716 **RESEARCH PAPER** NOVEMBER, 716–718 JOURNAL OF CHEMICAL RESEARCH 2005

Epoxidation of electron-deficient α,β-unsaturated carbonyl compounds over Keggin heteropoly compounds with aqueous H_2O_2

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The epoxidation of a variety of electron-deficient α,β-unsaturated carbonyl compounds has been studied using a series of heteropoly compounds and aqueous hydrogen peroxide in acetonitrile. Among the heteropoly compounds investigated, $(CTP)_3VMo_{12}O_{40}$ showed the highest catalytic performance for the epoxidation of these compounds.

Keywords: α,β-unsaturated carbonyl compounds; heteropoly compounds; $(CTP)_3VMo_{12}O_{40}$

Selective oxygen transfer to olefins remains an important research objective in view of the industrial importance of epoxides. Often epoxides formed in an initial step react further to provide industrially important products such as surfactants, corrosion protection agents, additives, *etc.* The α,β-epoxyketones are important starting materials for making α-hydroxyketones and β-hydroxyketones by reductive cleavage. These electron-deficient olefinic compounds are normally epoxidised with the sodium salt of hydrogen peroxide (NaOOH), the sodium salt of *t*-butyl hydroperoxide ($NaOOBu^t$), and peracids.[1-4] Basic catalysts such as $KF-Al_2O_3$ and $KOH-Al_2O_3$ have been used for the epoxidation of α,β-unsaturated ketones with TBHP.[5] The epoxidation of α,β-unsaturated ketones has been studied by using dilute H_2O_2 and various titanium-containing zeolites.[6] Ishii reported the epoxidation of 4-hexen-3-one using peroxotungstophosphate of $(CTP)_3\{PO_4[WO(O_2)_2]_4\}$ and H_2O_2.[7] Sharifi[8] reported that microwaves promoted the epoxidation of α,β-unsaturated ketones in aqueous sodium perborate. Recently Wang[9] reported the epoxidation of these compounds in an ionic liquid/water biphasic system using H_2O_2 as an oxidant.

The catalytic function of heteropoly compounds has attracted much attention[10,11] because their acidic and redox properties can be controlled at atomic or molecular levels by changing the chemical composition. Heteropolyanions having the Keggin structure are the most widely investigated as catalysts because of their stability and ease of synthesis. Here, we report the study of the epoxidation of α,β-unsaturated ketones over a series of Keggin heteropoly compounds using aqueous hydrogen peroxide as an oxidant.

Table 1 shows the effect of various Keggin structure HPAs and two-peroxo complexes on the epoxidation of 2-cyclohexen-1-one in acetonitrile. If no catalyst was added to the reaction system, no epoxide was detected after 5 h reaction (entry 1). Complete Keggin HPAs, in which the addenda atoms are all tungsten, such as $(CTP)_4SiW_{12}O_{40}$ (entry 2) exhibit no activity. Though the conversion for di-iron-substituted silicotungstate, of $(Bu_4N)_{3.5}H_{2.5}[\gamma\text{-}SiW_{10}\{Fe(OH_2)\}_2O_{38}]$ (entry 4), is relatively low (35%), the selectivity for epoxide is high (82%). The divacant lacunary silicotungstate, $(Bu_4N)_4[\gamma\text{-}SiW_{10}(H_2O)_2O_{34}]$ (entry 5), exhibits a higher activity; a conversion of 52 % and a selectivity of 87 % were obtained on this catalyst. All the HPAs containing molybdenum as addenda atoms do have catalytic performance. $(CTP)_4SiMo_{12}O_{40}$ (entry 6) and $(CTP)_3PMo_6W_6O_{40}$ (entry 7) exhibit a similar activity, but the epoxide selectivity is lower for the former (52%) than the latter (70%). $(CTP)_5PMo_{10}V_2O_{40}$ (entry 8) shows moderate activity compared with the former two catalysts. $(CTP)_3PMo_{12}O_{40}$ (entry 9) gives the highest activity among HPAs based on phosphorus as the heteroatom. The HPAs of $(CTP)_3VMo_{12}O_{40}$ (entry 10) whose heteroatom is vanadium exhibits the highest activity among all the catalysts investigated; a conversion of 93 % and a selectivity of 99 % were obtained on this catalyst. The peroxo compound, $(CTP)_3\{PO_4[WO(O_2)_2]_4\}$, shows better activity than $(Bu_4N)_3\{PO_4[MoO(O_2)_2]_4\}$ in the epoxidation of 2-cyclohexen-1-one.

Table 1 Epoxidation of 2-cyclohexen-1-one over different HPAs[a]

Entry	Catalyst	Conversion	Selectivity (%)[b]		
		(mol%)	Epoxide[14]	Diol[c]	Other
1	no	N.A[d]	–	–	–
2	$(CTP)_4SiW_{12}O_{40}$	N.A	–	–	–
3	$(CTP)_3PW_{12}O_{40}$	30	75	15	10
4	$(Bu_4N)_{3.5}H_{2.5}[\gamma\text{-}SiW_{10}\{Fe\ (OH_2)\}_2O_{38}]$	35	82	10	8
5	$(Bu_4N)_4[\gamma\text{-}SiW_{10}\ (H_2O)_2O_{34}]$	52	87	8	5
6	$(CTP)_4SiMo_{12}O_{40}$	21	52	41	7
7	$(CTP)_3PMo_6W_6O_{40}$	17	70	26	4
8	$(CTP)_5PMo_{10}V_2O_{40}$	45	74	20	6
9	$(CTP)_3PMo_{12}O_{40}$	80	86	9	5
10	$(CTP)_3VMo_{12}O_{40}$	93	99	1	
11	$(Bu_4N)_3\{PO_4[MoO(O_2)_2]_4\}$	31	65	30	5
12	$(CTP)_3\{PO_4[WO(O_2)_2]_4\}$	76	77	13	10

[a] Reaction condition: 3 mmol cyclohex-2-en-1-one, 0.75 mmol H_2O_2, 8 μmol catalyst, 3 ml acetonitrile; 0.56 mmol of butan-2-one as an internal standard; reaction temperature: 70 °C; reaction time: 5 h.

[b] Values were calculated assuming similar response of the FID detector to each of the products and butan-2-one.

[c] see refs 12,13

[d] No activity was observed.

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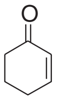
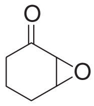
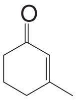
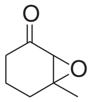
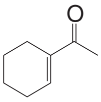
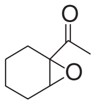
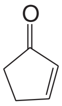
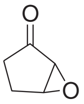
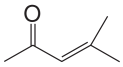
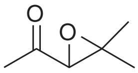
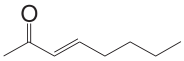
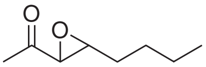
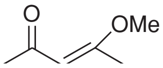
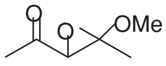
Table 2 Epoxidation of various unsaturated ketones over $(CTP)_3VMo_{12}O_{40}$[a]

Entry	Substrate	Product	Conversion[b] (mol %)	Selectivity[b] (mol %)	Ref.
1			93	99	*14*
2			22	98	*15*
3			73	97	*14*
4			52	98	*16*
5			82	95	*14*
6			56	92	*17,18*
7			16	93	

[a]Reaction condition: 3 mmol substrate, 0.75 mmol H_2O_2, 8 µmol catalyst, 3 ml acetonitrile; 0.56 mmol of butan-2-one as an internal standard; reaction temperature: 70 °C; reaction time: 5 h.

[b]Values were calculated assuming similar restore of the FID detector to each of the products and butan-2-one.

The results of epoxidation of various cyclic and open-chain α,β-unsaturated ketones over a $(CTP)_3VMo_{12}O_{40}/H_2O_2$ system are listed in Table 2. The substrates 1, 3, and 5 showed higher reactivity than substrates 4 and 6 for the epoxidation reaction, while entries 2 and 7 showed poor reactivity. Cyclohex-2-en-1-one showed best reactivity among the substrates investigated. The poor reactivity of substrate 2 compared with 1 is due to its steric hindrance with the presence of a methyl group at the β-position.[3] The open-chain α,β-unsaturated ketone with a long carbon chain (entry 6) was less active than that with a short chain (entry 5). Generally, it is difficult for the large and long substrate (oct-3-en-2-one) to contact the catalyst to form an intermediate (or transition state) and the solubility of the substrate with the longer alkyl chain in acetonitrile solution may be poor. Accordingly, the transfer of active oxygen to the C=C moiety of the alkene will be retarded. The methoxy group at the β position (entry 7) gives poor activity. This is probably due to the combined effects of the methoxy group, which not only makes the molecule more electron deficient by its electron-withdrawing nature but also provides steric hindrance.

Table 3 HOMO eigenvectors of various α,β-unsaturated ketones[a]

Unsaturated ketones	Eigenvectors /eV	Net electric charge of atoms on C=C double bond (Mulliken)	
		C_α	C_β
1	−10.0722	−0.2410	−0.1342
2	−9.7311	−0.2750	0.0745
3	−9.6294	−0.0735	−0.1641
4	−10.1913	−0.2133	−0.1540
5	−9.6868	−0.3184	0.1195
6	−9.8688	−0.2889	−0.0698
7	−9.5434	−0.3903	0.4928

[a]The HOMO eigenvectors of various α,β-unsaturated ketones were calculated using the PM3 semiempirical method, 6-31G base group. See refs 19,20.

Table 3 listed the HOMO orbital energies of substrates and the net electric charge of atoms on the C=C double bonds. Despite the eigenvector value in the HOMO of 2 being higher than that of substrates 3, 5 and 7, the reactivity of 2 is nearly as poor as 7 due to the steric hindrance discussed above. These results indicate that both electronic effects and steric effects play roles in the epoxidation of α,β-unsaturated ketones catalysed by $(CTP)_3VMo_{12}O_{40}/H_2O_2$. The steric hindrance effect is stronger than the effect of the electron-donating methyl group when substrate 2 is epoxidised. Thus the reactivity of 2 is poor compared with other cyclic substrates 1, 3, and 4. Although entries 5 and 6 have similar values of eigenvector, entry 5 shows higher reactivity which is attributed to substrate 6 having a longer carbon chain, and so it is difficult for it to contact the active oxygen compared with substrate 5.

In summary, we report the $(CTP)_3VMo_{12}O_{40}/H_2O_2/CH_3CN$ system for the epoxidation of α,β-unsaturated ketones. The true catalysts are probably peroxo heteropoly anions resulting from the reaction between $(CTP)_3VMo_{12}O_{40}$ and H_2O_2. The systematic investigation of these peroxo heteropoly anions is underway and will be reported later.

Experimental

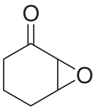
The catalysts of $(CTP)_4SiW_{12}O_{40}$ (cetylpyridinium abbreviated as CTP), $(CTP)_4SiMo_{12}O_{40}$, $(CTP)_3PW_{12}O_{40}$, $(CTP)_5PMo_{10}V_2O_{40}$, $(CTP)_3PMo_{12}O_{40}$, and $(CTP)_3VMo_{12}O_{40}$ were synthesised according to the literature.[21] $(CTP)_3PMo_6W_6O_{40}$ was synthesised according to Misono *et al.*[22] $(Bu_4N)_{3.5}H_{2.5}[\gamma\text{-}SiW_{10}\{Fe(OH_2)\}_2O_{38}]$ was prepared by the method of Nozaki *et al.*[23] $(Bu_4N)_4[\gamma\text{-}SiW_{10}(H_2O)_2O_{34}]$ was synthesised according to the literature.[24] $(Bu_4N)_3\{PO_4[MoO(O_2)_2]_4\}$ and $(CTP)_3\{PO_4[WO(O_2)_2]_4\}$ were synthesised according to the literature.[25]

The catalytic reactions were performed in a 10 ml two-necked round-bottomed flask equipped with a septum, a magnetic stirring bar, and a reflux condenser. Typically, substrate (3 mmol) and 0.56 mmol of butan-2-one as an internal standard were added to an acetonitrile solution (3 ml) of catalyst (8 μmol), and 30 % hydrogen peroxide (0.75 mmol). The flask was then placed in a hot oil bath at 70 °C and stirred for 5 h. The reaction solution was periodically sampled by syringe and analysed quantitatively by a Perkin Elmer XL gas chromatograph equipped with a 15 m SE-54 capillary column and FID detector. The qualitative analysis of liquid reaction mixture was carried out on an Agilent-6890/5973N GC/MS instrument equipped with an HP 5MS column (30) with helium as carrier gas. The column temperature was raised from 80 to 260 °C at a heating rate of $10\ ^\circ C\ min^{-1}$.

For the isolation experiments, the reaction scale was three times greater than that of the above reaction conditions. After reaction, the mixture was cooled and extracted with dichloromethane (50 ml × 3). The organic layer was separated and dried over magnesium sulfate. Evaporation of the solvent followed by purification by silica gel chromatography (eluent: light petroleum-dichloromethane, 10:1) gave the epoxides.

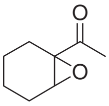
IR spectra were recorded on a *Nicolet* FT-170SX spectrometer as liquid film. ^1H and ^{13}C NMR spectra were taken on a Varian Mercury 300 MHz spectrometer with TMS as an internal standard and $CDCl_3$ as solvent unless otherwise noted.

Product 1[14]



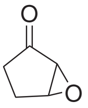
IR (film, cm^{-1}): 1718, 1272, 822; ^1H NMR (300 MHz, $CDCl_3$, ppm): 2.16–2.27 (m, $-CH_2$); 1.74–1.84 (m, $-CH_2$); 1.80–2.04 (m, $-CH_2$); 2.74 (m, -CH); 3.38 (d, -CH); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 16.9, 29.1, 37.1, 56.6, 64.4, 207.5. GC-MS (*m/z*): 112 (M^+), 97, 85, 83, 67, 57, 55.

Product 3[14]



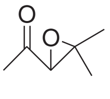
^1H NMR (300 MHz, $CDCl_3$, ppm): 1.39–1.50 (m, 4H); 1.46 (m, 1H); 1.70(m, 1H); 1.69 (m, 1H); 1.94 (m, 1H); 3.10 (t, -CH); 2.09 (s, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 21.3, 22.6, 23.9, 27.3, 28.8, 59.9, 63.2, 210.2.

Product 4[16]



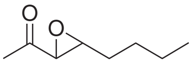
^1H NMR (300 MHz, $CDCl_3$, ppm): 2.02–2.12(m, $-CH_2$); 2.04–2.28 (m, $-CH_2$); 2.76(dd, -CH); 3.40 (d, -CH); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 20.5, 36.7, 47.1, 66.7, 212.0.

Product 5[14]



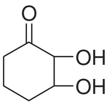
^1H NMR (300 MHz, $CDCl_3$, ppm): 1.26 (s, 6H); 2.09 (s, 3H); 3.38 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 22.7 (2C), 25.0, 58.0, 70.7, 207.2. GC-MS (*m/z*): 114(M^+), 99, 72, 57, 43.

Product 6[17,18]



^1H NMR (300 MHz, $CDCl_3$, ppm): 0.94 (t, 3H); 1.28 (m, 2H); 1.32 (m, 2H); 1.41(m, 2H); 2.09(s, 3H); 2.73 (m, 1H); 3.39 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.0, 22.4, 24.7, 27.4, 30.5, 54.2, 64.5, 207.2.

2,3-dihydrocycyclohexanone[12,13]



^1H NMR (300 MHz, CD_3OD, ppm): 1.74–1.85 (m, 2H); 1.83–2.07 (m, 2H); 2.0 (br, s, -OH); 2.16–2.26(m, 2H); 3.60(m, 1H); 4.02 (d, 1H); ^{13}C NMR (75 MHz, CD_3OD, ppm): 18.7, 29.4, 37.4, 73.5, 85.9, 207.5.

The nature of the products from entries 2 and 7 were inferred from GM/MS measurements and these compounds were not isolated.

Received 1 March 2005; accepted 13 June 2005
Paper 05/3095

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