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Copper-catalyzed regioselective allylic oxidation of olefins via C–H activation

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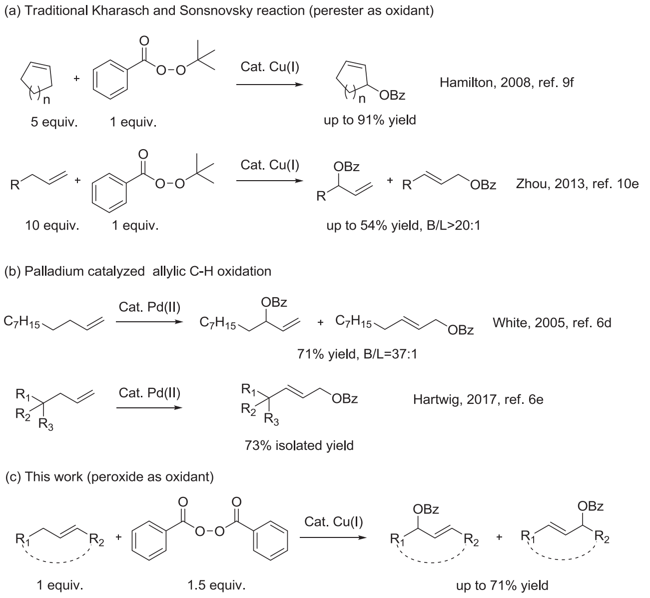
ABSTRACT

A regioselective oxidation of allylic C–H bond to C–O bond catalyzed by copper (I) was developed with diacyl peroxides as oxidants. The oxidation of allylic C–H bond was accomplished with good yield and regioselectivity under mild reaction conditions. This method has a broad substrate scope including cyclic olefins, terminal and internal acyclic olefins and allyl benzene compounds. The reaction proceeds by a radical mechanism as suggested by spin trapping experiments.

The direct functionalization of C–H bond is a key task in modern organic chemistry.[1] Allylic oxidation[2] of olefins is a typical C–H bond functionalization reaction which could directly convert C–H bond into diverse functional groups.[3] Allylic esters[4] are important intermediates which can be converted into allylic alcohols[5] and provide facile access to a variety of valuable compounds.[6] The first copper-catalyzed allylic oxidation[7] of olefins with perester was published by Kharasch and Sosnovsky in 1959.[8] As a useful tool for direct C–H bond functionalization at the allylic position of olefins, Kharasch-Sosnovsky reaction has been further developed by many researchers.[9] The results for cyclic olefins[9f] are excellent (Scheme 1a).[10] However, the yields for acyclic olefins are unsatisfying.[10] The best yield for allylic C–H oxidation was 54% using 10 equivalents of acyclic olefin (Scheme 1a).[10e] In 2005, White and coworkers developed a palladium-catalyzed allylic oxidation system affording branched products with moderate yield (Scheme 1b).[6d] Very recently, Hartwig and coworkers reported oxidation of hindered alkenes to form linear allylic esters (Scheme 1b).[6e] Herein, we report a copper-catalyzed regioselective allylic oxidation of olefins with high yield and broad substrate scope including cyclic olefins, terminal and internal acyclic olefins and allyl benzene compounds (Scheme 1c).



Scheme 1. Allylic C–H oxidation reactions: (a) Examples of traditional Kharasch and Sosnovsky reactions. (b) Examples of palladium catalyzed allylic C–H oxidation reactions. (c) This work.

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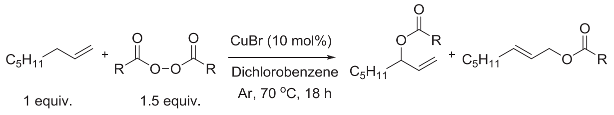
We initiated our studies by adopting benzoyl peroxide as the oxidant in the presence of various catalysts for the oxidation of 1-octene and the results are summarized in Table 1. During preliminary catalyst screening, CuBr and $CuBr_2$ were found effective in this system, gave the desired products in 61% and 58% yield, respectively (entries 5 and 6). It was found that 70 °C was the best reaction temperature when different temperatures were investigated using CuBr as catalyst (entries 6–8). At 70 °C using CuBr as the catalyst, the ratio of olefin: oxidant: catalyst was investigated. To our delight, when the ratio of olefin: oxidant: catalyst was 1:1.5:0.1, the reaction gave 71% yield and good regioselectivity (B/L is 8.2:1) (entry 12).

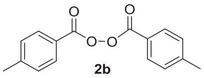
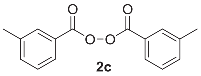
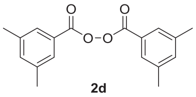
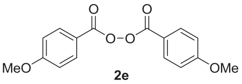
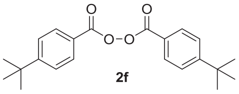
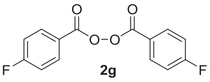
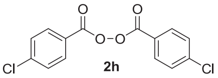
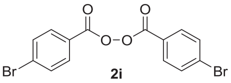
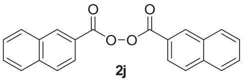
Under the optimized reaction conditions, the scope of oxidants was evaluated with 1-octene (Table 2). In general, the oxidants with the different substituents on the phenyl group can be transformed into the desired products with moderate yields and regioselectivities. The oxidants having 3-methyl and 3,5-dimethyl substituents gave 69% and 62% yields, respectively (entries 2 and 3). The oxidants with 4-fluoro and 4-chloro groups delivered the corresponding products in 62% and 72% yields, respectively (entries 6 and 7). Interestingly, sterically bulky 2-naphthoic peroxyanhydride (**2j**) can also be used as an oxidant for the reaction, although the yield and regioselectivity were lower than those of benzoyl peroxides (entry 9).

We next examined the scope of olefins (Table 3). A range of acyclic terminal olefins reacted smoothly and afforded the corresponding products in moderate to good yields (entries 1–5). Notably, TBS group is tolerated under the reaction condition. Moreover, the cyclic olefins, such as cyclohexene and 1,3-cyclooctadiene delivered allylic oxidation products in 71% and 57% yields, respectively (entries 6 and 7). 1,1-Disubstituted olefin **5h** 1-methylenecyclohexane (entry 8) afforded the products in 50% yield with moderate regioselectivity (**6h**/**7h** = 3.7:1). It is worth noting that the internal olefins worked well in this system. (*E*)-3-hexene gave 71% yield and 1:1 mixture of two phenyl esters was formed (entry 9). The substrate with two terminal alkenes (1,7-octadiene, entry 10) was studied and gave mono-fuctionalization products in moderate yield (53%, **6j**/**7j** = 5:1). Methyl 10-undecenoate (**5k**) afforded the desired products in 64% yield with B/L = 8.7:1. Finally, (but-3-enyloxy)benzene (**5l**) and (hept-6-enyloxy)benzene (**5m**) were

Table 2
Scope of benzoyl peroxides.[a]

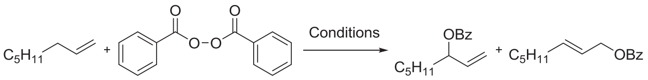


1 2 3 4

Entry	Benzoyl peroxide	Yield of (**3**+**4**)[b] (%)	**3**/**4**[c]
1	 **2b**	51	5.7:1
2	 **2c**	69	8.3:1
3	 **2d**	62	4.6:1
4	 **2e**	46	1.5:1
5	 **2f**	51	4.2:1
6	 **2g**	62	4.6:1
7	 **2h**	72	7:1
8	 **2i**	49	4.6:1
9	 **2j**	32	4.6:1

[a] The reaction was conducted on a 0.5 mmol scale in 4 mL of 1,2-dichlorobenzene under argon atmosphere.
[b] Isolated yield.
[c] Determined by ^{1}H NMR.

Table 1
Reaction conditions optimization.[a]



1 2a 3a 4a

Entry	Catalyst (mol%)	Temp. (°C)	Olefin/Oxidant	Yield (%)[b]	**3a**/**4a**[c]
1	CuTc (10)	70	1:1	7	0.6:1
2	CuOTf (10)	70	1:1	ND	
3	$NiCl_2$ (10)	70	1:1	Trace	
4	$Pd(TFA)_2$ (10)	70	1:1	13	0.6:1
5	$CuBr_2$ (10)	70	1:1	58	8.0:1
6	CuBr (10)	70	1:1	61	7.3:1
7	CuBr (10)	60	1:1	38	7.2:1
8	CuBr (10)	80	1:1	46	7.1:1
9	CuBr (5)	70	1:1	60	6.5:1
10	CuBr (15)	70	1:1	55	8.4:1
12	CuBr (10)	70	1:1.5	71[d]	8.2:1
13	None	70	1:1.5	ND	

[a] The reaction was conducted on a 0.5 mmol scale in 4 mL 1,2-diclorobenzene under argon atmosphere.
[b] GC yield (1,4-dimethoxybenzene as internal standard).
[c] Determined by GC.
[d] Isolated yield.