

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

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Olefins were smoothly epoxidized under O<sub>2</sub> (1 atm) in the presence of a hydrocarbon such as ethylbenzene or tetralin, using *N*-hydroxyphthalimide (NHPI) and Mo(CO)<sub>6</sub> 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)<sub>6</sub>; *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.<sup>1</sup> Since the direct epoxidation of alkenes with molecular oxygen, which lies in triplet ground state, is inhibited, epoxidation using O<sub>2</sub> is carried out in the presence of a compound like an aldehyde which serves as an active oxygen carrier.<sup>2</sup> Although there have been many reports on the metal-catalyzed epoxidation of alkenes by O<sub>2</sub> in the presence of aldehydes, only a limited number of methods using O<sub>2</sub> as terminal oxidant have been developed.<sup>3</sup> 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<sub>2</sub>. To the best of our knowledge, however, only one report has appeared on the epoxidation of alkenes by the use of cumene and O<sub>2</sub> with heteropolyoxometalates as catalyst.<sup>4</sup> 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<sub>2</sub>.<sup>5</sup> Therefore, stepwise procedures are commonly utilized in epoxidations using alkyl hydroperoxides. For example, the Halcon process consists of the aerobic oxidation of ethylbenzene to  $\alpha$ -hydroperoxyethylbenzene, and the Mo-catalyzed epoxidation of propylene with the  $\alpha$ -hydroperoxyethylbenzene.<sup>6</sup> 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.

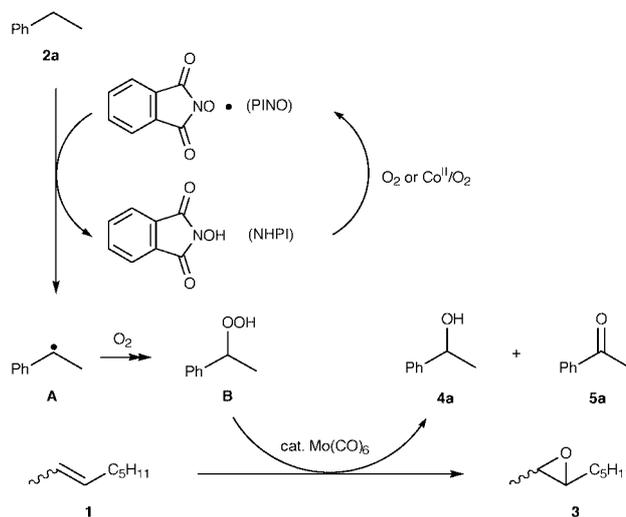
Recently, we have shown that hydrocarbons are efficiently oxidized with O<sub>2</sub> by *N*-hydroxyphthalimide (NHPI), which serves as a radical catalyst under mild conditions.<sup>7</sup> In this oxidation, hydrocarbons are converted into oxygen-containing compounds such as alcohols or ketones through *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<sub>2</sub> using hydrocarbons as a hydroperoxide source.† The epoxidation of **1** using ethylbenzene (**2a**) in the presence of NHPI (10 mol%), Co(OAc)<sub>2</sub> (0.1 mol%) and Mo(CO)<sub>6</sub> (5 mol%) at 60 °C under O<sub>2</sub> (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.<sup>8</sup> 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).<sup>9</sup> On the other hand, metal complexes such as MoO<sub>2</sub>(acac)<sub>2</sub>, VO(acac)<sub>2</sub> and TiO(acac)<sub>2</sub> 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,<sup>10</sup> MoO<sub>2</sub>(acac)<sub>2</sub> 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<sub>2</sub> using **2a** or **2b** was examined in the presence of catalytic amounts of NHPI, Co(OAc)<sub>2</sub> and Mo(CO)<sub>6</sub> 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<sub>2</sub> leads to a mixture of *cis*- and *trans*-epoxides.<sup>11</sup> 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<sub>2</sub> in the presence of hydrocarbons using NHPI, Co(OAc)<sub>2</sub> and various transition metals as catalysts<sup>a</sup>

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

<sup>a</sup> Oct-2-ene (**1**) (4 mmol) was allowed to react with O<sub>2</sub> (1 atm) in the presence of NHPI (10 mol%), Co(OAc)<sub>2</sub> (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. <sup>b</sup> MS-4A (200 mg) was added. <sup>c</sup> 6 h. <sup>d</sup> AIBN (5 mol%) was used instead of NHPI. <sup>e</sup> 8 h. <sup>f</sup> 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)<sub>2</sub> and Mo(CO)<sub>6</sub><sup>a</sup>

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

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

atom from NHPI or **2** to give hydroperoxide **B**, which serves as the oxidant of the molybdenum-catalyzed epoxidation of alkenes.<sup>‡</sup> Therefore, the present epoxidation of *cis*-olefin proceeds in a stereospecific manner, in contrast to the epoxidation of *cis*-alkene using aldehyde and O<sub>2</sub>, 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)<sub>2</sub> was employed instead of Mo(CO)<sub>6</sub>. 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.<sup>10</sup> It is interesting to note that the present epoxidation of allylic alcohols was promoted smoothly even with a very small amount of VO(acac)<sub>2</sub> (0.5 mol%) in the absence of Co(OAc)<sub>2</sub>. It is thought that VO(acac)<sub>2</sub> induces not only the generation of PINO from NHPI under O<sub>2</sub> 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.

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## Notes and References

† *Typical procedure for the epoxidation of 1*: A PhCN (2 ml) solution of **1** (4 mmol), NHPI (10 mol%), Co(OAc)<sub>2</sub> (0.1 mol%), Mo(CO)<sub>6</sub> (5 mol%) and **2a** (40 mmol) was placed in a two-necked flask equipped with a balloon filled with O<sub>2</sub>. 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<sup>5</sup> times faster than that of alkylperoxy radicals derived from hydrocarbons such as **2**: see Y. Sawaki and Y. Ogata, *J. Org. Chem.*, 1984, **49**, 3344.

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