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Dedicated to the 115th anniversary of B.A. Arbuzov's birth

Novel Cyanoarylporphyrazines with Triazole Groups at the Macrocycle Periphery as Potential Sensibilizers of Photodynamic Therapy and Optical Probes of Intracellular Viscosity

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Abstract—Novel fluorescent dyes of the cyanoarylporphyrazine series containing peripheral triazole groups have been synthesized. Their photophysical properties and the local viscosity effect on the fluorescence have been studied. The experiments with cell cultures have revealed rapid accumulation of the dyes in the cells cytoplasm. Photo- and dark cytotoxicity of the compounds have been evaluated by means of the MTT test.

Keywords: porphyrazines, template synthesis, ytterbium complexes, photosensibilizers, optical probes of intracellular viscosity

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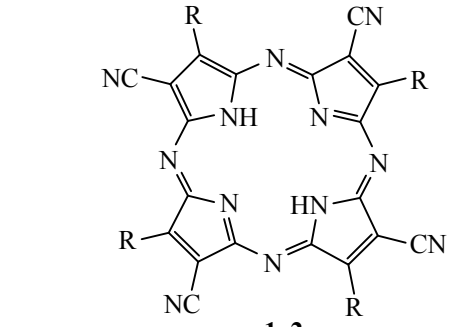
Tetrapyrrole macrocycles are important compounds in modern bioorganic chemistry, since they exhibit the property of selective accumulation in a tumor tissue and production of singlet oxygen (inducing cascade of oxidation reactions of cellular components resulting in the cancer cells death) under irradiation at a proper wavelength [1]. This concept lays the foundation of photodynamic therapy (PDT) of oncological diseases. In contrast to the porphyrins and phthalocyanines which have been widely applied as PDT agents [2–6], photosensitizing properties of porphyrazines in the form of free bases have been less studied [7–9]. The data on photodynamic activity of tetraaryltetracyanoporphyrazines have been absent until quite recently [10, 11]. We have earlier reported the synthesis of cyanoarylporphyrazines containing *para*-fluorophenyl (**1**) and *para*-benzyloxy (**2**) groups in the aryl frame of the macrocycle (Scheme 1) [10, 12]. The experiments with cancer cell cultures have revealed that the incorporation of *n*-donor oxygen atom in the aryl fragment significantly improves the efficiency of cycnoarylporphyrazine dyes as PDT sensibilizers.

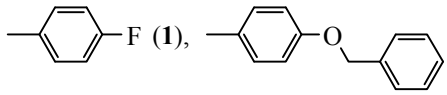
To elucidate the influence of the *n*-donor nitrogen atoms introduced in the aryl substituent on the photodynamic activity of porphyrazine, we herein synthesized novel cyanoarylporphyrazine dyes containing triazole moieties in the aryl substituents of the macrocycle. We studied their photophysical properties, the rate of accumulation in cancer cells, and cytotoxicity under irradiation and in dark. Overall, we demonstrated the prospects of those macrocycles use as photosensibilizers of PDT. As other cyanoarylporphyrazines synthesized by us [10–13], novel compounds of that series exhibited high sensitivity of the fluorescence parameters to local viscosity of their surrounding, which can be utilized in the development of optical viscosity probes.

To prepare the cyanoarylporphyrazine bases using click chemistry methods, we synthesized arylcarbaldehydes **5** and **6** bearing a propargyl group.

Scheme 1.



1, **2**

R =  (**1**), (**2**).

Aryltricyanoethylenes prepared from arylcarbaldehydes **7** and **8** bearing a triazole fragment (Scheme 2) were used as starting materials for template self-assembly of the porphyrazine macrocycle. Method of the synthesis of free cyanoarylporphyrazine bases is shown in Scheme 3.

The described synthetic route has been used by us earlier [12, 13], and it should be noted that the use of triazole-containing benzaldehydes as the precursors did not deteriorate the synthetic capability of the elaborated approach.

Table 1 displays spectral parameters of porphyrazines **17** and **18** in water; the data for tetra(4-fluorophenyl)tetracyanoporphyrazine **1**, photophysical properties and photodynamic properties of which have been described in detail in earlier [10], are given for reference. The introduction of triazole group led to noticeable shift of the absorption maximum to longer wavelength as compared to porphyrazine **1**. That ensured better optical transparency of biological tissue under irradiation, favorable for PDT.

A unique feature of cyanoarylporphyrazines is the combination of high photodynamic activity with strong sensitivity of the fluorescence parameters to the medium viscosity. Such fluorescent dyes known as "molecular rotors" are transformed into the dark state (when the excitation energy is fully or partially consumed on the internal rotation of the fluorophore molecule rather than fluorescence) upon photoexcitation in the low-viscosity medium. High local viscosity of the molecular rotor surrounding prevents the intermolecular movement, and therefore the intensity of fluorescence of such molecules is strongly increased in high-viscous media [14, 15]. The Förster–Hoffman equation (1) relates quantum yield of fluorescence (φ) with the solvent viscosity (η), z and α being numerical parameters.

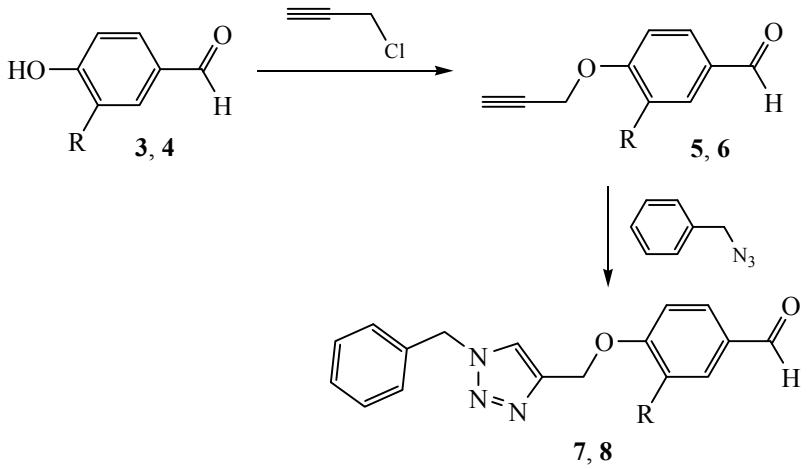
$$\log \varphi = z + \alpha \log \eta. \quad (1)$$

Similar equation is known for another fluorescence property, lifetime of the excited state τ [Eq. (2)] [16] (η being viscosity, z and α being numerical parameters, and k_r being the rate constant of the emitting transition).

$$\log \tau = \log (z/k_r) + \alpha \log \eta. \quad (2)$$

It has been earlier shown that tetra(4-fluorophenyl)-tetracyanoporphyrazine **1** is a typical fluorescent molecular rotor [10]. Its high photodynamic activity as well as the possibility of its use as a sensitive optical

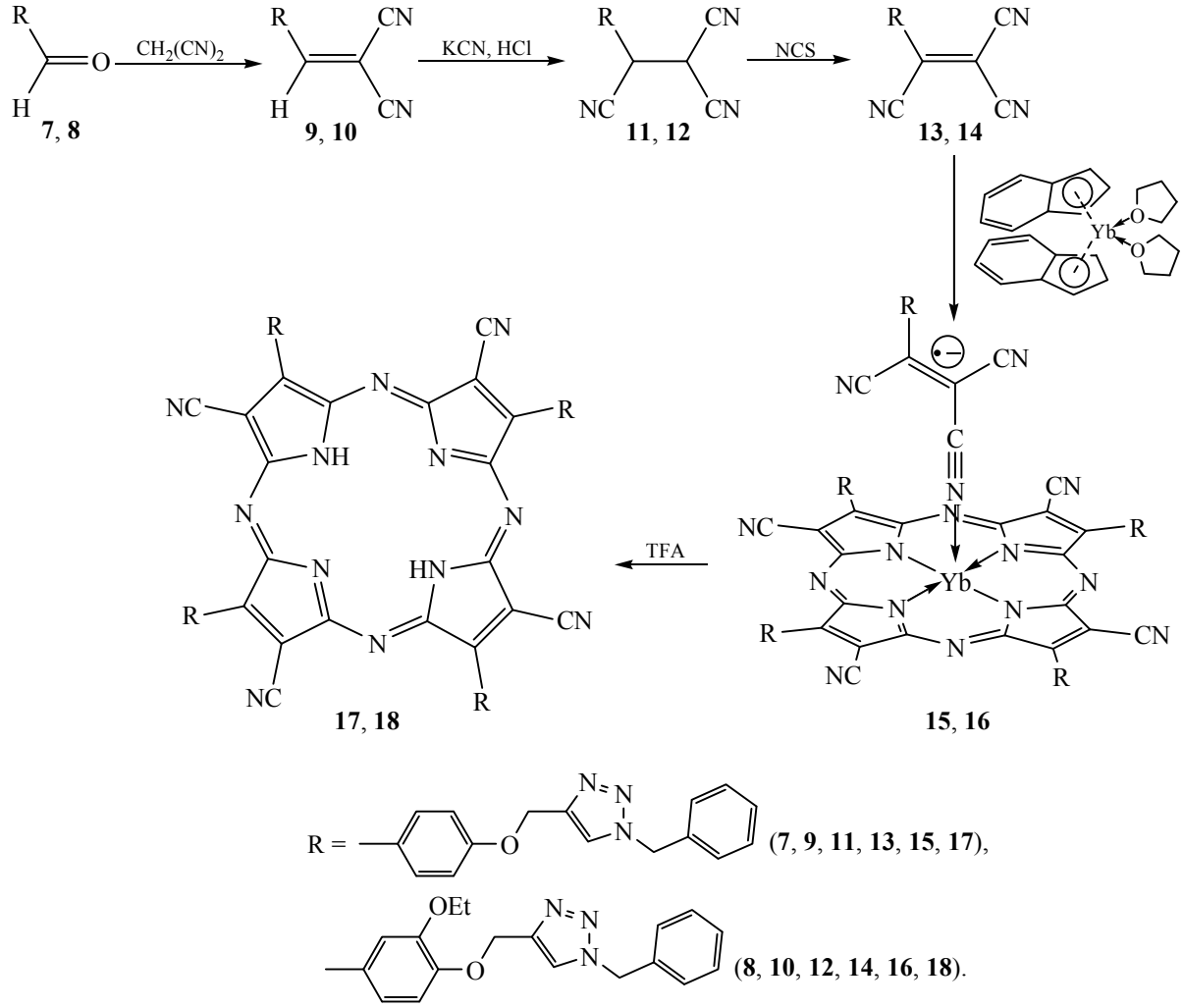
Scheme 2.



3, **4** **5**, **6** **7**, **8**

R = H (**3**, **5**, **7**), OEt (**4**, **6**, **8**).

Scheme 3.



sensor for intracellular viscosity have been demonstrated in the experiments with cancer cells culture. In is turn, this opens the possibility to perform real-time monitoring of cancer cells death from the change in the fluorescence parameters, since the intracellular viscosity is strongly increased during photodynamic action [17].

The parameter α reflecting the sensitivity of fluorescence of the molecular rotors to viscosity is of 0.3–0.6 [15]. The data in Fig. 1 show that porphyrazines containing triazole fragments in the cyanoarylporphyrazine macrocycle exhibited the sensitivity to viscosity close to that for the reference compound **1**. The *in vitro* studies demonstrated that both prepared porphyrazines were readily accumulated in the cells. To confirm the accumulation of the macrocycles in cancer cells, we performed fluorescence microscopy experiments. Using the strong red fluorescence signal, we determined that the introduced sensibilizer was accumulated in the cytoplasm of the A431 cells (epidermoid carcinoma of human skin) near the nucleus and in the nuclear shell. Accumulation of the

Table 1. Maximums of absorption and fluorescence in red spectral range and quantum yield of fluorescence of the prepared porphyrazines **17**, **18**, and **1** in water (c = 4 μmol/L)

Porphyrazine	**17**	**18**	**1** [10]
λ_{max} (Q-band), nm	593	591	579
log ε	4.32	4.38	4.42 [11]
λ_{fl}, nm (λ_{ex} = 590 nm)	640	650	650
φ[a], %	0.2	0.19	0.3

[a] Quantum yield of fluorescence was referenced to cresol violet (λ_{ex} = 590 nm).

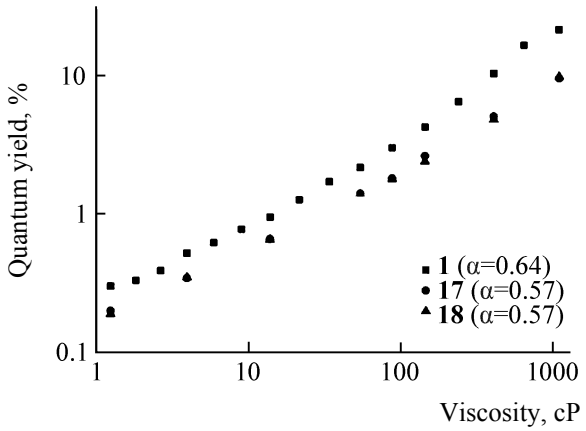


Fig. 1. Quantum yield of porphyrazines **1**, **17**, and **18** as function of the medium viscosity.

porphyrazines in the tumor cells in the course of the incubation of the cells culture is shown in Fig. 2. It is to be seen that porphyrazines **17** and **18** were readily accumulated by the tumor cells within first 60 min after their introduction in the culture.

To estimate the photodynamic activity of the novel tetraaryltetracyanoporphyrazines, we quantified their dark and photoinduced cytotoxicity towards the A431 cells. Those parameters can be determined using the MTT test [18], that is the measurement of concentration of the drug inducing the suppression of the cells growth or their death by 50% (inhibiting concentration IC_{50}). That value was measured in dark and under light irradiation. Figure 3 displays the plots of metabolic activity (viability) of the A431 cells as function of the concentration of porphyrazine **17** (a) and **18** (b) in dark and under light irradiation; the measured IC_{50} values are collected in Table 2. The obtained data revealed that the novel cyanoaryl-porphyrazines with triazole fragments in the aryl substituent exhibited pronounced photodynamic activity and could be used as photosensibilizers for PDT. As for the benzyloxy derivatives [12], the compounds investigated in this study revealed the reduced dark cytotoxicity in comparison with porphyrazine **1** [10], which is favorable for the application in optical anticancer therapy, since this factor will reduce the damage of healthy tissues in the absence of irradiation. On the other hand, it should be noted that the data in Table 2 showed that the triazole-containing cyanoarylporphyrazines revealed certain increase in the inhibiting concentration of the photo-sensibilizer under irradiation conditions [IC_{50}(light)], meaning weakening of the photodynamic effect. Nevertheless, the obtained data unambiguously demonstrated that cytotoxicity of novel potential photosensibilizers containing triazole fragments in the aryl substituent was largely caused by the photo-induced cell death rather than the inherent toxicity of the compounds. That was evidenced by the sufficiently high ratio IC_{50}(dark)/IC_{50}(light), so called therapeutic index. This parameter is important, yet the success of photodynamic therapy is often determined by the ability of the photosensibilizer to kill cancer cells and simultaneously induce the systemic immune reaction of the organism thus coping with the secondary neoplasms [19]. The probability of such response cannot be predicted from the MTT test results, since the massive immune response can be triggered by the type of the cell death [20]. The cyanoarylporphyrazine pigments being developed in our research group exhibit simultaneously the properties of efficient PDT photosensibilizers and fluorescent molecular rotors; this opens the way to investigate special features of the

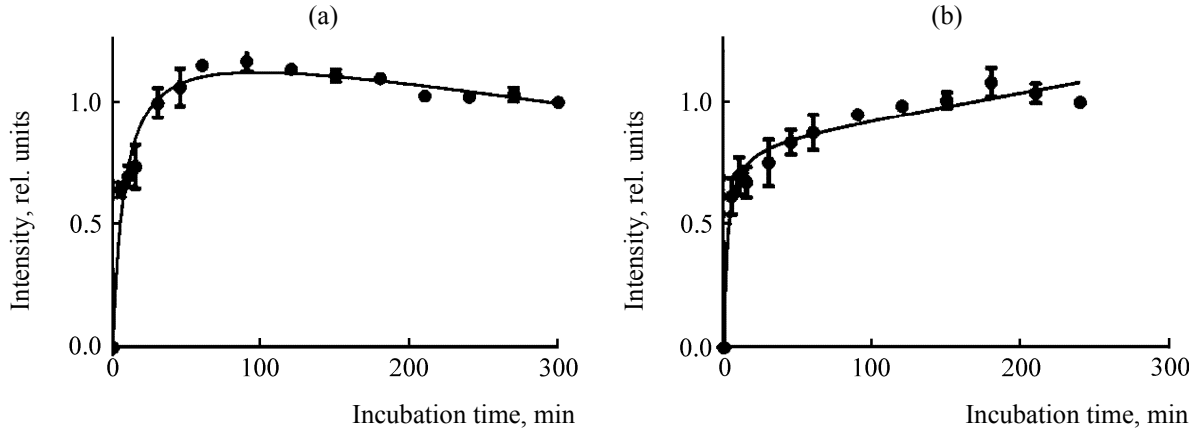


Fig. 2. Accumulation of porphyrazine **17** (a) and **18** (b) as function of the incubation time.

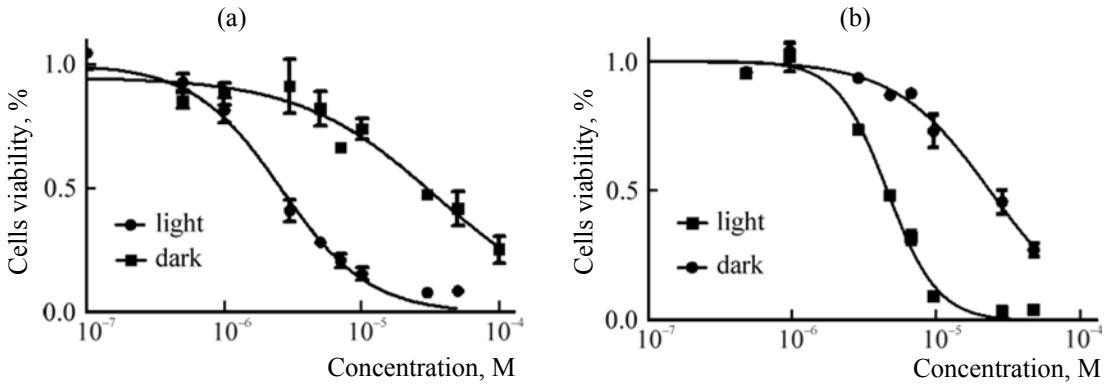


Fig. 3. Metabolic activity (viability) of the A 431 cells as function of the concentration of porphyrazine **17** (a) and **18** (b) in the medium in dark and during irradiation with 635 nm light at dose 20 J/cm^2.

cancer cells death in real time from the changes in the intracellular viscosity. This may allow distinguishing the types of cell death and reveal their relationship to the efficiency of therapeutic action.

EXPERIMENTAL

IR spectra of the suspensions in Vaseline oil were recorded using an FSM 1201 spectrometer. Electronic absorption spectra were recorded using a PerkinElmer Lambda 25 spectrometer. ^{1}H NMR spectra were recorded using a Bruker Avance II+ instrument [400 (^{1}H), 100 (^{13}C)] at 25°C. Steady-state fluorescence was studied using a PerkinElmer LS 55 spectrometer (wavelength range 300–800 nm). Mass spectra (MALDI TOF) were obtained using a Bruker Microflex LT mass spectrometer. Dynamic viscosity of the binary ethanol(methanol)–glycerol mixtures was measured using an SVM 3000 Stabinger viscometer (Anton Paar) with accuracy ±0.35%. Dissolution of porphyrazines was performed by mechanical stirring and ultrasonication during at least 15 min.

Viability of the cell culture was estimated by means of the MTT assay [18]. The cells were plated on a 96-well plate (4000 cells per a well) and incubated overnight. After that, the medium was replaced with 100 μL of the medium containing porphyrazine **17** or **18** in the appropriate concentration. The cells were incubated during 4 h, and then the medium was exchanged with a fresh portion. The cells were illuminated using a light diode array to ensure uniform irradiation of the plate [21]. The irradiation dose was 20 J/cm^2 (615–635 nm) at the areal power 20 mW/cm^2. 24 h after the irradiation, 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2*H*-tetrazolium bromide (MTT reagent, Alfa Aesar, UK) was introduced to the medium up to the final concentration 0.5 mg/mL, and the cells were incubated during 4 h. The medium was removed, and the formed colored crystals of MTT-formazan were dissolved in 100 μL of DMSO. The absorbance of the solutions at 570 nm was read using a Synergy MX plate spectrophotometer (BioTek, USA). Cells viability was estimated from the ratio of absorbance of the formazan solution in the sample to that in the reference (without irradiation and without porphyrazine). When dark cytotoxicity was determined, the samples were not irradiated.

To investigate the dynamics of porphyrazines **17** and **18** accumulation, the cells were incubated overnight in a 96-well plate with glass bottom (8000 cells per a well). Then the medium was exchanged with the medium containing 5 μmol/L of porphyrazine **17** or **18**. Fluorescence of the samples (excitation at 590 nm and registration at 640 nm) was measured 5, 10, 15, 30, 45, 60, 90, 120, 150, 180, 210, 240, 270, and 300 min after addition of the dye, without removal or washing of the cells (since the fluorescence was multiply enhanced in the cells in comparison with the medium). The spectrum of porphyrazine in the medium was recorded independently. The accumulation values were normalized to the signal obtained 300 min after the compound addition.

Table 2. The IC_{50} values of photodynamic activity and dark toxicity of porphyrazine with different peripheral aryl groups

Porphyrazine	IC_{50}(light), mol/L	IC_{50}(dark), mol/L	IC_{50}(dark)/IC_{50}(light)
1 [10]	8.0×10^{-7}	6.9×10^{-6}	8.6
2 [12]	1.0×10^{-6}	4.0×10^{-5}	40.0
17	2.7×10^{-6}	3.0×10^{-5}	11.1
18	3.5×10^{-6}	2.5×10^{-5}	7.1

Synthesis and analysis of the compounds were performed using anhydrous solvents. 4-Hydroxybenzaldehyde, ethylvaniline, propargyl chloride, benzyl chloride, sodium azide, malonodinitrile, and *N*-chlorosuccinimide were purchased from Sigma Aldrich. Bis(indenyl)ytterbium was prepared as described elsewhere [22].

Benzyl azide was prepared according to the procedure in [23]. A mixture of 20 mL of ethanol, 3 mL of water, benzyl chloride (25 mmol) and sodium azide (38 mmol) was stirred at boiling (95°C) during 20–24 h. After cooling down, the mixture was diluted with 100 mL of water. The product was exctracted with a CH_2Cl_2–hexane mixture (3×30 mL). The extract was washed several times with saturated solution of NaCl, and then the solvent was distilled off under reduced pressure. Yield 82%. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.38 s (2H), 7.35–7.45 m (5H).

Aldehydes 5 and **6** were synthesized via alkylation of 4-hydroxybenzaldehyde and ethylvaniline via a procedure adopted from [24]. A mixture of 15 mL of DMF, the aldehyde (25 mmol), propargyl chloride (24 mmol), K_2CO_3 (25 mmol), and KI (0.25 mmol) was stirred at 40°C during 20–24 h. After cooling down to ambient temperature, 100 mL of water was added. The precipitate was filtered off, washed with water several times, and dried.

4-(Prop-2-yn-1-yloxy)benzaldehyde (5). Yield 72%, white crystals, mp 78–80°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.59 t (1H, $\underline{HC}\equiv CCH_2O$, J = 2.4 Hz), 4.80 d (2H, $HC\equiv C\underline{CH_2}O$, J = 2.4 Hz), 7.11 d (2H, J = 8.7 Hz), 7.88 d (2H, J = 8.7 Hz), 9.92 s (1H, CHO). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 55.95, 76.37, 77.55, 115.19, 130.61, 131.89, 162.38, 190.77. Mass spectrum (ESI^+), *m/z*: 183.0420 $[M + Na]^+$.

4-(Prop-2-yn-1-yloxy)-3-ethoxybenzaldehyde (6). Yield 90%, white crystals, mp 79–80°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.50 t (3H, $\underline{CH_3}CH_2O$, J = 7.0 Hz), 2.57 t (1H, $\underline{HC}\equiv CCH_2O$, J = 2.4 Hz), 4.18 q (2H, $CH_3\underline{CH_2}O$, J = 7.0 Hz), 4.87 d (2H, $HC\equiv C\underline{CH_2}O$, J = 2.4 Hz), 7.17 d (1H, J = 8.2 Hz), 7.44–7.47 m (2H), 9.88 s (1H, CHO). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.62, 56.67, 64.56, 76.54, 77.69, 110.78, 113.14, 125.98, 130.99, 149.45, 152.37, 190.94. Mass spectrum (ESI^+), *m/z*: 227.0679 $[M + Na]^+$.

Synthesis of triazoles was performed via a procedure from [25]. A mixture of the aldehyde (6 mmol), benzyl azide (6 mmol), sodium ascorbate (0.6 mmol, 300 μL of freshly prepared 1 M. aqueous solution), $CuSO_4 \cdot 5H_2O$ (0.06 mmol), and 24 mL of a *tert*-butanol–water mixture (1 : 2) was stirred at room temperature during 20–24 h, diluted with 100 mL of water, and cooled. The precipitate was filtered off, washed with water several times, and dried.

4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]benzaldehyde (7). Yield 92%, light pink solid, mp 104–105°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.28 s (2H, CH_2N), 5.56 s (2H, CH_2O), 7.10 d (2H, J = 8.7 Hz), 7.30–7.31 m (2H), 7.38–7.40 m (3H), 7.58 s (1H, CHN), 7.84 d (2H, J = 8.7 Hz), 9.89 s (1H, CHO). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 54.34, 62.20, 115.10, 122.83, 128.15, 128.91, 129.20, 130.38, 131.97, 134.32, 143.65, 163.13, 190.74. Mass spectrum (ESI^+), *m/z*: 316.1048 $[M + Na]^+$.

4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]-3-ethoxybenzaldehyde (8). Yield 89%, light grey solid, mp 124–125°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 t (3H, $\underline{CH_3}CH_2O$, J = 7.0 Hz), 4.13 q (2H, $CH_3\underline{CH_2}O$, J = 7.0 Hz), 5.36 s (2H, CH_2N), 5.54 s (2H, CH_2O), 7.20 d (1H, J = 7.9 Hz), 7.26–7.28 m (2H), 7.37–7.43 m (5H), 7.58 s (1H, CHN), 9.84 s (1H, CHO). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.61, 54.30, 63.18, 64.50, 110.69, 113.22, 122.98, 126.43, 128.14, 128.87, 129.16, 130.69, 134.33, 149.34, 153.30, 190.95. Mass spectrum (ESI^+), *m/z*: 360.1316 $[M + Na]^+$.

Aryltricyanoethylenes were prepared as described in [26]. 0.56 g (10 mmol) of malonodinitrile and 2 drops of piperidine were added to a solution of 10 mmol of arylbenzaldehyde **7** or **8** in 100 mL of EtOH. The reaction mixture was stirred during 24 h at room temperature. The precipitate was filtered off, washed with water (4×80 mL), and dried at room temperature under reduced pressure.

2-{4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]phenyl}-1,1-dicyanoethylene (9). Yield 58%, light yellow solid. IR spectrum, ν, cm^{-1}: 2226 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.27 s (2H, CH_2N), 5.55 s (2H, CH_2O), 7.10 d (2H, J = 8.9 Hz), 7.29–7.31 m (2H), 7.37–7.39 m (3H), 7.57 s (1H, CHN), 7.64 s [1H, $CH{=}C(CN)_2$], 7.89 d (2H, J = 8.9 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 54.40, 62.33, 79.12, 113.24, 114.32, 115.91, 122.97, 124.47, 128.20, 128.98, 129.24, 133.41, 134.27, 143.14, 158.74, 163.34.

2-{4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]-3-ethoxyphenyl}-1,1-dicyanoethylene (10). Yield 81%, light yellow solid. IR spectrum, ν, cm^{-1}: 2224 (C≡N).

^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.43 t (3H, $\underline{CH_3}CH_2O$, J = 7.0 Hz), 4.11 q (2H, $CH_3\underline{CH_2}O$, J = 6.9 Hz), 5.35 s (2H, CH_2N), 5.53 s (2H, CH_2O), 7.17–7.36 m (8H), 7.62 s (1H, CHN), 7.67 s [1H, CH=C$(CN)_2$]. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.53, 54.44, 63.06, 64.76, 78.78, 112.27, 113.49, 113.65, 114.34, 124.82, 127.92, 128.20, 128.96, 129.21, 130.69, 134.25, 149.28, 153.73, 159.12.

Synthesis 2-aryl-1,1,2-tricyanoethanes 11 and 12. 1.62 g (25 mmol) of KCN dissolved in 80 mL of water was added to a solution of 2-aryl-1,1-dicyanoethylene **10** or **12** (12 mmol) in 150 mL of EtOH, and then 240 mL of water was added. The so obtained mixture was stirred during 45 min at room temperature, and then 6 mL of 37% HCl was added. After cooling on a water bath, the precipitate was filtered off, thoroughly washed with water, and dried at room temperature and reduced pressure.

2-{4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]phenyl}-1,1,2-tricyanoethane (11). Yield 95%, white solid. IR spectrum, ν, cm^{-1}: 2226 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.46 d. d (2H, CHCH, J = 32.1, 5.5 Hz), 5.28 s (2H, CH_2N), 5.53 s (2H, CH_2O), 7.05 d (2H, J = 8.3 Hz), 7.28–7.43 m (9H), 7.54 s (1H, CHN). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 29.77, 38.15, 54.39, 62.12, 109.64, 115.24, 116.16, 120.76, 123.06, 128.21, 128.96, 129.24, 129.68, 134.31, 143.14, 159.97.

2-{4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]-3-ethoxyphenyl}-1,1,2-tricyanoethane (12). Yield 62%, white solid. IR spectrum, ν, cm^{-1}: 2226 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.41 t (3H, $\underline{CH_3}CH_2O$, J = 6.9 Hz), 4.09 q (2H, $CH_3\underline{CH_2}O$, J = 7.0 Hz), 4.32 d. d (2H, CHCH, J = 32.1, 5.5 Hz), 5.28 s (2H, CH_2N), 5.53 s (2H, CH_2O), 6.98–7.39 m (8H), 7.61 s (1H, CHN), 7.66 s (1H, CH=C$(CN)_2$). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.63, 29.86, 38.68, 54.43, 63.32, 64.89, 77.22, 109.40, 112.59, 114.93, 115.43, 120.87, 121.19, 123.03, 128.21, 128.95, 129.22, 134.26, 149.88, 149.94.

Synthesis of 1-aryl-1,1,2-tricyanoethylenes 13 and 14. 1.20 g (9.0 mmol) of *N*-chlorosuccinimide was added to a solution of 2-aryl-1,1,2-tricyanoethane **1** or **12** (6.4 mmol) in 100 mL of Et_2O. The reaction mixture was stirred at cooling (ice bath). After 1 h, 150 mL of water was added, the organic layer was separated off, and the mixture was washed with water (3×150 mL). The solvent was removed under reduced pressure, and the product was sublimed under reduced pressure.

2-{4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]phenyl}-1,1,2-tricyanoethylene (13). Yield 90%, yellow solid. IR spectrum, ν, cm^{-1}: 2233, 2225 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.30 s (2H, CH_2N), 5.55 s (2H, CH_2O), 7.15–7.40 m (8H), 7.57 s (1H), 8.09 s (1H, CHN). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 54.46 62.56, 88.08, 93.17, 111.86, 113.79, 116.44, 121.80, 123.11, 128.22, 129.03, 129.27, 129.85, 132.47, 134.17, 140.29, 164.47. Mass spectrum, *m/z* (I_{rel}, %): 366 (22) $[M]^+$, 367 (75) $[M + 1]^+$, 368 (25) $[M + 2]^+$.

2-{4-[(1-Benzyl-1,2,3-triazol-4-yl)methoxy]-3-ethoxyphentyl}-1,1,2-tricyanoethylene (14). Yield 67%, yellow solid. IR spectrum, ν, cm^{-1}: 2224 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.45 t (3H, $\underline{CH_3}CH_2O$, J = 7.0 Hz), 4.11 q (2H, $CH_3\underline{CH_2}O$, J = 6.9 Hz), 5.38 s (2H, CH_2N), 5.54 s (2H, CH_2O), 7.28–7.40 m (7H), 7.57 s (1H), 7.64 s (1H, CHN). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.44, 54.42, 63.21, 65.04, 87.26, 93,24, 111.72, 113.82, 113.88, 122.16, 123.22, 126.48, 128.22, 129.00, 129.24, 134.19, 140.25, 142.93, 149.44, 155.11. Mass spectrum, *m/z* (I_{rel}, %): 409 (100) $[M]^+$.

Synthesis of ytterbium complexes 15 and 16. A solution of 2.3 mmol of the corresponding 2-aryl-1,1,2-tricyanoethylene **13** or **14** in a degassed THF (5 mL) was added in small portions under inert atmosphere to a solution of 0.25 g (0.46 mmol) of bisindenyl complex of ytterbium(II) in 5 mL of THF. After 1 day, the solution was filtered under vacuum. To remove the unreacted 2-aryl-1,1,2-tricyanoethylene and its complex with ytterbium, the obtained solution was washed with degassed toluene until discoloration. The product was dried under reduced pressure.

Synthesis of porphyrazines 17 and 18. A solution of 0.14 mmol of the corresponding ytterbium complex **15** or **16** in 2 mL of trifluoroacetic acid was stirred at room temperature during 30 min, and then 30 mL of water was added. The formed precipitate was centrifuged off and thoroughly washed with water to neutral reaction. The product was purified by column chromatography (silica gel 60, 40–60 μm, eluent—THF).

Tetra{4-[(1-benzyl-1,2,3-triazol-4-yl)methoxy]-phenyl}tetracyanoporphyrazine (17). Yield 23%, black solid, mp >300°C. IR spectrum, ν, cm^{-1}: 3394 (N–H), 2193 (C≡N), 1603 (C=C); 1218, 1030 (C_{Ar}–O–C). Electronic absorption spectrum (H_2O), λ_{max}, nm: 359 (Soret band), 593 (*Q*-band). Mass spectrum, *m/z*: 1465 $[M]^+$. Found, %: C 68.95; H 3.90; N 23.02. $C_{84}H_{58}N_{24}O_4$. Calculated, %: C 68.75; H 3.98; N 22.91.

Tetra{4-[(1-benzyl-1,2,3-triazol-4-yl)methoxy}-3-ethoxyphenyl}tetracyanoporphyrazine (18). Yield 27%, black solid, mp >300°C. IR spectrum, ν, cm^{-1}: 3403 (N–H), 2196 (C≡N), 2879, 2935 (C–H), 1596 (C=C); 1216, 1037 (C_{Ar}–O–C). Electronic absorption spectrum (H_2O), λ_{max}, nm: 362 (Soret band), 591 (*Q*-band). Mass spectrum, *m/z*: 1641 $[M]^+$. Found, %: C 67.56; H 4.41; N 20.67. $C_{92}H_{74}N_{24}O_8$. Calculated, %: C 67.22; H 4.54; N 20.45.

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CONFLICT OF INTERESTS

No conflict of interest was declared by the authors.

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