Effect of Halide Ligands on the Reactivity of Carbon−Palladium Bonds: Implications for Designing Catalytic Reactions

Zhong Wang, Zhaoguo Zhang, and Xiyan Lu*

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

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The integral role of halide ions as a ligand in divalent palladium-catalyzed nucleophile−alkyne−α,β-unsaturated carbonyl coupling reaction as well as in the stoichiometric reaction of arylpalladium reagents with acrolein was studied. Excess of halide ions can effectively inhibit the β-hydride elimination of a (2-oxoalkyl)palladium intermediate, giving preferentially the protonolysis product in acidic media. This result may have further implications for the design and development of divalent palladium-catalyzed reactions.

Introduction

Numerous ligands have been developed and applied in palladium-catalyzed reactions over the years. Coordination of these ligands not only improves the solubility and other physical properties of the complexes but also, more importantly, influences the chemical reactivities of the catalysts and intermediates.[1] There have been extensive studies on the effect of phosphine ligands in zerovalent palladium-catalyzed reactions.[2] The rich literature in this field has led to rational design of efficient catalytic systems as well as development of stereoselective and enantioselective catalysts. A number of studies also addressed the important effect of halide ligands in processes normally catalyzed by Pd(0).[3] Most of the papers described the increase of reactivity of the catalyst by eliminating halide ions in the reaction system. However, the integral role of halide ions as a ligand has been rarely considered in divalent palladium-catalyzed reactions, although they are often used in many Pd(II)-mediated processes.[4]

Palladium(II)-catalyzed reactions in the presence of halide ions were developed in early works.[5] Chloropalladate compounds are widely used as homogeneous catalysts because of their good solubilities in water and other polar solvents.[6] Recent studies revealed that halopalladate complexes can be generated in situ from various catalyst precursors and act as the actual catalytic species in a much wider range of Pd(II)-catalyzed reactions, e.g., $Pd_2(dba)_3{\cdot}CHCl_3$−benzoquinone−LiCl-promoted 1,4-difunctionalization of 1,3-dienes[7] and Pd(II)−LiX-mediated heteroatom addition to carbon−carbon multiple bonds.[8] In the former case, it was shown that the regio- and stereoselectivities of the reaction depend on the presence or absence of LiCl.[7]

Using the versatile Pd(II)−LiX system, we have also developed two highly selective reactions based on cyclization of allylic alkynoates (Scheme 1, a and b),[9] in which halide ion concentration significantly influences

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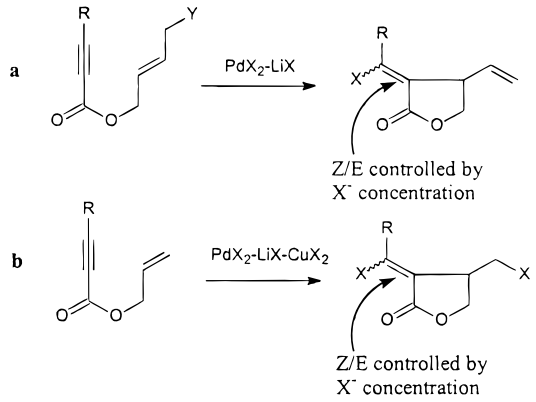
Scheme 1



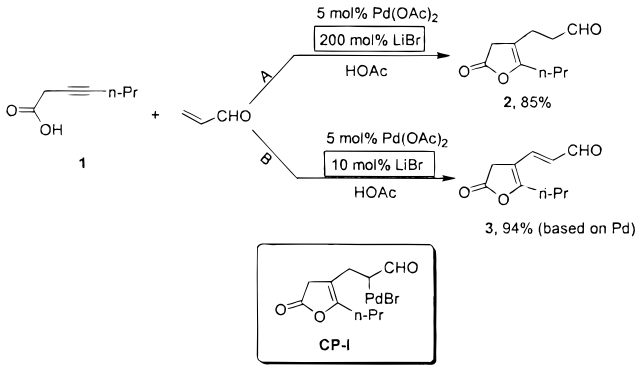
the Z/E selectivity of the exocyclic double bond. More recently, we discovered a series of Pd(II)-catalyzed nucleophile−alkyne−α,β-unsaturated carbonyl tandem additions where the halide ligand exhibits a more dramatic influence on the reaction course:[10] the presence of excess halide ion inhibits the usual β-hydride elimination (Heck-type reaction) and promotes protonolysis (conjugate addition) when alkenyl palladium species react with α,β-unsaturated carbonyl compounds; in these transformations, the halide alters the reaction pathway as a mechanistic switch. This significant observation roused our interest in the related mechanistic investigations. We not only studied the effect of halide amount on these catalytic reactions but also employed synthetic Pd(II) complexes to investigate the halide ligand effect and other controlling factors in their stoichiometric reaction with α,β-unsaturated carbonyl compounds. In this paper, we report these detailed studies addressing the important role of halide ions in palladium(II)-promoted conjugate addition reactions and discuss its potential application in the design of novel catalytic systems.

Results and Discussion

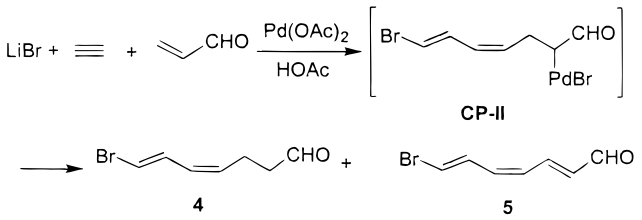
In the different effects of halide ions in Pd(II)-catalyzed reactions, we were most intrigued by the significant steering effect they exert to promote conjugate addition reactions. In these reactions, protonolysis of the C−Pd bond following carbon−carbon double-bond insertion is the key step to give the conjugate addition product and regenerate the catalytic Pd(II) species.[10] We thus concentrated our investigation on the transformations involving protonolysis of C−Pd bonds and the governing factors in this elementary reaction.[11,12]

Protonolysis of C−Pd Bond in Catalytic Reactions. In our preliminary communications,[10] we reported two catalytic reactions based on tandem nucleophile−alkyne−α,β-unsaturated carbonyl coupling. In both systems, we found that a halide ion is critical to the catalytic transformation. This prompted us to take a close look at the effect of halide amount on the two reactions.

Scheme 2



Scheme 3



We first examined the Pd(II)-promoted cyclization-coupling reaction of 3-heptynoic acid (**1**) with acrolein (Scheme 2): In this reaction, we propose that intramolecular oxypalladation followed by acrolein insertion generates a (2-oxoalkyl)palladium intermediate (**CP-I**). We found when **1** reacted with 5 equiv of acrolein in the presence of a catalytic amount of $Pd(OAc)_2$ (0.05 equiv) and excess LiBr (2 equiv) in HOAc, the reaction gave, via protonolysis of **CP-I**, the product **2** in 85% yield (based on **1**) (Scheme 2, A). However, in the presence of a decreased amount of LiBr ($LiBr/Pd(OAc)_2 = 2:1$), **3**, produced by β-H elimination, was obtained in 94% yield (based on Pd) together with precipitated palladium black (Scheme 2, B).

We then studied the halide effect in the bromide−acetylene−acrolein tandem addition reaction (Scheme 3). In this system (acetylene, LiBr, acrolein in HOAc solvent in the presence of a catalytic amount of $Pd(OAc)_2$), the (2-oxoalkyl)palladium intermediate **CP-II** is generated from bromopalladation of acetylene and consecutive insertion of acetylene and acrolein. From this intermediate, protonolysis leads to **4**, while β-H elimination gives **5**. When the $LiBr:Pd(OAc)_2$ ratio was changed from 10:1 to 200:1, we found not only the yield of the protonolysis product **4** increased dramatically (from 550% to 3980%, based on Pd) but also the formation of β-H elimination product **5** was diminished.

These above results with two catalytic reactions qualitatively suggest that low concentration of halide

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(11) Although protonolysis of the C−Pd bond is, in principle, also an important reaction of organopalladium compounds, its study and application are far less reported in the literature than the β-H elimination and other elementary reactions. (a) Cacchi, S.; La Torre, F.; Misisti, D. *Tetrahedron Lett*. **1979**, *25*, 4591−4594. (b) Cacchi, S. *Pure Appl. Chem*. **1990**, *62*, 713−722. (c) Coperet, C.; Sugihara, P.; Wu, G.; Shimovama, I.; Negishi, E.-I. *J. Am. Chem. Soc*. **1995**, *117*, 3422−3431.

(12) In the few studied systems involving protonolysis, the formation of protonolysis products was influenced by many factors, and there has been no consensus regarding the reaction mechanism. (a) Yamamura, K. *J. Org. Chem*. **1978**, *43*, 724−727. (b) Amorese, A.; Arcadi, A. Bernocchi, E.; Cacchi, S.; Cerrini, S. Fededi, W.; Ortar, G. *Tetrahedron* **1989**, *45*, 813−828. (c) Denmark, S. E.; Schnute, M. E. *J. Org. Chem*. **1995**, *60*, 1013−1019.

Scheme 4

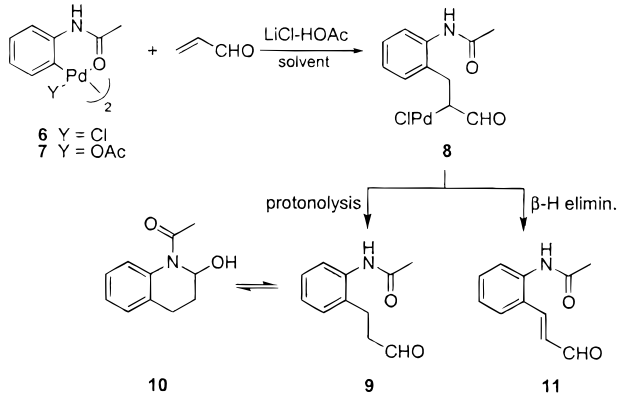
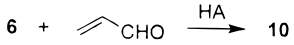


Table 1. Effect of Proton Source (HA) on the Protonolysis Reaction[a]



entry	HA	time (min)	**10**, yield (%)[b]
1	EtOH	>300	*c,d*
2	HOAc	<1	81
3	CF_3COOH	<1	70
4	HCl−MeCN	<1	65

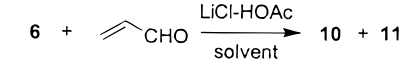
[a] Reaction conditions: **6** (0.2 mmol), acrolein (2 mmol), LiCl (1 mmol), HA (1 mL), room temperature. [b] Isolated yield based on **6**. [c] No organic product was detected after 5 h. [d] Product **10** can be isolated in 56% yield after addition of 2 equiv of HOAc.

ions favors formation of β-H elimination products, while high concentration of halide ions seems to inhibit β-H elimination, leading to exclusive protonolysis. However, the catalytic cycles involve multiple intermediates and reaction steps; this makes it more difficult to identify the halide effect on each individual step, e.g., the protonolysis step. To further explore the mechanism of protonolysis and to examine the generality of the halide effect observed in the catalytic reactions, we decided to study the stoichiometric reaction of palladium complexes **6** and **7** with acrolein (Scheme 4) as a model reaction.

Protonolysis of C−Pd Bond in Stoichiometric Reactions. Complexes **6** and **7** were prepared by literature methods.[13,14] The good solubility and stability of these complexes in a number of different solvents make them suitable probes to test the reaction with olefin compounds such as acrolein.

Effect of Proton Source. The reaction of **6** with acrolein was tested in a number of protic solvents, as well as in an aqueous HCl−acetonitrile mixture (Table 1). LiCl was added to provide a coordination environment similar to that in the tandem addition reactions.[10] Carboxylic acids were found to give superior yields of addition product than inorganic acid. Instead of **9**, the predicted protonolysis product, we isolated product **10**, which has a cyclic lactol-like structure, presumably formed by the interaction between the amide N−H group and the aldehyde group of **9** (Scheme 4).[15] In EtOH, the reaction gave no detectable products in 5 h (Table 1, entry 1); it is noteworthy that the β-H elimination product, **11**, was not formed and no Pd(0) precipitation was observed. When 2 equiv of HOAc was added to the above reaction mixture, the reaction proceeded to afford compound **10** in 56% isolated yield.

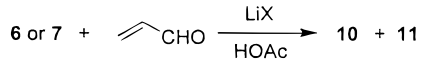
Table 2. Solvent Effect on Insertion−Protonolysis Reaction of C−Pd Bond[a]



			yield (%)[b]	
entry	solvent	time (min)	**10**	**11**
1	C_6H_6	2		87
2	MeCN	2	22	46
3	MeOH	2	40	35
4	HOAc	<1	81	

[a] Reaction conditions: **6** (0.2 mmol), LiCl (2 mmol), acrolein (2 mmol), HOAc (1 mmol), and solvent (1 mL), room temperature. [b] Isolated yield based on **6**.

Table 3. Effect of Halide Ions on Protonolysis and β-H Elimination of C−Pd Bond[a]



			yield (%)[b]	
X^-	[*c*] (M)	observation	**10**	**11**
none		Pd↓		87
OAc^-	1.0	Pd↓		78
ClO_4^-[c]	1.0	Pd↓		82
F^-	2.0	Pd↓	5	71
Cl^-	1.0	clear solution	84	
Br^-	1.0	clear solution	81	
I^-	1.0	clear solution	78	

[a] Reaction conditions: **6** (0.2 mmol), acrolein (1 mmol), LiX (10 mmol), HOAc (1 mL), room temperature. [b] Isolated yield based on **6**. [c] The acetate complex **7** was used in the reaction.

Influence of Solvent. Using HOAc as the protonating agent, solvents of different polarities were examined. In acetonitrile and methanol (Table 2, entries 2 and 3), the reaction gave a mixture of **10** and the β-H elimination product **11**, while in benzene (Table 2, entry 1), only the formation of **11** was observed.[16]

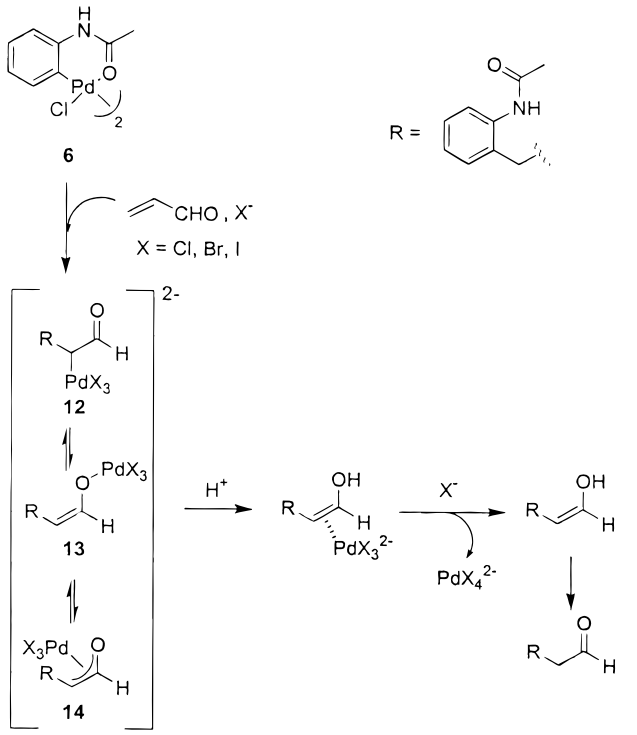
Ligand Effect. We studied the ligand effect of the reaction by providing different coordinating anions with lithium salts (LiOAc, LiF, $LiClO_4$, LiCl, LiBr, and LiI). As shown in Table 3, in the same solvent (HOAc), reactions with no extra anionic ligand or with ClO_4^- or OAc^- give only **11** as the product, while reactions with Cl^-, Br^-, or I^- afford exclusively the protonolysis product **10**. This indicates that the anions play a critical role in determining the reaction outcome.[17]

The significant differences in these results (Table 3) suggest that the reaction is governed by the coordination and electron-donating abilities of the anions. On the basis of these data, a mechanism involving a heterolytic C−Pd bond cleavage in the presence of an excess of halide ions is proposed (Scheme 5): Acrolein coordination and insertion first give the intermediate **12**. Protonation of the C−Pd bond in **12** then affords the addition product **10**.

(13) Horino, H.; Inoue, N. *J. Org. Chem.* **1981**, *46*, 4416−4422.
(14) Horino, H.; Inoue, N. *Tetrahedron Lett.* **1979**, 2403−2406.
(15) Kim, K. S.; Szarck, W. A. *Carbohydr. Res.* **1982**, *104*, 328−333.

(16) The "solvent effect" in benzene may actually be the result of low concentration of free dissociated halide ions. Please see the related discussion on ligand effect.
(17) The reactions of the acetate complex **7** with acrolein in the presence of different Li salts give similar results to chloro complex **6**. The data are included in Supplementary Table 1 (S-Table 1).

Scheme 5



This process is facilitated by the following factors.

(1) In structure **12**, a large excess of chloride, bromide, or iodide ions ($X = Cl^-$, Br^-, or I^-) effectively diminishes the β-H elimination by occupancy of the free coordination site. Also, the electron donation from X^- to the Pd results in a highly polarized C−Pd bond, which readily undergoes protonolysis in acidic media.

(2) The intermediate **12** has a mesomeric palladium enolate structure and is in equilibrium with a π-oxoallylpalladium form. The ionic character of Pd−O structures facilitates the protonation and heterolytic fission of the organopalladium bond.[11a,12b,18]

The data in Table 1 and Table 2 are also consistent with such a halide-assisted heterolytic mechanism.

(1) Table 1 shows that the reaction rate increases with increasing acidity of the proton source. This can be explained by the following: (a) protonation of the amide group of **6** or **7** helps release the Pd to react with acrolein, when acrolein insertion is the rate-determining step; or (b) the enolization of **12** is acid-catalyzed, if the protonolysis step is rate-limiting.

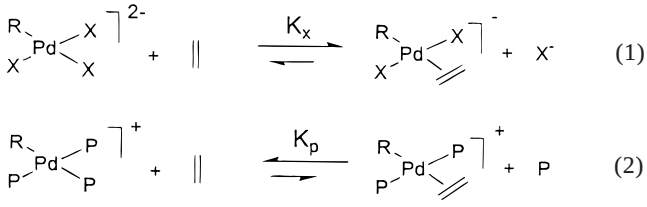
(2) Polar, dissociating solvents may provide higher concentration of free halide ions, which inhibits β-H elimination and promotes protonolysis, giving higher yields of **10** (Table 2).

An alternative possibility to account for the clean protonolysis (no β-H elimination) in the presence of excess of halide ions is that strong acids (HCl, HBr, or HI) formed in situ from HOAc and X^- might rapidly cleave the C−Pd bond. However, while strong acids do facilitate C−Pd bond cleavage and contribute to faster protonolysis reaction (Table 1, entries 1−4), the experiment with ClO_4^- (Table 3, entry 3) shows that, with a noncoordinating anion (ClO_4^-), the reaction exclusively gives β-H elimination product even though a strong acid ($HClO_4$) is also possibly formed in HOAc. The experiment using a weak Brønsted acid (Table 1, entry 1) further shows that coordination of X^- does inhibit the β-H elimination even when protonolysis is not in competition. These data strongly support that the inhibition of β-H elimination by an excess of halide ions is the major reason for the clean protonolysis reaction.

(18) Cacchi, S.; Palmier, G. *Tetrahedron* **1983**, *39*, 3373−3383.

Remarks

From the systematic studies of the reactions of stoichiometric arylpalladium complexes with acrolein, we have established that an excess of halide ions (Cl^-, Br^-, and I^-) can block β-H elimination while promoting protonolysis. These reactions cannot be achieved with phosphine ligands because under similar conditions excess phosphine shuts down the reaction completely by blocking the coordination of the olefin substrate.[19] This unique advantage of halide may result from the facile ligand exchange from a halide to an olefin, as opposed to the sluggish and unfavorable exchange from a phosphine to an olefin, $K_X > 1 > K_P$ (eqs 1 and 2).



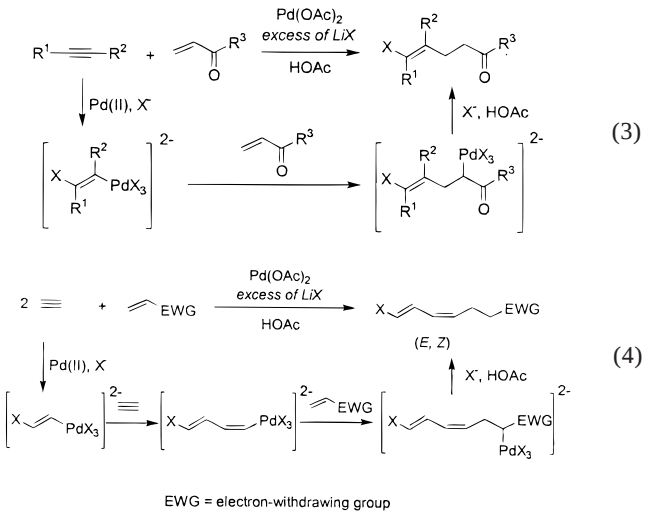
(1)

(2)

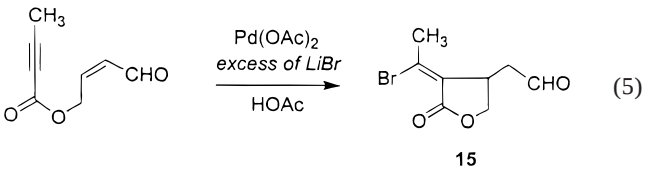
It is significant that by simply applying metal halides, the reaction pathway of an alkylpalladium intermediate can be cleanly switched from the normal β-H elimination (Heck-type reaction) to a heterolytic C−Pd bond cleavage process, i.e., protonolysis when the forming carbanion is stabilized by an electron-withdrawing group. Unlike β-H elimination, which normally leads to formation of Pd(0), protonolysis regenerates divalent palladium as the active species. On the basis of these findings and the many well-established Pd(II)-initiated C−Pd formation reactions,[5,20] an array of Pd(II)-catalyzed reactions can be designed. For example, combining halopalladation and halide-assisted protonolysis, we have developed two tandem addition reactions for the preparation of γ,δ-unsaturated carbonyls and functionalized (*E*,*Z*)-dienes, respectively[10a,d] (eqs 3 and 4). In these two reactions, halopalladation of the alkyne with $Pd(OAc)_2$−LiX generates the first vinylpalladium intermediate, which is followed by either insertion of an α,β-unsaturated carbonyl compound (eq 3) or consecutive insertion of acetylene and an electron-deficient olefin (eq 4) to give a (2-oxoalkyl)palladium intermediate. Upon halide-assisted protonolysis, the reaction gives the tandem addition product and regenerates the active Pd(II) species. An intramolecular version of eq 3 has also been developed to prepare the lactonic aldehyde **15** (eq

(19) When we attempted the reaction of acrolein with the vinylpalladium generated by halopalladation of an alkyne in the presence of excess triphenylphosphine, no acrolein insertion product was detected. Yagupsky, G.; Mowat, W.; Shortland, A.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1970**, 1369. Cross, R. J. In *The Chemistry of the Metal−Carbon Bond*; Hartley, F. R., Patai, S., Eds.; Wiley: Chichester, 1985; Vol. 2, p 559.

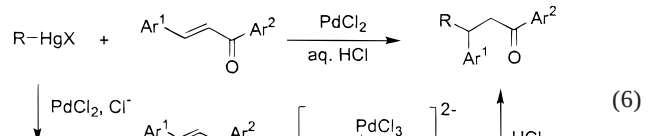
(20) Maitlis, P. M. *The Organic Chemistry of Palladium*; Academic Press: New York, 1971; Vols. 1−2.



5), a key intermediate used in a formal synthesis of (+)-pilocarpine.[10c]



Incorporating Pd(II)-mediated transmetalation with protonolysis, Cacchi et al. achieved Pd-catalyzed conjugate addition of organomercury reagents to α,β-unsaturated carbonyl compounds (eq 6).[11a,b]



The above examples demonstrate that halide-assisted protonolysis is an efficient method for regenerating catalytic Pd(II) species from organopalladium intermediates. Combined with other Pd(II)-initiated C−Pd formation reactions, such as oxypalladation and arene palladation, they might be used to develop a diversity of useful Pd(II)-catalyzed processes. Furthermore, simple palladium salts are used in these reactions; the ready availability, easy recovery and handling of the catalyst, and simplicity of operation (no O_2- or air-free requirements) should make them attractive choices in synthesis.

Conclusion

In conclusion, halide ions play an important role in Pd(II)-mediated conjugate addition reactions. The halide ion can block the β-H elimination of a (2-oxoalkyl)-palladium species, giving preferentially the protonolysis product in acidic media. It is significant that halide ions in these reactions do not inhibit the insertion of the double bond as phosphines usually do, but only inhibit the β-H elimination step. This important finding is expected to have a broad impact on the studies of Pd(II)-catalyzed reactions and lead to rational design of efficient catalytic systems.

Experimental Section

General Considerations. Spectral data were obtained by the use of the following instruments: Bruker AM-300 (^{1}H NMR), Shimadzu IR-440 (IR), Finnigan 4021 (MS), and Finnigan MAT8430 (HRMS). Complex **6** and **7** were prepared according to the literature procedure.[13,14]

Palladium-Catalyzed Cyclizing Coupling of 3-Heptynoic Acid with Acrolein. A mixture of 3-heptynoic acid (**1**, 126 mg, 1 mmol), $Pd(OAc)_2$ (11.3 mg, 0.05 mmol), acrolein (280 mg, 5 mmol), LiBr (174 mg, 2 mmol), and HOAc (5 mL) was stirred at room temperature until the reaction was complete as monitored by TLC. The reaction mixture was extracted with ether (80 mL) and washed with water (5 mL), and the ether layer was dried with Mg_2SO_4. After removal of ether, the residue was chromatographed on silica gel (eluent: 10:2 petroleum ether/ethyl acetate) gave **2** as an oil (155 mg, 85%). ^{1}H NMR ($CDCl_3$): δ 9.80 (s, 1H), 3.12 (s, 2H), 2.58 (t, J = 7.1 Hz, 2H), 2.45 (t, J = 7.1 Hz, 2H), 2.30 (t, J = 7.3 Hz, 2H), 1.56 (tq, J = 7.3, 7.3 Hz, 2H), 0.92 (t, J = 7.3 Hz, 3H). IR (neat): ν 2970, 2700, 1800, 1730, 1390, 1250, 1150, 980, 895 cm^{-1}. MS (m/z): 183 (M^+ + 1), 182 (M^+), 154, 139, 126, 111, 83, 71 (100), 55, 43. HRMS: Calcd for $C_{10}H_{14}O_3$ 182.0943; found 182.0957.

Effect of LiBr on the Cyclizing Coupling of 3-Heptynoic Acid with Acrolein. A mixture of 3-heptynoic acid (**1**, 252 mg, 2 mmol), $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), acrolein (280 mg, 5 mmol), LiBr (17.4 mg, 0.2 mmol), and HOAc (5 mL) was stirred at room temperature. The red solution gradually turned dark, and Pd metal began to precipitate out. After 5 h, the reaction was worked up as usual. Column chromatography on silica gel (eluent: 10:2 petroleum ether/ethyl acetate) gave **3** as an oil (17 mg, 94%, calculated on the basis of Pd) together with recovered **1** (230 mg). **3**: ^{1}H NMR ($CDCl_3$): δ 9.60 (d, J = 7.7 Hz, 1H), 7.28 (d, J = 15.5 Hz, 1H), 5.97 (dd, J = 15.5, 7.7 Hz, 1H), 3.37 (s, 2H), 2.56 (t, J = 7.3 Hz, 2H), 1.70 (tq, J = 7.3, 7.3 Hz, 2H), 1.00 (t, J = 7.3 Hz, 3H). IR (KBr): ν 2950, 1820, 1690, 1640, 1460, 1150, 1105, 980, 890 cm^{-1}. MS (m/z): 181 (M^+ + 1), 180 (M^+), 152, 137, 124, 109, 81, 71, 53, 43 (100). HRMS: Calcd for $C_{10}H_{12}O_3$ 180.0786; found 180.0829.

Palladium-Catalyzed Coupling of Acetylene with Acrolein in the Presence of Different Amounts of LiBr. Acetylene (passed successively through water, chromic acid, and concentrated sulfuric acid) was passed through a mixture of $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), LiBr (870 mg, 10 mmol), and acrolein (840 mg, 15 mmol) in HOAc (5 mL) at <15 °C for 24 h. Ether (100 mL) was added, and the mixture was washed with water (5 mL × 2). The organic layer was dried (Na_2SO_4) and concentrated, and the residue was subject to column chromatography on silica gel (eluent: 20:1 petroleum ether/ethyl acetate) to give the cotrimerization product **4** as an oil (yield: 3980% based on Pd). ^{1}H NMR ($CDCl_3$): δ 9.78 (s, 1H), 7.00 (ddd, J = 14, 11, 1.2 Hz, 1H), 6.34 (dd, J = 14, 0.3 Hz, 1H), 5.95 (ddd, J = 11, 11, 0.3 Hz, 1H), 5.44 (dtd, J = 11, 7, 1.2 Hz, 1H), 2.60−2.52 (m, 2H), 2.50 (t, J = 6.2 Hz, 2H). IR (neat): ν 2900, 2700, 1720, 1570, 1440, 1360, 1280, 1180, 1120, 1060, 970, 930, 800, 740 cm^{-1}. MS: (m/z): 189 [$M^+ - 1(^{81}Br)$], 187 [$M^+ - 1(^{79}Br)$], 161, 159, 149, 135, 133, 99, 83, 79, 69, 55 (100), 53. HRMS: Calcd for C_7H_9BrO [M^+ (^{79}Br)] 187.9837; found 187.9825.

In a similar experiment, acetylene was passed through a mixture of $Pd(OAc)_2$ (112 mg, 0.5 mmol), LiBr (435 mg, 5 mmol), and acrolein (10 mL) in HOAc (50 mmol) at room temperature. The solution gradually turned dark, and Pd metal began to precipitate out. After 24 h, the reaction mixture was worked up as above. The residue was subject to column chromatography on silica gel using gradient elution (eluent: from 100:1 to 50:1 to 25:1 hexane/ethyl acetate) to give **4** (210%

based on Pd) and **5** (82% based on Pd). ^{1}H NMR (400 MHz, $CDCl_3$) of **5**: δ 9.60 (d, J = 7.9 Hz, 1H), 7.19 (dd, J = 15.4, 11.1 Hz, 1H), 6.96 (dd, J = 11.1, 9.2 Hz, 1H), 6.75 (dd, J = 11.8, 9.2 Hz, 1H), 6.61 (dd, J = 15.0, 11.8 Hz, 1H), 6.50 (d, J = 15.0 Hz, 1H), 6.22 (dd, J = 15.4, 7.9 Hz, 1H). The presence of the trienal product **5** was further supported by GC−MS analysis [(m/z): 188 (M^+ (^{81}Br)), 186 (M^+ (^{79}Br)), 107 (M^+ − Br)] and UV spectra.

Reaction of Di-μ-chlorobis(2-actaminophenyl-2C,O)-dipalladium(II) (6) or Di-μ-acetatobis(2-actaminophenyl-2C,O)dipalladium(II) (7) with Acrolein. General Procedure. In a Schlenk tube, a mixture of complex **6** (or **7**), acrolein, LiY, HOAc, and solvent was stirred at room temperature until the reaction was complete as monitored by TLC. The reaction mixture was extracted with ether and washed with water, and the ether layer was dried with $MgSO_4$. After removal of ether, the residue was chromatographed on silica gel (8:2 petroleum ether/ethyl acetate) to give **10** and **11** (Tables 1−3).

10: oil. ^{1}H NMR ($CDCl_3$): δ 7.18−7.04 (m, 4H), 5.95 (t, J = 7.6 Hz, 1H), 4.31 (br, 1H), 2.55−2.52 (m, 1H), 2.46−2.38 (m, 2H), 2.20 (s, 3H), 1.59−1.57 (m, 1H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 172.6, 136.6, 134.6, 127.1, 126.5, 125.3, 124.4, 78.7, 31.8, 25.1, 23.2. ^{13}C NMR DEPT 135° spectra (90 MHz): δ 127.1, 126.6, 125.3, 124.4, 78.7, 31.8(−), 25.1(−), 23.2. IR (neat): ν 3394, 1647, 1584, 1493, 1373, 1334, 956, 789, 761 cm^{-1}. MS (m/z): 192 (M^+ + 1), 191 (M^+), 174, 163, 149, 148, 132, 130, 106(100), 93, 91, 77. HRMS: Calcd For $C_{11}H_{13}NO_2$ 191.0946; found 191.0938.

11: mp 148−150 °C (lit. 163−164 °C,[13,14] 140 °C[21]). ^{1}H NMR (CCl_4): δ 9.70 (d, J = 6.8 Hz, 1H), 9.45 (brs, 1H), 7.55−7.40 (m, 2H), 7.40−7.20 (m, 3H), 6.08 (dd, J = 15.5, 6.8 Hz, 1H), 2.01 (s, 3H). IR (KCl): ν 3286, 1685, 1657, 1580, 1482, 1371, 994, 916, 753 cm^{-1}. MS (m/z): 190 (M^+ + 1), 189 (M^+), 172, 161, 147, 146, 131, 129, 104(100), 77.

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Supporting Information Available: The experimental procedure and results for the reaction of **7** with acrolein; ^{1}H NMR spectra for compounds **2**, **3**, **4**, **5**, **10**; and ^{13}C NMR and DEPT spectra of compound **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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