Building an extended inverse crown motif *via* alkali-metal-mediated α-magnesiation of furan

David V. Graham, Eva Hevia, Alan R. Kennedy, Robert E. Mulvey,* Charles T. O'Hara and Christine Talmard†

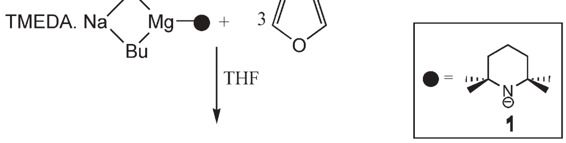
Received (in Cambridge, UK) 24th October 2005, Accepted 8th November 2005
First published as an Advance Article on the web 2nd December 2005
DOI: 10.1039/b514985a

The utility of inverse crown chemistry is extended to aromatic heterocycles, as furan is deprotonated selectively at the α-position by the mixed-metal alkyl-amido base [(TMEDA)·Na(Bu^n)(TMP)Mg(TMP)] to generate a transient intermediate which undergoes disproportionation to the disodium dimagnesium hexafuryl tri(thf) complex [{{(thf)$_3$·Na$_2$}{(TMEDA)·Mg$_2$}(2-C$_4$H$_3$O)$_6$}$_\infty$], a new type of inverse crown structure with triply-stabilized (through Mg–C σ, Na–O σ and Na···C–C π interactions) furyl 'guest' anions, and the tris(amide) [(TMEDA)$_x$·NaMg(TMP)$_3$].

Alkali metal TMP-based 'ates (where TMP is 2,2,6,6-tetramethylpiperidide, **1**) are developing into an extraordinarily versatile new class of organometallic reagent. With only a meagre number of studies carried out thus far, the best results are surely still to come; however, interesting and synthetically useful chemistry has already been demonstrated for TMP-aluminates, TMP-magnesiates, and TMP-zincates. In the first sub-class, which has been least developed, Uchiyama has shown that lithium tri-isobutyl(TMP)aluminate, empirically formulated as "Bu$^i_3$Al(TMP)Li", is an excellent regio- and chemoselective reagent for direct alumination of a wide range of functionalized aromatics including amides, cyanides, ethers, halides, indoles, and pyridines.[1] Mongin has reported the selective magnesiation of various chloro- and fluoro-aromatics[2,3] using the "highly coordinated" magnesiate "Bu$_3$(TMP)MgLi$_2$", designated as such because of the four-fold-anionic coordination of its Mg atom. Introduced by our own laboratory, the well-characterised monoalkyl-bis(TMP) magnesiate [(TMEDA)·Na(μ-Bu)(μ-TMP)Mg(TMP)],[4] **2**, exhibits remarkable selectivity in its deprotonating behaviour, which is *meta*-orientated in the case of toluene[5] and exclusive to one ring in bis(benzene)chromium.[6] Kondo *et al* have pioneered lithium TMP-zincate chemistry through the synthesis of lithium di-*tert*-butyl(TMP) zincate, empirically formulated as "Bu$^t_2$Zn(TMP)Li",[7] and subsequently the methyl analogue "Me$_2$Zn(TMP)Li".[8] Also developed by our own group, the structurally authenticated sodium TMP-zincate reagent [(TMEDA)·Na(μ-Bu^t)(μ-TMP)Zn(Bu^t)],[9] is found to act as a Bu^t transfer agent towards benzophenone, selectively adding the nucleophile to the *para*-position of one Ph ring, inducing dearomatisation.[10]

There is an additional attribute of TMP-magnesiate reagents which makes their chemistry even more special. Namely, in accomplishing deprotonation of a substrate, these mixed-metal reagents can often generate metallated intermediates in the form of "inverse crown" ring compounds.[11] Inverse crowns display polymetallic cationic "host" rings (residue of the reacted TMP-magnesiate base) surrounding an anionic "guest" (the deprotonated substrate) in an inverse Lewis acidic–Lewis basic arrangement to that encountered in conventional crown ether complexes. Their ability to encapsulate anions is a function of their mixed-metal (mixed-valence) synergic reactivity, which would be inoperative if all the metal atoms were alkali metal atoms as the host rings would be neutral not cationic. Previous inverse crowns based on TMP or diisopropylamide have resulted from the metallation of benzene,[11] toluene,[11] ferrocene,[12] ruthenocene,[13] and osmocene.[13] Here we extend the scope of this chemistry by reporting the first inverse crown synthesised *via* α-metallation of an aromatic heterocyclic compound (furan). X-Ray crystallography reveals that this alkali-metal-mediated magnesiation is manifested in a new type of inverse crown architecture constructed from a homoleptic anionic ligand set. Evidence that this inverse crown forms through disproportionation of a heteroleptic intermediate is also presented.

The synergic base used to deprotonate furan was aforementioned **2**, made as described previously.[4] Dissolving pure crystalline **2** in hexane solution and adding furan stoichiometrically (one or three molar equivalents) led to the precipitation of a pyrophoric white solid, formulated as [{Na$_2$}{(TMEDA)·Mg$_2$}(2-C$_4$H$_3$O)$_6$] **3** from NMR spectroscopic data. Growing crystals of this furanyl complex proved problematic; however, addition of THF afforded the analogous crystalline THF solvate **3·(thf)$_3$**.‡ There are at least two possible pathways through which the isolated product **3** could have been formed. If reagent **2** acts as a dual alkyl/amido base then the reaction would follow Scheme 1 with TMPH and butane co-products. This would run counter to the exclusive alkyl basicity



1/2 [{{(THF)$_3$.Na$_2$}{(TMEDA).Mg$_2$}(furyl)$_6$}$_\infty$]
3.(thf)$_3$
+ 2 TMP(H) + BuH + 1/2 TMEDA

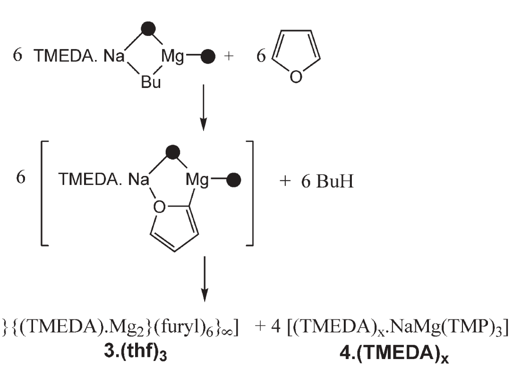
Scheme 1

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

† Participating in the ECTS-Scheme of the EC-Erasmus Programme. Resident university: Ecole Nationale Supérieure de Chimie de Montpellier.

exhibited by **2** in its reactions with benzene[4] and toluene.[5] Furthermore, the mass of **3** produced would be expected to increase *pro rata* on increasing the stoichiometry of furan from one to three molar equivalents [based on the formula of **3**, six molar equivalents of furan would be required for quantitative conversion]. Thus it appears safe to dismiss this first pathway. In the more plausible pathway (Scheme 2) **2** does act as an alkyl base, generating the intermediate [(TMEDA)·Na(μ-2-C_4H_3O)-(μ-TMP)Mg(TMP)], which in turn must disproportionate to **3** and the tris(amido)magnesiate [$(TMEDA)_x$·NaMg$(TMP)_3$] **4·(TMEDA)$_x$**, which remains in solution. NMR spectroscopic analysis of the oily residue left after removing the bulk solvent from this solution confirmed the presence of metal-bound TMP ligands and TMEDA, as well as a negligible amount of TMPH. Though we failed to isolate **4·(TMEDA)$_x$** in a pure solid form, by reacting a 1 : 1 : 3 : 2 mixture of BuNa, Bu_2Mg, TMPH and PMDETA (*N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine) in hexane solution under reflux conditions, we succeeded in synthesising, crystallising, and characterising (*vide infra*) the PMDETA analogue, [$\{(PMDETA)_2{\cdot}Na\}^+\{Mg(TMP)_3\}^-$], **4·(PMDETA)$_2$**.

The new inverse crown motif of **3·(thf)$_3$** (Fig. 1)§ can be regarded as a homoleptic inverse crown 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. Furan anions O(3)–O(6) act as η^2-O,C bridges linking Na to Mg through Na–O and Mg–C bonds, in constructing a 12-membered $(NaOCMgCO)_2$ host ring, which is severely puckered at the C–Mg–C junctions. A direct function of metallating the heterocycle at the α-site, this η^2-bridging contrasts with the η^1-bridges found in all amide-based inverse crowns to date.[11–13] Occupying near-central positions above and below the face of the host ring, guest furyl anions O(1) and O(2) also engage in η^2-O,C bridging to link Na(4) to Mg(1) and Mg(2) respectively, but in addition one π-bond from each of these guest furyls [C(7)–C(8) and C(11)–C(12)] forms short contacts to a third metal [Na(3)]. Thus **3·(thf)$_3$** exhibits the synergic bonding pattern (Mg–C σ bonds; Na···C π contacts) that has become the signature of inverse crowns[11] and related acyclic analogues.[4] Na(3) and Na(4) are therefore distinct, as the former is pseudo-trigonal bipyramidal, binding to two C=C bonds, two furyl (O) and one terminal THF (O) ligands, while the latter occupies a distorted $(O)_6$ octahedron comprising four μ-furyl and two terminal THF ligands. In contrast, Mg(1) and Mg(2) are chemically equivalent, their distorted tetrahedral coordinations made up of three furyl C atoms and one N atom of a TMEDA ligand. The second TMEDA N atom connects intermolecularly to a Mg of a neighbouring inverse crown molecule to build a one-dimensional chain polymer (Fig. 2).



Scheme 2

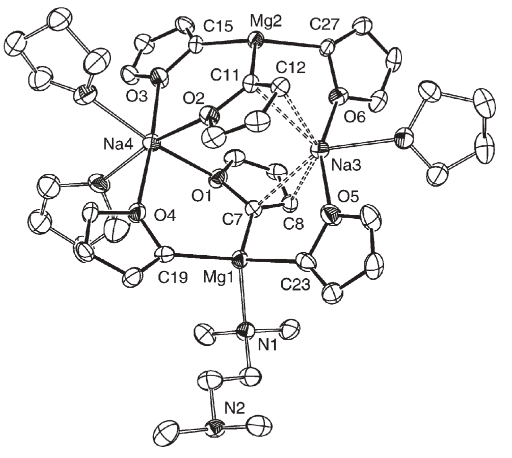


Fig. 1 Asymmetric unit of **3·(thf)$_3$** with selective atom labelling. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Mg(1)–C(23) 2.166(5), Mg(1)–C(19) 2.178(5), Mg(1)–C(7) 2.198(4), Mg(1)–N(1) 2.239(4), Mg(2)–C(15) 2.163(5), Mg(2)–C(27) 2.183(4), Mg(2)–C(11) 2.197(4), Mg(2)–N(2)#1 2.216(4), Na(3)–O(9) 2.330(3), Na(3)–O(5) 2.427(3), Na(3)–O(6) 2.476(3), Na(3)–C(11) 2.721(4), Na(3)–C(12) 2.784(5), Na(3)–C(7) 2.805(4), Na(3)–C(8) 2.821(5), Na(4)–O(3) 2.354(3), Na(4)–O(4) 2.363(3), Na(4)–O(1) 2.421(3), Na(4)–O(7) 2.427(3), Na(4)–O(2) 2.455(3), Na(4)–O(8) 2.458(3).

Searching further afield than inverse crowns, it is apparent that metallated furan structures are rare generally. There are no magnesium or sodium examples and only one mixed-metal precedent. This lithium–tin(II) complex formulated as the separated ion-pair [$\{Li(dioxane)_4\}^+\{Sn(2\text{-}C_4H_3O)_3Li(2\text{-}C_4H_3O)_3\}^-$·2dioxane] adopts a very different structure to **3·(thf)$_3$** with Li^+ sandwiched between two tripodal $(furyl)_3Sn^-$ anions.[14]

X-Ray crystallographic studies of **4·(PMDETA)$_2$**§ also reveal a solvent-separated ion pair structure. For different reasons both the cationic (Fig. 3) and anionic moieties (Fig. 4) are interesting. In the former, two PMDETA ligands struggle to simultaneously chelate to Na^+ with their usual tridentate grip, so as a compromise each forms two short Na–N bonds (mean length, 2.530Å) and one longer Na–N bond (mean length, 2.933Å) involving pseudo-axial N atoms. The latter displays a Mg centre in a trigonal planar environment of three N-attached TMP chair-shaped ligands (though one is disordered over two sites). It is the tris(TMP) content of this magnesiate anion which is surprising since previously attempts to react the Bu base of bis(TMP) **2** with TMPH failed, even under reflux conditions.[4] This emphasises how

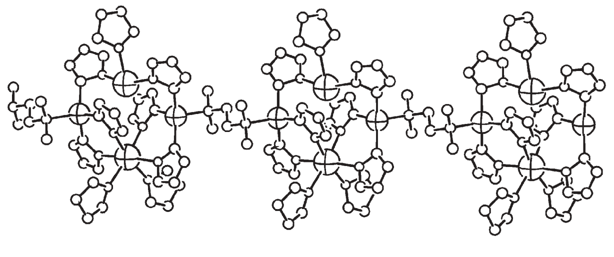


Fig. 2 Section of the extended inverse crown structure of **3·(thf)$_3$**.

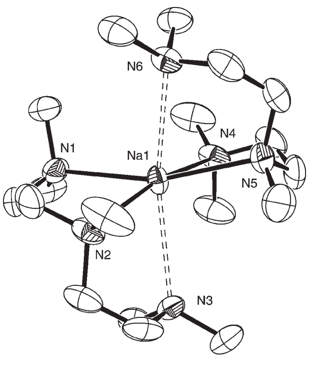


Fig. 3 Molecular structure of the cationic moiety $Na(PMDETA)_2^+$ of **4·(PMDETA)$_2$**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Na(1)–N(2) 2.4892(15), Na(1)–N(5) 2.5047(16), Na(1)–N(4) 2.5443(16), Na(1)–N(1) 2.5825(16), Na(1)–N(3) 2.9160(16), Na(1)–N(6) 2.9498(16).

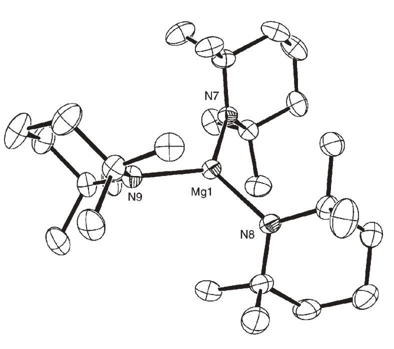


Fig. 4 Molecular structure of the anionic moiety $Mg(TMP)_3^-$ of **4·(PMDETA)$_2$**. Hydrogen atoms and disorder components are omitted for clarity. Selected bond lengths (Å): Mg(1)–N(7) 2.0576(13), Mg(1)–N(8) 2.0441(13).

critical the stoichiometry of the auxiliary ligand [2 PMDETA in **4·(PMDETA)$_2$**; 1 TMEDA in **2**] can be in these mixed-metal systems, and calls for a wider investigation of them under a range of different stoichiometries.

In conclusion, under alkali-metal-mediated magnesiation, furan is deprotonated selectively at the 2-position[15] and the α-furyl anion so produced is manifested in a new type of extended inverse crown structure.

We thank the EPSRC (grant award no. GR/R81183/01 and GR/T27228/01), the EU (Marie Curie Fellowship to E.H.), and the Royal Society/Leverhulme Trust (Fellowship to R.E.M.) for generously sponsoring this research.

Notes and references

‡ The reactions were carried out in a Schlenk tube under a protective argon atmosphere. *Synthesis of 3*. Freshly distilled furan (0.07 mL, 1 mmol) was added to a solution of [(TMEDA)·Na(μ-Bu)(μ-TMP)Mg(TMP)][4] (0.50 g, 1 mmol) in hexane (10 mL). The formation of a white solid was observed. The resulting suspension was stirred at room temperature for one hour. The white solid was collected by filtration, isolated and dried *in vacuo* (approx. 0.10 g: essentially quantitative yield based on Scheme 2 equations). Crystals of **3·(thf)$_3$** were obtained by recrystallising a portion of **3** from thf. ^{1}H NMR (400 MHz, 25°C, d^8-THF): 7.58 (m (br), 6H, H_3, furyl), 6.37 (m (br), 6H, H_5, furyl), 6.11 (m (br), 6H, H_4, furyl), 2.30 (s, 4H, CH_2, TMEDA), 2.15 (s, 12H, CH_3, TMEDA). $^{13}C\{^1H\}$ NMR (100.63 MHz, 25°C, d^8-THF): 201.2 (C_2–Mg, furyl), 144.15 (C_3, furyl), 121.36 (C_5, furyl), 108.10 (C_4, furyl), 58.65 (CH_2, TMEDA), 46.12 (CH_3, TMEDA). Minor traces of furan were also observed. *Synthesis of* ***4·(PMDETA)$_2$***. BuNa (0.4 g, 5 mmol) was suspended in hexane (10 mL). Next Bu_2Mg (5 mL of a 1 M solution in heptane, 5 mmol) was added to produce a white precipitate. TMPH (2.1 mL, 15 mmol) was then introduced. The mixture was stirred at room temperature for 15 min affording a pale yellow solution. PMDETA (2.1 mL, 10 mmol) was added and the solution was refluxed for 90 min affording an orange solution. This solution was allowed to reach room temperature slowly on the bench, affording after three days a crop of colourless crystals (0.42 g, 11%). ^{1}H NMR (400 MHz, 25°C, d^8-THF): 2.45 (m, 8H, CH_2, PMDETA), 2.34 (m, 8H, CH_2, PMDETA), .2.22 (s, 6H, CH_3, PMDETA), 2.18 (s, 36H, CH_3, PMDETA), 1.67 (m, 6H, H_γ, TMP), 1.32 (s, 24H, CH_3, TMP), 1.19 (m, 12H, H_β, TMP). $^{13}C\{^1H\}$ NMR (100.63 MHz, 25°C, d^8-THF): 58.95 (CH_2, PMDETA), 57.42 (CH_2, PMDETA), 53.99 (N–C_α, TMP), 46.43 (CH_3, PMDETA), 43.52 (CH_3, PMDETA), 42.13 (C_β, TMP), 36.39 (CH_3, TMP), 21.36 (C_γ, TMP).

§ Crystal data for **3·(thf)$_3$** $C_{42}H_{58}Mg_2N_2Na_2O_9$, $M_r = 829.50$, monoclinic, space group $P2_1/c$, $a = 15.5185(4)$, $b = 12.6919(5)$, $c = 22.3919(9)$ Å, $\beta = 90.043(2)°$, $V = 4410.3(3)$ Å^3, $Z = 4$, $\lambda = 0.71073$ Å, $\mu = 0.128$ mm^{-1}, $T = 123$ K; 49554 reflections, 6884 unique, R_{int} 0.148; final refinement to convergence on F^2 gave $R = 0.0551$ (F, 5165 obs. data only) and $R_w = 0.1245$ (F^2, all data), GOF = 1.029. The near 90° β angle is due to twinning and the data were treated as such. Crystal data for **4·(PMDETA)$_2$** $C_{45}H_{100}MgN_9Na$, $M_r = 814.64$, monoclinic, space group $P2_1/c$, $a = 16.3726(3)$, $b = 14.8374(2)$, $c = 21.3411(4)$ Å, $\beta = 90.145(1)°$, $V = 5184.31(15)$ Å^3, $Z = 4$, $\lambda = 0.71073$ Å, $\mu = 0.080$ mm^{-1}, $T = 123$ K; 92196 reflections, 11844 unique, R_{int} 0.0687; final refinement to convergence on F^2 gave $R = 0.0534$ (F, 8916 obs. data only) and $R_w = 0.1428$ (F^2, all data), GOF = 1.027. One TMP group is modelled as disordered over two sites. CCDC 287974 and 287985. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b514985a

1 M. Uchiyama, H. Naka, Y. Matsumoto and T. Ohwada, *J. Am. Chem. Soc.*, 2004, **126**, 10526.
2 H. Awad, F. Mongin, F. Trécourt, G. Quéguiner and F. Marsais, *Tetrahedron Lett.*, 2004, **45**, 7873.
3 H. Awad, F. Mongin, F. Trécourt, G. Quéguiner, F. Marsais, F. Blanco, B. Abarca and R. Ballesteros, *Tetrahedron Lett.*, 2004, **45**, 6697.
4 E. Hevia, D. J. Gallagher, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara and C. Talmard, *Chem. Commun.*, 2004, 2422.
5 P. C. Andrikopoulos, D. R. Armstrong, D. V. Graham, E. Hevia, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara and C. Talmard, *Angew. Chem., Int. Ed.*, 2005, **44**, 3459.
6 E. Hevia, G. W. Honeyman, A. R. Kennedy, R. E. Mulvey and D. C. Sherrington, *Angew. Chem., Int. Ed.*, 2005, **44**, 68.
7 Y. Kondo, M. Shilai, M. Uchiyama and T. Sakamoto, *J. Am. Chem. Soc.*, 1999, **121**, 3539.
8 M. Uchiyama, T. Miyoshi, Y. Kajihara, T. Sakamoto, Y. Otani, T. Ohwada and Y. Kondo, *J. Am. Chem. Soc.*, 2002, **124**, 8514.
9 P. C. Andrikopoulos, D. R. Armstrong, H. R. L. Barley, W. Clegg, S. H. Dale, E. Hevia, G. W. Honeyman, A. R. Kennedy and R. E. Mulvey, *J. Am. Chem. Soc.*, 2005, **127**, 6184.
10 E. Hevia, G. W. Honeyman, A. R. Kennedy and R. E. Mulvey, *J. Am. Chem. Soc.*, 2005, **127**, 13106.
11 R. E. Mulvey, *Chem. Commun.*, 2001, 1049.
12 W. Clegg, K. W. Henderson, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, R. B. Rowlings and D. M. Tooke, *Angew. Chem., Int. Ed.*, 2001, **40**, 3902.
13 P. C. Andrikopoulos, D. R. Armstrong, W. Clegg, C. J. Gilfillan, E. Hevia, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, J. A. Parkinson and D. M. Tooke, *J. Am. Chem. Soc.*, 2004, **126**, 11612.
14 M. Veith, C. Ruloff, V. Huch and F. Töllner, *Angew. Chem., Int. Ed.*, 1988, **27**, 1381.
15 For a recent study of the deprotonation of furans using lithium butylmagnesiates, and subsequent electrophilic trapping reactions, see: F. Mongin, A. Bucher, J. P. Bazureau, O. Bayh, H. Awad and F. Trécourt, *Tetrahedron Lett.*, 2005, **46**, 7989.