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Solvent effect on indocyanine dyes: A computational approach

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Abstract

The solvatochromic behaviour of a series of indocyanine dyes (Dyes I–VIII) was investigated by quantum chemical calculations. The effect of the polymethine chain length and of the indolenine structure has been satisfactorily reproduced by semiempirical Pariser–Parr–Pople (PPP) calculations. The solvatochromism of 3,3,3′,3′-tetramethyl-*N*,*N*′-diethylindocarbocyanine iodide (Dye I) has been deeply investigated within the *ab initio* time-dependent density functional theory (TD-DFT) approach. Dye I undergoes *non-polar* solvation and a linear correlation has been individuated between absorption shifts and refractive index. Computed absorption λ_{max} and oscillator strengths obtained by TD-DFT are in good agreement with the experimental data.

Keywords: Cyanine; TD-DFT; PCM; PPP

1. Introduction

Due to their bright colours and strong fluorescence, cyanine dyes are one of the most interesting class of dyes and, in the last 10 years, have grown in importance especially for their application in biotechnology. They show a very versatile structure that can be modified in order to obtain the desired optical properties.

In order to be useful in biotechnological applications, fluorophores must satisfy some specific requirements: (a) chemical and photochemical stability, (b) solubility in aqueous buffer solutions, (c) high molar extinction coefficients coupled with, (d) high quantum yield, (e) suitable functional groups for bioconjugation, (f) low overlap with biomolecules autofluorescence. Fluorophores need to be resistant to light and to pH variation, giving a consistent optical information. The introduction of SO_3^- groups in different positions of the structure increases the solubility in aqueous buffer solutions. Cyanine dyes show an intrinsic high molar extinction coefficient ($1.1–2.5 \times 10^5$ cm^{-1} M^{-1}) and a good quantum yield (0.15–0.35) that can be further improved by stiffening the structure. The addition of specific reactive group, such as *N*-hydroxysuccinimidyl esters, maleimide, or phosphoramidite, makes the dyes suitable for the bioconjugation to proteins, hormones, nucleotides and biomolecules in general. A major problem to solve is to obtain a good signal, despite the biomolecules intrinsic fluorescence, which usually falls in the UV–Vis region. For this reason our research is moving towards the design of near-infrared dyes [1–3].

We believe that a proper computational method able to give reliable prediction of the dyes' spectroscopic properties would render synthetic efforts more effective. Moreover, in sensors technology and life science in general, a proper knowledge of the interactions between dyes and solvents, considering as solvent also a protein environment or a solid surface of the sensor device, would definitely bring

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enormous advantages. However, computational methods coupling reliability and ease of use are just being developed and their systematic adoption is still quite limited.

This work aims at predicting and rationalizing the absorption properties of a series of 8 indocyanine dyes with increasing length of the main π conjugated system (Fig. 1). A satisfactory prediction of the $\lambda_{\max}$ has been achieved through semi-empirical Pariser–Parr–Pople (PPP) method [4]. In the PPP method the mathematical formalism is the same as that of the Hückel MO method, but its accuracy is enhanced because of the inclusion of electron interaction effects. Moreover, the method has a geometry sensitivity which allows geometrical isomerism to be taken into account. A strict limitation of the method is that it cannot include σ-electron effects directly, although one can generally allow for these empirically, thus avoiding the greater parameter and computational complexity.

Time-dependent density functional theory (TD-DFT) was found to be a robust and accurate method to investigate large organic molecules, for the calculation of excitation energies and oscillator strengths [5] and has recently met a certain success in the investigation of charged/radical dyes which take into account bulk solvation effects [6–17]. In this work 3,3,3′,3′-tetramethyl-*N*,*N*′-diethylindocarbocyanine iodide (Dye I) was taken as a model to investigate the effect of the solvent upon absorption wavelengths ($\lambda_{\max}$) at the TD-DFT level, giving an excellent agreement between theory and experiment. Furthermore, CASSCF method was performed as a preliminary analysis of the vertical excited state.

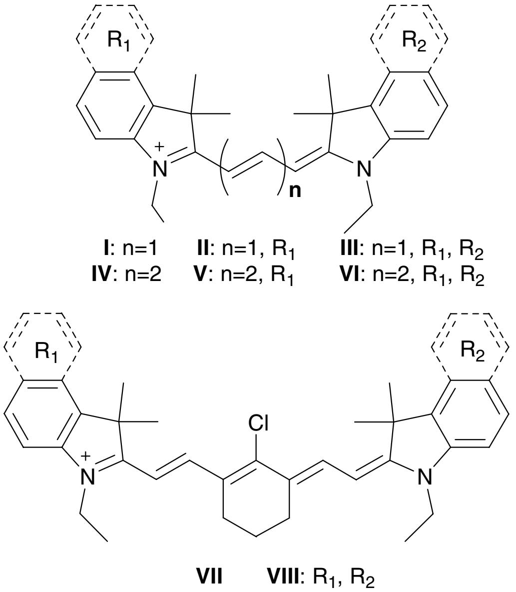

Fig. 1. Cyanine dyes structures (Dyes I, IV and VII do not contain a phenyl ring condensed with the indolenine ring, Dyes II and V contain a condensed phenyl ring on one of the indolenine rings, Dyes III, VI and VIII contain a condensed phenyl ring on each indolenine ring).

2. Experimental and computational details

Dyes I–VIII (Fig. 1) were synthesised in our laboratory, following the procedures listed in ref. 1–3. All the reagents were purchased from Sigma-Aldrich Italy. Absorption spectra were recorded by a Cary300 Varian UV–Vis spectrophotometer, using spectroscopic grade solvents.

Extinction coefficients at the absorption $\lambda_{\max}$ ($\varepsilon_{\max}$) were calculated from the slope of a Lambert–Beer plot. In order to compare calculated and experimental values more directly, oscillator strengths were determined from experimental absorption coefficients using the relation [5]:

$$f \approx 4.32 \times 10^{-9} \varepsilon_{\max} \Delta\omega_{1/2} \tag{1}$$

where $\varepsilon_{\max}$ is the experimental absorption coefficient ($M^{-1}cm^{-1}$) and $\Delta\omega_{1/2}$ corresponds to the halfwidth of the absorption band (cm^{-1}).

A standard PPP molecular orbital procedure was employed to investigate Dyes I–VIII, within the fixed β approximation. Electronic excitation energies were refined by a limited configurations interaction (CI) treatment involving the nine singly excited singlet configurations obtained by promoting an electron from the three highest occupied orbitals to the three lowest unoccupied orbitals. The parameters used (valence state ionisation potentials, resonance and electron repulsion integrals) were normally those compiled by Griffiths [4]. Standard bond lengths and angles were used in the computation whenever possible and literature values for β, the VSIP and the one-centre electron repulsion integral ($\gamma_{nm} = \mathrm{VSIP}_n - A_n$) were employed. Only certain parameters were reassessed by trial and error calculations, i.e. all the carbon atoms in heterocyclic nucleus and polymethine chains were considered as aromatic ones (C=C, Y = 1, $\beta_{nm} = -231.6$ kJ/mol, VSIP = 1076.8 kJ/mol, $A_m = 2.9$ kJ/mol); nitrogen atoms were considered equivalent and comparable to tri-arylmethane dye nitrogens (C–N, Y = 2, $\beta_{nm} = -265.3$ kJ/mol, VSIP = 1273.6 kJ/mol, $A_m = 687.0$ kJ/mol); chlorine was considered as substituent (C–Cl, Y = 2, $\beta_{nm} = -131.2$ kJ/mol, VSIP = 2248.0 kJ/mol, $A_m = 1206.1$ kJ/mol). Structures are assumed to be planar and configurations *all-trans*.

3,3,3′,3′-tetramethyl-*N*,*N*′-diethylindocarbocyanine iodide (Dye I) was taken as model molecule for a deeper investigation of the solvent effect at the TD-DFT level. TD-DFT method was applied within the adiabatic approximation. In this approach the excitation energies are determined from the linear response equations by solving the resulting non Hermitian eigenvalues problem by a modified Davidson algorithm as implemented in Gaussian03 [18,19]. The method is applicable to large molecules and it is known to work well for low-lying valence excited states with standard density functionals [19,20]. Several functionals have been tested in this work in order to set the optimal computational scheme, namely: the BLYP functional composed by the Becke exchange (B) [21] and Lee Yang and Parr (LYP) correlation functionals [22]; the Perdew and Wang (PW91) exchange-correlation functional [23]; the B3LYP, where