ChemComm

Epoxidation of alkenes using alkyl hydroperoxides generated *in situ* by catalytic autoxidation of hydrocarbons with dioxygen

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Received (in Cambridge, UK) 2nd November 1999, Accepted 10th December 1999

Olefins were smoothly epoxidized under O_2 (1 atm) in the presence of a hydrocarbon such as ethylbenzene or tetralin, using *N*-hydroxyphthalimide (NHPI) and $Mo(CO)_6$ as catalyst; the present reaction involves autoxidation of the hydrocarbon assisted by NHPI and epoxidation of alkenes with the resulting hydroperoxide catalyzed by $Mo(CO)_6$; *cis*-alkene was epoxidized in a stereospecific manner to form the corresponding *cis*-epoxide in high yield.

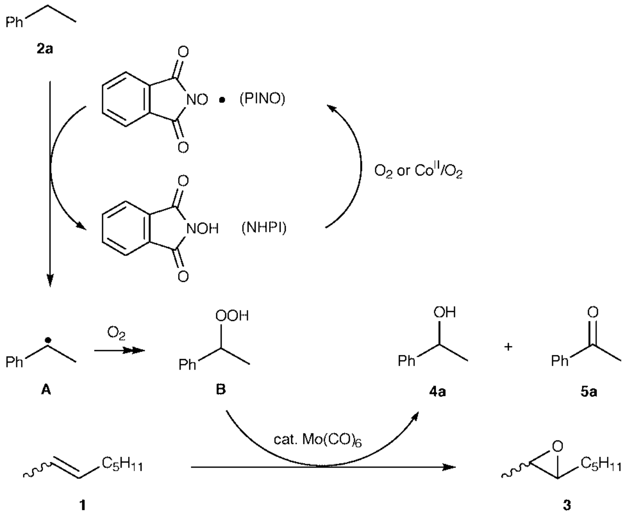
The epoxidation of alkenes using molecular oxygen *via* a catalytic process is a challenging subject in the field of oxidation chemistry.[1] Since the direct epoxidation of alkenes with molecular oxygen, which lies in triplet ground state, is inhibited, epoxidation using O_2 is carried out in the presence of a compound like an aldehyde which serves as an active oxygen carrier.[2] Although there have been many reports on the metal-catalyzed epoxidation of alkenes by O_2 in the presence of aldehydes, only a limited number of methods using O_2 as terminal oxidant have been developed.[3] There has been long-standing interest in the epoxidation of alkenes with alkyl hydroperoxides, as an active oxygen carrier, generated *in situ* from hydrocarbons and O_2. To the best of our knowledge, however, only one report has appeared on the epoxidation of alkenes by the use of cumene and O_2 with heteropolyoxometalates as catalyst.[4] A major difficulty in the epoxidation is attributed to the following: (i) autoxidation of aldehydes takes place very fast, at least two orders of magnitude faster than that of hydrocarbons; (ii) as a result, the epoxidation using hydrocarbons must be carried out under severe reaction conditions; and (iii) the epoxidizing ability of alkyl hydroperoxides is considerably lower than that of peracids or acylperoxy radicals derived from aldehydes and O_2.[5] Therefore, stepwise procedures are commonly utilized in epoxidations using alkyl hydroperoxides. For example, the Halcon process consists of the aerobic oxidation of ethylbenzene to α-hydroperoxyethylbenzene, and the Mo-catalyzed epoxidation of propylene with the α-hydroperoxyethylbenzene.[6] Consequently, development of an epoxidation system using a hydroperoxide generated *in situ* from ethylbenzene and molecular oxygen is very attractive from the synthetic and industrial points of view.

Recently, we have shown that hydrocarbons are efficiently oxidized with O_2 by *N*-hydroxyphthalimide (NHPI), which serves as a radical catalyst under mild conditions.[7] In this oxidation, hydrocarbons are converted into oxygen-containing compounds such as alcohols or ketones through *alkyl hydroperoxides (**B**)* as transient intermediates. If the alkyl hydroperoxides formed can be utilized as oxidants, it is possible to epoxidize alkenes using hydrocarbons and molecular oxygen. Here we report the Mo-catalyzed epoxidation of alkenes with hydroperoxides generated *in situ* by the NHPI-catalyzed aerobic oxidation of hydrocarbons such as ethylbenzene (Scheme 1).

Table 1 shows representative results for the epoxidation of oct-2-ene (**1**) with O_2 using hydrocarbons as a hydroperoxide source.† The epoxidation of **1** using ethylbenzene (**2a**) in the presence of NHPI (10 mol%), $Co(OAc)_2$ (0.1 mol%) and $Mo(CO)_6$ (5 mol%) at 60 °C under O_2 (1 atm) gave epoxide **3** in 61% selectivity at 67% conversion (run 1). An improvement of the present epoxidation by the addition of molecular sieves 4A (MS-4A) was observed, and thus the conversion of **1** and selectivity of epoxide **3** reached 81% and 70%, respectively (run 2). Using tetralin (**2b**) instead of **2a**, it was found that the selectivity of epoxide **3** was considerably improved (run 3). However, when toluene (**2c**) was employed as a hydrocarbon source, the selectivity of **3** was lowered to 44% (run 4). This is believed to be due to the occurrence of allylic hydrogen atom abstraction from **1** in competition with the benzylic hydrogen atom abstraction of **2c** by PINO.[8] Although AIBN was used as a radical source instead of NHPI, **1** was difficult to epoxidize to **3** (run 5). It is very interesting to note that the present epoxidation was induced even at room temperature to afford epoxide **3** in high selectivity (97%) at 31% conversion (run 7).[9] On the other hand, metal complexes such as $MoO_2(acac)_2$, $VO(acac)_2$ and $TiO(acac)_2$ were found to be inadequate for the present reaction (runs 8–10). Although molybdenum(VI) complexes have high catalytic activity for the epoxidation of alkenes with *tert*-butyl hydroperoxide,[10] $MoO_2(acac)_2$ was found to depress the formation of the hydroperoxide from **2b** under these conditions (run 8).

On the basis of these results, the epoxidation of various alkenes with O_2 using **2a** or **2b** was examined in the presence of catalytic amounts of NHPI, $Co(OAc)_2$ and $Mo(CO)_6$ under selected reaction conditions (Table 2).

trans-Oct-2-ene (*trans*-**1**) was epoxidized with excellent stereoselectivity to give *trans*-2,3-epoxyoctane (*trans*-**3**) (*trans* : *cis* = >99 : 1) with 88% selectivity together with a small amount of octane-2,3-diol (4%) in 78% conversion. Similarly, the epoxidation of *cis*-**1** gave *cis*-2,3-epoxyoctane (*cis*-**3**) (*cis* : *trans* = 99 : 1) in good selectivity. It is noteworthy that the present epoxidation of *cis*-olefin proceeds with nearly complete stereoselectivity to give *cis*-epoxide, although the metal-catalyzed epoxidation of *cis*-olefins using an aldehyde and O_2 leads to a mixture of *cis*- and *trans*-epoxides.[11] This is because the resulting alkylperoxyl radical can abstract the hydrogen



Scheme 1

Table 1 Epoxidation of oct-2-ene (**1**) to 2,3-epoxyoctane (**3**) with O_2 in the presence of hydrocarbons using NHPI, $Co(OAc)_2$ and various transition metals as catalysts[a]

				Conversion (%)		Selectivity (%)		
Run	Hydrocarbon	Transition metal	T/°C	**1**	**2a**,**b**	**3**	**4a**,**b**	**5a**,**b**
1	Ethylbenzene **2a**	$Mo(CO)_6$	60	67	10	61	65	25
2[b]	**2a**	$Mo(CO)_6$	60	81	12	70	71	19
3	Tetralin **2b**	$Mo(CO)_6$	50	67	25	86	62	30
4[c]	Toluene **2c**	$Mo(CO)_6$	60	59	—	44	—	—
5[d,e]	**2b**	$Mo(CO)_6$	80	12	7	67	88	11
6[f]	**2b**	$Mo(CO)_6$	50	58	18	91	79	17
7	**2b**	$Mo(CO)_6$	25	31	11	97	72	21
8	**2b**	$MoO_2(acac)_2$	50	8	<5	95	>90	<8
9	**2b**	$VO(acac)_2$	50	12	15	79	31	64
10	**2b**	$TiO(acac)_2$	50	15	21	80	47	40

[a] Oct-2-ene (**1**) (4 mmol) was allowed to react with O_2 (1 atm) in the presence of NHPI (10 mol%), $Co(OAc)_2$ (0.1 mol%), transition metal (5 mol%) and hydrocarbon (**2a**,**b**) in PhCN (2 mL) for 12 h. **2a** (40 mmol) and **2b** (20 mmol) were used, respectively. [b] MS-4A (200 mg) was added. [c] 6 h. [d] AIBN (5 mol%) was used instead of NHPI. [e] 8 h. [f] NHPI (5 mol%) was used.

Table 2 Epoxidation of various alkenes with molecular oxygen in the presence of tetralin (**2b**) or ethylbenzene (**2a**) catalyzed by NHPI, $Co(OAc)_2$ and $Mo(CO)_6$[a]

Run	Alkene	T/°C	Conversion (%)[b]	Selectivity (%)[b]
1	*trans*-Oct-2-ene	60 (60)	78 (71)	88 (79)[c]
2	*cis*-Oct-2-ene	50 (60)	83 (75)	87 (71)[d]
3	2,4,4-Trimethylpent-2-ene	70 (70)	90 (76)	84 (80)
4	Oct-1-ene	60 (70)	38 (37)	80 (81)
5[e]	Cyclohexene	60	80	74
6[e]	Cyclooctene	60	89	83
7	*trans*-Hex-2-ene-1-ol **6**	60	79	65
8[f,g]	**6**	60	97	92

[a] Alkenes (4 mmol) and **2a** (40 mmol) or **2b** (20 mmol) were allowed to react with O_2 (1 atm) in the presence of NHPI (10 mol%), $Co(OAc)_2$ (0.1 mol%), $Mo(CO)_6$ (5 mol%) and MS-4A (200 mg) in PhCN (2 ml) for 14 h. [b] The results using **2a** are in parentheses. [c] *trans*:*cis* = >99:1. [d] *cis*:*trans* = 99:1 for **2b**, 94:6 for **2a**. [e] **2b** (40 mmol) was used. [f] $VO(acac)_2$ (0.5 mol%) was used instead of $Co(OAc)_2$ and $Mo(CO)_6$. [g] 6 h.

atom from NHPI or **2** to give hydroperoxide **B**, which serves as the oxidant of the molybdenum-catalyzed epoxidation of alkenes.‡ Therefore, the present epoxidation of *cis*-olefin proceeds in a stereospecific manner, in contrast to the epoxidation of *cis*-alkene using aldehyde and O_2, which leads to a mixture of *cis*- and *trans*-epoxides.

Trisubstituted olefins afforded the corresponding epoxides in good selectivity. A terminal olefin, oct-1-ene, was a reluctant substrate for epoxidation using the present catalytic system, forming 1,2-epoxyoctane in moderate conversion. Cyclohexene was also epoxidized to 1,2-epoxycyclohexene in satisfactory yield.

On the other hand, the epoxidation of allylic alcohol, *trans*-hex-2-en-1-ol, to epoxy alcohol was achieved in high yield when $VO(acac)_2$ was employed instead of $Mo(CO)_6$. The epoxidation of allylic alcohols with *tert*-butyl hydroperoxide is known to result in epoxides with higher rates and better yields using vanadium(V) complexes rather than molybdenum(VI) catalysts.[10] It is interesting to note that the present epoxidation of allylic alcohols was promoted smoothly even with a very small amount of $VO(acac)_2$ (0.5 mol%) in the absence of $Co(OAc)_2$. It is thought that $VO(acac)_2$ induces not only the generation of PINO from NHPI under O_2 but also acts as the epoxidation catalyst of alkenes.

In conclusion, we have developed a selective one-pot epoxidation of alkenes with molecular oxygen using hydrocarbons such as ethylbenzene and tetralin as the hydroperoxide source under mild conditions.

This work was partly supported by the Japan Society for the Promotion of Science under the Research for the Future program JSPS.

Notes and References

† *Typical procedure for the epoxidation of* **1**: A PhCN (2 ml) solution of **1** (4 mmol), NHPI (10 mol%), $Co(OAc)_2$ (0.1 mol%), $Mo(CO)_6$ (5 mol%) and **2a** (40 mmol) was placed in a two-necked flask equipped with a balloon filled with O_2. The mixture was stirred at 60 °C for 12 h, and then analyzed by GLC with an internal standard.

‡ In general, the reaction of acylperoxy radicals derived from an aldehyde with olefins has been reported to be *ca.* 10^5 times faster than that of alkylperoxyl radicals derived from hydrocarbons such as **2**: see Y. Sawaki and Y. Ogata, *J. Org. Chem.*, 1984, **49**, 3344.

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Communication a908731a