RZnI vs. R_2Zn in Pd(0)-catalyzed cross-coupling reactions with thioimidates[1]

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Abstract: Thioimidates **1**-*Z* undergo facile cross-coupling with Pd(0)–RZnI but are inert to Pd(0)–R_2Zn. This difference is due to the lower Lewis acidity of R_2Zn, as opposed to lower nucleophilicity. Various sources of RZnI (R = Me, Et) and Pd(0) were evaluated for their convenience and reactivity.

Key words: thioimidates, cross-coupling, dialkylzincs, alkylzinc iodides.

Résumé : Les thioimidates (**1**-*Z*) donnent facilement des réactions de couplages croisés avec le Pd(0)–RZnI, mais ils sont inertes vis-à-vis du Pd(0)–R_2Zn. Cette différence est attribuée à l'acidité de Lewis plus faible du R_2Zn plutôt que d'un caractère nucléophile plus faible. On a évalué diverses sources de RZnI (R = Me, Et) pour leur facilité d'accès et leur réactivité.

Mots clés : thioimidates, couplage croisé, dialkylzinc, iodures d'alkylzinc.

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Introduction

Recently we described an unusual reactivity pattern of *E*- and *Z*-thioimidates **1**-*E,Z*, which undergo Pd(0)-catalyzed cross-coupling with alkyl zinc iodides at markedly different rates (Scheme 1) (1). Thioimidates **1**-*Z* were cleanly converted to imines **3**-*Z* using Pd(0)–RZnI, while the geometric isomers **1**-*E* were inert (R = Me, Et). This difference was traced to a previously unrecognized activating effect of RZnI and other Lewis acids, which serve to polarize the thioimidate C—S bond by complexing with the imidate nitrogen. NMR studies showed that the reactive *Z*-isomers readily coordinate Zn(II), most likely as η^1- or η^5-chelates (cf. **2**-*Z*) (2*a*, 2*b*). In either geometry, oxidative addition to Pd(0) is facilitated by the increased electrophilicity of the C—S bond. In contrast, Zn(II) chelation is not possible with **1**-*E*, and simple imine complexes of type **2**-*E* are sterically disfavored.[3] In the absence of such activation, oxidative addition does not occur, even with stoichiometric Pd(0). Cross-coupling to afford **3**-*E* therefore fails. Interestingly, however, addition of the smaller (and harder) Lewis acid BF_3 efficiently catalyzed the conversion of **1**-*E* to **3**-*E* when B = H. These conditions were also effective with other systems previously regarded as unreactive (2*c*).

In ongoing studies we have evaluated a number of procedures for preparing RZnI (R = Me, Et) (3). One of the most widely employed methods involves transmetallation of Grignard reagents with ZnI_2 (eq. [1], R = Me, Et) (4).

$$[1]\qquad RMgBr + ZnI_2 \longrightarrow RZnI + MgBrI$$

However, in our hands this reaction gave RZnI of relatively low reactivity. For example, MeZnI prepared by this route reacted sluggishly with **1**-*Z* when E = CO_2t-Bu and not at all when E = CHO (in general, the formyl derivatives of **1**-*Z* are slightly less reactive toward cross-coupling).[4] More satisfactory results were obtained following eq. [2] (R = Me, Et), involving oxidative addition of RI to activated Zn (5).

$$[2]\qquad RI + Zn \longrightarrow RZnI$$

Both MeZnI and EtZnI prepared in this manner were consistently more reactive, regardless of the substitution pattern of **1**-*Z* (E = CO_2t-Bu, CHO; B = H, Me, Ph). However, we also experienced a number of drawbacks to this procedure, which requires activation of Zn with 1,2-dibromoethane and trimethylsilyl chloride (5*b*–5*d*). In addition, one has to guard against competitive Wurtz coupling, and the RZnI must be prepared fresh before every reaction. Equation [3] (R = Me, Et) takes advantage of the Schlenk equilibrium between

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Dedicated to Professor Edward Piers, in appreciation of his seminal contributions to synthetic organic chemistry and chemical education.

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[3] Detailed NOE and X-ray studies showed that the imidate nitrogen in **1**-*E* is sterically shielded by the flanking S-Me and C-5-alkyl groups.

[4] Regardless of the method of preparation, we consistently found MeZnI to be less reactive than EtZnI.

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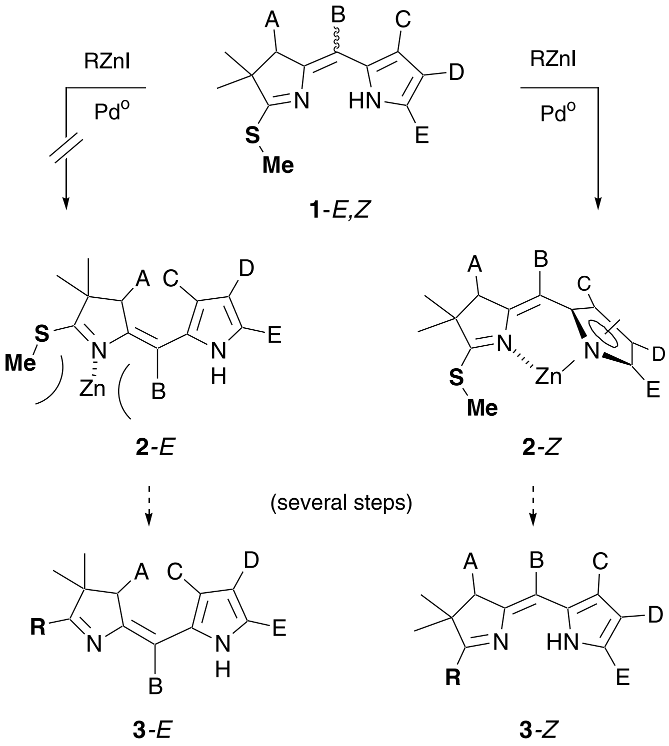
Scheme 1.



R_2Zn and ZnI_2, which Abraham and Rolfe (6) showed lies far to the right in polar solvents such as THF.

[3] $R_2Zn + ZnI_2 \rightleftarrows 2RZnI$

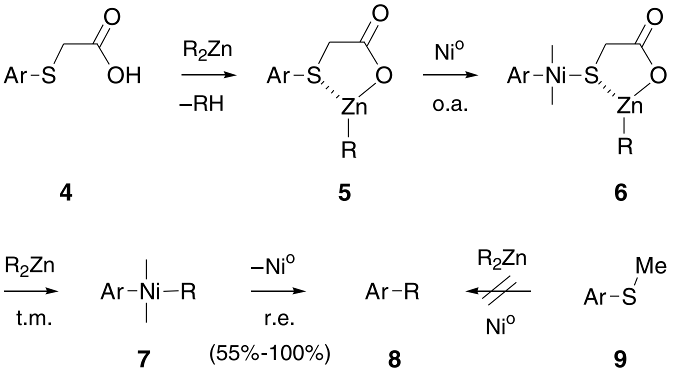
In general, this procedure worked well, but for reproducible results the ZnI_2 had to be freshly sublimed. By far the most convenient procedure for generating RZnI of uniform reactivity was the method of Charette and co-workers (eq. [4], R = Me, Et) (7).

[4] $R_2Zn + I_2 \longrightarrow RZnI + RI$

This method takes advantage of the nucleophilic character of R_2Zn and its ability to effect substitution on I_2. Among other advantages, displacement is carried out at –40 °C and is complete within minutes. Furthermore, both Me_2Zn and Et_2Zn are commercially available and relatively stable.

With a reliable means of preparing RZnI, we explored the effect of various Pd catalysts on converting **1**-*Z* to **3**-*Z* (cf. Scheme 1). Hayashi et al. (8) reported that dichloro[1.1′-bis-(diphenylphosphino)ferrocene]palladium(II) [($PdCl_2$(dppf)] was particularly effective in coupling *n*- and *sec*-BuZnCl with bromobenzene. The efficacy of $PdCl_2$(dppf) was ascribed to its large P-Pd-P bond angle, which presumably accelerates reductive elimination. In our case, however, we observed no significant advantage of $PdCl_2$(dppf) over a number of simpler homogeneous catalysts.[5] Perhaps the most convenient catalyst system tested was heterogeneous Pd–C, which has recently been employed in a number of related cross-coupling reactions (9). Although not quite as reactive as homogeneous PdL_4, Pd–C gave yields of imines **3**-*Z* in the range of 70%.

Scheme 2.



Given the ready availability of Me_2Zn and Et_2Zn (vide supra), it was of interest to examine the cross-coupling of these species with thioimidates **1**-*Z*. In contrast to the case with RZnI (5*c*), there are only scattered reports of transition-metal-catalyzed coupling of dialkylzincs R_2Zn with thioorganics. The most notable of these stem from the elegant studies of Liebeskind and co-workers (10),[6] who showed that thioglycolic acids **4** are excellent substrates for coupling with both RZnI and R_2Zn (Scheme 2). However, these examples represent a special case, since strong Zn-chelation assists both oxidative addition (o.a.) and subsequent transmetalation (t.m.). Under identical conditions, thiomethyl derivatives **9** are essentially inert.

In the present work we observed a dramatic difference in reactivity between RZnI and R_2Zn (R = Me, Et). As noted above, Pd(0)-catalyzed cross-coupling of thioimidates **1**-*Z* with RZnI occurred readily to give high yields of the corresponding imines **3**-*Z* (Scheme 1). In contrast, salt-free Me_2Zn and Et_2Zn failed to react under Pd(0) catalysis[7] and gave only trace amounts of **3**-*Z* when more reactive Ni catalysts were used (10).[6] The reasons for this difference were unclear. Previously we showed that the conversion of thioimidate **1**-*Z* to imine **3**-*Z* using Pd(0)–RZnI requires five steps, involving a minimum of 3 equiv. of RZnI for complete cross-coupling (Fig. 1) (1). Two equivalents are taken up in complexation (steps **1** and **3**), while the third is the source of RZnI for intermolecular transmetalation (step **4**) (10*a*). It seemed unlikely that the rate of reductive elimination (step **5**) would be greatly effected by a change from EtZnI to Et_2Zn. Therefore, we focused our attention on steps **1**–**4**, substituting R_2Zn for RZnI.

It was tempting to attribute this failure to a difference in nucleophilicity between RZnI and R_2Zn, which could have a significant impact on transmetallation (step **4**). However, there is some indication that dialkylzincs are at least as reactive as alkylzinc halides toward simple electrophiles (4). In one experiment we compared the relative rates of addition of

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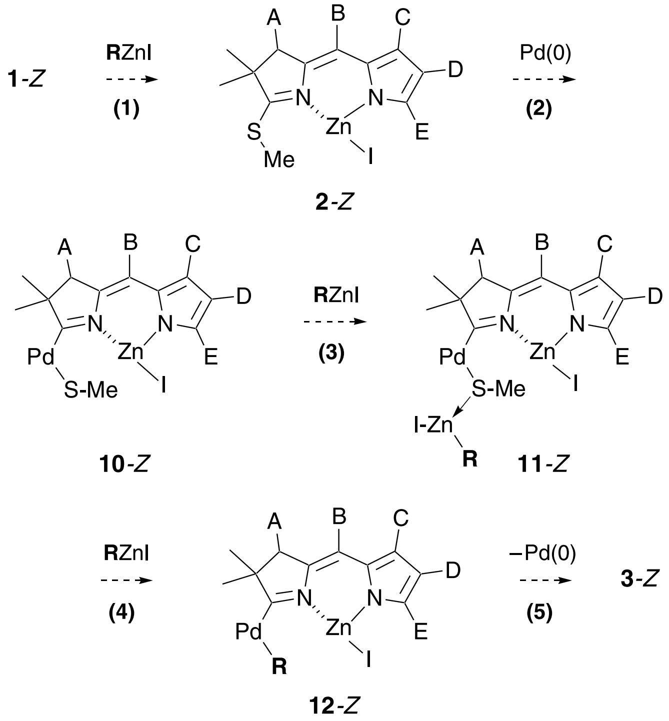
[5] Including, among others, $PdCl_2(PPh_3)_4$, $Pd(PPh_3)_4$, and $Pd_2(dba)_3$–*tris*(2-furylphosphine).

[6] See ref. 5*c* for an additional example.

[7] Me_2Zn and Et_2Zn were purchased neat from Strem Chemicals, Inc., and as toluene solutions from Sigma-Aldrich Chemical Co.

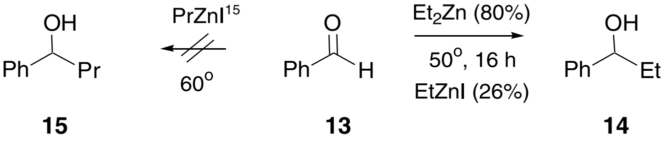
Fig. 1. Steps involved in conversion of thioimidates **1**-*Z* to imines **3**-*Z* using RZnI–Pd(0): (**1**) N-complexation with Zn; (**2**) oxidative addition; (**3**) S-complexation with Zn; (**4**) transmetalation; (**5**) reductive elimination.



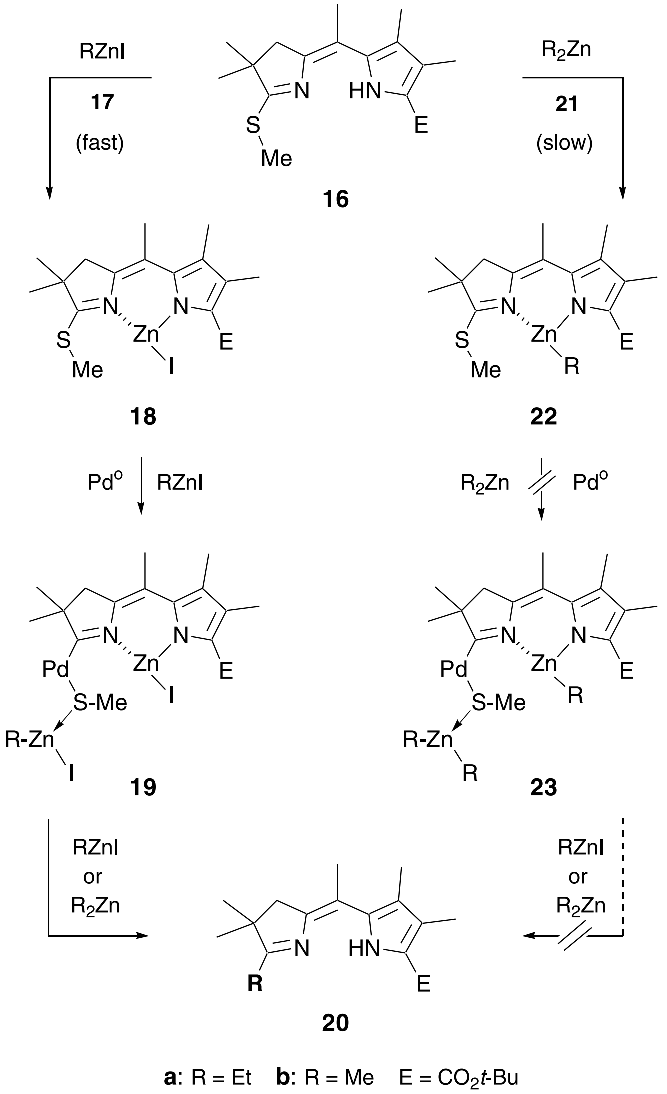
Et_2Zn and EtZnI to benzaldehyde. With Et_2Zn, GC analysis shows that the reaction is 80% complete after 16 h at 50 °C in THF–$PhCH_3$ (Scheme 3; see also Experimental section) (11).[8] During this same period, EtZnI reacts to the extent of 26%. Similar results have been found for PrZnI, which is reported to be unreactive at temperatures up to 60 °C (12).[9] In any event, both species are only weakly nucleophilic in the absence of added Lewis acids or bases (4).

A more likely possibility was that dialkylzincs are less effective activators for oxidative addition (step **2**) and (or) transmetalation (step **4**). Both processes require strong complexation with Zn (1, 10*a*). This argument finds support in the fact that dialkylzincs are generally poorer acceptors than alkylzinc iodides (i.e., weaker Lewis acids) (4, 13, 14). In both species, Zn has a low-lying, filled 3*d* shell, and its coordination chemistry is influenced mainly by electrostatic effects (14*b*). In alkylzinc iodides, the metal center is covalently bonded to an electronegative iodine atom, which renders Zn more electron deficient (13). Consequently, there is a strong driving force for coordination between alkylzinc iodides and Lewis bases (EtZnI exists as a coordination polymer in the solid state) (13). In contrast, dialkylzincs are bonded to two R groups, and Zn is less electron deficient. This is reflected in the fact that dialkylzincs are less prone to undergo association or complexation and always occur as monomers (14).

Scheme 3.



Scheme 4.



NMR studies demonstrated the difference in the complexing abilities of RZnI and R_2Zn with thioimidates of type **1**-*Z*. With thioimidate **16**, for example, addition of excess EtZnI (**17a**) effects immediate loss of the N-H proton and concomitant liberation of ethane (Scheme 4). The resulting Zn complex **18** readily undergoes oxidative addition to Pd(0) to afford **19a** and, ultimately, imine **20a** following transmetallation and reductive elimination. Under identical conditions, but employing Et_2Zn (**21a**), deprotonation and complexation of **16** requires several hours. At the end of this period, the resultant complex **22a** was treated with Pd(0), but little or no oxidative addition could be detected. These experiments were carried out with 6 equiv. of **21a** and stoichiometric Pd(0), which returned only unchanged **16**

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[8] See also ref. 4, p. 109.

[9] See also ref. 4.

upon quenching. It is worth noting that Zn complexes **18** and **22a** differ only in one ligand on Zn (I vs. Et). We believe it is the greater electron deficiency of Zn in **18** that provides the driving force for oxidative addition.

We performed a number of experiments to test this idea. Thioimidate **16** was first combined with 2 equiv. of Et_2Zn (**21a**) in THF–$PhCH_3$, and the resulting solution was allowed to stand at room temperature (RT) until complexation to give **22a** was complete. The reaction was then treated with catalytic Pd(0), and 1 equiv. of EtZnI (**17a**) was slowly added in the dark.[10] As expected based upon the pathway outlined in Scheme 4, we observed no formation of imine **20a**, since under these conditions oxidative addition to give **23a** does not occur. However, when this sequence was reversed the results were markedly different. Treatment of **16** with 2 equiv. of EtZnI (**17a**) and catalytic Pd(0), followed by 1 equiv. of *either* EtZnI (**17a**) *or* Et_2Zn (**21a**) led to formation of imine **20a** at approximately the same rate. This demonstrates that once oxidative addition *and S*-complexation with RZnI to give **19a** occurs, transmetalation and reductive elimination are equally facile with RZnI or R_2Zn. Next, we carried out a crossover experiment using MeZnI (**17b**) and Et_2Zn (**21a**). In this case, treatment of **16** with 2 equiv. of MeZnI – catalytic Pd(0), followed by slow addition of Et_2Zn, gave almost exclusively imine **20a** (R = Et). Interestingly, it was necessary to carry out this experiment with strict exclusion of light. Roughly equal amounts of **20a** and **20b** were obtained if this precaution was not taken.[11]

These experiments left unanswered the question of whether the lower complexing ability of R_2Zn also impacted on transmetallation. That is, do **19** and **23** undergo transmetallation at different rates? As shown by Liebeskind and co-workers (10*a*), this step requires considerable weakening of the Pd—S bond. Some indication that this was a problem could be inferred from our early experiments with Ni catalysts and R_2Zn (vide supra), which also produced little or no cross-coupling product **3**-*Z*. In these examples, however, oxidative addition to Ni almost certainly occurred (10).[6] To explore this issue further, we treated **16** with 0.9 equiv. of EtZnI, followed by catalytic Pd(0) and 2 equiv. of Et_2Zn. Our reasoning was that there should be sufficient EtZnI to produce complex **18**, which in turn is activated toward oxidative addition. At this point, however, there would be insufficient EtZnI to further activate the Pd—S bond to transmetalation.[12] Any such activation would have to come from Et_2Zn. Under these conditions we saw only very slow formation of imine **20a** (much slower than when employing 3 equiv. of EtZnI under otherwise identical conditions).

Finally, we briefly explored the possibility of in situ activation of both Et_2Zn and Me_2Zn toward Pd(0)-catalyzed cross-coupling. In this regard we were particularly drawn to the studies of Chastrette and Amouroux (15), who showed that the nucleophilic properties of linear dialkylzincs are markedly increased by tetra-*n*-butylammonium halides (Bu_4NX), while still maintaining the strong acceptor character of Zn (14*b*). Properties of this type might facilitate oxidative addition and (or) transmetallation. However, these modifications were only marginally successful in our case. Inclusion of either Bu_4NI or Bu_4NCl with Me_2Zn–Pd(0) had a modest effect in cross-coupling experiments with thioimidate **16**, raising the yield of imine **20b** from 0% to ~30% (cf. Scheme 4). It is possible, however, that more powerful donors might have a greater impact on accelerating these reactions, and this merits further investigation.

Experimental section

Melting points were determined in open capillaries and are uncorrected. ^1H NMR spectra were recorded at 300, 400, or 500 MHz and are expressed as parts per million (ppm) downfield from tetramethylsilane. All reactions were carried out in oven-dried glassware under an inert atmosphere of nitrogen or argon.

Formation of EtZnI

A flask containing 0.634 g (2.5 mmol) of iodine and 2.5 mL of THF was stirred at room temperature for 15 min to ensure that the iodine had completely dissolved. The solution was then cooled to –40 °C, and 2.5 mL (2.5 mmol, 1 equiv.) of 1 mol L^{-1} Et_2Zn in toluene was added in one portion. After an additional 5 min at –40 °C, the cold bath was removed, and the flask was allowed to warm to room temperature. This solution was then titrated against a freshly prepared 1 mol L^{-1} iodine-in-THF solution.

5-[1-(5-Ethyl-4,4-dimethyl-3,4-dihydro-pyrrol-2-ylidene)-ethyl]-3,4-dimethyl-1*H*-pyrrole-2-carboxylic acid *tert*-butyl ester (20a)

A solution of 25.0 mg (0.069 mmol) of thioimidate **16** and 4.8 mg (6.9 μmol, 0.1 equiv.) of $PdCl_2(PPh_3)_2$ in 1 mL of toluene was treated with 1.2 mL (0.414 mmol, 6 equiv.) of 0.4 mol L^{-1} EtZnI in THF–toluene (1:1) under argon. After stirring for 60 min at room temperature, the mixture was taken up in 5 mL of Et_2O, stirred for 10 min, and filtered through celite. To the filtrate was added 5 mL of saturated (sat'd) NH_4Cl, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with sat'd $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated to dryness under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc:hexanes = 1:9 to 1:5) to give 16 mg (70%) of the imine **20a** as an off-white solid. R_f (1:4 EtOAc:hexanes) 0.54. ^1H NMR (500 MHz, $CDCl_3$): 1.18 (s, 6H), 1.33 (t, *J* = 7.32, 3H), 1.57 (s, 9H), 2.11 (s, 2H), 2.18 (s, 3H), 2.29 (s, 3H), 2.42 (q, *J* = 7.32, 2H), 2.58 (s, 2H), 11.69 (br s, 1H). ^{13}C NMR (500 MHz, $CDCl_3$): 189.5, 161.36, 149.10, 132.16, 127.36, 119.06, 118.38, 114.26, 79.86, 47.83, 44.44, 28.87, 26.40, 22.19, 18.47, 11.73, 11.67, 10.54. HR-MS (FAB) calcd. for $C_{21}H_{32}N_2O_2$: 344.2464; found: 344.2543 ([M + H]). Anal. calcd. for $C_{21}H_{32}N_2O_2$: C 73.22, H 9.36, N 8.13; found: C 73.20, H 9.44, N 8.08.

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[10] Unless otherwise noted, the source of Pd(0) is $PdCl_2(PPh_3)_2$.

[11] The mechanism for this alkyl group exchange is unknown at present but may be related to the facile photoinduced synthesis of organozinc reagents recently described by Charette et al. (cf. ref. 7*b*).

[12] An alternative explanation is that oxidative addition to **18** requires activation by complexation of EtZnI at *both* the imidate N- and S-atoms. However, such a species would suffer prohibitive steric strain from the adjacent geminal dimethyl groups.

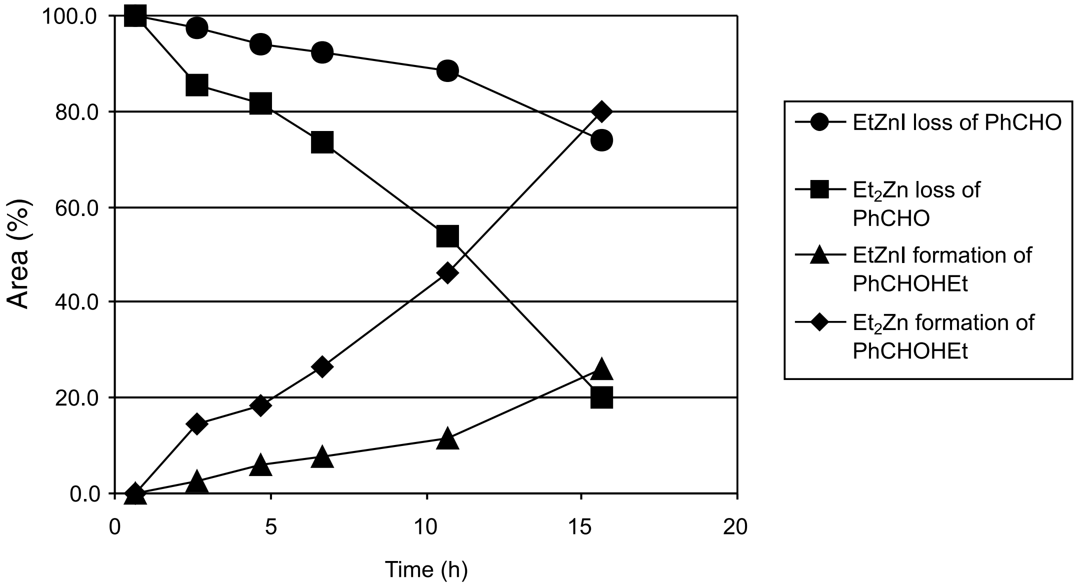

Fig. 2. The ratio of benzaldehyde to 1-phenyl-propan-1-ol.

Crossover experiment, 2 EtZnI + 1 Et_2Zn

A total of 10 mg (27.6 µmol) of thioimidate **16** was dissolved in 0.4 mL of toluene. To this was added 110 µL (55.2 µmol, 2 equiv.) of 0.5 mol L^{-1} EtZnI–THF, and the reaction was stirred at room temperature under argon. After stirring for 5 min, 2 mg (2.7 µmol, 0.1 equiv.) of $PdCl_2(PPh_3)_2$ was added, and the flask was purged with argon and wrapped in foil. After stirring for an additional 30 min, the reaction was checked by TLC, and no product was observed. At this time 28 µL (27.6 µmol, 1 equiv.) of 1 mol L^{-1} Et_2Zn in toluene was added dropwise over a period of 30 min. Monitoring of the reaction by TLC (1:9 EtOAc:hexanes) showed formation of **20a** after 30 min.

Crossover experiment, $2Et_2Zn$ + 1 EtZnI

A total of 10 mg (27.6 µmol) of thioimidate **16** was dissolved in 0.4 mL of toluene. To this was added 55 µL (55.2 µmol, 2 equiv.) of 1 mol L^{-1} Et_2Zn–THF, and the reaction was stirred at room temperature under argon. After stirring for 6 h to ensure complexation, 2 mg (2.7 µmol, 0.1 equiv.) of $PdCl_2(PPh_3)_2$ was added, and the flask was purged with argon and wrapped in foil. After an additional 30 min passed, the reaction was checked by TLC, and no products were observed. At this time, 55 µL (27.6 µmol, 1 equiv.) of 0.5 mol L^{-1} EtZnI in THF was added dropwise over 1 h. Monitoring of the reaction by TLC (1:9 EtOAc:hexanes) showed no formation of **20a**.

Crossover experiment, 2 MeZnI + $6Et_2Zn$

A solution of 10 mg (27.6 µmol) of thioimidate **16** in 0.4 mL of toluene was treated with 110 µL (55.2 µmol, 2 equiv.) of 0.5 mol L^{-1} MeZnI–THF, and the resultant solution was stirred at room temperature under argon. After stirring for 5 min, 2 mg (2.7 µmol, 0.1 equiv.) of $PdCl_2(PPh_3)_2$ was added, and the flask was purged with argon and wrapped in foil. After stirring an additional 30 min, the reaction was checked by TLC, and no products were observed. At this time, 10 µL (10 µmol, 0.4 equiv.) of 1 mol L^{-1} Et_2Zn in toluene was added dropwise every 10 min for 2.5 h. Monitoring of the reaction by TLC (1:9 EtOAc:hexanes) showed formation of **20a** after 30 min, and at no point was **20b** observed. Upon completion of the addition of Et_2Zn, the reaction was allowed to stir for an additional 3 h and then worked up as in the synthesis of **20a** (vide supra). ^1H NMR confirmed that no **20b** was formed. If no foil was employed and (or) addition of Et_2Zn was completed too quickly, both **20a** and **20b** were observed.

Crossover experiment, 0.9 EtZnI + $2Et_2Zn$

A solution of 10 mg (27.6 µmol) of thioimidate **16** in 0.4 mL of toluene was treated with 49 µL (25 µmol, 0.9 equiv.) of 0.5 mol L^{-1} EtZnI–THF, and the resultant solution was stirred at room temperature under argon. After stirring for 5 min, 2 mg (2.7 µmol, 0.1 equiv.) of $PdCl_2(PPh_3)_2$ was added, and the flask was purged with argon and wrapped in foil. After stirring an additional 30 min, the reaction was checked by TLC, and no products were observed. At this time, 55 µL (55 µmol, 2 equiv.) of 1 mol L^{-1} Et_2Zn in toluene was added dropwise over a period of 60 min. Monitoring of the reaction by TLC (1:9 EtOAc:hexanes) showed formation of **20a** after 50 min. The identical procedure employing 3 equiv. of EtZnI showed immediate formation of **20a**.

Addition of Et_2Zn to benzaldehyde

To 30 µL (3.3 mmol) benzaldehyde was added 1.2 mL of THF under argon. This solution was then treated with 1.0 mL (9.9 mmol, 3 equiv.) of 1 mol L^{-1} Et_2Zn–toluene, and the flask was immersed into an oil bath maintained at 50 °C. Using a 100 µL syringe, 50 µL aliquots were taken and quenched into 300 µL of MeOH. A 25 µL portion of each quenched aliquot was injected onto an HP 6890 GC, employing an HP-35 column (30 m × 0.25 mm × 0.25 µm film thickness). The temperature profile for the GC was as follows: 10 min at 60 °C, then an increase of 15 °C min^{-1} up to 220 °C, followed by 10 min at 220 °C. The ratio of benzaldehyde to 1-phenyl-propan-1-ol is plotted in Fig. 2 using Microsoft Excel 98®.

Addition of EtZnI to benzaldehyde

A solution consisting of 30 µL (3.3 mmol) of benzaldehyde and 2.2 mL (9.9 mmol, 3 equiv.) of 1 mol L^{-1} EtZnI in 1:1 THF:toluene was stirred in an oil bath maintained at 50 °C. The reaction progress was monitored and analyzed, as in the reaction employing Et_2Zn and benzaldehyde (see Fig. 2).

Acknowledgements

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References

1. I. Ghosh and P.A. Jacobi. J. Org. Chem, **67**, 9304 (2002).
2. F.C. March, D.A. Couch, K. Emerson, J.E. Fergusson, and W.T. Robinson. J. Chem. Soc. A, 440 (1971); (*b*) D.J. Burkey and Hanusa. J. Organomet. Chem. **512**, 165 (1996); (*c*) M.E. Angiolelli, A.L. Casalnuovo, and T.P. Selby. Synlett, **5**, 905 (2000).
3. For a general review for preparing organozinc reagents, see (*a*) P. Knochel and R.D. Singer. Chem. Rev. **93**, 2117 (1993); (*b*) P. Knochel and P. Jones (*Editors*). Organozinc reagents: A practical approach. Oxford University Press, New York. 1999.
4. E. Erdik. Organozinc reagents in organic synthesis. CRC Press, Boca Raton. 1996.
5. (*a*) A. Guijarro, D.M. Rosenberg, and R.D. Rieke. J. Am. Chem. Soc. **121**, 4155 (1999), and references cited therein; (*b*) C. Jubert and P. Knochel. J. Org. Chem. **57**, 5425 (1992); see also M.C.P. Yeh, H.G. Chen, and P. Knochel. Org. Synth. **70**, 195 (1991); (*c*) H. Tokuyama, S. Yokoshima, T. Yamashita, and T. Fukuyama. Tetrahedron Lett. **39**, 3189 (1998); ibid. J. Braz. Chem. Soc. **9**, 381 (1998); for an improved activation procedure, see (*d*) S. Huo. Organic Lett. **5**, 423 (2003).
6. M.H. Abraham and P.H. Rolfe. J. Organomet. Chem. **7**, 35 (1967).
7. (*a*) A.B. Charette and J.-F. Marcoux. J. Am. Chem. Soc. **118**, 4539 (1996); see also (*b*) A.B. Charette, A. Beauchemin, and J.-F. Marcoux. J. Am. Chem. Soc. **120**, 5114 (1998).
8. T. Hayashi, M. Konishi, Y. Kobori, M. Kumada, T. Higuci, and K. Hirotsu. J. Am. Chem. Soc. **106**, 158 (1984).
9. T. Shimizu and M. Seki. Tetrahedron Lett. **42**, 429 (2001), and references cited therein.
10. (*a*) J. Srogl, W. Liu, D. Marshall, and L.S. Liebeskind. J. Am. Chem. Soc. **121**, 9449 (1999); see also (*b*) C. Savarin, J. Srogl, and L.S. Liebeskind. Org. Lett. **2**, 3229 (2000); (*c*) L.S. Liebeskind and J. Srogl. J. Am. Chem. Soc. **122**, 11 260 (2000).
11. Marx reported a 40% yield for this reaction in diethyl ether: B. Marx. C.R. Hebd. Seances Acad. Sci. Ser. C, **266**, 1646 (1968).
12. Y. Tamaru, T. Nakamura, H. Sakaguchi, H. Ochiai, and Z-i Yoshida. J. Chem. Soc. Chem. Commun. 610 (1988).
13. N.A. Bell and P.T. Moseley. J. Organomet. Chem. **325**, 47 (1987).
14. (*a*) P.R. Markies, G. Schat, O.S. Akkerman, and F. Bickelhaupt. J. Organomet. Chem. **430**, 1 (1992); (*b*) J. Boersma. *In* Comprehensive organometallic chemistry. Vol. 2. *Edited by* G. Wilkinson, F.G.A. Stone, and E. Abel. Pergamon Press, Oxford. 1982. p. 823.
15. M. Chastrette and R. Amouroux. Tetrahedron Lett. **59**, 5165 (1970).