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Protonolysis of the carbon–palladium bond in palladium(II)-catalyzed enyne cyclization in imidazolium-type ionic liquids

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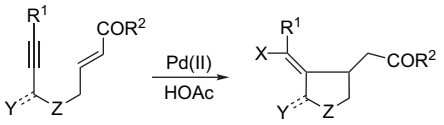
Abstract

The Pd-catalyzed cyclizations of 1,6-enynes are efficient reactions for the synthesis of α-methylene-γ-butyrolactones and lactams. The effects of solvent, proton source, chloride concentration, and temperature on the protonolysis of the carbon–Pd bond were investigated and the optimal reaction conditions were identified. We showed that imidazolium-type ionic liquids played an important role in the reaction both as a ligand for the palladium catalyst and as a solvent. The crystal structure of the Pd complex was obtained and the reaction mechanisms were discussed.

1. Introduction

Transition metal-catalyzed enyne cyclization[1] is a powerful reaction for the assembly of cyclic structures, which are important scaffolds in some bioactive compounds.[2] Up to date, a series of palladium-catalyzed enyne cyclization reactions have been developed.[3] In these processes, specific conditions are generally required to break the carbon–palladium bond and to regenerate the activated palladium species. Some of these reactions are β-H elimination,[4] β-heteroatom elimination,[5] reductive elimination,[6] oxidative cleavage,[7] reductive cleavage,[8] and protonolysis.[9]

As one of the fundamental reactions in organopalladium chemistry, protonolysis generally involves the reactions of Pd–aryl bond (sp^2-C–Pd bond), Pd–alkenyl bond (sp^2-C–Pd bond), and Pd–alkyl bond (sp^3-C–Pd bond). The sources of proton include an ammonium salt, CF_3CO_2H, HOAc, EtOH, and HCl.[10] Protonolysis is usually restricted to the sp^3-C–Pd bond adjacent to an electron-withdrawing group.[11] For example, the protonolysis of carbon–palladium bond in the cyclization of 1,6-enynes could be successfully carried out when the olefin bears an electron-withdrawing group (Scheme 1).[9] To our knowledge, few examples of protonolysis of sp^3-C–Pd bond adjacent to electron-rich groups have been reported.[12] For theoretical study and practical uses, it is important to have an effective method to carry out the protonolysis of sp^3-C–Pd bond. Therefore, we investigated various factors affected the protonolysis of the carbon–palladium bond in the palladium(II)-catalyzed cyclization of 2′-alkenyl 2-alkynoates and *N*-2′-alkenyl 2-alkynamides. Herein, we report the findings of our investigation.



R^1 = alkyl; R^2 = H, alkyl;
X = Cl, OAc; Y = H_2, O; Z = O, NTs, CH_2

Scheme 1. Schematic presentation of palladium(II)-catalyzed cyclization.

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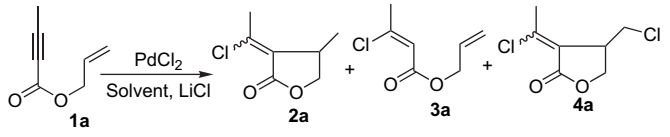
2. Results and discussion

2.1. Palladium-catalyzed reaction of allyl 2-butynoate under acidic conditions

Recently, we successfully performed the palladium(II)-catalyzed enyne cyclization of 2′-alkenyl 2-alkynoates in imidazolium-type ionic liquids (ILs) and in the presence of cupric chloride.[13] α-Chloroethylidene-β-chloromethyl-γ-butyrolactone **4a** was obtained in good yield. Accidentally we found that when cupric chloride was absent, the reaction proceeded through a protonolysis process to afford α-chloroethylidene-β-methyl-γ-butyrolactone **2a** as one of the main products. This finding encouraged us to explore new methods for the protonolysis of the sp^3-C–Pd bond in the final step of the cyclization reaction of 2′-alkenyl 2-alkynoates.[14]

Allyl 2-butynoate **1a** was used to optimize the reaction conditions. Under the atmosphere of dry hydrogen chloride,[15] the effects of several solvents on the reaction yield and product distribution were first investigated. The results are summarized in Table 1. With 6 mol % $PdCl_2$ as the catalyst in two different anion imidazolium-type ILs,[16] 1-butyl-3-methylimidazolium chloride ([bmim]Cl) and 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]), reaction of allyl 2-butynoate **1a** afforded protonolysis product **2a** predominantly, although the yields and the selectivity were not ideal (Table 1, entries 1 and 2). However, with the conventional solvents such as CH_3CN, CH_2Cl_2, and 1,4-dioxane, only traces of hydrochlorination product **3a** and oxidative cleavage product **4a** were detected after 12 h and there was no product **2a** detected (Table 1, entries 4–6). The oxidant of the oxidative cleavage reaction was oxygen in the air. Compound **1a** in HOAc was converted to **3a** or **4a** depending upon the concentration of HCl (Table 1, entries 7 and 8). Higher concentration of HCl favored the hydrochlorination of alkyne with HCl, and lower concentration of HCl favored the procedures of enyne cyclization and C–Cl bond formation. On the basis of the above results, it appeared that the efficient protonolysis of sp^3-C–Pd bond was accomplished only in ILs.

Table 1
Solvent effects of the cyclization of allyl 2-butynoate under acidic conditions[a]



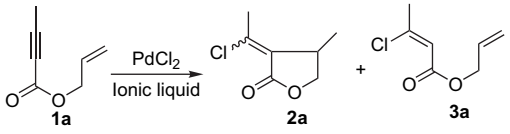
Entry	Solvent	Time (h)	GC yield (%)		
			2a	**3a**	**4a**
1	[bmim][BF_4]	12	73	4	0
2	[bmim]Cl	72	74	25	0
3[b,c]	HOAc	24	0	Trace	Trace
4[b]	CH_3CN	12	0	Trace	Trace
5[b]	CH_2Cl_2	12	0	Trace	Trace
6[d]	1,4-Dioxane	12	0	Trace	Trace
7	HOAc	12	0	87	0
8[e]	HOAc	12	0	6	65

[a] Reaction conditions: **1a** (1 mmol), $PdCl_2$ (0.056 mmol), and LiCl (6 mmol) were stirred in solvent (2 mL) under the atmosphere of 0.4 mmol/mL HCl at rt.
[b] The starting material was recovered.
[c] In the absence of HCl.
[d] The starting material was consumed.
[e] The reaction proceeded under the atmosphere of 0.05 mmol/mL HCl.

2.2. Effects of the proton source

During the early investigation of palladium-catalyzed cyclization in [bmim][BF_4], we found that the reaction was sensitive to water. The protonolysis of C–Pd bond in the cyclization of allyl 2-butynoate could proceed even in the presence of moisture absorbed by LiCl (Table 2, entry 1). However, the reaction was inconsistent in its conversion rate and selectivity. Later, we found that LiCl promoted the hydrolysis of BF_4^- anion in the presence of H_2O and produced HCl in the [bmim][BF_4]–LiCl–H_2O system. It was the proton provided by HCl that led to the protonolysis of C–Pd bond.[17] It was apparent that the amount of water affected the concentrations of produced HCl and chloride ions in the reaction system, which resulted in the inconsistent conversion rate and selectivity. To further investigate the effect of H_2O on protonolysis, dry $MgSO_4$ was added to the reaction mixture (Table 2, entry 2). As expected, the conversion rate decreased remarkably compared with that of the reaction without $MgSO_4$ (Table 2, entry 1). In order to keep the reaction to proceed under defined acidic condition, dry HCl gas was introduced to the reaction mixture containing dry $MgSO_4$. The expected conversion rate and yield were obtained (Table 2, entry 3). In the previous report,[9] HOAc was used as the proton source. However, in this work, the reaction did not occur when HCl was replaced with HOAc in [bmim]Cl (Table 2, entry 5), indicating that strong acid is required for the protonolysis and regeneration of active Pd(II) species.

Table 2
The effects of different proton sources[a]



Entry	Ionic liquid	LiCl (equiv)	HA	Time (h)	Conversion (%)	GC yield (%)	
						2a (*Z*/*E*)	**3a**
1	[bmim][BF_4]	6	H_2O[b]	12	100	62 (93:7)	1
2[c]	[bmim][BF_4]	6	H_2O[b]	12	27	56 (93:7)	4
3[c]	[bmim][BF_4]	6	HCl[d]	12	100	73 (94:6)	0.4
4	[bmim]Cl	6	H_2O[b]	96	No reaction		
5	[bmim]Cl	0	HOAc[e]	96	No reaction		

[a] Reaction conditions: **1a** (1 mmol), $PdCl_2$ (0.056 mmol), and LiCl were stirred in ionic liquid (2 mL) at rt.
[b] The water was formed from the moisture absorbed by LiCl.
[c] Dry $MgSO_4$ was added to the reaction system.
[d] The reaction proceeded under the atmosphere of 0.4 mmol/mL HCl.
[e] HOAc of 0.5 mL was added to the reaction system.

2.3. Effects of chloride ion concentration and reaction temperature

In bivalent palladium catalysis, the concentration of chloride ions plays an important role in the regioselectivity and stereoselectivity of the reaction.[3b] When [bmim][BF_4] is used as the solvent, the selectivity of the reaction can be controlled by the amount of LiCl. However, [bmim]Cl could play the roles of both as the solvent and as the source of chloride ion. When added different amounts of [bmim]Cl as the chloride source to the [bmim][BF_4] solution, experimental results showed that the *Z*/*E* ratio of product **2a** increased with the increase of the amount of [bmim]Cl (Table 3, entries 1–4). When [bmim]Cl was employed as the sole solvent (Table 3, entry 5), which provided a high concentration of chloride ion, the *Z*/*E* ratio of product **2a** was higher than 98:2. But the hydrochlorination product **3a** was also increased to 25% (Table 3, entry 5). Unexpectedly, the *Z*/*E* ratio changed from >98:2 to 13:87 when the temperature was raised from room temperature to 100 °C (Table 3, entries 5–7). When allyl 2-butynoate **1a** and HCl were mixed in [bmim]Cl without palladium catalyst at 70 °C for 2 days, the hydrochlorination product **3a** was obtained as the sole product (Table 3, entry 8), which confirmed that the competitive hydrochlorination reaction occurred in the system.

Finally, the optimal reaction conditions were determined as following: (A) substrate **1** (1 mmol) and $PdCl_2$ (0.178 mmol) were stirred in [bmim]Cl (2 mL) at room temperature under the atmosphere of 0.4 mmol/mL HCl (Table 3, entry 4); (B) substrate **1** (1 mmol), [bmim]Cl (6 mmol), and $PdCl_2$ (0.056 mmol) were stirred in [bmim][BF_4] (2 mL) at room temperature under the atmosphere of 0.4 mmol/mL HCl (Table 3, entry 4). When the protonolysis was carried out in these two conditions, the expected product **2a** was obtained in satisfactory yields with *Z*/*E* ratio ≥98:2.

2.4. Cyclization with recycled catalyst and solvent

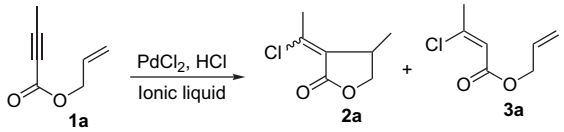
One of the most attractive features of using ionic liquids as the solvent for transition metal-catalyzed reactions is to recycle the catalyst–ionic liquid solution.[16] To confirm this possibility, we carried out cyclization reaction with the recovered catalyst–ionic liquid solution.

Allyl 2-butynoate **1a** was added to the reaction system composed of [bmim]Cl and $PdCl_2$ under the atmosphere of dry HCl. After complete reaction of **1a**, the ionic liquid reaction solution was extracted with ethyl acetate and then dried in vacuo for 1 h at 80 °C. To the recovered catalyst–ionic liquid solution was added substrate **1a** again and the reaction was allowed to proceed under the same reaction conditions. The experimental results are listed in Table 3 (entries 10 and 11). As shown, the cyclization reaction with recycled catalyst and solvent afforded the product in a little bit lower yield than that with fresh catalyst and solvent, indicating that the catalyst–ionic liquid solution could be reused to obtain satisfactory yields and stereoselectivity.

2.5. Cyclization of various 2′-alkenyl 2-alkynoates and N-alkenyl 2-alkyamides

Under the optimized reaction conditions, a variety of substituted 2′-alkenyl 2-alkynoates and *N*-2′-alkenyl 2-alkynamides were tested. As shown in Table 4, when substrates **1b**–**1e** were employed as the substrates, protonolysis products **2b**–**2e** were afforded with high *Z*-stereoselectivity in 60–88% isolated yields. It is interesting that no oxidative cleavage products **4** or β-H elimination products[4] were detected for substrates **1d** and **1e** (Table 4, entries 3 and 4). The reaction of **1f** yielded both the *E* and *Z* forms of cyclization product **2f** and hydrochlorination product **3f**, which was likely due to steric and electronic properties of the phenyl group (Table 4, entry

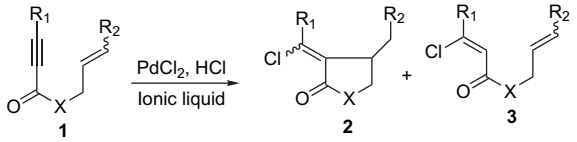
Table 3
Optimization of the reaction conditions of allyl 2-butynoate[a]

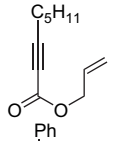
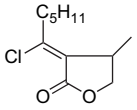
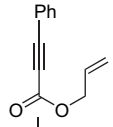
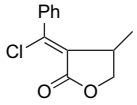
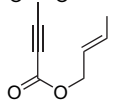
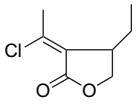
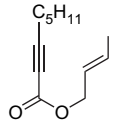
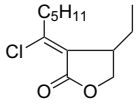
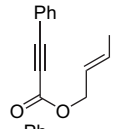
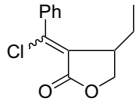
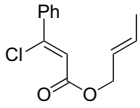
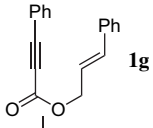
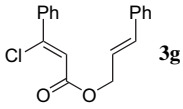
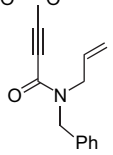
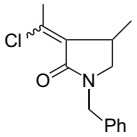
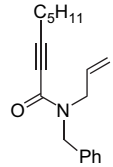
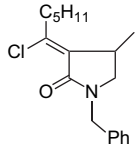


Entry	Ionic liquid	[bmim]Cl (equiv)	Pd catalyst (equiv)	*T*	Time (h)	GC yield (%)	
						2a (*Z*/*E*)	**3a**
1	[bmim][BF_4]	0	$[bmim]_4[Pd_3Cl_{10}]$ (0.056)	rt	24	65 (83:17)	8
2	[bmim][BF_4]	2	$PdCl_2$ (0.056)	rt	48	91 (92:8)	9
3	[bmim][BF_4]	4	$PdCl_2$ (0.056)	rt	48	94 (95:5)	6
4	[bmim][BF_4]	6	$PdCl_2$ (0.056)	rt	48	92 (98:2)	8
5	[bmim]Cl		$PdCl_2$ (0.056)	rt	72	74 (>98:2)	25
6	[bmim]Cl		$PdCl_2$ (0.056)	70 °C	9	78 (87:13)	22
7	[bmim]Cl		$PdCl_2$ (0.056)	100 °C	24	76 (13:87)	4
8	[bmim]Cl		0	70 °C	48	0	100
9	[bmim]Cl		$PdCl_2$ (0.178)	rt	72	93 (>98:2)	7
10[b]	Second run		Second run	rt	72	90 (>98:2)	7
11[c]	Third run		Third run	rt	72	88 (>98:2)	8

[a] Reaction conditions: **1a** (1 mmol) and $PdCl_2$ (0.056 mmol) were stirred in ionic liquid (2 mL) under the atmosphere of 0.4 mmol/mL HCl.
[b] The catalyst and ionic liquid mixture in entry 9 was reused in entry 10 after extracted with ethyl acetate.
[c] The catalyst and ionic liquid mixture in entry 10 was reused in entry 11 after extracted with ethyl acetate.

Table 4
Cyclization of different substrates in ILs



Entry	Substrates	Conditions[a]	Products[b]	Isolated yield (%)
1	 **1b**	A	 **2b**	72
2	 **1c**	A	 **2c**	60
3	 **1d**	A	 **2d**	80
4	 **1e**	A B	 **2e**	85 88
5	 **1f**	A	 **2f**  **3f**	*Z*-**2f**:40 *E*-**2f**:5 **3f**:5
6	 **1g**	A	 **3g**	10
7	 **1h**	A	 **2h**	*Z*-**2h**:68 *E*-**2h**:17
8	 **1i**	A B	 **2i**	87 83

[a] Condition A: **1** (1 mmol) and $PdCl_2$ (0.178 mmol) were stirred in [bmim]Cl (2 mL) under the atmosphere of 0.4 mmol/mL HCl. Condition B: **1** (1 mmol), [bmim]Cl (6 mmol), and $PdCl_2$ (0.056 mmol) were stirred in [bmim][BF_4] (2 mL) under the atmosphere of 0.4 mmol/mL HCl.
[b] Only *Z*-isomers of products **2** were purified and identified by ^{1}H NMR, ^{13}C NMR, IR, MS, and HRMS.

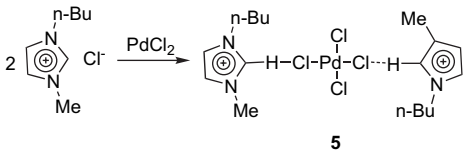
5). Another example of the effects of the phenyl group was the reaction of **1g** (Table 4, entry 6), which yielded only the hydrochlorination product of **3f**.

N-2′-Alkenyl 2-alkynamides were also smoothly cyclized under the given reaction conditions, and the protonolysis products were obtained in excellent isolated yields (Table 4, entries 7 and 8).

2.6. The structure of the Pd catalyst and proposed reaction mechanisms

After investigated the effects of proton sources, chloride ion concentration, and temperature on the protonolysis reaction and identified the optimal reaction conditions, we then carried out experiments to solve the structure of palladium complex and studied the role of imidazolium-type ionic liquids.

Dupont's group reported that a Pd complex **5** was formed through the reaction of $PdCl_2$ with [bmim]Cl (Scheme 2).[18] We postulated that **5** or a Pd complex similar to **5** might be



Scheme 2. The proposed Pd complex.

formed in situ in our reaction systems, even in the [bmim][BF_4]–LiCl–$PdCl_2$ system. To prove our hypothesis, the complex was prepared by mixing $PdCl_2$ (1 mmol) and LiCl (2 mmol) in [bmim][BF_4] (2 mmol) for 12 h at room temperature. A red-black crystal was obtained. The structure of the complex (**6**) was fully characterized by IR, ^1H, and ^{13}C NMR and its crystal structure was also determined by X-ray diffraction analysis (Figs. 1 and 2). The result showed that the structure of **6** was [bmim]$_4$[Pd_3Cl_{10}] and [bmim]Cl served as one of the ligands of palladium atom.

We examined the catalytic activity of Pd complex **6** in the reaction of **1a** in [bmim][BF_4] and some of the conventional solvents (Eq. 1). In [bmim][BF_4], the reaction gave the protonolysis product **2a** in 65% yield. However, in the conventional solvents including HOAc, CH_3CN, 1,4-dioxiane, and CH_2Cl_2, the reaction yielded the same product just as with $PdCl_2$. This observation suggested that imidazolium-type ionic liquids might serve as the stabilizer for the Pd complex in the reaction and enhance the protonolysis process. When the Pd complex **6** was dissolved in other solvents, $PdCl_2$ was released immediately and participated in the reaction as $PdCl_2$.

The reaction mechanisms of the palladium-catalyzed cyclization of enynes in ionic liquids are proposed (Scheme 3). Pd complex **6** is formed in situ in ILs, and chloropalladation of substrate **1**[2b] could generate the Pd–alkenyl intermediate **7**. Then, intermediate **7** could undergo intramolecular insertion to generate a Pd–alkyl intermediate **8**, which could complex with IL ligand efficiently to inhibit both β-hydride elimination and oxidative cleavage of C–Pd–Cl bond. Through the protonolysis of the C–Pd bond of **8** promoted by HCl, product **2** is therefore produced and active Pd(II) species could be regenerated.

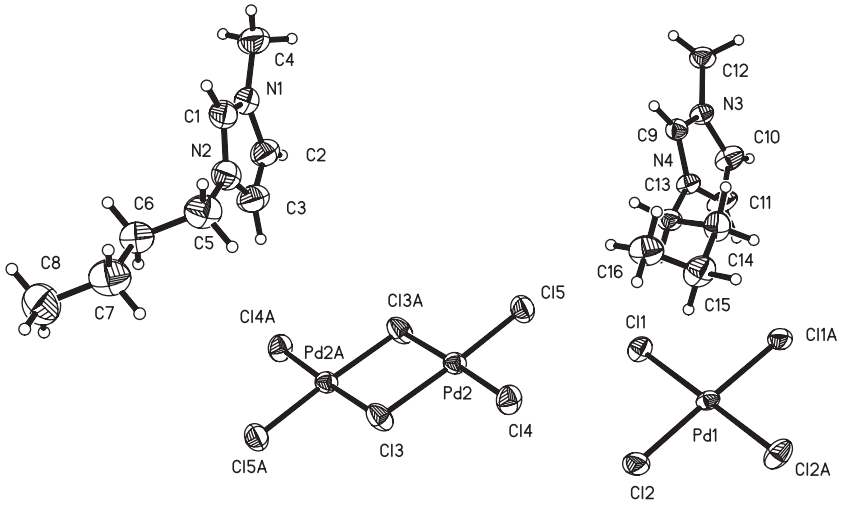


Figure 1. ORTEP plot with atom labeling scheme of the structure of Pd complex **6**.

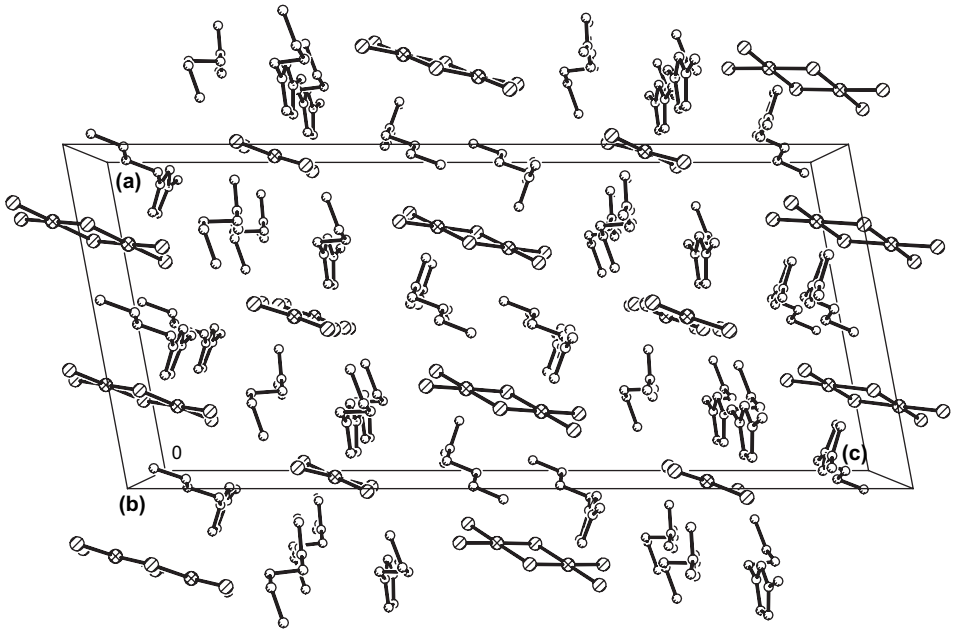
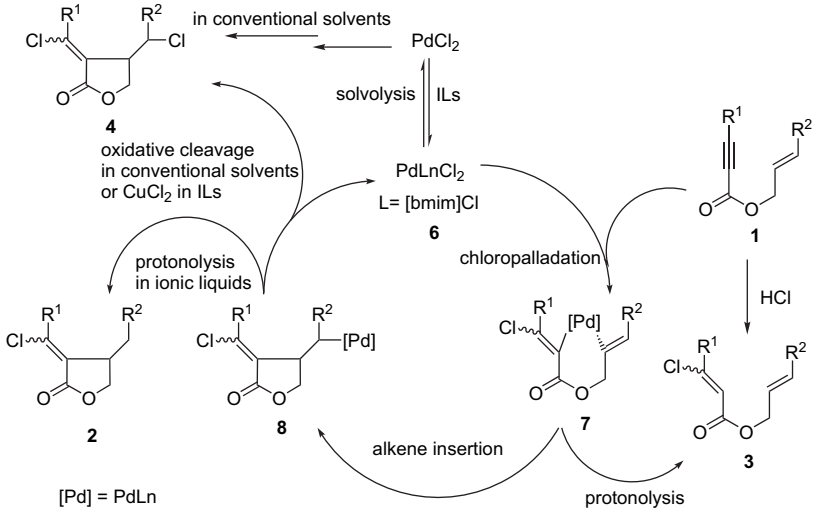
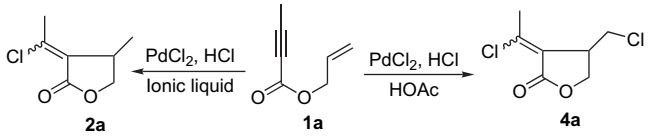


Figure 2. Crystal packing of Pd complex **6**.



Scheme 3. Proposed mechanistic cycle.

After chloropalladation of the triple bond, [bmim]Cl, as the ligand for the palladium, could enable **7** to undergo olefin insertion by activating the alkene. However, in HOAc, without the aid of [bmim]Cl ligand, the Pd–alkenyl bond could be easily protonolyzed to give product **3**. Alternatively, product **3** could also be formed by the direct reaction of **1** with HCl in [bmim]Cl in the absence of palladium catalyst. When catalyst **6** was used in a conventional solvent, it might be solvolyzed to $PdCl_2$ and the reaction might proceed through the normal process to form product **4**. Product **4** could also be formed through the oxidative cleavage of Pd–C bond of Pd–alkyl intermediate **8** in HOAc under low concentration of HCl or in the presence of $CuCl_2$.



2.7. Experimental section for the synthesis of $[bmim]_4[Pd_3Cl_{10}]$ and for the palladium-catalyzed cyclization and protonolysis of 2′-alkenyl 2-alkynoates in ionic liquids

2.7.1. General methods

^{1}H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded on BRUKER DRX-400 spectrometer using $CDCl_3$ as the solvent and TMS as the internal standard. GC analyses were performed on a GC-930 chromatography instrument (Shanghai Haixian Chromatography Instrument Ltd. Co.) with a flame ionization detector equipped with an OV-101 capillary column (internal diameter=0.25 mm, length=30 m). Mass spectra were recorded on a Shimadzu GCMS-QP5050A at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter=0.25 mm, length=30 m). IR spectra were recorded on Analect RFX-65A spectrometer.

2′-Alkenyl 2-alkynoates,[7a] *N*-alkenyl 2-alkyamides,[7c] and ionic liquids[19] were synthesized according to the reported procedures. All other reagents were used directly as obtained commercially. TLC was performed using commercially prepared 100–400 mesh silica gel plates (HF_{254}) and visualized at 254 nm.

2.7.2. Synthesis of $[bmim]_4[Pd_3Cl_{10}]$ **6**

A mixture of $PdCl_2$ (1 mmol), LiCl (2 mmol), and $[bmim][BF_4]$ (2 mmol) was stirred at room temperature for 12 h. A white precipitant was filtered after 5 mL of CH_2Cl_2 was added to the mixture. The dichloromethane was removed, and a red-black solid was obtained in 81% yield. Crystals suitable for X-ray diffraction study were obtained by slow volatilization of the dichloromethane solution of the compound at room temperature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.33 (s, 1H), 7.77–7.84 (m, 2H), 4.47 (t, 2H, J=7.4 Hz), 4.14 (s, 3H), 1.97–2.01 (m, 2H), 1.44 (q, 2H, J=7.4 Hz), 0.96 (t, 3H, J=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 124.2, 122.8, 49.7, 36.3, 32.1, 19.3, 13.0; IR (cm^{-1}) 3140, 3103, 3076, 2951, 2863, 1619, 1565, 1457, 1162, 850, 757.

2.7.3. General procedure for the palladium-catalyzed cyclization and protonolysis of 2′-alkenyl 2-alkynoates in ionic liquids

To a mixture of $PdCl_2$ (10 mg, 0.056 mmol), [bmim]Cl (1044 mg, 6 mmol), and ionic liquids (2 mL) was added **1a** (1 mmol). The reaction was stirred at room temperature under the atmosphere of 0.4 mmol/mL HCl and monitored by TLC with 10:3 petroleum ether and ethyl acetate as eluents. After the reaction was complete, the mixture was extracted with ethyl acetate (5×8 mL). The combined organic layers were washed with water (3×8 mL), dried over $MgSO_4$, and concentrated in vacuo. Purification of the residue on a preparative TLC afforded the pure product. The ionic liquid solution was dried in vacuo for 1 h at 80 °C and was ready for reuse in a repeated reaction.

*2.7.3.1. (Z)-α-(1′-Chloroethylidene)-β-methyl-γ-butyrolactone (Z-**2a**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.27 (dd, 1H, *J*=9.0, 7.2 Hz), 3.91 (dd, 1H, *J*=9.0, 1.7 Hz), 3.22–3.25 (m, 1H), 2.30 (d, 3H, *J*=0.92 Hz), 1.23 (d, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 140.8, 126.3, 71.0, 35.5, 25.7, 19.5; IR (cm^{-1}) 1759, 1651, 1442, 1376, 1224, 1139, 790, 674; MS (*m/z*): 162 (M^+ (^{37}Cl), 16), 160 (M^+ (^{35}Cl), 50), 145, 117, 102, 81, 67 (100); HRMS calcd for $C_7H_9O_2Cl$: 160.0286. Found: 160.0286.

*2.7.3.2. (E)-α-(1′-Chloroethylidene)-β-methyl-γ-butyrolactone (E-**2a**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.33 (dd, 1H, *J*=9.0, 7.2 Hz), 3.95 (dd, 1H, *J*=9.0, 1.7 Hz), 3.32 (m, 1H), 2.61 (d, 3H, *J*=0.92 Hz), 1.40 (d, 3H, *J*=7.2 Hz); MS (*m/z*): 162 (M^+ (^{37}Cl), 16), 160 (M^+ (^{35}Cl), 50), 145, 117, 102, 81, 67 (100).

*2.7.3.3. (Z)-α-(1′-Chlorohexylidene)-β-methyl-γ-butyrolactone (Z-**2b**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.27 (dd, 1H, *J*=9.0, 6.9 Hz), 3.92 (dd, 1H, *J*=9.0, 1.5 Hz), 3.22–3.26 (m, 1H), 2.45 (t, 2H, *J*=6.9 Hz), 1.62–1.71 (m, 2H), 1.32–136 (m, 4H), 1.24 (d, 3H, *J*=7.1 Hz), 0.88–0.91 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 145.1, 125.2, 70.3, 37.5, 34.7, 30.4, 26.4, 21.7, 19.5, 13.1; IR (cm^{-1}) 2960, 2865, 1760, 1644, 1456, 1374, 1222, 1135, 784, 675; MS (*m/z*): 218 (M^+ (^{37}Cl), 3), 216 (M^+ (^{35}Cl), 10), 181 (100); HRMS calcd for $C_{11}H_{17}O_2Cl$: 216.0912. Found: 216.0902.

*2.7.3.4. (Z)-α-(1′-Chlorobenzylidene)-β-methyl-γ-butyrolactone (Z-**2c**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (s, 5H), 4.33 (dd, 1H, *J*=9.0, 7.1 Hz), 3.88 (dd, 1H, *J*=9.0, 2.9 Hz), 3.28–3.33 (m, 1H), 0.98 (d, 3H, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 141.1, 137.9, 129.9, 128.7, 127.9, 127.6, 71.2, 35.9, 19.1; IR (cm^{-1}) 1746, 1640, 1446, 1371, 1210, 1091, 761, 693; MS (*m/z*): 224 (M^+ (^{37}Cl), 6), 222 (M^+ (^{35}Cl), 20), 207, 187, 177, 163, 141 (100); HRMS calcd for $C_{12}H_{11}O_2Cl$: 222.0442. Found: 222.0458.

*2.7.3.5. (Z)-α-(1′-Chloroethylidene)-β-ethyl-γ-butyrolactone (Z-**2d**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 (dd, 1H, *J*=9.0, 7.2 Hz), 4.11 (dd, 1H, *J*=9.0, 1.5 Hz), 3.11–3.13 (m, 1H), 2.33 (d, 3H, *J*=0.73 Hz), 1.59–1.67 (m, 2H), 0.98 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 140.8, 125.4, 68.8, 42.2, 27.0, 26.1, 10.8; IR (cm^{-1}) 1761, 1651, 1460, 1375, 1220, 1133, 775, 688; MS (*m/z*): 176 (M^+ (^{37}Cl), 12), 174 (M^+ (^{35}Cl), 36), 145, 117 (100); HRMS calcd for $C_8H_{11}O_2Cl$: 174.0442. Found: 174.0445.

*2.7.3.6. (Z)-α-(1′-Chlorohexylidene)-β-ethyl-γ-butyrolactone (Z-**2e**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.19 (dd, 1H, *J*=9.0, 7.1 Hz), 4.06 (dd, 1H, *J*=9.0, 1.5 Hz), 3.06–3.07 (m, 1H), 2.41–2.45 (m, 2H), 1.55–1.59 (m, 4H), 1.28–1.33 (m, 4H), 0.93 (t, 3H, *J*=7.6 Hz), 0.88 (t, 3H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 145.8, 124.9, 68.5, 41.9, 38.3, 31.1, 27.3, 27.0, 22.3, 13.8, 10.5; IR (cm^{-1}) 2961, 1760, 1642, 1460, 1374, 1220, 1134, 792, 687; MS (*m/z*): 232 (M^+ (^{37}Cl), 6), 230 (M^+ (^{35}Cl), 20), 195 (100); HRMS calcd for $C_{12}H_{19}O_2Cl$: 230.1068. Found: 230.1060.

*2.7.3.7. (Z)-α-(1′-Chlorobenzylidene)-β-ethyl-γ-butyrolactone (Z-**2f**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (s, 5H), 4.29 (dd, 1H, *J*=9.0, 7.1 Hz), 4.04 (dd, 1H, *J*=9.0, 2.5 Hz), 3.20–3.21 (m, 1H), 1.31–1.35 (m, 2H), 0.72 (t, 3H, *J*=7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 141.1, 138.2, 129.8, 128.7, 127.6, 126.7, 68.6, 41.9, 26.2, 10.2; IR (cm^{-1}) 1746, 1633, 1450, 1377, 1208, 1130, 758, 696; MS (*m/z*): 238 (M^+ (^{37}Cl), 18), 236 (M^+ (^{35}Cl), 55), 207, 179, 115 (100); HRMS calcd for $C_{13}H_{13}O_2Cl$: 236.0599. Found: 236.0595.

*2.7.3.8. (E)-α-(1′-Chlorobenzylidene)-β-ethyl-γ-butyrolactone (E-**2f**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.45 (m, 5H), 4.37 (dd, 1H, *J*=9.0, 7.1 Hz), 4.17 (dd, 1H, *J*=9.0, 2.5 Hz), 3.34–3.36 (m, 1H), 1.79–1.88 (m, 2H), 1.01 (t, 3H, *J*=7.6 Hz); MS (*m/z*): 238 (M^+ (^{37}Cl), 18), 236 (M^+ (^{35}Cl), 55), 207, 179, 115 (100).

*2.7.3.9. N-Benzyl-(Z)-α-(1′-chloroethylidene)-β-methyl-γ-butyrolactam (Z-**2h**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.32 (m, 5H), 4.64 (d, 1H, *J*=14.9 Hz), 4.40 (d, 1H, *J*=14.9 Hz), 3.35–3.40 (m, 1H), 3.01–3.04 (m, 1H), 2.75 (d, 1H, *J*=9.8 Hz), 2.23 (s, 3H), 1.12 (d, 3H, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1, 136.3, 133.5, 131.4, 128.6, 128.2, 127.5, 50.5, 46.9, 31.8, 24.9, 20.5; IR (cm^{-1}) 1683, 1628, 1427, 1362, 1281, 1171, 739, 701; MS (*m/z*): 251 (M^+ (^{37}Cl), 23), 249 (M^+ (^{35}Cl), 74), 234, 214, 91 (100); HRMS calcd for $C_{14}H_{16}ONCl$: 249.0915. Found: 249.0917.

*2.7.3.10. N-Benzyl-(E)-α-(1′-chloroethylidene)-β-methyl-γ-butyrolactam (E-**2h**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.35 (m, 5H), 4.59 (d, 1H, *J*=14.7 Hz), 4.40 (d, 1H, *J*=14.7 Hz), 3.38–3.42 (m, 1H), 3.09–3.13 (m, 1H), 2.76 (d, 1H, *J*=9.8 Hz), 2.68 (s, 3H), 1.17 (d, 3H, *J*=7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 140.3, 136.2, 132.9, 128.7, 128.1, 127.6, 50.9, 46.9, 32.3, 29.6, 22.1; MS (*m/z*): 251 (M^+ (^{37}Cl), 23), 249 (M^+ (^{35}Cl), 74), 234, 214, 91 (100).

*2.7.3.11. N-Benzyl-(Z)-α-(1′-chlorohexylidene)-β-methyl-γ-butyrolactam (Z-**2i**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.32 (m, 5H), 4.64 (d, 1H, *J*=14.7 Hz), 4.32 (d, 1H, *J*=14.7 Hz), 3.35 (dd, 1H, *J*=10.0, 7.3 Hz), 2.99–3.03 (m, 1H), 2.71 (d, 1H, *J*=9.6 Hz), 1.58–1.68 (m, 4H), 1.31–1.32 (m, 4H), 1.10 (d, 3H, *J*=7.1 Hz), 0.87–0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 138.8, 136.5, 131.1, 128.7, 128.3, 127.6, 50.8, 47.0, 37.5, 32.0, 31.2, 27.2, 22.4, 21.2, 13.9; IR (cm^{-1}) 2928, 2867, 1693, 1646, 1423, 1358, 1281, 1168, 748, 701; MS (*m/z*): 307 (M^+ (^{37}Cl), 13), 305 (M^+ (^{35}Cl), 41), 290, 270, 262, 91 (100); HRMS calcd for $C_{18}H_{24}ONCl$: 305.1541. Found: 305.1539.

*2.7.3.12. N-Benzyl-(E)-α-(1′-chlorohexylidene)-β-methyl-γ-butyrolactam (E-**2i**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.31 (m, 5H), 4.54 (d, 1H, *J*=14.7 Hz), 4.41 (d, 1H, *J*=14.7 Hz), 3.37 (dd, 1H, *J*=10.0, 7.6 Hz), 3.08–3.15 (m, 1H), 2.73 (d, 1H, *J*=9.5 Hz), 1.56–1.62 (m, 4H), 1.31–1.34 (m, 4H),

1.10 (d, 3H, J=7.1 Hz), 0.87–0.90 (m, 3H); MS (*m*/*z*): 307 (M^+ (^{37}Cl), 13), 305 (M^+ (^{35}Cl), 41), 290, 270, 262, 91 (100).

*2.7.3.13. 2′-Propenyl (Z)-2-chloro-2-butenoate (Z-**3a**).* ^1H NMR (400 MHz, $CDCl_3$): δ 6.04 (d, 1H, J=1.2 Hz), 5.89–5.96 (m, 1H), 5.32 (dm, 1H, J=17.1 Hz), 5.22 (dm, 1H, J=10.8 Hz), 4.63 (dm, 2H, J=5.6 Hz), 2.25 (d, 3H, J=1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 146.5, 132.0, 118.2, 116.5, 64.9, 28.1; MS (*m*/*z*): 162 (M^+ (^{37}Cl), 0), 160 (M^+ (^{35}Cl), 0), 125, 103 (100).

*2.7.3.14. (E)-2′-Butenyl (Z)-2-chloro-2-phenyl-2-propenoate (E,Z-**3f**).* ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.67 (m, 5H), 6.54 (d, 1H, J=1.2 Hz), 5.82–5.87 (m, 1H), 5.62–5.66 (m, 1H), 4.62 (dm, 2H, J=7.2 Hz), 1.73 (d, 3H, J=1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 146.5, 137.3, 131.9, 130.7, 128.6, 127.2, 124.9, 116.2, 65.4, 17.8; MS (*m*/*z*): 238 (M^+ (^{37}Cl), 1), 236 (M^+ (^{35}Cl), 4), 201, 181, 165 (100).

*2.7.3.15. (E)-3′-Phenyl-2′-propenyl (Z)-2-chloro-2-butenoate (E,Z-**3g**).* ^1H NMR (400 MHz, $CDCl_3$): δ 7.25–7.38 (m, 5H), 6.56 (d, 1H, J=16.0 Hz), 6.27–6.30 (dm, 1H, J=16.0 Hz), 6.05 (d, 1H, J=1.2 Hz), 4.79 (m, 2H), 2.25 (d, 3H, J=1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 146.8, 136.4, 134.5, 128.7, 128.2, 126.8, 123.2, 116.7, 65.0, 28.4; MS (*m*/*z*): 238 (M^+ (^{37}Cl), 1), 236 (M^+ (^{35}Cl), 3), 133, 115, 103 (100).

*2.7.3.16. (Z)-α-(1′-Chloroethylidene)-β-chloromethyl-γ-butyrolactone (Z-**4a**).*[7a] ^1H NMR (400 MHz, $CDCl_3$): δ 4.24–4.34 (m, 2H), 3.49–3.57 (m, 3H), 3.23 (m, 1H), 2.35 (s, 3H); MS (*m*/*z*): 198 (M^+ ($2^{37}Cl$), 1), 196 (M^+ (^{37}Cl, ^{35}Cl), 6), 194 (M^+ ($2^{35}Cl$), 11), 159, 145 (100).

3. Conclusions

In summary, we have developed an efficient method for the protonolysis of carbon–palladium bond in the palladium-catalyzed cyclization reaction of 1,6-enynes in imidazolium-type ionic liquid, which plays an important role in the reaction both as a ligand for the palladium catalyst and as a solvent. The process can be easily carried out with high conversion rate, yield, and stereoselectivity. Moreover, the catalyst–ionic liquid can be recycled several times without obvious loss of catalytic activity. This process provides a new methodology for constructing five-membered rings from 1,6-enynes. The compounds obtained from these reactions may have potential uses in pharmaceutical and natural product chemistry.

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