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Difluoroborates of Phenyl-Substituted Aza-Dipyrromethenes: Preparation, Spectral Properties, and Stability in Solution

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Abstract—Boron(III) complexes with phenyl-substituted meso-aza-dipyrromethenes (one of them 4,4'-brominated) have been prepared. The bromination has resulted in weakening of the compound fluorescence by more than ten-fold. The studied complexes are stable for a long time in the solutions in non-polar solvents both in the dark and exposed to light. The bromine-containing complex rapidly decomposes in the polar media.

Keywords: *ms*-aza-dipyrromethene, BODIPY, synthesis, absorption spectrum, fluorescence, stability

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The interest towards 4,4-difluoro-4-bora-3a,4a-diaza-s-indacenes (difluoroborates of dipyrromethenes also known as BODIPY dyes) has emerged in the recent years; these compounds have been recognized as universal phosphors exhibiting excellent thermal [1] and photochemical stability, a high quantum yield of fluorescence (most often independent of the solvent nature), and a high molar absorptivity [2]. BODIPY compounds have been applied as fluorescence labels, switches, chemosensors, and laser dyes [3–5]. Owing to the evident advantages of BODIPY over the conventional phosphors, new strategies of BODIPY structural modification and the respective properties optimization (including introduction of various substituents at pyrrole rings and the spacer of the dipyrromethene scaffold [6–8]) have been widely studied.

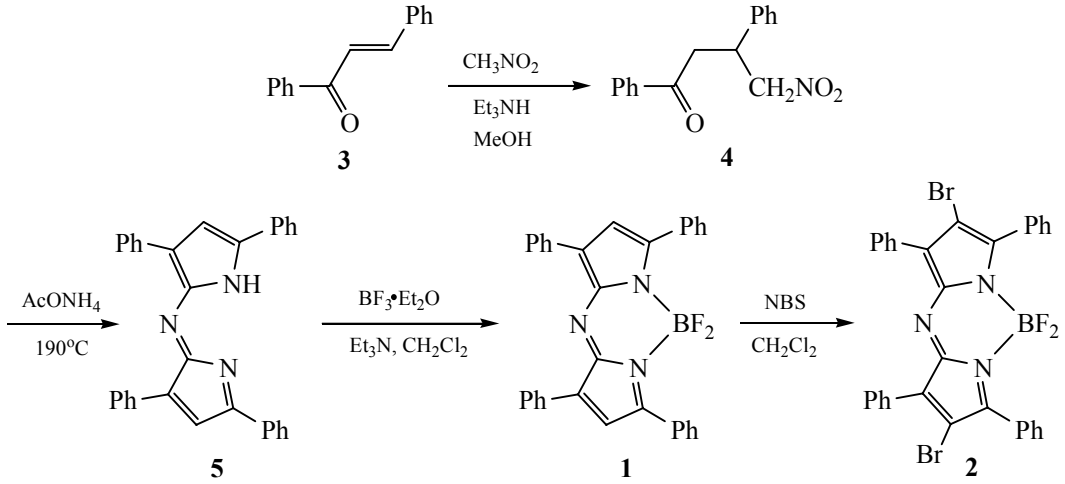
The dyes exhibiting strong absorption and fluorescence at the long-wave (600–800 nm) spectral range can be used as sensibilizers for photodynamic therapy and metabolism monitoring in biological systems [9]. The 4,4'-halogenated aza-derivatives of BODIPY are of specific interest in this regard. Besides the light absorption and emission efficiency, the stability in different media in the dark and at light is an important phosphors property in view of their practical application.

In this work we studied the effect of the substitution with heavy atoms (bromine) on spectral properties and stability in the solution of boron(III) complexes with phenyl-substituted aza-dipyrromethenes (compounds **1** and **2**).

Complexes **1** and **2** were prepared from chalcone **3**: the interaction of the latter with nitromethene in the presence of diethylamine afforded 1-nitro-2,4-diphenylbutan-4-one **4,** and its high-temperature intramolecular condensation in the presence of ammonium acetate gave 3,3',5,5'-tetraphenyl-*ms*-aza-2,2'-dipyrromethene **5**. Compound **5** was transformed into the difluoroborate complex **1** via treatment with boron trifluoride etherate in the presence of triethylamine; the subsequent bromination with *N*-bromosuccinimide yielded the corresponding dibrominated derivative **2** (Scheme 1).

Electron absorption spectra of complexes **1** and **2** in different organic solvents contained a strong band [λ_{max} = 643–653 (**1**) and 641–646 (**2**) nm], a weak broadened band [λ_{max} = 475–478 (**1**) and 504–511 (**2**) nm], and a near-UV band [λ_{max} = 307–308 (**1**) and 282–287 (**2**) nm] typical of the aryl-substituted compounds (Figs. 1 and 2). The spectra shape of complexes **1** and **2** was practically identical in all studied solvents: the non-polar (cyclohexane and dichloromethene) as well as polar proton-donor

Scheme 1.



(propanol-1, ethanol, and methanol) and electron-donor (DMF) ones. The solvatochromism was reflected in a slight blue (up to 4 nm, compound **1**) or red (up to 5 nm, compound **2**) shift of the maximum of the stronger absorption band for the solutions in cyclohexane as compared to the corresponding solutions in alcohols.

Fluorescence spectra of solutions of complexes **1** and **2** in cyclohexane ($c \approx 1 \times 10^{-6}$ mol/L) contained a single band with a maximum at 674 nm (Fig. 3), the fluorescence being by more than an order of magnitude stronger in the case of complex **1**.

Solutions of complex **1** in cyclohexane and alcohols were stable at light for over several weeks. Solutions of complex **2** in cyclohexane and other non-polar solvents were stable as well (Fig. 2a), whereas its solutions in alcohols and DMF became colorless within less than 24 h (Fig. 2b, curve *4*). For example, the absorption band with maximum at 641 nm became weaker upon storage of ethanol solution of compound **2**, and the absorbance in the near-UV region (λ_{max} = 286 nm) grew stronger; those changes evidenced practically complete decomposition of the chromophore into the colorless unsaturated or aromatic compounds. As seen from the data plotted in Fig. 4, the major changes of the electron absorption spectrum of ethanol solution of complex **2** were observed during the first 3 h of the exposure to light.

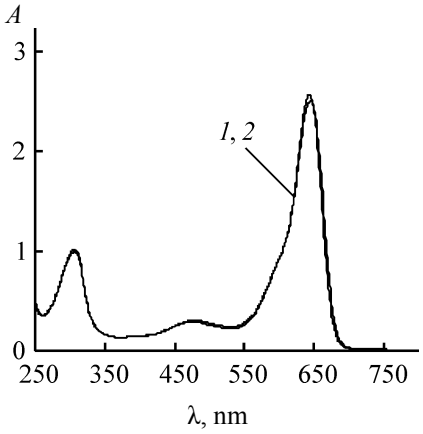


Fig. 1. Electron absorption spectra of complex **1** solutions in (*1*) cyclohexane and (*2*) propanol.

Most likely, the decomposition of complex **2** in the polar reactive solvents (alcohols and DMF) occurred via the nucleophilic substitution of bromine atoms followed by the reduction of the *meso*-aza bridge imine bond with bromide anions and oxidative decomposition of the aza-dipyrrin scaffold and the substituents with the formed bromine. Elucidation of the detailed mechanism of the process requires additional experiments falling outside the scope of this study.

To summarize, the bromination of compound **1** at the 4,4′ positions of the aza-dipyrrin scaffold significantly decreased the stability of that BODIPY dye in the polar electron- and proton-donor solvents and weakened its fluorescence, having no effect on the excellent stability of the studied compounds in inert non-polar organic media.

EXPERIMENTAL

Chalcon **3** and boron trifluoride etherate (both from Sigma-Aldrich) were used as received. Organic solvents (dichloromethane, ethanol, and DMF) were

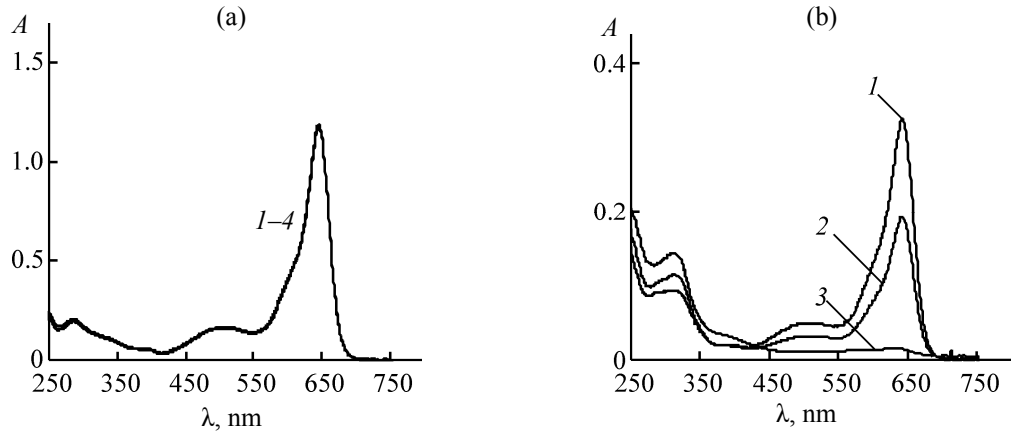


Fig. 2. Electron absorption spectra of complex **2** solutions in (a) cyclohexane and (b) propanol: (*1*) freshly prepared solution and the solution stored at light during (*2*) 3 h, (*3*) 1 day, and (*4*) 3 week.

purified by conventional methods [10]. Propanol-1 (UVIR-HPLC-HPLC preparative, PAI) and cyclohexane (Panreac) were used as received. Absorption and luminescence (λ_{ex} = 615 nm) spectra were registered using a CM2203 (SOLAR) spectrofluorimeter. ^{1}H NMR spectra of the solutions in $CDCl_3$ (298 K, 500 MHz) were recorded using an AVANCE III-500 (Bruker) spectrometer installed at the Upper-Volga Regional Center for Physicochemical Studies.

1-Nitro-2,4-diphenylbutan-4-one (4) was prepared via the procedure adopted from [9]. A solution of 10.0 g (48.0 mmol) of compound **3**, 10.4 mL (0.193 mol) of nitromethane, and 15.0 mL (0.145 mol) of diethylamine in 100 mL of methanol was refluxed during 24 h. After the solvent removal, the residue was recrystallized from methanol. Yield 8.14 g (63%), mp 97–99°C.

3,3',5,5'-Tetraphenyl-*ms*-aza-2,2'-dipyrromethene (5) was prepared via the procedure adopted from [11]. A mixture of 3 g (3.71 mmol) of compound **4** and 25 g of ammonium acetate was heated at 190°C during 2 h. The reaction mass was then cooled to ambient and diluted with water; the precipitate was filtered off, washed with water several times, and dried in air. The so obtained crude product was dissolved in dichloromethane and twice purified by chromatography on silica gel (L 40/100) collecting the medium part of the major elution zone. The solvent was evaporated, and the product was precipitated with methanol on cooling. Yield 2.35 g (70.2%). ^{1}H NMR spectrum, δ, ppm: 7.24 s (2H, 4,4'-H), 7.35–7.69 m (12H, *m,p*-H-Ph), 7.94–8.17 m (8H, *o*-H-Ph), 14.43 br.s (1H, NH). Found %: H 5.26; C 85.59; N 9.24. $C_{32}H_{23}N_3$. Calculated %: H 5.16; C 85.50; N 9.35.

3,3',5,5'-Tetraphenyl-*ms*-aza-2,2'-dipyrromethene difluoroborate (1). 1.32 g (13.1 mmol) of triethylamine and 1.86 g (13.1 mmol) of boron trifluoride etherate were added to a solution of 0.588 g (1.31 mmol) of 3,3',5,5'-tetraphenyl-*ms*-aza-2,2'-dipyrromethene in 40 mL of dichloromethane (room temperature, at stirring). The solution was stirred during 3 h, washed with water, and dried over sodium sulfate. After the solvent removal the residue was purified by chromatography on silica gel eluting with dichloromethane. The solvent was evaporated, and the product was precipitated with methanol upon cooling. Yield 0.426 g (65.4%). Electron absorption spectrum, λ_{max}, nm (log ε): 653(5.02), 478(4.05), 308(4.49) (benzene); 643, 475, 307 (cyclohexane); 649(4.91), 478, 308 (chloroform); 647, 478, 307 (propanol-1); 645, 477, 307 (ethanol). Fluorescence spectrum: λ^{fl}_{max} 674 nm (cyclohexane). ^{1}H NMR spectrum, δ, ppm: 7.07 s (2H,

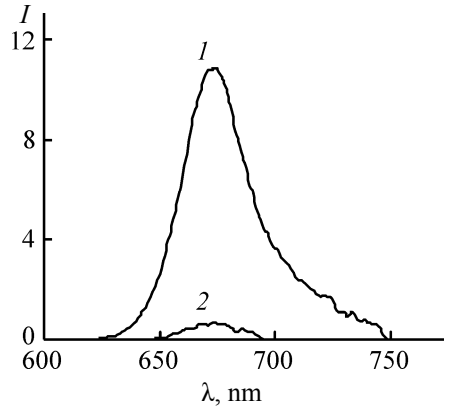


Fig. 3. Fluorescence spectra of solutions of complexes (*1*) **1** and (*2*) **2** in cyclohexane (equal concentration of the complexes).

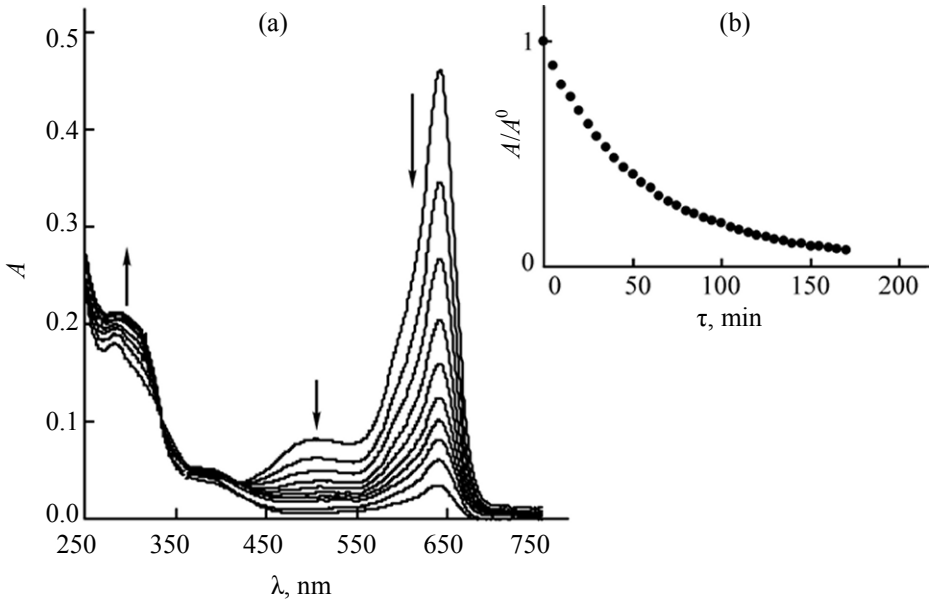


Fig. 4. Evolution of electron absorption spectrum of ethanol solution of complex **2** in the course of 210 min keeping at (a) light and (b) the corresponding change of the absorbance ($A_{641}/A_{641,0}$).

4,4'-H), 7.44–7.58 m (12H, *m,p*-H-Ph), 8.04–8.15 m (8H, *o*-H-Ph). Found, %: H 4.22; C 76.85; N 8.32. $C_{32}H_{22}BF_2N_3$. Calculated, %: H 4.46; C 77.28: N 8.45.

4,4'-Dibromo-3,3',5,5'-tetraphenyl-*ms*-aza-2,2'-dipyrromethene difluoroborate (2). 0.143 g (0.804 mmol) of *N*-bromosuccinimide was added to a solution of 0.1 g (0.201 mmol) of compound **4** in 20 mL of anhydrous dichloromethane. The solution was refluxed during 1 h, cooled to ambient, and subjected to chromatography on silica gel (L 40/100) eluting with dichloromethane. The solvent was evaporated, and the product was precipitated with methanol upon cooling. Yield 0.088 g (67%). Electron absorption spectrum, λ_{max}, nm: 646, 507, 287 (cyclohexane); 649 (4.91), 509, 287 (chloroform); 643, 510, 286 (propanol-1); 641, 511, 286 (ethanol). Fluorescence spectrum: λ^{fl}_{max} 674 nm (cyclohexane). ^{1}H NMR spectrum, δ, ppm: 7.46–7.51 m (12H, *m,p*-H-Ph), 7.74–7.91 m (8H, *o*-H-Ph). Found %: H 3.10; C 58.59; N 6.34. $BF_2C_{32}H_{20}Br_2N_3$. Calculated %: H 3.08; C 58.67; N 6.41.

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