Activation of Hydrogen Peroxide through Hydrogen-Bonding Interaction with Acidic Alcohols: Epoxidation of Alkenes in Phenol

Joos Wahlen, Dirk E. De Vos, and Pierre A. Jacobs*

Department of Interphase Chemistry, Centre for Surface Chemistry and Catalysis, Katholieke Universiteit Leuven, Kasteelpark Arenberg 23, B-3001 Heverlee, Belgium

pierre.jacobs@agr.kuleuven.ac.be

SUPPORTING INFORMATION

Materials

All materials were obtained from commercially available sources and were used without further purification. Hydrogen peroxide was a 50 wt.% aqueous solution from Acros.

Analysis, procedures and detailed results of control experiments

Hydrogen peroxide determination (Figure 1)

Hydrogen peroxide concentration was determined iodometrically. The composition of the reaction mixture was 5 mmol cyclooctene, 50 mmol phenol, and 5 mmol H₂O₂ (50 wt.%). The reaction was stirred at 40 °C. Typically, 200 μ L aliquots of the reaction mixture were quickly diluted into a solution of 20 mL H₂O, 2 mL 10 wt.% aqueous KI, and 2.5 mL of a 5 M H₂SO₄ solution containing a catalytic amount of (NH₄)₆Mo₇O₂₄·4H₂O. The mixture was titrated with a 0.1 M aqueous solution of Na₂S₂O₇ until the brown triiodide colour turned to a pale straw colour. Next, a few drops of a 10 g/L aqueous starch solution were added and titration was continued until the colour of the solution changed from blue to colourless.

GC and GC-MS analysis

For GC analysis, a Hewlett Packard 5890 gas chromatograph equipped with a 0.32 mm i.d. by 50 m WCOT fused silica column coated with a Chrompack CP-Sil 5 CB stationary phase (1.2 μ m d_f) was

used. The instrument was equipped with a flame ionization detector (FID) and coupled to a HP 3396 integrator. Quantification of the reaction products was based on the internal standard technique (*n*-alkanes) using suitable response factors. Products were identified by comparison of their GC retention times with authentic epoxides prepared by *m*-CPBA oxidation in CHCl₃ at 20 °C. All compounds in Table 1 have been previously isolated and characterized.¹ Additionally, GC-MS was used to confirm the identity of the products. A Fisons GC 8000 Series gas chromatograph equipped with a 0.32 mm i.d. by 60 m WCOT fused silica column coated with a Varian CP-Sil 5 CB Low bleed/MS stationary phase (0.25 μm df) was coupled to a Fisons MD 800 mass spectrometer.

General procedure for the phenol-promoted epoxidation of various alkenes (Table 1)

A 20 mL flask was charged with 50 mmol phenol, 5 mmol alkene, 0.05 mmol NaOAc, and 7.5 mmol H₂O₂ (50 wt.%). An appropriate alkane (*n*-octane, *n*-decane or *n*-tetradecane, 1 mmol) was added as an internal GC standard. The reaction mixture was stirred at the indicated temperature and the reaction was followed by GC analysis of the crude reaction mixture.

Reaction kinetics of the epoxidation of cyclooctene with H₂O₂ in differently substituted phenol solvents (Figure 2 and Figure 3)

All kinetic experiments were carried out using *cis*-cyclooctene as the alkene substrate and *n*-decane as an internal GC standard. The reaction was followed by monitoring the disappearance of cyclooctene as a function of time. In all cases a complete selectivity to cyclooctene oxide was observed.

In a typical reaction, a 50 mL three-neck round-bottom flask was charged with 100 mmol of the appropriate phenol, 10 mmol *cis*-cyclooctene, 2 mmol *n*-decane (internal GC standard), 0.1 mmol NaOAc, 15 mmol H₂O₂ (50 wt.%), and 16 mL 1,2-dichloroethane. 1,2-Dichloroethane was used as a co-solvent to dissolve the high-melting phenols. The flask was immersed in an oil bath thermostated at 60 °C and the mixture was stirred magnetically. Samples were withdrawn periodically, quickly diluted in tetrahydrofuran, and analyzed by GC.

Second-order rate constants were calculated by plotting the following function *Y* as a function of time:

$$Y = (1/s)\{\ln[(s + C_{\text{alkene}})/C_{\text{alkene}}] - \ln[(s + C_{\text{alkene,initial}})/C_{\text{alkene,initial}}]\} = kt, \quad \text{with } s = C_{\text{H}_2\text{O}_2} - C_{\text{alkene}}$$

This equation is the solution of the differential equation $dC_{\text{alkene}}/dt = -kC_{\text{alkene}}C_{\text{H}_2\text{O}_2}$ and is valid for $C_{\text{alkene,initial}} \neq C_{\text{H}_2\text{O}_2,\text{initial}}$. A plot of the concentration of cyclooctene *versus* time and the second-order plot

for each phenol are shown in Figure S1 – S4. The corresponding second-order rate constants are summarized in Table S1 and Figure 2 (see manuscript).

Table S1. Rate constants for epoxidation of cyclooctene with H₂O₂ in differently substituted phenols.

substituted phenol	k_{obs} [M ⁻¹ .h ⁻¹]
2-chlorophenol	0.035
4-methoxyphenol	0.044
4- <i>tert</i> -butylphenol	0.079
phenol	0.082
4-methylphenol	0.083
4-chlorophenol	0.224
4-nitrophenol	0.330
3-nitrophenol	0.339
3-chlorophenol	0.365

Under the same reaction conditions, but in the absence of phenol, a conversion of only 2 % was obtained after 23 h.

Figure S1. Epoxidation of cyclooctene with H₂O₂ in phenol.

Reaction conditions: 10 mmol cyclooctene, 2 mmol n-decane, 0.1 mmol NaOAc, 15 mmol H₂O₂, 100 mmol phenol, 16 mL 1,2-dichloroethane, 60 °C.

Figure S2. Epoxidation of cyclooctene with H_2O_2 in 4-methyl-, 4-*tert*-butyl-, and 4-methoxyphenol. Reaction conditions: 10 mmol cyclooctene, 2 mmol *n*-decane, 0.1 mmol NaOAc, 15 mmol H_2O_2 , 100 mmol *p*-substituted phenol, 16 mL 1,2-dichloroethane, 60 °C.

Figure S3. Epoxidation of cyclooctene with H_2O_2 in 2-, 3-, and 4-chlorophenol. Reaction conditions: 10 mmol cyclooctene, 2 mmol *n*-decane, 0.1 mmol NaOAc, 15 mmol H_2O_2 , 100 mmol chlorophenol, 16 mL 1,2-dichloroethane, 60 °C.

Figure S4. Epoxidation of cyclooctene with H₂O₂ in 3- and 4-nitrophenol.

Reaction conditions: 10 mmol cyclooctene, 2 mmol n-decane, 0.1 mmol NaOAc, 15 mmol H₂O₂, 100 mmol nitrophenol, 16 mL 1,2-dichloroethane, 60 °C.

Control experiment 1. Epoxidation of cyclooctene in various alcohol solvents

Figure S5. Epoxidation of cyclooctene with H₂O₂ in phenol, benzyl alcohol, and cyclohexanol.

Reaction conditions: 5 mmol cyclooctene, 1 mmol n-decane, 0.05 mmol NaOAc, 7.5 mmol H₂O₂, 50 mmol solvent, 40 °C.

Under the same reaction conditions, but using anisole (methoxybenzene) as a solvent, conversion was lower than 1 % after 24 h.

Control experiment 2. Effect of the addition of a metal-complexing agent on the epoxidation of cyclooctene

Figure S6. Epoxidation of cyclooctene with H_2O_2 in phenol in the presence or absence of EDTA.

*Reaction conditions: 5 mmol cyclooctene, 1 mmol *n*-decane, 0.05 mmol NaOAc, 7.5 mmol H_2O_2 , 50 mmol phenol, 40 °C, 0 or 0.25 mmol EDTA.*

Control experiment 3. Effect of the addition of a radical scavenger on the epoxidation of cyclooctene

Figure S7. Epoxidation of cyclooctene with H_2O_2 in phenol (PhOH) in the presence or absence of 2,6-di-*tert*-butyl-*p*-cresol (BHT).

*Reaction conditions: 10 mmol cyclooctene, 2 mmol *n*-decane, 0.1 mmol NaOAc, 10 mmol H_2O_2 , 100 mmol phenol, 40 °C, 0 or 0.5 mmol BHT.*

Control experiment 4. Effect of the addition of benzoquinone (BQ) on the epoxidation of cyclooctene with H₂O₂ in phenol

Figure S8. Epoxidation of cyclooctene with H₂O₂ in phenol (PhOH) or 1,2-dichloroethane (DCE) in the presence or absence of benzoquinone (BQ). Mol% is relative to cyclooctene.

Reaction conditions: 5 mmol cyclooctene, 1 mmol n-decane, 0.05 mmol NaOAc, 7.5 mmol H₂O₂, 50 mmol phenol or 8 mL 1,2-dichloroethane, 60 °C, 0 mmol, 0.1 mmol, or 0.5 mmol benzoquinone.

The added BQ (2 and 10 mol%) was detectable by GC analysis. The amount of BQ remained on an almost constant level, and slightly increased towards the end of the reaction.

Under the same reaction conditions, the epoxidation of cyclooctene with H₂O₂ in 1,2-dichloroethane (8 mL) instead of phenol in the presence of 1, 10, 100, and 1000 mol% benzoquinone relative to cyclooctene gave 3, 14, 20, and 22 % conversion after 22 h. In methanol (10 mL) instead of phenol in the presence of 10 mol% BQ relative to cyclooctene 2 % conversion was obtained after 22 h.

Note that in none of our reactions with pure phenol, benzoquinone was formed in a concentration larger than 1 mol% with respect to starting alkene. This demonstrates that BQ is a much less strong promotor of epoxidation than phenol itself; the fast epoxidation of cyclooctene in phenol cannot be due to the formation of a phenol oxidation product such as BQ.

Control experiment 5. Effect of the addition of catechol or hydroquinone on the epoxidation of cyclooctene with H_2O_2 in phenol

Figure S9. Epoxidation of cyclooctene with H_2O_2 in phenol (PhOH) in the presence of catechol (Cat) or hydroquinone (HQ). Mol% is relative to cyclooctene.

*Reaction conditions: 5 mmol cyclooctene, 1 mmol *n*-decane, 0.05 mmol NaOAc, 7.5 mmol H_2O_2 , 50 mmol phenol, 60 °C, 0 mmol or 0.5 mmol catechol or hydroquinone.*

Under the same reaction conditions, the epoxidation of cyclooctene with H_2O_2 in 1,2-dichloroethane (8 mL) instead of phenol in the presence of 10 mol% catechol or 10 mol% hydroquinone relative to cyclooctene gave 3 % and 3 % conversion after 22 h.

Epoxidation of cyclooctene with *tert*-butyl hydroperoxide (TBHP) in phenol

Figure S10. Epoxidation of cyclooctene with hydrogen peroxide or *tert*-butyl hydroperoxide in phenol.

*Reaction conditions: 5 mmol cyclooctene, 1 mmol *n*-nonane, 0.05 mmol NaOAc, 7.5 mmol H_2O_2 (50 wt.%) or 7.5 mmol TBHP (5.5 M in *n*-decane), 50 mmol phenol, 60 °C.*

Influence of the water content of H₂O₂ and the addition of epoxide product on the epoxidation of cyclooctene with H₂O₂ in phenol

Figure S11. Epoxidation of cyclooctene with 30 wt.% or 50 wt.% H₂O₂ in phenol.

Reaction conditions: 5 mmol cyclooctene, 1 mmol n-decane (internal standard), 0.05 mmol NaOAc, 5 mmol H₂O₂ (30 or 50 wt.%), 50 mmol phenol, 40 °C.

Figure S12. Effect of cyclooctene oxide addition on cyclooctene epoxidation with H₂O₂ in phenol.

Reaction conditions: 10 mmol cyclooctene, 2 mmol n-decane, 0.1 mmol NaOAc, 10 mmol H₂O₂, 100 mmol phenol, 40 °C, x mmol cyclooctene oxide added at the start of the reaction (see legend).

Influence of the amount of phenol on the epoxidation of cyclooctene with H₂O₂

Figure S13. Epoxidation of cyclooctene with H₂O₂ in 2, 3, and 5 mol equivalents of phenol.

Reaction conditions: 5 mmol cyclooctene, 1 mmol n-decane, 0.05 mmol NaOAc, 5 mmol H₂O₂, 10, 15, or 25 mmol phenol, 60 °C.

Figure S14. Epoxidation of cyclooctene with H₂O₂ in 5, 10, and 20 mol equivalents of phenol.

Reaction conditions: 5 mmol cyclooctene, 1 mmol n-decane, 0.05 mmol NaOAc, 5 mmol H₂O₂, 25, 50, or 100 mmol phenol, 60 °C.

References

- (1) Villa de P., A. L.; Sels, B. F.; De Vos, D. E.; Jacobs, P. A. *J. Org. Chem.* **1999**, *64*, 7267-7270 and references cited therein.