



Universidad Autónoma  
de Madrid

**Biblos-e Archivo**  
Repositorio Institucional UAM

**Repositorio Institucional de la Universidad Autónoma de Madrid**

<https://repositorio.uam.es>

Esta es la **versión de autor** del artículo publicado en:  
This is an **author produced version** of a paper published in:

**Journal of Physical Chemistry Letters 7.23 (2016): 4891-4897**

**DOI:** <https://doi.org/10.1021/acs.jpcllett.6b02484>

**Copyright:** © 2016 American Chemical Society

El acceso a la versión del editor puede requerir la suscripción del recurso

Access to the published version may require subscription

# Quantum/Classical Calculation of Vibronic Spectra along a Reaction Path: The case of the ECD of Easily Interconvertible Conformers with Opposite Chirality

Javier Cerezo,<sup>†</sup> Giuseppe Mazzeo,<sup>\*,‡</sup> Giovanna Longhi,<sup>‡</sup> Sergio Abbate,<sup>‡</sup> and  
Fabrizio Santoro<sup>\*,†</sup>

<sup>†</sup>*CNR–Consiglio Nazionale delle Ricerche, Istituto di Chimica dei Composti Organo  
Metallici (ICCOM-CNR), UOS di Pisa, Area della Ricerca, via G. Moruzzi 1, I-56124  
Pisa, Italy*

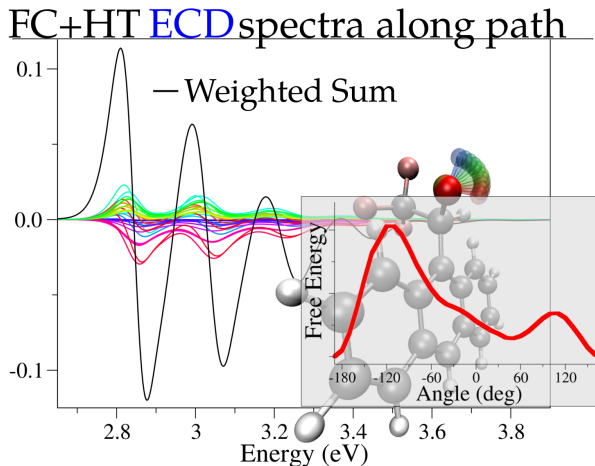
<sup>‡</sup>*Dipartimento di Medicina Molecolare e Traslazionale, Università di Brescia, Viale Europa  
11, I-25123 Brescia, Italy*

E-mail: giuseppe.mazzeo@unibs.it; fabrizio.santoro@iccom.cnr.it

## Abstract

We present a novel mixed method suitable for computing the low-to-middle resolution spectra of systems characterized by a large-amplitude motion  $s$  (defined by either a reaction or an internal path) coupled to a bath of harmonic oscillators  $\mathbf{r}$  which change with  $s$ . The method is based on an adiabatic approximation whereby  $s$  is considered much slower than  $\mathbf{r}$  degrees of freedom and is treated classically. We show that the spectrum can be obtained by a suitable average of quantum vibronic spectra of the fast coordinates computed at representative values of the slow coordinate along the path.

By our method we calculate the electronic circular dichroism (ECD) of 2,2,2-trifluoroanthryl-ethanol, which possesses two conformers with opposite chirality separated by a low-energy barrier. Path-averaged spectra are significantly different from those obtained only at the stable minima: agreement with experiment is improved. The method represents a generalization of those currently based on harmonic approximation.



TOC

There is great interest in developing robust methods to simulate the shape of electronic spectra in a non-phenomenological way. The scope is to get predictions directly comparable with experiments, improving our capability to extract detailed information from them. The spectral shape depends on the effect of nuclear dynamics of both the system and of the environment in which it is embedded and, in principle, the most accurate approach is to account for the quantum nature of molecular vibrations. Quantum effects are responsible for the appearance of line progressions and play an important role in determining the band widths, even when the shapes appear structureless.<sup>1,2</sup> Moreover, contributions beyond the so called Franck-Condon (FC) term, like Herzberg-Teller (HT) intensity-borrowing effects, can only be accurately described with a quantum (vibronic) calculation.<sup>3</sup>

Vibronic calculations for rigid systems, i.e. molecules whose initial and final state potential energy surfaces (PESs) may be represented in the harmonic approximation, are now rather standard thanks to recent advancements in time-independent (TI)<sup>4-9</sup> and time-

dependent (TD)<sup>10–17</sup> methods. Currently, a hot topic in computational electronic spectroscopy is the extension of these methods to flexible systems, i.e those in which at least one degree of freedom undergoes a large amplitude motion, possibly coupled to the other vibrational modes. The main route in these cases should be to work with full-dimensionality anharmonic PESs but this is only possible for systems with few coordinates. Our interest here is, instead, to develop (necessarily) approximate methods for the simulation of low- and medium-resolution spectra of large systems characterized by dozens or hundreds of coordinates, thus providing a generalization of the methods already available for rigid systems. For these cases it is necessary to work out a protocol to separate the anharmonic modes and treat them with more advanced methodologies. Some strategies were proposed to this scope in the past.<sup>18–23</sup> Typically they are based on the hypothesis that the harmonic and anharmonic degrees of freedom are not coupled, or that the coupling can be represented with a local expansion of the PES (for example, couplings are bilinear<sup>18</sup> and are usually estimated at the ground state geometry). While this approach can be very helpful in many cases, it is not adequate when the PES along the harmonic degrees of freedom, or the intensity of the electronic transition, remarkably depend on both the harmonic and the anharmonic coordinates.

A paradigmatic example is provided by systems characterized by different conformers separated by a low energy barrier, which can therefore easily interconvert along a large amplitude motion. The situation is sometimes dramatically evidenced by chiral spectroscopies, like e.g. electronic circular dichroism (ECD), since often different conformers may exhibit markedly different responses or even opposite chirality.<sup>24–26</sup> This is what happens in the case of 2,2,2-trifluoro-anthryl-ethanol, whose structure is reported in the inset of Figure 1, where we also report its energy profile and its rotatory strength along the 1-2-3-4 torsion ( $\theta$ ). All electronic calculations were performed in gas phase using the Gaussian09 program<sup>27</sup> adopting Density Functional Theory (DFT) and TD-DFT with the B3LYP functional and the TZVP basis. The system exhibits two stable conformers, Conf1 (more stable) and Conf2, with op-

posite rotatory strength (RS); notably, the RS changes remarkably with  $\theta$ . We measured the ECD spectrum of the system in acetonitrile and computed the corresponding vibronic profile for Conf1 and Conf2 including Duschinsky effects with the Vertical Hessian (VH) model,<sup>28</sup> and considering both FC and HT terms (FCHTi model).<sup>28</sup> Stick spectra were obtained from the TI expression

$$L(\omega) = \sum_{v_1, v_2} \rho_{v_1}(T) \Im(\langle \mathbf{v}_1 | \boldsymbol{\mu}_{12} | \mathbf{v}_2 \rangle \langle \mathbf{v}_2 | \mathbf{m}_{12} | \mathbf{v}_1 \rangle) \delta(\omega_{v_2} - \omega_{v_1} + (\Delta E/\hbar - \omega)) \quad (1)$$

where  $\rho_{v_1}$  is the Boltzmann population of the vibrational state  $|\mathbf{v}_1\rangle$ ,  $\Delta E$  the adiabatic energy difference between the minima of excited-state (ES) and ground-state (GS) PESs, and  $\boldsymbol{\mu}_{12}$  and  $\mathbf{m}_{12}$  (3-dimensional vectors) are respectively the electronic transition electric and magnetic transition dipole moments for the electronic transition  $1 \rightarrow 2$  ( $\Im$  indicates imaginary part), and we adopted the pre-screening method presented in refs. 4,5,9. Fully converged spectral shapes were simulated within the TD formulation,<sup>11,29</sup> using analytical expressions of the time correlation function including FC and HT terms<sup>10–15,30–32</sup> (see Supporting Information, SI, for further details). All vibronic spectra were computed with a development version of our code *FCclasses*.

Figure 2 compares experimental and computed spectra, the latter plotted as stick lines and convoluted line shapes.<sup>33</sup> Experimental vibrational circular dichroism (VCD) and ECD data were collected within the work at ref.,<sup>34</sup> but ECD data are reported for the first time here (VCD spectra reported in the SI of ref. 33 are also dependent on an adequate balance of Conf1 and Conf2). The experimental signal shows a very peculiar alternation of sign, which at temperature  $T=0$  K is only observed in the theoretical spectrum of the less populated conformer (Conf2). On the contrary, at  $T=300$  K, both conformers show sign alternation but still, the spectrum of Conf2 seems closer to the experimental one (notice the relative intensity of the two lowest-energy bands).

The rather flat energy profile with respect to  $K_B T$  ( $K_B$  is the Boltzmann constant) and the strong dependence of RS on  $\theta$  (Figure 1) suggest that structures different from those of

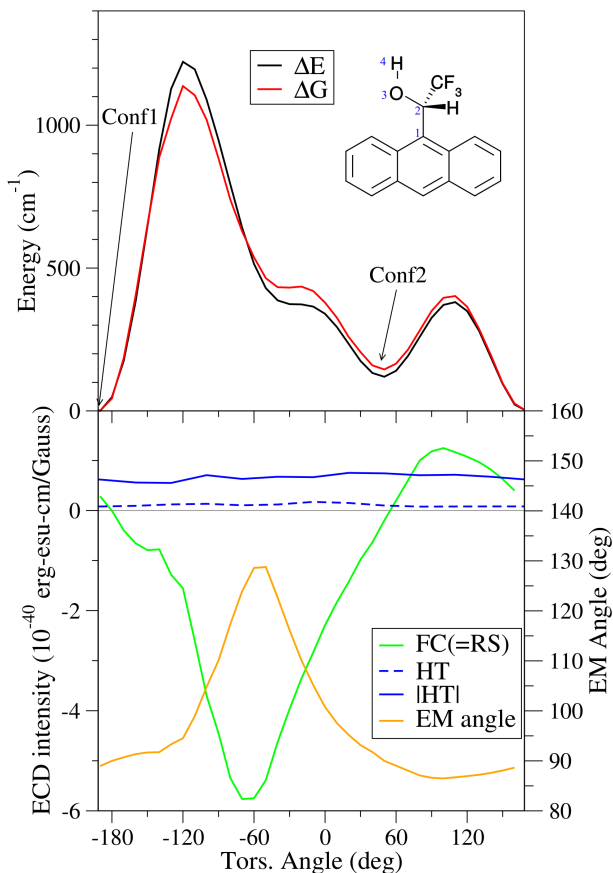


Figure 1: 2,2,2-trifluoro-anthryl-ethanol. Top: Potential ( $\Delta E$ ) and free energy ( $\Delta G$ ) profiles for the relaxed scan along  $\theta$  (dihedral angle described by labeled atoms on the molecular structure). Bottom: FC –equal to the rotatory strength– and HT contributions to the total ECD intensity of the spectra (defined in ref.<sup>24</sup> see also SI) computed along the path. The sum of the absolute HT contributions ( $|HT|$ , see SI) is also included. The angle between electric and magnetic transition dipole moments (EM angle) is shown.

the minima may contribute to the spectrum. In order to investigate this possibility a suitable computational model must be devised. The same results in Figure 2 indicate some desirable features the model should have. In fact, the sign alternation predicted for Conf2 arises from strong HT effects on fundamental transitions (by theory at FC level all the vibronic peaks share the same sign,<sup>26,35</sup> see comparison of FC and FCHT spectra in the SI). Such HT effects can only be described accounting for the quantum nature of the molecular vibrations. This fact, and the very same existence of vibronic experimental features, rule out the possibility to use classical Molecular Dynamics with the aim of obtaining a realistic sampling of the conformational variety and then obtain the spectrum from the classical FC principle. On the

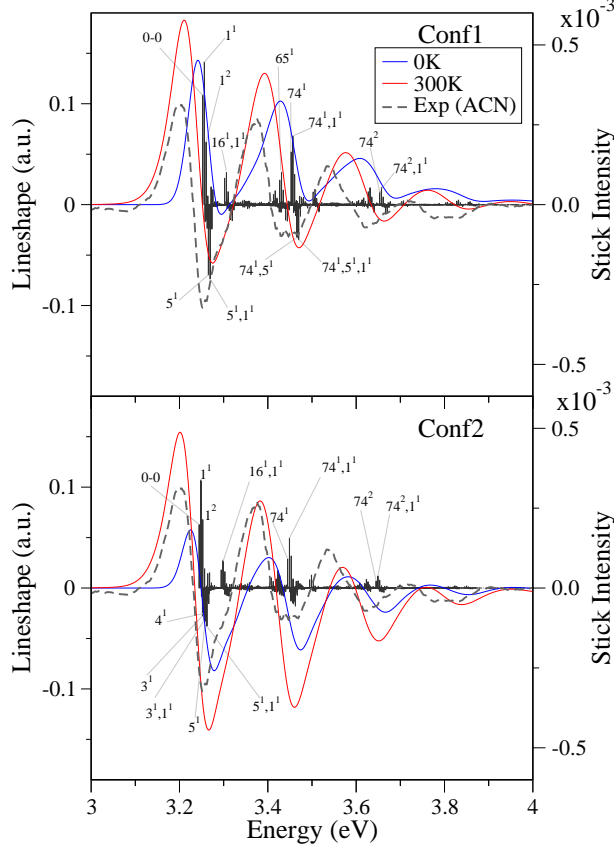


Figure 2: 2,2,2-trifluoro-anthryl-ethanol: experimental (0.01M/Acetonitrile) and simulated ECD spectral lineshapes (in atomic units, a.u.). Simulations at 0 and 300 K for Conf1 and Conf2 with the TD approach with a Gaussian broadening with half width at half maximum (HWHM) 0.03 eV. Stick transitions at 0 K computed with the TI approach are also included, labeling the most relevant ones as  $X_1^{y_1}, X_2^{y_2} \dots$  where  $X_1, X_2 \dots$  are the excited modes (sketched in the SI) in the final state and  $y_1, y_2 \dots$  their quantum numbers. 0 – 0 is the transition between the ground vibrational states. Simulated spectra are blue shifted by 0.39 eV.

other side, when using fully quantum models, results show that it is not possible to simply assume that  $\theta$  is separated from the other modes. In fact, the strong  $\theta$ -dependence of RS suggests that also HT effects along the other vibrational modes will depend on  $\theta$ .

On these grounds, here we adopt a hybrid quantum/classical approach based on the assumption that the other coordinates of the system are stiff (meaning harmonic) and much faster than the large amplitude motion (e.g.  $\theta$ ) and rearrange instantaneously at each change of the slow coordinate (adiabatic approximation).<sup>21,22</sup> Within this framework we propose a

novel general protocol to account for the dependence on the slow coordinate of the frequency and intensity of the vibronic transitions associated to the fast coordinates. The basic idea is to properly define and compute specific vibronic spectra corresponding to the “fast” degrees of freedom at each (non-equilibrium) value of the slow coordinate, and to obtain the total spectrum as a weighted average along the “slow” coordinate. Indeed, the adopted weights depend on the sampling performed on such coordinate. It has been shown that the contributions of low- frequency modes to low- medium-resolution spectra of semirigid dyes, can be treated classically,<sup>1,2,21</sup> thus the weights along the slow coordinate will be extracted from the Boltzmann distribution.

We start presenting our methodology by defining the slow coordinate in two ways. First, we adopt the so-called Intrinsic Reaction Coordinate (IRC)<sup>36</sup> that connects the two conformers. This choice is attractive because it allows one to use the elegant theory of the reaction path Hamiltonian (RPH)<sup>37</sup> as a reference for the definition of the initial-state PES. The IRC is a natural candidate for the slow “intrinsic” coordinate interconverting the two conformers and, moreover, a vibrational adiabatic approximation for the other modes along an IRC path has been often employed in literature.<sup>37–39</sup> As a second, more general, possibility, which we may call “a physically-motivated” choice, we will consider an internal coordinate (IC) of the system. In this context the reference Hamiltonian is the so called internal coordinate path Hamiltonian (ICPH).<sup>40</sup> Here we select the torsion  $\theta$ . This second strategy can be considered representative of cases where the slowness of the coordinate is not “intrinsic” but due to the interaction with the environment and therefore the coordinate cannot be defined by considering only intrinsic properties of the system, but it must be guessed on the grounds of chemical intuition or after analysis of preliminary MD studies. With both choices, a proper calculation of the spectrum requires an adequate definition of model PES along the quantum coordinates as a function of the slow coordinate and of an averaging strategy. The ICPH strategy is more general than the IRC because it does not require the presence of an energy barrier and it does not meet the IRC problems when it is necessary to extrapolate

the coordinate beyond the minima structures.<sup>40</sup>

When the IRC approach is adopted, the total Hamiltonian  $\hat{H}^{tot}$  of the system is evaluated according to the RPH theory, invoking the adiabatic approximation and neglecting all coupling terms between the IRC and the other  $3N-7$  coordinates both in the potential and in the kinetic energy. The same approximation is adopted for an IC path. In this case, the rotations are not exactly removed along the path, and their couplings should be accounted for.<sup>40</sup> Since here we are interested in medium-to- low-resolution spectra, we neglect such terms in the ICPH. With these assumptions, the Hamiltonian of the system is split in two terms: one depends on the slow coordinate ( $s$ ) only and the other one depends both on the fast coordinates ( $\mathbf{r}$ ) and, parametrically, on  $s$ . For each value of  $s$ , we consider the harmonic expansion of the PES along the  $\mathbf{r}$  and compute their energy levels, which depend on their frequencies  $\omega_{\mathbf{r}}(s)$  and quantum numbers  $\mathbf{v}_{\mathbf{r}}$ . The slow coordinate is treated classically so that the states of the system are characterized by  $\mathbf{v}_{\mathbf{r}}$  and the phase space of the slow coordinate,  $[s, p_s]$ . The energy is given by:

$$H(s, p_s, \mathbf{v}_{\mathbf{r}}) = T^s(p_s) + V^s(s) + E_{QM}^{fast}(s, \mathbf{v}_{\mathbf{r}}) \quad (2)$$

where  $T^s(p_s)$  and  $V^s(s)$  are the kinetic and potential energies corresponding to the slow coordinate and  $E_{QM}^{fast}(s, \mathbf{v}_{\mathbf{r}})$ , is the energy of the  $3N - 7$  quantum oscillators at the current value of  $s$ . Since the spectrum lineshape does not depend on  $p_s$ , the average at temperature  $T$  over all the states can be computed as (see SI for a detailed derivation),

$$L(\omega) = \int \frac{e^{-\Delta G(s)}}{\int e^{-\Delta G(s')} ds'} L^*(\omega; s) ds = \int \rho(s) L^*(\omega; s) ds \quad (3)$$

where  $L^*(\omega; s)$  is the Boltzmann-averaged lineshape at temperature  $T$  over all the possible harmonic vibrational states in the  $3N - 7$  space of the fast coordinates at a given  $s$ , and is computed with the TI formalism (Eq. 1) or the TD one (see SI).  $\Delta G(s)$  is the free energy including the entropic contribution of the  $3N - 7$  oscillators. The integral is evaluated

numerically, by dividing the conformational space into regions where  $L^*(\omega; s)$  is assumed constant (checks on the numerical integration procedure are given in the SI).

Let us first apply the above general framework to the specific case where  $s$  is the IRC ( $s_{IRC}$ ). This coordinate passes through the transition state connecting the two conformers following the gradient at each non-stationary point. The actual minima are never reached along the IRC path and independent IRC calculations need to be performed from each transition state (2 in our case). The distance from the last IRC point to the minima is computed integrating the reaction path<sup>41,42</sup> assuming a quadratic PES in that region (see SI for details).

In Figure 3, we present the potential and free energy profiles computed along the IRC path. The starting point ( $s_{IRC} = 0$ ) corresponds to the conformation of Conf1. We note that the path is periodic, i.e. the initial ( $s_{IRC} = 0$ ) and final ( $s_{IRC} \approx 19.9 \text{ amu}^{1/2}\text{bohr}$ ) conformations are identical. Compared with the torsional relaxed scan shown in Figure 1, the potential energy along the IRC path has a similar profile, with a higher barrier ( $\sim 1200 \text{ cm}^{-1}$ ) in one direction and a lower one ( $\sim 400 \text{ cm}^{-1}$ ) in the other direction. In both cases, the local minimum after the barriers (Conf2) is more energetic than Conf1. One relevant difference between the potential energy profiles is that, in the IRC, the slope of the curve significantly decreases around the minima and, consequently, the regions around these points appear to be wider. The same is observed around the inflection point ( $s \approx 10 \text{ amu}^{1/2}\text{bohr}$ ). This is related to the fact that in the vicinity of these stationary points, the nature of the IRC changes from the torsion of the hydroxyl, defined by atoms 1,2,3,4 in Figure 1, to that of the trifluoro-methyl group, which is associated to a lower frequency mode (see SI). Turning to the free energy, the profile along the IRC path is significantly perturbed in the vicinity of the minima and inflection points. Again, this effect can be explained by the change of the nature of the IRC: the torsional modes associated with the hydroxyl and trifluoro-methyl groups have different frequencies ( $\sim 300 \text{ cm}^{-1}$  and  $\sim 50 \text{ cm}^{-1}$ ), which result in very different entropic contributions.

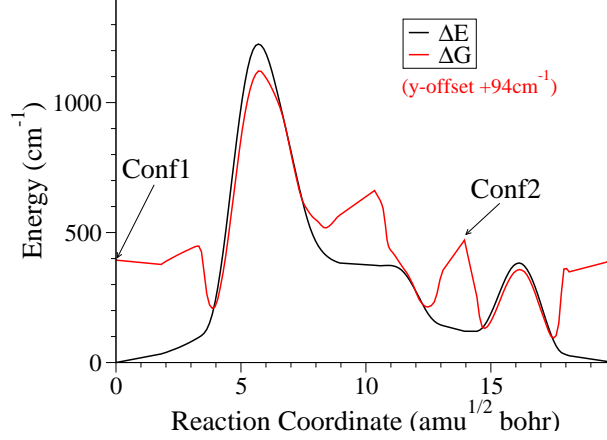


Figure 3: Potential ( $\Delta E$ ) and free energy ( $\Delta G$ ) profiles of 2,2,2-trifluoro-anthryl-ethanol along the IRC path connecting the conformers Conf1 and Conf2.

The alternative choice for the slow coordinate is  $\theta$ . In this case the energy profile is obtained through a relaxed scan, i.e. performing optimizations in the  $3N - 7$  space of the fast coordinates at selected values of  $\theta$ .

Once the path associated to the slow coordinate is defined using either the IRC or  $\theta$ , the spectra can be computed with Eq. 3. For this, we need two basic ingredients: the probability function,  $\rho(s)$ , which is computed from the free energy profiles presented in Figures 1 and 3, and the lineshape in terms of  $s$ ,  $L^*(\omega; s)$ . To compute the latter, we define the space of the fast degrees of freedom, as the orthogonal complement to  $s$ , which corresponds to the direction of the gradient in both the IRC and the relaxed scan. The gradient coordinate can be projected out from the Hessian in Cartesian coordinates ( $3N \times 3N$ ) by

$$\mathbf{H}_{\mathbf{x}}^{(r)} = (\mathbf{I} - \mathbf{t}_g \mathbf{t}_g^t) \mathbf{H}_{\mathbf{x}} (\mathbf{I} - \mathbf{t}_g \mathbf{t}_g^t) \quad (4)$$

where  $\mathbf{H}_{\mathbf{x}}$  and  $\mathbf{H}_{\mathbf{x}}^{(r)}$  are the Hessian matrices before and after the projection,  $\mathbf{I}$  is the  $(3N) \times (3N)$  identity matrix and  $\mathbf{t}_g$  is the normalized vector associated to the gradient. The translations and rotations of the systems are removed in a similar way, finally providing a Hessian with  $3N - 7$  roots.

To compute vibronic spectra, including Duschinsky effects, we need specific harmonic

models of the initial and final PES in the  $3N - 7$  space of the fast coordinates at each selected value of  $s$ . For the initial state, they are obtained by a second-order expansion at the minimum in the  $3N - 7$  space. This requires to compute the Hessian matrix in the reduced space according to Eq. 4. For the final state, for each  $s$  we could expand the harmonic PES at the  $3N - 7$  minimum of either the initial PES (VH model)<sup>28</sup> or the final state (AH model).<sup>28</sup> The AH approach is inconvenient in the case of the IRC, since, in order to locate the final-state minimum in the  $3N - 7$  space, it would be necessary to perform an optimization constraining the value of the IRC, not a trivial task. Therefore, in our protocol we adopt the VH model. This choice generally implies a normal mode analysis at a non-stationary point in the final state, which is problematic if Cartesian coordinates are used in the analysis. The problem is solved adopting curvilinear internal coordinates.<sup>43,44</sup> All frequencies computed in the initial and final states along the path were real. In order to properly describe the balance of FC and HT effects along the path,  $\mu_{12}$  and  $m_{12}$  were taken as linear functions of the fast coordinates and were computed by different Taylor expansions at each value of  $s$ . The expression of the initial and final state PES and the transition dipoles along the fast coordinates as a function of  $s$  are given in the SI.

Following the protocol described above, the spectra are computed along each path with the TD approach. Concretely, in the case of the IRC, the spectra are evaluated every  $\sim 0.54 \text{ amu}^{1/2} \text{ bohr}$ , including the spectra obtained at the minima. Note that the actual step depends on the values obtained along the IRC calculation, which may vary, especially when approaching a stationary point: e.g., the distance from Conf1 to the nearest IRC point is as large as  $2.4 \text{ amu}^{1/2} \text{ bohr}$ . In the case of the torsional path, the spectra are computed every  $30^\circ$  (starting from  $\theta=20^\circ$ ). In order to keep a constant step, the spectra corresponding to the minima are not included, although we considered structures that were very close to them:  $\theta = 170^\circ$  is near Conf1 ( $\theta = 168.3^\circ$ ) and  $\theta = 50^\circ$  is close to Conf2 ( $\theta = 48.9^\circ$ ). Preliminary calculations confirm the validity of this approach (see SI).

The final computed spectra depend on two main factors: the relative Boltzmann popula-

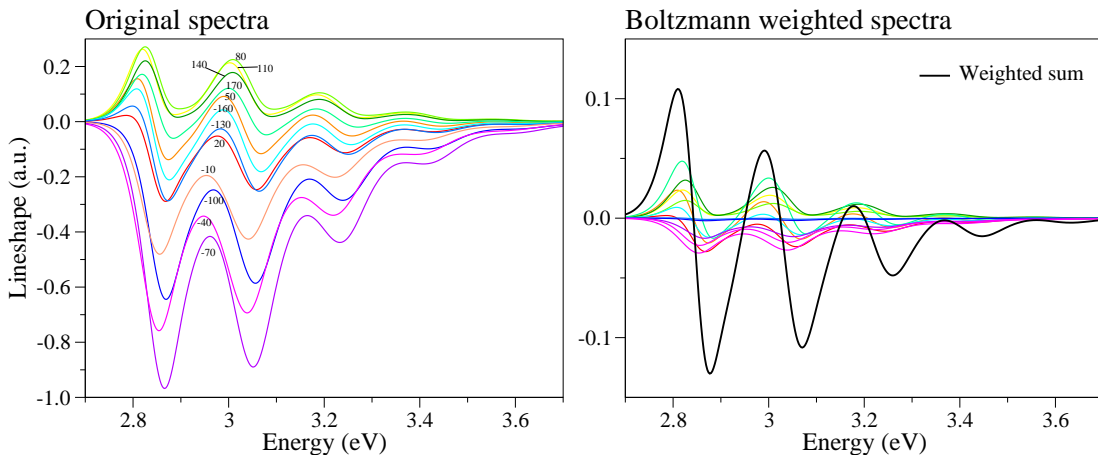


Figure 4: 2,2,2-trifluoro-anthryl-ethanol: Left: ECD lineshapes (in atomic units, a.u.) computed at different points along the torsional scan on the remaining  $3N - 7$  coordinates. The value of  $\theta$  is specified over the spectra. Right: each lineshape is scaled with the corresponding Boltzmann factor, and the sum is computed.

tion (distribution function) of each conformation and the total intensity of the spectra. In the left panel of Figure 4, we include all the spectra computed along the torsional path at 300 K. As indicated in Figure 1, in the conformations where the RS is large, the angle between electric and magnetic transition moments (EM angle) differs considerably from  $90^\circ$ , the spectra are mainly governed by the FC contribution and show a clear positive ( $80^\circ < \theta < 140^\circ$ ) or negative ( $-100^\circ < \theta < -10^\circ$ ) sign. On the contrary for intermediate structures (EM angle closer to  $90^\circ$ ), the HT contribution can be significantly larger than the FC ones, which leads to spectra with alternating signs. On the right panel, each spectrum is scaled by their Boltzmann weight, which provides the final contributions that sum up to the final lineshape. It is interesting to note that, although the conformations around ( $-100^\circ < \theta < -40^\circ$ ), i.e. around the inflection point of the PES, have a small Boltzmann weight, their high negative intensity has a relevant effect on the final spectrum.

A similar behavior is observed in the case of the IRC path (see Figure S5 in SI), since it involves similar  $\theta$  displacements, except in the vicinity of minima and inflection points where, as mentioned above, the path is mainly associated with the rotation of the trifluoro-methyl group (see Figure S4 in SI). In the case of Conf1, such motion spans over a large region of

the path ( $\sim 4 \text{ amu}^{1/2} \text{ bohr}$  around Conf1 geometry), but the change of the spectral shape is relatively small, as compared to the change along the torsion of the hydroxyl (see Figure S6 in SI). The extension of such region would increase, on the average, the relevance of spectral shapes similar to those of Conf1. However, at the same time the change in the IRC close to the minima leads to a remarkable increment of the free energy which, in turn, lowers the Boltzmann weight associated to this region. The two opposite effects compensate each other and the total spectrum calculated along the IRC path is very similar to the one calculated along  $\theta$  (Figure 5).

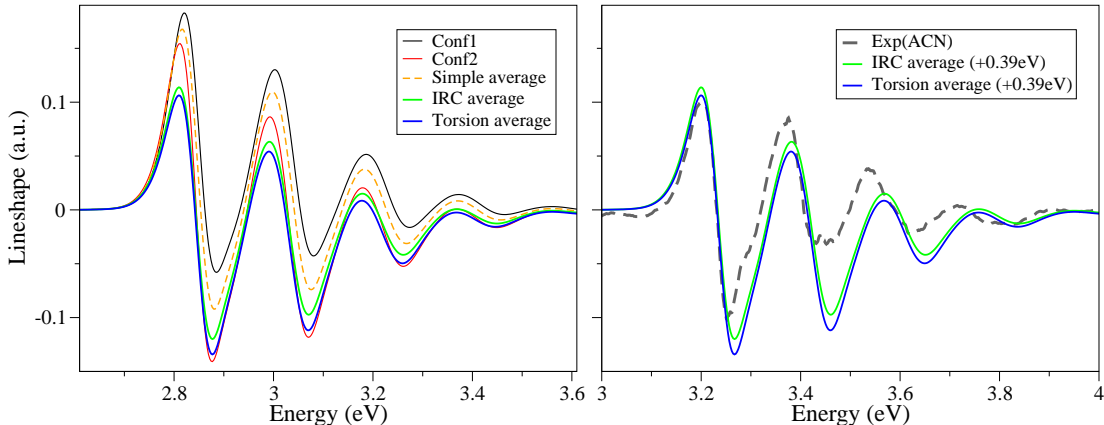


Figure 5: 2,2,2-trifluoro-anthryl-ethanol: **Left:** spectral lineshapes (in atomic units, a.u.) simulated for the two minima (Conf1 and Conf2) and for their weighted average (Simple average). The average spectra along the IRC and torsional paths are also shown. **Right:** the experimental lineshape spectrum in acetonitrile (ACN) is shown including the simulated spectra averaged along the paths, which are blue-shifted by 0.39 eV.

Figure 5 compares the spectra averaged along both IRC and internal paths with those computed for Conf1 and Conf2 structures and their simple Boltzmann average (SA). The final path-averaged spectra are also compared with the experiment. The main finding of this work is that the spectra computed taking into account the contribution of the structures along all the paths (either IRC or  $\theta$ ) are very similar and deviate significantly from the SA spectrum. Namely, at variance with the SA, the spectra obtained from the IRC and  $\theta$  paths do not fall in between those of Conf1 and Conf2. Indeed, the path-averaged spectra mainly depend on the balance of two uncorrelated factors: the probability distribution function  $\rho$ ,

and the relevance of FC and HT contributions, which control intensity and shape of each single spectrum along the path. As a consequence, the large negative intensity of some of the spectra, described above, results in average spectra that are, in some regions, below both spectra, the one of Conf1 and the one of Conf2, and normally closer to that of the less populated conformer, Conf2.

Overall the path-averaged spectra appear to be in better agreement with the experiment, as compared to the spectra simulated for Conf1, Conf2 or their SA. However, comparison with experiment clearly also depends on the adopted level of electronic theory, and we believe that, for this work, the improved agreement with experiment is less central than having shown that, in systems with conformers separated by a low barrier, structures out of equilibrium along the inter-conversion path may strongly contribute to the ECD shape. Keeping this in mind, we can further observe that the agreement with the experiment is very good but still not perfect, especially in the high energy region of the spectrum. For further analysis it might be useful to include the effect of the environment in the calculation of the PESs, i.e., with implicit solvation models, or to evaluate the dependence of the results on the DFT functional. Regarding the latter, we notice that B3LYP predicts a remarkable red-shift (0.39 eV) of the absolute position of the spectra. Such a deviation from the experiment can be related to a charge-transfer like character of the electronic transition,<sup>45</sup> which would not only affect the position of the spectrum, but also may have a significant impact on the vibrational reorganization energy, hence, on the relative intensity of the spectral progressions.<sup>46–48</sup> In this sense, the adoption of long-range corrected functionals may provide more realistic simulations.

In conclusion, we have presented a new effective method, based on a quantum/classical approach and on the adiabatic approximation, to compute the shape of the electronic spectra of flexible systems characterized by a slow large-amplitude motion coupled with the fast stiff coordinates. The proposed protocol may be easily standardized in a clear sequence of steps in the computation and therefore represents, in our opinion, a straightforward generalization

of the TI and TD harmonic approaches already available for rigid systems.<sup>4-17</sup> Going to the specific case of ECD spectroscopy, our method provides a consistent procedure to deal with systems where the rotatory strength varies significantly along a flexible coordinate and is expected to help in many cases already presented in literature.<sup>49</sup>

Of course the presented model has its own limitation. First, it is essentially tailored to simulate spectra with low to medium resolution, therefore it is adequate for systems in the condensed phase. The simulation of high-resolution spectra, e.g. in a jet cooled expansion, could not avoid a proper quantum treatment also for the slow coordinates. Second, the application of the method might become difficult when it is not clear which coordinates should be considered slow, or where several “slow” coordinates exist, or the coupling to the solvent motions is important. To the best of our knowledge, no general method is available nowadays for these cases if quantum vibrational effects need to be taken into account. Possible computational strategies for these cases might require the development of suitable protocols to separate quantum and classical degrees of freedom at representative snapshots of a preliminary MD simulation. First applications of this kind of hybrid approaches are appearing in literature,<sup>50,51</sup> and probably they will represent a hot topic in this research field in the next years.

## Acknowledgement

The support of MIUR (PRIN 2010-2011 prot. 2010ERFKXL) is acknowledged. JC acknowledges “Fundación Ramón Areces” for funding his postdoctoral position, and the Pisa Unit of ICCOM-CNR Pisa for hospitality.

## Supporting Information Available

Description of TI and TD approaches to simulate electronic spectra; expressions for the total intensity of FC and FCHT spectra; FC and FCHT stick spectra of the two stable conformers

and description of relevant normal modes; expression to compute the length of the IRC path; description of the equations to compute the spectra in the 3N-7 space of the fast coordinates; expression of the average spectra and investigation of its proper integration; description of the major structural displacements along the IRC path; ECD spectra computed along the IRC path. This material is available free of charge via the Internet at <http://pubs.acs.org/>.

## References

- (1) Cerezo, J.; Santoro, F.; Prampolini, G. Comparing classical approaches with empirical or quantum-mechanically derived force fields for the simulation electronic lineshapes: application to coumarin dyes. *Theor. Chem. Acc.* **2016**, *135*, 1–21.
- (2) Petrone, A.; Cerezo, J.; Ferrer, F. J. A.; Donati, G.; Improta, R.; Rega, N.; Santoro, F. Absorption and Emission Spectral Shapes of a Prototype Dye in Water by Combining Classical/Dynamical and Quantum/Static Approaches. *J. Phys. Chem. A* **2015**, *119*, 5426–5438.
- (3) Biczysko, M.; Bloino, J.; Santoro, F.; Barone, V. In *Computational Strategies for Spectroscopy*; Barone, V., Ed.; John Wiley & Sons, Inc., 2011; Chapter 8, pp 361–443.
- (4) Santoro, F.; Lami, A.; Improta, R.; Barone, V. Effective method to compute vibrationally resolved optical spectra of large molecules at finite temperature in the gas phase and in solution. *J. Chem. Phys.* **2007**, *126*, 184102.
- (5) Santoro, F.; Lami, A.; Improta, R.; Bloino, J.; Barone, V. Effective method for the computation of optical spectra of large molecules at finite temperature including the Duschinsky and Herzberg–Teller effect: The Qx band of porphyrin as a case study. *J. Chem. Phys.* **2008**, *128*, 224311.
- (6) Dierksen, M.; Grimme, S. An efficient approach for the calculation of Franck–Condon integrals of large molecules. *J. Chem. Phys.* **2005**, *122*, 244101.

- (7) Jankowiak, H.-C.; Stuber, J. L.; Berger, R. Vibronic transitions in large molecular systems: Rigorous prescreening conditions for Franck-Condon factors. *J. Chem. Phys.* **2007**, *127*, 234101.
- (8) Hazra, A.; Nooijen, M. Vibronic coupling in the excited cationic states of ethylene: Simulation of the photoelectron spectrum between 12 and 18 eV. *J. Chem. Phys.* **2005**, *122*, 204327.
- (9) Santoro, F.; Barone, V. Computational approach to the study of the lineshape of absorption and electronic circular dichroism spectra. *Int. J. Quantum Chem.* **2010**, *110*, 476–486.
- (10) Tang, J.; Lee, M. T.; Lin, S. H. Effects of the Duschinsky mode-mixing mechanism on temperature dependence of electron transfer processes. *J. Chem. Phys.* **2003**, *119*, 7188–7196.
- (11) Ianconescu, R.; Pollak, E. Photoinduced Cooling of Polyatomic Molecules in an Electronically Excited State in the Presence of Dushinskii Rotations. *J. Phys. Chem. A* **2004**, *108*, 7778–7784.
- (12) Peng, Q.; Niu, Y.; Deng, C.; Shuai, Z. Vibration correlation function formalism of radiative and non-radiative rates for complex molecules. *Chem. Phys.* **2010**, *370*, 215–222.
- (13) Borrelli, R.; Capobianco, A.; Peluso, A. Generating Function Approach to the Calculation of Spectral Band Shapes of Free-Base Chlorin Including Duschinsky and Herzberg-Teller Effects. *J. Phys. Chem. A* **2012**, *116*, 9934–9940.
- (14) Baiardi, A.; Bloino, J.; Barone, V. General Time Dependent Approach to Vibronic Spectroscopy Including Franck-Condon, Herzberg-Teller, and Duschinsky Effects. *J. Chem. Theory Comput.* **2013**, *9*, 4097–4115.

- (15) Avila Ferrer, F. J.; Cerezo, J.; Soto, J.; Improta, R.; Santoro, F. First-principle computation of absorption and fluorescence spectra in solution accounting for vibronic structure, temperature effects and solvent inhomogeneous broadening. *Comput. Theoret. Chem.* **2014**, *1040–1041*, 328–337.
- (16) Etinski, M.; Rai-Constapel, V.; Marian, C. M. Time-dependent approach to spin-vibronic coupling: Implementation and assessment. *J. Chem. Phys.* **2014**, *140*, 114104.
- (17) Tapavicza, E.; Furche, F.; Sundholm, D. Importance of Vibronic Effects in the UV-Vis Spectrum of the 7,7,8,8-Tetracyanoquinodimethane Anion. *J. Chem. Theory Comput.* **2016**, *12*, 5058–5066.
- (18) Hazra, A.; Nooijen, M. Comparison of various Franck-Condon and vibronic coupling approaches for simulating electronic spectra: The case of the lowest photoelectron band of ethylene. *Phys. Chem. Chem. Phys.* **2005**, *7*, 1759–1771.
- (19) Borrelli, R.; Peluso, A. The vibrational progressions of the  $N \rightarrow V$  electronic transition of ethylene: A test case for the computation of Franck-Condon factors of highly flexible photoexcited molecules. *J. Chem. Phys.* **2006**, *125*, 194308.
- (20) Borrelli, R.; Peluso, A. The electron photodetachment spectrum of  $c\text{-C}_4\text{F}_8^-$ : A test case for the computation of Franck-Condon factors of highly flexible molecules. *J. Chem. Phys.* **2008**, *128*, 044303.
- (21) Stendardo, E.; Avila Ferrer, F.; Santoro, F.; Improta, R. Vibrationally Resolved Absorption and Emission Spectra of Dithiophene in the Gas Phase and in Solution by First-Principle Quantum Mechanical Calculations. *J. Chem. Theory Comput.* **2012**, *8*, 4483–4493.
- (22) Liu, Y.; Cerezo, J.; Santoro, F.; Rizzo, A.; Lin, N.; Zhao, X. Theoretical investigation of the broad one-photon absorption line-shape of a flexible symmetric carbazole derivative. *Phys. Chem. Chem. Phys.* **2016**, *18*, 22889–22905.

- (23) Bloino, J.; Baiardi, A.; Biczysko, M. Aiming at an accurate prediction of vibrational and electronic spectra for medium-to-large molecules: An overview. *Int. J. Quantum Chem.* **2016**, DOI: 10.1002/qua.25188.
- (24) Lin, N.; Santoro, F.; Zhao, X.; Rizzo, A.; Barone, V. Vibronically Resolved Electronic Circular Dichroism Spectra of (R)-(+)-3-Methylcyclopentanone: A Theoretical Study. *J. Phys. Chem. A* **2008**, *112*, 12401–12411.
- (25) Rivera-Fuentes, P.; Alonso-Gómez, J.; Petrovic, A.; Santoro, F.; Harada, N.; Berova, N.; Diederich, F. Amplification of Chirality in Monodisperse, Enantiopure Allenol-Acetylenic Oligomers. *Angew. Chem. Int. Ed.* **2010**, *49*, 2247–2250.
- (26) Pescitelli, G.; Barone, V.; Di Bari, L.; Rizzo, A.; Santoro, F. Vibronic Coupling Dominates the Electronic Circular Dichroism of the Benzene Chromophore 1Lb band. *J. Org. Chem.* **2013**, *78*, 7398–7405.
- (27) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09 Revision A.2. 2009; Gaussian Inc. Wallingford CT.

- (28) Avila Ferrer, F. J.; Santoro, F. Comparison of vertical and adiabatic harmonic approaches for the calculation of the vibrational structure of electronic spectra. *Phys. Chem. Chem. Phys.* **2012**, *14*, 13549–13563.
- (29) Lami, A.; Santoro, F. In *Computational Strategies for Spectroscopy*; Barone, V., Ed.; John Wiley & Sons, Inc., 2011; Chapter 10, pp 475–516.
- (30) Tatchen, J.; Pollak, E. Ab initio spectroscopy and photoinduced cooling of the trans-stilbene molecule. *J. Chem. Phys.* **2008**, *128*, 164303.
- (31) Borrelli, R.; Peluso, A. The temperature dependence of radiationless transition rates from ab initio computations. *Phys. Chem. Chem. Phys.* **2011**, *13*, 4420–4426.
- (32) Huh, J.; Berger, R. Coherent state-based generating function approach for Franck-Condon transitions and beyond. *J. Phys.: Conf. Ser.* **2012**, *380*, 012019.
- (33) Avila Ferrer, F. J.; Cerezo, J.; Stendardo, E.; Improta, R.; Santoro, F. Insights for an Accurate Comparison of Computational Data to Experimental Absorption and Emission Spectra: Beyond the Vertical Transition Approximation. *J. Chem. Theory Comput.* **2013**, *9*, 2072–2082.
- (34) Abbate, S.; Lebon, F.; Longhi, G.; Gangemi, R.; Spizzichino, S.; Bellachioma, G.; Ruzziconi, R. Vibrational Circular Dichroism (VCD): a Valuable Tool for Conformational Analysis and Configuration Assignment of Chiral 1-([2.2]Paracyclophan-4-yl)-2,2,2-trifluoroethanol. *ChemPhysChem* **2011**, *12*, 3519–3523.
- (35) Lin, N.; Luo, Y.; Santoro, F.; Zhao, X.; Rizzo, A. Vibronically-induced change in the chiral response of molecules revealed by electronic circular dichroism spectroscopy. *Chem. Phys. Lett.* **2008**, *464*, 144 – 149.
- (36) Fukui, K. The path of chemical reactions - the IRC approach. *Acc. Chem. Res.* **1981**, *14*, 363–368.

- (37) Miller, W. H.; Handy, N. C.; Adams, J. E. Reaction path Hamiltonian for polyatomic molecules. *J. Chem. Phys.* **1980**, *72*, 99–112.
- (38) Marcus, R. A. Generalization of Activated-Complex Theory. III. Vibrational Adiabaticity, Separation of Variables, and a Connection with Analytical Mechanics. *J. Chem. Phys.* **1965**, *43*, 1598–1605.
- (39) Truhlar, D. G.; Garrett, B. C. Variational transition-state theory. *Acc. Chem. Res.* **1980**, *13*, 440–448.
- (40) Tew, D. P.; Handy, N. C.; Carter, S.; Irle, S.; Bowman, J. The internal coordinate path Hamiltonian; application to methanol and malonaldehyde. *Mol. Phys.* **2003**, *101*, 3513–3525.
- (41) Pechukas, P. On simple saddle points of a potential surface, the conservation of nuclear symmetry along paths of steepest descent, and the symmetry of transition states. *J. Chem. Phys.* **1976**, *64*, 1516–1521.
- (42) Page, M.; McIver, J. W. On evaluating the reaction path Hamiltonian. *J. Chem. Phys.* **1988**, *88*, 922–935.
- (43) Cerezo, J.; Santoro, F. Revisiting Vertical Models To Simulate the Line Shape of Electronic Spectra Adopting Cartesian and Internal Coordinates. *J. Chem. Theory Comput.* **2016**, *12*, 4970–4985.
- (44) Baiardi, A.; Bloino, J.; Barone, V. General formulation of vibronic spectroscopy in internal coordinates. *J. Chem. Phys.* **2016**, *144*, 084114.
- (45) Kuritz, N.; Stein, T.; Baer, R.; Kronik, L. Charge-Transfer-Like  $\pi \rightarrow \pi^*$  Excitations in Time-Dependent Density Functional Theory: A Conundrum and Its Solution. *J. Chem. Theory Comput.* **2011**, *7*, 2408–2415.

- (46) Silverstein, D. W.; Jensen, L. Vibronic coupling simulations for linear and nonlinear optical processes: Simulation results. *J. Chem. Phys.* **2012**, *136*, 064110.
- (47) Cerezo, J.; Avila Ferrer, F. J.; Santoro, F. Disentangling vibronic and solvent broadening effects in the absorption spectra of coumarin derivatives for dye sensitized solar cells. *Phys. Chem. Chem. Phys.* **2015**, *17*, 11401–11411.
- (48) Zaleśny, R.; Murugan, N. A.; Tian, G.; Medved', M.; Ågren, H. First-Principles Simulations of One- and Two-Photon Absorption Band Shapes of the Bis(BF<sub>2</sub>) Core Complex. *J. Phys. Chem. B* **2016**, *120*, 2323–2332.
- (49) Lightner, D.; Gurst, J. E. *Organic Conformational Analysis and Stereochemistry from Circular Dichroism Spectroscopy*; Wiley-VCH: New York, 2000.
- (50) Zaleśny, R.; Murugan, N. A.; Gelmukhanov, F.; Rinkevicius, Z.; Ośmiałowski, B.; Bartkowiak, W.; Ågren, H. Toward Fully Nonempirical Simulations of Optical Band Shapes of Molecules in Solution: a Case Study of Heterocyclic Ketoimine Difluoroborates. *J. Phys. Chem. A* **2015**, *119*, 5145–5152.
- (51) D'Abramo, M.; Aschi, M.; Amadei, A. Theoretical modeling of UV-Vis absorption and emission spectra in liquid state systems including vibrational and conformational effects: Explicit treatment of the vibronic transitions. *J. Chem. Phys.* **2014**, *140*, 164104.