

As **1a** is low soluble in water it can react readily with water at its interface to form a set of ionic products which can then diffuse rapidly to the bulk water phase [4a, 6b, 15,18,19]. The rate of dissolution of **1a** is so slow that these ionic products are produced at the interface even before **1a** is dissolved, and makes virtually impossible a detoxification process by a simple hydrolysis reaction. Furthermore, the first step being an equilibrium pathway, the return path to yperite is non negligible at high concentration [4a].

From these instances, it results that the hydrolysis of yperite (or its substitution to produce a non toxic derivative) can be improved taking into account three main conditions: (1) to increase the solubility of the substrate; (2) to ease the ionization of **1** into episulfonium ion; (3) to minimize the return reaction. These conditions can be achieved by coupling the use of strong nucleophiles such as oximate ions and the use of surfactants.

Considering the above investigations, extensive kinetics studies have to be made to assess the hydrolysis reaction (scheme 1). As a general feature, all our experiments were carried out in aqueous solution at constant pH with a large excess of the buffer over the substrate concentration so that the hydrolysis of **1** proceeds with no significant changes in the UV-Visible absorbance on going from **1** to **3** or **4**. This obviously excluded simple kinetic investigations by means of a conventional spectrophotometric procedure. In fact, different techniques have been developed by various authors to overcome this difficulty and to allow the measurement of accurate kinetic data for hydrolysis of yperite and its homologues. These include alkali and colorimetric titrations [6b, 17-21], polarographic monitoring [6b], conductimetric techniques [4b,15b,16d,16e,22], chromatography of aliquots [23] and lately, NMR spectroscopy [4d,10,15b,15c,16a]. But all of these techniques present a lack of accuracy when the rates involved are fast, and moreover, some of them (*i.e.* alkali titrations and conductimetric monitoring) are unusable in buffered systems or high ionic strength).

As evidenced by scheme 1, a most attractive alternative was, however, to use the increase in the concentration of the expelled chloride ion as the monitor to follow the kinetics of the processes. In this paper, we report for the first time our finding that a potentiometric cell involving a chloride ion selective electrode can actually be used to study relatively fast kinetic processes such as those depicted in scheme 1 which can take place with half reaction times of about 40 seconds for the fastest ones.

Experimental part

Material

A chloride ion selective electrode from Methrom coupled with a double junction ($\text{Hg}_2\text{SO}_4/\text{Hg}$) reference electrode were used. A high impedance millivoltmeter from Methrom and a data acquisition system from Eurosmart (Fast-Lab, Physcope, Synchronie) coupled to a PC computer were also

used. Each result potential comes from an average of 64 acquired potential values [14]. The reference electrode was directly in contact with the reaction mixture and bath thermostated ($25\text{ }^\circ\text{C} \pm 0.1$) cells were used. A constant and reproducible magnetic stirrer was used at maximum speed in the cell to provide sufficient mixing. As mentioned by Yang, it is necessary to predissolve the sulfide in a polar, organic solvent, and to keep its concentration low in solution. This limiting control allows to eliminate the slow dissolution step in the case of pure substrate injected and to ensure pure first-order kinetics. In consequence, the substrate concentration of **1a-d** is kept below $10^{-3}\text{ mol dm}^{-3}$ in the reaction mixture. Consequently all the kinetic runs described in the results-discussion section were carried in aqueous solution with chlorinated substrate concentration in **1b-d** equal up to $8 \times 10^{-4}\text{ mol dm}^{-3}$, prepared as following: a 2 % by volume stock solution was prepared in 1,4-dioxane and a 20 μL aliquot of predissolved substrate was then added in the 5 mL bulk reaction (0.4 % dioxane – 96.6 % H_2O v/v).

In all kinetic runs, the ionic strength was maintained constant at 0.1 mol dm^{-3} by adding KNO_3 .

Reagents

CEMS, CEES and HEPES were commercially available Aldrich products used without further purification. *Anti*-Pyruvic aldehyde 1-oxime (MINA) was a commercially available Aldrich product purified by crystallization in heptane. CEPS was synthesized using the method of Lion and co [7b]. ^1H NMR (CDCl_3) δ : 2.87(6H, t, CH_2), 3.62 (2H, t, CH_2), 7.27 (5H, m, Ph). Because of their aggressivity, CEPS, CEMS and CEES must be handled in a hood with protection suits and protection gloves.

Results and discussion

Selectivity of the process

In a first stage we investigated the selectivity limit of the chloride ion selective electrode to be used under the experimental conditions desired. A calibration procedure has then been carried out at constant pH and constant ionic strength, varying the chloride ion concentration and measuring the response of the electrode in different conditions: (a) KNO_3 0.1 mol dm^{-3} ; (b) HEPES buffer ($[\text{HEPES}] = 3 \times 10^{-2}\text{ mol dm}^{-3}$, $\text{pH} = 7.5$); (c) oximate buffer (MINA, $[\text{Mina}]_{\text{tot}} = 2 \times 10^{-2}\text{ mol dm}^{-3}$, $\text{pH} = 8.30$); (d) HEPES buffer containing oximates ($[\text{HEPES}] = 3 \times 10^{-2}\text{ mol dm}^{-3}$, $[\text{Mina}]_{\text{tot}} = 1.5 \times 10^{-2}\text{ mol dm}^{-3}$, $\text{pH} = 7.5$).

The calibration curves obtained plot the measured potential, E_{meas} , versus the reference electrode as a function of chloride ion concentration, following equation (1):

$$E_{\text{meas}} = \Delta - \frac{2.3 RT}{F} \log [\text{Cl}^-] \quad (1)$$

where Δ is a constant that depends of all the experimental conditions, R the perfect gas constant, T the temperature and F the Faraday constant.

Results are reported in figure 1. As can be seen, we obtained typical calibration curves with slopes of (-56.5 ± 0.8) mV per decade in their linear part [24]. The selectivity depends of the experimental conditions that induce interferences for the selective electrode and can perturb its response [25]. It is determined by the intersection between the two linear parts of the calibration curve. For conditions (a), (b) and (d), selectivity appears to be near the same (about 2×10^{-4} mol. dm $^{-3}$) and satisfactory for the range of chloride ion concentration required for the process. But figure 1 shows above all that a direct buffering by an oxime/oximate buffer (condition (c)) will be incompatible with our requirements, because of a too important loss of selectivity (up to 1×10^{-3} mol. dm $^{-3}$). However, figure 1 indicates that the use of oximate ions will be possible by coupling an external buffer in excess such as HEPES (conditions (d), with oximate ions in default).

Potentiometric measurements of the kinetic data

In a general way, reliable potentials can be obtained only if the potentiometric cell used for the measurements has reached chemical equilibrium [24b,25]. A first requirement for using a chloride ion selective electrode to follow fast variations in the Cl^- ion concentration of a solution was therefore to design experimental conditions minimizing as much as possible this equilibrium time [14]. This "dead" time can be strongly reduced providing that, prior to the addition of the chlorinated substrate, a 1×10^{-3} mol.dm $^{-3}$ chloride concentration is contained in the reaction vessel and a period of 15 mn was kept. Under these experimental conditions, the response of the electrode to the additional amounts of Cl^- resulting from the decomposition of the substrate at a concentration of less than 10^{-3} mol dm $^{-3}$ was sufficiently fast as to allow an adequate kinetic monitoring of the reactions proceeding with $t_{1/2} \geq 40$ seconds. Figure 2 shows the accurate first order decomposition of CEMS and CEES, at concentration of respectively 8.4×10^{-4} mol dm 3 and 7.8×10^{-4} mol dm 3 , in a HEPES buffer ([HEPES] = 3×10^{-2} mol dm $^{-3}$, pH = 7.5). After completion of the decomposition process, the final concentration of Cl^- was equal to the expected one. The linearity of the electrode response was further controlled by an internal calibration, introducing additional determined amounts of NaCl in the reaction mixture. The Cl^- ion concentration was determined from measured potentials using internal and external calibration parameters, in similar pH and ionic strength conditions.

Decomposition of **1b-d** in HEPES buffers

Using the potentiometric method described above, the kinetics of the decomposition of yperite simulants according to scheme 1 was studied under common pseudo-first

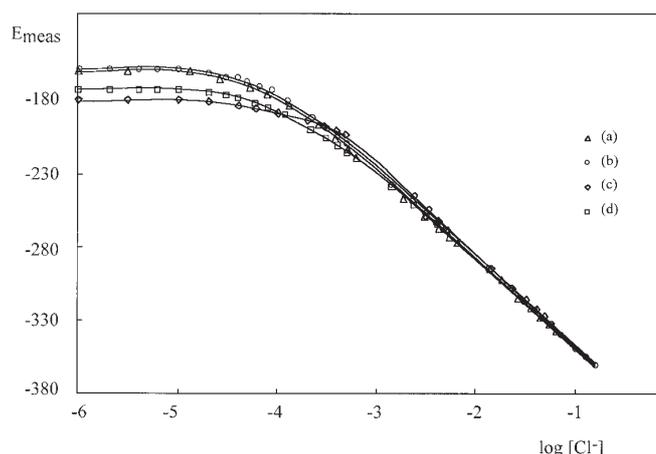


Figure 1. Limit of selectivity of the chloride ion selective electrode in (a) KNO_3 0.1 mol dm $^{-3}$, (b) a 3×10^{-2} mol dm $^{-3}$, 1:1 HEPES buffer (pH = 7.5); (c) a 2×10^{-2} mol dm $^{-3}$, 1:1 oximate (MINA) buffer (pH = 8.30); (d) a 1:1 HEPES buffer containing [Mina] $_0$ 1.5×10^{-2} mol dm $^{-3}$ (pH = 7.5).

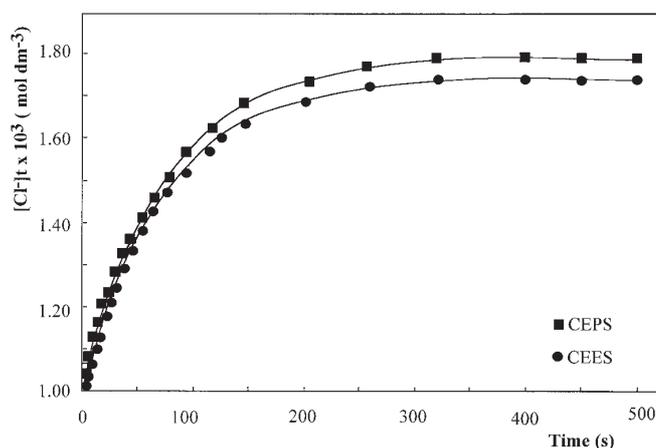


Figure 2. Kinetic monitoring of the increase in the Cl^- concentration produced by the decomposition of CEMS and CEES, with $C_0 = 8.4 \times 10^{-4}$ and 7.8×10^{-4} mol dm $^{-3}$ respectively, in a 1:1 HEPES buffer 3×10^{-2} mol dm 3 , in aqueous solution (pH = 7.5).

order conditions, with the HEPES buffer ([HEPES] = 3×10^{-2} mol dm $^{-3}$, pH = 7.5) in excess. Excellent first order kinetics up to at least 90 % of the total release of Cl^- ions were observed (Fig. 2).

Taking into account eq.(1) which relates the Cl^- concentration to the measured potential for the cell (eq.(2)), the simple rate law for the decomposition of **1b-d** corresponding to scheme 1 (eq.(3)) implies that the kinetic data obey eq.(4). In this equation, C_0 is the initial concentration of **1b-d**, E^0 the potential measured at zero time ($[\text{Cl}^-] = 8 \times 10^{-4}$ mol dm $^{-3}$), E_{meas} , the potential measured at any time t and F the Faraday constant. Δ is a constant deduced from the calibration of the cell.

$$[Cl^-] = 10^{-\frac{(E_{meas} - \Delta)F}{2.3RT}} \quad (2)$$

$$\frac{d[Cl^-]}{dt} = k_{obsd} [1] \quad (3)$$

with $k_{obsd} = k_1 \frac{k^w}{k^w + k_{-1} [Cl^-]}$, with $k^w = k^{H_2O} + k^{OH}[OH^-]$, that

represents the contribution in the reaction of water and OH⁻ ions, respectively.

$$k_{obsd} t = -\text{Ln} \frac{C_0 - 10^{-\frac{(E_{meas} - \Delta)F}{2.3RT}} - 10^{-\frac{(E_0 - \Delta)F}{2.3RT}}}{C_0} = -\text{Ln}(Y) \quad (4)$$

Figure 3 shows that good linear relationships were obtained by plotting Ln(Y) as a function of time, allowing a facile determination of the rate constant, k_{obsd} , from the slopes of the observed straight lines. These are reported in table I, with the corresponding half times, $t_{1/2}$, in the range 45-560 seconds, indicating at this stage that the technique is suitable for the kinetic study of the range of rate involved. These values are in good adequacy with those conductimetrically previously determined of $1.15 \times 10^{-2} \text{ s}^{-1}$ and $1.58 \times 10^{-2} \text{ s}^{-1}$ for respectively CEMS [22] and CEES [4b, 15d], in similar conditions. The value for CEPS can not be compared, because at this day, no hydrolysis kinetics data for CEPS is available in the literature.

Decomposition of 1b-d in presence of oximate ions

The decomposition of CEES, CEMS and CEPS were also studied in presence of oximate ions. As depicted by figure 1, the use of oximate ions in excess to buffer the mixture is not suitable because of the lost of selectivity. We employed in this case another experimental approach where the pH was kept constant by an HEPES buffer used as an external buffer ($[HEPES] = 3 \times 10^{-2} \text{ mol.dm}^{-3}$, $\text{pH} = 7.5$) in presence of oximate ions. Accordingly, the hydrolysis of the chlorinated substrate could be achieved in the presence of lower concentration of oximate reagents. In this condition, the

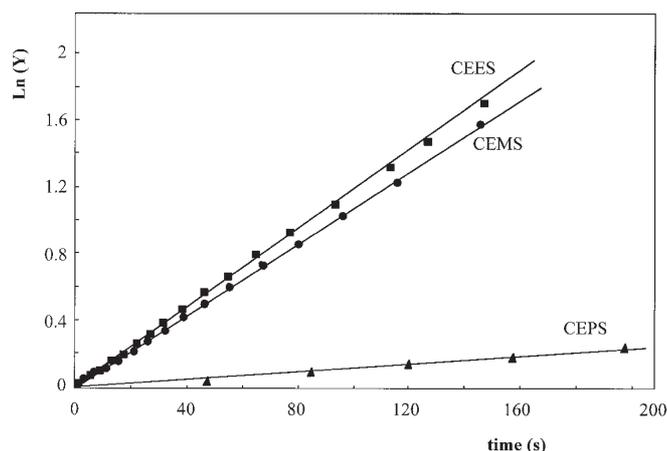


Figure 3. Plots of Ln Y vs t (see eq. 4) for the degradation of CEMS, CEES and CEPS, with $C_0 = 8.4 \times 10^{-4}$, 7.8×10^{-4} and $7.9 \times 10^{-4} \text{ mol dm}^{-3}$ respectively, in a 1:1 HEPES buffers $3 \times 10^{-2} \text{ mol dm}^{-3}$ in aqueous solution ($\text{pH} = 7.5$).

reactive oximate concentration at t time is given by equation (5):

$$[Ox^-] = \frac{[Ox]_0 - x}{1 + 10^{(\text{pK}_a^{Ox} - \text{pH})}} \quad (5)$$

In this equation, $[Ox]_0$ is the total concentration of the oxime introduced in the solution, and x, the concentration of the chloride ion generated by the reaction at time t ($x = [Cl^-]_t - [Cl^-]_0$ with $[Cl^-]_0 = 1 \times 10^{-3} \text{ mol dm}^{-3}$). The observed rate constant, k_{obsd} , obeys equation (6):

$$k_{obsd} = k_1 \frac{k^w + k^{Ox} [Ox^-]}{k^w + k_{-1} [Cl^-] + k^{Ox} [Ox^-]} \quad (6)$$

Considering the S_N1 mechanism for the hydrolysis reaction (scheme 1) depicted by various authors [4b, 6b, 15,16], the integration of eq.(3) in presence of nucleophiles, leads to the same eq.(4) as in absence of oximates ions and allows to

Table I. Pseudo first order rate constants, k_{obsd} , and corresponding half times, $t_{1/2}$, for decomposition of $8.4 \times 10^{-4} \text{ mol dm}^{-3}$, $7.8 \times 10^{-4} \text{ mol dm}^{-3}$ in (a) HEPES buffer and in (b) HEPES buffer containing oximates ($[HEPES] = 3 \times 10^{-2} \text{ mol dm}^{-3}$, $\text{pH} = 7.5$, $T = 25 \text{ }^\circ\text{C}$, $I = 0.1 \text{ mol dm}^{-3}$).

Substrate	HEPES (a)		HEPES(b) $[MINA]_0 = 1.5 \times 10^{-3} \text{ mol dm}^{-3}$	
	$K_{obsd} \text{ (s}^{-1}\text{)}$	$t_{1/2} \text{ (s)}$	$K_{obsd} \text{ (s}^{-1}\text{)}$	$t_{1/2} \text{ (c) (s)}$
CEES	$(1.40 \pm 0.10) \times 10^{-2}$	49	$(1.50 \pm 0.10) \times 10^{-2}$	46
CEMS	$(1.05 \pm 0.10) \times 10^{-2}$	66	$(1.10 \pm 0.10) \times 10^{-2}$	63
CEPS	$(1.25 \pm 0.05) \times 10^{-2}$	555	$(1.20 \pm 0.10) \times 10^{-2}$	575

(c) with an experimental error on $t_{1/2}$ of $\pm 5 \text{ s}$.

predicts that a plot of the right side term Y, versus time, will also afford a straight line passing through the origin, allowing a simple determination of k_{obsd} .

The above methodology was checked with an HEPES buffered system containing less than 10^{-3} mol dm $^{-3}$ in chlorinated substrate, an initial concentration of MINA $[\text{Ox}]_0 = 1.5 \times 10^{-2}$ mol dm $^{-3}$ and an initial concentration of Cl^- of 1×10^{-3} mol dm $^{-3}$. Nice first order kinetic monitorings were observed and after completion of the process, the final concentration of Cl^- was equal to the expected one. Good linear relationships were obtained by plotting $\text{Ln}(Y)$ as a function of time (Fig. 4) allowing the determination of the observed rate constant, k_{obsd} , from the slope. Values are reported in table I, with the corresponding half times, $t_{1/2}$.

As can be seen from the values listed in table I and within the experimental error, no effect of the presence of oximate ions was observed on the rate of decomposition of **1b-d** for a substrate concentration of less than 10^{-3} mol dm $^{-3}$. This is in agreement with the mechanism depicted by scheme 1 with the formation of the intermediate episulfonium ion **2** as the rate determining step [4,6b,15,16].

Decomposition of **1b-d** in presence of oximate ions at various concentrations

The above methodology has been used with systems containing 8×10^{-4} mol dm $^{-3}$ in CEMS substrate, an initial concentration of Cl^- of 1×10^{-3} mol dm $^{-3}$ and various initial concentration of MINA varying in the range $[\text{Ox}]_0 = 5.8 \times 10^{-3} - 5.8 \times 10^{-2}$ mol dm $^{-3}$. Applying eq.(6) and eq.(4) nice linear relationships were obtained and the rate constant, k_{obsd} , were deduced from the slopes. The values are reported in table II. As can be seen, no effect on the rate constant, k_{obsd} , was observed when varying the concentration in oximate. These results lead to two conclusions: (1-) they confirm the $\text{S}_{\text{N}}1$ mechanism depicted in scheme 1, (2-) above all, they indicate that in equation (6) and under these experimental conditions, the term $k_{-1}[\text{Cl}^-]$ is negligible compared to $k^{\text{Ox}}[\text{Ox}^-]$ and that k_{obsd} tends in fact toward k_1 . It affords in consequence a good estimation of the k_1 term, which depends only of the polarity of the solvent.

Table II. Pseudo first order rate constants, k_{obsd} , and corresponding half times, $t_{1/2}$, for decomposition of 8.4×10^{-4} mol dm $^{-3}$ CEMS in HEPES buffer containing various oximate concentrations ($[\text{HEPES}] = 3 \times 10^{-2}$ mol dm $^{-3}$, pH = 7.5, T = 25 °C, I = 0.1 mol dm $^{-3}$).

$[\text{MINA}]_0$ (mol dm $^{-3}$)	$k_{\text{obsd}} \times 10^{-2}$ (s $^{-1}$)	$t_{1/2}$ ^(a) (s)
5.8×10^{-3}	1.05 ± 0.10	66
1.5×10^{-2}	1.10 ± 0.10	63
4.2×10^{-2}	0.96 ± 0.04	72
5.8×10^{-2}	0.98 ± 0.04	71

^(a) with an experimental error on $t_{1/2}$ of ± 5 s.

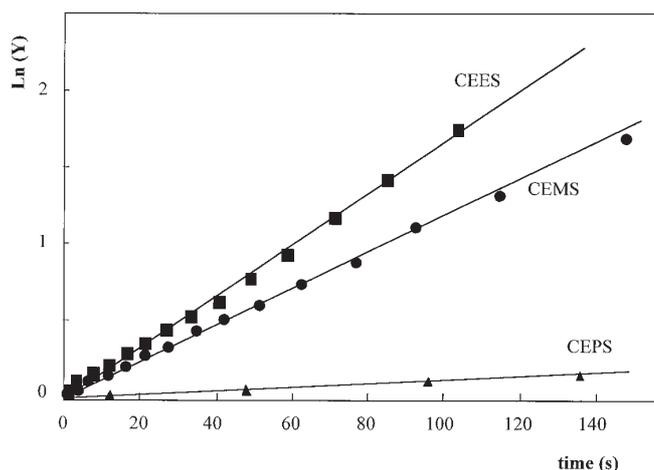


Figure 4. Plots of $\text{Ln} Y$ vs t (see eq. 4) for the degradation of CEMS, CEES and CEPS with $C_0 = 8.4 \times 10^{-4}$, 7.8×10^{-4} and 7.9×10^{-4} mol dm $^{-3}$ respectively, in a 1:1 HEPES buffers containing $[\text{Mina}]_0 = 1.5 \times 10^{-2}$ mol dm $^{-3}$ in aqueous solution (pH = 7.5).

Conclusion

It appears from this study that experimental conditions have been designed which allowed the use of a chloride ion selective electrode for the monitoring of reactions proceeding with a moderately fast departure of Cl^- ion, *i.e.* $t_{1/2} \approx 40$ seconds, in aqueous solution. The potentiometric measurement system is not perturbed by the presence of oximate ions even at moderately high concentrations, and adequate kinetic monitorings and kinetic data were obtained for the hydrolysis of yperite simulants (CEES, CEMS, CEPS) in aqueous solution in presence of HEPES buffer and oximate nucleophile agents. It affords then an experimental protocol for the monitoring of the destruction of Yperite and its simulants.

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