Isolation and structural characterisation of $[\{(Me_3Si)_2NMg[\mu\text{-}OC(H)Ph_2]\cdot(O{=}CPh_2)\}_2]$, an intermediate in the β-hydride transfer reaction between an alkyl(amido)magnesium and benzophenone

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The *in situ* reaction of Bu_2Mg with 2 mol. equiv. of $(Me_3Si)_2NH$ followed by addition of Ph_2CO yields the heteroleptic amide/alkoxide complex $[\{(Me_3Si)_2NMg[\mu\text{-}OC(H)Ph_2]\cdot(O{=}CPh_2)\}_2]$ 1, whereas reaction of purified $[\{(Me_3Si)_2N\}_2Mg]$ 2 with Ph_2CO results in formation of the solvate $[\{(Me_3Si)_2N\}_2Mg\cdot(O{=}CPh_2)_2]$ 3, the difference being due to incomplete amination of the bis(alkyl)magnesium compound resulting in β-hydride transfer to the ketone, which is the first example of this type of transformation using an alkyl(amido)magnesium reagent.

While Hauser bases[1] (R_2NMgX) and bis(amido)magnesium compounds[2] $[(R_2N)_2Mg]$ have been in the literature for some time, very little is known regarding their use as reagents to perform organic transformations. Magnesium amides are more thermally stable and less reactive than the widely used lithium amides (R_2NLi), leading to selectivity variations between these reagents.[3]

We are interested in studying selective deprotonation reactions between magnesium amide bases and ketones carrying an α-hydrogen, to yield magnesium enolates.[3b,4] With this in mind we decided to prepare a pre-enolisation complex[5] of a magnesium amide, for use as a model intermediate in the enolisation reaction. This involved reacting Bu_2Mg† (5 mmol) with hexamethyldisilazane, hmds, (10 mmol) in 10 ml of hexane for 3 h at 25 °C, followed by the addition of the non-enolisable ketone benzophenone (5 mmol).[6] It was expected that a simple ketone solvated bis(amido)magnesium complex would be produced, which could then be used for further analysis. To our surprise the only isolable product from the reaction was the crystalline compound $[\{(Me_3Si)_2NMg[\mu\text{-}OC(H)Ph_2]\cdot(O{=}CPh_2)\}_2]$ **1**.

The identity of **1** was confirmed by ^1H NMR analysis,‡ and its crystal structure was determined by an X-ray study (Fig. 1).§ Clearly, benzophenone had been reduced and the solvated, secondary alkoxide was obtained. The origin of the hydride was then investigated. A reaction was carried out in C_6D_6 to determine if the hydride was derived from the solvent; however, **1** was produced without deuterium incorporation. To exclude the possibility of moisture contamination as the hydride source, a reaction was conducted under strictly hydrophobic conditions, using triply distilled amine and sublimed Ph_2CO, again **1** was obtained. Our next avenue of inquiry proved to be more successful. Pure, crystalline $[\{(Me_3Si)_2N\}_2Mg]$ **2** was prepared by refluxing Bu_2Mg (20 mmol) and hmds (40 mmol) in 20 ml of heptane for 3 h and on cooling to approximately 40 °C, large, colourless, crystalline blocks of **2** were deposited from solution.¶ The solid was isolated by filtration and stored in an argon-filled glove box. This procedure is high yielding and much simpler than the recently reported electrochemical synthesis.[3b] Reaction of the pure bis(amide) (5 mmol) with benzophenone (10 mmol) in 5 ml of hexane gave a clear yellow solution, which yielded needle crystals of the solvated bis(amide) $[\{(Me_3Si)_2N\}_2Mg\cdot(O{=}CPh_2)_2]$ **3**, on standing at room temperature. Hence, the explanation for the preparation of **1** must lie in performing the amination reaction followed by solvation *in situ*.

To investigate the amination process, a reaction between Bu_2Mg and hmds was performed in C_6D_6 at 25 °C. A ^1H NMR spectrum of the solution after 3 h showed that alkyl peaks were still evident. This indicates that amination ceases or at least slows, at the alkyl(amido) state $[(Me_3Si)_2NMgBu]$[7] at this temperature. Using this information it is possible to propose a pathway for reduction of the ketone *via* β-hydride transfer from the alkyl(amido)magnesium intermediate (Scheme 1).[8]

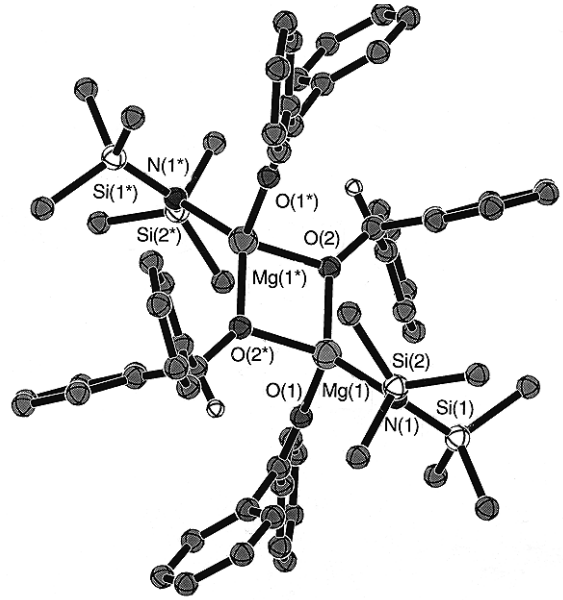
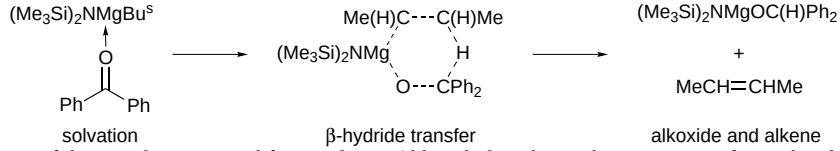


Fig. 1 Crystal structure of **1** with hydrogen atoms (except the alkoxide H) omitted for clarity. Starred atoms are related by the symmetry operation 1-*x*, -*y*, -*z*. Key bond lengths (Å) and angles (°): Mg(1)–N(1) 2.019(3), Mg(1)–O(1) 2.046(3), Mg(1)–O(2) 1.967(2), Mg(1)–O(2*) 1,991(2); O(2)–Mg(1)–O(2*) 82.9(1), O(2)–Mg(1)–N(1) 127.0(1), O(1)–Mg(1)–O(2) 109.1(1), O(1)–Mg(1)–O(2*) 98.1(1), O(2*)–Mg(1)–N(1) 129.5(1).



Scheme 1. The aggregation state of the complex is ignored for simplicity. Although the scheme shows reaction of a *sec*-butyl function, a similar reaction will occur with an *n*-butyl producing but-1-ene.

To test the feasibility of this route [$(Me_3Si)_2NMgBu^S$] was prepared and isolated as a pure compound[9] and reacted with benzophenone. The solid produced from this reaction was identified as **1**. It therefore appears that the origin of the hydride is indeed from the alkyl group attached to magnesium and that this is still present due to incomplete amination of the bis(alkyl)magnesium.

Complex **1** may be regarded as an intermediate in the reduction reaction of a ketone to an alcohol, *i.e.* prior to hydrolysis. To our knowledge, this is the only example of a magnesium alkoxide prepared *via* reduction to be structurally characterised. Although a wealth of information is available on the preparation of alcohols using metal reagents, the exact nature of the reacting species is still unclear. We also believe that this is the first report of the use of an alkyl(amido)magnesium compound as a hydride transfer reagent.[10] An alternative reaction possible between the alkyl(amido)magnesium and the ketone is alkylation, to give a tertiary alcohol (after hydrolysis). This is the preferred reaction mode between [$MeMgNR_2$] (NR_2 = NPr^i_2, NPh_2 or $NC_5H_8Me_2$) and the cyclic ketones 4-*tert*-butylcyclohexanone and 2,2,6,6-tetramethyl-4-*tert*-butylcyclohexanone.[11] The combined steric bulk of the alkyl anion and the phenyl groups of the ketone appear to negate this possibility in our system.

Turning to the structure of **1** a dimeric arrangement utilising bridging alkoxide anions is found. Each metal bonds terminally to one amide anion and tetracoordination is completed by carbonyl solvation from a benzophenone unit. Each magnesium adopts a distorted tetrahedral environment, with angles ranging from 82.9(1)° for O(2)–Mg(1)–O(2*) to 129.5(1)° for O(2*)–Mg(1)–N(1). Although the structural motif of a dimer is not unusual for magnesium,[12] the constitution of **1** is novel. Heteroleptic magnesium compounds where the metal is attached to two different anions are rare,[13] and surprisingly **1** is the first homometallic amide/alkoxide magnesium compound to be structurally characterised.[14]

Also noteworthy in **1** is the bis solvation by benzophenone. In this system **1** is prepared preferentially over further reduction by [$(Me_3Si)_2NMgBu$]. A maximum conversion of ketone to alcohol is therefore 50% due to deactivation of the coordinated Ph_2CO. Strong solvation of the highly Lewis-acidic magnesium centre by the carbonyl may disfavour the dissociation necessary for further reduction to take place.

The work reported herein illustrates the merit in isolating pure organometallic reagents before further reaction, as opposed to performing *in situ* transformations. We are currently studying the chemoselective properties of alkyl(amido)magnesium compounds and their use as asymmetric induction reagents.

Footnotes

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† Bu_2Mg is commercially available from Aldrich as a statistical 1 : 1 mixture of *n*- and *sec*-butylmagnesium.

‡ ^{1}H NMR (400 MHz, C_6D_6, 298 K) for **1**: δ 0.26 (s, 18 H, Me_3Si), 6.27 (s, 1 H, CH), 6.91 (t, 2 H, *p*-H), 7.00–7.14 (m, 10 H, *p*-, *m*-H ×2), 7.51 (d, 4 H, *o*-H), 7.61 (d, 4 H, *o*-H). Yield of first batch of crystals = 32% based on consumption of Ph_2CO, mp 128–131 °C.

§ *Crystal data* for **1**: $C_{64}H_{78}Mg_2N_2O_4Si_4$, M = 1100.28, T = 20 °C, monoclinic, space group $P2_1/n$, a = 12.837(1), b = 13.537(3), c = 18.049(2) Å, β = 93.741(9)°, U = 3129.8(8) Å^3, Z = 2, D_c = 1.167 Mg m^{-3}, $2\theta_{max}$ = 52°, 6719 reflections collected, 6429 unique reflections, R_{int} = 0.036, observed limit, $I > 2\sigma(I)$, observed reflections = 2771, number of variables = 382, full-matrix least-squares refinement on F converged to R = 0.044, R_w = 0.048 and S = 1.43. Structure solution using SAPI91 (F. Hai-Fu, 1991, structure analysis program with intelligent control, Rigaku Corporation, Tokyo, Japan). Calculation and graphics using TEXSAN (crystal structure analysis package, version 1.6, 1993, Molecular Structure Corporation, The Woodlands, Texas 77381). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/461.

¶ ^{1}H NMR (250 MHz, C_6D_6, 298 K) for **2**: δ 0.17 (s, Me_3Si), 0.39 (s, Me_3Si), 0.46 (s, Me_3Si). The two highest frequency singlets represent bridging and terminal anions in a dimer, and the low-frequency singlet is derived from monomeric amide. A concentration study showed increasing monomer present with increasing dilution. Yield = 70%, mp 122 °C.

‖ ^{1}H NMR (250 MHz, C_6D_6, 298 K) for **3**: δ 0.39 (s, 36 H, Me_3Si), 6.96–7.12 (m, 12 H, *m*-, *p*-H), 7.74 (d, 8 H, *o*-H). Yield = 78% based on consumption of Ph_2CO, mp 118–119 °C.

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