

Synthesis and structural characterisation of a magnesium bisenolate: a tetrameric (Mg₂O₂)₂ chain terminated by solvating ketone

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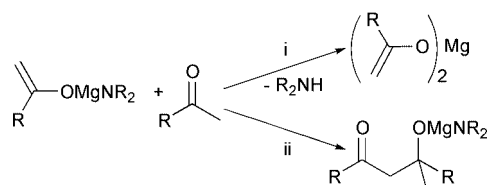
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A reactive magnesium enolate intermediate has been identified containing the remarkable composition of four metals, eight enolates (six bridging and two terminally bound) and two unenolised ketones, and its implications in the aldol addition reaction are discussed.

Enolate anions are key intermediates in numerous transformations including alkylations, Michael reactions, protonations, acylations and aldol additions.¹ We have recently begun an investigation into the use of magnesium bisamides, (R₂N)₂Mg, as reagents and have found significant differences in their reactivity, and more importantly in their selectivity, compared with their Li analogues. Recently reported uses of Mg-bisamides include the regio- and stereo-selective synthesis of kinetic silyl enol ethers,² the formation of secondary and tertiary β-hydroxy ketones via aldol addition reactions,³ and as asymmetric induction reagents in enantioselective deprotonation reactions.⁴ Herein, we discuss the formation and structure of a novel magnesium bisenolate and consider its role as a model complex in the aldol addition reaction.

The organometallic complexes produced by the reaction of magnesium bishexamethylsilylazide **1** with 2,4,6-trimethylacetophenone **2** (between 2 and 6 mol equiv.) in hexane solution were initially determined by ¹H NMR spectroscopic analysis of the solids precipitated from solution.[†] Only enolate and unenolised ketone were present in the solids, and the absence of any amide suggested formation of a magnesium bisenolate. This is in marked contrast with our previous studies³ of the reaction between **1** and 2 mol equiv. of a series of methyl ketones [O=C(Me)R, where R = Bu^t, Ph, Buⁿ, Prⁱ or cyclohexyl], which undergo aldol addition reactions. Furthermore, the aldol reaction sequence is supported by the structural characterisation of the amido(aldolate) [{(Me₃Si)₂NMg(μ-OC(Me)^tBuCH₂C(=O)Bu)=O}]₂ **3**,³ i.e. enolisation followed by aldol addition with retention of one amido unit attached to the metal. Following initial formation of an amido(enolate), two distinct routes are in competition either enolisation or aldol addition (Scheme 1). Formation of a bisenolate in preference to an amido(aldolate) for the reactions involving **2** is most likely due to a combination of the steric crowding and the electronics of the ketone which retard the addition reaction.⁵ The presence of an amido(enolate) intermediate in these reactions was confirmed by *in situ* ¹H NMR spectroscopic monitoring of the equimolar reaction between **1** and **2**. In addition, bisenolate was also detected in these mixtures demonstrating a competitive reaction even at this stage. Further support for an amido(enolate) reaction inter-



Scheme 1 Formation of (i) bisenolate or (ii) amido(aldolate) via an amido(enolate); aggregation state is ignored.

mediate comes from the recent structural elucidation of [{(Me₃Si)₂NMg{μ-OC(Ph)=CHMe}·THF}]₂ **4**, formed by reaction of **1** with 1 equiv. of propiophenone.^{2b}

Repeated attempts at crystal growth from the reactions between **1** and **2** resulted in the formation of crystallites too small for conventional single crystal diffraction but were suitable for analysis using synchrotron radiation.[‡] This study revealed the complex [Mg₄{OC(Mes)=CH₂}₈·{O=C(Mes)-Me}₂·(C₆H₅(Me)₂)] **5** (Mes = 2,4,6-Me₃C₆H₂), which is centrosymmetric and contains the novel composition (ignoring the inclusion solvent toluene) of four magnesiums, six bridging enolates, two terminal enolates (O2 and O2*) and two ketones (O1 and O1*) coordinated to the terminal metal centres (Fig. 1). The linear arrangement of the metals in a limited tetrameric complex represents a completely new structural motif in magnesium coordination chemistry.⁶ Although rare, tetrameric conformations, where the metals form either rhombohedral or tetrahedral geometries respectively, are known.⁶ The structure of **5** can be described as a section of polymeric bisenolate consisting of linked orthogonal Mg₂O₂ rings which has been intersected by donor solvent, interestingly in this case unenolised ketone.

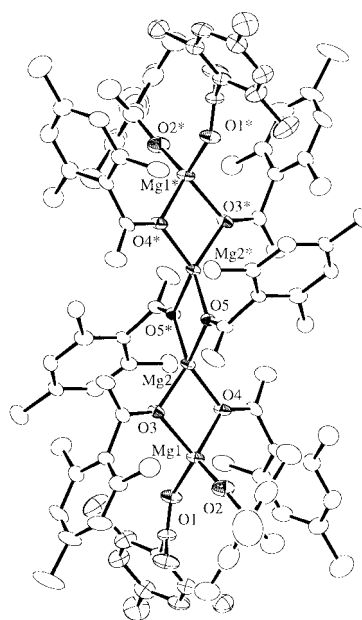


Fig. 1 Molecular structure of **5** with hydrogen atoms and solvents of crystallisation omitted for clarity. The ketone ligands are highlighted with hatched ellipses. Selected bond lengths (Å) and angles (°): Mg(1)–O(1) 2.012(3), Mg(1)–O(2) 1.845(3), Mg(1)–O(3) 1.991(3), Mg(1)–O(4) 1.970(3), Mg(2)–O(3) 1.969(3), Mg(2)–O(4) 1.965(3), Mg(2)–O(5) 1.978(3), Mg(2)–O(5*) 1.963(3); O(1)–Mg(1)–O(2) 110.08(13), O(1)–Mg(1)–O(3) 114.54(12), O(1)–Mg(1)–O(4) 108.28(12), O(2)–Mg(1)–O(3) 117.88(13), O(2)–Mg(1)–O(4) 122.24(14), O(3)–Mg(1)–O(4) 81.16(10), O(3)–Mg(2)–O(4) 81.83(11), O(4)–Mg(2)–O(5) 125.96(12), O(3)–Mg(2)–O(5) 117.87(11), O(3)–Mg(2)–O(5*) 135.08(12), O(4)–Mg(2)–O(5*) 121.39(11). * Indicates the transformation 1 – x, 1 – y, 1 – z.

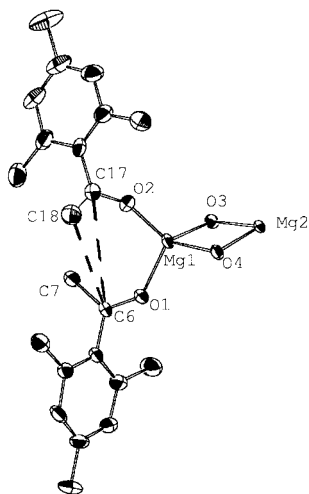


Fig. 2 View of the terminally bound groups in **5**. Important interatomic distances (Å): C(18)–C(6) 4.156(7), C(17)–C(6) 4.164(6), C(18)–O(1) 4.237(6), C(17)–O(1) 4.021(5).

Diphenylmagnesium adopts a polymeric structure⁷ similar to the core of **5** but deaggregates only to monomers on addition of either THF or TMEDA.⁸ The highly unusual tetrameric framework adopted by **5** may be explained by analysis of the structure. The two central aromatic rings, connected to O(5) and O(5*), are oriented *anti* to one another, whereas the aromatic groups of the terminal rings, connected to O(3) and O(4), are *syn* with respect to each other and are directed towards the terminal metal, Mg(1). If the polymeric form of the bisenolate has a similar structure the steric crowding induced by the *syn* aromatic groups may result in weak links in the polymer chain, leading to preferential scission at these sites. Alternatively, **5** may be the end product of chain growth with the *syn* aromatic groups on O(3) and O(4) blocking any further propagation.

The geometric parameters within **5** are in accord with those expected for Mg-alkoxides.⁶ Each metal is four coordinate with no significant interactions to either the arene rings or the olefinic groups (all Mg–C are > 3 Å). The central Mg₂O₂ ring is strictly planar, whereas the two terminal rings are buckled, with each of the atoms deviating from the mean plane by 0.56(1) Å, and with an interplanar angle between the central and outer rings of 80.13(9)°.

A remarkable feature of **5** is the presence of solvating ketone in addition to enolate groups, hence **5** can be considered as a model, aggregated, pre-aldol intermediate. Although there has been much speculation about the importance of pre-solvation in similar transformations, in particular for Li-mediated reactions,⁹ surprisingly little direct evidence for its existence has been reported.¹⁰ In part, this is due to the high reactivity of these complexes. In this instance the aldol addition reaction is disfavoured facilitating the isolation of **5**. Nevertheless, the self-coupled tertiary β-hydroxy ketone derived from **2** was detected in low yield (< 5%) on extended reaction times. In contrast, secondary β-hydroxy ketones could be readily prepared (> 80% yield) by reaction of the enolate solutions with aldehydes.

Finally, it is intriguing to speculate on the orientations adopted by the terminally bound enolate and ketone groups within **5**. The olefinic carbons C(17) and C(18) are essentially equidistant to the carbonyl carbon C(6) of the ketone and hence the centre of the π-bond is oriented appropriately for nucleophilic attack of the carbonyl through a six-membered transition state similar to that postulated in the Zimmerman–Traxler model (Fig. 2).¹¹ Such a mechanism would involve aldol addition *via* the terminal and not the bridging enolate groups of the aggregate.

Notes and references

† **5**: a solution of **1** (3 mmol) in hexane (10 mL) was cooled to –78 °C and **2** (6–18 mmol) was added dropwise by syringe over a period of 2 min. The mixture was allowed to warm to ambient temperature after 15 min and stirred for a further two days. The resulting white solids were filtered off, washed with hexane and analysed by ¹H NMR spectroscopy. Subsequent recrystallisation of the solids from hexane–toluene yielded small crystals, which were used for the X-ray diffraction analysis. The varying amount of unenolised ketone present (between 0.1 and 0.8 equiv.) is consistent with more than one type of solvated enolate present, most likely dimers or monomers. However, these could not be separated for unambiguous analysis and limited the analysis of the products to NMR spectroscopy. *In situ* ¹H NMR spectroscopic studies indicated complete reaction of **1** with available ketone after several hours at ambient temperature. ¹H NMR (400 MHz, [²H₅]pyridine, 25 °C): bisenolate: δ 7.00 (s, 2H, *m*-H, Mes), 3.91, 3.81 [d, ²J(HH) 1.7 Hz, 1H, C=CH₂] 2.63 (s, 6H, *o*-CH₃), 2.33 (s, 3H, *p*-CH₃); unenolised ketone: δ 6.78 (s, 2H, *m*-H, Mes), 2.42 (s, 3H, *p*-CH₃), 2.19 (s, 9H, *m*-CH₃ and CH₃); amido(enolate): δ 6.89 (s, 2H, *m*-H, Mes), 4.48, 3.91 [d, ²J(HH) 1.3 Hz, 1H, C=CH₂], 2.59 (s, 6H, *o*-CH₃), 2.27 (s, 3H, *p*-CH₃), 0.29 (s, 18H, SiMe₃).

‡ *Crystal data* for **5**: C₁₂₄H₁₄₈Mg₄O₁₀, *M* = 1895.66, *T* = 150(2) K, measurements were performed at Station 9.8, Daresbury SRS with Si111 monochromated radiation (λ = 0.6884 Å). A single crystal of dimensions 0.18 × 0.08 × 0.02 mm was mounted in inert oil and transferred to the cold N₂ gas stream of the diffractometer. Triclinic, space group *P* $\bar{1}$, *a* = 11.8142(7), *b* = 11.8617(7), *c* = 20.5469(13) Å, α = 74.844(2), β = 84.437(2), γ = 83.078(2)°, *U* = 2752.5(3) Å³, *Z* = 1, μ = 0.185 mm⁻¹, *D*_c = 1.144 Mg m⁻³, 2θ_{max} = 45°, 10156 reflections collected, 7669 unique, (*R*_{int} = 0.0425) all were used in the calculations. All non-hydrogen atoms were treated anisotropically and all hydrogens included in a riding model. The final *wR*(*F*²) was 0.1823, conventional *R* was 0.0680 and *S* = 1.002 for 637 parameters. Highest residual electron density 0.260 e Å⁻³. Programs were standard (G. M. Sheldrick, University of Göttingen, Germany) diffractometer control software and members of the SHELX family. The structure was solved using direct methods and refined by full-matrix least-squares refinement on *F*². The unit cells of several crystals from different reaction batches were checked to confirm that the synthesis of **5** was reproducible.

CCDC 182/1629. See <http://www.rsc.org/suppdata/cc/b0/b002892o/> for crystallographic files in .cif format.

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