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Recent progress in aerobic oxidation of hydrocarbons by *N*-hydroxyimides

Yasutaka Ishii *, Satoshi Sakaguchi

Department of Applied Chemistry & High Technology Research Center, Faculty of Engineering, Kansai University Suita, Osaka 564-8680, Japan

Abstract

Innovative carbon radical generation from hydrocarbons through a catalytic process under mild conditions has been achieved by the use of *N*-hydroxyphthalimide (NHPI) as a catalyst. This method can be successfully applied to a wide variety of functionalizations of hydrocarbons. Thus, alkanes are converted into alcohols, ketones, and carboxylic acids, through alkyl radicals generated by the action of NHPI. Cyclohexane was directly converted into adipic acid with O_2 by NHPI combined with $Mn(OAc)_2$. *p*-Xylene was oxidized to terephthalic acid in 95% yield by using an NHPI analogue as a catalyst. Alkenes could be epoxidized with H_2O_2 generated in situ from benzhydrol and O_2 under the influence of NHPI.
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Keywords: Aerobic oxidation; Dioxygen; *N*-Hydroxyphtahlimide; Radical

1. Introduction

The aerobic oxidation of hydrocarbons is a very important commercial process for the production of oxygen-containing compounds like alcohols, aldehydes, ketones, carboxylic acids, and epoxides from hydrocarbons. In particular, the production of carboxylic acids like adipic acid by direct aerobic oxidation of hydrocarbons has recently become environmentally important, since the adipic acid is currently synthesized by the nitric acid oxidation of K/A-oil (a mixture of cyclohexanone and cyclohexanol) which evolves a large amount of global-warming nitrous oxide (N_2O). Another important aerobic oxidation includes the transformation of *p*-xylene to terephthalic acid (TPA). Nowadays, most of TPA used worldwide is manufactured through the Amoco process using Co/Mn/Br system as a catalyst. This process, however, is operated at higher temperature (175–225 °C) and pressure (15–30 atm) of air using acetic acid as a solvent. Because of the use of corrosive bromine as an essential catalyst component, reactors lined with expensive titanium alloy must be employed. In addition, undesired side products like methyl bromide having remarkable global-warming effect cannot be avoided by employing this process. Therefore, the production of adipic acid not using nitric acid and of TPA by halogen-free method has been desired for long time in industrial chemistry.

Recently, we have successfully developed an innovative strategy for the catalytic carbon radical generation from hydrocarbons by a phthalimide *N*-oxyl (PINO) radical which can be generated from *N*-hydroxyphthalimide (NHPI) with oxygen in the presence or absence of a cobalt species under mild conditions (Scheme 1). The carbon radicals derived from a variety of hydrocarbons under dioxygen leads to oxygenated compounds like alcohols, ketones, and carboxylic acids. This paper summarizes a recent progress in the NHPI-catalyzed functionalization of hydrocarbons.

2. Oxidation of alkanes

As a raw material for nylon-6,6 and polyesters, adipic acid is the most important aliphatic dicarboxylic acid. The current production of adipic acid consists of a two-step oxidation process involving the aerobic oxidation of cyclohexane in the presence of a soluble Co catalyst at 150–170 °C to a K/A-oil and the nitric acid oxidation of the K/A-oil to adipic acid [1,2]. The drawbacks of this process are that the oxidation in the first step must be operated in 3–6% conversion of cyclohexane to keep a high selectivity (80%) of the K/A-oil, and that the nitric acid oxidation evolves a large amount of undesired global-warming nitrogen oxides, in particular N_2O. Therefore, the direct conversion of cyclohexane to adipic acid by the aerobic oxidation has long been sought after as a desirable and promising method in

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* Corresponding author. Tel.: +81 6 6368 0793; fax: +81 6 6339 4026.
E-mail address: ishii@ipcku.kansai-u.ac.jp (Y. Ishii).

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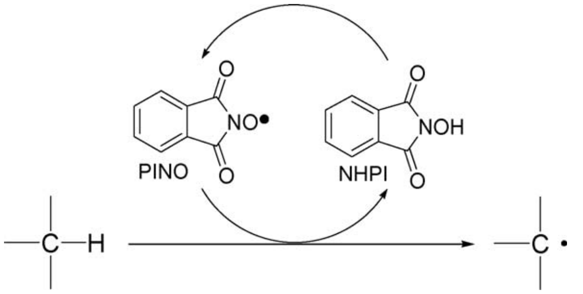
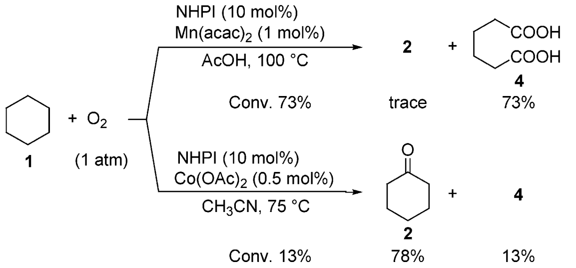


Scheme 1. Carbon radical generation by PINO.

industrial chemistry worldwide. Tanaka et al. succeeded in achieving conversion of cyclohexane to adipic acid under 30 atm of O_2 by the use of a higher concentration of Co(III) acetate combined with acetaldehyde or cyclohexanone which serves as promoter [3]. More recently, Ishii and Noyori reported the oxidation of cyclohexene to adipic acid with aqueous hydrogen peroxide by a polyoxometalate having a phase-transfer function as an alternative clean route [4].

The direct conversion of cyclohexane to adipic acid was successfully achieved by the use of a combined catalyst of NHPI with Co and Mn ions [5]. The oxidation of cyclohexane (**1**) in the presence of a catalytic amount of NHPI (10 mol%) and $Mn(acac)_2$ (1 mol%) under dioxygen atmosphere (1 atm) in acetic acid at 100 °C for 20 h gave adipic acid (**4**) in 73% selectivity at 73% conversion (Eq. (1)). This is the first example of a one-step oxidation of **1** to **4** under normal pressure of dioxygen at a reasonably low reaction temperature with high conversion and selectivity. The oxidation using the NHPI/$Co(OAc)_2$ system in acetonitrile, on the other hand, gave rise to cyclohexanone (**2**) in good selectivity (Eq. (1)) [6]. The oxidation by the NHPI/Co system in acetonitrile provides an alternative direct route to cyclohexanone, although the autoxidation of cyclohexane leads to a mixture of K/A-oil consisting of cyclohexanol as a main product [1,2]. The present catalytic system can be extended to the oxidation of large-membered cycloalkanes to the corresponding dicarboxylic acids. Cyclooctane, cyclodecane and cyclododecane were oxidized to suberic acid, sebacic acid and dodecanedioic acid, respectively.



(1)

The aerobic oxidations of **1** must be carried out in an appropriate solvent such as acetic acid or acetonitrile due to the lower solubility of NHPI in nonpolar solvents such as hydrocarbons. It is noteworthy that the NHPI-catalyzed reaction of **1** could proceed without any solvent by the use of a lipophilic NHPI derivative. Of a series of 4-alkyloxycarbonyl *N*-hydroxyphthalimides examined as lipophilic NHPI catalysts, 4-laulyloxycarbony *N*-hydroxyphthalimide was found to be an efficient catalyst for the aerobic oxidation of **1** under solvent-free conditions (Fig. 1) [7].

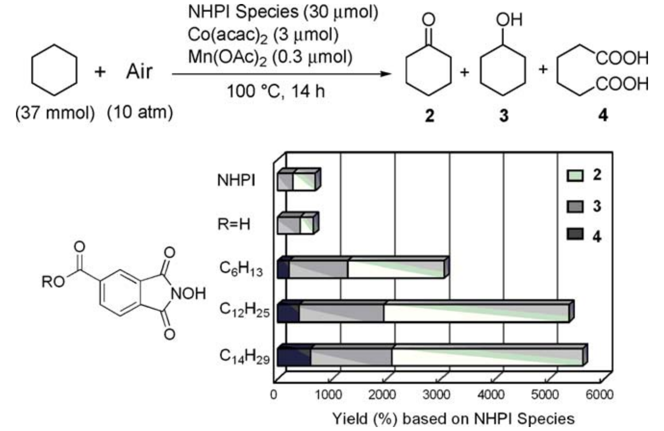
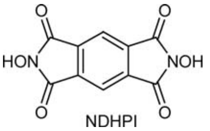


Fig. 1. Oxidation of **1** catalyzed by NHPI species tinder solvent-free conditions.

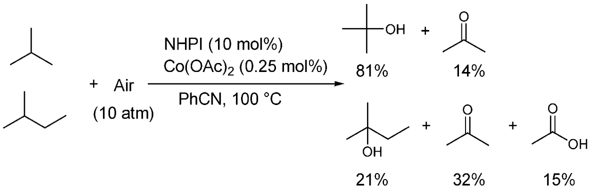
Catalytic aerobic oxidation of ethane to acetic acid was successfully performed through a catalytic radical process using NHPI derivatives combined with a Co(II) salt in acetonitrile or propionic acid. Among the catalysts examined, *N*,*N*-dihydroxypyromellitimide (NDHPI) was found to be the best catalyst. For instance, when a mixture of ethane (20 atm) and air (20 atm) in acetonitrile was allowed to react in the presence of NDHPI (100 μmol) and $Co(OAc)_2$ (30 μmol) at 150 °C for 15 h, 830 μmol of acetic acid was obtained and the turnover number (TON) of NDHPI reached 8.3 (Eq. (2)). In this reaction, other products such as ethanol or acetaldehyde were not detected at all. In the oxidation of ethane using NHPI as a catalyst under these conditions, the amount of NHPI used was two times that of NDHPI, but the yield of acetic acid and the TON of the catalyst were 530 μmol and 2.7, respectively. The highest TON (15.3) was obtained when the reaction was carried out using NDPHI combined with $CoCl_2$ in propionic acid [8].

$$\underset{20\,\text{atm}}{C_2H_6} + \underset{20\,\text{atm}}{\text{air}} \xrightarrow[150\,^{\circ}\text{C}]{\text{catalyst}} CH_3COOH \tag{2}$$

Catalyst (μmol)	Solvent	Yield (μmol)	TON
NHPI/$Co(OAc)_2$ (200/30)	CH_3CN	530	2.7
NDHPI/$Co(OAc)_2$ (100/30)	CH_3CN	830	8.3
NDHPI/$CoCl_2$ (100/30)	CH_3CH_2COOH	1532	15.3

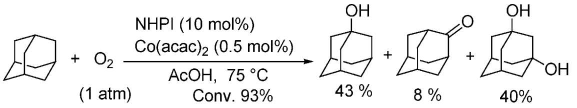


The autoxidation of isobutane is now carried out to mainly obtain *tert*-butyl hydroperoxide [9]. Halogenated metalloporphyrin complexes are reported to be efficient catalysts for the aerobic oxidation of isobutene [10,11]. It was found that the oxidation of isobutane by air (10 atm) catalyzed by NHPI and $Co(OAc)_2$ in benzonitrile at 100 °C produced *tert*-butyl alcohol in high yield (81%) along with acetone (14%) (Eq. (3)) [12]. 2-Methylbutane was converted into the carbon–carbon bond cleaved products, acetone and acetic acid, rather than the alcohols, as principal products. These cleaved products seem to be formed via β-scission of an alkoxy radical derived from the decomposition of a hydroperoxide by Co ions. The extent of the β-scission is known to depend on the stability of the radicals released from the alkoxy radicals [13]. It is thought that the β-scission of a *tert*-butoxy radical to acetone and a methyl radical occurs with more difficulty than that of a 2-methylbutoxy radical to acetone and an ethyl radical. As a result, isobutane produces *tert*-butyl alcohol as the principal product, while 2-methylbutane affords mainly acetone and acetic acid.



(3)

There have been a few reports on the catalytic hydroxylation of adamantane with dioxygen [14]. The NHPI-catalyzed aerobic oxidation of adamantane is considerably accelerated by adding a small amount of a Co salt [15]. Thus, the oxidation of adamantane in the presence of NHPI (10 mol%) and $Co(acac)_2$ (0.5 mol%) in acetic acid under dioxygen (1 atm) for 6 h produced 1-adamantanol (43%), 1,3-adamantanediol (40%), and 2-adamantanone (8%) (Eq. (4)). The relative reactivity of the tertiary C–H bond to the secondary C–H bond in the oxidation by NHPI/Co(II) was roughly 31. This value is considerably higher than that attained by the conventional autoxidation (3.8–5.4). The preferential oxidation of the tertiary C–H bond over the secondary bond may be attributed to the electron-deficient character of PINO which is a key radical species in the NHPI-catalyzed oxidation.



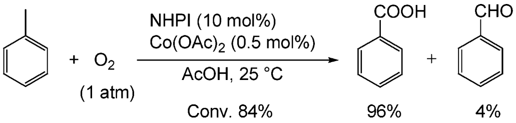
(4)

It is important that the oxidation led to diol in high selectivity, because it is rarely produced by conventional oxidation. Hirobe obtained diol in 25% yield by the oxidation of adamantane using a Ru complex with 2,6-dichloropyridine *N*-oxide as the oxidant [16]. In the stepwise hydroxylation of adamantanol by the NHPI/$Co(acac)_2$ system, the diol and triol were obtained in high selectivity. These alcohols are now manufactured as important components of photoresistant polymer materials on an industrial scale by Daicel Chemical Industry Ltd.

3. Oxidation of alkylbenzenes

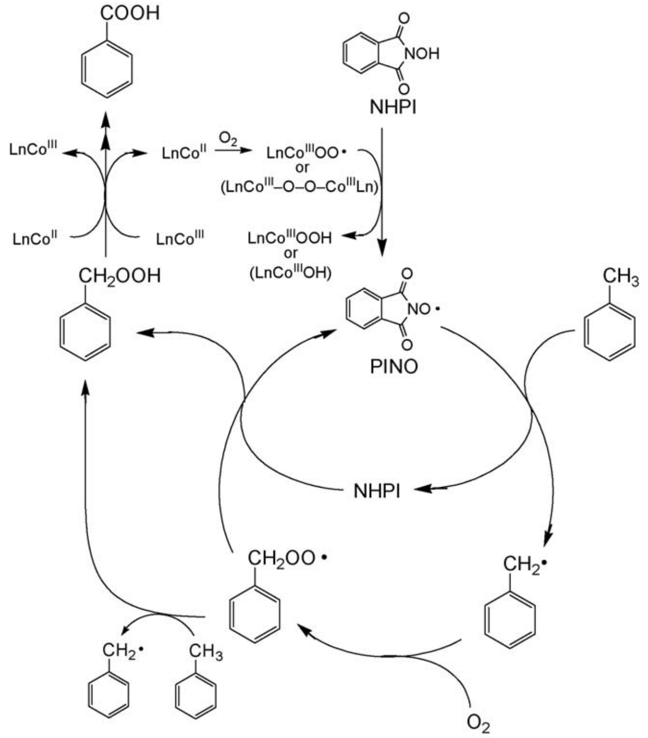
Aerobic oxidation of alkylbenzenes is a promising subject in industrial chemistry. Many bulk chemicals such as terephthalic acid, phenol, benzoic acid, etc. are manufactured by homogeneous liquid-phase oxidations with O_2 [1,17]. The largest-scale liquid-phase oxidation is the conversion of *p*-xylene to terephthalic acid, which is chiefly used as polyethylene terephthalate polymer material. Benzoic acid derived from the oxidation of toluene is an important raw material in the production of various pharmaceuticals and pesticides. These oxidation processes are usually operated at higher temperatures and pressures of air. A great deal of effort has been made to develop the homogeneous oxidations of alkylbenzenes with better selectivity under milder conditions. The first successful oxidation of a variety of alkylbenzenes with O_2 by the use of NHPI as the catalyst under very mild conditions is achieved.

Currently, the oxidation of toluene is commercially practiced in the presence of a catalytic amount of cobalt(II) 2-ethylhexanoate under a pressure of 10 atm of air at 140–190 °C [18]. The oxidation of toluene under normal pressure of dioxygen at room temperature is achieved by the use of a combined catalyst of NHPI and Co(II) species. The fact that the toluene was oxidized with dioxygen through the catalytic process in high yield under ambient conditions is very important from ecological and technical viewpoints as a promising strategy in oxidation chemistry. As a typical example, the oxidation of toluene in the presence of NHPI (10 mol%) and $Co(OAc)_2$ (0.5 mol%) in acetic acid under an atmosphere of O_2 at 25 °C for 20 h afforded benzoic acid and benzaldehyde in 96% and 4% selectivities, respectively, at 84% conversion (Eq. (5)) [19]. This finding suggests that an efficient cleavage of a C–H bond having the bond dissociation energy (BDE) of 88 kcal/mol (corresponding to the BDE of toluene) is possible at room temperature by the use of NHPI catalyst. However, when Co(III) was employed in place of Co(II), no reaction took place at all at room temperature.



(5)

A plausible reaction pathway for the aerobic oxidation of alkanes catalyzed by NHPI and Co(II) is illustrated in Scheme 2. A labile dioxygen complex such as superoxocobalt(III) or peroxocobalt(III) complexes is known to be formed by the complexation of Co(II) with O_2. The in situ generation of PINO from NHPI by the action of the cobalt(III)–oxygen complex formed is a key step in the present oxidation. The next step involves the hydrogen atom abstraction from alkanes by PINO to form alkyl radicals. Trapping the resulting alkyl radicals by dioxygen provides peroxy radicals, which are eventually converted into oxygenated products through alkyl hydroperoxides. In fact, on exposing NHPI in benzonitrile containing a small amount of $Co(OAc)_2$ to dioxygen at 80 °C, an ESR signal attributed to PINO as a triplet signal having hyperfine splitting (hfs) by the nitrogen atom ($g = 2.0074$, $A_N = 4.3$ G) is observed (Fig. 2). The *g*-value and hyperfine splitting constants observed here are consistent with those of PINO reported previously [20]. In addition, PINO is observed during the oxidation of toluene by the NHPI/Co(II) system under ambient conditions [19]. Recently,



Scheme 2. A plausible reaction path for the aerobic oxidation of toluene catalyzed by NHPI combined with Co(II).

Minisci, Pedulli and coworkers found that the BDE value of the O–H bond for NHPI is >86 kcal/mol by means of ESR spectroscopy. This suggests that PINO could abstract the benzylic hydrogen atom of toluene whose BDE is 88 kcal/mol [21].

Terephthalic acid (TPA) as well as dimethyl terephthalate (DMT) have recently become much important as raw material for polyethylene terephthalate [22]. In 2000, ca. 25 million tonnes of TPA were manufactured worldwide. Until the 1980s, the following four-step process developed by Witten and modified by Hercules and Dynamit–Nobel (Witten–Hercules process) had been mainly operated to produce DMT [22]. The first step is the conversion of *p*-xylene (PX) to *p*-toluic acid (PTA). It then passes to an esterification step to form methyl *p*-toluate, which is subjected to further oxidation to monomethyl terephthalate, followed by esterification to DMT. From the 1990s, these processes were changed to the aerobic one-stage oxidation of PX to TPA by the combined use of cobalt and manganese salts in the presence of bromide as a promoter in acetic acid at 175–225 °C under 15–30 atm of air, followed by hydrogenation of the crude TPA to remove 4-carboxybenzaldehyde (4-CBA) by a Pd catalyst [22–24]. This process was developed by Scientific Design and Amoco Ltd. (Amoco process). Currently, about 70% of TPA produced worldwide is based on the Amoco process, and almost all of the new plants adopt this method. However, there are several disadvantages in the Amoco process. Therefore, a new oxidation system for the production of TPA is desired to overcome these disadvantages. Partenheimer recently published some reviews devoted to the aerobic oxidation of alkylbenzenes, especially PX, using the Co/Mn/Br system [24].

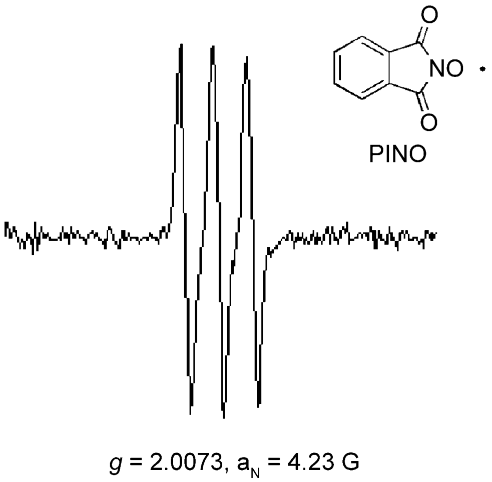
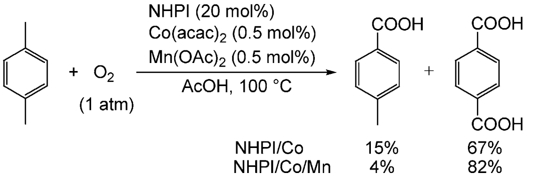


Fig. 2. ESR spectrum of PINO.

The aerobic oxidation of PX to TPA was examined by the NHPI catalyst to elaborate a halogen-free catalytic system [25]. The oxidation of PX with dioxygen (1 atm) in the presence of catalytic amounts of NHPI (20 mol%) and Co(OAc)$_2$ (0.5 mol%) in acetic acid at 100 °C for 14 h produced TPA in 67% yield and PTA (15%) together with small amounts of 4-CBA, 4-carboxybenzyl alcohol, 1,4-diacetoxymethylbenzene, and 4-acetoxymethylbenzoic acid as well as several unidentified compounds in 1–2% yields, respectively, at over 99% conversion (Eq. (6)). The yield of TPA is improved to 82%, when Mn(OAc)$_2$ (0.5 mol%) is added to the NHPI/Co(OAc)$_2$ system. The synergistic effect of Co and Mn salts in the aerobic oxidation of alkylbenzenes has been well documented [24]. From a practical point of view, it is important that the aerobic oxidation of PX under air (30 kg/cm^2) by the NHPI/Co/Mn system is completed within 3 h at 150 °C to form TPA in 84% yield.

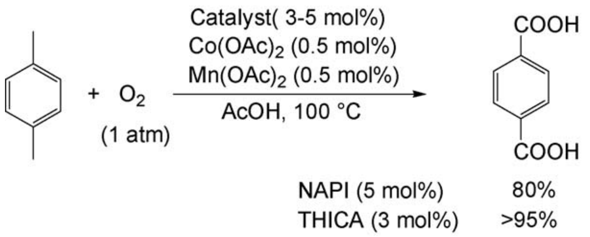


(6)

As shown in Eq. (6), ca. 20 mol% of NHPI must be used to obtain TPA in satisfactory yield (over 80%), because NHPI gradually decomposes to inert phthalimide and phthalic anhydride during the oxidation. If the NHPI used can be reduced by a simple modification, the present oxidation would be more desirable. Efforts to reduce the amount of the NHPI led to the discovery of an efficient catalyst, *N*-acetoxyphthalimide (NAPI), which can be easily prepared by the reaction of NHPI with acetic anhydride. Surprisingly, PX was oxidized to TPA in high yield (80%) even by the use of 5 mol% of NAPI, Co(OAc)$_2$ (0.5 mol%), and Mn(OAc)$_2$ (0.5 mol%) (Eq. (7)). The effect of NAPI is considered to be resistant to the rapid decomposition to phthalimide or phthalic anhydride at the early stage of the reaction where violent chain reactions take place, since NAPI is gradually hydrolyzed to NHPI by water present in acetic acid as well as the water resulting during the oxidation.

Furthermore, N,N',N''-trihydroxyisocianuric acid (THICA) was found to be a very efficient catalyst for the oxidation of alkylbenzenes with dioxygen. Thus, PX was efficiently oxidized by THICA to telephthalic acid in high yield. PX was allowed to react with O_2 (1 atm) in the presence of THICA (3 mol%) combined with $Co(OAc)_2$ (0.5 mol%) and $Mn(OAc)_2$ (0.5 mol%) in acetic acid at 100 °C gave TPA in >95% yield (Eq. (7)) [26]. In addition, we have established a new synthetic method for preparing of THICA [27]. The reaction of *O*-benzylhydroxyamine with phenyl chloroformate gave formbenzyloxycarbamic acid phenyl ester of which subsequent treatment with dimethylaminopyridine produced 1,3,5-tribenzyloxyisocyanurate leading to THICA by hydrogenation with H_2 on Pd/C. The other method involved the direct synthesis of 1,3,5-tribenzyloxyisocyanurate from *O*-benzylhydroxyamine and diphenyl carbonate (Scheme 3).

Phenol is one of the most important classes of raw materials in chemical industry, and a variety of compounds are derived from phenols like resins, dyes, pharmaceuticals, etc. [28]. In 2000, worldwide production of phenol was 6.6 Mt. Most of this phenol is produced by the Cumene process found by Hock and Lang in 1944 [29]. The Cumene process involves the aerobic oxidation of propylbenzene to cumene hydroperoxide followed by treatment with sulfuric acid to produce a 1:1 mixture of phenol and acetone. So far, a large quantity of acetone is used as a raw material of methacrylic acid (MA), but most of MA has currently been produced by aerobic oxidation of isobutene. Therefore, co-production of phenol and acetone by the Hock method incurs a serious drawback, since recent demand of acetone has been deceasing more and more in contrast to increasing need of phenol. Therefore, development of an alternative route to phenol without formation of acetone is an important subject in the chemical industry worldwide. From this point of view, Sheldon et al. have recently reported the aerobic oxidation of cyclohexylbenzene to cyclohexylbenzene-1-hydroperoxide (CHBPO), which is a precursor of phenol and cyclohexanone, using NHPI combined with several radical initiators [30].



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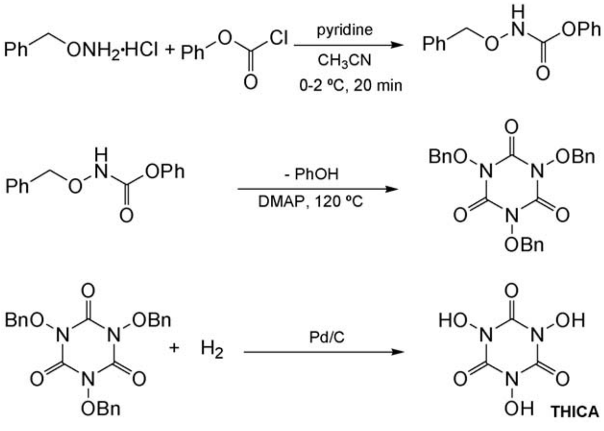
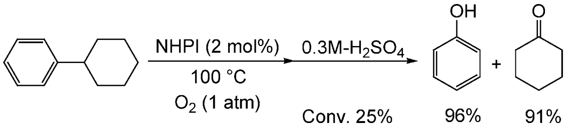


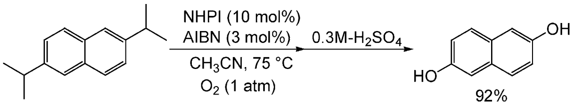
Scheme 3. A new route to THICA.

Synthesis of phenol and cyclohexanone in one pot was examined by means of the NHPI-catalyzed aerobic oxidation of cyclohexylbenzene. The aerobic oxidation of cyclohexylbenzene catalyzed by NHPI followed by treatment with sulfuric acid afforded phenol and cyclohexanone in good selectivities [31]. Thus, the reaction of cyclohexylbenzene under atmospheric dioxygen (1 atm) by NHPI at 100 °C for 3 h followed by treatment with 0.3 M sulfuric acid at room temperature for 2 h resulted in phenol and cyclohexanone in 96% and 91% selectivity, respectively, at 25% conversion (Eq. (8)). This method was successfully extended to the one-pot synthesis of 4-hydroxyacetophenone and cyclohexanone.



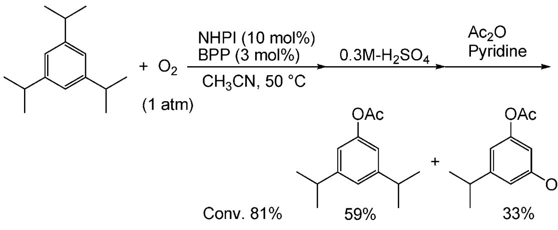
(8)

2,6-Naphthalenediol has attracted much attention for its chemical and physical properties as liquid crystalline monomer materials. A classical process is based on the sulfonation of naphthalene followed by alkali fusion of the resulting sulfonates [32]. However, 2,6-naphthalenediol is difficult to be synthesized in high yield by this method, which results in a complex mixture of several sulfonated products. There have been several patent works on the synthesis of 2,6-naphthalenediol by the oxidation of 2,6-diisopropylnaphthalene followed by treatment of the resulting 2,6-di(2-hydroxy-2-propyl)-naphthalene with H_2O_2 and H_2SO_4 [33]. Naphthalenediols were successfully synthesized by one-pot reaction through the oxidation of diisopropylnaphthalenes with air catalyzed by NHPI combined with α,α′-azobisisobutyronitrile (AIBN) followed by decomposition with sulfuric acid [34]. Thus, the oxidation of 2,6-diisopropylnphthalene with air (20 atm) in the presence of NHPI (10 mol%) and AIBN (3 mol%) in CH_3CN at 75 °C for 21 h followed by treatment with 0.3 M H_2SO_4 gave 2,6-naphtalenediol in 92% yield (Eq. (9)).



(9)

1,3,5-Triisopropylbenzene was efficiently oxidized with O_2 in the presence of a catalytic amount of NHPI and AIBN at 75 °C [35]. Upon treatment of the resulting products with sulfuric acid followed by acetic anhydride led to 5-acetoxy-1,3-diisopropylbenzene and 3,5-diacetoxy-1-isopropylbenzene as major products and a small amount of 1,3,5-triacetoxybenzene. When *tert*-butylperoxypivalate (BPP) was employed as a radical initiator, the oxidation could be achieved in good yield even at 50 °C (Eq. (10)).

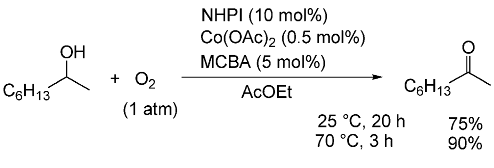


(10)

4. Oxidation of alcohols

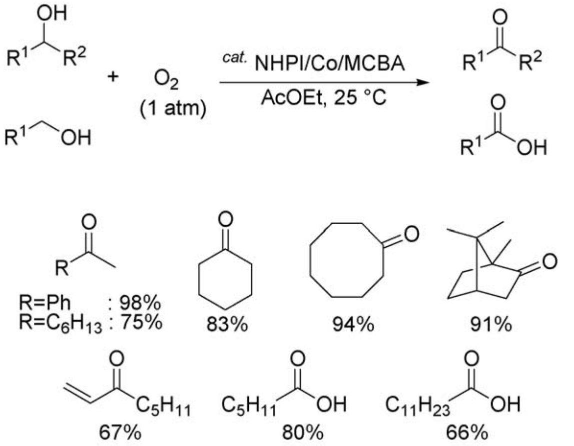
The oxidation of alcohols to the corresponding carbonyl compounds is a frequently used transformation in organic synthesis. There have been many catalytic methods for the aerobic oxidation of alcohols to the corresponding carbonyl compounds [36]. In 1996, Markó and coworkers developed an efficient aerobic oxidation system of aliphatic alcohols using an inexpensive $CuCl_2$/phenanthroline catalyst combined with azodicarboxylate [37]. Reusable heterogeneous catalysts consisting of Ru or Pd have been also reported [38]. Sheldon and coworkers have succeeded in the aerobic oxidation of alcohols by a water-soluble Pd catalyst [39].

As described in the preceding sections, alkanes are oxidized by the NHPI/Co(II) system with dioxygen under mild conditions. This catalytic system is expected to promote the aerobic oxidation of the hydroxy functions of alcohols to carbonyl functions [40]. The oxidation of 2-octanol in ethyl acetate at 70 °C in the presence of NHPI (10 mol%) and $Co(OAc)_2$ (0.5 mol%) under dioxygen (1 atm) gives rise to 2-octanone in quantitative yield. Benzoic acids such as *m*-chlorobenzoic acid (MCBA) enhance the oxidation of alcohols to carbonyl compounds. 2-Octanol can be converted into 2-octanone with O_2 even at room temperature by adding a catalytic amount of MCBA to the NHPI/$Co(OAc)_2$ system (Eq. (11)). The aerobic oxidation of aliphatic alcohols at room temperature has been reported only by Ley et al. who used $[Bu_4N]^+[RuO_4]^-$ assisted by 4A molecular sieves [41].



(11)

Scheme 4 shows the oxidation of secondary and primary alcohols under ambient conditions by the NHPI/$Co(OAc)_2$/MCBA system. Aromatic and cyclic alcohols afford the corresponding ketones in good to quantitative yields. Primary alcohols are also oxidized to carboxylic acids in good yields, although MCPBA is added instead of MCBA. Lauryl alcohol led to lauric acid (66% yield), which is used as a surfactant source. In this oxidation, which proceeds through a free radical process, primary alcohols are rapidly converted into carboxylic acids without isolation of aldehydes, because the hydrogen atom abstraction from aldehydes to afford acyl radicals takes place more easily than that from alcohols to furnish α-hydroxyalkyl radicals. The oxidation of allylic alcohols is easily achieved.

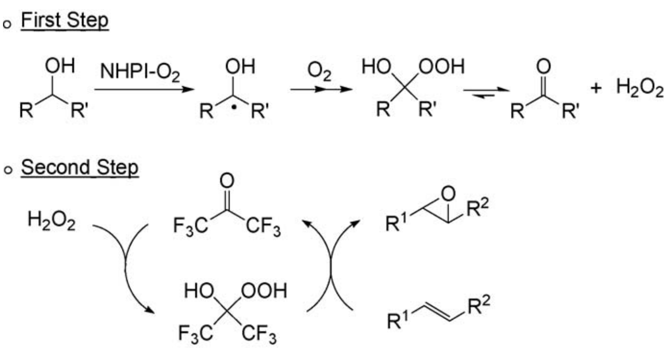


Scheme 4. Aerobic oxidation of alcohols by NHPI/Co/MCBA system.

5. Epoxidation of alkenes using dioxygen as terminal oxidant

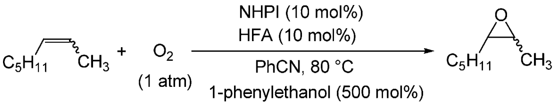
The epoxidation of alkenes using dioxygen via a catalytic process is a challenging subject in the field of oxidation chemistry. Much effort has been devoted to the epoxidation of alkenes with dioxygen using transition metals as catalysts. For instance, β-diketonate complexes of Ni, V, and Fe are reported to catalyze efficiently the epoxidation of alkenes with dioxygen in the presence of an aldehyde, alcohol, or acetal as a reducing agent under mild conditions [42]. On the other hand, Ru-porphyrin complexes and Ru-substituted polyoxometalates, $\{[WZnRu_2(OH)(H_2O)](ZnW_9O_{34})_2\}^{11-}$, catalyze the epoxidation of alkenes without any reducing agents [43].

The hexafluoroacetone (HFA)-catalyzed epoxidation of alkenes utilizing H_2O_2 obtained in situ by the NHPI-catalyzed aerobic oxidation of alcohols was examined (Scheme 5). A hydroperoxide derived from HFA and H_2O_2 has been reported to epoxidize various alkenes in fair to good yields [44]. This epoxidation system seems to be an interesting industrial



Scheme 5. A possible reaction path for the epoxidation of alkenes.

strategy, for it does not require the storage and transportation of explosive H_2O_2. In addition, the resulting ketones can be easily reduced to the original alcohols. 2-Octene was allowed to react under O_2 (1 atm) in the presence of 1-phenylethanol under the influence of catalytic amounts of NHPI (10 mol%) and HFA (10 mol%) in benzonitrile at 80 °C for 24 h, giving 2,3-epoxyoctane in 93% selectivity based on 93% conversion (Eq. (12)) [45]. This is the first successful epoxidation with H_2O_2 generated in situ from alcohols and O_2 without any metal catalysts. The important feature of this reaction is that the epoxidation of *cis*- and *trans*-2-octenes proceeded in a stereospecific manner to form *cis*- and *trans*-2,3-epoxyoctanes respectively, in high yields, although O_2 is used as a terminal oxidant.



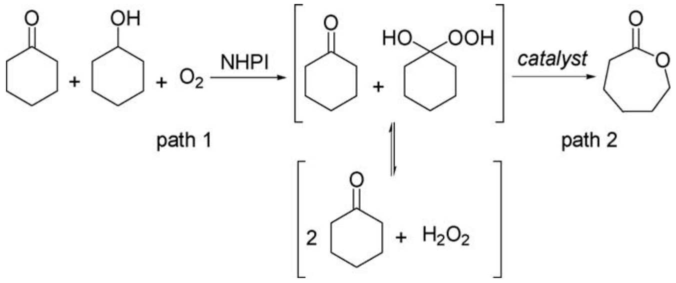
(12)

trans isomer	Conv. 93%	93% (*trans* : *cis* = 99 : 1)
cis isomer	Conv. 94%	86% (*cis* : *trans* = 98 : 2)

6. Baeyer–Villiger oxidation of K/A-Oil

K/A-oil, a mixture of cyclohexanone and cyclohexanol obtained by the aerobic oxidation of cyclohexane, is an important intermediate in petroleum industrial chemistry for the production of adipic acid and ε-caprolactam which are key materials for manufacturing 6,6-nylon and 6-nylon, respectively [46]. Baeyer–Villiger oxidation is a frequently used synthetic tool for conversion of cycloalkanones to lactones. Usually, this transformation is carried out by the use of peracids. However, the catalytic Baeyer–Villiger oxidation using dioxygen is limited to the in situ generation of peracids using excess aldehydes and O_2 [47]. From both a synthetic and an industrial points of view, it is very attractive that the K/A-oil can be used as the starting material for the production of ε-caprolactone with molecular oxygen via a catalytic process.

A new strategy for ε-caprolactone synthesis is outlined in Scheme 6. The aerobic oxidation of cyclohexanol catalyzed by NHPI gives a mixture of cyclohexanone and hydrogen peroxide through the formation of 1-hydroxy-1-hydroperoxycyclohexane (path 1). Treatment of the resulting reaction mixture with an appropriate catalyst would produce ε-caprolactone (path 2). Treatment of a 1:1 mixture of cyclohexanone (6 mmol) and cyclohexanol (6 mmol) by catalytic amounts of NHPI (0.6 mmol) and 2,2′-azobisisobutyronitrile (AIBN) (0.3 mmol) under O_2 atmosphere in CH_3CN at 75 °C for 15 h, followed by $InCl_3$ (0.45 mmol) at 25 °C for 6 h affords 12 in 57% selectivity based on the K/A-oil reacted, and 77% of K/A-oil was recovered [48].

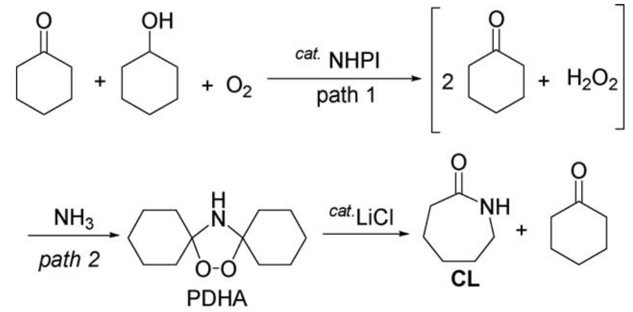


Scheme 6. A new strategy for the Baeyer–Villiger oxidation of K/A-oil.

7. Preparation of ε-caprolactam precursor from K/A-Oil

ε-Caprolactam (CL) is a very important monomer for the production of nylon-6, and about 4.2 million tonnes of CL were manufactured worldwide in 1998 [49]. Most methods of current CL production involve the conversion of cyclohexanone with hydroxylamine sulfate into cyclohexanone oxime followed by Beckmann rearrangement by the action of oleum and then treatment with ammonia giving CL. A serious drawback of this process is the co-production of a large amount of ammonium sulfate waste. Raja and Thomas reported a method for one-step production of cyclohexanone oxime and CL by the reaction of cyclohexanone with ammonia under pressure of air (34.5 atm) in the presence of a bifunctional molecular sieve catalyst [50]. In patent work, on the other hand, the transformation of 1,1′-peroxydicyclohexylamine (PDHA) to a 1:1 mixture of CL and cyclohexanone by LiBr has been reported [51].

It is interesting to develop a novel route to the CL precursor, PDHA, which was so far prepared by hydrogen peroxide oxidation of cyclohexanone followed by treatment with ammonia. Due to easy transformation of PDHA to a 1:1 mixture of CL and cyclohexanone under the influence of an appropriate catalyst such as lithium halides, the CL production via PDHA is considered to be a superior candidate of a next-generation waste-free process for CL. The NHPI-catalyzed aerobic oxidation of K/A-oil was applied to the synthesis of PDHA without formation of any ammonia sulfate waste. The strategy is outlined in Scheme 7. The NHPI-catalyzed oxidation of K/A-oil with O_2 produces 1,1′-dihydroxydicyclohexyl peroxide, which seems to exist in equilibrium with cyclohexanone and H_2O_2 (path 1). Subsequent treatment of the resulting reaction mixture with NH_3 would afford PDHA (path 2). A 1:2 mixture of cyclohexanone and cyclohexanone was reacted under dioxygen atmosphere (1 atm) in the presence of small amounts of NHPI and AIBN in ethyl acetate at 60 °C for 20 h, followed by the reaction with an atmospheric ammonia at 70 °C for 2 h to give 84% of PDHA at 24% conversion of K/A-oil



Scheme 7. A new strategy for the synthesis of ε-caprolactam precursor, PDHA.

[52]. This route provides a more economical and environmentally friendly process than that by the current method using hydroxylamine sulfate.

8. Conclusion

By employing *N*-hydroxyphthalimide (NHPI) as the catalyst, a novel aerobic oxidation of alkanes, which surpasses the conventional autoxidations in conversion and selectivity, has been achieved under mild conditions. This oxidation method provides entry to a diverse array of significant oxygen-containing compounds. Alcohols were successfully oxidized into the corresponding carbonyl compounds. The epoxidation of alkenes by in situ generated hydroperoxides or hydrogen peroxide has been explored for the first time. In addition, the oxidation of K/A-oil by NHPI could be applied to the preparation of ε-caprolactone and ε-caprolactam precursor.

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References

[1] G.W. Parshall, J. Mol. Catal. 4 (1978) 243.
[2] (a) D.D. Davis, in: W. Gerhartz (Ed.), 5th ed., Ullman's Encyclopedia of Industrial Chemistry, vol. A1, Wiley, New York, 1985, p. 270;
(b) D.D. Davis, D.R. Kemp, in: J.I. Kroschwitz, M. Howe-Grant (Eds.),4th ed., Kirk-Othmer Encyclopedia of Chemical Technology, vol. 1, Wiley, New York, 1990, , pp. 471–480and references cited therein.
[3] K. Tanaka, CHEMTECH 555 (1974), and references cited therein.
[4] (a) T. Oguchi, T. Ura, Y. Ishii, M. Ogawa, Chem. Lett. (1989) 857;
(b) K. Sato, M. Aoki, R. Noyori, Science 281 (1998) 1646.
[5] T. Iwahama, K. Syojyo, S. Sakaguchi, Y. Ishii, Org. Proc. Res. Dev. 2 (1998) 255.
[6] Y. Ishii, T. Iwahama, S. Sakaguchi, K. Nakayama, Y. Nishiyama, J. Org. Chem. 61 (1996) 4520.
[7] N. Sawatari, T. Yokota, S. Sakaguchi, Y. Ishii, J. Org. Chem. 66 (2001) 7889.
[8] A. Shibamoto, S. Sakaguchi, Y. Ishii, Tetrahedron Lett. 43 (2002) 8859.
[9] J.I. Kroschwitz, M. Howe-Grant (Eds.),4th ed., Kirk-Othmer Encyclopedia of Chemical Technology, vol. 1, Wiley, New York, 1990, See the following sections: (a) E. Billig, vol. 4, p. 691; (b) H.-D. Hahn, G. Dambkes, N. Rupprich, vol. A4, p. 463; (c) C.E. Loeffler, L. Stautzenberber, J.D. Unrun, vol. A4, p. 358, and references cited therein.
[10] (a) J.E. Lyons, P.E. Ellis Jr., in: R.A. Sheldon (Ed.), Metalloporphyrins in Catalytic Oxidations, vol. 291, Dekker, New York, 1994, and references cited therein;
(b) P.E. Ellis Jr., J.E. Lyons, Coord. Chem. Rev. 105 (1990) 181;
(c) H.L. Chen, P.E. Ellis Jr., T. Wijesekera, T.E. Hagan, S.E. Groh, J.E. Lyons, D.P. Ridge, J. Am. Chem. Soc. 116 (1994) 1086;
(d) M.W. Grinstaff, M.G. Hill, J.A. Labinger, H.B. Gray, Science 264 (1994) 1311.
[11] J.E. Lyons, P.E. Ellis Jr., H.K. Myers, J. Catal. 155 (1995) 59.
[12] S. Sakaguchi, S. Kato, T. Iwahama, Y. Ishii, Bull. Chem. Soc. Jpn. 71 (1998) 1240.
[13] (a) J.D. Bacha, J.K. Kochi, J. Org. Chem. 30 (1965) 3272;
(b) F.D. Greene, M.L. Savitz, F.D. Osterholts, H.H. Fau, W.H. Smith, P.M. Zanet, J. Org. Chem. 28 (1963) 55;
(c) J.K. Kochi, J. Am. Chem. Soc. 84 (1962) 1193.
[14] (a) S.-I. Murahashi, Y. Oda, T. Naota, J. Am. Chem. Soc. 114 (1992) 7913;
(b) N. Komiya, T. Naota, S.-I. Murahashi, Tetrahedron Lett. 37 (1996) 1633;
(c) N. Komiya, T. Naota, Y. Oda, S.-I. Murahashi, J. Mol. Catal. A: Chem. 117 (1997) 21;
(d) T. Punniyamurthy, S.J.S. Karla, J. Iqbal, Tetrahedron Lett. 36 (1995) 8497;
(e) P. Battioni, R. Iwanejko, D. Mansuy, T. Mlodnicka, J. Poltowicz, F. Sanches, J. Mol. Catal. A: Chem. 109 (1996) 91;
(f) A. Bravo, F. Fontana, F. Minisci, A. Serri, Chem. Commun. (1996) 1843;
(g) M.M. Dell'Anna, P. Mastrorilli, C.F. Nobile, J. Mol. Catal. A: Chem. 130 (1998) 65;
(h) N. Mizuno, M. Tateishi, T. Hirose, M. Iwamoto, Chem. Lett. (1993) 2137;
(i) S. Shinachi, M. Matsushita, K. Yamaguchi, N. Mizuno, J. Catal. 233 (2005) 81.
[15] Y. Ishii, S. Kato, T. Iwahama, S. Sakaguchi, Tetrahedron Lett. 37 (1996) 4993, We have found that quaternary ammonium bromides accelerate the NHPI-catalyzed aerobic oxidation even in the absence of any metal catalyst;
K. Matsunaka, T. Iwahama, S. Sakaguchi, Y. Ishii, Tetrahedron Lett. 40 (1999) 2165.
[16] H. Ohtake, T. Higuchi, M. Hirobe, J. Am. Chem. Soc. 114 (1992) 10660.
[17] R.A. Sheldon, in: L.I. Simándi (Ed.), Dioxygen Activation and Homogeneous Catalytic Oxidation, Elsevier, Amsterdam, 1991, p. 573.
[18] W.T. Reichle, F.M. Konrad, J.R. Brooks, in: E.G. Hancock (Ed.), Benzene and Its Industrial Derivatives, Benn, London, 1975.
[19] Y. Yoshino, Y. Hayashi, T. Iwahama, S. Sakaguchi, Y. Ishii, J. Org. Chem. 62 (1997) 6810.
[20] A. Mackor, T.A.J.W. Wajer, T. de Boer, Tetrahedron 24 (1968) 1623.
[21] F. Minisci, C. Punta, F. Recupero, F. Fontana, G.F. Pedulli, Chem. Commun. (2002) 688.
[22] (a) J.R. Sheehan, Ullman's Encyclopedia of Industrial Organic Chemicals, vol. 8, VCH, Weinheim, 1999, p. 4573;
(b) C. Park, J.R. Sheehan, in: J.I. Kroschwitz, M. Howe-Grant (Eds.),4th ed., Kirk-Othmer Encyclopedia of Chemical Technology, vol. 18, Wiley, New York, 1995, p. 991.
[23] (a) W.F. Brill, Ind. Eng. Chem. 52 (1960) 837;
(b) P. Raghavendrchar, S. Ramachandran, Ind. Eng. Chem. Res. 31 (1992) 453;
(c) K.A. Roby, P.J. Kingsley, CHEMTECH (1996) 39;
(d) A. Cincotti, R. Orru, G. Cao, Catal. Today 52 (1999) 331.
[24] (a) W. Partenheimer, Catal. Today 23 (1995) 69, and references cited therein;
(b) W. Partenheimer, Adv. Synth. Catal. 346 (2004) 1495;
(c) W. Partenheimer, J. Mol. Catal. A: Chem. 206 (2003) 105;
(d) W. Partenheimer, J. Mol. Catal. A: Chem. 206 (2003) 131.
[25] Y. Tashiro, T. Iwahama, S. Sakaguchi, Y. Ishii, Adv. Synth. Catal. 343 (2001) 220.
[26] N. Hirai, N. Sawatari, N. Nakamura, S. Sakaguchi, Y. Ishii, J. Org. Chem. 68 (2003) 6587.
[27] N. Hirai, T. Kagayama, Y. Tatsukawa, S. Sakaguchi, Y. Ishii, Tetrahedron Lett. 45 (2004) 8277.
[28] (a) J. Rigueras, P.W. Scullard, A.R. Mack, J. Org. Chem. 36 (1971) 3497;
(b) K. Haghbeen, E.W. Tan, J. Org. Chem. 63 (1998) 4503.
[29] (a) H. Hock, S. Lang, Ber. Dtsch, Chem. Ges. B77 (1944) 257;
(b) W. Jordan, H. van Barneveld, O. Gerlich, M.K. Boymann, J. Ullrich, Ullmann's Encyclopedia of Industrial Organic Chemicals, vol. A9, Wiley-VCH, Weinheim, 1985, p. 299;
(c) R.A. Sheldon, J.K. Kochi, Metal-catalyzed Oxidations of Organic Compounds, Academic, New York, 1981.

[30] I.W.C.E. Arends, M. Sasiidharan, A. Kuhnle, M. Duda, C. Jost, R.A. Sheldon, Tetrahedron 58 (2002) 9055.
[31] Y. Aoki, S. Sakaguchi, Y. Ishii, Tetrahedron 61 (2005) 5219.
[32] A.P. Kuriakose, J. Indian Chem. Soc. 43 (1966) 437.
[33] (a) T. Iwane, T. Sugawara, N. Suzuki, K. Kaneko, JP Patent 04099741 (1992).;
(b) T. Taguchi, H. Fukuhara, H. Miki, K. Saeki, JP Patent 62,238,225 (1987).
[34] Y. Aoki, S. Sakaguchi, Y. Ishii, Adv. Synth. Catal. 345 (2004) 199.
[35] Y. Aoki, S. Sakaguchi, Y. Ishii, Tetrahedron 61 (2005) 10995.
[36] (a) R.A. Sheldon, I.W.C.E. Arends, G.-J. Ten Brink, A. Dijksman, Acc. Chem. Res. 35 (2002) 774;
(b) R.A. Sheldon, I.W.C.E. Arends, Catal. Today 57 (2000) 157.
[37] (a) I.E. Markó, P.R. Giles, M. Tsukazaki, C.J. Urch, Science 274 (1996) 2044;
(b) I.E. Markó, P.R. Giles, M. Tsukazaki, I.C. Regnaut, A. Gautier, M. Brown, C.J. Urch, J. Org. Chem. 64 (1999) 2433.
[38] (a) K. Yamaguchi, K. Mori, T. Mizugaki, K. Ebitani, K. Kaneda, J. Am. Chem. Soc. 122 (2000) 7144;
(b) K. Yamaguchi, N. Mizuno, Angew. Chem. Int. Ed. 41 (2002) 4538;
(c) T. Nishimura, N. Kakiuchi, M. Inoue, S. Uemura, Chem. Commun. (2000) 1245.
[39] (a) G.-J. ten Brink, I.W.C.E. Arends, R.A. Sheldon, Science 287 (2000) 1636;
(b) Y. Uozumi, R. Nakao, Angew. Chem. Int. Ed. 42 (2003) 194.
[40] T. Iwahama, Y. Yoshino, T. Keitoku, S. Sakaguchi, Y. Ishii, J. Org. Chem. 65 (2000) 6502.
[41] R. Lenz, S.V. Ley, J. Chem. Soc., Perkin Trans. 1 (1997) 3291.
[42] T. Mukaiyama, T. Yamada, Bull. Chem. Soc. Jpn. 68 (17) (1995), and references cited therein.
[43] (a) J.T. Groves, R. Quinn, J. Am. Chem. Soc. 107 (1985) 5790;
(b) R. Neumann, M. Dahan, Nature 388 (1997) 24;
(c) Y. Nishiyama, Y. Nakagawa, N. Mizuno, Angew. Chem. Int. Ed. 40 (2001) 3639.
[44] (a) R.P. Heggs, B. Ganem, J. Am. Chem. Soc. 101 (1979) 2484;
(b) A.J. Biloski, R.P. Heggs, B. Ganem, Synthesis (1980) 810;
(c) M.C.A. van Vliet, I.W.C.E. Arends, R.A. Sheldon, Chem. Commun. (1999) 263.
[45] T. Iwahama, S. Sakaguchi, Y. Ishii, Chem. Commun. (1999) 727.
[46] (a) T. Michael, E.I. Musser, Ullman's Encyclopedia Industrial Organic Chemicals, vol. 3, Wiley-VCH, Weinheim, 1807;
(b) W.B. Fisher, J.F. Van Peppen, in: J.L. Kroshwite, M. Home-Grant (Eds.),4th ed., Kirk–Othmer Encyclopedia of Chemical Technology, vol. 7, John Wiley and Sons, New York, 1995, p. 851.
[47] (a) S. Murahashi, Y. Oda, T. Naota, Tetrahedron Lett. 33 (1992) 7557;
(b) T. Yamada, K. Takahashi, K. Kato, T. Takai, S. Inoki, T. Mukaiyama, Chem. Lett. (1991) 641.
[48] O. Fukuda, S. Sakaguchi, Y. Ishii, Tetrahedron Lett. 42 (2001) 3479.
[49] (a) V.D. Luedeke, in: J.J. Mcketta (Ed.), Encyclipedia of Chemical Processing and Design, Marcel Dekker, New York, 1978, p. 73;
(b) W.N. Fisher, L. Crescentini, in: J.I. Kroschwitz (Ed.), Kirk-Othmer Encyclopedia of Chemical Technology, vol. 4, John Wiley & Sons, New York, 1992, p. 827;
(c) J. Ritz, H. Fuchs, H. Kiecza, W.C. Moran, Ullmann's Encyclopedia of Industrial Organic Chemicals, vol. 2, Wiley-VCH, Weinheim, 1999, p. 1013.
[50] R. Raja, G. Sankar, J.M. Thomas, J. Am. Chem. Soc. 123 (2001) 8153.
[51] (a) N. Kakeya, T. Takai, JP Patent 2,001,122,851 (2001).;
(b) E.G.E. Hawkins, US Patent 3,947,406 (1976).;
(c) C.W. Capp, B.W. Harris, E.G.E. Hawkins, G.E. Edwin, FR Patent 1,567,559 (1969).
(d) J.S. Reddy, S. Sivasanker, P. Ratnasamy, J. Mol. Catal. 69 (1991) 383.
[52] S. Yamamoto, S. Sakaguchi, Y. Ishii, Green Chem. 5 (2003) 300.