s-Block metal inverse crowns: synthetic and structural synergism in mixed alkali metal–magnesium (or zinc) amide chemistry

Robert E. Mulvey

Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, UK G1 1XL.
E-mail: r.e.mulvey@strath.ac.uk

This article focuses on the special chemistry that can take place when certain lithium (or other heavier alkali metal) amides are combined with certain magnesium (or zinc) bisamides. Some of the reaction mixtures studied follow a straightforward path leading to simple heterobimetallic compositions with predictable structures, whereas others take an unexpected turn to behave as powerful oxygen scavengers or as regioselective bases to yield novel products with unpredictable host–guest macrocyclic structures. We refer to these new compounds as 'inverse crown ethers' or 'inverse crowns' because their arrangement of Lewis acidic and Lewis basic sites is opposite to that encountered in conventional crown ether complexes. This developing phenomenon appears to be a direct result of pairing together the two distinct metal types in the same complex, as the chemistry cannot be replicated by complexes containing one or the other metal type on its own.

Introduction

Diagonal neighbours in the periodic table, lithium and magnesium in the form of organolithium (pioneered by Schlenk) and organomagnesium halide (pioneered by Barbier and Grignard) reagents respectively, have both served the synthetic community for nearly one hundred years. Thumb through the pages of any current journal specialising in synthesis and you will almost certainly find several examples of these centenarians at work, performing some or other organic transformation. They are organometallic reagents *par excellence*. Accordingly, the literature on them is vast and ever increasing. Interested readers should consult the following sources[1,2] as a starting point for information. The present article does not deal with organolithium or organomagnesium compounds *per se*, but rather with organolithium–magnesium (and related organosodium–magnesium and organopotassium–magnesium) compounds, *i.e.* heterometallic mutations containing two different s-block metals. In theory, mixing the metal components in this way could promote beneficial synergic effects, and lead to mixed-metal

compounds having their own unique chemical profiles distinct from those of the homometallic compounds from which they are derived. This synergism could be manifested in altered reactivities and selectivities as a function of altered activated complexes and intermediates. It could also deliver new chemistry and new structures, not known or not possible for the conventional homometallic compounds. In practice, though as yet only a select few studies have addressed the application of mixed lithium–magnesium compounds in chemistry, several promising observations have already been recorded. Notably, Oshima and coworkers have demonstrated that magnesium-ate complexes 'LiMgR₃' are more effective than their Grignard counterparts (RMgX) in halogen–magnesium exchange reactions with organic halides for the preparation of aryl- and alkenyl-magnesium reagents, which are subsequently trapped by an assortment of electrophiles.[3] Also, following a systematic study of alkylation reactions of pyridine, Richey and Farkas concluded that 'solutions prepared by mixing solutions of dialkylmagnesium and alkyllithium compounds exhibit behaviour different from that of either organometallic compound alone'.[4] Turning from organic synthesis to coordination chemistry, Karsch and Reisky make the point that the key to the formation of the first magnesium compound with six Mg–P bonds lies in its 'ate formulation [Li(12-crown-4)₂]⁺[Mg{(PMe₂)₂C(SiMe₃)}₃]⁻, *i.e.* a mixed lithium–magnesium system albeit in the form of a solvent (crown ether)—separated ion pair.[5] Combining the two metals together has similarly proved advantageous in areas of polymer chemistry: Hsieh and Wang report that dialkylmagnesium, by itself, is not an active initiator for diene and styrene polymerization, but it participates in polymerization when complexed either with the alkyllithium initiator or with the propagating polymer–lithium molecules;[6] Antkowiak and Hall have patented the use of mixed lithium–magnesium amides based on hexamethyleneimine as anionic initiators for diene polymer and copolymer elastomers.[7] It is pertinent to note that in not one of these molecular/macromolecular applications is the structure of the active lithium–magnesium species known with any certainty. This general lack of knowledge coupled with the potential advantages alluded to earlier have prompted us to follow a programme of research designed to shed light on the fundamental structural consequences of mixing lithium (or another alkali metal) with magnesium (or zinc) in an organoelement environment. Mindful of the need to focus on synthetically useful compounds, we have directed our attention towards amide derivatives. Long-standing favourites of the synthetic chemist and thus commercially available, lithium amide reagents are specialists in the art of selective proton abstraction; recent studies have suggested that magnesium amides may also be useful and exhibit different reactivities/selectivities in this regard.[8] The extensive library of structural data available on these homometallic systems provides a further incentive for concentrating on amide derivatives because if any form of structural synergism were to result from pairing lithium and magnesium in a particular amide environment, then it should be easily recognised. It transpires that
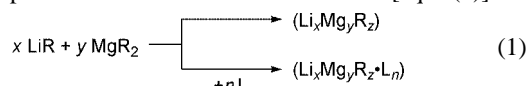
unique structural arrangements and, linked to this, unique chemistry, can indeed be generated by this heterobimetallic approach, as exemplified by the so-called 'inverse crown ether' complexes and related mixed-metal macrocycles which form the basis of this article. To put the novelty of this new class of compound into context, a brief survey of the contrasting structural types adopted by more mainstream mixed lithium–magnesium compounds is now presented.

## 'Ordinary' mixed lithium–magnesium compounds

Access to compounds of this type is usually achieved simply by mixing together the component homometallic compounds in the absence or presence of a Lewis base cosolvent [eqn. (1)]. In

$$x \text{ LiR} + y \text{ MgR}_2 \begin{array}{c} \longrightarrow (\text{Li}_x\text{Mg}_y\text{R}_z) \\ \longrightarrow (\text{Li}_x\text{Mg}_y\text{R}_z \cdot \text{L}_n) \\ +n\text{ L} \end{array} \qquad (1)$$

homoleptic cases (*i.e.* with only one type of anionic ligand) the product of such mixing need not necessarily be formulated as 'LiMgR$_3$', since products with stoichiometries discordant from that employed in the reaction can sometimes prevail. Especially common in this regard is 'Li$_2$MgR$_4$'. This phenomenon is a direct consequence of the fact that structural factors dictate the composition (in particular, the Li : Mg ratio) of the mixed-metal product. To elaborate, the building up of their molecular architectures can be formally regarded as a two-stage process, each stage of which involves a distinct type of bonding which may be designated as *anchoring* or *ancillary*.

The foundation/framework of the structure is provided by *anchoring* bonds as they comprise the stronger, more covalent, predominantly σ-based Mg–R interactions. Depending mainly on the steric requirements of the surrounding 'R' ligands, this framework is generally either tetrahedral or trigonal planar in disposition. *Ancillary* bonding can be defined as those more

ionic interactions, which enable the lithium ions to affix to this framework to give contacted ion pairs. To maximise the number of such electrostatic contacts the lithium atoms will affix μ_2 rather than terminally. Tetrahedral MgR$_4$ units have six edges, so three diagonally opposed pairs of edges to accommodate pairs of lithium ions, while triangular MgR$_3$ units have three edges, one of which can accommodate a single lithium ion (Fig. 1): in this way are formed the common Li$_2$MgR$_4$ and
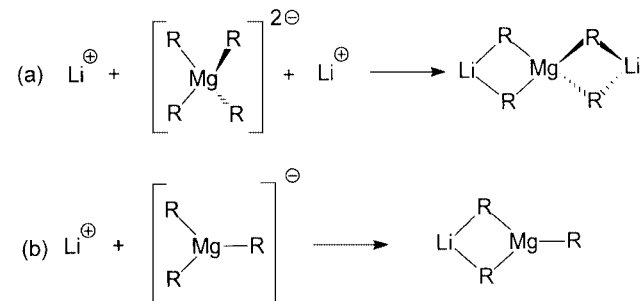
Fig. 1 Building up 2 : 1 and 1 : 1, Li : Mg stoichiometries through tetrahedral (a) and trigonal planar (b) 'anchoring' frameworks, respectively.

LiMgR$_3$ stoichiometries respectively, and charge neutrality is attained. Both of these scenarios can be found within the series of lithium organoC-magnesate structures **1–5**[9–12] shown in Scheme 1. An additional point is raised by the structure of **2**:[10] planar 'R' ligands (shown flat here, but in reality would be tilted out of the plane) can rotate to avoid interlocking with each other so creating a sterically relaxed opportunity for two or more Mg atoms to participate in the framework unit (in solvent-free homometallic [(MgPh$_2$)$_\infty$][13] this process occurs *ad infinitum* to give a polymeric arrangement). An alternative way to describe the anchoring/ancillary demarcation is to consider that anions will preferentially bind first to magnesium, on account of its
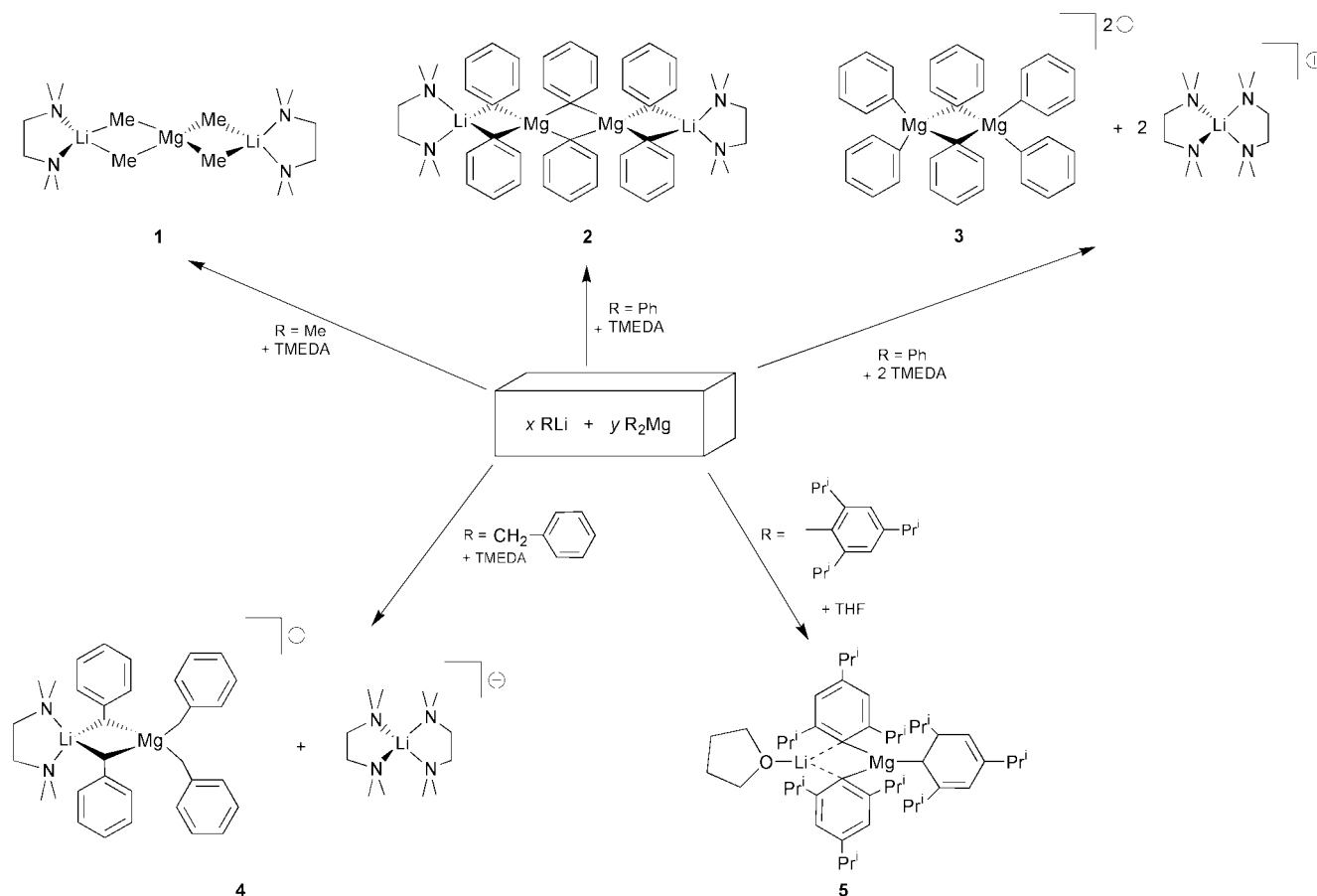
Scheme 1

greater Lewis acidity, until coordinative saturation is reached giving $(MgR_4)^{2-}$ or $(MgR_3)^-$ complex ions. These magnesium-fixed anions can therefore not usually satisfy the coordinative needs of approaching lithium cations within the limitations of a contacted ion pair arrangement and so solvent molecules are required to fill the remaining coordination sites. In certain cases, for example in structure **3**, solvent molecules can completely detach the lithium ions from the primary framework to generate solvent-separated ion pairs.

These basic structural types are not confined to alkyl and aryl ligands, as they also extend to amido systems. A clear example of the delicate balance between the tetrahedral and the trigonal planar frameworks is illustrated in a family of dibenzylamido [$^-N(CH_2Ph)_2$] systems (Scheme 2).[14,15] Sterically, the opti-
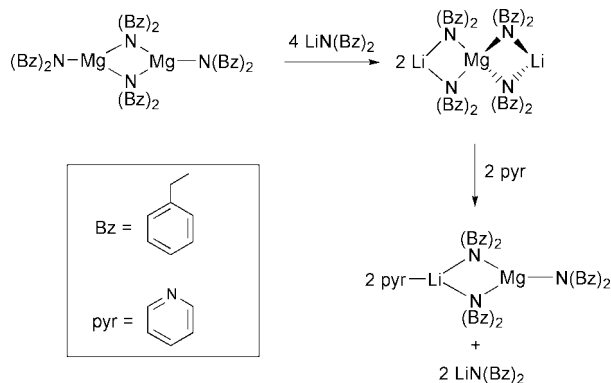
Scheme 2

mum number of dibenzylamido ligands to fit around a magnesium atom would appear to be three since homometallic [{Mg[N(CH_2Ph)_2]_2}_2] has a trigonal planar magnesium geometry within its dimeric solid-state constitution. However, introducing dibenzylamidolithium into this system induces coordination expansion about magnesium to create an alternative tetrahedral $(MgR_4)^{2-}$ framework made up of four dibenzyl-amido ligands R, set within a (Li_2MgR_4) formulation. This coordination expansion can be rationalised predominantly in terms of steric and valency effects: with the terminal coordination site on monovalent lithium vacant there is additional space for the benzyl arms of the bridging amido ligands to occupy. In the exclusively-magnesium structure this site is blocked by the presence of a terminally attached dibenzylamido ligand. When pyridine is added to the heterometallic structure a new dative Li–N bond is formed filling the terminal coordination site and forcing the bridging amido ligands closer towards the magnesium atom. This extra steric strain placed on magnesium reduces its ability to tolerate four (tetrahedral) coordination, thus prompting the displacement of one amide ligand (and its Li$^+$ partner) to leave a more sterically relaxed three-coordinate (trigonal planar) environment. Electronic effects must also be taken into consideration. Pyridine, a good σ donor, will also stabilise the lithium atom electronically. Other monodentate donor solvents such as THF will do likewise in other bulky amide systems, *e.g.* in [(THF)·LiMg{N(*c*-C_6H_{11})_2}_3].[16] The same basic motif can be found in mixed-anion systems, typified by the alkyl–amido complex [(py)·LiMg(HMDS)_2(Bu)][16] [HMDS = $^-$N(SiMe_3)_2]. Therefore the stabilising role of the solvent ligand in raising the coordination number of the lithium atom to three is an important factor in the conversion of lithium-rich Li_2MgR_4 structures into $LiMgR_3$ alternatives.

Pyridine or THF will also stabilise the tris(amide) derived from the sterically demanding hexamethyldisilazane [HMDS(H)]. Interestingly, however, the 1:1, Li:Mg motif remains intact even in the absence of any such solvent molecules.[17] As depicted in Fig. 2, the loss of solvent (N or O donor atom)—lithium dative bonding is balanced by the gain of $H_3C\cdots$Li interactions (mean length, 2.307 Å) made possible by
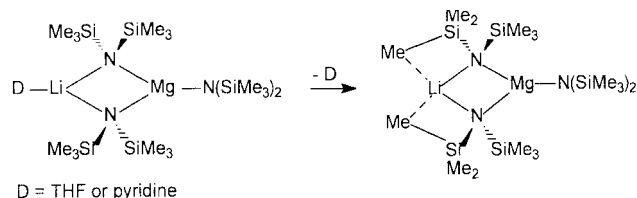
Fig. 2 Additional stabilisation of the Li atom can be achieved through a dative D–Li bond or, in the absence of a donor solvent, through $H_3C\cdots$Li agostic interactions.
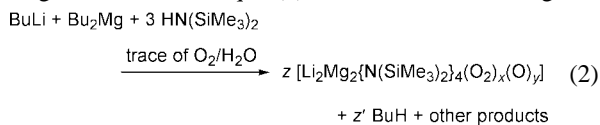
the bending of the SiMe_3 substituents towards the semi-naked lithium atom. Pseudo-agostic interactions of this type are becoming increasingly familiar in structures where alkali metals have low (formal) coordination numbers; here the affinity of the Li atom for the methyl substituent is heightened by the marked polarisation within the Si$^{\delta+}$–CH_3$^{\delta-}$ units, *i.e.* the carbon atoms of the methyl groups carry a substantial negative charge. It is therefore not surprising that, from a standpoint of length, these $H_3C\cdots$Li interactions can be likened to the electron-deficient C–Li bonds, which formally involve anions, of simple alkyllithiums such as [(Bu^{t}Li)_4][18] and [(EtLi)_4][19] (mean lengths, 2.246 and 2.25 Å, respectively).

Chelational stabilisation of lithium atoms is possible when the 'R' substituents within bridging amide ligands contain an additional heteroatom, two or three atoms removed from the amido nitrogen atom. The first mixed lithium–magnesium amide [Li_2Mg{N(CH_2CH_2NMe_2)CH_2Ph}_4], reported in 1993,[20] exhibits this feature in having five-membered (NCCNLi) chelate rings the tertiary amine nitrogen atoms of which serve to increase the coordination number of the lithium atoms from two to four.

'Extraordinary' mixed alkali metal–magnesium compounds

(i) Inverse crown ether complexes

During our attempts to reprepare the aforementioned solvent-free tris(amide) [LiMg{N(SiMe_3)_2}_3] **6** a surprising development came to light. It was found repeatedly that the reaction solutions preferentially crystallised an oxygen-contaminated variant of formula [Li_2Mg_2{N(SiMe_3)_2}_4(O_2)_x(O)_y] **7**, despite the fact that an inert-atmosphere protocol was employed throughout the synthetic procedure (or so we had assumed).[17] Reacting the mixtures [eqn. (2)] for 1 h then cooling the

BuLi + Bu_2Mg + 3 HN(SiMe_3)_2

$$\xrightarrow{\text{trace of O}_2/\text{H}_2\text{O}} z\,[Li_2Mg_2\{N(SiMe_3)_2\}_4(O_2)_x(O)_y] \quad (2)$$

+ z' BuH + other products

solutions afforded **7** in typically poor, but reproducible yields of 1–5%: none of the intended (oxygen-free) product **6** precipitated from solution, which perhaps reflects its previously noted high solubility (in arene or hydrocarbon solvents). Since the initial report of **7** we have managed to increase its yield five-fold (best to date, 24%). This improvement came as a direct result of deliberately exposing the reaction mixture to the atmosphere (!) whilst stirring it for four days. Clearly, as small quantities of **7** can be produced even when standard precautions are taken to avoid moisture/oxygen contamination, the mixed lithium–magnesium HMDS system must be an extremely efficient oxygen scavenger. However, the source of the oxygen contamination, whether it be dioxygen or moisture or a combination of both, is yet to be unambiguously established.

The molecular structure of **7** (Fig. 3) reveals a discrete eight-membered ring made up of alternating nitrogen and metal atoms, with the latter atoms themselves alternately lithium and magnesium. Peroxide or oxide ions occupy the core of the ring to render the molecule neutral overall. The peroxide and oxide-
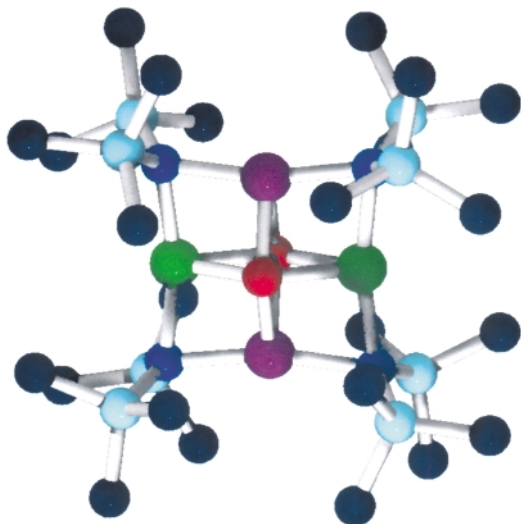
Fig. 3 Molecular structure of $[Li_2Mg_2\{N(SiMe_3)_2\}_4(O_2)_x(O)_y]$ showing peroxide core. Colour code for figures:[39] alkali metal, purple; Mg, green; Zn, yellow; N, dark blue; Si, light blue; C, black; O, red.

based molecules can be differentiated in arene solution by ^{1}H NMR spectroscopic studies. In the conventional host–guest chemistry of crown ether complexes,[21] electron-poor metal cation guests are stabilised by coordination to a series of Lewis basic oxygen centres fixed within a macrocyclic ligand host. Contrast that situation through a representative [12]crown-4 complex with the generalised structure of **7** (Fig. 4) and one can
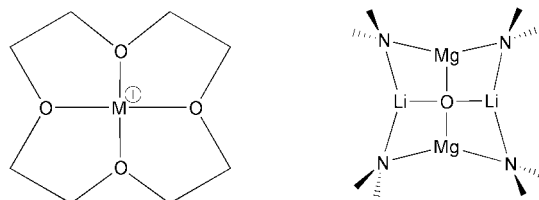
Fig. 4 A representative [12]crown-4 complex *vs.* the generalised structure of **7**.

see at a glance that while both macrocycles offer four built-in binding sites for the entertainment of the core guest the relative positions of metal and oxygen atoms have been interchanged. This topological comparison prompted us to coin the name 'inverse crown ether' complex to describe **7** and its isostructural analogues, even though no ether functionality is actually involved (a referee suggested an alternative name, metal amide chemistry, or 'MAC', crowns: but while this is perhaps more distinctive and certainly more apt given that they were discovered in Scotland, this description could be confused with metallo-crowns which are a known class of compound. In our view, the 'inverse' prefix is also essential to convey the difference with conventional crowns). The idea of a 'crown' made up of metal atoms would certainly sit easily with those people interested in royalty! At this juncture it is germane to mention that a similar description, 'anti-crowns', was introduced a few years prior to our work by Hawthorne and Zheng with regard to a series of [12]mercuracarborand-4 complexes in recognition of their charged-reversed relationship to normal [12]crown-4.[22] Contrary to the situation in the inverse crown systems, oxide or peroxide anions do not feature in anti-crown chemistry presumably because the softer acid Hg atoms prefer to bind softer bases such as Cl^-, Br^-, I^- or *closo*-$B_{10}H_{10}^{2-}$.

On further investigation it soon became apparent that the basic structural motif of **7** was not a unique, one-off oddity, but rather the progenitor of a family of such structures. The synthesis and crystallographic characterisation of **8**[23] (Fig. 5) established that inverse crown ethers could be made using other amide ligands, in this case derived from 2,2,6,6-tetramethyl-
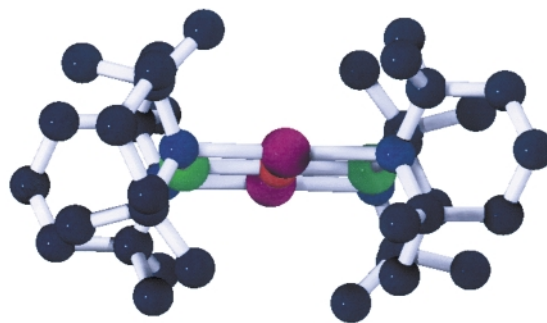
Fig. 5 Molecular structure of $[Li_2Mg_2(TMP)_4(O)]$ viewing the eight-membered ring from the side.

piperidine [TMPH = $\overline{HN(Me)_2CCH_2CH_2CH_2C(Me)_2}$]. Significantly this cyclic amide ligand is even more sterically demanding about its ligating N head than HMDS, which prompts the thought that extreme steric hindrance may be a prerequisite for the formation of an inverse crown ether. Preattached to the metal centres, these bulky ligands may on exposure to the oxygen contaminant, suppress altogether or at least kinetically inhibit the formation of metal oxide salts which would seem more likely products from lattice energy considerations.

More important extensions to the family followed on turning our attention from lithium to the heavier alkali metals. Applying the same synthetic approach but this time using butylsodium or butylpotassium in place of the lithium congener [eqn. (3)],

$$BuM + Bu_2Mg + 3\ HN(SiMe_3)_2$$

$$\xrightarrow{\text{trace of } O_2/H_2O} z\ [M_2Mg_2\{N(SiMe_3)_2\}_4(O_2)_x(O)_y] \quad (3)$$

$$+ z'\ BuH + \text{other products}$$

$$M = Na,\ K$$
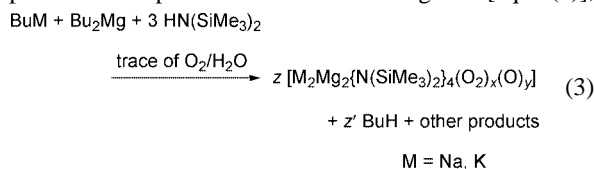
produced the first sodium–magnesium $[Na_2Mg_2\{N(SiMe_3)_2\}_4(O_2)_x(O)_y]$[23] **9** (Fig. 6) and potassium–magnesium
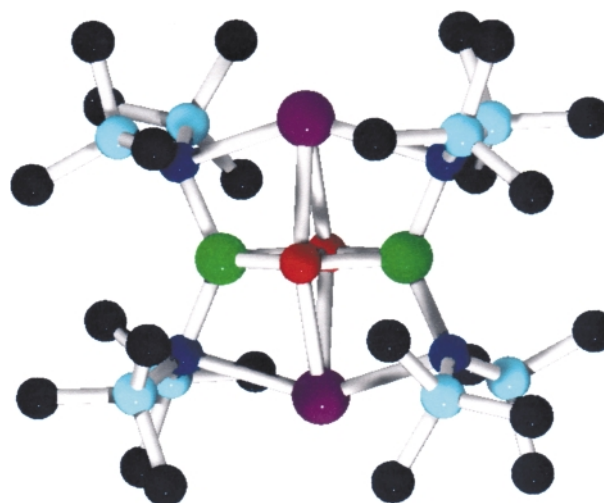
Fig. 6 Molecular structure of $[Na_2Mg_2\{N(SiMe_3)_2\}_4(O_2)_x(O)_y]$.

$[\{K_2Mg_2[N(SiMe_3)_2]_4(O_2)\}_\infty]$[24] **10** (Fig. 7) inverse crown ethers, respectively. Sodium can sometimes mimic the coordinative behaviour of its smaller Group 1 nearest neighbour so the existence of the former category of crown is not that surprising. On the other hand potassium organic derivatives normally exhibit marked structural differences to their lithium counterparts on account of the significantly larger size and softer, more polarisable nature of the K^+ cation; hence the fact that a potassium-based inverse crown ether is readily preparable bears testimony to the stability of these new macrocyclic systems. However there is one major distinction between **10** and **7** for while both have broadly similar molecular structures, in

Fig. 7 Double asymmetric unit of $[\{K_2Mg_2[N(SiMe_3)_2]_4(O_2)\}_\infty]$.

the latter it is discrete but in the former it joins up through intermolecular $(Me_2Si)H_3C\cdots K$ interactions to give a linear polymeric arrangement (Fig. 8). Therefore **10** could be

Fig. 8 Extended structure of $[\{K_2Mg_2[N(SiMe_3)_2]_4(O_2)\}_\infty]$.

described as the first supramolecular inverse crown ether structure, but this description exaggerates the distinction because such extended structures are quite common in the wider context of organopotassium chemistry.[25] Certain trends can be discerned from this Li/Na/K series of structures. Most obviously, the pairs of Mg atoms within the dicationic octagonal rings are always displaced towards the centre of the ring as a result of strong Mg–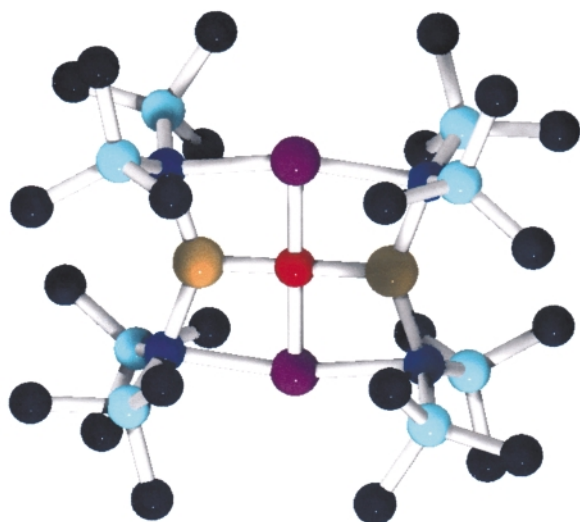O bonding. The magnitude of this displacement grows in concert with the increasing size of the alkali metal partner in the ring as gauged by the endocyclic N–Mg–N bond angles (mean values 193.3, 218.4 and 227.8° for the Li, Na and K structures respectively). Similarly, the small Li atom in **7** and **8** is pulled towards the centre of the ring through strong Li–O bonding, resulting in endocyclic N–Li–N bond angles greater than 180°. In contrast the Na and K atoms occupy peripheral ring sites with endocyclic N–Na–N and N–K–N bond

angles significantly less than 180°, reflecting longer, weaker Na–O/K–O bonding.

Extension to zinc. Having established that it is possible to vary the Group 1 metal in the inverse crown ether octagons, the next logical step was to consider possible replacement of the Group 2 metal, magnesium. The health problems associated with beryllium deterred us from experimenting with the lightest member of Group 2, so instead we turned our attention towards the next nearest neighbour, calcium. Though a significant size differential exists between Mg and Ca (*e.g.* 0.28 Å for ionic radii), that between Li and K is substantially greater (corresponding value, 0.60 Å). This favourable steric comparison, coupled with the knowledge that $[\{Ca[N(SiMe_3)_2]_2\}_2]^{26}$ is isostructural to the Mg congener, suggested to us that a calcium-based inverse crown would be an easily accessible target. In practice this has not been borne out. Thus far it has proved problematical to obtain any solids from mixtures of LiN-$(SiMe_3)_2$ and $Ca[N(SiMe_3)_2]_2$ as they generally remain in solution (in oxygenated arene media) even at subzero temperatures. However on one occasion we did manage to isolate and crystallographically characterise a solid product which transpired to be the calcium analogue of **6**, the tris(amide) $[LiCa\{N(SiMe_3)_2\}_3]$ **11**.[27] This solvent-free system (a THF-solvate was earlier reported by Davies[28]) adopts the same basic motif as **6** but with an additional feature, a double ration of intramolecular agostic interactions $H_3C\cdots Li$ and $H_3C\cdots Ca$, *i.e.* involving both types of metal atom separately. It is still an open question whether or not this extra coordinative stabilisation has a bearing on the failure (hitherto) to observe an inverse crown ether molecule within the mixed lithium–calcium system, but it most certainly contributes to its excellent solubility in organic solvents.

More success in this regard came upon switching our attention to the Group 12 metal zinc. This proved to be a perfect mimic for magnesium in all but one respect: attempts to prepare in donor-free media a lithium–zinc inverse crown ether complex analogous to **7** did not yield any products save unreacted starting material, namely $LiN(SiMe_3)_2$ and $Zn[N(SiMe_3)_2]_2$. This is consistent with the generalisation that reactivity (specifically here, Lewis acidity) diminishes on moving from magnesium to zinc. No such problems were encountered on replacing the lithium amide by its more reactive sodium or potassium congener. Thus the first inverse crown ether complexes of zinc, namely $[Na_2Zn_2\{N(SiMe_3)_2\}_4(O)]$ **12** and $[\{K_2Zn_2[N(SiMe_3)_2]_4(O_2)_x(O)_y\}_\infty]$ **13** were readily prepared by the method outlined in eqn. (4).[29] To obtain the former the

$$ZnCl_2 + 2\,LiN(SiMe_3)_2 \longrightarrow Zn[N(SiMe_3)_2]_2 + 2\,LiCl$$

$$\downarrow \begin{array}{l} MN(SiMe_3)_2 \\ trace\ of\ O_2/H_2O \end{array}$$

$$other\ products + [M_2Zn_2\{N(SiMe_3)_2\}_4(O_2)_x(O)_y]$$

$$M = Na,\ K$$

(4)

solution had to be heated to reflux, whereas to obtain the latter only gentle heating was necessary. This series of reactions therefore follows the classical reactivity trend associated with the alkali metal series (Li < Na < K). Future work will ascertain whether this trend holds for the complete homologous series, *i.e.* will formation of the (thus far hypothetical) Rb and Cs analogues be even more facile than that of K? The structures of **12** and **13** (Figs. 9 and 10, respectively) are isomorphous with each other and with their magnesium-based analogues **9** and **10**. Intermolecular $(Me_2Si)H_3C\cdots K$ contacts give a linear polymeric arrangement in the case of **13**, in the same way as that in **10**. Corresponding bond lengths and bond angles between **12** and **9** and between **13** and **10** show little variation, though the

Fig. 9 Molecular structure of [Na₂Zn₂{N(SiMe₃)₂}₄(O)].

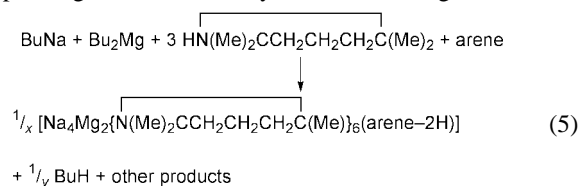**Fig. 10** Double asymmetric unit of [{K₂Zn₂[N(SiMe₃)₂]₄(O₂)}∞].

Zn–N bonds are systematically 0.07–0.08 Å shorter than the Mg–N bonds.

(ii) Inverse crown complexes

Pioneered by Pederson and first reported in 1967,[30] crown ether compounds and their many offshoots now make up a colossal field within supramolecular chemistry:[31] ring structures in this category come in countless different shapes and sizes, accumulated through the work of over thirty years of intensive research. This knowledge prompted us to pose the question, 'could we extend a stage further the analogy with conventional crown ether chemistry by also synthesising inverse analogues of different ring shapes and ring sizes?' We were pleased to discover that the answer is in the affirmative albeit at this stage to an extremely modest degree. Thus in this section two such types containing twelve or twenty-four ring atoms are discussed. Note that in labelling these larger ring systems 'inverse crown' complexes, as opposed to 'inverse crown ether' complexes, we simply want to draw the distinction that the former type do not contain any oxygen (atoms or anions) at all, though in common with the latter type their Lewis acidic (metal cation)–Lewis basic (heteroatom anion) positions are reversed relative to those in conventional crown ether complexes.

The breakthrough in our quest to prepare a larger inverse crown ring system came unexpectedly when the reaction that previously produced oxo-centred [Li₂Mg₂(TMP)₄(O)] **8**, was repeated but with butylsodium in place of butyllithium as the alkali-metallating source [eqn. (5)]. Remember that in the

corresponding HMDS-based system substituting sodium, or

BuNa + Bu₂Mg + 3 HN(Me)₂CCH₂CH₂CH₂C(Me)₂ + arene

$^{1}/_{x}$ [Na₄Mg₂{N(Me)₂CCH₂CH₂CH₂C(Me)}₆(arene–2H)]   (5)

+ $^{1}/_{y}$ BuH + other products

arene = C₆H₅Me, C₆H₆

even potassium, for lithium, does not alter the general nature of the product as all three metals give an inverse crown ether complex. However this time the move to the next heaviest alkali metal induces a dramatic chemical and structural transformation through the formation of the tetrasodium–dimagnesium amide-arenediide [Na₄Mg₂(TMP)₆{C₆H₃(CH₃)}] **14**, which is oxygen free.[32] We subsequently prepared a benzene-derived analogue [Na₄Mg₂(TMP)₆(C₆H₄)] **15**, to prove that this novel reaction chemistry is applicable to other arene solvents (toluene was the solvent used in the preparation of **14**). Structural preferences dictate the unusual 4Na : 2Mg stoichiometry of these products, not that used in the original reaction mixtures (*i.e.* 1Na : 1Mg). Yet, perplexingly, attempts to reprepare **14** and **15** using the 'correct' 4Na : 2Mg reaction stoichiometry are hampered by solubility problems. The structures of **14** (Fig. 11) and **15** (not
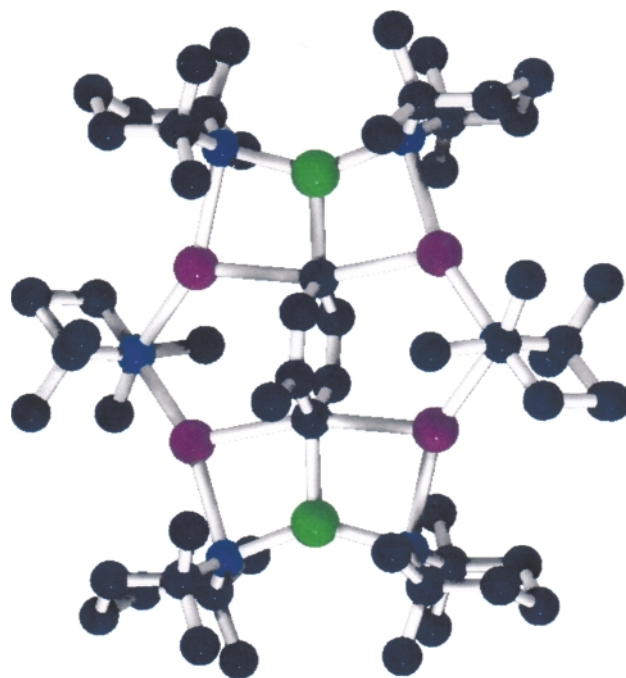

Fig. 11 Molecular structure of [Na₄Mg₂(TMP)₆(C₆H₃CH₃)].

shown) are essentially equivalent. Metal atoms and nitrogen atoms alternate within their Na₄Mg₂N₆ ring, which is severely puckered. The encapsulated arene molecules lie approximately orthogonal to the mean plane of this ring, locked into position by a combination of Mg–C σ bonds ('anchoring' bonds—see earlier) and Na–C π bonds ('ancillary' bonds). Of particular interest are the metallation sites of the toluene- and benzene-based dianions (2,5- and 1,4-positions, respectively) which are coincident with the placements of the Mg atoms within the dicationic Na₄Mg₂N₆ ring. This signifies that a special type of chemistry beyond the scope of mainstream organometallic reagents is operating here. To elaborate, while toluene can be easily monometallated to generate the resonance-stabilised benzyl carbanion, its dimetallation presents a much more challenging task. Reagents such as butyllithium/TMEDA can pull off more than one hydrogen atom, but only in a random unpredictable way which leads to a complex assortment of incompletely characterised polylithiated species.[33] Contrast this

with the controlled, regioselective dimetallation (dimagnesiation) of toluene facilitating the construction of pure **14**. However, there is another more important distinction: in the case of **14** the CH_3 substituent, which carries the most acidic hydrogen atom (by several pK_a units), remains fully intact (solution ^{1}H NMR studies support the crystal structure determination in this respect), as instead deprotonation occurs exclusively at ring sites. Treating toluene with an appropriate mainstream organometallic base normally leads (ultimately) to benzyl ($PhCH_2^-$) products,[34] since resonance stabilisation reaches a maximum when a hydrogen atom is removed from the CH_3 substituent. Hence it can be reasoned that a special ring template effect is responsible for directing the abnormal metallation chemistry inherent in the synthesis of **14** and for locking the toluene-based dianion in place to prevent any possible tautomerism from taking place which might have generated a thermodynamically more desirable benzyl isomer. The revelation that the weaker carbon acid benzene undergoes an identical double deprotonation during the formation of **15** is also highly significant. This would appear to be direct proof that a powerful synergic effect (the existence of which was speculated upon in the Introduction) is at work here because neither $Mg(TMP)_2$ on its own, nor NaTMP on its own, can metallate benzene (let alone regioselectively dimetallate it!) under the mild conditions used to make **15**. Almost certainly, a single type of structure, the immediate precursor to **14** and **15**, executes both the template effect and the mixed sodium–magnesium synergic effect.

The precise nature of this intermediate structure has not yet been established, but as a working model we tentatively suggest the (hypothetical) $[Na_4Mg_2(TMP)_8]$ molecule depicted in Scheme 3. Made up of authentic features seen in other structures such as mixed-metal Mg–N–Na bridges and tris-amido Mg coordination, this model appears ideally tailored for trapping an arene molecule and bringing about its twofold deprotonation by utilising the terminal amide ligands on the magnesium atoms, the diagonally opposed positions of which are fixed within the constraints of the twelve-membered ring. The byproduct of this process would therefore be the starting amine 2,2,6,6-tetra-methylpiperidine. While we are currently investigating the reaction of NaTMP and $Mg(TMP)_2$ in the absence of an arene solvent, it is conceivable that $[Na_4Mg_2(TMP)_8]$ may only have a transient existence (or may not exist at all without arene ligand stabilisation) and thus may not be isolable or easily detected.

The unpredictable nature of this area of heterometallic chemistry was demonstrated again, even more emphatically, when the reaction shown in eqn. (5) was repeated using butylpotassium in place of butylsodium. By analogy with the sodium and potassium inverse crown ether complexes **9** and **10**, it would be logical to expect that the potassium products would adopt the same basic structural motif as that found in **14** and **15**. This time, however, the introduction of the heavier alkali metal effects a spectacular ring expansion in the form of the unprecedented hexapotassium–hexamagnesium twenty-four membered macrocyclic amides $[K_6Mg_6(TMP)_{12}(C_6H_4CH_3)_6]$ **16** and $[K_6Mg_6(TMP)_{12}(C_6H_5)_6]$ **17**.[35] Fig. 12 shows the
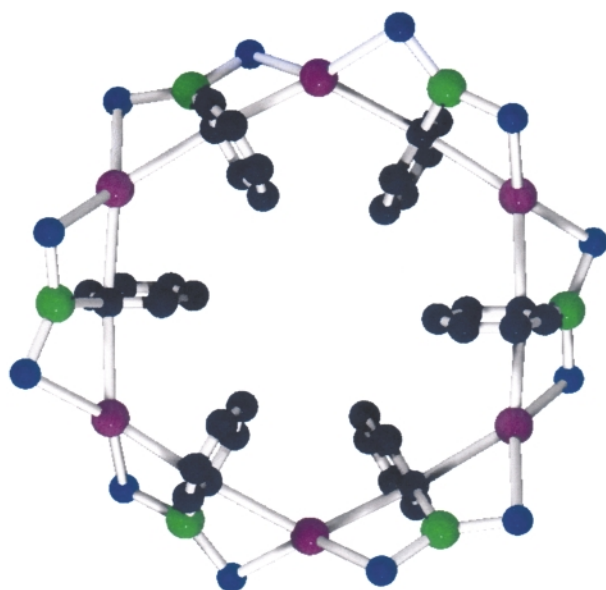

Fig. 12 Molecular structure of $[K_6Mg_6(TMP)_{12}(C_6H_5)_6]$.

structure of **17**, which is representative of both. Here the $[(KNMgN)_6]^{6+}$ ring system acts as a polymetallic host to six singly deprotonated arene anions. Mirroring the situation in **14**, the toluene-derived ligands in **16** have intact Me substituents and hydrogen atoms missing from ring sites, the positions of which are coincident with the placings of the magnesium atoms within the host ring. Thus a ring template effect appears to be operating in this system as well, though in this case the elusive templating molecule must be larger and have more breadth than its sodium counterpart (see Scheme 3) given that only one end of the arene molecule experiences deprotonation, implying that the other end lies distant from a magnesium atom. Following the pattern laid down in the smaller sodium ring systems, the encapsulation of the arene anions is achieved through a combination of anchoring Mg–C σ bonds and ancillary alkali metal–C π bonds but the hapticity of the phenyl rings changes from μ-η^1:η^1:η^1:η^1 to μ-η^3:η^2 in line with the larger size and coordinative capacity of the potassium atom. The interaction of alkali metal cations with π-systems is becoming an increasingly significant feature in chemistry with implications for biology as discussed in a recent review.[36] It will be interesting to ascertain the structural consequences of introducing rubidium or caesium as the alkali metal in this system: will the transition to a larger ring arrangement (here from one of twelve to one of twenty-four ring atoms) continue or more likely given their propensity for adopting polymeric arrangements, will cyclisation cease and
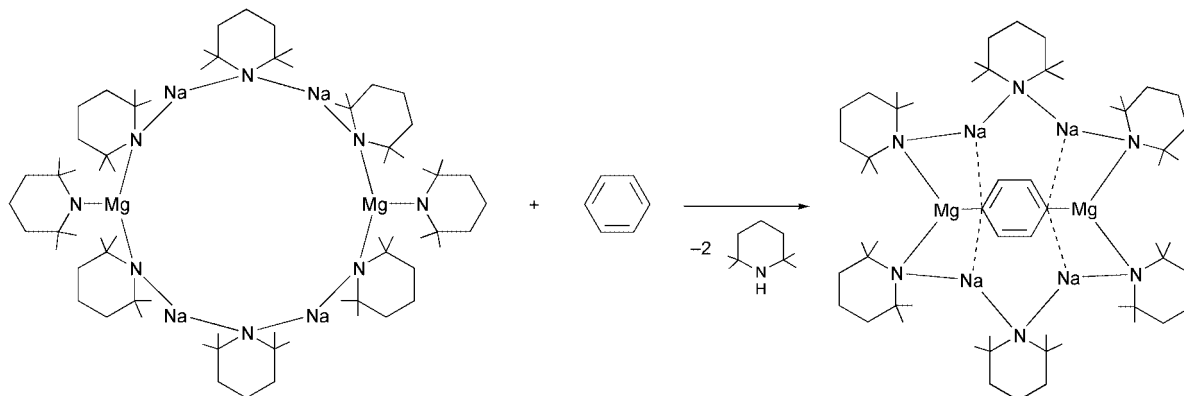
Scheme 3

cede to an infinite chain structure? Studies are in hand to find the answer to this question.

Outlook

Inverse crown ether and inverse crown complexes represent an important new class of s-block compound. The fundamental chemistry controlling their formation is intriguing and complex, and could not have been predicted from previous knowledge of s-block structural chemistry, even through a mountain of such data has been accumulated in recent years. There are clearly still some gaps in our understanding of these existing inverse crown ether complexes and their inverse crown relatives which ongoing research will hopefully soon resolve. Next it will be essential to establish the chemical profiles of this aesthetically attractive collection of ring compounds. For example, will the Mg–C σ bonded systems behave like typical Grignard reagents or will they have a unique chemical character of their own? We are particularly keen to ascertain how far we can extend this new class of compound. Bearing in mind that they are formally composite materials of four distinct component parts (M^+, M^{2+}, R_2N^-, and anion$^-$ or dianion^{2-}), the potential for permutation appears vast. There may even be scope for extending this chemistry beyond the s-block to, for example, the transition metal series in view of the availability therein of M^{2+} cations and the fact that $[LiMn\{N(SiMe_3)_2\}_3]$[37] is essentially iso-structural to $[LiMg\{N(SiMe_3)_2\}_3]$. We look forward to continuing this fundamental development work with one eye focussed on how we might usefully apply it in areas such as anion complexation and template synthesis. Artificial organic host molecules for anions are receiving considerable attention at present. Main group metal cations, especially Mg^{2+} and Ca^{2+}, are found in abundance in natural protein receptors where they play decisive roles in binding anionic substrates, in structure enforcement, or in allosteric switching. Yet their use in artificial receptors is not currently well developed. An expanded series of inverse crown type compounds might therefore serve a useful purpose as a database of model structures for learning more about the ways in which metal-based molecules selectively bind anions.[38]

Notes and references

1 B. J. Wakefield, *The Chemistry of Organolithium Compounds*, Pergamon, Oxford, 1974; B. J. Wakefield, *Organolithium Methods*, Academic Press, London, 1988; P. G. Williard, *Comprehensive Organic Synthesis*, ed. B. M. Trost, Pergamon Press plc, Oxford, 1991, vol. 1, p. 1; D. S. Wright and M. A. Beswick, *Comprehensive Organometallic Chemistry II*, ed. E. W. Abel, F. G. A. Stone and G. Wilkinson, Elsevier Science Ltd., Oxford, 1995, vol. 1, p. 1.

2 W. E. Lindsell, *Comprehensive Organometallic Chemistry II*, ed. E. W. Abel, F. G. A. Stone and G. Wilkinson, Elsevier Science Ltd., Oxford, 1995, vol. 1, p. 57; B. J. Wakefield, *Organomagnesium Methods in Organic Synthesis*, Academic Press, London, 1995; *Handbook of Grignard Reagents*, ed. G. S. Silverman and P. E. Rakita, Marcel Dekker, New York, 1996; *Grignard Reagents: New Developments*, ed. H. G. Richey Jr., Wiley, Chichester, 2000.
3 K. Kitagawa, A. Inoue, H. Shinokubo and K. Oshima, *Angew. Chem., Int. Ed.*, 2000, **39**, 2481.
4 H. G. Richey, Jr. and J. Farkas, Jr., *Organometallics*, 1990, **9**, 1778.
5 H. H. Karsch and M. Reisky, *Eur. J. Inorg. Chem.*, 1998, 905.
6 H. L. Hsieh and I. W. Wang, *Macromolecules*, 1986, **19**, 299.
7 T. A. Antkowiak and J. E. Hall, *Eur. Pat. Appl.* 0 747 405 A1, 1996.
8 J. F. Allan, K. W. Henderson and A. R. Kennedy, *Chem. Commun.*, 1999, 1325; K. W. Henderson, W. J. Kerr and J. H. Moir, *Chem. Commun.*, 2000, 479; G. Lessène, R. Tripoli, P. Cazeau, C. Biran and M. Bordeau, *Tetrahedron Lett.*, 1999, **40**, 4037.
9 T. Greiser, J. Kopf, D. Thoennes and E. Weiss, *Chem. Ber.*, 1981, **114**, 209.
10 D. Thoennes and E. Weiss, *Chem. Ber.*, 1978, **111**, 3726.
11 B. Schubert and E. Weiss, *Chem. Ber.*, 1984, **117**, 366.
12 K. M. Waggoner and P. P. Power, *Organometallics*, 1992, **11**, 3209.
13 P. R. Markies, G. Schat, O. S. Akkerman, F. Bickelhaupt, W. J. J. Smeets, P. van der Sluis and A. L. Spek, *J. Organomet. Chem.*, 1990, **393**, 315.
14 W. Clegg, K. W. Henderson, R. E. Mulvey and P. A. O'Neill, *J. Chem. Soc., Chem. Commun.*, 1994, 769.
15 W. Clegg, F. J. Craig, K. W. Henderson, A. R. Kennedy, R. E. Mulvey, P. A. O'Neil and D. Reed, *Inorg. Chem.*, 1997, **36**, 6238.
16 G. C. Forbes, A. R. Kennedy, R. E. Mulvey, P. J. A. Rodger and R. B. Rowlings, *J. Chem. Soc., Dalton Trans.*, 2001, DOI: 10.1039/b100052g.
17 A. R. Kennedy, R. E. Mulvey and R. B. Rowlings, *J. Am. Chem. Soc.*, 1998, **120**, 7816.
18 T. Kottke and D. Stalke, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 580.
19 H. Dietrich, *Acta Crystallogr.*, 1963, **16**, 681.
20 W. Clegg, K. W. Henderson, R. E. Mulvey and P. A. O'Neil, *J. Chem. Soc., Chem. Commun.*, 1993, 969.
21 G. Gokel, *Crown Ethers and Cryptands*, The Royal Society of Chemistry, Cambridge, 1991; G. Gokel, *Large Ring Molecules*, ed. J. A. Semlyen, John Wiley and Sons Ltd., Chichester, 1996, ch. 7, p. 263.
22 M. F. Hawthorne and Z. Zheng, *Acc. Chem. Res.*, 1997, **30**, 267.
23 A. R. Kennedy, R. E. Mulvey and R. B. Rowlings, *Angew. Chem., Int. Ed.*, 1998, **37**, 3180.
24 A. R. Kennedy, R. E. Mulvey, C. L. Raston, B. A. Roberts and R. B Rowlings, *Chem. Commun.*, 1999, 353.
25 C. Schade and P. v. R. Schleyer, *Adv. Organomet. Chem.*, 1987, **27**, 169.
26 M. Westerhausen and W. Schwarz, *Z. Anorg. Allg. Chem.*, 1991, **604**, 127.
27 A. R. Kennedy, R. E. Mulvey and R. B. Rowlings, unpublished work.
28 R. P. Davies, *Inorg. Chem. Commun.*, 2000, **3**, 13.
29 G. C. Forbes, A. R. Kennedy, R. E. Mulvey, R. B. Rowlings, W. Clegg, S. T. Liddle and C. C. Wilson, *Chem. Commun.*, 2000, 1759.
30 C. J. Pederson, *J. Am. Chem. Soc.*, 1967, **89**, 2495; C. J. Pederson, *J. Am. Chem. Soc.*, 1967, **89**, 7077.
31 For its many subareas, see: *Comprehensive Supramolecular Chemistry*, ed. J. L. Atwood, J. E. D. Davies, D. D. MacNicol and F. Vogtle, Elsevier Science Ltd., Oxford, 1996, vols. 1–11.
32 D. R. Armstrong, A. R. Kennedy, R. E. Mulvey and R. B. Rowlings, *Angew. Chem., Int. Ed.*, 1999, **38**, 131.
33 A. J. Chalk and T. J. Hoogeboom, *J. Organomet. Chem.*, 1968, **11**, 615.
34 D. Hoffman, W. Bauer, F. Hampel, N. J. R. van Eikema Hommes, P. v. R. Schleyer, P. Otto, U. Pieper, D. Stalke, D. S. Wright and R. Snaith, *J. Am. Chem. Soc.*, 1994, **116**, 528.
35 P. C. Andrews, A. R. Kennedy, R. E. Mulvey, C. L. Raston, B. A. Roberts and R. B. Rowlings, *Angew. Chem., Int. Ed.*, 2000, **39**, 1960.
36 G. W. Gokel, S. L. DeWall and E. S. Meadows, *Eur. J. Org. Chem.*, 2000, 2967.
37 B. D. Murray and P. P. Power, *Inorg. Chem.*, 1984, **23**, 4584.
38 Stalke and coworkers are developing other alkali metal molecules based on sulfur ligands which can also bind anions. For a selection of relevant papers, see: R. Fleischer and D. Stalke, *Coord. Chem. Rev.*, 1998, **176**, 431; R. Fleischer, S. Freitag and D. Stalke, *J. Chem. Soc., Dalton Trans.*, 1998, 193; R. Fleischer and D. Stalke, *Chem. Commun.*, 1998, 343.
39 J. W. Lauher, *Chemray: a Molecular Graphics Program, J. Mol. Graphics*, 1990, **8**, 34.