NIR dyes

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Near-Infrared Dyes and Fluorophores Based on Diketopyrrolopyrroles

*Georg M. Fischer, Andreas P. Ehlers, Andreas Zumbusch, and Ewald Daltrozzo**

Dedicated to Professor Friedrich Dörr on the occasion of his 85th birthday

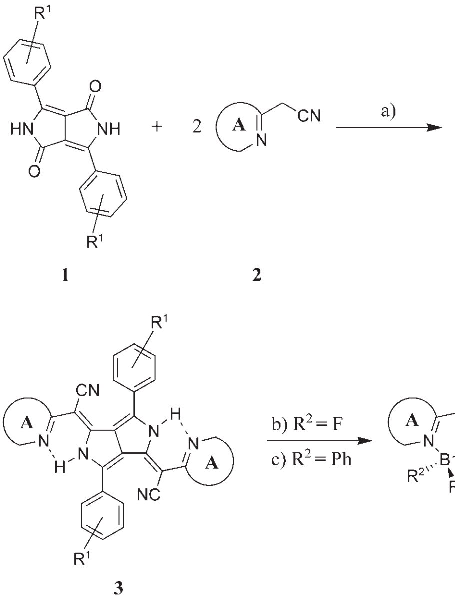
Our research activities over the last few decades have concerned correlations between molecular structure and fluorescence.[1,2] A central theme of the research has been the synthesis and spectroscopic investigations of near-infrared (NIR) dyes[3] to get insights into what degree the obtainable fluorescence quantum yields[4,5] are restricted by the $S_0 \leftrightarrow S_1$ energy gap.[6,7] Our results[8] on the condensation of 1,4-phthalazinediones with heteroarylacetonitriles in $POCl_3$ prompted us to carry out the reaction with diketopyrrolopyrroles (DPPs) **1**.[9] Herein we report the results of the investigations.

To date, attempts to activate the carbonyl group of DPPs with $POCl_3$, and to subsequently convert the intermediates with nucleophiles, only led to monosubstitution or to ring opening.[9,10] The reaction of **1** and **2** in refluxing toluene with an excess of $POCl_3$ according to Scheme 1 afforded disubstituted NIR dyes **3**. The progress of the reaction was controlled by recording absorption spectra and stopping the heating as soon as the DPP was used up and/or products absorbing at short wavelengths appeared. Purification was carried out by digesting the product in acetone and subsequent flash chromatography (silica gel/$CHCl_3$ or CH_2Cl_2).

The NIR dyes **3a**–**3h** (the structures and spectroscopic data of **3b**–**3h** can be found in the Supporting Information) were synthesized according to this procedure (Scheme 1) from the reaction of **1**[11] and **2**. The course of the reactions was the same in all cases and side-products with strong absorptions below 350 nm were observed. These side-products are most likely compounds formed by the opening of the DPPs pentalene ring system.

Prerequisite for the reactions is a certain solubility of the DPPs.[12] This is a feature of all of the DPPs used here with the exception of the 4-methoxy derivative **1b**. Remarkably, the 4-(*N*-methyl-*N*-octyl amino) derivative **1e** has a much better solubility than all the other DPPs used. Only in the case of the reaction of **1e** with **2a** were we able to isolate the 1:1 condensation product (13% yield).

The heteroarylacetonitriles **2a** and **2b** substituted with a *tert*-butyl group were used to improve the solubility of the condensation products **3**. In general, satisfying yields were obtained only if the solubility of both condensation partners was improved by having longer alkyl groups (Table 1). From these observations we draw the following conclusion concerning the reaction pathway: DPP reacts with $POCl_3$ to form a monophosphorylated intermediate,[9] which reacts with the



Scheme 1. Reagents and conditions: a) absolute toluene/$POCl_3$, reflux; b) 1,2-dichlorobenzene/$BF_3 \cdot Et_2O$, reflux, diisopropylethylamine; c) xylene/chlorodiphenylborane, reflux; DPPs **1**: R^1 = 4-octyloxy (**1a**), R^1 = 4-methoxy (**1b**), R^1 = 4-butyloxy (**1c**), R^1 = 4-(hex-5-enyloxy) (**1d**), R^1 = 4-(*N*-methyl-*N*-octylamino) (**1e**); heteroarylacetonitriles **2**: 2-(6-*tert*-butylquinolin-2-yl)acetonitrile (**2a**), 2-(6-*tert*-butylbenzothiazol-2-yl)acetonitrile (**2b**), 2-(quinoxalin-2-yl)acetonitrile (**2c**), 2-(6-methylpyridin-2-yl)acetonitrile (**2d**). A: aromatic ring.

Table 1: Yield and spectroscopic data of the first electronic transition ($S_0 \rightarrow S_1$) of **3a**–**3h**.[a]

Reactants		NIR dyes	Yield [%]	λ_{00} [nm]	ε_{00} [$M^{-1}cm^{-1}$]	f
1a	**2a**	**3a**	33	731	118000	0.71
1a	**2b**	**3b**	39	735	115000	0.74
1a	**2c**	**3c**	7	743	135000	0.72
1a	**2d**	**3d**	2	701	70000	0.48
1b	**2a**	**3e**	4	730	111000	0.68
1c	**2a**	**3f**	74	731	103000	0.62
1d	**2a**	**3g**	41	731	115000	0.69
1e	**2a**	**3h**	58	752	115000	0.64

[a] In chloroform at room temperature. λ_{00} = absorption wavelength, ε_{00} = molar decadic absorption coefficient, f = oscillator strength.

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[*] G. M. Fischer, A. P. Ehlers, Prof. Dr. A. Zumbusch,
Prof. Dr. E. Daltrozzo
Fachbereich Chemie
Universität Konstanz
Universitätstrasse 10, 78464 Konstanz (Germany)
Fax: (+49) 7531-883043
E-mail: ewald.daltrozzo@uni-konstanz.de

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heteroarylacetonitrile to give the 1:1 condensation product. Since the solubility of this product is higher than that of the DPP, it reacts faster with an additional equivalent of $POCl_3$ and heteroarylacetonitrile to yield **3**.

The NIR dyes **3a, 3e, 3f**, and **3g** differ only in the length of the alkyl groups on the alkoxy substituent. Consequently they show identical absorption spectra at room temperature. The effect of DPP substituents and of the nature of the heteroarylacetonitrile on both the yield and first electronic transition (λ_{00}, ε_{00}, and oscillatory strength f) is summarized in Table 1. Figure 1 shows the first electronic absorption of the dyes obtained from **1a** and **2a**–**2d**. Whereas the absorption of the quinoline, benzothiazole, and quinoxaline derivative differ only slightly, the absorption of the pyridine derivate is hypsochromically and hypochromically shifted, which agrees with theoretical predictions.

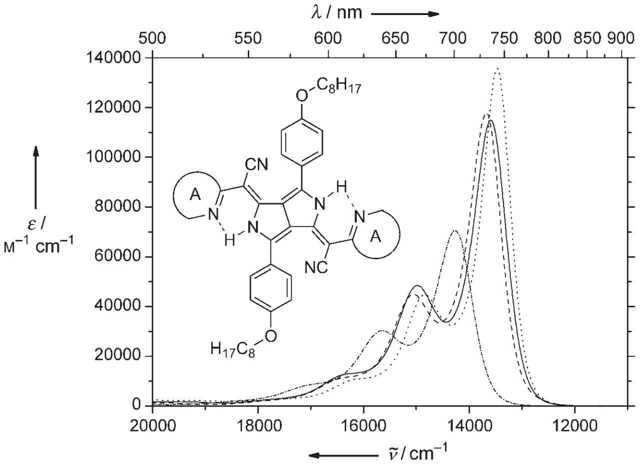

Figure 1. Absorption of the NIR dyes **3a** (——), **3b** (-----), **3c** (•••••), and **3d** (–•–•) with the DPP core **1a** in chloroform at room temperature.

The large intramolecular mobility (high amplitude torsional vibrations of the heteroaromatic terminal groups) of the NIR dyes **3** in solution results in no fluorescence being observed at room temperature. Substitution of the protons in both N–H···N bridges in **3** by a BF_2 or BPh_2 group proved to be the most convenient method to rigidize the chromophore and thus eliminate efficient torsions by radiationless S_1 decay.[2] The desired difluoroboryl chelates **4** were obtained by the reaction of **3** with boron trifluoride etherate and Hünig's base in refluxing 1,2-dichlorobenzene—for example, **4a** was obtained in 61% yield from **3a**. Compound **4a** is stable in dichloromethane: the absorption does not change upon illumination for several hours at 366 nm. Analogous results were obtained for **3e** and **3f**. To our surprise, the difluoroboryl derivate of the benzothiazole dye **3b** could not be isolated because of its lability. Heating **3a** in xylene and addition of chlorobiphenylborane afforded the diphenylboryl chelate **4a′** in a yield of 56%. As expected, all chelates **4** show intense NIR fluorescence at room temperature.

Table 2 gives the characterization data of the first electronic transition and the fluorescence for the boron chelates **4a** and **4a′**. A comparison of the long-wavelength absorptions of **3a**, **4a**, and **4a′** (Figure 2) clearly demonstrates the effects of chromophore stiffening: a) sharpening of the vibronic bands ($\Delta\tilde{\nu}_{1/2} \approx 750\,\mathrm{cm^{-1}}$ for **3a** versus $\Delta\tilde{\nu}_{1/2} \approx 500\,\mathrm{cm^{-1}}$ for **4a** and $\Delta\tilde{\nu}_{1/2} \approx 400\,\mathrm{cm^{-1}}$ for **4a′**), b) increase in the ε_{00} and $f(S_0 \rightarrow S_1)$ values, c) shift of the Franck–Condon factors in favor of the 00 transition.

Table 2: Spectroscopic data of the first electronic transition ($S_0 \leftrightarrow S_1$) of the difluoroboryl chelate **4a** and diphenylboryl chelate **4a′**.[a]

4	λ^A_{00} [nm]	λ^F_{00} [nm]	$\Delta\tilde{\nu}_{A\text{-}F}$ [cm^{-1}]	ε_{00} [M^{-1}cm^{-1}]	f	Φ_F
4a	754	773	320	205000	0.83	0.59
4a′	819	831	180	256000	0.76	0.53

[a] In chloroform at room temperature. $\lambda^A_{00}/\lambda^F_{00}$ = absorption/emission wavelength, $\Delta\tilde{\nu}_{A\text{-}F}$ = Stokes shift, ε_{00} = molar decadic absorption coefficient, f = oscillator strength, Φ_F = fluorescence quantum yield.

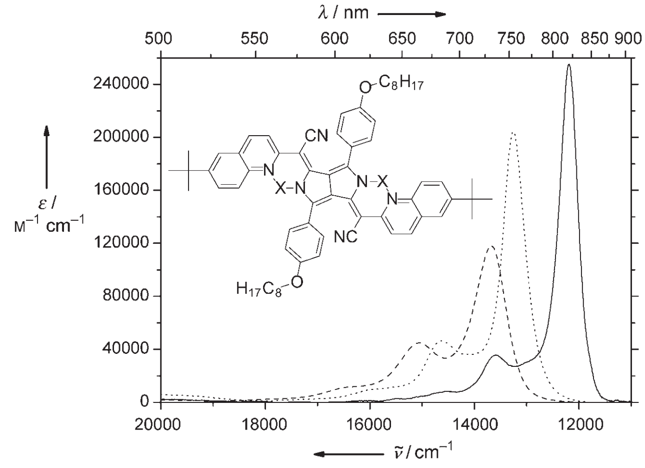

Figure 2. Absorption of **3a**, X = H (-----), **4a** (X = BF_2, •••••), and **4a′** (X = BPh_2, ——) in chloroform at room temperature.

Compound **4a** has a rigid planar chromophore, whereas **4a′** is somewhat twisted as a result of the steric requirements of the phenyl rings of the BPh_2 group. This finding explains the lower $S_0 \rightarrow S_1$ transition moment ($f = 0.76$ for **4a′** versus $f = 0.83$ for **4a**). The smaller half-width of the 00 band[13] indicates that the asymmetrical torsional potential for **4a′** on the side of the small torsional angle is steeper than the symmetrical torsional potential of **4a**. The bathochromic shift of **4a** to **4a′** is the expected consequence of the different σ-inductive effects of BF_2 and BPh_2 on the chromophoric system.

The room-temperature fluorescence quantum yields of 0.59 and 0.53 for **4a** and **4a′**, respectively (with an error of less than 10%), in chloroform at emission wavelengths (λ^F_{00}) of 773 nm and 831 nm, respectively, are, to our knowledge, far higher than for any other known fluorophore.

In contrast to the naphthalenediimides[14] and the rylenediimides,[15] there are only small changes in the molecular geometry resulting from the first electronic excitation in our systems, that is, the potential surfaces of S_0 and S_1 are very similar. Thus, the intensities of the vibrational transitions are strongly shifted towards the 00 transition. This effect combined with the appearance of the 00 band above 800 nm in the spectrum results in **4a′** coming close to being an ideal selective NIR absorber (intense absorption in the near-infrared range, but extremely low absorptions in the visible range from 700 to 380 nm), as is shown by the absorption of **4a′** in methylcyclohexane (Figure 3). Selective NIR absorbers are of technical interest for NIR laser welding of transparent polymers.[16]

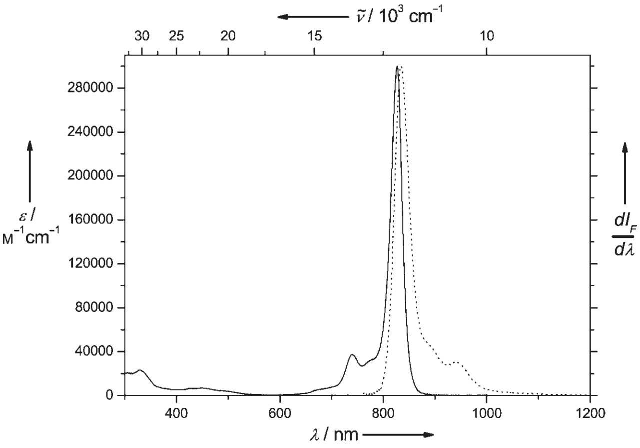

Figure 3. Absorption (——) and fluorescence (•••••) of **4a′** in methylcyclohexane at room temperature.

In conclusion, the condensation of sufficiently soluble diketopyrrolopyrroles with 2-heteroarylacetonitriles provides a new approach to dyes **3** with strong NIR absorptions. Stiffening the chromophore affords NIR fluorophores **4** which results in spectacular properties becoming available. Future applications of the dyes as NIR labels could be accomplished by their functionalization. The first steps towards this goal were already achieved by the synthesis of systems with terminal alkene groups.

Experimental Section

The fluorescence quantum yields were determined on diluted solutions ($c < 2\times10^{-6}$ M) with a home-made spectrometer.[7] A HeNe laser or a 804-nm diode laser were used as the excitation sources, and a germanium diode (NORTHCOAST) used as the detector. CZ 144 (= DY-665-X, Dyomics) was used as a reference dye ($\Phi_F = 0.60$ in $\mathrm{CH_2Cl_2}$).[17]

General procedure for the synthesis of NIR dyes **3**: $\mathrm{POCl_3}$ (8 mmol) was added to a mixture of DPP **1** (1 mmol) and heteroarylacetonitrile **2** (2.5 mmol) in absolute toluene (20 mL) at reflux in a nitrogen atmosphere. The reaction was monitored by UV/Vis/NIR spectroscopy and thin-layer chromatography. As soon as the DPP was used up or short-wavelength-absorbing by-products increased, the reaction was stopped. After removal of the toluene and excess $\mathrm{POCl_3}$ by vacuum distillation, the crude product was dissolved in $\mathrm{CH_2Cl_2}$ and neutralized with aqueous $\mathrm{NaHCO_3}$ solution. The organic phase was separated and dried with $\mathrm{MgSO_4}$. After removing the solvent, the residue was dissolved in acetone in an ultrasonic bath. The remaining solid was separated by filtration, washed with acetone, and purified by column chromatography.

3a: Column chromatography (silica gel/$\mathrm{CHCl_3}$) afforded **3a** as a green crystalline powder in 33% yield. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): $\delta = 14.78$ (br s, 2H; N-H), 7.96 (d, $^3J = 8.8$ Hz, 2H; H-4′), 7.77 (m, 8H; AA′, H-7′, H-8′), 7.65 (d, $^3J = 8.8$ Hz, 2H; H-3′), 7.63 (s, 2H; H-5′), 7.14 (m, 4H; XX′), 4.10 (t, $^3J = 6.6$ Hz, 4H; $\mathrm{OCH_2}$), 1.86 (m, 4H; $\mathrm{OCH_2}$*$\mathrm{CH_2}$*), 1.6–1.3 (m, 38H; alkyl, *tert*-butyl), 0.92 ppm (t, $^3J =$ 6,8 Hz, 6H; $\mathrm{CH_3}$). MALDI-MS: *m*/*z* calcd: 957.6 $[M+\mathrm{H}]^+$, 979.6 $[M+\mathrm{Na}]^+$, 995.5 $[M+\mathrm{K}]^+$; found: 956.8, 978.8, 995.7; UV/Vis/NIR ($\mathrm{CHCl_3}$): $\nu_{00} = 13700$ cm^{-1} ($\lambda_{00} = 731$ nm); $\varepsilon_{00} = 118000$ M^{-1}cm^{-1}, $f =$ 0.71. Elemental analysis calcd (%) for $\mathrm{C_{64}H_{72}N_6O_2}$ [$M =$ 957.30 g mol^{-1}]: C 80.30, H 7.58, N 8.78; found: C 80.36, H 7.67, N 8.37.

4a: $\mathrm{BF_3{\cdot}Et_2O}$ (0.98 mL, 1.77 g, 7.38 mmol) was added to a solution of **3a** (500 mg, 0.52 mmol) in *ortho*-dichlorobenzene (15 mL) at reflux in a nitrogen atmosphere. After 10 min, Hünig's base (0.22 mL, 169 mg, 1.31 mmol) was added and the mixture heated at reflux for a further 10 min. The reaction was then stopped. After removal of the solvent and excess $\mathrm{BF_3{\cdot}Et_2O}$, the crude product was dissolved in methanol in an ultrasonic bath and separated by filtration. Column chromatography (silica gel/$\mathrm{CH_2Cl_2}$) afforded **4a** in 76% yield (420 mg, 0.40 mmol) as a green powder. ^{1}H NMR (400 MHz, $\mathrm{C_2D_2Cl_4}$): $\delta = 8.42$ (m, 2H; H-8′), 8.14 (d, $^3J = 9.3$ Hz, 2H; H-4′), 7.74 (dd, $^3J = 9.5$ Hz, $^4J = 2.2$ Hz, 2H; H-7′), 7.72 (d, 4H; AA′), 7.66 (m, 4H; H-3′,H-5′), 7.06 (m, 4H; XX′), 4.08 (t, $^3J = 6.6$ Hz, 4H; $\mathrm{OCH_2}$), 1.85 (m, 4H; $\mathrm{OCH_2}$*$\mathrm{CH_2}$*), 1.53 (m, 4H; $\mathrm{O(CH_2)_2}$*$\mathrm{CH_2}$*), 1.45–1.2 (br s, 16H; alkyl), 1.36 (s, 18H; *tert*-butyl), 0.91 ppm (t, 6H; $\mathrm{CH_3}$). MALDI-MS: *m*/*z* calcd: 1053.6 $[M+\mathrm{H}]^+$, 1075.6 $[M+\mathrm{Na}]^+$; found: 1053.1, 1076.1; UV/Vis/NIR ($\mathrm{CHCl_3}$): $\nu^A_{00} = 13260$ cm^{-1} ($\lambda^A_{00} =$ 754 nm), $\varepsilon_{00} = 205000$ M^{-1}cm^{-1}, $f = 0.83$; $\nu^F_{00} = 12940$ cm^{-1} ($\lambda^F_{00} =$ 773 nm), $\Phi_F = 0.59$. Elemental analysis calcd (%) for $\mathrm{C_{64}H_{70}B_2F_4N_6O_2}$ [$M = 1052.90$ g mol^{-1}]: C 73.01, H 6.70, N 7.98; found: C 72.51, H 6.95, N 7.83.

4a′: A mixture of **3a** (250 mg, 0.26 mmol) and (321 mg, 1.6 mmol) chlorodiphenylborane was refluxed in absolute xylene (15 mL) under nitrogen. After 10 min at reflux, the reaction was stopped, xylene removed, and the residue purified by column chromatography (silica gel/$\mathrm{CH_2Cl_2}$) to afford **4a′** as a yellow solid in 56% yield (189 mg, 0.147 mmol). ^{1}H NMR (400 MHz, $\mathrm{C_2D_2Cl_4}$): $\delta = 8.18$ (d, $^3J = 9.5$ Hz, 2H; H-8′), 7.83 (d, $^3J = 9.3$ Hz, 2H; H-4′), 7.58 (d, $^3J = 9.3$ Hz, 2H; H-3′), 7.34 (m, 10H; H-5′, *m*-phenyl), 7.15 (dd, $^3J = 9.5$ Hz, $^4J = 2.2$ Hz, 2H; H-7′), 7.10 (m, 12H; *o*- ,*p*-phenyl), 6.52 (d, 4H; AA′), 6.06 (m, 4H; XX′), 4.02 (t, $J = 6.6$ Hz, 4H; $\mathrm{OCH_2}$), 1.86 (m, 4H; $\mathrm{OCH_2}$*$\mathrm{CH_2}$*), 1.53 (m, 4H; $\mathrm{O(CH_2)_2}$*$\mathrm{CH_2}$*), 1.48–1.25 (br s, 16H; alkyl), 1.16 (s, 18H; *tert*-butyl), 0.93 ppm (m, 6H; $\mathrm{CH_3}$). MALDI-MS: *m*/*z* calcd: 1285.7 $[M+\mathrm{H}]$, found: 1285.5; UV/Vis/NIR ($\mathrm{CHCl_3}$): $\nu^A_{00} = 12210$ cm^{-1} ($\lambda^A_{00} =$ 821 nm), $\varepsilon_{00} = 256000$ M^{-1}cm^{-1}, $f = 0.76$; $\nu\lambda^F_{00} = 12030$ cm^{-1} ($\lambda^F_{00} =$ 831 nm), $\Phi_F = 0.53$. Elemental analysis calcd (%) for $\mathrm{C_{88}H_{90}B_2N_6O_2}$ [$M = 1285.32$ g mol^{-1}]: C 82.23, H 7.06, N 6.54; found: C 81.59, H 7.11, N 6.49.

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[11] The starting materials **1a**–**1d** were obtained in 30–40% yields by heating the *para*-substituted benzonitriles with diethyl succinate in sodium 2-methylbutan-1-olate/2-methylbutan-2-ol at reflux as described in the Ref. [9]. By this method, **1e** could be obtained in only 7% yield.

[12] We are much obliged to Dr. H. J. Metz, Dr. K. Rode, Dr. J. Weber, and Dr.H. Wiezer, Clariant AG, for samples of 3,4-dimethoxyphenyl-, 3,5-dichlorophenyl-, 4-fluorophenyl-, 3,4,5-trimethoxyphenyl-, and 4-butoxyphenyl-DPP for test reactions.

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