

Prof. Giorgio Sartor

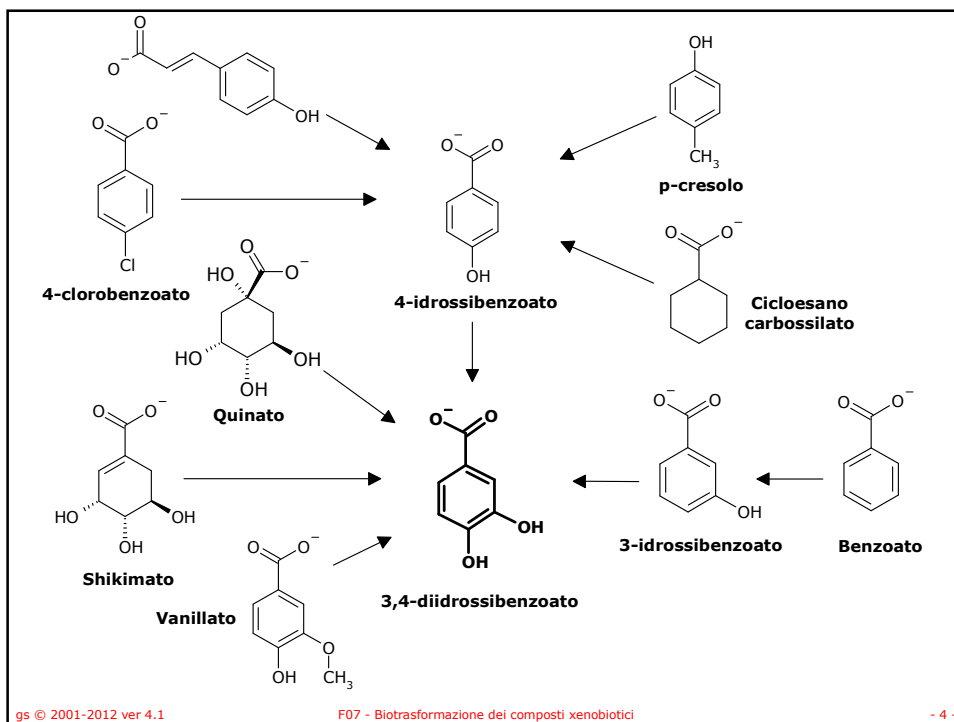
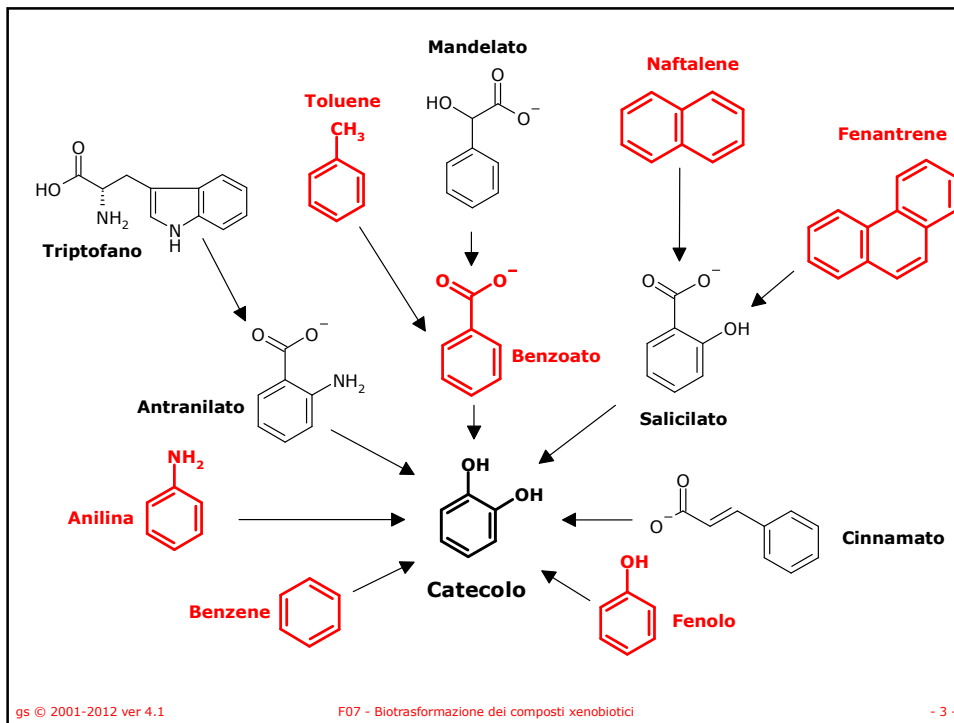
# Biotrasformazione dei composti aromatici

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Versione 4.1 – nov 2012

## Cosa consultare:

- KEGG – Metabolism of xenobiotics
  - <http://www.genome.jp/kegg/pathway.html#xenobiotics>
- BRENDA – The Comprehensive Enzyme Information System
  - <http://www.brenda-enzymes.info>
- The University of Minnesota - Biocatalysis/Biodegradation Database
  - <http://umbbd.msi.umn.edu/>



## Composti aromatici

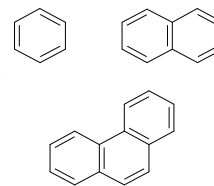
- Benzene, naftalene e fenantrene (IPA)
- Fluorene e derivati
- Bifenile
- Ftalati
- Benzoato
  - idrossilazione
  - coniugazione con CoA

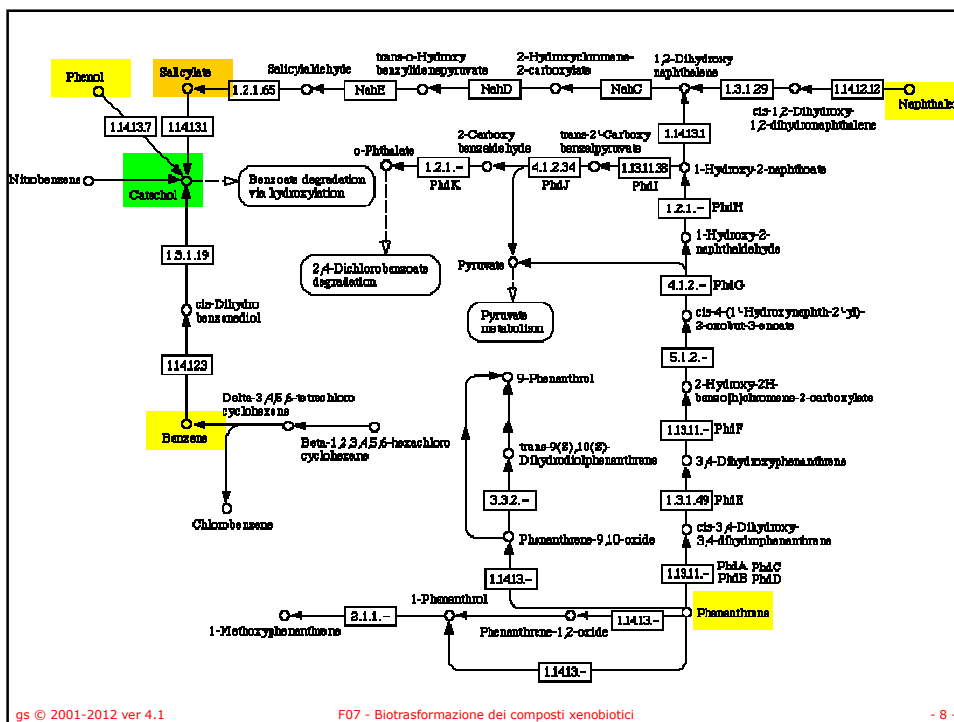
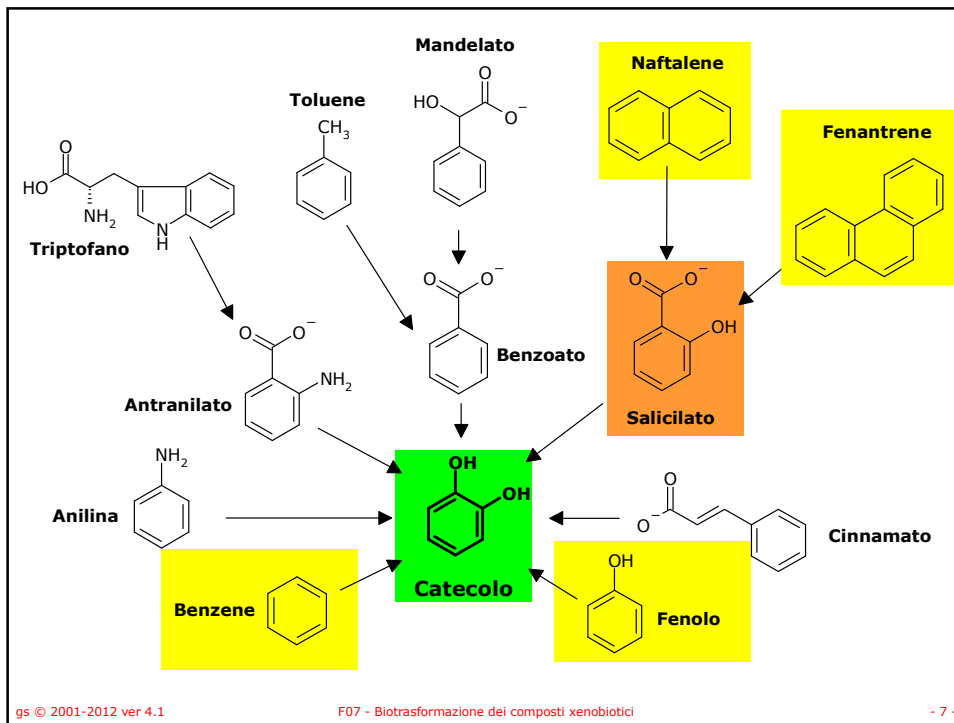
## Composti aromatici

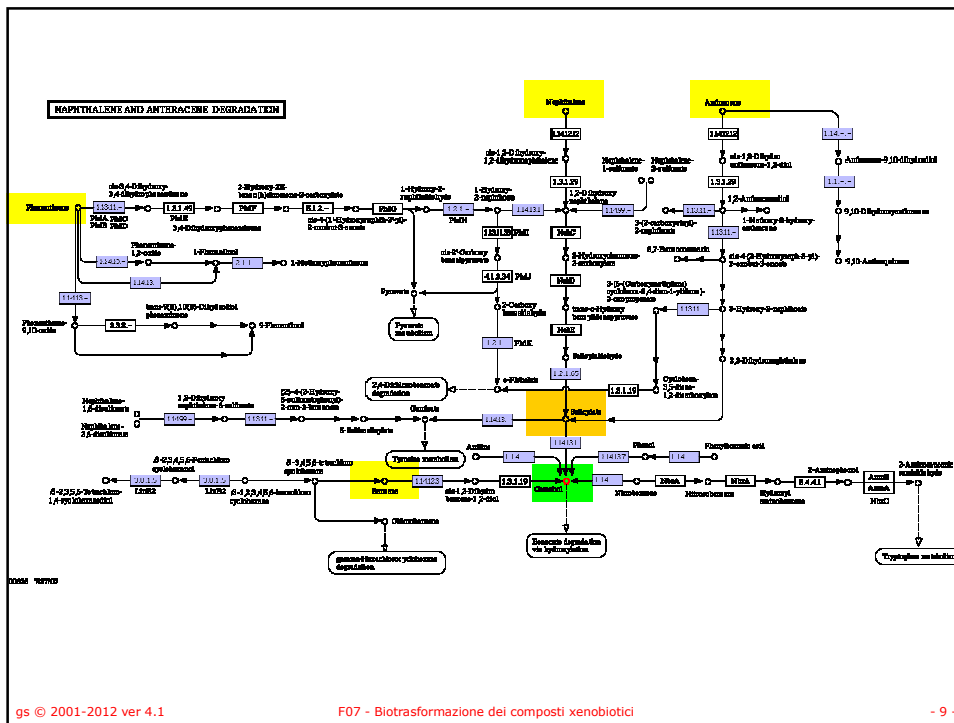
- Benzene, naftalene e fenantrene (IPA)

**Origine:** Naturale (vulcani, incendi), umana (industria chimica, fumi di sigaretta e scarichi automobili).

**Tossicità:** l'esposizione agli IPA provoca effetti sul midollo osseo (leucemia, anemia, ecc.). Sono possibili carcinogenici.





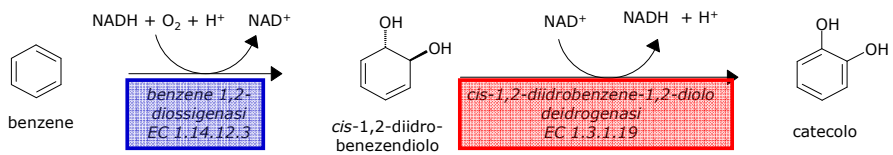


## Come metabolizzare un anello aromatico

- Il meccanismo per rendere più solubile un composto aromatico consiste nell'inserire uno o più gruppi idrofili.
- Per gli aromatici una delle vie è quella di inserire due gruppi -OH attraverso due reazioni successive:
  - La formazione di un diolo ciclico per azione di un riducente e di O<sub>2</sub>
    - Agisce una diossigenasi
  - La riossidazione del diolo ad aromatico
    - Agisce una deidrogenasi

# Diossigenasi

## Da benzene a catecolo



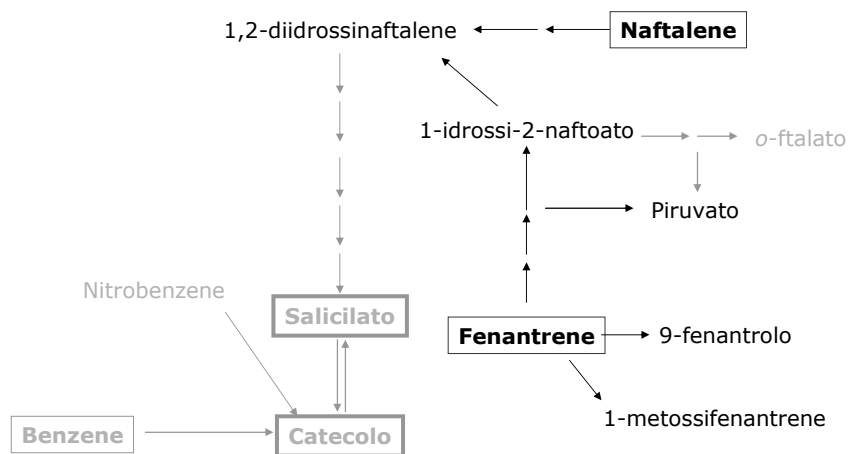
- EC 1.14.13.3

- Un sistema contenete una reduttasi costituita da una flavoproteina ferro-zolfo, una ossigenasi ferro-zolfo e ferredossina.
- Richiede  $\text{Fe}^{2+}$ .
- Gibson, D.T., Koch, J.R. and Kallio, R.E. Oxidative degradation of aromatic hydrocarbons by microorganisms. I. Enzymatic formation of catechol from benzene. *Biochemistry* 7 (1968) 2653-2662.

- EC 1.3.1.19

- Axcell, B.C. and Geary, P.J. The metabolism of benzene by bacteria. Purification and some properties of the enzyme *cis*-1,2-dihydroxycyclohexa-3,5-diene (nicotinamide adenine dinucleotide) oxidoreductase (*cis*-benzene glycol dehydrogenase). *Biochem. J.* 136 (1973) 927-934.

# Degradazione degli IPA

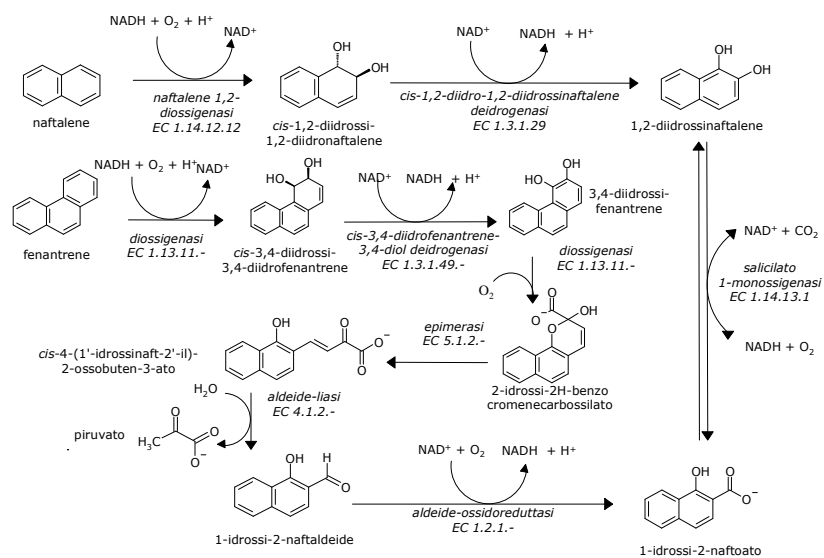


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## Da naftalene e fenantrene a 1,2-diidrossinaftalene

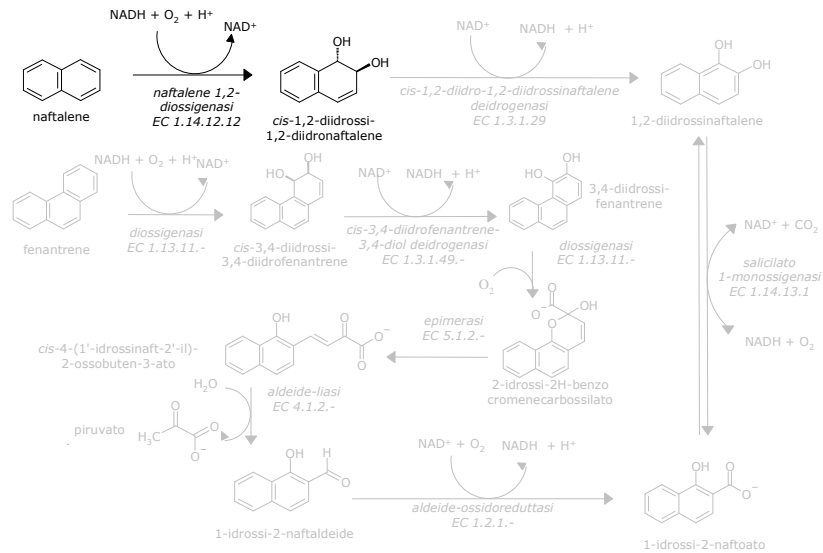


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## Da naftalene e fenantrene a 1,2-diidrossinaftalene



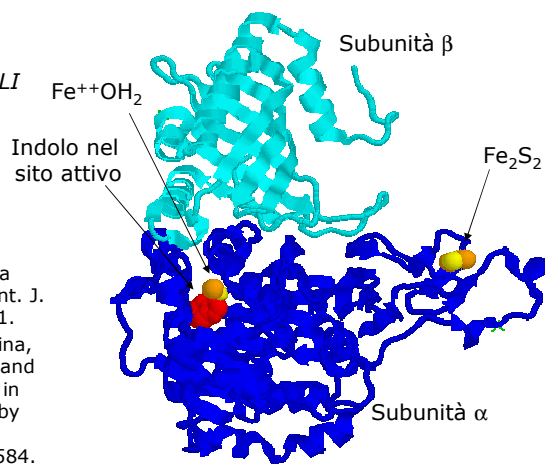
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## Naftalene 1,2-diossigenasi EC 1.14.12.12 (1EG9)

- Un esamero  $\alpha_3\beta_3$
- Da *PSEUDOMONAS PUTIDA*
- Espresso in *ESCHERICHIA COLI*
- Strutture: 1EG9; 1NDO; 1O7G; H; M; N; P; W;
- Referenze
  - Ensley, B.D. and Gibson, D.T. Naphthalene dioxygenase: purification and properties of a terminal oxygenase component. J. Bacteriol. 155 (1983) 505-511.
  - Jeffrey, A.M., Yeh, H.J.C., Jerina, D.M., Patel, T.R., Davey, J.F. and Gibson, D.T. Initial reactions in the oxidation of naphthalene by *Pseudomonas putida*. Biochemistry 14 (1975) 575-584.



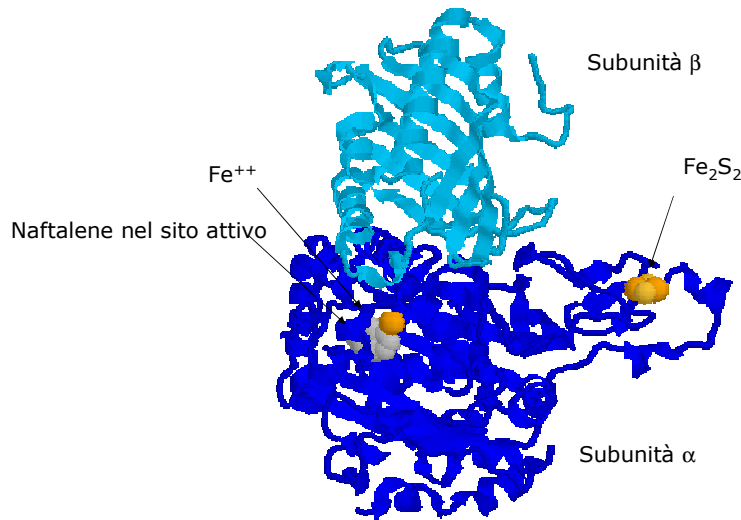
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# Naftalene 1,2-diossigenasi EC 1.14.12.12 (1O7G)

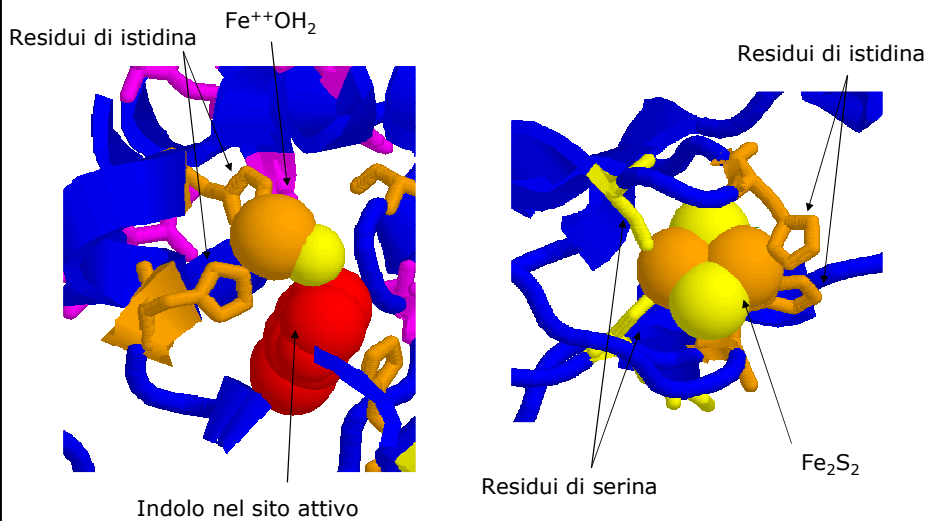


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# Naftalene 1,2-diossigenasi EC 1.14.12.12 (1EG9)

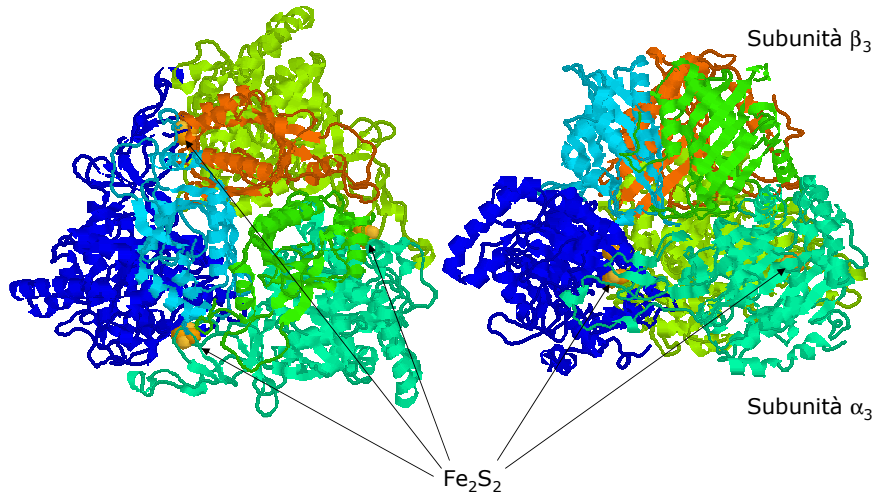


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# Naftalene 1,2-diossigenasi EC 1.14.12.12 (*1NDO*)

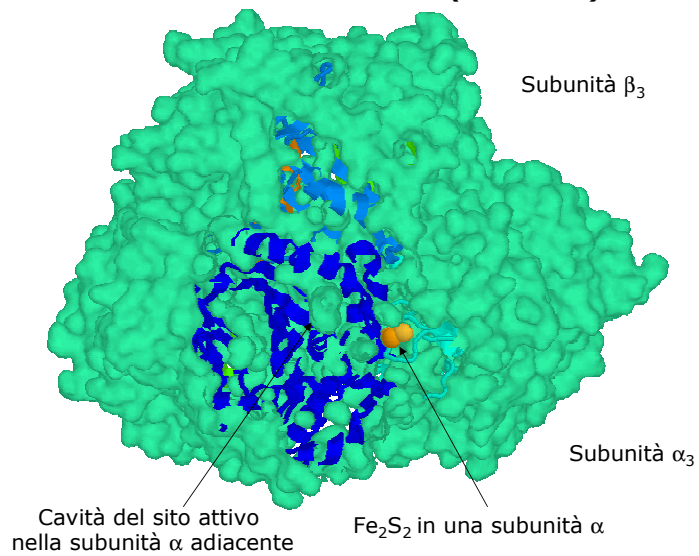


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# Naftalene 1,2-diossigenasi EC 1.14.12.12 (*1NDO*)

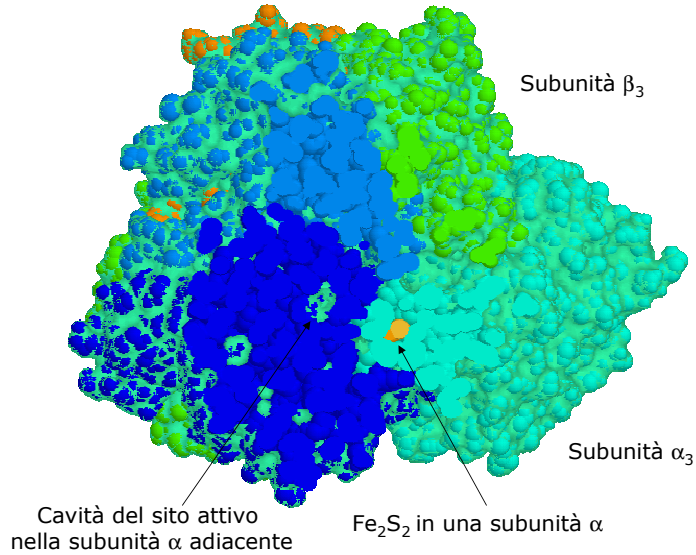


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## Naftalene 1,2-diossigenasi EC 1.14.12.12 (1NDO)

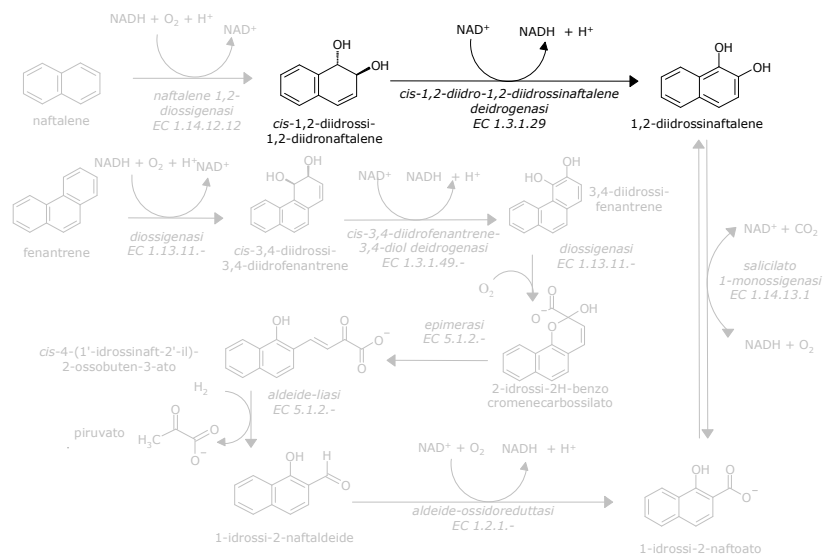


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## Da naftalene e fenantrene a 1,2-diidrossinaftalene

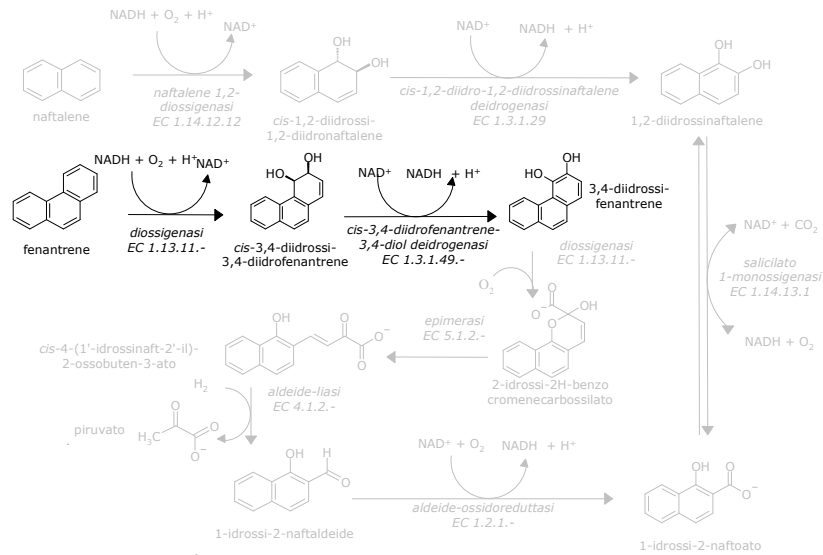


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## Da naftalene e fenantrene a 1,2-diidrossinaftalene

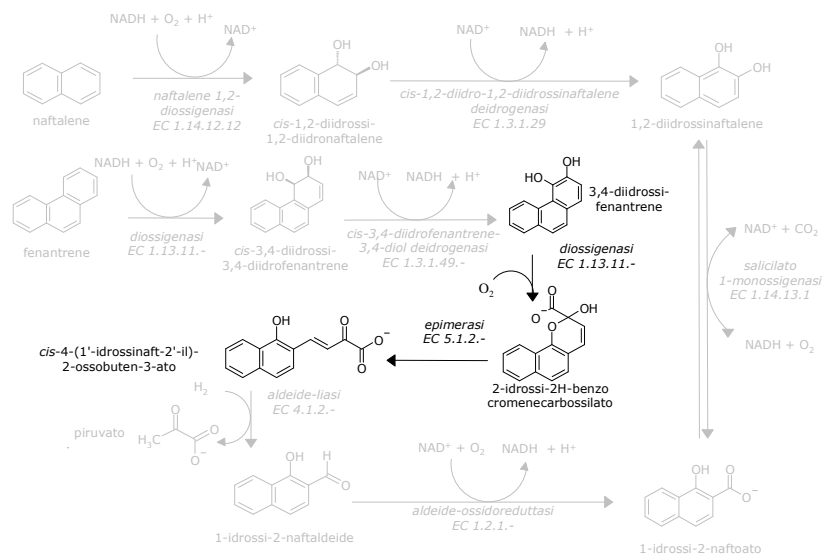


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## Da naftalene e fenantrene a 1,2-diidrossinaftalene

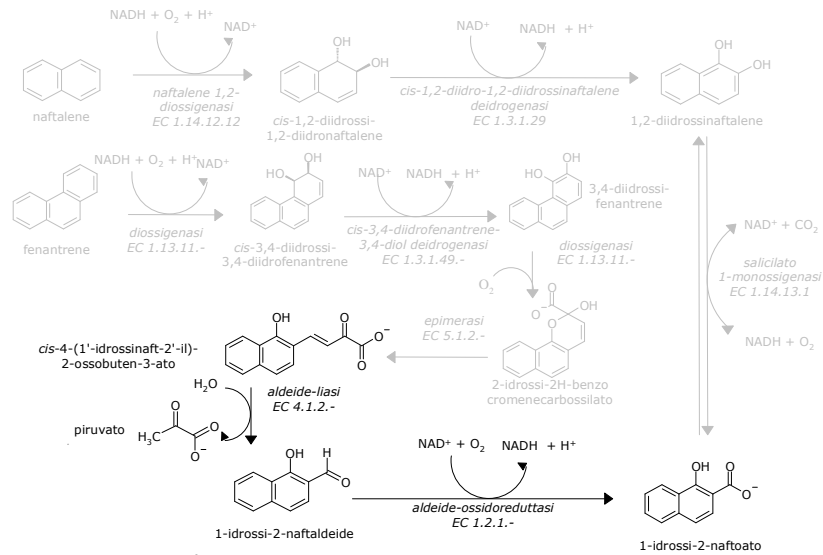


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## Da naftalene e fenantrene a 1,2-diidrossinaftalene

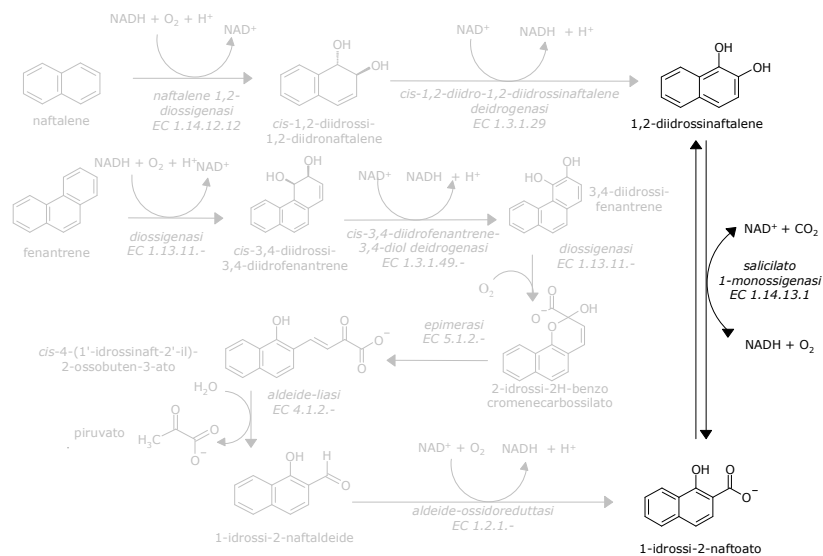


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## Da naftalene e fenantrene a 1,2-diidrossinaftalene

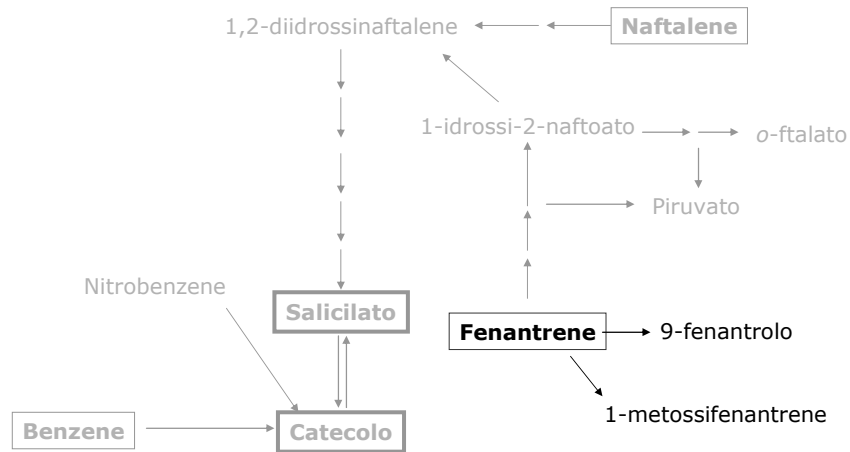


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## Degradazione degli IPA

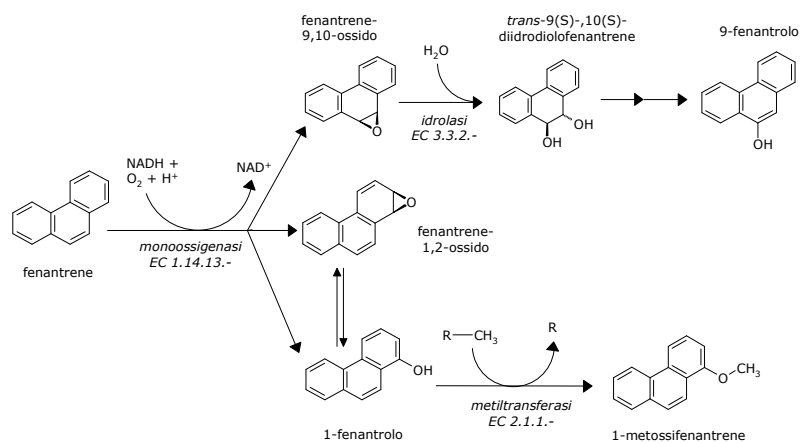


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## Epossidazione del fenantrene

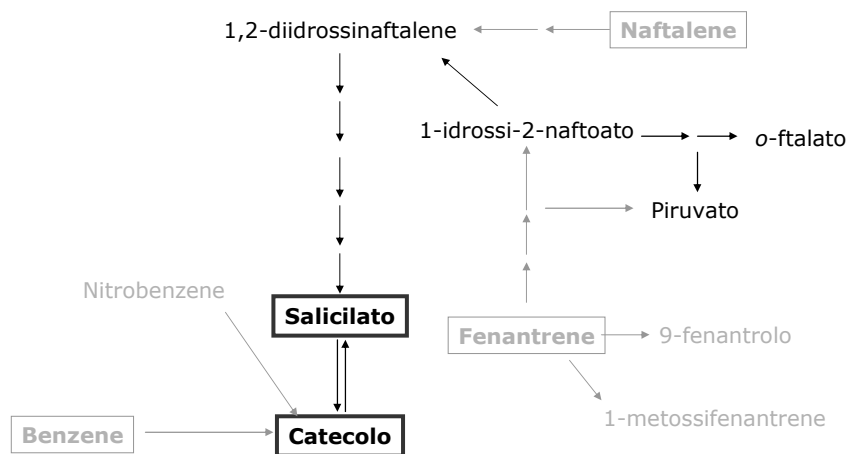


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## Degradazione degli IPA

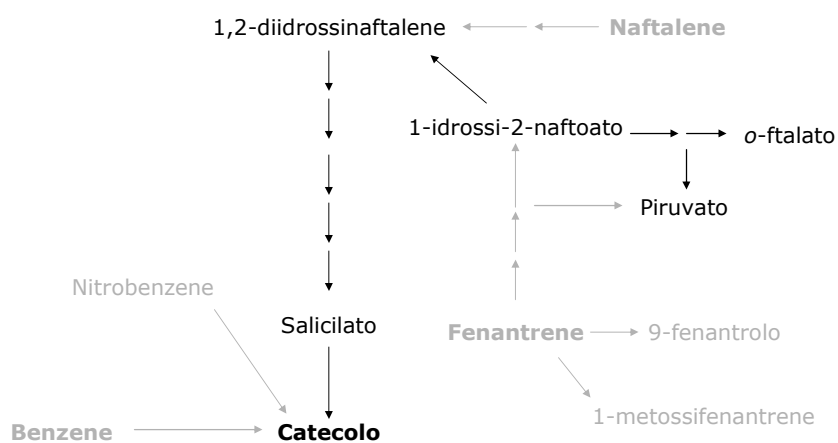


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## Degradazione degli IPA

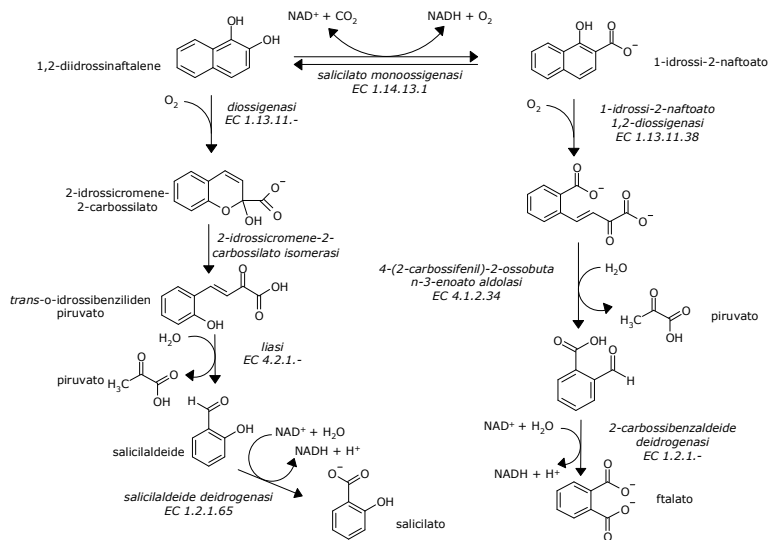


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## Degradazione dell'idrossinaftalene

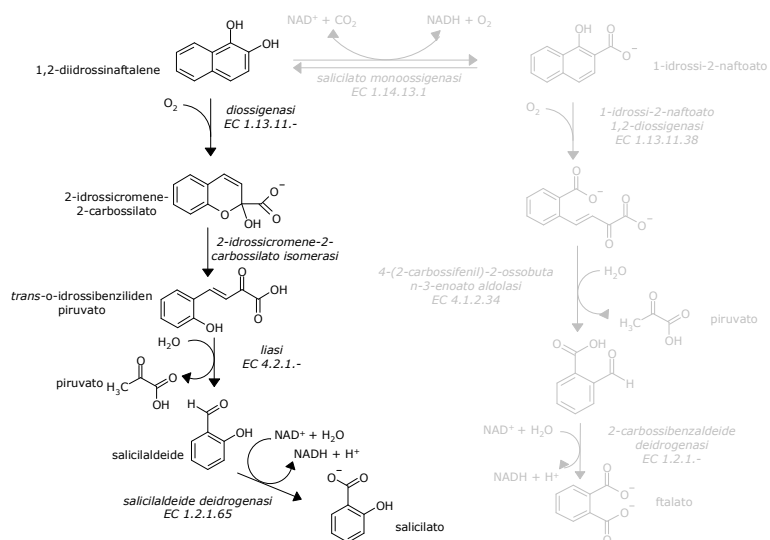


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## Degradazione dell'idrossinaftalene



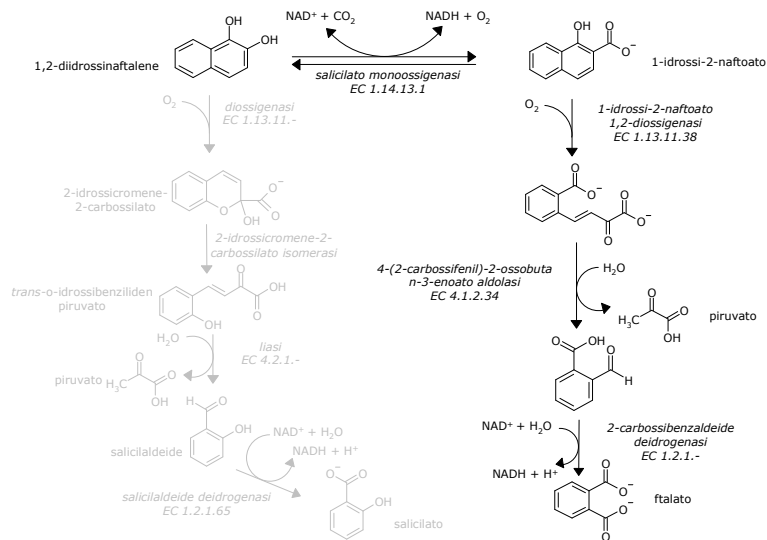
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## Degradazione dell'idrossinaftalene

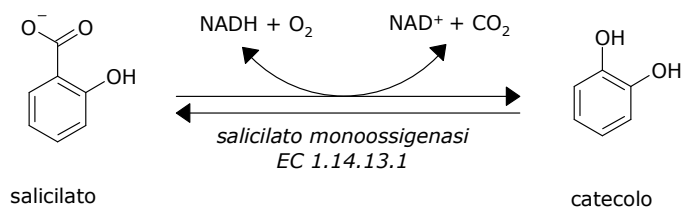


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## Da salicilato a catecolo



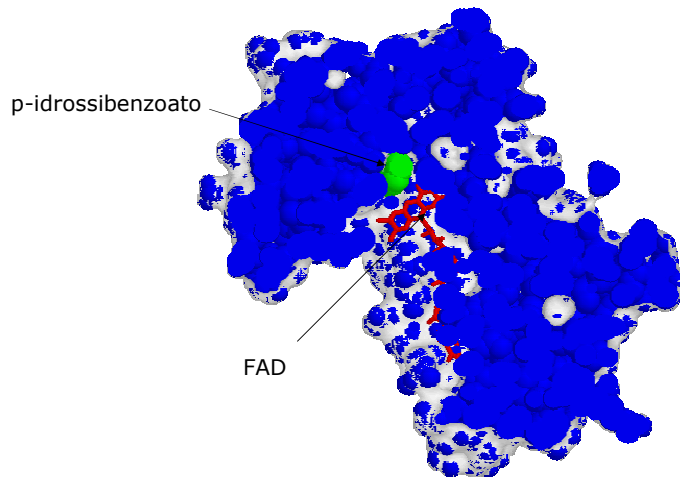
- Il meccanismo ipotizzato prevede la formazione di un o-chinone intermedio che viene ridotto a fenolo in maniera non enzimatica da una seconda molecola di NADH. La stechiometrica NADH:salicilato:ossigeno è 2:1:1
- L'enzima catalizza la formazione di catecolo da substrati diversi (o-nitro-, o-amino-, o-iodo-, o-bromo- and o-clorofenolo derivati) attraverso la rimozione del sostituente in orto.

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## p-idrossibenzoato idrolasi EC 1.14.13.2 (1IUU)



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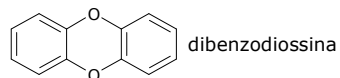
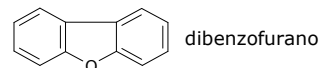
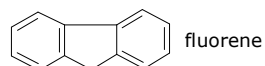
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## Composti aromatici

- Benzene, naftalene e fenantrene
- Fluorene e derivati

**Origine:** fumi da combustione di combustibili fossili e rifiuti (PVC). I loro derivati clorurati sono stati usati come defolianti

**Tossicità:** irritanti per la pelle, gli occhi, il sistema respiratorio. Hanno proprietà mutageniche. Provocano il cancro. Mimano gli ormoni. Esistono i loro derivati clorurati usati come defolianti, ancora più tossici. Non esiste una dose di sicurezza.

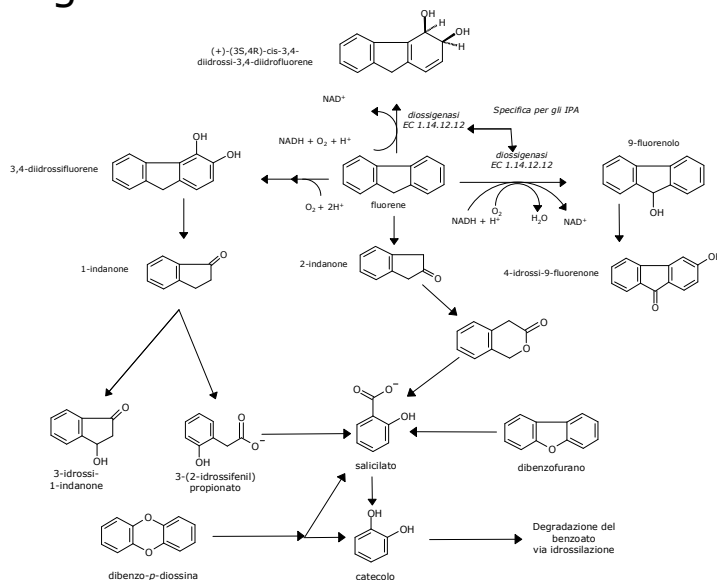


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## Degradazione ossidativa del fluorene

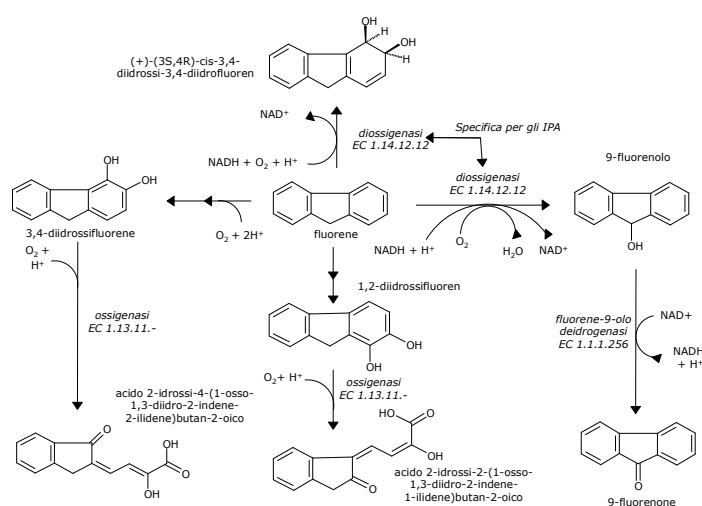


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## Degradazione ossidativa del fluorene - I

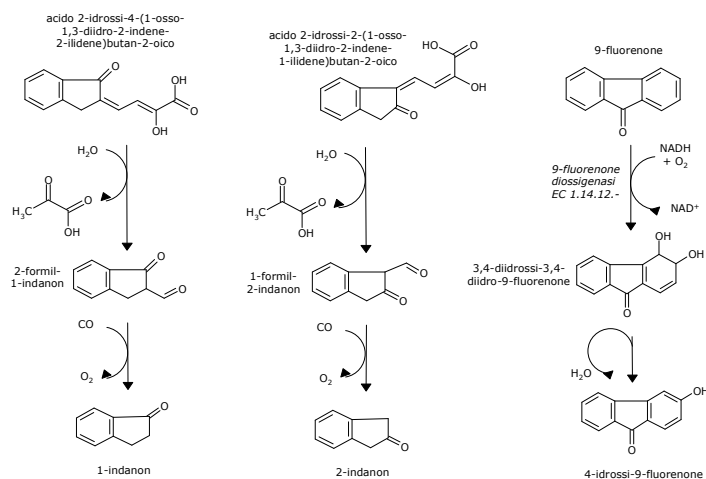


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## Degradazione ossidativa del fluorene - II

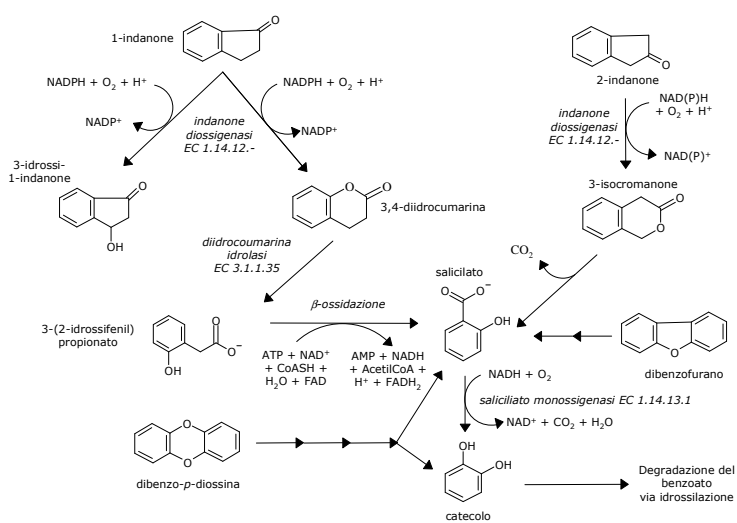


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## Degradazione ossidativa del fluorene - III

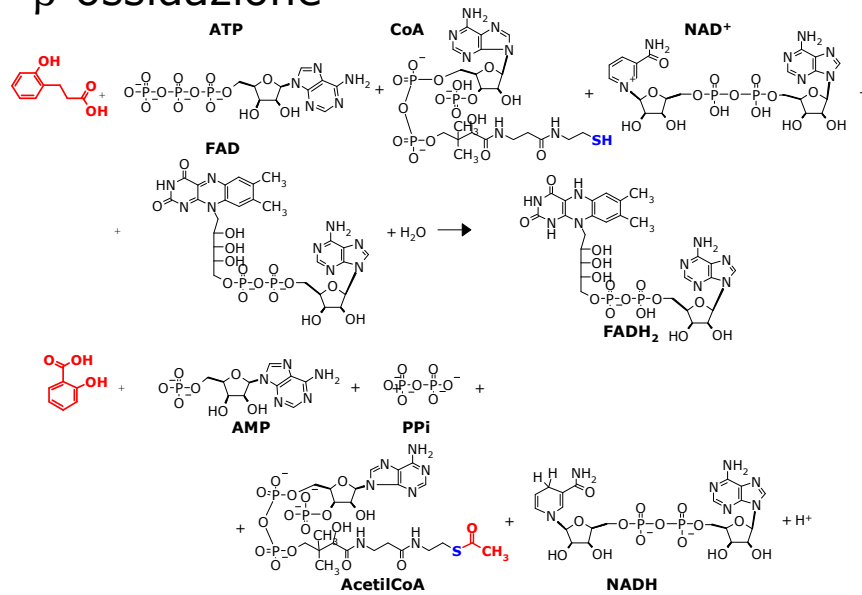


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# β-ossidazione

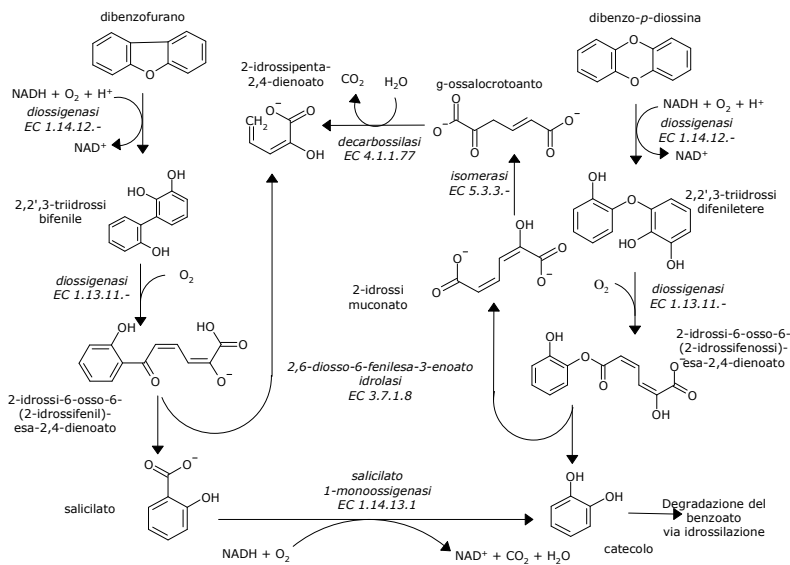


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# Degradazione di dibenzofurano e dibenzo-*p*-diossina

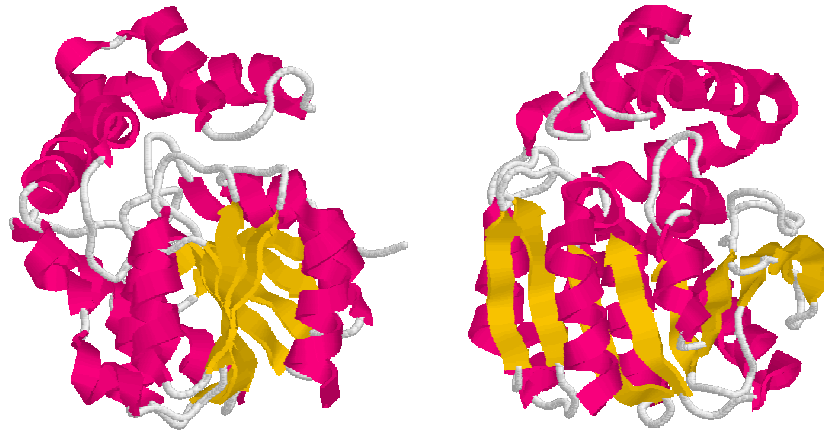


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2,6-diosso-6-fenileisa-3-enoato idrolasi  
*EC 3.7.1.8 (1C4X)*

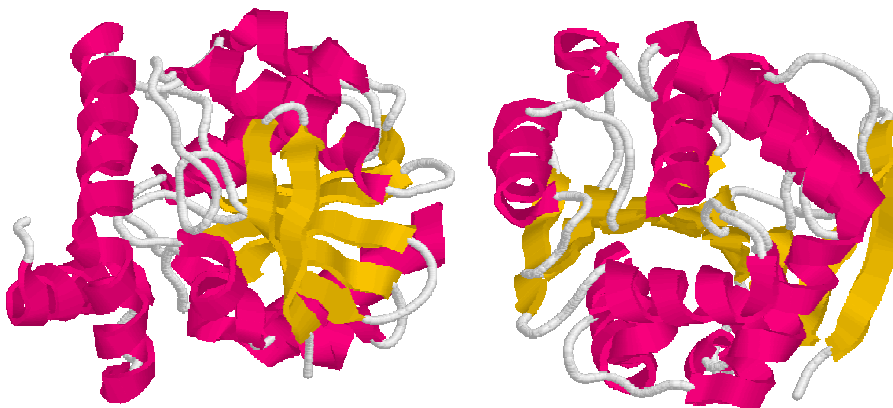


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2,6-diosso-6-fenileisa-3-enoato idrolasi  
*EC 3.7.1.8 (1J1I)*

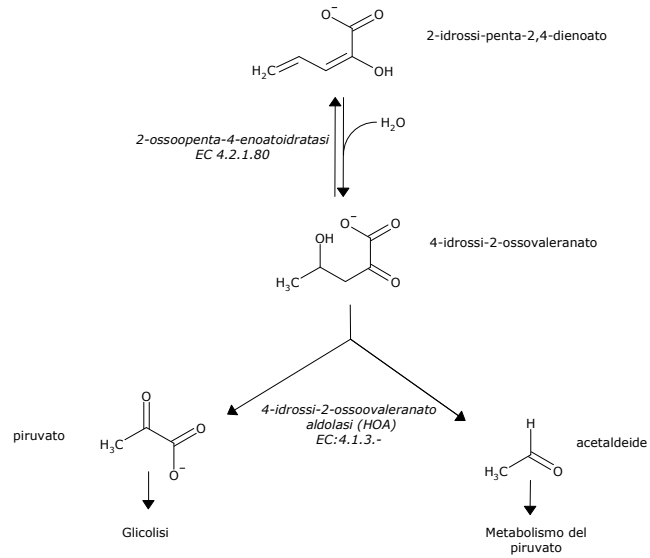


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## Scissione del 2-idrossi-2,4-pentadienoato

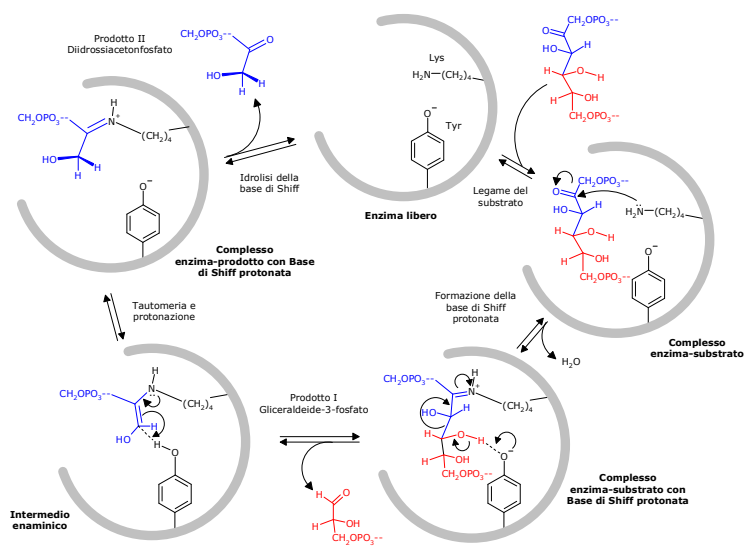


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## Aldolasi EC 4.2.1.13



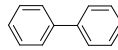
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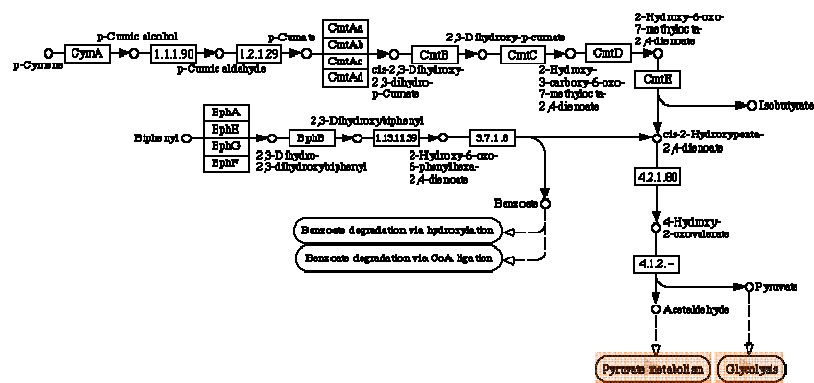
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# Composti aromatici

- Benzene, naftalene e fenantrene
- Fluorene e derivati
- Bifenile
- Ftalati
- Benzoato
  - idrossilazione
  - coniugazione con CoA

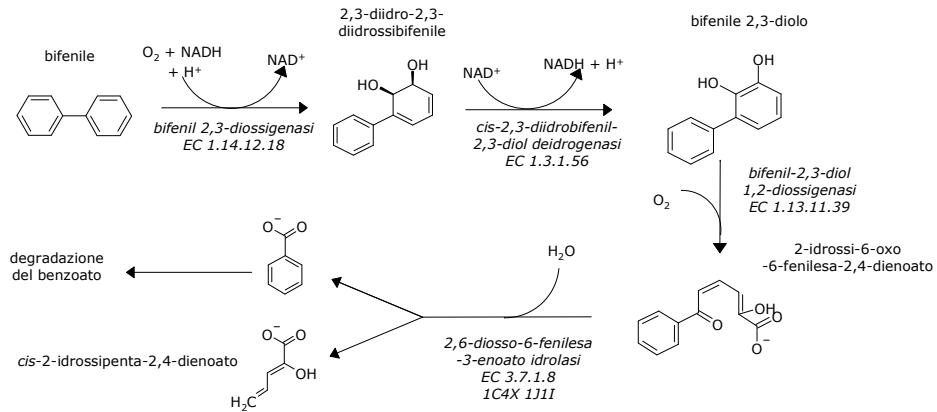


# Schema generale - bifenile





## Scissione del bifenile

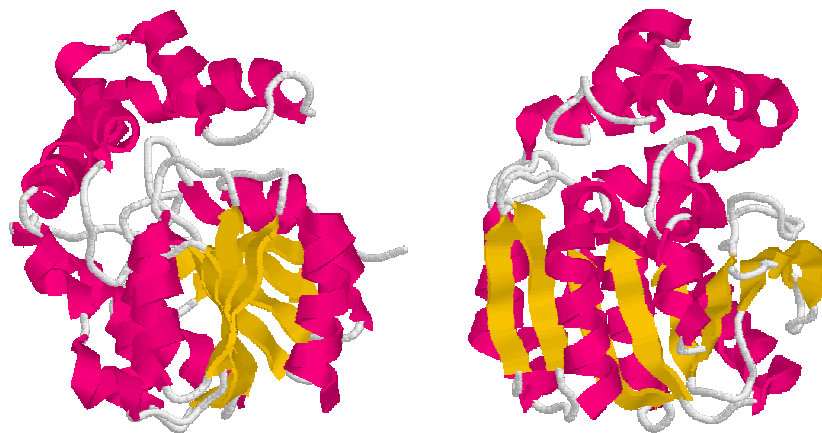


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## 2,6-diosso-6-fenilesa-3-enoato idrolasi EC 3.7.1.8 (1C4X)

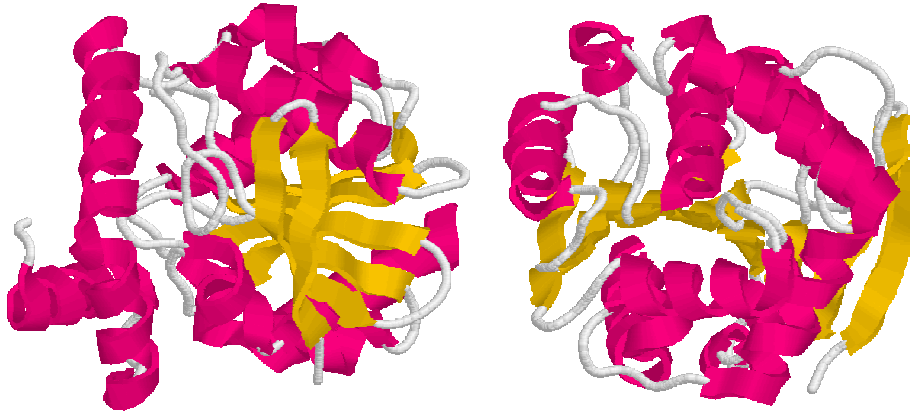


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## 2,6-diosso-6-fenilesa-3-enoato idrolasi EC 3.7.1.8 (1J1I)

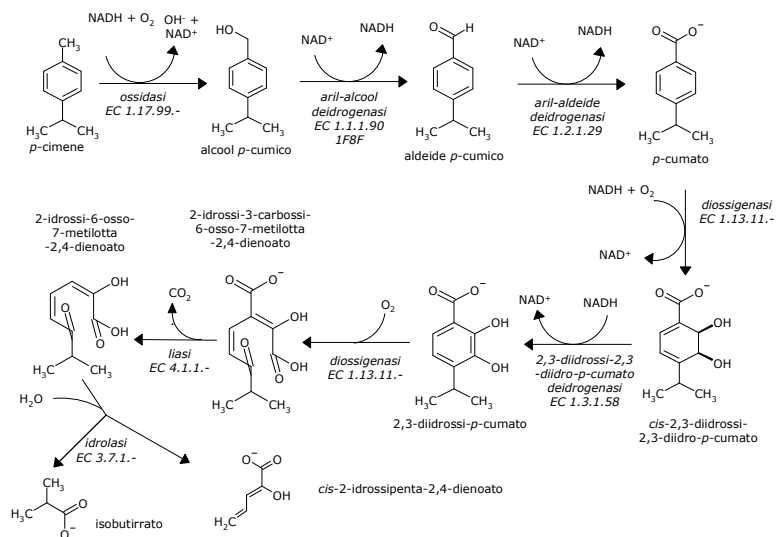


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## Scissione del *p*-cimene

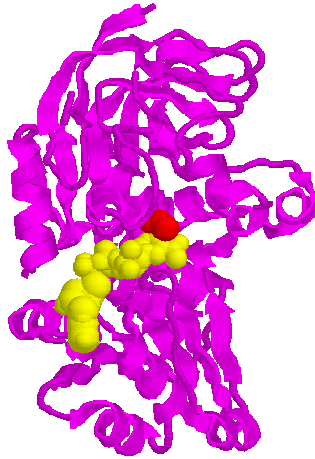


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Benzilalcol deidrogenasi  
*EC 1.1.1.90 (1F8F)*

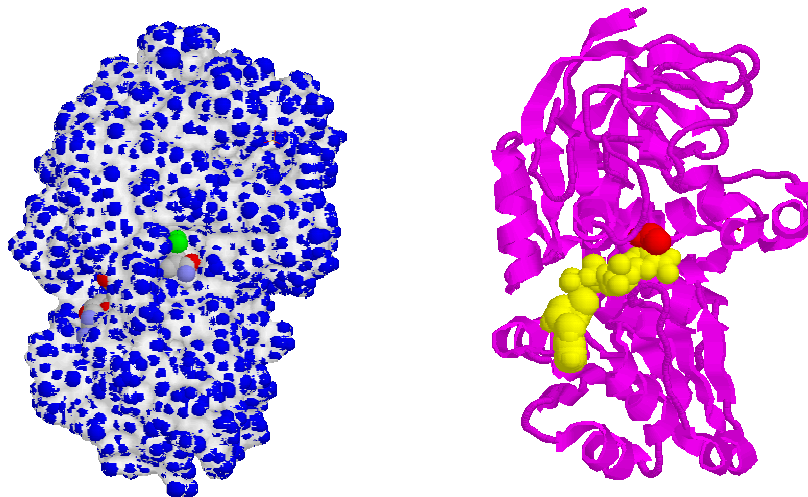


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Benzilalcol deidrogenasi  
*EC 1.1.1.90 (1F8F)*

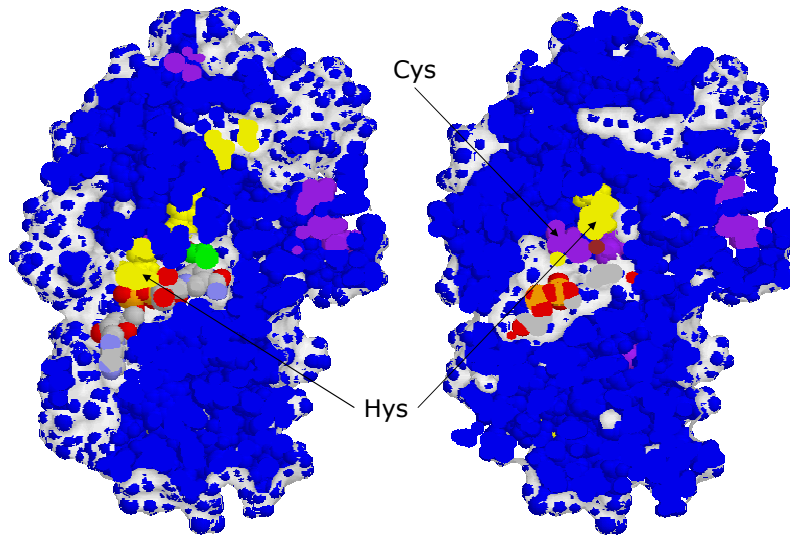


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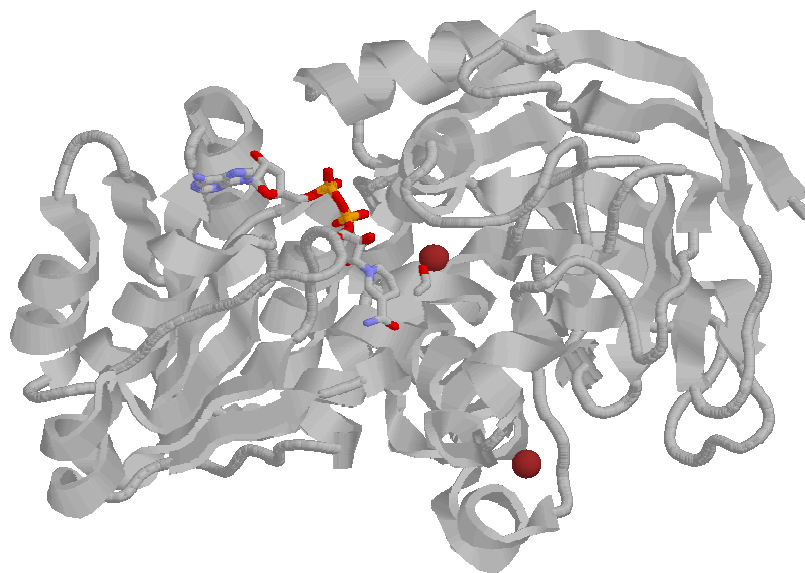
# Benzilalcol deidrogenasi *EC 1.1.1.90 (1F8F)*



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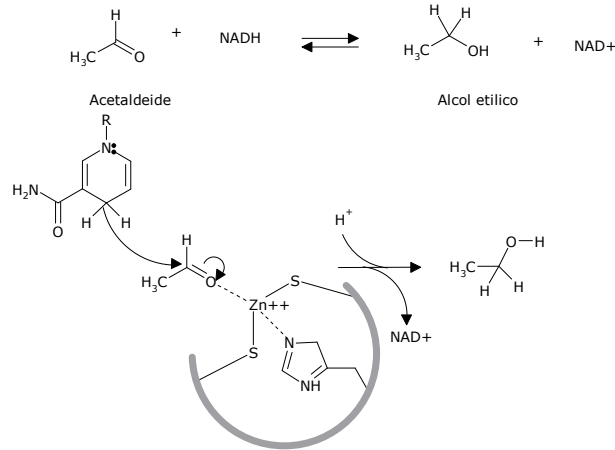
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## Alcool deidrogenasi EC 1.1.1.1

- Catalizza la reazione di ossidoriduzione:

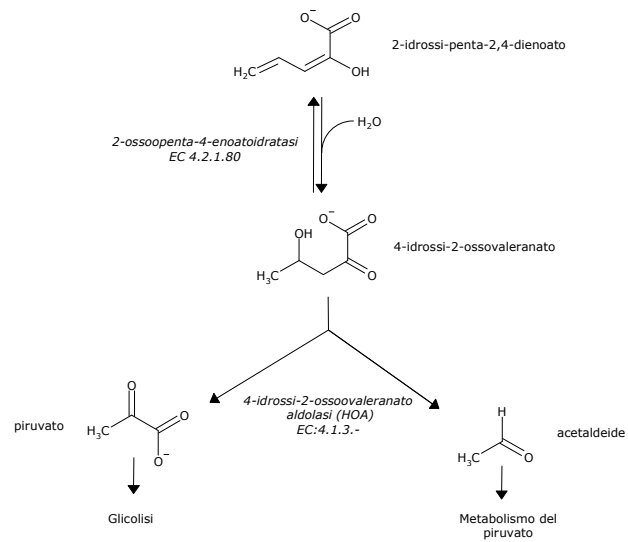


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F07 - Biotrasformazione dei composti xenobiotici

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## Scissione del 2-idrossi-2,4-pentadienoato



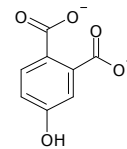
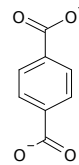
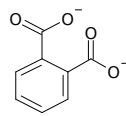
gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

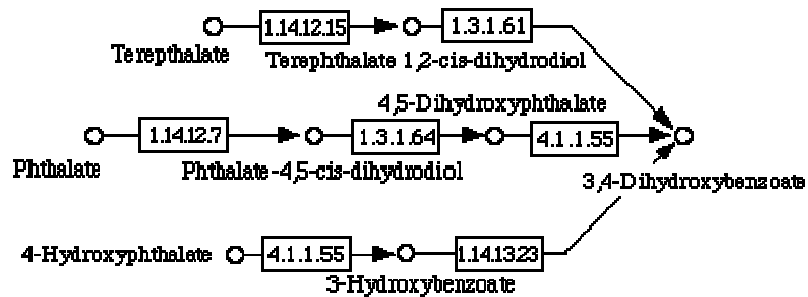
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## Composti aromatici

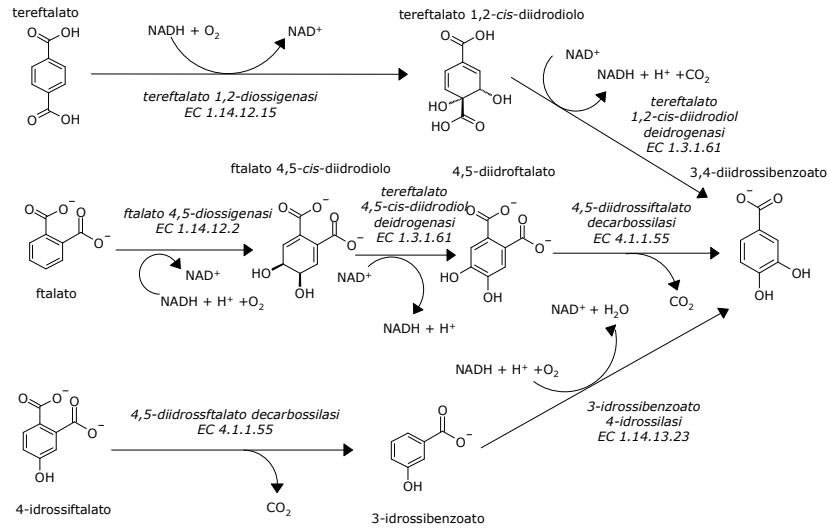
- Benzene, naftalene e fenantrene
- Fluorene e derivati
- Bifenile
- Ftalati
- Benzoato
  - idrossilazione
  - coniugazione con CoA



## Schema generale



## A 3,4-idrossibenzoato

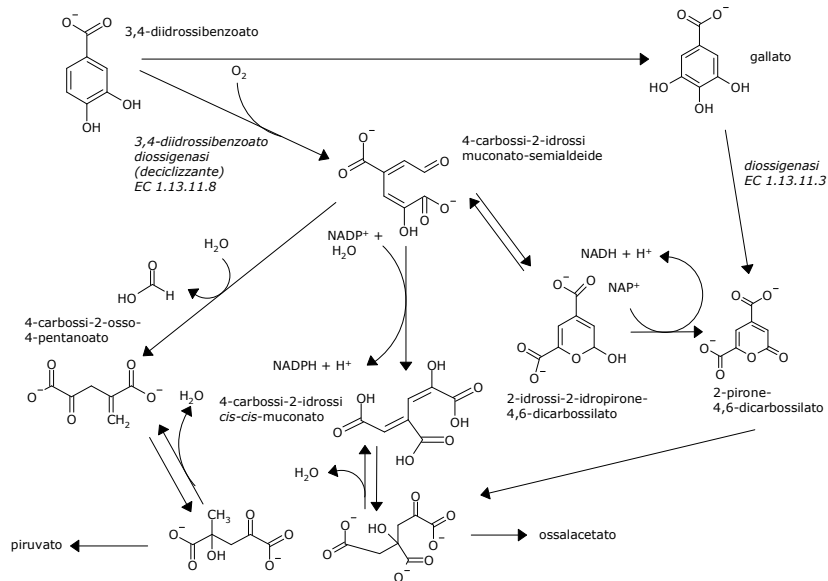


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F07 - Biotrasformazione dei composti xenobiotici

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## 3,4-diidrossibenzoato a piruvato e ossalacetato

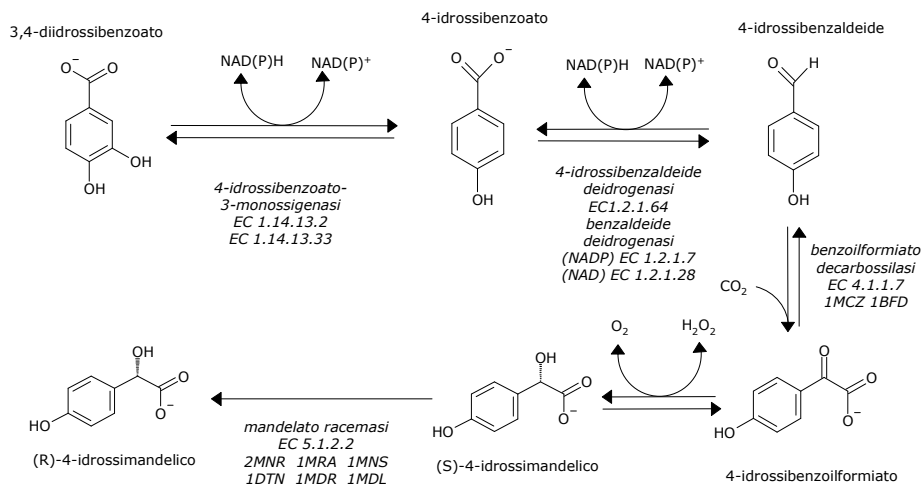


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Da 3,4-diidrossibenzoato a (R)-4-idrossimandelato



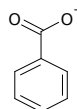
gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Composti aromatici

- Benzene, naftalene e fenantrene
- Fluorene e derivati
- Bifenile
- Ftalati
- **Benzoato**
  - idrossilazione
  - coniugazione con CoA



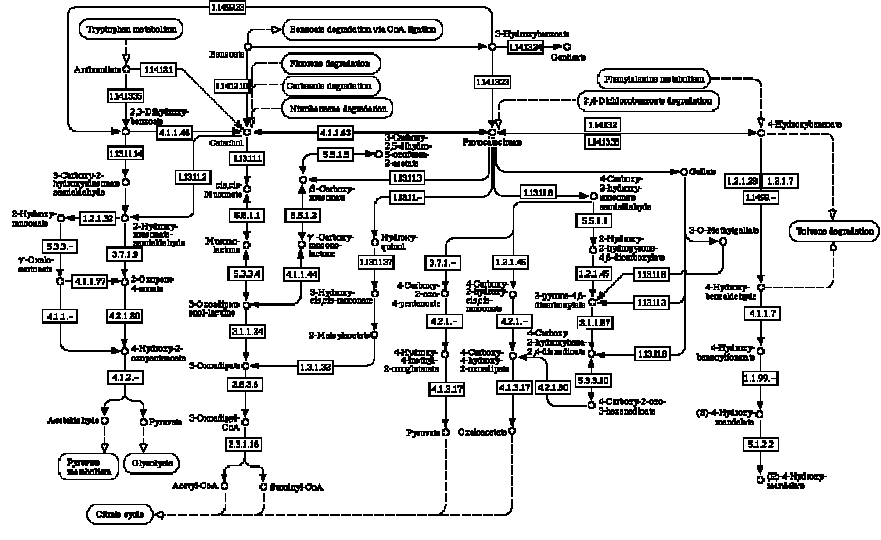
gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

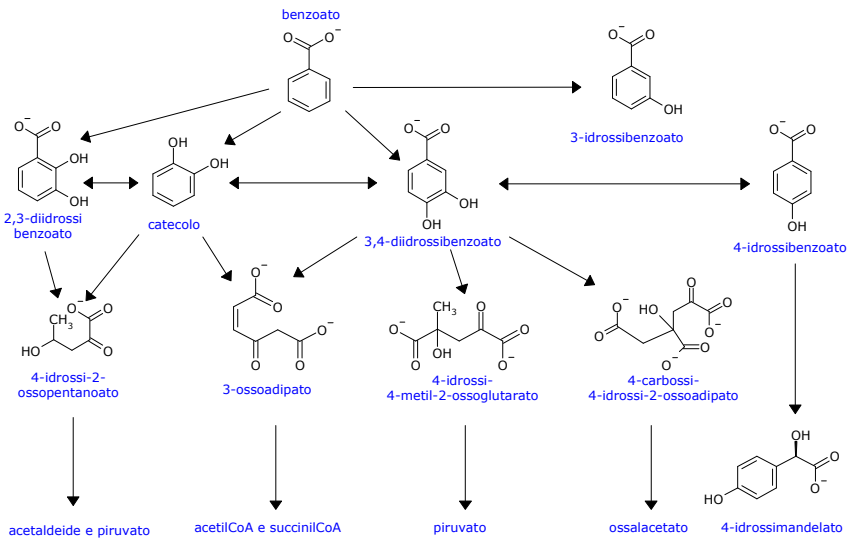
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# Schema generale

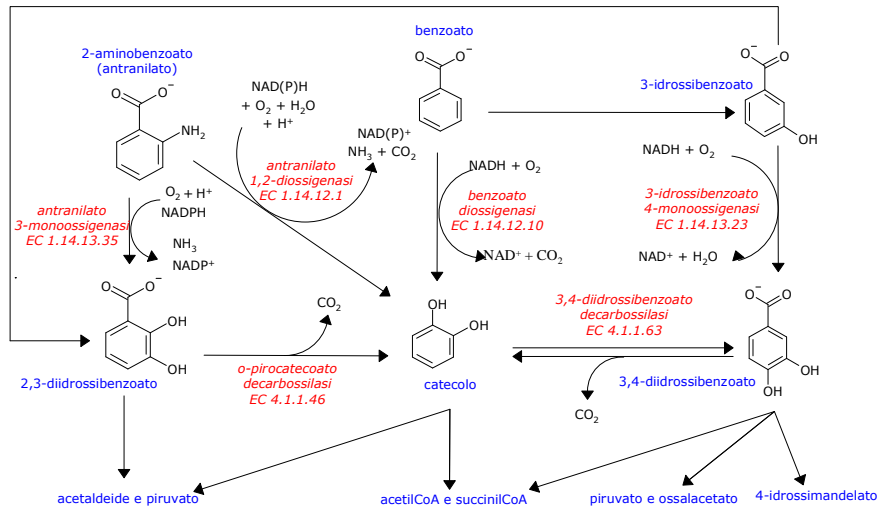


# In sintesi...



# Ossidazione del benzoato

*3-idrossibenzoato 2-monoossigenasi  
EC 1.14.99.23*

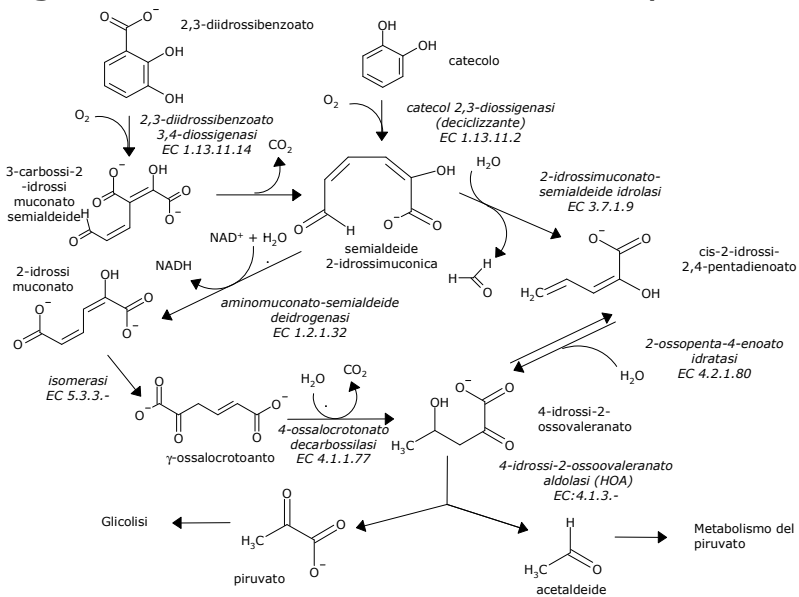


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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# Degradazione ad acetaldeide e piruvato

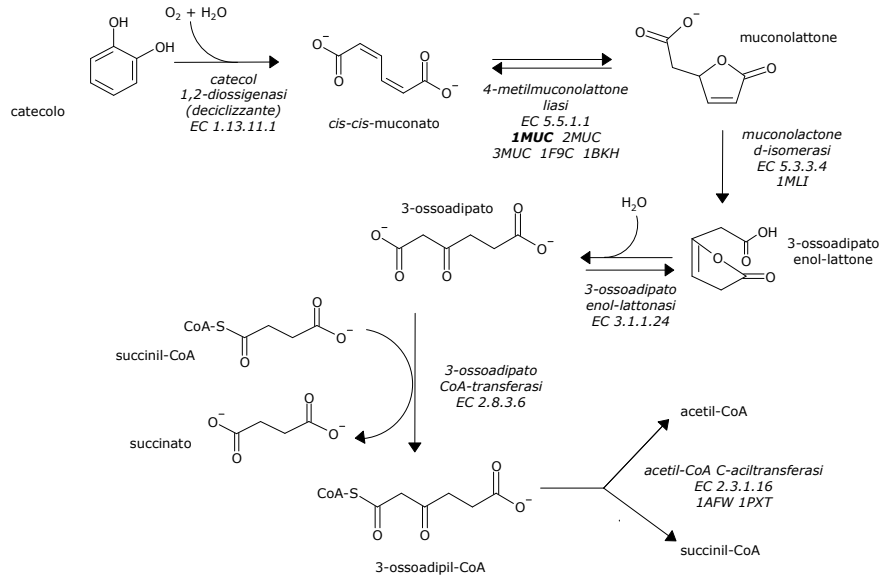


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F07 - Biotrasformazione dei composti xenobiotici

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## Da catecolo a acetilCoA e succinilCoA

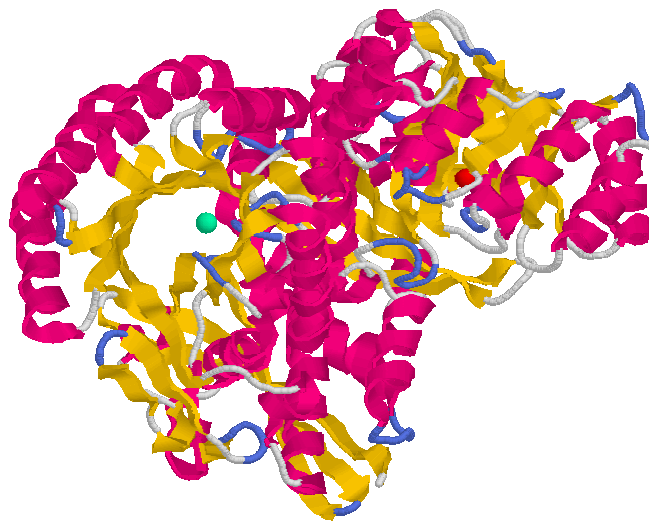


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## 4-metilmuconolattone liasi EC 5.5.1.1 (1MUC)

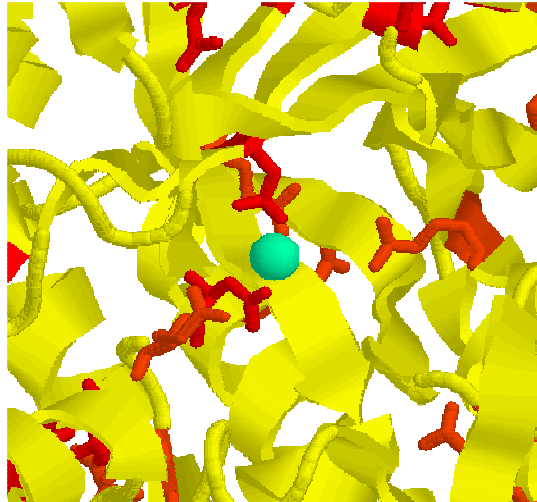


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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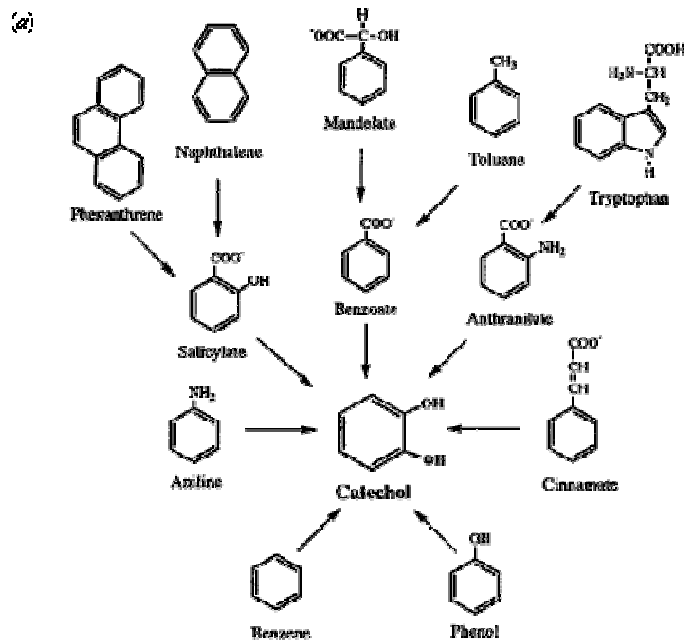
## 4-metilmuconolattone liasi EC 5.5.1.1 (1MUC)



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F07 - Biotrasformazione dei composti xenobiotici

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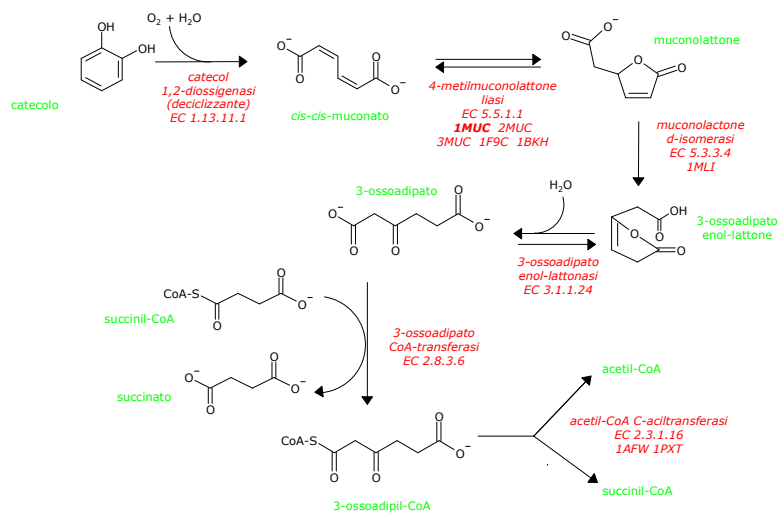


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Da catecolo a acetilCoA e succinilCoA

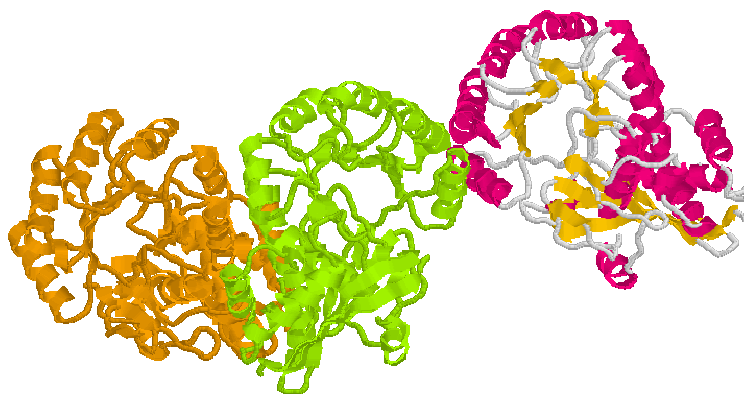


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## 4-metilmuconolattone liasi EC 5.5.1.1 (1BKH)

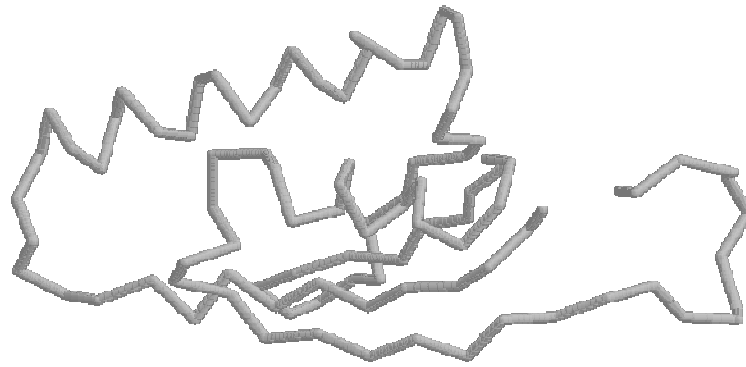


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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Muconolactone  $\delta$ -isomerasi  
*EC 5.3.3.4 (1MLI)*

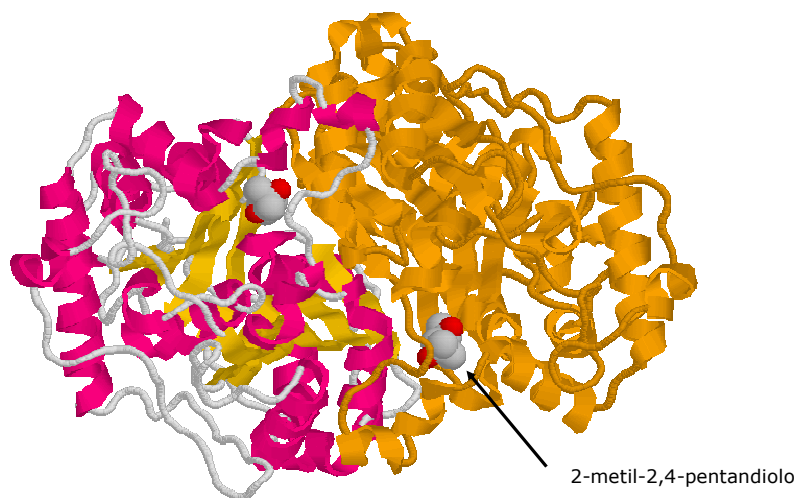


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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Acetil-CoA C-aciltransferasi  
*EC 2.3.1.16 (1AFW)*

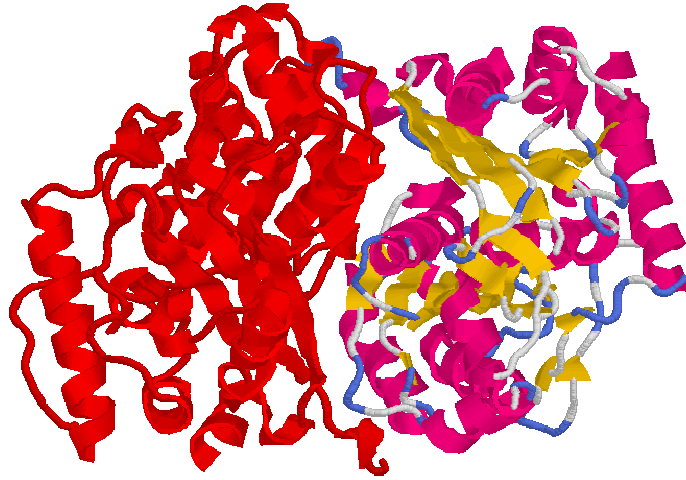


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F07 - Biotrasformazione dei composti xenobiotici

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## Acetil-CoA C-aciltransferasi EC 2.3.1.16 (1PXT)

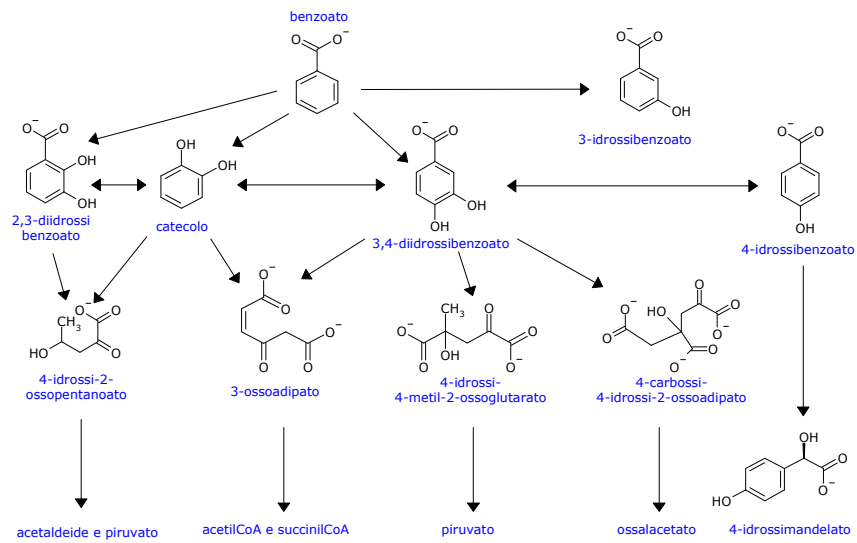


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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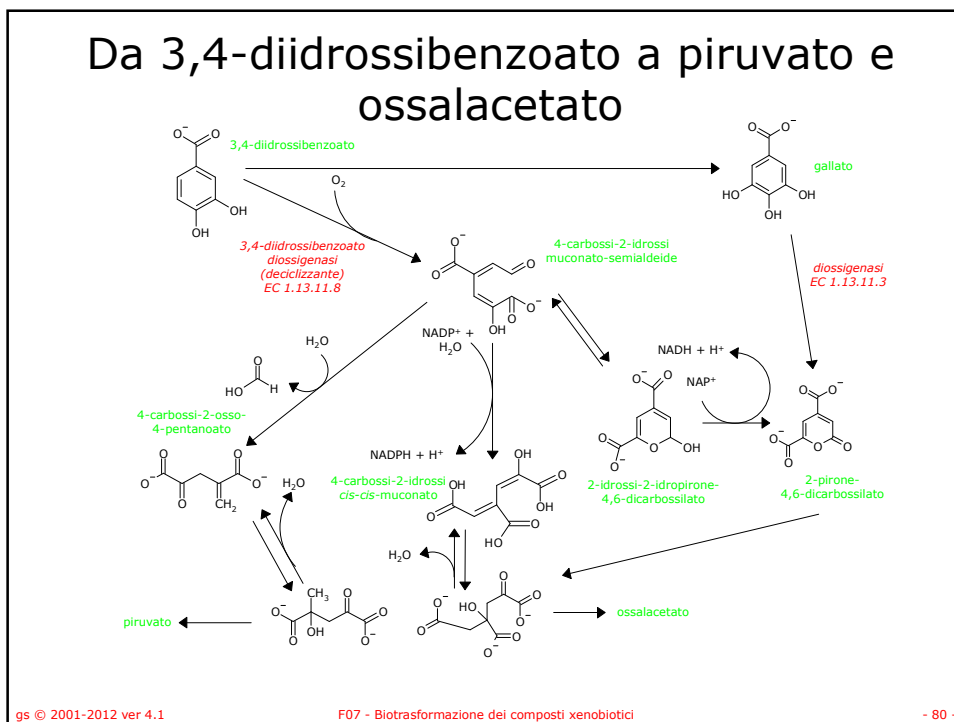
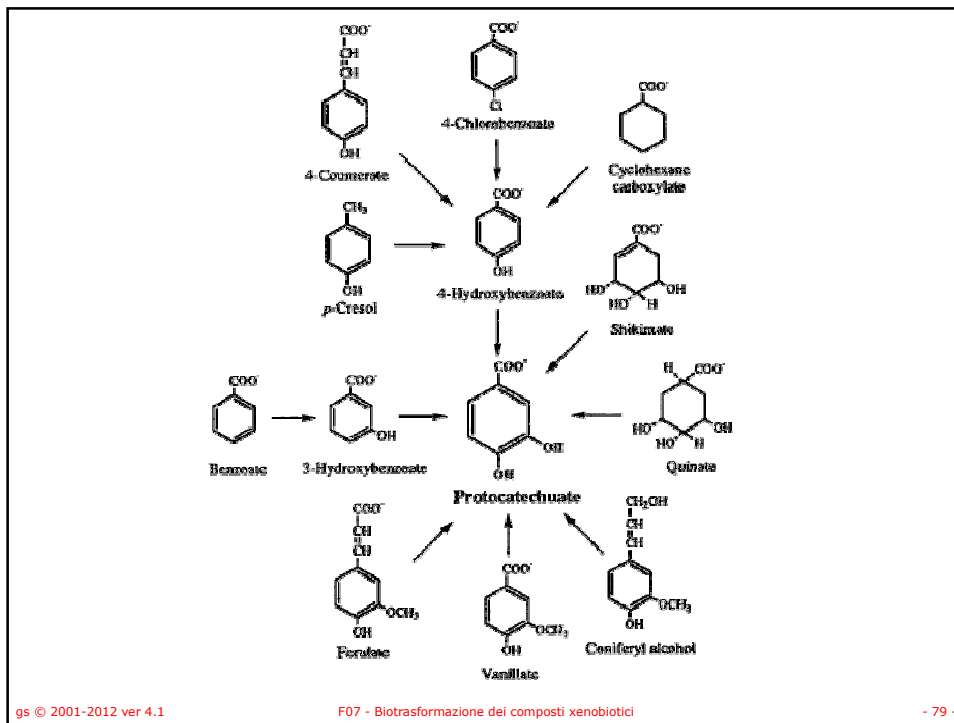
## In sintesi...



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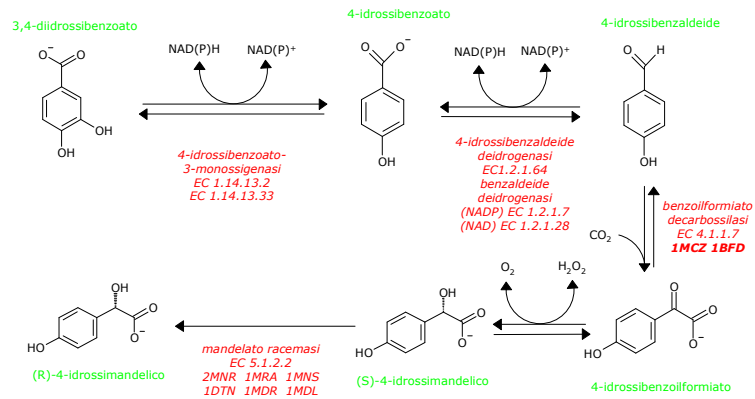
F07 - Biotrasformazione dei composti xenobiotici

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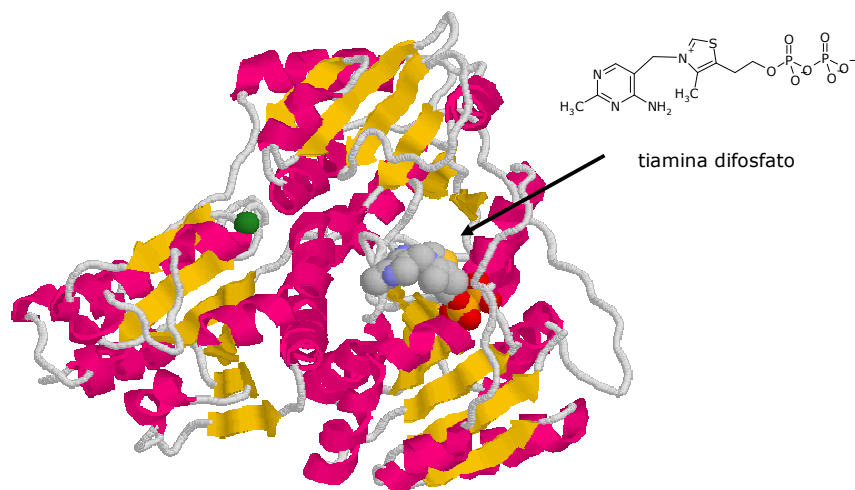




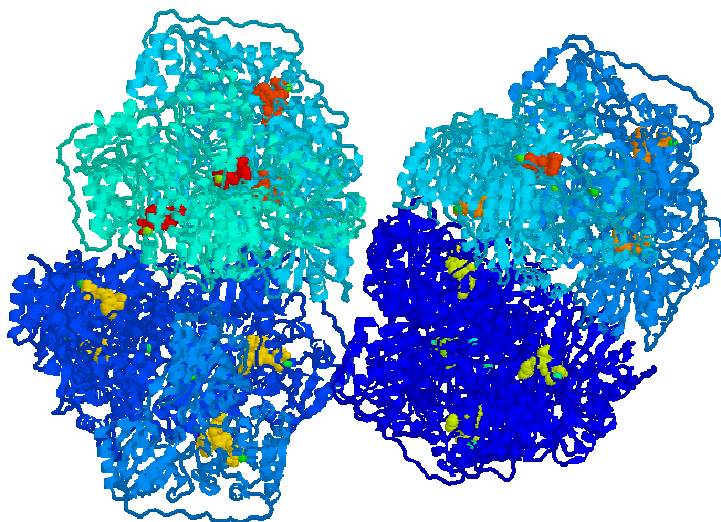
## Da 3,4-diidrossibenzoato a (R)-4-idrossimandelato



## Benzoilformiato decarbossilasi EC 4.1.1.7 (1BFD)



## Benzoilformiato decarbossilasi *EC 4.1.1.7 (1MCZ)*

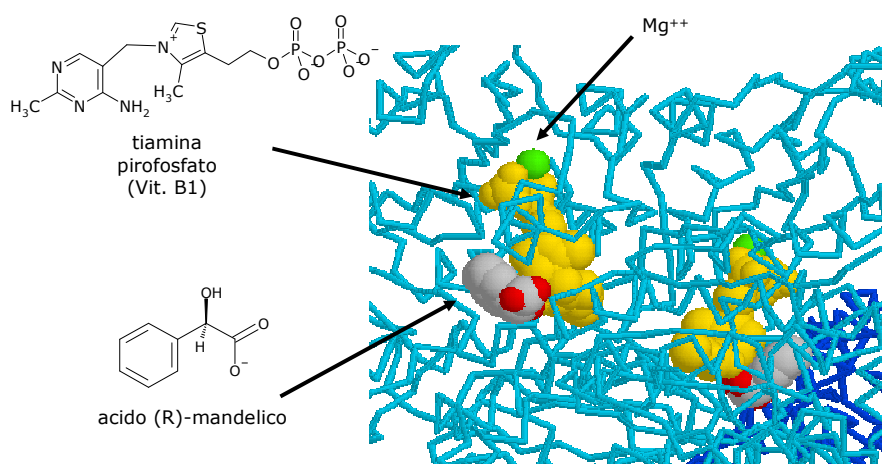


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## Benzoilformiato decarbossilasi *EC 4.1.1.7 (1MCZ)*

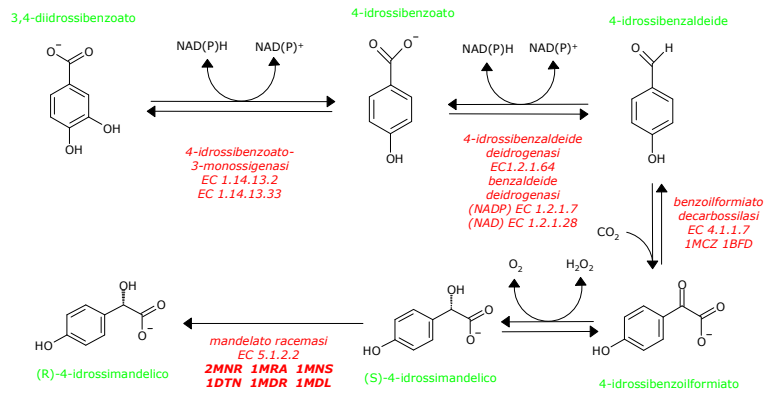


gs © 2001-2012 ver 4.1

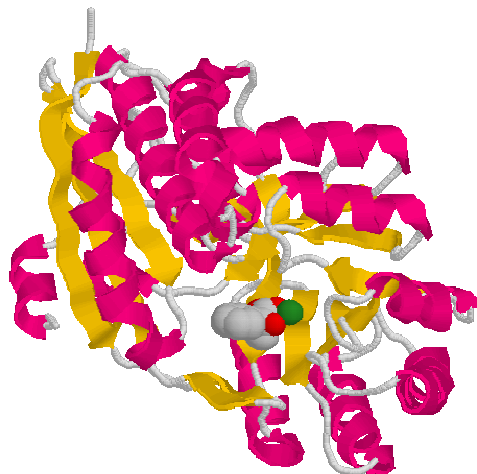
F07 - Biotrasformazione dei composti xenobiotici

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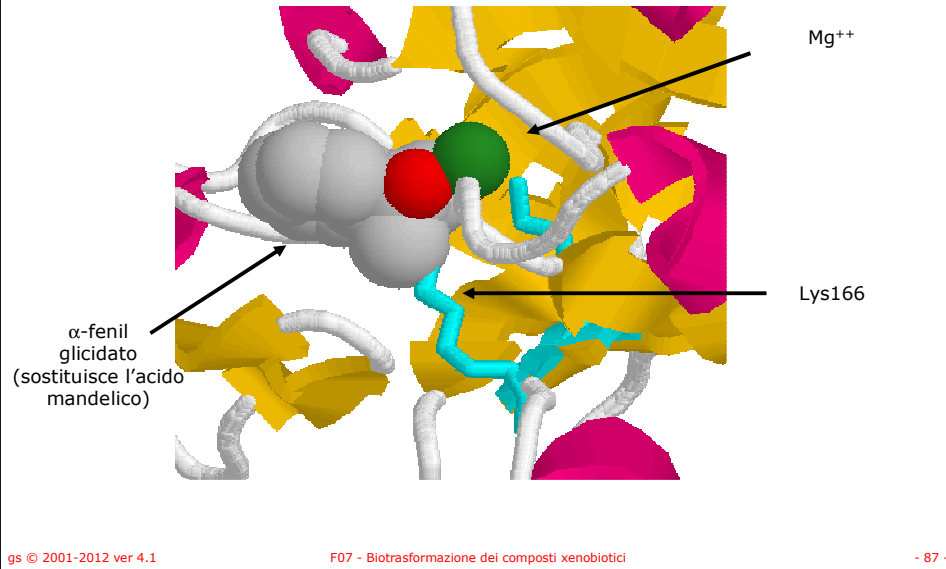
## Da 3,4-diidrossibenzoato a 4-idrossimandelato



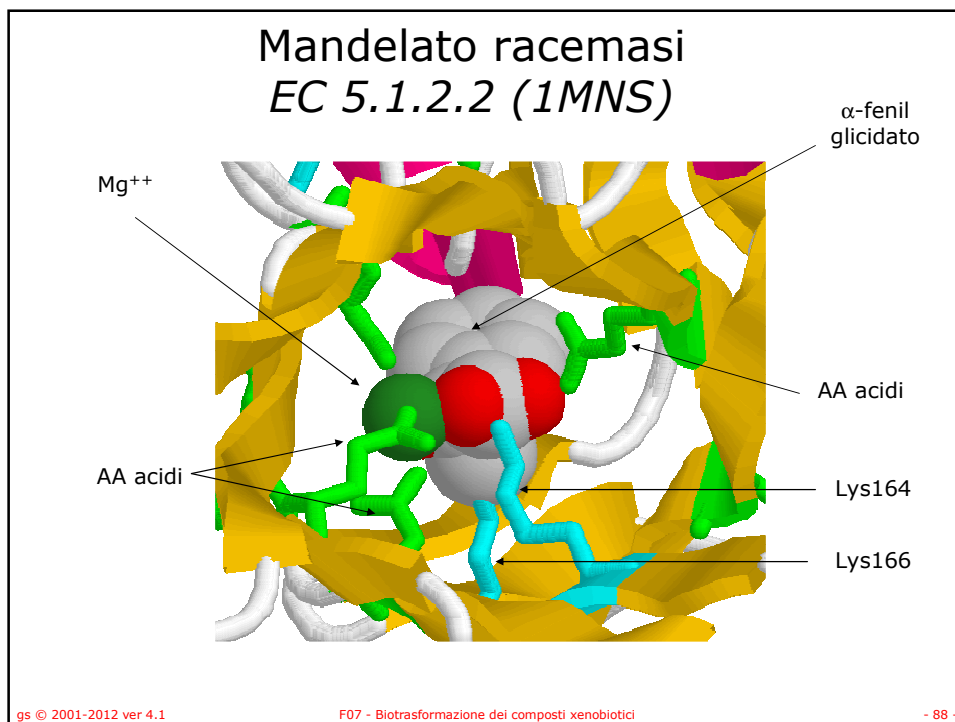
## Mandelato racemasi EC 5.1.2.2 (1MNS)



## Mandelato racemasi EC 5.1.2.2 (1MNS)

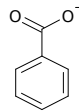


## Mandelato racemasi EC 5.1.2.2 (1MNS)

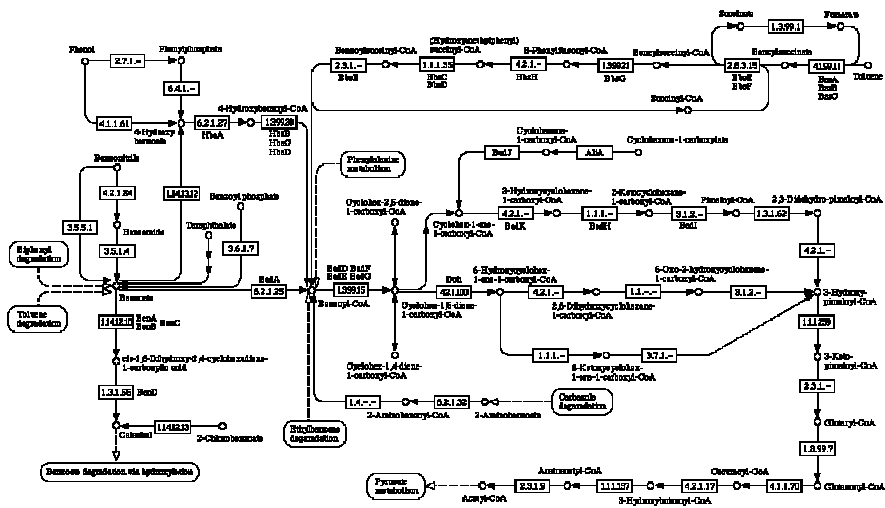


# Composti aromatici

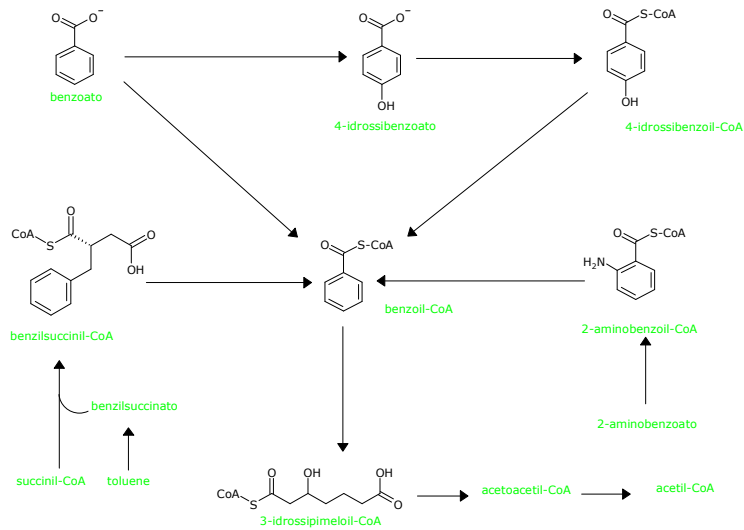
- Benzene, naftalene e fenantrene
- Fluorene e derivati
- Bifenile
- Ftalati
- Benzoato
  - *idrossilazione*
  - *coniugazione con CoA*



# Schema generale



## In sintesi...



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F07 - Biotrasformazione dei composti xenobiotici

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## Composti aromatici

- Toluene e xilene
- Carbazolo
- Stirene
- Etilbenzene
- Atrazina
- Caprolattame

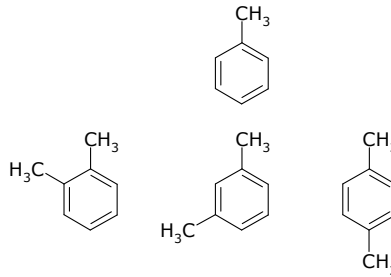
gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

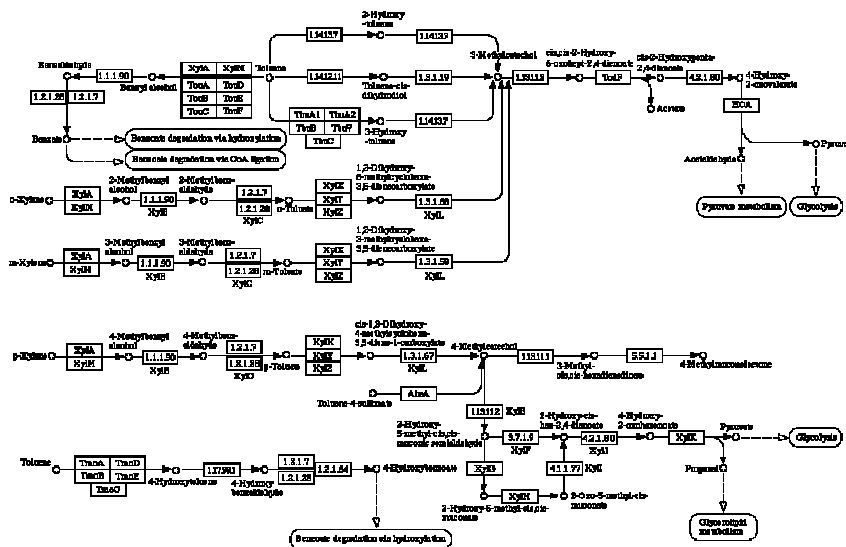
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# Composti aromatici

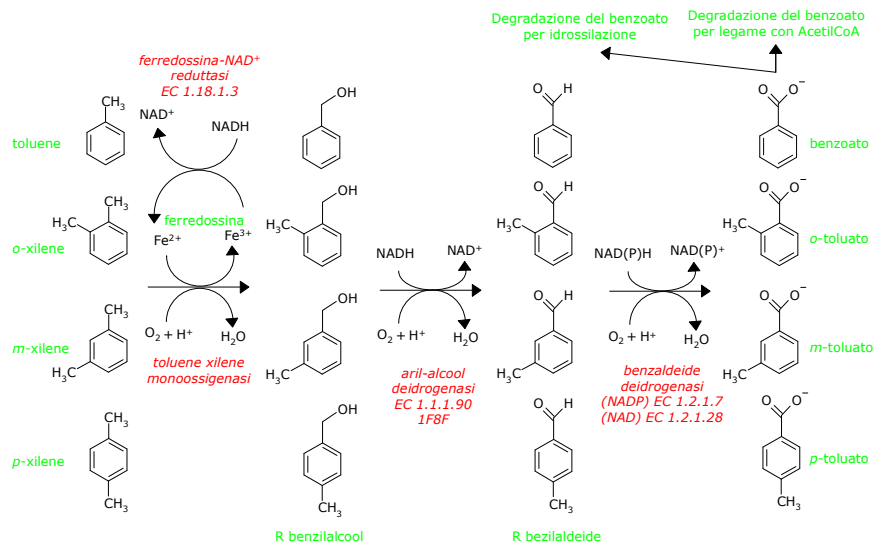
- Toluene e xilene
- Carbazolo
- Stirene
- Etilbenzene
- Atrazina
- Caprolattame



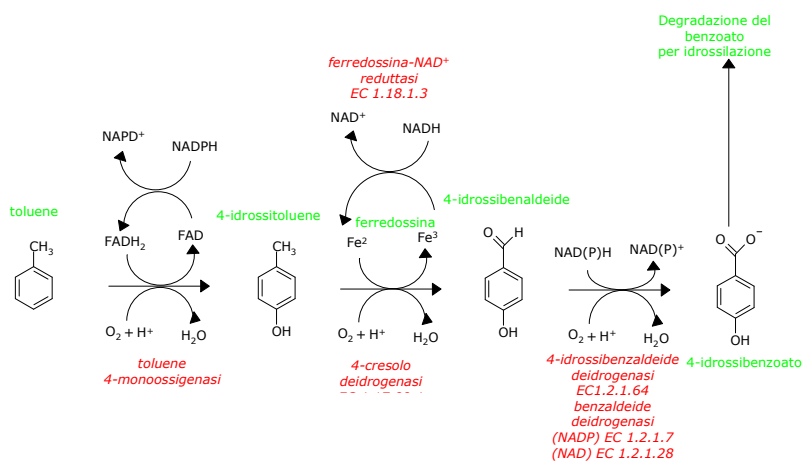
# Schema generale



## Ossidazione di toluene e xilene

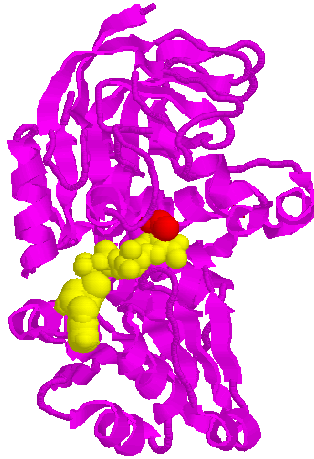


## Ossidazione del toluene





Benzilalcool deidrogenasi  
*EC 1.1.1.90 (1F8F)*

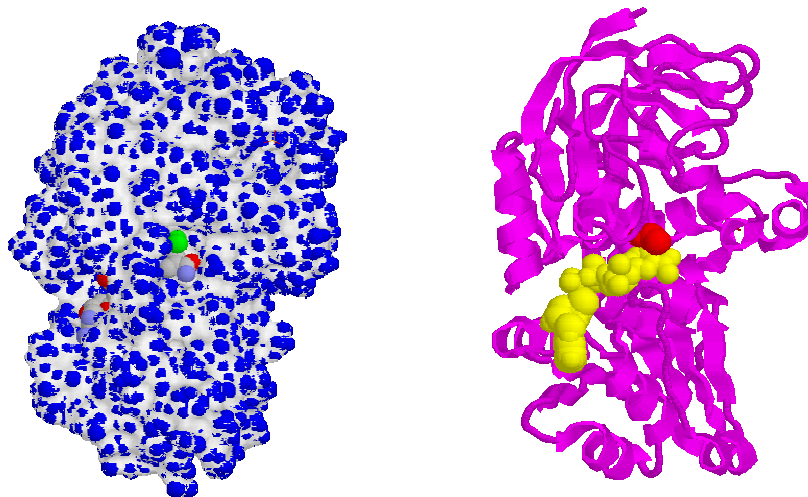


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F07 - Biotrasformazione dei composti xenobiotici

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Benzilalcool deidrogenasi  
*EC 1.1.1.90 (1F8F)*

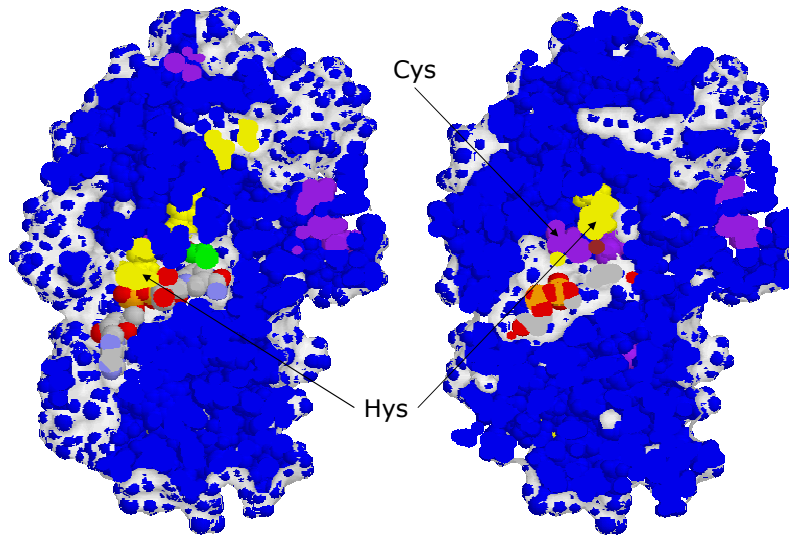


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Benzilalcol deidrogenasi EC 1.1.1.90 (1F8F)

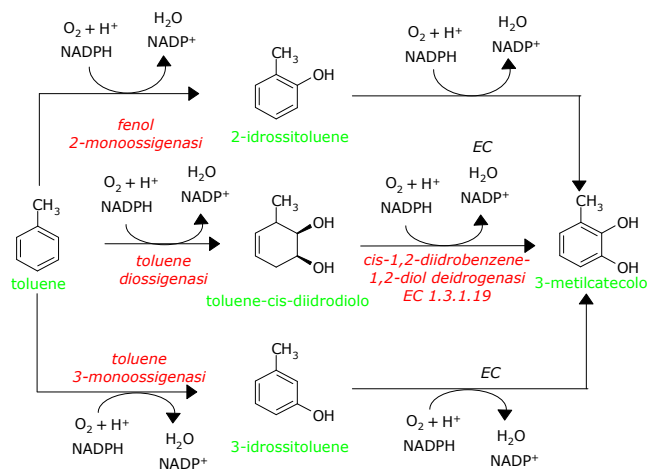


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Da toluene a 3-metilcatecolo

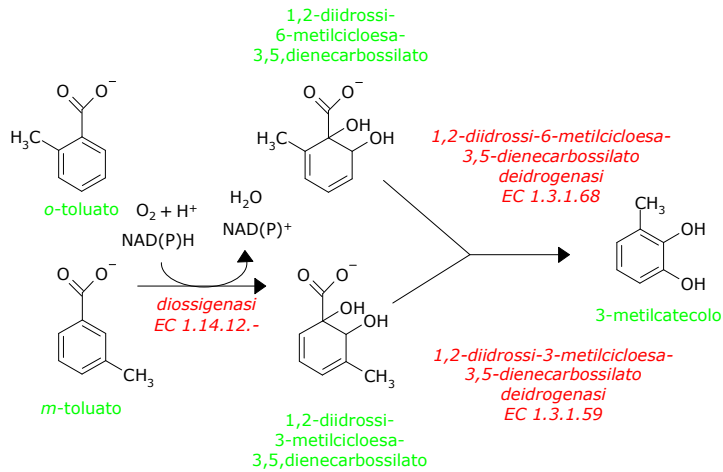


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F07 - Biotrasformazione dei composti xenobiotici

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## Da *o*-toluato e *m*-toluato a 3-metilcatecolo

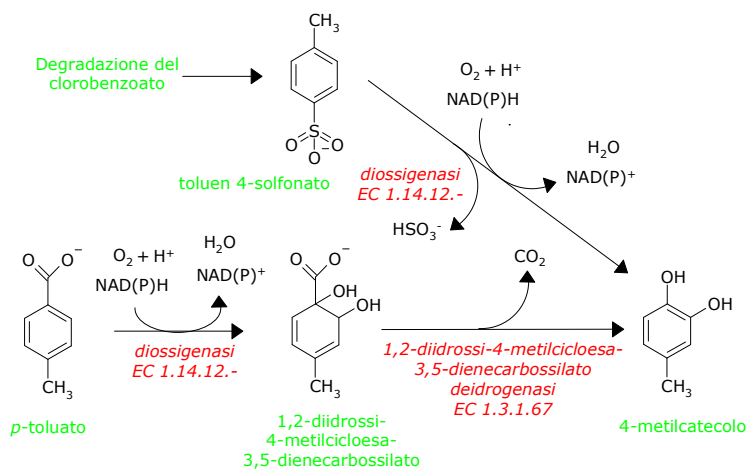


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Da *p*-toluato a 4-metilcatecolo

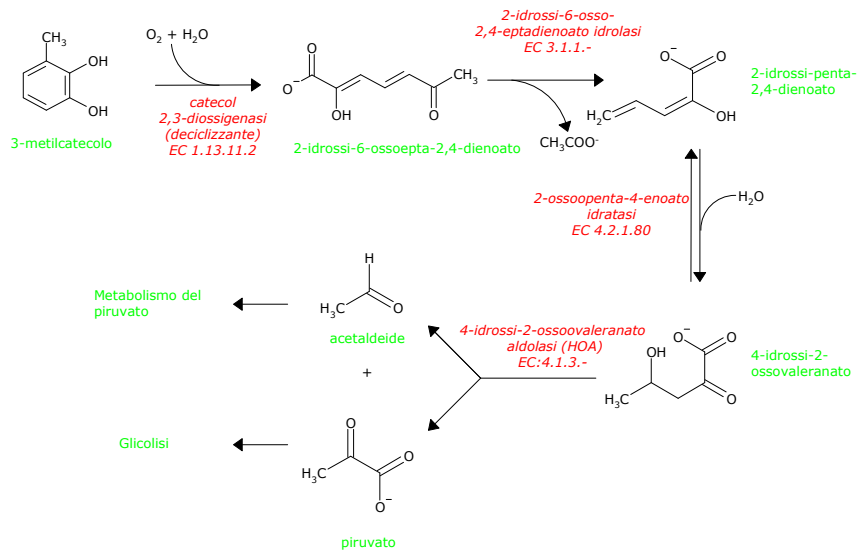


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Da 3-metilcatecolo a piruvato ed acetaldeide

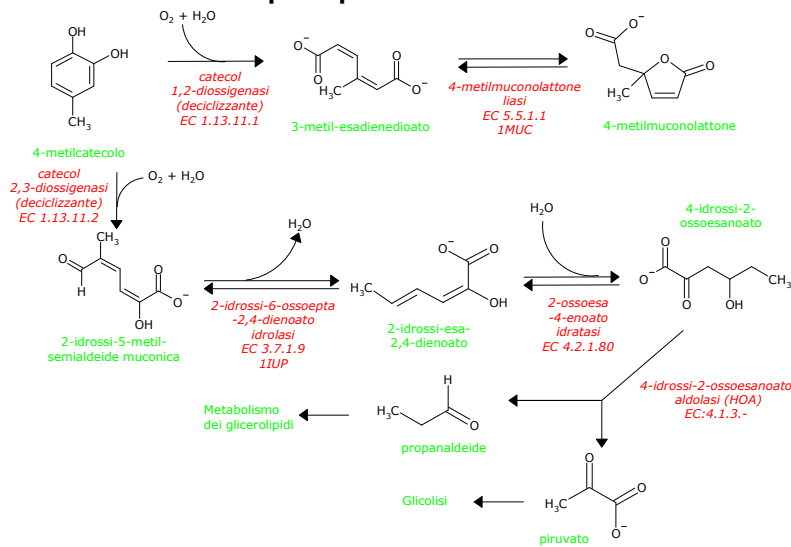


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Da 4-metilcatecolo a piruvato e propanaldeide

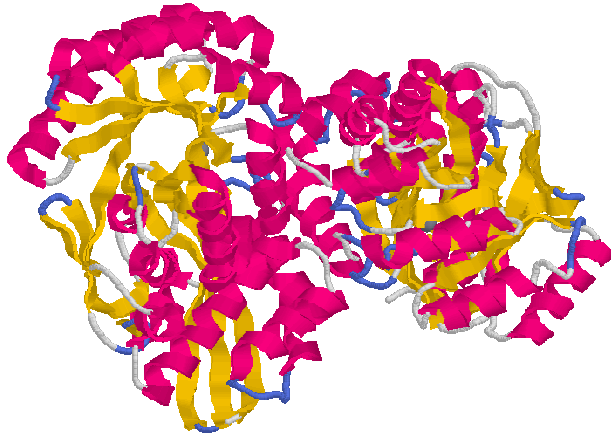


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F07 - Biotrasformazione dei composti xenobiotici

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## 4-metilmuconolattone liasi EC 5.5.1.1 (1MUC)



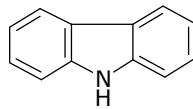
gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Composti aromatici

- Toluene e xilene
- **Carbazolo**
- Stirene
- Etilbenzene
- Atrazina
- Caprolattame

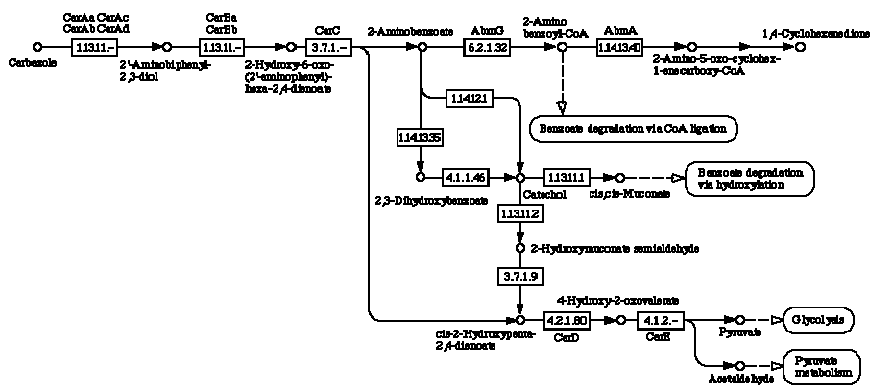


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Schema generale

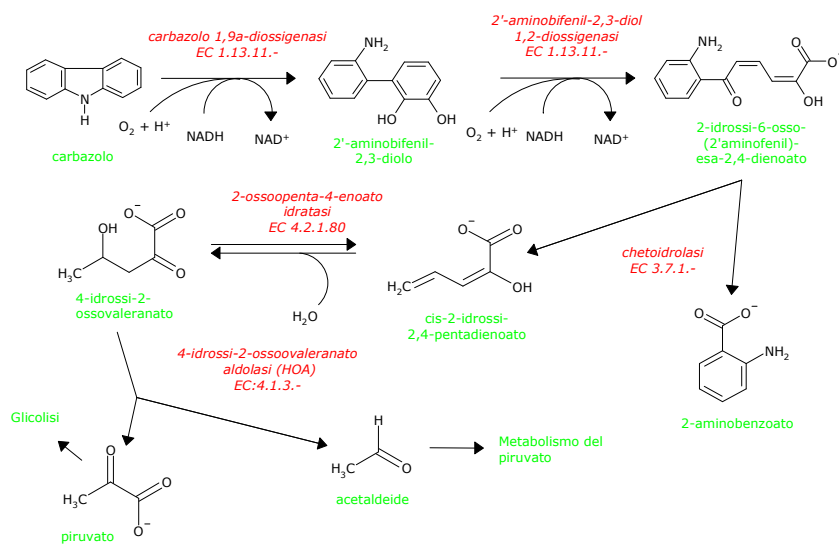


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Ossidazione e scissione del carbazolo

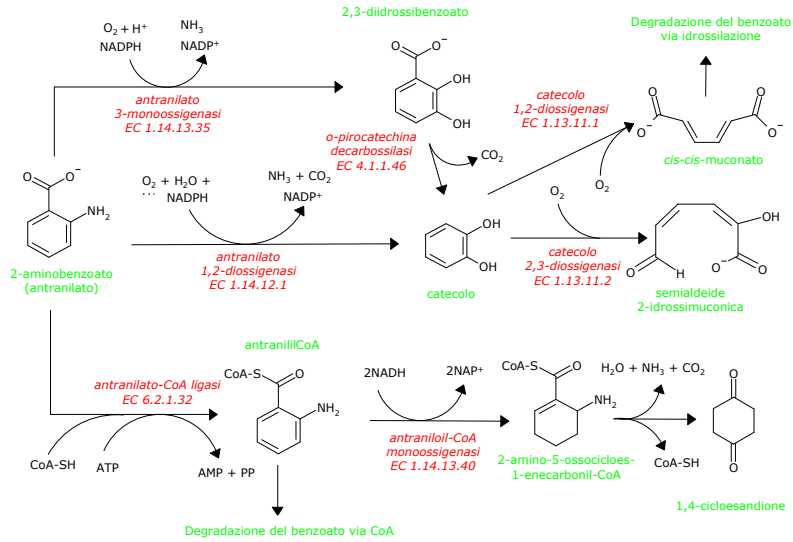


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Destino del 2-aminobenzoato

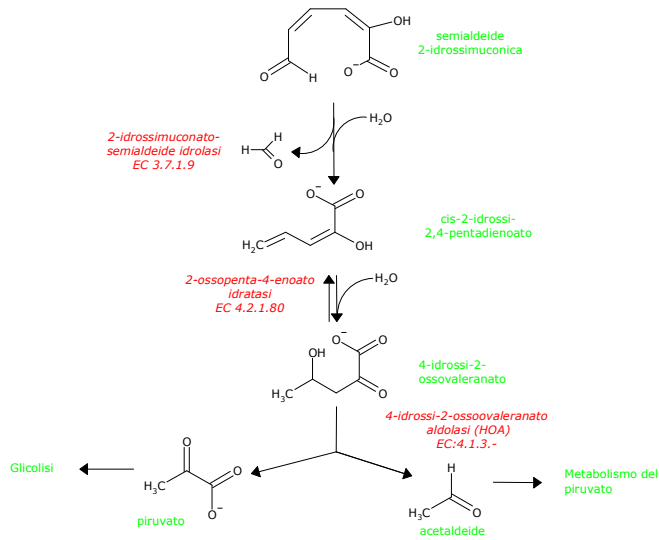


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Destino della semialdeide 2-idrossimuconica



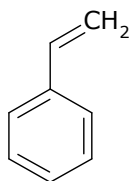
gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

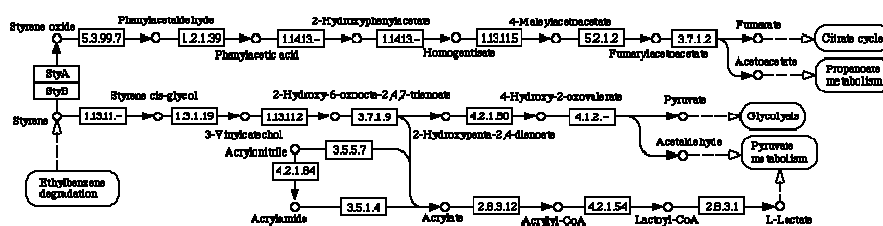
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## Composti aromatici

- Toluene e xilene
- Carbazolo
- **Stirene**
- Etilbenzene
- Atrazina
- Caprolattame

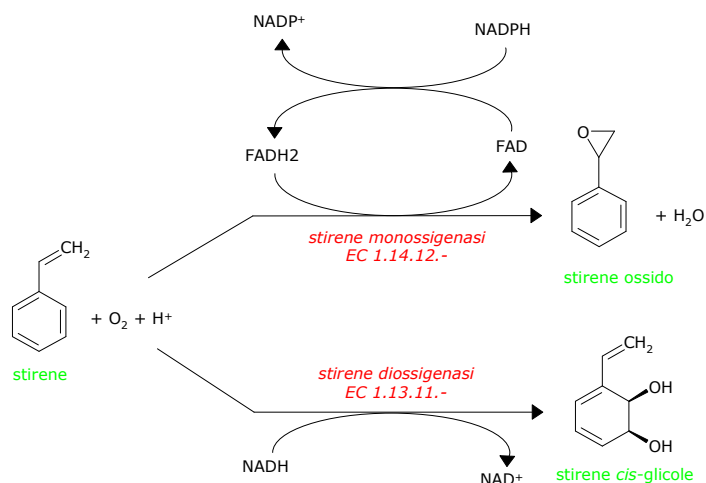


## Schema generale





## Ossidazione dello stirene

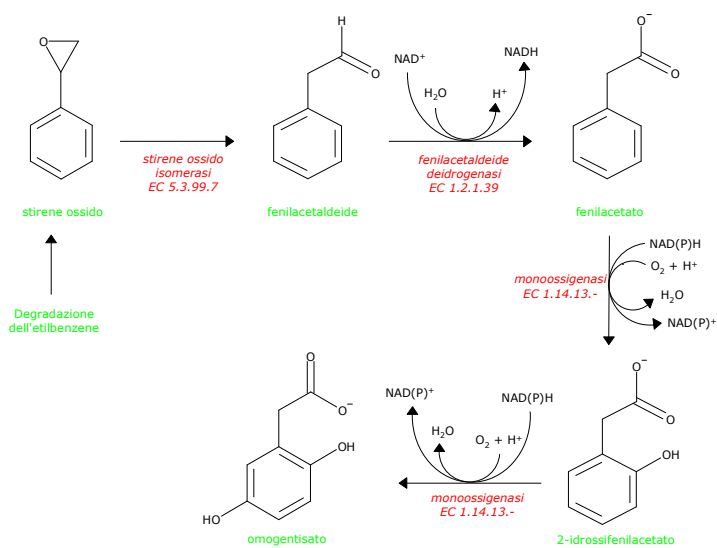


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Da stirene ossido a omogentisato

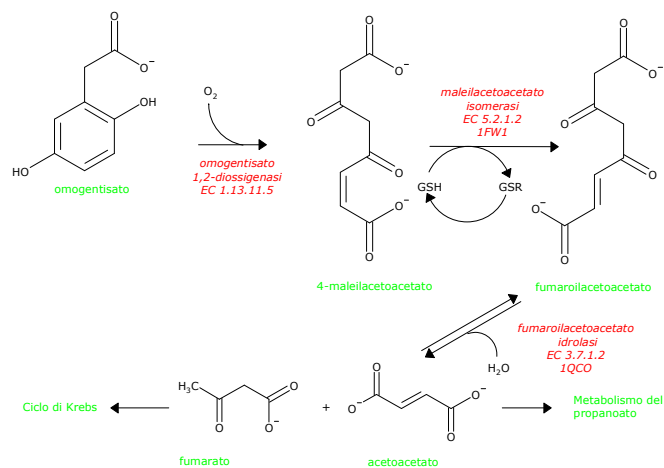


gs © 2001-2012 ver 4.1

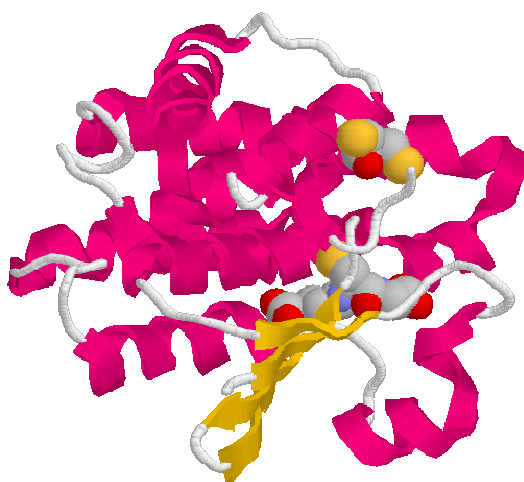
F07 - Biotrasformazione dei composti xenobiotici

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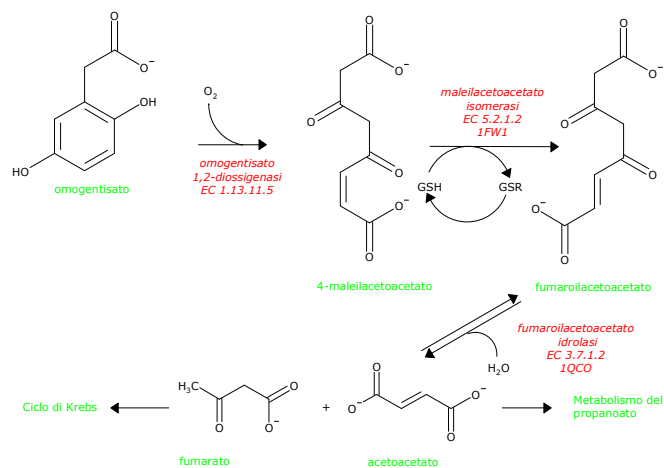
## Scissione dell'omogentisato



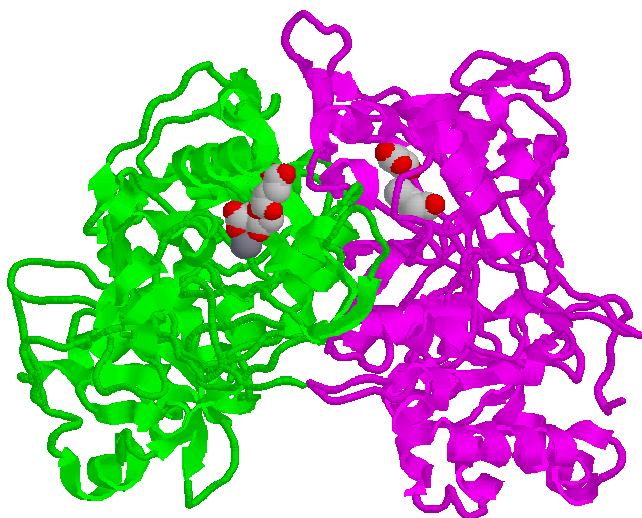
## Maleilacetoacetato isomerasi EC 5.2.1.2 (1FW1)



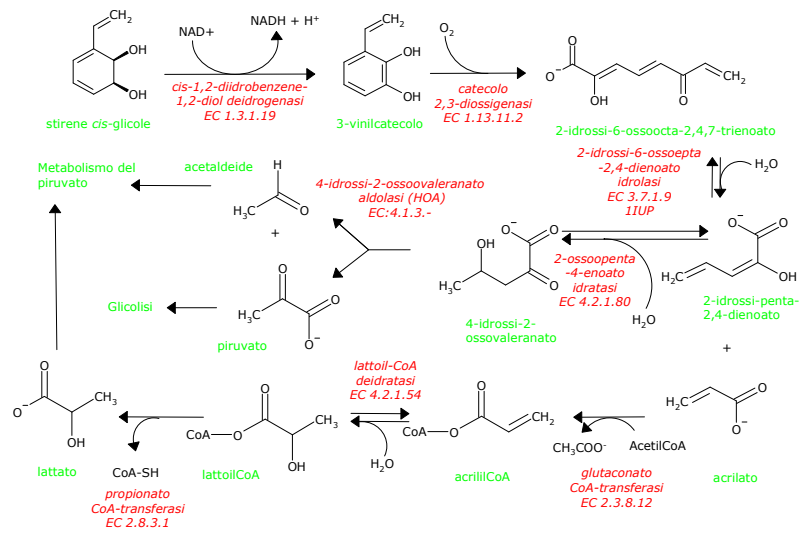
## Scissione dell'omogentisato



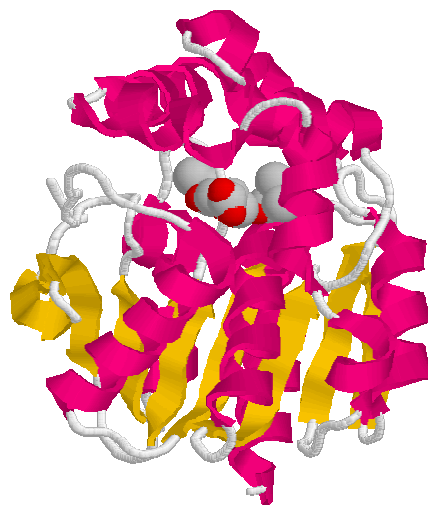
## Fumaroilacetoacetato idrolasi EC 3.7.1.2 (1QCO)



## Da stirene *cis*-glicole a lattato, piruvato ed acetaldeide

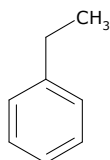


## 2-idrossi-6-ossoepta-2,4-dienoatoidrolasi EC 3.7.1.9 (1IUP)



## Composti aromatici

- Toluene e xilene
- Carbazolo
- Stirene
- **Etilbenzene**
- Atrazina
- Caprolattame

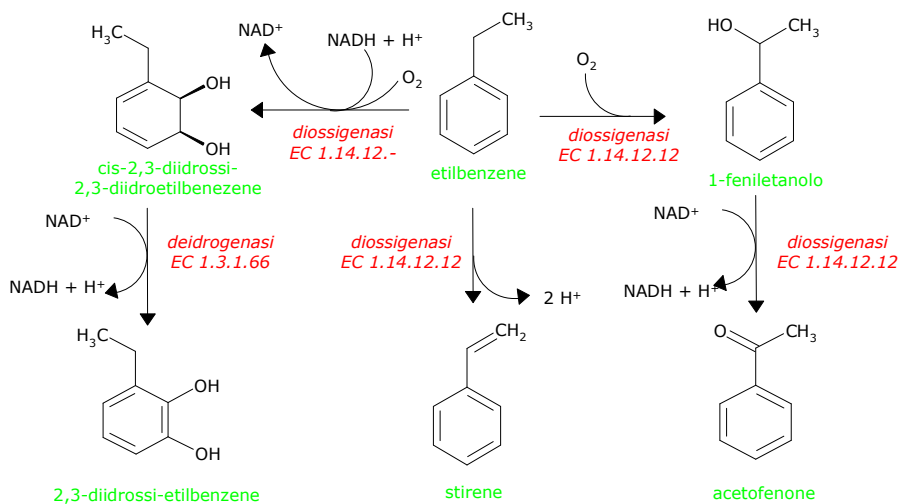


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## Ossidazione dell'etilbenzene - I

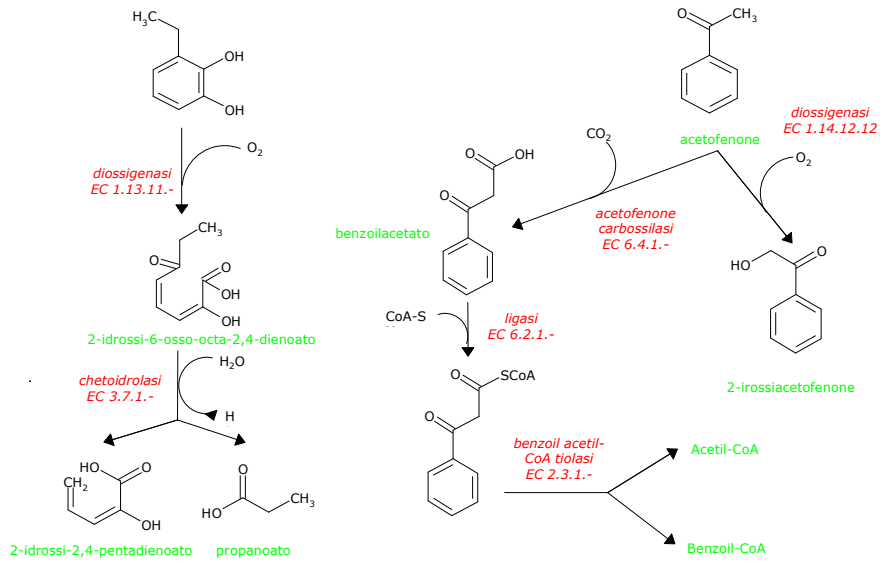


gs © 2001-2012 ver 4.1

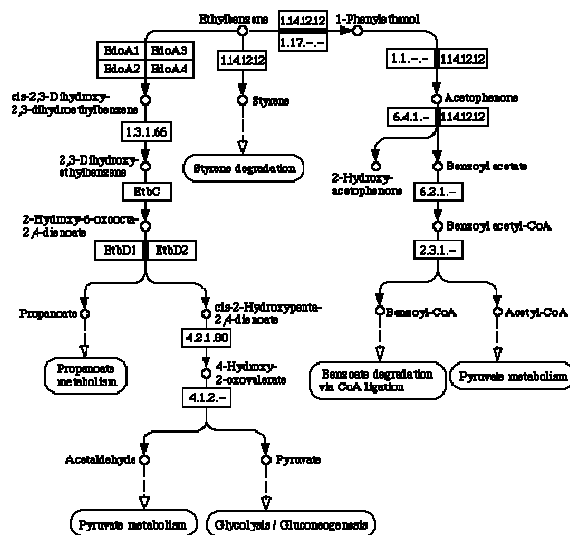
F07 - Biotrasformazione dei composti xenobiotici

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## Ossidazione dell'etilbenzene - II

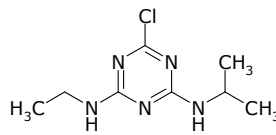


## Schema generale

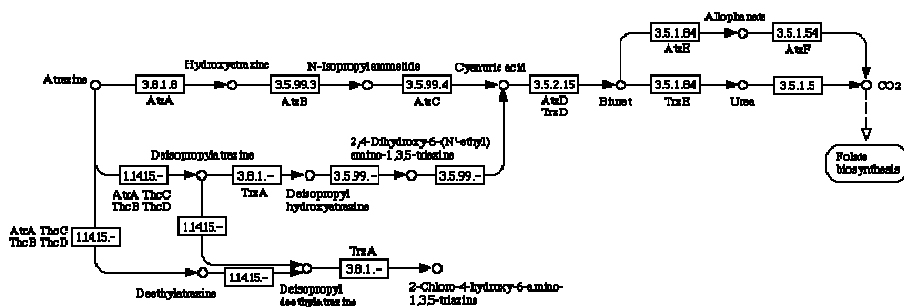


## Composti aromatici

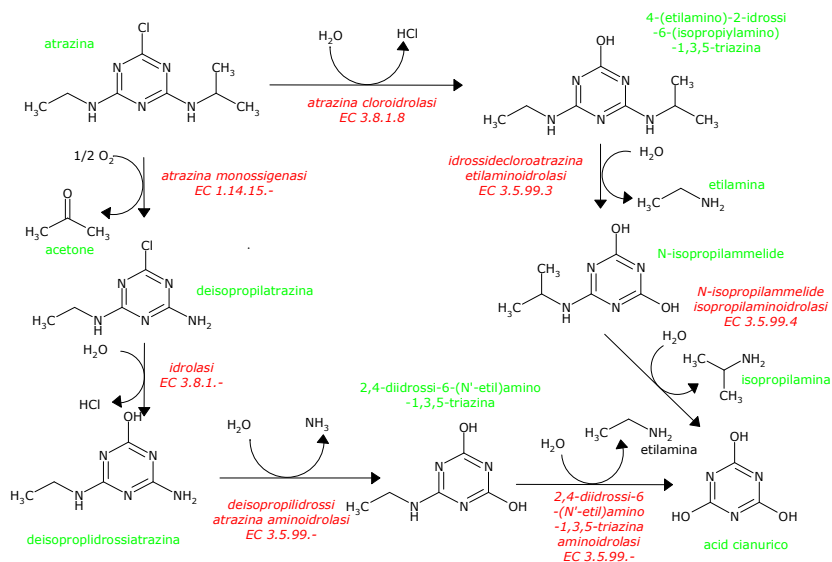
- Toluene e xilene
- Carbazolo
- Stirene
- Etilbenzene
- Atrazina
- Caprolattame



## Schema generale



## Formazione di acido cianurico

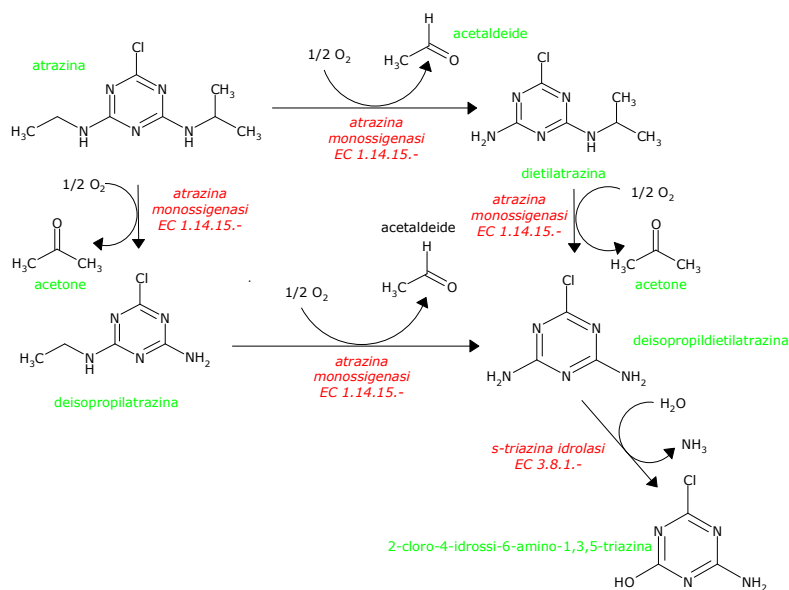


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## Via ossidativa



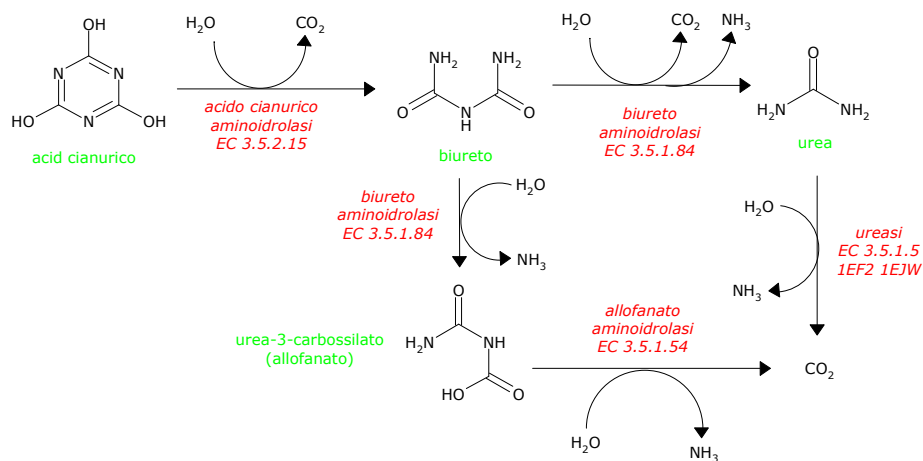
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## Destino dell'acido cianurico



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## Ureasi EC 3.5.1.15

Organismo	Subunità
Ureaplasma urealyticum	?
Glycine max	?
Brevibacterium	?
Canavalia ensiformis	?
Helicobacter pylori	?
Mycobacterium	?
Klebsiella aerogenes	10
Morus alba	2
Staphylococcus	12
Ureaplasma urealyticum	6
Spirulina maxima	6
Methylophilus	6
Helicobacter pylori	6
bacterium strain SL100	6
Ureaplasma urealyticum	5
Bacillus pasteurii	4
Brevibacterium	3

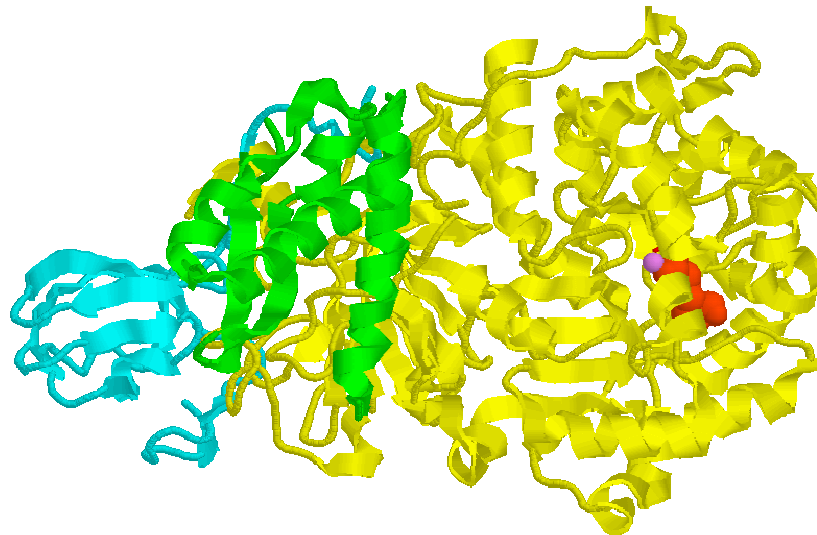
Organismo	Peso Molecolare (Kda)
Helicobacter pylori	600
Helicobacter pylori	484
Helicobacter mustelae	484
Helicobacter	484
Helicobacter felis	484
Glycine max	480
Staphylococcus	420
Staphylococcus xylosus	410
Ureaplasma urealyticum	380
Lactobacillus animalis	350
Glycine max	280
Arthrobacter oxydans	242
Spirulina maxima	232
Bacillus pasteurii	230
Klebsiella aerogenes	224
Lactobacillus fermentum	220
Lactobacillus reuteri	220
Brevibacterium	215
Streptococcus mitior	200
Methylophilus	190
Rhodobacter capsulatus	185
Mycobacterium	185
Rhodobacter capsulatus	180
Morus alba	175
Lactobacillus ruminis	150
Streptococcus salivarius	140
Bos taurus	135
Bos taurus	130
Bos taurus	125

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## Ureasi *EC 3.5.1.15 1EF2*

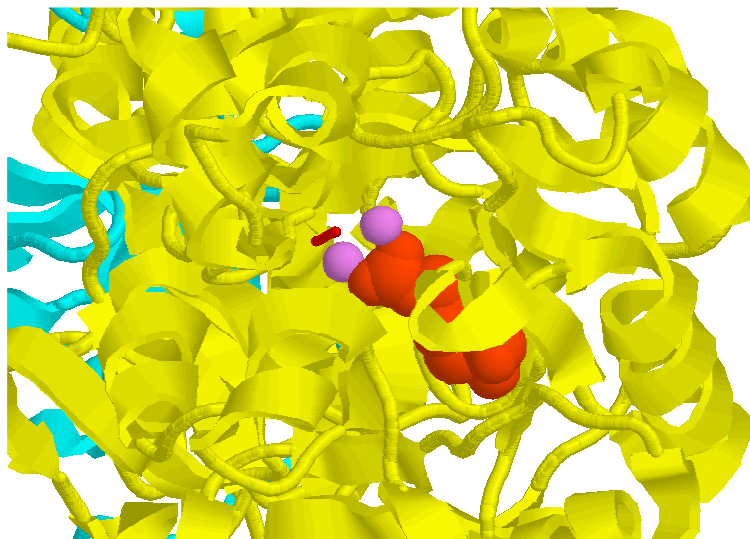


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## Ureasi *EC 3.5.1.15 1EF2*

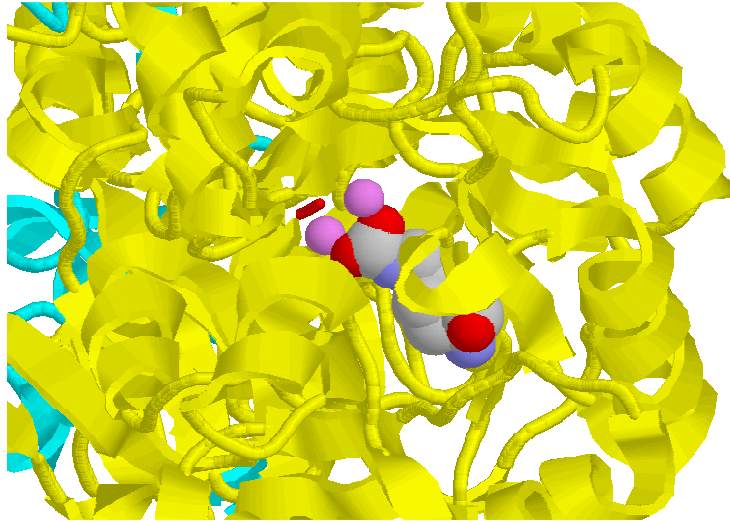


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## Ureasi *EC 3.5.1.15 1EF2*

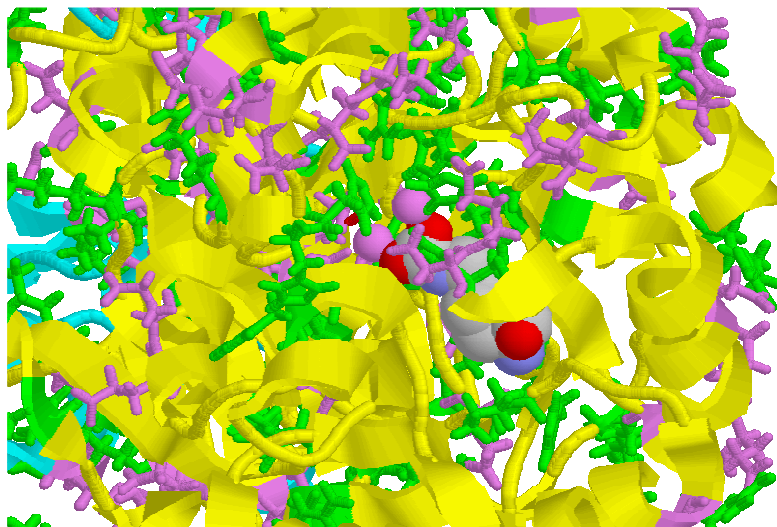


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## Ureasi *EC 3.5.1.15 1EF2*

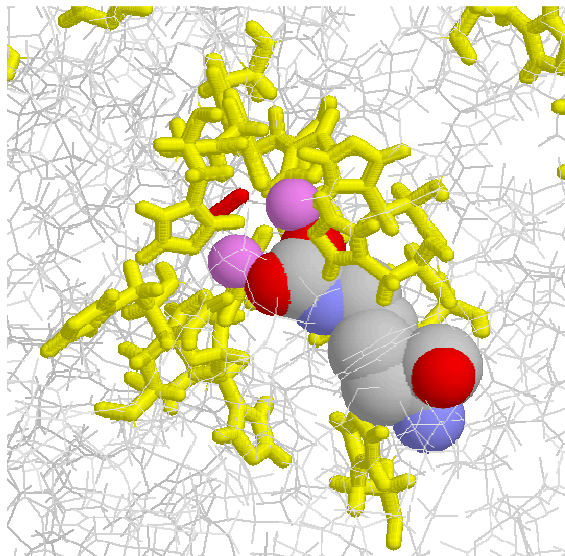


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## Ureasi *EC 3.5.1.15 1EF2*

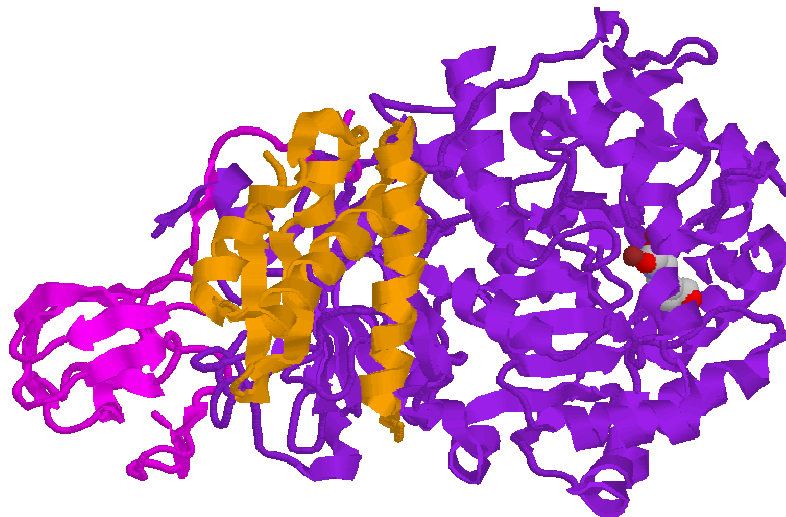


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## Ureasi *EC 3.5.1.15 1EJW (298K)*

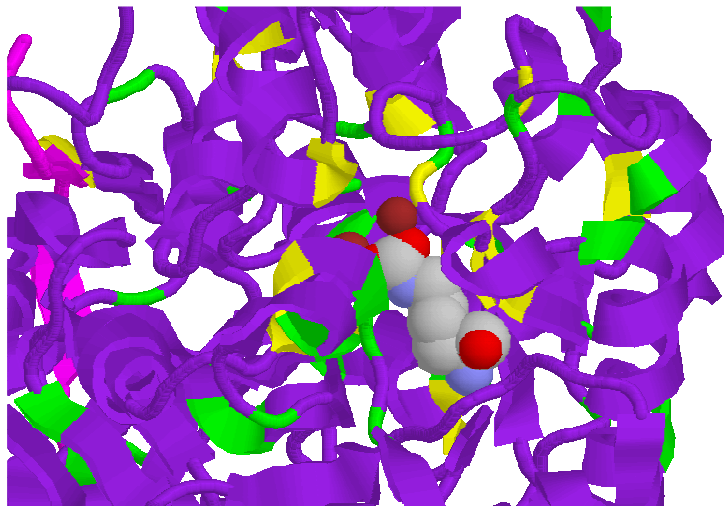


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## Ureasi *EC 3.5.1.15 1EJW*

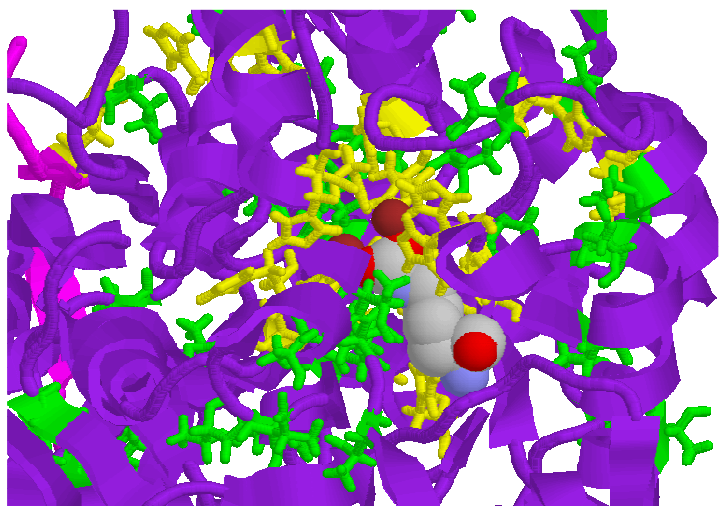


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## Ureasi *EC 3.5.1.15 1EJW*



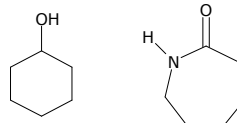
gs © 2001-2012 ver 4.1

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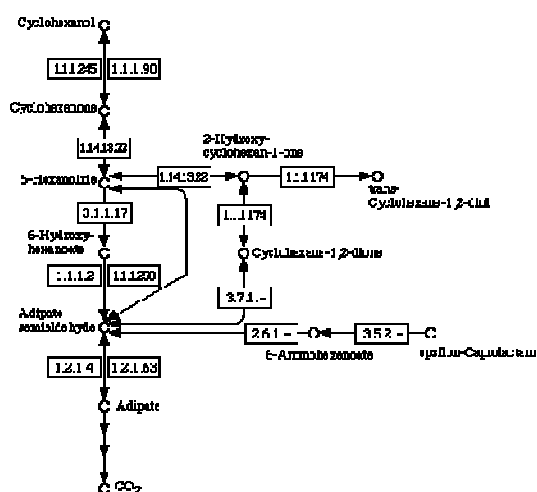
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## Composti aromatici

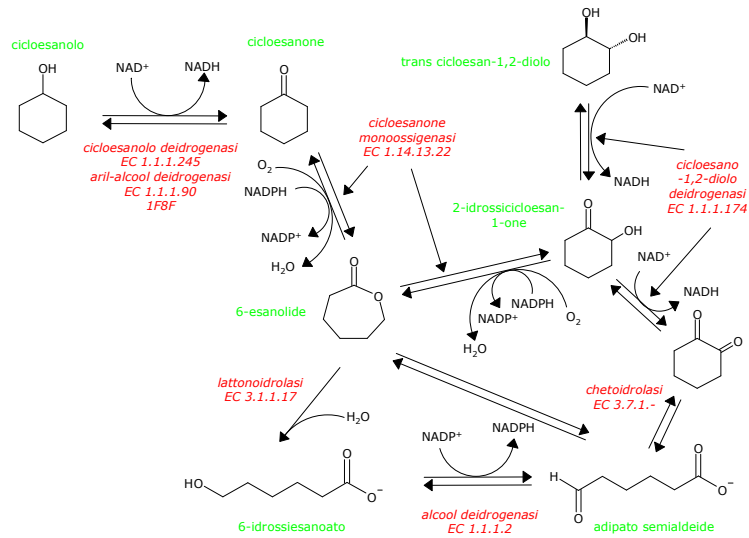
- Toluene e xilene
- Carbazolo
- Stirene
- Etilbenzene
- Atrazina
- Cicloesano e caprolattame



## Schema generale



## Da cicloesano e cicloesandiolo a adipato semiladeide

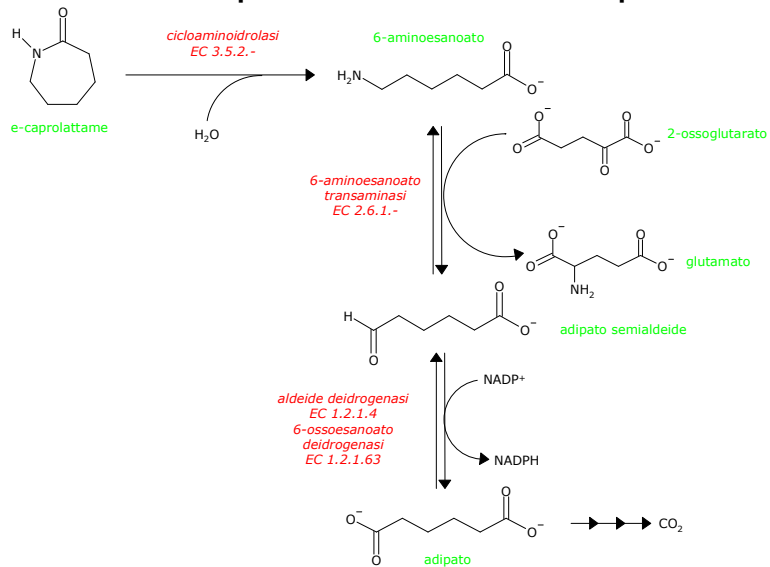


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## Da ε-caprolattame ad adipato



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F07 - Biotrasformazione dei composti xenobiotici

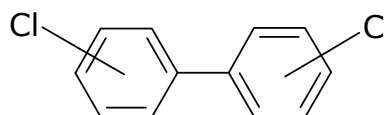
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## Composti organoclorurati e organofosfati

- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- 1,4-diclorobenzene
- 1,2-dicloroetano
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion

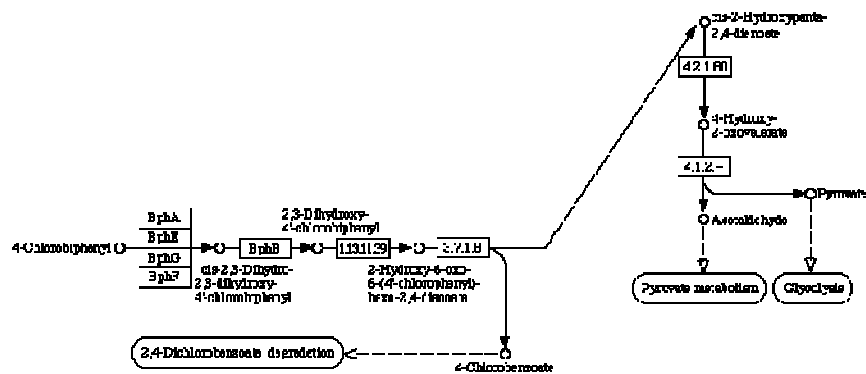
## Composti organoclorurati e organofosfati

- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- 1,4-diclorobenzene
- 1,2-dicloroetano
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion





## Schema generale – bifenile e PCB

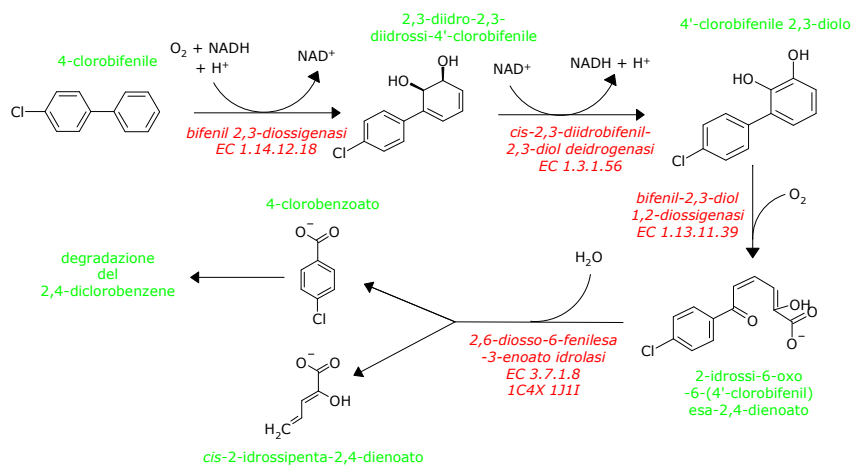


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## Scissione del 4-clorobifenile

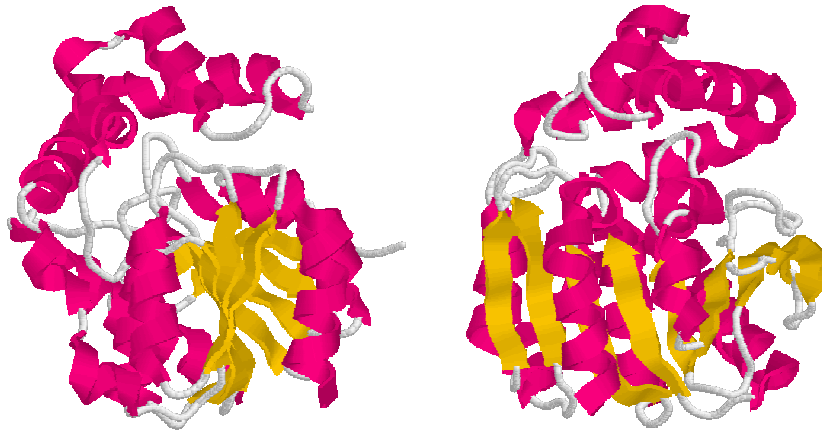


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2,6-diosso-6-fenilesa-3-enoato  
idrolasi *EC 3.7.1.8 (1C4X)*

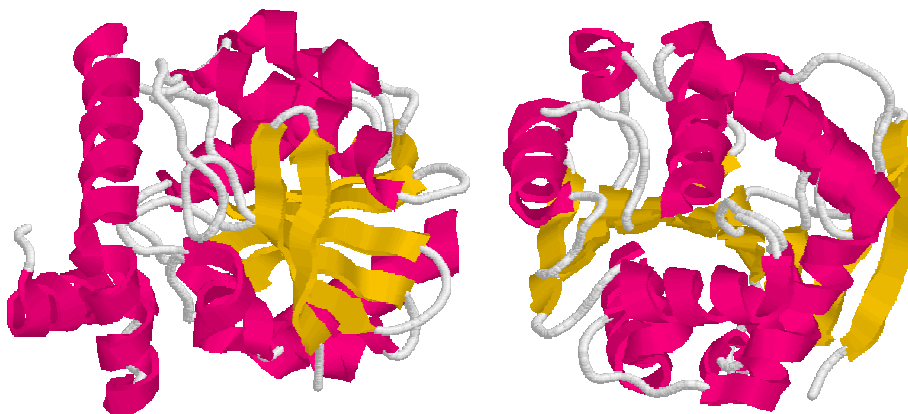


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2,6-diosso-6-fenilesa-3-enoato  
idrolasi *EC 3.7.1.8 (1J1I)*

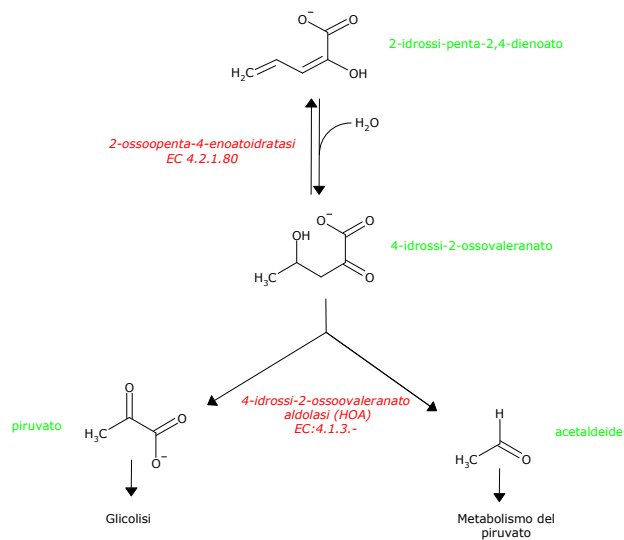


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## Scissione del 2-idrossi-2,4-pentadienoato



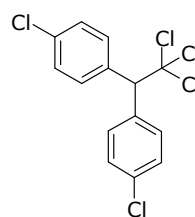
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## Composti organoclorurati e organofosfati

- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- 1,4-diclorobenzene
- 1,2-dicloroetano
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion



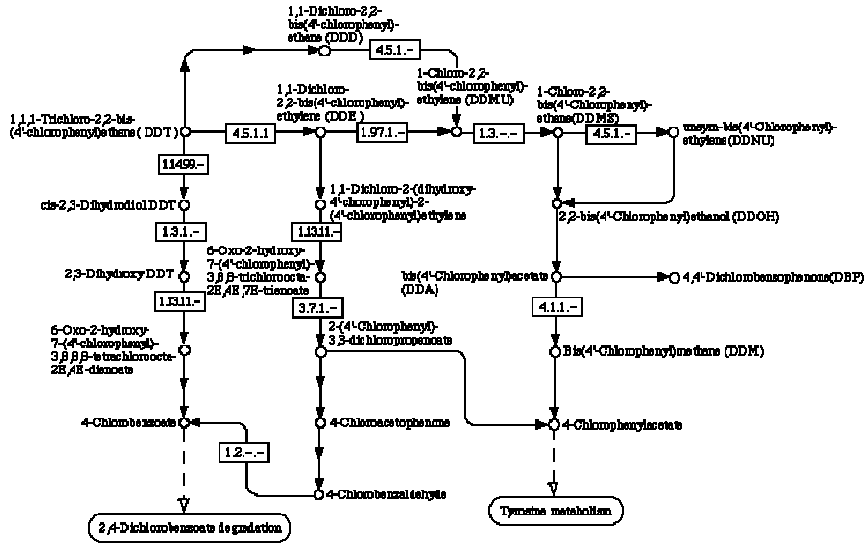
1,1,1-tricloro-2,2-bis-(4'-clorofenil)etano

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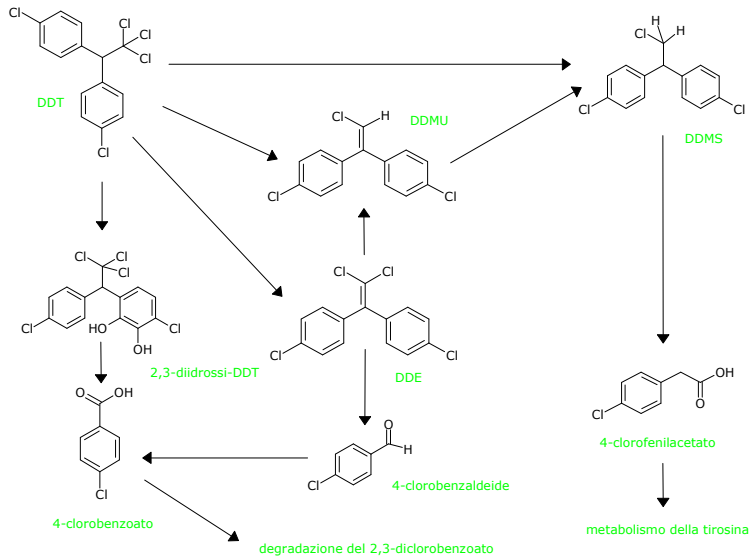
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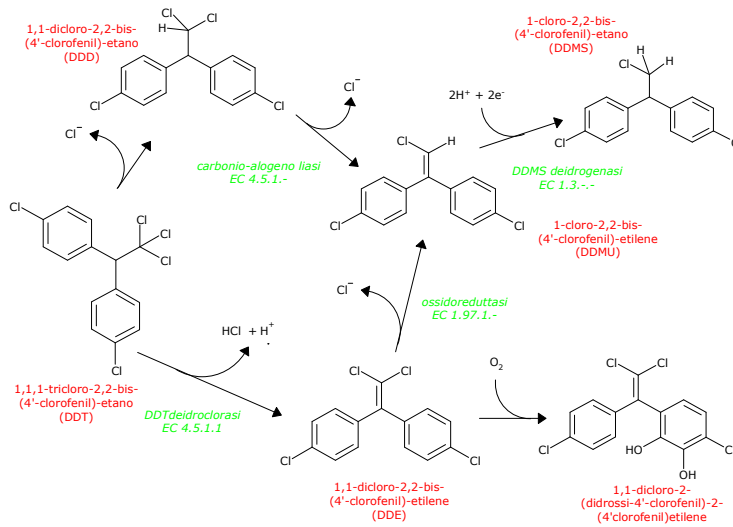
## Schema generale



## In sintesi



## Declorurazione del DDT

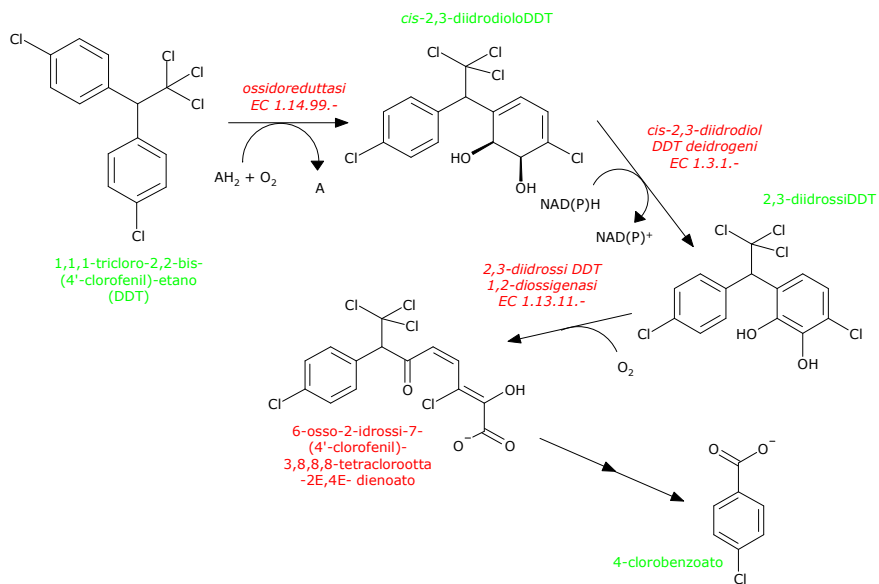


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## Ossidazione del DDT

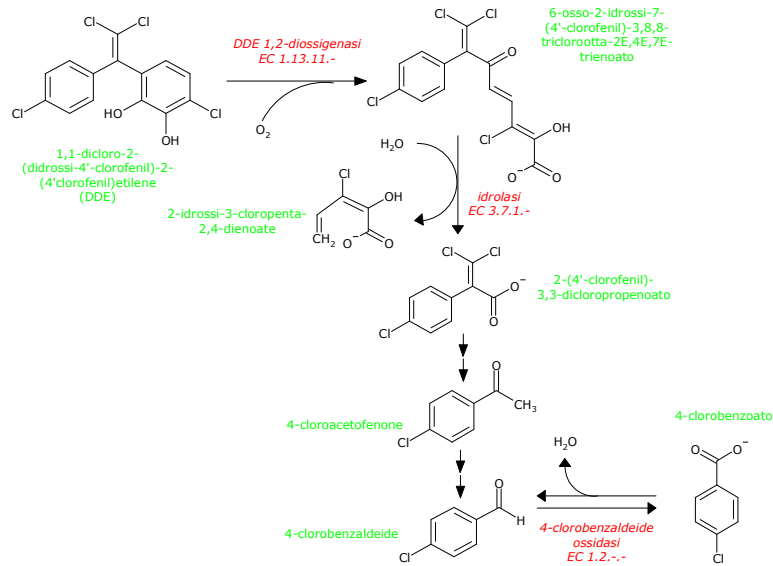


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## Ossidazione del DDE

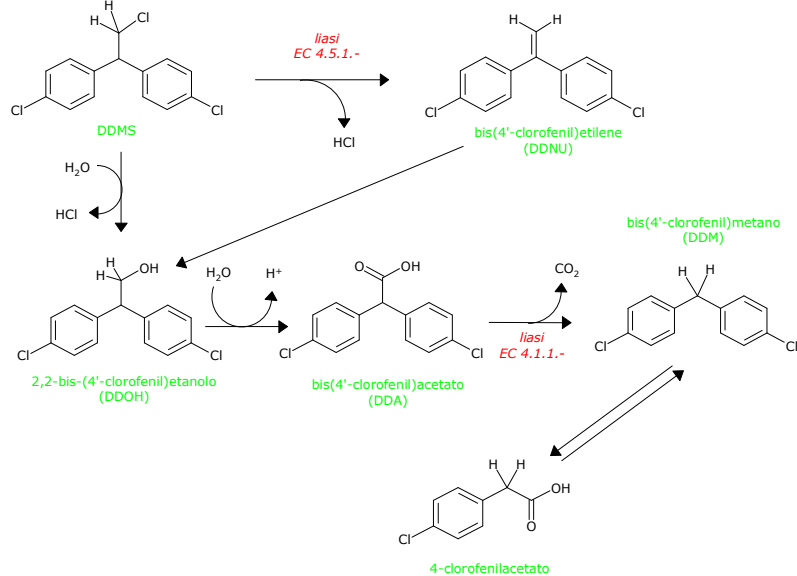


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## Ossidazione del DDMS

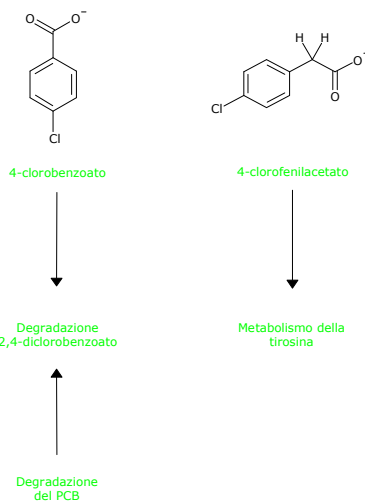


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## Prodotti finali



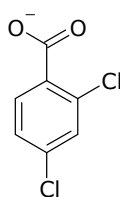
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## Composti organoclorurati e organofosfati

- Bifenile e PCB
- DDT
- **2,4-diclorobenzoato**
- 1,4-diclorobenzene
- 1,2-dicloroetano
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion



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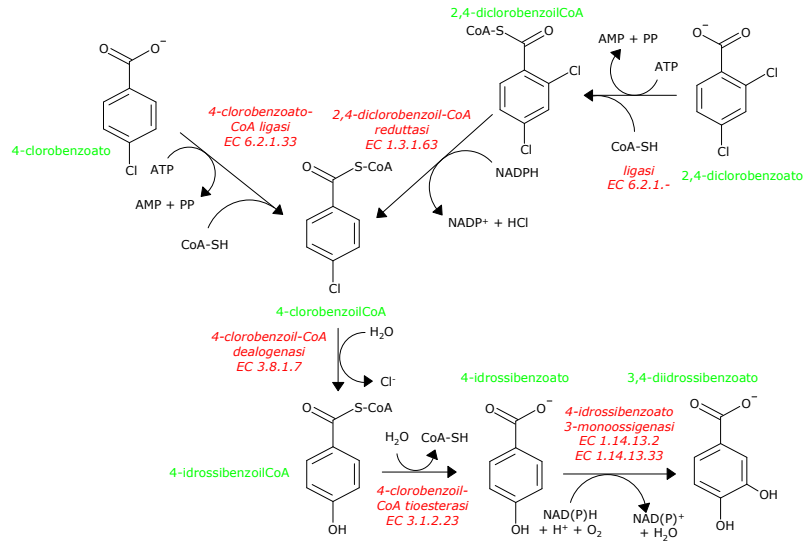
F07 - Biotrasformazione dei composti xenobiotici

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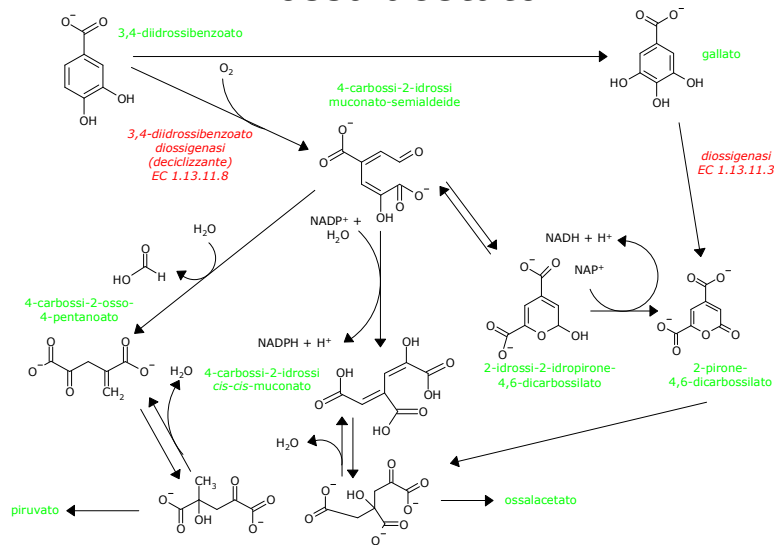




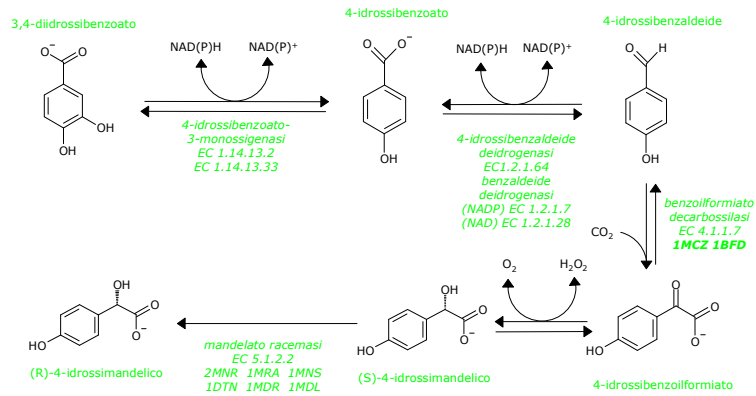
## Da 4-clorobenzoato e 2,4-diclorobenzoato a 3,4-diidrossibenzoato



## Da 3,4-diidrossibenzoato a piruvato e ossalacetato



## Da 3,4-diidrossibenzoato a (R)-4-idrossimandelato

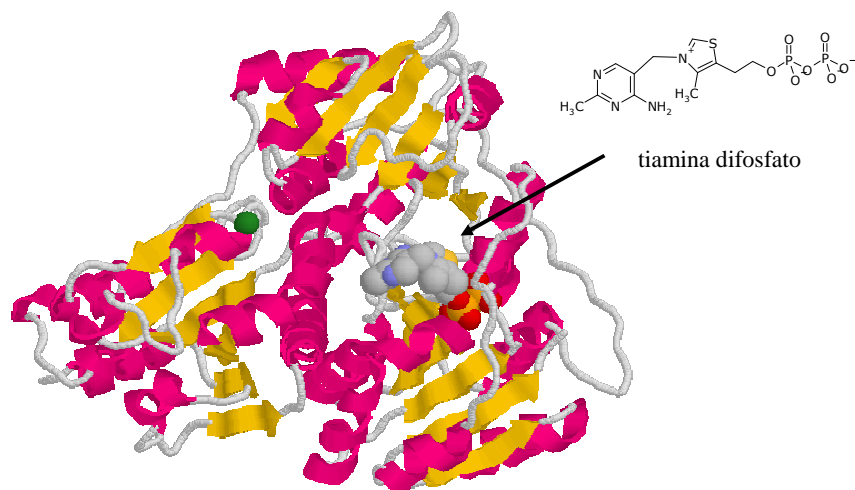


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## Benzoilformiato decarbossilasi EC 4.1.1.7 (1BFD)

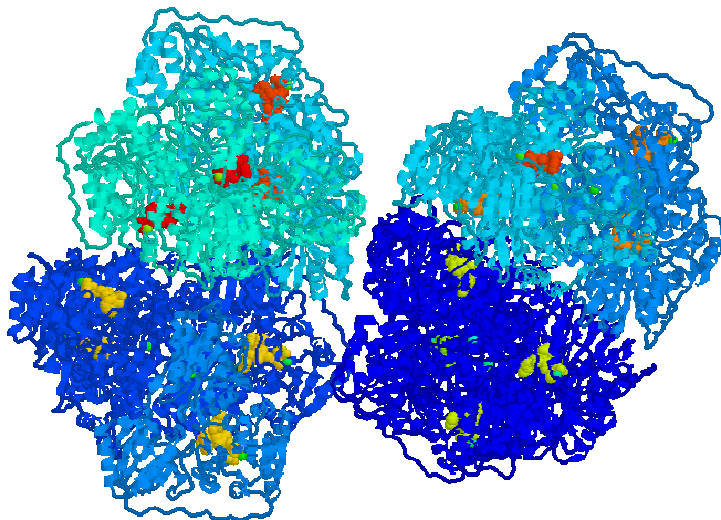


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## Benzoilformiato decarbossilasi EC 4.1.1.7 (1MCZ)

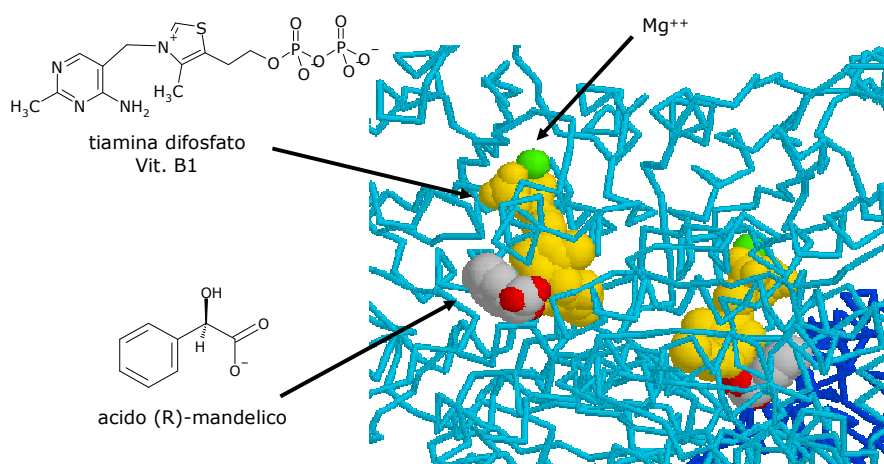


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## Benzoilformiato decarbossilasi EC 4.1.1.7 (1MCZ)

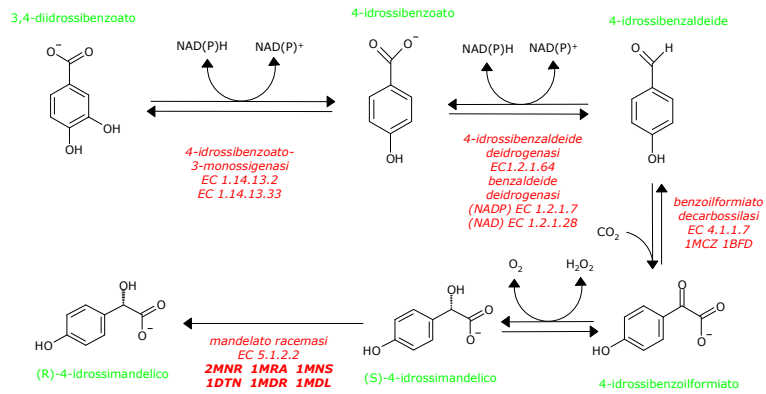


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## Da 3,4-diidrossibenzoato a 4-idrossimandelato

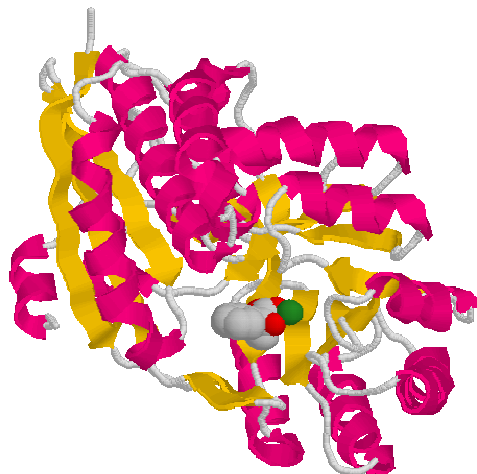


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## Mandelato racemasi EC 5.1.2.2 (1MNS)

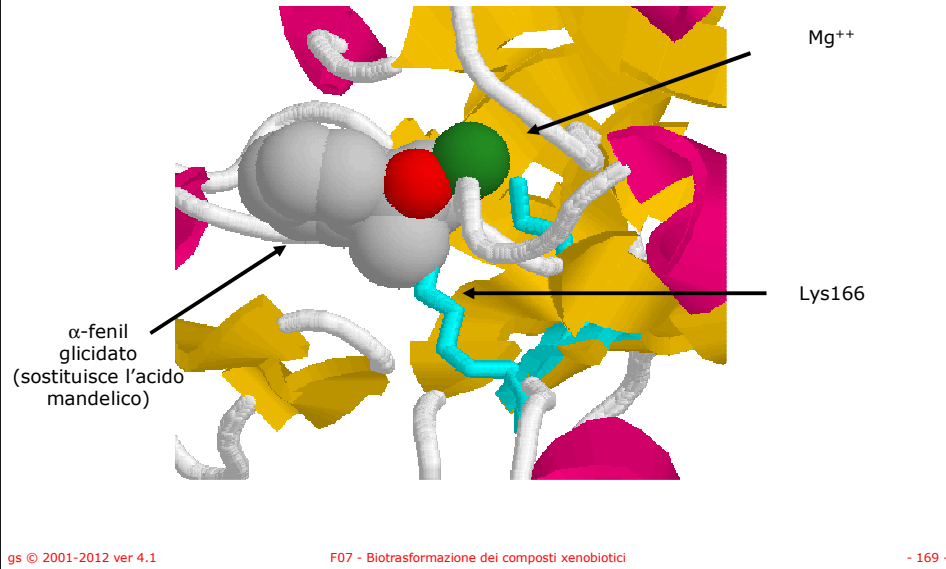


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## Mandelato racemasi EC 5.1.2.2 (1MNS)

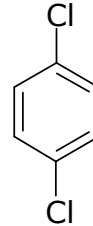


## Mandelato racemasi EC 5.1.2.2 (1MNS)

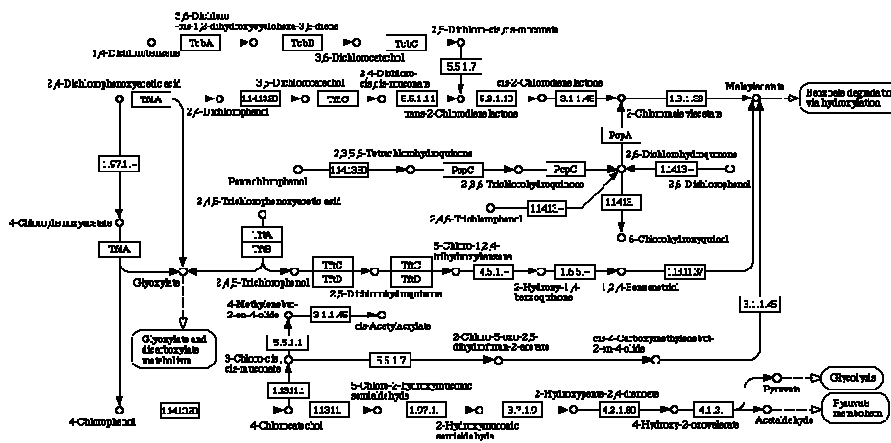


# Composti organoclorurati e organofosfati

- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- **1,4-diclorobenzene**
- 1,2-dicloroetano
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion

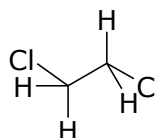


## Schema generale

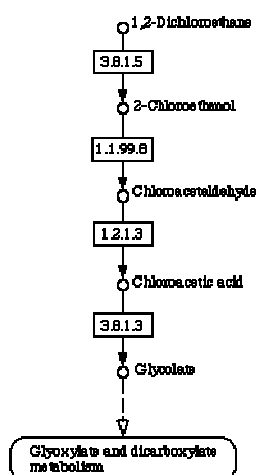


## Composti organoclorurati e organofosfati

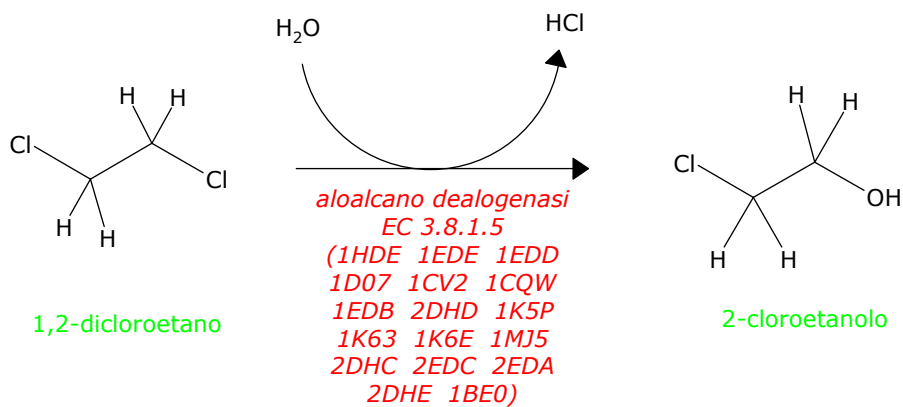
- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- 1,4-diclorobenzene
- **1,2-dicloroetano**
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion



## Schema generale



## Dealogenazione del 1,2-dicloroetano

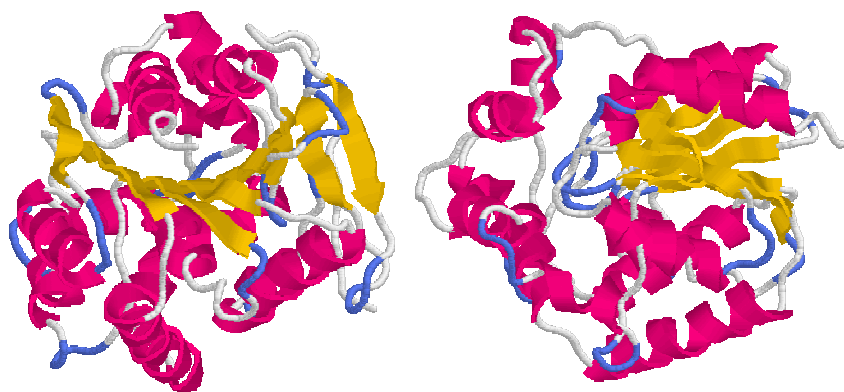


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## Aloalcano dealogenasi EC 3.8.1.5 (1EDE)



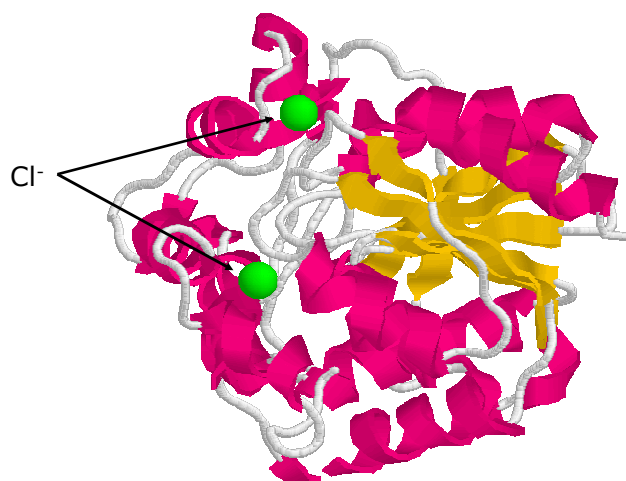
gs © 2001-2012 ver 4.1

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Aloalcano dealogenasi  
*EC 3.8.1.5 (1B6G)*

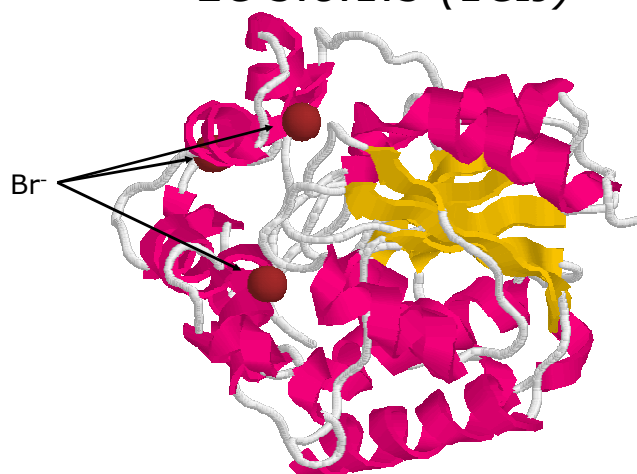


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Aloalcano dealogenasi  
*EC 3.8.1.5 (1CIJ)*

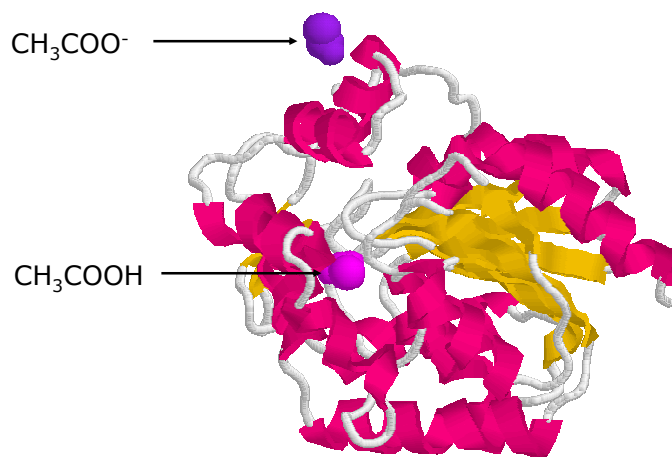


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### Aloalcano dealogenasi *EC 3.8.1.5 (1BE0)*

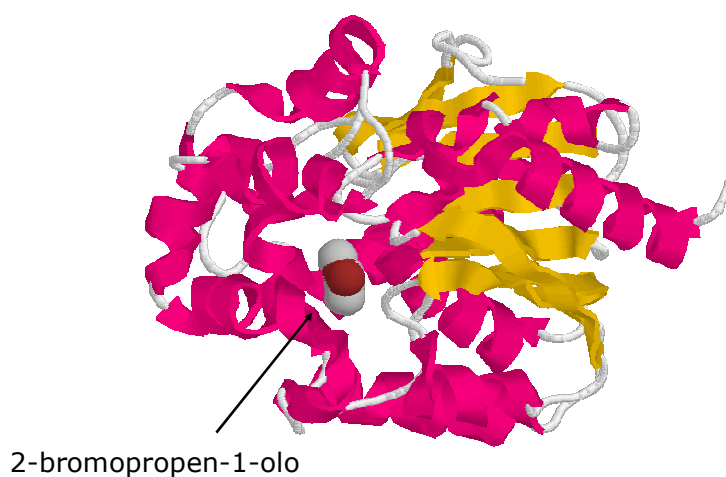


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### Aloalcano dealogenasi *EC 3.8.1.5 (1K63)*

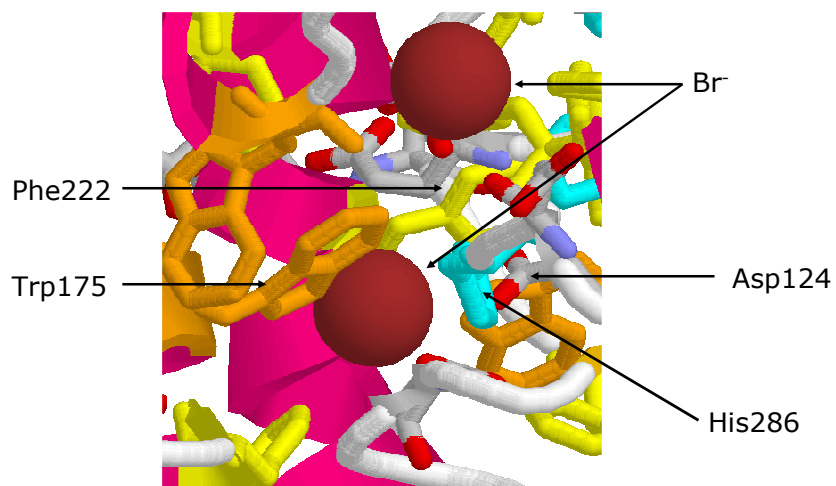


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## Aloalcano dealogenasi *EC 3.8.1.5 (1CIJ)*



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## Aloalcano dealogenasi *EC 3.8.1.5 (1BE0)*

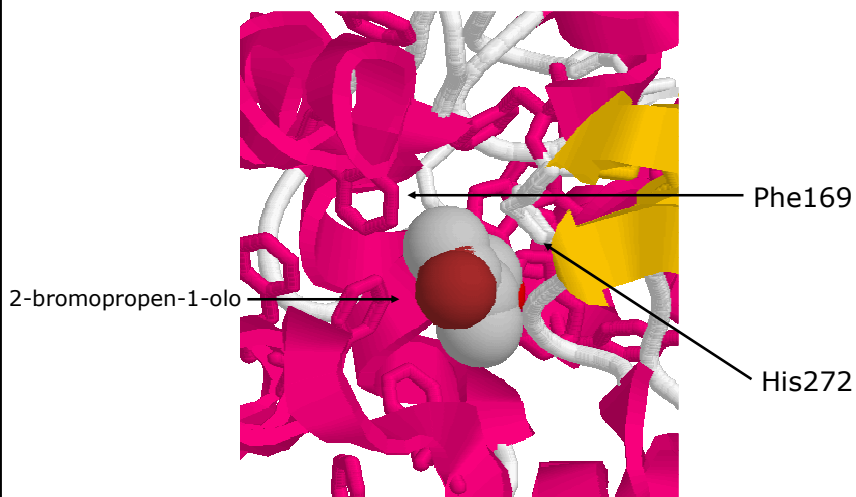


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## Aloalcano deidrogenasi EC 3.8.1.5 (1K63)

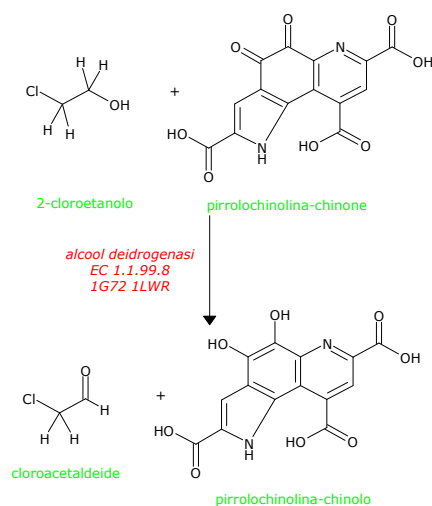


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## Deidrogenazione del 2-cloroetano

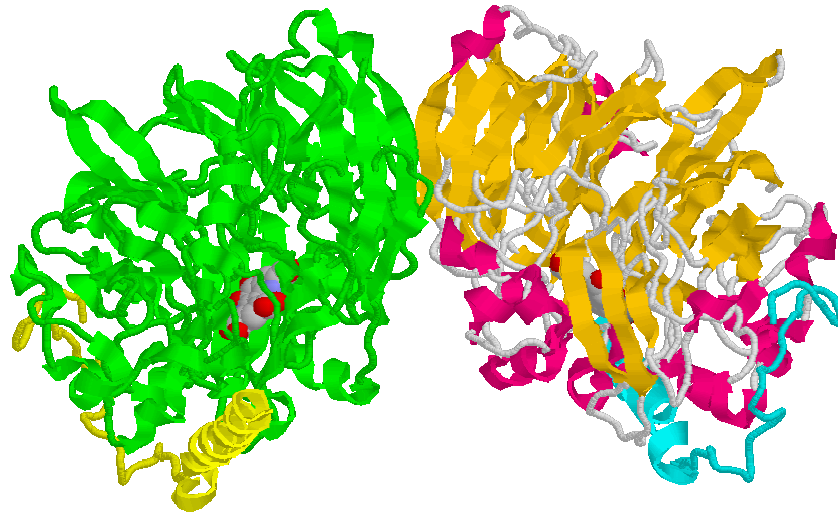


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Alcool deidrogenasi  
*EC 1.1.99.8 (1G72)*

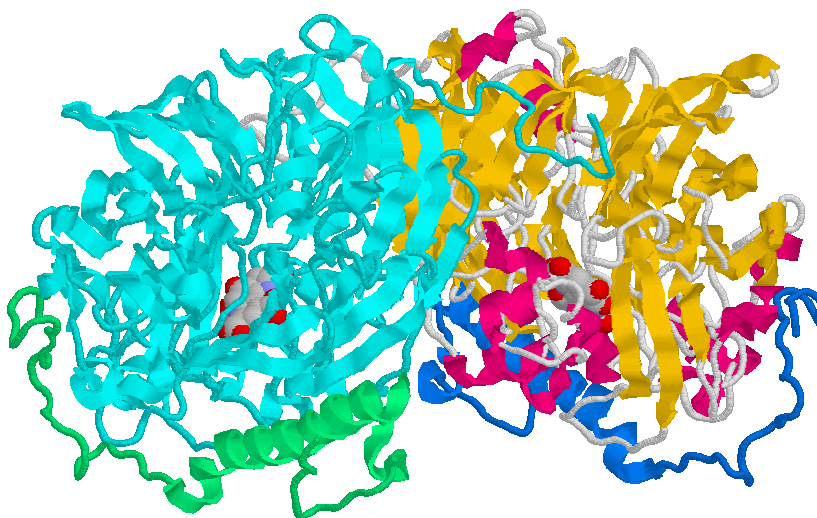


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Alcool deidrogenasi  
*EC 1.1.99.8 (1LW2)*

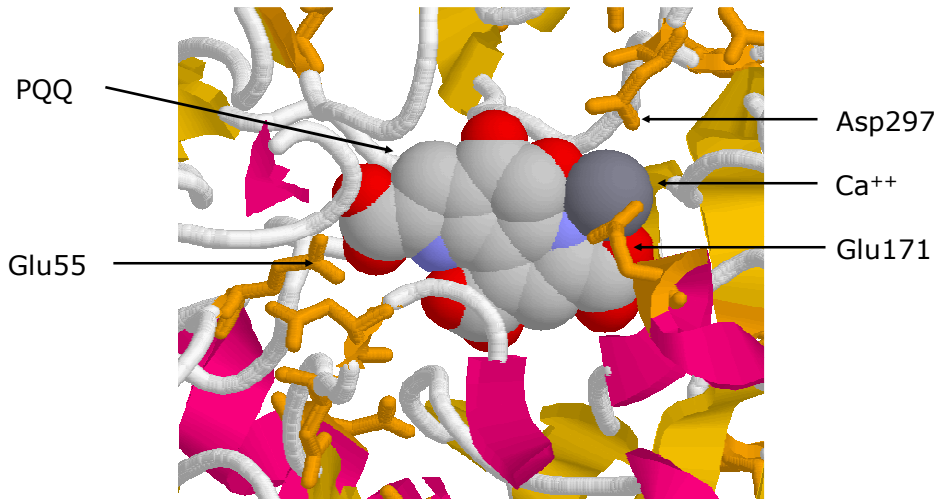


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## Alcool deidrogenasi EC 1.1.99.8 (1G72)

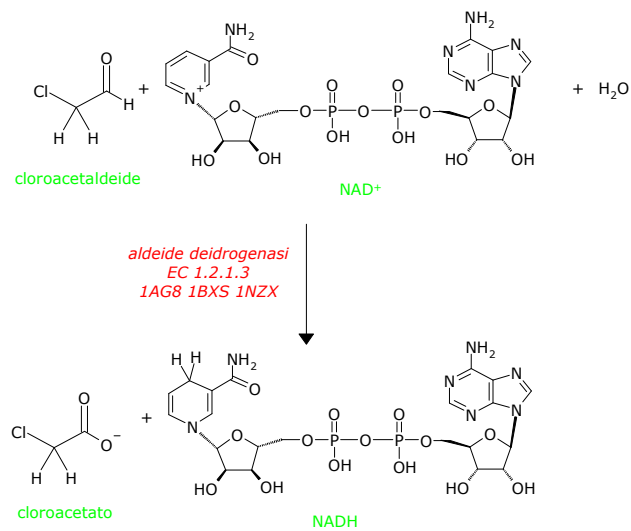


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## Deidrogenazione della cloroacetaldeide

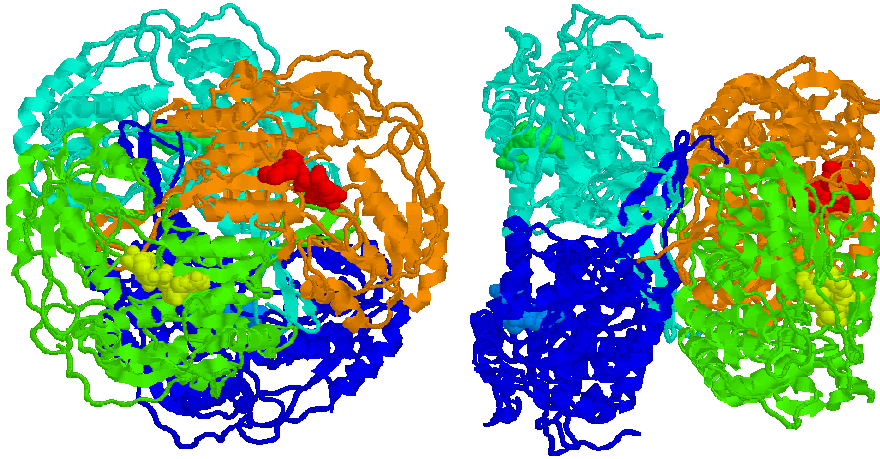


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Aldeide deidrogenasi  
*EC 1.2.1.3 (1BXS)*

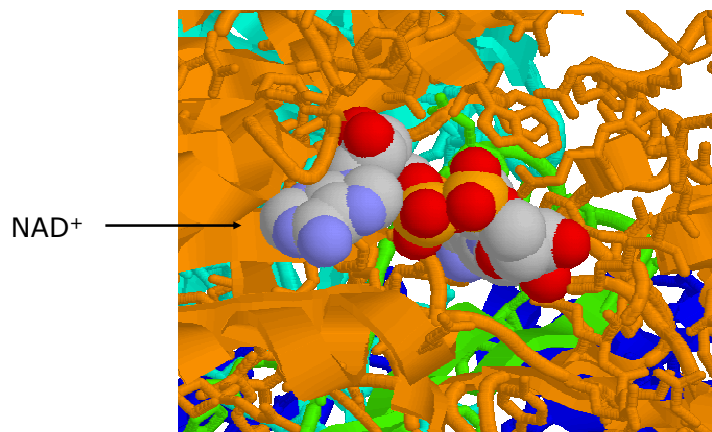


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Aldeide deidrogenasi  
*EC 1.2.1.3 (1BXS)*

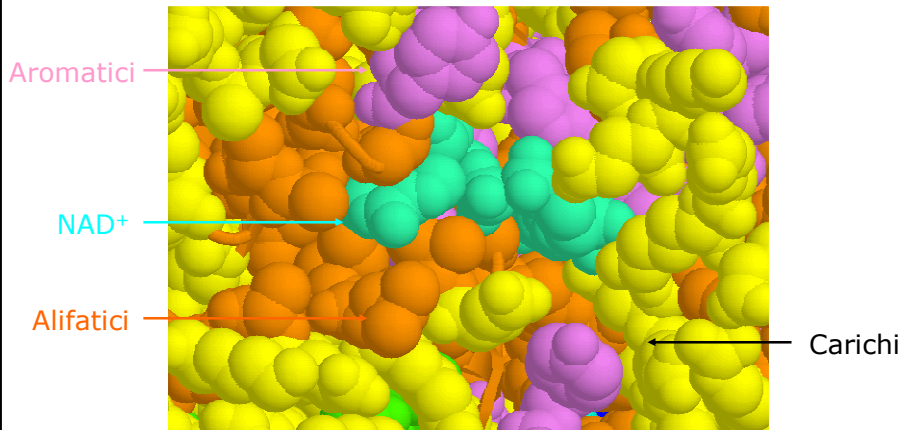


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## Aldeide deidrogenasi *EC 1.2.1.3 (1BXS)*

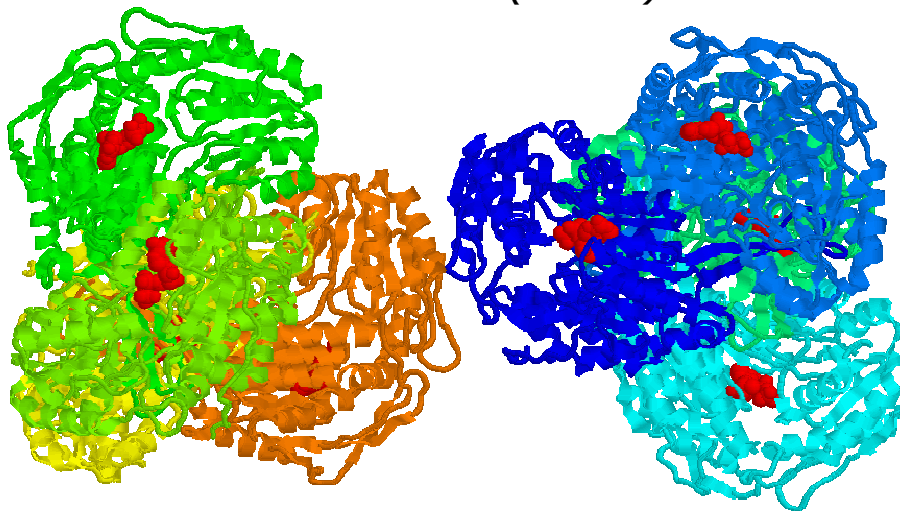


gs © 2001-2012 ver 4.1

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## Aldeide deidrogenasi *EC 1.2.1.3 (1NZX)*



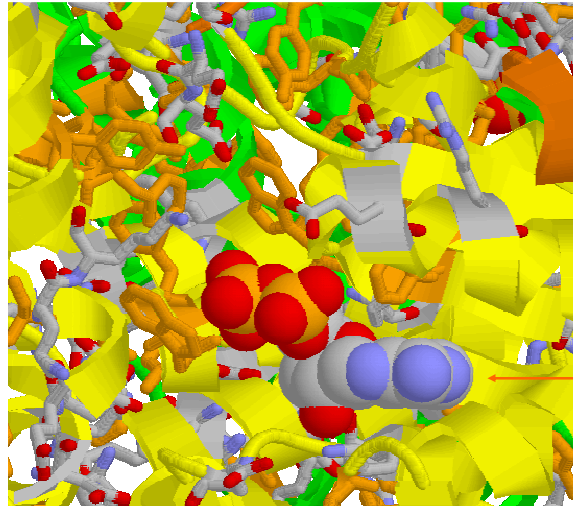
gs © 2001-2012 ver 4.1

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## Aldeide deidrogenasi EC 1.2.1.3 (1NZX)



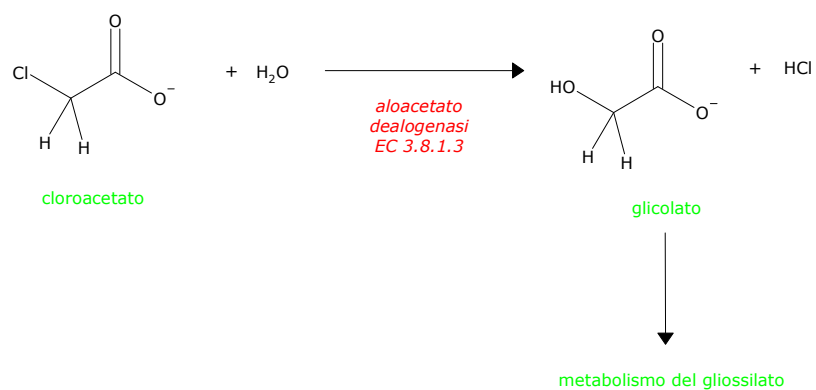
NAD<sup>+</sup>

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## Dealogenazione del cloroacetato



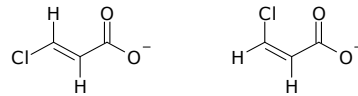
gs © 2001-2012 ver 4.1

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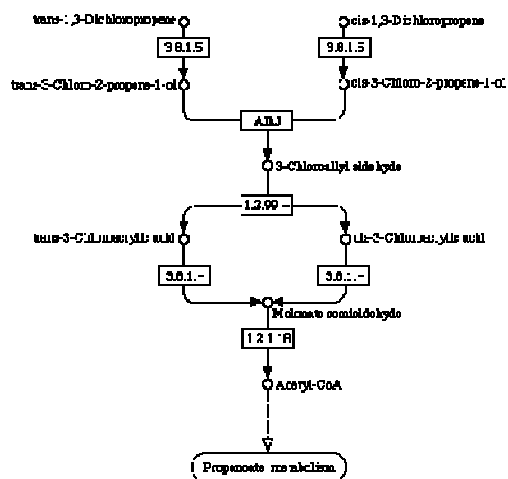
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## Composti organoclorurati e organofosfati

- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- 1,4-diclorobenzene
- 1,2-dicloroetano
- **Acido 3-cloroacrilico**
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion

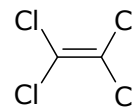


## Schema generale

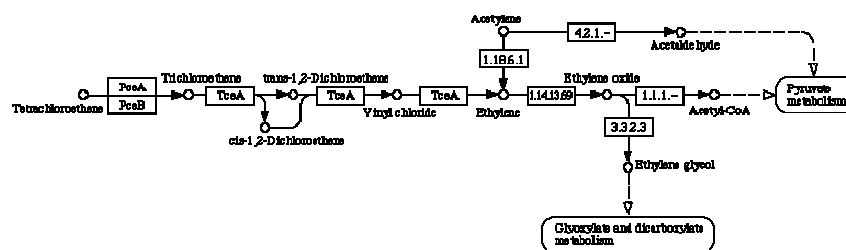


## Composti organoclorurati e organofosfati

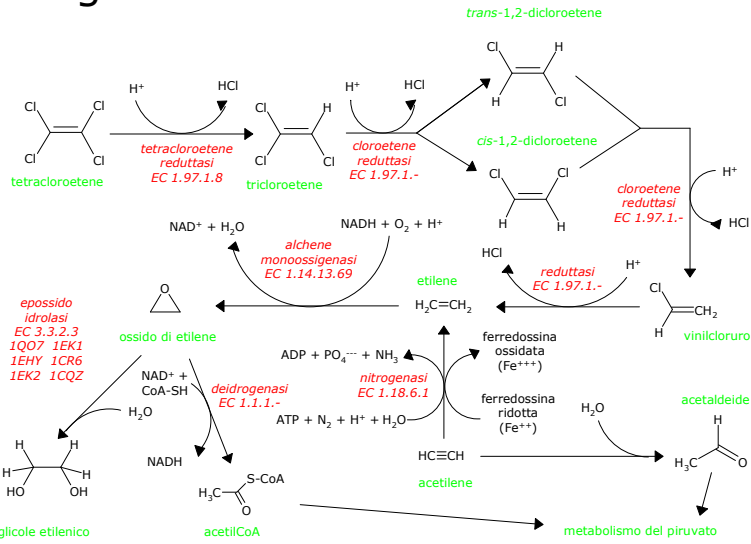
- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- 1,4-diclorobenzene
- 1,2-dicloroetano
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion



## Schema generale



# Degradazione del tetracloroetene

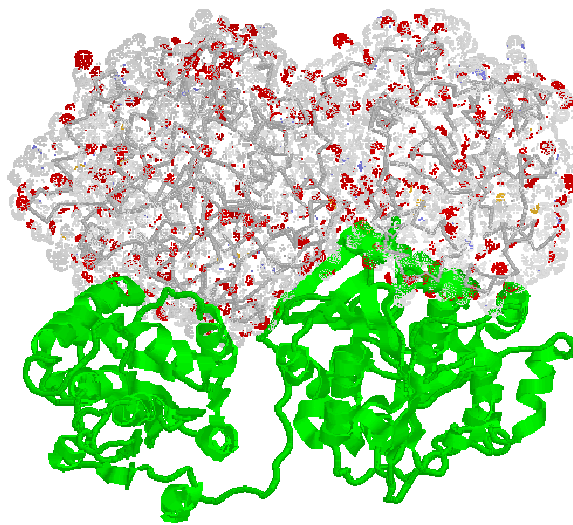


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# Epossido idrolasi EC 3.3.2.3 (1CQZ)

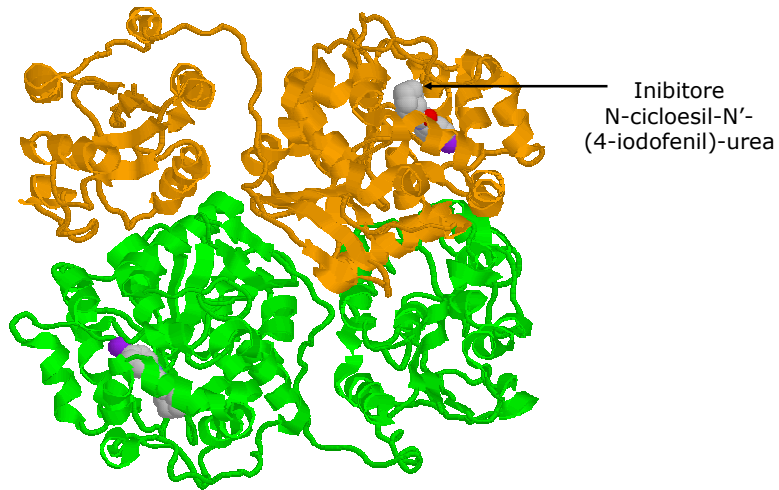


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## Epossido idrolasi EC 3.3.2.3 (1EK1)

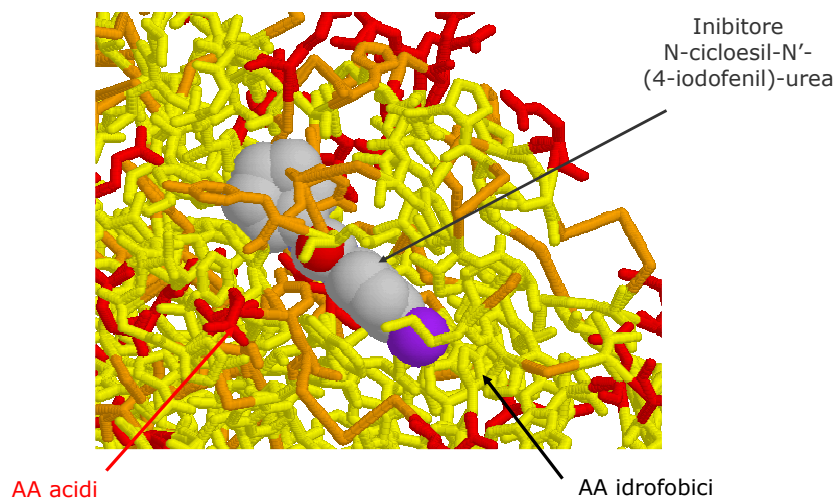


gs © 2001-2012 ver 4.1

F07 - Biotrasformazione dei composti xenobiotici

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## Epossido idrolasi EC 3.3.2.3 (1EK1)



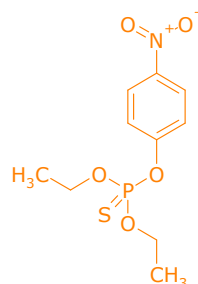
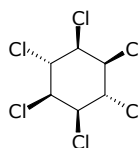
gs © 2001-2012 ver 4.1

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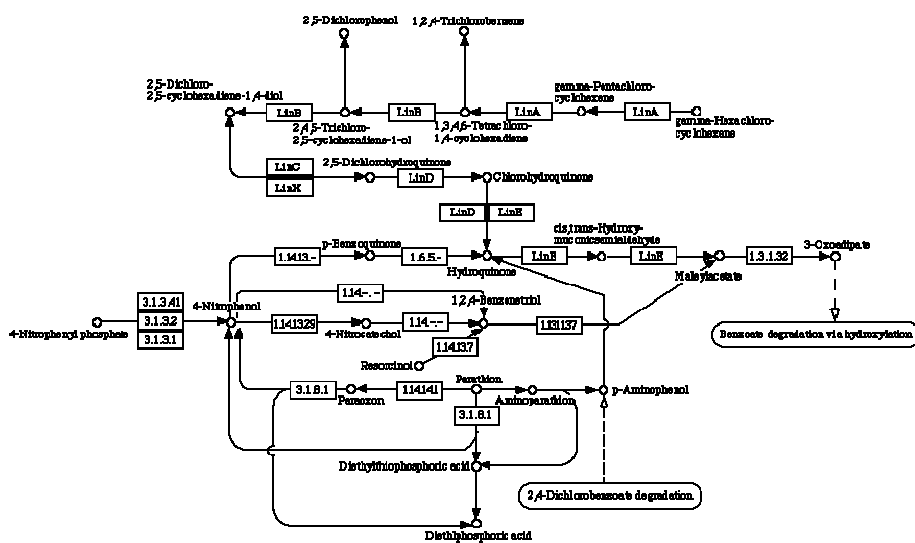
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## Composti organoclorurati e organofosfati

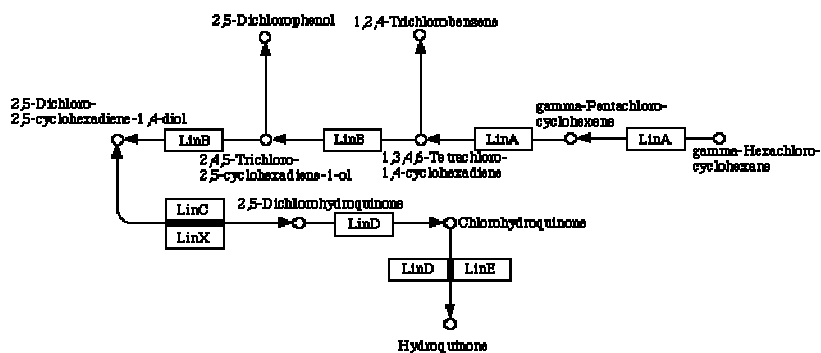
- Bifenile e PCB
- DDT
- 2,4-diclorobenzoato
- 1,4-diclorobenzene
- 1,2-dicloroetano
- Acido 3-cloroacrilico
- Tetracloroetene
- $\gamma$ -esaclorocicloesano e parathion



## Schema generale



## Degradazione del $\gamma$ -esaclorocicloesano (Lindano<sup>®</sup>)

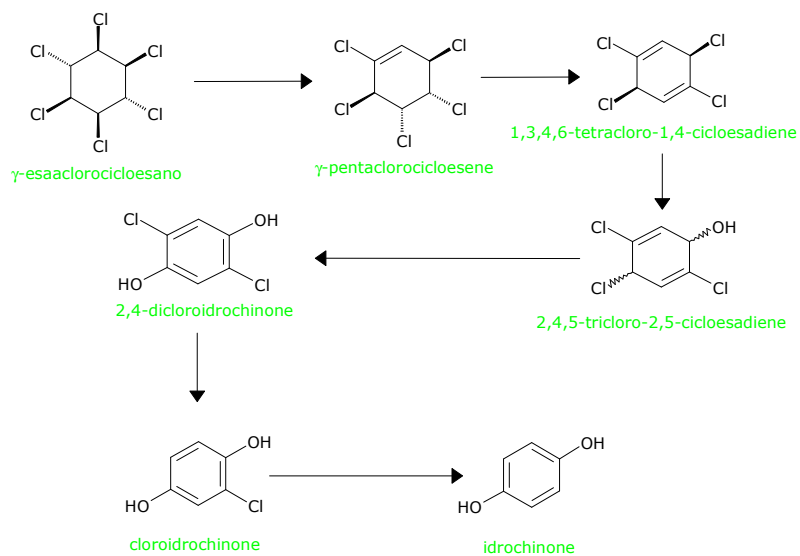


gs © 2001-2012 ver 4.1

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## In sintesi

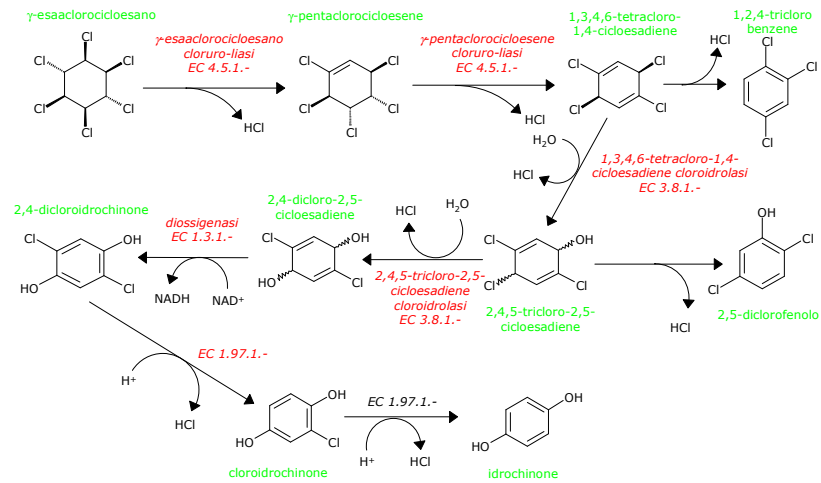


gs © 2001-2012 ver 4.1

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## Degradazione del $\gamma$ -esaclorocicloesano

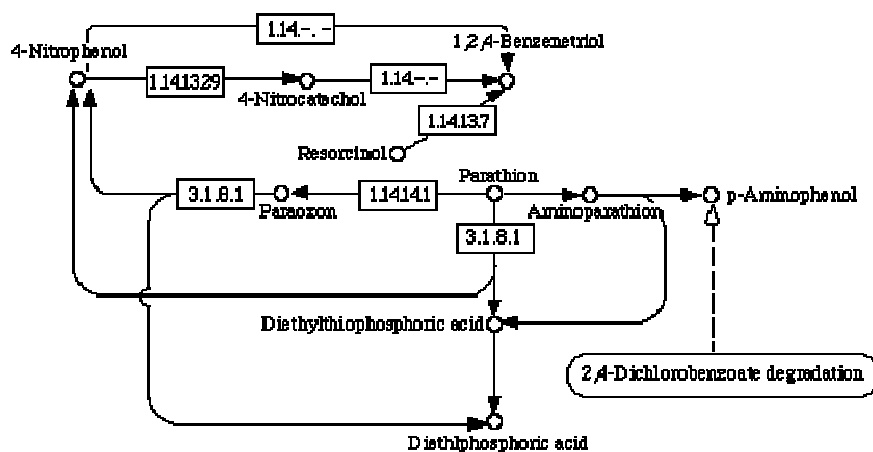


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## Degradazione del parathion<sup>®</sup>



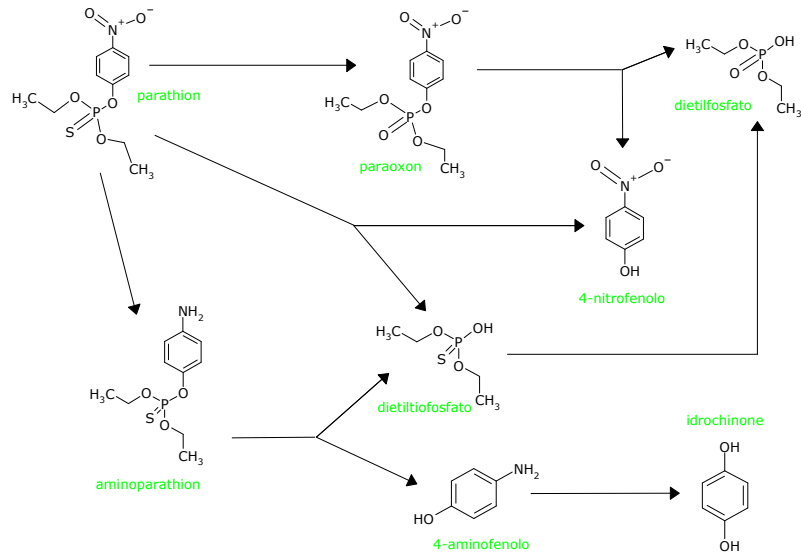
gs © 2001-2012 ver 4.1

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## In sintesi

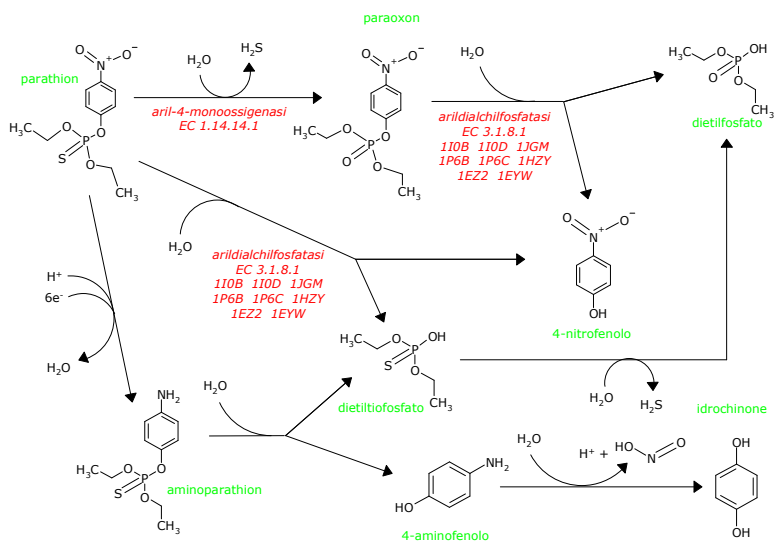


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## Degradazione del Parathion®



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## Monoossigenasi EC 1.14.14.1 - CYP

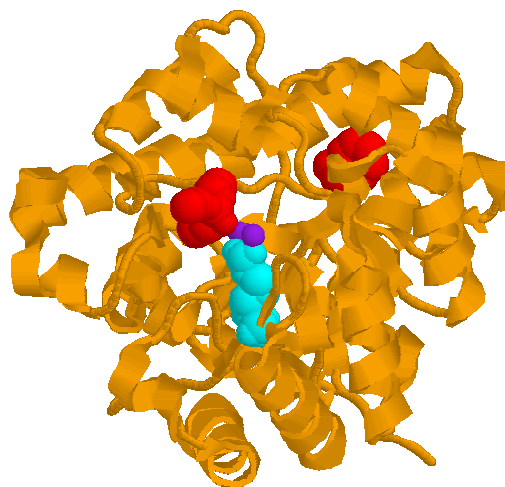
CYP1A1	CYP1A2	CYP1B1	CYP2A1	CYP2A2	CYP2A3A
CYP2A4	CYP2A5	CYP2A6	CYP2A7	CYP2A12	CYP2A13
CYP2B6	CYP2B9	CYP2B10	CYP2B15	CYP2B19	CYP2C
CYP2C8	CYP2C9	CYP2C12	CYP2C18	CYP2C19	CYP2C29
CYP2C37	CYP2C38	CYP2C39	CYP2C40	CYP2D10	CYP2D2
CYP2D6	CYP2D9	CYP2E1	CYP2F1	CYP2J2	CYP2J4
CYP2J5	CYP2J6	CYP3A3	CYP3A4	CYP3A5	CYP3A7
CYP3A11	CYP3A13	CYP3A16	CYP3A41	CYP3A43	CYP4B1
CYP4F8	CYP4F11	CYP4F12	CYP4F14	CYP19	CYP19A
CYP19A1	CYP19B	CYP26A1			

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## Arildialchilfosfatasi EC 3.1.8.1 (1EYW)

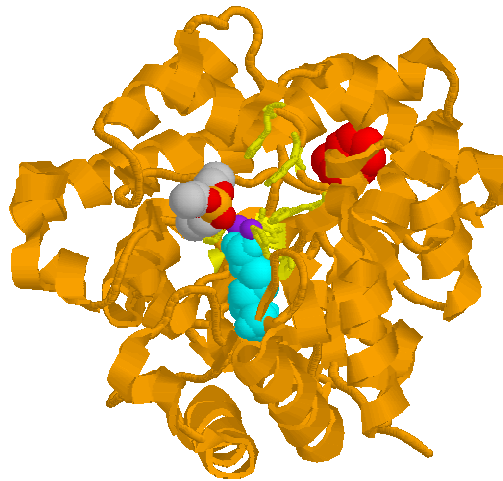


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Arildialchilfosfatasi  
*EC 3.1.8.1 (1EYW)*

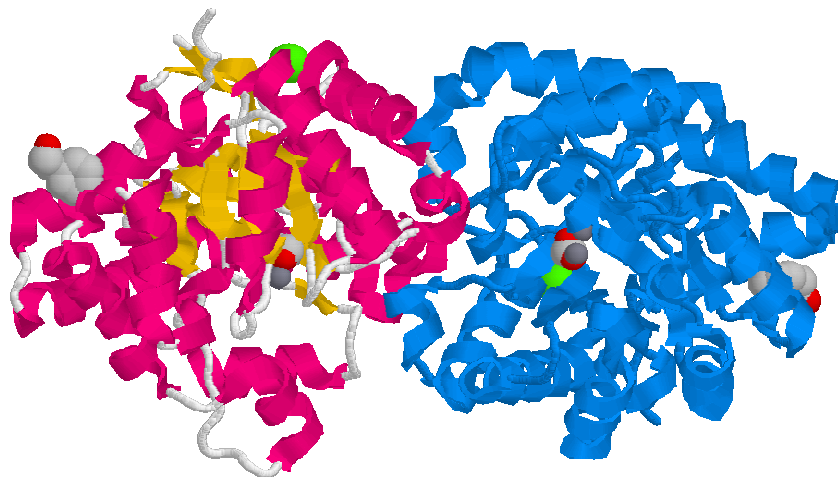


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Arildialchilfosfatasi  
*EC 3.1.8.1 (1I0B)*

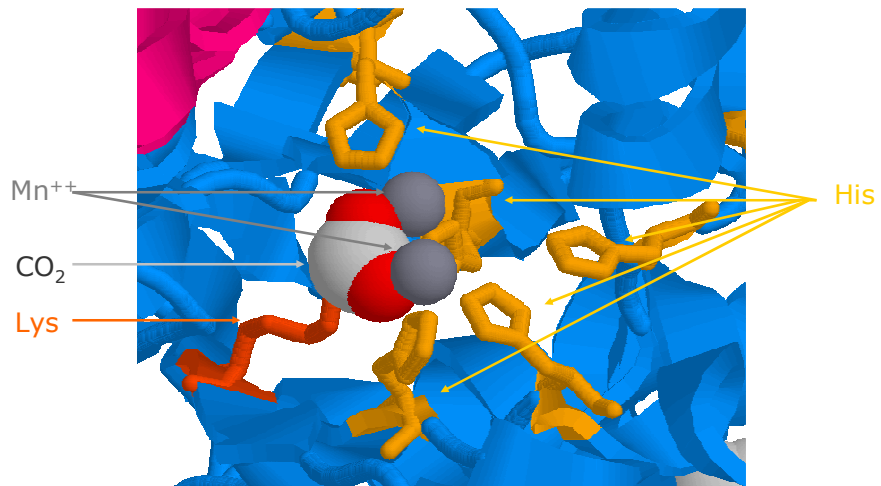


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## Arildialchilfosfatasi *EC 3.1.8.1 (1I0B)*

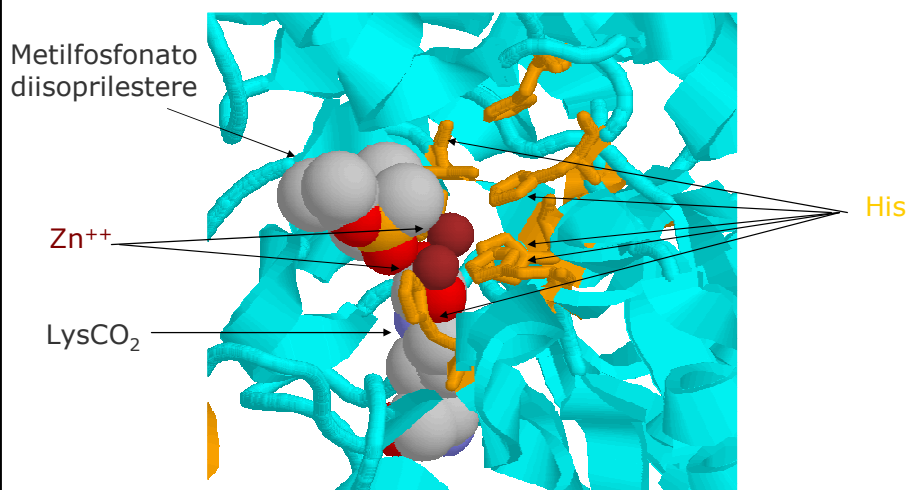


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## Arildialchilfosfatasi *EC 3.1.8.1 (1EZ2)*

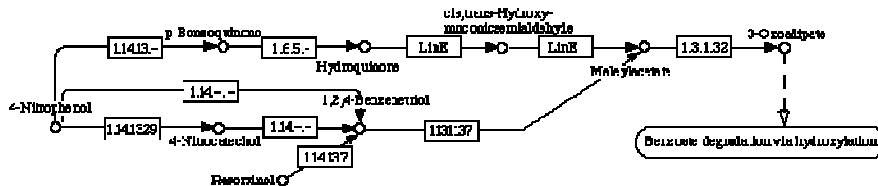


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## Destino del nitrofenolo e dell'idrochinone

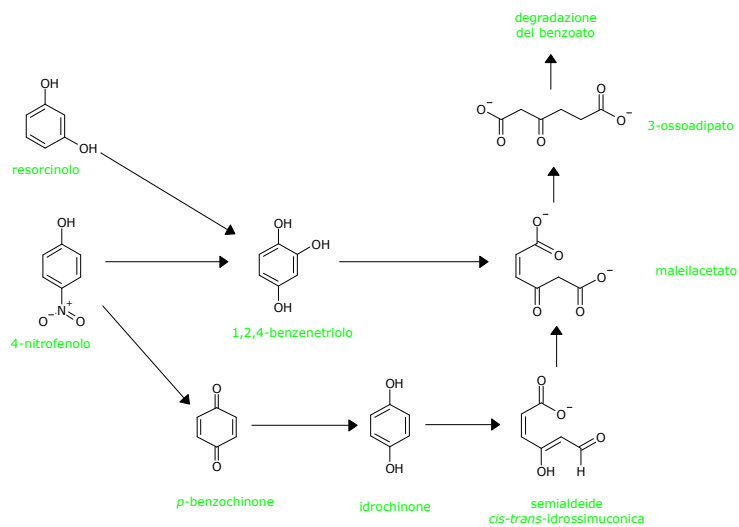


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## In sintesi

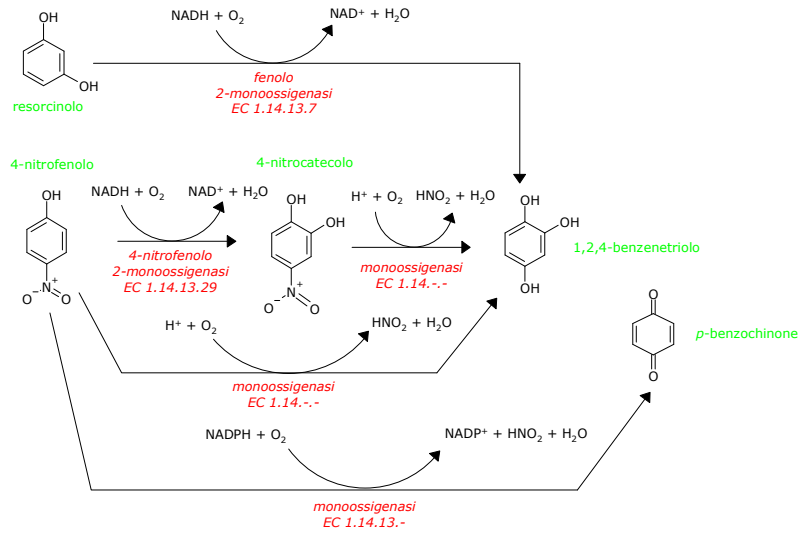


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## Destino del nitrofenolo

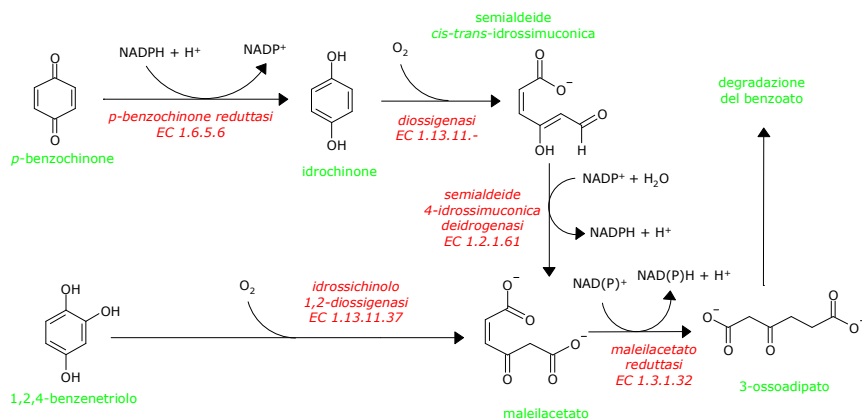


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## Destino del 1,2,4-benzenetriolo e del p-benzochinone



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## Referenze sul WEB

- Vie metaboliche
  - KEGG: <http://www.genome.ad.jp/kegg/>
    - Degradazione degli xenobiotici:  
<http://www.genome.ad.jp/kegg/pathway/map/map01196.html>
- Struttura delle proteine:
  - Protein data bank (Brookhaven): <http://www.rcsb.org/pdb/>
  - Hexpasy
    - Expert Protein Analysis System: <http://us.expasy.org/sprot/>
    - Prosite (protein families and domains): <http://www.expasy.org/prosite/>
    - Enzyme (Enzyme nomenclature database):  
<http://www.expasy.org/enzyme/>
  - Scop (famiglie strutturali): <http://scop.berkeley.edu/>
- Enzimi:
  - Nomenclatura - IUBMB: <http://www.chem.qmw.ac.uk/iubmb/>
  - Proprietà - Brenda: <http://www.brenda.uni-koeln.de/>
  - Expasy (Enzyme nomenclature database): <http://www.expasy.org/enzyme/>
- Database di biocatalisi e biodegradazione: <http://umbbd.ahc.umn.edu/>
- Citocromo P450: <http://www.icgeb.org/~p450srv/>
- Metallotioneine: <http://www.unizh.ch/~mtpage/MT.html>
- Tossicità degli xenobiotici: Agency for Toxic Substances and Disease Registry  
<http://www.atsdr.cdc.gov>

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**Materiale ottenuto dal Prof. Giorgio Sartor**

Università di Bologna – Alma Mater

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