# ORGANOMETALLICS

### Lithium Organozincate Complexes LiRZnX<sub>2</sub>: Common Species in **Organozinc Chemistry**

Julia E. Fleckenstein and Konrad Koszinowski\*

Department Chemie, Ludwig-Maximilians-Universität München, Butenandtstrasse 5-13, 81377 München, Germany

Supporting Information

ABSTRACT: We have used a combination of electrospray ionization (ESI) mass spectrometry, electrical conductivity measurements, and NMR spectroscopy to investigate the effect of LiCl on solutions of organylzinc halides RZnX (R = Bu, Bn, Ph; X = halogen) and dibutylzinc  $Bu_2Zn$  in tetrahydrofuran. In the case of RZnX, the addition of LiX (X = Cl) leads to  $ZnX_2 + 2 Li^+C_8H_{10}^- \xrightarrow{+RX} Zn^* + RX + 2 LiX + 2 C_8H_{10}$ a steep rise of the ESI signal intensities of  $RZnX_2^-$  organozincate anions.



At the same time, the electrical conductivities strongly increase and the NMR absorptions of the  $\alpha$ -H atoms of BuZnX shift upfield. These results consistently point to the formation of lithium organozincates  $Li^+RZnX_2^-$ . As the most common syntheses of RZnX reagents involve stoichiometric amounts of LiX salts, Li<sup>+</sup>RZnX<sub>2</sub><sup>-</sup> complexes are supposedly widespread and may hold the key to understanding the marked effects of LiCl on the reactivity of organozinc halides. In contrast, we find Bu<sub>2</sub>Zn to have a much lower tendency to add LiCl and form ate complexes. This result is in line with the weak effect of LiCl on the reactivity of diorganozinc compounds reported in the literature.

#### **1. INTRODUCTION**

Organozinc halides RZnX (R = organyl, X = Cl, Br, I) and diorganylzinc R<sub>2</sub>Zn are important reagents in modern organic synthesis.<sup>1</sup> Compared to organolithium and organomagnesium compounds, they have the advantage of much improved chemoselectivity and tolerance of functional groups.<sup>2</sup> As organozinc compounds at the same time readily undergo transmetalation, they are ideally suited as reagents for cross-coupling reactions. Indeed, Negishi cross-coupling reactions<sup>3</sup> constitute one of the most important and versatile methods in contemporary organic synthesis.4

A straightforward access to organozinc halides and diorganozinc compounds is given by transmetalation. The reaction of ethereal solutions of ZnX<sub>2</sub> with one or two equivalents of organolithium reagents produces RZnX and R2Zn along with one or two equivalents of LiX, eqs 1 and 2, respectively. Similarly, organomagnesium compounds may also be used for transmetalation.

$$ZnX_2 + RLi \rightarrow RZnX + LiX \tag{1}$$

$$ZnX_2 + 2RLi \rightarrow R_2Zn + 2LiX$$
(2)

Alternatively, organozinc halides can be generated by the insertion of Zn into organic halides RX.5 Because this reaction is relatively inefficient for commercially available Zn dust, several different ways for activating Zn have been developed. $^{6-10}$  Among these, for a long time arguably the most important was Rieke's method, which produces finely dispersed and highly active Zn\* by the reduction of  $ZnX_2$  by Li in the presence of catalytic amounts of naphthalene, eq 3.<sup>11</sup> Unless the active  $Zn^*$  metal is carefully washed, the finally obtained ethereal solution of RZnX contains substantial amounts of LiX. More recently, Knochel and

co-workers have demonstrated that stoichiometric amounts of LiCl greatly accelerate the insertion of Zn into organic halides, eq 4, thus providing a very convenient and practical access to organozinc halides.

$$ZnX_2 + 2Li \xrightarrow{[C_{10}H_8]} Zn^* + 2LiX \xrightarrow{+RX} RZnX + 2LiX$$
(3)

$$Zn + RX \xrightarrow{\text{LiCl}} RZnX + \text{LiCl}$$
 (4)

Although the most common syntheses of organozinc halides thus all produce these reagents in the presence of LiX, the possible role of the latter has been largely ignored<sup>13</sup> until Knochel's work on LiCl-promoted Zn insertion reactions has put them into the spotlight. Our group has recently used electrospray ionization (ESI) mass spectrometry to characterize organozinc intermediates produced by transmetalation<sup>14a</sup> and by LiCl-mediated Zn insertion reactions.<sup>14b</sup> For both reaction types, these qualitative studies pointed to the formation of organozincate anions RZnX<sub>2</sub><sup>-</sup> and R<sub>2</sub>ZnX<sup>-</sup> and related polynuclear complexes in the LiX-containing tetrahydrofuran (THF) solutions. In line with these findings, theoretical calculations by Liu et al. predicted the PhZnBr system to give a stable Li<sup>+</sup>PhZnBrCl<sup>-</sup> zincate complex in the presence of LiCl.<sup>16</sup> These workers also showed that the interaction of Zn/PhBr with LiCl lowered the energy of the transition structure of the Zn insertion, thus providing a rationale for the observed rate acceleration.<sup>15</sup> Growing evidence moreover suggests that the presence of LiX

Received: July 14, 2011 Published: August 25, 2011 additives also changes the reactivity of the in situ formed organozinc halides and enhances their nucleophilicity.<sup>16-21</sup> Organ and co-workers screened numerous simple salt additives and found LiCl and LiBr to be particularly effective in accelerating Negishi cross-coupling reactions in THF/dimethylimidazolidinone (DMI) mixtures.<sup>22</sup> On the basis of titration experiments, these authors proposed that here the active transmetalating agent corresponds to higher-order zincates  $\operatorname{Li}_{n}\operatorname{RZnBr_{3}}^{(2-n)-}$ , R = Bu.<sup>22</sup> As we learned while completing the present work, Organ and collaborators very recently also employed ESI mass spectrometry and NMR spectroscopy to support their hypothesis of higher-order zincates being present in THF/DMI mixtures.<sup>23</sup> Note that an analogous organozincate dianion is known from the structurally characterized salt [PPh4+]2[EtZnBr32-].24 Compared to the strong influence of lithium halides on organozinc halides, their effect on the reactivity of diorganylzinc compounds apparently is much smaller. As Kneisel, Dochnahl, and Knochel reported, LiCl does not activate 'Pr<sub>2</sub>Zn to undergo iodine-zinc exchange with methyl 4-iodobenzoate in diethyl ether/N-methyl-2-pyrrolidinone mixtures.<sup>25</sup> This reaction occurs efficiently in the presence of Li(acac) and Cs(acac), however. In these cases, the formation of  $\text{Li}^+/\text{Cs}^+(\text{CH}_3\text{OOC-C}_6\text{H}_4)\text{Zn}^i\text{Pr}(\text{acac})^-$  zincate complexes was surmised.<sup>25</sup>

To understand the effects of LiX salts on the reactivity of organozinc halides and diorganozinc compounds, more information on the interaction of these additives with organozinc species is needed. We have shown previously that ESI mass spectrometry is a useful method to obtain such qualitative information at the molecular level,<sup>14</sup> and we employ this technique for further experiments in the present study. However, ESI mass spectrometry is considered less suitable for quantitative analysis and thus offers only limited insight into the association and dissociation equilibria operative in solution, which are of key importance in the given context. Moreover, there is evidence that ESI mass spectrometry is incapable of detecting free zincate dianions.<sup>26</sup> To check for the presence of such dianions in LiX/RZnX and LiX/ R<sub>2</sub>Zn solutions and to probe the association/dissociation equilibria in these systems, we therefore turn to electrical conductivity measurements and NMR spectroscopy. These well-established methods provide quantitative information on speciation in solution and thus lend themselves to a combination with ESI mass spectrometry.

Throughout the present work, we have made special efforts to ensure well-defined reaction conditions and to control the concentration of LiX additives carefully. For the preparation of LiXfree RZnX reagents, we therefore have not relied on transmetalation reactions because the precipitation of the LiX (or MgX<sub>2</sub>) byproducts may possibly be incomplete even in apolar solvents. Instead, we have synthesized salt-free solutions of RZnX by Zn insertion into RX (in the absence of LiX) or by mixing R<sub>2</sub>Zn with ZnX<sub>2</sub>. Unlike Organ and co-workers,<sup>23</sup> we deliberately chose to sample solutions in THF without the addition of cosolvents, such as DMI, to keep the system as simple as possible. Note that solutions of RZnX·LiX and R<sub>2</sub>Zn·LiX in pure THF, i.e., without adding more polar cosolvents, show excellent reactivity in many synthetically valuable transformations, including Negishi crosscoupling reactions.<sup>2,3,12,21,27</sup>

#### 2. EXPERIMENTAL SECTION

2.1. General Procedures. Standard Schlenk techniques were applied in all cases to exclude moisture and oxygen. Gas-tight syringes

were used to transfer exact quantities of solutions under the exclusion of moisture and oxygen. ZnX<sub>2</sub> and LiX (X = Cl, Br, I) were rigorously dried by prolonged heating under vacuum. THF and diethyl ether were freshly distilled from sodium benzophenone ketyl under argon. THF-D<sub>8</sub> (Euriso-top, 99.50% D) was distilled and stored over molecular sieves (4 Å) under argon at 5 °C in the dark.

2.2. Synthesis of Bu<sub>2</sub>Zn (ref 28). A flame-dried flask under argon atmosphere was charged with a solution of BuLi in hexane ( $c \approx 2.4$  M) and the solvent was removed at 0 °C under reduced pressure. To the yellow residue was slowly added a solution of  $ZnCl_2$  in diethyl ether (c =1.00 M, 0.50 equiv) at -78 °C before the reaction mixture was allowed to warm to room temperature. After stirring for 15 h in the dark, the resulting suspension was subjected to centrifugation (1 h, 2000 rpm). The clear supernatant solution was separated and freed from diethyl ether under reduced pressure. Further purification could be achieved by distillation under high vacuum to give Bu<sub>2</sub>Zn as a colorless oil (65% yield), whose <sup>1</sup>H NMR spectroscopic properties (<sup>1</sup>H NMR (200 MHz, 296 K, C<sub>6</sub>D<sub>6</sub>)  $\delta$  0.35 (t, J = 7.7 Hz, 4H, CH<sub>2</sub>Zn), 1.08 (t, J = 7.2 Hz, 6H, CH<sub>3</sub>), 1.45–1.63 (m, 4H CH<sub>3</sub>CH<sub>2</sub>), 1.78–1.93 (m, 4H CH<sub>2</sub>CH<sub>2</sub>Zn)) agreed with those reported in the literature reasonably well.<sup>29</sup> Solutions of Bu<sub>2</sub>Zn in THF or THF-D $_8$  (c pprox 1.3 M, exact determination by iodiometric titration),<sup>30</sup> respectively, were stored under argon in the dark and found stable to degradation for >2 weeks.

**2.3.** Synthesis of Ph<sub>2</sub>Zn. A flamed-dried flask was charged with PhLi in Bu<sub>2</sub>O ( $c \approx 1.9$  M) under argon. A solution of ZnCl<sub>2</sub> in diethyl ether (c = 1.00 M, 0.50 equiv) was slowly added at -50 °C. After stirring for 3 h in the dark, the resulting suspension was subjected to centrifugation (0.5 h, 2000 rpm). The light yellow colored solution was separated, and the solvent was removed under reduced pressure at 50 °C. Sublimation (reduced pressure, 180 °C) gave Ph<sub>2</sub>Zn as a colorless powder (55% yield), whose <sup>1</sup>H NMR spectroscopic properties (<sup>1</sup>H NMR (200 MHz, 296 K, THF-D<sub>8</sub>)  $\delta$  6.95–7.10 (m, 6H, ArZn), 7.66–7.71 (m, 4H, ZnCCH)) agreed with those reported in the literature.<sup>31</sup>

**2.4. Synthesis of BuZnX and PhZnBr.** Combination of measured quantities of  $Bu_2Zn$  solutions with 1.00 equiv of  $ZnX_2$  (X = Cl, Br, I) in THF and stirring for 15 min produced solutions of BuZnX. Solutions of PhZnBr were prepared in an analogous way; in this case, stirring was continued for 24 h.

2.5. Synthesis of BuZnI and BnZnBr (ref 6b). A flask charged with Zn powder (1.4 equiv, 7.0 mmol) was flame-dried under high vacuum and allowed to cool under an argon atmosphere. The procedure was repeated twice, and THF or THF-D<sub>8</sub> (10 mL), respectively, was added. The zinc was activated by the addition of 1,2-dibromoethane (0.020 mL) followed by a short boiling-up of the suspension, and of chlorotrimethylsilane (0.020 mL), again followed by a short boiling-up. 1-Iodobutane or benzyl bromide (1.0 equiv, 5 mmol), respectively, was added, and the suspension was stirred overnight at room temperature. The remaining zinc powder was allowed to settle down, and the exact concentration of the supernatant solution of the organozinc reagent was determined by iodometric titration (yield: 90  $\pm$  10%).<sup>30</sup> Note that the thus produced organozinc reagents may contain small amounts of extra halide ions originating from the 1,2-dibromoethane and chlorotrimethylsilane additives (on the basis of the employed reagent quantities, maximum extra bromide and chloride contents of 0.09 and 0.03 equiv, respectively, can be calculated). These extra halide ions presumably form ZnX<sub>2</sub> salts, which are supposed to have only small effects on organozinc halides other than slightly reducing their stability.<sup>32</sup>

**2.6.** Sample Preparation. LiCl-free sample solutions of RZnX and Bu<sub>2</sub>Zn were prepared by diluting organylzinc reagents with THF to the desired concentration.  $RZnX/(LiCl)_n$  sample solutions were produced by dilution of the corresponding  $RZnX/(LiCl)_n$  reagents; the latter were generated as described above, but with *n* equivalents of LiCl added. Bu<sub>2</sub>Zn/(LiCl)<sub>n</sub> sample solutions were prepared by adding *n* equivalents of LiCl and extra THF to Bu<sub>2</sub>Zn.

**2.7. ESI Mass Spectrometry.** Solutions of  $BuZnI/(LiCl)_n$  (n = 0, 1, and 2, respectively, c = 5-15 mM) in THF were analyzed with a TSQ 7000 instrument described in detail previously.<sup>14a</sup> For all of the other ESI mass spectrometric experiments, an HCT quadrupole ion trap (Bruker Daltonik) was employed. Sample solutions ( $c \approx 5 \text{ mM}$ ) were administered at flow rates of 1 mL h<sup>-1</sup> into the instrument's ESI source, which was operated with  $N_2$  as sheath gas (0.7 bar backing pressure) and drying gas (5 L min<sup>-1</sup>) at an ESI voltage of 3 kV. To avoid unwanted decomposition reactions during the ESI process, we applied mild conditions very similar to those reported previously (60 °C drying gas temperature and low potential differences along the path of the ions).<sup>33</sup> The helium-filled quadrupole ion trap (estimated pressure  $p(\text{He}) \approx 2$ mTorr) was operated at trap drive values of 20-35. For the gas-phase fragmentation experiments, the mass-selected ions (typical isolation widths of 3-4 amu) were subjected to excitation voltages with amplitudes of  $V_{\text{exc}}$  and allowed to collide with the helium gas. Only fragment ions whose m/z ratio is larger than 27% of that of their parent ion can be detected efficiently in the ion trap.

Absolute ESI signal intensities are typically rather unstable and poorly reproducible, and so we only consider *relative* signal intensities in the present titration experiments. To this end, we have added to the sampled solutions of organozinc compounds small amounts of NaBPh<sub>4</sub> ( $c = 20 \mu M$ ) as internal standard and normalize the anion ESI signal intensities to that of BPh<sub>4</sub><sup>-</sup>. Because the concentration of NaBPh<sub>4</sub> is lower than that of the organozinc species by 2 orders of magnitude, we can exclude interferences with the dissociation equilibria of the latter. Note, however, that the addition of LiCl is likely to influence the concentration of free BPh<sub>4</sub><sup>-</sup> ions in a not easily predictable manner. While this problem somewhat complicates the comparison of signal intensities within a given titration experiment (same organozinc compound with varying LiCl concentrations), it does not affect the comparison between different systems (different organozinc compounds with the same LiCl concentration).

2.8. Conductivity Measurements. Electrical conductivity measurements were performed with a CDM230 instrument (Radiometer Analytical) and a standard platinum-electrode cell (cell constant  $\kappa_{cell}$  = 1 cm<sup>-1</sup>) or a SevenMulti instrument (Mettler Toledo) and a stainless steel electrode cell (InLab741, Mettler Toledo,  $\kappa_{cell} = 0.1 \text{ cm}^{-1}$ ). Both instruments were calibrated against 0.1 M solutions of aqueous KCl. In a first set of experiments, the specific conductivities of solutions of BuZnI in THF containing variable amounts of LiCl were measured. Performing these experiments by titration of a solution of BuZnI with a solution of LiCl and monitoring the increase in conductivity proved impractical because of the occurrence of hydrolysis reactions, despite the use of flame-dried glassware and careful observation of Schlenk techniques (hydrolysis of >25% of the original BuZnI as determined by iodometric titration of the sample solution). Instead, sample solutions of preformed  $BuZnX/(LiCl)_n$  (X = Cl, Br, I; n = 0, 0.50, 1.00, and 2.00, respectively, <math>c =0.157 M) in THF were analyzed (one data point per sample solution), which minimized the transfer of solutions via gastight syringes and reduced the extent of hydrolysis (as determined by iodometric titration for each sample solution).<sup>30</sup> The same method was also used for measurements of BnZnBr, PhZnBr, Bu<sub>2</sub>Zn, ZnCl<sub>2</sub>, and ZnBr<sub>2</sub> solutions containing various amounts of LiCl. In this way, we could reduce the extent of hydrolysis to <10% for the BuZnI and Bu<sub>2</sub>Zn reagents and <5% for the other organozinc samples.

In a second set of experiments, the specific conductivities of BuZnI/ LiCl solutions in THF were measured at different concentrations. These experiments were performed by adding portions of BuZnI/LiCl stock solutions to pure THF and monitoring the increase in conductivity. Because for these measurements the occurrence of hydrolysis reactions could not be rigorously excluded, additional experiments analyzed solutions of BuZnI/LiCl at fixed concentrations of c = 5.2, 9.6, 22, 39, and 76 mM, respectively (one data point per sample solution). For the sample solutions with concentrations c > 5.2 mM, iodometric titration<sup>30</sup> showed that <8% of the BuZnI was hydrolyzed, whereas no reliable determination was possible for the lowest concentration. Control experiments also probed solutions of pure LiX in THF. All conductometric measurements were performed at 258.15  $\pm$  0.10 K in order to slow down interfering hydrolysis reactions.<sup>34</sup>

**2.9. NMR Spectroscopy.** Defined quantities of BuZnX (X = Cl, Br, I) or Bu<sub>2</sub>Zn, respectively, and LiCl in THF-D<sub>8</sub> were added through rubber caps into flame-dried NMR tubes filled with argon. Room-temperature <sup>1</sup>H NMR spectra were recorded with a 200 MHz Varian Mercury and lowtemperature <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra with a 400 MHz Varian VNMRS instrument. The <sup>1</sup>H and <sup>13</sup>C chemical shifts are given relative to the signals of THF-D<sub>8</sub> ( $\delta$  1.73 and 25.5 ppm, respectively). To determine the exact concentration of intact BuZnX in the probed samples, the amount of BuH formed by hydrolysis (due to residual traces of moisture) was derived from the ratio of the integrated <sup>1</sup>H signals. Only <sup>1</sup>H NMR experiments with <25% hydrolysis (with respect to the initial concentration of the butylzinc reagent) were considered for further analysis, although the <sup>1</sup>H chemical shifts of samples with higher percentages of hydrolysis did not show significant deviations (at similar LiCl concentrations). <sup>7</sup>Li NMR spectra of BuZnCl/(LiCl) in THF-D<sub>8</sub> and of a control sample of pure LiCl in THF-D $_8$  were recorded with a 400-MHz JEOL EX-400 instrument at room temperature.

#### 3. RESULTS AND DISCUSSION

**3.1. ESI Mass Spectrometry.** *RZnX/(LiCl)<sub>n</sub>*. In the absence of LiCl, solutions of BuZnI in THF afford only very small amounts of butylzincate anions upon negative-ion mode ESI (Figure 1a). Similar behavior is observed for BnZnBr (Figure S1) and PhZnBr (Figure S2). These findings indicate that spontaneous ionic disproportionation of RZnX in pure THF is not favorable.<sup>35</sup> In the case of BuZnI, the presence of the purely inorganic ZnI<sub>3</sub><sup>-</sup> anion furthermore points to the occurrence of hydrolysis reactions. Such hydrolysis reactions cannot be completely avoided when introducing highly diluted solutions of moisture-sensitive organometallics into the ESI source of the mass spectrometer. Upon addition of one equivalent of LiCl, the butylzincate anion  $BuZnI_2^{-}$  appears and further increases in intensity when a second equivalent of LiCl is added. Similarly, the presence of LiCl also results in increased signal intensities of organylzincate anions for BnZnBr and PhZnBr; for the latter, the observed increase is rather small, however. For solutions of BuZnBr in DMI, Organ and collaborators also found higher ESI signal intensities of the butylzincate anion BuZnBr<sub>2</sub><sup>-</sup> upon the addition of LiBr.<sup>23</sup>

The experiments show that the formation of organylzincate anions directly correlates with the presence of LiCl. Thus, they are in accordance with our previous assumption that the LiCl adducts of organylzinc halides correspond to  $\text{Li}^+\text{RZnX}_2^-$  complexes, which undergo heterolytic dissociation to a measurable extent (Scheme 1). In line with this reasoning, positive-ion mode ESI of THF solutions of RZnX·LiCl affords virtually exclusively solvated Li(THF)<sub>n</sub><sup>+</sup> ions, n = 2-4.<sup>14a</sup>

The addition of LiCl not only leads to the formation of zincate complexes but presumably also gives rise to halide exchange reactions. Although the addition of two equivalents of LiCl results in a 100% excess of Cl<sup>-</sup> compared to Br<sup>-</sup> or I<sup>-</sup> anions in the overall solution, respectively, the bromine- and iodine-rich complexes still predominate in the ESI mass spectra. This predominance is particularly pronounced in the case of the BuZnI/(LiCl)<sub>2</sub> system, for which the signal intensity of BuZnI<sub>2</sub><sup>-</sup> exceeds those of BuZnICl<sup>-</sup> and BuZnCl<sub>2</sub><sup>-</sup> (m/z = 191/193/195, off-scale in Figure 1a) by factors of 5 and 50, respectively. A



**Figure 1.** Negative-ion mode ESI mass spectra of 5 mM solutions of (a) BuZnI/(LiCl)<sub>n</sub> in THF (n = 0-2) measured with the TSQ 7000 instrument and (b) Bu<sub>2</sub>Zn/(LiCl)<sub>n</sub> in THF (n = 0-2) measured with the HCT ion trap. The signal intensities are normalized to BPh<sub>4</sub><sup>-</sup>, whose sodium salt is added as an internal standard ( $c = 20 \ \mu$ M).

## Scheme 1. Formation and Heterolytic Dissociation of Li<sup>+</sup>RZnX<sub>2</sub><sup>-</sup> Complexes

$$RZnX + LiX \stackrel{K_{ass}}{\longleftrightarrow} Li^{+}RZnX_{2}^{-} \stackrel{K_{diss}}{\longleftrightarrow} Li^{+}(solv) + RZnX_{2}^{-}$$

possible reason for these large differences might be deviating dissociation constants of the corresponding  ${\rm Li}^+{\rm RZnX_2}^-$  complexes (see below).<sup>14b</sup>

Besides binding to Li<sup>+</sup>, the zincate anions can also attach to neutral RZnX, thus forming higher aggregates. Such higher aggregates of the general formula  $R_n Zn_n X_{n+1}$ , n = 2 and 3, are observed for all three systems  $BuZnI/(LiCl)_n$ ,  $BnZnBr/(LiCl)_n$ and  $PhZnBr/(LiCl)_n$ . The identities of these polynuclear anions are confirmed by gas-phase fragmentations of the mass-selected ions (Figures S3-S14 for the most abundant species; also compare ref 14). While the relative signal intensities of the larger aggregates are rather low in the case of  $BuZnI/(LiCl)_{w}$  they are higher for  $BnZnBr/(LiCl)_n$  and  $PhZnBr/(LiCl)_n$ . The present experiments alone cannot clearly distinguish whether these different tendencies toward aggregation are caused by the organyl or the halide substituents. Previous studies comparing BuZnI/LiCl and BuZnCl/LiCl as well as BnZnBr/LiCl and BnZnCl/LiCl, however, suggest that the halide has the bigger effect on the aggregation behavior.<sup>14</sup>

 $Bu_2Zn/(LiCl)_n$ . Without added LiCl, no zincate complexes are detected for solutions of  $Bu_2Zn$  in THF (Figure 1b), indicating that, like in the case of BuZnI, spontaneous ionic disproportionation does not occur to a significant extent. In the presence of LiCl, the  $Bu_2ZnCl^-$  anion appears but has a much lower normalized

signal intensity than its BuZnI<sub>2</sub><sup>-</sup>/BuZnICl<sup>-</sup> analogues observed for the BuZnI/(LiCl), system. This finding may be taken as a first indication that diorganylzinc compounds R<sub>2</sub>Zn have lower tendencies to add halide anions and form ate complexes than the corresponding organylzinc halides RZnX. Another difference between  $Bu_2Zn/(LiCl)_n$  and  $BuZnI/(LiCl)_n$  refers to their aggregation tendencies. Whereas several polynuclear anions are detected for the latter (although in relatively low signal intensities), no analogous aggregates are visible for the former. This observation fully agrees with our previous experiments on Bu<sub>2</sub>Zn/LiCl, which was produced by transmetalation of ZnCl with two equivalents of BuLi,<sup>14a</sup> and shows that the obtained reagent is the same, irrespective of the way it is prepared. In our previous study, we reasoned that a minimum number of halide substituents is needed for stabilizing polynuclear complexes by adopting bridging binding modes between different zinc centers.<sup>14b</sup> In the meantime, Clyburne and co-workers have reported the crystal structure of  $(Ph_4P^+)_2Et(Cl)Zn(\mu-Cl)_2Zn$ - $(Cl)Et^{2-}$  and thus provided direct evidence for the inferred bridging binding geometry in polynuclear zincates.<sup>24</sup>

 $ZnX_2/(LiCl)_n$ . For comparison, we also briefly consider the purely inorganic systems  $ZnCl_2/(LiCl)_n$  and  $ZnBr_2/(LiCl)_n$  in THF. In the absence of LiCl, we observe only little mononuclear zincates  $ZnCl_3^-$  and  $ZnBr_3^-$ , but abundant polynuclear complexes,  $Zn_nCl_{2n+1}^-$ , n = 2-5, and  $Zn_nBr_{2n+1}^-$ , n = 2 and 3 (Figures S15 and S16). This predominance of higher aggregation states once more points to the effectiveness of chloride and bromide in bridging multiple zinc centers. Upon the addition of LiCl, the size distributions of the zincates strongly shift to smaller aggregates, with the mononuclear species becoming more prominent. Here, the added chloride ions apparently help in breaking up the higher aggregates.<sup>36</sup> Therefore, it is somewhat surprising that with added LiCl the overall ESI signal intensities of the zincate ions seem to decrease, thus being in marked contrast to the behavior observed for RZnX/(LiCl)<sub>n</sub> and Bu<sub>2</sub>ZnCl/(LiCl)<sub>n</sub>.

Zincate Dianions. As mentioned above, zinc(+II) compounds may form not only monoanionic, tricoordinated ate complexes, but also dianionic, tetracoordinated zincates. In none of the present experiments did we observe such dianionic species. This result does not exclude the presence of dianionic zincates in solution, however. Estager et al. demonstrated that ESI mass spectrometry does not detect  $Zn_n Cl_{2n+2}^{2-}$  anions present in ionic liquids.<sup>26</sup> This incapability is not surprising, as small dianions are prone to undergo Coulomb fission in the gas phase. While we therefore cannot rely on ESI mass spectrometry for probing free zincate dianions, we should still be able to use this method for detecting the corresponding Li<sup>+</sup>-paired complexes. We indeed observe these species, such as  $LiZn_2X_6^-$  and  $LiPh_2Zn_2X_4^-$  (X = Cl and Br), in some cases (Figures S2, S13, S15, and S16). Similarly, Organ and collaborators found related LiBuZnBr<sub>3</sub><sup>-</sup> and LiZnBr<sub>4</sub><sup>-</sup> complexes in THF/DMI solutions of BuZnBr/(LiBr)<sub>2</sub>.<sup>23</sup> These results suggest that  $(Li^+)_2ZnX_4^{2-}$ ,  $(Li^+)_2PhZnX_3^{2-}$ ,  $(Li^+)_2BuZnX_3^{2-}$ , and analogous higher aggregates can form as intermediates in THF or THF/DMI solutions. However, the rather low signal intensities of Li<sup>+</sup>-paired dianions indicate that tetracoordinated zincates presumably constitute only relatively minor components of the equilibria operative under the given conditions.

**3.2. Conductivity Measurements.**  $RZnX/(LiCl)_n$ . Measurements of the electrical conductivity ideally complement ESI mass spectrometric experiments because both methods probe the charged components present in solution. Solutions of pure BuZnX (X = Cl, Br, I) as well as BnZnBr and PhZnBr in THF



**Figure 2.** Specific conductivities of BuZnX/(LiCl)<sub>n</sub> (X = Cl, Br, I,  $c \approx 157 \text{ mM}$ , T = 258 K) in THF as functions of c(LiX), X = Cl. In the absence of LiCl, specific conductivities  $\kappa < 7 \,\mu\text{S cm}^{-1}$  are measured. The open symbols represent the specific conductivities of pure LiX shown for comparison.

at 258 K show only very low specific conductivities (Figures 2 and 3, respectively). This finding is in full accordance with the low ion yields observed in the ESI mass spectrometric experiments of solutions of these reagents (see above). Note that for the case of BuZnI similarly low specific conductivities are measured irrespective of how it is prepared (by mixing Bu<sub>2</sub>Zn with ZnI<sub>2</sub> or by Zn insertion into BuI). In the presence of LiCl, the specific conductivities of the RZnX reagents drastically increase. This increase again fully matches the behavior observed by ESI mass spectrometry and the inferred formation of lithium butylzincate complexes, which undergo partial heterolytic dissociation according to Scheme 1. Control experiments, in agreement with the literature,<sup>37</sup> show that solutions of pure LiCl and LiBr in THF display only very low specific conductivities; the conductivity of LiI is higher but still well below that of BuZnI·LiCl (Figure 2). Thus, the steep increase in conductivity observed upon addition of LiCl apparently indeed reflects the formation of lithium organylzincate complexes.

While the individual systems  $RZnX/(LiCl)_n$ , X = Br and I, all exhibit very similar trends, their  $BuZnCl/(LiCl)_n$  counterpart shows somewhat lower specific conductivities. As already inferred from the ESI mass spectrometric experiments, the Li<sup>+</sup>BuZnCl<sub>2</sub><sup>-</sup> complex appears to have a lower dissociation constant. Presumably, the hard Li<sup>+</sup> cation interacts more strongly with the relatively small Cl atoms in the BuZnCl<sub>2</sub><sup>-</sup> anion than with the larger Br or I atoms of the other zincate anions.<sup>14b,38</sup> The  $BuZnCl/(LiCl)_n$  system is also special in that here no complicating halide exchange reactions can occur. Thus, it offers itself to a more detailed analysis. The measured specific conductivity clearly levels off after the addition of one equivalent of LiCl, indicating that almost all of the BuZnCl is transformed to Li<sup>+</sup>BuZnCl<sub>2</sub><sup>-</sup>. This finding suggests an appreciable association constant  $K_{ass}$ . The fact that the conductivity hardly further increases when a second equivalent of LiCl is added moreover contradicts the formation of significant amounts of BuZnCl<sub>3</sub><sup>2-</sup> dianions. For fitting the experimental data, the dependence of the conductivity on the concentration of the electrolyte must be known. This relation is straightforward if only simple dissociation



**Figure 3.** Specific conductivities of  $\text{RZnBr}/(\text{LiCl})_n$  (R = Bn, Ph,  $c \approx 157 \text{ mM}$ , T = 258 K) in THF as functions of c(LiCl). In the absence of LiCl, specific conductivities  $\kappa < 14 \,\mu\text{S cm}^{-1}$  are measured. For comparison, the specific conductivity of  $\text{BuZnBr}/(\text{LiCl})_n$  in THF is also shown.



Figure 4. Concentration dependence of the molar conductivity of BuZnI·LiCl in THF (T = 258 K). The open black symbols represent data points obtained from titration experiments, for which the extent of hydrolysis could not be rigorously controlled. The filled red symbols represent data points obtained from measurements at fixed concentrations, for which hydrolysis could be almost completely excluded (see Experimental Section for details). Activity coefficients are neglected.

processes according to Scheme 1 occur, but becomes much more complex if the ions form higher aggregates. In the case of the organozincates, both the ESI mass spectrometric and the conductometric experiments (see below) point to the occurrence of such processes to a certain, yet unknown extent. A reliable quantitative analysis of the measured data for the BuZnCl/  $(LiCl)_n$  system thus seems impossible.

For the Li<sup>+</sup>BuZnICl<sup>-</sup> system, we also studied the concentration dependence of the *molar* conductivity  $\Lambda$ . Starting at very low concentrations, the molar conductivity first declines with increasing concentration because ion pairing becomes more important (Figure 4). Interestingly, the molar conductivity then passes through a minimum and increases at higher concentrations.



**Figure 5.** Specific conductivities of  $\text{Bu}_2\text{Zn}/(\text{LiCl})_n$  and  $\text{ZnCl}_2/(\text{LiCl})_n$  ( $c \approx 157 \text{ mM}$ , T = 258 K) in THF as functions of c(LiCl). For comparison, the specific conductivity of  $\text{Bu}\text{ZnCl}/(\text{LiCl})_n$  in THF is also shown.

Two factors may cause this increase: (i) At higher concentration, the law of mass action favors the association of BuZnI and LiCl to produce the active electrolyte Li<sup>+</sup>BuZnICl<sup>-</sup>. (ii) With increasing concentration, the BuZnICl<sup>-</sup> ions can form so-called triple ions, i.e., larger ionic aggregates, which then contribute to the molar conductivity.<sup>39</sup>

To separate these two factors, we consider an effective molar conductivity  $\Lambda_{eff}$  based on the concentration of the active electrolyte Li<sup>+</sup>BuZnICl<sup>-</sup>, eq 5.

$$\Lambda_{\rm eff} = \kappa / [\rm Li^+ BuZnICl^-] \tag{5}$$

For calculating the actual concentration of Li<sup>+</sup>BuZnICl<sup>-</sup>, we approximate its formation constant  $K_{ass}$  by that of Li<sup>+</sup>BuZnCl<sub>2</sub><sup>-</sup>, for which we derive a value of  $K_{ass}$ (Li<sup>+</sup>BuZnCl<sub>2</sub><sup>-</sup>)  $\approx 100$  L mol<sup>-1</sup> from our <sup>1</sup>H NMR spectroscopic studies (see below). The resulting  $\Lambda_{eff}$  curve still shows a minimum, which is very shallow, though (Figure S17). We interpret this minimum as evidence for the formation of zincate ions in higher aggregation states. Independent support for the presence of such complexes is provided by the ESI mass spectrometric experiments, which detect Bu<sub>3</sub>Zn<sub>3</sub>I<sub>n</sub>Cl<sub>4-n</sub><sup>-</sup> complexes, n = 1 and 2 (see above). These species can form by the successive reaction of BuZnIX<sup>-</sup> with two molecules of BuZnCl, eq 6 with X = Cl and I.

$$BuZnIX^{-} + 2BuZnCl \rightleftharpoons Bu_2Zn_2IXCl^{-} + BuZnCl \rightleftharpoons Bu_3Zn_3IXCl_2^{-}$$
(6)

 $Bu_2Zn/(LiCl)_n$ . Solutions of  $Bu_2Zn$  in THF exhibit very low specific conductivities at 258 K (Figure 5). Upon the addition of LiCl, the conductivity increases, but much less than for the BuZnCl system. Three different factors may account for this deviating behavior: (i) The limiting molar conductivity of  $Bu_2ZnCl^-$  might be lower than that of  $BuZnCl_2^-$ . However, it seems very unlikely that this difference could be sufficiently large to cause the observed effect. (ii) The dissociation constant of  $Li^+Bu_2ZnCl^-$  may be lower than that of  $Li^+BuZnCl_2^-$ . Given that the ESI mass spectrometric experiments point to a reduced aggregation tendency of the  $Bu_2ZnCl^-$  ion (see above), this rationalization does not seem plausible either. (iii) The equilibrium constant for the association of  $Bu_2Zn$  and LiCl could be

Table 1.	H NMR Shifts of the $\alpha$ -H Atoms of Butylzinc
<b>Reagents</b>	in THF at 296 K

butylzinc species	$\delta$ ( $lpha$ -H) in ppm
BuZnCl	0.21
BuZnBr	0.23
BuZnI <sup>a</sup>	0.24
BuZnI <sup>b</sup>	0.24
Bu <sub>2</sub> Zn	0.14
$Li^{+}BuZnCl_{2}^{-}$	$0.08 \pm 0.01^c$
<sup><i>a</i></sup> Prepared from Bu <sub>2</sub> Zn/ZnI <sub>2</sub> . <sup><i>b</i></sup> Prep from fit.	ared by Zn insertion. <sup>c</sup> Derived

lower than that for the association of BuZnCl and LiCl. In line with this explanation, the specific conductivity of the  $Bu_2Zn/(LiCl)_n$  system does not level off after the addition of the first equivalent of LiCl but instead continues to rise almost linearly (Figure S18). This behavior provides clear evidence for the relatively low affinity of  $Bu_2Zn$  toward chloride ions and thus supports our interpretation of the ESI mass spectrometric results (see above).

 $ZnX_2/(LiCl)_n$ . The specific conductivities of ZnCl<sub>2</sub> and ZnBr<sub>2</sub> in THF at 258 K are again very low but strongly increase upon the addition of LiCl and then level off (Figures 5 and S19). In the case of  $ZnCl_2/(LiCl)_n$ , a constant plateau is already reached when exactly one equivalent of LiCl is added. This finding indicates a particularly high association constant for  $Li^{+}ZnCl_{3}^{-}$  (higher than for  $Li^{+}ZnBr_{3}^{-}$  and  $Li^{+}RZnX_{2}^{-}$ ). Moreover, the observed saturation after the addition of one equivalent of LiCl strongly suggests the absence of ZnCl<sub>4</sub><sup>2-</sup> dianions, in contrast to the situation found for ZnCl<sub>2</sub>-containing ionic liquids.<sup>26</sup> In the present experiments, the abundant Lewis-basic THF molecules presumably prevent further chloride anions from binding to the ZnCl<sub>3</sub><sup>-</sup> complexes.<sup>40</sup> With respect to the heterolytic dissociation of the inorganic lithium zincates, the higher conductivities measured for the  $ZnBr_2/(LiCl)_n$  system point to a more facile dissociation of the bromide-containing species. Thus, the inorganic Li<sup>+</sup>ZnX<sub>3</sub><sup>-</sup> complexes mimic the behavior of their Li<sup>+</sup>BuZnX<sub>2</sub><sup>-</sup> counterparts (see above).

**3.3.** NMR Spectroscopy.  $BuZnX/(LiCl)_n$ . In a careful study on lithium tri- and tetramethylzincate complexes, Uchiyama et al.<sup>41</sup> found the <sup>1</sup>H NMR signals of these species to display large upfield shifts in comparison to simple  $(CH_3)_2Zn$ . These upfield shifts correlate with the enhanced nucleophilic reactivity of LiZn- $(CH_3)_3$  and, particularly, Li<sub>2</sub>Zn $(CH_3)_4$  relative to  $(CH_3)_2Zn$ .<sup>41</sup> The chemical shift of the  $\alpha$ -H atoms thus apparently forms a sensitive probe of the electronic character of organozinc compounds and should also provide insight into the interaction of BuZnX with LiCl.

In the absence of LiCl, the  $\alpha$ -H atoms in BuZnCl, BuZnBr, and BuZnI exhibit quite similar chemical shifts (Table 1). For the latter, it does not make any difference whether it is prepared by mixing Bu<sub>2</sub>Zn with ZnI<sub>2</sub> or by Zn insertion into BuI, indicating that both samples are identical.

Upon the addition of one equivalent of LiCl, the absorptions of the  $\alpha$ -H atoms in BuZnCl shift upfield, while the absorptions of the H atoms further away from the Zn center hardly change (Figure 6). This behavior points to a specific interaction of LiCl with the Zn center and thus is fully in line with the inferred formation of a Li<sup>+</sup>BuZnCl<sub>2</sub><sup>-</sup> complex. The upfield shift observed



**Figure 6.** 200 MHz <sup>1</sup>H NMR spectrum of a solution of BuZnCl in THF-D<sub>8</sub> ( $c \approx 40$  mM) with and without the addition of one equivalent of LiCl (T = 296 K). The signal at  $\delta$  0.10 ppm (black trace) results from a contamination with silicon grease.

for the  $\alpha$ -H atoms demonstrates that the zincate species indeed exhibits a higher electron density than simple BuZnCl. Solutions of BuZnBr/(LiCl)<sub>n</sub> and BuZnI/(LiCl)<sub>n</sub> behave in a completely analogous fashion (Figures S20 and S21). Organ and collaborators also found a very similar behavior for BuZnBr/(LiBr)<sub>n</sub> in THF/DMI.<sup>23</sup>

At higher LiCl concentrations, the chemical shifts of the  $\alpha$ -H atoms move further upfield and finally level off (Figure 7). This behavior fully matches the results from the conductivity measurements and confirms our hypothesis that exactly one equivalent of LiCl reacts with BuZnX to produce Li<sup>+</sup>BuZnXCl<sup>-</sup>; higher adducts, such as (Li<sup>+</sup>)<sub>2</sub>BuZnXCl<sub>2</sub><sup>-</sup>, apparently do not form to a significant extent in the sampled concentration range. The fact that only one averaged signal is observed for the  $\alpha$ -H atoms furthermore indicates that the interconversion between BuZnX and Li<sup>+</sup>BuZnXCl<sup>-</sup> occurs fast on the NMR time scale. Lowering the temperature to 193 K does not resolve the individual NMR shifts of the two components either.

For a quantitative analysis, we focus on the BuZnCl/(LiCl)<sub>n</sub> system to avoid complications by X/Cl exchange processes. Our simplified model takes into account only the reaction of LiCl with BuZnCl according to Scheme 1 with X = Cl and neglects the formation of higher aggregates.<sup>42</sup> We thus assume that the measured chemical shift corresponds to the average of the shifts of BuZnCl and Li<sup>+</sup>BuZnCl<sub>2</sub><sup>-</sup> weighted according to their concentrations. The shift of the former is directly observable (Table 1), whereas that of the latter as well as the association constant  $K_{ass}$  can be obtained by fitting the experimental data on the basis of the law of mass action. The best fit obtained reproduces the experiment reasonably well (Figure 7) and affords an association constant of  $K_{ass} = 113 \text{ L mol}^{-1}$ . This finding implies that at synthetically relevant concentrations the equilibrium favors the formation of the Li<sup>+</sup>BuZnXCl<sup>-</sup> complex. The analogous trends observed for  $BuZnBr/(LiCl)_n$  and  $BuZnI/(LiCl)_n$  suggest a very similar behavior of these systems. In the case of  $BuZnI/(LiCl)_n$  we also investigate the effect of varying BuZnI concentrations and find that the more concentrated samples require higher amounts of LiCl to reach the full upfield shift of the  $\alpha$ -H atoms (Figure S22). This observation provides further evidence for the formation of specific 1:1 adducts of BuZnX and LiCl (X = I, Cl).

In addition to <sup>1</sup>H NMR spectroscopy, we also consider <sup>13</sup>C and <sup>7</sup>Li NMR spectroscopy as possible tools to characterize the



**Figure 7.** <sup>1</sup>H NMR shifts of the  $\alpha$ -protons of BuZnX/(LiCl)<sub>n</sub> (X = Cl, Br, I,  $c \approx 40$  mM, T = 296 K) in THF-D<sub>8</sub> as functions of c(LiCl). The solid line represents a fit of the BuZnCl/(LiCl)<sub>n</sub> shifts based on an association constant of  $K_{ass} = 113$  L mol<sup>-1</sup>.

complexation of BuZnX by LiCl. With increasing LiCl concentration, the absorbances of the  $\alpha$ -C atoms of BuZnCl and BuZnBr shift slightly downfield, thus opposing the behavior of the  $\alpha$ -H atoms (Figures S23 and S24). These results may at first sight appear surprising because both the  $\alpha$ -C and the  $\alpha$ -H atoms supposedly experience similar local electronic environments and might therefore be expected to display parallel trends in their NMR absorbances. However, an analysis of the relatively few available NMR data of organozinc compounds reported in the literature shows that opposing trends for <sup>1</sup>H and <sup>13</sup>C NMR shifts are actually the rule rather than the exception for these species.<sup>43,44</sup> <sup>7</sup>Li NMR spectroscopy of solutions of LiCl in THF-D<sub>8</sub> at room temperature finds a rather small upfield shift of the <sup>7</sup>Li signal from 0.38 to -0.05 ppm upon the addition of one equivalent of BuZnCl.

 $Bu_2Zn/(LiCl)_n$ . Compared to BuZnX, Bu<sub>2</sub>Zn shows an upfield shift of its  $\alpha$ -H atoms (Table 1), which reflects the enhanced electron density at the metal center and agrees with the wellknown higher nucleophilic reactivity of diorganozinc compounds.<sup>2d</sup> Upon treatment with LiCl, the signal of the  $\alpha$ -H atoms of Bu<sub>2</sub>Zn very slightly moves upfield (Figure S25). Unlike the case of BuZnX/(LiCl)<sub>n</sub>, we do not observe a saturation at a high excess of LiCl but instead find a continuous, though very small, upfield shift. This behavior indicates a lower tendency of Bu<sub>2</sub>Zn to add LiCl and form an ate complex, thus being fully in line with our ESI mass spectrometric and conductometric findings.

<sup>13</sup>C NMR spectroscopy of Bu<sub>2</sub>Zn measures an absorption of the  $\alpha$ -C atom that is shifted downfield relative to BuZnX (Figure S24), thus contrasting the trend in the corresponding <sup>1</sup>H NMR spectra. Organ and collaborators reported analogous opposing shifts of the <sup>1</sup>H and <sup>13</sup>C signals of BuZnBr and Bu<sub>2</sub>Zn in THF/ DMI.<sup>23</sup> Obviously, here we are dealing with another example of the above-discussed contrasting trends in <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy of organozinc compounds. The addition of one equivalent of LiCl results in a further downfield shift of the  $\alpha$ -C atom of Bu<sub>2</sub>Zn. This behavior resembles that of BuZnX/(LiCl)<sub>n</sub>, but the magnitude of the effect is smaller. We interpret this finding as additional evidence of the lower tendency of Bu<sub>2</sub>Zn toward complexation by LiCl. Scheme 2. Common Methods for the Synthesis of Organozinc Halides RZnX Involving LiX and Thus Giving Rise to the in Situ Formation of Lithium Organozincates



#### 4. CONCLUSIONS

Using a combination of ESI mass spectrometry, electrical conductivity measurements, and NMR spectroscopy, we have obtained consistent evidence that the action of LiCl on organylzinc halides RZnX (X = Cl, Br, I) in THF leads to the formation of lithium organylzincate complexes Li<sup>+</sup>RZnXCl<sup>-</sup> and the corresponding halide-exchanged Li<sup>+</sup>RZnX<sub>2</sub><sup>-</sup> species. These complexes can further undergo heterolytic dissociation to afford free Li<sup>+</sup>-(solv) and RZnXCl<sup>-</sup>/RZnX<sub>2</sub><sup>-</sup> ions. At higher concentrations, we also find evidence for the presence of polynuclear organozincate ions  $R_n Zn_n X_{n+1}^{-}$ . In the case of R = Ph, ESI mass spectrometry furthermore detects small amounts of  $LiR_2Zn_2X_4^{-}$ , which can be considered as the  $Li^+$  adduct of an  $R_2Zn_2X_4^{-2-}$  dianion. This observation indicates that the formation of Li<sup>+</sup>-paired organozincate dianions in THF solutions in principle may be feasible. The conductometric and NMR spectroscopic results show that such reactions only occur to a very low degree, however, if  $\leq 2$ equivalents of LiX are added.

Analogous experiments on  $Bu_2Zn/(LiCl)_n$  point to a significantly decreased tendency of diorganylzinc compounds to add halide anions and form the corresponding zincate complexes. This finding fully explains why LiCl does not activate 'Pr<sub>2</sub>Zn in iodine-zinc exchange reactions.<sup>25</sup> In contrast, the inorganic zinc halides ZnCl<sub>2</sub> and ZnBr<sub>2</sub> very readily form zincate anions in the presence of LiCl. As the ESI mass spectrometric measurements demonstrate, these species also easily give polynuclear aggregates, unlike Bu<sub>2</sub>Zn. The different behavior of ZnX<sub>2</sub>, RZnX, and R<sub>2</sub>Zn directly correlates with their Lewis acidities. Due to the electronegativity of the halogen atoms, ZnX<sub>2</sub> has an enhanced Lewis acidity and very easily adds X<sup>-</sup> and ZnX<sub>3</sub><sup>-</sup> anions to form monoand polynuclear zincate complexes, respectively. Substitution of one halogen by a less electronegative organyl group reduces the Lewis acidity of the resulting RZnX. Therefore, these species show a somewhat decreased affinity toward  $X^-$  and  $\text{ZnRX}_2^$ anions. Finally, the Lewis acidity of R<sub>2</sub>Zn is lowered to such an extent that complexation reactions become rather unfavorable. Note again that these findings are supported by three different, independent analytical methods. The good agreement between ESI mass spectrometry and electrical conductivity measurements as well as NMR spectroscopy suggests that the former technique indeed is well suitable for probing ion speciation in solution.

The inferred facile complexation of RZnX with LiX has farreaching implications for organozinc chemistry. The association constant of  $K_{\rm ass} \approx 100 \, {\rm L} \, {\rm mol}^{-1}$  derived for Li<sup>+</sup>BuZnCl<sub>2</sub><sup>-</sup> suggests that at synthetically relevant concentrations the lithium organozincate complex predominates. The most common synthetic routes to organylzinc halides, i.e., transmetalation of ZnX<sub>2</sub> with RLi, Knochel's LiCl-mediated Zn insertion into RX, as well as the insertion of Rieke Zn into RX, all involve stoichiometric amounts of LiX. We therefore conclude that the supposedly formed RZnX species in reality largely correspond to lithium organozincates Li<sup>+</sup>RZnX<sub>2</sub><sup>-</sup> (Scheme 2). The reactivities of the latter most likely differ from those of simple RZnX species and thus explain the pronounced effects of LiX in organozinc chemistry. Further efforts are needed for a better understanding of this interesting and important problem.

#### ASSOCIATED CONTENT

**Supporting Information.** Additional ESI mass spectra, concentration-dependent electrical conductivity plots, NMR spectra, and plots of concentration-dependent chemical shifts. This material is available free of charge via the Internet at http:// pubs.acs.org.

#### AUTHOR INFORMATION

#### **Corresponding Author**

\*E-mail: konrad.koszinowski@cup.uni-muenchen.de.

#### ACKNOWLEDGMENT

We thank Prof. Herbert Mayr for his continuous generous support, Dr. David S. Stephenson for performing the low-temperature NMR measurements, and Matthias A. Schade for assistance with synthetic procedures. K.K. also thanks Dr. Detlef Schröder for helpful discussions. We gratefully acknowledge financial support from the Deutsche Forschungsgemeinschaft (SFB 749 and KO 2875/4-1), LMU München (LMUexcellent), the Center for Integrated Protein Science Munich, and the Fonds der Chemischen Industrie.

#### REFERENCES

(1) The Chemistry of Organozinc Compounds; Rappoport, Z.; Marek, I., Eds.; Wiley: Chichester, 2006.

(2) (a) Knochel, P.; Singer, R. D. *Chem. Rev.* 1993, 93, 2117–2188.
(b) Knochel, P.; Perea, J. J. A.; Jones, P. *Tetrahedron* 1998, 54, 8275–8319.
(c) Knochel, P.; Leuser, H.; Gong, L.-Z.; Perrone, S.; Kneisel, F. F. In *Handbook of Functionalized Organometallics*; Knochel, P., Ed.; Wiley-VCH: Weinheim, 2005; Vol. 1, pp 251–346. (d) Knochel, P.; Leuser, H.; Gong, L.-Z.; Perrone, S.; Kneisel, F. F. *The Chemistry of Organozinc Compounds*; Rappoport, Z.; Marek, I., Eds.; Wiley: Chichester, 2006; pp 287–393.

(3) (a) Negishi, E.; King, A. O.; Okukado, N. J. Org. Chem. 1977,
 42, 1821–1823. (b) King, A. O.; Okukado, N.; Negishi, E. J. Chem. Soc.,
 Chem. Commun. 1977, 683–684.

(4) (a) Netherton, M. R.; Fu, G. C. Adv. Synth. Catal. 2004, 346, 1525–1532. (b) Frisch, A. C.; Beller, M. Angew. Chem. 2005, 117, 680–695. Angew. Chem., Int. Ed. 2005, 44, 674–688. (c) Negishi, E.; Hu, Q.; Huang, Z.; Wang, G.; Yin, N. In The Chemistry of Organozinc Compounds; Rappoport, Z.; Marek, I., Eds.; Wiley: Chichester, 2006; pp 457–553. (d) Phapale, V. B.; Cárdenas, D. J. Chem. Soc. Rev. 2009, 38, 1598–1607.

(5) Gaudemar, M. Bull. Soc. Chim. Fr. 1962, 974–987.

(6) (a) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. J. Org. *Chem.* **1988**, 53, 2392–2394. (b) Berk, S. C.; Yeh, M. C. P.; Jeong, N.; Knochel, P. *Organometallics* **1990**, *9*, 3053–3064.

(7) (a) Takagi, K. Chem. Lett. 1993, 469–472. (b) Ikegami, R.;
Koresawa, A.; Shibata, T.; Takagi, K. J. Org. Chem. 2003, 68, 2195–2199.
(8) Dexter, C. S.; Jackson, R. F. W. Chem. Commun. 1998, 75–76.

(9) Fillon, H.; Gosmini, C.; Périchon, J. J. Am. Chem. Soc. 2003, 125, 3867-3870.

(10) Huo, S. Org. Lett. 2003, 5, 423–425.

(11) (a) Rieke, R. D. Science 1989, 246, 1260–1264. (b) Zhu, L.;
 Wehmeyer, R. M.; Rieke, R. D. J. Org. Chem. 1991, 56, 1445–1453.

(12) (a) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. Angew. Chem. 2006, 118, 6186–6190. Angew. Chem., Int. Ed. 2006, 45, 6040–6044. (b) Ren, H.; Dunet, G.; Mayer, P.; Knochel, P. J. Am. Chem. Soc. 2007, 129, 5376–5377. (c) Boudet, N.; Sase, S.; Sinha, P.; Liu, C.-Y.; Krasovskiy, A.; Knochel, P. J. Am. Chem. Soc. 2007, 129, 12358–12359.

(13) For an earlier investigation, see: Huang, Z.; Qian, M.; Babinski, D. J.; Negishi, E. *Organometallics* **2005**, *25*, 475–478.

(14) (a) Koszinowski, K.; Böhrer, P. Organometallics **2009**, 28, 100–110. (b) Koszinowski, K.; Böhrer, P. Organometallics **2009**, 28, 771–779.

(15) Liu, C.-Y.; Wang, X.; Furuyama, T.; Yasuike, S.; Muranaka, A.; Morokuma, K.; Uchiyama, M. *Chem.—Eur. J.* **2010**, *16*, 1780–1784.

(16) Organ, M. G.; Avola, S.; Dubovyk, I.; Hadei, N.; Kantchev, E. A.
B; O'Brien, C. J.; Valente, C. *Chem.—Eur. J.* **2006**, *12*, 4749–4755.

(17) (a) Ochiai, H.; Jang, M.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2008**, *10*, 2681–2683. (b) Asada, Y.; Yasuda, S.; Yorimitsu, H.; Oshima, K. *Organometallics* **2008**, *27*, 6050–6052.

(18) Urkalan, K. B.; Sigman, M. S. J. Am. Chem. Soc. 2009, 131, 18042-18043.

(19) Glynn, D.; Shannon, J.; Woodward, S. Chem.—Eur. J. 2010, 16, 1053–1060.

(20) Hevia, E.; Mulvey, R. E. Angew. Chem. 2011, 123, 6575–6578. Angew. Chem., Int. Ed. 2011, 50, 6448–6450.

(21) For a recent report of a negative effect of lithium halides on the reactivity of RZnX, however, see: Joshi-Pangu, A.; Ganesh, M.; Biscoe, M. R. *Org. Lett.* **2011**, *13*, 1218–1221.

(22) Achonduh, G. T.; Hadei, N.; Valente, C.; Avola, S.; O'Brien, C. J.; Organ, M. G. *Chem. Commun.* **2010**, *46*, 4109–4111.

(23) Hunter, H. N.; Hadei, N.; Blagojevic, V.; Patschinski, P.; Achonduh, G. T.; Avola, S.; Bohme, D. K.; Organ, M. G. *Chem.—Eur. J.* **2011**, *17*, 7845–7851.

(24) MacIntosh, I. S.; Sherren, C. N.; Robertson, K. N.; Masuda, J. D.; Pye, C. C.; Clyburne, J. A. C. *Organometallics* **2010**, *29*, 2063–2068.

(25) Kneisel, F. F.; Dochnahl, M.; Knochel, P. Angew. Chem. 2004, 116, 1032–1036. Angew. Chem., Int. Ed. 2004, 43, 1017–1021.

(26) Estager, J.; Nockemann, P.; Seddon, K. R.; Swadźby-Kwaśny, M.; Tyrrell, S. *Inorg. Chem.* **2011**, *50*, 5258–5271.

(27) For selected recent examples, see: (a) Sase, S.; Jaric, M.;
Metzger, A.; Malakhov, V.; Knochel, P. J. Org. Chem. 2008, 73, 7380–7382. (b) Manolikakes, G.; Dong, M.; Mayr, H.; Li, J.; Knochel, P. Chem.—Eur. J. 2009, 15, 1324–1328. (c) Zhang, T.; Gao, X.; Wood, H. B. Tetrahedron Lett. 2011, 52, 311–313.

(28) Kneisel, F. F. Dissertation, LMU München, 2003.

(29) Hofstee, H. K.; Boersma, J.; van der Meulen, J. D.; van der Kerk,

G. J. M. J. Organomet. Chem. 1978, 153, 245-252.

(30) Krasovskiy, A.; Knochel, P. Synthesis 2006, 890-891.

(31) Markies, P. R.; Schat, G.; Akkermann, O. S.; Bickelhaupt, F. J. Organomet. Chem. **1992**, 430, 1–13.

(32) Rilatt, I.; Jackson, R. F. W. J. Org. Chem. 2008, 73, 8694–8704.
(33) (a) Koszinowski, K. J. Am. Chem. Soc. 2010, 132, 6032–6040.

(b) Putau, A.; Koszinowski, K. Organometallics **2010**, *29*, 3593–3601. Addition/correction: Organometallics **2010**, *29*, 6841–6842.

(34) Calculations of the temperature-dependent changes in sample volumes and, thus, in concentrations were based on data from Carvajal, C.; Tölle, K. J.; Smid, J.; Szwarc, M. J. Am. Chem. Soc. **1965**, 87, 5548–5553.

(35) Fleckenstein, J. E.; Koszinowski, K. Chem.—Eur. J. 2009, 15, 12745–12753.

(36) Also note that the shift to smaller zincates corresponds to an increase of the Cl:Zn ratio, thus reflecting the change in the overall composition of the solution. A similar correlation has been reported for ZnCl<sub>2</sub>-containing ionic liquids; see ref 26.

(37) (a) Hojo, M.; Ueda, T.; Chen, Z.; Nishimura, M. J. Electroanal. Chem. 1999, 468, 110–116. (b) Das, D. J. Solution Chem. 2008, 37, 947–955.

(38) However, similar arguments cannot explain why BuZnBr/ (LiCl)<sub>n</sub> displays higher conductivities than BuZnI/(LiCl)<sub>n</sub>. Clearly, the situation here is more complex.

(39) Fuoss, R. M.; Kraus, Ĉ. A. J. Am. Chem. Soc. 1933, 55, 2387-2399.

(40) Note that the  $(THF)ZnCl_3^-$  complexes are too weakly bound to survive the ESI process, however.

(41) Uchiyama, M.; Kameda, M.; Mishima, O.; Yokoyama, N.; Koike, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 4934– 4946.

(42) The related EtZnI has been shown to be monomeric in THF: Abraham, M. H.; Rolfe, P. H. J. Organomet. Chem. **1967**, *7*, 35–43.

(43) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. J. Am. Chem. Soc. 1992, 114, 2592–2602.

(44) (a) Boersma, J.; Noltes, J. G. J. Organomet. Chem. 1967, 8, 551–553. (b) Evans, D. F.; Fazakerley, G. V. J. Chem. Soc. (A) 1971, 182–183. (c) Blake, A. J.; Shannon, J.; Stephens, J. C.; Woodward,

S. Chem.—Eur. J. 2007, 13, 2462–2472.