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Simplifying metal-'ate' chemistry: formation and comprehensive characterisation of a homo-metallic amido lithiate complex

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Addition of TMEDA to lithium allyl-1-naphthylamide in a 1:1 ratio afforded the novel amido lithium/lithiate complex, [Li(TMEDA)$_2$][Li{N(1-naph)(CH$_2$CH=CH$_2$)}$_2$]. ^{7}Li NMR and computational calculations indicate this model to be representative of the solution state, with ^{1}H and ^{13}C NMR showing a 1,3-sigmatropic rearrangement. [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·Et$_2$O]$_2$ 1, and [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·PMDETA] 3, are presented for comparison.

Metal '-ate' chemistry, in which Li, Na and K are typically partnered with less electropositive elements, such Cu and Zn, has become a powerful synthetic tool; acting to greatly improving kinetic reactivity and providing new realms in selectivity.[1, 2] For example, lithium and sodium amido zincate complexes have been used to great effect in directed metallation of substituted homo- and hetero-aromatic systems including thiophenes, furans and quinolines,[3] as well as non-aromatic cyclic ethers[4] and halogen containing compounds.[5] Oshima has reported on the efficiency of lithium magnesiates as metal-halogen exchange reagents,[6] and Uchiyama and co-workers have shown mixed lithium-aluminium complexes to have a high tolerance to cyano, methoxy and carbonyl functional groups.[7] However, recently these lithium-aluminium reagents have been uncovered by Mulvey and co-workers to be trans-metal-trapping systems[8,9] rather than traditional 'ate' complexes. Recent research by Mulvey and co-workers has demonstrated their use in the synthesis of a diverse range of hetero-bimetallic ferrocene complexes[10] and some unique examples of ortho- and meta-directing properties of a sodium/magnesiate base.[11] There has also been notable progress in homo-metallic lithium 'superbases' with Gros and Fort using TMSCH$_2$Li/LiDMAE (trimethylsilylmethyl lithium/lithium dimethylaminoalkoxide) to selectively deprotonate pyridine and substituted derivatives. However, attention remains on lowering nucleophilicity and improving selectivity.[12, 13] Combining these two fields has the potential to provide new and interesting synthetic outcomes. However, amido lithiate species are very rare and have principally only been observed through solution NMR studies.[14-16]

In this paper, we now report on the formation and first comprehensive characterisation of a homo-metallic amido lithate complex [Li(TMEDA)$_2$][Li{N(1-naph)(CH$_2$CH=CH$_2$)}$_2$] which arises under highly specific conditions following the treatment of *N*-allyl-1-naphthylamine with BuLi and TMEDA (*N,N,N',N'*-tetramethylethane-1,2-diamine). The bidentate TMEDA donor appears critical in its formation as monodentate O donors (Et$_2$O and THF) and the tridentate donor PMDETA (*N,N,N',N',N''*-pentamethyldiethylenetriamine) lead to alternative outcomes.
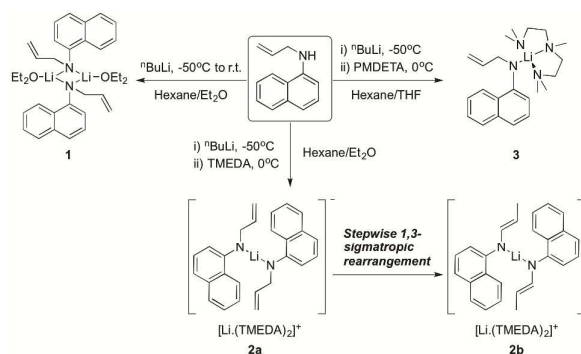
Scheme 1: Synthesis of [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·Et$_2$O]$_2$ **1**, [Li(TMEDA)$_2$][Li{N(1-naph)(CH$_2$CH=CH$_2$)}$_2$] **2a** and [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·PMDETA] **3**.

Following Scheme **1** we have isolated and structurally characterised the dimer [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·Et$_2$O]$_2$ **1**, the amido lithium/lithiate complex, [Li(TMEDA)$_2$][Li{N(1-naph)(CH$_2$CH=CH$_2$)}$_2$] **2a**, and the monomer, [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·PMDETA] **3**. The gradual appearance of an aza-allyl species, **2b**, has also been identified via NMR

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spectroscopy and has been further investigated by computational studies.

Homoallylic amines have been extensively investigated by Yus and co-workers for their capacity to be selectively dilithiated via sequential addition of [n]BuLi and [t]BuLi,[17,18] structural changes to these systems have also been shown to result from the use of different solvent systems, Lewis donors and alkali metals, as well as thermal history.[18-22] Our focus has primarily been concerned with various transformations of (S)-N-α(methylbenzyl)allylamine (S-α-mba), and related derivatives,[19-21] to aza-allyl or aza-enolate complexes and further research has demonstrated the dilithiation mechanism can extend to heavier alkali metal analogues.[23] Previously N-allyl-1-naphthylamine was used to form a trianionic species through this dilithiation mechanism and a rare addition across the allyl moiety that was identified via electrophile studies.[24]

In our experiments N-allyl-1-naphthylamine was reacted with 1.1 equivalents of [n]BuLi in hexane at -50°C and allowed to reach ambient temperature over 1 hour to afford a yellow/orange precipitate. Addition of the donor solvents Et$_2$O, TMEDA or PMDETA resulted in the isolation of complexes **1**, **2a** and **3** respectively as crystalline solids.
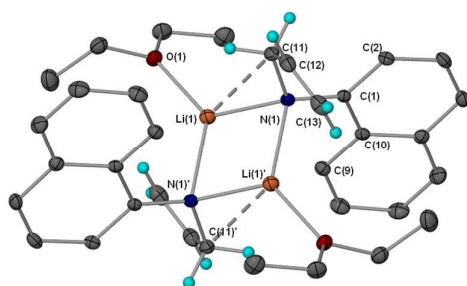

Fig. 1 Molecular structure of [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·Et$_2$O]$_2$ **1**. Thermal ellipsoids at 40% probability. Hydrogen atoms, except allyl ones, have been omitted for clarity. Symmetry operator '= 1-x, 1-y, 2-z.
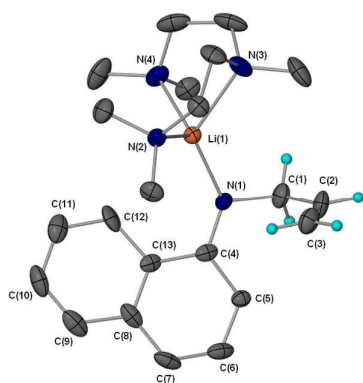

Fig. 2 Molecular structure of [Li{(1-naph)(CH$_2$CH=CH$_2$)N}·PMDETA] **3**. Thermal ellipsoids at 40% probability. Hydrogen atoms, except allyl hydrogens, have been omitted for clarity.

Single yellow/orange crystals suitable for X-ray diffraction studies of complexes **1** and **3** were grown from hexane/Et$_2$O and hexane/THF solutions, respectively, to reveal the dimeric complex [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·Et$_2$O]$_2$ **1** (Fig. 1) and the monomeric complex [Li{N(1-naph)(CH$_2$CH=CH$_2$)}·PMDETA] **3** (Fig 2). In both **1** and **3** the lithium cation bonds to the deprotonated amido N atom [Li(1)-N(1), 2.011(3) Å in **1** and Li(1)-N(1), 1.980 Å in **3**] and one molecule of the corresponding donor Et$_2$O in **1** [Li(1)-O(1), 1.924(3) Å] and PMDETA in **3** [Li(1)-N(2), 2.139 (2); Li(1)-N(3), 2.162(3); Li(1)-N(4), 2.175(3) Å]. Dimerisation of **1** results in a common central planar Li$_2$N$_2$ four membered ring[25-27] while **3** remains monomeric due to the steric strain imposed by the bulky PMDETA donor.[28, 29] Both Li atoms in **1** and **3** are formally four coordinate forming distorted tetrahedral geometries (sum of bond angles: 86.32° in **1** and 108.05° in **3**).
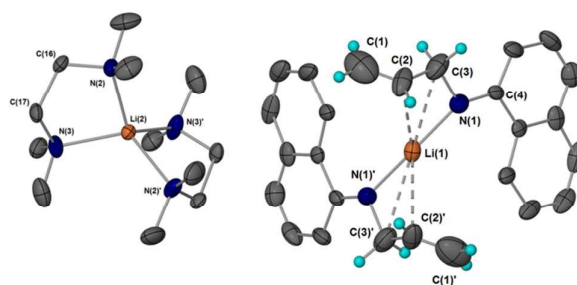

Fig. 3 Molecular structure of the two ion moieties in [Li(TMEDA)$_2$][Li{N(1-naph)(CH$_2$CH=CH$_2$)}$_2$] **2a**. Thermal ellipsoids at 40 % probability. Hydrogen atoms except allyl ones, have been omitted for clarity.

Addition of TMEDA to the lithiated allyl-1-naphthylamide resulted in the deposition of a yellow solid and a red oil which was then dissolved by adding Et$_2$O. Single crystals grown from this solution were suitable for X-ray diffraction studies revealing the novel amido lithium lithiate complex [Li(TMEDA)$_2$][Li{N(1-naph)(CH$_2$CH=CH$_2$)}$_2$] **2a** (Fig. 3). Complex **2a** formally adopts a separated ion pair (SIP) structure with the Li anion bonded to two deprotonated allyl-1-napthylamides [Li(1)-N(1),1.942(4) Å] countered by the cationic [Li(TMEDA)$_2$] moiety.[30-32] For clarity Figure 3 shows the two separate ion moieties, while the crystal structure showing the actual special arrangement of the two ions is provided in the ESI. The anionic Li ion makes two additional long electrostatic Li-C interactions with the allyl group [Li(1)-C(3), 2.714(7); Li(1)-C(2), 2.745(8) Å] making it overall formally six coordinate. Only one other amido lithium/lithate complex has been characterised in the solid-state system: [Li(12-crown-4)$_2$][Li{N(Me$_3$Si)$_2$}$_2$][34] which is provided as a private communication to the CCDC without any other further supporting data being available.

Solution studies of **1** were carried out in d$_8$-thf due to poor solubility in benzene (solvating Et$_2$O is lost under vacuum) and **3** was analysed in C$_6$D$_6$. Investigation into any anionic rearrangements was carried out by heating the solutions up to 60 °C for a period of 2 hours, however this failed to induce any structural change to the amide.
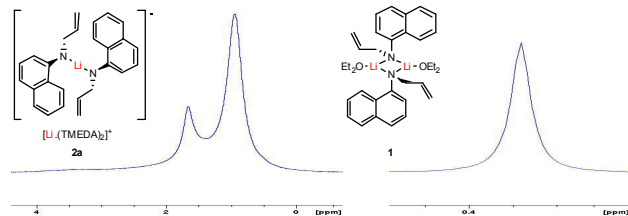
Fig. 4 ^{7}Li NMR spectrum of complex **2a** (in C_6D_6) showing two Li environments (left) vs. complex **1** (in d_8-THF).

Solution studies of **2a** were carried out in C_6D_6. ^{7}Li NMR spectroscopy showed two distinct signals indicating retention of the solid state structure in solution (Fig. 4). ^{1}H NMR spectroscopy of **2a** revealed a mixture of the aza-allyl and ally naphthylamide ascertained to have been induced by TMEDA. The aza-allyl species is easily distinguishable by the appearance of a doublet at 2.01 ppm representing a –CH_3 group as opposed to the doublet signals at 5.05 ppm which represent the C(1) protons. The C(2) proton also shifts upfield to 4.60 ppm (5.72 ppm in parent amine) and the splitting pattern changes to a doublet of quartets. Finally, the C(3) protons are drastically shifted into the aromatic region as a doublet at 7.60 ppm (3.49 ppm in parent amine). Notably, the ^{13}C NMR spectra also reveal significant shifts to higher frequencies for C(1) and C(3) to 12.6 ppm and 141.9 ppm respectively. At room temperature the rearrangement has been found to progress slowly with an approximate 60 % conversion to the aza-allyl species after 10 days (monitored via NMR study, see ESI‡).
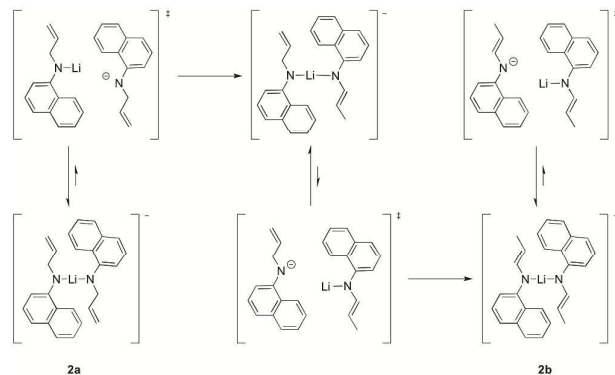
Scheme 2: Stepwise 1,3-sigmatropic rearrangement of **2a** → **2b.** Nb. The $[Li(TMEDA)_2]^+$ is omitted for clarity, but can be assumed to be associated with the anionic-complex in all examples above.

From these solution studies we have concluded this rearrangement progresses via a dissociated state whereby the isolated anion provides a lowered energy barrier in order to form the aza-allyl amide species (Scheme 2) occurring in a stepwise manner; the three lithiate species below are shown to be in a favourable equilibrium with their dissociated intermediates, this is assumed given the slow rate of the observed rearrangement. **2b** is expected to be the dominant species in solution given enough time.

Figure 3 summarises density functional calculations which were performed using the Gaussian 09 suite of software to investigate the thermodynamic profile of **2a** compared to other potential pathways. Molecular geometry calculations commenced at the B3LYP/6-31G(d) level using crystal structure data as a starting point. Complex **2a** was found to be substantially lower in energy than the alternative products by > 200 kJmol^{-1}. The calculated energy profile for the stepwise 1,3-sigmatropic rearrangement also found a 101 kJmol^{-1} gain for **2b** over **2a**, which is consistent with the solution studies.
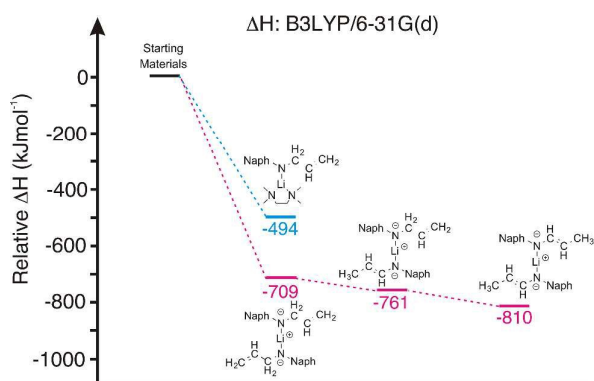

Fig. 5: B3LYP/6-31G(d) density functional theory calculations for **2a** and the alternative pathway. Nb. The $[Li(TMEDA)_2]^+$ is omitted for clarity, but can be assumed to be associated with the anionic-complex in all examples above.

From a subtle control of Lewis donor denticity and metal mediated anion rearrangements we have isolated, fully characterised and studied the formation of the homo-metallic amido lithate $[Li(TMEDA)_2][Li\{N(1\text{-}naph)(CH_2CH=CH_2)\}_2]$. It remains to be seen whether such a complex will deliver the diversity in reactivity and selectivity accessible through hetero-bimetallic amido 'ate' complexes coupled with the nuances of homo-metallic 'superbases'.

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Table of Contents

This manuscript describes the first comprehensive characterisation of a simple homo-metallic amido lithate complex, the crystals of which arise from treatment of *N*-allyl-1-naphthylamine with BuLi and TMEDA.