Chapter 1

Introduction

The shape of a molecule is important in determining its physical properties and reactivity. In addition, atoms can often be arranged in different ways to create different molecules. When two molecules have the same formula but have their atoms arranged differently, so-called isomers result. There are two kinds of isomerism that are, constitutional isomerism and stereoisomerism. In constitutional (or structural) isomerism, the molecular formula and molecular weight of the substances are the same, but their bonding differs. Constitutional isomers that can be readily converted from one to another are called tautomers. In stereoisomerism, substances with the same atoms are bonded in the same ways but differ in their three-dimensional configurations. Stereoisomers that are related to each other by a reflection (mirror images of each other) are called enantiomers.

The effects of isomerism on the chemical and biological properties of compounds are of great interest especially the biochemical and pharmaceutical applications [1]. The reason is that, for instance, it is shown that a proton transfer, which results in different tautomers, can lead to mispairing of purine and pyrimidine bases in DNA thus causing point mutations. Moreover, an enantiomer might be useful in a certain pharmaceutical application while the other might not. In this thesis, it is intended to achieve theoretically two different goals. The first one is studying hydrogen bond geometry and kinetics in porphycene (see section 3.1) as an example of proton tautomerization. Recently, a lot of interest has been centered, not only on the possibility of tautomerism in various molecules of biological interest, but also on the mechanism of proton transfer. In the present work a detailed study on the hydrogen bonding going from the tunneling splitting to the geometric and kinetic H/D isotope effects is offered. The second goal is controlling chirality (discussed in section 1.2.1) in the model system H_2POSD (see

section 4.1). Laser control of chemical reactions and in particular, the design of laser pulses to separate enantiomers is discussed in detail. This study may motivate experimentalists to use light to separate enantiomers; for a first experimental approach see Ref. [2].

1.1 Proton tautomerization

1.1.1 Hydrogen bonding

There is no doubt that hydrogen bonding is of great importance in chemistry and biology. Latimer and Rodebush published the first paper about the hydrogen bond phenomenon in 1920 [3]. In 1928, Pauling [4, 5] was the first to introduce the name hydrogen bond. Since then a lot of attention has been paid to hydrogen bonding [1, 6, 7]. The name hydrogen bond implies that the hydrogen atom should be a part of the bond. The hydrogen bond is an attractive interaction between a proton donor A-H and a proton acceptor B, in the same or a different molecule. For instance, the complex A-H...B (Fig. 1.1) has a bridge between the proton donor and acceptor, where A and B are electronegative atoms such as oxygen, nitrogen or fluorine. These electronegative atoms attract the electron cloud from around the hydrogen nucleus and leave the atom with a positive partial charge. A hydrogen bond results when this strong positive charge density attracts a lone pair of electrons on another electronegative atom. This different polarizabilities may result in a proton transfer between the electronegative atoms giving rise to different tautomeric structures.

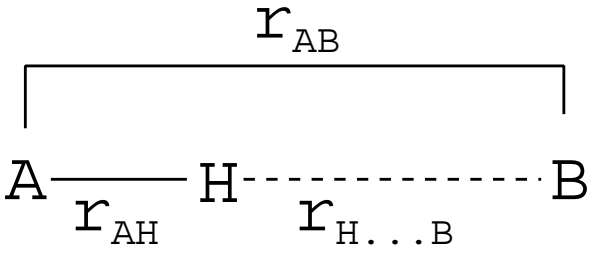

Figure 1.1: Schematic diagram of the hydrogen bond.

In the following, different types of hydrogen bonds are reviewed. Hydrogen bonds can be classified into three types [8] - **A) Traditional hydrogen bonds**: This is the most common type and designated as A-H..B. It has a shorter A-B

distance and a slightly longer A-H bond length with respect to the corresponding non-hydrogen-bonded system. For example, XH...NH_3 (X stands for F, Cl and Br) are stabilized by traditional hydrogen bonds in the gas phase [9, 10, 11]. **B) Ion-pair hydrogen bonds**: When the proton from the proton donor moiety A-H is transferred to the proton acceptor moiety B, the ion-pair hydrogen bond will be formed, which is designated as A^-...H^+-B. The distance B-H^+ is slightly longer than the corresponding free cation. Moreover, it has a similar A-B distance as the corresponding traditional hydrogen bond. For example, the BrH...$N(CH_3)_3$ complex has an ion-pair hydrogen bond in the gas phase [10]. **C) Proton-shared hydrogen bonds**: In this case the proton is shared between the two heavy atoms. It is designated as A...H...B. The A-B distance is shorter than the corresponding traditional and ion-pair hydrogen bonds. For example, ClH...$N(CH_3)_3$ is stabilized by a proton-shared hydrogen bond in the gas phase [10]

Part of the present study is concerned with the geometric H/D isotope effect in hydrogen bonded system and its firmly established relation to the shape of the potential energy surface (as discussed in section 1.1.3). It is, therefore, beneficial to explore different shapes of the potential energy surface according to the strength of the hydrogen bonds. The hydrogen bond can be classified, according to strength, into : **a) Strong**: This type of the hydrogen bond is represented by a single well potential energy surface or a double well potential surface with very low or vanishing barrier, see Fig. 1.2. The lowest vibrational wave functions are likely to lie above the barrier for the double minimum potential surface and are delocalized which makes such systems very sensitive to the environment. The hydrogen bond energy is about 14 to 40 kcal/mol. The distance between heavy atoms, r_{AB}, lies between 2.1Å and 2.6Å whereas the hydrogen bond distance $r_{H...B}$ ranges from 1.2Å to 1.5Å. A typical example is FHF^-.

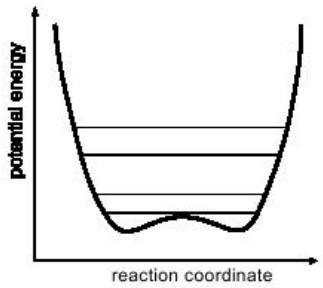

Figure 1.2: The potential energy function representing schematically the strong hydrogen bond with its vibrational eigen-energies above the vanishing barrier.

b) medium: This hydrogen bond is represented by a highly anharmonic single well potential energy surface (Fig. 1.3) compared to the non-hydrogen-bonded system. The lowest vibrational wave functions are localized. The hydrogen bond energy is about 4 to 14 kcal/mol. The distance between heavy atoms lies between 2.4Å and 3.3Å whereas the hydrogen bond distance ranges from 1.5Å to 2.2Å. It is prevalent in biological systems.

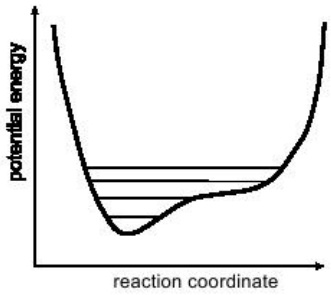

Figure 1.3: Schematic diagram of the potential energy surface for the moderate hydrogen bond.

c) weak: In the weak hydrogen bonds the potential energy surface is characterized by an asymmetric double minimum (symmetric double well in case of A=B, see Fig. 1.4). The wave functions of the lowest vibrational eigenstates cover both minima and lie under the potential barrier. The hydrogen bond energy is less than 4 kcal/mol. The distance between heavy atoms lies between 3.1Å and 4.3Å whereas the hydrogen bond distance ranges from 2.2Å to 3.2Å. This type of hydrogen bond is featured with, in addition to the local vibrational motion, tunneling between wave functions localized in the minima. As an example, ClH...benzene is characterized by a weak hydrogen bond.

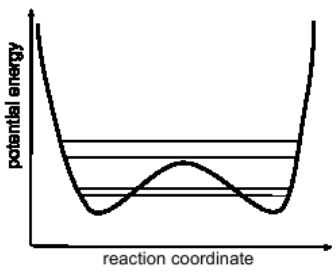

Figure 1.4: Double well model potential energy surface representing a weak symmetric hydrogen bond.

Understanding the hydrogen bond weak interaction is essential to explain many properties of molecules. The chemical structure of nucleic acids, proteins and many biological compounds is based on the nature of hydrogen bonds [12]. Moreover, hydrogen bonding controls many reactions such as e.g. enzymatic, solvation, and complex formation reactions [13, 14, 15, 16].

One of the most interesting aspects of intramolecular proton transfer processes is the nature in which structural rearrangements involving the proton are correlated with topological changes in the rest of the molecule as the reaction proceeds. Since these correlations reflect the reaction mechanism, study of the connection between the motion of the proton (kinetics) and the structure (geometry) can provide valuable insight into how a reaction proceeds. Here, deuteration provides a valuable means for a detailed investigation. The change in the geometry upon deuteration is called geometric isotope effect, while the change in the reaction rate upon deuteration is called kinetic isotope effect. As a matter of fact, this is one of the few instances where quantum mechanics surfaces even in complex biological systems (see, e.g., Refs. [17] and [18]).

1.1.2 Tunneling

It is well known that the wave functions of particles can extend beyond the classically accessible regions of potential energy surfaces, see Fig. 1.6. This important property is manifested in the so called quantum mechanical tunneling which enables particles to escape from the equilibrium region to the classically forbidden regions. Tunneling is most likely to happen for the very light atoms (like hydrogen and/or deuterium), therefore, the determination of its contribution to proton transfer is an important issue. Tunneling is quantitatively characterized by the observation of a splitting of the degenerate levels localized in either well of a symmetric double well potential, see Fig. 1.5. The tunneling splittings increase as the energy levels approach the top of the barrier.

Tunneling occurs when there is an overlap between the localized wave functions in different wells at the barrier region. This overlap will be obvious in case of symmetric double well potentials (e.g. some of proton transfer reactions), see Fig. 1.4. The associated tunneling splitting depends on the mass of the tunneling particle, the barrier height and width separating potential wells (Fig. 1.6).

The symmetry in the double well potential is a result of the equivalence of the two tautomeric structures. The symmetry remains unless there is an external interaction with e.g. the solvent. This coupling to the environment will cause

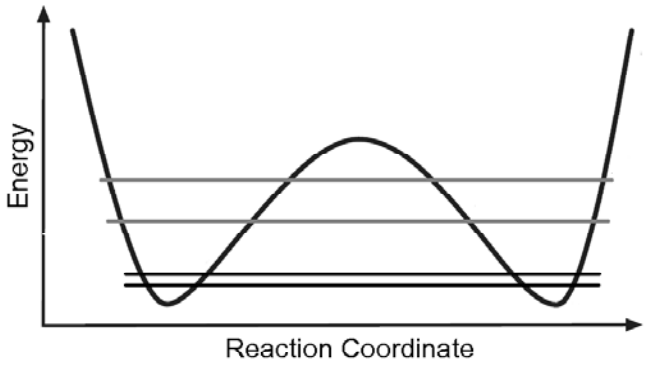

Figure 1.5: Schematic representation of a one dimensional potential energy curve and the tunneling splitting for the four lowest energy levels. The splitting of the first two energy levels (black) is smaller than that of the second two energy levels (grey).

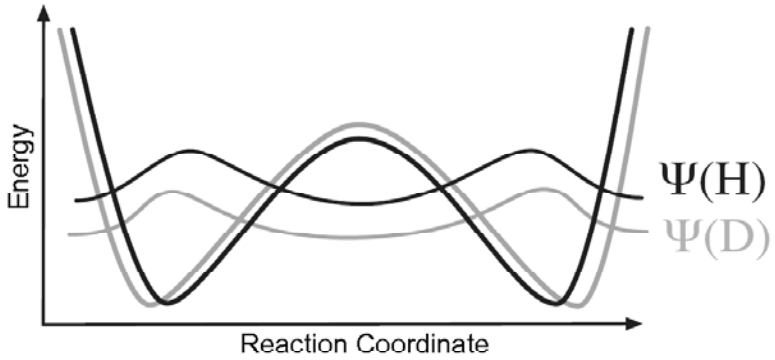

Figure 1.6: Schematic effective one-dimensional potentials and ground state vibrational wave functions for hydrogen (black) and deuterium (grey).

asymmetry in the potential energy surface and in turn modifies the conditions for tunneling. In the low temperature limit, the proton will be localized in the more stable well, see Fig. 1.7.

Isotope effects are especially pronounced when quantum tunneling is of importance such as for low-temperature reactions involving the motion of hydrogen/deuterium atoms. The importance of proton tunneling in chemical and biological systems is well known, e.g. for the DNA base pairing, as discussed e.g. by Löwdin [19].

The general requirements for the evaluation of the tunneling splitting are calculations of the potential energy surface as well as the vibrational eigenvalues.

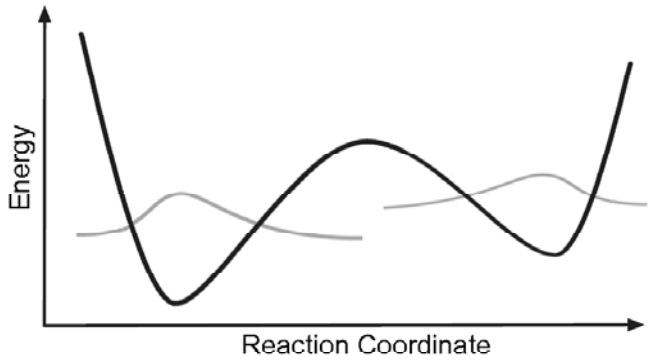

Figure 1.7: The two lowest vibrational wave functions for an asymmetric one dimensional potential energy curve. In the low temperature limit (T→0), the wave function corresponding to the proton will be localized in the more stable well (in this case the left well).

The problem which is faced is the choice of the employed coordinates (discussed in section 2.3). Moreover, the employed reaction coordinates can be coupled to the motion of other atoms which leads to the problem of multidimensionality, see Ref. [20]. This issue will be addressed in section 2.5.2.

1.1.3 Geometric isotope effect

It is well established that the hydrogen bond geometries depend on the chemical and/or the crystal structure [21, 22, 23] as well as the replacement of the hydrogen bond proton by a deuterium which defines the so called geometric H/D isotope effect (i.e. the hydrogen bond geometric change upon deuteration). Since deuterium has a heavier mass than the hydrogen atom, it affects to a certain extent the strength of the hydrogen bond which in turn changes the A-H (A stands for an electronegative atom) stretching vibration. These changes upon deuteration make the geometric isotope H/D effect (GIE) an important quantum phenomenon for the understanding of the nature of the hydrogen bonding. Further, isotopic substitution provides a rather specific way for obtaining information on the nature of potential energy surfaces and molecular wave functions [24]. In order to study the geometric H/D isotope effect, one conveniently defines the distances r_1 and r_2 or alternatively the coordinates q_1 and q_2 (see Scheme 1.8):

$$q_1 = (r_1 - r_2)/2 \tag{1.1}$$

and

$$q_2 = r_1 + r_2. \tag{1.2}$$

The coordinates q_1 and q_2 represent (in case of linear H-bond) the deviation of the hydrogen atom from the center of the H-bond (proton transfer coordinate) and the distance between the two heavy atoms (hydrogen bond length), respectively.

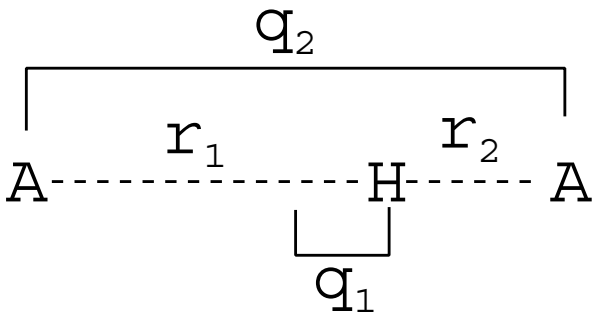

Figure 1.8: Scheme of the hydrogen bond coordinates q_1 and q_2. q_1 represents the deviation of the hydrogen from the hydrogen bond center (proton transfer coordinate) and q_2 represents the distance between the heavy atoms (hydrogen bond length).

Quantum mechanically, the average proton position in a harmonic potential energy surface (in case of non-deuterated and deuterated molecules) does not change from the classical equilibrium position, see Fig. 1.9.

As shown in Fig. 1.9 the wave function corresponding to the deuterated species has a lower energy level (zero point energy) in the potential well than that of the normal species (non-deuterated ones). Moreover, the expectation values of the wave functions corresponding to the normal and deuterated species are the same as the classical value of the equilibrium position, this leads to no change in the geometry upon deuteration, i.e. there is no geometric H/D isotope effect in the harmonic case.

On contrast, the average proton position in a hydrogen bonded system with medium strength does not coincide with the classical equilibrium position due to the anharmonicity in the proton potential, see Fig. 1.10.

Figure 1.10 reflects different expectation values of the normal and deuterated species, i.e. the expectation value of the deuterated species is closer to the classical equilibrium value than the normal ones. This is the so-called geometric H/D isotope effect. Since the coordinates q_1 and q_2 are coupled and cannot change

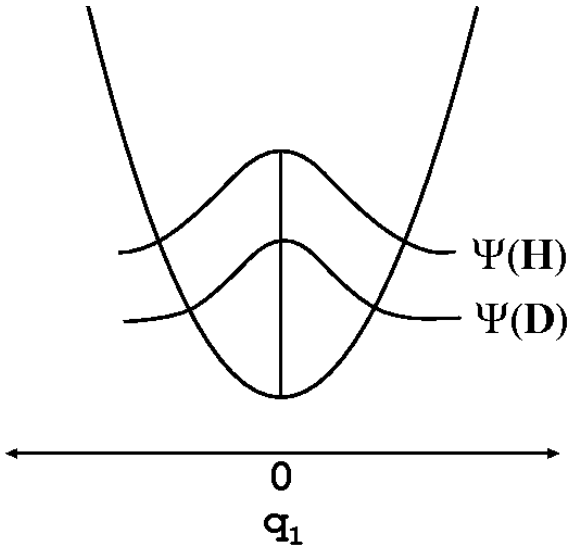

Figure 1.9: Schematic diagram of the ground state vibrational wave functions in a one dimensional harmonic potential energy curve. The lower vibrational wave function describes a deuterated molecule, whereas the higher wave function represents the non-deuterated species.

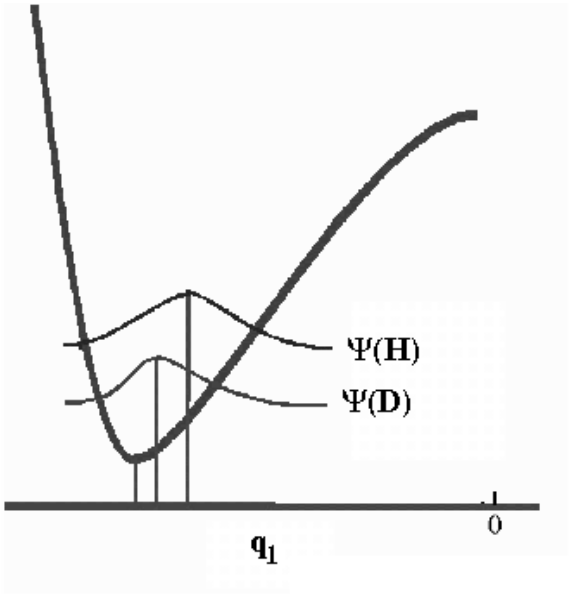

Figure 1.10: Schematic diagram of the ground state vibrational wave functions in a one dimensional anharmonic potential energy curve. The lower vibrational wave function describes a deuterated molecule, whereas the higher wave function represents the non-deuterated species.

independently (as will be shown in section 1.1.3), the potential energy surface, which describes well the geometric H/D isotope effect, should be at least two dimensional, see for instance Fig. 1.11. Notice that in this figure the symmetric case (i.e. A=B) is considered.

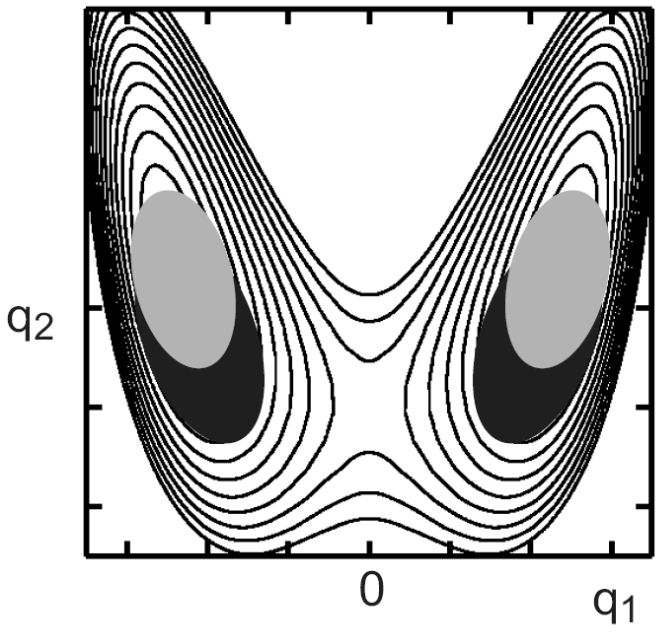

Figure 1.11: Schematic view of the ground state wave function for hydrogen (black) and deuterium (grey) in a two-dimensional potential surface.

In Fig. 1.11, one can see that the two coordinates are coupled causing a tilt of the two minima with respect to the harmonic potential surface which should have two minima with regular concentric contours. This tilt enforces the ground state wave functions (corresponding to the deuterated and non-deuterated species) to be tilted as well. Making a one-dimensional cut along the maxima of the wave functions and along the q_1 coordinate, one can get the potential energy curves depicted in Fig. 1.6. Notice that the shape and height of the barrier of the one-dimensional potential may be different for the two cases, indicating the interdependence between geometric and kinetic H/D isotope effects.

It is also clear that the maximum of the normal species wave function meets a different value, closer to the classical one, of q_2 than the deuterated species does: this is known as secondary geometric H/D isotope effect. In other words, the secondary geometric H/D isotope effect will refer to the change in q_2 upon deuteration. The so-called secondary GIE on the hydrogen bond distance q_2 was first

investigated for molecular crystals using X-ray crystallography by A. R. Ubbelohde (Ubbelohde effect) [25, 26, 27]. It was only recently that Benedict et al. have shown that primary and secondary GIEs in N$\cdots$H-N hydrogen bonds can be obtained as well from solid state ^{15}N NMR measurements [28]. It follows from Fig. 1.6 that the A-D distance is smaller than the A-H distance and the D...A distance is then longer than H...A because the maximum of the ground state wave function of the normal species is shifted to smaller q_1 value than that of deuterated ones (Fig. 1.10), i.e. the hydrogen atom gets close to the center of the hydrogen bond. This means that deuterium stays farther away from the center of the hydrogen bond than the hydrogen does giving rise to the primary geometric H/D isotope effect, i.e. this effect refers to the change in the value of q_1 upon deuteration. The cause of the geometric H/D isotope effect, regardless of tunneling, is twofold a) anharmonicity of the potential energy surface for vibrations of the hydrogen and that of the deuterium in the neighborhood of the two heavy atoms hosting the hydrogen bond and b) the fluctuations of the hydrogen and that of the deuterium are of different magnitude (different zero point energies).

As a consequence the ground state wave functions $\Psi(H)$ and $\Psi(D)$ will be different, see Fig. 1.6, and a local probe of the average position will detect a smaller A-D distance as compared to the A-H distance (primary GIE). Moreover, both distances differ from the predictions of the equilibrium distance within a classical nuclei approach as it is obtained, e.g., from a standard quantum chemical geometry optimization.

Multiple hydrogen bonds continue to attract considerable attention not least because of their prominent role in biological systems [1]. An issue of principal importance concerns the question whether proton dynamics in multiple hydrogen bonds takes place concertedly or by means of uncorrelated individual steps. NMR relaxometry measurements may give evidence for the preferred mode of transfer as shown, e.g. in Refs. [29] and [30]. At this point, one may ask whether the GIE contains such information as well. Previously, it has been shown for the intermolecular hydrogen bond in the acetic acid dimer that the GIE indicates cooperativity of the two hydrogen bonds [31]. "*Cooperativity*" implies that isotopic substitution in one hydrogen bond leads to a geometric change in the other hydrogen bond which goes into the same direction, for instance, both hydrogen bonds may contract or expand. To bring this into the context of proton transfer consider an intramolecular double hydrogen bond as shown in Fig. 1.12.

A concerted double proton transfer requires the molecular scaffold to follow

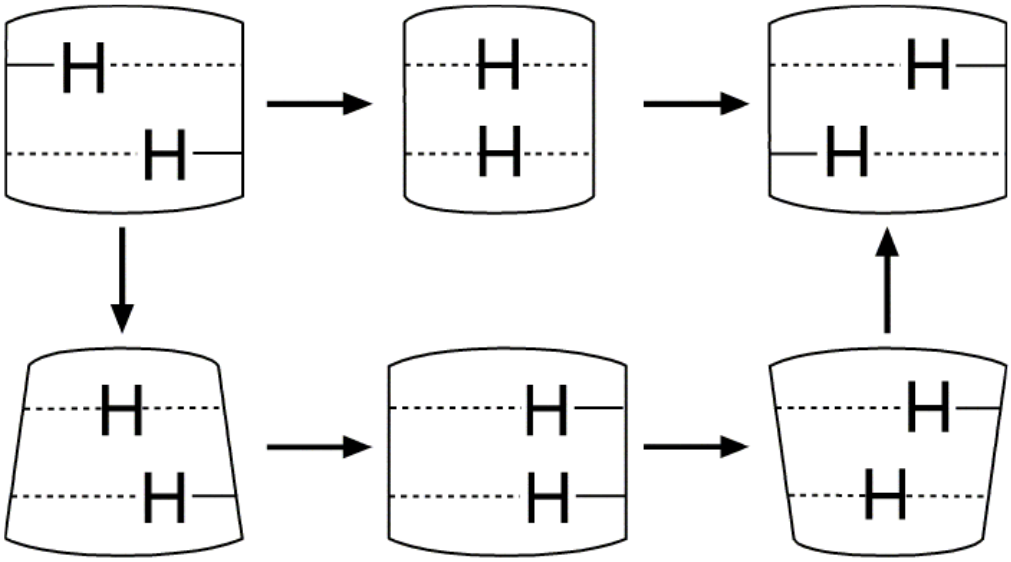

Figure 1.12: Sketch of concerted (upper path) and stepwise (lower path) double proton transfer and its relation to the likely rearrangement of the molecular skeleton.

the motion in a way such as to provide a simultaneous contraction of both hydrogen bonds, as shown in Fig. 1.12. Conversely, in a stepwise process the molecular rearrangement is most likely to be non-symmetric. The same would hold for double deuteron transfer. Now the question is what happens upon single deuteration. One may argue that the asymmetry introduced by the different masses will make the transfer stepwise in any case. On the other hand, another situation might be expected where despite the perturbation of the symmetry resulting from single deuteration the preferred mode of scaffold rearrangement is of symmetric type (cooperative hydrogen bonds). In other words, in the single deuteration case, one might expect either an elongation in both hydrogen bonds (the two hydrogen bonds are strongly coupled) or the elongation takes place for the deuterated hydrogen bond only (no coupling between the two hydrogen bonds). Assuming that these coupling patterns (the so-called vicinal effects) are reflecting the preferred mechanism of double proton transfer (concerted versus stepwise), the geometric H/D isotope effect could in principle be used for unveiling this mechanism.

The theoretical prediction of the geometric H/D isotope effects in the intramolecular double hydrogen bonded system requires to calculate the wave function for the nuclei involved in the hydrogen bonds. Here, one usually resorts to the Born-Oppenheimer separation, section 2.1.1, of electronic and nuclear co-

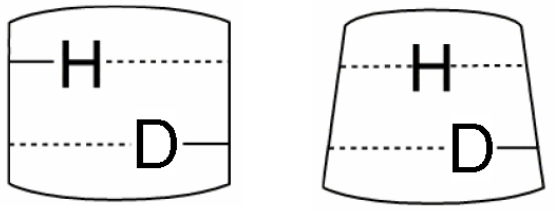

Figure 1.13: The possible geometries of the single deuteration of porphycene. The symmetric case (left) might indicate concertedness of the proton transfer, whereas the asymmetric case (right) might indicate a stepwise transfer.

ordinates being restricted to the electronic ground state. As outlined in section 2.3, in principle one needs to obtain a potential energy surface along relevant coordinates for which the nuclear Schrödinger equation can be solved (see, e.g., [8, 28, 32, 33]). Alternatively, the potential energy surface can be generated on the fly along with a molecular dynamics simulation [34] or the standard Born-Oppenheimer separation can be abandoned by treating the proton/deuteron on the same footing as the electrons [35]. The latter so-called multicomponent approach is computationally very demanding. For molecules of large size it requires to make further approximation degrading the quality of the quantum chemical level [36].

Experimental determination of the geometric H/D isotope effect

It is difficult to determine the geometric H/D isotope effect using X-ray diffraction with accuracy. Hydrogen atom positions are difficult to define with X-rays, even at resolutions between 1.2 and 1.0 Å (often considered as atomic resolution) [37]. The main problem to be solved using neutron diffraction are firstly the position of the hydrogen atoms (as deuterium) which are disordered or scatter too weakly to be detected with X-rays. Neutron diffraction has the advantage that, unlike an X-ray photon, which interacts with the electron cloud surrounding the nucleus, neutrons interact with the nucleus itself. Moreover, neutron diffraction is more able to probe the bulk material, since it is deeply penetrating. On the other hand, a neutron diffraction measurement requires a neutron source (e.g. a nuclear reactor), a target (the material to be studied), and a detector. Other components may be needed to select the desired neutron wavelength. All of these requirements makes the neutron diffraction method too expensive to be used in studying the geometric

H/D isotope effect. The NMR method as an alternative method can be used to detect the geometric H/D isotope effect without the special requirements needed for the neutron diffraction [38]. For the liquid state, the evaluation of NMR chemical shifts for different isotopes has been established as a tool that can characterize intramolecular hydrogen bonds [39]. However, liquid state NMR refers to hydrogen bonded systems experiencing an averaged solvent shell. This problem does not arise in case of studying crystalline solids using advanced solid state NMR. Dipolar solid state NMR techniques have been developed and used to study the geometric H/D isotope effects [40, 41, 42, 43]. In this respect, the information about distances obtained from hydrogen bond correlation techniques were found to be related to NMR chemical shifts of the hydrogens or the heavy atoms of the hydrogen bonds (Eq. (B.6)), see Appendix B. Then, a correlation between the experimentally measured chemical shifts and the geometrical changes of q_1 and q_2 can be established using Eq. (B.6) and with the help of the valence bond order and comparisons with some systems with known geometries. From the empirical values of q_1 and q_2, one can then calculate the primary and secondary geometric H/D isotope effects.

Limbach and coworkers have observed the H/D isotope effects by means of the solid state ^{15}N NMR chemical shifts of a series of homoconjugate model complexes of the N$\cdots$H$\cdots$N type [40]. The isotope effects on the NMR parameters for the strong hydrogen bonded systems like hydrogen fluoride anions and its anionic clusters were also studied by Limbach and coworkers [44, 45]. They predicted anti-cooperative hydrogen bonds in ionic clusters. On contrast, they have shown that the GIE indicates cooperative hydrogen bonds for the intermolecular hydrogen bonds in the acetic acid dimer [31]. The theoretical study of NMR isotope effects for simple molecules based on quantum mechanical calculations of nuclear shielding and scalar spin-spin couplings constants as functions of internal vibrational coordinates is well developed, see for example [46] and [47], and can be extended to isotopologs of hydrogen bonded complexes [48].

1.1.4 Kinetic isotope effect

As introduced in the previous section, the geometric H/D isotope effects may be used to extract information on the cooperativity of multiple hydrogen bonds. It should be noted that the cooperative/anticooperative changes in the geometry, although suggestive, do not show unambiguously whether the mechanism of double proton transfer is stepwise or concerted. Assuming such a correlation to exist

is the "*working hypothesis*" to be scrutinized in this thesis. Experimentally, the mechanism can be probed by dynamic NMR spectroscopy through measurement of rate constants for different isotopomers [49, 50]. Specifically the kinetic isotope effect is determined as the ratio between the rates of chemical reactions when a hydrogen in one of the reactants is replaced by a deuterium, i.e. k_H/k_D.

An isotopic substitution will greatly modify the measured reaction rate when the isotopic replacement is in a chemical bond that is broken or formed during the reaction course, i.e. the kinetic H/D isotope effect is large. In such a case, the rate change is termed a primary H/D isotope effect, see Fig. 1.14.

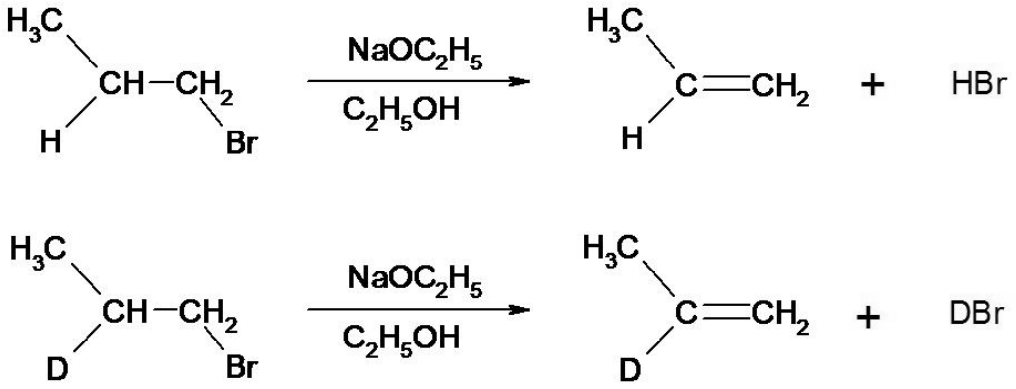

Figure 1.14: Exemplary reactions exhibiting a primary kinetic H/D isotope effect. The upper panel is for the reaction of the normal species while the lower panel is for the reaction of the deuterated one (adapted from Ref. [51]).

Here the base ($NaOC_2H_5$) abstracts first the proton/deuteron and leaves the lone pair of electrons which in turn repels away the bromide ion. The kinetic H/D isotope effect of the reactions shown in Fig. 1.14 can be calculated as $\frac{k_H}{k_D}$ to be 6.7 [51]. This value means that the rate is highly affected upon deuteration, i.e. the deuteration occurs at the bond involved in the rate determining step (primary kinetic H/D isotope effect).

Whereas, if the substitution is not in the chemical bond involved in the rate-determining step, one may still observe a smaller rate change compared to the primary effect, indicating the so-called secondary kinetic H/D isotope effect, see Fig. 1.15. Thus, the magnitude of the kinetic H/D isotope effect can be used to elucidate the reaction mechanism.

Here the inductive effect of the methyl group on the carbon atom, which carries the bromine atom, enforces the bromide ion to leave leaving a carbocation

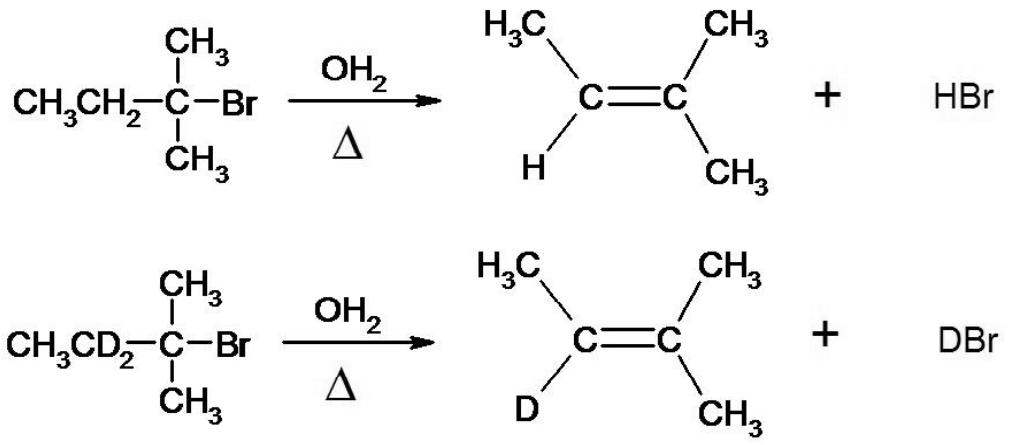

Figure 1.15: Exemplary reactions exhibiting a secondary kinetic H/D isotope effect. The upper panel is for the reaction of the normal species while the lower panel is for the reaction of the deuterated one (adapted from Ref. [51]).

which attracts then the C-H/D bond electrons. The kinetic H/D isotope effect of the reactions shown in Fig. 1.15 yields $\frac{k_H}{k_D}$ = 1.4 [51] which indicates a secondary H/D isotope effect, i.e. the deuteration takes place at a bond which is neighboring to the one involved in the rate determining step. For relations between different rates of different isotopes, see Ref. [17].

The rate change of reaction upon replacing one atom with its isotopomer can be attributed to the mass change between the isotopomers which in turn affects the vibration frequency of the bond that they form. Heavier atoms lead to lower vibration frequencies and have lower zero-point energy. With a lower zero-point energy, more energy must be supplied to break the bond, resulting in a higher activation energy for bond cleavage, which in turn lowers the measured rate according to Arrhenius equation, Eq. (1.3).

$$k(T) = Ae^{-E_a/RT}, \tag{1.3}$$

where k is the rate constant at certain temperature T, A is the frequency factor which is specific to a particular reaction, R is the gas constant and E_a is the activation energy. The actual rate might be higher than the rate calculated from Eq. (1.3), this means there is an additional rate enhancement for the lighter isotope. The reason for this rate enhancement is the quantum mechanical tunneling. This is typically only observed for hydrogen atoms, which are light enough to exhibit significant tunneling.

However, measurements of the kinetic isotope effect are not available for por-

phycene. Theoretically, the tautomerization mechanism can be determined by explicit consideration of the double proton kinetics, provided a reliable potential energy surface is available. Tautomerization rates of different mechanisms and isotopes can then be evaluated using the so called approximate instanton method [52] (tunneling rate) or transition state theory [53] (over-the-barrier rate). The calculated rate for different isotopes can be used to get the so-called kinetic H/D isotope effect [54]. The kinetic H/D isotope effects can be compared to probe the reaction mechanism. The present work presents a theoretical study of the potential and the kinetics of porphycene tautomerism with the aim of predicting the tautomerization mechanism and to provide a framework for the interpretation of kinetic and geometric isotope data in the context of our working hypothesis.

Transition state theory

In the following, the transition state theory [55, 56] which can be used to calculate the over-the-barrier proton transfer rate is outlined. The transition state approximation is a rather simple theory leading to an expression of the rate constant and depends mainly on the properties of the reactant and the transition state. Basically, it assumes that all reactants that reach the transition state are reactive and do not come back to the reactant region. A statistical description of the fraction of the reactive reactant with sufficient energy to reach the transition state leads to the rate expression. The resulting rate coefficient is proportional to the ratio of partition functions in the reactant well and at the transition state:

$$k_{TST}(T) = \frac{k_B T}{h} \frac{Q^{\ddagger}}{Q^R} e^{-E_a/RT}, \tag{1.4}$$

with k_B the Boltzmann constant, h Planck's constant, $Q^{\ddagger}$ the partition function of the transition state and Q^R the partition function of the reactant. The partition function comprises electronic, translational, rotational, and vibrational contributions. The vibrational partition function, in harmonic approximation, is

$$Q = \prod_k \frac{1}{1 - e^{-h\nu_k/k_B T}}, \tag{1.5}$$

where ν are the normal mode frequencies. The product runs over all vibrational degrees of freedom k of the system with the exception of the reaction coordinate for the transition state. Assuming that the degrees of freedom affected by the proton transfer have much higher frequencies than $k_B T$, the rate constant will take the familiar exponential form and the kinetic H/D isotope effect will then

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$$\frac{k_H}{k_D} = \eta_{TST} = e^{(\Delta E_0^D - \Delta E_0^H)/k_B T}, \tag{1.6}$$

where ΔE_0 is the zero point energy change between the reactant and the transition state. Therefore, the kinetic H/D isotope effect in the transition state theory is governed by the change in the zero point energy upon deuterium substitution (this indicates that the partition functions do not change). Equation (1.6) reveals that the kinetic H/D isotope effect in the transition state theory depends on the change of the zero point energies of different isotopes. In the next subsection how to calculate the tunneling rate using the so called approximate instanton method will be briefly discussed.

Approximate instanton method (AIM)

Approximate instanton method is designed to deal with tunneling in multidimensional systems. The instanton concept is based on the recognition that, under specified conditions, among the trajectories that connect reactant and product, there is one (the instanton path) which dominates the tunneling rate. Although this trajectory (tunneling trajectory) follows the minimum energy path in the vicinity of the equilibrium configurations of the reactant and product, it follows a shortest path in the region of the transition state. By "short" it is meant that the tunneling trajectory combines the path length and the energy that minimize the action [57, 58, 59, 60, 61]. This instanton action $S_I(T)$ is the quantity of interest, since the tunneling rate is proportional to $e^{-S_I(T)}$ [52, 54].

The approximate instanton method can be used in systems with multidimensional proton transfer for which the structure as well as the vibrational force field of the stationary points along the reaction path can be calculated using quantum mechanical methods. This method does not search for the Instanton trajectory explicitly but approximates the multidimensional Instanton action $S_I(T)$ directly using generalizations of exact instanton solutions for low-dimensional models [59, 62]. The tunneling rate can be calculated using the approximate instanton method from the expression:

$$k_{tun}(T) \approx k_{AIM}(T) = (\omega_0^R/2\pi)e^{-S_I(T)}, \tag{1.7}$$

where ω_0^R is the effective frequency of the tunneling mode in the reactant state, for more details see [52, 54]. The thermal (total) rate can be then calculated by:

$$k(T) = k_{AIM}(T) + k_{TST}(T). \tag{1.8}$$

By drawing the calculated rates for different isotopes as functions of inverse temperature, one can estimate the kinetic isotope effects, for instance see Fig. 1.16. This figure represents the calculated rates as functions of inverse temperatures of double proton transfer in porphine isotopomers. From the figure one can calculate the ratio between any two points on the curves (corresponding to different isotopes) at specific temperature. It is noteworthy that the mechanism of a specific reaction can be estimated from the agreement between the calculated rates for different mechanisms and the experimental data, see Fig. 1.16. As the calculated and

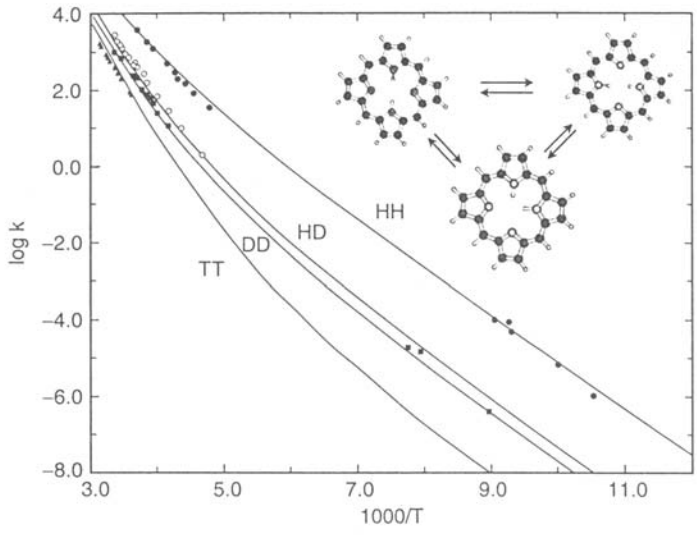

Figure 1.16: Temperature dependence of the rate constant (in sec^{-1}) of double proton transfer in porphine isotopomers evaluated for the stepwise mechanism. The symbols represent observed rate constants [63, 64] and the curves represent the results of a multidimensional AIM calculation [52]. The insert shows the concerted transfer (upper path) and the stepwise transfer (lower path) mechanisms. This figure is adapted from Ref. [54].

the experimental rate constants for different isotopomers are perfectly agreed for the stepwise mechanism, one can conclude that the double proton transfer reaction in porphine takes place stepwisely.

1.2 Control of isomerization reaction by laser pulses

1.2.1 Chirality

A molecule is chiral if it is not superimposable on its mirror image. For instance, the hands are natural chiral systems since they are mirror images of one another and non-superimposable. Achiral molecules, on contrast, are those that have a point of symmetry, plane of symmetry and/or improper axis of symmetry. The two non-superimposable, mirror-image forms of chiral molecules are referred to as enantiomers.

The phenomenon of chirality becomes more complicated if the molecule can change its shape by rotation about a certain bond. Let us consider first compounds that do not undergo rotations about any bond. It can be certainly said that methane is achiral as well as ethane, chloroform, cyclopropanol, etc. All of these compounds have different planes of symmetry. On contrast, bromochlorofluoromethane is chiral because it has no plane of symmetry, and it is nonsuperimposable with its mirror image [65].

Now, how about the compounds that change their shape by rotation? To answer this question, one can look at ethane. All the different conformers should be considered, because different conformers have different shapes, and chirality is a property of shape. Staggered ethane has planes of symmetry as does eclipsed ethane, see Fig. (1.17). But let us look at a conformation of ethane in between staggered and eclipsed, e.g. by starting with eclipsed ethane and twisting the H-C-C-H dihedral angle by 30° in one direction, one finds that this conformer has no plane of symmetry and then it is chiral. Its non-identical mirror image is a different conformer of ethane, obtained by starting with eclipsed ethane and twisting it 30° in the opposite direction. These two enantiomers can interconvert easily by rotation about the C-C bond.

Almost any compound with more than two C atoms has an infinite number of intermediate chiral conformers. In practice, though, it is said that a compound is chiral if any of its low-energy conformers are chiral. Therefore, ethane's staggered (low-energy conformer) and eclipsed conformers are achiral, and ethane is said to be achiral, even though it has many intermediate chiral conformers. This leads to the question, how low is "low-energy"? The answer depends on the considered time scale of the molecules' interconversion. For example, let us consider ns time scale which is very long with respect to the femtosecond, fs, time scale. According to femtosecond chemistry, if the interconversion from a molecule to

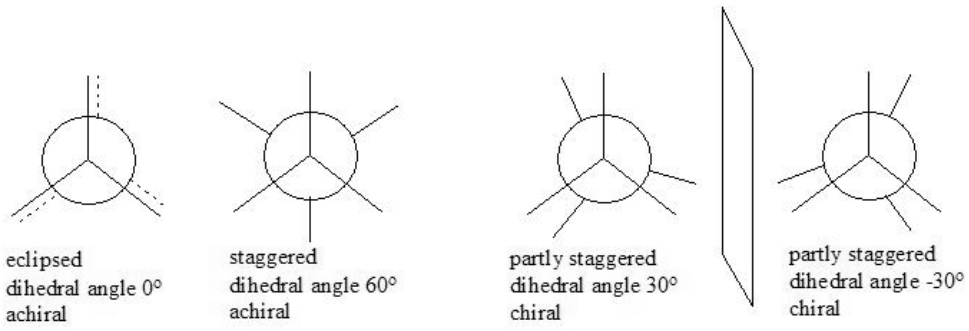

Figure 1.17: Eclipsed, staggered and partly staggered ethane.

the other takes place in ns time scale, one can say that the molecule is chiral. It will be shown in section 4.7 that the low-energy enantiomers (of deuterated phosphinothioic acid) interconvert to one another with a half-life of ns. This means that the studied molecule is chiral (prochiral) on the sub-ns time scale. There exist several kinds of chiral molecules depending on the source of chirality. Few examples are presented below [65]:

Molecules with a chiral center

Any molecule that contains a carbon atom with four non-identical groups attached is chiral. An example is shown in Fig. 1.18 (bromochlorofluoromethane) This molecule does not have any kind of symmetry and therefore does not superimpose on its mirror image.

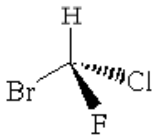

Figure 1.18: A molecule with one chiral carbon atom.

Molecules with restricted rotation

Restricted rotation about a double bond is well-known as a source of geometric isomerism, though it is not the only one. Restricted rotation can also give rise to chirality. Biphenyls consist of two benzene rings joined by a single bond. If each ring has large substituents on either side of this bond (the 2,6- and 2′-6′-

positions) then steric hindrance will prevent rotation. If the substituent groups are different, then the molecule will be chiral, see Fig. 1.19. Such enantiomers are called atropisomers.

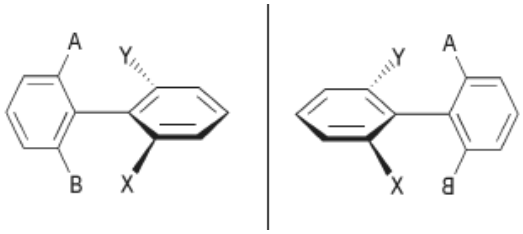

Figure 1.19: Compound with restricted rotation.

Restricted rotation can also be found in spiranes, compounds having two rings with one carbon atom in common. This makes the rings perpendicular, and suitable substitution gives rise to chirality. An exocyclic double bond can lead to the same kind of chirality as that present in spiranes, Fig. 1.20.

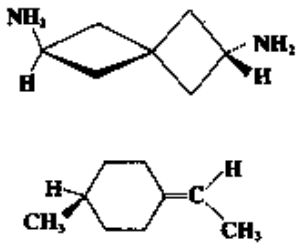

Figure 1.20: Spirane compound (top) and exocyclic double bond compound (bottom).

Restricted rotation of other types

There is a wide variety of compounds that show restricted rotation and consequently are chiral. Paracyclophanes are compounds having a benzene ring within a larger ring of methylene groups, Fig. 1.21. If substituted on the benzene ring, the molecule can be chiral, as is the example shown with ten methylene groups in the large ring. The layered cyclophane to its right is also chiral, Fig. 1.21.

1.2.2 Optical activity and enantioselection

A beam of light consists of waves that oscillate perpendicular to the direction of the beam. Normally, the waves oscillate in all planes perpendicular to the beam;

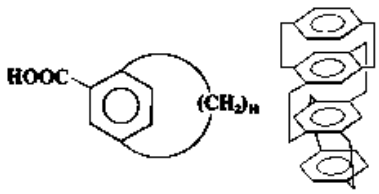

Figure 1.21: Paracyclophane compound (left) and layered cyclophane (right).

this is called unpolarized light. If the light is passed through a polarizer, the beam of light is altered so that the waves oscillate only in one plane. This kind of light is called plane- polarized light. A chiral compound interacts with plane polarized light in such a way that the plane of light is rotated in one direction or another. This phenomenon is called optical activity.

A sample of one enantiomer will rotate the plane of plane-polarized light in the opposite direction that a sample of the other enantiomer does. A sample of a compound that exists as a 1:1 mixture of enantiomers, a so-called racemic mixture, is optically inactive, because half of the molecules rotate light in one direction, and the other half rotate light in the other direction, so the net result is no rotation at all. Only samples of chiral compounds in which one enantiomer is in excess rotate plane-polarized light. A sample is called enantiomerically pure or enantiopure if it consists of only one enantiomer. It is called enantiomerically enriched or enantioenriched if it consists of both enantiomers, but one predominates.

Optically inactive starting materials always give optically inactive products in chemical reactions. Likewise, if a racemic compound is allowed to react with an achiral or a racemic compound, then the product(s) must be either achiral or racemic. Only when one of the starting materials is chiral and enantioenriched or enantiopure it is possible to obtain enantioenriched or enantiopure product.

The two enantiomers of a compound have identical physical properties in almost all respects. They have identical melting points, boiling points, solubilities, acidities, and spectroscopic characteristics. There are only two ways in which two enantiomers differ in their properties: in their interaction with other chiral molecule, and in their interaction with plane- polarized light. The difference in interaction of two enantiomers with a chiral compound is akin to the difference between the interaction of the left hand with a left glove and the interaction of the right hand with a left glove. Chemically, this means that two enantiomers of a compound will have different behaviors when they interact with another chiral, enantiopure compound.

The process of separating a racemic mixture into its enantiomers, resolution, can be affected by temporarily attaching a chiral, enantiopure reagent to the two enantiomers in the racemic mixture. This results in the formation of two diastereomers (stereoisomers that are not mirror images). There are two ways to make an enantiopure compound: (1) make a racemic mixture and carry out a resolution, or (2) carry out an asymmetric synthesis. An asymmetric synthesis uses an optically active starting material isolated from nature and uses its chirality to influence later reactions.

There exist several ways to separate enantiomers in traditional chemistry: case(1), a very extended procedure is to use chromatography on a chiral support. By means of paper chromatography one can separate a drop of ink into its colors. If the two enantiomers are placed on a piece of filter paper made up of a chiral material, one enantiomer will move faster than the other. In case of asymmetric synthesis, case(2), where does one get optically active starting materials to begin with? The answer is nature. Because organisms are made up of chiral, enantiopure molecules, they are able to make chiral, enantiopure compounds. These compounds can be extracted from living organisms and used in enantioselection. In the following, an alternative way to separate enantiomers, i.e. using coherent laser light, is suggested.

1.2.3 Chirality in quantum mechanics

This section addresses the issue of defining molecular chirality in quantum mechanics. The potential energy surface describing two equivalent enantiomers is a symmetric double well potential as the one shown in Fig. 1.22. The two minima correspond to the equilibrium configurations of the two enantiomers. Both conformers have the same energy values, except for the very small energy difference due to the parity violating weak interaction [66, 67, 68] which is not considered in this work. The two minima are separated by a potential barrier whose height depends on the reaction coordinate. Each enantiomer can be described by a wave function localized in one minimum [69]. For simplicity, the wave function localized in the left well is called $|\psi_L\rangle$ while the one localized in the right well will be symbolized by $|\psi_R\rangle$. $|\psi_L\rangle$ and $|\psi_R\rangle$ can be constructed by negative and positive superpositions of pairs of eigenfunctions $|\psi_\pm\rangle$, which appear as doublets under the barrier, see Fig. 1.22. In general, one can write $|\psi_{vL/R}\rangle$ to symbolize any

localized wave function constructed from the doublet v.

$$|\psi_{vL/R}\rangle = \frac{1}{\sqrt{2}}\big(|\psi_{v+}\rangle \pm |\psi_{v-}\rangle\big), \tag{1.9}$$

The quantum number v denotes the number of doublet. $+$ and $-$ refer to the symmetry of the wave function.

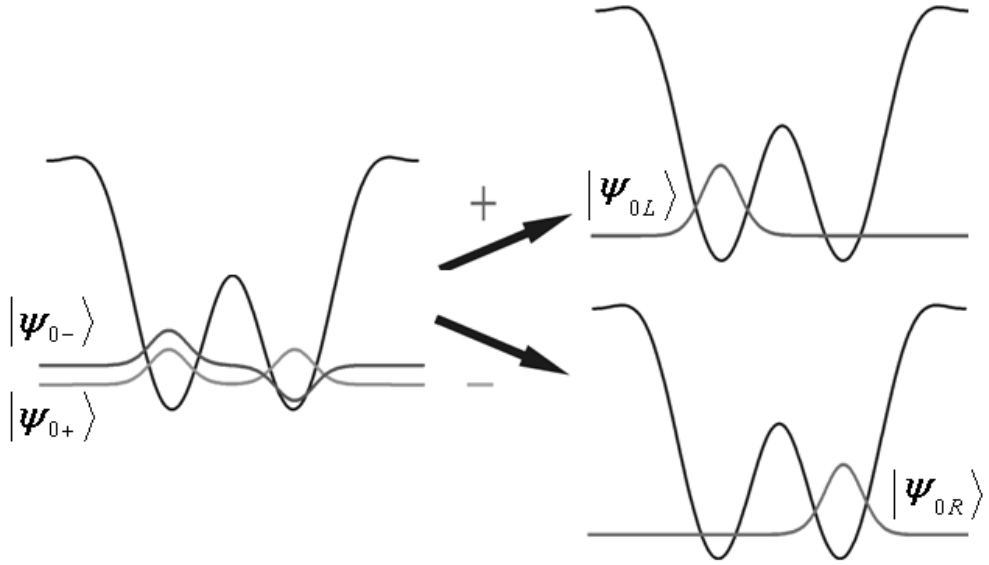

Figure 1.22: Construction of the localized wave functions by either + or - superposition of eigenstates.

The energy splitting ΔE_v between the two levels of each doublet depends on the height and width of the barrier, i.e. it decreases with increasing height and width till it arrives degeneracy.

$$\Delta E_v = E_{v-} - E_{v+}, \tag{1.10}$$

E_{v-} and E_{v+} are the eigenenergies of the eigenfunctions with $-$ and $+$ symmetries, respectively. The localized wave functions $|\Psi_{vL}\rangle$ and $|\Psi_{vR}\rangle$ corresponding to the two enantiomers are tunneling, with a tunneling time τ, that is related to the energy splitting by Heisenberg uncertainty principle:

$$\Delta E_v \times \tau = h. \tag{1.11}$$

The tunneling time, τ, is the time spent by the wave function of a specific doublet on going from the left well to the right and back to the left. The life time of each enantiomer is given by half of the tunneling time (see Fig. 1.23).

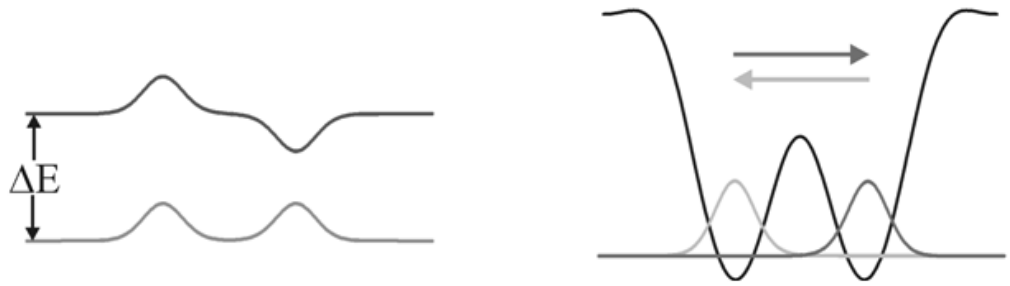

Figure 1.23: Tunneling splitting (left) and tunneling of the localized states (right).

After defining the enantiomers quantum mechanically, one has to think of a definition of a racemic mixture in order to have a complete picture of chirality. A racemic mixture in terms of quantum mechanics is a mixture of the two states describing the two enantiomers, i.e. $|\psi_{vL}\rangle$ and $|\psi_{vR}\rangle$. The mixture can be dealt as a mixed state described by the density matrix shown in Eq. (2.130) (Here: $|\psi_{vL/R}\rangle \equiv |+/-\rangle$), see section 2.6. Note that the probabilities of the two states, $|\psi_{vL}\rangle$ and $|\psi_{vR}\rangle$, must be the same and equal 1/2 to have a 50%:50% mixture.

1.2.4 Optical resolution of oriented enantiomers

Quantum control of nuclear wave packets guided by tailored laser pulses is now a major issue in femtosecond chemistry [70] because it can control a large variety of elementary reactions [71, 72]; photodissociation [73, 74], bond rearrangement [75], or selective molecular excitation [76] are just few examples, for recent reviews see Refs. [77, 78]. Photoisomerization of chiral molecules [79, 80, 81] is a fascinating target in the quantum control of molecules since molecular chirality is important not only in synthetic chemistry but also in biochemistry [82]. Control of photoisomerization, however, is in an early experimental stage, and in particular, control of molecular chirality still remains challenging. On the theoretical side, it is encouraging that different methods are being proposed to predict preferential synthesis of a single enantiomer from a racemic mixture of two enantiomers by means of laser pulses. These methods include the work of Fujimura and coworkers on helical enantiomers [83], as well as the method of laser distillation [80, 81] or two-step enantio-selective switch [84, 85, 86] proposed by Shapiro, Brumer and coworkers, with applications to 1,3-dimethylallene and S_2H_2. The so-called laser distillation method repeatedly makes use of three linearly polarized, perpendicular laser pulses to purify chiral substances in a randomly oriented sample [80, 81],

whereas the two-step method employs only two i.e. a pump and a dump laser pulses [84, 85, 86]. Another distillation approach has been discussed by Bychkov et al. employing coherent entanglement of the rotational-torsional states of the molecules [87]. In passing, it can be noticed that such molecular states can be used to prepare coherent superpositions with the purpose of quantum information processing, as shown e.g. by Sola and coworkers, who used H_2POSH to encode a two-qubit [88]. Last but not least, laser purification of a preoriented racemic sample has been suggested, with applications to H_2POSH [89, 90, 91, 92, 93, 94] and chiral olefins [95, 96, 97].

In this work a concept which should encourage experiments on enantiomer purification from a racemate is presented. As a prerequisite, it is assumed that the racemate is pre-oriented, e.g. in oriented environments, like surfaces or matrices, or e.g. by means of intense elliptically polarized laser fields, as suggested by Seideman and Stapelfeldt [98, 99]. Essentially our method is based on the following: a single linearly polarized laser pulse excites selectively the undesired enantiomer to a repulsive electronic excited state, this enantiomer dissociates, and in this way it is eliminated out of the racemic mixture. This approach was tested preliminarily in a single one-dimensional (1d) model of H_2POSD, using exclusively the chiral reaction coordinate, i.e. the OPDS torsional angle [95]. The first excited state of H_2POSD shows $n\sigma^*$ character and exhibits, therefore, a dissociative surface which leads to an electrostatic repulsion between the fragments H_2PO and SD. In the present work, the decisive dissociation coordinate is included, demonstrating that optical resolution of enantiomers is indeed feasible. Our simulations show, however, that due to weak dipole couplings between the initial and the intermediate excited state the amount of population transferred, and therefore, the efficiency is considerably reduced in comparison with our previous 1D model [95]. Note that in the present case, one can turn competing photodissociation to our advantage, that is, ultrafast dissociation is used to eliminate the undesired enantiomers. In contrast, if one aims at interconverting the undesired enantiomer into the useful one, it has been also shown that a sequential pump-dump scenario may be used to suppress the undesired photodissociation [100].

1.3 Outline

In chapter 2 the theoretical background of the work is reviewed. First, the molecular Schrödinger equation as well as the Born-Oppenheimer approximation are

discussed. Second, different methods to solve the electronic Schrödinger equation as well as the concept of the potential energy surface are outlined. Then, the Fourier grid Hamiltonian as a method for solving the nuclear Schrödinger equation is presented. How to solve the time dependent Schrödinger equation using the split operator method is shown. The multiconfiguration time dependent Hartree as another tool for the solution of the time dependent Schrödinger equation and imaginary time propagation is scouted. Finally, pure state dynamics is generalized to cover mixed states.

In Chapter 3, the results of the hydrogen bonding in porphycene are studied. Porphycene is presented and the previous work done on it is reviewed. Tunneling splitting in porphycene is evaluated and compared with experimental results obtained from fluorescence spectra. The properties of the potential energy surface in terms of atomic Cartesian coordinates are discussed. The atomic Cartesian coordinates and the reaction plane coordinates are correlated. Calculation of the anharmonic potential energy surface and how one simplifies the full- to reduced-dimensionality are also offered. The behaviour of the wave function in the vicinity of the equilibrium position and how to probe the geometric isotope effect are explored. Finally, a study of the kinetic isotope effect is presented.

Chapter 4 deals with the optical resolution of H_2POSD enantiomers. The model system is introduced and the previous work done on this model is reviewed. How to select the coordinates as well as the electronic structure of the model system are explained. The electronic ground and excited states potential energy surfaces and dipole moments as well as the electronic ground state vibrational eigenfunctions are computed. Finally, the separation method of the pre-oriented enantiomers via photodissociation is discussed.

Chapter 5 summarizes and outlines the future work. Various details are presented in the appendices.