Luminescent properties of substituted 4-aminophthalimides: computations vs. experiment

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Abstract. To perform a combined experimental and computational study on the luminescent properties of practically important class of organic dyes – 4-aminophthalimides.

Results and discussion. The absorption and fluorescence spectra of 4-aminophthalimide derivatives in polar protic and aprotic solvents were computed and matched vs. the experimental data. The changes in emission spectra are mainly related to the NH₂-group derivatization. The methyl substitution of amide hydrogen causes a bathochromic shift of about 7 nm in the absorption peak and a negligible hypsochromic shift in the fluorescence peak, while introducing alkyl substituents to the amine moiety causes bathochromic shifts in absorption and emission peaks of 30–40 nm and 10–60 nm, respectively.

Experimental part. Absorption and emission wavelengths were computed by the standard algorithm based on the ground state geometry optimization (equilibrium solvation), vertical excitation with nonequilibrium solvation, and the TD-DFT geometry optimization of the excited state structures. A reliable hybrid B3LYP functional was used in combination with DZ and TZ-quality basis sets.

Conclusions. The computed absorption wavelengths are in excellent agreement with the experimental data and are only slightly solvent-dependent. At the same time, the discrepancy with the experiment for Stokes shifts reaches about 20% at IEF-PCM-TD-B3LYP/6-31G(d). However, the general tendency for both absorption and fluorescence wavelengths is identical for all solvents within one molecule.

Key words: experimental luminescence spectra; absorption; fluorescence; Stokes shifts; 4-aminophthalimides; time-dependent density functional theory; polarizable continuum model

Experimental part

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Key words
4-Aminophthalimide 1 combines electron-donating amino group conjugated with the phthalimide moiety; this determines its distinct fluorescent properties (Stokes shifts > 100 nm) [1]. The derivatives of 1 continuously attract great attention because of biological applications [2], particularly as fluorescent markers [3] and environment-sensitive probes [4]. The fluorescence spectra of 1 not only strongly depend on the substituents [2, 5], but are remarkably solvent-sensitive due to the intramolecular charge transfer nature of the emitting state. It has been found that bathochromic shifts of the emission spectra of 1 in protic solvents are much greater than those observed in aprotic ones: the emission maximum shifts from 430 nm in toluene to 550 nm in water [6–7]. Additionally, the excited state of 1 has a relatively long lifetime of ca. 15 ns [8], but drops substantially in protic solvents, such as alcohols and especially in water [8, 9]. Due to its long excited state lifetime and high solvatochromism 1 is an ideal probe for monitoring the relaxation of various media, especially where H-bonds are involved [7]. It was extensively used to monitor microenvironments and solvation of a variety of substrates, including micelles, cyclodextrins, hydrogels, and ionic liquids [6,10]. Most recent studies include the synthesis of 4-amino-phthalimide C-nucleosides as isosteric fluorescent DNA base substitutes [11] probing the aggregation behavior of substituted 1 [12]. The modeling of hydrogen-bonding dynamics of 1 in aqueous solution [13] and modulation of 1 spectral properties by hydrogen bonds in water [14] were successfully performed using the time-dependent density functional theory (TD-DFT) approach. All above raises the importance of computational prediction of luminescent properties of the derivatives of 1, and it is the subject of current study.

**Results and discussion**

Herein, we studied the luminescent properties of 4-aminophthalimide 1 derivatives, namely 4-amino-N-methylphthalimide 2, 4-amino-N-ethylphthalimide 3, 4-amino-N-(n-propyl)phthalimide 4, 4-amino-N-(iso-propyl)phthalimide 5, 4-amino-N-cyclohexylyphthalimide 6, 4-amino-N-(1-adamantyl)phthalimide 7, 4-(N-ethyl)amino-N-methylphthalimide 8, and 4-(N,N-diethyl)amino-N-methylphthalimide 9 (Fig. 1) prepared as described earlier [2, 5].

Since the experimental fluorescence spectra of 4-aminophthalimide derivatives are determined by the allowed transitions between the $S_0/S_1$ electronic states [15], the frontier orbitals of 1 and its methyl derivative 2 were first analyzed through the optimization of their $S_1$-state geometries (Fig. 2).

As the amine nitrogen contributes substantially both to HOMO and LUMO, the introduction of substituents to the amino group should lead to shifts in both the absorption and emission bands. In contrast, the phthalimide nitrogen mostly contributes to the HOMO (Fig. 2). The above set of model molecules 1–9 allows us to vary the substitution pattern in both directions.

First, the ability of the TD-DFT approach to reproduce the experimental absorption spectra of compounds 1–9 was tested (Table 1). The computations of the vertical excitation step of substituted 1 with even relatively small basis sets provided absorption wavelengths in good agreement with the experiment.

![Fig. 1. The structures of 4-aminophthalimide derivatives studied](image-url)
It should be mentioned that the previous TD-DFT computations of the $S_0 \rightarrow S_1$ transition in 4-aminophthalimide (1, top) and 4-(N,N-diethyl)amino-N-methylphthalimide (9, bottom) computed at B3LYP/cc-pVTZ are remarkable bathochromic shifts for amine-substituted imide moiety (errors in computed Stokes shifts are less than 20%). At the same time, for 8, which has the ethyl substituent on the amine moiety, the theoretical emission wavelength is 42 nm larger than the experimental emission wavelength. General tendencies in fluorescence wavelengths (a negligible hypsochromic shift for imide-substituted 4-aminophthalimides and remarkable bathochromic shifts for amine-substituted derivatives) were reproduced appropriately by our computations with even rather narrow basis set – 6-31G(d). Calculations using ethanol as a model solvent showed the similar tendencies as observed in other solvents.

As noted above, the absorption wavelengths are well reproducible for the whole set of substituted 4-aminophthalimides even when a small basis set is used. Concerning the fluorescence wavelengths, deviations from the experimental spectral data are no more than 25 nm for molecules with only substituted imide moiety (errors in computed Stokes shifts are less than 20%). At the same time, for 8, which has the ethyl substituent on the amine moiety, the theoretical emission wavelength is 42 nm larger than the experimental emission wavelength. General tendencies in fluorescence wavelengths (a negligible hypsochromic shift for imide-substituted 4-aminophthalimides and remarkable bathochromic shifts for amine-substituted derivatives) were reproduced appropriately by our computations with even rather narrow basis set – 6-31G(d). Calculations using ethanol as a model solvent showed the similar tendencies as observed in other solvents.

As seen from Fig. 3, values of absorption and emission wavelengths for all molecules studied in different solvents are in direct relations with their dielectric constants. Thus, general tendencies in both absorption and fluorescence wavelengths are consistent for all solvents within one molecule.

**Experimental part**

Experimental spectra were obtained on a Jasco FP-8300 spectrometer. All calculations were performed with the Gaussian09 suite of programs [16]. The B3LYP [17] hybrid functional was selected for the TD-DFT [18–19] computations. The bulk solvent effects were assessed by means of the polarizable continuum model (PCM) [20] in its linear response (LR) formalism for geometry optimizations and frequency calculations, whereas both the LR and state-
Maximal absorption wavelengths ($\lambda_{\text{max}}^{\text{abs}}$, nm) determined for substituted 4-aminophthalimides using the TD-B3LYP functional with various basis sets (all data refer to methanol solutions)

| No. | Structure | B3LYP/6-31+G(d,p) | B3LYP/6-311++G(2d,2p) | B3LYP/cc-pVDZ | Exp. |
|-----|-----------|------------------|-----------------------|---------------|------|
| 1   |           | 380              | 372                   | 362           | 371  |
| 2   |           | 385              | 378                   | 368           | –    |
| 3   |           | 385              | 377                   | 368           | –    |
| 4   |           | 385              | 377                   | 369           | 376  |
| 5   |           | 384              | 376                   | 369           | 378  |
| 6   |           | 385              | 377                   | 370           | 378  |
| 7   |           | 381              | 375                   | 766           | 374  |
| 8   |           | 415              | 407                   | 391           | 391  |
| 9   |           | 426              | 419                   | 401           | 404  |

Maximal absorption and fluorescence wavelengths computed for 4-aminophthalimide 1 and 4-amino-N-methylphthalimide 2 with TD-B3LYP/cc-pVDZ with bulk solvation effects modeled for different solvents

| No. | Molecule | Solvent   | Theoretical | Experimental |
|-----|----------|-----------|-------------|--------------|
|     |          |           | $\lambda_{\text{max}}^{\text{abs}}$, nm | $\lambda_{\text{max}}^{\text{flu}}$, nm | $\lambda_{\text{max}}^{\text{abs}}$, nm | $\lambda_{\text{max}}^{\text{flu}}$, nm |
| 1   |          | methanol  | 362         | 589          | 371         | 530         |
|     |          | acetonitrile | 362       | 590          | –           | –           |
| 2   |          | methanol  | 368         | 585          | –           | 545         |
|     |          | acetonitrile | 369       | 586          | 366         | 475         |
specific formalisms were applied to compute transition energies. The Gaussian09 defaults for the PCM cavity definitions were retained in all calculations. The absorption maxima computed in the presence of the solvent reaction field were determined by using a non-equilibrium model, whereas the excited-state minimizations and the fluorescence calculations in solution were performed within the equilibrium approximation. Absorption and emission wavelengths were computed by the standard algorithm based on the ground state geometry optimization and frequencies (equilibrium solvation), vertical excitation with nonequilibrium solvation, TD-DFT geometry optimization of the excited state structure, computation of vibrational frequencies of the excited state structure, the state-specific equilibrium solvation of the excited state, and computation of the ground state energy with nonequilibrium solvation at the excited state geometry. Absorption wavelengths were obtained from the vertical absorption step; the emission wavelength was calculated by subtracting energies of the equilib-

**Table 3**

Theoretical and experimental absorption and fluorescence wavelengths, as well as Stokes shifts, computed for a set of 4-aminophthalimide derivatives using IEF-PCM-TD-B3LYP/6-31G(d) approach with bulk solvation effects modeled in methanol

| No. | Structure | Theoretical | Experimental |
|-----|-----------|-------------|--------------|
|     | \(\lambda_{\text{abs}}^{\text{max}}, \text{nm}\) | \(\lambda_{\text{abs}}^{\text{max}}, \text{nm}\) | \(\lambda_{\text{max}}, \text{nm}\) | \(\lambda_{\text{max}}, \text{nm}\) | Stokes shift, nm | Stokes shift, nm |
| 1   | ![Structure](image1.png) | 363 | 553 | 190 | 371 | 530 | 159 |
| 2   | ![Structure](image2.png) | 369 | 552 | 182 | – | 545 | – |
| 3   | ![Structure](image3.png) | 369 | 550 | 180 | – | 544 | – |
| 4   | ![Structure](image4.png) | 369 | 549 | 180 | 378 | 543 | 165 |
| 5   | ![Structure](image5.png) | 369 | 550 | 181 | 378 | 544 | 166 |
| 6   | ![Structure](image6.png) | 371 | – | – | 378 | 543 | 165 |
| 8   | ![Structure](image7.png) | 393 | 597 | 204 | 391 | 555 | 164 |
| 9   | ![Structure](image8.png) | 404 | 618 | 214 | 404 | – | – |

Fig. 3. Stokes shifts computed for a set of 4-aminophthalimide derivatives 1–9 using the IEFPCM-TD-B3LYP/6-31G(d) approach with the bulk solvation model in ethanol, acetonitrile, and dichloromethane.

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The absorption maxima computed in the presence of the solvent reaction field were determined by using a non-equilibrium model, whereas the excited-state minimizations and the fluorescence calculations in solution were performed within the equilibrium approximation. Absorption and emission wavelengths were computed by the standard algorithm based on the ground state geometry optimization and frequencies (equilibrium solvation), vertical excitation with nonequilibrium solvation, TD-DFT geometry optimization of the excited state structure, computation of vibrational frequencies of the excited state structure, the state-specific equilibrium solvation of the excited state, and computation of the ground state energy with nonequilibrium solvation at the excited state geometry. Absorption wavelengths were obtained from the vertical absorption step; the emission wavelength was calculated by subtracting energies of the equilib-

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rimum solvated excited state and solvating ground state and converting it to the wavelength scale. The Stokes shifts were computed by subtracting vertical absorption and emission energies and converting to the wavelength scale.

**Conclusions**

Using the TD-B3LYP/6-31G(d) method we computed the absorption and fluorescence wavelengths of 4-amino-4H-2,1,3-benzothiazole and 4-aminophthalimide derivatives in methanol, ethanol, acetonitrile, and dichloromethane. They were in good agreement with the experimental measurements. Substitution on the amino group had the most significant impact on the emission spectra. Theoretical errors in the computations of Stokes shifts did not exceed 20% at IEF-PCM-TD-B3LYP/6-31G(d). Absorption wavelengths computed with vertical approximation even with small basis sets reproduced well the experimental results for all molecules studied, excluding 4-amino-N-(1-adamantyl)phthalimide, which was the most challenging task. Using IEF-PCM-TD-B3LYP/6-31G(d) model computations we assessed solvent effects on absorption and emission wavelength in polar protic and aprotic solvents. It turned out that this combination of the solvation model and the basis set gave only approximate evaluation of the solvent effects. Thus, more advanced functional, different solvation models (including explicit solvation), and larger basis sets are needed to improve the computational prediction.

**Conflict of interests:** authors have no conflict of interests to declare.

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