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Pseudorotaxane complexes of naphthylpyridines and naphthylbipyridyl with β-cyclodextrin and hydroxypropyl-β-cyclodextrin

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The electronic absorption spectra and fluorescence spectra of 4-(2-naphthyl)pyridine (**1**), 2-(4-methyl-2-pyridyl)-4-(2-naphthyl)pyridine (**2**), and 4-(2-naphthyl)-2-phenylpyridine (**3**) in solutions and in complexes with β-cyclodextrin (β-CD) and well water-soluble hydroxypropyl-β-cyclodextrin (HP-β-CD) were studied. Fluorescence near 475 nm observed in aqueous solutions of compounds **1—3** arises from protonated forms of these compounds produced in the excited state. Results of DFT quantum chemical calculations show an increase in proton affinity energies of excited-state naphthylpyridines **2** and **3**. The formation of inclusion complexes with cyclodextrins makes protonation of compounds **2** and **3** more difficult, which manifests in large hypsochromic shifts of fluorescence band maxima. The stability constants of the complexes **1**•HP-β-CD and **2**•HP-β-CD determined from their fluorescence spectra are 3425 and 3760 L mol^{-1}, respectively. The stability constant of the complex **3**•HP-β-CD (5500±600 L mol^{-1}) was found from the changes in the solubility of naphthylpyridine **3** in water upon complexation. Semiempirical quantum chemical calculations of the molecular structures and thermodynamic characteristics of pseudorotaxane inclusion complexes of *trans*-**2**, *cis*-**2**, and *trans*-**2**•H_2O with HP-β-CD were carried out.

Key words: naphthylpyridines, naphthylbipyridyl, β-cyclodextrin, hydroxypropyl-β-cyclodextrin, pseudorotaxane complexes, molecular structure, quantum chemical calculations, density functional theory, PM3 method, electronic absorption spectra, fluorescence spectra.

"Guest—host" complexes of cyclodextrins (CD) with organic molecules can undergo various photochemical transformations, which are often impossible for unbound compounds.[1] Of particular interest are those cases where photoreactions and complexation efficiently affect one another.[2] Examples are provided by rotaxane and pseudorotaxane complexes of CD with long "guest' molecules that are considered as prototypes of shuffle-type molecular machines.[3] However, only a few photosensitive pseudorotaxane complexes, which are mainly based on cyclic charge-transfer complexes of viologen and cucurbituril analogs, were reported so far.[4,5] Possible advantages of CD-based photosensitive pseudorotaxane complexes are still unemployed.

Earlier,[6] taking 4-(2-naphthyl)pyridine (**1**) as an example, we established that (1) its electronic absorption spectra in different solvents and in neutral aqueous solution are slightly different from one another, but significantly change upon the addition of an acid due to the formation of the protonated form of **1**; (2) fluorescence spectrum of **1** in neutral aqueous solution arises from the protonated **1** produced in the excited state; and (3) fluorescence spectra of naphthylpyridine **1** in dehydrated solvents arise from the non-protonated **1** and are characterized by large hypsochromic shifts relative to the spectrum of the protonated **1**. We also found that complexation of **1** with β-cyclodextrin (β-CD) in neutral aqueous solution makes the formation of the protonated form of **1** in the excited state more difficult. This manifests itself in an increase in the intensity of the fluorescence band of the non-protonated form of compound **1** and simultaneous decrease in the intensity of the band corresponding to the protonated **1**.

Changes in the fluorescence spectrum of compound **1** upon complexation with β-CD could be more pronounced at higher concentrations of β-CD in the solution; how-

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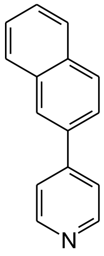
ever, β-CD is poorly soluble in water. Therefore, in this work we used well water-soluble hydroxypropyl-β-cyclodextrin (HP-β-CD). Hydroxypropyl groups in the β-CD molecule can also affect the formation of the inclusion complex. The aim of this work was to study the photophysical and spectral properties of (i) naphthylpyridines **1—3** having different-length molecules and different abilities to undergo photoinduced protonation and (ii) complexes of compounds **1—3** with HP-β-CD in solutions and to analyze the molecular structures of pseudorotaxane complexes thus obtained by quantum chemistry methods.



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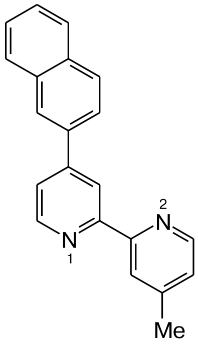

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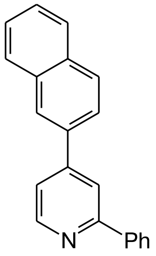

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Experimental and Calculation Procedure

4-(2-Naphthyl)pyridine (**1**), 2-(4-methyl-2-pyridyl)-4-(2-naphthyl)pyridine (**2**), and 4-(2-naphthyl)-2-phenylpyridine (**3**) were synthesized following known procedures.[7,8]

The stability constants were determined from fluorescence spectra by the parametric self-modeling of the spectral matrix (PSSM) method,[9] which was developed for calculating the stability constants from electronic absorption spectra using corresponding software. Experimental data were obtained by titrating the solution of the ligand—substrate complex with a solution of the ligand at a constant ligand concentration. The PSSM program can be adapted for processing of the fluorescence spectra recorded during titration of aqueous arene solution with an aqueous solution of the arene—β-CD complex at constant arene concentration. The procedure is as follows. Assuming optically thin layers in the sample, the arene fluorescence intensity (I_{fl}) is given by

$$I_{\text{fl}} = I_{\text{fl},1} + I_{\text{fl},2} = 2.3I_{\text{irr}}[A_1\Phi_1(\nu)\varphi_1 + A_2\Phi_2(\nu)\varphi_2] = $$
$$= 2.3I_{\text{irr}}d[C_1\varepsilon_1\Phi_1(\nu)\varphi_1 + C_2\varepsilon_2\Phi_2(\nu)\varphi_2]. \quad (1)$$

A spectrofluorimeter equipped with a quantum counter measures the ratio

$$I_{\text{fl}}/I_{\text{irr}} = 2.3Kd[C_1\varepsilon_1\Phi_1(\nu)\varphi_1 + C_2\varepsilon_2\Phi_2(\nu)\varphi_2]. \quad (2)$$

In expressions (1) and (2) the subscript "1" corresponds to the arene—β-CD complex and the subscript "2" corresponds to the unbound arene in solution; $I_{\text{fl},1}$ and $I_{\text{fl},2}$ are the intensities of the fluorescence spectra; A_1 and A_2 are the optical densities at the excitation light wavelength; $\Phi_1(\nu)$ and $\Phi_2(\nu)$ are the fluorescence lineshape functions normalized to unity with respect to the surface area under the curves; φ_1 and φ_2 are the quantum yields of fluorescence; ε_1 and ε_2 are the molar absorption coefficients at the excitation wavelength; C_1 and C_2 are the concentrations; I_{irr} is the excitation light intensity; d is the optical path length in the cell (usually, 1 cm); and K is the coefficient depending on the monochromator slits used in the acquisition of fluorescence.

Assuming that fluorescence is excited at a frequency at which $\varepsilon_1 = \varepsilon_2$ and treating the product $\Phi(\nu)\varphi K$ as an analog of the electronic absorption spectrum (*i.e.*, dependence of the molar absorption coefficient on the frequency of light), expression (2) has exactly the same form as the expression for thin-layer electronic absorption. Then, formally, all expressions and programs for spectral reconstruction from the optical density values[9] can be used for reconstruction of fluorescence spectra and calculations of stability constants.

The complexes under study were prepared from HP-β-CD (Aldrich) without additional purification. The inclusion complexes were prepared by adding the compounds under study to aqueous HP-β-CD solutions heated to 50 °C. Experiments were carried out at room temperature using bidistilled water and hexane purified by chromatography on a column with silica gel and subsequent distillation.

The electronic absorption spectra and luminescence spectra were recorded on a Specord-M40 spectrophotometer and on Elumin-2M (Russia) and Perkin LS55 spectrofluorimeters. The quantum yield of fluorescence (φ_{fl}) was measured using a conventional procedure with anthracene ($\varphi_{\text{fl}} = 0.3$ in ethanol[10]) as external reference.

To carry out a theoretical study of the chromophore properties of naphthylbipyridyl **4** (molecule **2** without methyl substituent), we calculated the $S_0 \rightarrow S_1$ transition energies and the proton affinity (PA) energies for the *trans*-**4** and *cis*-**4** conformers in the ground and singlet excited states. Calculations with full geometry optimization were carried out by the TDDFT (time-dependent DFT) method with the three-exponent basis set;[11] the exchange and correlation contributions were calculated using the PBE functional[12] (PRIRODA program Version 407).[13] The results obtained are listed in Table 1.

To determine which molecular fragment (naphthalene or pyridine moiety) mainly enters the cavity, we carried out quantum chemical calculations of the molecular structures of pseudorotaxane inclusion complexes of compound **2** with β-CD and HP-β-CD using the GAMESS program[14] and the PM3 method with standard parametrization.[15]

Results and Discussion

Electronic absorption spectra. The electronic absorption spectra of the compounds under study in hexane and water and those of their inclusion complexes with CD in neutral aqueous solutions almost match one another. The fluorescence spectra show more significant changes in those cases where the compound under study is in different environment including location in the cyclodextrin cavity upon complexation.

Fluorescence spectra. Similarly to the fluorescence spectrum of naphthylpyridine **1**,[6] those of compounds **2** and **3** in nonpolar solvent (hexane) exhibit a well-re-

Table 1. Ground-state (S_0) and excited-state (S_1) total energies (E_{tot}) and proton affinity (PA) energies of naphthylpyridine **4**

Compound	E_{tot} (a.u.)/kcal mol^{-1}		ΔE ($S_0 \rightarrow S_1$) /nm	PA/kcal mol^{-1}	
	S_0	S_1		S_0	S_1
trans-**4**	−879.28671/0.0	−879.17902/0.0	423.1	—	—
cis-**4**	−879.27663/6.3	−879.18595/−4.3	502.5	—	—
trans-**4**(N(1))•H$^+$	−879.67134/6.4	−879.62944/14.3	—	241.3	282.6
trans-**4**(N(2))•H$^+$	−879.663847/7.3	—	—	—	—
cis-**4**(N(1))•H$^+$	−879.68149/0.0	−879.63716/9.4	—	254.0	283.1
cis-**4**(N(2))•H$^+$	−879.67611/3.4	−879.65217/0.0	—	250.7	292.5

Note. PA = E_{tot}(**4**•H$^+$) − E_{tot}(**4**). The lack of excited-state data for the *trans*-**4** conformer protonated at the second nitrogen atom is due to the fact that this structure does not correspond to local energy minimum and rearranges into *cis*-**4**(N(2))•H$^+$ in the course of geometry optimization.

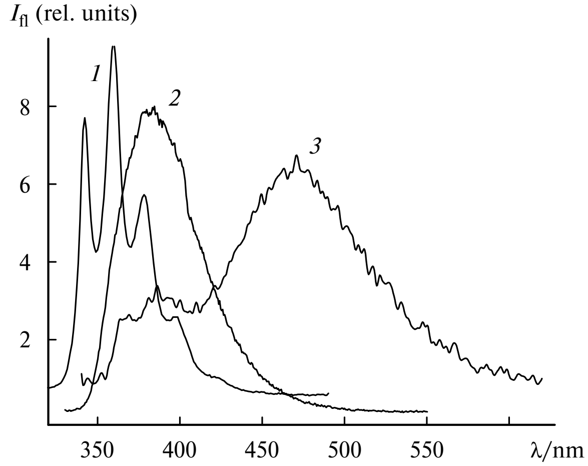


Fig. 1. Fluorescence spectra of compound **2** (C = 5•10^{-5} mol L^{-1}) at 293 K in hexane (*1*), ethanol (*2*), and water (*3*). The short-wavelength region of spectrum *3* arises from microcrystals of **2**.

solved vibronic structure, which disappears in the spectra recorded in polar solvents (EtOH, MeCN) (Fig. 1, spectra *1* and *2*). Again, like the fluorescence spectrum of compound **1**, the spectra of compounds **2** and **3** in aqueous solutions show a structureless band with a maximum at 475 nm, which arises from the corresponding protonated forms (see Fig. 1, spectrum *3*). This effect was also observed in the case of 4-phenylpyridine.[16] The appearance of this band is due to photoinduced protonation of the pyridine nitrogen atom, as illustrated in Scheme 1 taking compound **2** as an example.

Scheme 1

$$\mathbf{2} + H_2O \longrightarrow (\mathbf{2}\cdot H_2O) \xrightarrow{h\nu} (\mathbf{2}^{*}\cdot H_2O) \longrightarrow$$

$$\longrightarrow (\mathbf{2}\cdot H^+)^{*} \,\|\, OH^- \longrightarrow (\mathbf{2}\cdot H_2O) + h\nu_1 \text{ (475 nm)}$$

In contrast to the spectrum of compound **1**, a fluorescence band with a maximum near 380 nm appears in the spectra of aqueous solutions of compounds **2** and **3** at theoretical concentrations exceeding 5•10^{-5} mol L^{-1}. This band corresponds to fluorescence of the initial (non-protonated) compounds **2** and **3** (see Fig. 1, spectrum *3*), originates from microcrystals of these compounds, and appears due to lower solubility of naphthylpyridines **2** and **3** in water compared to **1**.

Pseudorotaxane inclusion complexes of compounds 1—3 with HP-β-CD. The addition of HP-β-CD to saturated aqueous solutions of compounds **1—3** results in the formation of inclusion complexes, which can be detected by an increase in the optical density in the electronic absorption spectra due to higher solubility of the complexes in water. Transformations of the fluorescence bands with maxima near 475 and 380 nm are more pronounced than those observed upon adding β-CD. Moreover, the band at 475 nm disappears at [HP-β-CD] > 10^{-2} mol L^{-1} and only fluorescence of the non-protonated forms of compounds **2** and **3** in the inclusion complexes is observed. The protonated form of naphthylpyridine **1** (maximum at 475 nm) fluoresces even at [HP-β-CD] = 10^{-2} mol L^{-1}. The fluorescence spectra of compounds **1** and **2** at HP-β-CD concentrations from 0 to ~10^{-3} mol L^{-1} are shown in Figs 2 and 3. The isobestic point seen in the spectra suggests that the solutions contain only these compounds and their complexes with HP-β-CD. The processes accompanying complexation are illustrated in Scheme 2 taking naphthylbipyridyl **2** as an example.

Scheme 2

$$(\mathbf{2}\cdot H_2O) + \text{HP-}\beta\text{-CD} \longrightarrow (\mathbf{2}\cdot\text{HP-}\beta\text{-CD}) + H_2O \xrightarrow{h\nu}$$

$$\longrightarrow (\mathbf{2}^{*}\cdot\text{HP-}\beta\text{-CD}) + H_2O \longrightarrow$$

$$\longrightarrow (\mathbf{2}\cdot\text{HP-}\beta\text{-CD}) + H_2O + h\nu_1 \text{ (380 nm)}$$

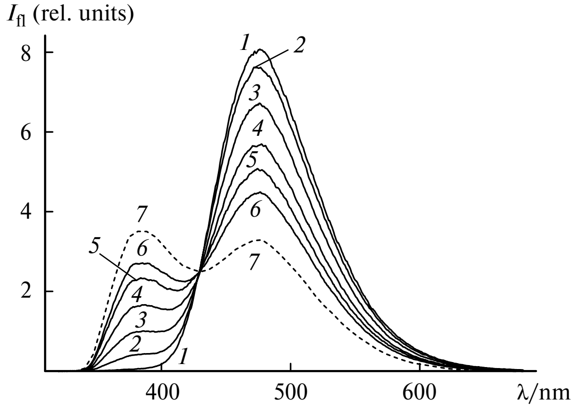


Fig. 2. Fluorescence spectra of aqueous solution of compound **1** ($C = 3 \cdot 10^{-5}$ mol L^{-1}) plotted *vs.* HP-β-CD concentration changed from 0 (*1*) to $9.5 \cdot 10^{-4}$ mol L^{-1} (*6*); calculated spectrum of the complex is shown in curve *7*. The minimum standard deviation (0.042) of the reconstructed spectra from experimental ones is attained at a stability constant of 3425 L mol^{-1} (1 : 1 complex).

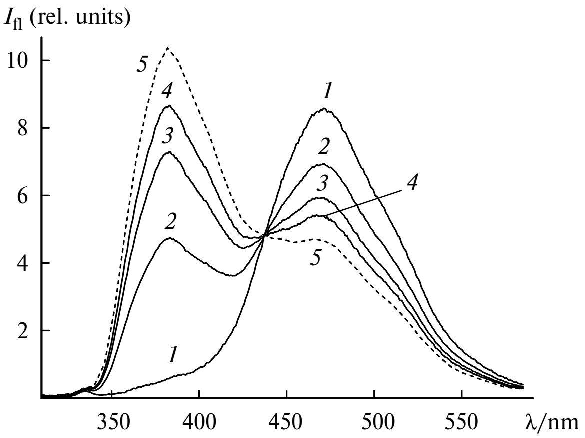


Fig. 3. Fluorescence spectra of aqueous solution of compound **2** ($C = 8 \cdot 10^{-6}$ mol L^{-1}) plotted *vs.* HP-β-CD concentration changed from 0 (*1*) to $1.2 \cdot 10^{-3}$ mol L^{-1} (*4*); calculated spectrum of the complex is shown in curve *5*. The minimum standard deviation (0.059) of the reconstructed spectra from experimental ones is attained at a stability constant of 3760 L mol^{-1} (1 : 1 complex).

Good agreement between the calculated and experimental spectra (see Figs 2 and 3) was obtained assuming the formation of 1 : 1 complexes. Minima in the plots of the root-mean-square deviation of the calculated spectra from experimental ones correspond to the stability constants of 3760 (**2**) and 3425 L mol^{-1} (**1**). The latter value exceeds than that reported for the complex of **1** with β-CD (2000 L mol^{-1}),[6] which is apparently due to the effect of the hydroxypropyl substituents in the β-CD molecule. As the concentration of HP-β-CD becomes higher than 10^{-2} mol L^{-1}, the intensity of the band at 380 nm arising from the non-protonated form of compound **2** continues to increase and does not reach a limiting value even at the maximum possible concentration of HP-β-CD. Most likely, these changes in fluorescence are due to the formation of a 2 : 1 complex characterized by very low stability constant.

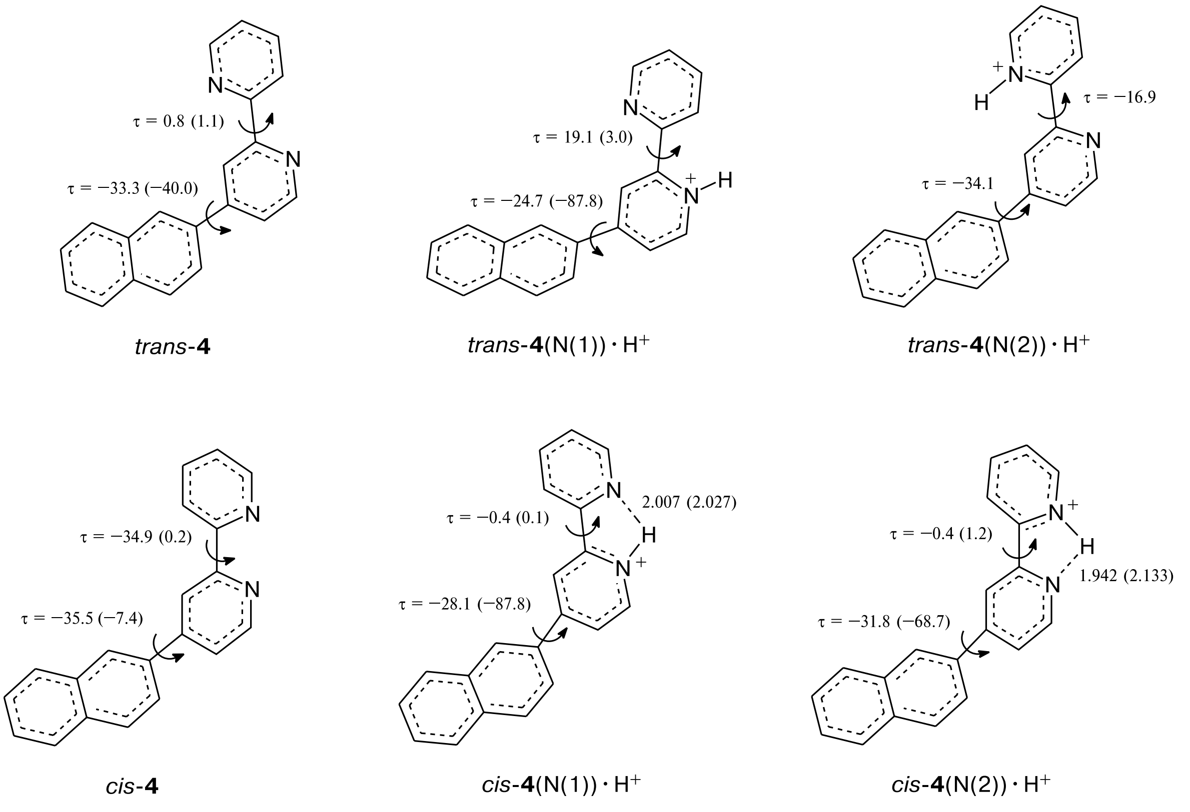
The calculated spectra of the 1 : 1 complexes are shown by dotted lines in Figs 2 and 3. They also exhibit fluorescence of the protonated forms of compounds **1** and **2**. In the course of complex formation, either the naphthyl or pyridine residues of these molecules can enter into the HP-β-CD cavity. According to estimates based on the results of quantum chemical calculations, both types of complexes can form nearly equiprobably. Fluorescence of the non-protonated forms of compounds **1** and **2** with a maximum at 380 nm is consistent with location of the pyridine residues of these molecules inside the HP-β-CD cavity. This makes contacts between water molecules and the nitrogen atom and thus the formation of excited-state protonated forms of **1** and **2** impossible. In other cases, fluorescence of the protonated forms of compounds **1** and **2** with a maximum at 475 nm is observed. The ratio of the maxima at 380 and 475 nm in the fluorescence spectra of the complexes depends not only on the concentration, but also on the quantum yields of fluorescence of the corresponding forms of compounds **1** and **2**.

The measured quantum yields, φ_{fl}, of the non-protonated forms of compounds **2** and **3** in the complexes with HP-β-CD are 0.34±0.1 and 0.6±0.1, respectively. The quantum yield of protonated naphthylpyridine **1** in aqueous solution is similar to unity[6] while fluorescence of non-protonated **1** in the complex is indiscernible even at maximum HP-β-CD concentrations. The quantum yield of fluorescence of protonated naphthylpyridine **2** in aqueous solution is at least an order of magnitude lower than that of protonated **1**. These data show that the fluorescence spectra of the 1 : 1 complexes should exhibit two maxima corresponding to two types of pseudorotaxane complexes with different mutual position of the HP-β-CD and long naphthylpyridine or naphthylbipyridyl molecules.

The dependences of the fluorescence spectra of complex **3** · HP-β-CD on the concentration of HP-β-CD at a constant concentration of compound **3** were not obtained due to very low solubility of compound **3** in water. However, the stability constant was evaluated from the changes in the solubility of naphthylpyridine **3** in water upon complexation with HP-β-CD. If we chose a weighed sample of compound **3** in such a manner that aqueous solution of **3** is saturated at all concentrations of HP-β-CD added, the concentration of the unbound compound **3** in the solution remains constant while the concentration of the complex increases as the HP-β-CD concentration increases. We established that the electronic absorption spectra of naphthylpyridine **3** in water and hexane and spectrum of its complex with HP-β-CD almost match one another. Therefore, we determined the concentrations of **3** in the aqueous solution and in the complexes with HP-β-CD at HP-β-CD concentrations from $7 \cdot 10^{-5}$ to $1 \cdot 10^{-3}$ mol L^{-1} using the electronic absorption spectra and the known molar absorption coefficient of compound **3** in hexane. The concentration of unbound compound **3** in the aqueous solution was $2.5 \cdot 10^{-6}$ mol L^{-1} at 294 K. The linear plot of [**3**·HP-β-CD] *vs.* [HP-β-CD] had a slope (R) of 0.014. The stability constant, K, was estimated at $R/2.5 \cdot 10^{-6} = 5524$ mol L^{-1}, which exceeds the values determined for compounds **1** and **2** probably due to higher hydrophobicity of naphthylpyridine **3**.

We compared the fluorescence spectra of compound **2** in solvents of different polarity and in the complex with HP-β-CD. Coincidence of the fluorescence bands of the non-protonated **2** at ~370 nm in MeCN and in the complex with HP-β-CD indicates that the HP-β-CD cavity acts on naphthylpyridine **2** as a polar solvent (MeCN), whereas the spectrum in the nonpolar solvent (hexane) exhibits a well-defined vibrational structure and experiences a hypsochromic shift. The formation of inclusion complexes between **2** and HP-β-CD in aqueous solution means that the molecules of compound **2** prefer a medium of lower polarity rather than water.

Quantum chemical calculations of the structure and energies of formation of pseudorotaxane inclusion complexes. The geometric parameters of the conformers of molecule **4**, their ground-state and excited-state protonated forms were optimized and the protonation energies were calculated by the DFT (S_0) and TDDFT (S_1) methods. The $S_0 \rightarrow S_1$ transition of the *trans*-**4** conformer is accompanied by an increase in the torsion angle between the naphthalene and pyridine residues, which indicates weakening of conjugation between them. On the contrary, transition of the *cis*-**4** conformer to the excited state causes the torsion angle to decrease, which favors better conjugation. In the ground state, the *trans*-**4** conformer is thermodynamically more stable than *cis*-**4** (energy difference is 6.3 kcal mol^{-1}), whereas the latter conformer is more preferable in the excited state S_1 (energy difference is 4.3 kcal mol^{-1}) (Fig. 4). This means that absorption of light induces *trans*—*cis*-isomerization of molecule **4** that fluoresces from the *cis*-form. Transitions of the protonated form to the excited states are followed by a dramatic increase in the torsion angles between the naphthalene and pyridine residues. In the *trans*-**4** and *cis*-**4** conformers, these angles are so similar to 90° that this can be treated as the loss of conjugation between the naphthalene and pyridine residues. At the same time photoexcitation has almost no effect on the torsion angles between two pyridine fragments, which are almost equal to



trans-**4** *trans*-**4**(N(1))·H^+ *trans*-**4**(N(2))·H^+

cis-**4** *cis*-**4**(N(1))·H^+ *cis*-**4**(N(2))·H^+

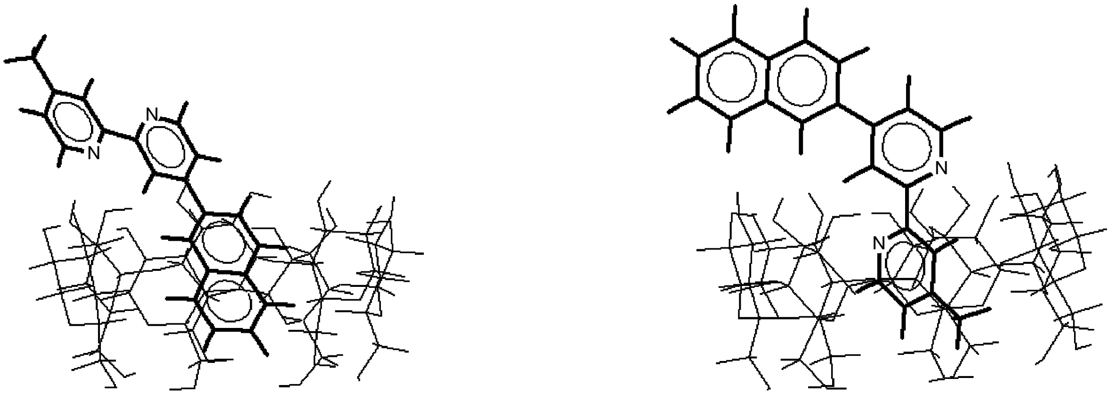
Fig. 4. Structures of the *trans*-**4** and *cis*-**4** conformers obtained from DFT calculations (torsion angles (τ) are given in degrees and distances are given in Å). The geometric parameters of the singlet excited states are given in parentheses. The *trans*-**4**(N(2))·H^+ form only exists in the ground state (see Note to Table 1).

zero in both states. This suggests that, owing to conjugation, both these chromophores are involved as a single species in all excitation and emission processes. The results of spectroscopic measurements show that naphthylpyridines in aqueous solutions fluoresce from the excited-state form protonated at the nitrogen atom. From the standpoint of quantum chemistry this can be due to higher excited-state proton affinity (PA) energies of these compounds compared to their ground-state PA energies. Table 1 shows that PA (S_1) > PA (S_0) for all possible protonated forms of the conformers of molecule **4**, the *cis*-**4**(N(2))$\cdot$H$^+$ form being the most thermodynamically favorable due to stabilization through the formation of a hydrogen bond between the proximate proton and the second nitrogen atom. Transition to the excited state leads to weakening of the hydrogen bond between the proton and the neighboring nitrogen atom in the *cis*-**4** conformer. This is indicated by somewhat greater excited-state N$^+$H...N hydrogen bond lengths compared to the ground-state N—H bond lengths in *cis*-**4**.

The PM3 semiempirical quantum chemical method permits reliable determination of the geometries of inclusion complexes of organic molecules (in particular, arenes) with β-CD.[6,16,17] In order to establish which molecular fragment (*i.e.*, naphthalene or bipyridyl residue) is mainly located in the cavity, we carried out PM3 calculations of pseudorotaxane complexes of naphthylpyridine **2** with β-CD.

PM3 calculations of the unbound conformers of molecule **2** showed that the *trans*-conformer is 2.3 kcal mol^{-1} thermodynamically more stable than the *cis*-conformer. This is in qualitative agreement with the results of more exact DFT calculations. For both conformers, penetration of the naphthalene residue into the β-CD cavity is thermodynamically more favorable than inclusion of the pyridine residue (Fig. 5). Changes in the Gibbs free energy (ΔG^*) were estimated using the calculated complexation energies (E_{bind}) and a correlation between these parameters.[18] By and large, the complexation energy difference between all types of pseudorotaxane complexes is small, which suggests an equilibrium between them in solution.

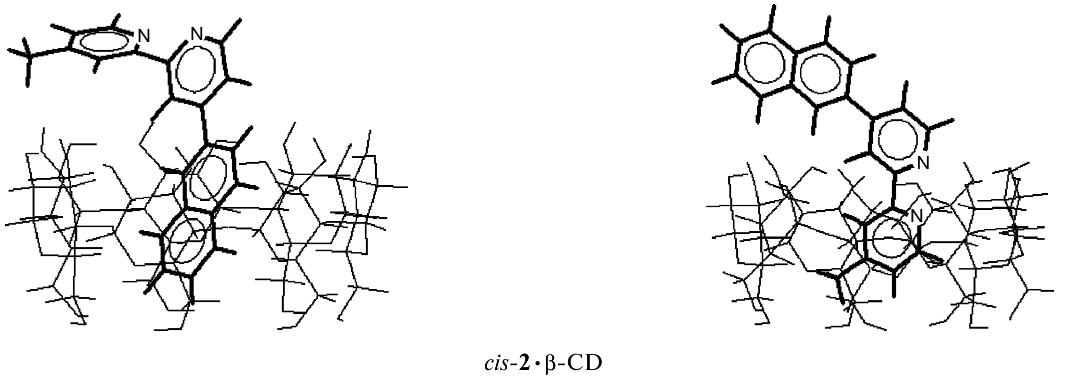
Recently, hydroxypropyl-β-cyclodextrin has become popular because of higher solubility in water compared



trans-**2**$\cdot$β-CD

E_{bind} = 12.6 kcal mol^{-1},
ΔG^* = –3.4 kcal mol^{-1}

E_{bind} = –11.1 kcal mol^{-1},
ΔG^* = –2.9 kcal mol^{-1}



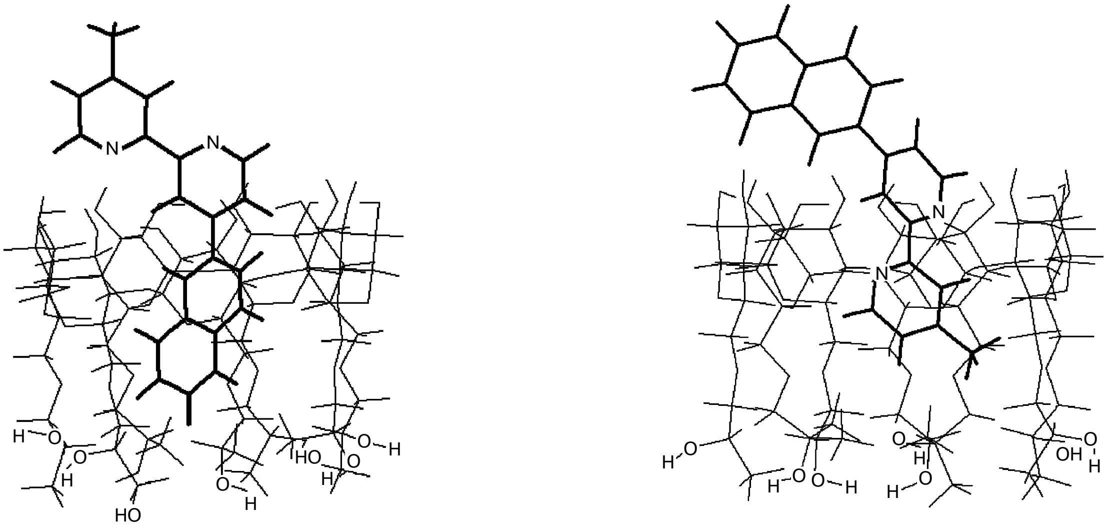
cis-**2**$\cdot$β-CD

E_{bind} = –14.3 kcal mol^{-1},
ΔG^* = –3.9 kcal mol^{-1}

E_{bind} = –13.1 kcal mol^{-1},
ΔG^* = –3.6 kcal mol^{-1}

Fig. 5. Structures of pseudorotaxane complexes of the *trans*-**2** and *cis*-**2** conformers with β-CD.

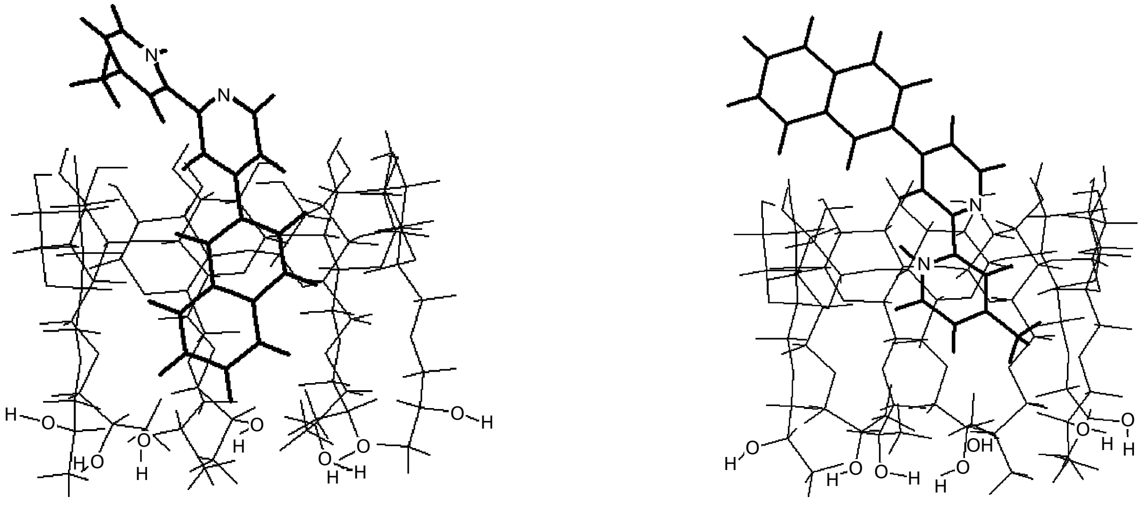
to β-CD. Exact molecular structure of HP-β-CD remains unknown as yet. Assuming that the primary hydroxyl groups of β-CD are more readily esterificated, we considered a structure in which all seven hydrogen atoms of $(CH_2)_3OH$ groups are replaced by $CH_2CH(OH)Me$ groups. PM3 calculations of unbound HP-β-CD molecules with C_7 symmetry gave two limiting structures. One of them has all OH groups of the hydroxypropyl fragments inside the cavity where they form a rim of hydrogen bonded hydroxyl groups. In the other structure the OH groups of the hydroxypropyl fragments are outside the cavity. The formation of intracavity hydrogen bonds between hydroxypropyl groups makes the first structure 16.4 kcal mol^{-1} thermodynamically more favorable than the second structure (*i.e.*, the energy of one hydrogen bond is estimated at 2.7 kcal mol^{-1}, which is quite realistic). At the same time the existence of the second form seems to be more preferable in aqueous solution, because in this case the hydroxyl groups can form hydrogen bonds with water molecules (*i.e.*, with the solvent used for preparation and investigations of CD complexes). Therefore, further calculations of the inclusion complexes of **2** with HP-β-CD were carried out with the second structure of the "host" molecule. Figures 6 and 7 show the structures



trans-**2**·HP-β-CD

$E_{\rm bind}$ = –16.3 kcal mol^{-1},
ΔG^* = –7.0 kcal mol^{-1}

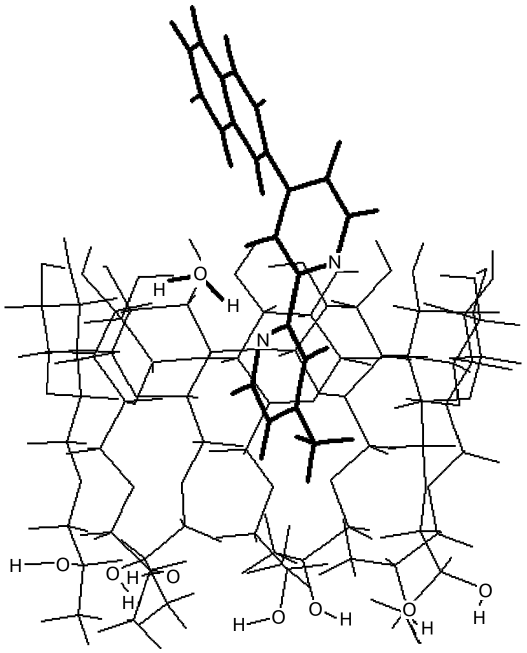
$E_{\rm bind}$ = –12.1 kcal mol^{-1},
ΔG^* = –4.3 kcal mol^{-1}



[*cis*-**2**(N(2))·H$^+$]·HP-β-CD
$E_{\rm bind}$ = –30.5 kcal mol^{-1},
ΔG^* = –13.1 kcal mol^{-1}

[*trans*-**2**(N(2))·H$^+$]·HP-β-CD
$E_{\rm bind}$ = –27.1 kcal mol^{-1},
ΔG^* = –11.7 kcal mol^{-1}

Fig. 6. Structures of pseudorotaxane complexes of HP-β-CD formed upon incorporation of the *trans*-**2** conformer and the conformers of the protonated forms of compound **2** from the wide rim of the HP-β-CD cavity.



(*trans*-**2** • H_2O) • HP-β-CD
$E_{bind} = -17.0$ kcal mol^{-1},
$\Delta G^* = -7.3$ kcal mol^{-1}

Fig. 7. Structure of the complex of *trans*-**2** • H_2O with HP-β-CD (bipyridyl residue is inside the cavity).

of pseudorotaxane inclusion complexes of compound **2** with HP-β-CD bearing outside OH groups of hydroxypropyl fragments.

According to calculations, the Gibbs free energy of inclusion of the naphthalene residue of the *trans*-**2** conformer into the HP-β-CD cavity from the wide rim formed by the secondary OH groups of glucose residues is 2.7 kcal mol^{-1} energetically more favorable than corresponding incorporation of the bipyridyl residue (see Fig. 6). Penetration into the HP-β-CD cavity from the narrow hydroxyl rim of the cavity is energetically less favorable, but here also the naphthalene residue of molecule **2** is 1.3 kcal mol^{-1} energetically more favorable for inclusion than the bipyridyl fragment. Comparison of the ΔG^* values calculated for the most preferable types of the complexes with β-CD and HP-β-CD shows that the Gibbs free energies of incorporation of compound **2** into the HP-β-CD cavity are higher than those of the processes involving β-CD. Probably, this can be due to the large volume of the HP-β-CD cavity, being consistent with a higher stability constant experimentally determined from fluorescence spectra. It should be noted that small differences between the ΔG^* values for both types of inclusion indicate the possibility of equilibrium between them in solution. Nevertheless, preferableness of inclusion of the naphthalene residue of molecule **2** into the cavity contradicts experimental observations, according to which the addition of CD to solution precludes protonation.

In searching for the origin of this effect we assumed that in aqueous solution compound **2** exists in the hydrated, at nitrogen atoms, form and that the energy of incorporation of this form into the cavity exceeds or is at least comparable with the ΔG^* value typical of the inclusion of the naphthalene residue. To confirm this hypothesis, we calculated the molecular structure of *trans*-**2** monohydrate (*trans*-**2** • H_2O) in which the water molecule forms a hydrogen bond with the more basic N(2) atom (according to PM3 calculations, *cis*-**2** monohydrate does not exist because optimization led to the *trans*-**2** structure). The energy of hydration of *trans*-**2** is 3.9 kcal mol^{-1}.

Then we calculated the complex of *trans*-**2** • H_2O with HP-β-CD (see Fig. 7). The cavity size at the wide hydroxyl rim of the host molecule is large enough to incorporate the substrate. The Gibbs free energy of inclusion of the bipyridyl residue of *trans*-**2** • H_2O (−7.3 kcal mol^{-1}) is comparable with the ΔG^* value determined for incorporation of the naphthalene residue of nonhydrated *trans*-**2** molecule into the cavity (−7.0 kcal mol^{-1}) and higher than the ΔG^* value for inclusion of the bipyridyl residue of nonhydrated *trans*-**2**. This supports nearly equal probabilities of the existence of different types of *trans*-**2** complexes with HP-β-CD and thus provides an explanation why the addition of HP-β-CD makes protonation difficult.

Incorporation of protonated forms into the HP-β-CD cavity is energetically more favorable than the inclusion of non-protonated ones (see Fig. 6). But in this case location of the naphthalene residue in the cavity also remains more preferable (energy difference is 2.6 kcal mol^{-1}). Although the energies of inclusion of protonated forms are higher than those of non-protonated species, we assume that the **2** • H^+ species (if any) diffuse from the HP-β-CD cavity to water. This assumption is based on the results of the Gibbs free energies calculations of naphthylpyridine inclusion into the β-CD cavity (ΔG_{ins}) and naphthylpyridine hydration (ΔG_{hydr}). Earlier,[6] we showed that the protonated form **1** • H^+ prefers aqueous environment rather than location in the β-CD cavity because $\Delta G_{hydr} > \Delta G_{ins}$.

PM3 calculations showed that HP-β-CD can form a "head-to-head" dimer with an energy of −18.2 kcal mol^{-1}, which is about 6 kcal mol^{-1} higher than the dimerization energy of β-CD. However, incorporation of naphthylpyridine **2** into the dimer was found to be energetically less favorable than inclusion of the naphthyl residue into the cavity of HP-β-CD monomer. These results are consistent with the experiment, because the fluorescence band of protonated compound **2** disappears only upon adding a large excess of HP-β-CD, which seemingly indicates the formation of a 2 : 1 complex.

* * *

Studies of the electronic absorption spectra and luminescence spectra of naphthylpyridine derivatives **1—3** revealed photo-induced protonation of these molecules in aqueous solutions. The interaction of HP-β-CD with naphthylpyridines **1—3** in aqueous solutions results in 1 : 1 complexes characterized by the stability constants ranging from 3425 to 5500 L $\mathrm{mol^{-1}}$. Complexation induces hypsochromic shifts of fluorescence maxima relative to the maxima in the spectra of neutral aqueous solutions. The complexes become more stable as the length (**2**) and hydrophobicity (**3**) of the "guest" molecules increase. According to calculations, the complexes have pseudorotaxane structures with predominant location of the hydrophobic naphthalene or pyridine residue in the CD cavity. However, the energy difference between the two situations in this type of complexes is small. This suggests the possibility of mechanical motion of CD along the naphthylpyridine derivative molecule in response to the action of external factors, which can be used in the design of corresponding molecular machines.

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