J. Org. Chem. **2000,** *65,* 6897−6903

Epoxidation of α,*β*-Unsaturated Ketones Using Hydrogen Peroxide in the Presence of Basic Hydrotalcite Catalysts

Kazuya Yamaguchi, Kohsuke Mori, Tomoo Mizugaki, Kohki Ebitani, and Kiyotomi Kaneda*

Department of Chemical Science and Engineering, Graduate School of Engineering Science,
Osaka University, 1-3 Machikaneyama, Toyonaka, Osaka 560-8531, Japan

kaneda@cheng.es.osaka-u.ac.jp

Received February 22, 2000

The basic layered hydrotalcites have been used as catalysts for the epoxidation of α,*β*-unsaturated ketones in heterogeneous reaction media using hydrogen peroxide as an oxidant. A wide variety of α,*β*-unsaturated ketones were oxidized to the corresponding epoxyketones in excellent yields under mild reaction conditions. For example, 2-cyclohexen-1-one gave 2,3-epoxycyclohexanone in 91% yield at 40 °C for 5 h with high efficiency in hydrogen peroxide. The catalytic activity of the hydrotalcites increased as the basicity of their surfaces increased. In the case of the epoxidation of less reactive substrates, adding a cationic surfactant such as *n*-dodecyltrimethylammonium bromide (DTMAB) to the above oxidation system accelerated the epoxidation reaction. These hydrotalcite catalysts were easily separated from the reaction mixture and were reusable.

Introduction

Epoxidation of electron-deficient carbon−carbon double bonds of α,*β*-unsaturated ketones is of great interest in organic chemistry because of the synthetic utility of the resulting intermediates for further functionalization of ketones.[1] In contrast to common olefins, nucleophilic oxidants are required for the epoxidation of electron-deficient olefins. Aqueous hydrogen peroxide is an ideal oxidant because it is both cheap and safe, yielding only water as a coproduct.[2] The epoxidation of α,*β*-unsaturated ketones using hydrogen peroxide under strongly alkaline conditions with bases such as NaOH, Na_2CO_3, KOH, and K_2CO_3 is still the most common procedure; it is not applicable for base-sensitive substrates such as cyclopentenones unless the pH of the reaction media is strictly controlled. Moreover, the use of such bases is undesirable because they are hazardous and lead to the production of a vast amount of wastes. With ever-growing environmental concern, much attention has been paid to the development of a “green protocol” using a “green oxidant” like hydrogen peroxide in a combination with reusable solid catalysts.[3]

We have recently developed a series of hydrotalcite catalysts as solid bases for various oxidation reactions using hydrogen peroxide or molecular oxygen as an oxidant.[4−8] The hydrotalcite, $Mg_{10}Al_2(OH)_{24}CO_3$, in the presence of an oxidant composed of hydrogen peroxide and a nitrile had high catalytic activity for the epoxidation of unfunctionalized olefins.[7a] In such epoxidations, hydrogen peroxide reacts with a basic hydroxyl function on the hydrotalcite surface to form a perhydroxyl anion species (HOO^-), which in turn nucleophilically attacks a nitrile to generate a peroxycarboximidic acid as an active intermediate oxidant. It is well-known that the epoxidation of α,*β*-unsaturated ketones using hydrogen peroxide under alkaline conditions proceeds by nucleophilic attack of a perhydroxyl anion on olefinic carbons.[3a] Since these hydrotalcite catalysts efficiently transform hydrogen peroxide into a perhydroxyl anion on the catalyst surface, we expected that the hydrotalcite-catalyzed system could be further extended for the epoxidation of α,*β*-unsaturated ketones.

Here, we report on the efficient heterogeneous epoxidation of α,*β*-unsaturated ketones by hydrogen peroxide using hydrotalcite catalysts under mild reaction conditions (eq 1). This heterogeneous hydrotalcite system can

---

* Phone and Fax: +81-6-6850-6260.

(1) (a) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737. (b) Rao, A. S. Paknikar, S. K.; Kirtane, J. G. *Tetrahedron Lett.* **1983**, *39*, 2323. (c) Smith, G. J. *Synthesis* **1984**, 629. (d) Kotsuki, H.; Kataoka, M.; Nishizawa, H. *Tetrahedron Lett.* **1993**, *34*, 4031. (e) Alcaraz, L.; Harnett, J. J.; Mioskowski, C.; Martel, J.-P.; Gall, T. L.; Shin, D.-S.; Falck, J. R. *Tetrahedron Lett.* **1994**, *35*, 5449.

(2) (a) *Green Chemistry: Theory and Practice*; Anastas, P. T., Warner, J. C., Eds.; Oxford University Press: New York, 1998. (b) Clark, J. H. *Green Chem.* **1999**, *1*, 1. (c) Sheldon, R. A. *Green Chem.* **2000**, *2*, G1. (d) Anastas, P. T.; Bartlett, L. B.; Kirchhoff, M. M.; Williamson, T. C. *Catal. Today* **2000**, *55*, 11.

(3) The following are works on the epoxidation of α,*β*-unsaturated carbonyl compounds using hydrogen peroxide as an oxideant: (a) Bunton, C. A.; Minkoff, G. J. *J. Chem. Soc.* **1949**, 665. (b) Greco, P. A.; Nishizawa, H.; Oguri, T.; Burkee, S. D.; Marinovic, N. *J. Am. Chem. Soc.* **1977**, *99*, 5773. (c) Julia, S.; Guixer, J.; Masana, J.; Rocas, J.; Colonna, S.; Molinari, H. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1317. (d) Ishii, Y.; Sakata, Y. *J. Org. Chem.* **1990**, *55*, 5545. (e) Banfi, S.; Colonna, S.; Molinari, H.; Julia, S.; Guixer, J., *Tetrahedron* **1984**, *40*, 5207. (f) Schulz, M.; Kluge, R.; Lipke, M. *Synlett* **1993**, 915. (g) Cativiela, C.; Figueras, F.; Fraile, J. M.; García, J. I.; Mayoral, J. A. *Tetrahedron Lett.* **1995**, *36*, 4125. (h) Kim, Y. H.; Hwang, J. P.; Yang, S. G. *Tetrahedron Lett.* **1997**, *38*, 3009. (i) Choudary, B. M.; Kantam, M. L.; Bharathi, B.; Reddy, C. V. *Synlett* **1998**, 1203.

(4) For Baeyer−Villiger oxidation of ketones, see: (a) Kaneda, K.: Ueno, S.; Imanaka, T. *J. Chem. Soc., Chem. Commun.* **1994**, 797. (b) Kaneda, K.; Ueno, S.; Imanaka, T. *J. Mol. Catal.* **1995**, *102*, 135. (c) Kaneda, K.; Yamashita, T. *Tetrahedron Lett.* **1996**, *37*, 4555. (d) Ueno, S.; Ebitani, K.; Ookubo, A.; Kaneda, K. *Appl. Surf. Sci.* **1997**, *121/122*, 366.

(5) For the oxidative dehydrogenation of alcohols, see: Kaneda, K.; Yamashita, T.; Matsushita, T.; Ebitani, K. *J. Org. Chem.* **1998**, *63*, 1750.

(6) For the oxygenation of aromatic compounds, see: Matsushita, T.; Ebitani, K.; Kaneda, K. *Chem. Commun.* **1999**, 265.

(7) For the epoxidation of olefins, see: (a) Ueno, S.; Yamaguchi, K.; Yoshida, K.: Ebitani, K.; Kaneda, K. *Chem. Commun.* **1998**, 295. (b) Yamaguchi, K.; Ebitani, K.; Kaneda, K. *J. Org. Chem.* **1999**, *64*, 2966.

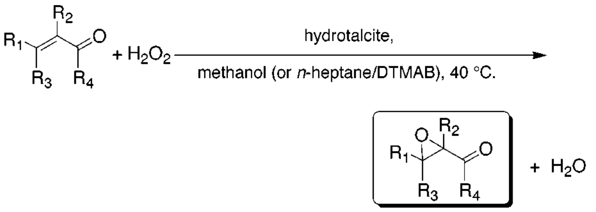
(8) For the *N*-oxidation of pyridines, see: Yamaguchi, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *New J. Chem.* **1999**, *23*, 799.

10.1021/jo000247e CCC: $19.00

Table 1. Effect of Solvents on the Epoxidation of 2-Cyclohexen-1-one Catalyzed by $Mg_{10}Al_2(OH)_{24}CO_3$ Using H_2O_2[a]

entry	solvent	convn[b] (%)	yield of epoxyketone[b] (%)
1	methanol	78	74
2	ethanol	30	26
3	2-propanol	15	10
4	ethyl acetate	79	78
5	1,2-dichloroethane	87	84
6	*n*-heptane	77	77
7	cyclohexane	71	71

[a] Reaction conditions: cyclohexenone (2 mmol), $Mg_{10}Al_2(OH)_{24}CO_3$ (0.15 g), 30% aq H_2O_2 (0.9 mL, 8 mmol), solvent (5 mL), 40 °C, 2 h. [b] Determined by GC using an internal standard technique.



(1)

be regarded as an environmentally friendly chemical process because it uses 30 wt % aqueous hydrogen peroxide, a simple workup procedure, and a reusable catalyst. In addition, cationic surfactants act as phase-transfer reagents to promote the epoxidation.

Results and Discussion

1. Triphasic Epoxidation System. 1-1. Survey of Reaction Conditions. Oxidations of 2-cyclohexen-1-one as a model substrate using 30 wt % aqueous hydrogen peroxide in various solvents were carried out in the presence of the hydrotalcite, $Mg_{10}Al_2(OH)_{24}CO_3$. The results are summarized in Table 1. 1,2-Dichloroethane was the most effective solvent for this oxidation; 2,3-epoxycyclohexanone was formed in 84% yield (40 °C, 2 h, entry 5). However, the use of halogenated solvents is undesirable from an environmental point of view.[2] Therefore, we had to try to use nonhalogenated solvents. It was then found that ethyl acetate, *n*-heptane, methanol, and cyclohexane were also good solvents, affording 78%, 77%, 74%, and 71% yields of the epoxyketone under the same reaction conditions, respectively (entries 1, 4, 6, and 7). Ethanol and 2-propanol were poor solvents (entries 2 and 3).

To optimize the amount of hydrogen peroxide required, epoxidations of 2-cyclohexen-1-one were carried out using various oxidant stoichiometries at 40 °C in methanol. When 4 equiv of hydrogen peroxide to a substrate were used, 2-cyclohexen-1-one gave an almost quantitative yield of the epoxyketone within 5 h. The epoxidation rate was slightly improved when a greater than 4-fold excess of hydrogen peroxide was used. *It is notable that excellent efficiency in hydrogen peroxide utilization could also be attained in this reaction system*. For example, 2,3-epoxycyclohexanone was obtained in 85% yield with only 1 equiv of hydrogen peroxide in methanol, although the reaction time was 24 h. The use of ethyl acetate, cyclohexane, and *n*-heptane solvents afforded the epoxyketone in 61%, 61%, and 58% yields, respectively.

The effect of reaction temperatures on the efficiency of hydrogen peroxide utilization was also examined in the case of the oxidation of 2-cyclohexen-1-one using 1 equiv of hydrogen peroxide in methanol solvent. High efficiency in hydrogen peroxide utilization was observed when the reaction was performed at low temperatures. However, attaining high yields of the epoxyketone required long reaction times below 20 °C, e.g., 82% yield at 20 °C for 48 h. The increase of reaction temperatures over 60 °C resulted in a decrease in efficiency; when the reaction temperature was changed from 40 to 60 °C, 85% yield of the epoxyketone after 24 h dropped to 73%. Epoxidation at 40 °C was the most suitable from the standpoints of the efficiency of hydrogen peroxide and the reaction rate.

Table 2. Recycling of the $Mg_{10}Al_2(OH)_{24}CO_3$ Catalyst in the Epoxidation of 2-Cyclohexen-1-one[a]

run	convn of cyclohexenone[b] (%)	yield of epoxyketone[b] (%)
1 (fresh)	94	91
2	91	90
3	92	90
4	91	89

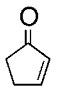
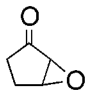
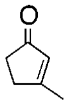
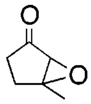
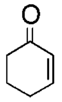
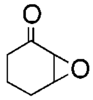
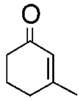
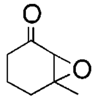
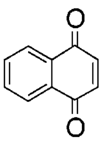
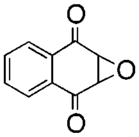
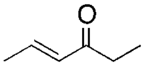
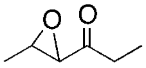
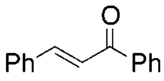
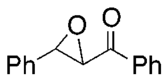
[a] Reaction conditions: cyclohexenone (2 mmol), $Mg_{10}Al_2(OH)_{24}CO_3$ (0.15 g), 30% aq H_2O_2 (0.9 mL, 8 mmol), methanol (5 mL), 40 °C, 5 h. [b] Determined by GC using an internal standard technique.

The use of a solid hydrotalcite makes the workup procedure very simple. The spent hydrotalcite, $Mg_{10}Al_2(OH)_{24}CO_3$, was easily separated from the reaction mixture by a simple filtration. The recovered catalyst was then reused for the epoxidation of 2-cyclohexen-1-one. The results are summarized in Table 2. The oxidation using the spent catalyst gave the epoxyketone in 90% yield under the same conditions as those of the first run. In the same manner, third and forth runs afforded the epoxyketone in 90% and 89% yields, respectively.

1-2. Epoxidation of Various α,β-Unsaturated Ketones. Oxidations of various α,β-unsaturated ketones using $Mg_{10}Al_2(OH)_{24}CO_3$ were carried out in methanol solvent at 40 °C and are summarized in Table 3. Simple cyclic enones such as cyclopentenone and cyclohexenone were smoothly oxidized to form the corresponding epoxyketones. 2-Cyclohexen-1-one was converted into 2,3-epoxycyclohexanone in 91% yield for 5 h (entry 3). A β-substituted cyclohexenone of 3-methyl-2-cyclohexen-1-one gave a high yield of the corresponding epoxyketone when the reaction time was prolonged to 24 h (entry 4). It is said that selective epoxidation of cyclopentenone is not attainable under basic conditions using NaOH and KOH because of competing aldol-type condensation. Notably, in the hydrotalcite catalyst system, 97% of 2,3-epoxycyclopentanone could be obtained from 2-cyclopenten-1-one in 3 h without formation of the aldol products (entry 1). Further, an alkyl-substituted cyclopentenone of 3-methyl-2-cyclopenten-1-one also could give the corresponding epoxyketone in excellent yield (entry 2). The oxidation of 1,4-naphthoquinone was very fast, affording the epoxyketone in an almost quantitative yield within 1 h (entry 5). Simple cyclic enones gave high yields of the corresponding epoxides, but the epoxidation of acyclic enones was difficult using the above reaction system. 4-Hexen-3-one, an aliphatic α,β-unsaturated ketone, was hardly oxidized under the above reaction conditions (entry 6). Further, oxidation of chalcone resulted in only 57% yield of 2,3-epoxy-1,3-diphenylpropanone (entry 7).

To explain the reactivity of the above α,β-unsaturated ketones, orbital energies in the LUMO of substrates **1**−**7**

Table 3. Epoxidation of Various α,β-Unsaturated Ketones Catalyzed by $Mg_{10}Al_2(OH)_{24}CO_3$ Using H_2O_2 in Methanol[a]

entry	substrate	product	time (h)	convn[b] (%)	yield[b] (%)	orbital energy[c] (eV)
1			3	99	97 (91)	-0.126
2			24	90	87 (80)	-0.128
3			5	94	91 (90)	-0.116
4			24	98	90 (80)	-0.121
5			1	99	97 (96)	-1.529
6			24	12	10	-0.008(*s-cis*) -0.047(*s-trans*)
7			24	57	57	-0.848

[a] Reaction conditions: substrate (2 mmol), $Mg_{10}Al_2(OH)_{24}CO_3$ (0.15 g), 30% aq H_2O_2 (0.9 mL, 8 mmol), methanol (5 mL), 40 °C. [b] Determined by GC or HPLC using an internal standard technique. Values in parentheses are isolated yields. For the isolation experiment, the reaction scale was three times as much as that of reaction conditions a. [c] Orbital energies in the LUMO were calculated by the PM3 semiempirical method.

were calculated (Table 3).[9] The orbital energies in the LUMO can be regarded as a measure of the electrophilicity of these enones.[10] The substrates **1**, **3**, and **5** having low LUMO orbital energies showed high reactivity for this epoxidation. The lower reactivity of substituted cyclic enones of **2** and **4** compared with nonsubstituted ones of **1**, **3**, and **5** might be due to the steric hindrance about olefinic double bonds. Vide supra, 4-hexen-3-one has a high LUMO orbital energy and gave an extremely low yield of the epoxyketone. The low reactivity of chalcone despite its low LUMO orbital energy might be related to its solubility into the water phase; the solubility is 0.16 mM for chalcone, whereas it is 157.7 mM for 2-cyclohexen-1-one at 25 °C.

2. Epoxidation under the Phase-Transfer Conditions. 2-1. Surfactant Effect. The above epoxidation mixture contains three phases: an organic ketone phase, an aqueous phase containing hydrogen peroxide, and the solid hydrotalcites. It is well-known that in a biphasic medium, surfactants can enhance the rates of many organic reactions by increasing the contact area of the interface between water and organic phases.[11,12] Since this oxidation occurs at the interface between water and organic phases, we expected that the use of surfactants might enhance the epoxidation of poorly reactive substrates such as 4-hexen-3-one and chalcone.

The effect of various surfactants on the epoxidation of chalcone was examined in *n*-heptane solvent as shown in Table 4. Interestingly, the use of cationic surfactants having long alkyl chains such as $[CH_3(CH_2)_{11}N(CH_3)_3]Br$ (DTMAB), $[CH_3(CH_2)_{15}N(CH_3)_3]Br$, and $[(n\text{-}C_{12}H_{25})_4N]Br$ gave high yields of 2,3-epoxy-1,3-diphenylpropanone (entries 2, 4, and 6), while $[CH_3(CH_2)_7N(CH_3)_3]Br$ and $[(n\text{-}C_4H_9)_4N]Br$ having short alkyl chains were not effective (entries 1 and 5). Both an anionic surfactant $[CH_3(CH_2)_{11}SO_4]Na$ (SDS) and a nonionic surfactant of sorbitan monolaurate (span 20) failed to promote the epoxidation

---

(9) The geometries of α,β-unsaturated ketones were calculated by the PM3 semiempirical method as implemented in the MOPAC version 97 system. The calculation was performed to localize the olefinic double bonds of α,β-unsaturated ketones into the *XY* plane: Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 221.

(10) Loncharich, R. J.; Brown, F. K.; Houk, K. N. *J. Org. Chem.* **1989**, *54*, 1129.

(11) Mathias, L. J.; Vaidys, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 1093 and references cited therein.

(12) Recently, phase-transfer oxidation systems using hydrogen peroxide have been developed. The followings are excellent examples of epoxidation under phase-transfer conditions: (a) Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1996**, *61*, 5307. (b) Boyer, B.; Hambardzoumian, A.; Lamaty, G.; Leydet, A.; Roque, J.-P.; Bouchet, P. *New J. Chem.* **1996**, *20*, 985. (c) Sato, K.; Aoki, M.; Ogawa, M.; Hashimoto, T.; Panyella, D.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 905. (d) Boyer, B.; Hambardzoumian, A.; Roque, J.-P. *Tetrahedron* **1999**, *55*, 6147.

Table 4. Effect of Surfactants on the Epoxidation of Chalcone Catalyzed by $Mg_{10}Al_2(OH)_{24}CO_3$ Using H_2O_2[a]

entry	surfactant	convn[b] (%)	yield of epoxyketone[b] (%)
1	$[CH_3(CH_2)_7N(CH_3)_3]Br$	12	12
2	$[CH_3(CH_2)_{11}N(CH_3)_3]Br$	100	98
3[c]	$[CH_3(CH_2)_{11}N(CH_3)_3]Br$	3	3
4	$[CH_3(CH_2)_{15}N(CH_3)_3]Br$	100	96
5	$[(n\text{-}C_4H_9)_4N]Br$	5	3
6	$[(n\text{-}C_{12}H_{25})_4N]Br$	100	96
7	$[CH_3(CH_2)_{11}SO_4]Na$	3	3
8	sorbitan monolaurate (span 20)	5	5
9	without	2	2

[a] Reaction conditions: chalcone (2 mmol), $Mg_{10}Al_2(OH)_{24}CO_3$ (0.15 g), 30% aq H_2O_2 (0.9 mL, 8 mmol), *n*-heptane (5 mL), surfactant (0.3 mmol), water (3 mL), 40 °C, 2 h. [b] Determined by HPLC using an internal standard technique, [c]Without hydrotalcite catalyst.

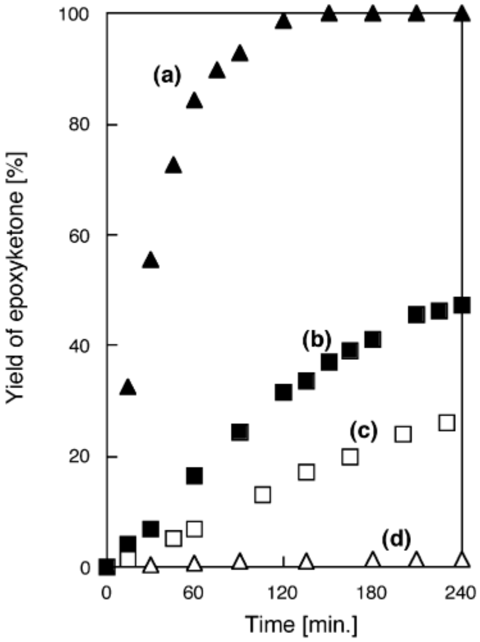


Figure 1. Reaction profiles of the $Mg_{10}Al_2(OH)_{24}CO_3$-catalyzed epoxidation of chalcone in (a) *n*-heptane with DTMAB, (b) methanol with DTMAB, (c) methanol without DTMAB, and (d) *n*-heptane without DTMAB.

(entries 7 and 8 vs entry 2). In addition, oxidation without the hydrotalcite catalyst gave only 3% of the epoxyketone even in the presence of DTMAB (entry 3).

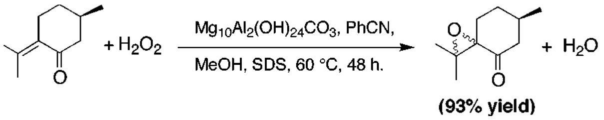
Oxidations of chalcone using DTMAB or no surfactant were carried out in various solvents at 40 °C, as shown in Figure 1. Adding DTMAB to the above oxidation system remarkably accelerated yields of the epoxyketone, particularly when nonpolar solvents such as *n*-hexane, cyclohexane, and *n*-heptane were used. For example, a quantitative yield of the epoxyketone was obtained in *n*-heptane within 2 h, while the epoxidation hardly proceeded in the absence of DTMAB. The use of methanol in the presence of DTMAB gave the epoxyketone in only 46% yield after 4 h.

Further, a similar phenomenon was observed also in the epoxidation of 2-cyclohexen-1-one (Table 5, entry 6). It is clear that this phase-transfer procedure by the use of DTMAB is very effective, especially for the epoxidation of hydrophobic enone substrates.

2-2. Substrate Scope. This phase-transfer procedure using DTMAB could be widely applied to various kinds of α,β-unsaturated ketones. Typical examples are collected in Table 5. Oxidations of common open-chain α,β-unsaturated ketones proceeded smoothly to give epoxyketones in high yields (entries 1−5). In the oxidation of the open-chain ketones using calcined hydrotalcites, Cativiela et al. reported the formation of 1,2-dioxolane products; mesityl oxide and 4-hexen-3-one gave the corresponding 3-hydroxy-1,2-dioxolanes in 36 %and 22% yields, respectively.[3g] Using our catalyst system, 13% yield of 3-hydroxy-3,3,5-trimethyl-1,2-dioxolane was obtained as a byproduct in the case of mesityl oxide (entry 1). Other open-chain aliphatic enones such as 4-hexen-3-one and 3-nonen-2-one gave high yields of epoxyketones as sole products, respectively (entries 2 and 3).

Generally, the epoxidation of isophorone does not easily proceed as a result of the steric hindrance of the β-substituted methyl group and *gem*-dimethyl group.[13] Isophorone, however, could be efficiently oxidized to form epoxyisophorone in 95% yield with this system (entry 7). In the case of (*R*)-(−)-carvone, hydrotalcite catalysts resulted in regioselective oxidation of the conjugated double bond to afford 2,3-epoxy-5-isopropenyl-2-methylcyclohexanone as a single diastereomer with the methyl group *cis* to the isopropenyl group (entry 8).[14] A similar selective formation of the *cis*-carvone oxide can be also observed in the base-catalyzed epoxidation using the hydrogen peroxide/NaOH system.[14]

The β,β-disubstituted acyclic enone, pulegone, hardly gave any epoxyketone, even after 48 h. Pulegone has high orbital energies both in the LUMO and HOMO, 0.273 and −9.605 eV, respectively. It is likely that electrophilic oxidants such as peracids might be preferable to a nucleophilic HOO^- species for the epoxidation of pulegone. Indeed, using a combined oxidant of benzonitrile and hydrogen peroxide in the presence of hydrotalcites,[7a] pulegone could be smoothly oxidized to give the corresponding epoxyketone in 93% yield (eq 2).



(2)

3. Catalyst Effect and Reaction Mechanism. Oxidations of isophorone using various kinds of base catalysts carried out in the presence of DTMAB are shown in Table 6. Yields of the epoxyketone increased with an increase in the heat of benzoic acid adsorption on hydrotalcites (entries 1, 3, and 5). The calorimetric heat of benzoic acid adsorption can be regarded as a measure of the basicity of the solid surfaces.[4d] The catalytic activity of MgO was lower than those of hydrotalcites and $Mg(OH)_2$, although MgO possesses a strong basicity (entry 6). The use of NaOH as a base catalyst resulted in a low selectivity as a result of oxidative cleavage of the epoxyketone to form 3,3-dimethyl-5-oxohexanoic acid (entry 9).[15] It is said that the calcined hydrotalcites of Mg−Al mixed oxides have high Lewis basicity derived from the surface oxygen species.[16] However, their catalytic activi-

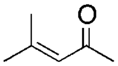
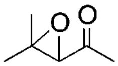
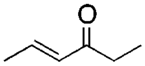
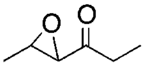
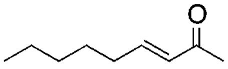
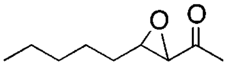
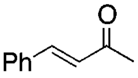
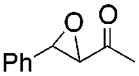
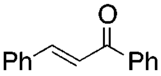
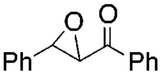
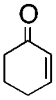
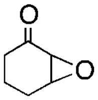
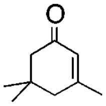
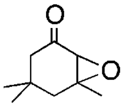
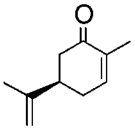
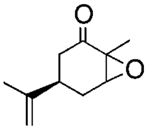
---

[13] (a) Yadav, V. K.; Kapoor, K. K. *Tetrahedron Lett.* **1994**, *35*, 9481. (b) Straub, T. S. *Tetrahedron Lett.* **1995**, *36*, 663. (c) Fraile, J. M.; García, J. I.; Cativiela, C.; Mayoral, J. A.; Figueras, F. *Tetrahedron Lett.* **1996**, *37*, 5995.

[14] Lindquist, N.; Battiste, M. A.; Whitten, W. M.; Williams, N. H.; Strekowski, L. *Phytochemistry* **1985**, *24*, 683.

[15] Temple, R. D. *J. Org. Chem.* **1970**, *35*, 1275.

Table 5. Epoxidation of Various α,β-Unsaturated Ketones Catalyzed by $Mg_{10}Al_2(OH)_{24}CO_3$ Using H_2O_2 under Phase-Transfer Conditions with DTMAB[a]

entry	substrate	product	time (h)	convn[b] (%)	yield[b] (%)
1			4	95	80[c]
2			4	99	96
3			6	95	94 (70)
4			24	79	72 (70)
5			2	99	99 (82)
6			3.5	95	92
7			24	97	95 (73)
8			24	99	99 (80) (*cis*:*trans* =96:4)

[a] Reaction conditions: substrate (2 mmol), $Mg_{10}Al_2(OH)_{24}CO_3$ (0.15 g), 30% aq H_2O_2 (0.9 mL, 8 mmol), *n*-heptane (5 mL), DTMAB (0.3 mmol), water (3 mL), 40 °C. [b] Determined by GC or HPLC using an internal standard technique. Values in parentheses are isolated yields. For the isolation experiment, the reaction scale was three times as much as that of reaction conditions a. [c] Yields were determined by ^1H NMR of the reaction mixture. 3-Hydroxy-3,3,5-trimethyl-1,2-dioxolane was also formed in 13% yield.

ties were slightly lower than those of the corresponding uncalcined hydrotalcites (entries 1 vs 2 and 3 vs 4). The XRD spectra revealed that calcined hydrotalcites were hydrated partially to rebuild the original hydrotalcite structure under our reaction conditions using aqueous hydrogen peroxide. Moreover, the calcined hydrotalcites have not only strong basic sites but also acidic sites.[16] Vide supra, in the oxidation of open-chain aliphatic enones using calcined hydrotalcites, the selectivities to epoxyketones were undesirable because of the acid-catalyzed formation of 1,2-dioxolanes.[3g,17] These results

Table 6. Epoxidation of Isophorone Catalyzed by Various Bases Using H_2O_2[a]

entry	catalyst	convn of isophorone (%)	yield of epoxyketone[b] (%)	heat of adsorption[c] (J g^{-1})
1	$Mg_{10}Al_2(OH)_{24}CO_3$	97	95	14.2
2[d]	$Mg_{10}Al_2(OH)_{24}CO_3$	88	84	20.2
3	$Mg_6Al_2(OH)_{16}CO_3$	77	73	6.3
4[d]	$Mg_6Al_2(OH)_{16}CO_3$	69	62	16.9
5	$Mg_6Al_2(OH)_{16}SO_4$	61	61	5.1
6[e]	MgO	51	40	8.4
7	$Mg(OH)_2$	60	60	6.4
8	$Al(OH)_3$	8	7	1.8
9[f]	NaOH	81	70[g]	
10[f]	Na_2CO_3	53	47	
11	without	<1	<1	

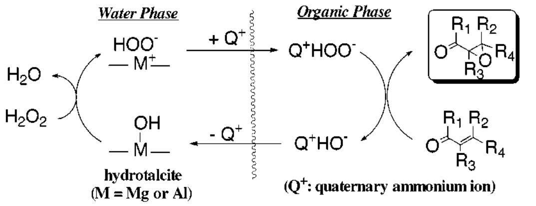
[a] Reaction conditions: isophorone (2 mmol), catalyst (0.15 g), *n*-heptane (5 mL), DTHMAB (0.3 mmol), water (3 mL), 30% aq H_2O_2 (0.9 mL, 8 mmol), 40 °C, 24 h. [b] Yields of the epoxide were determined by GC. [c] See ref 4d. [d] Catalysts calcined at 400 °C were used. [e] MgO calcined at 400 °C was used. [f] 0.2 mmol. [g] 3,3-Dimethyl-5-oxohexanoic acid was also formed as a byproduct.

---

(16) We have recently reported that the Mg–Al mixed oxides obtained by calcination of hydrotalcites were effective acid–base bifunctional catalysts for the fixation of CO_2 to various epoxides to form five-membered cyclic carbonates: Yamaguchi, K.; Ebitani, K.; Yoshida, T.; Yoshida, H.; Kaneda, K. *J. Am. Chem. Soc.* **1999**, *121*, 4526.

(17) It is known that 1,2-dioxolane compounds are formed by 1,4-addition reaction of hydrogen peroxide to the enone such as mesityl oxide and 4-hexen-3-one under acidic conditions: (a) Rieche, A.; Schmitz, E.; Gründemann, E. *Angew. Chem.* **1960**, *72*, 635. (b) Rieche, A.; Schmitz, E.; Gründemann, E. *Chem. Ber.* **1960**, *93*, 2443.

Scheme 1



indicate that basic sites due to the surface hydroxyl groups on uncalcined hydrotalcites might play an important role in this selective epoxidation.

A possible reaction mechanism for this epoxidation is shown in Scheme 1. Hydrogen peroxide reacts with a basic hydroxyl function on the surface of a hydrotalcite to form a perhydroxyl anion. This anionic species attacks the β-olefinic carbon atom of an α,β-unsaturated ketone, followed by the ring enclosure to give the corresponding epoxyketone, which regenerates the surface hydroxyl function of the hydrotalcite. Vide supra, α,β-unsaturated ketones having low LUMO orbital energies show high reactivity. The above results support that this epoxidation can occur via a nucleophilic attack of a perhydroxyl species. Oxidation of less reactive substrates with high LUMO energies and/or low solubility into the water phase is strongly promoted by cationic surfactants. Under these phase-transfer conditions, it is likely that a perhydroxyl anion species interacts with quaternary ammonium cation (Q^+) and then moves into organic phase by forming an ion pair such as a Q^+HOO^- species in order to react with a lipophilic α,β-unsaturated ketone substrate. The long alkyl chains of cationic surfactants bring about increasing the lipophilicity of cationic surfactant molecules, which facilitates the transporting of a lipophilic enone from the organic phase to the interface as a reaction zone. We think that main roles of the cationic surfactants are (1) to increase the contact area of the interface between water and organic phases, (2) to ensure the transfer of a substrate from the organic phase to the surface boundary, and (3) to gather the perhydroxyl anion from the water phase to the surface boundary.

Conclusion

Solid hydrotalcites efficiently catalyze the epoxidation of various kinds of α,β-unsaturated ketones using hydrogen peroxide under mild reaction conditions. In this epoxidation, basic sites due to surface hydroxyl functions of hydrotalcites promote the transformation of hydrogen peroxide into the perhydroxyl anion as an active species. For less reactive substrates, the phase-transfer procedure using a cationic surfactant of DTMAB is very effective for facile formation of epoxyketones. Further, these hydrotalcite catalysts are easily separated from the reaction mixture and can be reused with retention of their high catalytic activity and selectivity. We believe that this hydrotalcite-catalyzed system could have high potential in a wide variety of environment-friendly organic syntheses.

Experimental Section

General. $Al(NO_3)_3 \cdot 9H_2O$, $Al(OH)_3$, $Mg(NO_3)_2 \cdot 6H_2O$, and $Mg(OH)_2$ were purchased from Wako Pure Chemical as a special grade. MgO was supplied from the Catalyst Society of Japan as a reference catalyst, JRC-MGO-4 (1000 A) and used after the calcination at 400 °C. Hydrogen peroxide (30 wt %) and various kinds of surfactants were purchased from Wako Pure Chemical and used as received. α,β-Unsaturated ketones as substrates and solvents were purified by the standard procedures before use.[18] All of the epoxidation products are well-known compounds. Their identities were confirmed by comparison with mass spectroscopy and ^1H and ^{13}C NMR and infrared spectra.[14,19]

General Procedure for Preparation of Hydrotalcite Catalysts. Various hydrotalcites were prepared by the literature procedure.[20] A typical example is for $Mg_{10}Al_2(OH)_{24}CO_3$. $Al(NO_3)_3 \cdot 9H_2O$ (0.01 mol) and $Mg(NO_3)_2 \cdot 6H_2O$ (0.05 mol) were dissolved in deionized water (100 mL), and a second water solution (60 mL) of Na_2CO_3 (0.03 mol) and NaOH (0.07 mol) was prepared. After the first solution was slowly added to the second one, the resulting mixture was heated at 65 °C for 18 h with vigorous stirring. The white slurry was then cooled to room temperature, filtered, washed with large amount of deionized water, and dried overnight at 110 °C. The basal spacing was 7.93 Å determined from the XRD measurement. These hydrotalcite catalysts were stored in air and used without further pretreatment.

Measurement of the Basicity of Catalysts. The calorimetric heats of benzoic acid adsorption on the catalysts were measured by using a microdifferential scanning calorimeter.[4d] Catalyst (10 mg) was added into a cyclohexane solution (0.5 mL), and then a solution of benzoic acid (0.005 mmol) in cyclohexane (0.2 mL) was added into the above solution. The heat of generation was regarded as the calorimetric heat of benzoic acid adsorption.

General Procedure for the Epoxidation with Hydrotalcite Catalysts. Typical hydrotalcite-catalyzed epoxidation of α,β-unsaturated ketones is accomplished as follows. Into a reaction vessel with a reflux condenser were successively placed the hydrotalcite of $Mg_{10}Al_2(OH)_{24}CO_3$ (0.45 g), methanol (15 mL), 2-cyclohexen-1-one (6 mmol), and 30% aqueous hydrogen peroxide (2.7 mL, 24 mmol). After the resulting mixture was stirred at 40 °C for an appropriate time, the hydrotalcite was separated by a filtration. The filtrate was treated with MnO_2, followed by extraction with ethyl acetate (25 mL × 3). The extract was concentrated and subjected to column chromatography on silica gel (Wako gel C-200) with a mixture of *n*-hexane and ether (3:1) to afford 0.61 g of pure 2,3-epoxycyclohexanone (90% yield).

General Procedure for the Hydrotalcite-Catalyzed Epoxidation under Phase-Transfer Conditions. A typical example for the epoxidation under the phase-transfer conditions is as follows. Into a reaction vessel with a reflux condenser were successively placed the hydrotalcite of $Mg_{10}Al_2(OH)_{24}CO_3$ (0.45 g), methanol (15 mL), chalcone (6 mmol), 30% aqueous hydrogen peroxide (2.7 mL, 24 mmol), dodecyltrimethylammonium bromide (DTAB) (0.3 mmol), and water (0.9 mL). After the resulting mixture was stirred at 40 °C for an appropriate time, affording 1.10 g of pure 2,3-epoxy-1,3-diphenylpropanone (82% yield).

Recycling of the Hydrotalcite Catalyst for the Epoxidation of 2-Cyclohexen-1-one. Using the same procedure as described in the above, the first run for 2-cyclohexen-1-one (2 mmol scale) was carried out. After the oxidation, the spent hydrotalcite was recovered by filtration. The isolated hydrotalcite was washed with a small portion of deionized water and dried overnight at 110 °C before reuse. These recycling procedures were repeated three times in the same manner as for the first recycle.

---

[18] *Purification of Laboratory Chemicals*, 3rd ed.; Perrin, D. D., Armarego, W. L. F., Eds; Pergamon Press: Oxford, U.K., 1988.

[19] (a) Wyneberg, H.; Marsman, B. *J. Org. Chem.* **1980**, *45*, 158. (b) Reed, K. L.; Gupton, J. T.; Solarz, T. L. *Synth. Commun.* **1989**, *19*, 3579. (c) Adam, W.; Hadjiarapoglou, L.; Nester, B. *Tetrahedron Lett.* **1990**, *31*, 331. (d) Straub, T. S. *Tetrahedron Lett.* **1995**, *36*, 663.

[20] (a) Miyata, S. *Clays Clay Miner.* **1980**, *28*, 50. (b) Cavani, F.; Trifirò, F.; Voccari, A. *Catal. Today* **1991**, *11*, 173.

Acknowledgment. This work is supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan (11450307). We thank Prof. Yasunori Yoshioka at Osaka University for his help in MO calculations. We are also grateful to the Department of Chemical Science and Engineering, Osaka University, for scientific support by the Gas-Hydrate Analyzing System (GHAS).

JO000247E