Tailoring the Properties of Boron−Dipyrromethene Dyes with Acetylenic Functions at the 2,6,8 and 4-B Substitution Positions
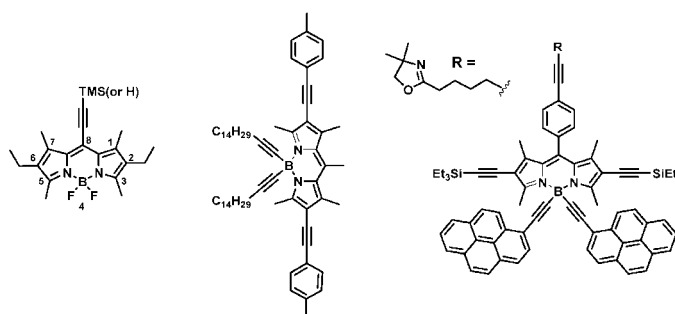
Laure Bonardi, Gilles Ulrich,* and Raymond Ziessel*

Laboratoire de Chimie Organique et Spectroscopies Avancées (LCOSA), Centre National de la Recherche Scientifique (CNRS), Université Louis Pasteur, Ecole de chimie, Polymères, Matériaux de Strasbourg (ECPM), 25 rue Becquerel, 67087 Strasbourg, Cedex 02, France

ziessel@chimie.u-strasbg.fr

ABSTRACT

Substitution of F-Bodipy with alkynylaryl residues at boron, at the pyrrolic core or at the meso position, provides unique tri-, tetra-, and pentasubstituted dyes. Substitution at the (pyrrolic) 2,6-positions provides substantial red shifts with quantum yields in the 40−90% range and excited-state lifetimes of 3−7 ns. ON/OFF fluorescence switching can be produced by protonation of dibutylamino subunits.

Difluoroboradiaza-*s*-indacene (*F*-Bodipy) derivatives are the subject of intense current research not only as convenient fluorescent dyes for biochemical labeling[1] but also as part of photonic molecular systems, laser dyes, mesomorphic materials, organogelators, and dopants in light-emitting devices.[2]

Strategies to extend the absorption properties to the near-infrared[3] have been based on (i) substitution of the 3,5-positions by styryl functions,[4] (ii) replacement of the meso 8-carbon by a nitrogen atom leading to aza-Bodipy,[5] (iii)

fusing some aromatic rings to the Bodipy core,[6] and finally, (iv) the replacement of pyrrole by isoindole.[7] The electronic absorption and emission profiles are clearly sensitive to the delocalization over the skeleton, and yellow to deep-green colors are provided routinely. The substitution of the central 8-position with aryl groups has little effect on the optical properties except where these groups incorporate electron-donating substituents like linear or cyclic tertiary amines or

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electron-withdrawing substituents like NO_2[8] or CN.[9] In these cases, photoinduced electron transfer (oxidative and reductive, respectively) are responsible for luminescence quenching. Otherwise, the orthogonality of the central fragment with respect to the dipyrromethene core prevents orbital interaction.

In considering the modification of Bodipy to induce properties such as high solubility, the capacity for ready linking to biological substrates, and enhanced absorptivity, it may be noted that 2,6-substitution has not been utilized much, probably because of the lack of general synthetic procedures.[10,11] The objective of the present work was therefore to develop procedures as part of a battery of methods for introducing these types of functionalities at all possible sites on the Bodipy molecule.

To this end, we first explored the synthesis of **1** by a classical route (Scheme 1). Condensation of Kryptopyrrole

Scheme 1
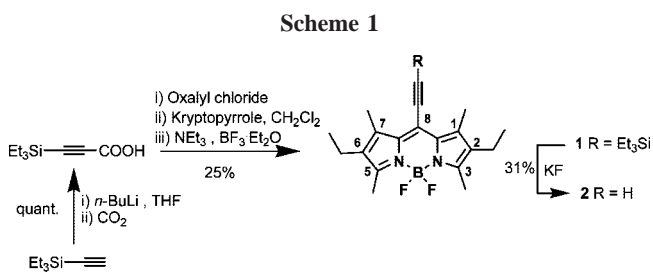
(2,4-dimethyl-3-ethylpyrrole) with the in situ generated triethylsilylacetylene acid chloride provided, in 25% yield, the target compound **1**, which could be deprotected to the corresponding terminal alkyne **2** in 31% yield. Both compounds show an intense $S_0 \rightarrow S_1$ absorption at 572 nm, red-shifted by 30 nm compared to the methyl-substituted derivative[12] due to extension of conjugation. Unfortunately, owing to the relatively high reactivity of the terminal alkyne, cross-coupling with various halogenoaryl derivatives failed under a variety of experimental conditions.

A strategy based on the Bodipy made from Knorrpyrrole (2,4-dimethylpyrrole) was more successful (Scheme 2). Here, the selective electrophilic attack of ICl provided either the monoiodo **4** and **5** or the bis-iodo derivatives **6** and **7** in excellent yields under mild conditions when compared to the previously described procedure.[13] Cross-coupling of *p*-tolylacetylene or di-*n*-butylaminophenylacetylene was straightforward, providing **8** to **11** in acceptable yields (Scheme 2).

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Scheme 2
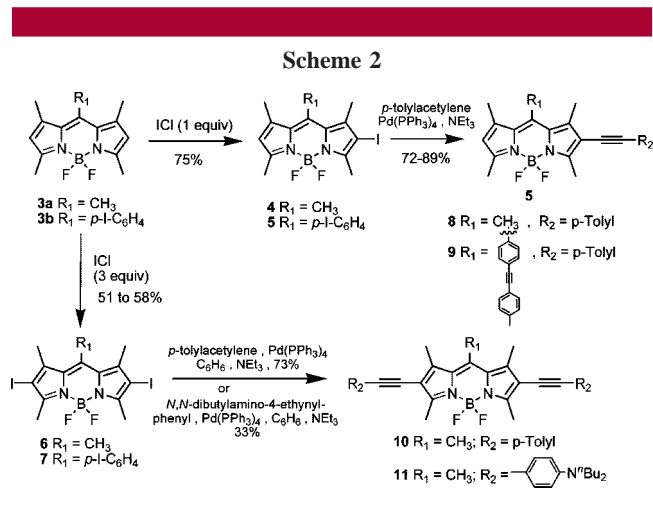
Under conventional Pd catalysis, iodophenyl and iodopyrrole substituents appear to react at similar rates, so that reactant **5** gives the disubstituted product **9**. As anticipated, the substitution of the β pyrrolic iodo substituent in **4**, **5**, and **6** by ethynyltolyl groups induces a bathochromic shift in the emission peaks by 64, 62, and 94 nm, respectively, for **8**, **9**, and **10** compared to the starting material.

For attachment of arylalkynyl fragments at boron, selective functionalization is feasible in the presence of halogenopyrrole residues: the use of alkynyl-Grignard reagents providing **13**−**16** in good yield (Scheme 3). The disappearence of the

Scheme 3
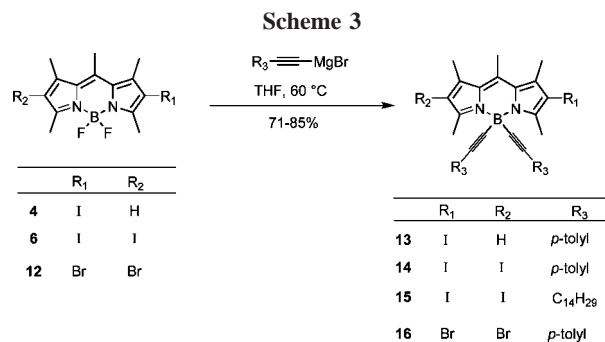
triplet at ca. 3.5 ppm in the ^{11}B NMR spectrum in favor of a singlet at ca. −9 ppm is good evidence for the substitution process.[14]

Our next target became the substitution of the iodo groups by arylalkynyl entities. Both mono- and double-cross-linking smoothly afforded the highly fluorescent dyes **17** and **18** in excellent yields, although the use of solubilizing alkyl groups on the boron center was crucial to avoid precipitation during the synthesis of **18** (Scheme 4).

As expected from earlier work on the substitution of fluoro by alkynyl fragments, no additional wavelength shift was observed. Thus, due to the absence of heavy atoms in **17**

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Scheme 4
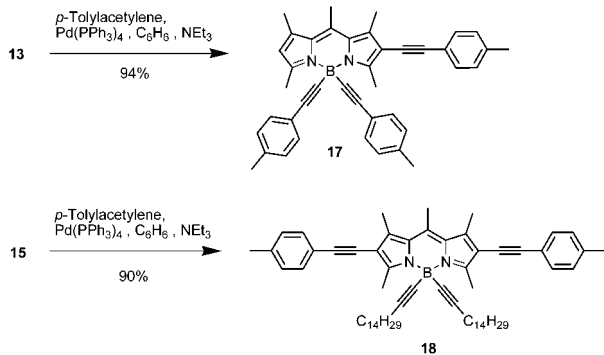
and **18** compared to **13** and **15**, the fluorescence quantum yields increase to 75 and 72%, respectively, and the excited-state lifetimes are ~4 ns.

To perform more sophisticated syntheses, discrimination between halogen substituents at the β pyrrolic and meso-phenyl centers was required. This was achieved as outlined in Scheme 5. Interestingly, despite the presence of acetylenic


Scheme 5
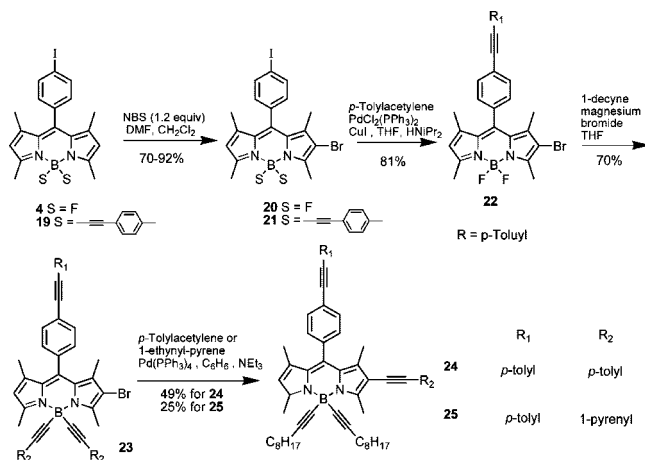
bonds linked to the boron atom in **19** and two phenyl moieties, the reaction with NBS nonetheless provided the monobromo compounds **20** and **21** in respectable yields. To circumvent the selectivity problem observed with **5** between the phenyl iodo in the 8-position and iodo in the 4-position, we reacted **20** and **21** under standard conditions with 1 equiv of *p*-tolylacetylene. Compound **20** reacted smoothly to give **22** in 81% yield, while **21** gave a mixture of insoluble derivatives which could not be fully separated by conventional procedures.

After some experimentation, we succeeded in preparing tetrasubstituted derivatives carrying three different acetylenic derivatives using a sequence of substitution at boron by means of C_{10}-Grignard reagents to give high solubility, followed by cross-coupling with different acetylenic reagents

such as *p*-tolylacetylene or 1-pyrenylacetylene. The highly soluble compounds **24** and **25** were easily purified.

These reactions demonstrated the possibility of preparing pentasubstituted dyes bearing three different acetylenic frameworks, each imparting different properties to the final fluorophore. As a prototypical example, we introduce an aliphatic alkyne first bearing a dimethyloxazoline group (as carboxylic acid protection) via Sonogashira coupling to the *meso*-iodophenyl subunit (Scheme 6). The compound **26** was

Scheme 6
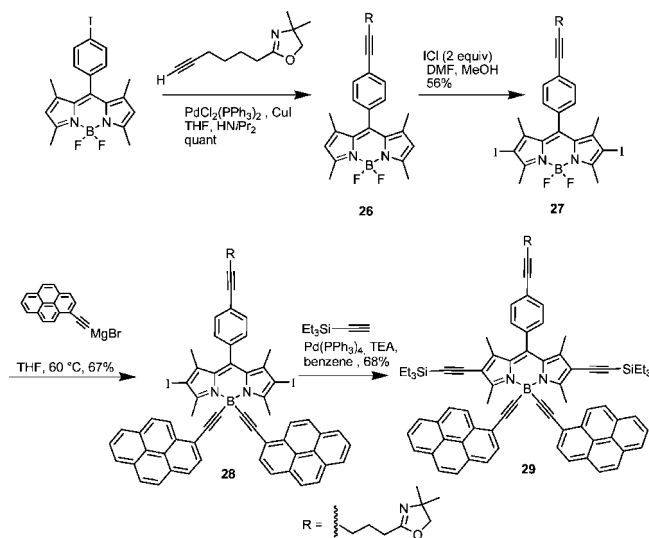
selectively iodinated by use of ICl in a polar solvent to give the nonfluorescent compound **27** in fair yield, despite the presence of an alkyne function. The use of two equivalents of ethynyl-Grignard allowed the replacement of both fluorine atoms by two ethynylpyrene units, leading to compound **28** in 67% yield. Triethylsilylacetylene functions were easily linked to the Bodipy core by standard procedures.

Some of the compounds described here show unusual photophysical behavior (Table 1). Molecules having a heavy halogen atom on the 2- or 2,6-positions show low quantum yields and reduced fluorescence lifetimes. This is largely due to efficient intersystem crossing leading to a low lying triplet state.[13]

Compound **11** is of particular interest in that its absorption spectrum displays a large and red-shifted band, and an additional intense band around 330 nm, presumably due to intramolecular charge transfer (ICT) from the *p*-dialkylaminophenyl-ethynyl residues to the Bodipy. This ICT would explain the fluorescence quenching, but additional photoinduced electron transfer is also possible.

Protonation of the amino groups induces a drastic change in the absorption and emission spectra, and restores the fluorescence. This phenomenon has been observed with other Bodipy derivatives bearing tertiary amine groups on the 8-[15] and 3-positions.[2,3]

As expected, compound **29** behaves like a known pyrene-substituted Bodipy:[14] an almost quantitative intramolecular

Table 1. Optical Properties of Selected Compounds in CH_2Cl_2 at rt[a]

| compd	λ_{abs} (nm)	ϵ (M^{-1} cm^{-1})	λ_{em} (nm)	τ (ns)	Φ^b (%)
1	571	57000	593	5.2	20
2	573	54000	591	5.1	40
4	509	90000	529	<1	14
6	527	90000	548	<1	6
8	526	72000	575	3.2	47
10	565	83000	603	3.5	46
11	599	40000	700	-	<1
11 + 2H^{+c}	554	65000	584	3.7	53
17	523	73000	561	4.2	75
18	557	89000	588	3.9	72
24	529	50000	570	4.3	55
25	540	62000	602	1.8	20
28	531	64400	549	<1	2
29	552	66700	571	6.5	99
	370	86000	571		90

[a] Determined in aerated dichloromethane solution, ca. 5×10^{-7} M. Using Rhodamine 6G as reference, $\Phi = 0.78$ in water, $\lambda_{exc} = 488$ nm. All Φ_F are corrected for changes in refractive index. [b] Excitation at the corresponding λ_{max} wavelength. [c] By addition of CF_3COOH in dichloromethane.

energy transfer being observed after excitation in the pyrene absorption bands. This is not the case with derivative **25**, where the ethynylpyrene group is connected to the 2-position (Figures 1 and 2). Here, the fluorescence of the dye drops
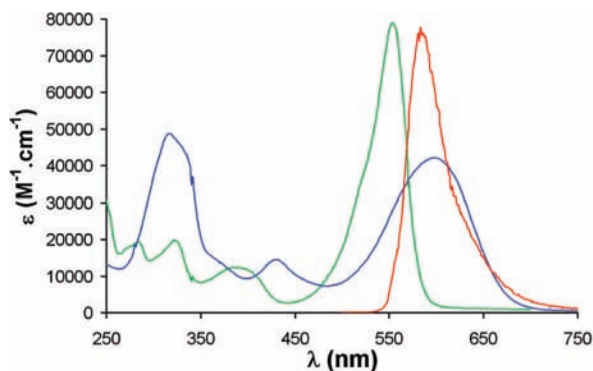
Figure 1. Absorption spectra of **11** (blue), **11** with 2 equiv of CF_3COOH (green), and emission of **11** with TFA (red).

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to 20% when excited in the Bodipy S_0-S_1 transition and weak energy transfer occurs after excitation of the pyrene moiety (residual quantum yield around 2%).
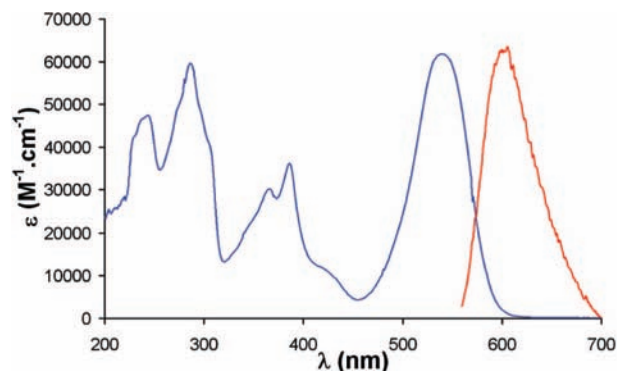
Figure 2. Absorption (blue line) and emission (red line) of **25** in CH_2Cl_2 at rt.

In conclusion, we have developed a new series of π-conjugated Bodipys based on the selective substitution either at the dipyrromethene core (2,6-positions), or at the 8 and 4 positions. The electrophilic iodination of the dipyrromethene core with ICl is significant even in the presence of alkyne fragments which remain inert. In comparison with standards, the obvious red-shift of λ_{max} of their absorption and PL spectra is in agreement with an increase of the effective conjugation length. Introduction of multiple substituents not only suppresses the formation of aggregates but also modifies the solubility and spectroscopic properties. We are currently synthesizing a complete library of novel compounds by adapting these strategies to investigate dendritic Bodipy scaffoldings for photon-concentrators.

Supporting Information Available: Experimental procedure and characterization; proton and carbon spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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