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*O.K. Farat, S.A. Varenichenko, V.I. Markov***SYNTHESIS AND SPECTRAL PROPERTIES OF NEW XANTHENE-LIKE FLUOROPHORE AND LIGHT-FILTER****Ukrainian State University of Chemical Technology, Dnipro, Ukraine**

By the reaction of N'-(4-formyl-2,3-dihydro-1H-benzo[b]xanthen-12-yl)-N,N-dimethylimidoforamide and N'-(6-formyl-7,8,9,10-tetrahydrocyclohepta[b]chromen-11-yl)-N,N-dimethylimidoforamide with malononitrile and cyanoacetic acid ethyl ester, the following two new dyes were synthesized by basic catalysis: N'-[4-(2,2-dicyanovinyl)-2,3-dihydro-1H-benzo[b]xanthen-12-yl]-N,N-dimethylimidoforamide and ethyl (2E)-2-cyano-3-(11-[(1E)-(dimethylamino)methylene]amino)-7,8,9,10-tetrahydrocyclohepta[b]chromen-6-yl)acrylate. Both dyes in solution have a purple color with high extinction coefficients, but due to the different size of the partially saturated cycle, the first one displays fluorescence, and the second one does not. The fluorescence quantum yields for N'-(4-formyl-2,3-dihydro-1H-benzo[b]xanthen-12-yl)-N,N-dimethylimidoforamide decrease with decreasing solvent polarity. For example, the highest emission quantum yield is observed in methanol (2.76%), while the smallest is observed in tetrahydrofuran (1.04%). It is due to the fact that methanol implies a lesser energy consumption during the redistribution of electron density in the excited state. N'-[4-(2,2-dicyanovinyl)-2,3-dihydro-1H-benzo[b]xanthen-12-yl]-N,N-dimethylimidoforamide dye can be used as a fluorophore, whereas ethyl (2E)-2-cyano-3-(11-[(1E)-(dimethylamino)methylene]amino)-7,8,9,10-tetrahydrocyclohepta[b]chromen-6-yl)acrylate dye can be used as a light filter to create a variety of materials and devices. In addition, the synthesized compounds can be used as building-blocks in organic chemistry.

Keywords: xanthene-like dye, fluorophore, light-filter, Knoevenagel reaction, quantum yield.

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Introduction

Xanthene derivatives, as well as its benzannulated analogs, are very important heterocyclic compounds that are widely used as fluorescent dyes for visualization of biomolecules, as well as in laser technologies due to their useful optical properties [1]. Their ability to convert light allows using them from optical fibers to filters [2]. In addition, some representatives of this heterocyclic series exhibit biological activity, for instance bactericidal [3], anti-inflammatory [4], antiviral effects [5], and many others [6]. Due to the presence of a wide range of useful properties of these compounds, the synthesis and study of their properties is receiving growing attention from scientists around the world.

Results and discussion

Previously, we developed new methods for the synthesis of xanthene derivatives and its benzanalogues by rearrangement of the corresponding 1,3-benz(naphth)oxazines [7,8] and 1,3-benzo(naphtho)dioxin-4-ones [9] under the action of the Vilsmeier-Haack reagent. Based on the obtained (benzo)xanthene derivatives, new fluorophores and dyes were synthesized and characterized [10–12].

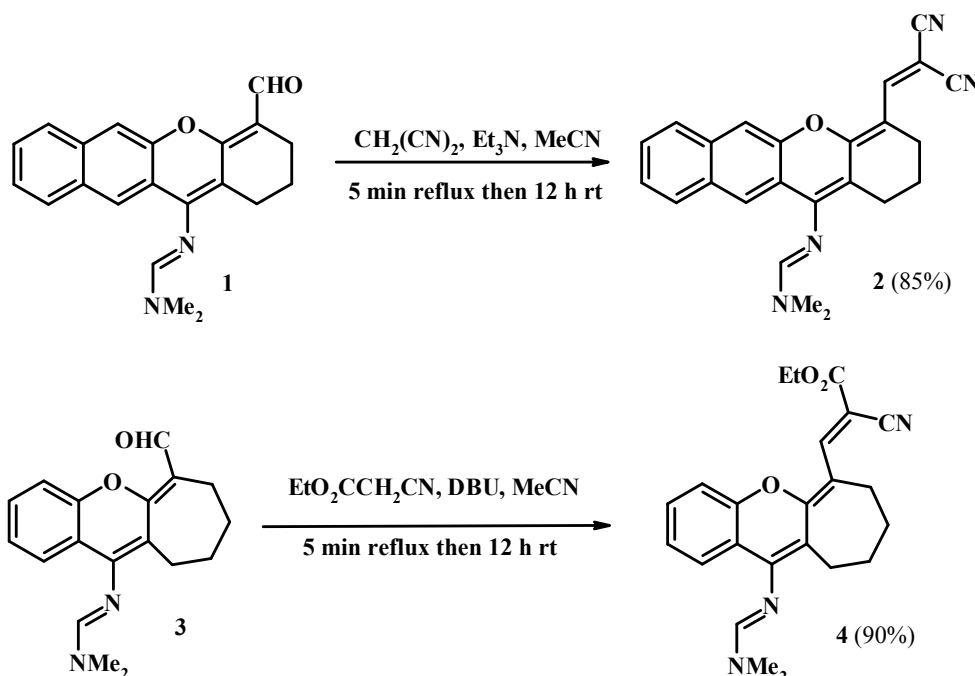
In continuation of these works, we synthesized dyes with predicted spectral properties. The reaction of aldehyde 1 [7] with malononitrile in the presence of triethylamine in acetonitrile produced benzoxanthene dye 2 with a high yield, and the reaction of chromene 3 [7] with cyanoacetic ester by DBU catalysis yielded the corresponding dye 4

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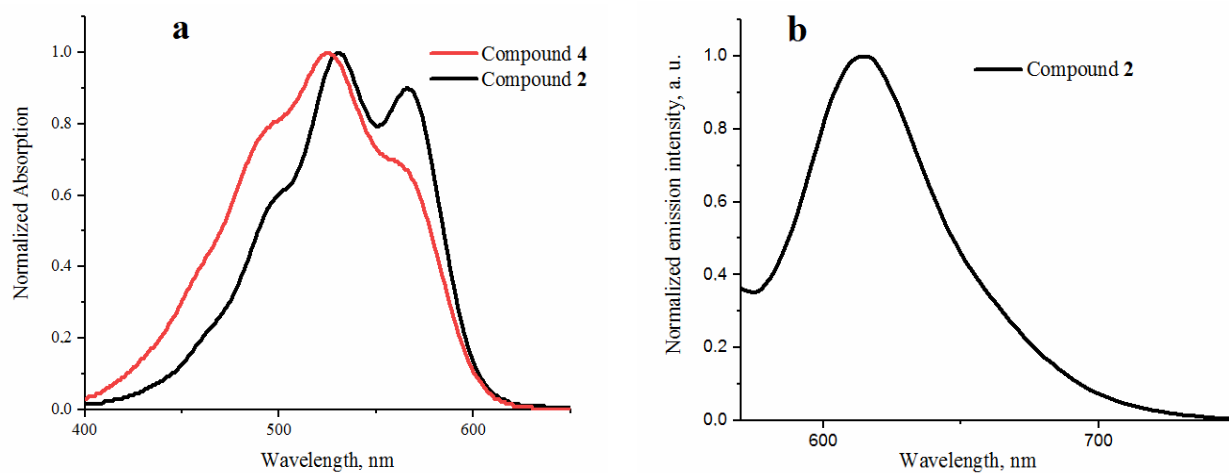
Scheme

(Scheme). The electrophilicity of the carbonyl group in aldehydes 1 and 3 is significantly reduced due to conjugation with an electron-donating oxygen atom. This is evidenced by the data of IR spectroscopy (absorption band at $\approx 1630\text{ cm}^{-1}$) and an X-ray structural study, according to which the length of the C=O double bond of $1.227(3)\text{ \AA}$ is significantly longer than the average length of C=O bonds in aldehydes 1.192 \AA [13]. Despite the reduced reactivity of the carbonyl group in these aldehydes, they react with active CH acids (malononitrile, cyanoacetic ester) under basic catalysis.

The structure of the synthesized compounds 2 and 4 has been rigorously proven by modern

physicochemical methods of analysis (^1H and ^{13}C NMR spectroscopy, as well as mass-spectrometry).

For compound 2, absorption and emission spectra were recorded in solvents with different polarity (Figure and Table). Compound 2 exhibits very similar optical properties in all solvents. The absorption maximum for compound 2 is observed at $\approx 530\text{ nm}$ with an extinction coefficient of $\approx 6.05 \cdot 10^4\text{ (M}^{-1}\text{ cm}^{-1}\text{)}$, and an emission maximum at $\approx 610\text{ nm}$. The shape and size of the absorption and emission spectra of this dye in different solvents almost do not change, therefore the spectra in the paper are given only for methanol (Figure). The fluorescence quantum yields for compound 2



Normalized absorption (a) and emission (b) spectra of compounds 2 and 4 in MeOH

Spectral properties* of compounds 2 and 4 in different solvents

Solvent	Solvent polarity**, E_T^N	Compound	$\lambda_{\text{abs-max}}$, nm	$\lambda_{\text{Em-max}}$, nm	$\epsilon_{\text{max}} \cdot 10^4$, $\text{M}^{-1}\text{cm}^{-1}$	λ_{Ex} , nm	Φ_F^{***} , %	Stokes shift, nm/cm^{-1}
CH ₂ Cl ₂	0.309	2	533	612	6.08	533	1.42	79/2500
MeOH	0.762	2	529	612	6.07	529	2.76	83/2645
MeCN	0.460	2	525	613	6.06	525	2.11	88/2710
THF	0.207	2	531	610	6.04	531	1.04	79/2420
MeOH	0.762	4	527	–	6.12	–	–	–

Notes: * – absorption ($\lambda_{\text{Abs-max}}$), emission ($\lambda_{\text{Em-max}}$), excitation (λ_{Ex}) maxima and extinction coefficients (ϵ_{max}) were determined; ** – normalized values of solvent polarity were taken from ref. [15]; *** – quantum yields (Φ_F) were determined at 20°C using Rhodamine B ($\Phi_F=0.68$ in EtOH) as a standard [14].

decrease with decreasing solvent polarity. For example, the highest emission quantum yield is observed in methanol (2.76%), while the smallest is observed in tetrahydrofuran (THF) (1.04%). This is due to the fact that methanol leads to less energy loss during the redistribution of electron density in the excited state. Presumably, the reconfiguration of the solvation shell in the excited state requires less energy for relaxation with methanol, which leads to stabilization of the excited state and an increase in the fluorescence quantum yield.

The absorption spectrum for compound 4 was recorded in methanol at a concentration of $2.5 \cdot 10^{-5}$ mol l⁻¹ (Figure and Table). The absorption maximum is observed at 527 nm with an extinction coefficient of $6.12 \cdot 10^4$ (M⁻¹ cm⁻¹). Emission for compound 4 is practically not observed, which allows us to recommend it as a red light filter.

The main difference between dyes 2 and 4 is the size of the saturated cycle, which affects the ability to fluorescence. The large Stokes shifts of dye 2 indicate a significant redistribution of the electron density in the molecules in the structurally and solvation-relaxed electronically excited state. The cyclohexene derivative 2 shows a more pronounced vibrational structure in the emission spectra than cycloheptene derivative 2. This proves that the flattening of the molecule 2 occurs in the excited state, while the vibrational motion of the more flexible cycloheptene ring prevents the molecules from flattening. The movement of the more flexible cycloheptene fragment in the excited state also leads to an increase in non-radiative energy dissipation and, as a result, to a decrease in fluorescence quantum yields.

Conclusions

Thus, the following two new dyes were synthesized and spectrally characterized: N²-[4-(2,2-dicyanovinyl)-2,3-dihydro-1H-benzo[b]xanthen-12-yl]-N,N-dimethylimidoforamide and ethyl (2E)-

2-cyano-3-(11-[(1E)-(dimethylamino)methylene]-amino)-7,8,9,10-tetrahydrocyclohepta[b]chromen-6-yl)acrylate. The former, due to its optical properties, can be used as a fluorophore, and the latter, due to the absence of fluorescence, as a magenta light filter.

Experimental

Unless otherwise stated, all reagents of analytical grade were purchased from commercial suppliers and used without any further purification. The ¹H NMR and ¹³C NMR spectra were performed on a Bruker Avance II 400 spectrometer (400.13 MHz and 100.62 MHz for ¹H and ¹³C, respectively) in DMSO-d₆, TFA-d or CDCl₃ using residual solvent peak as internal standard. The FTIR spectra were recorded in KBr pellets using a Varian 640 FT-IR spectrometer. The UV-vis spectra were measured by a Hitachi U-1900 spectrophotometer using quartz cuvette with optical path length 10 mm, the baseline was corrected relative to the solvent absorption. Excitation and emission luminescence spectra were collected using Hitachi F-7000 spectrofluorometer for solutions in different solvents placed in a standard quartz cuvette with an optical path length 10 mm, and 90° geometry. The EI mass spectra were recorded on Kratos MS 30 with direct injection of the sample to the ionization chamber at temperature of 250°C with 70 eV ionizing electrons. Elemental analysis was performed on a LECO CHN-900 instrument. Melting points were determined using an Electrothermal 9100 Digital Melting Point apparatus and were uncorrected. The control of reactions and the purity of the obtained compounds were monitored by TLC on Merck Silica gel 60 F-254 plates with 10:1, v/v CHCl₃/MeOH as an eluent.

N'-[4-(2,2-dicyanovinyl)-2,3-dihydro-1H-benzo[b]xanthen-12-yl]-N,N-dimethylimidoforamide(2)

Aldehyde 1 (0.5 g, 1.5 mmol) was dissolved in boiling MeCN (5 mL), then malononitrile 0.1 g (1.5 mmol) was added with a few drops of Et₃N.

The reaction mixture was refluxed for 5 min, and then left at room temperature for 12 h. The precipitate formed was filtered off and purified by recrystallization from *i*-PrOH. If no solid was formed, water was added to crystalize the product. Yield 0.48 g (85%), dark green powder, mp 241–243°C. FTIR (KBr pellets, ν , cm^{-1}): 3031, 2937, 2224, 1635, 1513, 1473. ^1H NMR (400 MHz, DMSO- d_6), δ , ppm: 8.23 (1H, s, CH), 8.19 (1H, s, CH), 8.16 (1H, s, H Ar), 7.98–8.03 (2H, m, H Ar), 7.91 (1H, d, $^3J=7.3$ Hz, H Ar), 7.58 (1H, t, $^3J=7.4$ Hz, H Ar), 7.50 (1H, t, $^3J=7.2$ Hz, H Ar), 3.25 (6H, s, 2CH₃), 2.78–2.82 (2H, m, CH₂), 2.65–2.68 (2H, m, CH₂), 1.76–1.78 (2H, m, CH₂). ^1H NMR (400 MHz, TFA-*d*), δ , ppm: 8.87 (1H, s, CH), 8.42 (1H, s, CH), 8.16–8.18 (3H, m, H Ar), 8.08 (1H, s, H Ar), 7.94 (1H, t, $^3J=7.2$ Hz, H Ar), 7.86 (1H, t, $^3J=7.4$ Hz, H Ar), 3.91 (6H, s, 2CH₃), 3.29–3.32 (2H, m, CH₂), 3.11–3.13 (2H, m, CH₂), 2.30–2.32 (2H, m, CH₂). ^{13}C NMR (100 MHz, TFA-*d*), δ , ppm: 161.0, 158.8, 156.6, 151.3, 138.2, 135.9, 133.4, 132.1, 130.9, 129.8, 129.6, 128.9, 125.3, 120.1, 117.8, 115.4, 47.0, 39.4, 27.4, 26.9, 22.3. Mass spectrum (EI), m/z (I_{rel} , %): 380 [M]⁺ (20). Found, %: C 75.56; H 5.23; N 14.82. Anal. calcd for C₂₄H₂₀N₄O (%): C 75.77; H 5.30; N 14.73.

Ethyl (2E)-2-cyano-3-(11-[(1E)-(dimethylamino)methylene]amino)-7,8,9,10-tetrahydro-cyclohepta[b]chromen-6-yl)acrylate(4)

Aldehyde 3 (0.5 g, 1.7 mmol) was dissolved in boiling MeCN (5 mL), then ethyl cyanoacetate 0.19 g (1.7 mmol) was added with a few drops of DBU. The reaction mixture was refluxed for 5 min, and then left at room temperature for 12 h. The precipitate formed was filtered off and purified by recrystallization from *i*-PrOH. If no solid was formed, water was added to crystalize the product. Yield 0.6 g (90%), dark green powder, mp 98–100°C. ^1H NMR (400 MHz, CDCl₃), δ , ppm: 8.72 (1H, s, CH), 7.56 (1H, d, $^3J=7.9$ Hz, H Ar), 7.39 (1H, s, CH), 7.35–7.40 (1H, m, H Ar), 7.24–7.26 (1H, m, H Ar), 7.13 (1H, t, $^3J=7.5$ Hz, H Ar), 4.29 (2H, q, $^3J=7.1$ Hz, OCH₂), 3.13 (3H, s, CH₃), 3.10 (3H, s, CH₃), 2.99–3.01 (2H, m, CH₂), 2.60–2.63 (2H, m, CH₂), 1.73–1.78 (4H, m, 2CH₂), 1.35 (3H, t, $^3J=7.1$ Hz, CH₃). ^{13}C NMR (100 MHz, CDCl₃), δ , ppm: 166.3, 165.3, 154.0, 152.9, 152.7, 149.5, 130.7, 124.1, 123.3, 120.5, 119.4, 116.5, 115.5, 111.2, 86.0, 60.6, 40.0, 34.1, 26.7, 25.5, 25.4, 24.5, 14.1. Mass spectrum (EI), m/z (I_{rel} , %): 391 [M]⁺ (100). Found, %: C 70.79; H 6.55; N 10.84. Anal. calcd for C₂₃H₂₅N₃O₃(%): C 70.57; H 6.44; N 10.73.

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СИНТЕЗ І СПЕКТРАЛЬНІ ВЛАСТИВОСТІ НОВИХ КСАНТЕНОПОДІБНИХ ФЛУОРОФОРА ТА СВІТЛОФІЛЬТРА

О.К. Фарат, С.А. Варениченко, В.І. Марков

Реакцією N'-(4-форміл-2,3-дигідро-1H-бензо[b]-ксантен-12-іл)-N,N-диметилімідоформаміду та N'-(6-форміл-7,8,9,10-тетрагідроциклогепта[b]хромен-11-іл)-N,N-диметилімідоформаміду з малонітрилом і етиловим естером ціанооцтової кислоти за основного каталізу синтезовано два нових барвники: N'-[4-(2,2-диціановініл)-2,3-дигідро-1H-бензо[b]ксантен-12-іл]-N,N-диметилімідоформамід і етил(2E)-2-ціано-3-(11-[(1E)-(диметиламіно)метиленаміно]-7,8,9,10-тетрагідроциклогепта[b]хромен-6-іл)акрилат. Обидва барвники в розчині мають пурпурове забарвлення з високими коефіцієнтами екстинкції, але через різний розмір частково насиченого циклу перший має флуоресценцію, а у другого вона відсутня. Квантовий вихід флуоресценції N'-(4-форміл-2,3-дигідро-1H-бензо[b]ксантен-12-іл)-N,N-диметилімідоформаміду зменшується зі зменшенням полярності розчинника. Наприклад, найбільший квантовий вихід емісії спостерігається у метанолі (2,76%), а найменший – у ТГФ (1,04%). Це пов'язано з тим, що метанол приводить до меншої втрати енергії під час перерозподілу електронної густини у збудженому стані. Барвник N'-[4-(2,2-диціановініл)-2,3-дигідро-1H-бензо[b]ксантен-12-іл]-N,N-диметилімідоформамід можна використовувати як флуорофор, а етил(2E)-2-ціано-3-(11-[(1E)-(диметиламіно)метиленаміно]-7,8,9,10-тетрагідроциклогепта[b]хромен-6-іл)акрилат – як світлофільтр для створення різних матеріалів і пристроїв. Крім того, синтезовані сполуки можна використовувати, як білдинг-блоки в органічній хімії.

Ключові слова: барвники ксантенового ряду, флуорофор, світловий фільтр, реакція Кньовенагеля, квантовий вихід.

SYNTHESIS AND SPECTRAL PROPERTIES OF NEW XANTHENE-LIKE FLUOROPHORE AND LIGHT-FILTER

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By the reaction of N'-(4-formyl-2,3-dihydro-1H-benzo[b]-xanthen-12-yl)-N,N-dimethylimidoforamamide and N'-(6-formyl-7,8,9,10-tetrahydrocyclohepta[b]chromen-11-yl)-N,N-dimethylimidoforamamide with malononitrile and cyano acetic acid ethyl ester, the following two new dyes were synthesized by basic catalysis: N'-[4-(2,2-dicyanovinyl)-2,3-dihydro-1H-benzo[b]xanthen-12-yl]-N,N-dimethylimidoforamamide and ethyl (2E)-2-cyano-3-(11-[(1E)-(dimethylamino)methylene]amino)-7,8,9,10-tetrahydro-cyclohepta[b]chromen-6-yl)acrylate. Both dyes in solution have a purple color with high extinction coefficients, but due to the different size of the partially saturated cycle, the first one displays fluorescence, and the second one does not. The fluorescence quantum yields for N'-(4-formyl-2,3-dihydro-1H-benzo[b]xanthen-12-yl)-N,N-dimethylimidoforamamide decrease with decreasing solvent polarity. For example, the highest emission quantum yield is observed in methanol (2.76%), while the smallest is observed in tetrahydrofuran (1.04%). It is due to the fact that methanol implies a lesser energy consumption during the redistribution of electron density in the excited state. N'-[4-(2,2-dicyanovinyl)-2,3-dihydro-1H-benzo[b]xanthen-12-yl]-N,N-dimethylimidoforamamide dye can be used as a fluorophore, whereas ethyl (2E)-2-cyano-3-(11-[(1E)-(dimethylamino)methylene]amino)-7,8,9,10-tetrahydro-cyclohepta[b]chromen-6-yl)acrylate dye can be used as a light filter to create a variety of materials and devices. In addition, the synthesized compounds can be used as building-blocks in organic chemistry.

Keywords: xanthene-like dye; fluorophore; light-filter; Knoevenagel reaction; quantum yield.

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