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The First Structural Characterization of α-Zincated (Reformatsky) Amides and Phosphine Oxides

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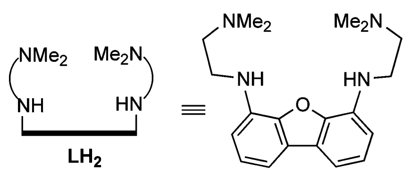
Reformatsky reagents comprise a class of α-functionalized organozincs that are widely used as C-nucleophiles in synthetic organic chemistry.[1] These mildly basic species tolerate most organic functionalities and therefore are well suited for uses involving complex functionalized molecules. There are several different types of Reformatsky reagents. The most extensively studied have been the Reformatsky esters, but related derivatives of amides, phosphonates, imines, and hydrazones are increasingly being used. Reformatsky reagents readily undergo transmetalation reactions with transition-metal salts. Consequently, they are useful intermediates in a variety of Cu- and Pd-mediated coupling reactions.[2] Reformatsky reagents also are frequently used in addition reactions to unsaturated substrates. For example, Reformatsky esters and amides readily add to aldehydes, ketones, and activated alkenes. The more reactive imine derivatives are even capable of adding to unactivated alkenes.[3] In the interest of understanding the reactivity patterns of the various Reformatsky reagents, it is important to develop a good understanding of their solution and solid-phase structures. Currently, this information is only available for Reformatsky esters.[4] The other types of Reformatsky reagents have been alternatively described as C-zincated organometallics and as Zn enolates. To provide insight into this area, we have prepared and fully characterized α-zincated derivatives of *N*,*N*-dimethylacetamide (DMA) and Me_3PO supported by a binucleating bis(amidoamine) ligand. Structural studies of these complexes show that the deprotonated DMA and Me_3PO molecules act as 1,3-bridging ligands between two Zn centers with the formation of Zn−C and Zn−O bonds. This structural motif is similar to that known for Reformatsky esters.

Chart 1



The bis(diamine) LH_2 (Chart 1) is conveniently prepared in multigram quantities by the Cu-catalyzed coupling[5] of 4,6-diiododibenzofuran and $Me_2NCH_2CH_2NH_2$. Analytically pure product was obtained in 51% yield by crystallization from Et_2O at −40 °C. LH_2 is deprotonated by basic organometallics to form isolable bis(amidoamine) derivatives.[6] For example, the reaction of LH_2 with 2 equiv of $ZnPh_2$ in toluene solution at 75 °C formed the dinuclear organozinc derivative LZn_2Ph_2 in 73% isolated yield. The solid-state structure[7,8] of LZn_2Ph_2 is shown in Figure 1. There are two molecules in the asymmetric unit. Both feature a parallelogram-shaped $[Zn_2(\mu\text{-}Ph)_2]^{2+}$ core with two typical Zn−C σ bonds (1.99−2.01 Å) and two weak bridging interactions (2.55−2.64 Å). The two molecules have Zn−Zn distances of 2.7279(6) and 2.7809(6) Å, reflecting modest core structural differences. In contrast to the solid-state structure, the ^1H NMR spectrum of LZn_2Ph_2 (CD_2Cl_2) indicates overall C_{2v} symmetry. Accordingly, the four Me groups of the bis(amidoamine) ligand are equivalent and are observed as a singlet at δ 2.10 ppm. The symmetric solution structure may result from cleavage of the weak Ph bridges and rotation about the dibenzofuran−N bonds. Alternatively, rapid Ph group trans-

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[6] (a) Hlavinka, M. L.; Hagadorn, J. R. *Chem. Commun.* **2003**, 2686−2687. (b) Related Zn derivatives supported by simple chelating amidoamine ligands: Malik, M. A.; O'Brien, P.; Motevalli, M.; Jones, A. C. *Inorg. Chem.* **1997**, *36*, 5076−5081.

[7] Crystal data for LZn_2Ph_2: $C_{32}H_{36}N_4OZn_2$, $P2_1/c$ (No. 14), a = 18.0749(7) Å, b = 10.7323(4) Å, c = 29.823(1) Å, β = 96.151(1)°, V = 5751.9(4) $Å^3$, T = −136 °C, Z = 8, d_{calcd} = 1.440 g cm^{-3}, μ = 1.70 mm^{-1}, 13 693 observed reflections, 711 parameters, R1 = 0.0548 (9091 data), GOF = 1.011. Crystal data for $LZn_2Ph_2(OPMe_3)_2(toluene)_{0.5}$: $C_{41.5}H_{66}N_4O_3P_2Zn_2$, $P\bar{1}$ (No. 2), a = 10.6982(5) Å, b = 13.7628(7) Å, c = 15.2245(7) Å, α = 81.638(2)°, β = 75.099(1)°, γ = 83.287(1)°, V = 2135.8(2) $Å^3$, T = −119 °C, Z = 2, d_{calcd} = 1.340 g cm^{-3}, μ = 1.24 mm^{-1}, 10 173 observed reflections, 442 parameters, R1 = 0.0915 (3936 data), GOF = 0.895. Crystal data for $LZn_2[CH_2P(O)Me_2]_2$: $C_{26}H_{42}N_4O_3P_2Zn_2$, $P2/n$ (No. 13), a = 13.3940(5) Å, b = 10.8162(4) Å, c = 21.5733(9) Å, β = 107.656(1)°, V = 2978.2(2) $Å^3$, T = −119 °C, Z = 4, d_{calcd} = 1.453 g cm^{-3}, μ = 1.75 mm^{-1}, 7113 observed reflections, 335 parameters, R1 = 0.0682 (4284 data), GOF = 1.008. Crystal data for $LZn_2[CH_2C(O)NMe_2]_2$: $C_{28}H_{42}N_6O_3Zn_2$, $P2_1/n$ (No. 14), a = 10.0092(9) Å, b = 12.912(1) Å, c = 22.700(2) Å, β = 98.982(3)°, V = 2897.6(5) $Å^3$, T = −118 °C, Z = 4, d_{calcd} = 1.470 g cm^{-3}, μ = 1.70 mm^{-1}, 6912 observed reflections, 352 parameters, R1 = 0.1198 (2897 data), GOF = 1.056.

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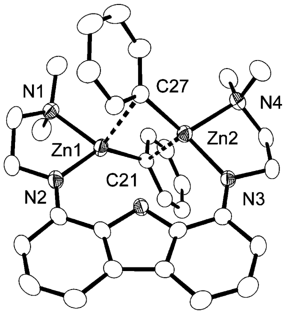
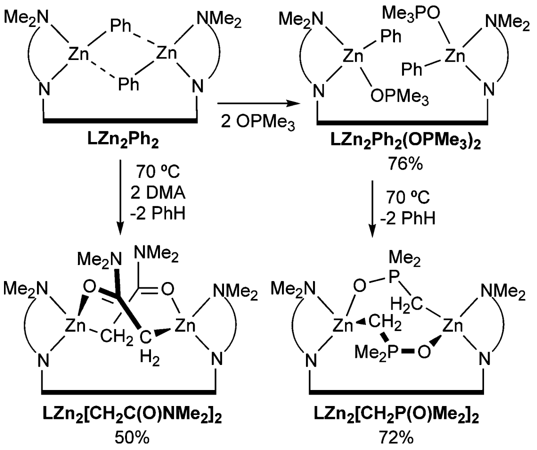


Figure 1. Structure of LZn_2Ph_2 drawn with 50% thermal ellipsoids. One of the two molecules in the asymmetric unit and the H atoms are omitted. Selected bond lengths (Å) and angles (deg): Zn1−N1, 2.149(3); Zn1−N2 1.922(3); Zn1−C21, 2.013(4); Zn1−C27, 2.618(3); Zn2−N3, 1.940(3); Zn2−N4, 2.139(3); Zn2−C27, 2.008(3); Zn2−C21, 2.546(3); Zn1−Zn2, 2.7279(6); N1−Zn1−N2, 85.8(1); N1−Zn1−C21, 115.2(1); N2−Zn1−C21, 136.9(1).

Scheme 1



fer between the Zn centers may occur. However, at −90 °C the ^1H NMR spectrum did not indicate lower symmetry, and so cleavage of the Ph bridges is likely responsible for the symmetric solution structure.

LZn_2Ph_2 coordinates Lewis bases with the cleavage of the Ph bridges. For example, the addition of 2 equiv of Me_3PO to a warm toluene solution of LZn_2Ph_2 formed $LZn_2Ph_2(OPMe_3)_2$ (Scheme 1), which was isolated as colorless crystals in 76% yield after cooling to ambient temperature. In the solid-state structure of $LZn_2Ph_2(OPMe_3)_2$ (see the Supporting Information) each Zn center adopts distorted-trigonal-monopyramidal geometry (∑(basal angles): Zn1, 351°; Zn2, 354°), with the $-NMe_2$ group occupying the apical position. This geometry occurs in $LZn_2Ph_2(OPMe_3)_2$ because the chelating amidoamines have N−Zn−N bite angles that are close to 90°. Also, the two donor groups are of different strengths; the weaker donor prefers the apical position. Heating a toluene solution of $LZn_2Ph_2(OPMe_3)_2$ to 70 °C for 2 days formed $LZn_2[CH_2P(O)Me_2]_2$ in 72% isolated yield. ^1H NMR spectroscopic data, combustion analysis, and single-crystal X-ray diffraction confirm its identity. This product is formed by the formal deprotonation of the Me_3PO ligands by the Zn−Ph groups. Zincation of functionalized organics by organozinc[9] and amidozinc[10] complexes has only been reported for substrates with C−H bonds that have pK_a[11] values below 29.[12] The pK_a of Me_3PO is unknown, but we estimate it to be between 32 and 36.[13] The solid-state structure of $LZn_2[CH_2P(O)Me_2]_2$ was determined by X-ray diffraction. One of the two independent molecules from the asymmetric unit is shown in Figure 2. Due to the great similarity of the two molecules, only one will be discussed. The molecule rests on a crystallographic C_2 axis of symmetry. Each Zn center adopts a distorted-trigonal-pyramidal geometry (∑(basal angles): 353°) with the apical position occupied by the weak 3° amine donor (N1). The deprotonated $[CH_2P(O)Me_2]^-$ ligands bridge the two Zn centers with the formation of Zn−C and Zn−O bonds. The P1−C11 bond length of 1.753(5) Å is ca. 0.04 Å shorter than the other P−Me bonds. Also, the P1−O2 length of 1.521(3) Å is 0.014 Å longer than the related parameter for $LZn_2Ph_2(OPMe_3)_2$. Thus, the anionic charge of $[CH_2P(O)Me_2]^-$ is delocalized.[14]

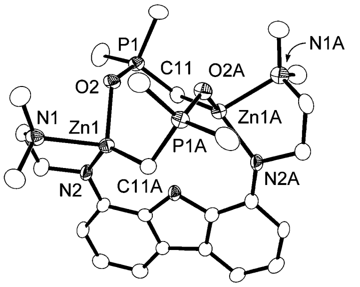


Figure 2. Solid-state structure of $LZn_2[CH_2P(O)Me_2]_2$ drawn with 50% thermal ellipsoids. One of the two molecules in the asymmetric unit and the H atoms are omitted. Selected bond lengths (Å) and angles (deg): Zn1−N1, 2.186(4); Zn1−N2, 1.980(4); Zn1−C11A, 2.011(5); Zn1−O2, 2.021(3); P1−O2, 1.521(3); P1−C11, 1.753(5); O2−Zn1−C11A, 113.8(2); O2−Zn1−N1; 90.8(1); O2−Zn1−N2, 105.7(2); N1−Zn1−N2, 84.0(2); N1−Zn1−C11A, 118.0(2); N2−Zn1−C11A, 133.4(2).

The ^1H NMR spectrum of $LZn_2[CH_2P(O)Me_2]_2$ (in CD_2Cl_2) is consistent with the C_2-symmetric structure observed in the solid state. The diastereotopic methylene ($Zn-CH_2-$) is observed as a pair of upfield resonances at δ 0.80 and 0.03 ppm. Each of these resonances is observed as a "doublet of doublets" due to coupling with ^{31}P ($^2J = 6.0$ Hz) and each other ($^2J = 12.8$ Hz). On the basis of these NMR data, it is very likely that the bridged structure is maintained in CD_2Cl_2 solution. Cleavage of the bridges would likely yield spectra of higher symmetry, as was observed with LZn_2Ph_2.

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(13) Estimation by comparison to related compounds listed in ref 11.

(14) The structure of $[Ph_2SnCl(CH_2P(O)Ph_2)]_2$ also features 1,3-bridging ligands with some delocalization of the anionic charge: Fackler, J. P., Jr.; Garzon, G.; Kresinski, R. A.; Murray, H. H., III; Raptis, R. G. *Polyhedron* **1994**, *13*, 1705−1713.

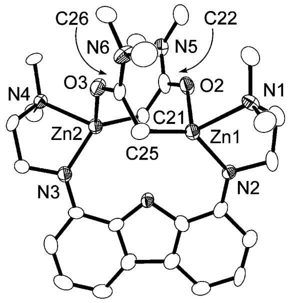
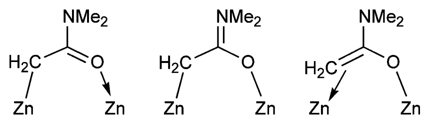


Figure 3. Solid-state structure of $LZn_2[CH_2C(O)NMe_2]_2$ drawn with 50% thermal ellipsoids. H atoms are omitted. Selected bond lengths (Å): Zn1−O2, 2.027(7); Zn1−C25, 2.024(10); Zn2−O3, 2.023(8); Zn2−C21, 2.028(10); O2−C22, 1.27(1); N5−C22, 1.37(1); C21−C22, 1.44(2); O3−C26, 1.29(1); N6−C26, 1.35(1); C25−C26, 1.43(1).

The reactivity of LZn_2Ph_2 toward relatively nonacidic C−H bonds is not limited to Me_3PO. Our preliminary studies indicate that LZn_2Ph_2 will undergo H−Zn exchange with a wide range of functionalized substrates. For instance, heating a C_6H_6 solution of LZn_2Ph_2 with 2 equiv of DMA ($pK_a \cong 35^{15}$) to 70 °C for 2 days afforded $LZn_2[CH_2C(O)NMe_2]_2$ in 50% isolated yield. The solid-state structure of $LZn_2[CH_2C(O)NMe_2]_2$ is shown in Figure 3. The molecule has approximate (noncrystallographic) C_2 symmetry. The pair of distorted-trigonal-pyramidal Zn centers (∑(basal angles): Zn1, 354°; Zn2, 352°) are bridged by the two $[CH_2C(NMe_2)O]^-$ ligands. Metrical parameters indicate that these ligands are extensively π delocalized; this is similar to the case for the deprotonated ester ligand of $\{BrZn[\mu\text{-}CH_2C(O)O^tBu]\}_2$.[4a] This delocalization is indicated in $LZn_2[CH_2C(O)NMe_2]_2$ by the C−O, C−N, and C−C distances of 1.28, 1.36, and 1.44 Å (averaged values), respectively. These bond lengths are consistent with bond orders between 1 and 2. Thus, all of the resonance structures shown in Chart 2 likely contribute to the ground-state electronic structure.

Chart 2



^1H NMR spectroscopic data indicate that $LZn_2[CH_2C(O)NMe_2]_2$ maintains C_2 symmetry when dissolved in CD_2Cl_2. The zincated methylene protons ($Zn-CH_2-$) are diastereotopic and are observed as upfield doublets (^2J = 8 Hz) at δ 2.30 and 1.74 ppm. No vinylic resonances were observed. Collectively these data suggest that the bridging structure observed in the solid state is maintained in solution.

In conclusion, we have reported the formation of α-zincated derivatives of *N*,*N*-dimethylacetamide and trimethylphosphine oxide by H−Zn exchange with the organozinc precursor LZn_2Ph_2. Structural characterization of these α-zincated derivatives reveal that the deprotonated amide and phosphine oxide molecules function as 1,3-bridging ligands between two Zn centers, both in solution and in the solid state.

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Supporting Information Available: Text giving experimental details and characterization data for all new compounds, a figure giving an additional view of $LZn_2Ph_2(OPMe_3)_2(toluene)_{0.5}$, and CIF files giving X-ray crystallographic data for LZn_2Ph_2, $LZn_2Ph_2(OPMe_3)_2$, $LZn_2[CH_2P(O)Me_2]_2$, and $LZn_2[CH_2C(O)NMe_2]_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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[15] The pK_a of $Et_2NC(O)Me$ is 35 (DMSO).[11]