1562 *Russian Chemical Bulletin, International Edition, Vol. 52, No. 7, pp. 1562—1566, July, 2003*

New phthalocyanine complexes based on 4,5-isopropylidenedioxyphthalonitrile

A. V. Ivanov,[a]★ *P. A. Svinareva,*[b] *I. V. Zhukov,*[a] *L. G. Tomilova,*[b] *and N. S. Zefirov*[b]

[a]*Institute of Physiologically Active Compounds, Russian Academy of Sciences,*
142432 Chernogolovka, Moscow region, Russian Federation.
Fax: (096) 785 7064. E-mail: kalashn2000@mail.ru
[b]*Department of Chemistry, Moscow State University,*
Leninskie Gory, 119992 Moscow, Russian Federation.
Fax: +7 (095) 939 0290. E-mail: phthal@org.chem.msu.su

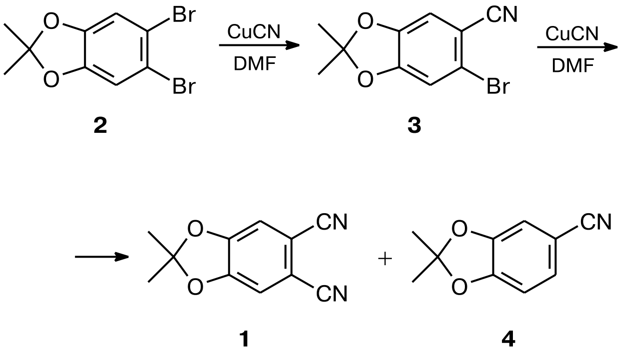
A series of new metal monophthalocyanine complexes were synthesized from 4,5-isopropylidenedioxyphthalonitrile and their spectroscopic and electrochemical properties were studied. The removal of the protective isopropylidene groups from these compounds afforded symmetrically substituted octahydroxyphthalocyanines.

Key words: 4,5-isopropylidenedioxyphthalonitrile, metal phthalocyanines, electrochemistry, electronic absorption spectra.

Tetrahydroxyphthalocyanines are of interest as potential pharmaceuticals for photodynamic therapy.[1] The presence of hydroxy groups in these compounds allows one to carry out chemical modifications of phthalocyanines.[2,3] However, tetrahydroxyphthalocyanines occur as unseparable mixtures of isomers. The problem of the synthesis of structurally homogeneous complexes can be solved by preparing symmetrically substituted phthalocyanines (Pc) containing eight hydroxy groups. 4,5-Dihydroxyphthalonitrile or its derivatives bearing readily removable protective groups can serve as precursors of these complexes.

With the aim of preparing symmetrically substituted polyhydroxyphthalocyanines, we synthesized 4,5-isopropylidenedioxyphthalonitrile (5,6-dicyano-2,2-dimethyl-1,3-benzodioxolane) (**1**) (Scheme 1).[4] It was found[4] that heating of 5,6-dibromo-2,2-dimethyl-1,3-benzodioxolane (**2**) with an excess of CuCN afforded 2-bromo-4,5-isopropylidenedioxybenzonitrile (**3**), which was then transformed into the target phthalonitrile **1**. However, compound **1** was prepared in a yield of no higher than 40—50%, because prolonged heating led to partial debromination of compound **3** giving rise to 3,4-isopropylidenedioxybenzonitrile (**4**).

Scheme 1



By analogy with the published data,[5,6] the reaction of dinitrile **1** with $Zn(OAc)_2$ (**5a**) in isopentyl alcohol in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded zinc 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine (**6a**) (Scheme 2). The use of lanthanide acetates **5b—g** in this reaction instead of zinc acetate yielded the corresponding 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanines **6b—g**. In an attempt to synthesize the praseodymium complex, metal-free phthalocyanine $(Me_2CO_2)_4PcH_2$ (**6h**) was isolated.

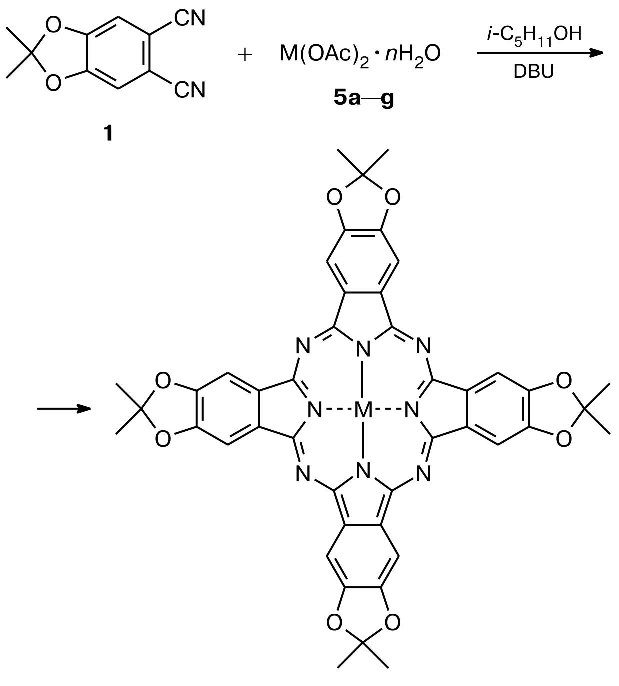
Metal-free phthalocyanine was also prepared by refluxing a mixture of phthalonitrile **1** and lithium methoxide in isopentyl alcohol followed by treatment with acetic acid.

Complexes of lanthanides were prepared for the purpose of studying the effect of the radius of the rare-earth element on the absorption maxima in electronic spectra. In the case of monophthalocyanine complexes, this effect is weak, but it is substantially enhanced on going to diphthalocyanines.

By analogy with the published data,[4,7] zinc 2,3,9,10,16,17,23,24-octahydroxyphthalocyanine (**7a**) was synthesized by dissolving complex **6a** in H_2SO_4 followed by treatment with water. The reaction of lutetium

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 7, pp. 1479—1483, July, 2003.

Scheme 2

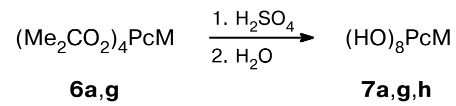


6a—h

M = Zn (**a**), SmOAc (**b**), EuOAc (**c**), TbOAc (**d**), DyOAc (**e**), YbOAc (**f**), LuOAc (**g**), 2 H (**h**)

monophthalocyanine (**6g**) with sulfuric acid for 2—3 min resulted in the removal of the isopropylidene groups (to give **7g**), whereas more prolonged treatment resulted in demetallation of the complex giving rise to metal-free 2,3,9,10,16,17,23,24-octahydroxyphthalocyanine (**7h**) (Scheme 3).

Scheme 3



$$\underset{\textbf{6a,g}}{(Me_2CO_2)_4PcM} \xrightarrow[2.\ H_2O]{1.\ H_2SO_4} \underset{\textbf{7a,g,h}}{(HO)_8PcM}$$

M = Zn (**a**), LuOAc (**g**), 2 H (**h**)

The MALDI-TOF mass spectra of the complexes were studied. The mass spectrum of compound **6a** has an intense molecular ion peak at m/z 865 with the isotope splitting characteristic of this type of complexes (Fig. 1). The mass spectra of complexes **6b—f** have peaks at m/z 950—1000 belonging to the macrocyclic ligands, which contain the corresponding metal ions and are devoid of acetate ions. The mass spectrum of compound **6g** has a molecular ion peak (m/z 1035).

The electronic absorption spectra of monophthalocyanines are characterized by an intense Q peak in the 660—675-nm region, which is typical of the Pc^{2-} ion and corresponds to the electron transition between the π and π^* orbitals. The Soret band has a maximum at 360 nm (Table 1).

In going from phthalocyanines **6** to octahydroxy derivatives **7**, the Q band is bathochromically shifted by 13—15 and 20 nm for the metal-containing phthalocyanines and metal-free phthalocyanine, respectively.

Compound	λ_{max}/nm	Compound	λ_{max}/nm
6a	670	**7a**	685
6g	668	**7g**	681
6h	658, 692	**7h**	678, 712

The typical spectra of the complexes under study are shown in Figs. 2 and 3.

Earlier, the electrochemical properties of rare-earth monophthalocyanines have been studied only for unsub-

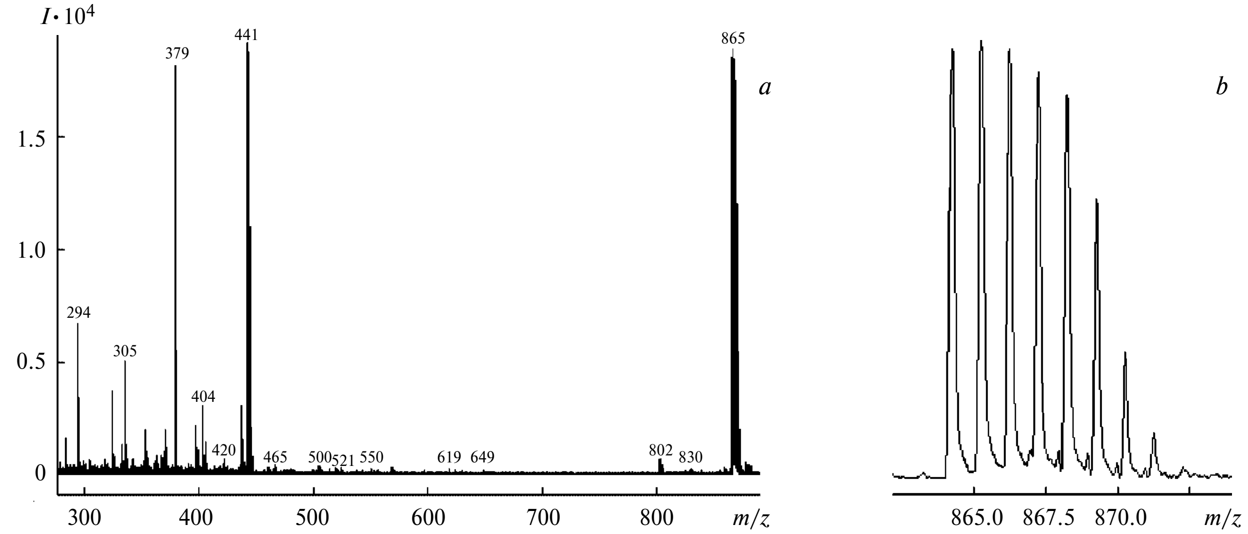


Fig. 1. Mass spectrum of complex **6a**: a, overall view, b, molecular ion peak.

Table 1. Positions of absorption bands in the electronic absorption spectra of solutions of phthalocyanines **6a—h** ($CHCl_3$)

Compound	λ_{max}/nm
$(Me_2CO_2)_4PcZn$ (**6a**)	363, 600, 638, 665
$(Me_2CO_2)_4PcSmOAc$ (**6b**)	357, 420, 610, 676
$(Me_2CO_2)_4PcEuOAc$ (**6c**)	359, 410, 602, 671
$(Me_2CO_2)_4PcTbOAc$ (**6d**)	353, 417, 606, 677
$(Me_2CO_2)_4PcDyOAc$ (**6e**)	358, 418, 604, 675
$(Me_2CO_2)_4PcYbOAc$ (**6f**)	360, 410, 607, 677
$(Me_2CO_2)_4PcLuOAc$ (**6g**)	355, 410, 605, 676
$(Me_2CO_2)_4PcH_2$ (**6h**)	348, 421, 593, 653, 693

stituted complexes in oxidation,[8] where two single-electron processes were observed. The redox potentials of lutetium 1,2-naphthalocyanine (the cathodic and anodic regions) were also reported.[9]

The electrochemical properties of zinc, terbium, and lutetium complexes (**6a**, **6d**, and **6g**, respectively) were studied by cyclic voltammetry on a graphite electrode (pyrolyzed polyacrylonitrile). The cyclic voltammogram of compound **6g** is shown in Fig. 4. For each of the three complexes under study, we observed two single-electron redox transitions both in the oxidation and reduction, whose potentials are given in Table 2. At a potential sweep rate of 100 mV s^{-1}, all redox transformations are quasi-reversible (the potential difference between the direct and reverse peaks was 60—160 mV), except for the second oxidation process of the lanthanide complexes for which reverse peaks were absent. The irreversibility of the second oxidation process of lanthanide monophthalocyanines has also been found earlier.[8] We observed that after oxidation at the second wave, the starting compound was regenerated only partially.

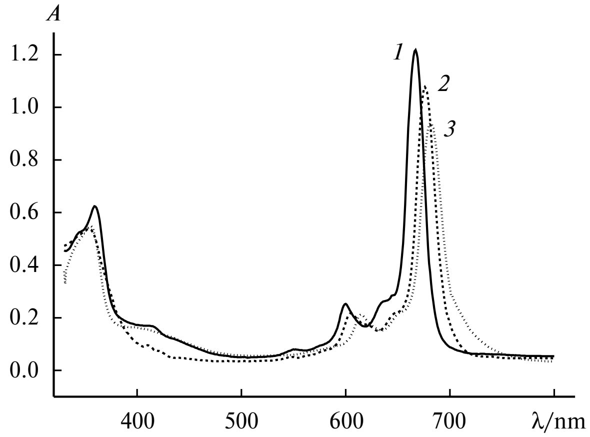


Fig. 2. Electronic absorption spectra of compounds **6g** (*1*, *2*) and **7g** (*3*) in $CHCl_3$ (*1*) and DMF (*2*, *3*).

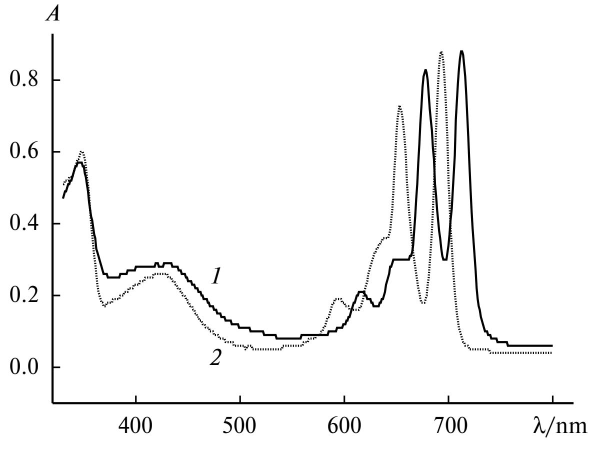


Fig. 3. Electronic absorption spectra of compounds **6h** (*1*) and **7h** (*2*) in DMF.

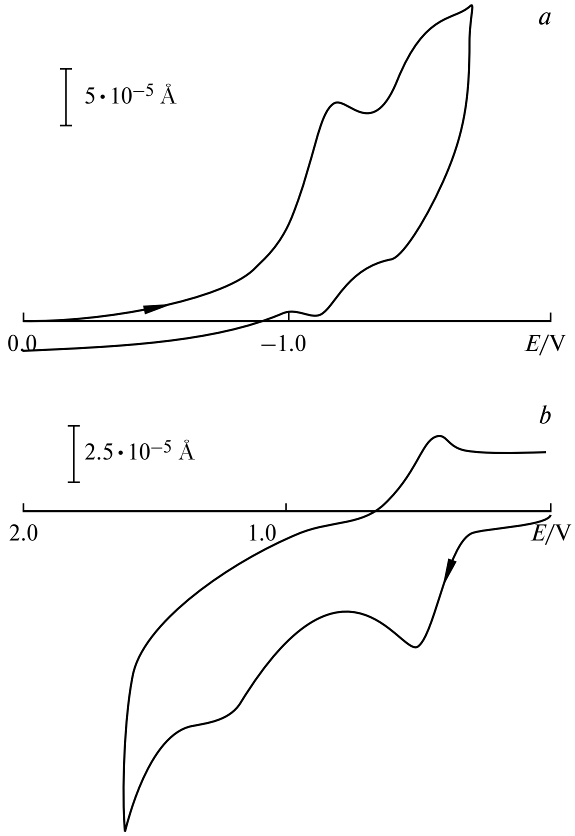


Fig. 4. Cyclic voltammogram of complex **6g** (graphite electrode, MeCN, 0.05 *M* $Bu^n{}_4NBF_4$, Ag|AgCl|KCl, $\nu = 100$ mV s^{-1}, 20 °C): *a*, cathodic region, *b*, anodic region.

For comparison, Table 2 gives the redox potentials of unsubstituted lutetium monophthalocyanine PcLiOAc (**8**), unsubstituted zinc phthalocyanine PcZn (**9**), zinc octabutoxyphthalocyanine (**10**), and zinc tetraneopentyloxyphthalocyanine (**11**). It can be seen that the introduction of the electron-withdrawing isopropylidenedioxy group into the phthalocyanine macrocycles causes a shift of the redox potentials of the complexes in the cathodic direction compared to the potentials of the unsubstituted complexes due to an increase in the electron density on the phthalocyanine rings. For complex **6a**, shifts

Table 2. Potentials of redox transitions of lanthanide and zinc monophthalocyanine complexes

Complex	Solvent	*E*/V				Reference
		Oxidation		Reduction		
6a ^{a}	*o*-DCB ^{b}	0.59	1.27	−0.99	−1.37	^{c}
6d ^{a}	MeCN	0.38	1.23 ^{d}	−1.17	−1.50	^{c}
6g ^{a}	MeCN	0.46	1.28 ^{c}	−1.13	−1.51	^{c}
8 ^{a}	MeCN	0.59	1.31	−1.08	−1.50	^{c}
9 ^{e}	DMF	0.67	—	−0.86	−1.30	**10**
10 ^{b}	DMF(Py)	0.50	—	−1.06	−1.53	**11**
11 ^{e}	*o*-DCB ^{b}	0.47	1.13	−1.17	−1.55	**12**

[a] *vs.* Ag|AgCl|KCl.

[b] *o*-DCB is *o*-dichlorobenzene.

[c] The present study.

[d] The peak potential, the redox process is irreversible.

[e] *vs.* SCE.

of the potential in the cathodic direction are smaller than those for the tetra- and octaalkoxy-substituted complexes. Therefore, the isopropylidenedioxy groups exhibit apparently the lower electron-withdrawing ability than two alkoxy groups at the same positions of the phthalocyanine macrocycle. A decrease in the ionic radius of lanthanide leads to a shift of the potentials of redox transitions in the anodic direction, which is consistent with the data published earlier for the first oxidation process of unsubstituted lanthanide monophthalocyanine complexes.[8]

Experimental

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 instrument (200 and 50.3 MHz, respectively) in $CDCl_3$ or $(CD_3)_2SO$ with Me_4Si as the internal standard. Thin-layer chromatography was carried out on Silufol UV-254 plates. Mass spectra were measured on Finnigan MAT INCOS-50 (EI, 70 eV, direct inlet) and VISION-2000 (MALDI-TOF) instruments.

Acetonitrile of analytical grade used for electrochemical studies was purified according to a procedure described earlier.[13] *o*-Dichlorobenzene of high-purity grade was passed through a column with neutral Al_2O_3 immediately before use; $Bu^n{}_4NBF_4$ (Aldrich) was twice recrystallized from Pr^iOH of special-purity grade and dried *in vacuo* at 110 °C.

Electrochemical measurements were carried out with a P-5827 potentiostat, a PR-8 programmator, and a two-coordinate PDA1 recorder using a three-electrode scheme on a graphite electrode (pyrolyzed polyacrylonitrile, $S_{spec} = 12$ m^2 g^{-1}, m ~1 mg) at 20 °C. Acetonitrile and *o*-dichlorobenzene were used as the solvents. The concentrations of the supporting electrolyte $Bu^n{}_4NBF_4$ were 0.05 and 0.15 mol L^{-1}, respectively. Platinum wire was used as the auxiliary electrode and a saturated Ag/AgCl/KCl electrode was used as the reference electrode. Oxygen was removed from the cell by a stream of dry argon. Voltammetric curves were recorded by cyclic voltammetry at a sweep rate of 100 mV s^{-1}. The measured peak potentials were recalculated taking into account the resistance of the electrolyte, which was calculated from the shifts of the anodic and cathodic peaks of oxidation of ferrocene according to the equation $(E^c - E^a) - 0.059 = IR$, where E^c and E^a are the cathodic and anodic peak potentials, respectively, I is the sum of the currents of the cathodic and anodic processes, respectively, and R is the resistance of the electrolyte. The concentrations of the complexes under study were $1 \cdot 10^{-4}$—$3 \cdot 10^{-4}$ mol L^{-1}.

4,5-Isopropylidenedioxyphthalonitrile (1) was prepared according to a procedure described by us earlier.[4]

3,4-Isopropylidenedioxybenzonitrile (4) was obtained in the chromatographic isolation of compound **1** (SiO_2 column, benzene as the eluent). Yield 15—22%, m.p. 75—76 °C. ^1H NMR, δ: 1.71 (s, 6 H, CMe_2); 6.77 (d, 1 H, H(5), $^3J = 8$ Hz); 6.96 (d, 1 H, H(2), $^4J = 1.75$ Hz); 7.18 (dd, 1 H, H(6), $^4J = 1.75$ Hz, $^3J = 8$ Hz). ^{13}C NMR, δ: 25.97 (Me); 104.23 (C(1)); 109.02 (C(5)); 111.28 (C(2)); 119.32 (CN); 120.21 (OCO); 127.79 (C(6)); 147.81 (C(3)); 151.37 (C(4)). MS (*m/z*): 865 [M]$^+$. Calculated (%): C, 68.56; H, 5.18; N, 8.00. $C_{10}H_9NO_2$. Found (%): C, 68.80; H, 5.33; N, 8.11.

Metal 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanines 6a—g (general procedure). A mixture of dinitrile **1** (0.5 g, 2.5 mmol), DBU (0.378 g, 2.5 mmol), and the corresponding metal acetate (0.625 mmol) was refluxed in isopentyl alcohol (5 mL) under argon until the reaction was completed (5—7 h). The reaction was monitored by TLC. After completion of the reaction, light petroleum (25 mL) was added to the reaction mixture. The precipitate that formed was filtered off, washed with a small amount of light petroleum, and dried in air. Phthalocyanine complexes were isolated by repeated extraction of the resulting powders with hot EtOAc. The phthalocyanines thus formed were purified by preparative TLC (Silufol UV-254, EtOAc).

Zinc 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine (6a). Yield 64%. ^1H NMR, δ: 2.21 (s, 24 H, $C(2)Me_2$); 8.72 (s, 8 H, H arom.). MS (*m/z*): 865 [M]$^+$. Found (%): C, 61.10; H, 3.68; N, 12.86. $C_{44}H_{32}N_8O_8Zn$. Calculated (%): C, 61.01; H, 3.72; N, 12.94.

Samarium 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine acetate (6b). Yield 22.4%. MS (*m/z*): 951 [M − AcO]$^+$. Found (%): C, 54.28; H, 3.50; N, 11.06. $C_{46}H_{35}N_8O_{10}Sm$. Calculated (%): C, 54.69; H, 3.49; N, 11.00.

Europium 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine acetate (6c). Yield 31%. MS (*m/z*): 952 [M − Ac]$^+$. Found (%): C, 54.32; H, 3.47; N, 10.98. $C_{46}H_{35}N_8O_{10}Eu$. Calculated (%): C, 54.61; H, 3.49; N, 11.07.

Terbium 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine acetate (6d). Yield 74.5%. MS (*m/z*): 959 [M − AcO]$^+$. Found (%): C, 54.18; H, 3.52; N, 10.96. $C_{46}H_{37}N_8O_{10}Tb$. Calculated (%): C, 54.23; H, 3.46; N, 11.00.

Dysprosium 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine acetate (6e). Yield 48%. MS (*m/z*): 963 [M − AcO]$^+$. Found (%): C, 54.10; H, 3.51; N, 10.71. $C_{46}H_{37}N_8O_{10}Dy$. Calculated (%): C, 54.04; H, 3.45; N, 10.96.

Ytterbium 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine acetate (6f). Yield 48%. MS (*m/z*): 972 [M − AcO]$^+$. Found (%): C, 53.12; H, 3.47; N, 10.79. $C_{46}H_{37}N_8O_{10}Yb$. Calculated (%): C, 53.49; H, 3.42; N, 10.85.

Lutetium 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine acetate (6g). Yield 45%. MS (*m/z*): 1035 [M]$^+$. Found (%): C, 53.46; H, 3.37; N, 10.68. $C_{46}H_{37}N_8O_{10}Lu$. Calculated (%): C, 53.39; H, 3.41; N, 10.83.

2,3,9,10,16,17,23,24-Tetra(isopropylidenedioxy)phthalocyanine (6h). A mixture of dinitrile **1** (0.5 g, 2.5 mmol) and

MeOLi (0.19 g, 5 mmol) was refluxed in isopentyl alcohol (5 mL) under argon for 6 h. After completion of the reaction, AcOH (0.5 mL) was added. The solvent was evaporated *in vacuo* and the residue was purified by column chromatography (Al_2O_3, $CHCl_3$) to give a blue powder in a yield of 0.32 g (64%). MS (*m/z*): 802 $[M]^+$. Found (%): C, 65.70; H, 4.53; N, 13.86. $C_{44}H_{34}N_8O_8$. Calculated (%): C, 65.83; H, 4.27; N, 13.96.

Zinc 2,3,9,10,16,17,23,24-octahydroxyphthalocyanine (7a). Zinc 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine (**6a**) (0.15 g) was dissolved in concentrated H_2SO_4 (5 mL). Immediately after complete dissolution, the resulting solution was poured onto ice. The precipitate that formed was filtered off, washed with water to the neutral reaction, dried, and reprecipitated with hexane from DMF. Yield 94%. ^1H NMR, δ: 10.14 (s, 8 H, OH); 8.68, (s, 8 H, H arom.). MS (*m/z*): 705 $[M]^+$. Found (%): C, 54.56; H, 2.32; N, 15.91. $C_{32}H_{16}N_8O_8Zn$. Calculated (%): C, 54.45; H, 2.28; N, 15.87.

Lutetium 2,3,9,10,16,17,23,24-octahydroxyphthalocyanine acetate (7g) was prepared analogously. Yield 72%. MS (*m/z*): 815 $[M]^+$.

This study was financially supported by the Russian Foundation for Basic Research (Project No. 00-03-32658) and the International Science and Technology Center (Grant 1526).

References

1. M. Hu, N. Brasseur, S. Z. Yildiz, J. E. van Lier, and C. C. Leznoff, *J. Med. Chem.*, 1998, **41**, 1789.
2. M. Kimura, T. Horai, K. Hanabusa, and H. Shirai, *Chem. Lett.*, 1997, **7**, 653.
3. X.-Y. Li and D. K. P. Ng, *Tetrahedron Lett.*, 2001, **42**, 305.
4. A. V. Ivanov, P. A. Svinareva, L. G. Tomilova, and N. S. Zefirov, *Izv. Akad. Nauk, Ser. Khim.*, 2001, 879 [*Russ. Chem. Bull.*, *Int. Ed.*, 2001, **50**, 919].
5. J. Li, J. R. Diers, J. Seth, S. I. Yang, D. F. Bocian, D. Holten, and J. S. Lindsey, *J. Org. Chem.*, 1999, **64**, 9090.
6. L. G. Tomilova, A. V. Ivanov, I. V. Kostuchenko, E. V. Shulishov, and O. M. Nefedov, *Mendeleev Commun.*, 2002, 149.
7. G. Sloff, *Rec. Trav. Chim. Pays-Bas.*, 1935, **54**, 995.
8. N. B. Subbotin, L. G. Tomilova, N. A. Kostromina, and E. A. Luk´yanets, *Zh. Obshch. Khim.*, 1986, **56**, 397 [*J. Gen. Chem. USSR*, 1986, **56** (Engl. Transl.)].
9. P. Guyon, A. Pondaven, J.-M. Kerbaol, and M. L´Her, *Inorg. Chem.*, 1998, **37**, 569.
10. A. Giraudeau, A. Louati, M. Gross, J. J. Andre, J. Simon, C. H. Su, and K. M. Kadish, *J. Am. Chem. Soc.*, 1983, **105**, 2917.
11. D. Wohrle and V. Schmidt, *J. Chem. Soc.*, *Dalton Trans.*, 1988, 549.
12. A. Manivannan, W. A. Nevin, C. C. Leznoff, and A. B. P. Lever, *J. Coord. Chem.*, 1988, **19**, 139.
13. T. V. Magdesieva, I. V. Zhukov, L. G. Tomilova, O. V. Korenchenko, I. P. Kalashnikova, and K. P. Butin, *Izv. Akad. Nauk, Ser. Khim.*, 2001, 379 [*Russ. Chem. Bull.*, *Int. Ed.*, 2001, **50**, 396].

Received December 26, 2002