Modifying Alkylzinc Reactivity with 2,2′-Dipyridylamide: Activation of tBu−Zn Bonds for *para*-Alkylation of Benzophenone**

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Many of the recent eye-catching advances in zincate executed metallation chemistry have centered on the secondary monoamide 2,2,6,6-tetramethylpiperidide (TMP). Developed by Kondo, Uchiyama, and co-workers, the original TMP zincate reagent [LiZn(TMP)tBu$_2$] is an effective base for both aromatic and heteroaromatic substrates.[1] Knochel and co-workers have since compiled a library of new TMP-based metalating agents, including the zinc pivalate [(TMP)Zn-(OPiv)·LiCl] (OPiv = pivalate), which like [LiZn(TMP)tBu$_2$], displays strong deprotonating power and exceptional functional-group tolerance but has the added advantage that its arylzincated derivatives boast prolonged air stability.[2] The area of zincate metalation chemistry that is best structurally defined is that involving the sodium TMP reagent [(TMEDA)Na(TMP)(tBu)Zn(tBu)] (**1**; TMEDA = *N,N,N′,N′*-tetramethylethylenediamine). This reagent, which exhibits enhanced reactivity over the aforementioned lithium zincates, and many of its arylzincated derivatives adopt similar structures, which are designed on an architectural template of a Na–anion–Zn–anion ring carrying terminal ligands, namely a neutral donor and an anion on Na and Zn, respectively (Figure 1). To break this template and develop new structural motifs that could stimulate new reactivity we have investigated replacing monofunctional TMP with multifunctional 2,2′-dipyridylamide [dpa, (2-NC$_5$H$_4$)$_2$N]. Offering three potential ligating N sites, this N-bridged bis(N heterocycle) finds utility in a diverse range of applications including medicine,[3] catalysis,[4] photoluminescence,[5] and supramolecular chemistry.[6] Herein we report a remarkable set of novel structures incorporating dpa into neutral zinc, sodium zincate, and potassium zincate modifications containing *tert*-butyl ligands. Preliminary reactivity studies reveal that the mixed sodium-zinc dpa complexes can *tert*-butylate the ketone benzophenone at the *para* (1,6-addition) position, which is
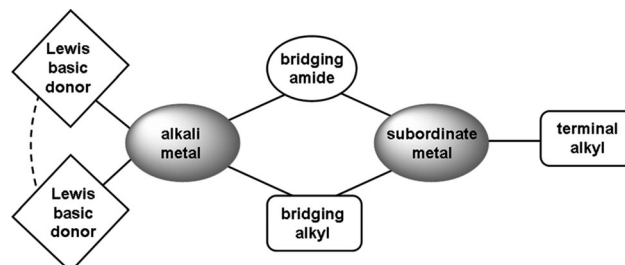
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Figure 1. General structural motif observed for heteroleptic ate bases. Here the subordinate metal is zinc.

challenging, and hint that the reaction can be made sub-stoichiometric in the sodium component.

The neutral, heteroleptic zinc complex [{(dpa)Zn(tBu)}$_2$] (**2**) was synthesized straightforwardly through the 1:1 stoichiometric combination of tBu$_2$Zn and the amine dpa(H) in a hexane solution. NMR studies of the filtrate revealed the absolute yield was higher than the 70% yield of the isolated crystals. Possessing an attractive hour-glass-shaped core, the centrosymmetric molecular structure of **2** (Scheme 1) is dimeric with the distorted tetrahedral zinc atom[7] bonded to the deprotonated N of one amido unit, which occupies the dipyridyl pocket of the other and completes its coordination with a terminal tBu ligand. In the hour-glass description (see the Supporting Information), each bulb comprises a puckered, six-atom (NCNCNZn) ring with Zn situated 1.0991(3) Å from the nearest NCNCN plane and 1.7143(3) Å from the second NCNCN plane. This motif bears a strong resemblance to that of the isoelectronic neutral zinc dimer [{MeZnC(H)-Py$_2$}$_2$](Py=2-pyridyl).[8] To our knowledge, **2** represents the first crystallographically characterized Zn/dpa complex showing a Zn−$_{(bridgehead)}$N bond, although it has been noted in alkylated dimeric derivatives wherein the mode of dimerization is distinct from that in **2**.[9] The *anti/anti* conformation[10] (i.e., both pyridyl N atoms directed away from the bridgehead N) within **2** also contrasts with the *syn/anti* conformations found in polymorphs of dpa(H)[11] and the aforementioned alkylated dpa derivatives.
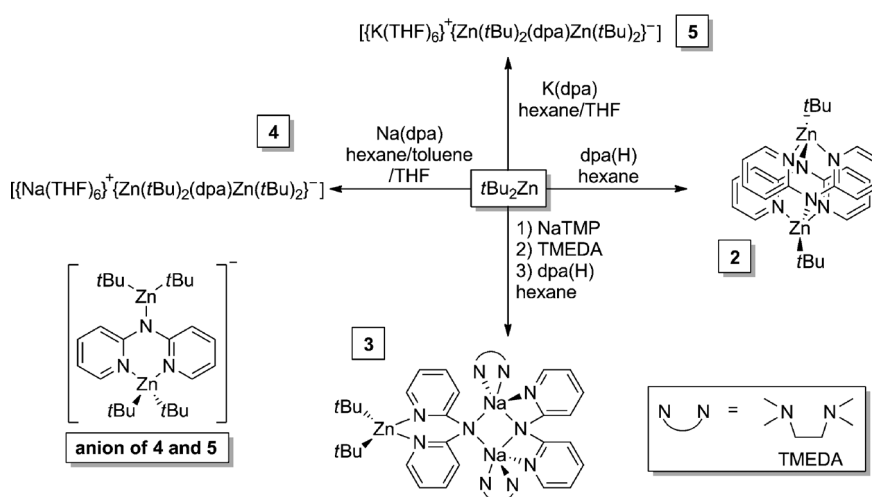
A simple transamination reaction[12] between TMP/zincate **1** and dpa(H) in a hexane solution was anticipated, but instead the isolated crystalline product was the disodium monozinc species [(TMEDA)$_2$Na$_2$(μ-dpa)$_2$Zn(tBu)$_2$] [**3**; 70% yield based on the dpa(H) stoichiometry]. Formally transamination has occurred but the 2:1 Na/Zn stoichiometry of **3** is inconsistent with the 1:1 stoichiometry of the reaction. Its molecular structure (Figure 2) can be viewed as a cocomplex between a TMEDA-complexed sodium amide dimer and

Scheme 1. Synthesis of the neutral zinc dimer 2, disodium zincate 3, sodium zinczincate 4, and potassium zinczincate 5.

1.347(2) Å; C15−N3, 1.346(2) Å; dihedral angle of unit bonded to Zn, 22.9°] suggest the degree of delocalization is small. This prompts the thought that though formally a higher-order zincate (conforming to the empirical formula $Na_2ZnR_2R'_2$), 3 is best interpreted as a neutral donor-acceptor bis(alkyl)zinc complex with a metalloligand as a donor. Supporting this view, the structure of 3 is novel as it bears little resemblance to the common Weiss motif of dialkali-metal zincate and related ate structures[14] (Figure 3) but shows more in common with homonuclear zinc complexes such as [tBu_2Zn-{(iPrN(H)CH$_2$CH$_2$N(H)iPr)}][15] or [(tBu_2Zn)$_3$(C$_4$H$_4$N$_2$)$_4$].[16]
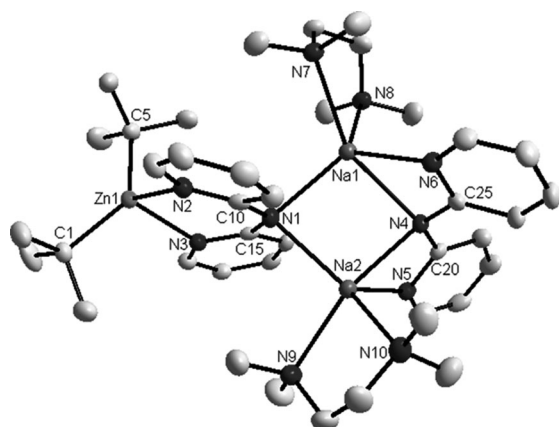

Figure 2. Molecular structure of 3[26] with thermal ellipsoids at 50% probability level. Hydrogen atoms omitted for clarity. Selected bond lengths (Å) and angles (°): Zn1−C1 2.048(2), Zn1−C5 2.044(2), Zn1−N2 2.185(2), Zn1−N3 2.157(2), C10−N1 1.371(2), C10−N2 1.347(2), C15−N1 1.373(2), C15−N3 1.346(2); C1-Zn1-C5 130.31(7), C1-Zn1-N2 111.19(6), C1-Zn1-N3 110.41(6), N2-Zn1-N3 82.42(6), N2-Zn1-C5 108.19(6), N3-Zn1-C5 103.65(7), C10-N1-C15 125.1(2).

a bis(alkyl) zinc monomer with the connection being two dative Zn−N$_{(pyr)}$ bonds completing a distorted tetrahedral (C$_2$N$_2$) zinc environment. To bind to Zn, one dipyridylamide must adopt an *anti/anti* disposition with its pyridine N atoms oriented away from the [{Na(amido)N}$_2$] ring, while the second has a *syn/syn* conformation with each Na bonded to the amido N and one or other of the pyridine N atoms. Resonance delocalization within the dipyridylamide scaffold is usually associated with shorter C-N$_{(amido)}$-C bridges (e.g., about 1.34 Å each), longer C-N$_{(pyr)}$ bonds (e.g., about 1.38 Å), and a dihedral angle between the two pyridine ring planes approaching 0° as ascertained by data from several neutral dpa(H) and anionic dpa complexes[11, 13] (see the Supporting Information). The corresponding dimensions within 3 [e.g., C10−N1, 1.371(2) Å; C15−N1, 1.373(2) Å; C10−N2,
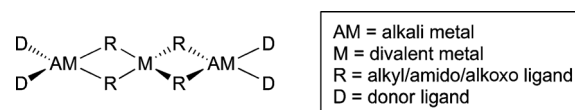

Figure 3. Graphical representation of a Weiss motif structure.

Surprisingly when the same metal components in 3 were mixed together in the presence of THF and in the absence of TMEDA, the structural outcome was remarkably different (Scheme 1). Substituting TMEDA by THF can be trivial in organoalkalimetal chemistry with one bidentate TMEDA being replaced by two monodentate THF molecules without altering the basic structure of the complex, but the reactivity may be changed.[17] However, here the structural effect is more profound. Unlike the contact ion-pair 3 with its 2:1 Na/Zn stoichiometry, the isolated product is the solvent-separated monosodium dizinc complex [{Na(THF)$_6$}$^+${Zn(tBu)$_2$-(dpa)Zn(tBu)$_2$}$^-$] (4). The octahedrally coordinated cation of 4 is known[18] but its anionic moiety (Figure 4) is unprecedented. Two tBu$_2$Zn monomers connect through one dpa anion which, lying flat in an *anti/anti* conformation, presents a chelating pyridyl pocket to one Zn atom, thus making it four coordinate, and the bridgehead amido N to the other Zn, thus
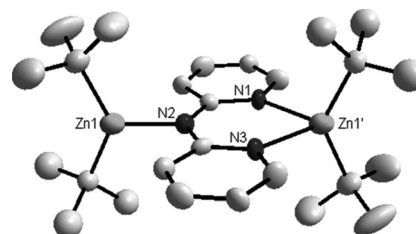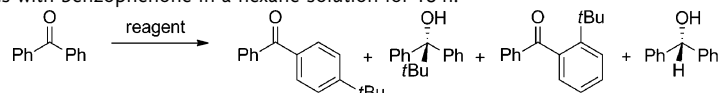

Figure 4. Anion of the solvent-separated ion pair structure of 4[26] with thermal ellipsoids at 50% probability level. Hydrogen atoms and disordered components omitted for clarity. The anionic moiety of 5 is effectively identical.

Table 1: Reaction of zinc reagents with benzophenone in a hexane solution for 18 h.

Entry	Reagent	T [°C]	Yield [%][a]				
			para addition (1,6)	Carbonyl addition (1,2)	*ortho* addition (1,4)	benzhydrol (H⁻ addition)	total
	Stoichiometric						
1	tBu$_2$Zn (1 equiv)	RT	1	0	0	0	1
2	tBu$_2$Zn·2 pyridine (1 equiv)	RT	1	0	0	0	1
3	tBu$_2$Zn·TMEDA (1 equiv)	RT	1	1	0	0	2
4	[(TMEDA)Na(TMP)(tBu)Zn(tBu)] (**1**; 1 equiv)	RT	58	14	3	0	75
5	[(TMEDA)$_2$Na$_2$(μ-dpa)$_2$Zn(tBu)$_2$] (**3**; 1 equiv)	RT	40	6	0	11	57
6	[{Na(THF)$_6$}⁺ {Zn(tBu)$_2$(dpa)Zn(tBu)$_2$}⁻] (**4**; 1 equiv)	RT	42	13	0	3	58
	Substoichiometric						
7	tBu$_2$Zn (1 equiv)	75	11	1	0	8	20
8	tBu$_2$Zn (1 equiv) + [(TMEDA)Na(TMP)] (0.1 equiv)	75	33	8	0	6	47
9	tBu$_2$Zn (1 equiv) + [(TMEDA)Na(dpa)]$_2$ (0.1 equiv)	75	52	12	0	7	71
10	tBu$_2$Zn (1 equiv) + [{Na(THF)$_6$}⁺{Zn(tBu)$_2$(dpa)Zn(tBu)$_2$}⁻] (0.1 equiv)	75	33	7	0	9	49

[a] Yields were determined by ¹H NMR spectroscopy using hexamethylbenzene (10 mol%) as an internal standard.

making it three coordinate. Unfortunately, the anion lies on a crystallographic center of symmetry, and as this symmetry can only be approximately satisfied by the dpa ligand, the structure is disordered over two sites. This prevents any discussion of dimensions, though the atomic connectivity is definite. We therefore turned to a DFT study using the B3LYP[19] method and the 6-311G (d,p)[20] basis set in which the anionic moiety of **4** was modeled. Its dimensions (see the Supporting Information for full details) revealed slightly more delocalization than that implied in **3**. Key indicators are the C−N$_{(amido)}$ bond lengths [1.363 Å; 1.372 Å (mean) in **3**] and the dihedral angle between the N$_{(pyr)}$−C(H) bonds [C-N···N-C is 3.9° in **4**; 26.0° in **3**]. Also within the pyridyl rings there are long C−N bonds and two relatively short C−C bonds akin to a N-C=C-C=C-C-N pattern (bond lengths 1.345/1.345, 1.380/1.380, 1.401/1.401, 1.374/1.374, 1.429/1.428, and 1.360/1.359 Å) similar to that found in a series of [Me$_2$MPy$_2$N]$_n$ complexes, where M is Al, Ga, In, or Tl.[13b] Formally **4** could be regarded as a sodium zinczincate[21] by combining a neutral tBu$_2$Zn unit with a [Zn(dpa)tBu$_2$]⁻ ate, though the true electronic distribution, as reflected by the theoretical calculations, lies between these two extremes. We also successfully prepared the potassium congener [{K(THF)$_6$}⁺{Zn(tBu)$_2$(dpa)Zn-(tBu)$_2$}⁻] (**5**; see the Supporting Information for details).

Alkylselective addition to ketones by Grignard reagents has been much studied with benzophenone, which is often used as a benchmark as its reactions can have several outcomes. Excellent progress has been made in carbonyl (1,2) additions most recently by Ishihara and co-workers who showed that catalytic amounts of ZnCl$_2$ (thus generating R$_3$ZnMgCl intermediates) can greatly enhance such reactions.[22] Hevia and co-workers also reported that adding just 10 mol% of the magnesium-zinc hybrid [(THF)$_6$Mg$_2$Cl$_3$]⁺-[Zn$_2$Et$_5$]⁻ to the reaction of EtMgCl and benzophenone gave the 1, 2-addition product in 90% yield.[23] These bimetallic zinc-mediated successes inspired us to test the *tert*-butylation

performance of **3** and **4** in a hexane solution, noting that **1** had previously delivered a tBu nucleophile to the *para* (1,6) position of benzophenone albeit on the sole evidence of an isolated crystalline enolato intermediate.[24] Table 1 reveals that the three sodium zincates **3**, **4**, and **1** give competitive yields of the challenging *para*-addition product 4-$t$butylbenzophenone in contrast to the near 0% yields witnessed for the homonuclear zinc species. A striking comparison is that the metalloligand solvated tBu$_2$Zn produces 40 times as much *para* product as unsolvated tBu$_2$Zn or its pyridine and TMEDA solvates. Olah and co-workers reported that reacting tBuLi with benzophenone in THF solvent gave a 52% yield of ring alkylation products (1:9, *ortho/para* ratio), but only at −100°C using toxic thionyl chloride as oxidant as an aqueous work-up dropped the combined yield to 28°C and running the reaction in hexane at ambient temperature switched the major product to that of 1,2 addition.[23] Clearly the zincate systems are advantageous since they give comparable yields at ambient temperature using a mild aqueous work-up. The most intriguing result came when a 1:1 mixture of tBu$_2$Zn and benzophenone was treated with only 10 mol% of the sodium amide [{(TMEDA)Na(dpa)}$_2$], presumably generating 10 mol% of **3** in situ in a hexane solution. At ambient temperature, 4-*tert*-butylbenzophenone was obtained in a low yield of 11% but this remarkably rose to 52% under reflux conditions, thus implying that the substoichiometric sodium amide is recycling in some way.

To conclude, this study has uncovered a set of alkylzinc-based compounds with unprecedented structures by utilizing a secondary amide equipped with two pyridyl appendages as a structural template-changing co-ligand. Unlike conventional alkylzinc reagents these heteroleptic compounds can directly alkylate (*tert*-butylate) benzophenone in the challenging *para* position. Most intriguingly, substoichiometric amounts of sodium amide [{(TMEDA)Na(dpa)}$_2$] can activate tBu$_2$Zn towards this *tert*-butylation through the inter-

mediacy of the zincate **3**, the structure of which masquerades as a neutral donor-acceptor complex.

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[26] Single-crystal data were measured at 123(2) K on Oxford Diffraction instruments using graphite-monochromated Mo$_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). The structures were refined to convergence on F^2 and against all independent reflections by full-matrix least-squares using the SHELXL-97 program.[27] Compounds **4** and **5** are structurally closely related. Both contain a large number of disordered groups (butyl, THF, and dipyr-idylamide) which required restraints and constraints to be applied to both bond lengths and displacement ellipsoids. Of particular relevance to the structural discussion is that the dipyridylamide ligands are disordered about the crystallographic center of symmetry. Selected parameters are given in the Supporting Information and full details are given in the deposited cif files. CCDC reference numbers 930517 (**2**), 930518 (**3**), 930519 (**4**), and 930520 (**5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Crystal data for **2**: C$_{28}$H$_{34}$N$_6$Zn$_2$; a colorless block gave monoclinic space group $P2_1/c$, $a = 9.4833(3)$, $b = 10.4377(4)$, $c = 14.0888(5)$ Å, $\beta = 105.844(4)°$, $V = 1341.58(8)$ Å^3, $Z = 2$, $R_{\text{calcd}} = 1.449$ Mg m^{-3}, $R1 = 0.0413$ [for 2840 reflections with $I > 2\sigma(I)$], $\omega R2 = 0.1039$ and $S = 1.065$ for 166 parameters and 3451 independent reflections. Crystal data for **3**: C$_{40}$H$_{66}$N$_{10}$Na$_2$Zn; an orange block gave monoclinic space group $P2_1/n$, $a = 11.5137(3)$, $b = 21.6403(4)$, $c = 18.3837(3)$ Å; $\beta = 93.636(2)°$, $V = 4571.26(16)$ Å^3, $Z = 4$, $R_{\text{calcd}} = 1.160$ Mg m^{-3}, $R1 = 0.0388$ [for 8121 reflections with $I > 2\sigma(I)$], $\omega R2 = 0.0864$ and $S = 1.032$ for 492 parameters and 10516 independent reflections. Crystal data for **4**: C$_{50}$H$_{92}$N$_3$NaO$_6$Zn$_2$; an orange block gave triclinic space group $P\bar{1}$, $a = 10.0075(11)$, $b = 11.1283(9)$, $c = 13.3084(15)$ Å; $\alpha = 69.353(9)$, $\beta = 85.491(9)$, $\gamma = 84.723(8)°$; $V = 1379.3(2)$ Å^3, $Z = 1$, $R_{\text{calcd}} = 1.186$ Mg m^{-3}, $R1 = 0.0606$ [for 5614 reflections with $I > 2\sigma(I)$], $\omega R2 = 0.1679$ and $S = 1.057$ for 321 parameters and 6820 independent reflections.

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