

Organozinc Pivalate Reagents: Segregation, Solubility, Stabilization, and Structural Insights**

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Abstract: The pivalates $RZnOPiv \cdot Mg(OPiv)X \cdot nLiCl$ ($OPiv$ = pivalate; R = aryl; X = Cl, Br, I) stand out amongst salt-supported organometallic reagents, because apart from their effectiveness in Negishi cross-coupling reactions, they show more resistance to attack by moist air than conventional organometallic compounds. Herein a combination of synthesis, coupling applications, X-ray crystallographic studies, NMR (including DOSY) studies, and ESI mass spectrometric studies provide details of these pivalate reagents in their own right. A *p*-tolyl case system shows that in $[D_8]THF$ solution these reagents exist as separated $Me(p-C_6H_4)ZnCl$ and $Mg(OPiv)_2$ species. Air exposure tests and X-ray crystallographic studies indicate that $Mg(OPiv)_2$ enhances the air stability of aryl zinc species by sequestering H_2O contaminants. Coupling reactions of $Me(p-C_6H_4)ZnX$ (where X = different salts) with 4-bromoanisole highlight the importance of the presence of $Mg(OPiv)_2$. Insight into the role of $LiCl$ in these multicomponent mixtures is provided by the molecular structure of $[(THF)_2Li_2(Cl)_2(OPiv)_2Zn]$.

It has long been known that salt additives can activate or deactivate organometallic compounds.^[1] The former has been demonstrated to great effect recently through new classes of organozinc and other organometallic reagents that exhibit enhanced reactivity owing to participation of halide salts within their THF solutions, as for example in $(TMP)_2Zn \cdot 2MgCl_2 \cdot 2LiCl$ (TMP is 2,2,6,6-tetramethylpiperide).^[2] Combined with activation, a new salt effect was

reported for the magnesium–zinc pivalate systems $RZnOPiv \cdot Mg(OPiv)X \cdot nLiCl$ (where $OPiv$ = pivalate; R = aryl, heteroaryl, or benzyl; X = Cl, Br, or I), namely stabilization as these systems boast a high degree of resistance to attack by air and moisture, especially when isolated as solids.^[3] Rapid decomposition is the normal outcome when such organometallic compounds are exposed to these antagonists, because metal–carbon bonds are generally thermodynamically unstable with respect to the metal–oxygen bonds that form as a result. Inert atmosphere procedures are thus mandatory for handling these air-sensitive organometallic compounds, so any advances that slow down or ideally stop such air degradation processes altogether would have a massive impact in the numerous academic and especially industrial laboratories that utilize these compounds. While the synthetic usefulness of these salt-stabilised pivalates in Negishi cross coupling or carbonyl addition applications has been documented,^[3] their multicomponent heterotrimetallic–heterotri-anionic compositions make for highly complicated chemistry, which challenges our understanding of them. To begin unravelling this complexity we present herein the opening study of these intriguing pivalate cocktails in their own right, gathering information from solutions, solids, and gas phase. As a consequence, light is thrown on solubility, segregation, and stabilisation issues.

Reported methods of synthesising these pivalates, by inserting Mg into an organic halide RX , magnesiating RX via salt-activated $(TMP)MgCl \cdot LiCl$, or performing $Mg-I/Mg-Br$ exchange on RI or RBr with $iPrMgCl \cdot LiCl$, involve a common second step, namely transmetalation with zinc pivalate [Eq. (1)]:



We initially probed this transmetalation studying the mixture of the arylester reagent $EtO_2C(p-C_6H_4)MgCl \cdot LiCl$ and zinc pivalate in THF solution by NMR spectroscopy.^[4] This solution was found previously to be effective in Negishi cross-coupling reactions under mild conditions, while the solid obtained on evaporation of solvent remained 45% active after 1 h air exposure. Surprisingly 1H NMR and COSY spectra of this mixture revealed only one pivalate signal and two distinct sets of aryl signals,^[4] in contrast to the two pivalate and one set of aryl signals expected from the transmetalation in Equation (1).

1H DOSY NMR^[5,6] experiments implied the presence of two major species^[7] with distinct diffusion coefficients, the lighter one of which could be assigned to free $C_6H_5CO_2Et$, presumably from partial hydrolysis after prolonged storage of

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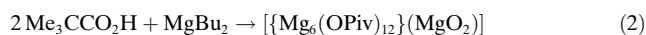
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the sample prior to NMR study. Supporting this hydrolysis presumption, crystals grown from THF solution were revealed by X-ray crystallography to be cocrystals that include a heptanuclear mixed cluster, the core of which can be formalized as $[\{\text{Mg}(\text{OPiv})_2\}_5\{\text{Mg}(\text{OH})_2\}(\text{MgO})\cdot 4\text{THF}]$ **1** (Supporting Information, Figure S4).^[4,8] The most telling features of **1** are OH^- or O^{2-} incorporation and the presence of excess pivalate, where a 1:1 $\text{Mg}/(\text{OPiv})$ stoichiometry would be expected from the transmetalation reaction in Equation (1). These observations prompted two questions. First, could the Mg pivalate products of these reactions be acting as moisture and/or oxygen scavengers? Second, could the transmetalation process be going beyond monopivalate $\text{Mg}(\text{OPiv})\text{Cl}$ products to bispivalate $\text{Mg}(\text{OPiv})_2$ products?^[9] Seeking possible answers to these questions, we devised different experiments. First we attempted to prepare an authentic sample of $\text{Mg}(\text{OPiv})_2$ by an alternative metalation approach, avoiding zinc transmetalation, by magnesiating pivalic acid in heptane/THF solution and crystallizing the product from hot toluene [Eq. (2)]:



Significantly, X-ray crystallography revealed this product $[\{\text{Mg}_6(\text{OPiv})_{12}\}(\text{MgO})_2]\cdot\text{C}_7\text{H}_8$, **2**, was also contaminated by O^{2-} ions, trapped within the discrete octanuclear cluster (Figure 1).^[4] As this preparation of **2** proved reproducible, we initially assumed that the O^{2-} was coming from pivalic acid solution as it was used as received without drying. However, on thoroughly drying the pivalic acid by using a desiccator filled with P_2O_5 , we still observed O^{2-} contamination. Eventually we traced the contamination to the commercial $\text{Mg}(n\text{Bu})_2$ used to prepare the pivalate [Eq. (2)] as on switching to $\text{Mg}(\text{CH}_2\text{SiMe}_3)_2$ which we prepared ourselves, purified by sublimation and stored as a solid in a dry box, no contamination was observed (confirmed by NMR and elemental analysis data; see the Supporting Information). This result suggests that $\text{Mg}(\text{OPiv})_2$ could be functioning as a decontaminating agent, mopping up any OH^- or related ions and trapping them in clusters, to thus protect zinc organometallic species present in the same solution from such contaminants.

Second, we revisited the transmetalation monitoring it by ^1H (including DOSY) and ^{13}C NMR spectroscopy in $[\text{D}_8]\text{THF}$ solution but now using a less sensitive *p*-tolyl probe to follow the fate of the aryl ligand [Eq. (3)]:

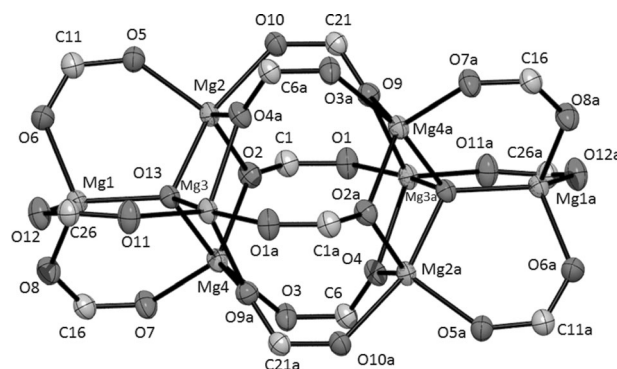
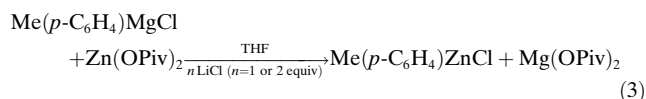


Figure 1. Molecular structure of $[\{\text{Mg}_6(\text{OPiv})_{12}\}(\text{MgO})_2]\cdot\text{C}_7\text{H}_8$ (**2**). Ellipsoids set at 50% probability; hydrogen atoms, solvent molecule, *t*Bu group, and disorder omitted for clarity.



For comparison, we also recorded the spectra of the individual components of the mixture $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}\cdot\text{LiCl}$ and $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl}\cdot\text{LiCl}$. Most informatively, ^{13}C NMR spectra (Figure 2) revealed well-separated C_{ipso} resonances for $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}\cdot\text{LiCl}$ (165.8 ppm) and $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl}\cdot\text{LiCl}$ (153.0 ppm).

Significantly, the reaction mixture of $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}$ and $\text{Zn}(\text{OPiv})_2\cdot n\text{LiCl}$ ($n = 1$ or 2) shows aromatic resonances matching those of $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl}\cdot\text{LiCl}$ with none corresponding to $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}\cdot\text{LiCl}$. Also, the ^1H DOSY NMR spectrum of the reaction mixture revealed that the aromatic resonances and pivalate resonance belong to distinct

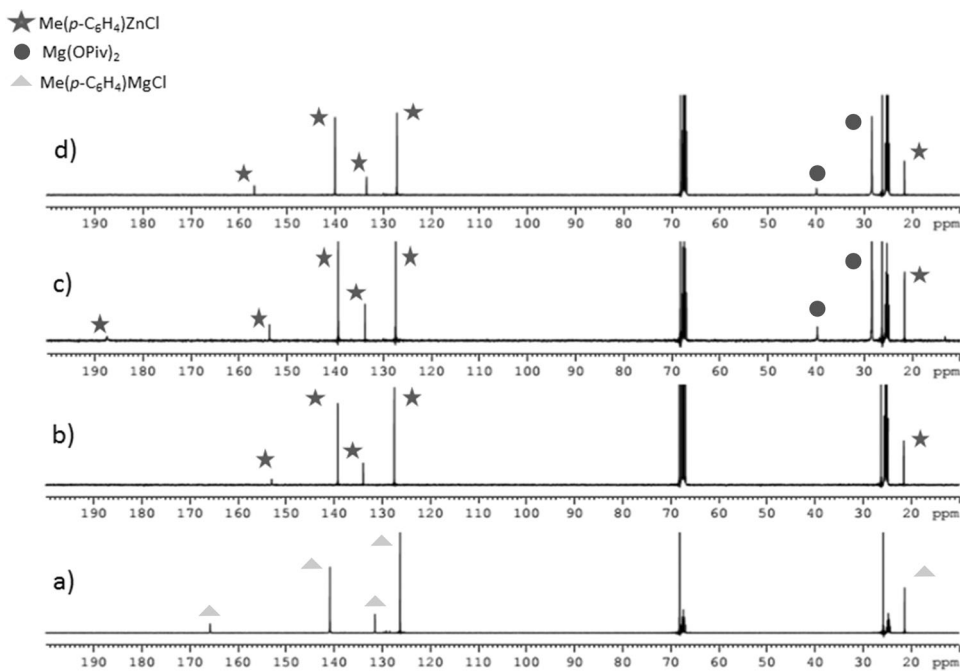


Figure 2. From bottom to top: ^{13}C NMR spectrum of a) $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}\cdot\text{LiCl}$, b) $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl}\cdot\text{LiCl}$, c) $\text{Zn}(\text{OPiv})_2\cdot\text{LiCl}$ and $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}$, and d) $\text{Zn}(\text{OPiv})_2\cdot 2\text{LiCl}$ and $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}$ in $[\text{D}_8]\text{THF}$ at 25°C .

molecules as their diffusion coefficients differ, being $6.87 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ and $5.42 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$, respectively.

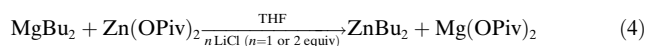
Complementary insight was obtained from electrospray ionization (ESI) mass spectrometry, which selectively probes the charged components of the sampled solution. Analysis of the reaction mixture of $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}$ and $\text{Zn}(\text{OPiv})_2 \cdot n\text{LiCl}$ ($n = 1$ or 2) in the negative-ion mode identified various zincate species $\text{Me}(p\text{-C}_6\text{H}_4)_y\text{Zn}_y\text{Cl}_y\text{X}(\text{LiCl})_z^-$ ($y = 1\text{--}3$; $z = 0, 1$; $\text{X} = \text{Cl}, \text{OPiv}$), which were largely depleted in pivalate ligands (Supporting Information, Figures S19 and S20). These complexes are similar to ordinary zincates formed by transmetalation of zinc halides by RLi reagents.^[10] In contrast, pivalate-rich species were detected upon positive-ion-mode ESI of the reaction mixture of $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}$ and $\text{Zn}(\text{OPiv})_2\text{LiCl}$ (Supporting Information, Figure S33). The most abundant cations observed also contained an OH group, thus resembling **1** in this respect.

Collectively these observations are consistent with almost complete transmetalation of $\text{Zn}(\text{OPiv})_2$ to $\text{Mg}(\text{OPiv})_2$, with Zn receiving the aryl and Cl ligands. This Zn heteroleptic complex was successfully trapped as its TMEDA solvate ($\text{TMEDA})\text{ZnMe}(p\text{-C}_6\text{H}_4)\text{Cl}$ (**3**). X-ray crystallography shows **3** is a simple distorted tetrahedral monomer.^[4] Unit cell checks of crystals grown by adding TMEDA to the original reaction mixture ($\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl} \cdot \text{LiCl}$ and $\text{Mg}(\text{OPiv})_2$ in toluene solution) also revealed **3**, confirming that complete transmetalation to $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl}$ had occurred and that the latter was not interacting with $\text{Mg}(\text{OPiv})_2$ co-product but segregated from it.

Light has also been shed on the solubilizing effect of LiCl on $\text{Zn}(\text{OPiv})_2$. Barely soluble in THF, $\text{Zn}(\text{OPiv})_2$ dissolves on addition of LiCl (one equivalent). The resulting solution deposited crystals elucidated by X-ray crystallography as $[(\text{THF})_2\text{Li}_2(\mu\text{-Cl})_2(\mu\text{-OPiv})_2\text{Zn}]$ (**4**). Solubility can therefore be attributed to forming this molecular complex (Figure 3) through the amphoteric Lewis acidic–Lewis basic resource of the salt, which completes the coordination of both the Lewis basic OPiv group and Lewis acidic Zn atom.

Having established that the reaction mixture in Eq. (3) gave $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl}$ and $\text{Mg}(\text{OPiv})_2$ products, we then studied the air stability of the former both in the absence and

presence of the latter (Supporting Information, Table S5). When a THF solution of the arylzinc reagent was exposed to air for 1 h, 90% survived with only 10% hydrolyzed to toluene (as determined from NMR spectra: note that the error associated with these values are accordingly $\pm 5\%$, so trends observed are more significant than absolute values).^[4] A modest increase in decomposition (to 12%) was observed on exposing solid $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnCl}$ in the same way. These already high stabilities increased to 95% (solution form) and slightly decreased to 83% (solid form) in the presence of $\text{Mg}(\text{OPiv})_2$ generated in situ. These values decreased to 87% and 69%, respectively, on using two equivalents of LiCl. The hygroscopic property of LiCl may be a factor in this deterioration, as captured H_2O could hydrolyze $p\text{-C}_6\text{H}_4\text{Me}$ anions to toluene, especially as the salt is incorporated within the molecular structure of Zn complex **4**. Changing the $p\text{-C}_6\text{H}_4\text{Me}$ ligand to Bu also proved insightful. NMR (^1H and ^{13}C) studies^[4] suggested reaction of Bu_2Mg and $\text{Zn}(\text{OPiv})_2$ with added LiCl (1 or 2 equivalents) in THF solution followed a similar complete transmetalation course [Eq. (4)] to that of its aryl analogue, generating $\text{Bu}_2\text{Zn} \cdot 2\text{LiCl}$ and $\text{Mg}(\text{OPiv})_2$.



Repeating air exposure experiments revealed that both $\text{Bu}_2\text{Zn} \cdot 2\text{LiCl}$ and the mixture $\text{Bu}_2\text{Zn} \cdot 2\text{LiCl}/\text{Mg}(\text{OPiv})_2$ hydrolyze completely in both THF solution and solid form. Remarkably, however, upon adding 5 equivalents of $\text{Mg}(\text{OPiv})_2$, 39% of $\text{Bu}_2\text{Zn} \cdot 2\text{LiCl}$ survived. Moreover, 51% survival was seen for a THF solution mixture of $\text{Bu}_2\text{Zn} \cdot \text{LiCl}$ and $\text{Mg}(\text{OPiv})_2$, as determined by the $\text{Bu}^-/\text{tBuCO}_2^-$ ratio seen in NMR spectra. Moist air had a slightly more detrimental effect than dry air as the mixture $\text{Me}(p\text{-C}_6\text{H}_4)\text{MgCl}/\text{Zn}(\text{OPiv})_2 \cdot 2\text{LiCl}$ experienced 13 and 7% decomposition, respectively, on such exposure, presumably because water reacts faster than O_2 with the aryl species. To study more the effect of moisture, we stored an NMR sample of a $[\text{D}_8]\text{THF}$ solution of $\text{Mg}(\text{OPiv})_2$ outside of the glovebox. After 3 days, a small amount of pivalic acid was detectable.^[4] Collectively these experiments suggest that $\text{Mg}(\text{OPiv})_2$ deprotonates water extremely slowly which supports our earlier view that the OH^- and O^{2-} contamination in **1** and **2** came “preformed” in the starting Mg reagent.

While these experiments show that $\text{Mg}(\text{OPiv})_2$ can mop up OH^- and O^{2-} ions in contaminated solutions, the question remains as to how $\text{Mg}(\text{OPiv})_2$ can protect organozinc compounds from air in non-contaminated solutions. A clue may lie in the way Mg salts incorporate water in their coordination spheres. For example, the acetate tetrahydrate $\text{Mg}(\text{MeCOO})_2(\text{H}_2\text{O})_4$ contains dative $\text{Mg} \cdots \text{O}(\text{H}_2\text{O})$ bonds but also intermolecular hydrogen bonds.^[11] To probe this idea with $\text{Mg}(\text{OPiv})_2$, we evaporated a THF solution containing this compound and water in a 1:3 ratio. This produced $[(\text{Mg}(\text{OPiv})(\text{THF})_2)(\mu\text{-OPiv})_2(\mu\text{-H}_2\text{O})\{\text{Mg}(\text{H}_2\text{O})(\text{OPiv})(\text{HOPIV})\}] \cdot \text{H}_2\text{O}$ (**5**). X-ray studies^[4] revealed a dinuclear subunit of two Mg centers linked by one H_2O and two pivalate anion bridges. Another pivalate and 2 THF ligands also terminally bind to one Mg, while the other Mg carries a terminal pivalate, pivalic acid, and H_2O ligand set.

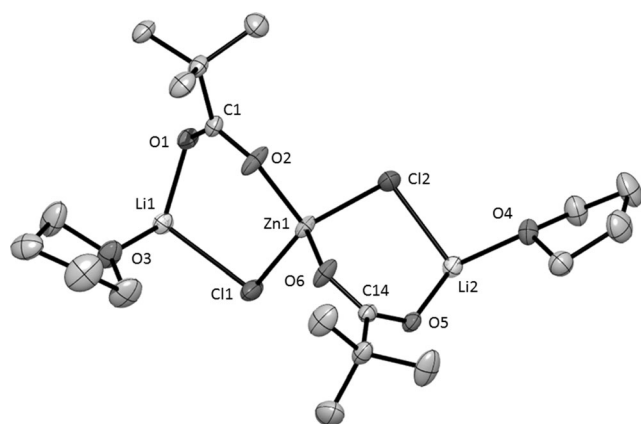


Figure 3. Molecular structure of $[(\text{THF})_2\text{Li}_2(\mu\text{-Cl})_2(\mu\text{-OPiv})_2\text{Zn}]$ (**4**). Ellipsoids set at 50% probability; hydrogen atoms omitted for clarity.

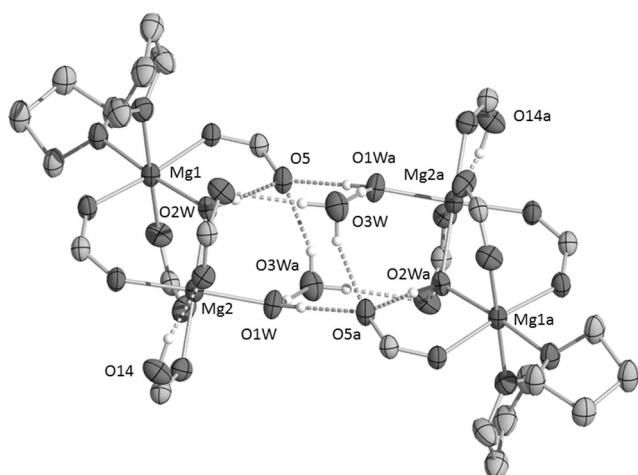


Figure 4. X-ray crystallographic structure of $[\{\text{Mg}(\text{OPiv})(\text{THF})_2\}(\mu\text{-OPiv})_2(\mu\text{-H}_2\text{O})\{\text{Mg}(\text{H}_2\text{O})(\text{OPiv})(\text{HOPiv})\}]\cdot\text{H}_2\text{O}$ (**5**). Ellipsoids set at 30% probability; tBu group and disorder omitted for clarity.

Completing the structure (Figure 4) is a H_2O molecule of crystallization, which engages in hydrogen bonds to two pivalates and one H_2O molecule from different dinuclear subunits to give a tetrameric unit overall. As pivalic acid was not observed in the characterization of the $\text{Mg}(\text{OPiv})_2$ used for crystallization, a small degree of metalation of H_2O by $\text{Mg}(\text{OPiv})_2$ takes place over the two-week period needed to grow crystals.

We then checked whether, apart from its stabilising role, $\text{Mg}(\text{OPiv})_2$ had any appreciable effect on the Negishi cross-coupling capability of the $\text{Me}(p\text{-C}_6\text{H}_4)\text{ZnX}$ reagent. The answer appears to be no, as indicated by the narrow range of high yields obtained for the biaryl product **11** (Table 1) from reactions of ethyl 4-iodobenzoate with different zinc reagents ($\text{X} = \text{Cl}\cdot\text{MgCl}_2\cdot\text{LiCl}$; $\text{Cl}\cdot\text{Mg}(\text{OPiv})_2\cdot\text{LiCl}$; $\text{Cl}\cdot\text{LiCl}$; or $\text{OPiv}\cdot\text{LiOPiv}$) in THF under identical conditions. We then turned to the much slower reaction with 4-bromoanisole to probe the effect of air and the more polar solvent EtOAc. To make sure the reactivity was the same, the cross-coupling with **12** (0.8 equiv) in the presence of 3 mol% $\text{Pd}(\text{OAc})_2$ and 6 mol% of DavePhos in THF under argon have been repeated to give biphenyl **13** in 82 to 86% yield (Table 2, entries 1, 5, 9, and 13; note that the homocoupled biphenyl **14** was also observed in reactions but always as the minor product in about 10% yield). Cross-couplings were then performed in air in non-dried glassware but in dry THF. For pivalate-free reactions, the yield dropped slightly from 85 to 77% for reagent **6** and from 86 to 81%

Table 1: Reactivity of zinc reagents **6–9** towards cross-coupling with ethyl 4-iodobenzoate (**10**).

Entry	X	Yield of 11 [%] ^[a]
1	$\text{Cl}\cdot\text{MgCl}_2\cdot\text{LiCl}$ (6)	91
2	$\text{Cl}\cdot\text{Mg}(\text{OPiv})_2\cdot\text{LiCl}$ (7)	89
3	$\text{Cl}\cdot\text{LiCl}$ (8)	94
4	$\text{OPiv}\cdot\text{LiOPiv}$ (9)	93

[a] Yield of isolated product.

for reagent **8** (entries 2 and 10). For pivalate-containing reagents **7** and **9** however, the yield increased from 82 to 88% for both reagents (entries 6 and 14).

When the cross-couplings were done in EtOAc and under Ar the yields for Mg salt containing reagents **6** and **7** increased to 91% and 85%, respectively (entries 3 and 7). However, the yield dropped slightly for both reagents when the reaction was done in air in non-dried glassware (entries 4 and 8). Remarkably when no Mg salt was present, cross-coupling did not work at all, no matter if it was performed under Ar or in air (entries 11–12, 15, 16). As GC samples quenched with I_2 showed, the metal species **8** and **9** did not decompose when the reaction was performed under Ar and nor did the amount of electrophile decrease significantly. A longer reaction time and a higher catalyst loading did not lead to any improvements. However, for the reactions carried out in air, a slow decomposition of the metal species could be observed.

Table 2: Reactivity of zinc reagents **6–9** towards cross-coupling with 4-bromoanisole (**12**).

Entry	X	Solvent	Reaction conditions	Yield of isolated 13 [%]
1	$\text{Cl}\cdot\text{MgCl}_2\cdot\text{LiCl}$ (6)	THF	under Ar	85
2	$\text{Cl}\cdot\text{MgCl}_2\cdot\text{LiCl}$ (6)	THF	in air	77
3	$\text{Cl}\cdot\text{MgCl}_2\cdot\text{LiCl}$ (6)	EtOAc ^a	under Ar	91
4	$\text{Cl}\cdot\text{MgCl}_2\cdot\text{LiCl}$ (6)	EtOAc ^a	in air	78
5	$\text{Cl}\cdot\text{Mg}(\text{OPiv})_2\cdot\text{LiCl}$ (7)	THF	under Ar	82
6	$\text{Cl}\cdot\text{Mg}(\text{OPiv})_2\cdot\text{LiCl}$ (7)	THF	in air	88
7	$\text{Cl}\cdot\text{Mg}(\text{OPiv})_2\cdot\text{LiCl}$ (7)	EtOAc ^a	under Ar	85
8	$\text{Cl}\cdot\text{Mg}(\text{OPiv})_2\cdot\text{LiCl}$ (7)	EtOAc ^a	in air	81
9	$\text{Cl}\cdot\text{LiCl}$ (8)	THF	under Ar	86
10	$\text{Cl}\cdot\text{LiCl}$ (8)	THF	in air	81
11	$\text{Cl}\cdot\text{LiCl}$ (8)	EtOAc ^a	under Ar	trace ^[b,c]
12	$\text{Cl}\cdot\text{LiCl}$ (8)	EtOAc ^a	in air	trace ^[b,c]
13	$\text{OPiv}\cdot\text{LiOPiv}$ (9)	THF	under Ar	82%
14	$\text{OPiv}\cdot\text{LiOPiv}$ (9)	THF	in air	88%
15	$\text{OPiv}\cdot\text{LiOPiv}$ (9)	EtOAc ^a	under Ar	trace ^[b,c]
16	$\text{OPiv}\cdot\text{LiOPiv}$ (9)	EtOAc ^a	in air	trace ^[b,c]

[a] Purchased from Fluka in analytical grade (99.9%). EtOAc was stored in air and used without further drying. [b] Only GC analysis of hydrolyzed/iodolyzed reaction aliquots was performed; no product was isolated. [c] Reaction was also carried out with 6 mol% $\text{Pd}(\text{OAc})_2$ and 12 mol% DavePhos and the reaction time increased to 24 h.

In summary, combining RMgX (R = aryl, alkyl) with Zn(OPiv)₂ in THF solution gives the fully transmetalated products RZnX and Mg(OPiv)₂, which from NMR and ESI-mass spectrometric evidence seem to exist separately. Air exposure tests disclose that while (aryl)ZnCl reagents show inherently better stability towards air than (alkyl)ZnCl reagents,^[12] remarkably, Mg(OPiv)₂ can enhance this stability by mopping up OH⁻ or O²⁻ antagonists and capturing and holding on to H₂O molecules, making them less accessible for hydrolyzing C–Zn bonds.^[13] LiCl appears to show an opposite effect in reducing the stability of organozinc pivalate reagents presumably because LiCl is incorporated within the Zn structure (unlike Mg(OPiv)₂, which is separated from it) and thus brings H₂O molecules into close proximity to Zn–C bonds.

Experimental Section

Full experimental details are included in the Supporting Information. CCDC 953398 (1), 953399 (2), 953400 (3), 953401 (4), and 971345 (5) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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- [1] a) D. Seebach, A. K. Beck, A. Studer in *Modern Synthetic Methods* (Eds.: B. Ernst, C. Leumann), Wiley-VCH, Weinheim, **1995**, pp. 1–178; b) E. Juaristi, A. K. Beck, J. Hansen, T. Matt, T. Mukhopadhyay, M. Simson, D. Seebach, *Synthesis* **1993**, 12, 1271; c) M. Hatano, K. Ishihara in *Acid Catalysis in Modern Organic Synthesis, Vol. 1*, (Eds.: H. Yamamoto, K. Ishihara), Wiley-VCH, Weinheim, **2008**, pp. 175–182; d) M. Hatano, S. Suzuki, K. Ishihara, *J. Am. Chem. Soc.* **2006**, 128, 9998; e) M. Hatano, O. Ito, S. Suzuki, K. Ishihara, *Chem. Commun.* **2010**, 46, 2674; f) M. Hatano, S. Suzuki, K. Ishihara, *Synlett* **2010**, 321; g) M. Hatano, K. Ishihara, *Synthesis* **2008**, 1647; h) L. Jin, C. Liu, J. Liu, F. Hu, Y. Lan, A. S. Batsanov, J. A. K. Howard, T. D. Marder, A. Lei, *J. Am. Chem. Soc.* **2009**, 131, 16656; i) A. Metzger, S. Bernhardt, G. Manolikakes, P. Knochel, *Angew. Chem.* **2010**, 122, 4769; *Angew. Chem. Int. Ed.* **2010**, 49, 4665; j) E. Hevia, R. E. Mulvey, *Angew. Chem.* **2011**, 123, 6576; *Angew. Chem. Int. Ed.* **2011**, 50, 6448.
- [2] a) B. Haag, M. Mosrin, H. Ila, V. Malakhov, P. Knochel, *Angew. Chem.* **2011**, 123, 9968; *Angew. Chem. Int. Ed.* **2011**, 50, 9794; b) R. R. Kadiyala, D. Tilly, E. Nagaradja, T. Roisnel, V. E. Matulis, O. A. Ivashkevich, Y. S. Halauko, F. Chevallier, P. C. Gros, F. Mongin, *Chem. Eur. J.* **2013**, 19, 7944; c) K. Snégaroff, S. Komagawa, F. Chevallier, P. C. Gros, S. Golhen, T. Roisnel, M. Uchiyama, F. Mongin, *Chem. Eur. J.* **2010**, 16, 8191.
- [3] a) S. Bernhardt, G. Manolikakes, T. Kunz, P. Knochel, *Angew. Chem.* **2011**, 123, 9372; *Angew. Chem. Int. Ed.* **2011**, 50, 9205; b) C. I. Stathakis, S. Bernhardt, V. Quint, P. Knochel, *Angew. Chem.* **2012**, 124, 9563; *Angew. Chem. Int. Ed.* **2012**, 51, 9428; c) C. I. Stathakis, S. M. Manolikakes, P. Knochel, *Org. Lett.* **2013**, 15, 1302.
- [4] See the Supporting Information for full experimental details.
- [5] a) D. Li, C. Sun, P. G. Williard, *J. Am. Chem. Soc.* **2008**, 130, 11726; b) D. Li, R. Hopson, W. Li, J. Liu, P. G. Williard, *Org. Lett.* **2008**, 10, 909; c) G. Kagan, W. Li, R. Hopson, P. G. Williard, *Org. Lett.* **2009**, 11, 4818; d) D. Li, G. Kagan, R. Hopson, P. G. Williard, *J. Am. Chem. Soc.* **2009**, 131, 5627; e) D. R. Armstrong, P. G. Alvarez, A. R. Kennedy, R. E. Mulvey, J. A. Parkinson, *Angew. Chem.* **2010**, 122, 3253; *Angew. Chem. Int. Ed.* **2010**, 49, 3185; f) D. R. Armstrong, A. R. Kennedy, R. E. Mulvey, J. A. Parkinson, S. D. Robertson, *Chem. Sci.* **2012**, 3, 2700.
- [6] For 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.
- [7] Additional small signals were observed in the aromatic region, which can possibly be assigned to the minor presence of a biaryl side product; see the Supporting Information for ¹H DOSY NMR spectroscopy.
- [8] Substitutional disorder for Mg₂ was observed with an occupancy of 87 % for Mg₂ and 13 % for Zn₂, which is possibly due to the presence of an excess of Zn(OPiv)₂ in the reaction media.
- [9] A. Côté, A. B. Charette, *J. Am. Chem. Soc.* **2008**, 130, 2771.
- [10] J. E. Fleckenstein, K. Koszinowski, *Organometallics* **2011**, 30, 5018.
- [11] D. E. Irish, J. Semmler, N. J. Taylor, G. E. Toogood, *Acta Crystallogr. Sect. C* **1991**, 47, 2322.
- [12] The diminished sensitivity of Zn–C(aryl) bonds has been commented on: A. R. Katritzky, Z. Luo, *Heterocycles* **2011**, 55, 1467.
- [13] R. E. Mulvey, *Dalton Trans.* **2013**, 42, 6676.