A Convenient Preparation of Aqueous Methyl Hydroperoxide and a Comparison of its Reactivity towards Triacetylethylenediamine with that of other Nucleophiles: The Mechanism of Peroxide Bleach Activation

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A less hazardous preparation of aqueous methyl hydroperoxide is described. The nucleophilic second-order rate constants for the reactions of triacetylethylenediamine (triAED) with a limited range of alkoxides, amines and peroxides exhibit Brønsted β-values of 0.7, 0.8 and 1.0 respectively. These values are consistent with transition states in which cleavage of one of the imide bonds of triAED is important. The rate constant for hydrogen peroxide shows a positive deviation from the Brønsted plot for the other peroxides. It is suggested that the hydrogen atom of the hydroperoxide anion causes the rate enhancement by hydrogen-bonding to the nitrogen of triAED. The results give an important insight into the mechanism of peroxide bleach activation.

Activated peroxide bleaching involves the formation of a peracid by acyl transfer to the hydroperoxide anion from esters and from imides such as tetraacetylethylenediamine (TAED). Hydrolysis of the activator represents an undesirable reaction that occurs in parallel to perhydrolysis. The aim of this and previous studies[1,2] is a detailed understanding of the mechanisms of the attack of hydrogen peroxide and other nucleophiles on activator molecules with a view to maximizing the efficiency of peracid release in activated bleaching systems. We have recently reported that the perhydrolysis of TAED is unexpectedly faster than its peracetolysis after taking into account the greater basicity of the hydroperoxide anion over peracetate.[1] The reaction of TAED with nucleophiles involves two acyl group transfers *via* the intermediate triacetylethylenediamine (triAED) so, in order to simplify the present kinetic study, isolated triAED was used.

Experimental

Preparation of Methyl Hydroperoxide.—In a fume cupboard, ensuring adequate cooling under ice and stirring with a magnetic follower, 30% hydrogen peroxide solution (BDH, AnalaR, 37.5 g), distilled water (62.5 cm^3), and dimethyl sulfate (98%, BDH, GPR, 25 g) were mixed in a resin pot fitted with condenser, dropping funnel and thermometer. Subsequently, 40% (w/w) potassium hydroxide solution (52.5 g) was run into the reaction mix over 40 min. Dimethyl peroxide, a by-product, escaped as a gas. The reaction mix was allowed to reach room temperature and aliquots taken to determine the peroxide concentrations. The determination of the total peroxide concentration was based on the method of Behrman *et al.*:[3] samples were generally diluted tenfold and to the diluted sample (5 cm^3) was added 2 mol dm^{-3} sulfuric acid (20 cm^3) and 100 g dm^{-3} aqueous potassium iodide (10 cm^3). A blank reaction was also carried out using distilled water. Immediately on adding the potassium iodide solution the assay mixtures were placed in the dark, this was found to slow down significantly the rate of iodine formation caused by dissolved oxygen. At regular intervals, 5 cm^3 samples were withdrawn from the assay mixtures and titrated with 0.01 mol dm^{-3} sodium thiosulfate solution (BDH, CONVOL). The value was corrected for the blank reading corresponding to oxidation of iodide by dissolved oxygen. This process was continued until steady readings for the peroxide content were obtained indicating that all the peroxide had reacted to form iodine: usually, this was found to take *ca.* 90 min. The hydrogen peroxide content of the reaction mixture was determined spectrophotometrically using the specific titanium(IV) oxalate assay of Sellers.[4] The methyl hydroperoxide concentration was taken as the difference between the total peroxide and the hydrogen peroxide concentrations.

Other Materials.—Butylamine hydrochloride (98% by titration with KOH) was prepared from butylamine (BDH, reagent grade) according to the standard procedure. Glycine (BDH, biochemical), methanol (BDH, reagent grade, 99%), trifluoroethanol (BDH, AnalaR), hydrogen peroxide (BDH, AnalaR, 30% w/v) potassium peroxomonosulfate triple salt ($2KHSO_5 \cdot K_2SO_4 \cdot KHSO_4$, Interox Chemicals Ltd.) and ethylenediaminetetramethylenephosphonic acid (EDTMP·H_2O, 92:8, Warwick International Ltd.) were used without further purification. The triAED was isolated from one of Warwick International Ltd. production streams which was rich in the desired compound, but also contained other acetylated ethylenediamine species. The crude material was initially extracted with boiling tolune to yield semi-pure (up to 70% by weight) triAED. Further purification was carried out by flash chromatography using a 650 mm × 52 mm diameter column packed with Sorbsil C 60-H, 40–60 μm silica gel and a 95:5 w/w chloroform–methanol eluent. The resulting material was up to 97% pure. A purity in excess of 98% can be achieved by high-vacuum distillation. Buffer components were AnalaR reagents and solutions were made up in distilled water.

Methods.—Carbon-dioxide-free conditions are particularly necessary with butylamine and were used routinely with all nucleophiles. Stock solutions of the amines and alcohols were made up by weight, hydrogen peroxide was standardized cerimetrically and the other peroxides using the standard iodometric methods. Unless stated otherwise kinetic runs were carried out in 0.05 mol dm^{-3} potassium carbonate–hydrogen carbonate buffers with the ionic strength adjusted to 1.00 mol dm^{-3} with potassium chloride. EDTMP, 1×10^{-5} mol dm^{-3} was used to suppress decomposition of the peroxides. Absorbances were measured at 25 °C using a Hewlett Packard HP 8451A spectrophotometer with a thermostatic cell holder. The drop in absorbance corresponding to the loss of triAED was monitored at a single wavelength in the region 220–250 nm depending upon the concentration of triAED. Pseudo-first-order conditions with the nucleophile in excess were used and for the amines and alcohols the observed first-order rate

Table 1 Variation with time of the peroxide concentrations in the methyl hydroperoxide reaction mix

Hours after addition of KOH	$[H_2O_2]$/ mol dm^{-3}	[MeOOH]/ mol dm^{-3}
0	2.10	0
1	0.586	0.380
24	0.110	0.450
196	0.0027	0.396
144	0.0001	0.279

Table 2 Effect of carbonate buffer concentration on the observed rate constant for the hydrolysis of triAED, pH 9.8,[a] ionic strength 1.0 mol dm^{-3} (KCl) at 25 °C

[buffer]/ mol dm^{-3}	k_{hyd}/ 10^{-5} s^{-1}
0.01	6.58
0.02	6.85
0.03	7.06
0.04	7.00
0.05	7.08
0.05[b]	10.14

[a] Slight differences in pH resulting from dilution of the stock buffer were corrected using 1.0 mol dm^{-3} KOH. [b] Using sodium salts.

constant (k_{obs}) was obtained from linear regression of $\ln(A - A_{inf})$ against time. In order to minimize photodegradation of the peroxides only 20–30 absorbance readings were taken over *ca.* four half-lives and k_{obs} was obtained from non-linear regression of the monoexponential change in absorbance with time. At least five different concentrations of each nucleophile were used and 90% confidence limits are quoted for the calculated rate constants.

The pK_a values of glycine and butylamine were determined at 25 °C, ionic strength 1.0 mol dm^{-1} with KCl, using the method of Albert and Sergeant.[5] The pH of the reaction and titration solutions was measured using an electrode calibrated with commercial standard buffer solutions and saturated calcium hydroxide, pH 12.45.[6]

Results

Preparation of Methyl Hydroperoxide.—The standard method of Reiche and Hitz[7] requires that, after addition of hydrogen peroxide, dimethyl sulfate and KOH the reaction mixture is acidified and then distilled. This is followed by extraction into diethyl ether and, after drying, fractionation of the raw product to obtain the pure methyl hydroperoxide. Behrman *et al.*[3] modified this procedure by omitting the diethyl ether extraction and subsequent procedures, since the methyl hydroperoxide was to be used in aqueous solution. They obtained a small volume (20 cm^3) of 3.3 mol dm^{-3} methyl hydroperoxide. We have found that the potentially hazardous distillation of the acidified reaction mix is not necessary since if the reaction mix (unacidified) is left for several days, the hydrogen peroxide concentration falls to below detectable limits, whilst the methyl hydroperoxide suffers only limited decomposition as shown in Table 1.

Hydrolysis of triAED.—Plots of $\ln(A - A_{inf})$ against time were linear for at least four half-lives. Table 2 shows that the effect of buffer concentration on the rate constant for hydrolysis, k_{hyd}, is small. This is reflected in a plot (not shown) of log k_{hyd} against pH in the region pH 9.8–11.1 that has slope 0.93 ± 0.09 (90% confidence limits). These results are consistent with rate-limiting attack of hydroxide on triAED at the lower concentrations of hydroxide and the higher buffer concentrations. Similar results have been obtained for the base hydrolysis of other imides.[1,8–13] The second-order rate constant, k_{OH^-}, for triAED was estimated as 1.01 dm^3 mol^{-1} s^{-1} (Table 3) and has a similar value to the corresponding rate constants published for *N*-methyldiacetamide,[9,10] 1.91 and 1.54 dm^3 mol^{-1} s^{-1}.

When the hydrolysis is conducted using sodium salts there is a *ca.* 40% increase in the rate of hydrolysis over that observed using potassium salts (Table 2). Similar cation effects have been observed for the base hydrolysis of phenylacetates.[14]

Aminolysis of triAED.—Plots of $\ln(A - A_{inf})$ against time were linear for at least four half-lives. Preliminary experiments (not conducted under carbon dioxide free conditions) with high concentrations of glycine buffer yielded values of k_{obs} that were independent of the nature of the cation, sodium or potassium, and second order with respect to the amine concentration, see the footnote to Table 3 for an example. The second order dependence on amine concentration in the aminolysis of amides[15–17] and esters[18,19] is well documented and predominantly due to general base catalysis by a second amine molecule which removes a proton from the attacking nucleophile in the activated complex.

At low amine concentrations plots (not shown) of k_{obs} against the total amine concentration ($[nuc]_T$) are linear with intercept equal to k_{hyd} and slope equal to the observed second-order rate constant, k_2, thus corresponding to the rate law shown in eqn. (1).

$$\text{rate}/[\text{triAED}] = k_{obs} = k_{hyd} + k_2[\text{nuc}]_T \quad (1)$$

Values of k_2 for glycine and butylamine varied with pH as shown in Table 3. The rate constant with respect to the free amine concentration, k_{nuc}, is calculated using eqn. (2) and the apparent pK_a values of the amines determined in this work, shown in Table 3.

$$k_{nuc} = k_2 (K_a + [H^+])/K_a \quad (2)$$

The calculated values of k_{nuc} for butylamine shown in Table 3 are clearly in agreement and thus the butylaminolysis of triAED does not appear to show any general acid or base catalysis or kinetic terms first order in both free base amine and hydroxide concentrations. The values of k_{nuc} for glycine show more variability, which may be due to small systematic errors in k_{obs} since the k_{hyd} term in eqn. (1) is predominant.[20]

Reactions of triAED and Oxygen Nucleophiles.—These were carried out at pH 10.03 except in the case of peroxomonosulfate. The decomposition of the peracid is relatively rapid at this pH which is close to its pK_a and therefore runs were carried out at pH 11.04 where the decomposition is much slower,[21,22] especially in the presence of polyaminomethylenephosphonic acid metal ion chelators.[23] Absorbance *versus* time traces were first order for at least four half-lives for the peroxide reactions. For the alcohol reactions positive deviations occurred, particularly at low alcohol concentrations, after 1–2 and 2–3 half-lives for trifluoroethanolysis and methanolysis respectively. Plots (not shown) of k_{obs} against total nucleophile concentration are linear and correspond to the rate law shown in eqn. (1). The alkoxides showed slight negative deviations from linearity due, presumably, to medium effects at the high alcohol concentrations used. Values of k_2 and the values of k_{nuc} calculated using eqn. (2) are shown in Table 3. The value of k_2 for methanol is much less than that of methyl hydroperoxide

Table 3 Rate constants (25 °C) for the reaction of triAED with nucleophiles in 0.05 mol dm^{-3} carbonate buffers, ionic strength 1.0 mol dm^{-3} with KCl.

Nucleophile	pH	$[nuc]_T$ range/ 10^{-3} mol dm^{-3}	$k_2/10^{-4}$ dm^3 mol^{-1} s^{-1}	pK_a	$k_{nuc}/10^{-3}$ dm^3 mol^{-1} s^{-1}
Glycine	9.80	3–64	15.8 ± 1.2[a]		3.17
Glycine	10.16	5–32	28.7 ± 1.0	9.80[b]	4.14
Glycine	10.42	4–17	24.2 ± 2.2		3.01
Butylamine	9.98	5–50	22.1 ± 2.2		33.7
Butylamine	10.03	5–18	26.3 ± 1.3	11.10[b]	33.7
Butylamine	10.39	8–20	55.0 ± 4.3		31.3
Anions of:					
water		0.03–1.1		15.75	1 010
methanol	10.03	150–580	2.1 ± 0.3	15.50[c]	61 000
trifluoroethanol	10.03	120–490	23 ± 3	12.37[c]	520
hydrogen peroxide	10.03	2–10	38 000 ± 2 000	11.6[d]	140 000
methyl hydroperoxide	10.03	9–23	1 900 ± 200	11.5[d]	5 900
peroxomonosulfuric acid	11.04	3–10	450 ± 40	9.3[e]	46

[a] k_3 0.0139 dm^6 mol^{-2} s^{-1} using $[glycine]_T$ 0.48–0.95 mol dm^{-3}. [b] This work. [c] P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, 1960, **82**, 795. [d] A. J. Everett and G. J. Minkoff, *Trans. Faraday Soc.*, 1953, **49**, 410. [e] Ref. 21.

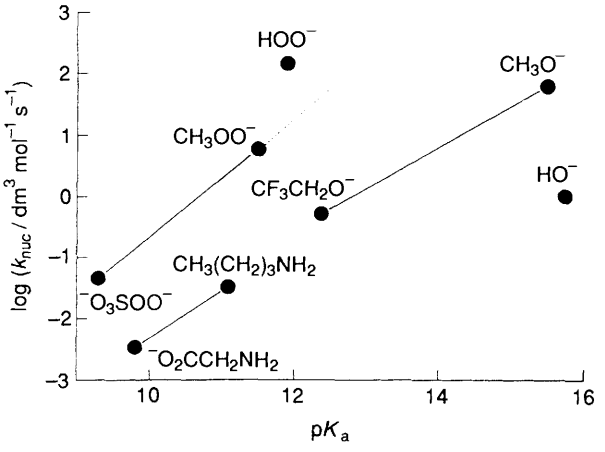


Fig. 1 Brønsted-type correlations of the dependence of the rate constants for the reactions of triAED with nucleophiles upon the pK_a of their conjugate acids, the pK_a of hydrogen peroxide is statistically corrected.

and so no correction has been made for the contribution of the methanol in the aqueous preparation of methyl hydroperoxide to the overall rate of reaction.

Discussion

A convenient preparation of aqueous methyl hydroperoxide for use in kinetic studies has been developed. Dimethyl peroxide is formed as a by-product of the reaction and adequate safety measures should be taken. The preparation contains methanol and, provided, as in this study, that its reactivity is low compared with that of methyl hydroperoxide, significant quantitative corrections to the measured rate constant are not required.

The effects of buffer concentration and pH on the rate of base hydrolysis of triAED are consistent with rate-limiting attack of hydroxide under conditions in which the general acid catalysed breakdown of the tetrahedral intermediate is rapid, and, as described in the results section, our results are similar to those obtained for other imides. Rate-limiting attack of the nucleophile is not unexpected in the case of hydroxide because of its highly solvated nature and relatively high basicity.

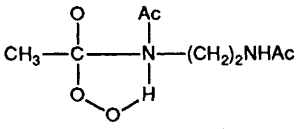
The measured rate constants for the reactions of triAED with the amines, alcohols, and peroxides correspond to nucleophilic attack by the conjugate bases rather than general acid or base catalysis of hydrolysis since, as stated above, the hydrolysis involves rate-limiting attack of hydroxide under the experimental conditions used.

For the attack of less basic nucleophiles on carboxylic acid derivatives it is generally accepted that the transition state involves cleavage of the leaving group–carbonyl carbon bond and plots of log k_{nuc} against the pK_a of the conjugate acid of the nucleophile yield Brønsted slopes, β_{nuc}, approaching unity.[20] Fig. 1 shows Brønsted-type plots of the data, using mean values of k_{nuc} for the amines and the statistically corrected pK_a of hydrogen peroxide. Values of β_{nuc} are, respectively, 0.66, 0.76 and 1.00 for the alcohols, amines, and the line joining methyl hydroperoxide and peroxomonosulfate. These results, within the limitations of the minimal number of points and the experimental variability with glycine, are therefore consistent with an activated complex in which cleavage of one of the imide bonds of triAED is important. The general pattern of the variation of reactivity of triAED between types of nucleophiles is similar to that of *p*-nitrophenyl acetate,[24–26] in that the peroxides, being α-nucleophiles, are the most reactive. The α-effect is, however, much smaller with triAED and similar to that observed for the aminolysis of benzoyl fluorides.[27] It is interesting to note that the peroxides show 'normal' β_{nuc} values with triAED since with *p*-nitrophenyl acetate a low (compared with other nucleophiles of similar basicity) value of β_{nuc}, 0.38, is observed with a range of perbenzoate anions and the anions of hydrogen peroxide and methyl hydroperoxide.[24] Jencks and co-workers have ruled out the possibility that the high reactivity and low β_{nuc} of certain α-nucleophiles, such as the perbenzoates, with esters actually represents an abnormally low reactivity of the resonance-stabilized, weakly basic phenolate ions to which they are compared, rather than an abnormally high reactivity of the α-effect compounds but have not established the reason for the unusual behaviour of the latter.[28] Our results with triAED show that abnormally low values of β_{nuc} are not a general property of peroxide nucleophiles resulting from ground-state factors.

The large reactivity toward TAED of the hydroperoxide anion compared with peracetate has been noted previously.[1,*] As shown in Fig. 1, hydrogen peroxide is significantly more reactive toward triAED than the other peroxides. It is possible that the hydrogen atom of the hydroperoxide anion causes the

* The ratio of reactivities calculated from the rate constants given in ref. 1 is 9.1 × 10^3 not 9.1 × 10^6 as quoted in the paper. Also the ratio of basicities, calculated from the pK_a values is 2.5 × 10^3 not 2.5 × 10^4 as quoted.

rate enhancement by hydrogen-bonding to the nitrogen of triAED in the cyclic structure **1** in which the distribution of the unit negative charge is not shown.



1

Jencks has invoked a similar cyclic structure to explain the rapid *O*-acylation of hydroxylamine by *p*-nitrophenyl acetate *via* an internal (intramolecular) general acid–base catalysed mechanism.[29] The rate-enhancement of HOO^- over $MeOO^-$ with *p*-nitrophenyl acetate and other esters is less than five-fold, however, and Jencks has concluded that in this case the hydrogen atom does not cause a large rate enhancement by hydrogen bonding to the ester.[30] The difference between esters and imides such as triAED and TAED may reflect a requirement for the leaving group of the latter compounds to be protonated. This is consistent with the absence of general acid catalysis that is observed for the perhydrolysis of TAED.[1]

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