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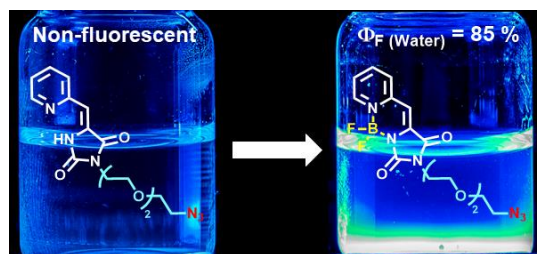
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Synthesis and Photophysical Behavior of a Highly Fluorescent Family of Unsymmetrical Organoboron Complexes Containing 5-(Pyridin-2-ylmethylene)imidazolidine-2,4-dione Moieties

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ABSTRACT: A new and highly fluorescent family of unsymmetrical organoboron complexes containing 5-(pyridin-2-ylmethylene)imidazolidine-2,4-dione moieties has been synthesized in three steps. These compounds show strong absorptions covering a wide range of the UV-Vis spectrum and are strongly emissive (ϕ_f of up to 0.92 in CH_3CN). Moreover, two fluorophores that include an alkyne or an azide group at the end of the alkyl chain, and with potential utility in bioorthogonal chemistry, have been developed. One of these, in which the glycol substituent provides an enhanced water solubility without compromising the fluorescence ($\phi_f = 0.85$ in water), may be of particular importance.

INTRODUCTION

The development of small organic fluorescent dyes has attracted widespread attention due to their applications in bioimaging, sensing and optoelectronics.¹ Among these synthetic fluorophores, organoboron complexes have received strong interest over the recent years, with boron dipyrromethenes (BODIPY, Figure 1) being particularly widely studied² as a result of the easy synthesis, tunable emission wavelengths, high quantum yields and good photostability of this family of dyes, and their wide-ranging applications.³

The success of BODIPY dyes has promoted research into similar systems with alternative bidentate ligands,⁴ and several analogs in which the pyrrole ring has been replaced by other heterocycles have recently been reported.⁵ Among these, two examples which use a BF_2 bridge to stiffen the structure of the Green fluorescent protein (GFP)-chromophore, thus preventing free rotation about the aryl-alkene bond, are worth noting.⁶ Both analogs of this well-known fluorophore⁷ have markedly higher quantum yields than the simplest chromophore derived from this protein

(*p*-HBDI, Figure 1), which does not exhibit significant fluorescence outside the protein environment.⁸

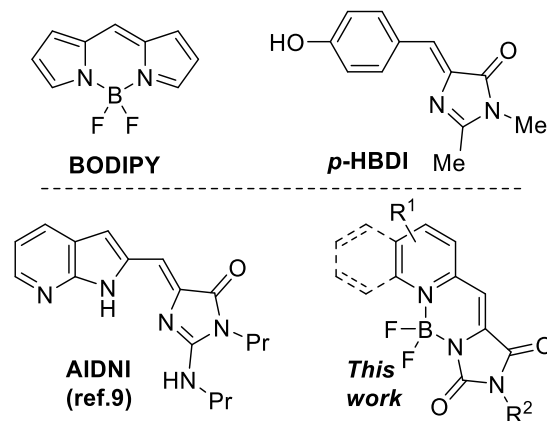


Figure 1. Molecular structures of BODIPY, *p*-HBDI, AIDNI and the family of organoboron complexes described in this work.

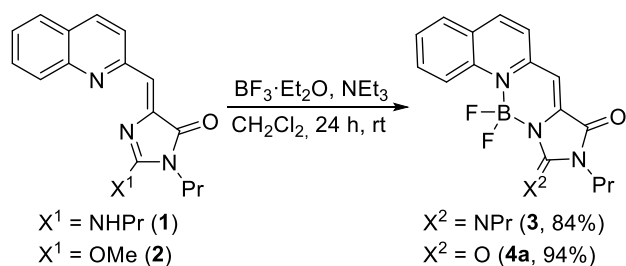
Very recently, we described an unexplored family of GFP-like chromophore analogs which exhibited significantly

enhanced fluorescence properties in comparison to the parent *p*-HBDI.⁹ This difference can be attributed to an extension of the conjugation in the chromophore thanks to the addition of an amino group at position 2 of the imidazolinone core, the lone electron pair of which could serve this purpose. Taking into account this previous work, and the possibility of using a BF₂ bridge to lock the conformation of this kind of fluorophore and increase their quantum yields, herein we report the synthesis and photophysical behavior of a highly fluorescent family of unsymmetrical organoboron complexes containing 5-(pyridin-2-ylmethylene) imidazolidine-2,4-dione moieties.

RESULTS AND DISCUSSION

With the aim of finding a method to form organoboron complexes derived from our previously described family of novel 2-amino-3,5-dihydro-4*H*-imidazol-4-one derivatives,⁹ we treated GFP-like chromophore analogs in which the 4-hydroxybenzyl group had been replaced by other heteroaryl moieties with BF₃·Et₂O in presence of a base. Although attempts with the most fluorescent compound synthesized in our previous work (AIDNI, Figure 1) were unsuccessful, and only decomposition products were obtained under all the reaction conditions tested, we found that quinoline derivatives **1** and **2** gave the organoboron complexes **3** and **4**, respectively, in excellent yields (Scheme 1).

Scheme 1. Synthesis of **3** and **4**



In order to explore the photophysics of the new compounds synthesized, their UV-Vis and fluorescence spectra were measured (see Supporting Information). In agreement with their similar chemical structures, both **3** and **4a** feature strong absorption bands centered between 400 and 450 nm. However, the fluorescence data are strikingly different. Thus, while **3** was found to be non-fluorescent ($\phi_f < 1\%$), **4a** shows intense fluorescence ($\phi_f = 68.6\%$) upon excitation at 360 nm. The presence of the imine moiety in **3** is probably responsible for the lack of emission, as the excited state may be deactivated through a non-radiative decay channel involving C=N isomerization. A complementary computational study was performed using Time-Dependent Density Functional Theory (TD-DFT, see SI for details). The absorption properties of **4a** were computed with the 6-31++G** basis set and using the Polarized Continuum Model (PCM) for acetonitrile to include solvent effects. Different functionals were evaluated (CAM-B3LYP,

Mo6-2X and PBE0), with all being expected to perform reasonably well for this type of species. The best agreement with experiment ($\lambda_{\text{max}} = 406$ nm) was found for PBE0 ($\lambda_{\text{max}} = 393$ nm, $f = 0.63$), although similar results were observed for the other functionals in terms of both the shape of the spectrum and the orbitals involved. A $\pi \rightarrow \pi^*$ transition between the HOMO and LUMO orbitals is responsible for the absorption. Both orbitals are delocalized over the whole π system. Likewise, the emission of **4a** was computed to be centered at 448 nm, in good agreement with the experimental value (460 nm, see Figure 2). The difference in the absorption and fluorescence spectra is assigned to a geometry relaxation process in the excited state. The minor computed geometrical changes are in agreement with the small Stokes shift and the large fluorescence quantum yields.

We then computationally evaluated the absorption properties of a series of derivatives in which substituents with different electron-donating abilities (methoxy and nitro groups) were included in diverse positions using the chemical structure of **4a** as the basic scaffold (1-4, see Table 1). In all cases, a strong absorption was found between 350 and 400 nm, thus indicating the possibility of tuning the optical properties while maintaining the same core structure.

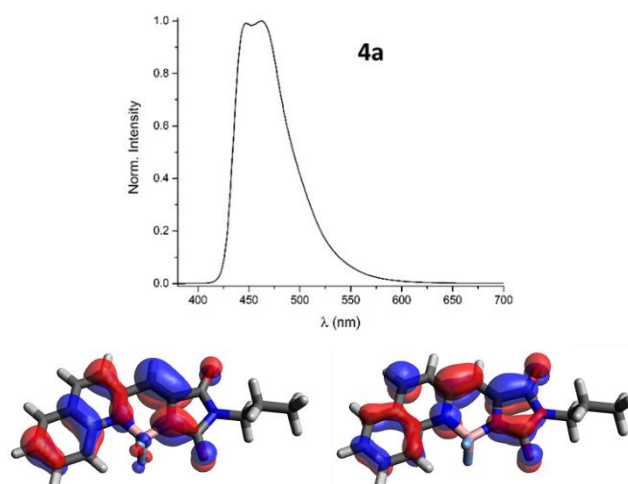
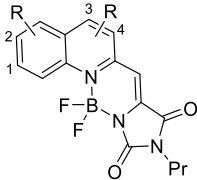


Figure 2. Fluorescence emission (top) and HOMO (bottom, left) and LUMO (bottom, right) orbitals computed for **4a**.

Inspired by the interesting fluorescence properties of **4a** and the option of controlling the photophysical properties, we considered it as a model compound for the design of an entire family of unsymmetrical organoboron complexes containing both a benzo-fused pyridine heterocycle or a pyridine and an imidazolidine-2,4-dione. In order to generate molecular diversity in both rings, we developed a new and more efficient three-step synthesis involving alkylation of the commercially available hydantoin with 1-iodopropane, Knoevenagel condensation, under microwave irradiation, of the alkylated product and the corresponding heteroaryl aldehyde using saturated NaHCO₃ as a base, and treatment of the synthesized heteroarylmethylene imidazolidinedione systems **6a-6f** with BF₃·Et₂O in the presence

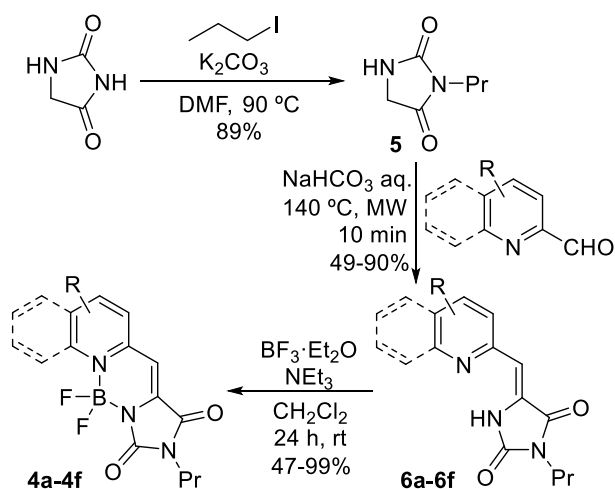
of NEt_3 (Scheme 2). This resulted in organoboron complexes **4a-4f** in moderate to good overall yields (Table 2).

Table 1. Computed absorption for analogues of **4a**



R	λ_{max} (nm)	compound
1-MeO	379	A
1-NO ₂	379	B
2-MeO	380	C
2-NO ₂	377	D
3-MeO	352	E
3-NO ₂	396	F
4-MeO	390	G
4-NO ₂	372	H



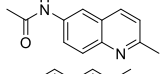



Scheme 2. Synthesis of organoboron complexes **4a-4f**



All the compounds prepared (**4a-4f**) exhibit strong absorptions covering a wide range of the UV-Vis spectrum and are strongly emissive upon excitation at 360 nm, presenting fluorescence lifetimes shorter than 5 ns (see Figure 3 and SI, respectively). This is in contrast with intermediates **6a-6f**, which show similar absorption bands but are not emissive (see SI), thus confirming the relevance of the BF_2 moiety for fluorescence. Compounds **4e** and **4f**, which exhibit a very intense fluorescence ($\phi_f = 0.92$ and 0.91 , respectively), are especially relevant. These two compounds share similar optical properties, with strong absorption bands around 350-370 nm and small Stokes shifts. In the case of **4e**, the emission is centered at 430 nm, while for **4f** it is located at 412 nm. The effect of the solvent on the optical properties of **4e** was explored by measuring the UV-Vis and fluorescence spectra in a range of solvents (see SI)

but only minor changes were found. The stronger absorption, very high fluorescence quantum yield and emission in the visible region mean that **4e** is an excellent fluorophore.

Table 2. Synthesis of organoboron complexes **4a-4f**

Ar	overall yield ^[a]	compound	ϕ_f ^[b]
	75	4a	0.69
	31	4b	0.47
	44	4c	0.42
	20	4d	0.19
	63	4e	0.92
	34	4f	0.91

[a] Three steps. [b] Acetonitrile solution, excitation at 360 nm.

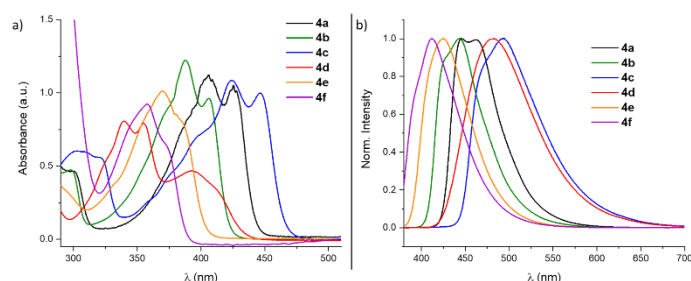
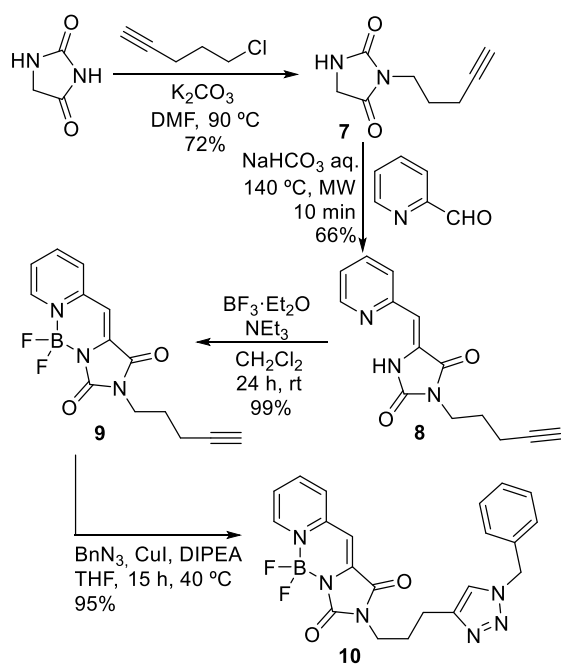


Figure 3. Absorption spectra (a) and fluorescence emission (b) for **4a-4f**.

Due to the excellent fluorescence properties of **4e**, this chromophore was chosen for the development of two fluorophores with potential utility in bioorthogonal chemistry.¹⁰ We envisaged that the incorporation of an alkyne or an azide group at the end of the alkyl chain attached to the imidazolidine-2,4-dione ring could serve for this purpose due to the participation of these groups in [3+2] cycloadditions.¹¹ For introduction of the terminal alkyne group, the same three-step synthesis was used but with 5-chloro-1-pentyne instead of 1-iodopropane. This gave derivative **9** in a 47% overall yield (Scheme 3). Compound **9** exhibits several absorption bands, and excitation at either 360 or 380 nm leads to an emission at 425 nm with $\phi_f = 0.72$ (see SI).

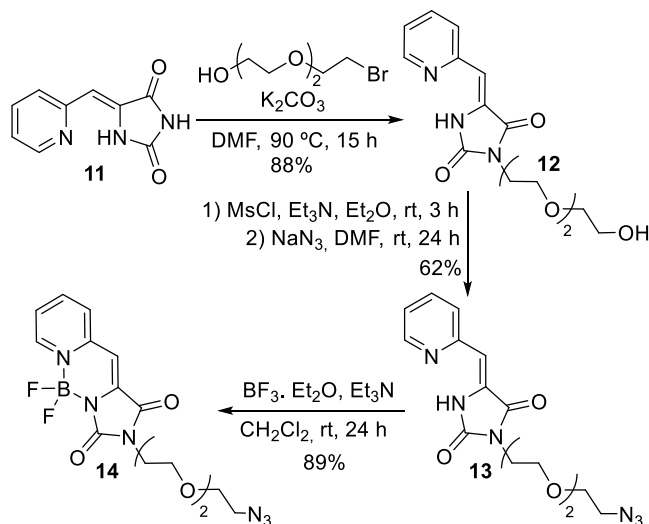
In order to demonstrate that triazole formation does not affect the fluorescence properties of these dyes, alkyne **9** was treated with benzyl azide under standard CuAAC conditions to get derivative **10** in a 95% yield. This compound showed a quantum yield of $\phi_f = 0.94$ in acetonitrile and $\phi_f = 0.67$ in water, which clearly retains a strong fluorescent emission enough to be used as dye in click chemistry. In addition, this derivative also presents a fluorescence lifetime shorter than 5 ns.

Scheme 3. Synthesis of derivatives **9** and **10**



For introduction of the azide group, we decided to synthesize a derivative that could also solve the most serious drawback of **4e** for use in biological applications, namely its poor solubility in water. With this idea in mind, compound **14**, which contains a highly polar substituent (diethylene glycol) attached to the imidazolidone-2,4-dione ring, was synthesized. To that end, 5-(pyridin-2-ylmethylene)imidazolidone-2,4-dione¹² (**11**) was treated with 2-[2-(2-bromoethoxy)ethoxy]ethan-1-ol¹³ in the presence of K_2CO_3 , then the hydroxyl group of **12** was replaced by an azide via a two-step strategy involving the formation of a methanesulfonate intermediate. Finally, the organoboron complex was easily formed from **13** by treatment with $BF_3 \cdot Et_2O$ and NEt_3 (Scheme 4). As expected, this compound (**14**) exhibits good water-solubility.

Scheme 4. Synthesis of derivative **14**



In acetonitrile, compound **14** maintains the optical properties of the basic core **4e**, such as the strong absorption band centered around 360 nm and the emission at 420 nm upon excitation at 360 nm, with a high quantum yield of $\phi_f = 0.89$, and the additional glycol substituent provides enhanced water-solubility without compromising the fluorescence. Thus, **14** also emits at 420 nm in water, with $\phi_f = 0.85$ (see Figure 4).

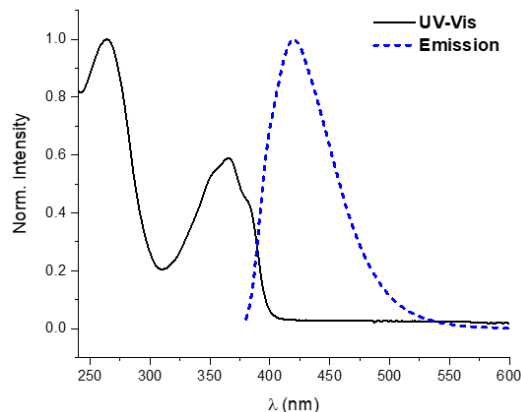


Figure 4. Optical properties of **14** in water.

CONCLUSIONS

We have described a new and highly fluorescent family of unsymmetrical organoboron complexes containing 5-(pyridin-2-ylmethylene)imidazolidone-2,4-dione moieties. Computational exploration of the optical properties of the core structure and the effect of substituents allowed us to design a set of compounds. In order to generate molecular diversity in both rings, an efficient three-step synthesis, which affords organoboron complexes in moderate to good overall yields, has been developed. These compounds show strong absorptions covering a wide range of the UV-Vis spectrum and are strongly emissive. This contrasts with intermediates lacking a BF_2 bridge, which show similar absorption bands but are not emissive. Due to the excellent fluorescence properties of **4e** ($\phi_f = 0.92$ in CH_3CN), we have chosen this chromophore for the development of two fluorophores, which include an alkyne or an azide group at the end of the alkyl chain, with potential uses in bioorthogonal chemistry. Derivative **14**, in which the glycol substituent provides an enhanced water-solubility without compromising the fluorescence properties ($\phi_f = 0.85$ in water), is particularly relevant in this regard.

EXPERIMENTAL SECTION

General Methods. All reactions involving air-sensitive compounds were carried out under an inert atmosphere (Ar). Starting materials sourced from commercial suppliers were used as received unless otherwise stated. Dry solvents, where necessary, were dried using an MBRAUN MB-SPS-800 apparatus. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60 F254, 70-200 mm) as the station-

ary phase. All reactions in a microwave reactor were carried out using a Biotage® Initiator 2.5 Microwave Synthesizer (temperature monitored by external surface sensor). All melting points were determined in open capillary tubes using a Stuart Scientific SMP3 melting point apparatus. ¹H and ¹³C spectra were recorded using either a Varian Mercury VX-300, Varian Unity 300 or Varian Unity 500 MHz spectrometer at room temperature. Chemical shifts are given in ppm (δ) downfield from TMS. Coupling constants (*J*) are in Hertz (Hz) and signals are described as follows: s, singlet; d, doublet; t, triplet; bs, broad singlet; dd, doublet of doublets; ddd, double doublet of doublets; dt, doublet of triplets; td, triplet of doublets; ap t, apparent triplet; ap q, apparent quadruplet; ap dt, apparent doublet of triplets; apparent triplet of doublets; ap quin, apparent quintuplet; sext, sextet; m, multiplet. High-resolution analysis (HRMS) was performed using an Agilent 6210 time-of-flight LC/MS. 4-Methoxyquinoline-2-carbaldehyde,¹⁴ isoquinoline-3-carbaldehyde,¹⁵ 4-methoxypicolinaldehyde¹⁶ and 2-(2'-(2''-bromoethoxy)ethoxy)ethanol¹³ were prepared as described previously. Absorption spectra were recorded using an Agilent 8453 spectrophotometer. Emission spectra were recorded using a Shimadzu RF6000 spectrofluorimeter.

(Z)-12,12-Difluoro-9-propyl-10-(propylimino)-9,10-dihydro-12λ⁴,13λ⁴-imidazo[1',5':3,4][1,3,2]diazaborinino[1,6-a]quinolin-8(12H)-one (3). Compound **19** (0.025 g, 0.078 mmol) was added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum and purged with argon. Dry CH₂Cl₂ (2 mL), dry NEt₃ (54 μL) and BF₃·Et₂O (96 μL) were then added and the resulting mixture was stirred for 24 h at room temperature. The reaction mixture was washed several times with water and the organic layer dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (50% EtOAc in hexane) to give **3** (0.024 g, 0.065 mmol) as an orange solid in 84% yield. M.p.: 187–190 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.88–8.82 (m, 1H), 8.19 (d, *J* = 8.6 Hz, 1H), 7.84–7.77 (m, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.7 Hz, 1H), 6.28 (s, 1H), 3.83 (t, *J* = 6.6 Hz, 2H), 3.72 (t, *J* = 7.3 Hz, 2H), 1.79–1.68 (m, 4H), 1.06 (t, *J* = 7.4 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 162.3, 152.8, 143.1, 141.6, 140.5, 140.1, 132.7, 129.0, 127.2, 123.8, 122.5, 91.3, 49.4, 41.6, 25.3, 21.5, 12.1, 11.5. ¹⁹F NMR (282 MHz, CDCl₃) δ -113.49 (q, *J* = 33.1 Hz, 2F). ¹¹B{¹H} NMR (160 MHz, CDCl₃) δ 2.84 (t, *J* = 33.1 Hz, 1B). HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₉H₂₂BF₂N₄O 371.1850; found 371.1860.

3-Propylimidazolidine-2,4-dione (5). Hydantoin (1.00 g, 10 mmol) and K₂CO₃ (1.38 g, 10 mmol) were added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum and purged with argon. 1-Iodopropane (0.97 mL, 10 mmol) and dry DMF (10 mL) were then added and the resulting mixture was stirred for 15 h at 90 °C. The reaction was quenched by addition of brine. The mixture was extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure to give **5** (1.27 g, 8.94

mmol) as a yellow solid in 89% yield. M.p.: 75–77 °C. ¹H NMR (500 MHz, CDCl₃) δ 6.56 (s, 1H), 3.96 (s, 2H), 3.46 (t, *J* = 7.4 Hz, 2H), 1.63 (sext, *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.5 Hz, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 171.6, 159.0, 46.5, 40.4, 21.5, 11.3. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₆H₁₁N₂O₂ 143.0815; found 143.0813.

General procedure for the synthesis of heteroaryl-methyleneimidazolidinedione systems 6. Compound **5** (1 equiv.), the corresponding aldehyde (1.2 equiv.) and aqueous saturated Na₂HCO₃ solution (0.12 M) were added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum. The resulting mixture was then stirred for 10 min at 140 °C in the microwave. The mixture was extracted with EtOAc (x3) and the combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel to give the corresponding compound **6**.

(Z)-3-Propyl-5-(quinoline-2-ylmethylene)imidazolidine-2,4-dione (6a). Following the general procedure, starting with 2-quinolinecarbaldehyde (0.066 g, 0.42 mmol). Purification by flash column chromatography on silica gel (10% EtOAc in hexane) gave **6a** (0.106 g, 0.38 mmol) as a yellow solid in 90% yield. M.p.: 160–162 °C. ¹H NMR (500 MHz, CDCl₃) δ 10.55 (bs, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.79 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.74 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.54 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 6.66 (s, 1H), 3.62 (ap t, *J* = 7.5 Hz, 2H), 1.73 (sext, *J* = 7.3 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 164.2, 154.6, 147.9, 137.0, 132.0, 130.5, 129.0, 127.8, 127.2, 127.0, 123.5, 106.1, 40.4, 21.7, 11.3. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₆H₁₆N₃O₂ 282.1237; found 282.1246.

(Z)-5-((4-Methoxyquinolin-2-yl)methylene)-3-propylimidazolidine-2,4-dione (6b). Following the general procedure, starting with 4-methoxyquinoline-2-carbaldehyde (0.079 g, 0.42 mmol). Purification by flash column chromatography on silica gel (30% EtOAc in hexane) gave **6b** (0.056 g, 0.18 mmol) as a yellow oil in 51% yield. ¹H NMR (500 MHz, CDCl₃) δ 10.60 (bs, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.97 (d, *J* = 8.6 Hz, 1H), 7.71 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.49 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 6.74 (s, 1H), 6.58 (s, 1H), 4.06 (s, 3H), 3.61 (t, *J* = 7.3 Hz, 2H), 1.73 (sext, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 164.1, 162.7, 155.5, 154.4, 148.6, 131.9, 130.6, 128.4, 126.1, 121.8, 120.1, 106.6, 102.2, 56.0, 40.5, 21.9, 11.5. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₇H₁₈N₃O₃ 312.1343; found 312.1354.

(Z)-N-(2-((2,5-Dioxo-1-propylimidazolidin-4-ylidene)methyl)quinoline-6-yl)acetamide (6c). Following the general procedure, starting with *N*-(2-formylquinolin-6-yl)acetamide (0.091 g, 0.42 mmol). The resulting residue was filtered over a plug of silica gel eluting with 30% EtOAc in hexane and was employed in the next step without further purification.

(Z)-5-(Isoquinolin-3-ylmethylene)-3-propylimidazolidine-2,4-dione (6d). Following the general procedure, starting with isoquinoline-3-carbaldehyde (0.066 g, 0.42

mmol). Purification by flash column chromatography on silica gel (50% EtOAc in hexane) gave **6d** (0.096 g, 0.34 mmol) as a white solid in 49% yield. M.p.: 166–168 °C. ¹H NMR (500 MHz, CDCl₃) δ 10.15 (bs, 1H), 9.17 (s, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.74–7.68 (m, 2H), 7.65–7.59 (m, 1H), 6.68 (s, 1H), 3.59 (t, *J* = 7.4 Hz, 2H), 1.72 (sext, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 164.3, 154.3, 152.5, 148.0, 136.1, 131.3, 130.0, 128.3, 128.0, 127.5, 127.0, 122.7, 107.6, 40.3, 21.8, 11.3. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₆H₁₆N₃O₂ 282.1237; found [M+H]⁺: 282.1248.

(Z)-3-Propyl-5-(pyridine-2-ylmethylene)imidazolidine-2,4-dione (6e). Following the general procedure, starting with 2-pyridinecarboxaldehyde (0.045 g, 0.42 mmol). Purification by flash column chromatography on silica gel (10% EtOAc in hexane) gave **6e** (0.059 g, 0.25 mmol) as a yellow oil in 72% yield. ¹H NMR (500 MHz, CDCl₃) δ 10.19 (bs, 1H), 8.58 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.70 (td, *J* = 7.8, 1.9 Hz, 1H), 7.33 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.18 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 6.52 (s, 1H), 3.60–3.55 (m, 2H), 1.70 (sext, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 164.2, 154.4, 149.4, 137.0, 131.0, 125.8, 122.4, 106.2, 40.3, 21.7, 11.3. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₂H₁₄N₃O₂ 232.1081; found 232.1080.

(Z)-5-((4-Methoxypyridine-2-yl)methylene)-3-propylimidazolidine-2,4-dione (6f). Following the general procedure, starting with 4-methoxypicolinaldehyde (0.029 g, 0.21 mmol). Purification by flash column chromatography on silica gel (40% EtOAc in hexane) gave **6f** (0.025 g, 0.097 mmol) as a yellow oil in 55% yield. ¹H NMR (500 MHz, CDCl₃) δ 10.26 (bs, 1H), 8.39 (d, *J* = 5.8 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.71 (dd, *J* = 5.8, 2.6 Hz, 1H), 6.45 (s, 1H), 3.86 (s, 3H), 3.57 (t, *J* = 7.3 Hz, 2H), 1.70 (sext, *J* = 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 166.1, 164.1, 155.7, 154.2, 150.5, 131.2, 111.6, 108.6, 106.4, 55.5, 40.4, 21.8, 11.5. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₃H₁₆N₃O₃ 262.1186; found 262.1191.

General procedure for the synthesis of organoboron complex 4. To a Biotage microwave vial equipped with a stir bar was added the corresponding compound **6** (1 equiv.). The vial was sealed with a cap line with a disposable Teflon septum and purged with argon. Dry CH₂Cl₂ (0.05 M), dry NEt₃ (5 equiv.) and BF₃·Et₂O (10 equiv.) were then added and the resulting mixture stirred for 24 h at room temperature. The reaction mixture was washed several times with water and the organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel to give the corresponding compound **4**.

12,12-Difluoro-8,10-dioxo-9-propyl-8,9,10,12-tetrahydroimidazo[1',5':3,4][1,3,2]diazaborinino[1,6-a]quinolin-13-ium-12-uide (4a). Following the general procedure, starting with compound **6a** (0.025 g, 0.088 mmol). Purification by flash column chromatography on silica gel (50% EtOAc in hexane) gave **4a** (0.027 g, 0.083 mmol) as a yellow solid in 94% yield. M.p.: 245–247 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.99 (dt, *J* = 9.1, 3.3 Hz, 1H), 8.42

(d, *J* = 8.5 Hz, 1H), 7.95–7.89 (m, 2H), 7.70 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 6.52 (s, 1H), 3.66–3.61 (m, 2H), 1.75 (sext, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 162.8, 155.4, 152.1, 143.2, 141.1, 139.6, 133.7, 129.1, 128.4, 128.2, 124.4, 123.0, 96.7, 40.9, 21.7, 11.4. ¹⁹F NMR (282 MHz, CDCl₃) δ -118.46 (q, *J* = 30.7 Hz, 2F). ¹¹B{¹H} NMR (160 MHz, CDCl₃) δ 2.00 (t, *J* = 30.7 Hz, 1B). HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₆H₁₅BF₂N₃O₂ 330.1223; found 330.1233.

12,12-Difluoro-5-methoxy-8,10-dioxo-9-propyl-8,9,10,12-tetrahydroimidazo[1',5':3,4][1,3,2]diazaborinino[1,6-a]quinolin-13-ium-12-uide (4b). Following the general procedure, starting with compound **6b** (0.056 g, 0.18 mmol). Purification by flash column chromatography on silica gel (50% EtOAc in hexane) gave **4b** (0.044 g, 0.12 mmol) as a yellow solid in 68% yield. M.p.: 248–250 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.64 (dt, *J* = 9.2, 3.0 Hz, 1H), 8.26 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.99 (ddd, *J* = 8.8, 6.9, 1.7 Hz, 1H), 7.74 (ddd, *J* = 8.0, 6.9, 0.8 Hz, 1H), 7.63 (s, 1H), 6.82 (s, 1H), 4.22 (s, 3H), 3.48 (t, *J* = 7.0 Hz, 2H), 1.62 (sext, *J* = 7.4 Hz, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 165.6, 162.2, 154.9, 153.5, 140.8, 137.8, 133.1, 127.4, 122.8, 122.6, 120.4, 103.1, 97.5, 57.9, 40.0, 21.0, 11.1. ¹⁹F NMR (282 MHz, DMSO-*d*₆) δ -129.22 (q, *J* = 29.8 Hz, 2F). ¹¹B{¹H} NMR (160 MHz, DMSO-*d*₆) δ 2.56 (t, *J* = 29.8 Hz, 1B). HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₇H₁₇BF₂N₃O₃ 360.1326; found 360.1335.

3-Acetamido-12,12-difluoro-8,10-dioxo-9-propyl-8,9,10,12-tetrahydroimidazo[1',5':3,4][1,3,2]diazaborinino[1,6-a]quinolin-13-ium-12-uide (4c). Following the general procedure, starting with compound **6c** (0.030 g, 0.089 mmol). Purification by flash column chromatography on silica gel (70% EtOAc in hexane) gave **4c** (0.017 g, 0.043 mmol) as a yellow solid in 49% yield. M.p.: 124–126 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 10.55 (s, 1H), 8.79 (d, *J* = 8.7 Hz, 1H), 8.66–8.61 (m, 1H), 8.57 (d, *J* = 2.5 Hz, 1H), 7.96–7.90 (m, 2H), 6.90 (s, 1H), 3.47 (t, *J* = 7.2 Hz, 2H), 2.13 (s, 3H), 1.61 (sext, *J* = 7.3 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆) δ 169.1, 162.1, 154.8, 149.9, 143.3, 138.4, 137.4, 135.8, 128.9, 125.9, 123.9, 123.5, 115.4, 97.3, 54.9, 24.2, 21.0, 11.2. ¹⁹F NMR (282 MHz, DMSO-*d*₆) δ -125.54 (m, 2F). ¹¹B{¹H} NMR (160 MHz, DMSO-*d*₆) δ 2.79 (s, 1B). HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₁₈H₁₇BF₂N₄O₃Na 409.1254; found 409.1256.

5,5-Difluoro-1,3-dioxo-2-propyl-1,2,3,5-tetrahydroimidazo[1',5':3,4][1,3,2]diazaborinino[1,6-b]isoquinolin-6-ium-5-uide (4d). Following the general procedure, starting with compound **6d** (0.032 g, 0.11 mmol). Purification by flash column chromatography on silica gel (30% EtOAc in hexane) gave **4d** (0.018 g, 0.053 mmol) as a white solid in 47% yield. M.p.: 278–280 °C (decomposition). ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.96 (s, 1H), 8.60 (d, *J* = 8.3 Hz, 1H), 8.47 (s, 1H), 8.19–8.07 (m, 2H), 7.91 (t, *J* = 7.6 Hz, 1H), 6.94 (s, 1H), 3.48 (ap t, *J* = 7.2 Hz, 2H), 1.61 (sext, *J* = 7.6 Hz, 2H), 0.88 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆) δ 152.3, 149.1, 137.4, 136.1, 131.2, 130.6, 129.9, 127.9, 126.8, 123.6, 121.9, 107.1, 98.7, 29.0, 21.1, 11.2. ¹⁹F NMR (282 MHz, DMSO-*d*₆) δ -134.91 (m, 2F). ¹¹B{¹H} NMR (160 MHz,

DMSO-*d*₆) δ 1.89 (s, 1B). HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₆H₁₅BF₂N₃O₂ 330.1220; found 330.1232.

5,5-Difluoro-1,3-dioxo-2-propyl-1,2,3,5-tetrahydroimidazo[1,5-*c*]pyrido[2,1-*f*][1,3,2]diazaborinin-6-ium-5-uide (4e). Following the general procedure, starting with compound **6e** (0.025 g, 0.11 mmol). Purification by flash column chromatography on silica gel (50% EtOAc in hexane) gave **4e** (0.030 g, 0.11 mmol) as a yellow solid in 99% yield. M.p.: 227–229 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.77 (d, *J* = 6.0 Hz, 1H), 8.17–8.09 (m, 1H), 7.63–7.55 (m, 2H), 6.50 (s, 1H), 3.66–3.59 (m, 2H), 1.74 (sext, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 162.8, 155.3, 149.3, 143.1, 142.5, 138.4, 125.7, 123.2, 96.0, 40.8, 21.8, 11.4. ¹⁹F NMR (282 MHz, CDCl₃) δ -135.30 (dd, *J* = 26.6 Hz, 2F). ¹¹B{¹H} NMR (160 MHz, CDCl₃) δ 1.19 (t, *J* = 26.6 Hz, 1B). HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₂H₁₃BF₂N₃O₂ 280.1066; found 280.1064.

5,5-Difluoro-9-methoxy-1,3-dioxo-2-propyl-1,2,3,5-tetrahydroimidazo[1,5-*c*]pyrido[2,1-*f*][1,3,2]diazaborinin-6-ium-5-uide (4f). Following the general procedure, starting with compound **6f** (0.025 g, 0.094 mmol). Purification by flash column chromatography on silica gel (50% EtOAc in hexane) gave **4f** (0.020 g, 0.065 mmol) as a white solid in 69% yield. M.p.: 209–210 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.56 (d, *J* = 7.0 Hz, 1H), 7.02 (dd, *J* = 7.0, 2.7 Hz, 1H), 6.91 (d, *J* = 2.7 Hz, 1H), 6.39 (s, 1H), 4.05 (s, 3H), 3.59 (t, *J* = 7.3 Hz, 2H), 1.71 (sext, *J* = 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 188.5, 169.6, 163.1, 151.1, 144.6, 138.5, 111.0, 108.8, 96.3, 57.0, 40.7, 21.7, 11.4. ¹⁹F NMR (282 MHz, CDCl₃) δ -131.49 (q, *J* = 26.9 Hz, 2F). ¹¹B{¹H} NMR (160 MHz, CDCl₃) δ 0.96 (t, *J* = 26.9 Hz, 1B). HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₃H₁₅BF₂N₃O₃ 310.1169; found 310.1173.

3-(Pent-4-yn-1-yl)imidazolidine-2,4-dione (7). Hydantoin (0.50 g, 5 mmol) and K₂CO₃ (0.69 g, 5 mmol) were added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum and purged with argon. 5-Chloro-1-pentyne (0.53 mL, 5 mmol) and dry DMF (5 mL) were then added and the resulting mixture was stirred for 15 h at 90 °C. The reaction was quenched by addition of brine. The mixture was extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure to give **7** (0.60 g, 3.59 mmol) as a yellow solid in 72% yield. M.p.: 78–79 °C. ¹H NMR (500 MHz, CDCl₃) δ 6.97 (s, 1H), 3.92 (s, 2H), 3.55 (t, *J* = 7.2 Hz, 2H), 2.22–2.16 (m, 2H), 1.95 (s, 1H), 1.80 (p, *J* = 7.1 Hz, 2H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 171.7, 158.9, 82.9, 69.1, 46.5, 37.9, 26.7, 16.2. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₈H₁₁N₂O₂ 167.0815; found 167.0810.

(Z)-3-(Pent-4-yn-1-yl)-5-(pyridin-2-ylmethylene)imidazolidine-2,4-dione (8). Compound **7** (0.058 g, 0.35 mmol), 2-pyridinecarboxaldehyde (0.04 mL, 0.42 mmol) and aqueous saturated Na₂HCO₃ solution (3 mL) were added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum. The resulting mixture was then stirred for 10 min at 140 °C in a microwave. The mixture was extracted with EtOAc (x3) and the combined organic layers were dried

over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (30% EtOAc in hexane) to give compound **8** (0.059 g, 0.23 mmol) as a white solid in 66% yield. M.p.: 115–117 °C. ¹H NMR (500 MHz, CDCl₃) δ 10.22 (bs, 1H), 8.61–8.58 (m, 1H), 7.71 (td, *J* = 7.7, 1.9 Hz, 1H), 7.36–7.32 (m, 1H), 7.19 (ddd, *J* = 7.7, 4.8, 1.0 Hz, 1H), 6.53 (s, 1H), 3.73 (t, *J* = 7.1 Hz, 2H), 2.27 (td, *J* = 7.1, 2.7 Hz, 2H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.93 (p, *J* = 7.1 Hz, 2H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 164.1, 154.3, 154.2, 149.5, 137.1, 130.9, 125.9, 122.5, 106.4, 82.9, 69.2, 37.9, 27.1, 16.3. HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₄H₁₄N₃O₂ 256.1081; found 256.1086.

5,5-Difluoro-1,3-dioxo-2-(pent-4-yn-1-yl)-1,2,3,5-tetrahydroimidazo[1,5-*c*]pyrido[2,1-*f*][1,3,2]diazaborinin-6-ium-5-uide (9). Compound **8** (0.026 g, 0.10 mmol) was added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum and purged with argon. Dry CH₂Cl₂ (2 mL), dry NEt₃ (0.07 mL) and BF₃·Et₂O (0.13 mL) were then added and the resulting mixture was stirred for 24 h at room temperature. The reaction mixture was washed several times with water and the organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (50% EtOAc in hexane) to give compound **9** (0.030 g, 0.099 mmol) as yellow solid in 99% yield. M.p.: 152–154 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.77 (d, *J* = 5.9 Hz, 1H), 8.16–8.11 (m, 1H), 7.64–7.57 (m, 2H), 6.51 (s, 1H), 3.76 (t, *J* = 7.1 Hz, 2H), 2.28 (td, *J* = 7.0, 2.7 Hz, 2H), 1.99–1.91 (m, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 162.9, 155.3, 149.3, 143.3, 142.7, 138.4, 125.8, 123.4, 96.2, 82.8, 69.3, 38.3, 26.9, 16.4. ¹⁹F NMR (282 MHz, CDCl₃) δ 129.39 (q, *J* = 25.6 Hz, 2F). ¹¹B{¹H} NMR (160 MHz, CDCl₃) δ 1.18 (t, *J* = 25.6 Hz, 1B). HRMS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₁₄H₁₃BF₂N₃O₂ 304.1064; found 304.1075.

2-(3-(1-Benzyl-1H-1,2,3-triazol-4-yl)propyl)-5,5-difluoro-1,3-dioxo-1,2,3,5-tetrahydroimidazo[1,5-*c*]pyrido[2,1-*f*][1,3,2]diazaborinin-6-ium-5-uide (10). To a round bottom flask were added **9** (15.0 mg, 0.0495 mmol) and BnN₃ (19.8 mg, 0.1485 mmol). Then the flask was degassed and filled with argon, and THF (0.7 mL) was injected. After that, DIPEA (25.9 mL, 0.1485 mmol) and CuI (30 mol%, 2.83 mg, 0.01485 mmol) were added. The resulting mixture was stirred at 40 °C for 15 h. The reaction was quenched by addition of NH₄Cl saturated aqueous solution mixed with NH₃ (3:1) and extracted with CH₂Cl₂. The organic layer was washed with brine and the combined aqueous layers were extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (80% EtOAc in hexane) to give compound **10** (0.60 g, 3.59 mmol) as a yellow solid in 95% yield. M.p.: 206–207 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.76 (d, *J* = 5.9 Hz, 1H), 8.19–8.11 (m, 1H), 7.66–7.57 (m, 2H), 7.40 (s, 1H), 7.39–7.21 (m, 5H), 6.51 (s, 1H), 5.49 (s, 2H), 3.68 (t, *J* = 6.9 Hz, 2H), 2.76 (t, *J* = 7.4 Hz, 2H), 2.07 (ap quin, *J* = 7.1 Hz, 2H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 162.8, 155.5, 149.3, 147.2,

143.2, 142.7, 138.3, 135.1, 129.2, 128.7, 128.1, 125.9, 123.4, 121.5, 96.3, 54.1, 38.3, 27.8, 23.1. ¹⁹F NMR (282 MHz, CDCl₃) δ -129.57 (m, 2F). ¹B{¹H} NMR (160 MHz, CDCl₃) δ 1.27 (t, J = 28.6 Hz, 1B). HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for C₂₁H₂₀BF₂N₆O₂ 437.1707; found 437.1716.

(Z)-5-(Pyridin-2-ylmethylene)imidazolidine-2,4-dione (11). Hydantoin (0.15 g, 1.5 mmol), 2-pyridinecarboxaldehyde (0.19 g, 1.8 mmol) and aqueous saturated Na₂HCO₃ solution (10 mL) were added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum. The resulting mixture was then stirred for 10 min at 140 °C in a microwave. The mixture was extracted with EtOAc (x3) and the combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (40% EtOAc in hexane) to give compound **11** (0.080 g, 0.42 mmol) as white solid in 28% yield. M.p.: 235–237 °C. ¹H NMR (500 MHz, CD₃OD) δ 8.69 (ddd, J = 4.8, 1.9, 0.9 Hz, 1H), 7.81 (td, J = 7.7, 1.8 Hz, 1H), 7.50 (dt, J = 7.9, 1.1 Hz, 1H), 7.28 (ddd, J = 7.6, 4.8, 1.1 Hz, 1H), 6.53 (s, 1H). ¹³C{¹H} NMR (75 MHz, CD₃OD) δ 166.8, 156.4, 155.3, 150.5, 138.0, 132.9, 126.7, 123.4, 107.0. HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for C₉H₈N₃O₂ 190.0611; found 190.0618.

(Z)-3-(2-(2-(2-hydroxyethoxy)ethyl)-5-(pyridin-2-ylmethylene)imidazolidine-2,4-dione (12). 2-(2'-(2'-Bromoethoxy)ethoxy)ethanol (0.11 g, 0.53 mmol), compound **11** (0.10 g, 0.53 mmol) and K₂CO₃ (0.073 g, 0.53 mmol) were added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum and purged with argon. Dry DMF (1.5 mL) was then added and the resulting mixture was stirred for 15 h at 90 °C. The reaction was quenched by addition of brine and the mixture was extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (in EtOAc) to give compound **12** (0.15 g, 0.47 mmol) as a yellow solid in 88% yield. M.p.: 90–93 °C. ¹H NMR (300 MHz, CDCl₃) δ 10.25 (bs, 1H), 8.63–8.58 (m, 1H), 7.71 (td, J = 7.7, 1.8 Hz, 1H), 7.38–7.32 (m, 1H), 7.20 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 6.55 (s, 1H), 3.88–3.82 (m, 2H), 3.79–3.55 (m, 10H), 2.16 (bs, 1H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 164.1, 154.2, 154.1, 149.4, 137.0, 130.8, 125.8, 122.5, 106.6, 72.7, 70.6, 70.2, 67.7, 62.0, 38.1. HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for C₁₅H₂₀N₃O₅ 322.1397; found 322.1403.

(Z)-3-(2-(2-(2-azidoethoxy)ethoxy)ethyl)-5-(pyridin-2-ylmethylene)imidazolidine-2,4-dione (13). Compound **12** (0.31 g, 0.96 mmol) was dissolved in dry CH₂Cl₂ (1 mL) in a round-bottomed flask and triethylamine (0.16 mL, 1.15 mmol) was added. The reaction mixture was then cooled to 0 °C and methanesulfonyl chloride (89 μL, 1.15 mmol) was added dropwise. The resulting mixture was stirred at room temperature until compound **12** had been completely consumed, which was determined by TLC analysis. The reaction was then quenched by addition of brine, and the mixture was extracted with CH₂Cl₂, dried over anhydrous

Na₂SO₄, filtered and concentrated under reduced pressure to give the desired methanesulfonate intermediate (0.26 g, 0.66 mmol) as a yellow oil (¹H NMR (300 MHz, CDCl₃) δ 10.13 (bs, 1H), 8.51–8.46 (m, 1H), 7.61 (td, J = 7.7, 1.8 Hz, 1H), 7.28–7.22 (m, 1H), 7.10 (ddd, J = 7.6, 4.8, 1.1 Hz, 1H), 6.42 (s, 1H), 4.27–4.22 (m, 2H), 3.75–3.69 (m, 2H), 3.66–3.60 (m, 4H), 3.54 (s, 4H), 2.98 (s, 3H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 163.5, 153.7, 153.6, 149.0, 136.7, 130.4, 125.5, 122.2, 106.1, 70.3, 69.9, 69.2, 68.8, 67.3, 37.7, 37.4. HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for C₁₆H₂₂N₃O₇S 400.1173; found 400.1176). This intermediate (0.26 g, 0.66 mmol) was subsequently dissolved in dry DMF (5 mL) in a round-bottomed flask, sodium azide (0.13 g, 1.98 mmol) was added, and the reaction mixture was stirred overnight at 50 °C. The reaction was quenched by addition of brine and the mixture was extracted with diethyl ether, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (80% EtOAc in hexane) to give compound **13** (0.21 g, 0.60 mmol) as a yellow solid in 62% overall yield. M.p.: 61–63 °C. ¹H NMR (300 MHz, CDCl₃) δ 10.13 (bs, 1H), 8.52–8.47 (m, 1H), 7.62 (tt, J = 7.8, 2.1 Hz, 1H), 7.27–7.22 (m, 1H), 7.14–7.07 (m, 1H), 6.43 (d, J = 2.1 Hz, 1H), 3.78–3.71 (m, 2H), 3.69–3.62 (m, 2H), 3.59–3.51 (m, 6H), 3.29–3.23 (m, 2H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 163.8, 154.0, 153.8, 149.1, 136.8, 130.6, 125.5, 122.2, 106.1, 70.4, 70.0, 69.8, 67.4, 50.5, 37.7. HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for C₁₅H₁₉N₆O₄ 347.1462; found 347.1470.

2-(2-(2-(2-Azidoethoxy)ethoxy)ethyl)-5,5-difluoro-1,3-dioxo-1,2,3,5-tetrahydropyridin-6-ium-5-uide (14). Compound **13** (0.060 g, 0.17 mmol) was added to a Biotage microwave vial equipped with a stir bar. The vial was sealed with a cap line with a disposable Teflon septum and purged with argon. Dry CH₂Cl₂ (3.5 mL), dry NEt₃ (36 μL, 0.26 mmol) and BF₃·Et₂O (64 μL, 0.52 mmol) were then added and the resulting mixture was stirred for 24 h at room temperature. The reaction mixture was washed several times with water and the organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (70% EtOAc in hexane) to give compound **14** (0.041 g, 0.10 mmol) as a yellow solid in 89% yield. M.p.: 101–103 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.78 (d, J = 6.0 Hz, 1H), 8.12 (ddd, J = 8.2, 7.5, 1.6 Hz, 1H), 7.62–7.56 (m, 2H), 6.50 (s, 1H), 3.86 (t, J = 5.7 Hz, 2H), 3.76 (t, J = 5.6 Hz, 2H), 3.68–3.61 (m, 6H), 3.36 (t, J = 5.2 Hz, 2H). ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 162.8, 156.4, 149.4, 143.3, 142.6, 138.5, 125.8, 123.3, 96.2, 70.8, 70.4, 70.2, 67.6, 50.9, 38.5. ¹⁹F NMR (282 MHz, CDCl₃) δ 129.53 (q, J = 27.1 Hz, 2F). ¹B{¹H} NMR (160 MHz, CDCl₃) δ 1.29 (t, J = 27.1 Hz, 1B). HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for C₁₅H₁₈BF₂N₆O₄ 395.1445; found 395.1448.

Computational details: Structures were optimized in the ground state at the DFT level of theory using the 6-31++G(d,p) basis set and the CAM-B3LYP,¹⁷ Mo6-2X and PBEo functionals. Frequency calculations were done to verify the stationary points as minima (zero imaginary frequencies). The solvent (acetonitrile) effect was considered

by means of the polarizable continuum model (PCM).¹⁸ Vertical transitions were computed at the TD-DFT level of theory including 10 states using the same functional and basis set. In addition, the Franck-Condon geometries were optimized in *S*₁ at the same level of theory to locate the emissive minima. All calculations were performed with the Gaussian 16 software package.¹⁹

ASSOCIATED CONTENT

Supporting Information

¹H, ¹³C, ¹⁹F and ¹¹B NMR spectra for new compounds, optical properties and Cartesian coordinates of computed structures.

The Supporting Information is available free of charge on the ACS Publications website.

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