New reactivity and structural insights of alkali-metal-mediated alumination in directed *ortho*-alumination of a tertiary aromatic amide

Joaquín García-Álvarez, David V. Graham, Alan R. Kennedy, Robert E. Mulvey* and Susan Weatherstone

Received (in Cambridge, UK) 28th April 2006, Accepted 26th May 2006
First published as an Advance Article on the web 19th June 2006
DOI: 10.1039/b606080c

The first reported sodium alkyl(TMP)aluminate reagent to be synthesised and crystallographically characterised, [TMEDA·Na(μ-TMP)(μ-^{i}Bu)Al(^{i}Bu)$_2$], reacts as an amido base towards phenylacetylene to form crystalline [(TMEDA)$_2$·Na(μ-CCPh)(μ-^{i}Bu)Al(^{i}Bu)$_2$]; whereas the congeneric TMEDA-stabilised lithium (TMP)aluminate exhibits dual alkyl/amido basicity in its reaction with *N*,*N*-diisopropylbenzamide to form a novel heterobimetallic-heterotrianionic crystalline complex [{PhC(=O)N(^{i}Pr)$_2$}·Li{2-[1-C(=O)N(^{i}Pr)$_2$]C$_6$H$_4$}{Me$_2$NCH$_2$-CH$_2$N(Me)CH$_2$}Al(^{i}Bu)$_2$], which, in addition to having an *ortho*-deprotonated benzamide ligand, also contains a methyl-deprotonated TMEDA ligand and a neutral benzamide molecule ligated to lithium.

Heterometallic and heteroleptic in composition, alkali metal alkyl-TMP-ates (where TMP is 2,2,6,6-tetramethylpiperidide) are currently being developed as an exciting new class of organometallic reagent. The few studies carried out thus far[1] have established that these new additions to one of the oldest dynasties in organometallic chemistry can offer unique (synergic) reactivities, and often improved regio- and chemoselectivities in their reactions, in comparison to the classical homometallic/homoleptic reagents (*e.g.*, lithium alkyls, lithium TMP) from which they are descended. Most of these studies have focused on TMP-zincates[2] or TMP-magnesiates.[3] To date, there has only been one communication on TMP-aluminates,[4] in which Uchiyama *et al.* reported the new reagent lithium triisobutyl(TMP)aluminate, empirically formulated as "^{i}Bu$_3$Al(TMP)Li". Opening-up a new means of approach to aromatic aluminum compounds, this reagent can effect the direct alumination of a wide range of functionalized aromatics. However, the structure of the reagent itself and those of the arylaluminated intermediates it generates (prior to electrophilic interception) are unknown, nor indeed have these important compounds been isolated from solution and characterized in their own right, though an *in situ* (in THF solution) NMR study of an anisole alumination[4] points to the TMP function as being the active base within this mixed alkyl-amido reagent. In this paper, by introducing a sodium TMP-aluminate reagent and reporting its reaction with phenylacetylene, we present unprecedented structural information on both the reagent itself and the aluminated acetylene intermediate. We also describe a remarkable reaction between the congeneric lithium TMP-aluminate and a tertiary aromatic amide, which affords a product that uniquely combines *ortho*-alumination of the amide, complexation of a non-metallated neutral amide molecule to lithium [prompting thoughts of the "complex-induced proximity effect" (CIPE)][5] and methyl-alumination of TMEDA (Me$_2$NCH$_2$CH$_2$NMe$_2$, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine).

The new sodium TMP-aluminate reagent [TMEDA·Na(μ-TMP)(μ-^{i}Bu)Al(^{i}Bu)$_2$] (**1**) can be synthesised simply by mixing together its component parts NaTMP, ^{i}Bu$_3$Al and TMEDA in a bulk hydrocarbon solution. Avoiding THF (used as the bulk solvent in the preparation of the aforementioned lithium TMP-aluminate) enabled **1** to be obtained in a crystalline form suitable for a X-ray crystallographic study.† The molecular structure of **1** (Fig. 1) features a planar, four-element NaCAlN ring with a mixed ^{i}Bu-TMP bridging ligand set, and is completed by two terminal ^{i}Bu ligands on Al and a chelating TMEDA (N,N-attached) on Na. The Al displays a distorted tetrahedral geometry (subtending bond angles from 99.85(11) (C9–Al1–C5) to 120.57(10)° (N1–Al1–C9)) and bridging/terminal Al–C bonds that are indistinguishable in length (2.038(2) and (mean) 2.037 Å, respectively). Lying only 0.293(2) Å out of the N1N2N3 basal plane, the Na geometry is best described as trigonal-pyramidal, with C1 at the apex (Na–C1 bond length 2.680(2) Å, *cf.* 2.468 Å (mean) for Na–N bonds). The bridge is stronger at the Na–N(TMP)–Al span, with lengths of 2.4368(19) and 1.9712(19) Å, respectively. A search of the Cambridge Structural Database[6] scored only 3 hits for other structures of general formula [Na(NR$_2$)Al(R)$_3$·±donor], but none of them adopt a *discrete* NaCAlN ring motif.

To establish the ligand transfer reactivity of **1** in a deprotonative application, we tested it in a 1 : 1 stoichiometry with phenylacetylene in hexane solution. Unexpectedly, the crystalline

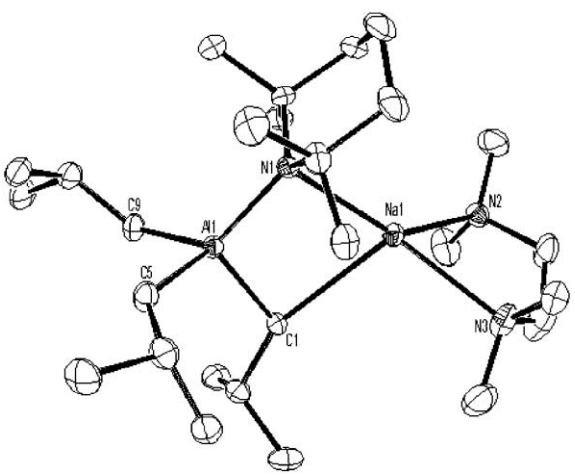


Fig. 1 Molecular structure of **1** with 30% probability displacement ellipsoids. H atoms have been omitted for clarity.

WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, UK G1 1XL. E-mail: r.e.mulvey@strath.ac.uk; Fax: +44 (0)141 552 0876

product $[(TMEDA)_2Na(\mu\text{-}^{i}Bu)(\mu\text{-}C{\equiv}CPh)Al(^{i}Bu)_2]$ (**2**) contains two molecules of TMEDA. The reaction was therefore repeated by adding an extra equivalent of TMEDA, this increasing the yield of **2**. On this evidence, **1** mimics the reactivity of "$^{i}Bu_3Al(TMP)Li$" by functioning as a TMP base. Heavily donor-solvated with respect to Na, the molecular structure of **2**† (Fig. 2) is strictly a contacted ion pair, but the contact (Na1–C1 (of C≡CPh) = 3.013(2) Å) is extremely loose. The Na–C(^{i}Bu) bridge in **1** is 2.680(2) Å in length, whereas in **2** it is significantly elongated (Na1–C(9), 3.250(3) Å). Other notable features of **2** include the contrast between the near-linearity of the C≡C–Al bond angle (163.85(19)°) and the near-perpendicularity of the C≡C–Na bond angle (94.75(15)°). This resembles the signature σ/π distinction of the metal (Mg or Zn/alkali metal)–deprotonated substrate bonding found in alkali metal magnesiates or zincates.[1] Also, while the geometry at Al is definitely tetrahedral, though distorted (range of C–Al–C bond angles 103.65(9)–118.44(10)°), the sodium coordination is less clear cut, as aside from the loose contact to $[Al(C{\equiv}CPh)(^{i}Bu)_3]^{-}$, the TMEDA ligands both bind asymmetrically (*i.e.*, N1: 2.539(2) *cf.* N2: 2.723(2) Å; N3: 2.628(2) *cf.* N4: 2.526(2) Å).

This success with **1** prompted us to investigate its lithium congener, that is a TMEDA-stabilised variant of Uchiyama *et al.*'s "$^{i}Bu_3Al(TMP)Li$". However, by following the same synthetic procedure as that for **1**, but substituting LiTMP for NaTMP, gave only a white oily product. As no useful structural information could be gleaned from this oil, we decided to utilise it *in situ* with *N*,*N*-diisopropylbenzamide in anticipation of a Directed *ortho* Alumination (DoAl), reaction. This was indeed realised, but in a most unexpected manner. Thus, remarkably, the solid product of the reaction was the heterobimetallic-heterotrianionic complex $[\{PhC(=O)N(^{i}Pr)_2\}\cdot Li\{2\text{-}[1\text{-}C(=O)N(^{i}Pr)_2]C_6H_4\}\{Me_2NCH_2CH_2\text{-}N(Me)CH_2\}Al(^{i}Bu)_2]$ (**3**), obtained in an isolated crystalline yield of 43%. Amenable to X-ray crystallographic study,† **3** provides not just the first structural insight into alkali-metal-mediated alumination (AMMA) but also reveals other surprising facts about the reaction.

Firstly, DoAl is confirmed since the Al bonds to the *ortho*-carbon (C15) of the deprotonated benzamide (Fig. 3). Three other

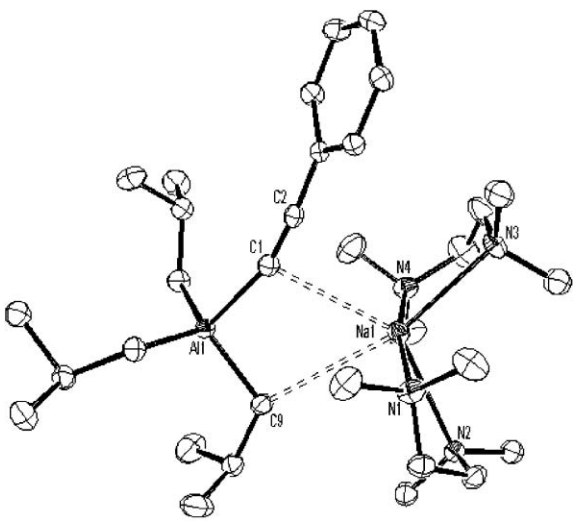


Fig. 2 Molecular structure of **2** with 30% probability displacement ellipsoids. H atoms have been omitted for clarity.

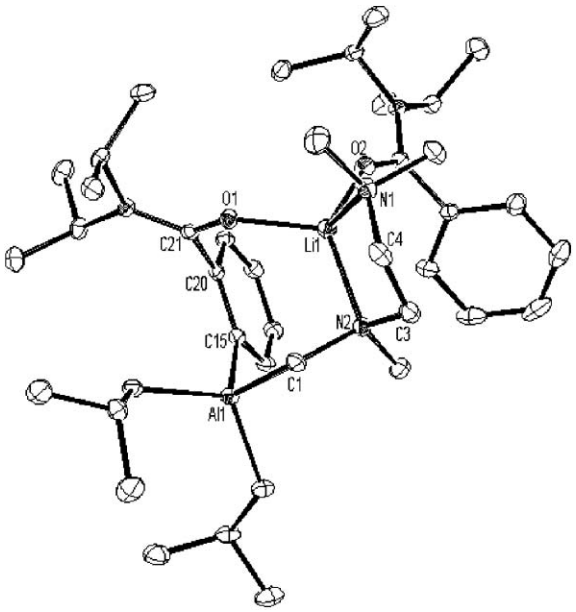
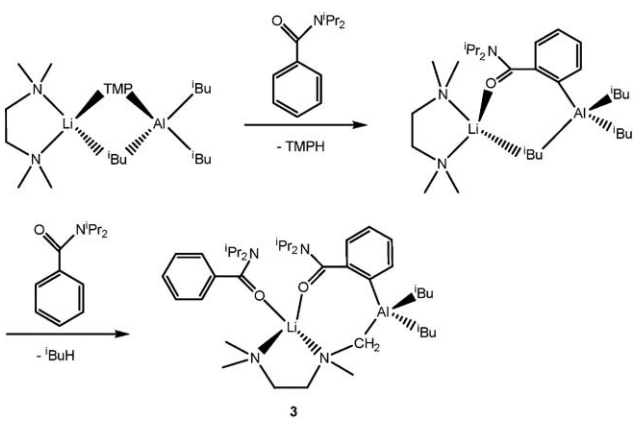


Fig. 3 Molecular structure of **3** with 30% probability displacement ellipsoids. H atoms have been omitted for clarity.

C atoms, two ^{i}Bu α-carbons and one CH_2 from "TMEDA", complete the distorted tetrahedral Al coordination. Secondly, closer inspection discloses that this CH_2 (C1) belongs to a methyl-deprotonated TMEDA, while, more normally, TMEDA's two N atoms (N1 and N2) chelate the Li in a five-membered LiNCCN ring. Thirdly, also bonded to O1 of the aluminated benzamide, the Li coordination sphere is completed by O2 of a second but non-metallated benzamide molecule. Overall, the Al and Li centres are held together in an irregularly-shaped undeca LiNCCNCAlCCCO ring. Based on the precedent of the conversion of **1** to **2**, a reaction sequence can be proposed (Scheme 1) to rationalise the formation of **3**.

In the first step, the benzamide is *ortho*-aluminated by TMP, with elimination of the amine TMPH. In the second step, a second benzamide molecule, by complexing to Li through its highly basic O,[7] appears to induce an intramolecular deprotonation of a TMEDA Me group *via* an Al-attached ^{i}Bu base, with concomitant elimination of ^{i}BuH. On its own, $^{i}Bu_3Al$ is not a strong enough base to metallate a tertiary aromatic amide or TMEDA,[8,9] so the



Scheme 1 Proposed stepwise reaction pathway for the formation of **3**.

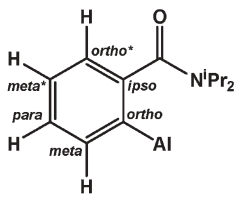
two distinct deprotonations of this reaction are synergic in origin, as the contacted Li appears to activate the Al-attached TMP and ^{i}Bu bases. This work thus establishes that TMP-aluminates can function as dual TMP/alkyl bases. It also establishes that normal patterns of reactivity can be reversed using AMMA, for although *N*,*N*-diisopropylbenzamide is significantly more acidic than TMEDA, TMEDA deprotonation is favoured over that of a second benzamide molecule. Finally, it further establishes that the extra stability inherent in these mixed-metal composites can allow normally "hot" interactions, such as the (neutral benzamide) O–Li donor–acceptor contact (of a type thought to be the foundation of the suspected pre-metallation complexes in the CIPE),[5] to be "frozen out", thus facilitating their direct study.

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

Notes and references

† Crystal data for **1**: $C_{27}H_{61}AlN_3Na$, M_r = 477.76, orthorhombic, space group $P2_12_12_1$, a = 10.3767(2), b = 16.9980(4), c = 17.8197(4) Å, V = 3143.09(12) Å^3, Z = 4, λ = 0.71073 Å, μ = 0.096 mm^{-1}, T = 150 K, 35650 reflections, 6929 unique (R_{int} = 0.045), final refinement to convergence on F^2 gave R = 0.0509 (F, 5768 obs. data only) and R_w = 0.1212 (F^2, all data), GOF = 1.059. CCDC 606350. Crystal data for **2**: $C_{32}H_{64}AlN_4Na$, M_r = 554.84, triclinic, space group $P\bar{1}$, a = 9.4085(4), b = 9.7578(4), c = 10.5611(4) Å, α = 102.489(2), β = 102.940(2), γ = 91.186(2)°, V = 920.16(6) Å^3, Z = 1, λ = 0.71073 Å, μ = 0.090 mm^{-1}, T = 123 K, 23628 reflections, 9674 unique (R_{int} 0.050), final refinement to convergence on F^2 gave R = 0.0537 (F, 7563 obs. data only) and R_w = 0.1163 (F^2, all data), GOF = 1.044. CCDC 606351. Crystal data for **3**: $C_{40}H_{70}AlLiN_4O_2$, M_r = 672.92, monoclinic, space group $P2_1/c$, a = 11.3307(3), b = 20.5770(5), c = 18.5945(5) Å, β = 100.5393(14)°, V = 4262.20(19) Å^3, Z = 4, λ = 0.71073 Å, μ = 0.082 mm^{-1}, T = 123 K, 17709 reflections, 9860 unique (R_{int} 0.040), final refinement to convergence on F^2 gave R = 0.0477 (F, 6609 obs. data only) and R_w = 0.1101 (F^2, all data), GOF = 1.025. CCDC 606352. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606080c

‡ All reactions were carried out under a protective argon atmosphere. **Synthesis of [TMEDA·Na(μ-TMP)(μ-^{i}Bu)Al(^{i}Bu$_2$)] (1)**: In a Schlenk tube, 3 mmol of BuNa (0.24 g) was suspended in 10 mL of hexane and a molar equivalent of (H)TMP (3 mmol, 0.51 mL) added *via* syringe. The resultant creamy white suspension was allowed to stir for 1 h, after which ^{i}Bu$_3$Al (3 mmol, 3 mL of a 1.0 M solution in hexane) was added at room temperature. The suspension changed from creamy white to a slightly cloudy, pale yellow solution. This was followed by the addition of a molar equivalent of TMEDA (3 mmol, 0.45 mL) to yield a clearer solution. The storage of this solution in a freezer (−27 °C) resulted in the precipitation of colourless crystals (0.47 g, 33%), which were isolated and dried in the form of a white powder. Reduction of the filtrate volume yielded only a pale yellow oil, from which no further solid precipitated. Recrystallisation of a portion of the solid from toluene yielded colourless crystals, suitable for solution and solid state analysis. ^{1}H NMR (400.13 MHz, d_6-benzene, 300 K): 2.45 (sept, 3 H, C*H*-^{i}Bu), 1.75 (s overlapping m, 16 H, 12 H of CH_3-TMEDA and 4 H of β-TMP), 1.64 (s overlapping m, 6 H, 4 H of CH_2-TMEDA and 2 H of γ-TMP), 1.49 (s br, 12 H, CH_3-TMP), 1.43 (d, 18 H, CH_3-^{i}Bu) and 0.21 (6 H, d, CH_2–Al-^{i}Bu). ^{13}C{H} NMR (100.63 MHz, d_6-benzene, 300 K): 56.95 (*C*H$_2$-TMEDA), 52.49 (α-TMP), 46.29 (β-TMP), 45.93 (*C*H$_3$-TMEDA), 30.5–31.5 (br, *C*H$_3$-TMP), 29.88 (*C*H$_3$-^{i}Bu), 27.94 (*C*H-^{i}Bu) and 18.81 (γ-TMP). The signal for the Al–*C*H$_2$ was not observed. **Synthesis of [(TMEDA)$_2$·Na(μ-^{i}Bu)(μ-C≡CPh)Al(^{i}Bu)$_2$] (2)**: Following the method above for **1**, but adding two molar equivalents of TMEDA (6 mmol, 0.9 mL), produced a cloudy yellow solution. PhC≡CH (3 mmol, 0.33 mL) was then introduced to give a transparent solution. Freezer cooling of this solution at −27 °C afforded colourless crystals of **2** (0.35 g, 21%). Note that adding only 1 molar equivalent of TMEDA also produced **2**, but in a smaller yield. ^{1}H NMR (400.13 MHz, d_6-benzene, 300 K): 7.34 (m, 2 H, *o*-C$_6$H$_5$), 6.96 (m, 3 H, 1 H *p*-C$_6$H$_5$ and 2 H *m*-C$_6$H$_5$), 2.46 (sept, 3 H, C*H*-^{i}Bu), 1.84 (s, 12 H, CH_3-TMEDA), 1.83 (s, 4 H, CH_2-TMEDA), 1.44 (d, 18 H, CH_3-^{i}Bu) and 0.29 (d, 6 H, CH_2–Al-^{i}Bu). ^{13}C{H} NMR (100.63 MHz, d_6-benzene, 300 K): 132.47 (*i*-C$_6$H$_5$), 129.13 (*o*-C$_6$H$_5$), 128.39 (*m*-C$_6$H$_5$), 127.90 (*p*-C$_6$H$_5$), 126.64 (*C*≡CPh), 109.58 (C≡*C*Ph), 57.81 (*C*H$_2$-TMEDA), 46.18 (*C*H$_3$-TMEDA), 30.01 (*C*H$_3$-^{i}Bu), 29.01 (*C*H-^{i}Bu) and 26.31 (*C*H$_2$–Al-^{i}Bu). **Synthesis of [{PhC(=O)N(^{i}Pr)$_2$}·Li{2-[1-C(=O)N(^{i}Pr)$_2$]C$_6$H$_4$}{Me$_2$NCH$_2$-CH$_2$N(Me)CH$_2$}Al(^{i}Bu)$_2$] (3)**: In a Schlenk tube, 2 mmol of TMEDA (0.3 mL) was added to a hexane solution of LiTMP (prepared freshly from a mixture of ^{n}BuLi (2 mmol, 1.25 mL of a 1.6 M solution in hexane) and TMPH (2 mmol, 0.34 mL)) to give a slightly opaque yellow solution. After the solution had been stirred for 30 min, ^{i}Bu$_3$Al (2 mmol, 2 mL of a 1.0 M solution in hexane) was introduced, and the mixture further stirred for 1 h. Addition of *N*,*N*-diisopropylbenzamide (4 mmol, 0.82 g) caused the precipitation of a colourless solid. This solid dissolved upon addition of hot toluene. Standing the solution on the bench afforded colourless crystals of **3** (0.58 g, 43%). Note that adding only 1 molar equivalent of the benzamide also produced **3**, but in a smaller yield. This suggests that the intermediate reacts more quickly with the benzamide than does the starting reagent. FT-IR (nujol): 1621 and 1614 cm^{-1} ($\nu_{C=O}$). ^{1}H NMR (400.13 MHz, d_4-THF, 300 K): 7.98 (m, 1 H, *m*-C$_6$H$_4$), 7.33 (m, 3 H, 2 H *m*-C$_6$H$_5$ and 1 H *p*-C$_6$H$_5$), 7.26 (m, 2 H, *o*-C$_6$H$_5$), 7.08 (m, 1 H, *p*-C$_6$H$_4$), 6.97 (m, 2 H, 1 H, *m**-C$_6$H$_4$ and 1 H *o*-C$_6$H$_4$), 4.09, 3.67, 2.04 and 1.86 (m, 1 H each, C*H*-^{i}Pr), 3.08 and 2.77 (m, 1 H each, C*H*-^{i}Bu), 2.31 (s, 6 H, 2CH_3-TMEDA), 2.25 (s, 4 H, CH_2-TMEDA), 2.13 and 1.97 (br s, 1 H each, N(CH_2)Al-TMEDA), 1.77 (s, 3 H, CH_3-TMEDA), 1.72, 1.57, 1.32, 1.26, 1.03 and 0.99 (d, 3 H each, CH_3-^{i}Pr), 0.93 (d, 6 H, 2CH_3-^{i}Pr), 0.85 and 0.83 (d, 6 H each, CH_3-^{i}Bu), 0.23, 0.11, −0.12 and −0.24 (m, 1 H each, CH_2–Al-^{i}Bu). ^{13}C{H} NMR (100.63 MHz, d_4-THF, 300 K): 177.98 (2 C, *C*=O), 169.81 (*o*-C$_6$H$_4$), 146.07 (*i*-C$_6$H$_4$), 141.08 (*m*-C$_6$H$_4$), 139.71 (*i*-C$_6$H$_5$), 128.05 (3 C, *m*-C$_6$H$_5$ and *p*-C$_6$H$_5$), 126.24 (*p**-C$_6$H$_4$), 125.59 (2 C, *o*-C$_6$H$_5$), 122.90 (*m**-C$_6$H$_4$), 122.86 (*o**-C$_6$H$_4$), 62.03 (*C*H$_3$-TMEDA), 69.58 and 51.36 (*C*H-^{i}Pr), 56.78 (*C*H$_2$-TMEDA), 48.46 (N(*C*H$_2$)Al-TMEDA), 45.63 (2*C*H$_3$-TMEDA), 28.79 (*C*H$_3$-^{i}Bu), 27.83 (*C*H-^{i}Bu), 20.09, 19.83, 19.68 and 19.36 (*C*H$_3$-^{i}Pr). The signal for the Al–*C*H$_2$ of ^{i}Bu was not observed. ^{7}Li NMR (155.50 MHz, d_4-THF, 300 K, reference LiCl in D$_2$O at 0.00 ppm): −0.05.



1 R. E. Mulvey, *Organometallics*, 2006, **25**, 1060.
2 (*a*) M. Uchiyama, T. Miyoshi, Y. Kajihara, T. Sakamoto, Y. Otani, T. Ohwada and Y. Kondo, *J. Am. Chem. Soc.*, 2002, **124**, 8514; (*b*) T. Imahori, M. Uchiyama, T. Sakamoto and Y. Kondo, *Chem. Commun.*, 2001, 2450; (*c*) Y. Kondo, M. Shilai, M. Uchiyama and T. Sakamoto, *J. Am. Chem. Soc.*, 1999, **121**, 3539.
3 (*a*) H. Awad, F. Mongin, F. Trécourt, G. Quéguiner and F. Marsais, *Tetrahedron Lett.*, 2004, **45**, 7873; (*b*) H. Awad, F. Mongin, F. Trécourt, G. Quéguiner, F. Marsais, F. Blanco, B. Abarca and R. Ballesteros, *Tetrahedron Lett.*, 2004, **45**, 6697; (*c*) D. V. Graham, E. Hevia, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara and C. Talmard, *Chem. Commun.*, 2006, 417.
4 M. Uchiyama, Y. Naka, Y. Matsumoto and T. Ohwada, *J. Am. Chem. Soc.*, 2004, **126**, 10526.
5 For an authoritative review, see: M. C. Whisler, S. MacNeil, V. Snieckus and P. Beak, *Angew. Chem., Int. Ed.*, 2004, **43**, 2206.
6 (*a*) F. H. Allen, *Acta Crystallogr., Sect. B: Struct. Sci.*, 2002, **58**, 380; (*b*) *Cambridge Structural Database*, version 5.25 with updates to March 2006; (*c*) For an example, see: M. Schiefer, H. Hatop, H. W. Roesky, H.-G. Schmidt and M. Noltemeyer, *Organometallics*, 2002, **21**, 1300.
7 For an example of a structure where this amide is complexed to a lithium zincate reagent, see: W. Clegg, S. H. Dale, E. Hevia, G. H. Honeyman and R. E. Mulvey, *Angew. Chem., Int. Ed.*, 2006, **45**, 2370.
8 TMEDA has recently been lithiated during the *ortho*-dilithiation of thiophenol or 2-trimethylsilylthiophenol, see: A. Hildebrand, P. Lönnecke, L. Silaghi-Dumitrescu, I. Silaghi-Dumitrescu and E. Hey-Hawkins, *Dalton Trans.*, 2006, 967.
9 For examples of alumino-TMEDA derivatives made by transmetallation as opposed to direct metallation see: X. Tian, R. Fröhlich, T. Pape and N. W. Mitzel, *Organometallics*, 2005, **24**, 5294.

