Electronic supplementary materials *Mendeleev Commun.*, 2024, **34**, 492–495

Nanosized systems of aluminum phthalocyanine and amphiphilic copolymers of *N*-vinylpyrrolidone with mono- and dimethacrylates for photodynamic therapy and fluorescence diagnostics

Svetlana V. Kurmaz, Ivan V. Ulyanov, Nina S. Emelyanova, Vladimir A. Kurmaz, Alexey V. Kozlov, Lev R. Sizov and Alexander Yu. Rybkin

Table of contents

Materials

N-vinylpyrrolidone (99%, Alfa Aesar) was distilled in vacuum to remove the inhibitor (NaOH). Triethylene glycol dimethacrylate (95%, Aldrich) and PEGMEM (Aldrich), 1-decanethiol (Aldrich) were used without additional purification; *i*-PrOH (“Khimmed”, Russia) was used as received. DMSO (“Lab-Scan”, Poland) was purified before use with freezing, aluminum phthalocyanine chloride were synthesized by the method.[S1]

The methods

Electronic absorption spectroscopy

The absorption spectra of PcAlCl solutions in DMSO, terpolymer and PcAlCl/copolymer compositions in water solution or DMSO were recorded on a Specord M40 in quartz cuvettes of 0.5 or 1 cm thickness.

Dynamic light scattering

The dynamic light scattering method was used to determine the hydrodynamic radii, R_h, of a terpolymer and its nanostructures with PcAlCl in phosphate-buffered saline solutions. To prepare samples for measurements, the solutions were filtered using a filter with a pore diameter of 0.45 μm. Before measuring, the vials with the solution were thermostated at a given temperature for 20 min. DLS measurements were carried out using a Photocor Compact setup (Photocor LTD, Russia) equipped with a diode laser operating at a wavelength of 654 nm. All solutions were analyzed at a detection angle of 90°. The processing of experimental data was carried out using the DynaLS software, version 2.8.3.

Synthesis of copolymers

The double copolymer CPL1 was obtained from the reaction mixture VP-TEGDM with a molar ratio 100 : 5. The terpolymers CPL3, CPL4 and CPL2 were obtained in toluene by a radical copolymerization in the presence of 1-decanethiol (DT) as a chain transfer agent or without any chain growth regulators at monomer molar ratio VP–PEGMEM–TEGDM–DT of 95 : 5 : 5 : 5, 98 : 2 : 5 : 0, 95 : 5 : 5 : 0, respectively. The terpolymer CPL5 has been developed from a reaction mixture VP–cyclo-HMA–TEGDM of 98 : 2 : 5 : 0 molar relation, respectively.

Physicochemical characteristics of VP copolymers

Table S1 Physicochemical characteristics of VP copolymers used to obtain water-soluble PcAlCl nanostructures

Copolymers	Monomer composition	Molar ratio of VP-(di)methacrylates units / %	M_w / kDa	Hydrodynamic radius, R_h / nm
CPL1	VP–TEGDM	94.6 : 5.4	24	4; 77
CPL2	VP–PEGMEM–TEGDM	89.0 : 11.0	260	5; 42
CPL3		86.5 : 9.9	19	4; 77
CPL4		90.7 : 9.3	120	2; 31
CPL5	VP–cyclo-HMA–TEGDM	90.9 : 9.1	126	49

PcAlCl encapsulation in copolymers

To encapsulate PcAlCl, solutions of copolymers in isopropyl alcohol (*i*-PrOH) with a concentration of 3.5 mg ml^{-1} and a solution of PcAlCl in DMSO (1.4 mg ml^{-1}) were prepared. To 32 ml of solutions of copolymers CPL1, CPL2, CPL3, CPL4, 1.2 ml of a solution of PcAlCl in DMSO was added dropwise with constant stirring, and 0.7 ml of the same solution was added with the same manner to CPL5. The calculated PcAlCl content per copolymer was ~1.5 and 0.88%, respectively. Solutions of copolymers with encapsulated PcAlCl were dried from organic solvents in air and in vacuum at room temperature and at 60 °C, and the dye/copolymer compositions in the form of the dry powder were obtained.

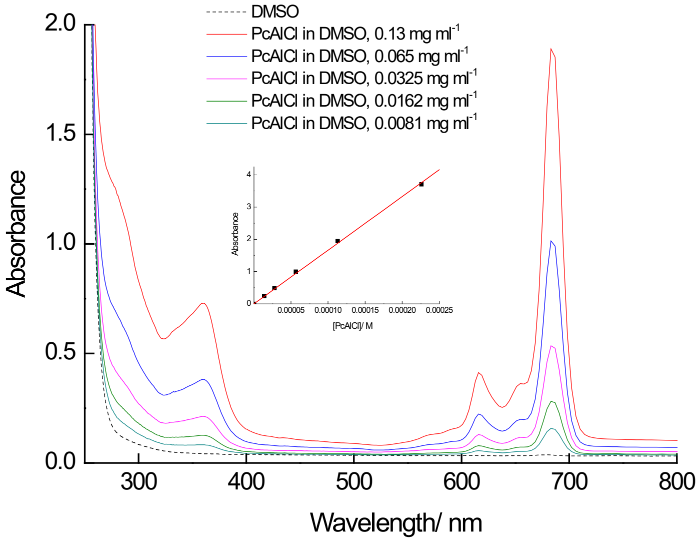


Figure S1 Dependence of the optical absorption density of PcAlCl on its concentration in DMSO in the range of 250–800 nm. Cuvette – 0.5 cm. The inset shows the dependence of the optical density of the

PcAlCl absorption band on its concentration in DMSO at λ = 683 nm. The extinction coefficient $\varepsilon = 1.7 \times 10^4$ M^{-1} cm^{-1}.

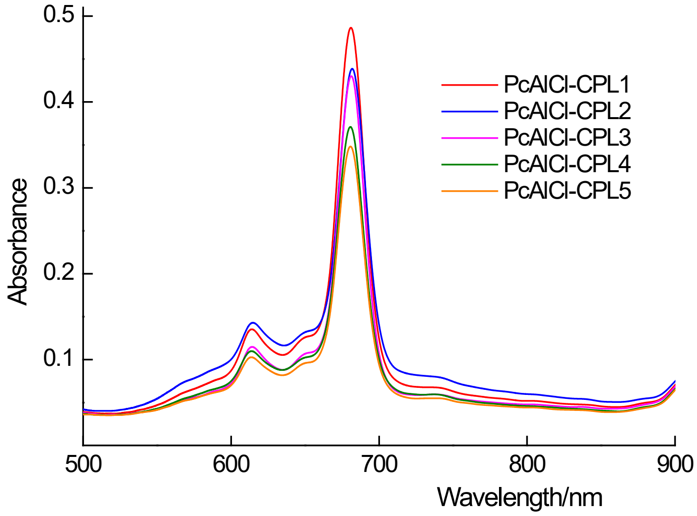


Figure S2 Absorption spectra of PcAlCl–CPL1, PcAlCl–CPL2, PcAlCl–CPL3, PcAlCl–CPL4 and PcAlCl–CPL5 in DMSO with concentrations of 1.2, 1.0, 1.0, 0.86 and 1.44 mg ml^{-1}, respectively. All measurements were taken in 1 cm quartz cuvette.

Fluorescence spectroscopy and quantum yield calculation

Fluorescence steady-state spectra were recorded by a Cary-Eclipse spectrofluorimeter. For measurements, we used aqueous solutions of compositions with an equal content of PcAlCl – 7.64×10^{-2} mg ml^{-1} (1.33×10^{-5} M). Fluorescence was excited at the wavelength of 630 nm, and the excitation and emission slits were 5 nm. Fluorescence spectra were recorded in the range of 650–800 nm.

Quantum yield was calculated using the formula:

$$\frac{\Phi_1^{fl}}{\Phi_2^{fl}} = \frac{(1 - 10^{-A_2})}{(1 - 10^{-A_1})} \frac{n_1^2}{n_2^2} \frac{\alpha_1}{\alpha_2},$$

where Φ^{fl} is the fluorescence quantum yield; A – optical density of the test solution; n is the refractive index of the solvent; α is the area of the fluorescence peak. Indices 1 and 2 refer to the standard dye and the composition under study, respectively. For the standard dye, $\Phi_1^{fl} = 0.15$,[S2] $A_1 = 0.00952$, $n_1 = 1.3396$ (ethanol) and $\alpha_1 = 700.9$ a.u.

Stability of PcAlCl–copolymer NPs aqueous solution

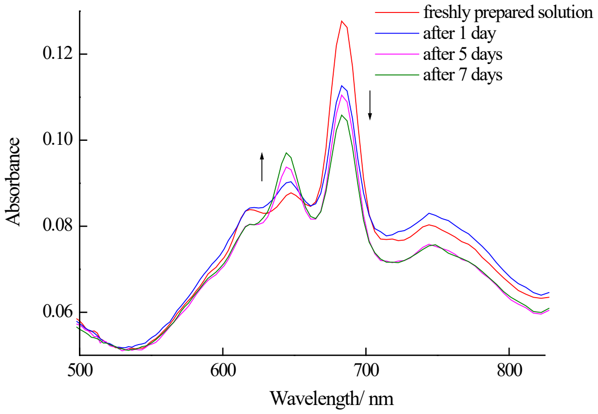


Figure S3 Absorption spectra of a freshly prepared aqueous solution of PcAlCl–CPL5 after 1, 5 and 7 days of storage at room temperature in the dark.

Distribution of light scattering intensity by size of scattering centers of PcAlCl–copolymer NPs in phosphate buffer saline solutions

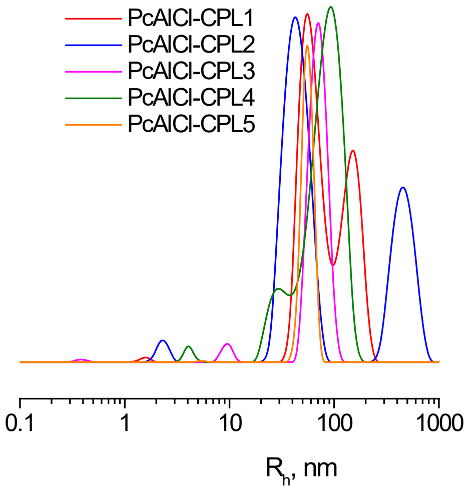
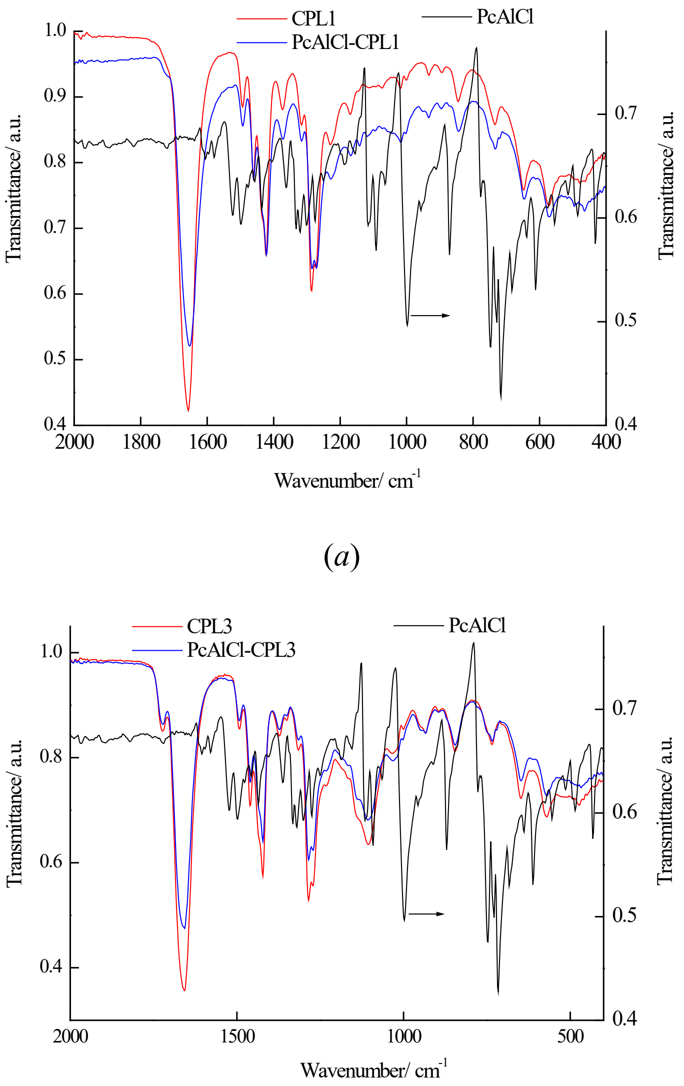


Figure S4 Light scattering intensity distribution curves by the size of scattering centers of PcAlCl–copolymer NPs based on CPL1, CPL2, CPL3, CPL4 and CPL5 in PBS, pH 7.4 (137 mM NaCl, 2.68 mM KCl, 4.29 mM Na_2HPO_4 and 1.47 mM KH_2PO_4).



(*a*)

(*b*)

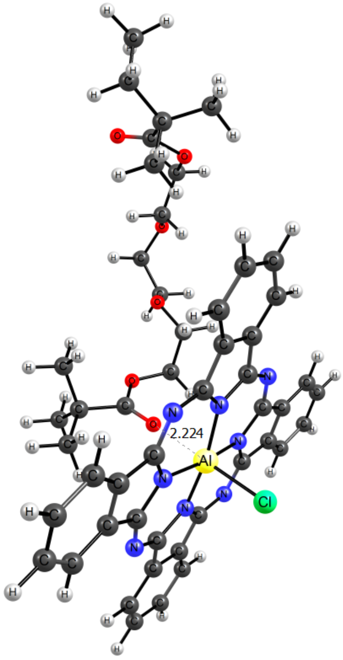
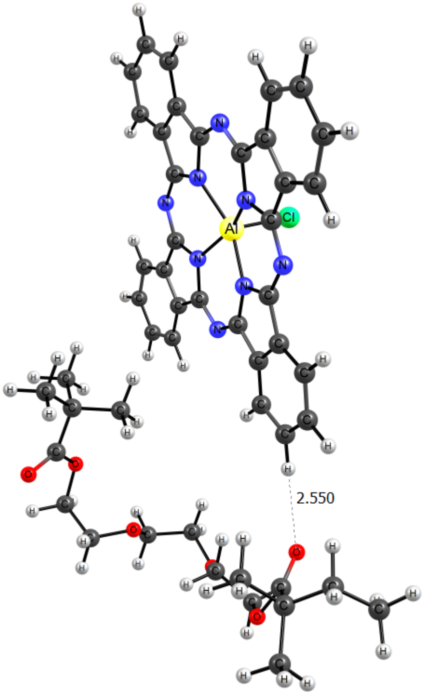
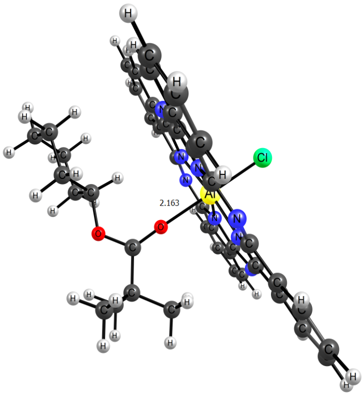
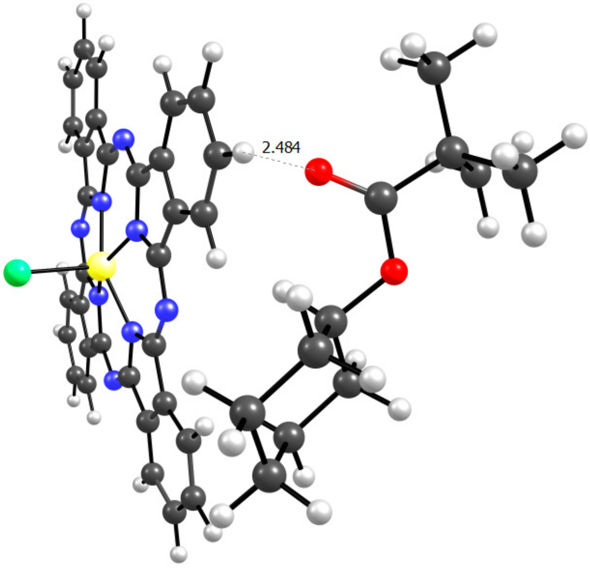
Figure S5 IR-FTIR spectra of PcAlCl, PcAlCl–CPL1 (*a*) and PcAlCl–CPL3 (*b*) powders.

Quantum-chemical modeling of PcAlCl–monomer units interactions

Quantum-chemical calculations were carried out within the framework of the density functional theory (DFT) with full optimization of the geometry of the initial molecules and their complexes in the Gaussian 09 program.[S3] The hybrid functional TPSSh[S4] and the basis set 6-31G*//6-311++G** were used as a method and basis. The influence of the solvent (water) was also taken into account using the polarizable continuum model (PCM). There are no imaginary vibration frequencies in the calculation results, all optimized structures correspond to the minimum potential energy.

To analyze the wave functions using the QTAIM method, the AIMALL software package (version 10.05.04)[S5] was used. The wave functions of the structures were calculated in the same approximations as the geometry optimization. In particular, from the analysis of the wave functions, we found the energies of intermolecular bonds (E_{bonds}), the electron density (ρ) and the Laplacian of the electron density ($\nabla^2\rho$) at the critical points of the bond. The energies of intermolecular bonds were calculated using the formula $E_{\text{a-b}} \approx 1/2 v_e(r)$,[S6] where $E_{\text{a-b}}$ is the A–B bond energy, and $v_e(r)$ is the potential energy density at the critical point of the A–B bond. The illustrations were made using the ChemCraft program (version 1.8).[S7]

Table S2. Possible structures of PcAlCl with TEGDM and cyclo-HMA monomer units

The monomer unit of a copolymer	Al (PcAlCl) as a center of the bonding	H (C–H) as a center of the bonding
TEGDM		
cyclo-HMA		

The work was performed on state assignment, state registration number 124013000722-8, 124020500019-2 and 124013000692-4.

References

S1 A. Ogunsipe and S. Opeolu, *Chem. Res. J.* 2020, **5**, 136–143.

S2 E. Zenkevich, E. Sagun, V. Knyukshto, A. Shulga, A. Mironov, O. Efremova, R. Bonnett, S. P. Songca and M. Kassem, *J. Photochem. Photobiol. B Biol*. 1996, **33**, 171.

S3 M. J. Frisch, G. W. Trucks, H. B. Schlegel et al (Gaussian, Inc., Wallingford CT, 2009).

S4 J. M. Tao, J. P. Perdew, V. N. Staroverov and G. E. Scuseria, *Phys Rev Lett.*, 2003, **91**, 146401.

S5 AIMAll (version 10.05.04), Todd A. Keith, T. K Gristmill Software, Overland Park KS, USA, 2010 (aim.tkgristmill.com).

S6 E. Espinosa, E. Molins and C. Lecomte, *Chem Phys Lett.*, 1998, **285**, 170.

S7 Chemcraft - graphical software for visualization of quantum chemistry computations. https://www.chemcraftprog.com