DOI: 10.1021/om900704m

ORGANOMETALLICS
Communication

Palladium-Catalyzed Diacetoxylation of Methylenecyclopropanes via C(sp^3)−C(sp^3) Bond Breaking

Min Jiang and Min Shi*

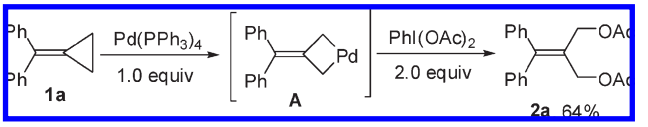
State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, People's Republic of China

Received August 9, 2009

Summary: Methylenecyclopropanes ***1*** *can undergo an effective palladium-catalyzed ring-opening reaction to give the diacetoxylated products* ***2*** *in good yields through C−C bond cleavage in the presence of* $Pd(OAc)_2$ *using* $PhI(OAc)_2$ *as the terminal oxidant and* Bu_4NI *as an additive under mild conditions. A plausible reaction mechanism has been also discussed on the basis of experimental results.*

Vicinal bifunctionalizations of alkenes are among the most important transformations in organic chemsitry.[1] Recently, palladium-catalyzed diamination[2] and amino oxygenation[3] of olefins or cyclopropanes as well as the functional-group- or ligand-directed acetoxylation of carbon−hydrogen bonds have been achieved on the basis of Pd(II)/Pd(IV) catalytic systems using $PhI(OAc)_2$ as the oxidant.[4] Inspired by these achievements, we envisaged that methylenecyclopropanes (MCPs) as highly strained and readily accessible starting materials can undergo an intriguing acetoxylation in the presence of palladium catalyst and $PhI(OAc)_2$. This cyclopropane ring opening can provide the kinetic processes for their strain unleashing,[5,6] and a variety of C−C bond cleavage products could be easily obtained using palladium complexes as the catalysts in the reactions with alcohols or amines.[7] We first attempted to use $Pd(PPh_3)_4$ (1.0 equiv) as the promoter and $PhI(OAc)_2$ (2.0 equiv) as the oxidant to examine the reaction outcome and found that the corresponding diacetoxylated product **2a** was obtained in 64% yield, presumably through the formation of the Pd(II) intermediate **A** and a subsequent Pd(II)/Pd(IV) catalytic cycle.[8] Several examinations revealed that 1.0 equiv of Pd(0) is necessary for this reaction to give **2a** in good yields (Scheme 1). We have now found that $Pd(OAc)_2$ can be used in a catalytic amount to replace $Pd(PPh_3)_4$. In this communication we report this novel palladium(II)-catalyzed diacetoxylation of methylenecyclopropanes **1** to produce the diacetoxylated products **2** via C−C bond cleavage in the presence of $PhI(OAc)_2$.

Scheme 1. Reaction of MCP 1a with $Pd(PPh_3)_4$ and $PhI(OAc)_2$



Initial studies using diphenylmethylenecyclopropane **1a** as the substrate were aimed at determining the optimal conditions for this palladium(II)-catalyzed ring opening and diacetoxylation. The results are summarized in Table 1. As revealed in Table 1, we found that the use of $Pd(OAc)_2$ (20 mol %, 0.2 or 1.0 equiv) as the catalyst afforded either **2a** in 6% yield or complex product mixtures when the reaction

*To whom correspondence should be addressed. Fax: 86-21-64166128. E-mail: Mshi@mail.sioc.ac.cn.

(1) (a) Block, E.; Schwan, A. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. *4*, pp 329−362. For various transition-metal-mediated difunctionalizations, see: (b) Kolb, H. C.; Vannieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547. (c) Muniz, K.; Iesato, A.; Nieger, M. *Chem. Eur. J.* **2003**, *9*, 5581–5596. (d) Li, G.; Wei, H.-X.; Kim, S. H. *Org. Lett.* **2000**, *2*, 2249–2252. (e) El-Qisairi, A. K.; Qaseer, H. A.; Katsigras, G.; Lorenzi, P.; Trivedi, U.; Tracz, S.; Hartman, A.; Miller, J. A.; Henry, P. M. *Org. Lett.* **2003**, *5*, 439–441. (f) Manzoni, M. R.; Zabawa, T. P.; Kasi, D.; Chemler, S. R. *Organometallics* **2004**, *23*, 5618–5621. (g) Lei, A.; Lu, X.; Liu, G. *Tetrahedron Lett.* **2004**, *45*, 1785–1788.

(2) (a) Streuff, J.; Hovelmann, C. H.; Nieger, M.; Muniz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586–14587. (b) Li, G.; Wei, H.-X.; Kim, S.-H.; Carducci, M. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 4277–4280. (c) Chen, D.; Timmons, C.; Wei, H.-X.; Li, G. *J. Org. Chem.* **2003**, *68*, 5742–5745.

(3) For aminoacetoxylation using the Pd(II)/Pd(IV) catalytic system, see: (a) Alexanian, E. J.; Lee, C.; Sorensen, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 7690–7691. (b) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179–7181. (c) Desai, L. V.; Sanford, M. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5737–5740.

(4) (a) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300–2301. (b) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542–9543. (c) Kalyani, D.; Sanford, M. S. *Org. Lett.* **2005**, *7*, 4149–4152. (d) Hull, K. L.; Anani, W. Q.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 7134–7135. (e) Desai, L. V.; Stowers, K. J.; Sanford, M. S. *J. Am. Chem. Soc.* **2008**, *130*, 13285–13293. (f) Ball, N. D.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 3796–3797. For a review, see: (g) Deprez, N. R.; Sanford, M. S. *Inorg. Chem.* **2007**, *46*, 1924–1935.

(5) Selected reviews: (a) Henry, N. C.; Wong, M. Y.; Chun, W. T.; Yu, C. Y. *Chem. Rev.* **1989**, *89*, 165–198. (b) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117–3179. (c) Nakamura, I.; Yamamoto, Y. *Adv. Synth. Catal.* **2002**, *344*, 111–129. (d) Brandi, A.; Cicchi, S.; Cordero, F. M.; Goti, A. *Chem. Rev.* **2003**, *103*, 1213–1269. (e) Nakamura, E.; Yamago, S. *Acc. Chem. Res.* **2002**, *35*, 867–877.

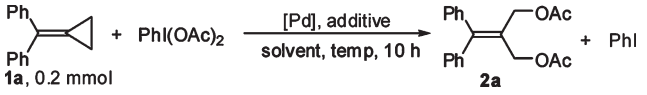
(6) Selected recent contributions from our group: (a) Shi, M.; Liu, L. P.; Tang, J. *J. Am. Chem. Soc.* **2006**, *128*, 7430–7431. (b) Shao, L.-X.; Xu, B.; Huang, J.-W.; Shi, M. *Chem. Eur. J.* **2006**, *12*, 510–517. (c) Shi, M.; Xu, B.; Huang, J.-W. *Org. Lett.* **2004**, *6*, 1175–1178. (d) Tian, G.-Q.; Shi, M. *Org. Lett.* **2007**, *9*, 4917–4920. (e) Shao, L.-X.; Li, Y.-X.; Shi, M. *Chem. Eur. J.* **2007**, *13*, 862–869. Recent examples on the metal-catalyzed C−C and C−H activation of MCPs: (f) Fürstner, A.; Aḷssa, C. *J. Am. Chem. Soc.* **2006**, *128*, 6306–6307. (g) Fürstner, A.; Aḷssa, C. *J. Am. Chem. Soc.* **2007**, *129*, 14836–14837.

(7) (a) Camacho, D. H.; Nakamura, I.; Saito, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 3365–3367. (b) Camacho, D. H.; Nakamura, I.; Saito, S.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 270–275. (c) Nakamura, I.; Itagaki, H.; Yamamoto, Y. *J. Org. Chem.* **1998**, *63*, 6458–6459. (d) Tsukada, N.; Shibuya, A.; Nakamura, I.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 8123–8124. (e) Scott, M. E.; Bathuel, Y.; Lautens, M. *J. Am. Chem. Soc.* **2007**, *129*, 1482.

(8) (a) Nakamura, I.; Oh, B.-H.; Saito, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1298–1300. (b) Oh, B.-H.; Nakamura, I.; Saito, S.; Yamamoto, Y. *Tetrahedron Lett.* **2001**, *42*, 6203–6205. (c) Nakamura, I.; Saito, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 2661–2663. (d) Nakamura, I.; Siriwardana, A. I.; Saito, S.; Yamamoto, Y. *J. Org. Chem.* **2002**, *67*, 3445–3449.

 Published on Web 09/17/2009

Table 1. Optimization of the Reaction Conditions



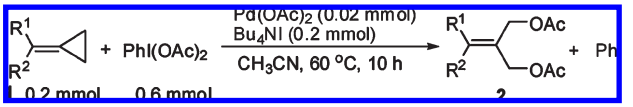
entry[a]	[Pd]	$PhI(OAc)_2$	additive	solvent	T/°C	yield (%)[b] 2a
1	$Pd(OAc)_2$, 0.2 eq	-	-	CH_3CN	60	6
2	-	2.0 eq	-	CH_3CN	60	-
3	$Pd(OAc)_2$, 1.0 eq	-	-	CH_3CN	60	complex
4	$Pd(OAc)_2$, 0.2 eq	2.0 eq	-	CH_3CN	60	8
5	$Pd(OAc)_2$, 0.2 eq	2.0 eq	Bu_4NI, 1.0 eq	CH_3CN	60	63
6	$Pd(OAc)_2$, 0.2 eq	2.0 eq	Bu_4NI, 0.2 eq	CH_3CN	60	complex
7	$Pd(OAc)_2$, 0.2 eq	-	Bu_4NI, 1.0 eq	CH_3CN	60	7
8	$Pd(OAc)_2$, 0.1 eq	2.0 eq	Bu_4NI, 2.0 eq	CH_3CN	60	68
9	***$Pd(OAc)_2$, 0.1 eq***	***3.0 eq***	***Bu_4NI, 1.0 eq***	***CH_3CN***	***60***	***71***
10	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NI, 1.0 eq	CH_3CN	rt	NR
11	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NI, 1.0 eq	DCE	60	60
12	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NI, 1.0 eq	toluene	60	54
13	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NI, 1.0 eq	HOAc	60	17
14	$PdCl_2$, 0.1 eq	3.0 eq	Bu_4NI, 1.0 eq	CH_3CN	60	68
15	$PdBr_2$, 0.1 eq	3.0 eq	Bu_4NI, 1.0 eq	CH_3CN	60	67
16	$Pd(OAc)_2$, 0.1 eq	3.0 eq[c]	-	HOAc	60	complex
17	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NOAc, 1.0 eq	CH_3CN	60	64
18	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NBr, 1.0 eq	CH_3CN	60	34
19	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NCl, 1.0 eq	CH_3CN	60	20
20	$Pd(OAc)_2$, 0.1 eq	3.0 eq	Bu_4NF, 1.0 eq	CH_3CN	60	trace

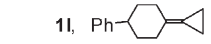
[a] Reaction conditions: **1** (0.2 mmol), [Pd] (0.1−1.0 equiv), $PhI(OAc)_2$ (2.0−3.0 equiv), additive (0.2−2.0 equiv), solvent (2.0 mL), room temperature or 60 °C. [b] Isolated yield. [c] Using benzoquinone instead of $PhI(OAc)_2$.

was performed in acetonitrile at 60 °C (Table 1, entries 1 and 3). Adding $PhI(OAc)_2$ (2.0 equiv) as the oxidant did not improve the reaction outcome (Table 1, entry 4). Without the use of Pd(II) catalyst, no reaction occurred (Table 1, entry 2). Also, we found that adding 1.0 equiv of Bu_4NI as a coadditive along with 0.2 equiv of $Pd(OAc)_2$ and 2.0 equiv of $PhI(OAc)_2$ produced **2a** in 63% yield (Table 1, entry 5). Reducing the amount of Bu_4NI to 0.2 equiv provided complex product mixtures. Increasing the amount of Bu_4NI to 2.0 equiv did not further improve the production of **2a** (Table 1, entries 6 and 8). The employment of 2.0 equiv of $PhI(OAc)_2$ was also found to be essential under the above conditions (Table 1, entry 7). Further examination of the employed amount of $PhI(OAc)_2$, temperature and solvent effects, palladium(II) source, and the counterions in ammonium salts revealed that using $Pd(OAc)_2$ (0.1 equiv), $PhI(OAc)_2$ (3.0 equiv), and Bu_4NI (1.0 equiv) resulted in a 71% yield of **2a** at 60 °C in MeCN (Table 1, entries 9−20), which serves as the optimal conditions for the diacetoxylation of **1a**.

With the optimized reaction conditions being identified, we next carried out this reaction using a variety of MCPs **1** to evaluate the generality of this reaction. The results are summarized in Table 2. As can be seen from Table 2, for various diarylmethylenecyclopropanes in which R^1 and R^2 are aromatic groups, the corresponding diacetoxylated products **2b**−**k** can be obtained in 72−83% yields within 10 h under the standard conditions. The electronic nature of the substituents on their benzene rings did not significantly influence the reaction outcome (Table 2, entries 1−10). Furthermore, using unsymmetrical MCPs **1n**−**r**, in which R^1 is an aromatic group and R^2 is a hydrogen atom, as the

Table 2. Palladium-Catalyzed Opening Reactions of MCPs 1 under the Optimal Conditions



entry[a]	**1**, R^1/R^2	yield (%)[b] **2**
1	**1b**, *p*-MeC_6H_4/*p*-MeC_6H_4	**2b**, 74
2	**1c**, *p*-$MeOC_6H_4$/*p*-$MeOC_6H_4$	**2c**, 72
3	**1d**, *m*,*p*-MeC_6H_3/C_6H_5	**2d**, 78
4	**1e**, *p*-MeC_6H_4/C_6H_5	**2e**, 83
5	**1f**, *o*,*m*-MeC_6H_3/C_6H_5	**2f**, 81
6	**1g**, *p*-ClC_6H_4/*p*-ClC_6H_4	**2g**, 63
7	**1h**, *p*-ClC_6H_4/*o*-ClC_6H_4	**2h**, 76
8	**1i**, *p*-ClC_6H_4/C_6H_5	**2i**, 77
9	**1j**, *p*-FC_6H_4/*p*-FC_6H_4	**2j**, 72
10	**1k**, *p*-FC_6H_4/C_6H_5	**2k**, 76
11	**1l**, 	**2l**, complex
12	**1m**, *p*-BrC_6H_4/CH_3	**2m**, complex
13	**1n**, C_6H_5/H	**2n**, 76
14	**1o**, *m*-MeC_6H_4/H	**2o**, 82
15	**1p**, *p*-ClC_6H_4/H	**2p**, 79
16	**1q**, *p*-BrC_6H_4/H	**2q**, 80
17	**1r**, *o*,*m*-$Cl_2C_6H_3$/H	**2r**, 84

[a] Reaction conditions: **1** (0.2 mmol), $PhI(QAc)_2$ (0.6 mmol, 3.0 equiv), Bu_4NI (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.02 mmol, 0.1 equiv), CH_3CN (2.0 mL), 60 °C. [b] Isolated yield.

substrates also produced the corresponding diacetoxylated products **2n**−**r** in 76−84% yields under identical conditions (Table 2, entries 13−17). Only in the cases of aliphatic MCP **1l** and unsymmetrical **1m**, in which R^1 is an aromatic group and R^2 is a methyl group or its analogue, were complex product mixtures formed under the standard conditions (Table 2, entries 11 and 12). The product structures of **2a**−**k** and **2n**−**r** were determined by NMR spectroscopic data, MS, HRMS, and microanalyses (see the Supporting Information).

Interestingly, in this catalytic system, the trimeric palladium complex **B** $[(Bu_4N)_2Pd_3I_8]$ was isolated and its crystal structure unambiguously determined by X-ray diffraction; CIF data are presented in the Supporting Information (Figure 1).[9,10] The control experiment indicated that palladium complex **B** is the real highly active species in this reaction, although $Pd(OAc)_2$ (10 mol %) itself can produce the corresponding product **2a** in 6% yield (Table 1, entry 1).

(9) The crystal data of palladium complex **B** have been deposited with the CCDC with the file number 721042: empirical formula, $C_{16}H_{36}I_4NPd_{1.5}$; formula weight, 909.66; crystal color and habit, colorless and prismatic; crystal dimensions, 0.176 × 0.127 × 0.062 mm; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 11.6372(9) Å, b = 11.7555(9) Å, c = 20.2311(14) Å, α = 90°, β = 106.217(2)°, γ = 90°, V = 2657.5(3) Å^3; space group, $P2_1/c$; Z = 4; D_{calcd} = 2.274 g/cm^3; F_{000} = 1680; diffractometer, Rigaku AFC7R; residuals R and R_w, 0.0492 and 0.0749.

(10) Examples of iodide-bridged dimeric palladium complexes: (a) Maassarani, F.; Pfeffer, M.; Borgneb, G. L. *J. Chem. Soc., Chem. Commun.* **1987**, 565–567. (b) Chan, S.; Lee, S. M.; Lin, Z. Y.; Wong, W. T. *J. Organomet. Chem.* **1996**, *510*, 219–231. (c) Tonde, S. S.; Kelkar, A. A.; Bhadbhade, M. M.; Chaudhari, R. V. *J. Organomet. Chem.* **2005**, *690*, 1677–1681.

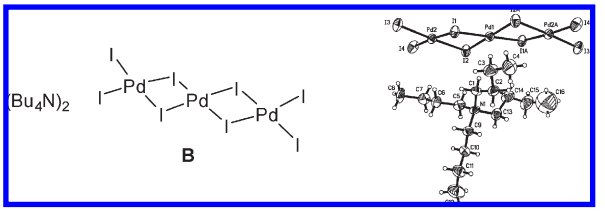


Figure 1. ORTEP drawing of palladium complex **B**.

1a affords **2a** in the presence of 1.0 equiv of palladium complex **B** in 65% yield within 1 h (condition A) or in the presence of 0.1 equiv of palladium complex **B** and 1.0 equiv of Bu_4NI in 67% yield within 1 h (condition B) (Scheme 2).

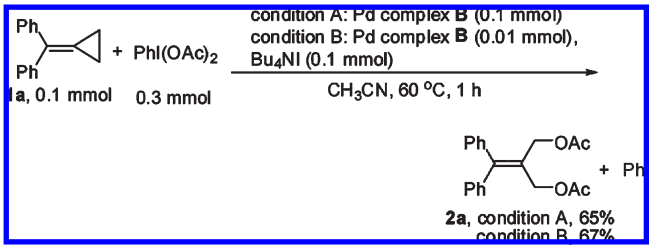
A plausible mechanism for the formation of the diacetoxylated derivatives **2** is outlined in Scheme 3 on the basis of the above experimental results. The active catalytic species **B** is in situ generated from $Pd(OAc)_2$ and Bu_4NI, which generates intermediate **C** through coordination to MCP **1**.[11] The anionic iodine species (I^-) attacks the cyclopropane of intermediate **C**, producing intermediate **D**, which undergoes the replacement of I with acetate anion (^-OAc) to afford intermediate **E**. At the same time, the acetate anion (^-OAc) from $PhI(OAc)_2$ may also attack intermediate **C** to provide intermediate **E**. According to the previous mechanistic proposal on the Pd(II)/Pd(IV) catalytic cycle,[2−4] oxidation of intermediate **E** with $PhI(OAc)_2$ generates Pd(IV) intermediate **F**. Then the corresponding diacetoxylated product **2** can be obtained via reductive elimination along with the regeneration of Pd(II) species.

In conclusion, we have developed a novel palladium-catalyzed ring-opening reaction of methylenecyclopropanes **1** to produce the corresponding diacetoxylated products **2** through C−C cleavage in good yields using $PhI(OAc)_2$ as the oxidant and Bu_4NI as an additive under mild conditions. This novel palladium-catalyzed process can provide an alternative approach to functionalized diacetoxylation products through C−C bond cleavage using highly strained small rings as the starting materials. Efforts are in progress to elucidate further mechanistic details of this reaction and to understand its scope and limitations.

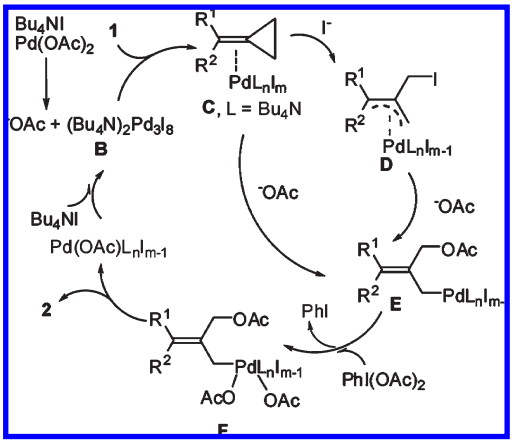
Experimental Section. Synthesis of 2a. Under ambient atmosphere, methylenecybutanes **1** (MCPs; 0.2 mmol), $PhI(OAc)_2$ (0.6 mmol), $Pd(OAc)_2$ (0.02 mmol), Bu_4NI (0.2 mmol), and CH_3CN (2 mL) were added into an Schlenk tube. The reaction mixture was stirred at 60 °C until the reaction was complete. Then, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO_2) to give the product **2a** in 71% yield as a colorless oil. IR (CH_2Cl_2): ν 3056, 3023, 1741, 1492, 1444, 1378, 1361, 1237, 1023, 969, 768, 703, 605 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 2.07 (6H, s, CH_3), 4.70 (4H, s, CH_2), 7.14−7.16 (4H, m, ArH), 7.25−7.33 (6H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 20.8, 62.8, 127.2, 127.8, 128.1, 129.1, 140.3, 148.7, 170.7. MS (EI) m/z (%): 324 (0.71) [M^+], 221 (11.35), 204 (100.00), 192 (16.26), 178 (11.84), 165 (8.24), 115 (29.60), 43 (48.72). Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21. Found: C, 74.06; H, 6.20.

(11) (a) Pohlmann, T.; de Meijere, A. *Org. Lett.* **2000**, *2*, 3877–3879. (b) Suginome, M.; Ito, Y. *J. Organomet. Chem.* **2003**, *680*, 43–50.

Scheme 2. Reaction of MCP 1a with $PhI(OAc)_2$ in the Presence of Palladium Complex B



Scheme 3. Plausible Reaction Mechanism



Acknowledgment. We thank the Shanghai Municipal Committee of Science and Technology (Grant No. 08dj1400100-2), the National Basic Research Program of China (Grant No. (973)-2009CB825300), and the National Natural Science Foundation of China (Grant Nos. 20872162, 20672127, 20872162, 20821002 and 20732008) for financial support.

Supporting Information Available: Text and figures giving detailed descriptions of experimental procedures and full characterization data for tge new compounds shown in Tables 1 and 2 and Schemes 1 and 2 and tables and a CIF file giving crystallographic data for palladium complex **B**. This material is available free of charge via the Internet at http://pubs.acs.org.