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An Electron-Deficient Diene as Ligand for Palladium-Catalyzed Cross-Coupling Reactions: An Efficient Alkylation of Aryl Iodides by Primary and Secondary Alkylzinc Reagents

Qiang Liu,[a] Hui Duan,[a] Xiancai Luo,[a] Yang Tang,[a] Gang Li,[a] Rong Huang,[a] and Aiwen Lei[a,*]

[a] The College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, People's Republic of China
Fax: (+86)-27-6875-4067
Phone: (+86)-27-6875-4672; e-mail: aiwenlei@whu.edu.cn

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Abstract: An electron-deficient diene, $\mathbf{L_1}$, was found to be an effective ligand in facilitating palladium-catalyzed Negishi couplings involving primary and secondary alkylzinc reagents. The reactions took place readily at 60 °C in THF with 5 mol% of a catalyst generated *in situ* from bis(acetonitrile)palladium dichloride [$PdCl_2(MeCN)_2$] and $\mathbf{L_1}$, and functional groups such as chloro, bromo, etc. attached to phenyl ring as well as β-H atoms adjacent to the reaction site were well tolerated. The problematic isomerizations in secondary alkyzinc reagents involved in the reactions reported in the literature were also observed in our system when isopropylzinc chloride was employed alone as the nucleophile. However, the isomerization was significantly suppressed when $i\text{-}Pr_2Zn$ was utilized in the presence of $\mathbf{L_1}$.

Keywords: alkylation; alkylzinc reagents; C–C coupling; diene ligand; palladium

Introduction

During the past three decades, Pd-catalyzed cross-coupling reactions have been explored energetically and now rank among the most fruitful transition metal-catalyzed bond formation processes in organic chemistry.[1,2] The methods for the formation of Csp–Csp^2, Csp^2–Csp^2 and C–N, etc. bonds have become well established after the development of various organometallic reagents to facilitate transmetallation processes in the 1970s[3–7] and the applications of electron-rich and/or sterically hindered ligands to mainly enhance oxidative additions since the 1990s.[8–20] However, Csp^3-related bond formations are still immature due to sluggish reductive elimination and competitive fast β-hydride elimination, although the methodologies, especially those invovling Csp^3–Ar bond formations, are of great importance both in laboratory synthesis and industrial application.[10,21,22]

Two options are viable for construction of the Csp^3–Ar bond utilizing cross-coupling methods. One is to use Csp^3–X as electrophile and ArM as nucleophile, which would involve oxidative addition of Csp^3–X to Pd(0). Recent applications of electron-rich and sterically hindered phosphine and carbene ligands have enabled the difficult oxidative addition of Csp^3–X,[23] but the formed Csp^3–Pd species is exposed to the risk of β-H elimination at the initial step and the electronic properties of the ligands are disadvantageous to the reductive elimination step.[22]

The other option is to use ArX as the electrophile and Csp^3M as the nucleophile, in which the oxidative addition of ArX to Pd(0) to form **II** is facile, but after transmetallation with a secondary alkylzinc reagent, the resultant complex **III** might undergo reductive elimination to afford the desired product **IV** (path a), or β-H elimination to form **V** (path b). Since the alkyl group is a good sigma donor ligand, the reductive elimination path is not easy. Consequently, path b is very competitive. At this point, **V** might go through olefin insertion and reductive elimination to give the isomerized product **VIII**, or undergo direct reductive elimination to form the dehalogenated compound **VI**. Therefore, accelerating the reductive elimination of **III** is the key to selectively gain the desired product **IV**.[24] π-Acidic ligands, which can accept electrons from the metal center, are known from many stoichiometric studies to be able to facilitate reductive eliminations.[25–34] For example, olefins were found to be able to accelerate reductive elimination in the 1960s.[35] However, as a labile type of ligand, olefins have rarely been applied in catalytic processes.[36–52] Recently, we have unexpectedly observed that $Pd(dba)_2$ could smoothly promote C*sp*–C*sp*^{3} bond formation with β-hydrogen in high yields,[53] indicating that dba might play an important role in forming the C*sp*–C*sp*^{3} bond. Afterwards, we designed a novel phosphine-olefin ligand and successfully applied it in C*sp*^{2}–C*sp*^{3} Negishi coupling.[54] But when a secondary alkylzinc chloride was used as nucleophile, isomerization to form **VIII** remained problematic. To further challenge the C*sp*^{3}-related bond formations and probe the application of olefin-type ligands in C*sp*^{3}-related cross-coupling reactions, we synthesized a bidentate olefin ligand **L$_1$** (Figure 1). Herein, we report our attempt to use **L$_1$** in Negishi couplings involving primary and secondary alkylzinc reagents.

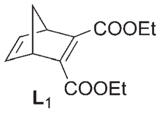
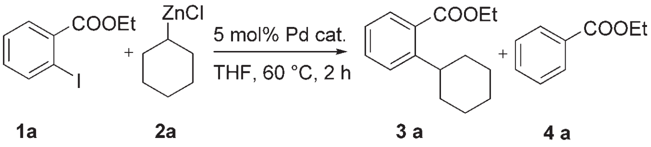


Figure 1. The diene ligand.

Table 1. The ligand effect in the C*sp*^{3}-related Negishi coupling.[a]



Entry	Pd Cat	Selectivity [%][b]	
		3a	4a
1	$PdCl_2(PPh_3)_2$	43	57
2	$PdCl_2(dppf)$	78	22
3	$PdCl_2(MeCN)_2$/DPPBz[c]	49	51
4	$PdCl_2(MeCN)_2/P^tBu_3{\cdot}HBF_4$	67	33
5	$Pd(dba)_2$	90	10
6	$PdCl_2(MeCN)_2/L_1$	92	8

[a] Reactions were carried out with ArI (0.5 mmol), Pd cat. (0.0025 mmol) and the zinc reagent (1.0 mmol) in THF at 60 °C for 2 h.

[b] The selectivity was determined by GC.

[c] DPPBz = 1,2-bis(diphenylphosphino)benzene.

Results and Discussion

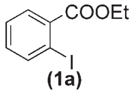
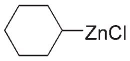
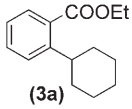
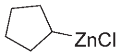
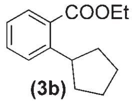
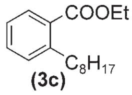
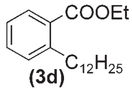
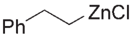
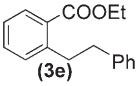
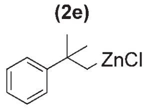
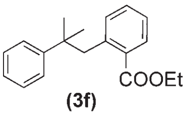
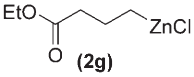
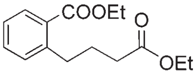
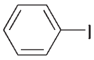
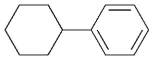
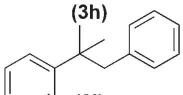
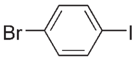
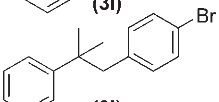
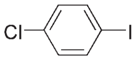
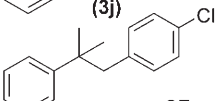
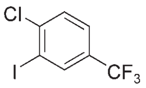
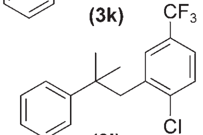
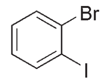
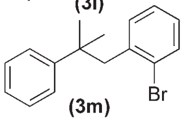
Ethyl 2-iodobenzoate **1a** and cyclohexylzinc chloride **2a** were chosen as benchmark substrates, different catalytic systems were tested at 60 °C in THF, and the results are compiled in Table 1. PPh_3 as ligand gave **3a** in 43% yield with 57% **4a**, and P(*t*-Bu)$_3$ promoted both the yield and selectivity to midrange (Table 1, entries 1 and 4). Bidentate ligand dppbz resulted in poor results, yet dppf achieved a moderate result (Table 1, entries 2 and 3). To our delight, the combination of 1 equivalent of $PdCl_2(MeCN)_2$ and 2 equivalents of **L$_1$** furnished the best result with a 92% yield of the desired product **3a** and only 8% dehalegenated side product **4a** (Table 1, entry 6). $Pd(dab)_2$ behaved well too albeit with slightly inferior yield and selectivity (Table 1, entry 5).

The substrate scope was next investigated under the optimized conditions with $PdCl_2(MeCN)_2$ and **L$_1$** as catalysts in THF at 60 °C, and the results are listed in Table 2. The couplings between **2a** and primary zinc reagents with β-H atoms (**2c**, **2d**, **2e**, **2g**), without β-H atoms (**2f**) and secondary zinc reagents (**2a**, **2b**) all took place readily and the yields were good to excellent (Table 2, entries 1–7). Furthermore, functional groups such as chloro, bromo, and trifluoromethyl, etc. in the aryl part were all well tolerated (Table 2, entries 8–13). It was noteworthy that when $Pd(dab)_2$ was utilized as catalyst, the reaction between **2c** and **1a** resulted in only 58% yield, and the reaction between **2d** and **1a** gave 88% desired product, both being inferior to those catalyzed by $PdCl_2(MeCN)_2$ and **L$_1$**, indicating the generality problem of $Pd(dba)_2$ in this reaction. In addition, the reaction of **1a** with **2f** on a 10-mmol scale was tested with 1 mol% catalyst loading, a 95% isolated yield of the desired cross-coupling product was obtained after 3 h.

In cross-coupling reactions involving secondary alkylzinc reagents, isomerization could hardly be evaded, i.e., path b in Scheme 1 is difficult to block.[24,54] When the catalyst generated *in situ* from $PdCl_2(MeCN)_2$ and **L$_1$** was tested in the reaction of **1a** and 1.5 equiv. of isopropylzinc chloride, the ratio between ethyl 2-isopropylbenzoate **5a** and ethyl 2-propylbenzoate **6a** was determined by GC to be 5:1 and the total yield was 91%. Using dba as the ligand resulted in even poorer selectivity (**5a**:**6a** = 2:1) and lower total yield (56%). However, the isomerization was almost completely inhibited when diisopropylzinc **4a** was used as the nucleophile and the selectivity for the desired product **5a** over the isomerized product **6a** was up to 97:3 (Table 3, entry 1). Dba afforded 74:26 selectivity under similar conditions (Table 3, entry 2).

Table 2. The Negishi coupling promoted by $\mathbf{L_1}$.[a]

$$\underset{\mathbf{1}}{\mathrm{Ar{-}I}} + \underset{\mathbf{2}}{\mathrm{R{-}ZnCl}} \xrightarrow[\text{THF, 2 h, 60 °C}]{\text{5 mol\% Pd Cat}} \underset{\mathbf{3}}{\mathrm{Ar{-}R}}$$

Entry	**1**	**2**[b]	**3**	Yield of **3** [%][c]
1	 **(1a)**	 **(2a)**	 **(3a)**	92
2	**1a**	 **(2b)**	 **(3b)**	94
3	**1a**	*n*-C_8H_{17}ZnCl **(2c)**	 **(3c)**	85 (58%)[d,e]
4	**1a**	*n*-$C_{12}H_{25}$ZnCl **(2d)**	 **(3d)**	93 (88%)[d,e]
5	**1a**	 **(2e)**	 **(3e)**	99
6	**1a**	 **(2f)**	 **(3f)**	99
7	**1a**	 **(2g)**	 **(3g)**	86
8	 **(1b)**	**2a**	 **(3h)**	70[d]
9	**1b**	**2f**	 **(3i)**	89
10	 **(1c)**	**2f**	 **(3j)**	98
11	 **(1d)**	**2f**	 **(3k)**	95
12	 **(1e)**	**2f**	 **(3l)**	96
13	 **(1f)**	**2f**	 **(3m)**	72

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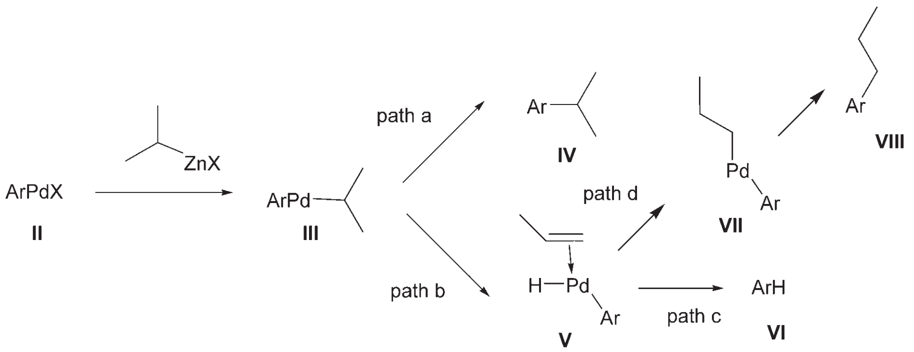
[a] Reactions were carried out with ArI (1.0 mmol), $PdCl_2(MeCN)_2$ (0.05 mmol), $\mathbf{L_1}$ (0.1mmol) and the zinc reagent (1.5 mmol) in THF at 60 °C for 2 h.

[b] RZnX was prepared *in situ* from RMgX and $ZnCl_2$.

[c] Isolated yields.

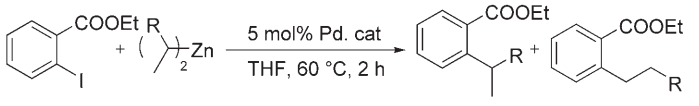
[d] GC yields.

[e] $Pd(dba)_2$ was used as the catalyst.



Scheme 1. Competitive paths of Negishi coupling involving secondary alkylzinc reagents.

Table 3. The Negishi coupling of secondary alkylzinc reagents.[a]



1a **4**[d] **5** **6**

Entry	Pd.Cat	R	Yield (**5** + **6**) [%]	Selectivity [%][e]	
				5	**6**
1	$PdCl_2(MeCN)/\mathbf{L_1}$	Me **(4a)**	92[b]	97	3
2	$Pd(dba)_2$	**4a**	90[c]	74	26
3	$Pd(dba)_2$ + 3 $\mathbf{L_1}$	**4a**	87[c]	91	9
4	$PdCl_2(MeCN)/\mathbf{L_1}$	n-C_2H_5 **(4b)**	88[b]	91	9
5	$PdCl_2(MeCN)/\mathbf{L_1}$	n-C_6H_{13} **(4c)**	90[b]	91	9

[a] Reactions were carried out with ArI (0.5 mmol), $PdCl_2(MeCN)_2$ (0.025 mmol), $\mathbf{L_1}$ (0.05 mmol) and the zinc reagent (1.5 mmol) in THF at 60 °C for 2 h.
[b] Isolated yields.
[c] GC yields.
[d] R'_2Zn was prepared *in situ* from R′MgBr and $ZnCl_2$.
[e] Determined by GC.

Yet the catalyst generated *in situ* from $Pd(dba)_2$ and 3 equiv, $\mathbf{L_1}$ improved the selectivity to 91:9 (Table 3, entry 3), clearly exhibiting the effectiveness of $\mathbf{L_1}$ in promoting the reductive elimination over the β-H elimination pathway (*vide supra*). Further extensions to diethylzinc **4b** and di(*n*-hexyl)zinc **4c** resulted in similar selectivities and yields (Table 3, entries 4 and 5).

What's more, a black powder, **Catalyst 1**, was prepared from $PdCl_2$ and $\mathbf{L_1}$ in MeOH following a similar procedure for synthesis of $Pd(dba)_2$. Its activity was tested and found to be similar to that of the catalyst generated *in situ* from $PdCl_2(MeCN)_2$ and $\mathbf{L_1}$ in several reactions. However, the spectroscopic data of the powder were difficult to assign, and it was not stable enough in solution to get a crystal for structure analysis. So further analysis is ongoing regarding the exact effect of $\mathbf{L_1}$ in the reaction.

Conclusions

In summary, we have designed and synthesized an electron-deficient olefin ligand $\mathbf{L_1}$, and applied it in Pd-catalyzed cross-coupling reaction of aryl iodides and alkylzinc reagents. β-H atoms and functional groups such as bromo, chloro, etc. were well tolerated, and $\mathbf{L_1}$ exhibited obvious effects in inhibiting isomerization when secondary dialkylzinc reagents were employed as the nucleophiles. Further studies on mechanistic aspects and extension of the scope are ungoing in our laborotary and will be reported in due course.

Experimental Section

Synthesis of L_1

Dicyclopentadiene (5 g) was heated to 180 °C, the cyclopenta-1,3-diene was then distilled out. To this cyclopenta-1,3-diene (3.3 g, 50 mmol), diethyl but-2-ynedioate (8.5 g, 50 mmol) was added dropwise. The color of the solution turned to light yellow. The reaction was exothermic. The product was distilled under vacuum to afford a colorless liquid; yield:. 10.4 g (88%).

Synthesis of Catalyst 1

Palladium(II) chloride (1.58 g, 8.94 mmol), ligand $\mathbf{L_1}$ (7.4 g, 31.3 mmol), anhydrous sodium acetate (5.87 g, 71 mmol) and anhydrous methanol (200 mL) were charged into a 500-mL oven-dried three-necked flask purged with N_2. The mixture was heated to reflux and stirred overnight. The solution was washed with degassed water. The aqueous phase was extracted with CH_2Cl_2. The organic phrase was dried with anhydrous sodium sulfate and the solvent evaporated under vacuum. Removal of further solvent using an oil pump provided a black crystalloid material; yield: 6.7 g.

General Procedure for Negishi Couplings Involving Primary Alkylzinc Reagents (Table 1 and Table 2)

Synthesis of the RZnX reagent: To a solution of $ZnCl_2$ (1.5 mmol) in dried THF (1 mmol), RMgX (1 mmol) was added. The gray solution was used directly in the following Negishi coupling reaction.

Under the protection of nitrogen gas, 0.025 mmol of Pd precursor or catalyst and the ligand (if it was used) was dissolved in THF(0.5 mL) and stirred for 20 min. To the THF solution, the iodoarene (0.5 mmol) was added. The RZnX reagent (1 mmol) was added to the mixture last. The mixture, which turned deep red immediately, was stirred for 2 h at 60 °C. The reaction was quenched with saturated aqueous ammonium chloride, separated and then extracted by Et_2O. The organic layer was dried over sodium sulfate, filtered, and concentrated. Purification of the products was accomplished by silica chromatography.

General Procedure for Negishi Coupling Involving Secondary Alkylzinc Reagents (Table 3)

Synthesis of the R_2Zn reagent: To a solution of $ZnCl_2$ (1.5 mmol) in dried THF (1 mmol), RMgX (3 mmol) was added. The gray solution was used directly in the following Negishi coupling reaction.

Under the protection of nitrogen gas, 0.025 mmol of Pd precursor or catalyst and the ligand (if it was used) was dissolved in THF(0.5 mL) and stirred for 20 min. To the THF solution, iodoarene (0.5 mmol) was added. The R_2Zn reagent (1.5 mmol) was added to the mixture last. The mixture, which turned deep red immediately, was stirred for 2 h at 60 °C. The reaction was quenched with saturated aqueous ammonium chloride, separated and then extracted by Et_2O. The organic layer was dried over sodium sulfate, filtered, and concentrated. Purification of products was accomplished by silica chromatography.

Supporting Information

The characterization data is available in a Supporting Information file.

Acknowledgements

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References

[1] F. Diederich, P. J. Stang, *Metal-catalyzed cross-coupling reactions*, 2nd edn., Wiley-VCH, John Wiley, Weinheim, Chichester, **2004**.

[2] E.-i. Negishi, *Handbook of organopalladium chemistry for organic synthesis*, Wiley, New York, Chichester, **2002**.

[3] K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc.* **1972**, *94*, 4374–4376.

[4] A. O. King, N. Okukado, E. Negishi, *J. Chem. Soc. Chem. Commun.* **1977**, 683–684.

[5] N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.* **1979**, 3437–3440.

[6] D. Milstein, J. K. Stille, *J. Am. Chem. Soc.* **1978**, *100*, 3636–3638.

[7] Y. Hatanaka, T. Hiyama, *J. Org. Chem.* **1988**, *53*, 918–920.

[8] N. Kataoka, Q. Shelby, J. P. Stambuli, J. F. Hartwig, *J. Org. Chem.* **2002**, *67*, 5553–5566.

[9] D. W. Old, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 9722–9723.

[10] D. J. Cardenas, *Angew. Chem.* **2003**, *115*, 398–401; *Angew. Chem. Int. Ed.* **2003**, *42*, 384–387.

[11] G. Altenhoff, R. Goddard, C. W. Lehmann, F. Glorius, *Angew. Chem.* **2003**, *115*, 3818–3821; *Angew. Chem. Int. Ed.* **2003**, *42*, 3690–3693.

[12] O. Navarro, R. A. Kelly, III, S. P. Nolan, *J. Am. Chem. Soc.* **2003**, *125*, 16194–16195.

[13] M. Eckhardt, G. C. Fu, *J. Am. Chem. Soc.* **2003**, *125*, 13642–13643.

[14] J. E. Milne, S. L. Buchwald, *J. Am. Chem. Soc.* **2004**, *126*, 13028–13032.

[15] B. C. Hamann, J. F. Hartwig, *J. Am. Chem. Soc.* **1998**, *120*, 7369–7370.

[16] A. F. Littke, G. C. Fu, *J. Org. Chem.* **1999**, *64*, 10–11.

[17] A. F. Littke, G. C. Fu, *Angew. Chem.* **1999**, *111*, 2568–2570; *Angew. Chem. Int. Ed.* **1999**, *38*, 2411–2413.

[18] C. Dai, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 2719–2724.

[19] N. Hadei, E. A. B. Kantchev, C. J. O'Brien, M. G. Organ, *Org. Lett.* **2005**, *7*, 3805–3807.

[20] N. Hadei, E. A. B. Kantchev, C. J. O'Brien, M. G. Organ, *J. Org. Chem.* **2005**, *70*, 8503–8507.

[21] D. J. Cardenas, *Angew. Chem.* **1999**, *111*, 3201–3203; *Angew. Chem. Int. Ed.* **1999**, *38*, 3018–3020.

[22] T.-Y. Luh, M.-k. Leung, K.-T. Wong, *Chem. Rev.* **2000**, *100*, 3187–3204.

[23] A. F. Littke, G. C. Fu, *Angew. Chem.* **2002**, *114*, 4350–4386; *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211.

[24] T. Hayashi, M. Konishi, Y. Kobori, M. Kumada, T. Higuchi, K. Hirotsu, *J. Am. Chem. Soc.* **1984**, *106*, 158–163.

[25] T. Yamamoto, A. Yamamoto, S. Ikeda, *J. Am. Chem. Soc.* **1971**, *93*, 3350–3359.

[26] R. Sustmann, J. Lau, *Chem. Ber.* **1986**, *119*, 2531–2541.

[27] R. Giovannini, T. Studemann, G. Dussin, P. Knochel, *Angew. Chem.* **1998**, *110*, 2512–2515; *Angew. Chem. Int. Ed.* **1998**, *37*, 2387–2390.

[28] R. Giovannini, T. Stuedemann, A. Devasagayaraj, G. Dussin, P. Knochel, *J. Org. Chem.* **1999**, *64*, 3544–3553.

[29] M. A. Grundl, J. J. Kennedy-Smith, D. Trauner, *Organometallics* **2005**, *24*, 2831–2833.

[30] A. Scrivanti, V. Beghetto, U. Matteoli, S. Antonaroli, A. Marini, B. Crociani, *Tetrahedron* **2005**, *61*, 9752–9758.

[31] D. B. G. Williams, M. L. Shaw, *Tetrahedron* **2007**, *63*, 1624–1629.

[32] I. J. S. Fairlamb, A. R. Kapdi, A. F. Lee, G. P. McGlacken, F. Weissburger, A. H. M. de Vries, L. Schmieder-van de Vondervoort, *Chem. Eur. J.* **2006**, *12*, 8750–8761.

[33] I. J. S. Fairlamb, A. R. Kapdi, A. F. Lee, *Org. Lett.* **2004**, *6*, 4435–4438.

[34] Y. Mace, A. R. Kapdi, I. J. S. Fairlamb, A. Jutand, *Organometallics* **2006**, *25*, 1795–1800.

[35] A. Yamamoto, S. Ikeda, *J. Am. Chem. Soc.* **1967**, *89*, 5989–5990.

[36] F. Glorius, *Angew. Chem.* **2004**, *116*, 3444–3446; *Angew. Chem. Int. Ed.* **2004**, *43*, 3364–3366.

[37] C. Fischer, C. Defieber, T. Suzuki, E. M. Carreira, *J. Am. Chem. Soc.* **2004**, *126*, 1628–1629.

[38] T. Hayashi, K. Ueyama, N. Tokunaga, K. Yoshida, *J. Am. Chem. Soc.* **2003**, *125*, 11508–11509.

[39] N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2004**, *126*, 13584–13585.

[40] Z.-Q. Wang, C.-G. Feng, M.-H. Xu, G.-Q. Lin, *J. Am. Chem. Soc.* **2007**, *129*, 5336–5337.

[41] C. Defieber, J.-F. Paquin, S. Serna, E. M. Carreira, *Org. Lett.* **2004**, *6*, 3873–3876.

[42] Y. Otomaru, N. Tokunaga, R. Shintani, T. Hayashi, *Org. Lett.* **2005**, *7*, 307–310.

[43] A. Goliaszewski, J. Schwartz, *J. Am. Chem. Soc.* **1984**, *106*, 5028–5030.

[44] A. Goliaszewski, J. Schwartz, *Organometallics* **1985**, *4*, 417–419.

[45] Y. Hayasi, M. Riediker, J. S. Temple, J. Schwartz, *Tetrahedron Lett.* **1981**, *22*, 2629–2632.

[46] J. S. Temple, M. Riediker, J. Schwartz, *J. Am. Chem. Soc.* **1982**, *104*, 1310–1315.

[47] J. Terao, Y. Naitoh, H. Kuniyasu, N. Kambe, *Chem. Lett.* **2003**, *32*, 890–891.

[48] J. Terao, Y. Naitoh, H. Kuniyasu, N. Kambe, *Chem. Commun.* **2007**, 825–827.

[49] J. Terao, H. Todo, S. A. Begum, H. Kuniyasu, N. Kambe, *Angew. Chem.* **2007**, *119*, 2132–2135; *Angew. Chem. Int. Ed.* **2007**, *46*, 2086–2089.

[50] J. Terao, H. Todo, H. Watanabe, A. Ikumi, N. Kambe, *Angew. Chem.* **2004**, *116*, 6306–6308; *Angew. Chem. Int. Ed.* **2004**, *43*, 6180–6182.

[51] J. Terao, H. Watanabe, A. Ikumi, H. Kuniyasu, N. Kambe, *J. Am. Chem. Soc.* **2002**, *124*, 4222–4223.

[52] B. M. Trost, P. J. Metzner, *J. Am. Chem. Soc.* **1980**, *102*, 3572–3577.

[53] Y. Zhao, H. Wang, X. Hou, Y. Hu, A. Lei, H. Zhang, L. Zhu, *J. Am. Chem. Soc.* **2006**, *128*, 15048–15049.

[54] X. Luo, H. Zhang, H. Duan, Q. Liu, L. Zhu, T. Zhang, A. Lei, *Org. Lett.* **2007**, *9*, 4571–4574.