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Bicyclic guanidinate compounds of magnesium and their activity as pre-catalysts in the Tishchenko reaction†

Benjamin M. Day, Natalie E. Mansfield, Martyn P. Coles* and Peter B. Hitchcock

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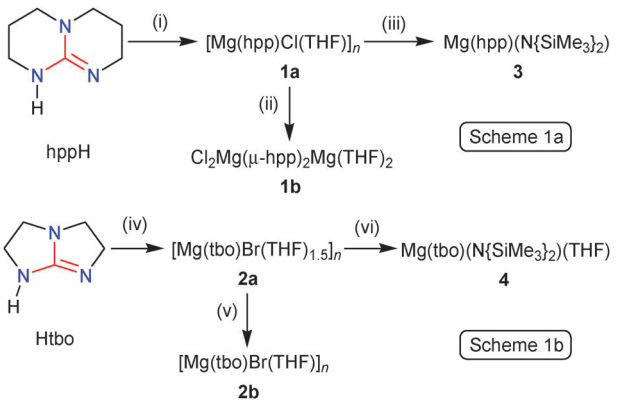
A synthetic route to magnesium guanidinate compounds that avoids ligand redistribution is reported; selected derivatives are active pre-catalysts in the dimerization of aldehydes.

The Tishchenko reaction is an industrially important process for the synthesis of esters *via* the simultaneous oxidation and reduction of two aldehydes.[1] Aluminium alkoxides were originally studied as catalysts,[2] with recent work including lanthanide[3] and actinide[4] systems, with particularly impressive results from lanthanum formamidinates.[5] Exploiting parallels between the 4f- and heavier group 2 elements, Hill *et al.* reported the catalytic activity of Ca, Sr, and Ba amides.[6] The only example of a homogeneous catalyst employing magnesium is a bio-inspired thiolate system,[7] in which bromomagnesium salts were prepared *in situ* from PhMgBr and thiols.

Isolable magnesium catalysts for the Tishchenko reaction remain an attractive goal due to the low cost/toxicity, and the commercial availability of magnesium in the form of Grignard reagents. An important consideration is the propensity for ligand redistribution *via* Schlenk equilibria,[8] and a judicious choice of supporting ligand is required. Our research interests include amidinate[9] and guanidinate[10] ligands in molecular catalysis, focussing on bicyclic derivatives.[11] We have demonstrated that the $[hpp]^-$ anion (Scheme 1a for hppH) is a stable ancillary ligand in titanium mediated olefin polymerization,[12,13] and that the zinc amide Zn(hpp)(N{SiMe$_3$}$_2$) is active in the ring-opening polymerization of lactide.[14] Whilst amidinate and guanidinate ligands have previously been used in the coordination chemistry of magnesium, few applications of the resultant compounds have been reported.

Most magnesium amidinates are solvated bis-ligand compounds, Mg(L)$_2$(solvent)$_n$ (L = amidinate; n = 0–3),[15–19] and mono-amidinate compounds are only isolable if the additional ligands are bulky (*e.g.* Cp,[19] N(Ar)(PR$_2$), Ar = 2,6-^{i}Pr$_2$C$_6$H$_3$)[20] or the amidinate has sterically encumbering substituents.[18] A self-assembled spirocyclic derivative incorporating $[PhC\{NSiMe_3\}_2]^-$ represents a recent additional structural type.[21] Despite their close relationship, corresponding guanidinate compounds are less common.[16,22] Only recently has the reaction between hppH and MgMeBr been reported to afford the tetramer, [Mg(hpp)Br]$_4$.[23] This compound is described as "extremely sensitive" and only a few crystals were isolated. We report high yielding routes to magnesium compounds supported by bicyclic guanidinates, and the application of examples as pre-catalysts in the Tishchenko reaction.



Scheme 1 (a) (i) MgMeCl, THF; (ii) THF, 65 °C, slow cool to room temperature, (iii) LiN{SiMe$_3$}$_2$, THF. (b) (iv) MgMeBr, THF; (v) vacuum; (vi) LiN{SiMe$_3$}$_2$, THF.

The reaction of one equivalent of hppH with MgMeCl in THF proceeded with gas evolution and precipitation of a white solid, **1a** (Scheme 1a). ^{1}H NMR spectroscopy and elemental analysis were consistent with Mg(hpp)Cl(THF),† which given the propensity for $[hpp]^-$ to bridge metal centres,[11,23] likely exists as an aggregate.[24] The corresponding reaction of Htbo with MeMgBr gave no precipitate and colourless crystals **2a** were obtained on work-up (Scheme 1b). ^{1}H NMR integrals for **2a** showed a $[tbo]^-$: THF ratio of 2 : 3; however, elemental analysis was consistent with loss of THF under vacuum to afford **2b**.† NMR data for **1a** and **2a** indicate symmetric environments for the guanidinates based on three and two groups of annular methylene resonances, respectively.

Colourless crystals **1b** (Fig. 1) were grown by slow cooling a hot (~65 °C) THF solution of **1a**.† The structure is comprised of two non-symmetry related Mg atoms supported by two

Department of Chemistry, University of Sussex, Falmer, Brighton BN1 9QJ, UK. E-mail: m.p.coles@sussex.ac.uk; Fax: +44 (0)1273 876687; Tel: +44 (0)1273 877339

† Electronic supplementary information (ESI) available: Experimental procedures, including details of the catalysis experiments, a description of crystallographic disorder, and characterizing data for all compounds. CCDC 799143–799146 for **1b**, **2a**, [**3**]$_2$ and [**4**]$_2$. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0cc04789a

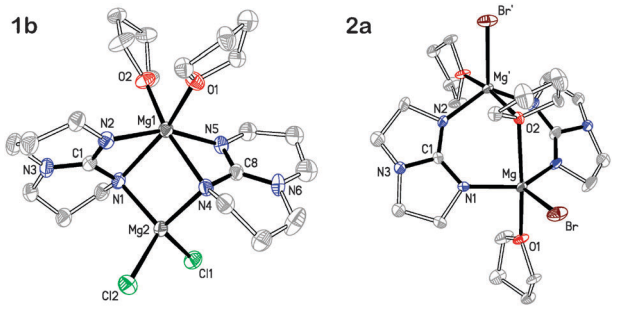
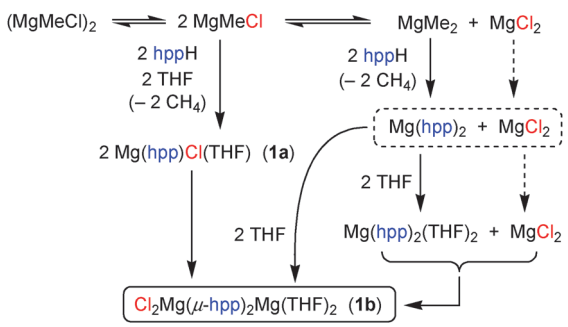


Fig. 1 Molecular structures of **1b** and **2a** (ellipsoids 30%, higher occupancy positions for disordered hpp and THF (**1b**) and tbo (**2a**) shown).† Selected bond lengths (Å) and angles (°): **1b** N1–Mg1 2.343(4), N2–Mg1 2.087(4), N4–Mg1 2.222(4), N5–Mg1 2.114(4), N1–Mg2 2.093(4), N4–Mg2 2.085(4); N1–Mg1–N2 61.08(15), N4–Mg1–N5 62.88(16), N1–Mg2–N4 99.35(17). **2a** Mg–N1 2.037(4), Mg′–N2 2.034(4), Mg–O1 2.093(3), Mg–O2 2.426(3); O1–Mg–O2 170.47(12), N1–Mg–N2′ 128.71(16), N1–Mg–Br 117.33(12), N2′–Mg–Br 113.48(12).

$[hpp]^-$ ligands with $(\kappa^1N,\kappa^{1,2}N')(\kappa^2N,\kappa^{1,2}N')$-bonding.‡ The octahedral geometry at Mg1 is highly distorted [range of angles: 61.08(15)°–102.78(16)°], with the chelated guanidinates describing the most acute angles. In contrast, Mg2 is a distorted tetrahedron [angles 99.35(17)°–113.37(13)°] defined by two terminal chlorides and a single nitrogen atom from each guanidinate.

Alternative routes to **1b** can be formulated considering methyl Grignard reagents that exist as equilibrium mixtures of $MgMe_2$ and MgX_2 in THF (Scheme 2). Initial protonation with hppH could lead to the (solvated) mixed ligand species **1a**, as observed for $[Mg(hpp)Br]_4$,[23] or the homoleptic bis-guanidine, $Mg(hpp)_2(THF)_n$.[25] In the latter case, partial transfer of the $[hpp]^-$ anion to a '$MgCl_2$' unit will afford **1b** (upon THF solvation), whereas if the reaction proceeded *via* **1a**, chloride transfer between magnesium centres would have to occur. We note that guanidinate bonding in **1b** is reminiscent of a previously reported Al/Ti complex,[12] which was shown to be an intermediate in the transfer of the guanidinate from titanium to aluminium.

The molecular structure of **2a** corresponds to $Mg_2(tbo)_2Br_2(THF)_3$. Each $[tbo]^-$ anion bridges the two metal atoms in a κ^1N,κ^2N'-bonding mode, reflecting the wider projection of the frontier orbitals.[26] The geometry at magnesium approaches trigonal bipyramidal (τ = 0.70),[27] with THF in axial positions, one of which adopts an unusual bridging mode.[17,28]



Scheme 2 Possible routes to the formation of **1b**.

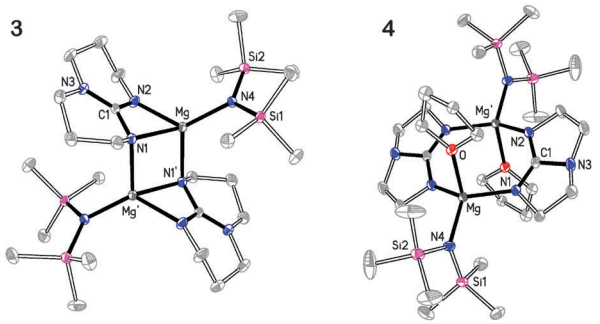


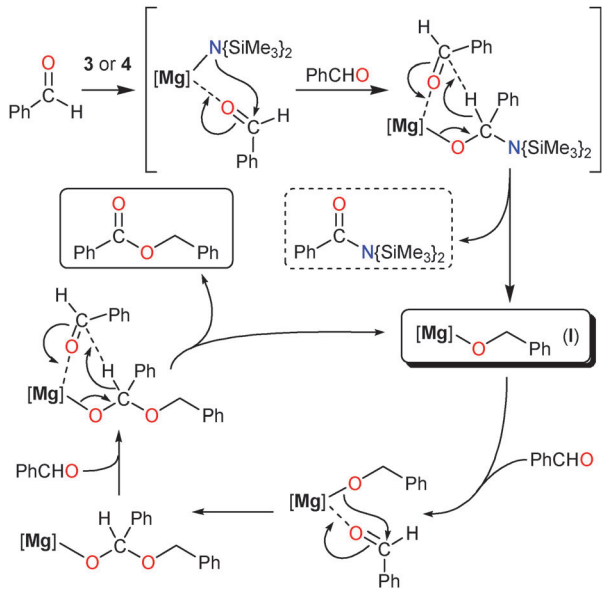
Fig. 2 Molecular structures of $[3]_2$ (ellipsoids 30%, higher occupancy position for disordered hpp group shown) and $[4]_2$ (ellipsoids 20%, higher occupancy positions for disordered $SiMe_3$ and THF groups shown). Selected bond lengths (Å) and angles (°): **3** Mg–N1 2.1752(14), Mg–N1′ 2.1255(14), Mg–N2 2.0738(14), Mg–N4 1.9798(14); N1–Mg–N2 64.19(5), N1–Mg–N1′ 94.17(5), Mg–N1–Mg′ 85.83(5). **4** Mg–N1 2.0468(15), Mg–N2′ 2.0507(15), Mg–N4 2.0205(15), Mg–O 2.0578(14); N1–Mg–N2′ 124.50(6), N1–C1–N2 132.07(15).

For catalytic applications, the magnesium amides, **3** and **4**, were synthesized (Schemes 1a and b). To minimize ligand redistribution both reactions were performed without isolation of the halide, affording the amides in overall yields of 68% (**3**) and 72% (**4**). Spectroscopic data show symmetric guanidinates, with one equivalent of THF in tbo derivative **4**.

X-Ray diffraction† shows that $[3]_2$ is isostructural with the zinc analogue,[14] consisting of $[(\kappa^1N,\kappa^{1,2}N')]_2$-bridging guanidinates‡ and terminal amides (Fig. 2). A strong association of the two '$Mg(hpp)(N\{SiMe_3\}_2)$' units is suggested by the short Mg–N1′ distance compared with Mg–N. In $[4]_2$, the guanidinates retain the κ^1N,κ^2N'-bonding observed in **2a**. The bulk of the amide ligands alleviate the need for a μ-THF group, although the magnesium centres retain a terminal THF resulting in a distorted tetrahedral geometry.

The activity of **3** and **4** towards the dimerization of benzaldehyde was examined on an NMR scale, using 1 mol% magnesium reagent and 1,4-dimethoxybenzene as an internal standard.† The initial reaction was rapid with both compounds, showing ~20% yield of the ester after 10 min (TOF 120 h^{-1}).[29] With hpp-derivative **3**, production is maintained at an approximately constant rate for an additional 20 min, whereas pre-catalyst **4** is notably slower, with 60% yield produced after 100 min. These data compare favourably with the reported magnesium thiolate systems,[7] where 5–20 mol% is required to give greater than 70% yield, and reaction times of 24–72 h.

Increasing the amount of **3** and **4** to 10 mol% enabled the catalysis to be examined in more detail. Under these conditions the final NMR yield of benzyl benzoate was 70–75% after essentially complete consumption of the substrate (< 5% remaining), indicating formation of side products incorporating benzaldehyde. This is expected based on the accepted mechanism derived from previously studied homogeneous catalyst systems, for which the proposed active species is the alkoxide, $[M]OCH_2Ph$.[1] A mechanism outlining the formation of $Mg(L')(OCH_2Ph)$ (**I**, L′ = $[hpp]^-$ or $[tbo]^-$) is given in Scheme 3.[30] In contrast to the reaction using $Ca(L'')(N\{SiMe_3\}_2)(THF)$ (L″ = $[HC\{C(Me)NAr\}_2]^-$, Ar = 2,6-^{i}Pr$_2$C$_6$H$_3$) in which L″H was liberated,[6] there is no indication of the neutral guanidine with **3** and **4**, providing evidence for



Scheme 3 Proposed mechanism for the Tishchenko reaction using **3** and **4** as pre-catalysts. [**Mg**] = 'Mg(guanidinate)', where guanidinate = $[hpp]^-$ (**3**) and $[tbo]^-$ (**4**).

the integrity of the Mg(L′) unit during catalysis. Furthermore, introduction of an additional 10 equiv. of benzaldehyde after complete consumption of the initial substrate reinitiated production of the ester, which proceeded to give a final yield of greater than 90% (24 h). These results demonstrate that once formed, the active species **I** are stable in solution, and offer intriguing possibilities for the synthesis of non-symmetrically coupled products.

To probe the scope of the substrate generality, the reactions of **3** (1 mol%) with pivaldehyde, cyclohexanecarbaldehyde, isovaleraldehyde and acetaldehyde were examined. The dimerization of pivaldehyde was slower than for benzaldehyde (10% yield of the ester after 10 min, TOF = 60 h^{-1}), with an 83% yield after 24 h and no observable side-products by NMR spectroscopy. Dimerization also occurred with the enolizable substrate cyclohexanecarbaldehyde. The catalysis was initially more rapid, with a 56% yield of the ester after 10 min (TOF = 336 h^{-1}). However, only a 75% yield of ester is produced after 24 h with almost full consumption of the aldehyde (~2% remaining), indicating the presence of side reactions. In contrast, the reactions of **3** with isovaleraldehyde and acetaldehyde gave complex mixtures of oligomeric species.

In summary, we have developed a viable synthetic route to heteroleptic magnesium compounds incorporating bicyclic guanidinate ligands and demonstrated their activity as pre-catalysts in the Tishchenko reaction.

Notes and references

‡ Expansion of the nomenclature used to describe guanidinates that bridge more than one metal centre is given in the ESI.†

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