Modelling of Formation Processes of Inclusion Complexes of Coumarin Laser Dyes and β-Cyclodextrin by the MM2 Force Field Method. I. 7-Amino-4-methylcoumarins

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Abstract. In order to improve the generating and photochemical properties of coumarin laser dyes, the following active media were synthesized: inclusion complexes of β-cyclodextrin (β-CD) and 7-amino-4-methylcoumarins (COU1, COU102, COU120). Complex formation processes were studied, and the structure of the inclusion complexes was estimated using the method of MM2 molecular mechanics. The data obtained suggest the reasons underlying the complex structure effects on their spectral, luminescent and generating characteristics.

Key words. Inclusion complexes, coumarin laser dyes, β-cyclodextrin, MM2 force-field method.

1. Introduction

β-Cyclodextrin (β-CD) is a cyclic oligosaccharide composed of seven α-D-glucopyranose rings connected at the 1- and 4-positions. The most important property of β-CD is its ability to form inclusion complexes with different guest molecules [1,2]. These 'host–guest' complexes are widely used in food technologies and pharmacology, but information on their phototechnological applications has appeared only recently [3]. Specifically, the effects of β-CD on the fluorescent characteristics [4] and generating properties [5] of some laser dyes have been reported. In some cases the formation of cyclodextrin is stated to increase fluorescence quantum yields and improve the generating characteristics of the laser dyes [5].

During our work on synthesizing active media for organic dye lasers we concluded that the development of such active media on the basis of cyclodextrin laser dye complexes is possible and promising [6,7]. The shell of α-D-glucopyranose nuclei, formed around the dye molecule, allows us:

- to increase the concentration of laser dye in aqueous solution;
- to relax photochemical processes induced by hard ultraviolet (UV) radiation due to proper shell absorption;
- to impede the diffusion of molecular oxygen of the active medium to the dye molecules and to delay photooxidation processes;

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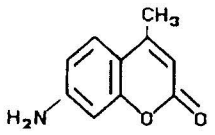
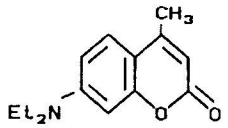
- to inhibit aggregation and solvation processes, which negatively affect the fluorescent and generating properties of the dye;
- and, in some cases, to increase the fluorescence quantum yield and generation efficiency of the laser dye.

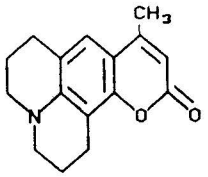
We paid attention to the 7-amino-4-methylcoumarins, widely known as highly efficient laser dyes, generating in a green-blue spectral region [8,9]. Up to the present no data on the effect of β-CD complex formation on generating characteristics have been available for these dyes:



7-Amino-4-methylcoumarin (COU120)



7-*N*, *N*-Diethylamino-4-methylcoumarin (COU1)



2,3,6,7-Tetrahydro-1*H*,5*H*,11*H*-1-benzopyran[6,7,8-*ij*]quinolysin-11-one (COU102)

It is known that ethanol or other organic solvents are usually used for preparation of active laser media (on the basis of aminocoumarin dyes) [10]. The majority of coumarin laser dyes have only limited solubility in water, which means that the use of water as an optimum solvent for laser media is problematic, in spite of its thermo-optical, chemical, toxicological and cost parameters.

Another important problem for the coumarin laser dyes used in this work is their relatively low photostability. Pumping radiation induces dye photodestruction processes that aggravate the generating properties of the active medium [11–15].

To increase the photoresource of such media, different adducts were recommended to inhibit the photodestruction processes [13, 14]; methods of deoxygenation of solutions and filtration of pumping radiation have also been used [15]. To increase the water solubility of the dyes, surface active substances have been used as adducts [16], or the dyes were structurally modified by the introduction of highly polar radicals [9].

In order to improve the generating and photochemical properties of coumarin dye active media we synthesized inclusion complexes of β-CD and 7-amino-4-methylcoumarins (COU1, COU102, COU120). The processes of complex formation were studied and the structure of the inclusion complexes was estimated using the method of MM2 molecular mechanics. On the basis of the data obtained we have tried to explain how the structure of the complexes affects their spectral, luminescent and generating characteristics.

2. Experimental

The spectral and luminescent characteristics of the complexes studied were measured using a Specord M-40 spectrometer and an LSM 4000 spectrofluorimeter.

The generating characteristics of the inclusion complexes were studied in solutions, the dye concentrations being 5×10^{-4} mol/L and 5×10^{-3} mol/L, the β-CD concentrations being 10^{-2} mol/L and 2×10^{-1} mol/L. The generating characteristics of aqueous solutions of the inclusion complexes were measured using a coaxial pumping flashlamp dye laser [17] as well as a pumping XeCl eximer laser ($\lambda = 308$ nm).

The maximum pumping energy of the lamp pumping laser was 395 J, the half-width impulse duration being 180 μs. The pumping energy of the XeCl eximer laser was 30 mJ at an impulse duration of 20 ns. The laser resonators were formed with flat mirrors, the reflectivity coefficients being 100, 35% and 100, 50% respectively. Generation energy and power were measured with an IMO-2H meter.

The photostability of the active medium was determined after multiple irradiation by light impulses until the generation disappeared completely in the case of impulse lamp excitation, or the generation energy decreased to 50% in the case of XeCl eximer laser excitation. Simultaniously the number of impulses was calculated, and the total value of absorption energy per litre of solution was then determined.

3. Calculations

The structure of β-CD, the inclusion complexes and the host–guest interaction energy were determined using Allinger's molecular mechanics method [18] (force field MM2 [19]). The calculations took account of the following factors: deformations of the stretching bonds and the stretching angles as well as nonstretching Coulomb and vander Waals' interactions. The atomic charges of the coumarin derivatives were calculated by the SCF MO LCAO method in the MNDO approximation [20]. The charges on β-CD atoms were determined from calculations on the trisaccharide of α-D-glucopyranoze in the C_1 chair conformation (MNDO approximation). Atom charges of the central trisaccharide fragment were supposed to correspond to atom charges of β-CD links (Table I). The sevenfold symmetry axis of the β-CD molecules was taken into account in the calculations. The molecule was disposed in such a way that the Z axis coincided with the symmetry axis and O_4 atoms were fixed in the X–Y plane. The β-CD structure was calculated under a complete geometry optimization. Such an optimized β-CD structure is shown in Figure 1. The β-CD structure obtained correlates with experimental data as well as with analogous calculations [21].

Further, the interaction energies of β-CD with coumarin derivatives were calculated on complex formation; the structure of such complexes was determined, too. Besides, the structure of α-D-glucopyranose macrocycle was frozen and only the optimization of the 'guest' molecule position was carried out in the β-CD cavity, taking nonstretching interactions into account. In some cases the position of the hydroxyl groups of cyclodextrine was changed. In the calculations the 'guest' molecule had three degrees of freedom, including X- and Y-axis shifts as well as

Table I
Atomic charges for the α-glucopyranose fragment of the cyclodextrin macrocycle

Atom	Charge	Atom	Charge
C_1	0.296	O_3'	−0.309
C_2	0.103	(O_3')—H	0.193
C_3	0.120	H_4'	0.017
C_4	0.140	O_4'	−0.327
C_5	0.144	C_6	0.156
O_5	−0.385	H_6'	0.000
H_1	0.005	H_6'	0.015
H_2	0.010	O_6'	−0.327
O_2'	−0.299	(O_6')—H	0.185
(O_2')—H	0.191	H_5'	0.063
H_3'	0.010		

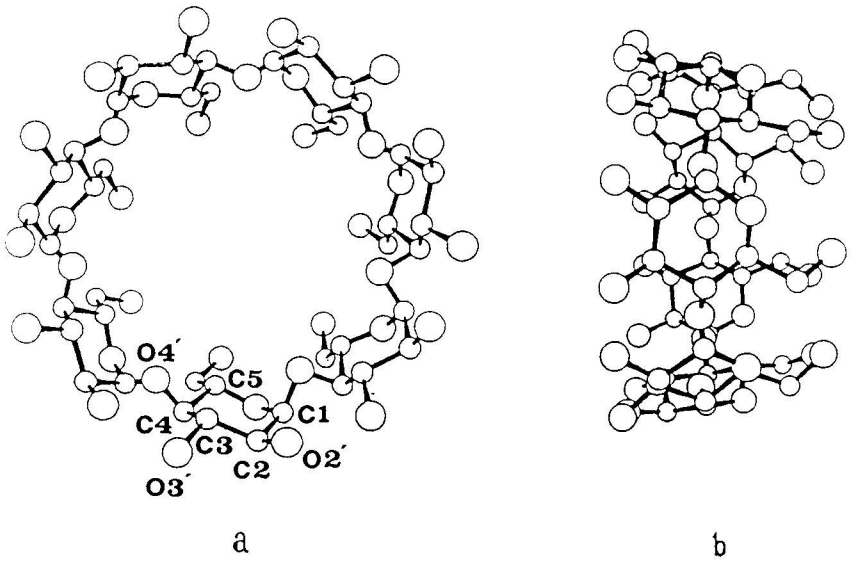


Fig. 1. Stick and ball model of β-cyclodextrin molecule: (a) view from the top; (b) side view.

rotation around the Z-axis. The 'guest' molecule position was changed by 0.5 Å along the Z-axis, and the interaction energy was minimized for each point.

Two calculation cycles were carried out for every compound studied, corresponding to the introduction of the molecule into the β-cyclodextrin cavity from the broad end via the pyranone (normal position) and benzene (reverse position) rings.

Figures 2–6 show the calculated results.

4. Results and Discussion

The β-CD molecule has a truncated cone form, the angle between the Z axis and the line connecting C_3 and C_5 atoms being 11°. Seven H_3' and H_5' atoms are on the broad and narrow ends, respectively. These atoms are on a circumference of ≈9 Å diameter for the broad end and of ≈8 Å for the narrow one. Seven O_4

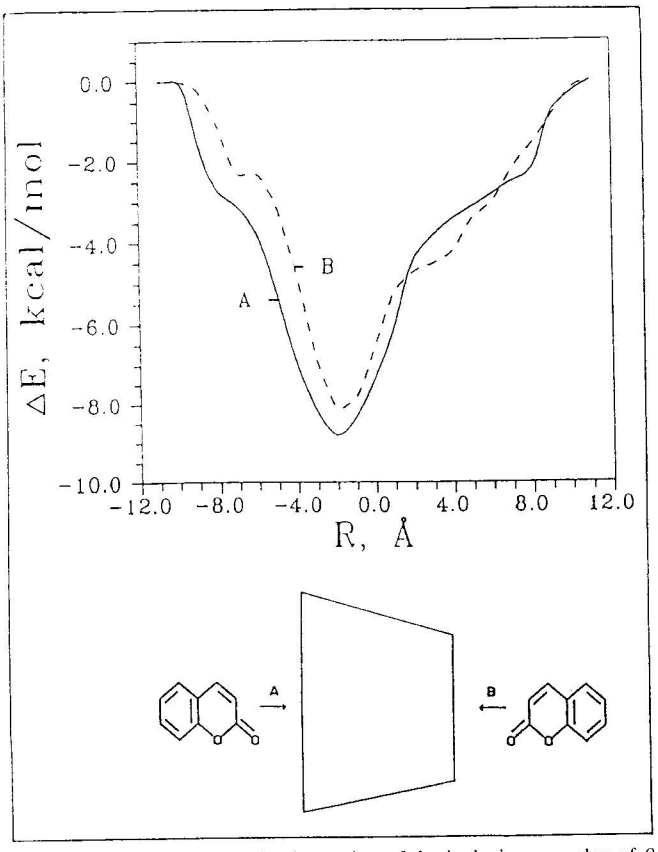


Fig. 2. Changes in stabilization energy on the formation of the inclusion complex of β-CD with COU.

atoms are turned into the macrocycle, forming a hydrophilic zone of ≈10 Å diameter.

Figure 6 schematically shows the structure of β-CD inclusion complexes with coumarin derivatives and presents their stabilization energies. As can be seen, COU and COU120 can form both normal inclusion complexes and reverse ones, having very similar stabilization energies. The reduction of the interaction energy from −8.8 to −8.1 kcal/mol on going from COU to COU120 in the case of normal orientation is due to the methyl group appearing at the C_4 position of coumarin, which results in an increase of the number of H · · · H contacts in the complex. At the same time the amino group appearing in the molecule increases the complex stability of the compound in the reverse orientation. In this case the energy minimum corresponds to the complex amino group protons which are close to the O_4 plane (hydrogen bonding is possible), and the oxygen atoms of the COU120 molecule interact with the H_3 atoms of the broad end of the macrocycle.

In the case of the COU1 molecule the complex with the reverse orientated 'guest' has a significantly low stabilization energy of −3.6 kcal/mol. This is due to the fact that the volume of the diethylamino group of the benzene fragment is such that it cannot be included deeply into β-CD cavity. Besides, even in the

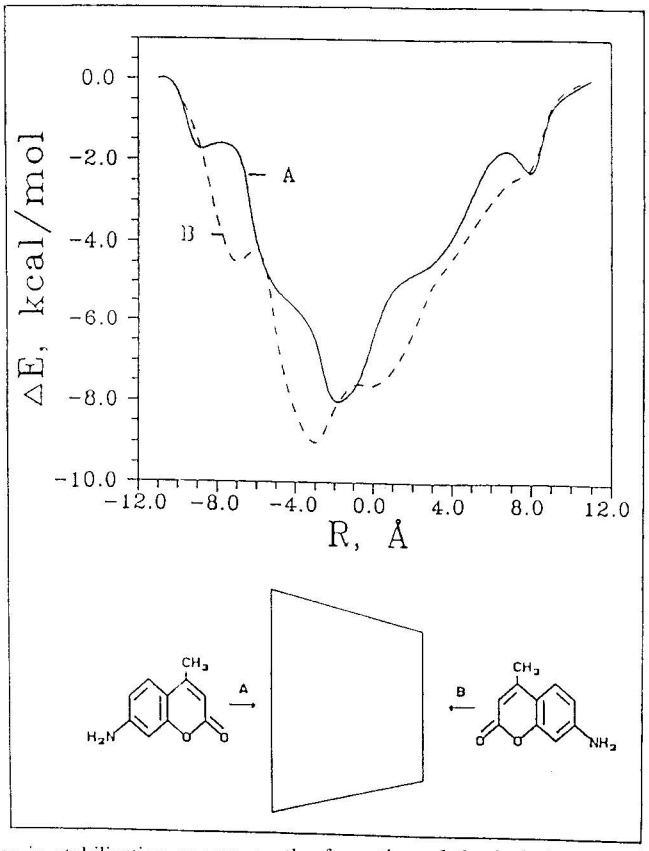


Fig. 3. Changes in stabilization energy on the formation of the inclusion complex of β-CD with COU120.

normal orientation, the stabilization energy decreases (in comparison with COU and COU120) by up to −7.2 kcal/mol. This is due to the fact that the diethylamino group makes the complete inclusion of the COU1 molecule into the macrocycle cavity difficult. At the same time the diethylamino group itself is left projecting out of the cavity.

The increased volume of the COU102 molecule makes the formation of the reverse orientated complex impossible. In the case of normal orientation the interaction energy is low, too (−4.5 kcal/mol.), which is explained by the insignificant inclusion of COU102 into the β-CD cavity: it only penetrates into the region of H_3' atoms at the broad end.

Thus, the calculated interaction energy of the complexes shows that COU and COU120 form both normal structures and reverse ones having similar values of stabilization energies. In the case of the normal position of COU102 and the reverse one of COU1, the complexes are formed upon incomplete introduction of 'guest' into the β-CD cavity, and in the case of the reverse position of COU102 the complex formation is improbable.

Figures 2–5 show curves corresponding to changes in interaction energies of β-

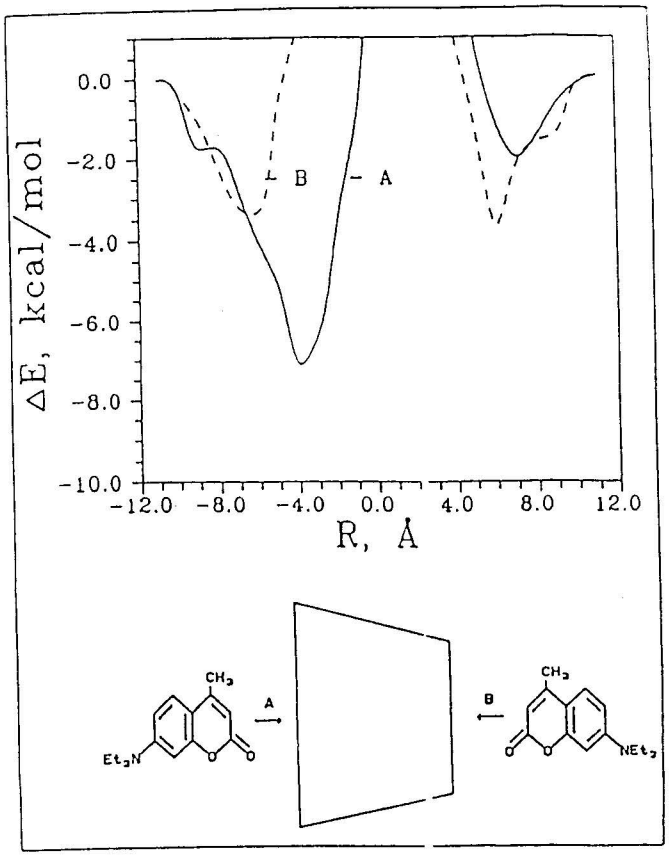


Fig. 4. Changes in stabilization energy on the formation of the inclusion complex of β-CD with COU1.

CD of the molecules studied on passing through the macrocycle cavity. The schemes are shown at the bottom of Figures 2–5, demonstrating normal (A) and reverse (B) orientations of coumarin derivatives in the β-CD cavity. Two curves (schemes in the top part of the figures) correspond to these orientations. The zero point on the X axis corresponds to the mutual position of the molecules in the complex when the plane passing through the O_4' atoms of the macrocycle coincides with the C_9—C_{10} bond of coumarin.

As can be seen from these figures, the energetic curves for COU (Figure 2) and COU120 (Figure 3) differ fundamentally from the curves for COU1 (Figure 4) and COU102 (Figure 5). Plots for COU and COU120 have global minima corresponding to the positions of molecules of these compounds in the macrocycle cavity. The continuity of the curves demonstrates the possibility of passing 'guest' molecules through the 'host' cavity. Actually, plots for COU1 and COU102 consist of two parts having their own minimum. The forbidden zone is located between these minima, and its width is determined by the physical structure of the molecules.

The complex form of the energetic curves are determined by the interaction

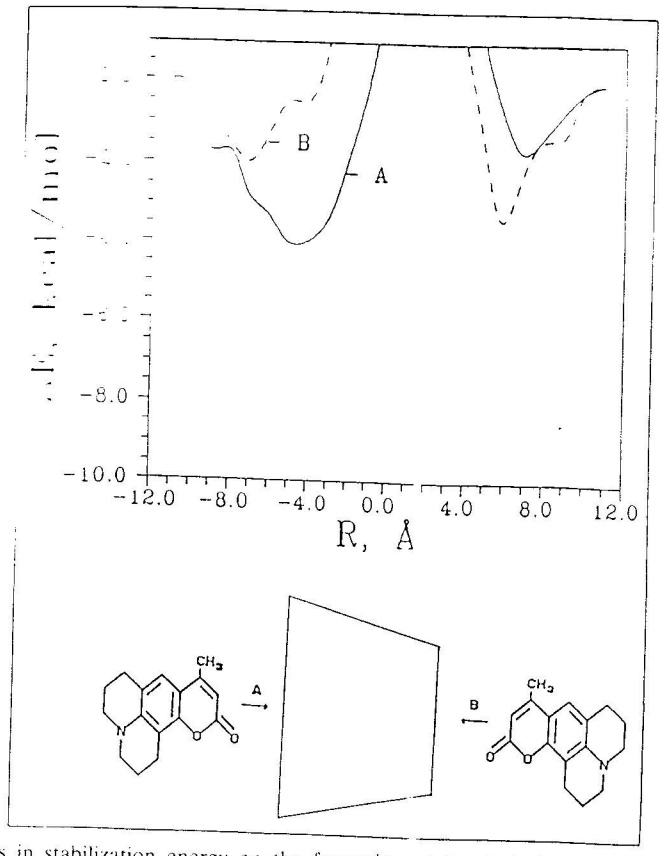


Fig. 5. Changes in stabilization energy on the formation of the inclusion complex of β-CD with COU102.

between concrete molecular fragments of β-CD and coumarin derivatives. So, for example, bands appearing in the R regions of all the plots result from the intermolecular interactions of CH_3'—CH_5' atoms of β-CD. For coumarin derivatives having a methyl group in position 4 such an interaction manifests itself more strongly (Figure 3) than for coumarin itself (Figure 2). In the case of COU120 molecules containing an NH_2-group the energetic curves (Figure 3) have some peculiarities. These are due to the possibility of the formation of additional N—H · · · O hydrogen bonds between β-CD and COU120. These peculiarities exactly explain the local minima appearing in the regions −7 Å and +1 Å (Figure 3, curve B corresponding to the reverse position). The minima correspond to intermolecular hydrogen bonds of the amino group proton with O_4' and O_6' atoms of β-CD, respectively.

As has been noted, plots for COU1 and COU120 have two minima corresponding to the incomplete inclusion of the molecules into the β-CD cavity. As the calculations show, more stable intermolecular structures are formed in the case of the interaction of the carboxyl oxygen atom of coumarin derivatives.

Differences in the structure and stabilization energy of β-cyclodextrin complexes

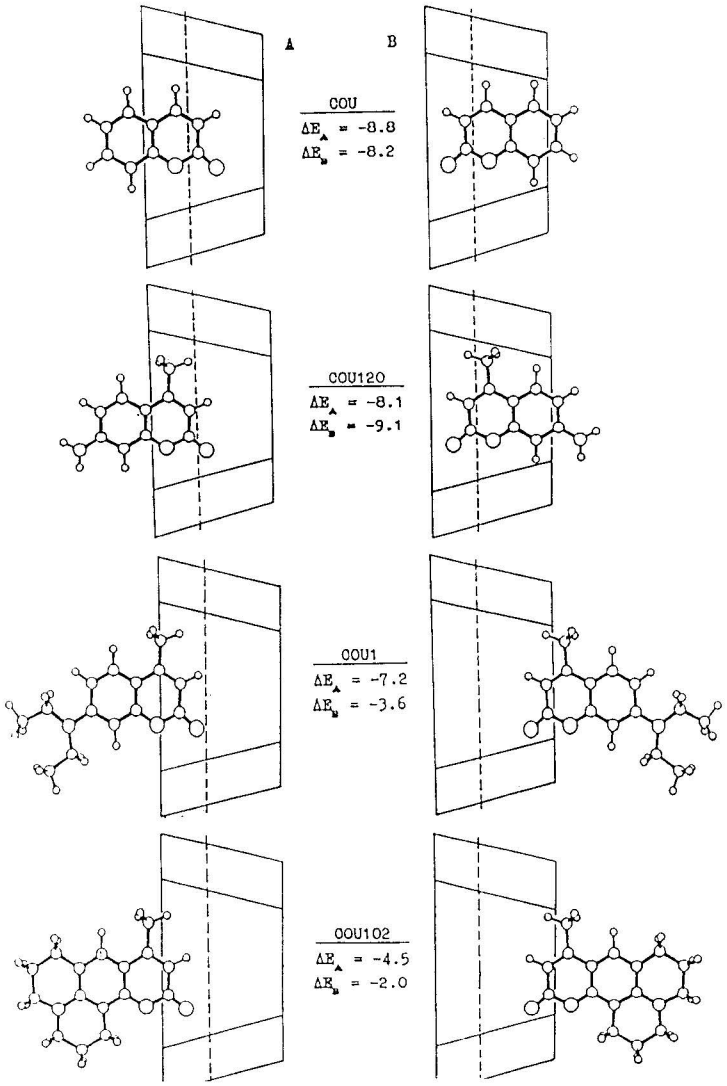


Fig. 6. Coumarin positions in β-cyclodextrin cavity at minimum of stabilization energy in inclusion complexes of normal (A) and reverse (B) types.

COU, COU120, COU1 and COU102 (Figure 6) possibly account for the fact that their aqueous solutions differ in their optical properties. Thus, β-CD complex with COU120 is strongly fluorescent and generates, whereas β-CD complexes with COU1 and COU102 are weakly fluorescent and do not generate.

It is known [9] that the low solubility of coumarin laser dyes in water means that the laser concentrations (5×10^{-4} mol/L) can be obtained only in some cases. For example, the optical density (D) of the saturated solution of one of the most effective laser dyes (COU120) is ~0.6 (the layer thickness being 1 mm). The optical density of the saturated solution of the complex of this compound and β-

Table II
Generating characteristics of inclusion complexes of coumarins with β-CD

No.	Dye	Concentration mol/L	β-CD concentration mol/L	Efficiency %	Energy mJ	Phopto-stability kJ/L
1	COU120	5×10^{-4}	10^{-2}	0.1	400	166
2	COU120	5×10^{-5}	–	0.03	120	71
3	COU120*	5×10^{-4}	–	0.3	1200	48
4	COU175	5×10^{-4}	–	–	–	–
5	COU1	5×10^{-4}	10^{-2}	–	< 5	–
6	COU102	5×10^{-4}	10^{-2}	–	< 10	–

* Alcohol solution.

CD (10^{-2} mol/L) increased up to $D > 2$, which allows the preparation of active media with the optimum optical density ($D \sim 1.2$). It can be seen from Table II, representing laser characteristics of inclusion complexes of the studied LD with β-CD, that the complex formation of β-CD and COU120 results both in an increase of generation efficiency (3.3 times), in comparison with the aqueous solution of COU120, and in an increase of photostability by 2.3 times. It should be noted that under the same conditions of generation excitations a water-soluble LD COU175, which is more photostable than the well-known water-soluble coumarin LD, does not generate. The generation energy of the complex is three times lower than an alcohol solution of COU120 but, at the same time, the angular brightness of the laser radiation increases significantly. Furthermore, the photostability of the aqueous solution of the inclusion complex of β-CD and COU120 is 3.5 times greater than the analogous characteristics of the alcohol solution.

In the case of complexes of β-CD + COU1 and β-CD + COU102 the solubility of LD in water increases, too, but for COU102 it does not achieve the laser concentration. The generation efficiency of these complexes is extremely low under the same excitation conditions. Besides, even if aqueous solutions of these dyes do not operate at all, their inclusion complexes reveal their generating abilities.

This sharp difference in generating characteristics of β-cyclodextrin complexes of COU120, COU1 and COU102 can experimentally demonstrate the different structures of these inclusion complexes. These differences manifest themselves particularly convincingly when comparing the generating properties of the β-CD + COU120 and β-CD + COU1 complexes. These two LD operate well in alcohol, and, besides, their complexes are highly water soluble. However, these factors are not enough for effective generation of β-CD complex with COU1 (Table II). Perhaps this is due to the different structures of the complexes. And generation sensitive to the changes in LD structure and medium parameters demonstrates these changes indirectly. Actually, as can be seen from Figure 6, the inclusion of a COU1 molecule into the β-cyclodextrin cavity is difficult, and the diethylamino group in COU1 is less protected from solvation effects than the amino group in COU120. This results in greater COU1 fluorescence quenching in comparison with an alcohol solution. On the other hand, the improved fluorescent characteristics and generation of the β-CD + COU1 complex (in comparison with COU1 aqueous solution) appear to provide evidence that β-CD partly contributes to the decrease of the solvation effect.

The other possible method of radiationless deactivation of the fluorescent state of coumarin LD including the amino group is caused by the possibility of free rotation of the amino group and the formation of the twist form on energy absorption [22]. On the formation of β-CD + COU120 complex the LD penetrates deeply into the cyclodextrin cavity ($R_o = -3$ Å), which makes the free rotation of the amino group difficult. For COU1 this effect is significantly less marked. Therefore fluorescent and generating characteristics of the β-CD + COU120 complex should be more pronounced than those of β-CD + COU1, in agreement with the experimental evidence.

Thus, the results obtained testify the possibilities of modification of generating properties of laser dyes by the formation of complexes with cyclodextrins. Besides, using the molecular mechanics methods the experimentalist can avoid routine procedures of examining all possible alternatives and determining the most complementary combinations of the complex former and included molecule.

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