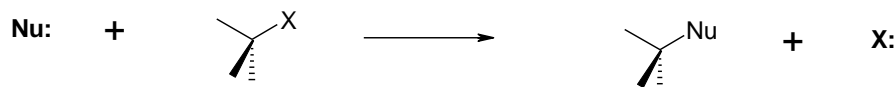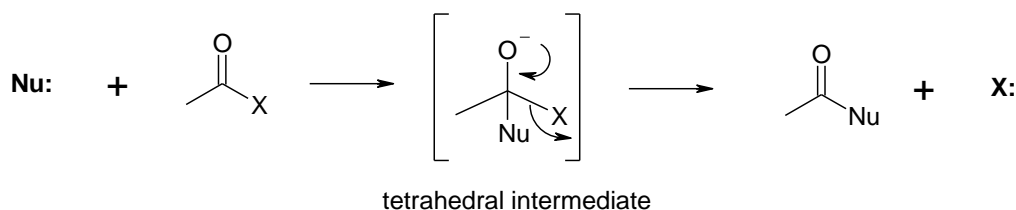# HYDROLYSIS

Hydrolysis reactions of organic substrates are ubiquitous (common) in the environment. Hydrolysis is an important degradation reaction in surface, ground, fog and porewaters and can be a dominant pathway in biological systems as well. In general, hydrolysis occurs via one of two classes of mechanisms;

i) *Nucleophilic Substitution* (S_N1 and S_N2), generally occurs when the leaving group is attached to sp^3 hybridized carbon centre, such as alkyl halides, epoxides and phosphate esters.

Nu: + X ⟶ Nu + **X:**

And

ii) *Addition – Elimination*, generally occurs when the leaving group is attached to sp^2 hybridized acyl carbon centre, such as with carboxylic acid derivatives including esters, anhydrides, amides, carbamates and ureas.

Nu: + X ⟶ [tetrahedral intermediate] ⟶ Nu + **X:**

tetrahedral intermediate

Kinetics

Hydrolysis rates are generally first order or *pseudo* first order under most environmental conditions (where the pH is generally buffered) with an overall observed hydrolysis rate constant k_h. The half life can therefore be expressed as;

$$t_{1/2} = \frac{\ln 2}{k_h}$$

Hydrolysis reactions are generally enhanced by both acids and bases and three independent reaction mechanisms account for neutral, acid and base hydrolysis. Therefore, the overall hydrolysis kinetics has three contributing components.

$$\text{Rate of hydrolysis} = k_h \, [RX]$$

where, $k_h = k_A[H^+] + k_N + k_B[OH^-]$

NUCLEOPHILIC SUBSTITUTION/ELIMINATION MECHANISM

HALOGENATED HYDROCARBONS

The hydrolysis of halogenated hydrocarbons leads to alcohols (or poly alcohols, which rapidly equilibrate to corresponding carbonyl compounds). The reaction is often accompanied by competing elimination to form alkene products, which can be more environmentally persistent and hazardous. In general, hydrolysis products predominant under neutral conditions, whereas elimination products are often more significant under basic conditions. The hydrolysis rates of halogenated aliphatic compounds is influenced by bond strength to the leaving group, stability of the incipient carbocation (S_N1) and steric interactions (S_N2). The following data can be interpreted in terms of these factors and consideration of the dominant substitution mechanism.

Mechanisms and Half-lives at pH 7 for hydrolysis of some monohalogenated hydrocarbons at 25°C

a) Effect of leaving group

Compound	**CH_3F**	**CH_3Cl**	**CH_3Br**
$t_{1/2}$	30 yr	0.9 yr	30 d
Mechanism	S_N2	S_N2	S_N2

b) Chloroform
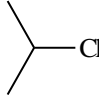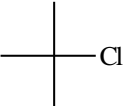
Compound	**$CHCl_3$**
$t_{1/2}$	3500 yr
Mechanism	E1cB
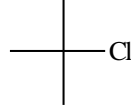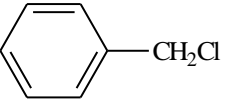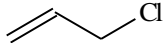
via CCl_3^-

c) Effect of halogenation on carbon

Compound	**CH_3Cl**	**CH_2Cl_2**	**CCl_4**
$t_{1/2}$	0.9 yr	704 yr	7000 yr
Mechanism	S_N2	S_N2	S_N2

d) Effect of substitution on carbon

Compound	**CH_3Cl**		
$t_{1/2}$	0.9 yr	38 d	23 s
Mechanism	S_N2	S_N2......S_N1	S_N1

e) Effect of stable carbocations

Compound		CH_3OCH_2Cl		
$t_{1/2}$	23 s	2 min	15 hr	69 d
Mechanism	S_N1	S_N1	S_N1	S_N1

BASE CATALYSED ELIMINATION WITH POLYHALOGENATED ALIPHATICS

Base catalysed elimination (E2 or E1cB) becomes important relative to neutral hydrolysis (S_N2, S_N1) as the degree of chlorination increases. This is the result of the increasing acidity of hydrogens on the β-carbon and as the increased steric bulk at the α-carbon as the number of chlorines increases.

Hydrolysis of Alkyl Halides Which Can Undergo Elimination At pH 7 And 25°C

| Compound	$ClCH_2\!-\!CH_2Cl$	$Cl_2CH\!-\!CH_2Cl$	$Cl_2CH\!-\!CHCl_2$	$Cl_2CH\!-\!CCl_3$
$k_B[OH^-]$ (min^{-1})	1.0×10^{-11}	9.4×10^{-9}	3.0×10^{-6}	1.3×10^{-4}
k_N (min^{-1})	1.8×10^{-8}	5.2×10^{-11}	9.7×10^{-9}	4.9×10^{-8}
$t_{1/2}$ (yr)	72	139	0.4	0.01
k_{hyd} (min^{-1})	1.8×10^{-8}	9.5×10^{-9}	3.0×10^{-6}	1.3×10^{-4}
Mechanism	S_N2	E2	E2	E2

Kinetic Data on Nucleophilic Substitution and Nonreductive Elimination (Dehydrohalogenation) Reactions of Some Polyhalogenated Hydrocarbons at 25°C and pH 7

Compound	k_N (s^{-1})	k_B (M^{-1}.s^{-1})	$t_{1/2}$	log A	E_a (kJ.mol^{-1})
CH_2Cl_2	3×10^{-11}	2×10^{-8}	700 yr		
$CHCl_3$	7×10^{-13}	7×10^{-5}	3500 yr		
$CHBr_3$		3×10^{-4}	700 yr		
$BrCH_2\!-\!CH_2Br$	6×10^{-9}		4 yr	10.5	105
$Cl_2CH\!-\!CHCl_2$		2	40 d		
$CH_3\!-\!CCl_3$	2×10^{-8}		400 d	13	118
$BrCH_2\!-\!CHBr\!-\!CH_2Cl$	10^{-10}	6×10^{-3}	40 yr	14	93

Products from Nucleophilic Substitution and Nonreductive Elimination (Dehydrohalogenation) Reactions of Some Polyhalogenated Hydrocarbons at 25°C and pH 7

Compound	Product	Yield	Product	Yield
CH_2Cl_2	CH_2O			
$CHCl_3$	HCOOH			
$CHBr_3$	HCOOH			
$BrCH_2\!-\!CH_2Br$	$HOCH_2CH_2OH$	>75%	$CH_2\!\!=\!\!CHBr$	
$Cl_2CH\!-\!CHCl_2$			$ClCH\!\!=\!\!CCl_2$	
$CH_3\!-\!CCl_3$	CH_3COOH	80%	$CH_2\!\!=\!\!CCl_2$	20%
$BrCH_2\!-\!CHBr\!-\!CH_2Cl$	$CH_2\!\!=\!\!CHBr\!-\!CH_2OH$	>95%		

Mechanism of 'hydrolysis' of DDT at pH 7

DDT → E2 → DDE
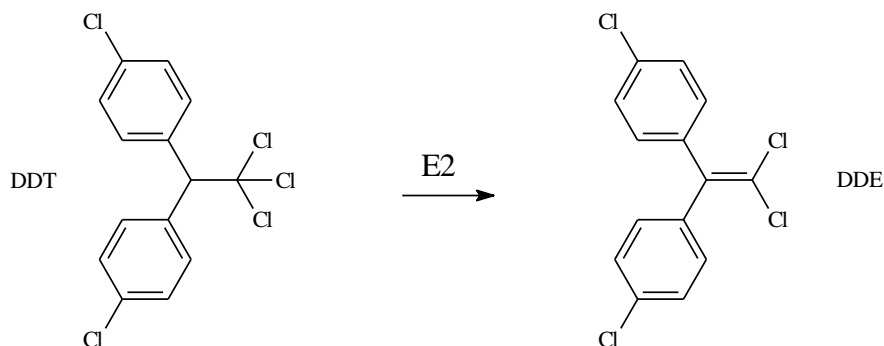
The dominant natural degradation of DDT in neutral aqueous solution is actually an elimination via an E2 mechanism. The hydrogen on the β carbon is somewhat acidic as a result of the inductively withdrawing chlorine atoms in the para positions on the aromatic rings. The developing negative charge on the β carbon is stabilized by resonance to the *ortho* and *para* positions of the aromatic rings.

# Mechanism of hydrolysis of methoxychlor at pH 7
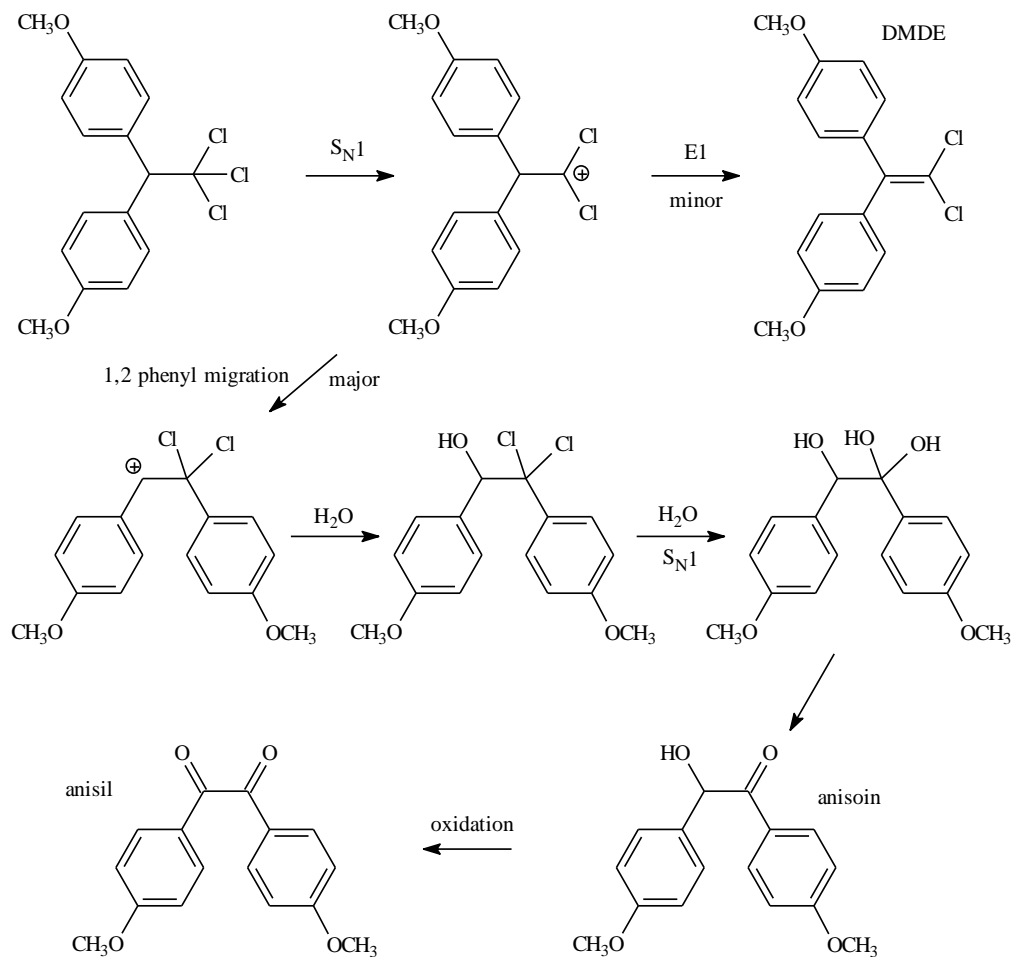
EPOXIDES

Epoxides undergo hydrolysis by neutral and acid catalyzed mechanisms under environmentally relevant conditions. The hydrolysis of epoxides generally leads to diols and to a lesser extent ketones (via carbocation rearrangement). Mechanisms analogous to S_N1 and S_N2 operate under neutral and acid catalyzed conditions.
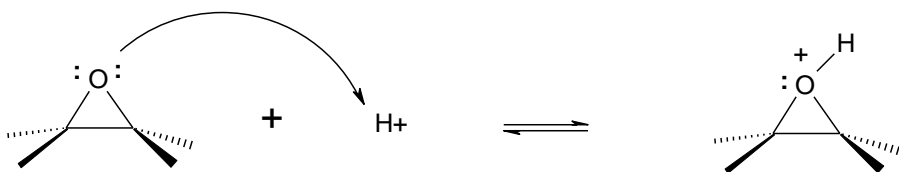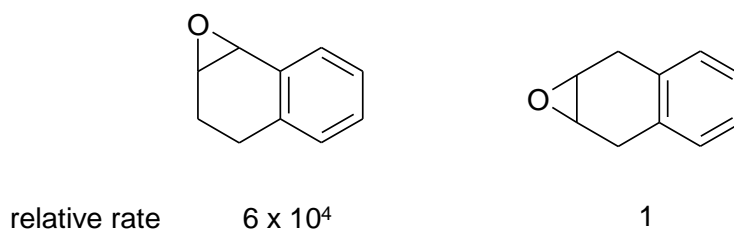
*neutral S_N1 mechanism*
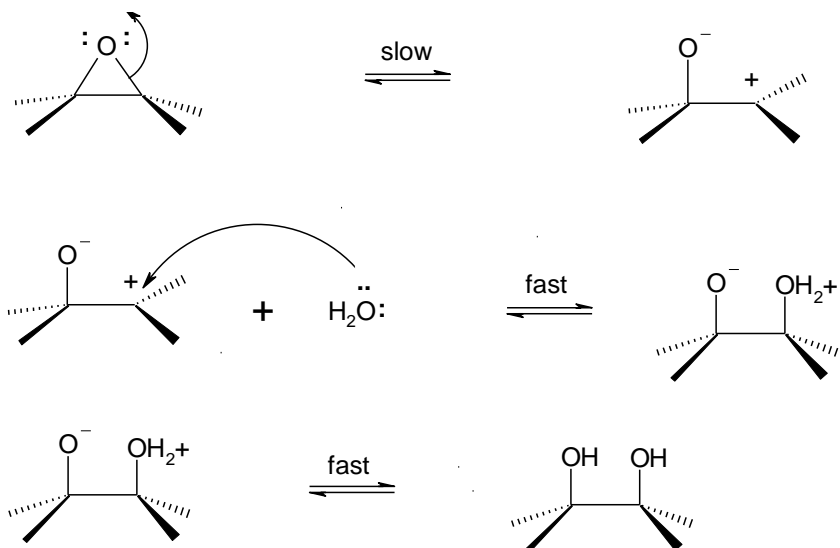
neutral S_N2 mechanism
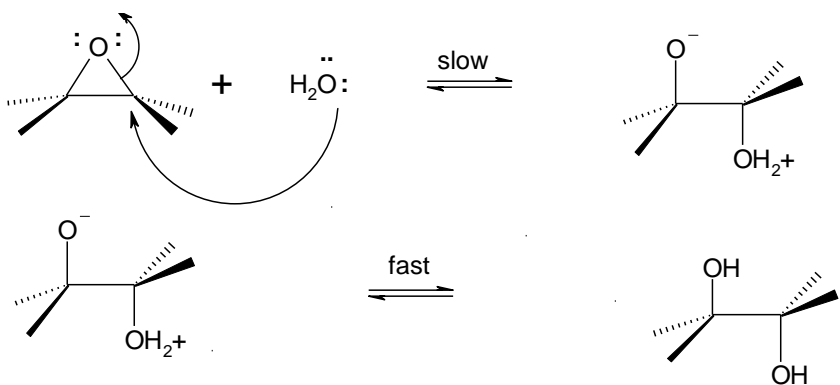
Acid catalyzed pre-equilibrium creates more electrophilic reaction centre.

Hydrolysis rates of epoxides are accelerated by structural features that stabilize the incipient carbocation and therefore favour an S_N1 reaction, such as in the case of allylic or benzylic epoxides.


relative rate 6×10^4 1

In the absence of structural features that stabilize carbocation intermediates, the S_N2 reaction will predominant. In this case, hydrolysis rates are greatly reduced by steric interactions that impede incoming nucleophiles thus slowing the S_N2 reaction. The polycyclic agrochemicals dieldrin and endrin are examples of persistent epoxides resistant to hydrolysis.

dieldrin   endrin
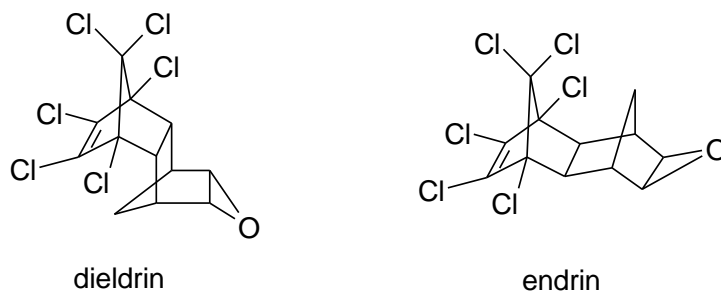
PHOSPHORIC ACID ESTERS

Organophosphorous esters represent an important class of environmental chemicals used mostly as insecticides for agriculture. Hydrolysis generally involves conversion of phosphate tri-esters to the corresponding di-ester derivatives. Substitution can occur at both the central phosphorus atom as well as at the sp^3 carbon of one of the attached alkyl groups. It is generally observed that base catalyzed hydrolysis favours P-O or P-S cleavage, whereas neutral or acid catalyzed hydrolysis favours C-O or C-S cleavage.
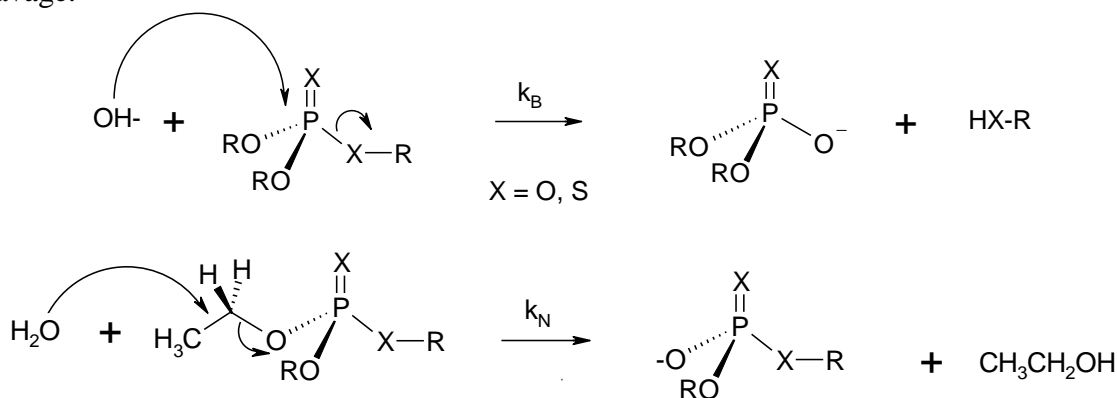
As a result, the product distribution for the hydrolysis of organophosphorus esters is pH dependent. In the P-O cleavage reaction, the mechanism appears to involve a direct displacement (S_N2-like – no pentavalent intermediate). In the C-O cleavage reaction, the mechanism is also a direct displacement S_N2 reaction, where the phosphate ester anion is acting as the leaving group.
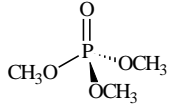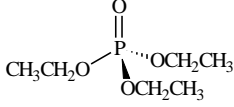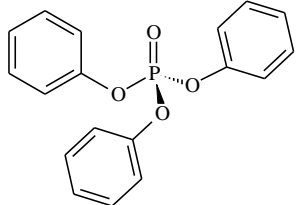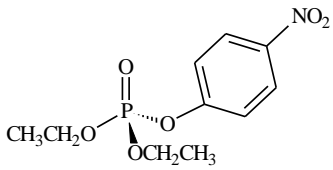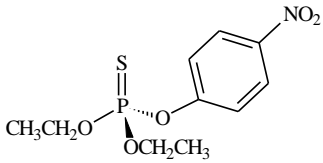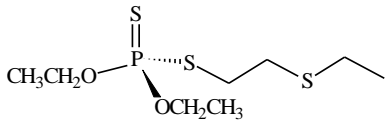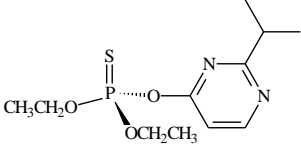
Hydrolysis rates are enhanced by EWGs attached to the central phosphorus atom. Phosphate esters with electron withdrawing groups on –X-R (conjugate acids with pK_a ~ 6-8) have enough biological activity (phosphorylation of acetylcholinesterase) and hydrolytic stability to be effective insecticides without being persistence in the aquatic environment. With weaker electron withdrawing or electron donating groups ($pK_a < 6$) are biologically inactive and persistent environmentally. When the –X-R has strong electron withdrawing groups ($pK_a > 8$), the hydrolysis reaction is so rapid that the organophosphate esters do not have sufficient time to reach their target organisms and are consequently ineffective as insecticides. Hydrolytic stability is also effected by replacing P=O with P=S. Since sulfur is less electronegative than oxygen, thiophosphate esters exhibit greater stability toward neutral and base catalyzed hydrolysis than the corresponding phosphate esters.

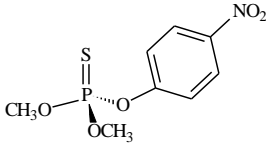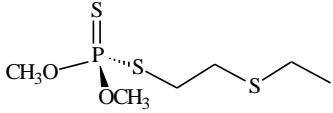The table below summarizes the rate constants for a number of important phosphoric acid esters. In general, stabilization of leaving group enhances the base catalyzed rate constant (k_B).
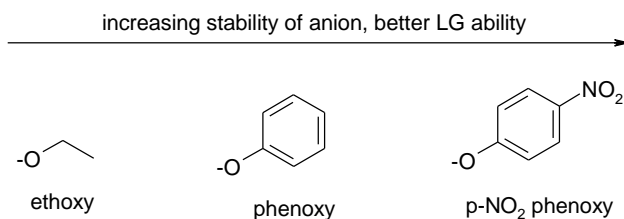
The acid catalyzed reaction is generally unimportant, however in the case of Diazinon which bears the basic pyrimidine group, protonation of one of the nitrogens improves the leaving group ability and enhances P-O cleavage.

Rate constants, half-lives at pH 7 for hydrolysis of some phosphoric and thiophosphoric acid triesters at 25°C

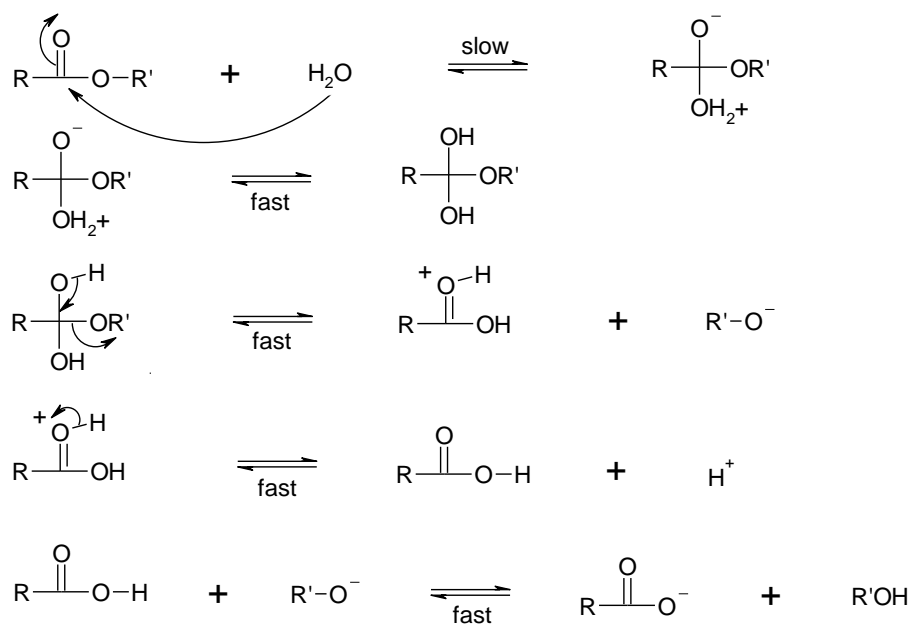| Name	Structure	k_A (M^{-1}.s^{-1})	k_N (s^{-1})	k_B (M^{-1}.s^{-1})	$t_{1/2}$ (pH 7)
Trimethylphosphate	CH$_3$O–P(=O)(OCH$_3$)OCH$_3$	NI	1.8×10^{-8}	1.6×10^{-4}	1.2 yr
Triethylphosphate	CH$_3$CH$_2$O–P(=O)(OCH$_2$CH$_3$)OCH$_2$CH$_3$	NI	$\sim 4 \times 10^{-9}$	8.2×10^{-6}	~5.5 yr
Triphenylphosphate	(C$_6$H$_5$O)$_3$P=O	NI	$< 3 \times 10^{-9}$	0.25	320 d
Paraoxon	CH$_3$CH$_2$O–P(=O)(OCH$_2$CH$_3$)O–C$_6$H$_4$–NO$_2$	NI	7.3×10^{-8}	0.39	72 d
Parathion	CH$_3$CH$_2$O–P(=S)(OCH$_2$CH$_3$)O–C$_6$H$_4$–NO$_2$	NI	8.3×10^{-8}	5.7×10^{-2}	89 d
Methylparathion	CH$_3$O–P(=S)(OCH$_3$)O–C$_6$H$_4$–NO$_2$	NI	1.2×10^{-7}	1.1×10^{-2}	67 d
Thiometon	CH$_3$O–P(=S)(OCH$_3$)S–CH$_2$CH$_2$–S–CH$_2$CH$_3$	NI	1.1×10^{-7}	6.4×10^{-3}	73 d
Disulfoton	CH$_3$CH$_2$O–P(=S)(OCH$_2$CH$_3$)S–CH$_2$CH$_2$–S–CH$_2$CH$_3$	NI	1.4×10^{-7}	2.0×10^{-3}	57 d
Diazinon	CH$_3$CH$_2$O–P(=S)(OCH$_2$CH$_3$)O–(isopropylpyrimidine)	2.1×10^{-2}	4.3×10^{-8}	5.3×10^{-3}	178 d

NI = not important

ADDITION-ELIMINATION MECHANISM

CARBOXYLIC ACID ESTERS

In general, nucleophilic displacement at an acyl carbon is faster than that at a saturated alkyl halide. This is because of the greater electronegativity of oxygen over most halides and the reduced steric hindrance at the trigonal planar acyl carbon. The most common reaction mechanisms involve acyl-oxygen cleavage and are show below.

neutral hydrolysis

$$R-C(=O)-O-R' \quad + \quad H_2O \quad \underset{}{\overset{\text{slow}}{\rightleftharpoons}} \quad R-\underset{OH_2+}{\overset{O^-}{\underset{|}{\overset{|}{C}}}}-OR'$$

$$R-\underset{OH_2+}{\overset{O^-}{\underset{|}{\overset{|}{C}}}}-OR' \quad \underset{\text{fast}}{\rightleftharpoons} \quad R-\underset{OH}{\overset{OH}{\underset{|}{\overset{|}{C}}}}-OR'$$

$$R-\underset{OH}{\overset{O-H}{\underset{|}{\overset{|}{C}}}}-OR' \quad \underset{\text{fast}}{\rightleftharpoons} \quad R-C(=\overset{+}{O}-H)-OH \quad + \quad R'-O^-$$

$$R-C(=\overset{+}{O}-H)-OH \quad \underset{\text{fast}}{\rightleftharpoons} \quad R-C(=O)-O-H \quad + \quad H^+$$

$$R-C(=O)-O-H \quad + \quad R'-O^- \quad \underset{\text{fast}}{\rightleftharpoons} \quad R-C(=O)-O^- \quad + \quad R'OH$$
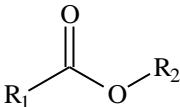
*acid catalyzed hydrolysis* ($A_{AC}2$)

base catalyzed hydrolysis (B$_{AC}$2)

As can be seen from the data below, the half-lives of carboxylic acid esters range from hrs to years depending on the structure. The rate constants for the neutral and base catalyzed reactions are sensitive to structural changes. In general, k_N and k_B increase with EWGs on R$_1$ and decrease with increasing steric bulk on R$_2$.
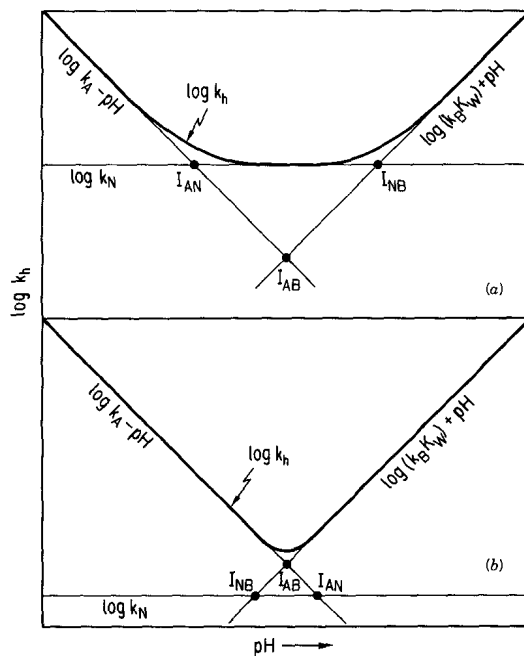
Rate constants, half-lives at pH 7 for hydrolysis of some carboxylic acid esters at 25°C

R$_1$	R$_2$	k_A (M^{-1}.s^{-1})	k_N (s^{-1})	k_B (M^{-1}.s^{-1})	t$_{1/2}$ (pH 7)
methyl	ethyl	1.1 x 10^{-4}	1.5 x 10^{-10}	0.11	2 yr
methyl	*tert*-butyl	1.3 x 10^{-4}		1.5 x 10^{-3}	140 yr
methyl	vinyl	1.4 x 10^{-4}	1.1 x 10^{-7}	10	7 d
methyl	phenyl	7.8 x 10^{-5}	6.6 x 10^{-8}	1.4	38 d
methyl	2,4-dinitrophenyl		1.1 x 10^{-5}	94	10 h
chloromethyl	methyl	8.5 x 10^{-5}	2.1 x 10^{-7}	140	14 h
dichloromethyl	methyl	2.3 x 10^{-4}	1.5 x 10^{-5}	2.8 x 10^{3}	40 min
dichloromethyl	phenyl		1.8 x 10^{-3}	1.3 x 10^{4}	4 min

Variation of hydrolysis half-life at 25°C for several carboxylic acid esters as a function of solution pH caused by changing contributions of the acid-catalysed, neutral and base-catalysed mechanisms.
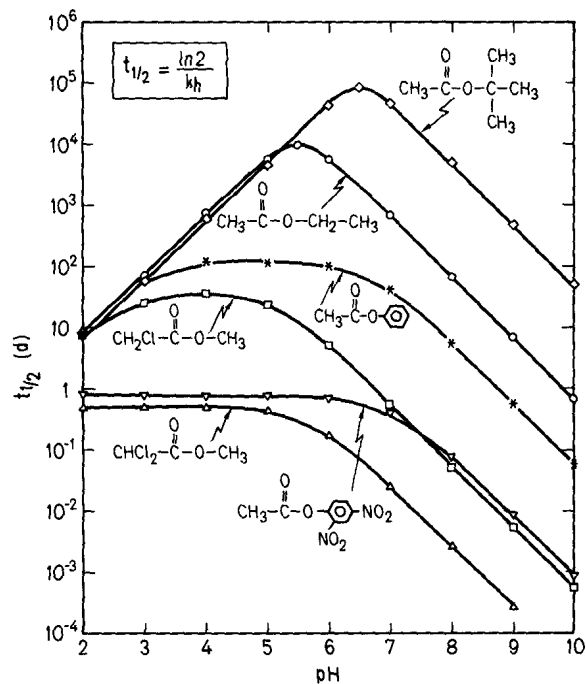

Schematic representation of the relative contribution of the acid-catalysed, the neutral, and the base-catalysed reactions to the overall hydrolysis rate as a function of solution pH. a) neutral reaction rate is significant over some pH range b) the contributions of the neutral reaction can be neglected.

AMIDES

Amides are inherently less reactive than carboxylic acid esters with half-lives typically $> 10^3$ yrs. The decreased hydrolysis rates are the result of a less electrophilic acyl carbon due to the electron donating resonance characteristics of the amide nitrogen. Neutral hydrolysis is very slow and under most conditions and either acid or base catalysis is required ($A_{AC}2$ or $B_{AC}2$).
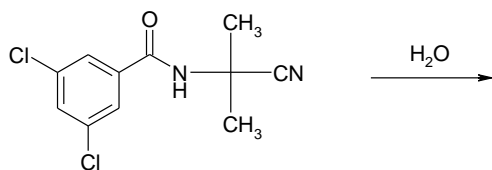

pronamide; $t_{1/2} \sim$ 700 yrs

Rate constants, half-lives at pH 7 for hydrolysis of some simple amides at 25°C

R_1	R_2	R_3	k_A ($M^{-1}.s^{-1}$)	k_B ($M^{-1}.s^{-1}$)	$t_{1/2}$ (pH 7)
methyl	H	H	8.4 x 10^{-6}	4.7 x 10^{-5}	4000 yr
isopropyl	H	H	4.6 x 10^{-6}	2.4 x 10^{-5}	7700 yr
chloromethyl	H	H	1.1 x 10^{-5}	0.15	1.5 yr
methyl	methyl	H	3.2 x 10^{-7}	5.5 x 10^{-6}	40,000 yr
methyl	methyl	methyl	5.2 x 10^{-7}	1.1 x 10^{-5}	20,000 yr

As can be seen by the data above, both k_A and k_B are increased with the addition of EWGs on R_1. Bulky groups on R_2 decrease k_A and k_B.
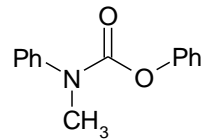
CARBAMATES

Carbamates are a very important class of environmentally relevant compounds used in agriculture as both insecticides and herbicides. Hydrolysis half-lives range dramatically from seconds to 10^5 years. Base catalysis dominants over environmental pHs. Primary carbamates (R_1 or R_2 = H) undergo hydrolysis via an E1cB type mechanism much faster than secondary carbamates, which hydrolyze via a $B_{AC}2$ mechanism.
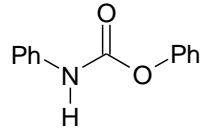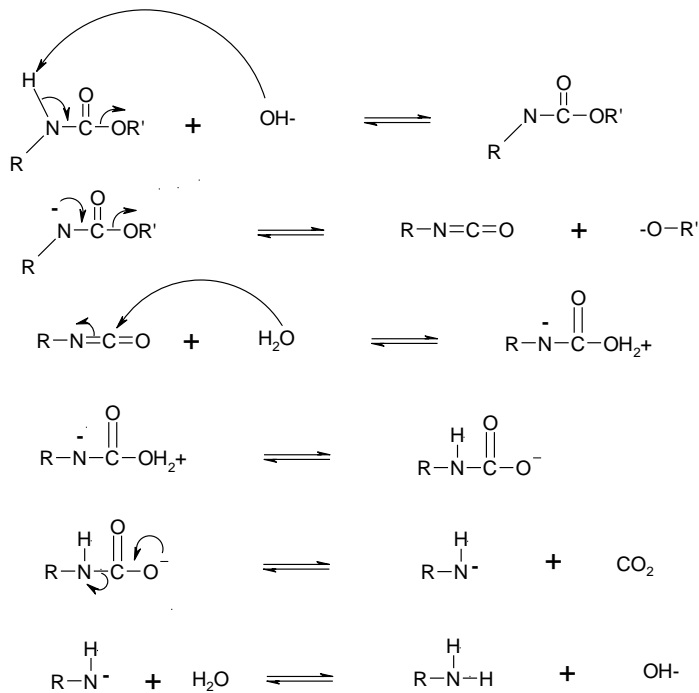

$k_h = 5.4 \times 10^{-5}$ s^{-1}

$t_{1/2} = 1.5$ d

$k_h = 4.2 \times 10^{-11}$ s^{-1}

$t_{1/2} = 5200$ yrs

1° carbamates (E1cB)

2° carbamates ($B_{AC}2$)

Rate constants, half-lives at pH 7 for hydrolysis of some simple carbamates at 25°C


R_1	R_2	R_3	k_N (s^{-1})	k_B ($M^{-1}.s^{-1}$)	$t_{1/2}$ (pH 7)
methyl	methyl	ethyl		4.5×10^{-6}	50,000 yr
methyl	phenyl	ethyl		4.0×10^{-6}	55,000 yr
methyl	methyl	4-nitrophenyl		4.0×10^{-4}	550 yr
methyl	phenyl	4-nitrophenyl		8.0×10^{-4}	275 yr
H	methyl	ethyl		5.5×10^{-6}	40,000 yr
H	phenyl	ethyl		3.2×10^{-5}	7,000 yr
H	methyl	4-nitrophenyl		600	3 h
H	phenyl	4-nitrophenyl		2.7×10^5	25 s
H	methyl	4-methylphenyl	6.0×10^{-8}	0.56	70 d
H	methyl	1-naphthyl	9.0×10^{-7}	50	33 h

Correlation of the base-catalysed hydrolysis rates (log k_B) of carbamates as a function of the pK$_a$ of the alcohol moiety for a series of N-phenyl and N-methyl-N-phenyl carbamates.
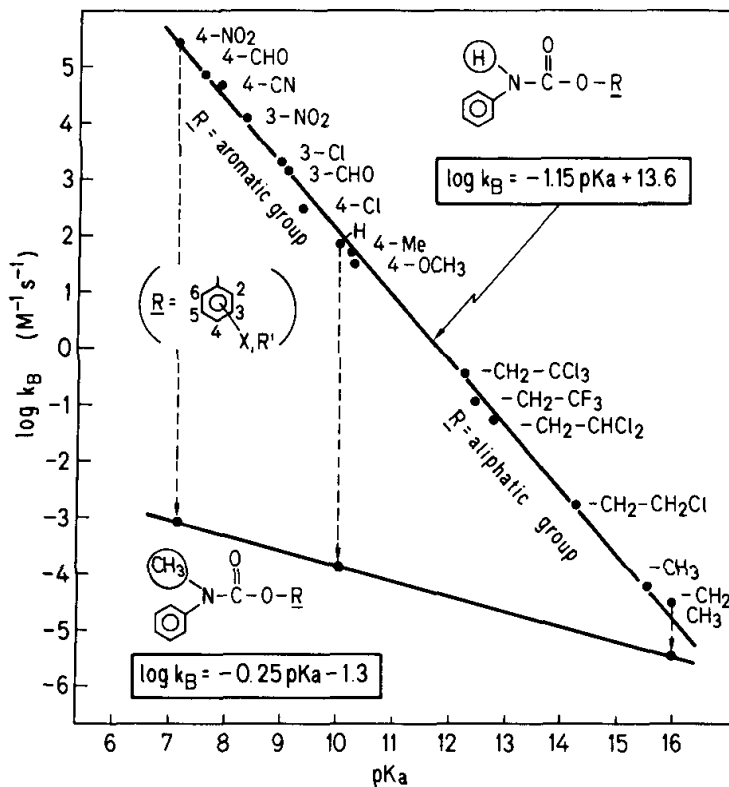
SULFONYL UREAS

This relatively new class of herbicides has very powerful herbicidal properties and very low mammalian toxicity. The hydrolysis rates are greatly reduced at pHs > 6 due to the enhanced acidity of one of the N-H hydrogens. The resonance stabilized conjugate base is much less electrophilic and considerably more water soluble than the protanated form. Therefore this class of compounds is both environmentally persistent and readily transported in aquatic ecosystems.


pH > 6

delocalized anion

acidic hydrogen
pKa ~ 3-5

pH < 6

hydrolysis products
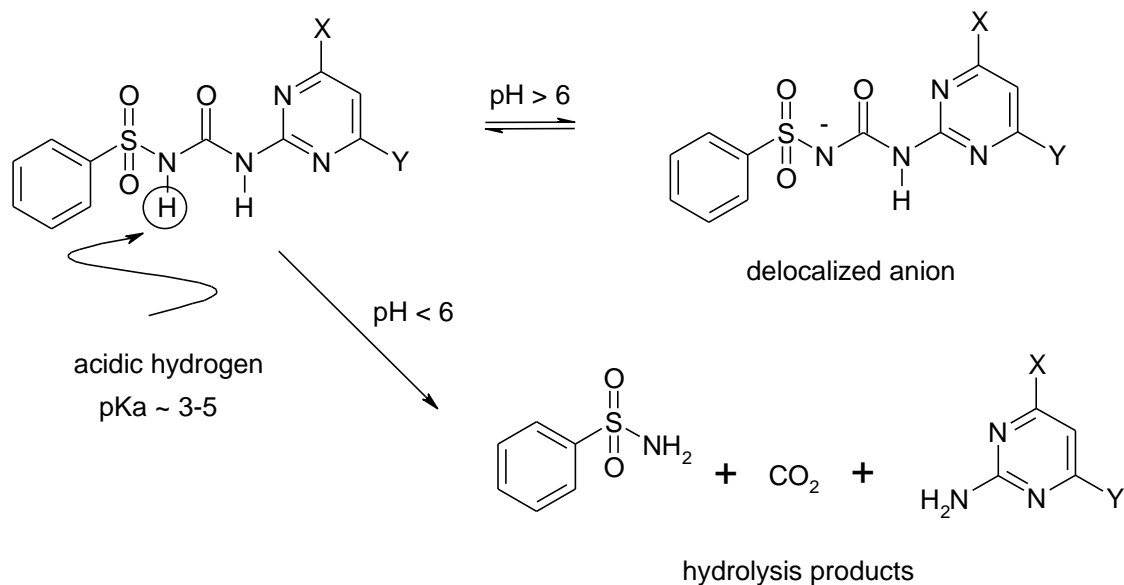
OTHER NUCLEOPHILIC REACTIONS

NATURALLY OCCURRING NUCLOPHILES

A direct comparison of nucleophilic strength is given by the Swain – Scott equation, where k_{Nu} and k_{H2O} are the second order rate constants for the reaction with R-X, n is the nucleophilicity and s is a reaction constant parameter related to the sensititivity of the reaction to nucleophiles.

$$\log\left(\frac{k_{Nu}}{k_{H2O}}\right) = n\,s$$

This approach is analogous to the Hammett equation and a reference reaction is used to define nucleophilicity constant. The S_N2 substitution of methyl bromide is assigned a value of $s =1$ and so nucleophilicity is defined by the value of n for this reaction.

$$Nu^- \;+\; CH_3\text{-}Br \;\rightarrow\; Nu\text{-}CH_3 \;+\; Br^-$$
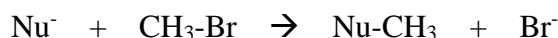
$$\log\left(\frac{k_{Nu}}{k_{H2O}}\right)_{CH3Br} = n$$

Examples of important environmental nucleophiles and their nucleophilicities relative to water based on reaction with methyl bromide.

Nucleophile	n	Nucleophile	n
ClO_4^-	< 0	HPO_4^{2-}	3.8
H_2O	0.0	Br^-	3.9
NO_3^-	1.0	OH^-	4.2
F^-	2.0	I^-	5.0
SO_4^{2-}	2.5	CN^-	5.1
CH_3COO^-	2.7	HS^-	5.1
Cl^-	3.0	SO_3^{2-}	5.1
HCO_3^-	3.8	S_4^{2-}	7.1

As can be seen by the nucleophilicity values reported above, reduced sulfur based nucleophiles have the greatest reactivity towards halogenated aliphatic compounds. Although not commonly encountered in surface waters, reduced sulfur species are often present in anoxic environments such as in sediments and ground waters. Substitution reactions with groundwater contaminants have been observed to produce significant amounts thiols, dialkyl sulfides and dialkyl disulfides in addition to the expected hydrolysis products.
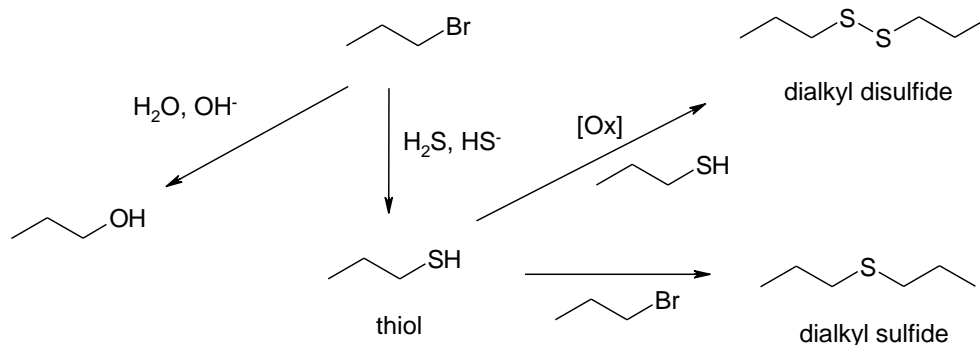
To calculate the overall hydrolysis rate in natural waters with a variety of possible nucleophiles, sum over the individual reaction rates.

$$k_h = k_N + \Sigma k_{Nu}[Nu] = k_{H2O}[H_2O] + \Sigma k_{Nu}[Nu]$$

where $k_{Nu} = k_{H2O}10^{ns}$, n and s are the Swain – Scott nucleophilicity and reaction constant, respectively.

Example:

In pure water at pH = 7.0 and 25°C the hydrolysis half-life of methyl bromide is 20 days. Estimate the half-life of CH_3Br present at low concentration (i.e., < 1 μM) in a homogeneous settling pond at the same pH and temperature containing 100 mM Cl^-, 2 mM NO_3^-, 1 mM HCO_3^- and 0.1 mM CN^-.

Solution: Methyl bromide reacts with nucleophiles by an S_N2 mechanism. Since all nucleophiles are present at concentrations in excess over that of the electrophile, the reaction can be expressed as a *pseudo*-first order rate law. Thus, the *pseudo* first order rate constant can be expressed as;

$$k_h = k_N + \Sigma \, k_{Nu} \, [Nu]$$

and we can estimate the rate constants for all nucleophiles from the Swain-Scott equation.

$$\log \frac{k_{Nu}}{k_{H2O}} = n \, s \qquad\qquad \text{so} \qquad\qquad k_{Nu} = k_{H2O} \, 10^{ns}$$

Since $s = 1$ for methyl bromide,

$k_h = k_N + \Sigma k_{Nu}[Nu]$

$= k_{H2O} [H_2O] + k_{H2O} 10^1 [NO_3^-] + k_{H2O} 10^3 [Cl^-] + k_{H2O} 10^{3.8} [HCO_3^-] + k_{H2O} 10^{4.2} [OH^-] + k_{H2O} 10^{5.1} [CN^-]$

$= 175 \, k_{H2O}$

Since $k_N = 55.5 \, k_{H2O}$, $k_h = (175/55.5) \, k_N = 3.14 \, k_N$

The half life in pure water is 20 days so, $k_N = 0.693/20 \text{ d} = 3.47 \times 10^{-2} \text{ d}^{-1}$

And k_h in the settling pond is $(3.14) (3.47 \times 10^{-2} \text{ d}^{-1})$
so, $t_{1/2}$ is now **6.4 days**

HARD-SOFT ACID-BASE BEHAVIOUR

Qualitative predictions can be made regarding the product distribution of hydrolysis reactions using the principles of the hard-soft acid-base model (HSAB). In this treatment, nucleophiles and electrophiles are categorized into 'hard' and 'soft' depending on their size, electronegativity and polarizability. Hard acids/bases are relatively small, of high electronegativity and low polarizability. Soft acids/bases are relatively large, of lower electronegativity and more polarizable.

Hard	Borderline	Soft
OH^-, $H_2PO_4^-$, HCO_3^-, NO_3^-, SO_4^{2-}, Cl^-, F^-, NH_3, $CH_3CO_2^-$	H_2O, NO_2^-, SO_3^{2-}, Br^-, $PhNH_2$	HS^-, RS^-, PhS^-, $S_2O_3^{2-}$, I^-, CN^-

The general principle is that hard acids prefer to bind with hard bases and soft acids prefer to bind with soft bases. Since electrophiles and nucleophiles can be thought of as Lewis acids and bases, respectively, the HSAB principle can be applied to the hydrolysis reactions considered here. For example, in the hydrolysis of phosphoric acid esters, nucleophilic attack can occur at either carbon (a soft electrophile) or phosphorous (a hard electrophile). Thus, attack by a soft nucleophile, such as H_2O or HS^- will tend to occur at the carbon leading to C-O cleavage. On the other hand, attack by OH^- will preferentially occur at the phosphorus atom leading to P-O cleavage.

'soft-soft' interaction S_N2

'hard-hard' interaction S_N2
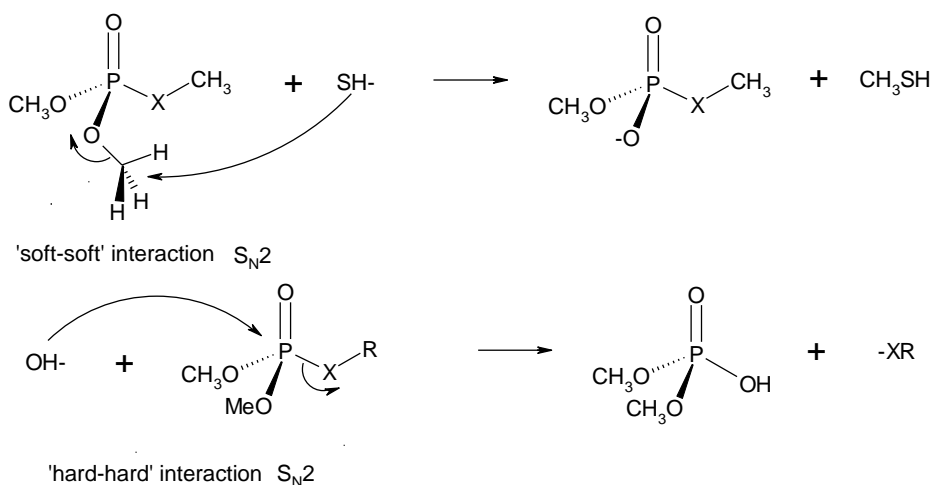
The HSAB model can also be used to predict the relative reactivities of HS^-, H_2O and OH^- towards halogenated aliphatics and consequently predict the dominant reaction products. Nucleophilic substitution of the 'soft' HS^- at the 'soft' electrophilic carbon centre predominates to yield the dithiol product, whereas, the 'hard' nucleophile OH^- is more likely to react with the 'hard' electrophilic proton to yield the elimination product. Water, which is of intermediate 'softness', reacts to give a mixture of both the diol and alkene product.
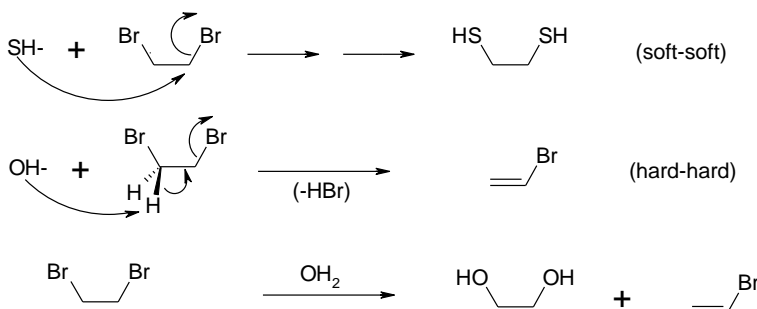
GENERAL ACID AND GENERAL BASE CATALYSIS

In contrast to catalysis mechanisms involving H^+ or OH^- (specific acid/base catalysis), hydrolysis reactions can be enhanced by the presence of weak Bronsted acids and/or bases. Such catalysis is known as general acid/base catalysis (or buffer catalysis). A wide variety of weak acids and bases can be found in aquatic ecosystems that can potentially enhance hydrolysis rates of organic pollutants. It has observed however, that in most natural waters buffer catalysis accounts for $< 5\%$ rate enhancement and can generally be ignored. However, the use of high buffer concentrations often employed in laboratory experiments can result in enhanced hydrolysis rates that are significant.
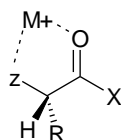
METAL IONS

Metal ion – catalyzed hydrolysis occurs primarily through two types of mechanisms.
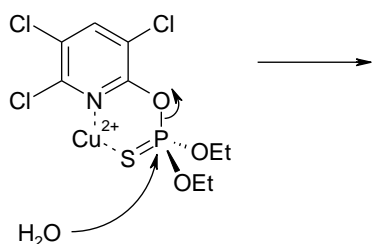
i) Lewis acid complexation; hydrolysable functional more susceptible to nucleophilic attack
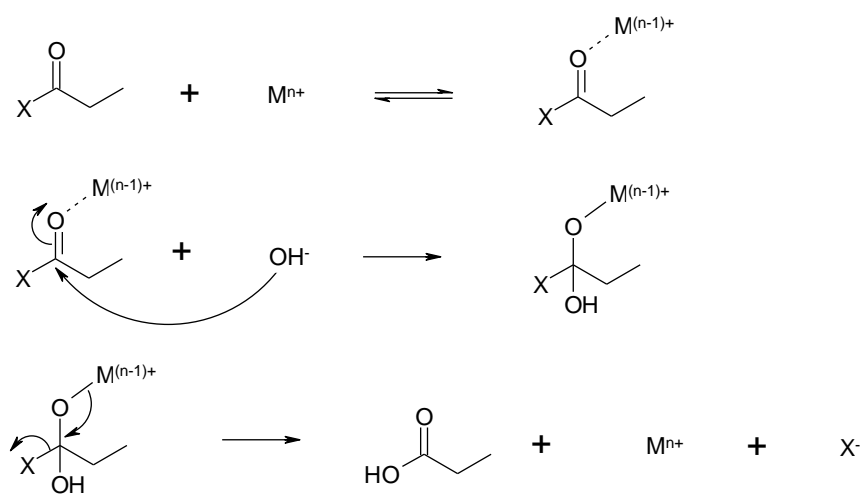
The complexation and rate enhancements greater when bidentate complexes are formed. For example,

$$Z = -CO_2R, -OCH_3, -OH, -NH_2$$

For phosphorus esters, metal ion complexation favours P-O cleavage even and lower pHs (e.g., Cu^{2+} catalyzed hydrolysis of chlorpyrifos).

ii) reactive metal hydroxo species; increased acidity of metal aquo complexes generates OH- in situ

A number of 'hard' metal ions (Fe^{3+}, Al^{3+}, Zn^{2+}) effectively increase the acidity of water by formation of metal hydroxo complexes. These metal complexed (OH⁻) groups are effectively 'delivered' to the acyl carbons either by an intermolecular or intramolecular process, increasing the rate of nucleophilic attack and hence the hydrolysis rate.

$$Fe(H_2O)_6{}^{3+} \quad \rightarrow \quad (Fe(H_2O)_5OH)^{2+} \quad + \quad H^+$$

intermolecular   intramolecular