# Isolation and structural elucidation of a key aluminoaromatic intermediate and evidence for dismutation phenomena in TMP-alumination chemistry†

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Lithium TMP-aluminate "$^i$Bu$_3$Al(TMP)Li" undergoes dismutation in THF solution to precipitate the tetraalkylaluminate [{Li·(THF)$_4$}$^+${Al($^i$Bu)$_4$}$^-$], but reacts kinetically as a TMP base towards *N*,*N*-diisopropylbenzamide to afford the crystalline ortho-aluminated species [(THF)$_3$·Li{O(=C)N($^i$Pr)$_2$(C$_6$H$_4$)}Al-($^i$Bu)$_3$] and TMPH.

First reported in 2004 by Uchiyama *et al.*, lithium TMP-aluminate "$^i$Bu$_3$Al(TMP)Li" (where TMP is the amide 2,2,6,6-tetramethyl-piperidide) is an excellent reagent in THF solution for selectively deprotonating and concomitantly aluminating a wide range of functionalized aromatics.[1] This new direct alumination method possesses many advantages over the indirect two-step metathesis approach (for example, synthesis of an aromatic lithium or Grignard species, followed by reaction with an aluminium salt) usually employed for preparing aromatic aluminium compounds.[2] In formal equation terms, these reactions of $^i$Bu$_3$Al(TMP)Li represent a simple exchange of an aromatic hydrogen for a triorganoaluminium–lithium (R$_3$Al, Li$^+$) fragment, but in reality they can be extraordinarily complex. This is because the base itself is bimetallic, multi-Lewis acidic, heteroleptic and highly coordinated about the (ultimately) active anionic Al centre, combined with the fact that organoaluminium compounds have a strong propensity for undergoing ligand exchange, aggregation, and solvation phenomena.[2] Structural information on the nature of the base in solution and in the solid-state is therefore vital to help unravel this inherent complexity, which is exacerbated on addition of the aromatic molecule to be aluminated. We started along this path by reporting[3] the crystal structure of the Lewis base-stabilized derivative [L·Li(µ-TMP)(µ-$^i$Bu)Al($^i$Bu)$_2$] (L = *N*,*N*-diisopropyl-benzamide = [PhC(=O)N$^i$Pr$_2$]), the synthesis of which revealed the marked solvent dependency of the basic performance of $^i$Bu$_3$Al(TMP)Li: it metallates the benzamide essentially quantitatively (starting with 2.2 molar equivalents of base) in bulk THF, negligibly in a stoichiometric quantity of THF, and essentially not at all in bulk hexane. Most recently, Uchiyama and co-workers carried out a combined experimental and theoretical study[4] which concluded that the active base of lithium TMP-aluminate is the mono-THF solvate [THF·Li(µ-TMP)(µ-$^i$Bu)Al($^i$Bu)$_2$], **1**, though there was some inconsistency as to its origin with the paper stating

that crystalline **1** was obtained from bulk THF solution, whereas the supporting information indicated it was prepared in hexane solution with a stoichiometric quantity of THF. This report stimulated us to revisit the reaction between $^i$Bu$_3$Al(TMP)Li and [PhC(=O)N$^i$Pr$_2$] to attempt to extract structural information from bulk THF solutions, to add to the knowledge gleamed previously from hexane solutions. As revealed herein, we can now report the first successful isolation and spectroscopic/crystallographic characterization of an aluminoaromatic intermediate[5] obtained *via* the actual experimental conditions used to effect direct alumination of the benzamide. Our study also sheds new and surprising light on the constitution of the base in solution, which points to an inherently more complicated chemistry than that previously described.

We began the study by re-preparing the "base" **1** following the literature procedures. In our hands, **1** failed to crystallise (or even deposit as a solid) from neat THF solution despite several attempts; but was readily produced *via* a hexane solution containing a stoichiometric quantity of THF. To our surprise, **1** did not metallate the benzamide to any appreciable extent in hexane or benzene solution. Taken together with previous findings, the implication of this unexpected failure is that excess THF is necessary for metallation efficacy, thus casting doubt on the case for **1** being the true active base. We therefore switched our focus to bulk THF solutions. Following exactly the original literature procedure,[1] we treated the benzamide with 2.2 molar equivalents of $^i$Bu$_3$Al(TMP)Li in neat THF solution but omitted any subsequent electrophilic trapping step. Initially this gave a homogeneous yellow solution, but after 1 h deposited a colourless crystalline solid identified directly by $^1$H, $^7$Li and $^{13}$C NMR spectroscopy (and indirectly by comparison with its known crystallographically characterised dioxane analogue [{Li·(dioxane)$_4$}$^+${Al($^i$Bu)$_4$}$^-$] **I**,[6] Fig. 1) as the solvent-separated ionic aluminate [{Li·(THF)$_4$}$^+$-{Al($^i$Bu)$_4$}$^-$] **2**.‡ Precipitation of **2** was also observed in THF solutions of $^i$Bu$_3$Al(TMP)Li in the absence of the benzamide. On
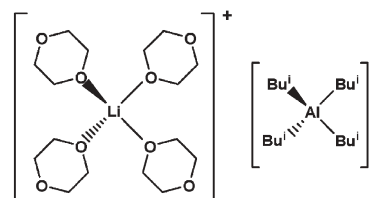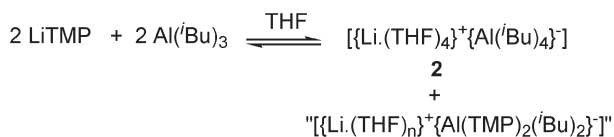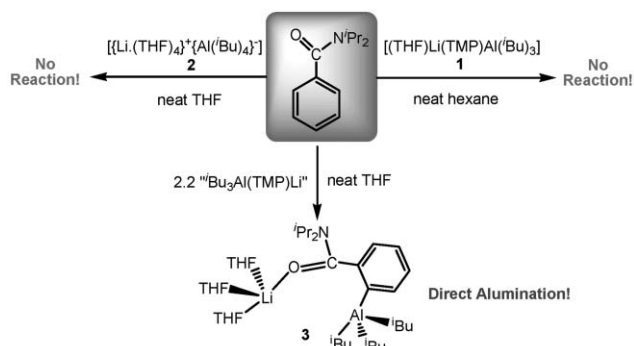
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† The HTML version of this article has been enhanced with colour images.



**Fig. 1** Chemdraw representation of [{Li·(dioxane)$_4$}$^+${Al($^i$Bu)$_4$}$^-$] **I**.

**Scheme 1** Dismutation of putative $^i\text{Bu}_3\text{Al(TMP)Li}$ in neat THF solution.



**Scheme 2** How the identity of the aluminate reagent greatly influences the course of the direct alumination reaction.

this evidence, dismutation, previously unconsidered,[4] depicted in its simplest possible form in Scheme 1, must clearly contribute to the solution chemistry of the putative $^i\text{Bu}_3\text{Al(TMP)Li}$ formulated reagent.

Interestingly, isolated **2** is inert towards the benzamide in neat THF solution (Scheme 2). This inactive component of the $^i\text{Bu}_3\text{Al(TMP)Li}$ THF-solution could explain why 2.2 molar equivalents of the base are required to effect 94% metallation of the benzamide as determined by electrophilic quenching with iodine.[1] Returning to our investigation of the $^i\text{Bu}_3\text{Al(TMP)Li}$, benzamide, THF mixture, after isolating **2** from the solution, the filtrate deposited a second crystalline product, characterised by $^1\text{H}$, $^7\text{Li}$ and $^{13}\text{C}$ NMR spectroscopy, and X-ray crystallography, as the tris(THF)-solvated lithium trialkyl-monoorthoarylaluminate $[(\text{THF})_3\cdot\text{Li}\{O(=C)N(^i\text{Pr})_2(C_6H_4)\}Al(^i\text{Bu})_3]$, **3**.‡ This complex represents the first tangible metallo intermediate of a direct alumination reaction (performed in THF solution) of a benzamide, or indeed of any functionalised aromatic compound, to be structurally defined and well characterised.[7] Its molecular structure§ (Fig. 2) can be considered a contacted ion pair. The anionic moiety comprises a distorted tetrahedral Al centre made up of four C atoms, three from terminal $^i\text{Bu}$ ligands and one from the deprotonated *ortho* position of the benzamide fragment. Contact to the cationic moiety is through the carbonyl O atom which binds terminally to Li to complete a distorted tetrahedral coordination sphere of O atoms, the remaining three of which belong to THF ligands. Key bond lengths and bond angles are listed in the figure legend. There is no contact between the Li and the deprotonated *ortho* C atom of the benzamide fragment (separation distance, Li···C7 4.759(8) Å). In contrast, the Li–O1 (carbonyl) bond length is short at 1.860(7) Å, though essentially equidistant to that in aforementioned $[\text{L}\cdot\text{Li}(\mu\text{-TMP})(\mu\text{-}^i\text{Bu})Al(^i\text{Bu})_2]^3$ [1.872(4) Å], where the benzamide is neutral, not anionic. To make this short Li–O1 bond the carbonyl function lies almost perpendicular [C7C2C1O1 99.7(4)°] to the aromatic plane. Consistent with the alumination
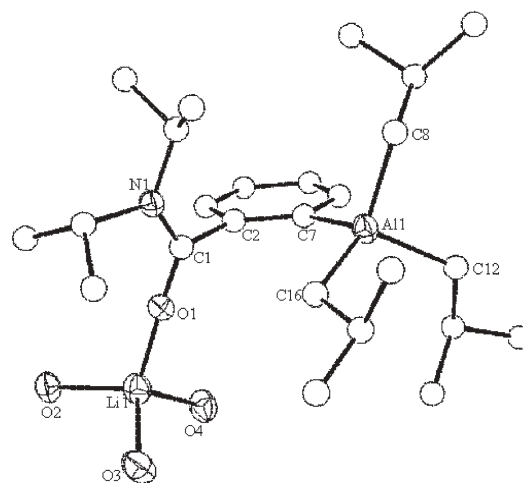


**Fig. 2** Molecular structure of **3** with thermal ellipsoids at 50% probability level. The hydrocarbon backbones of the three THF molecules and all hydrogen atoms are omitted for clarity: Selected bond lengths (Å) and bond angles (°): Li1–O1 1.860(7), Li1–O2 1.954(7), Li1–O3 1.956(7), Li1–O4 1.945(7), Al1–C7 2.050(4), Al1–C8 2.013(4), Al1–C12 2.017(4), Al1–C16 2.023(4); O1–Li1–O2 113.4(4), O1–Li1–O3 110.4(3), O1–Li1–O4 108.1(3), O2–Li1–O3 107.2(3) O2–Li1–O4 110.2(3), O3–Li1–O4 107.4(3), C7–Al1–C8 109.84(16), C7–Al1–C12 105.44(16), C7–Al1–C16 110.16(16), C8–Al1–C12 103.26(17), C8–Al1–C16 113.73(17), C12–Al1–C16 113.90(17).

(Al–H exchange) nature of the reaction,[8] the Al resides almost coplanar with the aromatic plane [175.9(3)°] with the newly developed Al–arylC7 bond [2.050(4) Å] modestly longer than the Al–alkyl bonds (mean length, 2.018 Å).

On adding the new substantial information gleaned from unearthing **2** and **3** to the existing body of evidence, a more realistic picture of the constitution of the base and its reaction with the benzamide begins to emerge. With **1** ruled out as a candidate for the active base, Scheme 3 shows the likely other species involved with **2** and **3**, the participation of which has been established. The existence of molecular "$^i\text{Bu}_3\text{Al(TMP)Li}$" can be inferred from its trapping by benzamide L in the Lewis-base adduct $[\text{L}\cdot\text{Li}(\mu\text{-TMP})(\mu\text{-}^i\text{Bu})Al(^i\text{Bu})_2]$.[3] Within a bulk THF medium, this heteroleptic trisalkyl-monoamido coordination of Al is likely to be maintained (at least transiently) and probably to be accompanied by a tetra (THF)-solvated $Li^+$, a commonly found cation.[9] The detection of **2** proves unequivocally that $[\{Li\cdot(THF)_4\}^+\{Al(TMP)(^i\text{Bu})_3\}^-]$ must undergo a dismutation process, the third component of which can be formulated formally as $[\{Li\cdot(THF)_n\}^+\{Al(TMP)_2(^i\text{Bu})_2\}^-]$ from stoichiometric balance.
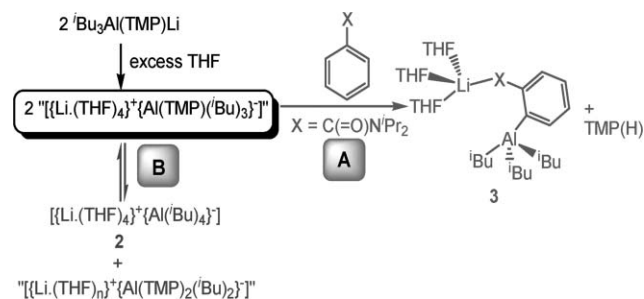


**Scheme 3** Postulated pathway for the formation of **3**.

As it has been demonstrated that **2** is inert towards the benzamide, alumination of the benzamide must be effected by one (or potentially both) of the TMP-aluminates. Proof of the TMP ligand transfer selectivity occurring within the reaction comes from the detection of TMPH in filtrates following the isolation of crystalline product **3** from THF solutions. The TMP-free, tris(alkyl) composition of **3** combined with its high isolated yield (54% with respect to the benzamide) would appear to provide clinching evidence that the dominant active base within the mixture is a tris(alkyl) composed, mono-TMP aluminate with a stoichiometric excess (with respect to lithium) of THF, namely $[Li \cdot (THF)_x Al(TMP)(^iBu)_3]$. Tetra-solvated, solvent separated $[\{Li \cdot (THF)_4\}^+ \{Al(TMP)(^iBu)_3\}^-]$ is the most likely candidate, but a kinetically labile, lower-solvated ($x = 2$ or $3$), contacted ion-pair variant cannot be unequivocally ruled out.

In conclusion, the solution and structural chemistry of "$^iBu_3Al(TMP)Li$" has now been shown to be decidedly more intricate than previously thought.[4] Based on our synthetic, reactivity, NMR spectroscopic and X-ray crystallographic studies, a reaction scheme involving previously unconsidered solvent-separated ion-pair species and a dismutation process can be postulated. In the presence of the benzamide, or another strongly Lewis basic aromatic substrate susceptible to metallation, pathway **A** will be predominant, whereas if the base is left alone dissolved in THF solution or treated with slower reacting substrates the dismutation pathway **B** will take on more prominence.

## Notes and references

‡ All reactions were carried out under a protective argon blanket.

*Synthesis* of $[\{Li \cdot (THF)_4\}^+ \{Al(^iBu)_4\}^-]$ (**2**): BuLi (5 mmol, 3.13 ml of a 1.6 M solution in hexane) was added to a mixture of THF (4 mL) and TMPH (5 mmol, (0.85 mL)) at $-78\ ^\circ C$ and the mixture was stirred for 10 min at $0\ ^\circ C$. Then, $^iBu_3Al$ (5 mmol, 5 mL of a 1 M solution in hexane) was added to the mixture at $-78\ ^\circ C$ and the mixture was stirred for 30 min at $0\ ^\circ C$ to give a pale yellow solution and a white solid. Heating the solution to refluxing temperature was needed to form a clear solution. Bench cooling of this solution afforded colourless crystals of **2** (0.71 g, 23%). Under these conditions, $[THF \cdot Li(\mu\text{-}TMP)(\mu\text{-}^iBu)Al(^iBu)_2]$, **1**, failed to crystallise despite several attempts (the only product deposited as a solid was **2**). $^1H$ NMR (400.13 MHz, $d_6$-benzene, 293 K): $\delta$ 3.48 (m, 16H, OC$H_2$ THF), 2.45 (sept, 4H, $^3J_{HH} = 6.6$ Hz, CH$_2$C$H$(CH$_3$)$_2$), 1.45 (d, 24H, $^3J_{HH} = 6.6$ Hz, CH$_2$CH(C$H_3$)$_2$), 1.40 (m, 16H, CH$_2$ THF), 0.17 (d, 8H, $^3J_{HH} = 6.6$ Hz, C$H_2$CH(CH$_3$)$_2$). $^{13}C\{H\}$ NMR (100.63 MHz, $d_6$-benzene, 293 K): $\delta$ 67.75 (OC$H_2$ THF), 28.96 (CH$_2$CH(CH$_3$)$_2$), 27.45 (C$H_2$CH(CH$_3$)$_2$), 24.75 (C$H_2$ THF), 22.92 (CH$_2$CH(C$H_3$)$_2$). $^7Li$ NMR (155.50 MHz, $d_6$-benzene, 293 K, reference LiCl in D$_2$O at 0.00 ppm): $\delta$ $-0.95$ ppm.

*Reaction* between $[\{Li \cdot (THF)_4\}^+ \{Al(^iBu)_4\}^-]$ (**2**) and $[PhC(=O)N^iPr_2]$: In a Schlenk tube, isolated **2** was dissolved in neat THF solution to give a pale yellow solution. A molar equivalent of *N,N*-diisopropylbenzamide was introduced, and the mixture was further stirred for 3 h. $^1H$ NMR spectroscopic analysis of this mixture established that **2** does not metallate the benzamide.

*Synthesis* of $[(THF)_3 \cdot Li\{O(=C)N(^iPr)_2(C_6H_4)\}Al(^iBu)_3]$ (**3**): Under Ar atmosphere, BuLi (5 mmol, 3.13 ml of a 1.6 M solution in hexane) was added to a mixture of THF (4 mL) and TMPH (5 mmol, (0.85 mL)) at $-78\ ^\circ C$ and the mixture was stirred for 10 min at $0\ ^\circ C$. Then, $^iBu_3Al$ (5 mmol, 5 mL of a 1 M solution in hexane) was added to the mixture at

$-78\ ^\circ C$ and the mixture was stirred for 30 min at $0\ ^\circ C$. *N,N*-Diisopropylbenzamide (2.5 mmol, 0.53 g) was added at $-78\ ^\circ C$ and the mixture was stirred during 3 h at r.t. to give a yellow solution and a white solid. Heating the solution to refluxing temperature was needed to form a clear solution. Bench cooling of this solution afforded again colourless crystals of **2** (0.71 g, 23%). All the solvent of the filtrate was removed *in vacuo*, followed by the addition of 10 mL of hexane to form a yellow solution. Freezer cooling of this solution at $-27\ ^\circ C$ afforded colourless crystals of **3** (0.84 g, 54% based on benzamide). $^1H$ NMR (400.13 MHz, $d_6$-benzene, 293 K): $\delta$ 8.45 (d, 1H, $^3J_{HH} = 7.5$ Hz, 1H *m*-C$_6$H$_4$), 7.25 (m, 1H, *p*-C$_6$H$_4$), 7.08 (m, 1H, *m**-C$_6$H$_4$), 6.88 (d, 1H, $^3J_{HH} = 7.5$ Hz, *o**-C$_6$H$_4$), 4.07 and 3.19 (sept, 1H each, $^3J_{HH} = 6.7$ Hz, NC$H$(CH$_3$)$_2$), 3.23 (m, 12H, OC$H_2$ THF), 2.45 (sept, 3H, $^3J_{HH} = 6.6$ Hz, CH$_2$C$H$(CH$_3$)$_2$), 1.43 (m, 24H, 18H CH$_2$CH(C$H_3$)$_2$ and 6H NCH(C$H_3$)$_2$), 1.32 (m, 12H, CH$_2$ THF), 1.71, 1.09 and 0.85 (d, 6H each, $^3J_{HH} = 6.7$ Hz, NCH(C$H_3$)$_2$), 0.28 (m, 6H, C$H_2$CH(CH$_3$)$_2$). $^{13}C\{H\}$ NMR (100.63 MHz, $d_6$-benzene, 293 K): $\delta$ 177.98 (*C*=O), 160.57 (*o*-C$_6$H$_4$), 144.43 (*i*-C$_6$H$_4$), 141.18 (*m*-C$_6$H$_4$), 125.59 (*p*-C$_6$H$_4$), 124.05 (*m**-C$_6$H$_4$), 122.67 (*o**-C$_6$H$_4$), 67.69 (OC$H_2$ THF), 51.36 and 45.42 (C$H$ $^iPr$), 29.13 and 28.88 (C$H_3$ of $^iBu$), 27.67 (C$H$ of $^iBu$), 24.62 (C$H_2$ THF), 20.64 and 19.57 (C$H_3$ $^iPr$), 19.45 (2C, C$H_3$ $^iPr$). Signal for Al–C$H_2$ of $^iBu$ was not observed. $^7Li$ NMR (155.50 MHz, $d_6$-benzene, 293 K, reference LiCl in D$_2$O at 0.00 ppm): $\delta$ $-0.14$ ppm. TMPH was detected in the $^1H$ NMR spectra of the filtrates after the isolation of crystalline product **3** from THF solutions.
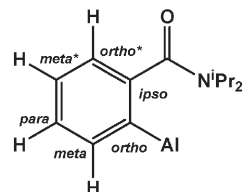


§ *Crystal data* for **3**: $C_{37}H_{69}AlLiNO_4$, $M_r = 625.85$, triclinic, space group $P\bar{1}$, $a = 9.8880(6)$, $b = 10.5709(8)$, $c = 10.8837(8)$ Å, $\alpha = 108.652(3)$, $\beta = 107.329(4)$, $\gamma = 99.374(4)^\circ$, $V = 986.15(12)$ Å$^3$, $Z = 1$, $\lambda = 0.71073$ Å, $\mu = 0.086$ mm$^{-1}$, $T = 123$ K; 20423 reflections, 3833 unique, $R_{int} = 0.061$; final refinement to convergence on $F^2$ gave $R = 0.0494$ ($F$, 2688 obs. data only) and $R_w = 0.1087$ ($F^2$, all unique data), GOF = 1.017. CCDC 660804. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b713913f

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5  "Intermediate" in the sense that it is still carbanionically active and has not been subjected to a subsequent electrophilic quenching step.

6  For full spectroscopic and crystallographic characterization of this compound see the Electronic Supplementary Information (ESI) associated with the paper cited in ref. 3.

7  For a structural study of a reaction carried out in hexane solution where a TMEDA-stabilised lithium TMP-aluminate functions as a dibasic alkyl-amido base, see: J. García-Álvarez, D. V. Graham, A. R. Kennedy, R. E. Mulvey and S. Weatherstone, *Chem. Commun.*, 2006, 3208.

8  For a review of such alkali-metal-mediated alumination (and metallation in general), see: R. E. Mulvey, F. Mongin, M. Uchiyama and Y. Kondo, *Angew. Chem., Int. Ed.*, 2007, **46**, 3802.

9  A search of the Cambridge Structural Database scored 296 hits for structures containing the cation $[Li(THF)_4]^+$, 17 of which have an Al atom in the counterion. Cambridge Structural Database, Version 5.28 with updates to May 2007. For an example, see: J. Vollet, G. Stosser and H. Schnöckel, *Inorg. Chim. Acta*, 2007, **360**, 1298.