A hybrid TDDFT/MM investigation of the optical properties of aminocoumarins in water and acetonitrile solution

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Abstract

We present a hybrid Time-Dependent Density Functional /Molecular Mechanics (TDDFT/MM) simulation study on the optical properties of aminocoumarins in gas phase and solution. As solvation is described through a molecular approach, the effects due to the inhomogeneities of the electric field of the solvent molecules are fully included. We focus on the ground state and first excited singlet state properties of C151, C35 and C153, three aminocoumarins for which a homogeneous set of experimental data is available. Our approach is able to give quantitative information on the redshifts in water and acetonitrile, two solvents which show different H-bonding properties. In addition, it is able to quantify the effects of chemical substituents, such as the spectral redshift due to the increased alkylation at the amino position.

Keywords: aminocoumarins, solvent effects, TDDFT, spectral shifts
Introduction

The 7-aminocoumarins represent an important class of organic compounds with extensive and diverse applications\textsuperscript{1-3}. They possess distinct biological activity\textsuperscript{4} and have been indicated as agents with potential anticancer, antibiotic and anticoagulant activity. However, the main reason for their popularity lies mostly in their excited state properties. They exhibit a strong fluorescence in the visible region (from 350 nm to 500 nm), which makes them suitable for use as laser dyes and non-linear optical chromophores. More recently, they have been exploited to monitor the enzymatic activities of several classes of proteases\textsuperscript{5}. In the latter case, they are linked to specific peptide recognition sequences and the enzymatic proteolysis induces changes in the substrate emission wavelength allowing a determination of the enzymatic activity. However, the domain of application of these compounds is hampered by a variety of factors since the spectra are affected by temperature and protein environment, and a thorough understanding will be needed for the design of highly optimized compounds for specific applications. In particular, full understanding of the spectral properties of coumarins is of crucial importance for the design of new and more efficient substrates acting as fluorescence probes.

The solvation behavior of coumarins has also attracted great interest. Aminocoumarins exhibit a strong solvatochromism resulting from a substantial increase of the dipole moment when going from the ground to the excited state. This causes a redshift in both the absorption and the fluorescence spectra, which is a function of the solvent polarity. Moreover, the interactions between the excited solute and solvent dipoles dominate the subsequent relaxation phase and are responsible for a complex reorganization dynamics.

Several experimental studies using time-resolved emission methods, such as fluorescence spectroscopy\textsuperscript{6-13} or UV photoelectron spectroscopy\textsuperscript{14}, have permitted to measure and resolve in time the emission redshift for solvents of different polarity. In particular, Gustavsson and coworkers have given a description of the fluorescence spectra on the femtosecond time scale\textsuperscript{8}.

The optical properties of coumarins in the gas phase have been described by several theoretical studies, performed with both semi-empirical\textsuperscript{14-17} and ab initio methods\textsuperscript{10;18;19}. Some facts have been established so far by these studies: (i) the transitions, which are responsible for the luminescent properties, are $S_0 \rightarrow S_1$ transitions; (ii) the nature of the excitation is a $\pi-\pi^*$ excitation, involving a charge displacement, with an increased charge density on the carbonyl and a correspondent depletion at the ring oxygen. In particular, the
first excited state \( S_1 \) has a large dipole moment, highly enhanced with respect to the ground state and resulting from the electron donor nature of the amino-group. (iii) Electron donor substituents (e.g. amino or methoxy groups) in position fifteen or seven, respectively (see numbering in Chart 1) induce redshifts of the longest wavelength absorption maxima and are responsible for an enhancement of band intensity. In fact electrons donors in position 7 extend the \( \pi \)-electron conjugation while substituents in position 15 increase the electron acceptor strength with the global effect of increasing the charge displacement which stabilizes the excited state \( S_1 \).

The optical properties of coumarins in polar and apolar solvents have also been extensively studied using continuum models \(^7\text{;}^{18,20-23}\). Considerations based on continuum theory or the mean spherical approximation (MSA) have given a first theoretical insight into the contribution of the solvent interaction to the solvation response \(^24\). An overall correlation is found between the steady state absorption wavelength and the reaction field as calculated from dielectric continuum theories for polar solvents, even if significant deviations occur in the case of aromatic solvents \(^22\) where the solvent response is dominated by the solvent quadrupole moment.

As previously pointed out, the inhomogeneities of molecular interactions plays an important role in the solvation behavior \(^20,23,25-28\). In particular, Cave and coworkers \(^18\) showed that for coumarin C151 a continuum model description of the solvent tends to overestimate the excitation energies, in particular for protic solvents, suggesting the presence of specific H-bonding effects.

Here, we address this issue by combining a detailed first-principles description of the solute, with a molecular dynamics description of the solvent. A classical treatment of the solvent has revealed itself a helpful tool to understand solvent and solvent-mixture behavior \(^25-30\). The method used here is hybrid Car-Parrinello quantum-mechanical /molecular mechanical (QM/MM) approach, in which the solvent is treated with a classical force field and the ground state potential energy surface and the excitation energies of the solute (aminocoumarins) are described within density functional theory (DFT) and time dependent (TD) DFT, respectively. In the latter case, linear response theory together with the adiabatic approximation to the exchange and correlation functionals allow for a calculation of the excited states. Such a TDDFT/MM treatment is expected to be adequate for cases where the excited state is strictly localized on the solute (QM part restricted to solute) or near the solute (inclusion of the first solvent shell in the QM part). Such an approach can probe the direct influence of chemical substituents and of the polar solvation. Moreover it can also take into account solvent electric field inhomogeneities and the explicit effects of H-bonding, which are
e.g. not included in a continuum solvent model. In fact, this approach has been demonstrated to successfully reproduce the optical properties of acetone in water\textsuperscript{31}.

Here, calculations are carried out on three selected aminocoumarin derivatives in vacuo and in two solvents with comparable dipole moments, but different H-bond donor/acceptor properties, namely water and acetonitrile (ACN). For these systems a homogeneous set of time resolved absorption and fluorescence spectra have been reported\textsuperscript{8}. These compounds are 7-amino-4-trifluoromethylcoumarin (C151), 7-diethylamino-4-trifluoromethylcoumarin (C35) and a rigidified aminocoumarin with a julolidine moiety (C153) (Chart 1). Because C153 exhibit different conformations of the aliphatic ring sharing the nitrogen, four conformers (C153s, C153s2, C153a and C153a2, see Chart 2) are considered. These correspond to two possible syn and anti conformations, respectively (which differ in the conformation of the saturated ring sharing the nitrogen). The presence of at least two of them has been detected experimentally\textsuperscript{16}.

These compounds differ from each other in several properties, such as the number of internal degrees of freedom, dipole moments, and capabilities for H-bond formation with the solvent. In particular, C35 and C153 are acceptors of H-bonds, while C151 is both acceptor and donor. All the three coumarins may accept H-bonds at the nitrogen lone pair and the carbonyl group from H-bond donating solvents, but only C151 may establish such bonds with H-bond acceptors via the two H-atoms on the amino-group.

Our QM/MM approach turns out to describe accurately the solvent inhomogeneities and to reproduce solvent induced redshifts on the absorption spectra for all three coumarin dyes, in good agreement with the experimental data. Thus, this methodology opens the way to the treatment of more complex environments, such as chromophores in a protein environment.

\section*{Methods}

\textbf{Ground state properties of the molecules in gas phase.} Geometry optimization in vacuum for C151, C35, C153s C153s2, C153a and C153a2, was performed in the ground state within a standard DFT approach, using gradient corrections due to Becke\textsuperscript{32}, Lee, Yang and Parr\textsuperscript{33} (BLYP), a plane wave basis set up to a kinetic energy cutoff of 70 Ry and norm-conserving Troullier-Martins (TM) pseudopotentials\textsuperscript{341}. The molecules were treated as isolated systems using the Poisson solver by Martyna and Tuckerman to decouple periodic images\textsuperscript{35}. Energy minima were defined with a residual maximal nuclear gradient norm of

\textsuperscript{1} Pseudopotential parameter description.
\textsuperscript{2} Atom type r = \texttt{pseudopotential/O1.2\textsuperscript{Kleiman-Bylander}S nonlocal, P localN1.2\textsuperscript{Kleiman-Bylander}S nonlocal, P localH1.2\textsuperscript{Kleiman-Bylander}S localC1.2\textsuperscript{Kleiman-Bylander}S nonlocal, P localF1.2\textsuperscript{Kleiman-Bylander}S nonlocal, P local
10⁻⁵ a.u. using a direct inversion of the iterative subspace algorithm (DIIS). Cubic boxes of edges 17, 18 and 18 Å edges were used for C151, C35 and C153, respectively. Dipole moments were calculated from the electronic density and nuclear positions and their values were checked for convergence with respect to increasing box size. Kohn-Sham orbitals were calculated for the optimized ground state geometry. To estimate finite temperature effects on the dipole moment, a 5 ps molecular dynamics run at 300 K was performed for C151 in vacuum, with a time step of 6 a.u. and temperature control with a Nose–Hoover thermostat. The dipole moment for C151 at 300 K has been estimated as average over ~75 snapshots along this MD trajectory.

Absorption spectra for the lowest excited singlet state were calculated for C151, C35 and C153a with TDDFT within the Tamm-Dancoff approximation. Within this approach the interacting system in a time-dependent external field is mapped exactly to a non-interacting time-dependent Kohn-Sham (KS) system with the same time-dependent density. If a weak time-dependent electrical field is considered, this leads to a Dyson-like response equation for the exact susceptibility of the interacting electronic system. Poles of this susceptibility occur at the true transition frequencies. TDDFT in general yields excitation energies and properties in good agreement with experimental values. Calculations were performed with the program package CPMD 3.5. In analogy to the ground state calculations, the BLYP DFT functional and TM pseudopotentials were used.

**QM/MM Car-Parrinello calculations in different solvents.** Solvent effects were determined as average values of the absorption spectra over snapshots from a QM/MM trajectory. Calculations were carried out in ACN for all three molecules and in water solution for C151 only, as the other molecules are not soluble in water. The optimized structure for each of the coumarins has been immersed in a solvent box and equilibrated with constant temperature and constant pressure (NTP) classical MD.

Specifically, C151 was immersed in a box of 46.1 X 41.6 X 45.6 Å³ containing 1046 ACN molecules; C35 in a box of 46.5 X 46.0 X 45.4 Å³ containing 1166 ACN molecules and C153 in a box of 46.9 X 42.3 X 46.9 Å³ containing 1106 ACN molecules. In all three cases, the resulting ACN density after temperature and pressure equilibration is 0.76 g/cm³, in agreement with the experimental data. For C151 a water box of 45.5 X 40.5 X 44.7 Å³ containing 2711 molecules was used, with a resulting density after temperature and pressure equilibration of 1 g/cm³. Initially the systems were equilibrated performing 500 ps of purely classical NPT molecular dynamics at 300 K using a time step of 1.5 fs. The solvent molecules are treated with rigid
bond constraints (Shake algorithm\textsuperscript{45}). Particle mesh Ewald (PME\textsuperscript{46,47}) was used for the treatment of the electrostatic interactions. The TIP3P\textsuperscript{48} and ACN models from ref\textsuperscript{44} were used for water and acetonitrile force field, respectively. The ACN model is a three atom model with a united atom representation of the methyl group (C\textsubscript{3}ACN).

The purely classical equilibration was followed by mixed QM/MM simulations, performed in the ground state, in which the aminocoumarin was considered at the quantum mechanical level (DFT). The electrostatic interactions between the QM and the neighboring MM atoms is taken into account by a Coulomb potential modified at short range in order to avoid spurious overpolarization effects. The electrostatic interaction between the QM system and the more distant MM atoms (here a cutoff of 10 a.u. around each QM atom is used) is modeled by coupling the multiple moments of the quantum charge distribution with the classical point charges. The steric interaction between QM and MM part is modeled by a Lennard-Jones potential as described by the AMBER\textsuperscript{48} force field. Details of the mixed QM/MM Car-Parrinello simulation method are given in Refs \textsuperscript{43,49}. For each of these simulations an overall simulation time of 5 ps with a time step of 6 a.u. was performed.

Dipole moments of all coumarins were calculated in solution starting from the electronic density distribution as average of \textasciitilde 120 snapshots taken at equal time intervals over a 5 ps trajectory.

For the analysis of the solvation shell effects, radial distribution functions (RDFs) were calculated. Dynamical fluctuations of the electric field were estimated through the cross-correlation function C\textsubscript{ij} of the electric field vectors E\textsubscript{i}(t) and E\textsubscript{j}(t) acting on the atoms i and j, C\textsubscript{ij}= E\textsubscript{i}(t) * E\textsubscript{j}(t) /(|E\textsubscript{i}(t)| |E\textsubscript{j}(t)|).

The vertical excitation energies were calculated for C151, C35 and C153 in ACN and for C151 in WAT within the TDDFT/Tamm-Dancoff approach as average values over \textasciitilde 120 snapshots taken at equal time intervals over a trajectory of 5 ps. Average values and root mean square deviations (rms) deviations were calculated for all the simulations and compared with the experimental values.

**Results and Discussion**

**Calculations in vacuum.** The geometries of C151, C35, C153s, C153s2, C153a and C153a2 were optimized in the ground state. The four different conformations for C153 are characterized in Table 1 by the sequence of torsional angles for the two rings lobes of the joulidine group. The anti conformer C153a has the
lowest energy; however, the difference among the ground state energies of the four conformers turns out to be only about 1 kcal/mol (see Table 1).

The coumarin dipole moment increases from 7.1 up to 8.4 Debye with the alkylation at the amino group, passing from C151, to C35 and C153 (Table 2, column 1). The calculated relative shifts turn out to be in quantitative agreement with experimental measurements\(^{30}\).

The absolute value of the coumarin dipole moments on the other hand is overestimated. Previous studies on C151, on the basis of various methods (TDDFT/B3LYP, CIS, MCASPT2, and ZINDO SC), suggested that experimental estimates may be too low, or may represent a thermally averaged geometry in which rotation about the amine-ring bond could lead to a significant lowering of the ground state dipole moment as compared to the equilibrium geometry\(^{18}\).

The latter proposal was tested by carrying out Car-Parrinello MD at 300 K of C151. The large value of the fluctuations of the torsional angle of the amine group with respect to the ring plane (175±20 degrees) shows that the rotation about the amine-ring bond is possible. However, the resulting dipole moment is (6.5±0.6) Debye, that is only 0.5 Debye lower than the dipole moment of the optimized structure. Thus, even this temperature correction to the dipole moment cannot account completely for the discrepancy with the experimental value.

We now turn our attention to the electronic structure. As expected, in all cases, the HOMO-1, HOMO, LUMO and LUMO+1 orbitals have \(\pi\) character. The HOMO-1 can essentially be described as a \(\pi\) orbital localized on the aromatic rings. The HOMO is mainly localized on the nitrogen atom and on the \(\pi\) system of the two coumaric rings and partially on the acceptor group, whereas the LUMO is dominated by contributions on the acceptor part (see Fig. 1). Thus, upon HOMO-LUMO excitation, the charge on the amino group is transferred to the carbonyl group. As effect of the sigma-donation, the charge displacement appears more pronounced as the alkylation degree on the nitrogen increases. Our results are in accord with the widely accepted picture of a sizeable charge displacement connected to the first (HOMO - LUMO) excitation. In particular, in the case of C153, our results are in agreement with previous DFT calculations in vacuum\(^{10}\).

The vertical excitation energies to the first four singlet states of C151, C35, C153s and C153a were calculated with TDDFT / BLYP (Table 2) on the geometry-optimized structures.

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\(^{30}\) Reference number.

\(^{18}\) Reference number.

\(^{10}\) Reference number.
In the first excited singlet state (corresponding to the HOMO-LUMO excitation), C151 has the highest absorption energy of 3.32 eV, while increasingly lower values are found for C35 (2.99 eV) and for C153 (2.91 eV and 2.90 eV, respectively for the anti and syn conformers C153a and C153s). The calculated absorption spectra indicate an increasing red shift with increasing degree of alkylation of the amino group (C151<C35<C153) as also found experimentally. The calculated substituent shifts with respect to C151 (Table 2, column 2, values in parenthesis) turn out to be 0.33 and 0.41 eV for C35 and C153a, respectively, and are in very good agreement with the experimental data (0.33 and 0.45 eV for C35 and C153, respectively) (Table 2, column 3, values in parenthesis).

**Calculations in water and ACN solution.** Subsequently, we considered the properties of coumarins in solution of water and ACN. In the case of C153, only the C153a conformer was considered in solution, since the calculated excitation spectra in vacuum gave similar results for all the conformers.

The solvation structure was analyzed in terms of different RDFs (Fig.2 for the three coumarins in ACN solution and Fig. 3 for a comparison of water and ACN solution in the case of C151). The resulting RDFs are rather noisy due to the relatively short simulation time which is accessible with a first-principles based approach.

In ACN, the substituents at the amino group produce a shift in the maximum peak of the RDFs N-C$_3^{ACN}$ (the distribution of C$_3^{ACN}$ atom around the N atoms) of C35 and C153 due to the bulky diethyl and julolidine groups. The substituents at the amino group increase the nucleophilicity of the carbonyl oxygen O$_4$ in C35 and C153, as it appears in the increased weight of the first peak in RDF O-C$_3^{ACN}$ (C$_3^{ACN}$ distribution around O). Spherical integration of this peak up to 3.5 Å yields coordination numbers of 1.7, 2.1 and 2.3 for C151, C35 and C153, respectively, which indicate an increase of the ACN coordination around the carbonyl oxygen with increasing alkylation at the amino position. For C153, where a comparison with previously published data is possible, our results are in accord with Ref. 28.

In the case of C151, the effects of different solvents (water and ACN) can be compared (Fig. 3). In the RDF N-C$_3^{ACN}$, the maximum peak is shifted towards larger radial distances respect to the corresponding maximum peak in the RDF N-O (the distribution of water oxygens around the N atom in water solution) (Fig. 3a), possibly because of the presence of the spherically more demanding methyl group of ACN, instead of the water. This effect is also evident when comparing the RDF O$_4$-C$_3^{ACN}$ with the RDF O$_4$-O (the distribution of water protons around the carbonyl oxygen atom in water solution) (Fig. 3b). In the case of water solvation a direct H-bond is established between carbonyl oxygen O$_4$ and the water protons, while in the case of ACN...
solvation, the slightly positive charged (\(C_3\)ACN charge = 0.15) methyl group of ACN cannot approach as close to \(O_4\), and the maximum peak in the RDF \(O_4-C_3\)ACN is shifted towards higher values of the \(O_4-C_3\)ACN distance.

The solute-solvent electrostatic interactions were also analyzed in terms of the MD-averaged electric (reaction) field at the atomic sites. (In Fig. 4 the reaction field at the single atomic positions is reported for the three coumarin structures; left: C151 (top), C35 (middle) and C153 (bottom)). Average values are calculated for ~ 120 snapshots, over 5 ps trajectory. The polar nature of all three solutes determines a solvent polarization, which tends to compensate the electric field of the solute. Our simulations show that such a field is not homogeneous across the solute (Fig. 4) and in particular there are large inhomogeneities between the donor and acceptor ends, with a stronger polarization at the former. A possible rationalization for this effect can be provided by considering that ACN can form stronger H-bonds at the amino group, but weaker H-bonding contacts at the carbonyl group, through the -CH\(_3\) group. A measure of the field inhomogeneity over the solute molecule can be provided by calculating the electric field cross correlation for couples of reaction field vectors at different atomic positions. In particular, in Table 3 the average value of these quantities has been reported as a function of time for pairs of nearby atoms (3/4, 15/20) and pairs of atoms at the opposite ends of the solute molecule (20/4, 20/5). For couples of nearby atoms the electric field fluctuations are strongly correlated and the average value of the cross correlation is in the range of 0.7-0.9 (Table 3), while for couples of atoms at the opposite ends of the solute molecule, the electric field fluctuations are only weakly correlated, with an average value of the cross correlation around 0.2-0.3 (Table 3). The correlation coefficient shows a similar behavior for all coumarins (C151, C35 and C153) in ACN.

For coumarin C151, we compare ACN and WAT solvation. Water produces a stronger reaction field around the solute. In particular this field has, on average, a stronger dipolar behavior (see Fig. 5) with respect to the one of the ACN. This is mostly due to the stronger solvation at the \(O_4\) position. For WAT, correlation between the solvent electric field at the opposite ends of the molecule is higher than for ACN, also for pairs of atoms at the opposite ends of the solute molecule (see Table 3). The sizeable dynamical electric field inhomogeneities that we find support the use of a molecular solvent (QM/MM) approach and the choice of our simulation protocol to explicitly include H-bonding which cannot be treated within a continuum solvent approach.

Dipole moments in solution were compared for all the coumarins with the corresponding values in vacuum. For C151 in ACN the average value (9.4±1.0 Debye) is highly enhanced with respect to the vacuum
calculation (6.5±0.6 Debye). In the same way, also the dipole moments of C35 and C153 increase and their average values over the simulations turn out to be 10.5±1.4 Debye and 13.7±1.7 Debye, respectively. Effects of the ACN polarization are more pronounced for the more rigid C153, whose dipole shift with respect to vacuum reaches 4.3 Debye. Water solvation produces a stronger effect on coumarin C151 with respect to ACN. In particular for C151 the dipole moment in water turns out to be 15.3±1.5 Debye. The higher dipole moment with respect to ACN solvation can be explained with the stronger H-bond network around the solute, and in particular around the CO group as indirect effect of the increased alkylation degree of the amino group in C153.

Average absorption spectra in WAT and ACN indicate that the solvent produces a redshift in the absorption of the three coumarins with respect to the vacuum values. Both solvents cause quite a similar absorption shift in the case of C151, in agreement with the experimental data\(^8\). Averages and rms deviations for the absorptions are reported in Table 4. As for the vacuum spectra, also for the solution case the calculated absolute values are slightly underestimated, however the calculated relative redshifts with respect to the vacuum are in very good agreement with the experimental values of ref\(^8\).

Fluctuations of the absorption gap around the average values along the QM/MM trajectory can be related to the dynamical changes in electrostatic properties of the systems. The correlation coefficient between the electrostatic potential value due to the solvent and the absorption gap is reported for each atom in Fig. 6. It is always negative at the carbonyl end (atom numbers 3,4,5,6; numbering according to Chart 1), while it is positive at the amino end (atom numbers 20,21,22; numbering according to Chart 1). This means that changes in the solvent electric potential have opposite effects on the two ends of the molecule, as it can be expected since the absorption gap is related to a charge displacement between the two ends of the molecule.

The dipole moment in solution can be used as a direct measure of the global external electrostatic field in solution. Interestingly, an anticorrelation between the coumarin dipole moment and the absorption gap is found. In particular, an increase of the dipole moment (related to an increase of the external field) is associated with a redshift of the absorption gap. Higher correlation values are found for C151 and C35 in ACN, while a lower value is found for C153 in ACN (values for correlation coefficients are reported in Figure 7).
However, for C151 in water, the dipole-absorption correlation is not very pronounced. In this case, a description of the solvation effect in terms of only the dipolar field is not sufficient to explain the fluctuations of the absorption gap as consequence of the environmental changes. In other words, this means that the atomic positions which mostly influence the absorption gap are not the main contribution to the coumarin dipole moment. In particular, water solvation enhances the contribution of the carbonyl end to the dipole moment. However, the increased polarization at the carbonyl end does not result in the same enhancement of the redshift of the absorption gap. For this reason, even a higher dipole moment in WAT, does not necessarily correspond to a larger redshift in the absorption gap.

Conclusions

Our QM/MM method, which has given good results for the description of ground state systems, is also providing a useful description of the environment effects on excitation energies.

The accuracy in reproducing the solvent shift on the optical spectra has been shown for a test case (acetone) in a previous paper. Here, we present more complex systems, coumarin derivatives, in which effects of the chemical substituents on the solute and the solvent effects are combined. In particular, our calculations reproduce the redshift due to water and ACN solvation, providing a good agreement with previously published experimental data.

We find that the dipole moment of these compounds increases in solution. The interaction of this induced dipole with the solvent, along with induced higher moments, increases the absorption redshift with respect to vacuum transition energies. However absorption spectra are not only determined by the dipolar contribution coming from the external-solvent field. When effects of solvation in ACN and water are compared in the case of C151, we find that correlation between the coumarin dipole moment and the absorption gap is less important in water than in ACN.

Thus, our method turns out be accurate enough to reproduce both substituent and solvent effects on the optical properties of coumarins. We believe that our TDDFT/MM approach can be extended to more complex environments, such as chromophores in a protein environment and can have also practical applications for the design of compounds with tailored optical properties.

Acknowledgments We acknowledge the allocation of computer resources from INFM Progetto Calcolo Parallelo. Calculations have been carried out on the IBM SP4 at CINECA, Italy.
Reference List


42. CPMD code by J. Hutter et al., MPI für Festkörperforschung and IBM Zurich Research Laboratory 1995-2002.

Table 1

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Table 2

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Table 3

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<td>C35 ACN</td>
<td>0.87</td>
<td>0.79</td>
<td>0.32</td>
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<td>0.88</td>
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<tr>
<td>C151 WAT</td>
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<td>0.87</td>
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Table 4

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<tr>
<th>Compound</th>
<th>GS dipole moment (Debye)</th>
<th>ΔE1 (ACN)</th>
<th>ΔE1′′ (ACN)</th>
<th>ΔE1 (ACN)-ΔE1 (vacuum)</th>
<th>ΔE1 (ACN)-ΔE1 (hexane)</th>
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<tr>
<td>C151</td>
<td>9.4 ±1.0 (2.3)</td>
<td>3.10 ±0.08</td>
<td>3.48</td>
<td>0.22</td>
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<td>C35</td>
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<td>2.85 ±0.08</td>
<td>3.19</td>
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<td>0.18</td>
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<td>C153a</td>
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<td>2.99 ±0.10</td>
<td>3.48</td>
<td>0.33</td>
<td>0.22</td>
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Table Captions

Table 1 Torsional angles in the optimized structures for the four conformers of C153 in vacuum (columns 1 to 4). The numbering scheme is given in Chart 1. Ground state energy differences with respect to conformer C153a (last column) in kcal/mol.

Table 2. Selected electronic properties for coumarins C151, C35 and C153a and C153s optimized structures in vacuo. In the first column the ground state dipole moments are reported (Debye). In the second column the first singlet absorption energies are given (eV). In the third column the experimental value for the absorption from ref. 8 are reported (eV). For both the second and the third columns the values in brackets are the red shift with respect to the C151 value (eV). In the fourth, fifth and sixth columns, the second, third and fourth singlet state absorptions are reported, respectively (eV).

Table 3 Electric field cross-correlation for selected pairs of atoms. In particular, correlation between pairs of nearby atoms (3/4, 15/20) and atom pairs located at opposite ends (20/4, 20/5) are presented for comparison. Numbering scheme is given in Fig.6.

Table 4 Solution properties for coumarin C151, C35 and C153a. First column: ground state dipole moments (Debye) (average values and standard deviations), in brackets the difference with respect to the ground state values is reported (Debye); second column: calculated absorption energy (average values and standard deviations). Third column: experimental value for the absorption spectra from ref. 8. Fourth column: red shift values for the absorption gap with respect to the structures optimized in vacuo. Fifth column: experimental red shift for the absorption gap with respect to hexane from ref. 8.
Figure Captions

**Figure 1** Chemically active orbitals for C151, C35, C153a and C153s in vacuum. In white the positive phase of the wavefunctions (the isosurfaces are drawn at a value of $5 (\text{a.u.})^{3/2}$), in black the negative phase of the wavefunctions (the isosurfaces are drawn at a function value of $-5 (\text{a.u.})^{3/2}$) are reported.

**Figure 2** Radial distribution functions (RDFs) in ACN. (a) RDF between atom N and the methyl group carbon atom of ACN ($C_3^{\text{ACN}}$) for C151 (continuum line), C35 (dotted line), C153 (dash-dotted line). (b) RDF between atom $O_4$ and $C_3^{\text{ACN}}$ for C151 (continuum line), C35 (dotted line), C153 (dash-dotted line). The numbering is according to Chart 1.

**Figure 3** Radial distribution functions (RDF) in water and ACN (dotted line) for C151 selected atoms. (a) RDF N-X. In water solution, X stands for O and RDF N-O represents the radial distribution function between atom N and the water oxygens (continuum line); In ACN solution, X stands for $C_3^{\text{ACN}}$ and RDF N-X represents the radial distribution function between atom N and $C_3^{\text{ACN}}$ (dotted line). (b) RDF $O_4$-X. In water solution X stands for O and RDF $O_4$-O represents the radial distribution function between atom $O_4$ and the water oxygens (continuum line); In ACN solution X stands for $C_3^{\text{ACN}}$ and RDF $O_4$-X represents the radial distribution function between atom $O_4$ and $C_3^{\text{ACN}}$ (dotted line).

**Figure 4** Average direction and magnitude of the electric field generated by ACN at the positions of the C151 (a), C35 (b) and C153 (c) atoms. The average is over ~120 snapshots along a trajectory of ~5 ps. The direction of the dipole moment is reported as dashed line.

**Figure 5** Average direction and magnitude of the electric field generated by the water at the positions of the C151 atoms. The average is over ~120 snapshots along a trajectory of ~5 ps.

**Figure 6** Correlation coefficients between the absorption gap and the electrostatic potential on the atomic positions as function of the atom numbers. (a) Correlation coefficients for C151 (grey), C35 (black) and C153 (white) in ACN. (b) C151 in ACN. Correlation coefficients between the absorption gap and the electric field at
the atomic positions (white boxes); correlation coefficients between the solute dipole moment and the electric field at the atomic positions (black boxes) (c) C151 in water. Correlation coefficients between the absorption gap and the electric field at the atomic positions (white boxes); correlation coefficients between the solute dipole moment and the electric field at the atomic positions (black boxes). The atom numbering is according to Chart I.

Figure 7 Correlation plot between the absorption gap (x axis) and the dipole moment of the solute in solution (y axis). (a), (b) and (c) represent correlation plots for C151, C35 and C153 in ACN, respectively.
Chart 1
Chart 2
<table>
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<tr>
<th></th>
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Figure 2

(a) RDF N-\text{C}^{\text{ACN}}_3 (Å)

(b) RDF O-\text{C}^{\text{ACN}}_3 (Å)
Figure 6
Figure 7

(a) Dipole moment vs. absorption gap for C151 (Debye) with correlation coefficient R = 0.61.

(b) Dipole moment vs. absorption gap for C35 (Debye) with correlation coefficient R = 0.74.

(c) Dipole moment vs. absorption gap for C153 (Debye) with correlation coefficient R = 0.35.