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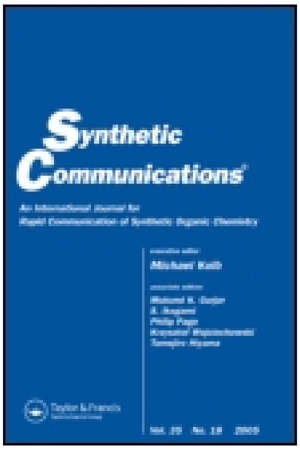

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Efficient Aerobic Oxidation of Alcohols to Carbonyl Compounds with NHPI/CAN Catalytic System

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ABSTRACT

Aerobic oxidation of various secondary alcohols into their corresponding carbonyl compounds has been accomplished by using *N*-hydroxy phthalimide (NHPI)/ceric ammonium nitrate (CAN). Primary alcohol and allylic alcohols were transformed in relatively moderate yield.

Key Words: Carbonyl compounds; Catalytic system; Aerobic oxidation; Secondary alcohols.

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INTRODUCTION

The development of efficient catalytic system for selective organic transformation is currently one of the challenging tasks in synthetic organic chemistry. The oxidation of alcohol into their corresponding carbonyl compounds is one of the most important transformations in organic synthesis.[1] *N*-Hydroxy phthalimide (NHPI) has first been used as an efficient electron carrier for the electrochemical oxidation of alcohols. [2] Then Ishii et al. found that NHPI efficiently catalyzes the aerobic oxidation of various organic substrates to oxygen containing compounds, under non-electrochemical conditions.[3] An efficient catalytic method for the low temperature oxygenation of organic compound with dioxygen was developed by using NHPI as a catalyst and a metal salt as co-catalyst. With this system, organic compounds containing sufficiently reactive C–H bonds, e.g., (cyclic)alkanes,[4] sulfoxides,[5] alkyl benzenes,[6] and aromatic compounds containing benzylic functions,[7–9] have been oxidized at moderate temperature up to high conversion. A methodology for the aerobic oxidation of organic compounds has been established using a combined catalytic system consisting of NHPI/quaternary ammonium bromide.[10] Hydroxylations of polycyclic alkanes [11] with molecular oxygen in the presence of NHPI combined with cobalt salts under mild conditions have been reported. A variety of alkenes were epoxidized in a regio- and stereoselective manner with oxygen in the presence of benzhydrol catalyzed by NHPI and hexafluroacetone.[12] Electro catalytic oxidation of several alcohols have been performed by using a new series of substituted NHPI[13] as catalysts. Ceric ammonium nitrate (CAN) itself is a well-known oxidizing agent that oxidizes various organic substrates.[14–16] Aerobic oxidation of alkyl malonates into ketomalonates[17]employs catalytic amount of CAN. In the continuing interest of our alcohol oxidation studies,[18–21] we would like to herein report the aerobic oxidation of benzylic alcohols using NHPI/CAN system.

RESULTS AND DISCUSSION

sec-Phenylethyl alcohol was chosen for several control experiments to study the role of the each reagent utilized in the reaction (Table 1). NHPI and CAN are the most important species for the oxidation process. Without these reagents, there is very little oxidation reaction (entries 1 and 2) taking place. Without oxygen bubbling, the oxidation gives only 51% of acetophenone (entry 3). Elevated temperature is also needed for efficient oxidation (entry 4). An efficient oxidative condition is described with entry 6.

Investigations of the scope of the substrates were conducted under the optimized condition as mentioned above and the results were given in

Table 1. Oxidation of *sec*-phenethyl alcohol under various condition by using NHPI/CAN system in CH_3CN.[a]

Entry	CAN (mol%)	NHPI (mol%)	O_2[b]	Time (hr)	Yield (%)
1	—	10	O_2	5	Trace
2	20	—	O_2	1.15	Trace
3	20	10	—	1.15	51
4	20	10	O_2	4	48
5	10	10	O_2	1.15	68
6	20	10	O_2	1.15	91

[a] All the reactions except for entry 4 were carried out with reflux temperature of CH_3CN (b.p. 82°C). Entry 4 was reacted at RT.

[b] O_2 was bubbled in all reactions except for entry 3. Entry 3 was reacted on the air without O_2 bubbling.

Table 2. Unsubstituted and substituted phenylethanols (entries 1–6) were efficiently oxidized to corresponding ketones with excellent yield (>90%). The change of methyl group of 1-phenylethanol into larger groups prolongs the reaction time (entries 7–10). 1-Indanol and 1,2,3,4-tetrahydro-1-naphthol were converted into their corresponding ketones with good yields (entries 11 and 12). Cyclopropyl benzyl alcohol has undergone smooth oxidation with moderate yield (entry 13). Benzyl alcohol, cinnamyl alcohol and (−) carveol produced poor yield of ketones (49–61%).

On the basis of previous oxidation studies,[3,20] the following mechanism has been proposed as indicated in Sch. 1. Dioxygen is reduced to H_2O_2 by the oxidation of Ce^{3+} to Ce^{4+}. NHPI can be converted into phthalimide-*N*-oxyl (PINO) radical. PINO then oxidizes the alcohol to corresponding ketone.

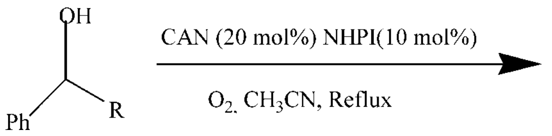
In conclusion, present catalytic system is useful for the oxidation of secondary benzylic alcohols to ketones. Primary and allylic alcohol reveal poor oxidation tendency.

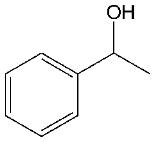
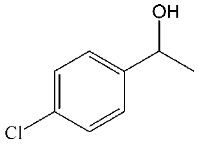
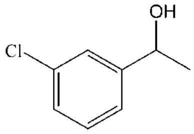
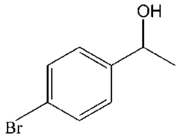
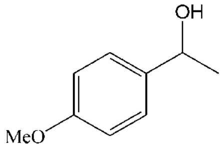
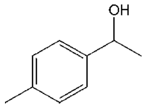
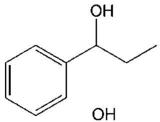
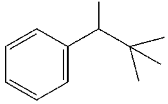
EXPERIMENTAL

General Procedure for the Oxidation of Alcohols Catalyzed by NHPI/CAN System

Alcohol (1 mmol), CAN (20 mol%), and NHPI (10 mol%) were dissolved in 3 mL of CH_3CN in a three necked round-bottom flask equipped

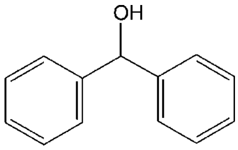
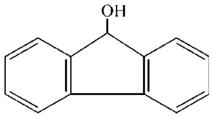
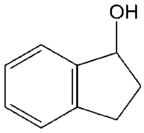
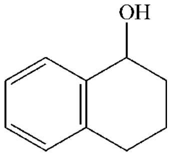
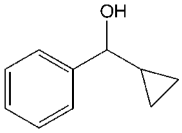
Table 2. Oxidation of alcohols by NHPI/CAN system in CH$_3$CN.



Entry	Substrate	Time (hr)	Yield^{a,b} (%)
1		1.2	91
2		1.3	95
3		1.5	96
4		1.3	97
5		1	93
6		1.3	90
7		1.3	95
8		2.3	93

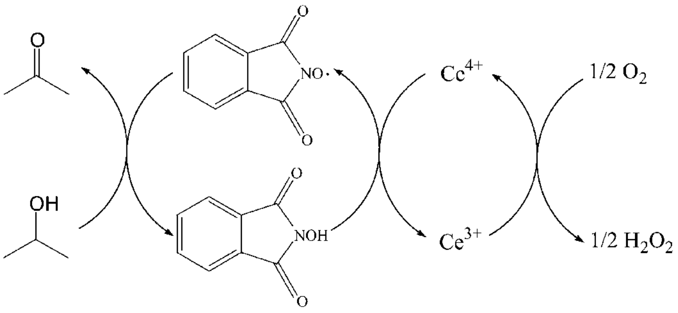
(*continued*)

Table 2. Continued.

Entry	Substrate	Time (hr)	Yield[a,b] (%)
9		2.3	92
10		2.5	96
11		45 min	86
12		1.3	88
13		2.3	83

[a] Isolated yield.

[b] All the ^1H NMR spectra of ketones and aldehydes exactly match with those tabulated in the Aldrich library of ^{13}C and ^1H FT NMR spectra edited by Charles J. Pouchert, Jacqlynn Behnke.



Scheme 1.

with a condenser and magnetic bar. This mixture was heated to reflux with an oil bath under continuous stream of oxygen. The progress of the reaction was monitored by using TLC. After completion of the reaction, excess solvent was evaporated under reduced pressure and the product was purified by flash column chromatography on silica gel by using ethyl acetate/hexane mixture as eluent. The products thus separated were identified by ^{1}H NMR spectroscopy.

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