

Direct lateral metallation using alkali-metal mediated zincation (AMMZn): SiC–H vs. Si–O bond cleavage†

Eva Hevia,* Alan R. Kennedy, Jan Klett and Matthew D. McCall

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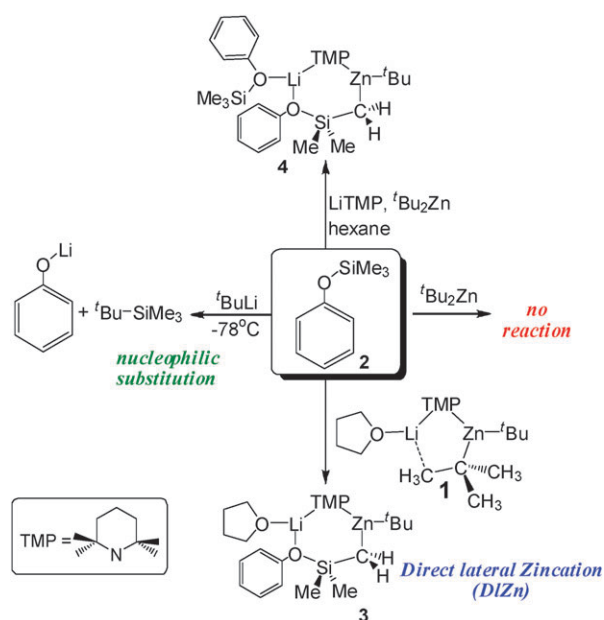
A new application of zincate [(THF)Li(TMP)(^tBu)Zn(^tBu)] (1) in alkali-metal mediated zincation (AMMZn) is reported by isolating and structurally defining the first intermediates of direct lateral zincation (DIZn) of trimethyl(phenoxy)silane (2) both of which adopt novel six-element {ZnCSiOLi} ring structures.

Pioneered 150 years ago by Wanklyn, alkali-metal zincates constitute the oldest known heterobimetallic ('ate') compounds.¹ Neglected for a long time by synthetic chemists, they have recently proved to be outstanding reagents for functionalisation of a broad range of organic molecules *via* different fundamental transformations such as metal–halogen exchange, deprotonative metallation or nucleophilic addition.² TMP–dialkyl zincates (TMP = 2,2,6,6-tetramethylpiperidine) have received special attention due to their highly chemo- and regioselectivities shown in deprotonative metallation reactions, allowing the direct (one-step) zincation of a wide range of aromatic substrates under mild conditions.³ Combining the high reactivity typically associated with alkali-metal amides with the exceptional functional group tolerance and the greater selectivity of neutral organozinc reagents (R₂Zn), lithium TMP–zincate [(THF)Li(TMP)(^tBu)Zn(^tBu)] (1),⁴ has directly zincated anisole,^{4a,b,5} benzonitrile,^{4a} methyl benzoate^{4a} and *N,N*-diisopropyl benzamide.^{4a,6} These deprotonations where the departing hydrogen is replaced by zinc but require the presence of the alkali-metal to succeed are best regarded as alkali-metal mediated zincations (AMMZn).³ To date all reported examples of AMMZn using TMP–zincates involve the regioselective removal of a proton from an aromatic carbon. In this paper we reveal the first example of direct lateral zincation (DIZn) of an aromatic molecule, trimethyl(phenoxy)silane (2), by 1 establishing a new synthetic route to α -zincated aryloxysilanes.

α -Metallated silanes (α -carbanions) have attracted considerable attention due to their numerous applications in synthesis.⁷ They can participate in similar reactions to other heteroatom-substituted carbanions but, in addition, the presence of a silyl group in the α -position provides additional stabilisation of their negative charge.⁸ Although there are several indirect routes to prepare these important reaction intermediates, there are only a handful of examples that involve a direct metal–hydrogen

exchange reaction. This is due, to a great extent, to the poor acidity of silyl methyl protons. This problem can be overcome when more activated heteroatom-substituted silanes are employed such as alkoxy-silanes.⁹ Thus, the latter can be easily lithiated by ^tBuLi in pentane at low temperatures (–78 °C). However, when the same methodology is extended to phenyl-substituted alkoxy-silanes, significant amounts of a silicon-substituted product, resulting from the cleavage of the Si–O bond, are formed.⁹

In our hands when trimethyl(phenoxy)silane (2) is treated with ^tBuLi in THF at –78 °C, no net C–H metallation occurs and LiOPh and ^tBu–SiMe₃ are the sole products observed resulting from the competing nucleophilic substitution reaction at silicon (Scheme 1).¹⁰ This difference in comparison with alkoxy-silane reactivity is probably due to the better leaving ability of the OPh group. When LiTMP is employed, the reaction gave a complicated mixture of products including the substitution products LiOPh and TMP–SiMe₃ and a marginal amount of the lithiated product. We next probed the reaction of 2 with the lithium zincate 1 at room temperature which afforded [(THF)Li(TMP){PhOSi(CH₃)₂CH₂}Zn(^tBu)] (3) as determined by NMR spectroscopy and X-ray crystallography, in an isolated yield of 52% (Scheme 1).¹¹ Multinuclear (¹H, ¹³C and ⁷Li) NMR studies carried out in C₆D₆ solutions established that α -deprotonation of 2 had occurred, which was indicated by an informative singlet at –0.52 ppm in the



Scheme 1

WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, UK G1 1XL. E-mail: eva.hevia@strath.ac.uk
† Electronic supplementary information (ESI) available: Full experimental details and NMR spectra. CCDC 721173 and 721174. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b903592c

^1H NMR spectrum and a remarkable downfield resonance at -3.9 ppm in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for the SiCH_2 group. These chemical shifts contrast with those found for the remaining non-metallated CH_3 groups attached to silicon (0.29 and 0.14 ppm in the ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum, respectively) which are similar to those found in **2** for the SiMe_3 moiety (0.15 and 0.2 ppm in the ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum, respectively).

The molecular structure of **3** established by X-ray crystallographic studies \ddagger confirms that the metallation of **2** is actually a zincation (Fig. 1a). Retaining the backbone of **1** $\{(\text{THF})\text{Li}(\text{TMP})\text{Zn}(\text{tBu})\}$, the structure of **3** is completed by the α -zincated trimethyl(phenoxy)silane that coordinates asymmetrically through a methyl C to Zn, forming a strong (short) sigma bond [Zn1-C14 , $2.0769(15)$ Å] and through the oxygen to Li via a dative bond [Li1-O1 , $1.974(3)$ Å]. This gives rise to a novel six-element $\{\text{ZnCSiOLiN}\}$ ring which adopts a pseudo-boat conformation, where Si1, Zn1, N1 and O1 lie almost coplanar (torsion angle $4.84(2)^\circ$) whereas Li1 and C14 constitute the boat vertices (Fig. 1b). This boat conformation is presumably influenced by the secondary interaction between Li1 and C14; the C atom of the silane experiences the metallation and therefore bears a partial negative charge (shown with a dashed line in Fig. 1a and 1b). This contact is relatively long (weak) [Li1-C14 , $2.568(3)$ Å] in comparison with other related compounds such as dimeric $\{[(\text{TMEDA})\text{Li}(\text{CH}_2\text{SiMe}_3)]_2\}$ (mean Li-C bond length, 2.264 Å). 12 Both metals exhibit a distorted trigonal planar geometry, with Zn coordination (sum of the angles around Zn, 360°) accomplished by a terminal tBu group whereas Li completes its coordination sphere with a terminal THF molecule. The structure of **3** in the solid state appears to be retained in C_6D_6 solution as shown by the inequivalence of the α -Me groups and β -H of the TMP ligand (at $1.38/1.18$ ppm and at $1.68/1.45$ ppm, respectively, in the ^1H NMR spectrum).

Thus, in **3**, the original molecule of trimethyl(phenoxy)silane (**2**) has been regioselectively deprotonated at one of the methyl groups of the SiMe_3 group, leaving intact the Si-O bond. Zn occupies the position previously filled by a hydrogen atom, binding strongly to an sp^3 carbon. Therefore, the dialkyl(amido) base **1** has behaved as an overall alkyl base, where the co-product of the reaction is tBuH. This reaction constitutes to the best of our knowledge the first example of direct lateral zincation (DIZn). Note that in stark contrast with **3**, in all

previous examples of AMMZn of arenes the deprotonations always occur at the aromatic ring, leaving the lateral groups (methyl) untouched. 13 In addition, it is noteworthy that tBu $_2$ Zn on its own failed to metallate (even to react) with **2** which shows that this unprecedented zinc-hydrogen exchange accomplished by **1** is a genuine example of synergic bimetallic induced reaction. 3 Furthermore, the synthesis of α -zincated trimethyl(aryloxy)silanes through an indirect route, which involves firstly deprotonation of the substrate by a more reactive group 1 organometallic reagent (such as tBuLi or LiTMP) followed by a metathesis reaction with ZnCl_2 , is not viable since as previously mentioned organolithium reagents fail to selectively deprotonate **2** at the methyl position, favouring Si-O bond cleavage or affording an undesirable complex mixture of products. This illustrates the great scope that AMMZn offers as a synthetic tool, achieving the regioselective metallation of **2** that is otherwise inaccessible when conventional monometallic reagents are employed.

In order to gain more understanding of the metallation of **2** by **1**, we next endeavoured to perform the reaction of **2** with an unco-complexed mixture of LiTMP and tBu $_2$ Zn. 14 Previous studies by Thomas and Bates 15 on α -lithiation of methoxytrimethylsilane by tBuLi have revealed that at low temperatures (-78°C) a transient premetallation complex between the relevant alkoxy silane and tBuLi ($[\text{tBuLi}\cdot 2\text{S}]_2$; $\text{S} = \text{MeOSiMe}_3$) can be detected and spectroscopically characterised (^{13}C and ^7Li NMR) which is in dynamic equilibrium with the starting materials (tetrameric tBuLi and $\text{S} = \text{MeOSiMe}_3$). When **2** was reacted with an equimolar mixture of LiTMP and tBu $_2$ Zn in hexane at room temperature colourless crystals of mixed-metal compound $[(\text{PhOSiMe}_3)\text{Li}(\text{TMP})\{\text{PhOSi}(\text{CH}_3)_2\text{CH}_2\}\text{Zn}(\text{tBu})]$ (**4**) were obtained in an isolated 16% yield (Scheme 1). NMR spectroscopic analysis of **4** in C_6D_6 revealed the presence of α -deprotonated **2** as indicated by an informative resonance at -0.68 ppm in the ^1H NMR spectrum for the SiCH_2 moiety (similar to that found for **3**, -0.59 ppm). Remarkably the ^1H NMR also showed the signals corresponding to non-metallated **2** in a ratio of 1 : 1 with the α -metallated fragment, at slightly different chemical shifts (7.10 , 6.84 , 0.15 ppm) to those found for free **2** in the same deuterated solvent (7.10 , 6.88 , 0.15 ppm). X-Ray crystallographic studies established the molecular structure of **4** \ddagger (Fig. 2) which is similar to that of **3**. Li and Zn are connected through a mixed TMP- α -deprotonated trimethyl(phenoxy)silane ligand

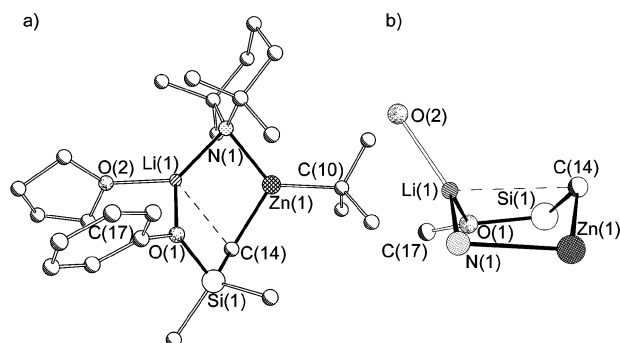


Fig. 1 (a) Molecular structure of **3**. (b) Inorganic core of **3** highlighting the pseudo-boat conformation of the $\{\text{ZnCSiOLiN}\}$ ring.

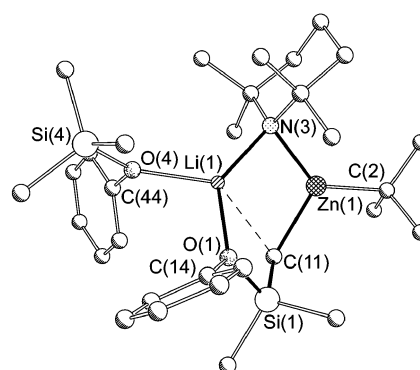


Fig. 2 Molecular structure of **4**.

set, forming a six-element {ZnCSiOLiN} ring which displays a pseudo-boat conformation. As found in **3**, both metals have distorted trigonal planar geometries; Zn binds to a terminal ^tBu ligand, whereas lithium is now coordinated to a non-metallated molecule of **2** which acts as Lewis donor through the oxygen atom (Li–O4, 2.075(3) Å) mimicking the role previously played by THF in **3**. Remarkably in contrast with **3**, the lithium–carbon contact in **4** is significantly weaker (as indicated by the elongated value found for the Li–C11 bond length, 2.776(3) Å). This is probably a consequence of the increase in steric hindrance about Li by coordinating a molecule of **2** which contains a highly sterically demanding SiMe₃ group instead of THF, which prevents it approaching closer to C11.

The yield of **4** can be improved (to 37%) when two equivalents of silane **2** are employed. The fact that **4** is obtained, even when only one molar equivalent of **2** is used, implies that the rate of metallation of **2** is faster than the rate of formation of the putative mixed-metal intermediate [(PhOSiMe₃)Li(TMP)(^tBu)Zn(^tBu)] (**I**) (Scheme 2) which once formed must react with the remaining non-coordinated silane **2** to generate **4**. In order to detect the formation of **I**, the reaction was carried out at –78 °C; however, this resulted in the precipitation of a white solid which was isolated and identified as LiTMP using NMR analysis. Thus, these results suggest that LiTMP, ^tBu₂Zn and **2** in hexane solution must be in equilibrium with the mixed-metal compound **I** (Scheme 2). The latter as soon as it is formed reacts with some non-coordinated **2**, driving the equilibrium towards **I** and therefore towards the formation of the metallated product **4**. At low temperatures, the solubility of LiTMP in hexane decreases, causing its precipitation, and therefore shifting the equilibrium towards the monometallic reagents (left) and inhibiting metallation of **2**.

In summary this work has revealed a new application of **1** in AMMZn, by isolating and structurally defining the first intermediates of direct lateral zincation (DLZn) of the trimethyl(phenoxy)silane **2**. These compounds are not accessible by a conventional two-step metathesis reaction, using monometallic reagents, illustrating the large potential that mixed-metal chemistry can offer to synthetic chemists. In addition the reaction of the unco-complexed LiTMP and ^tBu₂Zn with **2** has also been explored, which shows that these

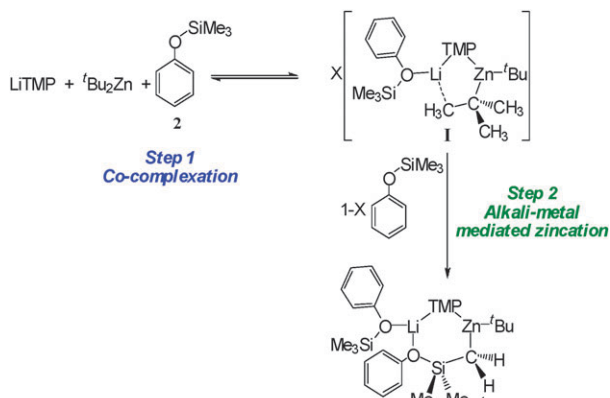
two monometallic reagents must form mixed-metal reagent analogues of **1** but with a molecule of trimethyl(phenoxy)silane acting as a donor on the lithium reagent. Once formed in solution it must react rapidly with some non-coordinated (free) trimethyl(phenoxy)silane to afford the metallated intermediate **4**.

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Notes and references

‡ Crystal data for **3**: C₂₆H₄₈LiNO₂SiZn, *M_r* = 507.05, triclinic, space group *P*1̄, *a* = 11.2813(5), *b* = 11.3700(6), *c* = 13.0987(6) Å, α = 79.264(4)°, β = 79.106(4)°, γ = 61.575(5)°, *V* = 1441.91(12) Å³, *Z* = 2, λ = 0.71073 Å, μ = 0.913 mm^{–1}, *T* = 123 K; 20 418 reflections, 7908 unique, *R_{int}* 0.0326; final refinement to convergence on *F*² gave *R* = 0.0314 (*F*, 6081 obs. data only) and *R_w* = 0.0725 (*F*², all data), GOF = 0.967. Crystal data for **4**: C₃₁H₅₄LiNO₂Si₂Zn, *M_r* = 601.23, monoclinic, space group *P*2₁/c, *a* = 12.4930(3), *b* = 12.8910(3), *c* = 20.8841(5) Å, β = 92.494(2)°, *V* = 3360.14(14) Å³, *Z* = 4, λ = 0.71073 Å, μ = 0.828 mm^{–1}, *T* = 123 K; 55 721 reflections, 9627 unique, *R_{int}* 0.0426; final refinement to convergence on *F*² gave *R* = 0.0352 (*F*, 7223 obs. data only) and *R_w* = 0.0742 (*F*², all data), GOF = 0.997.

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Scheme 2