Technical Piece
THE STABILITY OF ORGANOMETALLICS
Understanding their common decomposition pathways

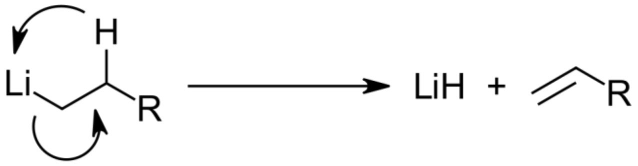
INTRODUCTION

Organometallic reagents find wide use in multiple realms of chemistry, from the formation of highly nucleophilic species to applications in cross coupling reactions. Due to their ubiquitous use, the storage, safe handling, and successful use of such highly reactive species are important. A successful reaction can be dependent on the impurities present, which in turn arise from their methods of production and storage. Understanding the common decomposition pathways for such reagents, and how this may affect a given reaction where such compounds are used is therefore desirable.

METAL-CARBON SPECIES

Perhaps the most ubiquitously used of all the organometallics, metal-carbon species contain two chief groups – carbon-lithium species, and Grignard reagents.

First, carbon-lithium species will be discussed. Much work has been performed in recent years on the solution structure-activity relationships of these compounds,[1] which has led to the understanding of how altering the composition of lithium species can lead to entirely altered reactivity – a danger of improper storage or handling.



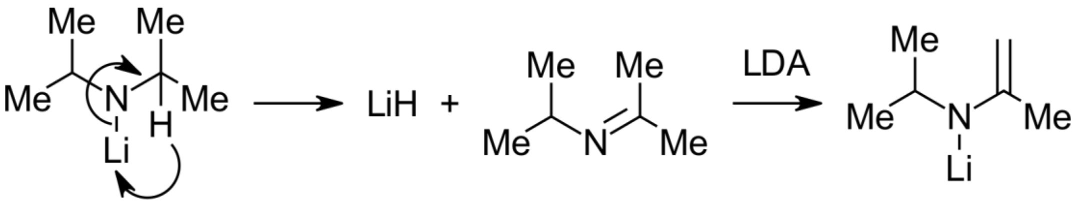
Scheme 1: Thermal degradation of alkyllithiums

However, proper handling of these reagents still leads to very slow decomposition of these reagents. Even when stored at 0 °C, many of the commercial solutions of alkyllithium reagents lose up to 0.02% of the active alkyllithium per day to thermal degradation.[2] This effect is only compounded with increasing temperature. This thermal degradation arises from β-hydride elimination, forming lithium hydride (LiH) and simple olefins (Scheme 1). These olefins are typically highly soluble in organic media, however the lithium hydride is an insoluble, grey powder. Visual analysis can be used to observe the hydride in more degraded samples. The presence of lithium alkoxide (formed by the reaction of an alkyllithium with oxygen) accelerates this degradation.[3] Additionally, alkyllithiums that are synthesised or stored in aromatic solvents (such as toluene or xylenes) will slowly lithiate the solvent, forming alternative lithium species and causing even greater losses of the desired compound. Other formulations in ethereal solvents, even where no β-hydrogens are present, may also decompose by attacking and cleaving the solvent itself.[4] Indeed, in such ethereal solvents these compounds have half lives that are most commonly measured in minutes, and such rapid half lives persist until cryogenic temperatures are reached.[5]

Secondly, Grignard reagents. Similarly widespread in their use, the Grignard reagents are almost exclusively manufactured in ethereal solvents, which provide these species with much enhanced stability.[6] Indeed, while some highly electron-poor Grignards display very poor thermal stability above cryogenic temperatures,[7] many Grignards are stable up to high temperatures in excess of 100 °C. Excepting the reactions with oxygen (leading to peroxymagnesium compounds) and moisture (leading to magnesium alkoxides), the Grignard reagents are relatively stable and long-lasting when not exposed to oxygen and moisture.

METAL AMIDES

Another distinct class of organometallic reagent, metal amides are highly common in their use as strong bases. This is especially apparent in the deprotonation of carbonyl compounds, where LDA or LHMS find common use. Such compounds are often made up fresh from strongly basic species and the corresponding amide, but are also sold as commercial solutions.

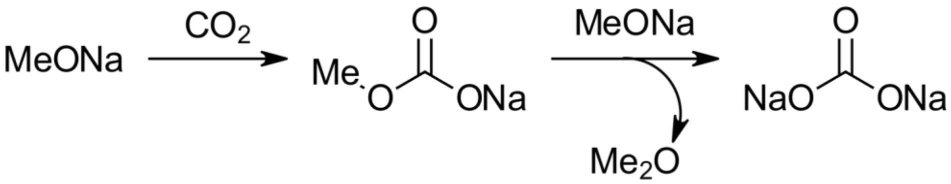


Scheme 2: Thermal degradation of LDA

One of the most widely employed metal amides is LDA. This compound has found much use across synthetic organic chemistry.[8] However, in similar fashion to the carbon-lithium species discussed earlier, LDA can thermally decompose through β-hydride elimination (Scheme 2).[2] A solution of 26 wt% LDA in THF/ethyl benzene (produced from a styrene-Lithium metal suspension)[8] loses 0.2 wt% of LDA per day when stored at room temperature.[9] Besides the production of LiH, this reaction also generates an imine with acidic protons, capable of generating an enamine by consuming another molecule of LDA. This degradation is part of the reason that commercial forms of this base are produced at lower temperatures.[10] By contrast bases such as LiHMDS (while less basic) are significantly more stable, due to both a lack of β-hydrogens for elimination, and that these species are not basic enough to attack ethereal solvents.

SODIUM ALKOXIDES

Predominantly used as bases for cross coupling reactions, but also finding wide use in more generic organic synthesis, sodium alkoxides are a typical class of organometallic reagent. An excellent example of the instability of these compounds can be found in the work of the Engle group.[11] During research into metal cross couplings, the authors observed high batch to batch variance where sodium methoxide or ethoxide was used. Classically, visual analysis has been conducted to assess the purity of such batches – assuming that degraded batches were not free flowing powders. However, the research performed by the authors employed a variety of spectroscopic techniques for purity analysis: ^{1}H and ^{13}C NMR spectroscopy, ^{23}Na ssNMR spectroscopy, Raman spectroscopy and Karl Fischer analysis. All this analysis led to the conclusion that under air or CO_2, degradation of both organometallic bases were rapid, with decomposition beginning almost immediately upon exposure to air. A decomposition pathway suggested by the authors is shown below (Scheme 3).



Scheme 3: The degradation of sodium methoxide by CO_2

This reaction leads to the formation of sodium methyl carbonate, which can be further degraded to sodium carbonate where excess CO_2 is present to fully degrade these materials. Additionally, the formation of sodium formate was also observed after prolonged storage under air (several days). These reactions occur very rapidly under solid state conditions, leading to full consumption of the exposed sodium methoxide after three days under air storage. However, the authors noted that they were unable to observe decomposition where freshly purchased or prepared sodium methoxide was immediately stored under inert conditions. Analogous results were observed with sodium ethoxide. The authors recommend that all purchased samples of these materials are immediately assayed for purity.

While it is plausible that other metal alkoxides (such as lithium alkoxides) undergo similar side reactions, in the absence of supporting literature this remains speculation.

SUMMARY

In summary there are pathways by which organometallic species may thermally decompose, even when protected from the ambient lab atmosphere. As such, greater understanding of these compounds and the pathways or conditions by which they decompose is key for the further safe use of such compounds. However, ongoing work in this field is providing remarkable jumps towards the use of these compounds under more benign conditions. Such developments include the use of green solvents, such as deep eutectic solvents (DES) or ionic liquids to bring great stability to these reactive compounds.[12] An example can be found in the work of Vidal *et al*., who described the use of organolithium and Grignard reagents under air, at room temperature, and with water present.[13] In time further procedures to this theme will arise that will shape the way we handle organometallic compounds, and vastly improve their ease of use and stability.

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