An Unexpected Reaction of Allylic Propynoate under Palladium(II) Catalysis†

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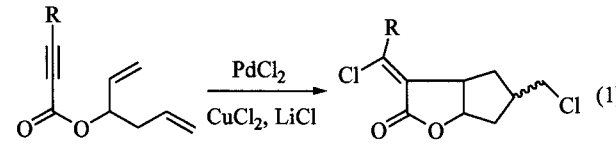
Palladium(II) catalyzed reactions of allyl propynoate in the presence of excess halide ions with or without allyl halide or acrolein were studied, yielding (*E*)-3-halo-2-allyl-acrylic acid as the sole product. A mechanism involving halopalladation, carbopalladation, ring opening and *β*-heteroatom elimination was proposed and was further justified by the reaction with deuterated substrate.

Keywords palladium, enyne, halopalladation, carbopalladation, *β*-heteroatom elimination

Introduction

In the past several years, palladium-catalyzed enyne coupling reactions have been explored as tools for the synthesis of lactones from acyclic allylic alkynoates.[1] *α*-Alkylidene-*γ*-butyrolactone structure unit could be easily assembled through halopalladation,[2] intramolecular olefin insertion and finally quenching of the carbon-palladium bond by *β*-heteroatom elimination,[1,3,4] copper halide mediated oxidative cleavage,[5] carbonylation[6] and protonolysis,[7] respectively. We also developed the facile intramolecular enyne cyclization of 1′, 5′-hexadien-3-yl alkynoates (**1**) to construct bicyclic *α*-(*Z*)-chloralkylidiene-*γ*-butyrolactone derivatives (**2**) [Eq. (1)].[5b]

Based on these results, we designed a tandem reaction starting from the allyl alkynoates, allyl halide or acrolein catalyzed by Pd(II) species in the presence of excess halide. The first step was supposed to be halopalladation, followed by intramolecular insertion, then intermolecular insertion, and the finally formed C—Pd bond was quenched by different methods as shown in Scheme 1. Here we describe the unexpected results of preliminary research.



(1)

1 **2**

Results and discussion

The reaction of enyne ester **3a** (110 mg, 1 mmol) with allyl bromide (600 mg, 5 mmol) in the presence of palladium acetate (11 mg, 0.05 mmol) and lithium bromide (430 mg, 5 mmol) in HOAc (5 mL) was tried first. An acid (*E*)-**10a** (Scheme 2) was obtained as the only product in 89% isolated yield instead of the proposed compound **8a**. The structure and stereochemistry of product (*E*)-**10a** were confirmed by spectroscopic data and HRMS analysis.

Surprisingly, if allyl bromide was replaced by acrolein, the same product was obtained in good yield (85%) (Scheme 2).

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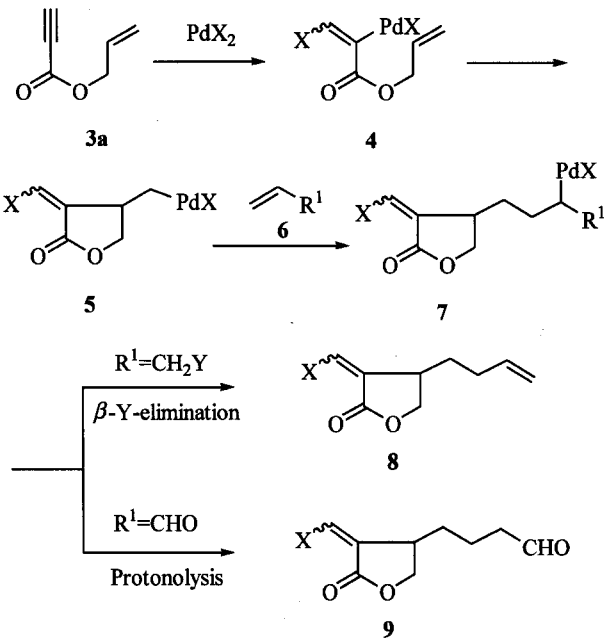
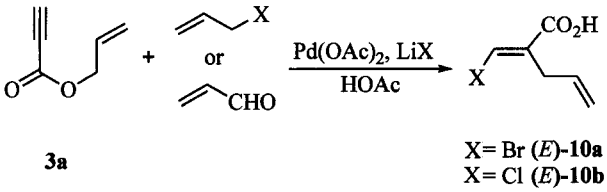
Scheme 1 Designed tandem reactions

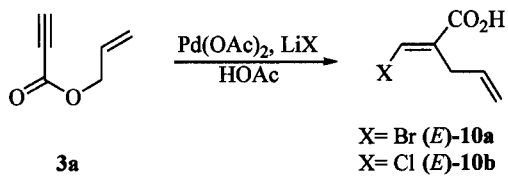


Scheme 2 Reaction of allyl propynoate with alkenes



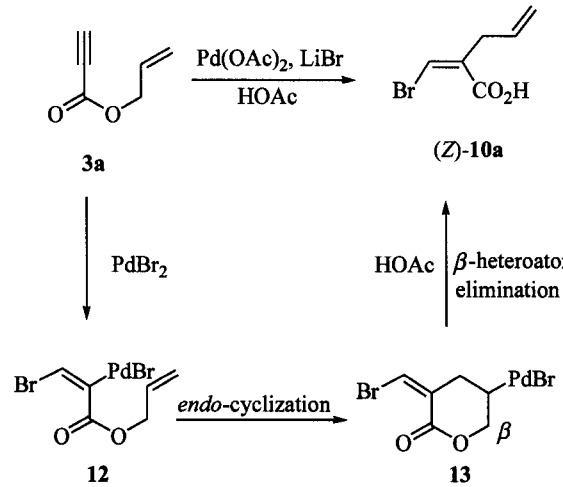
On further study, we found that even without allyl halide or acrolein, (*E*)-**10a** was also obtained satisfactorily (88% isolated yield) in the presence of LiBr, and (*E*)-**10b** was obtained with 87% yield when LiCl was used (Scheme 3). Apparently, a new intramolecular tandem HX-addition-rearrangement reaction occurred in this reaction condition.

Scheme 3 Tandem HX-addition-rearrangement reaction



It was observed in our previous studies that the Pd(II) species is regenerated in the catalytic reaction quenched by β-heteroatom elimination or protonolysis in the presence of excess halide ions.[8] The formation of the product is better to be explained by a palladium(II) catalyzed pathway. Thus, a mechanism involving *trans*-halopalladation of **3a**, direct *endo*-mode insertion of the C = C bond of **12** to the vinylic C—Pd bond, followed by β-heteroatom elimination of **13** was suggested to account for the formation of **10a**, as outlined in Scheme 4. Following this mechanism, the stereochemistry of the product **10a** should be in (*Z*)-form, while the product we obtained was in (*E*)-form, which can be obtained only in the case that the first step is *cis*-halopalladation. Unfortunately, *cis*-halopalladation is much less possible than *trans*-halopalladation under high concentration of halide ion and in polar solvents.[9]

Scheme 4 *Endo*-mode C = C insertion yielding product (*Z*)-**10a**

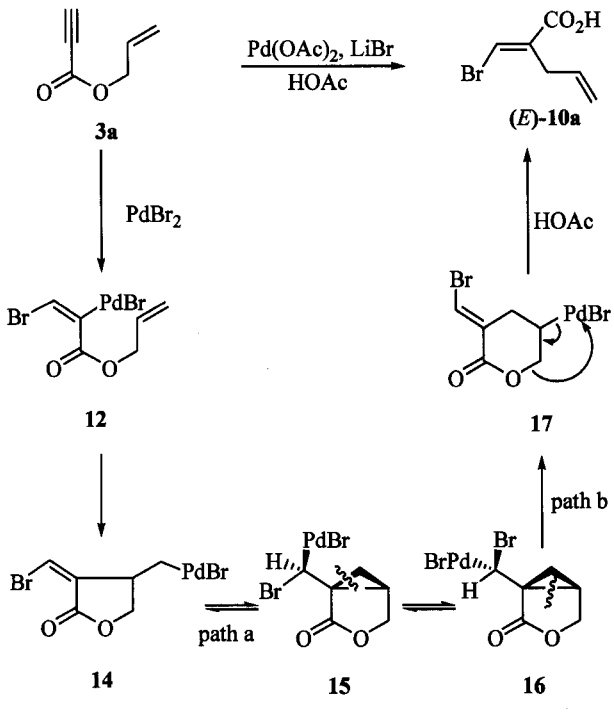


Another proposed speculation for the formation of (*E*)-**10a** is as follows. The reaction involves *trans*-halopalladation of **3a**, followed by intramolecular insertion of the terminal alkene into the resulting (*E*)-alkyenylpalladium species in **12** with overall retention of (*Z*)-enyl configuration, giving the alkylpalladium intermediate (*Z*)-**14**. At this stage, two competitive pathways are possible. One is β-H elimination of the palladium species, which yields Pd(0) species thus leading the catalytic cycle to the end. In addition, in our previous studies, we have reported that in the presence of excess halide ions, β-H elimination was prohibited,[8b,c] thus, the first pathway is much less possible. Another pathway is the insertion of the exocyclic double bond into the car-

bon-palladium bond, forming the cyclopropane derivative **15**.[10] Intermediate **15** could go further ring-opening reaction to yield either (*Z*)-**14** (via path a) or (*E*)-**17** (via path b).[10] During the ring-opening reaction, the C—C bond of **15** must be rotated to **16** in order to satisfy the coplanarity of C—Pd bond and the C—C bond to be cleaved, resulting in the formation of **17** with (*E*)-configuration of the *exo*-cyclic double bond.

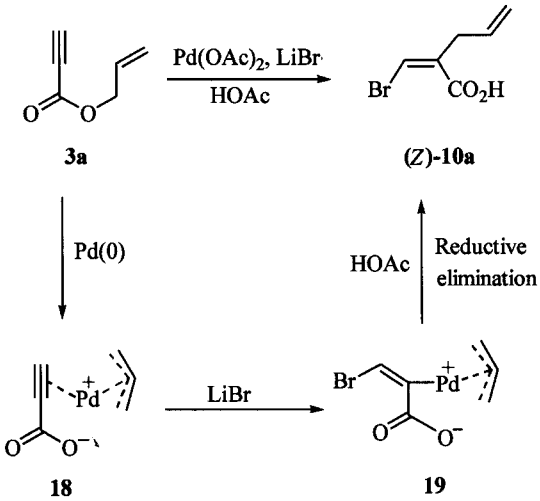
As we discussed above, in the presence of excess halide ions, for intermediate (*Z*)-**14**, β-hydrogen elimination that results in the end of the catalytic cycle is not possible to occur, while intermediate (*E*)-**17** undergoes β-oxy elimination to give (*E*)-**10a**. This mechanism, which involves a sequence of (i) *trans*-halopalladation, (ii) β-heteroatom elimination, is more consistent with the stereochemistry of the product and the results of the reaction (Scheme 5).

Scheme 5 Proposed mechanism for the reaction



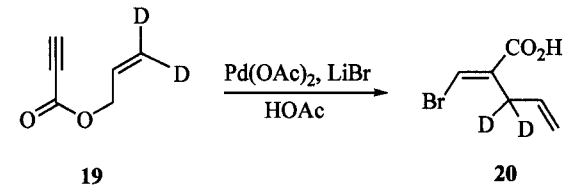
It is also possible that Pd(0) is the key catalytic species reacting with **3a** to form the π-allyl Pd species **18** which coordinates with the triple bond and halide attacks preferentially at the opposite side of the Pd species to form **19**, followed by reductive elimination of **19** to give the product **10a**. But, in this reaction, the stereochemistry of the double bond of the final product is still in *Z*-configuration, what is more, in the presence of excess halide, Pd(II) is not easily reduced to Pd(0) (Scheme 6).[1,3,4]

Scheme 6 Pd(0) catalyzed intramolecular reaction



To make sure whether Pd(0) can catalyze this reaction or not, and to verify the mechanism proposed, we tried the reaction with deuterium-labeled substrate. If the reaction was catalyzed by a Pd(0) species, the deuterium-hydrogen scrambled products will be obtained. The reaction gave only product **20** (Scheme 7), thus, the the possibility of a Pd(0) species as the catalyst is ruled out. Further study to explore broader substrates is ongoing in our laboratory.

Scheme 7 Reaction of the deuterated substrate



Experimental

Materials

Pd(OAc)$_2$ and 1, 1-dideuterioallyl propynoate was prepared according to the literature.[11a,11b] LiBr and LiCl were dried over P_2O_5 under vacuum. Acetic acid was refluxed with acetic anhydride and distilled from $KMnO_7$. Allyl bromide, allyl chloride and acrolein were distilled before use.

Reaction of allyl propynoate with allyl bromide

A Schlenk reaction tube was charged with palladium acetate (11 mg, 0.05 mmol), lithium bromide (430 mg, 5 mmol) and HOAc (5 mL). After the mixture became homogeneous, **3a** (110 mg, 1 mmol) was added, followed by the addition of allyl bromide (605 mg, 5 mmol). The mixture was stirred at r.t. (~30 ℃) till the starting material was consumed. After removal of the solvent under vacuum, the residue was diluted with ether and washed with water. Acid (*E*)-**10a** (Scheme 2) was obtained as the only product in 88% yield after column chromatography.

(*E*)-**10a** ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 11.7—11.2 (br, 1H), 7.79 (s, 1H), 5.95—5.85 (m, 1H), 5.20—5.00 (m, 2H), 3.24 (d, J = 6.2 Hz, 2H); IR (neat) ν: 3086—2500 (broad), 1693, 1640, 1604, 992, 918 cm^{-1}; MS m/z: 192 (M^+, ^{81}Br), 190 (M^+, ^{79}Br), 111, 93, 67 (base); HRMS calcd for $C_6H_7BrO_2$ 189.9629 (^{79}Br), 191.9609 (^{81}Br), found 189.9667 (^{79}Br), 191.9621 (^{81}Br).

Reaction of allyl propynoate with acrolein

The reaction is essentially the same as the reaction of allyl propynoate with allyl bromide, albeit allyl bromide was replaced with acrolein. The same product (*E*)-**10a** was obtained in 85% yield.

Reaction of allyl propynoate in the absence of allyl bromide or acrolein

The reaction is essentially the same as the reaction of allyl propynoate with allyl bromide, albeit neither allyl bromide nor acrolein was added. The same product (*E*)-**10a** was obtained in 87% yield.

Reaction of 1,1-dideuterioallyl propynoate in the presence of excess halide and $Pd(OAc)_2$

The reaction follows the above reaction conditions to give **20** in 60% yield.

20 ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 10.99 (br, 1H), 7.79 (s, 1H), 5.85—5.76 (m, 1H), 5.17—5.06 (m, 2H), 3.28—3.17 (m, 0.15H); IR (neat) ν: 3000—2500 (broad), 1610, 1500, 1410, 1300, 920 cm^{-1}; MS m/z: 194 (M^+, ^{81}Br), 192 (M^+, ^{79}Br), 169, 113 (base), 85, 67; HRMS calcd for $C_6H_5D_2{}^{79}BrO_2$ 191.9843, found 191.9799.

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