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Inverse Phase Transfer Catalysis. III.- Optimization of the Epoxidation Reaction of α,β-Unsaturated Ketones by Hydrogen Peroxide.

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Abstract

The epoxidation of chalcone using hydrogen peroxide in the presence of a base in a two-phase medium system following the so-called Inverse Phase Transfer Catalysis (IPTC) process was investigated. Careful examination of various parameters including surfactant concentration, pH, H_2O_2 decomposition side-reactions and epoxide ring-opening, allowed us to determine optimal experimental conditions

Keywords: epoxidation, hydrogen peroxide, surfactant, phase-transfer catalysis.

Introduction

We recently reported[1,2] that the rate of the reaction of a lipophilic substrate, dissolved in an organic phase, with a hydrophilic reactant solubilized in an aqueous phase, was highly enhanced by adding a water soluble surfactant to the reaction mixture. The surfactant allows the transfer of the lipophilic substrate into the water phase, via the formation of micellar aggregates. In addition, the product of the reaction, which is also hydrophobic , is transferred into the organic phase as soon as it is formed.

Such a process is called Inverse Phase Transfer Catalysis[3] (IPTC), as the reaction takes place into the aqueous phase[4].

We have already illustrated the efficiency of the procedure in the case of sodium borohydride reduction of highly hydrophobic ketones[1] as well as for the epoxidation of α,β-unsaturated ketones[2] by the perhydroxyl ion (HOO^-).

However, the epoxidation reaction was not fully satisfactory. Due to its rapid decomposition, H_2O_2 must be used in large excess[2] in order to achieve maximum conversion of the ketone into its epoxide derivative.

Our goal was to control several key parameters including:

i) adjustment of the hydrogen peroxide excess,
ii) efficiency of the mass transfer,
iii) minimization of an undesirable subsequent reaction: epoxide ring-opening.

The study of these different factors has been achieved using chalcone as a model[5]. We report herein our results.

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Results and Discussion

Adjustment of the hydrogen peroxide excess

Preliminary results[2] were obtained using a large excess of hydrogen peroxide ($R = [H_2O_2]_o / [\text{ketone}]_o = 50$). In the present work the epoxidation of the chalcone was performed for several values of R: 50, 10, 5 and 2 respectively. The reaction was performed in a water/heptane 1/1 two-phase medium in the presence of dodecyltrimethylammonium bromide (DTAB) using the following initial conditions(concentrations quoted are in the aqueous phase in the case of the inorganic reagent and in heptane for the ketone):

$$[\text{DTAB}] = 0.1\text{M};\ [Na_2CO_3] = 0.05\text{M};\ [\text{chalcone}] = 0.1\text{M}.$$

The course of the reaction was monitored by measuring the absorbance of the reaction mixture at 300nm (λ_{max} of the chalcone) versus time[2].

Results are reported in fig.1 for four H_2O_2 concentrations: R = 50, 10, 5 and 2.

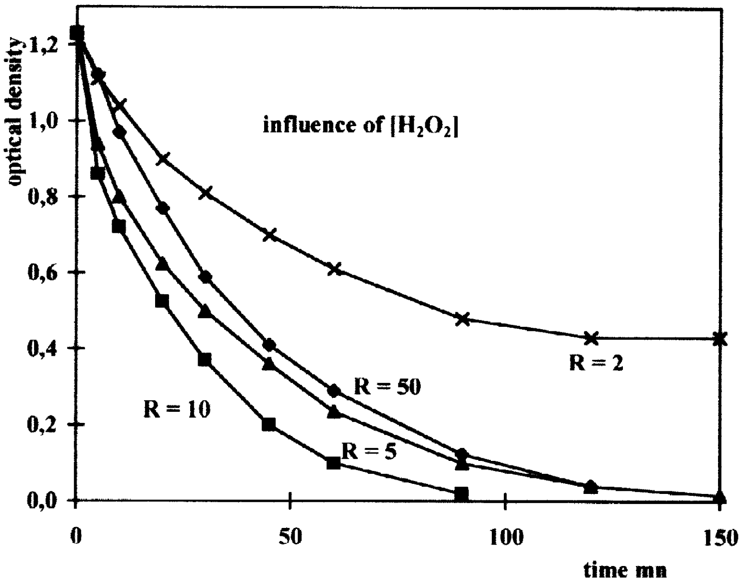


Figure 1. Epoxidation reaction of chalcone: influence of the hydrogen peroxide concentration; [DTAB] = 0.1M; [Na_2CO_3] = 0.05M; [chalcone] = 0.1M.

The fastest reaction is observed for R = 10. With R = 5 and 50, reaction rates are similar. For R = 2, the reaction reaches a plateau, presumably as a consequence of the lack of hydrogen peroxide (as shown by the fact the reaction can be reiniated by adding small amount of H_2O_2). The value R = 5 appeared to be a good compromise to achieve complete epoxidation with a limited excess of oxidizing reactant. We used this ratio to perform the work reported below.

Efficiency of the mass transfer

An efficient transfer of the hydrophobic substrate into the aqueous phase can unquestionably contribute to accelerate the epoxidation reaction. This transfer being ensured by the surfactant, we examined how its concentration could influence the reaction rate.

DTAB concentrations ranging from 0 to 1M were experimented, in the following conditions:

$$[H_2O_2] = 0.5\text{M};\ [\text{chalcone}] = 0.1\text{M};\ [Na_2CO_3] = 0.05\text{M}.$$

Variation of chalcone concentration are reported in the figure 2.

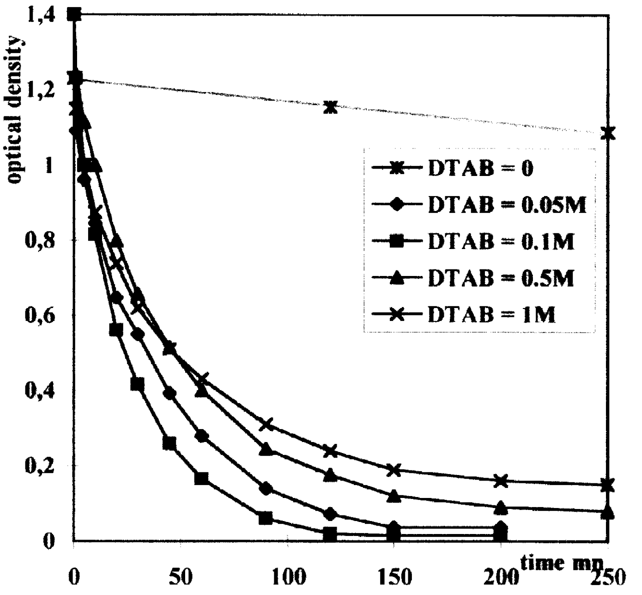


Figure 2. Epoxidation reaction of chalcone: influence of the surfactant (DTAB) concentration; $[H_2O_2] = 0.5M$; [chalcone] = 0.1M; $[Na_2CO_3] = 0.05M$.

Figure 2 illustrates the crucial role played by the surfactant: in its absence the reaction prove to be extremely slow. For surfactant concentrations above its cmc[2]($1.44\ 10^{-2}M$) ranging from 0.05M and 1M, reaction rate increased significantly.

Surprisingly, the rate is higher for a DTAB intermediate concentration (0.1M) than for the maximum concentration (1M). We could have expected transfer efficiency increasing with surfactant concentration.

In fact, this unexpected behaviour illustrates the influence of the surfactant on the pH of the medium. DTAB displays a slightly acidic character so that the pH of the medium[6] takes successive values of 9.98; 9.88; 9.76 and 9.48 when DTAB concentration reaches 0.05, 0.1, 0.5 and 1M respectively. The decrease of the pH certainly causes a diminution of the concentration of the reactive species; the perhydroxyl ion (scheme 2). It would appear therefore that the reaction rate is more sensitive to the pH than to the concentration of the surfactant. However, experiments performed at higher pH ([DTAB] = 0.05M and $[Na_2CO_3] = 0.5M$; pH = 10.56) shows that despite a faster initial rate, the reaction stops after 85% conversion by lack of oxidizing reactant (addition of a small amount of hydrogen peroxide allows completion of reaction). In the above conditions, H_2O_2 decomposition reaction becomes faster than epoxidation. Therefore it is essential to minimize this side reaction.

Minimization of the decomposition of H_2O_2

Hydrogen peroxide decomposition is base-catalyzed[7] (see scheme 1)

$$H_2O_2 + OH^- \xrightleftharpoons{\text{fast}} HOO^- + H_2O$$

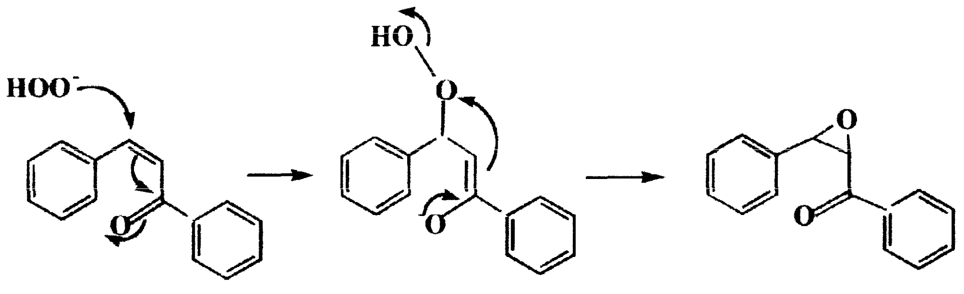
$$HOO^- + H_2O_2 \xrightarrow[\text{slow}]{} O_2 + H_2O + OH^-$$

Scheme 1

The reaction rate depends on both H_2O_2 and HOO^- concentrations. For a given H_2O_2 concentration, the decomposition rate is maximum when the product of the concentrations of these two species is maximum, i.e.

when [H_2O_2] = [HOO^-]. This occurs when the pH equals the H_2O_2 pK_a (11.13)[7,8]. Therefore, to minimize H_2O_2 decomposition, the pH must be remote from 11.13.

The mechanism[9]of epoxidation involves the two following steps (scheme 2):



Scheme 2

HOO^- is the reactive species. When pH << 11.13, H_2O_2 decomposes slowly. However the HOO^- concentration being small, the epoxidation reaction is similarly slow.

If pH >> 11.13, H_2O_2 decomposition decreases and HOO^- concentration increases resulting in a faster epoxidation. According to these observations, the reaction was performed using the following conditions: $[NaOH]_o = 0.5M$, $[H_2O_2]_o = 0.5M$, $[DTAB] = 0.1M$ and $[ketone]_o = 0.1M$ ($R = 5$; $pH = 12.53$). Figure 3 shows that in such conditions the chalcone is very quickly (< 20mn) converted into the corresponding epoxide.

Control of the ring-opening reaction of the epoxide

However in these conditions both OH^- and HOO^- concentrations are relatively high.Both nucleophilic reagents are able to open the epoxide ring. Therefore, it was important to assess the stability of the latter. In that respect we monitored the concentration of the epoxide at $\lambda = 245.5nm$ (λ_{max} of the epoxide). The plot of the absorbance versus time reported in figure 3

indicates a slight decrease of epoxide concentration following its formation. However, concentration varies weakly between 20 and 80 mn, which allows a facile isolation.

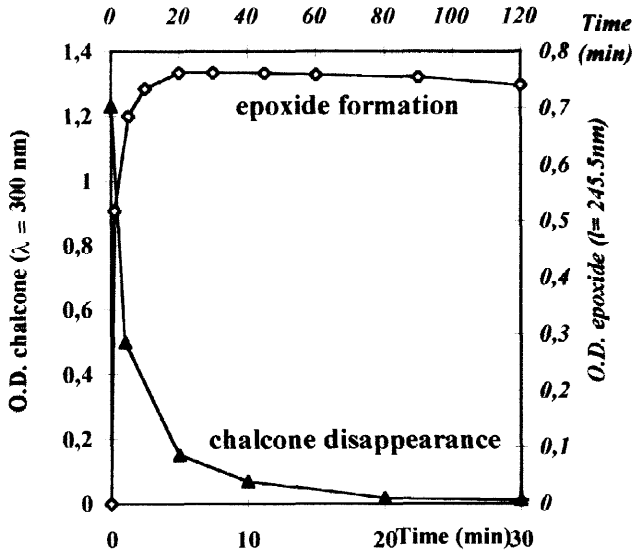


Figure 3. Epoxidation reaction of chalcone and stability of the formed epoxide; [NaOH] = 0.5M; [H_2O_2] = 0.5M; [chalcone] = 0.1M; [DTAB] = 0.1M.

We applied these kinetic results to a laboratory scale experiment as described in the experimental section. A series of α,β-unsaturated ketones was reacted using following experimental conditions:

$$[NaOH] = 0.5M;\ [H_2O_2] = 0.5M;\ [DTAB] = 0.1M$$

Experiments were achieved at a scale (5mmole) that allows isolation of products
Results are reported in table 1.

Table 1.- Epoxidation of α,β-unsaturated ketones with H_2O_2 in a two-phase medium at 25°C[a].

Ketones	reaction time (mn)	% yield[b]	Ketones	reaction time (mn)	% yield[b]
chalcone	10	88	naphtoquinone	48[c]	60
mesityl oxide	10	76	citral	10	98
isophorone	120	65	methyl cinnamate	480	60
cyclohexenone	5	70	cinnamamide	480	70
carvone	60	95			

[a] Heptane was generally used as the organic phase.
[b] Isolated yield of pure product exhibiting ^1H NMR data consistent with their assigned structures.
[c] Calculated value in heptane from that measured in CH_2Cl_2, see note 10.

From the data reported in table 1, one can see that the new experimental conditions determined in this work improve strongly earlier results[2].

i) time reactions are shorter. For example, epoxidation of isophorone is performed in 2 hours compared to 20h as previously reported[2].

ii) We can also note an interesting functional group selectivity. Thus, for carvone and citral, only electron-deficient C-C double bonds are fully converted into the corresponding epoxide; the unconjugated C = C proved to be unaffected.

Conclusion

In summary, these results prove the validity of the phase-transfer procedure promoted by micellar aggregates. The main role played by the surfactant is to ensure the transfer of the lipophilic substrate to the water phase.

In addition, our study permitted to show that good results were obtained when the pH of the medium is set beyond the H_2O_2 pK_a. In our case, oxirane ring-opening in general is largely prevented by isolating the product as soon as the ketone is consumed.

Experimental section

Dodecyltrimethylammonium bromide (DTAB), α,β-unsaturated ketones, sodium carbonate and hydroxide, 30% hydrogen peroxide were obtained from commercial sources.

UV studies were performed on a SAFAS DES-170 spectrophotometer. ^1H NMR spectra were recorded in a Brucker ACE-250 apparatus at 250 MHz with $CDCl_3$ solutions.

General procedure for epoxidation reactions.

Reactions in two-phase media were studied according to the procedure already described[2]. For large scale studies, the procedure is the same but at the end of the reaction (checked by UV), the resulting solution was extracted with CH_2Cl_2. The extract was treated with Na_2SO_3 to destroy peroxides, dried (Na_2SO_4) and evaporated. The residue, which was essentially pure product, was purified by silica gel column chromatography and studied by ^1H NMR spectrometry.

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The reactivity ratio heptane/CH_2Cl_2 is close to 10; besides this result is consistent with what has been observed in homogeneous medium[11].
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