EPOXIDATION OF ALKENES WITH H_2O_2 GENERATED *IN SITU* FROM ALCOHOLS AND MOLECULAR OXYGEN USING *N*-HYDROXYPHTHALIMIDE AND HEXAFLUOROACETONE AS CATALYSTS

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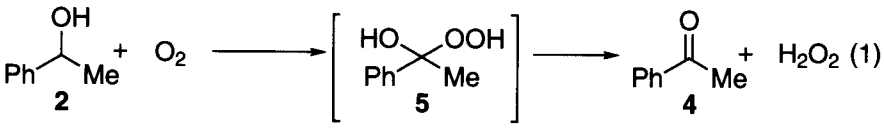
Abstract——A new epoxidation method of olefins with hydrogen peroxide and/or α-hydroxy hydroperoxide which are generated *in situ* from an alcohol and molecular oxygen was developed. A variety of alkenes were smoothly epoxidized with molecular oxygen in the presence of an alcohol under the influence of hexafluoroacetone (HFA) and *N*-hydroxyphthalimide (NHPI) as catalysts. The reaction involves the formation of α-hydroxy hydroperoxide and/or hydrogen peroxide derived from 1-phenylethanol and dioxygen by the action of NHPI and the active oxygen transfer from these hydroperoxides to HFA, giving 2-hydroperoxyhexafluoro-2-propanol which serves as the actual epoxidizing agent.

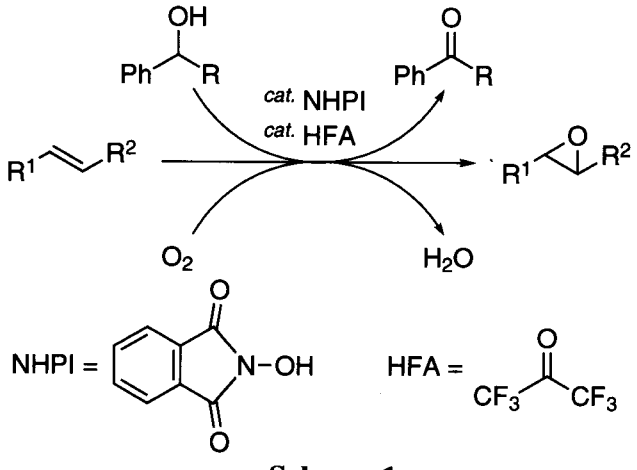
INTRODUCTION

The selective oxidation of olefins to the corresponding epoxides is an important and frequently used transformation in organic synthesis. Hence, numerous methods using various oxidants have been developed for this purpose.[1] Although the epoxidation utilizing molecular oxygen as the oxidant is a very useful and promising synthetic tool, the direct introduction of molecular oxygen into a carbon-carbon double bond of alkenes is difficult to carry out because of the restriction by spin conservation for the reaction of organic compounds with molecular oxygen in the ground state (triplet). Thus, much effort has been paid to develop the epoxidation of alkenes using molecular oxygen.[2] In recent years, the epoxidation of alkenes has been successfully performed by using methods combined with molecular oxygen and various reducing reagents such as aldehydes under the influence of metal complexes and heteropolyoxometalates.[3] For instance, β-diketonate complexes of Ni,[3a,b,r] V[3c,q] and Fe[3d] catalyze efficiently the epoxidation of alkenes with molecular oxygen in the presence of an aldehyde, alcohol or acetal as a reducing agent under mild conditions.

In previous papers, we reported that *N*-hydroxyphthalimide (NHPI), which serves as the radical catalyst, promotes the aerobic oxidations of benzylic compounds,[4] cycloalkanes,[5] polycyclic alkanes,[6] alkylbenzenes[7] and lower alkanes[8] in the presence or absence of a transition metal under mild conditions. These oxidations have been found to proceed *via* a radical process which involves the homolytic cleavage of a carbon-hydrogen bond of substrates and the addition of dioxygen to the resulting alkyl radicals giving peroxy radicals which are eventually converted into alcohols or ketones through alkyl hydroperoxides.[5,7] Similarly, in the NHPI-catalyzed oxidation of secondary alcohols with dioxygen, the alcohols are converted into ketones *via* the formation of α-hydroxy hydroperoxides which are formed in the same manner as the oxidation of alkyl hydroperoxides. For instance, 1-phenylethanol is oxidized by autoxidation to 1-hydroperoxy-1-phenylethanol which is known to readily liberate hydrogen peroxide (H_2O_2) to form acetophenone (eq. 1).[9] In the course of our work on the NHPI-catalyzed aerobic oxidation of various alcohols, we have interested in the epoxidation of olefins utilizing the H_2O_2 formed by the aerobic oxidation of alcohols without any metal catalyst.[10] Since H_2O_2 has been manufactured commercially by process based on the autoxidation of anthrahydroquinones to anthraquinones, the one-pot epoxidation of olefins with molecular oxygen involving the *in situ* generation of H_2O_2 is one of the most desirable straightforward methods. In addition, from safety reasons, it is convenient to exclude the storage and transportation of explosive hydrogen peroxide, especially in industrial scale.

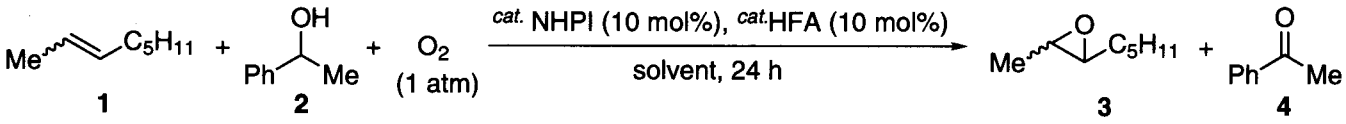


In this paper, we report in detail a new aerobic epoxidation method of alkenes using fluorinated ketones such as hexafluoroacetone (HFA) as a catalyst which transfer an active oxygen of H_2O_2 generated *in situ* by the NHPI-catalyzed oxidation of alcohols with molecular oxygen (Scheme 1).



Scheme 1.

Table 1. Epoxidation of 2-Octene (1) to 2,3-Epoxyoctane (3) with Molecular Oxygen Catalyzed by NHPI and HFA in the Presence of 1-Phenylethanol (2) under Various Conditions [a)]



run[b)]	solvent[c)]	temp. / °C	conv. of **1** / %	yield of **3** / %[d)]	conv. of **2** / %	yield of **4** / %[d)]
1[e)]	PhCN	80	7	3 (43)	34	32 (94)
2[f)]	PhCN	80	90	66 (73)	30	29 (97)
3	PhCN	70	53	46 (87)	20	20 (99)
4[g)]	PhCN	80	80	58 (72)	46	45 (98)
5	TFT	80	25	25 (99)	9	9 (100)
6[h)]	TFT	80	62	60 (96)	22	22 (99)
7[i)]	PhCN	80	<6	n.d.	<2	trace

a) **1** (3 mmol) was allowed to react with dioxygen (1 atm) in the presence of NHPI (49 mg, 0.3 mmol), HFA•3H_2O (66 mg, 0.3 mmol) and 1-phenylethanol (1.86g, 15 mmol) in solvent (6 mL) for 24 h. b) In every run, small amounts of 2,3-octanediol and hexanoic acid were formed other than epoxide (**3**). c) TFT = α, α, α-Trifluorotoluene d) Based on substrate used. Selectivity is in parentheses. e) In the absence of HFA. f) 2,3-Octanediol (13 %), hexanoic acid (3 %) and small amounts of unidentified products were obtained. g) **2** (9 mmol) was used. h) NHPI (0.6 mmol) was used. i) In the absence of NHPI.

RESULTS

Epoxidation of 2-Octene (1) with Dioxygen in the Presence of 1-Phenylethanol (2) Catalyzed by NHPI and HFA under Various Conditions. We first examined the NHPI-catalyzed epoxidation of 2-octene (**1**) with dioxygen in the presence of 1-phenylethanol (**2**) under various reaction conditions (Table 1). In spite of the successful conversion of alcohol (**2**) into acetophenone (**4**), a trace amount of 2,3-epoxyoctane (**3**) was formed (run 1). If the active oxygen of the resulting H_2O_2 can be transferred to a ketone bearing a strong electron-withdrawing substituent like hexafluoroacetone (HFA), 2-hydroperoxyhexafluoro-2-propanol (**6**) having higher oxidizing potential is expected to be formed.[11] Indeed, **6** derived from HFA and H_2O_2 has been reported to epoxidize various olefins in fair to good yields.[12] Thus, the epoxidation of **1** (3 mmol) using **2** (5 equiv) in the presence of a catalytic amount of NHPI (10 mol%) and HFA (10 mol%) at 80 °C was examined. As expected, **1** was epoxidized to give **3** (66 %) along with its cleaved products, 2,3-octanediol (13 %) and hexanoic acid (3 %) (run 2). In this reaction, about 30 % (4.5 mmol) of **2** used was found to be converted into acetophenone (**4**). This means that a sufficient amount of hydroperoxide (**5**) to epoxidize the olefin (**1**) (3 mmol) is supplied during the reaction course, because **4** is formed through **5**. The reaction of **1** at 70 °C led to **3** in 46 % yield at moderate conversion (53 %) (run 3). Even when alcohol (**2**) was reduced from 5 to 3 equiv, **3** was obtained in 58 % yield at relatively higher conversion (80 %) (run 4). Needless to say, in the absence of NHPI, neither the oxidation of **2** nor of **1** took place (run 7). In these reactions using benzonitrile as solvent, cleaved products of **3** such as 2,3-octanediol and hexanoic acid were formed as by-products. To prevent the formation of such products, lipophilic solvents like 1,2-dichloroethane, chloroform

Table 2. Effect of Fluorinated Ketones on the Epoxidation of 2-Octene (1) to 2,3-Epoxyoctane (3) with Molecular Oxygen Catalyzed by NHPI in the Presence of 2 [a)]

run	fluorinated ketone[b)]	conv. / %	yield / %[c)]
1	HFA	60	51
2	TFA	<8	3
3	TFAP	4	2
4	PFAP	5	3
5	OFAP	55	42

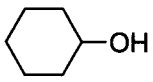
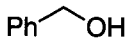
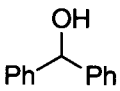
a) **1** (3 mmol) was allowed to react with dioxygen (1 atm) in the presence of NHPI (49 mg, 0.3 mmol), fluorinated ketone (66 mg, 0.3 mmol) and 1-phenylethanol (1.86 g, 15 mmol) in benzonitrile (6 mL) at 80 °C for 15 h. b) HFA = hexafluoroacetone; TFA = 1,1,1-trifluoroacetone; TFAP = 2, 2, 2-trifluoroacetophenone; PFAP = 2', 3', 4', 5', 6'-pentafluoroacetophenone; OFAP = octafluoroacetophenone c) Based on substrate used.

and benzene are usually used in the epoxidation by a hydroperoxide. From an environmental point of view, it is preferable to avoid the employment of these solvents. Thus, we employed α, α, α-trifluorotoluene (TFT) which well meets the present requirements, *i.e.* hydrophobic solvent and depression of the formation of cleaved products such as diols. As expected, the epoxidation of **1** using TFT as a solvent produced the epoxide (**3**) in high selectivity (99 %) without formation of cleaved products, although the conversion was low (25 %) (run 5). When 20 mol% of NHPI was used in this epoxidation, the conversion was improved to 62 % to form **3** in 96 % selectivity (run 6).

Effect of Fluorinated Ketones and Alcohols on the Present Epoxidation. In order to know the potential of fluorinated ketones using as active oxygen carriers in the present epoxidation, **1** was allowed to react at 80 °C for 15 h under the influence of several fluorinated ketones (Table 2). Epoxidations employing 1,1,1-trifuoroacetone (TFA), 2',3',4',5',6'-pentafluoroacetophenone (PFAP) and 2,2,2-trifluoroacetophenone (TFAP) in place of HFA resulted in low conversion of **1** and poor yields of the epoxide (**3**) (runs 2 ~ 4). These results indicate that the extent of the polarization of the α-hydroxy hydroperoxide derived from these fluorinated ketones and H_2O_2 is insufficient to epoxidize thoroughly the olefin (**1**). In fact, the reaction using octafluoroacetophenone (OFAP) in which all hydrogens were substituted by fluorine gave the epoxide (**3**) in 42 % yield at moderate conversion (55 %) (run 5).

Since alcohols are also a dominant factor in regulation of the present epoxidation, the effect of alcohols was examined (Table 3). The epoxidation of **1**, as expected, was markedly affected by the alcohols employed. Isopropanol and cyclohexanol reduced the conversion and selectivity of **1** to **3** (runs 1, 2). This is believed that the abstraction of the α-hydrogen from these alcohols by phthalimide *N*-oxyl radical (PINO)[13] derived from NHPI and dioxygen takes place in competition with that of allylic hydrogen from the olefin (**1**). In the electrochemical oxidation using NHPI as the mediator, Masui *et al.* reported that the allylic oxidation of olefins occurs more easily than the dehydrogenation of alcohols such as isopropanol and cyclohexanol to ketones.[14] Hence, in the epoxidation using an alcohol whose α-hydrogen is more easily abstracted than that

Table 3. Effect of Alcohol on the Epoxidation of 2-Octene (1) to 2,3-Epoxyoctane (3) with Molecular Oxygen Catalyzed by NHPI and HFA [a)]

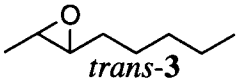
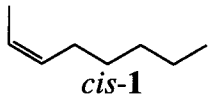
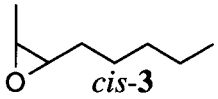
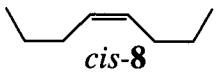
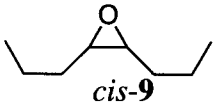
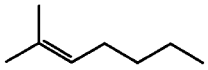
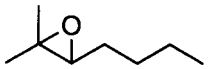
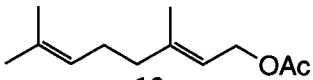
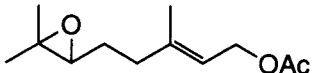
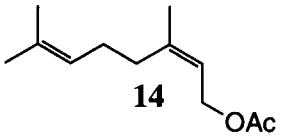
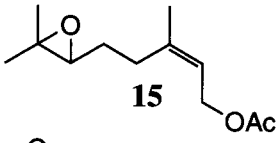
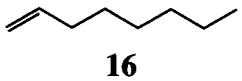
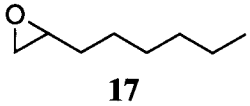
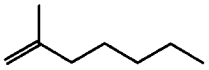
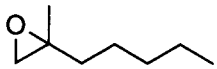
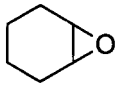
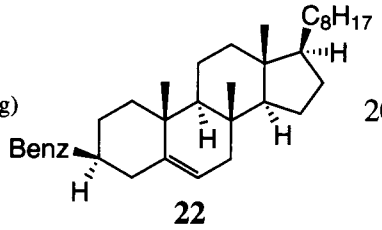
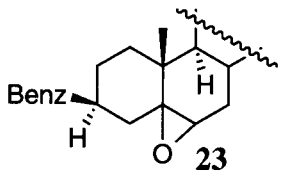
run	alcohol	conv. / %	yield / %[b)]
1		58	24 (42)
2		55	32 (58)
3		84	60 (71)
4		90	66 (73)
5[c)]	 (7)	94	85 (90)

a) **1** (3 mmol) was allowed to react with dioxygen (1 atm) in the presence of NHPI (49 mg, 0.3 mmol), HFA (66 mg, 0.3 mmol) and alcohol (15 mmol) in benzonitrile (6 mL) at 80 °C for 24 h.
b) Based on substrate used. Selectivity is in parentheses. c) Reaction was carried out for 18 h.

of isopropanol and cyclohexanol, the epoxidation is expected to proceed more selectively. Indeed, the reaction of **1** using benzyl alcohol led to **3** in higher selectivity (71 %) and conversion (84 %) (run 3). Among the alcohols examined, benzhydrol (**7**) afforded **3** in the highest selectivity (90 %) and conversion (94 %) (run 5).

Epoxidation of Various Olefins. The epoxidation of various olefins by molecular oxygen was run using benzhydrol (**7**) in the presence of catalytic amounts of HFA and NHPI in benzonitrile at 80 °C (Table 4). *trans*-2-Octene (*trans*-**1**) yielded *trans*-2,3-epoxyoctane (*trans*-**3**) in complete stereospecific manner in 87 % yield (run 1). Similarly, the epoxidation of *cis*-**1** gave *cis*-2,3-epoxyoctane (*cis*-**3**) in good yield (81 %) (run 3). Interestingly, it was found that the epoxidation of *cis*-**1** by the present catalytic system proceeds with retention of the configuration to form **3** in high selectivity (*cis*-**3**/*trans*-**3** = 98/2). Like *cis*-**1**, *cis*-4-octene (**8**) was epoxidized selectively to *cis*-epoxide (**9**) (*cis*/*trans* = 99/1) (run 4). Trisubstituted olefin such as 2-methyl-2-heptene (**10**) was also oxidized to the corresponding epoxide (**11**) in satisfactory yield (run 5). Geranyl acetate (**12**) and neryl acetate (**14**) afforded the corresponding epoxides (**13** and **15**), respectively, in which the double bonds remote from their acetoxy groups were epoxidized with high regioselectivity (runs 6, 7). It is noteworthy that the epoxidation of terminal olefins such as 1-octene (**16**) and 2-methyl-1-heptene (**18**), which are difficult to be oxidized compared with internal olefins, gave the corresponding epoxides in satisfactory yields (runs 8 and 9). However, cyclohexene (**20**) was difficult to be selectively epoxidized to cyclohexeneoxide (**21**) because of the concomitant formation of the allylic oxidation products, *e.g.* cyclohexenone (5 %) and cyclohexenol (1 %), and diol (1 %) (run 10). Cholesteryl benzoate (**22**) gave 5,6-α-epoxide (α-**23**) in preference to 5,6-β-epoxide (β-**23**) (α-**23**/β-**23** = 75/25) (run 11).

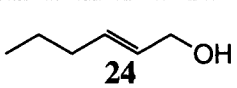
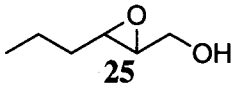
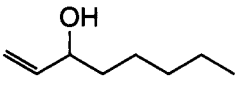
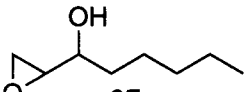
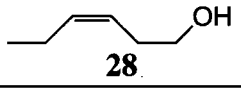
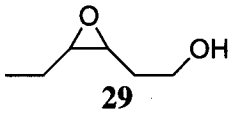
Table 4. Epoxidation of Various Olefins with Dioxygen Catalyzed by NHPI and HFA in the Presence of Benzhydrol (7) [a)]

run	substrate	time / h	conv. / %	product	yield / %	select. / %
1	 *trans*-**1**	18	93	 *trans*-**3**	87	93 (*trans/cis* = >99/1)
2[b)]	*trans*-**1**	24	90	*trans*-**3**	72	80 (*trans/cis* = >99/1)
3	 *cis*-**1**	16	94	 *cis*-**3**	81	86 (*cis/trans* = 98/2)
4	 *cis*-**8**	16	96	 *cis*-**9**	80	83 (*cis/trans* = 99/1)
5	 **10**	15	90	 **11**	74	82
6[c)]	 **12**	20	88	 **13**	71	81
7[d)]	 **14**	20	89	 **15**	74	83
8[e,f)]	 **16**	24	80	 **17**	72	90
9[f,g)]	 **18**	24	83	 **19**	70	84
10[f,h)]	 **20**	24	78	 **21**	63	80
11[f,g)]	 **22**	20	72	 **23**	60	83 (75/25)[i)]

a) Substrate (3 mmol) was allowed to react under dioxygen (1 atm) in the presence of NHPI (49 mg, 0.3 mmol), HFA (66 mg, 0.3 mmol) and benzhydrol (**7**) (2.76 g, 15 mmol) in benzonitrile (6 mL) at 80 °C. b) 1-Phenylethanol (**2**) was used in place of benzhydrol (**7**). c) 2,3-Epoxide (3 %) and diepoxide (4 %) were obtained. d) 2,3-Epoxide (4 %) and diepoxide (4 %) were obtained. e) Reaction was carried out at 90 °C. f) α, α, α-Trifluorotoluene was used as solvent. g) NHPI (0.6 mmol) was used. h) Cyclohexenone (5 %), cyclohexenol (1 %) and 1,2-cyclohexanediol (1 %) were obtained other than 21. i) Ratio of *α/β*.

Epoxidation of Allylic and Homoallylic Alcohols. In the present epoxidation, allylic alcohols were difficult to be epoxidized selectively under the above conditions owing to the cleavage of oxirane ring of the resulting epoxides. For example, the reaction of *trans*-2-hexen-1-ol (**24**) using **7** under dioxygen (1 atm) in the presence of NHPI and HFA produced epoxy alcohol (**25**) in 49 % yield, although the conversion was high

Table 5. Epoxidation of Allylic and Homoallylic Alcohols with Dioxygen Catalyzed by NHPI and HFA in the Presence of Benzhydrol (7) [a)]

run	olefin	$Co(OAc)_2$ / mol %	temp. / °C	time / h	conv. / %	product	yield / %	select. / %
1	 **24**	-	80	12	92	 **25**	49	53
2	**24**	-	70	24	72	**25**	50	69
3	**24**	0.05	50	24	82	**25**	71	87
4	 **26**	0.05	60	24	48	 **27**	43	90
5	 **28**	0.05	60	18	90	 **29**	74	82

a) Substrate (3 mmol) was allowed to react under dioxygen (1 atm) in the presence of NHPI (49 mg, 0.3 mmol), HFA (66 mg, 0.3 mmol) and benzhydrol (2.76 g, 15 mmol) in TFT (3 mL).

(92 %) (Table 5, run 1). In order to depress the cleavage of the oxirane ring, it is desired to carry out the reaction at lower temperature.

In a previous paper, we reported that the NHPI-catalyzed aerobic oxidation of alcohols was facilitated at lower temperature by adding a small amount of a cobalt ion.[15] Therefore, the addition of a cobalt ion to the present epoxidation system was expected to result in the lowering of the reaction temperature. By adding $Co(OAc)_2$ (0.05 mol%) to the reaction system, the epoxidation of **24** proceeded smoothly even at 50 °C to give epoxide (**25**) in higher yield and selectivity (run 3). Similarly, *cis*-3-hexen-1-ol (**28**) was epoxidized in stereoselective manner to form the corresponding *cis*-epoxy alcohol (**29**) in good selectivity (82 %).

Stereochemistry in Epoxidation. To know the characteristics of the present epoxidation method, the selectivity in the epoxidation of cis olefins by this system was compared with that by the conventional epoxidation methods (Table 6). As shown in runs 3 and 4 in Table 4, the epoxidation of cis olefins, *cis*-**1** and *cis*-**8**, led to the corresponding cis epoxides, *cis*-**3** and *cis*-**9**, with complete stereoselectivity. Inspection of

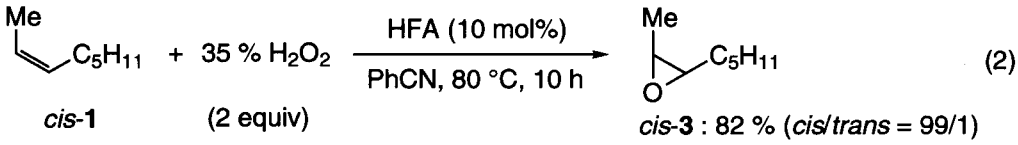
Table 6. Stereochemistry in Epoxidation of *cis*-2-Octene (1) and Cholesteryl Benzoate (22) under Various Oxidation Conditions

run	oxidation method	ratio of *cis*-**3**:*trans*-**3**	ratio of α-**23**:β-**23**
1	present	98:2[a)]	75:25[b)]
2[c)]	$Ni(dmp)_2$ / aldehyde - O_2	51:49	31:69
3[d)]	*m*CPBA	98:2	71:29
4[d,e)]	MMPP	—	85:15

a) Determined by GLC b) Determined by HPLC (*n*-hexane/chloroform=10/1). c) Cited from ref. 3b
d) Cited from ref. 16a e) MMPP=magnesium monoperoxyphthalate hexahydrate

Table 6 indicates that the present results closely resemble to the epoxidation of *cis*-**1** by *m*CPBA in contrast to that by the Ni(dmp)$_2$/aldehyde-O_2 system which affords a mixture of *cis*- and *trans*-**3** (runs 2 and 3).[3b,c] Similarly, the epoxidation of **22** resulted in 5,6-α-epoxide (α-**23**) and 5,6-β-epoxide (β-**23**) in a ratio of 75:25 which is comparable to that by peroxy acids exemplified by *m*CPBA (α–**23**/β–**23** = 71/29) and MMPP (α–**23**/β–**23** = 85/15) (runs 3 and 4).[16] However, the same epoxidation by the aldehyde-O_2 system is reported to produce β-**23** in preference to α-**23** (α–**23**/β–**23** = 31/69) (run 2).[3e,17]

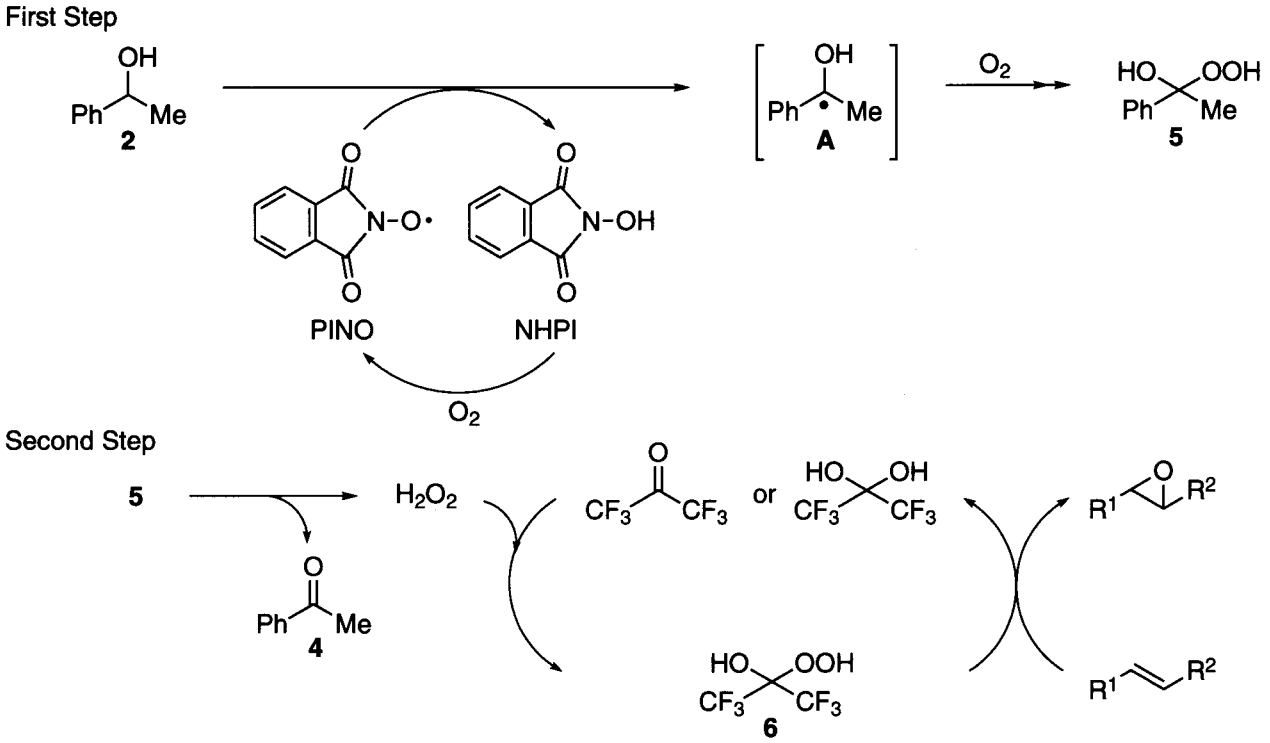
It is interesting to note that the present catalytic system provides a stereospecific epoxidation route with molecular oxygen similar to that with *m*CPBA. So far no such selectivity has been observed in the epoxidation of *cis* olefins using molecular oxygen. This may be attributed to that an actual epoxidizing species is a hydroperoxide (**6**) derived from HFA and H_2O_2, and the epoxidation of olefins by **6** would proceed *via* a reaction sequence as shown in Scheme 2. Indeed, the independent epoxidation of *cis*-**1** with 35%-H_2O_2 (2 equiv) in the presence of HFA gave *cis*-**3** in stereospecific manner in 82 % yield (eq. 2).



DISCUSSION

It is well known that the autoxidation of an alcohol gives H_2O_2 *via* an α-hydroxy hydroperoxide as a transient intermediate.[9] To obtain the information on the formation of H_2O_2 in the present reaction system, the aerobic oxidation of **2** under the influence of NHPI was carried out in CD_3CN at 75 °C, and the resulting reaction mixture was subjected to the ^1H NMR measurement. A broad peak was observed at δ 8.8 attributed to the proton of H_2O_2, and the remaining were assigned to peaks arising from **2** and **4**. However, peaks assigned to the α-hydroxy hydroperoxide (**5**) were rarely observed. These observations suggest that most of the formed hydroperoxide (**5**) liberates H_2O_2 relatively with ease under these conditions to give acetophenone (**4**),[18] although a mixture of cyclohexanone or acetaldehyde and H_2O_2 is reported to lie in equilibrium with its α-hydroxy hydroperoxide, respectively.[19]

We next tried the estimation of the amount of H_2O_2 formed by the aerobic oxidation of **2**. The oxidation of **2** was carried out under the same reaction conditions employed as the epoxidation of **1**. After the reaction, the solution was diluted with dichloromethane, and then enough water required to separate the organic phase was added to the mixture. The aqueous phase was separated out and extracted with dichloromethane three times to remove organic compounds. GC measurement of the aqueous phase showed no contamination with organic compounds such as the starting materials and the products. The amount of H_2O_2 in aqueous phase was determined by iodometry. It was found that 21 % (3.1 mmol) of **2** was converted into H_2O_2.



Scheme 2. A Possible Reaction Path for Epoxidation of Olefin in the Presence of 2 by NHPI/HFA.

From the organic residue, 27 % (4 mmol) of acetophenone (**3**) and 73 % (11 mmol) of alcohol (**2**) were obtained. The total amounts of **2**, **4**, recovered from the organic phase, and H_2O_2 from the aqueous phase were almost balanced with the quantity of **2** employed, and the quantity of H_2O_2 formed in this reaction was comparable to that of **4**. This shows that the H_2O_2 in the present reaction medium can exist without significant loss.

On the basis of these results, the epoxidation by the present system can be accounted for the following reaction sequence (Scheme 2). In the first step, phthalimide *N*-oxyl, PINO, generated *in situ* from NHPI and dioxygen abstracts an α-hydrogen atom from alcohol to give hydroxy radical (**A**) which is readily trapped by O_2 and eventually converted into α-hydroxy hydroperoxide (**5**).[20] The resulting **5** would rapidly liberate H_2O_2 to form **4**. The second step is the formation of 2-hydroperoxyhexafluoro-2-propanol (**6**) by the reaction of HFA (or HFA-hydrate) with the H_2O_2, and then olefins are oxidized by **6** to yield epoxides and HFA-hydrate. The formation of the hydroperoxide (**6**) which serves as an actual epoxidizing species in this reaction is confirmed by the following observations; (i) the epoxidation did not take place in the absence of HFA, (ii) the selectivity of the epoxidation of cis olefins closely resembles to that by peracids, (iii) the amount of H_2O_2 formed is comparable to that of acetophenone (**4**), (iv) the results of the independent epoxidation of *cis*-**1** by H_2O_2 using HFA were almost the same as those of the epoxidation by the present system.

In conclusion, we have developed the epoxidation of olefins by *in situ* generation of H_2O_2 from alcohols and molecular oxygen under the influence of NHPI and HFA without any metal catalyst. This method provides an alternative epoxidation route of olefins by molecular oxygen in stereospecific manner.

EXPERIMENTAL

General. ^1H and ^{13}C NMR were measured at 270 and 67.5 MHz, respectively, with tetramethylsilane as the internal standard. IR spectra were measured using NaCl pellets. A GC analysis was performed with a flame ionization detector using a 0.22 mm x 25 m capillary column (SGE BP–5). A HPLC analysis was performed with UV-VIS detector using a 4.6 mm x 25 cm normal phase column (Shimadzu CLC-SIL).

All starting materials, solvents 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.

General Procedure for the Epoxidation of 1. A benzonitrile (6 mL) solution of **1** (3 mmol), NHPI (49 mg, 10 mol%), HFA•$3H_2O$ (66 mg, 10 mol%), and **2** (15 mmol) was placed in a two–necked flask equipped with a balloon filled with O_2. The mixture was stirred at 80 °C for 24 h. After the reaction, the reaction mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and analyzed by GLC with an internal standard. The products were separated from the solvent under reduced pressure and purified by column chromatography on silica gel (*n*-hexane/AcOEt = 20/1) to give the corresponding epoxides.

Epoxides *trans*-**3**,[3b] *cis*-**3**,[3b] **13**,[21] **15**,[21] **17**, **21** and **23**[3e] were identified through the comparison of their ^1H and ^{13}C NMR with those of authentic samples or with literature values.

***cis*-4,5-Epoxyoctane (*cis*-9)**: Obtained as a colorless liquid. ^1H-NMR ($CDCl_3$, 270 MHz) δ 2.92 (br, 2H), 1.42-1.58 (m, 8H), 0.98 (t, J = 6.92 Hz, 6H); ^{13}C-NMR ($CDCl_3$, 67.5 MHz) δ 57.3, 30.2, 20.2, 14.3.

2,3-Epoxy-2-methylheptane (11): Obtained as a colorless liquid. ^1H-NMR ($CDCl_3$, 270 MHz) δ 2.72 (t, J = 6.27 Hz, 1H), 1.34-1.55 (m, 6H), 1.31 (s, 3H), 1.27 (S, 3H), 0.92 (t, J = 6.93 Hz, 3H); ^{13}C-NMR ($CDCl_3$, 67.5 MHz) δ 64.9, 58.5, 28.9, 28.8, 25.2, 22.9, 19.0, 14.3.

1,2-Epoxy-2-methylheptane (19): Obtained as a colorless liquid. ^1H-NMR ($CDCl_3$, 270 MHz) δ 2.60 (d, J = 4.95 Hz, 1H), 2.58 (d, J = 4.95 Hz, 1H), 1.36-1.57 (m, 8H), 1.31 (s, 3H), 0.89 (t, J = 6.93, 3H); ^{13}C-NMR ($CDCl_3$, 67.5 MHz) δ 57.4, 54.3, 37.0, 32.1, 25.2, 22.9, 21.2, 14.3.

Procedure for the Isolation of Hydrogen Peroxide in the Oxidation of 1-Phenylethanol (2). A benzonitrile (5 mL) solution of **2** (15 mmol), NHPI (49 mg, 0.3 mmol) was placed in a two–necked flask equipped with a balloon filled with O_2. The mixture was stirred at 80 °C for 24 h. After the reaction, water (5 mL) and dichloromethane (10 mL) were added to the reactant, and then the aqueous phase was separated and extracted with dichloromethane (5 mL x 3) to remove organic compounds. The quantity of hydrogen peroxide in the aqueous solution was determined by iodometry.[22] The organic layer was dried over $MgSO_4$ and analyzed by GLC with an internal standard.

This work was partly supported by Research for the Future program JSPS.

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Received, 30th April, 1999