Chapter 3

Chirality

3.1 Outline of the chapter

All investigations within the scope of this work are based on the chirality of molecules and the control of these chiral molecules by means of laser pulses. This chapter gives a short overview on the phenomenon of chirality. The first section will focus on the definitions of enantiomers and racemates as well as on their physical and chemical properties. In the following section the reader will also be introduced to the proper nomenclature of chiral molecules. The last section treats enantiomers and racemates in terms of quantum mechanics.

3.2 Enantiomers and racemates

Molecules consisting of the same number and types of atoms with the same connectivity of the atoms can form *stereo-isomers*, i.e. isomers that differ from each other by the spatial distribution of their atoms. The conceptional easiest case of stereo-isomerism is the so-called *cis-trans isomerism* where the two isomers only differ in their spatial configuration of e.g. four atoms connected by a C=C double bond. If two stereo isomers are mirror images of each other then they are called *enantiomers* (from *Greek* enantio = opposite)[1]. Enantiomers always form a pair with one molecule being the mirror image of the other

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[1]Stereo-isomers that are not mirror images of each other are called *diastereomers*.

one. Still both molecules cannot be superimposed since they are not identical. This phenomenon is called *chirality*. In general, a molecule that is not superimposable on its mirror image is *chiral*.[2] Hence, if it is superimposable on its mirror image it is *achiral*.
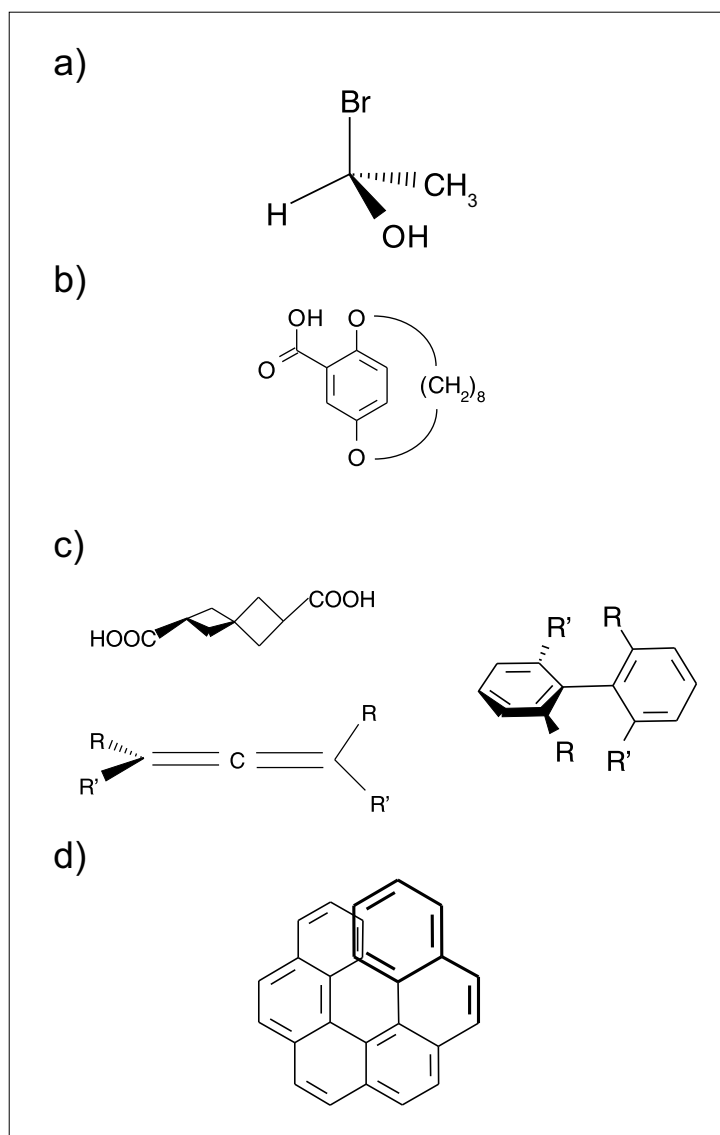

Figure 3.1: Examples of different kinds of chiral molecules: a) Chiral center: C-atom with 4 different substituents; b) Chiral plane: cyclophanes; c) Chiral axis: spiranes, allenes, biphenyles (atropisomers); d) Helical chirality: helicenes.

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[2]The absense of a symmetry element of second order (σ,i,S_n) makes a molecule chiral.

The source of chirality in molecules can originate from different types of configurations of their atoms. The most common one is the chiral center usually generated by a Carbon atom with four different substituents. Other types are chiral axis, chiral plane and a helix. Figure 3.1 shows examples of all four different kinds of chiral molecules. A chiral molecule as part of a polymer causes this also to be chiral. Proteins consisting of chiral amino acids form, for example, helices with a fixed sense of rotation.

Enantiomers have the same physical properties[3] except for the fact that they rotate the direction of the polarization vector of electromagnetic fields by the same angle but in opposite directions. This behavior is called *optical activity* and it is connected to the phenomenon of chirality. Chiral substances show optical activity, hence, a pure enantiomer is optically active. A 50%:50% mixture of two enantiomers exhibits no optical activity because the effect of both enantiomers on the polarization vector cancels out. Such a mixture is called a *racemate* and it is not chiral.

The explanation for the optical activity of chiral compounds is connected with the polarizability of the molecule and the fact that light is slowed down by the interaction with a molecule. Linearly polarized light may be regarded as a superposition of left- and right-handed circularly polarized light. As long as linearly polarized light is passing through a symmetrical region of the material both circularly polarized components travel at the same speed. However, a chiral molecule has a different polarizability depending on whether it is approached from the left or the right. One circularly polarized component approaching the chiral molecule "from one side" sees a different polarizability than the other one and is slowed down to a different extent. Hence, the left- and right-handed circularly polarized components travel at different velocities causing the vector of the linearly polarized light to rotate towards the left or the right. In liquids and gases the molecules are randomly oriented. Hence, there are molecules that rotate the polarization vector of the light in one direction while others rotate it in the other. Even though nearly all molecules rotate the polarization vector individually, the net effect for a achiral substance is that the polarization angle of the light will not change, since there is always a molecule which is oriented opposite to a previous one canceling the rotation effect. For chiral substances, however, no opposite orientation is present and there is a net rotation.

The chemical properties of enantiomers are identical in a symmetrical environment but different in an unsymmetrical environment. Enantiomers react at the same rate with achiral compounds, but at different rates with chiral compounds[4]. In general, it is impossible to synthesize an chiral substance in a chemical reaction without any source

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[3]The parity-violating weak interaction is not considered. At the atomic level enantiomers differ in total energy by a tiny energy difference.

[4]This is the reason why for many chiral molecules only one enantiomeric form is biologically active while the other form is not, see e.g. ref. [15].

of chirality (see Figure 3.2). If achiral educts (A and B) form a chiral product (P) always both enantiomers (S- and R-Form) will be yielded to the same amount forming an achiral racemic mixture. If, however, a chiral source (M*) is present in the reaction an *enantiomeric excess* will be produced. A reaction is called *enantio-selective* if achiral substrates form exclusively or predominantly one enantiomer at the expense of the other enantiomer. The source of chirality in an enantio-selective reaction is a chiral reagent, e.g. a chiral auxiliary forming a chiral precursor, a chiral catalysator [118, 16, 17, 18], or a chiral solvent causing an unsymmetric environment [119]. In theory, also in the presence of circularly polarized light a chiral product richer in one enantiomer should be obtained from achiral reagents (for a review see ref. [20]). However, such experiments have not yet proven to be very efficient since the extent of creating pure enantiomers has always been found less than 1% [120, 121, 21, 23].

Achiral reactants give a 50%:50% mixture of both enantiomers:

$$A + B \longrightarrow (S)\text{-}P + (R)\text{-}P$$

racemate
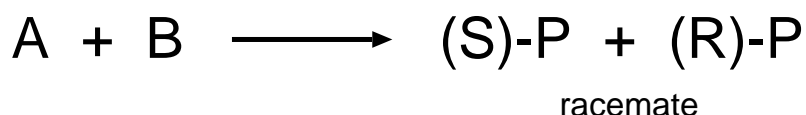
Chiral auxiliaries induce enantio-selectivity:

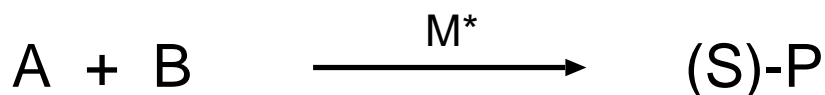$$A + B \xrightarrow{\quad M^* \quad} (S)\text{-}P$$

Figure 3.2: Only in the presence of a chiral reagent enantio-selectivity is gained.

Instead of obtaining a pure enantiomer from an enantio-selective synthesis, which is not always possible, a racemate can be separated to gain the desired chiral molecule. The separation of a racemic mixture is difficult since both enantiomers behave chemically identically unless they are in contact with a substance carrying chiral information. Most commonly used is the conversion of the both enantiomers into *diastereomers*, which can easily be separated, e.g. by fractional crystallization, since diastereomers have different physical and chemical properties. A different method to separate enantiomers is by using a chromatographic column which consists of chiral substances; because of the chiral environment the enantiomers are adsorbed to a different extent and, therefore, move along the column at different rates. If only one enantiomer is desired the undesired one can also be destroyed by a biochemical process. Certain bacteria differentiate between the two enantiomeric forms of a substance and digest only one of them. In general, the separation of enantiomers has always the disadvantage that half of the sample has to be discarded

unless both enantiomers are desired.

3.3   Cahn-Ingold-Prelog nomenclature

In this work only molecules with axial chirality are discussed. The chiral axis [5] can be derived in the conceptual easiest way from the four fold rotational mirror axis by annihilation of this symmetry. Around this axis four substituents a, b, c, d are arranged in pairs, but do not lie in a plane (see Figure 3.3). Within each pair the substituents must be different ($a \neq b, c \neq d$), but substituents of the two different pairs may be identical (e.g. $a = c$), in contrast to a chiral center. Molecules with the configuration ab, ab are still chiral. This kind of enantiomerism can be found in allenes, alkylidene-cycloalkanes, spiranes, adamantanes, biphenyls and related categories of compounds.
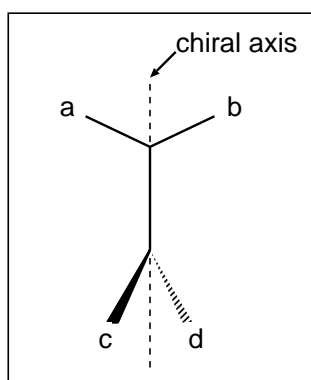

Figure 3.3: Chiral axis connecting four atoms a,b,c and d

For all kind of stereo-isomers different types of nomenclature are used. In the case of enantiomers the goal is to distinguish between the two forms by defining their configuration. The *Fischer nomenclature* (see e.g. ref. [12]) for sugar molecules is historically the oldest way to define the configuration of a chiral molecule. The letters D (from dexter = right) and L (from laevus = left) are used to distinguish between the configuration of a sugar and its mirror image relative to the configuration of (R)- or (S)-glyceraldehyde, respectively, which is used as reference. Since this reference cannot be used for all kind of stereo-isomerism the Fischer nomenclature is nowadays only used for certain sugars. A more general approach is the *Cahn-Ingold-Prelog nomenclature* (CIP) [6] which allows to define an *absolute* configuration. A so-called sequence rule is applied to put all substituents around the chiral center, axis, or plane in an order of priority. By viewing the

molecule along a certain bond the absolute configuration labeled R (from rectus = right) or S (from sinister = left) can be derived.

It is important to note that the configuration of a molecule using neither the Cahn-Ingold-Prelog nor the Fischer nomenclature matches the direction of the change of the polarization vector of light caused by the molecule. The direction of the change of the polarization vector of light can only be obtained experimentally and it is denoted by a *(+)* or *(−)* in front of the name of the substance. By chance, the configuration of a molecule derived from the CIP nomenclature may coincide with the direction of turning the polarization vector of light.
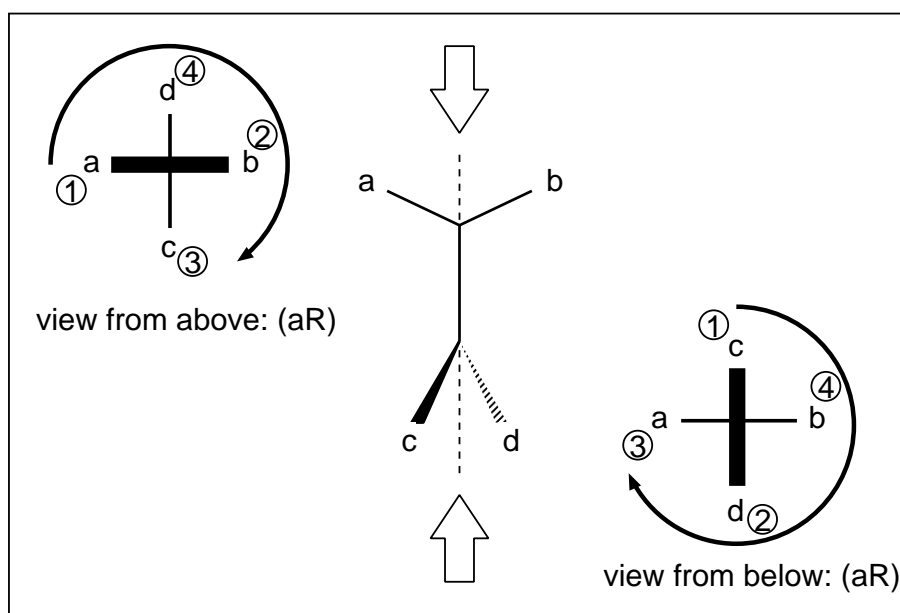

Figure 3.4: Determination of the stereo descriptor for a molecule with chiral axis. (adapted from ref. [122])

The CIP nomenclature of molecules with chiral axes is based on a simple sequence rule: closer groups have a higher priority than distant groups. The molecule must be viewed along its chiral axis; the direction is not important as long as the above rule is followed. The order of priority for atoms is in general given by their atomic numbers, i.e. fluor has a higher priority than hydrogen. Let the priority be $a > b > c > d$. Then, viewing the molecule from above as shown in figure 3.4 the sequence of substituents is clockwise (a, b, c). Therefore, the configuration of the molecule is (aR) where the prefix a stands for axial but it is not compulsory. The same result is also derived if the molecule

is viewed from below. Here, the closer substituents (c, d) have higher priority than the distant ones (a, b). Thus, the sequence is again clockwise (c, d, a) and the chiral axis is called (aR).

3.4   Localized wave functions

In quantum chemistry two enantiomers can be described by localized wave functions in a symmetric double well potential. Each well is the minimum energy configuration of one of the two enantiomers. The wells must be energetically equivalent because both enantiomers have the same molecular energy[5]. A potential barrier with a height which depends on the coordinate chosen to transform one enantiomer into the other one separates the two wells. In case of molecules having a chiral axis this energy barrier is the torsional barrier around the chiral axis.[6] Each enantiomer is described by means of a single wave function localized in either of the two wells [30]. These localized wave functions $|\Psi_{vL}\rangle$ for the wave function localized in the left potential well and $|\Psi_{vR}\rangle$ for the wave function localized in the right potential well are constructed by positive and negative superposition of pairs of eigenstates $|\Phi_{v\pm}\rangle$ of the system [30]:

$$|\Psi_{vL}\rangle = \frac{1}{\sqrt{2}} \left(|\Phi_{v+}\rangle + |\Phi_{v-}\rangle \right)$$
$$|\Psi_{vR}\rangle = \frac{1}{\sqrt{2}} \left(|\Phi_{v+}\rangle - |\Phi_{v-}\rangle \right) \tag{3.1}$$

The eigenstates of a double well potential form doublets v below the barrier and are denoted by $v+$ and $v-$, e.g. $0+, 0-, 1+, 1-$, where $+$ (*gerade* or *even*) is used for functions which are symmetric with respect to inversion and $-$ (*ungerade* or *odd*) for functions which are anti-symmetric with respect to inversion. Figure 3.5 shows the construction of $|\Psi_{0L}\rangle$ and $|\Psi_{0R}\rangle$ from $|\Phi_{0+}\rangle$ and $|\Phi_{0-}\rangle$ of the energetically lowest doublet $v = 0$.

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[5]The very tiny difference in energy (10^{-14} J/mol [43]) due to the parity-violating weak interaction is not considered. For further discussion see refs. [39, 40]

[6]For molecules with a chiral center a bond must be broken and reformed 'on the other side' to transform one enantiomer into the other. In this case, an appropriate reaction coordinate might be difficult to find since dissociation must be included. The potential barrier will be very high.
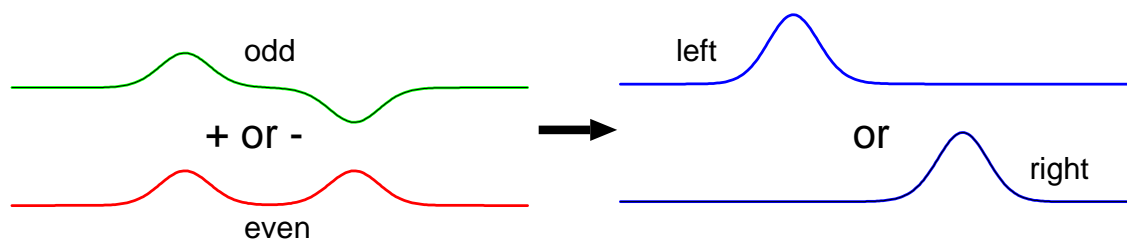
Figure 3.5: The $+$ or $-$ superposition of the energetically lowest doublet of eigenstates $|\Phi_{0+}\rangle$ and $|\Phi_{0-}\rangle$ produces the left or right localized wave function $|\Psi_{0L}\rangle$ or $|\Psi_{0R}\rangle$, respectively.

For a potential barrier of finite height and width the eigenenergies E_v in the left and right well are not exactly degenerate below the barrier. The energy splitting ΔE_v of the doublets depends on the height and width of the potential barrier. ΔE_v increases with increasing energy, i.e. with decreasing height and width of the barrier. The lifetime of an enantiomer is given by the energy splitting ΔE_v of the doublet via the *Heisenberg uncertainty principle*:

$$\Delta E_v \cdot \tau_v = h, \qquad \Delta E_v = E_{v-} - E_{v+} \tag{3.2}$$

where E_{v+} and E_{v-} are the eigenenergies of the eigenfunctions v with $+$ and $-$ symmetry, respectively. The tunneling time of a wave function τ_v of a specific doublet v is the full period of tunneling from the left well to the right well and back. The lifetime of an enantiomer is given by half the tunneling time. For very high potential barriers the doublet states will be almost degenerate, at least for the energetically lowest doublets. Therefore, the lifetime of the enantiomer will be quasi infinite compared to the timescale of the simulated control of the chemical reaction.[7]

Since the choice of calling the (aR)-enantiomer Ψ_R or Ψ_L is completely arbitrary and has no effect on the outcome of the calculations, for simplification and better understanding of the text, the enantiomer described by a wave function localized in the left potential well will be called the L-enantiomer and the one described by a wave function localized in the right potential well R-enantiomer. This nomenclature is not to be confused with the CIP nomenclature discussed in section 3.3.

A racemate is a *mixture* of two enantiomers (see section 3.2). In terms of quantum mechanics a mixture of n states $|\Psi_v\rangle$ which have been prepared independently is described

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[7]Barron introduced the concept of "true" chirality for quantum systems describing time-invariant molecular chirality in contrast to "false" chirality in case of time-variant enantiomorphism [123].

by the density matrix operator ρ, also called statistical operator[8]

$$\rho = \sum_{v=0}^{n} |\Psi_v\rangle W_v \langle \Psi_v| , \qquad (3.4)$$

where W_v is the (Boltzmann) weight of the state v. Below a certain temperature the eigenstates of the system above the potential barrier are not populated and may be neglected

$$
\begin{aligned}
\rho &= \rho_{\text{above the barrier}} + \rho_{\text{below the barrier}} \\
&= \rho_{\text{below the barrier}}.
\end{aligned}
\qquad (3.5)
$$

Then, a racemate is described as a density ρ_{rac} which is derived from a wave function localized in the left potential well and a wave function in the right well, forming an *incoherent* superposition of $|\Psi_L\rangle$ and $|\Psi_R\rangle$

$$
\begin{aligned}
\rho &= \rho_{\text{below the barrier}} \\
&= \sum_v \left(|\Psi_{vL}\rangle W_v \langle \Psi_{vL}| + |\Psi_{vR}\rangle W_v \langle \Psi_{vR}| \right) \\
&= \frac{1}{2}\rho_L + \frac{1}{2}\rho_R = \rho_{\text{rac}}.
\end{aligned}
\qquad (3.6)
$$

Here ρ_L and ρ_R are the density matrix operators for all population localized in the left and right well, respectively. Both wave functions, $|\Psi_L\rangle$ and $|\Psi_R\rangle$, must have the same weight W to make it a 50%:50% mixture. If the temperature is low enough the system can even be prepared so that approximately only the energetically lowest doublet $v = 0$ is populated (see section 4.5).

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[8]The dynamics of an incoherent mixture of n wave functions is determined by the *Liouville-von Neuman equation*, see section 4.5:

$$i\hbar \frac{\partial}{\partial t}\rho = \left[\hat{\mathbf{H}}, \rho\right]. \qquad (3.3)$$