Palladium(II)-Catalyzed Oxidative Ring Cleavage of *tert*-Cyclobutanols under Oxygen Atmosphere

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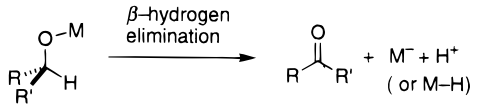
Transition-metal alcoholates have been widely explored in organic and inorganic chemistry, since they have the interesting reactivity and structural diversity.[1] In sharp contrast to stability of early transition-metal alcoholates, late transition-metal ones are labile due to weak M−O bond.[2b] Thus, the late transition-metal alcoholates, although they lack M−C bonds, show certain similarities to alkyls and are prone to β-hydrogen elimination to give a carbonyl compound and a reduced metal as shown in Scheme 1.[2] On the other hand, the examples of dealkylation reactions of *tert*-alcoholates via β-carbon elimination catalyzed by the late transition metal (Scheme 2) similar to β-hydrogen elimination are still few in number.[3]

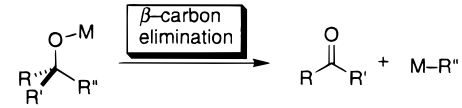
Recently, we have succeeded in the aerobic oxidation of *primary* and *secondary* alcohols to aldehydes and ketones in the $Pd(OAc)_2$/pyridine/MS3A catalyst system.[4] This dehydrogenative reaction proceeds via a palladium alcoholate and catalytically on palladium under oxygen atmosphere. Thus, we undertook the reaction of *tert*-alcohols. Cyclic *tert*-cyclobutanol could merit being used to pursue the β-carbon elimination without the loss of the carbon atom because it was expected to favor β-carbon elimination at the endo-carbon by relief of the ring strain.[5,6] Now we wish to report the novel palladium-catalyzed reaction of several *tert*-cyclobutanols involving selective β-carbon elimination (bond **a** breaking) from the palladium alcoholate under the aerobic conditions (Scheme 3).

Ring expansion reaction of 1-alkenyl or 1-alkynyl cyclobutanols is a well-investigated reaction that can be promoted or catalyzed by a divalent palladium.[7] This reaction is suggested by the required formation of palladium alkene or alkyne π-complex prior to migration of a secondary carbon (Scheme 4). Our approach to find a different bond-cleavage reaction is performed by the application of the recently discovered aerobic conditions employing Pd(II) (vide supra)[4] to *tert*-cyclobutanols. Treatment of 7-vinylbicyclo[4.2.0]octan-7-ol[8] (**1a**) (0.5 mmol) in toluene at 80 °C for 20 h with 10 mol % $Pd(OAc)_2$, pyridine (1.0 mmol) and MS3A (50 mg) under oxygen atmosphere afforded 1-(2-methylenecyclohexan-1-yl)-2-propen-1-one (**2a**) in 56% isolated yield as a dehydrogenative ring opening product (eq 1). This result suggested that our reaction condition favored the cleavage of C−C bond of cyclobutanol giving a less hindered primary alkylpalladium intermediate (bond **a** breaking). The amount of pyridine used was crucial to obtain the product **2a** selectively. Reducing the amount of pyridine to 0.2 mmol, the yield of **2a** decreased (30%).[9] Next, the reaction of 7-phenylbicyclo[4.2.0]octan-7-ol (**1b**) under the same conditions for 48 h afforded 2-methylenecyclohexan-1-yl phenyl ketone (**2b**) in 60% isolated yield. Interestingly, the addition of a catalytic amount of ethyl acrylate (0.2 mmol) dramatically increased the yield of **2b** up to 97% isolated yield.[10] These successful reaction conditions could be applied to

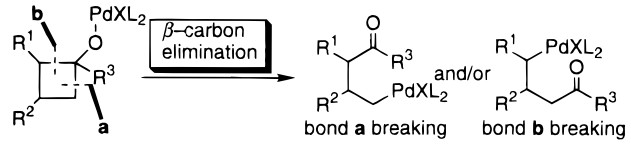
Scheme 1



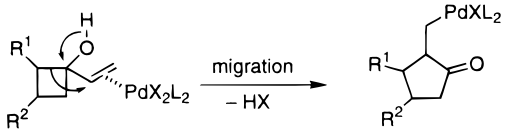
Scheme 2



Scheme 3



Scheme 4



(1)

substrate	time (h)	isolated yield (%)
1a: R = vinyl	20	**2a** 56
1b: R = Ph	48	**2b** 60
1b: R = Ph	16	**2b** 97 [a]
1c: R = Bu	38	**2c** 71 [a]

a) In the presence of ethyl acrylate (0.2 mmol)

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(4) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **1998**, *39*, 6011.

(5) The ring expansion reactions of siloxycyclopropanes, see: (a) Kuwajima, I.; Nakamura, E. *Top. Curr. Chem.* **1990**, *155*, 1. (b) Kirihara, M.; Ichinose, M.; Takizawa, S.; Momose, T. *Chem. Commun.* **1998**, 1691 and references therein. The oxidative rearrangement reactions of cyclobutanols, see: Schlecht, M. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ley, S. V., Eds.; Pergamon: Oxford, U.K., 1991; Vol.7, pp 824−826. The recent advance of β-carbon elimination in the reaction sequence using spiro cyclobutanones, see: Murakami, M.; Takahashi, K.; Amii, H.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 9307.

(6) The study on the strain energy, see: Schleyer, P. v. R.; Williams, J. E.; Blanchard, K. R. *J. Am. Chem. Soc.* **1970**, *92*, 2377.

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(8) Cyclobutanols are readily accessible from the corresponding cyclobutanones and Grignard reagent or alkyllithium. Typical methods for cyclobutanones, see: (a) Krepski, L. R.; Hassner, A. *J. Org. Chem.* **1978**, *43*, 2879. (b) Greene, A. E.; Luche, M.-J.; Serra, A. A. *J. Org. Chem.* **1985**, *50*, 3957.

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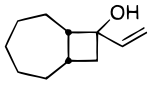
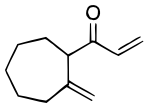
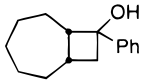
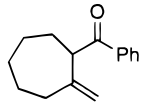
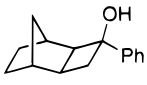
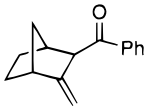
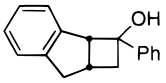
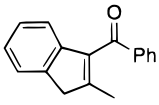
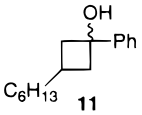
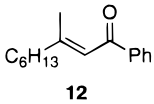
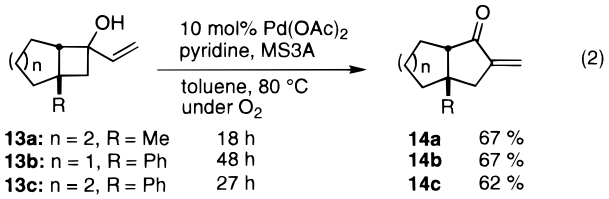
Table 1. $Pd(OAc)_2$ Catalyzed Reaction of Cyclobutanols*

entry	substrate	time (h)	product and yield (%) [a]
1 [b]	 **3**	23	 **4** 52
2	 **5**	21	 **6** 93
3	 **7**	17	 **8** 91
4	 **9**	22	 **10** 81
5	 **11**	48	 **12** 52

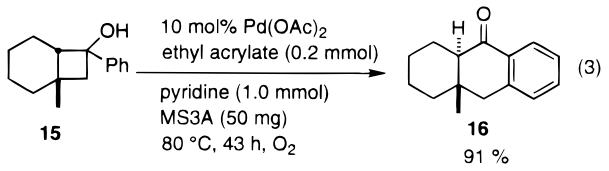
* Reaction conditions: alcohol (0.5 mmol), $Pd(OAc)_2$ (0.05 mmol), pyridine (1.0 mmol), ethyl acrylate (0.2 mmol), MS3A (50 mg), toluene (5 mL), at 80 °C under atmospheric O_2. [a] Isolated yield. [b] In the absence of ethyl acrylate.

the reaction of alkyl-substituted bicyclic cyclobutanol **1c** leading to β,γ-unsaturated ketone 1-(2-methylenecyclohexan-1-yl)pentan-1-one (**2c**) in 71% yield. This means that the formation of palladium alcoholate is a crucial step and the pre-coordination of π-bond with palladium is not required prior to C−C bond cleavage. Other examples of the selective C−C bond cleavage of cyclobutanols are listed in Table 1. Several bicyclic cyclobutanols **3**, **5**, and **7** produced the corresponding β,γ-unsaturated ketones **4**, **6**, and **8** in good to high yields (entries 1−3). Cyclobutanol **9** yielded α,β-unsaturated ketone **10** (81%) isomerized from the initially formed β,γ-unsaturated ketone (entry 4). The reaction of monocyclic cyclobutanol **11** was relatively slow, but α,β-unsaturated ketone **12** was obtained in moderate yield (entry 5).

The reaction could also be applied to bicyclic cyclobutanols **13a**−**c** having an angular substituent (eq 2). Cyclobutanols **13a**−**c** afforded cyclopentanones **14a**−**c** in good yield. Each product was apparently different from products obtained in the previous palladium(II)-mediated reactions.[7] These results show that an alkylpalladium intermediate which is formed by β-carbon elimination from palladium alcoholate undergoes cyclization in 5-*exo* mode and subsequent β-hydrogen elimination to give an α-methylenecyclopentanone. In the case of substrate **15** having phenyl group instead of vinyl, the interesting reaction took place to give ketone **16**[11] in 91% yield (eq 3). The formation of **16** can



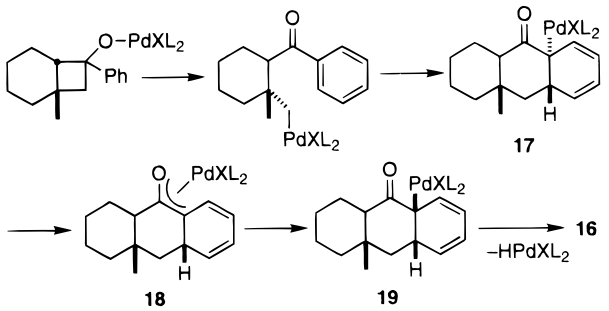
(2)



(3)

be explained by assuming the reaction sequence shown in Scheme 5. An alkylpalladium intermediate by β-carbon elimination undergoes intramolecular endo cyclization with phenyl ring to give *trans*-organopalladium complex **17**. This *trans*-complex isomerizes via palladium enolate **18** to *cis*-organopalladium complex **19**, which affords the product **16** via β-hydrogen *syn*-elimination.

Scheme 5



We suppose that these catalytic reactions proceed via the formation of a Pd(II)−alcoholate species[12] from alcohol and Pd(II)−pyridine complex[13] followed by β-carbon elimination giving an alkylpalladium species. This alkylpalladium species is prone to eliminate palladium with β-hydride to give β,γ-unsaturated ketones or cyclize with an alkenyl bond in the same molecule to give cyclic ketones. The Pd(II)−hydride species produced at the final stage can be converted again to active Pd(II) species by molecular oxygen. The salient features of this catalytic behavior deserves detailed study in this C−C bond cleavage reaction as well as in the aerobic oxidation of *primary* and *secondary* alcohols.

Supporting Information Available: Experimental procedures and analytical and spectroscopic data of compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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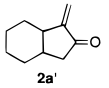
(9) The byproduct, 7-methylenebicyclo[4.3.0]nonan-8-one (**2a′**) was also obtained in 21% yield. The formation of **2a′** might stem from bond **b** breaking as indicated in Scheme 3 or palladium catalyzed rearrangement as shown in Scheme 4.


2a′

(10) This effect of ethyl acrylate is not clear at present, but it might accelerate the β-carbon and hydrogen elimination. In the reaction of 1-vinylcyclobutanols the addition of ethyl acrylate did not show significant difference in the yield of the products.

(11) ^1H NMR for compound **16**, see: Thompson, H. W.; Long, D. J. *J. Org. Chem.* **1988**, *53*, 4201. Ring juncture was isomerized in some stage during the reaction. The stereochemistry of **16** was confirmed by X-ray crystallographic analysis in our hands: see Supporting Information.

(12) Blackburn, T. F.; Schwartz, J. *J. Chem. Soc., Chem. Commun.* **1977**, 157.

(13) Kravtsova, S. V.; Romm, I. P.; Stash, A. I.; Belsky, V. K. *Acta Crystallogr.* **1996**, *C52*, 2201.