



*Dedicated to the memory of  
Professor Ioan Silaghi-Dumitrescu (1950 – 2009)*

## EXPERIMENTAL AND THEORETICAL STUDY ON THE PHOTOPHYSICAL PROPERTIES OF A PYRROLYL-ISOXAZOLE DERIVATIVE

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The paper aims at characterizing the excited state of a pyrrolyl-isoxazole derivative containing, apart from these two fragments with electron donor (D) – pyrrolyl – and acceptor (A) – isoxazole – character, a third one – methylenephthalidyl – having also an A character. They are single bonded in an A-D-A arrangement. It is shown that the presence of the second A fragment in the molecule modifies the photophysical properties comparing to D-A pyrrolyl-isoxazole derivatives: lower Stokes shift, band width practically independent on the polarity of the solvent, linear dependence of the Stokes shift on the solvent polarity function. The spectral study of the inclusion complex of the studied compound in  $\beta$ -cyclodextrin reveals a decrease in the emission intensity in the presence of cyclodextrin. These experimental findings are consistent with the lack of a twisted intramolecular charge transfer (TICT) excited state, which in turn is present for pyrrolyl-isoxazole derivatives of the D-A type. The lack of a TICT state is further ascertained by theoretical calculations of sections through the potential energy surfaces along both possible A to D rotation dihedrals. The stable conformations are quasiplanar, while the orthogonal conformations are unstable.

### INTRODUCTION

The literature data concerning pyrrolyl derivatives in which pyrrolyl is single bonded to another aromatic fragment have shown the twisted intramolecular charge transfer (TICT) nature of their first excited singlet state.<sup>1-5</sup> Such molecules contain two single-bonded fragments with donor (D, pyrrole) and acceptor (A, aromatic moiety) character. Due to the D→A intramolecular charge transfer occurring in the excited state, a twisted orthogonal conformation characterized by a large dipole moment is stabilized in polar solvents.<sup>6,7</sup> Inclusion of these non-rigid D–A molecules into cyclodextrins (CDs) may prevent the geometrical changes occurring in the excited state.<sup>8,9</sup> Therefore

information on the rotation of the D and A fragments around the joint  $\sigma$  bond can be also obtained from the study of the inclusion process of the molecule into CDs.

Our previous experimental and theoretical study on some pyrrolyl-isoxazole derivatives of the D-A type revealed that they are only weakly fluorescent, due to TICT state formation.<sup>10</sup> The present paper deals with another compound of this class, 5-(2'-(3-methylenephthalidyl)-pyrrolyl)-3,4-dimethylisoxazole (PPI) (Figure 1), for which there is the possibility of a free rotation about both the inter-ring bonds, but the charge distribution in both the ground and excited states is different, due to the methylenephthalidyl substituent, a second A fragment in the molecule. This determines an A-D-A

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fragment arrangement. It is known from the literature that a D-A-A structure can lead to an enhanced charge transfer character of the excited state.<sup>11</sup> We aimed to experimentally and theoretically characterize the photophysical properties and the nature of the excited state of the studied compound and to stress on the differences induced by the presence of a second A fragment in an A-D-A arrangement comparing to other known pyrrolyl-isoxazole derivatives of the D-A type.

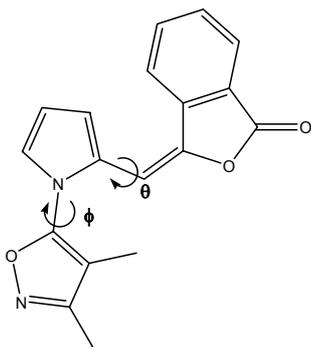


Fig. 1 – Structural formula of 5-(2'-(3-methylenephthalidyl)pyrrolyl)-3,4-dimethylisoxazole (PPI).

## RESULTS AND DISCUSSIONS

### Solvent effects on the photophysical properties of PPI

The photophysical parameters of PPI in solvents of different polarity are listed in Table 1. The  $S_0 \rightarrow S_1$  PPI absorption band is situated in the UV region (Figure 2A). The large molar absorption coefficients ( $\sim 10^4 \text{ M}^{-1}\text{cm}^{-1}$ ) and the bathochromic shift in polar solvents (from 358 nm in CHX to 368

nm in DMSO) reflect a  $\pi \rightarrow \pi^*$  character for this transition.

The bathochromic shift is much more pronounced in the case of the fluorescence emission peak, situated in the visible region of the spectrum. The fluorescence maximum lies in the interval 460–480 nm, depending on the solvent polarity (Figure 2B). The  $\pi \rightarrow \pi^*$  nature of the transition, correlated to the significant solvent effect observed, make us presume that the PPI molecule is submitted to charge transfer accompanying excitation. However, the magnitude of this charge transfer is not large, as the Stokes shift values are below  $7000 \text{ cm}^{-1}$ , even in polar solvents. The value in dioxane,<sup>10</sup> a non-polar solvent, for pyrrolyl-isoxazole derivatives of the D-A type is around  $9000 \text{ cm}^{-1}$ , whereas for PPI it is only  $6424 \text{ cm}^{-1}$ . It is considered that a charge transfer excited state yields Stokes shifts of around  $9000 \text{ cm}^{-1}$  and it can be as high as  $30000 \text{ cm}^{-1}$  for TICT forming compounds.<sup>3,12,13</sup> Furthermore, in the case of a TICT excited state a broadening of the fluorescence spectrum towards larger wavelengths should be observed in polar solvents, as a result of the stabilization of this state on the expense of the locally excited state. The full-width-at-half-maximum (FWHM) does not vary significantly with solvent polarity for PPI, as it is obvious from Table 1.

The experimental data show that the quantum yield increases in polar solvents. This is another argument to disfavor the TICT state hypothesis, because this non-fluorescent state should be stabilized in polar solvents and as a consequence the emission efficiency should decrease.

Table 1

The photophysical parameters of PPI in different solvents

No.	Solvent	$\lambda_a$ (nm)	$\epsilon$ ( $\text{M}^{-1}\text{cm}^{-1}$ )	$\lambda_f$ (nm)	$\Delta\nu_{Stokes}$ ( $\text{cm}^{-1}$ )	$\Phi$	FWHM ( $\text{cm}^{-1}$ )	$\tau_0$ (ns)
1	CHX	358	5719	457	6051	0.01	3696	–*
2	$\text{CCl}_4$	362	8012	461	5932	0.01	3708	–*
3	$\text{CHCl}_3$	365	18104	467	5984	0.06	3395	0.37
4	Dioxane	361	10826	469	6424	0.01	3499	–*
5	DCM	364	10917	472	6287	0.05	3462	0.42
6	Butanol	363	9939	475	6495	0.07	3331	1.36
7	Ethanol	362	14128	477	6660	0.11	3303	1.26
8	Methanol	360	14954	481	6987	0.08	3244	1.26
9	DMF	364	14862	477	6509	0.12	3428	0.65
10	$\text{CH}_3\text{CN}$	362	12324	477	6660	0.08	3431	0.76
11	DMSO	368	12875	482	6427	0.22	3328	1.51

Note: CHX = cyclohexane, DMF = dimethylformamide, DMSO = dimethylsulfoxide;  $\epsilon$  = molar absorptivity coefficient. \* - lifetime under the resolution of the device.

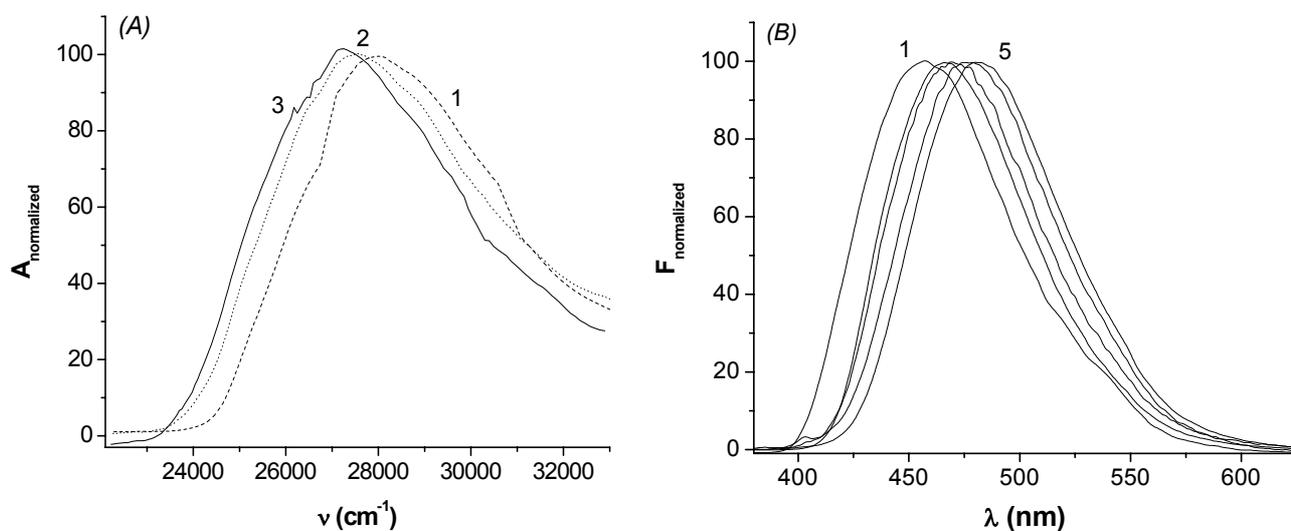


Fig. 2 – The normalized absorption spectra (A) (1-CHX, 2-DCM, 3-DMSO) and fluorescence spectra (B) (1-CHX, 2-DCM, 3-DMF, 4-Butanol, 5-DMSO) of PPI in solvents of different polarities.

The fluorescence decays were biexponential in all the solvents for which the lifetime fell within the resolution of the device ( $\tau > 0.1$  ns). The average lifetime rises with the polarity of the solvent.

The dependence of  $\nu_f$  and  $\Delta\nu_{Stokes}$  on the bulk polarity function of the solvent was studied by means of the Lippert-Mataga and Reichardt-Dimroth models (Figure 3). The corresponding linear regression data, as well as the values for the change in the dipole moment of PPI molecule upon excitation, evaluated from the slopes of these plots, are listed in Table 2. These values vary in the interval 3.4–4.8 D and, although they are consistent with the existence of a charge transfer in the excited state, they are smaller than the ones

obtained for TICT forming compounds.<sup>13-15</sup> There are no deviations from the linear behavior in polar protic solvents, indicating the presence of only one excited state.<sup>14</sup> As regards the Kamlet-Taft model, the experimental fluorescence maxima were plotted against the calculated ones in Figure 3C and the regression equation is given as an inset. It shows that the most important contribution to the solute–solvent interaction is the polarization one (the  $p$  coefficient is larger than  $a$  and  $b$ , which have similar values). The contribution from the overall interaction is of 61.4% for polarity *vs.* 19.9% and 18.7%, for H bond formation in which the solvent acts as a donor and acceptor, respectively.

Table 2

Linear regression data for the plots of Stokes shift *vs.* solvent polarity function and the calculated variation of the dipole moment of PPI upon excitation ( $\Delta\mu$ )

Model	Equation	Slope (absolute value)	R	$\Delta\mu$ (D)
Lippert-Mataga	$\nu_f = f(F(\epsilon, n))$	3326±395	0.961	–
	$\Delta\nu_{Stokes} = f(F(\epsilon, n))$	2555±514	0.856	4.81
Reichardt-Dimroth	$\Delta\nu_{Stokes} = f(E_T^N)$	1234±295	0.863	3.35

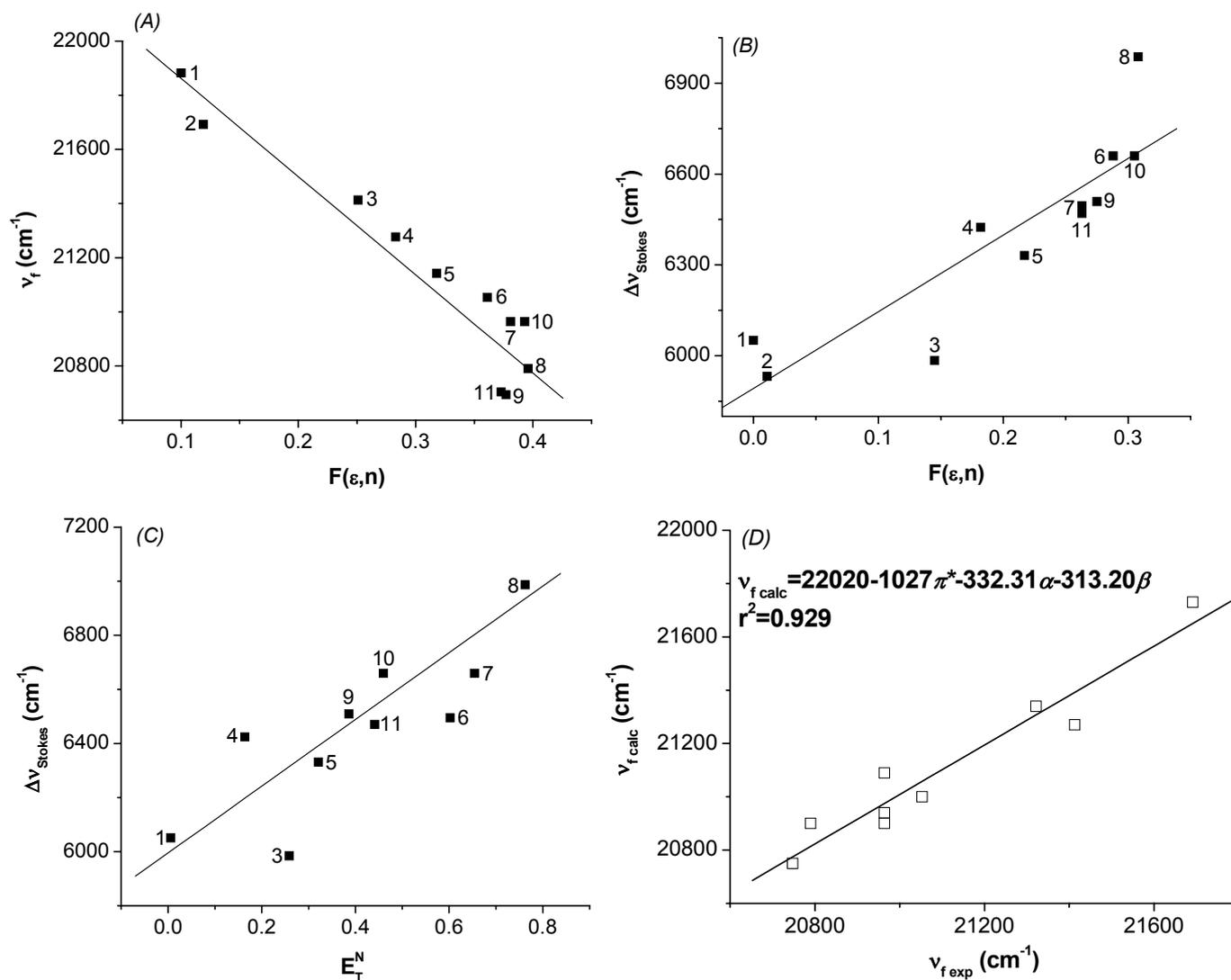


Fig. 3 – Plots of the fluorescence wavenumbers or Stokes shifts vs. the solvent polarity functions in the Lippert-Mataga (A, B) and Reichardt-Dimroth (C) models. The solvents are noted as in Table 1. (D) Plot of the calculated vs. experimental fluorescence wavenumber of PPI in different solvents in the frame of the Kamlet-Taft model. The regression equation is given as inset.

### Study of PPI- $\beta$ -CD inclusion complex

It is known that inclusion of a TICT state forming compound into the cavity of a CD hinders the free rotation around the  $\sigma$  bond. That means an increase of the fluorescence intensity, as the TICT state is non-fluorescent in nature, and, on the other hand, a blue shift of the CT band, due to the hydrophobic cavity.<sup>13,16</sup>

The steady-state fluorescence data have shown that PPI and  $\beta$ -CD indeed form an inclusion complex. Addition of  $\beta$ -CD to the PPI solution

results in the decrease of the fluorescence intensity and the association constant ( $K$ ) of the 1:1 host (CD)-guest (PPI) complex is determined by way of equation (6) to be  $K = 8893.3 \pm 2031.0 \text{ M}^{-1}$  in water-methanol,  $R^2 = 0.965$ . The wavelength of the fluorescence maximum of the complex corresponds to the value obtained for PPI in the neat solvent (Figure 4). These two observations are consistent with the lack of the TICT excited state.

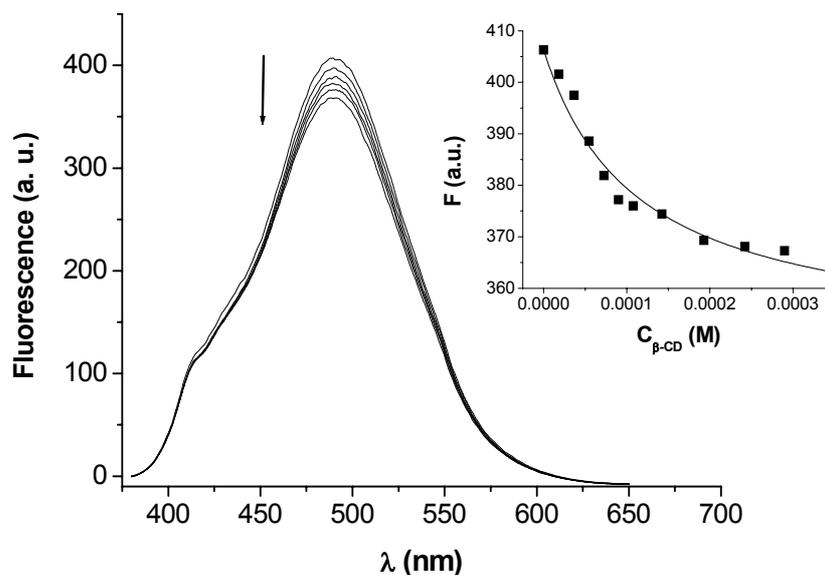


Fig. 4 – Fluorescence spectra of PPI in water:methanol 9:1 in absence and presence of increasing amounts of  $\beta$ -CD. Inset: plot of the fluorescence intensity of complexed PPI vs.  $\beta$ -CD concentration according to Eq. (6).

### Theoretical results

The nature of the first excited singlet state was investigated by performing in vacuo molecular orbitals calculations. The possibility of rotation of the isoxazole and methylenephthalidyl moieties with respect to the pyrrolyl-isoxazole and pyrrolyl-methylenephthalidyl bonds, respectively, was discussed in terms of sections through potential energy surfaces (PESs).<sup>17,18</sup> The most stable conformations of the molecule in the ground and in the excited states were determined.

The analysis of the PES sections reveals a non-planar equilibrium conformation of the molecule in its ground state (Figure 5), with a local minimum for a torsion angle between pyrrolyl and isoxazole ( $\phi$ ) of 45 deg and an absolute minimum for 158 deg. The calculated energetic barrier for the rotation of the isoxazole moiety was 2 kcal/mol. In the case of the first singlet excited state, the shape of the PES changes upon excitation, but the torsion angle corresponding to the most stable state of the excited molecule is 150 deg. The orthogonal conformation is not a stable one, as it does not correspond to a minimum on the PES, unlike the

pyrrolyl-isoxazole derivatives of the D-A type, for which the only minimum on the excited state PES is for  $90^\circ$ .<sup>10</sup> On the other hand, rotation of the second A fragment, methylenephthalidyl ( $\theta$ ), yields an absolute minimum for the planar conformation (Figure 5) in the ground state and for a dihedral of  $-60$  deg in the first excited state. The orthogonal conformation does not correspond to a minimum.

The dipole moment obtained for the excited state was 8.7 D, comparing to the one in the ground state of 4.6 D. This means a difference  $\Delta\mu$  of 4.1 D, in a fairly good agreement with the experimental values of 3.4 or 4.8 D, depending on the solvatochromic method used. As the dipole moment rises upon excitation, this proves a charge transfer character for the excited state. The frontier MOs are both located on the pyrrolyl-methylenephthalidyl fragment (see Figure 5) for  $\phi=90^\circ$ , but HOMO is mainly located on pyrrolyl and LUMO on methylenephthalidyl for  $\theta=90^\circ$  so the charge transfer upon excitation is most probably from pyrrolyl to methylenephthalidyl.

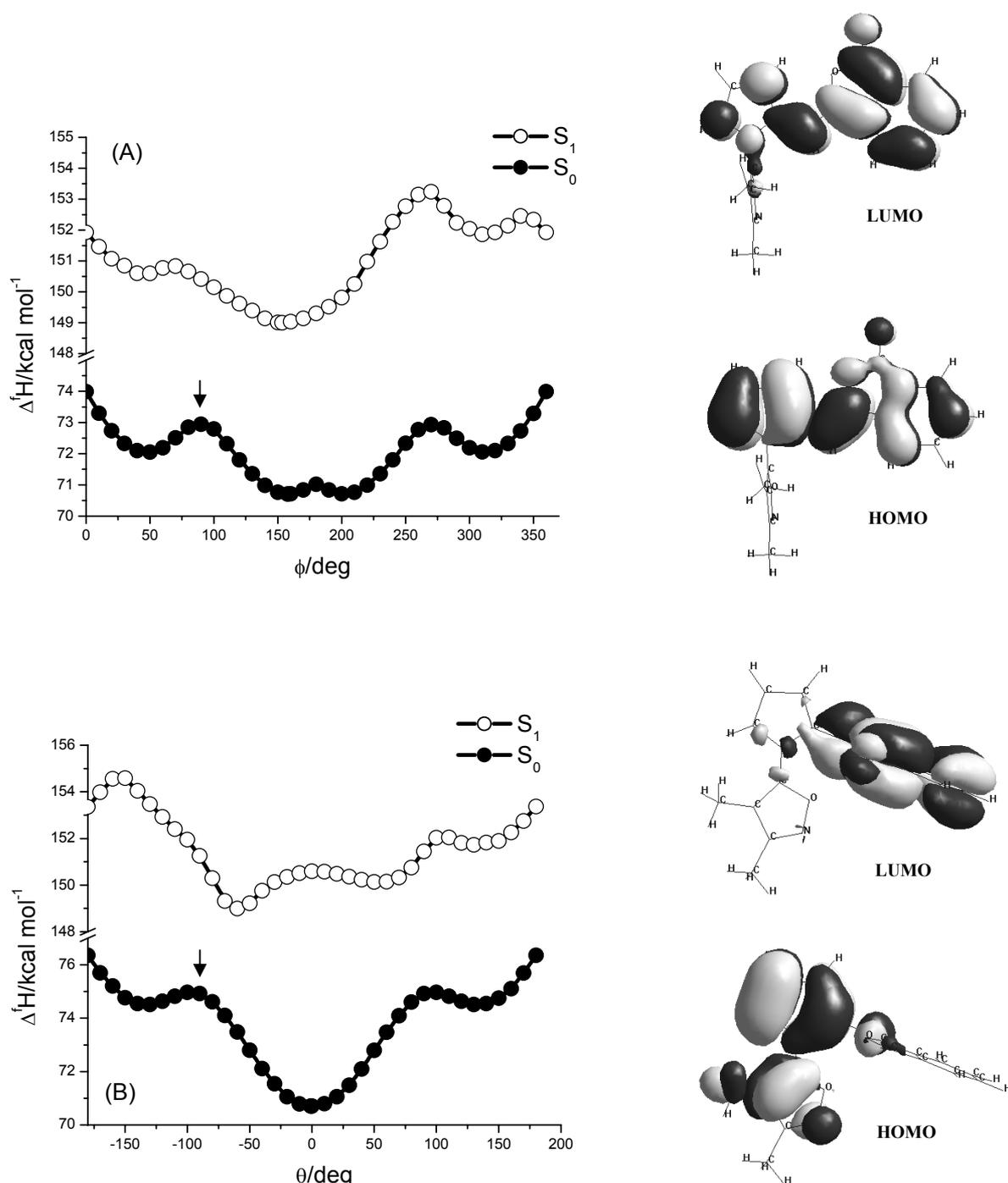


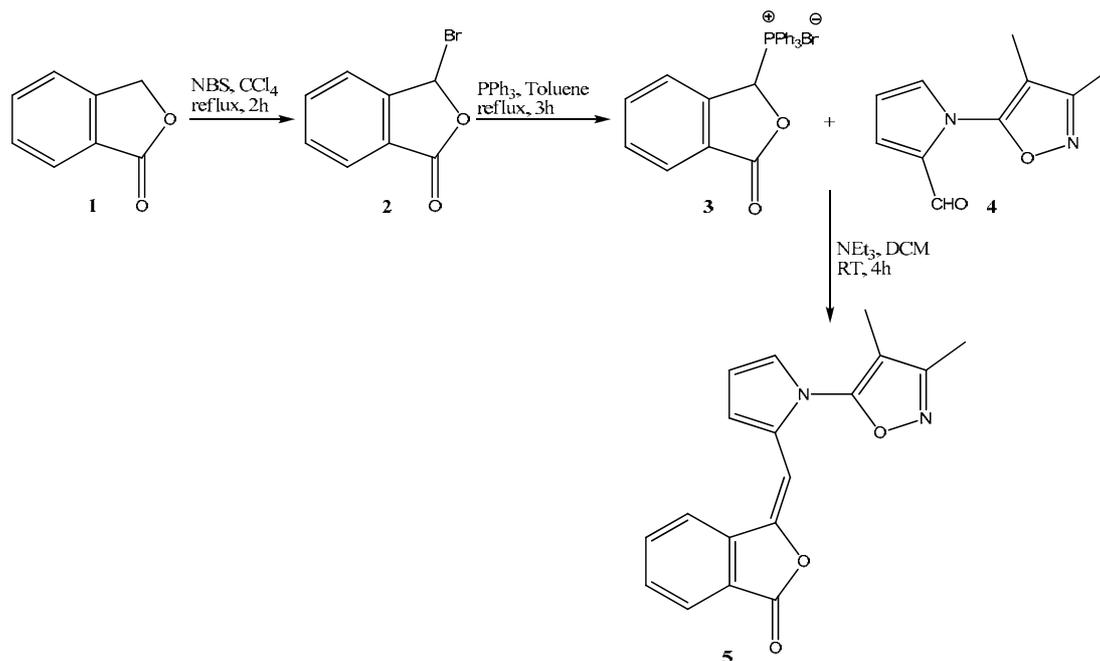
Fig. 5 – (left) Sections through the PESs for the ground ( $S_0$ ) and excited ( $S_1$ ) states of PPI. (A) rotation of isoxazolyl,  $\Phi$  in Figure 1 and (B) rotation of methylenephthalidyl,  $\theta$  in Figure 1; (right) Frontier MOs for the respective orthogonal conformation – indicated with an arrow on the PES.

## EXPERIMENTAL

### Synthesis

Bromination of phtalide **1** with NBS in  $\text{CCl}_4$  led to 3-bromophthalide in 82%.<sup>19</sup> Triphenyl(phtalid-3-yl)phosphonium

bromide salt **3** has been isolated in a 85% yield by refluxing 3-bromophthalide **2** with triphenyl phosphite in toluene.<sup>20</sup> The Wittig reaction<sup>21</sup> of 1-(3,4-dimethyl-isoxazol-5-yl)-1*H*-pyrrole-2-carbaldehyde **4**<sup>22</sup> with the salt **3** gives the final product **5** as a mixture of isomers *cis/trans* in a ratio of 1:1 and 62% yield.<sup>23</sup>



Scheme 1 – Synthesis of 5-(2'-(3-methylenephthalidyl)-pyrrolyl)-3,4-dimethylisoxazole (PPI).

### Spectroscopic measurements

The characteristics of the absorption and fluorescence spectra of PPI in several organic solvents of various polarities were compared. The absorption spectra were recorded on a Helios- $\alpha$  UV-VIS spectrophotometer and the fluorescence emission spectra on a FP-6300 Jasco spectrofluorimeter (360 nm excitation wavelength). All these measurements were conducted for  $10^{-5}$  M solutions, at room temperature. The spectroscopic solvents were checked for fluorescence before use in the emission domain of PPI. The lifetime was measured on an Edinburgh Instruments FLS920 spectrofluorometer with a 375.6 nm laser. The intensity decay was fitted to biexponential functions and the accuracy of the fit was tested by the values of  $\chi^2$  and residuals. The average lifetime  $\langle\tau\rangle$  was calculated as:<sup>24</sup>

$$\langle\tau\rangle = \frac{B_1\tau_1^2 + B_2\tau_2^2}{B_1\tau_1 + B_2\tau_2} \quad (1)$$

where  $\tau_1$ ,  $\tau_2$  are the lifetimes of the excited species and  $B_1$ ,  $B_2$  the preexponential factors.

### Solvatochromic study

The experimental data in solvents of different polarity were plotted against different polarity functions:

$$\nu_f = \frac{2\mu_e\Delta\mu}{cha^3} \times F(\varepsilon, n) \quad (2)$$

$$\Delta\nu_{Stokes} = \frac{2(\Delta\mu)^2}{cha^3} \times F(\varepsilon, n) \quad (3)$$

where  $\nu_f$  is the fluorescence maximum,  $\Delta\nu_{Stokes}$  the Stokes shift,  $\mu_e$  – the excited state dipole moment,  $\Delta\mu$  – the difference between the excited and ground state dipole,  $c$  is the speed of light in vacuum,  $h$  is Planck's constant and  $a$  is the Onsager cavity radius (taken as 40% of the longest molecular axis, i.e.

$4.5 \text{ \AA}$ ).<sup>11</sup>  $F(\varepsilon, n)$  is a bulk solvent polarity function, its expression depending on the solvatochromic model used: the Lippert-Mataga model<sup>25</sup> considers the dependencies of the Stokes shift,  $\Delta\nu_{Stokes}$ , on  $F(\varepsilon, n) = \frac{\varepsilon - 1}{2\varepsilon + 1} - \frac{n^2 - 1}{2(2n^2 + 1)}$ , while the Reichardt-Dimroth model<sup>26</sup> considers the dependency of  $\Delta\nu_{Stokes}$  on the experimentally determined polarity function,  $E_T^{30}$ , normalized as:  $E_T^N = \frac{E_T^{30}(\text{solvent}) - E_T^{30}(\text{TMS})}{E_T^{30}(\text{water}) - E_T^{30}(\text{TMS})}$ .

Another way of studying solvatochromism is to consider both polarization and H bond formation through the Kamlet-Taft model<sup>27</sup> of the form:

$$\nu = \nu_0 + p\pi^* + a\alpha + b\beta \quad (4)$$

where  $\pi^*$  is the solvent dipolarity/polarizability function, while  $\alpha$  and  $\beta$  measure the ability of the solvent to donate or to accept a proton, respectively, in a solvent-to-solute H bond.

### Estimation of fluorescence quantum yields

The fluorescence quantum yield of PPI ( $\Phi_{f,PPI}$ ) was estimated with respect to the fluorescence quantum yield of a standard solution of quinine sulfate in 0.5 M  $\text{H}_2\text{SO}_4$  ( $\Phi_{f,reference} = 0.55$ ).<sup>28</sup>

$$\phi_{f,PPI} = \phi_{f,reference} \frac{S_{PPI} \cdot D_{reference}}{D_{PPI} \cdot S_{reference}} \quad (5)$$

where  $S$  represent the corresponding integrated emission band areas and  $D$  are the absorbances at the excitation wavelength.

### Study of the inclusion of PPI into $\beta$ -cyclodextrin ( $\beta$ -CD)

The formation of a  $PPI$ - $\beta$ -CD guest-host complex was studied by means of steady-state fluorescence measurements, at room temperature. A  $10^{-6}$  M solution of PPI in methanol:water (1:9) was titrated with aliquots of  $10^{-3}$  M

$\beta$ -CD solution prepared by adding  $\beta$ -CD powder to the PPI solution above.

The association constant ( $K$ ) of the inclusion complex was estimated by non-linear regression analysis. The fluorescence intensity ( $F$ ) was plotted as a function of the  $\beta$ -CD concentration ( $C$ ) and the data were fitted by the equation 6, corresponding to the formation of a 1:1 inclusion complex:

$$F = \frac{F_0 + K \cdot I_f \cdot C}{1 + K \cdot C} \quad (6)$$

where  $F_0$  is the fluorescence intensity in the absence of  $\beta$ -CD and  $I_f$  is the fluorescence intensity of the complex at maximum  $\beta$ -CD concentration.

### Theoretical calculations

Semi-empirical calculations were performed using the MOPAC2007<sup>29</sup> program (*in vacuo* optimization, AM1 Hamiltonian). The geometries of the ground and excited states were optimized in internal coordinates. In order to check the presence of a TICT excited state, sections through the PESs were built with respect to the torsion angle about the pyrrolyl-isoxazole bond, angle  $\theta$  in Fig.1 and the methylenephthalidyl-pyrrolyl bond, angle  $\phi$  in Figure 1. These angles were increased by 10 degrees (deg) steps in the interval 0–360 deg and all other internal coordinates were fully optimized.

## CONCLUSIONS

In the aim of characterizing the excited states of a pyrrolyl-isoxazole derivative that contains also a methylenephthalidyl fragment, PPI, we conducted an experimental and theoretical study. The measured photophysical properties of PPI such as Stokes shift, solvatochromism, FWHM, emission intensity and maximum in the presence of CD indicate the lack of the TICT excited state, in spite of the free rotation of the constitutive fragments. Other arguments in this respect are provided by the theoretical calculations, which reveal that the twisted excited state is not stable.

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