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# Selective C–O bond formation: highly efficient radical dioxygenation of alkenes initiated by catalytic amount of *tert*-butyl hydroperoxide

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A highly selective radical dioxygenation of alkenes using hydroxamic acid and $O_2$ with 5–10 mol % of *tert*-butyl hydroperoxide as a catalyst was developed. On the basis of this newly developed strategy, a wide range of phenylethanol derivatives with a variety of functional groups can be effectively synthesized.

## 1. Introduction

Selective oxidation and oxidative functionalization of organic molecules under mild reaction conditions to construct various oxygenated compounds would be the most important strategy and considered to be an essential area of research in modern organic synthesis.[1] Molecular oxygen is a perfect source to incorporate into organic molecules because of environmentally safe and abundantly available in nature.[2] A variety of transition-metal catalyzed oxygen incorporation in organic molecules have been developed, however, limited reports talk about such activation of molecular oxygen under metal-free conditions.[3] Alkenes are abundant simple chemical feedstocks and organic molecules, which have been used widely in organic synthesis, and methods for their concise, selective oxidative functionalization are attractive to assemble substituted alcohols[4] and ketones.[2c] A number of transition-metal-catalyzed reactions have been developed for the incorporation of oxygen in alkenes by the activation of molecular oxygen.[2c] For instance, in 2010, Jiang group reported a palladium-catalyzed dihydroxylation of olefins with oxygen as sole oxidant, but 8 atm of molecular oxygen was needed, which limited the utility of this reaction.[5] In 2015, a copper-/cobalt-catalyzed highly selective radical dioxygenation of alkenes was achieved by Lei group.[6] However, a metal-free conditions for this transformation have not been widely studied up to now,[7] and thus the search for alternatives which allows to control the selectivity of the alkene dioxygenation, particularly involving environmental friendly pathway, still remains challenging.

Recently, *N*-hydroxyphthalimide (NHPI) and *N*-hydroxybenzotriazole were used as hydroxylamine reagent via an radical pathway to synthesize α-oxygenated ketones by the Lei,[6] Adimurthy,[7a] Punniyamurthy,[8] Woerpel,[9] and our group.[10] In our previous work, we successfully realized 1-phenylethanol derivatives synthesis using TsOH as catalyst, 4 equiv *tert*-butyl hydroperoxide (TBHP) as the oxidant. Lei group also discovered the same reaction using cobalt as the catalyst.[6] Considering the importance of these phenylethanols, the development of metal-free and acid-free conditions is desirable to avoid the possible contamination of metals and acid to environment. In 2015, Zou group reported an air oxidative radical hydroxysulfurization of styrenes initiated by 0.5 mol % of TBHP.[11] Inspired by this work and in continuation of our efforts on the difunctionalization of alkenes,[12] we envisaged whether 1-phenylethanol derivatives can be obtained via an radical addition, when catalysis loading of TBHP was used under oxygen atmosphere (Scheme 1-b).

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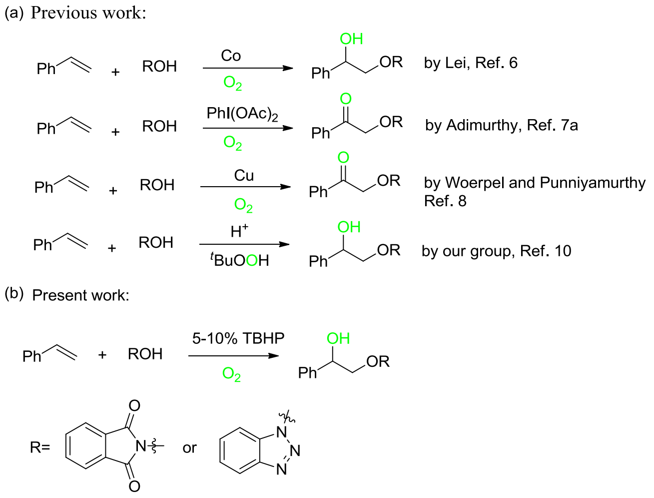
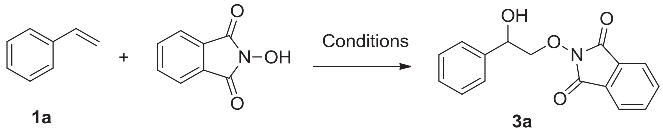


**Scheme 1.** Dioxygenation of alkenes.

## 2. Results/Discussion

In order to screen the suitable reaction condition according to our assumptions, first, omission of the catalyst was carried out, and an 80% yield of product was separated but for a longer reaction time (22 h, Table 1, entry 2). Decreasing the oxidant loading to 2.0 equiv, the yield was decreased to 61% in the air. Interestingly, using 1 atm oxygen as the co-oxidant, 1.2 equiv of TBHP can give an 89% yield (12 h). Then, the loading of TBHP was further decreased to 0.1 equiv, and a 90% yield of **3a** was detected under 1 atm oxygen conditions (entry 9, 24 h). A 95% yield of product was also obtained using 0.05 equiv of TBHP and 1 atm oxygen as the oxidant but for about 48 h (entry 10). Only using oxygen as the oxidant, no target product was observed at room temperature (entry 11), and only 40% yield was obtained at 60 °C, indicating the importance of TBHP. In addition, only using 0.1 equiv of TBHP as the oxidant under argon atmosphere, no reaction occurred. It was noteworthy that using 3.0 equiv of TBHP as oxidant under argon atmosphere, no product was achieved. These phenomena meant the oxygen was very significant for this transformation (entries 13 and 14).

**Table 1**
Initial studies for the reaction of dioxygenation of alkenes[a]



| Entry | Oxidative condition | Solvent | Time | Yield[b] |
|---|---|---|---|---|
| 1 | 4.0 equiv TBHP (5–6 M in decane)+ air | $CH_3CN$ | 76 h | 80% |
| 2 | 4.0 equiv TBHP (5–6 M in decane)+air | DCE | 22 h | 80% |
| 3 | 3.0 equiv TBHP (5–6 M in decane)+air | DCE | 22 h | 93% |
| 4 | 2.0 equiv TBHP (5–6 M in decane)+air | DCE | 22 h | 61% |
| 5 | 2.0 equiv TBHP (5–6 M in decane)+1 atm $O_2$ | DCE | 12 h | 69% |
| 6 | 1.2 equiv TBHP (5–6 M in decane)+1 atm $O_2$ | DCE | 12 h | 89% |
| 7 | 0.4 equiv TBHP (5–6 M in decane)+1 atm $O_2$ | DCE | 24 h | 84% |
| 8 | 0.2 equiv TBHP (5–6 M in decane)+1 atm $O_2$ | DCE | 24 h | 98% |
| **9** | **0.1 equiv. TBHP (5–6 M in decane)+1 atm $O_2$** | **DCE** | **24 h** | **90%** |
| 10 | 0.05 equiv TBHP (5–6 M in decane)+1 atm $O_2$ | DCE | 48 h | 95% |
| 11 | 1 atm $O_2$ | DCE | 48 h | N.R. |
| 12 | 1 atm $O_2$ | DCE | 48 h | 40% [c] |
| 13 | 0.1 equiv TBHP (5–6 M in decane)+1 atm Ar | DCE | 24 h | N.R. |
| 14 | 3.0 equiv TBHP (5–6 M in decane)+1 atm Ar | DCE | 24 h | N.R. |

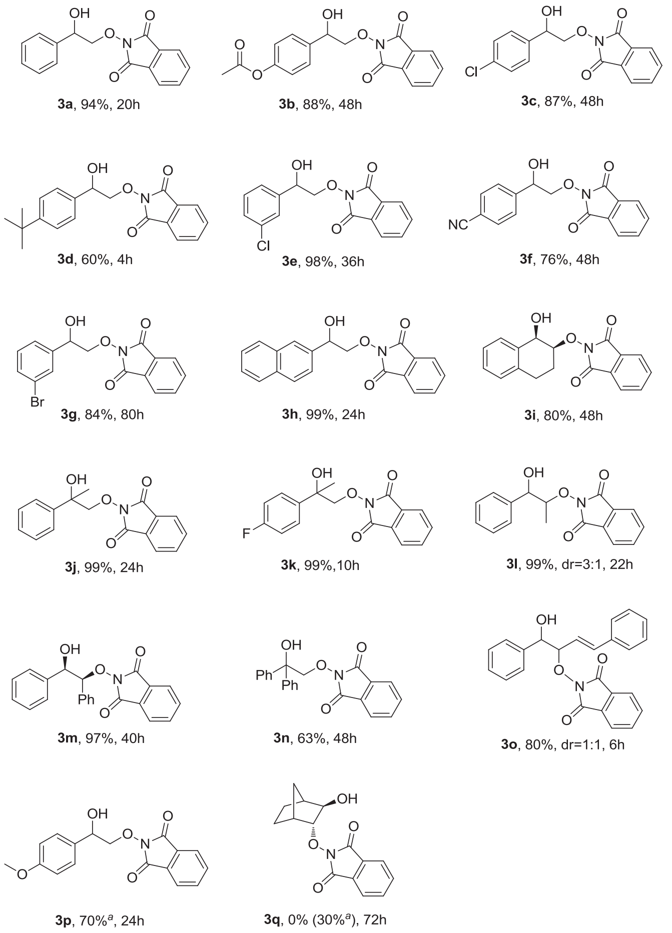
The best reaction conditions are indicated in bold.

[a] Reaction conditions: **1a** (2.0 equiv, 0.6 mmol), NHPI (0.3 mmol), oxidant, and solvent (3.0 mL), at room temperature.

[b] Isolated yield.

[c] The reaction was carried out at 60 °C.

Under the optimized conditions (Table 1, entry 9), the alkene substrate scope was proved to be quite general with activated terminal alkenes and disubstituted alkenes participating in the dioxygenation reaction effectively (Scheme 2). A wide range of substrates and functional groups are tolerated including fluoro, chloro, bromo, methoxy, cyano, tertiary butyl and ester substituents at the different positions of styrenes. Cyclic alkenes such as 1,2-dihydronaphthalene can provide the dioxygenation product **3i** in 80% yield. $\alpha$-Methylstyrene and corresponding substituents can participate in this transformation in a short time (**3j** and **3k**). Notably, 1,1-diphenylethylene proved to be an effective alkene substrate, yielding tertiary alcohol **3n** in 63% yield. Phenyl substituted conjugated diene such as (1*E*,3*E*)-1,4-diphenylbuta-1,3-diene was tolerated to deliver a isomer **3o** (dr=1:1) in a high yield only for 6 h. Unactivated alkenes such as norbornene can also produce the target product **3q**, and only the major isomer was separated, but 3.0 equiv of TBHP was needed, and the same for the synthesis of product **3p**. In addition, *N*-hydroxybenzotriazole was also suitable for this transformation, and the corresponding products **4a**–**e** were obtained in good to high yields under optimized conditions (Scheme 3).



**Scheme 2.** The scope of the activated alkenes. [a]3.0 equiv of TBHP was added in the systems.