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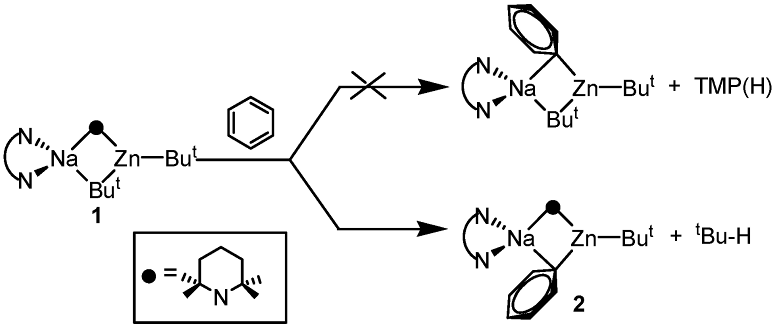

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Sodium Dialkyl-amidozincates: Alkyl or Amido Bases? An Experimental and Theoretical Case Study

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Alkali metal zincates are fast establishing themselves as a new vanguard class of organozinc reagent,[1] to add to the old guard of organozinc halides and diorganozincs, which have long been actively engaged in organic synthesis. Among the best developed alkali metal zincates are homoleptic triorganozincates $[M^+ZnR_3^-]$[2] and heteroleptic diorgano-amidozincates $[M^+ ZnR_2(R_2N)^-]$.[3] In the latter category, lithium di-*tert*-butyltetramethylpiperidinozincate (TMP-zincate) is receiving special attention in view of its high chemo-/regioselectivity in deprotonative reactions of, for example, functionalized aromatics (including benzyne precursors)[3a] and functionalized heteroaromatics (including halopyridines).[3b] The heteroleptic character of TMP-zincate makes ligand-transfer selectivity an issue, as in theory either the amido ligand or the alkyl ligand could function as the base (zincating agent) in these metal−hydrogen exchange applications. Though hitherto no definitive structural evidence has been forthcoming to decide between the two possibilities, it has been presumed[3] that TMP-zincate is an amide base, that is, following deprotonation the new (putative) zincate retains both *tert*-butyl ligands and TMPH is formed (eq 1).

$$R{-}H + Li^+Zn^tBu_2(TMP)^- \xrightarrow{-TMPH} Li^+Zn^tBu_2R^- \quad (1)$$

During our own investigations into the special synergic effects of mixed alkali metal-magnesium amide bases, we have found that the identity of the alkali metal can profoundly affect the course of a reaction. A germane example is the reactions of ^{n}BuM/Bu$_2$Mg/3TMPH mixtures (tantamount to TMP-magnesiates) with benzene, which produce either a 12-membered $[Na_4Mg_2(TMP)_6(C_6H_4)]$[4] or a 24-membered $[K_6Mg_6(TMP)_{12}(C_6H_5)_6]$[5] "inverse crown" ring when M = Na or K. This challenged us to test whether TMP-zincate chemistry could exhibit comparable alkali metal effects. Thus we report here the synthesis of a sodium TMP-zincate and the successful isolation of the metallo-intermediate it forms on deprotonating benzene. By crystallographically characterizing both new compounds, we have established unequivocally the ligand-transfer selectivity (in this specific application basicity) of the sodium zincate toward benzene, which appears to run counter to the presumed[6] basic behavior of lithium TMP-zincate.

Sodium di-*tert*-butyltetramethylpiperidinozincate was prepared as its TMEDA (*N,N,N′,N′*-tetramethylethylenediamine) adduct [TMEDA·Na(μ-^{t}Bu)(μ-TMP)Zn(^{t}Bu)], **1**. In a variation of the method used to make TMP-zincate,[3c] which was performed in the bulk polar solvent THF, the addition reaction of a 1:1 mixture of ^{t}Bu$_2$Zn and NaTMP was carried out in nonpolar hexane, with 1 molar equiv of polar TMEDA added, with gentle warming, to effect complete dissolution. We anticipated correctly that avoidance of a bulk polar solvent would increase the opportunity for crystallization of the zincate, and thus cooling the resulting pale yellow solution afforded colorless crystals of **1** (isolated yield, 58%). The reactivity of **1** toward arene solvents (vide infra) necessitated the recording of its NMR spectra in inert d_{12}-cyclohexane, which confirmed its molecular formula.

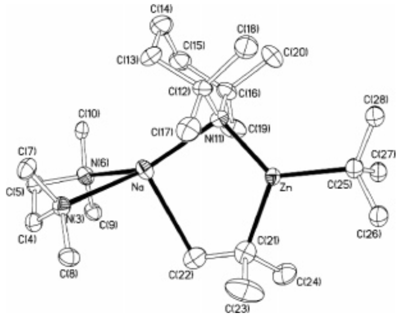

Figure 1. Molecular structure of **1** with second disorder components and hydrogen atoms omitted for clarity, showing atom-labeling scheme and 30% probability displacement ellipsoids.

Counting a medium-long Na···Me agostic contact [Na2−C22, 2.750(10) Å], the molecular structure of **1**[7] (Figure 1) can be viewed as a five-membered (NaNZnCC) ring system, incorporating a TMP bridge and an unusual ^{t}Bu bridge. The latter bridges asymmetrically to Zn through quaternary C21 and to Na through methyl C22. On forming this ^{t}Bu$_2$Zn·NaTMP cocomplex, Zn expands its coordination from linear in ^{t}Bu$_2$Zn to distorted trigonal planar in **1**. The distortion is mainly located at the N11−Zn1−C21 bond angle, which has to narrow [116.9(3)°, cf. 126.2(2)° for N11−Zn1−C25] to make the Na···C22 agostic interaction.

Crystal structures of zincates, especially synthetically useful types, are scarce. To our knowledge there is no other sodium diorgano-amidozincate structure available for direct comparison. There is one example each of a lithium diorgano-amidozincate [TMTA·Li{μ-N(SiMe$_3$)$_2$}Zn(CH$_2$SiMe$_3$)$_2$][8] and a sodium triorganozincate [{NaZn(neo-pentyl)$_3$}$_2$],[9] but these differ markedly from **1** in adopting open-cyclic and bicyclic-dimeric structures, respectively. A closer analogy, at least in a connectivity sense, is the monoorgano TMP-magnesiate [TMEDA·Na(μ-^{n}Bu)(μ-TMP)-Mg(TMP)],[10] though its ^{n}Bu bridge is constructed symmetrically through the α-C.

Endeavoring to establish whether **1** functions preferentially as an amido or alkyl base toward protic substrates, we stirred a hexane solution of it with 1 molar equiv of benzene for only 30 min at ambient temperature. Transferring the solution to a freezer at −20 °C produced colorless crystals. NMR spectroscopic studies, which could be recorded passively in d_6-benzene solution, showing most informatively a set of Ph resonances and integration ratios consistent with a 1:1 ^{t}Bu:TMP stoichiometry, combined with X-ray crystal-

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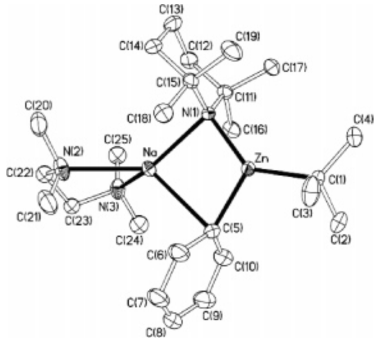
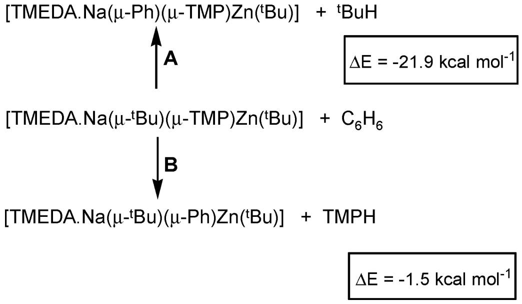


Figure 2. Molecular structure of **2** with second disorder components and hydrogen atoms omitted for clarity, showing atom-labeling scheme and 30% probability displacement ellipsoids.

Scheme 1



lography, identified these crystals as the new hetero(tri)leptic zincate [TMEDA·Na(μ-Ph)(μ-TMP)Zn(^{t}Bu)], **2** (isolated yield, 51%). Thus, it has been established absolutely that, in this specific application, the mixed-ligand zincate **1** operates as an alkyl base, with elimination of one ^{t}Bu ligand as ^{t}BuH. The other potential basic ligand within **1**, TMP, retains its original bridging position in the molecular structure of **2** (Figure 2).[7] Moreover, a comparison of **1** and **2** reveals that the selective expulsion of ^{t}Bu is accompanied by a remarkable retention in structure of the dormant backbone of the complex base as the deprotonated substrate Ph essentially reoccupies the site left by the expelled ^{t}Bu [the Na-ipsoC5 bond in **2**, length 2.706(3) Å, is only marginally shorter than the agostic Na···Me contact in **1**], while the rest of the structure remains unchanged. A notable geometrical feature of **2** is that Zn lies almost coplanar with the Ph ring plane [+0.213(4) Å out of it], whereas Na lies far removed from this plane [at a distance of −2.566(3) Å]. This appears indicative of a σ/π demarcation in the metal-Ph bonding, which is also prevalent in Mg-Na “inverse crown” and related complexes.[11]

To attempt to understand the preference for ^{t}Bu over TMP transfer, we next carried out a theoretical study (at the DFT level, using B3LYP functionals and the 6-311G** basis set) of the reaction between **1** and benzene. Modeling all reactants and products (Scheme 1), it was calculated that route **A**, which mimics the experimental reaction, and route **B**, a hypothetical reaction where TMP acts as the base, are both exothermic processes. However, the energy released is far greater for **A** (by a margin of 20.4 kcal mol^{-1}), suggesting that the preference for ^{t}Bu ligand transfer is, at least in part, thermodynamically driven. Of course, an alternative mechanism could be that route **B** occurs first, followed by a second deprotonation step in which TMPH is deprotonated by the sodium triorganozincate [TMEDA·Na(μ-^{t}Bu)(μ-Ph)Zn(^{t}Bu)]. However, as there would be no additional energy gained by this two-step process (calculated to be −1.5 and then −20.4 kcal mol^{-1} sequentially) over the one-step mechanism (−21.9 kcal mol^{-1}) and it would involve the cleavage of a short, strong Na−N(TMP) bond in preference to a very weak, long Na−C(^{t}Bu) contact, this two-step alternative appears highly unlikely.[13]

Finally, it should be emphasized that neither ^{t}Bu$_2$Zn nor NaTMP can unilaterally deprotonate benzene under the same conditions as that achieved by the special zincate **1**. Therefore the reaction between **1** and benzene represents an example of *synergic metalation*, or more specifically, of *alkali metal-mediated zincation*.

Acknowledgment. We thank the EPSRC (grant award no. GR/R81183/01), the EU (Marie Curie Fellowship to E.H.), and the Royal Society/Leverhulme Trust (Fellowship to R.E.M.) for generously sponsoring this research.

Supporting Information Available: Full experimental details, theoretical calculations, and crystallographic data of **1** and **2** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) No specific evidence has been presented in the papers listed in ref 3 as to the nature of the zincate intermediates formed when TMP-zincate is used as a base, though the equations therein show it as an amide base. In general, it appears that these intermediates are not isolated from solution. Note also that the reactivity of the TMEDA-ligated lithium TMP-zincate has not yet been studied.
(7) Crystal data for (**1**): $C_{23}H_{52}N_3NaZn$, $M = 459.0$, orthorhombic, *Pbcn*, $a = 27.382(4)$, $b = 10.834(2)$, $c = 18.963(5)$ Å, $V = 5625.6(19)$ Å^3, $Z = 8$, $T = 150$ K; $R = 0.080$ ($I > 2\sigma$), $R_w(F^2) = 0.241$ (all 4050 unique data, from 16772 measured data, $R_{int} = 0.037$), largest residual electron density = 1.28 e Å^{-3}. Crystal data for (**2**): $C_{25}H_{48}N_3NaZn$, $M = 479.0$, monoclinic, $P2_1/n$, $a = 16.5118(5)$, $b = 10.9189(2)$, $c = 16.8603(5)$ Å, $\beta = 111.755(1)°$, $V = 2823.25(13)$ Å^3, $Z = 4$, $T = 123$ K; $R = 0.047$ ($I > 2\sigma$), $R_w(F^2) = 0.096$ (all 6461 unique data, from 52923 measured data, $R_{int} = 0.074$), largest residual electron density = 0.42 e Å^{-3}. Data were collected on Nonius KappaCCD diffractometers with Mo Kα radiation ($\lambda = 0.71073$ Å). Both structures show disorder in some ligand atoms; these were refined with isotropic displacement parameters for **2**. All other non-hydrogen atoms were refined anisotropically, while H atoms were constrained with a riding model (SHELXS, SHELXL and SHELXTL software).
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(13) Even more reassuringly when routes **A** and **B** are recalculated without TMEDA, the former is exothermic by −19.2 kcal mol^{-1}, whereas the latter is endothermic by +6.3 kcal mol^{-1}.

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