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Facile Palladium(0)-Catalyzed Ring Expansion Reactions of Hydroxy Methoxyallenyl Cyclic Compounds via Hydropalladation

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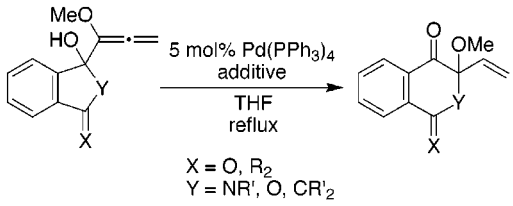
ABSTRACT



Palladium(0)-catalyzed one-atom ring expansion of various hydroxy methoxyallenyl compounds has been achieved in excellent yields without the use of aryl halides. Hydroxy methoxyallenylisoindolinones, -indanones, and -phthalans have been readily converted to the corresponding isoquinolones, naphthoquinones, and isochromanones in the presence of P(*o*-tolyl)$_3$.

Ring expansion reactions have provided efficient tactics for the construction of various biologically active natural products and drugs.[1] We have performed base-mediated tandem heterocyclic and carbocyclic two-atoms ring expansion reactions and palladium(0)-catalyzed tandem carbopalladation-heterocyclic and -carbocyclic one-atom ring expansion reactions by employing various hydroxy allenic compounds.[2] Recently, Clark et al. and various other groups have reported palladium-catalyzed ring expansion reactions using cyclobutanols.[3,4] However, the palladium(0)-catalyzed ring expansion reactions described above should be initiated by carbopalladation with aryl halides based on Heck-type reactions,[3] except for the palladium(II)-catalyzed ring expansion reactions of alkenyl- and alkynylcyclobutanols. Thus, we envisioned that desirable palladium(0)-catalyzed one-atom ring expansion reactions seem to proceed via hydro-

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palladation (vide infra) onto the allenic moiety without the use of aryl or alkenyl halides; this process is described below.

Several substrates, hydroxy methoxyallenylisoindolinones **1a**,**c**−**e**, -indanones **3a**,**b**,**e**, and -phthalans **5a**,**b** were made readily accessible by previously reported reactions of the corresponding *N*-alkylphthalimides, dialkylindandiones, and dialkylphthalides with lithio methoxyallene; in each case, good yields were obtained.[2,5]

First of all, hydroxy methoxyallenylisoindolinone **1a** was refluxed in the presence of 5 mol % $Pd(PPh_3)_4$ and 3 mole equiv of K_2CO_3 in THF. The desired one-atom ring expansion proceeded even in the absence of aryl halides to afford isoquinoline **2a** in a 79% yield (entry 1 in Table 1). Similar

Table 1. Palladium(0)-Catalyzed One-Atom Ring Expansion of Hydroxy Methoxyallenyl Cyclic Compounds **1**, **3**, and **5**

entry	compound	additive	time (h)	product	yield (%)
1	**1a**	K_2CO_3[a]	19	**2a**	79
2	**1c**	K_2CO_3[a]	19	**2c**	63
3	**1d**	K_2CO_3[a]	19	**2d**	69
4	**1e**	K_2CO_3[a]	17	**2e**	88
5	**3a**	K_2CO_3[a]	24	**4a**	36
6	**5a**	K_2CO_3[a]	24	**6a**	63
7	**3a**	PPh_3[b]	18	**4a**	90
8	**1a**	P(*o*-tolyl)$_3$[b]	3	**2a**	93
9	**1c**	P(*o*-tolyl)$_3$[b]	2	**2c**	83
10	**1d**	P(*o*-tolyl)$_3$[b]	3	**2d**	71
11	**1e**	P(*o*-tolyl)$_3$[b]	1	**2e**	93
12	**3a**	P(*o*-tolyl)$_3$[b]	9	**4a**	96
13	**3b**	P(*o*-tolyl)$_3$[b]	9	**4b**	96
14	**3e**	P(*o*-tolyl)$_3$[b]	9	**4e**	98
15	**5a**	P(*o*-tolyl)$_3$[b]	2	**6a**	81
16	**5b**	P(*o*-tolyl)$_3$[b]	1	**6b**	91

[a] Three mole equiv of K_2CO_3 was used. [b] Ten mole percent PPh_3 or P(*o*-tolyl)$_3$ was used.

treatment of other isoindolinones **1c**−**e**, indanone **3a**, and phthalan **5a** furnished the corresponding isoquinolones **2c**−**e** in 63−88% yields (entries 2−4), naphthoquinone **4a** in a 36% yield (entry 5), and isochromanone **6a** in a 63% yield (entry 6). All experimental results are summarized in Scheme 1 and Table 1. The structures of all products were explicitly determined by their characteristic spectroscopic data and/or X-ray crystallographic analysis of **2a** and **4a**, as shown in Figure 1.[6,7]

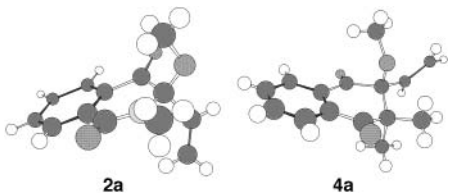
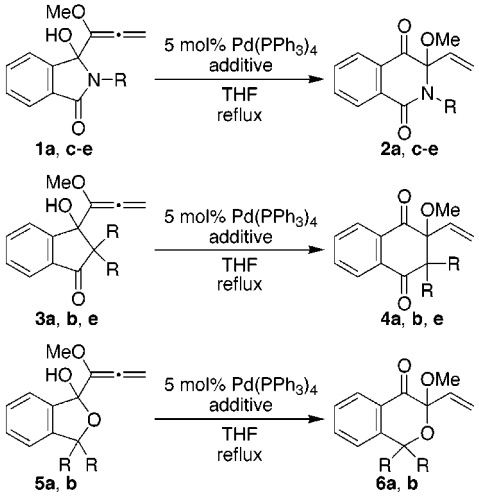


Figure 1. Computer-generated drawing from the X-ray coordinates of compounds **2a** and **4a**.

Scheme 1



Because of the poor yield (36%) and lengthy reaction time (24 h) required for the reaction to obtain naphthoquinone **4a** as described above, the Pd(0)-promoted reaction of **3a** was tentatively undertaken by employing 10 mol % PPh_3 as an additive instead of K_2CO_3. Fortunately, the yield and reaction time were improved to be 90% and 18 h (entry 7), respectively. We considered that decomposition of palladium catalyst and the allenic substrates under the reaction conditions with K_2CO_3 for 17−24 h turned out to provide an unsatisfied yield of each product, as shown in Table 1.

Subsequently, the $Pd(PPh_3)_4$-catalyzed reactions of **1a**,**c**−**e**, **3a**,**b**,**e**, and **5a**,**b** were similarly performed in the presence of 10 mol % of P(*o*-tolyl)$_3$ as an additive,[8] which is known to stabilize the Pd catalyst and improve its turnover. Surprisingly, all one-atom ring expansion reactions in the present study were easily generated to afford the corresponding desired products in 71−98% yields after refluxing for 1−9 h, as shown in Table 1 (entries 8−16).

To learn reactivity of the palladium(II) species to the methoxyallenic moiety, compound **3a** was treated with 5 mol % $Pd(OAc)_2$ in the presence of 1 mole equiv of DDQ in THF under reflux for 3 h.[4o] The reaction did not furnish the desirable naphthoquinone **4a** at all, but dimethylindanedione was obtained in a 37% yield. Similar treatment of **3a** with 1 mole equiv of $Pd(OAc)_2$ in THF under reflux for 1.5 h[4p] resulted in decomposition of **3a**.

A plausible mechanism for the cascade hydropalladation-ring expansion reaction can be represented on the basis of

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(6) X-ray data for **2a** and **4a**. **2a**: $C_{13}H_{13}NO_3$, MW = 231.25, colorless prismatic crystal, triclinic, space group *P*1 (No. 2), a = 7.879(2) Å, b = 11.512(4) Å, c = 7.282(2) Å, V = 592.0(3) Å^3, α = 101.50(1)°, β = 111.50(1)°, γ = 74.840(8)°, Z = 2, R = 0.088, Rw = 0.141. **4a**: $C_{15}H_{16}O_3$, MW = 244.21, colorless prismatic crystal, monoclinic, space group: $P2_1/a$ (No. 14), a = 11.7404(4) Å, b = 8.8228(3) Å, c = 12.3876(4) Å, β = 100.042(2)°, V = 1263.49(7) Å^3, Z = 4, R = 0.062, Rw = 0.097. Structure factors are available from author upon request.

(7) Supporting Information available.

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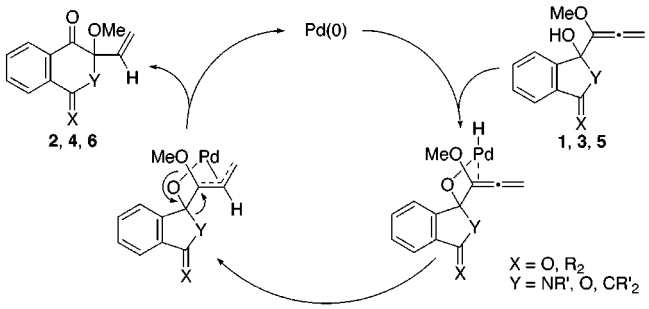

Figure 2. Proposed mechanism for the cascade hydropalladation-ring expansion reactions using $Pd(PPh_3)_4$.

earlier reports as follows (Figure 2).[9,10] In the first step of the catalytic cycle, oxidative addition of the hydroxy group of a hydroxy methoxyallenyl cyclic compound is presumed to occur onto the Pd(0) catalyst. In the second step, a π-allylpalladium complex can be generated by hydropalladation. Then, release of the Pd(0) and rearrangement of the Y group in the π-allylpalladium complex may concertedly proceed to give the one-atom ring expanded product.

In conclusion, we have successfully developed new palladium(0)-catalyzed one-atom ring expansion reactions of various hydroxy methoxyallenyl cyclic compounds via hydropalladation without the use of aryl halides. Further application of the products bearing vinyl and methoxy groups to the syntheses of biologically active natural products and drugs is now ongoing.

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Supporting Information Available: Typical experimental procedure for the synthesis of compounds **2a**,**c**−**e**, **4a**,**b**,**e**, and **6a**,**b** and their physical and spectroscopic data, and X-ray structural data on compounds **2a** and **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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