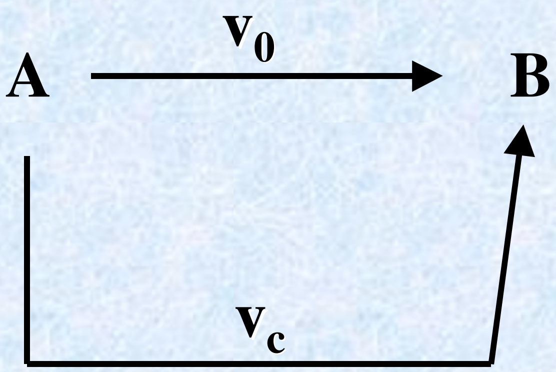
Catalysis

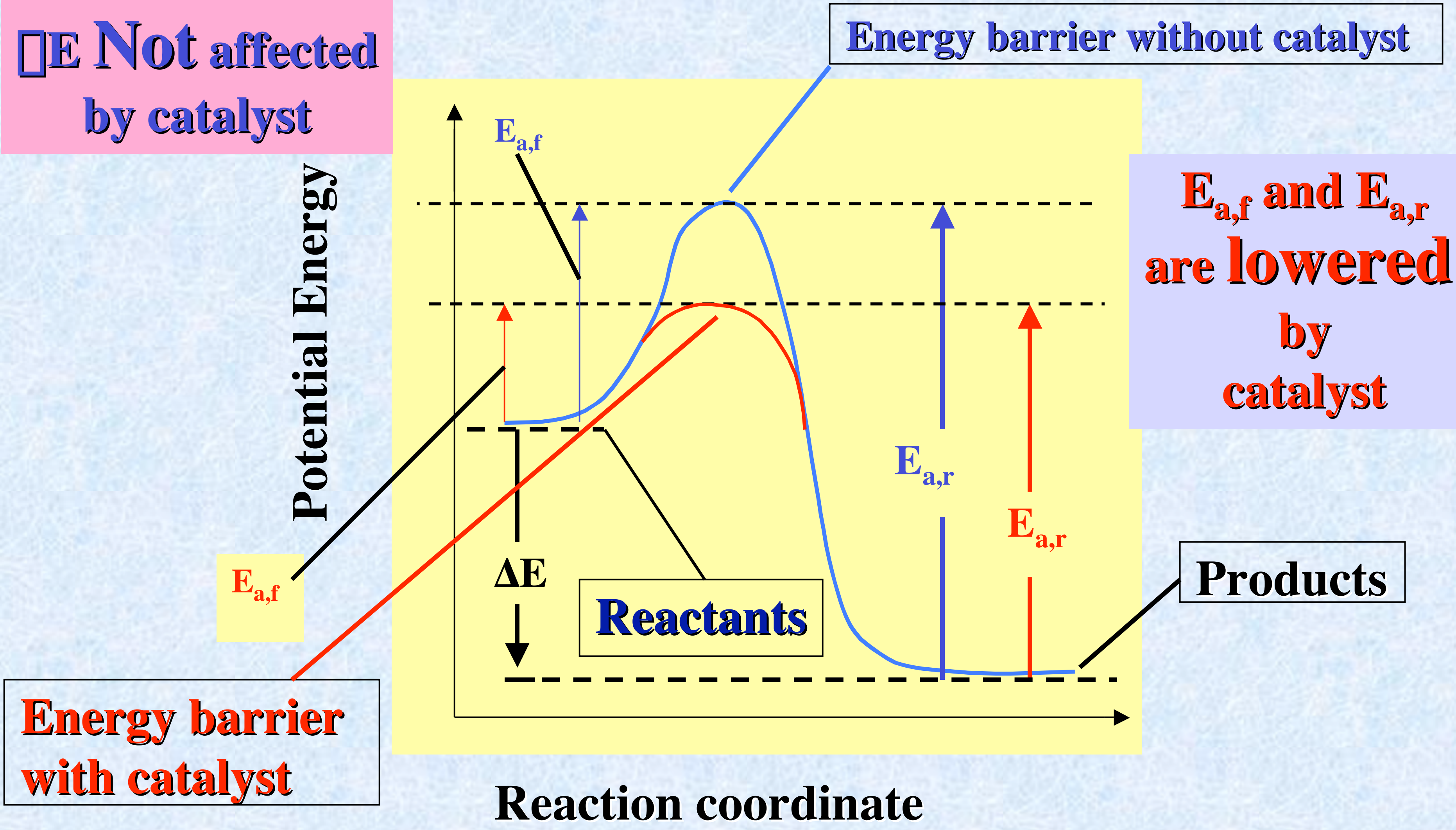
Catalysis provides an additional mechanism by which reactants can be converted to products. The alternative mechanism has a lower activation energy than the reaction in the absence of a catalyst.



v_0 no catalyst
v_c -- catalyst present

($v_0 = -d[A]/dt$ with no catalyst)
($v_c = -d[A]/dt$ with a catalyst)

ΔE **Not** affected by catalyst



$E_{a,f}$ and $E_{a,r}$ are **lowered** by catalyst

Generally a catalyst is defined as a substance which increases the rate of a reaction without itself being changed at the end of the reaction.

This is strictly speaking not a good definition because some things catalyze themselves, but we will use this definition for now.

Catalyst supplies a reaction path which has a lower activation energy than the reaction in the absence of a catalyst.

Catalysis by Enzymes

Enzymes may be loosely defined as catalysts for biological systems. They increase the rate of reactions involving biologically important systems.

Enzymes are remarkable as catalysts because they are usually **amazingly specific** (work only for a particular kind of reaction.)

They are also generally **very efficient**, achieving substantial Rate increases at concentrations as low as 10^{-8} M!

Typical enzyme molecular weights are 10^4-10^6 gm/mole (protein molecules)

Summary of Enzyme Characteristics

1) Proteins of large to moderate weight 10^4 - 10^6.

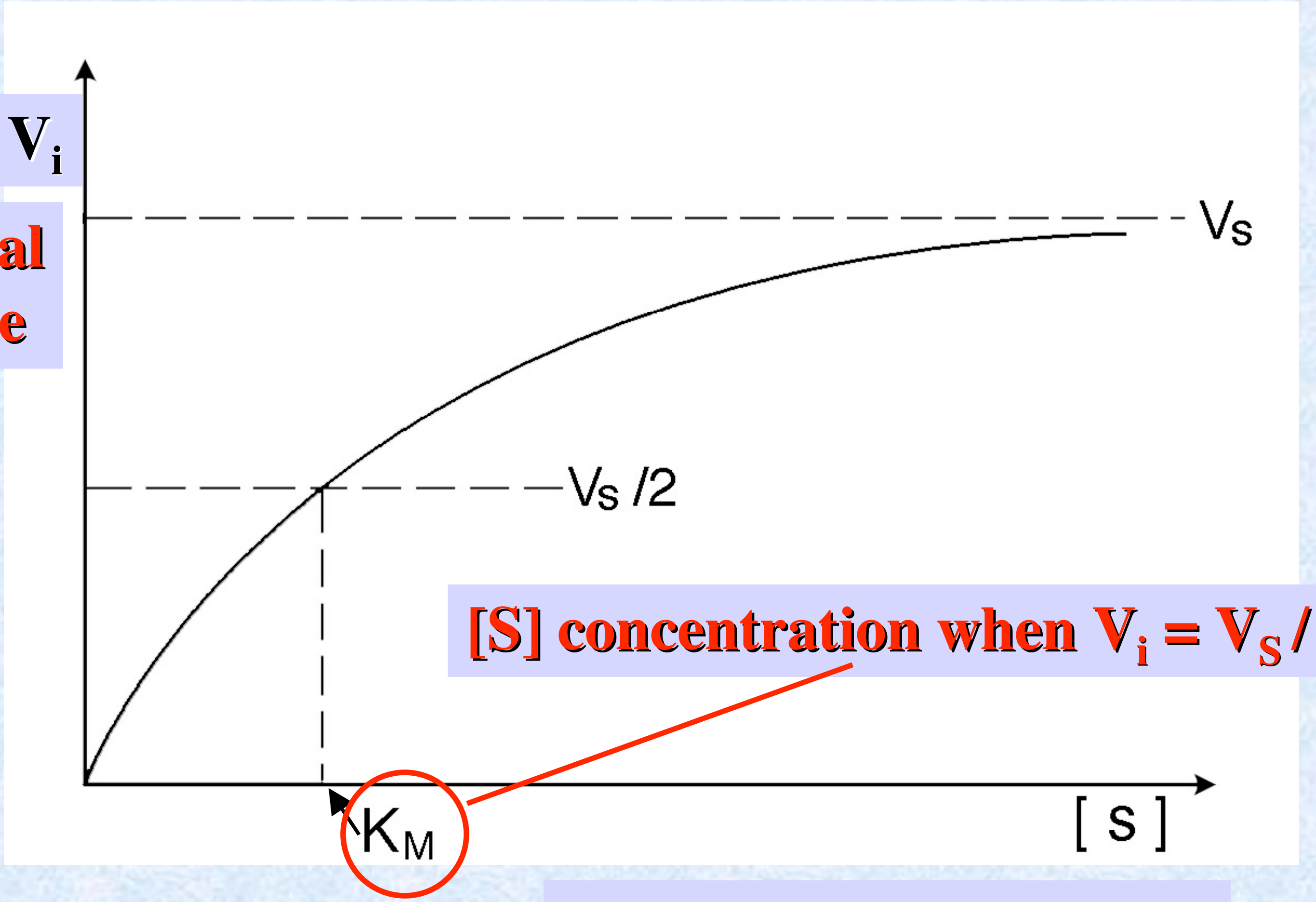
2) Extremely efficient (work at 10^{-8} M)

3) Very specific (work only on special types of reactions).

General Behavior of Enzyme Catalyzed Reactions

S (substrate) $\xrightarrow{E}$ Products

If the initial rate of the reaction is plotted versus the initial concentration of substrate S for a constant enzyme concentration, the following behavior is found:

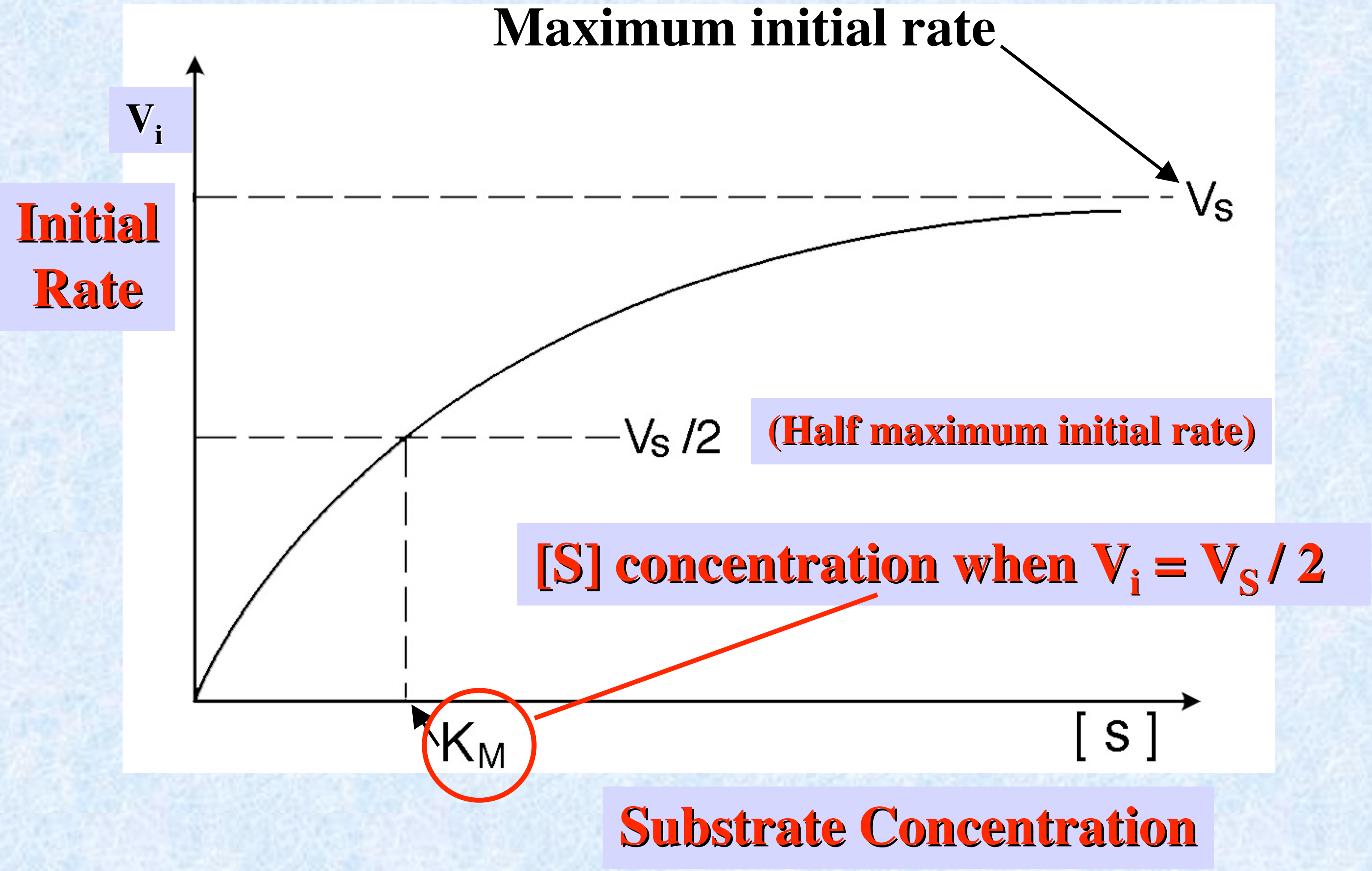


V_i

Initial Rate

[S] concentration when $V_i = V_S / 2$

Substrate Concentration



Maximum initial rate

V_i

Initial Rate

(Half maximum initial rate)

[S] concentration when $V_i = V_S / 2$

Substrate Concentration

V_s is found to be directly proportional to the total enzyme concentration (E_o): $V_s \sim (E_o)$

(S) concentration required to reach half maximum initial velocity $(V_i = V_S/2)$ found to be independent of (E_o). $(S)_{1/2} = K_M$

Explanation: Michaelis-Menten Mechanism

E is free enzyme and ES is an enzyme-substrate complex

It may generally be assumed that (S) >> (E) since E are so efficient they catalyze reaction at very small concentration.

$$d\frac{(ES)}{dt} = k_1\,(E)\,(S) - k_{-1}\,(ES) - k_2\,(ES)$$

Step 1 Step 2 Step 3

First Order Process

First Order Process

Steady State assumption:

$$0 = \frac{\text{`}\qquad\text{´}}{dt}$$

Second Order Process

$$(ES) = \frac{k_1(E_0)(S)}{k_{\square 1} + k_2 + k_1(S)} = k_1E_0/[k_1+(k_{-1}+k_2)/(S)]$$

Mechanism

$E + S \overset{k_1}{\square} ES$ Step 1

$ES \overset{k_{-1}}{\square} E + S$ Step 2

$ES \overset{k_2}{\square} P + E$ Step 3

All are elementary kinetic steps.

Divide top and bottom by k_1 to get $\square$

Bonus * Bonus * Bonus * Bonus * Bonus * Bonus

$$\underbrace{\frac{k_2}{2}(E_0)}_{V_S/2} = \frac{k_2(E_0)}{1+\dfrac{K_m}{\boxed{(S)_{\frac{1}{2}}}}}$$

$(S)_{1/2}$ is the substrate concentration when the initial rate reaches half its maximum value.

Case III : $\dfrac{K_m}{(S)} >> 1$

$$\frac{dP}{dt} = \frac{k_2(E_0)}{1+\dfrac{K_m}{(S)}}$$

Depends linearly on [S] in region of low substrate concentration.

$$\frac{dP}{dt} = V = \frac{V_{max}}{1 + \frac{K_m}{(S)}}$$

Invert this equation to get-->

Mechanism

$E + S \overset{k_1}{\square} ES$ **Step 1**

$ES \overset{k_{-1}}{\square} E + S$ **Step 2**

$ES \overset{k_2}{\square} P + E$ **Step 3**

{Lineweaver-Burke Plot}

K_m is rate at which ES decomposes by two mechanisms (k_{-1} or k_2) divided by rate constant for formation of ES.

Large K_m □ weak binding of E to S

Small K_m □ strong binding of E to S

$$K_m = \frac{k_{\square 1} + k_2}{k_1}$$

The binding of a substrate to an enzyme and the subsequent reaction of the substrate.

Application of chemical kinetics to ecological and toxicological problems

I. Application of enzyme kinetics:

- Degradation of organophosphate pesticides

Enzymes can be used to catalyze degradation of pesticides

While extremely beneficial for protection of crops, pesticides can have serious environmental impact

Possible deleterious consequences include seepage of these otherwise helpful chemicals into soil and ground water

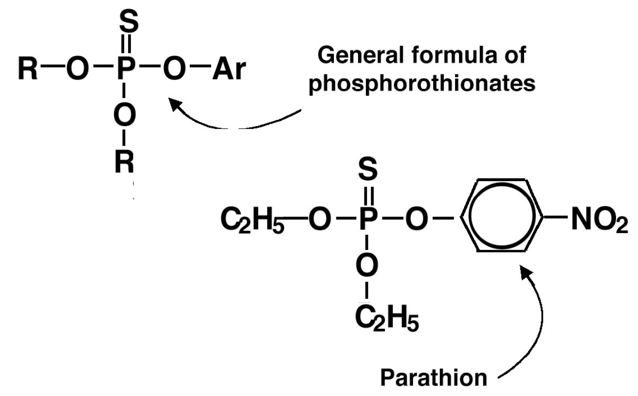
Case study: organophosphate pesticides

- abundant
- highly toxic
- "neutralized" via reaction

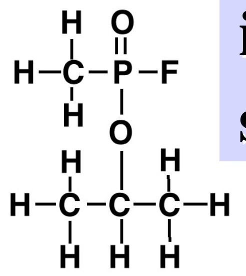
The *same* enzyme catalysts which can neutralize these pesticides can also be used to **detoxify** chemical nerve agents.

- nerve agents are structurally similar to organophosphate pesticides

General formula for pesticides

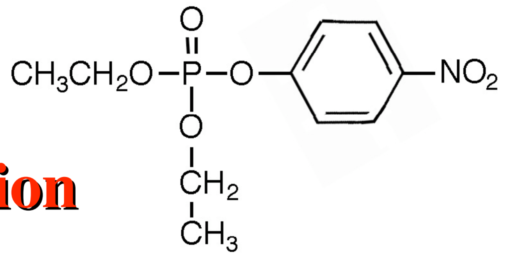


Nerve gas used in Japanese subway attack.



- both contain organophosphate esters

Degradation product produced in body from parathion



paraoxon

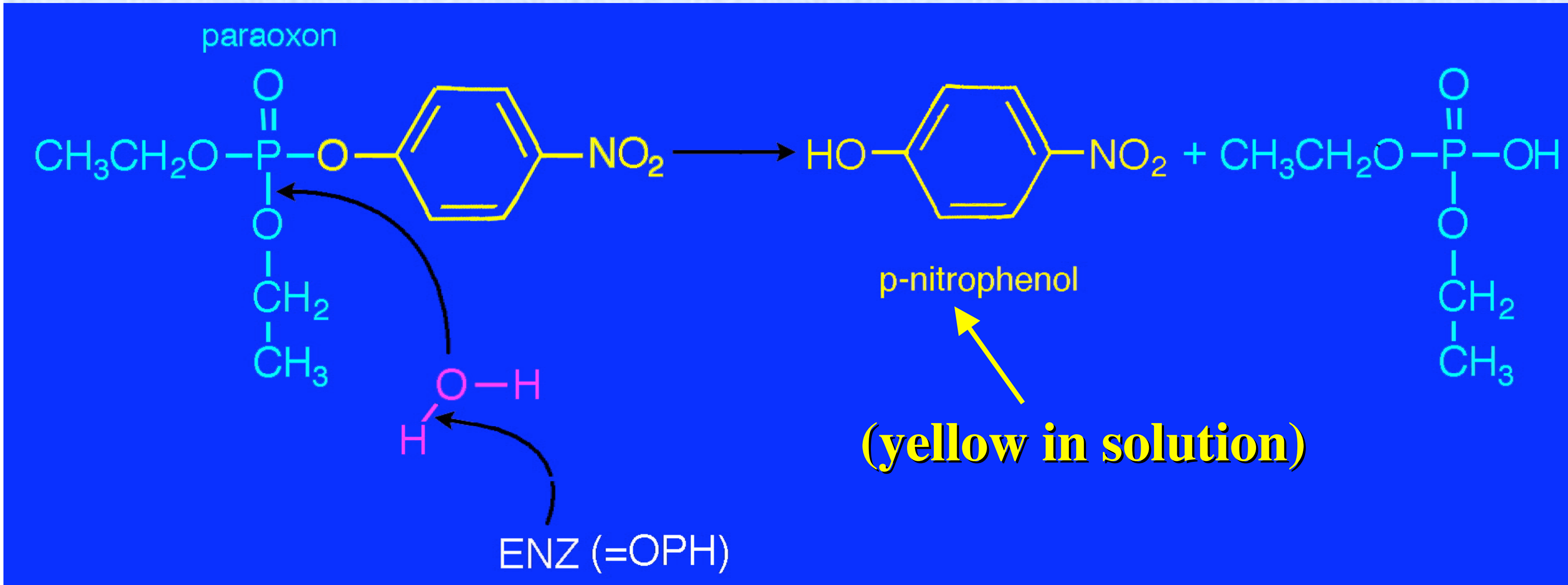
Recent studies have shown that enzymes, which effectively degrade organophosphates, can be incorporated into polymers -- specifically, foams -- in order to aid in their practical application.

One enzyme under current investigation is organophosphorus hydrolase (OPH) a.k.a. phosphotriesterase.

[derived from *Escherichia coli*]

Attack by water

The degradation reaction of organophosphates works via hydrolysis.



paraoxon

p-nitrophenol

(yellow in solution)

ENZ (=OPH)

K.E. LeJeune and A. J. Russell, Biotechnology and Bioengineering, Vol. 51, pp. 450-457 (1996)