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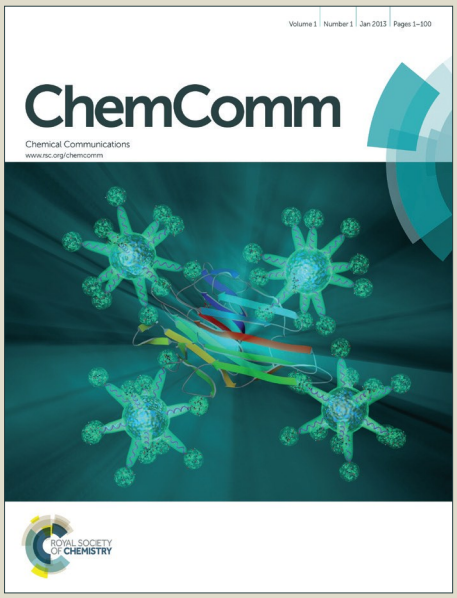

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ARTICLE

The importance of the Lewis base in lithium mediated metalation and bond cleavage reaction of allyl amines and allyl phosphines.

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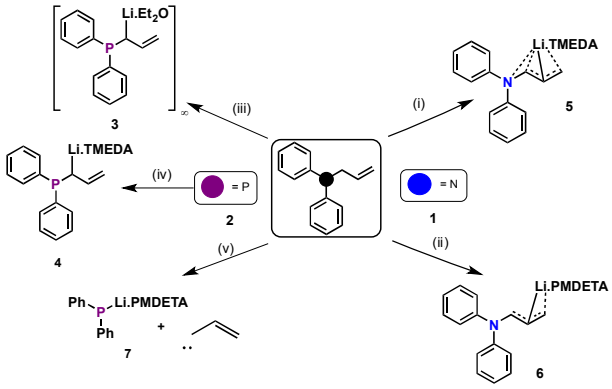
Metallation of two analogus N- and P-allyl molecules $Ph_2NCH_2CHCH_2$ **1** and $Ph_2PCH_2CHCH_2$ **2** with *n*BuLi have show contrasting reactivites based on the choice of Lewis donor. With **1** metallation of the alpha carbon atom was achieved regardless of the Lewis donor used while in comparison metallation of **2** showed an unexpected donor denticity dependance with P-C bond clevage induced with the tri-dentate PMDETA. Complementary DFT and solution studies rationalise this outcome.

The importance of alkali metal amide[1,2] complexes in synthesis is reflected in their versatility as essential building blocks used by synthetic chemists. In particular, allyl amides have played a significant role as bases in deprotonation, alkylation and desymmetrisation reactions, while their use as nucleophiles, through homochiral ammonia equivalents, has allowed the synthesis of ß-amino acids and ß-lactams.[3] Their importance and synthetic utility is further highlighted by their prevalence in diverse drug molecules and their use as 'unexpected' protecting groups[4] in the synthesis of polyfunctional compounds. Our research has focused on the reactivity, facile rearrangements and unusual decomposition pathways of metal allyl amides in which solvents, Lewis donors and temperature choice play significant roles. [3,5–8]

What is apparent is that in contrast to the breadth of N-allyl based chemistry there have been very few studies on their phosphorus analogues. Such comparative studies of homologous molecules[9] allows fundamental concepts to be built while probing contrasting reactivity and molecular structures. Recently research on new phosphorus analogues of some 'classic' long known nitrogen complexes urea and N_2O_4 revealed them to be no mere carbon copies.[10–12] The electronic properties conferred on compounds by the heavier elements in a group can differ dramatically from the lighter ones.

In this paper we report a comparative reactivity study of two analogous N- and P-allyl molecules; diphenylallylamine **1** and diphenylallylphosphine **2**. The reactions reveal an unprecedented dependence on donor denticity in competitive deprotonation versus N/P-C bond cleavage reactions. Both X-ray crystallography and solution studies reveal contrasting behaviours and spatial electronic arrangements.



Scheme 1 Reagents and conditions: (i) *n*BuLi, hexane, TMEDA, -40°C—r.t, 62% (ii) *n*BuLi, hexane, PMDETA, -40°C—r.t, 42% (iii) *n*BuLi, hexane, Et_2O, -40°C—r.t, 75% (iv) *n*BuLi, hexane, TMEDA, -40°C—r.t, 75% (v) *n*BuLi, hexane, PMDETA, -40°C—r.t, 73%. (ESI‡)

Reaction of **1** or **2** with an equimolar amount of *n*BuLi at -40°C in hexane solution gave an immediate bright yellow solution. Addition of Et_2O to the lithiated P-allyl system afforded X-ray quality single yellow crystals identified as the polymeric lithium phosphine complex $[(Ph_2PCHCH{=}CH_2)Li.Et_2O]_\infty$ **3**. (Scheme 1) Unfortunately, addition of Et_2O or THF to the analogous lithiated N-allyl complex resulted in uncharacterizable viscous red oils (^{1}H and ^{7}Li NMR spectroscopy revealed a complicated mixture of species which could not be easily identified ESI‡). Use of bi-dentate donor TMEDA (N,N,N',N'-tetramethylethylenediamine), results in orange crystalline solids, identified as $[(Ph_2PCHCH{=}CH_2)Li.TMEDA]$ **4** and

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‡Electronic Supplementary Information (ESI) available: Full experimental and X-ray crystallographic data. CCDC 1452499(3), 1452498(5), 1452869(6). For ESI and crystallographic data in CIF or other electronic form See DOI: 10.1039/x0xx00000x

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[(Ph_2NCHCH=CH_2)Li.TMEDA] **5**. Lastly, addition of the tri-dentate donor PMDETA (N,N,N′,N′′,N′′-pentamethyldiethylenetriamine) results in two different reaction pathways; the expected deprotonation of the N-allyl complex to afford [(Ph_2NCHCH=CH_2)Li.PMDETA] **6**, while isolation of [Ph_2PLi.PMDETA] **7**, from the P-allyl reaction indicates an unexpected P-C bond cleavage reaction has to have occurred.

Single crystal X-ray diffraction studies of complexes **3**, **5** and **6** revealed very different spatial electronic arrangements. In all three cases metallation at the C1 position of the allyl group has taken place. In the ASU of complex **3**, [(Ph_2PCHCH=CH_2)Li.Et_2O]$_\infty$, the Li cation bonds to the P atom [Li1-P1 2.592(3) Å] (Fig.1) and the O atom of a coordinated Et_2O molecule, and does not interact with the deprotonated allyl chain (shortest Li-C_{allyl} distance Li1-C1 4.23 Å). However, extending the coordination environment of the Li atom, four short electrostatic interactions happen with a neighbouring deprotonated allyldiphenylphosphine molecule (Fig.1) [Li-C range; 2.203(3) – 2.432(3) Å], and help form an overall polymeric chain and a six-coordinate Li atom. To the best of our knowledge **3** represents the first structurally characterized example of a metallated allylphosphine. The majority of structurally characterized examples[13,14] are simple diorganophosphides [R_2PLi.donor] or phosphinomethanides [(R_2P)CR′$_2$Li.donor] where R = H, Aryl, sub-Aryl or silyl.

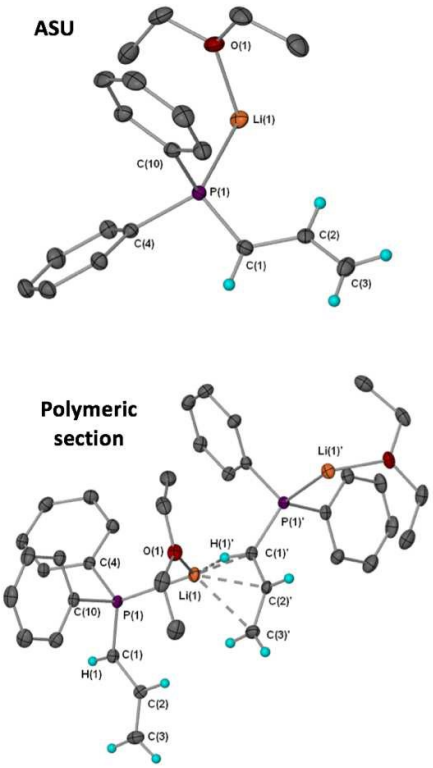

Fig. 1 Molecular structure of **3** (ESI‡). Ellipsoids shown at 45% probability. Hydrogen atoms (except allyl ones) have been omitted for clarity

The organolithium amido complexes [(Ph_2NCHCH=CH_2)Li.TMEDA] **5** and [(Ph_2NCHCH=CH_2)Li.PMDETA] **6** (Fig 2) both show deprotonation at the C1 position. In **5** the shortest Li-C bond is located at C2 [Li1-C2 2.175(3) Å] while in **6** at C3 [Li1-C3 2.197(3) Å]. This difference can be attributed to the steric strain imposed by the bulkier PMDETA molecule pushing the Li cation in **6** further along the deprotonated allyl group. Both **5** and **6** make additional electrostatic interactions with the fully delocalized allyl group which has lost its single/double bond character (average C-C bond lengths of 1.379 Å in **5** and of 1.375 Å in **6**).[15–17]

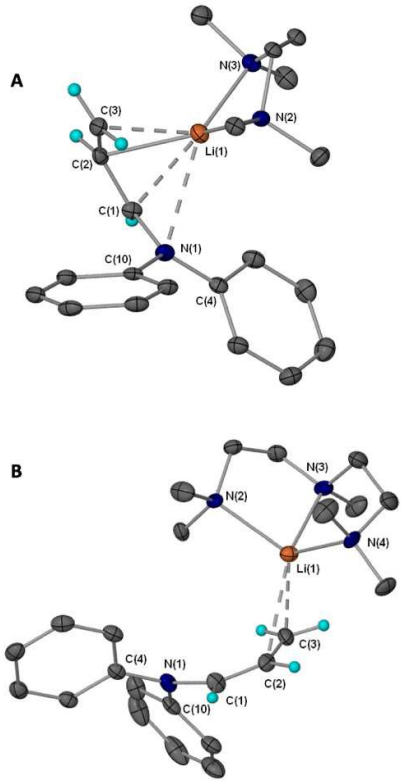

Fig. 2 Molecular structure of **5** (A ESI‡) and **6** (B ESI‡). Hydrogen atoms (except allyl ones) and one disordered PMDETA molecule have been omitted for clarity. Ellipsoids shown at 45% probability

^{1}H NMR spectroscopy studies on complexes **3**-**6** in C_6D_6 solution confirmed metallation at the C1 position through the presence of a new doublet of doublets located at 3.67 ppm (**3**), 3.53 ppm (**4**), 4.58 (**5**) and 5.06 ppm (**6**) when compared to the corresponding free parent amine **1** (4.23 ppm) and phosphine **2** (2.80 ppm). The lithio-phosphine complexes **3** and **4** preserve their solid state composition in solution with delocalization of the allyl chain retained. In contrast, the dramatic respective upfield shifts of C3 in **5** and **6** to 1.96 ppm and 1.51 ppm in the ^{1}H spectra and to 56.6 ppm and 57.1 ppm in the ^{13}C NMR spectra (*c.f.* 5.20 ppm and 116.2 ppm in parent amine

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respectively) highlights the complex is undergoing a 1,2-shift of the double bond in solution giving the isomeric species [$Ph_2NCH{=}CHCH_2Li$] (Figure S9 ESI‡). Low temperature ^1H and ^7Li NMR studies on **5** in d_8-toluene reveal only one species is observed in solution down to -60°C (Figure S10 and 11 ESI‡).

Subsequent quenching studies of complexes **3**-**6** with D_2O confirmed the retention (**3** and **4**) and movement of the double bond (**5** and **6**) affording isomeric mono-deuterio-complexes [Ph_2**P**$CHDCH{=}CH_2$] and [Ph_2**N**$CH{=}CHCH_2D$]. The monodeutero-amido colmplex is in keeping with Eisch[18] and Barretts[19] predicted intermediate organolithium species [$Ph_2NCH{=}CHCH_2Li$].

Unexpectedly, lithiation of **2** followed by addition of PMDETA produced [Ph_2Li.PMDETA] **7** (73% crystalline yield)[20] presumably through a P-C bond cleavage. Detailed mechanistic studies of such lithium induced P-C bond cleavage in tertiary and bis(phosphides), indicate that both temperature and the nature of the bond (P-C_{aryl} versus P-C_{alkyl}) are important factors in the release of the leaving group as the most stable anion or radical.[21–24] This resulting P-C cleavage reaction can be considered as a product of cleave and capture chemistry – a concept recently introduced by Mulvey and co-workers.[25,26]

To understand the PMDETA dependent P-C bond cleavage reaction in **3** we conducted an *in-situ* NMR experiment to monitor the formation of 7 and possibly identify the 'C_3H_4' by-product. Thus, complex **3** was dissolved in C_6D_6, cooled to -10°C and PMDETA added. The reaction was warmed to room temperature and monitored by ^1H NMR over a period of 1 day. The NMR showed complexation of PMDETA (significant broadening of signals) coincided with the formation of **7** and of a secondary species indicated by two new signals 6.23 ppm and 1.56 ppm (ESI‡) which we propose to be a cyclohexadiene species resulting from the homocoupling of two 'C_3H_4' – 'allene' or 'carbenoid' species. Propene elimination from allylphosphines under pyrolysis has previously been reported[22] while computational[27,28] and experimental studies indicate that dimerisation of allene into a 1,2-dimethylenecyclobutane is thermodynamically stable.

The cleavage of allylic and propargylic C-N bonds in amines and amides is not particularly unusual and N-C_{allyl} cleavage can be achieved by a variety of methods including hydrolysis, nucleophilic displacement and, most commonly transition-metal-catalysed.[4] Our own research has shown alkali-metal sources[16,29] also to be effective. However, in this study **5** and **6** are stable in solution over long periods of time (3-4 weeks).

Wanting to establish the difference in relative energies between the initial complex and cleavage products, we turned to density functional calculations (DFT) using the Gaussian 09 suite of software (ESI‡). Geometry optimisations and frequency calculations were performed at the B3LYP/6-31G(d) level and basis set, in order to compare ΔG values for the competing pathways, for each of the mono-, bi- and tri-dentate donors. As can be seen in Fig. 3, the free energy ΔG for the monomeric complex (0 kJ/mol) is compared to the relative free energy of (i) the dimeric complex, (ii) the elimination of allene, C_3H_4 and (iii) the dimerisation product of two allene molecules, C_6H_8. ΔG for transition states were not calculated due to the uncertainty which remains around the mechanism in play.

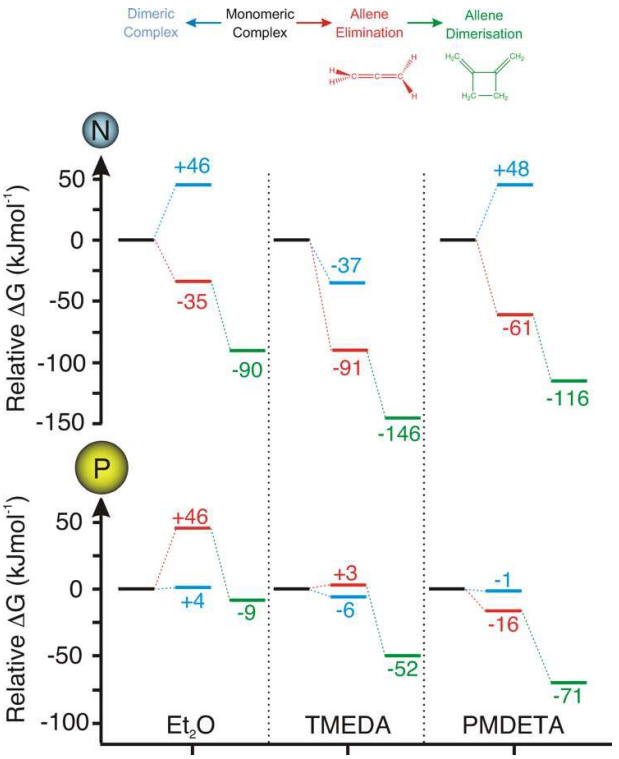

Fig 3 Comparative DFT calculation for both N- and P-based systems with relative ΔG values for the two competing pathways.

In comparing the N- and P-containing systems, several differences are evident. Firstly, the formation of a dimeric complex for the N-containing systems suggests this is not favourable where Et_2O or PMDETA are the donor, yet is predicted to be more stable with TMEDA. Experimentally, the dimeric complex is not observed. Secondly, while the cleavage products for the N-containing systems are predicted to be lower in energy, none are observed experimentally, suggesting the barrier to elimination is large.

In contrast, DFT calculations for the P-containing systems reveal a variety of possibilities, in each case agreeing very well with experiment. Where Et_2O is the donor, the monomeric complex is more stable than the dimeric complex (+4 kJ/mol) or elimination of allene (+46 kJ/mol), neither of which is observed experimentally. Using TMEDA as the donor, a dimeric complex is predicted with the relative free energy slightly lower (-6 kJ/mol) -in comparison to the monomeric complex When the tridentate PMDETA donor is used, the relative free energies change preference, with the pathway for allene

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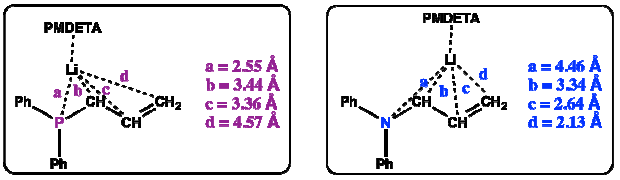
elimination now substantially more favourable (-16 kJ/mol). The dimerization of two allene molecules is well known to proceed as a spontaneous and exothermic reaction to give 1,2-dimethylenecyclobutane.[27,28] The corresponding free energies for this product are also shown. It should be noted that while the NMR experiment described above reveals evidence for a C_6H_8 molecule (two signals 6.23 ppm and 1.56 ppm), unresolved splitting means it is difficult distinguish between 1,2-dimethylenecyclobutane, hexa-1,3-diene or hexa-1,4-diene.



Scheme 2 DFT calculated Li bond lengths to allyl and N/P atoms.

These calculations strongly support the hypothesis that the position of the Li atom has implications for the cleavage mechanism. For instance, when PMDETA is used as a donor, the Li-N distance is calculated to be 4.46 Å (Li cation is closer to C3), and experimentally N-C bond cleavage is not observed. In contrast, in the P-containing analogue the Li-P distance is significantly shorter 2.55 Å, and in this case the elimination of C_3H_4 is readily observed (Scheme 2).

In conclusion we have shown that the choice of Lewis donor in these lithium mediated metallation or cleavage reactions of two analogous N-allyl and P-allyl systems dictates the experimental outcome. Structural and DFT calculations suggest the location of the Li cation, influenced by Lewis donor denticity, plays a crucial role in facilitating P-C or N-C bond cleavage.

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Notes and references

‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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