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Practical Epoxidation of α, β-Unsaturated Ketones with Tetra-n-butylammonium Peroxydisulfate

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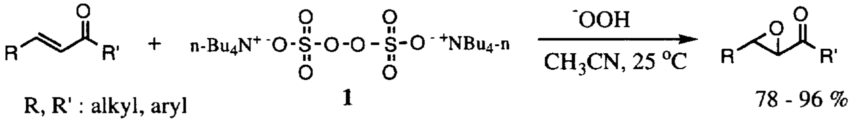
Abstract : α,β-Unsaturated ketones reacted with tetra-n-butylammonium peroxydisulfate in the presence of hydrogen peroxide and base in acetonitrile at 25 °C to give the corresponding epoxides in excellent yields.

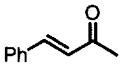
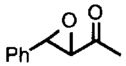
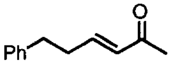
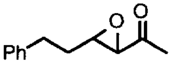
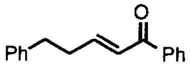
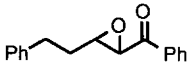
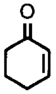
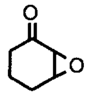
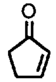
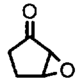
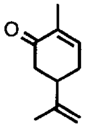
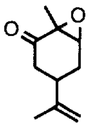
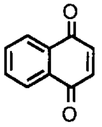
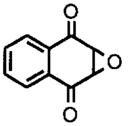
Epoxidation of electron deficient olefins such as α,β-unsaturated ketones has been an important target for the functionalizations of ketones. In contrast to the electrophilic epoxidation of general alkenes, epoxidation of electron deficient olefins requires a nucleophilic oxidation in the alkaline condition. A number of epoxidation of electron deficient olefins have been developed using tertiary butyl peroxide,[1] *m*-chloroperbenzoic acid,[2] hydrogen peroxide,[3] peroxide-ammonium fluoride,[4] or sodium perborate[5] under strong alkaline conditions. The yields are generally varied depend on substrates and reaction conditions. We have interested in epoxidation of electron deficient olefins such as α,β-unsaturated ketones utilizing peroxysulfonate.[6] However, it was failed to epoxidize the electron deficient double bond.[6] But ring double bonds or chain double bonds were regioselectively epoxidized by electrophilic oxidation rather than nucleophilic oxidation in even basic conditions.[6] Such a peroxysulfonate ($RS(O_2)OO^-$) or peroxysulfate (**2**) has neither been isolated nor confirmed.

We have successfully prepared tetra-n-butylammonium peroxydisulfate ($TBA_2S_2O_8$: **1**),[7a] which shows oxidizing ability for the cleavage of C=N bond and it may involve formation of an oxaziridine intermediate.[7b] We have now found that various α,β-unsaturated ketones reacted with $TBA_2S_2O_8$ and H_2O_2 under basic conditions at 25 °C to result in the corresponding epoxides in excellent yields.



The following experimental procedure is representative. 2-Cyclohexen-1-one (1.0 mmol, 98 mg) was dissolved in anhydrous acetonitrile (1 ml). The solution of **1** (1.0 mmol, 667 mg) and sodium hydroxide (1.0 mmol, 40 mg) in anhydrous acetonitrile (4 ml) was added and then hydrogen peroxide (50 % w/w, 1.0 mmol, 0.052 ml) slowly added to the reaction mixture. After stirring 0.5 hour at 25 °C by monitoring the reaction on thin layer chromatography, the reaction mixture was extracted with methylene chloride (30 ml x 3), washed with water, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give a crude product which was purified by a flash column chromatography (silica gel 230-400 mesh, 20 x 2 cm, eluent; EtOAc : n-Hexane = 1 : 5, 95 %). The results obtained are summarized in Table 1.

Table 1. Epoxidation of α,β-Unsaturated Ketones with Tetra-n-butylammonium Peroxydisulfate **1** and Hydrogen Peroxide in the Presence of Sodium Hydroxide in Acetonitrile at 25 °C

Run	Substrates	**1** (eq.)	H_2O_2 (eq.)	Base (eq.)	Reaction Time (h)	Products	Yield [a] (%)
1		1	1	K_2CO_3 (1)	1		50
2		1	none	NaOH (1)	1		trace
3		none	1	NaOH (1)	1		30
4		1	1	NaOH (1)	0.5		95 [b]
5		1	1	NaOH (1)	2.5		88
6		1	1	NaOH (1)	2.0		98
7		0.5	0.5	NaOH (0.5)	0.1		90 [c]
8		1	1	NaOH (1)	0.5		95
9		1	1	NaOH (1)	0.5		85
10		1	1	NaOH (1)	2		92
11		1	1	NaOH (1)	0.5		95

a) Isolated yields. b) When the same reaction was carried out in benzene, CH_2Cl_2, or $CHCl_3$ for 1h, the product was isolated in 10 %, 65 %, or 73 % respectively. c) The reaction was carried out in a mixture solvent of MeCN and MeOH (v/v = 1/1)

The peroxydisulfate ($TBA_2S_2O_8$, **1**) may convert to tetra-n-butylammonium peroxysulfate (**2**) by attacking of HOO^- of which 1,4-addition to α,β-unsaturated ketone produces the epoxide product together with tetra-n-butylammonium sulfate (**3**) as shown in Figure 1.

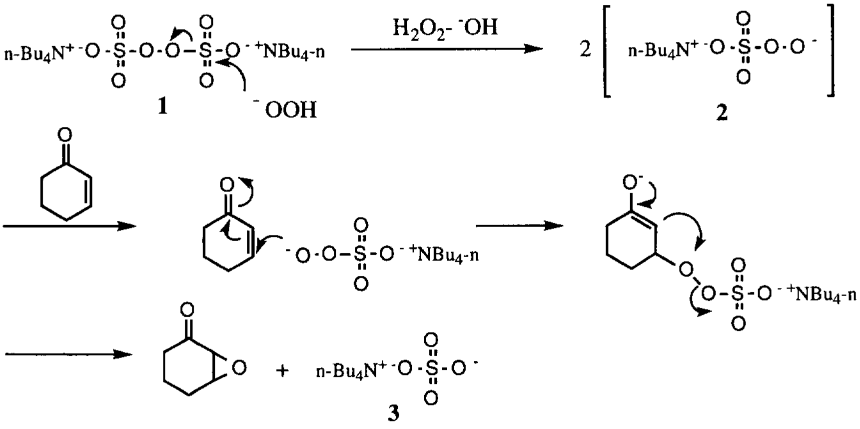


Figure 1. Epoxidation of α,β-Unsaturated Ketones with **1** - H_2O_2 - ^-OH

In this reaction, **3** was actually isolated in 80 % and confirmed. There are two competitive routes for the epoxidation of **1**; one is epoxidation by **2**, and the other one is by HOO^-. In the Table 1, equivalent amounts of **1**, H_2O_2, and NaOH in acetonitrile gave the best yields of epoxides (run 4: 95 % and run 8: 95 %). Equivalent amount of H_2O_2 and NaOH in the absence of **1**, resulted in low yield (run 3: 30 %) under the same reaction conditions. In the absence of H_2O_2, traceable amount of epoxide was isolated (run 2). The stronger nucleophile of HOO^- than HO^- may be attributed to form **2** more easily. Such a peroxysulfate ($RS(O)_3O$-O^-) has been neither isolated nor confirmed. But peroxydisulfate **2** is considered to be involved in this new epoxidation. Both cyclic and acyclic α,β-unsaturated ketones were smoothly oxidized into the corresponding epoxides. In the case of L-carvone, the ring double bond of α-substituted α,β-unsaturated carbonyl was selectively epoxidized (run 10 in Table I). On the other hand, β-substituted α,β-unsaturated ketones such as α-ionone and pulegone were not epoxidized probably due to the steric hindrance of β-subsituents : Starting materials were recovered quantitatively.[8] Furthermore, acetal, ketal, and thioether moieties have been found to be inert to **1** in the furanylation and pyranylation of alcohols [7a, 9] and in the oxidation of alcohols.[10]

The present epoxidation may provide a practically efficient method for epoxidations of α,β-unsaturated ketones containing various functional groups under mild conditions.

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References and Notes

1. a) Wynberg, H.; Marsman, B. *J. Org. Chem.*, **1980**, *45*, 158. b) Pluim, H.; Wynberg, H. *J. Org. Chem.*, **1980**, *45*, 2498. c) Bruke, S. D.; Murtiashaw, C. W.; Saunders, J. O.; Oplinger, J. A.; Dike, M. S. *J. Am. Chem. Soc.*, **1984**, *106*, 4558. d) Yadav, V. K.; Kapoor, K. K. *Tetrahedron Lett.*, **1994**, *35*, 9481. e) Acena, J. L.; Arjona, O.; Pradilla, R. F.; Plumet, J.; Viso, A. *J. Org. Chem.*, **1994**, *59*, 6419.
2. Martinelli, M. J.; Peterson, B. C.; Khau, V. V.; Hutchison, D. R.; Leanna, M. R.; Audia, J. E.; Droste, J. J.; Wu, Y. D.; Houk, K. N. *J. Org. Chem.*, **1994,** *59*, 2204.
3. a) Greene, A. E.; Luche, M. J.; Depres, J. P. *J. Am. Chem. Soc.*, **1983**, *105*, 2435. b) Baggiolini, E. G.; Iacobelli, J. A.; Hennessy, B. M.; Batcho, A. D.; Sereno, J. F.; Uskokovic, M. R. *J. Org. Chem.*, **1986**, *51*, 3098. c) Guy Solladie, G. S.; Hutt, J. *J. Org. Chem.*, **1987**, *52,* 3560. d) Hoeger, C. A.; Johnston, A. D.; Okamura, W. H. *J. Am. Chem. Soc.*, **1987**, *109*, 4690. e) Benzuidenhoudt, B. C. B.; Swanepoel, A.; Augustyn, J. A. N.; Ferreira, D. *Tetrahedron Lett.*, **1987**, *28*, 4857. f) Baures, P. W.; Eggleston, D. S.; Flisak, J. R.; Gombatz, K.; Lantos, I.; Mendelson, W.; Remich, J. J. *Tetrahedron Lett.*, **1990**, *31*, 6501. g) Itsuno, S.; Sakakura, M.; Ito, K. *J. Org. Chem.*, **1990**, *55*, 6047. h) Shulz, M.; Kluge, R.; Lipke, M. *Synlett,* **1993**, 915.
4. Miyashita, M; Suzuki, T.; Yoshikoshi, A. *Chem. Lett.*, **1987**, 285.
5. Straub, T. S. *Tetrahedron Lett.*, **1995**, *36*, 663.
6. Kim, Y. H.; Chung, B. C. *J. Org. Chem.*, **1983**, *48*, 1562.
7. a) Jung, J. C.; Choi, H. C.; Kim,Y. H. *Tetrahedron Lett.*, **1993**, *34*, 3581. b) Choi, H. C.; Kim, Y. H. *Syn. Commun.*, **1994**, *24*, 2307.
8. A present limitation scope of the progress is not available for β-substituted compounds of α,β-unsaturated ketones probably due to a steric hindrance of the substituents at β-position.
9. Choi, H. C.; Jung, J. C.; Kim,Y. H. *Heteroatom Chem.*, **1996**, *6*, 333.
10. Kim,Y. H.; Jung, J. C. unpublished data.

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