Макрогетероциклы
http://macroheterocycles.isuct.ru

Synthesis and Spectral Characteristic of Ytterbium Complexes with Asymmetric Tetraarylporphyrins

Lilia D. Fedorova,[a] Valentina D. Rumyantseva,[a@] Natal'ya V. Roshchina,[a] Andrey F. Mironov,[a] Valery M. Markushev,[b] and Igor P. Shilov[b]

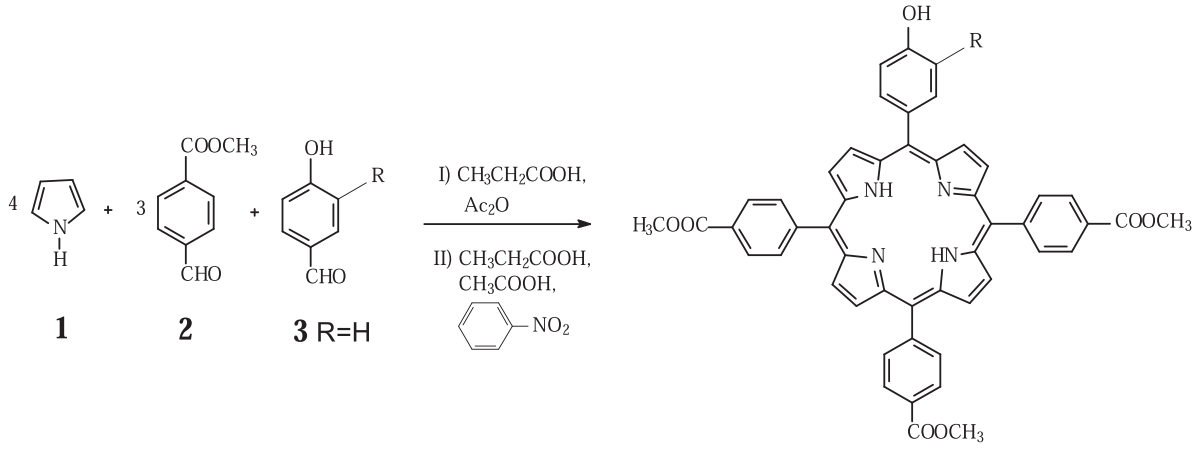
[a]*Lomonosov Moscow State Academy of Fine Chemical Technology, 119571 Moscow, Russia*
[b]*Kotel'nikov Institute of Radioengineering and Electronics RAS, 141190 Fryazino, Moscow region, Russia*
[@]*Corresponding author E-mail: vdrum@mail.ru*

Asymmetric substituted tetraarylporphyrins, containing 4-hydroxyphenyl and isomeric 3- and 4-pyridyl substituents, were synthesized. Ytterbium complexes of the both hydrophobic and hydrophilic derivatives were obtained. Luminescence spectrum and the curves of kinetic fluorescence decay were studied. O-Alkyl derivatives at 4-hydroxyphenyl moiety were prepared.

Keywords: Tetraarylporphyrins, ytterbium complexes, luminescence spectra.

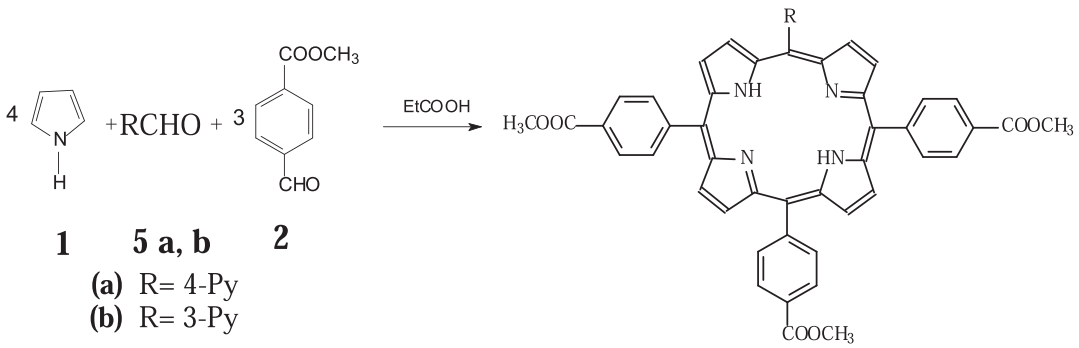
This work is the continuation of investigation on the synthesis of ytterbium complexes for cancer diagnostic. Purpose of our work was synthesis of asymmetric tetraarylporphyrins, containing hydroxyphenyl groups and one isomeric pyridyl substituent.

The development of luminescent diagnostics method of the visually and endoscopically reachable tumors in the IR-spectral range is presented in Table 1. Luminescence-spectral characteristics of Yb-complexes of porphyrins of non-phototoxic ytterbium complexes of porphyrins shows, that such substances practically do not generate



1 **2** **3** R=H

4 R=H



1 **5 a, b** **2**

(a) R= 4-Py
(b) R= 3-Py

6 a, b

(a) R= 4-Py
(b) R= 3-Py

Table 1. Luminescence-spectral characteristics of Yb complexes of porphyrins.

Yb complexes of porphyrins	UV-vis, λ_{max}, nm ($\varepsilon\cdot10^{-3}$, $l\cdot M^{-1}\cdot cm^{-1}$)	Luminescence spectrum, λ_{max}, DMSO	τ, μs
Yb(acac)-**4**	424.6(271), 516(5.5), 554.4(15.2), 593.2(4.6)	982	16.3
Yb(acac)-**6a**	418, 555.4, 590.8	983	13.4
Yb(acac)-**6b**	416.8, 551.4, 588	983	14.8
Yb(acac)-2,4-dimethoxy-HP IX	398(196.0), 532(9.15), 568.2(10.6).	975	8-11
Yb(acac)-5,10,15,20-tetrakis(1-*N*-(*p*-fluorophenyl)-3-(*o*-chlorophenyl)-pyrazole-4-yl)porphyrin	429.6(234), 557.6(14.5), 596(4.1)	976	20

singlet oxygen and at the same time have high luminescent characteristics and possess the tumor-tropic properties of the therapeutic photosensitizers.[1] Synthesis of hydrophobic asymmetric esters ytterbium complexes was carried out by known method.[2]

Results of our investigation and lifetimes for obtained complexes are presented in Table 1.

Studying of luminescent spectra and kinetics of decay of metalloporphyrins in DMSO showed that lifetimes for triesters are higher in 2 times, than for Yb(acac)-2,4-dimethoxyhematoporphyrin IX,[1] and similar to Yb(acac)-5,10,15,20-tetrakis(1-*N*-(*p*-fluorophenyl)-3-(*o*-chlorophenyl)pyrazole-4-yl)porphyrin.[3] These compounds could be the markers with low toxicity in luminescent diagnostic of malignant tumors.

Experimental

Spectra ^{1}H NMR (δ, ppm) were obtained on Brucker DPX-300 (300 MHz) (Germany) in $CDCl_3$. Spectra of UV-vis (nm) were registered on spectrometer Jasco 7800 (Japan) in $CHCl_3$. Mass-spectra were measured on a Brucker Ultraflex TOF (Germany). IR-spectrum (ν, cm^{-1}) were registered on a FT-spectrometer Brucker EQUINOX55 (Germany) by a method diffuse reflection. HPLC was carried out on a Waters Breeze chromatograph using a column Nova-Pack 18.4 μm 4.6×150 mm (Germany). Study of luminescence and temporal parameters of Yb metallocomplexes was carried out at experimental measuring stroboscopic test-bench prototype developed in IRE RAS.

5-(4-Hydroxyphenyl)-10,15,20-tris(4-methoxycarboxyphenyl)porphyrin, **4**. Nitrobenzene (20 ml), propionic acid (40 ml) and acetic acid (20 ml) were refluxed during 30 minutes. Then 4-hydroxybenzaldehyde (300 mg, 2.5 mmol) and methyl ester of 4-formylbenzoic acid (1.23 g, 7.5 mmol) in propionic acid (20 ml) were slowly dropped. Pyrrol (705 mg, 10.5 mmol) in nitrobenzene was gradually added and the mixture was refluxed during 2 hours, cooled, than methanol was added (20 ml) and the mixture was kept in refrigerator. The precipitation obtained was filtrated and washed by methanol. Chromatography of the obtained mixture of porphyrins was done on Kieselgel 60 in $CHCl_3$–CCl_4 (1:5). The first and second fractions, containing 5,10,15,20- tetrakis(4-methoxycarbonylphenyl)porphyrin and **4**, correspondingly, were evaporated and crystallized. Yield: 212 mg (11%). R_f 0.3; RT (retention time) 4.505 min; UV-vis λ_{max} ($\varepsilon\cdot10^{-3}$, $l\cdot M^{-1}\cdot cm^{-1}$): 419.8 (256), 516.2 (12.7), 551.4 (6.7), 590.2 (4.3), 646.8 (3.1). IR ν cm^{-1}: 3428 (OH), 1723 ($COOCH_3$). *m/z*: 805.458 $[M+H]^+$, account for $C_{50}H_{36}N_4O_7$ 804.85. ^{1}H NMR δ ppm: 8.92 (2H, m, H^3, H^7); 8.80 (6H, m, H^2, H^8, H^{12}, H^{13}, H^{17}, H^{18}); 8.45 (6H, m, 10,15,20-*ortho*-Ar); 8.30 (6H, m, 10,15,20-*meta*-Ar), 8.08 (2H, m, 5-*ortho*-Ar), 7.21 (2H, m, 5-*meta*-Ar), 4.12 (9H, s, $COOCH_3$), -2.78 (2H, s, NH).

5-(4-Pyridyl)-10,15,20-tris(4-methoxycarboxyphenyl)-porphyrin, **6a**. Propionic acid (20 ml) was added to the mixture of 4-pyridinaldehyde (180 mg, 1.685 mmol) and methyl ester of 4-formylbenzoic acid (830 mg, 5.06 mmol), and refluxed at 140°C. Pyrrol (425 mg, 6.74 mmol) in propionic acid (3 ml) was slowly dropped and the mixture was refluxed during 30 minutes. Than warm methanol (10 ml) was added and the obtained solution was kept in refrigerator. The precipitation obtained was filtrated and washed by methanol. Weight of porphyrin mixture was 240 mg. Chromatography of the obtained mixture of porphyrins was done on Kieselgel 60 in $CHCl_3$–diethyl ester (94:6). The second fraction was evaporated and crystallized. Yield: 90 mg (7.5%). Found: C 74.49; H 4.41; N 8.54 %. $C_{49}H_{35}N_5O_6$ requires C 74.51; H 4.47; N 8.87 %. R_f 0.68; RT 7.457 min. UV-vis λ_{max} ($\varepsilon\cdot10^{-3}$, $l\cdot M^{-1}\cdot cm^{-1}$): 419.8 (281.0), 514.8 (20.2), 549.0 (7.8), 588.8 (6.7), 644.4 (3.4); *m/z*: 790.373 $[M+H]^+$. ^{1}H NMR δ ppm: 9.032 (2H, d, J = 5.92 Hz, Py); 8.86 (8H, s, H^2, H^3, H^7, H^8, H^{12}, H^{13}, H^{17}, H^{18}); 8.47 (6H, m, Ph); 8.32 (6H, m, Ph); 8.149 (2H, d, J = 5.92 Hz, Py); 4.14 (9H, s, $COOCH_3$).

5-(3-Pyridyl)-10,15,20-tris(4-methoxycarbonylphenyl) porphyrin, **6b**. Propionic acid (15 ml) was added to the mixture of 3-pyridinaldehyde (180 mg, 1.685 mmol) and methyl ester of 4-formylbenzoic acid (830 mg, 5.06 mmol), and refluxed at 140°C. Pyrrol (425 mg, 6.74 mmol) in propionic acid (3 ml) was slowly dropped and the mixture was refluxed during 30 minutes. Than warm methanol (10 ml) was added and the obtained solution was kept in refrigerator. The precipitation obtained was filtered and washed by methanol. Chromatography of the obtained mixture of porphyrins was done on Kieselgel 60 in $CHCl_3$ – diethyl ester (5:1). Fraction, containing target product, was evaporated and recrystallized. Yield: 40 mg (5.1%). R_f 0.66; RT 6.496 min. UV-vis λ_{max}: 420, 515, 550, 589, 645. ^{1}H NMR δ ppm: 9.44 (H, s, Py-H^2); 9.04 (H, s, Py-H^4), 8.83 (8H, s, H^2, H^3, H^7, H^8, H^{12}, H^{13}, H^{17}, H^{18}), 8.47 (H, s, Py-H^6), 7.76 (H, t, Py-H^5), 4.12 (9H, s, $COOCH_3$).

References

1. Rumyantseva V.D., Mironov A.F., Shilov I.P., Shchamchalov K.S., Ivanov A.V., Baryshnikov A.Yu. Patent RU № 2411243, published 10.02.112.
2. Wong C.P., Venteicher R.F., Horrocks W. De W. *J. Am. Chem. Soc*. **1974**, *96*, 7149-7150.
3. Rumyantseva V.D., Markushev V.M., Panas A.M. *et al.* Patent RU № 2372099 published 10.11.09

Received 29.04.2011
Accepted 15.06.2011