Palladium-Catalyzed Vinylation of Aryl Chlorides. Chelate Effect in Catalysis

Y. Ben-David, M. Portnoy, M. Gozin, and D. Milstein*

Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot 76100, Israel

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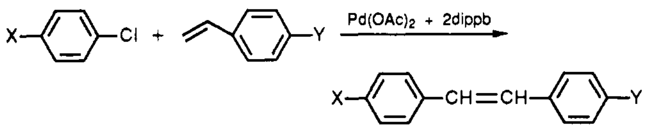
Summary: **By use of the dippb ligand (dippb = 1,4-bis(diisopropylphosphino)butane) it is possible to effect the synthetically useful Pd-catalyzed direct vinylation of aryl chlorides; the reaction tolerates various substituents and generally results in high yields. The reaction is very sensitive to the nature of the chelating ligand, probably as a result of the need for chelate opening to allow olefin coordination and chelate closure to promote insertion. Monophosphines are ineffective. A mechanistic scheme is presented.**

Palladium-catalyzed vinylation of aryl halides, also known as the "Heck reaction", is a useful synthetic method for generation of carbon–carbon bonds. No other general single-step method for accomplishing this transformation is known. One limitation of this reaction is that aryl chlorides are usually unreactive.[1] Various efforts to develop synthetically useful vinylation reactions based on aryl chlorides have resulted in low yields[2,3] and low catalyst stability.[3] A recent approach to solve this problem involves a two-stage process based on Ni(II)-catalyzed substitution of the chloride by iodide, followed by Pd-catalyzed vinylation.[4] We report here that direct vinylation of aryl chlorides is possible in high yield in a single step. This work also demonstrates a dramatic chelate effect on catalytic activity.

We have recently discovered that the complex Pd(dippp)$_2$ (1; dippp = 1,3-bis(diisopropylphosphino)propane) is an efficient catalyst for carbonylation[5] and formylation[6] of aryl chlorides. Since the vinylation reaction also involves oxidative addition of the aryl chloride, followed by coordination of the unsaturated molecule and insertion, we tried complex 1 as a catalyst for vinylation of chlorobenzene with styrene. Surprisingly, no catalysis was observed. Since 1 is known to undergo oxidative addition of chlorobenzene to yield the complex *cis*-(dippp)Pd(Ph)Cl (2),[5] we assumed that the problem rests with the insertion step. Indeed, 2 does not react with styrene (in the presence or absence of triethylamine) even upon heating at 150 °C in DMF (DMF = dimethylformamide). Because the olefin insertion step is likely to proceed from a 4-coordinate intermediate,[7] i.e., it may require chelate opening to allow for coordination of the olefin, we decided to choose a larger diphosphine of similar steric properties to facilitate this process.

Indeed, when dippb (1,4-bis(diisopropylphosphino)butane) is utilized in conjunction with Pd(OAc)$_2$ and sodium acetate in DMF, high-yield catalytic vinylation of chlorobenzene is observed (Table I). Essentially the same results are obtained when (dippb)$_2$Pd is used as a catalyst.

Table I



X	Y	base	solvent	amt of Ar–Cl, %	amt of ArCH=CHAr, %^{a}	
					cis	trans
H	H	NaOAc	DMF	15.6	4.4	80
H	H	NaOAc	CH$_3$CN	100	0	0
H	H	NEt$_3$	DMF	91.1	0.7	8.2
MeO	H	NaOAc	DMF	78.8	2.2	19
H	MeO	NaOAc	DMF	23	7	70
Me	H	NaOAc	DMF	45	5	50
NO$_2$	H	NaOAc	DMF	6.5	8.9	84.6
PhCO	MeO	NaOAc	DMF	0	3	97
CHO	H	NaOAc	DMF	5	5	90

[a] GC yields based on the aryl chloride. Reaction conditions: A solution containing the aryl chloride (10.0 mmol), styrene (12.0 mmol), Pd(OAc)$_2$ (0.1 mmol), dippb (0.2 mmol), base (10 mmol), and 4 mL of solvent was heated at 150 °C for 24 h in a closed vessel under nitrogen.

Table II

$$\mathrm{Ph{-}Cl + PhCH{=}CH_2 \xrightarrow{Pd(OAc)_2 + L} PhCH{=}CHPh}$$

L	amt of Ph—Cl, %	amt of stilbene, %^{a}	
		cis	trans
dippb	15.6	4.4	80
dippp	97	0	3
dippe	100	0	0
dppe	83.4	1.6	15
iPr$_2$P-nBu	85.0	3.0	12.
i-Pr$_3$P	74.4	1.6	24

[a] Reaction conditions as described in Table I, with sodium acetate as the base and DMF as the solvent.

It is noteworthy that in contrast to the normal Heck reaction conditions of aryl bromide and iodide vinylations, which frequently utilize a tertiary amine as a base, very little reaction is observed here with NEt$_3$. Also, changing the solvent to CH$_3$CN results in complete recovery of the starting chlorobenzene. Both observations may be rationalized in terms of competition for a coordination site between these good ligands and the olefin.

Various substituents can be utilized. Qualitatively, electron-donating groups (Me, MeO) on the aryl chloride result in slower reactions, whereas electron-withdrawing substituents (NO$_2$, PhCO, CHO) result in higher rates, compatible with a rate-determining oxidative-addition step. In accordance with this, a methoxy substituent on the olefin has no significant effect. The formyl substituent, which may be susceptible to side reactions such as the base-catalyzed Cannizzaro reaction, is unaffected under the reaction conditions.

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(1) (a) Heck, R. F. *Org. React.* **1982**, *27*, 345. (b) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985; pp 276–287. (c) For a recent example, see: Cabri, W.; Candiani, I.; De Bernardinis, S.; Francalanci, F.; Penco, S. *J. Org. Chem.* **1991**, *56*, 5796.

(2) Julia, M.; Duteil, M.; Grard, C.; Kuntz, E. *Bull. Soc. Chim. Fr.* **1973**, 2791.

(3) (a) Spencer, A. *J. Organomet. Chem.* **1984**, *270*, 115. (b) Davidson, J. B.; Simon, N. M.; Sojka, S. A. *J. Mol. Catal.* **1984**, *22*, 349.

(4) Bozell, J. J.; Vogt, C. E. *J. Am. Chem. Soc.* **1988**, *110*, 2655.

(5) Ben-David, Y.; Portnoy, M.; Milstein, D. *J. Am. Chem. Soc.* **1989**, *111*, 8742.

(6) Ben-David, Y.; Portnoy, M.; Milstein, D. *J. Chem. Soc., Chem. Commun.* **1989**, 1816.

(7) (a) Thorn, D. L.; Hoffmann, R. J. *J. Am. Chem. Soc.* **1978**, *100*, 2079. (b) Koga, N.; Obara, B.; Kitaura, K.; Morokuma, K. *J. Am. Chem. Soc.* **1985**, *107*, 7109.

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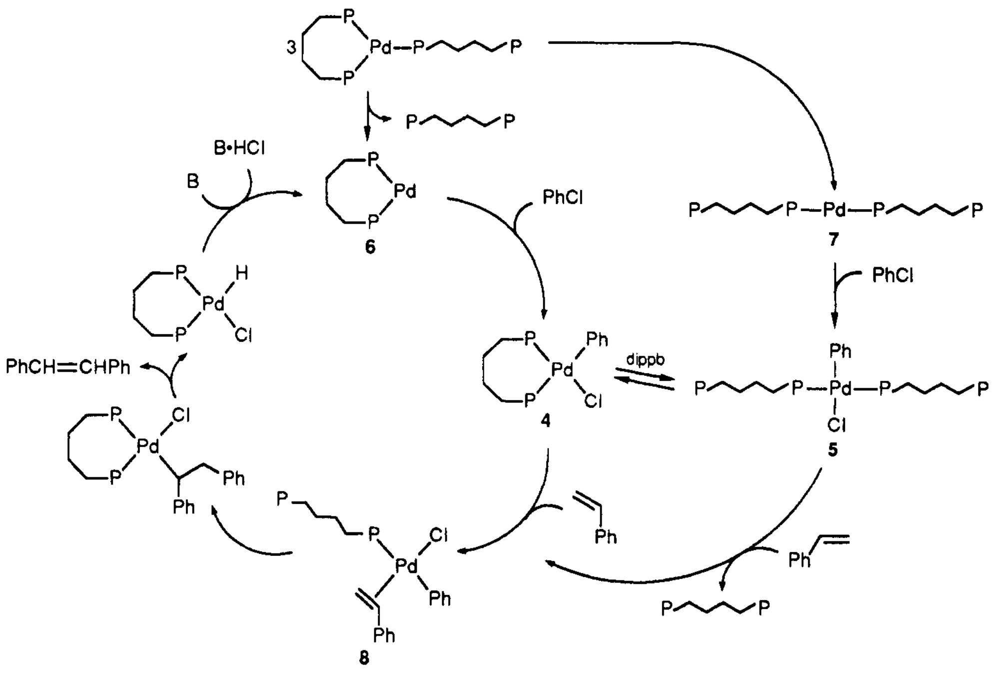
Scheme I



A striking chelate effect on catalytic activity is presented in Table II. In contrast to the observed reaction with dippb as a ligand, almost no reaction takes place when dippp and dippe (dippe = 1,2-bis(diisopropylphosphino)ethane) are utilized, whereas a low yield is observed with monophosphines. In no case have we observed catalyst decomposition and palladium metal formation.

Some observations of mechanistic relevance are as folows. Pd(dippb)$_2$ (**3**), which is present in solution in a trigonal form, similar to the case for Pd(dippp)$_2$,[5] oxidatively adds chlorobenzene at 50 °C to yield in parallel pathways *cis*-(dippb)Pd(Ph)Cl (**4**) and *trans*-(dippb)$_2$Pd(Ph)Cl (**5**). **4** and **5** are in an equilibrium favoring **5**.[8,9] **5** reacts with styrene in DMF at 140 °C to yield stilbene quantitatively, while *cis*-(dippp)Pd(Ph)Cl is inert under these conditions.

A plausible mechanism is presented in Scheme I. Chlorobenzene oxidative addition probably involves a 14e Pd(0) complex, as has been shown for Pd(dippp)$_2$.[9] The intermediate can be the chelated complex **6** and complex **7**. Oxidative addition to **6** is expected to be faster than to **7**, due to the smaller P–Pd–P angle.[10] Chelate opening in **4** or ligand dissociation from **5** will allow generation of the 4-coordinate olefin complex **8**. Olefin insertion in this complex may be promoted by synchronous chelate closure. β-H elimination followed by deprotonation completes the catalytic cycle. The observed prominent chelate effect is likely to be associated with both the oxidative-addition and insertion steps. Dippe and dippp form stronger chelates than dippb,[9] rendering formation of an intermediate analogous to **8** difficult. The advantage of dippb over monophosphines probably lies in the faster oxidative addition to **6** and promotion of the insertion in **8** by the potentially chelating dippb. Sterics or basicity is not responsible for this difference, since the ineffective iPr$_2$P-nBu has a basicity and cone angle similar to those of dippb.[11]

In conclusion, the nature of the chelate may have a dramatic effect on catalytic activity, allowing specific catalyst tailoring. This is exemplified nicely in catalytic reactions of aryl chlorides—the dippp ligand allows carbonylation[5] and formylation,[6] whereas dippb is specific for vinylation. Chelating ligand effects in other palladium-catalyzed reactions have also been reported.[1c,12]

Further studies aimed at evaluation of the scope (primarily with regard to the olefin) and mechanism of this synthetically useful vinylation reaction are in progress.

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Registry No. dippb, 80499-19-0; dippp, 91159-11-4; dippe, 87532-69-2; dppe, 1663-45-2; PhCl, 108-90-7; 4-MeOC$_6$H$_4$Cl, 623-12-1; 4-MeC$_6$H$_4$Cl, 106-43-4; 4-O$_2$NC$_6$H$_4$Cl, 100-00-5; 4-PhCOC$_6$H$_4$Cl, 134-85-0; 4-OHCC$_6$H$_4$Cl, 104-88-1; H$_2$C=CHPh, 100-42-5; 4-H$_2$C=CHC$_6$H$_4$OMe, 637-69-4; *cis*-PhCH=CHPh, 645-49-8; *trans*-PhCH=CHPh, 103-30-0; *cis*-PhCH=CHC$_6$H$_4$-*p*-OMe, 1657-53-0; *trans*-PhCH=CHC$_6$H$_4$-*p*-OMe, 1694-19-5; *cis*-4-MeC$_6$H$_4$CH=CHPh, 1657-45-0; *trans*-4-MeC$_6$H$_4$CH=CHPh, 1860-17-9; *cis*-O$_2$NC$_6$H$_4$CH=CHPh, 6624-53-9; *trans*-O$_2$NC$_6$H$_4$CH=CHPh, 1694-20-8; *cis*-4-MeOC$_6$H$_4$CH=CHCOPh, 141063-03-8; *trans*-4-MeOC$_6$H$_4$CH=CHCOPh, 141063-04-9; *cis*-4-OHCC$_6$H$_4$CH=CHPh, 71093-80-6; *trans*-4-OHCC$_6$H$_4$CH=CHPh, 40200-69-9; iPr$_2$P-nBu, 63059-00-7; i-Pr$_3$P, 6476-36-4.

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(8) This oxidative-addition reaction is expected to be much slower under the conditions of the catalytic reactions, which employ a large excess (compared to **3**) of the reactant π-accepting olefin.

(9) Portnoy, M.; Milstein, D. To be submitted for publication.

(10) It has been shown that nucleophilicity of ML$_2$ d^{10} complexes increases with a decrease in the L–M–L angle: (a) Otsuka, S. *J. Organomet. Chem.* **1980**, *200*, 191. (b) Hofmann, P.; Heiss, H.; Müller, G. *Z. Naturforsch.* **1987**, *B42*, 395.

(11) The basicities of R$_2$P(CH$_2$)$_n$PR$_2$ and R$_2$P(CH$_2$)$_{n-1}$CH$_3$ are expected to be similar for $n \geq 3$. See, for example, Table I of: Sowa, J. R.; Angelici, R. J. *Inorg. Chem.* **1991**, *30*, 3534.

(12) For example: (a) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158. (b) Dolle, R. E.; Schmidt, S. J.; Kruse, L. I. *J. Chem. Soc., Chem. Commun.* **1987**, 904. (c) Pisano, C.; Mezzett, A.; Consiglio, G. *Organometallics* **1992**, *11*, 20.