

# **Valutazione del rischio chimico**

CdL Magistrale Interateneo in  
Scienze e Tecnologie per l'Ambiente e il Territorio  
Università di Udine e Università di Trieste

CdL Magistrale in Chimica  
Università di Trieste

Docente  
Pierluigi Barbieri

**SSD Chimica dell'ambiente e dei beni culturali, CHIM/12**

# *Valutazione del rischio chimico*

Processo chimico



(Emissioni)



(Dispersione  
Trasferimenti di fase  
trasformazioni ambientali)



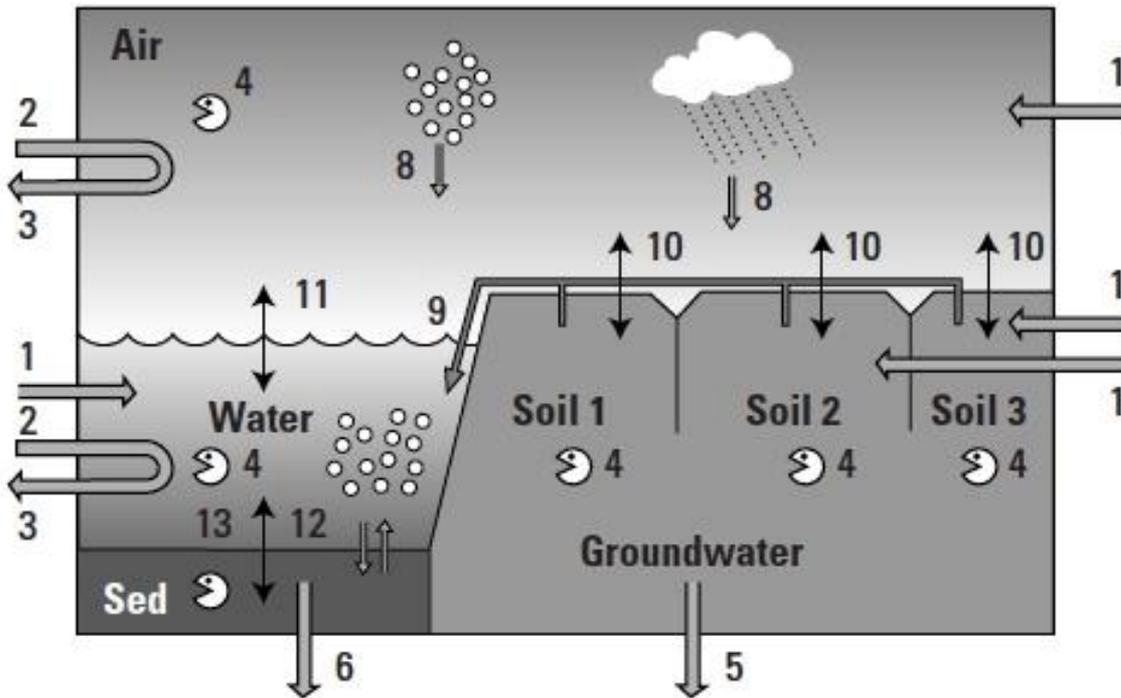
**Esposizione** / PEC



**Valutazione  
del rischio**



Valutazione degli **effetti** dell'esposizione  
a sostanze singole e a miscele /  
NOAEC /tossicologia



*I processi di **degradazione** abiotica e biologica*



Figure 4.11. Diagram of a multimedia mass balance model concept. 1 = Emission, 2 = Import, 3 = Export, 4 = Degradation, 5 = Leaching, 6 = Burial, 7 = Wet deposition, 8 = Dry aerosol deposition, 9 = Run-off, 10, 11 = Gas absorption and volatilization, 12 = Sedimentation and resuspension, 13 = Sorption and desorption. From [61]

# **BIODEGRADAZIONE**

La degradazione microbica ha un ruolo chiave nella rimozione delle sostanze chimiche di sintesi negli *ambienti acquatici e terrestri*.

Inizialmente era vista come aspetto indesiderato, associato a ridotta durata di prodotti dell'industria (perseguita "persistenza")

Successivamente si è realizzato che biodegradazione troppo lenta può provocare accumulo nei comparti ambientali e negli organismi / avvelenamento primario e secondario nelle reti trofiche / compromissione delle risorse idriche.

Impatto estetico (plastiche, schiume)

Rischio ecologico (tensioattivi, PCB, DDT, aldrin ect.)

Pericolo per la salute umana (diossine e pesticidi nel cibo e nelle acque potabili)

# BIODEGRADAZIONE

- Trasformazione da prodotto genitore a altro composto organico è nota come biodegradazione “primaria”
- Biodegradazione in ambienti aerobici -> prodotti finali  $\text{CO}_2$  e  $\text{H}_2\text{O}$  (mineralizzazione)

**In ambienti aerobici** la sopravvivenza dei microorganismi eterotrofi è spesso condizionata dalla disponibilità di fonti di carbonio.

**In ambienti anaerobici** i processi di degradazione microbica sono in genere più lenti e possono non portare alla mineralizzazione. In comparti metanogeni si intende per mineralizzazione la conversione a prodotti finali con un solo atomo di carbonio

**L'organizzazione dei microorganismi eterotrofi è caratterizzata da versatilità catabolica** (adattamento o acclimatemento)

Microflore in miscela - piuttosto che monoculture - degradano i *chemicals*

**L'adattamento** è un cambiamento nella comunità microbiologica eterotrofa che realizza cambiamenti metabolici (es. induzione enzimatica, cambiamenti di popolazione, trasferimento genetico, mutazione) e aumenta la velocità di biodegradazione di una specie chimica come risultato di una precedente esposizione al composto. L'apparato enzimatico consiste in enzimi coinvolti in cicli metabolici fondamentali (es. idrolisi) e enzimi adattivi o indotti. Questi enzimi consentono ai batteri di usare composti organici (substrati) non adatti per l'uso immediato.

Fattori ambientali: aerobicità (sedimenti e suoli) è condizionata da rapporto tra velocità di consumo microbiologico di  $O_2$  e velocità di diffusione  $O_2$

- *Batteri aerobi* usano  $O_2$  sia come reagente per l'ossidazione dei composti organici che come accettore terminale degli elettroni (serve per la *dissimilazione* : conversione del composto organico - come sorgente energetica - in  $CO_2$ ).
- *Batteri anaerobi facoltativi* usano l' $O_2$  ma hanno la possibilità di usare un altro accettore di elettroni se l'ambiente diviene anaerobico (es. batteri denitrificanti e solforiduttori)
- *Batteri anaerobi obbligati* : per essi  $O_2$  è tossico

Table 3.10. Free energy of redox reactions in the saturated zone of soil. Calculations are based on data from [126,127].

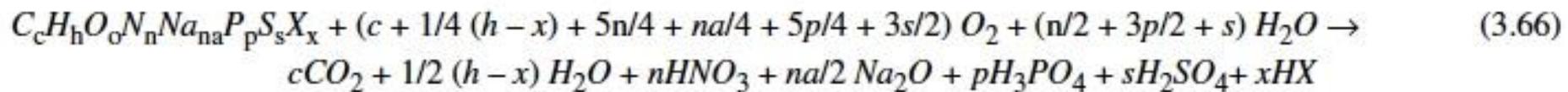
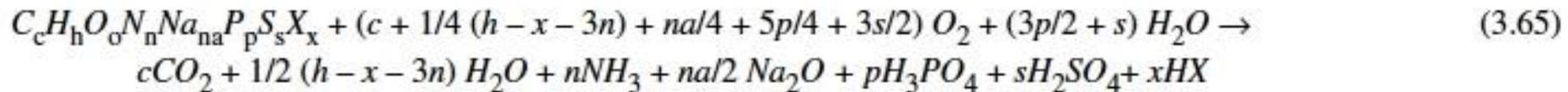
Environment (electron acceptor)	-DG (kJ)	Relative to oxygen %	Reaction equation
Oxygen	472.5	100	$O_2 + CH_2O \rightarrow CO_2 + H_2O$
Nitrate	462.8	97.9	$4/5 NO_3^- + 4/5 H^+ + CH_2O \rightarrow 2/5 N_2 + CO_2 + 7/5 H_2O$
Nitrate/nitrite	332.8	70.4	$2 NO_3^- + CH_2O \rightarrow 2 NO_2^- + CO_2 + H_2O$
Pyrolusite	364.2	77.1	$2 MnO_2 + 4 H^+ + CH_2O \rightarrow 2 Mn^{2+} + CO_2 + 3 H_2O$
Manganite	320.9	67.9	$4 MnOOH + 8 H^+ + CH_2O \rightarrow 4 Mn^{2+} + CO_2 + 7 H_2O$
Hausmannite	330.6	70.0	$2 Mn_3O_4 + 12 H^+ + CH_2O \rightarrow 6 Mn^{2+} + CO_2 + 7 H_2O$
Hematite	60.0	12.7	$2 Fe_2O_3 + 8 H^+ + CH_2O \rightarrow 4 Fe^{2+} + CO_2 + 5 H_2O$
Magnetite	27.1	5.7	$2 Fe_3O_4 + 12 H^+ + CH_2O \rightarrow 6 Fe^{2+} + CO_2 + 7 H_2O$
Sulphate	98.1	20.8	$1/2 SO_4^{2-} + H^+ + CH_2O \rightarrow 1/2 H_2S + CO_2 + H_2O$
H <sub>2</sub> production	26.0	5.5	$H_2O + CH_2O \rightarrow 2 H_2 + CO_2$
Methanogenic	91.4	19.3	$CH_2O \rightarrow 1/2 CH_4 + 1/2 CO_2$

- Energia guadagnata da batteri con ossidazione di un atomo di C per diversi elettroni accettori è molto diversa -> diversa velocità di degradazione
- Se biodegradazione di specie chimiche di sintesi non sufficiente per generare crescita batterica si può avere cometabolismo

# **Biodegradazione aerobica e pathways metabolici**

Chemicals come nutrienti per batteri con varietà di meccanismi biochimici.

Per reazioni senza e con nitrificazione si ha:



Se sostanza è completamente mineralizzata, sono calcolabili richiesta di ossigeno teorica *ThOD* e

produzione di diossido di carbonio teorica *ThCO<sub>2</sub>*

$$ThOD (mg O_2 / mg subst.) = (MW Oxygen / MW subst.) \times (c + 1/4 (h - x - 3n) + na/4 + 5p/4 + 3s/2) \quad (3.67)$$

$$ThOD (mg O_2 / mg subst.) = (MW Oxygen / MW subst.) \times (c + 1/4 (h - x) + 5n/4 + na/4 + 5p/4 + 3s/2) \quad (3.68)$$

$$ThCO_2 (mg CO_2 / mg subst.) = (MW Carbondioxide / MW subst.) \times c$$

- Home
- Search
- About
  - EAWAG-BBD | PPS | BPT
- What's New
- FAQs
- Join E-mail List
- Contributors
- Publications
- Links
- Acknowledgements
- Contact Us

[Pathway Prediction System](#) | [PredictBT Workshops](#) | [Biochemical Periodic Tables](#)

<http://eawag-bbd.ethz.ch/>

*Microbial biocatalytic reactions and biodegradation pathways.*

- [What's New?](#) Last updated January 18, 2016.
- [Search](#) the EAWAG-BBD for compound, enzyme, microorganism, pathway, or BT rule name; chemical formula; chemical structure; CAS Registry Number; or EC code.
- Pathways and Metapathways in the EAWAG-BBD

Benzo(a)pyrene

- Lists of [219 pathways](#); [1503 reaction entries](#); [249 biotransformation rule entries](#); [109 reactions of toxicology](#) ([Metapathway and Pathway Graphics](#))
- Derivative work: [xenobiotic pathway](#)
- *cite using:*  
Gao J, Ellis LBM, Wackett LP (2014) Database: improving public access to microbial biocatalytic reactions and biodegradation pathways.
- For more information [join our email list](#).

KEGG PATHWAY Database  
Wiring diagrams of molecular interactions, reactions, and relations

KEGG2 PATHWAY BRITE KO GENES LIGAND DISEASE DRUG DBGET

Select prefix: map Organism Enter keywords: [ ] Go Help

### Pathway Maps

KEGG PATHWAY is a collection of manually drawn pathway maps (see [last updates](#) and [change history](#)) representing our knowledge on the molecular interaction and reaction networks for:

- 1. Metabolism**  
Carbohydrate Energy Lipid Nucleotide Amino acid Other amino acid Glycan PK/NRP Cofactor/vitamin Secondary metabolite Xenobiotics Overview
- 2. Genetic Information Processing**
- 3. Environmental Information Processing**
- 4. Cellular Processes**
- 5. Human Diseases**

and also on the structure relationships (KEGG drug structure maps) in:

- 6. Drug Development**

KEGG Atlas may now be used to examine any of the KEGG pathway maps.

### Pathway Entries and Pathway Modules

Pathway entries are text representation of pathway maps, containing descriptions (for a limited number of entries, at the moment), **Pathway modules** are specification of subnetworks that correspond to tighter functional units, each represented as a list of KO identifiers (K numbers).

Search Pathway entries for [ ] Go Clear

Pathways di degradazione  
microbica

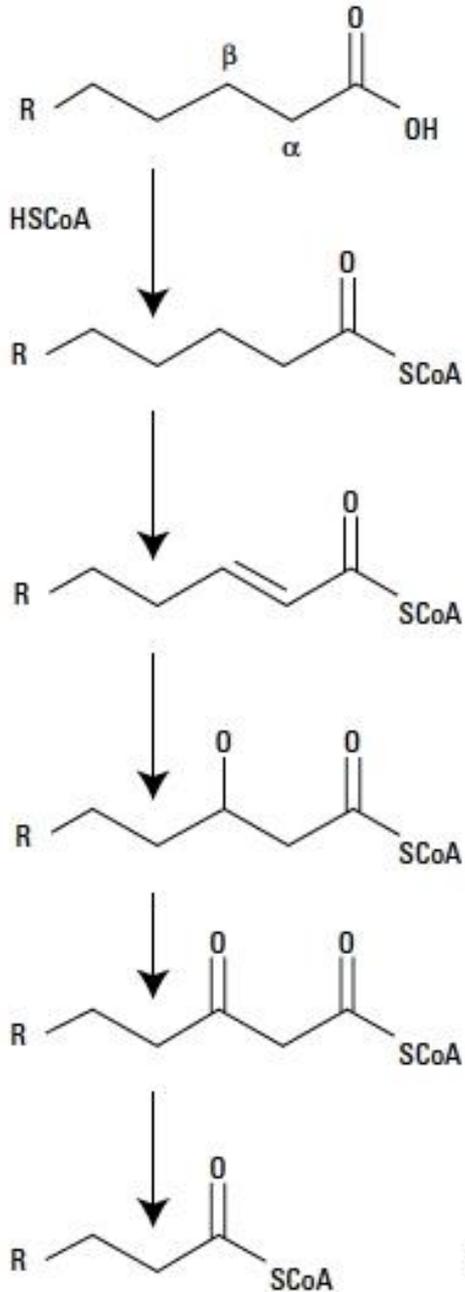
<https://www.genome.jp/kegg/pathway.html>

## Biodegradazione aerobica

- Ossidazione **omega** (metile terminale -> alcol -> acido carbossilico , richiede *ossigenasi*)
- Ossidazione **beta** a un doppio legame di un acido grasso
- Ossidazione **aromatica**

# ***Ossidazione omega***

*[http://en.wikipedia.org/wiki/Omega\\_oxidation](http://en.wikipedia.org/wiki/Omega_oxidation)*



Tio-estere

(+  $\text{H}_2\text{O}$ )

Prodotto insaturo

(+ 2H)

Beta idrossi-derivato

Beta cheto-derivato

(+ 2H)

## Ossidazione beta

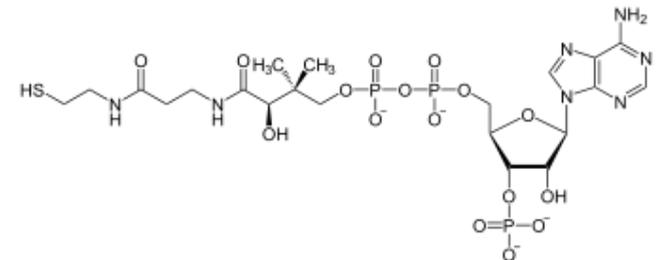


Figure 3.34.  $\beta$ -oxidation of aliphatic hydrocarbons by bacteria.  
(H)SCoA = Coenzyme A.

# Ossidazione aromatica

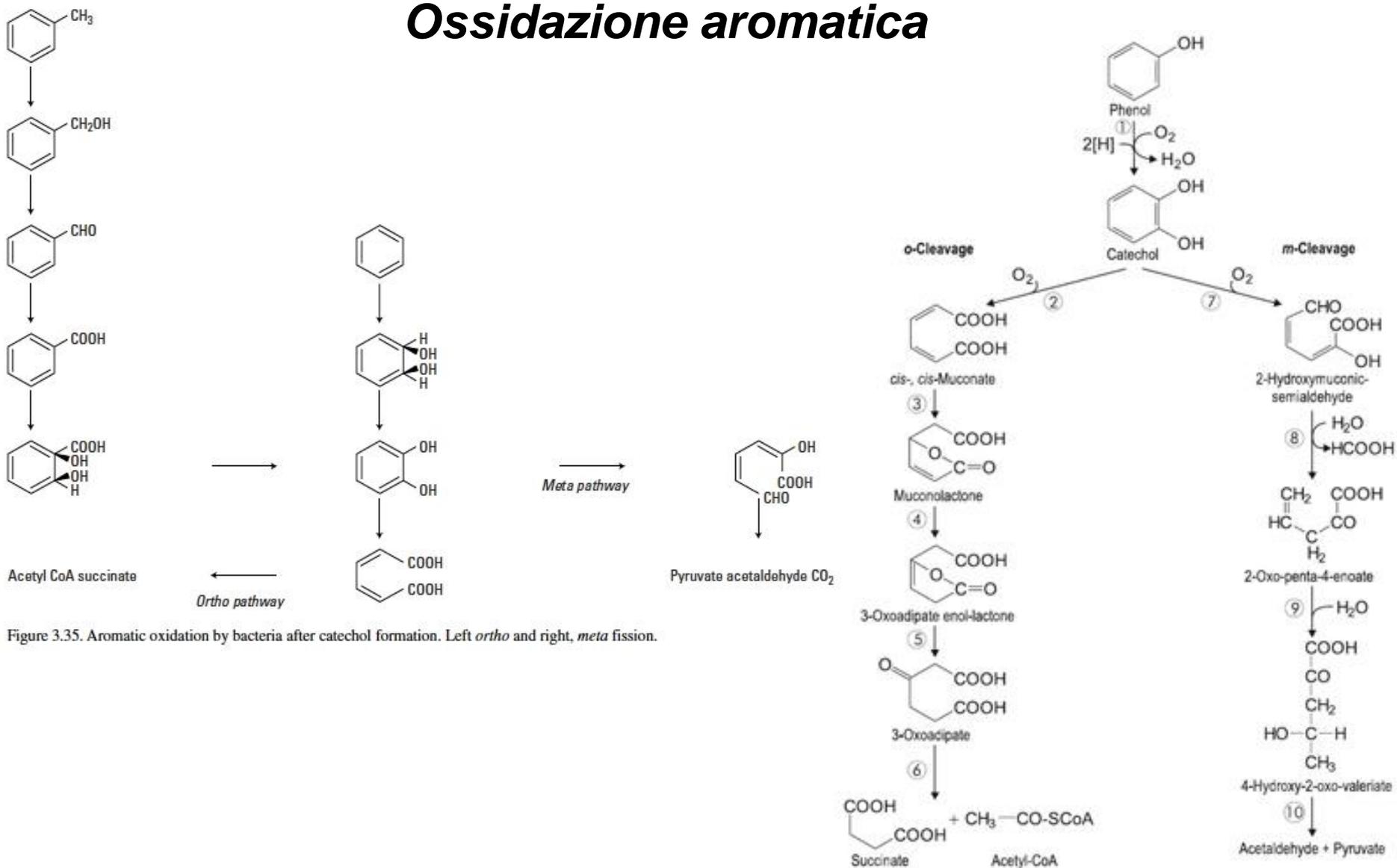


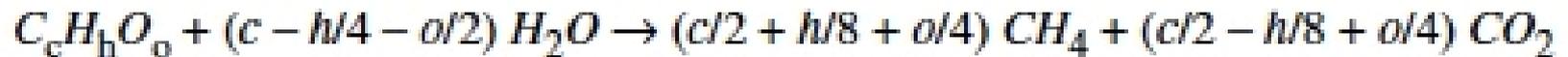
Figure 3.35. Aromatic oxidation by bacteria after catechol formation. Left *ortho* and right, *meta* fission.

# ***Degradazioni anaerobiche***

Assenza di O<sub>2</sub> quale accettore terminale di elettroni

Ambienti con riduzione di Nitrati, di Ferro (FeIII), di Manganese (Mn IV), di Solfati e perfino CO<sub>2</sub>

Nella metanogenesi si ha mineralizzazione con conversione in prodotti che contengono un atomo di carbonio



Rilevanti per dealogenazione riduttiva nei sedimenti

MTBE biodegrada più favorevolmente in condizioni anaerobiche che aerobiche

Dealogenazione riduttiva

Esistono protocolli OECD per valutare la biodegradabilità in ambiente metanogeno

Table 3.12 Ready biodegradability tests (RBT) and inherent biodegradability tests (IBT) according to the OECD.  
Population densities are in colony forming units (CFU) per ml. From [133,141].

OECD test guideline	Summary parameter	Population density (CFU/ml)
<i>Ready biodegradability</i>		
301E: Modified OECD screening test	DOC	$(0.5 - 2.5) \times 10^2$
301B: CO <sub>2</sub> evolution	CO <sub>2</sub>	$(2 - 10) \times 10^5$
301F: Manometric respirometry test	O <sub>2</sub>	$(2 - 10) \times 10^5$
301A: DOC Die-away test	DOC	$(2 - 10) \times 10^5$
301D: Closed bottle test	O <sub>2</sub>	$(0.5 - 2.5) \times 10^3$
301C: Modified MITI(I) test	O <sub>2</sub>	$(2 - 10) \times 10^5$
306: Biodegradability in Seawater	DOC	
<i>Inherent biodegradability</i>		
302B: Zahn-Wellens test	DOC	$(0.7 - 3) \times 10^7$
302A: Modified SCAS test	DOC	$(2 - 10) \times 10^7$
302C: Modified MITI(II) test	O <sub>2</sub>	$(0.7 - 3) \times 10^6$
<i>Simulation tests</i>		
303A: Activated Sludge Units	DOC	
303B: Biofilms	DOC	
304A: Inherent Biodegradability in Soil	<sup>14</sup> CO <sub>2</sub>	
307: Aerobic and Anaerobic Transformation in Soil	<sup>14</sup> CO <sub>2</sub> / CO <sub>2</sub>	
308: Aerobic and Anaerobic Transformation in Aquatic Sediment Systems	<sup>14</sup> CO <sub>2</sub> / CO <sub>2</sub>	
309: Aerobic Mineralization in Surface Water	<sup>14</sup> CO <sub>2</sub> / CO <sub>2</sub>	

Table 3.11. Influence of molecular structure on the biodegradability of chemicals in the aerobic environment.

Type of compounds or substituents	More biodegradable	Less biodegradable
Hydrocarbons	linear alkanes > C <sub>12</sub> alkanes with not too high molecular weight linear chain -C-C-C- aliphatic mono- and bicyclic aromatic	linear alkanes < C <sub>12</sub> high molecular weight alkanes branched chain -C-O-C- aromatic polycyclic aromatic
Aliphatic chlorine	Cl more than 6 carbons from terminal carbon	Cl at 6 or less carbon atoms from terminal C
Substituents to an aromatic ring	-OH -CO <sub>2</sub> H -NH <sub>2</sub> -OCH <sub>3</sub>	-F -Cl -NO <sub>2</sub> -CF <sub>3</sub>

Una molecola persistente:

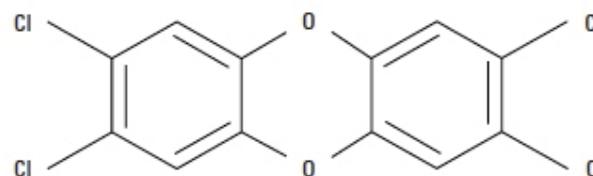


Figure 3.36. Molecular structure of 2,3,7,8-tetrachloro-*p*-dioxin (TCDD).

Table 3.13 Ready biodegradability tests (RBT) and inherent biodegradability tests (IBT) according to the OECD.  
Population densities are in colony forming units (CFU) per ml. From [61,62]

Type of test	Summary parameter	Population density (CFU/ml)
<i>Ready biodegradability test</i> [61]		
Modified OECD screening test	DOC	$(0.5 - 2.5) \times 10^2$
CO <sub>2</sub> evolution	CO <sub>2</sub>	$(2 - 10) \times 10^5$
Manometric respirometry	O <sub>2</sub>	$(2 - 10) \times 10^5$
DOC die-away	DOC	$(2 - 10) \times 10^5$
Closed bottle	O <sub>2</sub>	$(0.5 - 2.5) \times 10^3$
MITI(I)	O <sub>2</sub>	$(2 - 10) \times 10^5$
<i>Inherent biodegradability</i> [61]		
Zahn-Wellens test	DOC	$(0.7 - 3) \times 10^7$
SCAS test	DOC	$(2 - 10) \times 10^7$
MITI(II)	O <sub>2</sub>	$(0.7 - 3) \times 10^6$

# BIOTRASFORMAZIONI

Le specie chimiche nell'ambiente entrano in contatto con e sono assorbite da organismi

Se le concentrazioni negli organismi raggiungono valori critici ci possono essere alterazioni della normale fisiologia.

Le specie chimiche possono essere eliminate per escrezione nella forma originale o modificandone la struttura

- Microorganismi -> *biodegradazione*
- Altri organismi -> ***biotrasformazioni***

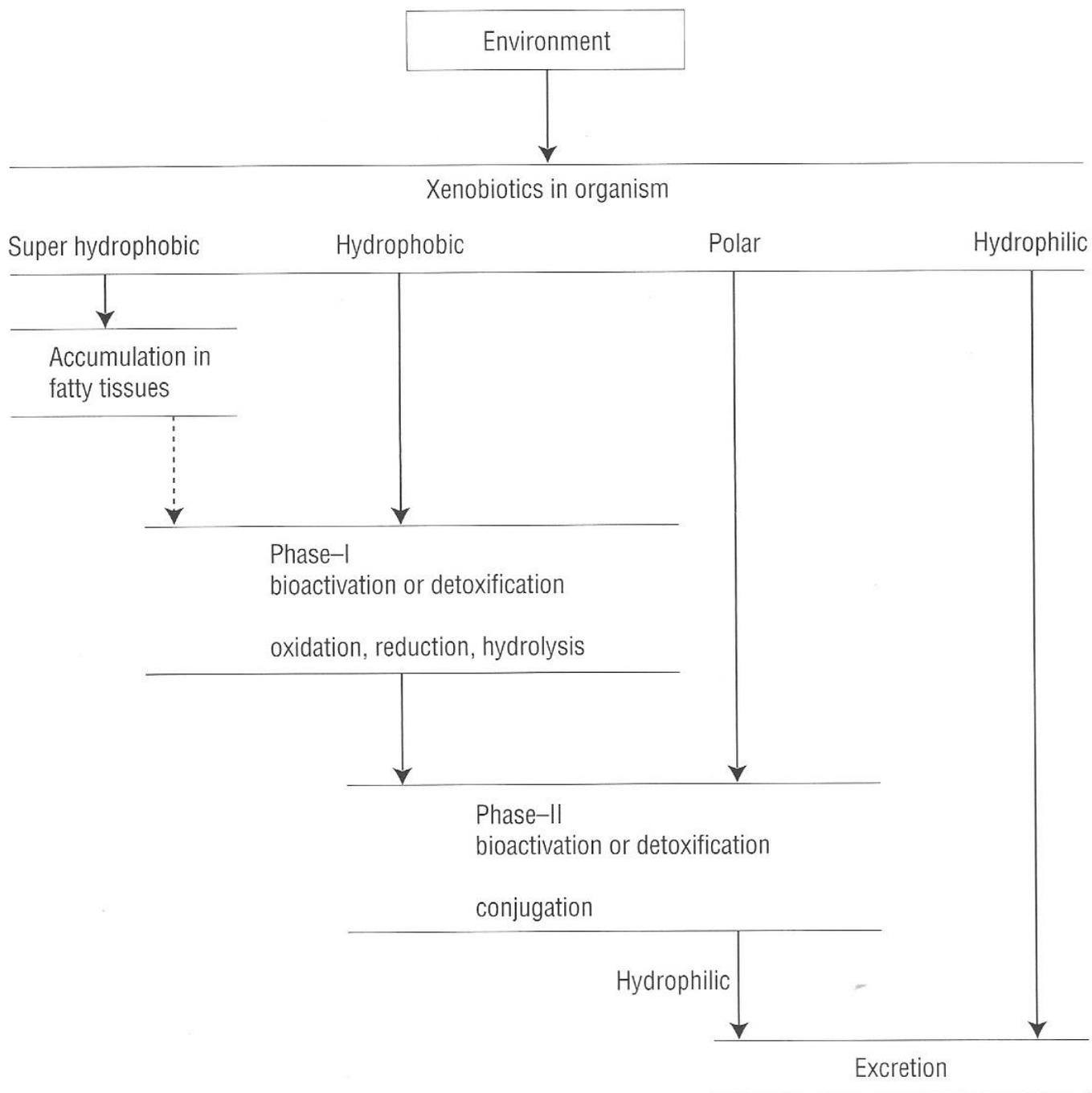
Enzimi (catalizzatori biologici)

Per lipidi / proteine /carboidrati -> metabolismo

Per xenobiotici -> biotrasformazione

Bioattivazione o Detossificazione

Prodotti meno idrofobici dei composti genitori



3.38. General pathways of biotransformation of xenobiotics in living organisms.

Reazioni di Fase I : *non sintetiche* (idrolisi, ossidazioni e riduzioni)

Reazioni di Fase II : *sintetiche* (coniugazioni)

Reazioni di Fase I Introducono nelle specie chimiche gruppi  $-OH$ ,  $-COOH$ ,  $-NH_2$ , che generano specie reattive che possono essere facilmente coniugate (Fase II) ed escrete

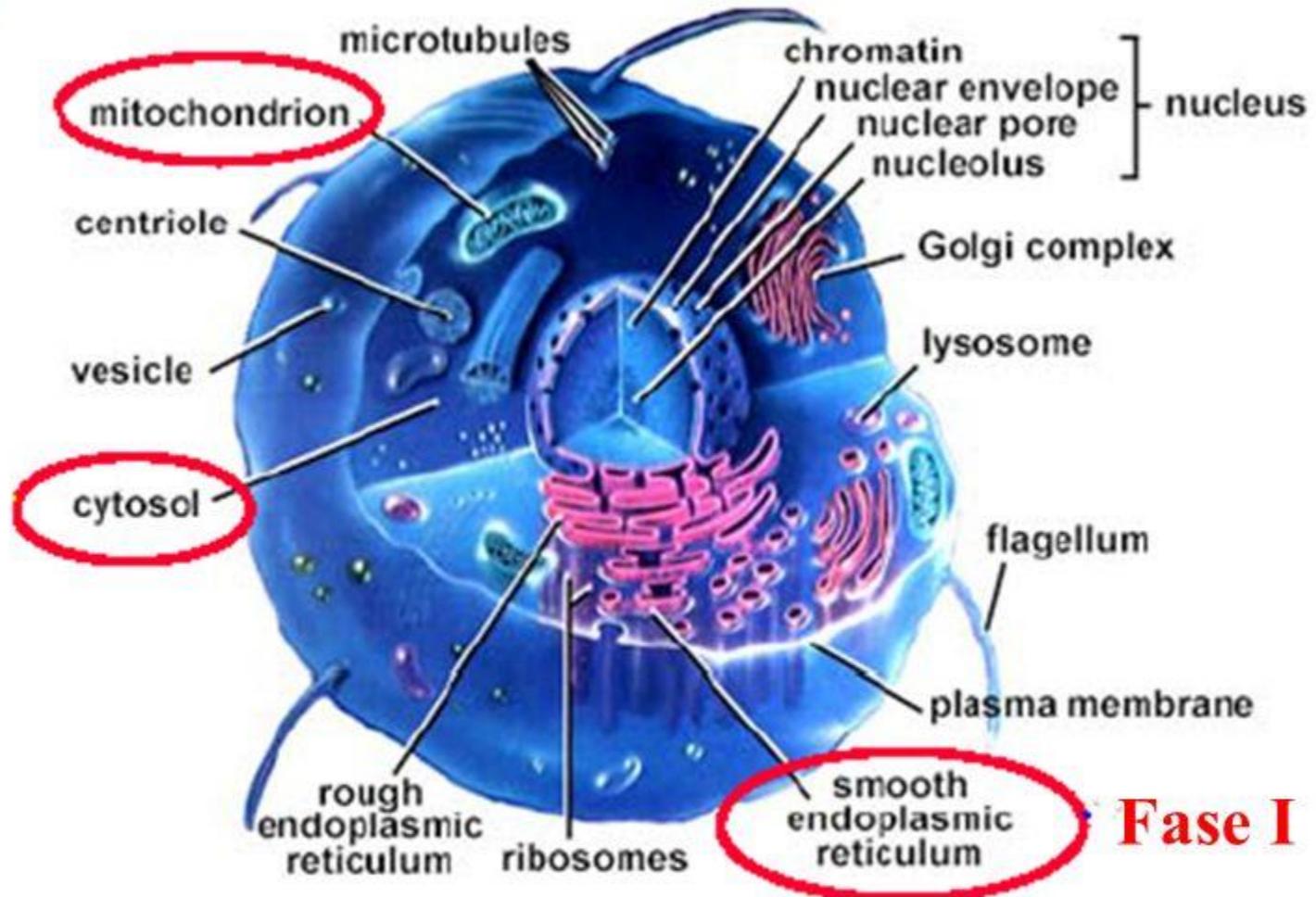
# Tipi di reazione di biotrasformazione

Table 3.14 The most important enzyme systems which metabolize pesticides [63]

Enzyme system	Location	Compounds metabolized
<i>Phase-I reactions:</i>		
Mixed function oxidases	Microsomes, notably from vertebrate liver and insect fat body	Many liposoluble pesticides
Phosphatases	Present in nearly all tissues and subcellular fractions of species	Organophosphorus insecticides and "nerve gases"
Carboxyesterases	In most tissues of insects and vertebrates	Malathion and malaoxon
Epoxide hydroxylase	Microsomes, particularly in the mammalian liver	Dieldrin, heptachlor and arene epoxides
DDT dehydrochlorinase	Virtually all insects and vertebrates	<i>p,p'</i> -DDT and <i>p,p'</i> -DDD
<i>Phase-II reactions:</i>		
Glucuronyl transferases	Mainly in microsomes; widespread in vertebrates other than fish and insects	Compounds with labile hydrogen, including hydroxylated metabolites
Glutathione-S-transferases	70,000 g supernatants of vertebrates livers and also insects	Chlorinated compounds, e.g. $\gamma$ -HCH; also some epoxides

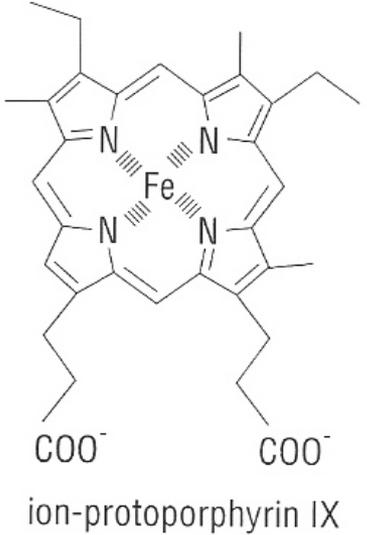
# Fase I

# Fase II



**Gli enzimi della fase I predominano nel reticolo endoplasmatico liscio (microsomi), quelli della fase II nel citosol**

Sistema enzimatico **ossidasi a funzione mista** (*Mixed Function Oxidase –MFO*), di cui il **citocromo P450** è parte, inserisce un atomo di O sul substrato e riduce l'altro atomo di O ad acqua



Widely distributed enzymes that carry out oxidation-reduction reactions in which one atom of the oxygen molecule is incorporated into the organic substrate; the other oxygen atom is reduced and combined with hydrogen ions to form water. They are also known as

Citocromo P450 superfamiglia enzimatica di **emoproteine** presente in tutti i **domini** dei viventi (sono note più di 7.700 distinte macromolecole di tipo CYP), appartenente alla sottoclasse enzimatica delle **ossidasi a funzione mista** (o monoossigenasi)

monooxygenases or hydroxylases. These reactions require two substrates as reductants for each of the two oxygen atoms. There are different classes of monooxygenases depending on the type of hydrogen-providing cosubstrate (COENZYMES) required in the mixed-function oxidation

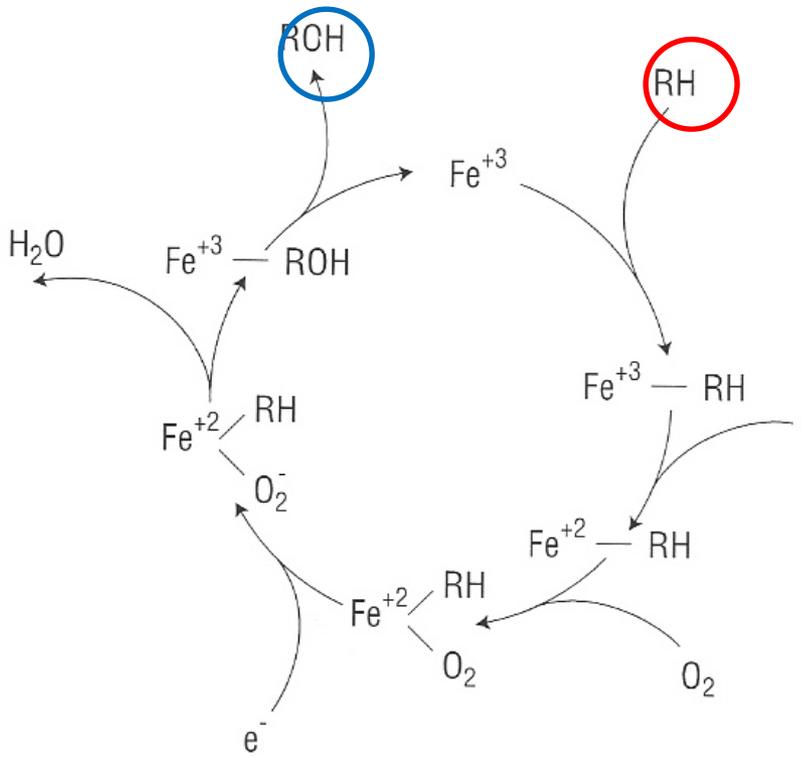
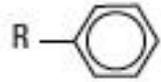


Figure 3.40. Mechanism of oxidation by cytochrome P-450. **MFO**

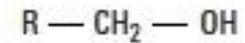
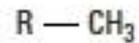
# Le più comuni reazioni di biotrasformazione degli xenobiotici nel biota (continua)

## Oxidations

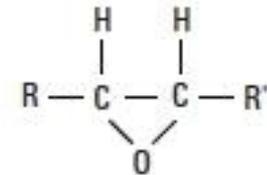
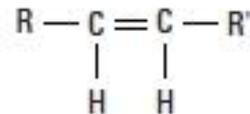
1. Aromatic hydroxylation



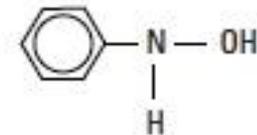
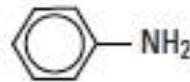
2. Aliphatic hydroxylation



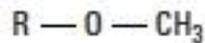
3. Epoxidation



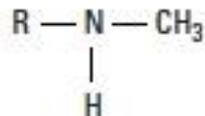
4. N-hydroxylation



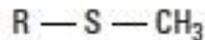
5. O-dealkylation



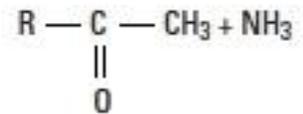
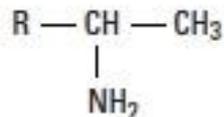
6. N-dealkylation



7. S-dealkylation



8. Deamination



(continua) le più comuni reazioni di biotrasformazione degli xenobiotici nel biota

9. Sulphoxidation



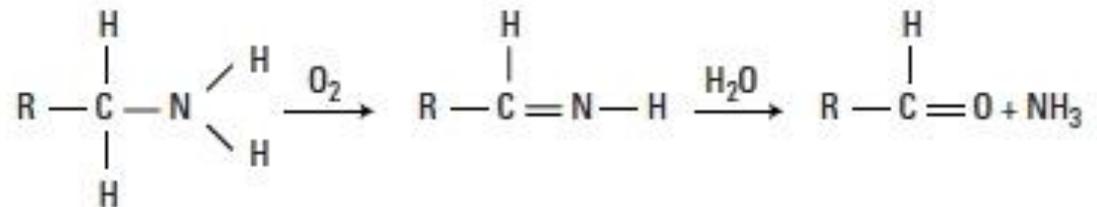
10. Dehalogenation



11. Desulphuration



12. Monoamine and diamine oxidation



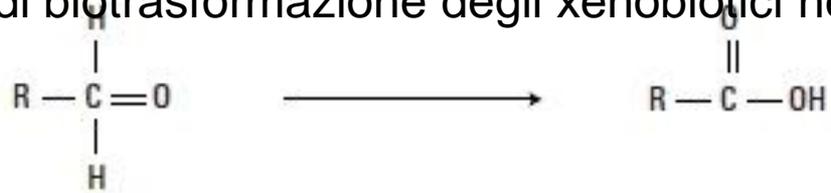
13. Alcohol dehydrogenation



(continua) le più comuni reazioni di biotrasformazione degli xenobiotici nel biota

*Oxidations (continued)*

14. Aldehyde dehydrogenation



*Reductions*

15. Azo reduction



16. Nitro reduction



17. Dehalogenation  
non-microsomal reduction



18. Aldehyde



*Hydrolysis*

19. Ester



20. Amide



21. Epoxide



Nelle reazioni di Fase II si introducono nella molecola gruppi polari di dimensioni relativamente grandi .

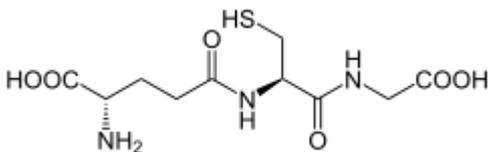
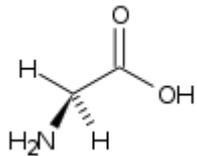
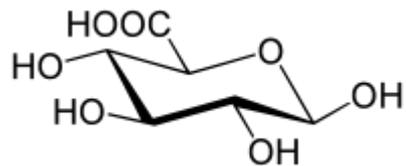


Table 3.15. Phase-II conjugation reactions [65]

Reaction	Functional group
Glucuronic acid Sulphate	-OH, -COOH, -NH <sub>2</sub> , -NH, -SH, -CH aromatic -OH, aromatic -NH <sub>2</sub> , alcohols
Glycine Acetyl	-COOH aromatic -NH <sub>2</sub> , aliphatic -NH <sub>2</sub> , hydrazides, -SO <sub>2</sub> , -NH <sub>2</sub>
Methyl Glutathion	aromatic -OH, -NH <sub>2</sub> , -NH, -SH epoxides, organic halides

## Phase-II reactions

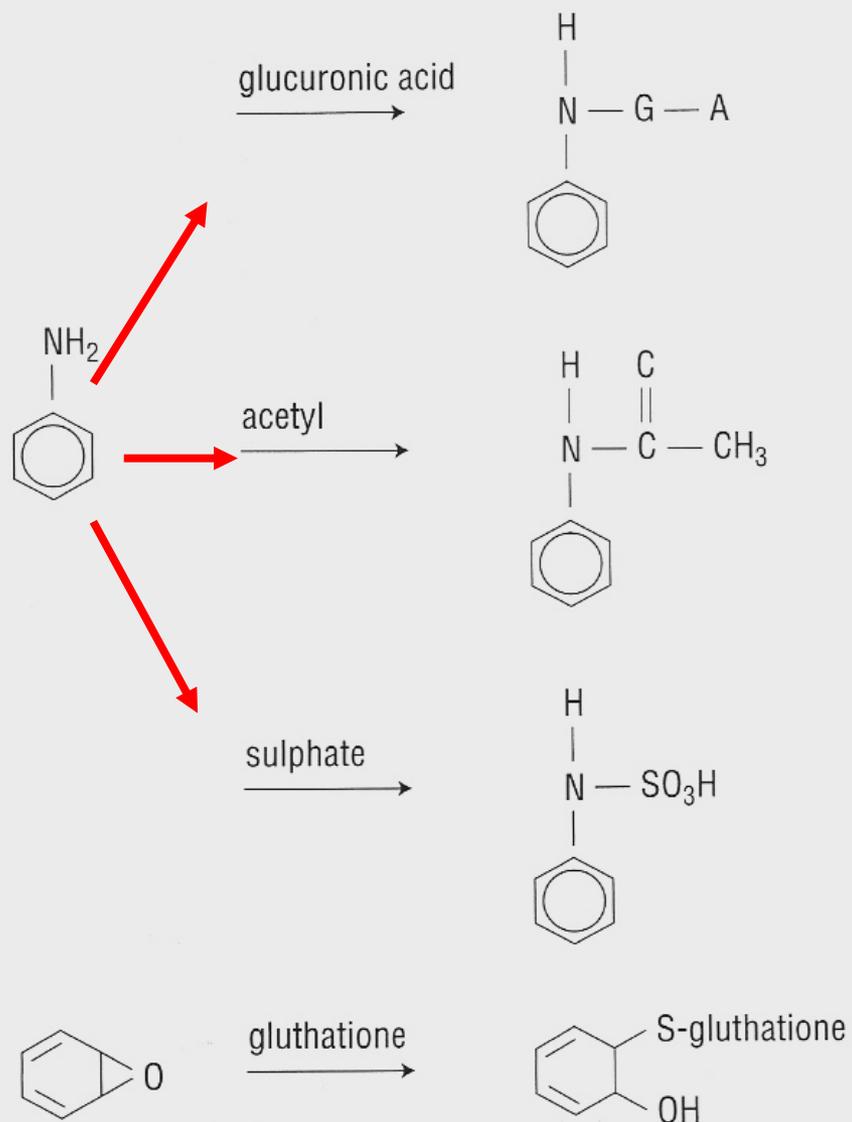
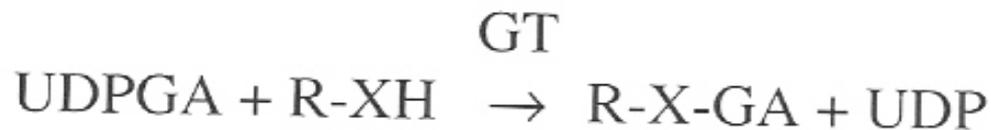


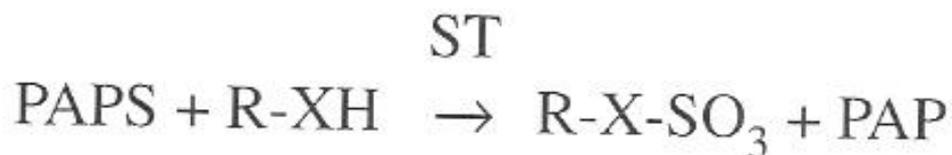
Figure 3.41. Some general phase-II biotransformation reactions involving aniline and benzene.

The general reaction for glucuronic acid conjugation is:



where X is O, COO or NH, UDPGA is uridine diphosphoglucuronic acid and GT is glucuronyltransferase.

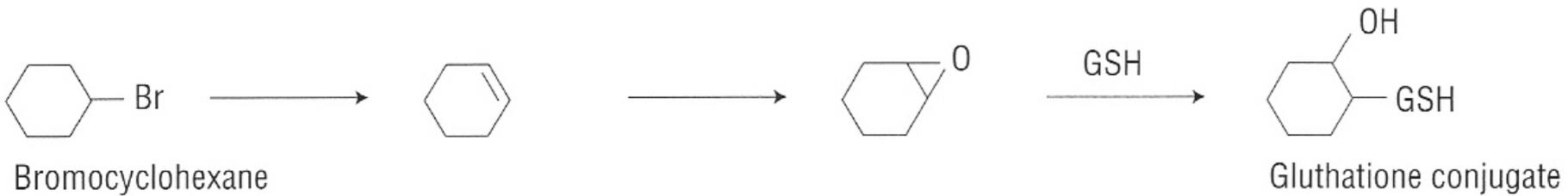
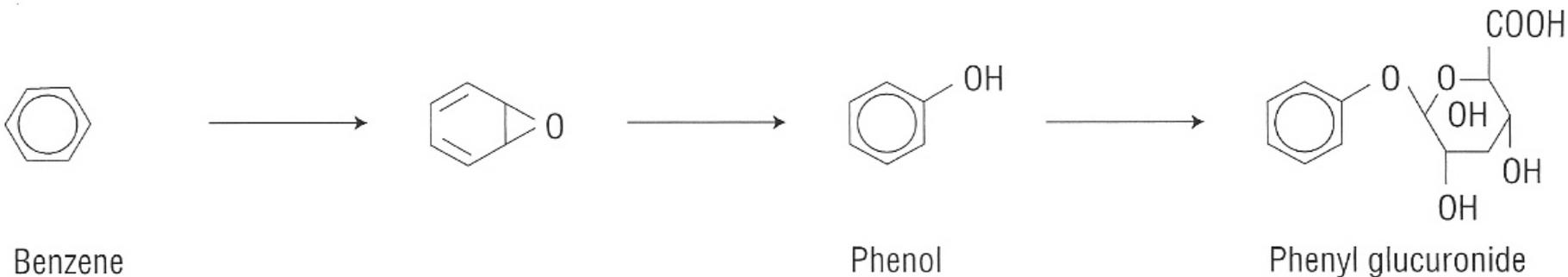
The general reaction for sulphate conjugation is:



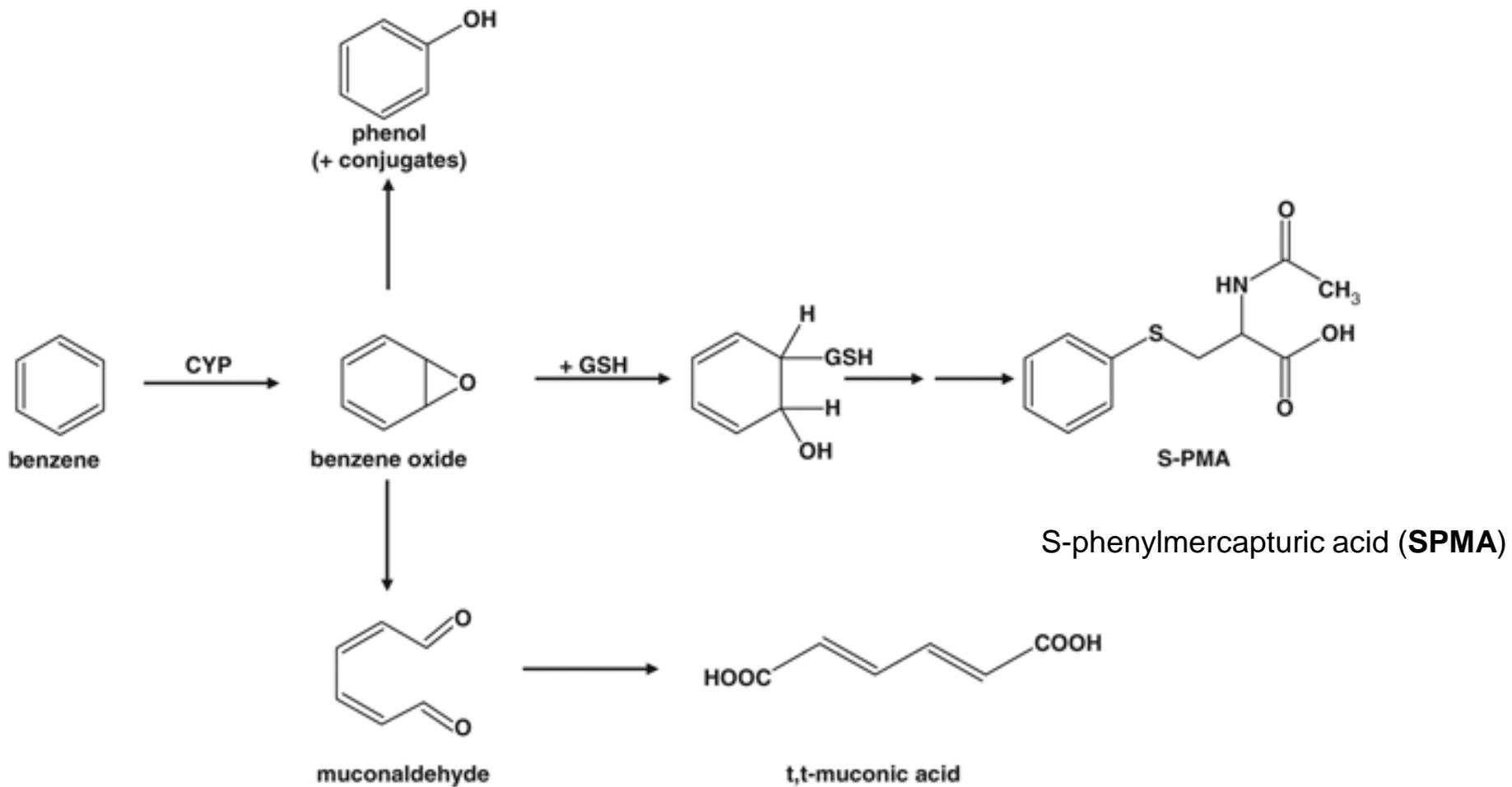
where X is O or NH, PAPS is 3'-phosphoadenosyl-5-phosphosulphate, ST is sulfotransferase and PAP is 3'-5'-adenosine diphosphate.

## Phase-I + phase-II reactions

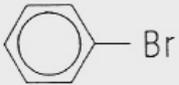
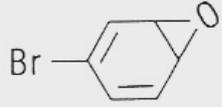
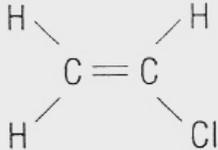
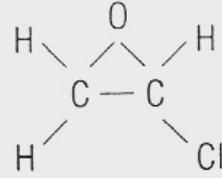
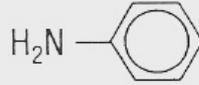
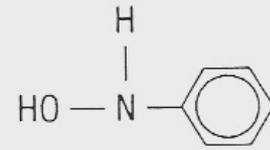
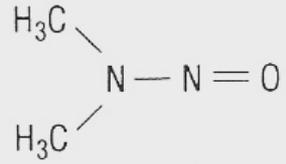
---



3.42. The role of phase-I and phase-II reactions in the mechanism of biotransformation of benzene and bromocyclohexane



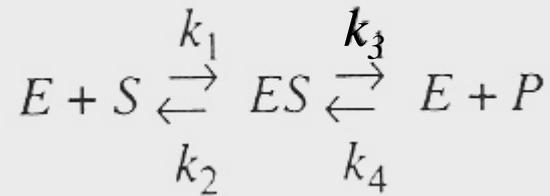
*Prodotti tossici  
delle bio-  
trasformazioni*

Compound	Proposed intermediate	Toxic effect
 Bromobenzene		Liver necrosis
 Vinyl chloride		Liver tumour
 Aniline		Methemoglobine
 Dimethylnitrosamine	$\text{CH}_3^+$	Carcinogenicity
Tetrachloromethane	$\text{CCl}_3$	Liver necrosis
Chloroform	$\text{CHCl}_3, \text{CCl}_3$	Kidney necrosis

3.43. The biotransformation of different xenobiotic compounds to reactive intermediates.

Table 3.16. Species variation for phenol conjugation with glucuronic acid and sulphate [64]

Species	Conjugation of phenol (percentage of total excretion)	
	glucuronic acid	sulphate
Pig	100	0
Rabbit	46	45
Rat	25	68
Man	23	71
Cat	0	87



where  $E$  is enzyme,  $S$  is substrate,  $P$  is product,  $k_1$ ,  $k_2$ ,  $k_3$  and  $k_4$  are rate constants.

$$V = V_{\max} [S] / (K_m + [S]) \quad (3.67)$$

Eqz. di Michaelis Menten

Costante di Michaelis  $K_m$ ,  
valore caratteristico per reazione enzimatica,  
indipendente da concentrazione dell'enzima

## Biotrasformazione degli IPA

<http://monographs.iarc.fr/ENG/Monographs/vol92/mono92.pdf>

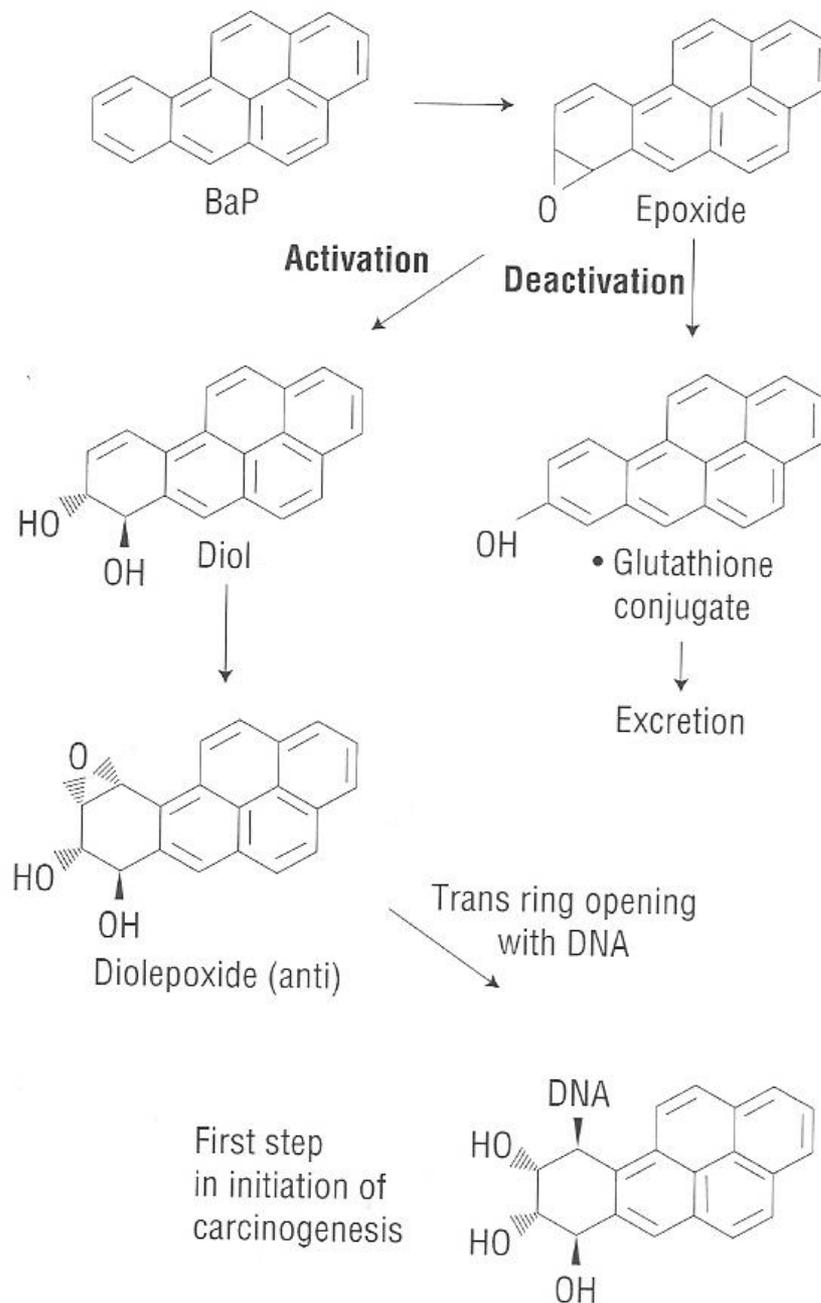
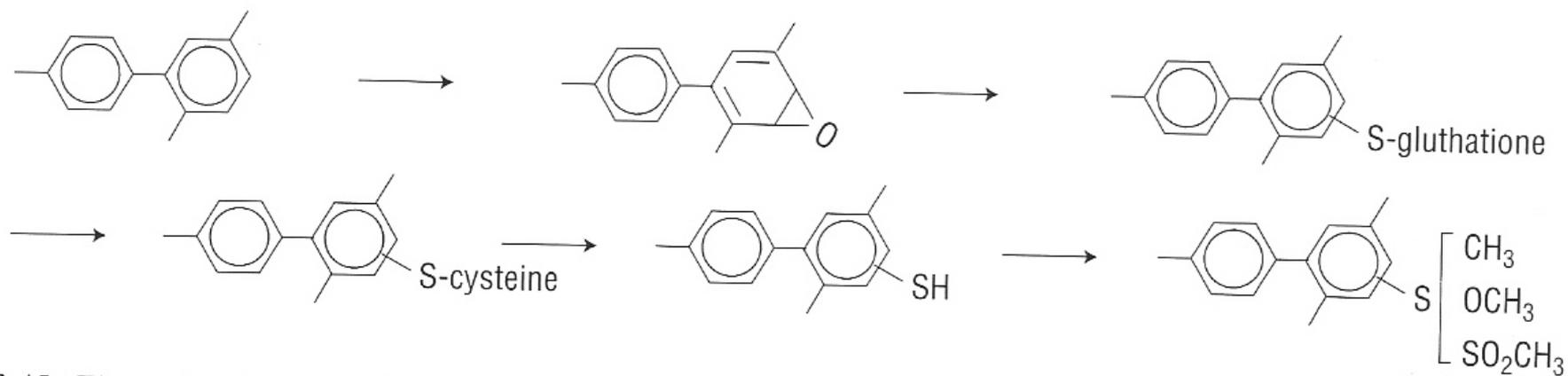


Figure 3.44. The biotransformation pathways of benzo(a)pyrene and binding to the DNA of reactive intermediates. From [66].



3.45. The major biotransformation route of PCBs. From Safe [72]. With permission.

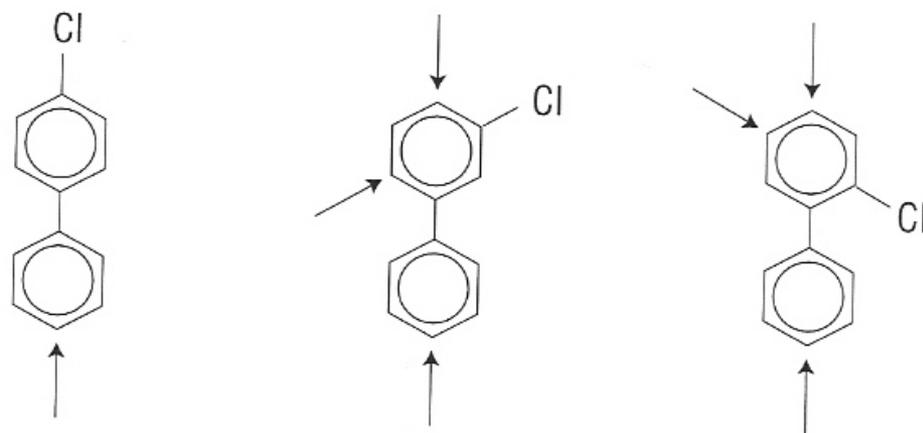
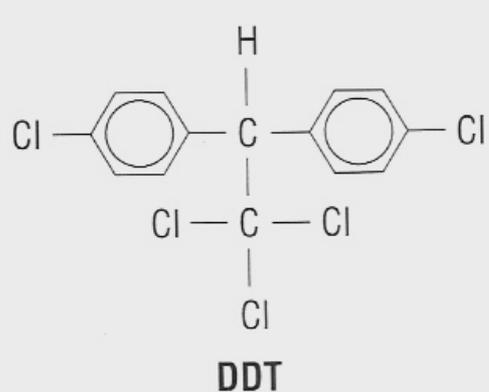
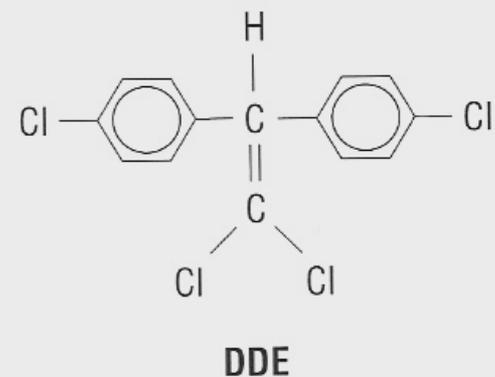


Figure 3.46. The preferred oxidation positions in a PCB molecule and the role of the chlorine position in the molecule in cytochrome P-450 catalyzed biotransformation reactions. From [67].

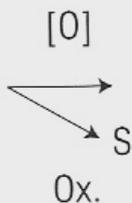
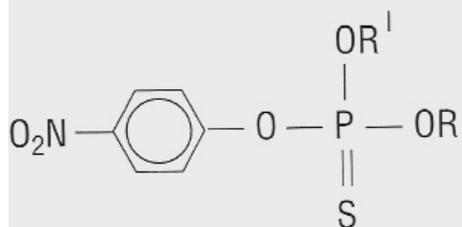


Insects  
Birds  
Mammals

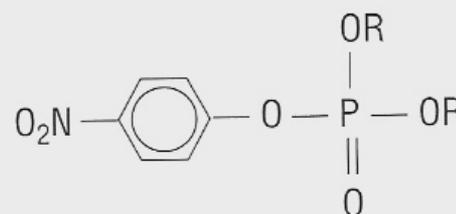


3.47. The main route of biotransformation of DDT to DDE.

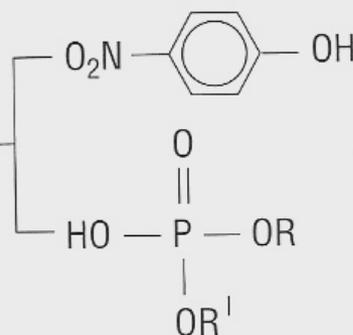
Parathion



Paraoxon



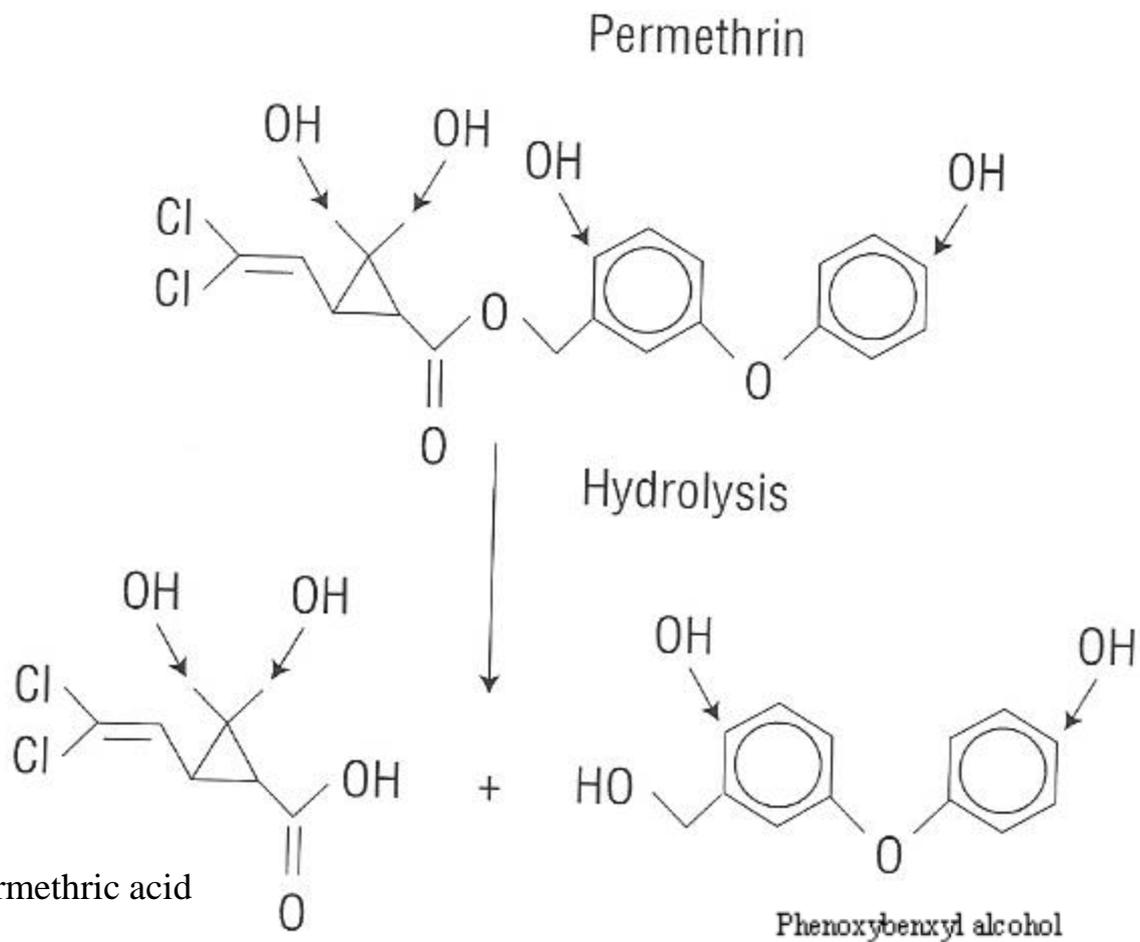
Hydrolysis products



Hydrolysis

3.48. The biotransformation routes of organophosphorus compounds.

O,O-Diethyl O-(4-nitrophenyl) phosphorothioate



Dichlorovinyl acid; Permethric acid

Phenoxybenzyl alcohol

Figure 3.49. The hydrolytic degradation of synthetic pyrethroids.

Table 3.17. Characteristics of the hepatic effects of PB and 3-MC [64]

Characteristic	PB	3-MC
Onset of effects	8-12 h	3-6 h
Time of maximal effect	3-5 d	1-2 d
Persistence of induction	5-7 d	5-12 d
Liver enlargement	marked	slight
Protein synthesis	large increase	small increase
Liver blood flow	increase	no effect
Biliary flow	increase	no effect
Enzymes:		
– cytochrome P-450 1A1 + 1A2	increase	no effect
– cytochrome P-450 2B1 + 2B2	no effect	increase
– NADPH-cytochrome reductase	increase	no effect

# A proposito di composti organici fluorurati...

- [http://www.oecd.org/ehs/pfc/Scheringer\\_OECD\\_webinar\\_2%20\(2\).pdf](http://www.oecd.org/ehs/pfc/Scheringer_OECD_webinar_2%20(2).pdf)
- [http://www.oecd.org/env/ehs/risk-management/PFC\\_FINAL-Web.pdf](http://www.oecd.org/env/ehs/risk-management/PFC_FINAL-Web.pdf)
- <http://www.sciencedirect.com/science/article/pii/S0269749106006038>
- <http://gimle.fsm.it/30/4/01.pdf>