1,10a-Dihydro-1-aza-10a-boraphenanthrene and 6a,7-Dihydro-7-aza-6a-boratetraphene: Two New Fluorescent BN-PAHs

Isabel Valencia, Patricia García-García, David Sucunza, * Francisco Mendicuti, and Juan J. Vaquero *

ABSTRACT: Previously unknown 1,10a-dihydro-1-aza-10a-boraphenanthrene and 6a,7-dihydro-7-aza-6a-boratetraphene have been efficiently synthesized. Bromination of these BN-PAHs proceeds with complete regioselectivity, resulting in the formation of different substituted derivatives via cross-coupling reactions. These compounds exhibit rather high fluorescence quantum yields (up to $\phi_F = 0.80$).

INTRODUCTION

BN/CC-isosterism in aromatic compounds leads to BN-polycyclic aromatic hydrocarbons (BN-PAHs),1 which retain their aromaticity but exhibit different properties as a result of a dipole in the molecule.2 This formal replacement of a C=C unit by an isoelectronic B=N bond has been exploited for the design of new materials. Thus, BN-arenes have been investigated as promising components for improved optoelectronic devices,3 as well as in the search for new pharmacophores in medicinal chemistry4 and in the development of novel ligands for transition metal-based catalysis.5

As a result of the significant progress seen in the field of BN-PAHs over the past few years, several BN-arenes have been prepared in sufficient quantities, thus facilitating further studies into the properties of these heterocycles.6 Nevertheless, as these examples cover only a small part of all the possible permutations of this BN/CC-isosterism, a basic understanding of the simplest of these systems is still highly desirable.

In this regard, several BN-isosteres of mono-, bi-, tri-, and tetracyclic aromatic compounds have been reported.7 In particular, with respect to tri- and tetracyclic BN-PAHs, different anthracene,8 phenanthrene,9 tetracene,10 tetraphene,11 chrysene,12 pyrene,12b,13 benzo[cd]phenanthrene,14 and triphenylene15 analogues in which a C=C unit has been replaced by a B=N bond have been described, showing that the position of the B=N unit has a crucial effect on both their reactivity and photophysical properties.7,9a−c,16 Herein, we report an efficient synthesis for two novel systems, namely, isosteres of phenanthrene and tetraphene (Figure 1), as well as their derivatization via a bromination-cross coupling reaction methodology and a study of their main optical properties.

RESULTS AND DISCUSSION

The synthesis of BN-phenanthrene 1 (Scheme 1) started with regioselective bromination of the commercially available monocyclic BN-arene 317 and subsequent treatment with two equivalents of vinylmagnesium bromide to give 4. Removal of the tert-butyldimethylsilyl ether (TBS)-protecting group from this substrate, followed by a Suzuki−Miyaura cross-coupling reaction, using chloro[(tri-tert-butylphosphine)-2-(2-aminobiphenyl)] palladium(II) (tBu3P−Pd-G2) as a catalyst and Cs2CO3 as a base,18 afforded biphosphol derivative 5. Finally, a ring-closing metathesis of this intermediate using...
the second-generation Grubbs catalyst gave the desired compound 1. Altogether, this novel BN-phenanthrene was prepared in five steps, with only three purifications, in 46% overall yield.

BN-tetraphene 2 was prepared in five steps (three purification processes), using a slightly modified methodology, in 27% overall yield (Scheme 2). Thus, this synthesis started with the formation of the bicyclic BN-arene 7 via the treatment of 2-vinylaniline 6 with boron trichloride to force a borylative cyclization,19 regioselective bromination,18 and nucleophilic substitution at the boron position using vinylmagnesium bromide. A subsequent Suzuki−Miyaura cross-coupling reaction with intermediate 7, using tBu3P−Pd-G2 as a catalyst and Cs2CO3 as a base, and a final ring-closing metathesis using the second-generation Grubbs catalyst gave compound 2.

The reactivity of both BN-phenanthrene 1 and BN-tetraphene 2 was explored to obtain functionalized derivatives. Thus, we evaluated their behavior in the presence of brominating agents as electrophilic aromatic substitution is a well-established tool for the functionalization of BN-PAHs.7 In this regard, although the use of Br2 in CH2Cl2 was not successful, regioselective bromination was achieved at the carbon next to the boron, the most reactive position in related BN-aromatics according to the literature, when compounds 1 and 2 were treated with NBS/AlCl3 in CH2Cl2 (Scheme 3). Under these reaction conditions, no traces of other regioisomers or dibrominated compounds were observed.

Bromo-substituted BN-arenes 9 and 10 are suitable for further functionalization by palladium-catalyzed cross-coupling reactions. Thus, standard Suzuki, Sonogashira, and Buchwald−Hartwig amination coupling conditions were employed to obtain phenyl-, alkynyl-, and morpholinyl-substituted derivatives 11−16 in high yields (Scheme 4).

Alkylation of BN-tetraphene 2 was also tested, with moderate success (Scheme 5). Thus, treatment of this BN-PAH with two equivalents of the base lithium bis(trimethylsilyl)amide (LiHMDS) and iodomethane led to the formation of methylated BN-tetraphene derivative 17 in 52% yield.

Once the efficient synthesis for BN-phenanthrene 1 and BN-tetraphene 2 had been developed and various functionalized derivatives were synthesized, we focused on the evaluation of their main photophysical properties. The absorption and emission data for parent compounds 1 and 2 and their derivatives 11−16 in cyclohexane are summarized in Table 1.

UV−vis absorption spectra for BN-phenanthrenes 1, 11−13 and BN-tetraphenes 2, 14−16 as well as their PAH phenanthrene (18) and tetraphene (19) isostere analogues of 1 and 2 derivatives, respectively, were monitored in the 250−500 nm range. All spectra show two main structureless bands (Figure 3 and Figure S1); however, both bands for 18 and 19 are shifted slightly to the blue relative to those for BN-
phenanthrene and BN-tetraphene derivatives. Besides, less energetic bands for 18 and 19 are much less intense. The presence of the fourth aromatic ring in 19 and the BN-tetraphenes favors ring conjugation, shifting all spectra by about 8–14 nm to the red with respect to those obtained for 18 and BN-phenanthrene derivatives. The effect of a larger contribution to the ring conjugation of some substituents over others (H < Ph < PhC≡C) is also the reason for the observed bathochromic displacements of the absorption peaks for the less energetic bands in 11 (14) and 12 (15) with respect to their parent 1 (2). As reported previously, the peaks for the morpholinyl-containing derivatives 13 and 16 displayed additional broad fluorescence bands centered at 521 and 545 nm, respectively. Both of these bands, the intensity of which depends on the nature of the solvent and which were previously observed in a morpholinyl-functionalized 4a-aza-12a-borachrysene,12a were attributed to the presence of rather stable π−π stacking aggregates in solution (see Supporting Information, pages S10–13, for confirmation).

With the exception of the two morpholinyl-functionalized derivatives 13 and 16, the rest of the BN-PAHs studied showed relatively high quantum yields (\(\phi_F > 0.33\)), much higher than the PAHs 18 and 19, whose fluorescence is very weak. In particular, 12, 14, 15, and 16 exhibited rather high fluorescence, with quantum yields of 0.63, 0.68, 0.80, and 0.66, respectively. The effect of phenylalkynyl substituents on the

Table 1. UV/Vis and Fluorescence Parameters for BN-PAHs 1, 2, and 11−16

| cmpnd | \(\epsilon\) (10^3 × M⁻¹ cm⁻¹) | \(\lambda_{\text{abs max}} (\lambda_{\text{exc}})\) (nm)^b | \(\lambda_{\text{em}}\) (nm) | \(\phi_F\) c | \(\tau\) (ns)^f |
|-------|-----------------|-----------------|----------------|-------|-------|
| 1     | 9.6             | 338, 354, 372 (354) | 395           | 0.33  | 1.9   |
| 11    | 12.0            | 342, 358, 377 (343) | 405           | 0.47  | 6.9   |
| 12    | 19.1            | 350, 366, 386 (351) | 432           | 0.63  | 6.1   |
| 13    | 4.9             | 350, 365(s) (350)  | 388 (351)     | 0.21  | 2.3 (13.3) |
| 18    | 11.1            | 244(s), 251, 274, 281, 293, 315, 323, 330, 337, 346 (293) | 365           | 0.01  | 15.5  |
| 2     | 24.1            | 348, 365, 385 (365) | 405           | 0.68  | 4.1   |
| 14    | 22.7            | 351, 368, 387 (368) | 441           | 0.80  | 8.9   |
| 15    | 28.8            | 357, 375, 394 (375) | 463           | 0.66  | 7.1   |
| 16    | 15.3            | 342, 359, 376 (323) | 364 (545)     | 0.17  | 1.7 (12.3) |
| 19    | 5.7             | 255, 267, 277, 287, 299(s) 313, 327, 340, 358 (358) | 386           | 0.02  | 15.0   |

aCyclohexane was used as a solvent. bMolar absorptivities measured at \(\lambda_{\text{max}}\). cPeaks (maxima of the band to the red in black) and shoulders (s) for the bands that appear to the red. dStandard for fluorescence quantum yield was 9,10-diphenylanthracene in cyclohexane (\(\phi_F = 0.93\)). eFluorescence lifetimes were obtained upon 335 nm (or 296 nm) nanoled excitation by fixing the emission at \(\lambda_{\text{em}}\). fNanoled excitation by fixing the emission at \(\lambda_{\text{em}}\).
fluorescence increase in BN-aromatic compounds has been reported previously.\textsuperscript{12a,16a} Fluorescence intensity profiles for 18 and 19 and BN-phenanthrene and tetrphenylen derivatives (Figure S2) were reasonably adjusted to monoeponential decays. Lifetimes (Table 1) are, in general, slightly larger for BN-phenanthrene counterparts (~2–7 ns) than for their corresponding BN-phenanthrene counterparts (~2–7 ns). PAHs 18 and 19 again deviate from this trend. They show rather high and similar lifetime values near 15 ns.

Additionally, we studied the ability of 1 and 2 to react with \textit{n}-tetrabutylammonium fluoride (TBAF) as the p-orbital of the boron center in BN-PAHs can accept an electron pair from Lewis bases such as F\textsuperscript{−}.\textsuperscript{9e,12a,22} To that end, fluorescence titration experiments were carried out on 1 and 2 with TBAF\textsuperscript{23} (Figure S3). The addition of aliquots of fluoride led to a monotonic quenching of the fluorescence intensity in both cases, which can presumably be attributed to the formation of 2 and 2 fluoroborate complexes. The titrations were verified by \textsuperscript{19}F, \textsuperscript{11}B, and \textsuperscript{10}B NMR measurements. Upon addition of 4 equiv of TBAF to BN-phenanthrene 1, a new signal appeared at −144 ppm in \textsuperscript{19}F NMR and 0 ppm in \textsuperscript{11}B and \textsuperscript{10}B NMR spectra, which could indicate the formation of a fluoroborate complex (Figures S10–S13).\textsuperscript{9e} On the other hand, the comparative analysis of the results from the titrations by TBAF of 2 and the methylated BN-tetrphenylen derivative 17 (Figures S4 and S5) led us to discard that quenching was due to the F\textsuperscript{−} binding to the NH via hydrogen bonding. The Stern–Volmer plots of fluorescence intensities (Figure S4) and lifetimes (τ/τ = 1 at any [TBAF]) also confirmed that the decrease in fluorescence intensity was due to the likely formation of ground-state fluoroborate complexes. However, these complexes seem to be significantly less stable (Figures S4 and S5) than those reported previously by us for 4a-aza-12a-borachrysene whose complexation constant was a magnitude order larger.\textsuperscript{12a}

\section*{CONCLUSIONS}

Syntheses of the previously unknown compounds 1,10a-di-hydro-1-aza-10a-borophanthenene and 6a,7-di-hydro-7-aza-6a-boratetraphene have been described in five steps (three purification processes). The reactivity of these BN-PAHs with brominating agents was explored in order to obtain function-alized derivatives. Treatment with NBS/AlCl\textsubscript{3} proceeded with complete regioselectivity, thus allowing subsequent derivatization based on palladium-catalyzed cross-coupling reactions under standard conditions. The fluorescence of these BN-PAHs was also tested, showing rather high fluorescence quantum yields (up to φ\textsubscript{F} = 0.80).

\section*{EXPERIMENTAL SECTION}

**General Methods.** Reagents were acquired from commercial sources and used without further purification. When required, solvents were dried using an MBRAUN MB-SPS-800 apparatus. In general, reactions were carried out under an argon atmosphere using oven-dried glassware with magnetic stirring and dry solvents. For reactions that required heating, the heat source was a sand bath. Reactions were monitored using analytical TLC plates (silica gel 60 F254, 0.25 mm), and compounds were visualized with UV radiation. Silica gel grade 60 (70–230 mesh) was used for column chromatography. All melting points were determined in open capillary tubes using a Stuart Scientific SMP3 melting point apparatus (uncorrected). IR spectra were obtained using a PerkinElmer FTIR spectrum 2000 spectrophotometer. \textsuperscript{1}H, \textsuperscript{13}C\{\textsuperscript{1}H\} and \textsuperscript{11}B\{\textsuperscript{1}H\} NMR 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, with calibration with respect to the residual protonated solvent used (δ\textsuperscript{H} = 7.24 ppm and δ\textsuperscript{B} = 77.0 ppm for CDCl\textsubscript{3}). \textsuperscript{11}B\{\textsuperscript{1}H\} NMR spectra were referenced externally to BF\textsubscript{3}·O\textsubscript{2}O\textsubscript{3} (δ = 0 ppm). HRMS was performed using an Agilent 6210 time-of-flight LC/MS. Absorption spectra were recorded using a UVikon 941 (Kontron Instruments) UV–vis spectrophotometer. Steady-state fluorescence measurements were carried out using a PTI Quanta Master spectrophotometer equipped with a Xenon flash lamp as a light source, single concave grating monochromators, and Glan-Thompson polarizers in the excitation and emission paths. Detection was allowed by a photomultiplier cooled by a Peltier system. Slit widths were set at 6 nm for both excitation and emission paths, and polarizers were fixed at the "magic angle" condition. Right angle geometry and rectangular 10 mm path cells were used for the fluorescence measurements.

3-Bromo-2-vinyl-1-(tert-butylidemethylsilyl)-1,2-dihydro-1,2-aza-borine (4). To the Schlenk containing the 1-(tert-butylidemethylsilyl)-2-chloro-1,2-di-hydro-1,2-azaborine 3 (250 mg, 1.10 mmol, 1.0 equiv) was added anhydrous CH\textsubscript{2}Cl\textsubscript{2} (55 mL, 0.2 M), and the resulting solution was cooled to 0 °C. A recently prepared bromine solution (56 μL, 1.10 mmol, 1.0 equiv) in anhydrous CH\textsubscript{2}Cl\textsubscript{2} (5.5 mL, 0.2 M) was added under argon at a rate of 1.1 mmol/h. The reaction was stirred for 15 additional minutes at 0 °C and was allowed to warm to room temperature for four hours and a half. The mixture was concentrated under reduced pressure to afford the corresponding intermediate 3-bromo-1-(tert-butylidemethylsilyl)-2-chloro-1,2-di-hydro-1,2-azaborine as an air- and moisture-sensitive oil, which could be used as is in the next step without further purification. To the Schlenk containing the 3-bromo-1-(tert-butylidemethylsilyl)-2-chloro-1,2-di-hydro-1,2-azaborine was added anhydrous THF (5.5 mL, 0.2 M), and the resulting solution was cooled to −30 °C. The vinylmagnesium bromide solution (1.0 M in Et\textsubscript{2}O; 2.20 mL, 2.20 mmol, 2.0 equiv) was added dropwise using a syringe, and then the reaction mixture was allowed to warm to room temperature and stirred for 18 h. At the end of the reaction, the mixture was concentrated under reduced pressure, and the remaining residue was purified by flash column chromatography (hexane) to afford the corresponding 3-bromo-2-vinyl-1-(tert-butylidemethylsilyl)-1,2-di-hydro-1,2-azaborine 4 (194 mg, 0.65 mmol, 60%) as a yellow oil. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): δ (ppm) 7.90 (d, J = 7.0 Hz, 1H), 7.29 (d, J = 7.0 Hz, 1H), 6.46 (dd, J = 20.1, 15.0 Hz, 1H), 6.17 (ap, J = 7.0 Hz, 1H), 5.91 (dd, J = 15.0, 3.0 Hz, 1H), 5.80 (dd, J = 20.1, 3.0 Hz, 1H), 0.92 (s, 9H), 0.45 (s, 6H). \textsuperscript{13}C\{\textsuperscript{1}H\} NMR (125 MHz, CDCl\textsubscript{3}): δ (ppm) 135.9 (s, 1H), 133.4 (s, 1H), 128.5 (s, 1H), 127.0 (s, 1H), 124.7 (s, 1H), 121.7 (dd, J = 20.1, 3.0 Hz, 1H), 119.3 (s, 1H), 118.6 (s, 1H), 112.6 (s, 1H), 111.7 (s, 1H), 101.6 (s, 1H), 66.4 (s, 1H), 38.9 (s, 1H), 28.8 (s, 1H), 27.6 (s, 1H), 27.4 (s, 1H), 24.3 (s, 1H), 23.5 (s, 1H), 22.8 (s, 1H), 21.9 (s, 1H), 19.4 (s, 1H), 13.3 (s, 1H).
δ (ppm) 145.6 (CH), 138.1 (CH), 131.0 (C**, 130.0 (CH), 111.3 (CH), 26.7 (3CH3), 11.2 (2CH3). **Carbon not observed in 13C{1H} NMR, assigned by gHMBC. 11B{1H} NMR (160 MHz, CDCl3): δ (ppm) 35.86. HRMS (APCI) calcld for C14H14BN: [M + H]+: 207.1228. Found [M]+: 207.1219.

3-(2-Vinylphenyl)-2-vinyl-1,2-dihydro-1,2-azaborine (5). Compound 4 (103 mg, 0.347 mmol, 1.0 equiv) was dissolved in 1.7 mL of THF. A TBAB solution (1.0 M; 0.36 mL, 0.364 mmol, 1.0 equiv) was added, and the mixture was stirred for 10 min at room temperature. At the conclusion of the reaction, the solvent was removed under reduced pressure. The resulting crude material was filtered through a pad of silica gel (eluent EtOAc) to afford the corresponding 3-bromo-2-vinyl-1,2-dihydro-1,2-azaborine as a white oil, which could be used as is in the next step without further purification. In an oven-dried Biotage microwave vial equipped with a stir bar, the 3-bromo-2-vinyl-1,2-dihydro-1,2-azaborine (52 mg, 0.28 mmol, 1.0 equiv) and 2-vinylphenylboronic acid (55 mg, 0.37 mmol, 1.3 equiv) were dissolved in dioxane (2.87 mL). The resulting solution was treated with a suspension of cesium carbonate (1.73 mmol, 0.5 equiv) and the 2-vinylphenylboronic acid (134 mg, 0.58 mmol, 1.0 equiv) in dioxane (2.87 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The remaining residue was purified by flash column chromatography on silica gel (1% EtOAc/hexane) to give the corresponding 3-bromo-2-vinyl-1,2-dihydro-1,2-azaborine (52 mg, 0.28 mmol, 1.0 equiv) as a brown oil. 1H NMR (500 MHz, CDCl3): δ (ppm) 8.30 (s, 1H), 7.91 (br s, NH), 7.55 (d, J = 9.1 Hz, 1H), 7.44 (ap t, J = 8.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.21−7.17 (m, 1H), 6.68 (dd, J = 20.0, 13.9 Hz, 1H), 6.17 (dd, J = 20.0, 3.0 Hz, 1H), 6.03 (dd, J = 13.9, 3.0 Hz, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ (ppm) 145.9 (CH), 139.1 (C), 131.4 (CH*), 131.4 (CH*), 128.9 (CH), 128.8 (CH), 127.9 (C**), 125.3 (C), 121.9 (CH), 118.2 (CH). *Carbon not observed in 13C{1H} NMR, assigned by gHMBC. **Carbon not observed in 13C{1H} NMR, assigned by gHMBC.
arg. The reaction mixture was heated at reflux for 24 h. The crude product was cooled to room temperature, diluted with dichloromethane (10 mL), and filtered through a pad of silica gel. The filtrate was concentrated in vacuo, and the remaining residue was purified by flash column chromatography on silica gel (2% EtOAc/Hex) to give the corresponding 6,7-dihydro-7-aza-6a-boratetraphene 2 (94 mg, 0.41 mmol, 93%) as a white solid. Mp: 130−132 °C. 1H NMR (500 MHz, CDCl3): δ (ppm) 9.19 (s, 1H), 8.56 (d, J = 7.9 Hz, 1H), 8.46 (br s, NH), 8.03 (d, J = 11.9 Hz, 1H), 7.99 (dd, J = 8.0, 0.8 Hz, 1H), 7.68 (dd, J = 7.7, 1.5 Hz, 1H), 7.60−7.53 (m, 2H), 7.51−7.46 (m, 2H), 7.34 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 7.01 (d, J = 11.9 Hz, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ ppm 149.9 (CH), 139.8 (CH), 138.3 (CH), 134.8 (CH), 134.2 (CH), 134.0 (C*), 130.9 (CH), 130.7 (CH), 129.0 (CH), 127.1 (CH), 127.1 (CH*), 126.7 (CH), 125.1 (CH), 122.2 (CH), 118.5 (CH). **Carbon not observed in 13C{1H} NMR, assigned by gHSQC. 11B{1H} NMR (160 MHz, CDCl3): δ ppm 27.47. HRMS (APCI) calcd for C12H9BN [M + H]+: 256.1385. Found [M + H]+: 256.1289.

10-Phenyl(ethyl)-1,10a-dihydro-1-aza-10a-boraphenanthrene (12). To an oven-dried Schlenk flask charged with 9 (20.0 mg, 0.08 mmol, 1.0 equiv), phenylacetylene (26 μL, 0.24 mmol, 3.0 equiv), Pd(PPh3)2Cl2 (2.8 mg, 0.004 mmol, 5 mol %), and CuI (0.6 mg, 0.004 mmol, 5 mol %) was added, and the mixture was stirred at 80 °C for 2 h. The resulting mixture was successively washed with water (5 mL) and with dichloromethane (3 × 5 mL). The combined organic layers were dried over Na2SO4, filtered, and concentrated to a vacuum. The resulting product was purified by flash column chromatography on silica gel (hexanes/EtOAc 95:5) to give 12 as a brown oil (19 mg, 0.07 mmol, 88%). 1H NMR (500 MHz, CDCl3): δ (ppm) 9.25 (br s, NH), 8.97 (d, J = 7.4, 1.0 Hz, 1H), 8.47 (dd, J = 8.2, 1.2 Hz, 1H), 8.28 (s, 1H), 7.90−7.86 (m, 6H), 7.75 (dd, J = 8.1, 1.4 Hz, 1H), 7.64−7.61 (m, 2H), 7.55 (dd, J = 8.2, 7.1, 1.4 Hz, 1H), 7.45 (dd, J = 8.4, 7.1, 1.2 Hz, 1H), 7.42−7.34 (m, 3H), 6.93 (dd, J = 7.3, 6.1, 1.7 Hz, 1H). 13C{1H} NMR (125 MHz, CDCl3): δ (ppm) 147.8 (CH), 138.7 (CH), 135.3 (CH), 135.0 (C*), 134.6 (C), 133.4 (C), 131.7 (2CH), 131.1 (CH), 128.5 (2CH), 128.0 (CH), 127.4 (CH), 125.9 (C), 124.4 (C), 121.6 (11C*), 112.0 (CH), 94.9 (C), 90.6 (C). **Carbon not observed in 13C{1H} NMR, assigned by gHMBC. 11B{1H} NMR (160 MHz, CDCl3): δ (ppm) 27.47. HRMS (APCI) calcd for C12H9BN [M + H]+: 256.1385. Found [M + H]+: 256.1289. https://doi.org/10.1021/acs.joc.1c01095
(125 MHz, CDCl3; δ (ppm) 137.9 (CH), 135.8 (C*), 134.4 (CH), 134.1 (C*), 133.6 (CH), 131.9 (C), 129.5 (CH), 125.9 (CH), 125.1 (CH), 124.8 (CH), 121.3 (CH), 111.4 (CH), 67.4 (2CH2), 53.1 (2CH3)).**Carbon not observed in 13C(1H) NMR, assigned by gHMBC. 11B(1H) NMR (160 MHz, CDCl3; δ (ppm) 26.93. HRMS (APCI) calcd for C6H9BN2O [M + H]+: 264.1543. Found [M + H]+: 264.1549.

6-Phenyl-7-aza-6-boratetraphene (14). In a round-bottom flask equipped with a stir bar, the brominated BN-tetraphene (30.0 mg, 0.10 mmol, 1.0 equiv) and phenylboronic acid (33.0 mg, 0.27 mmol, 2.8 equiv) were dissolved in 0.40 mL of toluene and treated with a suspension of Na2CO3 (238.0 mg) in 1.0 mL of water. Then Pd(PPh3)4 (3.0 mg, 0.005 mmol, 5 mol %), and CuI (0.9 mg, 0.005 mmol, 5 mol %), phenylacetylene (32.0 mg, 0.30 mmol, 1.0 equiv), and CuI (0.9 mg, 0.005 mmol, 5 mol %) were added at this time, and the resulting solution was stirred for 6 h at room temperature. The reaction mixture was cooled to room temperature, diluted with methanol and treated with a suspension of Na2CO3 (238.0 mg) in 1.0 mL of water. Then Pd(PPh3)4 (5.6 mg, 0.005 mmol, 5 mol %) was added, and the mixture was heated to 70 °C and stirred overnight. After the addition of water (4 mL) and extraction with dichloromethane (3 mL). The combined organic layers were dried over Na2SO4, filtered, and concentrated under a vacuum. The crude organic product was purified by flash column chromatography on silica gel (1% AcOEt/hexane) to give the desired product as a yellow solid (16 mg, 0.05 mmol, 50%). Mp: 138–140 °C. 1H NMR (300 MHz, CDCl3; δ (ppm) 9.10 (s, 1H), 8.44 (br s, 1H), 8.38–8.40 (m, 1H), 7.96 (dd, J = 7.9; 1.3 Hz, 1H), 7.59–7.56 (m, 1H), 7.54–7.52 (m, 2H), 7.40–7.38 (m, 2H), 7.36–7.33 (m, 1H), 7.12 (s, 1H), 4.03–4.01 (m, 4H), 3.21–3.19 (m, 4H). 13C(1H) NMR (125 MHz, CDCl3; δ (ppm) 152.4 (C*), 138.9 (C), 138.3 (C), 134.1 (C*), 131.7 (C), 130.5 (CH), 129.6 (CH), 129.0 (CH), 127.1 (CH), 126.3 (CH), 125.3 (CH), 125.1 (C), 122.0 (CH), 121.5 (CH), 118.6 (CH), 67.4 (2CH2), 52.7 (2CH3).**Carbon not observed in 13C(1H) NMR, assigned by gHMBC. 11B(1H) NMR (160 MHz, CDCl3; δ (ppm) 27.51. HRMS (APCI) calcd for C6H9BN2O [M + H]+: 315.1667. Found [M + H]+: 315.1675.

7-Methyl-7-aza-6-boratetraphene (17). To a 4 mL reaction vial equipped with a stir bar was added 7-aza-6-boratetraphene (2 mg, 0.09 mmol, 1 equiv) followed by THF (0.18 mL). The vial was sealed and placed under an Ar atmosphere. LiHMDS (25 μL, 0.13 mmol, 1.5 equiv) was added dropwise via a syringe. The solution was stirred for 4 h at room temperature. After this time, the reaction mixture was cooled to 0 °C, and iodomethane (25 μL, 0.13 mmol, 1.5 equiv) was added. The reaction mixture was allowed to stir at 0 °C for 10 min, then warmed to room temperature. The solution was stirred at this temperature overnight. A second addition of LiHMDS (8 μL, 0.04 mmol, 0.5 equiv) and iodomethane (8 μL, 0.04 mmol, 0.5 equiv) were added at this time, and the resulting solution was stirred for 6 h at room temperature. The reaction was quenched with deionized H2O, and the aqueous layer was extracted with EtO. The organic layer was dried (Na2SO4), filtered, and concentrated under a vacuum. The resulting product was purified by flash column chromatography on silica gel (hexanes) to give the desired product 17 as a white solid (11.0 mg, 0.05 mmol, 52%). Mp: 114–116 °C. 1H NMR (500 MHz, CDCl3; δ (ppm) 9.19 (s, 1H), 8.57 (d, J = 7.9 Hz, 1H), 8.07–8.02 (m, 2H), 7.80 (d, J = 8.6 Hz, 1H), 7.71–7.67 (m, 2H), 7.56–5.3 (m, 1H), 7.47–7.41 (m, 1H), 7.39 (djd, J = 7.9, 1.0, 1.0 Hz, 1H), 7.24 (d, f = 12.2 Hz, 1H), 4.06 (s, 3H). 13C(1H) NMR (125 MHz, CDCl3; δ (ppm) 147.7 (CH), 141.8 (C), 138.5 (CH), 134.4 (C), 134.2 (C), 133.3 (C*), 131.5 (CH), 130.7 (CH), 129.4 (CH), 127.1 (CH), 127.1 (C), 126.6 (CH), 125.8 (C), 122.2 (CH), 120.8 (CH), 115.0 (CH), 35.2 (CH3).**Carbon not observed in 13C(1H) NMR, assigned by gHSQC. **Carbon not observed in 13C(1H) NMR, assigned by gHMBC. 11B(1H) NMR (160 MHz, CDCl3; δ (ppm) 29.51. HRMS (APCI) calcd for C7H10BN [M + H]+: 244.1295. Found [M + H]+: 244.1296.

**ASSOCIATED CONTENT**

Supporting Information
The Supporting Information is available free of charge at https://pubs.acs.org/10.1021/acs.joc.1c01095.

Photophysical data, X-ray crystallographic data for 2, and 1H, 13C(1H), and 11B(1H) NMR spectra for new compounds (PDF)

Accession Codes
CCDC 2073370 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

**AUTHOR INFORMATION**

Corresponding Authors
David Sucunza – Departamento de Química Orgánica y Química Inorgánica, Instituto de Investigación Química “Andrés M. del Río” (IQAR), Universidad de Alcalá, IRYCIS, 28805 Alcalá de Henares, Spain; orcid.org/0000-0002-3307-4204; Email: david.sucunza@uah.es
Juan J. Vaquero – Departamento de Química Orgánica y Química Inorgánica, Instituto de Investigación Química

The Journal of Organic Chemistry pubs.acs.org/joc

Article

16265

https://doi.org/10.1021/acs.joc.1c01095

J. Org. Chem. 2021, 86, 16259–16267
Authors
Isabel Valencia – Departamento de Química Orgánica y Química Inorgánica, Instituto de Investigación Química “Andrés M. del Río” (IQAR), Universidad de Alcalá, IRYCIS, 28805 Alcalá de Henares, Spain; orcid.org/0000-0002-3820-9673; Email: juanjose.vaquero@uah.es
Patricia García-García – Departamento de Química Orgánica y Química Inorgánica, Instituto de Investigación Química “Andrés M. del Río” (IQAR), Universidad de Alcalá, IRYCIS, 28805 Alcalá de Henares, Spain; orcid.org/0000-0003-3671-5828
Francisco Mendicuti – Departamento de Química Analítica, Química Física e Ingeniería Química, Instituto de Investigación Química “Andrés M. del Río” (IQAR), Universidad de Alcalá, 28805 Alcalá de Henares, Spain
Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c01095

Notes
The authors declare no competing financial interest.

ACKNOWLEDGMENTS
We are grateful to the Ministerio de Ciencia e Innovación, AEI and FEDER (projects CTP2017-85263-R, RTI2018-097609-B-C21 and FPU predoctoral grant for I.V.), Instituto de Salud Carlos III (FEDER funds, ISCIII RETIC REDINREN RD16/009/0015), and the University of Alcalá (projects CCG19/CC-017 and CCG19/CC-033) for financial support.

REFERENCES
(1) (a) Giustra, Z. X.; Liu, S.-Y. The State of the Art in Azaborine Chemistry: New Synthetic Methods and Applications. J. Am. Chem. Soc. 2018, 140, 1184−1194. (b) Bosdet, M. J. D.; Piers, W. E. B-N as a C-C substitute in aromatic versus C-C: how similar are they? Can. J. Chem. 2009, 87, 3669−3678. (c) Zhang, C.; Zhang, L.; Sun, C.; Sun, W.; Liu, X. BN-Phenanthrenes: Synthesis, Reactivity, and Optical Properties. Org. Lett. 2019, 21, 3476−3480. (d) Yruegas, S.; Martinez, J. J.; Martin, C. D. Intermolecular insertion reactions of azides into 9-borafuroles to generate 9,10-B,N-azaborine chemistry. Chem. Commun. 2018, 54, 6808−6811. (e) Zhang, W.; Li, G.; Xu, L.; Zhou, Y.; Wan, W.; Yan, N.; He, G. 9,10-Azaborphenanthrene-containing small molecules and conjugated polymers: synthesis and their application in chemodosimeters for the ratiometric detection of fluoride ions. Chem. Sci. 2018, 9, 4444−4450. (f) Abengózar, A.; García-García, P.; Sucunza, D.; Frutos, L. M.; Castroño, O.; Sampedro, D.; Pérez-Redondo, A.; Vaquero, J. J. Synthesis, Functionalization, and Optical Properties of 1,2-Dihydro-1-aza-2-boraphenanthrene and Several Highly Fluorocent Derivatives. Org. Lett. 2019, 21, 2550−2554. (g) Zhang, C.; Zhang, L.; Sun, C.; Sun, W.; Liu, X. BN-Phenanthrenes: Synthesis, Reactivity, and Optical Properties. Org. Lett. 2019, 21, 3476−3480. (d) Yruegas, S.; Martinez, J. J.; Martin, C. D. Intermolecular insertion reactions of azides into 9-borafuroles to generate 9,10-B,N-azaborine chemistry. Chem. Commun. 2018, 54, 6808−6811. (e) Zhang, W.; Li, G.; Xu, L.; Zhou, Y.; Wan, W.; Yan, N.; He, G. 9,10-Azaborphenanthrene-containing small molecules and conjugated polymers: synthesis and their application in chemodosimeters for the ratiometric detection of fluoride ions. Chem. Sci. 2018, 9, 4444−4450. (f) Abengózar, A.; García-García, P.; Sucunza, D.; Frutos, L. M.; Castroño, O.; Sampedro, D.; Pérez-Redondo, A.; Vaquero, J. J. Synthesis, Optical Properties, and Regioselective Functionalization of 4a-Aza-10a-boraphenanthrene. Org. Lett. 2017, 19, 3458−3461 and references cited therein.
(10) Ishibashi, J. S. A.; Dargelos, A.; Darrigan, C.; Chrostowska, A.; Liu, S.-Y. BN Tetracene: Extending the Reach of BN/CC Isosterism in Acenes. Organometallics 2017, 36, 2499−2497.
(11) (a) Huang, J.; Li, Y. BN Embedded Polycyclic π-Conjugated Oligomers and Polymers. Chem. - Eur. J. 2016, 22, 12972−12982. (b) Bosdet, M. J. D.; Piers, W. E. B-N as a C-C substitute in aromatic systems. Can. J. Chem. 2009, 87, 8−29. (c) Liu, Z.; Marder, T. B. B-N versus C-C: how similar are they? Angew. Chem., Int. Ed. 2008, 47, 242−244.
(3) For reviews, see: (a) Huang, J.; Li, Y. BN Embedded Polycyclic π-Conjugated Systems: Synthesis, Optoelectronic Properties, and Photovoltaic Applications. Front. Chem. 2018, 6, 341. (b) Wang, J.-Y.; Pei, J. BN-embedded aromatics for optoelectronic applications. Chin. Chem. Lett. 2016, 27, 1139−1146. (4) (a) Zhao, P.; Nettleton, D. O.; Karki, R. G.; Zecchi, F. J.; Liu, S.-Y. Medicinal Chemistry Profiling of Monocyclic 1,2-Azaborines. ChemMedChem 2017, 12, 358−361. (b) Lee, H.; Fischer, M.; Shoichet, B. K.; Liu, S.-Y. Hydrogen Bonding of 1,2-Azaborines in the Binding Cavity of T4 Lysozyme Mutants: Structures and Thermodynamics. J. Am. Chem. Soc. 2016, 138, 12021−12024. (c) Vasceanu, A.; Jessing, M.; Kilburn, J. P. BN/CC isosterism in borazaronaphthalenes towards phosphodiesterase 10A (PDE10A) inhibitors. Bioorg. Med. Chem. 2015, 23, 4435−4461. (d) Rombouts, F. J. R.; Tovar, F.; Austin, N.; Tresadern, G.; Trabanco, A. A. Benzazaborinines as Novel Bioisosteric Replacements of Naphthalene: Propanolol as an Example. J. Med. Chem. 2015, 58, 9287−9295. (e) Knack, D. H.; Marshall, J. L.; Harlow, G. P.; Dudzik, A.; Szałeniec, M.; Liu, S.-Y.; Heider, J. BN/CC isosteric compounds as enzyme inhibitors: N- and B-ethyl-1,2-azaborine inhibit ethylbenzene hydroxylation as nonconvertible substrate analogues. Angew. Chem., Int. Ed. 2013, 52, 2599−2601. (5) (a) McConnell, C. R.; Campbell, P. G.; Fristoe, C. R.; Memmel, P.; Zakharov, L. N.; Li, B.; Darrigan, C.; Chrostowska, A.; Liu, S.-Y. Synthesis and Characterization of 1,2-Azaborine-Containing Phosphine Ligands: A Comparative Electronic Structure Analysis. Eur. J. Inorg. Chem. 2017, 2017, 2207−2210. (b) Son, F.; Huang, M.; Zhou, Z.; Fang, X. 4a,8a-Azaboronaphthalene-4-yl phosphine ligands: synthesis and electronic modulation in Suzuki−Miyaura coupling reactions. RSC Adv. 2015, 5, 75607−75611. (6) (a) McConnell, C. R.; Liu, S.-Y. Late-stage functionalization of BN-heterocycles. Chem. Soc. Rev. 2019, 48, 3436−3453. (b) Béland-Chabot, G.; Braunschweig, H.; Roy, D. K. Recent Developments in Azaborinone Chemistry. Eur. J. Inorg. Chem. 2017, 2017, 4353−4368. (c) Campbell, P. G.; Marwitz, A. J. V.; Liu, S.-Y. Recent advances in azaborine chemistry. Angew. Chem., Int. Ed. 2012, 51, 6074−6092. (7) Abengózar, A.; García-García, P.; Fernández-Rodríguez, M. A.; Sucunza, D.; Vaquero, J. J. Recent developments in the chemistry of BN-aromatic hydrocarbons. Adv. Heterocycl. Chem. 2021, 135, 197−258.
(16) Abengózar, A.; Sucunza, D.; García-García, P.; Vaquero, J. J. Remarkable effect of alkynyl substituents on the fluorescence properties of a BN-phenanthrene. Beilstein J. Org. Chem. 2019, 15, 1257–1261.

(b) Huang, H.; Zhou, Y.; Wang, M.; Zhang, J.; Cao, X.; Wang, S.; Cao, D.; Cui, C. Regioselective Functionalization of Stable BN-Modified Luminescent Tetraphenes for High-Resolution Fingerprint Imaging. Angew. Chem., Int. Ed. 2019, 58, 10132–10137.

(c) Abengózar, A.; Fernández-González, M. A.; Sucunza, D.; Frutos, L. M.; Salgado, A.; García-García, P.; Vaquero, J. J. C–H Functionalization of BN-Aromatics Promoted by Addition of Organolithium Compounds to the Boron Atom. Org. Lett. 2018, 20, 4902–4906.

(17) Brown, A. N.; Li, B.; Liu, S.-Y. Negishi Cross-Coupling Is Compatible with a Reactive B–Cl Bond: Development of a Versatile Late-Stage Functionalization of 1,2-Azaborines and Its Application to the Synthesis of New BN Isosteres of Naphthalene and Indenyl. J. Am. Chem. Soc. 2015, 137, 8932–8935.

(18) Molander, G. A.; Wisniewski, S. R. Accessing Molecularly Complex Azaborines: Palladium-Catalyzed Suzuki–Miyaura Cross-Couplings of Brominated 2,1-Borazaronaphthalenes and Potassium Organotrifluoroborates. J. Org. Chem. 2014, 79, 6663–6678.

(19) Dewar, M. J. S.; Dietz, R. New heteroaromatic compounds. Part III. 2,1-Borazaro-naphthalene (1,2-dihydro-1-aza-2-boranaphthalene). J. Chem. Soc. 1959, 2728–2730.

(20) CCDC 2073370 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

(21) Brouwer, A. M. Standards for photoluminescence quantum yield measurements in solution (IUPAC Technical Report). Pure Appl. Chem. 2011, 83, 2213–2228.

(22) (a) Li, G.; Chen, Y.; Qiao, Y.; Lu, Y.; Zhou, G. Charge Transfer Switching in Donor–Acceptor Systems Based on BN-Fused Naphthalimides. J. Org. Chem. 2018, 83, 5577–5587. (b) Han, Y.; Yuan, W.; Wang, H.; Li, M.; Zhang, W.; Chen, Y. Dual-responsive BN-embedded phenacenes featuring mechanochromic luminescence and ratiometric sensing of fluoride ions. J. Mater. Chem. C 2018, 6, 10456–10463. (c) Zhou, J.; Tang, R.; Wang, X.; Zhang, W.; Zhuang, X.; Zhang, F. BN-heteroacene-cored luminogens with dual channel detection for fluoride anions. J. Mater. Chem. C 2016, 4, 1159–1164.

(23) Brettell-Adams, I. A.; Andreen, A. V.; Bhattacharyya, S.; Rupar, P. A. Iodine is a common impurity in tetrabutylammonium fluoride. Sens. Actuators, B 2018, 258, 597–601.