

Determination of the absolute configuration of a chiral epoxide using foil induced Coulomb explosion imaging

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Abstract. We have applied the method of foil-induced Coulomb Explosion Imaging (FCEI) to determine the handedness of a homochiral sample of the compound trans-2,3-dideuterooxirane C₂OH₂D₂. We determined the compound to be of the (*R,R*)-configuration with a statistical significance of 5 σ . As the molecular sample was chemically linked to the stereochemical reference standard glyceraldehyde, our assignment constitutes an independent verification of the absolute handedness of all compounds linked to this reference substance.

1. Introduction

Chiral molecules exist in two spatial isomeric configurations made out of the same atoms. The spatial structures of the two isomers (enantiomers) are different in such a way that one configuration is the incongruent mirror image of the other. Both configurations cannot be superimposed to each other by translations and/or rotations. Louis Pasteur was the first who noticed that ammonium sodium tartrate crystals exist as two mirror images which rotate linearly polarized light in opposite directions [1]. In fact, the optical activity of chiral substances remained to be the only physical property chiral molecules seem to differentiate in. On the other hand, the chemical behavior of the different enantiomers can change dramatically in homochiral environments, something which is impressively demonstrated by the well known fact that the human DNA exists only in one spatial configuration.

A link between spatial structure and optical activity was tentatively introduced by Fischer in 1894, since at this time no theory or experimental technique was available to determine the stereostructure of chiral molecules [2]. He arbitrarily related dextrorotatory and levorotatory glyceraldehyde to a spatial configuration he named D and L, respectively. By this, glyceraldehyde became the stereochemical reference standard, and via chemical correlations the stereostructure of many chiral molecules was determined relative to glyceraldehyde [3]. Meanwhile, the D/L system introduced by Fischer has been replaced by the more rigorously defined R/S nomenclature using the Cahn-Ingold-Prelog priority rules [4, 5].



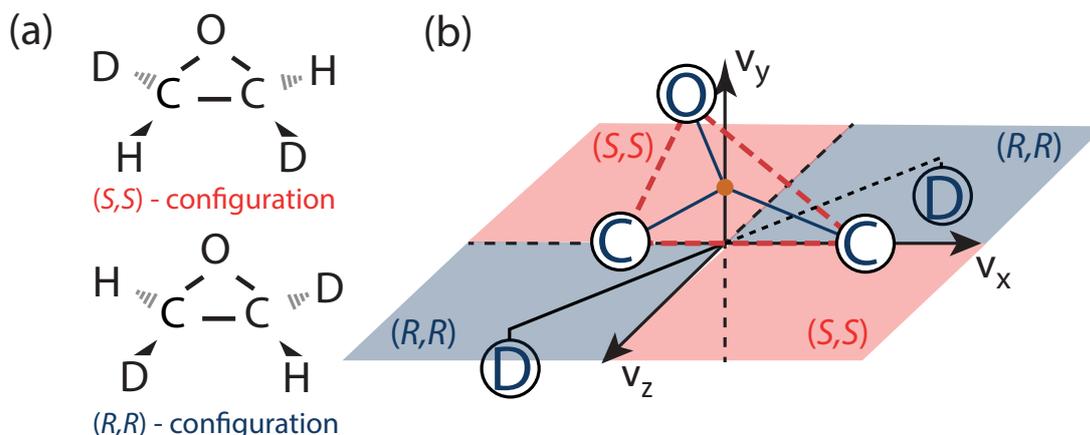


Figure 1. (a) Enantiomeric structure of trans-2,3-dideuteriooxirane. The two enantiomers differ by the interchanged positions of the H and D's. (b) Chirality measurement: The molecular fixed coordinate system is defined in such a way that the C's lie on the v_x axis and the center of mass of the C-O-C triangle (orange) lies on the positive v_y axis. The position of the D is exchange symmetrized, exploiting the C_2 symmetry of the molecule. To determine the absolute configuration, the D's are projected into the v_x - v_z plane. The handedness is now given by the quadrant the D lies in, as depicted.

It took more than 50 years before Fischer's arbitrary assignment was experimentally verified by Bijvoet et al. [6], who finally succeeded to determine the absolute stereostructure of sodium rubidium tartrate crystals by anomalous X-Ray diffraction (XRD). To this date, anomalous XRD is the method of choice for absolute configuration determination of chiral substances which can be crystallized. Other more recent techniques to determine the handedness of a molecule are vibrational circular dichroism [7] and vibrational Raman optical activity [8], however, both methods rely heavily on quantum mechanical calculations.

The present investigation constitutes the first measurement of the handedness of isolated chiral molecules in gas phase. The experiment was performed on a homochiral sample of trans-2,3-dideuteriooxirane ($C_2OH_2D_2$) [9, 10] using foil-induced Coulomb Explosion Imaging (FCEI) [11]. As the sample was chemically linked to glyceraldehyde [12], the experiment serves moreover as an independent proof of the correctness of Fischer's original guess.

2. Principle of FCEI for chirality measurements on $C_2OH_2D_2$

In foil-induced CEI measurements, single molecules are ionized, accelerated to velocities of a few percent of the speed of light and then directed onto a thin stripping foil [11]. When penetrating the foil, the molecules are stripped off their binding electrons. The stripping process occurs within 1 fs, thus it is much faster than the molecular vibrations, and the internuclear distances can therefore be considered to be frozen during the ionization process. After the stripping, the mutual Coulomb potential between the charged atoms is transferred into kinetic energy, and already after a separation of $\sim 1 \mu\text{m}$ asymptotic velocities are reached. They carry the information of the spatial position of the atoms in the molecule at the moment they hit the stripping foil. After a distance of $\sim 3 \text{ m}$ the ions drift apart from each other (the molecular structure magnifies) until they are detected by a time- and position-sensitive detector system that records the relative fragment positions \vec{r}_{ij} between fragments i and j from which the asymptotic velocities \vec{v}_{ij} can be calculated.

The CEI technique is a well established method to determine the structure of small molecules

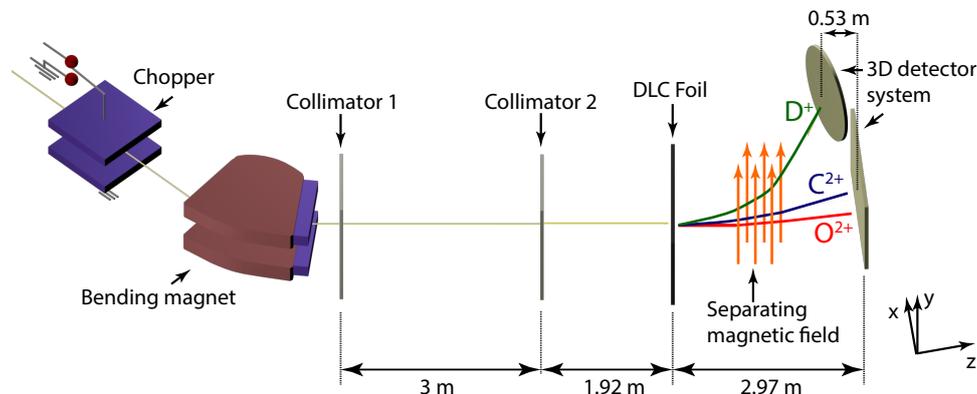


Figure 2. The FCEI beamline. After the last bending magnet, two collimators are used to define the shape of the ion beam. The Coulomb explosion process is triggered when the molecules penetrate the DLC foil. A separating magnetic dipole field located after the foil guides the fragments onto either the round or the rectangle detector. As soon as the first fragment impinges on the round detector, the chopper is charged and further molecules are prevented from entering the beamline. The coordinate system in which the events are recorded is depicted. The distance in transverse horizontal direction between the middle of both detectors is ~ 31 cm (not in scale).

[13, 14]. For the first time, the present measurement aimed at the assignment of the handedness of a homochiral sample via foil-induced CEI. Independent from our work, chirality measurements with laser-induced CEI on racemic samples were performed by Pitzer *et al.* [15].

We chose the molecule *trans*-2,3-dideuteriooxirane ($C_2OH_2D_2$) for our studies. The two enantiomers of the molecule are shown in Fig. 1(a). The measurements were performed with both racemic and enantiopure samples of oxirane. To determine the handedness, single molecular events with two C^{2+} , one O^{2+} and one D^+ in coincidence were recorded and analyzed. This selection represents the minimum number of atoms needed to determine the absolute configuration. The charge states selected are a compromise between production probability (lower charge state more likely to be produced) and an optimized Coulomb explosion process (higher charge state preferred). Although the ionization of the constituents is only partial, the information on handedness of the molecule is conserved during the Coulomb explosion process as the electro-magnetic interaction does not violate parity and the process happens in a non chiral environment. The handedness is therefore directly imprinted in the break-up geometry and thereby in the asymptotic velocities \vec{v}_{ij} .

The analysis is performed by defining for each single molecular event a right-handed coordinate system (v_x, v_y, v_z) in such a way that both C's lie on the v_x axis (see Fig. 1(b)). The center of mass of the C-O-C triangle is positioned on the positive v_y axis. Since the direction of the v_x axis is arbitrary and only one D is detected, the position of the D is exchange symmetrized and projected onto the v_x - v_z plane. The handedness of the oxirane is then given by the quadrant the D lies in: a D in quadrant II and IV identifies the (*S,S*)-configuration, a D in quadrant I and III identifies the (*R,R*)-configuration (compare Fig. 1(a) and Fig. 1(b)).

3. Experimental setup

The measurements were performed at the Max Planck Institute for Nuclear Physics and described in detail in [9, 10]. The molecules were ionized in a cold cathode ion source. As shown by density functional calculations, the ionization leads most likely to a removal of one

electron from the oxygen and should leave the structure of the oxirane intact. After ionization, the ions were accelerated to a kinetic energy of 2.02 MeV ($\sim 1\%$ of the speed of light) using a single-ended Van-de-Graff accelerator. A dipole magnet was used to mass select the ions before they were guided into the FCEI beam line using additional magnets.

The FCEI beamline is discussed in detail in [16] and is depicted in Fig.2. Behind the last bending magnet two collimators with a distance of ~ 3 m are used to create a pencil-like beam profile. The aperture diameter of both collimators was 1 mm during our measurements. Following the ion flight direction, the next component of the FCEI beamline is the stripping foil, a $0.8 \mu\text{g}/\text{cm}^2$ thick diamond like carbon (DLC) foil, in which the Coulomb explosion process is triggered. To identify the ion species, a dipole magnet is installed behind the stripping foil that separates the fragments by their charge-to-mass ratio. About 2.5 m behind the field, two synchronized position and time sensitive detectors are installed. C^{2+} - and O^{2+} -fragments were guided onto the rectangular detector. Due to the separating dipole, these fragments hit the detector at different spots, which allowed us to identify them. D^+ -fragments were guided onto the round detector.

Both detectors consist of a MCP, combined with a phosphor screen and monitored by a camera, to determine the transverse fragment positions with an accuracy of $\sim 0.1 \mu\text{m}$. To measure the relative longitudinal fragment position, vertical wires in a distance of ~ 0.75 mm are used to determine the relative fragment impact times with an accuracy of ~ 200 ps.

The coordinate system (x,y,z) in which the fragment positions are recorded is aligned with the rectangular detector. The x axis follows the intersection line between the detector plane and the plane of deflection, and points into the direction of increasing deflection. The y axis lies in the detector plane and is pointing upwards. The z axis is perpendicular to the detector plane and forms a right-handed coordinate system with the x and y axis. The origin of the coordinate system is the middle of the rectangular detector plane. This coordinate system is not to be confused with the molecular fixed coordinate system discussed in the section before.

4. Data analysis

The data analysis can be divided into three main steps, which are described in length in [10]: Ion species identification, molecular vibration reduction, and subtraction of events with falsely identified ion species.

Ion species identification: The round detector is hit exclusively by D^+ fragments, their identification is therefore trivial. The rectangular detector is hit by C^+ , O^{2+} and C^{2+} fragments which could only be partially separated (see Fig.3(a)). We therefore fitted the fragment distribution observed for three coincident ions per event with individually determined fragment distributions of C^+ , O^{2+} and C^{2+} , and defined an O^{2+} and C^{2+} identification window as indicated in Fig. 3(a).

In the analysis we accepted only events with one hit in the O^{2+} - and two hits in the C^{2+} -window. The window width was chosen as a compromise of the absolute number of events and events with a correct ion identification. It is obvious that this procedure will lead to some false ion identifications.

Molecular vibration reduction: The ionization process in the ion source is known to lead to vibrational excitation of the molecules. These vibrations typically cool within a second, but since the $\sim 40 \mu\text{s}$ flight time between source and stripping foil is significantly shorter, the imaging experiment is performed with excited molecules. These vibrations deform the C-O-C triangle and therefore potentially compromise the information on the handedness. In Fig. 3(b) the experimental area of the C-O-C triangle is plotted (lower panel) and compared with the result (upper panel) of a Monte Carlo simulation of the oxirane molecule with its atoms in the equilibrium rest positions [17, 18]. To suppress the vibrations in the next step of the analysis, we accepted only events with an area of the C-O-C triangle between 16×10^{-5} a.u. and 28×10^{-5}

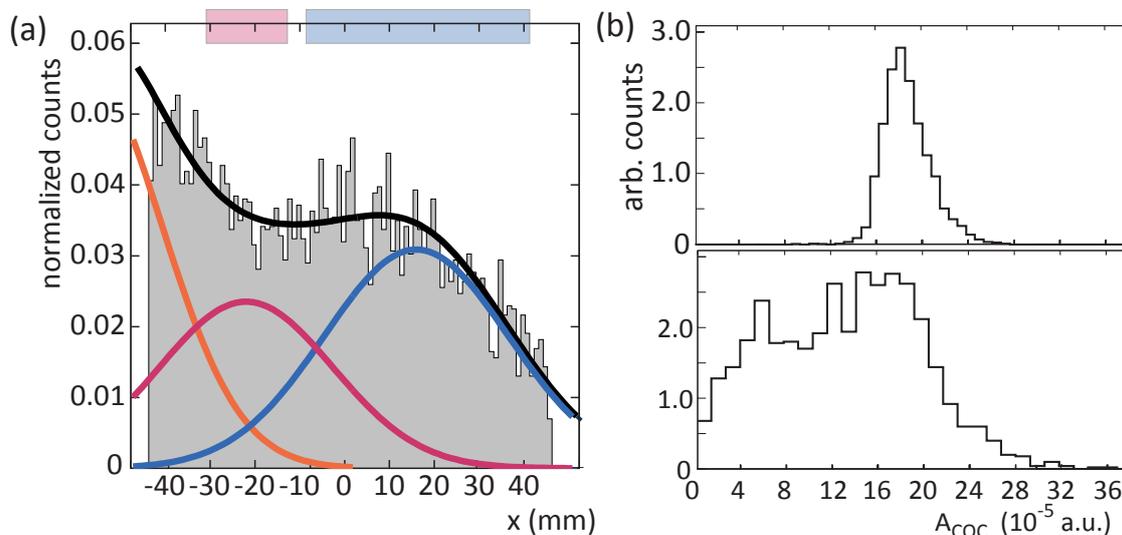


Figure 3. Ion identification and triangle cut. (a) The fragment distribution of three ions in coincidence (grey area) is fitted with the superposition (black) of the individually determined fragment distributions of C^+ (orange), O^{2+} (red) and C^{2+} (blue). The windows used to assign O^{2+} and C^{2+} ions are indicated by the bars at the top of the plot. (b) The measured C-O-C area distribution (bottom) is deformed by molecular vibration when compared to simulations of a non vibrating molecule (top).

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Correcting for misidentified ion events: Background events can be caused by falsely identified ions, e.g., when an O^{2+} is identified as C^{2+} and vice versa. From simulations based on the individually measured fragment distributions shown in Fig. 3(a), we estimated the probability of our identification scheme to assign events correctly to be 73%. To correct the final (v_x, v_z) distribution (see Fig. 4) for the 27% contribution of misassigned events, we created a second sample of events from the same original data set by re-defining the analysis windows and modifying the assignment procedure. This background sample is analyzed in the same way as the original one, and results in a (v_x, v_z) distribution containing 75% of misassigned events. This distribution is scaled to yield the same number of total events, then multiplied by $0.27/0.75$, and finally subtracted from the (v_x, v_z) distribution derived from the original sample.

5. Results

We performed our measurements on two different samples. The first sample contained a mixture of both enantiomers of the oxirane to equal amounts. The second sample contained almost exclusively (enantiomeric ratio 97.5 : 2.5) either the (R, R) - or the (S, S) -enantiomer. The handedness of the sample was unambiguously linked to (+)-glyceraldehyde by chemical correlation, however, the analysis of the FCEI results was performed without knowing the outcome of the chemical correlation process.

The results for each step in the analysis are depicted in Fig. 4. To get a statistical handle on the results, we counted the number of D's (N_i) in quadrant II and III. D's in quadrant II identify the (S, S) -enantiomer ($i = S$), while D's in quadrant III identify the (R, R) -enantiomer ($i = R$). Both values define an asymmetry

$$a = \frac{N_R - N_S}{N_R + N_S}. \quad (1)$$

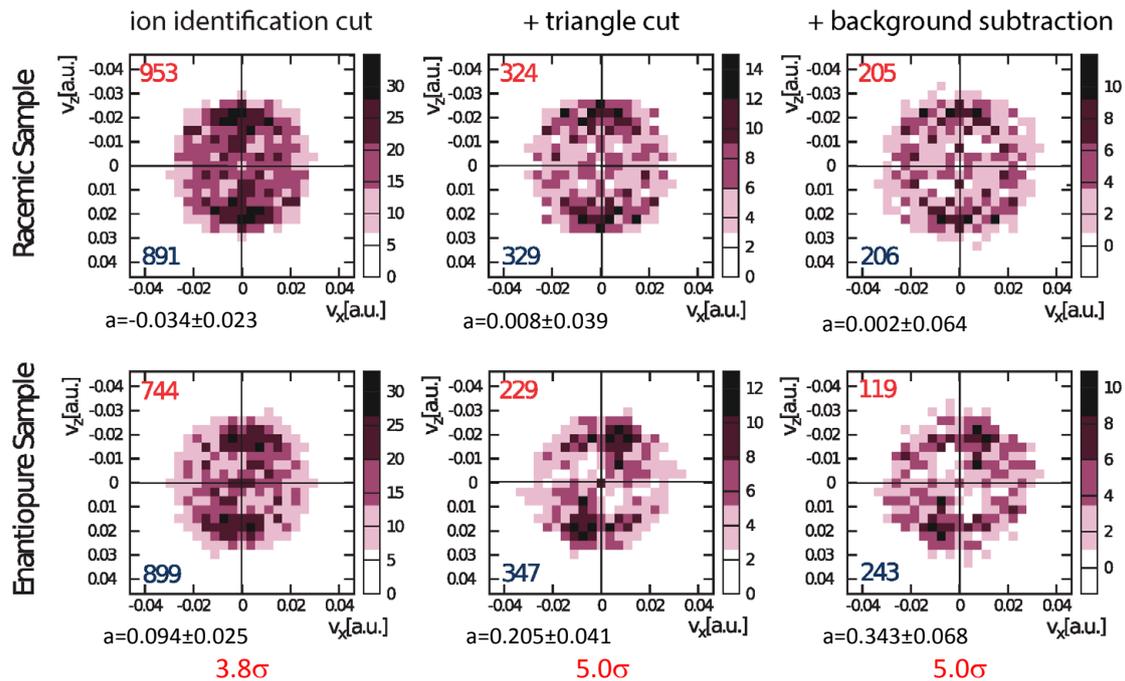


Figure 4. The density plots show the position of the D's in the molecular fixed v_x - v_z coordinate system. The upper and lower panel show the results for the racemic and enantiopure sample, respectively. The plots on the left are after the ion identification cut, the plots in the middle are after applying in addition the triangle cut, and the plots on the right are after performing also the background subtraction. The number of D's in the (S,S) -quadrant (red) and the (R,R) -quadrant (blue) are given together with the resulting asymmetries a . The red numbers on the bottom of each column denote the statistical significance for the enantiopure sample to have an (R,R) -configuration.

A positive and negative a indicate the (R,R) -enantiomer and (S,S) -enantiomer, respectively. The statistical uncertainty of a is given by

$$\sigma = 2\sqrt{\frac{N_R N_S}{(N_R + N_S)^3}} \quad (2)$$

for the data displayed in the left and middle column of Fig. 4, while for the background corrected results the statistical error of the background distribution has to be included in the calculation of σ as well.

After the ion identification cut, the racemic sample is almost symmetric, while the enantiopure sample shows a slight propensity for the (R,R) configuration, albeit with low contrast. After the triangle cut and the background subtraction of falsely assigned events, the racemic sample is perfectly symmetric, while the asymmetry of the enantiopure sample increases with each step. Since for a racemic sample the asymmetry is expected and measured to be zero, we express the statistical significance by which the enantiopure sample is shown to contain the (R,R) -enantiomer by quoting a in units of σ (red numbers given at the bottom of Fig. 4).

6. Conclusion

We performed FCEI measurements to determine the absolute configuration of a homochiral trans-2,3-dideuteriooxirane sample. We found with a statistical significance of 5σ that the sample is of the (R,R) -configuration. This is the first time that the absolute configuration of a chiral molecule in the gas phase has been determined by direct imaging. As the sample was chemically linked to the stereo-chemical standard molecule (+)-glyceraldehyde, we could confirm Fischer's assignment and by this also the absolute stereo-structure of all chiral molecules linked to (+)-glyceraldehyde.

Acknowledgments

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