

## 8-Alkoxy- and 8-Aryloxy-BODIPYs: Straightforward Fluorescent Tagging of Alcohols and Phenols

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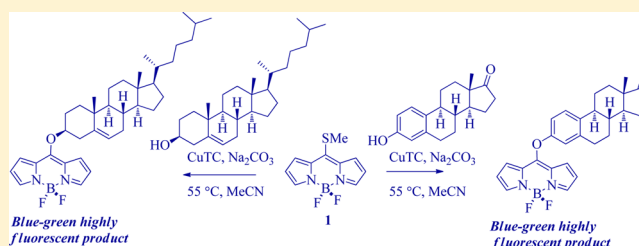
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### S Supporting Information

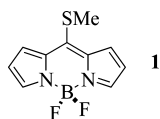
**ABSTRACT:** We demonstrate herein that both alcohols and phenols can be tagged with a BODIPY (borondipyrromethene) moiety to yield highly fluorescent products. Thus, 8-(methylthio)-BODIPY (**1**) undergoes an  $S_NAr$ -type reaction with a host of alcohols and phenols in the presence of a base and a Cu(I) additive. The BODIPY dyes bearing alkoxy or nonfunctionalized phenoxy moieties are characterized by a highly efficient fluorescence emission, regardless of the media, in the blue-green part of the visible region. Complementary to this, the presence of electron-donor groups at the aryl ring leads to an intramolecular charge-transfer process, which quenches the fluorescence mainly in polar media. In addition to simple alcohols and phenols, four natural products (eugenol, menthol, cholesterol, and estrone) were labeled in a simple fashion. X-ray structures of the cholesterol and estrone derivatives are discussed. In fact, the BODIPY bearing cholesterol stands out as a bright fluorescence biological marker.



## INTRODUCTION

Applications seemingly unrelated such as the design of drug nanocarriers used in theranostics (area of research that combines diagnostic detection agents with therapeutic drug delivery carriers)<sup>1</sup> and recently reported conjugated materials used in solution-processed solar cells<sup>2</sup> have one thing in common: they both contain one or several BODIPY (borondipyrromethene) units. Among their most useful properties are strong absorbance in the visible wavelengths, narrow absorption bands, and tunable photophysics that can allow one to vary both the quantum yield ( $\phi_F$ ) and emission wavelength ( $\lambda_{em}$ ).<sup>4</sup> These types of dye have found ample use in biology<sup>5</sup> and materials science,<sup>6</sup> due to the fact that they can be grafted onto the substrate of interest, thereby making it fluorescent or fluorescent-prone.

After a seminal report by Biellmann et al. in 2006, which described the synthesis and optical properties of 8-(methylthio)-BODIPY (**1**),<sup>7</sup> our research groups have demonstrated that such a compound can efficiently participate in a variety of useful chemical transformations.



For example, **1** participates in the Liebeskind–Srogl cross-coupling reaction<sup>8</sup> with boronic acids to yield the correspond-

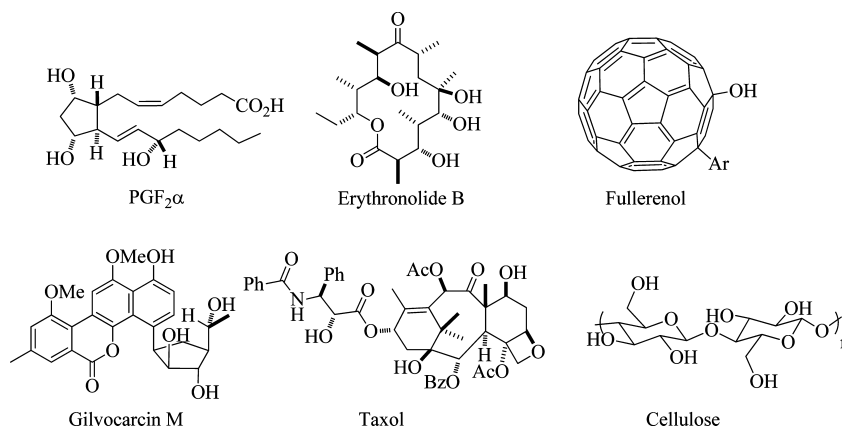
ing 8-substituted BODIPY derivatives.<sup>9</sup> Also, the methylthio group can be replaced by a proton to produce the parent unsubstituted BODIPY system in almost quantitative yield.<sup>10</sup> We have shown as well that the methylthio group could be substituted by primary and secondary amines to give highly fluorescent blue-emitting analogues, a property hitherto unknown for BODIPY dyes.<sup>11</sup> In this way, blue-emitting BODIPYs were developed with improving fluorescence and lasing performance with regard to commercially available laser dyes in that region. The reason for such unexpected behavior was that the BODIPY delocalized  $\pi$  system, characterized as a cyclic cyanine, changes to a hemicyanine-like system with the presence of the amino group. However, the fluorescence efficiency of the derivatives bearing secondary and tertiary amines was limited in polar media by the activation of a quenching intramolecular charge-transfer (ICT) process.

Although BODIPY dyes have been conjugated to many biologically relevant molecules,<sup>12</sup> a great synthetic effort has to be devoted to the modification of the BODIPY core in order to add a functional group that would allow the attachment to the target molecule under mild conditions. Alternatively, one can purchase the commercially available dyes<sup>3</sup> already functionalized for the desired purposes, albeit at sky-high prices.

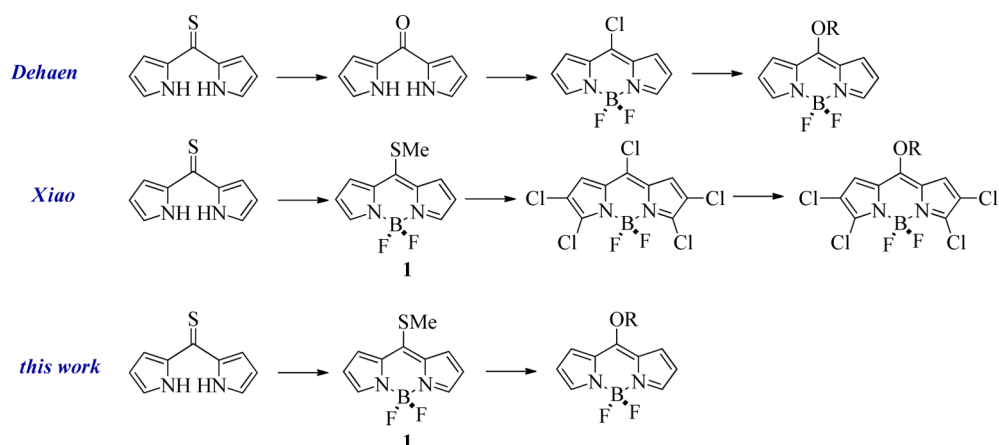
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Chart 1. Hydroxylated Complex Products



Scheme 1. Different Ways To Prepare Alkoxy-BODIPYs



On the other hand, intriguing research possibilities have arisen that give the opportunity to tag hydroxylated complex molecules (i.e., the molecules in Chart 1) with a fluorescent moiety under mild reaction conditions.

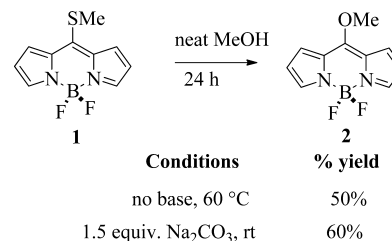
The mode of action of important drugs may be elucidated using highly sensitive fluorescent techniques. The fabrication of fluorescent new materials, with potentially very useful properties, may become a reality. In this context, we wish to disclose our efforts to *directly* attach alcohols and phenols to the BODIPY core via de displacement of the methylthio group to yield highly fluorescent dyes. Recently, both Dehaen and Xiao have reported the properties of a few examples of similar compounds by means of somewhat longer routes (Scheme 1).<sup>13</sup>

Herein, we have carried out a more comprehensive study of this family of compounds. In addition to demonstrating the synthetic utility of this methodology, we have introduced alkoxy and aryloxy groups in the *meso* BODIPY position with the aim to modulate the extension of the blue shift, looking for tailor-made BODIPYs in an almost unexploited region with this fluorophore. In contrast to the fluorescence behavior of the amino-BODIPYs in polar solvents, 8-alkoxy-BODIPYs developed herein excel by their bright green fluorescence, regardless of the media.

## RESULTS AND DISCUSSION

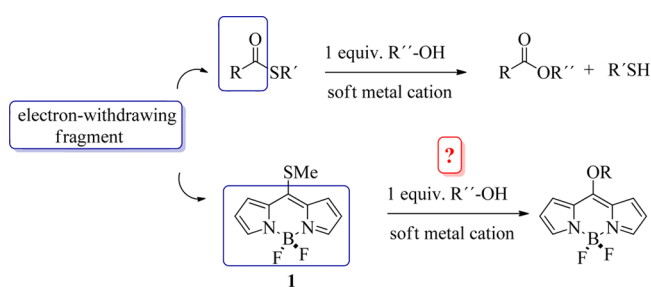
**Synthesis.** Prompted by our reports of the mild S<sub>N</sub>Ar-like displacement of the methylthio group in **1** with amines,<sup>11</sup> we

set out to investigate similar displacement reactions with alcohols and phenols. In the initial trials, the desired product was obtained in 50% yield simply by stirring **1** in neat MeOH at 60 °C for 24 h. A slight yield increase (60%) was observed after 24 h at room temperature if 1.5 equiv of Na<sub>2</sub>CO<sub>3</sub> was added (Scheme 2).

Scheme 2. Initial Reactions of **1** with Neat MeOH

Realizing that these results were useful only for simple alcohols, we decided to investigate a more general and efficient way to carry out the same transformation using stoichiometric amounts of the reactants. The transformation of a thiol ester into an ester has been reported in the literature.<sup>14</sup> This process is mediated by soft metal cations: Hg(II), Cu(I), Cu(II), and Ag(I). Coordination of the metal cation with the sulfur atom in the thiol ester weakens the S–C bond, thereby facilitating the attack of the incoming alcohol. We hypothesized that a similar

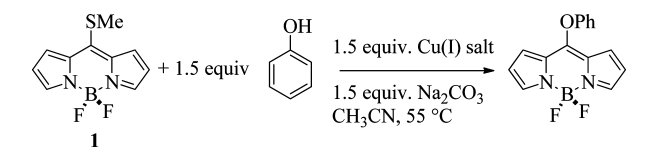
reactivity might be displayed by **1**, drawing an analogy with thiol esters (Figure 1).



**Figure 1.** Analogy of the electronic properties of a thiol ester and those of **1**.

Since Cu(I) salts were considered to have the right combination of both low toxicity and cost, in comparison to other soft metal cations such as Hg(II), a survey of the reactivities of different Cu(I) salts was undertaken (Table 1).

**Table 1. Survey of Cu(I) Salts on the Formation of 8-Alkoxy-BODIPY Dyes**



entry	Cu(I) salt	conversion after 1 h (%) <sup>a</sup>
1	none	0
2	CuCl	34
3	CuCN	9
4	CuI	36
5	Cu(I)-3-methylsalicylate	67
6	CuI-SMe <sub>2</sub>	31
7	Cu(I)OP(O)Ph <sub>2</sub>	47
8	Cu(I)OTf	21
9	CuTC <sup>b</sup>	100 <sup>c</sup>

<sup>a</sup>Determined by <sup>1</sup>H NMR. <sup>b</sup>Copper(I) thiophene-2-carboxylate. <sup>c</sup>90% isolated yield.

Although the majority of the Cu(I) salts showed some degree of activity, it was clear that copper(I) thiophene-2-carboxylate (CuTC) was the most effective Cu(I) source, since the desired product was obtained in 90% isolated yield with a complete conversion in under 1 h. Although no mechanistic study was undertaken, it might be argued that the driving force for the CuTC-mediated reaction is the formation of a strong S–CuTC bond (45–55 kcal/mol), thereby labilizing further the C–S bond.<sup>15</sup> The presence of a Cu(I) salt was essential, as demonstrated by the control experiment shown in entry 1. After the best reaction conditions were identified (CuTC, Na<sub>2</sub>CO<sub>3</sub>, CH<sub>3</sub>CN), the generality of the process was investigated with a series of both alcohols and phenols (Table 2). In method 1, simple alcohols were used both as solvents and reactants, while in method 2, the alcohol or phenol was used in slight excess in CH<sub>3</sub>CN.

Using method 1, simple alcohols added to **1** after only a few hours (entries 1–3) to yield the corresponding 8-alkoxy dyes in acceptable yields. However, for reasons at this point unclear to us, *i*-PrOH failed to give the desired product, for only decomposition was observed (entry 4). Using method 2,

aliphatic alcohols displaced the methylthio group of **1** in moderate yields (entries 5, 6, 8, and 13). This reaction appears to be sensitive to steric effects; primary alcohols added within 3–6 h, while menthol and cholesterol added only after 24 and 36 h, respectively. Triphenylcarbinol failed to give the product altogether (entry 15).

Phenols with different substitution patterns were added to **1** (entries 7, 9–12, and 14). Phenol was the most reactive nucleophile, since it efficiently added to **1** in 90% yield in less than 1 h (entry 7). Addition of either electron-withdrawing or electron-donating substituents resulted in longer reaction times and moderate yields, with no discernible apparent pattern, at least in the sample of examples examined. As in the aliphatic alcohol series, steric crowding had a deleterious effect; pyrogallol also failed to add (entry 15).

The functional group tolerance of particularly method 2 is worth mentioning. As is hinted by the examples presented herein, the potential of this method for numerous applications becomes clear. For instance, complex natural hydroxylated products (entries 8, 9, 12, and 13) can be rendered fluorescent in one step via a very simple reaction. Similarly, some of the products prepared in this work contain functional groups that can be used as connecting points with other target molecules or that can be interconverted to other species for a specific application: for example, the bromine atom in **6**, the allyl group in **9**, the formyl group in **10**, the *p*-iodo atom in **11**, the carbonyl group in **12**, and the *p*-OH group in **14**.

**Optical Properties.** With the results previously reported by us<sup>11</sup> for the 8-amino-BODIPY dyes as background, the properties of the new alkoxy and phenoxy derivatives are better understood. Figure 2 shows that both the absorption and fluorescence spectra of the methoxy derivative **2** are blue-shifted with regard to the parent BODIPY chromophore, but to a lesser extent than for the corresponding methylamino counterpart. Thus, while the amino substitution placed the absorption and emission bands at 418 and 463 nm, respectively, the alkoxy group placed them at 452 and 487 nm, enlarging the Stokes shift in relation to the parent BODIPY (Figure 2). Theoretical calculations confirm this tendency. In general, the inclusion of electron-donor substituents at the central position, characterized by a high enhancement of the electronic density upon excitation, increased the LUMO energy, whereas the HOMO remained almost unaltered (Figure 3). Such an increase of the energy gap depends on the electron-releasing ability of the substituent. Thus, the methoxy group (Hammett parameter  $\sigma_p = -0.268$ ) has a lower electron-donor character in comparison with the methylamino group ( $\sigma_p = -0.84$ ) and, consequently, the increase of the energy gap is lower with the former substituent. Reported electrochemical measurements for a similar 8-methoxy-BODIPY pointed out that the dye was more difficult to reduce, while the oxidation half-wave potential remained almost unaltered, confirming the increase cited above of the LUMO energy as the reason for the spectral blue shift.<sup>13b</sup>

The hypsochromic shift induced by the presence of heteroatoms at the *meso* position is due to an important rearrangement of the electronic delocalization of the chromophore. The formation of a hemicyanine-like delocalized  $\pi$  system due to the electron coupling of the amine and the BODIPY core (Figure 4) explains the shift induced by the amino group.<sup>11</sup> According to this argument, a methoxy group should also be able to interact by resonance with the chromophore and, hence, enable the formation of a merocyanine-like delocalization. The optimized ground-state

Table 2. Scope and Limitations of the Reaction of Alcohols and Phenols with 1

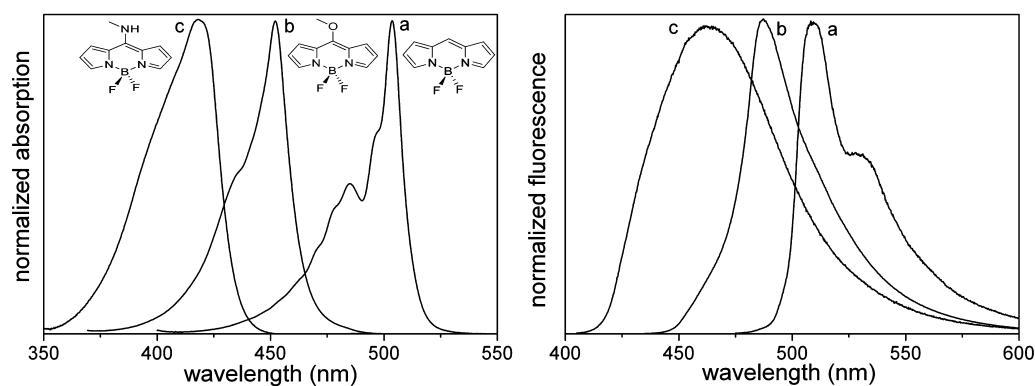
Entry	R-OH/Method	Compound	Reaction time (h)	% Yield <sup>a</sup>	Entry	R-OH/Method	Compound	Reaction time (h)	% Yield <sup>a</sup>
1	MeOH Method 1		1	73	10			12	41
2	EtOH Method 1		3	62	11			5	57
3	Pr-OH Method 1		4	70	12			5	76
4	<sup>t</sup> Pr-OH Method 1	-	-	-	13			36	60
5	Bu-OH Method 2		3	67	14			2.5	56
6	Br-CH <sub>2</sub> -CH <sub>2</sub> -OH Method 2		6	66	15		-	-	-
7	PhOH Method 2		0.9	90	16		-	-	-
8			24	53					
9			12	52					

<sup>a</sup>Isolated yields.

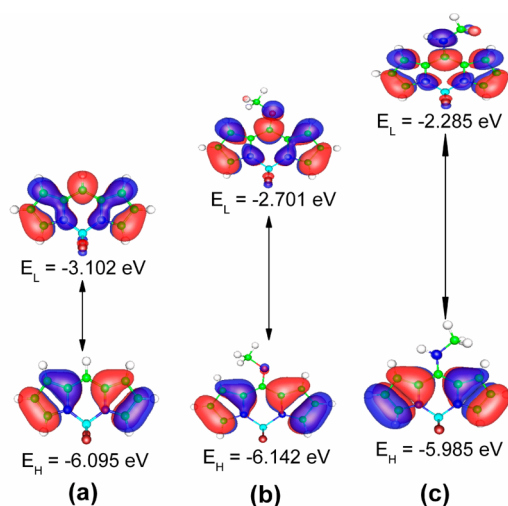
geometry places the oxygen coplanar with the chromophore, making possible the required electron coupling favoring the new resonant structure. The formation of these hemi- and merocyanine delocalized  $\pi$  systems from the cyanine system, upon grafting an amino or methoxy group, should imply an important charge rearrangement, since both pyrroles are no longer equivalent. Accordingly, the shape of the spectral bands is altered (mainly in absorption, where these resonant structures prevail) and they become broader and have lower vibrational resolution (Figure 2). This feature is more evident

with the amino group, since the induced change in the chromophoric charge density by its higher electron-releasing ability is stronger (Figure 4).

The fluorescence quantum yield of the BODIPY 2 is very high (around 0.8), regardless of the surrounding environment. At this point, it is important to note that the primary amino derivatives were highly fluorescent; however, secondary and tertiary amines caused a decrease of the fluorescence capacity in polar solvents because of activation of a quenching ICT state. Taking into account that the formation of such a state depends



**Figure 2.** Normalized absorption and fluorescence spectra of BODIPY (a) and its methoxy (b) and methylamino (c) derivatives at central *meso* positions in cyclohexane.

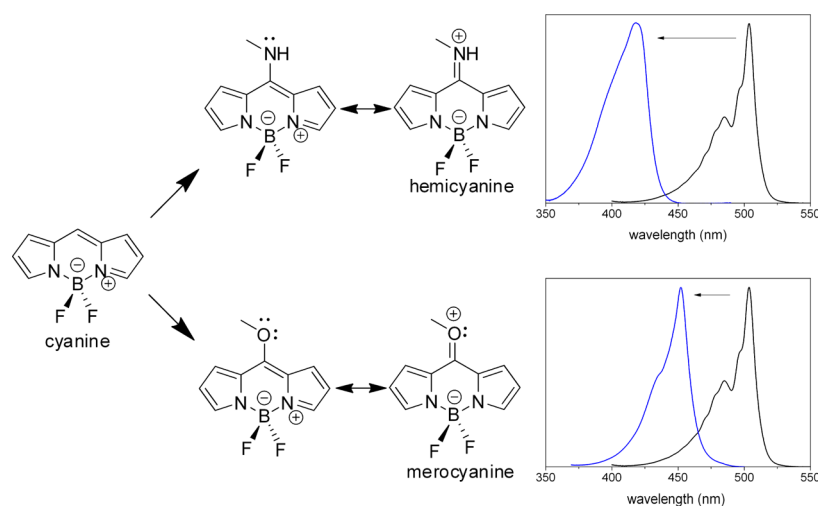


**Figure 3.** HOMO and LUMO eigenvalues for the parent BODIPY (a) and its derivatives bearing methoxy (b) and methylamino groups (c) at the central position.

directly on the electron-releasing ability of the donor unit, the population of the ICT state should be hampered by the

replacement of the methylamino group by the methoxy fragment. In fact, the high fluorescence efficiencies of dye 2 in all the considered solvents (Table 3) indicates that the ICT state is not taking place. This is a very important advantage, since 8-methoxy-BODIPY overcomes the limited fluorescence emission of 8-amino-BODIPYs in polar solvents.

Neither the length of the alkyl chain (from methyl to butyl) nor the size of the substituent (cf. 8 and 13) had a significant impact on photophysical properties, except for the fluorescent quantum yield that ranges from 0.80 to 0.95 (Table 3 and Figure 1S in the Supporting Information). Even the heavy bromine atom in 6 had no influence because of its location far from the BODIPY core. It should be pointed out that for the menthol derivative 8, with a more constrained structure due to steric hindrance, the fluorescence decay curve is better described as a growth and a decay. Such a growth component should be associated with the steric hindrance, which slows down the structural rearrangement upon excitation. Nonetheless, slight differences are observed in the fluorescence abilities among the aliphatic derivatives. Thus, from methoxy to propoxy the fluorescence quantum yield improves from 0.84 to 0.96 and 0.93, which could be due to the increase of the electron-donor character of the alkoxy group with the number



**Figure 4.** Hemicyanine and merocyanine resonance structures from a cyanine delocalized  $\pi$  system upon the incorporation of heteroatoms (nitrogen and oxygen, respectively), at the central position of the BODIPY. The corresponding spectral hypsochromic shift of each new resonant structure is also plotted.

**Table 3. Photophysical Properties of the Parent Unsubstituted BODIPY and Its Derivatives Bearing Alkoxy Groups in a Common Apolar Solvent (Cyclohexane)<sup>a</sup>**

	$\lambda_{ab}$ (nm)	$\epsilon_{max}$ ( $10^4$ M <sup>-1</sup> cm <sup>-1</sup> )	$\lambda_{fl}$ (nm)	$\phi$	$\tau$ (ns)	$k_{fl}$ ( $10^8$ s <sup>-1</sup> )	$k_{nr}$ ( $10^8$ s <sup>-1</sup> )
BODIPY	503.5	7.6	510.5	0.96	6.47	1.48	0.06
2 (cyclohexane)	452.0	6.0	487.0	0.84	5.41	1.55	0.29
2 (methanol)	441.0	4.6	485.5	0.75	6.14	1.22	0.41
8-MAB (cyclohexane)	418.5	2.4	463.0	0.70	4.67	1.50	0.64
8-MAB (methanol)	394.5	3.0	440.0	0.10	0.52	1.91	17.2
3	451.0	6.2	486.5	0.96	5.44	1.76	0.07
4	450.5	6.4	486.0	0.93	5.43	1.71	0.13
5	450.0	6.0	486.0	0.80	5.43	1.47	0.37
13	451.5	5.3	485.0	0.91	5.58	1.63	0.16
8	450.5	6.2	486.0	0.88	5.63	1.56	0.21
6	455.5	4.5	491.0	0.91	5.57	1.63	0.16

<sup>a</sup>The corresponding photophysical properties of 8-methylamino-BODIPY (8-MAB) have been included.<sup>11b</sup> The data in a polar solvent (methanol) for methoxy and methylamino derivatives are also collected. The complete photophysical data in several solvents are included in Table 1S in the Supporting Information.

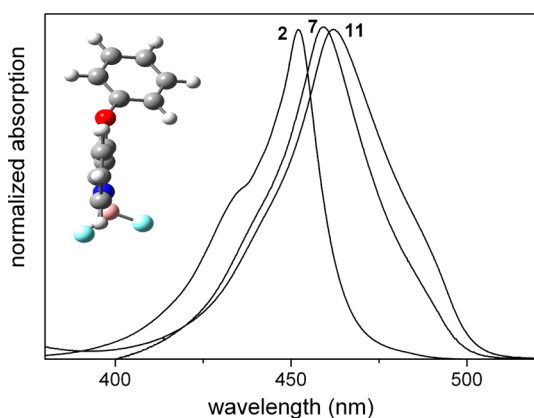
of methylene units. Accordingly, the merocyanine form is better stabilized and the fluorescence quantum yield is slightly ameliorated. However, a longer aliphatic chain (i.e., butoxy) leads to a more flexible structure, which favors the vibrational decay pathways, as is reflected in the increase in the nonradiative rate constant for compound **5** (Table 3). Therefore, all these derivatives are characterized by very high fluorescence quantum yields (>0.80) in all the solvents studied and should be ideal for the vast applications that make use of BODIPYs, i.e., as active media of tunable dye lasers, with the additional advantage of their large Stokes shift (>2000 cm<sup>-1</sup>).

Of special interest is the cholesterol derivative **13**. In this case, the BODIPY core was successfully functionalized with a biomolecule, and the fluorescence properties of the chromophore remained unaltered. In brief, a fluorescence marker to monitor biological events has been developed with emission in the blue-green part of the electromagnetic spectrum. This region is not generally used in studies in most of the molecular probes based on BODIPYs (generally from yellow to red).

In addition to alcohols, several phenol derivatives have been prepared. First of all, the phenyl ring did not seem to participate in the delocalized  $\pi$  system of the indacene core, since the spectral band positions were similar to those of the alkoxy-BODIPYs (Figure 5); otherwise, a red-shifted emission

should have been observed corresponding to an extended delocalization. The optimized geometry revealed that the phenyl ring was twisted with respect to the oxo-BODIPY plane, hampering the electronic coupling (Figure 5). Instead, the lone pair of electrons on oxygen seems to still interact mainly with the BODIPY core, leading to the merocyanine (Figure 4), maintaining the previously discussed blue-shifted spectral bands. However, such hypsochromic shifts are slightly lower than the shifts in related aliphatic derivatives, as theoretically corroborated by the energy of the frontier orbitals (Figure 2S in the Supporting Information). This tendency is extrapolated to all phenoxy derivatives, especially those bearing electron-withdrawing substituents, such as dyes **10** and **11**, which should remove more electronic density from the oxygen (Figure 5). Therefore, the aromatic substituent could slightly remove the electronic density from the oxygen and consequently decrease the extension of the spectral blue shift.

Table 4 gives the photophysical properties of the aryloxy derivatives of BODIPY. It is worth noting that derivatives bearing hydroxyl, methoxy, or iodine at the phenyl ring were

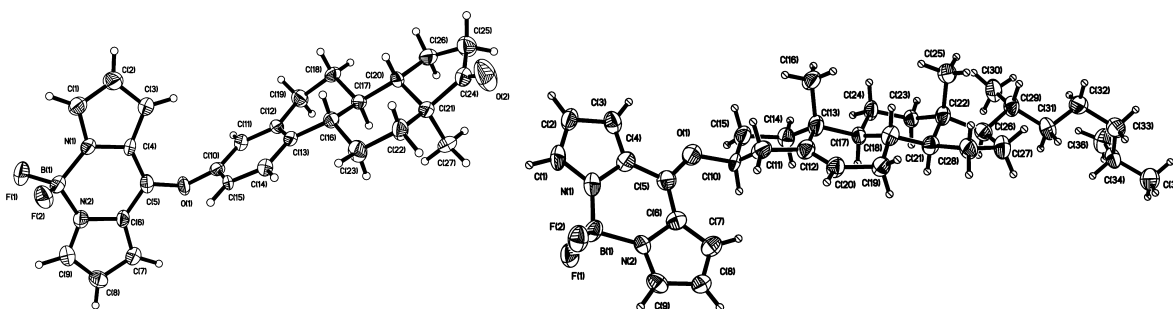


**Figure 5.** Normalized absorption spectra of BODIPY derivatives bearing methoxy (compound **2**), phenoxy (**7**), and *p*-iodophenoxy groups (**11**) in a common solvent (cyclohexane). The optimized ground-state geometry of **7** is also shown.

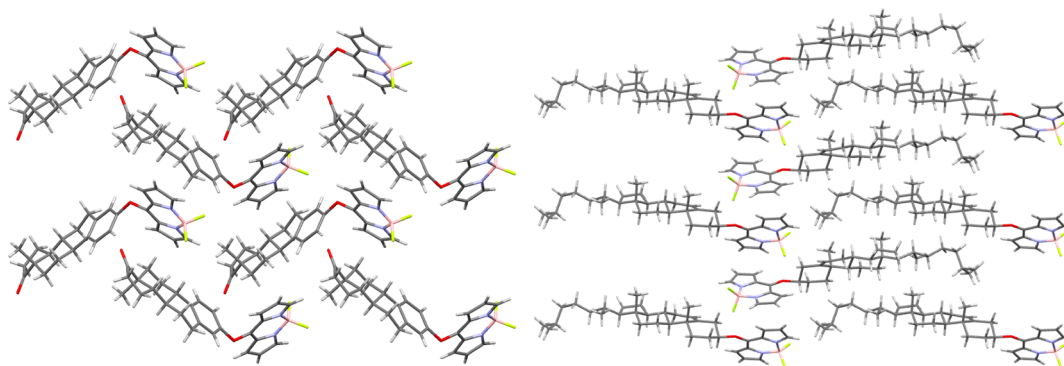
**Table 4. Photophysical Properties of BODIPYs Bearing Different Aryloxy Substituents at the Meso Position in Apolar (Cyclohexane) and Polar/Protic (Trifluoroethanol) Solvents<sup>a</sup>**

	$\lambda_{ab}$ (nm)	$\epsilon_{max}$ ( $10^4$ M <sup>-1</sup> cm <sup>-1</sup> )	$\lambda_{fl}$ (nm)	$\phi$	$\tau$ (ns)	$k_{fl}$ ( $10^8$ s <sup>-1</sup> )	$k_{nr}$ ( $10^8$ s <sup>-1</sup> )
Cyclohexane							
<b>7</b>	459.0	3.5	495.0	0.97	5.78	1.68	0.05
<b>10</b>	466.0	3.8	498.5	0.99	6.03	1.64	0.02
<b>12</b>	458.0	3.4	495.0	0.89	5.84	1.52	0.19
<b>11</b>	462.0	4.7	497.0	0.81	5.66	1.43	0.33
<b>14</b>	458.0	4.2	495.5	0.76	5.25	1.45	0.46
<b>9</b>	457.0	4.9	494.0	0.91	5.60	1.62	0.16
Trifluoroethanol							
<b>7</b>	449.0	2.9	491.5	0.54	4.71	1.04	1.08
<b>10</b>	456.0	0.7	494.5	0.81	7.68	1.05	0.25
<b>12</b>	448.0	2.9	488.5	0.005			
<b>11</b>	452.5	4.0	492.0	0.05	0.33	1.51	28.8
<b>14</b>	448.5	3.6	491.0	0.002			
<b>9</b>	448.5	3.8	484.0	0.001			

<sup>a</sup>The complete photophysical data in several solvents are included in Table 2S in the Supporting Information.



**Figure 6.** Conformations adopted in the crystal form for compounds **12** (left) and **13** (right). The ellipsoids are drawn at the 50% probability level.



**Figure 7.** Crystal packing of **12** (left) and **13** (right) showing the difference between them due to the size of cholesterol in comparison to estrone.

not stable in nucleophilic solvents (such as alcohols and amides). Their photophysical properties change as the solution ages. Probably, these types of solvents act as reactants displacing the initial alkoxy or phenoxy fragments, which may behave as good leaving groups. No effort was made to pursue this observation. For this reason, these solvents were excluded from the photophysical characterization. The phenyl ring in **7** did not affect the fluorescence properties, and very high efficiencies were achieved (up to 0.97, Table 4) in all solvents. However, functionalization of the aryl group completely changes the situation. Substitution on the phenyl ring (i.e., **11**, **14**, **9**, and **12**) had a drastic effect on the fluorescence properties of the BODIPY, particularly when the substituent was characterized by its electron-releasing ability. Thus, although high fluorescence quantum yields were recorded in apolar media (approaching 1 in most cases), the emission efficiency strongly decreased in polar solvents (Table 4). The exception to this behavior was the formyl-substituted derivative **10**, with an electron-withdrawing group ( $\sigma_p = 0.22$ ) at the *para* position of the aryl, where high fluorescence efficiencies were achieved in all considered media, in a way similar to that for the parent unsubstituted phenyl derivative **7**.

The presence of the electron-donor groups methoxy (**9**,  $\sigma_p = -0.268$ ) and hydroxyl (**14**,  $\sigma_p = -0.37$ ) in *ortho* and *para* positions of the phenyl ring, respectively, induced a strong quenching of the fluorescence emission even in low-polarity solvents (e.g., ethyl acetate, Table 2S in the Supporting Information). This is attributed to the formation of an ICT state that leads to a negligible emission in polar media (Table 4). Considering the evolution of the fluorescence efficiency with the solvent polarity for compound **11** (bearing a *p*-iodo group), an ICT should also take place in this derivative. The effect of the heavy atom should be very low because of its distant location from the chromophore. However, the iodine behaved like an electron acceptor ( $\sigma_p = 0.35$ ) and the ICT

should occur from the BODIPY to the aryl fragment. Furthermore, the quenching effect of the ICT induced by the halogen (compound **11**) is less effective than that described above for compounds **9** and **14**, since higher fluorescence quantum yields are achieved for the former derivative in polar media (Table 4).

Dye **12** is structurally very similar to **13**. Both are functionalized with biomolecules (estrone and cholesterol, respectively), but their photophysical properties are quite different. The presence of cholesterol (cyclohexane attached to oxygen) leads to high fluorescence efficiencies regardless of the media (Table 3); on the other hand, the presence of estrone (phenyl linked to the oxygen) decreases the fluorescence ability of the derivative, especially in polar solvents (Table 4), in accord with the presence of a quenching ICT state. The phenyl ring can behave as an electron donor or acceptor depending on its substitution pattern, as we have stated before (i.e., donor in the presence of hydroxyl or acceptor with the attachment of iodine). In **12** the phenyl ring is fused to an aliphatic ring, increasing its electron-donor ability, which seems to be high enough to activate the ICT state.

To summarize, BODIPY derivatives bearing aliphatic alkoxy or phenoxy groups are characterized by high fluorescence efficiency in all media. Complementing this, the attachment of sufficiently strong electron-donating or -withdrawing groups (methoxy, hydroxyl, etc.) at the aryl ring leads to a fluorescence emission sensitive to the environment, making feasible their use as polarity sensors.

**X-ray Structures of 12 and 13.** Cholesterol is a very important organic structure, but previous crystal reports show that it is quite difficult structure to solve.<sup>16</sup> Due to this feature, the number of crystal reports is scarce, and in order to modify some properties, functionalization at the OH has been carried out. This modification has an impact on the crystal structure, allowing a more efficient packing, therefore upgrading the

symmetry from  $P1$  for the nonfunctionalized cholesterol to  $P2_1$  and even  $P2_12_1$ .<sup>17</sup> For BODIPY 13, the space group is  $P2_1$ . Due to the fused polycyclic nature of the cholesterol, no changes in the conformation are observed with the functionalization; however, the alkyl chain attached to it has more freedom, which allows it to acquire a better orientation to maximize the packing.

As observed in other BODIPY systems,<sup>7</sup> the  $O-C_{\text{BODIPY}}$  distance is shorter than the  $O-C_{\text{chol}}$  distance due to the merocyanine character of this oxygen (Figure 4). The distances in the BODIPY moiety are not statistically differentiable due to the equivalent resonance structures in the conjugate system. There is a small dihedral angle of  $5.7^\circ$  between the pyrrole rings, but the BODIPY moiety could be considered as planar. Cholesterol is tilted from this plane by about  $39^\circ$  (Figure 6).

The crystal packing is bilayer type, expected because of the amphiphilic character of this derivative (Figure 7). The short contact distances  $H\cdots H$  in the cholesterol moiety range from 2.16 to 2.37 Å, showing that these contacts, albeit being unfavorable (considering the London forces), are present due to the stabilization energy introduced by the BODIPY fragment. The BODIPY moieties are arranged in a parallel fashion (Figure 7), although it is not a  $\pi-\pi$  interaction because the interplanar distance is 3.34 Å, but the offset is  $\sim 3.0$  Å. The most important interactions are those formed by one of the fluorine atoms, which behaves as a bidentate HB acceptor ( $C3-H3\cdots F1 = 2.53$  Å and  $C11-H11B\cdots F1 = 2.65$  Å)<sup>18</sup> generating a 2-D layer (the BODIPY layer or polar domain).

The conformation of the estrone moiety remains unchanged in BODIPY 12 (Figure 6). It can be compared to the reported structure of the unfunctionalized estrone by Busetta et al.<sup>19</sup> However, the functionalization in this case, in contrast to that of cholesterol, reduces the symmetry of the crystal, bringing it from  $P2_12_12_1$  to  $P2_1$ , because of the elimination of the hydroxyl group and further removal of the intramolecular HB between it and the carbonyl group.

The other difference with respect to derivative 13 is the size; estrone is smaller and thus the hydrophobic character is not as strong as in 13; therefore, the packing is different. In this derivative the bilayer arrangement is not the favored one, but a zigzag chain arrangement (Figure 7). However, as in 13, the strongest interactions are formed by the F atoms; in this case both F atoms participate in the HB to generate the 3-D structure ( $C7-H7\cdots F1 = 2.36$  Å,  $C22-H22\cdots F2 = 2.52$  Å, and  $C2-H2\cdots F2 = 2.60$  Å).<sup>20</sup> In addition, the tilt of the BODIPY moiety against the estrone mean plane is  $79.6^\circ$ .

## CONCLUSIONS

We have successfully prepared a family of 8-alkoxy- and 8-aryloxy-BODIPY dyes in a straightforward manner in moderate to good yields. The substituents at the meso position carry functional groups that will allow further elaboration for specific applications. Four biomolecules (eugenol, menthol, cholesterol, and estrone) were easily attached to the BODIPY core, which demonstrates the usefulness of this method to label biologically relevant molecules.

The inclusion of heteroatoms at the central position of the BODIPY is an adequate strategy to achieve BODIPY-based blue-green emitting fluorophores. Furthermore, the proper selection of the heteroatom, in terms of its electronegativity, allows the modulation of the extension of the blue shift. Accordingly, the amino group induces a more pronounced spectral shift to higher energies than the alkoxy group.

However, the fluorescence performance of the mono- and disubstituted 8-amino-BODIPYs was limited in polar media. Herein, we show that 8-alkoxy-BODIPYs overcome such problems and display high fluorescence efficiencies irrespective of the media. The lower electron donor character of the alkoxy group, with regard to the amino group, prevents the formation of quenching intramolecular charge transfer states, which limits the fluorescence performance of the latter dyes in polar media. Of course, the inclusion of electron-donor or -acceptor substituents at the oxygen fragment can also lead to the formation of the ICT state, with the consequent reduction in fluorescence efficiency.

In summation, BODIPY dyes bearing heteroatoms (N and O) allow for a wide coverage of the visible electromagnetic region (from yellow to blue). Taking into account the reported BODIPYs with red-shifted emission, it is in fact possible to span the whole visible spectrum, by just choosing the adequate modification of the chromophoric core.

## EXPERIMENTAL SECTION

**Photophysical Properties.** The photophysical properties were registered in dilute solutions (around  $2 \times 10^{-6}$  M), prepared by adding the corresponding solvent to the residue from the adequate amount of a concentrated stock solution in acetone, after vacuum evaporation of this solvent. The fluorescence spectra were corrected from the wavelength dependence of the detector sensibility. The fluorescence quantum yield ( $\phi$ ) was obtained using a 0.1 M NaOH aqueous solution of fluorescein ( $\phi_r = 0.79$ ) as reference and corrected by the different refractive indexes of the solvents used for the sample and the reference. Radiative decay curves were registered with the time-correlated single-photon counting technique using a microchannel plate detector, with picosecond time resolution ( $\sim 20$  ps). Fluorescence emission was monitored at the maximum emission wavelength after excitation at 440 nm by means of a diode laser with 150 ps fwhm pulses. The fluorescence lifetime ( $\tau$ ) was obtained from the slope after the deconvolution of the instrumental response signal from the recorded decay curves by means of an iterative method. The goodness of the exponential fit was controlled by statistical parameters ( $\chi^2$ , Durbin–Watson, the analysis of the residuals). The radiative ( $k_r$ ) and nonradiative deactivation ( $k_{nr}$ ) rate constants were calculated by means of  $k_r = \phi/\tau$  and  $k_{nr} = (1 - \phi)/\tau$ , respectively.

**Theoretical Calculations.** The ground-state geometry was optimized by the hybrid DFT method B3LYP, using a double-valence basis set (6-31G), as implemented in Gaussian 09. The geometry was considered as a minimum of energy after the analysis of the frequencies did not yield any negative value.

**X-ray Diffraction Measurements.** Each crystal was mounted on a glass fiber using Paratone, and its crystal data were acquired at room temperature and processed with the suite APEX 2.<sup>21</sup> The structure solution was obtained through direct methods. Absorption corrections were applied. The hydrogens were placed by geometry and restrained to ride on the heavy atoms.

**Synthesis and Characterization.** <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a 200 MHz spectrometer in deuteriochloroform ( $CDCl_3$ ), with tetramethylsilane (TMS; 0.00 ppm <sup>1</sup>H, 0.00 ppm <sup>13</sup>C), chloroform (7.26 ppm <sup>1</sup>H, 77.00 ppm <sup>13</sup>C), acetonitrile-*d*<sub>3</sub> (1.94 ppm <sup>1</sup>H, 118.3, 1.3 ppm <sup>13</sup>C), or acetone-*d*<sub>6</sub> (2.05 ppm <sup>1</sup>H, 206.0, 29.8 ppm <sup>13</sup>C) as internal reference. Data are reported in the following order: chemical shift in ppm, multiplicity (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), sex (sextet), hep (heptet), m (multiplet), exch (exchangeable), app (apparent)), coupling constant *J* (Hz), and integration. Infrared spectra were recorded on a FTIR spectrophotometer; peaks are reported ( $cm^{-1}$ ) with the following relative intensities: s (strong, 67–100%), m (medium, 40–67%), and w (weak, 20–40%). Melting points are not corrected. Mass spectrometry data were collected on a TOF analyzer.



**Typical Method 1 (TM1).** A Schlenk tube equipped with a stir bar under  $N_2$  was charged with BODIPY 1 (0.10 g, 0.42 mmol, 1 equiv). The corresponding alcohol (5 mL) was added, and the mixture was stirred until the solids dissolved. The mixture was purged with  $N_2$  for 5 min, whereupon CuTC (0.119 g, 0.63 mmol, 1.5 equiv) and  $Na_2CO_3$  (0.07 g, 0.63 mmol, 1.5 equiv) were added. The Schlenk tube was immersed in a preheated oil bath at 55 °C and the stirring continued until the consumption of the starting material. The solvent was removed in vacuo, and the crude material was adsorbed in  $SiO_2$  gel. The product was purified by column chromatography using a hexane/EtOAc gradient. For purposes of characterization, the products were crystallized from  $CH_2Cl_2$ /hexanes.

**Typical Method 2 (TM2).** A Schlenk tube equipped with a stir bar under  $N_2$  was charged with BODIPY 1 (0.10 g, 0.42 mmol, 1 equiv) and  $CH_3CN$  (6 mL). The mixture was purged with  $N_2$  for 5 min, whereupon CuTC (0.119 g, 0.63 mmol, 1.5 equiv) and the corresponding alcohol or phenol was added (0.63 mmol, 1.5 equiv). The reaction mixture was stirred for 5 min, upon which  $Na_2CO_3$  (0.07 g, 0.63 mmol, 1.5 equiv) was added. The Schlenk tube was immersed in a preheated oil bath at 55 °C and the stirring continued until the consumption of the starting material. The solvent was removed in vacuo, and the crude material was adsorbed in  $SiO_2$  gel. The product was purified by column chromatography using a hexane/EtOAc gradient. For purposes of characterization, the products were crystallized from  $CH_2Cl_2$ /hexanes.

**BODIPY 2:** following TM1; product (68.5 mg, 73%) obtained as a yellow solid;  $R_f = 0.3$  (30% EtOAc/hexanes); mp 137–139 °C; IR (KBr;  $cm^{-1}$ ) 3127 (w), 3116 (w), 2925 (w), 1739 (w), 1559 (s), 1533 (s), 1465 (s), 1395 (s), 1366 (s), 1335 (m), 1291 (s), 1263 (s), 1231 (s), 1186 (m), 1131 (s), 1085 (s), 1002 (m), 971 (s), 938 (m), 866 (w), 779 (m), 730 (m), 647 (m), 551 (w), 443 (w);  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  7.74 (s, 2H), 7.37 (d,  $J = 6.0$  Hz, 2H), 6.54 (s, 2H), 4.49 (s, 3H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  162.00, 139.58, 126.22, 125.52, 116.69, 62.15.<sup>13a</sup>

**BODIPY 3:** following TM1; product (62.0 mg, 62%) obtained as a yellow solid;  $R_f = 0.5$  (30% EtOAc/hexanes); mp 118–119 °C; IR (KBr;  $cm^{-1}$ ) 2925 (w), 1736 (w), 1558 (s), 1529 (m), 1474 (w), 1445 (s), 1402 (s), 1351 (m), 1331 (m), 1292 (s), 1262 (s), 1232 (m), 1151 (m), 1132 (s), 1100 (s), 1073 (s), 1008 (m), 960 (s), 787 (w), 861 (w), 763 (m), 728 (m), 643 (w), 582 (w), 435 (w);  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  7.66 (s, 2H), 7.27 (d,  $J = 3.6$  Hz, 2H), 6.45 (d,  $J = 1.8$  Hz, 2H), 4.68 (q,  $J = 7.2$  Hz, 2H), 1.54 (t,  $J = 6.9$  Hz, 3H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  161.62, 139.371, 126.54, 125.54, 116.54, 71.51, 15.51; HRMS FABS ( $M + H^+$ ) calcd for  $C_{11}H_{12}BF_2N_2O$  237.1011, found 237.1015.

**BODIPY 4:** following TM1; product (73.5 mg, 70%) obtained as a yellow solid;  $R_f = 0.4$  (30% EtOAc/hexanes); mp 99–100 °C; IR (KBr;  $cm^{-1}$ ) 3123 (w), 2972 (w), 2885 (w), 1730 (w), 1554 (s), 1471 (m), 1441 (s), 1399 (s), 1365 (m), 1333 (w), 1290 (m), 1264 (s), 1225 (s), 1151 (m), 1130 (s), 1096 (s), 1079 (s), 1040 (m), 995 (w), 970 (s), 862 (w), 769 (s), 728 (s), 644 (m), 583 (w), 453 (w);  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  7.73 (s, 2H), 7.34 (d,  $J = 3.6$  Hz, 2H), 6.51 (d,  $J = 3.6$  Hz, 2H), 4.66 (t,  $J = 6.0$  Hz, 2H), 1.98 (m, 2H), 1.13 (t,  $J = 7.2$  Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  161.893, 139.45, 125.47, 116.53, 77.78, 23.395, 10.662; HRMS FABS ( $M + H^+$ ) calcd for  $C_{12}H_{14}BF_2N_2O$  251.1167, found 251.1171.

**BODIPY 5:** following TM2; product (74.3 mg, 67%) obtained as yellow crystals;  $R_f = 0.6$  (30% EtOAc/hexanes); mp 79–80 °C; IR (KBr;  $cm^{-1}$ ) 3125 (w), 2963 (w), 1565 (s), 1474 (w), 1438 (m), 1405 (s), 1368 (w), 1350 (w), 1262 (s), 1226 (m), 1127 (m), 1094 (s), 1076 (m), 1043 (m), 992 (w), 968 (m), 768 (m), 730 (m);  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.71 (s, 2H), 7.32 (s, 2H), 6.50 (s, 2H), 4.68 (m,  $J = 5.7$  Hz, 2H), 1.93 (m,  $J = 6.6$  Hz, 2H), 1.56 (m,  $J = 7.2$  Hz, 2H), 1.03 (m,  $J = 6.6$  Hz, 2H);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  161.8, 139.3, 126.5, 125.5, 116.5, 75.4, 31.8, 19.3, 13.9; HRMS FABS ( $M + H^+$ ) calcd for  $C_{13}H_{16}BF_2N_2O$  265.1324, found 265.1320.

**BODIPY 6:** following TM2; product (87.5 mg, 66%) obtained as a bright yellow solid;  $R_f = 0.4$  (30% EtOAc/hexanes); mp 120.5–122.0 °C; IR (KBr;  $cm^{-1}$ ) 2975 (w), 2940 (w), 2634 (w) 1709 (s), 1649 (s), 1545 (s), 1460 (m), 1422 (s), 1402 (m), 1365 (m), 1311 (w),

1276 (m), 1090 (s), 1012 (m), 982 (m), 967 (w), 946 (m), 778 (m), 759 (m), 646 (w), 660 (m), 586 (w);  $^1H$  NMR ( $CDCl_3$ , 200 MHz)  $\delta$  7.77 (s, 1H), 7.35 (d,  $J = 4.0$  Hz, 2H), 6.55 (s, 2H), 4.99 (t,  $J = 6$  Hz, 2H), 3.77 (t,  $J = 6$  Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  160.30, 140.23, 126.38, 125.88, 74.01, 2810; HRMS FABS ( $M + H^+$ ) calcd for  $C_{11}H_{11}BBrF_2N_2O$  315.0116, found 315.0119.

**BODIPY 7:** following TM2; product (107.5 mg, 90%) obtained as a bright yellow solid;  $R_f = 0.67$  (30% EtOAc/hexanes); mp 129.8–131.4 °C; IR (KBr;  $cm^{-1}$ ) 3122 (w), 1740 (w), 1573 (s), 1526 (m), 1486 (m), 1398 (s), 1364 (s), 1332 (w), 1283 (s), 1251 (s), 1225 (s), 1187 (w), 1118 (s), 1073 (s), 1040 (s), 960 (s), 868 (w), 786 (m), 768 (s), 721 (m), 694 (m), 638 (m), 568 (w), 478 (w);  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  7.74 (s, 2H), 7.52–7.47 (t, 2H,  $J = 7.32$  Hz), 7.41–7.36 (t, 1H,  $J = 7.32$  Hz), 7.24 (s, 2H), 6.67 (s, 2H), 6.39 (s, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  156.04, 141.08, 130.85, 130.85, 127.33, 126.457, 120.44, 117.08.<sup>13a</sup>

**BODIPY 8:** following TM2; product (76.7 mg, 53%) obtained as a light olive green solid;  $R_f = 0.4$  (30% EtOAc/hexanes); mp 149.4–250.4 °C; IR (KBr;  $cm^{-1}$ ) 2944 (m), 2871 (m), 1550 (s), 1469 (m), 1428 (s), 1407 (s), 1322 (m), 1290 (m), 1256 (s), 1223 (s), 1186 (w), 1147 (w), 1126 (s), 1094 (s), 1076 (s), 1052 (m), 963 (s), 847 (w), 781 (m), 766 (m), 734 (m), 676 (w), 64 (m), 585 (w), 525 (w);  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  7.71 (s, 2H), 7.28 (s, 2H), 6.52 (s, 2H), 4.97 (m, 1H), 2.37 (d,  $J = 12.3$  Hz, 1H), 2.09–0.745 (m, 17H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  161.42, 139.03, 126.61, 124.88, 116.528, 85.56, 48.86, 40.01, 34.27, 31.77, 27.01, 24.08, 22.22, 20.78, 17.01; HRMS FABS ( $M + H^+$ ) calcd for  $C_{19}H_{26}BF_2N_2O$  347.2106, found 347.2104.

**BODIPY 9:** following TM2; product (77.3 mg, 52%) obtained as a yellow solid;  $R_f = 0.7$  (30% EtOAc/hexanes); mp 273–274 °C; IR (KBr;  $cm^{-1}$ ) 3130 (w), 1637 (s), 1612 (m), 1569 (s), 1540 (s), 1513 (m), 1461 (m), 1413 (s), 1395 (s), 1380 (s), 1267 (m), 1235 (w), 1117 (m), 1032 (m), 944 (w), 792 (m);  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.71 (s, 2H), 7.15 (d,  $J = 9$  Hz, 1H), 6.88 (d,  $J = 3$  Hz, 2H), 6.70 (d,  $J = 3$  Hz, 2H), 6.37 (d,  $J = 3$  Hz, 2H), 6.05–5.96 (m, 1H), 5.17–5.11 (m,  $J = 9$  Hz, 2H), 3.72 (s, 3H), 3.46 (d,  $J = 6$  Hz, 2H);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  160.8, 150.6, 142.6, 141.0, 140.3, 136.8, 126.7, 125.5, 121.7, 121.5, 116.9, 116.7, 114.1, 56.3, 40.3; HRMS FABS ( $M + H^+$ ) calcd for  $C_{19}H_{18}BF_2N_2O_2$  355.1429, found 355.1423.

**BODIPY 10:** following TM2; product (53.6 mg, 41%) obtained as a bright yellow solid;  $R_f = 0.4$  (30% EtOAc/hexanes); mp 195 °C dec; IR (KBr;  $cm^{-1}$ ) 3114 (w), 2857 (w), 1695 (m), 1597 (m), 1565 (s), 1495 (m), 1473 (m), 1407 (s), 1395 (s), 1365 (m), 1332 (w), 1287 (m), 1255 (s), 1226 (s), 1202 (m), 1158 (w), 1124 (s), 1088 (s), 1065 (s), 1044 (m), 954 (s), 874 (w), 849 (w), 775 (m), 766 (m), 724 (w), 638 (w), 607 (w), 577 (w), 504 (w);  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  10.04 (s, 1H), 8.01 (d,  $J = 8.4$  Hz), 7.80 (s, 2H), 7.41 (d,  $J = 8.7$  Hz), 6.82 (s, 2H), 6.46 (s, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz)  $\delta$  189.16, 159.96, 141.35, 133.22, 131.06, 126.46, 125.45, 118.99, 116.57; HRMS FABS ( $M + H^+$ ) calcd for  $C_{16}H_{12}BF_2N_2O_2$  313.0960, found 313.0963.

**BODIPY 11:** following TM2; product (98.1 mg, 57%) obtained as yellow crystals;  $R_f = 0.6$  (30% EtOAc/hexanes); mp 122–124 °C; IR (KBr;  $cm^{-1}$ ) 3130 (w), 3109 (w), 2865 (w), 2353 (m), 2342 (m), 1569 (s), 1541 (s), 1414 (s), 1400 (s), 1263 (s), 1155 (m), 1120 (s), 1082 (s), 1053 (m), 1000 (w), 977 (m);  $^1H$  NMR (200 MHz,  $CDCl_3$ )  $\delta$  7.79 (d,  $J = 9$  Hz, 2H), 7.02 (d,  $J = 9$  Hz, 2H), 6.75 (d,  $J = 3.6$  Hz, 2H), 6.43 (s, 2H);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  156.2, 141.7, 138.8, 128.1, 126.6, 122.3, 117.5, 114.3, 90.8; HRMS FABS ( $M + H^+$ ) calcd for  $C_{15}H_{11}BF_2IN_2O$  410.9977, found 410.9975.

**BODIPY 12:** following TM2; product (147.0 mg, 76%) obtained as yellow crystals;  $R_f = 0.36$  (30% EtOAc/hexanes); mp 202–204 °C; IR (KBr;  $cm^{-1}$ ) 3120 (w), 3066 (w), 2943 (m), 2865 (w), 1718 (s), 1619 (w), 1582 (w), 1567 (s), 1538 (s), 1462 (m), 1409 (s), 1400 (s), 1380 (m), 1356 (w), 1287 (m), 1259 (s), 1165 (s), 1157 (w), 1115 (s), 970 (m);  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.72 (s, 2H), 7.37 (d,  $J = 7.8$  Hz, 1H), 7.00 (m,  $J = 7.8$  Hz, 1H), 6.97 (s, 1H), 6.72 (s, 2H), 6.39 (s, 2H), 2.91 (s, 3H), 2.58–2.35 (m, 4H), 2.20–2.02 (m, 6H), 1.98–1.463 (m, 9H), 0.90 (s, 3H);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  207.5, 159.9, 153.9, 140.8, 139.7, 139.0, 132.0, 127.6, 126.3, 120.0, 116.9, 115.6, 113.2, 50.8, 48.3, 44.4, 38.2, 36.2, 36.1, 31.8, 29.7, 26.5, 21.9, 14.2;

HRMS FABS ( $M + H^+$ ) calcd for  $C_{27}H_{28}BF_2N_2O_2$  461.2212, found 461.2215.

**BODIPY 13:** following TM2; product (145.2 mg, 60%) obtained as yellow crystals;  $R_f = 0.7$  (30% EtOAc/hexanes); mp 171–173 °C; IR (KBr,  $cm^{-1}$ ) 2938 (w), 2893 (w), 2865 (w), 1738 (w), 1668 (w), 1565 (s), 1471 (w), 1431 (s), 1400 (s), 1371 (w), 1341 (w), 1290 (m), 1263 (s), 1225 (m), 1151 (w), 1126 (m), 1095 (s), 1075 (s), 1053 (w), 1000 (w), 972 (m), 766 (m), 728 (m);  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  7.62 (s, 2H), 7.19 (s, 2H), 6.42 (s, 2H), 5.4 (s, 1H), 2.57 (d,  $J = 6$  Hz, 2H), 2.134–0.765 (m), 0.62 (s, 3H);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  160.9, 139.3, 138.8, 133.4, 132.3, 127.9, 126.9, 125.2, 124.4, 123.1, 116.6, 85.0, 75.3, 57.0, 56.5, 50.4, 42.6, 39.9, 38.9, 37.2, 36.5, 36.1, 32.2, 30.0, 28.2, 24.6, 24.2, 23.1, 21.4, 19.7, 19.0, 12.2; HRMS FABS ( $M + H^+$ ) calcd for  $C_{36}H_{35}BF_2N_2O$  577.4141, found 577.4139.

**BODIPY 14:** following TM2; product (70.5 mg, 56%) obtained as yellow crystals;  $R_f = 0.4$  (30% EtOAc/hexanes); mp 198–200 °C; IR (KBr,  $cm^{-1}$ ) 3506 (w), 3129 (w), 1601 (w), 1568 (s), 1503 (s), 1399 (s), 1366 (m), 1289 (m), 1256 (s), 1230 (s), 1216 (w), 1188 (m), 1113 (s), 1088 (s), 1013 (m), 946 (w), 930 (m), 842 (w), 762 (s);  $^1H$  NMR (200 MHz,  $CDCl_3$ )  $\delta$  7.7 (s, 2H), 7.12 (d,  $J = 9$  Hz, 2H), 6.92 (d,  $J = 9$  Hz, 2H), 6.70 (m,  $J = 4$  Hz, 2H), 6.40 (d,  $J = 4$  Hz, 2H);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  154.9, 149.2, 140.7, 128.1, 126.4, 121.6, 117.2, 117.01, 116.5; HRMS FABS ( $M + H^+$ ) calcd for  $C_{15}H_{12}BF_2N_2O_2$  301.0960, found 301.0964.

## ■ ASSOCIATED CONTENT

### ● Supporting Information

Figures, tables, and CIF files giving  $^1H$  and  $^{13}C$  NMR spectra of all the compounds described, full photophysical data in several solvents, calculated energies of the frontier orbitals, tables of atom coordinates and absolute energies, and crystallographic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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