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Exploring the Application of the Negishi Reaction of HaloBODIPYs: Generality, Regioselectivity and Synthetic Utility in the Development of BODIPY Laser Dyes

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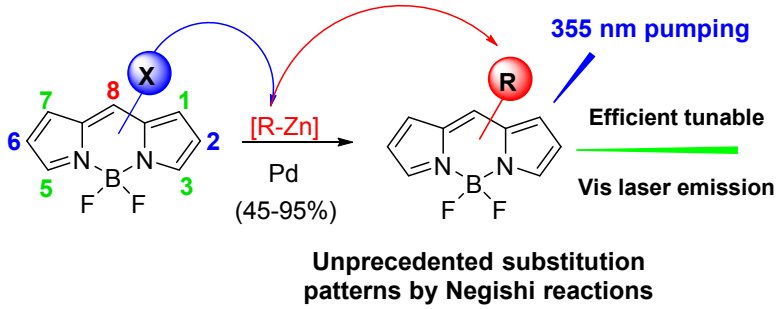
KEYWORDS: C-C coupling reactions; BODIPYs; Laser Dyes; Regioselectivity



ABSTRACT: The generality of the palladium-catalyzed C-C coupling Negishi reaction when applied to haloBODIPYs is demonstrated on the basis of selected starting BODIPYs, including polyhalogenated and/or asymmetrical systems, and organozinc reagents. This reaction is an interesting synthetic tool in BODIPY chemistry, mainly because it allows a valuable regioselective post-functionalization of BODIPY chromophores with different functional groups. In this way, functional patterns that are difficult to obtain by other procedures (*e.g.*, asymmetrically functionalized BODIPYs involving halogenated positions) can now be made. The regioselectivity is achieved by controlling the reaction conditions, and is based on almost-general reactivity

preferences, and nature of the involved halogens and their positions. This ability is exemplified by the preparation of a series of new BODIPY dyes with unprecedented substitution patterns allowing noticeable lasing properties.

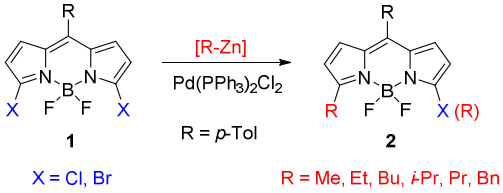
INTRODUCTION

During the last two decades, BODIPYs (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes, also known as boron dipyrromethenes or boron dipyrrins)[1] have become important molecules for the development of valuable photonic tools,[2] such as chemosensors,[3] laser dyes,[4] potential photodynamic therapy agents,[5] or photoactive organic materials for photovoltaic devices.[6] The vast increase in the use of these dyes is undoubtedly due to their many excellent characteristics, such a bright fluorescence in the visible (Vis) spectral range, and a good robustness towards light and chemicals.[2]

The synthetic accessibility when constructing BODIPYs is certainly another major reason for the attractiveness of these dyes. Functionalized BODIPYs can be obtained from suitably functionalized pyrroles (pre-functionalization),[7] or the desired functional pattern can be introduced in a later stage after the construction of the BODIPY core (post-functionalization).[8] In particular, post-functionalization, which requires the use of reactive BODIPYs is highly attractive. This is because post-functionalization limits the manipulation of unstable pyrrole derivatives, and allows the straightforward introduction of a greater variety of functional groups. In fact, with a limited synthetic effort, a large number of functional groups can be introduced onto the BODIPY core by post-functionalization methodologies.[8] However, introducting certain functionalities (*e.g.*, alkyl groups substituted with additional reactive functional groups) or achieving certain functional patterns onto the BODIPY core (*e.g.*, involving reactive functional

groups) cannot easily be done by post-fuctionalization methods, and are thus instead prepared by complex pre-functionalization routes.[9]

Among the palladium catalyzed C-C coupling reactions, Negishi reaction on easily accessible haloBODIPYs could offer a solution for these problematic cases , due to the high functional-group compatibility (including the labile BODIPY BF_2 group) of organozinc reagents ([R-Zn]) compared to other organometal compounds. Strickingly, Negishi reaction has been scarcely used in the development of BODIPY dyes, despite its demonstrated utility in the synthesis of advanced photonic materials.[10] In fact, the unique Negishi reactions of BODIPYs (involving 3,5-dihaloBODIPYs; Scheme 1) were reported by us recently.[10b] In this seminal work, 8-(4-methylphenyl)-3,5-dihaloBODIPY (**1**) was used as the starting material to exemplify the effectiveness of Negishi reaction to prepare alkylated derivatives **2**. This was done by introducing one or two identical alkyl groups (*i.e.*, di- *vs.* mono-coupling) selectively onto the BODIPY core. Furthemore, two different alkyl groups could be introduced by using two consecutive controlled Negishi reactions.



Scheme 1. Preliminary Negishi reactions of 3,5-dihaloBODIPYs

On the basis of these preliminary results, we became interested in studying the versatility and selectivity of the Negishi reaction when applied to haloBODIPYs. For this purpose, we have used different starting halogenated and (poly)halogenated BODIPYs, including those bearing different halogens (chlorine, bromine and iodine), on different BODIPY positions, and having different starting symmetries (symmetrical

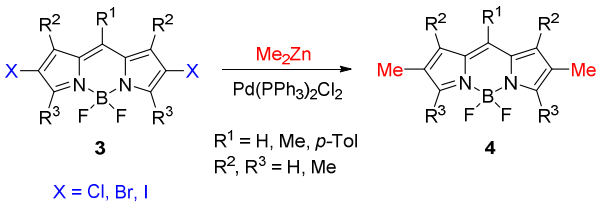
vs. asymmetrical haloBODIPYs). The results obtained from this systematic study have allowed us to establish straightforward synthetic protocols to obtain unprecedented substitution patterns onto the BODIPY core, surmounting the limits imposed by the known pre- and post-functionalization methods. The utility of these protocols has been exemplified by the preparation of a series of new alkylated BODIPYs, including halogenated ones, with noticeable lasing properties.[2d,4a,11]

RESULTS AND DISCUSSION

Generality and regioselectivity. Since our preliminary results confirmed that the Negishi reaction works well in symmetrical 3,5-dihaloBODIPYs (at least for the essayed BODIPYs and organozinc reagents; Scheme 1),[10b] our first objective was to explore the feasibility of similar C-C couplings in symmetrical 2,6-dihaloBODIPYs. For this purpose we selected a small series of related 2,6-dihaloBODIPYs (**3a-i**, Table 1) to test the influence of the halogen involved (chlorine, bromine *vs.* iodine; *e.g.*, *cf.* **3a**, **3b** and **3c**), and of the BODIPY substrate (*e.g.*, *cf.* **3c** and **3d**, or **3f**, **3h** and **3i** for stereoelectronic effects, or **3b**, **3e** and **3g** for electronic effects without steric influence). The starting BODIPYs were also selected on the basis of their synthetic accessibility. Thus, 2,6-dichloroBODIPY **3a**,[12] 2,6-dibromoBODIPY **3b**,[13] and 2,6-diiodoBODIPYs **3c**[5a] and **3i**[14] were prepared straighforwardly using described procedures, which involve electrophilic halogenation of the corresponding parent (non-halogenated) BODIPY as the key step. For example, dibromoBODIPYs **3e** and **3g** were obtained by electrophilic bromination of the corresponding parent BODIPY with *N*-bromosuccinimide (NBS) or pyridine hydrobromide perbromide ($PyHBr_3$) (60% and 68% isolated yield, respectively; see Experimental Section), whereas 2,6-diiodoBODIPYs **3d**, **3f** and **3h** were obtained by electrophilic iodination of the corresponding non-halogenated parent

BODIPY with commercial ICl (69%, 70%, 93% and 85% isolated yield, respectively; see Experimental Section). The reactivity of these substrates in a Negishi reaction was tested at room temperature (r.t.) by coupling with commercial Me_2Zn using $Pd(PPh_3)_2Cl_2$ as pre-catalyst in toluene (Table 1).

Table 1. Negishi methylation of 2,6-dihaloBODIPYs (Scheme 2).[a]



Entry	3	X	R^1	R^2	R^3	4 (yield)[b]
1	**3a**	Cl	*p*-Tol	H	H	-
2[c]	**3a**	Cl	*p*-Tol	H	H	**4a** (69)[c]
3	**3b**	Br	*p*-Tol	H	H	**4a** (41)[d]
4	**3c**	I	*p*-Tol	H	H	**4a** (42)[e]
5	**3d**	I	*p*-Tol	H	Me	**4b** (40)[f]
6	**3e**	Br	H	H	Me	**4c** (70)
7	**3f**	I	H	H	Me	**4c** (71)
8	**3g**	Br	Me	H	Me	**4d** (59)[g]
9	**3h**	I	Me	H	Me	**4d** (68)[g]
10	**3i**	I	Me	Me	Me	**4e** (69)[h]

[a]Me_2Zn (1.2 M in toluene); $Pd(PPh_3)_2Cl_2$ (10 mol%); toluene as solvent; r.t. (for details, see Experimental Section). [b]Isolated yield. [c]XPhos (10 mol%) was added to the reaction mixture (see Experimental Section). [d]**5a** (10%) and **6** (9%) were also isolated (Figure 1). [e]**6** (11%) and **7a** (11%) were also isolated (Figure 1). [f]**5b** (16%), and **7b** (14%) were isolated also (Figure 1). [g]**8a** (13%). [h]**8b** (9%) were isolated also (Figure 1).

In contranst to what was found previously with the Negishi dimethylation of *meso*-tolylated **1** (Scheme 1), where the nature of the involved halogen atom (chlorine *vs.* bromine) did not have any appreciable influence on the obtained yield (*ca.* 80%),[10b] the dimethylation yield of related *meso*-tolylated **3** under similar reaction conditions showed a clear dependence on the nature of the halogen involved (chlorine *vs.* bromine; see entries 1 and 3 in Table 1). Thus, the dichlorinated dye **3a**, which is expected to be less reactive when compared with related dibrominated dye **3b**, did indeed not react under the selected reaction conditions. However, when a more efficient palladium catalytic system, involving 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (XPhos) as electron-rich phosphine ligand,[15] was used instead reaction did ocurr (*cf.* entries 1 and 2 in Table 1). These results demonstrate the higher Negishi reactivity of 3,5-dihaloBODIPYs compared to the related 2,6-dihaloBODIPYs. On the other hand, no significant differences were observed for dibrominated **3b** *vs.* diiodinated **3c** compounds under the selected conditions (*cf.* entries 3 and 4 in Table 1), neither for dibrominated **3e** or **3g** *vs.* related diiodinated **3f** or **3h** (*cf.* entries 6 and 7, or 8 and 9, respectively, in Table 1).

Changing the hydrogens at the 3,5-positions of BODIPY by methyl groups, did not seems to influence the reactivity, although the steric hindrance around of the reactive C-halogen bond was increased (*cf.* entries 4 and 5 in Table 1). There was also no effect on the reactivity observed when an additional neighboring methyl group was introduced on the system (*cf.* entries 9 and 10 in Table 1). On the other hand, the presence of *p*-tolyl (*p*-Tol) group instead of hydrogen at the *meso* (8) position produced a noticeable lower yield (*cf.* entries 3 and 6, and 4 and 7 in Table 1), which could be due to differential electronic effect, but not to difference in steric hindrance. However, appreciable reactivity differences could not be detected when changing *meso* hydrogen by *meso*

methyl (*cf.* entries 6 and 8, and 7 and 9 in Table 1); *i.e.*, where only different inductive effects are involved. Interestingly, the loss of Negishi reactivity towards dimethylation observed for *meso*-tolylated 2,6-dihaloBODIPYs **3b-d** and **3g-i** was accompanied by the detection of minor side-products (see **5-8** in Figure 1, and Table 1), whose competitive formation could explain the lower yields for the formation of desired compound **4**.

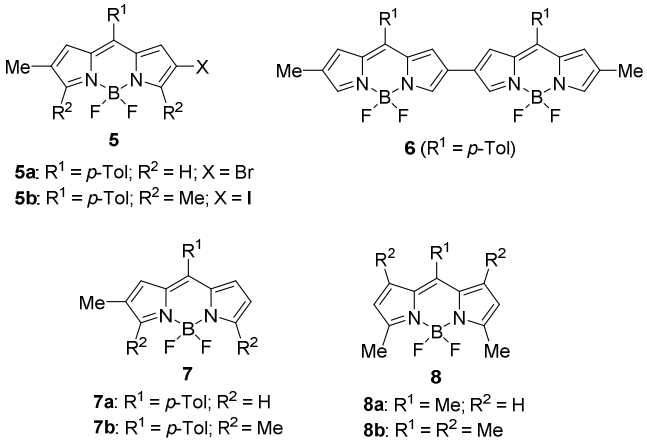
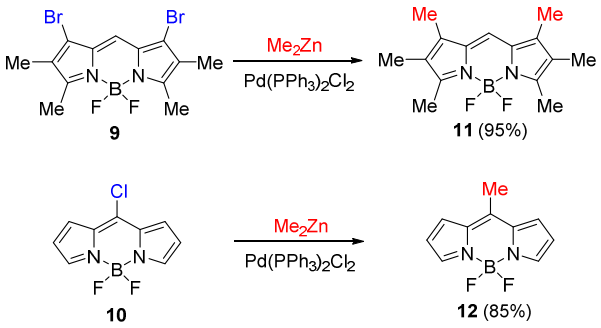


Figure 1. Minor side-products isolated after Negishi methylation of **3b-d**, **3g-i** (Table 1).

Once it was confirmed that Negishi reaction can be applied to standard BODIPYs halogenated at their 2,6-, or 3,5-positions, we became interested in investigating if such synthetical valuable C-C forming reactions could be applied also when the reactive halogen is located at other BODIPY positions (*i.e.*, at 1,7 or 8). For this purpose, we selected the methylation of the synthetically-accessible symmetrical 1,7-dibromoBODIPY **9**[7c] and 8-chloroBODIPY **10**[16] (Scheme 2) under the same reaction conditions (*i.e.*, excess of Me_2Zn, $Pd(PPh_3)_2Cl_2$ as the pre-catalyst, and toluene as the solvent; see Experimental Section). The expected 1,7-dimethylated and 8-methylated BODIPYs (**11** and **12**, respectively) were obtained in excellent yields (Scheme 2), even starting from **10**, where a less reactive chlorinated position is involved.

Comparison of these last two results with those obtained for the methylation of related symmetrical BODIPYs halogenated at 2,6 (Table 1) or 3,5 (Scheme 1) position using the same coupling conditions, seems to show the following preferences (halogen and BODIPY position) for the Negishi reaction in haloBODIPYs: I > Br > Cl; 8 > 3,5 ~ 1,7 > 2,6. The halogen preference agrees with that found for related palladium-catalyzed C-C couplings in other halogenated electron-poor aromatic systems (*e.g.*, halopyridines);[17] whereas the position preference agrees with that reported for Suzuki and Shonogashira reactions in chlorinated BODIPYs.[8a,8d-e,18]



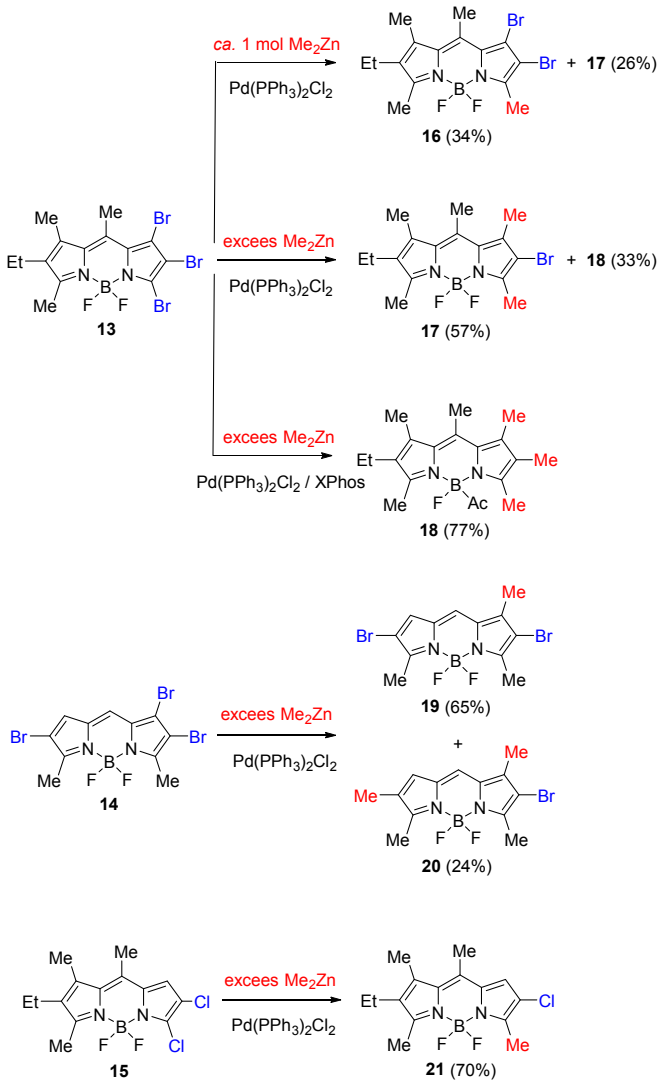
Scheme 2. Negishi methylations in 1,7-dihalo and 8-haloBODIPYs (for details, see Experimental Section).

In our preliminary communication on the Negishi coupling of 3,5-dihaloBODIPYs,[10b] we demonstrated that the controlled Negishi coupling of a single halogenated position in symmetrical 3,5-dihaloBODIPYs (partial Negishi coupling leading to still-halogenated systems) is possible under stoichiometrically controlled reaction conditions (Scheme 1). This is highly interesting for two reasons: (1) the higher accessibility to starting polyhalogenated BODIPYs involving symmetrical halogenated positions; (2) the utility of the obtained asymmetrical haloBODIPYs as synthetic intermediates in the preparation of other asymmetrical BODIPY derivatives (*e.g.*, by a subsequent coupling

reaction).[10b] Regarding this, the influence of the halogenated BODIPY positions on the reactivity of the Negishi reaction (see above) prompted us to test if this difference could be used to allow a controlled partial Negishi coupling in asymmetrical polyhalogenated BODIPY systems. We selected trihaloBODIPYs **13**-**15** (Scheme 3) as the starting asymmetrical polyhalogenated systems due to their synthetic accessibility. Thus, tribromoBODIPY **13** was prepared in a straightforward fashion by electrophilic bromination of the corresponding non-halogenated parent BODIPY with Br_2 (75% isolated yield; see Experimental Section), whereas tribromoBODIPY **14** was obtained as minor product in the preparation of **3e** (28% isolated yield; see Experimental Section). On the other hand, dichloroBODIPY **15** was obtained following a described procedure.[12]

Methylation reactions (using Me_2Zn) essayed on asymmetrical polyhaloBODIPYs **13**-**15** (Scheme 3) demonstrated the possibility of undergoing partial Negishi reactions in such systems, by selecting properly the reaction conditions on the basis of the expected reactivity of the involved halogenated positions. Thus, for 1,2,3-tribromoBODIPY **13**, where two similar highly-reactive 1 and 3 brominated positions are involved, it was possible to obtain a separable mixture of monomethylated **16** and dimethylated **17** (34% and 26% isolated yield, respectively) when *ca.* 1 mol equiv. of Me_2Zn was used under standard reaction conditions (10 mol% $Pd(PPh_3)_2Cl_2$; Scheme 3). However, when the same starting tribromoBODIPY was treated under the same conditions with a large excess of Me_2Zn (20 mol equiv.) a separable mixture of major dimethylated **17** and minor trimethylated **18** was obtained (57% and 33% isolated yield, respectively; Scheme 3). On the other hand, using an ample excess of Me_2Zn together with XPhos as an additive allows the isolation of trimethylated **18** as the major reaction product (77% isolated yield; Scheme 3). These results confirm the higher reactivity of the 1- and 3-

BODIPY positions, when compared to the 2-positions, as well as the mentioned influence of stereolectronic factors in such reactivity.



Scheme 3. Selectivity of Negishi methylation of asymmetrical polyhalogentated BODIPYs (for details, see Experimental Section).

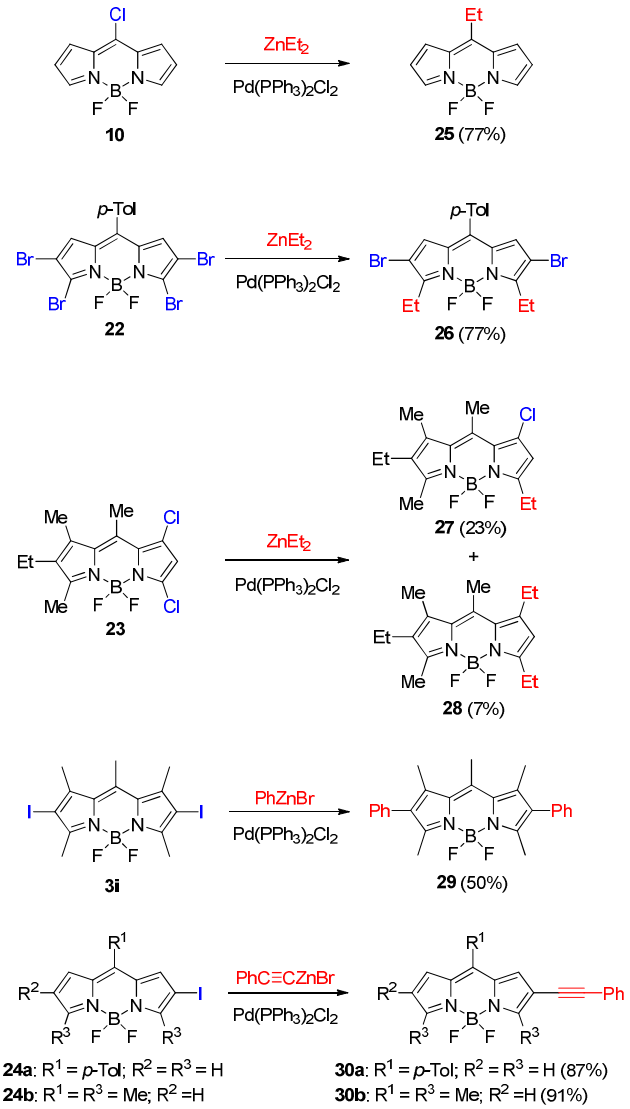
Similar reactivity was confirmed for asymmetrical haloBODIPYs **14** and **15** (Scheme 3 and note the different reactivity depending on position and stereoelectronic factors). Thus, the treatment of tribromoBODIPY **14** with excess of Me_2Zn, using the less reactive catalyst under standard reaction conditions, allowed the formation of a

separable mixture of major monomethylated **19** and minor dimethylated **20** (65% and 24 % isolated yield, respectively; Scheme 3), whereas dichlorinated **15** under the same conditions gave monomethylated **21** (70% isolated yield) as the only reaction product.

The structures of BODIPYs **16**, **17**, **19** and **20**, according to the above-mentioned regioselectivity, were inequivocally assigned by 1D and 2D NMR experimts (see Experimental Section).

In our preliminary communication on the Negishi coupling,[10b] we also demonstrated utility of this reaction to introduce other alkyl groups than methyl, as well as alkynyl and aryl groups at the halogenated positions of symmetrical 3,5-dibromoBODIPYs (Scheme 1). To check this possibility of these reactions at other BODIPY positions, we studied at small, but representative, series of reactions shown in Scheme 4. Criteria of accessibility for the chosen starting haloBODIPYs and organozinc reagents were taken into account for the selection.

Thus, Negishi ethylation of **10**,[16] **22**[8b] and **23**[12] under simple standard conditions (excess of Et_2Zn and 10 mol% $Pd(PPh_3)_2Cl_2$; Scheme 4) yielded the corresponding expected ethylated BODIPY according to the demonstrated general reactive preference for the halogenated position (8 > 3,5 ~ 1,7 > 2,6; Scheme 3). Thus, it was possible to easily ethylate 8-chloroBODIPY **10** to form 8-ethylBODIPY **25** in an excellent yield (Scheme 4). It was also possible to undergo the partial ethylation of 2,3,5,6-tetrabromoBODPYs **22**, without reacting the less reactive 2- and 6-positions, to generate 3,5-diethylBODIY **26** (Scheme 4). Noticeably, it was even possible to conduct the partial ethylation of 5,7-dichloroBODIPY **23**, which involves more similar reactive positions, to generate selectively major 5-ethylBODIPY **27** together with minor 5,7-diethylBODIPY **28** (Scheme 4).

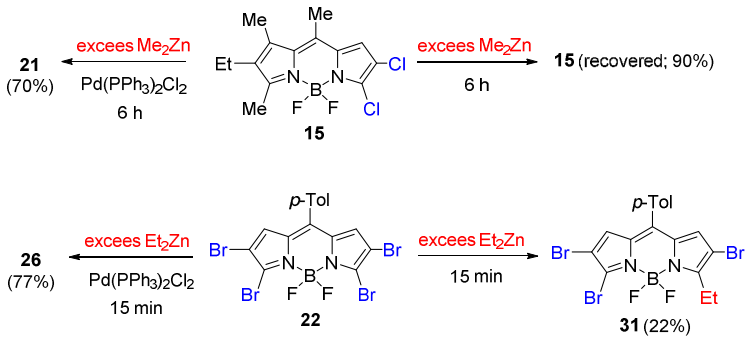


Scheme 4. Additional Negishi reactions of different haloBODIPYs (for details, see Experimental Section).

The reactivity of the 2,6-positions towards Negishi reaction could be enhanced by using iodoBODIPYs. In fact, we were able to arylate and alkynylate these iodinated positions under standard catalytic conditions (10 mol% of $Pd(PPh_3)_2Cl_2$). Thus, as an example, the highly sterical-hindered positions of 2,6-diiodoBODIPY **3i**[14] were easily phenylated using commercial PhZnBr to yield 2,6-diphenylBODIPY **29** (Scheme 4). On the other hand, photophysical-interesting π-extended 2-(phenylethynyl)BODIPYs[14,19] **30a-b**

could be straightforwardly obtained by Negishi phenylethynylation of the corresponding 2-iodoBODIPYs **24a-b** (Scheme 3). The novel starting maerial **24b** was obtained similarly to **24a**,[5a] by iodination of the corresponding non-halogenated parent BOPIPY[20] with ICl (see Experimental Section).

Certain electron-poor enough BODIPYs conveniently substituted in specific positions with good leaving groups (*e.g.*, polyhaloBODIPYs with halogen located at 1,7 or/and 3,5 BODIPY positions) are known to undergo aromatic nucleophilic substitution (S_NAr) easily.[5a,8f,21] Therefore, S_NAr could be competitive with the Negisthi reaction in some of the above studied cases (*i.e.*, the organozinc reagent acting as a nucleophile without requiring any palladium catalyst). To test this possibility, we selected polyhaloBODIPYs **15** and **22** (Schemes 3 y 4, respectively), which are specially activated for S_NAr. These BODIPYs were reacted with organozinc reagent in absence of palladium, but maintining the rest of the reaction conditions previously essayed for them (Scheme 5), showing no reaction in the case of **15**, and partial reaction in the case of **22** to afford monoehtylated **31** (22% isolated yield). Therefore, it is concluded that S_NAr could compite with the Negishi reaction in special cases involving strongly activated BODIPYs, as it ocurrs for polybrominated **22**. Nonetheless, this competitive pathway is surpassed by the faster Negishi one.



Scheme 5. Nucleophilic aromatic substitution *vs.* Negishi reaction in parallel conditions (for details, see Experimental Section).

Photophysical properties and laser activity. Most of the above conducted Negishi reactions allowed the straightforward synthesis (as single or major reaction products) unprecedented BODIPY dyes with interesting substitution patterns (most of them involving asymmetrical chromophoric systems with multiple alkyl groups). These compounds could be interesting as potential laser dyes.[2d,11] 8-(4-methylphenyl)BODIPYs (*e.g.,* see **4a** in Table 1) and polybromoBODIPYs (*e.g.*, see **19** in Scheme 3) were discarded for this study due to their expected poor fluorescence.[22] Nonetheless, the fluorescence ability of the selected BODIPYs (**17**, **18**, **20**, **21, 25**, **27** and **30b**; Schemes 3 and 4) was tested before studying their lasing behavior (Table 2).

The compounds investigated exhibited the typical absorption and fluorescence spectra of BODIPY dyes,[2,11] with maximum absorption at *ca.* 500 nm, which can in somes cases be shifted up to *ca.* 530 nm by well-known stereolectronic effects in BODIPYs (*e.g.*, in π-extended 3**0b**).[14,19] The Stokes shifts also agreed with those values expected for similar BODIPY chromophores.[11] The different fluorescence ability of the studied BODIPYs (quantum yields from 0.27 to 1.00; Table 2) can be explained also by known factors quenching the fluorescence of BODIPYs, such as loss of symmetry, presence of heavy atoms, conformational flexibility, etc.[2b-c,11c,22] Thus, as examples, the fluorescent quantum yield of *quasi* symmetrical **18** is similar to that observed for symmetrical PM546 (4,4-difluoro-1,3,5,7,8-pentamethylBODIPY),whereas asymmetrical and chlorinated **21** exhibited a clear loss of fluorescence (Table 2 and Scheme 3). However, similar asymmetrical and chlorinated **27** (Scheme 4), but halogenated at the 3-position instead of the 2-position, exhibited a noticeable high fluorescent quantum yield (0.88; Table 2), which demonstrated the importance of the position of the substitution pattern for balancing opposite factors affecting photophysical properties. Also remarkable is the extraordinarily high fluorescence quantum yield (Φ = 1.00) measured for structurally-

simple symmetrical **25** (Scheme 4), which is superior to that measured for the commercial BODIPY laser dye PM546 under the same solution conditions (Table 2).

Table 2. Basic phothophysical properties,[a] and lasing behavior[b] of selected BODIPYs in ethyl acetate solution. Commercial PM546 has been included for comparison.

Dye	λ_{abs}[c] (nm)	λ_{em}[d] (nm)	$\Delta\nu$[e] (cm^{-1})	Φ[f]	[c][g] (mM)	Eff.[h] (%)	λ_{las}[i] (nm)
PM546	494	502	402	0.85	2.5[j]	23[j]	541[j]
17	514	535	764	0.51	0.5	26	582
18	517	536	686	0.81	0.5	44	560
20	526	538	424	0.55	2.0	30	572
21	513	521	425	0.27	1.0	35	554
25	491	500	367	1.00	0.7	55	510
27	502	518	615	0.88	2.0	46	543
30b	533	566	1094	0.43	1.0	18	600

[a]Dye concentration *ca* 10^{-5} M. [b]Under transversal pumping at 355 nm. [c]Maximum absorption wavelength. [d]Maximum emission wavelength upon irradiation at the maximum absorption. [e]Stokes shift. [f]Fluorescence quantum yield. [g]Optimal concentration for maximum laser efficiency. [h]Laser efficiency. [i]Peak wavelength for the laser emission. [j]Data from reference **4b**.

According to their absorption properties, the lasing action of the selected new dyes was studied under pumping at 355 nm dye solutions in ethyl acetate (see Experimental Section). All the solutions, placed in a simple plane-plane non-tunable resonator, exhibited broad-line-width laser emission (pump threshold energy of ~0.8 mJ, divergence of 5 mrad; pulse duration of 8 ns full-width at half maximum (FWHM)). To

optimize the laser action from the different dyes, we first analyzed the dependence of the lasing properties with the dye concentration in ethyl acetate solution, by varying the optical densities from 8 to 30 while keeping all other experimental parameters constant. In all cases, the studied dye solutions followed the typical behavior, with the laser efficiency (Eff.; defined as the ratio between the energy of the dye laser output and the input energy incident on the sample surface) first increasing with the dye concentration until an optical density (*ca.* 15) where a maximum efficiency is reached. From this point on, further increasing the dye concentration resulted in a loss of the laser efficiency. This fact can be accounted for an increase of the re-absorption/re-emission processes, with deleterious effect on the laser action. The results obtained are collected in Table 2, where the wavelength for the peak of the laser emission (λ_{las}) and the laser efficiency (Eff.) are presented, as well as the corresponding optimal concentration ([c]) for each dye solution. To facilitate the interpretation and comparison of the obtained lasing results, Figure 2 shows the laser emission spectra of the studied dye solutions, the height of the peak being proportional to the laser efficiency.

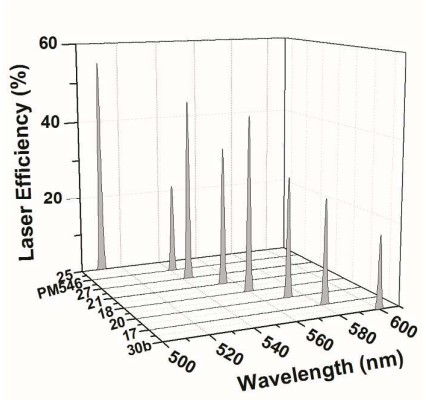


Figure 2. Laser emission spectra for the studied selected BODIPYs (data from Table 2).

The comparison of the results collected in Table 2 (or Figure 2) with the photophysical properties in the same table demonstrates that the lasing behavior of the studied dyes in

ethyl acetate solution correlates well with their photophysical properties: the higher the fluorescence quantum yield, the higher is the laser efficiency, the longer the fluorescence wavelength, the more red-shifted becomes the lasing emission. Noticeably, the measured maximum laser efficiencies (up to 55%) were superior to that exhibited by the commercial laser dye PM546,[4b] with the only exception of **30b** (Table 2), and required a minor optimal concentration, which is a valuable advantage when developing dye lasers. Thus, for example, alkylBODIPYs **18** and **25** exhibited laser efficiencies much higher than those exhibited by PM546 (44% and 55%, *vs*. 23%; Table 2) by using significant smaller dye concentrations (0.5 mM and 0.7 mM, *vs.* 2.5 mM; Table 2). In this regard, the high laser efficiency measured for **25**, despite its extraordinarely simple (almost naked) structure (Scheme 4), must be highlighted. On the other hand, the laser behavior of bromoBODIPYs **17** and **20** is also remarkable, with both exhibiting high-enough laser efficiencies (26% and 30%, *vs.* 23%; Table 2) despite the expected adverse heavy-atom effect.[5e,22]

Finally, it must be emphasized that the laser emissions of the studied series of Negishi-accesible BODIPYs are well distributed into a wide spectral range (510-600 nm; Figure 2). In other words, the laser emission can be fine-tuned by the substitution pattern of the BODIPY chromophore, which is achieved using straightforward Negishi reactions involving easily accessible haloBODIPYs.

CONCLUSION

We have systematically studied the workability of the Negishi reaction when applied to haloBODIPYs, showing it interest as a valuable synthetic tool for the development of BODIPY dyes. The high accessibility to haloBODIPYs and organozinc reagents, as well as the known high compatibility of these organometal reagents with multiple functional

groups, undoubtedly makes Negishi reaction to be an unavoidable synthetic tool to take into account when planning the synthesis of a new BODIPY dye, mainly when reactive groups are required in the final dye structure. Interestingly, it is shown that the Negishi reaction of haloBODIPYs is deeply affected by the involved BODIPY position, as well as by the nature of the halogen atom, making possible to conduct partial (regiocontrolled) functionalizations in polyhalogenated systems by selecting properly the reaction conditions. The so-obtained still-halogenated BODIPYs are valuable synthetic intermediates to other asymmetrical BODIPYs, which cannot be easily prepared by different synthetic routes. To exemplify this synthetic advantage, we have conducted Negishi of accessible haloBODIPYs to generate easily a small series of unprecedented alkylated BODIPYs with specific substitution patterns, most of them umprecedented. The study of the lasing behavior of these new dyes has allowed discovering unexpected noticeable lasing properties for unconventional BODIPY laser dyes, which becames to demonstrate the capacity of the Negishi reaction for the development of smarter BODIPY dyes for advanced photonic applications.

EXPERIMENTAL SECTION

General remarks. All starting materials and reagents were commercially, unless indicated otherwise, and used without further purifications. Common solvents were dried and distilled by standard procedures. Flash chromatography was performed using silica gel (230-400 mesh). Melting points were determined on a standard melting point apparatus, and are uncorrected. NMR spectra were recorded at 20 ºC in $CDCl_3$. ^1H chemical shifts are dated in ppm relative to tetramethylsilane (δ = 0.00 ppm) as internal reference. ^{13}C chemical shifts are dated in ppm with $CDCl_3$ (δ = 77.67 ppm) as the

internal standard. DEPT 135 experiment was used to assignate the type of carbon nucleous (C *vs*. CH *vs*. CH_2 *vs.* CH_3). In specific cases, combination of 2D HMQC and HMBC experiments with selective gradient-enhanced 1D NOESY experiments was used to unequivocally discern between regioisomeric structures (in these cases, the unequivocal assignation of NMR signals is dated). FTIR spectra were obtained from neat samples using the ATR technique. High resolution mass spectrometry HRMS) was conduced using the EI technique and electrostatic sector and magnetic sector mass analyzers.

Photophysical properties were measured for diluted (*ca.* 10^{-5} M) dye solutions in acethyl acetate. UV-Vis absorption and fluorescence spectra were recorded on standard spectrophotometer and spectrofluorimeter, respectively. The fluorescence spectra were corrected from the wavelength dependence of the detector sensibility. Commercial BODIPY PM546 was used as the reference dye (Φ = 0.85 in ethyl acetate).[4b]

Lasing properties were measured for liquid solutions of dyes contained in 1 cm optical-path rectangular quartz cuvettes carefully sealed to avoid solvent evaporation during the experiments. The liquid solutions were transversely pumped at 355 nm, with 5 mJ, 8 ns FWHM pulses from the third-harmonic of a Q-switched Nd:YAG laser at a repetition rate of up to 10 Hz. The exciting pulses were line-focused onto the cuvette, providing pump fluences on the active medium in the range 110-180 mJ/cm^2. The oscillation cavity (2 cm length) consisted of a 90% reflectivity aluminum mirror, with the lateral face of the cuvette acting as output coupler.

Synthesis of halogenated BODIPYs

Halogenated BODIPYs **3a**,[12] **3b**,[13] **3c**,[5a] **3i**,[14] **9**,[7c] **10**,[16] **15**,[12] **22**,[8c] **23**,[12] and **24a**[5a] were synthesized by the corresponding described methods.

*4,4-Difluoro-2,6-diiodo-3,5-dimethyl-8-(4-methylphenyl)BODIPY (**3d**).* To a solution of 4,4-difluoro-3,5-dimethyl-8-(4-methylphenyl)BODIPY[23] (40 mg, 0.13 mmol) in a CH_2Cl_2/MeOH mixture (10 mL/10 mL) was added dropwise a solution of ICl (0.32 mL, 0.32 mmol) in MeOH (5 mL), and the mixture stirred at r. t. for 10 min. The solvent was evapored under vacuum and the crude product was dissolved in CH_2Cl_2, washed with water, dried over $MgSO_4$, filtered and concentrated to dryness. Flash chromatography on silica gel using hexane/EtOAc (98:2) afforded **3d** (50 mg, 69%) as a red solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, J = 8.1 Hz, 2H, tolyl), 7.23 (d, J = 8.1 Hz, 2H, tolyl), 6.89 (s, 2H, 2CH), 2.58 (s, 6H, $2CH_3$), 2.38 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 141.8, 141.2, 136.8 (CH), 135.2, 130.4, 130.3 (CH), 129.3 (CH), 21.5 (CH_3), 15.5 (CH_3) ppm, (C-I) not observed. FTIR υ 2921, 1556, 1437, 1231, 1124, 998 cm^{-1}. HRMS *m/z* 561.9377 (calcd for $C_{18}H_{15}BF_2I_2N_2$: 561.9384).

*2,6-Dibromo-4,4-difluoro-3,5-dimethylBODIPY (**3e**) and 1,2,6-tribromo-4,4-difluoro-3,5-dimethylBODIPY (**14**).* To a solution of 4,4-difluoro-3,5-dimethylBODIPY[24] (41 mg, 0.19 mmol) in dry CH_2Cl_2 (10 mL) was added, under argon atmosphere, $PyHBr_3$ (125 mg, 0.39 mmol) and the mixture was stirred at r.t. for 2 h. The mixture was washed with saturated aqueous NH_4Cl and water, dried over $MgSO_4$, filtered and concentrated to dryness. Flash chromatography using hexane/CH_2Cl_2 (95:5) afforded tribromoBODIPY **14** (24 mg, 28%) and dibromoBODIPY **3e** (58 mg, 60%), as red solids.

3e: ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.96 (s, 2H, 2CH), 6.94 (s, 1H, CH), 2.53 (s, 6H, $2CH_3$) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 156.7, 133.3, 130.0 (CH), 126.2 (CH), 109.0 (C-Br), 13.5 (CH_3) ppm. FTIR υ 2926, 1545, 1450, 1254, 1100, 989 cm^{-1}. HRMS *m/z* 375.9199 (calcd for $C_{11}H_9BBr_2F_2N_2$: 375.9193).

14: M.p.: 215-217 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.08 (s, 1H, CH), 7.05 (s, 1H, CH), 2.56 (s, 3H, CH_3), 2.53 (s, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 158.2, 155.2, 133.7, 131.9, 130.8 (CH), 124.5 (CH), 121.2 (C-Br), 110.9 (C-Br), 110.1 (C-Br), 14.1 (CH_3), 13.7 (CH_3) ppm. FTIR υ 2928, 1525, 1453, 1214, 1076, 1065, 993 cm^{-1}. HRMS *m/z* 453.8286 (calcd for $C_{11}H_8BBr_3F_2N_2$: 453.8298).

*4,4-Difluoro-2,6-diiodo-3,5-dimethylBODIPY (**3f**).* According to the procedure described for **3d**, 4,4-difluoro-3,5-dimethylBODIPY[24] (102 mg, 0.47 mmol) in CH_2Cl_2/MeOH (10 mL/10 mL), and a solution of 1.7 mL of ICl (1 M in CH_2Cl_2, 1.17 mmol) in MeOH (5 mL) were reacted for 15 min. Flash chromatography on silica gel using hexane/CH_2Cl_2 (8:2) afforded diiodoBODIPY **3f** (150 mg, 68%) as a red solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (s, 2H, 2CH), 6.88 (s, 1H, CH), 2.54 (s, 6H, $2CH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 136.5 (CH), 135.3, 125.1 (CH), 77.2 (C-I), 15.6 (CH_3) ppm. FTIR υ 2921, 1555, 1447, 1235, 1114, 991 cm^{-1}. HRMS *m/z* 471.8909 (calcd for $C_{11}H_9BF_2I_2N_2$: 471.8915).

*2,6-Dibromo-4,4-difluoro-3,5,8-trimethylBODIPY (**3g**).* To a solution of 4,4-difluoro-3,5,8-trimethylBODIPY[20] (51 mg, 0.22 mmol) in dry THF (5 mL) was added, under argon atmosphere, *N*-bromosuccinimide (78 mg, 0.44 mmol) in dry THF (5 mL), and the mixture stirred at r.t. for 24 h. Flash chromatography using hexane/EtOAc (98:2) afforded dibromoBODIPY 3g (51 mg, 70%) as a red-orange solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (s, 2H, 2CH), 2.51 (s, 6H, $2CH_3$), 2.34 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 140.3, 133.9, 127.6 (CH), 108.6 (C-Br), 15.8 (CH_3), 13.7 (CH_3) ppm. FTIR υ 2923, 1565, 1457, 1254, 1080, 1072, 980 cm^{-1}. HRMS *m/z* 389.9334 (calcd for $C_{12}H_{11}BBr_2F_2N_2$: 389.9348).

*4,4-Difluoro-2,6-diiodo-3,5,8-trimethylBODIPY (**3h**).* According to the same procedure described for **3d** (see above), 4,4-difluoro-3,5,8-trimethylBODIPY[20] (120 mg, 0.52 mmol) in CH_2Cl_2/MeOH (10 mL/10 mL), and 1.13 mL of ICl (1 M in CH_2Cl_2, 1.13 mmol) in MeOH (5 mL) were reacted for 20 min. Flash chromatography on silica gel using hexane/CH_2Cl_2 (5:5) afforded diiodoBODIPY **3h** (235 mg, 93%) as a red solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (s, 2H, 2CH), 2.54 (s, 6H, $2CH_3$), 2.35 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 139.1, 135.7, 133.7 (CH), 77.2 (C-I), 15.4 (CH_3) ppm. FTIR υ 2920, 1566, 1422, 1245, 1126, 1061, 991 cm^{-1}. HRMS *m/z* 485.9066 (calcd for $C_{12}H_{11}BF_2I_2N_2$: 485.9071).

*1,2,3-Tribromo-6-ethyl-4,4-difluoro-5,7,8-trimethylBODIPY (**13**).* To a solution of 2-ethyl-4,4-difluoro-1,3,8-trimethylBODIPY[7a] (170 mg, 0.65 mmol) in dry CH_2Cl_2 (20 mL) was added, under argon atmosphere, Br_2 (0.033 mL, 0.65 mmol), and the mixture was stirred at r.t. for 90 min. The mixture was treated with saturated aqueous $Na_2S_2O_3$, decanted, and the organic layer washed with water, dried over $MgSO_4$, filtered and concentrated to dryness. Flash chromatography using hexane/$CHCl_3$ (8:2) afforded tribromoBODIPY **13** (242 mg, 75%) as a red solid.

M.p.: 260-263 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 2.76 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 2.37 (q, J = 7.7 Hz, 2H, CH_2) 2.30 (s, 3H, CH_3), 1.00 (t, J = 7.7 Hz, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 164.1, 142.5, 139.1, 137.6, 135.6, 130.0, 120.4 (C-Br), 112.4 (C-Br), 111.2 (C-Br), 17.3 (CH_3), 17.2 (CH_2), 15.1 (CH_3), 14.3 (CH_3), 13.5 (CH_3) ppm. FTIR υ 2973, 1578, 1396, 1369, 1211, 1190, 1085, 978 cm^{-1}. HRMS *m/z* 495.8758 (calcd for $C_{14}H_{14}BBr_3F_2N_2$: 495.8766).

*4,4-Difluoro-2-iodo-3,5,8-trimethylBODIPY (**24b**).* According to the same procedure described for **3d** (see above), 4,4-difluoro-3,5,8-trimethylBODIPY[20] (50 mg, 0.26 mmol) in CH_2Cl_2/MeOH mixture (7 mL/7 mL), and 0.31 mL of ICl (1 M in CH_2Cl_2,

0.31 mmol) in MeOH (5 mL) were reacted for 2 h. Flash chromatography on silica gel using hexane/CH_2Cl_2 (8:2) afforded diiodoBODIPY **3h** (24 mg, 22%) and iodoBODIPY **24b** (50 mg, 65%) as orange-red solids.

24b: M.p.: 149-151 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (s, 1H, CH), 7.10 (d, J = 4.2 Hz, 1H, CH), 6.25 (d, J = 4.2 Hz, 1H, CH), 2.54 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 2.37 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 155.4, 139.6, 135.4, 135.3, 131.9 (CH), 128.7 (CH), 120.2 (CH), 75.1 (C-I), 15.3 (CH_3), 15.0 (CH_3) ppm. FTIR υ 2928, 1565, 1418, 1237, 1110, 1051, 998 cm^{-1}. HRMS *m/z* 360.0100 (calcd for $C_{12}H_{12}BF_2IN_2$: 360.0106).

General procedure for Negishi reactions

Method A. A Schlenk tube was capped with a rubber septum, air evacuated, and backfilled with argon (this sequence was repited three times). Then, the halogenated BODIPY (1 mol), $Pd(PPh_3)_2Cl_2$ (10 mol%) and dry toluene (1-2 mL) were added under argon atmosphere. R_2Zn or RZnBr (0.7-20 mol) were added dropwise, and the mixture was stirred at r.t. for 5-120 min. The reaction solution was then filtered (CH_2Cl_2 was used for elution and washing), the solvent removed under vacuum, and the obtained residue submitted to flash chromatography on silica gel.

Method A+XPhos. XPhos (10 mol%) was also added.

Method B. To a flame-dried 100 mL two-neck flask was added phenylacetylene (5.5 mol) and dry THF (5 mL). Then, BuLi (1.6 M in hexane, 5.5 mol) was added dropwise under argon atmosphere at -78 ºC, and the resulting mixture stirred for 30 min. Then, a solution of $ZnBr_2$ (5.5 mol) in dry THF (2 mL) was added over the mixture at -78 ºC, and 5 min later the reaction was allowed to reach r.t. Then, the halogenated BODIPY (1 mol), $Pd(PPh_3)_2Cl_2$ (10 mol%) and dry toluene (10 mL) were added over the mixture at r.t., and the resulting reaction mixture was stirred for 1-4 h. Finally, the reaction mixture

was disolved with EtOAc and the resulting solution washed with 10% HCl, saturated aqueous $NaHCO_3$ and water, dried over $MgSO_4$, filtered and concentrated to dryness. The resulting residue was submitted to flash chromatography on silica gel.

*Negishi reaction of BODIPY **3a** and Me_2Zn:* According to method A, BODIPY **3a**[12] (31 mg, 0.09 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 0.009 mmol) in dry toluene (1 mL), and 1.5 ml of Me_2Zn (1.2 M in toluene, 1.8 mmol) were reacted for 24 h. Flash chromatography using hexane/EtOAc (95:5) afforded unreacted starting BODIPY **3a** (26 mg, 82%).

According to method A+XPhos, BODIPY **3a** (30 mg, 0.085 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 0.009 mmol) and XPhos (4 mg, 0.009 mmol) in dry toluene (1 mL), and 0.6 mL of Me_2Zn (1.2 M in toluene, 0.68 mmol) were reacted for 60 min. Flash chromatography using hexane/EtOAc (95:5) afforded BODIPY **4a** (18 mg, 69%) as a brown solid.

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.62 (s, 2H, 2CH), 7.36 (d, J = 8.4 Hz, 2H, tolyl), 7.24 (d, J = 8.4 Hz, 2H, tolyl), 6.58 (s, 2H, 2CH), 2.39 (s, 3H, CH_3), 2.03 (s, 6H, $2CH_3$) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 145.3, 143.5 (CH), 140.9, 134.7, 131.3, 130.5 (CH), 129.7 (CH), 129.2, 129.0 (CH), 21.5 (CH_3), 11.7 (CH_3) ppm. FTIR υ 2922, 1567, 1519, 1312, 1255, 1090, 988 cm^{-1}. HRMS *m/z* 310.1443 (calcd for $C_{18}H_{17}BF_2N_2$: 310.1450).

*Negishi reaction of BODIPY **3b** and Me_2Zn:* According to method A, BODIPY **3b**[13] (35 mg, 0.08 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 0.009 mmol) in dry toluene (1 mL), and 1.3 mL of Me_2Zn (1.2 M in toluene, 1.6 mmol) were reacted for 120 min. Flash chromatography using hexane/EtOAc (97:3) afforded BODIPYs **4a** (10 mg, 41%) and **5a** (3 mg, 10%) as brown solids, and bis(BODIPY) **6** (4 mg, 9%) as a purple solid.

5a: ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.78 (s, 1H, CH), 7.62 (s, 1H, CH), 7.36 (d, J = 7.7 Hz, 2H, tolyl), 7.26 (d, J = 7.7 Hz, 2H, tolyl), 6.75 (s, 1H, CH), 6.70 (s, 1H, CH), 2.40 (s, 3H, CH_3), 2.06 (s, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 147.6 (CH), 145.9, 141.6, 140.1 (CH), 135.6, 133.9, 131.8 (CH), 131.3, 130.7, 130.5 (CH), 129.3 (CH),

129.1 (CH), 104.8 (C-Br), 21.5 (CH_3), 11.8 (CH_3) ppm. FTIR υ 2950, 2921, 1567, 1544, 1358, 1250, 1098, 1065, 988 cm^{-1}. HRMS *m/z* 374.0411 (calcd for $C_{17}H_{14}BBrF_2N_2$: 374.0400).

6: M. p.: 168-169 ºC. ^1H NMR (700 MHz, $CDCl_3$) δ 7.94 (s, 2H, 2CH), 7.71 (s, 2H, 2CH), 7.39 (d, J = 7.7 Hz, 4H, tolyl), 7.28 (d, J = 7.7 Hz, 2H, tolyl), 6.79 (s, 2H, 2CH), 6.64 (s, 2H, 2CH), 2.42 (s, 6H, $2CH_3$), 2.05 (s, 6H, $2CH_3$) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 145.7, 145.6, 141.3, 139.6 (CH), 135.5, 135.0, 131.1, 130.6 (CH), 130.5 (CH), 130.3, 129.3 (CH), 123.7 (CH), 21.5 (CH_3), 11.7 (CH_3) ppm. FTIR υ 2932, 1566, 1524, 1310, 1235, 1190, 978 cm^{-1}. HRMS *m/z*: 590.2440 (calcd for $C_{34}H_{28}B_2F_4N_4$: 590.2434).

*Negishi reaction of BODIPY **3c** and Me_2Zn:* According to the method A, BODIPY **3c**[5a] (48 mg, 0.09 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 0.009 mmol) in dry toluene (2 mL), and Me_2Zn (0.9 mL, 1.2 M in toluene, 1.08 mmol) were reacted for 2 h. Flash chromatography using hexane/EtOAc (98:2) afforded BODIPYs **4a** (12 mg, 42%) and **7a** (3 mg, 11%) as brown solids, and bis(BODIPY) **6** (6 mg, 11%) as a purple solid.

7a: ^1H NMR (700 MHz, $CDCl_3$) δ 7.77 (s, 1H, CH), 7.75 (s, 1H, CH), 7.38 (d, J = 7.7 Hz, 2H, tolyl), 7.25 (d, J = 7.7 Hz, 2H, tolyl), 6.80 (d, J = 3.5 Hz, 1H, CH), 6.65 (s, 1H, CH), 6.41 (d, J = 3.5 Hz, 1H, CH), 2.39 (s, 3H, CH_3), 2.03 (s, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 146.4, 144.4 (CH), 142.1 (CH), 141.1, 137.2, 135.1, 134.5, 131.2, 130.5 (CH), 130.3 (CH), 129.4 (CH), 129.1 (CH), 117.5 (CH), 21.5 (CH_3), 11.7 (CH_3) ppm. FTIR υ 2920, 1569, 1534, 1310, 1245, 1093, 978 cm^{-1}. HRMS *m/z* 296.1286 (calcd for $C_{17}H_{15}BF_2N_2$: 296.1294).

*Negishi reaction of BODIPY **3d** with Me_2Zn.* According to method A, BODIPY **3d** (62 mg, 0.111 mmol), $Pd(PPh_3)_2Cl_2$ (8 mg, 0.011 mmol) in dry toluene (2 mL), and 1.9 mL of Me_2Zn (1.2 M in toluene, 2.22 mmol) were reacted for 60 min. Flash

chromatography using hexane/EtOAc (98:2) afforded BODIPYs **5b** (8 mg, 16%) as a red solid, **4b** (15 mg, 40%) as a brown-red solid, and **7b** (5 mg, 14%) as a purple solid.

4b: ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.29 (d, J = 7.7 Hz, 2H, tolyl), 7.19 (d, J = 7.7 Hz, 2H, tolyl), 6.41 (s, 2H, 2CH), 2.47 (s, 6H, $2CH_3$), 2.37 (s, 3H, CH_3), 1.92 (s, 6H, $2CH_3$) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 155.3, 140.4, 139.8, 132.8, 131.7, 130.3 (CH), 128.8 (CH), 128.4 (CH), 127.7, 21.4 (CH_3), 12.7 (CH_3), 11.1 (CH_3) ppm. FTIR υ 2934, 1566, 1540, 1312, 1250, 1099, 979 cm^{-1}. HRMS *m/z* 338.1755 (calcd for $C_{20}H_{21}BF_2N_2$: 338.1764).

5b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, J = 8.1 Hz, 2H, tolyl), 7.20 (d, J = 8.1 Hz, 2H, tolyl), 6.70 (s, 1H, CH), 6.54 (s, 1H, CH), 2.54 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 1.94 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2, 154.1, 140.7, 140.4, 134.5, 133.7, 133.6 (CH), 131.0, 130.6 (CH), 130.3 (CH), 129.0 (CH), 74.4 (C-I), 21.4 (CH_3), 15.1 (CH_3), 13.1 (CH_3), 11.2 (CH_3) ppm. FTIR υ 2919, 1573, 1544, 1420, 1236, 1129, 1084, 970 cm^{-1}. HRMS *m/z* 450.0569 (calcd for $C_{19}H_{18}BF_2N_2I$: 450.0575).

7b: ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.29 (d, J = 7.7 Hz, 2H, tolyl), 7.19 (d, J = 7.7 Hz, 2H, tolyl), 6.58 (d, J = 3.5 Hz, 1H, CH), 6.48 (s, 1H, CH), 6.13 (d, J = 3.5 Hz, 1H, CH), 2.55 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 1.94 (s, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 157.5, 155.3, 141.5, 140.0, 134.0, 133.4, 132.8, 131.5, 130.4 (CH), 129.4 (CH), 129.0 (CH), 128.8 (CH), 118.1 (CH), 21.4 (CH_3), 14.8 (CH_3), 12.8 (CH_3), 11.2 (CH_3) ppm. FTIR υ 2920, 1560, 1556, 1323, 1245, 1090, 989 cm^{-1}. HRMS *m/z* 324.1600 (calcd for $C_{19}H_{19}BF_2N_2$: 324.1607.

*Negishi reaction of BODIPY **3e** with Me_2Zn.* According to method A, BODIPY **3e** (39 mg, 0.103 mmol), $Pd(PPh_3)_2Cl_2$ (8 mg, 0.010 mmol) in dry toluene (1 mL), and 1.7 mL

of Me_2Zn (1.2 M in toluene, 2.07 mmol) were reacted for 24 h. Flash chromatography using hexane/EtOAc (95:5) afforded BODIPY **4c**[7c] (18 mg, 70%) as an orange solid.

*Negishi reaction of BODIPY **3f** with Me_2Zn.* According to the method A, BODIPY **3f** (62 mg, 0.13 mmol), $Pd(PPh_3)_2Cl_2$ (9 mg, 0.013 mmol) in dry toluene (2 mL), and Me_2Zn (2.2 mL, 1.2 M in toluene, 2.65 mmol) were reacted for 3 h. Flash chromatography using hexane/CH_2Cl_2 (8:2) afforded BODIPY **4c**[7c] (23 mg, 71%) as an orange solid.

*Negishi reaction of BODIPY **3g** with Me_2Zn.* According to method A, BODIPY **3g** (24 mg, 0.06 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 0.006 mmol) in dry toluene (1 mL) and 1 mL of Me_2Zn (1.2 M in toluene, 1.2 mmol) were reacted for 4 h. Flash chromatography using hexane/EtOAc (98:2) afforded BODIPYs **4d**[7c] (9.3 mg, 59%) and **8a**[20] (2 mg, 13%) as orange solids.

*Negishi reaction of BODIPY **3h** with Me_2Zn.* According to method A, BODIPY **3h** (120 mg, 0.25 mmol), $Pd(PPh_3)_2Cl_2$ (17 mg, 0.025 mmol) in dry toluene (2 mL), and 2.48 mL of Me_2Zn (1.2 M in toluene, 2.98 mmol) were reacted for 40 min. Flash chromatography using hexane/EtOAc (95:5) afforded BODIPYs **4d**[7c] (44 mg, 68%) and **8a**[20] (8 mg, 13%) as orange solids.

*Negishi reaction of BODIPY **3i** with Me_2Zn.* According to method A, BODIPY **3i**[14] (50 mg, 0.1 mmol), $Pd(PPh_3)_2Cl_2$ (8 mg, 0.011 mmol) in dry toluene (2 mL), and 1 mL of Me_2Zn (1.2 M in toluene, 1.2 mmol) were reacted for 40 min. Flash chromatography using hexane/CH_2Cl_2 (5:5) afforded BODIPYs **4e**[11a] (20 mg, 69%) and **8b**[11a] (PM546) (3 mg, 9%) as orange solids.

*Negishi reaction of BODIPY **9** with Me_2Zn.* According to method A, BODIPY **9**[7c] (17 mg, 0.042 mmol), $Pd(PPh_3)_2Cl_2$ (3 mg, 0.004 mmol) in dry toluene (1 mL), and 0.7 mL

of Me2Zn (1.2 M in toluene, 0.84 mmol) were reacted for 1 h. Flash chromatography using hexane/AcOEt (98:2) afforded BODIPY **11**[24] (11 mg, 95%) as an orange solid.

*Negishi reaction of BODIPY **10** with Me_2Zn.* According to method A, BODIPY **10**[16] (30 mg, 0.13 mmol), $Pd(PPh_3)_2Cl_2$ (9 mg, 0.013 mmol) in dry toluene (1 mL), and 0.9 mL of Me_2Zn (1.2 M in toluene, 1.08 mmol) were reacted for 30 min. Flash chromatography using hexane/EtOAc (8:2) afforded BODIPY **12**[25] (23 mg, 85%) as a yellow solid.

*Negishi reactions of BODIPY **13** with Me_2Zn.* According method A, BODIPY **13** (30 mg, 0.06 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 0.006 mmol) in dry toluene (1 mL), and 0.035 mL of Me_2Zn (1.2 M in toluene, 0.04 mmol) were reacted for 24 h. Flash chromatography using hexane/$CHCl_3$ (9:1) afforded BODIPYs **16** (9 mg, 34%) and **17** (6 mg, 26%) as red solids, and BODIPY **13** (9 mg, 30%).

According to method A, BODIPY **13** (40 mg, 0.08 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 0.008 mmol) in dry toluene (1 mL) and 1.3 mL of Me_2Zn (1.2 M in toluene, 1.6 mmol) were reacted for 22 h. Flash chromatography using hexane/CH_2Cl_2 (9:1) afforded BODIPYs **17** (17 mg, 57%) and **18** (8 mg, 33%) as red solids.

According to method A+XPhos, BODIPY **13** (30 mg, 0.06 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 0.006 mmol), X-Phos (3 mg, 0.006 mmol) in dry toluene (1 mL), and 1 mL of Me_2Zn (1.2 M in toluene, 1.2 mmol) were reacted for 24 h. Flash chromatography using hexane/CH_2Cl_2 (9:1) afforded BODIPY **18** (14 mg, 77%) as a red solid.

16: M.p.: 222-224 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 2.78 (s, 3H, CH_3-C8), 2.51 (s, 3H, CH_3-C3), 2.47 (s, 3H, CH_3-C5), 2.36 (q, J = 7.7 Hz, 2H, CH_2), 2.30 (s, 3H, CH_3-C7), 1.00 (t, J = 7.7 Hz, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 160.3 (C5), 146.1 (C3), 141.1 (C7), 140.0 (C8), 136.0 (C6), 134.2 (C7a), 128.1 (C8a), 113.7 (C1), 109.6 (C2), 17.2 ($\underline{C}H_3$-C8), 17.1 (CH_2), 14.9 ($\underline{C}H_3$-C7), 14.4 ($\underline{C}H_3$-CH_2), 13.6 ($\underline{C}H_3$-C3), 13.1

(CH$_3$-C5) ppm. FTIR υ 2922, 2853, 1563, 1465, 1192, 1075, 1029 cm^{-1}. HRMS *m/z* 431.9812 (calcd for $C_{15}H_{17}BBr_2F_2N_2$: 431.9820).

17: M.p.: 174-177 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 2.52 (s, 3H, CH$_3$-8), 2.47 (s, 3H, CH$_3$-C3), 2.45 (s, 3H, CH$_3$-C5), 2.34 (q, *J* = 7.7 Hz, 2H, CH$_2$), 2.33 (s, 3H, CH$_3$-C1), 2.27 (s, 3H, CH$_3$-C7), 0.98 (t, *J* = 7.7 Hz, 3H, CH$_3$) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 156.3 (C5), 148.0 (C3), 140.4 (C8), 139.0 (C7), 135.1 (C1), 134.2 (C6), 132.8 (C7a), 130.2 (C8a), 109.7 (C2), 17.1 (CH$_3$-C8), 17.0 (CH$_2$), 16.0 (CH$_3$-C1), 14.7 (CH$_3$-CH$_2$), 14.6 (CH$_3$-C7), 13.3 (CH$_3$-C3), 12.7 (CH$_3$-C5) ppm. FTIR υ 2923, 2854, 1557, 1471, 1205, 1070, 995 cm^{-1}. HRMS *m/z* 368.0863 (calcd for $C_{16}H_{20}BBrF_2N_2$: 368.0871).

18: M.p.: 222-224 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 2.53 (s, 3H, CH$_3$), 2.42 (s, 3H, CH$_3$), 2.41 (s, 3H, CH$_3$), 2.33 (q, *J* = 7.7 Hz, 2H, CH$_2$), 2.26 (s, 3H, CH$_3$), 2.25 (s, 3H, CH$_3$), 1.87 (s, 3H, CH$_3$), 0.97 (t, *J* = 7.7 Hz, 3H, CH$_3$) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 152.2, 151.7, 139.6, 136.8, 136.3, 132.3, 131.6, 125.9, 17.1 (CH$_2$), 16.9 (CH$_3$), 14.9 (CH$_3$), 14.6 (CH$_3$), 14.4 (CH$_3$), 12.6 (CH$_3$), 12.4 (CH$_3$), 9.1 (CH$_3$) ppm. FTIR υ 2965, 2922, 2856, 1556, 1477, 1318, 1207, 1047, 979, 958 cm^{-1}. HRMS *m/z* 304.1912 (calcd for $C_{17}H_{23}BF_2N_2$: 304.1922).

*Negishi reaction of BODIPY **14** with Me_2Zn.* According to method A, BODIPY **14** (23.5 mg, 0.051 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 0.005 mmol) in dry toluene (1 mL), and 0.9 mL Me_2Zn (1.2 M in toluene, 1.02 mmol) were reacted for 4 h. Flash chromatography using hexane/AcOEt (98:2) afforded BODIPYs **19** (13 mg, 65%) and **20** (4 mg, 24%) as brown solids.

19: M.p.: 200-204 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.97 (s, 1H, CH-8), 6.89 (s, 1H, CH-C7), 2.52 (s, 3H, CH$_3$-C3), 2.50 (s, 3H, CH$_3$-C5), 2.15 (s, 3H, CH$_3$-C1) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 157.7 (C3), 154.0 (C5), 141.0 (C8a), 133.2 (C1), 132.1

(C7a), 128.6 (CH-C7), 123.4 (CH-C8), 110.7 (C2), 107.5 (C6), 13.8 (CH_3-C3), 13.3 (CH_3-C5), 11.1 (CH_3-C1) ppm. FTIR υ 2963, 2927, 1546, 1457, 1270, 1210, 1143, 1073, 977 cm^{-1}. HRMS *m/z* 389.9341 (calcd for $C_{12}H_{11}BBr_2F_2N_2$: 389.9350).

20: M.p.: 140-143 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.90 (s, 1H, CH-C8), 6.68 (s, 1H, CH-C7), 2.48 (s, 3H, CH_3-C3), 2.46 (s, 3H, CH_3-C5), 2.12 (s, 3H, CH_3-C1), 1.98 (s, 3H, CH_3-C6) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 158.9 (C5), 152.6 (C3), 137.6 (C1), 133.3 (C7a), 131.5 (C8a), 129.5 (C6), 129.0 (C7), 122.5 (C8), 108.3 (C2), 13.3 (CH_3-C3), 13.0 (CH_3-C5), 11.2 (CH_3-C6), 10.9 (CH_3-C1) ppm. FTIR υ 2970, 2941, 1559, 1466, 1288, 1206, 1163, 1058, 972 cm^{-1}. HRMS *m/z* 326.0409 (calcd for $C_{13}H_{14}BBrF_2N_2$: 326.0401).

*Negishi reaction of BODIPY **15** with Me_2Zn.* According to method A, BODIPY **15**[12] (60 mg, 0.18 mmol), $Pd(PPh_3)_2Cl_2$ (12 mg, 0.018 mmol) in dry toluene (2 mL), and 1.5 mL of Me_2Zn (1.2 M in toluene, 1.8 mmol) were reacted for 6 h. Flash chromatography using hexane/CH_2Cl_2 (9:1) afforded BODIPY **21** (40 mg, 70%) as a yellow-brown solid.

M.p.: 177-180 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.76 (s, 1H, CH), 2.46 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 2.31 (q, J = 7.5 Hz, 2H, CH_2), 2.19 (s, 3H, CH_3), 0.96 (t, J = 7.5 Hz, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 146.6, 140.2, 138.7, 134.8, 133.4, 131.5, 120.6 (CH), 118.2, 17.0 (CH_2), 16.1 (CH_3), 14.6 (CH_3), 13.9 (CH_3), 12.9 (CH_3), 11.6 (CH_3) ppm. FTIR υ 2969, 2930, 1564, 1476, 1292, 1212, 1153, 1063, 967 cm^{-1}. HRMS *m/z* 310.1210 (calcd for $C_{15}H_{18}BClF_2N_2$: 310.1218).

*Negishi reaction of BODIPY **10** with Et_2Zn.* According to method A, BODIPY **10**[16] (30 mg, 0.13 mmol), $Pd(PPh_3)_2Cl_2$ (9 mg, 0.013 mmol) in dry toluene (1 mL), and 0.2 mL

of Et_2Zn (1 M in hexane, 0.2 mmol) were reacted for 20 min. Flash chromatography using hexane/EtOAc (8:2) afforded BODIPY **25** (22 mg, 77%) as a yellow solid.

M.p.: 115-116 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 2H, 2CH), 7.22 (d, J = 4.2 Hz, 2H, 2CH), 6.47 (d, J = 4.2 Hz, 2H, 2CH), 2.90 (q, J = 7.8 Hz, 2H, CH_2), 1.37 (t, J = 7.8 Hz, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5, 143.4 (CH), 134.8, 127.6 (CH), 118.0 (CH), 24.5 (CH_2), 18.3 (CH_3) ppm. FTIR υ 2920, 1569, 1534, 1310, 1245, 1093, 978 cm^{-1}. HRMS-EI *m/z* 220.0978 (calcd for $C_{11}H_{11}BF_2N_2$: 220.0981).

*Negishi reaction of BODIPY **22** with Et_2Zn.* According to method A, BODIPY **22**[8c] (50 mg, 0.084 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 0.008 mmol) in dry toluene (2 mL), and 0.5 mL of Et_2Zn (1 M in hexane, 0.5 mmol) were reacted for 15 min. Flash chromatography using hexane/EtOAc (8:2) afforded BODIPY **26** (32 mg, 77%) as a red solid.

M.p.: 182-183 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 8.1 Hz, 2H, tolyl), 7.23 (d, J = 8.1 Hz, 2H, tolyl), 6.76 (s, 2H, 2CH), 2.95 (q, J = 7.5 Hz, 4H, $2CH_2$), 2.38 (s, 3H, CH_3), 1.27 (t, J = 7.5 Hz, 6H, $2CH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 142.8, 141.1, 132.9, 130.9 (CH), 130.5, 130.3 (CH), 129.3 (CH), 107.9 (C-Br), 21.5 (CH_3), 21.3 (CH_2), 13.1 (CH_3) ppm. FTIR υ 2930, 1545, 1470, 1352, 1234, 1136, 980 cm^{-1}. HRMS *m/z* 493.9968 (calcd for $C_{20}H_{19}BBr_2F_2N_2$: 493.9974).

*Negishi reaction of BODIPY **23** with Et_2Zn.* According to method A, BODIPY **23**[12] (52 mg, 0.157 mmol), $Pd(PPh_3)_2Cl_2$ (11 mg, 0.016 mmol) in dry toluene (2 mL), and 2.1 mL of $ZnEt_2$ (1.5 M in toluene, 3.145 mmol) were reacted for 3 h. Flash chromatography using hexane/AcOEt (98:2) afforded BODIPYs **27** (12 mg, 23%) and **28** (4 mg, 7 %) as yellow-brown solids.

27: M.p.: 128-130 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.16 (s, 1H, CH), 2.87 (q, J = 7.7 Hz, 2H, CH_2), 2.72 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.35 (q, J = 7.7 Hz, 2H, CH_2), 2.29

(s, 3H, CH_3), 1.20 (t, J = 7.7 Hz, 3H, CH_3), 0.98 (t, J = 7.7 Hz, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 158.1, 154.9, 140.6, 139.9, 135.1, 133.6, 128.3, 127.3, 115.5 (CH), 21.4 (CH_2), 17.1 (CH_2), 16.1 (CH_3), 14.7 (CH_3), 14.6 (CH_3), 12.9 (CH_3), 12.7 (CH_3) ppm. FTIR υ 2970, 2927, 1556, 1466, 1280, 1210, 1145, 1033, 977 cm^{-1}. HRMS *m/z* 324.1368 (calcd for $C_{16}H_{20}BClF_2N_2$: 324.1374).

28: M.p.: 140-142 ºC. ^1H NMR (700 MHz, $CDCl_3$) δ 6.10 (s, 1H, CH), 2.90 (q, J = 7.7 Hz, 2H, CH_2), 2.75 (q, J = 7.7 Hz, 2H, CH_2), 2.54 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 2.34 (q, J = 7.7 Hz, 2H, CH_2), 2.27 (s, 3H, CH_3), 1.23 (t, J = 7.7 Hz, 3H, CH_3), 1.22 (t, J = 7.7 Hz, 3H, CH_3), 0.97 (t, J = 7.7 Hz, 3H, CH_3) ppm. ^{13}C NMR (176 MHz, $CDCl_3$) δ 158.5, 153.1, 146.8, 140.6, 137.1, 133.0, 132.1, 130.9, 115.9 (CH), 24.0 (CH_2), 21.6 (CH_2), 17.1 (CH_2), 16.8 (CH_3), 14.9 (CH_3), 14.5 (CH_3), 14.2 (CH_3), 12.9 (CH_3) 12.5 (CH_3) ppm. FTIR υ 2973, 2928, 1556, 1469, 1273, 1208, 1149, 1073, 987 cm^{-1}. HRMS *m/z* 318.2071 (calcd for $C_{18}H_{25}BF_2N_2$: 318.2077).

*Negishi reaction of BODIPY **3i** with PhZnBr.* According to method A, BODIPY **3i**[14] (70 mg, 0.136 mmol), $Pd(PPh_3)_2Cl_2$ (9 mg, 0.013 mmol) in dry toluene (2 mL), and 1.1 mL of PhZnBr (0.5 M in THF, 0.54 mmol) were reacted for 40 min. Flash chromatography using hexane/AcOEt (95:5) afforded BODIPY **29**[26] (28 mg, 50%) as a red solid.

*Negishi reaction of BODIPY **24a** with PhC≡CZnBr.* According to method B, phenylacetylene (0.07 mL, 0.605 mmol) in THF (5 mL), 0.34 mL of BuLi (1.6 M in hexane, 0.55 mmol), $ZnBr_2$ (136 mg, 0.605 mmol) and BODIPY **24a**[5a] (45 mg, 0.11 mmol), $Pd(PPh_3)_2Cl_2$ (8 mg, 0.011 mmol) in dry toluene (10 mL) were reacted for 75 min. Flash chromatography using hexane/CH_2Cl_2 (85:15) afforded BODIPY **30a** (37 mg, 87%) as a purple solid.

M.p.: 193-194 ºC. ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 (s, 1H, CH), 7.90 (s, 1H, CH), 7.41-7.36 (m, 4H, phenyl), 7.28-7.23 (m, 5H, phenyl), 6.96-6.93 (m, 2H, 2CH), 6.50

(broad s, 1H, CH), 2.40 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 145.3 (CH), 145.2 (CH), 141.8, 135.6, 134.2, 132.6 (CH), 131.9 (CH), 131.4 (CH), 130.7, 130.6 (CH), 129.4 (CH), 128.4 (CH), 128.3 (CH), 123.1, 119.2 (CH), 114.2, 91.9 (C≡C), 82.2 (C≡C), 21.5 (CH_3) ppm. FTIR υ 2923, 2220, 1544, 1480, 1399, 1348, 1255, 1101 cm^{-1}. HRMS *m/z* 382.1448 (calcd for $C_{24}H_{17}BF_2N_2$: 382.1451).

*Negishi reaction of BODIPY **24b** with PhC≡CZnBr.* According to method B, phenylacetylene (0.07 mL, 0.61 mmol) in THF (5 mL), 0.35 mL of BuLi (1.6 M hexano, 0.55 mmol), $ZnBr_2$ (137 mg, 0.61 mmol), BODIPY **24b** (40 mg, 0.11 mmol) and $Pd(PPh_3)_2Cl_2$ (8 mg, 0.011 mmol) in dry toluene (10 mL) were reacted for 4 h. Flash chromatography using hexane/EtOAc (97:3) afforded BODIPY **30b** (30 mg, 80%) as a purple solid.

M.p.: 150-153 ºC. ^1H NMR (300 MHz, $CDCl_3$) δ 7.45-7.41 (m, 2H, phenyl), 7.31-7.26 (m, 3H, phenyl), 7.13 (s, 1H, CH), 7.10 (d, J = 4.2 Hz, 1H, CH), 6.25 (d, J = 4.2 Hz, 1H, CH), 2.64 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 2.42 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 157.8, 140.3, 135.9, 135.2, 133.4, 131.4 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 126.7 (CH), 123.4, 119.9 (CH), 93.5 (C≡C), 82.5 (C≡C), 15.4 (CH_3), 15.0 (CH_3), 13.4 (CH_3) ppm. FTIR υ 2210, 1579, 1232, 1146, 1056 cm^{-1}. HRMS *m/z* 334.1445 (calcd for $C_{20}H_{17}BF_2N_2$: 334.1451).

Test reactions in absence of palladium

*Reaction of BODIPY **15** with Me_2Zn without palladium.* Following the procedure indicated in method A (see above) without adding the palladium precatalyst, BODIPY **15** (20 mg, 0.06 mmol) in dry toluene (2 mL) was submitted to react with 0.5 mL of Me_2Zn (1.2 M in THF, 0.60 mmol) for 6 h. No reaction took place. Flash chromatography using hexane/CH_2Cl_2 (9:1) afforded unalterated **15** (18 mg, 90%).

*Reaction of BODIPY **22** with Et_2Zn without palladium*. Following the procedure indicated in method A (see above) without adding the palladium precatalyst, BODIPY **22**[8c] (20 mg, 0.033 mmol) in dry toluene (2 mL) was submitted to react with 0.2 mL of Et_2Zn (1 M in hexane, 0.5 mmol) for 15 min. Flash chromatography using hexane/EtOAc (8:2) afforded 3-ethylBODIPY **31** (4 mg, 22%) as a red solid, and unalterated **22** (14 mg, 70%).

31: M.p.: 195-197 ºC. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.30 (d, J = 8.4 Hz, 2H, tolyl), 7.26 (d, J = 8.4 Hz, 2H, tolyl), 6.90 (s, 1H, CH), 6.73 (s, 1H, CH), 2.99 (q, J = 7.7 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 1.29 (t, J = 7.7 Hz, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 142.7, 141.7, 134.1, 133.9, 133.0, 130.4 (CH), 129.6 (CH), 129.5 (CH), 129.2 (CH), 127.9 (C-Br), 110.5 (C-Br), 109.4 (C-Br), 21.7 (CH_3), 21.5 (CH_2), 12.9 (CH_3) ppm. FTIR υ 2940, 1556, 1466, 1350, 1222, 1130, 988 cm^{-1}. HRMS *m/z* 543.8760 (calcd for $C_{18}H_{14}BBr_3F_2N_2$: 543.8768).

ASSOCIATE CONTENT

Supporting Information

Copies of the ^{1}H-NMR spectra of all compounds, copies of the ^{13}C-NMR spectra of all new compounds, as well as copies of the spectra corresponding to the conducted selective grandient-enhanced 1D NOESY and 2D HMBC experiments.

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All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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