New fluorescent aryl- or ethynylaryl-boron-substituted indacenes as promising dyes

Gilles Ulrich,*[a] Christine Goze,[a] Sébastien Goeb,[a] Pascal Retailleau[b] and Raymond Ziessel*[a]

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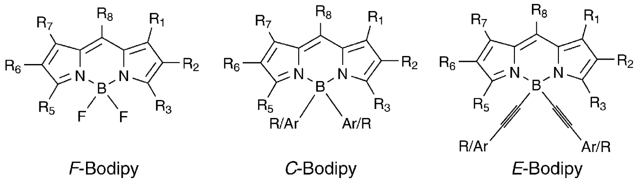
A generic design principle based on the use of organometallic (Li or Mg) reagents for the substitution of the fluoro ligands in difluoroboradiazaindacene is described. A library of compounds bearing various substituents (butyl, phenyl, naphthyl, pyrenyl, ethynylnaphthyl, ethynylfluorenyl, ethynylcarbazoyl, ethynylperylenyl, ethynylthiophenyl and ethynylterpyridinyl) has been prepared and characterized. Electrochemical and photochemical measurements show that these novel dyes remain redox-active and strongly luminescent. They offer an interesting perspective for applications in labelling and electroluminescence.

Active current interests in light-emitting molecules encompass both biological and materials sciences, as well as chemistry. Many highly efficient luminescent molecules have been used as chemical probes, sensors and tracers,[1] as well as in biosensing[2] and optoelectronics.[3] Essential to the further development of these fields is the design and synthesis of chemically stable luminescent molecules emitting at selected wavelengths. The ease and flexibility of synthesis, stability to heat and light, redox activity and toxicity are other important properties of such molecules. Useful platforms for their construction include acridines,[4] anthracene,[5] phenanthrene,[6] pyrene,[7] coumarins[8] and indacene dyes.[9,10]

Recently, it has been shown that the intense fluorescence of rod-shaped oligo-(*para*-phenylene ethynylene) systems can be finely tuned by incorporating donor–acceptor groups.[10] Very convincing relationships between the fluorescence quantum yield and the nature of electron-withdrawing[11] or electron-donating[12] substituents have recently been reported, providing valuable information for the molecular design of novel dyes.

Our interests have been focused on the planar difluoroboradiazaindacene (*F*-Bodipy, Chart 1) framework because its optical properties (absorption, emission and quantum yield) can be tuned at will by modifying the pyrrole substituents,[13] the central *meso* position,[14] and the boron substituents.[15] Nevertheless, knowledge of the structures and properties of *F*-Bodipy chemically modified at the boron center[16] is very limited, and surprisingly little is known about the replacement of fluoride by aryl, ethynylaryl, ethynylthienyl or ethynyl-polypyridine residues, although such derivatives might play significant roles given recent advances in plastic electronics.[17]



F-Bodipy *C*-Bodipy *E*-Bodipy

Chart 1

Herein, we wish to report that the replacement of the fluoro ligands in *F*-Bodipy can be readily achieved by reactions with organometallic reagents under mild conditions. In some cases, mono-aryl/mono-fluoro Bodipys were prepared, and in all cases the optical and redox properties remain very intriguing. The synthesis of alkyl- or aryl-boron-substituted Bodipys (*C*-Bodipy, Chart 1) was effectively accomplished with lithio derivatives, as shown in Scheme 1. These reactions can be readily followed by thin-layer chromatography, useful because this technique is essential for the successful purification of the target fluorophores to make sure that polar side products and unreacted starting materials are present at minimal levels.

The successful syntheses of boron-disubstituted Bodipys using alkyl-lithium reagents prompted us to also examine the use of Grignard reagents. As expected, the reactions were less vigorous and could be conducted at higher temperatures. Again, the *C*-Bodipy species, isolated in fair yields, were chemically, thermally and photochemically stable.† The highly fluorescent monosubstituted reaction intermediates could be isolated more readily from the reactions involving Grignard reagents (Scheme 2). The use of one equivalent of the Grignard reagent at 0 °C enabled, for example, the isolation of the monosubstituted compounds **6** and **7** in fair yield, though both the disubstituted derivatives **3** and **4** and some unreacted starting materials were also present in the product mixture. Increasing the temperature dramatically decreased the yield of the monosubstituted derivatives, while decreasing the temperature to −78 °C inhibited the substitution process completely.

Two conformers of **4**, displaying minor differences, were identified in the crystal state (Fig. 1),‡ confirming both the stoichiometry and the structure anticipated on the basis of the synthetic procedure.§ The boron center is a distorted tetrahedron, with B–N1, B–N2 and B–C1″ equivalent bonds of 1.580(8), 1.579(7) and 1.608(6) Å, respectively, and an

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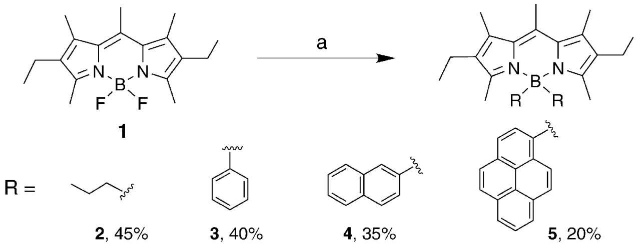
[a] *Laboratoire de Chimie Moléculaire, École de Chimie, Polymères, Matériaux (ECPM), 25 rue Becquerel, 67087 Strasbourg Cedex 02, France. E-mail: gulrich@chimie.u-strasbg.fr. E-mail: ziessel@chimie.u-strasbg.fr; Fax: +33 3 90 24 26 35; Tel: +33 3 90 24 26 89*
[b] *Laboratoire de Cristallochimie, ICSN-CNRS, Bât 27-1 avenue de la Terrasse, 91198 Gif-sur-Yvette Cedex, France*



Scheme 1 a: RLi, THF, 0–20 °C.

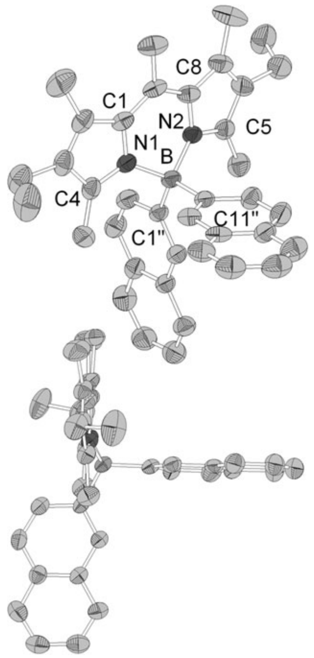


Fig. 1 ORTEP views of **4** with ellipsoids at the 50% probability level.

elongated B–C113 bond of $<$1.641(9) Å, with bond angles N1–B–N2, C1″–B–C11″, N1–B–C1″ and N2–B–C11″ of $<$104.3(3), 115.3(4), 108.9(3) and 110.9(3)°, respectively. In the B–C11″ equivalent direction, the boron is displaced from the mean plane of the dipyrromethene by 0.39 Å, a deformation not observed in the related *F*-Bodipy.[14,18]

Subsequent to the syntheses of the alkyl- and aryl-Bodipy compounds, we examined the reactions of various lithiated arylacetylenes with *F*-Bodipy **1**, leading to *E*-Bodipy (Chart 1). Here, the reaction is very fast, with the intermediate monosubstituted compounds being undetectable and a temperature higher than 20 °C being detrimental. Under optimal conditions, the naphthalene, fluorene and perylene compounds are readily prepared, but the isolated yields decrease with increasing size and electron density of the aryl residues (Scheme 3). Interestingly, this reaction tolerates heteroatoms (S and N), but the yield dramatically decreases with the terpyridine fragment, possibly due to the lithiation of the terpyridine unit in the *ortho*-position of the pyridine ring.

To demonstrate the generality of this protocol, we have replaced the methyl group on the dipyrromethene unit by a *para*-tolyl group (**14**) or a proton (**15**). No significant loss of reactivity was found when similar conditions were applied (Chart 2). Also, the successful introduction of ethynylpyrene fragments in compound **16**, carrying an empty terpyridine fragment in the *meso* position, is noteworthy.

Interestingly, the ^{1}H NMR chemical shifts of the methyl groups *ortho* to the nitrogen in the indacene core depend upon the nature of the boron substituents (Table 1). A strong shielding of these methyl groups is observed, and is more pronounced when two bulky aromatic groups are grafted onto the boron center: 2.49 ppm for **1** (phenyl) and 1.38 ppm for **5** (pyrene). In contrast, the substitution of the fluorine by ethynyl groups gives a small downfield shift of the methyl residues by up to *ca.* 3 ppm.

Replacement of the fluorine of *F*-Bodipy causes the loss of the triplet at 3.8 ppm in the ^{11}B NMR spectrum and the appearance of a singlet, even for the monofluoro compounds. The chemical shift of this singlet is sensitive to the boron substituent, with a small downfield shift for the aryl-substituted compounds (just above 3.8 ppm) but a very strong upfield shift to *ca.* −9 ppm for the ethynyl derivatives. This effect probably reflects the strong σ-donor character of the ethynyl carbon. In the *E*-Bodipy compounds, the $\nu_{\mathrm{C\equiv C}}$ stretching vibration is found in the 2100 to 2200 cm^{-1} range (Table 1).

All the newly synthesized molecules were also characterized by cyclic voltammetry, and some of the traces are given in Fig. 2. In all cases, quasi-reversible oxidation and reduction processes were found around ≈+0.9 and ≈−1.4 V, which can be straightforwardly assigned to the formation of the Bodipy radical cation (Bodipy$^{+\bullet}$) and radical anion (Bodipy$^{-\bullet}$), respectively. Remarkably, replacing the fluoro groups by butyl fragments in **2** has no influence on either redox process. Switching from butyl to ethynylthienyl facilitates the oxidation by 100 mV and shifts the reduction by 210 mV to more anodic potentials (Fig. 2a). In the ethynylthienyl series of compounds (**11**, **14** and **15**), the Bodipy$^{+\bullet}$ species are formed at nearly the same potential (+0.87 V), whereas the formation of the Bodipy$^{-\bullet}$ species is shifted by 50 to 60 mV from **16** (R = H) to **15** (R = *para*-tolyl) and from the latter to **11** (R = CH$_3$) (Fig. 2b). This reflects the better electron-donating ability of the central methyl group with respect to *para*-tolyl and proton units.

All the new *C*-Bodipy and *E*-Bodipy compounds exhibit an intense absorption around 520 nm, with extinction coefficients of ~70 000 M^{-1} cm^{-1} assigned to a spin-allowed S$_0$ → S$_1$ transition centered on the indacene core (Table 1). A second weak and broad S$_0$ → S$_2$ (π–π*) transition located at *ca.*

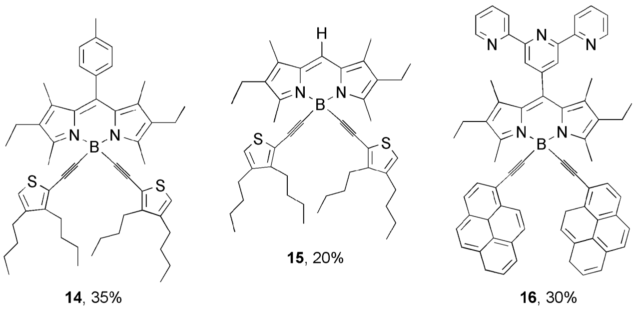
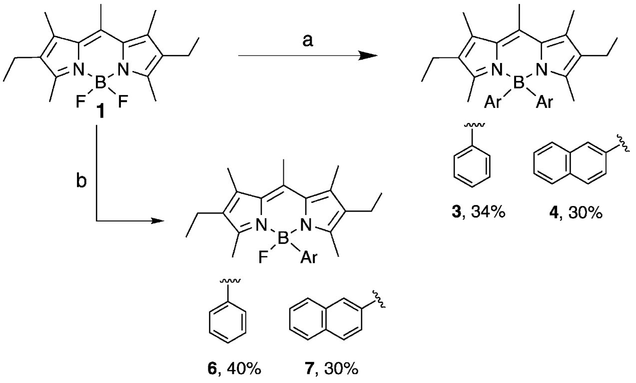


Chart 2



Scheme 2 a: 2 RMgBr, Et_2O, 20 °C. b: RMgBr, Et_2O, 0 °C.

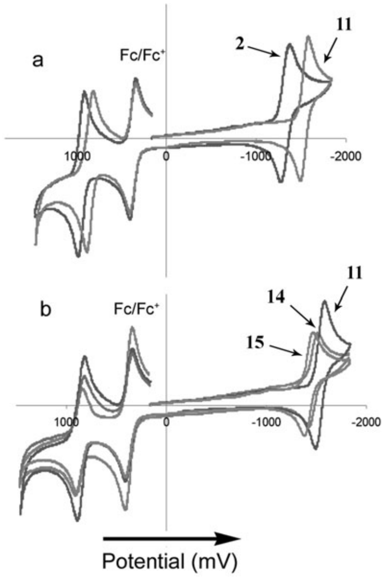


Fig. 2 (a) Cyclic voltammograms of compounds **2** and **11**. (b) Cyclic voltammograms of compounds **11**, **14** and **15** in CH_2Cl_2, at rt, using 0.1 M $^{n}Bu_4PF_6$ as the supporting electrolyte, at a scan rate of 200 mV s^{-1}. Potentials were standardized using ferrocene (Fc) as an internal reference and converted to SCE, assuming that $E_{\frac{1}{2}}(Fc/Fc^+) = +0.38$ V ($\Delta E_p = 60$ mV) *vs.* SCE. $E_{\frac{1}{2}}$ accounts for half peak potential and ΔE_p accounts for peak difference, SCE for saturated calomel electrode.

380 nm was also clearly evident for most of the new species. The peak appearing in the high energy region around 250–300 nm may be assigned to spin-allowed π–π* transitions centered on the aromatic rings grafted either onto the boron or onto the indacene core (Fig. 3). Very strong fluorescence, with quantum yields reaching 98% in some cases, was measured using Rhodamine 6G, as in ref. 19, and is in keeping with that of *F*-Bodipy analogues.[9,18] The excitation spectra, performed under similar conditions, perfectly match the absorption spectra, indicating that the emitted light originates from a single excited state, with almost no contribution from alternative radiative deactivation pathways. The absence of any significant dynamic quenching of the luminescence by molecular oxygen excludes the presence of an emissive triplet excited state.

In summary, we have established a synthetic route for substitution of the fluoro ligands in difluoroindacene derivatives by alkyl, aryl and ethynylaryl fragments. Fifteen new dyes have been successfully synthesized and characterized by various methods, including, in the case of naphthyl, X-ray crystallography. The redox properties of these molecules differ significantly from those of their *F*-Bodipy parent compounds, although both the photochemical stability† and high quantum yields are retained. This design strategy paves the way for the construction of optical tags suitable for labelling biological materials. Further work will explore the design of dendritic-like frameworks for biphotonic studies.

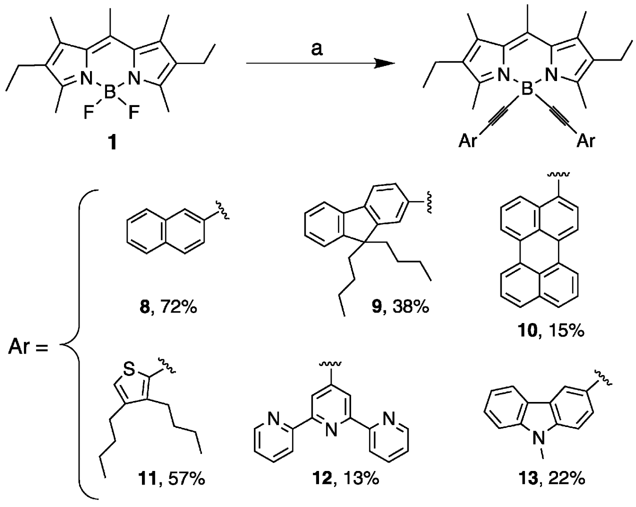
Experimental

A typical example of the synthesis of **16** is described: Butyllithium (0.15 mL, 1.55 M in hexane) was added to a solution of 1-ethynylpyrene (0.041 g, 0.179 mmol) in 5 mL of THF at

Table 1 Selected spectroscopic data of the novel dyes

Compound	^{1}H NMR/ppm[a]	^{11}B{^{1}H}/ppm[b]	IR[c] $\nu_{C\equiv C}$/cm^{-1}	λ_{max}/nm[d] (ε/M^{-1} cm^{-1})	λ_{em}/nm[d]	Φ (%)[e]
1	2.49	3.82	–	517 (64 500)	538	83
2	2.41	3.83	–	527 (60 000)	538	95
3	1.70	2.70	–	514 (64 500)	548	91
4	1.73	2.87	–	516 (74 500)	552	50
5	1.38	4.97	–	524 (46 300)	577	25
6	2.16	5.73	–	519 (75 000)	543	90
7	2.17	5.75	–	516 (57 000)	543	92
8	2.93	−9.63	2172	517 (77 700)	537	90
9	2.96	−9.60	2122	517 (70 000)	535	94
10	3.00	−9.40	2125	517 (53 500)	535	95
11	2.79	−9.60	2168	516 (67 000)	536	98
12	2.84	−9.88	[f]	517 (87 000)	536	80
13	2.98	−9.48	2165	515 (81 000)	536	97
14	2.79	−9.60	2167	519 (60 000)	533	89
15	3.02	−9.24	2167	526 (76 800)	537	95
16	3.15	−8.92	2164	526 (70 000)	590	40

[a] Chemical shift of the methyl groups in the position *ortho* to the nitrogen atoms. [b] Determined in $CDCl_3$. [c] KBr pellets. [d] Measured in CH_2Cl_2 at 23 °C, λ_{max} maximum absorption and λ_{em} maximum emission. [e] Relative quantum yields determined using Rhodamine 6G as in ref. 19 ($\Phi = 0.78\%$, $\lambda_{exc} = 488$ nm). Excitation wavelength is λ_{max} of the boradiazaindacene entity. [f] Not observed.



Scheme 3 a: ArC≡CLi, THF, 0–20 °C.

−78 °C. The dark green anion was allowed to slowly warm up 0 °C and was then transferred *via* cannula to a solution of 2,6-diethyl-4,4-difluoro-1,3,5,7-tetramethyl-8-(2:2′:6′:2″-terpyridin-4′-yl)-4-bora-3a,4a-diaza-*s*-indacene[14] (0.048 g, 0.089 mmol) in 10 mL of THF. Complete consumption of the starting material was observed after 10 min. The solution was then readily quenched with water and the compound extracted with dichloromethane. Column chromatography (alumina, CH_2Cl_2/cyclohexane 20 : 80) followed by recrystallization (CH_2Cl_2/cyclohexane) gave the desired compound **16** (0.025 g, 30% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) (δ/ppm): 8.82 (d, 2 H, ^3J = 9.0 Hz), 8.75–8.69 (m, 6 H), 8.22–7.98 (m, 16 H), 7.91 (dt, 2H, ^3J = 8.0, ^4J = 2.0 Hz), 7.37 (m, 2 H), 3.15 (s, 6 H), 2.45 (q, 4 H, ^3J = 7.6 Hz), 1.57 (s, 6 H) and 1.09 (t, 6 H, ^3J = 7.5 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) (δ/ppm): 156.4, 155.7, 154.6, 149.5, 147.1, 137.0, 136.3, 133.6, 132.3, 131.5, 131.4, 130.5, 129.9, 128.6, 128.0, 127.6, 127.5, 126.5, 126.1, 125.3, 125.2, 124.75, 124.70, 124.6, 124.3, 121.5, 121.3, 120.8, 17.2, 15.0, 14.7 and 12.9; ^{11}B{^{1}H} NMR ($CDCl_3$, 128 MHz) (δ/ppm): −8.92 (s); UV-vis (CH_2Cl_2) (λ/nm (ε/M^{-1} cm^{-1})): 526 (70 000), 370 (103 000), 358 (78 000), 285 (111 400), 275 (74 400) and 248 (106 000); IR (KBr) (ν/cm^{-1}): 2961 (s), 2164 (m), 1582 (s), 1402 (s), 1178 (s), 978 (s) and 845 (s); FAB$^+$ (*m*/*z* (nature of peak, relative intensity (%))): 948.2 ([M + H]$^+$, 100), 722.2 ([M–pyr–≡–]$^+$, 20); anal. calc. for $C_{68}H_{50}BN_5$: C, 86.16; H, 5.32; N, 7.39. Found: C, 85.95; H, 5.12; N, 7.27%.

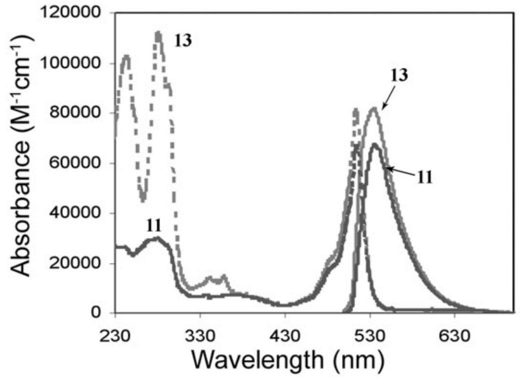


Fig. 3 Absorption spectra (dotted) and emission spectra (full line) for compounds **11** and **13**. All spectra were measured in CH_2Cl_2 at rt.

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† In our hands, no obvious degradation of the novel dyes has been observed by treatment with water, protic solvents, acids or strong bases in daylight. For instance, these dyes are stable in hot piperidine overnight. No particular precautions have to be taken during the work-up of these compounds, or during chromatography, crystallization or spectroscopic studies. Compounds could be stored at rt in air and in daylight. However, some decomposition might occur in excess F$^-$ anions or strong oxidants. This statement of stability is based on current observations.

‡ X-ray crystal data for **4** at 293 K. Formula sum: $C_{38}H_{39}BN_2$, formula weight: 534.52, crystal system: triclinic, space group: *P*-1 (no. 2). Unit cell dimensions: a = 13.236(5), b = 13.934(5), c = 18.545(5) Å, α = 102.109(5), β = 90.215(5), γ = 112.416(5)°, unit cell volume: 3075.05(180) Å^3, Z = 4, density (calculated): 1.153 g cm^{-3}. Reflections collected/unique 15816/6224 (R_{int} = 0.0304), data/restraints/parameters 6224/4/768. Final R indices [$I > 2\sigma(I)$]: $R1$ = 0.0587, w$R2$ = 0.1565; R indices (all data): $R1$ = 0.0881, w$R2$ = 0.1809. CCDC 606381. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b604830g.

§ Indeed, there are two independent molecules in the asymmetric unit of the triclinic cell (Z = 4). If the rms coordinate difference between boradiazaindacene moieties is only 0.136 Å, the main differences between them mainly reside in the relative orientations of the naphtyl groups.

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