Molecular Structures of THF-Solvated Alkali-Metal 2,2,6,6-Tetramethylpiperidides Finally Revealed: X-ray Crystallographic, DFT, and NMR (including DOSY) Spectroscopic Studies

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Abstract: The often studied THF solvates of the utility alkali-metal amides lithium and sodium 2,2,6,6-tetramethylpiperidide are shown to exist in the solid state as asymmetric cyclic dimers containing a central M₂N₂ ring and one molecule of donor per metal to give a distorted trigonal planar metal coordination. DFT studies support these structures and confirm the asymmetry in the ring. In C₆D₁₂ solution, the lithium amide displays a concentration-dependent equilibrium between a solvated and unsolvated species which have been shown by diffusion-ordered NMR spectroscopy (DOSY) to be a dimer and larger oligomer, respectively. A third species, a solvated monomer, is also present in very low concentration, as proven by spiking the NMR sample with THF. In contrast, the sodium amide displays a far simpler C₆D₁₂ solution chemistry, consistent with the solid-state dimeric arrangement but with labile THF ligands.

Keywords: alkali metals · amides · crystal structures · density functional calculations · NMR spectroscopy

Introduction

Bulky alkali-metal amides reside at the forefront of organometallic chemistry as a result of their substantial synthetic value; their considerable Brønsted basicity coupled with weak nucleophilicity makes them excellent tools for carrying out deprotonation reactions (the conversion of a relatively inert C–H bond into a more useful polar C···M⁺ bond). The common utility amides are 2,2,6,6-tetramethylpiperidide (TMP),[1] 1,1,1,3,3,3,-hexamethyldisilazide (HMDS)[2] and diisopropylamide (DA).[3] As a general rule, the introduction of a Lewis donor to a solution of a utility amide can inhibit its aggregation, boosting reactivity and thus enhancing its synthetic practicality. However, there can be a trade off, since the possibility of an undesirable side reaction between the alkali-metal amide and the Lewis donor exists.[4] It is therefore desirable to investigate and understand the structures of such complexes, both in the solid state and most importantly in solution, since such structural knowledge can help rationalise their behaviour and allow for future tailoring of synthetic applications. One such system on which an extensive body of knowledge is known and continues to be amassed is that of TMP, due to its mounting role in complex multicomponent bases.[5,6] The molecular structures of unsolvated (M=Li,[1a] Na,[1c]) and N,N',N'-tetramethylethylenediamine (TMEDA)-solvated (M=Li,[1b] Na,[1d] K,[1d]) MTMP have been determined (Scheme 1), whereas in solution Collum and co-workers have reported a prodigious volume of work on the solution chemistry, focusing on the synthetically popular lithium system.[7] On traversing to the equally prevalent donor tetrahydrofuran (THF), much less is known. Renaud and Fox have reported that LiTMP exists as a solvated dimer (A, Scheme 2) in bulk THF solution at higher concentrations with a small amount of monomeric product (E/F) being co-present in more dilute solution.[8] Romesberg and Collum predicted, by early MNDO calculations, that the “open dimer” (B) is slightly favoured over the di-solvated isomeric closed dimer (A) and that monosol-
vation (as in C) would cause a ring distortion that would prevent coordination by the second molecule of THF (as in A).\[9\] However, the solid-state structure of the THF-solvated species is conspicuous by its absence in contrast to the large portfolio of structures of other THF-solvated organolithium compounds.[10] We now unequivocally establish that THF-solvated MTMP complexes (M = Li, Na) are isostructural closed dimers (A) with one molecule of donor per metal centre and we present contrasting NMR spectroscopic data for these species in a hydrocarbon medium, that is, with a stoichiometric rather than an excess amount of donor present.

### Results and Discussion

In the synthetic work, THF was added dropwise to a suspension of MTMP in hexane until a homogeneous yellow solution was obtained. This was immediately cooled to −35°C, which in the case of lithium (1) and sodium (2) precipitated a crop of crystals overnight that were suitable for X-ray crystallographic analysis (see Figure 1 and Table 1) and were shown to be [(LiTMP·THF)\(_2\)] and [(NaTMP·THF)\(_2\)], respectively. In contrast, the potassium congener degraded to a brown oil, even at low temperature. This suggests that it is too unstable to be isolated, possibly due to attack of the base on THF. In the solid state, complex 1 is stable under an inert (argon) atmosphere for at least a month, whereas complex 2 degrades to a brown/black oil within 72 h. The heavier alkali metal amide 2 is however sufficiently stable to be isolated from solution and dried, making it a synthetically useful material.

The molecular structure of 1\[11\] mirrors that seen in solution by Fox and is in contrast to the gas-phase structure predicted by MNDO calculations. Such monosolvated cyclic dimers (that is, possessing one donor ligand per metal) have been witnessed before for LiHMDS,\[2c\] NaHMDS\[2f\] and LiDA\[3c\] but the structures reported here represent the first such examples for an alkali-metal TMP species. The four-membered planar central ring is moderately distorted with each Li atom displaying a longer and a shorter Li–N bond. The average length (2.053 Å) along with the average Li–O bond length (1.973 Å) are marginally longer than those in the related structure [LiHMDS·THF]\(_2\) (2.025 and 1.882 Å respectively) probably as a consequence of the bulkier amide in 1.

Despite the bulk of the amide being less important in 2 (given that Na–N bonds are proportionately longer than Li–N bonds), this structure\[12\] also shows asymmetry in the four-membered ring with a pair of longer and shorter Li–N bonds. The average length (2.053 Å), along with the average Li–O bond length (1.973 Å), are marginally longer than those in the related structure [LiHMDS·THF]\(_2\), Li–O (1.882 Å respectively) probably as a consequence of the bulkier amide in 1.

To help rationalise these molecular structures we performed an ab initio (DFT) computational study of some hypotheti-
(A) was the lowest energy structure (by 4.41 and 8.28 kcal mol\(^{-1}\)) from the open di-solvated structure B, for Li and Na, respectively, corroborating the experimentally observed molecular structures. Further to this, the bond parameters predicted for structure A (Table 1) were in accord with the experimentally determined results. Although the absolute values vary marginally from those observed, the trends are clear and consistent, in particular the DFT calculations predicted the asymmetry in the four membered M\(_2\)N\(_2\) ring with each metal centre displaying a longer and shorter M–N bond.

Previous NMR spectroscopic studies on LiTMP have been carried out either in the complete absence of a Lewis donor or in neat donor, that is, with a huge excess. The isolated crystals of 1 (and 2) were thus suitable for a study with a precisely stoichiometric amount of THF in a bulk hydrocarbon solvent. The \(^1\)H (Figure S1 in the Supporting Information) and \(^7\)Li NMR spectra (Figure S2 in the Supporting Information) of 1 reveals that more than one species (1a and 1b) are the principal species, with a minor amount of a third product 1c in the \(^7\)Li spectrum) are present in solution\(^{[13]}\) (with the overall integration confirming the 1:1 THF/TMP ratio). A 2D-HOESY spectrum (\(^1\)H–\(^7\)Li, Figure S3 in the Supporting Information) intimates that one of the two main species, 1b, has metal-coordinated THF. A variable concentration study was consequently embarked upon. Although the \(\beta\) and \(\gamma\) hydrogen resonances of the TMP anions are low intensity broad multiplets in the \(^1\)H spectrum, the sharp methyl group singlets are particularly informative. What is immediately noticeable at low concentration is the loss of the methyl signal of 1b (Figure S4 in the Supporting Information), such loss being mirrored in the \(^7\)Li spectrum (Figures S5a and b in the Supporting Information). This leads us to surmise that a dynamic coordination/decoordination equilibrium of the THF to lithium is occurring, with decoordination habitually being favoured at lower concentration. The addition of a few drops of \([\text{D}_3]\)THF to the concentrated sample resulted in complete loss of the unsolvated species 1a, whereas the resonance for 1c grew noticeably, suggesting that it too is a THF-solvated species (Figure S5c in the Supporting Information). This spectrum resembles that witnessed by Fox in neat THF, allowing us to conclude that 1c is almost certainly a solvated monomer as seen previously\(^{[8]}\).

To obtain further understanding of the true nature of species 1a and 1b in solution, the sample was subjected to a \(^1\)H DOSY NMR experiment (1c is present in such small amounts in \(\text{C}_2\text{D}_2\) solution (Figure S5b in the Supporting Information) that no useful information on it could be gleaned from the DOSY study). This technique can be considered as a type of NMR chromatography\(^{[14]}\) in which resonances of different components in a solution can be separated by their molecular weight, which in turn can be estimated provided inert standards of known weight are present for calibration (the log of molecular weight can be linearly correlated to \(\log D\) (diffusion coefficient)). In this instance, the internal standards employed were tetramethyilsilane (TMS, MW = 88), 1-phenyl naphthalene (PhN, MW = 204) and tetraphenylnaphthalene (TPhN, MW = 433). Our study (see the Supporting Information for full details) shows that the two major TMP-containing molecules in solution (1a and 1b, Figure 2) are of significantly different size with the unsolvated species (1a) being of greater molecular weight (i.e., correlated with a lower diffusion coefficient) than the solvated species (1b).

The estimated molecular weight, or MW\(_{\text{DOSY}}\) of 1a (Figure S6 in the Supporting Information) is greater than 432 g mol\(^{-1}\), since it comes at a higher molecular weight than the largest internal standard (tetraphenylnaphthalene, MW = 432), a result consistent with the unsolvated species being either trimeric (MW = 442) or tetrameric (MW = 589) LiTMP, as witnessed by Collum in hydrocarbon solution in the complete absence of donor\(^{[20]}\). Interestingly, the solvated species does not display the same diffusion coefficient as THF. However, the estimated size of THF from this study (MW\(_{\text{DOSY}}\) = 141) is greater than “free THF” (MW = 72) and is indicative of the dynamic coordination/decoordination event (see above).\(^{[15]}\) The predicted weight of 1b (MW\(_{\text{DOSY}}\) = 356) is very close to that of the species \([\text{LiTMP}]_2\cdot\text{THF}\) (C/D) (MW = 367), which was predicted to exist by MNDO calculations.\(^{[9]}\) However, for the same reason that a dynamic coordination/decoordination event gives an artificially high estimate of the molecular weight of THF, so too can it give an artificially low estimate of the molecular weight for the solvated species, meaning that it is impossible to rule out the identity of 1b being di-solvated \([\text{LiTMP}-\text{THF}]_2\).\(^{[9]}\) We note here that this result in no way allows us to speculate whether 1b adopts the closed (A) or open (B) dimeric form since both should have the same diffusion coefficient.

The solution behaviour of 2 appears to be considerably more straightforward. \(^1\)H and \(^13\)C NMR suggest the presence of only one TMP containing species in solution, consequently, a \(^1\)H DOSY spectrum (Figure S8 in the Supporting Information) was also obtained to confirm this assertion. Like 1b, the THF resonances of 2 suggest a lower molecular weight than those of TMP, but the plot of log \(D\) versus log MW (Figure S9 in the Supporting Information) insinu-
ates a higher molecular weight than free THF (MW\textsubscript{DOSY} = 149). Likewise, the predicted molecular weight of the NaTMP species is lower (MW\textsubscript{DOSY} = 370) than that of the parent molecular structure (NaTMP)\textsubscript{2}·2THF (MW = 471). However, all the evidence combined is sufficient to predict that the TMP-containing species in 2 is a solvated dimer with a dynamic coordination/decoordination of THF occurring such as that previously described for 1b. The lack of a second set of signals representing an unsolvated species suggests that the equilibrium lies heavily in favour of the solvated species due to the steric relaxation introduced by having a heavier, longer-bond-forming alkali metal making it more favourable than its lithium congener.

**Conclusion**

In summary, the solid state structures of the THF-solvated alkali-metal utility amides M(TMP) (M = Li, Na) have belatedly been shown to exist as solvated dimers with a central distorted M\textsubscript{2}N\textsubscript{2} ring. A variety of NMR spectroscopic experiments confirm the lithium congener disproportionates in non-polar solvent to yield a solvated and unsolvated species, the ratios of which are strongly concentration dependent. A third (more heavily solvated) species is also present in minor amounts. There is no evidence for disproportionation in the case of the more reactive sodium congener, with only a fast coordination/decoordination of THF seemingly occurring in solution.

**Experimental Section**

**General methods:** To avoid hydrolysis and/or oxidation of the metal amide compounds, all reactions and manipulations were carried out in an atmosphere of dry pure argon gas using standard Schlenk and glovebox techniques. Hexane and THF were distilled over sodium-benzophenone. nBuNa\textsuperscript{[16]} was prepared by a literature method. nBuLi (1.6 M in hexanes) and TMP(H) were purchased from Aldrich and Merck respectively and were used as received. TMEDA was distilled over CaH\textsubscript{2} and stored over molecular sieves. Elemental analyses were performed by the University of Strathclyde Elemental Analysis Service. NMR spectra were recorded on a Bruker AVANCE 400 NMR spectrometer, operating at 400.13 MHz for \textsuperscript{1}H, 155.50 MHz for \textsuperscript{7}Li and 100.62 MHz for \textsuperscript{13}C. DOSY experiments were performed on a Bruker AVANCE 400 NMR spectrometer operating at 400.13 MHz for proton resonance under TopSpin (version 2.0, Bruker Biospin, Karlsruhe) and equipped with a BBFO-2-atm probe with actively shielded z-gradient coil capable of delivering a maximum gradient strength of 54 G cm\textsuperscript{-1}. Diffusion-ordered NMR data were acquired using the Bruker pulse program dstegp3s employing a double stimulated echo with sine-shaped gradient pulses were used with a duration of 4 ms (P30) together with a diffusion period of 100 ms (D20). Gradient recovery delays of 200 ms followed the application of each gradient pulse. Data were systematically accumulated by linearly varying the diffusion encoding gradients over a range from 2 to 95 % for 64 gradient increment values. The signal decay dimension on the pseudo-2D data was generated by Fourier transformation of the time-domain data. DOSY plots were generated by use of the DOSY processing module of TopSpin. Parameters were optimized empirically to find the best quality of data for presentation purposes. Diffusion coefficients were calculated by fitting intensity data to the Stejskal–Tanner expression with estimates of errors taken from the variability in the calculated diffusion coefficients by consideration of different NMR responses for the same molecules of interest.

**Computational details:** A series of calculations using the Gaussian 03 package\textsuperscript{[27]} were performed to enhance our understanding of the THF-
solvated structures 1 and 2. For each species A–E, geometry optimization was undertaken at the HF/6-31G** [18] level, followed by a frequency analysis. Then the geometry was refined by further calculation at the B3LYP/6-31G** level. The structural parameters reported were taken from the DFT calculations, whereas the total energy abstracted from the DFT calculation was adjusted by inclusion of the zero-point energy value from the HF calculation modified by the factor 0.91.

Crystal structure determinations: Crystallographic data were collected at 123(2) K on Oxford Diffraction Diffractometers with MoKα (λ = 0.71073 Å) radiation. Structures were solved using SHELXL-97,[21] and refined to convergence on F² against all independent reflections by the full-matrix least-squares method using the SHELXL97 program.[22] For compound 1, disorder in the THF groups was modelled with C and H atoms. For compound 2, disorder in the THF groups was modelled with C and H atoms.

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[11] Crystal data for I: C6H9Li2NaO2, M = 438.58, orthorhombic, space group Pnca, a = 15.2093(4), b = 15.6979(5), c = 23.0539(6) Å, V = 5949.2(3) Å³, Z = 8, ρc = 1.060 Mg m⁻³, T = 123(3) K, 14004 reflections collected, 5394 unique (Rwp = 0.0504), R1 = 0.0585, based on F for 2892 reflections with I > 2σ(I), wR2 = 0.1336 based on F² for all reflections, min/max residual electron density 0.464–0.444 e Å⁻³.

[12] Crystal data for II: C21H32Li4N2O2, M = 470.68, triclinic, space group P1, a = 10.7969(6), b = 11.2737(6), c = 12.2982(7) Å, α = 88.1844(4), β = 73.3185(4), γ = 84.4244(4), V = 1418.93(14) Å³, Z = 2, ρc = 1.102 Mg m⁻³, T = 123(2) K, 11150 reflections collected, 563 unique (Rwp = 0.0493), R1 = 0.0465, based on F for 2525 reflections with I > 2σ(I), wR2 = 0.0936 based on F² for all reflections, min/max residual electron density 0.256–0.165 e Å⁻³.
This is in contrast to the related species [LiDA-THF]2 which maintains its integrity in solution as evidenced by ¹³C INEPT DOSY NMR: D. Li, R. Hopson, W. Li, J. Liu, P. G. Williard, Org. Lett. 2008, 10, 909.


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