Lithium Zincate Reagents

DOI: 10.1002/ange.201104297

"LiZn(TMP)$_3$", a Zincate or a Turbo-Lithium Amide Reagent? DOSY NMR Spectroscopic Evidence**

Pablo García-Álvarez, Robert E. Mulvey,* and John A. Parkinson*

Combining common organometallic reagents (e.g. organolithium, -magnesium or -zinc compounds) with certain additives, in order to increase their reactivity and/or chemoselectivity for the functionalization of sensitive aromatic or heteroaromatic substrates, is a rapidly developing research area. In this context, several groups around the world have together developed a new library shelf of "superbases" that can have abilities surpassing those of their ancestors. The additives employed cover a wide range of species, from simple donor ligands or inorganic salts, to other organometallic bases also effective on their own. For instance, the degree of aggregation of alkyllithium reagents in non-polar solvents can usually be reduced using donors such as TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine), that empower their reactivity.[1] Simple LiCl can enhance the kinetic basicity of Grignard reagents in THF media, resulting in the formation of so called Turbo-bases (e.g. "RMgCl·LiCl" where R = amide or alkyl), that exhibit much better regioselectivity and higher functional group tolerance than their parent non-activated Grignard reagents.[2] The combination of soft organometallic compounds with highly reactive hard alkali metal bases (forming 'ate complexes) provides a new class of mixed-metal reagents. These execute reactions never before imagined by their separate counterparts thereby introducing new patterns of reactivity classified as alkali metal mediated metalation.[3] Some successful members of these bimetallic 'ate complexes, for deprotonation reactions, are the bases "LiZn*t*Bu$_2$(TMP)" (Kondo and Uchiyama),[4] "Bu$_4$MgLi$_2$" (Mongin),[5] and [(TMEDA)·Na(μ-TMP)(μ-*t*Bu)Zn(*t*Bu)] (Mulvey; TMP = 2,2,6,6-tetramethylpiperidide), which as a proof of concept easily zincates non-activated unsubstituted benzene.[6]

Despite the growing number of applications of these superbases, and considering the importance that structural elucidation provides in the understanding of active species (in order to rationalize reactivity patterns and/or propose reaction mechanisms), structural studies in the area of bimetallic 'ate type complexes are mostly limited to those systems developed in non-polar solvents (aliphatic and aromatic hydrocarbons), probably due to the easier obtainment of suitable crystals for X-ray analysis from such media.[7] The true nature of those mixed-reagents that operate in polar solvents, commonly THF, and therefore the role of the additives employed, is generally unknown and they are frequently treated as black-box mixtures.

As part of our ongoing structural elucidation studies, herein we shed light on the constitution of an important member of this family of basic mixtures, the a priori lithium zincate "(TMEDA)·LiZn(TMP)$_3$", developed by Mongin et al., which can chemoselectively functionalize many aromatic substrates in an improved way compared to that of their lithium and zinc counterparts (implying synergistic behavior).[8] This reagent is usually made in situ by a metathesis reaction involving (TMEDA)·ZnCl$_2$ in THF media [Eq. (1)].

$$3\,\mathrm{LiTMP}+(\mathrm{TMEDA})\cdot\mathrm{ZnCl_2} \rightarrow \text{“}(\mathrm{TMEDA})\cdot\mathrm{LiZn(TMP)_3}\text{”}+2\,\mathrm{LiCl} \tag{1}$$

We chose this reagent as a focus for attention because of: 1) the blurred nature of the base as a contacted lithium zinc species and therefore of its 'ate formulation and 2) the possibility that LiCl, also present in the reaction media, has a role in the constitution of the base. In relation to reason (1) the authors were led to interpret the base in different ways, it being generally treated as a simple 1:1 mixture of LiTMP and Zn(TMP)$_2$, where its synergistic performance is explained according to the in situ trapping of generated lithio species with zinc compounds.[8a–c] This agrees with the detection of free LiTMP and Zn(TMP)$_2$ in ^{13}C NMR spectra of the base[8d] and with calculations predicting that LiTMP and Zn(TMP)$_2$ are more stable separately than their co-complex.[8c] Initially, reaction pathways and DFT calculations considering an "LiZn(TMP)$_3$" 'ate were proposed, for example during the metalation/zincation of N-phenylpyrrole.[8e] Regarding reason (2), LiCl has not been considered when formulating the basic mixture or in mechanistic studies.[8c,e] This lack of "consideration" towards LiCl is quite surprising in view of Knochel's comprehensive work especially considering the established participation of LiCl in processes such as the oxidative insertion of zinc dust into aryl halides,[9] or in S$_N$2′ reactions of organozinc reagents.[10] Also, Collum revealed the remarkable fact that trace quantities of LiCl (as small as 0.5 mol%) can greatly accelerate ortholithiation reactions of certain arenes using the protocol commonly practiced by organic chemists (lithium diisopropylamide; THF; −78 °C).[11] It is noteworthy in contrast that one of the first reports regarding the

---

[*] Prof. R. E. Mulvey, Dr. J. A. Parkinson
WestCHEM, Department of Pure and Applied Chemistry
University of Strathclyde, Glasgow, G1 1XL (UK)
E-mail: r.e.mulvey@strath.ac.uk

Dr. P. García-Álvarez
Departamento de Química Orgánica e Inorgánica IUQOEM
Universidad de Oviedo-CSIC, Oviedo, 33071 (Spain)
E-mail: pga@uniovi.es

[**] This research was supported by the UK Engineering and Physical Science Research Council (award no. EP/F063733/1), the Royal Society (Wolfson research merit award to R.E.M.), the Spanish MICINN (DELACIERVA-09-05 to P.G.-A.), and the EU (Marie Curie FP7-2010-RG-268329 to P.G.-A).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201104297.

application of lithium zincate reagents in THF media, by Isobe in 1977, does explicitly include LiCl in their formulae ($R_3LiZn{\cdot}2\,LiCl$).[12]

Therefore, it is essential that a fully defined understanding should be sought regarding the true nature of the basic solution phase mixture developed by Mongin, which, when all its components are included, can be empirically formulated as "(TMEDA)·LiTMP·Zn(TMP)$_2$·2 LiCl", referred to here as **A**. As crystallization of active species does not always reflect the reality occurring in solution (particularly in THF),[13,14] we decided to study **A** using DOSY NMR spectroscopy. DOSY techniques can be used to identify individual components of solution mixtures (comparable to chromatography in NMR terms), and to estimate their "sizes", which are inversely proportional to their diffusion coefficients (D).[15] For example, Stalke has demonstrated qualitatively how the solid-state X-ray determined structures of lithium zincates [(pmdeta)Li(μ-Me)$_2$ZnMe] (pmdeta = *N,N,N′,N″,N″*-pentamethyldiethylenetriamine) and [(diglyme)$_2$Li][ZnMe$_3$] are retained in aromatic solvents.[7b] Williard has corroborated that the THF-solvated LiDA, dimeric in the solid state, retains its integrity in [D$_8$]toluene solution.[16] Hevia established that the aggregation state in the crystal of three-dimensional networks exhibited by unsolvated lithium magnesiates are far from being mirrored in solution thereby uniquely identifying DOSY NMR spectroscopy as of particularly powerful relevance if the solution phase material can only be generated in situ.[17] Also the complex composition in THF solution of some of Knochel's Turbo-Grignard bases in [D$_8$]THF media have been disclosed in own laboratories only by virtue of using the same DOSY technique.[13a]

In a slight variation of Mongin's original synthesis,[8d,e] we prepared the basic mixture (TMEDA)·LiTMP·Zn(TMP)$_2$·2 LiCl (**A**) by mixing LiTMP with (TMEDA)·ZnCl$_2$ in a 3:1 ratio.[18] **A** was analyzed by ^{1}H NMR spectroscopy in [D$_8$]THF and showed sets of resonances corresponding to a 1:1:1 mixture of TMEDA [$\delta^1H = 2.31$ ppm (4H, CH_2), 2.17 (12H, CH_3)], Zn(TMP)$_2$ [$\delta^1H = 1.20$ ppm (24H, CH_3)], and LiTMP [$\delta^1H = 1.09$ ppm (12H, CH_3)]. The presence of lithium was confirmed by a unique broad singlet in the ^{7}Li NMR spectrum at $\delta^7Li = 1.09$ ppm, which encompasses the two different sources of lithium in the mixture, thus hinting at some type of co-complexation between LiTMP and LiCl (note that preliminary low-temperature NMR studies reveals the splitting of this broad signal into three separate resonances hinting at a fast equilibrium between some sort of mixed LiTMP·LiCl co-complex and possibly free LiTMP and LiCl species; see Supporting Information for details). NMR analysis of a standard sample of LiCl of equal concentration to that formally present in **A** reveals a singlet at $\delta^7Li = 0.55$ ppm,[18] which a priori rules out the possibility that in **A** LiCl is "swimming" free in solution (unless by coincidence the chemical shift difference is due to the dielectric constant varying between solutions[19]).

To gain further information about the existing interactions between the components of **A**, ^{1}H and ^{7}Li DOSY NMR experiments were carried out in the presence of internal standards of known molecular weight (FW). Figure 1 shows a superposition of the ^{1}H and ^{7}Li DOSY NMR spectra of **A** and the standards tetraphenylnaphthalene (TPhN), phenylnaphthalene (PhN) and tetramethylsilane (TMS) at 27 °C in [D$_8$]THF. The various components of the mixture all separate clearly in the diffusion dimension[18] with a relative size sequence of TPhN > LiTMP ≈ "Li"[20] > Zn(TMP)$_2$ > PhN > TMEDA > TMS, according to their increasing D values [D(TPhN) $= 7.06(4)\times10^{-10}$ < D(LiTMP) $= 7.37\times10^{-10}$ ≈ D("Li") $= 7.56\times10^{-10}$ < D(Zn(TMP)$_2$) $= 9.51(8)\times10^{-10}$ < D(PhN) $= 1.21(2)\times10^{-9}$ < D(TMEDA) $= 1.42(1)\times10^{-9}$ < D(TMS) $= 1.83\times10^{-9}\,m^2s^{-1}$]. Qualitatively the ^{1}H DOSY data clearly indicate that TMEDA, Zn(TMP)$_2$ and LiTMP do not belong to the same sized molecule, which refutes the possibility of any kind of lithium zincate formulation for the basic mixture **A**. The relationship between log$D$ and log FW for the internal standards used proved to be approximately linear (Supporting Information, Figure S4) and the trend-line generated showed a very good fit ($r^2 = 0.99$). As the signals corresponding to the components of **A** lie in the range of diffusion coefficients delimited by the trend-line, this can be used to infer their size (expressed in formula weight), which turn out to be approximately 425 g mol^{-1} (LiTMP), 407 g mol^{-1} ("Li"), 277 g mol^{-1} [Zn(TMP)$_2$], and 141 g mol^{-1} (TMEDA). A similar approach has been used by other groups to estimate sizes in solution carrying out diffusion measurements in the presence of internal references.[13a,14a,17,21] From these estimated sizes a comparison between these unknowns and the true components of **A** were realized, extracting the following conclusions. Excluding Zn(TMP)$_2$, every forming part of **A** exhibits in the DOSY study a larger size than that corresponding to its actual molecular weight (LiTMP = 147 g mol^{-1}, TMEDA = 116 g mol^{-1}, LiCl = 42 g mol^{-1}), which can be explained according to possible aggregation and/or interactions between them and the solvent THF. For example, there are several reports that experimentally and theoretically indicate that in THF solution LiTMP predominates as a dimer in dynamic equilibrium with monomeric species [Eq. (2)].[22]

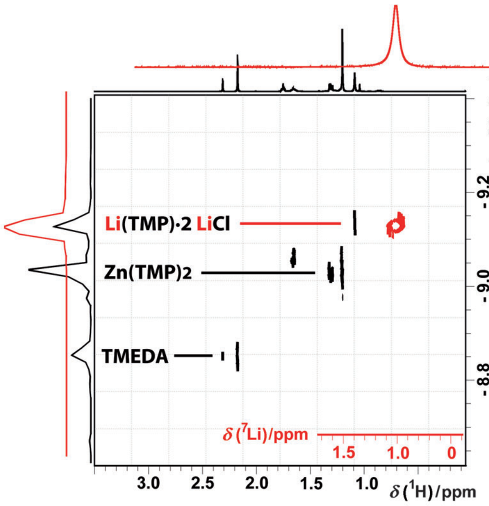

Figure 1. Superposition of ^{1}H and ^{7}Li DOSY NMR spectra of **A** and the standards TPhN, PhN, TMS at 27 °C in [D$_8$]THF. The region corresponding to TPhN, PhN, and TMS is omitted for clarity.

$$(\mathrm{THF})_x \cdot (\mathrm{LiTMP})_2 \rightleftharpoons 2\,(\mathrm{THF})_x \cdot \mathrm{LiTMP};\ x = 1, 2 \qquad (2)$$

A comparison between the DOSY estimates and possible species in THF solution would be tedious (there are hundreds of possible aggregates with different solvations) and could cause misleading results (possible interactions between **A** components would give average values), so we decided to carry out a direct comparison with DOSY data extracted from the individual constituents of **A** and some of their most likely combinations. Therefore ^{1}H,^{7}Li DOSY experiments were carried out with TMEDA, Zn(TMP)$_2$, LiTMP, LiCl, LiTMP·2LiCl, (TMEDA)·LiTMP·2LiCl, (TMEDA)·LiTMP, and TMEDA·2LiCl, in the presence of the same internal standards and under the same conditions of temperature and concentration as used for the parent mixture **A**.[18] All the data obtained are summarized by Table 1, from which emerges a much brighter picture of the real scenario concerning **A**. The principal conclusions extracted from these data are the following:

Table 1: DOSY sizes estimated (expressed in FW; g mol^{-1}) for every component of **A** for all reasonable combinations.[a]

Entry	Combination	"TMEDA"	"Zn(TMP)$_2$"	"LiTMP"	"Li"
1	**A**	141	277	425	407
2	TMEDA, 116[b]	110	–	–	–
3	Zn(TMP)$_2$, 346[b]	–	280	–	–
4	LiTMP, 147[b]	–	–	336	–
5	LiCl, 42[b]	–	–	–	342
6	LiTMP·2LiCl	–	–	401	400
7	LiTMP·2LiCl·TMEDA	148	–	406	393
8	LiTMP·TMEDA	116	–	361	–
9	2LiCl·TMEDA	140	–	–	326

[a] The species in quotation marks are the components of these entities in solution and "Li" refers to the unique lithium-containing species extracted from the ^{7}Li DOSY data. [b] Real FW value of the pure compounds.

a) Neutral zinc amide Zn(TMP)$_2$ is not interacting with the rest of the components of **A**. Entries 1 and 3 show an almost identical FW value. The large difference between the estimated size for Zn(TMP)$_2$ (277 g mol^{-1}) and its real FW value (346 g mol^{-1}) can be explained due to the low accuracy of the method when a single atom of the molecule of study, in this case Zn, is much heavier than the rest of the atoms involved (C, H, N).[23] This phenomenon has been reported previously in other DOSY studies involving Zn complexes.[14a] Entry 7 shows the data obtained when analyzing a LiTMP·2LiCl·TMEDA mixture [note the absence of Zn(TMP)$_2$], which fits reasonably well with what is observed for TMEDA, LiTMP and LiCl in **A**.

b) LiTMP (estimated from ^{1}H-DOSY) and remaining "Li"-containing molecules (estimated from ^{7}Li DOSY), always possess very similar sizes (entries 1, 6 and 7) hinting at the aforementioned interaction between LiTMP and LiCl. LiCl (entry 5) and LiTMP (entry 4) on their own, both exhibit a smaller size than what is observed in **A** (entry 1), which is in agreement with their co-complexation when they are linked together. There are also other facts supporting this co-complexation: namely, 1) the unique singlet observed in the lithium NMR spectrum of **A**, LiTMP·2LiCl, or (TMEDA)·LiTMP·2LiCl; 2) LiTMP (Figures S11, S23) is much more prone to hydrolysis when it is not accompanied by LiCl (Figures S1, S17, S20); and 3) no ^{7}Li-DOSY data could be obtained for LiTMP when LiCl is absent due to very fast relaxation of the lithium nuclei of LiTMP. However, for **A**, LiTMP·2LiCl or (TMEDA)·LiTMP·2LiCl this fast relaxation is not observed indicating some sort of cooperation between both lithium sources that somehow reduces this phenomenon.

c) Free TMEDA has a smaller size (entry 2) than when measured upon inclusion in **A**. This indicates an interaction with the remaining components but which excludes Zn(TMP)$_2$. However, the estimated size of TMEDA in **A** is clearly smaller than that of the LiTMP·2LiCl species, which puts TMEDA in a possible dynamic coordination/decoordination equilibrium event with them,[24] and it is in agreement with its lack of participation when used in a strongly coordinating polar solvent such as THF.[25] Comparing entries 8 and 9, this interaction is probably with LiCl, because when TMEDA is mixed with LiTMP, no significant changes in its apparent size are detected.

On balance, it seems reasonable to suggest that **A** in solution consists of a co-complexation between LiTMP and two equivalents of LiCl, with a degree of solvation by THF together with weak involvement in an equilibrium with TMEDA. However, it appears that Zn(TMP)$_2$ is just a spectator, probably due its high steric demands. Knochel has also discussed a fast magnesium-to-zinc transmetalation process using his (TMP)$_2$Zn·MgCl$_2$·2LiCl system since adding ZnCl$_2$ to a substrate followed by (TMP)$_2$Mg·2LiCl produces faster deprotonation reactions than using preformed (TMP)$_2$Zn·MgCl$_2$·2LiCl.[26] This hints that (TMP)$_2$Zn·MgCl$_2$·2LiCl is, in analogy with our study, a Zn(TMP)$_2$ base weakly interacting with the other inorganic salts of the mixture, which possesses a much lower kinetic basicity than the Mg Turbo-base (TMP)$_2$Mg·2LiCl.

In conclusion, using DOSY NMR spectroscopy, enlightening information about the true nature in solution of basic mixtures of substantial importance in organic synthesis has been revealed. These findings concur with Mongin's view that with this mixture lithiation occurs first, followed by a transmetalation through Zn(TMP)$_2$, but goes beyond that by pinpointing LiTMP·2LiCl ± TMEDA as the possible active lithiating base. Also, this study demands that LiCl should be a priori considered for transmetalation reactions in THF, when the nature of the reagents of study are not known with any certainty.

Received: June 21, 2011

Keywords: amides · DOSY NMR spectroscopy · lithium chloride · lithium zincates · structure elucidation

---

[1] a) V. H. Gessner, C. Däschlein, C. Strohmann, *Chem. Eur. J.* **2009**, *15*, 3320; b) D. B. Collum, *Acc. Chem. Res.* **1992**, *25*, 448.

[2] For key papers on RMgCl·LiCl Turbo-bases, see: a) C. J. Rohbogner, S. H. Wunderlich, G. C. Clososki, P. Knochel, *Eur. J. Org. Chem.* **2009**, 1781; b) A. Krasovskiy, B. F. Straub, P. Knochel, *Angew. Chem.* **2006**, *118*, 165; *Angew. Chem. Int. Ed.*

2006, *45*, 159; c) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem.* **2006**, *118*, 3024; *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; d) A. Krasovskiy, P. Knochel, *Angew. Chem.* **2004**, *116*, 3396; *Angew. Chem. Int. Ed.* **2004**, *43*, 3333.

[3] a) R. E. Mulvey, *Acc. Chem. Res.* **2009**, *42*, 743; b) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem.* **2007**, *119*, 3876; *Angew. Chem. Int. Ed.* **2007**, *46*, 3802; c) R. E. Mulvey, *Organometallics* **2006**, *25*, 1060.

[4] Y. Kondo, M. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539.

[5] F. Mongin, A. Bucher, J. P. Bazureau, O. Bayh, H. Awad, F. Trécourt, *Tetrahedron Lett.* **2005**, *46*, 7989.

[6] P. C. Andrikopoulos, D. R. Armstrong, H. R. L. Barley, W. Clegg, S. H. Dale, E. Hevia, G. W. Honeyman, A. R. Kennedy, R. E. Mulvey, *J. Am. Chem. Soc.* **2005**, *127*, 6184.

[7] For some examples on structural characterization in non-polar solvents of bimetallic 'ate type complexes, see: a) Refs. [3c, 6]; b) S. Merkel, D. Stern, J. Henn, D. Stalke, *Angew. Chem.* **2009**, *121*, 6468; *Angew. Chem. Int. Ed.* **2009**, *48*, 6350.

[8] a) F. Chevallier, Y. S. Halauko, C. Pecceu, I. F. Nassar, T. U. Dam, T. Roisnel, V. E. Matulis, O. A. Ivashkevich, F. Mongin, *Org. Biomol. Chem.* **2011**, *9*, 4671; b) K. Snégaroff, S. Komagawa, F. Chevallier, P. C. Gros, S. Golhen, T. Roisnel, M. Uchiyama, F. Mongin, *Chem. Eur. J.* **2010**, *16*, 8191; c) J.-M. L'Helgoual'ch, A. Seggio, F. Chevallier, M. Yonehara, E. Jeanneau, M. Uchiyama, F. Mongin, *J. Org. Chem.* **2008**, *73*, 177; d) A. Seggio, F. Chevallier, M. Vaultier, F. Mongin, *J. Org. Chem.* **2007**, *72*, 6602; e) A. Seggio, M.-I. Lannou, F. Chevallier, D. Nobuto, M. Uchiyama, S. Golhen, T. Roisnel, F. Mongin, *Chem. Eur. J.* **2007**, *13*, 9982.

[9] a) C-Y. Liu, X. Wang, T. Furuyama, S. Yasuike, A. Muranaka, K. Morokuma, M. Uchiyama, *Chem. Eur. J.* **2010**, *16*, 1780; b) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem.* **2006**, *118*, 6186; *Angew. Chem. Int. Ed.* **2006**, *45*, 6040.

[10] K. Kobayashi, M. Ueno, H. Naka, Y. Kondo, *Chem. Eur. J.* **2009**, *15*, 9805.

[11] L. Gupta, A. C. Hoepker, K. J. Singh, D. B. Collum, *J. Org. Chem.* **2009**, *74*, 2231.

[12] M. Isobe, S. Kondo, N. Nagasawa, T. Goto, *Chem. Lett.* **1977**, *8*, 679.

[13] a) D. R. Armstrong, P. García-Álvarez, A. R. Kennedy, R. E. Mulvey, J. A. Parkinson, *Angew. Chem.* **2010**, *122*, 3253; *Angew. Chem. Int. Ed.* **2010**, *49*, 3185; b) P. García-Álvarez, D. V. Graham, E. Hevia, A. R. Kennedy, J. Klett, R. E. Mulvey, C. T. O'Hara, S. Weatherstone, *Angew. Chem.* **2008**, *120*, 8199; *Angew. Chem. Int. Ed.* **2008**, *47*, 8079.

[14] a) D. R. Armstrong, W. Clegg, P. García-Álvarez, M. D. McCall, L. Nuttall, A. R. Kennedy, L. Russo, E. Hevia, *Chem. Eur. J.* **2011**, *17*, 4470; b) E. Hevia, J. Z. Chua, P. García-Álvarez, A. R. Kennedy, M. D. McCall, *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 5294.

[15] For recent DOSY reviews see: a) D. Li, I. Keresztes, R. Hopson, P. Williard, *Acc. Chem. Res.* **2009**, *42*, 270; b) A, Macchioni, G. Ciancaleoni, C. Zuccaccia, D. Zuccaccia, *Chem. Soc. Rev.* **2008**, *37*, 479; c) B. Antalek, *Concepts Magn. Reson. Part A* **2007**, *30*, 219.

[16] D. Li, R. Hopson, W. Li, J. Liu, P. G. Williard, *Org. Lett.* **2008**, *10*, 909.

[17] S. E. Baillie, W. Clegg, P. García-Álvarez, E. Hevia, A. R. Kennedy, J. Klett, L. Russo, *Chem. Commun.* **2011**, *47*, 388.

[18] See Supporting Information for full experimental and spectroscopic details.

[19] For example: T. Takayama, I. Ando, T. Asakura, *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1233.

[20] "Li" refers to the unique lithium-containing species extracted from the ^{7}Li DOSY data.

[21] a) G. Kagan, W. Li, R. Hopson, P. G. Williard, *Org. Lett.* **2009**, *11*, 4818; b) D. Li, G. Kagan, R. Hopson, P. G. Williard, *J. Am. Chem. Soc.* **2009**, *131*, 5627.

[22] a) P. Renaud, M. A. Fox, *J. Am. Chem. Soc.* **1988**, *110*, 5702; b) F. E. Romesberg, D. B. Collum, *J. Am. Chem. Soc.* **1992**, *114*, 2112.

[23] The logarithm of the diffusion coefficients can be correlated with the logarithm of the molecular weights (assuming that the size of a molecule is proportional to its FW). However, for Zn(TMP)$_2$, which contains a single atom (Zn) considerably heavier than the rest of the atoms involved (C, H, N), the accuracy of this approximation can be compromised.

[24] E. Crosbie, P. García-Álvarez, A. R. Kennedy, J. Klett, R. E. Mulvey, S. D. Robertson, *Angew. Chem.* **2010**, *122*, 9578; *Angew. Chem. Int. Ed.* **2010**, *49*, 9388.

[25] Ref. [1].

[26] Z. Dong, G. C. Clososki, S. H. Wunderlich, A. Unsinn, J. Li, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 457.