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Synthesis of 4,4'-functionalized BODIPYs from dipyrrens

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ABSTRACT

A series of 14 symmetric (**1a-g**) and asymmetric (**2a-g**) BODIPYs bearing two different substituents at the boron center were synthesized in a one-pot reaction from dipyrrens **1** and **2**, respectively, in 14-63% isolated yields. The reaction involves the treatment of dipyrren with phenylboron dichloride followed by nucleophilic substitution of the chloride group using various nucleophiles, including TBAF, TMSCN, ROH, acetate and alkoxides. The reactions are completed within 2 h at room temperature. The spectroscopic and ^{11}B NMR properties of the new BODIPYs were investigated and three crystal structures are presented.

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4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (known as BODIPY) dyes have been intensely investigated in recent years for a variety of bioimaging, biosensing and bioanalytical applications. They possess unique properties that include large molar extinction coefficients, high fluorescence quantum yields, high photochemical and thermal stabilities, and ease of synthesis and functionalization.¹⁻³ Among the various methods developed for BODIPY functionalization, reactions at the boron center have lagged behind those at the carbon atoms, and usually employ nucleophilic substitution of one or both fluorides with alkyl, aryl, alkynyl, alkoxy and aryloxy groups. These reactions require strong nucleophilic agents, such as Grignard or organolithium reagents,⁴⁻¹² and alkoxides,^{13,14} or alternatively, can be accomplished under milder reactions in the presence of a Lewis acid (usually AlCl_3 or $\text{BF}_3 \cdot \text{OEt}_2$).¹⁵⁻²¹ These methodologies afford either the 4-mono- or 4,4'-disubstituted BODIPYs via careful control of the reaction conditions, and additional synthetic steps are required for the preparation of 4,4'-difunctionalized BODIPYs bearing two different substituents at the boron center. Alternatively, mono- and disubstituted BODIPYs can be prepared by reaction of dipyrrens with haloboranes.^{22,23}

Recently, the synthesis of 4-chloro-4-phenyl-1,3,5,7,8-pentamethyl-BODIPY was reported from the corresponding dipyrren hydrochloride salt, by reaction with sodium hydride followed by dichlorophenylborane; this BODIPY was sensitive to moisture and was rapidly converted into the corresponding 4-hydroxy-4-phenyl-BODIPY, which afforded 4-phenyl-BODIPY upon reaction with potassium bifluoride.²⁴ This methodology was employed for the [^{18}F]-radiolabelling of BODIPY for its investigation in positron emission tomography (PET)/fluorescence dual imaging.^{25,26} The combination of PET

and fluorescence in dual modality imaging is advantageous for clinical applications since it provides complementary and faster diagnosis. While the use of PET is limited to macroscopic spatial and temporal imaging, fluorescence-based imaging allows visualization over a much broader range, including at the subcellular level, thus enabling much higher spatial and temporal resolution. BODIPYs are particularly suitable as dual PET/fluorescence agents due to their inherent high fluorescence and ease of radiofluorination under both aqueous and organic conditions.²⁵⁻²⁷

Herein we further investigate the preparation of functionalized BODIPYs at the boron center, using one-flask reactions between dipyrrens and dichlorophenylborane, at room temperature, followed by substitution of the chloride with fluoride and various other carbon- and oxygen-centered nucleophiles, as shown in Scheme 1.

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Scheme 1. One-pot synthesis of BODIPYs from dipyrin.

Figure 1: Molecular structure of BODIPYs **1b**, **1c** and **2c** from X-ray crystal structure analysis, with 50% ellipsoids.

The starting dipyrins were synthesized as previously described¹⁵ and were isolated as the hydrochloride salts **1** and **2**. In our three-step one-flask procedure, dipyrins **1** or **2** were first dissolved in anhydrous dichloromethane and treated with 5 equiv of triethylamine (TEA). To this solution were added 5 equiv of phenylboron dichloride followed by 10 equiv of a nucleophile, and the mixture was stirred at room temperature for 1–2 h, until complete disappearance of the starting dipyrin, as monitored by TLC. The target 4,4'-difunctionalized BODIPYs **1a–g** and **2a–g**²⁸ were purified by preparative TLC, and isolated in yields ranging from 14% to 63%, as shown in Table 1. The lower yields obtained with the softer nucleophiles (ROH, TMSCN, AcO-) are due to the concomitant formation of the corresponding hydroxide derivative as by-product. Such 4-hydroxy-4-phenyl-BODIPYs have been previously isolated and characterized.^{24,25} For comparison purposes, the BF₂-BODIPYs **3** and **4** were also obtained from dipyrins **1** and **2** via complexation with BF₃•OEt₂ in the presence of TEA, in 68 and 41% yields, respectively.²⁹ Interestingly, under conditions similar to those described above for the dipyrins, BODIPYs **3** and **4** did not produce any of the targeted 4,4'-difunctionalized BODIPYs, although it has been recently reported that BODIPYs can react with boron trichloride followed by a Grignard reagent or alkoxide, to afford the corresponding difunctionalized BODIPYs.³⁰

BODIPYs **1a** and **2a** were obtained from the corresponding chloro-derivatives using tetrabutylammonium fluoride (TBAF) as the nucleophile, under milder conditions than those previously reported.^{24–26,28} Indeed, the B–Cl bond is weaker and more labile than the B–F bond, and does not require heating or the presence of activators, such as TMSOTf or a Lewis acid. Under the above reaction conditions, both hard and soft nucleophiles, such as alkoxides, acetate and trimethylsilyl cyanide (TMSCN), reacted to give the target BODIPYs in moderate yields (Table 1). TMSCN has been previously employed for substitution of the fluorides in a BF₂-BODIPY, although the reaction proceeds only in the presence of a Lewis acid, such as tin tetrachloride or boron trifluoride.⁹ Under these milder reaction conditions, nucleophiles functionalized with amine, ester and acetylene functionalities can be used, allowing for further derivatization or conjugation of the BODIPY,^{9,20,21} as well as the introduction of a polyethylene glycol group for increased solubility.

All BODIPYs were characterized by ¹H, ¹³C, and ¹¹B NMR, HRMS (ESI-TOF), and in the case of BODIPYs **1b**, **1c**, and **2c** also by X-ray crystallography (see Figure 1). The ¹H- and ¹³C-NMR spectra indicated that the introduction of different substituents on boron has no significant effect on the chemical shifts of the methyl and ethyl BODIPY core groups. For example in the ¹H NMR of BODIPYs **1a–g** the 3,5-methyls consistently appear as a singlet around 2.2 ppm and the 1,7-methyls at 1.3 ppm. On the other hand, the asymmetric BODIPYs **2a–g** show 4 singlets for the 1,3,5,7-methyl groups at around 2.2, 2.1, 1.4 and 1.3 ppm. Compared to BODIPYs **3** and **4**, the 3,5-methyls in BODIPYs **1a–g** and **2a–g** appear upfield shifted due to shielding caused by the 4-phenyl ring.

Significant differences were observed in the ¹¹B NMR of the BODIPYs using BF₃•OEt₂ as reference (δ = 0 ppm), as shown in Table 1. The characteristic triplet seen at 0.7 ppm for BODIPYs **3** and **4** bearing two fluorides, with ca. *J*(¹¹B–¹⁹F) = 33 Hz, is replaced by a singlet for all other BODIPYs spanning the range from 2.43 (for the mono-fluoride **1a**) to –9.42 ppm (for the cyano derivative **1c**). The lack of boron-fluorine coupling in **1a** and **2a**, as previously observed,^{5,24} might be due to quadrupolar broadening. On the other hand, the ¹¹B chemical shifts depend on the electron density on the groups bound to boron, which is greater for the CN derivatives **1c** and **2c**, and lowest for the mono-fluorides **1a** and **2a**.

Table 1. Yields and ¹¹B NMR chemical shifts (128 MHz, CDCl₃, all singlets) for BODIPYs **1a–g** and **2a–g**.

BODIPY	R	R ¹	Yield (%)	δ(ppm)
1a	Et	F	52	2.43
1b	Et	OMe	63	2.18
1c	Et	CN	17	–9.42
1d	Et	OAc	25	–0.48
1e	Et	OCH ₂ CH ₂ NHBoc	32	1.54
1f	Et	O(CH ₂ CH ₂ O) ₃ Me	21	1.63
1g	Et	OCH ₂ C≡CH	25	1.73
2a	H	F	41	2.23
2b	H	OMe	49	2.10
2c	H	CN	18	–7.43
2d	H	OAc	16	–0.34
2e	H	OCH ₂ CH ₂ NHBoc	14	1.10
2f	H	O(CH ₂ CH ₂ O) ₃ Me	15	1.21
2g	H	OCH ₂ C≡CH	31	1.65

For X-ray diffraction structure analysis, crystals were grown by slow evaporation of hexane diffused in dichloromethane (for BODIPYs **1c** and **2c**) or in ethyl acetate (for BODIPY **1b**). In all cases, the central BN_2C_3 ring is fairly planar, with mean deviation of 0.020 Å for both **1b** and **1c** and 0.056 Å for **2c** (Figure 1). The 8-mesophenyl is oriented approximately perpendicular to the BODIPY core plane, to avoid steric hindrance from the 1,7-dimethyl substituents, the dihedral angles being 84.1° for **1b**, 85.3° for **1c**, and 87.6° for **2c**. Likewise, the phenyl group on B forms dihedral angles with the central ring of 86.1° for **1b**, 85.9° for **1c**, and 83.2° for **2c**.

The spectroscopic properties and fluorescence quantum yields of BODIPYs **1a-g** and **2a-g** in dichloromethane at room temperature were determined and are summarized in Table 2. All BODIPYs showed absorptions in the visible range with high molar absorption coefficients ($\log \epsilon = 4.5\text{--}5.0$) that correspond to the $S_0\text{--}S_1$ ($\pi\text{--}\pi^*$) transition. The symmetric BODIPYs **1a-g** showed absorptions in the range of 521–524 nm and emission bands between 533–537 nm with 11–15 nm Stokes shifts. The asymmetric BODIPYs **2a-g** showed blue-shifted absorption and emission bands, in the ranges 511–513 and 521–523 nm, respectively, and slightly smaller Stokes shifts (9–11 nm). The fluorescence quantum yields decreased slightly for all BODIPYs compared with compounds **3** and **4** bearing two fluorides. These results are in agreement with previous observations showing that BODIPYs bearing methoxy and other flexible groups on boron show decreased fluorescence quantum yields due to increased energy lost to non-radiative decay to the ground state.^{20,21} Among the 4-phenyl-BODIPYs, those bearing the cyano group showed the highest fluorescence quantum yields, 0.65 for **1c** and 0.78 for **2c**.

Table 2. Spectroscopic properties of BODIPYs **1a-g**, **2a-g**, **3**, and **4** in CH_2Cl_2 at room temperature; Abs: absorption; Em: emission; SS: Stokes shift; a: excitation at 480 nm; b: calculated using rhodamine 6G as the standard.

BODIPY	Abs (λ_{max} , nm)	Em ^a (λ_{max} , nm)	Φ_f^b	$\log \epsilon$ ($\text{M}^{-1} \text{cm}^{-1}$)	SS (nm)
1a	524	535	0.53	4.86	11
1b	522	537	0.42	4.77	15
1c	521	533	0.65	4.63	12
1d	522	533	0.64	4.63	11
1e	523	533	0.60	4.73	11
1f	523	534	0.48	4.82	11
1g	523	534	0.51	4.61	11
2a	513	523	0.61	4.85	10
2b	512	523	0.50	4.92	11
2c	511	521	0.78	4.97	10
2d	512	522	0.68	4.81	10
2e	513	523	0.60	4.76	10
2f	512	521	0.51	4.72	9
2g	513	523	0.64	4.78	10
3	526	536	0.74	4.68	10
4	514	524	0.82	4.49	10

In summary, we developed a synthetic route for the functionalization of BODIPYs bearing two different substituents on the boron center, via a one-pot reaction of dipyrins with phenylboron dichloride followed by treatment with a nucleophile. BODIPYs **1a-g** and **2a-g** were isolated in moderate yields (14–

63%) under these mild conditions, while **3** and **4** were unreactive. The highest yields were obtained for BODIPYs **1b** and **2b** using sodium methoxide; milder nucleophiles (alcohols, TMSCN, acetate ion) also produced the target BODIPYs albeit in lower yields, due to formation of the corresponding hydroxyl derivatives as by-product. The mild reaction conditions allow the preparation of functionalized BODIPYs with increased solubility, for various biomedical applications. All BODIPYs show intense absorptions ($\log \epsilon = 4.5\text{--}5.0$) and emissions in the visible range, and decreased fluorescence quantum yields relative to the parent BODIPYs **3** and **4**. Among this series of 14 new BODIPYs, **1c** and **2c** bearing cyano groups on boron display the highest quantum yields.

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28. *NMR and HRMS data for new BODIPYs: 1a:* ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.57-7.51 (m, 3H), 7.43-7.40 (m, 3H), 7.37-7.35 (m, 1H), 7.20 (t, 2H, $J = 6.9$ Hz), 7.15-7.11 (m, 1H), 2.23 (q, 4H, $J = 7.6$ Hz), 2.17 (s, 6H), 1.32 (s, 6H), 0.91 (t, 6H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 153.91, 140.55, 137.07, 136.54, 132.81, 132.10, 132.07, 130.48, 129.11, 128.80, 128.58, 127.00, 126.09, 17.25, 14.78, 13.20, 13.16, 11.89; HRMS (ESI-TOF) m/z 438.2752 $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{32}\text{BFN}_2$: 438.2740. **1b:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.56-7.50 (m, 3H), 7.43-7.36 (m, 4H), 7.15 (t, 2H, $J = 7.4$ Hz), 7.10-7.05 (m, 1H), 3.09 (s, 3H), 2.23 (q, 4H, $J = 7.6$ Hz), 2.16 (s, 6H), 1.32 (s, 6H), 0.90 (t, 6H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 153.66, 140.51, 136.91, 136.00, 132.51, 132.36, 131.32, 129.08, 128.89, 128.83, 128.58, 126.79, 125.59, 49.20, 17.31, 14.85, 12.86, 11.93; HRMS (ESI-TOF) m/z 472.2771 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{35}\text{BN}_2\text{O}$: 472.2775. **1c:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.56-7.54 (m, 3H), 7.49 (d, 2H, $J = 6.6$ Hz), 7.42-7.38 (m, 1H), 7.25 (t, 2H, $J = 6.9$ Hz), 7.21-7.17 (m, 1H), 2.25 (q, 4H, $J = 7.6$ Hz), 2.15 (s, 6H), 1.34 (s, 6H), 0.91 (t, 6H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 154.0, 140.43, 136.89, 136.18, 132.76, 132.29, 130.57, 129.11, 128.99, 128.78, 128.73, 128.64, 126.90, 125.70, 17.30, 14.83, 13.55, 11.89; HRMS (ESI-TOF) m/z 467.2618 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{32}\text{BN}_3$: 467.2613. **1d:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.56-7.48 (m, 5H), 7.44-7.41 (m, 1H), 7.39-7.36 (m, 1H), 7.21 (t, 2H, $J = 6.8$ Hz), 7.17-7.12 (m, 1H), 2.22 (q, 4H, $J = 7.6$ Hz), 2.07 (s, 3H), 2.04 (s, 6H), 1.33 (s, 6H), 0.89 (t, 6H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 172.40, 152.41, 140.56, 136.76, 136.71, 132.47, 131.25, 129.10, 129.06, 128.89, 128.60, 126.94, 126.06, 23.19, 17.38, 14.75, 13.12, 12.09; HRMS (ESI-TOF) m/z 500.2720 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{31}\text{H}_{35}\text{BN}_2\text{O}_2$: 500.2737. **1e:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.56-7.51 (m, 3H), 7.45-7.36 (m, 3H), 7.37-7.35 (m, 1H), 7.15 (t, 2H, $J = 7.4$ Hz), 7.10-7.05 (m, 1H), 3.24-3.18 (m, 2H), 3.16-3.15 (m, 2H), 2.21 (q, 4H, $J = 7.6$ Hz), 2.12 (s, 6H), 1.42 (s, 9H), 1.31 (s, 6H), 0.89 (t, 6H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 156.34, 153.54, 140.56, 136.81, 136.14, 132.57, 131.21, 129.07, 128.99, 128.83, 128.76, 128.63, 126.71, 125.64, 78.96, 60.60, 42.81, 28.65, 17.30, 14.80, 13.06, 11.93; HRMS (ESI-TOF) m/z 601.3561 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{36}\text{H}_{46}\text{BN}_3\text{O}_3$: 601.3573. **1f:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.56-7.50 (m, 3H), 7.44-7.40 (m, 3H), 7.38-7.36 (m, 1H), 7.15 (t, 2H, $J = 8.0$ Hz), 7.10-7.06 (m, 1H), 3.64-3.62 (m, 2H), 3.60-3.57 (m, 6H), 3.51-3.48 (m, 2H), 3.33 (s, 3H), 3.30 (t, 2H, $J = 5.6$ Hz), 2.22 (q, 4H, $J = 7.6$ Hz), 2.15 (s, 6H), 1.31 (s, 6H), 0.89 (t, 6H, $J = 7.5$ Hz); ^{13}C NMR (CD_2Cl_2 , 100 MHz) δ 154.09, 137.26, 136.64, 133.02, 132.64, 131.67, 129.53, 129.41, 129.32, 129.23, 129.00, 127.09, 126.02, 73.21, 72.51, 71.23, 71.14, 70.99, 61.49, 59.18, 17.62, 15.06, 13.21, 12.12; HRMS (ESI-TOF) m/z 604.3557 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{36}\text{H}_{47}\text{BN}_2\text{O}_4$: 604.3565. **1g:** ^1H NMR (CDCl_3 , 400 MHz) δ 7.56-7.50 (m, 3H), 7.42 (d, 3H, $J = 6.6$ Hz), 7.38-7.34 (m, 1H), 7.17 (t, 2H, $J = 8.1$ Hz), 7.10 (t, 1H, $J = 7.2$ Hz), 3.92 (d, 1H, $J = 2.4$ Hz), 2.22 (q, 4H, $J = 6.6$ Hz), 2.21 (s, 3H), 2.17 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H), 1.27 (s, 1H), 0.90 (t, 6H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 154.19, 140.33, 136.79, 136.34, 132.73, 132.55, 131.20, 129.10, 128.96, 128.81, 128.79, 128.64, 126.73, 125.69, 70.92, 50.09, 17.28, 14.80, 13.22, 11.93; HRMS (ESI-TOF) m/z 496.2771 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{32}\text{H}_{35}\text{BN}_3\text{O}$: 496.2754. **2a:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.57-7.51 (m, 3H), 7.43-7.40 (m, 3H), 7.37-7.35 (m, 1H), 7.20 (t, 2H, $J = 6.8$ Hz), 7.16-7.12 (m, 1H), 5.88 (s, 1H), 2.24 (q, 2H, $J = 7.6$ Hz), 2.19 (s, 3H), 2.15 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 0.91 (t, 3H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 141.27, 140.64, 136.12, 133.58, 132.06, 132.02, 129.17, 129.11, 128.84, 128.62, 128.43, 127.05, 126.19, 120.85, 17.25, 15.35, 14.68, 14.56, 13.32, 11.94; HRMS (ESI-TOF) m/z 410.2439 $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{28}\text{BFN}_2$: 410.2398. **2b:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.57-7.51 (m, 3H), 7.43-7.36 (m, 4H), 7.15 (t, 2H, $J = 7.3$ Hz), 7.10-7.06 (m, 1H), 5.86 (s, 1H), 3.10 (s, 3H), 2.24 (q, 2H, $J = 7.5$ Hz), 2.19 (s, 3H), 2.13 (s, 3H), 1.38 (s, 3H), 1.34 (s, 3H), 0.91 (t, 3H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 155.53, 153.61, 141.23, 139.60, 137.03, 136.47, 133.34, 132.31, 131.87, 131.48, 129.14, 128.96, 128.69, 128.65, 126.84, 125.70, 120.63, 49.20, 17.30, 15.16, 14.74, 14.64, 12.97, 11.98; HRMS (ESI-TOF) m/z 444.2458 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{31}\text{BN}_2\text{O}$: 444.2468. **2c:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.57-7.53 (m, 3H), 7.50-7.48 (m, 2H), 7.42-7.38 (m, 2H), 7.25 (t, 2H, $J = 6.8$ Hz), 7.22-7.18 (m, 1H), 5.96 (s, 1H), 2.26 (q, 2H, $J = 9.3$ Hz), 2.17 (s, 3H), 2.13 (s, 3H), 1.40 (s, 3H), 1.37 (s, 3H), 0.92 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (CD_2Cl_2 , 100 MHz) δ 154.03, 141.53, 133.25, 129.78, 129.71, 129.49, 128.94, 128.80, 128.01, 127.39, 121.82, 112.37, 17.66, 16.00, 14.84, 14.06, 12.28; HRMS (ESI-TOF) m/z 439.2305 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{28}\text{BN}_3$: 439.2297. **2d:** ^1H NMR (CDCl_3 , 400 MHz) δ 7.55-7.49 (m, 5H), 7.45-7.43 (m, 2H), 7.22 (t, 2H, $J = 7.1$ Hz), 7.19-7.16 (m, 1H), 5.82 (s, 1H), 2.24 (q, 2H, $J = 7.5$ Hz), 2.11 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 0.88 (t, 3H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 172.45, 154.27, 152.31, 146.25, 141.63, 140.05, 137.76, 136.32, 133.25, 132.42, 132.21, 131.78, 129.15, 128.95, 128.90, 128.70, 128.43, 127.01, 126.19, 120.86, 23.15, 17.35, 15.35, 14.69, 14.65, 13.24, 12.06; HRMS (ESI-TOF) m/z 472.2407 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{29}\text{H}_{31}\text{BN}_3\text{O}_2$: 472.2397. **2e:** ^1H NMR (CDCl_3 , 400 MHz) δ 7.56-7.51 (m, 3H), 7.45-7.41 (m, 3H), 7.37-7.36 (m, 1H), 7.17 (t, 2H, $J = 6.8$ Hz), 7.10 (t, 1H, $J = 7.0$ Hz), 5.85 (s, 1H), 3.24 (t, 2H, $J = 5.0$ Hz), 3.18 (t, 2H, $J = 4.6$ Hz), 2.22 (q, 2H, $J = 7.9$ Hz), 2.15 (s, 3H), 2.09 (s, 3H), 1.43 (s, 9H), 1.37 (s, 3H), 1.33 (s, 3H), 0.90 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (CD_2Cl_2 , 100 MHz) δ 132.78, 129.60, 129.50, 129.15, 129.03, 127.15, 126.21, 120.97, 61.04, 28.74, 28.64, 17.61, 15.46, 14.92, 14.78, 13.38, 12.18; HRMS (ESI-TOF) m/z 601.3561 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{36}\text{H}_{46}\text{BN}_3\text{O}_3$: 601.3573. **2f:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.56-7.51 (m, 3H), 7.42 (t, 3H, $J = 6.3$ Hz), 7.38-7.34 (m, 1H), 7.16 (t, 2H, $J = 6.8$ Hz), 7.12-7.07 (m, 1H), 5.85 (s, 1H), 3.64-3.61 (m, 2H), 3.60-3.56 (m, 6H), 3.51-3.48 (m, 2H), 3.33 (s, 3H), 3.33-3.28 (m, 2H), 2.23 (q, 2H, $J = 7.8$ Hz), 2.17 (s, 3H), 2.12 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 0.90 (t, 3H, $J = 7.6$ Hz); ^{13}C NMR (CD_2Cl_2 , 100 MHz) δ 156.02, 154.00, 141.85, 140.19, 137.69, 136.84, 133.86, 132.81, 132.49, 132.24, 129.58, 129.46, 129.15, 129.10, 127.30, 127.12, 126.21, 126.12, 120.90, 73.22, 72.52, 71.23, 71.16, 70.99, 61.54, 59.18, 17.63, 15.43, 14.96, 14.78, 13.34, 12.18; HRMS (ESI-TOF) m/z 576.3244 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{34}\text{H}_{43}\text{BN}_2\text{O}_4$: 576.3240. **2g:** ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.57-7.51 (m, 3H), 7.43-7.41 (m, 3H), 7.38-7.36 (m, 1H), 7.17 (t, 2H, $J = 6.9$ Hz), 7.13-7.09 (m, 1H), 5.87 (s, 1H), 2.24-2.22 (dd, 2H, $J = 1.2$ Hz), 2.19 (s, 3H), 2.14 (s, 3H), 1.38 (s, 3H), 1.34 (s, 3H), 1.27 (s, 1H), 0.90 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (CD_2Cl_2 , 100 MHz) δ 156.38, 154.17, 141.85, 140.58, 138.17, 136.66, 134.12, 132.70, 132.25, 129.63, 129.51, 129.18, 129.06, 129.02, 127.23, 126.30, 121.09, 71.40, 50.35, 17.60, 15.56, 14.90, 14.78, 13.55, 12.20; HRMS (ESI-TOF) m/z 468.2458 $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{31}\text{BN}_2\text{O}$: 468.2449.
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