Zincation

DOI: 10.1002/ange.200501560

Alkali-Metal-Mediated Zincation of Ferrocene: Synthesis, Structure, and Reactivity of a Lithium Tmp/Zincate Reagent**

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Lithium dialkyl tetramethylpiperidino zincates of the general formula "[$LiR_2Zn(tmp)$]" (tmp = 2,2,6,6-tetramethylpiperidine) represent an important subfamily of organozincate reagent. Established only in 1999 through the pioneering work on "[Li*t*Bu_2Zn(tmp)]" by Kondo et al.,[1] "tmp zincates" have found application as highly chemo- and/or regioselective bases for the metalation of alkyl benzoates and related aza aromatic compounds, bromopyridines, and various halobenzenes.[2,3] Recent reports[4] have highlighted the poverty of structural information available on lithium zincates in general. Tmp zincates are no exception in this regard, with a ^{13}C NMR spectroscopic study of "[Li*t*Bu_2Zn(tmp)]" in solution[1] providing the only morsel of structural evidence

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[**] This work was supported by the UK Engineering and Physical Science Research Council through grant award no. GR/R81183/01 and use of the National Crystallography Service Synchrotron Component; the UK Council for the Central Laboratories of the Research Councils through a Synchrotron beamtime allocation; and the EU through a Marie Curie Fellowship to E.H. We also thank Dr. D. R. Armstrong and Dr. P. C. Andrews for many helpful discussions. tmp = 2,2,6,6-tetramethylpiperidine.

gathered hitherto. Elucidation of the structures of zincate reagents and the intermediates formed in deprotonative zincation processes would enhance our understanding of zincate chemistry; not least in the case of tmp zincates, which because of their heteroleptic formulation can act as alkyl, amido, or dual alkyl/amido bases. Previously, we reported a series of mixed alkali-metal/magnesium amides, a number of which are tmp magnesiates.[5] This magnesium-based research uncovered several remarkable mixed-metal-induced synergic effects, which most notably lead to "inverse-crown" ring compounds.[6] The likelihood that mixed alkali-metal/zinc amides would exhibit similar synergic behavior provided a further incentive to extend our studies to the tmp zincates. Thus, we introduce herein the lithium tmp/zincate reagent [(tmeda)Li(μ-*n*Bu)(μ-tmp)Zn(*n*Bu)] (**1**; tmeda = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine) and break new ground with a report of its structure and the structure of two zincated intermediates generated when **1** is used to selectively (mono)deprotonate ferrocene (Fc) in the first example of direct zincation of a metallocene.

It is surprising that prior to this investigation $n\mathrm{Bu_2Zn}$ had not been subjected to a transformation to prepare a tmp zincate system given that both the parent organozinc reagent[7] and its homoleptic zincate derivative "[Li$n\mathrm{Bu_3Zn}$]"[8] have reasonably well developed chemistries. In the event, the transformation proved straightforward by applying the same method of addition as that used previously to prepare "[Li$t\mathrm{Bu_2Zn}$(tmp)]";[1] however, the bulk solvent was changed from polar THF to nonpolar hexane and then the reaction was completed with the introduction of a stoichiometric amount of the donor solvent, TMEDA, in a deliberate attempt to afford a crystalline zincate [Eq. (1)].[9]

$$\mathrm{Li(tmp)} + n\mathrm{Bu_2Zn} + \mathrm{TMEDA} \xrightarrow{\text{hexane}} [\mathrm{Li}n\mathrm{Bu_2Zn(tmp)(tmeda)}] \qquad (1)$$

The new zincate **1** was produced as colorless crystals (65% yield of the isolated product). NMR (^{1}H, ^{7}Li, and ^{13}C) spectroscopic characterization of these crystals in a solution of deuterated benzene established the co-complexed nature of **1**, as revealed most diagnostically in the chemical shift of the M−C*H*$_2$ resonance of the M−*n*Bu linkage. This signal appears at $\delta = 0.24$ ppm in **1** relative to $\delta = 0.27$, -0.23, and -0.83 ppm in $n\mathrm{Bu_2Zn}$, "[Li$n\mathrm{Bu_3Zn}$]", and *n*BuLi, respectively, thus suggesting that the *n*Bu group in the new mixed-metal co-complex retains much of its original "zinc character".

This last point was confirmed when the complete molecular structure of **1** was revealed through an X-ray crystallographic study (Figure 1).[10] Both *n*Bu ligands remain attached to the Zn center, one at a modestly shorter distance than the other (namely, C(5)−Zn: 2.011(2) Å; compare with C(1)−Zn: 2.041(2) Å). The *n*Bu attachment is terminal for the shorter bond; however, the other *n*Bu ligand bridges to the Li center, which explains the slight bond elongation. The Li−C(1) connection is relatively long (2.551(5) Å) relative to corresponding bonds in, for example, [{(Li*n*Bu)$_4$(tmeda)}$_\infty$] (2.131(8)–2.326(8) Å)[11] but markedly shorter than the Li···C separation (2.736 Å) in the hexamethyldisilazido zincate [Li{μ-N(SiMe$_3$)$_2$}Zn(CH$_2$SiMe$_3$)$_2$(tmta)] (tmta = trimethylenediamine-*N*,*N*,*N*′,*N*′-tetraacetic acid),[12] which is considered to have an open rather than a closed cyclic arrangement, such as the {LiNZnC} unit. This weak, but significant, attraction of the Li center to the C(1) center results in a slight pyramidalization of the {LiNNN} coordination sphere (sum of the N-Li-N bond angles: 350.98°) that is made up of μ-tmp and bidentate tmeda ligands. In contrast, the {Zn-N(1)-C(1)-C(5)} coordination is nearly perfectly planar (sum of the bond angles around Zn: 359.98°). Completing the four-membered {LiNZnC} ring, the tmp nitrogen bridge, unlike its *n*Bu carbon bridge counterpart, is much more symmetrical (span lengths: 2.047(4) and 2.0612(18) Å to the Li and Zn centers, respectively).

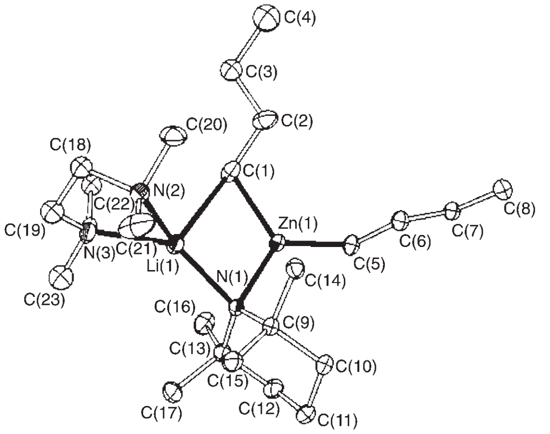
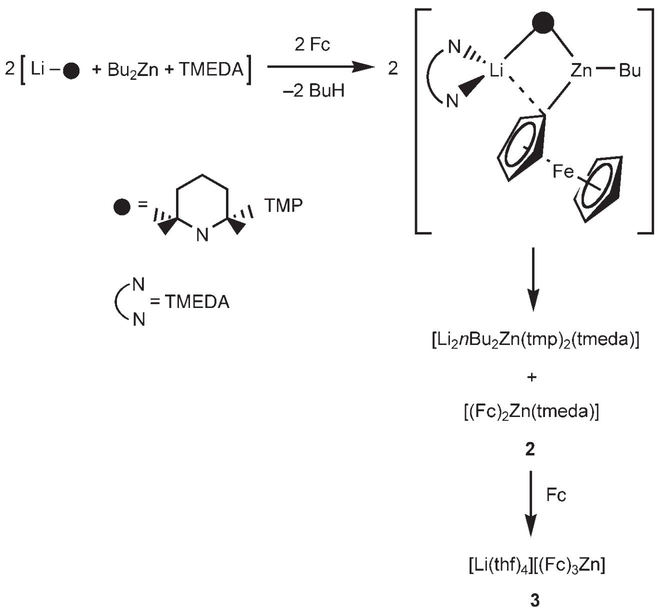


Figure 1. Molecular structure of **1**. The hydrogen atoms are omitted for clarity. Only one component is shown for each disordered group. Displacement ellipsoids are shown at the 30% probability level.

We explored the reactivity of **1** toward ferrocene under a range of conditions to probe its deprotonative metalation ability in solution. This investigation revealed a complicated sequence of stoichiometry- and time-dependent reactions (Scheme 1). The first detectable (and isolable) metalated product was the lithium-free neutral bis(ferrocenyl) zinc complex [(Fc)$_2$Zn(tmeda)] (**2**). This orange solid, which precipitated from the reaction mixture within minutes, was characterized by NMR spectroscopy and X-ray crystallography (see below). Its formation is both surprising and significant, as it establishes for the first time that intermediate metalo products from the deprotonative metalation of a substrate by a lithium zincate (prior to any electrophilic workup) are not necessarily zincates themselves (in contrast to what appears to be the case with "[Li$t\mathrm{Bu_2Zn}$(tmp)]" and related reagents)[1–3] but could possibly be, depending on the conditions, distinct Li and Zn compounds. No lithium-containing products could be isolated from solution at this stage, though investigation of the filtrate following removal of **2** suggested the presence of [Li$_2$$nBu_2$Zn(tmp)$_2$(tmeda)], which exists as an oil when prepared independently from a Li(tmp)/nBu$_2$Zn/tmeda (2:1:1) mixture. When the reaction is repeated over a longer time (24 h), a small amount of tris(ferrocenyl) zincate separated from the solvent. This product was characterized as the THF adduct [Li(thf)$_4$][(Fc)$_3$Zn] (**3**) and is formed in addition to **2**. On repeating the reaction with two equivalents of ferrocene, precipitation of **2** still occurred but the yield of **3** was significantly increased. In support of the



Scheme 1. Reaction of **1** (formed in situ) with ferrocene in hexane to yield both neutral zinc and anionic zincate products.

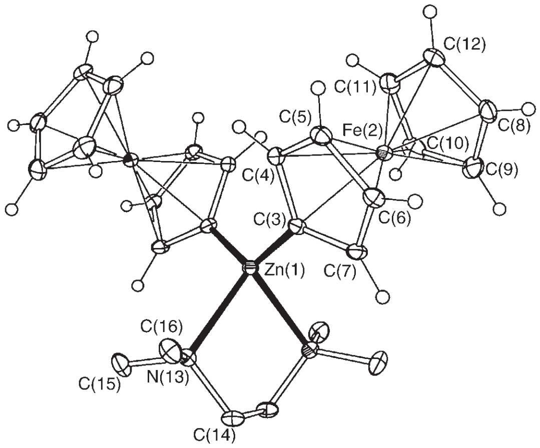


Figure 2. Molecular structure of **2**. The hydrogen atoms, except those belonging to the ferrocene rings, are omitted for clarity. Displacement ellipsoids are shown at the 30% probability level.

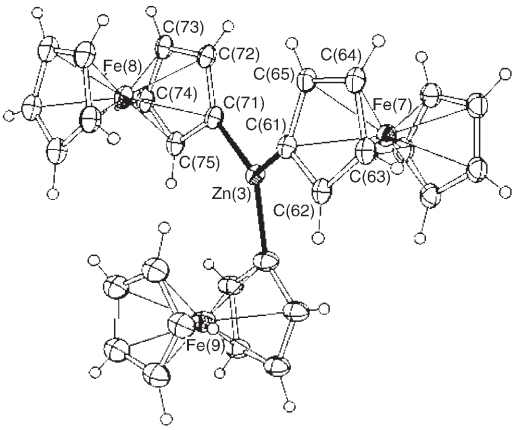


Figure 3. Molecular structure of one anion of **3**. Displacement ellipsoids are shown at the 10% probability level. Only one component of the disorder is shown.

reaction pathway shown in Scheme 1, it was found that pure "[Li$_2$*n*Bu$_2$Zn(tmp)$_2$(tmeda)]" also metalates ferrocene to yield **3**. The first step in the pathway remains an open question as no intermediate could be detected/isolated at this juncture, though logically it is likely to be the hypothetical "[Li*n*Bu(Fc)Zn(tmp)]", which must undergo a fast disproportionation reaction to the neutral zinc and the zincate species [(Fc)$_2$Zn(tmeda)] and "[Li$_2$*n*Bu$_2$Zn(tmp)$_2$(tmeda)]", respectively.

Two polymorphs of **2** crystallize from hexane/toluene and hexane/THF solutions to form monoclinic and orthorhombic systems, respectively. Because of the general similarity of these systems, only the former is discussed herein. A simple mononuclear arrangement is revealed,[13] with Zn at the center of a distorted (2 × C; 2 × N) tetrahedron, which is made up of two monodeprotonated ferrocene units and one bidentate tmeda ligand (Figure 2). The Zn center, on a twofold rotation axis, is almost coplanar (0.064 Å deviation) with each of the C_5H_4 rings to which it is bonded. This structure bears some similarity to [Zn{2-(CH$_2$NMe$_2$)$_2$C$_5$H$_3$FeC$_5$H$_5$}$_2$],[14] though the ligating nitrogen atoms belong to *N*,*N*-dimethylaminomethyl side arms on the ferrocenyl framework. However, there is a major synthetic distinction, as the latter compound is not prepared through direct zincation but by a common metathetical approach from $ZnCl_2$ and the analogous ferrocenyllithium. Three crystallographically independent ion pairs that have essentially the same structure make up the asymmetric unit of **3**, together with three uncoordinated THF molecules.[15] The anion is unprecedented, with the Zn center in a distorted trigonal planar (3 × C) arrangement comprising three monodeprotonated ferrocenyl ligands (Figure 3). The countercation, pseudotetrahedral [Li(thf)$_4$]$^+$ ion, is known. The crystal structure shows extensive disorder, thus requiring the use of synchrotron radiation for data collection and a combination of constraints and restraints in the refinement.

Control reactions have established that the monometallic reagents Li(tmp) and *n*Bu$_2$Zn are both inert towards ferrocene, even in the presence of TMEDA. Therefore the success of the solution of **1** formed in situ in the production of **2** and **3** can be attributed to a mixed-metal synergic effect or, more specifically, to alkali-metal-mediated zincation. Future work will now be directed towards pinpointing the active base species in solution that produce such an alkali-metal-mediated zincation of organic substrates.[16,17]

Experimental Section

All reactions were carried out in a protective argon atmosphere.

1: Bu$_2$Zn (5 mL, 1M solution in hexane, 5 mmol) was added to a suspension of Li(tmp) in hexane (prepared in situ by reaction of BuLi (3.1 mL, 1.6M solution in hexane, 5 mmol) with TMP(H) (0.85 mL, 5 mmol)). The reaction mixture was stirred for 30 min, thus affording a pale yellow solution. At this stage, TMEDA (0.75 mL, 5 mmol) was introduced. After the solution was stirred for 15 min, it was concentrated by removal of some solvent in vacuo. Placed in the refrigerator at 0 °C, the resulting pale yellow solution deposited a crop of colorless crystals (1.42 g, 64 %). ^{1}H NMR (400 MHz, 25 °C, C_6D_6): $\delta = 2.08$ (m, 4H; CH_2 Bu), 1.84 (m, 14H; CH_3 tmeda and H_γ tmp), 1.79 (s 4H; CH_2 tmeda), 1.69 (m, 4H; CH_2 Bu), 1.51 (m, 4H; H_β tmp), 1.21 (m, 18H; 12H of CH_3 tmp and 6H of CH_3 Bu), 0.28 ppm (m, 4H; Zn$-CH_2$ Bu); ^{13}C{^{1}H} NMR (100.63 MHz, 25 °C, C_6D_6): $\delta = 57.70$ (CH_2 tmeda), 53.47(C_α tmp), 47.30 (CH_3 tmeda), 39.04 (C_β tmp), 36.24, 34.28 (CH_3 tmp), 33.53 (CH_2 Bu), 31.44 (CH_2 Bu), 20.41 (C_γ tmp), 16.42 (Zn$-CH_2$ Bu), 15.15 ppm (CH_3 Bu); ^{7}Li NMR (155.50 MHz, 25 °C, C_6D_6, reference LiCl in D_2O at 0.00 ppm): $\delta =$ 0.561 ppm.

2: Bu_2Zn (1 mL, 1 M solution in hexane, 1 mmol) was added to a solution of Li(tmp) in hexane (prepared in situ by reaction of BuLi (0.62 mL, 1.6 M solution in hexane, 1 mmol) with TMP(H) (0.17 mL, 1 mmol)), and TMEDA (0.15 mL, 1 mmol) was introduced, thus affording a pale yellow solution. Ferrocene was added (0.18 g, 1 mmol), and the reaction mixture was stirred for 12 h. An orange solid started to precipitate after 0.5 h. THF (2 mL) was added to this suspension to afford an orange solution that was placed in the freezer at −20 °C. A crop of orange crystals was obtained after 24 h (0.20 g, 35 %; note: maximum yield possible is only 50 %). ^{1}H NMR (400 MHz, 25 °C, C_6D_6): $\delta = 4.55$ (m, 4H; CH_β C_5H_4 Fc), 4.30 (s, 10H; C_5H_5 Fc), 4.17 (m, 4H; CH_γ C_5H_4 Fc), 1.97 (s, 12H; CH_3 tmeda), 1.60 ppm (s, 4H; CH_2 tmeda); ^{13}C{^{1}H} NMR (100.63 MHz, 25 °C, C_6D_6): $\delta = 79.39$ (Zn$-C_\alpha$ Fc), 77.94 (C_β Fc), 70.60 (C_γ Fc), 68.04 (C_5H_5 Fc), 57.45 (CH_2 tmeda), 48.10 ppm (CH_3 tmeda).

3: A solution of **1** in hexane was prepared in situ as described above for **2** by reaction of Bu_2Zn (1 mmol), Li(tmp) (1 mmol), and TMEDA (1 mmol). Two equivalents of ferrocene (0.37 g, 2 mmol) were then introduced, and the reaction mixture was stirred for 24 h, thus producing an orange solid. THF (2 mL) was added to the reaction mixture to afford an orange solution. Placed in the refrigerator at 0 °C, this solution deposited a crop of orange crystals (0.34 g, 34 %). ^{1}H NMR (400 MHz, 25 °C, C_6D_6): $\delta = 4.57$ (m, 6H; CH_β C_5H_4 Fc), 4.49 (m, broad, 21H; 6H of CH_γ C_5H_4 and 15H of C_5H_5 Fc), 3.41 (m, 16H; CH_2O thf), 1.36 ppm (m, 16H; CH_2 thf); ^{13}C{^{1}H} NMR (100.63 MHz, 25 °C, C_6D_6): $\delta = 86.70$ (Zn$-C_\alpha$ Fc), 79.38 (C_β Fc), 70.33 (C_γ Fc), 68.37 (CH_2O thf), 67.67 (C_5H_5 Fc), 26.11 ppm (CH_2 thf); ^{7}Li NMR (155.50 MHz, 25 °C, C_6D_6, reference LiCl in D_2O at 0.00 ppm): $\delta = -1.05$ ppm.

Received: May 7, 2005

Keywords: amides · ferrocene · metalation · synergy · zinc

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