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Supplementary Information

Carbocyanine-Based Fluorescent and Colorimetric Sensor Array for the Discrimination of Medicinal Compounds

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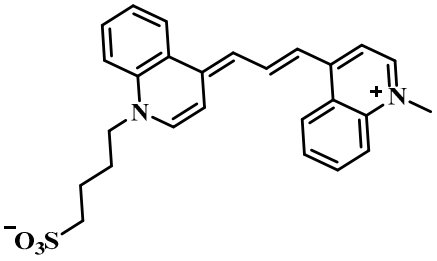
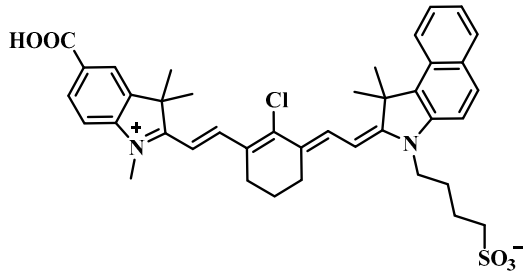
Protocols for the Syntheses of Dyes 2–4 And Spectral Data



Dye 2: 4-((E)-4-((E)-3-(1-methylquinolin-1-ium-4-yl)allylidene)quinolin-1(4H)-yl)butan-1-sulfonate.

0.50 g (1.2 mmol) of (E)-1-methyl-4-(2-(N-phenylacetamide)vinyl)quinolin-1-ium iodide and 0.32 g (1.2 mmol) of 4-(4-methylquinoline-1-ium-1-yl)butan-1-sulfate, 1.5 mL (12 mmol) of triethylamine and 20 mL of methylene chloride were mixed in a vial. The reaction mixture was kept for 16 h at room temperature with stirring. Methylene chloride was evaporated in a vacuum, the residue was dissolved in a mixture of methylene and methanol, after which an excess of acetone was added. The precipitate formed was filtered off, washed with acetone, and dried. Yield: 1.5 g (84%), dark blue powder. λ_{abs} = 705 nm (methanol), λ_{fl} = 729 nm (ethanol), ε = 1.2×10^5 L·mol·cm^{-1}.

^{1}H NMR spectrum (DMSO, δ, ppm; J/Hz): 1.56-1.71(m, 2H, CH_2), 1.78-1.91(m, 2H, CH_2), 2.53(t, 2H, $^3J_{HH}$ = 5.4, $CH_2SO_3^-$), 3.98 (s, 3H, N^+CH_3), 4.33 (t, 2H, $^3J_{HH}$ = 6.8, NCH_2), 7.01 (d, 1H, $^3J_{HH}$ = 12.6, =CH), 7.04 (d, 1H, $^3J_{HH}$ = 12.6, =CH), 7.49–7.66 (m, 4H, arom.), 7.71–7.87 (m, 4H, arom.), 7.96 (t, 2H $^3J_{HH}$ = 7.2, arom.), 8.33 (t, 2H, $^3J_{HH}$ = 9.29, arom.), 8.55 (t, 1H, $^3J_{HH}$ = 13.0, =CH). ^{13}C NMR spectrum (DMSO, δ, ppm): 21.64 (CH_2), 27.26 (CH_2), 45.01 (NCH_2), 50.07 ($CH_2SO_3^-$), 51.47 (N^+CH_3), 107.83, 109.78, 116.90, 117.13 (all arom.), 118.40 (=CH), 122.35, (arom.), 122.40 (=CH), 123.37 (arom.), 123.57 (=CH), 124.00, 124.22, 125.36, 128.03, 132.02, 137.40, 138.40, 138.76, 140.24, 140.80, 141.95, 147.86 (all arom.). IR, ν/cm^{-1}: 1134.9 (SO_3), 1463.22 (CH_3), 1613.13 ($C=N^+$), 2851.72 (N-CH_3), 2922.11 (CH_2). HRMS-ESI: found m/z 447.1746 $[M+H]^+$. $C_{48}H_{53}N_2O_9S_2$. Calculated: M = 447.1737.

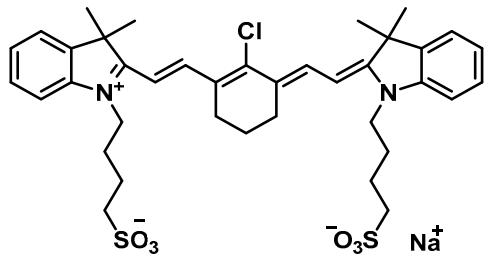


Dye 3:

4-(2-((E)-2-((E)-3-((E)-2-(5-carboxy-1,3,3-trimethylindolin-2-ylidene)ethylidene)-2-chlorocyclohex-1-en-1-yl)vinyl)-1,1-dimethyl-1H-benzo[e]indol-3-ium-3-yl) butane-1-sulfonate.

0.021 g (0.037 mmol) 3-(2-((E)-2-((E)-2-chloro-3-((N-phenylacetamide)methylene) cyclohex-1-en-1-yl)vinyl)-1,1-dimethyl-1H-benzo[e]indol-3-ium-3-yl)propan-1-sulfonate, 0.026 g (0.037 mmol) 5-carboxy-1,2,3,3-tetramethyl-3H-indol-1-ium iodide and 0.03 g (0.37 mmol) sodium acetate were mixed in a vial. The resulting mixture was dissolved in 4 mL of acetonitrile. The reaction mixture was heated at 70°C for 9 h, after which it was cooled to room temperature. The precipitate formed upon addition of excess diethyl ether was filtered off and dried. The target compound was purified by flash chromatography on silica gel (CH_2Cl_2:MeOH = 50:1). Yield 0.026 g (36%), dark green powder. λ_{abs} = 790 nm (methanol), λ_{fl} = 830 nm.

^{1}H NMR spectrum (CD_3OD, δ, ppm; J/Hz): 1.91 (s, 6H, $C(CH_3)_2$), 1.92-1.96 (m, 4H, CH_2), 1.98 (s, 6H, $C(CH_3)_2$), 2.02-2.07 (m, 2H, CH_2), 2,69 (t, 2H, $^3J_{HH}$ = 6.0, CH_2), 2,75 (t, 2H, $^3J_{HH}$ = 5.9, CH_2), 2,89 (t, 2H, $^3J_{HH}$ = 7.2, CH_2), 3.63 (s, 3H, NCH_3), 4.32 (t, 2H, $^3J_{HH}$ = 7.0, N^+CH_2), 6.15 (d, 1H, $^3J_{HH}$ = 14.0, =CH), 6.36 (d, 1H, $^3J_{HH}$ = 14.3, =CH), 7.37 (d, 1H, $^3J_{HH}$ = 7.8, arom.), 7.41-7.48 (m, 2H, arom.), 7.60 (d, 2H, $^3J_{HH}$ = 8.0, arom.), 7.65 (d, 1H, $^3J_{HH}$ = 8.8, arom.), 7.96 (d, 1H, $^3J_{HH}$ = 8.2, arom.), 8.00 (d, 1H, $^3J_{HH}$ = 8.8, arom.), 8.23 (d, 1H, $^3J_{HH}$ = 8.5, arom.), 8.42 (d, 1H, $^3J_{HH}$ = 14.0, =CH), 8.52 (d, 1H, $^3J_{HH}$ = 14.3, =CH). IR, ν/cm–1: 1711 (COOH). HRMS-ESI: found m/z 699.2644 $[M+H]^+$. $C_{40}H_{43}ClN_2O_5S$. Calculated: M = 699.2654.



Dye 4:

4-((E)-2-((E)-2-(2-chloro-3-((E)-2-(3,3-dimethyl-1-(4-sulfonatobutyl)-3H-indole-1-i-2-yl)vinyl)cyclohex-2-en-1-ylidene)ethylidene)-3,3-dimethylindolin-1-yl)butan-1-sulfonate sodium. The dye was synthesized following paper [1].

^{1}H NMR spectrum (DMSO, δ, ppm.; *J*/Hz): 1.65 (s, 12 H, 2 $C(CH_3)_2$), 1.69-1.75 (m, 4 H, 2 CH_2), 1.76-1.87 (m, 6 H, 3 CH_2), 2.72 (t, 4 H, $^3J_{HH}$ = 5.8, 2 CH_2), 3.13-3.18 (m, 4 H, 2 CH_2SO_3), 4.20 (t, 4 H, $^3J_{HH}$ = 7.0, 2 CH_2N^+), 6.36 (d, 2 H, $^3J_{HH}$ = 14.2, 2 =CH), 7.23-7.30 (m, 2 H, arom.), 7.37-7.44 (m, 2 H, arom.), 7.45-7.50 (d, 2 H, arom.), 7.61 (d, 2 H, $^3J_{HH}$ = 7.3, arom.), 8.24 (d, 2 H, $^3J_{HH}$ = 14.1, 2 =CH). λ_{abs} = 780 nm (in methanol). λ_{fl} = 799 нм (in ethanol).

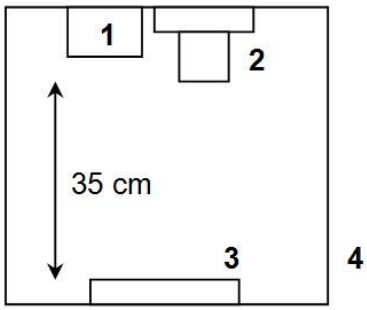


Figure S1. Scheme of the NIR visualizer: 1 – light source (eleven 3-Wt red LEDs with an emission maximum of 660 nm, Minifermer, Moscow, Russia); 2 – a NIR digital camera (modernized Nikon D80 photo camera with a light filter transmitting only light with wavelengths above 700 nm). (Photodrom, Moscow); 3 – fluorimetric plate; 4 – light-protective casing.

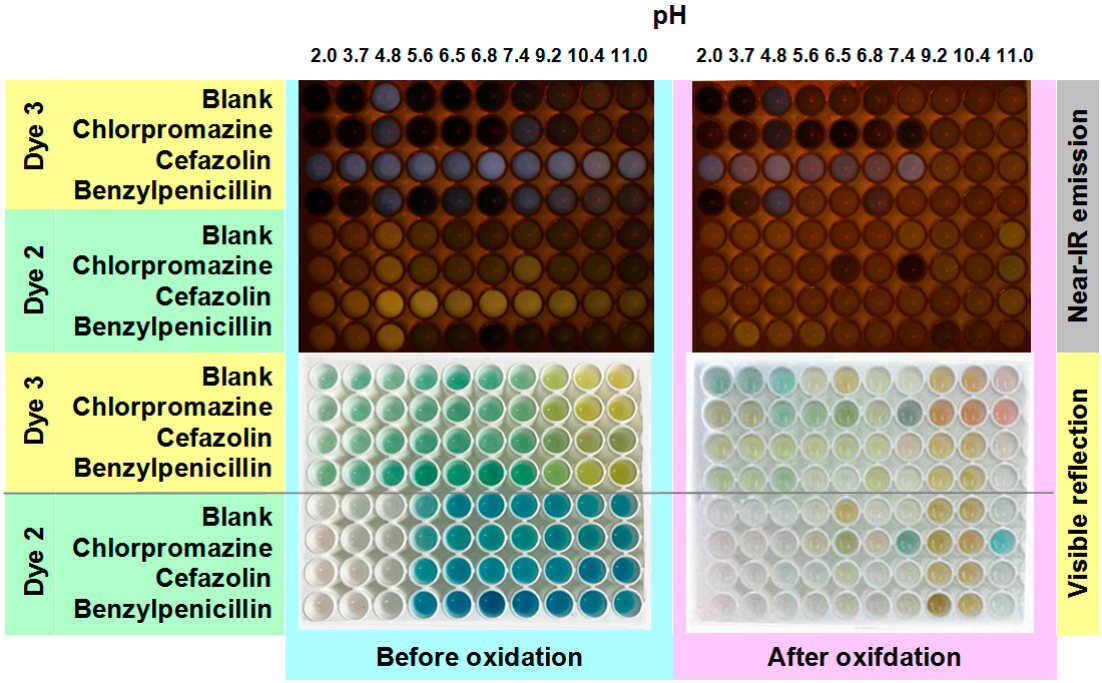


Figure S2. Effect of pH on the NIR fluorescence (two upper photographs) and visible images (two lower photographs) in the presence of carbocyanine dyes **2** and **3** and three model analytes (chlorpromazine, cefazolin, benzylpenicillin) and the blank. Every analyte occupies two rows of the plate: in the presence of dye **3** in one of the first rows (A–D) and in the presence dye **2** in one of the last 4 rows (F–H). Equal pH values are in columns. The left-hand pair of photographs was obtained before oxidizing, while the right-hand photographs were taken 4 min (NIR) and 5 min (vis) after the start of the redox reaction (Cu^{2+}, H_2O_2). Conditions: 30 µL of buffer (0.1M HCl for pH 2.0, 0.1M acetate buffer (pH 3.6–6.8), 0.067M phosphate buffer (pH 7.4), 0.05M borate buffer (pH 9.2–10.4) or 0.1M glycinate buffer (pH 11.0); 180 µL of water, 30 µL of 1 mM CTAB, 30 µL of 5 mM model analyte, 30 µL of 0.1 g/L dye, 30 µL of 1M H_2O_2, and 30 µL of 1 mM $CuSO_4$.

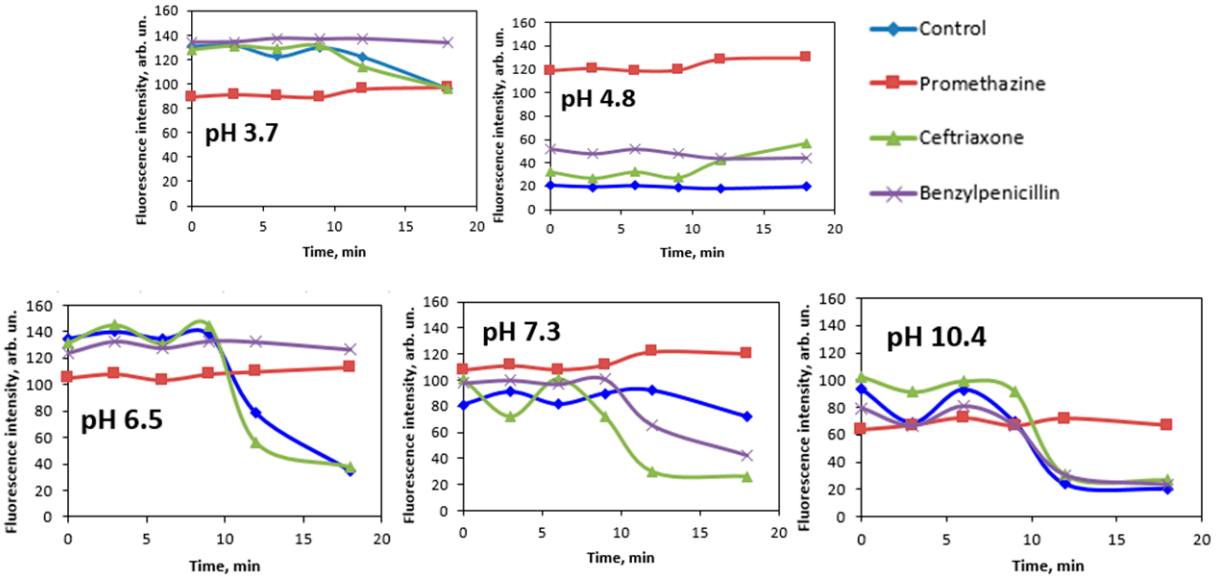


Figure S3. Kinetic curves for the redox system *dye 4 – H_2O_2 – Cu(2+)* with three selected analytes (shown in the legend) and the blank experiment for pH 3.6–10.4. The reaction was conducted in a 96-well plate, see Fig. S2 for concentrations. The fluorescence intensity was obtained from the NIR photographs taken every several minutes.

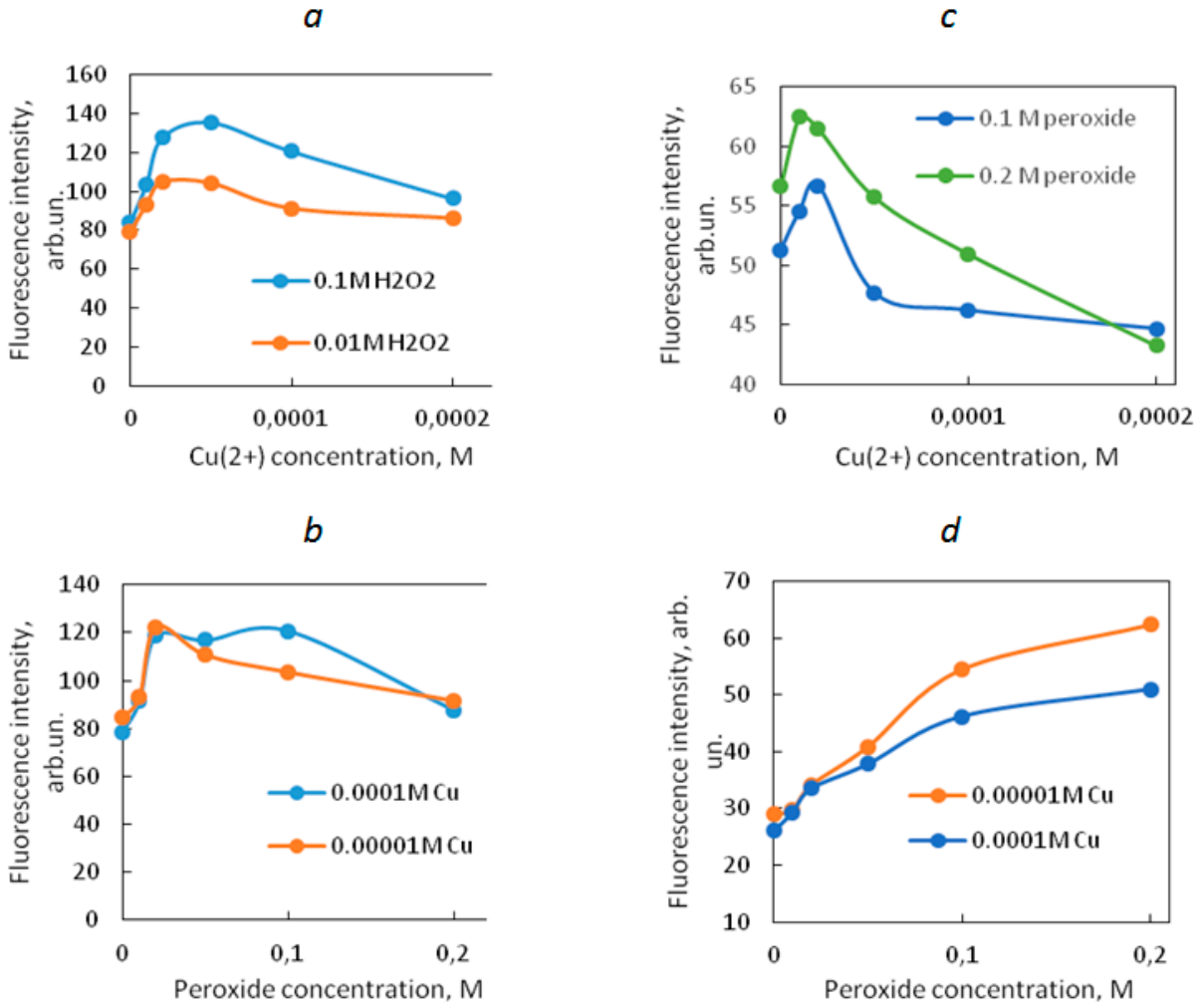


Figure S4. Effect of the concentration of hydrogen peroxide and $CuSO_4$ on the NIR fluorescence intensity of reaction products (*a, b* – dye **1**; *c, d* – dye **3**) at 2 min after the reaction start. The concentrations shown in the graphs are final in the 96-well plate. Other conditions: 0.0067M phosphate buffer (pH 7.4), 0.1 mM CTAB, 0.01 g/L dye.

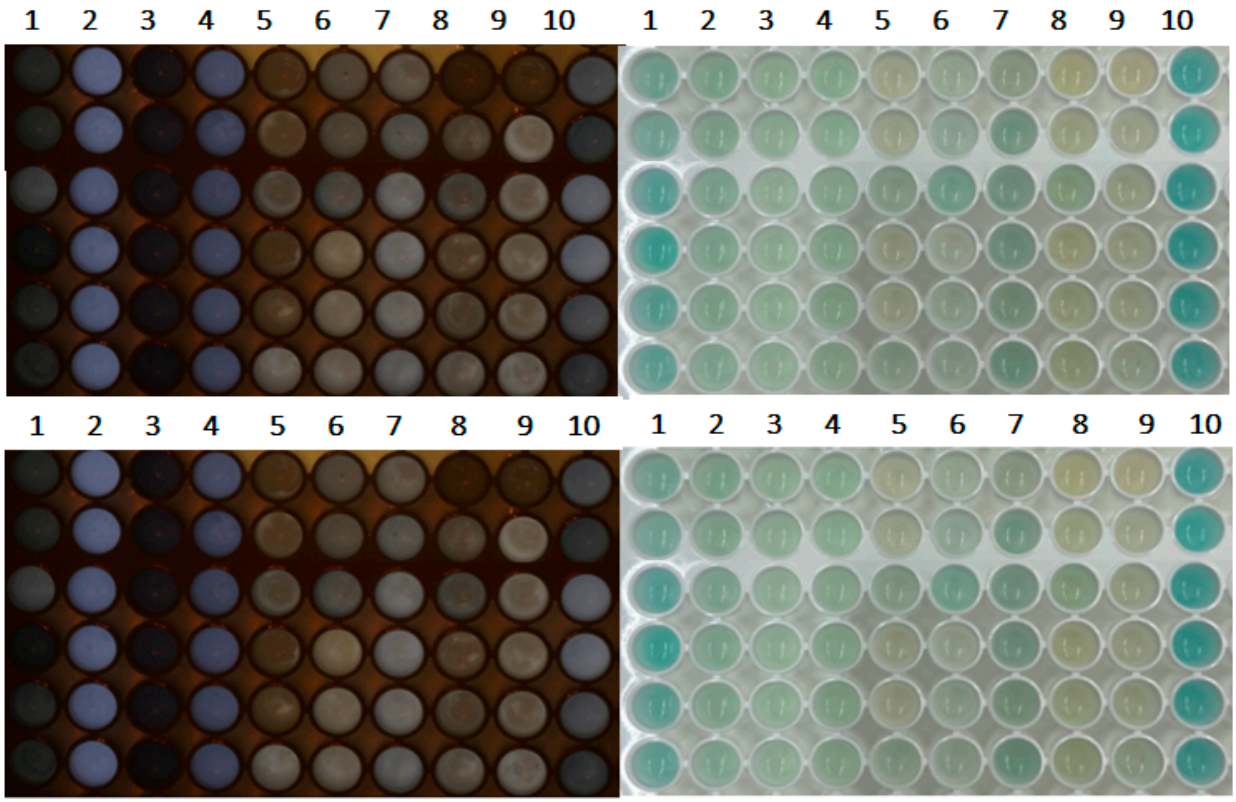
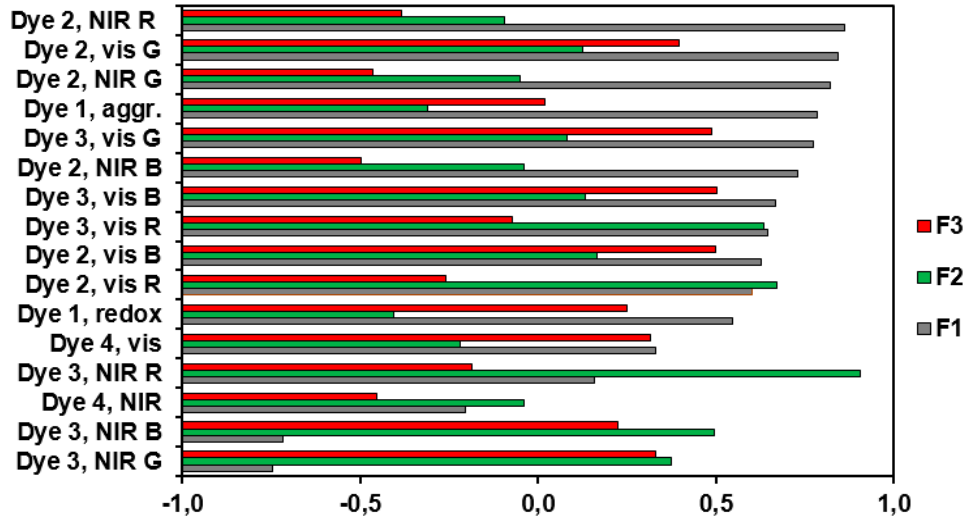
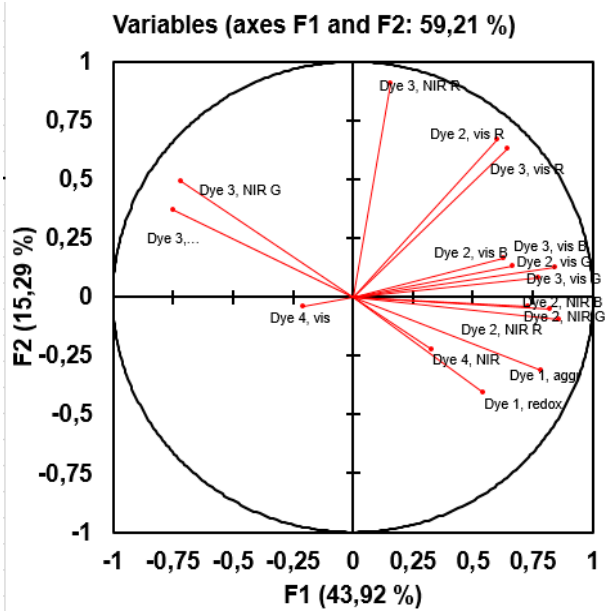


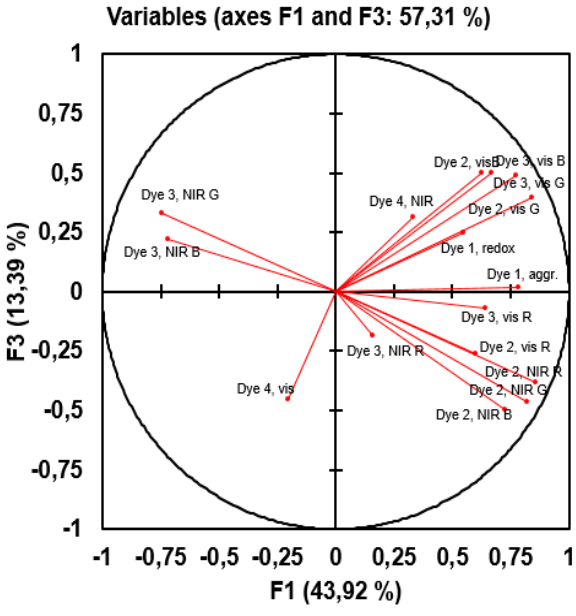
Figure S5. Images used for the data treatment obtained with 9 analytes after 4 min of oxidation of dye **4** with H_2O_2. First column – without analyte, 2nd column – with promethazine, 3rd – promazine, 4 – chlorpromazine, 5 – ceftriaxone, 6 – cefazolin, 7 – ceftazidime, 8 – cefotaxime, 9 – benzylpenicillin, 10 – ampicillin. All wells in a column represent 6 parallel runs. Conditions: a 30 µL volume of each of the following solutions were added to a 96-plate well: 0.067M phosphate buffer (pH 7.4), 8 mM SDS, 5 mM model analyte, 0.1 g/L dye 3, 1M H_2O_2, and 60 µL of 0.3 mM $CuSO_4$, 180 µL of water.



(a)



(b)



(c)

Figure S6. a: Loadings plot for the first three principal components for the basic data set (16 data columns); **b, c**: circular factor diagrams representing the correlations between variables and factors for the basic data set: ***b*** – PC2 vs PC1, ***c*** – PC3 vs PC1.

Reference:

1. Narayanan, N.; Patonay, G. A New Method for the Synthesis of Heptamethine Cyanine Dyes: Synthesis of New Near-Infrared Fluorescent Labels. *J. Org. Chem*. **1995**, *60*, 2391–2395. https://doi.org/10.1021/jo00113a018.