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Palladium-Catalyzed Intramolecular 1,2-Oxidation of Allenes.

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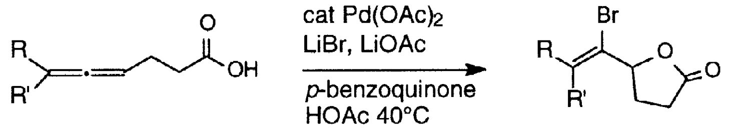
Abstract. Palladium(II)-catalyzed intramolecular 1,2-oxidation of allenic acids proceeds smoothly under mild conditions in the presence of LiBr and *p*-benzoquinone to give bromolactones in good to high yields.

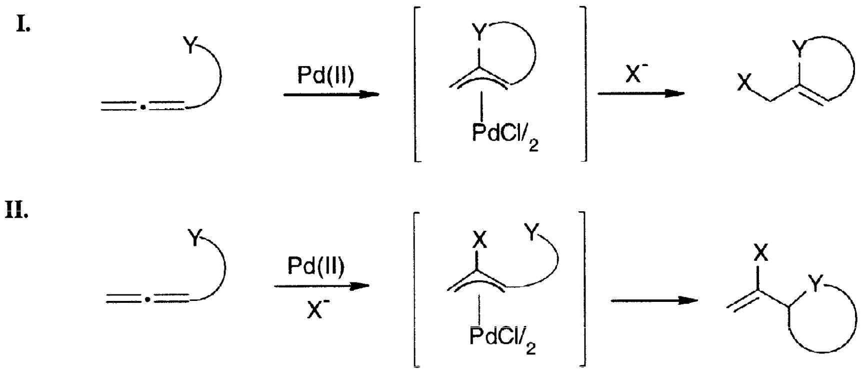
Transition metal-catalyzed nucleophilic additions to unsaturated hydrocarbons are important organometallic reactions which are widely used in organic synthesis.[1] In particular, palladium-catalyzed reactions of olefins and dienes have been extensively studied and a large number of selective organic transformations have been reported.[2] Recently, palladium-catalyzed reactions of allenes have attracted considerable interest. These reactions have mainly involved Pd(0) catalysis[3-6] and only to a minor extent Pd(II) catalysis.[7,8] We recently reported on a mild procedure for palladium-catalyzed 1,2-oxidation of allenes.[8] We have now extended this 1,2-oxidation to an intramolecular version in which an allenic acid is transformed to a bromolactone under mild reaction conditions (eq 1).



(eq 1)

In our search to extend the 1,2-oxidation of allenes to an intramolecular version we considered two possible cyclization modes (Scheme1). The intermediate (π-allyl)palladium complex could be formed either from an intramolecular nucleophilic attack on the palladium-coordinated allene (path I) or from an external attack according to path II. The two mechanistic pathways have been examined and each of these will be discussed below.

Scheme 1



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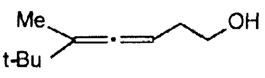
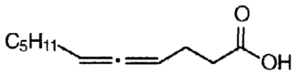
The starting materials for the cyclization experiments, the γ-allenic alcohol 1[9] and the allenic acid 2[10] are readily available by standard methods. We first studied the cyclization using γ-allenic alcohol 1 as the substrate. With this substrate only cyclization according to path I is likely since path II would give a 4-membered ring.



1



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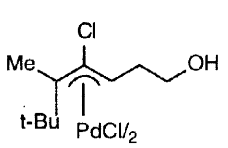
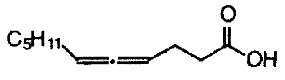
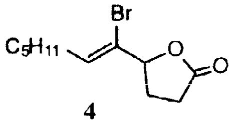
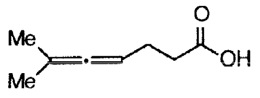
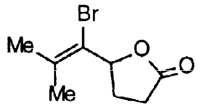
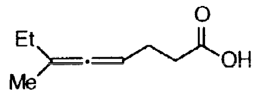
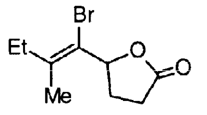
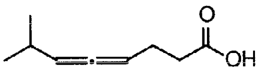
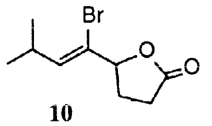
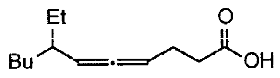
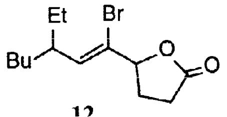


3

Palladium-catalyzed oxidation of allene 1 in acetic acid employing *p*-benzoquinone as the oxidant and LiBr as the external nucleophile gave no trace of 1,2-oxidation products. A stoichiometric reaction was made in order to study the reaction intermediate. Thus, β-allenic alcohol 1 was reacted with a stoichiometric amount of $Pd(PhCN)_2Cl_2$ which afforded the π-(chloroallyl)palladium complex 3. The result indicates that an external nucleophile (Cl^-) has attacked the palladium activated allene, and that no intramolecular attack takes place. Apparently, an intramolecular attack by oxygen at the central allene carbon under the reaction conditions employed is unfavored. We therefore turned our attention to the other possible pathway (path II, Scheme1), using substrate 2 with one carbon more in the side chain.

Reaction of allenic acid 2 in the presence of a catalytic amount of $Pd(OAc)_2$, *p*-benzoquinone, LiOAc and LiBr in acetic acid afforded γ-lactone product 4 in 84 % yield, with mainly Z stereochemistry (*Z*/*E*=92/8). The stereochemical assignment was made by NOE measurements. A few other allenic acids were also shown

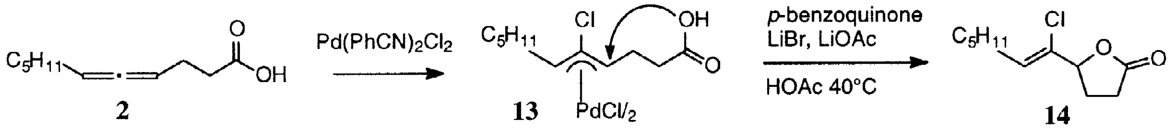
Table 1. Palladium-Catalyzed 1,2-Oxidation of Substituted γ allenic acids [a]

Entry	Allene	Product	Method [a]	Z/E [b]	Yield [c]
1	 2	 4	B	92/8	84
2	 5	 6	A	-	68
3	 7	 8	A	59/41	67
4	 9	 10	A	76/24	70
5	 11	 12	B	82/18	52

(a) Method A (see note 11): The reaction was performed in acetic acid at 40°C employing 5 mol% of $Pd(OAc)_2$, 5 equiv. of LiBr, 1.5-2.5 equiv. of LiOAc and 2.5 equiv. of *p*-benzoquinone. The substrate was added over 16-18h. The reaction time was 20-48 h.; Method B (see note 11): As for method A but with 6-10 equiv. of LiBr, 5-6 equiv. of LiOAc, and 5-6 equiv. of *p*-benzoquinone. (b) Determined by NOE measurements. (c) Isolated yield after flash chromatography.

to undergo the palladium-catalyzed bromolactonization reaction (Table 1). Thus, allenes **5**, **7**, **9**, and **11** afforded the corresponding γ lactones **6**, **8**, **10**, and **12** in good isolated yields (entries 2-5).[11,12]

The fact that allenic acids, such as **2**, undergo the intramolecular 1,2-oxidation whereas the allenic alcohol **1** does not, suggests that path II is a more favored pathway than path I. Further evidence for a mechanism according to pathway II was provided by the reaction of allenic acid **2** with a stoichiometric amount of $Pd(PhCN)_2Cl_2$ in benzene which afforded the (π-allyl)palladium complex **13** (eq 2). Complex **13** was isolated and characterized and subsequently treated with *p*-benzoquinone, LiBr and LiOAc in acetic acid, which resulted in a fast intramolecular cyclization to give the γ-lactone **14**.[13]

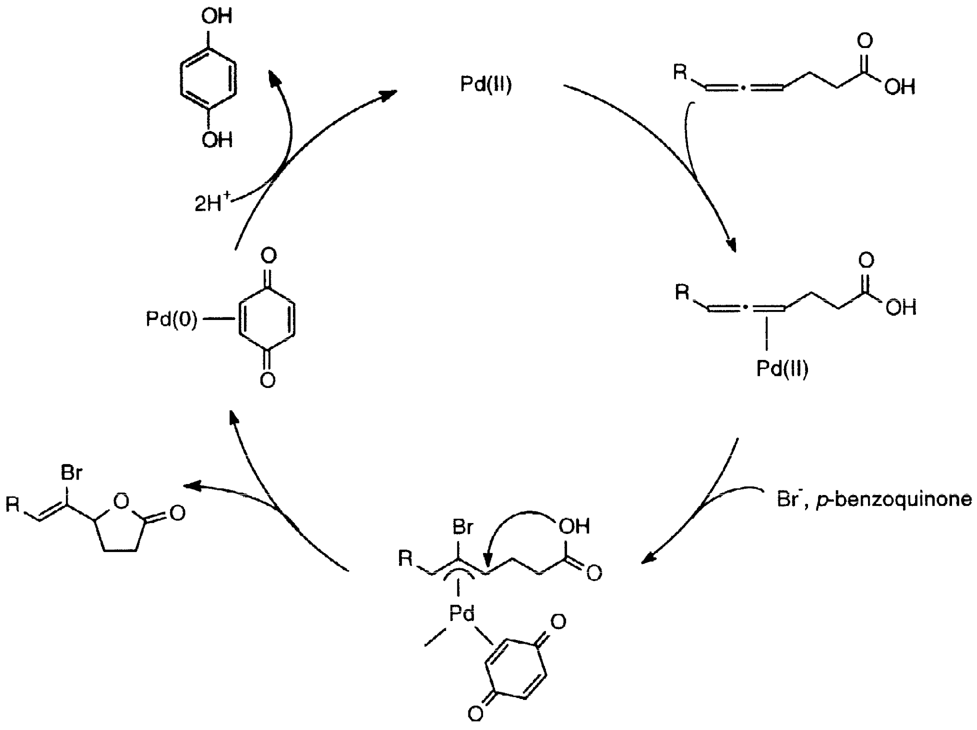


2 **13** **14**

(eq 2)

A likely mechanism for the palladium-catalyzed intramolecular oxidation is given in Scheme 2. Coordination of the allene to palladium and subsequent nucleophilic attack produces a π-allyl palladium intermediate, which undergoes a quinone-induced intramolecular attack to give the product and a Pd(0)-quinone complex. The latter complex then undergoes an internal redox reaction to give Pd(II) and hydroquinone.

Scheme 2



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11. **General procedure for allene cyclisation. Method A: 5-(1-bromo-2-methyl-propenyl)-dihydrofuran-2-one (6).** The allenic acid (1.43 mmol) in a 0.55M solution of acetic acid, was added during 18h to a stirred solution of $Pd(OAc)_2$ (0.071 mmol, 0.05 equiv.), LiBr (7.1 mmol, 5 equiv.), LiOAc (2.1 mmol, 1.5 equiv.), and p-benzoquinone (3.6 mmol, 2.5 equiv.) in 5.2 ml of acetic acid (0.68M towards p-benzoquinone) at 40°C. The mixture was stirred for 48h. The reaction mixture was diluted with water and extracted with ether. The combined extracts were washed with ice-cold 2M NaOH and water then dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (2:1 pentane/ether) to afford the cyclized product. **Method B:** The same procedure as for method A but with 6-10 equiv. of LiBr, 5-6 equiv. of LiOAc, and 5-6 equiv. of BQ in 0.55M acetic acid (towards p-benzoquinone).
12. Selected NMR data: **5-(1-bromo-2-methyl-propenyl)-dihydrofuran-2-one (6)** ^1H NMR ($CDCl_3$) δ 5.51 (dd, J=6.5, 7.8, 1H), 2.74 (ddd, J=5.7, 10.2, 17.9, 1H), 2.54 (ddd, J=8.2, 10.1, 17.9, 1H), 2.40-2.24 (m, 2H) 1.95 (s, 3H), 1.93 (s, 3H) ^{13}C NMR ($CDCl_3$) δ 176.5, 137.4, 120.3, 77.5, 28.4, 26.9, 25.8, 20.9.
13. This rules out an alternative mechanism of the 1,2-oxidation via an oxypalladation to give a vinylpalladium species followed by reductive elimination to form the vinyl bromide bond.