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An Efficient Aerobic Oxidation of Isobutane to *t*-Butyl Alcohol by *N*-Hydroxyphthalimide Combined with Co(II) Species

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Highly selective aerobic oxidation of isobutane to *t*-butyl alcohol was successfully achieved by the use of a radical catalyst, *N*-hydroxyphthalimide (NHPI) in the presence of Co(II) salt under relatively mild conditions. The oxidation of isobutane by NHPI combined with $Co(acac)_2$ under a pressure of air (10 atm) in benzonitrile at 100 °C gave *t*-butyl alcohol in high yield (84%) along with acetone (13%). The reaction is thought to proceed via hydrogen abstraction from isobutane by the phthalimidooxyl radical (PINO), which seems to be a key active species. The formation of acetone can be explained by a partial β-scission of the *t*-butoxy radical, generated from the redox decomposition of *t*-butyl hydroperoxide by cobalt ion. Alkyl-substituted butanes and pentanes were difficult to be oxidized selectively under these conditions because of easy degradation to smaller fragments of the resulting alkoxyl radical intermediates.

The conversion of alkanes to oxygen-containing compounds is one of the most important and fundamental transformations in synthetic organic chemistry. For instance, the oxidation of lower alkanes to alcohols and carbonyl compounds is a promising subject in industrial organic chemistry.[1] Lower alkanes, such as butane and isobutane, are currently converted into acetic acid and *t*-butyl alcohol or hydroperoxide, respectively, by homogeneous liquid-phase oxidation with molecular oxygen using a cobalt salt, which is commonly referred to as autoxidation.[2] However, since the autoxidation of alkanes involves a homolytic cleavage of a carbon-hydrogen bond having a high bond dissociation energy (90—100 $\mathrm{kcal\,mol^{-1}}$) in the reaction sequence, the reaction must be carried out under relatively severe reaction conditions, higher temperature (150—250 °C) and oxygen (or air) pressure (10—30 atm).[2,3] As a consequence, the oxidation must be practiced in a lower conversion of alkanes to prevent the formation of undesired side products.

In response to increasing demand for mild aerobic oxidation in the area of synthetic organic chemistry, both in large-scale processes and in the manufacturing of fine chemicals, considerable efforts have been paid to the liquid-phase oxidation of alkanes with molecular oxygen by a variety of transion-metal complexes, such as Mn,[4] Ru, Fe,[5] Cu,[6] Eu,[7] Co,[8] and V.[9] However, the oxidations using these complexes have called for either the coexistence of a reducing reagent[4—9] or photo-[10] and electrochemical assistances.[11]

Recently, Lyons and Ellies showed that halogenated metalloporphyrin complexes are efficient catalysts for the direct oxygenation of acyclic alkanes with molecular oxygen under relatively mild conditions (i.e., at around 100 °C, and 6.8 atm of O_2).[12—14] For instance, the oxidation of isobutane catalyzed by 5,10,15,20-terakis(pentafluorophenyl)-2,3,7,8,12,13,17,18-octabromoporphrin iron complex gave *t*-butyl alcohol (89% selectivity) in 45% conversion.[12a] More recent patent work by their group has shown that *t*-butyl alcohol was produced in 81—90% yield by the use of a new type of 5,10,15,20-terakis(haloalkyl)porphrin iron complex.[15] Based on economical and environmental importance, the selective catalytic oxidation of lower alkanes with molecular oxygen without any co-reductant or photo- and electrochemical assistances is an area in which continued research and technical breakthroughs will be required.

In previous papers we have reported that various organic substrates, such as diols, alkylbenzenes, cycloalkanes, and adamantanes, are smoothly oxidized with molecular oxygen (1 atm) by *N*-hydroxyphthalimide (NHPI), which serves as a radical catalyst, in the absence or presence of $Co(acac)_n$ ($n = 2$ or 3) under mild conditions.[16] We now wish to report on the selective oxidation of isobutane to *t*-butyl alcohol with dioxygen by NHPI combined with the Co(II) species.

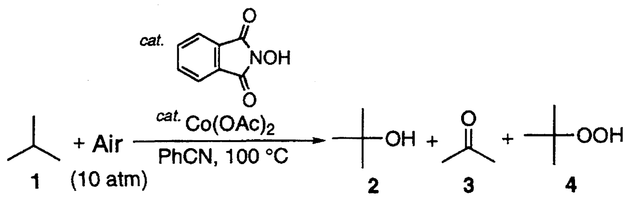
Results and Discussion

The representative results for the oxidation of isobutane (**1**) with air catalyzed by NHPI under various reaction conditions are given in Table 1. The oxidation of **1** by air (10 atm) in the presence of NHPI (10 mol%) in benzonitrile at 100 °C produced *t*-butyl hydroperoxide (**4**) (8%) as a major product along with small amounts of *t*-butyl alcohol (**2**) (3%) and acetone (**3**) (4%) (Run 1) (Eq. 1). Interestingly, the oxidation of **1** with air by NHPI was markedly enhanced by adding a slight amount of $Co(OAc)_2$ (0.25 mol%) to produce **2** in higher yield (81%) and **3** (14%) (Run 2).

Table 1. Oxidation of Isobutane (**1**) with Dioxygen Catalyzed by NHPI and $Co(OAc)_2$ [a]

Run	NHPI	$Co(OAc)_2$	Temp	Yield (%)		
	mol%	mol%	°C	**2**	**3**	**4**
1	10	0	100	3	4	8
2	10	0.25	100	81	14	0
3	0	0.25	100	2	<1	0
4[b]	10	0.25	100	66	16	0
5	10	0.25	80	63	8	6
6[c]	10	0.25	50	32	5	5
7	5	0.25	100	63	11	0
8[d]	10	0.25	100	No reaction		
9[e]	10	0.25	100	21	22	0

a) **1** (5 mmol) was allowed to react in the presence of NHPI and $Co(OAc)_2$ under a pressure of air (10 atm) in benzonitrile (10 mL) for 8 h. b) A pressure of air was 5 atm. c) Reaction was carried out for 48 h. d) 2,4-Di-*t*-butyl-*p*-cresol (1 mol%) was added. e) Acetic acid (10 mL) was used as solvent.



(1)

It is noteworthy that **2** was produced in satisfactory yield even under 5 atm of air (Run 4). The oxidation at 80 °C gave **2** (63%), **3** (8%), and **4** (6%) (Run 5). **1** was oxidized even at 50 °C by the present catalytic system, although a somewhat longer reaction time was needed (Run 6). When the amount of NHPI was halved, **2** was obtained in 63% yield (Run 7). These findings show that the present oxidation provides a practical method for the oxidation of **1** to **2** under mild conditions.

In contrast to the oxidation of cycloalkanes and alkylbenzenes where acetic acid serves as a good solvent,[16] the oxidation of **1** in acetic acid resulted in a considerable amount of cleaved product **3** (Run 9). It is thus believed that the *t*-butyl hydroperoxide **4**, formed as the primary product, is labile in acetic acid. Hydroperoxides are known to be easily degraded to carbonyl compounds by acids.[17] Among the solvents examined, benzonitrile was found to be the best. The reaction did not take place at all in the presence of a radical scavenger, 2,4-di-*t*-butyl-*p*-cresol (1 mol%) (Run 8). No oxidation of **1** by $Co(OAc)_2$ without NHPI under these conditions took place, and a large part of the starting material, **1**, was recovered unchanged (Run 3).

Figure 1 shows time-dependence curves of products, **2**, **3**, and **4** in the oxidation of **1** with air (10 atm) by NHPI combined with $Co(OAc)_2$. This indicates that **4** is the primary product during the early stage of oxidation.

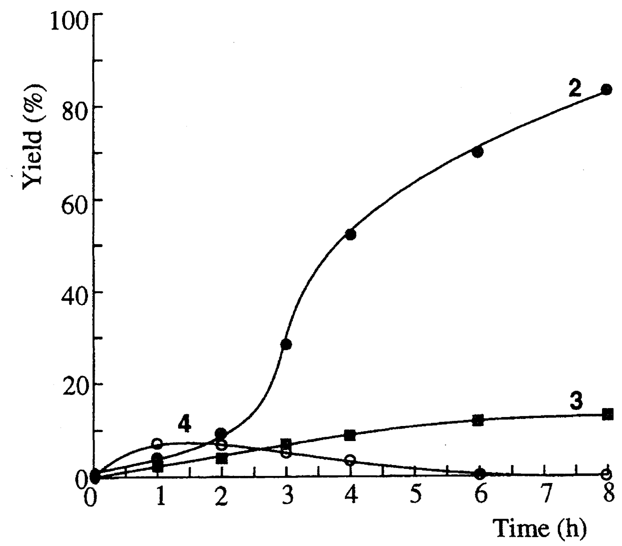


Fig. 1. Time-dependence curves for the oxidation of isobutane (**1**) with dioxygen catalyzed by *N*-hydroxyphthalimide (NHPI) Combined with $Co(OAc)_2$ in PhCN at 100 °C.

Table 2. Effect of Transion Metal Salt in the Oxidation of Isobutane (**1**) with Dioxygen Catalyzed by NHPI[a]

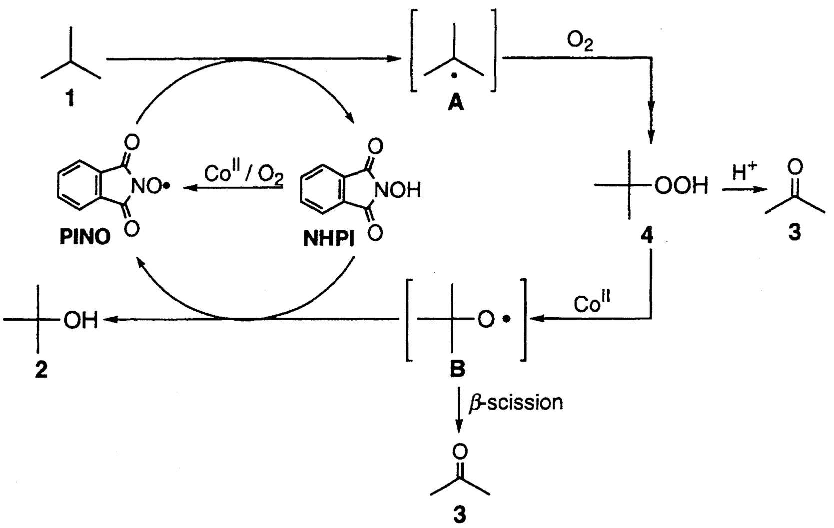
Metal	Yield/%		Metal	Yield/%	
	2	**3**		**2**	**3**
—	3	4	$Fe(acac)_3$	52	9
$TiO(acac)_2$	6	2	$Co(acac)_2$	84	13
$V(acac)_3$	18	9	$Co(acac)_3$	58	10
$Cr(acac)_3$	52	9	$Ni(acac)_2$	25	6
$Mn(acac)_2$	28	8	$Cu(acac)_2$	47	11
$Mn(acac)_3$	48	12	$Zn(acac)_2$	2	1

a) **1** (5 mmol) was allowed to react in the presence of NHPI (10 mol%) and metal complex (0.25 mol%) under a pressure of air (10 atm) in benzonitrile (10 mL) at 100 °C for 8 h.

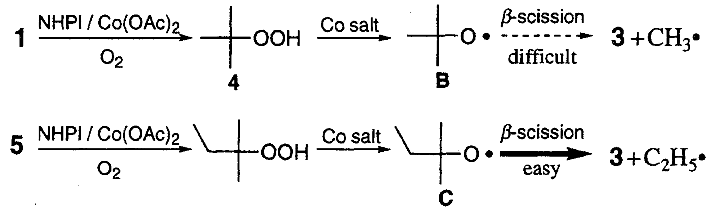
In order to obtain information about metal ions on the NHPI-catalyzed oxidation of **1**, various acetylacetonato complexes of the fourth-period transition metals were examined (Table 2). Among them, Co(II) was found to be the best additive, followed by Co(III), Cr(III), Mn(III), Fe(III), and Cu(II); however, Ti(IV) and Zn(II) were inert in this oxidation.

Since molecular oxygen, due to its triplet ground state, cannot react with alkanes in the singlet ground state, the major role of metal ions is to bind and activate the dioxygen as well as to facilitate the decomposition of any intermediates, such as hydroperoxides. The metal ions that accelerate the present NHPI-catalyzed aerobic oxidation of **1** are known to form some metal–oxygen complexes that react with molecular oxygen.[18] For instance, the Co(II) species have been reported to react with dioxygen to form a cobalt–oxygen complex, $L_2CoOO\cdot$, as well as $L_2CoOOCoL_2$.[19] The thus generated cobalt–oxygen complexes abstract the hydrogen atom from the NHPI to produce phthalimidooxyl (PINO).[20]

Therefore, a possible reaction path for the present oxidation is illustrated in Scheme 1. The reaction is initiated by the abstraction of hydrogen from NHPI with a cobalt-oxygen complex to generate PINO. The resulting PINO abstracts hydrogen from **1** to produce isobutyl radical (**A**), which is readily trapped by dioxygen to give the *t*-butyl hydroperoxy radical, and eventually **4**. Under these conditions, **4** is



Scheme 1. A possible reaction path for the aerobic oxidation of isobutane (**1**) catalyzed by NHPI combined with $Co(OAc)_2$.



Scheme 2.

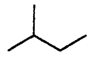
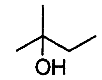
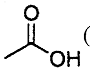
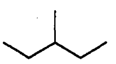
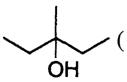
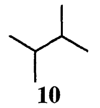
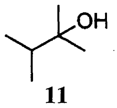
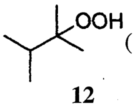
rapidly decomposed by metal ions, such as the Co(II) ion, to the *t*-butoxy radical (**B**), on which subsequent abstraction of the hydrogen atom from NHPI or **1** produces PINO or **A**, respectively. Therefore, such metal species as Cr, Mn, Fe, and Cu, which are commonly used as catalysts for autoxidation, participate in the generation of organic radicals, such as **B**, which can react with dioxygen to produce hydroperoxides. A part of the **B** undergoes a β-scission to form cleaved product **3**, as described later.

We next examined the NHPI-catalyzed aerobic oxidation of several lower alkanes (Table 3). Methyl-substituted butane and pentane, such as 2-methylbutane (**5**) and 3-methylpentane (**8**), were oxidized under air pressure (10 atm) in the presence of NHPI and $Co(OAc)_2$ in benzonitrile at 100 °C to afford carbon–carbon bond cleaved products, acetone **3** and acetic acid **7**, as major products in preference to the corresponding alcohols. In the oxidation of 2,3-dimethylbutane (**10**) under these conditions, 1,2,2-trimethylpropyl hydroperoxide (**12**) (23%) was obtained as the major product together with the corresponding alcohol, 2,3-dimethyl-2-butanol (**11**) (11%), and cleaved product **3** (12%).

Alkyl hydroperoxides by metal ions, such as $FeSO_4$, brought about carbon–carbon bond cleaved products through the β-scission of alkoxyl radical intermediates; the extent of the β-scission depends on the structure of the resulting alkoxyl radicals.[21] Since the *t*-butoxy radical (**B**) is more stable than the *t*-pentyloxyl radical (**C**), it is though that **1** produced alcohol **2** as the principal product, while **5** gave cleaved products **3** and **7** (Scheme 2).

In conclusion, the selective catalytic oxidation of isobutane **1** to *t*-butyl alcohol **2** with air was successfully achieved using the radical catalyst, NHPI, combined with Co(II) salt with high selectivity under relatively mild conditions. This oxidation provides a practical method for the conversion of **1** into *t*-butyl alcohol **2**.

Table 3. Oxidation of Several Alkanes with Dioxygen Catalyzed by NHPI and $Co(OAc)_2$ [a]

Substrate	Products (Yield/%)		
 5	 6 (21)	3 (32)	 7 (15)
 8	 9 (13)	7 (24)	
 10	 11 (11)	 12 (23)	3 (12)

a) Substrate (5 mmol) was allowed to react in the presence of NHPI (10 mol%) and $Co(OAc)_2$ (0.25 mol%) under a pressure of air (10 atm) in benzonitrile (10 mL) at 100 °C for 8 h.

Experimental

General. All starting materials and catalysts were purchased from commercial sources and used without further treatment. The yields of products were estimated from the peak areas based on the internal standard technique. A GC analysis was performed with a flame ionization detector using a 0.2 mm×25 m capillary column

(OV-1). GC-MS spectra were obtained at an ionization energy of 70 eV.

General Procedure for Oxidation of Isobutane (1). The reaction was carried out in autoclave. Isobutane (**1**) was treated as liquid at −15 °C. To benzonitrile (10 mL) was added isobutane (**1**) (5 mmol), NHPI (0.5 mmol, 10 mol%), and $Co(OAc)_2$ (0.0125 mmol, 0.25 mol%) in an autoclave. The autoclave was pressurized to 10 atm with air. The mixture was stirred at 100 °C for 8 h. After the reaction, the GC and GC-MS analyses were performed. The products were identified through a comparison of the MS spectral data of the products with that of the authentic samples.

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