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A Remarkable Effect of Quaternary Ammonium Bromide for the *N*-Hydroxyphthalimide-Catalyzed Aerobic Oxidation of Hydrocarbons

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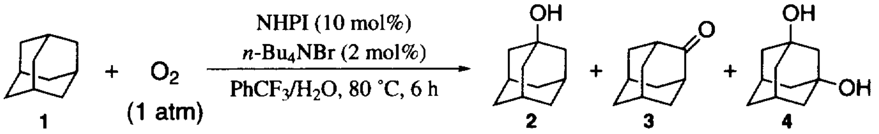
Abstract : A methodology for the aerobic oxidation of organic substrates in the absence of any metal catalyst has been established using combined catalytic system consisting of *N*-hydroxyphthalimide and quaternary ammonium bromide. Thus, various hydrocarbons were successfully oxidized under dioxygen atmosphere to the corresponding oxygenated compounds in good selectivities.

The development of a catalytic oxidation system using molecular oxygen as an oxidant is a major challenge in organic chemistry.[1] Such a system would have high economic and environmental values in industrial chemistry. The autoxidation of hydrocarbons, which is currently carried out on commercial scale, calls for the coexistence of a bromide ion in addition to cobalt and/or manganese salts to accelerate the reaction.[2] Recently, it has been reported that the autoxidation of hydrocarbons is enhanced in the presence of a quaternary ammonium salt under a two-phase condition.[3]

We have shown that a variety of organic substrates are successfully oxidized with molecular oxygen using *N*-hydroxyphthalimide (NHPI) as the radical catalyst,[4] and that the oxidation is considerably facilitated by adding a small amount of a transition metal salt such as $Co(OAc)_2$.[5] Now, we have found that a quaternary ammonium bromide accelerates the NHPI-catalyzed aerobic oxidation even in the absence of any metal catalyst. Thus, various hydrocarbons were oxidized with dioxygen in the presence of a catalytic amount of NHPI and quaternary ammonium bromide in $PhCF_3$ containing a very small amount of water. In this paper, we wish to report the scope and limitations in the aerobic oxidation catalyzed by NHPI combined with quaternary ammonium bromide.

A typical reaction was carried out as follows. To a solution of adamantane (**1**) (2 mmol) in trifluorotoluene and water (6/0.03 mL) in a three-necked flask were added NHPI (0.2 mmol) and n-Bu_4NBr (0.04 mmol), and then the flask was flushed with oxygen and equipped with a balloon filled with O_2. The reaction mixture was allowed to react at 80 °C for 6 h (standard conditions). After removing the solvent *in vacuo*, the products were



(1)

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Table 1 Aerobic oxidation of **1** catalyzed by NHPI under selected conditions[a]

Entry	Additive	Solvent (mL)	Conv.(%)	Selectivity (%)[b]		
				2	**3**	**4**
1	–	$PhCF_3$ (6)	12	58	<1	42
2	n-Bu_4NBr	$PhCF_3$ (6)	13	54	8	<1
3	n-Bu_4NBr	$PhCF_3/H_2O$ (6/0.03)	73	60	12	23
4	n-Bu_4NBr	$PhCF_3/H_2O$ (6/0.01)	40	65	10	6
5	n-Bu_4NBr	$PhCF_3/H_2O$ (6/0.06)	42	63	10	6
6	n-Bu_4NBr	$PhCl/H_2O$ (6/0.03)	43	58	12	7
7	Me_4NBr	$PhCF_3/H_2O$ (6/0.03)	55	65	10	16
8	$(n$-$C_5H_{11})_4NBr$	$PhCF_3/H_2O$ (6/0.03)	62	65	11	21
9	LiBr	$PhCF_3/H_2O$ (6/0.03)	no reaction			
10	n-Bu_4NCl	$PhCF_3/H_2O$ (6/0.03)	46	67	11	15
11	n-Bu_4PBr	$PhCF_3/H_2O$ (6/0.03)	56	61	10	7

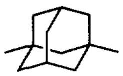
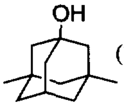
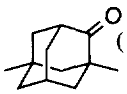
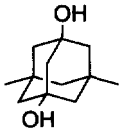
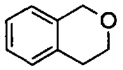
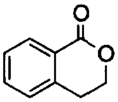
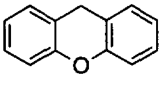
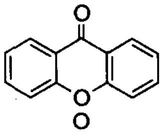
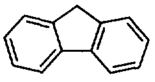
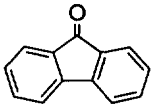
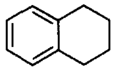
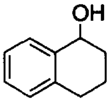
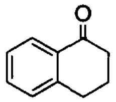
[a]**1** (2 mmol) was allowed to react under dioxygen atmosphere (1 atm) in the presence of NHPI (10 mol%) and additive (2 mol%) at 80 °C for 6 h. [b]Selectivity of the product was determined by GC analysis using internal standard.

isolated by column chromatography on silica gel (hexane/ethyl acetate).

The oxidation of adamantane (**1**) with molecular oxygen was chosen as a model reaction and carried out under various conditions (Table 1). The oxidation of **1** in the presence of a catalytic amount of NHPI (10 mol%) at 80 °C for 6 h produced 1-adamantanol (**2**) and 1,3-adamantanediol (**4**) in 58% and 42% selectivity, respectively, but the conversion was low (entry 1). However, when the reaction was carried out in the presence of tetra-*n*-butylammonium bromide (TBAB) (2 mol%) in $PhCF_3$ containing a small amount of H_2O, the conversion of **1** markedly increased from 12% to 73% to give **2** in 60% selectivity along with 2-adamantanone (**3**) (12%) and **4** (23%) (entry 3). However, in the absence of H_2O, no acceleration by TBAB was observed (entry 2). The reaction was found to be very sensitive to water content (entries 4 and 5). The use of PhCl as a solvent resulted in a moderate conversion, probably because of lower solubility of dioxygen in PhCl than that in $PhCF_3$ (entry 6).[6] The effect of Me_4NBr and $(n$-$C_5H_{11})_4NBr$ was almost the same as that of TBAB, but LiBr was inert (entries 7 to 9). n-Bu_4NCl and quaternary phosphonium bromide, n-Bu_4PBr, showed moderate effects in this oxidation (entries 10 and 11). At the end of the reaction NHPI was almost converted into phthalimide, which does not catalyze the reaction.

The relative reactivity of the tertiary hydrogen of **1** to the secondary one after statistical correction for the number of hydrogen atoms was ca. 21 (entry 3), although for simple free-radical hydrogen abstraction by Br• the value of 3°/2° is reported to be between 3.8 and 5.4.[7] In contrast, the 3°/2° value is 31 in the aerobic oxidation of **1** catalyzed by NHPI combined with $Co(acac)_2$.[5a] This indicates that the present oxidation by the NHPI/TBAB system takes place through a similar way as the NHPI/$Co(acac)_2$ system, in which phthalimide-*N*-oxyl (PINO) was thought to be an active species. Hence, we assume that the abstraction of a hydrogen atom from **1** by phthalimide-*N*-oxyl is a key step in this oxidation. It seems likely that the reaction is initiated by the hydrogen abstraction by PINO generated from NHPI and dioxygen[5a] and that the TBAB acts as a surfactant to generate reversed micelles in a mixed solvent of $PhCF_3$ and H_2O, and assists the decomposition of the resulting

Table 2 Aerobic oxidation of various compounds catalyzed by NHPI and TBAB[a]

Entry	Substrate	Time (h)	Conv. (%)	Product (Selectivity / %)[b]
1		24	68	 (74)  (15)  (9)
2		0.5	98	 (92)
3		6	64	 (86)
4		6	45 (3)[c]	 (99)
5		6	49 (14)[c]	 (53)  (20)

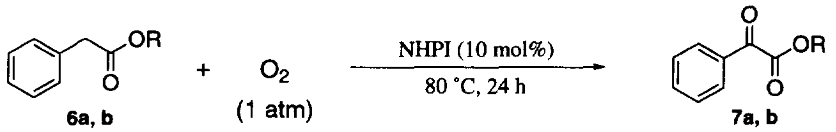
[a] Substrate (2 mmol) was allowed to react under dioxygen atmosphere (1 atm) in the presence of NHPI (10 mol%) and TBAB (2 mol%) in $PhCF_3/H_2O$ (6/0.03 mL) at 80 °C. [b] Selectivity of the product was determined by GC analysis using internal standard. [c] Conversions in the absence of TBAB.

hydroperoxides to alkoxy radicals which promote the radical transfer.[2,3] In fact, in a separate experiment cumene hydroperoxide (5) was rapidly decomposed within 1 h in the presence of a catalytic amount of TBAB (2 mol%) in $PhCF_3/H_2O$ at 80 °C (the conversion of **5** was 83%), while most of **5** was recovered unchanged in the absence of TBAB under these conditions (the conversion of **5** was 7%).

On the basis of these results, various organic substrates were oxidized with dioxygen catalyzed by the combined catalytic system of NHPI and TBAB (Table 2). 1,3-Dimethyladamantane was also oxidized in the presence of NHPI and TBAB at 80 °C for 24 h to form the corresponding oxygenated products, alcohol (74%), diol (9%), and ketone (15%) (entry 1). On the other hand, isochromane was rapidly converted into isochromanone within 30 min under standard conditions. The oxidation of fluorene and tetralin proceeded in moderate conversions forming the corresponding ketones and alcohols, although in the absence of TBAB, the conversions of these oxidations were only 3% and 14%, respectively (entries 4 and 5).

Interestingly, the oxidation of ethyl phenylacetate (**6a**) was successfully performed by the present catalytic system. The oxidation of **6a** catalyzed by NHPI/TBAB gave ethyl 2-oxo-phenylacetate (**7a**) in excellent selectivity (99%) at 59% conversion, while the oxidation by NHPI/$Co(acac)_2$ in acetic acid failed (eq. 2).[8] Although the oxidation of esters to the corresponding α-keto esters was achieved by the CrO_3-Ac_2O system,[9] there is no report for the oxidation using dioxygen as an oxidant. Like **6a**, isopropyl phenylacetate (**6b**) was successfully oxidized to the corresponding α-keto esters **7b** without the oxygenation of the isopropyl moiety. However, no reaction occurred when ethyl hexanoate was allowed to react under these conditions.

In conclusion, a catalytic amount of quaternary ammonium bromide was found to accelerate the aerobic



(2)

R	additive (mol%)	solvent	conv. (%)	select. (%)
Et (**6a**)	*n*-Bu_4NBr (2)	$PhCF_3/H_2O$	59	99
Et (**6a**)	$Co(acac)_2$ (0.5)	AcOH	26	57
^{i}Pr (**6b**)	*n*-Bu_4NBr (2)	$PhCF_3/H_2O$	65	97

oxidation of various hydrocarbons by NHPI catalyst in $PhCF_3$ containing a very small amount of water in the absence of any metal catalyst. In addition, phenylacetates were successfully oxidized to the corresponding α-keto esters which are difficult to prepare by conventional oxidation methods.

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8 Under these conditions a variety of organic substrates, such as adamantanes, alkylbenzens, and cycloalkanes, were oxidized to produce the corresponding alcohols, carbonyl compounds, and carboxylic acids in good yields (See ref. 5).

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