Spectroscopic properties, structure, and photoinduced motion of 4-(2-naphthyl)pyridine in cyclodextrin cavities

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Spontaneous and photoinduced protonation of 4-(2-naphthyl)pyridine (**1**) in solutions and in complexes with β-cyclodextrin (β-CD) and 2-hydroxypropyl-β-cyclodextrin (HP-β-CD) was studied using the absorption and fluorescence spectroscopies. The structures and stabilities of complexes of compound **1** and its quaternized derivative, 1-methyl-4-(2-naphthyl)pyridinium perchlorate (**3**), with β-CD and HP-β-CD were examined by ^{1}H NMR titration ($\log K = 1.5$—2.3). The molecule of naphthylpyridine **1** is always in the cyclodextrin cavity, regardless of the pH value of the solution. 2-Hydroxypropyl-β-cyclodextrin binds better the neutral form of compound **1** than does β-CD, while naphthylpyridinium salts exhibit nearly equal affinities to both cavitands. According to spectroscopic data, pK_a (**1**) is 5.12 in water, which favors protonation of the N atom both in the ground and excited states; as a result, the fluorescence spectrum exhibits only the band of the protonated form with a lifetime of 15 ns. The addition of HP-β-CD to a solution of naphthylpyridine **1** results in the formation of inclusion complex **1**@HP-β-CD, lowers pK_a to 4.62, and gives rise to a fluorescence band of the nonprotonated form of compound **1** with a lifetime of 1.25 ns. Therefore, the presence of compound **1** in the HP-β-CD cavity precludes its protonation in the excited state. The initial portions of the fluorescence curves for compound **1** in solution and in its complex with HP-β-CD obtained upon pulsed excitation were compared to propose the initiation mechanism of short-lived fluorescence of the nonprotonated form of naphthylpyridine **1**. Quantum chemical modeling of the protonation and complexation of compound **1** in the presence of water was performed. Based on the results obtained, a reversible photoinduced mechanical motion of naphthylpyridine **1** in the HP-β-CD cavity was suggested.

Key words: naphthylpyridine, β-cyclodextrin, hydroxypropyl-β-cyclodextrin, inclusion complexes, stability constants, electronic absorption spectroscopy, fluorescence, quantum chemical modeling, NMR spectroscopy.

Earlier, photoinduced intra- and intermolecular proton transfer in excited organic systems has been studied in solutions (see, *e.g.*, Ref. 1). We have demonstrated[2] that 4-(2-naphthyl)pyridine (**1**) in the excited state in aqueous solution adds a water proton to the N atom, which gives rise to an intense fluorescence band (λ_{max} = 475 nm) considerably (by 100 nm) shifted to the longer-wavelength region with respect to the fluorescence maximum of compound **1** in aprotic solvents. Derivatives of naphthylpyridine **1** exhibit similar properties.[3] The addition of β-cyclodextrin (β-CD) or 2-hydroxypropyl-β-cyclodextrin (HP-β-CD) to an aqueous solution of compound **1** results in the fluorescence of both protonated and nonprotonated forms of **1** (FPF and FNF, respectively). This suggests that the formation of inclusion complexes of compound **1** with cyclodextrins precludes its protonation in the excited state. In a complex, protonation can be hindered by penetration of the pyridine residue of compound **1** into the β-CD cavity, which is more hydrophobic than water. However, in structure **1** the naphthalene residue is more hydrophobic than the pyridine residue. Therefore, the formation of an inclusion complex with the naphthalene residue in the cavity and the hydrophilic pyridine residue contacting the aqueous environment outside the cavity seems *a priori* more probable. In this case, however, a question arises as to how complexation can preclude the protonation of naphthylpyridine **1**.

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In this work, we examined the structures and stabilities of the inclusion complexes of compound **1** and its protonated and quaternized forms with β-CD and HP-β-CD (the latter is soluble in water better than the former) using ^{1}H NMR titration. Photophysical processes giving rise to FNF in these complexes were studied by measuring the absorption and fluorescence spectra. The fluorescence kinetics was measured on the nanosecond time scale; quantum chemical modeling was used to determine the structures and energies of formation of the inclusion complexes of naphthylpyridine **1** with HP-β-CD and to study the influence of water on the protonation of **1**. In addition, we estimated for the first time the distance travelled by the "guest" molecule in the cyclodextrin cavity upon the photoinduced protonation.

Experimental

Hydroxypropyl-β-cyclodextrin (degree of substitution is 4.5; Aldrich) and β-cyclodextrin (Cyclolab, Hungary) were used as is. 4-(2-Naphthyl)pyridine (**1**) was prepared as described earlier.[4]

Elemental analysis was carried out at the Microanalysis Laboratory, A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences. Melting points were determined in capillaries on a MEL-Temp II instrument.

^{1}H NMR spectra were recorded on a Bruker DRX-500 spectrometer in $CDCl_3$ and D_2O—MeCN-d_3 (4 : 1) at 30 °C with the solvent or HOD signals (δ_H 7.27 or 4.70, respectively) as the internal standards. Homonuclear 2D NMR spectra (^{1}H—^{1}H COSY and ROESY) were used to assign the proton signals and to refine the structures of the complexes. 2D experiments were carried out with the standard parameters specified in the Bruker software. The mixing time in the ROESY experiment was 300 μs.

4-(2-Naphthyl)pyridin-1-ium perchlorate (2). A 70% solution of $HClO_4$ (30 μL) was added to a solution of naphthylpyridine **1** (21 mg, 0.1 mmol) in EtOH (1 mL). The reaction mixture was kept at −6 °C for six days. The precipitate that formed was filtered off, washed with benzene, and recrystallized from benzene—EtOH (1 : 1). The yield of compound **2** was 13 mg (42%), m.p. 236—238 °C. ^{1}H NMR (D_2O—MeCN-d_3 (4 : 1), 30 °C), δ: 7.84—7.90 (m, 2 H, H(6), H(7)); 8.18—8.23 (m, 2 H, H(5), H(8)); 8.28—8.30 (m, 1 H, H(3)); 8.34 (d, 1 H, H(4), J = 8.6 Hz); 8.52—8.53 (m, 2 H, H(3′), H(5′)); 8.71 (s, 1 H, H(1)); 8.94—8.95 (m, 2 H, H(2′), H(6′)). Found (%): C, 59.11; H, 3.79; N, 4.51. $C_{15}H_{12}ClNO_4$. Calculated (%): C, 58.93; H, 3.96; N, 4.58.

1-Methyl-4-(2-naphthyl)pyridinium iodide. Methyl iodide (47 μL, 0.75 mmol) was added to a solution of compound **1** (100 mg, 0.5 mmol) in benzene (7 mL). The reaction mixture was kept at room temperature for five days. The precipitate that formed was filtered off and washed with benzene (3×5 mL) and pentane (3×5 mL). The yield was 146 mg (86%), m.p. 215—216 °C (from EtOH). ^{1}H NMR ($CDCl_3$, 25 °C), δ: 4.67 (s, 3 H, NMe); 7.58—7.64 (m, 2 H, H(6), H(7)); 7.79 (d, 1 H, H(3), J = 7.4 Hz); 7.88 (d, 1 H, H(4), J = 7.4 Hz); 7.97—8.01 (m, 2 H, H(5), H(8)); 8.34—8.36 (m, 3 H, H(1), H(3′), H(5′)); 9.24—9.26 (m, 2 H, H(2′), H(6′)). Found (%): C, 54.91; H, 4.04; N, 3.89. $C_{16}H_{14}IN$. Calculated (%): C, 55.35; H, 4.06; N, 4.03.

1-Methyl-4-(2-naphthyl)pyridinium perchlorate (3). A 70% solution of $HClO_4$ (30 μL) was added to a solution of 1-methyl-4-(2-naphthyl)pyridinium iodide (35 mg, 0.1 mmol) in MeOH (3 mL). The reaction mixture was kept at room temperature for 24 h. The precipitate that formed was filtered off and recrystallized from MeOH. The yield of compound **3** was 17 mg (52%), m.p. 199—201 °C. ^{1}H NMR (D_2O—MeCN-d_3 (4 : 1), 30 °C), δ: 4.52 (s, 3 H, NMe); 7.85—7.91 (m, 2 H, H(6), H(7)); 8.18—8.22 (m, 2 H, H(5), H(8)); 8.29—8.30 (m, 1 H, H(3)); 8.34 (d, 1 H, H(4), J = 8.6 Hz); 8.58—8.59 (m, 2 H, H(3′), H(5′)); 8.75 (br.s, 1 H, H(1)); 8.92—8.94 (m, 2 H, H(2′), H(6′)). Found (%): C, 59.84; H, 4.56; N, 4.31. $C_{16}H_{14}ClNO_4$. Calculated (%): C, 59.91; H, 4.71; N, 4.37.

During **^{1}H NMR titration**, the stoichiometries and the stability constants of the complexes of compounds **1**—**3** with cyclodextrins were determined by analyzing the shifts of the substrate proton signals ($\Delta\delta_H$) at different ratios of the cavitand and substrate concentrations. The cyclodextrin concentration was varied from 0 to $3 \cdot 10^{-3}$ mol L^{-1}, the total concentration of compounds **1**—**3** being always constant (~$1 \cdot 10^{-3}$ mol L^{-1}). The $\Delta\delta_H$ values were measured to within 0.001 ppm with a correction for the shift of the signal of MeCN-d_2. The stability constants of the complexes were calculated with the HYPNMR program;[5] the logarithms of the constants are given in Table 1.

Complexes of naphthylpyridine **1** with cyclodextrins for spectroscopic measurements were obtained by adding the substrate to aqueous solutions of cavitands heated to 50 °C; the resulting complexes were kept at room temperature for at least 24 h before spectroscopic investigations. The concentration of compound **1** in the solutions was 10^{-6}—10^{-4} mol L^{-1}; the concentrations of the cyclodextrins were $5 \cdot 10^{-3}$ mol L^{-1}. Twice-distilled water, hexane (purified by column chromatography on silica gel followed by distillation), and acetonitrile (Grade-F, Reakhim, water content less than 0.01%) were used as solvents.

Electronic absorption spectra were recorded on a Specord M-40 spectrophotometer; fluorescence spectra were recorded on Elyumin 2-M and Perkin—Elmer LS55 spectrofluorimeters. The fluorescence kinetics and lifetimes were measured on a Fluotime 200 fluorescence spectrometer (PicoQuant GmbH). The pK_a values were determined from the electronic absorption spectra recorded at different pH values of the solution. The quantum yield of fluorescence (φ_f) was calculated with anthracene as a standard (φ_f = 0.3 in ethanol[6]).

Quantum chemical calculations with full geometry optimization for all compounds and complexes were carried out by the PM3 semiempirical method with a standard set of parameters[7]

Table 1. Stability constants K of the complexes of compounds **1**—**3** with β-CD and HP-β-CD[a]

Compound	log$K$[b]	
	β-CD	HP-β-CD
1	1.9	2.3
2	1.7	1.7
3	1.6	1.5

[a] ^{1}H NMR titration in D_2O—MeCN-d_3 (4 : 1), 30 °C.
[b] K/L mol^{-1} = [(**1**—**3**)@CD]/([**1**—**3**] • [CD]); the error of determination is ±30%.

(the PC GAMESS program). The enthalpies of formation (ΔH_f), the binding energies of the components of the complexes (E_{bind}), and the energies of penetration of naphthylpyridine with allowance for water molecules were calculated (in the designations $\mathbf{1_n}$ and $\mathbf{1_p}$, the subscripts "n" and "p" indicate that the HP-β-CD cavity accommodates the naphthalene or pyridine residue of naphthylpyridine **1**, respectively). The energies E_{bind} were calculated as the difference between the ΔH_f values of the optimized complexes and the sums of the ΔH_f values of their components.

The protonation of compound **1** in the ground and excited states was calculated using the TDDFT/PBE method incorporated into the Priroda 6 program package.[8]

The exact structure of 2-hydroxypropyl-β-cyclodextrin is unknown.[9] This is due to the fact that the base-catalyzed synthesis of HP-β-CD from propylene oxide and β-CD gives an inseparable mixture of alkylation products in which the alcoholic OH protons are randomly replaced by the hydroxypropyl groups, the primary O(6) groups being mainly replaced under more strongly basic conditions.[9] In accord with the structural characteristics of the HP-β-CD used, as well as for certainty in the geometry optimization of HP-β-CD, the starting structure was a symmetric β-CD molecule (symmetry group C_7) in which seven primary OH groups are replaced by 2-hydroxypropyl groups in such a conformation that all OH groups are oriented toward the outside of the hydrophobic cavity (*i.e.*, toward the aqueous environment) to provide the highest possible solubility of HP-β-CD. The resulting fully optimized structure of HP-β-CD (also with C_7 symmetry) was used to design the model inclusion complexes; the results of the calculations are given in Table 2. It should be noted that the model structure with seven 2-hydroxypropyl groups ($CH_2CH(OH)CH_3$) on the narrower portal of HP-β-CD has the deepest possible cavity compared to the structures in which H atoms of the primary OH groups are only partially replaced by 2-hydroxypropyl fragments. Therefore, the E_{bind} values calculated for such a HP-β-CD model can be regarded as the upper bound for the energies of formation of the complexes.

Table 2. PM3-calculated enthalpies of formation and relative energies of the compounds and the complexes

Compound or complex	ΔH_f [a]	E_{bind} [b]	ΔE_{bind} [c]
	kcal mol^{-1}		
H_2O	−53.4	—	—
$5H_2O$	−291.0	−23.9[d]	—
HP-β-CD	−1792.2	—	—
$5H_2O$@HP-β-CD	−2090.9	−7.7	—
1	71.7	—	—
$\mathbf{1}\cdot H^+$ [e]	221.9	—	—
$\mathbf{1}\cdot 5H_2O$	−215.2	—	—
$\mathbf{1}\cdot H^+OH^-\cdot 4H_2O$	−189.5	—	25.7
$\mathbf{1_p}\cdot 5H_2O$@HP-β-CD	−2020.4	−13.0	—
$\mathbf{1_n}\cdot 5H_2O$@HP-β-CD	−2019.1	−11.7	—
$\mathbf{1_p}\cdot H^+OH^-\cdot 4H_2O$@HP-β-CD	−1996.1	−14.4	24.3
$\mathbf{1_n}\cdot H^+OH^-\cdot 4H_2O$@HP-β-CD	−1997.4	−15.7	22.0

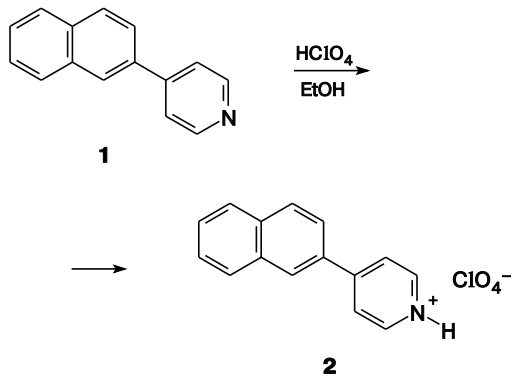
[a] The calculated enthalpy of formation.
[b] The energy of binding of "guest" molecules with $5H_2O$@HP-β-CD.
[c] The energy of penetration of naphthylpyridine **1** into the HP-β-CD cavity calculated as the difference between the energy of filling the empty space in $5H_2O$@HP-β-CD with an additional water pentamer (so that the cavity accommodates ten water molecules) and the energy of binding of "guest" molecules with $5H_2O$@HP-β-CD.
[d] The energy of formation of a cluster pentahydrate.
[e] The proton affinity is 231.3 kcal mol^{-1}.

Results and Discussion

Synthesis of pyridine derivatives 1—3. To study the structures and stabilities of the complexes of 4-(2-naphthyl)pyridine (**1**) with β-CD and HP-β-CD, we obtained its derivatives, *viz.*, naphthylpyridinium perchlorate (**2**) and 1-methyl-4-(2-naphthyl)pyridinium perchlorate (**3**). The synthesis of 4-(2-naphthyl)pyridine (**1**) has been described earlier.[4]

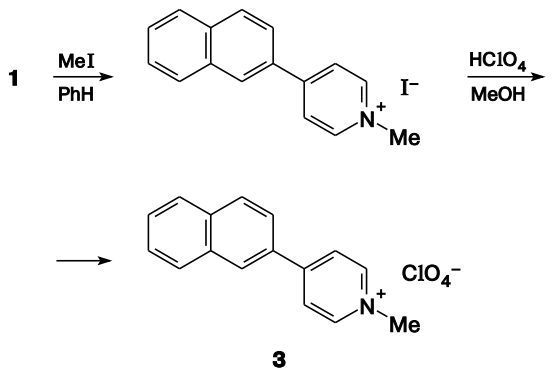
Naphthylpyridinium perchlorate **2** was obtained in 42% yield by treatment of compound **1** with an excess of conc. $HClO_4$ in ethanol (Scheme 1).

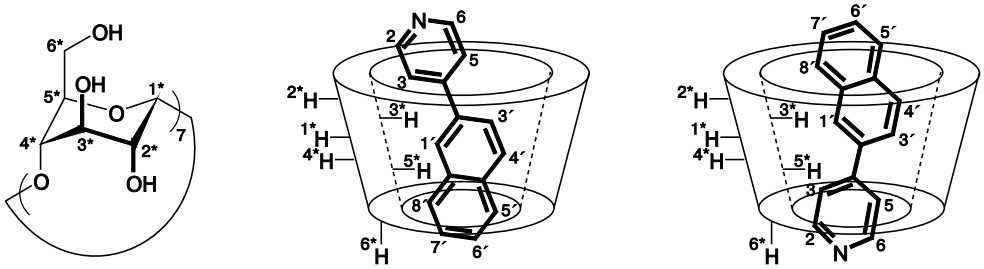
Scheme 1



1-Methyl-4-(2-naphthyl)pyridinium perchlorate **3** was obtained by quaternization of compound **1** with methyl iodide followed by a metathesis reaction with conc. $HClO_4$ in methanol (Scheme 2). The yield of **3** was 52%.

Scheme 2





^{1}H NMR spectroscopy. NMR spectroscopy is widely used for structure determination and measurement of the stabilities of various supramolecular complexes in solution, in particular, for the determination of the way in which the "guest" molecule is included in the cyclodextrin cavity, the stoichiometry of the complexation, and the stabilities of such complexes.[10] We studied mixtures of compounds **1**—**3** with β-CD and HP-β-CD using 2D NMR spectroscopy and ^{1}H NMR titration. According to preliminary data, the hydrophobic substrate should be dissolved in a mixture of water and an organic solvent to provide a concentration required for NMR experiments (~$1 \cdot 10^{-3}$ mol L^{-1} and higher). We used a D_2O—MeCN-d_3 (4 : 1) mixture in which the solubility of the most hydrophobic compound **1** is ~$1.6 \cdot 10^{-3}$ mol L^{-1} and the solubilities of the cyclodextrins under study are at least $6 \cdot 10^{-3}$ mol L^{-1} at 30 °C.

The macrocycle of β-CD comprises seven α-glucopyranose units attached to one another through positions 1* and 4*.

The resulting cavity is shaped like a truncated cone with two unequal portals. In this structure, only the H(3*) and H(5*) protons are directed toward the inside of the cavity. A fragment of the ROESY NMR spectrum of a mixture of naphthylpyridine **1** and β-CD illustrating intermolecular interactions is shown in Fig. 1. The spec-

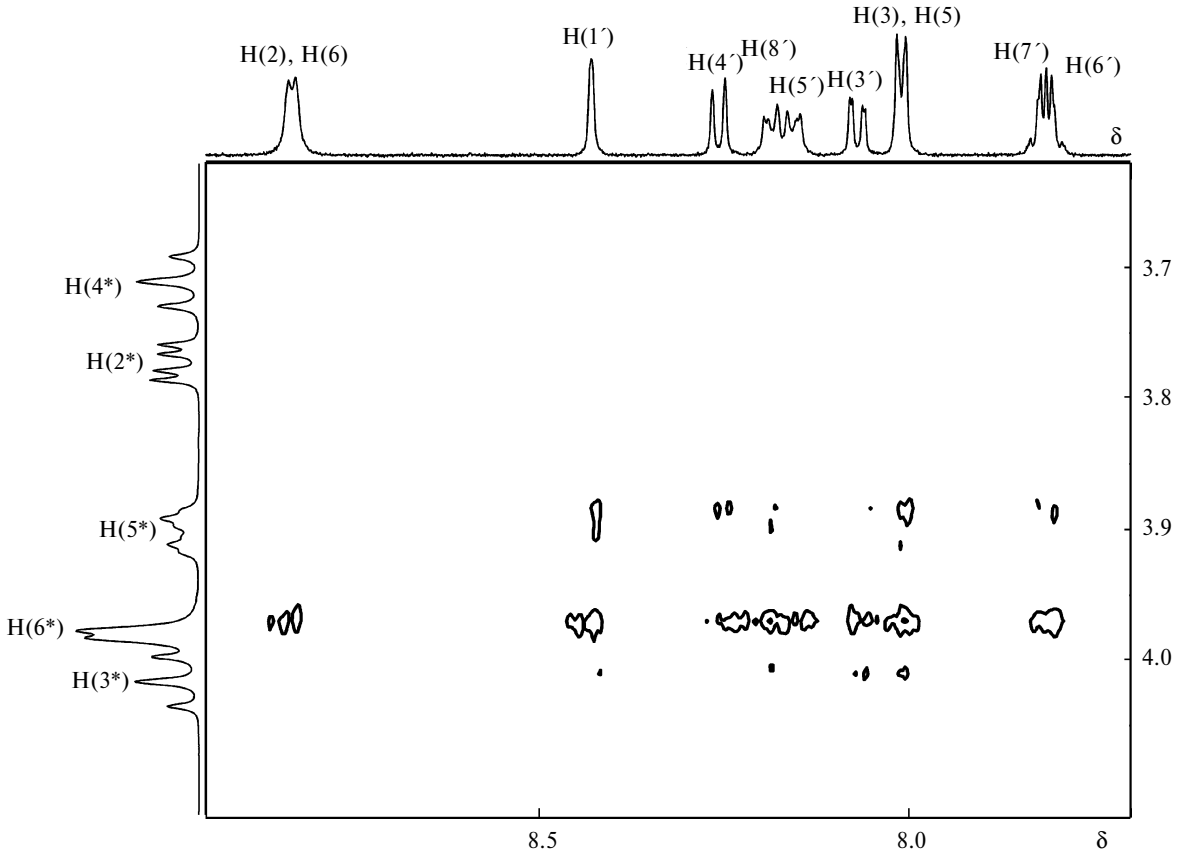


Fig. 1. Fragment of the ROESY NMR spectrum of a mixture of compound **1** ($C_1 = 1.6 \cdot 10^{-3}$ mol L^{-1}) and β-CD ($C_{\beta\text{-CD}} = 6 \cdot 10^{-3}$ mol L^{-1}) in D_2O—MeCN-d_3 (4 : 1), 30 °C.

trum reveals relatively weak cross peaks for dipolar couplings of most of the substrate protons with the "inner" H(3*) and H(5*) protons and the methylene H(6*) protons of the cyclodextrin. This suggests that the hydrophobic molecule **1** is in the lipophilic cavity of the cavitand. According to the spectral pattern, the asymmetric "guest" molecule is accommodated in the β-CD cavity in both possible ways.

The ROESY NMR spectra of the mixtures of salts **2** and **3** with β-CD show a similar pattern of intermolecular interactions (see, *e.g.*, Fig. 2). A slight difference from the ROESY NMR spectrum of the mixture of neutral compound **1** with β-CD is that the cross peaks between the pyridine H(3) and H(5) protons in molecules **2** and **3** and the "inner" protons of the cyclodextrin are less intense. This suggests that the positively charged hydrophilic pyridine residue in the complexes **2**(**3**)@β-CD protrudes more into the water—acetonitrile environment than in the complex **1**@β-CD.

Because of the incomplete replacement of the protons of the primary OH groups in HP-β-CD by 2-hydroxypropyl groups, the ^{1}H NMR spectrum of HP-β-CD exhibits a set of strongly broadened lines. The ROESY NMR spectra of the mixtures of compounds **1**—**3** with HP-β-CD show very weak, difficult-to-interpret cross peaks due to intermolecular interactions. However, the positions of these cross peaks (δ 3.9—4.0 for aliphatic protons) most likely suggest the formation of inclusion complexes **1**—**3**@HP-β-CD, which are structurally similar to the β-CD complexes.

The stabilities of the complexes of compounds **1**—**3** with the cyclodextrins were quantified using ^{1}H NMR titration. It should be noted that mixing of the components results in relatively small and differently directed shifts of the signals of the substrate and cavitand protons ($\Delta\delta_H$ up to 0.10 ppm). Such a behavior is characteristic of cyclodextrin-based supramolecular systems.[10] The variation of the chemical shifts of the substrate protons with the ratio of the concentrations of the CD and the substrate is well described by the model considering the sole equilibrium

$$\mathbf{1—3} + \mathrm{CD} \overset{K}{\rightleftharpoons} (\mathbf{1—3})@\mathrm{CD}, \qquad (1)$$

where K/L mol^{-1} is the stability constant of the 1 : 1 complex. The stability constants (log$K$) obtained are given in Table 1.

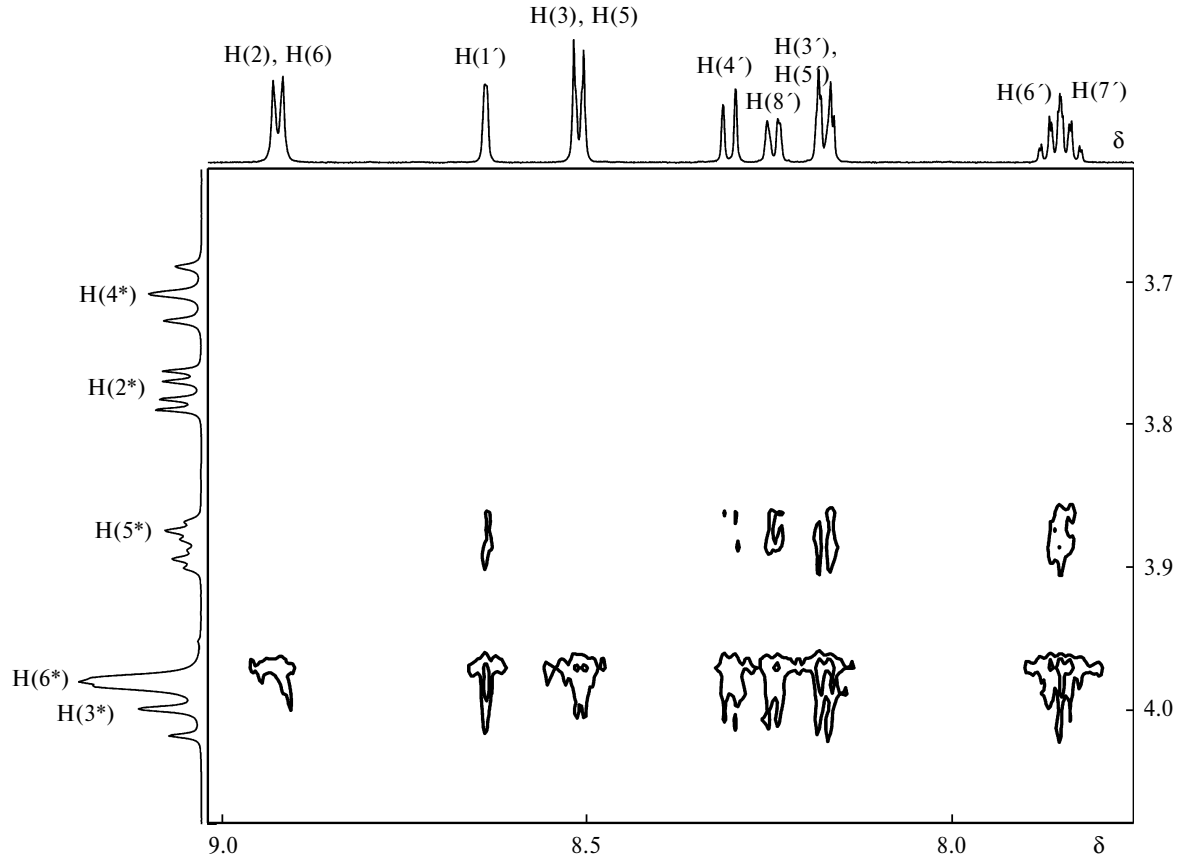


Fig. 2. Fragment of the ROESY NMR spectrum of a mixture of compound **2** and β-CD ($C_2 = C_{\beta\text{-CD}} = 6 \cdot 10^{-3}$ mol L^{-1}) in D_2O—MeCN-d_3 (4 : 1), 30 °C.

It can be seen in Table 1 that the complexes of compound **1** with β-CD and HP-β-CD in the water—acetonitrile mixture are less stable than in water (in water, $\log K$ = 3.30 and 3.54,[3] respectively). Obviously, this reflects the less hydrophilic character of the mixed solvent, which makes it difficult to retain the hydrophobic substrate within the cavity of the cavitand. Noteworthy is a parallel decrease in $\log K$; *i.e.*, the complex **1**@β-CD remains less stable than the complex **1**@HP-β-CD because of the stronger lipophilicity of the cavity of the latter cavitand bearing hydrophobic substituents at the primary OH groups. The complexes of salts **2** and **3** with both cavitands have nearly equal stabilities ($\log K$ = 1.5—1.7) but are less stable than the complexes of compound **1**. This also reflects the higher hydrophilicity of the cationic form of the substrate compared to its neutral form, which reduces its affinity for the lipophilic cavity of the cyclodextrin. Note, however, that the aforementioned increase in the hydrophilicity of salts **2** and **3** does not lead to complete decomposition of the inclusion complexes, probably because of the hydrophobic nature of the naphthalene residue in all the substrates studied.

Electronic absorption spectra. The spectra of naphthylpyridine **1** relatively slightly depend on the solvent. However, in aqueous solutions with low pH values, protonation of the N atom results in a considerable bathochromic shift of the spectrum (Fig. 3). Processing of the absorption spectra of compound **1** in water at different concentrations of $HClO_4$ (see Fig. 3) gave pK_a = 5.18, which is close to the experimental value found for pyridine (pK_a = 5.21).[11]

Compound **1** is efficiently protonated when its solution is stored in air, probably because of the generation of carbonic acid in water; the absorption spectrum shows the corresponding changes.

A freshly prepared neutral aqueous solution of naphthylpyridine **1** also contains its hydrated form, which absorbs weakly at the longer wavelengths compared to the spectrum of compound **1** in hexane. A similar change in the spectrum has been reported for an aqueous solution of 4,4′-bipyridyl.[12]

The addition of HP-β-CD, which is more soluble than β-CD, to an aqueous solution of compound **1** also has little effect on the absorption spectrum of the nonprotonated form. However, the protonated species of compound **1** partially formed in the presence of carbon dioxide disappears upon the addition of HP-β-CD. This suggests that compound **1** is deprotonated after its accommodation in the HP-β-CD cavity. A similar effect was observed in the formation of the complex **1**@β-CD in aqueous solution.

Fluorescence spectra and lifetimes of naphthylpyridine 1 in solutions. The fluorescence spectra of compound **1** in various solvents are shown in Fig. 4. In the spectrum of a neutral aqueous solution, the broad band with λ_{max} = 475 nm relates to its protonated species formed in the excited state.[2] The processes that occur can be described as follows (Scheme 3).

Scheme 3

$$\mathbf{1} + H_2O \longrightarrow \mathbf{1}\cdot H_2O \xrightarrow{h\nu} \mathbf{1}^*\cdot H_2O \longrightarrow$$
$$\longrightarrow (\mathbf{1}\cdot H^+)^* \,||\, OH^- \longrightarrow \mathbf{1}\cdot H_2O + h\nu_1\ (475\ nm)$$

The fluorescence quantum yield of naphthylpyridine **1** in water is nearly unity. The fluorescence lifetime for an argon-purged aqueous solution is 15±0.1 ns; after the addition of $HClO_4$, the lifetime is 14.7±0.1 ns. In both

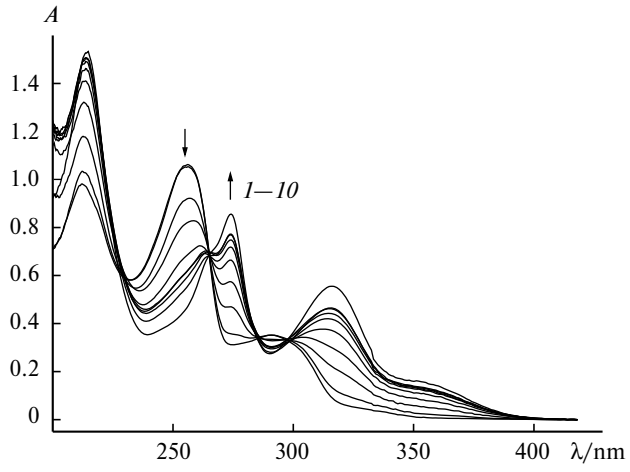


Fig. 3. Absorption spectra of an aqueous solution of compound **1** ($3\cdot10^{-5}$ mol L^{-1}, 1-cm cell) upon the addition of an aqueous solution of compound **1** ($3\cdot10^{-5}$ mol L^{-1}) containing $HClO_4$. Curves *1—10* correspond to a successive decrease in the pH value of the solution from 6.3 to 3.9.

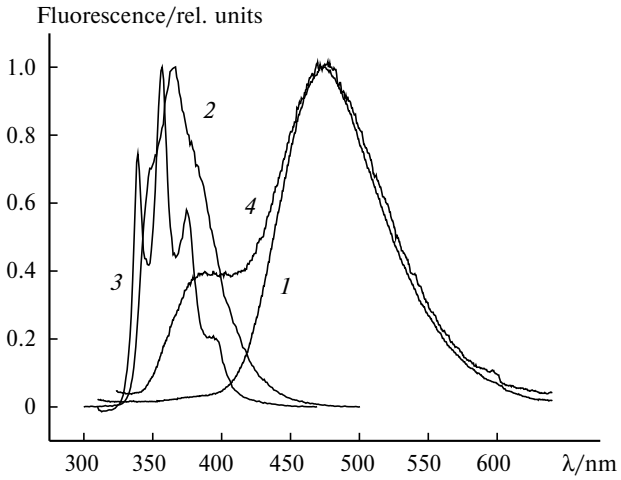


Fig. 4. Normalized fluorescence spectra of compound **1** in neutral aqueous solution (*1*), MeCN (*2*), and hexane (*3*) and its complex with HP-β-CD in water (*4*).

cases, the fluorescence decay obeys a monoexponential law. In hexane and MeCN, the fluorescence quantum yields of the nonprotonated form of compound **1** are 0.09±0.02 and 0.7±0.15, respectively.

In aprotic solvents, the fluorescence peak of compound **1** experiences a hypsochromic shift by ~100 nm compared to its aqueous solution. In nonpolar hexane, the FNF band of compound **1** shows a pronounced vibronic structure, while in polar MeCN, it is indistinct (see Fig. 4).

Spectroscopic properties and fluorescence lifetimes of naphthylpyridine 1 in the complex with HP-β-CD. The addition of β-CD or HP-β-CD to an aqueous solution of compound **1** substantially changes its fluorescence spectra because of the formation of the inclusion complexes with these cyclodextrins.[2,3] The main changes include the appearance of the FNF of compound **1** with λ_{max} = 375 nm (see Fig. 4, curve *4*) and the simultaneous weakening of the fluorescence of its protonated form at 475 nm. In addition, since the protonation becomes less probable, the complex of compound **1** with HP-β-CD has pK_a = 4.62, which favors the appearance of FNF. Obviously, FNF is possible only if the formation of the inclusion complex in the excited state prevents the protonation of compound **1**.

Compound **1** can form two types of inclusion complexes with HP-β-CD, depending on the fragment (naphthalene or pyridine) in the HP-β-CD cavity. At first glance, the structure with the more hydrophobic naphthalene residue fully immersed in the cavity and the more hydrophilic pyridine residue being partially outside the cavity and contacting the aqueous phase is more preferred. However, the fact that protonation is prevented in the presence of HP-β-CD suggests that the pyridine residue can also be in the cavity of the cavitand; most likely, both these types of complexes are in equilibrium (NMR data). Otherwise (*i.e.*, when the cavity accommodates only the naphthalene residue, while the pyridine residue is outside the cavity), the formation of an inclusion complex could hardly influence the protonation. Thus, the protonation rate of compound **1** is generally determined by the location of its pyridine residue in the HP-β-CD cavity.

For a more detailed study of this phenomenon, we measured the fluorescence lifetimes of compounds **1**—**3** in solutions and in their complexes with HP-β-CD. Fluorescence of compound **1** was excited at 280 nm (for its protonated forms, additionally at 375 nm). The results obtained are given in Table 3. The fluorescence decays of naphthylpyridine **1** in the complex, which was observed at 370 nm for FNF **1** and at 490 nm for FPF **1**, have a biexponential character, while its fluorescence in solutions shows only monoexponential decays. The fluorescence lifetimes given in Table 3 are interpreted in terms of the existence of two types of complexes differing in the location of the pyridine residue of compound **1** relative to the HP-β-CD cavity.

Table 3. Fluorescence lifetimes τ for compounds **1**—**3** in MeCN and water and for their complexes with HP-β-CD

Compound or complex	λ_{obs}/nm	τ/ns	Relative amplitude
1@HP-β-CD	370 (FNF)	1.25±0.3	6
		4.87±0.13	1
	490 (FPF)	17.1±0.1	3
		6.2±0.4	1
1—H_2O	470	15±0.1	Monoexponential
1—MeCN	370	9.5±0.05	The same
2@HP-β-CD	480	16.1±0.1	»
2—H_2O	480	14.7±0.03	»
2—MeCN	480	13.3±0.03	»
3@HP-β-CD	480	15.32±0.05	»
3—H_2O	480	14.55±0.05	»
3—MeCN	480	12.73±0.03	»

Pulsed excitation of compound **1** will always immediately causes FNF unless the protonation of the N atom occurs. However, the spectrum of an aqueous solution of compound **1** shows no FNF on the nanosecond scale; only the steady-state FPF instead occurs instead. This suggests a high protonation rate of compound **1** in the excited state. According to quantum chemical calculations (see below), after the formation of the complex $\mathbf{1}_n$@HP-β-CD in which the pyridine residue of compound **1** is outside the HP-β-CD cavity, its contact with water is somewhat limited since water molecules cannot approach it from the cavitand side. Because of this, short-lived FNF (1.25 ns) becomes possible.

For the complex in which the pyridine residue of naphthylpyridine **1** is in the HP-β-CD cavity (Fig. 5, *a*)*, protonation of compound **1** in the excited state is substantially limited because a proton from the aqueous phase has difficulty in reaching the N atom and proton transfer from the water pentamer seems to be less efficient: four surrounding water molecules may be insufficient for stabilization of the protonated form existing as the ion pair $C_{15}H_{11}N^+$—H...$^-$OH (Fig. 5, *b*). That is why the FNF lifetime in this complex increases to 4.87 ns; however, it is shorter than in MeCN, in which no protonation of excited naphthylpyridine **1** competing with FNF occurs. Thus, the FNF lifetimes are determined by the protonation rate of compound **1** in the excited state, which in turn depends on the structures of the resulting inclusion complexes.

The FPF of compound **1** in the complex after pulsed excitation (Fig. 6, curve *2*) is noticeably delayed compared to FNF (see Fig. 6, curve *1*) and FNF in anhydrous

* Five water molecules hydrating the pyridine N atom that were considered in the calculations are shown only.

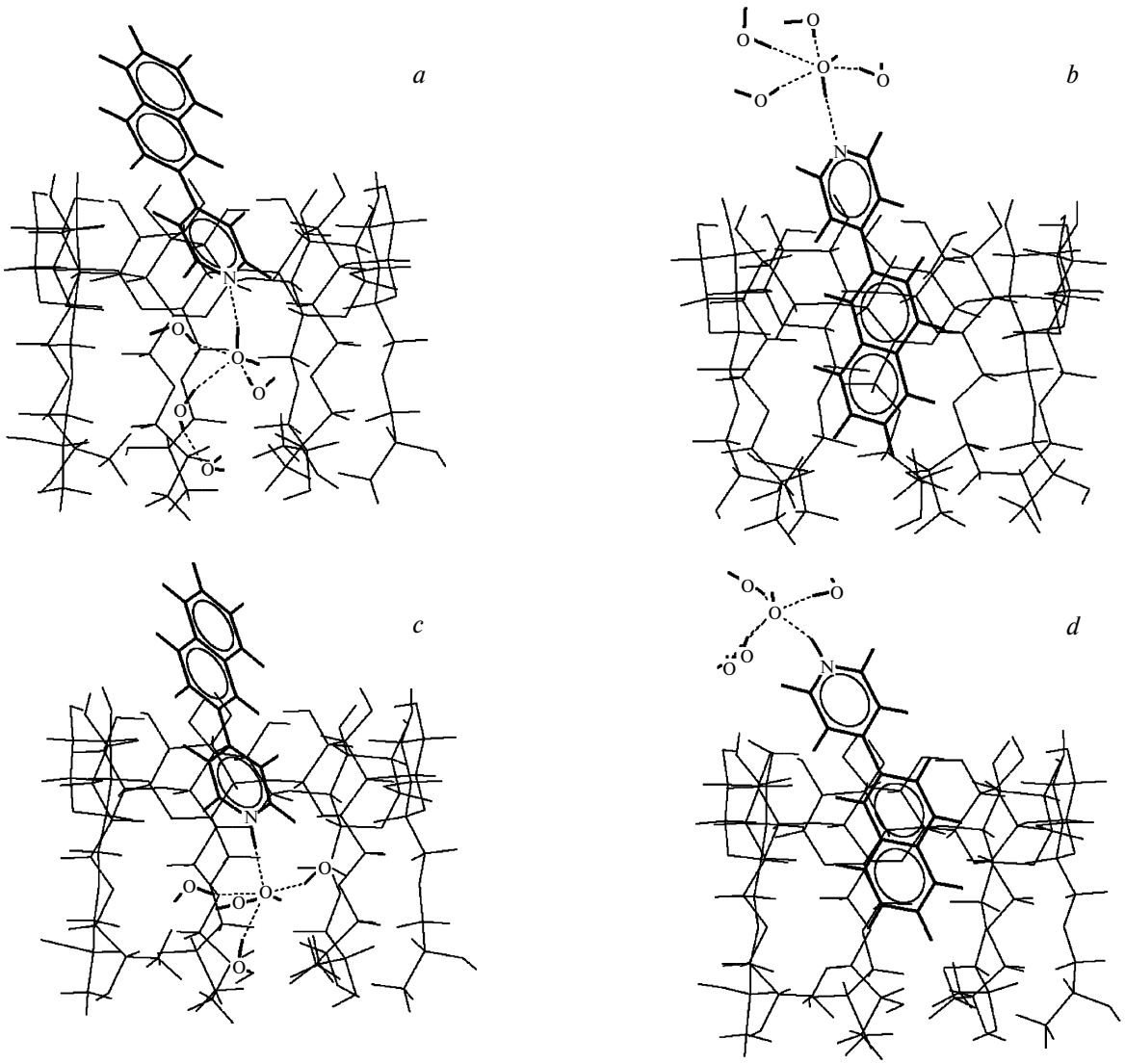


Fig. 5. PM3-calculated structures of the complexes **1** • $5H_2O$@HP-β-CD (*a*, *b*) and **1** • H^+OH^- • $4H_2O$@HP-β-CD (*c*, *d*): the pyridine (*a*, *c*) and naphthalene residues (*b*, *d*) in the HP-β-CD cavity.

MeCN (see Fig. 6, curve *3*), where compound **1** in the excited state is not protonated. The initial portions of the kinetic curves show a rise of FPF and a decay of FNF in the complex, which reveals a correlation between these processes. Therefore, FPF is in fact due to the protonation of compound **1** in the excited state, thus competing with FNF and determining its lifetime.

If the pyridine residue of naphthylpyridine **1** is outside the HP-β-CD cavity (*i.e.*, the N atom is surrounded by water molecules), after its protonation in the excited state one can expect that the FPF lifetime will be of the same order of magnitude as the lifetime observed in the aqueous solution of compound **1**. That is why the lifetime $\tau = 17.1$ ns should be related to the FPF of the complex $\mathbf{1}_n$@HP-β-CD.

A comparison of the fluorescence spectra of a naphthylpyridine derivative in a complex with HP-β-CD and in an aprotic solvent (MeCN) suggested close values of the polarities of MeCN and the HP-β-CD cavity.[3] In anhydrous MeCN, the fluorescence lifetimes of compounds **2** and **3** (both are ionic derivatives of naphthylpyridine **1**) are 13.3 and 12.73 ns, respectively, which is substantially shorter than in water. Therefore, one would expect that the FPF lifetime of the excited-state complex with the protonated form of compound **1**, in which the pyridine fragment is in the cavity, will be shorter than in water (actually, this lifetime is 6.2 ns). The difference of this lifetime from the aforementioned ones is probably due to the dissimilar counterions (ClO_4^- or OH^-) accompanying the protonation and to an equilibrium between the protonated and neutral forms of compound **1**. The increase in the fluorescence lifetimes of compounds **2** and **3** in aqueous solution upon the addition of HP-β-CD (16.1 and 15.32 ns, respectively) suggests the formation of

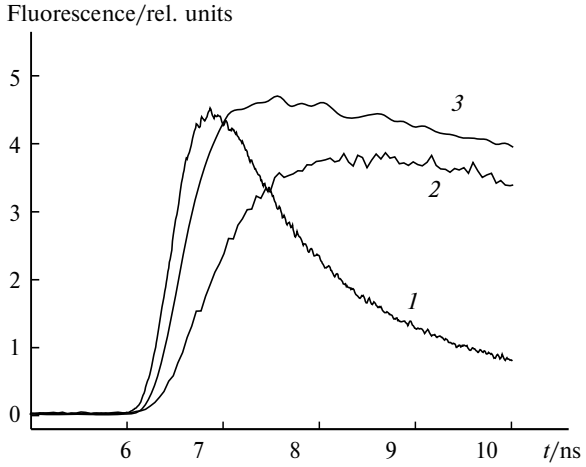


Fig. 6. Initial portions of the curves of the fluorescence kinetics of compound **1** upon the pulsed excitation (λ = 280 nm): in the complex with HP-β-CD observed at a wavelength of 370 nm (FNF) (*1*), in the complex with HP-β-CD observed at a wavelength of 490 nm (FPF) (*2*), and in MeCN observed at a wavelength of 370 nm (FNF) (*3*).

inclusion complexes with sufficiently hydrophilic compounds as well, which agrees with NMR spectroscopic data.

Schemes 4 and 5 show the processes occurring in the formation of inclusion complexes of compound **1** with HP-β-CD in aqueous solution and in the fluorescence excitation of compound **1** (for the complexes with the naphthalene and pyridine residues in the HP-β-CD cavity, respectively).

Scheme 4

$$\mathbf{1}\cdot H_2O + 10H_2O@\text{HP-}\beta\text{-CD} \longrightarrow \mathbf{1_n}\cdot 5H_2O@\text{HP-}\beta\text{-CD} +$$
$$+ 6H_2O \xrightarrow{h\nu} \mathbf{1_n}^*\cdot 5H_2O@\text{HP-}\beta\text{-CD} \xrightarrow{\tau = 1.25\ \text{ns}}$$
$$\longrightarrow \mathbf{1_n}\cdot 5H_2O@\text{HP-}\beta\text{-CD} + h\nu_1\ (375\ \text{nm})$$

$$\mathbf{1_n}^*\cdot 5H_2O@\text{HP-}\beta\text{-CD} \longrightarrow$$
$$\longrightarrow \mathbf{1_n}^*\cdot H^+OH^-\cdot 4H_2O@\text{HP-}\beta\text{-CD} \xrightarrow{\tau = 17.1\ \text{ns}}$$
$$\longrightarrow \mathbf{1_n}\cdot H^+OH^-\cdot 4H_2O@\text{HP-}\beta\text{-CD} + h\nu_2\ (475\ \text{nm})$$

$$\mathbf{1_n}\cdot H^+OH^-\cdot 4H_2O@\text{HP-}\beta\text{-CD} \longrightarrow \mathbf{1_n}\cdot 5H_2O@\text{HP-}\beta\text{-CD}$$

Quantum chemical modeling. The aim of our quantum chemical calculations was to consider the thermodynamics of protonation/deprotonation in an aqueous solution of naphthylpyridine **1** in the absence and in the presence of HP-β-CD. Additional tasks included structural determination of the "guests", the "hosts", and the complexes and calculations of the corresponding energies of formation. We took into account the fact that the experimentally found influence of complexation on the spontaneous

Scheme 5

$$\mathbf{1}\cdot H_2O + 10H_2O@\text{HP-}\beta\text{-CD} \longrightarrow \mathbf{1_p}\cdot 5H_2O@\text{HP-}\beta\text{-CD} +$$
$$+ 6H_2O \xrightarrow{h\nu} \mathbf{1_p}^*\cdot 5H_2O@\text{HP-}\beta\text{-CD} \xrightarrow{\tau = 4.87\ \text{ns}}$$
$$\longrightarrow \mathbf{1_p}\cdot 5H_2O@\text{HP-}\beta\text{-CD} + h\nu_1\ (375\ \text{nm})$$

$$\mathbf{1_p}^*\cdot 5H_2O@\text{HP-}\beta\text{-CD} \longrightarrow$$
$$\longrightarrow \mathbf{1_p}^*\cdot H^+OH^-\cdot 4H_2O@\text{HP-}\beta\text{-CD} \xrightarrow{\tau = 6.2\ \text{ns}}$$
$$\longrightarrow \mathbf{1_p}\cdot H^+OH^-\cdot 4H_2O@\text{HP-}\beta\text{-CD} + h\nu_2\ (475\ \text{nm})$$

$$\mathbf{1_p}\cdot H^+OH^-\cdot 4H_2O@\text{HP-}\beta\text{-CD} \longrightarrow \mathbf{1_p}\cdot 5H_2O@\text{HP-}\beta\text{-CD}$$

and photoinduced protonation, as well as NMR spectroscopic data, suggest the existence of complexes in which the pyridine residue can be both inside and outside the cavity. In addition, we tried to answer the question as to whether photoinduced protonation causes a mechanical displacement of the "guest" molecule within the cyclodextrin cavity. This process is of interest because this type of inclusion complexes could be used for the design of molecular machines.

Taking into account a conditional choice of the HP-β-CD structure (see Experimental) and limitations in studies of the influence of hydration on the protonation of compound **1** (only five water molecules were considered, see below), the results obtained were used for qualitative interpretation of the facts observed and for demonstration of the general trend of the displacement of substrates in the HP-β-CD cavity.

Calculations were carried out by the PM3 semiempirical method,[7] which has been often used earlier to calculate the structures and energies of formation of the complexes of cyclodextrins with various "guests". Although complexes of cyclodextrins are formed in aqueous solutions, the results obtained for separate complexes of hydrophobic molecules with cyclodextrins were quite realistic.[13] Since in the present work we studied the properties of complexes of the compound comprising the hydrophilic (pyridine) and hydrophobic fragments (naphthalene) and the protonation of compound **1** is possible only in the presence of water, the role of water as an essential component was examined in detail. Although the PM3 method is a semiempirical one, it is the only method that allows a consecutive computational procedure "guest" molecule (**1**)—"host" molecule (HP-β-CD)—"guest—host" inclusion complex because HP-β-CD and its complexes contain many atoms. It is known[7] that this method is parametrized to obtain realistic structural data and enthalpies of formation of molecules (ΔH_f). The latter circumstance makes it possible to directly calculate the energy of complexation and other energy characteristics and to estimate the stabilizing or destabilizing effects. The PM3 method provides good results in calculations of

hydrogen bonds and proton transfer for hydrogen-bonded complexes with conventional distances (*e.g.*, *l*(N...H—O)) no longer than 2.5 Å.[14]

An important quantity for estimation of the reliability of the method is the proton affinity (PA) energy. Calculations for naphthylpyridine give PA = 221.9 kcal mol^{-1}, which agrees well with the pyridine PA (222.3 kcal mol^{-1}) and with the PA values determined using ion cyclotron resonance.[15]

When considering protonation of naphthylpyridine, first we calculated the monohydrate **1** • H_2O since only a water molecule can act as a proton donor. According to our calculations, only one isomer has the structure of hydrate **1** • H_2O, in which a water proton forms a bond to the N atom ($C_{15}H_{11}N$...H—OH). For the second isomer (the ion pair $C_{15}H_{11}N^+$—H...$^-$OH; *i.e.*, the protonated form of **1** with the counterion HO^-), no local minimum was located on the potential energy surface. Therefore, spontaneous proton transfer in separate monohydrate **1** • H_2O is very unlikely.

A neutron diffraction study of the influence of humidity on the number of water molecules around β-CD at 120 K revealed[16] that there are 11—12 water molecules per β-CD molecule, of which five to six are in the cavity and the rest are near the hydrophilic portals of β-CD. The results obtained by molecular dynamic calculations were, on the whole, consistent with experimental data: five water molecules are constantly in the cavity when its number has been varied from 12 (see Ref. 16) to 258 (see Ref. 17) and seven water molecules are in the β-CD cavity surrounded by 827 water molecules.[18] It is essential that the water molecules in the β-CD cavity are hydrogen bonded to form a closed cluster (cyclic pentamer). The formation of a cluster has been assumed[17] to be the main factor favoring its retention in the hydrophobic cavity because such a cluster is more covalent (and hence hydrophobic) than the same number of nonbonded water molecules.

Since (1) the cavity volume in HP-β-CD is greater than in β-CD, (2) data on the structures of complexes with HP-β-CD are lacking, and (3) the number of water molecules in the cavity is unknown, first we ascertained that the HP-β-CD cavity can accommodate up to ten water molecules in the form of two cyclic pentamers. Their calculated energy of inclusion was −13.1 kcal mol^{-1}. Therefore, in the absence of any substrate, the HP-β-CD cavity is filled with water molecules and a hydrophobic molecule of compound **1** can penetrate into the cavity by displacing some water molecules from it. Because molecule **1** does not reach the bottom of the HP-β-CD cavity for geometrical reasons, we also ascertained that the remaining space suffices to accommodate a water pentamer. That is why we performed our calculations assuming that the cavity comprises naphthylpyridine **1** and a water pentamer.

To verify the possibility of protonation of naphthylpyridine in the presence of five water molecules, we calculated a pentahydrate of compound **1** and the ion pair **1** • H^+OH^- stabilized by four water molecules. We assumed that, according to the Grotthuss mechanism,[19] proton transfer occurs in the channel of the hydrogen bond $C_{15}H_{11}N$...H—OH, giving rise to the ion pair $C_{15}H_{11}N^+$—H...$^-$OH, while the other four water molecules stabilize this structure with separated charges. The optimized structures of the pentahydrate **1** • $5H_2O$ and the tetrahydrate of the ion pair **1** • H^+OH^- are shown in Fig. 7.

In the pentahydrate, the water molecule nearest to the N atom, as well as the OH group in the ion pair, is hydrogen bonded to four surrounding water molecules. One of them is also hydrogen bonded to the H atom of naphthylpyridine that is *ortho* to the N atom (see Fig. 7). The participation of the H atom in the *ortho*-position relative to the pyridine N atom in hydrogen bonding to an adjacent water molecule has been noted in the protonation of pyridine.[11] In addition, because of the negative charge on the OH group, the hydrogen bonds between it and the surrounding water molecules are appreciably shortened.

Our calculations of the system naphthylpyridine—five water molecules revealed two energy minima for the pentahydrate **1** • $5H_2O$ and the ion pair **1** • H^+OH^- • $4H_2O$, the former being 25.7 kcal mol^{-1} more favorable (see Table 2). This difference agrees well with the data obtained for the protonation of pyridine using a more precise method (B3LYP/cc-pVDZ): the pyridine pentahydrate proves to be more stable (by 28 kcal mol^{-1}) than its protonated form hydrogen-bonded to four water mol-

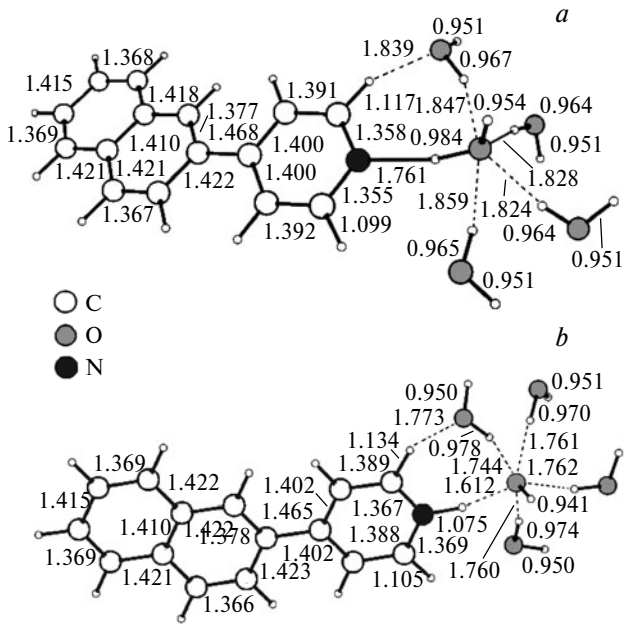


Fig. 7. PM3-optimized structures **1** • $5H_2O$ (μ = 3.21 D) (*a*) and **1** • H^+...$^-$OH • $4H_2O$ (μ = 11.22 D) (*b*).

ecules.[11] Therefore, protonation in the ground state is an endothermic process characterized by fluctuations,[19] which accounts for the weak basic properties of pyridine and its derivatives.

Because the energy barrier between the protonated form and the transition state (TS_b) in the proton transfer between the N and O atoms in the system RN...H...OH is very low (<1 kcal mol^{-1}),[11] the reverse process (deprotonation) can occur spontaneously. However, this holds for pyridine pentahydrate in the gas phase; in the bulk of aqueous solution, stabilization by surrounding water can weaken the endothermic effect of protonation and increase the height of the barrier TS_b. Therefore, a light quantum giving an energy to a naphthylpyridine molecule exposed to radiation not only brings it to the excited state S_1 but also provides its protonation.

Protonation in the excited state is facilitated because compound **1** in the state S_1 has a higher proton affinity than in the ground state S_0. This conclusion was drawn from the calculations of the structures **1** and **1** • H^+ in the ground and excited states using the DFT and TDDFT methods with the exchange-correlation functional PBE and agrees with the published data, according to which the basicity of pyridine derivatives increases with PA.[20] The structures with fully optimized geometries are shown in Fig. 8.

The transition $S_0 \rightarrow S_1$ changes the geometries of the molecules (see Fig. 8). For instance, structure **1** in the state S_1 is more planar and the electron density in its triad CNC is higher. As a result, the average charge on this fragment increases from –0.15 *e* in the state S_0 to –0.166 *e* in the state S_1 and the bonds are noticeably shorter. At the same time, while the formation of the protonated species **1** • H^+ makes the structure more planar, its transition into the state S_1 abruptly increases the torsion angle between both aromatic residues. This breaks their conjugation, leading to the more pronounced "quinonoid" character of the pyridine residue and to the highly delocalized electron density in the naphthalene residue of **1** • H^+.

Let us consider the protonation of compound **1** in the presence of HP-β-CD whose cavity contains, as we assumed, ten water molecules. Because the energy of their inclusion is –13.1 kcal mol^{-1} and E_{bind} of the pentahydrate is –7.9 kcal mol^{-1} (see Table 2), removal of five water molecules from the complex $10H_2O$@HP-β-CD for liberation of the space in the HP-β-CD cavity for a "guest" molecule is an endothermic process consuming 5.1 kcal mol^{-1}. However, this energy loss is compensated by the inclusion of the molecule of compound **1** into the HP-β-CD cavity. The resulting energy gains are 6.7 and 9.8 kcal mol^{-1} for the pyridine and naphthalene fragments in the cavity, respectively. Therefore, the overall inclusion of the molecule of compound **1** into the HP-β-CD cavity is a thermodynamically favorable process.

The optimized structures of the pentahydrate **1** • $5H_2O$ and the tetrahydrate of the ion pair **1** • H^+OH^- inserted into the HP-β-CD cavity are displayed in Fig. 5. Note that the computer-assisted models of $\mathbf{1_p} \cdot 5H_2O$@HP-β-CD and $\mathbf{1_p} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD provide better fits for possible structures of the complexes with the pyri-

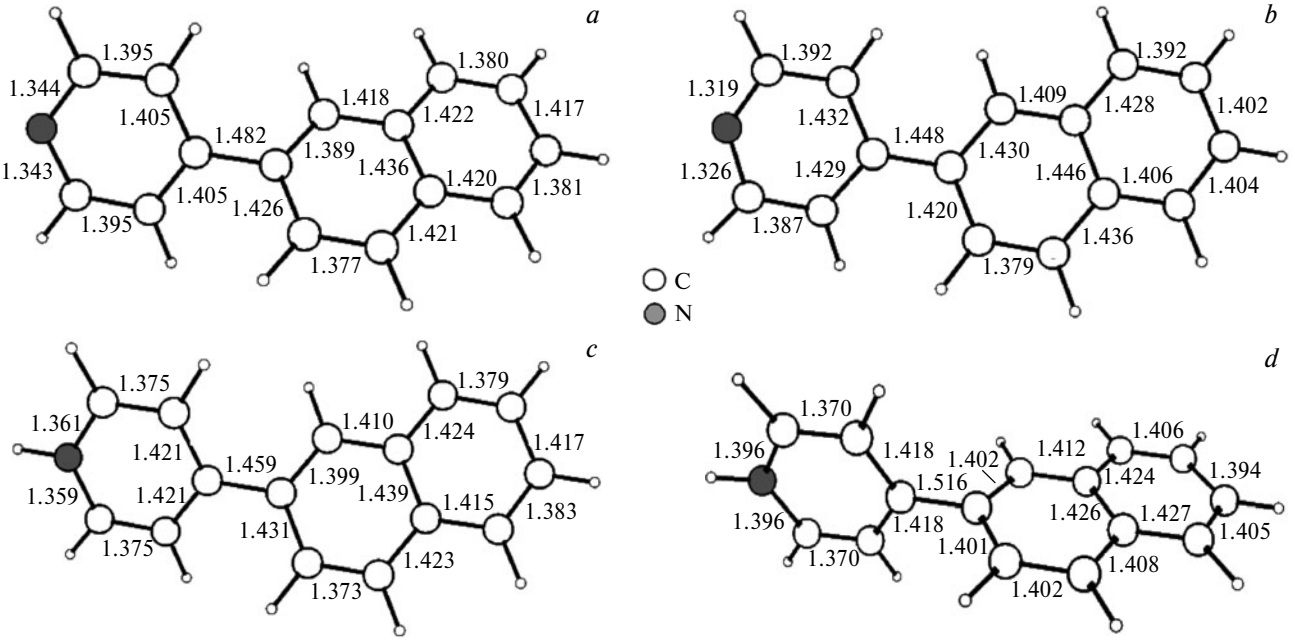


Fig. 8. Structures of the ground and first excited states calculated at the DFT/PBE and TDDFT/PBE levels, respectively: S_0(**1**), τ = 34.7°, q_N = –0.225 *e*, $q_{C(1)}$ = –0.113 *e*, $q_{C(6)}$ = –0.112 *e* (*a*); S_1(**1**), τ = 12.2°, q_N = –0.192 *e*, $q_{C(1)}$ = –0.154 *e*, $q_{C(6)}$ = –0.152 *e* (*b*); S_0(**1** • H^+), τ = –22.4°, PA = 239.9 kcal mol^{-1} (*c*); S_1(**1** • H^+), τ = –88.4°, PA = 283.2 kcal mol^{-1} (*d*).

dine fragment is in the cavity than do the models of $\mathbf{1_n} \cdot 5H_2O$@HP-β-CD and $\mathbf{1_n} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD with the pyridine fragment outside the cavity. It can clearly be seen in Figs 5, *a* and *c*, that the number of water molecules hydrating the pyridine N atom in the cavity cannot exceed five. As for the pyridine fragment located outside the cavity, it is obviously hydrated by more than five water molecules (though their number is actually unknown). However, for estimation of the energies of insertion, we had to calculate the structures with equal numbers of partners.

The thermodynamics of the interaction of molecule **1** with water in the cavity is schematically shown in Fig. 9 in the form of energy changes in the formation of the complexes **1**@HP-β-CD $\cdot 5H_2O$, $\mathbf{1} \cdot 5H_2O$@HP-β-CD, and $\mathbf{1} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD (see Table 2), in which the "guest" molecule is inserted into the cavity by its pyridine and naphthalene fragments. It can be seen in Fig. 9 that in the complex **1**@HP-β-CD $\cdot 5H_2O$ (*i.e.*, when the "guest" does not react with water in the cavity), location of the naphthalene residue in the cavity provides an energy gain compared to the pyridine residue. This is due to the fact that before a chemical reaction between the "guest" and water begins, it is more favorable for the hydrophobic component to be in the cavity. The formation of the pentahydrate stabilizes the complex $\mathbf{1} \cdot 5H_2O$@HP-β-CD (by 1.7 kcal mol^{-1}) if the pyridine residue is in the cavity and destabilizes it if the fragment $N \cdot 5H_2O$ is outside the cavity. Finally, in the complex of the ion pair $\mathbf{1} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD, location of the naphthalene residue in the cavity is more favorable than location of the pyridine one because the charged fragment $N^+—H...^-OH \cdot 4H_2O$ is more hydrophilic than the naphthalene fragment and tends to be surrounded by water (*i.e.*, outside the cavity). However, the absolute energies of binding (E_{bind}) of the protonated and non-protonated forms of compound **1** in the complexes are close. In addition, in any case the difference between E_{bind} for two types of complexes is not so large as to exclude an equilibrium between them. The PM3-calculated structures of the complexes of the ion pairs $\mathbf{1} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD are shown in Fig. 5.

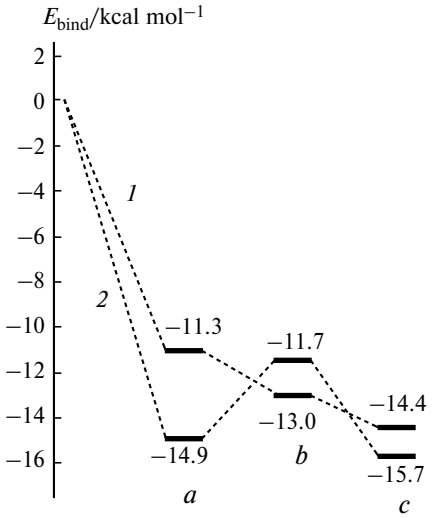


Fig. 9. Diagram of the energies of formation (E_{bind}) of the complexes **1**@HP-β-CD $\cdot 5H_2O$ (*a*), $\mathbf{1} \cdot 5H_2O$@HP-β-CD (*b*), and $\mathbf{1} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD (*c*) with the pyridine (*1*) and naphthalene residues in the cavity (*2*).

The deprotonation of naphthylpyridine in the cavity can be explained as follows. According to our calculations and the available data,[11] the ion pair, which is less stable because of the separated charges, has a higher energy than the hydrate, and four water molecules do not suffice for its stabilization. In the bulk of water, the ion pair is stabilized by coordination of a substantially greater number of water molecules (though this number is unknown and, of course, variable) forming a water "cloud" around $\mathbf{1} \cdot H^+OH^-$. However, the hydrophobic character and small volume of the HP-β-CD cavity prevents the hydration of $\mathbf{1} \cdot H^+OH^-$ inside so that the ion pair for its stabilization has to either leave the cavity or give back the proton to the water environment of the complex $\mathbf{1} \cdot H^+OH^-$@HP-β-CD, which actually takes place according to spectroscopic data. Therefore, although the energy of formation of the complex of $\mathbf{1} \cdot H^+OH^-$ with HP-β-CD is somewhat higher than that for the neutral hydrate $\mathbf{1} \cdot H_2O$ (see Table 2), this energy is too low to stabilize the ion pair, which results in the loss of the proton.

Motion of the "guest" in the cyclodextrin cavity upon photoinduced protonation. To answer the question as to whether the protonated "guest" can move in the cavity, we calculated the distances *L* between the centroids of the HP-β-CD and naphthylpyridine molecules for the complexes with the naphthalene or pyridine residues in the cavity prior to and after protonation. It was assumed that if the protonation decreases *L*, then the "guest" molecule penetrates more deeply into the cavity, and *vice versa*. The results obtained are given in Table 4.

Table 4. Distances *L* between the centroids of HP-β-CD and naphthylpyridine **1** before and after the protonation

Complex	*L*	Δ*L**
	Å	
$\mathbf{1_p} \cdot 5H_2O$@HP-β-CD	3.490	0
$\mathbf{1_p} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD	2.737	−0.75
$\mathbf{1_n} \cdot 5H_2O$@HP-β-CD	4.608	0
$\mathbf{1_n} \cdot H^+OH^- \cdot 4H_2O$@HP-β-CD	5.407	0.80

* The negative Δ*L* value indicates that the centroids come closer to each other (*i.e.*, the "guest" penetrates more deeply in the cavity); the positive Δ*L* value indicates that the "guest" protrudes from the cavity.

The protonation decreases L for the complexes with the pyridine residue in the cavity and increases L for the complexes with the naphthalene residue in the cavity. In other words, the "guest" penetrates more deeply into the cavity upon protonation in the former case and protrudes from the cavity in the latter case (see Fig. 5). Because, with consideration of the van der Waals atomic radii, the height of the HP-β-CD "basket" is ~13.5 Å, the "guest" moves inside the cavity through a noticeable distance. This behavior can be explained by comparing the magnitudes and orientations of the dipole moments of HP-β-CD (μ = 1.88 D), the pentahydrate of compound **1**, and the tetrahydrate of the ion pair.

The dipole moment of the tetrahydrate $\mathbf{1} \cdot H^+OH^- \cdot 4H_2O$ is ~3 times higher than that of the pentahydrate $\mathbf{1} \cdot 5H_2O$, which is due to charge separation. Since the negative end of the dipole in both forms of compound **1** is directed toward the N atom, then if the latter is in the HP-β-CD cavity, the dipole moments of the "guest" and the "host" are nearly antiparallel. In this case, the protonated "guest" should penetrate more deeply into the cavity because the dipole-dipole attraction increases. When the naphthalene residue is in the cavity, the dipoles are parallel to each other. The protonated molecule **1** will, in contrast, protrude from the cavity because of the sharply increased dipole-dipole repulsion (see Fig. 5). In conclusion, it should be noted that the actual distance travelled by the "guest" molecule in the latter case upon photoinduced protonation can be longer since our calculations considered only a little extent of hydration.

To sum up, the formation of an inclusion complex of compound **1** with HP-β-CD in aqueous solution precludes its protonation. This is a prerequisite for the fluorescence of the nonprotonated form of naphthylpyridine **1** with a lifetime of 1.25 ns, which is determined by the retarded (compared to the aqueous solution) protonation of compound **1** in its complex with CD. Apparently, the processes that take place are accompanied by a photoinduced reversible mechanical motion of naphthylpyridine in the cyclodextrin cavity. The trends revealed for the photoinduced proton transfer in pseudorotaxane complexes of cyclodextrin can be used in the design of molecular machines.

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