Amphiphilic α-alkoxyalkyl hydroperoxide (α-AHP): a new oxidising reagent in aqueous media

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Effective oxidation of benzyl sulfide to the corresponding sulfoxide in water was achieved by using amphiphilic α-alkoxyalkyl hydroperoxide (α-AHP) in the presence of a catalytic amount of $MoO_2(acac)_2$ under mild conditions.

Exploration of organic reactions in aqueous media is now becoming important from the standpoint of environmentally benign processes.[1] One of the major problems in these reactions, however, is the poor solubility of most organic substrates in water. The application of micellar or vesicular systems made from amphiphilic molecules to organic reactions in water is an effective device to overcome this substantial problem.[2] For example, Jaeger *et al.* have studied in detail the rate and/or regioselectivities of certain reactions, such as monohalogenation of alkyl phenyl ethers or Diels–Alder reactions, in specially designed micellar or vesicular systems.[3] Kobayashi *et al.* have developed Lewis acid–surfactant combined catalysts and have applied micellar systems made from these functional surfactants to aldol or Mannich-type reactions.[4] A number of other papers concerning organic reactions in aqueous micellar systems have been published over the past decade.[5]

For oxidation reactions in aqueous media, commercially available 30–60% hydrogen peroxide has been used as an oxidising reagent because its oxygen efficiency is excellent and water is a resultant side product.[6] *tert*-Butyl hydroperoxide (TBHP) is another choice of reagent in aqueous media.[7] Because these hydroperoxides are potentially hazardous compounds, however, they must be handled with special care. With this in mind, we developed a unique amphiphilic α-alkoxyalkyl hydroperoxide (α-AHP) to act both as a micellar-forming reagent to solubilise organic substrates and as an oxidising reagent. The compounds designed for this work could be easily prepared by ozonation of α-olefins in the presence of oligo-(ethylene glycol)s† (Scheme 1).

Fundamental surface-active properties of **1** were as follows: T_{cp} (cloud point at 1 wt%) = 40 °C; cmc = 3.1×10^{-3} mol dm^{-3}; γ_{cmc} (the surface tension at cmc, as an indication of the effectiveness of adsorption at the air/water interface)[8] = 30 mM m^{-1}; pC_{20} (the efficiency of adsorption)[8] = 3.7.‡ This cloud point means that **1** is soluble in water at rt and forms micelles at any concentration above its cmc. Compound **2** was additionally

synthesised as a reference because it was freely soluble in water but showed no surface-active properties.

Differential thermal analyses (DTA/TG) of **1** and **2** were carried out.§ Both compounds were stable up to about 100 °C but gradually decomposed above that temperature. These results indicate that this type of α-AHP is moderately thermostable. Although careful treatment is still required, the α-AHP is easier to handle than TBHP. The ^{1}H and ^{13}C NMR spectra of a 5 wt% D_2O solution of **1** did not change at all after the solution was kept at 60 °C for 24 h.

Oxidation of benzyl sulfide was chosen to determine the effectiveness of α-AHP as an oxidising reagent in aqueous media. The reaction was run at rt and the reaction products were directly monitored by HPLC.¶ The oxidation reaction in each system was carried out at least three times to confirm its reproducibility. The results are summarised in Table 1 along with data for the same reaction conducted in dichloromethane.

It was confirmed that **1** certainly acted as an oxidising reagent in the presence of $MoO_2(acac)_2$ catalyst[9] under homogeneous conditions in dichloromethane (entry 8). In an aqueous system, too, **1** could oxidise water-insoluble benzyl sulfide very effectively (entries 1 and 2). The reaction proceeded cleanly. In no cases, were any compounds other than unreacted substrate, unreacted α-AHP, benzyl sulfoxide, (benzyl sulfone), alkyl aldehyde and tetra(ethylene glycol) detected in the reaction mixture after 24 h. Aldehyde and tetra(ethylene glycol) were fragments derived from the corresponding α-AHP through the oxidation reaction. Addition of a catalytic amount of MoO_2-$(acac)_2$ to the aqueous micellar system promoted the reaction. In the presence of excess α-AHP, however, benzyl sulfone as well as benzyl sulfoxide was formed in quantity (entry 4). In contrast to the $MoO_2(acac)_2$ system, addition of $VO(acac)_2$[9] caused no acceleration of the reaction in aqueous media (entries 5 and 6). The conversion of the substrate was only 16% when **2** was employed as an oxidising reagent (entry 7). Compound **2** is water-soluble but does not form micelles in water. Evidently, a

Table 1 Oxidation of benzyl sulfide with α-AHP **1** or compound **2** at room temperature[a]

Entry	Oxidant/ mmol dm^{-3}	System[b]	Metal-catalyst[c]	Conver- sion (%)	Molar ratio sulfoxide : sulfone
1	**1** (10)	A	None	52	100:0
2	**1** (20)	A	None	89	100:0
3	**1** (10)	A	$MoO_2(acac)_2$	72	100:0
4	**1** (20)	A	$MoO_2(acac)_2$	100	80:20
5	**1** (10)	A	$VO(acac)_2$	52	100:0
6	**1** (20)	A	$VO(acac)_2$	88	100:0
7	**2** (10)	A	$MoO_2(acac)_2$	16	100:0
8	**1** (10)	B	$MoO_2(acac)_2$	90	80:20

[a] In 10 mmol dm^{-3} benzyl sulfide dispersion (or solution) of water (or dichloromethane) (0.01 dm^3) containing 10 or 20 mmol dm^{-3} of oxidant, at rt for 24 h. [b] A: in water and B: in dichloromethane. [c] Three mol% toward benzyl sulfide.
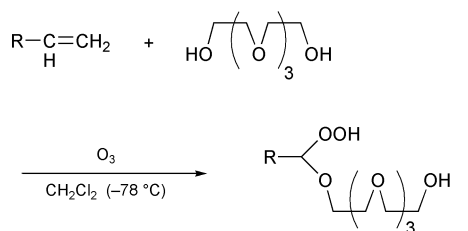
1 R = n-C_8H_{17} (44%)

2 R = n-C_4H_9 (34%)

Scheme 1

key feature of success in promotion of this oxidation in water is the formation of micelles.

When the concentration of **1** in water was 10 mmol dm^{-3}, the maximum conversion was only 72% (entry 3). It is surmised that the oxygen atom transfer from **1** to benzyle sulfide results in the formation of the corresponding hemiacetal, which in turn is easily decomposed into non-surface-active nonanal and tetra(ethylene glycol). Because the cmc of **1** is 3.1 mmol dm^{-3}, most of the micelles will disappear at the final stage of the reaction. This results in the loss of effective solubilisation of substrate in the system. The appearance of insoluble solids in the reaction system was actually observed after 18 h with the naked eye. However, when using excess **1** (20 mmol dm^{-3}) micelles were still present after 24 h, so that the conversion of substrate in each system was higher than in the corresponding system containing 10 mmol dm^{-3} of **1**.

The precise mechanism of these micellar oxidation systems has not yet been established, but it seems reasonable to surmise that benzyl sulfide solubilised within the α-AHP micelles will be oxidised effectively by hydroperoxy groups of α-AHP, which will exist in the vicinity of the solubilised site.

In summary, effective oxidation of benzyl sufide to the corresponding sulfoxide (and sulfone) in water has been achieved by using micellar α-AHP **1** in the presence of a catalytic amount of MoO$_2$(acac)$_2$ under very mild conditions. Studies on the preparation of a series of α-AHPs and their application to other oxidation reactions in these micellar systems are now in progress.

Notes and references

† Over a solution of 1-alkene (10 mmol) and tetra(ethylene glycol) (80 mmol) in dichloromethane (0.04 dm³) was passed a slow stream of ozone (1.2 equiv.) at −78 °C. Then, the mixture was poured into aqueous NaHCO$_3$ and was extracted with ether. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether–methanol (95:5, v/v) gave the target α-AHP as an oil. *Selected data* for compound **1** (R = n-C$_8$H$_{17}$), δ_H(270 MHz; CDCl$_3$) 0.88 (t, 3H), 1.15–1.45 (m, 12H), 1.60–1.85 (m, 2H), 3.1 (s, 1H), 3.52–3.90 (m, 16H), 4.84 (t, 1H), 10.66 (s, 1H); δ_C(67.5 MHz) 13.98, 22.53, 24.71, 29.07, 29.23, 29.32, 31.05, 31.71, 61.49, 65.12, 69.95, 70.02, 70.19, 70.42, 70.92, 72.38, 107.00 (Calc. for C$_{17}$H$_{36}$O$_7$: C, 57.93; H, 10.30. Found: C, 58.12; H, 10.09%). For compound **2** (R = n-C$_4$H$_9$), similar NMR data were recorded (Calc. for C$_{13}$H$_{28}$O$_7$: C, 52.69; H, 9.52. Found: C, 52.39; H, 9.37%).

‡ Cmc, γ_{cmc} and pC_{20} values were obtained from a surface tension *vs.* concentration (on a log scale) curve measured by the Wilhelmy method (Kyowa CBVP-A3 model; platinum plate) at 20 °C.

§ DTA/TG measurements were performed in a stream of nitrogen at 2 °C min^{-1} of programming rate (Seiko DTA/TG30 model).

¶ Oxidation of benzyl sulfide in aqueous systems was conducted as follows: to a stirred aqueous solution of α-AHP (0.01 dm³, 10 or 20 mmol dm^{-3}) in a 0.05 dm³ sample vial equipped with a magnetic bar and a septum were added benzyl sulfide (0.1 mmol) and metal catalyst (3 mol%). The reaction mixture was stirred in dark at rt for 24 h. Then, acetonitrile (0.015 dm³) was poured into the mixture and bromobenzene as an internal standard was added to the solution. The resultant solution was injected directly into the HPLC apparatus equipped with a TSKgel ODS-80Ts column (eluate: water–acetonitrile = 2/3, flow rate: 8 × 10^{-4} dm³ min^{-1}). From the comparison with authentic samples, formation of nonanal (in the case of α-AHP **1**) or pentanal (in the case of compound **2**), and tetra(ethylene glycol) was confirmed in the reaction mixture.

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