Enantioselective analysis of chiral enviromental contaminants

A versatile tool for ecotoxicological risk assessment

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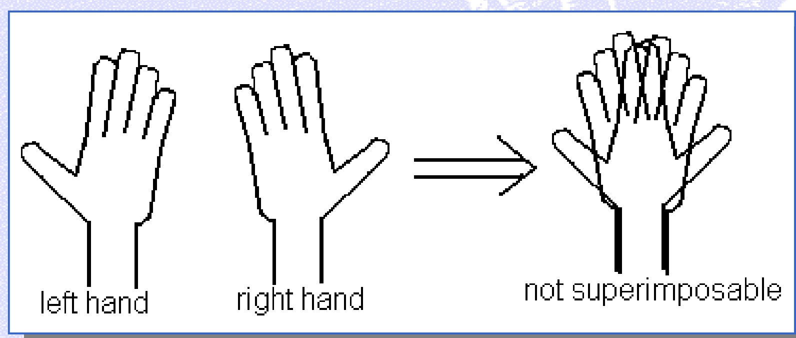
Chirality

Chirality (from the Greek word for "hand") describes the property of having a non-superimposable mirror image.

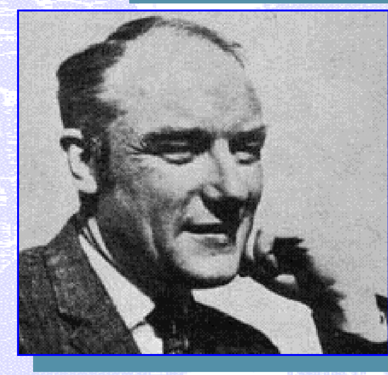
A pair of hands also possess chirality, and are analogous to an enantiomeric pair of molecules.

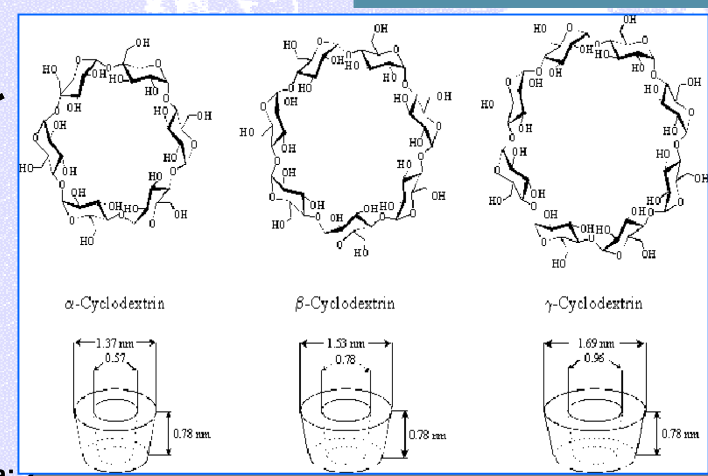
Molecules or objects that cannot have a noncongruent mirror image are said to be achiral.



Historical review

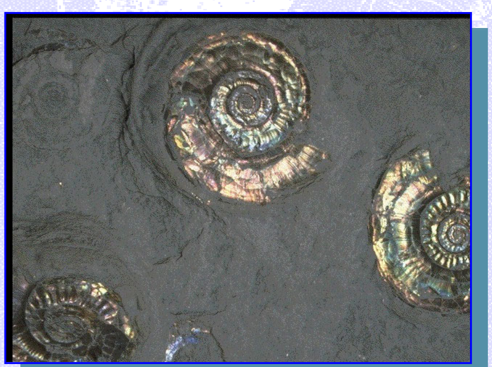
- 1847 Pasteur, Biot
- 1880 Lord Kelvin
- 1953 Watson Crick
- 1960 Thalidomide
- 1970 chiral HPLC
- 1980 chiral GC
- 1990 chiral trace analysis (ng/pg-range)





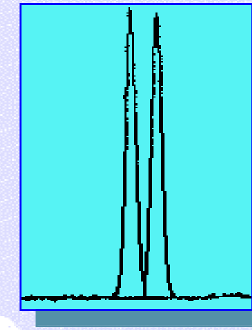
Generell Background

- Chirality is considered as a principal feature of “life processes”
- All biochemical mechanisms are potentially enantioselective.
- Deviation from the racemic distribution (Enantiomeric ratio (ER) = 1, Enatiomeric fraction (EF) = 0.5) indicates biochemical degradation or/ and enantioselective accumulation.



$$EF = \frac{Ena.\text{-}area\ 1}{Ena.\text{-}area\ 1 + Ena.\text{-}area\ 2}$$

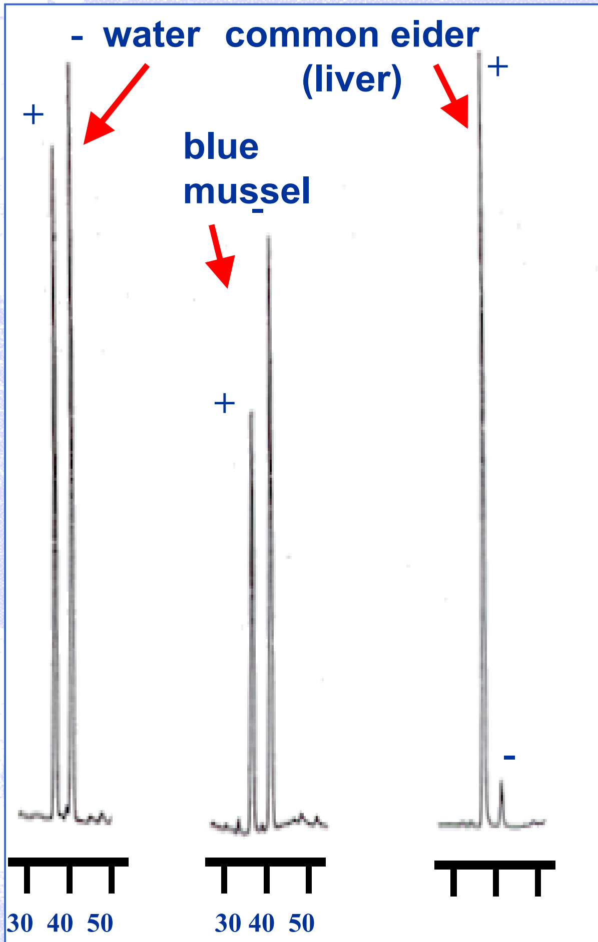
Analytical applications

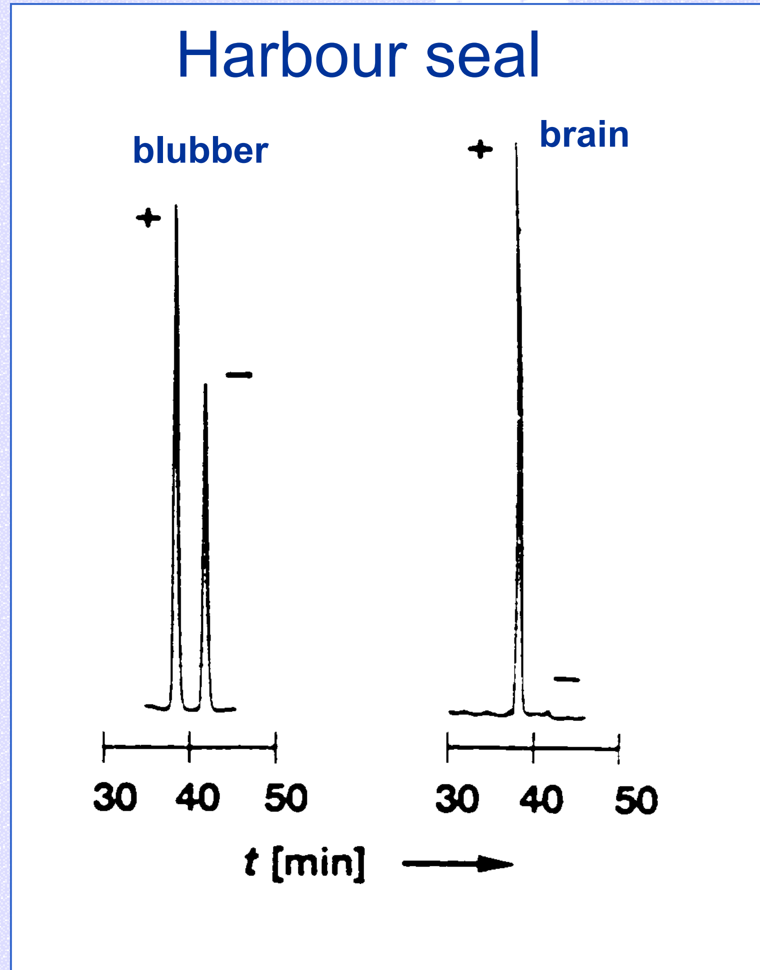


- Process applications and quality control in the pharmaceutical industry.
- Separation and “clean-up of pharmaceutical end products as well as toxicological studies.
- Enantioselective separation of chiral environmental contaminants for structure elucidation and ecotoxicological assessments.
- Level and environmental fate as well as bioavailability studies for chiral contaminants.

Chirality and bioavailability

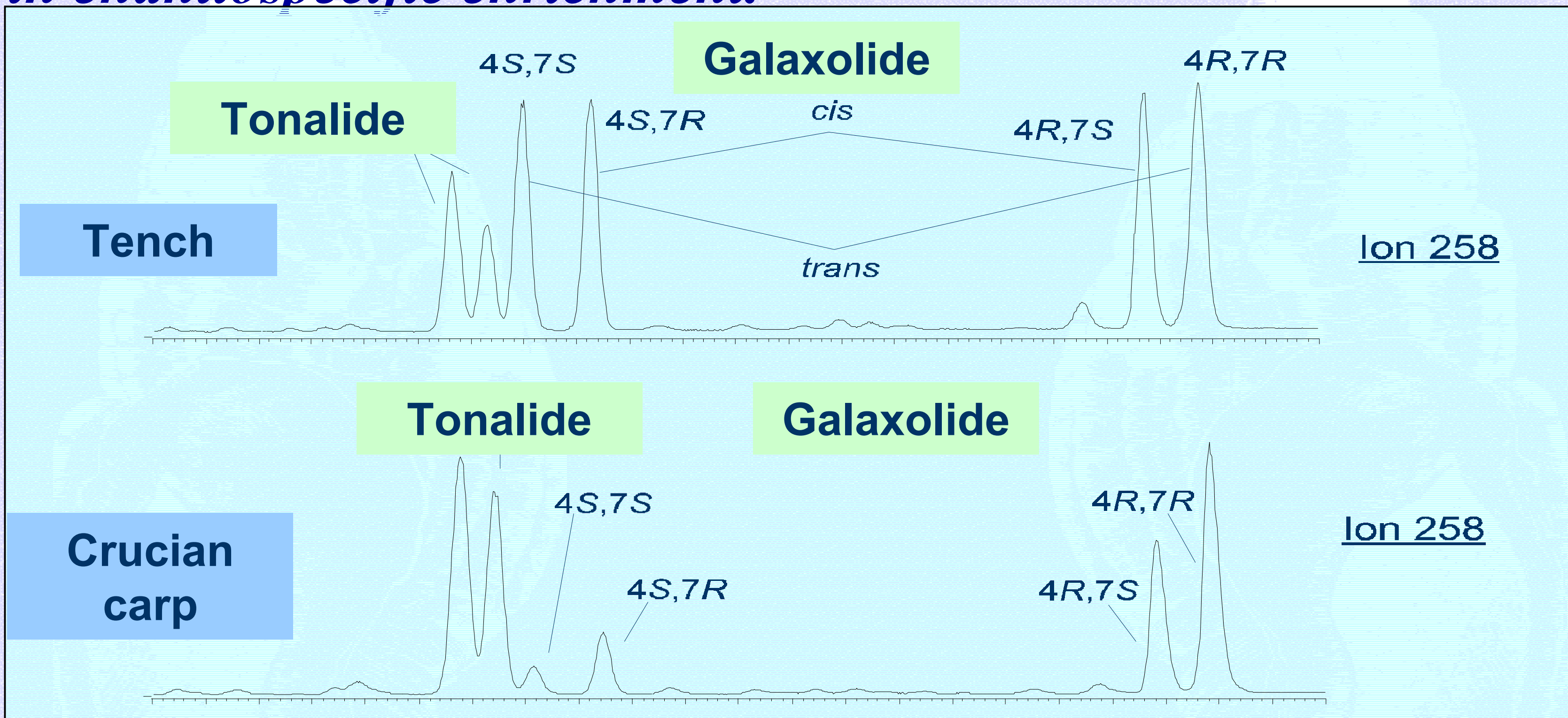
α-HCH:





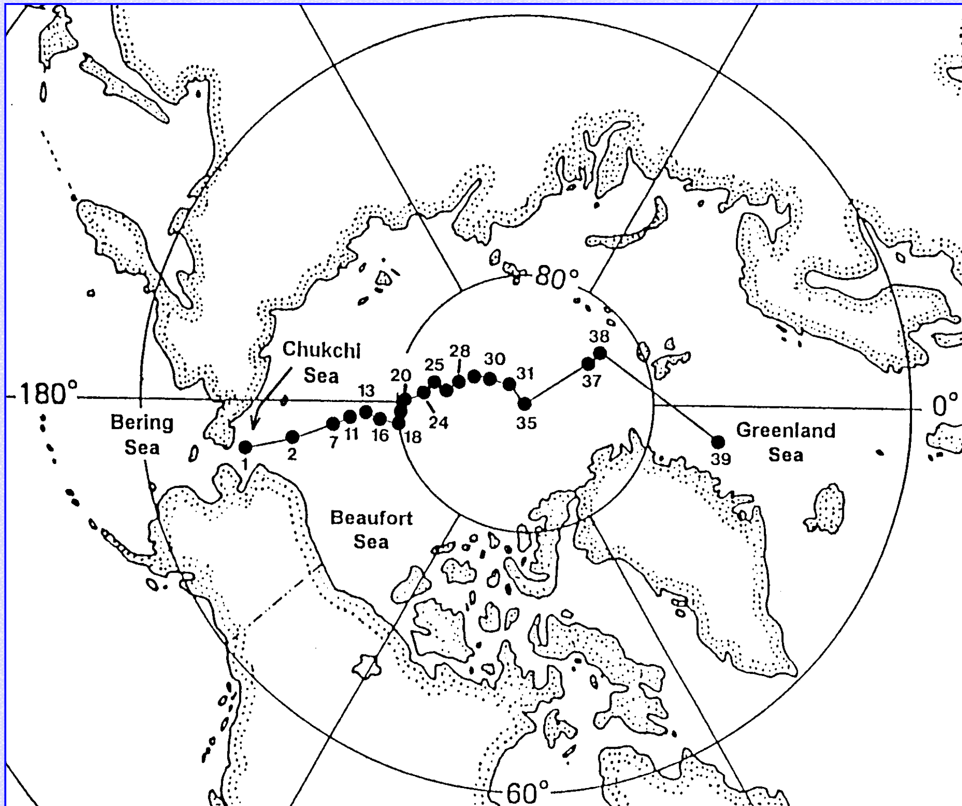
Chirality and fragrances

Species depending metabolisation of the polycyclic musks resulted in enantiospecific enrichment.

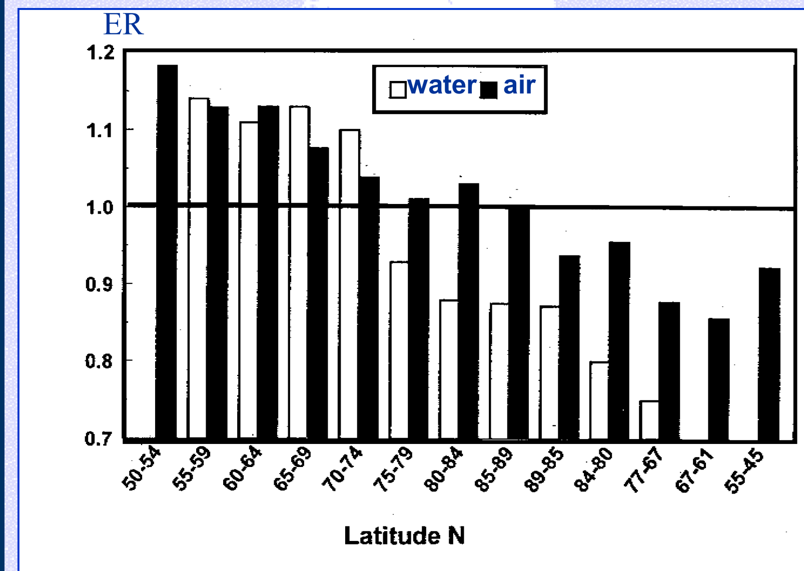


Gatermann R., S. Biselli, H.Hühnerfuss, G.G. Rimkus, S. Franke, M.Hecker, R.Kallenborn, L. Karbe & W.A. König (2002). Synthetic musks in the environment. Part 2: Enantioselective transformation of the polycyclic musk fragrances HHCB, AHTN, AHDI, and ATII in freshwater fish. Archives of Environmental Contamination and Toxicolgy, 42/4: 447-453

Chirality and atmospheric transport



α-HCH



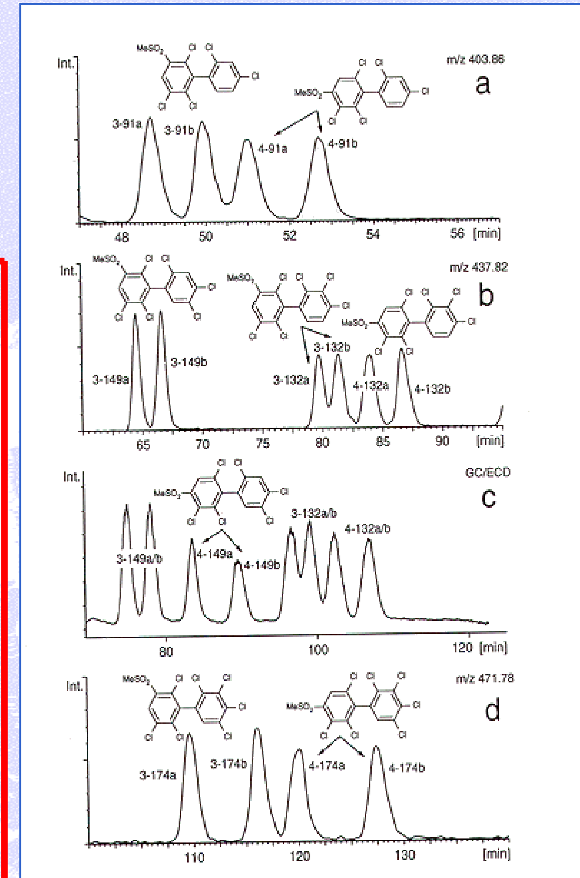
Jantunen LMM and Bidleman TF (1998) Organochlorine pesticides and enantiomers of chiral pesticides in Arctic ocean water. Arch Environ Contam Toxicol 35: 218-228.

Bidleman TF, Jantunen LM, Harner, T, Wiberg K, Wideman JL, Brice K, Su K, Falconer RL, Aigner E J, Leone AD, Ridal JJ, Kerman B, Finizio A, Alegria H, Parkhurst WJ, Szeto S Y (1998) Chiral pesticides as tracers of air-surface exchange. Environ Pollut 101: 1-7

Chirality and 'new contaminants'

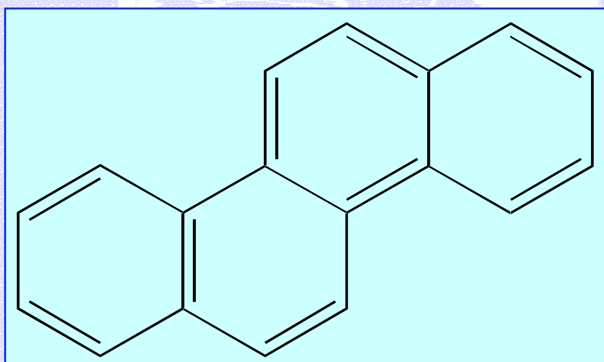
Metabolites: $MeSO_2$-PCBs

Ellerichmann T, Bergman Å, Franke S, Hühnerfuss H, Jakobsson E, König WA, Larsson C (1998) Gas chromatographic enantiomer separation of chiral PCB methyl sulfons and identification of selectively retained enantiomers in human liver. Fresenius Envir Bull 7: 244-257

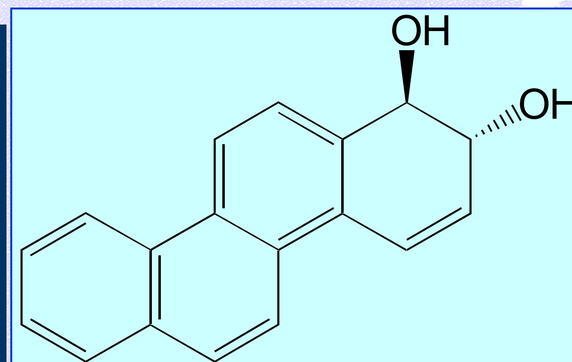


PAH: metabolites : Chrysene

Chang RL, Levin VV, Wood AW, Yagi H, Tada M, Vyas KP, Jerina DM and Conney AH (1983) Tumorigenicity of enantiomers of chrysene 1,2-dihydrodiol and of the diastereomeric bay-region chrysene 1,2-diol-3,4-epoxides on mouse skin and in newborn mice. Cancer Res 43: 192



Chrysene

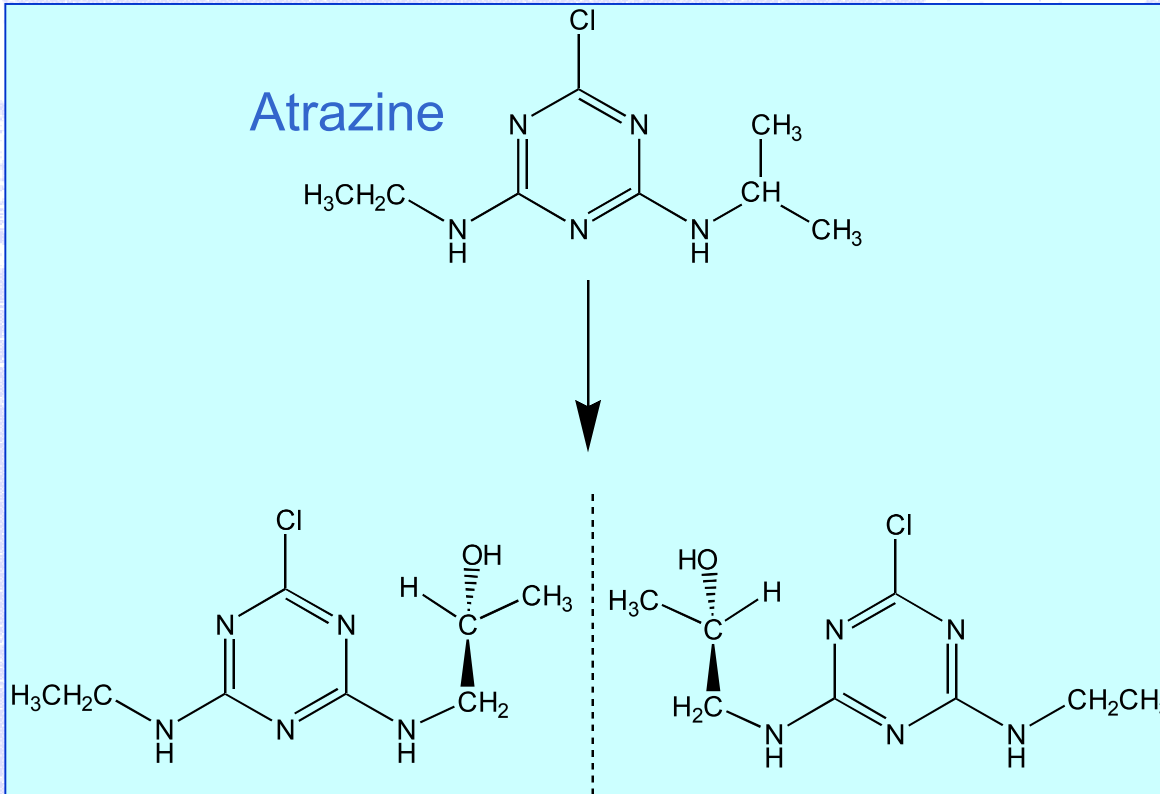


(+/-)-*trans*-1,2,-dihdroxy-1,2-dihydrochrysene

Chirality and 'new contaminants'

Metabolites: Atrazine

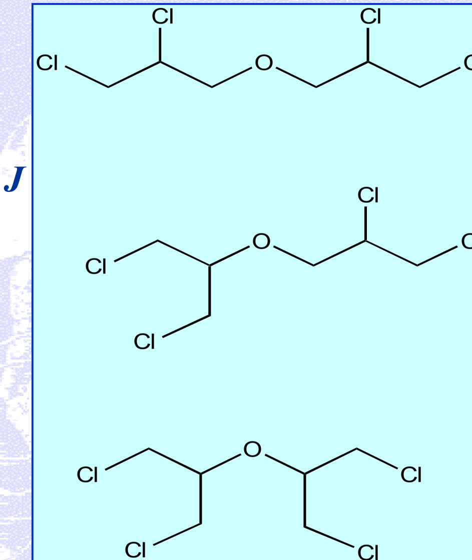
Lang D, Criegee D, Grothusen A, Saalfrank RW and Böcker RH (1996) In vitro metabolism of atrazine, terbuthylazine, ametryne, and terbutryne in rats, pigs and humans. Drug Metab Dispos 24: 859-65



(*R*)-1-hydroxy-iso-propylatrazine

(*S*)-1-hydroxy-iso-propylatrazine

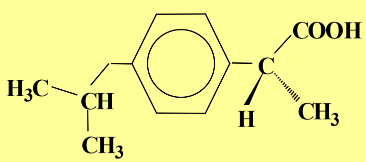
Chirality and 'new contaminants'



New Compounds: Chlorinated bis-propyl ethers

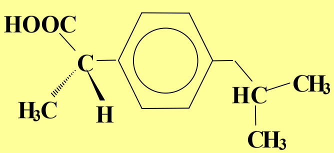
Franke S, Meyer C., Specht M, König WA, Francke W (1998) Chloro-bis-propy ethers in the Elbe river - isomeric distribution and enantioselective degradation. J High Resolut Chromatogr 21: 113-120

Pharmaceutical products:



(*R*)-(-)-Ibuprofen

inactive

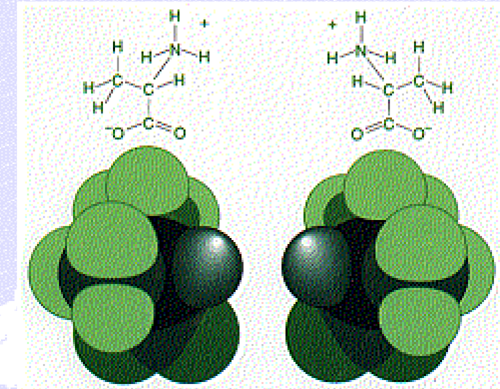


(*S*)-(+)-Ibuprofen

pharmacologically active

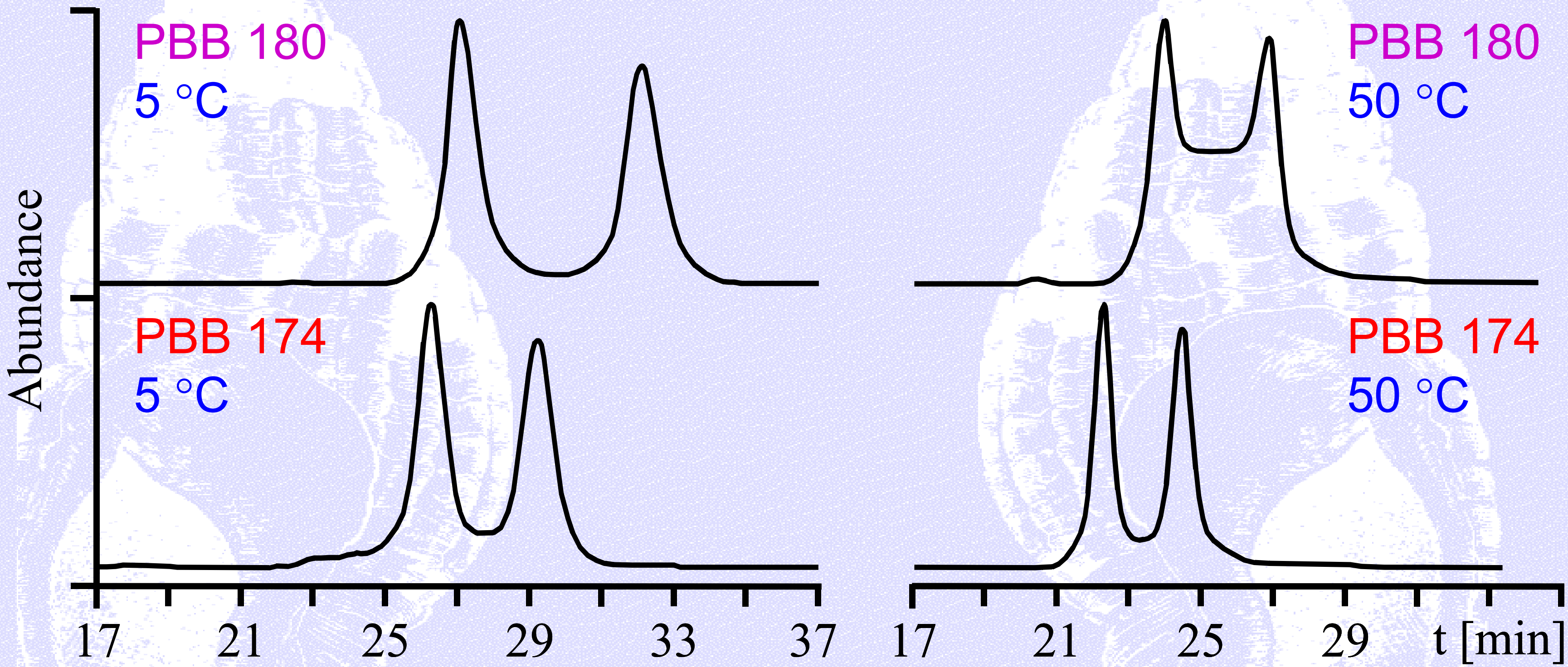
Buser H-R, Poiger T, Müller MD (1999) Occurrence and environmental behaviour of the chiral pharmaceutical drug Ibuprofen in surface waters and in wastewater. Environ Sci Technol 33: 2529-2535

Restrictions and challenges



- Racemic distribution in the environment does not exclude biochemical transformation,
- Combination of degradation and selective accumulation can possibly bias the final picture
- Not possible to discriminate between passive and active biological processes.

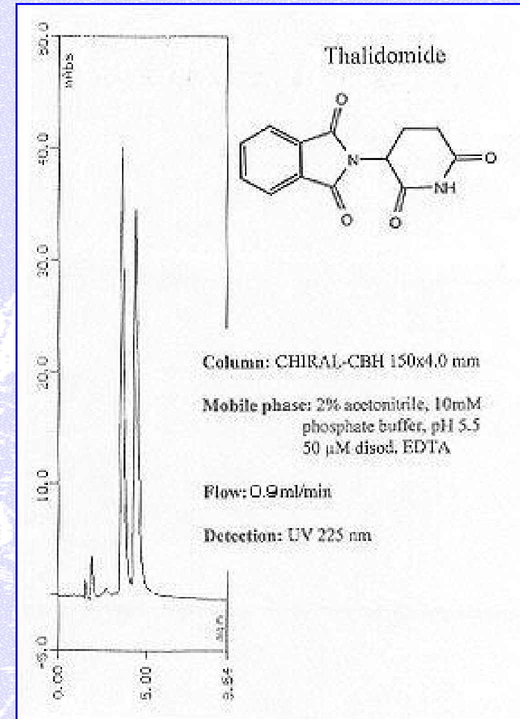
Enantiomer separation of brominated biphenyls (PBB)



Purple: "Buttressed" di-*ortho* substituted PBB
Red: Tri-*ortho* substituted PBB

- β-PMCD
- UV 220 nm

Toxicology



- Active transport through biological membranes is usually enantioselective (BBB)
- Binding affinity to receptors is potentially enantioselective.
- Enzymatic processes are potentially enantioselective (eg., cytochrome P 450)
- Xeno-endocrine and pheromone-like effects are likely to be enantioselective

Ecotoxicology

- Elevated levels in combination with deviation from the racemic distribution indicate high bioavailablility (eg., α-HCH, chlordanes).
- High levels in combination with (nearly) racemic distibution indicate passive accumulation processes/ biomagnification (eg., Toxaphene)

Challenges and perspectives

- Investigations on metabolisation/ transformation in biological systems must be performed enantioselective when chiral compounds are investigated.
- Risk assessment modeling i combination with enantioselective analysis can support the evaluation of the environmental hazards posed by chiral environmental contaminants.