



# Highly efficient epoxidation of $\alpha,\beta$ -unsaturated ketones by hydrogen peroxide with a base hydrotalcite catalyst prepared from metal oxides

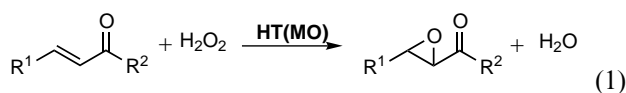
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**Abstract**—The base hydrotalcite, prepared from MgO and Al<sub>2</sub>O<sub>3</sub>, acted as a highly efficient catalyst for the epoxidation of  $\alpha,\beta$ -unsaturated ketones using aqueous hydrogen peroxide as an oxidant. This heterogeneous epoxidation has the advantages of a high efficiency of H<sub>2</sub>O<sub>2</sub> utilization without organic solvents, a simple workup procedure, and reusability of the hydrotalcite catalyst. © 2002 Elsevier Science Ltd. All rights reserved.

Epoxidation of electron-deficient carbon–carbon double bonds of  $\alpha,\beta$ -unsaturated ketones is of great interest because epoxyketones can be important building blocks in organic synthesis.<sup>1</sup> Aqueous hydrogen peroxide is an ideal oxidant because of its high oxygen content and the production of water as the sole by-product.<sup>2</sup> The homogeneous epoxidation of the enones using H<sub>2</sub>O<sub>2</sub> with bases such as NaOH and KOH remains a common procedure.<sup>3</sup> Use of recyclable solid base catalysts addresses the environmental issues of the present epoxidation processes.<sup>4</sup> We have already reported the heterogeneous epoxidation of  $\alpha,\beta$ -unsaturated ketones with hydrotalcites as solid bases.<sup>4c</sup> In this paper, a hydrotalcite, prepared from metal oxides, was found to be a highly efficient heterogeneous catalyst for the epoxidation of various  $\alpha,\beta$ -unsaturated ketones, and required only 1.5 equiv. of H<sub>2</sub>O<sub>2</sub> without organic solvents (Eq. (1)).



A hydrotalcite, designated as HT(MO), was easily prepared according to a modified procedure by Rajamathi et al.<sup>5</sup> A heterogeneous mixture of 0.43 g of MgO and 0.14 g of  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>,<sup>6</sup> was vigorously stirred in 50 mL of

0.5 M aqueous Na<sub>2</sub>CO<sub>3</sub> solution at 110°C for 24 h. The obtained slurry was filtered and washed with water, followed by drying at 110°C to afford 0.92 g of HT(MO), Mg<sub>9.5</sub>Al<sub>2.6</sub>(OH)<sub>24.8</sub>CO<sub>3</sub>·*n*H<sub>2</sub>O, as a white powder. Elemental analysis: Mg, 20.8; Al, 6.4; C, 1.1%. XRD showed a layered-structure of the hydrotalcite with an interlayer distance of 2.9 Å. The specific BET surface area, determined by N<sub>2</sub> adsorption at 77 K, was 106 m<sup>2</sup> g<sup>-1</sup>, which is more than two times larger than that of the Mg<sub>10</sub>Al<sub>2</sub>(OH)<sub>24</sub>CO<sub>3</sub> hydrotalcite prepared by the conventional co-precipitation method using metal chlorides and nitrates in aqueous NaOH solution.<sup>7</sup> A titration experiment using benzoic acid on the hydrotalcite surface showed that the number of surface base sites was about 2 mmol g<sup>-1</sup>.

Epoxidations of isophorone using H<sub>2</sub>O<sub>2</sub> with various base catalysts were examined in the presence of *n*-dodecyltrimethylammonium bromide (DTMAB) in *n*-heptane solvent as shown in Table 1. It should be noted that the HT(MO) exhibited higher catalytic activity than other solid base catalysts such as conventional hydrotalcites (entries 2 and 3), MgO, Mg(OH)<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub> and Al(OH)<sub>3</sub> (entries 4 and 6–8). The activity of the HT(MO) was greatly larger than that of a physical mixture of MgO and Al<sub>2</sub>O<sub>3</sub> (entry 5). Use of NaOH as a water-soluble base resulted in a low selectivity of the epoxide as a result of oxidative cleavage of the epoxyketone (entry 10). *To our knowledge, this hydrotalcite is one of the most effective catalyst for the epoxidation of  $\alpha,\beta$ -unsaturated ketones using H<sub>2</sub>O<sub>2</sub> as an oxidant.*<sup>3,4</sup>

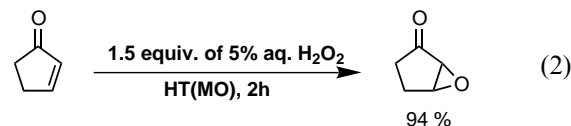
**Keywords:** epoxidation;  $\alpha,\beta$ -unsaturated ketone; hydrotalcite catalyst; hydrogen peroxide; solid base.

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Table 2 shows the epoxidation of various  $\alpha,\beta$ -unsaturated ketones catalyzed by the HT(MO) using 1.5 equiv. of  $\text{H}_2\text{O}_2$  at  $40^\circ\text{C}$ .<sup>8</sup> Cyclic enones such as 2-cyclopenten-1-one, 3-methyl-2-cyclopenten-1-one, 2-cyclohexen-1-one and 3-methyl-2-cyclohexen-1-one were smoothly oxidized to form the corresponding epoxyketones quantitatively without organic solvents (entries 1, 6, 9, and 11).<sup>†</sup> Although acyclic enones of 4-hexen-3-one and 3-nonen-2-one showed low reactivity for the epoxidation,<sup>‡</sup> use of a phase-transfer reagent of DTMAB in *n*-heptane solvent produced epoxyketones in high yields (entries 14 and 15).<sup>4c</sup> Generally, the epoxidation of isophorone does not easily occur due to the steric hindrance of  $\beta$ -substituted methyl and *gem*-dimethyl groups.<sup>4a</sup> However, the present phase-transfer system enhanced the oxidation to give epoxyisophorone in 95% yield (entry 16). Chemoselective epoxidation was exemplified with (*R*)-(-)-carvone to afford 2,3-epoxy-5-isopropenyl-2-methylcyclohexanone as a major diastereomer with a methyl group *cis* to the isopropenyl group (entry 18). It is clear that the HT(MO) showed much higher activity for many  $\alpha,\beta$ -

unsaturated ketones than the conventional hydrotalcite<sup>4c</sup> (entries 4, 7, 17 and 19).

Use of the solid hydrotalcite makes the workup procedure strikingly simple. The spent hydrotalcite was easily separated from the reaction mixture by filtration. The recovered catalyst was then reused for the epoxidation of 2-cyclopenten-1-one, as shown in Table 2 (entries 2 and 3).<sup>§</sup> The oxidation with the spent catalyst gave the epoxyketone in greater than 93% yield under the same conditions as those of the first run. *Notably, even in low concentration of  $\text{H}_2\text{O}_2$ , this HT(MO) catalyst showed high catalytic activity for the epoxidation without organic solvents.* Reaction of 2-cyclopenten-1-one using 1.5 equiv. of 5%  $\text{H}_2\text{O}_2$  for 2 h gave the corresponding epoxyketone in 94% yield (Eq. (2)).<sup>9</sup> Using 5%  $\text{H}_2\text{O}_2$ , other cyclic enones were also smoothly epoxidized in high yields, as shown in Table 2 (entries 5, 8, 10 and 12). Utilization of the low concentration  $\text{H}_2\text{O}_2$ <sup>10</sup> will open new chemical processes, e.g. the epoxidation of propylene using  $\text{H}_2\text{O}_2$  produced in situ from  $\text{H}_2$  and  $\text{O}_2$ .<sup>11</sup>



**Table 1.** Epoxidation of isophorone catalyzed by various bases using 4 equiv. of  $\text{H}_2\text{O}_2$  in the presence of DTMAB<sup>a</sup>

Entry	Catalyst	Conv'n (%) <sup>b</sup>	Yield of epoxyketone (%) <sup>b</sup>
1 <sup>c</sup>	HT(MO)	100	95
2	$\text{Mg}_{10}\text{Al}_2(\text{OH})_{24}\text{CO}_3$	97	95
3	$\text{Mg}_6\text{Al}_2(\text{OH})_{16}\text{CO}_3$	77	73
4 <sup>d</sup>	MgO	68	67
5 <sup>d,e</sup>	$\text{MgO} + \text{Al}_2\text{O}_3$	74	73
6	$\text{Mg}(\text{OH})_2$	60	60
7	$\text{Al}_2\text{O}_3$	28	26
8	$\text{Al}(\text{OH})_3$	8	7
9 <sup>f</sup>	NaOH	81	70 <sup>g</sup>
10 <sup>f</sup>	$\text{Na}_2\text{CO}_3$	53	47
11	Without	<1	<1

<sup>a</sup> Reaction conditions: isophorone (2 mmol), catalyst (0.15 g), *n*-heptane (5 mL),  $\text{H}_2\text{O}$  (4 mL), *n*-dodecyltrimethylammonium bromide (0.3 mmol), 30 % aq.  $\text{H}_2\text{O}_2$  (0.9 mL, 8 mmol),  $40^\circ\text{C}$ , 24 h.

<sup>b</sup> Determined by GC using an internal standard technique.

<sup>c</sup> Reaction time; 12 h.

<sup>d</sup> MgO calcined at  $400^\circ\text{C}$  was used.

<sup>e</sup> A physical mixture of MgO (0.052 g) and  $\text{Al}_2\text{O}_3$  (0.018 g) was used (Mg/Al mol ratio=4).

<sup>f</sup> 0.2 mmol was used.

<sup>g</sup> 3,3-Dimethyl-5-oxohexanoic acid was also formed as a by-product.

<sup>†</sup> To optimize Mg/Al ratios in the HT(MO), hydrotalcites with Mg/Al ratios from 3 to 5 were prepared from metal oxides. We found that the HT(MO) with the Mg/Al ratio of 4 was the most active catalyst for the epoxidation of 2-cyclopenten-1-one.

<sup>‡</sup> The low reactivity of these enones could be explained by their low electrophilicities evaluated from LUMO orbital energy, calculated by the PM3 semiempirical method.<sup>4c</sup>

























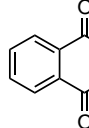
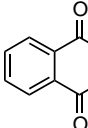


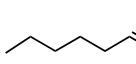
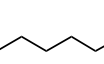








A possible reaction mechanism for this epoxidation can be postulated as follows.  $\text{H}_2\text{O}_2$  reacts with a surface base site, i.e.,  $\text{OH}^-$ , of the hydrotalcite to form a  $\text{HOO}^-$  species.<sup>4c</sup> The  $\text{HOO}^-$  attacks the electrophilic  $\beta$ -olefinic carbon atom of an  $\alpha,\beta$ -unsaturated ketone, followed by a ring enclosure to give a corresponding epoxyketone, which regenerates an  $\text{OH}^-$  on the hydrotalcite surface. At present, we think that high activity of the HT(MO) might be ascribed to its large surface area and high hydrophilicity.<sup>¶</sup>

In conclusion, the hydrotalcite, prepared from MgO and  $\text{Al}_2\text{O}_3$ , proved to be a highly effective base catalyst in the epoxidation of  $\alpha,\beta$ -unsaturated ketones using aqueous hydrogen peroxide. The present heterogeneous catalyst system provides an ideal epoxidation protocol with high atom economy because of the efficient utility of  $\text{H}_2\text{O}_2$ .

<sup>§</sup> We confirmed that the present epoxidation was catalyzed by the HT(MO) surface. The solid HT(MO) catalyst was removed by filtration from the reaction mixture at 70% conversion of 2-cyclopenten-1-one. No epoxidation occurred while the colorless filtrate was further treated at  $40^\circ\text{C}$  for 3 h.

<sup>¶</sup> The  $\nu(\text{O}-\text{H})$  of the HT(MO) in FT-IR measurement appeared at  $3437 \text{ cm}^{-1}$ , which is significantly lower than that of the conventional  $\text{Mg}_{10}\text{Al}_2(\text{OH})_{24}\text{CO}_3$  hydrotalcite ( $3493 \text{ cm}^{-1}$ ). The above shift can be attributed to hydrogen bonding between surface OH functions and/or adsorbed waters, suggesting a high hydrophilicity of the HT(MO) surface.

**Table 2.** Epoxidation of various  $\alpha,\beta$ -unsaturated ketones catalyzed by hydrotalcites using  $\text{H}_2\text{O}_2^{\text{a}}$ 

entry	substrate	product	method	time (h)	convn <sup>b</sup> (%)	yield of epoxyketone <sup>b</sup> (%)
1			A	1	100	95 (88)
2 <sup>c</sup>			A	1	100	95
3 <sup>d</sup>			A	1	100	93
4 <sup>e</sup>			B	1	31	29
5			C	2	100	94
6			A	2.5	97	92 (91)
7 <sup>e</sup>			B	4	27	24
8			C	5	93	92
9			A	1	96	95 (87)
10			C	4	98	97
11			A	3	100	97 (90)
12			C	4	95	94
13			B	7	100	96
14			D	7	100	92
15			D	16	95	89
16 <sup>f</sup>			D	12	100	95
17 <sup>e, f</sup>			D	24	97	95
18			D	30	97	95 (74)
19 <sup>e</sup>			D	30	18	16

<sup>a</sup> Reaction conditions: method (A) HT(MO) (0.15 g), substrate (2 mmol), 30 % aq.  $\text{H}_2\text{O}_2$  (0.34 mL, 3 mmol), 40 °C; method (B) HT(MO) (0.15 g), substrate (2 mmol), methanol (5 mL), 30 % aq.  $\text{H}_2\text{O}_2$  (0.34 mL, 3 mmol), 40 °C; method (C) HT(MO) (0.15 g), substrate (10 mmol), 5 % aq.  $\text{H}_2\text{O}_2$  (9 mL, 15mmol), 40 °C; method (D) HT(MO) (0.15 g), substrate (2 mmol), *n*-heptane (5 mL), DTMAB (0.3 mmol),  $\text{H}_2\text{O}$  (5 mL), 30 % aq.  $\text{H}_2\text{O}_2$  (0.34 mL, 3 mmol), 40 °C. <sup>b</sup> Determined by GC or HPLC using an internal standard technique. Values in parentheses are isolated yields using 20 mmol of substrate and 30 mmol of 30 % aq.  $\text{H}_2\text{O}_2$ . <sup>c</sup> Reuse-1. <sup>d</sup> Reuse-2. <sup>e</sup> The conventional  $\text{Mg}_{10}\text{Al}_2(\text{OH})_{24}\text{CO}_3$  (0.15 g) was used as a catalyst. <sup>f</sup> 4 equiv. of  $\text{H}_2\text{O}_2$  was used.

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- A typical procedure for the heterogeneous epoxidation of  $\alpha,\beta$ -unsaturated ketones is as follows. Into a reaction vessel with a reflux condenser were successively placed the HT(MO) (0.15 g), 2-cyclopenten-1-one (1.7 g, 20 mmol) and 30% aqueous hydrogen peroxide (3.4 mL, 30 mmol). After the resultant heterogeneous mixture was stirred at  $40^\circ\text{C}$  for 3 h, the hydrotalcite was separated by filtration. The filtrate was treated with aqueous  $\text{Na}_2\text{SO}_3$ , followed by extraction with ethyl acetate. Removal of the solvent under reduced pressure afforded 1.8 g of pure 2,3-epoxycyclopentanone (88%).
- The epoxidation of  $\alpha,\beta$ -unsaturated ketones using low concentration  $\text{H}_2\text{O}_2$  is as follows. Into a reaction vessel with a reflux condenser were successively placed the HT(MO) (0.15 g) and 2-cyclopenten-1-one (0.82 g, 10 mmol). Then the 5% aqueous hydrogen peroxide (10 mL, 15 mmol) was added. The resultant heterogeneous mixture was stirred at  $40^\circ\text{C}$  for 2 h, afforded the corresponding epoxyketone in 94% GC yield.
- The oxometalate-catalyzed hydrocarbon oxidations using low concentration  $\text{H}_2\text{O}_2$ , see: alcohol: (a) Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 12386; (b) Sato, K.; Takagi, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.* **1998**, *39*, 7549; common olefin: (c) Venturello, C.; D'Aloisio, R. *J. Org. Chem.* **1988**, *53*, 1533; (d) Sakamoto, T.; Pac, C. *Tetrahedron Lett.* **2000**, *41*, 10009.
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