1,3,2-(2*H*)-Dioxaborine Polymethine Dyes on the Base of Dehydroacetic Acid – Effective Fluorescent Amine Probes

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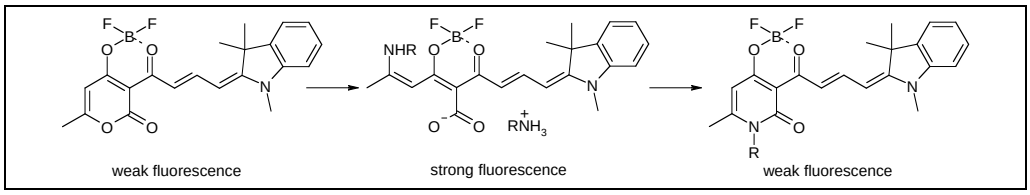

A number of new polymethine dyes based on the boron difluoride complexes of dehydroacetic acid and 3-acetyl-4-hydroxypyridone has been synthesized. Their spectral-luminescent properties have been investigated. The reaction of obtained merocyanines with primary and secondary amines has been studied. These low fluorescent dyes gave highly fluorescent open chain products, which on further heating cyclized to weakly fluorescent pyridone dyes.

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INTRODUCTION

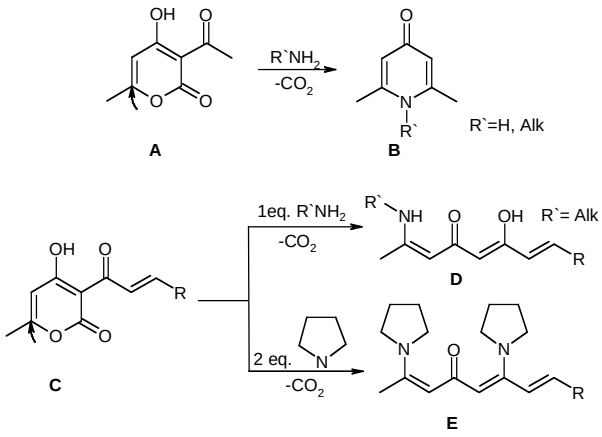
The reaction of 4-hydroxypyran-2-ones with amines is well known as the method for the preparation of pyridone system. In 1885 Heitinger first obtained 2,6-dimethyl-pyridine-4-one **B** (R = H) *via* reaction of dehydroacetic acid **A** with ammonia [1]. A large amount of works related to the reactions of dehydroacetic acid [2-7] and its derivatives of type **C** [8-10] with the amines have been published since then. The latter form open-chain decarboxylated products by the reaction with amines. Depending on the nature of substituents, amines and the reaction conditions the monosubstituted enamine derivatives of 1,3,5-triketones of type **D** [8,9] or disubstituted derivatives of type **E** could be obtained [10]. In all cases amine attacks the C-6 position of the pyranone system which leads to its further opening and decarboxylation of the obtained acid (Scheme 1).

It is well-known, that structural analogs of dehydroacetic acid – 4-hydroxy-3-acetylcumarines easily form boron difluoride complexes which can provide intense and deep colored polymethine dyes with high ability to fluorescence [11,12]. Moreover, the interest to none-linear optical properties (NLO) of 2,2-difluoro-1,3,2-(2*H*)-dioxaborine dyes, recently tends to increase [13-18]. Consequently, it was decided to synthesize and investigate chemical and structural properties of the dyes based on the derivatives of dehydroacetic acid.

RESULTS AND DISCUSSION

The starting boron difluoride complex **2a** was described earlier, however, it was prepared not as a desired product [19]. For our purposes this compound was obtained with

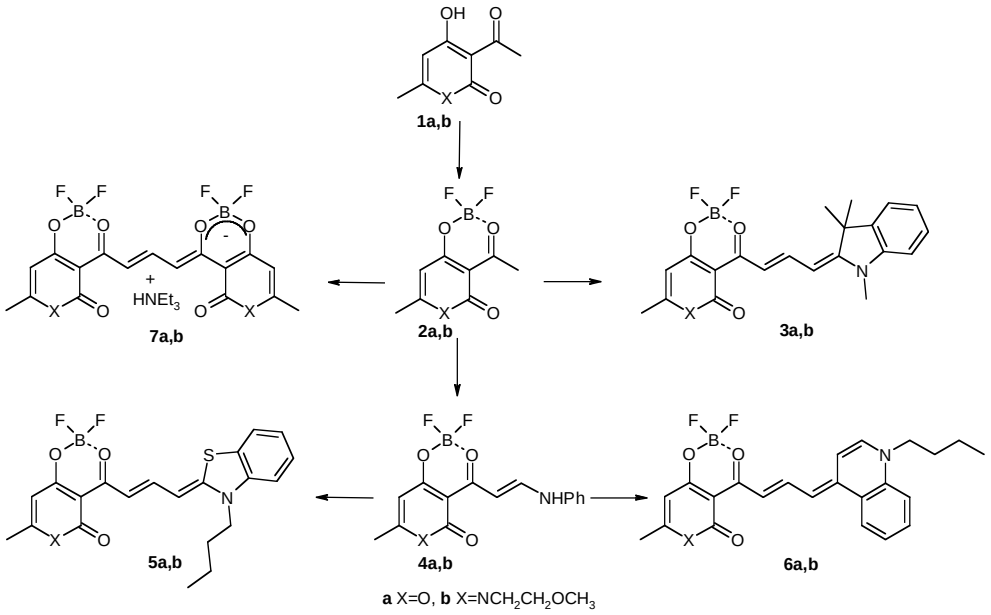
Scheme 1



the reaction of boron trifluoride etherate and dehydroacetic acid in the presence of acetic anhydride. The melting point of the prepared compound is 48 ºC higher than reported in literature, but the NMR spectra are coincident.

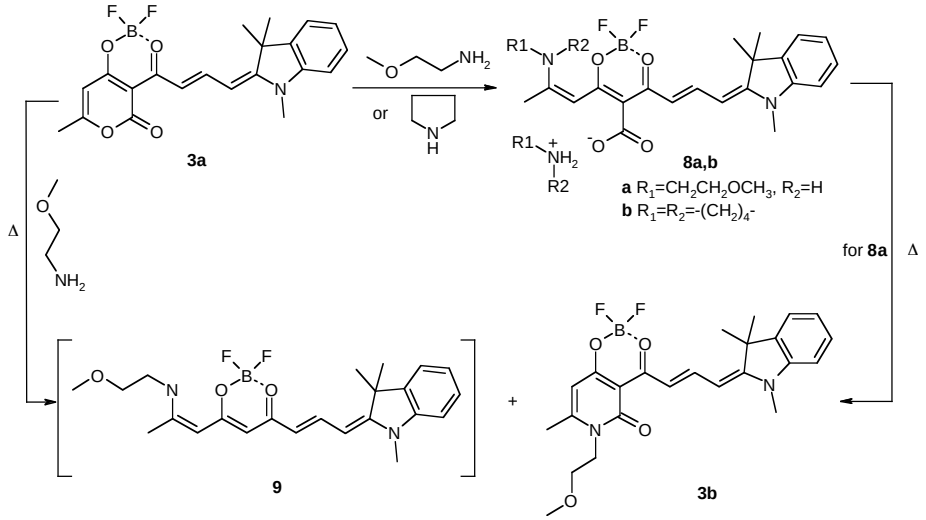
This complex easily reacts with 2-(1,3,3-trimethyl-indolin-2-ylidene)acetaldehyde to form dye **3a**. The reaction of the complex **2a** with ethyl isoformanilide leads to hemicyanine **4a**, which forms merocyanines **5a** and **6a** with quaternary salts of the heterocycles. The reaction of the compound **2a** with triethylorthoformate and triethylamine in acetic anhydride media leads to symmetrical anionic dye **7a** (Scheme 2). Compound **2a**, as well as other boron difluoride complexes of 1,3-diketones are stable in aprotic solvents, but easily hydrolyzes in alcohol/water media. The dyes **3** – **7** are stable in protic solvents.

Scheme 2



The prepared dyes are relatively weak luminophors. Only symmetrical dye **7a** has a fluorescent quantum yield 12 % (Table 1). However, some interesting spectral effects were observed on addition of primary and secondary aliphatic amines to their solutions. For instance, after short time treatment of merocyanine **3a** with 2-methoxyethylamine (this amine was chosen for the convenience due to its low volatility and easy identification with ^{1}H NMR spectroscopy), intense fluorescence appeared, TLC analysis showed the formation of a new dye. Though, the absorption maxima of the prepared dye is a little different from that of starting compound, which points on the retaining of the dioxaborine cycle. When equimolecular quantities of dye **3a** and amine were mixed, the TLC analysis of the reaction mixture always showed the presence of the significant quantity of starting dye. The reaction of **3a** with an excess of amine in acetonitrile at room temperature was carried out and the dye which can not be purified to the analytical purity grade was isolated. However, according to the ^{1}H NMR data that dye has the structure **8a**. The ^{1}H NMR spectrum ($CDCl_3$) of prepared

Scheme 3



compound showed two none-equivalent amine residues, one proton of NH group (9.43 ppm), the protons of polymethine chain (8.03; 6.40; 5.68 ppm), one proton of enamine fragment (5.47 ppm), and match to the structure **8a** (Scheme 3). The mass-spectrum of this dye gave molecular ion with mass number [475] which corresponds to the anionic part of the molecule ($474+H^+$).

The reaction of dye **3a** with amine in boiling ethanol forms intermediate compound **8a**, which transforms to the mixture of two other dyes. The less soluble product of structure **3b** was isolated (Scheme 3). The analogous result was obtained on heating of the isolated dye **8a** in acetonitrile: the mixture of two different dyes in proportion 1:1 (according to ^{1}H NMR data) was formed. One of them was isolated and identified as pyridone dye **3b**, other possibly has the structure of decarboxylated product **9** (due to the appearance of the singlet at 4.72 ppm, which could correspond to the proton of dioxaborine cycle).

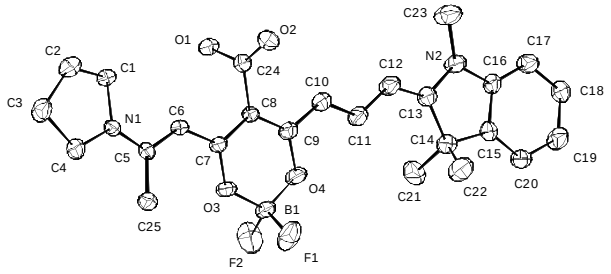


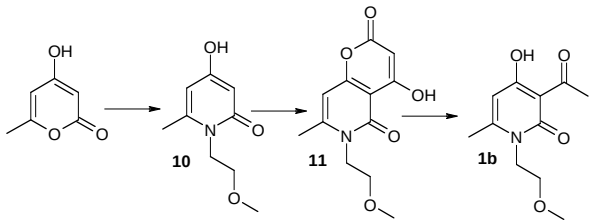
Figure 1. Molecular structure of **8b**. Selected bond lengths and angles for **8b**: N(1)-C(1) 1.482(4), N(1)-C(4) 1.474(4), N(1)-C(5) 1.335(3), O(3)-C(7) 1.321(3), O(4)-C(9) 1.338(4), O(4)-B(1) 1.447(4), O(3)-B(1) 1.471(4), N(2)-C(16) 1.400(4), N(2)-C(13) 1.384(4), C(5)-C(6) 1.389(4), C(6)-C(7) 1.407(4), C(9)-C(10) 1.436(4), C(10)-C(11) 1.342(4), C(11)-C(12) 1.437(5), C(12)-C(13) 1.345(4); C(1)N(1)C(4) 111.6(2), C(7)O(3)B(1) 123.8(2), O(3)B(1)O(4) 113.7(3), C(9)O(4)B(1) 121.9(2), C(13)N(2)C(16) 111.9(3)

To ensure the legitimization of our assumptions for the structure of the compound **8a**, its structural analog – enamine **8b** was prepared by the reaction of the dye **3a** with pyrrolidine. It appears more stable than **8a**, which allows the establishment of its exact structure. The NMR spectra and X-ray structural analysis (Figure 1) uniquely determined the structure **8b**. In the ^{1}H NMR spectra (DMSO-d^6) the mixture of *E*- and *Z*- isomers (enamine fragment) was observed, which is evidenced by doublet splitting of the enamine proton. However, in the solid state, according to X-ray data, the molecule exists only as *E*- isomer and has almost planar structure. Interestingly, the alternation of the bonds through the chromophore could be found even in dioxaborine cycle (the bond lengths values for C7-C8 and C8-C9 are 1.367 and 1.428 Å correspondingly).

Therefore, in the case of boron difluoride complexes of chalcones of dehydroacetic acid, which *per se* are dyes **3a**, **5a**, and **6a** (the dyes **5a** and **6a** react with amines similar to dye **3a**), the similar mechanism for the opening the pyran cycle possibly realizes, that was previously observed for free chalcones of the type **C** [8-10]. Due to the higher electron accepting properties of annelated 2,2-difluoro-1,3,2-(2*H*)-dioxaborine fragment in comparison with free β-diketonate group, the carboxylic acid formed by opening of the pyran cycle is stronger, than formed from **C**. That's why probable formation of more stable salt is more evident. This fact partly prevents decarboxylation and allows to provide cyclization to pyridone cycle by heating of open cycle product.

Thus, these dyes are effective fluorescent indicators with high speed of response on the amino group. To investigate this phenomenon in details on several examples, some pyridone dyes were prepared for comparison (Scheme 2). As it was already mentioned, they can be synthesized from enamines **8**. Although, using direct synthesis is much more convenient. The nessessary 3-acetyl-4-hydroxypyrid-2-one **1b** was obtained analogously to [20] (Scheme 4). Pyridone dyes **3b** – **7b** were synthesized similarly to their oxygen analogs. According to analytical and spectral data merocyanine **3b**, prepared from pyridone complex **2b**, and the compound prepared earlier by alternative method have completely identical constants.

Scheme 4



Bathochromic shift of the absorption maxima of 14 nm is observed upon the transition from symmetrical pyranone dye **7a** to pyridone **7b**, the absorption intensity hardly changed (Table 1). The similar tendency is observed in the fluorescence spectra of this part of the symmetrical dyes. In case of merocyanines **3b**, **5b** and **6b** insignificant bathochromic shift of the absorption and fluorescence maxima takes place in comparison with their oxygen analogs. The fluorescent quantum yields of the merocyanines remain low, but molar absorptivity, contrarily to the symmetrical dyes, increases by almost 1.5 times.

The reaction of the dehydroacetic acid derivatives with amines was investigated in detail rely on spectral properties of the dioxaborine dyes based on pyranone and

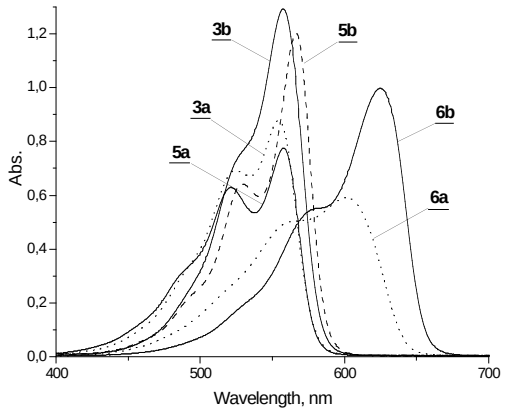


Figure 2. The absorption spectra of merocyanines **3a**,**b**, **5a**,**b** and **6a**,**b** in acetonitrile ($C=1\cdot10^{-5}$ mol·l^{-1}).

pyridone moiety. In the case of symmetrical dye **7a**, reaction with amines in acetonitrile occurs immediately, but all attempts to isolate any individual product from the reaction mixture failed. The absorption and fluorescence bands become broad and the fluorescent intensity decreases greatly.

In the case of merocyanine dyes **3a**, **5a** and **6a** spectral changes occur slower (from several minutes for dye **3a** to

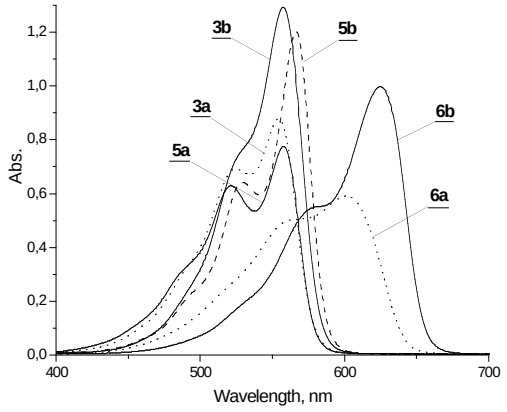


Figure 3. The changes occurring in the absorption spectra of the solutions of merocyanines **3a**, **5a** and **6a** in acetonitrile ($C=1\cdot10^{-5}$ mol·l^{-1}) after the addition of 10 eq. of 2-methoxyethylamine

several hours for **6a**). It means that pyranone nuclei opening rate decreases as well as electron-donating ability of other end nuclei get stronger. It is obvious because more electron-donating end groups strongly deliver electron density to the pyranone fragment, and decrease its sensitivity to the nucleopfilic attack.

The investigated reaction is sensitive to polarity of the solvent. For instance, after addition of the excess of amine to acetonitrile solution of the dye **3a**, spectral changes finished for the first minutes, but when reaction was carried out in dichloromethane changes lasted about 15 min.

The absorption maxima of the merocyanine **3a** hardly changes after addition of 2-methoxyethylamine, only the absorption band becomes slightly broader and less intense. Although, addition of the amines to the solutions of the dyes **5a** and **6a** leads to bathochromic shift of the absorption maxima of 20 and 44 nm correspondingly (Figure 3). It means that the enamine derivatives in this case are colored deeper in comparison with the pyridone analogs **5b** and **6b**. The absorption intensity insignificantly increases.

The fluorescence spectra recorded after reaction of the dyes **3** and **5** with alkylamines showed the most significant changes (Figure 4). Decreasing of electron-accepting properties of the dioxaborine cycle, (because

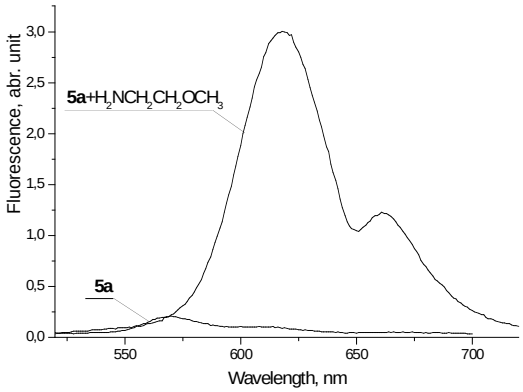


Figure 4. The changes occurring in the fluorescence spectra of the solutions of dye **5** in acetonitrile after the addition of 10 eq. of 2-methoxyethylamine (excitation at 500 nm).

of presence of the electron-donating enamine fragment in the open chain products) leads to increase of the fluorescent quantum yield (up to 19 % for the compound **3** and to 13 % for **5**) in comparison with the analogous pyranone or pyridone dyes. The fluorescence maxima batochromically shift on 33 and 48 nm for the compounds **3** and **5** correspondingly. The similar spectral effect was observed for the dioxaborine dyes based on coumarine nuclei. For instance, in the acetonitrile solution of the dye **12** with unsubstituted coumarine nuclei $\varphi = 0.2\%$ whereas the quantum yield increases to 11% with the introduction of the electron donating diethylamino group (dye **13**) [12].

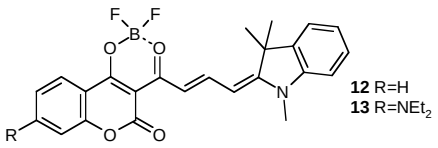


Table 1

Spectral-luminescent properties of the dyes

№	Absorption $\lambda_{max(MeCN)}$, nm ($\varepsilon*10^{-5}$)	Emission (excitation 500 nm) $\lambda_{max(MeCN)}$, nm (φ)
3a	554 (0.88)	566 (0.013)
3a+$H_2NCH_2CH_2OCH_3$ [a]	551 (0.71)	599 (0.19)
5a	558 (0.77)	570 (0.012)
5a+$H_2NCH_2CH_2OCH_3$ [b]	578 (0.78)	618 (0.13)
6a	601 (0.59)	630 (0.008)
6a+$H_2NCH_2CH_2OCH_3$ [c]	645 (0.69)	-
7a	554 (1.55)	560 (0.12)
3b	558 (1.29)	575 (0.021)
5b	567 (1.20)	576 (0.019)
6b	625 (1.00)	641 (<0.005)
7b	568 (1.47)	575 (0.20)
8b	554 (0,44)	598 (0.085)

[a] After 5 min of the reaction. [b] After 20 min of the reaction. [c] After 5 h of the reaction.

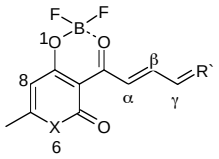
Therefore, the boron difluoride complexes of the merocyanines based on dehydroacetic acid were found to be sensitive fluorescence indicators for primary and secondary aliphatic amines. The speed of response can be regulated by nature of the second end nuclei and media polarity. This allows them to be utilized for the detection of the nature based amines, which is going to be reported later

EXPERIMENTAL

Electronic absorption spectra were recorded on a Shimadzu UV-3100 spectrophotometer in acetonitrile. NMR spectra were obtained with a Varian VXR-300 instrument (300 MHz) at 25°C using tetramethylsilane as an internal standard. LC/MS spectra were recorded using a liquid chromatography/mass spectrometric system consisting of an Agilent 1100 Series high-performance liquid chromatograph equipped with a diode-matrix and an Agilent LC/MSD SL mass-selective detector. Fluorescence spectra were recorded on a Signe-4M fluorescence spectrophotometer and are not corrected. Relative fluorescence quantum yields (ϕ) were determined relative to Rhodamine 6G (ϕ=0.95, EtOH) [21].

X-ray Structure determination for **8b:** Crystal data: $C_{29}H_{38}B_1F_2N_3O_4$, M 541.45, monoclinic, space group P 2_1/c (N 14), *a* = 16.9422(8), *b* = 7.5994(4), *c* = 24.671(1) Å, β = 94.620(2)°, V = 3166.1(3) Å^3, Z = 4, d_c = 1.14 g·cm^{-3}, μ = 0.083 mm^{-1}, F(000) = 1152, crystal size ca. 0.08 × 0.21 × 0.48 mm. All crystallographic measurements were performed at 173 K on a Bruker Smart Apex II diffractometer operating in the ω and φ scans mode. The intensity data were collected within the range of 1.2 ≤ θ ≤ 26.9° using Mo-K_α radiation (λ = 0.71078 Å). The intensities of 22378 reflections were collected (6676 unique reflections). Data were corrected for Lorentz and polarization effects. The structure was solved by direct methods and refined by the full-matrix least-squares technique in the anisotropic approximation for non-hydrogen atoms using the CRYSTALS program package [22]. Hydrogen atoms were located in the difference Fourier maps and refined with fixed positional and thermal parameters (only H(1) and H(2) atoms which take part in the hydrogen bonds were refined isotropically). The SADABS [23] absorption correction (the ratio of minimum to maximum apparent transmission is 0.416803) was applied. In the refinement 6676 reflections (2308 reflections with I ≥ 3σ(I)) were used. Convergence was obtained at R1 = 0.042 and wR2 = 0.046, GOF = 1.113 (360 parameters; observed/variable ratio 6.41; the largest and minimal peaks in the final difference map 0.17 and –0.18 e/Å^3, Chebychev weighting scheme [24] with 3 parameters (24.2, -17.6, 19.5) was used.

The full crystaltallographic data sets (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 681809. Copies of data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].



2,2-Difluoro-4,7-dimethyl-5-oxo-(5*H*)-pyrano[4.3-*d*][1,3,2]-(2*H*)-dioxaborine (2a). The mixture of dehydroacetic acid (**1a**) (8.4 g, 0.05 mol), acetic anhydride (3 mL) and boron trifluoride etherate (8 mL, 0.063 mol) in toluene (25 mL) was refluxed for 1-2 min. The solution was cooled; the product was filtered off and washed with toluene. Yield 8.4 g (78%). M.p. 135°. ^{1}H NMR ($CDCl_3$): 2.40 (s, 3 H, CH_3), 2.87 (s, 3 H, CH_3), 6.14 (s, 1 H, 8-H). Anal. calcd. for $C_8H_7BF_2O_4$: C, 44.50; H, 3.27. Found: C, 44.59; H, 3.36.

2,2-Difluoro-7-methyl-5-oxo-(5*H*)-4-[3-(1,3,3-trimethyl-indolin-2-ylidene)-1-propenyl]-pyrano[4,3-*d*][1,3,2]-(2*H*)-dioxaborine (**3a**).The mixture of complex **2a** (0.43 g, 2 mmol) and 2-(1,3,3-trimethylindolin-2-ylidene)acetaldehyde (0.42 g, 2 mmol) was refluxed for 2 min in acetic anhydride (3 mL). The mixture was cooled and allowed to stand for 12 h to crystallize. The product was collected by filtration, washed

with acetic acid, and diethyl ether. Yield: 0.72 g (90 %). M.p. 288-289°. ^{1}H NMR (DMSO-d_6): 1.65 (s, 6 H, CH_3), 2.28 (s, 3 H, CH_3), 3.73 (s, 3 H, NCH_3), 6.26 (s, 1 H, 8-H), 6.61 (d, $^3J_{H,H}$ = 14.7 Hz, 1 H, γ-H), 7.27 (d, $^3J_{H,H}$ = 12.3 Hz, 1 H, α-H), 7.36 (m, 1 H, 5`-H), 7.48 (m, 1 H, 6`-H), 7.53 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, 7`-H), 7.67 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, 4`-H), 8.59 (t, $^3J_{H,H}$ = 13.5 Hz, 1 H, β-H). APSI MS: M^++1 = 400. Anal. calcd. for $C_{21}H_{20}BF_2NO_4$: C, 63.18; H, 5.05; N, 3.51. Found: C, 63.21; H, 5.01; N, 3.53.

2,2-Difluoro-7-methyl-5-oxo-4-(2-(phenylamino)vinyl)-(5*H*)-pyrano[4,3-*d*][1,3,2]-(2*H*)-dioxaborine (**4a**). Complex **2a** (1.08 g, 5 mmol) was dissolved in warm acetic anhydride (3 mL), cooled down, treated with ethyl isoformanilide (1 g, 6.7 mmol), and kept for 1 h at room temperature. The reaction mixture was diluted with ethylacetate (10 mL), and the precipitate was collected by filtration. Yield: 1.25 g (78 %). M.p. 280- 282° (dec). ^{1}H NMR (DMSO-d_6): 2.30 (s, 3 H, CH_3), 6.32 (s, 1 H, 8-H), 7.27 (m, 2 H, Ph-H), 7.49 (m, 4 H, α-H, Ph-H), 8.86 (t, $^3J_{H,H}$ = 13.0 Hz, 1 H, β-H), 12.31 (d, $^3J_{H,H}$ = 15.0 Hz, 1 H, NH). λ_{max} 416 nm(MeCN). Anal. calcd. for $C_{15}H_{12}BF_2NO_4$: C, 56.47; H, 3.79; N, 4.39. Found: C, 56.61; H, 3.86; N, 4.45.

4-[3-(3-butylbenzothiazol-2(3*H*)-ylidene)-1-propenyl]-2,2-difluoro-7-methyl-5-oxo-(5*H*)-pyrano[4.3-*d*][1,3,2]-(2*H*)-dioxaborine (**5a**). A mixture of hemicyanine **4a** (160 mg, 0.5 mmol), 3-butyl-2-methylbenzothiazolium iodide (170 mg, 0.51 mmol) and diisopropylethylamine (100 mg, 0.78 mmol) in dry acetonitrile was refluxed for 10 min. The mixture was cooled and allowed to stand for 12 h to crystallize. The product was collected by filtration, washed with acetic acid, and diethyl ether. Yield: 130 mg (60%). M.p. 257-258°. ^{1}H NMR (DMSO-d_6): 0.95 (m, 3 H, CH_3), 1.45 (m, 2 H, CH_2), 1.76 (m, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 4.52 (m, 2 H, NCH_2), 6.16 (s, 1 H, 8-H), 6.97 (d, $^3J_{H,H}$ = 13.2 Hz, 1 H, γ-H), 7.17 (d, $^3J_{H,H}$ = 11.7 Hz, 1 H, α-H), 7.54 (m, 1 H, 6`-H), 7.66 (m, 1 H, 5`-H), 7.91 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 4`-H), 8.09 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, 7`-H), 8.29 (t, $^3J_{H,H}$ = 13.4 Hz, 1 H, β-H). Anal. calcd. for $C_{21}H_{20}BF_2NO_4S$: C, 58.49; H, 4.67; N, 3.25. Found: C, 58.37; H, 4.61; N, 3.30.

4-[3-(1-Butylquinolin-4(1*H*)-ylidene)-1-propenyl]-2,2-difluoro-7-methyl-5-oxo-(5*H*)-pyrano[4,3-*d*][1,3,2]-(2*H*)-dioxaborine (**6a**). A mixture of hemicyanine **4a** (160 mg, 0.5 mmol), 1-butyl-4-methylquinolinium iodide (165 mg, 0.505 mmol) and diisopropylethylamine (100 mg, 0.78 mmol) in acetic anhydride (1 mL) was stirred at room temperature for 1 h. The dye was precipitated by 2-propanol and recrystallized from DMF/2-propanol mixture. Yield: 75 mg (35%). M.p. 284-285°. ^{1}H NMR (DMSO-d_6): 0.92 (m, 3 H, CH_3), 1.38 (m, 2 H, CH_2), 1.84 (m, 2 H, CH_2), 2.23 (s, 3 H, CH_3), 4.73 (m, 2 H, NCH_2), 6.13 (s, 1 H, 8-H), 7.15 (d, $^3J_{H,H}$ = 11.4 Hz, 1 H, γ-H), 7.34 (d, $^3J_{H,H}$ = 14.4 Hz, 1 H, α-H), 7.80 (m, 1 H, 6`-H), 8.00 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, 8`-H), 8.07 (m, 1 H, 7`-H), 8.26 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 5`-H), 8.41 (dd, $^3J_{H,H}$ = 14.4 Hz, $^3J_{H,H}$ = 11.4 Hz, 1 H, β-H), 8.73 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, 5`-H), 8.77 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H, 2`-H). Anal. calcd. for $C_{23}H_{22}BF_2NO_4$: C, 64.96; H, 5.21; N, 3.29. Found: C, 65.12; H, 5.34; N, 3.36.

Triethylammonium 2,2-difluoro-4-[3-(2,2-difluoro-7-methyl-5-oxo-(5*H*)-pyrano[4,3-*d*][1,3,2]-(2*H*)-dioxaborin-4-ylidene)-1-propenyl]-7-methyl-5-oxo-(5*H*)-pyrano[4,3-*d*][1,3,2]-(2*H*)-dioxaborinate (**7a**). A mixture of complex **2a** (432 mg, 2 mmol) and triethylorthoformiate (150 mg, 1 mmol) in acetic anhydride (2 mL) was refluxed for 1 min. The reaction mixture was cooled down to room temperature; triethylamine (121 mg, 1.2 mmol) was added, and stirred at room temperature for 30 min. The dye **7a** was precipitated by the addition of 2-propanol. The product was recrystallized from EtOH. Yield: 230 mg (43%). M.p. 233-234°. ^{1}H NMR (DMSO-d_6): 1.17 (m, 9 H, CH_3), 2.28 (s, 6 H, CH_3), 3.10 (m, 6 H, NCH_2), 6.29 (s, 2 H, 8-H), 7.23 (d, $^3J_{H,H}$ = 13.5 Hz, 2 H, α-H, α`-H), 8.70 (t, $^3J_{H,H}$ = 13.5 Hz, 1 H, β-H), 8.85 (br s, 1 H, N^+H). Anal. calcd. for $C_{23}H_{27}B_2F_4NO_8$: C, 50.83; H, 4.97; N, 2.58. Found: C, 50.86; H, 5.08; N, 2.49.

8a: A mixture of dye **3a** (105 mg, 0.26 mmol) and 2-methoxyethylamine (100 mg, 1.3 mmol) in dichloromethane was stirred at room temperature for 1.5 h. The solvent was evaporated *in vacuo* without heat, the residue treated with 2-propanol and collected by filtration. Yield: 120 mg (86%).^{1}H NMR ($CDCl_3$): 1.54 (s, 6 H, CH_3), 2.06 (s, 3 H, CH), 3.03 (m, 2 H, NCH_2), 3.16-3.53 (m, 15 H, NCH_3, NCH_2, 2-OCH_2, 2-OCH_3), 5.47 (s, 1 H, NCH_2), 5.68 (d, $^3J_{H,H}$ = 13.2 Hz, 1 H, CH), 5.94 (br s, 3 H, $H_3N^+CH_2$), 6.40 (d, $^3J_{H,H}$ = 14.1 Hz, 1 H, CH), 6.70 (m, 1 H, 7`-H), 6.90 (m, 1 H, 5`-H), 7.15 (m, 2 H, 4`-H, 6`-H), 8.03 (m, 1 H, CH), 9.73 (s, 1 H, NH).

Pyrrolidinium 2,2-difluoro-4-[2-(pyrrolidin-1-yl)-1-propenyl]-6-[3-(1,3,3-trimethylindolin-2-ylidene)-1-propenyl]-1,3,2-(2*H*)-dioxaborine-5-carboxylate (**8b**). Pyrollydine (178 mg, 2.5 mmol) was added to the solution of dye **3a** (200 mg, 0.5 mmol) in dichloromethane. The reaction mixture was stirred at room temperature for 30 min, and the precipitate collected by filtration. The product was recrystallized from acetonitrile. Yield: 170 mg (63%). M.p. 170-1° (dec). ^{1}H NMR (DMSO-d_6): 1.53 (s, 6 H, CH_3), 1.80 (m, 4 H, CH_2), 1.92 (m, 4 H, CH_2), 2.52 (s, 3 H, CH_3), 3.04 (m, 4 H, NCH_2), 3.20 (s, 3 H, NCH_3), 3.32 (m, 2 H, NCH_2), 3.60 (m, 2 H, NCH_2), 5.56 (m, 1.5 H, γ-H+5-H), 5.75 (s, 0.5 H, 5-H), 6.29 (d, $^3J_{H,H}$ = 14.7 Hz, 1 H, α-H), 6.88 (m, 2 H, 5`-H, 7`-H), 7.19 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H, 6`-H), 7.30 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, 4`-H), 7.66 (t, $^3J_{H,H}$ = 13.2 Hz, 1 H, β-H). Anal. calcd. for $C_{29}H_{36}BF_2N_3O_3$: C, 64,33; H, 7,02; N, 7,76. Found: C, 64,45; H, 7,11; N, 7,68.

4-Hydroxy-1-(2-methoxyethyl)-6-methylpyridin-2(1*H*)-one (**10**). A mixture of 4-hydroxy-6-methylpyran-2-one (25.2 g, 0.2 mol) and 2-methoxyethylamine (15 g, 0.2 mol) in water (50 mL) was refluxed for 6 h. The mixture was cooled and the product was collected by filtration. Yield: 27.5 g (75%). M.p. 203-205°. ^{1}H NMR (DMSO-d_6): 2.30 (s, 3 H, CH_3), 3.20 (s, 3 H, OCH_3), 3.47 (m, 2 H, OCH_2), 3,98 (m, 2 H, NCH_2), 5.47 (s, 1 H, 3-H), 5.72 (s, 1 H, 5-H), 10,39 (s, 1 H, OH). Anal. calcd. for $C_9H_{13}NO_3$: C, 59.02; H, 7.10; N, 7.65. Found: C, 58.86; H, 7,20; N, 7,69.

3-Acetyl-4-hydroxy-1-(2-methoxyethyl)-6-methylpyridin-2(1*H*)-one (**1b**). A mixture of hydroxypyridone **10** (18.3 g, 0.1 mol) and diethylmalonate (18.3 g, 0.11 mol) in diphenyl ether was slowly heated to 215 °C and kept at this temperature for 2 h. The reaction mixture was cooled, 2-propanol (50 mL) was added, the precipitate collected by filtration and recrystallized from 2-propanol. Yield: 16 g (64%). M.p. 171-172°.

A mixture of compounds **11** (15 g, 0.06 mol), ethylene glycol (260 mL), sodium hydroxide (30 g, 0.75 mol) and water (38 mL) was heated to 175 – 180 °C (bath temperature) and refluxed with stirring for 2 h. The solution was poured into water (1000 mL), and neutralized with hydrochloric acid. The warm solution was filtered, and after cooling down the precipitate was collected by filtration. Yield: 8.4 g (62%). M.p. 108-110°. ^{1}H NMR ($CDCl_3$): 2.45 (s, 3 H, CH_3), 2.73 (s, 3 H, CH_3), 3.32 (s, 3 H, OCH_3), 3.67 (m, 2 H, OCH_2), 4.15 (m, 2 H, NCH_2), 5.83 (s, 1 H, 8-H), 15.51 (s, 1 H, OH). Anal. calcd. for $C_{11}H_{15}NO_4$: C, 58.66; H, 6.71; N, 6.22. Found: C, 58.61; H, 6.73; N, 6.19.

2,2-Difluoro-4,7-dimethyl-6-(2-methoxyethyl)-5-oxo-(5*H*)-pyrido[4,3-*d*][1,3,2]-(2*H*)-dioxaborine (**2b**). A mixture of acetylpyridone **1b** (4.5 g, 0.02 mol), boron trifluoride etherate (4.5 g, 0.032 mol) and acetic anhydride (3.5 g) in diethyl ether (15 mL) was stirred at room temperature for 7 h. The precipitate was collected by filtration, and washed with ether. Yield: 5.06 g (93 %). M.p. 135-136º. 1H ^{1}H NMR ($CDCl_3$): 2.53 (s, 3 H, CH_3), 2.85 (s, 3 H, CH_3), 3.30 (s, 3 H, OCH_3), 3.63 (m, 2 H, OCH_2), 4.16 (m, 2 H, NCH_2), 5.96 (s, 1 H, 8-H). Anal. calcd. for $C_{11}H_{14}BF_2NO_4$: C, 48.39; H, 5.17; N, 5.13. Found: C, 48.55; H, 5.28; N, 5.19.

2,2-Difluoro-6-(2-methoxyethyl)-7-methyl-5-oxo-(5*H*)-4-[3-(1,3,3-trimethylindolin-2-ylidene)-1-propenyl]-pyrido[4,3-*d*]-[1,3,2]-(2*H*)-dioxaborine (3b).

From compound 3a: A mixture of dye **3a** (0.2 g, 0.5 mmol) and 2-methoxyethylamine (0.18 g, 2.4 mmol) was refluxed in ethanol for 2 h. The hot reaction mixture was filtered off, the precipitate collected. Yield: 70 mg (31 %).

From boron difluoride complex 2b: A mixture of compound **2b** (273 mg, 1 mmol) and 2-(1,3,3-trimethylindolin-2-ylidene)-acetaldehyde (212 mg, 1.05 mmol) in acetic anhydride (0.5 mL) was refluxed for 2 min. The mixture was cooled and allowed to stand for 12 h to crystallize. The product was collected by filtration and washed with acetic anhydride and ether. Yield: 275 mg (60 %). M.p. 264-265º. ^{1}H NMR (DMSO-d_6): 1.63 (s, 6 H, CH_3), 2.44 (s, 3 H, CH_3), 3.25 (s, 3 H, OCH_3), 3.57 (m, 2 H, OCH_2), 3.64 (s, 3 H, NCH_3), 4.11 (m, 2 H, NCH_2), 5.98 (s, 1 H, 8-H), 6.40 (d, $^3J_{H,H}$ = 14.4 Hz, 1 H, γ-H), 7.27 (m, 1 H, 5`-H), 7.42 (m, 2 H, 6`-H, 7`-H), 7.60 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, 4`-H), 7.71 (d, $^3J_{H,H}$ = 13.2 Hz, 1 H, α-H), 8.59 (t, $^3J_{H,H}$ = 13.5 Hz, 1 H, β-H). APSI MS: M^++1 = 457.Anal. calcd. for $C_{24}H_{27}BF_2N_2O_4$: C, 63.17; H, 5.96; N, 6.14. Found: C, 63.15; H, 5.92; N, 6.16.

2,2-Difluoro-6-(2-methoxyethyl)-7-methyl-5-oxo-4-(2-(phenyl-amino)vinyl)-(5*H*)-pyrido[4,3-*d*][1,3,2]-(2*H*)-dioxaborine (**4b**). A mixture of complex **2b** (550 mg, 2 mmol) and ethylisoformanilide (600 mg, 4 mmol) was fused at 120 ºC during for 1 h. The melt was cooled and triturated with chloroform. The resulting solid was collected by filtration and washed with chloroform. Yield: 515 mg (69 %). M.p. 208-210º. ^{1}H NMR (DMSO-d_6): 2.46 (s, 3 H, CH_3), 3.26 (s, 3 H, OCH_3), 3.58 (m, 2 H, OCH_2), 4.13 (m, 2 H, NCH_2), 6.02 (s, 1 H, 8-H), 7.25 (m, 1 H, Ph-H), 7.44 (m, 4 H, Ph-H), 7.68 (d, $^3J_{H,H}$ = 12.0 Hz, 1 H, α-H), 8.81 (t, $^3J_{H,H}$ = 12.0 Hz, 1 H, β-H), 11.97 (d, $^3J_{H,H}$ = 13.5 Hz, 1 H, NH). λ_{max} 431 nm (MeCN). Anal. calcd. for $C_{18}H_{19}BF_2N_2O_4$: C, 57.47; H, 5.09; N, 7.45. Found: C, 57.58; H, 5.17; N, 7.51.

4-[3-(3-Butylbenzothiazol-2(3*H*)-ylidene)-1-propenyl]-2,2-difluoro-6-(2-methoxyethyl)-7-methyl-5-oxo-(5*H*)-pyrido-[4.3-*d*][1,3,2]-(2*H*)-dioxaborine (**5b**). Triethylamine (101 mg, 1 mmol) was added at room temperature to the mixture of hemicyanine **4b** (174 mg, 0.46 mmol) and 3-butyl-2-methylbenzothiazolium iodide (180 mg, 0.54 mmol) in acetic anhydride (5 mL). The reaction mixture was stirred at room temperature for 2 h, and the precipitate was collected by filtration. The product was recrystallized from acetonitrile. Yield: 200 mg (82 %). M.p. 267-268º. ^{1}H NMR (DMSO-d_6): 0.93 (m, 3 H, CH_3), 1.44 (m, 2 H, CH_2), 1.72 (m, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.25 (s, 3 H, OCH_3), 3.56 (m, 2 H, OCH_2), 4.10 (m, 2 H, NCH_2), 4.46 (m, 2 H, NCH_2), 5.94 (s, 1 H, 8-H), 6.86 (d, $^3J_{H,H}$ = 13.8 Hz, 1 H, γ-H), 7.49 (m, 1 H, 6`-H), 7.62 (m, 2 H, α-H, 5`-H), 7.86 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 4`-H), 8.04 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 7`-H), 8.29 (t, $^3J_{H,H}$ = 12.8 Hz, 1 H, β-H). Anal. calcd. for $C_{24}H_{27}BF_2N_2O_4S$: C, 59.03; H, 5.57; N, 5.74. Found: C, 59.14; H, 5.66; N, 5.79.

4-[3-(1-Butylquinolin-4(1*H*)-ylidene)-1-propenyl]-2,2-difluoro-6-(2-methoxyethyl)-7-methyl-5-oxo-(5*H*)-pyrido [4,3-*d*][1,3,2]-(2*H*)-dioxaborine (**6b**). Triethylamine (101 mg, 1 mmol) was added to the mixture of hemicyanine **4b** (174 mg, 0.46 mmol) and 1-butyl-4-methylquinolinium iodide (150 mg, 0.46 mmol) in acetic anhydride (4 mL). The reaction mixture was stirred for 3 h at room temperature, and the precipitate was collected by filtration. The product was recrystallized from acetonitrile. Yield: 135 mg (61 %). M.p. 236-238º. ^{1}H NMR (DMSO-d_6): 0.92 (m, 3 H, CH_3), 1.38 (m, 2 H, CH_2), 1.82 (m, 2 H, CH_2), 2.40 (s, 3 H, CH_3), 3.25 (s, 3 H, OCH_3), 3.57 (m, 2 H, OCH_2), 4.11 (m, 2 H, NCH_2), 4.65 (m, 2 H, NCH_2), 5.88 (s, 1 H, 8-H), 7.21 (d, $^3J_{H,H}$ = 14.1 Hz, 1 H, γ-H), 7.64 (d, $^3J_{H,H}$ = 12.3 Hz, 1 H, α-H), 7.74 (t, $^3J_{H,H}$ = 8.1 Hz, 1 H, 6`-H), 7.85 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, 8`-H), 8.01 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, 7`-H), 8.18 (d, $^3J_{H,H}$ = 9.0 Hz, 1 H, 3`-H), 8.50 (t, $^3J_{H,H}$ = 13.8 Hz, 1 H, β-H), 8.56 (d, $^3J_{H,H}$ = 6.9 Hz, 1 H, 5`-H), 8.69 (d, $^3J_{H,H}$ = 9.0 Hz, 1 H, 2`-H). Anal. calcd. for $C_{26}H_{29}BF_2N_2O_4$: C, 64.74; H, 6.06; N, 5.81. Found: C, 64.89; H, 6.18; N, 5.90.

Triethylammonium 2,2-difluoro-4-[3-(2,2-difluoro-6-(2-methoxyethyl)-7-methyl-5-oxo-(5*H*)-pyrido[4,3-*d*][1,3,2]-(2*H*)-dioxaborin-4-ylidene)-1-propenyl]-6-(2-methoxyethyl)-7-methyl-5-oxo-(5*H*)-pyrido[4,3-*d*][1,3,2]-(2*H*)-dioxaborinate (**7b**). A mixture of complex **2b** (273 mg, 1 mmol) and diphenylformamidine (100 mg, 0.51 mmol) in acetic anhydride (0.5 mL) was refluxed for 1 min. The solution was cooled down to room temperature, triethylamine (150 mg, 1.49 mmol) was added, and the reaction mixture was stirred at room temperature for 2 h. 2-Propanol was added, the precipitate collected by filtration, and finally recrystallized from 2-propanol. Yield: 120 mg (40 %). M.p. 194-195º. ^{1}H NMR (DMSO-d_6): 1.17 (m, 9 H, CH_3), 2.44 (s, 6 H, CH_3), 3.10 (m, 6 H, NCH_2), 3.24 (s, 6 H, OCH_3), 3.56 (m, 4 H, OCH_2), 4.11 (m, 4 H, NCH_2), 5.98 (s, 2 H, 8-H), 7.60 (d, $^3J_{H,H}$ = 13.5 Hz, 2 H, α-H, α`-H), 8.73 (t, $^3J_{H,H}$ = 13.5 Hz, 1 H, β-H), 8.81 (br s, 1 H, N^+H). Anal. calcd. for $C_{29}H_{41}B_2F_4N_3O_8$: C, 52.97; H, 6.24; N, 6.39. Found: C, 52.83; H, 6.34; N, 6.37.

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