N-Methyl-3,4-dihydroisoquinolinium-catalysed oxidation of calmagite by peracetic acid: kinetics and mechanism of catalyst inactivation

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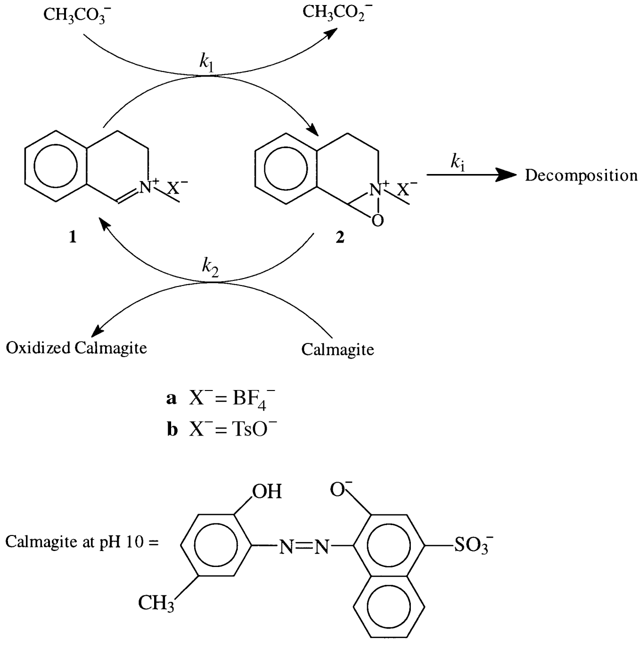
The azo dye, calmagite, is oxidized by peracetic acid and a catalytic amount of *N*-methyl-3,4-dihydroisoquinolinium *p*-toluenesulfonate by *in situ* formation of the corresponding oxaziridinium salt. The kinetics of the reaction have been examined under steady-state conditions in aqueous solution at pH 10. Under pseudo-first-order conditions employing an excess of calmagite relative to peracetic acid, no catalyst degradation is observed. Under near equimolar concentration of reactants, however, catalyst inactivation is found to be significant. Two major decomposition products have been isolated. Kinetic and product analyses indicate that catalyst inactivation occurs through the oxaziridinium salt intermediate by two major pathways; alkaline hydrolysis, which accounts for 60% of catalyst decomposition, and nucleophilic attack by peracid on the oxaziridinium salt.

Introduction

Oxaziridines are a class of three-membered ring heterocyclic compounds containing oxygen, nitrogen and carbon atoms. While these compounds have long been known as oxidizing agents, capable of oxidizing iodide to iodine and triphenylphosphine to triphenylphosphine oxide, their synthetic utility was not exploited until the discovery by Davis and co-workers in 1978 of the more electron-deficient *N*-sulfonyloxaziridines.[1] These neutral, aprotic oxidizing agents have found use in a variety of synthetic transformations such as conversion of sulfides to sulfoxides[2] and asymmetric oxidation of enolates to optically active α-hydroxy carbonyl compounds.[3] These molecules are prepared from *N*-sulfonylimines and a peracid and are typically isolated prior to use. *In situ* generation of the oxaziridine using catalytic amounts of *N*-(*p*-nitrobenzylidene) benzenesulfonamide (0.2 equiv.) and potassium monopersulfate (from Oxone®) in a biphasic solvent system has been shown to convert sulfides to sulfoxides in yields as high as 96%.[4] Sulfonylimines have also been used catalytically with hydrogen peroxide to effect enantioselective oxidation of sulfides.[5]

More recently, Hanquet, Lusinchi and Milliet have shown that the oxaziridinium salt *N*-methyl-1,2-oxo-1,2,3,4-tetrahydroisoquinolinium tetrafluoroborate **2a** is an effective oxygen transfer agent for the oxidation of sulfides,[6] amines and imines[7] and the epoxidation of olefins.[8] This more electron deficient oxaziridine is more reactive than the *N*-sulfonyloxaziridines. For example, epoxidation of *trans*-stilbene by *N*-(*p*-nitrobenzylidene)benzenesulfonamide was only 25% complete after 7 days at 25 °C, and 95% complete after 12 h at 60 °C.[9] In contrast, the oxaziridinium salt **2a** gave 96% conversion to the epoxide after just 30 mins at ambient temperature.[8] This oxaziridinium salt can similarly be generated *in situ* from monopersulfate and catalytic amounts of *N*-methyl-3,4-dihydroisoquinolinium tetrafluoroborate **1a** in acetonitrile–aqueous hydrogencarbonate solvent. Thus, (*E*)-2-undecen-1-ol was converted to its epoxide[10] and a variety of sulfides were converted selectively to either sulfoxide or sulfone depending on whether 1 or 2 equiv. of Oxone® were used.[6] A chiral binaphthyl iminium salt has recently been used catalytically with Oxone® to achieve asymmetric epoxidations of olefins.[11] The above are the only reports of which we are aware, describing the catalytic generation of oxaziridines from imines to effect oxidations, yet clearly this is the most cost effective way to generate these oxidants.

In this paper, we have examined the kinetics of the *N*-methyl-3,4-dihydroisoquinolinium *p*-toluenesulfonate **1b** oxidation of the azo dye, calmagite {3-hydroxy-4-[(2-hydroxy-5-methylphenyl)azo]1-naphthalenesulfonic acid} using peracetic acid in aqueous solution (Scheme 1). Calmagite was chosen as a model water-soluble substrate whose oxidation is easily followed spectrophotometrically. Rate constants were determined for peracetic acid oxidation of the iminium salt **1b** to the oxaziridinium salt **2b** (k_1) and for the oxidation of calmagite by **2b** (k_2). Catalyst decomposition was found to be significant under certain conditions and the rate constant for catalyst inactivation (k_i) was also determined. The major products of this decomposition were isolated and a mechanism for catalyst inactivation is proposed.



a $X^- = BF_4^-$
b $X^- = TsO^-$

Scheme 1

Results

Kinetics

The oxidation of calmagite using catalytic amounts of **1b** and

Table 1 Rate constants for the catalytic oxidation of calmagite by **1b** using peracetic acid

[**1b**]/μmol dm^{-3}	$k_1/10^{-2}$ dm^3 mol^{-1} s^{-1}	$k_2/10^{-3}$ dm^3 mol^{-1} s^{-1}	$k_i/10^2$ s^{-1}
7.500	6.56	2.29	6.00
3.750	6.20	2.31	5.45
1.875	7.19	1.85	4.42

peracetic acid in aqueous solution was examined at 30 °C at pH 10 under steady-state conditions. The reaction was conducted at pH 10 because peracid anion is required for transformation of the imine to the oxaziridine, and because this pH is 2 pK units away from both the pK_a of peracetic acid (8.20) and the pK_1 (8.14) and pK_2 (12.35) of calmagite.[12] Thus, the species involved in this reaction are the peracetate anion and the monophenolate dianion of calmagite. Under pseudo-first-order conditions employing an excess of calmagite, the consumption of calmagite is stoichiometric with respect to peracid although identification of the product was not made. At higher peracid concentrations the catalyst degrades before all of the peracid is consumed, as explained below. Overall, the kinetics are consistent with a second-order catalysed reaction in which peracid oxidation of the iminium salt forms the oxaziridinium salt **2b**, which then acts as the oxygen transfer agent for the oxidation of calmagite (Scheme 1). Oxidation of calmagite by peracetic acid in the absence of catalyst was negligible under the time period examined.

Determination of k_1. The rate constant k_1 was determined under pseudo-first-order conditions by employing an excess of calmagite relative to peracetic acid (Table 1). Under these conditions, the formation of **2b** is rate determining, $k_1 = (6.65 \pm 0.41) \times 10^2$ dm^3 mol^{-1} s^{-1} and no catalyst degradation was observed.

Attempted determination of k_2. Under near equimolar concentration of reactants, the rate of calmagite oxidation becomes rate determining. Because the equilibrium constant for the oxidation of **1b** is strongly in favour of oxaziridine formation, this leads to build up of the oxaziridinium salt **2b**. Under these conditions, the kinetics deviated from a second-order catalysed reaction. The final concentration of oxidized calmagite was dependent on the catalyst concentration with none of the concentrations of catalyst tested achieving complete oxidation of calmagite. The addition of more peracetic acid provided no additional oxidation of calmagite while the addition of more **1b** caused an increase in calmagite oxidation indicating that catalyst poisoning was occurring during the reaction.

Determination of k_2 and k_i. Although there is more than one pathway for catalyst degradation (*vida infra*), as a first approximation, the decomposition was modelled as a pseudo-first-order decomposition with respect to **1b**.[13] A catalyst undergoing a pseudo-first-order decomposition can be expressed as eqn. (1):

$$(\text{iminium salt})_{\mathbf{a}} \xrightarrow{k_i} (\text{iminium salt})_{\mathbf{i}} \qquad (1)$$

where the subscripts a and i indicate the active and inactive form of **1b**. The concentration of active catalyst at any time t is thus:

$$[\text{iminium salt}_{\mathbf{a}}] = [\text{iminium salt}]_0 \exp(-k_i t) \qquad (2)$$

The rate of calmagite oxidation at steady-state where $[CH_3CO_3H] > [\text{calmagite}]$, and where the catalyst concentration is constant can be written as:

$$\frac{-\mathrm{d}[\text{calmagite}]}{\mathrm{d}t} = k_2 [\text{calmagite}]\,[\text{iminium salt}]_0 \qquad (3)$$

Under conditions where catalyst decomposition occurs, the rate of calmagite oxidation will be a function of active catalyst concentration. In this case, the rate of calmagite oxidation becomes:

$$\frac{-\mathrm{d}[\text{calmagite}]}{\mathrm{d}t} = k_2[\text{calmagite}]\,[\text{iminium salt}]_0 \exp(-k_i t) = k_{\text{eff}}\,[\text{calmagite}] \exp(-k_i t) \qquad (4)$$

Upon rearrangement and integration, eqn. (4) can be written as:

$$-\ln \frac{[\text{calmagite}]}{[\text{calmagite}]_0} = -\left(\frac{k_{\text{eff}}}{k_i}\right)[\exp(-k_i t) - 1] \qquad (5)$$

At $t = \infty$, eqn. (5) becomes:

$$\ln\,[\text{calmagite}]_\infty = \ln\,[\text{calmagite}]_0 - \left(\frac{k_{\text{eff}}}{k_i}\right) \qquad (6)$$

Rearranging eqn. (5) and substituting eqn. (6):

$$\ln\,[\text{calmagite}] - \ln\,[\text{calmagite}]_\infty = \left(\frac{k_{\text{eff}}}{k_i}\right) \exp(-k_i t) \qquad (7)$$

or

$$\ln(\Delta\ln\,[\text{calmagite}]) = \ln\left(\frac{k_{\text{eff}}}{k_i}\right) - k_i t \qquad (8)$$

where $\Delta\ln\,[\text{calmagite}] = \ln\,[\text{calmagite}] - \ln\,[\text{calmagite}]_\infty$. A plot of $\ln(\Delta\ln\,[\text{calmagite}])$ *versus* t allowed direct measurement of a k_i of $(5.29 \pm 0.66) \times 10^{-2}$ s^{-1} from the slope (Table 1). The rate constant, k_2, for the oxidation of calmagite by **2b** was then measured indirectly from the intercept $\ln(k_{\text{eff}}/k_i)$ and was found to be $(2.15 \pm 0.2) \times 10^3$ dm^3 mol^{-1} s^{-1}.

Determination of $k_{i(OH)}$. The contribution to catalyst inactivation (k_i) from hydrolysis of the oxaziridinium salt was determined under the reaction conditions of calmagite oxidation using preformed **2b**. The pseudo-first-order hydrolysis rate constant ($k_{i(OH)}$) was obtained by iodometric analysis of the active oxygen concentration with time. The rate constant for oxaziridinium salt hydrolysis, $k_{i(OH)}$, was $(3.22 \pm 0.12) \times 10^{-2}$ s^{-1}.

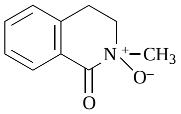
Identification of decomposition products

Stability of iminium salt 1a in alkaline solution. A solution of **1a** (32 mmol dm^{-3}) was dissolved in 0.1 mol dm^{-3} sodium hydrogencarbonate in D_2O (measured pH 10). The ^1H NMR spectrum of this solution was identical to a [$^2H_6$]DMSO solution of **1a**, indicating hydrolytic stability. No detectable decomposition was observed in 2 h at 42 °C or in three weeks at ambient temperature, as monitored by NMR spectroscopy.

Decomposition products from iminium salt 1a and excess oxidant. The iminium salt **1a** (15.8 mmol dm^{-3}) and monopersulfate (78.8 mmol dm^{-3}) were combined in a carbonate buffer solution of D_2O (measured pH 9.5). Following the progress of the reaction by ^1H NMR spectroscopy, the first spectrum taken 3 min after mixing showed complete loss of iminium salt, formation of oxaziridinium salt (55%) and appearance of decomposition products. After 2 h at ambient temperature, there was no oxaziridinium salt and a stable mixture of decomposition products remained; the pH had fallen to 8. The pH was maintained to within 0.5 units and a similar mixture resulted by use of 0.2 mol dm^{-3} sodium carbonate buffer (pH 10) and replacement of monopersulfate with either peracetic acid or *m*-

chloroperbenzoic acid. Repeating the reaction with monopersulfate on a larger scale in H_2O, the major two decomposition products were isolated from methylene dichloride extracts and were identified as the *O*-acyl hydroxylamine **4** and lactam **5**. Spectral data for **5** match the assignments made by Hanquet for this compound which he obtained by treatment of **1a** with aqueous sodium hydroxide and hydrogen peroxide.[16]

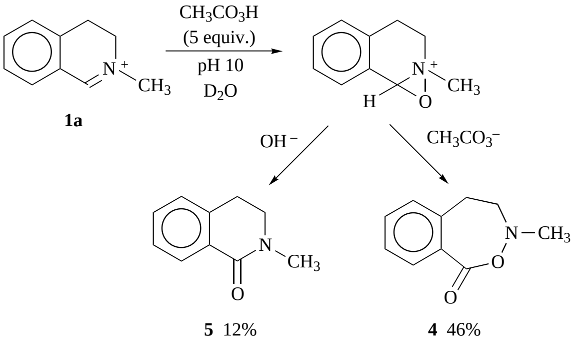
Compound **4** is new. On the basis of MS and ^{1}H NMR data,



6

the acylamine *N*-oxide **6** was also considered. Very few reports of these compounds were found, and no spectral data was located. An acylamine *N*-oxide was presumed to be the intermediate of the hydrogen peroxide oxidation of acetanilide to nitrobenzene; however, it could not be isolated.[14] The IR stretch for the isolated material was at 1731 cm^{-1}. The carbonyl frequency for aliphatic *O*-acyl hydroxylamines is between 1742 and 1761 cm^{-1}.[15] The 11 cm^{-1} shift to lower frequency is reasonable for the aryl substitution of **4**. For compound **6** to possess an IR band at 1731 cm^{-1}, one would have to propose a shift of 80 cm^{-1} to higher frequency from lactam **5** (1650 cm^{-1}) due to oxygen substitution on the nitrogen. Additionally, the isolated material is less polar than lactam **5** since its R_f value on silica gel is higher than the lactam. Compound **6** would be more polar than **5**.

Integration of aliphatic resonances due to compounds **4** and **5** relative to the total aromatic region in the ^{1}H NMR spectrum of the reaction mixture with peracetic acid provided the percentages shown in Scheme 2.



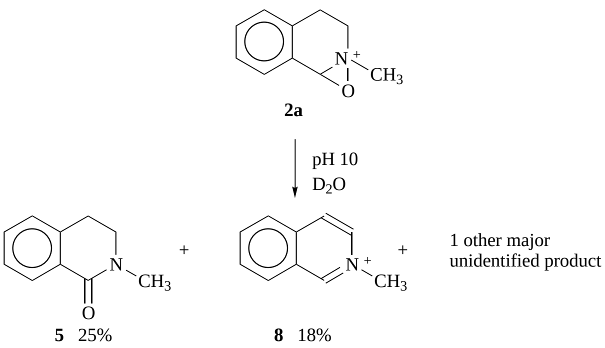
Scheme 2 Decomposition products from reaction of peracetic acid (5 equiv.) with **1a** in aqueous solution (pH 10)

Decomposition products from oxaziridinium salt 2a in aqueous alkali. Hydrolysis of **2a** (15.8 mmol dm^{-3}) in pH 10 D_2O resulted in an 18% yield of *N*-methylisoquinolinium **8** and a 25% yield of lactam **5** as shown in Scheme 3. A third major component remains unidentified.

Decomposition products from oxaziridinium salt 2a and excess monopersulfate. Treatment of **2a** (15 mmol dm^{-3}) with 4 equiv. of monopersulfate in D_2O, buffered to a measured pH of 10, provided 78% acyl hydroxylamine **4** after 40 mins at ambient temperature as determined by comparing the ^{1}H NMR spectrum of this mixture with that of the pure product.

Discussion

Under pseudo-first-order conditions by employing an excess of calmagite relative to peracetic acid, **1b** is converted to **2b** which then acts as an oxygen transfer agent for the oxidation of calmagite. Under these conditions, near complete conversion of peracetic acid is achieved and little catalyst degradation is observed. No background reaction with peracetic acid was observed even when a 10-fold excess was used. The rate enhancement by **1b** may in part be due to a favourable interaction of the iminium cation and the peracetate anion compared to less favourable interaction of the peracetate anion and the monophenolate dianion of calmagite which exists at pH 10.

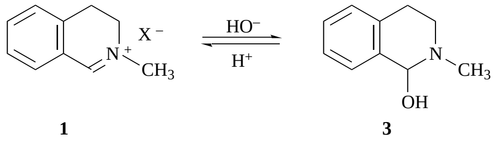


Scheme 3 Decomposition products from hydrolysis (pH 10) of **2a**

Under conditions where the reactants are present at near equimolar concentrations, the behaviour of **1b** deviates from a second-order catalysed reaction and the final concentration of oxidized calmagite becomes dependent on the concentration of catalyst. None of the concentrations of catalyst tested resulted in complete oxidation of calmagite. The addition of peracetic acid provided no additional oxidation of calmagite while the addition of more **1b** caused an increase in calmagite oxidation indicating that catalyst decomposition occurs during the reaction.

Decomposition of **1a** in the presence of peracid has been reported by Hanquet *et al.* in their attempts to optimize the synthesis of **2a**.[16] Using 1 equiv. each of *p*-nitroperbenzoic acid and sodium hydrogencarbonate in methylene dichloride, they obtained 60% *N*-methylisoquinolinium tetrafluoroborate **8**, 20% **1a** and 20% of the ring opened aldehyde, 2-(*N*-methyl-*N*-*p*-nitrobenzoyloxy)-2-aminoethylbenzaldehyde. Since the decomposition had only been studied in organic solvent with stoichiometric amounts of peracid, we examined the decomposition under the aqueous conditions of our experiments.

In the absence of peracid, the iminium salt **1a** was stable for more than 2 h at 42 °C at pH 10. The pseudo base **3** was not detected under our conditions. Hanquet *et al.* obtained a 68% yield of **3** by treating a methylene dichloride solution of **1a** with 2.5 mol dm^{-3} aqueous sodium hydroxide.[16] The iminium salt was regenerated upon treatment with *p*-nitrobenzoic acid. Cook *et al.* observed **3** from a 0.5 mol dm^{-3} aqueous sodium hydroxide solution of **1** and measured a pK_{ROH} of 10.75 for the equilibrium.[17] The hydrolytic stability of **1a** contrasts with the very short lifetimes (10^{-7}–10^{-8} s) recently reported for *N*-phenyliminium ions in aqueous solution.[18] Nevertheless, catalyst inactivation in our system is not due to iminium hydrolysis.



Treatment of **1a** with excess peracid at alkaline pH resulted in two major CH_2Cl_2 soluble products which were isolated; *O*-acylated hydroxylamine **4** (46%) and lactam **5** (12%) (Scheme 2); a third water-soluble product was not identified. Alkaline hydrolysis of **2a** gave 25% of lactam **5** and 18% of *N*-methylisoquinolinium tetrafluoroborate **8**, and a third major product which remains unidentified (Scheme 3). Formation of **4** is the result of peracid attack on the oxaziridinium salt since this is the major product (78%) from treatment of **2a** with monopersufate. Since lactam **5** forms from both the oxaziridinium salt and the catalyst/peracid decomposition it likely forms *via* alkaline hydrolysis of the oxaziridinium salt, presumably by hydroxide removal of the C1 proton followed by opening of the oxaziridine ring. Hanquet *et al.* proposed a reasonable mechanism for *N*-methylisoquinolinium formation involving base removal of the C3 proton on the oxaziridinium salt followed by cleavage of the N–O bond to give 4-hydro-1-hydroxy-*N*-methylisoquinolinium salt, which then eliminates water.[16]

It is clear from the analysis of the decomposition products that there is more than one pathway for the degradation of **1b**. Two major decomposition pathways involve reaction from the oxaziridinium salt. In an effort to determine the rate of decomposition of the catalyst relative to the rate of calmagite oxidation, the decomposition was consequently modelled as a pseudo-first-order decomposition with respect to **1b** as a first approximation. At high levels of peracid relative to calmagite, the catalyst exists in solution as the oxaziridinium **2b**, and the rate of calmagite oxidation will be a function of the concentration of calmagite and the concentration of catalyst undergoing a first-order decay, eqn. (4). A plot of ln (Δln [calmagite]) *versus* t allows direct measurement of k_i. The rate of calmagite oxidation (k_2) is then measured indirectly from the intercept ln (k_{eff}/k_i). It is apparent from this that the partitioning ratio (k_2[calmagite]/k_i) is a function of calmagite concentration. As the calmagite concentration is increased, the catalyst lifetime is prolonged by drawing the reaction towards product formation and effectively reducing the rate of inactivation. The rate of hydrolysis of **2b** was obtained independently using preformed **2b**. The pseudo-first-order rate constant $k_{i(OH)}$ accounts for 60% of the total rate of inactivation.

Conclusions

The kinetic evidence and product analysis presented here are consistent with catalyst degradation occurring from the oxaziridine. When peracetic acid is used as the oxidant, the rate constant for the formation of the oxaziridine is smaller than the rate constant for calmagite oxidation of the oxaziridine. Under conditions that favour oxaziridinium formation, the decomposition of catalyst is maximized suggesting that the decomposition occurs from the oxaziridine. Decomposition is primarily due to reaction with peracid or hydrolysis of the oxaziridine, the latter accounting for 60% of the overall rate of inactivation. The rate of catalyst decomposition is minimized by reducing the peracid concentration or increasing the calmagite concentration. Both of these approaches have the effect of favouring product formation over catalyst inactivation.

Experimental

Materials

All reagents used were ACS grade. Peracetic acid was used as obtained from Aldrich as a 32% solution containing 40–45% acetic acid and < 6% hydrogen peroxide. Calmagite (triethanolammonium salt), *m*-chloroperbenzoic acid (73% active) and monopersulfate, which was delivered as Oxone® ($2KHSO_5·KHSO_4·K_2SO_4$), were obtained from Aldrich.

General

Spectra taken in acetonitrile and D_2O were referenced to residual protons in the solvent at 1.93 and 4.63 ppm, respectively, unless otherwise noted; spectra taken in other solvents were referenced to tetramethylsilane (TMS); coupling constants (J) are reported in Hertz. pH values reported in deuterium oxide were measured with pH strips calibrated in 0.5 units and are uncorrected.

N-Methyl-3,4-dihydroisoquinolinium tetrafluoroborate 1a[16]

Prepared from *N*-methyl-3,4-dihydroisoquinoline.[19] The ^1H NMR spectrum corresponds to the literature.

N-Methyl-3,4-dihydroisoquinolinium *p*-toluenesulfonate 1b

Prepared from *N*-methyl-3,4-dihydroisoquinoline[20] and methyl *p*-toluenesulfonate using the general literature procedure.[21] Yield 88%; recrystallized to constant melting point: mp 126–128 °C (methanol–THF). δ_H(200 MHz; D_2O $Me_3SiCD_2CD_2CO_2Na$) 8.77 (1 H, s, CH=N), 7.78–7.18 (8 H, m), 3.93 [2 H, t $J_{3,4}$ 8.7, C(3)H], 3.73 (3 H, s, NCH_3 $J_{3,4}$ 8.7), 3.15 [2 H, t C(4)H], 2.27 (3 H, s, OTs); δ_C(75 MHz, [$^2H_6$]DMSO) 166.3 (C1), 145.6, 137.7, 137.2, 136.0, 133.0, 128.2, 128.1, 128.0, 125.4, 124.6, 49.4 (C3), 47.2 (N-Me), 24.2 (C4), 20.7 (OTs); *m*/*z* (FAB) 146 (M^+). Found M, 146.098 23. $C_{10}H_{12}N$ requires 146.096 97. *m*/*z* (FAB negative ion) 171 (M^-).

1,2-Oxo-3,4-tetrahydroisoquinoline[16,23]

Iodometric titration gave 75% activity. δ_H(200 MHz; CD_3CN) 8.10–7.10 (4 H, m), 4.95 [1 H, s, C(1)H], 3.90 [1 H, m, C(3)H], 2.90 [2 H, m, C(4)H], 2.55 [1 H, m, C(3)H].

N-Methyl-1,2-oxo-3,4-tetrahydroisoquinolinium tetrafluoroborate 2a[16]

Iodometric titration gave 87% activity; mp 85–102 °C; δ_H(300 MHz, CD_3CN) 7.83–7.39 (4 H, m, Ar), 6.15 [1 H, s, C(1)H], 4.33 [1 H, ddd, J_{AB} 13.4, $J_{3,4a}$ 6.2, $J_{3,4b}$ 2.0, C(3)H], 3.88 [1 H, ddd, J_{AB} 13.4, $J_{3,4a}$ 5, $J_{3,4b}$ 12.3, C(3)H], 3.31 (3 H, s, NCH_3), 3.21–2.86 [2 H, m, C(4)H].

The ^1H NMR assignments in the literature for 1,2-oxo-3,4-tetrahydroisoquinoline[22] and **2a** do not include the resonances at 3.90 and 3.88, respectively. COSY experiments on **2a** show strong coupling between the protons at 4.33, 3.88 and 3.21–2.86 ppm; therefore, these protons must be part of the same molecule.

Kinetic study of catalytic oxidation of calmagite by 1b and peracetic acid

Reactions (300 mm^3) containing calmagite (20–120 μmol dm^{-3}), peracetic acid (12.5–400 μmol dm^{-3}) and **1b** (1.875–7.5 μmol dm^{-3}) were conducted at 30 °C in a 0.1 mol dm^{-3} sodium hydrogencarbonate buffer (pH 10). The progress of the reaction was monitored spectrophotometrically by following a decrease in absorbance of calmagite at 600 nm ($\varepsilon_{600} = 20\,640$ dm^3 mol^{-1} cm^{-1}) using a Cobas-Fara II Autoanalyser. Pseudo-first-order rate constants for the formation of **2b** were calculated from the slopes of lines obtained from plots of the ln[CH_3CO_3H] *versus* t at fixed concentrations of calmagite and varying fixed concentrations of **1b**. Slopes were determined using least-squares analysis. The pseudo-first-order rate constant for the decomposition of **1b** was measured directly from the slope of a plot of ln (Δln [calmagite]) *versus* t. The rate constant for calmagite oxidation (k_2) was measured indirectly from the intercept, ln (k_2[calmagite]/k_i), of the same plot. pH measurements before and after the runs dropped by less than 0.05 units from a starting pH ranging from 10.10 to 10.15.

Isolation of decomposition products of reaction of 1a and monopersulfate

1a (15.8 mmol dm^{-3}) and monopersulfate (78.8 mmol dm^{-3}) in 0.1 mol dm^{-3} sodium hydrogencarbonate (pH 9.5) were stirred at ambient temperature for 2 h. The final pH was 6.9. Water was removed by freeze-drying, the solids were extracted with CH_2Cl_2, the extracts dried over $MgSO_4$ and the solvent evaporated. Remaining in the solids were water-soluble materials with NMR peaks at 8.3, 3.6 and 3.35. GC–MS of the methylene dichloride residue showed two major products; the major $t_R = 10.26$ min and $m/z = 177$; the minor $t_R = 10.46$ min and $m/z = 161$. Silica gel column chromatography (ethyl acetate–

hexane, 3 : 1) was used to isolate these two major components which had R_f values of 0.11 and 0.50.

2-Methylbenzo[*e*]-1-oxa-2-azacycloheptan-7-one, **4**, major product, GC $t_R = 10.26$; $R_f = 0.50$ (ethyl acetate–hexane 3 : 1); ν_{max}(neat)/cm^{-1} 1731; δ_H(200 MHz, $CDCl_3$) 7.75–7.25 (4 H, m, Ar), 3.25 (2 H, t, $J_{4,5}$ 6.8), 3.05 (2 H, t, $J_{4,5}$ 6.8), 2.9 (3 H, s); δ_C(200 MHz, $CDCl_3$) 31.6, 46.1, 58.5, 127.3, 128.2, 129.4, 132.4, 137.0, 172.0; *m*/*z* (EI) 177 ($M^{\cdot +}$); *m*/*z* (FAB) 178 [$(M + H)^{\cdot +}$, 52%], 160 (32), 147 (43), 73 (100). Found M + H 178.087 60. $C_{10}H_{12}NO_2$ requires 178.086 80.

2-Methyl-3,4-dihydro-2*H*-isoquinolin-1-one, **5**, GC, minor product, $t_R = 10.46$; $R_f = 0.11$ (ethyl acetate–hexane 3 : 1). ^{1}H and ^{13}C NMR and IR spectra match those reported in the literature for the title compound.[23]

Identification of products from hydrolysis of 2a

2a (15.8 mmol dm^{-3}) was dissolved in D_2O buffered with sodium carbonate (0.10 mol dm^{-3}) to pH 10. After 20 min, decomposition was complete and provided a ^{1}H NMR spectrum which was a mixture of three major products. This reaction was repeated in H_2O using 150 mg **2a**. After the mixture had stood for 1 h the water was removed by freeze-drying. ^{1}H NMR spectroscopy of an aliquot of these solids in D_2O showed the same mixture as obtained from conducting the reaction in D_2O. The solids were extracted with methylene dichloride, dried over $MgSO_4$ and the solvent removed *in vacuo* to give 113 mg of a brown liquid. The ^{1}H NMR spectrum of the methylene dichloride extracts was simplified, showing only 2 products. *N*-Methylisoquinolinium, **8**, was readily identified from singlets at 9.46 (C1) and 4.32 (N-CH_3) which correspond to chemical shifts in this solvent of an authentic sample[16] which we prepared. Lactam **5** was similarly identified from the ^{1}H NMR spectrum of the mixture by comparison with the authentic isolated material. GC–MS of the methylene dichloride extracts further confirm these two products by comparison with the authentic samples. Integration of the decomposition mixture in D_2O provides the percentages shown in Scheme 3.

Kinetic study of the hydrolysis of 2b at pH 10

An acetonitrile solution of **2b** (500 cm^3 of a 10^{-2} mol dm^{-3} solution) was pipetted into 50 cm^3 of a pH 10 carbonate buffer (0.10 mol dm^{-3}) at 30 °C. Aliquots (1.5 cm^3) of the oxaziridinium solution (10^{-4} mol dm^{-3}) were removed at 10 s time intervals and quenched by addition to a solution of potassium iodide (6.6 g dm^{-3}) and potassium hydrogenphthalate (80 g dm^{-3}) at pH 3. Triiodide concentration was measured by UV spectroscopy at 352 nm according to the method of Davies and Deary.[24] The pseudo-first-order rate constant was obtained from the average of the slopes of three plots of ln (absorbance) *versus* time.

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