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Enantiomeric Enrichment of Chiral Pesticides in the Environment

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Contents

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I. Introduction

Many agrochemicals consist of chiral compounds and about 25% of all agrochemicals used worldwide are chiral compounds (Williams 1996). In the Netherlands, approximately 23% of the total number of 265 permitted agrochemicals consist of a mixture of chiral compounds (CTB 1999). Only a small fraction of all agrochemicals are manufactured and used in the form of a pure enantiomeric compound. For example, in Switzerland and the Netherlands, the only type of chiral phenoxy herbicides permitted is the type containing only the active enantiomer (Williams 1996). For compounds that possess more than one chiral center, more than half of the compound may enter the environment as enantiomer ballast (Kohler et al. 1997; Eckhardt et al. 1992; Moser et al. 1982). There are advantages to be gained from using pure enantiomers rather than the racemate. Enantiomeric agrochemicals, in which one enantiomer is significantly more active than the other, are likely to cost less to produce, can be used in smaller quantities, and cause less environmental damage (Spangler et al. 1999; Renner 2000). Asymmetrical synthesis of pure enantiomers can be profitable because the patents of the racemic compounds expire in due course and because pure enantiomers are authorized exclusively in crop protection (Blaser and Spindler 1997; Williams 1996). However, most of the chiral agrochemicals found in the environment originate from symmetrical synthesis and are applied as such in the field.

Organisms produce or degrade chiral compounds by stereospecific enzymatic processes (Wiberg et al. 1998a). Therefore, application of chiral mixtures may result in a change in the concentration of the enantiomers that deviates from the racemic composition originally applied (Kohler et al. 1997; Faller et al. 1991a). As a result, the enantiomeric ratio (ER), defined as the ratio of the concentrations of the (+)-enantiomer and the (−)-enantiomer, will deviate from the racemic composition (ER = 1) (Vetter and Schurig 1997).

Enantiomer enrichment processes for chiral drugs in humans and laboratory animals have been studied extensively (Simonyi 1984; Brossi 1994; Caldwell 1996). Deviations from the racemic mixture have been found in plasma protein binding (Bertilsson et al. 1991; Hashimoto et al. 1992; Nordin and Bertilsson 1995; Rochat et al. 1995; Baudry et al. 1997; Sidhu et al. 1997; Yu et al. 1997), brain tissue (Hashimoto et al. 1992; Fuller and Snoddy 1993; Aoyama et al. 1994; Aspeslet et al. 1994; Baldessarini et al. 1994; Nybäck et al. 1994; Scanley et al. 1994; Baudry et al. 1997; Sam et al. 1997; Yu et al. 1997), brain fluid (Smith and Peterson 1982; Bertilsson et al. 1991; LaManna et al. 1993; Nordin and Bertilsson 1995; Sam et al. 1997), liver tissue (Püttman et al. 1989; Nordin and Bertilsson 1995; Rochat et al. 1997), and kidney tissue/urine (McErlane et al. 1990; Aspeslet et al. 1994; Prien et al. 1997). However, despite considerable pharmacological research, the processes such as stereoselective active transportation through membranes, stereoselective degradation, and stereoselective binding are not completely understood on the molecular scale. In general, it is assumed that active sites are able to select monomers of matching chirality from

a racemic mixture, thus giving rise to the formation of diastereomeric complexes between the active sites of enzymes and the chiral compounds (Hühnerfuss 2000). Diastereomeric complexes differ in their physical properties (Ternay 1979).

Abiotic enantioselective transformations can also change the ER. However, for these enantioselective processes a chiral catalyst or an excess of one enantiomer from a reactive chiral compound is required (March 1985). However, no such process condition has been reported in enantiomeric environmental studies (Zipper et al. 1998a). Enantiomerization reactions, which can also lead to changes in the ER, are biologically mediated (Buser and Müller 1998; Reist et al. 1995).

The ER can be used as a tracer tool in environmental studies (Bidleman 1998; Bidleman and Falconer 1999a,b). A distinction can be made between "old" and "new" sources of a chemical, and the fate of a compound can be traced in water and air (Bidleman et al. 1998a; Jantunen et al. 1998; Falconer et al. 1998; Ridal et al. 1997). For example, enantiomer profiles of nonracemic pesticide residues in soil and water are preserved on volatilization; the "old source" signature can be distinguished from a freshly applied racemic pesticide. Even an abnormal source of chiral herbicides, such as roof sealing as a source of mecoprop,[1] can be identified by measuring ERs (Bucheli et al. 1998a,b).

In general, hydrophobic persistent organic compounds accumulate from a lower trophic level to a higher trophic level. In a food web, the concentration increases to the highest trophic level (de Voogt 1996). Wiberg et al. (1998a, 2000) showed that concentrations of the enantiomers of α-HCH (hexachlorocyclohexane)[1] and chlordane compounds became biomagnified in the polar bear food chain. Additionally, ERs increased from total cod (ER ≈ 1) to blubber and liver samples of ringed seals to liver samples of polar bear (ER = 2.3). Multivariate statistical methods have been used to investigate the relationships between ERs, chemical residue concentration, and biological data (Wiberg et al. 2000). ERs of α-HCH and chlordane compounds were the most important variables for the sample groupings and for the class separation of male/female seals and fat/liver tissues (Wiberg et al. 2000). Therefore, ER measurements are likely to be a valuable distinctive tool for food chain analysis. Tanabe et al. (1996) showed that the ERs of α-HCH increased from ER = 0.8–1 for water, air, and lower trophic levels to ER = 1.6–2.8 for higher trophic levels such as pinnipeds and blubber of cetaceans. Iwata et al. (1998) studied the biological and ecological factors of enantioselective accumulation of α-HCH. They found that the ERs in higher trophic animals were influenced by species-specific metabolism and transport processes in the body as well as by biological factors, whereas the ERs were also changed by ecological factors such as feeding habits. Deviations in ER as a result of sexual maturity, aging, and breeding activities were not significant (Iwata et al. 1998).

[1]For precise chemical nomenclature and Chemical Abstract Numbers (CAS), see the Appendix.

Changes in ER caused by differences in habitat and food sources were also found by Kallenborn et al. (1998). These results are in contrast to those found by Wiberg et al. (1998b), who showed that the sampling site (habitat) played a minor role in ER changes. In general, changes in ER are larger in seals than in herrings. According to Vetter and Muraya (2000), this is true because in higher organisms pollutants are subjected to an increased specialization of enzyme systems. Also, the health status of the animal may be a factor in the enantiomer-specific metabolism of chiral pesticides (Wiberg et al. 1998b). Wiberg et al. (1998b) showed that species-specific differences, e.g., inverse ERs of *cis*-chlordane[1] and *trans*-chlordane[1] in ringed seal versus harbor and grey seal, are important factors controlling ERs in Baltic seals. Their conclusions agree with results reported in the work of Iwata et al. (1998). Karlsson et al. (2000) showed that ERs of *cis*-chlordane and *trans*-chlordane were gender specific in cod. The female cod preferentially accumulated (−)-*cis*-chlordane and (−)-*trans*-chlordane.

ERs found in environmental compartments change in time and place (Zipper et al. 1998a; Jantunen and Bidleman 1998), but a theory explaining these changes has not yet been developed. The purpose of this review is to develop a model to predict enantiomeric enrichment in the environment for persistent pesticides. The model will be based on published ERs for six chiral compounds in air, water, soil, and biotic compartments.

II. Methodology and Data Selection

A. Enantiomeric Ratios

An enantiomeric ratio (ER) is defined as the (+)-enantiomer concentration of a chiral compound divided by its (−)-enantiomer concentration (Vetter and Schurig 1997):

$$ER = \frac{(+)\text{-}enantiomer}{(-)\text{-}enantiomer} \tag{1}$$

The (+)-sign indicates that the enantiomer rotates a plane of polarized light to the right, clockwise (March 1985). The isomer with the (−)-sign rotates the light to the left, counterclockwise. Chiroptical detection is not always included in chiral chromatographic analysis. Also, pure enantiomers or enantiomeric-enriched reference materials may not be available; therefore, the enantiomer elution sequence cannot be achieved. In such cases, the ER is defined as the concentration of the first eluting enantiomer divided by the second enantiomer, under precisely defined chromatographic conditions (Vetter and Schurig 1997). Nowadays, pure enantiomer or enantiomer-enriched standards are often available and the elution sequence can be easily determined (Müller and Buser 1994). In this study, we use the ERs as presented in the literature.

B. Enantiomer Fractions

The enantiomeric ratio data were transformed into enantiomer fractions (EFs) as a standard descriptor (Harner et al. 2000). The EF can be calculated from ER by the formula:

$$EF = \frac{ER}{ER + 1} \tag{2}$$

This descriptor provides a more meaningful representation of graphical data than the ER and is more easily employed in mathematical fate expressions (Harner et al. 2000). On the basis of an earlier draft version of this article, we found that the graphical representation of EFs is superior to the plotting of ERs and to the plotting of ERs in combination with inverse ERs (1/ER). EFs can always be plotted, even for ERs that reach infinity; the EF can only range from 0 to 1.0, with EF = 0.5 representing the racemic mixture.

C. Measurements

Measurements of the ERs of chiral organochlorine compounds in environmental samples started around 1990 (König et al. 1991) when highly selective chiral chromatographic columns were used. Chiral column material based on cyclodextrines yielded good separation of enantiomers (Vetter and Schurig 1997). Nevertheless, separation of enantiomers is not always successful. Chiral compounds with C-asymmetry are often easier to separate than compounds with axial asymmetry, known as atropisomers (Buser and Müller 1995a). Chiral gas chromatography was generally used to separate chiral organochlorine compounds in very low quantities, but electrophoresis (El Rassi 1997; Garrison et al. 1996; Penmetsa et al. 1997), micellar electrokinetic chromatography (Schmitt et al. 1997), and HPLC (Sevcik et al. 1997) have also been used.

D. Database

Data were selected from publications in which enantiomers were determined in different environmental compartments: water (dissolved phase and suspended particulates), air, soil, and biota. Only field data were used; no results from laboratory studies using field material were incorporated (Tett et al. 1994, 1997; Buser and Müller 1997, 1998; Zipper et al. 1998a,b; Zipper 1998). The references for the ERs are grouped by the chiral compounds in Table 1.

Six xenobiotics—α-HCH, mecoprop, *cis*-chlordane (CC), *trans*-chlordane (TC), oxychlordane (OXY), and heptachlor *exo*-epoxide (HEPX)—were selected from Table 1. These compounds were measured in several environmental compartments. The absolute configuration of the (+)- and (−)-enantiomers are shown in Fig. 1.

Table 2 lists the numbers of samples for the compartments water, air, soil, and biota. The ERs of the same origin (location, organism, organ) were grouped and an average ER was calculated. Every group or compartment is given a compartment number, *n*. For α-HCH, the total of 618 separate ERs could be grouped in 99 different compartments. Statistical calculations were performed in the database but were not used in the figures because they did not improve the distinctness. EFs were calculated according to Eq. 2 (Harner et al. 2000). The complete data set contains ER, organism name, the organs on which analy-

Table 1. List of chiral compounds with references.

Compound	Reference
α-HCH (hexachlorocyclohexane)	Faller et al. (1991a,b)
	Kallenborn et al. (1991, 1998)
	Müller et al. (1992)
	Hühnerfuss et al. (1992a,b, 1993)
	Mössner et al. (1992)
	Pfaffenberger et al. (1992, 1994a)
	Möller et al. (1993)
	Hummert et al. (1995)
	Falconer et al. (1995a,b, 1997)
	Jantunen and Bidleman (1996, 1997, 1998)
	Finizio et al. (1998)
	Klobes et al. (1998a)
	Oehme et al. (1995)
	Tanabe et al. (1996)
	Ridal et al. (1997)
	Aigner et al. (1998)
	Iwata et al. (1998)
	Wiberg et al. (1998a,b)
	Jantunen et al. (1998)
	Harner et al. (1999)
Phenoxypropanoic acids	Buser and Müller (1998)
(e.g. mecoprop and dichlorprop)	Buser et al. (1998)
	Bucheli et al. (1998a,b)
	Zipper et al. (1998a)
Chlordane compounds:	Buser et al. (1992)
cis-Chlordane (CC)	Büser and Müller (1993)
	Falconer et al. (1997)
	Müller et al. (1997)
	Wiberg et al. (1997, 1998a)
	Jantunen and Bidleman (1998)
	Aigner et al. (1998)
	Ulrich and Hites (1998)
trans-Chlordane (TC)	Aigner et al. (1998)
	Büser and Müller (1993)
	Buser et al. (1992)
	Falconer et al. (1997)
	Jantunen and Bidleman (1998)
	Müller et al. (1997)
	Ulrich and Hites (1998)
	Wiberg et al. (1997, 1998a)

Table 1. Continued.

Compound	Reference
Heptachlor *exo*-epoxide[1] (HEPX)	Hühnerfuss et al. (1993)
	Büser and Müller (1993)
	König et al. (1994)
	Müller et al. (1997)
	Finizio et al. (1998)
	Falconer et al. (1997)
	Wiberg et al. (1997, 1998a)
	Aigner et al. (1998)
	Bidleman et al. (1998b)
	Ulrich and Hites (1998)
	Jantunen and Bidleman (1998)
	Pfaffenberger et al. (1994a)
Oxychlordane[1] (OXY)	Hühnerfuss et al. (1993)
	König et al. (1994)
	Müller et al. (1997)
	Aigner et al. (1998)
	Klobes et al. (1998a)
	Pfaffenberger et al. (1994a)
	Vetter et al. (1997a)
	Wiberg et al. (1998a)
β- and γ- pentachlorocyclohexene	Hühnerfuss et al. (1992b, 1993)
atropisomers of PCBs	Vetter et al. (1997a)
	Glausch et al. (1995)
	Hühnerfuss et al. (1995)
	Blanch et al. (1996)
	Haglund and Wiberg (1996)
	Reich et al. (1999)
	Klobes et al. (1998a)
Atropisomer of methylsulfonyl-PCBs	Ellerichmann et al. (1998)
	Bergman et al. (1998)
	Wiberg et al. (1998c)
Toxaphene/polychlorinated bornanes	Kallenborn et al. (1994)
	Vetter et al. (1997a,b, 1998, 1999)
	Klobes et al. (1998b)
2,4′-DDD and 2,4′-DDT	Buser and Müller (1995a)
	Falconer et al. (1997)
	Finizio et al. (1998)
	Aigner et al. (1998)
Bromocyclen	Pfaffenberger et al. (1994b)

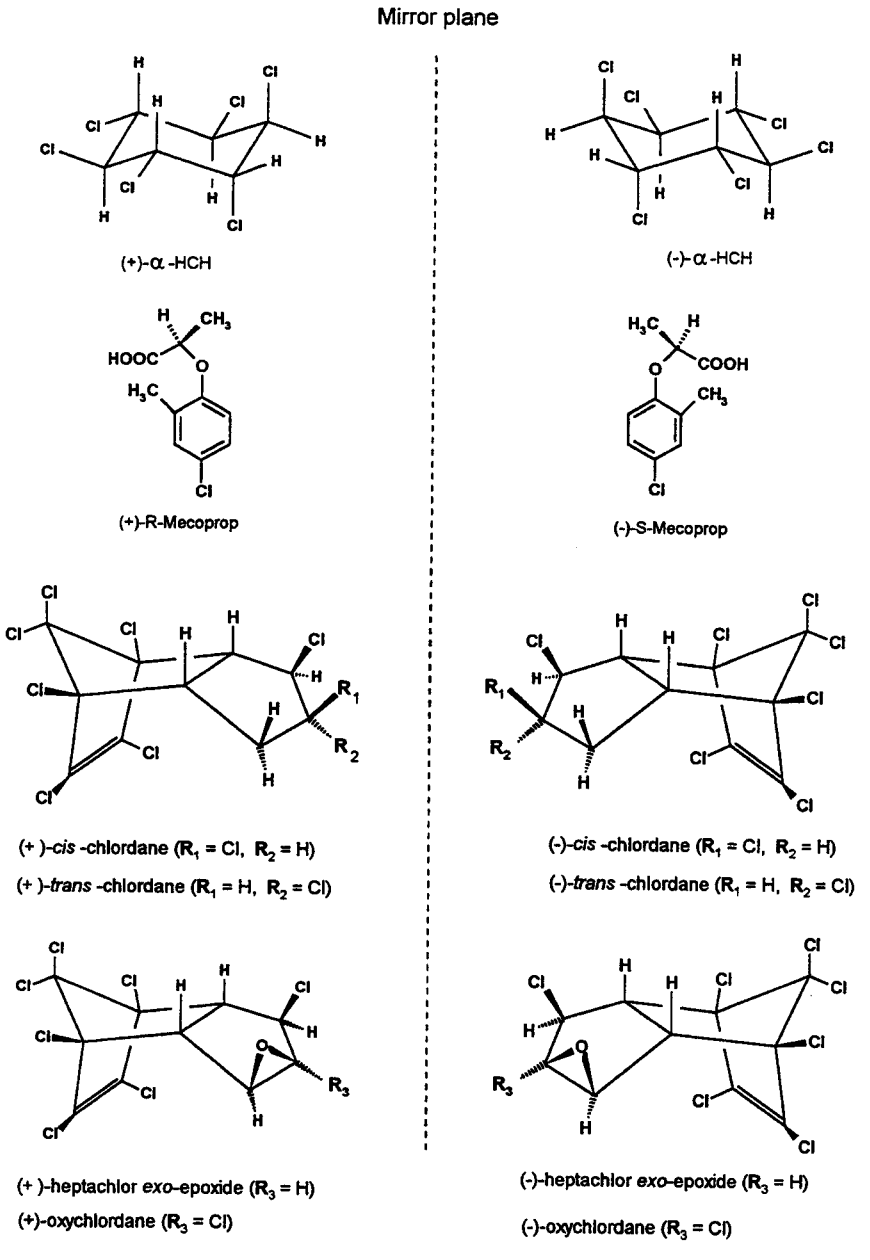

Fig. 1. Structures of the enantiomers of α-hexachlorocyclohexane (α-HCH), mecoprop, *cis*-chlordane, *trans*-chlordane, heptachlor *exo*-epoxide, and oxychlordane. The (+)-enantiomer cannot be superimposed upon its mirror image, the (−)-enantiomer. Note: α-HCH has *aaeeee*-conformation. Absolute configuration is according to Buser and Müller (1995b) (α-HCH); Zipper et al. (1998b) (mecoprop), and Miyazaki et al. (1980) (chlordane compounds).

Table 2. Number of samples in different compartments for which enantiomeric ratios (ER) were determined.

Compound	Total	Water	Air	Soil	Biota
α-HCH	618	269 (12)[a],(7)[b]	89 (9)[c]	10	250
Mecoprop	92	92[d]	—	—	—
cis-Chlordane	86	11	16	31	28
trans-Chlordane	96	14	17	32	33
Heptachlor *exo*-epoxide	105	12	17	26	50
Oxychlordane	99	—	—	17	82

—, no values found.
[a]Suspended particulates are assigned to the water compartment.
[b]Snow is assigned to water compartment.
[c]Rain is assigned to the air compartment.
[d]Groundwater samples belong to the water compartment.

sis was made, sampling area, date (when available), and the references. This data set is available on the Internet at **HTTP://www.waterresearch.nl/ERDATA.HTM** or from the author on request.

III. Selected Chiral Compounds

A. α-HCH

Technical hexachlorocyclohexane (HCH) used to be an important insecticide in agriculture and in forestry, and served as a wood preservative (Slooff and Matthijsen 1988). The technical mixture of HCH, which is produced by chlorination of benzene under UV light, consists of 60%–70% α-HCH, 5%–12% β-HCH, 10%–15% γ-HCH, and 6%–10% δ-HCH and smaller amounts of other isomers and congeners. The cumulative world emission of technical HCH between 1947 and 1997 amounted to 6800 kton (Wania and Mackay 1999). The use of technical HCH was discontinued in the United States in 1978 (Falconer et al. 1995b) and other industrialized countries but continues in Third World countries (Buser and Müller 1995a). Nine stereoisomers of 1,2,3,4,5,6-hexachlorocyclohexane, seven mesoforms and a *dl*-pair, exist in theory (March 1985). Eight unique isomers can be derived: α-, β-, γ-, δ-, ε-, η-, θ-, and ι-HCH (Deo et al. 1994). Only α-HCH consists of a pair of enantiomers. γ-HCH or lindane is an insecticide (Slooff and Matthijsen 1988). The chair conformer of HCH is stable at room temperature. The six chlorosubstituents are either in axial (*a*) or in equatorial (*e*) positions. The chair conformer can be involved in chair–chair interconversion, also called cyclohexane ring inversion (Ternay 1979). In this process, all the bonds that are axial become equatorial whereas those that are equatorial become axial. Therefore, α-HCH with the *aaeeee*-conformation is equal to α-HCH with the *eeaaaa*-conformation. The equatorial position is the more favorable one for a relatively large substituent such as chlo-

rine. The molecule will acquire the conformation in which most chlorine atoms are situated in an equatorial position. For α-HCH, *aaeeee* is the preferred conformation (Fig. 1).

Distribution and Metabolism. Relatively high concentrations of HCHs (sum of α- and γ-HCH) in air samples were found in the Northern hemisphere in tropical Asia (Bay of Bengal and Arabian Sea: 690–32,000 pg/m^3; Iwata et al. 1993). Water samples showed a considerable increase in HCH concentration above 40° N latitude in the North Pacific (Northern North Pacific: 240–1600 pg/L; Iwata et al. 1993). The global distribution of HCH isomers is controlled by their physicochemical properties and by meteorological conditions (Iwata et al. 1993). α-HCH is the most stable isomer on photolysis in the presence of iron salts (Malaiyandi and Shah 1984), which explains the persistence of α-HCH in the environment. Deo et al. (1994) concluded that any stereoisomer of HCH added to the environment is vulnerable to interconversion and degradation, processes that continue until an equilibrium is reached between the different isomers. The toxicity and the fate of HCH isomers in humans, wildlife, plant, soil, water, and atmosphere were reviewed by Willett et al. (1998). They concluded that the reasons for differences in the enantiomeric enrichment of α-HCH in environmental and biological samples are still largely unclear.

B. Mecoprop

Mecoprop belongs to the phenoxyalkanoic acids, or, simply, the phenoxy herbicide group. It is the most widely used herbicide for broadleaf weed control in cereal crops throughout the world (Worthing and Hance 1991). In the U.S., 23,000 kt of mecoprop and dichlorprop are used annually (Schneiderheinze et al. 1999). Of the total amount of mecoprop produced in the European Union (5000 t/yr), only 5% is applied in the form of the pure, active enantiomer (+)-(R)-mecoprop (Zipper 1998). The phenoxyalkanoic herbicides are highly water soluble acids ($pK_a = 3.11$) and have a low tendency to accumulate in organic matter. At pH 7, they are not sorbed to most soil types (Zipper et al. 1998a).

Distribution. Residues of phenoxyalkanoic herbicides are often found in subsurface and groundwater samples (Felding 1995; Fielding et al. 1991; Gintautas et al. 1992). Because of the hydrophilic character of Mecoprop, all ER measurements from field studies were in the dissolved phase (see Table 2). In European countries (Denmark, Germany, Great Britain, The Netherlands, Italy, Sweden), residues of (*R*,*S*)-mecoprop were found in drinking water in concentrations higher than the maximum allowable concentration for an individual pesticide, i.e., 100 ng/L (Zipper 1998).

C. Chlordane Compounds

Technical-grade chlordane was used extensively as a pesticide in the U.S. from 1948 to 1988 (ATSDR 1994). The cumulative world production is 70,000 tons (Christen 1999). Technical chlordane consists of more than 100 different com-

pounds that are structurally related (Vetter and Schurig 1997). *cis*-Chlordane, *trans*-chlordane, and heptachlor are the major compounds, accounting for 19%, 24%, and 22% of technical chlordane, respectively (Verschueren 1996). *cis*- and *trans*-Chlordane (CC and TC) are the insecticidally relevant parts of the formulations (Vetter and Schurig 1997). Heptachlor *exo*-epoxide (HEPX) was tested as an insecticide, (+)-HEPX exhibiting stronger insecticidal activity than (–)-HEPX (Miyazaki et al. 1978). Oxychordane (OXY) is the common metabolite of *cis*- and *trans*-chlordane in biota (Vetter and Schurig 1997). Oxychlordane can also be formed from octachlors and nonachlors (Aigner et al. 1998; Müller and Buser 1994). Heptachlor *exo*-epoxide (HEPX) is the major metabolite of heptachlor. The epoxidation of heptachlor occurs stereoselectively with conversion of the absolute configuration (Müller and Buser 1994).

Distribution. Chlordane compounds (sum of TC, CC, and *trans*-nonachlor) have relatively high Henry's law constant values. Consequently, atmospheric transport is an important migration route (Iwata et al. 1993). Chlordane compounds can be deposited in the Arctic and adjacent water bodies. Air concentrations of 8.1–160 pg/m^3 were found in the South China Sea and 5.5–55 pg/m^3 in the northern North Pacific (Iwata et al. 1993). Aqueous concentrations of chlordane compounds (sum of TC, CC, and *trans*-nonachlor) amounted to 3.9–22 pg/L in the East China Sea and 4.3–17 pg/L in the northern North Pacific (Iwata et al. 1993).

IV. Results

A. α-HCH

According to the literature, α-HCH is the compound with the highest number of measurements (Table 2). The average enantiomer fractions (EFs) in a group *n* of the same origin are plotted in ascending order in Fig. 2. The racemic composition has an EF of 0.5 (line). Compartments with an EF higher than 0.5

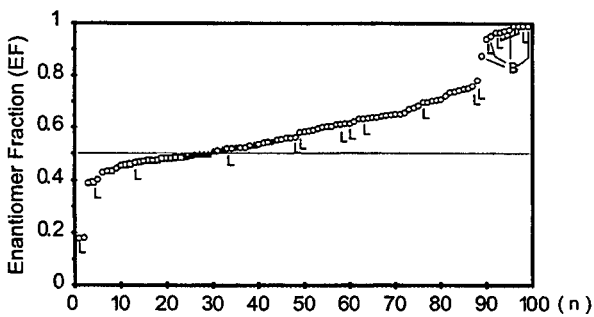

Fig. 2. Average enantiomer fraction (EF) of α-HCH in soil (◆), air (▲), water (□), and biotic compartments (○) in ascending order by compartment number (*n*). L, liver tissue; B, brain tissue.

have higher (+)-enantiomer concentrations, whereas EFs below the line EF = 0.5 have higher (−)-enantiomer concentrations (Fig. 2). Equal distances above and below the line EF = 0.5 indicate equal but opposite stereoselective behavior. There are two main groups, the abiotic compartments consisting of soil, air, and water and the biotic compartments consisting of all data from different organisms and organs. Extremely high EFs for the biotic compartments are shown in the upper right section of Fig. 2 whereas low EFs are shown in the lower left section. The EF of α-HCH in Arctic particulate material (Fig. 2, $n = 14$) was assigned to the water compartment because it interacts strongly with water. On the basis of studies of mecoprop behavior (Zipper et al. 1998a), we assume that sorption processes for chiral compounds are nonstereoselective.

In general, the abiotic compartments showed average EFs close to 0.5 (from 0.39 to 0.55; Fig. 2), whereas average EFs in biotic compartments showed a much higher deviation, from EF = 0.5 (0.18–0.99; Fig. 2). In biota, the enrichment in either (+)-α-HCH or (−)-α-HCH is often higher than in soil, air, and water. Most soil compartments (Fig. 2) showed a higher (+)-α-HCH concentration than their enantiomer because the (−)-α-HCH degrades faster than (+)-α-HCH (Finizio et al. 1998; Falconer et al. 1997). Nonenantiomer-selective photochemical reactions from γ-HCH are additional sources of α-HCH (Müller et al. 1992). Enantiomer enrichment of α-HCH from γ-HCH is mediated microbially (Faller et al. 1991a). In most cases, the air compartment (Fig. 2) shows EFs close to the racemic mixture of α-HCH. Only Arctic samples ($n = 30$, 32) and air samples taken above agricultural areas ($n = 39$) yielded slightly higher EFs. The aqueous compartment shows values close to EF = 0.5 or just below EF = 0.5, indicating that (+)-α-HCH degrades faster than (−)-α-HCH. The biotic compartments show EFs that are generally much higher than 0.5. Biotic compartments with EF < 0.5 are roe-deer liver ($n = 1$), blubber of hooded seal (Arctic) ($n = 2$), blubber of Antarctic Weddell seals ($n = 3$), Baltic blue mussel ($n = 5$), hooded seal from the North Sea ($n = 6$), fat ($n = 7$), and liver ($n = 9$) of sheep, herring $n = 10$), liver of flounder ($n = 13$), blue mussel from the North Sea ($n = 15$), and cod ($n = 17$). Liver and brain organs, especially in seal and bird samples, show EFs close to 1 ($n = 86$–99; Fig. 2); this indicates strong enrichment of (+)-α-HCH in these compartments.

B. Mecoprop

Average enantiomer fractions (EFs) of mecoprop are plotted in ascending order in Fig. 3. The majority of the studies were performed in Swiss groundwater and surface waters. Mecoprop is one of the few pesticides applied as a pure enantiomer (Williams 1996). In Switzerland, only (+)-*R*-mecoprop is registered for agricultural use (Williams 1996). Therefore, it was expected that EFs close to 1 would be found; in fact, EFs of less than 0.5 were found in Swiss wastewater treatment plants ($n = 1$), Swiss streams ($n = 2$, 3), roof water ($n = 4$, 8), and lakes ($n = 6$, 7, 10, 11) (Buser and Müller 1998; Bucheli et al. 1998a,b). These EFs are the result of selective breakdown of the *R*-enantiomer. EFs of less than

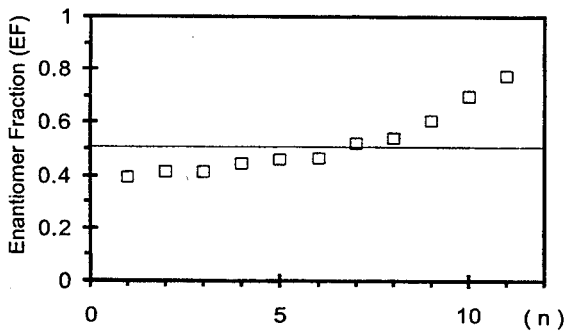

Fig. 3. Average enantiomer fraction of mecoprop in water compartments (□) in ascending order by compartment number (n).

0.5 were also found in the North Sea ($n = 5$) (Buser et al. 1998). The highest EFs ($n = 9$; Fig. 3) were found in groundwater wells at a former chemical waste disposal site at Kölliken, Switzerland (Zipper et al. 1998a). A range of EFs were found here but they depended on the site, the depth of the well, and sampling time. High EFs were often found in deep wells sampled in November, whereas in the same wells in February some EFs were close to 0.5 (Zipper et al. 1998a). High average EFs ($R > S$), up to 0.78, were found in Lakes Sempachersee ($n = 10$) and Hallwilersee ($n = 11$) in 1997 (Buser and Müller 1998). These values are the result of agricultural practices in combination with degradation of the R-enantiomer in soils (Buser and Müller 1998). The lowest EF (0.39) (Fig. 3) was from a wastewater treatment plant near Lake Greifensee ($n = 1$); the S-enantiomer had the highest concentration (Bucheli et al. 1998b). Apparently a bituminous roof sealing membrane impregnated with a Preventol B2 rubber seal protectant against root penetration was responsible for the high concentration of racemic mecoprop detected in municipal wastewater in Grüze, Switzerland (Bucheli et al. 1998a). Preventol B2 is a technical product of polyethylene glycol and releases (R,S)-mecoprop when hydrolyzed (Bucheli et al. 1998a).

C. *cis*-Chlordane (CC)

Average enantiomer fractions (EFs) of *cis*-chlordane are plotted in ascending order in Fig. 4. Soil samples in agricultural areas showed EFs higher than 0.5 ($n = 6$, 11–16). Air compartments in Southern Norway ($n = 8$), Southern U.S. ($n = 9$), and the Great Lakes ($n = 10$) show EFs of approximately 0.5. The deviation from EF = 0.5 in air compartments is very small (range, 0.50–0.52). The EFs in the surface water from the Arctic (Jantunen and Bidleman 1998) were close to 0.5 ($n = 7$). EFs in biotic compartments of *cis*-chlordane varied from 0.15 ($n = 1$) to 0.72 ($n = 20$). Average EFs in harbor seal blubber ($n = 1$), grey seal liver ($n = 2$), grey seal blubber ($n = 4$), and Baltic salmon ($n = 3$) samples showed relatively higher concentrations of the (–)-enantiomer; average EFs of

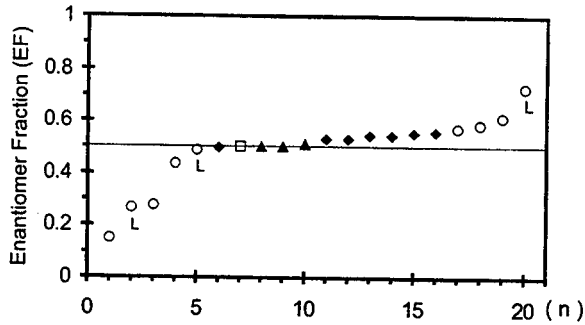

Fig. 4. Average enantiomer fraction of *cis*-chlordane (CC) in soil (◆), air (▲), water (□), and biotic compartments (○) in ascending order by compartment number (*n*). L, liver tissue.

herring ($n = 18$) and ringed seal blubber ($n = 19$) and liver ($n = 20$) of samples showed higher concentrations of the (+)-enantiomer concentration.

D. *trans*-Chlordane (TC)

Average *trans*-chlordane EFs are plotted in ascending order in Fig. 5. The EF in all agricultural soil compartments ($n = 11–15$, 18, 19; Fig. 5) is below the line EF = 0.5, which indicates that an enantioselective process has been in operation. The air compartments showed EFs close to 0.5 ($n = 17$, 20, 21; Fig. 5). The air above the Great Lakes (Ontario, Michigan, Erie, Superior; $n = 17$) showed an average EF of 0.47. Wiberg et al. (1997) proposed three possible sources for *trans*-chlordane in air: termiticides used in households, long-range transport from regions where chlordane is still in use, and, finally, volatilization from agricultural soil or from the Lakes themselves. Air samples from the Southern

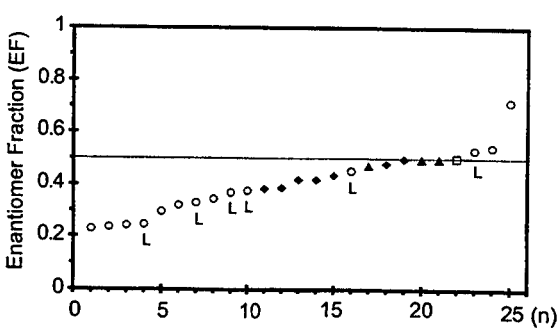

Fig. 5. Average enantiomer fraction of *trans*-chlordane (TC) in soil (◆), air (▲), water (□), and biotic compartments (○) in ascending order by compartment number (*n*). L, liver tissue.

U.S. (Alabama, South Carolina; $n = 21$) were close to 0.5 and showed no enantiomeric enrichment (Wiberg et al. 1997). Indoor air showed a high concentration of chlordane compounds, probably resulting from the use of termiticides (Wiberg et al. 1997). The EFs in air from the Norwegian south coast ($n = 20$) were 0.49 and showed no enantiomeric enrichment. It was concluded that the decline in concentration could only result from abiotic degradation processes of chlordane compounds (Buser and Müller 1993). Surface water in the Arctic showed EFs close to 0.5 (range, 0.49–0.51). In the Chukchi Sea, some values for EF were less than 0.5 and in the Greenland Sea higher EFs were more than 0.5 (Jantunen and Bidleman 1998), indicating reversed enantiospecific processes in different seas. *trans*-Chlordane enantiomers in biotic samples showed the EF to be less than 0.5 in several compartments ($n = 1–10$). Most organs in different seal species ($n = 1–4, 7–10, 16$) from Swedish waters showed enantiomeric enrichment of the (–)-enantiomers (Wiberg et al. 1998b; Buser et al. 1992). In addition, herring ($n = 2, 3, 6$), which is a food source for seals, showed an EF of less than 0.5 (Wiberg et al. 1998a). Salmon caught in the Swedish River Ume ($n = 24$) showed an EF greater than 0.5 in muscle (Buser et al. 1992). Blubber of the harbor seal ($n = 25$) in Swedish waters showed EFs greater than 0.5 (Wiberg et al. 1998a). These EFs showed enantiospecific processes to be the opposite of those found in liver samples of harbor seal ($n = 9$).

E. Heptachlor *exo*-Epoxide (HEPX)

Average heptachlor *exo*-epoxide EFs are depicted in ascending order in Fig. 6. Soil samples from the Fraser Valley, Canada ($n = 8$) showed EFs of 0.52 (Falconer et al. 1997). Samples from the U.S. agricultural areas showed EFs between 0.73 and 0.75 ($n = 17–21$). The average EFs in air compartments were between 0.58 and 0.67 ($n = 9, 10, 13, 14$). The highest EFs were found in air from Lake Ontario (0.65) and Lake Superior (0.67) (Wiberg et al. 1997). The average EF of HEPX in surface water at the North Pole ($n = 12$) was 0.62

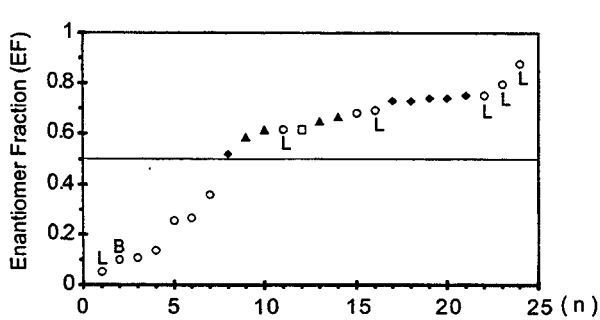

Fig. 6. Average enantiomer fraction of heptachlor *exo*-epoxide (HEPX) in soil (◆), air (▲), water (□), and biotic compartments (○) in ascending order by compartment number (n). L, liver tissue; B, brain tissue.

(Jantunen and Bidleman 1998). The EFs of HEPX in biotic compartments ranged from 0.05 to 0.14 for the organs liver ($n = 1$), brain ($n = 2$), and blubber ($n = 4$) in seals from Iceland (König et al. 1994). Blubber samples of harbor seal ($n = 3$), grey seal ($n = 5$), and ringed seal ($n = 6$) from Swedish waters yielded EFs below 0.5 (Wiberg et al. 1998b). On the other hand, samples of seagull ($n = 15$), hare liver ($n = 22$), rat liver ($n = 23$), and roe-deer liver from Baden-Württemberg and Schleswig-Holstein ($n = 24$) yielded EFs higher than 0.5 (König et al. 1994; Pfaffenberger et al. 1994a; Buser and Müller 1993.

F. Oxychlordane (OXY)

Average EFs of oxychlordane are depicted in ascending order in Fig. 7. EFs for OXY were determined only in soil and in biotic compartments. Average EFs of agricultural soils were higher than 0.5 ($n = 11$, 13, 19), except for Illinois soils ($n = 7$) (Aigner et al. 1998). The lowest EF was found in liver of harbor seal ($n = 1$, 2) and in brain of seal ($n = 3$) (Wiberg et al. 1998b; König et al. 1994). Exceptionally high average EFs of 0.92 and 0.95 were found in roe-deer liver samples from the German states Schleswig-Holstein ($n = 22$) and Baden-Württemberg ($n = 23$), respectively (Pfaffenberger et al. 1994a).

V. Discussion

A. Deviations from the Racemic Mixture

From the literature, we selected the enantiomer ratios (ERs) of six chiral organochlorine pesticides that were measured in air, water, soil, and biota. Enantiomeric processes in a compartment cause the enantiomer fraction (EF) to deviate from the racemic composition (EF = 0.5). For air, water, soils, and organisms, there is a general trend in the deviation of EF from 0.5 for the six compounds. First, the EFs in air are close to 0.5 in the abiotic compartments; second, the

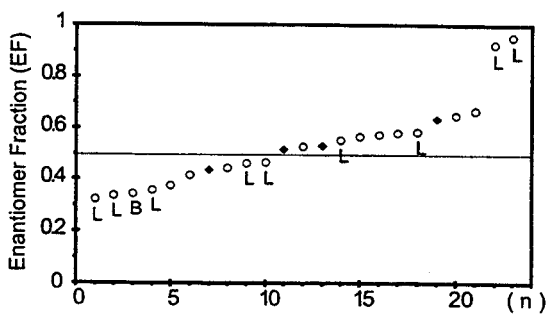

Fig. 7. Average enantiomer fraction of oxychlordane (OXY) in soil (◆) and biotic compartments (○) in ascending order by compartment number (n). L, liver tissue; B, brain tissue.

EFs in water compartments deviate slightly from 0.5. The highest deviations from EF = 0.5 in abiotic compartments occurred in soils. For the compounds considered, the order of the deviation from EF = 0.5 is air < water < soil. Enantioselective biodegradation of pesticides has a stronger effect on the EF in soils than in air or water compartments because pesticides from other sources with EFs close to 0.5 exchange easily between air and water. Also, compounds in a compartment with EFs close to 0.5 in a huge reservoir like an ocean are not affected by minor changes in EFs from other sources.

In general, biotic compartments (whole organisms, tissues, and organs) showed a higher deviation from EF = 0.5 than abiotic compartments; this is attributed to stereospecific metabolization and enzymatic transport processes. For the different compounds studied, lower trophic biota (e.g., mussels, cod, flounder) showed a smaller deviation from EF = 0.5 than higher trophic organisms (e.g., seals, birds, and terrestrial animals), as was also the case with α-HCH and octachlordane in the polar bear food chain (Wiberg et al. 1998a). A possible reason for these differences is that higher trophic level organisms have a higher metabolic capacity than cold water organisms (Karlsson et al. 2000).

High deviations from EF = 0.5 were found for the different pesticides in specific organs in biota, for example, in liver, kidney, brain tissue, and spinal marrow (Figs. 2, 4, 5, 6, 7). For the biotic compartments, a general trend in the deviation of EF = 0.5 was found in the following sequence: lower trophic biota < higher trophic biota < liver/kidney < brain. This sequence is the result of the combined effect of stereoselective degradation/metabolization, complexation, uptake, and excretion within an organism or its organ. Unfortunately, the mechanistic molecular processes are not understood, but progress has been made in understanding the mechanisms of chiral drugs applied to humans (Rochat et al. 1999).

B. Constant Enantiomer Fraction

After application, chiral xenobiotic compounds in the environment are redistributed over different compartments. In general, uptake and release of hydrophobic compounds are controlled by kinetic processes (de Wolf 1992) and hydrophobic compounds biomagnify from lower trophic to higher trophic organisms (de Voogt 1996).

When hydrophobic chiral compounds with EFs close to 0.5 are outside an organism, they can exchange with tissue and organs inside the organism. If no enantioselective processes occurred, the EFs of chiral compounds would have the same values inside as outside the organisms; however, enantioselective processes in different organs or tissues push the EF away from 0.5. The EF represents the result of these enantioselective exchange processes, enantioselective metabolization processes, and nonenantioselective exchange processes. Therefore, every organism and every organ in an organism will obtain its constant EF for a chiral compound that is typical for the compartment selected. In fact, the

observed concentration of enantiomers is a combined effect of nonenantioselective exchange and enantioselective processes in which every biotic compartment attains a constant EF. In these processes, it is not important how the EFs of a compounds are achieved; they can be the result of several processes, such as enantiomer-selective transport, enantioselective metabolization, kinetic exchange, or food web accumulation.

C. Model Scheme

Deviations from EF = 0.5 in abiotic and biotic compartments were found for the six selected pesticides but also occurred for other chiral compounds released to the natural environment. In Fig. 8, we present a general scheme for the deviation of EF from the racemic mixture that is applicable to various chiral compounds. Nearly every chiral compound is induced in the environment as a racemate (EF = 0.5) as a result of a nonenantioselective chemical synthesis. Enantioselective processes are responsible for the deviations from EF = 0.5. The EFs of chiral compounds in the air, water, and soil compartments are close to the EF of the racemic mixture (Fig. 8). In organisms such as mollusks, fish, birds, and marine mammals the deviations from EF = 0.5 increase as a result of the active uptake from lower trophic organisms and further enantiomer enrichment. The strong enrichment of one enantiomer in a higher trophic level overrules that of the existing EF in a lower trophic organism, even if the enrichment favors the opposite enantiomer in the lower trophic level. This mechanism has been demonstrated in a polar bear food chain (Wiberg et al. 1998a) for α-HCH where cod showed enantioselective behavior opposite to that of the predatory ringed

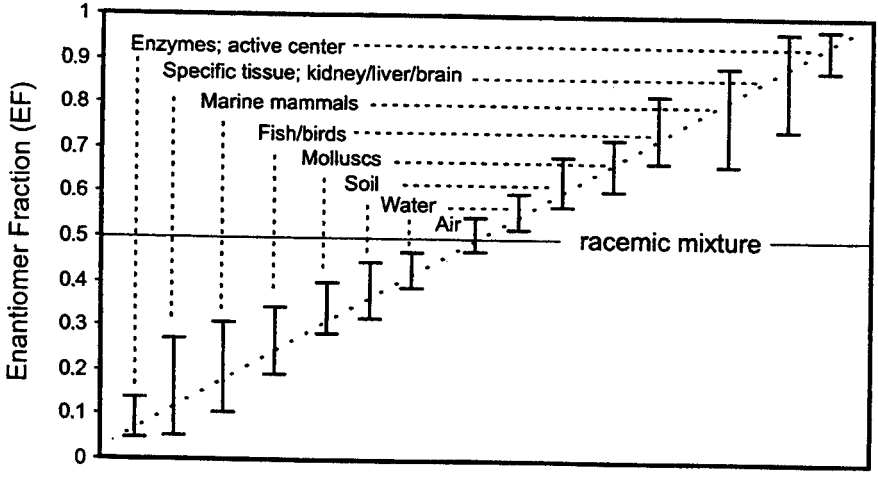

Fig. 8. Hypothetical model of enantiomer fractions (EFs) for a chiral compound in different compartments. Deviations from the racemic mixture are above or below the line EF = 0.5.

seal. However, by contrast, toxaphene compounds showed enantiomer enrichment in the lower trophic levels and racemic composition in the higher food web levels (Vetter and Maruya 2000).

The enrichment within a compartment shows a preference for one enantiomer; the EF is either above or below 0.5. (Fig. 8). The highest deviation of EF from the racemic mixture can be observed in liver, kidney, and brain tissue because in these compartments many stereoselective processes are in operation, i.e., enzymatic degradation and stereoselective transportation across membranes. On a molecular scale, we expect very high deviations of EF = 0.5 in the active centers of enzymes (Fig. 8) because this is where the chemical recognition of the chiral compound takes place. However, no data are available concerning enantiomer enrichment from enzyme active centers. Nonenantioselective biomagnification of a hydrophobic compound in a higher trophic organism will not alter the enantiomeric ratio; only enantioselective metabolization or enantioselective uptake or release can alter the EF. Although the processes leading to enantiomeric enrichment are not completely understood (Dugas and Penney 1981), we expect that the deviation from EF = 0.5 for various chiral compounds entering the environment will generally follow the scheme in Fig. 8.

D. Stereochemical Recognition of Chlordane Compounds

The structures of *cis*-chlordane (CC) and *trans*-chlordane (TC) in Fig. 1 show that these compounds differ only in the position of one Cl atom (R_1 versus R_2). These compounds enter the environment as racemic mixtures. If the stereochemical behavior is the same for each of these compounds, i.e., each compound is attacked at a topological congruent position, then we expect the deviation from EF = 0.5 to be in the same direction. In comparable compartments, we expect the EF to be either higher or lower than 0.5 for CC and TC. The direction of the deviation from the racemic mixture is shown in Table 3 for comparable compartments. CC and TC showed opposite behavior for most comparable compartments, which indicates opposite stereochemical behavior. The R_1 or R_2 position of the Cl atom (Fig. 1) proved to be the important structural position.

The structures of heptachlor *exo*-epoxide (HEPX) and oxychlordane (OXY) in Fig. 1 differ only in the R_3-substituent (Cl or H). These compounds enter the environment through the metabolism of chlordane compounds (Müller and Buser 1994). The direction of the deviation from EF = 0.5 (see Table 3) does not allow a similar conclusion to be drawn with regard to the stereochemical behavior of CC and TC. In some compartments similar stereochemical behavior was observed for HEPX and OXY whereas in other compartments opposite stereochemical behavior was observed (Table 3). On the molecular scale, the precise nature of the metabolization is complicated. The tertiary structure of a protein may be responsible for the stereochemical recognition of compounds and not the reaction center itself (Kaye 1991). However, certain structural elements can influence the observed enantiomer enrichment (Karlsson et al. 2000).

Table 3. Enantiospecific processes for the average enantiomer fraction (EF) of *cis*-chlordane (CC), *trans*-chlordane (TC), heptachlor *exo*-epoxide (HEPX), and oxychlordane (OXY) in soil, air, water, and biotic compartments.

Compartment	CC	TC	HEPX	OXY
Agricultural soils[a]	+	—	+	+
Air[b]	+	—	+	n.a.
Arctic water	+	—	+	n.a.
Grey seal, liver	—	—	n.a.	—
Grey seal, blubber	—	—	—	+
Harbor seal, blubber	—	+	—	—
Ringed seal, liver	+	—	n.a.	—
Ringed seal, blubber	+	—	—	+
Baltic herring, oil	+	—	n.a.	n.a.
Herring, total	+	—	—	+
Baltic salmon	—	+	n.a.	n.a.
Cod, liver oil	—	+	+	—
Seagull, egg	n.a.	n.a.	+	+
Hare, liver	n.a.	n.a.	+	+
Roe-deer, liver	n.a.	n.a.	+	+

Enantiomer-specific process: +, EF ≥ 0.5; —, EF < 0.5.
n.a., not available.
[a]CC and TC, 7 comparable compartments; HEPX and OXY, 3 comparable compartments.
[b]CC and TC, 3 comparable compartments; HEPX, 3 compartments.
Note: only grey seal compartments had the same sign for CC and TC.

E. Shielding from the Racemate

A deviation from EF = 0.5 can occur only by chemical binding of compounds where the enantiomers form diastereomers or by the formation of diastereomeric associations in which the interactions are weaker. Living systems, which range from simple to complex organisms, are homochiral and provide diastereomeric associations in enzymes that may result in stereoselective metabolization. Also, chiral compounds can be stereoselectively transported through biological membranes. For a deviation from EF = 0.5 to occur in any compartment, enantiomers have to be separated in a physical or a biochemical way to avoid a selective exchange with compartments that are not enriched in enantiomers. This "shielding from the racemate" can be obtained via membranes in living organisms, via semiisolated water bodies, by movements of percolating groundwater, or by sedimentation. Shielding of organisms from the surrounding water (EF ≈ 0.5) may be the result of the metabolism of chiral compounds and the selective passage of chiral compounds through biological membranes. This passage through biological membranes, the mechanisms of which are not completely understood (Baudry et al. 1997), can lead to different EFs within compartments.

For example, the EF of a organism can differ from the EF of water or the EF of liver can differ from the EF of brain (Figs. 2, 4, 5, 6, 7). In Arctic water, deep water is isolated from exchange processes with the atmosphere by overlying water bodies. In the Arctic atmosphere, the EF of α-HCH is approximately 0.5 whereas in subsurface water EFs of α-HCH reached 0.17–0.23 at depths of 250–1000 m (Harner et al. 1999).

Enantioselective processes in microorganisms may also alter the EF considerably (Harner et al. 1999). For instance, percolation water from waste disposal sites polluted with mecoprop has revealed EFs as high as 0.88 as a result of the groundwater being cut off from the racemic bulk by its movement in the ground (Zipper et al. 1998a). Shielding effects can be expected in sediment cores where each sediment layer is cut off from layers above or below. Only small changes in EF have been reported in sediment cores in which enantiomers of toxaphene compounds were measured (Vetter et al. 1998, 1999). The EFs of heptachlorobornane changed from 0.41 (in 1992) to approximately 0.44 (in 1935). The EFs of hepatchlorbornane were about 0.5 in all sediment layers. Changes in EFs in sediment cores were attributed to different types of microorganisms in different layers (Vetter et al. 1998, 1999).

F. Chiral Enrichment Processes

The extreme EFs depicted in Figs. 2 to 7 are found almost exclusively in the brain tissue of various organisms. Hühnerfuss et al. (1992a) attributed this high enrichment of one enantiomer relative to the other to the blood–brain barrier (BBB). BBB transport processes are currently under study by pharmacologists who seek to understand the action of chiral drugs (Rochat et al. 1999). The microvessels of the BBB consist of a single continuous layer of cerebral endothelial cells that are effectively sealed together by tight intercellular junctions (Ghersi-Egea et al. 1995). These junctions eliminate the paracellular pathway of solute movement through the BBB; there is practically no transcellular bulk flow of solute through the BBB (Baudry et al. 1997). Rochat et al. (1999) recognized three transport routes through the BBB: (1) passive passage, bidirectional, saturable transport that is characteristic of a mechanism requiring no energy; (2) carrier-mediated, by the presence of the efflux pump P-glycoprotein (Pgp) at the apical membrane of brain endothelial cells which effluxes many drugs and peptides back into the blood; and (3) metabolism, as brain endothelial cells contain a substantial volume of mitochondria, indicating that the BBB could contribute to significant monoamine oxidase (MAO) biotransformation of xenobiotics. Carrier-mediated transport and metabolism may result in the stereoselective passage of chiral compounds through the BBB, which in turn could lead to the observed changes in enantiomer fractions. If a chiral compound is to pass stereoselectively through a membrane, it has to create diastereomeric associations or complexes with its host, the membrane. Therefore, passive passage will not discriminate between enantiomers because there is practically no interaction with the membrane. Enantiomeric enrichments can be observed in liver samples

(see Figs. 2, 4, 5, 6, 7). The liver is a detoxification organ for xenobiotics. The metabolization of atropisomers of polychlorobiphenyls (PCBs) in human liver samples produced exclusively one atropisomer of methylsulfonyl PCBs (Ellerichmann et al. 1998; Bergman et al. 1998).

We suggest that two processes lead to chiral enrichment, resulting in higher concentrations of one enantiomer: the first process is stereoselective degradation and the second is stereoselective separation. We refer here to the first process as the chiral machine and to the second as the chiral guard. The chiral machine denotes the enzymatic recognition and metabolization of chiral compounds. The chiral guard is nondestructive, and its principal process is chiral recognition by the endothelial cells and stereochemical effluxing of the chiral compound by Pgp. An EF higher or lower than 0.5 is the result of one or more stereospecific processes. We assume that in the liver the chiral machine is the main stereospecific process. The chiral enrichment in the brain is the result of the chiral guard in combination with the chiral machine.

G. Environmental Regulations

The EFs of several chiral compounds show that biotic processes treat enantiomers differently, resulting in unequal enantiomer concentrations even in abiotic compartments such as water, air, and soil. Enantiomers can have different biological and physiological properties and can affect plants and organisms in different ways. Therefore, investigations that treat racemates as though they were single entities can produce inaccurate and misleading results (Amstrong et al. 1993). In the U.S., almost all environmental regulations, which are based on toxicological studies, treat racemates as single molecules with the same properties (Schneiderheinze et al. 1999; Kohler et al. 1997). In the European Union, also, the possible different effects of enantiomers are not taken into account. Further research into enantioselective biodegradation and toxicology is needed to investigate the distribution effect and fate of chiral agrochemicals (Schneiderheinze et al. 1999). Therefore, toxicological studies for chiral agrochemicals do not have a sound scientific basis.

Summary

Enantiomer fractions (EFs) of chiral compounds have been used to explain the mechanisms of enantiomer enrichment in air, soil, water, and biota. The EFs were calculated from enantiomeric ratios (ERs) of chiral compounds measured by researchers during the past 10 years. Six compounds were selected from different abiotic and biotic compartments: α-hexachlorocyclohexane (α-HCH), mecoprop, *cis*-chlordane (CC), *trans*-chlordane (TC), heptachlor *exo*-epoxide (HEPX), and oxychlordane (OXY). The EF was used as a general descriptor for enantiomer enrichment. In environmental compartments the EFs of chiral pesticides deviated from those of the racemic composition (EF = 0.5). The deviations from EF = 0.5 in the different compartments show similar patterns for

several compounds, i.e., air < water < soil < biota. In biota the order was lower trophic level < higher trophic level and liver or kidney tissue < brain tissue. Explanations for stereoselective behavior were found in pharmacology and brain research. The enantiomeric enrichments in environmental compartments were visualized in a general scheme applicable to other persistent chiral compounds. The mechanisms of enantiomer enrichment were conceptualized by a hypothetical model of a chiral machine (enzymatic degradation) and a chiral guard (stereospecific efflux). Environmental regulation authorities should treat chiral pesticides as a composition of enantiomers because biotic processes handle enantiomers as separate chemical entities.

Appendix. Chemical nomenclature.

Common name (abbreviation)	IUPAC	CAS number
HCH	Technical hexachlorocyclohexane	608-73-1
rac. (±)-α-HCH	(1a,2a,3b,4a,5b,6b)-Hexachlorocyclohexane	319-84-6
(+)-α-HCH	(1a,2a,3b,4a,5b,6b)-Hexachlorocyclohexane	119911-69-2
(−)-α-HCH	(1a,2a,3b,4a,5b,6b)-Hexachlorocyclohexane	119911-70-5
rac. (±)-(*RS*)-Mecoprop	(±)-(*RS*)-2-(4-Chloro-2-methylphenoxy)propanoic acid	7085-19-0
(+)-(*R*)-Mecoprop	(+)-(R)-2-(4-chloro-2-methylphenoxy)propanoic acid	16484-77-8
rac. (±)-*cis*-Chlordane (CC)	1-*exo*-2-*exo*,4,5,6,7,8,8-Octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindane	5103-71-9
rac. (±)-*trans*-Chlordane (TC)	1-*exo*-2-*endo*,4,5,6,7,8,8-octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindane	5103-74-2
rac. (±)-Heptachlor *exo*-epoxide or *cis*-heptachlorepoxide (HEPX)	1-*exo*-4,5,6,7,8,8-Heptachloro-2,3-*exo*-epoxy-3a,4,7,7a-tetrahydro-4,7-methanoindane	1024-57-3
rac. (±)-Oxychlordane (OXY)	1-*exo*,2-*exo*,4,5,6,7,8,8-Octachloro-2,4-*exo*-epoxy-3a,4,7,7a-tetrahydro-4,7-methanoindane	27304-13-8

rac., racemic.

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