Structure and Dynamics of Chiral Molecules **

By Martin Quack *

Could there be chiral methane? What is the characteristic structural feature (in a physicochemical sense) of a molecule? This question dates back to *Louis Pasteur*, the discoverer of molecular chirality, and since the work of *van't Hoff* and *Le Bel* is generally considered by chemists as solved. In the present article it is pointed out that there exist fundamentally conflicting theoretical views of the physical origin of molecular chirality. These views predict consequences that could, in principle, be distinguished experimentally, but at present there is no conclusive experimental evidence available. Possible experiments are suggested that test different hypotheses. The importance of the magnitude of the parity-violating energy difference ΔE_{pv} in molecules due to the weak nuclear force for both the structure and spectra of chiral molecules and for the kinetics of racemization is discussed. The chemical relaxation rate coefficient of chiral molecules with some appreciable energy of excitation is derived for several limiting cases of a simple statistical mechanical model, which takes ΔE_{pv} into account.

> *"Si les principes immédiats de la vie immédiate sont dissymétriques, c'est que, à leur élaboration, président des forces cosmiques dissymétriques; c'est là, suivant moi, un des liens entre la vie à la surface de la terre et le cosmos, c'est-à-dire l'ensemble des forces répandues dans l'univers".*[***]
>
> *L. Pasteur*[19]

1. Introduction

Since Pasteur's first separation of crystals of racemic organic compounds (such as the sodium ammonium salt of tartaric acid) into left- and right-handed, optically active compounds 140 years ago,[1] two major questions related to this observation of chirality have been addressed repeatedly:

1. What is the origin of chirality in *molecular physics* and thus the "nature" or intrinsic structural feature of a chiral molecule or chiral substance?
2. What is the origin of chirality in (molecular) *biology* (i.e. the *chiral bias* favoring some enantiomers over others)?

These two questions are quite distinct, although related to each other. The second question concerns one of the more obvious, major unsolved problems in biochemical research.[2−17] We shall concentrate here on the first question, which is considered by many to be solved. This is not so, as we shall demonstrate. It may be that proper consideration of the first question will help to solve the second.

Even today the "structure" of chiral molecules is discussed by most chemists in terms of *macroscopic molecular models* in three dimensional space in the framework of conventional

stereochemistry.[1c, 3, 18−23] It was recognized by *Friedrich Hund*[24] that in the framework of quantum mechanics certain problems arise with classical stereochemistry due to the possibility of tunneling, which connects left- and right-handed structures. *Hund* provided an immediate apparent solution to these problems by considering the time scales for interconversion between enantiomers (see Section 2.2). *Primas*[25] pointed out, however, that this solution does not explain, why one cannot buy in a drug store the substance corresponding to the coherent superposition of left- and right-handed states of chiral molecules such as alanine. Of course the reason for this may be trivial, the superposition states may be unstable and thus difficult to store in bottles (one cannot buy free radicals such as CH_3 in bottles in a drug store, but there is good evidence for their existence). However, a *possible* solution of "Primas' paradox" is the nonexistence of these achiral states of chiral molecules, which leads to the more recent discussions of chirality.[26−32] These invoke either essential interactions with the radiation field, or else with other external agents in order to explain the physics of chiral molecules.

Finally, after the discovery of the chiral symmetry violating weak nuclear interaction[33−41] it would appear natural to assume that this force has also fundamental implications for the physics of chiral molecules.[10, 11, 17,42−54] In contrast to the other three fundamental forces of physics (strong nuclear forces, electromagnetic interaction, and gravitation) this "weak interaction" is intrinsically chiral. It is responsible for the β-decay of the neutron. It has been shown to lead to a nonconservation of the quantum number "parity" in nuclear decay processes[34] and in atomic spectroscopy.[40] In chemistry it has a most striking, as yet hypothetical, consequence: Under appropriate conditions it leads to a parity-violating energy difference E_{pv}[10, 11] between two enantiomers **R** and **L**, in thermodynamic terms, i.e. to a thermodynamic reaction energy $\Delta_R U_0^0$ different from zero

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[***] If the foundations of life are dissymmetric, then because of dissymmetric cosmic forces operating at their origin; this, I think, is one of the links between the life on this earth and the cosmos, that is the totality of forces in the universe.

for the racemization (a) (leaving the sign undetermined; see also appendix); $|\Delta_R U_0^0| \equiv |\Delta E_{PV}|$.

$$L \rightleftharpoons R \qquad\qquad (a)$$

All of the above mentioned discussions of molecular chirality result in differing views about the actual "structure" (in a general, physicochemical sense) of chiral molecules and substances. These differences should not be dismissed entirely as problems in the realm of bad terminology or philosophy. Rather, we shall demonstrate that the different views correspond to different theories of chirality with conflicting predictions concerning the outcome of certain experiments. To decide unequivocally which theories must be dismissed, one must perform an experiment which discriminates between them. To date, there is essentially no experimental evidence available on some central questions and this aspect has been largely overlooked in the theoretical discussions of the problem. The present paper is intended to fill this gap. Some possible experiments[50] will be discussed.

2. A Critical Discussion of Different Points of View Concerning Molecular Chirality

In this section we shall summarize some of the general aspects and predictions of the various theories of chirality. Predictions for specific experiments will be given in Section 3.

2.1. Macroscopic Molecular Models and Classical Mechanics: "The Classical Hypothesis"

The original description of chiral molecules was given in terms of molecular models that are the microscopic analogue of macroscopic models satisfying the laws of classical mechanics of our everyday world.[1, 18–21] It is in essence also the starting point of the organic stereochemists models. In modern language one would take the approximate Born-Oppenheimer potentials as true effective potential functions for the essentially classical motion of the heavy nuclei. These potentials may then either be symmetrical with respect to space inversion or there may be a slight asymmetry if there is a parity-violating term. In the former case the occurrence of left- and right-handed enantiomers arises from the initial conditions of a given experiment. It would arise quite naturally and is not difficult to understand. Because of the experimentally established energetic equivalence (to within rather large experimental error!) this was the historically prevalent point of view.[18–21] Pasteur seems to have seriously considered also an intrinsic asymmetry. In this latter case enantiomerism would be rather similar to all other kinds of isomerism with a small $\Delta_R U_0^0$.

With the advent of quantum mechanics, governing also molecular vibrations and rotations, one might consider the classical point of view as irrelevant and superseded.[24] However, one might also take an extreme outsider's point of view along the following lines: The motion corresponding to the interconversion of enantiomers in complex organic molecules is of very low frequency. It may be that for such

motions quantum mechanics becomes invalid, and classical mechanics (or something similar) is intrinsically valid (i.e. not just as an approximation to quantum mechanics). There is no computational test of sufficient accuracy in the quantum chemistry of enantiomers, which could disprove such a hypothesis. More interestingly, we are not aware of any direct experimental test. Such tests might search for either tunneling in the symmetric case (absent in classical mechanics) or look for direct violations of the quantum mechanical superposition principle, which is irrelevant for Newtonian mechanics both in the symmetric and asymmetric cases.

Before discussing specific experiments, it should be pointed out, that the "classical hypothesis" seems rather inconsistent and theoretically remote. There is no good reason for treating electrons and nuclei on a totally different footing, which is implied by taking the Born-Oppenheimer potentials as more than an approximate trick. In reality there is no good reason to assume that there are such potentials and one should consistently treat both electrons and nuclei by the same mechanics (quantum or classical). There is sufficient evidence for excluding a classical mechanical treatment for the electronic motions in enantiomers. One would thus be tempted to discard the classical hypothesis on theoretical grounds. In the absence of direct experimental tests, some might wish to resist this temptation.

2.2. The Quantum Mechanical Point of View with a Space Reflection Invariant Hamiltonian: "Hund's Hypothesis"

Hund[24] recognized that in quantum mechanics there will be a small splitting $\Delta E_\pm$ due to tunneling between eigenstates of positive and negative overall parity, if the total hamiltonian H is invariant under space reflection for the potentially enantiomeric molecular system. The eigenfunctions of H would thus be achiral. Their superposition results in left- and right-handed enantiomers, which are time dependent molecular states. Hund estimated the time dependence for typical compounds and concluded that on ordinary time scales the tunneling contribution to interconversion would be negligible: The enantiomers are predicted to be kinetically stable.

In order to avoid certain confusions that sometimes arise, we should stress that there is no reason whatsoever to request that a molecule or chemical compound should correspond to an eigenstate of H. Many molecules are known to exist as kinetically stable entities, often even as scattering resonances in the continuum far above the ground state of H. A simple example is formaldehyde H_2CO, which is unstable with respect to decomposition into $H_2 + CO$, according to current thermodynamic data ($\Delta_R H_0^0 = -1.7 \pm 6$ kJ mol^{-1}, a more pronounced example is $N_2H_4 = N_2 + 2 H_2$, $\Delta_R H_0^0 = -109$ kJ mol^{-1}). These molecules are kinetically stable. In this context it may be useful to provide some orders of magnitude. The racemization of aspartic acid is among the fastest for amino acids and is believed to occur unimolecularly under certain conditions.[56, 60] At 310 K the rate constant is $k_{rac} \simeq 2.7 \times 10^{-11}$ s, corresponding to a chemical relaxation time of about 1200 years. Most of the reaction occurs by thermal excitation over a barrier of about 125 kJ mol^{-1}.

Hund's hypothesis is perfectly consistent with all available experimental evidence. One may raise, however, some theoretical objections. The first, and certainly most serious one, concerns the influence of parity-violating perturbations due to the weak nuclear force. As this was only discovered in 1956,[133–35] Hund could not know about it. In 1927 it seemed apparently too remote to even hypothesize about this possibility. Today we must take it into account.[6, 10, 11, 42–55] However, this does not automatically invalidate Hund's hypothesis for the fundamental structure and dynamics of enantiomers, whose properties depend critically on certain parameters, the splitting $\Delta E_\pm$ due to tunneling and the parity-violating splitting ΔE_{PV} (see appendix). Only when the inequality (1) holds will Hund's hypothesis be valid. Current theory would seem to exclude the inequality (1) for a number of typical cases.[10, 111] However, from an experimental point of view the question is open.[50]

$$\Delta E_\pm \gg E_{PV} \tag{1}$$

The second objection was raised by Pfeifer.[26] He points out that Hund's treatment neglects some interactions with the radiation field. If these are included, Pfeifer finds that the achiral eigenstates are removed and that the chiral states correspond to stable states of the system due to a superselection rule. Experimentally, this point also remains open.[50]

The third and perhaps least serious objection comes from a discussion of collisional effects by Harris and Stodolsky.[30] To the extent that at very low gas densities the idealization of a collision free molecule is adequate, this work complements Hund's work but does not reject his hypothesis (for a discussion of crystallization see Ref. [57]).

2.3. Influence of the Radiation Field: Pfeifer's "Superselection Rule Hypothesis"

Pfeifer pointed out two weaknesses of Hund's treatment.[26, 58, 59] Firstly, Hund does not explicitly account for the *apparent* absence of "isomers of well defined parity".[50] These would thus seem to be unstable or nonexistent, in contrast to the established high stability of enantiomers. This objection may or may not be taken seriously. Certainly the repeated statement[58, 27] that "according to experiment space reflection invariant pure states for enantiomeric molecules do not exist" is incorrect, as to the best of our knowledge no experimental evidence has ever been presented for the *absence* of states of well defined parity (there is no evidence for their *existence* either, but that is a different matter, see Section 3.1). Thus, Hund's treatment would seem to be somewhat incomplete but not necessarily incorrect. However, the first observation led Pfeifer to note that secondly, Hund omits to treat the interactions with the radiation field, which cannot be entirely removed. When Pfeifer includes these, he finds[58] within the framework of algebraic quantum mechanics (see also Ref. [27]) a superselection rule, which, indeed, excludes on theoretical grounds the existence of states of well defined parity under certain conditions for enantiomeric systems. Thus, even without parity violating terms in the hamiltonian, the stable ground state of enantiomeric systems corresponds to left- and right-handed isomers and not to the symmetric state of positive parity.

Pfeifer's superselection rule certainly constitutes a most striking theoretical finding. He also gives some numerical estimates for molecules.[26, 58] However, there is no direct experimental test of the superselection rule hypothesis as yet.[26, 50] On the theoretical side, some aspects of Pfeifer's treatment have been revised or extended.[27] One might also raise at least two general theoretical objections to Pfeifer's treatment:

1. *Maxwell's* equations and quantum field theory have equations of motion that are space reflection invariant, as is the molecular hamiltonian in the approximation used by Pfeifer. Thus from general symmetry considerations his result would seem undesirable, if not impossible.

2. It is not clear whether the infinite boundary conditions for the field used by Pfeifer, excluding gravitation, can correspond to any real physical situation or are meaningful idealizations. The two objections are related and we realize, of course, that the symmetry breaking is the *essence* of Pfeifer's theory. As the theoretical situation is not entirely clear, we would summarize that *experimentally* the question is definitely open.

2.4. The Stabilization of Enantiomers by Collision: "The Collision Hypothesis"

It has been suggested that interactions with some external medium, in particular also collisions in a gas, tend to stabilize enantiomers (L and R) and destabilize parity isomers (+ and −)[30, 31, 32] (see also Ref. [59]). In discussing a Bloch type relaxation equation for the density matrix P of a two level problem in the $|L>$ and $|R>$ basis, Harris and Stodolsky derive the equation (2) for the relaxation to equilibrium for the population difference Δp of L and R (if $p_L^e \simeq p_R^e$ for the equilibrium population p^e).

$$\Delta p(t) = P_{LL} - P_{RR} = \Delta p(0) \exp[-(\bar{\delta}^2/\bar{\lambda})t] \tag{2}$$

Here, one has $\bar{\lambda}^{-1} \approx T_2$, the phase relaxation rate constant that can be assumed to be proportional to the collision frequency in a gas, and $\Delta E_\pm = 2\bar{\delta}$, the tunneling splitting for the parity states, which can be related to the rate of racemization in the absence of collisions (Section 4). Equation (2) is assumed to hold in the case of strong damping, i.e. $(\bar{\lambda}/\bar{\delta}) \gg 1$. One has the seemingly paradoxical result that the *population relaxation rate* $T_1^{-1} \simeq \bar{\delta}^2/\bar{\lambda}$ and thus the racemization rate constant k_{rac} are inversely proportional to the collision rate. But, normally, in the low pressure range of unimolecular reactions (of which racemizations are special cases) one has $k \propto$ collision rate, i.e. just the opposite behavior. This results from the mechanism of an ordinary unimolecular reaction, which involves a collisional activation process to energized states with fast reaction.[60, 70] The model of Harris and Stodolsky applies to the "low temperature limit" two state model of racemization only.

It is this starting point which one may criticize: In real polyatomic molecules, the two state model would apply only at exceedingly low temperatures $T \ll 1$ K, where all molecules are in the rotational and vibrational ground state. This will be difficult to achieve. A second criticism of the model comes from its neglect of the radiation field. One can

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estimate that under dilute beam conditions thermal radiative transitions between ground and vibrationally excited states may be at least as important if not more so than transitions by collisions.[50] Thirdly, as noted also by *Harris* and *Stodolsky*, there are cases of low collision rate and sufficiently fast inversion rate, where *Hund*'s model would be applicable. One might then ask for the "structure" of the isolated molecule.

Whether or not the *Harris* and *Stodolsky* model is relevant to the stabilization or existence of long-lived enantiomers in dilute gases for real molecules at ordinary temperatures could be decided only by the direct experimental determination of the molecular relaxation parameters. To our knowledge, there exists no experimental evidence either supporting or denying this hypothesis. Thus, the theory merits an experimental test, possibilities for which will be discussed in Section 3.

2.5. Weak Nuclear Interaction and Parity Violation in Molecules

The first new aspect (after quantum mechanics and *Hund*) in terms of the *physics* of molecular chirality was certainly the discovery of the parity-violating weak nuclear force.[33–35] Parity violation in physics in general and for chiral molecules in particular clearly was not foreseen by theoretical reasoning alone. Parity violation leads to a slight energy difference for the **L** and **R** isomers. Recent estimates on the basis of fairly detailed quantum chemical calculations place the parity-violating energy difference of enantiomers ΔE_{PV} in the range of 10^{-14} J mol^{-1} or about 10^{-4} to 10^{-5} Hz in frequency units.[10, 11] If this is accepted, the structure of enantiomers would be dominated by this energy difference. Tunneling from **L** to **R** would be quite negligible for typical molecules at low temperatures and the probability density for true molecular eigenstates associated mostly with one enantiomer (say **L**) would be negligible for that part of the configuration space associated with the other enantiomer (**R**). Optical isomers would then resemble ordinary isomers **A** and **B**, such as *cis-trans* isomers, separated by an energy difference ΔE_{AB} at the zero-point level. For these the eigenstates of the molecular hamiltonian are sufficiently well localized at low energies that they may be associated with one isomer only.

From the theoretical side this situation appears to be fairly well understood. However, there exists no experimental test yet. Clearly, a direct experimental measurement of the parity-violating energy difference would be in order.[50] If the experimentally measured ΔE_{PV} were to be much smaller than the theoretical prediction, it might be that there are many optically active molecules, for which parity violation would be dynamically unimportant.

From a fundamental point of view the structural hypothesis of enantiomers based upon parity violation is the most interesting one, as it is based on symmetry arguments[61] closely related to general conservation laws[71] following the thoughts of *A. E. Noether*. Understanding the structure of enantiomers in terms of the parity-violating energy difference by a quantitative measurement might have conse-quences beyond physical stereochemistry in the realm of the physics of fundamental symmetries.[50, 62]

2.6. Symmetry Breaking *de facto* or *de lege*

At this point it may be useful to distinguish the symmetry breaking through initial conditions in the ordinary classical (Section 2.1) or quantum (Section 2.2) theory from the symmetry breaking by *violation* of the fundamental symmetry law of parity conservation (Section 2.5).

If the initial conditions of a physical system can be chosen in different, but symmetrically equivalent ways, the symmetry of the *phenomena* or the actual state of motion will not necessarily reflect the underlying symmetry. A classical mass point moving in a symmetrical double well potential will be localized on one side, if it lies below the barrier of the double well. The direction of motion of the planets around the sun is well defined and does not reflect the symmetry of the law of motion or of space. The same is true for the **L** and **R** enantiomers in the classical situation or *Hund*'s hypothesis. And a cigarette without filter will be lit at *one end*, even if it is symmetrical.

The symmetry of the underlying law or structure is broken *de facto* by the chosen initial conditions. But the underlying symmetrical law allows also the opposite, *symmetrically equivalent* solution. In the quantum case (Section 2.2) one has then the interesting possibility of a symmetrical state of motion by the superposition principle, but such a symmetrical state is no more likely than the asymmetrical state. In classical mechanics this symmetrical state does not exist, as the superposition principle is lacking.

If, however, the symmetry is already broken in the underlying law of motion (asymmetrical double well for the classical mass point, parity violation for **L** and **R**, cigarette with a filter), then the two states of motion are not symmetrically equivalent, and we speak of symmetry breaking *de lege*. If the symmetry breaking *de lege* is small, then in quantum mechanics a very nearly symmetrical state can be generated by linear superposition, which will evolve slowly in time with respect to its symmetry properties (time-dependent symmetry violation).

These two situations of symmetry breaking *de facto* and *de lege* are obviously quite different and should be distinguished by appropriate terminology, as proposed. There is a third class of symmetry breaking, which is commonly named "*spontaneous*".[63] It arises with an intrinsically symmetrical dynamical structure and *Pfeifer*'s hypothesis is an example of this. One might add that one view of parity violation introduces this as a spontaneous symmetry breaking in a cosmological context. Thus, the parity-violating molecular hamiltonian of our present world arises as a particular solution out of a fundamentally symmetrical situation at the origin of our universe. It may be that the **L** isomer of a given molecule is more stable than the **R** isomer in our world; this view implies that another world may exist in which the reverse would be true. This view of parity violation is nevertheless consistent with the statement that the left-right symmetry-breaking in our world is *de lege*, as the laws of motion are now defined in the present context.

2.7. "Totaliter aliter"

Before discussing experiments discriminating between current hypotheses of the structure of chiral molecules, one should consider the possibility that the experimental result will contradict *all* current hypotheses and is thus "totally different" (totaliter aliter[64]). Such a discussion must necessarily be speculative, as otherwise we could have listed yet another, specific alternative. Effects that have not been considered so far and that may influence the structure of chiral molecules are time reversal symmetry violation and gravitation. Both are very small at the molecular level, but one is talking about small effects anyway. At the other end of the spectrum one has configuration interaction of the molecular low energy states with excited electronic states and dissociative states that are achiral. This might influence the $\Delta E_\pm$ in an unpredicted way, as it is usually calculated as a tunneling splitting in the electronic ground state. At still higher energies there are states, where the particle concept (electrons and nuclei) of molecular structure is no longer useful. The effects of configuration interaction with such high energy field states (including increasing numbers of positrons, antiprotons etc.) are small, but not easy to predict and may perhaps lead to surprising consequences for the very small energy effects that we consider in chiral molecules. Finally, there might be effects from an as yet unknown force.

Even this list is not complete. Together with the five specific alternatives mentioned before it should convince the reader, that no definite statement on the structure of chiral molecules will be possible without direct experimental tests, even if *some* of the theoretical alternatives may seem remote or might even be excluded as inconsistent with currently established facts by a sufficiently careful analysis.

3. Experimental Tests

We shall discuss possible experimental tests of the hypotheses, labeled 1–5 following the order of Section 2. In each case we shall discuss the *principle* of the experiment, not the details of its realization, which are complex and often not obvious, and its capabilities to distinguish between the various hypotheses.

3.1. The Principles of the Experimental Testing of Various Hypotheses Concerning Molecular Chirality

1. The first class of experiments concerns the spectroscopy of separate enantiomers. Proposals and actual experiments of high accuracy have been communicated in the radiofrequency and infrared ranges. If the weak nuclear force has sufficient influence, the absorption frequencies for the individual **R** and **L** isomers will be slightly different. Measurements with CO_2 lasers have been attempted on CHFClBr by *Kompanets* et al.[43] but gave a null result. Experiments on camphor by *Arimondo* et al.[52] gave the same absorption frequencies for D and L to an accuracy $\Delta v/v$ of 10^{-8}, probably still far away from an expected effect, although no accurate calculations have been carried out. Calculations for NMR chemical shifts predict differences of

about 1 mHz, which may be measurable but have not yet been proven experimentally.[47−49] If successful, these experiments are, in principle, able to discriminate the inversion symmetrical hypotheses 1–4 from the asymmetrical 5. They do not give, however, a direct measure of the parity-violating energy difference of enantiomers ΔE_{PV}. We note that in atomic spectroscopy the search for effects from the weak nuclear force has been successful,[39−41] and for diatomic molecules there are some null results available in searches for both parity and time-reversal symmetry-violation.[51, 53, 54]

2. The second class of experiments concerns spectroscopic transitions *between* the **R** and **L** isomers. When ΔE_{PV} is much larger than the splitting due to tunneling, one-photon transitions (at mHz frequencies) are strictly forbidden. However, a two-photon transition with an intermediate state of well defined parity will be allowed according to the following scheme:
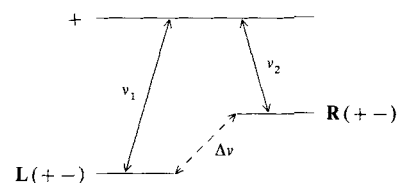
Scheme 1. Two-photon transfer between the enantiomers **R** and **L**.

Possible transitions in this case may involve an excited electronic state that is achiral and has rovibronic levels of well defined parity. The corresponding transitions would occur in the visible or UV part of the spectrum.

Stabilizing two lasers at the transition frequencies v_1 and v_2 of the **L** and **R** isomers one could measure the beating between them, which may occur on the time scale of hours. This experiment is technically very difficult as it requires long time stabilization of the frequency to within $\Delta v/v \approx 10^{-19}$, quite apart from other difficulties. A slightly more favorable situation would occur for special molecules, having a small tunneling splitting ($\Delta E_\pm \ll \Delta E_{PV}$) in the vibrational ground state and a large one ($\Delta E_\pm \geq \Delta E_{PV}$) in a vibrationally excited state of the electronic ground state. Scheme 1 would then allow a measurement in the IR with a gain of a factor of about ten concerning the required accuracy. In even more special cases, it may be possible to measure the highly forbidden transition $\mathbf{L} \leftrightarrow \mathbf{R}$ at the frequency Δv directly. This will happen, when tunneling is just sufficient to mix the **L** and **R** wave functions slightly, still preserving the dominant asymmetry. The $\mathbf{L} \leftrightarrow \mathbf{R}$ transition will then be slightly allowed as it acquires a weak inversion transition character. Of course, such optical isomers are necessarily rather short-lived, and are not the most typical cases. The second class of experiments allows us to measure ΔE_{PV} and thus to decide to what extent inversion symmetry is violated *de lege* or not (i.e. preferring hypothesis 5 to the others).

3. A third class of experiments is somewhat speculative at present. It would be based on the kinetic selection of **L** and **R** isomers due to the asymmetric kinetics in the case of an appreciable ΔE_{PV}:

$$\mathbf{L} \underset{k_{LR}}{\overset{k_{RL}}{\rightleftarrows}} \mathbf{R} \tag{b}$$

$$\frac{k_{RL}}{k_{LR}} = 1 \pm \bar{A} \tag{3}$$

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with $\bar{A}$ of the order of 10^{-18}. This is not directly measurable, but in relation with nonequilibrium kinetic schemes in evolutionary times, mechanisms have been discussed that would lead to a measurable selection of **L** or **R**.[7-9, 12] If a mechanism of this kind could be found for a quantitatively well understood laboratory reaction, the measured selection rate for **L** or **R** could be interpreted in terms of $\bar{A}$ and finally ΔE_{PV}. Such an experiment would be an outstanding achievement in chemical kinetics, but at present there are no ideas as to how it could be realized. It might also be possible to unravel the mechanism of the natural selection of optical isomers in prebiotic times from fossil documents and thereby obtain the relevant parameters. Again this is at present a remote possibility. If ever such evaluations became possible they would discriminate hypothesis **5** against the others and, perhaps, provide a result for ΔE_{PV} in certain molecules.

4. Another experiment has been proposed, which is based on the generation of states of well defined parity and the observation of the time dependence of parity.[50] The principle of the experiment is based on three steps: a) Preparation of molecular states of well defined parity (for instance ($+$) from optically active molecules (**R** or **L**) of ill defined parity in the electronic ground state. b) Free evolution of the isolated molecule with initially well defined parity ($+$). Under this condition the probability for negative parity will increase quadratically with time; for short times Equation (4) holds.[50] For long times one has an oscillation with period τ [Eq. (5)].

$$p_{-} = (\pi \Delta E_{PV} t/h)^2 \tag{4}$$

$$\tau_{\pm} = h/\Delta E_{PV} \tag{5}$$

c) Spectroscopic observation of the population of states of the "forbidden" parity (for example p_{-}) as a function of time. According to Equations (4) or (5) one can evaluate ΔE_{PV} and again distinguish hypothesis **5** from the others. This experiment allows us, however, also to decide between hypothesis **2** and **1** or **3**. In the preparation step [Eq. (6)] of the experiment one generates a linear superposition state λ_+ [Eq. (6)],

$$\chi_+ = (\lambda + \varrho)/\sqrt{2} \tag{6}$$

where λ and ϱ are the eigenfunctions of the **L** and **R** isomers (cf. Appendix). According to the quantum mechanical superposition principle this is always possible whether or not there is a sizeable ΔE_{PV} (hypotheses **2** and **5**). According to the classical hypothesis **1** or the superselection rule hypothesis **3**[26] the preparation step will generate only **R** or **L** or mixtures of **R** and **L**. These can be distinguished experimentally from the χ_+ state by the dipole absorption spectrum. χ_+ has only strong electric dipole absorptions to states of negative parity whereas **L** and **R** and mixtures have strong electric dipole absorption to both positive and negative rovibronic states. Thus, in an appropriate electronic transition, for example,[50] hypotheses **1** and **3** would predict a spectrum with about twice as many lines than predicted by hypotheses **2** and **5**. The experiment provides a direct test of the superposition principle for enantiomers. It would not allow one to differentiate between hypotheses **1** and **3**, which both require violation of the quantum mechanical superposition princi-

ple. Hypothesis **1** is in a sense a very general hypothesis and **3** might be thought to be a special, precise formulation. In that sense a distinction between **1** and **3** would become meaningful only if precise alternatives were formulated. This class of experiments would be a test for all possible hypotheses except **4** and is thus very powerful. We have also discussed in detail[50] that the experiment should be practical, even if difficult and expensive in its setup. Although the experiment is subject to numerous obvious complications, the evidence presented in Ref. [50] and further investigations[65] all suggest that the experiment can be realized with a guarantee of a definite outcome, whichever this may be. Complications could arise if ΔE_{PV} is either very small or much larger than currently predicted. If ΔE_{PV} is very small, from the absence of parity evolution one could then only derive an upper *limit* on ΔE_{PV}. If ΔE_{PV} is very large, the oscillation of parity might be so fast that it would *simulate* an **L** - **R** mixture, leading to the incorrect conclusion that hypotheses **1** or **3** are appropriate. By increasing time resolution, it should be easy to avoid such an error. Also, a very large ΔE_{PV} would be easily measured by a class 2 experiment and if established, proper precautions could be taken. We might also mention that the technique of *Kukolich* et al.[68] could be useful in the realization of our experiment (see also the related discussion below). Another realization involving excited electronic states is sketched in Figure 1.[50]
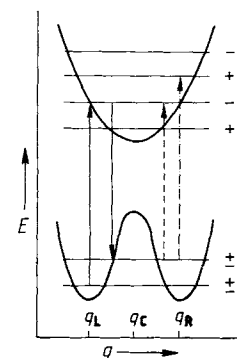

Fig. 1. Scheme for the generation of states of well defined parity (if possible) in a molecule that is chiral in the electronic ground state. The ground state potential has a high barrier for racemization, the excited state a low barrier or none as shown. q = inversion coordinate. In a first optical transition ($\uparrow$) one generates a state of well defined parity ($-$) in the excited state, and in the second ($\downarrow$) in the ground state. The dashed lines indicate the spectroscopic observation of the outcome of the experiment (after Ref. [50]).

5. The final class of experiments would test the collisional hypothesis **4** perhaps by observation of the time dependence of optical activity.[30] A nontrivial time dependence will only be observed for rather quickly interconverting enantiomers, according to current estimates of ΔE_{PV}. A possible realization of the experiment would follow Scheme 2.

In a molecular beam of stable **L** and **R** isomers a pump laser would be used to excite the **L** isomer, for example, to an electronic or vibrational state in which the splitting due to tunneling is sufficient to allow interconversion at an observable rate, ideally complete inversion to **R** within a time of free flight in the beam. This transformation could be followed as a function of the length of flight along the beam by measuring the optical activity by Raman scattering[66] perhaps with CARS or Fourier transform techniques[67] in or-

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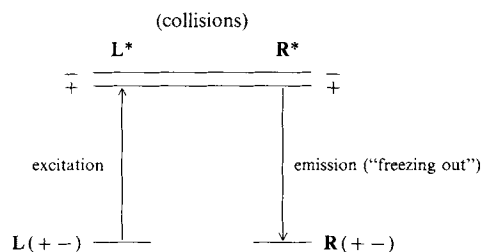
Scheme 2. Experiment for testing the collision hypothesis 4 via the time dependence of the optical activity.

der to increase sensitivity (a serious problem in measuring optical activity). One might also increase sensitivity by freezing out the transformed molecules with a dump laser and collecting the stable "product" R for some time until sufficient material for the experimental sensitivity is available. In the free evolution stage of the experiment p_+ and p_- would remain constant and p_R and p_L would oscillate as suggested by *Harris* and *Stodolsky*. According to their prediction, this oscillation should *be slowed down* if we allow for collisions with some background gas in the molecular beam chamber. One needs just to investigate the L → R interconversion as a function of gas pressure, using Equation (2) for the evaluation of the relevant parameters. If the effect predicted by *Harris* and *Stodolsky* is observed, their hypothesis 4 would be confirmed for the molecular system in question, and one might, by systematic investigations, obtain an understanding of the circumstances in which the collisional stabilization of enantiomers is relevant (see also Section 4). A complication will arise in all these experiments, because a real molecule is not a two level system and even if the initial state is a coherent superposition of just two states, collisions will tend to transfer excitation to other states. It may also be useful to study the L → R oscillations by observations of quantities other than optical activity. A promising technique could be based upon the experiment of *Kukolich* et al.,[68] who studied collision cross sections of parity states (−) and of superposition states (+ −) in ammonia. They used the measurement of polarization in a microwave cavity (their case 2 experiment), which may be more sensitive than the measurement of optical activity. Indeed this experiment could be carried out in a very imaginative way in selected high *J, K* states of *near* symmetric tops with almost oriented molecules:

(c)

As indicated by the dipole moment arrows in Equation (c), the L → R interconversion in an oriented molecular beam will change the macroscopic electric dipole moment orientation and this could be detected. The dynamic situation can again become very complex with collisions.[69]

We have shown in this section that meaningful *real* experiments (as opposed to thought experiments) could test the different hypotheses on the structure of enantiomers. The hypotheses provide significantly different predictions for the various experiments. An appropriate combination of the different experiments discussed here would allow us to exclude all but one of the hypotheses, but we do not know which one

would remain intact, even though intuition may suggest one. As discussed in Section 2.7, perhaps none of the hypotheses would survive the test, but this appears unlikely. At present, to the best of our knowledge, there is no definite experimental evidence available whatsoever. It should be obvious that the outcome of the experiments will depend in general also upon molecular parameters. Different hypotheses may therefore be correct for different molecules. It is then in order to discuss the scope of these hypotheses to make predictions concerning the influence of molecular parameters.

3.2. The Influence of Molecular Parameters

Molecular properties can influence considerably the nature of chirality in a given molecule. The most obvious case in question arises for *Hund*'s hypothesis and the parity-violation hypothesis. The inequality (1) determines which one applies. We have fairly standard techniques to estimate $\Delta E_\pm$, although it may sometimes be difficult to calculate the reaction path and barrier height for racemization by accurate ab initio techniques. The calculation of ΔE_{PV} by ab initio methods has just started.[10, 11] It is not clear yet (to the author) to what extent one can be certain that all the important effects have been included in the calculations. In this sense, too, an experimental test would be important. If current theoretical results are accepted, one would be able to calculate the relevant parameters in inequality (1) for simple molecules. More investigations of ΔE_{PV} are needed.

The classical hypothesis (1) is, at present, purely qualitative. *Pfeifer* has tried to make some estimates, for which molecular parameters his superselection rule should be applicable.[26, 58] The problem deserves more quantitative theoretical investigations.[27] The interested experimentalist would like to know from the theoretician, for which molecules and at what energies the symmetry breaking phase transition occurs, if it happens at all. Probably the isolated two-level approximation has to be abandoned for realistic estimates.

Harris and *Stodolsky*[30] have provided a collision theory formulation for their hypothesis. So far, no one has actually calculated quantitative cross sections for specific examples. Before planning experiments, such calculations would be helpful. The most serious problems will arise from the multistate nature of real molecules. That is, a large multichannel scattering calculation will be required, even if many channels are closed.

For the purpose of estimating collisional effects on the various doublet states of enantiomers, one may consider the results on ammonia inversion sublevels.[68] Here it is found that in the basis of parity states effective cross sections for T_1 and T_2 processes are somewhat larger than gas kinetic values and of about the same order of magnitude in inert gas collision partners, T_1 being shorter than T_2 with dipolar collision partners. This can be understood by a mechanism of dipolar relaxation connecting the parity sublevels but not the R–L sublevels. One can show that for a *degenerate* two-level problem, T_1 for the parity basis χ corresponds to T_2 for the $\varrho-\lambda$ basis (see Appendix). Extrapolating from these results one would thus assume fast, approximately gas kinetic phase relaxation for the density matrix in the (ϱ, λ) basis and fast

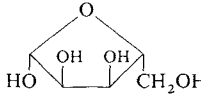Table 1. Some chiral molecules of particular theoretical or experimental interest.
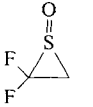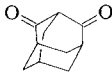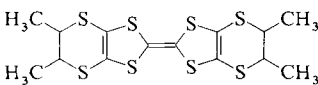
Molecule	Name	Remarks and references
CHFClBr (H, F, Cl, Br)		volatile, gas phase spectroscopy [43] possible: IR-laser chemistry
(camphor structure)	camphor	(volatile) gas phase spectroscopy [52]
$H_3C-CH-CO_2H$ with NH_2	alanine	theory: $\Delta E_{PV}^{max} \approx 10^{-13}$ J mol^{-1} (L more stable [10, 11])
$HO_2C-CH_2-CH-CO_2H$ with NH_2	aspartate	theory: $\Delta E_{PV}^{max} \approx 8 \times 10^{-14}$ J mol^{-1} (L more stable [11]), well known racemization rate [56]
(ribose ring structure: O, OH, OH, HO, CH_2OH)	ribose	theory: $\Delta E_{PV} \approx 2 \times 10^{-14}$ J mol^{-1} (D more stable [11])
H−Te−Te−H (hypothetical structure, twisted 90°)		relativistic theory $\Delta E_{PV} \approx 10^{-8}$ J mol^{-1} [49]
$Pt(C_2H_2)_2$ (hypothetical structure)		relativistic theory [49] $\Delta E_{PV} \approx 10^{-7}$ J mol^{-1}
$[CHCl_2CH_2TlH]^{\ominus}$ (hypothetical structure)		calculated difference in NMR chemical shift of enantiomers ≈ 1 mHz [47, 48]
O=S with F, Cl		suitable for spectroscopy
(N,N'-dimethyl-2,3-diazabicyclo[2.2.1]hept-5-ene structure)	N,N'-dimethyl-2,3-diazabicyclo[2.2.1]hept-5-ene	modest barrier, NMR spectroscopy [91]
(1,2,2-trimethylaziridine structure)	1,2,2-trimethylaziridine (also 1H-aziridine and oxaziridines)	modest barrier [90], expected low barrier in excited electronic states vibrational and electronic spectroscopy. Higher barriers with NCl [92]
(sulfoxide structure: O, S, F, F)	(general sulfoxides)	modest barrier, laser chemistry and spectroscopy
H−P with F, D	(general phosphanes)	intermediate barrier, spectroscopy and IR laser chemistry (similar also PX$_5$)
CHD=C=CHD	dideuterioallene	isotopic chirality, very small ΔE_{PV} expected
CHF^{37}Cl^{35}Cl (C with H, F, ^{37}Cl, ^{35}Cl)		isotopic chirality, suitable for spectroscopy in jets and overtones [93], very small ΔE_{PV} expected
(CH_3, Re, ^{16}O, ^{18}O, ^{17}O structure)		isotopic chirality with heavy atom, volatile compound for spectroscopy [94] and laser chemistry
S,O−C=C=C−S,O		hypothetical spinless chiral molecule
(O=C, S, S, C=S with O double bond structure)		hypothetical spinless chiral molecule (also related derivatives)
(S−S, O, O=C, C=O, O structure)		hypothetical spinless chiral molecule [96]
DFC=C=CH*H	allene (vibrationally twisted)	dynamic chirality [88] locally CH* excited dynamical chirality (Section 4)

Table 1. (Continued)

Molecule	Name	Remarks and references
	adamantanedione	proposed dynamical (electronic) chirality [86]
	methane	dynamic chirality of certain levels (Section 4)
		basis for chiral conductor [95], macroscopic electronic effects in ΔE_{PV}?

population relaxation in the χ_+, χ_- basis. On the other hand, by the same argument as for other isomerizations with high barriers, one would assume slow population relaxation T_1 in the (ϱ, λ) basis. This would easily explain why the "isomers of well defined parity" are not normally found in nature (*Primas'* paradox): They are collisionally unstable and equilibrate at about the gas kinetic collision rate. The arguments given above for collisions hold also for thermal background radiation, which will probably, via vibrationally excited states, quickly interconvert the $+$ and $-$ isomers but not L and R.[50] Quantitative experimental results on these cross sections are lacking, however, and would be obtained by a combination of experiments of type (4) and (5). Thus, some of the experiments discussed in Section 3.1 would provide information on molecular stationary state, collisional and radiative kinetic properties.

For carrying out spectroscopic experiments on the foundations of molecular chirality, it may be useful to choose from a list of suitable molecules. Criteria are: 1. Simplicity (few atoms); 2. volatile compounds; 3. heavy nuclei (for a large ΔE_{PV}); 4. a limited number of nuclei with spin (perhaps a "spinless" molecule, except for the NMR experiments) in order to remove close degeneracies in the spectra; 5. for some investigations molecules with modest energy barriers for racemization. Table 1 summarizes some molecules that may be considered, including a few for which ΔE_{PV} has been calculated. In a search, it transpired that "spinless" enantiomeric compounds are not known, and some are proposed to stimulate the imagination of the synthetic chemist.

4. The Kinetics of Racemization

Molecular structures are in general time dependent and thus an understanding of the dynamics of chiral molecules and of the kinetics of racemization is required in relation to their structural properties. Racemization reactions are a special class of isomerization reactions, which can be dealt within the framework of unimolecular rate theory.[70] Under ordinary "high temperature" conditions they can be discussed approximately in terms of a quasiclassical barrier crossing in the theory of reversible unimolecular reactions[72] or, even more simply by the kinetic scheme in Eqs. (b) and (3) with a very small $\bar{A}$. The rate constants will follow the Arrhenius law (7).

$$k_{RL} \simeq k_{LR} \simeq A \exp(-E_A/RT) \tag{7}$$

Another limit is the symmetrical two level tunneling model of racemization which does not lead to kinetic equations but to oscillatory motion.[24] The period of oscillation ($\Delta E_{PV} \simeq 0$) is given by Equation (8).

$$\tau = h/\Delta E_\pm \tag{8}$$

These descriptions are textbook material in the realm of kinetics[60] or of spectroscopy ("ammonia inversion").[73] The treatment of *Harris* and *Stodolsky*[30] extends the "low temperature" two-level tunneling model to cases involving parity violation and collisions. We shall not discuss these simplified models further but rather refer to the extensive literature on this subject.

Closer inspection of the dynamics of racemization shows, however, that it has certain very special features because of the *approximate* nonrigid molecular symmetry of space inversion and energy equivalence of L and R isomers.[71, 74-76] These special kinetic properties have not been discussed before for real chiral molecules at finite energies, where, in general, a very large number of quantum states renders statistical approximations useful.[77] We shall consider the strongly quantized case at energies below the classical energy barrier. Here, the reaction is dominated by quantum tunneling and quasiclassical barrier crossing is not a useful concept. In this case, the molecular spectrum shows close degeneracies associated with the interplay of ΔE_{PV} and $\Delta E_\pm$ and the average spacing of molecular states $\delta = \varrho^{-1}$ (ϱ = density of rovibronic or nurovibronic states subject to symmetry constraints[76]). This situation leads to very peculiar kinetic properties, depending on these three parameters. Similar behavior is expected for other isomerizations with a very small energy difference between reactant and product states, but in the case of chiral molecules it is essential for symmetry reasons and it thus reveals some of the fundamental properties of chiral molecules. We shall discuss some simple limiting cases of the kinetics of racemization in turn. We start by disregarding collisional and radiative transitions and give a phenomenological discussion of their effects at the end.

The experimental situation that one should have in mind in the following discussion of racemization of an ensemble of isolated molecules is a cold molecular beam in high vacuum, for instance a supersonic jet, excited to some energy $E \pm \Delta E$, for instance with a laser, such that $\Delta E \gg \delta$ but $\Delta E \ll E < E_0$ (classical threshold for racemization). We shall thus calculate the statistical, microcanonical racemization rate under these conditions. Thermal rate constants can be derived from this.

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If an ordinary microcanonical equilibrium were obtained in these racemizations, it would be governed by the densities of states ϱ of the **R** and **L** enantiomers. In order to get an estimate for this we may use a semiclassical approximation for the harmonic density of states [Eqs. (9) and (10)][70] and neglect to a first approximation the differences between the frequencies v_i^L and v_i^R of the isomers (but not ΔE_{PV}).

$$\varrho_L = \frac{(E + a E_Z^L)^{s-1}}{\prod_i h v_i^L} \tag{9}$$

$$\varrho_R = \frac{(E + a E_Z^R + \Delta E_{PV})^{s-1}}{\prod_i h v_i^R} \tag{10}$$

Hence, with s vibrational degrees of freedom, and with vibrational zero point energies $E_Z^L \simeq E_Z^R$ and vibration frequencies $v_i^L \simeq v_i^R$ one gets, setting $E' = E + a E_Z$ (with an energy dependent "constant" $0 \le a \le 1$) the Equations (11) and (12).

$$K_{micro} = \frac{k_{RL}^{micro}}{k_{LR}^{micro}} \simeq \left(\frac{E' + \Delta E_{PV}}{E'} \right)^{s-1} \tag{11}$$

$$\ln(K_{micro}) = (s-1)\ln\left(1 + \frac{\Delta E_{PV}}{E'} \right) \simeq (s-1)\frac{\Delta E_{PV}}{E'} \tag{12}$$

Thus, with $\Delta E_{PV} \ll E'$, K_{micro} will deviate very little from 1 (say, typically, by 10^{-18}). The actual situation is more complicated.

4.1. "Fast Tunneling" with Negligible Parity Violation and Small Densities of States

The time evolution for the isolated chiral molecule is governed by the differential equation (13) for the time evolution operator U,[78] which solves the time-dependent Schrödinger equation for Ψ and the Liouville-von Neumann equation for P according to equations (14)–(16).

$$i\hbar \frac{\partial U}{\partial t} = H U \tag{13}$$

$$U(t) = \exp(-i H t/\hbar) \tag{14}$$

$$\Psi(t) = U(t) \Psi(0) \tag{15}$$

$$P(t) = U(t) P(0) U^+(t) \tag{16}$$

$\Psi(t)$ is the wave function of a molecule and $P(t)$ the density operator of an ensemble, respectively. In order to consider racemization or the time dependence of optical activity, we could write these equations as matrix equations in the basis of molecular states of well defined handedness (ϱ_i and λ_i). These are not generally eigenstates of H and thus the matrix representation of H will contain off-diagonal contributions. One can calculate these off-diagonal contributions by means of the Born Oppenheimer approximation in terms of a tunneling through the potential barrier, but this is by no means a necessary or exact description of the problem and is

given here only for visualization. If the rovibronic density ϱ of molecular states is low [inequality (17)],

$$\delta = \varrho^{-1} \gg \Delta E_\pm, \Delta E_{PV} \tag{17}$$

the total hamiltonian matrix is approximately block diagonal, with two dimensional blocks of the form (18),

$$H^{(2)} = \begin{pmatrix} \langle E_k \rangle - \Delta E_{PV}^{(k)}/2 & \Delta E_\pm^{(k)}/2 \\ \Delta E_\pm^{(k)}/2 & \langle E_k \rangle + \Delta E_{PV}^k/2 \end{pmatrix} \tag{18}$$

$\langle E_k \rangle$ is the average diagonal energy of the k th two-dimensional block. We shall make use of circular frequencies instead of energy parameters [Eqs. (12) and (20)].

$$D_k = 2 \pi \Delta E_\pm^{(k)}/h \tag{19}$$

$$\Delta_k = 2 \pi \Delta E_{PV}^{(k)}/h \tag{20}$$

Suppose we have an equal initial population in N quantum states of the pure **L** isomer [Eq. (21)].

$$p_L(0) = \sum_{j=1}^{N} P_{jj(L)}(0) = 1 \tag{21}$$

The time evolution of the population of the **R** isomer is given by (22) (cf. Ref. [77] and Appendix).

$$p_R(t) = N^{-1} \sum_{i=1}^{N} \frac{D_i^2}{D_i^2 + \Delta_i^2} \left[\sin\left(\frac{t}{2}\sqrt{D_i^2 + \Delta_i^2} \right) \right]^2 \tag{22}$$

We consider now the special case $D_k \gg \Delta_k \approx 0$. In practice this applies always at high energies, with large tunneling frequencies (say 10^6 s^{-1} or more); one then obtains (23).

$$p_R(t) \simeq N^{-1} \sum_{i=1}^{N} \left[\sin\left(\frac{t D_i}{2} \right) \right]^2 \tag{23}$$

The D_i at energy $E \pm \Delta E$ will vary widely. For states that are highly excited in the coordinate associated with the tunneling motion, D_i will be large, for other states it will be small. This situation is well known for the case of ammonia, where excitation of the NH stretching modes increases the inversion splitting only slightly.[73] Even if the coupling of vibrational modes is large, at high energies, the most reasonable assumption would be that the D_i are randomly distributed according to some distribution function $G(D)$ with the average $\langle D_i^2(E) \rangle$ increasing with molecular energy E. If N is very large, we can replace the sum in Eq. (23) by an integral, neglecting terms of the order 1/N [Eq. (24)].

$$p_R(t) = \int_{-\infty}^{+\infty} d D\, G(D) [\sin t D/2]^2 / \int_{-\infty}^{+\infty} d D\, G(D) \tag{24}$$

In this description, the detailed rovibrational molecular dynamics is contained in the spectral distribution function $G(D)$. Little is known as to what this may be. We shall

consider two possible assumptions: (25) and the Lorentz function (27). From (25) we get (26), while (27) gives (28).

$$G(D) = \begin{cases} \text{constant}, & -D_{\max} < D < D_{\max} \\ 0 & \text{otherwise} \end{cases} \quad (25)$$

$$p_{\mathbf{R}}(t) = \frac{1}{2}\left[1 - \frac{\sin(D_{\max} t)}{D_{\max} t}\right] \quad (26)$$

$$G(D) = D_{\mathbf{L}}/[\pi(D^2 + D_{\mathbf{L}}^2)] \quad (27)$$

$$p_{\mathbf{R}}(t) = \frac{1}{2}[1 - \exp(-D_{\mathbf{L}} t)] \quad (28)$$

Both approaches give an approximate relaxation to the expected microcanonical equilibrium $(t \to \infty)\, p_{\mathbf{L}} \approx p_{\mathbf{R}} \approx 1/2$ (for $\Delta E_{\mathrm{PV}} \to 0$). Only in the second case is this relaxation truly exponential with a chemical relaxation time $\tau_{\mathbf{R}} = 1/D_{\mathbf{L}}$. Real distribution functions for D will probably be characterized by some maximum value $D_{\max}$ such as in Equation (26), corresponding to the one-dimensional model with a tunneling splitting $D_{\max}$ calculated with *all* the energy in the racemization mode. One can develop detailed models for $G(D)$. The main result here is that in real, excited molecules under the conditions discussed *one will observe relaxation to zero optical activity even without collisions*. This is in contrast with the two-level prediction of oscillatory optical activity. Before discussing other limiting cases we should give typical experimental conditions, in which the present case will apply. For a molecule SOFCl after IR multiphoton excitation or a molecule such as ($\overline{\mathrm{CF_2NClCH_2}}$) after overtone laser excitation of CH modes one will expect such a behavior. The density of states is still quite small and the tunneling splitting can always be made sufficiently large $(D \gg \Delta)$ by adequate excitation. Racemization in the beam can then be sufficiently fast (ns to ms time range) that both collisions and spontaneous and thermally induced radiative transitions are negligible: we are talking about conditions that may prevail in real experiments. In principle, one can also excite selectively one pair of tunneling levels and observe oscillatory dependence, but this is less important in practice.

4.2. Large Parity-Violating Energy Difference ΔE_{PV} and "Slow Tunneling", with a Small Density of States

Current calculations suggest that, at low energies, ΔE_{PV} will exceed $\Delta E_\pm$ in chiral molecules. As long as Equation (17) is satisfied, we still obtain the block diagonal structure of H as given by Equation (18). By the arguments given in Section 4.1 one obtains from Equation (22) with normalized distribution functions $F(\Delta)$ and $G(D)$ Equation (29).

$$p_{\mathbf{R}}(t) = \int_{-\infty}^{+\infty} \mathrm{d}\Delta F(\Delta) \int_{-\infty}^{+\infty} \mathrm{d}D\, G(D) \frac{D^2}{D^2 + \Delta^2}\left[\sin\left(\frac{t}{2}\sqrt{D^2 + \Delta^2}\right)\right]^2 \quad (29)$$

ΔE_{PV} is essentially an electronic property depending upon the electronic wave function at the positions of the nuclei.[6,10,11,45,49] Although this certainly depends on the rovibrational state, it makes sense to take it as being constant, particularly for rigid molecules without large amplitude motions (except for racemization). The distribution

function $F(\Delta)$ is thus approximately a Dirac delta distribution $\delta(\Delta - \Delta_c)$. On the other hand, D will vary in a wide range from D_a to D_b, as discussed before. In order to obtain a simple result we assume that (30) applies.

$$G(D) = \frac{\sqrt{D^2 + \Delta_c^2}}{N_0 D} \text{ for } D_a < D < D_b \quad (30)$$

with N_0 as normalization constant, so that $\int_{-\infty}^{+\infty} G(D)\,\mathrm{d}D = 1$.

$$N_0 = \sqrt{D_b^2 + \Delta_c^2} - \sqrt{D_a^2 + \Delta_c^2} - \Delta \ln\left\{\frac{D_a(\Delta + \sqrt{D_b^2 + \Delta_c^2})}{D_b(\Delta + \sqrt{D_a^2 + \Delta_c^2})}\right\} \quad (31)$$

For $\Delta_c \ll D$ one obtains a constant distribution and results equivalent to Equation (26). For $\Delta_c \gg D$, $G(D)$ is proportional to $1/D$ (assuming positive D_a and D_b). One obtains Equation (32).

$$p_{\mathbf{R}}(t) = \frac{1}{2N_0}\left\{(\sqrt{\Delta_c^2 + D_b^2} - \sqrt{\Delta_c^2 + D_a^2}) - \frac{1}{t}[\sin(t\sqrt{\Delta_c^2 + D_b^2}) - \sin(t\sqrt{\Delta_c^2 + D_a^2})]\right\} \quad (32)$$

As $t \to \infty$ this relaxes, with some oscillations, to a stationary value [Eq. (33)].

$$p_{\mathbf{R}}(\infty) = \frac{1}{2N_0}\{\sqrt{D_b^2 + \Delta_c^2} - \sqrt{D_a^2 + \Delta_c^2}\} \quad (33)$$

These expressions are valid for all ratios of Δ_c, D_a, and D_b. When we assume $\Delta_c \gg D_a, D_b$, we find the somewhat simpler result (34).

$$p_{\mathbf{R}}(\infty) = \left\{1 + \frac{4\Delta_c^2}{D_b^2 - D_a^2} \ln\left(\frac{D_b}{D_a}\right)\right\}^{-1} \quad (34)$$

Only in Equation (34) have we made use of $\Delta_c \gg D_a, D_b$, thus that $p_{\mathbf{R}}(\infty)$ remains small. *Again $p_{\mathbf{R}}$ does not oscillate as* $t \to \infty$ (neglecting terms of the order $1/N$). Under these conditions an initial optical activity due to the condition $p_{\mathbf{L}}(0) = 1$ will relax to a somewhat smaller than initial but still large value. In contrast to the result of Section 4.1, one cannot be sure that this result will be applicable in practice, neglecting collisional and radiative effects. This will only be true, if for some molecule the ΔE_{PV} is quite large. In this case we could learn about ΔE_{PV} from the kinetics of racemization. Fundamentally similar results are also obtained for the physically less likely case that ΔE_{PV} varies strongly with the rovibrational quantum state. Assuming for instance $F(\Delta)$ and $G(D)$ to be constant in the interval $-\Delta_m \leq \Delta \leq +\Delta_m$ and $-D_m \leq D \leq +D_m$ and zero outside, one finds a relaxed $(t \to \infty)$ population $(\Delta_m \gg D_m)$ [Eq. (35)].

$$p_{\mathbf{R}}(\infty) = \left(\frac{\pi D_m}{8\Delta_m}\right) + \frac{1}{4}\left[1 - \left(\frac{D_m^2 + \Delta_m^2}{D_m \Delta_m}\right)\arctan\left(\frac{D_m}{\Delta_m}\right)\right] \quad (35)$$

Separate forward and backward fluxes cannot be defined in any of these cases. Probability "appears" through tunnel-

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ing across the boundary. Nevertheless, if one defines forward and backward rate coefficients in a kinetic relaxation scheme [Eq. (b) in Section 3.1], which is approximately possible, the rate coefficients depend upon the initial state and do not satisfy the detailed balance relationship Equations (3) or (11). This is an unusual situation in kinetics, which has, however, been encountered before.[77]

4.3. Very Large Densities of States: Pauli Equation for Racemization

For polyatomic molecules with more than 10 to 20 heavy atoms one can estimate with approximations such as Eq. (9) or by more accurate calculations[76] that the density of rovibronic states even at modest energies ($\approx 50 \, kJ \, mol^{-1}$) quickly becomes sufficiently large that (36) holds true.

$$\delta = \varrho^{-1} \ll \Delta E_{\pm}, (\Delta E_{PV}) \tag{36}$$

The hamiltonian matrix can no longer be brought into the block diagonal structure as in Equation (18) and, in general, any level of the R isomer will be coupled to many levels of the L isomer and vice versa. A finite matrix expansion of Equations (13)–(16) would then require matrices of the order of at least many times $\Delta E_{\pm} \varrho$ or $\Delta E_{PV} \varrho$, which will be large numbers. Making use of statistical assumptions that have been discussed in detail elsewhere[77, 79] one can derive a Pauli equation for the specific rate coefficients $k_{RL}^{micro}(E)$ and $k_{LR}^{micro}(E)$ as a function of excitation energy E [Eqs. (37) and (38)].

$$k_{RL}^{micro}(E) = 2\pi \langle D_{RL}^2 \rangle \varrho_R^\omega \tag{37}$$

$$k_{LR}^{micro}(E) = 2\pi \langle D_{LR}^2 \rangle \varrho_L^\omega \tag{38}$$

$\langle D_{LR}^2 \rangle$ is the mean square "tunneling" coupling between all quantum states of R and L isomers at energy E in an interval ΔE which is large enough to render the average meaningful (D_{RL} cannot be calculated directly by a two-level tunneling model). The $\varrho^\omega = h\varrho/2\pi$ are the densities of states in circular frequency units. In contrast to the results of Section 4.2, Equations (37) and (38) satisfy the detailed balance relationship in Equations (11) and (12). The optical activity will relax to zero (practically) with a relaxation time $\tau_R = 1/(k_{RL} + k_{LR})$. Again, it will not oscillate. The density of states ϱ that has to be considered in the inequality (36) is not the full density of states but rather only the density of those states that are effectively coupled (by matrix elements of the order $\sqrt{\langle D_{LR}^2 \rangle}$). The transition between the situations in Sections 4.1 and 4.2 ("cases C" of Ref. [77]) and the Pauli equation ("case B" of Ref. [77]) will happen at values $\varrho^{-1} \simeq \Delta E_{\pm}$. From studying this transition experimentally one would thus learn about the coupling dynamics between the R and L isomers in real polyatomic molecules, beyond the two-level approximation. The experiment would simply use the rapid increase of both ϱ and $\Delta E_{\pm}$ with excitation energy. The infrared laser chemistry of racemization has recently been discussed in this context.[77b]

4.4. Dynamic Chirality and the Possible Existence of Chiral Methane

The common description of chiral molecules is based upon a Born-Oppenheimer potential with a double well and a barrier (such as in Fig. 1), which separates the two enantiomers. Racemization may occur in this description either by quantum tunneling through the barrier or by a quasiclassical barrier crossing above the barrier. We have stressed before that this description is unnecessary. This may appear obvious, because an observed *phenomenon* such as chirality, cannot depend on some arbitrary approximation that we use for its description. Atomic chirality is known to occur where this description would be meaningless.[41] It may be useful to complement these general observations with specific *molecular* examples of *dynamical chirality* beyond Born-Oppenheimer potentials.

Work by *Mecke*[80] and more recently by *Child* and *Lawton*[81] and others[82] suggests that high overtone excitation of high frequency modes in molecules with equivalent X–H modes may lead to long-lived localized vibrational excitations ("local modes"), in the following examples marked by asterisks.

(d)

(e)

(f)
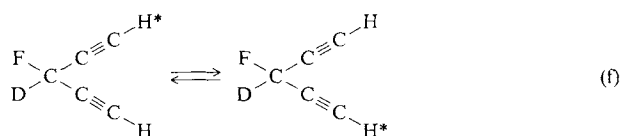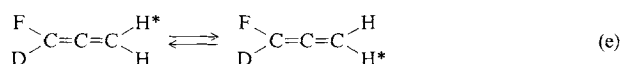
Molecules with such localized vibrational excitations are chiral. The coupling including racemization is entirely vibrational (rotational) and unrelated to any electronic potential barriers. Although the lifetimes for localized states have probably been overestimated in early work,[81, 83] current evidence suggests that whereas the racemization (d) may occur on the subpicosecond time scale, the racemization (e) should be slower and in the case of acetylenic CH (or also alcoholic OH) stretching modes may exceed many picoseconds.[84] Such dynamic chirality could be studied by time resolved vibrational spectroscopy.[85] No direct experimental evidence has yet been presented, but one can be fairly certain from indirect evidence that the phenomenon exists.

Another kind of dynamic chirality has recently been proposed on the basis of localized *electronic* carbonyl excitation in an adamantanedione.[86] The chirality and its lifetime has not yet been established experimentally. Optical activity in vibrationally twisted allene has been discussed as well.[88] One should realize that also *rotation* may induce a dynamic asymmetry or chirality, for example by centrifugal distortion (for magnetic effects see Ref. [89]).

A particularly interesting case of dynamic chirality is methane, by tradition the prototype of an achiral, highly symmetric, tetrahedral molecule.[20] We shall discuss the consequences of parity violation and methane inversion from the present point of view. Figure 2 gives a rotational
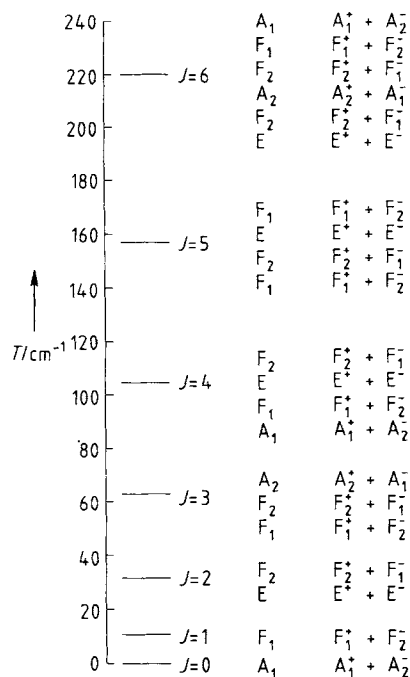
Fig. 2. Rotational energy level scheme for methane with symmetry assignments as explained in the text (after Ref. [100]). T = term value = $E/(hc)$ (for nomenclature cf. also Ref. [75]).

energy level scheme for methane. The zero order spherical top levels shown at the left-hand side are split by centrifugal distortion into sublevels, classified in the point group species (A_1, A_2, E, F_1, F_2) as shown in the middle. These strongly J-dependent splittings are large, of the order of $0.1\ \mathrm{cm}^{-1}$ here, and can be much larger. Each of these levels is further split by a very small amount into a sublevel of positive and negative parity ($+$, $-$) as indicated by the molecular symmetry group species notation on the right-hand side.[74, 75] (In Ref. [99] a different nomenclature has been used. According to the authors involved, the current nomenclature from Ref. [75] should be preferred.) It turns out that for CH_4 only the $A_2^{\pm}$ (combining with nuclear spin $I = 2$), the $F_1^{\pm}$ (combining with nuclear spin $I = 1$) and the $E^{\pm}$ (combining with nuclear spin $I = 0$) exist, because of the Pauli principle. Thus the $A_{1,2}$ and $F_{1,2}$ levels in T_D have all well defined parity (either $+$ or $-$) and there is no inversion splitting for these. However, the $E^{\pm}$ pair does occur. Whereas in an asymmetrically substituted molecule with a high barrier the $\pm$ splitting due to tunneling must be very small for symmetry reasons, in a symmetrical molecule such as methane there are further contributions to this splitting, which are still very small but which are potentially much larger than the tunneling splitting. According to all current quantum chemical evidence the inversion splitting must be very small in methane.[97] There have also been experimental investigations on this question.[98, 99]

Nevertheless, for special dynamical reasons, or by using the influence of external fields as in atoms,[40, 41] the splitting may be made very small for some E^+, E^- level pair, so that $\Delta E_{\pm} \ll \Delta E_{PV}$. In this case ΔE_{PV} will generate new levels ϱ and λ (see Appendix), which have no well defined parity and are chiral: The probability density distribution $|\Psi_{\lambda, \varrho}(x,y,z)|^2$ for the four protons around the carbon nucleus will be asymmet-

ric. This effect can be tested by a spectroscopic experiment (in principle also by diffraction methods, but accuracy will be too low there). It leads in any case to a fundamental revision of the stereochemical concepts introduced by *van't Hoff* and *Le Bel* some 100 years ago.[20]

4.5. Effects of Collisional and Radiative Processes

A complete treatment of collisional and radiative processes in a complex multilevel problem is beyond the scope of this article. However, we shall provide a phenomenological discussion of the effects expected in relation to the kinetic schemes in Sections 4.1. to 4.3. These complement the two-level treatment of collisions given by *Harris* and *Stodolsky*.[44]

Collisional and radiative effects can be introduced in general in a *reduced* density matrix equation of motion by adding non-Hamiltonian terms (cf. Eq. (16)). They can also be simulated approximately by phenomenologically adding contributions from a continuous spectrum to the molecular hamiltonian (Eqs. (13) and (18)), for instance in the form of complex energies $E_k - i\Gamma_k/2$ with a width Γ_k. The effect on kinetic schemes as described in Sections 4.1 to 4.3 is known. The width has the effect of changing the density of states from a Dirac δ-distribution to a more continuous function.[77] Then, by connecting the blocks of the effective hamiltonian instead of the relaxation [Eqs. (26), (28) or (32)] one has a transition to the Pauli equation rate coefficients (37) and (38). This changes somewhat the relaxation rate, but always leads to *complete racemization* at $t \to \infty$. In this sense collisions and spontaneous and thermal radiative processes *promote* racemization. This is somewhat in contrast to the result of *Harris* and *Stodolsky*,[44] not because their theoretical result would be subject to doubt, but because here we consider a complex multilevel problem at finite energy, whereas their result refers to the $T \to 0$, $E \to 0$ limit of a pure two-level problem. Of course, the present qualitative predictions can be tested by experiments similar to those we have proposed in Section 3. There is no evidence available on chiral molecules. However, in a dynamically very similar case of IR-multiphoton excitation, collisions were, indeed, found to enhance the corresponding equilibration process by the mechanism discussed above, which has also been established experimentally.[87]

5. Conclusions

We have demonstrated that different current hypotheses about the physical-chemical structure of chiral molecules lead to experimentally distinguishable consequences. Possible experiments using spectroscopic probes of molecular quantum state structure or probing the kinetics of racemization have been proposed. Although difficult and expensive (on the chemical, not particle physics scale) they would seem worthwhile in order to experimentally settle the questions posed.

It has been known to chemists and biologists for 140 years that chiral molecules carry a message for living beings: Chirality determines the fragrance of fruits, it can make all the

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difference between bitter and sweet and it may distinguish healthy drug from deadly poison.[101] Chiral molecules recognize each other not just as key and lock but as hand and glove. It is also believed by many that chiral compounds in nature are messengers of the evolution of living beings.

It seems to be much less well known that molecular chirality may carry an as yet hidden message on the subtle physical forces governing molecular structure and dynamics and, perhaps, following the motto by *Pasteur*, on the structure of our universe.

Appendix: Some equations for the matrix representations of the two level problem with near degeneracies.

The hamiltonian matrix has the form (A 1). The eigenvalues for a hermitian operator H (A 2) follow from (A 3).

$$H = \begin{pmatrix} H_{11} & H_{12} \\ H_{21} & H_{22} \end{pmatrix} \tag{A 1}$$

$$H_{12} H_{21} = H_{12} H_{12}^* = |H_{12}|^2 \tag{A 2}$$

$$E_{1,2} = \frac{H_{11} + H_{22}}{2} \pm \frac{1}{2}[(H_{11} - H_{22})^2 + 4|H_{12}|^2]^{\frac{1}{2}} \tag{A 3}$$

If we work in the basis $\chi_\pm$ of states of well defined parity and take ΔE_{PV} as perturbation one may identify (with real H_{12} and positive $\Delta E_\pm$) the expressions (A 4) and (A 5).

$$\Delta E_{PV} = 2 H_{12} \tag{A 4}$$

$$H_{11} = - \Delta E_\pm/2 = -H_{22} \tag{A 5}$$

If we work in the basis of "left" and "right" handed states λ and ϱ, one has (positive ΔE_{PV}) the equations (A 6) and (A 7).

$$H_{11}' = - \Delta E_{PV}/2 = -H_{22}' \tag{A 6}$$

$$\Delta E_\pm = 2 H_{12}' \tag{A 7}$$

The eigenvalues with respect to the average energy $(E_1 + E_2)/2 = \langle E \rangle \equiv 0$ are obviously the same ($\Delta E_\pm$ and ΔE_{PV} are defined real, positive) [(A 8)]. It is immaterial, whether ΔE_{PV} (Ref. [50]) or the tunneling $\Delta E_\pm$ (Section 4) is introduced as "perturbation".

$$E_{1,2} = \langle E \rangle \pm \frac{1}{2}(\Delta E_\pm^2 + \Delta E_{PV}^2)^{\frac{1}{2}} \tag{A 8}$$

Eigenvectors for the example of basis χ are given by (A 9) where x and y are defined via S [Eq. (A 10)] according to (A 11) and (A 12).

$$C = \begin{pmatrix} x & y \\ -y & x \end{pmatrix} \tag{A 9}$$

$$S = (\Delta E_\pm^2 + \Delta E_{PV}^2)^{\frac{1}{2}} \tag{A 10}$$

$$x^2 = \frac{S + \Delta E_\pm}{2 S} \tag{A 11}$$

$$y^2 = \frac{S - \Delta E_\pm}{2 S} \tag{A 12}$$

The signs of the roots $\sqrt{x^2}$ and $\sqrt{y^2}$ can be taken in various combinations respecting $C^T C = 1$ (S is defined positive). One has by convention $E_1 < E_2$ and $H_{11} < H_{22}$. Some sign combinations in Ref. [50] were inconsistent with the correct figure ($E_\lambda < E_\varrho$). Figure 3 represents the situation ($x = y = 1/\sqrt{2}$ [Eq. (A 13)–(A 16)].
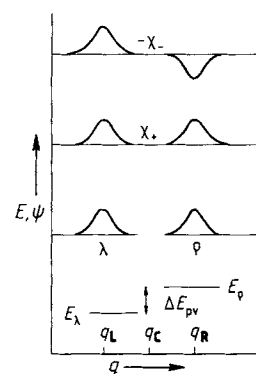

Fig. 3. Scheme for wave functions in a nearly degenerate situation ($\Delta E_\pm \approx 0$) in a chiral molecule (see text).

$$\lambda = \frac{1}{\sqrt{2}}(\chi_+ - \chi_-) \tag{A 13}$$

$$\varrho = \frac{1}{\sqrt{2}}(\chi_+ + \chi_-) \tag{A 14}$$

$$\chi_+ = \frac{1}{\sqrt{2}}(\lambda + \varrho) \tag{A 15}$$

$$-\chi_- = \frac{1}{\sqrt{2}}(\lambda + \varrho) \tag{A 16}$$

According to the superposition principle (if valid) these can always be generated by one of the methods of Section 3. The time evolution results from Equation (A 17) giving Equation (22) for $P_{RR} = p_R$, for example.

$$U = C \begin{pmatrix} \exp(-i E_1 t/\hbar) & 0 \\ 0 & \exp(-i E_2 t/\hbar) \end{pmatrix} C^T \tag{A 17}$$

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The density matrix with the elements $P_{ij} = \langle c_i c_j^* \rangle$ ($\langle \ \rangle$ = average over an appropriate ensemble) has the form (A 18) in the λ-ϱ basis and the form (A 19) in the $\chi_\pm$ basis.

$$\begin{pmatrix} P_{RR} & P_{RL} \\ P_{LR} & P_{LL} \end{pmatrix} = P^{\lambda,\varrho} \tag{A 18}$$

$$\begin{pmatrix} P_{++} & P_{+-} \\ P_{-+} & P_{--} \end{pmatrix} = P^{\chi_\pm} \tag{A 19}$$

For the degenerate system (or nearly degenerate system) at any temperature with $kT \gg S$ (A 10) Equation (A 20) holds.

$$P^{\lambda,\varrho} = P^{\chi_\pm} = \begin{pmatrix} \frac{1}{2} & 0 \\ 0 & \frac{1}{2} \end{pmatrix} \tag{A 20}$$

P is invariant under the basis transformation (as any other constant diagonal matrix), also in the many level case, if H is block diagonal as in Equation (18). A racemic mixture of R and L is identical to a mixture of $+$ and $-$ in terms of any observable ensemble property. A common model for P, simplified for the degenerate case, considered as a reduced density matrix of the molecule interacting by collisions or otherwise with a thermal bath gives the expressions (A 21) and (A 22), from which the relationships (A 24) and (A 25) can be derived for the relaxation times given here by τ_1 and τ_2 with the basis transformation (A 23).

$$(P_{11} - P_{22}) = (P_{11}^0 - P_{22}^0)\exp(-t/\tau_1) \tag{A 21}$$

$$P_{12} = P_{12}^0 \exp(-t/\tau_2) \tag{A 22}$$

$$P^{\chi_\pm} = C P^{\varrho,\lambda} C^{T} \tag{A 23}$$

$$\tau_1^{\chi_\pm} = \tau_2^{\varrho,\lambda} \tag{A 24}$$

$$\tau_2^{\chi_\pm} = \tau_1^{\varrho,\lambda} \tag{A 25}$$

Here we have made use of the reality of P in the case of a degenerate model, because $E_{1,2}$ can be set to zero without loss of generality. To within this approximation the assignment of "phase" or "population" relaxation times τ_1 and τ_2 is arbitrary in the two level problem (cf. Section 3).

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[101] *S*-asparagine has a bitter taste, whereas *R*-asparagine has a sweet taste; *S*-contergan® is teratogenic (with potential lethal consequences for the feti), *R*-contergan® seems to be harmless and a useful drug; *S*-penicillamine is an antiarthritic drug, *R*-penicilliamine is highly toxic; certain benzpyrene metabolites are extremely carcinogenic in one form and apparently harmless in the other.

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