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Isolation and characterisation of the mixed-metal alkyl amide [(TMEDA)Na(μ-Bu)(μ-TMP)Mg(TMP)], an unexpected chelate-trapped intermediate in the formation of inverse crowns

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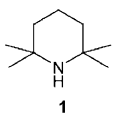
Only two-fold amination occurs when 3 molar equivalents of TMPH are offered to a 1 : 1 BuNa–Bu_2Mg mixture; adding TMEDA gives the mixed alkyl amide [(TMEDA)Na(μ-Bu)-(μ-TMP)Mg(TMP)], which itself affords the phenyl-bridged analogue when reacted with benzene.

Deprotonative metallation is one of the most widely studied and widely utilised transformational tools in chemical synthesis, though comparatively little work has been carried out on mixed-metal reagents[1] in this context. The recently reported[2] synergic (mixed sodium–magnesium) metallation of the cyclic amine TMPH (**1**; 2,2,6,6-tetramethylpiperidine) by a butylsodium–dibutylmagnesium mixture in the presence of toluene (eqn. (1)) sparked interest on two main counts: first, in producing $[Na_4Mg_2(TMP)_6(C_6H_3CH_3)]$ **2**, it established that inverse crowns (Lewis acidic host–Lewis basic guest macrocyclic heterometallic amides)[3] with deprotonated arene guests could be synthesised; second, it introduced a new methodology for the selective metallation of alkylarenes in a ring as opposed to alkyl positions (toluene is two-fold deprotonated in the 2,5 ring positions when encapsulated within the 12-membered host ring). With a view to shedding light on how this synergic phenomenon operates to harvest inverse crowns, hitherto a grey area, we have endeavoured to isolate intermediates from such reactions by exploiting the trapping ability of the chelating auxiliary TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) molecule. Thus this paper describes a successful TMEDA-trapping that has enabled the isolation of an informatory intermediate, the surprising identity of which has been established through crystallographic and spectroscopic characterisation. Having a hybrid composition, part inverse crown, part Lochmann–Schlosser superbase,[1] the intermediate's deprotonative reactivity has been tested through its reaction with benzene, the product of which has also been crystallographically characterised.

$$\mathrm{BuNa} + \mathrm{Bu_2Mg} + 3\mathrm{TMP(H)} + \text{toluene} \rightarrow \mathbf{2} + \text{other products} \quad (1)$$



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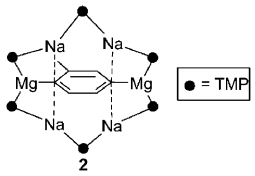

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In order to try to trap a mixed-metallo intermediate prior to the (arene) metallation step, TMEDA was added stoichiometrically (one molar equivalent) to the reaction mixture in eqn. (1) but in the absence of toluene (the pro-guest substrate). This stoichiometry was expected to yield the putative 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 interesting monoalkyl-bis(amido) complex [(TMEDA)-Na(μ-Bu)(μ-TMP)Mg(TMP)], **3**, as isolable colourless crystals.‡ To rule out TMEDA as the instigator of this incomplete amination, we examined TMEDA-free solutions containing butylsodium, dibutylmagnesium and TMPH (in a 1 : 1 : 3 ratio) by ^{1}H and ^{13}C NMR spectroscopy: this confirmed in addition to TMP resonances, the presence of butyl groups and concomitant TMPH molecules, with integration ratios suggesting that the composition of the oil so obtained was predominately [(TMPH)NaMg-(Bu)$(TMP)_2$], that is the TMPH analogue of TMEDA-solvated **3**. When we reflux the reaction mixture containing **3** for 5 hours, Bu and TMPH resonances are still observed in NMR spectra of the residue; however, in a control experiment, only pure Bu-free $Mg(TMP)_2$ is seen when dibutylmagnesium on its own is refluxed in hexane solution. Eaton also observes[4] complete conversion to $Mg(TMP)_2$ on refluxing Bu_2Mg–2TMPH in THF solution. Henderson reported[5] a similar observation in the reaction between dibutylmagnesium and the bulky silylamine hexamethyldisilazane $[(Me_3Si)_2NH$:HMDS(H)] in hydrocarbon solution: the first amination is easy, the second proceeds under forcing reflux conditions producing Bu-free $Mg(HMDS)_2$.

$$2\mathrm{BuNa} + 2\mathrm{Bu_2Mg} + 2\mathrm{TMP(H)} + 2\mathrm{TMEDA} \xrightarrow{-2\mathrm{BuH}} [(\mathrm{TMEDA})\mathrm{Na(Bu)(TMP)Mg(TMP)}] + \mathrm{NaMgBu_3(TMDEDA)} \quad (2)$$

Optimisation of the synthesis of **3** revealed that the best yield (42%: maximum possible 50%) is achieved using only one molar equivalent of TMPH, allowing the balanced reaction in eqn. (2) to be constructed. The suspected co-product $[NaMg(Bu)_3\cdot(TMEDA)]$, which we could not obtain in solid form, appears as a residual, impure, colourless oil following filtration/isolation of crystalline **3** and removal of solvent *in vacuo* from the filtrate of the reaction mixture. NMR spectroscopic analysis of this oil confirmed the predominance of Bu and (coordinated) TMEDA resonances, and near negligible quantity of TMPH. It should be noted that the "$NaMg(Bu)_3$" formulation is precedented as, termed sodium tributylmagnesiate,[6] it was employed in anionic polymerisations of isoprene and styrene; however, no characterisation details were reported in this paper.

A four-element NaNMgC ring, with a mixed TMP–Bu bridging ligand set, forms the central feature of the molecular structure of **3** (Fig. 1),§ which is completed by a terminal TMP on Mg and a chelating TMEDA on Na. This central ring is modestly puckered [the NaNMgC atoms sit 0.110(1), −0.149(1), 0.170(1) and −0.131(1) Å respectively out of the best fit plane, with a fold angle of 161.14(8)°]. Adhering to an interpretation defined previously for mixed Li–Mg compounds,[3] the Mg anchors the anionic ligand set into a trigonal planar framework (sum of bond angles, 359.94°) through strong bonds of relatively high covalency, offering one triangular edge for the weaker, more electrostatic ancillary bonding of Na. The large disparity in bond lengths in the mixed bridges of the central ring [Na1–C1, 2.669(2) Å, Mg1–C1, 2.200(2) Å, Na1–N1, 2.4523(18) Å, Mg1–N1, 2.0791(17) Å] is consistent with this picture. The trigonal planar Mg geometry is distorted by the vast bulk of two adjacent TMP ligands leading to a

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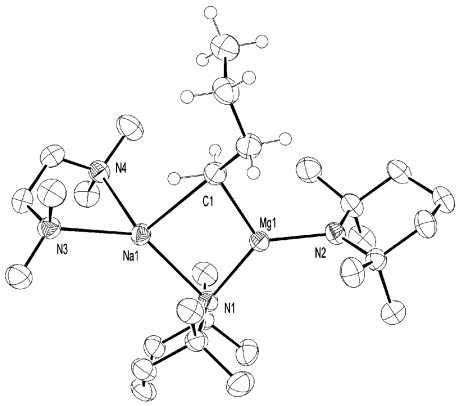

Fig. 1 Molecular structure of **3** with selective atom labelling. Hydrogen atoms (except Bu ones) omitted for clarity.

wide N1Mg1N2 angle [132.20(7)°], which is counterbalanced by a constricted N1Mg1C1 endocyclic bond angle [108.57(8)°]. Lying only 0.369(1) Å above the N1N3N4 plane (compared to between 0.642 and 1.199 Å to the other CNN planes surrounding it), Na1 occupies a geometry best described as distorted trigonal pyramidal with the apex C1. Pentacoordinate C1 assumes a distorted tetrahedral geometry if the contact to Na1 is discounted: the odd positioning of Na1 within the coordination sphere of C1 is best illustrated by the extreme Na1C1C2 [155.50(19)°] and Na1C1H1B [55.7(17)°] bond angles (H1B is a methylene H atom attached to C1).

Identifying the 'intermediate' trapped within **3** provides persuasive evidence that the active base in the formation of inverse crown **2** is '[Na(Bu)(TMP)Mg(TMP) ± TMPH]' which itself could be considered a co-complex of BuNa and $Mg(TMP)_2$, in the same way that the best known superbase is a co-complex of BuLi and $KOBu^t$.[7] Thus, complex **3** represents an intriguing, potentially useful, base in its own right possessing (in theory) dual alkyl and amido basicity, as well as the 'activating' effect of the auxiliary TMEDA ligand. We have therefore examined its deprotonative ability in a reaction with benzene. Deprotonation is smoothly accomplished and the resulting Ph^- is encapsulated within [(TMEDA)Na(μ-Ph)(μ-TMP)Mg(TMP)], **4**. Its molecular structure (Fig. 2)§ exhibits similar gross features to those of **3** with Ph^- occupying the vacancy left by Bu^- (hence, here, **3** acts as an alkyl base). Mimicking the situation recurrent in inverse crowns, Mg lies close to the Ph ring plane [C4···C1–Mg1 angle, 170.9(1)°], while Na binds to its face in a η^1-fashion, indicative of a σ/π demarcation in the bonding. It is worth reiterating that **3** does not appear to deprotonate TMPH, which significantly is more acidic (in pK_a terms) than benzene. Thus, in the guise of a magnesium amide–TMEDA co-stabilised, sterically hindered variant of butylsodium, **3** offers promise as a selective base, readily available in an amenable crystalline form.

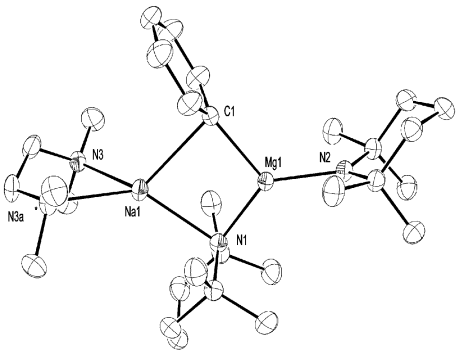

Fig. 2 Molecular structure of **4** with selective atom labelling. Hydrogen atoms omitted for clarity.

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Notes and references

‡ All reactions were carried out under a protective argon atmosphere. *Synthesis of [(TMEDA)Na(μ-Bu)(μ-TMP)Mg(TMP)] (**3**):* BuNa (0.4 g, 5 mmol) was suspended in hexane (10 mL). Bu_2Mg (5 mL of a 1 M solution in heptane, 5 mmol) was then added to produce a white precipitate. TMP(H) (0.85 mL, 5 mmol) was then introduced and the mixture was stirred at room temperature for 30 minutes until all the solid had dissolved. At this stage TMEDA (0.75 mL, 5 mmol) was added. After stirring for 15 minutes, the solution was concentrated by removing some solvent in vacuo. Placed in the freezer at −28 °C, the resulting pale yellow solution deposited a crop of colourless crystals (1.02 g, 42%). ^{1}H NMR (400 MHz, 25 °C, C_6D_6): δ 2.05 (m, 2H, CH_2, Bu), 1.92 (m, 4H, TMP), 1.79 (m, 14H, CH_3, TMEDA and CH_2, Bu), 1.73 (m, 4H, CH_2, TMEDA), 1.53 (s, 24H, CH_3, TMP), 1.44 (m, 8H, TMP), 1.23 (t, 3H, CH_3, Bu), −0.78 (m, 2H, Mg–CH_2, Bu). $^{13}C\{^1H\}$ NMR (100.63 MHz, 25 °C, C_6D_6): δ 57.34 (CH_2, TMEDA), 52.72 (N–C, TMP), 46.36 (CH_3, TMEDA), 42.78 (TMP), 36.03 (CH_3, TMP), 33.41 (CH_2, Bu), 32.94 (CH_3, Bu), 20.93 (TMP), 14.90 (CH_2, Bu), 14.85 (Mg–CH_2, Bu). Synthesis of [(TMEDA)-Na(μ-Ph)(μ-TMP)Mg(TMP)] (**4**): Compound **3** (1.0 g, 2 mmol) was dissolved in hexane (10 mL). Then 2 mL of benzene (22 mmol) were added and the colourless solution obtained was refluxed for 90 minutes. The resulting yellow solution was placed in a Dewar flask of hot water and allowed to cool slowly to room temperature affording colourless crystals of **4** (0.46 g, 44%).^{1}H NMR (400 MHz, 25 °C, C_6D_6): δ 7.88 (m, 2H, H_{ortho}, Ph), 7.16 (m, H_{meta}, Ph, obscured by the solvent), 7.09 (m, 1H, H_{para}, Ph), 1.90 (m, 4H, TMP), 1.63 (m, 24H, CH_3, TMP), 1.54 (s, 12H, CH_3, TMEDA), 1.49 (s, 4H, CH_2, TMEDA), 1.37 (m, 8H, TMP). $^{13}C\{^1H\}$ NMR (100.63 MHz, 25 °C, C_6D_6): δ 173.35 (C_{ipso}, Ph), 140.91 (C_{ortho}, Ph), 127.86 (C_{meta}, Ph), 125.44 (C_{para}, Ph), 57.26 (CH_2, TMEDA), 52.60 (N–C, TMP), 46.23 (CH_3, TMEDA), 42.72 (TMP), 36.22 (CH_3, TMP), 20.68 (TMP).

§ Crystal data for **3**: $C_{28}H_{61}MgN_4Na$, M_r = 501.11, triclinic, space group $P\bar{1}$, a = 10.2664(6), b = 10.9478(7), c = 15.3294(8) Å, α = 97.037(3), β = 106.436(4), γ = 96.617(2)°, V = 1619.62(16) Å^3, Z = 2, λ = 0.71073 Å, μ = 0.089 mm^{-1}, T = 123 K; 23255 reflections, 6474 unique, R_{int} 0.0693; final refinement to convergence on F^2 gave R = 0.0601 (F, 5441 obs. data only) and R_w = 0.1734 (F^2, all data), GOF = 1.102. Crystal data for **4**: $C_{30}H_{57}MgN_4Na$, M_r = 521.10, orthorhombic, space group *Pnma*, a = 22.7801(4), b = 14.7272(3), c = 9.7007(2) Å, V = 3254.46(11) Å^3, Z = 4, λ = 0.71073 Å, μ = 0.091 mm^{-1}, T = 123 K; 7159 reflections, 3877 unique, R_{int} 0.0360; final refinement to convergence on F^2 gave R = 0.0467 (F, 2722 obs. data only) and R_w = 0.1244 (F^2, all data), GOF = 1.028. CCDC 244499 and 244500. See http://www.rsc.org/suppdata/cc/b4/b410293b/ for crystallographic data in .cif or other electronic format.

1 An exception is the so called Lochmann–Schlosser superbases: see (*a*) L. Lochmann, *Eur. J. Inorg. Chem.*, 2000, 115; (*b*) M. Schlosser, *Organometallics in Synthesis*, Wiley, Chichester, 2nd edn., 2002, pp. 1–353.
2 D. R. Armstrong, A. R. Kennedy, R. E. Mulvey and R. B. Rowlings, *Angew. Chem., Int. Ed.*, 1999, **38**, 131.
3 R. E. Mulvey, *Chem. Commun.*, 2001, 1049.
4 P. E. Eaton, C.-H. Lee and Y. Xiang, *J. Am. Chem. Soc.*, 1989, **111**, 8016.
5 K. W. Henderson, J. F. Allan and A. R. Kennedy, *Chem. Commun.*, 1997, 1149.
6 M. Liu, C. Kamienski, M. Morton and L. J. Fetters, *J. Macromol. Sci., Chem.*, 1986, **A23**, 1387.
7 M. Schlosser, *Mod. Synth. Methods*, 1992, **6**, 227.