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Synthesis of BF_2 Complexes of Prodigiosin Type Oligopyrroles

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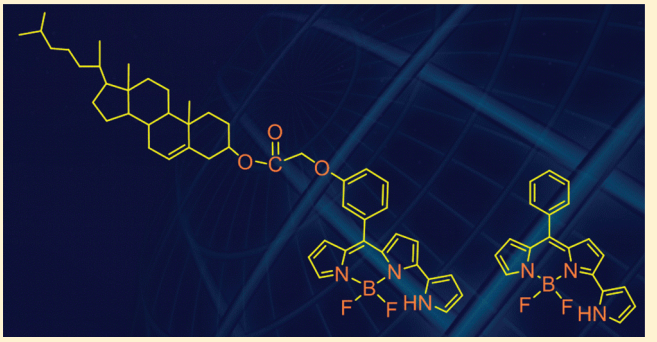
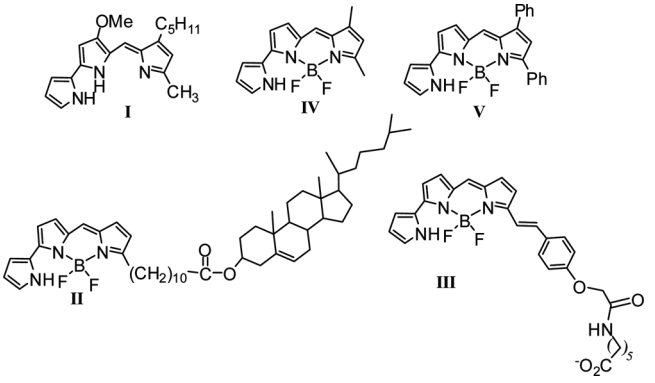
Supporting Information

ABSTRACT: We developed a simple, facile route for the synthesis of BF_2 complexes of prodigiosin type oligopyrroles and their cholesterol conjugates. This route gives an access to synthesize any desired *meso*-aryl-substituted 3-pyrrolyl BODIPYs which were not easily accessible earlier.

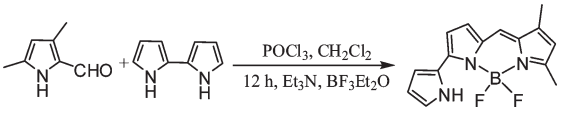


Prodigiosins **I**, the open-chain pyrrolyldipyrrin type oligopyrroles isolated from microorganisms such as *Streptomyces* and *Serratia*,[1] are red pigments and currently under study for their potential use as antineoplastic and immunosuppressive agents.[2] Prodigiosins are known to raise the intralysosomal pH and to stimulate apoptosis; these are proposed to be protonation−counteranion-based modes of action. Prodigiosins provided inspiration to researchers to synthesize and study the anion recognition properties of several oligopyrrolic systems[3] which are formally related to the naturally occurring prodigiosins. The coordination of boron to a range of polypyrrole-containing ligands that includes simple dipyrrins,[4] porphyrins,[5] corroles,[6] and expanded porphyrins[7] have received tremendous attention in recent years. The most widely utilized class of pyrrolyl boron complexes are dipyrrin-BF_2 complexes (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene, BODIPY), which are highly fluorescent dyes and are used as biolabels, light harvesters, sensitizers for solar cells, fluorescent sensors, molecular photonic wires, and electron- and energy-transfer reagents and in laser applications[4] due to their remarkable photophysical properties such as photostability, sharp absorption, large extinction coefficients, tunable absorption and emission wavelengths, and high fluorescent quantum yields. BF_2 complexes of the prodigiosin types of structures **II** and **III** (Chart 1) marketed by Invitrogen (formerly Molecular Probes) have been used as biological labels because of their excellent photophysical properties and biocompatibility. However, the BF_2 complexes **II** and **III** are very expensive and are only available in small quantities. The original synthesis of the BF_2 complexes of prodigiosins **IV** and **V** is available as patent literature,[8] and the synthesis of **IV** obtained from a U.S. patent[8] is presented in Scheme 1. This route is applicable only to the synthesis of *meso* free 3-pyrrolyl BODIPYs and involves complicated reaction steps and expensive precursors. In this paper, we report a simple synthetic route for *meso*-aryl-substituted 3-pyrrolyl BODIPYs **1**−**7** (Chart 2) and biocompatible 3-pyrrolyl BODIPY-cholesterol conjugates **12** and **13**.

Chart 1



Scheme 1. Reported Synthesis of 3-Pyrrolyl BODIPY[8]



To synthesize the target compound 3-pyrrolyl *meso*-phenyl boron dipyrromethene **1**, we first investigated the possibility of introducing pyrrole at the 3-position of readily available

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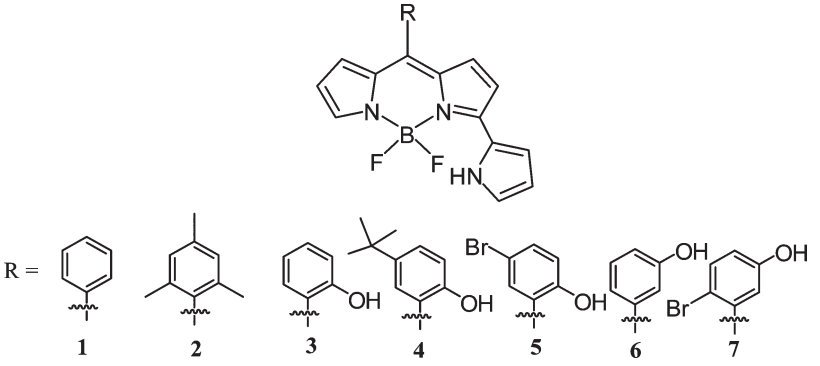
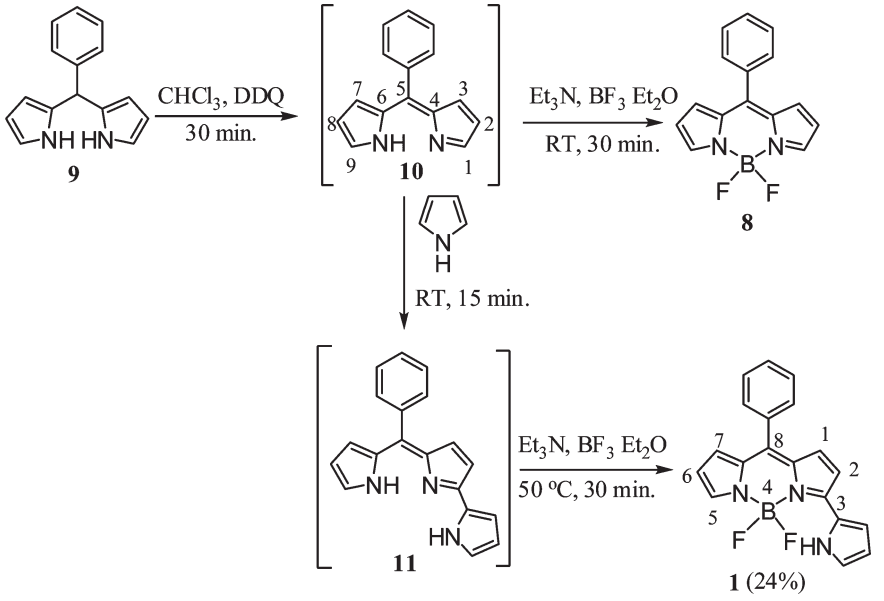
Chart 2



Scheme 2. Synthesis of 3-Pyrrolyl BODIPY 1



meso-phenyl boron dipyrromethene[9] **8** by performing nucleophilic substitution with pyrrole under various reaction conditions on the basis of the recent report by Dehaen and co-workers.[10] Addition of pyrrole and DDQ to **8** in chloroform in the presence or absence of acid catalyst at room temperature or elevated temperature conditions did not yield the product. We then carried out the reaction with *meso*-phenyl dipyrromethene[11] **10**, since the 1-position is susceptible to nucleophilic substitution similarly to the 3-position in **8** and successfully synthesized 3-pyrrolyl *meso*-phenyl boron dipyrromethene **1** as well as other 3-pyrrolyl BODIPYs **2**−**7** by adopting a three-step, one-pot reaction method (Scheme 2). In the first step, the *meso*-phenyl dipyrromethane **9** in $CHCl_3$ was oxidized with 1.5 equiv of DDQ at room temperature for 30 min. The resultant *meso*-phenyl dipyrromethene **10** without isolation was treated with 1 equiv of pyrrole at room temperature for 15 min to form the prodigiosin type of 1-pyrrolyl *meso*-phenyl dipyrromethene **11**. The mechanism of formation of **11** may be either by oxidative nucleophilic substitution[10] or radical substitution[12] (Supporting Information). However, without isolation of this intermediate **11**, the reaction mixture was treated further with triethylamine and $BF_3 \cdot OEt_2$ at room temperature for 30 min. TLC analysis indicated the formation of the desired compound **1** along with BODIPY **8**. Column chromatographic purification on silica gave compound **1** in low yield (2%). We varied the reaction conditions such as changing the amounts of DDQ and pyrrole and altering the reaction temperature of the last step. The best yield for compound **1** (24%) was obtained when we used 2.5 equiv of DDQ and 3 equiv of pyrrole while maintaining the reaction temperature of the last step at 50 °C. Under these reaction conditions, we did not observe any 3,5-disubstituted product. Compounds **2**−**7** were also prepared under same optimized reaction conditions by using the corresponding *meso*-aryl dipyrromethanes (Supporting Information).

Compounds **1**−**7** are soluble in common organic solvents and have been characterized by mass, NMR, absorption, electrochemical, and fluorescence techniques. The molecular ion peak in HR-MS mass spectra confirmed the identity of compounds **1**−**7**. ^1H, ^{13}C, ^{19}F, and ^{11}B along with $^1H-^1H$ COSY NMR were used to characterize compounds **1**−**7** in detail. In ^1H NMR spectra,

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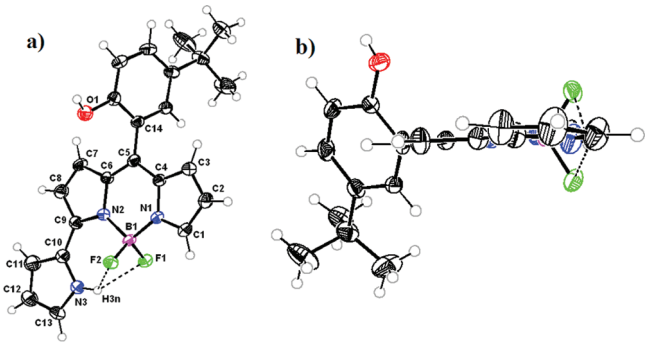

Figure 1. Crystal structure of **4** with 50% probability ellipsoids, with hydrogen bonds denoted by dashed lines: (a) top view; (b) side view. The cocrystallized water molecule is omitted for clarity.

Table 1. Photophysical Data of Compound 1

solvent	λ_{abs} (nm)	ε	λ_{em} (nm)	$\Delta\nu_{st}$ (cm^{-1})	Φ
hexane	542, 579	4.55, 4.72	599	577	0.41
toluene	547, 584	4.45, 4.66	608	676	0.35
$CHCl_3$	545, 582	4.43, 4.66	606	681	0.32
MeOH	540, 575	4.27, 4.58	602	780	0.13
DMSO	551, 587	4.37, 4.56	619	880	0.07

the eight protons of three pyrrole rings appeared as eight distinct signals in the 6.3−7.8 ppm region; the *meso*-aryl protons appeared as a multiplet at ∼7.50 ppm, and the NH signal of the pyrrole group appeared as a broad singlet at 10.6 ppm -(Supporting Information). The pyrrole NH proton appeared more downfield because of its involvement in intramolecular hydrogen bonding with the fluoride ion of the BF_2 group. The presence of hydrogen bonding was also clearly evident in ^{19}F NMR spectra of compounds **1**−**7**, which exhibited a doublet of quartets at ∼−141.5 ppm. In ^{11}B NMR spectra, compounds **1**−**7** experienced downfield shifts by 1 ppm compared to the signals for **8**, which is attributed to alteration of π-delocalization caused by the pyrrole group present at the 3-position of the BODIPY ring (Supporting Information).

The presence of intramolecular hydrogen bonding between the pyrrole NH and the fluoride ion of the BF_2 group was also established by the X-ray structure solved for compound **4** (Figure 1). The single crystal of compound **4** was obtained on slow evaporation of a $CHCl_3$ solution over a period of 2 weeks. The structure was solved under space group $P4_2/n$ and showed the expected chemical composition and connectivity. The dipyrrin ring was essentially planar, and the *meso*-aryl group was twisted at a 68° dihedral angle relative to the BODIPY core. The pyrrole group lies almost in the same plane as the BODIPY core, with a deviation of 9.8°. The NH- - -F distances were 2.15 and 2.33 Å, supporting the existence of intramolecular hydrogen bonding between the pyrrole NH and the fluoride ions of the BF_2 group.

The absorption and fluorescence properties of compounds **1**−**7** were studied in five different solvents of varying polarities (Supporting Information), and the data for compound **1** are presented in Table 1. A comparison of the absorption and emission spectra of **1** and **8** is shown in parts a and b of Figure 2, respectively. As is evident from Figure 2, the absorption and emission bands of compound **1** experienced a red shift

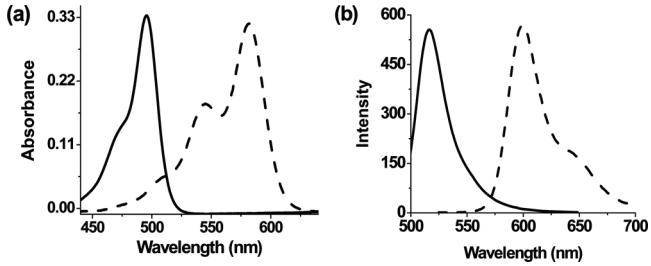

Figure 2. Comparison of normalized (a) absorption and (b) emission spectra of compounds **1** and **8** recorded in $CHCl_3$.

(∼70−75 nm) compared to the signals for **8**, indicating an enhancement in the π-electron delocalization. Furthermore, in the absorption spectra, the vibronic transition which appears as a shoulder in **8** was clearly separated as a band in compound **1**. The absorption and emission spectra of compounds **1**−**7** were hardly affected by solvent polarity, the maximum being slightly shifted bathochromically when the solvent was changed from hexane to DMSO, which is consistent with the general behavior of BODIPY chromophores.[9] The quantum yields of compounds **1**−**7** were increased by 4−8 times in comparison to that for **8**, indicating that compounds **1**−**7** are more fluorescent compared to **8**. The cyclic voltammetric studies of compounds **1**−**7** showed one reversible reduction and one irreversible reduction along with an ill-defined oxidation. The reduction potentials of compounds **1**−**7** were shifted toward less negative potential compared to that of **8** by ∼150−200 mV, indicating that compounds **1**−**7** were much easier to reduce (Supporting Information).

The use of 3-pyrrolyl BODIPYs for the synthesis of biocompatible compounds was demonstrated by synthesizing the 3-pyrrolyl BODIPY-cholesterol conjugates **12** and **13** (Scheme 3). The commercially available cholesterol was reacted with bromoacetic acid under DCC coupling conditions followed by column chromatographic purification, affording the bromo ester of cholesterol **14**. Compound **14** was treated further with either **3** or **6** in the presence of K_2CO_3 in DMF at room temperature for 15 min followed by purification on silica, affording **12** and **13**, respectively, in 60−70% yields. Compounds **12** and **13** are freely soluble in solvents such as *n*-hexane, $CHCl_3$, CH_3OH, DMF, and DMSO and were characterized by various techniques (Supporting Information). The fluorescence studies of compounds **12** and **13** indicated that these compounds are more fluorescent with decent quantum yields (0.3−0.5) compared to those of their corresponding 3-pyrrolyl BODIPYs **3** and **6**, respectively.

Due to their excellent fluorescence properties, the commercially available as well as synthesized BODIPY-cholesterol conjugates have found extensive usage in various biological applications,[13] especially visualization of sterol trafficking in living cells and organisms. Since the pyrrolyl BODIPY-cholesterol conjugates **12** and **13** exhibited photophysical properties similar to those of existing BODIPY-cholesterol conjugates, we carried out preliminary investigations on their cellular interaction and uptake by HepG2 cells. The confocal micrographs of HepG2 cells incubated with **12** for 12 h at 37 °C under 5% CO_2 are shown in Figure 3. As can be seen, the fluorescent molecule dispersed almost uniformly at the cell boundary by labeling the cell membrane efficiently without disrupting its architecture, even at a high concentration of 50 mM. This finding concurs with literature reports[13] which showed that the BODIPY-cholesterol molecule partitions itself into ordered domains in the cell membrane, presumably by

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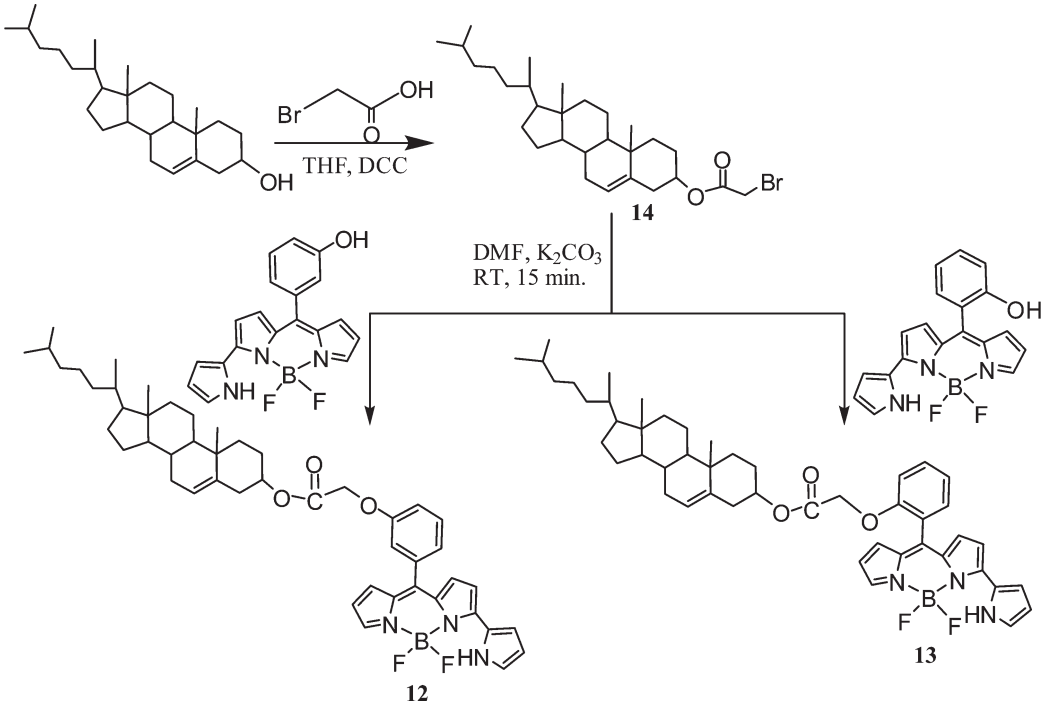
Scheme 3. Synthesis of BODIPY-Cholesterol Conjugates 12 and 13



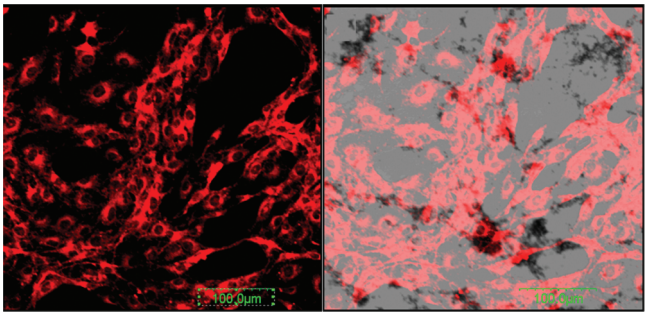


Figure 3. Uptake of BODIPY-cholesterol **12** (50 mM) by HepG2 cells: (left) confocal micrograph; (right) corresponding overlay picture.

establishing a dynamic equilibrium with the cholesterol moieties of the cell membrane. Thus, these conjugates can be used as potential markers to study sterol trafficking in cellular membranes and for live cell imaging.

In conclusion, we have developed a simple and efficient synthetic route for the synthesis of BF_2 complexes of prodigiosin type oligopyrroles (3-pyrrolyl BODIPYs). The presence of a pyrrole group at 3-position resulted in better photophysical properties. We also showed that the pyrrolyl BODIPYs can be made suitable for biological studies by covalent attachment to cholesterol.

EXPERIMENTAL SECTION

General Considerations. All NMR spectra (δ values, ppm) were recorded using 300 and 400 MHz spectrometers. Tetramethylsilane (TMS) was used as an external reference for recording ^1H (of residual protons; δ 7.26 ppm) and ^{13}C (δ 77.0 ppm) spectra in $CDCl_3$. $^1H-^1H$ COSY was used to confirm proton assignments. Cyclic voltammetric (CV) studies were carried out with an electrochemical system utilizing a three-electrode configuration consisting of a glassy-carbon working electrode, platinum-wire auxiliary electrode, and a saturated calomel reference electrode. The experiments were performed in dry CH_2Cl_2 using 0.1 M TBAP as the supporting electrolyte. Half-wave potentials were measured using DPV and also calculated manually by taking the average of the cathodic and anodic peak potentials.

Materials. Dulbecco's Modified Eagle's Medium (DMEM), fetal calf serum (FCS), trypsin-EDTA, L-glutamine, penicillin (50 U/mL), and streptomycin (50 μg/mL) were obtained from HiMedia Laboratories.

Culture of HepG2 cells. HepG2 cells were obtained from the National Centre for Cell Science, Pune, India, and cultured on DMEM supplemented with 10% FCS, 2 mM L-glutamine, penicillin (50 U/mL), and streptomycin (50 μg/mL) under an atmosphere of 5% CO_2 at 37 °C. At confluence, the cells were passaged by rinsing the cell monolayer twice with phosphate-buffered saline (pH 7.4) and adding prewarmed 0.05% trypsin-EDTA solution for 5 min. After detachment of the cell layer from the surface, complete growth medium was added in an equal amount to the trypsin-EDTA solution; the cells were then split 1/3 and seeded into fresh complete growth medium.

Visualization of BODIPY-Cholesterol Uptake by Confocal Microscopy. For confocal microscopy experiments, HepG2 cells were incubated with BODIPY-cholesterol at concentrations of 5−50 mM (in DMSO; final volume less than 1% of total medium) and seeded onto six-well plates containing 3 mL of complete medium with 5×10^5 cells per well. The plates were then incubated for 12 h at 37 °C and 5% CO_2. After incubation, cells were washed twice with prewarmed (37 °C) phosphate-buffered saline (pH 7.4) and visualized under a laser scanning confocal microscope.

Synthesis of 3-Pyrrolyl BODIPYs 1−7. A sample of *meso*-aryl dipyrromethane (1.35 mmol) was taken up into $CHCl_3$ (30 mL) and oxidized with DDQ (3.37 mmol) at room temperature for 30 min. Pyrrole (4.0 mmol) was added and the reaction mixture stirred for an additional 15 min. During this period, the reaction mixture turned from yellow to red. Triethylamine (54 mmol) followed by $BF_3 \cdot Et_2O$ (67.5

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mmol) was added, and the reaction mixture was heated at 50 °C for an additional 30 min. The reaction mixture was diluted with CH_2Cl_2 and washed thoroughly with 0.1 M NaOH solution and water. The organic layers were combined, dried over Na_2SO_4, and filtered, and the solvent was removed on a rotary evaporator under vacuum. The resulting crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (92/8) and afforded pure compounds **1**−**7** as brown solids.

1: yield 24%; mp 259−260 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 6.39−6.41 (m, 1H; py), 6.45−6.46 (m, 1H; py), 6.65 (d, 1H, ^3J(H,H) = 3.7 Hz; py), 6.90 (d, 1H, ^3J(H,H) = 4.7 Hz; py), 6.93 (d, 1H, ^3J(H,H) = 4.7 Hz; py), 7.02−7.03 (m, 1H; Py), 7.20−7.21 (m, 1H; Py), 7.51−7.53 (m, 5H; Ar), 7.94 (s, 1H; py), 10.56 (s, 1H, -NH); ^{19}F NMR (282.2 MHz, $CDCl_3$, δ in ppm) −141.1 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm) 1.30 (t); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) 111.8, 116.1, 118.7, 121.2, 123.7, 125.2, 126.6, 128.4, 130.0, 130.5, 133.3, 133.5, 134.6, 136.8, 137.8, 139.8, 151.7; HRMS calcd for $C_{19}H_{14}N_3BF$ 314.1265, found 314.1260 [M^+ − F].

2: yield 21%; mp 265−267 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 2.11 (s, 6H; $-CH_3$), 2.35 (s, 3H; $-CH_3$), 6.38−6.40 (m, 3H; py), 6.66 (d, 1H, ^3J(H,H) = 4.6 Hz; py), 6.84 (d, 1H, ^3J(H,H) = 4.6 Hz; py), 6.95 (s, 2H; Ar), 7.02−7.03 (m, 1H; Py), 7.20−7.21 (m, 1H; Py), 7.65 (s, 1H; py), 10.56 (s, 1H, −NH); ^{19}F NMR (282.2 MHz, $CDCl_3$, δ in ppm) −141.4 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm) 1.29 (t); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) 111.8, 116.1, 118.6, 121.2, 123.8, 123.9, 126.5, 128.2, 130.4, 132.0, 133.5, 136.8, 136.9, 138.1, 138.5, 139.4, 151.8; HRMS calcd for $C_{22}H_{20}N_3BF$ 356.1734, found 356.1745 [M^+ − F].

3: yield 15%; mp 262−263 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 5.46 (bs, 1H; −OH), 6.42−6.46 (m, 2H; py), 6.62 (d, 1H; ^3J(H,H) = 3.7 Hz; py), 6.90−6.95 (m, 3H; py), 7.09−7.11 (m, 1H; Py), 7.26−7.28 (m, 2H; Ar), 7.41 (d, 1H, ^3J(H,H) = 2.5 Hz; Ar), 7.48−7.51 (dd, 1H, ^3J(H,H) = 8.6 Hz, ^3J(H,H) = 4.4 Hz; Ar), 7.67 (s, 1H; py), 10.59 (bs, 1H; −NH); ^{19}F NMR ($CDCl_3$) −141.1 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm) 1.48 (t); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) 112.1, 116.2, 116.8, 119.4, 120.1, 120.7, 121.6, 123.7, 124.7, 127.1, 131.3, 131.7, 133.3, 134.7, 136.8, 138.3, 152.1, 155.0; HRMS calcd for $C_{19}H_{14}BFON_3$ 330.1214, found 330.1203 [M^+ − F].

4: yield 16%; mp 234−235 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 1.27 (s, 9H; *t*-Bu), 5.25 (bs, 1H; −OH), 6.42−6.46 (m, 2H; py), 6.45−6.46 (m, 1H; py), 6.93−6.97 (m, 3H; py), 7.07−7.08 (m, 1H; Py), 7.26−7.28 (m, 2H; Ar), 7.40 (d, 1H, ^3J(H,H) = 8.2 Hz; Ar), 7.67 (s, 1H; py), 10.58 (s, 1H, −NH); ^{19}F NMR (282.2 MHz, $CDCl_3$, δ in ppm) −141.1(dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm) 1.28 (t); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) 29.6, 30.3, 112.1, 116.3, 119.4, 120.0, 121.8, 123.7, 124.7, 127.2, 128.4, 128.7, 133.1, 133.3, 135.0, 137.0, 138.3, 139.4, 143.1, 151.3, 152.2; HRMS calcd for $C_{23}H_{22}N_3BOF$ 386.1840, found 386.1826 [M^+ − F].

5: yield 15%; mp 227−229 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 5.29 (bs, 1H; −OH), 6.41−6.44 (m, 2H; py), 6.60 (d, 1H, ^3J(H,H) = 4.4 Hz; py), 6.87−6.93 (m, 3H; py), 7.07 (s, 1H; Py), 7.40−7.51 (m, 3H; Ar), 7.65 (s, 1H; py), 10.55 (s, 1H, −NH); ^{19}F NMR (282.2 MHz, $CDCl_3$, δ in ppm) −140.9 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm): 1.26 (t); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) 112.4, 112.5, 116.6, 118.6, 120.2, 122.4, 122.5, 123.6, 124.2, 127.9, 131.3, 132.5, 132.7, 133.7, 134.2, 137.3, 138.2, 152.8, 152.9; HRMS calcd for $C_{19}H_{13}N_3BOFBr$ 408.0319, found 408.0303 [M^+ − F].

6: yield 18%; mp 230−232 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 6.40−6.45 (m, 2H; py), 6.70 (d, 1H, ^3J(H,H) = 4.1 Hz; py), 6.91 (d, 1H, ^3J(H,H) = 4.0 Hz; py), 6.99−7.08 (m, 3H; py), 7.08 (d, 1H, ^3J(H,H) = 7.0 Hz; Ar), 7.22−7.23 (m, 2H; Ar), 7.34 (t, 1H, ^3J(H,H) = 7.6 Hz; Ar), 7.67 (s, 1H; py), 10.57 (s, 1H, −NH); ^{19}F NMR (282.2 MHz, $CDCl_3$, δ in ppm) −141.0 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm) 1.27 (t); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) 29.6, 30.3, 112.1, 116.3, 119.4, 120.0, 121.8, 123.7, 124.7, 127.2, 128.4, 128.7, 133.1, 133.3, 135.0, 137.0, 138.3, 139.4, 143.1, 151.3, 152.2; HRMS calcd for $C_{19}H_{14}N_3BOF$ 330.1214, found 330.1226 [M^+ − F].

7: yield 18%; mp 236−237 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 5.85 (bs, 1H; −OH), 6.42−6.44 (m, 3H; py), 6.74 (d, 1H, ^3J(H,H) = 4.4 Hz; py), 6.90 (d, 1H, ^3J(H,H) = 4.0 Hz; py), 6.98−7.00 (m, 1H; py), 7.07−7.08 (m, 1H; Py), 7.18 (d, 1H, ^3J(H,H) = 8.4 Hz; Ar), 7.28 (d, 1H, ^3J(H,H) = 8.4 Hz; Ar), 7.32−7.36 (m, 1H; Ar), 7.67 (s, 1H; py), 10.58 (s, 1H, −NH); ^{19}F NMR (282.2 MHz, $CDCl_3$, δ in ppm) −141.2 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm): 1.29 (t); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): 111.8, 112.1, 116.2, 116.8, 119.5, 121.8, 123.8, 124.3, 127.3, 128.6, 132.6, 133.1, 135.9, 136.4, 137.1, 138.0, 152.4, 152.9; HRMS calcd for $C_{19}H_{13}N_3BOFBr$ 408.0319, found 408.0324 [M^+ − F].

Synthesis of BODIPY-Cholesterol Conjugates 12 and 13. A mixture of bromo-cholesterol **14** (42 mg, 0.085 mmol), BODIPY **3** or **6** (20 mg, 0.057 mmol), and anhydrous K_2CO_3 (24 mg, 0.171 mmol) was stirred in 5 mL of dry DMF for 1 h at room temperature. The DMF was removed under reduced pressure. The resulting reaction mixture was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (96/4) and afforded pure compounds **12** and **13** as brown solids.

12: yield 30 mg, (70%); mp 270−271 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 0.6−2.4 (m, 43H; cholesterol), 4.61 (s, 2H; $-CH_2$), 6.41−6.44 (m, 2H; py), 6.64 (d, 1H, ^3J(H,H) = 4.2 Hz; py), 6.91 (d, 1H, ^3J(H,H) = 4.3 Hz; py), 6.96 (d, 1H, ^3J(H,H) = 4.3 Hz; py), 7.03 (m, 2H; py), 7.09 (d, 1H, ^3J(H,H) = 7.3 Hz; Ar), 7.14 (d, 1H, ^3J(H,H) = 6.9 Hz; Ar), 7.21 (s, 1H; Ar), 7.40 (t, 1H, ^3J(H,H) = 6.9 Hz; Ar), 7.69 (s, 1H; py), 10.55 (s, 1H, −NH); ^{19}F NMR (282.2 MHz, $CDCl_3$, δ in ppm) −141.3 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm) 1.25 (t); HRMS calcd for $C_{48}H_{61}N_3O_3BF_2$ 776.4729, found 776.4736 [M + 1]$^+$.

13: yield 27 mg (59%); mp 267−268 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ in ppm) 0.6−2.4 (m, 43H; cholesterol), 4.55 (s, 2H; $-CH_2$), 6.38−6.39 (m, 2H; py), 6.62 (s, 1H; py), 6.82−6.84 (m, 2H; py), 6.95−6.96 (m, 2H; Py), 7.06 (t, 1H, ^3J(H,H) = 7.3 Hz; Ar), 7.18 (s, 1H; Ar), 7.34 (d, 1H, ^3J(H,H) = 7.7 Hz; Ar), 7.42 (t, 1H, ^3J(H,H) = 8.1 Hz; Ar), 7.62 (s, 1H; py), 10.55 (bs, 1H; −NH); ^{19}F NMR ($CDCl_3$) −141.1 (dq, J(B,F), J(H,F)); ^{11}B NMR (96.3 MHz, $CDCl_3$, δ in ppm) 1.28 (t); HRMS calcd for $C_{48}H_{61}N_3O_3BF_2$ 776.4729, found 776.4738 [M + 1]$^+$.

■ ASSOCIATED CONTENT

Supporting Information. Tables, figures, and a CIF file giving characterization data for all new compounds and crystallographic data for compound **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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