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**Title:** The Role of LiBr and ZnBr2 on the Coupling of sp2-Hybridized Oxidative Addition Partners with sp3-Hybridized Organozincs

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COMMUNICATION

# The role of LiBr and $ZnBr_2$ on the cross-coupling of aryl bromides with $Bu_2Zn$ or BuZnBr.

Philip Eckert,[a] and Michael G. Organ*[a]

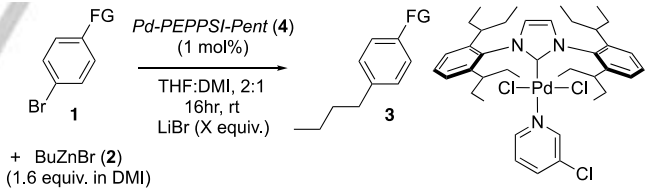
**Abstract:** The impact of LiBr and $ZnBr_2$ salts on the Negishi coupling of alkylZnBr and dialkylzinc nucleophiles with both electron-rich and electron-poor aryl electrophiles has been examined. Focusing only on the more difficult coupling of deactivated (electron-rich) oxidative addition partners, LiBr promotes coupling with BuZnBr, but does not have such an effect with $Bu_2Zn$. The presence of exogenous $ZnBr_2$ shuts down the coupling of both BuZnBr and $Bu_2Zn$, which has been shown before with alkyl electrophiles. Strikingly, the addition of LiBr to $Bu_2Zn$ reactions containing exogenous $ZnBr_2$ now fully restores coupling to levels seen without any salt present. This suggests that there is a very important interaction between LiBr and $ZnBr_2$. It is proposed that Lewis acid adducts are forming between $ZnBr_2$ and the electron-rich Pd(0) centre and the bromide from LiBr forms inorganic zincates that prevent the catalyst from binding to $ZnBr_2$. This idea has been supported by catalyst design as chlorinating the backbone of the NHC ring of *Pd-PEPPSI-IPent* to produce *Pd-PEPPSI-IPent*$^{Cl}$ catalyst now gives quantitative conversion, up from a ceiling of only 50% with the former catalyst.

Interest in the Negishi Reaction[1] has soared as more organozinc reagents have come available, in particular air-stabile versions,[2] as more catalysts have been invented that are especially adept at cross-coupling organozinc partners,[3] and as key mechanistic details have been elucidated that have helped broaden application through increased understanding.[4] Important to the last point is the key role that salts play in this Nobel Prize-winning transformation.[4e,5,6] Unnoticed, or perhaps just ignored for years, LiBr (or LiCl) is the natural byproduct of the Rieke protocol to make alkylzincs,[7] which remains the most common method used to prepare these reagents. Similarly, the same salts are also the byproduct of the preparation of sp2 hybridized organozincs that come from transmetallation (TM) of the corresponding organolithium or Grignard reagent.[8] The necessity of LiX or $MgX_2$ salts was not made clear until methods were developed to stringently remove them. When the Hou protocol[9] was used to eliminate LiX formation, alkyl-alkyl (sp3-sp3) couplings were shown to go from rapid, quantitative transformations to no reaction at all.[4c,6] In the case of aryl-aryl couplings, diarylzinc reagents were found not to have a reliance on the presence of alkali salts whereas with arylzinc halides (ArZnX) they were again shown to be essential for any coupling whatsoever.[6c]

With RZnX structured reagents we have argued that LiX has a significant impact on the structure of the organozinc in solution, be it through the formation of zincates[4c,6a,b] and/or alterations in the aggregation state of the organozinc,[6c] and this markedly impacts the coupling at the TM stage with our Pd-NHC (N-heterocyclic carbene) coupling system. We have shown that *Pd-PEPPSI* catalysts are able to couple organolithium reagents at -78 ºC, which shows the very high reactivity of these complexes.[10] The corresponding Negishi couplings with otherwise identical substrates and reaction conditions could be done as low as -20 ºC, but no lower.[8,11] This illustrates that oxidative addition (OA) and reductive elimination (RE) are indeed very rapid process for bulky *Pd-PEPPSI* catalysts and suggests that the rate-limiting step of the process involves the organometallic, at least when NHC ligands are employed. Again, this points to a likely and significant involvement of the salts at the TM stage of the catalytic cycle.

The TM of an alkyl group is known to be intrinsically more difficult that the corresponding sp2 hybridized carbon fragment.[12] In the case of our sp3-sp3 coupling, TM is doubly difficult as the OA partner is also alkyl and therefore electron-donating making the OA intermediate less electrophilic and less able to undergo TM.[4c,6] This is why we believe that LiX salt is so critical to enhancing the nucleophilicity of the alkylzinc halide, thereby helping to facilitate TM. We envisioned that if instead we focused on the OA partner and enhanced its electrophilicity, then the need for the LiX salt might diminish, if not disappear. One way to do that is to use aryl bromides, which are intrinsically electron-poor, where the electronics can be tuned further (i.e., Hammett-type analysis) without a significant alteration in the physical footprint.

**Table 1.** Negishi Coupling of BuZnBr with arylbromides with, and without, LiBr.




| Entry 1 (compound) | FG | Percent Conv. No LiBr[a] | Percent Conv. 3.2 equiv. LiBr[a] |
|---|---|---|---|
| 1 (**3a**) | $NO_2$ | 93 | 98 |
| 2 (**3b**) | CHO | 88 | 90 |
| 3 (**3c**) | $COCH_3$ | 82 | 86 |
| 4 (**3d**) | $CO_2CH_3$ | 96 | 92 |
| 5 (**3e**) | H | 60 | 72 |
| 6 (**3f**) | $OCH_3$ | 28 | 65 |
| 7 (**3g**) | $N(CH_3)_2$ | trace | 25 |

[a] Percent conversion was determined by $^1$H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Experiments were carried out in duplicate and the average result is reported.

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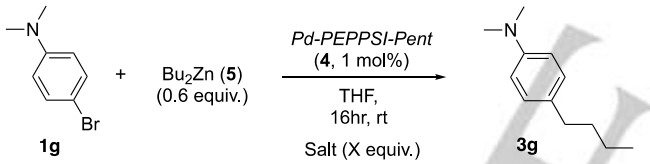
In our initial experiments, salt-free BuZnBr was prepared using the Hou protocol[9] and reacted with a series of aryl bromides (Table 1). Whereas alkylzinc reagents experienced zero coupling with alkyl electrophiles until at least 1.0 equivalents of LiBr was present,[4c,6] bromobenzene could be coupled to 60% conversion without any LiBr added (entry 5).[13] When electron-poor electro-philes were examined, all gave excellent conversion without LiBr, which did improve slightly when it was added (entries 1-5). In the case of electron-donating groups, conversion without salt was low (entry 6) or non-existent (entry 7), yet when LiBr was added a dramatic increase in conversion was observed in all cases.

If an argument can be made that the LiBr is enhancing the nucleophilicity of the organozinc reagent as we have suggested previously,[4c,6] and this is why we see such a stark increase in conversion in entries 5-7 in Table 1, we should expect to see a similarly dramatic increase in conversion simply by constructing a more electron-rich organozinc reagent. Indeed, when we prepared dibutylzinc ($Bu_2Zn$ (**5**)), freshly distilled) and reacted it with **1g**, a poorly reactive OA partner, under similar conditions to those used in Table 1, 50% conversion was attained without any LiBr (Table 2, Series 1, Entry a). Interestingly, now adding any amount of this salt (0.3 – 1.2 equiv., series 1, entries b-e) did not further increase conversion. Even 3.2 equivalents of LiBr made no difference (series 1, entries f).

**Table 2.** Impact of LiBr and $ZnBr_2$ on Negishi Coupling using $Bu_2Zn$ nucleophile and 4-bromo-*N,N*-dimethylaniline (**1g**).[a]




| | | Entry (Equivalents of Salt Employed) | | | | | |
|---|---|---|---|---|---|---|---|
| Series | Salt | a (0) | b (0.3) | c (0.6) | d (0.9) | e (1.2) | f (3.2) |
| 1 | LiBr | 50[b] | 50 | 49 | 52 | 50 | 43 |
| 2 | $ZnBr_2$ | 50[b] | 39 | 20 | 13 | 10 | - |

[a] Percent conversion to **3g** was determined by $^1$H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Experiments were carried out in duplicate and the average result is reported. [b] Under otherwise identical reaction conditions, 1.0 equivalents of $Bu_2Zn$ led to 55% conversion.

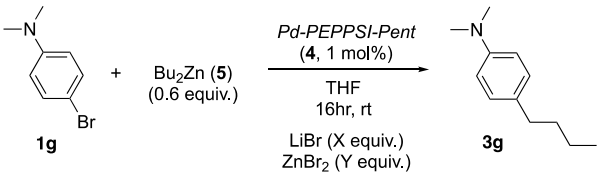
Since both butyl groups could be transferred there could/should have been full conversion to **3g** with only 0.6 equiv. of $Bu_2Zn$. This raised the question as to whether the Schlenk equilibrium was active under our coupling conditions. That is, without LiBr, BuZnBr may not be active enough to couple with a deactivated OA partner (e.g., Table 1, Entry 7), and $Bu_2Zn$ is not forming in these runs so no coupling takes place. Conversely, if only $Bu_2Zn$ is able to react (in the absence of LiBr) when it is all consumed there is nothing left that is competent to couple, so the reactions halts near 50% conversion. When we increased the amount of $Bu_2Zn$ to 1.0 equiv., there was only ~5% increase in conversion (Table 2, Footnote [b]). This implies that the mechanism is more involved when poorly reactive OA partners, such as **1g**, are employed.

The impact of salts on the coupling of $Bu_2Zn$ was next evaluated. Interestingly, whereas adding LiBr had a major effect on BuZnBr, it failed to move coupling beyond the 50% conversion that was attained in its absence. In fact, increasing equivalence of the salt from 0.3 to 1.2 did not statistically alter conversion at all (Table 2, Series 1, Entry a vs. Entries b-e). Conversely, when $ZnBr_2$ was added to the transformation in increasing amounts, coupling was proportionally reduced (Table 2, Series 2, Entry a vs. Entries b-e). There are two possible explanations for this result. The increasing amounts of $ZnBr_2$ could allow the Schlenk equilibrium to become active and more BuZnBr forms but it is not capable of coupling with such a deactivated electrophile and conversion plummets.[4-6] Alternatively, $ZnBr_2$ is certainly more Lewis acidic than LiBr and can bind to the reduced Pd(0) strongly enough following RE to poison it in an off-cycle resting state.[14]

In the case of $Bu_2Zn$, neither LiBr nor $ZnBr_2$ (both natural byproducts of making the organometallic and the coupling, respectively) seem to help the transformation. Structurally and functionally, these two salts are quite different. LiBr has significant, often overlooked Lewis basic behaviour through the halide as a consequence of a looser ion pair with the low electronegativity lithium ($\chi$ = 1.0). Conversely, the more electronegative zinc ($\chi$ = 1.6) creates a tighter metal-halide bond and the Lewis acidic properties of zinc dominate for the salt as a whole.

We wondered if LiBr and $ZnBr_2$, might interact in some way to exert either a positive or negative influence over the coupling (Table 3). With no LiBr added we are reminded of the increasingly negative impact of the presence of exogenous $ZnBr_2$ as conversion drops from 39 to 13 percent as the amount of this salt is increased from 0.3 to 0.9 equivalents (Series 1-3, Entry a). Strikingly, when equi-molar or slightly higher amounts of LiBr were added to the reaction mixtures containing $ZnBr_2$ cross-coupling was restored to the level seen with no salt at all (Series 1-3, Entries d and e compared with Table 2, entry a).

**Table 3.** Impact of adding LiBr and $ZnBr_2$ together on Negishi Coupling using $Bu_2Zn$ nucleophile with 4-bromo-*N,N*-dimethylaniline.[a]




| | | Entry (LiBr Equivalents Used) | | | | |
|---|---|---|---|---|---|---|
| | | a (0) | b (0.3) | c (0.6) | d (0.9) | e (1.2) |
| Series (ZnBr Equiv. Used) | 1 (0.3) | 39 | 49 | 48 | 52 | 61 |
| | 2 (0.6) | 20 | 37 | 38 | 46 | 49 |
| | 3 (0.9) | 13 | 23 | 30 | 36 | 44 |

[a] Percent conversion was determined by $^1$H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Experiments were carried out in duplicate and the average result is reported.

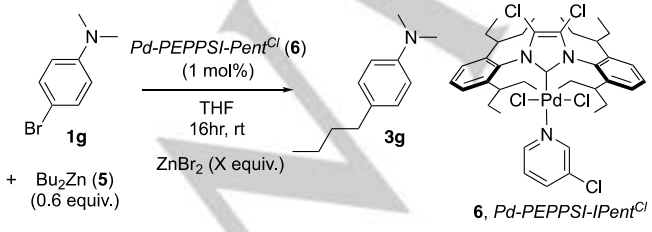
That LiBr failed to improve conversion of the dialkylzinc nucleophile in the absence of $ZnBr_2$, but so profoundly increased conversion when $ZnBr_2$ was present, suggests that the most important interaction of LiBr is not with $Bu_2Zn$, which may be different in the case of BuZnBr, but rather with $ZnBr_2$. We propose that the Lewis basic bromide ion coordinates to $ZnBr_2$ to form $LiZnBr_3$ and/or possibly $Li_2ZnBr_4$. This eliminates the Lewis acidic nature of zinc by strong coordinative saturation of the metal centre. A related hypothesis has been proposed by Koszinowski using a Pd S-PHOS complex.[4e] If this situation is operative, we envisioned that we could incorporate catalyst design elements to aid in circumventing poisoning.

Chlorinating the backbone of *Pd-PEPPSI-IPent* to produce *Pd-PEPPSI-IPent$^{Cl}$* (**6**) has been shown to profoundly accelerate the rate of cross-coupling in general,[15] while at the same time improving selectivity in the coupling of secondary alkyl nucleophiles.[16] The dramatic improvements in these reaction attributes were ascribed to electronic and steric influences of the chlorines.[15,16] N-heterocyclic carbene (NHC) ligands are among the strongest σ donators making the metal centre quite electron rich.[17] While this is beneficial for OA, it makes TM and RE more difficult. It also renders the metal more susceptible to Lewis acids, such as $ZnBr_2$,[14] so chlorinating the NHC reduces the Lewis basic nature of Pd(0),[16,17] thereby making it less susceptible to poisoning.

From a steric perspective, chlorinating the NHC backbone forces the N-aryl substituents in toward the metal, which was shown to be the primary reason for selectivity in the aforementioned selective secondary alkyl cross-coupling reactions.[16] In that case, pushing the aryl groups forward hindered the formation of the 4-centred transition state necessary for β-hydride elimination that is necessary for migratory insertion leading to isomerization, while at the same time driving RE, a 3-centred transition state. Perhaps, sterically, this might disfavour the ability of $ZnBr_2$ from binding to Pd(0). Taken together, chlorinating the NHC core should aid in resisting poisoning, both sterically and electronically.

When *Pd-PEPPSI-IPent$^{Cl}$* (**6**) was substituted for *Pd-PEPPSI-IPent* (**4**) consumption of **1g** was now quantitative with 80% conversion to **3g** (Table 4, Entry a), up from 50% with **4** (Table 2, Series 1, Entry a). Consistent with the developing hypothesis above, when $ZnBr_2$ was added in increasing amounts (Table 4, Entries b-d) conversion to **3g** slightly decreased whereas when the same amounts of this salt were added to the reaction with **4**, conversion dropped by a factor of four (Table 2, Series 2).

**Table 4.** Influence of NHC backbone chlorination of *Pd-PEPPSI-IPent* (to create *Pd-PEPPSI-IPent$^{Cl}$* (**6**)) on the negative impacts of $ZnBr_2$ in the Negishi Coupling of $Bu_2Zn$ nucleophile (**5**) with 4-bromo-*N,N*-dimethylaniline (**1g**).[a]




| Entry ($ZnBr_2$ Equivalents Employed) | | | |
|---|---|---|---|
| a (0) | b (0.3) | c (0.6) | d (0.9) |
| 80 | 77 | 69 | 60 |

[a] Percent conversion was determined by $^1$H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Experiments were carried out in duplicate and the average result is reported.

In this manuscript we have shown that LiBr has a profound effect on the coupling of alkylZnBr nucleophiles with deactivated (electron-rich) aryl OA partners, but its role is less important with activated (electron-deficient) ones. We propose that in this case, like with alkyl OA partners that we have investigated in the past,[4c,6a,6b] that alkyl zincates are again forming with LiBr that are necessary to help drive TM. If the OA arene is electron-poor, this makes Pd more electron-deficient and this helps to drive TM and LiBr is much less important.

Dialkylzincs, which are now much more nucleophilic than alkylZnBr, might be anticipated to undergo TM more readily with the deactivated (electron-rich) OA partners. Indeed, this is what we observed; whereas **1g** did not react at all with BuZnBr (**2**), it reacted to 50% conversion with $Bu_2Zn$. Interestingly, now the addition of LiBr had zero impact on conversion. When $ZnBr_2$ was added to the reaction with **1g** with $Bu_2Zn$ (**5**), coupling plummeted. However, the addition now of LiBr, which initially had no impact, restored full coupling in the presence of $ZnBr_2$ to levels seen when no salt was present at all.

The fact that $Bu_2Zn$ couplings see no benefit upon the addition of LiBr, but shows dramatic improvement when $ZnBr_2$ is in the mixture points to a different, or at least an additional, important role. We propose this role is to coordinatively saturate $ZnBr_2$, a Lewis acid that can bind to the electron-rich NHC-Pd(0) centre, thereby helping to keep the catalyst on cycle. In support of this, when we modified the catalyst with two chlorines on the back of the NHC ring, coupling dramatically increased (still in the absence of any LiBr). One can argue that the chlorines withdraw electron density away from Pd(0) making it less basic. In addition, there in now an increased steric presence in the coordination sphere of the metal as repulsion between the chlorines and N-aryl substituents on the NHC force these two rings toward Pd. Together these two features disfavour binding to $ZnBr_2$, thus avoiding the formation of off-cycle resting states.

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**Keywords:** PEPPSI • Negishi coupling • salt effect • catalyst poisoning

[1] A. O. King, N. Okukado, E.-i. Negishi, *J. Chem. Soc. Chem. Commun.*, **1977**, 683-684.

[2] S. Bernhardt, G. Manolikakes, T. Kunz, P. Knochel, *Angew. Chem. Int. Ed.* **2011**,*50*, 9205-9209.

[3] a) E. Gioria, J. M. Martínez-Ilarduya, P. Espinet, *Organometallics* **2014**, *33*, 4394−4400; b) J. E. Milne, S. L. Buchwald, *J. Am. Chem. Soc*. **2004**, *126*, 13028-13032 ; c) Valente, C.; Çalimsiz, S.; Hoi, K. H.; Mallik, D.; Sayah, M.; Organ, M. G. *Angew. Chem*. **2012**, *124*, 3370–3388 (*Angew. Chem. Int. Ed*. **2012**, 51, 3314-3332).

[4] a) Z. Huang, M. Qian, D. J. Babinski, E. Negishi, *Organometallics* **2005**, *24*, 475–478; b) J. A. Casares, P. Espinet, B. Fuentes, G. Salas, *J. Am. Chem. Soc.* **2007**, *129*, 3508-3509; c) G. T. Achonduh, N. Hadei, C. Valente, S. Avola, C. J. O'Brien, M. G. Organ, *Chem. Commun*. **2010**, *46*, 4109-4111; d) A. González-Põrez, R. Álvarez, O. N. Faza, A. R. de Lera, J. M. Aurrecoechea, *Organometallics* **2012**, *31*, 2053–2058, e) K. Böck, J. E. Feil, K. Karaghiosoff, K. Koszinowski, *Chem. Eur. J.* **2015**, *21*, 5548-5560.

[5] a) M. A. Schade, J. E. Fleckenstein, P. Knochel, K. Koszinowski, *J. Org. Chem.* **2010**, *75*, 6848–6857; b) A. Hern.n-Gûmez, E. Herd, E. Hevia, A. R. Kennedy, P. Knochel, K. Koszinowski, S. M. Manolikakes, R. E. Mulvey, C. Schnegelsberg, *Angew. Chem*. **2014**, *126*, 2744–2748 (*Angew. Chem. Int. Ed*. **2014**, *53*, 2706–2710).

[6] a) H. N. Hunter, N. Hadei, V. Blagojevic, P. Patschinski, G. T. Achonduh, S. Avola, D. K. Bohme, M. G. Organ, *Chem. Eur. J.* **2011**, *17*, 7845–7851; b) L. C. McCann, H. N. Hunter, J. A. C. Clyburne, M. G. Organ, Angew. Chem. 2012, 124, 7130-7133 (*Angew. Chem. Int. Ed*. **2012**, *51*, 7024–7027); c) McCann, L. A.; Organ, M. G. *Angew. Chem.* **2014**, *126*, 4475-4478 (*Angew. Chem. Int. Ed.* **2014**, *53*, 4386-4389).

[7] R. D. Rieke, M. V. Hanson, J. D. Brown, *J. Org. Chem.,* **1996**, *61*, 2726–2730; (b) L. Zhu, R. M. Wehmeyer, R. D. Rieke, *J. Org. Chem*., **1991**, *56*, 1445–1453.

[8] S. Çalimsiz, M. Sayah, D. Mallik, M. G. Organ, *Angew. Chem.* **2010**, *122*, 2058–2061 (*Angew. Chem. Int. Ed.* **2010**, *49*, 2014–2017).

[9] S. Huo, *Org. Lett.,* **2003***, 5*, 423-425.

[10] N. Sinha, D. Heijnen, B. L. Feringa, M. G. Organ, *Chem. Eur. J.* **2019**, 25, 9180 – 9184

[11] N. Sinha, P. A. Champagne, M. J. Rodriguez, Y. Lu, M. E. Kopach, D. Mitchell, M. G. Organ, *Chem. Eur. J.* **2019**, *25*, 6508-6512.

[12] V. Farina, X. Krishnan *J. Am. Chem. Soc.* **1991**, *113*, 9585-9595.

[13] As a control, the Pd catalyst was omitted from the transformations in Table 1. Only **3a** containing a nitro group showed background conversion when no Pd was used (~30% conversion).

[14] a) R. Álvarez, A. R. De Lera, J. M. Aurrecoechea, A. Durana, *Organometallics* **2007**, *26*, 2799-2802; b) G. A. Chass, C. J. O'Brien, N. Hadei, E. A. B. Kantchev, W.-H. Mu, D.-C.Fang, A. C. Hopkinson, I. G. Csizmadia, M. G. Organ, M. G. *Chem. Eur. J.* **2009**, *15*, 4281-4288; c) M. G. Organ, G. A. Chass, D.-C. Fang, A. C. Hopkinson, C. Valente, *Synthesis* **2008**, 2776-2797.

[15] a) S. Sharif, R. P. Rucker; N. Chandrasoma, D. Mitchell, M. J. Rodriguez, M. Pompeo, R. D. J. Froese, M. G. Organ, *Angew. Chem.* **2015**, *127*, 9643–9647 (*Angew. Chem. Int. Ed.* **2015**, *54*, 9507-9511); b) M. Pompeo, J. L. Farmer, R. D. J. Froese, M. G. Organ, *Angew. Chem.* **2014**, *126*, 3287-3290 (*Angew. Chem. Int. Ed.* **2014**, *53*, 3223-3226); c) C. Valente, M. Pompeo, M. Sayah, M. G. Organ, *Org. Proc. Dev. Res.* **2014**, *18*, 180-190; d) M. Sayah, M. G. Organ, *Chem. Eur. J.* **2013**, *19*, 16196-16199; e) K. H. Hoi, J. A. Coggan, M. G. Organ, *Chem. Eur. J.* **2013**, *19*, 843–845; e) M. Sayah, A. Lough, M. G. Organ, *Chem. Eur. J.* **2013**, *19*, 2749-2756; f) C. Valente, S. Çalimsiz, K. H. Hoi, D. Mallik, M. Sayah, M. G. Organ, *Angew. Chem.* **2014**, *126*, 3287-329 (*Angew. Chem. Int. Ed.* **2012**, *51*, 3314-3332).

[16] a) B. Atwater, N. Chandrasoma, D. Mitchell, M. J. Rodriguez, M. Pompeo, R. D. J. Froese, M. G. Organ, *Angew. Chem.* **2015**, *127*, 9638–9642 (*Angew. Chem. Int. Ed.* **2015**, *54*, 9502 –9506); b) B. Atwater, N. Chandrasoma, D. Mitchell, M. J. Rodriguez, M. G. Organ, *Chem. Eur. J.* **2016,** *22*, 14531-14534; c) M. Pompeo, R. D. J. Froese, N. Hadei, M. G. Organ, *Angew. Chem.* **2012**, *124*, 11516-11519 (*Angew. Chem. Int. Ed.* **2012**, *51*, 11354 –11357)

[17] R. A. Kelly III, H. Clavier, S. Giudice, N. M. Scott, E. D. Stevens, J. Bordner, I. Samardjiev, C. D. Hoff, L. Cavallo, S. P. Nolan, *Organometallics* **2008**, *27*, 202–210.

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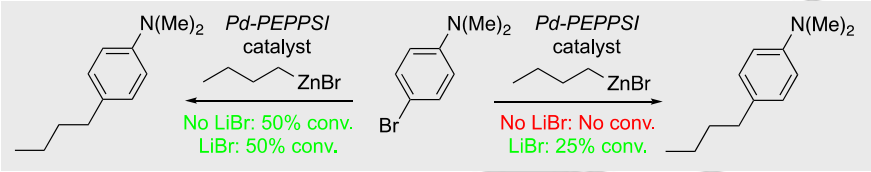


*Philip Eckert and Michael G. Organ**

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**The role of LiBr and $ZnBr_2$ on the cross-coupling of aryl bromides with $Bu_2Zn$ or BuZnBr**

Butylzinc bromide requires LiBr to cross-couple with alkylbromides, presumably to form zincates to enhance transmetallation given the electron richness (deactivation) of the electrophile. Here we show that butylzinc bromide will couple with electron poor (activated) arylbromides without salt, but will not couple electron-rich ones until salt is added. Dibutylzinc, a more powerful nucleophile, now couples deactivated aryl bromides without LiBr and adding the salt fails to further enhance conversion.