Aerobic oxidation of secondary alcohols using NHPI and iron salt as catalysts at room temperature

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ABSTRACT

Aerobic oxidation of various alcohols has been accomplished by using a novel catalytic system, *N*-hydroxyphthalimide (NHPI) combined with $Fe(NO_3)_3 \cdot 9H_2O$. Secondary alcohols, especially benzylic and aliphatic alcohols, were smoothly transformed into corresponding ketones with up to 92% yields at room temperature under one atmosphere pressure of oxygen. The influences of reaction conditions such as solvent, different metal catalyst, catalyst loading and the structure of alcohols on the promotion effect were studied. And a possible radical mechanism for the oxidation of secondary alcohols in $Fe(NO_3)_3 \cdot 9H_2O/NHPI/O_2$ system was proposed.

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1. Introduction

The selective oxidation of alcohols into their corresponding carbonyl compounds is a frequently used transformation in organic synthesis [1–5], and most of the resulting carbonyl compounds are important synthetic intermediates in chemicals and pharmaceuticals [6,7], hence many scientists tried their best to develop a wide variety of methods for oxidation of alcohols. Traditional oxidants mainly include permanganate [8], manganese (IV) oxide [9,10], chromium (VI) oxide [11], and ruthenium reagents [12,13]. In general, these oxidants are needed at least a stoichiometric amount and usually bring about noxious byproducts. Therefore, oxygen as clean oxidant for the selective oxidation of alcohols to carbonyl compounds under mild conditions is more attractive since the main by-product is water [14–16]. And NHPI is recognized as one of powerful catalysts for aerobic oxidation of various organic compounds [17–22].

Up to now, very few catalytic systems have more advantages than using NHPI for the oxidation of alcohols with O_2 as terminal oxidant [23–26], thus, either from the viewpoint of green or sustainable chemistry, developing a highly efficient catalytic system based on NHPI is very interesting and valuable. However, because oxygen molecule cannot be activated directly by NHPI in the absence of co-catalyst at room temperature, a co-catalyst is required for this catalytic reaction. Iron has a number of advantages over other transition metals for it's relatively non-toxic, cheap and environmentally friendly [27], and iron-based catalyst systems have been applied in a variety of organic transformations [28–36], especially in some oxidation reactions using oxygen as oxidant [37–39]. Therefore, we supposed iron salts have a potential as good co-catalysts in NHPI catalytic system and applied NHPI and iron salts as the catalytic system to the oxidation of alcohols. As we expected, a series of secondary aliphatic and aromatic alcohols were smoothly converted to corresponding ketones at room temperature under an atmosphere pressure of oxygen (Scheme 1).

2. Experimental

2.1. General remarks

All starting materials and catalysts were purchased from commercial suppliers and used without further purification. Column chromatography was generally performed on silica gel (200–300 mesh) and TLC inspections were on silica gel GF254 plates.

GC–MS spectra were recorded on an Agilent Technologies 7890A GC-system with an Agilent 5975 inert Mass Selective Detector (EI) and a HP-5MS column (0.25 mm × 30 m, Film: 0.25 μm). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker spectrometer 400 MHz using $CDCl_3$ as the solvent with TMS as an internal reference.
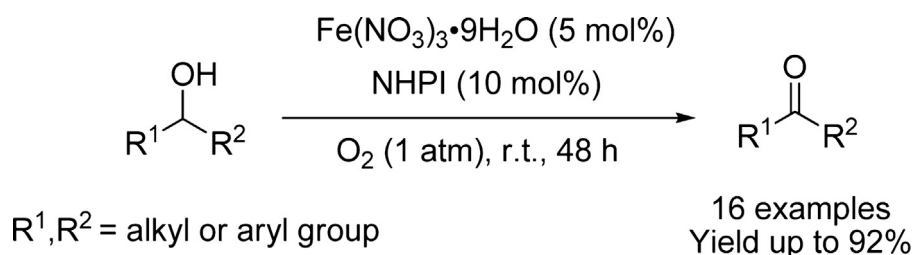
Scheme 1. Oxidation of secondary alcohols into corresponding ketones at room temperature in the presence of Fe(NO$_3$)$_3$·9H$_2$O and NHPI under an atmosphere pressure of oxygen.

2.2. General procedure of oxidation of secondary alcohols

Substrate (1 mmol) and the desired amounts of Fe(NO$_3$)$_3$·9H$_2$O and NHPI were added to 1.5 mL of acetonitrile in a 15 mL test tube. The solution was maintained for 20 h under an atmospheric pressure of O$_2$ and at 25 °C. After the reaction was quenched by Na$_2$S$_2$O$_3$ solution, 60 mg of nitrobenzene, serving as an internal standard, was added to the reaction system. The solution was centrifuged and the supernatant was diluted with diethyl ether and dried with anhydrous Na$_2$SO$_4$ for 30 min. The products were analyzed by GC, and further confirmed by GC–MS. The isolated yield was obtained through column chromatography generally performed on silica gel (200–300 mesh).

3. Results and discussion

3.1. Influence of metal salts

The exploratory experiments were started by testing this protocol and screening the metal salts using α-phenylethanol as the model substrate in the presence of NHPI (10 mol%) under the identical conditions (Table 1). Initially, a variety of iron salts were used and their reaction activities were evaluated. We found only Fe(NO$_3$)$_3$·9H$_2$O as co-catalyst could obtain high conversion and selectivity (Table 1, entry 8), other iron salts were almost inert for the reaction (Table 1, entries 1–7); moreover, Fe(NO$_3$)$_3$·9H$_2$O, NHPI and oxygen were essential to the aerobic

oxidation of α-phenylethanol (Table 1, entries 9–11). Obtaining 19% of acetophenone under dinitrogen atmosphere may ascribe to the oxidation of Fe(NO$_3$)$_3$·9H$_2$O [40]. The results suggested that the anions of iron salts had a great effect on the oxidation of α-phenylethanol. That's to say, nitrate ion may play an important role in the oxidation. Subsequently, a series of nitrates were investigated to test whether the metal cation also had certain effect for the reaction (Table 1, entries 12–19). The results showed Cu(NO$_3$)$_2$·3H$_2$O and Zr(NO$_3$)$_4$·5H$_2$O could give 39% and 55% yields respectively (Table 1, entries 13 and 14). As for Co(NO$_3$)$_2$·6H$_2$O, only 6% yield was provided (Table 1, entry 12), and for other nitrates, no products were detected (Table 1, entries 15–19). The results indicated that metal cation also has some influence on the reaction. Among tested metal salts, Fe(NO$_3$)$_3$·9H$_2$O exhibited best activity. Maybe, this good performance is attributed to the synergistic effect between iron cation and nitrate anion.

3.2. Influence of different solvent

The effect of the solvents on the oxidation of alcohols was also evaluated (Table 2). It is clear that the solvent has an important effect on the reaction. Under the same condition, the conversion of α-phenylethanol to acetophenone was achieved in higher yield in acetonitrile compared to other solvents such as DMSO, THF, dichloroethane, and toluene and so on (Table 2, entry 1 *vs* entries 2–7).

3.3. Influence of the amount of Fe(NO$_3$)$_3$·9H$_2$O and NHPI

Subsequently, the influence of the amount of Fe(NO$_3$)$_3$·9H$_2$O and NHPI on the oxidation was examined under the identical reaction conditions, as listed in Table 3. The yield of acetophenone was 14% in the presence of 0.5 mol% Fe(NO$_3$)$_3$·9H$_2$O and 5 mol% NHPI (Table 3, entry 5). And the yield increased to 75% when the amount of Fe(NO$_3$)$_3$·9H$_2$O reached to 5 mol% (Table 3, entries 2–4), but there was almost no change by further increasing Fe(NO$_3$)$_3$·9H$_2$O to 8 mol% (Table 3, entry 1). Therefore, 5 mol% of Fe(NO$_3$)$_3$·9H$_2$O is a desired catalyst loading. Based on that, the desired loading amount of the NHPI was investigated also (Table 3, entries 6–10).

Table 1
Screening of metal salt as catalyst for the oxidation of α-phenylethanol.[a]

Entry	Metal salt	Conv. (%)[b]	Yield (%)[b]
1	K$_4$[Fe(CN)$_6$]·3H$_2$O	NR[c]	–
2	K$_3$[Fe(CN)$_6$]	NR[c]	–
3	Fe$_2$(SO$_4$)$_3$·XH$_2$O	NR[c]	–
4	FeCl$_2$·4H$_2$O	NR[c]	–
5	FeCl$_2$	NR[c]	–
6	FeCl$_3$	6	–
7	Fe(OTf)$_2$	9	8
8	Fe(NO$_3$)$_3$·9H$_2$O	84	83
9	–	NR[c]	–
10[d]	Fe(NO$_3$)$_3$·9H$_2$O	20	19
11[e]	Fe(NO$_3$)$_3$·9H$_2$O	NR[c]	–
12	Co(NO$_3$)$_2$·6H$_2$O	6	6
13	Cu(NO$_3$)$_2$·3H$_2$O	39	39
14	Zr(NO$_3$)$_4$·5H$_2$O	56	55
15	Mg(NO$_3$)$_2$·6H$_2$O	NR[c]	–
16	Ni(NO$_3$)$_2$·6H$_2$O	NR[c]	–
17	Zn(NO$_3$)$_2$·6H$_2$O	NR[c]	–
18	Al(NO$_3$)$_3$·9H$_2$O	Trace	Trace
19	In(NO$_3$)$_3$·5H$_2$O	Trace	Trace

[a] α-Phenylethanol (1 mmol), metal salt (5 mol%), NHPI (10 mol%), acetonitrile (1.5 mL), O$_2$ (1 atm), room temperature, 20 h.
[b] Determined by GC using nitrobenzene as an internal standard.
[c] NR = No reaction.
[d] Under dinitrogen atmosphere.
[e] Without NHPI.

Table 2
Solvent optimization.[a]

Entry	Solvent	Conv. (%)[b]	Yield (%)[b]
1	Acetonitrile	84	83
2	CH$_2$Cl$_2$	38	38
3	ClCH$_2$CH$_2$Cl	7	7
4	THF	13	13
5	DMSO	NR[c]	–
6	H$_2$O	NR[c]	–
7	Toluene	NR[c]	–

[a] α-Phenylethanol (1 mmol), Fe(NO$_3$)$_3$·9H$_2$O (5 mol%), NHPI (10 mol%), solvent (1.5 mL), O$_2$ (1 atm), room temperature, 20 h.
[b] Determined by GC using nitrobenzene as an internal standard.
[c] NR = No reaction.