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Indium(III) chloride-catalyzed oxidative cleavage of carbon–carbon multiple bonds by *tert*-butyl hydroperoxide in water—a safer alternative to ozonolysis

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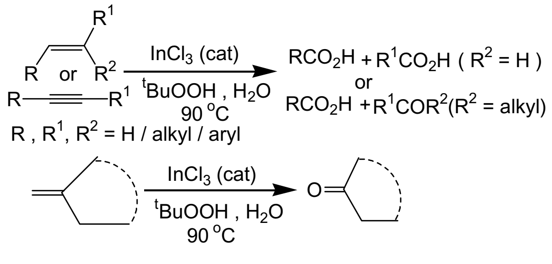
Abstract

An efficient and general method for the oxidative cleavage of alkenes and alkynes using *tert*-butyl hydroperoxide and indium(III) chloride as catalyst in water to give the corresponding carboxylic acids or ketones has been achieved. The reaction conditions are compatible with sensitive moieties such as peptide bonds, *tert*-butyl carboxylic esters and *N*-Boc-protected tryptophan. The catalyst could be recycled.

Keywords: Oxidative cleavage; Alkenes; *tert*-Butyl hydroperoxide; Indium(III) chloride; Water

The oxidative cleavage of alkenes to carboxylic acids and ketones is a very useful reaction in organic synthesis.[1] The commonly used reagents for this transformation include ozone and several metal oxides such as OsO_4 and RuO_4 in combination with a co-oxidant like $NaIO_4$ and Oxone.[1,2] Although ozonolysis is a very reliable method, a major issue is the concern for safety; serious or fatal accidents may occur.[3] In addition, ozone gas is highly toxic and damaging to human health and its generation requires special instrumentation. On the other hand OsO_4[4] because of its high volatility and toxicity[4c] is not environmentally acceptable and thus restricts its use for large-scale applications in industry. Ruthenium compounds,[5] being very expensive, are also disadvantaged. An efficient and green protocol for the oxidation of alkenes to the corresponding carboxylic acids using hydrogen peroxide and Na_2WO_4 as a catalyst has been demonstrated by Noyori et al.[6e,g] Other procedures involving relatively less toxic reagents[6] such as titanium based catalysts[6a] and heteropolyacids on oxide supports[6b] have been reported. However, they lack general applicability and do not provide satisfactory yields. Therefore, a simple, efficient and safe procedure for oxidative cleavage of olefins, which can excel ozonolysis, is highly desirable. Recently, a gold(I)-catalyzed oxidative cleavage of alkenes to carbonyl compounds using *tert*-butyl hydroperoxide as oxidant and neocuproine as ligand was reported.[6f] This has led us to report our results on the oxidative cleavage of alkenes and alkynes with *t*-BuOOH catalyzed by $InCl_3$ in H_2O in the absence of any ligand (Scheme 1).



Scheme 1.

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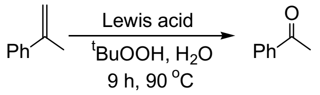
The experimental procedure is very simple.[7] A mixture of alkene/alkyne, *t*-BuOOH and $InCl_3$ in water was heated at 90 °C for a certain period of time (TLC). Standard work up provided the product. The aqueous solution of $InCl_3$ and *t*-BuOH left after work up was recycled for subsequent reactions without any appreciable loss of efficiency. Several experiments were carried out using various reagents and catalysts to optimize the reaction conditions. When *t*-BuOOH was replaced by H_2O_2 the yields of products did not rise above 25%. $InCl_3$ gave the best results of the several Lewis acid catalysts investigated (Table 1).

Several diversely substituted alkenes underwent clean cleavage using this procedure to furnish the corresponding products. The results are summarized in Table 2. The open chain mono- substituted (Table 2, entries 1–5) and 1,2-disubstituted (Table 2, entries 6–7) olefins were oxidized to the corresponding carboxylic acids, while the 1,1-disubstituted substrate (Table 2, entry 11) provided the corresponding ketone. The unsubstituted cyclic olefins, cyclohexene (Table 2, entry 8) and cyclooctene (Table 2, entry 10) produced adipic and suberic acids, respectively, in very high yields. These carboxylic acids were obtained as crystals after work up and did not require any further purification. These reactions were also scaled up to multigram quantities without any difficulty. Both adipic and suberic acids are industrially very important[6e] and this procedure may serve as an alternative to existing methods.[6] The substituted cyclic olefin, 1-methylcyclohexene (Table 2, entry 9), upon oxidative cleavage, furnished the corresponding keto acid. The exocyclic olefins (entries 12 and 13) were cleaved to the corresponding ketones very efficiently. A few complex olefins containing peptide bonds together with *t*-butyl ester groups and Boc-protected tryptophan moiety (Table 2, entries 14–17) underwent cleavage to the corresponding carboxylic acids without affecting these sensitive functionalities. These substituted peptide carboxylic acids are highly useful compounds and are not easy to prepare using standard methods.[8] The optically active peptides (Table 2, entries 15–17) retained their optical purity under the reaction conditions. The aromatic as well as aliphatic alkynes (Table 2, entries 18–21) were also cleaved to produce the corresponding carboxylic acids without the formation of α-diketones[9a] or α,α′-dioxygenated derivatives.[9b]

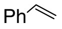
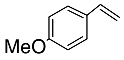
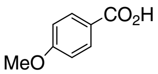
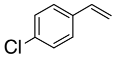
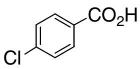
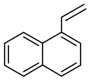
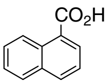
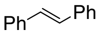
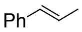
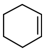
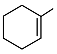
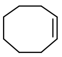
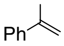
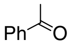
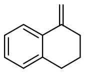
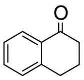
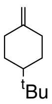
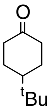
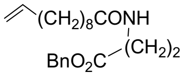
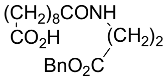
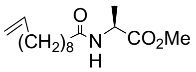
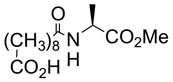
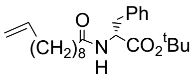
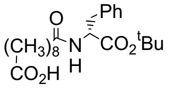
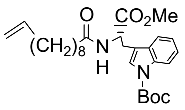
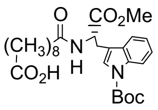
Table 1
Results of the cleavage reaction using different Lewis acids



Lewis acid	Yield[a] (%)	Lewis acid	Yield[a] (%)
$CuCl_2$	38	$ZnCl_2$	39
$CeCl_3$	37	$TiCl_4$	55
$FeCl_3$	42	$InCl_3$	84

[a] Yields calculated from ^{1}H NMR spectra of the crude products.

Table 2
Oxidative cleavage of alkenes and alkynes

Entry	Substrate	Product	Time (h)	Yield[a] (%)	Ref.
1		$PhCO_2H$	8	88	4c
2			8.5	78	6e
3			8.6	75	6e
4			9	81	11
5	$CH_3(CH_2)_5CH{=}CH_2$	$CH_3(CH_2)_5COOH$	8	81	5d
6		$PhCO_2H$	8.5	83	4c
7		$PhCO_2H$	8	85	4c
8		$HO_2C(CH_2)_4CO_2H$	9	92	5d
9		$CH_3CO(CH_2)_4CO_2H$	8.2	84	6b
10		$HOOC(CH_2)_6CO_2H$	8	94	5d
11			8	84	4c
12			8	80	11
13			8.2	68	6e
14			9	72	—
15			8.5	78	—
16			10	68	—
17			10	62	—
18	Ph–C≡CH	$PhCO_2H$	9	76	4c
19	$CH_3(CH_2)_3C{\equiv}CH$	$CH_3(CH_2)_3CO_2H$	12	68	5d
20	Ph–C≡C–Ph	$PhCO_2H$	11	71	5d
21	Et–C≡C–Et	$EtCO_2H$	12	64	5d

[a] Isolated yields of pure products (^{1}H and ^{13}C NMR).

The reactions, are in general very clean and high yielding and no side products were isolated. The majority of the products were obtained in high purities (>98%) after work up and a few were purified by crystallization or column chromatography. When the reaction was carried out