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Vanadium-catalyzed chlorination under molecular oxygen

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ABSTRACT

A catalytic chlorination of ketones was performed by using a vanadium catalyst in the presence of Bu_4NI and $AlCl_3$ under atmospheric molecular oxygen. This catalytic chlorination could be applied to the chlorination of alkenes to give the corresponding *vic*-dichlorides. $AlCl_3$ was found to serve as both a Lewis acid and a chloride source to induce the facile chlorination. A combination of Bu_4NI and AlI_3 in the presence of a vanadium catalyst under atmospheric molecular oxygen induced the iodination of ketones.

1. Introduction

Halogenation reaction is one of the most important reactions in the field of organic synthesis, providing versatile precursors and substrates in a variety of coupling reactions. Haloperoxidases are enzymes that catalyze the oxidation of halide ions in the presence of H_2O_2 as an oxidant [1–5]. Haloperoxidases have attracted extensive interest due to their capability to halogenate a range of organic compounds. Various bromination reactions mimicking a catalytic activity of vanadium bromoperoxidase [6], which is a naturally occurring enzyme found in marine algae, have been reported [7–17]. Tungsten [18] or molybdenum [19] complexes have been also demonstrated to serve as a bromination catalyst in the presence of stoichiometric hydrogen peroxide. However, these oxidative bromination systems require a stoichiometric amount of a strong oxidant to generate the bromonium-like species. Some catalytic oxidative bromination reactions with molecular oxygen as a terminal oxidant instead of a strong oxidant have been achieved [20–24]. Recently, we have performed the combination of a vanadium catalyst, a bromide salt, and a Brønsted acid or a Lewis acid in the presence of molecular oxygen induces catalytic oxidative bromination of various arenes, alkenes, alkynes, and ketones without the usage of a strong oxidant [25–27]. These findings prompted us to develop an efficient halogenation method. In this paper, we report the catalytic chlorination reaction of ketones and alkenes without a need of a strong oxidant by using a vanadium catalyst in the presence of Bu_4NI and $AlCl_3$ with molecular oxygen as a terminal oxidant.

2. Experimental

2.1. General materials and experimental procedures

All reagents and solvents were purchased from commercial sources and were further purified by the standard methods, if necessary. ^1H NMR spectra were recorded in $CDCl_3$ on a JNM-ECS 400 (400 MHz) spectrometer. Chemical shifts were determined by using of tetramethylsilane as an internal standard.

2.2. General procedure for vanadium-catalyzed chlorination under atmospheric molecular oxygen

In a 5 mL three-necked flask, Bu_4NI (111 mg, 0.3 mmol), $AlCl_3$ (40 mg, 0.3 mmol), and $VO(O^iPr)_3$ (15 μL, 0.063 mmol) were placed. The flask was evacuated and backfilled with molecular oxygen. To the mixture, acetonitrile (1 mL) and a substrate (0.25 mmol) were added. The mixture was stirred at 80 °C under atmospheric molecular oxygen, followed by treatment with 1:1 mixture of saturated $Na_2S_2O_3$ aqueous solution and saturated $NaHCO_3$ aqueous solution, and extraction with ether. The organic layer was dried over $MgSO_4$, filtered, and evaporated. 1,3,5-Trimethoxybenzene or 1,2,4,5-tetramethylbenzene was added as an internal standard, and ^1H NMR analysis was performed to determine an NMR yield. Spectral data of the products were identical with those of commercially available and authentic samples.

2.3. General procedure for vanadium-catalyzed iodination under atmospheric molecular oxygen

In a 5 mL three-necked flask, Bu_4NI (111 mg, 0.3 mmol), AlI_3 (122 mg, 0.3 mmol), and NH_4VO_3 (2.9 mg, 0.025 mmol) were placed. The flask was evacuated and backfilled with molecular oxygen. To the mixture, acetonitrile (1 mL) and a substrate (0.25 mmol) were added.

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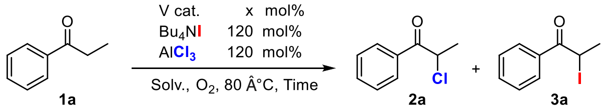
0162-0134/

Table 1
Catalytic chlorination of propiophenone by using vanadium catalyst/$Bu_4NI/AlCl_3/O_2$ system.

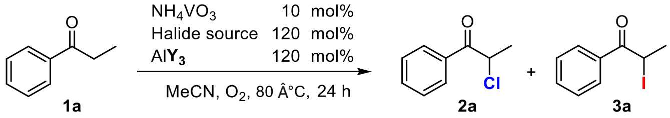


Entry	V cat.	V cat. x (mol%)	Solv.	Time (h)	NMR yield (%)	
					2a	3a
1	NH_4VO_3	10	MeCN	24	60	0
2	–	–	MeCN	24	0	0
3[a]	NH_4VO_3	10	MeCN	24	7	0
4	NH_4VO_3	10	DME[b]	24	31	0
5	NH_4VO_3	10	CPME[c]	24	36	0
6[d]	NH_4VO_3	10	ether	24	0	0
7[e]	NH_4VO_3	10	MeCN	24	64	0
8	NH_4VO_3	20	MeCN	24	77	0
9	$VO(O^iPr)_3$	20	MeCN	24	90	3
10	$VO(acac)_2$	20	MeCN	24	69	9
11	$VOCl_3$	20	MeCN	24	70	0
12	NH_4VO_3	20	MeCN	36	98	0

[a] Ar atmosphere.
[b] 1,2-Dimethoxyethane.
[c] Cyclopentyl methyl ether.
[d] Room temperature.
[e] 200 mol% of Bu_4NI and $AlCl_3$ were used.

The mixture was stirred at 80 °C under atmospheric molecular oxygen, followed by treatment with 1:1 mixture of saturated $Na_2S_2O_3$ aqueous solution and saturated $NaHCO_3$ aqueous solution, and extraction with ether. The organic layer was dried over $MgSO_4$, filtered, and evaporated. 1,2,4,5-Tetramethylbenzene was added as an internal standard, and ^1H NMR analysis was performed to determine an NMR yield. Spectral data of the products were identical with those of commercially available and authentic samples.

Table 2
The effect of a halide source and aluminium halide in catalytic halogenation of propiophenone by using cat. NH_4VO_3.

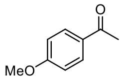
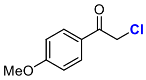
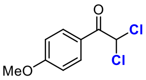
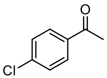
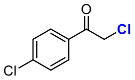
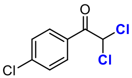
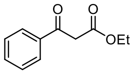
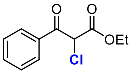
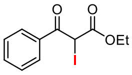


Entry	Halide source	AlY_3	NMR yield (%)	
			2a	3a
1	Bu_4NI	$AlCl_3$	60	0
2	KI	$AlCl_3$	7	9
3	Bu_4NCl	AlI_3	58	16
4	Bu_4NCl	$AlCl_3$	5	0
5	Bu_4NI	AlI_3	0	33[a]
6[b]	Bu_4NI	AlI_3	0	49[a]

[a] Benzoic acid was obtained as a by-product.
[b] Reaction time: 48 h.

Table 3
Catalytic chlorination of ketones by using cat. $NH_4VO_3/Bu_4NI/AlCl_3/O_2$ system.

$$\text{Substrate} \xrightarrow[\text{MeCN, O}_2\text{, 80 °C, Time}]{\substack{NH_4VO_3 \ \ 20 \ \ \text{mol\%} \\ Bu_4NI \ \ 120 \ \ \text{mol\%} \\ AlCl_3 \ \ 120 \ \ \text{mol\%}}} \text{Product}$$

Entry	Substrate	Time (h)	Products NMR yield (%)	
1	 1b	36	 2b 49	 2bb 3
2		48	53	4
3	 1c	36	 2c 55	 2cc 3
4	 1d	24	 2d 63	 3d trace

2.4. Gram-scale reaction of propiophenone

In a 50 mL three-necked flask, Bu_4NI (4.43 g, 12 mmol), $AlCl_3$ (1.60 g, 12 mmol), and $VO(O^iPr)_3$ (472 μL, 2.0 mmol) were placed. The flask was evacuated and backfilled with molecular oxygen. To the mixture, acetonitrile (30 mL) and propiophenone (1.33 mL, 10 mmol) were added. The mixture was stirred at 80 °C under atmospheric molecular oxygen for 24 h, followed by treatment with 1:1 mixture of saturated $Na_2S_2O_3$ aqueous solution and saturated $NaHCO_3$ aqueous solution, and extraction with ether. The organic layer was dried over $MgSO_4$, filtered, and evaporated. The residue was chromatographed on a silica gel column eluting with hexane and dichloromethane to give 1.32 g (78% yield) of 2-chloro-1-phenylpropan-1-one.

3. Results and discussion

α-Halocarbonyl compounds are regarded as important precursors for various transformations employed in organic and pharmaceutical syntheses. The chlorination reaction of propiophenone in the presence of 10 mol% of NH_4VO_3, 120 mol% of Bu_4NI, and 120 mol% of $AlCl_3$ as a Lewis acid in MeCN at 80 °C for 24 h under atmospheric molecular oxygen was performed (Table 1, entry 1). The chlorination reaction proceeded well to afford the α-chlorocarbonyl compound **2a** in 60% yield. No chlorination product was obtained in the absence of NH_4VO_3 (entry 2). This catalytic chlorination reaction was not effectively performed under argon atmosphere (entry 3). The chlorination reaction in other solvents, such as dimethoxyethane (DME), cyclopentyl methyl ether (CPME), and ether resulted in a slightly decreased yield (entries 4–6). The use of 200 mol% of Bu_4NI, and 200 mol% of $AlCl_3$ did not show a drastically enhanced yield (entry 7). With an increased amount (20 mol%) of NH_4VO_3, the α-chlorocarbonyl derivative **2a** was produced in a good yield (entry 8). Highly active catalysis was observed with $VO(O^iPr)_3$ (entry 9) although $VO(acac)_2$ and $VOCl_3$ exhibited a similar catalytic activity (entries 10–11). The α-chlorocarbonyl compound **2a** was obtained quantitatively by extending the reaction time (entry 12).