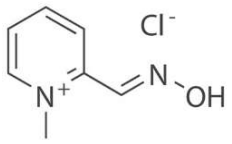
3. This question is about treating nerve agent poisoning

Nerve agents bind to and inhibit an enzyme called acetylcholinesterase (AChE). The inhibited AChE can no longer hydrolyse a key neurotransmitter, which leads to paralysis and ultimately death.

One of the main treatments for nerve agent poisoning is a group of chemicals containing the oxime functional group (C=NOH). These reactivate the inhibited AChE by removing the bound nerve agent. An important reactivator is the salt 2-pyridine aldoxime methyl chloride (PAM).

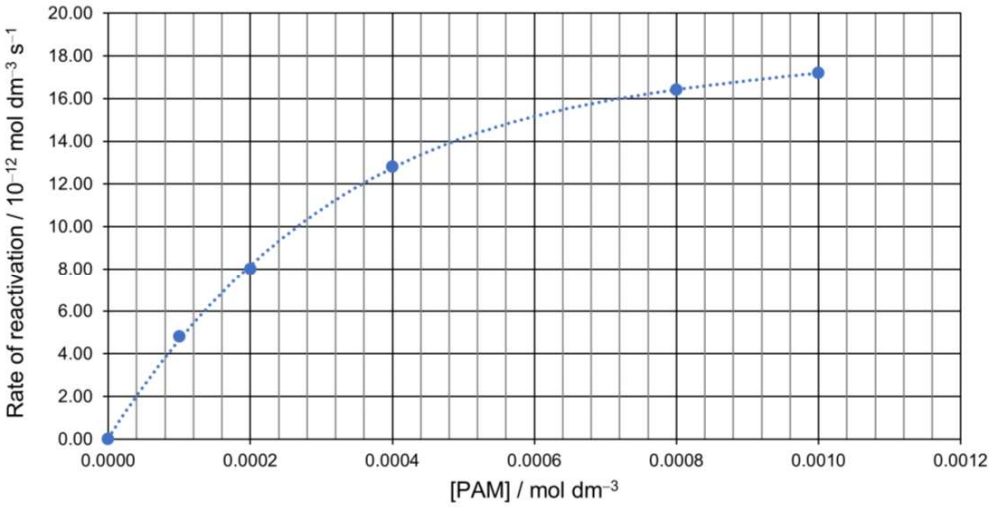


PAM

(a) **(i)** Calculate the molar mass of PAM.

(ii) An adult poisoned by a nerve agent requires an hourly dose of 3.00 mmol of PAM for every kilogram of body mass. Calculate the mass of PAM required for an 80 kg person over a 24-hour treatment period.

Nerve agents work very quickly. Kinetic studies of oximes treatments are an important area of study. The rate of reactivation of inhibited AChE by PAM is shown below.



(b) **(i)** Give the approximate order of reaction with respect to PAM at concentrations of PAM below 0.0002 mol dm^{-3}.

(ii) Give the approximate order of reaction with respect to PAM at concentrations of PAM above 0.0008 mol dm^{-3}.

The following two-step mechanism was proposed to explain these results:

$$\text{AChE-I} + \text{PAM} \underset{}{\overset{K_c}{\rightleftharpoons}} \text{AChE-I-PAM} \xrightarrow{k_2} \text{AChE} + \text{I-PAM}$$

where AChE-I is the inhibited AChE, AChE-I-PAM is a complex of the inhibited AChE and PAM, and I-PAM is PAM with the nerve agent attached.

(c) K_c is the equilibrium constant for the the first step. Write an expression for K_c.

Based on this model, the following expression can be derived for the observed first-order rate constant with respect to the concentration of inhibited AChE (k_{obs}):

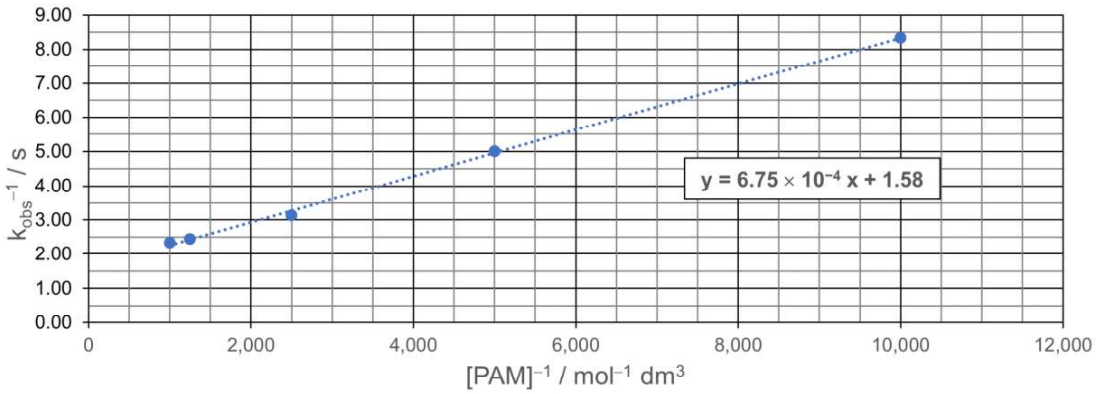
$$k_{obs} = \frac{k_2[PAM]}{[PAM] + \frac{1}{K_c}}$$

k_{obs} is the observed rate constant

K_c is the equilibrium constant for the the first step

k_2 is the rate constant for the second step

A graph of $\frac{1}{k_{obs}}$ was plotted against $\frac{1}{[PAM]}$:



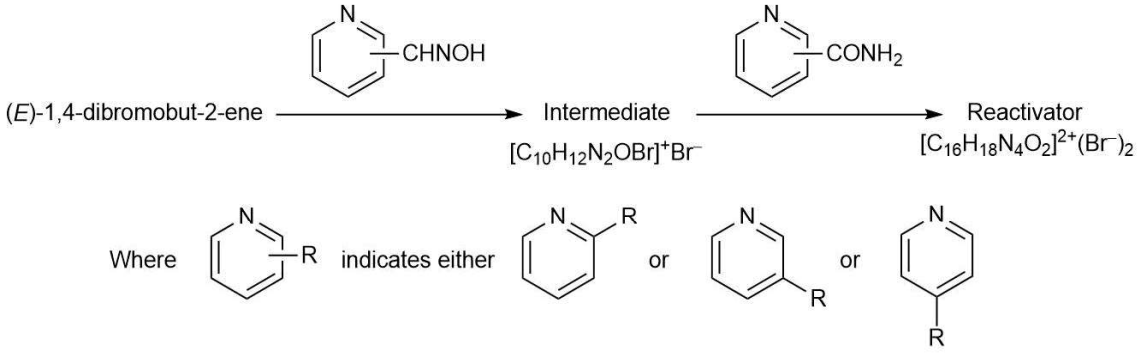
(d) **(i)** Calculate k_2.

(ii) Calculate K_c.

Another important research area is developing more effective AChE reactivators for treating nerve agent poisoning. One new group of reactivators was developed using (*E*)-1,4-dibromobut-2-ene as a starting material.

(e) Draw the structure of (*E*)-1,4-dibromobut-2-ene.

This group of reactivators was synthesised via a 2-step pathway, using a series of related reagents:



(f) How many different reactivators could be made with the above set of reagents?

The most potent reactivator **Y** had 12 signals in its ^{13}C NMR and was obtained from intermediate **X** that had 8 signals in its ^{13}C NMR.

(g) Draw the structures of **X** and **Y**.