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Convenient Synthesis of Green Diisoindolodithienylpyrromethene–Dialkynyl Borane Dyes

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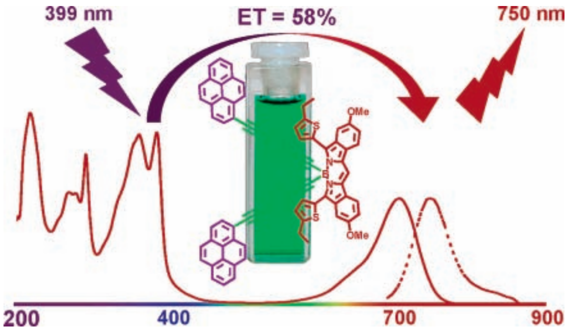
ABSTRACT



Versatile dyes based on diisoindolodithienylpyrromethene substituted at the boron center by alkynylaryl chromophores have been developed that efficiently fluorescence in the near infrared. Fast intramolecular energy transfer from the appended alkynyl units to the central core provides Stokes shifts above 16 000 cm^{-1}.

The engineering of light-emitting molecules for practical applications[1] depends upon the achievement of the right balance between the electronic interactions and their effects upon the excited-state lifetimes of the chromophoric subunits. The development of high-performance, environmentally stable fluorescent probes has been largely a consequence of efforts to mimic the light-harvesting complexes and reaction centers of natural photosynthetic systems.[2] While highly fluorescent molecules derived from acridine,[3] anthracene,[4] phenanthrene,[5] pyrene,[6] dansyl,[7] and indacene[8−11] cores display a rich variety of optical properties, challenges remain in the control of nonradiative decay pathways and in the conversion of often fragile organic frameworks to more robust species. Partial success in enhancing stability has, however, been achieved by encapsulating dyes within nanoparticles.[12] To overcome the problems of generally low yields in the synthesis of complex chromophores and rather

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(1) Valeur, B. In *Molecular Fluorescence*: *Principles and Applications*; Wiley-VCH: Weiheim, Germany, 2002.

(2) (a) Olson, J. M. *Photochem. Photobiol.* **1998**, *67*, 61. (b) Gust, D.; Moore, T. A.; Moore, A. L. *Acc. Chem. Res.* **2001**, *34*, 40.

(3) Herbich, J.; Kapturkiewicz, A. *J. Am. Chem. Soc.* **1998**, *120*, 1014.

(4) (a) Mataga, N.; Nishikawa, S.; Asahi, T.; Okada, T. *J. Phys. Chem.* **1988**, *92*, 6233. (b) Wiessner, A.; Hüttmann, G.; Kühnle, W.; Staerk, H. *J. Phys. Chem.* **1995**, *99*, 14923.

(5) Onkelinx, A.; De Schryver, F. C.; Viaene, L.; Van der Aueraer, M.; Iwai, K.; Yamamoto, M.; Ichikawa, M.; Masuhara, M.; Maus, M.; Rettig, W. *J. Am. Chem. Soc.* **1996**, *118*, 2892.

(6) (a) Herbich, J.; Kapturkiewicz, A. *Chem. Phys.* **1993**, *170*, 221. (b) Harriman, A.; Hissler, M.; Ziessel, R. *Phys. Chem. Chem. Phys.* **1999**, *1*, 4203. (c) Hissler, M.; Harriman, A.; Khatyr, A.; Ziessel, R. *Chem. Eur. J.* **1999**, *5*, 3366. (d) Shen, Z.; Procházka, R.; Daub, J.; Fritz, N.; Acar, N.; Schneider, S. *Phys. Chem. Chem. Phys.* **2003**, *5*, 3257.

(7) Prodi, L.; Bolletta, F.; Montalti, M.; Zaccheroni, N. *Eur. J. Inorg. Chem.* **1999**, 455.

(8) Kollmannsberger, M.; Rurack, K.; Resch-Genger, U.; Daub, J. *J. Phys. Chem.* **1998**, *102*, 10211.

(9) Wan, C.-W.; Burghart, A.; Chen, J.; Bergström, F.; Johanson, L. B.-A.; Wolford, M. F.; Kim, T. G.; Topp, M. R.; Hochstrasser, R. M.; Burgess, K. *Chem. Eur. J.* **2003**, *9*, 4430.

(10) Yilmaz, M. D.; Bozdemir, O. A.; Akkaya, E. U. *Org. Lett.* **2006**, *8*, 2871.

(11) McDonnell, S. O.; O'Shea, D. F. *Org. Lett.* **2006**, *8*, 3493.

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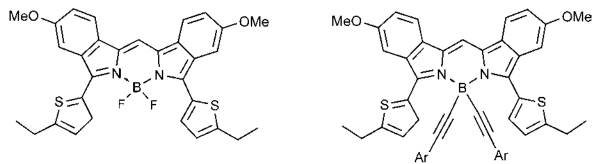
limited possibilities for varying these syntheses, we have turned our attention to the remarkable family of difluoro-bora-diaza-s-indacene ("*F*-Bodipy") dyes. These are particularly intriguing molecules for several reasons:[8,9,13] (i) they combine high molar absorptivities with very high fluorescence quantum yields; (ii) their optical properties can be tuned by modifying the pyrrole unit and/or the bridge of the pyrromethene unit and/or, as shown recently, the boron substituents; (iii) they are chemically and photochemically stable in solution and in the solid state; and (iv) they are redox active both as oxidants and as reductants.

The focus of the present work is the issue of whether or not a range of *F*-Bodipy derivatives can be obtained showing both absorption and emission in the near-infrared area (in particular, 720−780 nm; Figure 1A). To this end, we have explored the substitution of the fluoride ligands on boron by polyaryl-alkynide ligands (Figure 1B), the aryl substituents being designed to produce large virtual Stokes' shifts by virtue of intramolecular energy transfer.



A **B**

Figure 1. General formulas for *F*-Bodipy and *E*-Bodipy.

While trigonal alkynylboranes[14] are well-characterized species, much less is known of tetrahedral alkynylborates[15,16] and thus we have explored their synthesis in some detail. The systems developed significantly extend the scope of available indacene-dye derivatives and provide photo- and electroactive materials with potential applications in both biological analysis and various light-emitting devices.

Our earlier work involving introduction of oligopyridine substituents onto the *meso* position of *F*-Bodipy's demonstrated that this could produce highly luminescent materials, soluble in polymeric matrices, of considerable promise in sensors[17] and electroluminescent devices.[18] The pivotal building block **1**[19] absorbs at 727 nm ($\epsilon = 90\,000$ M^{-1} cm^{-1}) and emits at 780 nm with a quantum yield of 20% when excited in the lower energy absorption band (Figure 2), thus largely satisfying the demands specified above for a near-infrared active material. Its excitation and absorption spectra match precisely, indicating that the emission results from the $S_1 \rightarrow S_0$ transition. The Stokes' shift, however, as expected for an organic singlet emitter, is relatively small ($\Delta\nu = 930$ cm^{-1}), but slightly larger than in dipyrromethene dyes.[17]

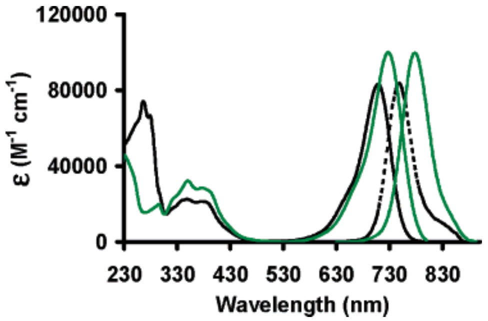
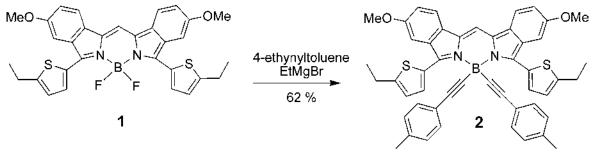


Figure 2. Absorption, emission spectra of starting material **1** (green) and pivotal intermediate **5** (black) in CH_2Cl_2, at rt.

The promising characteristics of **1** prompted us to examine further functionalization involving attachment of arylalkynide fragments at boron, the aryl substituents involving both metal ion chelating and luminescent polycyclic aromatic units. Our earlier observation was that **1** was not resistant to substitution using 4-lithioethynyltoluene or 1-lithioethynylpyrene, probably as a result of deprotonation of the relatively acidic *meso*-proton. This problem could be readily circumvented, however, by using alkynyl-Grignard reagents in place of the lithium species, enabling **2** to be obtained readily and in good yield (Scheme 1).

Scheme 1



Thus, our present target became the substitution of the fluoro ligands by sophisticated arylalkynyl entities. Crucial to the success of the strategy adopted was the unsymmetrical functionalization of 1,4-diiodobenzene with acetylenic units bearing different protecting groups (Scheme 2).

Our earlier work on bipyridine derivatives provided appropriate inspiration.[20] Thus, compound **6** could be selectively deprotected on the 2-hydroxyprop-2-yl side by using an alkali metal hydroxide under anhydrous conditions.

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(12) Montalti, M.; Prodi, L.; Zaccheroni, N.; Zattoni, A.; Reschiglian, P.; Falini, G. *Langmuir* **2004**, *20*, 2989.

(13) (a) Ulrich, G.; Ziessel, R. *Synlet.* **2004**, 439. (b) Ulrich, G.; Ziessel, R. *J. Org. Chem.* **2004**, *69*, 2070. (c) Ulrich, G.; Ziessel, R. *Tetrahedron Lett.* **2004**, *45*, 1949.

(14) (a) Yamaguchi, S.; Akiyama, S.; Tamao, K. *J. Am. Chem. Soc.* **2000**, *122*, 6335. (b) Jia, W.-L.; Saong, D.; Wang, S. *J. Org. Chem.* **2003**, *68*, 701. (c) Kubo, Y.; Yamamoto, M.; Ikeda, M.; Takeuchi, M.; Shinkai, S.; Yamaguchi, S.; Tamao, K. *Angew. Chem., Int. Ed* **2003**, *42*, 2036.

(15) (a) Qian, B.; Baek, S. W.; Smith, M. R., III *Polyhedron* **1999**, *18*, 2405. (b) Ding, L.; Ma, K.; Dürner, G.; Bolte, M.; Fabrizi de Biani, F.; Zanello, P.; Wagner M. *J. Chem. Soc., Dalton Trans*. **2002**, 1566.

(16) Ulrich, G.; Goze, C.; Guardigli, M.; Roda, A.; Ziessel, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 3694.

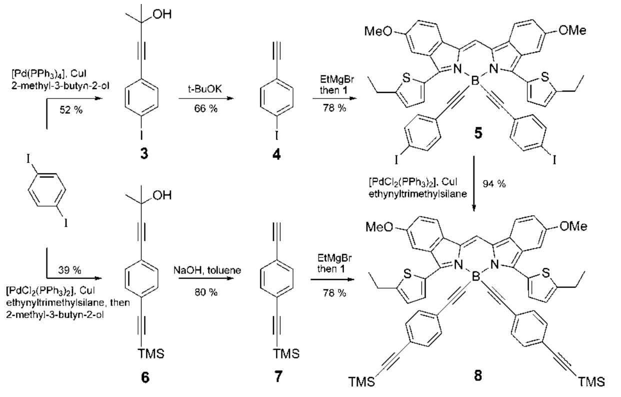
(17) Goze, C.; Ulrich, G.; Charbonnière, L.; Ziessel, R. *Chem. Eur. J.* **2003**, *9*, 3748.

(18) Hepp, A.; Ulrich, G.; Schmechel, R.; von Seggern, H.; Ziessel, R. *Synth. Met.* **2004**, *146*, 11.

(19) Kang, H. C.; Haugland, R. P. U.S. Patent 5,433,896, July 18, 1995.

(20) Goeb, S.; De Nicola, A.; Ziessel, R. *J. Org. Chem.* **2005**, *70*, 1518.

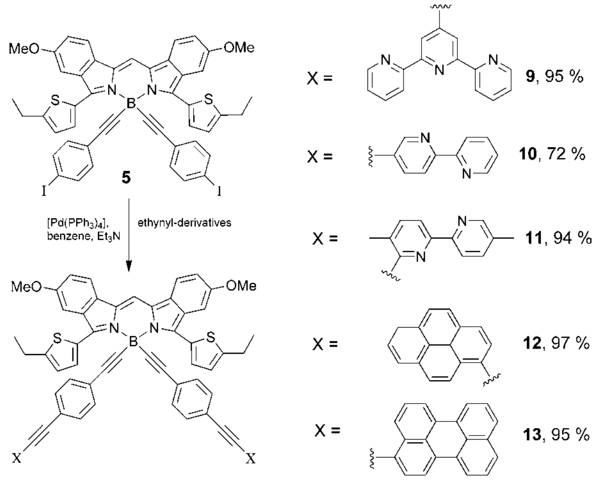
Scheme 2



The Grignard derivatives were prepared by reactions of **4** and **7** with EtMgBr in THF at 50 °C and their reactions with **1** at room temperature provided the target alkynylboron derivatives **5** (78%) and **8** (80%). Note that the conversion of **5** to **8** is also possible by using standard Pd-catalyzed cross-coupling (Scheme 2).

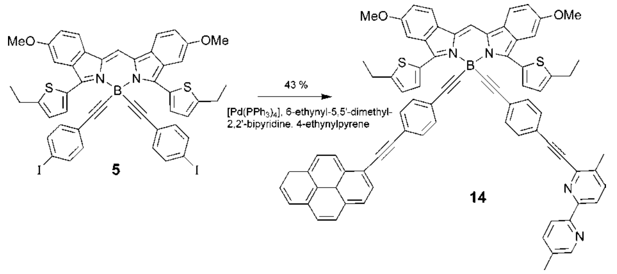
While deprotection of **8** with K_2CO_3 in a protic solvent does produce the terminal alkyne, this was too reactive to be conveniently isolated. Further, in situ deprotection and cross-coupling with 4′-{[(trifluoromethyl)sulfonyl]oxy}-2,2′;6′,2′′-terpyridine[21] results only in an intractable mixture of products, so that, to bypass such problems, we developed a cross-coupling reaction of the bis-iodo compound **5** and a stable terminal alkyne. An outline of the reactions involved is given in Scheme 3.

Scheme 3



With use of known terminal alkynes,[22] reaction occurs under mild conditions and no decomposition of the dyes was observed. Despite the presence of a chelating unit, the catalyst is not deactivated and an excess of triphenylphosphine is not required. Despite their low solubility, both 1-ethynylpyrene and 1-ethynylperylene also reacted efficiently. Interestingly, the mixed species **14** was obtained in 43% isolated yield by using two different ethynyl derivatives mixed immediately, the resulting three components of the product mixture being easily separated by column chromatography (Scheme 4). This design opens up the possibility of preparing new dyes bearing an activated function suitable for protein labeling. The approach is unique in that it uses an easy access to dissymmetric fluorescent dyes.

Scheme 4



All the new dyes are deep emerald-green crystalline solids which show a metallic luster. The electronic absorption spectra all exhibit a structureless maximum near 708 nm with a molar absorptivity of ~80 000 M^{-1} cm^{-1}. A higher energy absorption found near 350 nm in **12** and near 450 nm in **13** can be assigned to spin-allowed $\pi-\pi^*$ transitions centered on the pyrene and perylene fragments, respectively. Note that in some cases the absorption in the near-UV is very strong (Table 1) due to an overlapping of these absorption

Table 1. Optical Properties in CH_2Cl_2, at Room Temperature

compd	λ_{abs} (nm)	ϵ (M^{-1} cm^{-1})	λ_{em} (nm)	ΔS^a (cm^{-1})	Φ^b (%)
1	727	90 000	780	930	20
2	709	86 000	750	771	42
5	709	84 000	750	771	45
8	707	81 000	750	790	43
9	709	86 000	750	771	22
	335	130 000	750	16 500	8
10	708	80 000	750	790	21
	335	123 000	750	16 600	9
11	708	81 000	750	790	19
	342	95 000	750	16 000	9
12	708	83 000	750	790	40
	399	135 000	750	11 800	23
13	708	84 000	750	790	40
	474	122 000	750	7 800	15
14	708	80 000	750	790	34
	399	71 000	750	11 800	18
	344	76 000	750	15 700	15

[a] Stokes shifts calculated from the absorption and emission energies. [b] Relative quantum yields (±20%) determined with use of Cresyl violet as reference[23] ($\Phi = 0.51\%$, $\lambda_{exc} = 578$ nm). Concentration range 0.9×10^{-8} to 1.2×10^{-7} M.

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(21) Potts, K. T.; Konwar, D. *J. Org. Chem.* **1991**, *56*, 4815.

(22) Grosshenny, V.; Romero, F. M.; Ziessel, R. *J. Org. Chem.* **1997**, *62*, 1491.

bands with the one localized on the di-isoindolodithienylpyrromethene skeleton (see Figure 2). In the bipyridine and terpyridine derivatives **9**, **10**, and **11**, absorptions assigned to $\pi-\pi^*$ and $n-\pi^*$ transitions are observed between 290 and 350 nm. In all cases, irradiation in the band near 708 nm gives rise to a broad emission at 780 nm, with quantum yields between 18% and 45%. Selected data are gathered in Table 1.

Intriguing observations were made on irradiating compound **12** in the pyrene band (399 nm) and compound **13** in the perylene band (474 nm). Some very weak residual emission (<1%) from the polyaromatic entities was detectable but far more efficient emission occurred through the bis-isoindolemethene unit near 750 nm (Figure 3). This corresponds to virtual Stokes' shifts of 11 800 and 7 800 cm^{-1}, respectively. Consideration of the quantum yields indicates that intramolecular energy transfer must occur with 58% and 38% efficiency respectively for compounds **12** and **13**. Provided only very dilute solutions (about 1 10^{-7} M) are considered, the absorption and excitation spectra match perfectly, indicating that a single excited state is the source of the observed emission. The use of higher concentration shows aggregate formation, which perturbs the optical behavior.

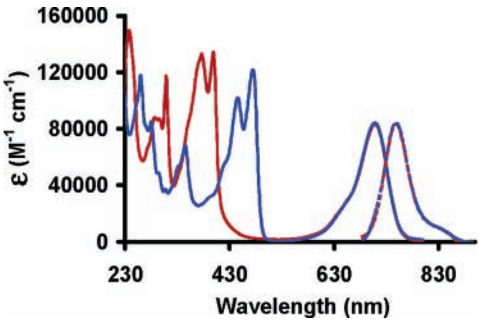

Figure 3. Absorption, emission spectra of **12** (red) and **13** (blue) in CH_2Cl_2, at rt.

The substitution of both fluoro ligands by polyaromatic or polypyridine units in the previously described di-isoindolodipyrromethene frameworks[19] is a nice tool to engender light-emission in the near-infrared region. The virtual Stoke shifts obtained by irradiation in the imported fragments around 400 nm are very high, >16 000 cm^{-1} in some cases due to an efficient intramolecular singlet energy transfer process. For comparison, recently reported work involving the modification of an *F*-Bodipy by a conformationally restricted substituent with less extended conjugation resulted in displacement of the fluorescence only between 630 and 680 nm with Stokes' shifts lying between 240 and 800 cm^{-1}. An added advantage of the presently described compounds is the variation in characteristics associated with the substituted alkynyl ligands on boron. Compounds **12** and **13** have particularly useful characteristics in regard to application as fluorescent labels. They absorb and emit at exceptionally long wavelengths when compared to known Bodipy species and the quantum yields remain satisfactory given the low energy of the emission. We contend that the present work paves the way for the development of a new generation of stable, functionalized luminophores.

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

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(23) Olmsted, J., III *J. Phys. Chem*. **1979**, *83*, 2581.
(24) Chen, J.; Burghart, A.; Derecskei-Kovacs, A.; Burgess, K. *J. Org. Chem.* **2000**, *65*, 2900.