Dizincation and dimagnesiation of benzene using alkali-metal-mediated metallation†

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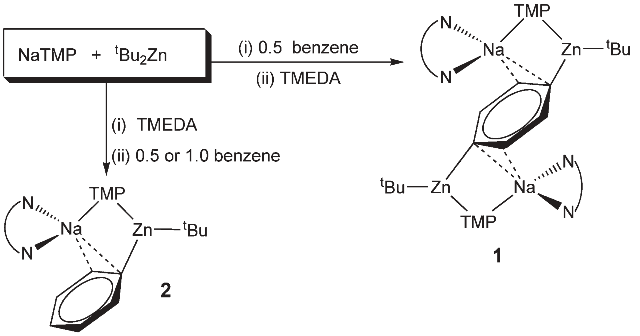
Benzene can be easily 1,4-dideprotonated stoichiometrically on reaction with two equivalents of a synergic mixture of $^{t}Bu_2Zn$, NaTMP and TMEDA to give a unique 1,4-dizincated benzene product which has been characterised by X-ray crystallography and NMR spectroscopy as well as modelled theoretically by DFT computational studies; a related synergic dimagnesiation of benzene is also reported.

Benzene is the ideal model aromatic hydrocarbon with which to measure the metallating, and in rarer cases, the polymetallating ability of new organometallic bases in view of its minimal steric hindrance and lack of directing substituents *cf.* the classical functional groups such as O-carbamates, amides, sulfones, oxazolines *etc.* which drive directed *ortho*-metallation (DoM) reactions.[1–3] Dideprotonation and concomitant dimetallation of benzene is a particularly desirable goal since in general it is difficult to achieve even with highly reactive polar metal reagents such as organolithium compounds. Several studies have found that usually less than 10% dilithiation is achievable using organolithium reagents as determined indirectly by quantifying the metal-free products obtained following electrophilic (commonly carboxylation) quenching protocols.[4] Increasing the reactivity power of the metallating agent by adding potassium *t*-butoxide to the organolithium reagent *n*-butyllithium to generate the 'LICKOR' superbase leads to an improvement in the total amount of dimetallation, though a mixture of 1,4- and 1,3-phenylene isomers (respective yields, 26 and 24%) is obtained, a threefold excess of the superbase is employed, and the nature of dimetallation (dilithiation, dipotassiation, or a mixture of monolithiation/monopotassiation?) is cloaked in mystery.[4] The notion that dimetallation of benzene could be accomplished to any useful extent *via* an organozinc reagent would hitherto have been dismissed as fanciful given the low chemical reactivity that characterises the chemistry of these much less polar Group 12 metal reagents.[5] Here, however, we report that such a seemingly far-fetched reaction can indeed now be realised. Thus, in a sense journeying back nearly 150 years to the roots of organometallic chemistry, we describe how a sodium zincate reagent (one of the earliest recorded organometallic compounds was Wanklyn's sodium triethylzincate "$NaZnEt_3$" in 1858[6]) can smoothly effect 1,4-dideprotonation of benzene. Moreover, in contrast to the case of the superbase-induced dimetallation, the structure of this benzenediide complex has successfully been uncloaked through an X-ray crystallographic study, unequivocally establishing the dizincation as opposed to disodiation nature of its formation reaction. For comparison, we also report a sodium magnesiate-effected dideprotonation of benzene and the crystal structure of the 1,4-dimagnesiated product.

Experimentally, we note that in the absence of TMEDA, $^{t}Bu_2Zn$ and NaTMP (TMP is 2,2,6,6-tetramethylpiperidide) do not form a complex as the mixture is insoluble in pure hydrocarbon media. Dissolution and complex formation can, however, be achieved by adding 0.5 molar equivalents of benzene, which implies an initial solution complex of formula $[\{(\text{benzene})_{0.5}\text{Na}(^{t}\text{Bu})(\text{TMP})\text{Zn}(^{t}\text{Bu})\}_2]$, prompting thoughts of an inverse sandwich arrangement. Its additional stabilising (solubilising) feature, not possible in pure hydrocarbon media, would be Na···π–benzene interactions, which belong to a general class of alkali metal···π–arene interaction that is becoming ever more prevalent.[7] Stirring this reaction mixture for 48 h and then introducing TMEDA at the end of this period promotes crystallisation of the product: X-ray crystallographic and NMR spectroscopic characterisation reveal it to be the 1,4-diphenylenezinc complex $[1,4\text{-}\{\text{TMEDA.Na}(\mu\text{-TMP})\text{Zn}(^{t}\text{Bu})\}_2\text{C}_6\text{H}_4]$, **1**.‡ Isolated in a yield of 39%, **1** was confirmed to be pure by NMR spectra in d_6-benzene solution, which most informatively show a significant downfield shift (at 7.62 ppm) for the aromatic C_6H_4 singlet resonance relative to that of benzene (7.16 ppm). Note that TMEDA exerts a deactivating effect on the bimetallic base's ability to dideprotonate benzene; for if it is introduced at an early stage of the reaction, only the known monodeprotonated benzene complex $[\text{TMEDA}\cdot\text{Na}(\mu\text{-TMP})(\mu\text{-C}_6\text{H}_5)\text{Zn}(^{t}\text{Bu})]$ **2** is produced (Scheme 1).[8] Hence TMEDA acts only as a crystallisation aid in



Scheme 1 Dizincation (in **1**) and monozincation (in **2**) of benzene, highlighting the importance of the order of reagent addition.

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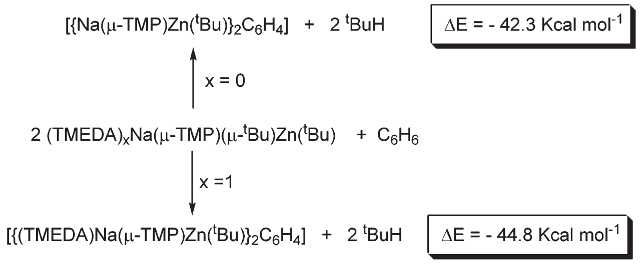
the formation of **1** and appears not to be involved in the transition structures of the deprotonation steps.[9]

The centrosymmetric molecular structure of **1** (Fig. 1)§ reveals a dideprotonated benzene ring substituted at the sterically least congested 1,4-positions by zinc atoms, lying only 0.124 Å out of the C_6H_4 ring plane. Carrying a terminal ^{t}Bu ligand, trigonal planar Zn(1) connects to Na(1) through a TMP N(1) bridge. Pyramidally surrounded by 3 N atoms [N(1) from TMP; N(2)/N(3) from TMEDA], Na(1) also engages with the C_6H_4 ring in a η^2-manner through C(1) and C(2), but lies far removed from the plane of this ring (2.389 Å). Dideprotonation *versus* monodeprotonation of benzene impacts remarkably little on bond dimensions as gauged by comparing those in **1** with those in **2**. Illustrating this point, the bond lengths of Zn–N(1) are 2.0339(16) and 1.9984(18) Å, respectively, and of Zn–C(Ar) are 2.0657(18) and 2.057(3) Å, respectively. Similarly, the bond angles of Zn–N–Na are 89.03(6) and 87.74(7)°, respectively, and of Zn–C(Ar)–Na are 79.43(6) and 79.51(8)°, respectively. This pattern reflects a combination of the lack of electronic perturbation about the deprotonated C centre (*i.e.*, when an aryl C–H bond is transformed to C–Zn) and the low steric requirement involved in 1,4-disubstitution. More flexibility is apparent in the inherently weaker, π-dominated Na···C(Ar) bonding, as in **1** there are two relatively short such contacts [to (C(1), 2.733(2) Å; to C(2), 2.801(2) Å compared to one in **2** [2.706(3) Å].

To estimate the energetics involved in the formation of **1**, we modelled all the reactants and products in Scheme 2 at the DFT level using B3LYP functionals and the 6-311G** basis set.[10] As previously noted,[8] monozincation of benzene is exothermic by 21.9 kcal mol^{-1} (or 19.2 kcal mol^{-1} in the absence of TMEDA). We find here that dizincation is even more favourable with overall energy gains of 44.8 and 42.3 kcal mol^{-1}, respectively (*i.e.* the second deprotonations are exothermic by 22.9 and 23.1 kcal mol^{-1}, respectively).



Scheme 2 Dizincation reactions of benzene modelled by DFT calculations, showing the energies of formation.

While the above zincate used to effect alkali-metal-mediated zincation (AMMZ) is a monoamido-bisalkyl formulation, alkali-metal-mediated magnesiation (AMMM) is usually effected by the reverse combination (*i.e.*, bisamido-monoalkyl fomulations).[11] This was previously illustrated by the reaction of "NaMg(^{n}Bu)(TMP)$_2$" with benzene (in a vast molar excess) to produce $[Na_4Mg_2(TMP)_6(C_6H_4)]$, **3**, a 12-membered ring (inverse crown) structure with a 1,4-dideprotonated benzene core.[12] The mismatch between the Na : Mg stoichiometry in the precursor (1 : 1) and product (2 : 1) intimates that this is not a simple deprotonation reaction, but must involve an additional disproportionation or elimination step, presumably giving $Mg(TMP)_2$. Given the success with **1**, we pondered whether a more straightforward, stoichiometrically-efficient, dimagnesiation of benzene was possible. Subjecting a stoichiometric amount of benzene (0.5 molar equivalents) to a bisamido-monoalkyl mixture of NaTMP, ^{t}BuMgTMP, and TMEDA readily achieved this, producing the 1,4-diphenylenedimagnesio complex $[1,4\text{-}\{TMEDA.Na(\mu\text{-}TMP)Mg(TMP)\}_2C_6H_4]$, **4**.† In contrast to **3**, **4** exhibits the desired 1 : 1 Na : Mg ratio and has an acyclic (with respect to metal coordination) structure. Isolated in a yield of 46%, **4** exhibits poor solubility in d_6-benzene solution, though a C_6H_4 singlet resonance at 7.60 ppm (*cf*, 7.62 ppm in **1**) could still be discerned. This feature fits with the molecular structure (Fig. 2)‡ in the crystalline state which bears strong resemblance to that of **1** but with terminal TMP(Mg) units replacing ^{t}Bu(Zn) units. Mimicking the situation in **1**, in centrosymmetric **4** each of the divalent metal atoms lies only 0.082 Å out of the C_6H_4 plane, while each Na atom is 2.541 Å out of this plane. Consistent with relative metal sizes, the

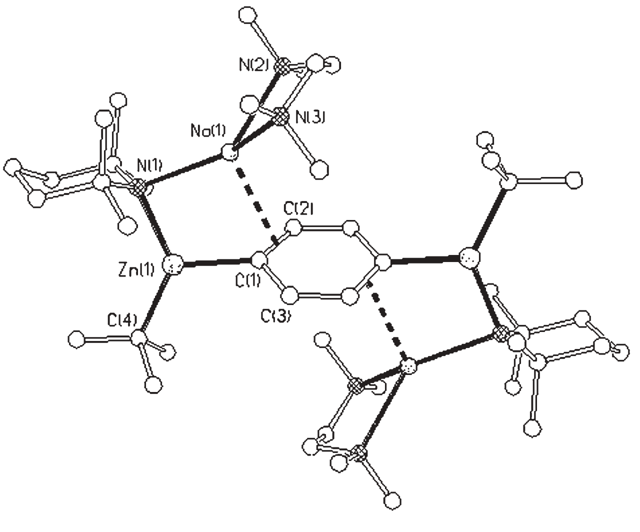


Fig. 1 Molecular structure of **1** with hydrogen atoms omitted for clarity, showing Na···π-C_6H_4 interactions as dashed lines.

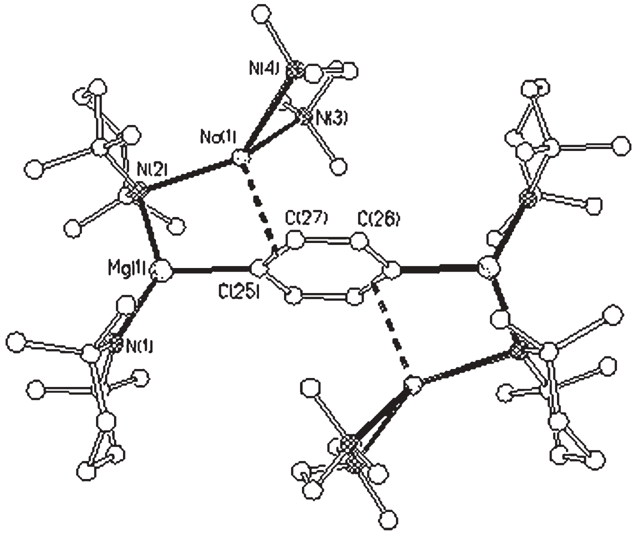


Fig. 2 Molecular structure of **4** with hydrogen atoms omitted for clarity, showing Na···π–C_6H_4 interactions as dashed lines.

Mg–C(Ar) [2.176(4) Å] and Mg–N(TMP)$_{br}$ [2.084(3) Å] bonds are modestly longer than their zinc counterparts in **1** [2.0657(18) and 2.0339(16) Å, respectively], while the remaining Mg–N(TMP)$_t$ bond [1.997(3) Å] is slightly shorter than the remaining Zn–C(^{t}Bu) bond [2.0485(19) Å] in **1**, reflecting the different ligands involved. As in **1** the C_6H_4 ring in **4** interacts in a η^2-manner with Na, with Na···C lengths of 2.677(4) and 2.866(4) Å.

A key distinction between the reaction systems producing **1** and **4** is that without TMEDA the NaTMP/^{t}BuMgTMP mixture is not soluble in hexane with 0.5 molar equivalents of benzene added. Solubility is a critical factor in switching on the synergy (note that ^{t}Bu$_2$Zn on its own is incapable of effecting benzene zincation, let alone its dizincation!) of these mixed-metal reagents;[11] hence, on that criterion the zincation method offers more flexibility than the magnesiation method. Further work is in progress developing and comparing AMMZ and AMMM.

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Notes and references

‡ All reactions were performed under a protective argon atmosphere.

Synthesis of [1,4-{TMEDA.Na(μ-TMP)Zn(^{t}Bu)}$_2$C$_6$H$_4$], 1). A solution of ^{t}Bu$_2$Zn (0.358 g, 2 mmol) in hexane (10 mL) was transferred *via* cannula to a suspension of NaTMP in hexane [prepared *in situ* by reaction of BuNa (0.16 g, 2 mmol) with TMP(H) (0.34 mL, 2 mmol)]. At this stage, half a molar equivalent (1 mmol, 0.1 mL) of benzene was added to the solution and heated gently until the entire solid dissolved forming a yellow coloured solution. It was then allowed to stir for 48 h before the addition of a molar equivalent of TMEDA (2 mmol, 0.30 mL). The resultant solution was moved to the freezer to aid the crystallisation. A crop (0.34 g, 39%) of colourless crystals formed in solution which were suitable for X-ray crystallographic analysis. ^{1}H NMR (400.13 MHz d_6-benzene): 7.62 (s, 4H, C*H*, phenyl), 1.85(m, 8H, H$_\beta$, TMP), 1.79 (m, 4H, H$_\gamma$, TMP), 1.76 (s, 8H, CH$_2$, TMEDA, 1.74 (s, 24H, CH$_3$, TMEDA), 1.60 (s, 18H, CH$_3$, ^{t}Bu), 1.50 (s, 12H, CH$_3$, TMP), 1.18 (s, 12H, CH$_3$, TMP). ^{13}C{H} NMR (100.63 MHz d_6-benzene): 163.73 (C$_{ipso}$, C$_6$H$_4$), 139.23 (C$_{2,3}$, C$_6$H$_4$), 56.67 (CH$_2$, TMEDA), 52.99 (C$_\alpha$, TMP), 46.45 (CH$_3$, TMEDA), 52.99 (C$_\beta$, TMP), 37.92 (CH$_3$, TMP), 35.29 (CH$_3$, ^{t}Bu), 35.28 (CH$_3$, TMP), 20.75 (C, ^{t}Bu), 20.65 (C$_\gamma$, TMP).

Synthesis of [1,4-{TMEDA.Na(μ-TMP)Mg(TMP)}$_2$C$_6$H$_4$], **4** A Schlenk tube was charged with 0.32 g (4 mmol) BuNa which was suspended in freshly distilled hexane (15 ml) and stirred in an ultrasonic bath for 10 min. The suspension was then treated with one molar equivalent (0.68 ml, 4 mmol) of the amine TMPH (2,2,6,6-tetramethylpiperidine). The resultant off-white suspension was stirred at room temperature for 2 h. One molar equivalent (0.88 g, 4 mmol) of ^{t}BuMgTMP was introduced to the suspension *via* a solids addition tube. 0.60 ml (4 mmol) TMEDA were added to the suspension *via* an argon purged syringe, and dissolution was achieved on gentle warming. 0.18 ml (180 μL, 2 mmol) benzene was introduced to the solution, and the mixture was heated to reflux for 1 h. The solution was left to cool slowly overnight in a Dewar flask of hot water. A crop of colourless crystals (needles) formed, isolated in a yield of 0.89 g (46% based on consumption of benzene). ^{1}H NMR (400.13 MHz d_6-benzene): 7.60 (s, 4H, C*H*, C$_6$H$_4$), 1.93–1.07 (series of overlapping signals TMP and TMEDA).

§ Crystal data for (**1**): $C_{44}H_{90}N_6Na_2Zn_2$, $M = 879.9$, monoclinic, space group $P2_1/n$, $a = 8.3869(17)$, $b = 21.158(4)$, $c = 14.333(3)$ Å, $\beta = 90.72(3)°$, $V = 2543.2(9)$ Å^3, $Z = 2$, $D_c = 1.149$ g cm^{-3}, $\mu = 0.99$ mm^{-1} (Mo Kα, $\lambda = 0.71073$ Å), $T = 150$ K; 24259 reflections measured ($\theta < 27.5°$), 5770 unique, $R_{int} = 0.057$, R (F, $F^2 > 2\sigma$) = 0.037, R_w (F^2, all data) = 0.072, goodness of fit on $F^2 = 1.02$, 255 refined parameters, constrained riding H atoms, final difference map within ± 0.32 e Å^{-3}. Crystal data for (**4**): $C_{54}H_{108}Mg_2N_8Na_2$, $M = 964.1$, monoclinic, space group $P2_1/n$, $a = 8.3042(3)$, $b = 21.9621(8)$, $c = 16.3052(6)$ Å, $\beta = 91.458(2)°$, $V = 2972.7(2)$ Å^3, $Z = 2$, $D_c = 1.077$ g cm^{-3}, $\mu = 0.10$ mm^{-1} (Mo Kα, $\lambda = 0.71073$ Å), $T = 123$ K; 61353 reflections measured ($\theta < 25.0°$), 5225 unique, $R_{int} = 0.133$, R (F, $F^2 > 2\sigma$) = 0.068, R_w (F^2, all data) = 0.147, goodness of fit on $F^2 = 1.01$, 310 refined parameters, constrained riding H atoms, final difference map within ± 0.35 e Å^{-3}. CCDC 621932 and 621933. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b613655a

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