Sodium Hexamethyldisilazide: Using ^{15}N–^{29}Si Scalar Coupling to Determine Aggregation and Solvation States

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ABSTRACT: ^{29}Si NMR spectroscopy, the method of continuous variations, and density functional theory computations show that sodium hexamethyldisilazide (NaHMDS) is a disolvated dimer in toluene, a mixture of disolvated dimer and tetrasolvated monomer in THF/toluene, and exclusively monomer in neat THF. The dioxane-solvated NaHMDS only partially deaggregates to monomer even in neat dioxane. ^{15}N–^{29}Si coupling constants and ^{29}Si chemical shifts show a high and dependable correlation with the aggregation state. Monitoring either chemical shift or coupling constant versus THF concentration even in the high-temperature, rapid-exchange limit affords the solvation numbers consistent with DFT computations. The preparation of ^{15}N-labeled NaHMDS has been improved.

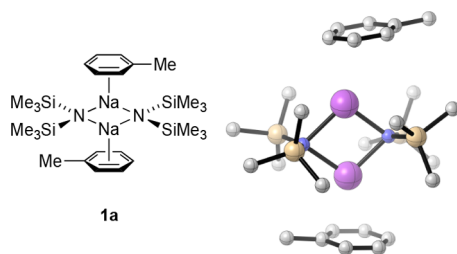A select few groups have been hailing the organic chemistry community to pay more attention to organosodium chemistry. We joined in only recently and possibly may not be the last to do so. To this end, sodium hexamethyldisilazide (NaHMDS) is arguably *the* preeminent organosodium reagent in both academic and industrial laboratories.[1] Despite its prominence, studies of its properties in solution are restricted to a couple of NMR spectra[2,3] and a handful of computations.[4]

We have embarked on an extensive study using a combination of methods to determine the structure of NaHMDS in over 30 commonly employed organic solvents to begin to study how aggregation and solvation influence reactivity and selectivity.[5] An unexpectedly important protocol revolves around the interrogation of structure using ^{15}N–^{29}Si coupling observed in ^{15}N-labeled NaHMDS. Lukevics and co-workers used natural abundance to examine $^{1}J_{N–Si}$ coupling in a series of disilazanes including NaHMDS in benzene.[3] Unaided by additional data, their suggestion that NaHMDS is tetrameric in benzene was suspect,[2a,b] but the tactic had merit.

We find a highly predictable correlation of ^{15}N–^{29}Si coupling with aggregation state. The high sensitivity, resolution, and quantitation offered by ^{29}Si NMR spectroscopy and the low cost of the ^{15}N label (7% the cost of an NMR tube) render this of potential interest to those studying M–
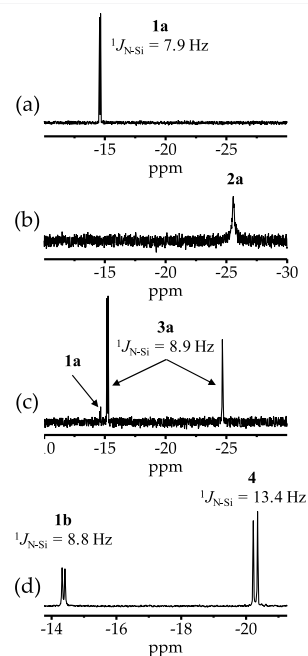

Figure 1. DFT-computed, toluene-complexed dimer **1a**.

Figure 2. ^{29}Si NMR spectra of (a) [^{15}N]NaHMDS (0.20 M) in toluene at −80 °C showing homodimer **1a**, (b) NaTMDS (0.20 M) in toluene at −80 °C showing homodimer **2a**, and (c) a 1:1 mixture of [^{15}N]NaHMDS and NaTMDS (0.20 M total titer) in toluene recorded at −80 °C showing homo- and heterodimers **1a** and **3a**. (d) ^{29}Si NMR spectrum of 0.15 M [^{15}N]NaHMDS in 0.75 M THF with Me$_2$NEt (DMEA) as cosolvent recorded at −120 °C shows dimer **1b** and monomer **4**.

(1)

1a; S = toluene
1b; S = THF

2a; S = toluene
2b; S = THF

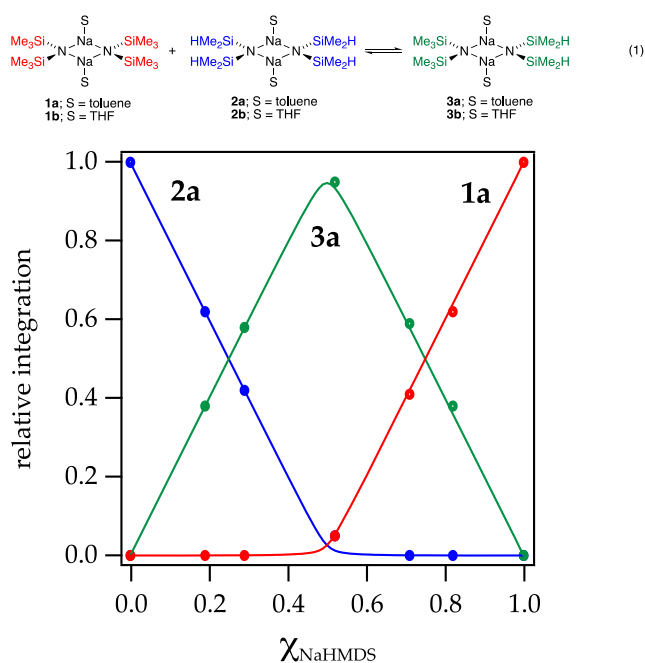**3a**; S = toluene
3b; S = THF

Figure 3. Job plot showing relative integrations of the ^{29}Si resonances of NaHMDS homodimer **1a** (red), NaTMDS-derived homodimer **2a** (blue), and heterodimer **3a** (green; eq 1) versus the measured[16] mole fraction of NaHMDS (X_{NaHMDS}) at 0.20 total molarity[17] in neat toluene-d_8 at −80 °C.
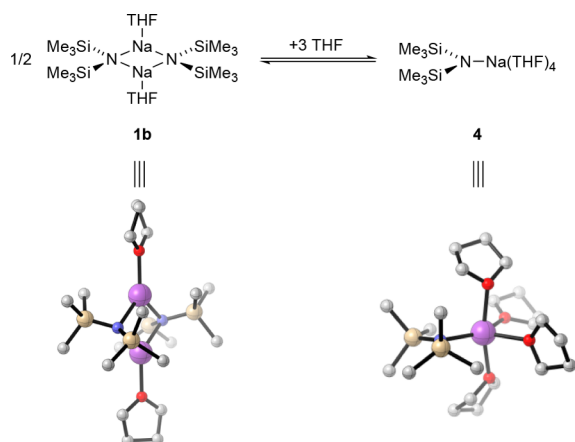

Figure 4. DFT-computed, THF-complexed dimer **1a** and monomer **4**.

N(SiR$_3$)$_2$ and M−N(SiR$_3$)(R) derivatives. We present herein preliminary studies that focus on three prominent solvents: toluene, THF, and dioxane.

A ^{29}Si{^{1}H} INEPT experiment circumvented the problems posed by background signal from glass NMR tubes and NOE effects,[6] allowing the relative integrations to be ascertained. [^{15}N]NaHMDS was prepared in 45% overall yield from ^{15}NH$_4$Cl by an optimized protocol.[7] ^{1}H and ^{13}C NMR spectra are archived Supporting Information. Density functional theory (DFT) computations were carried out at the M06-2X level of theory[8,9] for geometry optimizations and single-point calculations.[10] The standard Def2-SVP basis set was used for geometry optimizations, and the expanded basis set Def2-TZVP for single point calculations.[11,12]

The high solubility of NaHMDS in toluene and insolubility in hexane implicated an explicit π complexation, as observed
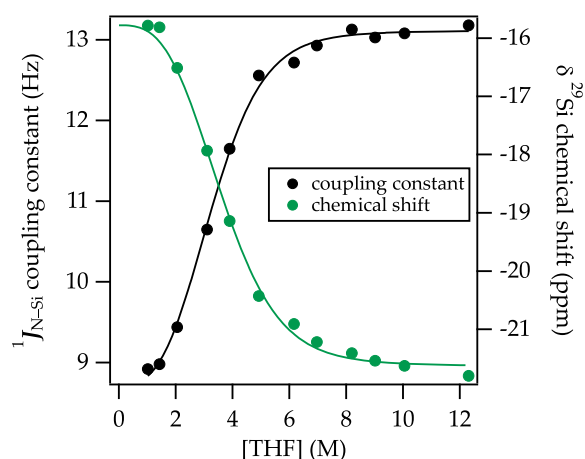

Figure 5. ^{29}Si chemical shift (green) and ^{15}N−^{29}Si coupling constants (black) plotted versus [THF] in 2:1 pentane/toluene as cosolvent measured at −20 °C. The curves are fits to a model based on an A$_2$S$_2$−AS$_4$ equilibrium (Supporting Information).

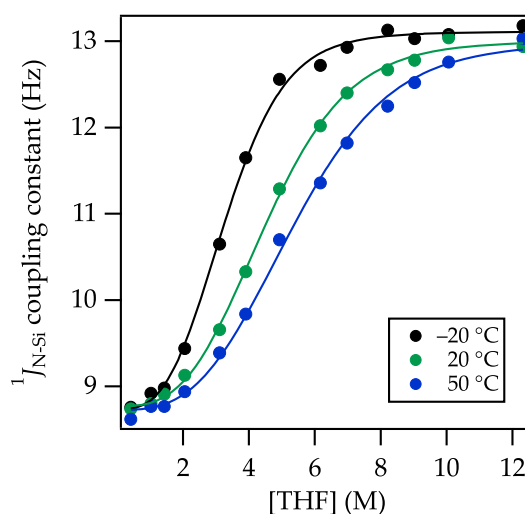**Figure 6.** ^{15}N−^{29}Si coupling constants plotted versus [THF] in 2:1 pentane/toluene as cosolvent measured at −20 °C (black), 20 °C (green), and 50 °C (blue). The functions are fits to a model based on an A$_2$S$_2$−AS$_4$ equilibrium (Supporting Information).

crystallographically for many metals, including sodium.[13] The ^{29}Si NMR spectrum shows a doublet with $^1J_{N−Si}$ = 7.9 Hz akin to that for the benzene solvate noted by Lukevics, which proves to be characteristic of dimeric NaHMDS (Figure 1).

The dimer assignment was secured using the method of continuous variations (MCV).[14] Mixtures of NaHMDS and the structurally similar sodium tetramethyldisilazide [NaTMDS; (HMe$_2$Si)$_2$NNa][15] in toluene show two homo-dimers along with a heterodimer manifesting a ^{29}Si singlet corresponding to the TMDS fragment and a doublet with coupling characteristic of dimers ($^1J_{N−Si}$ = 8.9 Hz; Figure 2c). Plotting the proportions of homo- and heteroaggregates versus measured[16] mole fraction of NaHMDS (X_{NaHMDS}) affords the Job plot in Figure 3. Quantitative heterodimerization is supported computationally (eq 1) and presumably derives from steric relief in the NaHMDS homodimer **1**. An analogous Job plot is obtained in toluene with 5.0 equiv of THF, conditions in which THF quantitatively displaces toluene to
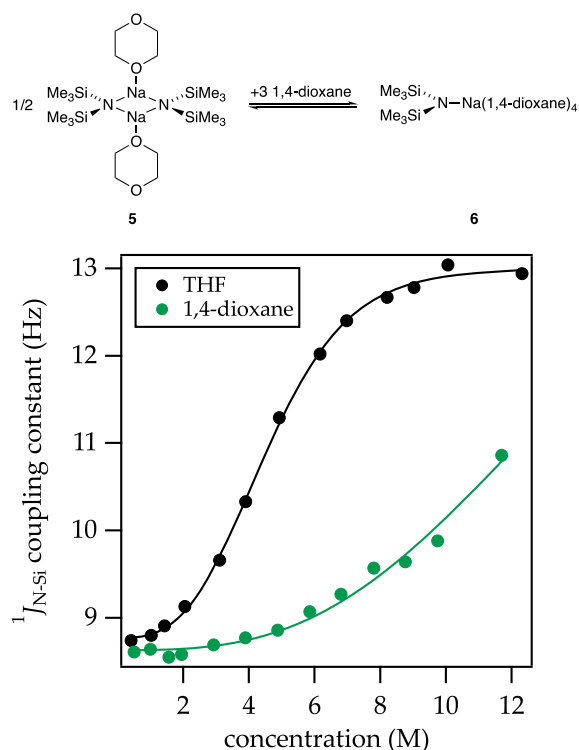
Figure 7. $^{15}N-^{29}Si$ coupling constants plotted versus [THF] (black) and [1,4-dioxane] (green) in 2:1 pentane/toluene as cosolvent measured at 20 °C. The functions are fit to a model based on an $A_2S_2-AS_4$ equilibrium (Supporting Information).

form **1b** as shown by titrations.[13] Dimer **1b** has been characterized crystallographically.[2c]

Titration of solutions of [^{15}N]NaHMDS (0.15 M) in DMEA to record ^{29}Si NMR spectra with added THF at −120 °C reveals a markedly upfield-shifted resonance displaying a large coupling ($^1J_{N-Si}$ = 13.4 Hz, Figure 2d) characteristic of NaHMDS monomers (Figure 4). The monomer becomes the sole observable form by 10 equiv (1.50 M).

Exchange of free and sodium-bound THF is rapid even at −120 °C. Although computations are supportive of both di- and tetrasolvated dimer, a host of other monodentate solvents show disolvation to be the norm.[5] Couplings and chemical shifts are proxies for aggregation even in the high-temperature, rapid-exchange limit as illustrated in Figure 5. Figure 6 shows the temperature dependence of the deaggregation, revealing the anticipated preference for monomer at lower temperatures. Moreover, the curves in Figures 5 and 6 result from fits according to the equilibrium in Figure 4 with tetrasolvated monomer **4**. Analogous fits assuming a trisolvated monomer are decidedly inferior.

The correlation of coupling constant to aggregation state can also be used to assign dimer−monomer ratios in solvents that eluded assignment at lower temperatures. The prominent ethereal solvent 1,4-dioxane produced a highly insoluble white crystalline material at low temperature probably owing to a polymeric network of monomers characterized crystallographically,[18] precluding solution structural studies. ^{29}Si spectra in the rapid exchange limit at 20 °C show dioxane-concentration-dependent coupling consistent with partial deaggregation of dimer **5** to monomer **6** at 20 °C. In neat dioxane, the 10.7 Hz coupling indicates that approximately

50% of the titer derives from monomer **6** (Figure 7). DFT computations indicate monomer **6** is only trisolvated.

We have shown that chemical shift and $^{15}N-^{29}Si$ coupling for the dimers (7.5−8.5 Hz) and monomers (13.0−13.5 Hz), in conjunction with results from a much more broadly based study,[5] are *highly* diagnostic of aggregation state. From a single spectrum, even at ambient temperatures, one can assess the relative proportions of monomers and dimers. Ironically, in over a dozen papers describing the structure of lithium hexamethyldisilazide using ^{15}N-labeled substrate in >100 solvents, we did not record a single ^{29}Si NMR spectrum: we did not need them. Belatedly, we find the analogous [^{15}N]LiHMDS/THF dimer and monomer $^{15}N-^{29}Si$ couplings are 7.0 and 11.7 Hz, respectively. We suspect that other organometallic complexes with silazide-based ligands are likely to show diagnostic trends as well.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.0c00331.

Spectroscopic, computational, and MCV data (PDF)

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Notes

The authors declare no competing financial interest.

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(7) (a) [^{15}N]Hexamethyldisilazane was prepared from [^{15}N]NH$_3$[19] by mixing [^{15}N]ammonium chloride (3.0 g, 55.0 mmol, >99% ^{15}N isotopic purity) with 6.00 g (0.15 mol) of granular NaOH in a 25 mL in a one-neck, round-bottom flask cooled to −78 °C. The mixture was warmed with a heat gun for approximately 20 min. After the transfer of ammonia was complete, 1-(trimethylsilyl)imidazole (14.7 g, 15.3 mL, 105 mmol, 98% purity) was added to ammonia at −78 °C and stirred. HCl begins to off-gas, and imidazole precipitates immediately. Anhydrous diethyl ether (20 mL) is then added to the flask, and the mixture is held at 0 °C for 40 min. Cholesterol (3.0 g) was added to the [^{15}N]hexamethyldisilazane with stirring for 45 min to remove excess 1-(trimethylsilyl)imidazole. Short-path distillation at atmospheric pressure removed the diethyl ether. Vacuum distillation (40 mm Hg, 20 °C) afforded 4.75 mL (47% yield) of (Me$_3$Si)$_2$^{15}NH. (b) [^{15}N]-Sodium hexamethyldisilazide (**1**) was prepared by a known procedure as follows.[20] Sliced sodium metal (1.20 g, 52.4 mmol) was added to a flame-dried, fine-mesh swivel frit setup (Supporting Information) in the glovebox. The apparatus was moved to a Schlenk line for the remainder of the procedure. Under an argon atmosphere, [^{15}N]HMDS (7.31 g, 9.45 mL, 45.0 mmol) and 40 mL of DMEA were added to the reaction flask at room temperature. Isoprene (2.62 mL, 26.2 mmol) dissolved in 8 mL of dry DMEA was then added over 1 h via syringe pump to the mixture. After addition of isoprene, the reaction was stirred at rt for an additional 2 h. The solution was then filtered through the frit and canula transferred to a second coarse swivel frit setup, and the solution was evaporated to dryness under vacuum for at least 10 h to yield a white powder. The powder was then suspended in dry pentane (~20 mL), stirred for 1 h, and filtered. Washing with an additional 20 mL of pentane yielded 6.70 g (91% yield) of [^{15}N]NaHMDS, which was transferred to a glovebox and stored at room temperature. It should be noted that NaHMDS can be recrystallized as described previously[20] but with no detectable improvement. ^{1}H NMR spectrum (500 MHz, toluene-d_8) δ 0.160 ppm; ^{13}C NMR spectrum (125.72 MHz, toluene-d_8) δ 7.28 ppm; ^{29}Si NMR spectrum (99.36 MHz, toluene-d_8) −14.6 ppm. (c) NaTMDS (**2**) was prepared using the same method described for NaHMDS. ^{13}C NMR spectrum (125.72 MHz, toluene-d_8) δ 5.93 ppm; ^{29}Si NMR spectrum (99.36 MHz, toluene-d_8) −25.57 ppm.

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