Reviews

Modern Ate Chemistry: Applications of Synergic Mixed Alkali-Metal−Magnesium or −Zinc Reagents in Synthesis and Structure Building

Robert E. Mulvey

WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, U.K.

Received November 28, 2005

The special synergic reactivity exhibited by certain heterobimetallic ate compounds in which magnesium or zinc is paired together with an alkali metal such as lithium, sodium, or potassium provides the theme of this review. The emerging concepts of alkali-metal-mediated magnesiation and alkali-metal-mediated zincation are introduced with respect to the selective deprotonation and/or polydeprotonation of a series of arene, aromatic heterocyclic, metallocene, and metal π-arene substrates. It is shown that, in accomplishing such deprotonations, alkali metal−magnesium amide based reagents can often generate “inverse crown” ring compounds. Inverse crowns display polymetallic cationic “host” rings (residue of the reacted mixed-metal base) surrounding an anionic “guest” (the deprotonated substrate) in a Lewis acidic−Lewis basic arrangement inverse to that encountered in conventional crown ether complexes. A signature feature of inverse crown ring and related mixed-metal structures is a synergic combination of Mg−C (or Zn−C) σ bonds and alkali-metal−π contacts. Also included are related inverse crown ether complexes in which the guest can be an oxo, peroxo, hydrido, alkoxo, or enolato anion and the first example of the concept of synergic nucleophilic addition involving the action of a new sodium dialkylamidozincate reagent toward benzophenone.

Introduction

This article is intended to provide the reader with a glimpse of the special chemistry that one can observe when an alkali metal (usually Li, Na, or K) is combined with either magnesium or zinc within the same organoelement compound (usually the element is C, N, or O). Strictly, all of these mixed-metal formulations could be classified under the generic term “ates” and, as such, subdivided into contacted ion-pair (e.g., $LiMgR_3$, $LiZnR_3$) or separated ion-pair (e.g., $Li^+MgR_3^-$, $Li^+ZnR_3^-$) types, but grouping them together in this way implies a commonality in their chemical profiles/structures that is all too often wide of the mark. In the most interesting cases, the reactivity and/or selectivity of the heterobimetallic composite cannot be replicated by either of its homometallic component parts; therefore, in effect one could argue that this behavior is neither conventional alkali-metal chemistry nor conventional magnesium or zinc chemistry but a unique new synergic chemistry. As this article will set out to demonstrate, reactions of these mixed-metal compounds can in fact be special magnesiations or zincations, and are therefore best regarded as *alkali-metal-mediated* magnesiations or zincations. Thus, the synergy is commonly marked by a reversal in the normal order of reactivity, because whereas in conventional homometallic chemistry organoalkali-metal reagents are orders of magnitude more reactive than their organomagnesium or organozinc counterparts, when an alkali metal and magnesium or zinc are paired together in the same molecule, the seat of reactivity (which is often enhanced in comparison to that of R_2Mg or R_2Zn compounds) is transferred to Mg or Zn. Simplistically, this may appear entirely logical, especially in the case of $M^+MgR_3^-$ or $M^+ZnR_3^-$ formulations where the negative charge resides solely on the anionic MgR_3^- or ZnR_3^- moiety, but the complete picture of how reactivity is arrived at has a more mosaic complexity about it. For example, Richey has shown[1] that the rate of addition of “$KZnEt_3$” to di-*tert*-butyl ketone is less than 10^{-4} that of “$LiZnEt_3$”, dismissing any assumption that reactivity is controlled exclusively by the anionic moiety; moreover, in homometallic chemistry organopotassium compounds are generally considered to be significantly more reactive than organolithium congeners, yet here the reverse is true. Similarly, in our own laboratory we have discovered that the mixed potassium−zinc silylamide “$KZn(HMDS)_3$” (HMDS = $(Me_3Si)_2N^-$; see later) readily deprotonates toluene at the methyl position to give the polymeric benzyl product $[\{KZn(HMDS)_2(CH_2Ph)\}_\infty]$, whereas the magnesium analogue “$KMg(HMDS)_3$” fails miserably under the same conditions.[2] Again this runs counter to the normal reactivity order (Mg > Zn) expected in the homometallic world.

We have become increasingly aware of such “synergic surprises” in our ongoing investigations of mixed alkali-metal−magnesium and alkali-metal−zinc compounds. Centered mainly, but not exclusively, on organonitrogen (amido; R_2N^- ligands), this research forms the basis of this review. Our approach has been to study metal-containing compounds (both the mixed-metal reagents themselves and the metalated intermediates they generate on reaction with organic substrates) directly, by, where

---

(1) Maclin, K. M.; Richey, H. G., Jr. *J. Org. Chem.* **2002**, *67*, 4602.

(2) Clegg. W.; Forbes, G. C.; Kennedy, A. R.; Mulvey, R. E.; Liddle, S. T. *Chem. Commun.* **2003**, 406.

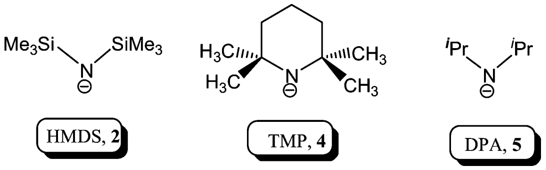
10.1021/om0510223 CCC: $33.50

possible, isolating them and subjecting them to structural analysis. The more traditional organic chemistry of magnesiates and zincates, the investigation of which is largely focused on the organic products further down the line, that is, after the metalated intermediates have been consumed by reaction with an electrophile, is not covered here. This organic product driven research, which nicely complements our own metal-centered studies, is presently a burgeoning field following many years of relatively stunted growth in comparison to that of Grignard reagents or diorganozinc reagents.[3]

As a preface to the discussion of inverse crown ether complexes, one possible class of compound originating from a mixed-metal synergy, it is worth reflecting on some early findings within the general area of ate chemistry.

Historical Notes

It is noteworthy that the preparation of the first alkali-metal ate compound actually predates by about six decades the pioneering preparations of neutral organosodium and organolithium compounds by Schlenk.[4] This landmark distinction belongs to sodium triethylzincate, “$NaZnEt_3$”,[5] made by Wanklyn in 1858 by the action of sodium on diethylzinc, which itself had been synthesized a few years earlier by Frankland.[6] Nearly a century would pass by before Wittig would coin the term “ate” in the realization that classes of such metal compounds with anionic formulations could be developed. He introduced lithium triphenylzincate, “$LiZnPh_3$”, as well as the analogous magnesium species, “$LiMgPh_3$”, the first magnesiate, both prepared by direct combination of their homometallic component compounds, in a seminal paper from 1951.[7] Though Wittig did not explicitly describe ate chemistry in terms of synergy, he was clearly conscious of the possible unique reactivity characteristics of ates, for example, in exclaiming that “$LiMgPh_3$” in reaction with benzalacetophenone yields a product of mainly 1,4-addition, whereas on its own LiPh yields mainly a 1,2-addition product. Wittig rationalized the early chemistry of ates[8] collectively in terms of an anionic activation, with the negative charge activating “anionically” all of the ligands surrounding the metal through an inductive effect. This idea was emphasized by Tochtermann in an early review of “structures and reactions of organic ate-complexes” from 1966.[9] As we often note today in our own work, enhanced solubility in organic solvents can usually be a reliable indication that a diorganomagnesium− or diorganozinc−organo-alkali-metal mixture has formed a mixed-metal ate complex. One of the first observations of this effect was recorded by Coates in 1968,[10] who noticed that dimethylmagnesium, Me_2Mg, dissolves better in ether solutions containing *n*-butyllithium, $^{n}BuLi$, than in neat ether solvent. He attributed this to the formation of lithium *n*-butyldimethylmagnesium, which was separated as the viscous liquid ether solvate “$LiMg(^{n}Bu)(Me)_2{\cdot}OEt_2$”. The occurrence of more than one stoichiometry for the same metal^1:metal^2:ligand trilogy (the formulas “$MMgR_3$” and “M_2MgR_4”, and their zinc equivalents, are particularly common) is another special feature of ate chemistry that was recognized at an early stage. Detailed NMR studies by Brown, Seitz, et al. between 1966 and 1969 of solutions prepared by mixing organolithium and diorganomagnesium compounds in various proportions established the formation of rapidly equilibrating ate complexes of at least three distinct stoichiometries.[11] The groundbreaking X-ray crystallographic research of Weiss, which led to the determination of the solid-state structures of many important organo-alkali-metal compounds from the early 1960s and beyond, also included a series of simple magnesiate and zincate complexes. These studies revealed the common M^{II} trigonal-planar and tetrahedral geometries associated with the distinct stoichiometries mentioned above. For brevity this early structural work is not covered here, as Weiss has summarized it in a review from 1993.[12]



HMDS, **2** TMP, **4** DPA, **5**

Figure 1. Structural formulas of the three most synthetically useful (metal) amide reagents.

Inverse Crown Ether Complexes

A detailed account of how the idea of “ inverse crown ethers” was conceived was included in a feature article from 2001.[13,14] To avoid unnecessary repetition and for brevity, only a summary of this early work is reproduced here, while new developments since 2001 are given greater coverage and discussion.

Reported in 1998,[15] the first inverse crown ether (though not interpreted as such in this original paper) was an HMDS-based complex of lithium and magnesium, namely $[Li_2Mg_2(HMDS)_4(O)_x(O_2)_y]$ (**1**) (HMDS is 1,1,1,3,3,3-hexamethyldisilazide, $(Me_3Si)_2N^-$ (**2**; Figure 1), also commonly referred to as bis(trimethylsilyl)amide). The synthesis of **1** was fortuitous, as the intention was to prepare a mixed lithium−magnesium variant of lithium HMDS, namely $[LiMg(HMDS)_3]$ (**3**). From a fundamental viewpoint, the preparation and study of **3** seemed long overdue, given the widespread utility of lithium HMDS, the recent surge of interest in magnesium amide reagents,[16] and the literature precedents of mixed-metal HMDS complexes, including the isovalent manganese(II) species $[LiMn(HMDS)_3]$ (by Power)[17] and the series of mixed-alkali-metal species $[3THF{\cdot}M^1M^2(HMDS)_2]$ (by Williard).[18] Adopting Williard’s direct method of simply adding together the component single-metal HMDS complexes or alternatively treating a 1:1 mixture of butyllithium and dibutylmagnesium with 3 molar equiv of the parent amine HMDS(H) (Scheme 1) undoubtedly produces **3**, but its high solubility in arene or hydrocarbon solvent tends

---

[3] For leading references to recent organic literature see: (a) Kitagawa, K.; Inoue, A.; Shinokubo, H.: Oshima, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 2481. (b) Inoue, A.; Kitagawa, K.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2001**, *66*, 4333. (c) Mongin, F.; Bucher, A.; Bazureau, J. P.; Bayh, O.; Awad, H.; Trécourt, F. *Tetrahedron Lett.* **2005**, *46*, 7989. (d) Uchiyama, M.; Naka, H.; Matsumoto, Y.; Ohwada, T. *J. Am. Chem.* Soc. **2004**, *126*, 10526. (e) Hatano, M.; Matsumura, T.; Ishihara, K. *Org. Lett.* **2005**, *7*, 573.

[4] Schlenk, W.; Holtz, J. *Ber*. **1917**, *50*, 262.

[5] Wanklyn, J. A. *Ann*. **1858**, *108*, 67.

[6] For an essay on zinc alkyls, Edward Frankland, and the beginnings of main-group organometallic chemistry, see: Seyferth, D. *Organometallics* **2001**, *20*, 2940.

[7] Wittig, G.; Meyer, F. J.; Lange, G. *Ann.* **1951**, *571*, 167.

[8] Wittig, G. *Angew. Chem.* **1958**, *70*, 65.

[9] Tochtermann, W. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 351.

[10] Coates, G. E.; Heslop, J. A. *J. Chem. Soc. A* **1968**, 514.

[11] (a) Seitz, L. M.; Brown, T. L. *J. Am. Chem. Soc.* **1966**, *88*, 4140. (b) Seitz, L. M.; Brown, T. L. *J. Am. Chem. Soc.* **1967**, *89*, 1602. (c) Seitz, L. M.; Little, B. F. *J. Organomet. Chem.* **1969**, *18*, 227.

[12] Weiss, E. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1501.

[13] Mulvey, R. E. *Chem. Commun.* **2001**, 1049.

[14] See also Driess, M.; Mulvey, R. E.; Westerhausen, M. In *Molecular Clusters of the Main Group Elements*; Driess, M., Nöth, H., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Chapter 3.6.

[15] Kennedy, A. R.; Mulvey, R. E.; Rowlings, R. B. *J. Am. Chem. Soc.* **1998**, *120*, 7816.

[16] Henderson, K. W.; Kerr, W. J. *Chem. Eur. J.* **2001**, *7*, 3430.

Scheme 1. Synthesis of the Mixed Lithium−Magnesium Tris(HMDS) Complex 3 and Its Oxygen-Contaminated Variant 1, the First s-Block Metal Inverse Crown

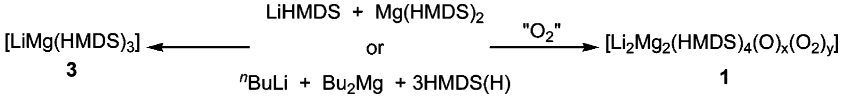


Table 1. Representative Selection of Crystallographically Characterized Inverse Crown Ethers $[M^I_2M^{II}_2(amide)_4(O)_x(O_2)_y]$

M^I	M^{II}	amide	x	y	ref
Li	Mg	HMDS	0.28	0.72	15
Li	Mg	TMP	1.00	0.00	20
Na	Mg	TMP	1.00	0.00	23
Na	Mg	HMDS	0.68	0.32	20
K[a]	Mg	HMDS	0.00	1.00	21
Na	Zn	HMDS	1.00	0.00	22
K[a]	Zn	HMDS	0.18	0.82	22

[a] These potassium-based inverse crown ethers are not molecular but link up intermolecularly through $(Me_2Si)H_3C\cdots K$ agostic contacts to generate linear polymeric chains.

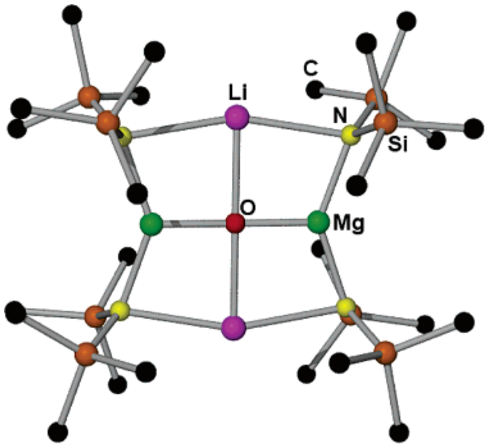


Figure 2. Molecular structure of the oxo inverse crown ether **1**.

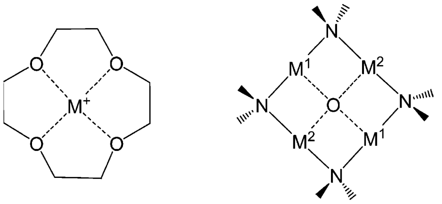


Figure 3. Topological comparison between generalized crown ether and inverse crown complexes.

to keep it dissolved, leaving the oxygen-contaminated "impurity" **1** to crystallize preferentially from the solution. Thus, more often than not, we isolated crystals of **1** from solutions expected to yield **3**. Clearly, as trace quantities of **1** can still be produced even when standard precautions are followed to avoid moisture/oxygen ingress (thought to be the source of the "foreign" oxo anions in **1**), solutions of **3** must be super-efficient oxygen scavengers.

The inverse crown motif of **1** (Figure 2) is designed around an anionic core filled by either a single oxide or peroxide ion. Surrounding this core is an eight-membered cationic ring made up of alternating nitrogen and metal atoms, with the latter atoms themselves alternately lithium and magnesium. The mutual interchange of these Lewis basic (anionic) and Lewis acidic (cationic) sites compared to their disposition in conventional crown ether complexes[19] (host rings Lewis basic and guests Lewis acidic; see Figure 3 for a generalized comparison) prompted the coining of the term "inverse crown ethers" to describe what emerged as a family of new mixed-metal macrocyclic amides. Note that the designation "ether" is used loosely here, as these compounds are clearly not ethers in the normal organic functional group sense. Table 1 lists the compositions of a representative selection of crystallographically characterized inverse crown ethers, which conform to the general formula $[M^I_2M^{II}_2(Amide)_4(O)_x(O_2)_y]$, where M^I is an alkali metal and M^{II} is Mg or Zn. It is noteworthy that lithium, sodium, or potassium can fulfill the role of the alkali metal in this structural motif, though in the potassium cases the larger size of the cation encourages these motifs to link up intermolecularly through $(Me_2Si)H_3C\cdots K$ agostic interactions to generate linear polymers, in contrast to the discrete arrangements found for lithium and sodium. In the magnesium structures the group 2 metal is displaced toward the center of the octagonal ring, as a consequence of its strong oxophilicity. Magnesium can also be exchanged for zinc in the heavier alkali-metal HMDS inverse crown ethers, but significantly seemingly not in the lithium case. This is related to the failure of $Zn(HMDS)_2$ to form a cocomplex with LiHMDS (akin to the magnesium cocomplex **3**) in aliphatic hydrocarbon solution (the medium generally employed for the preparation of inverse crown ethers), though mixed alkyl−HMDS cocomplexes such as $[\{Li(\mu\text{-HMDS})_2ZnMe\}_\infty]$[22] and $[Li(\mu\text{-HMDS})_2Zn^nBu]$[24] are readily accessible. Emphasizing the importance of the solvent medium, in neat hexane solution we prepared the oxo inverse crown ether $[Na_2Zn_2(HMDS)_4(O)]$,[22] whereas Dehnicke reported that in the presence of 12-crown-4 the solvent-separated zincate $[\{Na(12\text{-crown-}4)_2\}^+\{Zn(HMDS)_3\}^-]$[25] is obtained. Both potassium-based inverse crown ethers in Table 1[21,22] are rich in peroxide (one exclusively so, the other showing an 82:18 peroxide:oxide discrimination). It is tempting to rationalize this trend in terms of a host-ring−guest-anion size match, i.e., the larger eight-membered $(KNMgN)_2$ ring having a preference for the larger anion peroxo $(O_2)^{2-}$ over oxo $(O)^{2-}$, but in view of the limited sample size and the fact that the smaller $(LiNMgN)_2$ ring in **1**[15] also shows a substantial peroxide bias (72% versus 28% oxide), judgment on the reasons for these peroxide:oxide ratios must remain reserved. The precise mechanism for how these oxygen-based anions end up encapsulated within the polynuclear mixed-metal amide rings is not yet known. Adventitious moisture, oxygen, or both could be the source of the guest anion. Intuitively, in view of the presence of peroxide with its two linked O atoms, one might assume that molecular oxygen is the principal culprit,

---

[17] Murray, B. D.; Power, P. P. *Inorg. Chem.* **1984**, *23*, 4584.

[18] Williard, P. G.; Nichols, M. A. *J. Am. Chem. Soc.* **1991**, *113*, 9671.

[19] Gokel, G. *Crown Ethers and Cryptands*; The Royal Society of Chemistry: Cambridge, U.K., 1991.

[20] Kennedy, A. R.; Mulvey, R. E.; Rowlings, R. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 3180.

[21] Kennedy, A. R.; Mulvey, R. E.; Raston, C. L.; Roberts, B. A.; Rowlings, R. B. *Chem. Commun.* **1999**, 353.

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

[23] Kennedy, A. R.; MacLellan, J. G.; Mulvey, R. E. *Acta Crystallogr.* **2003**, *C59*, m302.

[24] Forbes, G. C.; Kennedy, A. R.; Mulvey, R. E. Unpublished work.

[25] Putzer, M. A.; Neumüller, B.; Dehnicke, K. *Z. Anorg. Allg. Chem.* **1997**, *623*, 539.

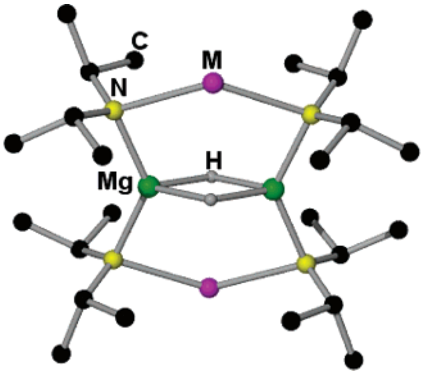


Figure 4. Molecular structure of the hydrido inverse crown **6**.

and to an extent this is backed up experimentally by the observation that the yields of certain inverse crown ethers are increased when dry oxygen is deliberately added to reaction solutions. However, the "problem" of oxygen contamination of organometallic compounds (especially those of the oxygen-loving small, hard, s-block metals) is a minefield of complexity. As long ago as 1964, Stucky and Rundle reported the crystal structure of the contaminated "Grignard reagent" $Mg_4Br_6(O)\cdot 4Et_2O$,[26] and since then the number of similar unexpected findings of oxygen ingress has risen sharply as major technological advances in X-ray crystallography and computing have made it decidedly easier to determine crystal structures. As our mixed-metal research has veered off in different directions, we have not investigated further the questions of where the O_2^{2-} or O^{2-} ions come from and how they get there (if the source is moisture, then the reaction is presumably a deprotonation, whereas with oxygen a redox reaction must take place in which the inverse crown ether is the reduced product and a hydrazine such as $(Me_3Si)_2N-N(SiMe_3)_2$ could be the oxidized product). In general, where oxygen contamination of an s-block organometallic compound has taken place but was unplanned, little definite information exists on the mechanism involved.

Two inverse crown ethers in Table 1[20,23] have TMP (2,2,6,6-tetramethylpiperidide (**4**); Figure 1) amide bridges instead of HMDS bridges. TMP is cyclic, is more sterically demanding, and is more basic in pK_a terms than acyclic HMDS. Together with DPA (diisopropylamide (**5**); Figure 1), TMP and HMDS, when partnered with lithium, represent the three most important amides worldwide in terms of their synthetic usefulness. This is one of the main reasons why our mixed-metal research has focused predominately on this indispensable set of bulky amides. Inspecting Table 1, one notes that DPA is conspicuously missing; that is, there is no example hitherto of a DPA-based oxo- or peroxo-centered inverse crown ether. However, attempts to prepare such a compound following the same protocol as that used in the HMDS and TMP cases (i.e., a 1:1:3 mixture of RM, Bu_2Mg, and amine) produced a new category of inverse crown ether with hydride "guest" anions of general formula $[M_2Mg_2(DPA)_4(\mu\text{-}H)_2\cdot 2(\text{toluene})]$ (**6**, where M = Na,[27] K[28]). Their common structural motif (Figure 4) is also based upon an eight-membered $[(MNMgN)_4]^{2+}$ ring, but unlike the planar rings of the oxo/peroxo inverse crown ethers, this one adopts a chair conformation with a planar NMgN···NMgN chair seat and alkali metal M in the head- and foot-rest positions. Toluene molecules solvate the M^+ cations electrostatically through their π-systems, and interestingly the M−arene centroid distances are significantly shorter (by 0.159 Å) when M = K. This observation may appear counter-logical against the fact that sodium is much smaller than potassium, but the explanation lies in the greater separation of the DPA groups within the N−K−N ring bonding compared to that in the N−Na−N ring bonding, which creates a wider coordination around the K^+ center and allows for a closer approach of the toluene molecule. Lying on either side of the chair seat, the hydride ions form a planar $(MgH)_2$ ring and do not interact with the M^+ cations. As supported by DFT calculations, the proposed reaction pathway for the formation of **6** (Scheme 2) necessitates a β-hydride elimination step from an ^{i}Pr substituent of a DPA ligand. Since TMP and HMDS do not contain any β-C−H functionality, this alternative reaction to oxo/peroxo encapsulation is not feasible for them. In the cases of **6**, β-hydride elimination is thermally induced by heating the reaction solutions to reflux temperatures. Under milder conditions, β-hydride elimination can be suppressed and tris(amide) complexes can be formed and isolated from solution. Thus, the solvent-free potassium−magnesium tris(amide) $[\{KMg(DPA)_3\}_\infty]$ adopts an infinite spiral chain of ···K−(μ-N)$_2$−Mg−N··· links, while the isostructural TMEDA solvates $[TMEDA\cdot K(\mu\text{-}DPA)_2Mg(DPA)]$ and $[TMEDA\cdot Na(\mu\text{-}DPA)_2Mg(DPA)]$ adopt a discrete dinuclear arrangement as TMEDA blocks the propagating terminal site on the alkali metal.[29]

Mixed alkali metal−magnesium tris(diisopropylamides) can in turn be utilized to produce inverse crowns with alkoxo "guest" anions.[30] Having the general formula $[MMg(DPA)_2(OR)_2]$ (**7**: M = Li, R = ^{n}Oct; M = Na, R = ^{n}Bu, ^{n}Oct), these mixed-ligand amido−alkoxo composites are prepared by treating hydrocarbon solutions of "$MMg(DPA)_3$" (sodium DPA is essentially insoluble in hydrocarbon solvents; thus, the fact that it is rendered soluble when combined with magnesium bis-DPA can be attributed to a synergic effect) with 1 molar equiv of the appropriate *n*-alcohol (Scheme 3). X-ray crystallographic studies of **7** reveal a structural motif closely related to that of **6**. Thus, a chair-shaped octagonal $(MNMgN)_2$ ring has M "tips" displaced on either side of a plane defined by NMgN···NMgN, and each side contains an O atom of an alkoxide anion which caps a MMgMg triangular face (Figure 5). The main distinction with **6** is the absence of any terminal solvent ligands such as toluene on the alkali metal M. This is compensated for by M−O (guest) bonding, whereas in **6** the hydride guest is far removed from the alkali-metal tips. Since **7** could be viewed as a cocomplex between an alkali-metal alkoxide (MOR) and a magnesium bis(amide) $(Mg(NR_2)_2)$, we pondered whether it would be possible to substitute the latter component for a magnesium bis(alkyl) (MgR_2) to generate the first alkyl inverse crown, as hitherto all s-block inverse crowns had been amide-based. This was readily accomplished[31] via direct addition (cocomplexation) of an alkali-metal *tert*-butoxide and dibutylmagnesium (Scheme 4), in a procedure adapted from that used previously by Richey in the preparation of the potassium zincate $[\{[KZn(Et)_2(O^tBu)]_2\}_\infty]$.[32] The alkyl inverse crown products $[\{TMEDA\cdot MMg(Bu)_2(O^tBu)\}_2]$ (**8**, where M = Na, K) adopt the same basic motif as that of **7** but with added TMEDA ligands chelating to the M^+ cations (Figure 6) made possible by the attenuation in steric strain on substituting smaller Bu bridges for the bulkier

---

[26] Stucky, G. D.; Rundle, R. E. *J. Am. Chem. Soc.* **1964**, *86*, 4821.

[27] Gallagher, D. J.; Henderson, K. W.; Kennedy, A. R.; O'Hara, C. T.; Mulvey, R. E.; Rowlings, R. B. *Chem. Commun.* **2002**, 376.

[28] Andrikopoulos, P. C.; Armstrong, D. R.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Rowlings, R. B. *Eur. J. Inorg. Chem.* **2003**, 3354.

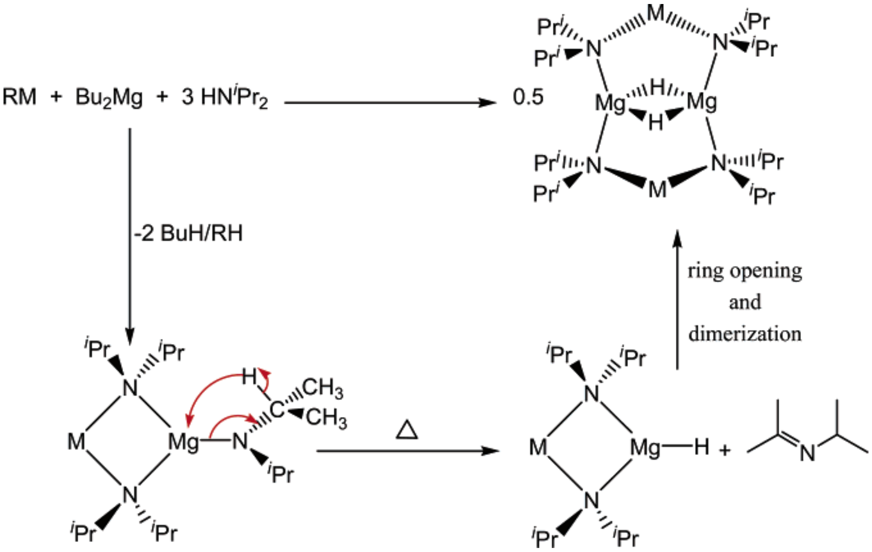
[29] Hevia, E.; Kenley, F. R.; Kennedy, A. R.; Mulvey, R. E.; Rowlings, R. B. *Eur. J. Inorg. Chem.* **2003**, 3347.

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

[31] Barnett, N. D. R.; Clegg, W.; Kennedy, A. R.; Mulvey, R. E.; Weatherstone, S. *Chem. Commun.* **2005**, 375.

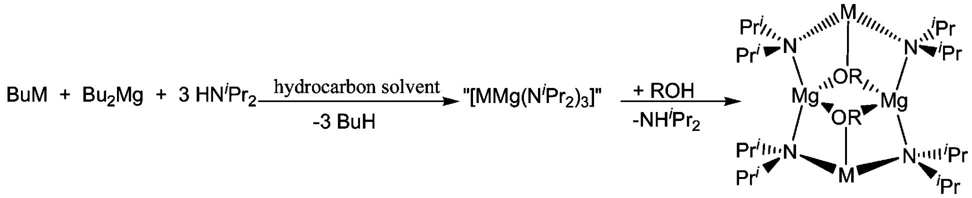
[32] Fabicon, R. M.; Parvez, M.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 1412.

Scheme 2. Proposed Pathway for the Formation of Inverse Crowns with Hydride "Guest" Anions (M = Na, R = Bu; M = K, R = $PhCH_2$)[a]

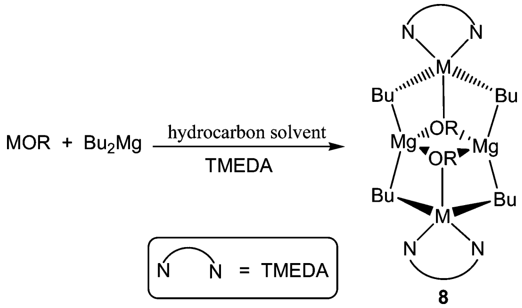


[a] For clarity, solvating toluene ligands in the final product have been omitted.

Scheme 3. Synthesis of Inverse Crowns with Alkoxo "Guest" Anions (M = Li, R = ⁿOct; M = Na, R= ⁿBu, ⁿOct)



Scheme 4. Synthesis of Alkyl Inverse Crowns (M = Na, K; R = ᵗBu)



8

secondary amide bridges in **7**. Interestingly, analysis of the dimensions of the sodium and potassium versions of **8** reveals that, in binding to the (2 × C; 1 × O) tripodal face of a common organomagnesiate anion, Na^+ prefers O coordination, whereas K^+ prefers C coordination (Figure 7), though both structures are identical in terms of connectivity. As further examples later in the discussion testify to, alkali-metal effects, especially between lithium and sodium, are relatively common in these mixed-metal complexes; therefore, it is erroneous to regard their chemistry as simply that of the anionic ate moiety with a passive (or dummy) alkali-metal partner.

In collaboration with Henderson, we successfully extended this octagonal ring family of inverse crowns to mixed potassium−calcium enolates, generated by HMDS deprotonation of ketones (Scheme 5).[33] Though it has the same basic motif as those of **7** and **8**, $[\{KCaR_3{\cdot}THF\}_2]$ (**9**) is homoleptic, not heteroleptic, since enolate anions (R is $OC(Mes){=}CH_2$) occupy both host ring and guest sites (Figure 8). Again the "soft" C

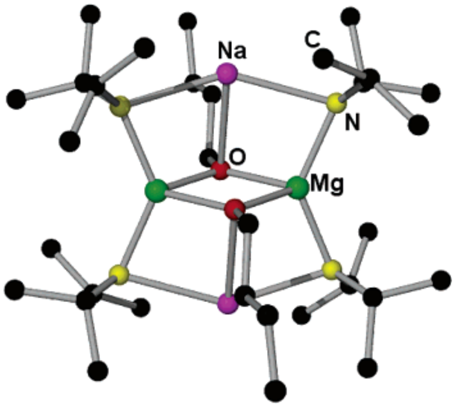


Figure 5. Molecular structure of the alkoxo inverse crown **7** (where M = Na).

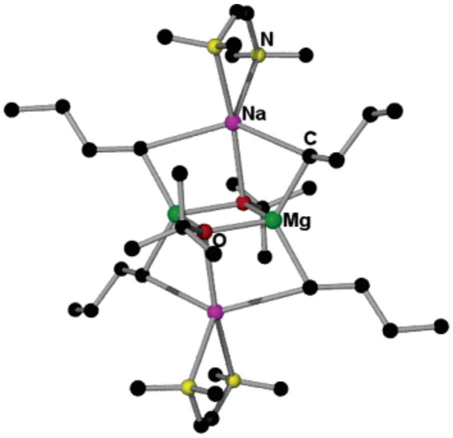


Figure 6. Molecular structure of the alkyl inverse crown **8** (where M = Na).

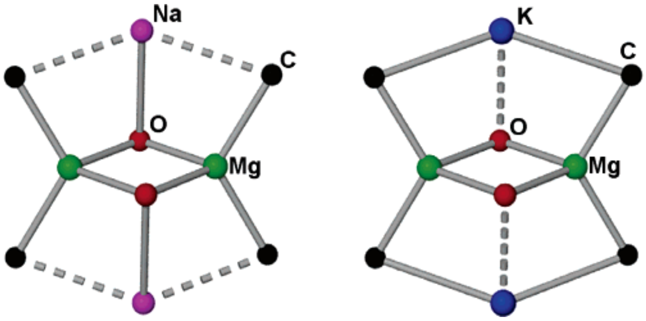


Figure 7. Depiction of the structure of **8** showing the differential binding of Na^+ and K^+ to a common dinuclear diorganomagnesiate.

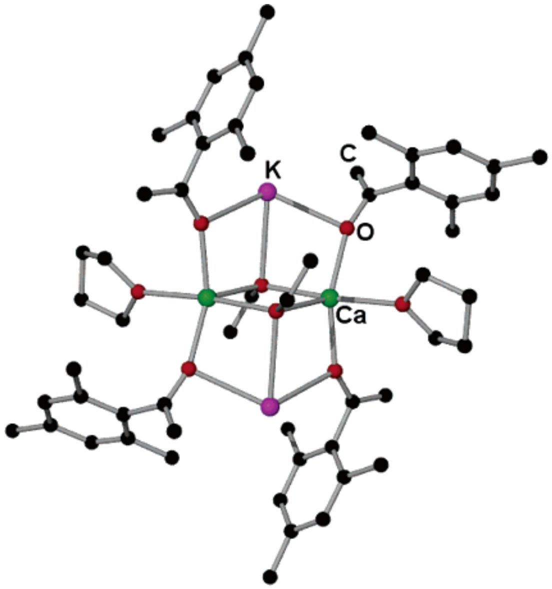


Figure 8. Molecular structure of the enolato inverse crown **9**.

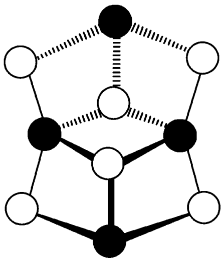


Figure 9. Common structural motif found in **7**−**9** and many other inorganic complexes.

preference of potassium is evident in **9**, as it interacts only weakly with the anionic enolate oxygens but engages in a plethora of interactions with the π-systems of the olefinic and aryl bonds. In a search of the crystallographic literature, it is clear that this homoleptic motif of **9** (sometimes interpreted as two cuboidal arrays, each "missing" a corner atom, and sharing a common face—the guest−Mg four-membered ring in our inverse crown notation) is widespread and fast becoming a general structural type in inorganic chemistry. This motif (generalized in Figure 9) may represent the whole structure or part of a more complicated architecture. Table 2 lists a representative sample of both mixed-metal and homometallic compounds that share this basic motif. Of special note is the alkylmagnesium amide [{^{n}BuMg$_2$[μ-N(H)Dipp]$_2$(μ_3-O^{n}Bu)}$_2$] (**10**; Scheme 6), made in our own laboratory, which by invoking the isovalency between $(MgBu)^+$ and M^+ (e.g., Na^+) can be described as a homometallic magnesium−magnesium′ inverse crown.[34] When **10** is compared with **7**, it can be observed that the basic motif of each is essentially the same but that the former has two types of Mg centers, those carrying exo-Bu substituents in the alkali metal (M) positions of the latter and those without exo-Bu substituents in the Mg positions of the latter. Given that this type of structure (Figure 9) is relatively common across both homometallic and heterometallic chemistries and was known long before the idea of inverse crowns was raised (for example, in 1996, Power reported a zinc analogue closely related to **10** in [{EtZn$_2$[N(H)Dipp]$_2$(OEt)}$_2$]),[35] the description of them as "inverse crowns" should carry less weight and significance than it does for the other structural types so named in this review.

Scheme 5. Synthesis of a Potassium−Calcium Enolato Inverse Crown

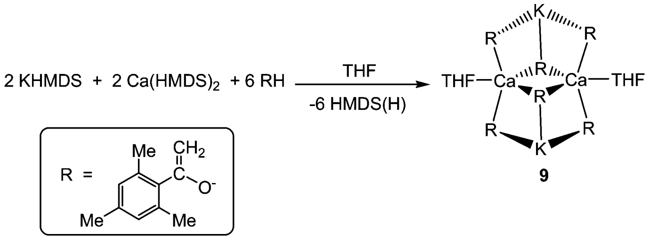
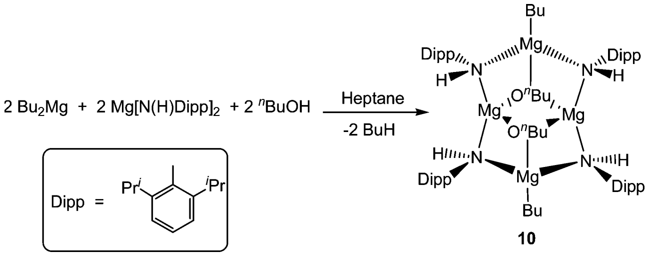


Table 2. Representative Sample of Compounds That Exhibit a Structural Motif Similar to That of the Mixed-Metal Enolate 9

compd	ref
[{^{n}BuMg$_2$[μ-N(H)Dipp]$_2$(μ_3-O^{n}Bu)}$_2$]	34
[{EtZn$_2$[N(H)Dipp]$_2$(OEt)}]	35
[{(PhCH$_2$)Mg$_2$Cl$_3$·3THF}$_2$]	36
[Sr$_4$(OPh)$_8$·6THF·2PhOH]	37
[Mg$_4$(OMe)$_6$(Br)$_2$·6C$_4$D$_8$O]	38
[{NaFe(O^{t}Bu)$_3$·THF}$_2$]	39
[{KZn(OSiMe$_3$)$_3$·TMEDA}$_2$]	40
[{LiNb(OEt)$_5$(OH)}$_2$]	41
[{LiHf(O^{i}Pr)$_5$}$_2$]	42

Scheme 6. Synthesis of a Homometallic Magnesium−Magnesium' Inverse Crown



Inverse Crowns and Alkali-Metal-Mediated Magnesiation

While the aforementioned inverse crown ethers are generally synthesized in a hydrocarbon medium, in the presence of an arene solvent reactions can change course and new categories of mixed-metal host−guest type complexes can be generated. Since these new complexes do not contain oxo or peroxo anions

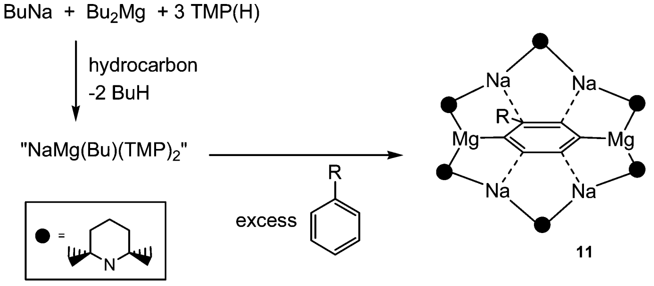
---

[33] He, X.; Noll, B. C.; Beatty, A.; Mulvey, R. E.; Henderson, K. W. *J. Am. Chem. Soc.* **2004**, *126*, 7444.

[34] Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; Weatherstone, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 1709.

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

Scheme 7. Synthesis of Inverse Crowns with Arenediide "Guest" Anions (R = H, Me)



but still have Lewis acidic host rings entertaining Lewis basic guest anions, we retain the label inverse crown but drop the suffix ether in describing them. We now present a few key examples to show that these alternative inverse crowns are products of *alkali-metal-mediated magnesiation.*

Toluene (or benzene) can be twofold deprotonated by a synergic base mixture of *n*-butylsodium, dibutylmagnesium, and 3 molar equiv of the bulky amine TMPH (Scheme 7).[43] In these exploratory syntheses the arene was present in excess as a cosolvent rather than as a stoichiometric reactant. From an organic synthetic perspective these reactions are unusual on two main counts. First, while toluene can be easily monometalated to generate the resonance-stabilized benzyl carbanion, its dimetalation (and that of benzene) presents a much more challenging task. Conventional homometallic reagents such as (butyllithium)·TMEDA can pull off more than one hydrogen atom, but only in a random unpredictable way, leading to a complex assortment of incompletely characterized polylithiated species. Second, these mixed-metal-mediated twofold deprotonations are regioselective: toluene is metalated in the 2,5-positions and benzene in the 1,4-positions. The former regioselectivity is especially noteworthy, as the most acidic hydrogen by several pK_a units belongs to the methyl sustituent of toluene, which is why mainstream organometallic bases usually attack at this position (lateral metalation) to produce benzyl ($PhCH_2^-$) products, since resonance stabilization reaches a maximum when a hydrogen atom is removed from the methyl site. These twofold deprotonative metalations give rise to isostructural 12-membered inverse crown ring products of the formula [$Na_4Mg_2(TMP)_6$(arene-2H)] (**11**, where arene-2H is $C_6H_3CH_3$ or C_6H_4; Figure 10). Metal atoms and nitrogen atoms alternate within the $(NaNNaNMgN)_2$ ring, which is severely puckered. The encapsulated arene molecules lie approximately orthogonal to the mean plane of the host ring through a combination of Mg−C σ bonds and Na−π-arene interactions. This bonding description can be inferred from the coplanarity of both Mg atoms with the arenediide ring planes—in effect, the Mg atoms act as pseudo hydrogen atoms! The number of hydrogen atoms lost from the parent arenes (two) tallies exactly with the number of Mg atoms in the inverse crown products (two), whereas in contrast there are four Na atoms present. This is reason enough to classify these twofold deprotonations as *magnesiations*; however, a qualification is necessary, as more accurately these are *alkali-metal-mediated magnesiations* because neither Bu_2Mg nor $Mg(TMP)_2$ on their own can metalate benzene (let alone dimetalate it regioselectively), as they require the mediation of the added sodium component. Previously[13] we had speculated that this special regioselective twofold deprotonation could be a function of a ring template effect whereupon the (hypothetical) [$Na_4Mg_2(TMP)_8$] cyclic dodecamer would react with the arene to generate **11** and 2 molar equiv of the amine TMPH. This possibility has now been disproven by compelling evidence, as outlined below.

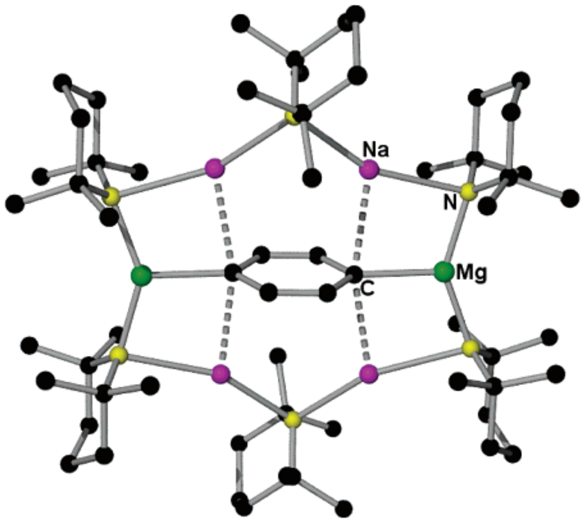
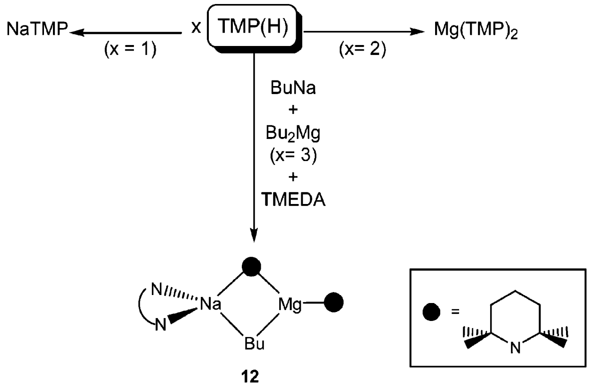


Figure 10. Molecular structure of the arenediide inverse crown **11** (where arene = benzene).

Scheme 8. Synergic Synthesis of the Mono(alkyl)−Bis(amido) Complex 12



To try and establish the identity of the active base in this system, we sought to exploit the intermediate-trapping ability of the chelating auxiliary TMEDA (*N,N,N′,N′*-tetramethylethylenediamine, $Me_2NCH_2CH_2NMe_2$) by adding it stoichiometrically to the same reaction that affords **11**, but in the absence of toluene or benzene (Scheme 8). The stoichiometry employed was expected to yield the tris(amide) "$NaMg(TMP)_3$" complexed by TMEDA, with all the butyl carbanions consumed as butane. Surprisingly, however, in practice the reaction reproducibly affords the monoalkyl−bis(amido) complex [(TMEDA)·Na(μ-Bu)(μ-TMP)Mg(TMP)] (**12**) as colorless crystals in a high isolated yield; that is, one butyl ligand remains in the product.[44] Optimization of the synthesis of **12** revealed that the best yield (42%; maximum possible 50%) is achieved using only 1 molar

---

(36) Sakamoto, S.; Imamoto, T.; Yamaguchi, K. *Org. Lett.* **2001**, *3*, 1793.

(37) Drake, S. R.; Streib, W. E.; Chisholm, M. H.; Caulton, K. G. *Inorg. Chem.* **1990**, *29*, 2707.

(38) Walfort, B.; Yousef, R. I.; Ruffer, T.; Steinborn, D. *Acta Crystallogr.* **2004**, *C60*, m482.

(39) Gun'ko, Y. K.; Cristmann, U.; Kessler, V. G. *Eur. J. Inorg. Chem.* **2002**, 1029.

(40) Merz, K.; Block, S.; Schoenen, R.; Driess, M. *Dalton Trans.* **2003**, 3365.

(41) Yanovsky, A. I.; Turevskaya, E. P.; Turova, N. Ya.; Struchkov, Yu. T. *Koord. Khim.* **1985**, *11*, 110.

(42) Veith, M.; Mathur, S.; Mathur, C.; Huch, V. *J. Chem. Soc., Dalton Trans.* **1997**, 2101.

(43) Armstrong, D. R.; Kennedy, A. R.; Mulvey, R. E.; Rowlings, R. B. *Angew. Chem., Int. Ed.* **1999**, *38*, 131.

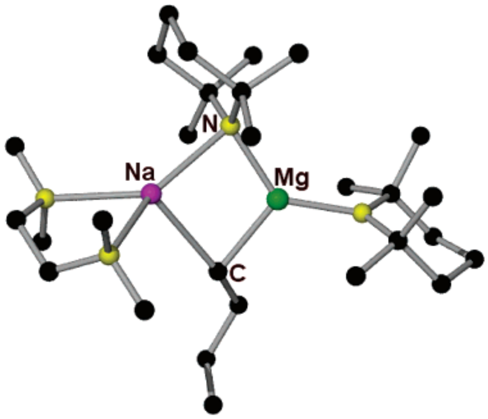


Figure 11. Molecular structure of the sodium−magnesium monoalkyl−bis(amido) complex **12**.

equiv of TMPH, as the reaction always affords a second organometallic product, namely the tris(alkyl) complex [(TMEDA)·NaMg(Bu)$_3$]. The unexpected presence of the Bu ligand in **12**, which could not be expelled as butane on refluxing the reaction solution for several hours, can be attributed to a synergic effect, as on their own both butylsodium and dibutylmagnesium react fully with TMPH to form Na(TMP) and Mg(TMP)$_2$, respectively. A four-element NaNMgC ring, with a mixed TMP−Bu bridging ligand set, forms the central feature of the molecular structure of **12** (Figure 11), which is completed by terminal TMEDA and TMP ligands on the Na and Mg atoms, respectively. Complex **12** could be considered a cocomplex of BuNa and Mg(TMP)$_2$ in the same way that the best known Lochmann−Schlosser superbase could represent a cocomplex between BuLi and KO^{t}Bu.[45] With the added ingredient of TMEDA, which often activates organolithium reagents, the composition of **12** is intriguing from the viewpoint of its potential as a new base possessing both alkyl and amido functionalities. Using NMR spectroscopy we reexamined the reaction solution that affords **11** prior to introducing the arene, and this confirmed that the alkyl group was still present in a mixture of composition "[Na(Bu)(TMP)Mg(TMP)] and TMPH"; hence, logically it would appear that this is the active base behind at least one of the deprotonations (see below) involved in the formation of **11**.

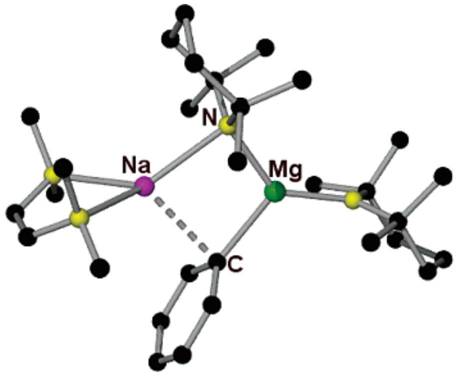
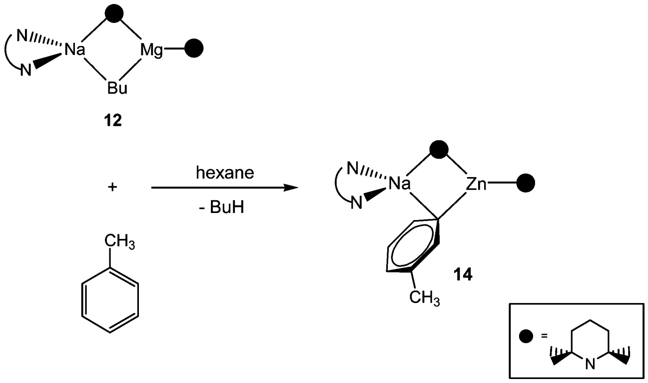


Figure 12. Molecular structure of the sodium−magnesium alkyl-/arylamido complex **13**.

Scheme 9. Synergic Meta Deprotonation of Toluene



Readily available in a pure crystalline form, **12** has been tested in a few preliminary reactions to assess its deprotonative ability. It behaves as an alkyl base toward benzene to produce another crystalline compound in [(TMEDA)·Na(μ-Ph)(μ-TMP)Mg(TMP)] (**13**), the molecular structure of which (Figure 12) essentially mimics that of **12** but with the Ph$^-$ anion occupying the same position as that vacated by Bu$^-$.[44] Deprotonation of toluene, where regioselectivity becomes an issue, also proves to be straightforward under reflux conditions, producing [(TMEDA)·Na(μ-C$_6$H$_4$CH$_3$)(μ-TMP)Mg(TMP)] (**14**), in a best isolated yield of 58% (Scheme 9).[46] The molecular structure of **14** (Figure 13) reveals most importantly, and remarkably, that the deprotonation of toluene is exclusively meta oriented. Here, therefore, the new reagent **12** is functioning as a selective alkyl base and effecting a unique meta selectivity that cannot be replicated by any known homometallic base. The basic connectivity in the structure of **14** is the same as that in **12** and **13**, with only the identity of the carbon bridge between sodium and magnesium altering. Both areneide bridges in **14** and **13** exhibit the same bonding pattern: lying almost coplanar with the arene ring, the Mg engages with the deprotonated C atom (meta in the case of **14**) through σ-bonding, whereas Na lies almost perpendicular to this ring to set up an interaction with its π-system. This σ- and π-bonding distinction has become a signature feature of arene-based inverse crowns and related mixed-metal structures. DFT calculations modeling the four regioisomers of **14** (but without TMEDA) possible when toluene is deprotonated in different positions (Figure 14) implicate the Na···C π-interactions as the major factor in the meta isomer being the most stable model in a validation of the experimental structure. The meta isomer displays several medium-to-long Na···C π-interactions (spanning 2.453−2.960 Å), whereas the benzylic isomer, surprisingly the least stable of the four regioisomers, has no Na···C π-contacts below 4.8 Å (the Na−C

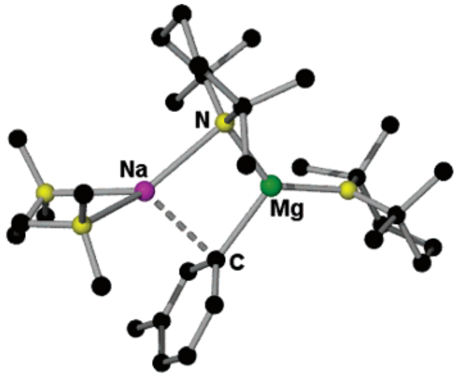


Figure 13. Molecular structure of the synergically meta-deprotonated toluene complex **14**.

---

[44] Hevia, E.; Gallagher, D. J.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Talmard, C. *Chem. Commun.* **2004**, 2422.

[45] (a) Lochmann, L. *Eur. J. Inorg. Chem.* **2000**, 115. (b) Schlosser, M. *Mod. Synth. Methods* **1992**, *6*, 227.

[46] Andrikopoulos, P. C.; Armstrong, D. R.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Talmard, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 3459.

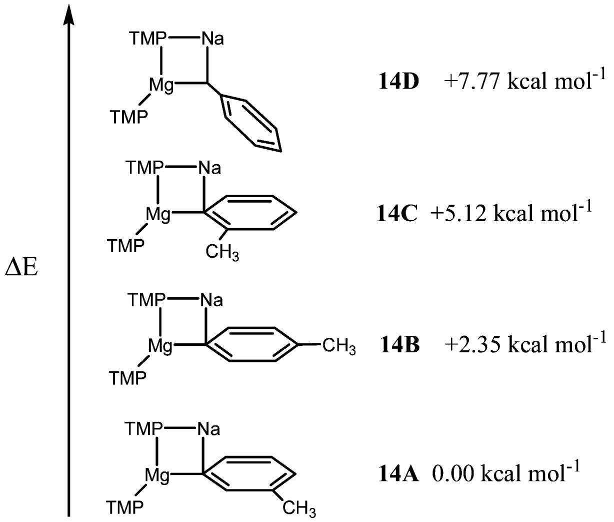


Figure 14. Relative energies and structures of the theoretical regioisomers of **14** (without TMEDA) in which toluene is deprotonated at the meta (**A**), para (**B**), ortho (**C**), or methyl (**D**) position.

benzylic bond length is 2.475 Å). The benzyl isomer, produced by deprotonation at the most acidic methyl site, is the one expected experimentally and the most stable theoretically when deprotonation is carried out using a homometallic base such as butylsodium. In the bimetallic models the stability order is meta isomer > para > ortho > benzyl. Hence, the normal order of thermodynamic stability of toluene metalation products (lateral isomer > ring isomer) has been reversed using this special Na–Mg bimetallic approach. This is an extraordinary result, which could open doors to new organometallic aromatic chemistry if the methodology is found to be applicable to a broad range of compounds. Evidence of the promise of this methodology toward the synthesis of meta-substituted aromatics was established through the almost quantitative conversion of **14** to trimethyl(*m*-tolyl)silane using the strong electrophilic reagent trimethylsilyl triflate. As in the case of **11**, the synthesis of **14** represents another example of alkali-metal-mediated magnesiation. Both results appear to suggest that the alkali-metal (sodium) mediation predominately involves an electrostatic interaction with the π-system of the arene. Moreover, the contrast between them, a singlefold deprotonation of toluene in **14** versus a twofold deprotonation in **11**, provides a strong clue that the two deprotonations involved in the latter occur in a stepwise manner, and not simultaneously through a ring template effect. It is therefore likely that the low-yield product **11** forms via a subsequent intramolecular deprotonation of a meta-deprotonated intermediate related to **14** but without TMEDA, effected by strong heating, which is accompanied by elimination of Mg(TMP)$_2$ (this accounts for the Na:Mg stoichiometry change from 1:1 in **14** to 2:1 in **11**).

A spectacular ring expansion takes place on substituting sodium by potassium in the reactions that yield **11**.[47] The 12-membered host ring of **11** is now replaced by a 24-membered hexapotassium–hexamagnesium–dodecaamide ring, which acts as a polymetallic host to 6 singlefold deprotonated arene anions in products of the general formula [K$_6$Mg$_6$(TMP)$_{12}$(arene-1H)$_6$], where arene is benzene or toluene (Figure 15). Again, the trapped arene anions receive dual (σ and π) stabilization from the Mg and K atoms, respectively.

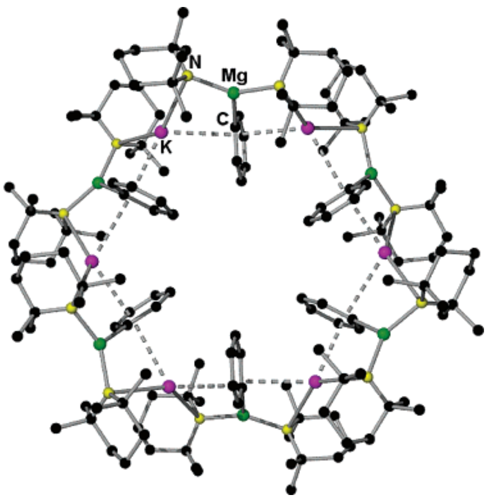


Figure 15. Molecular structure of the potassium–magnesium areneide inverse crown where arene = benzene.

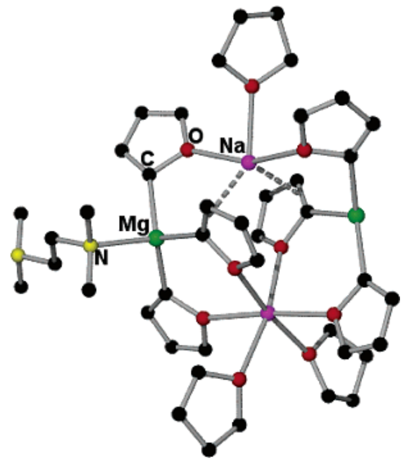


Figure 16. Molecular structure of the polymeric furyl inverse crown **15**.

Extension to Aromatic Heterocycles

The utility of the mixed sodium–magnesium mixed alkyl–amido base **12** has been extended to aromatic heterocyclic compounds. Furan undergoes alkali-metal-mediated α-magnesiation (Scheme 10).[48] While in terms of selectivity this α-metalation is far from unusual—as long ago as 1934 Gilman had used ethylsodium for this purpose[49]—it is manifested in the product [{{3THF·Na$_2$}{(TMEDA)·Mg$_2$}(2-C$_4$H$_3$O)$_6$}$_\infty$] (**15**), which has a novel structure (Figure 16) that establishes a new inverse crown architecture. Illustrating beautifully the synergic signature σ–π bonding of inverse crowns, this structure is homoleptic in the sense that the same anion, furan deprotonated in the 2-position, is found in both the "host" ring and "guest" sites, though each type is clearly distinguishable. One set of furan anions act as η^2(O,C) bridges linking Na to Mg through Na–O and Mg–C bonds, in constructing a puckered 12-membered (NaOCMgCO)$_2$ host ring; while occupying central positions above and below the face of the host ring, the other two furyl guests also engage in η^2(O,C) bridging to link one Na to the two Mg centers but in addition use one C=C π-bond each to supplement the coordinative requirements of the other Na. The structure builds into a one-dimensional chain polymer

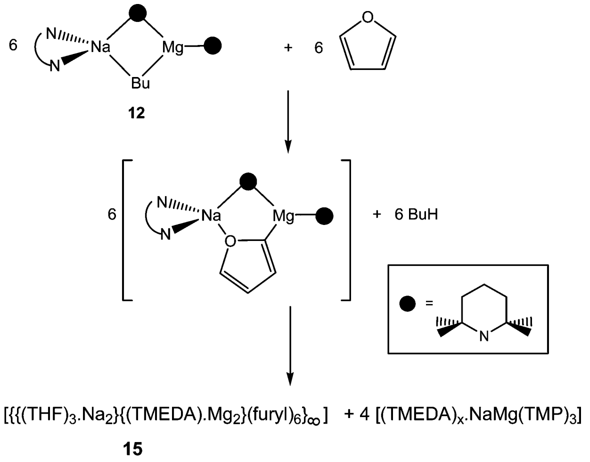
---

[47] Andrews, P. C.; Kennedy, A. R.; Mulvey, R. E.; Raston, C. L.; Roberts, B. A.; Rowlings, R. B. *Angew. Chem., Int. Ed.* **2000**, *39*, 1960.

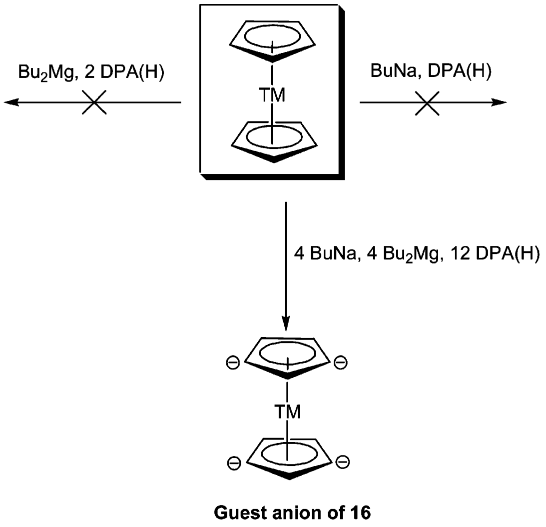
[48] Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Talmard, C. *Chem. Commun.* **2006**, 417.

[49] Gilman, H.; Breuer, F. *J. Am. Chem. Soc.* **1934**, *56*, 1123.

Scheme 10. Proposed Disproportionation Pathway for the Formation of a Furyl Inverse Crown



Scheme 11. Synergic Fourfold Deprotonation of Ferrocene, Ruthenocene, and Osmocene



via Mg(μ-TMEDA)Mg intermolecular bonding. Note that this homoleptic arrangement is thought to be the product of disproportionation of a mixed mono(furyl)−bis(amido) intermediate, the coproduct being TMEDA-solvated NaMg(TMP)$_3$ (Scheme 10).

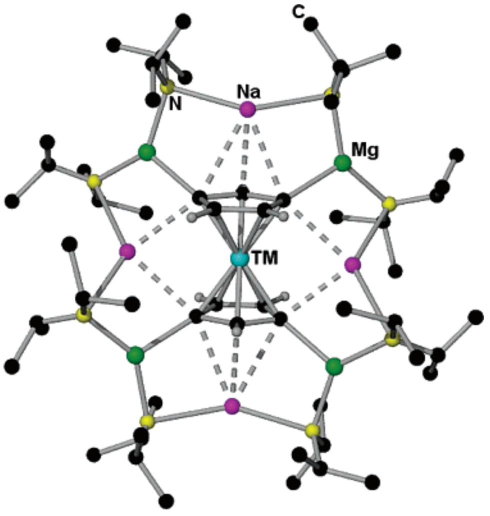


Figure 17. Molecular structure of the metallocenyl inverse crown **16**.

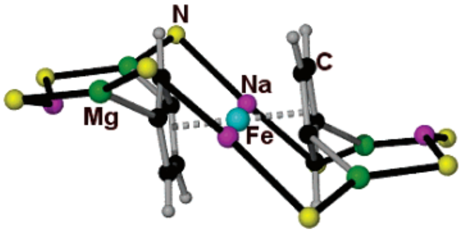


Figure 18. Side view of **16** (where TM = Fe), highlighting its stretched *Z* conformation.

Extension to Metallocenes and Metal π-Arene Complexes

To date the most spectacular demonstration of the extraordinary power of the synergic effect has come in the area of metallocene deprotonation chemistry. The ability to regioselectively metalate parent metallocene molecules (most especially ferrocene) is of fundamental importance. Entry can be gained to a vast pool of ring-substituted derivatives, compounds much in demand across the borders of science, medicine, and technology,[50] by exploiting the metal-activated metallocenes as synthetic intermediates. Lithiation is the tool most often put to use for this purpose. For example, monolithioferrocene is accessible in high yield by treating ferrocene with a *tert*-butyllithium solution in THF.[51] When more than one hydrogen atom needs removing from a parent metallocene (or an already substituted derivative), then regioselective polymetalation is usually required. Dilithiation of ferrocene (orientated mainly in the 1,1′-positions) can be accomplished by adding 2 equiv of the alkyllithium base in the presence of an activating tertiary amine such as TMEDA.[52] Controlled, higher lithiation (or any higher polar metalation) of ferrocene has not yet proved possible to any synthetically useful extent. However, using a synergic synthetic strategy similar to that applied to the arene substrates, a path has now been opened to pure, well-defined, polymetalated metallocenes. Thus, subjecting ferrocene, ruthenocene, or osmocene to the synergic amide base sodium−magnesium tris(diisopropylamide) affords a unique group 8 homologous series of polymetalated metallocenes of general formula [{M(C$_5$H$_3$)$_2$}Na$_4$Mg$_4$(DPA)$_8$] (**16**, where M = Fe, Ru, Os; Scheme 11).[53] Their common molecular, new inverse crown motif is spectacular (Figure 17), comprising a 16-membered [(NaNMgN)$_4$]$^{4+}$ host ring and a metallocenetetraide [M(C$_5$H$_3$)$_2$]$^{4-}$ guest core. The azametalla host ring is severely puckered, adopting a stretched Z-like conformation (Figure 18). Hydrogen atoms have been selectively cleaved from the 1,1′,3,3′-positions of the parent metallocene in generating the tetraanionic guest. Since magnesium atoms refill these cleaved hydrogen atom sites, in keeping with the pattern observed in other deprotonation-derived inverse crowns, these novel metallocenetetraide complexes can also be classified as products of (tetra)magnesiation.

---

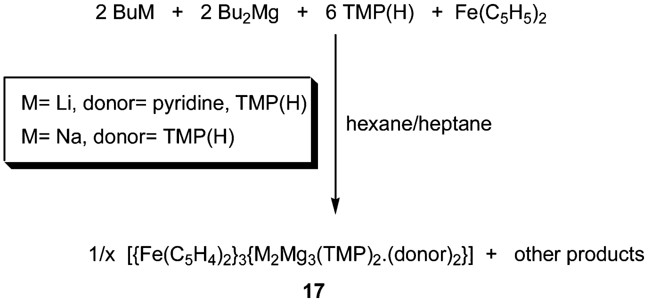
(50) Togni, A.; Hayashi, T. *Ferrocenes*; VCH: Weinheim, Germany, 1995.

(51) (a) Rebieré, F.; Samuel, O.; Kagan, H. B. *Tetrahedron Lett.* **1990**, *31*, 3121. (b) Sanders, R.; Mueller-Westerhoff, U. T. *J. Organomet. Chem.* **1996**, *512*, 219.

(52) Butler, I. R.; Cullen, W. R.; Ni, J.; Rettig, S. J. *Organometallics* **1985**, *4*, 2196.

(53) (a) Clegg, W.; Henderson, K. W.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Rowlings, R. B.; Tooke, D. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 3902. (b) Andrikopoulos, P. C.; Armstrong, D. R.; Clegg, W.; Gilfillan, C. J.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Parkinson, J. A.; Tooke, D. M. *J. Am. Chem. Soc.* **2004**, *126*, 11612.

Scheme 12. Synthesis of Mixed Alkali-Metal−Magnesium Trinuclear Ferrocenophanes



The critical nature of the alkali metal (sodium) in mediating this magnesiation can be appreciated by the knowledge that the parent magnesium bis(diisopropylamide) is inert toward ferrocene (and its group 8 congeners) and, even more remarkably, that *direct* magnesiation of them is not possible using any conventional organomagnesium base (Grignard reagents, bis(alkyls), etc.). Ferrocenylmagnesium compounds are known, for example $[(FcN)_2Mg{\cdot}THF]$[54] (where FcNH is dimethylaminomethylferrocene), but these are not synthesized via direct magnesiation but usually by metathesis from a lithioferrocene and a magnesium halide. Clearly the mediation of the sodium amide greatly enhances the basicity of its magnesium bis(amide) partner, enabling deprotonation of not just one metallocene C−H bond but four such bonds. The signature synergic σ/π bonding of inverse crowns is also featured in the structures of **16**, though the Mg atoms do not lie exactly coplanar with the aromatic ring planes (deviation range 0.875−1.141 Å) as they do in the arenediide inverse crowns **11**. The bridge span in the host ring may be a factor in this distinction, as in **11** the Mg atoms are joined by five-membered N−Na−N−Na−N bridges, whereas in **16** they are joined by more restrictive three-membered N−Na−N bridges. In contrast, the π-bonding preference of sodium for the guest is more clear-cut, especially those in the pseudoaxial sites, which engage with the π-face of the Cp′ ring in a η^3 manner. NMR spectroscopic studies of **16**[53b] indicate that each congener exists as two distinct interconverting conformers in arene solution, one of which is thought to resemble the molecular structure in the crystal.

TMP is generally regarded to be a stronger base than DPA. Logically it should be expected, therefore, that an in situ solution of "$NaMg(TMP)_3$" (which we now know is actually a mixture of $NaMgBu(TMP)_2$ and TMPH) would be more basic than "$NaMg(DPA)_3$". However, this is where the unpredictability and counterlogic of this synergic mixed-metal amide chemistry comes to the fore. The DPA base can effect fourfold deprotonation of ferrocene as outlined above, but the TMP analogue proves to be less effective, as it can only pull off two hydrogen atoms from ferrocene. Nonetheless, this more usual 1,1′-twofold deprotonation reaction (Scheme 12)[55] is manifested in a novel series of trinuclear ferrocenophanes of general formula $[\{Fe(C_5H_4)_2\}_3\{M_2Mg_3(TMP)_2{\cdot}2(donor)\}]$ (**17**: M = Na, donor = TMPH; M = Li, donor = TMPH, pyridine). In the common structural motif of **17** (Figure 19) each of the three Mg atoms independently stitches together the three ferrocene-1,1′-diyl units, with the centric Mg binding exclusively to ferrocenyl C atoms. The two peripheral Mg atoms also bind to a TMP ligand, which bridges to a donor-stabilized alkali-metal center (lithium or sodium). No precedent exists for this extraordinary class of heterotrimetallic ocmplex, in either composition or structure. The closest analogy to date is the homo main group metallic gallium-bridged species $[\{Fe(C_5H_4)_2\}_3\{Ga{\cdot}(pyridine)\}_2]$ reported by Jutzi et al.[56] At present the mechanism involved in the formation of **17** has not yet been elucidated. However, a clue is perhaps provided by its odd 2:3 Na:Mg stoichiometry (though equimolar proportions were present in the reaction mixture) coupled with the fact that, although six C−H deprotonations have occurred, the structure of **17** contains only three residues (two complete with Na and Mg atoms and one incomplete with Mg only) of the base. This implies that both intermolecular and intramolecular deprotonations have taken place, accompanied by a disproportionation or cleavage of a metal-containing fragment (Na(TMP) is an obvious candidate). Given the high steric demands of both ferrocene and TMP individually, and especially collectively when linked together via short Mg bridges, it is reasonable that such a cleavage would be strongly favored to relieve steric strain. Therefore, it is likely that the diminished (poly)basicity of "$NaMg(TMP)_3$" compared to that of "$NaMg(DPA)_3$" is steric in origin rather than electronic.

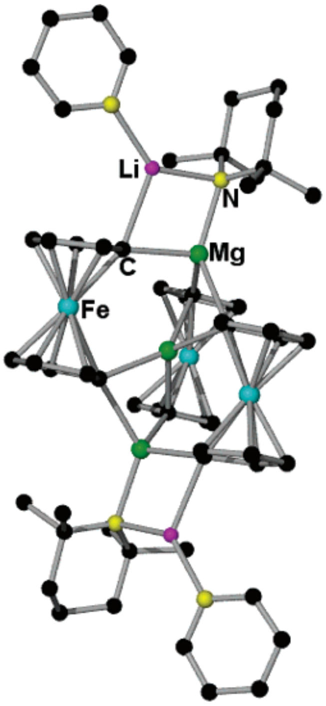


Figure 19. Molecular structure of the mixed lithium−magnesium trinuclear ferrocenophane **17** (where donor = pyridine).

The metal π-arene complex bis(benzene)chromium,[57] another classical organometallic molecule like ferrocene, has also been subjected to alkali-metal-mediated magnesiation. Elschenbroich has studied the metalation of bis(benzene)chromium using mainstream organometallic bases since the 1960s and found that it is best accomplished by TMEDA-activated butyllithium.[58] The heteroannular dilithio derivative "$[Cr(C_6H_5Li)_2]$" is the major product, since lithiation of one chromium-bound benzene ring activates the compound toward a second lithiation (on the other ring); hence, the yield of the monolithio derivative "[Cr(C_6H_5-

---

[54] Seidel, N.; Jacob, K.; Fischer, A. K.; Pietzsch, C.; Zanello, P.; Fontani, M. *Eur. J. Inorg. Chem.* **2001**, 145.

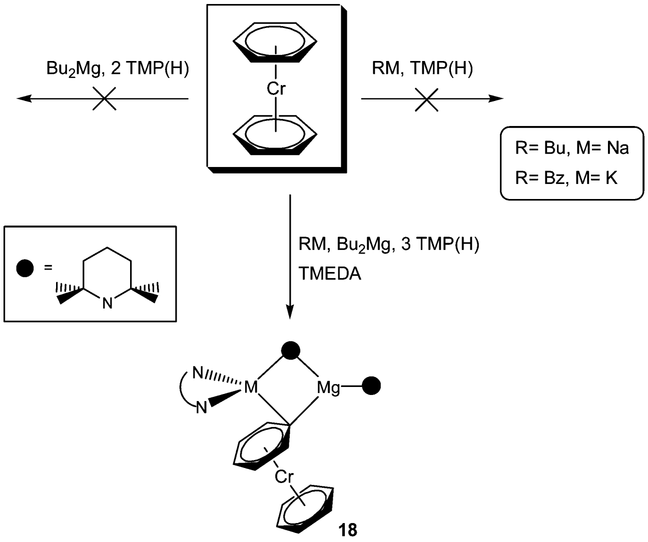
[55] Henderson, K. W.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Rowlings, R. B. *Chem. Commun.* **2001**, 1678.

[56] Jutzi, P.; Lenze, N.; Neumann, B.; Stammler, H.-G. *Angew. Chem., Int. Ed.* **2001**, *40*, 1424.

[57] For a historical account of the human and chemical story behind bis(benzene)chromium see: Seyferth, D. *Organometallics* **2002**, *21*, 1520, 2800.

[58] Elschenbroich, C. *J. Organomet. Chem.* **1968**, *14*, 157.

Scheme 13. Synergic Monodeprotonation of Bis(benzene)chromium



Li)(C_6H_6)]” is always much poorer, irrespective of the initial stoichiometry used in the reaction. Note also that neither of these lithio intermediates have been crystallographically characterized. In view of this background, the result of reacting bis(benzene)chromium with either a sodium−magnesium or potassium−magnesium amide mixture in the presence of TMEDA (Scheme 13) is surprising:[59] even when the synergic base is employed in a 4:1 molar excess with respect to the reactant, metalation (magnesiation) occurs selectively on only one benzene ring, manifested in red crystalline products of the general formula [TMEDA·MMg{Cr(C_6H_5)(C_6H_6)}($TMP)_2$] (**18**, M = Na, K). Thus, this synergic metalation strategy provides (potentially) the best method yet (isolated yields of crystalline **18** are typically greater than 60%) for entry into regioselectively monofunctionalized bis(benzene)chromium complexes (which may be particularly useful in asymmetric synthesis). Homometallic (that is, nonsynergic) control experiments that employ the same TMPH/TMEDA mixtures but with only a single metalating reagent (butylsodium, benzylpotassium, or dibutylmagnesium) fail to similarly promote metalation of bis(benzene)chromium, thus establishing that the selective monodeprotonation behind the synthesis of **18** is genuinely synergic in origin. Moreover, direct magnesiation of bis(benzene)chromium is not possible with a Grignard reagent or with any homometallic magnesium bis(alkyl) or bis(amido) base; hence, these reactions also belong in the category of alkali-metal-mediated magnesiations. Strictly the prefix “TMEDA-activated” should be added here, as a donor ligand (even excess TMPH will suffice) is necessary to effect metalation (TMEDA also aids crystallization of **18**). The molecular structures of **18** are basically the same (for brevity only the potassium example is shown in Figure 20). They resemble closely the structure of **13** but have an additional exo “Cr(C_6H_6)” fragment attached to the phenyl ring, which bridges M and Mg centers as part of a near-planar, four-element MNMgC ring (also observed in **12**). The signature synergic σ/π bonding is also evident, since Mg is only slightly off-coplanar with the Ph ring plane, while the Na and K cations engage in a η^2 and η^3 mode, respectively, with the Ph π-system. A question still remains as to why twofold deprotonation of bis(benzene)chromium does not occur when the synergic base is present in a large molar excess. From molecular models it is clear that twofold deprotonation is not blocked sterically, as a second TMP−Mg−TMP−M−TMEDA coordination arc could be easily added to the second benzene ring if it too was monodeprotonated. The explanation must therefore involve electronics, though the precise reason for this electronic inertness toward a second metalation is as yet unknown.

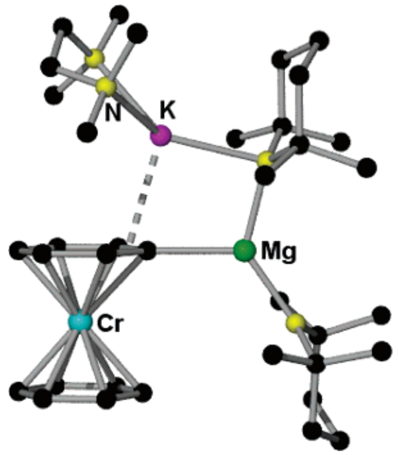


Figure 20. Molecular structure of the synergically magnesiated bis(benzene)chromium complex **18**.

Alkali-Metal-Mediated Zincation

Though zinc is in group 12, due to its stable filled d shell it exhibits few of the characteristic properties of the transition elements. As its reactivity is centered on its s^2 valence shell configuration, zinc has more in common with magnesium, and indeed, many of their inorganic compounds are isomorphous. The important similarities in the context of the present discussion are similar ion size, stability of the +2 oxidation state, ability to assume a trigonal-planar (ate) coordination geometry, and a propensity to form strong σ-bonds with carbon. In general, due in part to zinc’s greater electronegativity, zinc−carbon bonds are several picometers shorter, and consequently stronger, than corresponding magnesium−carbon bonds; hence, in theory zinc could be even better than magnesium in fulfilling the σ-bonding role within synergic σ-/π-bonded divalent-metal/alkali-metal complexes (that is, the greater stability of Zn−C σ-bonds should be transmitted to the overall stability of the complex). The development of this alternative concept of *alkali-metal-mediated* zincation is still in its early stages; however, as now outlined, on the basis of the results of the first few “synergic trials”, its promise as a novel new synthetic methodology appears likely to be realized.

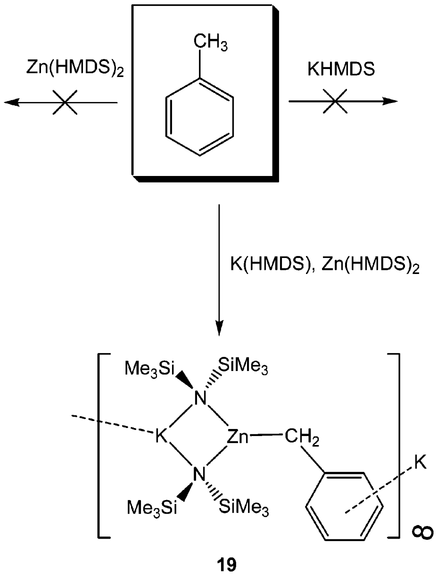
Neither KHMDS nor Zn($HMDS)_2$ can unilaterally metalate toluene. The former reagent is actually sold commercially as a solution in toluene. Surprisingly, however, when these HMDS reagents are combined in “KZn($HMDS)_3$”, toluene is smoothly deprotonated at the thermodynamically most acidic methyl site, to generate the benzyl product [{KZn($HMDS)_2$ (CH_2Ph)}$_\infty$] (**19**; Scheme 14).[2] This synergic deprotonation can also be applied to other methylbenzene molecules such as *m*-xylene and mesitylene. What is perhaps most intriguing in the case of **19** is that the synergy appears to switch off when zinc is substituted by magnesium. Toluene is not deprotonated by the analogous magnesium complex “KMg($HMDS)_3$”; instead, it is utilized as a neutral π-arene ligand in the magnesiate [{[K(toluene)$_2$]$^+$[Mg($HMDS)_3$]$^-$}$_n$] (where $n = 2, \infty$).[60] Switching from potassium

---

[59] Hevia, E.; Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E.; Sherrington, D. C. *Angew. Chem., Int. Ed.* **2005**, *44*, 68.

[60] Forbes, G. C.; Kennedy, A. R.; Mulvey, R. E.; Roberts, B. A.; Rowlings, R. B. *Organometallics* **2002**, *21*, 5115.

Scheme 14. Synergic Deprotonation of Toluene Using Mixed Potassium−Zinc Tris(HMDS)



to the heavier alkali metal rubidium in the zincate system[60] appears to suppress deprotonation as well, because a similar neutral π-toluene complex, $[\{Rb(toluene)_3]^+[Zn(HMDS)_3]^-\}_\infty]$, is produced. Clearly there are alkali-metal effects as well as magnesium zinc effects at play in these mixed-metal compositions. The signature synergic σ-/π-bonding characteristic of the magnesium systems is present but is expressed in a new way in the crystal structure of zincate **19** (Figure 21): the benzyl $C(H)_2$ forms a strong σ-bond to the zinc terminus of a rhomboidal $[K(\mu\text{-HMDS})_2Zn]$ ring, while, electron-rich from the negative charge, the benzyl π-face coordinates intermolecularly to K^+ in the adjacent (KNZnN) ring to extend the structure supramolecularly through a chain with a glide plane.

The success of this alkali-metal-mediated zincation of toluene using moderately basic HMDS heightened our expectations of what might be achievable using the stronger base TMP. Searching the literature raised expectations even higher, as we noted that Kondo and Uchiyama had recently developed the lithium TMP−zincate "$LiZn^tBu_2(TMP)$" and showed that it exhibited high levels of chemo- and regioselectivity toward the deprotonation of a series of functionalized aromatics[61] and heteroaromatics.[62] No structural details of the zincate reagent or of any metalated intermediates were reported in these studies. Wishing to explore the synergic consequences of mixing sodium and zinc (inspired by the novel chemistry of the sodium−magnesium systems), we prepared a sodium TMP−zincate as its TMEDA adduct, $[(TMEDA)\cdot Na(\mu\text{-}^tBu)(\mu\text{-TMP})Zn(^tBu)]$ (**20**; Scheme 15).[63] The lithium TMP−zincate had been prepared in the bulk (polar) solvent THF, but to increase the opportunity for crystallization, **20** was made in nonpolar hexane to which was added 1 molar equiv of polar TMEDA. Accordingly, crystallization proved remarkably easy, allowing its crystal structure (Figure 22) to be determined. This molecular structure, at least in a connectivity sense, bears a close resemblance to that of the sodium−magnesium mono(alkyl)−bis(amido) complex **12**: thus, a TMEDA-chelated Na bridges through TMP to a Zn or Mg carrying a terminal ligand (^{t}Bu in **20,** TMP in **12**), while an alkyl (^{t}Bu in **20,** ^{n}Bu in **12**) ligand forms a second bridge between Na and Zn or Mg. The zincate or magnesiate character of these structures is best gauged by their trigonal-planar coordination geometries, which include short Zn−μ-C or Mg−μ-C alkyl bonds; however, in contrast the Na−C(alkyl) bridges are long and weak and, moreover, distinct, involving an agostic Me contact in **20** and an α-CH_2^- atom on **12**. Therefore, in the absence of an aromatic ligand the structure of **20** improvises by introducing a new type of synergic bonding, a σ/agostic combination, to help satisfy the coordination requirements of the Mg/Na partnership. Agostic contacts are inherently weak; thus, the Na···Me agostic contact could be viewed as a potential reactivity hotspot within **20**. This appears to be the case in its reaction with benzene (Scheme 15), as in affording the hetero(tri)leptic zincate $[(TMEDA)\cdot Na(\mu\text{-Ph})(\mu\text{-TMP})Zn(^tBu)]$ (**21**) the deprotonated substrate Ph reoccupies

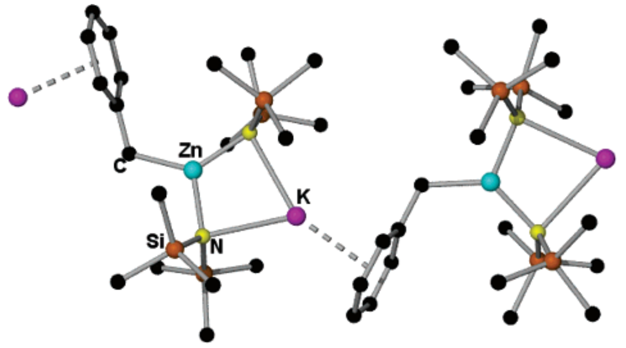
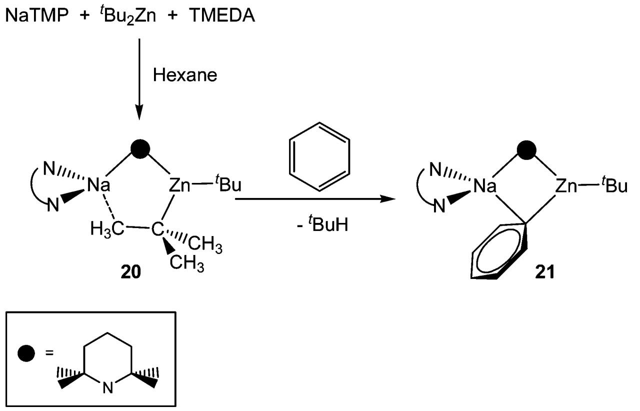


Figure 21. Section of the polymeric structure of the mixed potassium−zinc mono(benzyl)−bis(HMDS) complex **19**.

Scheme 15. Synthesis of the Sodium TMP−Zincate Reagent 20 and Its Reaction with Benzene



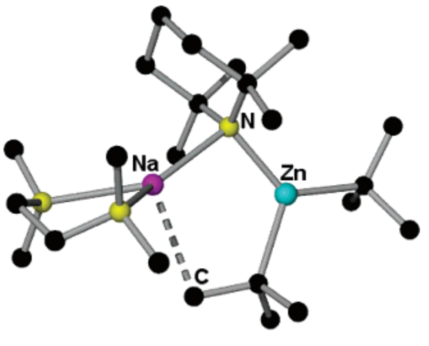


Figure 22. Molecular structure of the sodium dialkyl amido zincate reagent **20**.

---

[61] (a) Uchiyama, M.; Miyoshi, T.; Kajihara, Y.; Sakamoto, T.; Otani, Y.; Ohwada, T.; Kondo, Y. *J. Am. Chem. Soc.* **2002**, *124*, 8514. (b) Kondo, Y.; Shilai, M.; Uchiyama, M.; Sakamoto, T. *J. Am. Chem. Soc.* **1999**, *121*, 3539.

[62] Imahori, T.; Uchiyama, M.; Sakamoto, T.; Kondo, Y. *Chem. Commun.* **2001**, 2450.

[63] Andrikopoulos, P. C.; Armstrong, D. R.; Barley, H. R. L.; Clegg, W.; Dale, S. H.; Hevia, E.; Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E. *J. Am. Chem. Soc.* **2005**, *127*, 6184.

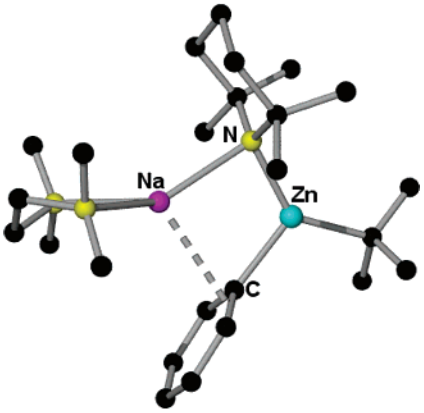


Figure 23. Molecular structure of the hetero(tri)leptic zincate **21**.

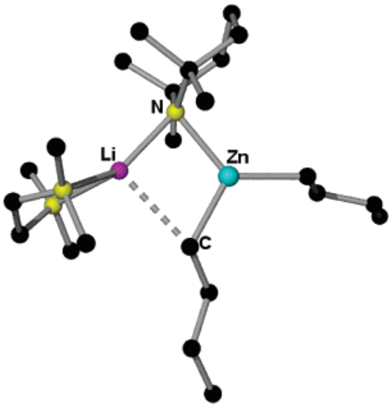


Figure 24. Molecular structure of the lithium TMP−zincate reagent **22**.

the bridging site left by the expelled ^{t}Bu, with Na⋯Ph π-contacts replacing Na⋯Me agostic contacts (Figure 23). Here **20** functions as an alkyl base, in contrast to the TMP basicity exhibited by "LiZn^{t}Bu$_2$(TMP)" in the Kondo/Uchiyama work. A major factor in the distinction could be that the two metal centers hold on strongly to the TMP bridge in the backbone of **20**, diminishing its deprotonating power, which leads to the backbone being retained in **21**, whereas as "LiZn^{t}Bu$_2$(TMP)" is employed in neat THF solution the solvent-separated ion pair [{Li(THF)$_x$}$^+${Zn^{t}Bu$_2$(TMP)}$^-$] is more likely, in which TMP is bound to Zn only and consequently is endowed with enhanced deprotonating power. It should be emphasized that neither the alkyl basicity of ^{t}Bu$_2$Zn nor the amido basicity of Na(TMP) is strong enough on its own to inflict deprotonation upon benzene; hence, the reaction of **20** with benzene represents a synergic metalation or, more specifically, a sodium-mediated zincation.

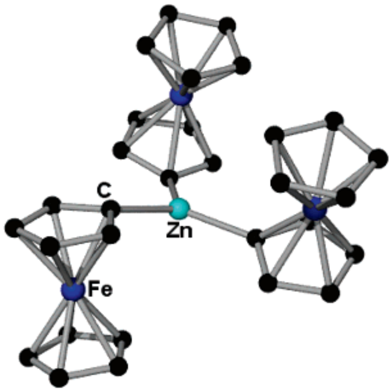
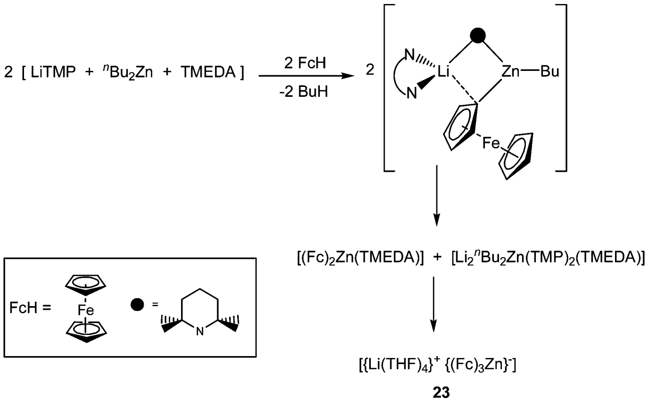


Figure 25. Anionic moiety of the lithium triferrocenylzincate **23**.

Scheme 16. Synergic Zincation of Ferrocene



A complementary lithium-mediated zincation is starting to be developed as well. Under bulk apolar conditions, the crystalline lithium TMP−zincate reagent [(TMEDA)·Li(μ-^{n}Bu)(μ-TMP)Zn(μ-^{n}Bu)] (**22**) has been synthesized by mixing together LiTMP, ^{n}Bu$_2$Zn, and TMEDA in equimolar proportions.[64] The molecular structure of **22** (Figure 24), appears cast from the same mould as that of magnesiate **12**, having an ion-contacted ate arrangement, with the contact through a short Li−N(TMP) bond and a long (weak) Li−C(n-butyl) bond. Confirming its synergic reactivity, reagent **22** can effect the zincation of ferrocene, in contrast to its homometallic component parts LiTMP and ^{n}Bu$_2$Zn, which are both inert toward ferrocene even in the presence of TMEDA. Following a disproportionation pathway (Scheme 16), the reaction with ferrocene produces sequentially two monodeprotonated ferrocene (C$_5$H$_4$FeC$_5$H$_5$, Fc) products: initially the lithium-free neutral bis(ferrocenyl) zinc complex [(Fc)$_2$Zn·(TMEDA)] and finally the tris(ferrocenyl)-zincate [{Li(THF)$_4$}$^+${(Fc)$_3$Zn}$^-$] (**23**; Figure 25).[64] This result highlights the promise of alkali-metal-mediated zincation as a new synthetic tool, since this represents the first example of *direct* zincation of a metallocene, whereas in general mainstream zinc alkyl reagents are not basic enough for this purpose. Previously it was necessary to use a metathetical approach involving a zinc halide and a premetalated (often lithiated) metallocene to generate a compound with zinc directly attached to the carbon framework of the metallocene.[65]

Synergic Nucleophilic Addition

To date our studies of mixed alkali-metal zincate reagents have been almost entirely confined to deprotonative metalation applications. Another cornerstone technique of synthetic chemistry in which organometallic (especially organolithium) reagents are utilized heavily is in nucleophilic addition. This poses the question "How would the new reagents behave as nucleophiles?". Our first exploration in this area has produced a remarkable result. Thus, we have probed the reactivity of [(TMEDA)·Na(μ-^{t}Bu)(μ-TMP)Zn(^{t}Bu)] (**20**) toward benzophenone.[66] This ketone was chosen because it lacks acidic H atoms, thus preventing competing deprotonation reactions, and because a previous study by Uchiyama ascertained that it is reduced nonselectively by a NaH/ZnCl$_2$/2^{t}BuLi mixture (a solution

---

(64) Barley, H. R. L.; Clegg, W.; Dale, S. H.; Hevia, E.; Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E. *Angew. Chem., Int. Ed.* **2005**, *44*, 6018.

(65) Seidel, N.; Jacob, K.; Zanello, P.; Fontani, M. *J. Organomet. Chem.* **2001**, *620*, 243.

(66) Hevia, E.; Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E. *J. Am. Chem. Soc.* **2005**, *127*, 13106.

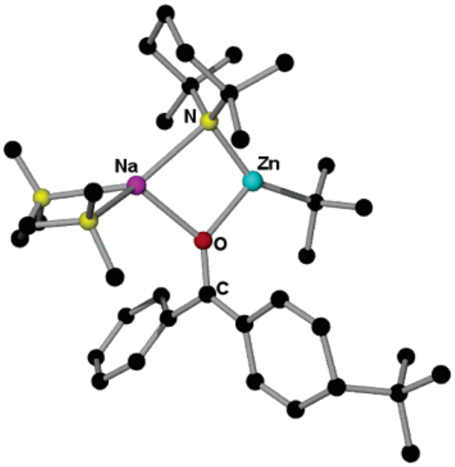
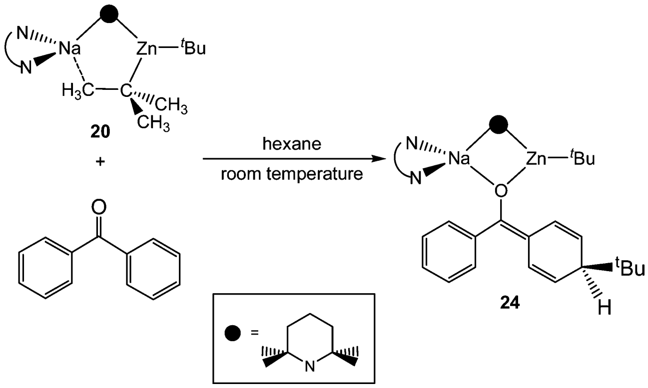


Figure 26. Molecular structure of the 1,6-adduct of benzophenone **24**.

Scheme 17. Synergic 1,6-Addition of Sodium TMP−Zincate 20 to Benzophenone



synthon of the zincate $Zn^tBu_2H^-$) to give both $^tBu^-$ and H^- 1,2-addition products in poor yield (18 and 4%, respectively).[67] In contrast, **20** converts benzophenone selectively to the mono-*tert*-butylated 1,6-adduct **24** (Scheme 17), which remarkably, due to stabilization of the dearomatized enolato anion by coordination to the bulky sodium alkylamidozincate cation left following alkyl transfer, has been obtained in an isolable crystalline form (yield 60%). Comparing the molecular structure of **24** (Figure 26) with that of the reactant alkylating agent **20** reveals that the ^{t}Bu exit and butylated-enolato entry occurs with retention of connectivity within the remaining backbone of the structure. This again points to the $Na\cdots(\mu\text{-Me})(Me)_2C-Zn$ junction being the reactivity hotspot of **20**, as was the case in its aforementioned reaction with benzene in producing **21**. Olah previously reported[68] that benzophenone could be efficiently *tert*-butylated to 4-*tert*-butylbenzophenone (yield 52%) with *tert*-butyllithium and oxidizing thionyl chloride, though no lithium enolates were observed in this study. However, the new zincate reagent method has the added advantages that it permits isolation/crystallization/characterization of the reactive enolate and, most importantly, the butylation is carried out at room temperature, whereas the more aggressive lithium reagent has to be employed at −100 °C.

Clearly if this result could be built upon in the future, then it could have major repercussions for synthesis. Nucleophilic addition protocols involving lithium reagents, an indispensable tool of the synthetic chemist's repertoire, are routinely performed at subambient temperature (usually −78 °C) to avoid side reactions and decomposition pathways. If a complementary chemistry could be developed at room temperature based on synergic alkali-metal zincates, then this would be good news both economically, with the prospect of energy savings for industrial-scale reactions on circumventing the need for coolants, and chemically, as it would allow the study and potential isolation/characterization of reactive intermediates such as **24**.

Closing Remarks: The Origins of Synergy

Considering that directed metalation reactions utilizing organolithium reagents (for example, directed ortho metalation (DOM)[69] and lithiation α to heteroatoms[70]) have been studied for several decades and are still not fully understood except in selected special cases, then clearly it will take some time to unravel the complexities of the chemistry of the mixed-metal systems described in this article. The synergic effect(s) probably involves a superimposition of several factors, which are difficult to delineate precisely at this stage. However, on the basis of the work carried out thus far, it appears that there are at least three key aspects to achieving special mixed-metal-induced regioselective magnesiations or zincations. First, there must be an intimate contact between the alkali metal and magnesium or zinc, either through an amido bridge or alkyl bridge or some combination thereof. DFT calculations on model systems (mostly unpublished work) show that more often than not mixed-metal structures are energetically preferred to their two homometallic component structures. Thus, the formation of mixed-metal structures is thermodynamically driven. Second, the substrate to be deprotonated apparently enters the coordination sphere of the alkali metal (consistent with the notion of alkali-metal mediation) and is locked in through metal−π-arene or some other type of interaction (possibly agostic bonding). This can be likened to the "complex-induced proximity effect"[71] that is believed to be a key contributing factor in DOM reactions. Supporting this idea, we have crystallographically characterized a sizable number of mixed alkali-metal−magnesium or −zinc tris(HMDS) complexes in which an arene such as benzene, toluene, or *o*-xylene engages in π-interactions with the alkali-metal component. The anionic $M^{II}(HMDS)_3^-$ moiety (M^{II} = Mg, Zn) can be contacted to the alkali metal via agostic $(Me_2Si)H_3C\cdots M$ interactions, as in the aforementioned $[\{[K(toluene)_2]^+[Mg(HMDS)_3]^-\}_n]$, or separated, as in the novel mixed π-ferrocene π-toluene complex $[\{K(\eta^5\text{-ferrocene})_2(\eta^3\text{-toluene})_2\}^+\{Mg(HMDS)_3\}^-]$.[72] In these cases it is assumed that $Mg(HMDS)_3^-$ is not sufficiently basic enough under the conditions studied to effect deprotonation of the alkali-metal-coordinated substrate. In the other cases the alkali-metal−substrate interaction must help fix the stereochemistry of the complex and thus be a major factor in directing the subsequent deprotonation regioselectively (Figure 27). The third key aspect is that an alkali-metal-mediated magnesiation or zincation must then take place and, as the prebinding of the substrate molecule would lower the entropy of the deprotonation reaction, the

---

(67) Uchiyama, M.; Koike, M.; Kameda, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1996**, *118*, 8733.

(68) Olah, G. A.; Wu, A.-H.; Farooq, O. *Synthesis* **1991**, 1179.

(69) For leading references see: Hartung, C. G.; Snieckus, V. The Directed *ortho* Metalation Reaction. A Point of Departure for New Synthetic Aromatic Chemistry. In *Modern Arene Chemistry,*; Astruc, D., Ed.; Wiley-VCH: New York, 2002; pp 330−367.

(70) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon/Elsevier Science: Oxford, U.K., 2002.

(71) Schlosser, M. *Organometallics in Synthesis*; Wiley: Chichester, U.K., 1994; pp 1−167.

(72) Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E.; Sherrington, D. C. *Organometallics* **2004**, *23*, 1197.

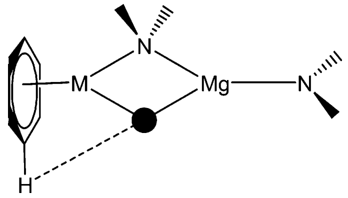


Figure 27. Hypothetical alkali-metal π-arene complex with a fixed stereochemistry primed for regioselective intramolecular deprotonation.

basicity of the magnesium or zinc center is greatly enhanced compared to that of mainstream homometallic magnesium or zinc bases, in which such prebinding is not possible.

Finally, in the course of writing this review, my research group has made several important new discoveries, especially in the context of synergic zincation, which significantly broadens the scope of this chemistry. These new results will be published shortly.

Acknowledgment. I owe a great deal of thanks to past and present members of my research group, not only for helping to develop this work but also for the friendship and fun they have shared with me and each other along the way. Special thanks go to the recent members of my group Eva Hevia, Gordon Honeyman, and Charlie O'Hara, whose research in particular has given us a far greater understanding of the area, and to Allison Drummond, who ensures the smooth running of our laboratory. Moreover, I am sincerely grateful for the indispensable collaborations with the X-ray crystallographic experts (Alan Kennedy at Strathclyde and Bill Clegg and Sophie Dale at Newcastle) and the theoreticians (Dave Armstrong and Prokopis Andrikopoulos). Financial support from the UK EPSRC, the Royal Society/Leverhulme Trust, and the EU is gratefully acknowledged. Finally I thank Dwight Sweigart for inviting me to write this review.

OM0510223