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**Synthesis of conjugates of 5,15-disubstituted aminoporphyrins
and terpyridine derivatives with potential chelating properties**

**Fedor Y. Vyalba, Anastasia V. Ivantsova, Kseniya A. Zhdanova, Maxim N. Usachev,
Margarita A. Gradova and Natal'ya A. Bragina**

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Materials and methods

The following reagents were used: calcium hydride, phosphorus pentoxide, domestic organic solvents, *p*-nitrobenzaldehyde, pyrrole, G60 silica gel (Merck). *p*-Hexyloxybenzaldehyde **2** was synthesized according to the method.^{S1} Dichloromethane was distilled over phosphorus pentoxide; pyrrole and THF over calcium hydride. NMR (¹H and ¹³C) spectra of the solutions under study in CDCl₃ or DMSO-d₆ were recorded on a Bruker MSL-300 pulse Fourier transform spectrometer. Tetramethylsilane or boron trifluoride etherate were used as external standard. MALDI mass spectra were recorded on a Bruker autoflex time-of-flight (TOF) mass spectrometer (Bruker Daltonics Inc., Germany) equipped with a 355 nm solid-state UV laser (1 kHz frequency, 1000 pulses for each sample) and operating in the positively charged ion detection mode with $\lambda = 355$ nm (repeated in the text) and a reflectron. An MTP 384 ground steel target (Bruker Daltonics Inc., Germany) was used to record the MALDI mass spectra. Electronic spectra were recorded on TermoSpectronic Helios Alpha spectrophotometer in quartz cuvettes with optical path length of 1 cm using HACH DR-4000V spectrophotometer (Hach-Lange, USA) in the range of 320-800 nm in steps of 1 nm in quartz cuvettes with optical path length of 10 mm at room temperature.

Fluorescence spectra were recorded on a Cary Eclipse spectrofluorimeter (Agilent) Perkin Elmer LS-50 fluorescence spectrometer (USA) in quartz cuvettes with an optical path length of 10 mm at room temperature. Fluorescence quantum yield values were calculated according to the known methodology^{S2,S3} using ZnTPP ($\Phi_F = 0.033$ in DMF) as a standard.^{S4} HPLC MSWP analysis was performed on a Vanquish ultra-high performance liquid chromatographic system coupled to a Q-Exactive HF-X high-resolution hybrid mass spectrometer under electrospray ionization. The chromatographic separation was performed using reverse-phase column "Hypersil Gold C8" with length of 50 mm, inner diameter of 2.1 mm, particle diameter of the sorbent 1.9 μm (production of "Thermo Scientific", Germany, catalog number 10238700). Deionized water Mili Q with a resistivity of 18.2 Ohm cm^{-1} was used as component A of the mobile phase. Isopropyl alcohol of HPLC grade ("Scharlau", Spain, catalog number 603-117-00-0) was used as component B of the mobile phase. The volume flow rate of the mobile phase was 0.25 ml min^{-1} . Column temperature was 40°C. Aliquot volume applied to the column is 3 μl . Mode of elution - gradient. Gradient of the mobile phase composition: 0.0 - 1.0 min - component B - 5%; 1.0 - 12.0 min - linear increase of component B to 95%; 12.0 - 14.0 min. - B component - 95%; 14.0 - 14.1 min - step decrease of component B to 5%; 14.1 - 15.0 min - component B - 5%. Ionization conditions: spray capillary voltage = +/-4.0 kV (depending on polarity); atomizing gas flow rate = 35 c.u.; auxiliary gas flow rate = 15 c.u.; drying gas flow rate = 5 c.u.; spray capillary temperature =

200°C; mass spectrometer inlet capillary temperature = 350°C; auxiliary gas temperature = 200°C; ion optics inlet lens voltage = 50 V.

Compounds were recorded in two sequentially switching mass spectrometer operating modes:

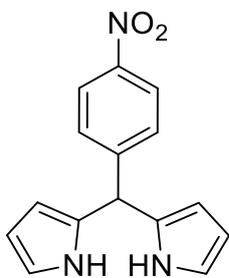
- Full Scan MS Positive/Negative (Full Scan) - full current scanning of positively/negatively charged precursor ions in the range of m/z values from 300 to 1600 Da with a resolution of 70000 rms.

Identification of compounds was performed by coincidence of m/z values of theoretically predicted and experimentally obtained adducts $[M^+H]^+$ and $[M^+Na]^+$.

Photochemical studies. The quantum yield of singlet oxygen generation was determined by the relative method using the chemical trap, 1,3-diphenylisobenzofuran (DPBF).^{S5,S6} ZnTPP ($\Phi_{\Delta} = 0.74$ in DMF)^{S7} was used as a standard. The samples were irradiated in 10 mm wide quartz cuvettes at room temperature in air-saturated solutions. Illumination system consisting of 150 W halogen bulb, three-lens spherical condenser with reflector, thermal and UV filters and light filter ZhS-18, transmitting light at $\lambda \geq 500$ nm, was used as a source. The luminous flux power was 10 $mW\ cm^{-2}$. The efficiency of singlet oxygen generation in the irradiated solutions of porphyrins was evaluated by the dynamics of optical density decrease in the absorption band of DPBF at 415 nm (CDPBF = 0.1 mM). In all photochemical experiments, the concentration of porphyrins was maintained at 1-2 μM , while the optical density of the solutions in the Q-band region did not exceed 0.05 in order to minimize the light filter effect.

References

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- S6 Ahmad S., Yadav K.K., Narang U., Bhattacharya S., Singh S.J., Chauhan S.M.S. *RSC Advances.*, 2016, **6**, 36090-36095.
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Synthesis and data 5-(4-nitrophenyl)dipyrromethane (1):

Pyrrole (0.03 mol) was added to aqueous HCl (0.18 M, 100 mL, 1.5:98.5), then 4-nitrobenzaldehyde (0.01 mol) was added. The reaction mixture was stirred at room temperature (TLC control). After 2 h the precipitated (semi)solid was filtered off and washed with water and petroleum ether to give 5-(4-nitrophenyl)dipyrromethane (**1**) as bright yellow crystals: mp 160-161 °C. Yield: Quantitative. ¹H NMR (300 MHz, dms^o-d₆) δ, ppm: 9.20 (br s, 2H, N-H), 8.71 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.93 (dd, *J* = 8.7, 3.3 Hz, 2H, Ar-H), 7.25 (s, 2H, 2C₅-H), 6.65 (s, 2H, 2C₄-H), 6.37 (s, 2H, 2C₃-H), 6.13 (s, 1H, meso-H). ¹³C NMR (75 MHz, CDCl₃) δ, ppm: 149.64, 146.89, 130.79, 129.22, 123.77, 117.95, 108.77, 107.80, 43.78.

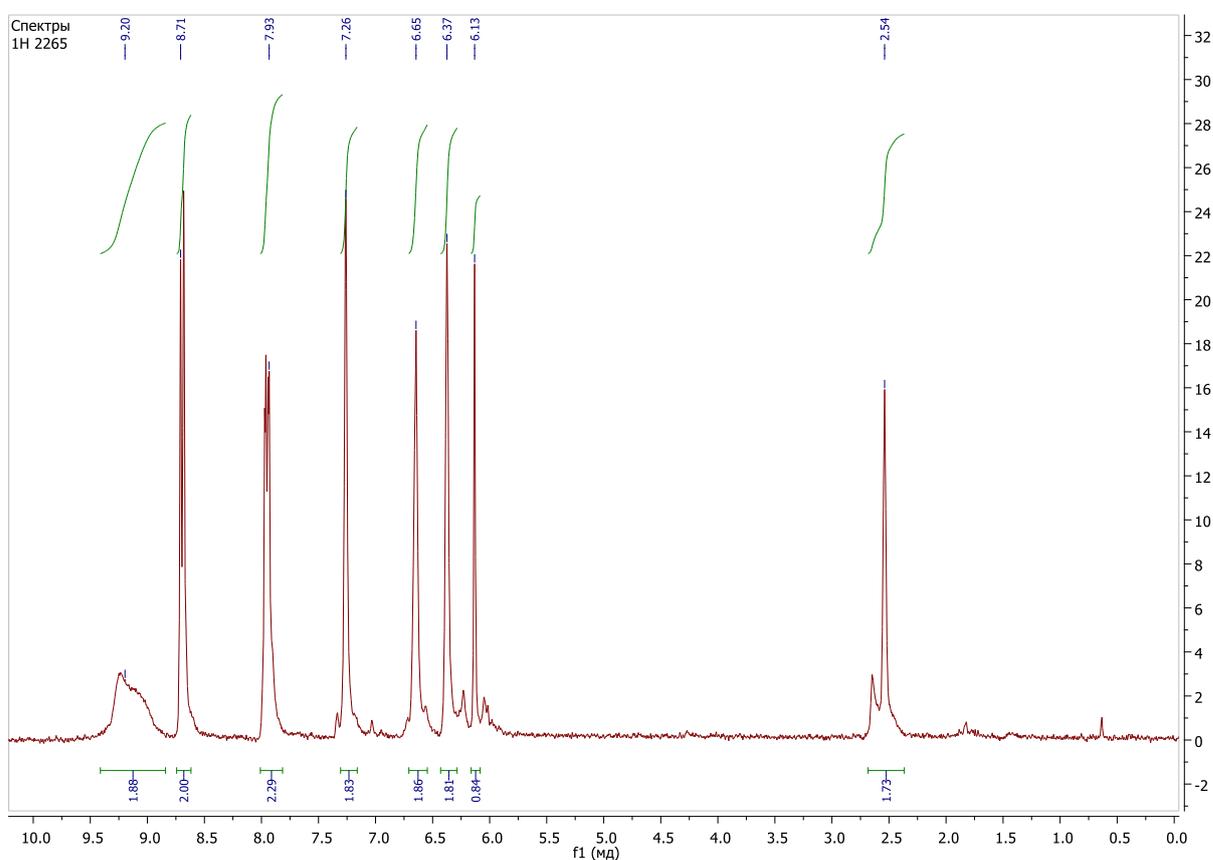
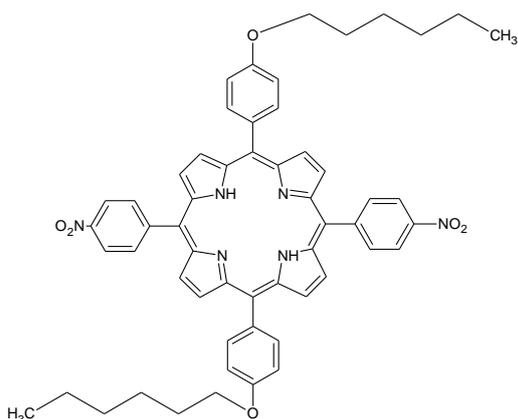


Figure S1. ¹H NMR spectrum of **1**



5,15-Bis(4-nitrophenyl)-10,20-bis(4-*n*-hexyloxyphenyl)porphyrin (2):

5-(4-Nitrophenyl)dipyrromethane (1 mmol) and 4-hexyloxybenzaldehyde (1 mmol) were added to a mixture of nitrobenzene (5 ml) and acetic acid (2.5 ml) preheated to 100°C. After 1 h of stirring, the mixture was cooled to room temperature. Then the nitrobenzene and the acetic acid were evaporated under reduced

pressure, and the residue was purified by column chromatography on silica gel with a mixture of CH₂Cl₂ and *n*-hexane. After evaporation, the crude product was washed with methanol by centrifugation resulting in pure 5,15-bis(*p*-nitrophenyl)-10,20-bis(*p*-hexyloxyphenyl)porphyrin **3** as a purple powder. The yield is 20%.

¹H NMR (300 MHz, CDCl₃, 25 °C) δ, ppm: 8.90 – 8.82 (m, 4H; H-β), 8.70 – 8.63 (m, 4H; H-β). 8.60 – 8.54 (m, 4H; Ph-H), 8.35 – 8.27 (m, 4H; Ph-H), 8.06 – 7.98 (m, 4H; Ph-H), 7.22 (d, J = 8.6 Hz, 4H; -Ph-H), 4.19 (t, J = 6.5 Hz, 4H; -O-CH₂-), 1.96 – 1.89 (m, 4H; -CH₂-), 1.55 (q, J = 7.1 Hz, 4H; -CH₂-), 1.42 – 1.36 (m, 8H; -CH₂-CH₂-), 0.94 – 0.89 (m, 6H, -CH₃), -2.83 (s, 2H, -NH-). UV-vis [CHCl₃; λ_{max}, nm (lg ε)]: 423.4 (5.58), 518.2 (4.49), 555.5 (3.38), 592.9 (3.23), 649 (3.22). HRMS calculated 904.4009 for C₅₆H₅₂N₆O₆ ([M+H]⁺) found 905.4012.

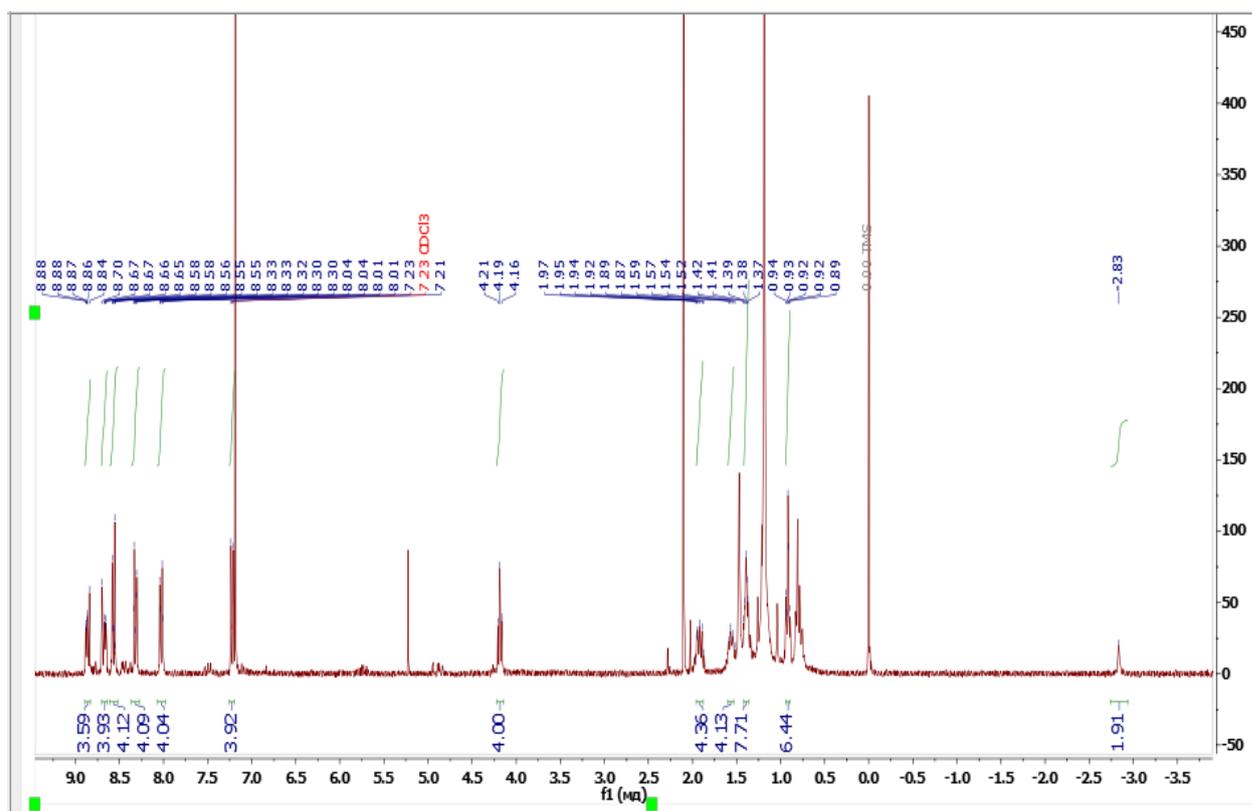


Figure S2. ¹H NMR spectrum of **2**

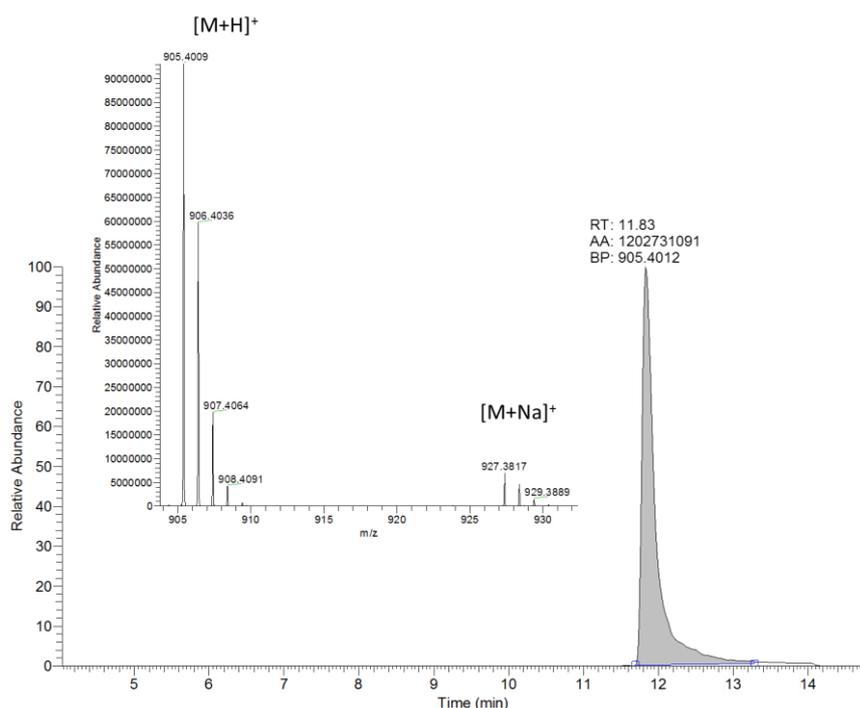
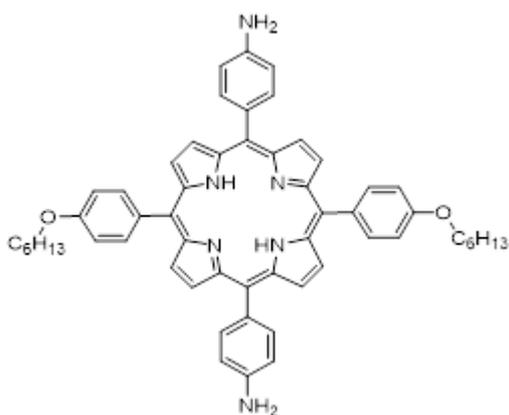


Figure S3. HRMS spectrum of compound **2** when recording positively charged ions.



5,15-Bis(4-aminophenyl)-10,20-bis-(4-*n*-hexyloxyphenyl)porphyrin (3a**):**

To a solution of compound **2** (57 mmol) in a CHCl₃/HOAc mixture (1:2, 30 ml) was added a solution of SnCl₂·2H₂O (4 mol) in concentrated HCl (10 ml). The mixture was stirred vigorously in a preheated oil bath (65-70°C) for 30 min, boiled for 7 h, and then neutralized with ammonia solution (25%) to pH 8-9. Chloroform (100 ml) was added, and the mixture was stirred for 1 h. The organic phase was separated and the aqueous phase was extracted with CHCl₃ (2×100 ml). The combined organic layers were washed once with diluted ammonia solution, three times with water and then concentrated to dryness. The residue was purified by column chromatography (silica gel, chloroform) to give the product (**3**). The yield (85%).

¹H NMR (300 MHz, CDCl₃, 25 °C) δ, ppm: 9.01 – 8.80 (m, 8H; H-β), 8.59 – 8.29 (m, 6H), 8.21 – 8.08 (m, 4H), 8.04 – 7.93 (m, 2H), 7.46 (d, J = 8.2 Hz, 2H), 7.32 – 7.27 (m, 4H; Ph-H), 7.13 – 6.97 (m, 4H; Ph-H), 4.25 (t, J = 6.5 Hz, 4H; -O-CH₂-), 4.10 (br-s, 4H; -NH₂), 1.97 (q, J = 7.1

Hz, 4H;-CH₂-), 1.76 – 1.55 (m, 4H; -CH₂-), 1.53 – 1.39 (m, 8H; -CH₂-CH₂-), 1.08 – 0.92 (m, 6H, -CH₃), -2.72 (s, 2H, -NH-)

¹³C NMR (75 MHz, CDCl₃, 25°C) δ,ppm: 159.08 (PhC-OCH₂), 149.88 (C₄, C₆ pyr), 146.92 (C₁₄, C₁₆ pyr), 146.10 (PhC-NH₂), 140.85 (C₁, C₉ pyr), 140.17 (C₁₁, C₁₉ pyr), 135.82 (CH Pyr), 134.70 (meso-C_{5,15}), 132.74 (meso-C_{10,20}), 127.34 (CH Pyr), 120.53 (αCH Ph), 119.69 (αCH Ph), 113.57 (βCH Ph), 112.84 (βCH Ph), 68.47 (OCH₂), 31.88 (OCH₂CH₂), 29.64 (O(CH₂)₂CH₂), 26.08 (OCH₂CH₂CH₃), 22.86 (CH₂CH₃), 14.27 (CH₃).

MS (MALDI-TOF):m/z found 869.44 ([M⁺Na]⁺ calculated for C₅₆H₅₆N₆O₂[Na⁺]=869.09), 883.64 ([M⁺K]⁺ calculated for C₅₆H₅₆N₆O₂[K⁺]=883.41). UV-vis [CHCl₃; λ_{max}, nm (lg ε)]: 425 (5.29), 520 (4.08), 557 (3.94), 594 (3.67), 653 (3.69).

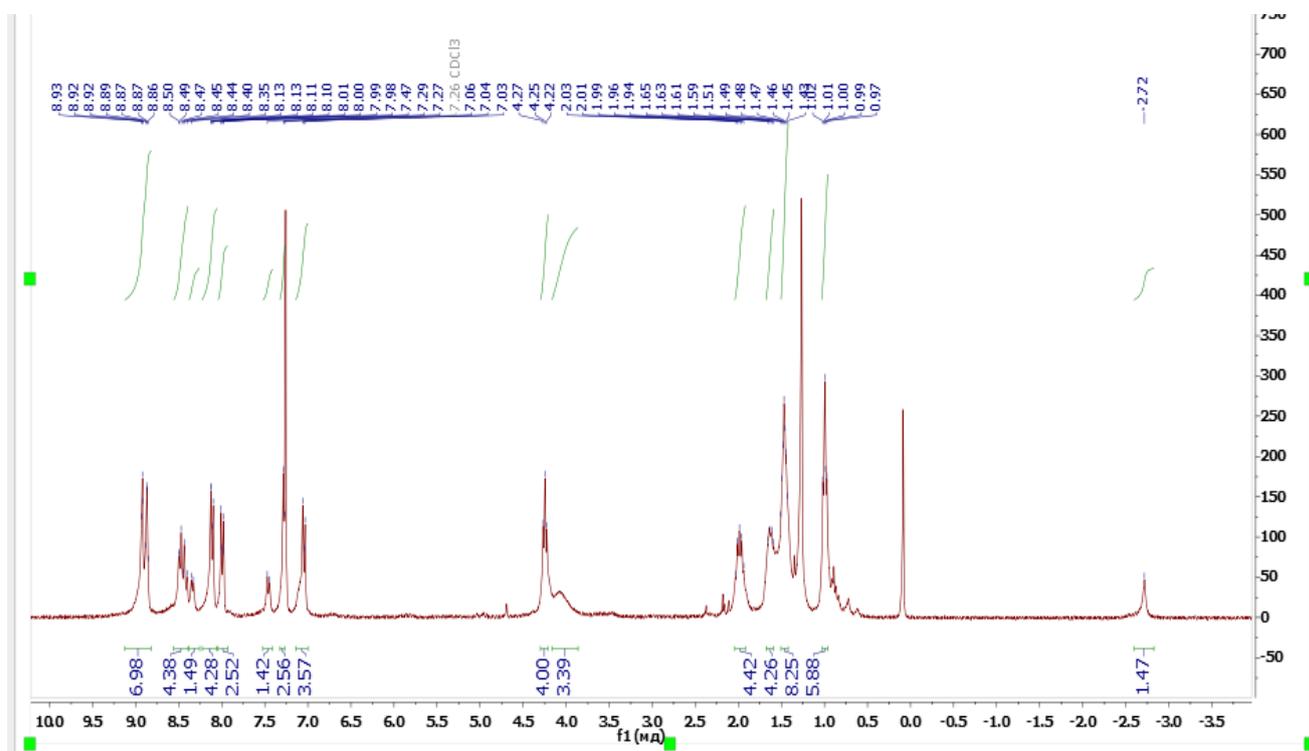


Figure S4. ¹H NMR spectrum of **3a**

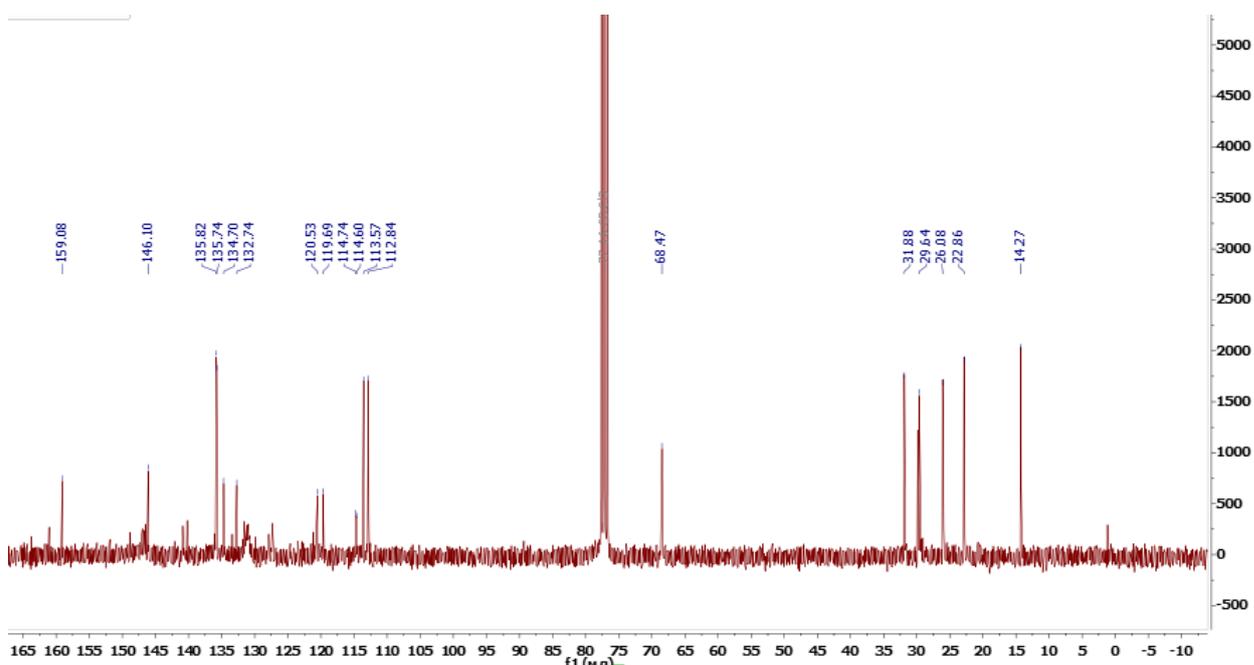


Figure S5. ^{13}C NMR spectrum of **3a**

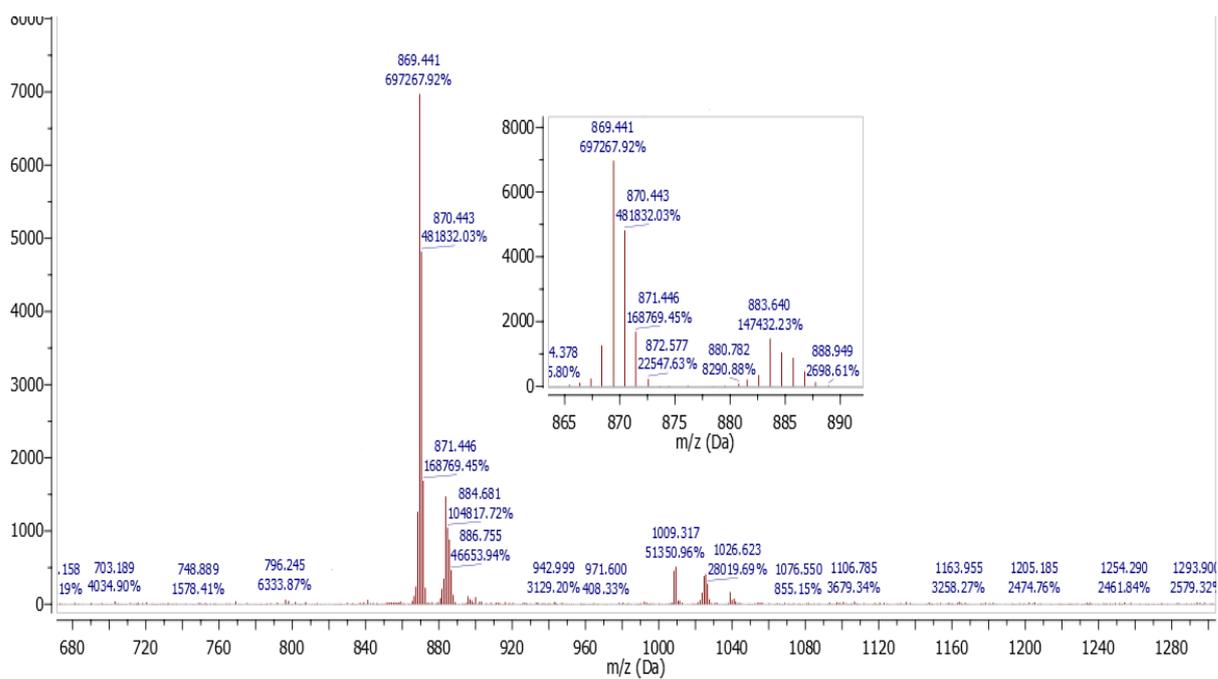
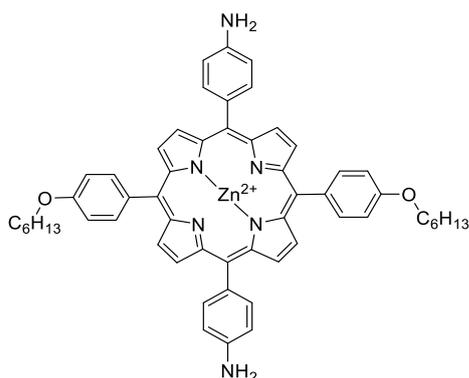
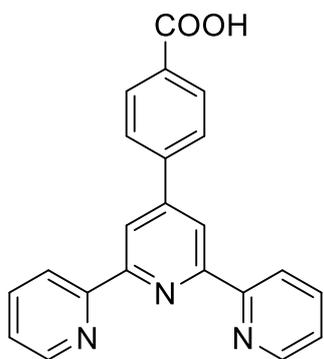


Figure S6. MS (MALDI-TOF) spectrum of compound **3a**.



5,15-Bis(4-aminophenyl)-10,20-bis-(4-n-hexyloxy phenyl)porphyrinato zinc (3b):

Zinc acetate dihydrate (0.516 mmol) was added to a solution of porphyrin **3** (0.344 mmol) in THF (50 mL). The mixture was boiled for 1 h and then extracted with dichloromethane, concentrated and the resulting solid was washed with *n*-hexane. According to TLC (ethyl acetate/hexane 1:4) no initial porphyrin was detected. The product was isolated with a yield of 91% (0.315 mmol) as a violet powder. The yield of the reaction is quantitative. UV-vis [CHCl₃; λ_{max}, nm (log ε)]: 426 (5.56), 520 (4.21), 557 (3.79).



4'-(4-Carboxyphenyl)-2,2':6',2'-terpyridine (4):

4-Carboxybenzaldehyde (6.7 mmol) was dissolved in absolute ethanol (20 mL) under stirring for 5 min. 2-Acetylpyridine (12.5 mmol), concentrated NH₄OH (1 mL) and NaOH solution (0.45 g in 1 mL H₂O) were added successively. The mixture was stirred at 45°C for 48 h and a white precipitate was observed. The solid was filtered off and washed with CH₂Cl₂ (3×4 mL) and a 1:1 mixture of cold methanol:H₂O (3×5 mL). A beige coloured solid was obtained after drying in an air current for 2 h. The product obtained in this step was the corresponding Na-salt of the compound. The crude product was suspended in CH₃OH/H₂O (80:20), stirred and sonicated at 35°C until complete dissolution. The solution was acidified to pH 2 with 1M HCl. The resulting white solid was filtered off and dried by vacuum filtration after washing with cold water. This compound was used without further purification. The yield was 82%. ¹H NMR (300 MHz, DMSO-d₆) δ, ppm: 8.83 (d, *J* = 8.6 Hz, 6H), 8.25 – 8.00 (m, 6H), 7.74 – 7.60 (ddd, 2H). ¹H NMR of the Na salt (300 MHz, D₂O) δ 7.67 (d, *J* = 8.9 Hz, 2H), 7.48 – 7.33 (m, 2H), 7.26 (q, *J* = 8.9 Hz, 2H), 7.11 (t, *J* = 8.8 Hz, 2H), 7.05 – 6.93 (m, 2H), 6.84 (dd, *J* = 10.0, 5.6 Hz, 4H). ¹³C NMR (75 MHz, DMSO-d₆) δ, ppm: 167.18; 156.25; 155.07; 149.60; 148.85; 137.92; 130.61; 127.55; 125.04; 121.12; 118.44. UV-Vis: (1.25M NaOH in water, 30μM): λ_{max} 275 nm.

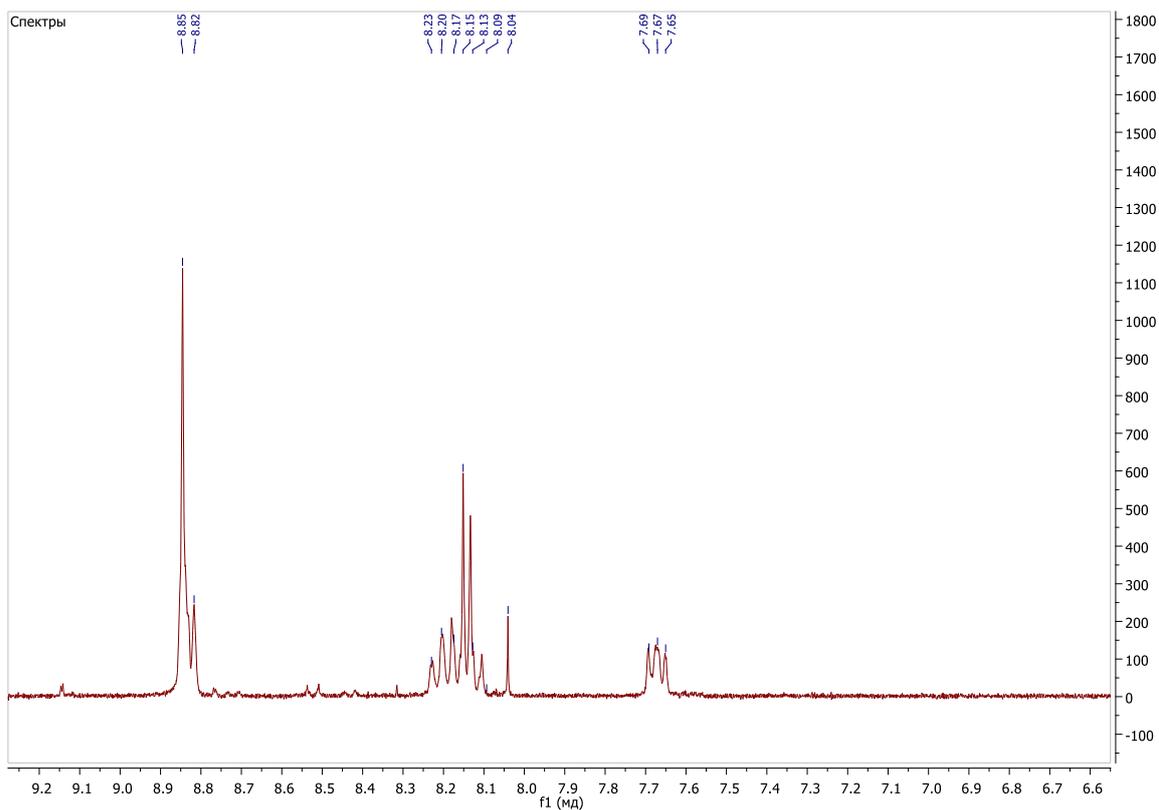


Figure S7. ^1H NMR spectrum of **4** in DMSO-d_6

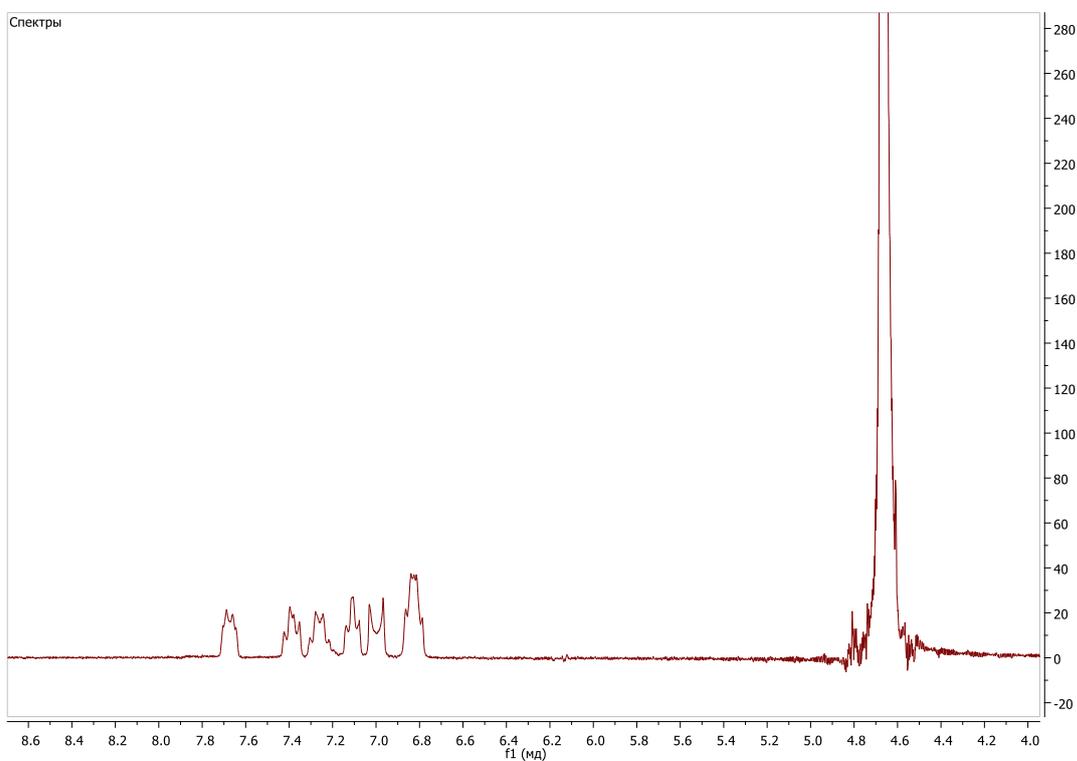
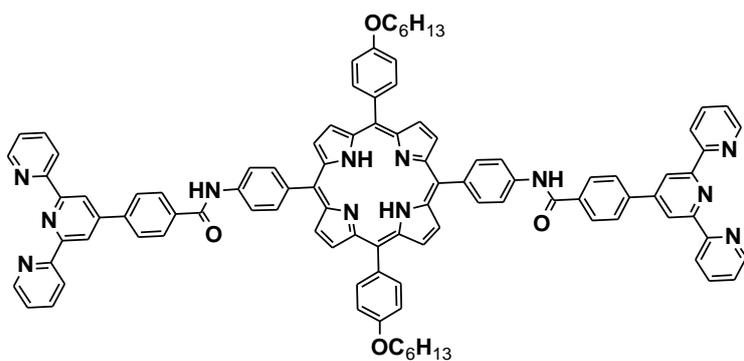


Figure S8. ^1H NMR spectrum of Na salt of **4** in D_2O



***N,N'*-((10,20-Bis(4-hexyloxyphenyl)porphyrin-5,15-diyl)-bis(4,1-phenylene))bis(4-([2,2':6',2''-terpyridin]-4'-yl)-benzamide) (5a):**

4'-([2,2':6',2''-terpyridin]-4'-yl)-benzamide **4** (0.40 mmol) was dissolved in SOCl_2 (6 ml) and stirred at 80°C for 2 h in an argon atmosphere. Afterwards SOCl_2 was removed under reduced pressure and the resulting terpyridine acyl chloride was dried under deep vacuum at 50°C for 1 hour. The resulting solid was dissolved in anhydrous THF (9 mL), and then aminoporphyrin **3a** (0.04 mmol) and anhydrous triethylamine (0.20 mL) were added. The mixture was heated to 70°C in an argon atmosphere overnight. The solvent was removed under reduced pressure, CHCl_3 (80 ml) was added, and the mixture was washed with water (3x50 mL). The organic layer was dried with Na_2SO_4 , filtered and concentrated. The residue was purified by column chromatography (silica gel G60) (CH_2Cl_2 :MeOH (100:6)) to give the target product **6** as a violet solid (90%).

^1H NMR (300 MHz, CDCl_3 , 25°C) δ , ppm: 9.00 (m, 4H- β -pyrrole), 8.83 (m, 4H- β -pyrrole), 8.77 (s, 4H-3'5'), 8.75 (4H, dm, 6, 6''), 8.71 (4H, dm, 3', 3''), 8.25 – 8.16 (4H, m, α Ph), 8.13 (4H, d, $J = 7.1$ Hz, α Ph), 7.90 ppm (td, $J = 7.8, 1.8$ Hz, 4H- 5, 5''), 7.38 (ddd, $J = 7.5, 4.7, 1.2$ Hz, 4H- 4, 4''), 7.30 (m, 8H, β Ph), 4.5 (t, $J = 6.6$ Hz, 4H, OCH_2), 2.00 (m, 4H, OCH_2CH_2), 1.63-1.70 (m, 4H, $\text{O}(\text{CH}_2)_2\text{CH}_2$), 1.53-1.44 (m, 4H, $\text{O}(\text{CH}_2)_3\text{CH}_2$), 1.25 – 1.33 (m, 4H $\text{O}(\text{CH}_2)_4\text{CH}_2$), 1.09 – 0.86 (m, 6H, CH_3), 0.10 (s, 2H).

^{13}C NMR (75 MHz, CDCl_3 , 25°C) δ , ppm: 165.42 ($\text{C}(\text{O})\text{NH}$), 159.05 ($\text{C}-\text{OHex}$), 156.15 (tpy 2:2''), 155.92 (tpy 2':6'), 149.15 (tpy: C6, C6''), 148.96 (tpy 4'), 147.43 (tpy: C4'), 147.00 (PhC-NH), 142.117, 139.22 (Ph1C), 138.56, 138.24, 137.68, 137.50, 136.92 (tpy 6:6''), 135.51 (C pyr), 135.14 (tpy $\text{C}-\text{C}(\text{O})$), 134.27 (meso-10,20), 133.89 (meso-5,15), 130.13 (C pyr), 128.21 (β Ph tpy), 127.81, 127.31 (α Ph tpy), 124.39, 123.93 (tpy 5':5), 121.37 (tpy 3:3''), 118.87 (tpy 3':5'), 118.38, 114.00 (β Ph), 112.62 (α Ph), 68.81 (OCH_2), 31.60 (OCH_2CH_2), 29.44 ($\text{O}(\text{CH}_2)_2\text{CH}_2$), 25.70 (CH_2CH_3), 23.54 (CH_2CH_3), 14.13. UV-vis [CHCl_3 ; λ_{max} , nm (log ϵ): 424(5.71). 519(4.30). 558(4.16). 594(3.8). 652(3.74)]. MALDI-TOF HRMS calculated 1515.6513 for $\text{C}_{100}\text{H}_{82}\text{N}_{12}\text{O}_4$, found 1515.6655.

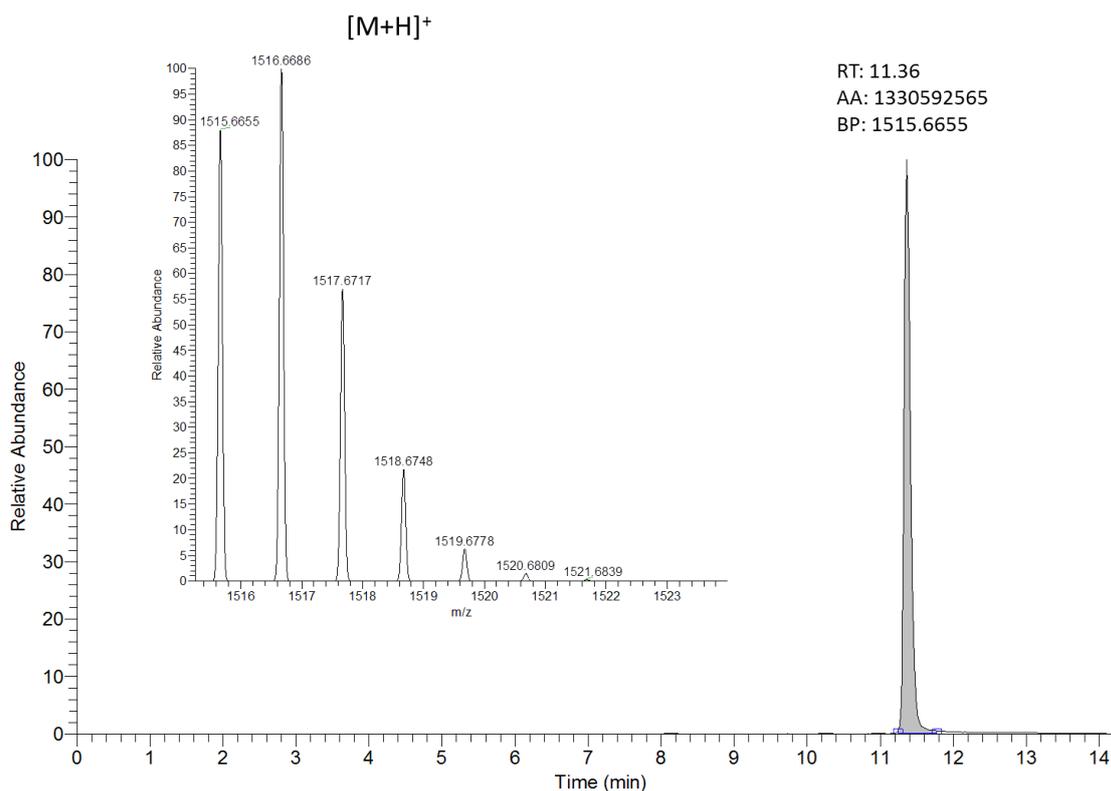
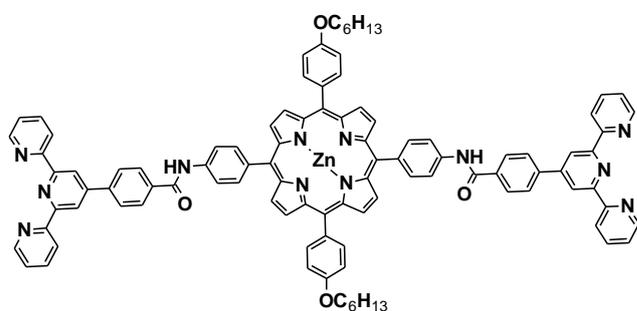


Figure S11. HRMS spectrum of compound **5a** when recording positively charged ions.



Zinc (II) complex of *N,N'*-((10,20-bis(4-hexyloxyphenyl)porphyrin-5,15-diyl)bis(4,1-phenylene))bis(4-([2,2':6',2''-terpyridin]-4'-yl)benzamide) (5b**):**

4'-([2,2':6',2''-terpyridin]-4'-yl)benzamide (**4**

(0.4 mmol) was dissolved in SOCl_2 (6 mL) and stirred at 80°C for 2 h in an argon atmosphere. Afterwards SOCl_2 was removed under reduced pressure and the resulting terpyridine acyl chloride was dried under deep vacuum at 50°C for 1 hour. The resulting solid was dissolved in anhydrous THF (9 mL) and then porphyrin **3b** (0.04 mmol) and anhydrous triethylamine (0.200 mL) were added. The reaction mixture was heated to 70°C in argon atmosphere overnight. The solvent was removed under reduced pressure, CHCl_3 (80 mL) was added, and the mixture was washed with washed with water (3x50 mL). The organic layer was dried with Na_2SO_4 , filtered and concentrated. The residue was purified by silica column chromatography (CH_2Cl_2 :MeOH (100:6)) to give the target product **5b** as a violet solid (90%).

^1H NMR (300 MHz, Chloroform- d) δ , ppm: 8.90 (m, 8H- β -pyrrole), 8.84 (s, 4H- 3'5'), 8.79 (4H, dm, 6, 6''), 8.71-8.75 (4H, dm, 3', 3''), 8.26 (m, 4H, α Ph), 8.21 (d, $J = 7.1$ Hz, 4H, α Ph), 7.88-

7.95 (td, $J = 7.8, 1.8$ Hz, 4H- 5, 5''), 7.38 (ddd, $J = 7.5, 4.7, 1.2$ Hz, 4H- 4, 4''), 7.25-7.32 (m, 8H, β Ph), 4.26 (t, $J = 6.6$ Hz, 4H, OCH_2), 1.96-2.08 (m, 4H, OCH_2CH_2), 1.56-1.70 (m, 8H, $\text{O}(\text{CH}_2)_2\text{CH}_2$), 1.43-1.52 (m, 4H, $\text{O}(\text{CH}_2)_3\text{CH}_2$), 1.39 – 1.18 (m, 4H, $\text{O}(\text{CH}_2)_4\text{CH}_2$), 1.09 – 0.86 (m, 6H, CH_3).

^{13}C NMR (75 MHz, CDCl_3 , 25 °C) δ , ppm: 166.27, 154.72, 150.22, 149.51, 148.35, 147.11, 146.52, 146.13, 141.29, 140.93, 139.32, 137.12, 136.08, 135.51, 134.14, 133.71, 132.83, 129.84, 129.18, 126.81, 126.26, 124.09, 121.75 – 121.05 (m), 120.53, 120.26, 119.08, 117.86, 115.11, 68.81, 31.60, 29.44, 25.70, 23.54, 14.10. MALDI-TOF HRMS calculated 1577.5814 for $\text{C}_{100}\text{H}_{80}\text{N}_{12}\text{O}_4\text{Zn}$, found 1577.5790.

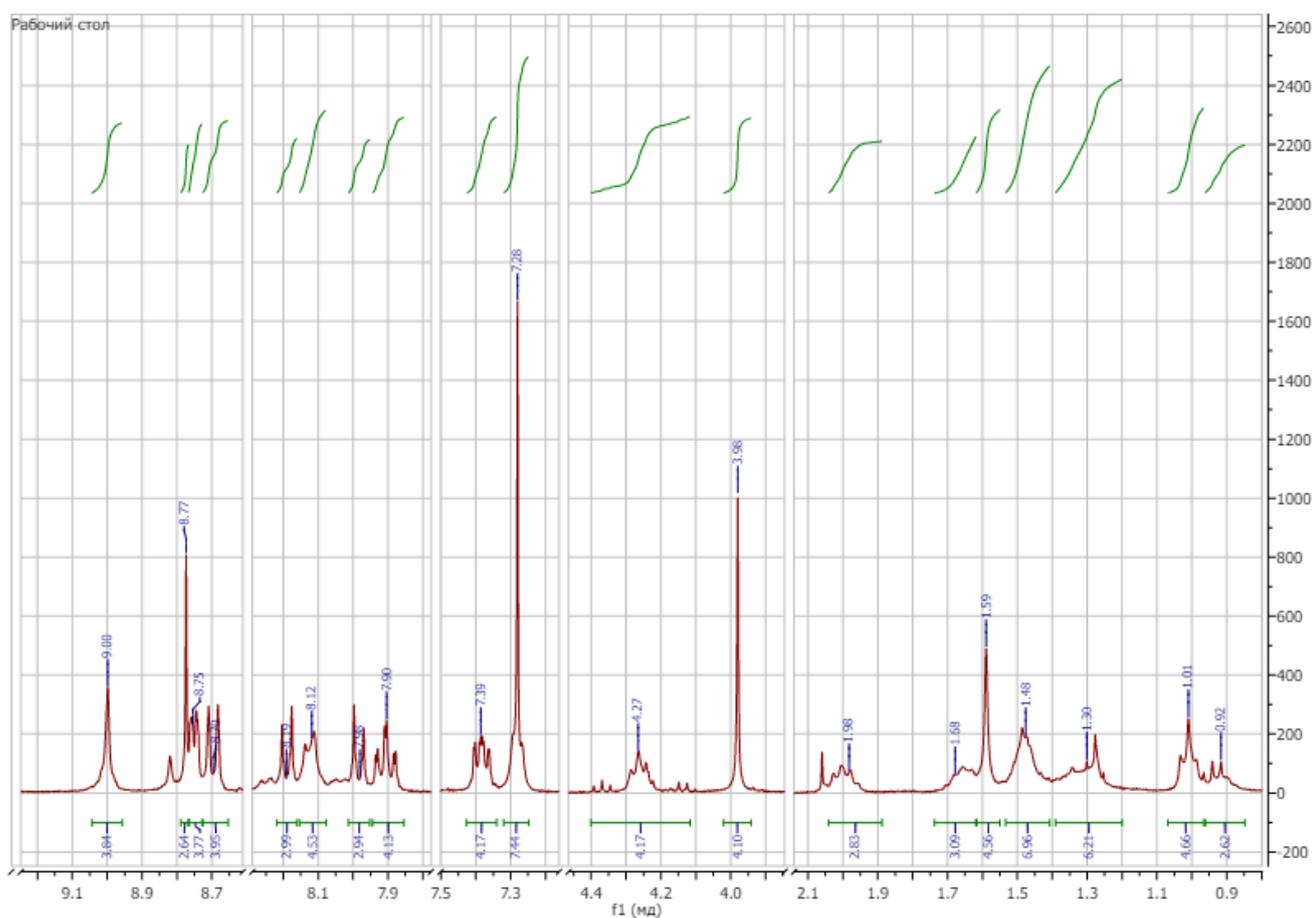


Figure S12. ^1H NMR spectrum of **5b**.

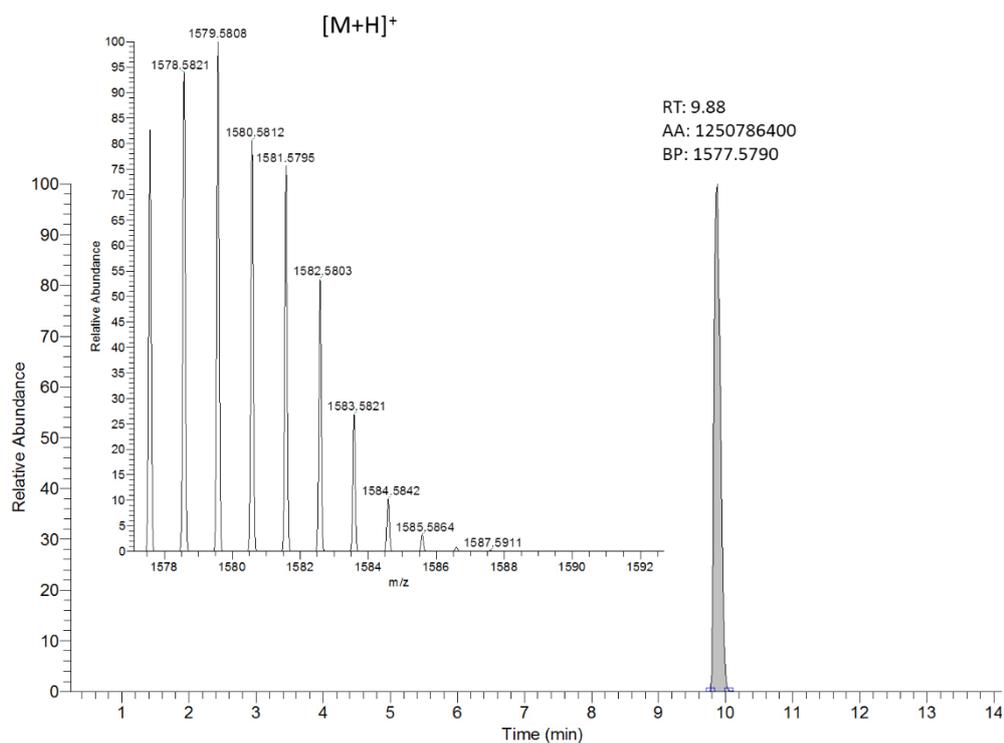


Figure S13. HRMS spectrum of compound **5b** when recording positively charged ions.

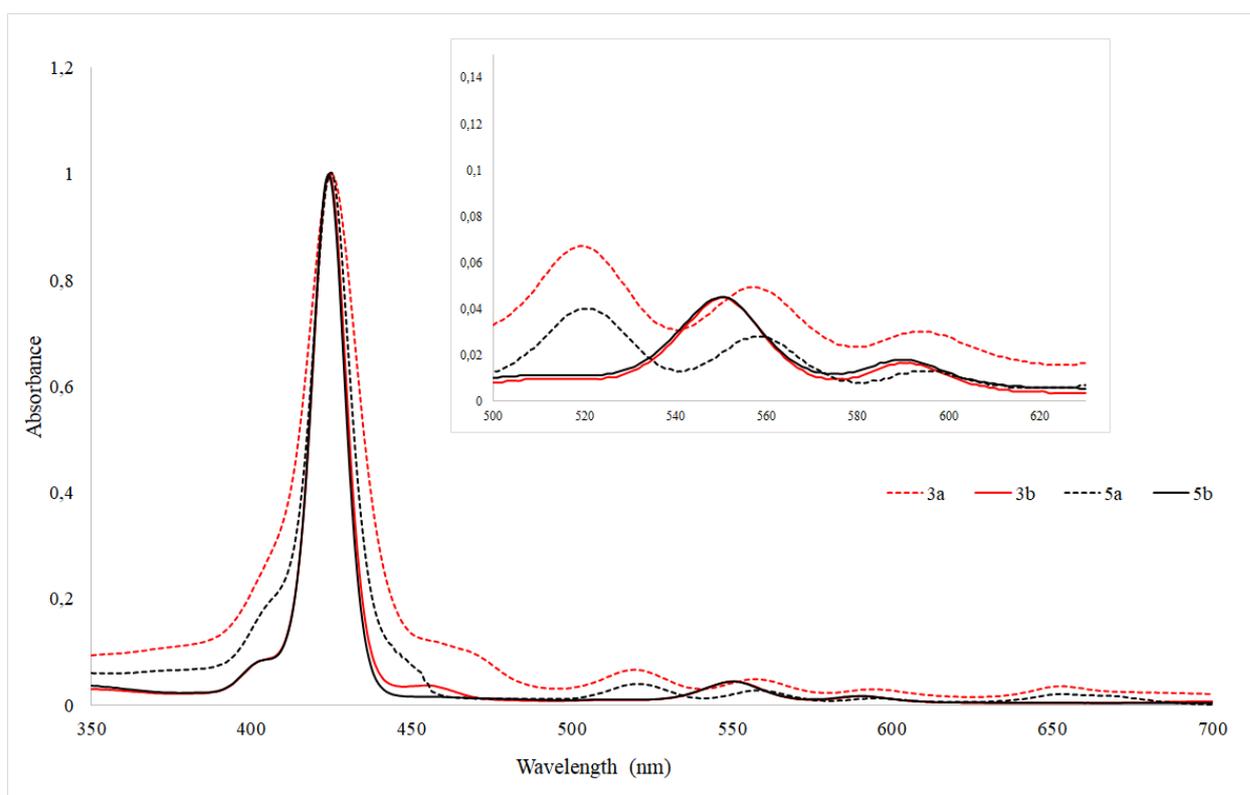


Figure S14. Normalized UV-Vis spectra of compounds **3a,b** and **5a,b**, inset region 490-670 nm.