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Stereoselective Epoxidation with Dioxiranes Generated from Ketones

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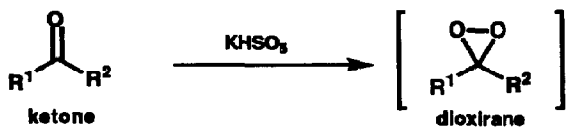
Abstract: Dioxiranes generated *in situ* from potassium monoperoxysulfate and cyclohexanones stereoselectively oxidized cyclohexene derivatives to afford epoxides.

Dioxiranes[1] have recently been shown to be important and versatile oxidants, which are generated from potassium monoperoxysulfate (KHSO5) and ketones. (Fig. 1) Dimethyldioxirane, a dioxirane generated from acetone as a ketone, is particularly useful as an oxidation reagent with a broad scope of synthetic applications[2]. Several papers have been reported about stereoselective epoxidation using dimethyldioxirane[3]. However, there have been only a few examples using dioxiranes generated from other ketones[4]. In this paper, we report the stereoselective epoxidation of cyclohexene derivatives with dioxiranes generated *in situ* from cyclohexanones, and the stereoselectivities due to ketone structure are also discussed. (Fig. 2)

Fig 1



Dioxiranes were prepared *in situ* by reactions of potassium monoperoxysulfate (commercially available as OXONE) with cyclohexanones. Epoxidation was carried out in a CH_2Cl_2-MeOH-buffer solvent system at pH 11.

Fig 2

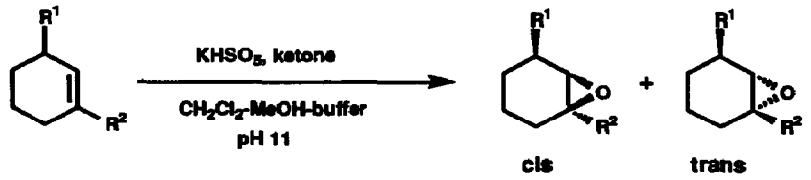
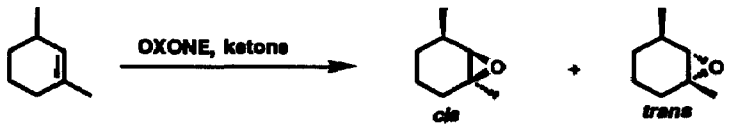
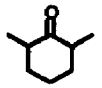
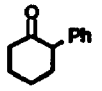
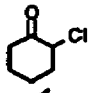


Table 1 shows the results of the epoxidation of 1,3-dimethyl-1-cyclohexene with potassium monoperoxysulfate in the presence of cyclohexanones. Dioxiranes as oxidants gave rise to *trans* selectivity while only slight selectivity was noted with *m*-CPBA. The best selectivity (96 : 4) was achieved with 2-

chlorocyclohexanone as a ketone. (entry 5) More sterically hindered ketones generally gave better selectivities.(entry 1-5)

Table 1. Stereoselective Epoxidation of 1,3-Dimethyl-1-cyclohexene



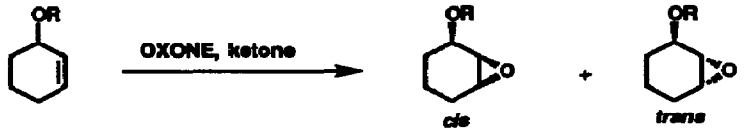
Entry	Reagent	Method[a]	Reaction time (h)	Yield(%)[b]	Selectivity[c] (*cis*:*trans*)
1	OXONE 	A	3.0	55	14 : 86
2	OXONE 	A	3.5	80	9 : 91
3	OXONE 	A	3.5	83	12 : 88
4	OXONE 	A	4.0	68	7 : 93
5	OXONE 	A	3.0	100	4 : 96
6	OXONE 	A	18.5	70	23 : 77
7	OXONE, no ketone	A	2.5	28	25 : 75
8	m-CPBA	B	1.0	76	46 : 54

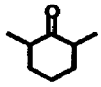
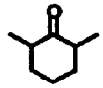
a) Method A : a solution of OXONE (5 mmol) in water was added dropwise to a well-stirred mixture of CH_2Cl_2 (2.5 ml), MeOH (20 ml), and buffered water (6 ml, pH 11.0, 0.5 M phosphate buffer) containing 1,3-dimethy-1-cyclohexene (0.5 mmol), ketone (5.0 mmol),and 18-crown-6 as a phase-transfer catalyst at 0-5 °C. During the addition, pH of the reaction mixture was monitored and kept constant using a pH-stat (1N KOH).
Method B: a mixture of 1,3-dimethyl-1-cyclohexene (5 mmol) and *m*-CPBA (15 mmol) in CH_2Cl_2 was stirred at r.t.
b) Determined by GLC.
c) Determined by GLC.

The epoxidation of 2-cyclohexen-1-ol and its TBDMS derivatives was carried out and the results are summarized in Table 2. With 2-cyclohexen-1-ol, use of dioxiranes as oxidants led to *trans* selectivity in contrast to *cis* selectivity in m-CPBA. (entry 1-6, 8) Epoxidation with $KHSO_5$ in the absence of a ketone indicated *cis* selectivity. (entry 7) For TBDMS derivatives, epoxidation with dioxiranes brought about *trans*

selectivity. Selectivity (93 : 7) was maximal with dioxirane derived from 2,6-dimethylcyclohexanone.(entry 8) In either case, more sterically hindered ketones provided better selectivities. (entry 1-3, 6-8)

Table 2. Stereoselective Epoxidation of Cyclohexenol Derivatives



Olefine	Entry	Reagent	Method[a]	Reaction time (h)	Yield (%)[b]	Selectivity[c] (*cis*:*trans*)
	1	OXONE 	C	1.5	69	36 : 64
	2	OXONE 	C	3.5	63	29 : 71
	3	OXONE 	C	3.0	66	23 : 77
	4	OXONE, no ketone	C	3.0	46	73 : 27
	5	m-CPBA	B	3.0	83	95 : 5
	6	OXONE 	C	3.5	40	13 : 87
	7	OXONE 	C	1.5	77	10 : 90
	8	OXONE 	C	3.0	65	7 : 93
	9	OXONE, no ketone	C	3.0	0	-
	10	m-CPBA	B	3.5	85	18 : 82

a) Method C: a solution of OXONE (4 mmol) in water was added dropwise to a well-stirred mixture of CH_2Cl_2 (10 ml), MeOH (40 ml) and buffered water (20 ml, pH 11.0, 0.5 M phosphate buffer) containing 1,3-dimethy-1-cyclohexene (2 mmol), ketone (20mmol) at r.t.. During the addition, pH of the reaction mixture was monitored and kept constant using a pH-stat (1N KOH).
Method B: mixture of 1,3-dimethyl-1-cyclohexene (2 mmol) and m-CPBA (6 mmol) in CH_2Cl_2 was stirred at r.t.

b) Isolated yield.

c) Determined by GLC. d) TBDMS : *tert*-butyldimethylsilyl

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