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Articles

Enantiomeric Excess Sensitivity to Below One Percent by Using Femtosecond Photoelectron Circular Dichroism

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Photoelectron circular dichroism (PECD) is experimentally investigated with chiral specimens with varying amounts of enantiomeric excess (ee). As a prototype, we measure and analyze the photoelectron angular distribution from randomly oriented fenchone molecules in the gas phase that result from ionization with circularly polarized femtosecond laser pulses. The quantification of these measurements shows a linear dependence with respect to the ee values. In addition, differences in the ee values (denoted as detection limit) of below one percent can be distinguished for nearly enantiopure samples, as well as for almost racemates. In combination with the use of a reference, the assignment of absolute ee values is possible. The present measurement time is a few minutes, but this could be reduced. This table-top laser-based approach should facilitate widespread implementation in chiral analysis.

1. Introduction

The recognition of chiral molecules has been a challenge for a long period of time. Since the first chiral distinction through optical activity,[1] the detection sensitivity has been improved, for example, by exploiting the different behaviors of chiral molecules in chiral environments.

Chiral chromatography is widely used to determine enantiomeric excess (ee) to an accuracy of a few percent and below.[2] In additon, nuclear magnetic resonance (NMR) spectroscopy can be employed to determine ee values by studying the chirality-dependent chemical shifts in the NMR spectra.[3]

Approaches based on light–matter interactions pave the way to spectrally resolved multichannel investigations of chirality. Recently, it has been shown that Fourier transform microwave three-wave mixing in supersonic gas jets can be used to determine ee to an accuracy of a few percent.[4,5] By using Fourier transform vibrational circular dichroism spectroscopy in the near- to mid-infrared spectral region, it is feasible to combine real-time tracking of chemical reactions with ee detection that is accurate to the few percent.[6]

A complementary technique to study ee values with accuracy to below one percent is to measure the optical rotation in the liquid phase through femtosecond spectroscopy.[7]

The detection of charged particles after photoionization offers high efficiency. With respect to ions, laser mass spectrometry is a well-established technique to investigate circular dichroism.[8,9] With respect to electrons, theoretical calculations have predicted an asymmetry that arises in the photoelectron angular distribution (PAD) of chiral molecules ionized by circularly polarized light.[10] This effect is termed photoelectron circular dichroism[11] (PECD) and has been investigated experimentally by using vacuum ultraviolet light either from synchrotron[12] or high-harmonic generation sources.[13] By utilizing a femtosecond laser system, the PECD effect has been demonstrated[14] and confirmed[15] in 2+1 resonance-enhanced multiphoton ionization (REMPI) of bicyclic ketones. In addition, mass tagging has been employed to differentiate chiral molecules in mixtures.[16,17] It has been suggested that this technique could be used as a highly sensitive analytic tool for even low particle densities,[14,18] due to the strength of the underlying electric dipole interaction.

Suggestions of a linear dependence of the PECD effect with respect to ee have already been given in Ref. [18], to explain the difference in PECD strength for measurements on enantiopure (R)-(−)- and (S)-(+)-fenchone. Recently, the measurement of two substances in Ref. [16] has supported the assumption of a linear dependence on ee.

Herein, the high accuracy of laser-based chiral recognition using the PECD effect is demonstrated for different mixtures of (R)-(−)- and (S)-(+)-fenchone molecules.

Experimental Section

The enantiomers of fenchone were purchased from Sigma–Aldrich with a specified purity of 99.2%. Gas chromatography (GC) was performed by Chemische Laboratorien Dr. Soenke Petersen using a γ-cyclodextrin capillary column[19,20] as a reference when obtaining the ee values of the different specimens investigated herein. In addition to the purchased enantiopure (S)-(+)-fenchone with an ee value of 99.9% and the purchased (R)-(−)-fenchone with an ee value of 84.0%, five mixtures of both enantiomers were characterized. The measurement uncertainty for the GC was ±0.1% ee. The

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ee values of the mixtures that were used for the coarse scan were derived from the specified *ee* values of both enantiomers.

For the experimental setup, data acquisition, and data evaluation, see the Supporting Information and in more detail in Ref. [18]. In brief, femtosecond laser pulses centered at 398 nm having a full width at half maximum (FWHM) pulse duration of 25 fs at a repetition rate of 1 kHz were focused into an effusive gas beam of the sample. The preponderance of circular polarization is reflected in the high value of the measured Stokes parameter $|S_3| = 99\%$. At 3 μJ pulse energy, a focal peak intensity (I_0) of approximately 2×10^{12} W cm^{-2} was achieved in the interaction region of a velocity map imaging (VMI) spectrometer.[21,22]

The 3D photoelectron momentum distribution was projected onto a detector (Abel projection). These PAD images were measured and the PECD image was derived by subtracting the PAD image resulting from ionization with the right circularly polarized light (RCP) from the PAD image by using left circularly polarized light (LCP).

2. Results and Discussion

To compare the PECD effect from the specimens with various *ee* values, we evaluated the linear PECD (LPECD), as a quantitative measure. LPECD compares the number of electrons emitted into the forward hemisphere relative to the laser beam, with those emitted into the backward hemisphere, and can be calculated from the projected PECD images by using Equation (1):

$$LPECD = \frac{2(F - B)}{T/2},\qquad(1)$$

where F and B denote the forward and the backward hemisphere of a PECD image, respectively, and T is the total photoelectron signal for both helicities of the light.[18] Owing to the projected nature of the detector image, the LPECD calculated by using Equation (1) covers all electrons from zero to the maximum kinetic energy; this can include several ionization channels and background electrons.

To separate the different contributions to the detector image, one needs to reconstruct the 3D momentum, which we did through an Abel-inversion algorithm that expands the PADs into Legendre polynomials.[18] Following Yang's theorem, the expansion was truncated after the eighth order[23] for an unbiased evaluation.

Using the polynomial expansion as a basis, LPECD can be expressed in terms of the retrieved odd order Legendre coefficients normalized to the total signal c_0 [Eq. (2)]:[18]

$$LPECD = \frac{1}{c_0}\left(2c_1 - \frac{1}{2}c_3 + \frac{1}{4}c_5 - \frac{5}{32}c_7\right)\qquad(2)$$

where c_l are the Legendre coefficients of order l averaged over the FWHM of about 200 meV around the excess energy of the fenchone parent molecule centered at approximately 0.56 eV.[18] This width amounts to twelve sampling points in our Abel inversion algorithm.

Taking Equation (2) and the orthogonality of the Legendre polynomials into account, a linear relation between the *ee* values and LPECD is expected.

We measured the LPECD for a total of ten different samples spanning a wide range of *ee* values in two campaigns. In the first (coarse scan), some of the samples, which spanned the full range of *ee* values, were measured once. During the second campaign (precise scan, taken five months later), each of the six specimens was measured repeatedly to improve the statistics.

The experimentally observed relationship between LPECD and *ee* values is depicted in Figure 1, which contains data from the coarse scan (purple diamonds) and the precise scan (black diamonds, also shown in Figure 2). Fitting a linear function of the form [Eq. (3)]:

$$LPECD(\%) = t + m \cdot ee(\%)\qquad(3)$$

to the datapoints shown in Figure 1 yields $t = (-0.39 \pm 0.07)\%$ and $m = -0.1401 \pm 0.0009$.

To determine the detection limit of our approach in the limiting cases around racemates and nearly enantiopure mixtures, the measurements of the precise scan were investigated in more detail. The LPECD values of the investigated specimens are depicted in Figure 2, which displays two measurement series, one in the racemate region (upper panel) and the other one close to enantiopure (*S*)-(+)-fenchone (lower panel).

For each measurement, three different specimens were measured permutatively, yielding four data points each to exclude possible systematic trends. Every datapoint represents approximately 3×10^5 laser pulses, generating an ionization signal of about 50 molecules each. The total amount of ionized molecules is thereby in the 10^{-17} mol. region.

Fitting a linear function to the datapoints of the precise scan yields even lower errors for the coefficients in Equation (3): $t = (-0.39 \pm 0.02)\%$ and $m = -0.1379 \pm 0.0006$.

We note that the linear regression for both the coarse and the precise scan, yields an offset of the LPECD. For achiral specimens as well as racemates, the LPECD and residual CD
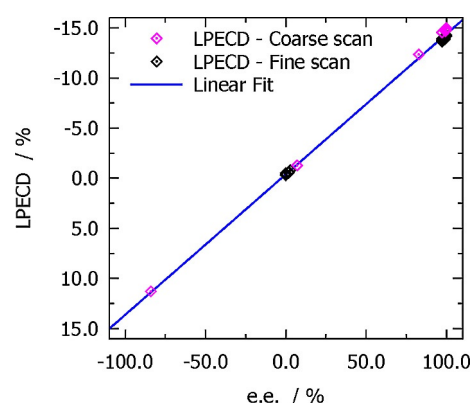
Figure 1. LPECD values for ten different mixtures of (*R*)-(−)- and (*S*)-(+)-fenchone calculated by using Equation (2) with a linear regression to all data points (——). The quantity *ee* denotes the enantiomeric excess of (*S*)-(+)-fenchone. Coarse scan: ◇); precise scan: ◇.
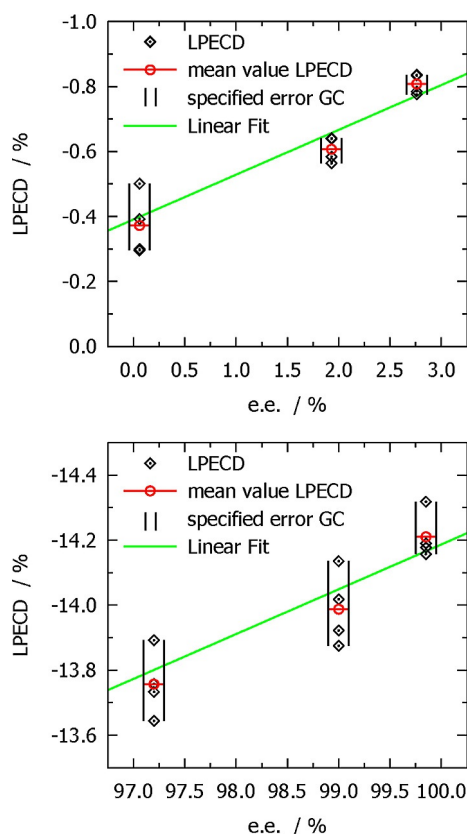
Figure 2. LPECD values for six different mixtures of (*R*)-(−)- and (*S*)-(+)-fenchone calculated by using Equation (2). The quantity *ee* denotes the enantiomeric excess of (*S*)-(+)-fenchone. Each graph represents one measurement series. In both measurements, the three specimens were measured permutatively to yield four data points each.

should vanish. Residual imperfections as, for example, the offset are taken into account in the calibration curve.

To determine the enantiomeric excess of an unknown specimen of fenchone, we inverted the linear relation given in Equation (3):

$$ee(\%) = \frac{\text{LPECD}(\%) - t}{m} \qquad (4)$$

Furthermore, we used error propagation to estimate the uncertainty of the calculated *ee* values. Whereas the errors of *m* and *t* are obtained by linear regression, the largest standard error of the mean LPECD values in the precise scan was used as the uncertainty for the maximum LPECD. With this we obtained $\delta_{ee} = 0.6\%$ as the sensitivity of our method based on the Legendre coefficients obtained through Abel inversion. When evaluating the LPECD directly from the PECD raw images by using Equation (1) we obtained $\delta_{ee}^{\text{raw}} = 0.8\%$, which still lies well below one percent.

3. Conclusions

In this work, by using fenchone as a prototype, we demonstrated that a laser-based femtosecond PECD technique is sensitive to *ee* in specimens of randomly oriented molecules in the gas phase.

To that end we used LPECD as a quantitative measure, which compares the number of electrons emitted into the forward hemisphere, relative to the laser beam, with those emitted into the backward hemisphere. We showed that LPECD had a linear dependence with respect to the *ee* values. Our analysis revealed that this method is sensitive to differences in *ee* to below one percent in nearly racemic as well as nearly enantiopure samples; this is comparable to other established methods. In combination with the use of a reference the assignment of absolute *ee* values was possible.

These results may open the door to many implementations of femtosecond PECD in chiral analysis. By using higher repetition rate laser systems, the measurement time could be decreased significantly and as the experiments were carried out on a dilute gas sample, we expect many applications in cases where time-dependent variations in *ee* values of small sample amounts are crucial.

Acknowledgements

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Supporting Information

Enantiomeric Excess Sensitivity to Below One Percent by Using Femtosecond Photoelectron Circular Dichroism

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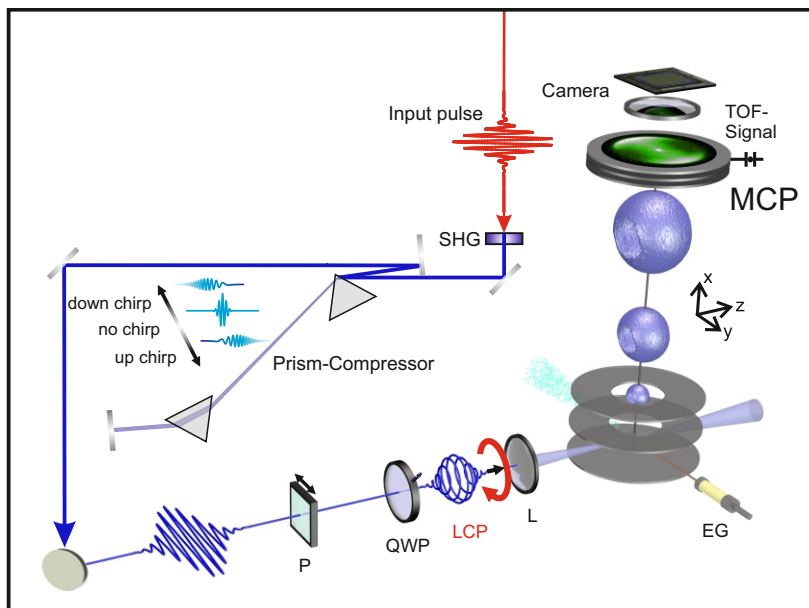phone: +49 (0)561 804 4452   fax: +49 (0)561 804 4453

Figure 1: Layout of the femtosecond photoelectron circular dichroism apparatus

The experimental setup is depicted in figure 1 (adapted from [1]). The output of a Ti:Sa laser (*Femtolasers Femtopower Pro*) with 1 kHz repetition rate and a central wavelength of 795 nm is frequency doubled in a 100 μm thick β-bariumborate (BBO, *Dayoptics, Inc.*) crystal. The UV pulses centered around 398 nm are compressed using a prism compressor allowing for in situ dispersion management via ionization of Xe atoms.

A thin-film polarizer (P, *CODIXX*) ensures horizontal input polarization. A quarter-wave plate (QWP, *B.Halle*) is used to convert linearly polarized (LIN) into left circularly polarized (LCP) or right circularly polarized light (RCP). Therefore the plate is rotated to $\pm$ 45° with respect to the input polarization. The degree of polarization is determined using an additional polarizer after the QWP and measuring the transmitted laser power with a powermeter.

The beam is focused into the interaction region of the spectrometer by a lens (L) with a focal length of 200 mm where the laser is intersected with an effusive gas beam (EG). A pulse duration of approximately 25 fs and a pulse energy of 3 μJ result in a peak intensity I_0 of about $2 \cdot 10^{12} \frac{\text{W}}{\text{cm}^2}$.

The three-dimensional electron momentum distribution is projected onto a detector comprising a multi-channel plate (MCP) assembly and a phosphor screen (*SI-Instruments GmbH* model S3075-10-I60-PS-FM, 75 mm effective diameter). The projections can be recorded using a 1.4 million pixel CCD camera (Lumenera Lw165m). Alternatively ion time-of-flight (TOF) mass spectra can be recorded via a capacitive coupled output.

For one datapoint, we record 50 times 50 images for LCP and RCP alternately

at an exposure time of 132 ms and a gain of 1 on the CCD camera. The RCP and LCP photoelectron angular distribution (PAD)-images are derived by averaging over the 50 recorded images. The PECD image is calculated by subtracting the RCP PAD-image from the LCP PAD-image.

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