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Diverse Pathways for the Palladium(II)-Mediated Oxidation of Olefins by *tert*-Butylhydroperoxide

Jin-Quan Yu and E. J. Corey*

Department of Chemistry and Chemical Biology, Harvard University,
12 Oxford Street, Cambridge, Massachusetts 02138

corey@chemistry.harvard.edu

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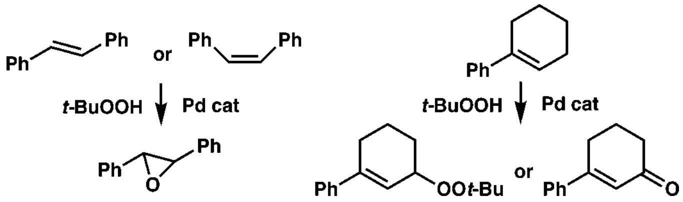
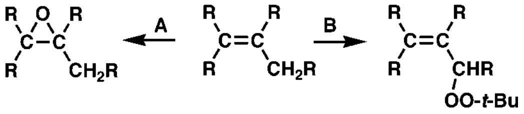
ABSTRACT



New procedures are described for the palladium-catalyzed oxidation of olefins by *tert*-butylhydroperoxide under slightly basic conditions in CH_2Cl_2 solution at 0–25 °C.

The selective oxidative functionalization of organic compounds under the catalytic influence of transition metal complexes continues to be a fascinating and useful area of research.[1] We describe herein some novel results of an exploratory study of the oxidation of various olefins by *tert*-butylhydroperoxide in the presence of catalytic amounts of palladium(II) acetate or trifluoroacetate. Two different reaction pathways have been observed using a mixture of the catalytic Pd(II) salt, *t*-BuOOH, and olefin in CH_2Cl_2 at 0−25 °C in the presence of catalytic amounts of K_2CO_3: (1) allylic peroxy ether formation and (2) epoxidation, as shown in Scheme 1. In terms of conditions, product, and reaction pathway, the new allylic peroxidation is decidedly different from the well-known $Pd(OAc)_2$-catalyzed allylic oxidation of olefins to form allylic acetates.[2]

Scheme 1



A variety of olefins have been converted to epoxides (Scheme 1, path A) using 5 equiv of *t*-BuOOH, 10 mol % $Pd(OAc)_2$, or $Pd(OAc)_2$•BINAP complex in the presence of 25 mol % K_2CO_3 in CH_2Cl_2 at 0 °C, as summarized in Table 1. Both carboxylate ligands appear to be displaced from PdX_2 by *tert*-butylperoxy ligands as shown by ^1H NMR analysis and also mass spectral analysis, which indicated the species $Pd(OO\textit{t}\text{-}Bu)_2{\cdot}2C_5D_5N$ after coordination with pyridine-d_5. At room temperature the mixture of catalyst and *t*-BuOOH gives rise to liberation of O_2, indicative of the formation of the peroxy radical *t*-Bu−OO•, which can dimerize to the unstable di-*tert*-butyltetraoxide.[3,4] The simplest and clearest explanation for the epoxidation reaction is the free radical chain process shown in Scheme 2 for (*Z*)-stilbene → *trans*-stilbene oxide. The formation of epoxides by the cyclization of

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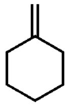
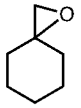
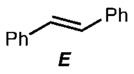
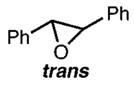
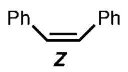
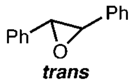
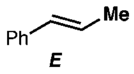
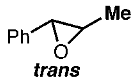
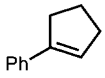
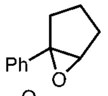
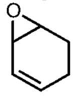
(1) For some recent examples, see: (a) Andrus, M. B.; Lashley, J. C. *Tetrahedron* **2002**, *58*, 845. (b) Eames, J.; Watkinson, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 3567. (c) Chen, H.; Hartwig, J. F. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 3391. (d) Espino, C. G.; Wehn, P. M.; Chow, J.; DuBois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935. (e) Kohmura, Y.; Kawasaki, K.-i.; Katsuki, T. *Synlett* **1997**, 1456.

(2) Heumann, A.; Reglier, M.; Waegell, B. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 366. (b) Heumann, A.; Akermark, B. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 453. (c) McMurry, J. E.; Korovsky, P. *Tetrahedron Lett.* **1984**, *25*, 4187. (d) Backvall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335.

(3) See: (a) Bartlett, P. D.; Günther, P. *J. Am. Chem. Soc.* **1966**, *88*, 3288. (b) Bartlett, P. D.; Guaraldi, G. *J. Am. Chem. Soc.* **1967**, *89*, 4799.

10.1021/ol0262340 CCC: $22.00

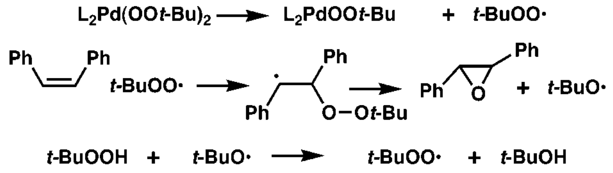
Table 1. Expoxidation of Olefins by *t*-BuOOH in CH_2Cl_2 at 0 °C Catalyzed by $Pd(OAc)_2-K_2CO_3$

olefin	epoxide	yield, %
		80[a]
		82
		70[a]
		76[a]
		65
		75
		90

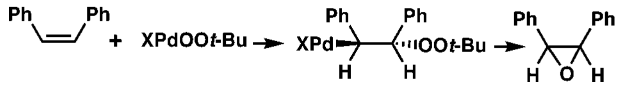
[a] Reaction was carried out at 23 °C.

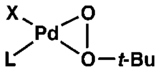
β-alkylperoxy carbon radicals is clearly documented.[5] The production of *trans*-stilbene oxide from either (*E*)- or (*Z*)-stilbene is clearly consistent with this two-step epoxidation pathway and inconsistent with either direct O atom transfer from a *μ*2-peroxo palladium intermediate of type **1** or a trans *tert*-butylperoxy palladation and 1,3-elimination as shown in Scheme 3. Additional support for the radical epoxidation pathway shown in Scheme 2 derives from the reaction of styrene with *t*-BuOOH at 0 °C in CH_2Cl_2 in the presence of $Pd(OAc)_2$ and K_2CO_3 (same conditions as for the examples in Table 1), which produced styrene oxide only as a minor product (ca. 5%) and mainly the 1,2-bis-*t*-butylperoxy ether **2** in 85% yield. Similarly, α-methylstyrene was converted to a mixture of epoxide (5%) and 1,2-bis-*tert*-butylperoxy adduct (65%). 1,4-Diphenylbutadiene was oxidized to (*E*)-1,4-diphenyl-1,4-bis-*tert*-butylperoxy-2-butene in an unusual example of chemical (i.e., nonphotochemical) 1,4-dioxygenation of a 1,3-diene (Scheme 4).

Scheme 2

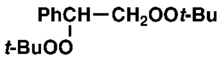


Scheme 3



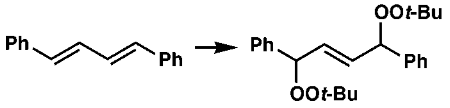


1



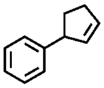
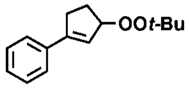
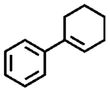
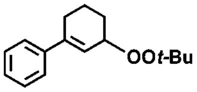
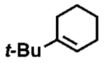
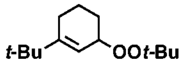
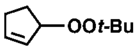
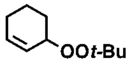
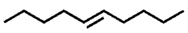
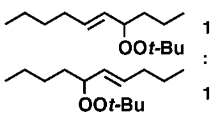
2

Scheme 4



Numerous olefinic substrates that possess allylic hydrogen are oxidized by the *t*-BuOOH–$Pd(OAc)_2-K_2CO_3-CH_2Cl_2$ system to allylic *tert*-butylperoxy ethers as major products (Scheme 1, path B) with only minor competition from the epoxidation pathway. Table 2 summarizes several examples of this type of reaction. These allylic oxidations can also be rationalized in terms of *tert*-butylperoxy radical intermedi-

Table 2. Allylic *t*-Butylperoxidation of Olefins by *t*-BuOOH–$Pd(OAc)_2-K_2CO_3$ in CH_2Cl_2 at 0 °C

entry	olefin	product	time (h)	major prod., isol. yield, %
1			40	75%
2			72	62%
3			72	68%
4			48	63% (82% GC)
5			72	65% (80% GC)
6			48	70%

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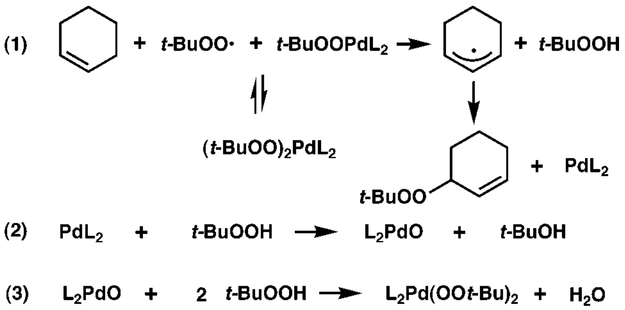
[4] For the oxidative formation of peroxy radicals from hydroperoxides, see: (a) Haynes, R. K.; Vonwiller, S. C. *J. Chem. Soc., Chem. Commun.* **1990**, 1102. (b) Kharasch, M. S.; Pauson, P.; Nudenberg, W. *J. Org. Chem.* **1953**, *18*, 323. (c) Araneo, S.; Fontana, F.; Minisci, F.; Recupero, F.; Serri, A. *J. Chem. Soc., Chem. Commun.* **1995**, 1399.

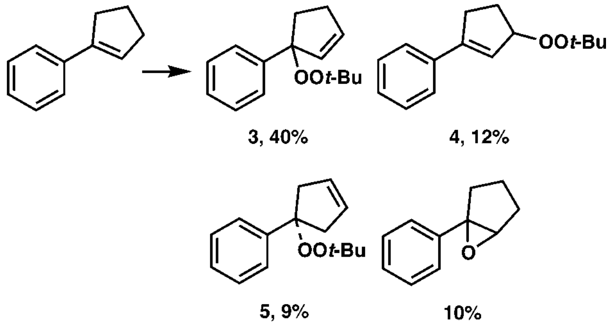
ates, a key step being the hydrogen atom abstraction shown in step 1 of Scheme 5. Steps 2 and 3, which explain catalyst regeneration, are hypothetical, but reasonable. In entries 4−6 of Table 2, a catalytic amount of 2,2′-diphenylphosphino-1,1′-binaphthyl (BINAP) was also used to prevent deposition of metallic Pd and thus enhance conversion of $L_2Pd(0)$ to $L_2Pd(II)$. The balance between epoxidation and allylic peroxidation pathways depends sensitively on the olefin structure for substrates in which both types of oxidation are possible. Steric effects and relative stabilities of the allylic radical from H atom abstraction and the *β*-*tert*-butylperoxy radical from addition of *t*-$BuOO^•$ to the double bond are clearly important determinants.

Scheme 5

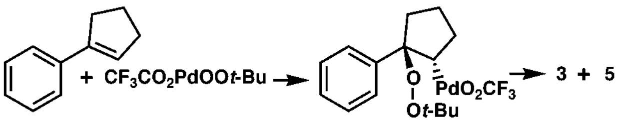


The ligands attached to palladium and the reaction conditions can also play a role in deciding the nature of the products from allylic peroxidation. Oxidation of 1-phenylcyclopentene with 5 equiv of *t*-BuOOH in CH_2Cl_2 at 0 °C in the presence of 10 mol % $Pd(OCOCF_3)_2$ and 20 mol % NaH_2PO_4 for 24 h produces only 10% of the corresponding epoxide along with *tert*-butylperoxy ethers **3**−**5**, as shown in Scheme 6. Upon prolonged reaction, peroxy ether **3** undergoes rearrangement to **4** because the reaction mixture is slightly acidic. ^{1}H NMR studies have revealed that $Pd(OCOCF_3)_2$ is converted under these reaction conditions to CF_3CO_2PdOO*t*-Bu. Although this reagent could conceivably lead to the formation of *t*-$BuOO^•$ and products derived therefrom, it appears more likely that **3** and **5** result instead from the peroxy palladation of the olefinic linkage as shown in Scheme 7. This type of peroxy palladation has also been proposed to account for the conversion of terminal olefins to methyl ketones.[6] In fact, the formation of epoxide (a marker for *t*-$BuOO^•$ radical formation) is completely suppressed by the use of a minimum amount of NaH_2PO_4 (2.5 mol %) with the result that only *tert*-butylperoxy ethers are formed (65% isolated yield).

Scheme 6

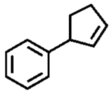
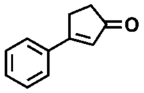
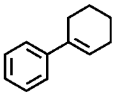
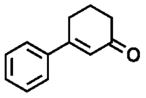
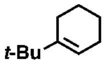
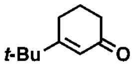
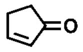
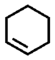
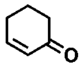
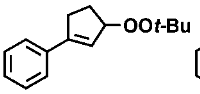
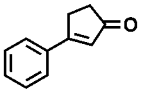


Scheme 7



We have also developed a heterogeneous version of the allylic oxidation using 2.5 mol % Pd on charcoal or $Pd(OAc)_2$ on charcoal as the catalyst, an olefin, 5 equiv of *t*-BuOOH as the oxidant, and 25 mol % of K_2CO_3. Under these conditions under an atmosphere of nitrogen, various olefins have been oxidized to α,*β*-enones under extraordinarily mild, nearly neutral reaction conditions (0 °C in CH_2Cl_2), as summarized in Table 3. The α,*β*-enones are formed by way of allylic *tert*-butylperoxy ether intermediates (which have been detected by chromatographic analysis, isolated and characterized) under these conditions, evidently by a *t*-$BuOO^•$-

Table 3. Pd−C-Catalyzed Allylic Oxidation of Olefins to α,*β*-Enones by *t*-BuOOH

entry	substrate	products	isolated yields
1			71%
2			75%
3			85%
4			71%
5			79%
6			86%

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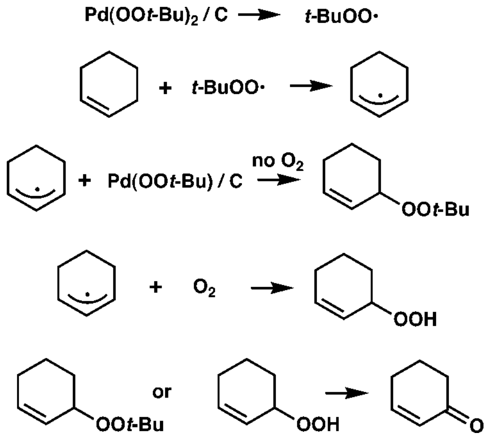
(5) (a) Bloodworth, A. J.; Bylina, G. S. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2433. (b) Schmidt, G. E. Ph.D. Dissertation, Harvard University, Cambridge, MA, 1981; Part II, pp 195−278.

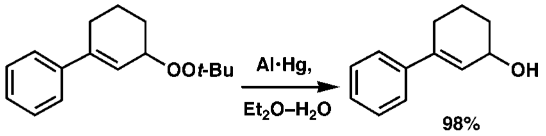
initiated reaction sequence. These ethers undergo rapid further reaction with *t*-BuOO$^{\bullet}$ under the reaction conditions to form the terminal α,*β*-enone products. This radical-mediated oxidative sequence is summarized in Scheme 8 for cyclohexene as the substrate. It has also been found that the α,*β*-enones can be formed without the intermediacy of allylic *tert*-butylperoxy ethers if the reactions are conducted under 1 atm of O_2. Under these conditions, the allylic radicals formed from the olefin by *t*-BuOO$^{\bullet}$-induced allylic H abstraction are intercepted by O_2 to form an allylic hydroperoxide, which is then further oxidized to α,*β*-enone (Scheme 8).

Scheme 8



The *tert*-butylperoxy ethers obtained by the Pd-mediated allylic oxidation described above are readily transformed into the corresponding allylic alcohols. For example, as indicated in Scheme 9, 3-phenyl-2-cyclohexenyl-*tert*-butylperoxide upon stirring with aluminum amalgam in wet ether at 23 °C is reduced exothermically (spontaneous heating to reflux) in 1 h to 3-phenyl-2-cyclohexen-1-ol, which can be isolated in 98% yield (Scheme 9).

Scheme 9



Further studies are required to ascertain the most useful applications of the catalytic methodology described herein. Once issues of relative reactivity, selectivity (especially for polyfunctional or more complex molecules), and scope are more sharply defined, it is likely that the new reagents will find a place in the synthetic chemist's toolbox, since *t*-BuOOH is a relatively safe and inexpensive peroxy reagent.

In conclusion, a number of new oxidative reactions of olefins are described that involve *t*-BuOOH and various palladium catalysts. These include *t*-BuOO$^{\bullet}$-mediated epoxide formation, allylic peroxy ether or hydroperoxide formation, and conversion to α,*β*-enones, all of which occur under basic (K_2CO_3) conditions. The initiating *t*-BuOO$^{\bullet}$ radical appears to be formed by homolysis of L_2Pd(OO*t*-Bu)$_2$, which leads also to L_2Pd(OO*t*-Bu), a species that can provide a second *t*-BuOO group by either radical transfer or dissociation. Oxidation of L_2Pd by *t*-BuOOH regenerates the key reactant L_2Pd(OO*t*-Bu)$_2$. Another, nonradical pathway to allylic peroxy ethers is followed under nonbasic conditions with more electrophilic palladium species. A self-consistent and rational mechanistic explanation for these useful processes has been presented.

Acknowledgment. We are grateful to St. John's College, Cambridge University, for a Research Fellowship to J.-Q. Yu.

Supporting Information Available: Several representative experimental procedures and appropriate product data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0262340

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(6) Pd(OAc)$_2$ undergoes a similar ligand exchange with *t*-BuOOH to form the known AcOPdOO*t*-Bu. See: Mimoun, H.; Charpentier, R.; Mitschler, A.; Fischer, J.; Weiss, R. *J. Am. Chem. Soc.* **1980**, *102*, 1047.