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Two-Photon Absorption Circular Dichroism: A New Twist in Nonlinear Spectroscopy

Carlos Toro,[a] Leonardo De Boni,[a] Na Lin,[b] Fabrizio Santoro,[c] Antonio Rizzo,[c] and Florencio E. Hernandez*[a, d]

Abstract: Herein we report on the full experimental measurement of the two-photon absorption circular dichroism spectra of (S)-(−)-1,1′-bi(2-naphthol) and (R)-(+)-1,1′-bi(2-naphthol), their analysis, and theoretical support. The finding of new nonlinear optical fingerprints in chiral molecules offers new opportunities in the recognition and understanding of optically active systems in regions where CD could present strong limitations.

Introduction

Among several phenomena, homochirality seems to rule the activity of nearly all natural products in nature, from proteins, nucleic acids, lipids, sugars, and amino acids to hormones, antibiotics, and vitamins.[1] Because the specificity of ligand–receptor interactions plays a dominant role in life processes, a better understanding of the chiroptical properties of optically active molecules has been fundamental for all studies in biological activity, essentially those associated with the origin of life itself.[2]

Molecules that are not superimposable on their mirror image, such as pure enantiomers, present differences in linear absorption coefficients and refractive indices for left and right circularly polarized light. The former effect is the so-called circular dichroism (CD), whereas the latter is known as optical rotation (OR).[3] CD and OR are a manifestation of the interaction between the radiation fields and the induced electric-dipole, magnetic-dipole and electric-quadrupole moments. Because the latter vanishes in isotropic media due to rotational averaging, the former two in cooperation determine the intensity of a transition by the action of photons in solution. Because of the OR, chiral molecules rotate the plane of polarization of light, a well recognized effect known as optical activity.

During the last two decades, CD and OR have facilitated remarkable progress in the understanding of principles underlying chirality and the development of new applications. CD has strongly contributed to the study of the physical-chemical and conformational properties of chiral molecules, proteins, and polypeptides, in solutions and at interfaces.[4] Nonetheless, the progress and current status of this method presents an important limitation: it is based on the linear absorption (one-photon absorption, 1PA) of optically active compounds, which is typically observed in the far and near UV region of the spectrum. In addition, when working in solution, the linear absorption of common organic solvents in the same spectral region usually overwhelms the CD signal from the sample of interest. Despite the success of techniques such as vibrational circular dichroism (VCD)[5] and Raman optical activity (ROA),[6] which have yielded major advances in the determination of the absolute configuration of small molecules as well as in the elucidation of secondary structure in proteins, we believe that the analysis of interesting biological systems such as natural amino acid structures and the study of innovative optically active drugs soluble in organic solvents demands alternative approaches

[a] C. Toro, Dr. L. De Boni, Dr. F. E. Hernandez
Department of Chemistry, University of Central Florida
P. O. Box 162366, Orlando, Fl 32816-2366 (USA)
E-mail: florenzi@mail.ucf.edu

[b] Dr. N. Lin
Department of Theoretical Chemistry, Royal Institute of Technology
AlbaNova, 106 91 Stockolm (Sweden)

[c] Dr. F. Santoro, Dr. A. Rizzo
Istituto per i Processi Chimico-Fisici del Consiglio Nazionale delle Ricerche (IPCF-CNR)
Area della Ricerca, G. Via Moruzzi 1, 56124 Pisa (Italy)

[d] Dr. F. E. Hernandez
The College of Optics and Photonics, CREOL
University of Central Florida
P. O. Box 162366, Orlando, Fl 32816-2366 (USA)

that can reveal unique spectroscopic and structural features at short wavelengths.

Nonlinear optics has opened new frontiers in this direction. Processes such as sum-frequency generation (SFG), second harmonic generation (SHG), and nonlinear optical activity have been lately reported for the study of chemical and biological chiral systems.[7] More recently, two-photon absorption circular dichroism (2PA-CD) in optically active molecules, first proposed theoretically by Tinoco[8] and Power[9] in the 1970s, has regained the attention of the scientific community because of its potential applications in the fundamental study of such structures.[10] Two-photon absorption, a third-order nonlinear optical effect, is based on the simultaneous absorption of two photons with less energy (i.e. longer wavelength) than that required for an electronic transition induced by one photon.[11] Then, for two photons of the same energy, that is, the degenerate case, 2PA-CD can be defined as $\Delta\delta^{2PA\text{-}CD}(\omega) = \delta^{2PA}_L(\omega) - \delta^{2PA}_R(\omega)$, where $\delta^{2PA}_L(\omega)$ and $\delta^{2PA}_R(\omega)$ are the 2PA cross-sections (δ^{2PA}) for left and right circular polarization, respectively (Figure 1). In
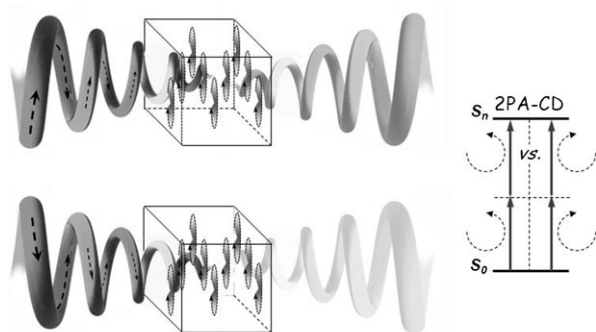

Figure 1. Schematic of the 2PA-CD phenomenon. The degenerated two-photon absorption of a chiral molecule using two photons with either circular left polarization (top-left) or circular right polarization (bottom-left) are compared. A simplified Jablonski diagram for 2PA-CD (right) is also depicted.

these processes there is usually no significant linear absorption in the excitation region, hence, the study of short wavelengths absorbing molecules using 2PA becomes possible. A key feature of this process in centrosymmetric molecules is that two-photon transitions obey an even-parity selection rule instead of an odd-parity one for one-photon. Consequently, in optically active molecules with an approximate center of symmetry one could anticipate significant relative intensity differences between 1PA and 2PA transitions. Therefore, having access to 2PA-CD in chiral molecules will help obtain structural and conformational information analogous to that which can be derived from linear CD in compounds whose excitation energies are in the inaccessible far UV.

2PA processes in chiral molecules depend on the transition electric- and magnetic-dipole moments and the transition electric-quadrupole moment. Therefore, one can anticipate that a gate to 2PA-CD will also open access to under-

standing the contribution of different transition moments. For instance, information on the importance of the induced quadrupole moment, whose contribution averages to zero in isotropic samples in linear CD, in electronic transitions of chiral molecules can be obtained. As a consequence of the small magnitude of the magnetic-dipole and electric-quadrupole transition moments, the measurement of a full 2PA-CD spectrum has been challenging. Although other interesting approaches related to third-order nonlinear optical effects have been recently proposed experimentally,[12] only resonance-enhanced multiphoton ionization circular dichroism (REMPICD) can give information close to 2PA-CD.[13] However, its signal is a mixture of 2PA and excited-state absorption. In addition, REMPICD is a destructive technique that can only provide analysis in the gas phase.

Recently, we have reported the first experimental measurements of the 2PA-CD spectrum of (S)-(−)-1,1′-bi(2-naphthol) in solution using the novel double L-scan technique.[14] The development of this new method, with high sensitivity, has permitted us to perform simultaneous measurements of the 2PA polarization dependence using "twin" pulses.

Herein, we present the experimental 2PA-CD spectra of (S)-(−)-1,1′-bi(2-naphthol) and (R)-(+)-1,1′-bi(2-naphthol) (enantiomeric ratio S:R ≥ 99:1 and R:S ≥ 99:1, respectively), hereafter SBN and RBN, respectively, in solutions of tetrahydrofuran and their corresponding theoretical spectra, in the 200 nm to 350 nm wavelength range. We demonstrate the mirror image of the 2PA-CD spectra for the two enantiomers and infer, based on the theoretical results, the origin of the observed peaks in terms of the allowed transitions, their mixing, and probabilities. Because it is well known that the linear and nonlinear circular dichroism spectra of optical isomers are expected to be mirror images,[15] we show the theoretical 2PA-CD spectrum of SBN as the reverse of that of RBN.

The nonlinear experimental characterization of these two enantiomers was performed by using the mentioned double L-scan technique.[14] The two-photon excitation was performed with an optical parametric generator, pumped by the third harmonic of a mode-locked Nd:YAG laser, operating at 10 Hz repetition rate and a pulse width of 25 ps (FWHM). The circular polarization state of the incoming radiation was controlled with achromatic zero-order broadband quarter-waveplates (400–700 nm), placed right before the focusing lenses (see Figure 1 in reference [14]). To truly obtain a phase difference of π/2 between the electric-field components at wavelengths closer to the spectral edge of the quarter-waveplates, a small tilt angle was introduced with respect to the incident beam. The circular polarization of the excitation beam was carefully corroborated at all wavelengths before any nonlinear measurements by measuring the transmittance intensity versus angle through a broadband polarizer (Malu's Law). Herein, we define the rotation direction of the circularly polarized light from the observer and not from the transmitter as previously delineated in reference [14]. This is the convention adopted in applications of CD and magnetic CD (MCD) spectroscopy.

The theoretical calculations, considering the electronic contribution to the 2PA-CD, were carried out within the density functional theory (DFT) employing the Becke three parameters Lee Yang and Parr (B3LYP)[16] hybrid functional. The structure of the most stable isomer of RBN, taken from reference [17], was optimized at a DFT/B3LYP level of theory using the 6-31G+G(d,p) basis set from Gaussian 03.[18] We performed calculations in the gas phase as well as in solvent. To include solvent effects, we used the polarizable continuum model (PCM) in a non-equilibrium regime.[19] Calculations were performed over the first 25 excited states. To obtain information on the spectroscopic properties from the binaphthol optical isomers, we used the aug-cc-pVDZ basis set which has been proven to properly reproduce 1PA, CD, 2PA, and 2PA-CD in different organic compounds.[10]

Then, the formalism proposed by Tinoco,[8] and recently implemented by Rizzo et al.,[10] was followed to calculate the degenerate two-photon absorption circular dichroism, $\Delta\delta^{2PA-CD}(\omega)$:

$$\Delta\delta^{2PA-CD}(\omega) \propto \omega^2 \times g(2\omega) \times {}^f R^{2PA-CD} \qquad (1)$$

In this equation, ${}^f R^{2PA-CD}$ represents the two-photon circular dichroism rotatory strength which depends on the polarization and propagation status of the beam as well as electronic contributions defined according to Sum-Over-States model.[10] In Equation (1), ω and $g(2\omega)$ are the circular frequencies and normalized line shape, respectively.

Results and Discussion

Figure 2 displays the experimental 2PA spectra of RBN and SBN (plotted at half of the excitation wavelength) for three different electromagnetic field polarization states as well as the linear absorption spectra, inserted for comparison. These results reveal that the probability of transition from the ground state to an excited stated is reduced using circularly polarized radiation through almost the entire wavelength range. Also, the two discrete bands observed with linear polarization, centered at approximately 230 and 275 nm, are less pronounced with circular polarization. The observed reduction in the 2PA cross-sections using circularly polarized radiation can be attributed to restrictions on the number of molecular transitions due to the dipole–dipole selection rules (the spin angular momentum of a photon). Because the angular momentum of the photon is completely independent of its energy, a similar effect can be observed in non-chiral molecules as well. This phenomenon is called circular-linear dichroism (CLD).[20] However, in nonoptically active molecules CLD does not depend on the polarization handedness of the input radiation.

Going into some details, at 220 and 250 nm one can observe a relative decrease in the linear/circular 2PA cross-sections ratio. In the former, δ^{2PA} seems to have a strong contribution from the tails of two distinct adjacent bands, that is, that corresponding to the π–π* transition of the C=C cen-

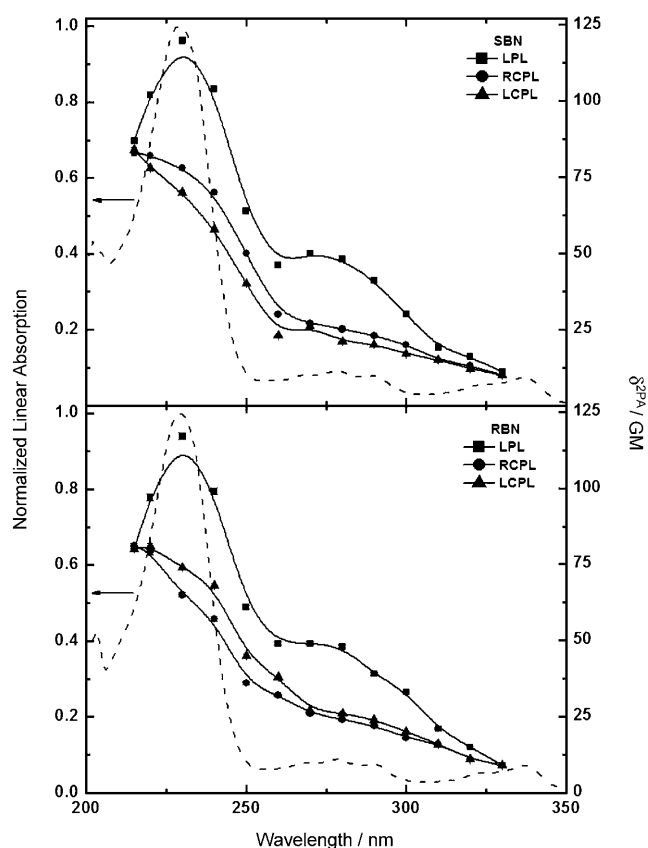Figure 2. Polarization dependent two-photon absorption cross-section (δ^{2PA}) spectra for SBN and RBN. The linear absorption spectra (dashed line) and 2PA spectra for linearly (■), left (▲) and right circularly (●) polarized light are depicted. Solid lines are used to guide the reader.

tered at about 180 nm and that of ring resonance of benzene located at approximately 230 nm. Therefore, the convolution of different excited states within this spectral region, contributes with different transition probabilities for circular and linear polarized light. A similar behavior can be observed at 250 nm where a low energy band centered at about 275 nm and assigned to the on-axis π–π* transition of the naphthalene overlaps with that at 230 nm.

In Figure 2, one can identify differences in cross-sections for left and right circularly polarized radiation. These originate in the molecular chirality, and are a consequence of the coupling between the optical fields and the magnetic and electric induced multipoles. Furthermore, the dominant contribution to δ^{2PA} from left and right circularly polarized light is reversed for RBN and SBN, as expected. This is in agreement with the model of π electrons constrained to move in the rotation direction imposed by a helical frame (molecular constraints).[8,9] While conventional electric dipole strength in unpolarized light is indeed usually dominated by the linear electronic displacement that appears in the transition moment operator, in optically active systems the rotatory strength is determined by the mixing of magnetic and electric multipole transition moments, translated, in the model given in references [8] and [9], which is independent of the

origin of the chirality, into an electronic displacement along an helical pattern.

The difference between δ_L^{2PA} and δ_R^{2PA} determines the 2PA-CD, as illustrated in Figure 3a. It can be noticed that the spectrum of one isomer is the specular image of the
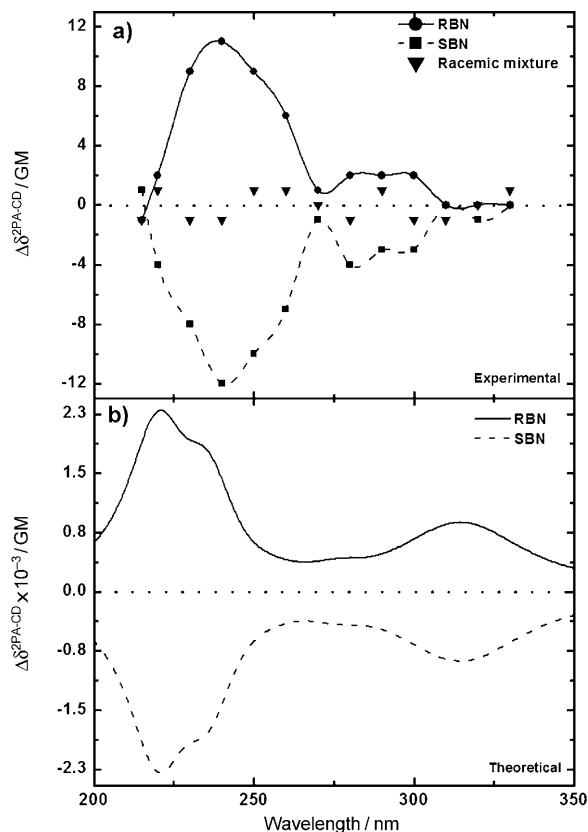

Figure 3. Experimental (a) and theoretical (b) two-photon absorption circular dichroism spectra for SBN and RBN. The experimental signal for a racemic mixture is also depicted.

other as expected. The spectral features obtained by means of 2PA-CD are different from those reported by using CD, for the same compounds.[21] This outcome was certainly anticipated based on symmetry selection rules for 1PA and 2PA. Since linear CD is related to certain allowed transitions in the chiral system, 2PA-CD offers the opportunity to evaluate chiroptical effects in transitions that are otherwise one-photon forbidden. Measurements of the 2PA-CD attempted on a racemic mixture of SBN and RBN did not give any significant signal, as expected and as can be seen in Figure 3a. Accordingly, it can be inferred that our approach can determine the two-photon circular dichroism with a sensitivity of ± 1 GM.

The theoretical 2PA-CD spectra of RBN and SBN are displayed in Figure 3b. The theoretical convoluted spectra are in agreement with experiment. An orbital analysis of the excited states reveals that each experimental band results from a complicated balance of contributions, of opposite sign, coming from several electronic excited states. Within

the C_2 framework of our molecules, the ground and excited states are classified as belonging to A and B symmetry representations, with the ground state being of A character. Excited states in the range of frequencies of relevance, can be classified in pairs of near lying excitations of different symmetry (A and B), deriving from a mixing of intra- and inter-naphthol moiety $\pi-\pi^*$ excitations, and with rotatory strengths of opposite sign, yielding a significant amount of cancellation to the 2PA-CD spectrum (see Figure 4 and the
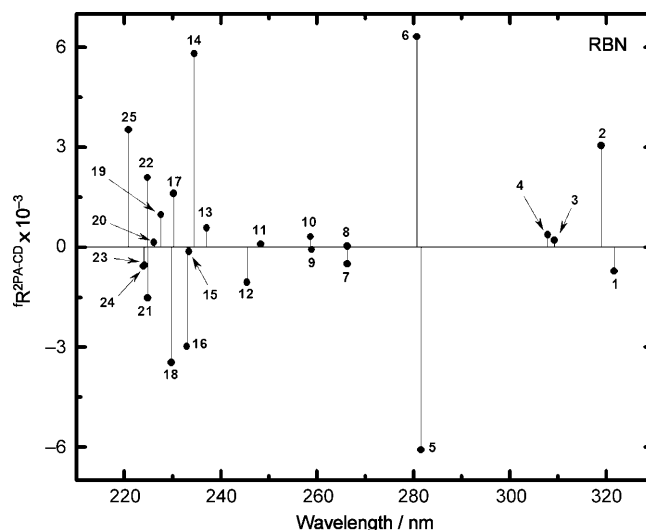

Figure 4. Two-photon circular dichroism rotatory strength of RBN calculated at a B3LYP/aug-cc-pVDZ level of theory. Numbers 1–25 label each excited state.

Supporting Information). Prior calculations of the CD spectra of RBN and SBN using this theoretical approach revealed the accuracy of our method. A good agreement between theory and experiment was obtained (for more details see the Supporting Information).

Now a more extensive elucidation of the 2PA-CD spectrum can be completed. From now on we will mainly concentrate our discussion on RBN since similar arguments apply to SBN. Our calculations properly reproduce the short wavelength band observed at approximately 240 nm which appear at about 220 nm in the theoretical spectrum. This peak results from the rotatory strengths of several electronic excited states clustered around 230 nm, with a state lying at 234.5 nm yielding the most intense (positive) signal. Its contribution (106 % of the area of the peak) is, nevertheless, only 25 % of the sum of the absolute rotatory strengths of the states lying in the region. Cancellation effects appear to be therefore extremely important in this case. On the other hand, the peak centered at about 315 nm, which is slightly red shifted with respect to that obtained in the experiment (ca. 290 nm), is ascribed to the contribution of two pairs of states with opposite symmetry, with a net dominance of the second lowest excited state of A symmetry. Note also that the near transparency around 270 nm, between the two major bands in experiment, hides a very strong, almost com-

plete, cancellation of rotator strengths of a pair of excited states (the fifth and sixth lowest in our calculations) again of opposite symmetry. In addition, the slightly red shifted shoulder observed at about 230 nm in the calculation corresponds to that at approximately 260 nm in the experiment. Finally, the fact that the 2PA-CD spectrum for RBN is positive through the whole spectral range is apparently due to the strong compensation of positive and negative signals of states. The notable differences in magnitude between the experimental and theoretical spectra, a factor of more than three orders of magnitude, can be perhaps attributed to conformational effects, such as exciton coupling for dimers undergoing electrically allowed transitions.[22] The evidence deserves further detailed scrutiny. The effect of changes in the dihedral angle formed by the two naphthols in RBN was analyzed by performing a Boltzmann average (based on total energy) over a choice of five conformers (the increase towards 180° corresponds to the two OH groups getting closer) differing in the relative orientations of the two rings (see Figure 5). This is an admittedly approximate and yet
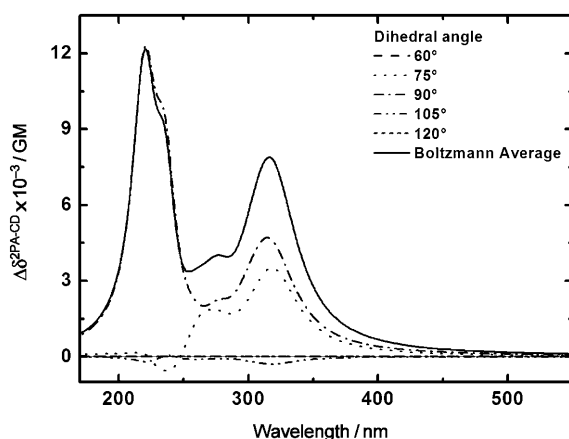

Figure 5. Analysis of the effect of a change in the dihedral angle between the two naphthols in RBN on the 2PA-CD spectrum. DFT/B3LYP/aug-cc-pVDZ calculations, and convolution with Lorentzian functions were performed with HWHM of 0.3 eV in the energy domain. Curves at 60° and 120° overlap at 0 GM.

reasonable way to describe the effect of slow vibrational motions in condensed phase. At each wavelength, the thicker curve (corresponding to the Boltzmann average) is the algebraic sum of the individual contributions. This preliminary study does not seem to indicate that the 2PA-CD spectrum might be particularly sensitive to the change in the angle between the planes of the naphthol rings. In addition, a greater contribution to the 2PA is expected for picosecond excitation pulses and excited state absorption.[23]

Conclusions

We have measured the polarization-dependent two-photon absorption cross-section of a chiral sample in solution. Slight

differences between the nonlinear absorption cross-sections for left and right circularly polarized light allowed the measurement of the 2PA-CD spectrum for each enantiomer. Ascertained differences in symmetry selection rules and spectral information between 2PA-CD and CD revealed the existence of complementary information in both approaches. These results, along with linear and vibrational circular dichroism and Raman optical activity fingerprints, especially when coupled with state-of-the-art theoretical modeling, establish a cooperative strategy to unveil molecular characteristics in chiral systems. Our findings are envisaged to open new opportunities in the recognition and understanding of optically active systems.

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