Assessing Alkali-Metal Effects in the Structures and Reactivity of Mixed-Ligand Alkyl/Alkoxide Alkali-Metal Magnesiates

Neil R. Judge,[a] Leonie J. Bole,[a] and Eva Hevia*[a]

Abstract: Advancing the understanding of using alkali-metal alkoxides as additives to organomagnesium reagents in Mg—Br exchange reactions, a homologous series of mixed-ligand alkyl/alkoxide alkali-metal magnesiates [MMg(CH$_2$SiMe$_3$)$_2$(dmem)]$_2$ [dmem = 2-{[2-(dimethylamino)ethyl]methylamino} ethoxide; M = Li, **1**; Na, **2**; (THF)K, **3**] has been prepared. Structural and spectroscopic studies have established the constitutions of these heteroleptic/heterometallic species, which are retained in arene solution. Evaluation of their reactivity towards 2-bromoanisole has uncovered a marked alkali-metal effect with potassium magnesiate **3** being the most efficient of the three ate reagents. Studies probing the constitution of the exchange product from this reaction suggest that the putative [KMgAr$_2$(dmem)]$_2$ (Ar = o-OMe—C$_6$H$_4$) intermediate undergoes redistribution into its single metal components [KAr]$_n$ and [MgAr(dmem)]$_2$ (**5**). This process can be circumvented by using a different potassium alkoxide containing an aliphatic chain such as KOR′ (R′ = 2-ethylhexyl) which undergoes co-complexation with Mg(CH$_2$SiMe$_3$) to give [KMg(CH$_2$SiMe$_3$)$_2$(OR′)]$_2$ (**7**). This ate, in turn, reacts quantitatively with 2-bromoanisole furnishing [KMgAr$_2$(OR′)]$_2$ (**9**) which is stable in solution as a bimetallic compound. Collectively this work highlights the complexity of these alkali-metal mediated Mg—Br exchange reactions, where each reaction component can have a profound effect not only on the success of the reaction; but also the stability of the final metalated intermediates prior to their electrophilic interception.

Introduction

The unique activating effects of alkali-metal alkoxides when added to other s-block organometallics is a well-established phenomenon in polar organometallic chemistry.[1–4] Typified by the LIC-KOR (Lochmann-Schlosser) superbase, combining potassium *tert*-butoxide with *n*-butyllithium greatly enhances the metalation capabilities of this mixture when compared to those of their monometallic counterparts.[5–8] This synergistic behavior has been attributed to the formation of mixed alkyl/alkoxy bimetallic [LiK(OR′)R]$_n$ aggregates though the true constitution of these species has remained a matter of debate for many years.[9,10] Using the more hydrocarbon soluble bimetallic combination, namely NpLi/KO*t*Bu (Np = Neopentyl), Klett has impressively structurally characterised the [Li$_4$K$_4$Np$_3$(O*t*Bu)$_5$] aggregate where the alkyl groups bind to both potassium and lithium leading to an intermediary bond polarity and distinct reactivity to those observed for alkyl potassium or alkyl lithium reagents.[11] The constitution of these bimetallic aggregates seems fluid with several species of distinct composition co-existing in solution. These alkoxide-mediated activating effects are known beyond organolithium chemistry. Thus, early studies by Richey Jr have shown that various dialkylmagnesium reagents can effectively undergo Mg-halogen exchange reactions with several aryl bromides and iodides when group 1 metal alkoxides are used as additives.[12] This boost in reactivity was attributed to the formation of more reactive triorganomagnesiate anions, although the role that the alkali-metal could play in these transformations was not really considered at the time. More recently, Knochel has exploited the synthetic utility of these alkyl/alkoxide systems combining *s*Bu$_2$Mg with two equivalents of LiOR′ (R′ = 2-ethylhexyl) to promote fast and regioselective Mg—Br exchange of a wide range of aryl and heteroaryl bromides. The power of this approach has also been demonstrated by accomplishing more challenging Mg—Cl exchange of significantly less reactive aryl chlorides.[13] Further studies assessing Mg—Br exchanges on dibromo-substituted heterocyclic substrates have revealed that their regioselectivity is intimately connected to the presence of Lewis donors as additives.[14] Thus, when 2,5-dibromopyridine is reacted with *s*Bu$_2$Mg·2LiOR′ selective activation of the C2 position is observed whereas the presence of one equivalent of PMDETA (*N,N,N′,N″,N″*-pentamethyldiethylenetriamine) triggers a regioselectivity switch inducing selective Mg—Br exchange at the C5-position (Figure 1a). Through isolation of key organometallic intermediates and NMR spectroscopic investigations, our collab-

[a] N. R. Judge, Dr. L. J. Bole, Prof. E. Hevia
Department für Chemie und Biochemie
Universität Bern
3012 Bern (Switzerland)
E-mail: eva.hevia@dcb.unibe.ch

Chemistry–A European Journal

Research Article
doi.org/10.1002/chem.202104164

Chemistry Europe
European Chemical
Societies Publishing

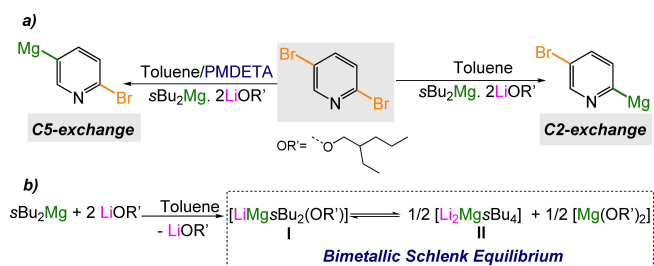**Figure 1.** (a) Regioselectivity switch of Mg—Br exchange reactions of 2, 5-dibromopyridine mediated by $sBu_2Mg \cdot 2LiOR'$ combination. (b) Bimetallic Schlenk equilibrium for [LiMgsBu$_2$(OR')] (**I**).

orative work with Knochel established that lithium and its coordinative saturation play a key role in controlling the regioselectivity of these reactions. Intrigued by these findings we took a closer look into the constitution of the exchange reagent, uncovering the presence of a bimetallic Schlenk-type equilibrium between the mixed alkyl/alkoxy magnesiate [LiMgsBu$_2$(OR')] (**I**), alkyl rich [Li$_2$MgsBu$_4$] (**II**) and magnesium alkoxide Mg(OR')$_2$ (Figure 1b). Surprisingly, these studies suggest that [Li$_2$MgsBu$_4$] (**II**) is the active species performing the Mg—Br exchange, the mixed alkyl/alkoxy magnesiate [LiMgsBu$_2$(OR')] (**I**) species is actually unreactive in this process.[15] Building on this work and inspired by recent studies in s-block bimetallic chemistry which have established the key mediating role played by the alkali-metal in main group heterobimetallic systems with applications in homogeneous catalysis,[16–18] organic synthesis[19,20] and small molecule activation processes,[21] here we extend our studies on mixed-alkyl/alkoxide alkali-metal magnesiate chemistry to sodium and potassium. By systematically changing the alkali-metal, we evaluate the constitution of these heterobimetallic systems in both solution and in the solid state and investigate their reactivity towards Mg—Br exchange reactions using 2-bromoanisole which has been chosen as a model substrate.

Results and Discussion

Synthesis and characterisation of mixed alkyl/alkoxide alkali-metal magnesiates

An effective strategy to access heterobimetallic complexes is the combination (or more accurately co-complexation) of the required monometallic counterparts.[22,23] This approach has been successfully used by Mulvey for the synthesis of mixed alkyl/alkoxide [(TMEDA)MMg(OtBu)nBu$_2$]$_2$ complexes by combining MOtBu (M = Na, K) with nBu$_2$Mg in the presence of bidentate Lewis donor TMEDA (TMEDA = *N,N,N′,N′*-tetramethylethylenediamine).[24] For our studies we chose the alkoxide derived from 2-{[2-(dimethylamino)ethyl] methylamino}ethanol (dmemH) which has already shown promise in lithium zincate chemistry.[25] Thus, addition of 2 molar equivalents of Li(dmem) to sBu_2Zn allows the activation of both alkyl groups on zinc to promote challenging Zn—I and Zn—Br exchanges. Moreover, the

two additional N-coordinating sites located in the backbone of the alkoxide ligand should allow for intramolecular stabilisation of the alkali metals via chelation and subsequently preclude aggregation, which can also contribute towards the formation of kinetically more reactive species. Homometallic M(dmem) (M = Li, Na, K) were prepared in situ by straightforward deprotonation of dmemH with MCH$_2$SiMe$_3$ in hexane (see Supporting Information for details). Co-complexation reactions of equimolar amounts of M(dmem) and Mg(CH$_2$SiMe$_3$)$_2$ were then investigated (Figure 2). Lacking of β-hydrogens, this dialkyl(magnesium) offers more thermal stability than sBu$_2$Mg,[26] making the isolation of the organometallic intermediates more accessible. These reactions lead to the isolation of mixed alkyl/alkoxy alkali-metal magnesiates [MMg(CH$_2$SiMe$_3$)$_2$(dmem)]$_2$ (M = Li, **1**; Na, **2**; (THF)K, **3**) (Figure 2) as crystalline solids in a 54, 35 and 29% yields respectively. While these isolated yields are moderate, NMR analysis of the reaction filtrates showed that they formed quantitatively. These mixed-metal species could also be prepared using a second co-complexation approach, by reacting heteroleptic [Mg-(CH$_2$SiMe$_3$)(dmem)] (**4**) (obtained by deprotonation of dmemH with Mg(CH$_2$SiMe$_3$)$_2$ with the relevant MCH$_2$SiMe$_3$ (Figure 2). Compounds **1**–**4** were characterised by multinuclear NMR and their molecular structures were established by X-ray crystallography. All are dimers featuring a central four-membered {MgOMgO} unit. For heterobimetallic compounds **1**–**3**, while each Mg center binds to two alkoxide and two alkyl groups, the presence of a different alkali-metal and its coordination preferences dictates the overall structure of the complex. In each case the alkoxide ligand binds in a tridentate fashion to the alkali-metal, via its O and two N sites. Featuring a centrosymmetric structure, lithium magnesiate **1** exhibits a ladder motif reminiscent to those previously reported for lithium amides[27–32] comprising outer Li—C rungs and inner alkoxy O—Mg rungs. Completing the structure along the ladder edge internal NMe$_2$ and NMe coordinate to Li whereas a terminal alkyl group binds to Mg. This structure can also be envisaged as two dinuclear {LiOMgC} rings which combine laterally via their Mg—O edges to generate this tetranuclear ladder. Within this motif one alkyl group is terminal on Mg (Mg—C5, 2.146(14) Å) whereas the other bridges Mg and Li (Mg—C1 2.205(14) Å, Li—C1, 2.273(3) Å) (Table 1). This structure is analogous to that previously reported by us for [LiMgs-Bu$_2$(dmem)]$_2$ using the same chelating alkoxide ligand.[15]

Contrastingly, heavier congeners sodium and potassium magnesiates **2** and **3** exhibit a different dimeric motif where now all alkyl groups bridge the alkali-metal and Mg. Instead of forming a ladder-type structure, **2** and **3** display an incomplete double cubane motif with a missing vertex in each cube. This arrangement is known for other monometallic and heterobimetallic complexes[33–37] including mixed alkyl alkoxide alkali-metal magnesiate[38,39] and manganate complexes.[40] The structures of **2** and **3** can also be described as inverse crowns,[41–44] comprising a cationic octagonal {(MCMgC)}$_2^+$ ring which hosts two alkoxide anions in its core. Each alkoxide coordinates to two Mg atoms and one alkali-metal (M) using its O atom and two N atoms to chelate the latter. Thus in **2** Na displays
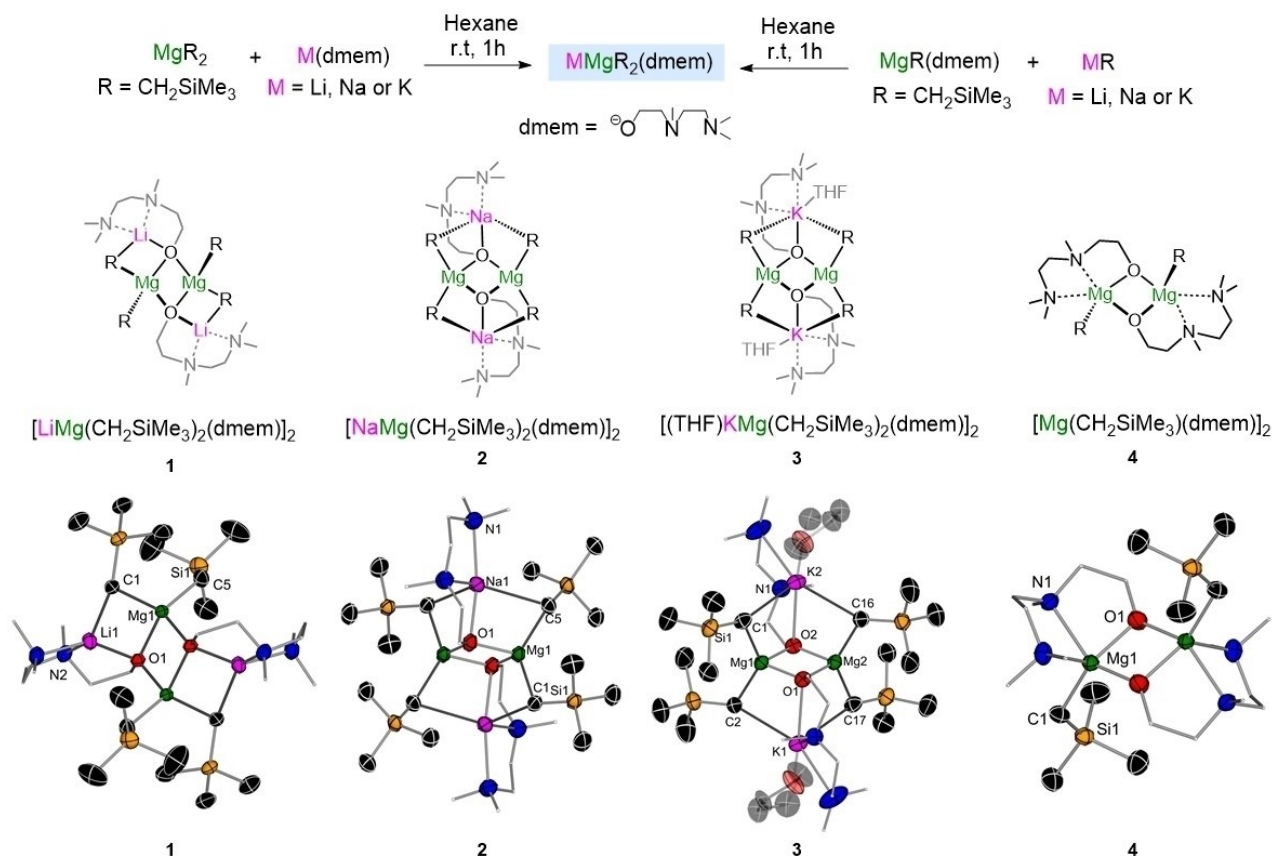
Chemistry–A European Journal

Research Article
doi.org/10.1002/chem.202104164

Chemistry Europe
European Chemical
Societies Publishing

Figure 2. Co-complexation routes to access mixed alkyl/alkoxy alkali-metal magnesiates **1–3**. Molecular structures of compounds **1–4** with displacement ellipsoids at 50% probability, all H atoms omitted and with C atoms in the alkoxide substituent drawn as wire frames only for clarity. Equivalent atoms in **1**, **2**, and **4** generated by (3/2−x, 1/2−y, 2/3−z), (1−x, 1−y, 1−z) and (1−x, −y, 1−z) respectively.

Table 1. Selected bond distances (Å) and angles (°) in the crystal structures of compounds **1–4**.

[LiMg(CH₂SiMe₃)₂(dmem)]₂ **1**			
Mg1−C1	2.205(14)	Li1−C1	2.273(3)
Mg1−C5	2.146(14)	Li1−O1	1.978(2)
Mg1−O1	2.033(9)	Li1···Mg1	2.779(2)
Mg···Mg	3.030(8)	Mg1−O1−Mg1	96.350(4)
O1−Mg1−O1	83.650(4)		

[NaMg(CH₂SiMe₃)₂(dmem)]₂ **2**			
Mg1−C1	2.191(2)	Na1−C1	2.686(3)
Mg1−C5	2.204(3)	Na1−C5	2.882(3)
Mg1−O1	2.018(16)	Na1−O1	2.421(18)
Mg···Mg	3.057(14)	Mg1···Na1	3.132(12)
O1−Mg1−O1	81.613(8)	Mg1−O1−Mg1	98.387(7)

[(THF)KMg(CH₂SiMe₃)₂(dmem)]₂ **3**			
Mg1−C1	2.188(3)	K1−C2	3.131(3)
Mg1−C2	2.193(3)	K2−C1	3.173(3)
Mg1−O1	2.027(18)	K1−O1	2.740(17)
Mg···Mg	2.996(11)	Mg1···K1	3.589(10)
O1−Mg1−O2	84.610(7)	Mg1−O1−Mg2	95.320(7)
O1−Mg2−O2	84.80(7)	Mg1−O2−Mg2	95.253(7)

[Mg(CH₂SiMe₃)(dmem)]₂ **4**			
Mg1−C1	2.177(2)	Mg···Mg	3.090(13)
Mg1−O1	1.995(17)	Mg1−O1−Mg1	101.476(7)
O1−Mg1−O1	78.524(7)		

pentacoordination, whereas in **3** K attains hexacoordination by solvation of a molecule of THF (Figure 2). Inspecting the Mg−C and Mg−O bond distances in these compounds did not reveal any significant differences (Table 1). These bonds anchor the structure to which the alkali-metals are affixed by a combination of M−C and M−O ancillary bonds which as expected become more elongated as the size of the alkali metal cation increases (Table 1). The structures of **1–3** can be compared to that of the monometallic alkylmagnesium alkoxide **4** which also exhibits a dimeric motif with a similar {MgOMgO} ring, although in this case the Mg atoms are also chelated by the N atoms on the alkoxide chain. Consistent with its neutral constitution, the Mg−O distance in **4** (1.995(17) Å) is slightly shorter than those found in magnesiate species **1–3**. This trend is also observed for the Mg−C bond distances (2.177(2) Å) although it should also be noted that in **4** the alkyl groups bind terminal to the Mg centers (Table 1). Using cryoscopic molecular weight determinations Coates reported in 1968 that alkylmagnesium alkoxides tend to form tetramers and higher oligomers via intermolecular Mg−O donor acceptor bonds in non-coordinating solvents such as benzene; whereas coordinating solvents such as THF can favour the formation of dimeric structures.[45] Many examples of structurally characterised alkylmagnesium alkoxides adopt tetrameric structures[46,47] or higher oligomer biscubanes.[48] The

Chemistry–A European Journal

Research Article
doi.org/10.1002/chem.202104164

Chemistry Europe
European Chemical
Societies Publishing

intramolecular coordinating abilities of the tridentate chelating alkoxide used here prevents the oligomerisation of **4** where the dimer is soluble even in non-polar solvents such as hexane.

The solution constitution of mixed alkyl/alkoxy magnesiates **1**–**3** in C_6D_6 was also studied using multinuclear NMR spectroscopy including ^{1}H-DOSY NMR studies. This was imperative to assess if these complexes exist as the sole compounds in solution or if alternatively they are in equilibrium with other organometallic species as previously shown for related lithium magnesiates [LiMgsBu$_2$(OR')] (R' = 2-ethylhexyl) (Figure 1b).[15] Related to these findings, O'Hara has also reported that heteroleptic alkali metal magnesiates [(rac)BIPHEN]M$_2$MgnBu$_2$(THF)$_4$ (M = Li or Na), containing the bis(aryloxide) group BIPHEN (BIPHEN = 5,5',6,6'-tetramethyl-3,3'-di-tert-butyl-1,1'-biphenyl-2,2'-diol) undergo a redistribution process in THF solution to form homoleptic alkoxy [(rac)BIPHEN]$_2$M$_2$Mg(THF)$_4$ and alkyl rich magnesiate [M$_2$MgnBu$_4$(THF)$_4$].[49,50] Interestingly, for **1**–**3**, the presence of the tridentate alkoxide ligand seems to impose a greater stability of these bimetallic species in solution as no evidence of ligand redistribution and formation of other organometallic compounds in solution were observed. This was supported by ^{1}H-DOSY NMR spectroscopic studies which indicated that in all cases a single molecular entity is formed containing both alkyl and alkoxide groups (see Supporting Information). In the case of **1**, two different signals are observed for the M–CH$_2$ groups in the ^{1}H and ^{13}C NMR spectra (δ^1H = −1.56 and −1.96 ppm; δ^{13}C = −4.8 and −6.7 ppm) which is consistent with the retention, in solution, of its structure in the solid state where one alkyl group is terminal while the other one bridges. In contrast, sodium magnesiate **2** and potassium magnesiate **3** display only one signal in the ^{1}H and ^{13}C NMR (δ^1H = −1.8 and −6.3 ppm; δ^{13}C = −1.78 and −6.3 ppm,) for the equivalent M–CH$_2$ groups which bridge between the Mg and alkali metal centres in the solid-state structures. While the M–CH$_2$ signal at 298 K in the ^{1}H NMR spectra for **2** is broad; at 333 K this peak converges to a sharp singlet suggesting there is a degree of fluxionality in solution. ^{1}H DOSY NMR studies suggest that this is most likely due to a monomer/dimer equilibrium (See Supporting Information for details).

Assessing alkali-metal effects in Mg-Br exchange reactions

Next, we investigated the ability of magnesiates **1**–**3** to undergo Mg–Br exchange using 2-bromoanisole as a model substrate. Since these bimetallic complexes contain two alkyl groups which potentially can undergo exchange, reactions were carried out with two equivalents of 2-bromoanisole in benzene at room temperature for one hour, followed by an aqueous quench and subsequent analysis by GC to determine the extent of Mg–Br exchange (Table 2). Significantly, monometallic Mg species, Mg(CH$_2$SiMe$_3$)$_2$ and [Mg(CH$_2$SiMe$_3$)(dmem)]$_2$ **4**, are completely inactive towards 2-bromoanisole (entries 1 and 2). In contrast, lithium magnesiate **1** gave a 41% conversion to anisole (entry 3). While this yield is moderate, it should be noted that our previous studies using [LiMgsBu$_2$(OR')] (R' = 2-ethylhexyl)

Table 2. Screening of Mg–Br exchange capabilities of mixed alkyl/alkoxy alkali metal magnesiates towards 2-bromoanisole.

i) Exchange Reagent (1 equiv)
Benzene, RT, 1h
ii) NH_4Cl

Entry	Exchange reagent[a]	Yield [%][b]
1	R$_2$Mg	0
2	RMg(dmem) (**4**)	0
3	LiMgR$_2$(dmem) (**1**)	41
4	NaMgR$_2$(dmem) (**2**)	45
5	KMgR$_2$(dmem) (**3**)	59
6	K(dmen) + nBu$_2$Mg	75
7	K(dmen) + sBu$_2$Mg	52

[a] R = CH$_2$SiMe$_3$. [b] Yields were determined by GC analysis of reaction aliquots after an aqueous quench using hexamethylbenzene as internal standard. Formation only of anisole and unreacted 2-bromoanisole were observed.

have shown that this mixed alkyl(alkoxide) magnesiate reacts sluggishly towards 2-bromoanisole.[15] Replacing Li by Na, using magnesiate **2** slightly increased in the yield of the exchange product (45%, entry 4) which can be further improved to 59% (entry 5) using potassium magnesiate **3**.

Intrigued by these findings that show a clear alkali-metal and alkoxide effect, we next assessed the influence of the alkyl groups, combining equimolar amounts of K(dmem) with equimolar amounts of nBu$_2$Mg and sBu$_2$Mg which a priori can be expected to be more reactive than Mg(CH$_2$SiMe$_3$)$_2$. Interestingly, while this was the case for nBu$_2$Mg (75%, entry 6), using sBu$_2$Mg gave similar conversions to those observed for **3** (52%, entry 7) which was somewhat surprising given that the sBu group has been the alkyl substituent of choice in related Li/Mg and Li/Zn systems investigating Mg–X and Zn–X exchange using alkoxide ligands.[13,25] It should be noted that when LiOR' (R' = 2-ethylhexyl) is paired with sBu$_2$Mg, the active exchange reagent is Li$_2$MgsBu$_4$ due to the presence of the bimetallic Schlenk equilibrium depicted in Figure 1b and that when this equilibrium is manipulated towards the exclusive formation of mixed alkyl/alkoxide [LiMgsBu$_2$(OR')] the exchange process is suppressed.[15] This scenario is not possible for magnesiates **1**–**3** which in solution retain their mixed alkyl/alkoxide constitution (see above). Our studies show a clear enhancement of reactivity when potassium is used as a metal partner with Mg contrasting with early work by Richey Jr. where adding different group 1 metal alkoxides to MgEt$_2$ enabled Mg–Br exchange in bromobenzene, though no definite trend in reactivity could be seen dependent on the alkali-metal.[12]

To gain further insights into the reactivity of **3** with 2-bromoanisole we next turned our focus to the isolation of the metalated intermediate prior to hydrolysis. Carrying the reaction out in benzene we noticed the almost immediate formation of a white precipitate which could not be redissolved in other organic solvents including polar THF. Removal of this solid by filtration furnished a light-yellow solution which on cooling deposited crystals of [MgAr(dmem)]$_2$ (**5**)

Chemistry–A European Journal

Research Article
doi.org/10.1002/chem.202104164

Chemistry
Europe
European Chemical
Societies Publishing

(Ar = o-OMe–C_6H_4) in a 30% crystalline yield (Figure 3). X-ray crystallographic studies established the molecular structure of **5** which shares the same dimeric motif as that described for **4** but now each Mg binds to an *ortho*-metalated anisyl group via its C atom. Despite their structural similarity, it should be noted that **5** is not accessible by reacting **4** with 2-bromoanisole (Table 2, entry 2), demonstrating that its formation is synergic in origin as it is mediated by potassium magnesiate **3**. ^{1}H NMR analysis of the reaction filtrates also confirm that **5** is the only organometallic species present in solution. While the lack of solubility in organic solvents of the solid formed during this reaction precluded its NMR characterisation, its aqueous quench with subsequent GC analysis showed the formation of anisole. Thus, we can tentatively propose that the formation of **5** occurs with the concomitant precipitation of [KAr]$_n$ (Ar = o-OMe–C_6H_4) (Figure 3). Adding a new layer of complexity to the behaviour of these mixed alkyl/alkoxide species, these results indicate that while potassium magnesiate **3** can efficiently promote Mg–Br exchange of 2-bromoanisole, the putative intermediate of this reaction [KMgAr$_2$(OR')] (**int-1**) undergoes redistribution into single metal components **5** and [KAr]$_n$ which may be driven by the poor solubility of the potassium species. This type of equilibrium is reminiscent to that present in Lochman-Schlosser nBuLi/KOtBu combinations, where an initial mixed metal alkyl/alkoxide intermediate is formed which eventually evolves into the exchange products LiOtBu and nBuK.[6] Ultimately, caution should be taken when using these bimetallic reagents in organic synthesis, since while 2-bromoanisole can be efficiently converted into anisole via Mg–Br exchange, two entirely different organometallic species are formed which could be expected to have very different properties in terms of stability, reactivity and functional group tolerance, and could therefore affect further functionalisation of their aromatic moieties.
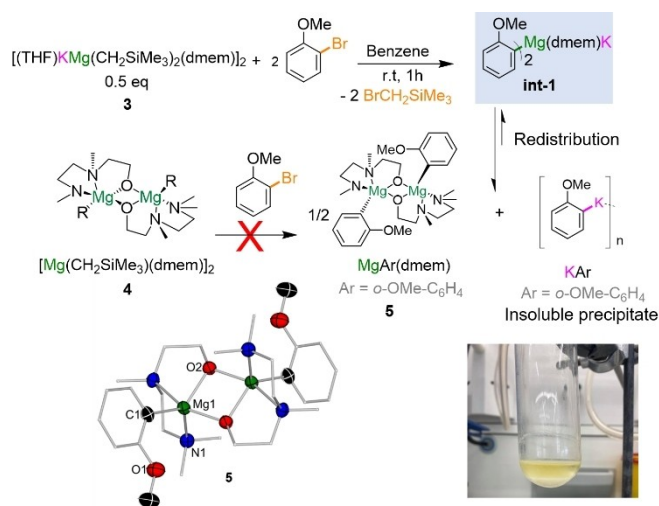
Puzzled by these findings, we next decided to probe whether the redistribution process shown in Figure 3 would also affect related potassium and sodium magnesiates containing the long chain aliphatic alkoxide OR' (R' = 2-ethylhexyl). Co-complexation of MOR' with equimolar amounts of Mg-$(CH_2SiMe_3)_2$ led to the formation of [MMg$(CH_2SiMe_3)_2$(OR')]$_2$ (M = Na, **6**; K, **7**). Whilst sodium magnesiate **6** could only be isolated as a colourless oil, potassium magnesiate **7** was isolated as crystalline solid in a 55% yield. ^{1}H and ^{13}C NMR characterisation of these compounds show similar behaviour as **2** and **3**, existing as single intact entities in C_6D_6 solutions without undergoing the bimetallic Schlenk equilibrium depicted in Figure 1b, previously reported for [LiMgsBu$_2$(OR')]$_2$.[15] The molecular structure of **7** was established by X-ray crystallographic studies (Figure 4). Despite the aliphatic constitution of the alkoxide groups lacking additional coordination sites the core structure of **7** is almost identical to that described for **3**, displaying comparable geometrical parameters (see Table S2 in Supporting Information). Coordinatively unsaturated K centres in **7** attain further stabilisation by forming anagostic K···Me interactions with one Me group from the CH_2SiMe_3 ligands on a neighbouring [KMg$(CH_2SiMe_3)_2$(OR')]$_2$ dimeric unit giving rise to a linear 1D polymeric arrangement (see Figure S9 in Supporting Information).

Both **6** and **7** react with two equivalents of our 2-bromoanisole in benzene at room temperature affording conversions to anisole, after a hydrolysis step, of 75 and 76% respectively after just one hour. Contrasting with **3**, using potassium magnesiate **7**, no solid precipitation is observed before the hydrolysis step. ^{1}H NMR monitoring of this reaction showed that after 3 h, all starting material **7** has reacted with 2-bromoanisole producing two equivalents of BrCH$_2$SiMe$_3$ and mixed aryl/alkoxide [KMgAr$_2$(OR')]$_2$ (**9**) which is stable in solution and does not undergo any redistribution process. The same reactivity was observed for sodium derivative **6** in forming [NaMgAr$_2$(OR')]$_2$ (**8**) (Scheme 1) although in this case after 3 h at room temperature unreacted 2-bromoanisole is detected in solution (75% conversion), illustrating the importance of the choice of alkali-metal for the efficiency of the Mg–Br exchange
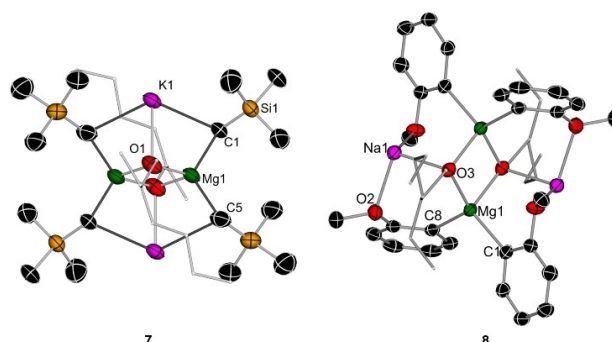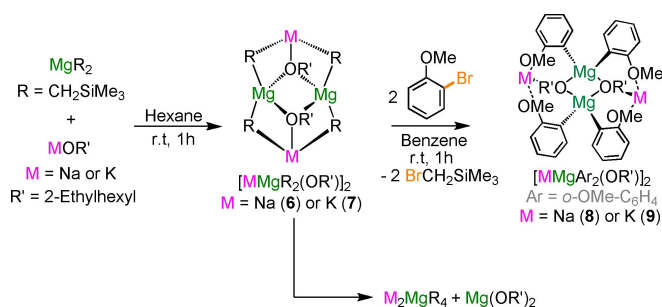

Figure 3. Isolation of [MgAr$_2$(dmem)] (**5**) via reaction of potassium magnesiate **3** with two equivalents of 2-bromoanisole and proposed concomitant formation of an insoluble potassium aryl [KAr]$_n$. Molecular structure of compound **5** with displacement ellipsoids at 50% probability, all H atoms omitted and with C atoms in the alkoxide substituent drawn as wire frames only for clarity. Equivalent atoms in **5** generated by (1−x, 1−y, 1−z).

Figure 4. Molecular structures of alkly/alkoxy potassium magnesiate **7** and aryl/alkoxy sodium magnesiate **8** with displacement ellipsoids at 50% probability, all H atoms omitted and with C atoms in the alkoxide substituent drawn as wire frames only for clarity. Equivalent atoms in **7** and **8** generated by (1−x, 1−y, 1−z) and (4/3−x, 5/3−y, 2/3−z) respectively.

Chemistry–A European Journal

Research Article
doi.org/10.1002/chem.202104164

Chemistry
Europe
European Chemical
Societies Publishing

Scheme 1. Synthesis of alkyl/alkoxy magnesiates **6** and **7** and their reactivity with 2-bromoanisole to form metallated intermediates **8** and **9** respectively.

process (See Supporting Information for details). Magnesiates **8** and **9** were characterised in solution by ^{1}H and ^{13}C NMR spectroscopy. ^{1}H DOSY NMR studies on these species confirm their mixed aryl/alkoxide constitution. The molecular structure of **8** was also confirmed by X-ray crystallographic studies (Figure 4), in which each Mg binds to two *ortho*-metallated anisole groups, occupying the position previously filled by the Br atoms, completing their coordination by bonding to two alkoxide ligands. Each Na binds to one alkoxide group and two OMe substituents from the anisyl fragments. The Na atoms in **8** find additional stabilisation by π-engaging in a preferred η^3-fashion with the aryl groups of neighbouring dimeric units creating an intricate 3D polymeric arrangement overall (see Figure S10 in Supporting Information).

This motif is closely related to the one we have previously reported for the product of Mg–Br exchange obtained from treating 2-bromoanisole with an equimolar mixture of Mg*s*Bu$_2$ and LiOR′.[14] However on this occasion this compound is obtained by direct exchange with Li$_2$Mg*s*Bu$_4$ to give a Li$_2$MgAr$_4$ intermediate which in turn undergoes co-complexation with Mg(OR′)$_2$ also present in the reaction media via the bimetallic Schlenk equilibrium depicted in Figure 1.[15] As aforementioned, while we do not observe the presence of this equilibrium for potassium magnesiate **3**, we decided to benchmark its reactivity towards to 2-bromoanisole against that of higher order potassium magnesiate K$_2$Mg(CH$_2$SiMe$_3$)$_4$ which can be isolated as its TMEDA solvate by combining TMEDA, KCH$_2$SiMe$_3$ and Mg(CH$_2$SiMe$_3$)$_2$ in a 2:2:1 ratio.[51] Interestingly, when reacting this alkyl rich reagent with four equivalents of 2-bromoanisole we only observed a 57% conversion, revealing that the mixed alkyl/alkoxide species is in this specific case a more powerful exchange reagent.

Conclusion

By assessing the reactivity of several mixed alkyl/alkoxide alkali-metal magnesiates towards 2-bromoanisole, systematically changing the alkali-metal and alkoxide group, new light has been shed on the activating effect of alkali-metal alkoxides when used as additives with organomagnesium reagents to mediate Mg–Br exchanges. A notable alkali-metal effect has

been uncovered, with the formation of the stable mixed alkyl/alkoxide [MMg(alkyl)$_2$(alkoxide)] species when M = Na, K in solution are not affected by the bimetallic Schlenk equilibrium previously reported for related lithium/magnesiates. Furthermore, an increase in reactivity has been noticed when using K instead of Li as a bimetallic partner with Mg, consistent with the alkali-metal playing a prominent role in mediating the Mg–Br exchange process. These findings also show the close interplay between the nature of the alkoxide group employed and the constitution of the exchange products prior to electrophilic interception. Thus, uncovering a new element of complexity, while the long aliphatic alkoxide OR′ bimetallic intermediate [KMgAr$_2$(OR′)]$_2$ is stable in arene solutions, employing dmem led to the formation of the single metal species [MgAr(dmem)]$_2$ (**5**) with concomitant precipitation of [KAr]$_n$. The different composition of these exchange products can profoundly affect the further functionalization of the aryl fragment when using these systems in organic synthetic transformations.

Experimental Section

Acknowledgements

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

[1] M. Schlosser, *J. Organomet. Chem.* **1967**, *8*, 9–16.

[2] P. Caubère, *Chem. Rev.* **1993**, *93*, 2317–2334.

[3] L. Lochmann, J. Pospíšil, D. Lím, *Tetrahedron Lett.* **1966**, *7*, 257–262.

[4] L. Lochmann, M. Janata, *Cent. Eur. J. Chem.* **2014**, *12*, 537–548.

[5] M. Schlosser, *Angew. Chem. Int. Ed.* **2005**, *44*, 376–393; *Angew. Chem.* **2005**, *117*, 380–398.

[6] M. Schlosser, S. Strunk, *Tetrahedron Lett.* **1984**, *25*, 741–744.

[7] L. Lochmann, *Eur. J. Inorg. Chem.* **2000**, 1115–1126.

[8] F. Mongin, A. Harrison-Marchand, *Chem. Rev.* **2013**, *113*, 7563–7727.

[9] S. D. Robertson, M. Uzelac, R. E. Mulvey, *Chem. Rev.* **2019**, *119*, 8332–8405.

[10] J. Klett, *Chem. Eur. J.* **2021**, *27*, 888–904.

[11] P. Benrath, M. Kaiser, T. Limbach, M. Mondeshki, J. Klett, *Angew. Chem. Int. Ed.* **2016**, *55*, 10886–10889; *Angew. Chem.* **2016**, *128*, 11045–11049.

[12] J. Farkas, S. J. Stoudt, E. M. Hanawalt, A. D. Pajerski, H. G. Richey, *Organometallics* **2004**, *23*, 423–427.

[13] D. S. Ziegler, K. Karaghiosoff, P. Knochel, *Angew. Chem. Int. Ed.* **2018**, *57*, 6701–6704; *Angew. Chem.* **2018**, *130*, 6811–6815.

[14] A. Desaintjean, T. Haupt, L. J. Bole, N. R. Judge, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2021**, *60*, 1513–1518; *Angew. Chem.* **2021**, *133*, 1536–1541.

[15] L. J. Bole, N. R. Judge, E. Hevia, *Angew. Chem. Int. Ed.* **2021**, *60*, 7626–7631; *Angew. Chem.* **2021**, *133*, 7704–7709.

[16] J. M. Gil-Negrete, E. Hevia, *Chem. Sci.* **2021**, *12*, 1982–1992.

[17] A. M. Borys, E. Hevia, *Trends Chem.* **2021**, *xx*, 8–11.

[18] M. De Tullio, A. M. Borys, A. Hernán-Gómez, A. R. Kennedy, E. Hevia, *Chem. Catal.* **2021**, *1*, 1308–1321.

[19] T. X. Gentner, R. E. Mulvey, *Angew. Chem. Int. Ed.* **2021**, *60*, 9247–9262; *Angew. Chem.* **2021**, *133*, 9331–9348.

[20] A. Harrison-Marchand, F. Mongin, *Chem. Rev.* **2013**, *113*, 7470–7562.

[21] M. J. Evans, M. D. Anker, C. L. McMullin, S. E. Neale, M. P. Coles, *Angew. Chem. Int. Ed.* **2021**, *60*, 22289–22292; *Angew. Chem.* **2021**, *133*, 22463–22466.

[22] P. Mastropierro, Z. Livingstone, S. D. Robertson, A. R. Kennedy, E. Hevia, *Organometallics* **2020**, *39*, 4273–4281.

[23] P. Mastropierro, A. R. Kennedy, E. Hevia, *Eur. J. Inorg. Chem.* **2020**, *2*, 1016–1022.

[24] N. D. R. Barnett, W. Clegg, A. R. Kennedy, R. E. Mulvey, S. Weatherstone, *Chem. Commun.* **2005**, *190*, 375–377.

[25] M. Balkenhohl, D. S. Ziegler, A. Desaintjean, L. J. Bole, A. R. Kennedy, E. Hevia, P. Knochel, *Angew. Chem. Int. Ed.* **2019**, *58*, 12898–12902; *Angew. Chem.* **2019**, *131*, 13030–13034.

[26] A. R. Kennedy, J. Klett, R. E. Mulvey, S. D. Robertson, *Eur. J. Inorg. Chem.* **2011**, 4675–4679.

[27] D. R. Armstrong, D. Barr, W. Clegg, S. M. Hodgson, R. E. Mulvey, D. Reed, R. Snaith, D. S. Wright, *J. Am. Chem. Soc.* **1989**, *111*, 4719–4727.

[28] R. E. Mulvey, *Chem. Soc. Rev.* **1991**, *20*, 167.

[29] D. R. Baker, R. E. Mulvey, W. Clegg, P. A. O'Neil, *J. Am. Chem. Soc.* **1993**, *115*, 6472–6473.

[30] A. R. Kennedy, R. E. Mulvey, A. Robertson, *Chem. Commun.* **1998**, *0*, 89–90.

[31] R. E. Mulvey, *Chem. Soc. Rev.* **1998**, *27*, 339–346.

[32] A. Downard, T. Chivers, *Eur. J. Inorg. Chem.* **2001**, 2193–2201.

[33] W. Clegg, S. H. Dale, D. V. Graham, R. W. Harrington, E. Hevia, L. M. Hogg, A. R. Kennedy, R. E. Mulvey, *Chem. Commun.* **2007**, 1641–1643.

[34] M. M. Olmstead, W. J. Grigsby, D. R. Chacon, T. Hascall, P. P. Power, *Inorg. Chim. Acta* **1996**, *251*, 273–284.

[35] S. Sakamoto, T. Imamoto, K. Yamaguchi, *Org. Lett.* **2001**, *3*, 1793–1795.

[36] K. Merz, S. Block, R. Schoenen, M. Driess, *J. Chem. Soc. Dalton Trans.* **2003**, *3*, 3365–3369.

[37] S. E. Baillie, E. Hevia, A. R. Kennedy, R. E. Mulvey, *Organometallics* **2007**, *26*, 204–209.

[38] E. Hevia, A. R. Kennedy, R. E. Mulvey, S. Weatherstone, *Angew. Chem. Int. Ed.* **2004**, *43*, 1709–1712; *Angew. Chem.* **2004**, *116*, 1741–1744.

[39] K. J. Drewette, K. W. Henderson, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, R. B. Rowlings, *Chem. Commun.* **2002**, *2*, 1176–1177.

[40] M. Uzelac, I. Borilovic, M. Amores, T. Cadenbach, A. R. Kennedy, G. Aromí, E. Hevia, *Chem. Eur. J.* **2016**, *22*, 4843–4854.

[41] R. E. Mulvey, *Chem. Commun.* **2001**, 1049–1056.

[42] A. R. Kennedy, R. E. Mulvey, C. L. Raston, B. A. Roberts, R. B. Rowlings, *Chem. Commun.* **1999**, *2*, 353–354.

[43] G. C. Forbes, A. R. Kennedy, R. E. Mulvey, R. B. Rowlings, W. Clegg, S. T. Liddle, C. C. Wilson, *Chem. Commun.* **2000**, *2*, 1759–1760.

[44] A. R. Kennedy, J. Klett, R. E. Mulvey, S. Newton, D. S. Wright, *Chem. Commun.* **2008**, *7345*, 308–310.

[45] G. E. Coates, J. A. Heslop, M. E. Redwood, D. Ridley, *J. Chem. Soc. A Inorganic, Phys. Theor.* **1968**, *5*, 1118.

[46] M. M. Sung, C. G. Kim, J. Kim, Y. Kim, *Chem. Mater.* **2002**, *14*, 826–831.

[47] C. A. Moreno, D. L. Hughes, M. Bochmann, *Polyhedron* **2007**, *26*, 2523–2526.

[48] S. Heitz, Y. Aksu, C. Merschjann, M. Driess, *Chem. Mater.* **2010**, *22*, 1376–1385.

[49] J. Francos, P. C. Gros, A. R. Kennedy, C. T. O'Hara, *Organometallics* **2015**, *34*, 2550–2557.

[50] C. Yeardley, A. R. Kennedy, P. C. Gros, S. Touchet, M. Fairley, R. McLellan, A. J. Martínez-Martínez, C. T. O'Hara, *Dalton Trans.* **2020**, *49*, 5257–5263.

[51] M. Fairley, L. Davin, A. Hernán-Gómez, J. García-Álvarez, C. T. O'Hara, E. Hevia, *Chem. Sci.* **2019**, *10*, 5821–5831.