Alkali Metal Metal(*ates*) Containing Divalent Earth Abundant Transition Metals

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Abstract: Recent advances in cooperative chemistry have shown the enormous potential of main group hetero-bimetallic complexes for the functionalisation of aromatic molecules. Going beyond main group metal chemistry, here we provide an overview on the synthesis, structure and reactivity of bimetallic complexes which combine an alkali-metal (AM= Li, Na) with a divalent earth abundant transition metal (M= Mn, Fe, Co, Ni), containing the utility silyl amide HMDS [HMDS = N(SiMe$_3$)$_2$]. Advancing the understanding on how cooperative effects operate in these bimetallic (*ate*) systems, selected examples of their applications in deprotonative metalation are also discussed with special emphasis on the constitution of the metalated intermediates.

Keywords: Alkali metals · Amides · *Ate* complexes · Cooperative effects · Transition metals

Alessandra Logallo was born in Matera (Italy) and moved to Bari to obtain her Master degree in Medicinal Chemistry at the University of Bari in 2019. During this time, she also worked on asymmetric autocatalytic reactions at the University of Oslo under the supervision of Prof. M. Amedjkouh to then move to Strathclyde University in Glasgow where she investigated the reactivity of zincate complexes in the group of Prof. Eva Hevia. She is currently studying synthesis and reactivity of cobalt bimetallic complexes as PhD student in the same group at the University of Bern.

1. Cooperative Bimetallics in Main Group Chemistry

Group 1 metal amides such as LiHMDS (HMDS = N{SiMe$_3$}$_2$) and LiTMP (TMP = 2,2,6,6- tetramethylpiperidide) are amongst the most widely used reagents in synthesis, finding numerous applications in deprotonative metalation for arene functionalisation.[1] However, despite their popularity, their use to metalate arenes containing sensitive functional groups such as halogens, CN or NO$_2$ can be compromised by the limited selectivity of these reagents and the fragility of the relevant metalated intermediates which can undergo unwanted side reactions, even under strict cryogenic conditions.[2,3] An alternative approach is the use of bimetallic reagents which combine a group 1 metal with a more electronegative main group metal such as Mg, Zn or Al.[4,5] Typically the single metal amide complexes of these metals are not reactive enough to promote the deprotonation of arenes.

However, seminal work by Knochel,[6] Mulvey,[4,7–9] Uchiyama[10] and Mongin[11] has shown that this lack of reactivity can be overcome by forming heterobimetallic 'ate' complexes.

By switching on 'metal/metal' cooperation, these bimetallic systems often display unique synergic reactivities, offering enhanced selectivities and greater functional group tolerances than their relevant single-metal components.[4]

Selected examples which highlight the special metalating power of these bimetallic combinations include the synergic meta/meta' dimagnesiation of *N,N*-dimethylaniline using sodium magnesiate [Na$_2$Mg(TMP)$_3$(*n*Bu)] (**1**) as a base.

Here the synergic effect between the metals overcomes the *ortho*-directing effect of the NMe$_2$ substituent. Thus, when the same substrate is reacted with Group 1 organometallics such as *n*BuNa.TMEDA (TMEDA= *N,N,N',N'*-tetramethylethylenediamine) *ortho*-metalation is observed whereas with Mg(TMP)$_2$ no metalation is observed (Fig. 1a).[12,13]
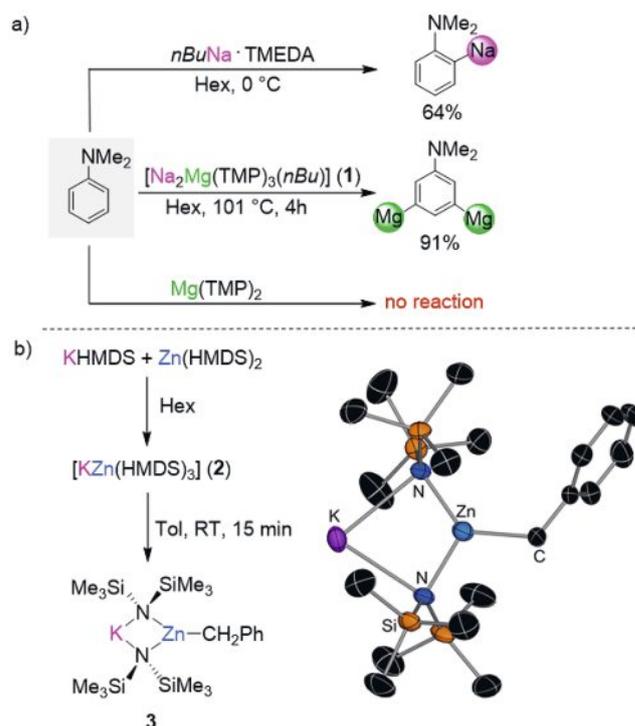
Fig. 1. a) Example of selective metalation of *N,N*-dimethylaniline; b) metalation of toluene with [KZn(HMDS)$_3$]. On the right molecular structure of **3**. Hydrogen atoms are omitted for clarity. Ellipsoids are set at 50% probability.

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Similarly, while KHMDS can be commercially purchased as toluene solution and $Zn(HMDS)_2$ is inert towards toluene metalation, when combined together to form $[KZn(HMDS)_3]$ (**2**) lateral zincation of this arene is observed to give $[KZn(HMDS)_2(CH_2Ph)]$ (**3**, Fig. 1b).[14] Interestingly, potassium zincate **3** has recently been reported as a catalyst for benzylic C–H bond addition of diarylmethanes to styrenes and to conjugated dienes.[15]

Building on these intriguing findings our group has recently become interested in extending these special cooperative effects beyond main group metal chemistry, focussing on divalent earth abundant metals M (M= Mn, Fe, Co and Ni). Most of our work has focussed on systems which contain the utility amide HMDS $[HMDS= N(SiMe_3)_2]$.[1] This bulky amide group has been successfully used before to prepare monometallic amide complexes of these divalent transition metals.[16,17] Furthermore previous studies have already shown the excellent potential of main group metal *ates* containing HMDS substituents in deprotonative metalation[8,18,19] and catalysis.[20,21] Here we provide an overview on the synthesis, structure and reactivity of these heterobimetallic compounds.

2. Synthesis and Characterisation of Alkali Metal Metal(*ates*)

Within main group chemistry, one of the most versatile methods to access alkali-metal *ates* is the use of co-complexation approaches where the monometallic components are combined, typically in the presence of a Lewis donor (L).[7] This approach has also been successfully applied to the synthesis of a variety of alkali-metal-mediated HMDS complexes $[AMM(HMDS)_3]$ (AM= Li, Na; M= Mn, Fe, Co, Ni).[17,22,23,30] Depending on the type of Lewis donor present in the co-complexation reaction, different structural motifs have been unveiled (Fig. 2a–d). Thus monodentate ligands (such as THF or Et_2O) favour the formation of contacted ion metal pairs where the alkali-metal and the transition metal are connected by two bridging amide groups whereas the Lewis donor stabilises the alkali-metal as shown in Fig. 2a for $[(THF)NaCo(HMDS)_3]$ (**4**).[23] Using higher hapticity donors such as PMDETA (PMDETA= *N,N,N',N'',N''*-pentamethyldiethylenetriamine) or 12-crown-4, or a large excess of the Lewis base furnish solvent-separated ion pair motifs where now the transition metal binds to three terminal HMDS groups forming a well-defined *ate* anion with the alkali-metal being fully solvated by the Lewis donor. Examples of this structural motif are complexes like $[\{Na(12\text{-crown-}4)_2\}^+\{M(HMDS)_3\}^-]$ (M = Mn, **5a**; Fe, **5b**; Co, **5c**)[24] or the recently characterised $[Na(PMDETA)_2][Ni(HMDS)_3]$ (**6**) (Fig. 2b).[21] Co-complexation can also be accomplished in the absence of a Lewis donor in a non-coordinating solvent such as hexane as shown in Fig. 2c and 2d for $[LiFe(HMDS)_3]$ (**7**) and $[\{NaFe(HMDS)_3\}_\infty]$ (**8**) respectively.[23,30] In **8** sodium achieves further coordinative stabilisation by forming intermolecular interactions with the terminal HMDS group of an adjacent molecular unit (*via* Na···Me electrostatic contacts), giving rise to a 1D polymeric chain arrangement. Contrastingly, showing an interesting alkali-metal effect, **7** displays a discrete monomeric structure where Li attains a distorted tetrahedral geometry, interacting with a Me group from each of the bridging HMDS ligands.[23]
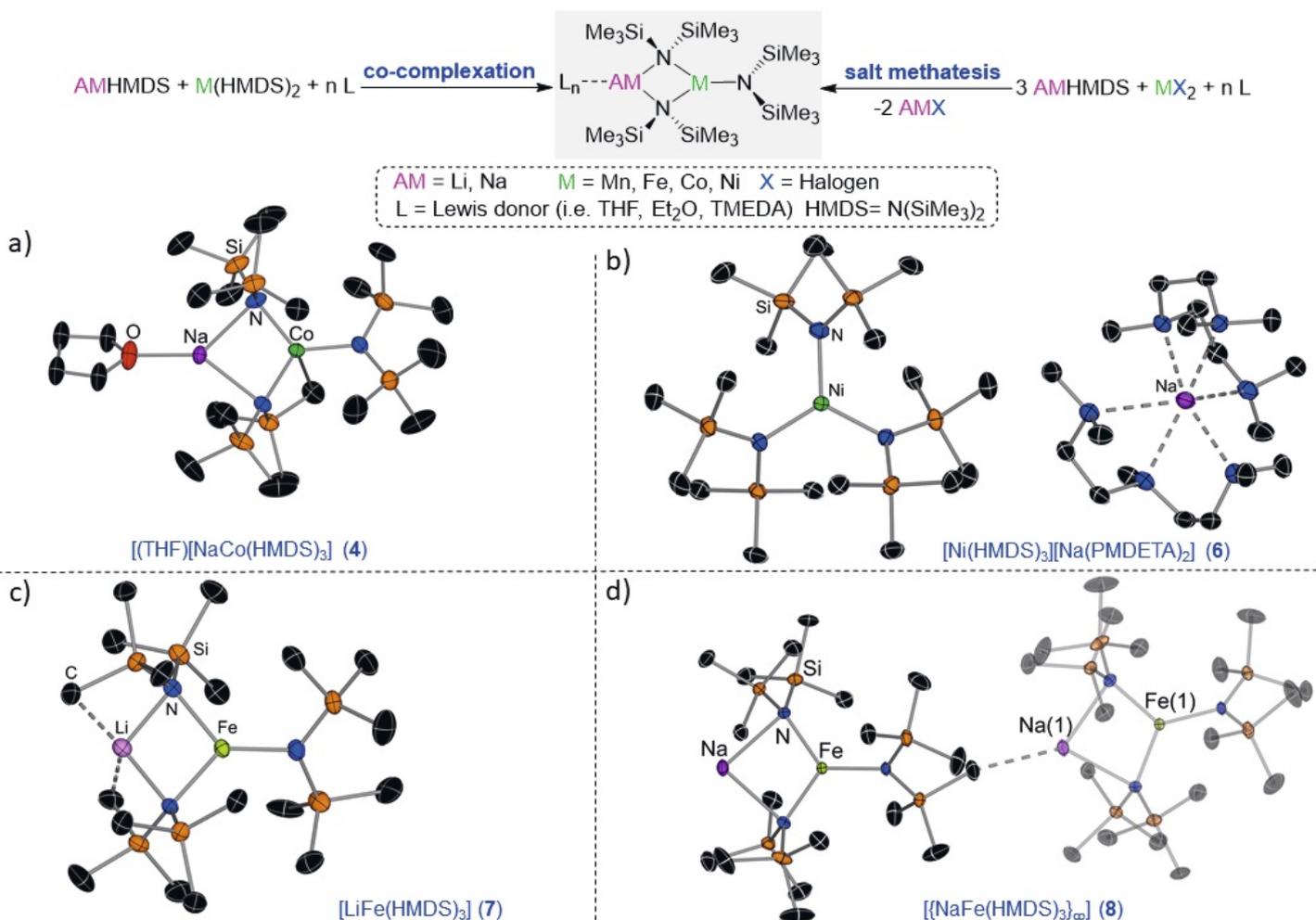
Fig. 2. General synthesis of alkali metal metal(*ates*). Selected examples of: a) contacted ion pair $(THF)[NaCo(HMDS)_3]$ (**4**); b) solvent-separated ion pair $[Ni(HMDS)_3][Na(PMDETA)_2]$ (**6**); c) and d) unsolvated alkali metal metal(*ates*) $[LiFe(HMDS)_3]$ (**7**) and $[\{NaFe(HMDS)_3\}_\infty]$ (**8**).

Careful evaluation of the main structural parameters of these heterobimetallic complexes has revealed two distinct types of bonding present in these structures. Thus, the shorter and more covalent M–N bonds provide the foundation for the $\{M(HMDS)_3\}^-$ units to which the alkali-metal cations are affixed by a combination of weaker AM–N and AM–Me ancillary bonds. This is a trend that has also previously been found for main group heterobimetallic complexes.[4]

Along with co-complexation approaches, another method to access these heterobimetallic complexes is salt-metathesis reactions. In this case an excess of the AM(HMDS) precursor is reacted with a halide salt of the transition metal (Fig. 2). This approach was successfully employed to prepare $[Ni(HMDS)_3]$ $[Na(PMDETA)_2]$ (6), circumventing the need of preparing $Ni(HMDS)_2$ which is thermally unstable.[17,25] In most cases alkali-metal metal (ates) $[AMM(HMDS)_3]$ have been further characterised by other techniques which include NMR and EPR spectroscopies as well as SQUID magnetometry. Reactivity studies have also revealed the high sensitivity of these compounds to oxygen and water as shown for $[\{NaMn(HMDS)_2(CH_2SiMe_3)\}_\infty]$ (9) which in the presence of oxygen affords inverse crown ether complex $[Na_2Mn_2(HMDS)_4(O)]$ (10, Fig. 3).[26]

Fig. 3. Synthesis of complex $[\{NaMn(HMDS)_2(CH_2SiMe_3\}_\infty]$ (9) and reaction with dry air to give $[Na_2Mn_2(HMDS)_4(O)]$ (10).

The molecular structure of 10 displays a centrosymmetric motif with alternating Na and Mn(II) atoms, linked through N bridges in a $(NaNMnN)_2$ octagonal ring, which encapsulates an oxo anion. A similar structure has also been reported for $[Na_2Co_2(HMDS)_4(O)]$ (11), obtained as a side product of the synthesis of $(THF)NaCo(HMDS)_3$ (4). While its synthesis appears to be unreproducible, formation of isostructural 11 can be attributed to serendipitous presence of air and/or moisture when preparing 4.[27]

3. Applications in Deprotonative Metalation

Building on these initial studies our group has investigated the reactivity of alkali-metal *ates* $[AMM(HMDS)_3]$ in deprotonative metalation reactions. Initial studies assessing the reactivity of $[\{NaFe(HMDS)_3\}_\infty]$ (8) towards amines have shown its ability to promote transamination reactions (Fig. 4).[28,29] An interesting steric effect has been noted. Thus while 8 can react with three equivalents of 2,2'-dipyridylamine (DPAH) to form $[\{(THF)$

$NaFe(DPA)_3\}_\infty]$ (12), when treated with three equivalents of $HN(SiMe_3)Ar^*$ ($Ar^* = 2,6\text{-}i\text{Pr-C}_6H_4$) only one out of the three HMDS groups undergo transmetalation furnishing $[\{NaFe(HMDS)_2[NAr^*(SiMe_3)]_2\}_\infty]$ (13). Related to these findings, $[Na(PMDETA)_2][Ni(HMDS)_3]$ (4) can also undergo 3-fold transmetalation with DPAH, although in this case the putative nickelate from this reaction undergoes a redistribution process affording its single-metal components $[(DPAH)Ni(DPA)_2]$ (14), which can be isolated as a crystalline solid and Na(DPA) which is detected by ^{1}H NMR spectroscopy (Fig. 4).[21]

Fig. 4. Representation of transamination products $[\{(THF)NaFe(DPA)_3\}_\infty]$ (12);$[\{NaFe(HMDS)_2[NAr^*(SiMe_3)]_2\}_\infty]$ (13) and $[(DPAH)Ni(DPA)_2]$ (14).

Alkali-metal ferrates $[AMFe(HMDS)_3]$ (AM= Li, Na) have proved to be excellent metallating reagents for the ferration of fluoroarenes.[29–34]

Deprotonation of these substrates using conventional organolithium reagents can be difficult due to the exceptional fragility of the relevant metalated intermediates which can undergo unwanted side reactions even at extremely low temperatures.[2] However, using $[(dioxane)_{0.5}\cdot NaFe(HMDS)_3]$ (15) regioselective ferration of a wide range of fluoroarenes can be achieved while operating at room temperature as shown in Fig. 5a for 1,3,5-trifluorobenzene furnishing $[(dioxane)\cdot NaFe(HMDS)_2(1,3,5\text{-}F_2C_6H_3)]$ (16).[31] X-ray crystallographic studies demonstrated that these reaction is a genuine ferration, with the iron centre occupying the position previously filled by a hydrogen centre. Formation of 16 nicely illustrates the synergic reactivity of these bimetallic combinations since neither of the single metal components of the bimetallic base 15 is able to selectively metalate these substrates. $Fe(HMDS)_2$ is completely inert towards 1,3,5-trifluorobenzene whereas NaHMDS deprotonates this molecule but the relevant intermediate is not stable at room temperature and undergoes decomposition affording a mixture of products. The reactivity of 15 towards fluoroarenes is also very unusual from the perspective of the expected reactivity of transition metal complexes with this type of substrates, which typically tend to undergo either C–H or C–F bond activation reactions with the subsequent change on the oxidation state of the transition metal.[35] Interestingly, these ferrations showed an excellent stoichiometric control. Thus when reacting 1,2,4,5-tetrafluorobenzene with two molar equivalents of 15 at room temperature, selective two-fold ferration at its C3,C6 positions is observed affording $[[\{dioxane\cdot NaFe(HMDS)_2\}_2(1,2,4,5\text{-}C_6F_4)]_\infty]$ (17).

While compounds 16 and 17 show a remarkable thermal stability, when the reaction conditions are pushed, reacting a 3 molar excess of the base 15 with 1,3,5-trifluorobenzene at 80 °C, the unexpected C–F bond activation complex $[[1,3\text{-}bis(FeHMDS)\text{-}$

Fig. 5. a) Examples of mono-ferration, di-ferrration and two-fold C–H/three-fold C–F activation of fluoroarenes using sodium ferrate [(diox-ane)$_{0.5}$·NaFe(HMDS)$_3$] (**15**) to give respectively [(dioxane)·NaFe(HMDS)$_2$(1,3,5-F$_2$C$_6$H$_3$)] (**16**), [[{dioxane·NaFe(HMDS)$_2$}$_2$(1,2,4,5-C$_6$F$_4$)]$_\infty$] (**17**) and [[1,3-bis(FeHMDS)-2,4,6-tris(HMDS)-C$_6$H]] (**18**). c) From left to right molecular structures of complexes **16**, **17** and **18**. Hydrogen atoms are omitted for clarity. Ellipsoids are set at 50% probability.

2,4,6-tris(HMDS)-C$_6$H]] (**18**) is obtained along with the precipitation of NaF (Fig. 5a). Exhibiting a homometallic constitution, **18** is the result of an unprecedented 2-fold C–H/3-fold C–F activation. Thus each F atom present in the starting material has now been replaced by an HMDS grop, whereas two new Fe–C bonds have been formed at the C2 and C6 positions of the ring.[31]

Mechanistic studies combining NMR spectroscopic analysis, isolation of key reaction intermediates and DFT calculations have shed some light on how these ferration processes take place (Fig. 5b). [34] Studies on the reactivity of sodium ferrate [{NaFe(HMDS)$_3$}$_\infty$] (**8**) with pentafluorobenzene revealed that initially coordination of the substrate to the alkali-metal *via* Na–F interactions take place, activating it towards the metalation step as well as causing a shift on one of the amide groups on the ferrate which binds terminally to Na in **I1** (Fig. 5b). This amide group is now in prime position to perform the metalation of C$_6$F$_5$H *via* Na–H exchange furnishing **I2**, which, in turn, will undergo fast intramolecular transmetalation to the Fe(II) centre to give **I3**. Isomerisation of **I3**, with its aryl group adopting a terminal position gives [{NaFe(HMDS)$_2$(C$_6$F$_5$)}$_\infty$] (**19**) which can be isolated and structurally characterised. Reflecting the importance of the coordination ability of Na and the close contact between Na and Fe in **8**, when the reaction was repeated with solvent-separated ion pair [{Na(15-crown-5)$_2$}$^+${Fe(HMDS)$_3$}$^-$] (**20**) no metalation is observed.[31] Collectively these findings showed that these ferration reactions are genuine examples of bimetallic cooperation, where each metal plays a key role, with sodium performing the metalation of the substrate whereas Fe traps and stabilises the fragile C$_6$F$_5$ fragment. Extending these studies to the more basic amide TMP have enabled the ferration of less activating substrates such as toluene, benzene and pyridine.[36]

Encouraged by the unique synergic reactivities of these systems our group is currently exploring the ability of these and other heterobimetallic combinations in deprotonative metalation reactions of a wide range of aromatic substrates.

4. Outlook

Heterobimetallic complexes combining an alkali-metal with an earth abundant transition metal can offer synergic reactivities that cannot be replicated by its single metal components on their own. Considering the redox potential of these metals, these systems offer a wide range of opportunities for the development of new chemical transformations or for upgrading some of these stoichiometric successes to catalytic regimes. It is anticipated that some of the results presented in this contribution can inspire more innovations in these evolving areas of research.

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