Angewandte
Highlights

Rotating Enantiomers

DOI: 10.1002/anie.201307159

Fourier Transform Microwave Spectroscopy: Handedness Caught by Rotational Coherence**

*Jens-Uwe Grabow**

chirality · enantiomers · handedness · microwave spectroscopy · molecular rotation

In memory of Neil E. Shafer-Ray

That molecular structure can be chiral, that is, exhibit handedness, is of profound importance to chemistry and biology: As with our left and right hands, chiral molecules exist as otherwise equivalent mirror images of the opposite chirality. Such stereoisomers are called enantiomers. The detection and identification of enantiomers relies on the concept that the mirror symmetry of enantiomers is broken by exposure to circularly polarized radiation where the electromagnetic field vector rotates either clockwise or counterclockwise once per wavelength. This symmetry breaking is the foundation of three widely used forms of "chiroptical" spectroscopies employing ultraviolet/visible light or infrared radiation and involving electronic or vibrational transitions: Optical rotation measures the difference in index of refraction for left-circularly polarized (LCP) and right-circularly polarized (RCP) radiation; Circular dichroism measures the difference in the absorption of LCP and RCP radiation. Also Raman optical activity can be used as a chiroptical technique to determine the excess of one enantiomer over the other in a mixture or the absolute configuration, that is, specific handedness, of a given enantiomer under investigation. The optical activity can be positive or negative depending on whether the electric and magnetic dipole transition moments point into the same or opposite halves of a sphere centered on the molecule.

A technique reported by Patterson et al.[1] takes a new route: Radiation associated with a loop of three dipole-allowed transitions between rotational states emitted by molecules of opposite chirality is exactly out of phase, thus providing a direct signal of molecular chirality. After the sample is subjected to two transient electromagnetic fields, the molecular ensemble emits microwave radiation of an intensity that is proportional to the product of the chiral molecule's three orthogonal rotational electric dipole moments μ_X, μ_Y, μ_Z. This product is independent of the choice of the molecule's inertia principal axes $g = a, b, c$, but changes sign if any two moments are interchanged. Therefore, the scalar triple product of $\boldsymbol{\mu}_a \cdot \boldsymbol{\mu}_b \times \boldsymbol{\mu}_c$ will be positive or negative depending on the enantiomer under investigation, and thus establishes a new measure of chirality. The approach offers an advantage over existing chiroptical spectroscopy techniques because of its independence from the weak magnetic dipole transition moment, while the unrivaled resolution of Fourier transform microwave (FT-MW) spectroscopy virtually always discriminates the molecules of interest even in complex mixtures—at measurement times as fast as seconds rather than minutes to hours for traditional chiroptical spectroscopy techniques. But how can one say which microwave signal is produced by an enantiomer associated with a positive product and which belongs to a negative one?

The evolution in time of the molecular system is usually described by the density matrix formalism,[2] starting with Equation (1),

$$i\hbar \frac{\partial}{\partial t'} \boldsymbol{\varrho}'(\mathbf{r}',\mathbf{v},t') = [\mathbf{H},\boldsymbol{\varrho}'(\mathbf{r}',\mathbf{v},t')] \tag{1}$$

where $'$ denotes the molecular rest frame of a subsystem with velocity $\mathbf{v}$ at position $\mathbf{r}$. In this equation, $\boldsymbol{\varrho}$ is the density matrix and $\mathbf{H} = \mathbf{H}_0 + \mathbf{H}_e + \mathbf{H}_i$ is the matrix representation of the time-dependent Hamilton operator describing the system, where $\mathbf{H}_0$ is the unperturbed operator describing its stationary states, $\mathbf{H}_e$ denotes the interaction with external radiation, and $\mathbf{H}_i$ accounts for collisional interactions. We assume an isolated system of three states $|a\rangle$, $|b\rangle$ and $|c\rangle$; these eigenstates of the unperturbed Hamiltonian $\mathbf{H}_0$ with the eigenvalues E_a, E_b, and E_c, respectively, are defined by Equation (2).

$$\mathbf{H}_0 \equiv \begin{pmatrix} E_\mathrm{a} & 0 & 0 \\ 0 & E_\mathrm{b} & 0 \\ 0 & 0 & E_\mathrm{c} \end{pmatrix} \tag{2}$$

Irradiating with an $\mathbf{e}_z$ plane-polarized microwave (MW) field propagating in the direction of the y axis and then subjecting the molecular ensemble to a field along the $\mathbf{e}_y$ axis oscillating on radiofrequency (RF) timescales, the field amplitudes ε_g of the radiation resonant to the transitions $|b\rangle \leftrightarrow |a\rangle$ and $|c\rangle \leftrightarrow |b\rangle$ for a volume element of the sample at position $\mathbf{r}$ are defined by Equation (3) which accounts for the relative phases $\theta_{kl}{}^{(e)}$ and wave constants $k_{kl}^{(e)} = \omega_{kl}^{(e)}/c_p$ with $c_p^{(e)}$ being the phase velocity. Suspending collisional interactions,

---

[*] Prof. Dr. J.-U. Grabow
Institut für Physikalische Chemie und Elektrochemie
Gottfried-Wilhelm-Leibniz-Universität
Callinstrasse 3A, 30167 Hannover (Germany)
E-mail: jens-uwe.grabow@pci.uni-hannover.de
Homepage: http://www.grabow.pci.uni-hannover.de

[**] Support by the Deutsche Forschungsgemeinschaft (DFG) and the Land Niedersachsen is gratefully acknowledged.

the total Hamiltonian is given by Equation (4) where the space-fixed components of the dipole moment operator $\boldsymbol{\mu}$ are assumed to be described by Equation (5).

$$\mathbf{E}^{(e)}(\mathbf{r},t) = \varepsilon_{ab}^{(e)}(\mathbf{r},t)\mathbf{e}_z \cos\left(\omega_{ab}^{(e)}t + \theta_{ab}^{(e)} - k_{ab}^{(e)}y\right) + \varepsilon_{bc}^{(e)}(\mathbf{r},t)\mathbf{e}_y \cos\left(\omega_{bc}^{(e)}t + \theta_{bc}^{(e)}\right) \tag{3}$$

$$\mathbf{H}(t) = \mathbf{H}_0 + \mathbf{H}_e = \mathbf{H}_0 - \boldsymbol{\mu}\cdot\mathbf{E}^{(e)}(\mathbf{r},t) \tag{4}$$

$$\boldsymbol{\mu} \equiv \begin{pmatrix} 0 & \mu_{ab}\mathbf{e}_z & \mu_{ac}\mathbf{e}_x \\ \mu_{ba}\mathbf{e}_z & 0 & \mu_{bc}\mathbf{e}_y \\ \mu_{ca}\mathbf{e}_x & \mu_{cb}\mathbf{e}_y & 0 \end{pmatrix} \tag{5}$$

This implies that the transition $|c\rangle \leftrightarrow |a\rangle$ is dipole-allowed also. The angular frequencies $\omega_{ab}^{(e)}$ and $\omega_{bc}^{(e)}$ of the external electromagnetic radiation are chosen to be close to the molecular resonance frequencies $\omega_{ab}^{(0)}$ and $\omega_{bc}^{(0)}$ of the transitions $|b\rangle \leftrightarrow |a\rangle$ and $|c\rangle \leftrightarrow |b\rangle$, having $\omega_{kl}^{(0)} = (E_t - E_k)/\hbar$. To solve Equation (1) for a three-level system, the problem is transformed to the interaction representation, that is, the rotating frame, using Equations (6) and (7).

$$\boldsymbol{\varrho}(\mathbf{r},t) = e^{-i\mathbf{S}(\mathbf{r},t)}\boldsymbol{\rho}(\mathbf{r},t)\mathrm{e}^{i\mathbf{S}(\mathbf{r},t)} \tag{6}$$

$$\mathbf{S}(\mathbf{r},t) \equiv \begin{pmatrix} \frac{E_a}{\hbar}t & 0 & 0 \\ 0 & \frac{E_a}{\hbar}t + \omega_{ab}^{(e)}t + \theta_{ab}^{(e)} - k_{ab}^{(e)}y & 0 \\ 0 & 0 & \frac{E_a}{\hbar}t + \omega_{ab}^{(e)}t + \theta_{ab}^{(e)} - k_{ab}^{(e)}y + \omega_{bc}^{(e)}t + \theta_{bc}^{(e)} \end{pmatrix} \tag{7}$$

With the quantization axis z chosen to be parallel to the polarization direction $\mathbf{e}_z$ of the MW field, we have $\mu_{ab} = \mu_{ba} = \mu_c\sqrt{s_{ab}}$, $\mu_{bc} = -\mu_{cb} = i\mu_a\sqrt{s_{bc}}$, $\mu_{ac} = \mu_{ca} = \mu_b\sqrt{s_{ac}}$, with $\Delta M = \pm 1$ selection rules for $\mathbf{e}_g \perp \mathbf{e}_z$ in the transition loop.[3] It is then possible to define real dimensionless linear combinations which describe the transformed density matrix ρ of the three-level molecular system [Eq. (8a–d)].

$$s_{kl}(\mathbf{r},t) \equiv \rho_{kk}(\mathbf{r},t) + \rho_{ll}(\mathbf{r},t) \tag{8a}$$

$$u_{kl}(\mathbf{r},t) \equiv \frac{\mu_{lk}\rho_{kl}(\mathbf{r},t) + \mu_{kl}\rho_{lk}(\mathbf{r},t)}{\mu_g\sqrt{s_{kl}}} \tag{8b}$$

$$v_{kl}(\mathbf{r},t) \equiv -i\frac{\mu_{lk}\rho_{kl}(\mathbf{r},t) - \mu_{kl}\rho_{lk}(\mathbf{r},t)}{\mu_g\sqrt{s_{kl}}} \tag{8c}$$

$$w_{kl}(\mathbf{r},t) \equiv \rho_{kk}(\mathbf{r},t) - \rho_{ll}(\mathbf{r},t) \tag{8d}$$

The expectation values of observables are determined by the time-dependence of $\boldsymbol{\varrho}$. The transient observable of the molecular ensemble at number density ${}^1N$ is the macroscopic dipole moment, that is, the polarization $\mathbf{P} = \mathbf{P}_{ab} + \mathbf{P}_{ac} + \mathbf{P}_{bc}$ originating from the dipole-allowed transitions. Its expectation value is given by the trace of the product of dipole moment operator $\boldsymbol{\mu}$ and density matrix $\boldsymbol{\varrho}$ according to Equation (9). For chiroptical spectroscopy, only the molecular signal near the angular frequency $\omega_{ac}^{(e)}$ is utilized. With $\kappa_{kl} \equiv \mu_g\sqrt{s_{kl}}/\hbar$, we have Equation (10).

$$\mathbf{P}(\mathbf{r},t) = {}^1N(\mathbf{r},t)\langle\boldsymbol{\mu}(\mathbf{r},t)\rangle = {}^1N(\mathbf{r},t)\mathrm{Tr}[\boldsymbol{\mu}\cdot\boldsymbol{\varrho}(\mathbf{r},t)] \tag{9}$$

$$P_{\mathrm{ac}}(\mathbf{r},t) = {}^1N(\mathbf{r},t)\hbar\kappa_{\mathrm{ac}}\left[u_{ac}(\mathbf{r},t)\cos\left(\omega_{ac}^{(e)}t + \theta_{ac}^{(e)} - k_{ab}^{(e)}y\right) - v_{ac}(\mathbf{r},t)\sin\left(\omega_{ac}^{(e)}t + \theta_{ac}^{(e)} - k_{ab}^{(e)}y\right)\right] \tag{10}$$

The values of u_{ac} and v_{ac} are determined by Equation (1) together with Equations (2)–(5). After employing the interaction representation given with Equation (7), we apply the rotating wave approximation[4] which neglects all terms oscillating with $2\omega_{ij}^{(e)}$. Introducing the angular Rabi frequency $x_{kl} = \kappa_{kl}\varepsilon_{kl}^{(e)}$ and the Doppler-shifted frequency offset $\Delta\omega_{kl} = \omega_{kl}^{(0)}\left(1 + v_y/c_p^{(0)}\right) - \omega_{kl}^{(e)}$, we can give the optical Bloch equations for the three-level system [Eq. (11)–(13)].

$$\frac{\partial}{\partial t'}\boldsymbol{\Theta}'(\mathbf{r}',t') = \boldsymbol{\Lambda}'(\mathbf{r}',t')\cdot\boldsymbol{\Theta}'(\mathbf{r}',t') \tag{11}$$

$$\boldsymbol{\Theta}'(\mathbf{r}',t') \equiv \begin{pmatrix} u'_{ab}(\mathbf{r}',t') \\ v'_{ab}(\mathbf{r}',t') \\ w'_{ab}(\mathbf{r}',t') \\ u'_{ac}(\mathbf{r}',t') \\ v'_{ac}(\mathbf{r}',t') \\ u'_{bc}(\mathbf{r}',t') \\ v'_{bc}(\mathbf{r}',t') \\ w'_{bc}(\mathbf{r}',t') \end{pmatrix} \tag{12}$$

$$\boldsymbol{\Lambda}'(\mathbf{r}',t') \equiv \begin{pmatrix} 0 & -\Delta\omega_{ab} & 0 & 0 & \frac{x'_{bc}}{2} & 0 & 0 & 0 \\ \Delta\omega_{ab} & 0 & -x'_{ab} & -\frac{x'_{bc}}{2} & 0 & 0 & 0 & 0 \\ 0 & x'_{ab} & 0 & 0 & 0 & 0 & -\frac{x'_{bc}}{2} & 0 \\ 0 & \frac{x'_{bc}}{2} & 0 & 0 & \Delta\omega_{ac} & 0 & \frac{x'_{ab}}{2} & 0 \\ -\frac{x'_{bc}}{2} & 0 & 0 & \Delta\omega_{ac} & 0 & \frac{x'_{ab}}{2} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{x'_{ab}}{2} & 0 & -\Delta\omega_{bc} & 0 \\ 0 & 0 & 0 & \frac{x'_{ab}}{2} & 0 & \Delta\omega_{bc} & 0 & -x'_{bc} \\ 0 & -\frac{x'_{ab}}{2} & 0 & 0 & 0 & 0 & x'_{bc} & 0 \end{pmatrix} \tag{13}$$

Here $\Delta\omega_{\mathrm{ac}} = \Delta\omega_{\mathrm{ab}} + \Delta\omega_{\mathrm{bc}}$ is the sum of both Doppler-shifted angular frequency offsets and the spatial and time coordinates of the matrix elements are omitted for simplicity. For the quantitative discussion of the complete experiment sequence we use the concept of strong, selective pulses with Rabi frequencies that are large compared to the frequency offsets $x_{kl} \gg \varDelta\omega_{kl}$, such that the resonant solutions with $\varDelta\omega_{kl} = 0$ are sufficiently accurate. Starting at quasi-thermal equilibrium conditions of the jet-cooled ensemble and applying the hypothesis of random phases, we then solve Equation (11) using the initial condition of Equation (14).

$$\begin{pmatrix} u'_{ab}(\mathbf{r}',t') \\ v'_{ab}(\mathbf{r}',t') \\ w'_{ab}(\mathbf{r}',t') \\ u'_{ac}(\mathbf{r}',t') \\ v'_{ac}(\mathbf{r}',t') \\ u'_{bc}(\mathbf{r}',t') \\ v'_{bc}(\mathbf{r}',t') \\ w'_{bc}(\mathbf{r}',t') \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ w_{ab}^{(0)} \\ 0 \\ 0 \\ 0 \\ 0 \\ w_{bc}^{(0)} \end{pmatrix} \tag{14}$$

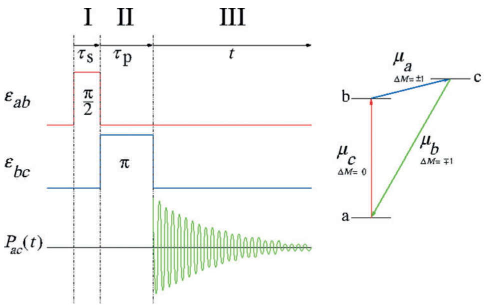

Figure 1. FT-MW chiroptical pulse sequence: I) excitation, II) preparation, III) evolution. See text for details.

The pulse sequence shown in Figure 1 yields the chiroptical spectrum: In the excitation period (I) the initial signal pulse of length τ_s converts the b←a population difference ΔN_{ab} into b←a coherence v_{ab}, which corresponds to a complete transfer for a π/2 pulse defined as $\tau_s = \tau_{s,opt} = x_{ab}^{-1}(\mathbf{r})\pi/2$. The pump pulse in the preparation period (II) of length τ_p converts the b←a coherence v_{ab} into double-quantum (DQ) c←a coherence u_{ac}. This transfer is complete for an ideal π pulse defined as $\tau_p = \tau_{p,opt} = x_{bc}^{-1}(\mathbf{r})\pi$. In the *evolution period* (III) the c←a DQ coherences u_{ac} and v_{ac}, exhibiting an angular frequency of $\omega_{ac} = \omega_{ab} + \omega_{bc}$, evolve freely for the time t'. The *probe* coherences u_{ac} and v_{ac} contain the chiroptical information of the DQ sequence performed [Eq. (15a, b)][5] with the group velocity $c_g^{(e)}$. Finally, Equation (10) yields in the laboratory frame Equation (16) having $P_{\mathrm{ac}} \propto \kappa_{\mathrm{ac}}\kappa_{\mathrm{ab}}\kappa_{\mathrm{bc}}$ in the linear regime for both pulses.

$$u'_{ac}\left(\mathbf{r}', t' + \tau_p + \tau_s + \frac{y'}{c_g^{(e)}}\right) = -w_{ab}^{(0)} \sin[x'_{ab}(\mathbf{r}')\tau_s] \sin\left[\frac{x'_{bc}(\mathbf{r}')}{2}\tau_p\right] \cos[\Delta w_{ac} t'] \tag{15a}$$

$$v'_{ac}\left(\mathbf{r}', t' + \tau_p + \tau_s + \frac{y'}{c_g^{(e)}}\right) = -w_{ab}^{(0)} \sin[x'_{ab}(\mathbf{r}')\tau_s] \sin\left[\frac{x'_{bc}(\mathbf{r}')}{2}\tau_p\right] \sin[\Delta w_{ac} t'] \tag{15b}$$

$$\begin{aligned} P_{\mathrm{ac}}(\mathbf{r},t) ={}& -^{1}N(\mathbf{r},t)\hbar\kappa_{ac} w_{ab}^{(0)} \sin[x'_{ab}(\mathbf{r}')\tau_s] \sin\left[\frac{x'_{bc}(\mathbf{r}')}{2}\tau_p\right] \\ & \left\{\cos\left(\omega_{ac}^{(e)} t + \theta_{ac}^{(e)} - k_{ab}^{(e)} y\right) \cos\left[\Delta\omega_{ac}\left(t - \frac{y}{c_g^{(e)}}\right)\right] - \right. \\ & \left. \sin\left(\omega_{ac}^{(e)} t + \theta_{ac}^{(e)} - k_{ab}^{(e)} y\right) \sin\left[\Delta\omega_{ac}\left(t - \frac{y}{c_g^{(e)}}\right)\right]\right\} \end{aligned} \tag{16}$$

Thus, the enantiomer-specific information is unambiguously encoded in the microwave emission of a particular enantiomer by acquisition of the phase $\theta_{ac}^{(e)} = \theta_{ab}^{(e)} + \theta_{bc}^{(e)}$ from the driving DQ fields, or the opposite one. While we have only considered a progressive scheme in detail here, where the common level E_b for both transitions is the intermediate level, the results can be applied to all other progressive and regressive schemes by interchanging the indices $kl \leftrightarrow lk$ according to the energy-level ordering and inverting signs according to $\Delta\omega_{kl} \rightarrow -\Delta\omega_{lk}$, $v_{kl} \rightarrow -v_{lk}$, and $w_{kl} \rightarrow -w_{lk}$ if the indices would be interchanged.

With only the signs of the enantiomer-specific dipole moment components to be connected to the absolute configuration of a chiral molecule, quantum-chemical calculations are required that are less costly than the traditional chiroptical spectroscopy techniques that depend on the orientation of the electric and magnetic dipole transition moments with respect to the molecule's absolute configuration.

While routine application might still take a while, the Patterson group's conceptually new approach to chiroptical spectroscopy offers an unprecedented potential to determine the absolute configuration of previously unassigned chiral molecules.

Received: August 14, 2013

[1] A. Patterson, M. Schnell, J. M. Doyle, *Nature* **2013**, *497*, 475–477.
[2] K. Blum, *Density Matrix Theory and Applications*, Plenum Press, New York, **1981**, pp. 37–62.
[3] C. H. Townes, A. L. Schawlow, *Microwave Spectroscopy*, Dover Publications, New York, **1975**, pp. 95–100.
[4] J. I. Steinfeld, P. L. Houston, in *Laser and coherence spectroscopy* (Ed.: J. I. Steinfeld), Plenum, New York, **1978**, pp. 1–123.
[5] J.-U. Grabow, in *Handbook of High-Resolution Spectroscopy* (Eds.: M. Quack, F. Merkt), Wiley, Chichester, **2011**, pp. 723–799.