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Lanthanide porphyrin complexes

A F Mironov

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Abstract. The review summarizes literature data and results of the author's research on the synthesis, properties and possible fields of practical application of lanthanide porphyrin complexes. Emphasis is given to the application of luminescence properties of lanthanide derivatives in medicine. The bibliography includes 108 references.

I. Introduction

Lanthanide complexes hold a prominent position among a wide diversity of metalloporphyrins. As opposed to transition metals with a partially filled 4d shell, which are very sensitive to the number and distribution of d electrons, 4f orbitals of lanthanides are buried deep inside the electron shell and their 4f electrons are strongly shielded by the outer 5s and 5p shells. The interaction between 4f electrons and adjacent atoms is weakly reflected in the chemical behaviour of lanthanides, and, consequently, their complexes have quite similar chemical properties.[1–3] Depending on the size, the lanthanide ions can be located either directly above the plane of the porphyrin macrocycle or at the periphery of the porphyrin in special chelate groups. Lanthanide porphyrin complexes have attracted attention due to their potential practical use for the design of various optical materials and lasers. Emphasis is given to the application of the unique luminescence properties of these compounds in biology and medicine.

Intrinsic luminescence of lanthanide ions (Ln) is rather weak, but it is substantially enhanced in complexes with porphyrins due to the energy transfer from the excited macrocycle to the Ln^{III} ion. Solovyov, Tsvirko and their co-workers[4–9] studied ethioporphyrin I, octaethylporphyrin (OEP), tetrabenzoporphyrin, *meso*-tetraphenylporphyrin (TPP) and *meso*-tetra(*p*-tolyl)porphyrin (TTP) complexes of a large group of lanthanides and classified these compounds into three groups.

1. Complexes of La, Gd and Lu, whose 4f-electron levels are higher than singlet (S_1 and S_2) and triplet (T_1) levels of porphyrins.

2. Complexes of Sm, Eu, Tb, Ho and Tm with a triplet level T_1 lower in energy than the luminescent level of Ln^{III}.

3. Complexes of Er, Nd and Yb, in which the luminescent level of Ln^{III} is lower in energy than the T_1 level.

In the first group of complexes, the energy transfer is impossible, and their luminescence properties are similar to those of porphyrin complexes of other metals, whose ions do not have low-lying localized energy levels. Diamagnetic lanthanum and lutetium complexes exhibit weak fluorescence but rather strong phosphorescence at 77 K. The paramagnetic gadolinium complex has intense phosphorescence but does not have fluorescence. The absence of the latter is apparently associated with the intersystem crossing to the T_1 state. Metal complexes of the Groups 2 and 3 do not exhibit molecular fluorescence and phosphorescence for the same reason. By contrast, erbium, neodymium and ytterbium porphyrin complexes are characterized by near-infrared 4f luminescence, which is possible due to the intramolecular energy transfer from the triplet level of porphyrin located in the region of 12 500 – 13 500 cm^{-1} to lower-lying resonant levels of Er^{3+}, Nd^{3+} and Yb^{3+} (6450, 11 500 and 10 200 cm^{-1}, respectively) (Fig. 1).[9,10] Infrared 4f luminescence of lanthanide complexes with porphyrins and other macrocyclic ligands is considered in reviews.[11,12]

Table 1 summarizes principal characteristics of lanthanide atoms and ions. Starting with the first element (lanthanum), the electron shell of lanthanides gradually becomes filled, 14 electrons being added one at a time mainly to the

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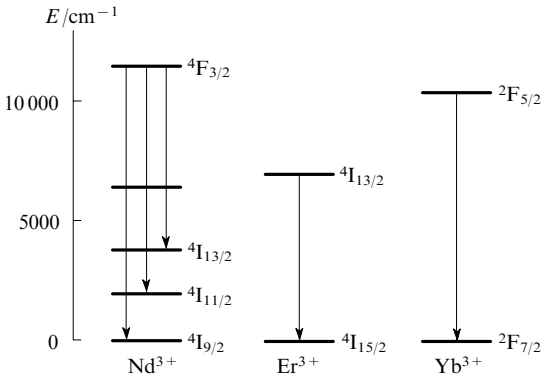


Figure 1. Energy level diagram of Nd^{3+}, Er^{3+} and Yb^{3+} ions.[9]

4f sublevel and, in three cases (cerium, gadolinium and lutetium) to the 5d sublevel. A sharp decrease in the atomic radius of cerium and lowering of the energy of its 4f orbital compared to lanthanum are insufficient to prevent the filling of the 5d sublevel. For gadolinium, this is due to the stability of the half-filled 4f sublevel. In the latter case (in lutetium), the 4f sublevel is completely filled and the next 71th electron is forced to occupy the 5d orbital.

The chemical bonds of lanthanides have a predominantly ionic character and their properties are determined by the size of the ion in the oxidation state +3. The oxidation states +4 (Ce, Pr, Tb) and +2 (Sm, Eu, Yb) are less characteristic. An important feature of lanthanides is a decrease in the ionic radius in the series from lanthanum to lutetium. The so-called lanthanide contraction is attributed to the growing attraction between the outer electron shells and the positively charged nucleus. The size of the Ln^{3+} ion has a substantial effect on the character of complexation. Thus, the Yb^{3+} ion is smaller than La^{3+} by 0.16 Å and it easily forms complexes with porphyrins.

Table 1. Outer electron configurations of lanthanide atoms and ions, the oxidation states and radii of M^{3+} ions.[2]

Atomic number	Element	Electron configuration [a]		Ionic radius of M^{3+} /Å	Oxidation state [b]
		of atom	of M^{3+} ion		
57	La	$5d^16s^2$	[Xe]	1.03	+3
58	Ce	$4f^15d^16s^2$	$4f^1$	1.02	+3, +4
59	Pr	$4f^35d^06s^2$	$4f^2$	0.99	+3, +4
60	Nd	$4f^45d^06s^2$	$4f^3$	0.98	+3 (+4)
61	Pm	$4f^55d^06s^2$	$4f^4$	0.97	+3 (+4)
62	Sm	$4f^65d^06s^2$	$4f^5$	0.96	+3, +2 (+4)
63	Eu	$4f^75d^06s^2$	$4f^6$	0.95	+3, +2
64	Gd	$4f^75d^16s^2$	$4f^7$	0.94	+3
65	Tb	$4f^95d^06s^2$	$4f^8$	0.92	+3, +4
66	Dy	$4f^{10}5d^06s^2$	$4f^9$	0.91	+3 (+4)
67	Ho	$4f^{11}5d^06s^2$	$4f^{10}$	0.90	+3
68	Er	$4f^{12}5d^06s^2$	$4f^{11}$	0.89	+3
69	Tm	$4f^{13}5d^06s^2$	$4f^{12}$	0.88	+3 (+2, +4)
70	Yb	$4f^{14}5d^06s^2$	$4f^{13}$	0.87	+3, +2
71	Lu	$4f^{14}5d^16s^2$	$4f^{14}$	0.86	+3

[a] Valence-shell electrons, which are outer with respect to the xenon electron shell, are given; [b] unstable oxidation states are enclosed in parentheses.

II. Porphyrin and phthalocyanine complexes of lanthanides with large ionic radii

Lanthanum and other lanthanides can also form rather stable complexes with porphyrins and related macrocycles. In these complexes, a metal ion is located above the plane of the macrocycle and often forms structures composed of two or three porphyrin or phthalocyanine molecules. These are so-called double- and triple-decker sandwich complexes, in which Ln^{3+} acts as a linking unit.

Tsivadze and co-workers [13–17] proposed a facile method for the synthesis of such heteroleptic structures with different ions, from lanthanum to terbium, as the central elements. Tetraarylporphyrin **1**, crown-substituted phthalonitrile and acetylacetonate of the corresponding lanthanide served as the starting compounds (Scheme 1). The heating of this mixture in n-octanol in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) results in the formation of dimeric (**2**)† and trimeric (**3**) structures in a total yield of ~50%. The authors suggest that dimer **2**, which is initially formed from two tetrapyrrole macrocycles, binds a porphyrin molecule to yield trimer **3**.

Compounds **2** and **3** can be easily separated on an alumina chromatography column. The yields and ratios of double- and triple-decker complexes essentially depend on the reaction conditions. Thus, even traces of water in n-octanol sharply decrease the yield of compounds **3**.

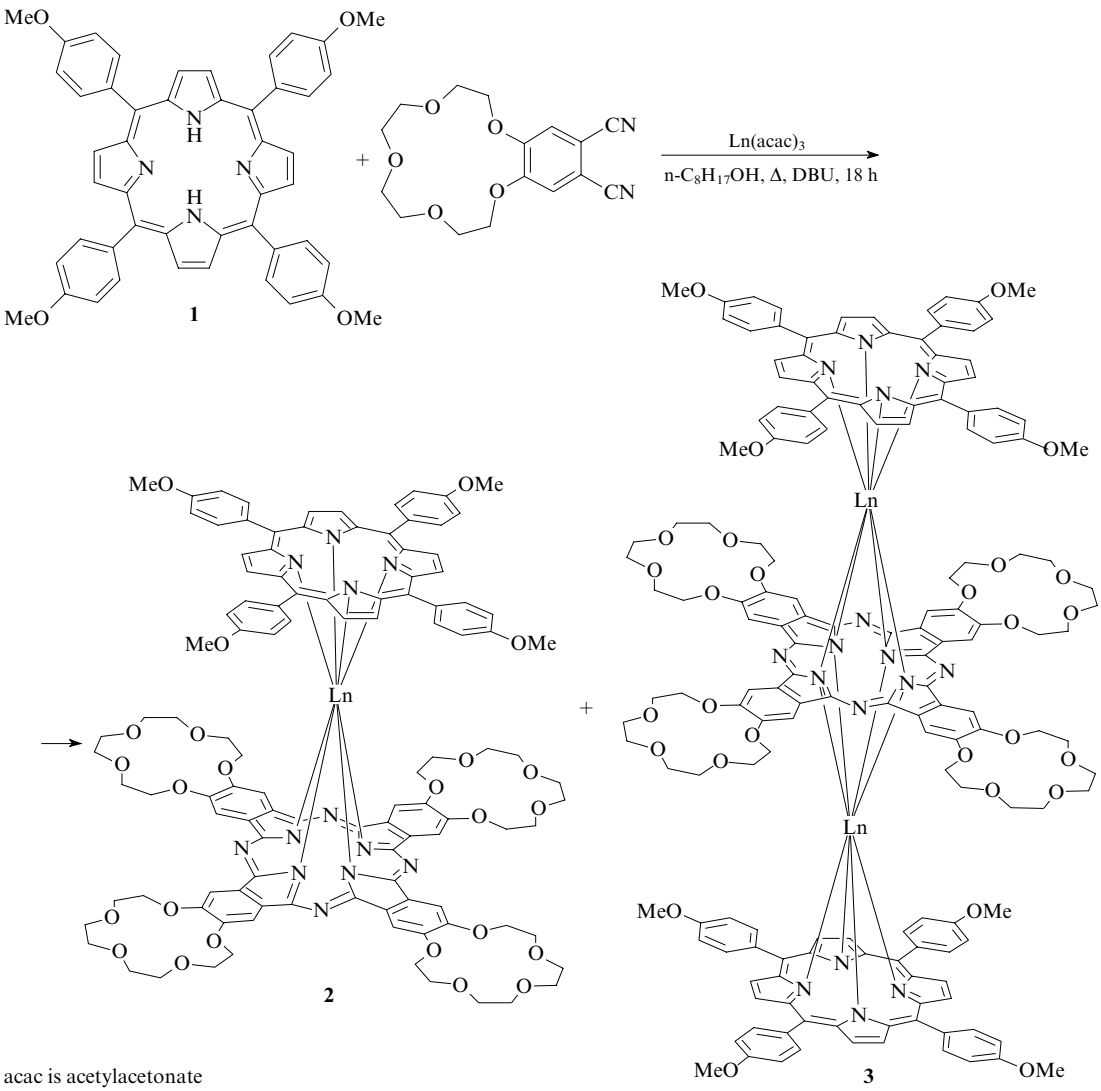
An analysis of the electronic absorption spectra of complexes **2** and **3** showed that the intensity of the bands belonging to phthalocyanine in triple-decker complexes is substantially weaker than that of the bands assigned to porphyrins. However, the most interesting information was obtained when comparing the positions of long-wavelength absorption bands of double- (750–830 nm) and triple-decker (860–950 nm) complexes, on the one hand, and the ionic radii of lanthanides, on the other hand. In both cases, there is a clear pattern that the Q band is linearly shifted to the IR region as the ionic radius of Ln^{3+} decreases (Fig. 2 *a*, *b*). Moreover, this correlation made it possible to determine the real oxidation state of the cerium ion in the double-decker complex, which exhibits a bathochromic shift of the Q band unusually large for this element. It appeared that the synthesis is accompanied by the oxidation of the Ce^{3+} ion to Ce^{4+}. The treatment of the Ce^{4+} complex with hydrazine hydrate affords the Ce^{3+} ion, whose ionic radius fits well to the general pattern (see Fig. 2 *a*).

The ability of the cerium atom to be oxidized to Ce^{4+} is evidently associated with the specific electron density distribution in double-decker complexes of this metal because the Ce^{3+} ion in the corresponding tetraphenylporphyrin derivative does not exhibit the tendency to the oxidation.[18]

The oxidation of compounds **2** and **3** with *N*-bromosuccinimide was investigated by Tsivadze and co-workers.[14] It was shown that both the metal (for example, cerium) ion

† Double-decker complexes crystallize in the monoprotonated neutral form (except for Ce^{4+} complexes). However, the proton is not given in the structural formula. The authors of original studies often omit this proton in the empirical formulas.

Scheme 1



acac is acetylacetonate

Ln	Yields (%)	
	2	**3**
La	26	32
Ce	20	20
Pr	18	24
Nd	15	20
Sm	16	35
Eu	30	12

and the π system of the ligands of the double-decker complexes can be oxidized. In the triple-decker complexes, only the ligand part of the molecule is subjected to oxidation.

For triple-decker complexes **3**, the effect of paramagnetic lanthanide ions on the ^{1}H and ^{13}C NMR spectra was studied in-depth.[19–22] The elaborated method can serve as a reliable tool for the establishment of structures of new

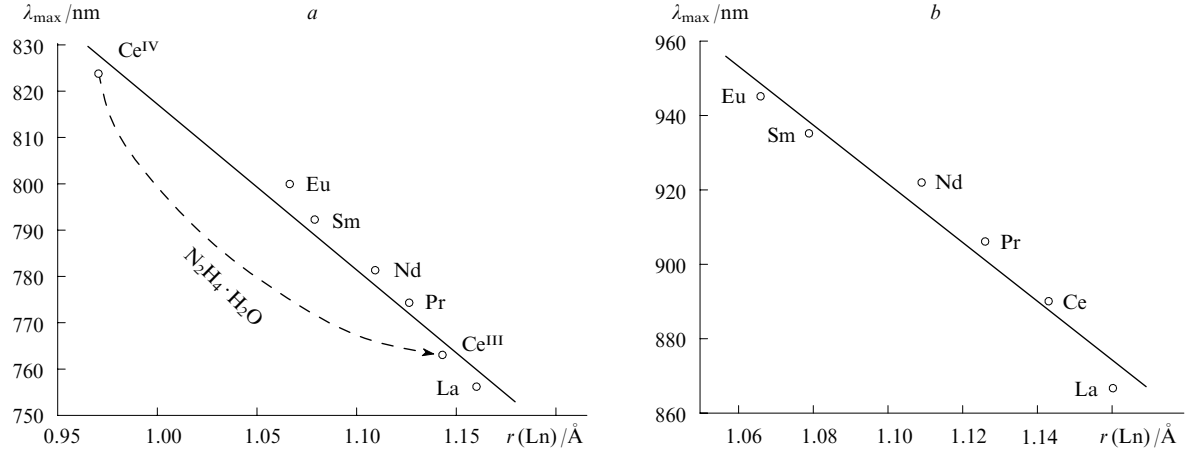
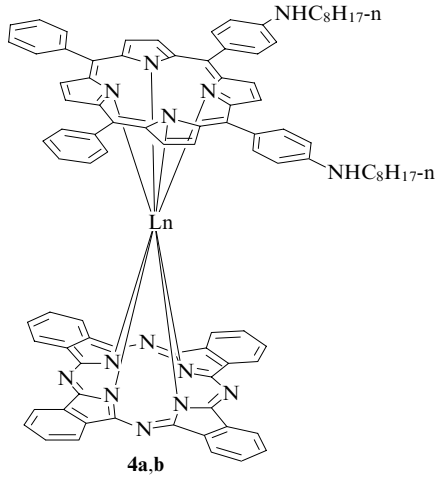


Figure 2. Position of the Q band in the absorption spectra of double- (*a*) and triple-decker (*b*) complexes against the ionic radius of lanthanides.[14]

heteroleptic tetrapyrrole compounds and their supramolecular ensembles.

Double-decker complexes of lanthanides (Yb^{3+}, Dy^{3+} and Lu^{3+}) with porphyrins (OEP and TPP) were studied by NMR spectroscopy.[23,24] It was found that the enthalpy of the activation for the rotation of phenyl rings of porphyrins increases with increasing atomic number of Ln, which is attributed to the effect of lanthanide contraction. In the authors' opinion, these are prerequisites for the application of these compounds as thermometric NMR sensors directly in reaction media. They can be employed to measure the temperature in solution and investigate endothermic or exothermic processes.[25]

Two new double-decker complexes were synthesized from 5,10-diphenyl-15,20-di(4-n-octylaminophenyl)porphyrin and unsubstituted phthalocyanine with Eu (**4a**) and Lu (**4b**) and characterized by physicochemical methods and X-ray diffraction.[26] Complexes **4a**,**b** can form nanostructures 220–250 and 300 nm in width and 10 and 3–5 μm in length.



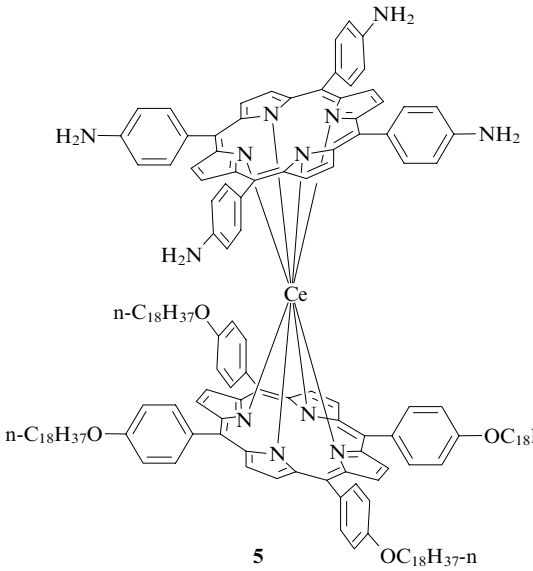
4a,**b**

Ln = Eu (**a**), Lu (**b**)

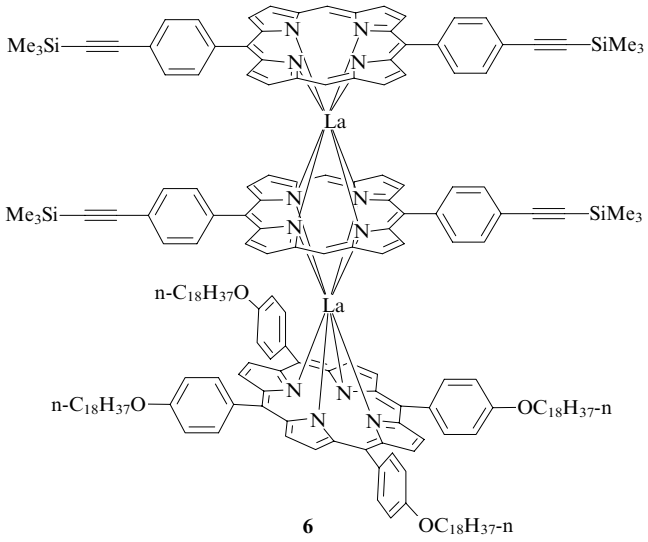
An interesting feature of the behaviour of double- and triple-decker porphyrins is that individual macrocycles can undergo rotational and vibrational motion with respect to the metal ion.[27,28] A NMR spectroscopic study showed that in solution the rotation strongly depends on the ionic radius of the metal lying on a rotation axis. The use of lanthanides with large ionic radii leads to a decrease in the barrier to the rotation, thus facilitating this process compared to metal ions with smaller ionic radii.[29]

The investigation of the possibility of the rotation for lanthanide porphyrin complexes immobilized onto the Au(111) surface was the next important step in the research of this phenomenon.[30] A Ce^{IV} double-decker complex (**5**) and a La^{III} triple-decker complex (**6**) were synthesized starting from two porphyrins containing relatively small substituents, *meso*-tetrakis(4-aminophenyl)porphyrin and 10,20-bis(4-trimethylsilylethynylphenyl)porphyrin, and a macrocycle bearing large hydrophobic substituents, *meso*-tetrakis(4-n-octadecyloxyphenyl)porphyrin.

Due to the adsorption of porphyrin with long-chain substituents on an Au(111) substrate, the above-mentioned complexes form well-organized monolayers. The investigation of the latter by low-temperature scanning electron microscopy showed a slight rotation of the upper porphyrin in complex **5** under non-destructive conditions, whereas the labile porphyrin in complex **6** is, on the contrary, characterized by strong rotation even in the absence of any considerable external effect.



5



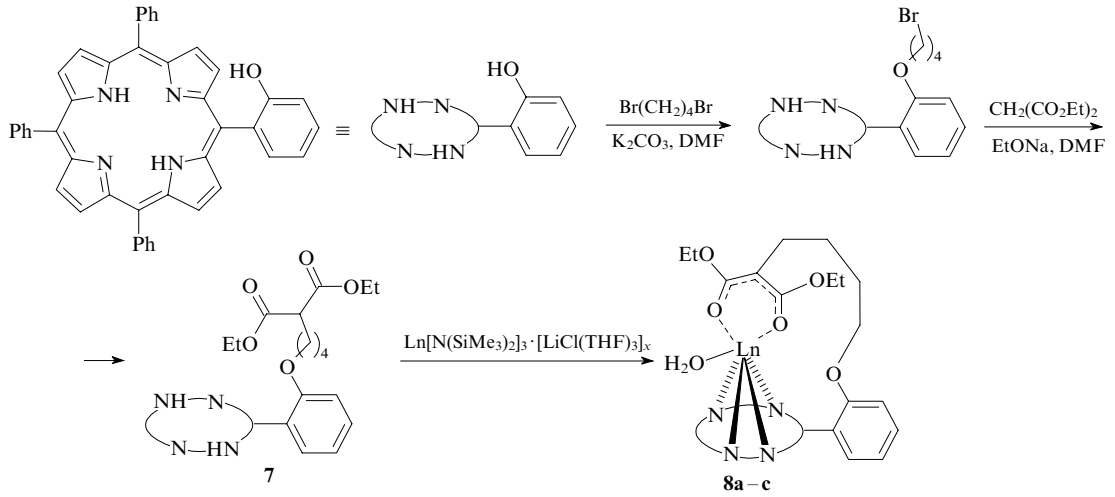
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Therefore, evidence was obtained that the size of the central metal ion affects the ease of rotation of individual porphyrin moieties around the Ce^{IV} and La^{III} atoms in lanthanide multiple-decker complexes. It should be noted that the effect of the porphyrin structure in the complex on the rotation remains unclear because the rotation was compared for complexes **5** and **6**, in which porphyrins contain different substituents.[30] However, the authors believed that these results are an important step toward creating mechanical machines and memory cells based on supramolecular ensembles.

III. Lanthanide mono- and bisporphyrin complexes

In addition to double- and triple-decker structures, other types of structural organization of porphyrin lanthanide complexes are also possible. Thus, the Nd^{3+} ion and even smaller Er^{3+} and Yb^{3+} ions can be located above the plane of the porphyrin but be coordinated not to the second macrocycle but to other ligands (for example, to two oxygen

Scheme 2

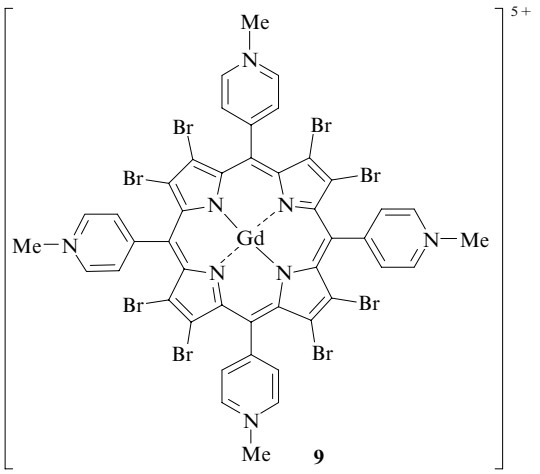


Ln = Nd (**a**), Er (**b**), Yb (**c**)

atoms of the diethyl malonic moiety and a water molecule).[31] The synthesis of the starting porphyrin **7** for such complexes involves the addition of 1,4-dibromobutane at the hydroxy group of 5-(2-hydroxyphenyl)-10,15,20-triphenylporphyrin followed by the reaction of the resulting bromo derivatives with diethyl malonate in the presence of sodium ethoxide (Scheme 2).

Porphyrin **7** was transformed into the corresponding complexes **8a–c** by being treated with $Ln[N(SiMe_3)_2]_3 \cdot [LiCl(THF)_3]_x$. The resulting compounds proved to be rather stable and did not decompose during chromatography. The conclusion about the strength of the bonds between the metal ion and four nitrogen atoms can be drawn from the intensity ratio of α bands to β bands in the absorption spectra, which are 0.17, 0.19 and 0.25 for Nd^{3+}, Er^{3+} and Yb^{3+}, respectively. These values are indicative of an increase in the strength of the Ln–N bonds as the ionic radius of lanthanides decreases. A study of photoluminescence of complexes **8** showed that, when excited with light, the porphyrin macrocycle transfers the energy to the Ln^{3+} ion causing near-infrared luminescence.

Due to the smaller ionic radii, gadolinium and the next following lanthanides can form complexes, in which the Ln^{3+} ion lies in the plane of the porphyrin macrocycle. In addition to conventional methods for the synthesis of lanthanide complexes based on the reactions of porphyrins with salts or acetylacetonates of the corresponding lanthanides, an original approach was proposed for gadolinium.[32, 33] The latter is based on the ability of water-soluble octahalogenated porphyrins to bind lithium ions selectively and strongly even in the presence of other alkali metal ions (Na^+ and K^+). When treated with gadolinium salts under mild conditions (water, 20 °C), the lithium complex with 2,3,7,8,12,13,17,18-octabromo-*meso*-tetrakis(*N*-methylpyridinio-4-yl)porphyrin gives compound **9**.

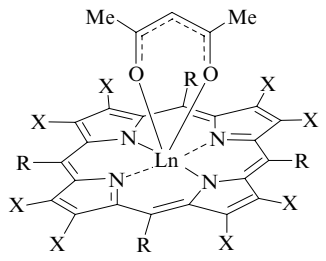


Among numerous lanthanide complexes, gadolinium and ytterbium derivatives are the most promising compounds for medical applications. Their use is associated primarily with strong near-infrared fluorescence, where biological tissues are most transparent.

The luminescence of porphyrin complexes of a series of lanthanides (Nd, Eu, Gd, Tb, Dy, Ho, Er, Yb) and their sensitivity to oxygen were investigated by Khalil *et al.*[34] Neodymium, erbium and ytterbium complexes show luminescence due to the f–f transition of lanthanide ions with maxima at 890, 1068 and 1348 nm (for Nd^{3+}), 1530 nm (for Er^{3+}), 970, 1002 and 1020 nm (for Yb^{3+}). Gadolinium porphyrins exhibit emission from the triplet state of the porphyrin macrocycle at 726, 810, 922 and 1056 nm.

Europium, terbium, dysprosium and holmium complexes do not show luminescence in the region of 700–1700 nm. The dependence of phosphorescence of Gd^{3+} complexes with *meso*-tetraphenylporphyrin, octaethylporphyrin, *meso*-tetrakis(pentafluorophenyl)porphyrin (TPFPP) and *meso*-tetra(4-pyridyl)porphyrin (TPyP) on the concentration of O_2 in solution and gas-permeable polymer films was studied. The quenching rate constant of phosphorescence was shown to depend linearly on the O_2 concentration.

The relaxation through radiationless excitation of vibrations of the surrounding C–H bonds is one of the main factors responsible for the low efficiency of infrared luminescence of lanthanide complexes.[35–37] With the goal of investigating the effect of this factor on the luminescence quenching of erbium complexes, hydrogen atoms in porphyrins were successively replaced by halogen atoms first in the *meso*-phenyl substituents and then in the β positions of the macrocycle.[38] The following metalloporphyrins were synthesized: Er^{III}-TPP (**10a**), Er^{III}-TPFPP (**10b**) and Er^{III}-2,3,7,8,12,13,17,18-Br_8-TPFPP (**10c**).



10a–f

Ln = Er (**10a–c**), Gd (**10d–f**); R = Ph, X = H (**a**, **d**); R = C_6F_5: X = H (**b**, **e**), Br (**c**, **f**)

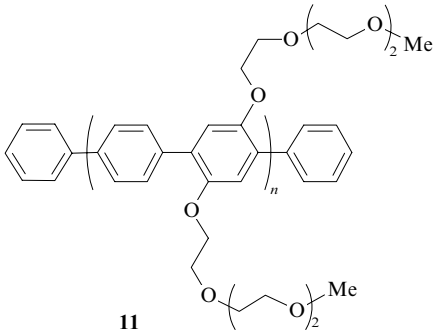
An analysis of the absorption spectra of complex **10a** and its halogenated derivatives **10b**,**c** showed that the introduction of a fluorine or bromine atom has only a slight effect on the position and intensity of the maxima of the Soret band and Q bands. The introduction of the Er^{3+} ion leads to the shift of the fluorescence maximum compared to that of the starting TPP (653 and 720 nm) through the transition from an excited singlet state of the porphyrin to the triplet state.[10] This results in the further energy transfer to the energy level of lanthanide, which is accompanied by the characteristic IR emission corresponding to the $^4I_{13/2} \rightarrow {}^4I_{15/2}$ transition of the Er^{3+} ion and the appearance of a luminescence band at 1540 nm. The emission of all erbium complexes in the visible region is determined only by the singlet state of the porphyrin macrocycle.

Related halogenated gadolinium complexes **10e**,**f** were used as model systems.[39] In these complexes, the introduction of substituents does not lead to a substantial change in the energy of the triplet state of the ligand. However, it was shown that the energy levels of the triplet state of metal complexes are much more sensitive to the halogenation compared to the singlet state. Therefore, the halogenation of porphyrins results in an increase in the infrared luminescence efficiency of Ln^{3+} complexes.

Among lanthanides, ytterbium is most widely used for the synthesis of complexes with porphyrins and it was studied in most detail. This is due to several reasons, including the small size of the Yb^{III} ion and, as a consequence, high stability of its complexes, as well as a low-lying triplet level, which ensures the efficient intramolecular energy transfer from the triplet level of porphyrins and the characteristic 4f luminescence of Yb^{III} ions in the region of 960–1010 nm with a maximum at 980 nm. In most complexes, the ytterbium ion is located slightly above the plane of the macrocycle with specially organized ligands (Scheme 3).

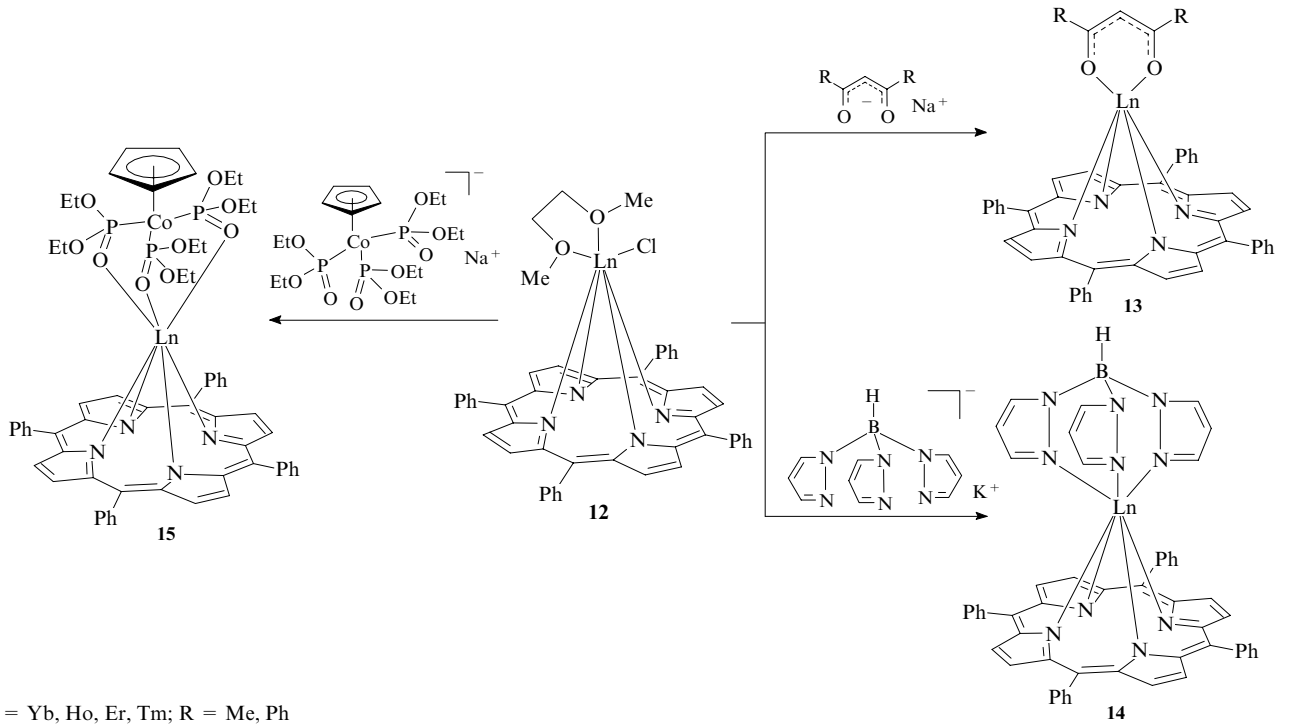
The main fields of application of ytterbium porphyrin complexes are related to the design of light-electricity conversion devices, chemical sensors, catalysts and near-infrared luminescent probes for biology and medicine.

For instance, near-infrared organic light-emitting diodes, which are based on a composite consisting of lanthanide TPP complexes and conjugated polymers, were described.[40] Blue poly(paraphenylene) was used as the polymer (**11**).



11

Scheme 3



Ln = Yb, Ho, Er, Tm; R = Me, Ph

In addition to ytterbium (λ_{max} = 977 nm), the following lanthanides were introduced into TPP complexes to vary the luminescence wavelength in the range of 950–1800 nm: Ho (λ_{max} = 1197 nm), Er (λ_{max} = 1570 nm) and Tm (λ_{max} = 1800 nm). Complexes **13**–**15** with different 'covering' ligands were synthesized based on complexes **12** (see Scheme 3)[40] according to a procedure developed by Foley *et al.*[41]

The proposed composite for light diodes has the optimal overlap of blue emission of the polymer (419 nm) with the Soret band of metalloporphyrins (427 nm), thus ensuring the efficient energy transfer to the corresponding ligand.

Near-infrared electroluminescent devices were created.[40] Figure 3 depicts the corresponding spectra for TPP complexes of Yb^{III}, Ho^{III} and Er^{III}. These devices require a relatively small voltage for the switching on and a weak current is consumed for their efficient operation.

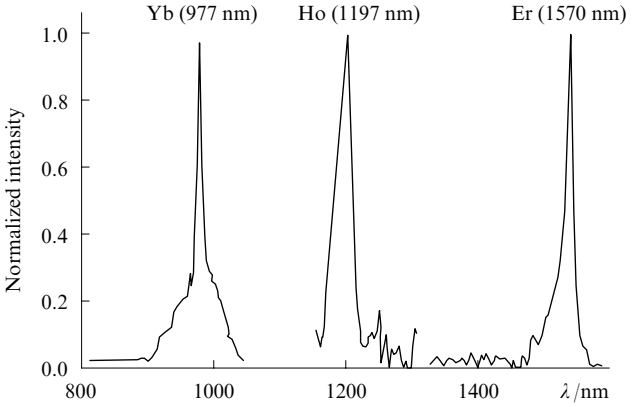
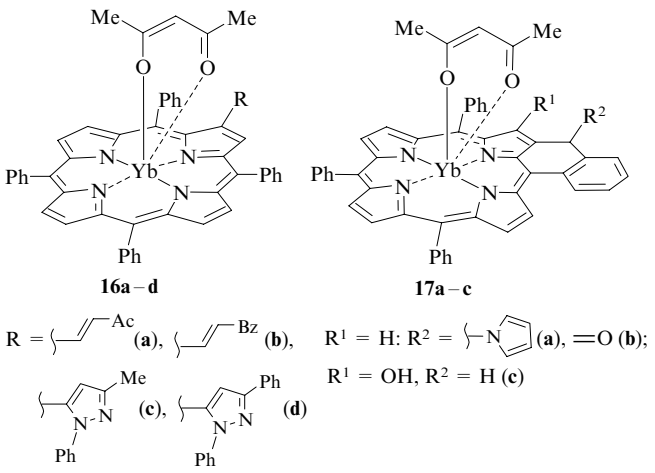


Figure 3. Infrared eletroluminescence of lanthanide tetraphenylporphyrin complexes.[40]

Korovin and co-workers[42–49] carried out a series of works on the synthesis of a large group of ytterbium porphyrin complexes and investigation of their fluorescence. Twelve Yb^{III} complexes with symmetrically tetrasubstituted porphyrins containing isomeric pyridine, quinoline and quinoxaline moieties in the *meso* positions were synthesized.[45] The 4f-luminescence maximum of Yb^{3+} ions in the complexes was observed at 980 nm under excitation at a wavelength from 250 to 600 nm. The fact that the excitation 4f luminescence spectra of Yb^{III} in porphyrin complexes coincide with their absorption spectra attests to the energy transfer from the macrocycle to the lanthanide ion. The luminescence quantum yields, particularly of 4-pyridyl- and 4-quinolyl-substituted porphyrins, are higher (up to 2.5 times) compared to phenyl and naphthyl derivatives.

The synthesis of a series of Yb^{III} porphyrins containing crown ether and other oxygen-containing rings in the *meso* positions was documented.[46] Interesting results were obtained in the study of unsymmetrically substituted porphyrins **16a**–**d** and **17a**–**c**.[44]

It was shown that the efficiency of 4f luminescence of Yb^{III} complexes with such porphyrins depends to a substantial degree on the nature of the substituents in the macrocycle. The calculations using the ELZA program and the construction of three-dimensional models of porphyrins and Yb^{III} complexes using the Hyper-Chem 7.0



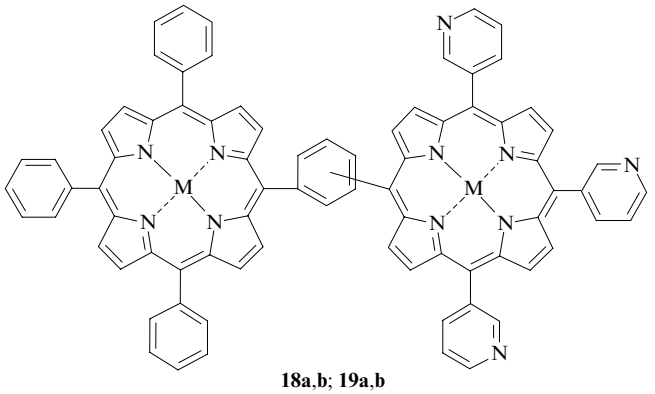
16a–**d** **17a**–**c**

R = Ac (**a**), Bz (**b**), Me (**c**), Ph (**d**)

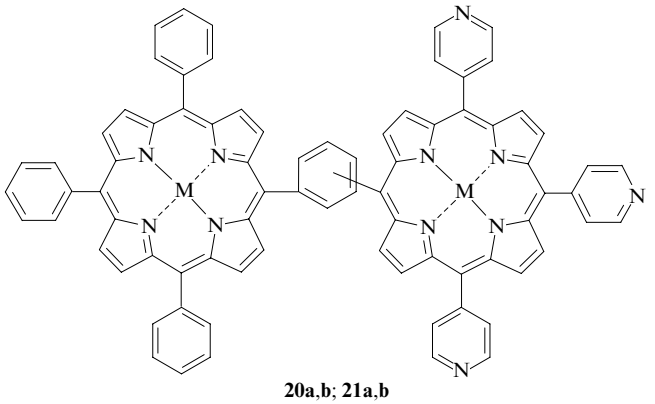
R^1 = H: R^2 = N (**a**), =O (**b**); R^1 = OH, R^2 = H (**c**)

showed that, as opposed to TPP in which all four nitrogen atoms bear equal charges, the introduction of substituents into porphyrins (see complexes **16** and **17**) leads to a change in the charges, this effect being most pronounced for the N atom nearest to the substituent. The larger the negative charge on the nitrogen atom and the smaller the positive charge on the ytterbium ion, the higher the luminescence quantum yield. However, the strengthening of the covalent bond between ytterbium and the outer ligand results in that the Yb^{3+} ion is forced to be displaced from the plane of the macrocycle and, as a consequence, in a decrease in the 4f-luminescence intensity.

The electronic and luminescence spectra of ytterbium bisporphyrin complexes **18b**–**21b** were investigated by Korovin *et al.*[45]



18a,**b**; **19a**,**b**



20a,**b**; **21a**,**b**

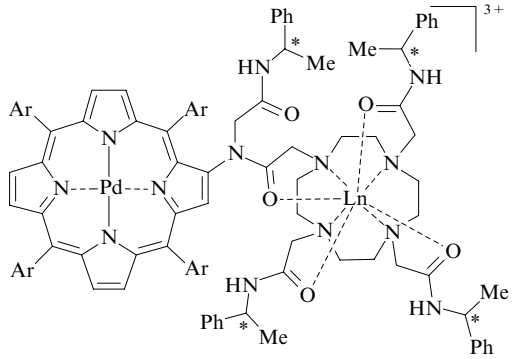
M = 2 H (**a**), Yb (**b**); isomers: *para* (**18**, **20**), *meta* (**19**, **21**)

The introduction of an Yb^{3+} ion into bisporphyrins **18a**–**21a** leads to a decrease in the number of Q bands from four to two and the disappearance of the splitting of the Soret band. It was found that luminescence of *p*-phenylene derivatives **18b** and **20b** is somewhat higher than that of *meta* isomers **19b** and **21b**. Apparently, this is attributed to the interaction between the more closely spaced ytterbium ions in the *meta* isomers (the distance is 10.8 ± 0.1 Å) compared with the *para* isomers (12.0 ± 0.1 Å). This is evidenced by a substantially higher luminescence quantum yield ($\Phi = 10.1$ when Zn-TPP with $\Phi = 0.03$ was used as the reference) and the luminescence lifetime ($\tau = 10.9$ ms) for *meso*-tetra(4-pyridyl)porphyrin. For dimers **18b**–**21b**, the corresponding values are as follows: $\Phi = 2.7-5.4$ and $\tau = 3.7-6.0$ ms.

IV. Heteronuclear lanthanide-containing complexes

The synthesis of heteronuclear structures, which involve both lanthanide-containing moieties and porphyrin complexes of other metals (Pt, Pd, Ru, Cr, Zn, *etc.*), was described. These structures can serve different functions.

Complexes **22a**,**b**, in which the porphyrin is covalently bonded to chiral lanthanide-containing moieties, were synthesized [50] with the aim of investigating the sensitizing effect of Pd porphyrin on the Yb^{3+} and Nd^{3+} ions.



22a,**b**

Ar = $C_6H_3Bu^t_2$-3,5; Ln = Yb^{3+} (**a**), Nd^{3+} (**b**)

The choice of Pd complexes was dictated by the fact that they have exceptionally long lifetimes of the triplet state, which is efficiently quenched by molecular oxygen in a polar medium.[51]

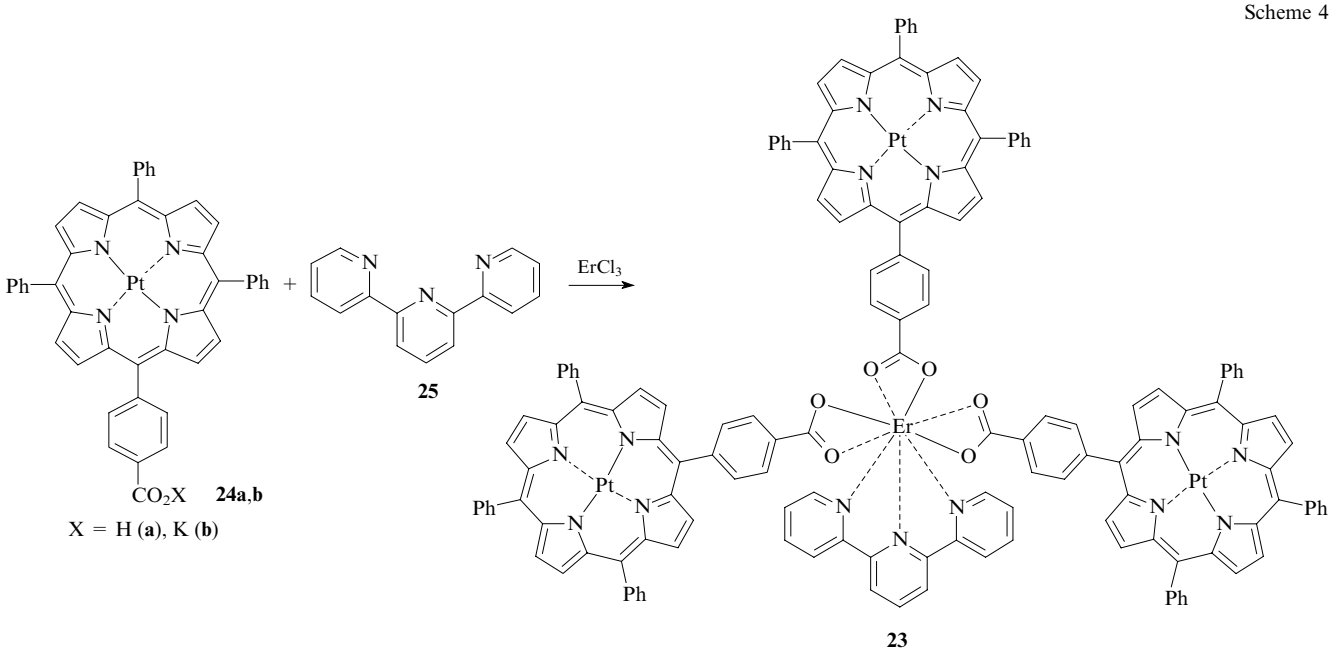
Earlier, it has been shown that tetracationic Pd porphyrins bind to DNA,[52] resulting in an enhancement of their fluorescence by a factor of 20. In the absence of O_2, the phosphorescence of Pd porphyrin appears as broadened maxima at 735 and 800 nm with the simultaneous enhancement of phosphorescence of lanthanides (by a factor of 7 and 2 for Yb^{3+} and Nd^{3+} ions, respectively), whose emission maxima are observed at 980 nm for Yb^{3+} and at 870 and 1064 nm for Nd^{3+}. In the presence of a 20-fold excess of the oligonucleotide $[(CG)_6]_2$ in an aerated solution (20% D_2O in CD_3OD), the emission of porphyrin increases to 30% of the emission in an deoxygenated medium; the phosphorescence of Yb^{3+} is enhanced in approximately the same degree. Evidently, the binding to nucleotides inhibits the quenching of the triplet state of porphyrin by oxygen.

The synthesis of Er^{III} complex **23** containing three Pt porphyrins as the ligands was documented.[53] Initially, Pt complexes with 5,10,15-triphenyl-20-(4-carboxyphenyl)porphyrin (**24a**) and its potassium salt (**24b**) were synthesized,[54] and their threefold excess was used in the reaction with tripyridine (**25**) and $ErCl_3$ (Scheme 4).

When exposed to light, both Pt porphyrin and tripyridine act as antennas that transfer the energy to an erbium ion; however, the contribution of the porphyrin is the major one. In the absence of oxygen, the luminescence quantum yield of complex **23** is 0.015%. Photophysical studies and theoretical calculations confirmed that the energy transfer to an Er^{III} ion occurs through the first excited state of the metal porphyrin complex. A study of luminescence of Er^{III} complex **23** under deoxygenated conditions and in the presence of O_2 showed that the latter substantially affects the energy transfer.

It was found [31, 55–58] that porphyrin ligands act as efficient antennas for increasing near-infrared luminescence

Scheme 4



24a,**b**

X = H (**a**), K (**b**)

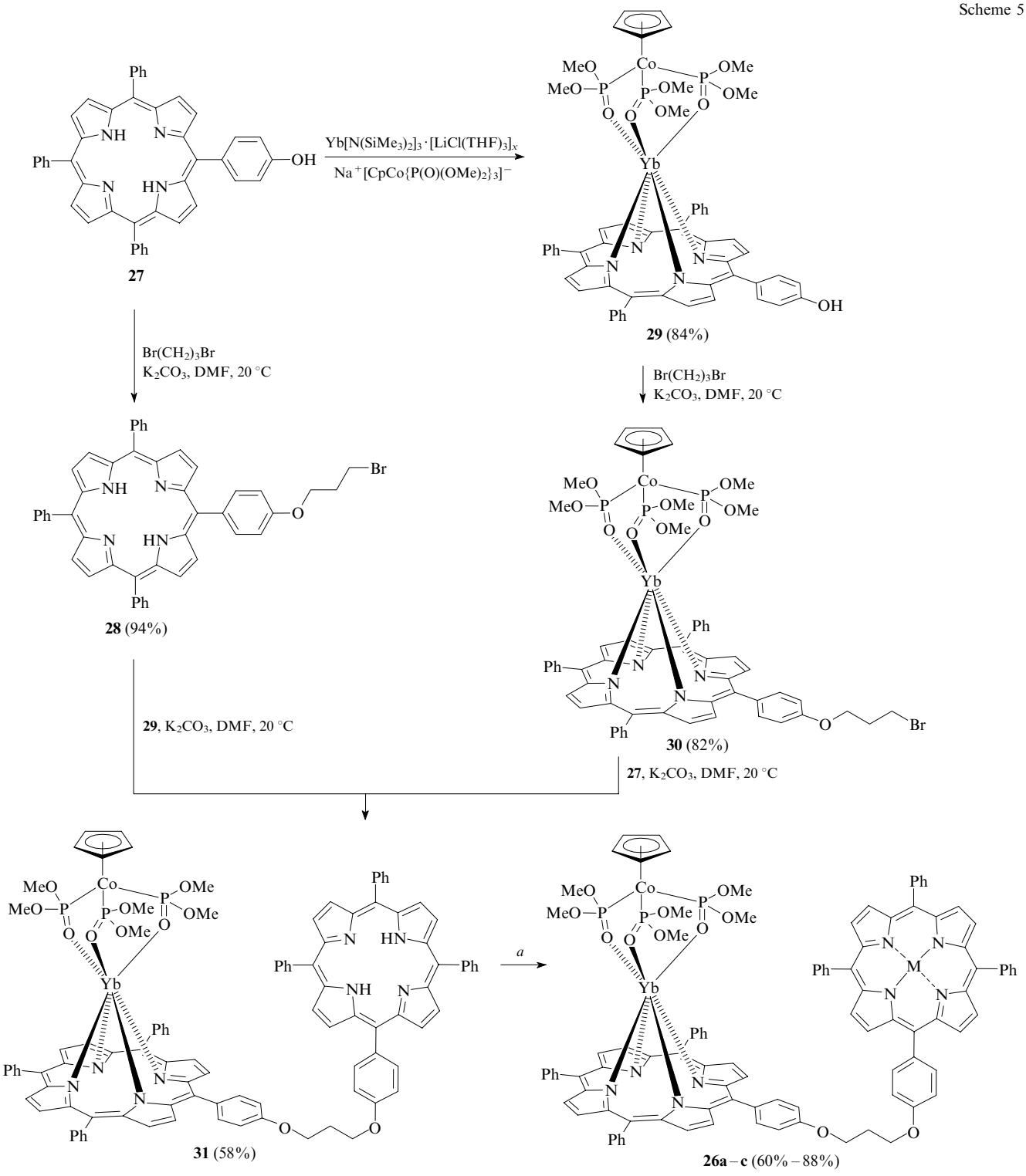
25

23

of Yb^{III}, Er^{III} and Nd^{III}. With the aim of increasing the excited-state lifetime of lanthanides and enhancing luminescence, d–f heterometallic complexes of transition metal ions (Cr^{3+}, Ru^{2+} and Pt^{2+}) and lanthanides (Yb^{3+} and Nb^{3+}) were synthesized.[59,60] The $Cr^{3+} \rightarrow Ln^{3+}$ system proved to be the most efficient one and enables increasing the excited-state lifetime of lanthanide ions at 10 K by three orders of magnitude (from several microseconds to milliseconds). However, the ligands in these assemblies absorb light only at 247 and 334 nm.

It would be expected that systems containing Zn, Pd or Pt complexes with TPP as antennas will be efficient systems.[61] The route to the synthesis of such d–f bimetallic bisporphyrins **26a–c**, in which the macrocycles are linked by a flexible three-carbon spacer, is depicted in Scheme 5. The Yb^{III} porphyrin contains rare pentadienyl(dimethoxy-

Scheme 5



(*a*) $M(OAc)_2 \cdot 2H_2O$, $CHCl_3$–MeOH (1 : 1), Δ or $PtCl_2(PhCN)_2$, Δ; M = Zn (**a**), Pd (**b**), Pt (**c**); Cp = η^5-C_5H_5

phosphate)cobalt as an auxiliary ligand. 5-(4-Hydroxyphenyl)-10,15,20-triphenylporphyrin (**27**) served as the starting compound to prepare Yb complex **31** according to two procedures (through the formation of complexes **28**–**30**). Complex **31** gave compounds **26a**–**c** when refluxed with salts of the corresponding metals.

Dyads **31** and **26a**–**c** were characterized by ^{1}H NMR spectroscopy, mass spectrometry and electronic spectroscopy. According to the X-ray diffraction data, the Yb^{3+} ion is held by seven coordination bonds with four nitrogen atoms of the macrocycle and three oxygen atoms of the phosphate groups.

The investigation of the photophysical properties of dyads **26a**–**c** showed that the emission of the Yb^{3+} ion corresponding to the $^2F_{5/2} \rightarrow {}^2F_{7/2}$ transition is observed at 998 nm, and the luminescence lifetime at room temperature is 30–40 μs, which is much longer than the emission time of porphyrin. It was found that the emission depends on the $\pi \rightarrow \pi^*$ transition of the porphyrin moiety both in the visible and near-IR regions. The intensity of infrared luminescence increases in the following series: **29** (1.0) < **26a** (1.8) < **26b** (4.0) < **26c** (5.0) (Fig. 4). This confirms the energy transfer from the porphyrin antenna to the Yb^{3+} ion.[61]

The lowering of the temperature from 298 to 77 K leads to an increase in the luminescence lifetime for complexes **31b**,**c** to 40 and 70 μs, respectively. In addition, a considerable two-photon transfer was observed for these dyads. This process is apparently associated with the interactions of the porphyrin macrocycles and the fact that the macrocycle is no longer centrosymmetric. It is expected that the resulting complexes will find use in nonlinear optics.

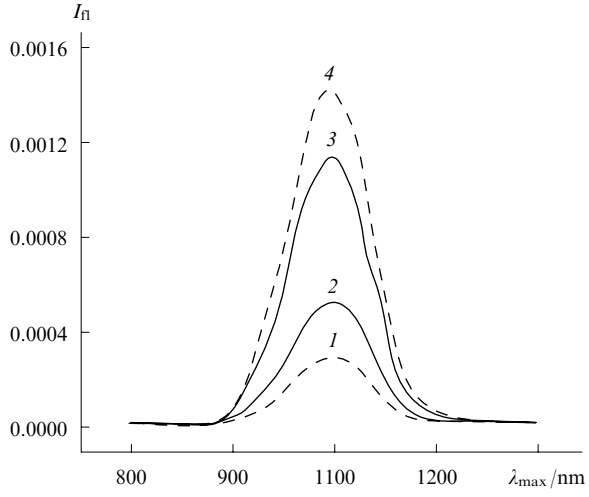


Figure 4. Near-infrared photoluminescence of d,f metal dyads **29** (*1*), **26a** (*2*), **26b** (*3*) and **26c** (*4*).[61]

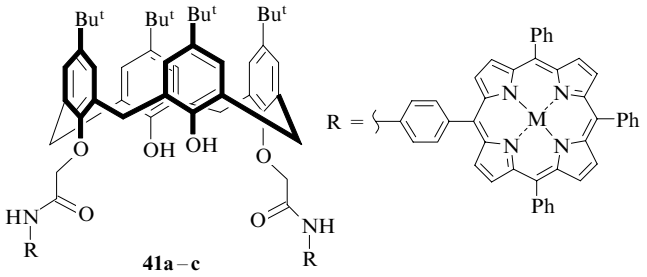
Another approach to the synthesis of heteronuclear lanthanide-containing complexes was described by Rusakova *et al.*[42] In such complexes, the porphyrin coordinates d metals (Zn and Cu), and the Yb^{III} and Lu^{III} ions are linked to aminopolycarboxylic acids, *viz.*, ethylenediaminetetraacetic (EDTA) and diethylenetriaminepentaacetic (DTPA) acids (Scheme 6). The use of aminopolycarboxylic acids makes it possible not only to increase the stability of lanthanide complexes but also to improve substantially the shielding of the lanthanide ion from solvent molecules causing luminescence quenching.

The first step (see Scheme 6) involves the condensation of 5-(4-aminophenyl)-10,15,20-triphenylporphyrin (**32**) with dianhydrides **33** and **34** giving compounds **35** and **36**, respectively, in high yields (up to 95%). The treatment of the latter with Yb^{III} and Lu^{III} chlorides in dimethylformamide at 50 °C for 10 min followed by cooling with water and recrystallization also afforded chelates **37a**,**b** and **38a**,**b** in high yields. It should be noted that lanthanides are not included in the porphyrin macrocycle. In the final step, Yb chelates of Zn and Cu porphyrin complexes **39a**,**b** and **40a**,**b** were synthesized.

A study of luminescence of complexes **37a** and **38a** showed that the addition of Yb^{III}-EDTA and Yb^{III}-DTPA to porphyrin **32** leads to a substantial increase in the quantum yield of 4f luminescence ($\Phi = 1.1 \times 10^{-3}$ and 1.5×10^{-3}, respectively; the calculations with respect to Zn-TPP as the reference, for which $\Phi = 0.03$).[62] This attests to the energy transfer from porphyrin to the Yb^{III} ion. On the contrary, the introduction of Zn^{II} into the porphyrin macrocycle leads to a decrease in the quantum yield to 0.39×10^{-3} and 0.55×10^{-3} for compounds **39a** and **40a**, respectively. For Cu complexes **39b** and **40b**, the luminescence signal of the Yb^{3+} ion was not detected at all.

It is interesting that the same tendency is observed also for bisporphyrin complexes, in which the Yb^{III} ion is located in one of the macrocycles (see structures **26** and **31**).[61] The emission at 651–652 nm associated with the $\pi \rightarrow \pi^*$ interaction of the porphyrin macrocycles is weaker for Zn complex **26a** (3.9×10^{-2}) than for unsubstituted porphyrin antenna **31** (9.1×10^{-2}; H_2TPP with $\Phi = 0.11$ at 298 K was used as the standard).

Noncovalently bound heteronuclear lanthanide-containing supramolecular ensembles based on compounds **41a**–**c** containing porphyrin and calix[4]arene macrocycles were synthesized and their spectral luminescent properties were studied by Snurikova *et al.*[48]

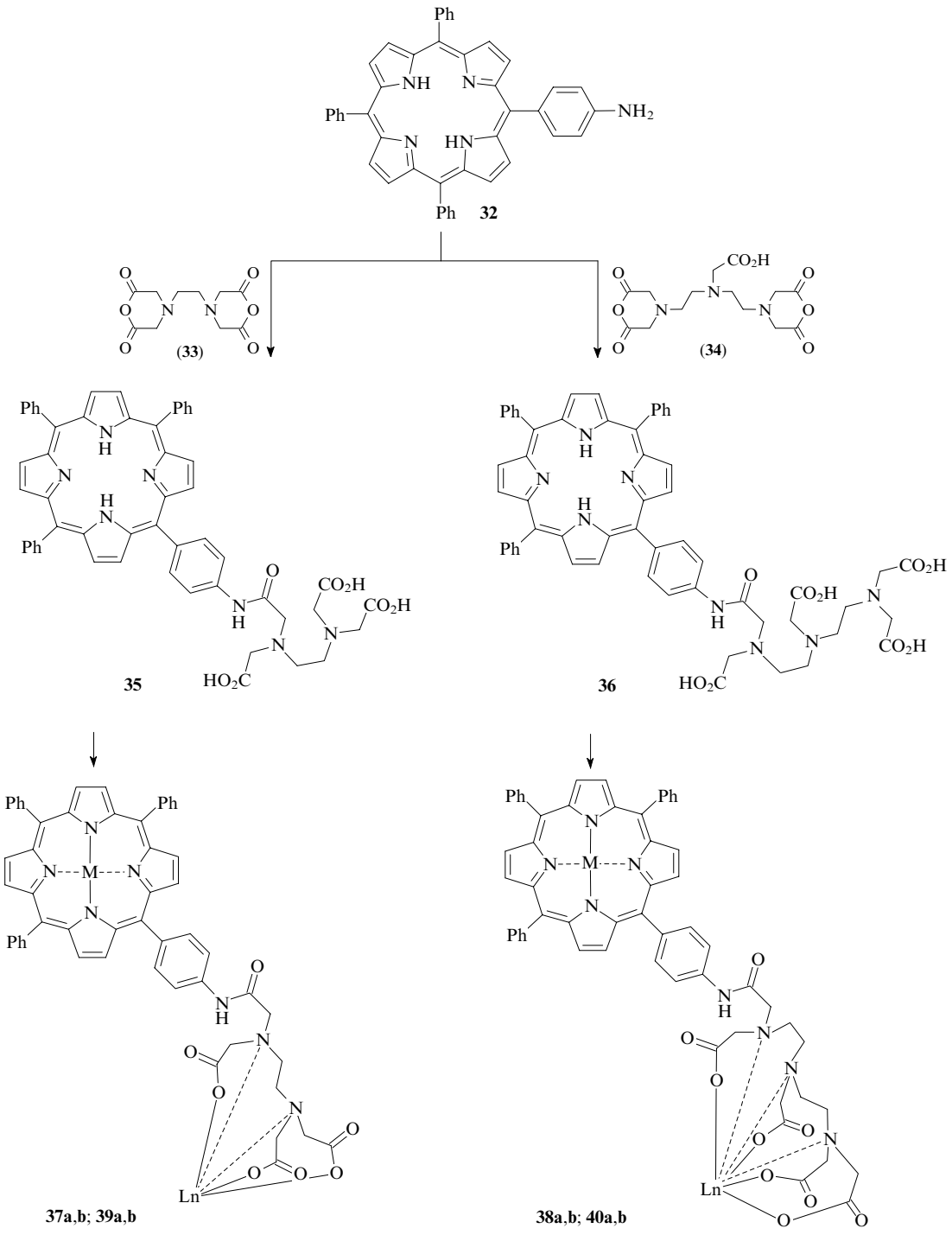


41a–**c**

M = 2 H (**a**), Cu (**b**), Zn (**c**)

It was shown that the presence of a Zn ion in the porphyrin moieties of complex **41c** has no effect on the 4f-luminescence intensity of the corresponding Yb derivatives. On the contrary, 4f-luminescence quenching is observed for copper compounds **41b**. The authors believed that this is associated with the excitation-level energy of d metals: 5015 cm^{-1} and 17520–19510 cm^{-1} for Cu and Zn derivatives, respectively. In other words, the 4f-luminescence intensity of these complexes varies only slightly if the excitation level of the d metal is higher than the emission level of lanthanide. On the contrary, the low-lying energy level of excitation of copper is responsible for 4f-luminescence quenching.

Scheme 6



Assemblies based on complexes **41** may be of interest as receptors for other cations, anions and neutral molecules.

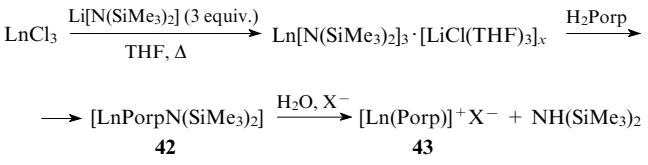
V. Lanthanide cationic porphyrin complexes

Cationic derivatives belong to a special group of lanthanide porphyrin complexes.[63] Their properties substantially differ from those of the above-considered Ln^{III} porphyrins containing acetylacetone, β-diketones, diethyl malonate and other auxiliary ligands. The transformation of these neutral complexes into cationic complexes is practically impossible because of the problems with the displacement of axial ligands.

A radically different method was developed for the synthesis of Ln^{III} cationic porphyrins (Scheme 7).[63] It is based on the use of lanthanide amide derivatives prepared *in situ* from anhydrous $LnCl_3$ and 3 equivalents of $Li[N(SiMe_3)_2]$ in refluxing tetrahydrofuran. The resulting complex $Ln[N(SiMe_3)_2]_3 \cdot [LiCl(THF)_3]_x$ was added *in situ*

to free porphyrin (H_2Porp). The subsequent hydrolysis of porphyrinate **42** afforded cationic complex **43**.

Scheme 7

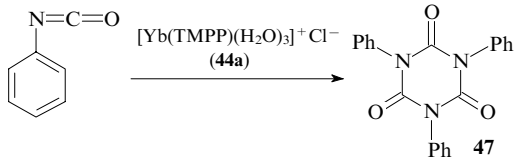


The above-described method was used to synthesize complexes with *meso*-tetrakis(*p*-methoxyphenyl)- (TMPP) and *meso*-tetrakis(*p*-tolyl)porphyrins: $[Yb^{III}(TMPP).(H_2O)_3]^+Cl^-$ (**44a**), $[Er^{III}(TMPP)(H_2O)_3]^+Cl^-$ (**45**) and $[Yb^{III}(TTP)(H_2O)_2(THF)]^+Cl^-$ (**46**). According to the X-ray diffraction data, the lanthanide ion in these compounds forms seven coordination bonds: four bonds with the nitrogen atoms of the porphyrin ring and three bonds with the oxygen atoms of the solvent.

The reaction of compound **44a** with $AgBF_4$ in THF is accompanied by the disproportionation of Ag^+ ions to Ag^0 and Ag^{2+} {in the complex $[Ag^{II}(TMPP)]$}.[63]

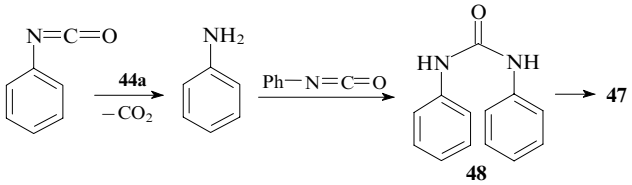
Complex **44a** catalyzes the conversion of phenyl isocyanate at 30 °C for 24 h giving rise to the cyclic trimer, 1,3,5-triphenyl-*symm*-triazine-2,4,6-trione (**47**), in quantitative yield at a monomer : catalyst ratio of 600 : 1 (Scheme 8).[63]

Scheme 8



The proposed reaction mechanism involves the formation of aniline, its reaction with phenyl isocyanate and the cyclization of diphenylurea (**48**) (Scheme 9).

Scheme 9



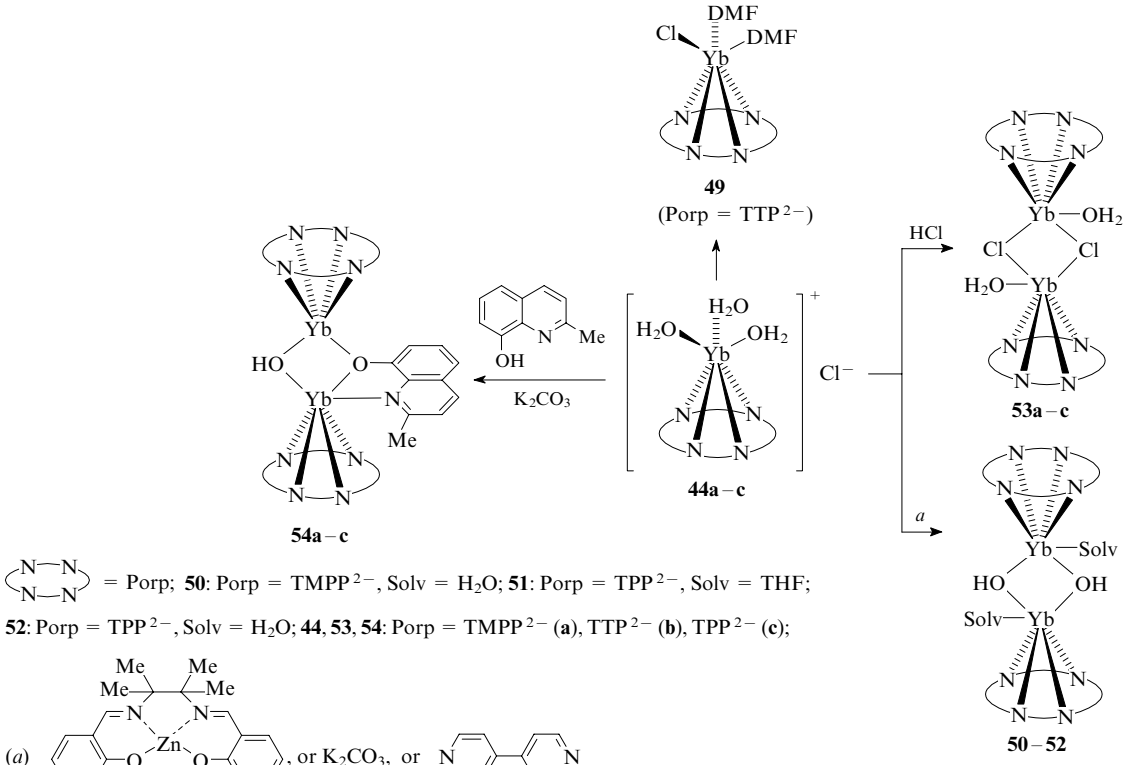
It should be noted that the erbium analogue of Yb^{III} complex **44a** does not catalyze this reaction.

The lanthanide cationic complexes $[Yb^{III}(Porp).(H_2O)_3]^+Cl^-$ are highly prone to the formation of neutral dimeric structures, in which two ytterbium ions can be linked by the bridging HO^- or Cl^- anions depending on the synthesis procedure.[64] Neutral monomeric (**49**) and dimeric complexes (**50**–**54**) were synthesized from Yb^{III} cationic complexes **44a**–**c** containing three porphyrins, *viz*., TMPP, TTP and TPP (Scheme 10).

As opposed to neutral mononuclear complexes with the general formula [Ln(Porp)(β-Dik)] (β-Dik is diketonate), in which the six-coordinate lanthanide ion forms four bonds with the nitrogen atoms of porphyrin and two bonds with the oxygen atoms of β-diketone, and neutral sandwich-type complexes with the general formula $Ln_m(Porp)_n$, in which the lanthanide ion is coordinated to eight nitrogen atoms of two macrocycles, the ytterbium and other lanthanides in the cationic monoporphyrin complexes $[Ln(Porp)(H_2O)_3]^+Cl^-$ form seven-coordinate structures with four nitrogen atoms of the macrocycle and three oxygen atoms of water.

The water molecules in the cationic complexes $[Yb(Porp)(H_2O)_3]^+Cl^-$ are very labile and are easily

Scheme 10



= Porp; **50**: Porp = $TMPP^{2-}$, Solv = H_2O; **51**: Porp = TPP^{2-}, Solv = THF;

52: Porp = TPP^{2-}, Solv = H_2O; **44**, **53**, **54**: Porp = $TMPP^{2-}$ (**a**), TTP^{2-} (**b**), TPP^{2-} (**c**);

replaced by other electron-donating molecules. Thus, complex **44b** is easily transformed into neutral compound **49** in virtually quantitative yield upon dissolution in DMF (see Scheme 10). In this complex, the seven-coordinate ytterbium ion is bound to four nitrogen atoms, one chloride ion and two oxygen atoms of DMF. The Yb^{3+} ion lies above the plane of the macrocycle at a distance of 1.131 Å.

The reaction of $[Yb(Porp)(H_2O)_3]^+Cl^-$ with the Zn complex of the Schiff base, 4,4′-bipyridine or K_2CO_3 in the $H_2O-CH_2Cl_2$ two-phase system produces neutral dimeric complexes **50**–**52** in high yields. In these complexes, the Yb^{3+} ions are linked by two hydroxy bridges.

The treatment of complexes **44a**–**c** with hydrochloric acid in the $H_2O-CH_2Cl_2$ system affords dimers **53a**–**c** with two bridging chloride ions between Yb^{3+} ions.

The most unusual dimer **54** was produced by the reaction of compounds **44a**–**c** with 8-hydroxyquinaldine (see Scheme 10). This compound contains ytterbium ions with different coordination numbers (6 and 7).

Since Yb^{III} porphyrins, along with Er^{III} and Nd^{III} complexes, exhibit near-infrared luminescence, they are considered as promising diagnostic agents for medicine.[65–70] Complexes **49** and **52**–**54** show luminescence at 980 nm and have the lifetime of 1.02–3.17 ms, These values are considerably larger than the corresponding parameters for porphyrins. The intensity of infrared emission of the dimers is substantially higher than that of the monomers. However, it noticeably decreases with increasing number of OH groups.[71] The relative luminescence intensity decreases in the series of dimers **54** > **53** > **52**. Unfortunately, data on biological studies of these complexes are lacking.

VI. Ytterbium porphyrins as photosensitizers for fluorescence diagnosis of cancer

It is known that cancer is the No. 2 cause of death after cardiovascular diseases. In Russia, 470 000 new cases of cancer are diagnosed per year and about 300 000 death cases by cancer are reported.[72] The World Health Organization estimates that the cancer cases will increase by 50% in 2020. This is to a substantial extent due to the lack of reliable methods for early diagnosis of malignant tumours.

Photodynamic therapy (PDT) of cancer is a new actively developed efficient method for the treatment of malignant tumours.[73] The following photosensitizers were proposed: Photofrin, Photogem, Photosense, Photoditazine, Radachlorin, and so on. These agents are selectively accumulated in the tumour and, when exposed to light at a particular wavelength (generally, laser radiation is used), efficiently generate singlet oxygen and other active forms that destroy malignant tumours.[74, 75]

Attempts to use these photosensitizers for the primary cancer diagnosis are usually inefficient due to their relatively low luminescence. The use of higher concentrations of photosensitizers and an increase in the radiation dose are also undesirable because they lead to an increase in the generation of singlet oxygen and the occurrence of a number of dangerous reactions in the body. The replacement of porphyrins having high tumour tropism by their ytterbium complexes results in a substantial suppression of undesirable photoactivity.[76] This is due to the fact that the luminescent level of the Yb^{III} ion is lower than the triplet level of porphyrin but is higher than the singlet oxygen

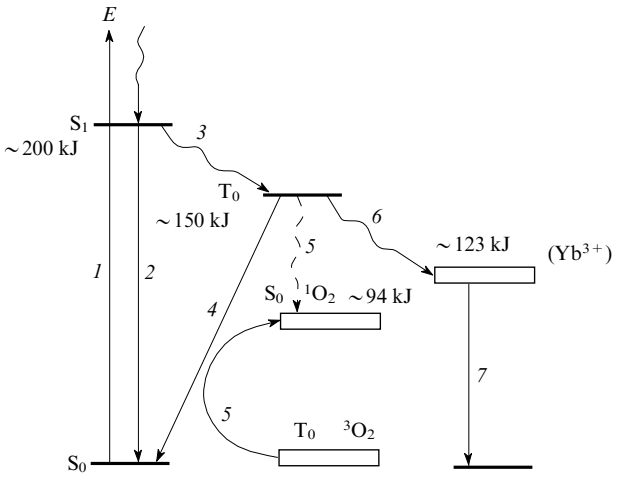


Figure 5. Pattern of electronic transitions in porphyrin sensitizers and the formation of the singlet oxygen atom: (*1*) absorption, (*2*) fluorescence, (*3*) intersystem crossing, (*4*) phosphorescence, (*5*) excitation transfer to the oxygen and the transition of $^3O_2$ into $^1O_2$, (*6*) excitation transfer to the Yb^{3+} ion (*7*) luminescence of the Yb^{3+} ion.[76]

level. As a result, the photoexcitation of the porphyrin macrocycle is transferred not to the oxygen atom but to the ytterbium ion and causes intense infrared luminescence (Fig. 5).

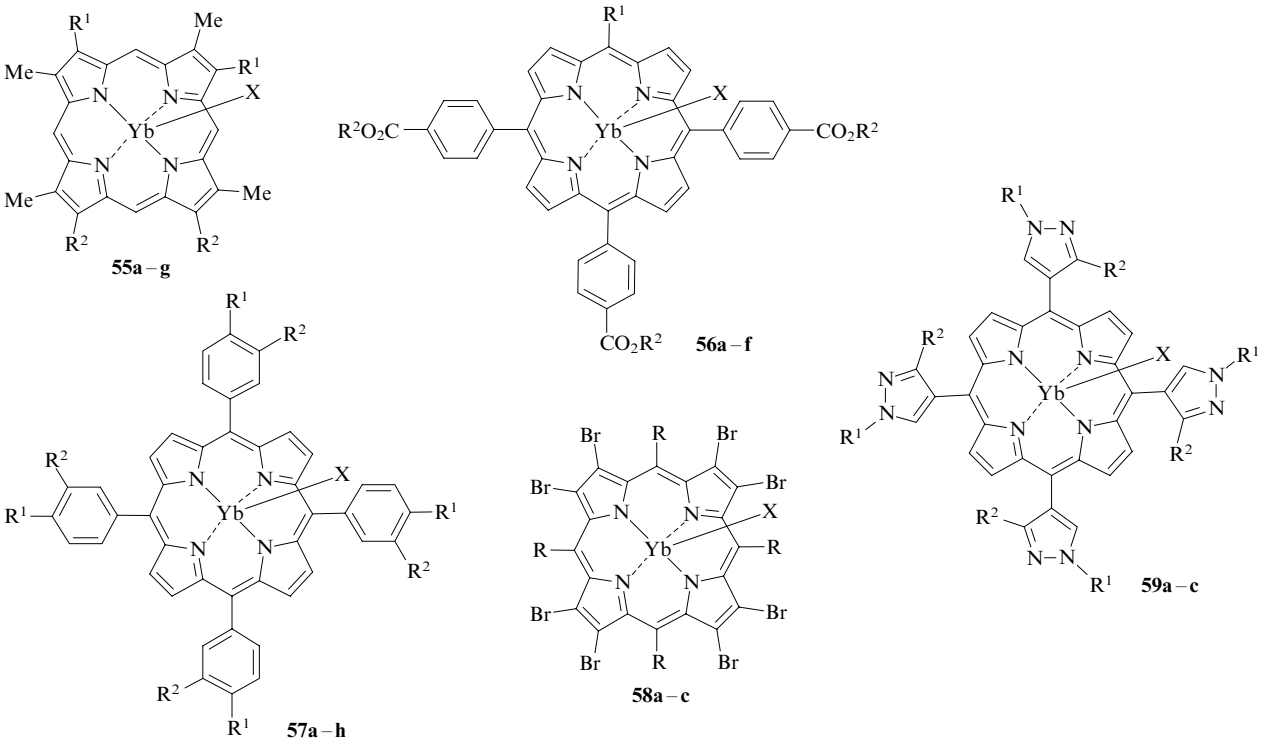
Among lanthanides only Yb^{III}, Nd^{III} and Er^{III} can form porphyrin complexes having such properties, because the luminescent levels of other elements are higher than the triplet level of the porphyrin macrocycle and the emission is unlikely to originate. Due to the smaller ionic radius of Yb^{3+} and high stability, Yb porphyrins are the most promising photosensitizers for fluorescence diagnosis of malignant tumours. The possibility of the practical use of luminescence properties of Yb^{III} porphyrins for this purpose was shown for the first time in the studies[77–89] performed with the participation of the author of the present review.

Approximately 30 ytterbium complexes **55**–**59** were synthesized based on natural porphyrins (hematoporphyrin IX, coproporphyrin III) and synthetic *meso*-tetraarylporphyrins, their absorption and luminescence spectra were measured, and the kinetics of the luminescence decay was studied.

Ytterbium complexes of octabromo- and pentafluorophenyl-substituted porphyrins **58a**–**c** were synthesized to reduce the role of high-frequency intramolecular C–H vibrations in radiationless transitions. For the most promising compounds, toxicological and pharmacokinetic investigations were carried out in laboratory animals.

A comparison of the absorption and luminescence excitation spectra of the starting porphyrins and Yb complexes showed their good coincidence, which attests to the efficient absorbed energy transfer from the porphyrin macrocycle to the ytterbium ion. High absorption coefficients were observed for all synthesized complexes. Thus, this coefficient for the Yb^{III} derivative of 2,4-dimethoxyhematoporphyrin IX (**55e**) at 976 nm is 1.3×10^5 litre mol^{-1} cm^{-1}.

All complexes **55**–**59** have an intense luminescence band in the range of 975–985 nm. The average lifetime of the



55: X = acac; $R^2 = (CH_2)_2CO_2Me$: R^1 = H (**a**), CH=CH_2 (**b**), CH(OMe)Me (**c**), $(CH_2)_2CO_2Me$ (**d**); $R^2 = (CH_2)_2CO_2H$: R^1 = CH(OMe)Me (**e**), $(CH_2)_2CO_2H$ (**f**); R^1 = CH(OMe)Me, $R^2 = (CH_2)_2CO_2K$ (**g**); **56**: X = Im_2, R^2 = H: R^1 = 4-HOC_6H_4 (**a**), 3-Py (**b**), 4-Py (**c**); X = acac, R^2 = Me: R^1 = 4-HOC_6H_4 (**d**), 3-Py (**e**), 4-Py (**f**); Im is imidazolyl, Py is pyridyl; **57**: X = Im_2; R^2 = H: R^1 = H (**a**), Me (**b**), Et (**c**), SO_3H (**d**), CO_2H (**e**), CO_2Me (**f**); R^1 = OMe, $R^2 = SO_3H$ (**g**); $R^1 = SO_3H$, R^2 = OMe (**h**); **58**: X = acac; R = Ph (**a**), 2,4,6-$Me_3C_6H_2$ (**b**), C_6F_5 (**c**); **59**: X = acac; R^1 = Ph, R^2 = 3-$MeOC_6H_4$ (**a**); R^1 = 4-MeC_6H_4, R^2 = 4-FC_6H_4 (**b**); R^1 = 4-FC_6H_4, R^2 = 4-ClC_6H_4 (**c**)

excited state is 5–10 μs. Table 2 summarizes the spectral luminescent parameters and lifetimes of selected Yb^{III} porphyrins. As can be seen from this table, the lifetimes of methyl esters **56d–f**, **57f** (13.4–20 and 3–8 μs, respectively) are much longer than those of the corresponding acids **56a–c** and **57e**. Large values of τ are also observed for pyrazole derivatives **59a–c**. For example, this parameter for compound **59c** is ~20 μs. Hence, these complexes can be considered as promising luminescent markers of tumours.[88]

Pharmacokinetic studies showed that, of the synthesized complexes, dipotassium salt of Yb^{III} 3,7-dimethoxyhematoporphyrin (**55g**) is the most promising marker for PDT of tumours. The contrast factor calculated from the ratio of luminescence indices of the tumour and surrounding tissues was 51 after 48 h the administration of the agent. This

Table 2. Spectroscopic properties of Yb-porphyrins.[82]

Compound	λ_{max}/nm ($\varepsilon \times 10^{-3}$/litre mol^{-1} cm^{-1})		τ/μs
	electronic absorption spectrum	luminescence spectrum [a]	
55c	398 (196), 532 (9.15), 568 (10.6)	975	10
56a	417.4 (128), 549.6 (6.1), 585.6 (2.5)	982	3
56b	416.8, 551.4, 588.8	983	5
56c	417 (322), 548.4 (11.7), 585 (2.6)	976	6.5
56d	424.6 (271), 516 (5.5), 554.4 (15.2), 593.2 (4.6)	982	16.3
56e	416.8, 551.4, 588	983	14.8
56f	418, 555.4, 590.8	983	13.4
57e	417 (405), 510 (2.5), 548.7 (15.6)	980	8
57f	421.4, 515.4, 553, 591.6	974	20
59c	429.6 (234.2), 557.6 (14.5), 596.0 (4.1)	973	20

[a] In DMSO.

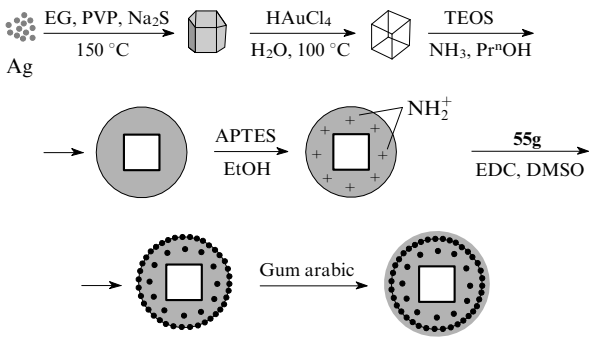


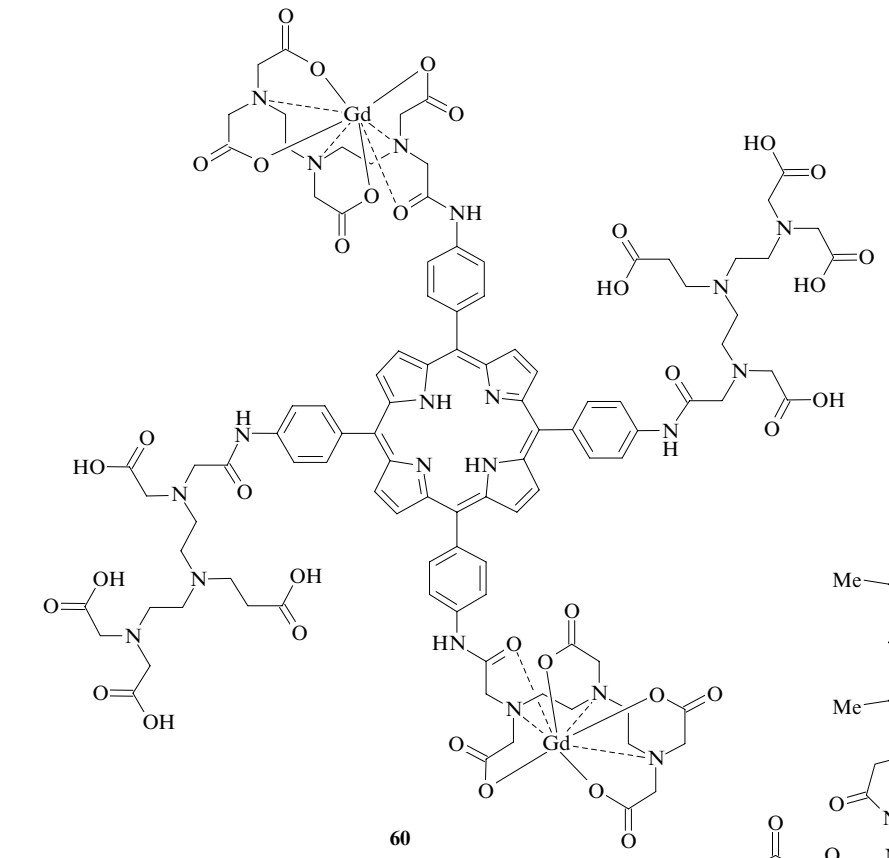
Figure 6. Synthesis of silicon dioxide-coated gold–silver nanoparticles immobilized onto Yb^{III} complex **55g**.[91]
Notations: EG is ethylene glycol, PVP is polyvinylpyrrolidone, TEOS is tetraethyl orthosilicate, APTES is (3-aminopropyl)triethoxysilane, EDC is 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide.

photosensitizer has a very low photo- and cytotoxicity, is readily soluble in water and is stable during storage.[89]

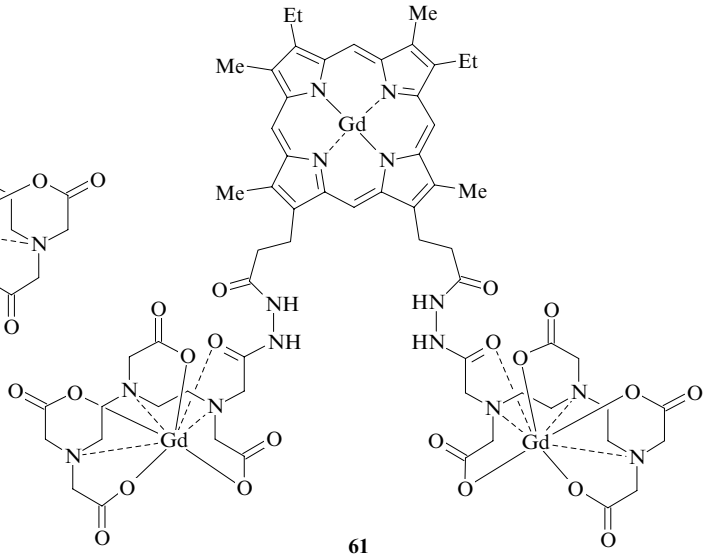
The possibility of the deposition of complex **55g** onto silicon dioxide-coated composite gold–silver nanoparticles was studied.[90–92] Figure 6 depicts the principal scheme of the synthesis of these nanoparticles. The average size of the particles was 40–60 nm, and each particle contained about 1500 porphyrin molecules. Biological studies in mice bearing Ehrlich carcinoma showed a 50% increase in the activity of Yb^{III} complex **55g** upon its deposition on the substrate.

VII. Application of gadolinium derivatives of porphyrins in photodynamic therapy and magnetic resonance imaging

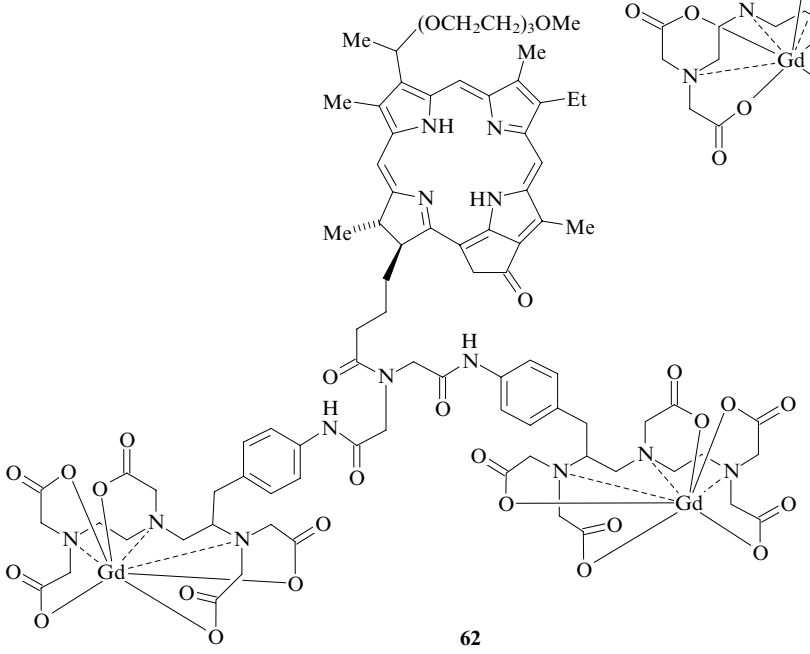
The use of gadolinium-containing compounds for the dual-target drug design was described in a number of works.[93–102] These compounds are employed as photosensitizers for PDT of cancer and contrast agents in magnetic resonance imaging. The gadolinium ion can either be located in the porphyrin macrocycle or be bound by special



60

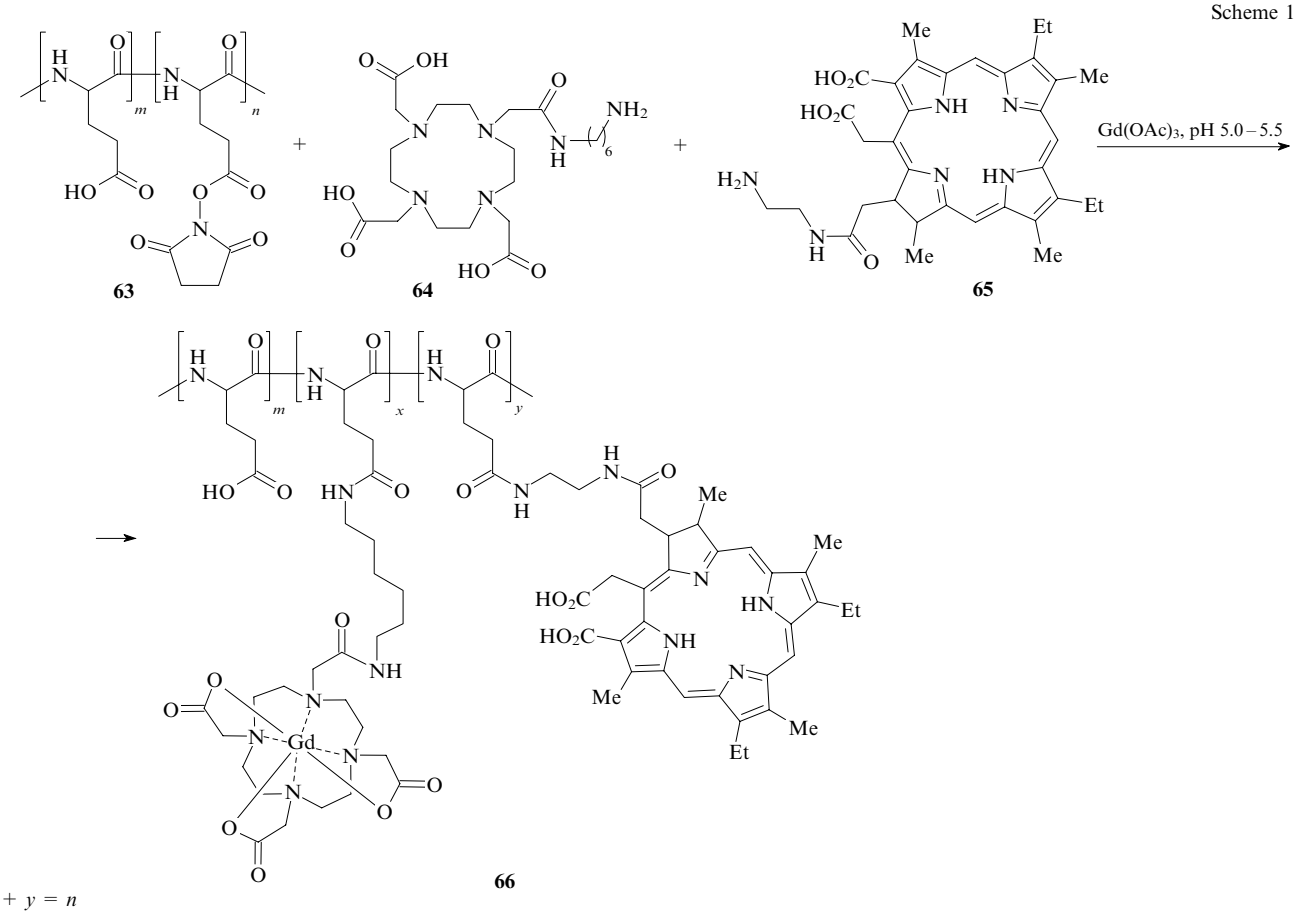


61



62

Scheme 11



ligands attached to porphyrins (for example, by DTPA). Structures **60** and **61** are such examples.[93,94]

However, biological studies showed that these complexes are weakly adsorbed in the tumour but have high tropism for necrotic tissues.[94–96] Based on the latter fact, these complexes were proposed as agents for myocardial perfusion imaging showing the quantity of damaged tissues.[97–99]

Pandey *et al.*[100] synthesized a gadolinium complex based on a pyropheophorbide *a* derivative displaying high tropism for tumours. Conjugate **62** is well accumulated in tumours and enhances magnetic resonance imaging of the tumour by 57%.[101] The enhanced contrast and brightness of the image were retained for more than 24 h, which substantially exceed the performance characteristics of the commercial agent Gd-DTPA (Magnavist®). The presence of the Gd^{3+} ion does not reduce the photodynamic activity of chlorin. After 90 days, 80% of PDT-treated C3H mice bearing Rif tumours survived.

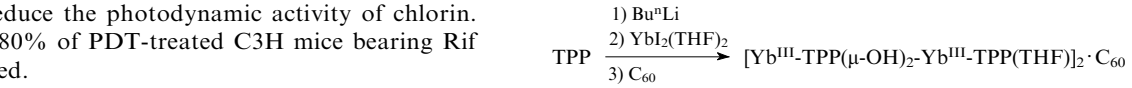
Scheme 11 depicts the route to the synthesis of a conjugate for the combined PDT-MRT method based on poly-L-glutamate (**63**), the amide derivative of mesochlorin e_6 (**65**) and cyclene **64**, in which a gadolinium ion was incorporated.[102] To obtain the optimal results after the combined treatment with compound **66**, the ratio of cyclene derivative **64** to photosensitizer **65** attached to the polymer should be 8 : 1.

Experiments in athymic mice bearing human breast cancer showed that conjugate **66** is well accumulated in the tumour and reaches the maximum concentration 18 h after the administration. After irradiation, a substantial tumour growth retardation was observed compared with the control group.

VIII. Supramolecular structures involving ytterbium porphyrin complexes and fullerenes

An interesting feature of the behaviour of ytterbium porphyrin complexes is their ability to form three-dimensional assemblies with fullerene C_{60}.[103] These structures were synthesized by the treatment of TPP with n-butyllithium followed by the condensation with $YbI_2(THF)_2$ in THF (Scheme 12). Then fullerene C_{60} (0.5 equiv.) was added *in situ* to the resulting dimeric ytterbium complex to form sandwich-type structure **67**.

Scheme 12



67

The presence of trivalent ytterbium in the final product is associated with the oxidation of Yb^{II} with atmospheric oxygen. According to the X-ray diffraction data (Fig. 7), the assembly consists of C_{60} molecules and two Yb^{III} porphyrins, in which Yb^{III} ions are linked by two hydroxy groups. Complex **67** crystallizes so that two Yb^{III}-TPP subunits surround each fullerene molecule. The latter is unsymmetically located between two [Yb^{III}-TPP(μ-OH)$_2$-Yb^{III}-TPP(THF)] moieties and is held by noncovalent interactions between the porphyrin macrocycle and the

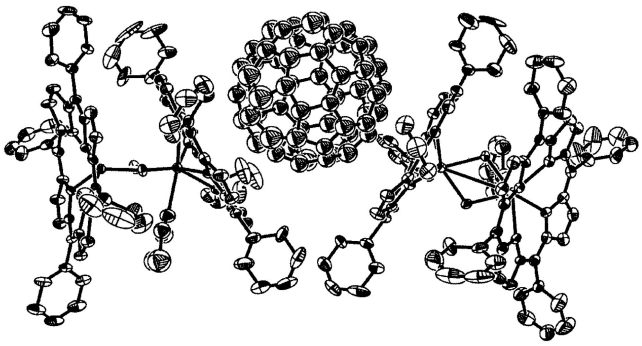


Figure 7. Proposed structure of complex **67**.[103]

sphere-like surface of the fullerene. One porphyrin macrocycle interacts with the C—C bonds of the five- and six-membered rings of C_{60}, and another macrocycle interacts with the C—C bonds between the five- and six-membered rings (5 : 6) and between two six-membered rings (6 : 6) of another C_{60} molecule. This pattern substantially differs from the above-described interactions of porphyrins and their metal complexes containing electron-rich six-membered rings.[104–107] As can be seen from Fig. 7, the ytterbium ions deviate from the plane of the porphyrin and are on the opposite side with respect to C_{60}, due to which they cannot form direct interactions with each other.

As opposed to noncovalent interactions between fullerene and two TPP molecules, the Yb^{III} ions in structure **68** are covalently linked through two hydroxy bridges (Fig. 8). This combination of covalent and noncovalent interactions results in the formation of helically twisted ribbons $\{[Yb^{III}\text{-}TPP(\mu\text{-}OH)_2\text{-}Yb^{III}\text{-}TPP(THF)]\cdot C_{60}\}_n$ (**69**) running through the crystal (Fig. 9).

In supramolecular structure **69**, there are noncovalent interactions between the phenyl substituents of porphyrin and fullerene. In contrast to a large number of available structurally characterized crystalline fullerene complexes with transition metal porphyrins, a few successful examples of the synthesis of aryl-substituted metalloporphyrin-fullerene assemblies are known. In structure **69**, one of the phenyl substituents of dimer **68** forms a contact with the third C_{60} molecule; the shortest C···C distance is 3.35 Å. This type of noncovalent interactions between the phenyl ring and the C_{60} molecule is very rare. For tetraarylporphyrin H_2Porp, only one example of such contacts was reported.[108] In structure **69**, this interaction can occur in the

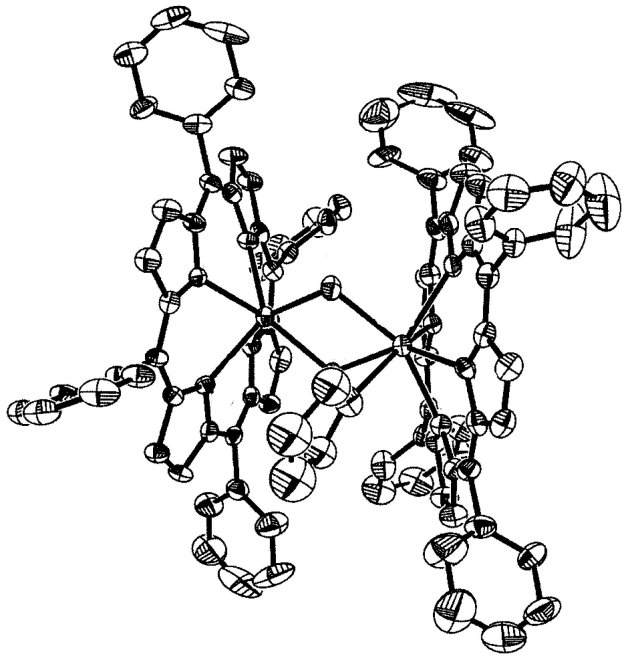


Figure 8. Proposed structure of the dimer $[Yb^{III}\text{-}TPP(\mu\text{-}OH)_2.Yb^{III}\text{-}TPP(THF)]$ (**68**).[103]

case of the non-parallel arrangement of porphyrin macrocycles, which allows the phenyl substituents to come close to fullerene C_{60} molecules.

* * *

The above-considered lanthanide porphyrin complexes show that 4f transition metals are of considerable interest. The development of new methods for the synthesis of these compounds, investigations of their structures, spectroscopic and other physicochemical properties provide a great scope for their use in medicine, as catalysts for chemical transformations, in light-conversion systems and other practical applications in science and engineering. It should be emphasized that transition metal complexes with porphyrins can be used for the synthesis of various supramolecular structures, which will find application in nanotechnology for the design of materials with unique properties.

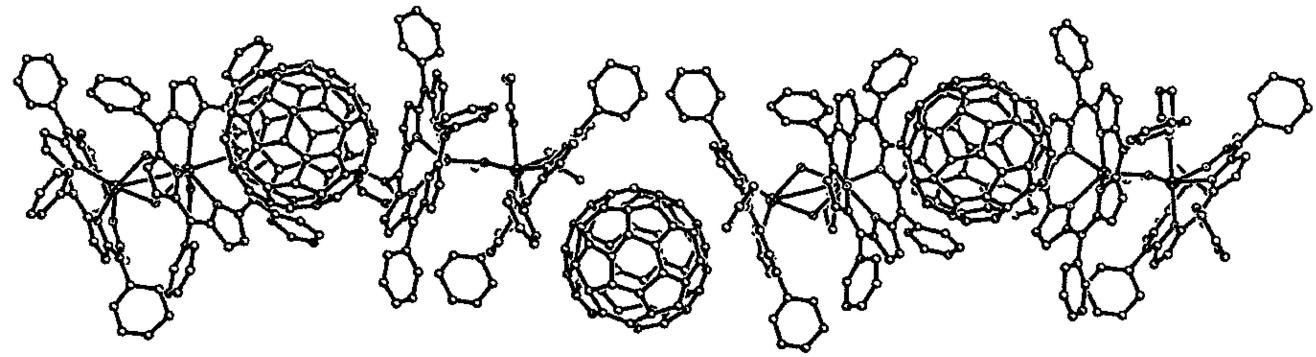


Figure 9. Supramolecular helix of **69**.[103]

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