

Alkali-Metal Heavyweights: Up and Coming Contenders in Homogeneous Catalysis?

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ABSTRACT: Alkali-metal compounds particularly organolithium and lithium amide reagents are indispensable organometallic reagents in synthesis, finding widespread applications in cornerstone stoichiometric organic processes. Recent advances in the development of heavier alkali-metal analogues have revealed their emerging potential not only to participate in stoichiometric processes but also to catalyze transformations traditionally dominated by precious transition metals. This perspective provides an overview of a selection of these applications focusing on hydrogen isotope exchange, alkene isomerization, C-C bond formation, hydrophosphination and hydrogenation. Special focus is placed on current mechanistic understanding and alkali-metal effects, aiming to draw out key challenges and opportunities that may guide the future development of alkali-metal-mediated catalysis.

INTRODUCTION

For main group chemists excursions into homogeneous catalysis have been mainly a pleasure of curiosity as main group elements generally do not have the required combination of properties, most significantly the ability to lose and gain electrons easily to cycle between different oxidation states, to match transition metals in important organic reactions which have dominated catalysis both fundamentally and in industrial applications. However, the whirlwind currently blowing through global science to achieve more sustainability in our practices, has stimulated mounting interest in the development of catalytically active main group compounds across the whole periodic table. Within *p*-block, Group 13 elements have excelled in their use as strong Lewis acid catalysts,¹⁻³ whereas heavier pnictogens, in particular bismuth, have also demonstrated the redox flexibility traditionally ascribed exclusively to transition metals.^{4,5} Early main group elements, on the other hand, display more uniform reactivity resulting in compounds with a higher ionic character, where their direct applications in catalysis have mainly stemmed from polar organometallics.⁶

To date, Group 2 has set the pace in *s*-block metal catalysis, including key synthetic protocols such as hydrogenation and hydroelementation reactions.⁷⁻¹⁰ This dominance can be attributed in part to their divalent nature which brings in versatility through the participation of a second ionic ligand when compared to alkali-metal complexes, often helping to deliver better stability and control over aggregation processes. Since alkali metal compounds are

monovalent, they have no access to such ligand rich formulations unless as part of heterobimetallic compositions. Nevertheless, ongoing efforts on Group 1 catalysis have demonstrated considerable potential in this area.¹¹⁻¹³ For example, the use of polydentate neutral ligands such as polyamines or crown ethers has allowed to partially overcome the aggregation issues encountered historically with alkali-metal compounds.¹⁴ However, as evidenced in some of the catalytic exemplars noted in this perspective article, aggregation seems to become less of a hindrance when dealing with the heaviest most reactive alkali metals particularly rubidium and caesium. With the aim of drawing attention to this evolving topic, this perspective article focuses exclusively on recent applications in catalysis of complexes which contain the non-radioactive alkali metals (Li, Na, K, Rb, Cs).

It is widely accepted that organometallic chemistry started with the discovery of Zeise's Salt, $\text{KPtCl}_3(\text{C}_2\text{H}_4)\cdot\text{H}_2\text{O}$, which was first discovered in the period 1825 – 1827 as researched by Seyferth in one of his classic cover essays,¹⁵ so a heavier alkali metal participated at the launch of organometallic chemistry albeit for charge balance purposes with K^+ supporting the complex anion $[\text{PtCl}_3(\text{C}_2\text{H}_4)]^-$, the moiety containing the landmark side-on bond between the ethene and the transition metal. Though the first organometallic compound of the alkali metals is credited to sodium in Wanklyn's alkylzincate $\text{NaZn}(\text{C}_2\text{H}_5)_3$ in 1847,¹⁶ it is organolithium compounds first prepared by Schlenk and Holtz in 1917,¹⁷ that, by a considerable margin, have been the most widely studied of the

alkali metals in the context of organometallic chemistry. These extensive studies have uncovered the remarkable diversity of reactivities possessed by this class of organolithium compounds⁸ including deprotonative metalation, metal-halogen exchange, ligand transfer, nucleophilic addition, reduction and transmetalation, to name just a few. Common alkyl and aryl types, as well as some sterically demanding secondary amides, have long been, and continue to be, commercial heavily used frontline reagents, while in multistep procedures, several organolithium intermediates may also be utilised in the journeys further along the roadmaps. A limitation is that this vast contribution to the development of synthetic chemistry has been mainly confined to stoichiometric organic reactions, not to catalytic reactions. Sodium and potassium have a track record in stoichiometric synthesis too, particularly their amides,¹⁹⁻²⁰ but to a far lesser extent than that of lithium. This vast library of stoichiometric applications of the lighter alkali metals contrasts sharply with the paucity of historical data of their employment in organic catalysis. Of course, some anomalous early examples exist, such as the Takasago process that introduced alkali-metal-catalyzed hydroamination, to the fragrance industry²¹ and the sodium-naphthalene addition reactions to conjugated olefins²² that established "living" anionic polymerization chemistry.

Due primarily to the phenomenal success of these lighter alkali-metal compounds in stoichiometric synthesis, there has been little enthusiasm to develop organocaesium and organorubidium chemistry with one mindset of this reluctance being that organic compounds of such highly electropositive metals would be over-reactive with highly polar $M^{\delta+}C^{\delta-}$ or $M^{\delta+}N^{\delta-}$ bonds, so expectations of widespread selective utility are understandably low. There are other factors that inevitably have held back this development such as the high cost of caesium metal and the fact that organocaesium and organorubidium compounds are pyrophoric. But in mitigation it should be noted that the source of caesium in the selected reactions described in this article start off from commercial caesium salts such as caesium fluoride which are relatively inexpensive. Moreover, the Schlenk line and glovebox techniques²³ used widely throughout chemistry for the safe handling of pyrophoric organo-lithium, -sodium and -potassium compounds are equally effective for performing organo-rubidium and -caesium chemistry.

This perspective article asks the question, "on moving from stoichiometric synthesis to homogeneous catalysis can the current accepted order of chemical utility, high for lithium, low for sodium, potassium, rubidium and caesium, be flipped?" It is important to stress here the idiom "one size does not fit all", since the chemical reaction landscape is so vast that one could never envision a single class of organometallic reagent being capable of performing every transformation. Therefore, increasing the library of accessible polar organometallic reagents will help ensure the security of the World's future supplies of important commodity chemicals and pharmaceuticals. This

aspiration has become a more pressing issue with the news that the most recent 2023 EuChemS endangered elements periodic table²⁴⁷ has lithium downgraded from limited availability/future risk to supply to under a rising threat due to its escalating demand in energy technology, prompting the European Commission to add it in 2020 to their critical raw materials list for low-carbon technologies,²⁵ whereas all other alkali metals are designated green, meaning in "plentiful supply". In terms of earth crustal abundance, the heavyweight alkali metals have a sizable advantage over precious transition metals that dominate catalysis at present since Rb's abundance is similar to that of Cu or Co (and interestingly, higher than Li), whereas Cs is about 3 orders of magnitude more abundant than Au, Pd or Ir.²⁶ On the other hand, when it comes to the catalyst loadings and turnover numbers these heavyweight contenders are not in the same class as their transition metal counterparts, though it should not be overlooked that the Rb and Cd pre-catalysts/catalysts used to date have been commercial or easy to synthesise compounds where ligand design has not featured. The onus now, and a principal reason for writing this article, is to encourage the community to come up with innovative ways of closing the gap between transition metal performance and that of the heavyweight alkali metals.

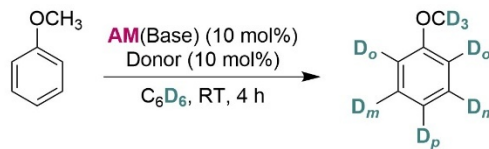
To start answering this question, herein we provide selective recent exemplars of catalytic reactions that showcase the potential of heavy alkali metals, mainly amide compounds but also phosphide compounds, in applications of hydrogen isotope exchange, alkene isomerization, C-C bond formation, hydrophosphination, and hydrogenation. Special focus is on investigations that consider the full set of alkali metals (Li - Cs).

HYDROGEN ISOTOPE EXCHANGE AND ALKENE ISOMERIZATION

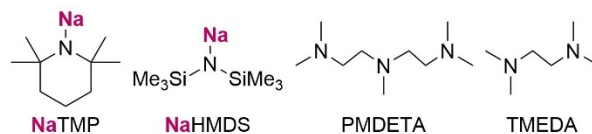
The field of hydrogen isotope exchange (HIE) has been traditionally dominated by transition metal catalysis,²⁷ providing a gateway for the synthesis of labelled molecules containing deuterium (or tritium) isotopes through the selective replacement of existing hydrogen atoms.²⁸ Although numerous strategies based on main group elements have been described in the literature, these usually depend to some extent on the pH of the targeted hydrogen atom, requiring the use of strong acids/bases and often limiting the applicability of each methodology.²⁹ For instance, alkali-metal alkoxides and carbonates have been employed in combination with D_2O or acetone- d_6 as deuterium sources for the base-mediated HIE of relatively acidic C-H bonds,³⁰ e.g. those of carbonyl derivatives, terminal alkynes,³¹ pyridines³² or fluoroarenes;³³ but experiencing a total lack of reactivity towards more challenging substrates such as non-activated arenes. Furthermore, these methods are usually not well understood mechanistically, with the alkali metal frequently overlooked as a mere counter-cation of the proton acceptor anion.

In response to the restricted reactivity exhibited by alkali-metal alkoxides and other oxygen-based anions as catalysts, the use of more basic analogous amides has opened up new avenues in the HIE field, that demonstrate a superior capacity for the deprotonation of weakly acidic C–H bonds. For example, the deprotonative metalation of arenes can be readily accessed under mild conditions employing highly encumbered NaTMP (TMP = 2,2,6,6-tetramethylpiperidine), which facilitates the formation of the corresponding sodiated arenes with concomitant formation of the amine TMP(H).³⁴ Though this metalation is low yielding due to the dynamic equilibrium established between the Ar(H)/NaTMP and NaAr/TMP(H) pairs, the relative stability of the sodiated intermediates allows for further *in situ* functionalization. In this regard, deuteration of anisole was investigated employing NaTMP with C₆D₆ as both solvent and deuterium source (Figure 1a).³⁵ Under catalytic conditions (10 mol% of base), partial deuterium incorporation was observed in the *ortho* position to the methoxy group, demonstrating the capability of this bulky sodium amide to promote the HIE process. In this work, the use of catalytic amounts of the polydentate amine PMDETA (*N,N,N',N'',N'''*-pentamethyldiethylenetriamine) proved critical as it reduces the aggregation of NaTMP, which in turn facilitates solubility in C₆D₆ and enhances its kinetic basicity. Under these conditions almost quantitative deuterium incorporation was achieved, not only in the *ortho* position, but in every C–H bond including those in the methyl group. Furthermore, the combined effect of the Na⁺ cation with the TMP moiety provided by far the best outcome, since the less basic NaHMDS (HMDS = hexamethyldisilazide) and the lighter congener LiTMP gave negligible H/D exchange. Counter-intuitively, the more basic alkyl sodium NaCH₂SiMe₃ also failed to provide any conversion, informing that base strength is not the only contributing factor, but that the reversibility of the deprotonation step is also important. Based on these results, the perdeuteration of different substrates was investigated, including non-activated arenes, toluene derivatives and π -conjugated aromatic systems (Figure 1b). Excellent deuterium incorporations were found in most cases, including the hydrogen atoms in benzylic positions, from methoxy groups or α to a silicon atom, presumably due to the lower pK_a values of these Csp³–H bonds. Steric factors were found to be of major relevance, leading to a lower H/D exchange in the most hindered positions without any *ortho*-directing groups (OCH₃, CF₃, NMe₂).

a) Base-catalyzed HIE studies on the deuteration of anisole



AM(Base) / Donor	Degree of deuteration
NaTMP / none	20 % (<i>ortho</i>)
NaTMP / PMDETA	> 95 %
NaHMDS / PMDETA	< 5 %
LiTMP / PMDETA	< 5 %
NaCH ₂ SiMe ₃ / PMDETA	< 5 %



b) NaTMP-catalyzed perdeuteration of arenes: selected substrates

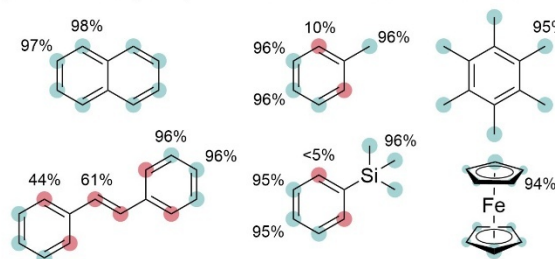


Figure 1. Perdeuteration of arenes via Hydrogen Isotope Exchange (HIE) catalyzed by alkali-metal bases in C₆D₆.

Experimental investigations of the NaTMP-catalyzed perdeuteration mechanism revealed that the process occurs with concomitant formation of C₆D₅H, which implies the parallel sodiation of the solvent to yield NaC₆D₅ and TMP(D). Further insights into the constitution of the organometallic intermediates led to structural elucidation of [(TMEDA)₂Na₃(TMP)₂(Ph)], obtained from a mixture of NaTMP/TMEDA/C₆H₆ in hexane (TMEDA = *N,N,N',N'*-tetramethylethylenediamine) (Figure 2a). The isolation of this intermediate confirms the capability of NaTMP to deprotonate benzene, and the presence of the two NaTMP units co-complexed with the NaPh moiety illustrates the partial metalation of the aromatic substrates. Moreover, sodiated 2-methoxynaphthalene was independently prepared and dissolved in C₆D₆ leading to no deuterium incorporation until catalytic amounts (10 mol%) of TMP(H) were added. This result indicates that TMP is required as a shuttle to perform the H/D exchange, engaging in the catalytic cycle in the forms of TMP(H) and TMP(D) and regenerating NaTMP (Figure 2b).

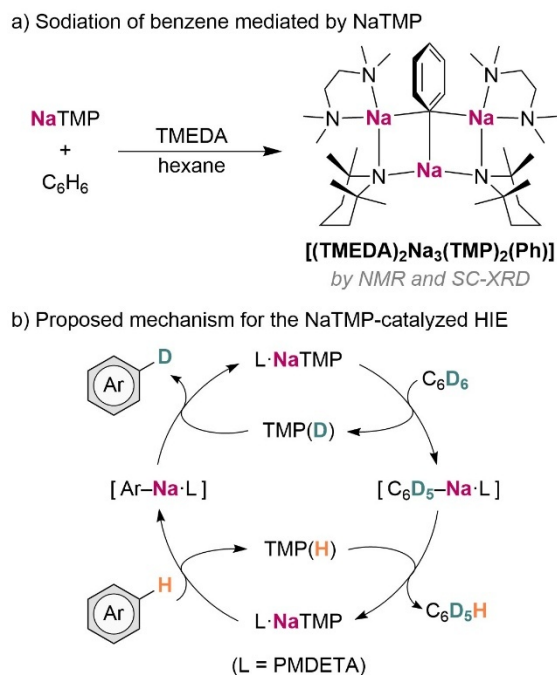
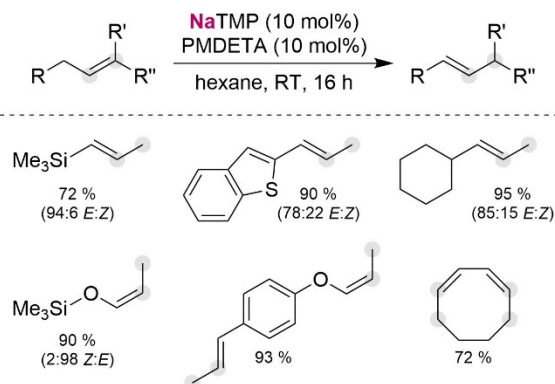


Figure 2. Mechanistic investigations on the perdeuteration of arenes catalyzed by NaTMP.

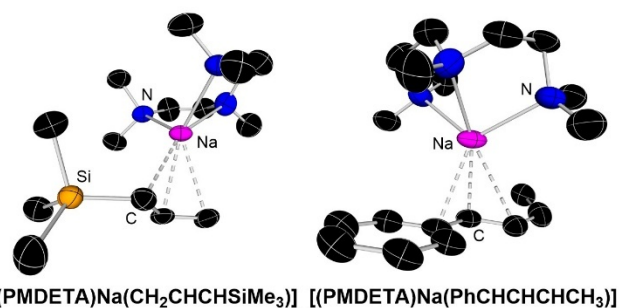
Interestingly, this catalytic system based on the reversibility of the deprotonative metalation mediated by the NaTMP·PMDETA/TMP(H) pairing has been further exploited to catalyze the isomerization of alkenes (Figure 3).³⁶ Showing a similar trend to that observed for the perdeuteration of arenes when assessing the isomerization of allyltrimethylsilane into the corresponding vinylsilane, that is, negligible conversions when using NaHMDS, LiTMP or *n*BuNa, this system provided a higher activity under milder conditions when compared to other main-group element catalyzed isomerizations as for example on using Lewis acid $B(C_6F_5)_3$ (20 °C, 16 h vs. 140 °C, 48 h).³⁷ Excellent conversions to the internal olefins were obtained for allyl-substituted derivatives (Figure 3a), such as amines, arenes, ethers and silanes, demonstrating a remarkable regioselectivity for the *E* isomer (*Z* for allyl ethers). Reactions occur by the formation of π -allyl sodium intermediates as those shown in Figure 3b. Moreover, the alkene isomerization process could be combined with the deuteration strategy when C_6D_6 was used as solvent. For example, employing cyclohexene an overall 75 % of deuterium incorporation was found in every position of the ring, which is consistent with the displacement of the double bond around the six-membered ring while the re-protonation occurred mediated by coexisting TMP(D) (Figure 3c). DFT studies on these transformations using allyltrimethylsilane as model substrate showed that its coordination to the sodium centre prior to the metalation fixes the preferred *E*-selectivity observed in the isomerization process. These studies also support the active involvement of TMP(H) as a proton source over the allyltrimethylsilane, allowing for regeneration of NaTMP·PMDETA. When exploring the

potential of LiTMP, experimental studies showed that this reaction is significantly slower (6% conversion after 2 h vs. 86% for NaTMP). DFT calculations also revealed noticeably larger activation energies for the metalation/protonation steps using this lighter alkali-metal amide as a catalyst.

a) NaTMP-catalyzed isomerization of alkenes: selected substrates



b) Molecular structure of isolated π -allyl sodium intermediates



c) Catalytic cycloalkene metalation and deuteration

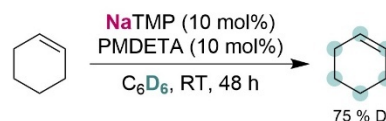
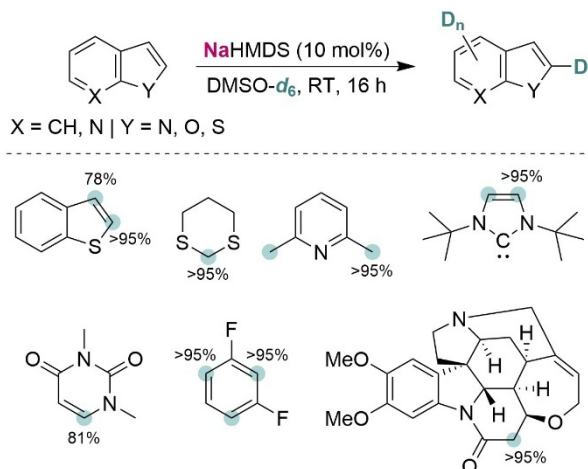


Figure 3. Isomerization of alkenes catalyzed by NaTMP.

Within HIE, building on the results using NaTMP as a catalyst and C_6D_6 as a deuterium source, an alternative catalytic strategy was developed in 2025 which relied on the ability of alkali-metal amides to access the single-site labelling of Csp^2 and Csp^3 -H bonds.³⁸ This approach employs the more acidic solvent $DMSO-d_6$ as a deuterium source in combination with NaHMDS, reasoning that similar pK_a values should be necessary to deuterate specific positions of more acidic substrates (Figure 4a). This strategy was tested against a diverse selection of heterocycles, including thiophene, furan, pyrazoles, fluoroarenes, N-heterocyclic carbenes and carbonyl compounds, among others. Almost quantitative deuterium incorporations were found in the most acidic position of each substrate, with partial H/D exchange in the second most acidic C-H bond in a few cases. For fluoroarenes and carbonyl derivatives, there were

complete and selective labelling in the *ortho* and α positions respectively on operating at room temperature.

a) NaHMDS-catalyzed selective HIE: selected substrates



b) Proposed mechanism for the AM(HMDS)-catalyzed HIE

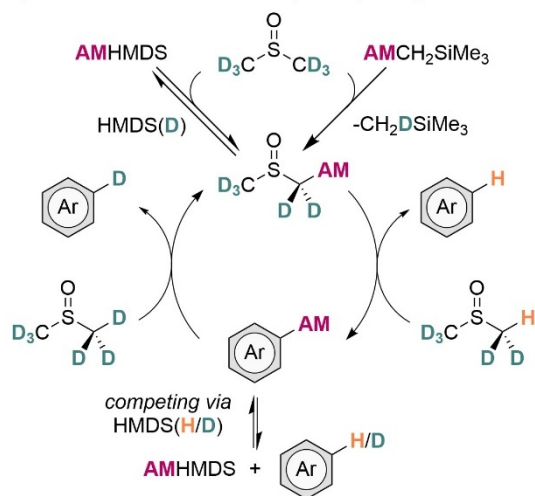
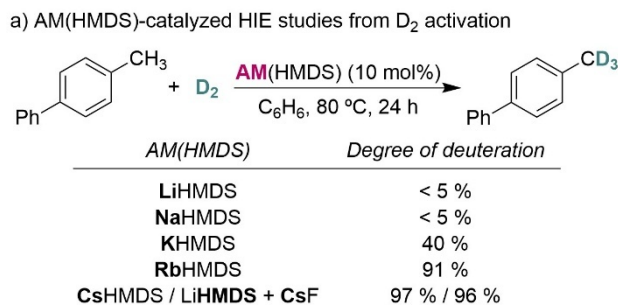


Figure 4. Site-selective Csp^2 and Csp^3 -H deuteration catalyzed by NaHMDS in $DMSO-d_6$.

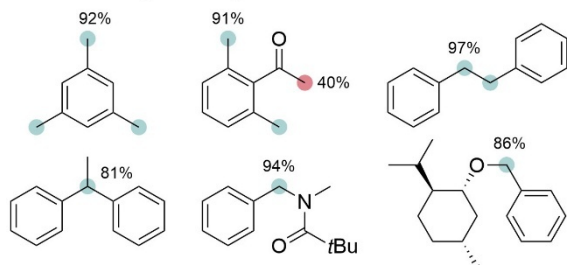
Investigating the reaction mechanism for the NaHMDS/ $DMSO-d_6$ system, it was observed that a faster deuterium incorporation could be achieved when employing the amide-free alkyl sodium $NaCH_2SiMe_3$, indicating that the amine HMDS(H/D) is not required for an efficient HIE, and the presence of the latter is detrimental for the reaction kinetics. However, the study noted that the milder reactivity exhibited by the sodium amide concurrently provides a greater functional group tolerance, expanding its applicability beyond unsubstituted toluene derivatives or simple heterocycles. Furthermore, higher rates of isotope labelling were obtained on descending Group 1 ($Li < Na < K < Cs$), which were attributed to the stronger metalating power of the heavier alkali-metal bases. It was also remarked that no donor was necessary for efficient HIE, since DMSO provides excellent solubility for the AM(HMDS), which could also explain the less marked alkali-metal effect observed compared to that of the AM(TMP)/ C_6D_6

system. Based on these observations, a slightly different mechanism was proposed, where the addition of the AM(HMDS) leads to the partial deprotonative metalation of the $DMSO-d_6$, forming the active catalyst $AM[CD_2S(O)CD_3]$ (isolated in the Na case) which can also partially metalate the substrate (Figure 4b). Then, the surrounding molecules of $DMSO-d_6$ are acidic enough to perform the H/D exchange without the need of the HMDS(H/D) as a shuttle, although the contribution of the latter cannot be ruled out in the overall HIE process, especially with substrates with lower pK_a values than DMSO.

Related to these findings, but using D_2 as a deuterium source, it has been reported that heavier alkali-metal amides can selectively catalyze deuteration of benzylic C-H bonds.³⁹ Subsequently, these studies were extended to tritiation protocols by employing T_2 , a radioactive yet important isotope for drug discovery.⁴⁰⁻⁴¹ Probing the capability of different alkali-metal bases to activate D_2 , it was found that neither KH or KCH_2Ph could conduct HIE for 4-phenyltoluene under catalytic conditions (10 mol%, 4 bar D_2 , 80 °C, 24 h), whereas the amide KHMDS provided 40% deuterium enrichment in the benzylic position (Figure 5a). Additionally, a strong alkali-metal effect was discernible, since the Li and Na analogues provided negligible reactivity. On the other hand, Rb (91%) and Cs (97%) gave outstanding results, even if the latter was generated in situ from LiHMDS and CsF (96%). These sizeable differences were attributed to the greater kinetic basicity of the heavier AM(HMDS), in combination with the lesser lattice energy of the potential in situ generated alkali-metal hydrides from the D_2 activation. Under the aforementioned conditions and employing CsHMDS as catalyst, different toluene, xylene and mesitylene derivatives were successfully and selectively labelled in the available methyl, methylene or methine benzylic C-H bonds (Figure 5b). Expanding on molecular complexity, these studies were extended towards the late-stage deuteration and tritiation of pharmaceuticals, which exhibited excellent isotope incorporations. For the tritiated drugs, which showed high specific activities, conditions were modified to work under a low pressure of T_2 (150 mol%, 0.3 bar T_2 , 90 °C), and HIE was confirmed by 3H NMR and mass spectrometry. Control experiments were performed in order to trap the potential carbanion or hydride intermediates arising from the deprotonation of 4-phenyltoluene or H_2 with CsHMDS, however, these could not be detected. Nevertheless, isotope exchange was observed in the presence of CsHMDS between H_2 and D_2 , and 4-phenyltoluene and deuterated diphenyl methane (Figure 5c). These results were considered to suggest the presence of the hydride and benzyl intermediates, but in a very low concentration due to a high thermodynamic cost.



b) CsHMDS-catalyzed benzylic deuteration: selected substrates



c) Control experiments with CsHMDS

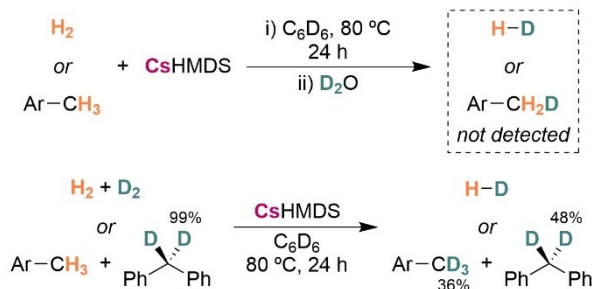
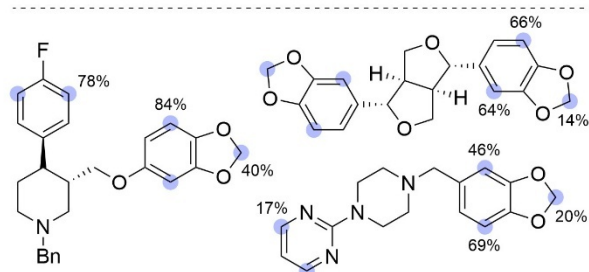
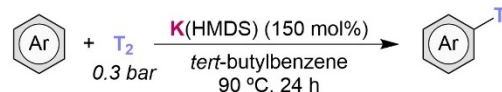


Figure 5. Benzylic HIE catalyzed by alkali-metal amides AM(HMDS) from D₂/T₂ activation.

As an extension of this system, the isotopic labelling of Csp²-H bonds in arenes was explored.⁴² The same pattern was observed regarding the activity of the alkali-metal amides, with CsHMDS outperforming its lighter congeners. In this case, selective deuteration or tritium incorporation was observed *ortho* to strong directing groups, such as ethers, amides or fluorine atoms, as well as for more acidic substrates such as furan or thiophene (Figure 6a). Mechanistic studies were conducted to assess the role of the alkali metals, comparing K against Cs. Interestingly, a primary kinetic isotopic effect was found for KHMDS (KIE = 2.7), while for the caesium amide the difference was less pronounced (KIE = 1.6). A plausible mechanism was evaluated by DFT calculations, showing the initial metalation of the substrate through a σ -bond metathesis transition state to be lower in energy for Cs (26.1 vs. 30.2 kcal·mol⁻¹ for K). The metalated intermediate would react with D₂ via another σ -bond metathesis, affording the labelled product and the metal hydride, which would regenerate the catalyst on reacting with the free amine HMDS(H) (Figure 6b). Energy profiles indicated that the first deprotonation is the rate-determining step for KHMDS, in line with the KIE value experimentally determined, whereas for CsHMDS the activation of D₂ was predicted to be more energetically

demanding. This proposed mechanism sharply contrasts with that reported earlier for alkaline earth metal amide complexes, where the hydride intermediate is formed by D₂ activation from the metal amide and HIE occurs via nucleophilic aromatic substitution of the hydride species in the aromatic ring.⁴³

a) K(HMDS)-catalyzed HIE of pharmaceuticals from T₂ activation



b) Proposed cycle for the AM(HMDS)-catalyzed HIE of arenes

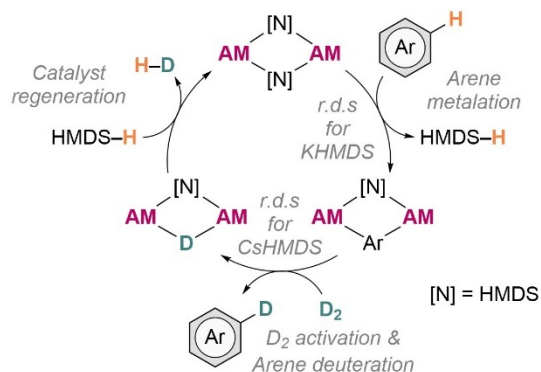


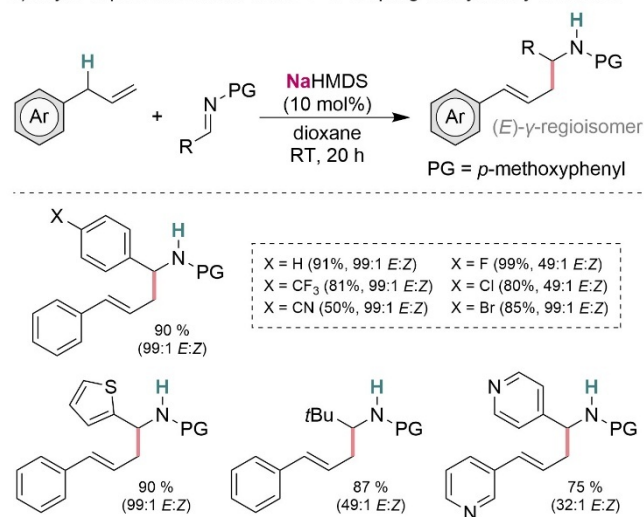
Figure 6. Directed aromatic HIE catalyzed by alkali-metal amides AM(HMDS) from D₂/T₂ activation.

C-C BOND FORMATION VIA C-H BOND ADDITION ACROSS UNSATURATED ORGANIC MOLECULES

Since the development of transition metal-catalyzed cross-coupling reactions during the second half of the 20th century, the construction of new C-C bonds has been a primary goal in the organometallic chemistry field. Although metals such as Pd, Cu or Ni have been and continue to be the leading drivers of these processes, Group 1 elements have also played an active role in catalytic C-C bond formation. For instance, the Murahashi coupling usually involves a Pd or Ni catalyst in combination with organolithium reagents, albeit in stoichiometric amounts as the source of the nucleophilic agent.⁴⁴ However, the incorporation of alkali-metal bases can also modify the reactivity of certain catalytic systems. As an example, the deprotonative cross-coupling of allylbenzenes with aryl bromides can be accessed from stoichiometric LiHMDS with a Pd catalyst, leading to the selective formation of the α -regioisomer instead of a mixture of γ -regioisomers expected under

Heck-type conditions (that is, using a weaker base that cannot deprotonate the allylbenzene reagent).⁴⁵ However, the integration of the alkali metal into the catalytic species without the requirement for a transition metal remains challenging due to the impossibility to enter a typical redox manifold and provide catalytic turnover.

a) Allylic deprotonation and imine C–C coupling catalyzed by NaHMDS



b) Mechanistic experiments for the NaHMDS-catalyzed C–C coupling

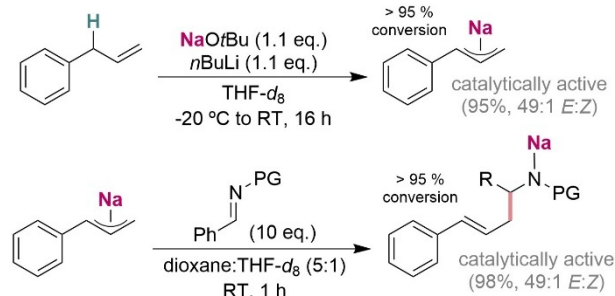


Figure 7. NaHMDS-catalyzed C–C bond formation through allylic Csp^3 -H deprotonation followed by imine coupling: selected substrates and mechanistic experiments.

In spite of their inability to access different oxidation states, alkali metals can make exceptionally basic reagents and intermediates that have been exploited for the formation of C–C bonds under catalytic regimes. Similar to the aforementioned deprotonative cross-coupling work using LiHMDS, NaHMDS was used for the allylic deprotonation of alkenes.⁴⁶ The in situ generated allyl sodium species engaged in catalytic C–C bond formation with imines without requiring a transition metal (Figure 7a). The formal Csp^3 -H bond activation and C–C coupling occurred under mild conditions upon using NaHMDS (10 mol%, 25 °C, 20 h), whereas other Li, K or alkaline-earth amides failed to catalyze this transformation. This marked alkali-metal effect was ascribed to a combination of the different electronegativities, formal charges and ionic radius, which collectively influence the Lewis acidity of the metal and the relative Brønsted basicity of the amides and organometallic

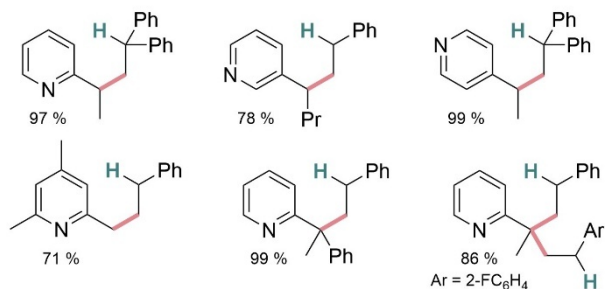
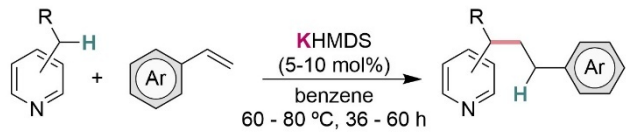
intermediates. The NaHMDS-catalyzed process was tested towards a range of electron-poor and electron-rich aromatic amines bearing sensitive functional groups, together with different substituted allylbenzenes. In general, excellent yields were recorded with total selectivity towards the (*E*)- γ -regioisomer (*E:Z* ratio from 24:1 to 99:1), as opposed to the aforementioned Pd-catalyzed system.²⁶ Although from the deprotonation of allylbenzene with NaHMDS no intermediates were isolated, the proposed allyl sodium complex was prepared using NaOtBu/*n*BuLi, and it was found to undergo addition towards a model imine (Figure 7b). The resulting amide from the C–C bond formation was proven to be catalytically active like the allyl sodium species, giving analogous results to those obtained from NaHMDS and suggesting that both sodium compounds are the potential intermediates for this amide-catalyzed process.

Similar strategies have been developed employing different alkali-metal HMDS amides (of Li, Na and K) to couple esters, amides or alkylpyridines as pronucleophiles with α,β -unsaturated carbonyl compounds or styrene derivatives as electrophilic partners.^{47–49} Although KOtBu or Na or K metal have proved active catalysts for some of these couplings,^{50–51} using alkali-metal amides provides a platform with a higher activity than their alkoxide analogues and a more controlled and predictable behavior than that of the neat metal catalysts. An illustrative example can be found in the coupling of alkylpyridines with styrenes,⁵² where KOtBu failed to afford any conversion whereas KCH₂Ph, a significantly stronger base, initiated anionic oligomerization of styrene, seen with Na or K metal.⁵⁰ In contrast, KHMDS catalyzed the C–C bond formation from 2-ethylpyridine and styrene under relatively mild conditions (5 mol%, 60 °C, 36 h), enabling the extension of this transformation to different functionalised substrates (Figure 8a). It should be noted that the selectivity of these reactions is usually controlled by the acidity of the different C–H bonds and the relative stability of the different intermediates. This means that only deprotonation of the benzylic position was observed for the alkylpyridines, and that addition into the styrene substrate always leads to the β -regioisomer, whose anionic intermediate is stabilised by charge delocalization across the phenyl ring.

As previously observed for allylbenzene with NaHMDS, trapping the intermediate from the deprotonation of 2-methylpyridine with KHMDS proved unsuccessful, which was ascribed to the low acidity of these substrates preventing a significant amount of the metalated species and HMDS(H) to be formed within the existing equilibrium. Accordingly, the expected potassium intermediate was prepared and reacted with HMDS(H), producing immediately 2-methylpyridine and KHMDS. Although this potassium species was found to catalyze the transformation, it mainly gave oligomerization products, suggesting that the presence of HMDS(H) controls the chemoselectivity of the process, potentially by re-protonation of the C–C coupling intermediate (Figure 8b). Consistent with the

experimental KIE value of 2.7, further computational investigations revealed that proton transfer between the organic substrate and KHMDS/HMDS(H) is involved in the rate-determining step, rather than C–C bond formation.⁵³

a) KHMDS-catalyzed C–C coupling of alkylpyridines with styrenes



b) Proposed mechanism for the KHMDS-catalyzed C–C coupling

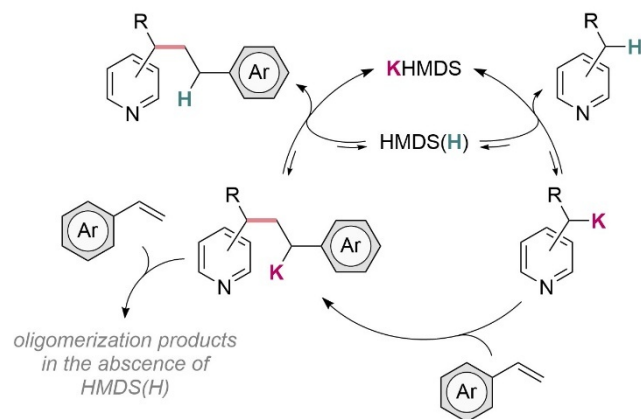


Figure 8. KHMDS-catalyzed C–C bond formation through benzylic Csp^3 -H deprotonation of alkylpyridines followed by styrene coupling: selected substrates and mechanistic experiments.

Moving towards more challenging substrates, another study reported the aminobenylation of aldehydes with toluene derivatives (Figure 9).⁵⁴ Whereas for carbonyl compounds, allylbenzenes, or alkylpyridines ($pK_a \approx 25 - 35$ in DMSO)⁵⁵ the deprotonation step is more accessible, especially when they have electron-withdrawing groups that increase the acidity, toluene ($pK_a \approx 43$ in DMSO)⁵⁶ demonstrates a lower susceptibility to react with bases. Screening different alkali-metal amides ($pK_a \approx 26$ for HMDS(H) in THF),⁵⁷ it was observed that neither LiHMDS nor NaHMDS were able to catalyze the aforementioned transformation under catalytic conditions (10 mol%, 110 °C, 12 h), while KHMDS only afforded a poor 35% yield. However, combining 1.1 equivalents of NaHMDS (where 1 equivalent is consumed for in situ generation of the corresponding imine from the aldehyde) with a 10 mol% of a caesium salt as additive resulted in an increased activity of the catalytic

system, where Cs_2CO_3 gave the best result (93% yield). These conditions were successfully applied to different aldehydes and toluene derivatives producing good yields, indicative of the strong influence of the Cs additive. It was proposed that during the process CsHMDS could be formed via a metathesis between NaHMDS and Cs_2CO_3 . To test this, CsHMDS was independently synthesised, and it was proved to be catalytically active, showing a comparable result to the NaHMDS/ Cs_2CO_3 pairing (94% yield). This outcome could be attributed to the enhanced kinetic basicity of the Cs amide, although it was also proposed that the capability of Cs^+ to engage in π -interactions with the aromatic system could play a major role, increasing the acidity of the benzylic C–H bond.⁵⁸

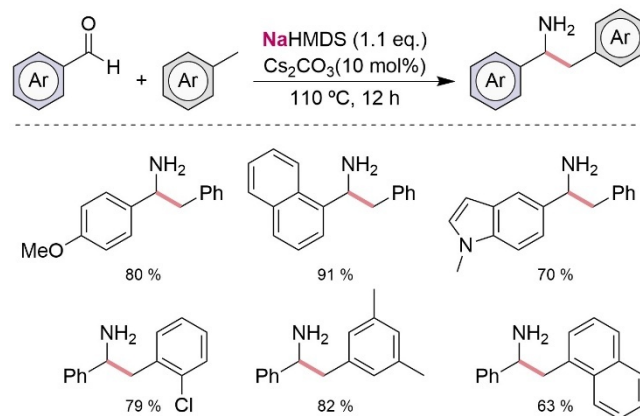
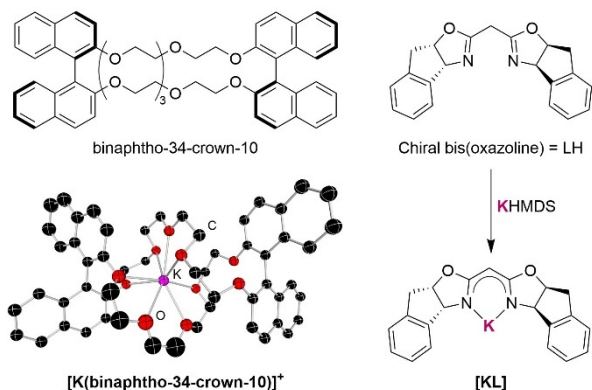


Figure 9. Catalytic aminobenylation of aldehydes from toluene derivatives.

The construction of new molecular architectures through C–C bond formation often implies the use of chiral or prochiral substrates, for which stereoselective methodologies are highly desirable. However, examples of asymmetric catalysis employing alkali-metal bases have been rather limited to date, especially for congeners heavier than lithium.⁵⁹ Chiral Lewis donors such as crown ethers or bis(oxazoline) ligands have proved effective for inducing asymmetry through coordination to the metal centre (Figure 10a). This strategy has been exploited to access the coupling of carbonyl compounds with α,β -unsaturated substrates or imines catalyzed by KHMDS, achieving excellent diastereo- (anti/syn > 99:1) and enantioselectivities (e.e. > 95%) (Figure 10b).⁶⁰⁻⁶¹ For bis(oxazoline) ligands, it was found that their potassium salts formed by deprotonation with KHMDS were the source of the chirality. DFT calculations suggested that the asymmetric environment of the potassium enolate intermediate is modulated by the deprotonated bis(oxazolidine) ligand, further influencing the coupling with the imine.

a) Chiral Lewis donor ligands employed in AM-catalyzed asymmetric synthesis



b) Catalytic asymmetric coupling of carbonyl compounds with imines

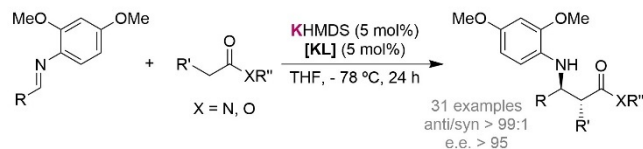
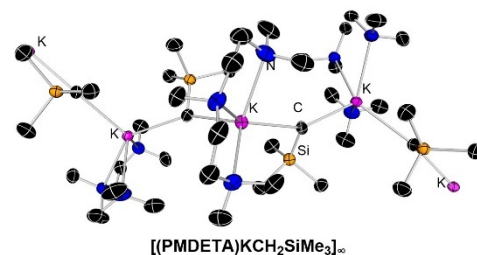


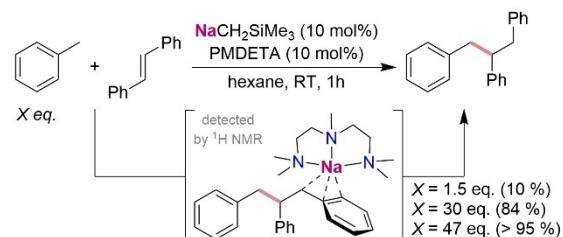
Figure 10. KHMDS-catalyzed stereoselective strategy for the C–C coupling of carbonyl compounds and imines.

Alkali-metal organometallic derivatives have also been employed in catalytic asymmetric synthesis to access synthons from weakly acidic substrates. For example, the strong basicity of $\text{KCH}_2\text{SiMe}_3$ and $\text{NaCH}_2\text{SiMe}_3$, typically supported by a Lewis donor such as PMDETA to reduce their aggregation and facilitate their solubility in apolar solvents (Figure 11a),⁶² enables the $\text{Csp}^3\text{-H}$ deprotonation of toluene derivatives, generating highly reactive intermediates ($\text{AM-CH}_2\text{Ar}$) that can engage in catalytic C–C bond formation.⁶³ Illustrating this strategy, another study reported the addition of toluene to *trans*-stilbene employing $\text{NaCH}_2\text{SiMe}_3$ -PMDETA as catalyst (10 mol%), though it was observed that a considerable excess of toluene was necessary to promote catalytic turnover from the sodiated intermediate (Figure 11b).⁶⁴ A different study explored the benzylation of imines from $\text{KCH}_2\text{SiMe}_3$ and toluene, introducing a chiral amine and KHMDS as additives to impart asymmetry in the resulting amines (Figure 11c).⁶⁵ Although other combinations such as KOtBu/LiTMP proved capable of promoting this transformation catalytically, the $\text{KCH}_2\text{SiMe}_3/\text{KHMDS}$ system proved superior at transferring the chiral information. Thus, it was reasoned that formation of chiral oligomeric species involved in the C–C coupling stage, where the chiral amine binds to the KCH_2Ph intermediate and KHMDS, have a significant influence in the stereochemistry of the process.

a) Polymeric structure of $[(\text{PMDETA})\text{KCH}_2\text{SiMe}_3]$



b) Catalytic benzylation of *trans*-stilbene mediated by $\text{NaCH}_2\text{SiMe}_3$



c) Catalytic stereoselective C–C coupling in the presence of a chiral amine

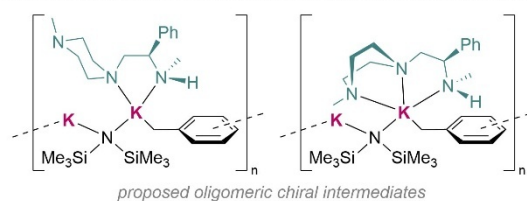
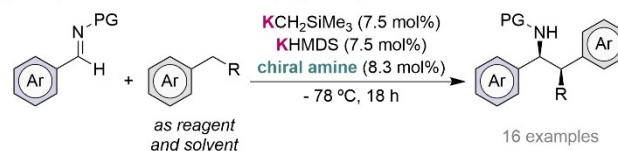


Figure 11. AM-catalyzed C–C coupling of toluene derivatives with unsaturated substrates.

CATALYTIC HYDROPHOSPHINATION

Catalytic hydrophosphination (HP) and related reactions such as hydrophosphorylation⁶⁶ and hydrophosphinylation⁶⁷ are atom-economical approaches for the synthesis of phosphorus compounds which is plagued by a significant number of challenges (Figure 12).⁶⁸ Meeting these challenges in controlling chemo-, regio-, and stereo-selectivity, as well as in increasing substantially the number of participating substrates (Figure 12), are nontrivial considering that the first example of catalytic HP of an alkene appeared 35 years ago.⁶⁹ The catalyst used then was the $\text{Pt}(0)$ complex $[\text{Pt}\{\text{P}(\text{CH}_2\text{CH}_2\text{CN})_3\}]$ and ever since transition metal catalysts have played a major role in the development of catalytic hydrophosphination though this has spread to other metals across the periodic table as described in a 2023 comprehensive review.⁷⁰ Conspicuously, this 31-page review contains only one brief paragraph on the alkali metals, thus emphasizing the underdevelopment of alkali metals in this important reaction class which at its best can produce phosphorus compounds atom-economically and without waste, for exploitation in agriculture,

medicinal chemistry, and organocatalysis, as well as for a vast library of ligands used in transition metal catalysis.⁷¹

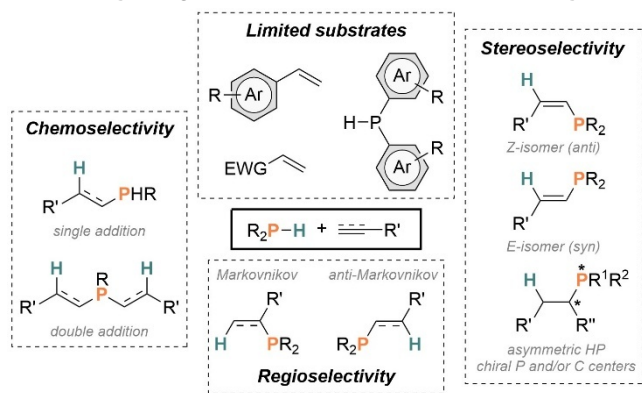


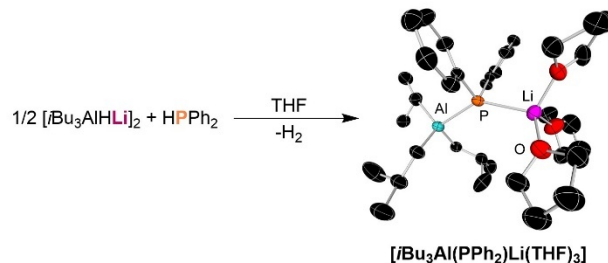
Figure 12. Current challenges in hydrophosphination reactions.

Enhanced performance of homogeneous catalysts where enhancement is delivered by setting two metal centres into well-defined structures is becoming more prominent across the periodic table in areas such as transition metal chemistry,⁷² main group chemistry⁷³ and polymerization chemistry.⁷⁴ The bimetallic input in these reactions has been labelled in different terms such as cooperative, synergic, or synergistic, or the more specific term "alkali-metal-mediation" in the sense that the Group 1 metal mediates reactions that are impossible or low yielding with the second metal without the presence of an alkali metal component. It is often prudent to work with well-defined compounds known to be bimetallic in solution as one can be led into misinterpreting reactions, even stoichiometric reactions, on the basis of a known solid-state structure when the solution chemistry is complicated involving multiple species in equilibria. For example, selective aluminium of a set of substituted aromatic substrates was thought to be carried out by the crystallographically characterised lithium aluminum compound, $[i\text{Bu}_3\text{Al}(\text{TMP})\text{Li}]$,⁷⁵ described as a Brønsted base ate, but a subsequent detailed NMR study concluded that, in fact, the metalations were C–H to C–metal transformations performed by monometallic LiTMP with the produced carbanion subsequently trapped by an aluminum species in the solution,⁷⁶ in what is referred to as a *trans-metal-trapping* process that is still synergistic in origin.⁷⁷

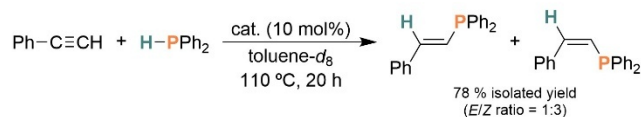
In 2019 the related lithium phosphidoaluminate $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ was structurally defined in both the crystal and in solution and found to be a capable catalyst for HP of alkynes, alkenes, and carbodiimides (Figure 13a).⁷⁸ Made by adding the common phosphine Ph_2PH to the pre-catalytic hydridoaluminate $[i\text{Bu}_3\text{AlHLi}]$ in hydrocarbon/THF solution, $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ was optimised as a catalyst via its performance with the terminal alkyne $\text{PhC}\equiv\text{CH}$, but at 10 mol% under the high temperature of 110 °C achieving a yield of 78% – over 20 h in toluene- d_8 with a poor *E/Z* ratio of 1:3 – to the anti-Markovnikov phosphidoalkene product, indicative of *anti*-addition

of the P–H bond across the $\text{C}\equiv\text{C}$ triple bond (Figure 13b). Catalytic performance was faster with the internal alkynes ($\text{PhC}\equiv\text{CPh}$) and $\text{PhC}\equiv\text{CMe}$ with both reaching yields about 80% in only 1 h, though $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ failed to react at all with the more challenging unactivated alkynes, 1-hexyne, and 3-hexyne. In an interesting observation the addition of assorted Lewis base donors to the pre-catalyst $i\text{Bu}_3\text{AlHLi}$ and catalyst $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ did not significantly impact the rate of the hydrophosphination reaction of $\text{PhC}\equiv\text{CPh}$ and Ph_2PH in toluene- d_8 solution but selectivity was impacted with the *E/Z* ratio varying from 2:1 to 19:1, with the latter high value obtained when $[i\text{Bu}_3\text{AlHLi}]$ was activated by two equivalents of TMEDA. The reaction of $\text{PhC}\equiv\text{CPh}$ with $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ was probed by kinetics using $\text{Ph}_2\text{PH}/\text{Ph}_2\text{PD}$ and found to be pseudo first order with a small kinetic isotope effect (KIE) implying the turnover determining step is not P–H bond cleavage but alkyne insertion into $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$. A reaction scheme was proposed for this catalytic hydrophosphination process (Figure 13c). In the same study $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ was also successful in catalytic hydrophosphination of styrenic substrates though only under similarly harsh conditions, but even these conditions failed to work with the more challenging alkenes α -methyl styrene, *trans*- β -methyl styrene and 1-hexene.

a) Synthesis and molecular structure of $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$



b) Hydrophosphination catalyzed by $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$



c) Proposed mechanism for hydrophosphination of phenylacetylene

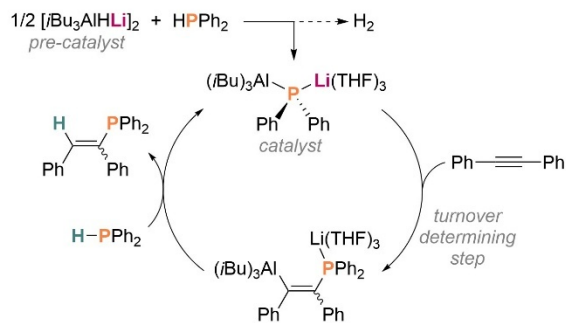


Figure 13. Synthesis of $[i\text{Bu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ and catalytic application in the hydrophosphination of alkynes.

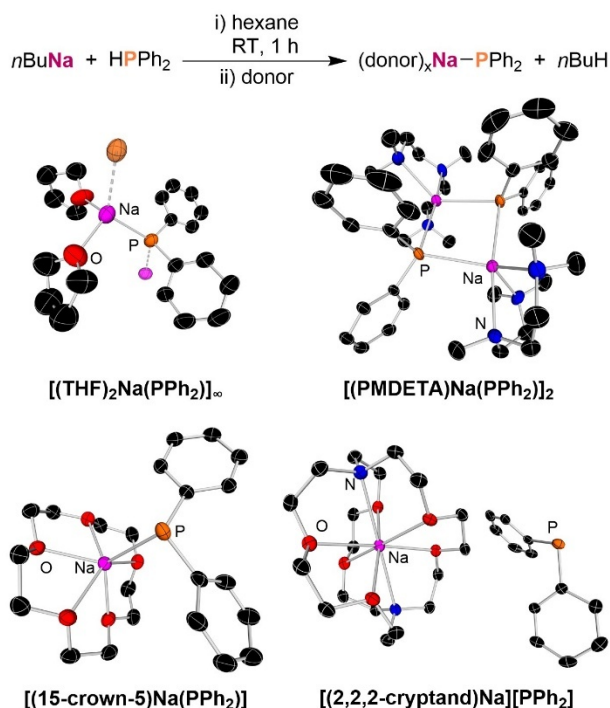


Figure 14. Synthesis and molecular structures of sodium diphenylphosphides bearing different Lewis donors.

Learning from the work involving $[\text{iBu}_3\text{Al}(\text{PPh}_2)\text{Li}(\text{THF})_3]$ a follow-up study pondered whether its high steric bulk was a detrimental factor behind its modest catalytic capacity. Could this be improved by removing the aluminum moiety to lower the steric bulk to enhance the lability of lithium phosphide Ph_2PLi though at the cost of losing any possible beneficial bimetallic cooperative effects? Well-defined donor adducts (with THF,⁷⁹ and also with DME,⁸⁰ Et_2O ,⁷⁹ PMDETA⁸¹ and TMEDA⁸¹) were already known since 1986 so were easily accessible for study. However, unpublished studies with these monometallic lithium phosphides proved disappointing, therefore focus moved to the less studied sodium analogs. Part of the reasoning for this choice is that sodium is approximately 1500 times more earth abundant than lithium,⁸² is also environmentally benign and has relatively low toxicity compared to precious d-block metals so in theory sodium could potentially fill the role of an alternative, more sustainable metal for exploitation in HP catalysis. A hint of the potential of heavier alkali metals in this HP field came in a 2018 report⁸³ that established that potassium amide KHMDS was catalytically competent in double HP of terminal alkynes with Ph_2PH to access 1,1-diphosphines. NaHMDS was also considered in this 2018 study during the catalyst optimization using the test alkyne ethyl propionate, but no further information was reported in the paper. Adhering to the practice of testing well-defined compounds in catalytic trials, another study synthesised a series of crystallographically characterised adducts with decreasing aggregation state (polymeric; dimeric; monomeric; and separated ion pair), directly dependent on the

dentistry of the Lewis donor used, namely monodentate THF; tridentate PMDETA; pentadentate 15-crown-5; octadentate 2,2,2-cryptand, respectively (Figure 14).⁸⁴ Results on the catalytic HP of alkynes were much better in comparison to those of the aforementioned bimetallic and monometallic lithium phosphides, with a direct correlation being established between the adduct aggregation state and its catalytic performance. Thus, the lower aggregates with 15-crown-5 or 2,2,2-cryptand were the best performing catalysts with a range of alkynes able to reach quantitative conversions in 30 min at room temperature on a 10 mol% scale. Isolated yields measured for the 15-crown-5 adduct were slightly lower in the range 73-86%. As is common in such reactions, *E/Z* isomeric ratios were generally poor with some exceptions, though increasing the reaction temperature to 110 °C, generally improved selectivity. Using 1-propyne as the model substrate with the 15-crown-5 adduct as the catalyst, DFT studies examined possible mechanisms for these catalytic reactions providing some insight into the complicated pattern of the *E/Z* isomer ratios obtained in these catalytic reactions that suggested a high dependency on the specific substrate used.

Stimulated by the success of monomeric Ph_2PNa -15-crown-5 in the aforementioned HP applications,⁸⁴ research was extended to the whole of Group 1, with a complete set of well-defined crown-ether adducts synthesised and crystallographically characterised⁸⁵ which, including structures published earlier,⁸⁶ totalled 9 structures, 7 of which feature the common diphenylphosphide in $[(12\text{-crown-}4)\text{Li}(\text{PPh}_2)]$, $[(15\text{-crown-}5)\text{Li}(\text{PPh}_2)]$, $[(15\text{-crown-}5)\text{Na}(\text{PPh}_2)]$, $[(18\text{-crown-}6)\text{K}(\text{PPh}_2)]$, $[(18\text{-crown-}6)\text{Rb}(\text{PPh}_2)]$ (2 variants), and $[(18\text{-crown-}6)\text{Cs}(\text{PPh}_2)]$, while the less common *t*-butyl(phenyl)phosphide and di-*t*-butylphosphide appear in $[(18\text{-crown-}6)\text{Cs}(\text{P}(\text{tBu})\text{Ph})]$ and $[(18\text{-crown-}6)\text{Cs}(\text{P}(\text{tBu})_2)]$, respectively (Figure 15). A subsequent 2025 study of this set of alkali metal crown-ether adducts⁸⁷ underlines the prospect of lithium passing on the baton to its heavier congeners when it comes to utilization in homogeneous catalytic reactions such as HP, which if developed much further may help the chemistry community's race towards a more sustainable future of the chemical industry. In benchmarking reactions with Ph_2PH and the alkene $\text{Ph}_2\text{C}=\text{CH}_2$, Ph_2PLi -15-crown-5 failed to show any conversion on a 1 mol% scale in C_6D_6 solution at room temperature over 24 h. In contrast, all the heavier alkali metal crown ether adducts showed catalytic competency to diverse degrees under these conditions. $[(15\text{-crown-}5)\text{Na}(\text{PPh}_2)]$ reached only a poor 30% conversion after 14 h, whereas $[(18\text{-crown-}6)\text{K}(\text{PPh}_2)]$ is more active reaching full completion in about 1 h. However, it is the performances of $[(18\text{-crown-}6)\text{Rb}(\text{PPh}_2)]$ and $[(18\text{-crown-}6)\text{Cs}(\text{PPh}_2)]$ that catch the eye with quantitative conversion in 28 and 12 min respectively, leading to turnover frequencies (ToFs) of 211 h^{-1} and 493 h^{-1} . Solvent dependence was found to be operating on moving from C_6D_6 to the polar solvent $\text{MeCN-}d_3$, with all four Na-Cs adducts achieving near complete conversion on a 1 mol% scale in a few minutes though again

the performance of [(15-crown-5)Li(PPh₂)] was poor. This augmented reactivity was attributed to the increased nucleophilicity of the Ph₂P⁻ moiety in polar solvents. The overall conclusion from the comparative Ph₂C=CH₂ HP study is that the Cs adduct can achieve the maximum nucleophilicity of Ph₂P⁻ in non-polar solvents such as C₆D₆, whereas the lighter congeners need polar solvents to reach the maximum (for K and Rb) or high nucleophilicity (with Na but less so with Li) in polar solvents such as MeCN-*d*₃. Addressing some of the challenges mentioned above (Figure 12),⁶⁸ this study also probed various aspects of scope. Rarely used in HP catalysis or found to be inactive in it, the challenging electron-donating alkyl-containing phosphines *t*BuPhPH, *t*Bu₂PH and *n*Bu₂PH with lower acidity P-H bonds were benchmarked with Ph₂C=CH₂ and shown to be successful with [(18-crown-6)Cs(PPh₂)] proving to be the best catalyst (Figure 16). Extending the scope further, this Cs catalyst worked well in HP reactions with assorted styrenic substrates with all four phosphines to afford trialkylphosphine products including examples chiral at phosphorus. A selection of activated and non-activated alkynes as well as related unsaturated species combined with the same phosphine substrates also proved amenable to HP via the Cs catalyst.

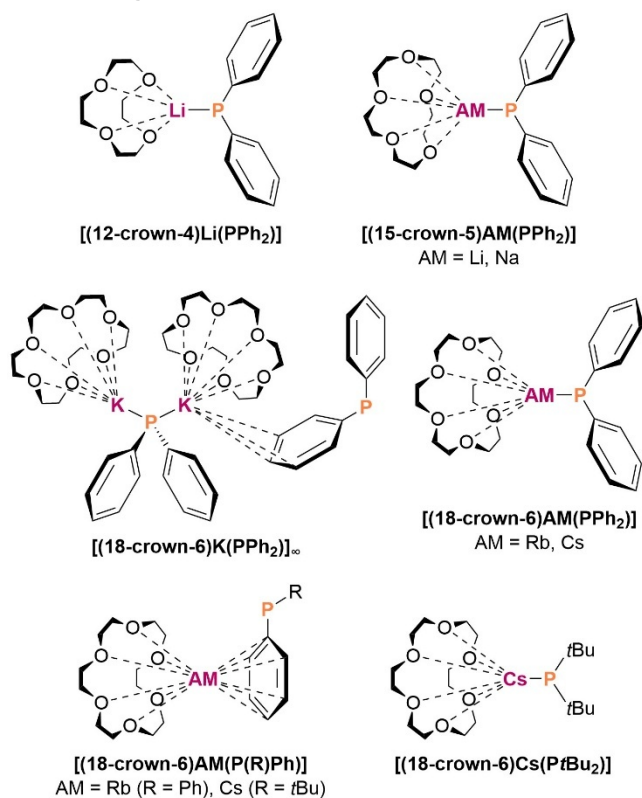


Figure 15. Complete series of crystallographically characterized alkali-metal phosphides supported by crown-ether ligands.

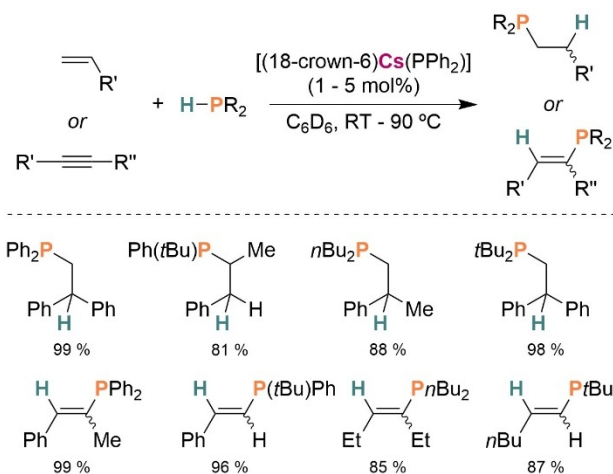


Figure 16. Hydrophosphination of alkenes and alkynes catalyzed by [(18-crown-6)Cs(PPh₂)].

It is encouraging for the development of new catalysts that different research groups are beginning to see the benefit of including the complete set of alkali metals in their programs, with the higher reactivity descending the group being a key factor. An exemplar in hydrophosphination catalysis was the recent report⁸⁸ of the first use of Group 1 salt alkoxides, *tert*-amylates AMOC(CH₃)₂CH₂CH₃ (AM = Li-Cs), as precatalysts for HP of styrenes with Ph₂PH (Figure 17). Matching the Li-Cs trend reported earlier in an investigation of transfer hydrogenation catalysis,⁸⁹ Li is inactive and activity rises in line with the increasing size of the cations from Na to Cs. The trend with these salt precatalysts essentially follows that witnessed in the aforementioned alkali-metal organophosphide crown ether study,⁸⁷ but in that previous case the catalyst loading can be reduced to 1 mol% compared to 5 mol% for the salts which suggests these well-defined organophosphide compounds generated in situ by adding an alkali-metal base to the substrate/phosphine mixture are the bona fide catalysts.

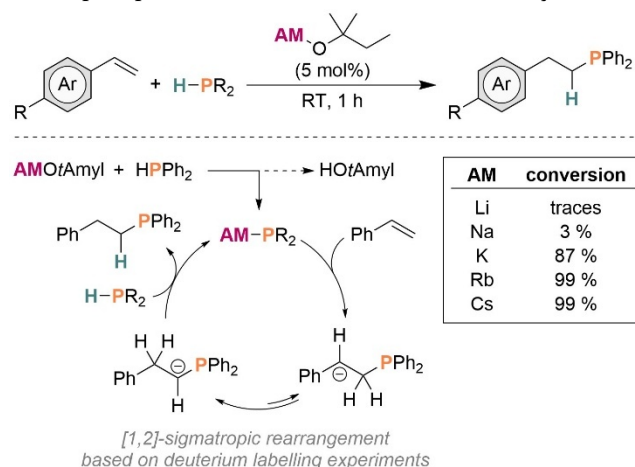


Figure 17. Hydrophosphination of alkenes catalyzed by alkali-metal *tert*-amylates.

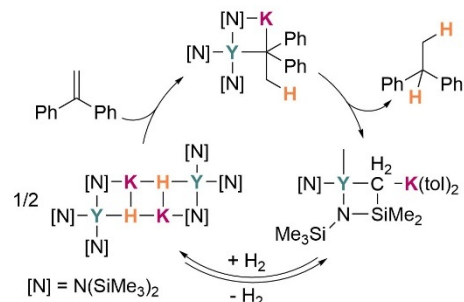
CATALYTIC HYDROGENATION

The use of precious transition metal catalysts in homogeneous catalysis has long been essential in many fundamental organic reaction classes including hydrogenation,⁹⁰ formally the direct addition of H₂ across an unsaturated bond (direct hydrogenation) or accomplishing the same outcome via a surrogate of H₂ (indirect hydrogenation) for example, as in transfer hydrogenation.⁹¹ Though Group 1 chemistry is renowned for its general synthetic utility, this does not encompass catalytic hydrogenation, which may seem odd initially since alkali-metal hydrides have the perfect pair of electronic charges, formally AM⁺H⁻, to carry out such nucleophilic addition reactions. However, the problem is that such microscopic charges at the macroscopic level produce ionic salt structures with large lattice energies that are insoluble in the organic solvents required for many catalytic hydrogenation reactions. As aforementioned, the whirlwind currently blowing through global science to achieve better sustainability in chemistry practices making more use of earth abundant elements and causing less damage to the environment and its inhabitants, is incentivizing chemists to develop new catalytic methods for important reactions already well covered by precious transition metals, which are under rising threat of supply and generally have toxicity concerns. Synthesizing alkali-metal organometallic compounds having non-lattice type structures and containing a hydride component can induce good solubility in organic solvents, thus opening up the potential of delivering alkali-metal-based hydrogenation catalysts. This research is still immature, while the current leadership in catalytic hydrogenations is predominantly found in Group 2 metal complexes.⁹²⁻⁹⁴ Nevertheless, examples of active alkali-metal-based catalysts are being drip-fed into the literature, a representative selection of which are outlined here.

Valency and lattice energy considerations mean it appears unlikely that a binary AM⁺H⁻ pairing can be designed for example with a Lewis base donor supporting ligand that would instill it with the required solubility properties to make it a potential hydrogenation catalyst. But as mentioned elsewhere in this article, synergistic bimetallic compounds can offer potential solutions. For example, a simple co-complexation reaction between benzyl potassium and yttrium tris-HMDS in the presence of THF affords the potassium yttrium ate complex [(THF)K(CH₂Ph)Y(HMDS)₃], which operates synergistically to activate H₂ to generate the amido-hydrido complex [K(H)Y(HMDS)₃]₂, in effect a hydrocarbon soluble molecular variant of K⁺H⁻. Strong heating of [K(H)Y(HMDS)₃]₂ provokes an internal deprotonation reaction at one HMDS Me group to form cyclopotassiated [(tol)₂K{H₂C(Me)₂SiSiMe₃}Y(HMDS)₂] and H₂ in a reversible process that generates H⁻ and H⁺, which in turn can effect catalytic hydrogenation of alkenes to alkanes (Figure 18a).⁹⁵ Note the optimization reaction using 1-

octene as the model alkene and replacing benzylpotassium by *ortho*-dimethylaminobenzyl lithium, in combination with yttrium tris-HMDS, worked too but gave lower conversions even under higher catalytic loadings. With [K(H)Y(HMDS)₃]₂, the reaction scope was extended to assorted alkenes, alkynes and imines, with good conversions but under relatively harsh conditions (6 bar H₂, 80 - 100 °C, 4 - 96 h) dependent on the activated or non-activated nature of the unsaturated substrate. Similar synergistic effects were uncovered in a related study⁹⁶ substituting the transition metal yttrium HMDS complex by the Group 2 base metal analogues Mg(HMDS)₂·Et₂O and Ca(HMDS)₂·(THF)₂ (Figure 18b). Again, catalytic hydrogenation of various styrenes and alkenes was achieved though the conditions were mostly severe (6 bar H₂, 80 - 100 °C, 24 - 72 h) with 10 mol% of the catalyst needed for the best NMR yields in C₆D₆ solution. However, this time the hydride source for the catalyst was the salt K⁺H⁻, the poor solubility of which was singled out by the authors as one main reason for the long reaction times needed to effect catalysis. They reasoned that over time the Group 2 metal amides would disrupt the crystal lattice of K⁺H⁻, causing its partial degradation, which, in turn, produces some soluble heterobimetallic hydride ate complexes for the catalytic process.

a) Proposed mechanism for the reversible H₂ activation and hydrogenation



b) Catalytic olefin hydrogenation mediated by KH: selected substrates

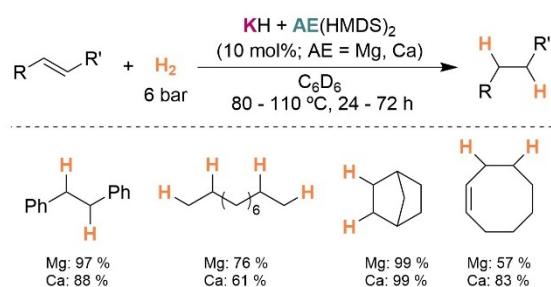
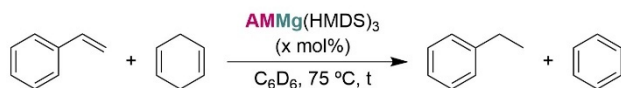


Figure 18. KH-mediated hydrogenation of alkenes.

While such lattice salts can act as pre-catalysts, it is clear that well-defined organometallic species can be more effective catalytically and sometimes are likely to be the *bona fide* catalysts in organic transformations. While a recent study established catalytic transfer hydrogenation for alkene to alkane reactions with the aforementioned Ca(HMDS)₂ and its heavier congeners M(HMDS)₂ (M = Sr, Ba) using 1,4-cyclohexadiene (1,4-CHD) as a convenient,

easily handled liquid transfer hydrogenation H_2 source, it is conspicuous that the lighter congener $Mg(HMDS)_2$ failed in such transformations.⁹⁷ Subsequently, the challenge of empowering the magnesium amide with catalytic competence was met by synthesising bimetallic ate modifications of it with the full set of Group 1 metals.⁸⁹ Screening $Mg(HMDS)_2$ and all of the Group 1 magnesiate with styrene under the same conditions (1,4-CHD, 10 mol% catalyst, 75 °C, in C_6D_6 solution) confirmed $Mg(HMDS)_2$ did not react and revealed a trend of increasing activity with increasing size of the alkali metal (Figure 19a) with $LiMg(HMDS)_3$ completely inert and $NaMg(HMDS)_3$ essentially inert, whereas $KMg(HMDS)_3$, $RbMg(HMDS)_3$ and $CsMg(HMDS)_3$ all reach full conversion to the ethylbenzene product in sequential decreasing reaction times of 3.5 h, 0.75 h and 0.5 h respectively. $CsMg(HMDS)_3$ also performed well on lowering its loading to 1 mol% with only a small degree of decomposition on isolation of the product. On changing the alkene to the more sterically hindered 1,1-diphenylethylene, which prevents styrene polymerization, the three heaviest alkali-metal amides also performed well reaching full conversion in 2.5 h or less. It is postulated that the alkali-metal trisamidomagnesiate are pre-catalysts and that the actual catalysts could be monohydrido-bisamidomagnesiate, which have been established to have well-defined structures such as the crystalline benzene adduct $[(C_6H_6)KMg(HMDS)_2H]_2$ (Figure 19b).

a) Alkali-metal magnesiate amide-catalyzed styrene hydrogenation



catalyst	x [mol%]	t [h]	yield [%]
$Mg(HMDS)_2$	10	16	0
$LiMg(HMDS)_3$	10	16	0
$NaMg(HMDS)_3$	10	16	4
$KMg(HMDS)_3$	10	3.5	> 98
$RbMg(HMDS)_3$	10	0.75	93
$CsMg(HMDS)_3$	10	0.5	89
$CsMg(HMDS)_3$	5	0.5	92
$CsMg(HMDS)_3$	1	1.5	90

b) Molecular structure of $[(C_6H_6)KMg(HMDS)_2H]_2$

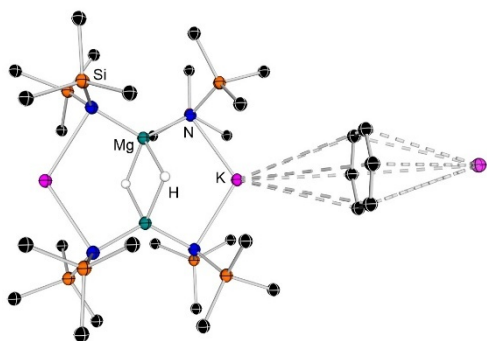
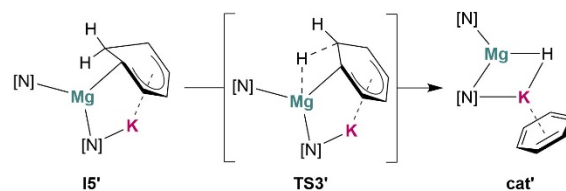


Figure 19. Application of alkali-metal magnesiate in hydrogenation of styrene and proposed catalytic species.

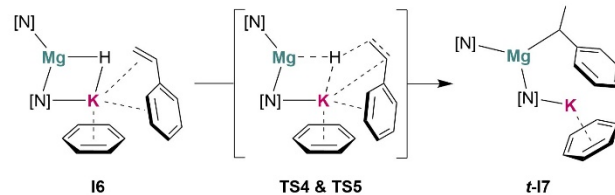
A follow-up DFT study strengthens this view,⁹⁸ since the calculations demonstrate the multistep cooperativities

between the metal centres within the bimetallic complex, as neither the monometallic potassium amide $K(HMDS)$ nor the magnesium amide $Mg(HMDS)_2$ can separately execute this styrene to ethylbenzene transformation under the conditions employed experimentally. Several distinct mechanistic pathways were computed, leading to the identification of the most plausible sequence in which the metal centres act synchronistically (to see the non-synergistic single metal pathways we refer the reader to the primary source).⁹⁸ Four key steps in this plausible mechanism are shown in Figure 20. In (A), the K centre stabilises and anchors the Meisenheimer complex in $I5'$ setting up hydride transfer from 1,4-CHD to the Mg centre to form the monohydrido-bisamidomagnesiate catalyst. The insertion of the Mg-H bond into the styrenic C=C takes place in (B), with the structure of the intermediate $t-I7$ stabilised by a short Mg-C bond (2.22Å) and a η^6 -interaction between K^+ and the phenyl ring. In (C), the Mg switches from the α -bond in $t-I7$ to the *para*-C, again K^+ acts as anchor, (D) delivering $HMDS(H)$ to the styryl moiety via TS8 protonating the α -C atom to generate ethylbenzene and the starting potassium trisamidomagnesiate $KMg(HMDS)_3$.

(A) Formation of bimetallic hydride



(B) Insertion of Mg-H bond into the C=C bond



(C) Isomerization of new formed alkyl potassium magnesiate



(D) Product release and catalyst regeneration

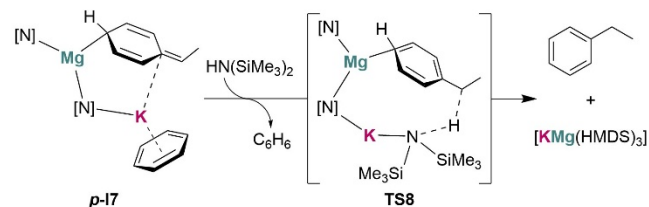
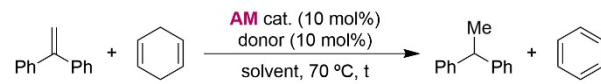


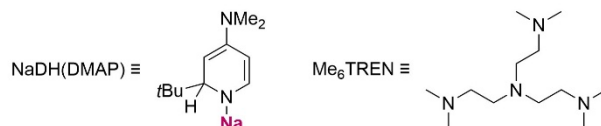
Figure 20. Catalytic hydrogenation of styrene: synergistic effect of the K-Mg bimetallic system.

Recent research has also revealed that the heavier alkali metals do not need the presence of a second metal within a bimetallic system to be effective in homogeneous catalytic hydrogenation reactions. Much less studied than their HMDS counterparts, alkali-metal dihydropyridinates are showing promise across different catalytic regimes including dehydrocoupling of aminoboranes,⁹⁹ hydroboration of carbonyl substrates,⁹⁹ dehydrocyclization of diamine boranes,¹⁰⁰ and transfer hydrogenation of imines to amines (see below). In alkene to alkane catalytic transfer hydrogenation again using 1,4-CHD as the H₂ source, the key to effective catalytic performance seems to be obtaining a monomeric form of the dihydropyridylsodium compound, Na-1,2-*t*Bu-DH(DMAP).¹⁰¹ This is attainable by either using the polar Lewis base THF as the reaction solvent or by using the well-defined monomeric variant [Me₆TREN-Na-1,2-*t*Bu-DH(DMAP)] [DMAP = 4-dimethylaminopyridine; Me₆TREN = tris(N,N-dimethyl-2-aminoethyl)amine], which has been crystallographically characterised. Selected data from the reduction reactions of 1,1-diphenylethylene to 1,1-diphenylethane in Figure 21a show that in non-polar C₆H₆ solution Na-1,2-*t*Bu-DH(DMAP) takes a full day to reach full conversion, but repeating the reaction in THF-*d*₈ solution or adding one equivalent of Me₆TREN to a C₆D₆ solution reduces the time to 0.5 h. These two faster reaction successes have been attributed to the monomeric forms of Na-1,2-*t*Bu-DH(DMAP) in their respective solutions, namely one multi-THF-solvated and the other Me₆TREN-solvated as determined from DOSY experiments. Unlike alkali-metal HMDS compounds and other utility amides, which generally act as Brønsted bases in reactions, alkali-metal dihydropyridinates can either act as Brønsted bases or surrogate hydrides. In this specific case, Na-1,2-*t*Bu-DH(DMAP) can in theory enter the proposed catalytic cycle in either of these ways (Figure 21b). Both possibilities are feasible experimentally from NMR studies since stoichiometric control reactions of Na-1,2-*t*Bu-DH(DMAP) with 1,4-CHD produced the rearomatised 2-*t*Bu-DMAP and H₂, corresponding to a base pathway, while with the substrate Ph₂C=CH₂ essentially full conversion to Ph₂C(Na)-CH₃ and 2-*t*Bu-DMAP was observed corresponding to a hydride pathway. When entries 5 and 6 in Figure 21a show that saline Na⁺H⁻ is completely inert in these reactions, the headline in the paper claiming Na-1,2-*t*Bu-DH(DMAP) to be a soluble molecular carrier of sodium hydride seems apt.

a) Alkali-metal dihydropyridinate-catalyzed diphenylethylene hydrogenation



catalyst	donor	solvent	t [h]	yield [%]
NaDH(DMAP)	-	C ₆ D ₆	24	99
NaDH(DMAP)	Me ₆ TREN	C ₆ D ₆	0.5	93
NaDH(DMAP)	-	THF- <i>d</i> ₈	0.5	98
NaDH(DMAP)	Me ₆ TREN	THF- <i>d</i> ₈	1	89
NaH	Me ₆ TREN	C ₆ D ₆	24	0
NaH	Me ₆ TREN	THF- <i>d</i> ₈	24	0
LiDH(DMAP)	-	C ₆ D ₆	24	24
LiDH(DMAP)	Me ₆ TREN	C ₆ D ₆	24	31
LiDH(DMAP)	-	THF- <i>d</i> ₈	6	68
LiDH(DMAP)	Me ₆ TREN	THF- <i>d</i> ₈	3	44



b) Proposed mechanism for catalytic transfer hydrogenation

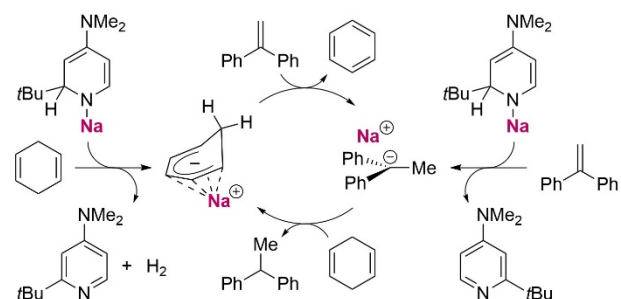


Figure 21. Catalytic applications of alkali-metal dihydropyridinates in transfer hydrogenation.

Staying with 1,4-CHD and dihydropyridinates, but derivatives of pyridine rather than of DMAP, a full set of alkali-metal dihydropyridinates have been screened in catalytic hydrogenation of imines to amines from which a clear trend in activity is discernible.¹⁰² With all three imines probed the activity gradually increased from the lighter to the heavier alkali metals and quite markedly so over the Group with maximum yields for lithium (21 - 93 %) requiring 24 h; whereas for caesium essentially quantitative yields were reached within minutes (range 15 - 180) (Figure 22). The most impressive results for the caesium dihydropyridinate at 5 mol% loadings were those ran at 25 °C where near quantitative yields were obtained in just 60 and 15 min for Ph(H)C=NPh and Ph₂C=NH respectively in THF-*d*₈ solution. The lighter congeners could not match these performances as they required heating to 70 °C. The essential take home messages from the DFT computation part of the study are that in the postulated initiation pathways the dihydropyridinates can act either as bases or as surrogate hydrides akin to those in the aforementioned alkene to alkane transfer hydrogenation study, that Cs follows a pathway with a significantly lower turnover determining step than that of the Li congener, mainly due to the greater π -philicity of Cs over Li in the transition state (see inset in Figure 22).

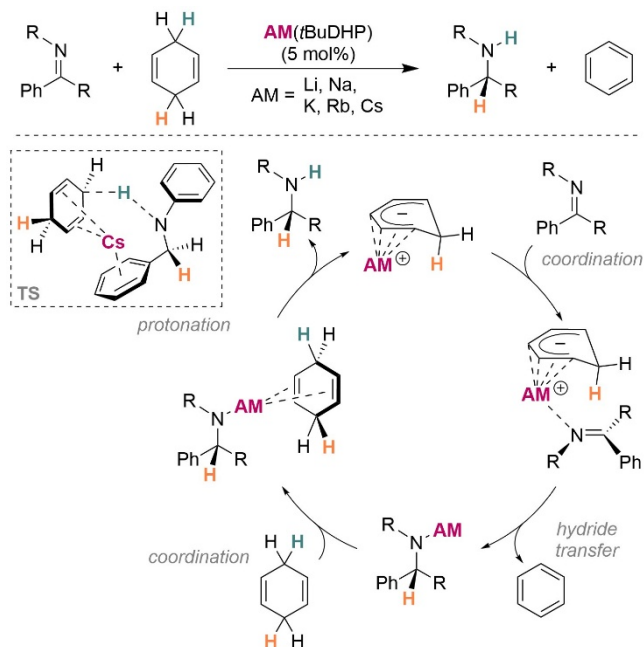


Figure 22. Proposed catalytic cycle for transfer hydrogenation of imines using AM(*t*BuDHP).

CONCLUSIONS AND OUTLOOK

This perspective article describes a selection of recent advances in alkali-metal-mediated catalysis which highlights the exciting potential that the heavier alkali-metal amides offer to catalyze processes that typically require the use of precious transition-metals. It aims to inform the wider community of this potential in the hope that more chemists will be attracted to it. Promising progress has certainly been made in hydrogen isotope exchange, alkene isomerization, C–C bond formation, hydrophosphination, and hydrogenation, and on the evidence presented here the current trend looks like the heavier alkali metals sodium, potassium, rubidium, and caesium are better prospects for mediating catalytic reactions than their lighter lithium congener. Sodium and potassium have already made valuable contributions to stoichiometric synthesis though much less so in the catalytic regime, whereas Rb and Cs organometallic chemistries are essentially unknown to practitioners of synthesis and catalysis. Perhaps the most exciting aspect of this Perspective is that the heavier alkali metals could in time be useful alternatives to both lithium, in stoichiometric applications, and transition metals, in homogeneous catalysis, that could profoundly benefit the material aspects of sustainability, help reduce environmental impact and lower costs. Some transition metal chemists may be rather sceptical about this possibility given that significant improvements would have to be made in terms of scope, substrate diversity, turnover frequency, functional group tolerance, etc. before alkali metals could become competitively viable to transition metals, but it could be argued that the latter have been studied extensively for 75 years or more, whereas studies on the

former are only at a formative stage. There is still much more to be done even in understanding the fundamental coordination chemistry of the heavier alkali metals, especially for caesium and rubidium, and such knowledge could be the key to making improvements in existing catalytic selectivities and to discovering brand new catalytic applications. In that regard it is interesting to note that the aforementioned Takasago process, in the hydroamination of myrcene with morpholine,¹⁰³ has been upgraded from using an uneconomical Li or Na catalyst loading of 4–40% to a Pd-catalyzed process with a low loading of 0.02% in the converse of our transition metal to alkali metal approach, emphasising that catalyst loading and recyclability are key factors in such reactions. Significant recyclability has still to be achieved with the heavyweight alkali metals as is the development of catalytic processes beyond those that require metal hydride intermediates. The challenges are there, but will they be met?

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