Pergamon

Tetrahedron Letters 43 (2002) 6791–6794

TETRAHEDRON
LETTERS

# Palladium(II)-catalyzed coupling reactions of alkynes and allylic compounds initiated by intramolecular carbopalladation of alkynes

Guosheng Liu and Xiyan Lu*

*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*

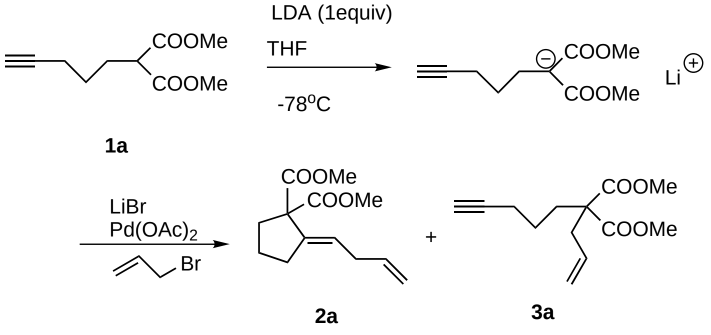
Received 22 May 2002; revised 10 July 2002; accepted 19 July 2002

**Abstract**—Under divalent palladium catalysis, a highly regio- and stereoselective coupling reaction of alkynes with allyl halides initiated by cyclocarbopalladation of alkynes proceeded smoothly in the presence of excess halide ions. The reaction involves intramolecular carbopalladation, allylic compound insertion into the vinylic–Pd bond and quenching the C–Pd bond by β-heteroatom elimination in one step without using oxidants.

Vinylpalladium species are versatile organic intermediate in palladium-catalyzed coupling reactions.[1] Besides the well studied oxidative addition of Pd(0) with vinylic halides or triflates to generate vinylic palladium species,[1] they can be also obtained from the addition of a nucleophile to alkynes coordinated with divalent palladium species.[1,2] In this case, oxygen,[2d,g] nitrogen[3] and halide[2e,f] nucleophiles have been reported. While the carbopalladation reactions of alkynes catalyzed by Pd(0) have been extensively studied,[4] palladium(II)-catalyzed reactions involving a carbanion as the nucleophile have scarcely been reported.[5]

Although the Pd(II) species is the most common active species in palladium-catalyzed carbon–carbon bond forming reactions, most of the carbon–carbon coupling reactions initially mediated by Pd(II) species are stoichiometric.[1,6] Compared with the Pd(0) species, Pd(II) species are less used as catalysts.[7] The main reason is that methods for quenching the carbon–palladium bond to regenerate the divalent palladium species are rarely reported,[2] and the carbon–palladium bond is easily quenched by β-hydride elimination or reductive elimination, which in general generates the Pd(0) species. Thus, oxidants are necessary to regenerate the divalent palladium catalyst to make the catalytic cycle possible.

In our previous work, we used β-heteroatom elimination to quench the carbon–palladium bond in the pres-



**Scheme 1.**

---

*Keywords*: carbopalladation; coupling reaction; divalent palladium; β-heteroatom elimination.

* Corresponding author. Tel.: +86-21-64163300 (ext. 3333); fax: +86-21-64166128; e-mail: xylu@pub.sioc.ac.cn

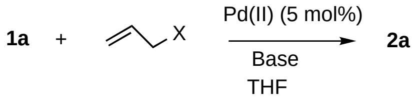
PII: S0040-4039(02)01512-5

ence of halide ions and regenerate the divalent palladium species.[2e,f] We wish to report herein the results of palladium(II)-catalyzed coupling reactions initiated by intramolecular carbopalladation of alkynes with allylic compounds.

Firstly, we investigated the reaction of **1a** (0.5 mmol), LDA (0.5 mmol) and allyl bromide (2.5 mmol) in the presence of $Pd(OAc)_2$ (5 mol%) and LiBr (2 mmol) in dry THF (4 mL) (Scheme 1). The reaction was completed in 4 h to give the cyclization product **2a** (38% yield) via the coupling reaction and another product **3a** (31% yield) from an allylic substitution reaction. When allyl chloride was used instead of allyl bromide, the reaction gave product **2a** in 85% yield with high stereo- and regioselectivity (Table 1, entry 1). The stereoconfiguration of **2a** is *E* according to the H–H NOESY spectra. Changing the base (entry 2) or the leaving group of the allylic compound (entries 3 and 4) also gave excellent yields. Excess halide ions play an important role in this reaction. In the absence of halide ions, no reaction occurred with the formation of a black precipitate (entry 5). The reaction catalyzed by $PdCl_2(PhCN)_2$ also proceeded smoothly and gave **2a** in 65% yield in the presence of an excess of chloride ions (entry 6). The reaction using the weak base, $Et_3N$, gave **2a** in 51% yield (entry 7), while no cyclization product was obtained using other bases such as $K_2CO_3$ and DBU (entries 8 and 9).

Using identical reaction conditions to those of **1a**,[8] the results of carbopalladation coupling reactions with various active methylene compounds are shown in Table 2. Similar to the malonate derivative **1a**, the reactions of

**Table 1.** Reaction of **1a** with allylic compounds catalyzed by Pd(II) species



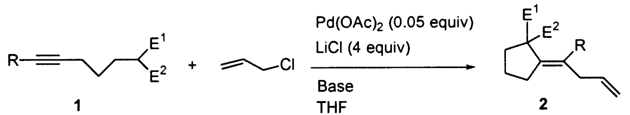
| Entry | X | Base | Pd | Additive | **2** (yield, %)[a] |
|---|---|---|---|---|---|
| 1 | Cl | LDA (1 equiv.) | $Pd(OAc)_2$ | LiCl (4 equiv.) | 85 |
| 2 | Cl | BSA (1.5 equiv.) | $Pd(OAc)_2$ | LiCl (4 equiv.) | 87 |
| 3 | OAc | LDA (1 equiv.) | $Pd(OAc)_2$ | LiBr (4 equiv.) | 80 |
| 4 | OAc | BSA (1.5 equiv.) | $Pd(OAc)_2$ | LiBr (4 equiv.) | 91 |
| 5 | OAc | BSA (1.5 equiv.) | $Pd(OAc)_2$ | – | NR[b] |
| 6 | OAc | BSA (1.5 equiv.) | $PdCl_2(PhCN)_2$ | LiCl (4 equiv.) | 65 |
| 7 | Cl | $Et_3N$ (2 equiv.) | $Pd(OAc)_2$ | LiCl (4 equiv.) | 51 |
| 8 | OAc | $K_2CO_3$ (2 equiv.) | $Pd(OAc)_2$ | LiBr (4 equiv.) | Trace |
| 9 | Cl | DBU (1 equiv.) | $Pd(OAc)_2$ | LiCl (4 equiv.) | Trace[c] |

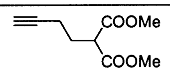
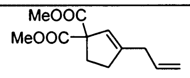
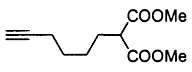
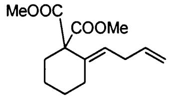
[a] Isolated yield.

[b] Black precipitate was formed.

[c] White precipitate appeared when DBU was added to the mixture.

**Table 2.** Reactions of **1** with allyl chloride catalyzed by Pd(II)



| Entry | 1 | R | $E^1$ | $E^2$ | Base | Yield % (2)[a] |
|---|---|---|---|---|---|---|
| 1 | **1a** | H | COOMe | COOMe | BSA | 87 (**2a**) |
| 2 | **1b** | H | COOEt | $COCH_3$ | BSA | 72 (**2b**) |
| 3 | **1c** | H | COOEt | CN | BSA | 68 (**2c**) |
| 4 | **1d** | H | COOMe | $(EtO)_2P(O)$ | LDA | 61 (**2d**) |
| 5 | **1e** | *n*-Bu | COOMe | COOMe | BSA | 71 (**2e**) |
| 6 | **1f** | H | CN | CN | BSA/LiOAc | 45 (**2f**) |
| 7[b] | **1h** | |  | |  | trace (**2h**) |
| 8[b] | **1i** | |  | |  | trace (**2i**) |

[a]Isolated yield. [b]BSA was used as the base

**1b**, **1c** and **1d** gave the products **2b**, **2c** and **2d** in moderate yields (entries 2, 3 and 4). Although a longer time is required, this reaction can also be applied to disubstituted alkyne **1e** and gave the product **2e** in 71% yield with high stereoselectivity (entry 5). For the malononitrile derivative **1f**, a considerable decrease in reaction rate was observed, but on addition of LiOAc, the reaction rate increased giving **2f** in 45% yield (entry 6). The stereo-configuration of products **2a**–**f** are all in the *E*-form (*trans* addition). In contrast to the reaction of **1a**, the reaction of **1h** and **1i** gave only a trace of the *endo*-five-membered ring product **2h** and six-membered ring product **2i**, respectively (entries 7 and 8).[9]

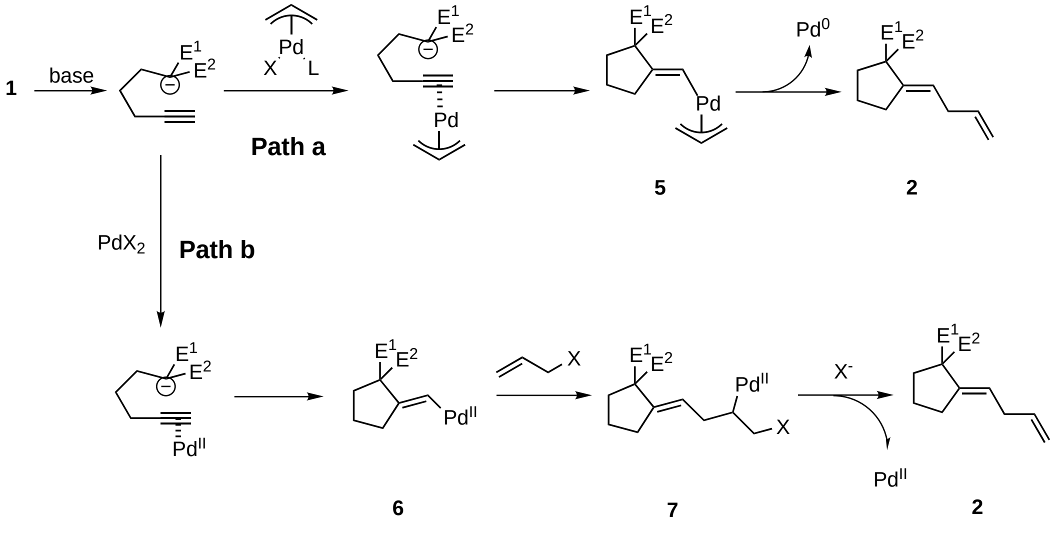
The reaction mechanism may be speculated to occur via two separate pathways (Scheme 2): **Path a** is a Pd(0)-catalyzed route starting from the reaction of Pd(0) with the allylic halide to form the π-allylpalladium(II) species which coordinates with the triple bond of **1**, followed by cyclocarbopalladation of **1** to give vinylpalladium(II) **5** and finally reductive elimination of **5** to give **2** and regenerate Pd(0).[10] On the other hand, the nucleophilic addition of the carbanion to the alkynes coordinated by Pd(II) can proceed via a different pathway (**path b**). It might be initiated by a cyclocarbopalladation of **1** to form vinylpalladium(II) **6**, followed by insertion of the allylic compound to the carbon-palladium bond of **6** to give intermediate **7** and quenching of the carbon–palladium bond by β-heteroatom elimination in the presence of excess halide ions to give **2** and regenerate Pd(II). Here, the halide ion plays a very important role in inhibiting the β-H elimination of **7**.[11]

In order to gain further support for the mechanism, 3-deuterio-allyl acetate was used in this reaction. Compound **8**[12] was obtained in 75% yield without the detection of the isomeric product (Scheme 3), which indicated that **path b** would be acceptable. Thus, a catalytic cycle involving divalent palladium did proceed in this reaction.

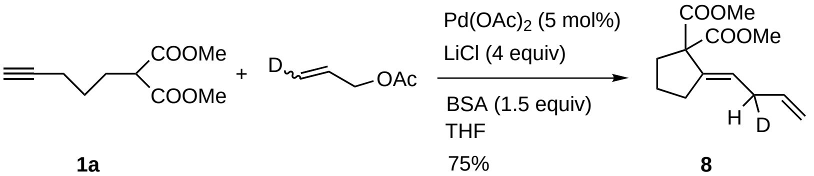
In conclusion, we have reported a divalent palladium-catalyzed coupling reaction initiated by cyclocarbopalladation of alkynes with allylic compounds. The reaction involved intramolecular carbopalladation of alkynes, allylic compound insertion to the C–Pd bond and quenching the C–Pd bond by β-heteroatom elimination in one-step without using oxidants. In the presence of halide ions, the reaction gave products with high regio- and stereoselectivity.

## Acknowledgements

The Major State Basic Research Program (Grant No, G2000077502-A). We thank the National Natural Sciences Foundation of China and Chinese Academy of Sciences for financial support.



Scheme 2.



Scheme 3.

## References

1. (a) Tsuji, J. *Palladium Reagents and Catalysis: Innovations in Organic Synthesis*; John Wiley: Chichester, 1995; (b) Soderberg, B. C. *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon, 1995; Vol. 12, Chapter 3.5, p. 241.
2. (a) Maitlis, P. M. *The Organic Chemistry of Palladium*; Academic Press: New York, 1971; Vol. 1, p. 79; (b) Maitlis, P. M. *Acc. Chem. Res.* **1976**, *9*, 93–99; (c) Kaneda, K.; Uchiyama, T.; Fujiwarka, Y.; Teranishi, S. *J. Org. Chem.* **1979**, *44*, 55; (d) Yanagihara, N.; Lambert, C.; Iritani, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 2753; (e) Lu, X.; Zhu, G.; Wang, Z. *Synlett* **1998**, 115; (f) Lu, X.; Ma, S. In *New Age of Divalent Palladium Catalysis*; Murahashi, S.-I.; Davies, S. G., Eds. Transition metal catalyzed reactions, 1999; Chapter 6, p. 133; (g) Zhang, Q.; Lu, X. *J. Am. Chem. Soc.* **2000**, *122*, 7604.
3. (a) Iritani, K.; Matsubara, S.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 1799; (b) Lei, A.; Lu, X. *Org. Lett.* **2000**, *2*, 2699.
4. (a) Monteiro, N.; Gore, J.; Balme, G. *Tetrahedron Lett.* **1991**, *32*, 1645; (b) Monteiro, N.; Gore, J.; Balme, G. *Tetrahedron* **1992**, *48*, 10103; (c) Fournet, G.; Blame, G.; Hemelryck, B.; Gore, J. *Tetrahedron Lett.* **1990**, *31*, 5147.
5. Although Pd(II) complexes mediate the addition of both stabilized carbanions and silyl enol ethers to unactivated olefins, efficient catalysis has scarcely been reported. Recently, a Pd(II)-catalyzed intramolecular addition of a 1,3-dione to unactivated olefins was reported, see: Pei, T.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2001**, *123*, 11290.
6. (a) Malleron, J. L.; Fiaud, J. C.; Legros, J. Y. *Handbook of Palladium-Catalyzed Organic Reactions*; Academic Press: San Diego, 1997; (b) Tsuji, J. *Perspectives in Organopalladium Chemistry for the XXI Century*; Elsevier Science: Lausanne, 1999.
7. (a) Perch, N. S.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **1999**, *121*, 6960; (b) Shibashaki, M.; Boden, C. D. J.; Kojima, A. *Tetrahedron* **1997**, *53*, 7371; (c) Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 2950; (d) Goeke, A.; Sawamura, M.; Kuwano, R.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 662.
8. Typical procedure using LDA as the base: LDA (0.5 mmol) was added to the mixture of compound **1** (0.5 mmol) in dry THF (4 mL) at −78°C, and the mixture was stirred for 10 min at this temperature. Then, LiCl (2 mmol), allylic compound (2.5 mmol) and Pd(OAc)$_2$ (5 mol%) were added successively. After the reaction was complete, as monitored by TLC, the mixture was allowed to warm to room temperature and 10 mL water was added. The mixture was extracted with diethyl ether. The combined extracts were dried, filtered, and the solvent was evaporated under vacuum. The resulting crude oil was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/15) to give **2**. Typical procedure using BSA as the base: BSA (0.75 mmol) was added to a mixture of LiCl (2 mmol), allylic compound (2.5 mmol), Pd(OAc)$_2$ (5 mol%) and **1** (0.5 mmol) in dry THF (4 mL) at room temperature. The work-up procedure is the same as above. All the products were characterized by spectroscopic data. Typical spectroscopic data for compound **2a**: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 5.80 (m, 1H), 5.69 (t, $J = 6.4$ Hz, 1H), 5.05 (d, $J = 17.1$ Hz, 1H), 4.97 (d, $J = 10.1$, 1H), 3.70 (s, 6H), 2.78 (t, $J = 6.4$ Hz, 2H), 2.35 (t, $J = 7.3$ Hz, 2H), 2.29 (t, $J = 7.0$ Hz, 2H), 1.72 (m, 2H). IR (neat): 2955, 1734, 1638, 1435, 1261, 1143 cm$^{-1}$; MS (*m/e*): 238 (M$^+$), 178, 145, 119 (100), 91, 77, 59; HRMS (M$^+$): calcd for $C_{13}H_{18}O_4$: 238.1205; found: 238.1177.
9. The reactions of **1h** and **1i** are complicated, and it is difficult to obtain pure compounds **2h** and **2i**.
10. A similar mechanism involved coordination of π-allylpalladium(II) with allenes, see: Kimura, M.; Fugami, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1992**, *57*, 6377.
11. In divalent palladium-catalyzed reactions, the excess halide ions can prohibit the β-H elimination, see: Zhang, Z.; Lu, X.; Xu, Z.; Zhang, Q.; Han, X. *Organometallics* **2001**, *20*, 3724.
12. Data for compound **8**: colorless oil, $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 5.81 (m, 1H), 5.69 (m, 1H), 5.06 (d, $J = 17.1$ Hz, 1H), 4.97 (d, $J = 10.2$ Hz, 1H), 3.73 (s, 6H), 2.80 (dd, $J = 6.7$, 7.9 Hz, 1H), 2.39 (t, $J = 7.3$ Hz, 2H), 2.32 (t, $J = 6.7$ Hz, 2H), 1.74 (m, 2H); IR (neat): 2956, 1733, 1636, 1435, 1264, 1140 cm$^{-1}$; MS (*m/e*): 239 (M$^+$), 208, 179, 145, 120 (100), 92, 77, 59; HRMS (M$^+$–OMe): calcd for $C_{12}H_{14}DO_3$: 208.1084; found: 208.1122.