ISSN 1070-3632, Russian Journal of General Chemistry, 2007, Vol. 77, No. 6, pp. 1117–1125. © Pleiades Publishing, Ltd., 2007.
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Phthalocyanines and Related Compounds: XLIV.[1] Synthesis of Conjugates of Phthalocyanines with Rhodamines

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Received September 14, 2006

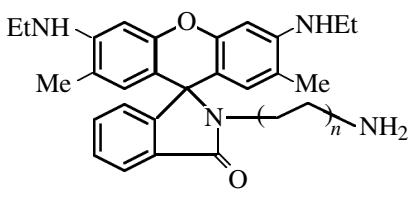
Abstract — A series of conjugates of sulfo- and carboxy-substituted phthalocyanines with rhodamines were prepared, and their electronic absorption and luminescence spectra were studied. An intramolecular transfer of the excitation energy from the rhodamine moiety (donor) to the phthalocyanine moiety (acceptor) was revealed.

DOI: 10.1134/S1070363207060291

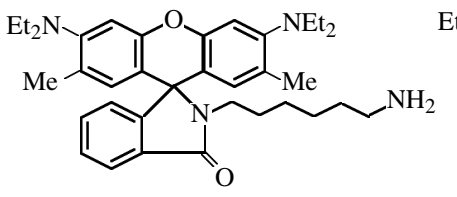
Synthesis of molecular systems combining nonconjugated dye fragments that have different physical and chemical properties is of theoretical and practical importance. Intramolecular transfer of the excitation energy is used for the development of cascade laserable dyes [2]. Li et al. [3] recently reported on a tetraconjugate of zinc octa[4,5]carboxyphthalocyanine with substituted perylenetetracarboxylic acid diimide, which is a model of a light-collecting antenna [4]. Combination in one molecule of two chromophores exhibiting intense absorption in the visible range allows expansion of the spectrum of photosensitizers for photodynamic therapy with increased selectivity of tumor uptake. It can be expected that the rhodamine fragment absorbing in the range 500–600 nm will transfer the excitation energy to the phthalocyanine (Pc) or porphyrin fragment and thus enhance the efficiency of generation of active oxygen species by the latter. Such composite photosensitizers can be used, in particular, for photodynamic water treatment using solar radiation.

The rhodamine fragment can be used as a fluorescence marker for determining the localization in the body of cobalt complexes catalyzing the formation of active oxygen species in catalytic (dark) therapy [5].

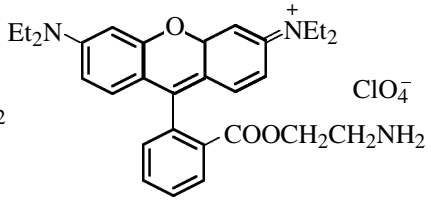
From spirolactams derived from *N*-(2-aminoethyl)-rhodamine 6G (**I**), *N*-(6-aminohexyl)rhodamine 6G (**II**), and *N*-(6-aminohexyl)rhodamine 4C (III), and also from Rhodamine C 2-aminoethyl ester perhlorate (**IV**), we prepared a series of conjugates with sulfo- and carboxy-substituted phthalocyanines: tetraconjugates of metal-free tetra(4-R-sulfamoyl)phthalocyanine (**V**, **VII**) and its aluminum complex (**VI**, **VIII**) with spirolactam **I** and Rhodamine C ester **IV**, and also monoconjugates **IX**–**XII** of the cobalt complex of octa[4,5]carboxyphthalocyanine with rhodamines **I**–



I, II



III



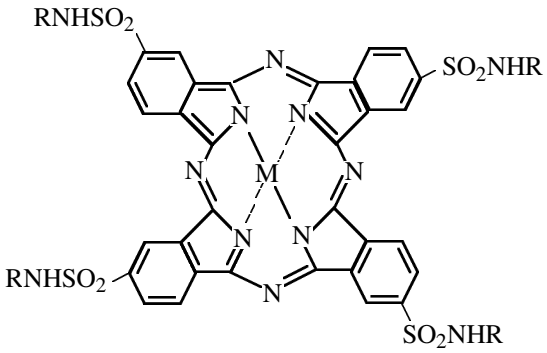
IV

n = 1 (**I**), 2 (**II**).

[1] For comminication XLIII, see [1].

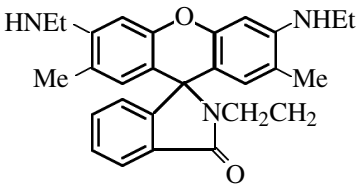
IV, monoconjugate **XIII** of the hydroxyaluminum phthalocyanine with spirolactam **I**, diconjugate **XIV** of cobalt octa[4,5]carboxyphthalocyanine with spirolactam **I**, and tetraconjugate **XV** with Rhodamine C ester **IV**.

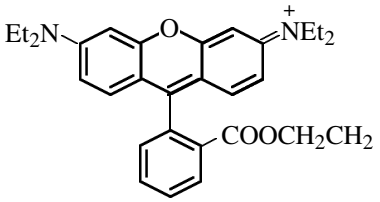
The starting spirolactams **I**–**IV** were prepared by reactions of Rhodamines 6G and 4C with appropriate diamines until the dye become colorless. Rhodamine C 2-aminoethyl ester **IV** was prepared by esterification of Rhodamine C with 2-aminoethanol in the presence of concentrated H_2SO_4 on heating.



V–**VIII**

M = HH (**V, VII**), AlCl (**VI, VIII**),

R =  (**V, VI**),

 (**VII, VIII**).

Conjugates **V**–**VIII** were prepared by amidation of tetra(4-chlorosulfonyl)phthalocyanine **XVI** or its aluminum complex **XVII** with colorless spirolactam **I** or Rhodamine C aminoethyl ester **IV** in the presence of triethylamine.

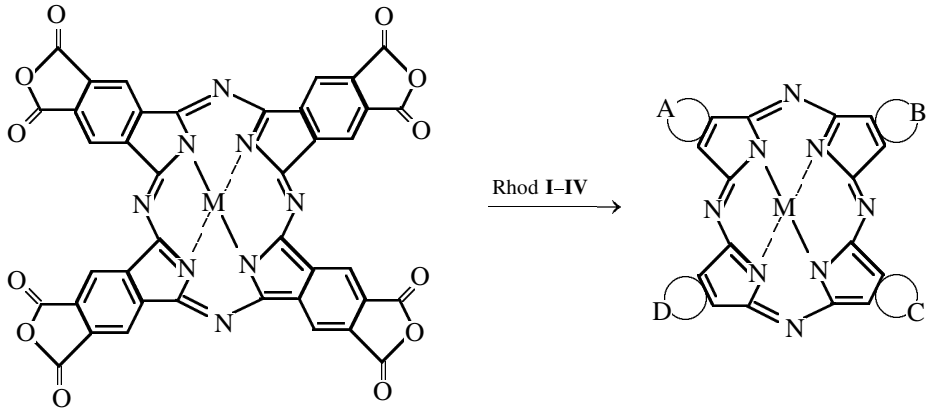
The starting sulfochlorides **XVI** and **XVII** were prepared by treatment of the corresponding tetra(4-sulfo)phthalocyanines **XVIII** and **XIX** with thionyl chloride in the presence of DMF. Compound **XVIII** was prepared by demetallation in acid solution of zinc tetra(4-sulfo)phthalocyanine **XX**, which, in turn, was prepared by fusion of 4-sulfophthalic acid monopotassium salt with zinc acetate in the presence of urea. Hydroxyaluminum tetra(4-sulfophthalocyanine) **XIX** was prepared similarly to **XX**, with aluminum sulfate used as the metal source.

Conjugates **IX**–**XV** of carboxy-substituted phthalocyanines with rhodamines were prepared by reactions of cobalt and hydroxyaluminum octa[4,5]carboxyphthalocyanine tetraanhydrides **XXI** and **XXII** with rhodamines **I**–**IV**. Monoconjugates **IX**–**XI** were prepared by reactions of tetraanhydrides **XXI** and **XXII** with rhodamines **I**–**IV** in 1 : 1 molar ratio in *N*-methylpyrrolidone in a helium flow at 150–155°C.

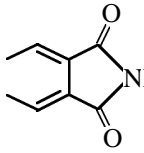
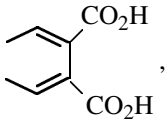
By the reaction of cobalt octa[4,5]carboxyphthalocyanine tetraanhydride **XXI** with lactam of *N*-(2-aminoethyl)rhodamine 6G (**I**) in 1 : 5 molar ratio at 175–180°C, we prepared diconjugate **XI**, and with Rhodamine C ester **IV** at 1 : 15 molar ratio of the tetraanhydride and ester at 150–155°C, tetraconjugate **XV**.

Conjugates **V** and **VI** with spirolactam derived from Rhodamine 6G (**I**) are well soluble in organic solvents such as toluene and chloroform, which allowed their chromatographic purification. In neutral and alkaline solutions, these compounds have a blue-green color and the absorption spectra typical of phthalocyanines. Treatment with acids causes opening of the lactam ring in the rhodamine moiety; it is converted to the ionic form, and the solutions become lilac-violet. The forming compounds are insoluble in nonpolar solvents and soluble in polar solvents; an additional absorption band at 530 nm (rhodamine moiety), exceeding in the intensity the *Q* band of the

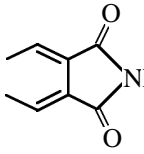
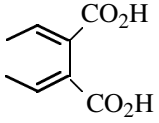
phthalocyanine moiety (Fig. 1), appears in their electronic absorption spectra. As the solution acidity is decreased, the band with a maximum at 530 nm decreases in the intensity and then completely disappears. Such acid–base transformations of conjugates **V** and **VI** (Fig. 1, table), like those of the initial spirolactam **I**, are reversible and independent of particular acid or base. However, in contrast to the initial Rhodamine 6G, compounds **V** and **VI** are insoluble in water even in the ionic form.

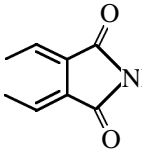


XXI, XXII

A =  , B = C = D =  ,

R = Rhod **I**, M = AlX (**XIII**), M = Co (**IX**); R = Rhod **II**, M = Co (**X**); R = Rhod **III**, M = Co (**XI**); R = Rhod **IV**, M = Co (**XII**).

A = C =  , B = D =  ; R = Rhod **I**, M = Co (**XIV**),

A = B = C = D =  ; R = Rhod **IV**, M = Co (**XV**).

In the electronic absorption spectrum of **V** in the open protonated form (after treatment with trifluoroacetic acid), the long-wave *Q* band is split in two bands of approximately equal intensity (Fig. 1, table), which is typical of metal-free phthalocyanines, whereas compound **VI** in the open form, like the starting aluminum phthalocyanine, shows no such splitting.

Conjugates **VII** and **VIII** with the ester bond are readily soluble in $CHCl_3$–MeOH (10 : 1), DMSO, and concentrated HCl but insoluble in water. In a suspension in 1% aqueous NaOH, these compounds are gradually hydrolyzed with the elimination of rhodamine residues; in the process, the phthalocyanines pass into the aqueous-alkaline solution. Apparently, the instability of the conjugates in alkaline solutions is also responsible for the appearance in the reaction mixture, after the reaction completion, of a relatively large amount of phthalocyanine containing, along with sulfamoyl groups, also free sulfo groups.

In contrast to conjugates **V** and **VI** exhibiting the characteristic strong absorption band of rhodamine in acid solutions, conjugates of phthalocyanines with Rhodamine C aminoethyl ester (**VII**, **VIII**), like the initial rhodamine ester, preserve the spectral pattern

Absorption and luminescence spectra of conjugates of phthalocyanines with rhodamines

Conjugate no.	M	Absorption, λ_{max}, nm (relative intensity), solvent	Luminescence,[a] λ_{max}, nm (solvent)
V	HH	700, 663, 645, 637, 346 (1.88 : 1.67 : 0.68 : 0.67 : 1); $CHCl_3$	No luminescence
VI	AlX	686, 617, 355 (2.22 : 0.55 : 1); acetone	No luminescence
V, salt	HH	700, 663, 637, 602, 528, 349 (0.44 : 0.60 : 0.58 : 0.38 : 1.95 : 1); 10% EtOH in $CHCl_3$	708, 562 (20% EtOH in $CHCl_3$)
VI, salt	AlX	681, 618, 530, 350 (1.20 : 0.25 : 2.59 : 1); 10% EtOH in $CHCl_3$	698, 566 (20% EtOH in $CHCl_3$)
VII	HH	694, 674, 640, 566, 341 (1.02 : 1.05 : 0.65 : 1.42 : 1), DMSO	700, 578 (20% EtOH in $CHCl_3$)
VIII	AlCl	691, 683, 650, 618, 565, 357 (1.68 : 1.67 : 0.88 : 0.59 : 2.82 : 1), DMSO	695, 578 (20% EtOH in $CHCl_3$)
XIII	AlOH	708, 683, 536, 338 (1.80 : 0.45 : 0.25 : 1), DMSO	708 (DMSO)
IX	Co	681, 610 sh, 536, 365 (1.13 : 0.60 : 0.37 : 1), DMSO	No luminescence
X	Co	678, 561, 329 (0.90 : 0.10 : 1), DMSO	Not measured
XII	Co	675, 566, 337 (1 : 1.16 : 1), DMSO	578 (0.01 N NaOH); 590 (DMSO)
XIV	Co	686, 630 sh, 535, 340 (1.25 : 1.06 : 0.42 : 1), DMSO with addition of AcOH	Not measured
XV	Co	683, 565, 354 (0.60 : 3.90 : 1), DMSO	590 (DMSO); 573 (MeOH–$CHCl_3$, 1 : 20)

[a] Upon excitation of the rhodamine moiety.

irrespective of the solution acidity (Fig. 2). It should be noted that compound **VII** occurs in the aggregated state in solution and has a broadened *Q* band in the absorption spectrum.

Monoconjugates **IX**–**XI** and **XIII** are soluble in dilute aqueous solutions of alkalis and organic bases; however, in the spectra of their acetates and perchlorates in these solutions, the rhodamine absorption bands fully disappear because of transition into the colorless lactam form. An exception is monoconjugate **XII** with Rhodamine C 2-aminoethyl ester, which is resistant to dilute aqueous alkalis.

We have examined the luminescence spectra of the conjugates (Figs. 3–5). By the example of conjugates **V**, **VI**, and **XIII**, we demonstrated the occurrence of the intramolecular transfer of the excitation energy

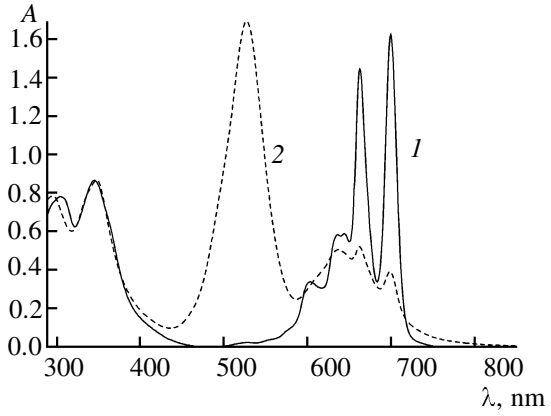


Fig. 1. Electronic absorption spectra of the conjugate of metal-free phthalocyanine with Rhodamine 6G (**V**): (*1*) in chloroform and (*2*) in a 1% solution of ethanol in chloroform (after treatment with trifluoroacetic acid).

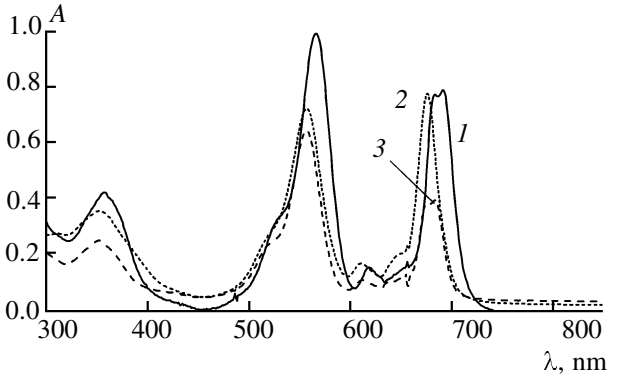


Fig. 2. Electronic absorption spectra of the conjugate of aluminum phthalocyanine with Rhodamine C (**VIII**): (*1*) in DMSO, (*2*) in 1% aqueous NaOH, and (*3*) in ethanol.

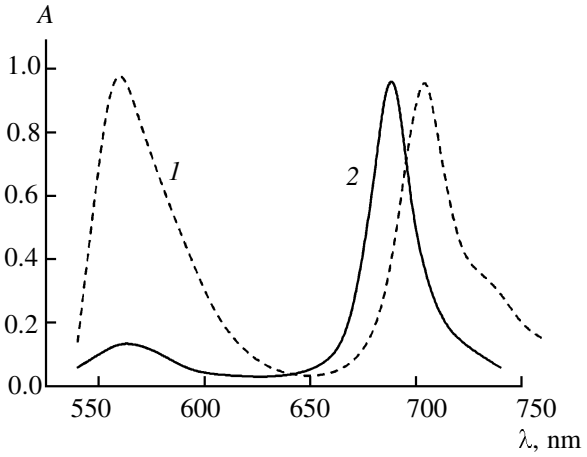


Fig. 3. Fluorescence spectra of the salt forms of the conjugates of (*1*) tetra(3-sulfo)PcH_2 (**V**) and (*2*) tetra-(4-sulfo)PcAlX (**VI**) with spirolactam derived from Rhodamine 6G (**I**) in EtOH–$CHCl_3$.

from the rhodamine moiety (donor) to the phthalocyanine moiety (acceptor). In excitation of conjugates **V** and **VI** with the 528-nm radiation, both donor and acceptor moieties showed fluorecscence (560–570 and 690–705 nm, respectively; Fig. 3). In the case of **XIII**, the fluorescence of the rhodamine moiety was weak; only strong fluorescence of the phthalocyanine moiety was observed (λ_{max} 708 nm).

We revealed strong remote quenching of the fluorescence of the rhodamine moiety by the cobalt ion of the phthalocyanine moiety. However, monoconjugate **XII** and its sodium salt still exhibit noticeable fluorescence of the rhodamine moiety in aqueous solutions and aprotic solvents. Hence, as expected, the remote quenching of the rhodamine fluorescence is incomplete (Fig. 4, table). Tetraconjugate **XV** exhibits strong fluorescence of the rhodamine moiety; λ_{max} in DMSO 590 nm (Fig. 5, table).

The use of a narrow-band narrow-beam excitation source, a solid-state laser with diode pumping, λ 532 nm (sharp peak in the fluorescence spectra), allowed fairly accurate (within 10 rel. %) comparative measurements of the fluorescence quantum yield for the compounds under consideration. Assuming that the quantum yields of the fluorescence of Rhodamine C proper and its 2-aminoethyl ester are equal (60% [7]), we find that the absolute quantum yield for the tetraconjugate is no less than 5%. This can be sufficient for in vivo luminescence imaging of agents for catalytic therapy of the Teraphthal type [5].

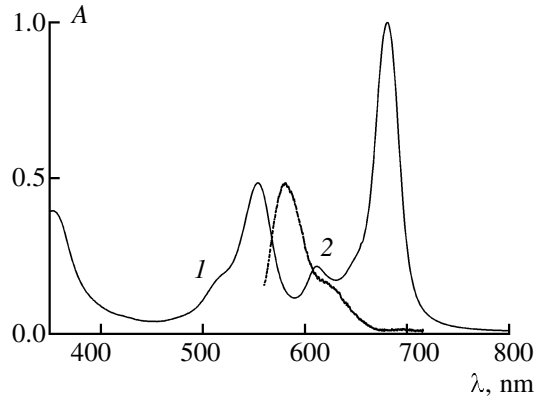


Fig. 4. Normalized (*1*) absorption and (**2**) fluorescence spectra of monoconjugate **XII** of octa[4,5]carboxy-PcCo with Rhodamine C 2-aminoethyl ester **IV** in 0.01 N aqueous NaOH.

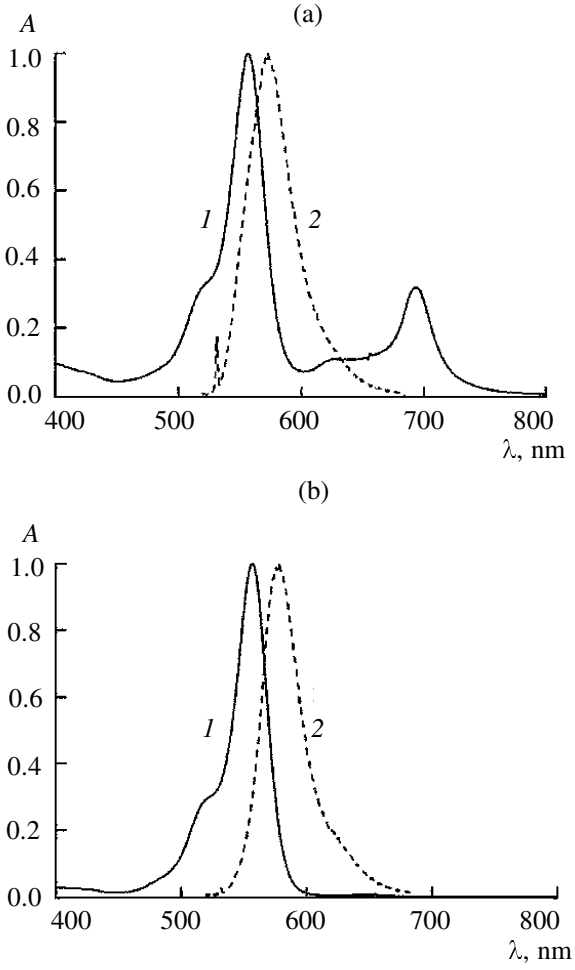


Fig. 5. Normalized (*1*) absorption and (*2*) fluorescence spectra of (a) tetraconjugate **XV** of octa[4,5]carboxy-PcCo with Rhodamine C 2-aminoethyl ester and (b) initial Rhodamine C ester in methanol–chloroform, 1 : 20.

EXPERIMENTAL

The electronic absorption spectra were recorded on an HP8453 spectrophotometer, and the IR spectra, on an FSM-1201 spectrophotometer. The mass spectra of **V** and **VI** were taken using matrix-assisted laser desorption/ionization (MALDI-TOF) technique with a Bruker Reflex **III** mass spectrometer equipped with a nitrogen laser (λ 337 nm) at an accelerating voltage of 20 kV. α-Cyano-4-hydroxycinnamic acid was used as a matrix.

The luminescence spectra were studied with an OSA WP4 optical spectrum analyzer. To enhance the sensitivity, we arranged a brightness amplifier, an electron-optical image intensifier, before the photodetector line. The luminescence was excited with an OI-18A lighter, with a DRK-120 mercury lamp as light source. A 546-nm line was cut out using a standard set of color filters. To reduce the scattered exciting radiation, an OS12 filter cutting the radiation with $\lambda < 540$ nm was arranged in the observation channel. A solid-state laser with diode pumping (BioSpek, λ 532 nm) was used for measuring the fluorescence quantum yield. The spectra obtained were normalized to the extinction coefficient of the test solution at the excitation wavelength.

Spirolactam I derived from Rhodamine 6G and ethylenediamine. *a*. A mixture of 9.6 g of Rhodamine 6G and 14 ml of ethylenediamine was kept for 96 h at room temperature (or for 4 h with heating on a water bath to 30°C under stirring) until the dye became colorless. The pink precipitate thus obtained was filtered off, washed with water to neutral reaction, and dried. After recrystallization from benzene, yield of **I** 7.0 g (70%), mp 221°C. Found, %: C 73.71, 73.90; H 7.05, 7.10; N 11.96, 12.10. M^+ 456. $C_{28}H_{32}N_4O_2$. Calculated, %: C 73.70; H 7.02; N 12.28.

b. Ethylenediamine (2.7 ml) was added to a solution of 9.6 g of Rhodamine 6G in 100 ml of anhydrous DMF. The solution was allowed to stand until it become colorless (3 days). Then the solution was diluted with water, and the pink precipitate was worked up as in procedure *a*. Yield of **I** 7.3 g (73%), mp 221°C.

Hydrochloride of I. Spirolactam **I** (0.483 g) was dissolved in chloroform, and 3 ml of concentrated HCl was added. In so doing, a bright orange fluorescent solution formed, from which after a certain period, upon evaporation of chloroform, salt **I**·HCl precipitated. Yield 0.4 g (70%). Electronic absorption spectrum in ethanol, λ_{max}, nm ($\log\varepsilon$): 528 (4.60). The product is spectroscopically identical to the trifluoroacetate described in the literature [6].

Spirolactam II derived from Rhodamine 6G and hexamethylenediamine. *a*. A mixture of 4.8 g of Rhodamine 6G and 7 g of hexamethylenediamine was heated for 6 h at 45°C until the dye became colorless. The light pink precipitate thus obtained was filtered off, washed with water to neutral reaction, dried, and recrystallized from benzene. Yield of spirolactam **II** 3.6 g (65%), mp 175°C. Found, %: C 74.73, 74.93; H 7.71, 7.89; N 10.46, 10.62. $C_{32}H_{40}N_4O_2$. Calculated, %: C 74.97; H 7.86; N 10.93.

Spirolactam **III** was prepared similarly from a mixture of 5.07 g of Rhodamine 4C and 7 g of hexamethylenediamine; yield 3.6 g (61%), mp 71°C.

b. Hexamethylenediamine (1.8 g) was added to a solution of 4.8 g of Rhodamine 6G in 100 ml of DMF; the solution was allowed to stand at room temperature until it became colorless, after which it was diluted with water, and the precipitate was worked up as in procedure *a*. Yield of **II** 4.0 g (72%), mp 175°C.

Hydrochloride of **II** was prepared similarly to hydrochloride of **I**. From 0.511 g of **II**, 0.39 g (68%) of **II**·HCl was obtained. Electronic absorption spectrum in ethanol, λ_{max}, nm ($\log\varepsilon$): 528 (4.57).

Rhodamine C 2-aminoethyl ester perchlorate IV. A mixture of 19.2 g of Rhodamine C, 24 ml of 2-aminoethanol, and 66 g of concentrated H_2SO_4 was heated at 155°C for 7 h. Then the mixture was poured into water and filtered. Unchanged Rhodamine C was extracted from the filtrate with chloroform (yield 11 g after distilling the solvent off). Perchloric acid was added to the aqueous solution, and the precipitate formed in the process was filtered off, washed with water, and dried. Yield of **IV** 8 g (90% based on converted Rhodamine C). Electronic absorption spectrum in ethanol, λ_{max}, nm ($\log\varepsilon$): 557 (4.90). Luminescence (ethanol), λ_{max}, nm: 585.

Zinc tetra(4-sulfo)phthalocyanine XX. A mixture of 0.6 g of zinc acetate dihydrate, 2.84 g of potassium salt of 4-sulfophthalic acid prepared by oxidation of sodium 2-hydroxynaphthalene-6-sulfonate with potassium permanganate [7], 7.2 g of urea, 0.53 g of ammonium chloride, and 0.05 g of ammonium molybdate was heated for 0.5 h at 160–170°C, after which the temperature of the reaction mixture was raised to 210°C and then gradually, over a period of 6–8 h, to 230°C until the mixture completely solidified. Then the fusion cake was cooled, ground, suspended in 50 ml of 10% aqueous HCl saturated with NaCl, and heated to boil. After cooling, the precipitate was filtered off, washed with 10% aqueous HCl, thoroughly squeezed, dried on the filter, and washed successively

with acetone, hot acetone, and acetone–ethanol–water mixture (10 : 10 : 1). The residue was dissolved in 50 ml of 1% aqueous ammonia, the solution was filtered, the mother liquor was acidified with HCl, 15–20 g of NaCl was added, and the mixture was heated to 50–60°C. The precipitate formed in the process was filtered off, repeatedly washed with a 2 : 1 mixture of 80% aqueous ethanol and acetone, and reprecipitated from water with acetone. Yield of tetrasulfonic acid sodium salt **XX** after drying 0.33 g (15%).

Similarly, from a mixture of 0.4 g of aluminum sulfate, 1.61 g of 4-sulfophthalic acid potassium salt, 3.6 g of urea, 0.3 g of ammonium chloide, and 0.04 g of ammonium molybdate we prepared 0.4 g (30%) of aluminum tetrasulfophthalocyanine **XIX**.

Tetra(4-sulfo)phthalocyanine XVIII. Sodium salt of tetrasulfonic acid **XX** (1.94 g) was heated at 80–90°C for 0.5 h in 18% aqueous HCl; the mixture was cooled and filtered. The precipitate of the undissolved complex was dissolved in 0.1% aqueous NaOH and combined with the acidic mother liquor; the product was precipitated under heating with concentrated HCl containing NaCl. The precipitate was filtered off and washed successively with 18% HCl, 16% aqueous NaCl to neutral reaction, and 80% aqueous ethanol (or 90% aqueous 2-propanol) until the filtrate became salt-free. Yield of sodium salt of tetrasulfonic acid **XVIII** after drying 1.06 g (59%).

Conjugate V of metal-free phthalocyanine with spirolactam I. A mixture of 0.37 g of sodium salt of tetrasulfonic acid **XVIII**, 3 ml of thionyl chloride, and 0.1 ml of DMF was heated to 70°C and kept at this temperature for 1 h, after which 1.5 ml of thionyl chloride was added, and the mixture was heated at 70–75°C for an additional 1.5 h. Then the mixture was cooled and poured onto ice; the precipitate of sulfonyl chloride **XVI** was filtered off and washed with water to neutral reaction of the wash water. The thoroughly squeezed paste was suspended in a cold (0–5°C) mixture of 20 ml of chloroform and 5 ml of acetone. To the cooled suspension (3–5°C), we added 0.75 g of spirolactam **I** and then, over a period of 2 h at the same temperature, 0.5 ml of triethylamine. Then the mixture was allowed to warm up to room temperature. The stirring was continued for an additional 6 h; if necesssary, triethylamine was added to maintain the basicity of the medium. After that, the mixture was refluxed for 2 h, cooled, and filtered to remove insoluble impurities; the mother liquor was evaporated to dryness, and the residue was dissolved in concentrated HCl. The hydrochloric acid solution was diluted with a fivefold volume of water to completely precipitate the product. The precipitate of the conjugate was filtered off, reprecipitated from ethanol with 1% aqueous NaOH, washed with water, dissolved in chloroform, and chromatographed on Al_2O_3 with a 1% solution of methanol in chloroform used as eluent. Yield of **V** 0.15 g (14%). Mass spectrum, 2587.65, 2588.67, 2589.67, 2590.67. *M* 2589.1. Found, %: N 12.53, 12.48; S 5.11, 5.15. $C_{144}H_{138}N_{24}O_{16}S_4$. Calculated, %: N 12.98; S 4.95.

Conjugate VII of the metal-free phthalocyanine with Rhodamine C aminoethyl ester (IV). The paste of sulfonyl chloride **XVI** prepared from 0.197 g of tetrasulfonic acid **XVIII** was added to 25 ml of acetone cooled to 0–5°C, after which 0.56 g of aminoethyl ester **IV** was added at 3–5°C, and the mixture was treated with triethylamine as described above. The cooled reaction mixture was filtered, and the precipitate on the filter was washed with chloroform and acetone and then was dissolved in concentrated HCl. The hydrochloric acid solution was filtered, and the precipitate on the filter was washed with water and acetone and dried; 0.043 g of **VII** was obtained. The mother liquor was diluted with a twofold amount of water, and the precipitate was filtered off, washed on the filter with 18% aqueous HCl, water, and acetone, and dried. For additional purification, the combined precipitates were dissolved in DMSO and precipitated with 10% aqueous HCl; the precipitate was filtered off and washed on the filter with water and acetone. Yield of conjugate **VII** 0.036 g (5%).

Conjugate VI of hydroxyaluminum phthalocyanine with spirolactam I. To a solution of 0.56 g (1.23 mmol) of spirolactam **I** in 15 ml of chloroform, cooled to 3–5°C, we added the thoroughly squeezed paste of sulfonyl chloride **XVII** prepared similarly to **XVI** from 0.243 g of sulfonic acid **XIX**; the mixture was treated with triethylamine as described above. To the cooled reaction mixture, after filtering undissolved impurities off, we added several drops of concentrated HCl; the precipitate was filtered off and repeatedly washed with chloroform to obtain a colorless filtrate, after which it was reprecipitated from ethanol with 1% aqueous NaOH and washed with water. The phthalocyanine obtained (base form) was dissolved in chloroform and chromatographed on Al_2O_3 (eluent: 2% solution of methanol in chloroform). Yield of conjugate **VI** 0.13 g (17%). Mass spectrum, *m/z*: 2631.74, 2632.73, 2633.73, 2634.8. *M* 2631.04. Found, %: C 64.85, 64.90; H 5.23, 5.27; Cl 1.23, 1.15; S 5.39, 5.35. $C_{144}H_{137}AlN_{24}O_{17}S_4$. Calculated, %: C 65.73; H 5.25; S 4.87 (the compound contains an impurity of the chloroaluminum analog).

Conjugate VIII of hydroxyaluminum phthalocyanine with Rhodamine C aminoethyl ester IV. To a

mixture of aqueous paste of sulfonyl chloride **XVII** (prepared from 0.086 h of tetrasulfonic acid **XIX**), 10 ml of chloroform, and 10 ml of acetone, cooled to 3–5°C, we added at the same temperature 0.17 g of rhodamine **IV**, after which the mixture was treated with triethylamine as in the case of **V**. The solvent was evaporated, methanol was added to the residue, the mixture was stirred for 30 min, and the precipitate was filtered off, washed with methanol, dried, and dissolved in concentrated HCl. The solution was filtered, and the precipitate on the filter was washed with water, reprecipitated with concentrated HCl from a solution in 1% aqueous NaOH, and washed with 10% aqueous HCl and water. After drying, 0.036 g of **VIII** was obtained. The mother liquor was diluted with water until the product completely precipitated (fourfold volume of water), and the precipitate was filtered off, washed on the filter with 10% aqueous HCl and water, and dried. The products were combined and reprecipitated two times more. Yield of **VIII** 0.056 g (26%).

Monoconjugate IX of cobalt octa[4,5]carboxyphthalocyanine with spirolactam I. To a solution of 0.35 g of tetraanhydride **XXI** in 35 ml of anhydrous *N*-methylpyrrolidone, we added 0.22 g of spirolactam **I**; the mixture was stirred for 20 h at 150–155°C in a helium flow, cooled, and poured into benzene–hexane (2 : 1); the resulting suspension was filtered, and the precipitate was washed with hexane and benzene, squeezed, and dried. The precipitate (0.55 g) was refluxed for 15 min in glacial acetic acid; the suspension was filtered, and the procedure was repeated until the filtrate became virtually colorless. The precipitate was washed with water to neutral reaction, refluxed with distilled water for 5 h, filtered off, squeezed, and dried. Yield of acetate **IX** · AcOH 0.45 g (75%). IR spectrum (KBr), ν, cm^{-1}: 1635, 1709, 1768 (C=O). Found, %: C 59.61, 59.66; H 3.12, 3.31; N 12.21, 12.24. $C_{70}H_{48}CoN_{12}O_{18}$. Calculated, %: C 59.88; H 3.45; N 11.97.

Perchlorate IX · $HClO_4$. A 0.2-g portion of monoconjugate **IX** was stirred with 3 ml of 60% perchloric acid for 4 h at room temperature. The suspension was filtered, and the precipitate on the filter was washed with 2 ml of perchloric acid, thoroughly squeezed, washed with water to neutral reaction, and dried. Yield of the salt 0.16 g. Electronic absorption spectrum (DMSO), freshly prepared solution, λ_{max}, nm: 681, 535 sh, 337 (relative intensity 1.06 : 0.38 : 1); after 20 h: 685, 535 sh, 337 (1.08 : 0.05 : 1).

Diconjugate XIV of cobalt octa[4,5]carboxyphthalocyanine with spirolactam I. To a solution of 0.08 g of tetraanhydride **XXI** in 8 ml of *N*-methylpyrrolidone, we added 0.11 g of spirolactam **I**; the mixture was stirred for 6 h at 175–180°C in a helium flow, after which 0.1 g of **I** was added, and the mixture was stirred at the same temperature for 14 h. Then the mixture was poured into benzene–hexane (2 : 1), the suspension was filtered, and the precipitate was washed with hexane, benzene, and water (until the filtrates became colorless), squeezed, and dried. By repeated chromatography on SiO_2 (eluent: chloroform–methanol, 10 : 1), we isolated 0.08 g (47%) of diconjugate **XIV**. IR spectrum (KBr), ν, cm^{-1}: 1673, 1709, 1768 (C=O), 2854, 2928 (C–H). Found, %: C 64.01, 64.15; H 4.63, 4.40; N 12.17, 12.46. $C_{96}H_{72} \cdot CoN_{16}O_{16}$. Calculated, %: C 65.34; H 4.11; N 12.70.

Monoconjugate XIII of hydroxyaluminum octa[4,5]carboxyphthalocyanine with spirolactam I was prepared similarly to **IX** from 0.35 g of tetraanhydride **XXII** and 0.22 g of spirolactam **I**. Yield 0.53 g. After treatment with acetic acid, acetate **XIII** · AcOH was obtained in 80% yield. IR spectrum (KBr pellet), ν, cm^{-1}: 1667, 1710, 1774 (C=O), 2800–2950 (C–H). Electronic absorption spectrum (DMSO), freshly prepared solution, λ_{max}, nm: 708, 683, 536, 365 (relative intensity 1.80 : 0.45 : 0.25 : 1; after 20 h: 1.83 : 0.45 : 0.16 : 1). Found, %: C 60.54, 60.72; H 3.30, 3.20; N 12.39, 12.61. $C_{70}H_{49}AlN_{12}O_{19}$. Calculated, %: C 60.51; H 2.46; N 12.10.

Monoconjugate X of cobalt octa[4,5]carboxyphthalocyanine with lactam II was prepared by heating a mixture of 0.35 g of tetraanhydride **XXI** with 0.35 g of Rhodamine C spirolactam **II** in *N*-methylpyrrolidone; the product was isolated similarly to **IX**. Yield 0.54 g.

Acetate X · AcOH was prepared in 78% yield from **X** similarly to **IX** · AcOH. IR spectrum (KBr), ν, cm^{-1}: 1631, 1702, 1761 (C=O), 2820–2970 (C–H). Electronic absorption spectrum (DMSO), freshly prepared solution, λ_{max}, nm: 678, 561, 329 (relative intensity 0.90 : 0.10 : 1); after 20 h: 679, 328 (0.92 : 1). Found, %: C 60.46, 60.90; H 3.73, 4.02; N 11.87, 11.92. $C_{76}H_{60}CoN_{12}O_{18}$. Calculated, %: C 60.33; H 4.07; N 11.30.

Perchlorate X · $HClO_4$. Electronic absorption spectrum (DMSO), freshly prepared solution, λ_{max}, nm: 677, 560, 328 (relative intensity 0.95 : 0.15 : 1); after 1 h: 677, 329 (0.98 : 1).

Monoconjugate XI of cobalt octa[4,5]carboxyphthalocyanine with spirolactam III was prepared in a good yield by heating a mixture of 0.35 g of tetraanhydride **XXI** with 0.35 g of spirolactam **III** in *N*-methylpyrrolidone; the product was isolated similarly to **IX** in the form of acetate **XI** · AcOH. IR spec-

trum (KBr), ν, cm^{-1}: 1631, 1702, 1761 (C=O), 2820–2970 (CH). Found, %: C 60.46, 60.90; H 3.73, 4.02; N 11.87, 11.92. $C_{76}H_{60}CoN_{12}O_{18}$. Calculated, %: C 60.33; H 4.07; N 11.30.

Monoconjugate XII of cobalt octa[4,5]carboxyphthalocyanine with Rhodamine C ester IV was prepared similarly from 0.35 g of tetraanhydride **XXI** and 0.28 g of rhodamine **IV**; the product was isolated by the extraction with hot chloroform. Yield 0.45 g (77%). IR spectrum (KBr pellet), ν, cm^{-1}: 1642, 1711, 1770, 1836 (C=O). Electronic absorption spectrum (DMSO), λ_{max}, nm: 675, 566, 337 (relative intensity 1 : 1.16 : 1). Found, %: C 59.35, 59.14; H 2.90, 2.99; Cl 2.55, 2.49; N 11.13, 11.03. $C_{70}H_{42}ClCoN_{11}\cdot O_{18}$. Calculated, %: C 59.22; H 2.99; Cl 2.50; N 10.86.

Sodium salt of monoconjugate XII. To a suspension of 0.1 g of **XII** in 15 ml of distilled water, we added 0.1 N aqueous NaOH to pH 7. The resulting solution was filtered to remove mechanical impurities and evaporated to dryness on a rotary evaporator in a vacuum (20 mm Hg). The residue was mixed with 10 ml of ethanol; the undissolved residue was filtered off and dried at 100–105°C. Yield ~90%. The salt is readily soluble in water and phosphate buffer (pH 6.75).

Tetraconjugate XV of cobalt octa[4,5]carboxyphthalocyanine with Rhodamine C 2-aminoethyl ester IV. To a solution of 0.05 g of tetraanhydride **XXI** in 7 ml of anhydrous *N*-methylpyrrolidone, we added 0.5 g of perchlorate of rhodamine **IV**; the mixture was stirred for 20 h at 150–155°C in a helium flow. The cooled reaction mixture was poured into water; the suspension was filtered, and the precipitate was washed with hot distilled water, squeezed, and dried. The product was purified by chromatography on silica gel; impurities were eluted with chloroform and chloroform–methanol (20 : 1), and the conjugate, with tetrahydrofuran. Then the eluate was diluted with benzene, the suspension was filtered, and the precipitate was washed successively with benzene, ether, and ethanol until the filtrate became colorless. Yield of **XV** 0.16 g (84%). IR spectrum (KBr), ν, cm^{-1}: 1647, 1703, 1764 (C=O), 2929, 2972 (CH). Found, %: C 62.33, 62.06; H 4.19, 4.32; Cl 2.68; N 9.24, 9.25. $C_{160}H_{144}Cl_4CoN_{20}O_{36}$. Calculated, %: C 61.51; H 4.66; Cl 4.54; N 8.97.

ACKNOWLEDGMENTS

The study was financially supported by the Moscow City Government.

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