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Catalysis Today 117 (2006) 138–140
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Oxidative cleavage of C–C bond of 2-phenylpropionaldehyde using molecular oxygen

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Abstract

Oxidative C–C bond cleavage between carbonyl carbon and vicinal carbon of 2-phenylpropionaldehyde to give acetophenone using 1 atm molecular oxygen as oxidant was catalyzed by Ce(IV), V(IV) and Brønsted acids. Among the examined catalysts, sulfuric acid exhibited the highest activity and gave the product in 99% yield.

Keywords: Oxidation; Molecular oxygen; C–C bond cleavage; Aldehydes; Metal salt catalysts; Brønsted acid catalysts

1. Introduction

Catalytic oxidation is a fundamental reaction in fine chemical synthesis as well as petroleum-based feedstock transformations. During the recent years, there is a considerable demands to replace the oxidation methods using stoichiometric amounts of heavy metal reagents or moisture-sensitive expensive oxidants with more environmentally benign, economical ones [1]. In this regard, molecular oxygen (O_2) is obviously an ideal oxidant to perform the transformation. Therefore, development of catalysts, which can employ molecular oxygen has been extensively studied especially in alcohol oxidation to carbonyl compounds in the field of homogeneous catalysis [2]. On the other hand, oxidative cleavage of carbon–carbon bond is also an important reaction in organic synthesis. Very recently, during the course of the study of asymmetric hydrolysis and alcoholysis [3], we found a copper-catalyzed carbon–carbon double bond cleavage of aromatic enol ethers to give ketones using molecular oxygen as oxidant [4]. Generally, this transformation requires activated oxygen, such as ozone or singlet oxygen, which is generated by the use of a special equipment, such as an ozonizer or a photochemical apparatus. Nevertheless, in our copper-catalyzed system, unactivated 1 atm O_2 is only necessary to perform it (Scheme 1).

The C=C cleavage reaction is accelerated in the presence of 5 equiv of H_2O, but the water brought about hydrolysis reaction into **3** under argon atmosphere. The selectivity of **2/3** was completely controlled by the surrounding gas. The oxidative cleavage seems to involve radical cation intermediate generated by Cu(II) via one-electron oxidation, followed by the formation of dioxetane. An alternative route, oxidative cleavage of the aldehyde **3** to the ketone **2** (via enolization) is unlikely because the conversion of **3** into **2** under the condition found to be very slow (5% after 52 h) [4].

Next our interest turned into this aldehyde C–C bond cleavage reaction. Although oxidative C–C bond cleavage between carbonyl carbon and vicinal carbon of cycloalkanone derivatives with stoichiometric metal reagents are known [5], few report have been made on aldehydes. In addition, Baeyer–Villiger oxidation of **3** gives formate and carboxylic acid as products but does not **2** [6]. In this paper, we disclose catalytic C–C bond cleavage of the aldehyde **3** using molecular oxygen as oxidant to give the ketone **2** in high yield.

2. Results and discussion

2.1. Oxidative C–C bond cleavage of aldehyde 3

We have tested several metals and acids as catalyst for the oxidative C–C bond cleavage of **3**. The results are shown in Table 1. Using $CuCl_2$, which is the best catalyst for the reaction

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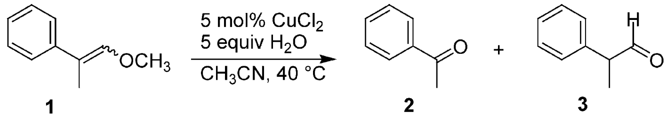
doi:10.1016/j.cattod.2006.05.020



atmosphere	time, h	% yield 2	% yield 3
1 atm O_2	1	86	0
1 atm Ar	24	0	>99

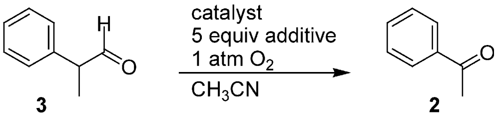
Scheme 1.

of enol ether **1**, yield of **2** were less than 5% at 40 °C (entries 1 and 2) and 13% at 70 °C (entry 3). Cerium and vanadium salts gave better results (entries 4–7). A reaction at 40 °C with $Ce(SO_4)_2{\cdot}4H_2O$ as catalyst gave 44% of **2** at 68 h (entry 4), and the yield was improved to 82% at 70 °C (entry 6). Though the activity was slightly low, $VO(acac)_2$ also gave **2** in favorable yield (entry 7). Interestingly, Brønsted acids catalyzed the reaction effectively (entries 8–17). Sulfuric acid catalyst (10 mol%) gave **2** in 92% yield and the addition of 5 equiv of H_2O improved the yield up to 99%. The reaction under Ar showed almost no conversion of **3** (entry 10), which suggest O_2 is essential in this reaction. The reactions with lower catalyst loadings of sulfuric acid were examined (entries 11–13). It was found that 5 and 2 mol% catalyst afforded the product in comparable yield (99 and 96%), but 1 mol% catalyst resulted in a lower yield (77%). Other homogeneous Brønsted acid catalysts, such as *p*-toluenesulfonic acid (10 mol%) and hydrochloric acid (9 mol%; added as aqueous 1 M HCl resulted in the addition of 5 equiv of H_2O as additive) showed slightly lower activities than sulfuric acid (entries 14 and 15). Solid acid catalysts also exhibited comparable catalytic activity (entries 16 and 17). The activity of Amberlist-15 was rather higher than Montmorillonite K10.

In our previous work, Brønsted acids also catalyzed the C═C cleavage reaction of **1**, however, the activity was rather lower than $CuCl_2$. In addition, considerable amount of hydrolyzed product **3** was formed (at 40 °C) [4]. Control experiments suggest autooxidation without any catalyst under the condition of present work (at 70 °C) is not negligible (entries 18 and 19). Since C═C cleavage autooxidation of styrene derivatives is common process [7], the present reaction seems to proceed through the enol form. We expect Brønsted acids act as a catalyst for enolization. The effect of additive (H_2O, CH_3OH and t-C_4H_9OH), whose role is considered to accelerate the decomposition of dioxetane intermediate into carbonyl compounds [8], appeared to be smaller compared to the C═C cleavage reaction of **1** [4]. Measurement of gas uptake under the condition of entry 9 (1 mmol scale, 3 h, 60% convn) revealed reasonable consumption of molecular oxygen: ca. 15 mL, 0.6 mmol of O_2 was consumed.

The C–C cleavage reaction was found to be applicable to 2,2-diphenylacetaldehyde to give benzophenone in high

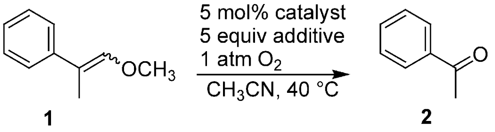
Table 1
Oxidative cleavage of C–C bond of **3** into **2**



Entry	Catalyst	Cat. (mol%)	Additive	*T* (°C)	Time (h)	Yield (%)[a]
1	$CuCl_2$	5	H_2O	40	52	5
2	$CuCl_2$	5	CH_3OH	40	18	3
3	$CuCl_2$	5	H_2O	70	18	13
4	$Ce(SO_4)_2{\cdot}4H_2O$	5	t-C_4H_9OH	40	18	31
					68	44
5	$Ce(SO_4)_2{\cdot}4H_2O$	5	t-C_4H_9OH	70	19	67
6	$Ce(SO_4)_2{\cdot}4H_2O$	5	H_2O	70	22	82
7	$VO(acac)_2$[b]	5	H_2O	70	24	69
					43	82
8	H_2SO_4	10	None	70	14	92
9	H_2SO_4	10	H_2O	70	15	99
10[c]	H_2SO_4	10	H_2O	70	14	2
11	H_2SO_4	5	H_2O	70	14	99
12	H_2SO_4	2	H_2O	70	14	96
13	H_2SO_4	1	H_2O	70	14	77
14	p-$CH_3C_6H_4SO_3H{\cdot}H_2O$	10	H_2O	70	14	74
15	HCl	9	H_2O	70	14	65
16	Amberlist-15	10[d]	H_2O	70	14	87
17	Montmorillonite K10	10[e]	H_2O	70	14	46
18	None		H_2O	70	39	34
19	None		None	70	14	17

[a] GC yield.
[b] $VO(acac)_2$ = vanadium(IV) bis(acetylacetonate)oxide.
[c] Under 1 atm Ar.
[d] Catalyst loadings were calculated based on 4.7 mmol/g [10].
[e] Catalyst loadings were estimated based on 0.5 mmol/g [11].

Table 2
Oxidative cleavage of C═C bond of **1** into **2**



Entry	Catalyst	Additive	Time (h)	Yield (%)[a]
1	None	H_2O	24	0
2[b]	$CuCl_2$	H_2O	24	0[c]
3	$CuCl_2$	H_2O	1	86
4	$Ce(SO_4)_2{\cdot}4H_2O$	H_2O	1	26
5	$Ce(SO_4)_2{\cdot}4H_2O$	CH_3OH	1	34
			41	44
6	$Ce(SO_4)_2{\cdot}4H_2O$	t-C_4H_9OH	1	44
			17	81
7	$VO(acac)_2$[d]	H_2O	6	33
			52	87
8	$VO(acac)_2$[d]	CH_3OH	29	56
9	H_2SO_4	H_2O	1	Trace[e]
			18	38[f]
10[b]	H_2SO_4	H_2O	18	Trace[g]

[a] GC yield.
[b] Under 1 atm Ar atmosphere.
[c] The aldehyde **3** was obtained in >99% yield.
[d] $VO(acac)_2$ = vanadium(IV) bis(acetylacetonate)oxide.
[e] The aldehyde **3** was obtained in 49% yield.
[f] The aldehyde **3** was obtained in 43% yield.
[g] The aldehyde **3** was obtained in 95% yield.

yields (up to 97%). However, control experiments elucidated that the rate of background reaction (autooxidation without catalyst) is larger than **3** [9], which is close to the rate observed in the presence of the catalysts. Thus, it is uncertain whether the metal salts and Brønsted acids accelerate the reaction or not in this substrate. We will make a further investigation on mechanism and substrate scope of the reaction in near future.

*2.2. Oxidative C=C bond cleavage of enol ether **1***

The study of oxidative C–C bond cleavage of **3** disclosed Ce(IV) and V(IV) salt were effective catalyst for the reaction. Thus we examined these catalyst for the oxidative C=C bond cleavage of enol ether **1** (Table 2). The results of control experiments without the catalyst or molecular oxygen (entries 1 and 2) and $CuCl_2$ catalyzed reaction under 1 atm oxygen (entry 3) are picked up from the previous report [4] (see also Scheme 1). Although the catalytic activity found to be lower than $CuCl_2$, the examined catalysts $Ce(SO_4)_2 \cdot 4H_2O$ (entries 4–6) and $VO(acac)_2$ (entries 7 and 8) gave **2** as major product (up to 87%) associated with trace amount of **3**. Under the condition of entry 6 (at 40 °C), **3** was gradually converted to **2** (Table 1, entry 4), therefore the pathway through **3** by hydrolysis cannot be excluded completely. As described in the previous paper [4], employing *p*-toluenesulfonic acid as a catalyst, Brønsted acids were not suitable for this direct C=C bond cleavage reaction, because those brought about hydrolysis reaction into **3** considerably. Indeed, the reaction under 1 atm O_2 with 5 mol% sulfuric acid gave **3** in 49% yield with trace amount of **2** at 1 h. Then, the amount of **3** was decreased to 43% accompanying the formation of **2** in 38% at 18 h (Table 2, entry 9). The result clearly suggests indirect formation of **2** from **3**. In fact, the reaction under 1 atm Ar atmosphere gave only **3** in 95% yield.

3. Summary

Oxidative C–C bond cleavage of the aldehyde **2** to the ketone **3** using molecular oxygen was achieved by the use of Ce(IV), V(IV) and Brønsted acids as catalyst. Especially, sulfuric acid exhibited the highest activity and gave the product almost quantitatively.

4. Experimental

*4.1. Typical procedure of the oxidative C–C bond cleavage of aldehyde **3** (Table 1, entry 9)*

A 20 mL Schlenck flask was charged with **3** (134 mg, 1.00 mmol), diglyme (internal standard for GC analysis, 33.8 mg, 0.252 mmol), H_2O (90.1 mg, 5.00 mmol), 50 mM acetonitrile solution of H_2SO_4 (2.0 mL, 0.100 mmol) and then the mixture was stirred at 70 °C under 1 atm O_2 for 15 h. The yield of the product **2** was determined as 99% by GC analysis (Agilent HP-1 column, length 30 m, 0.32 mm i.d.).

Acknowledgment

This work was supported by Grant-in-Aid for Scientific Research on Priority Areas (No. 16033204, Reaction Control of Dynamic Complexes) from Ministry of Education, Culture, Sports, Science and Technology, Japan.

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