Synthesis of 2,8-Disubstituted Analogues of Troeger's Base

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Abstract: Starting from the 2,8-dibromo- and the 2,8-diiodo-substituted Troeger's base analogues **1** and **2**, several new symmetrically disubstituted derivatives **4**, **5**, and **7**–**17** could be obtained by transition metal-catalyzed cross-coupling reactions or other functionalizations like borylation or protecting group operations. For the first time, conditions for a highly efficient Suzuki cross-coupling reaction involving the Troeger's base core were established.

Key words: Troeger's base, cross-coupling reactions, Suzuki reaction

Troeger's base (Figure 1) was first synthesized more than hundred years ago in 1887.[1] However, its structure was not eludicated until 1935.[2] Due to the rigid shape of the molecule, both N-atoms are sterically fixed. Thus, the molecule is dissymmetric and therefore chiral.

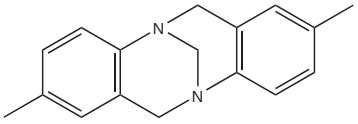

Figure 1 Troeger's base

Besides this special stereochemical situation that made this molecule become one of the textbook examples for explaining dissymmetry,[3] it is the unique V-shaped structure of the compound that has attracted the interest of many chemists, since its rigid conformation makes it an almost ideal building block to introduce curvature into larger molecules. This is, of course, of major importance in supramolecular chemistry, e.g. in order to achieve concave structures of receptor molecules.[4–6]

Troeger's base derivatives are usually formed by reaction of an aniline, formaldehyde, and a strong acid.[7] This condensation has been limited to electron-rich anilines for a long time. Only recently, however, Wärnmark and coworkers succeeded in the synthesis of halo-substituted analogues of Troeger's base using paraformaldehyde, trifluoroacetic acid, and the corresponding aniline.[8] Although they showed that the formation is very sensitive to the reaction conditions, especially the scale,[9] this method allows easy access to symmetrically dihalogen-substituted analogues in almost any position in each of the two aromatic rings.[10] Independent of the scale, however, the reaction generally works best with 4-halo-2-methylanilines because the electron-donating character of the methyl group facilitates the electrophilic aromatic substitution being part of the formation mechanism.[8]

Within the course of our studies concerning the formation of self-assembled supramolecular receptors[11,12] the 2,8-dibromo- and 2,8-diiodo analogues **1** and **2** (Figure 2) of Troeger's base attracted our interest and prompted us to evaluate the possibilities to apply them as substrates in a number of transition-metal catalyzed cross-coupling reactions[13] and some other transformations in order to get access to versatile difunctionalized rigid molecules with extended V-shaped cores. This paper describes the synthesis of a number of racemic 2,8-disubstituted derivatives of Troeger's Base (Table 1) that were prepared from **1** and **2** in Ullmann, Sonogashira, and Suzuki cross-coupling reactions as well as by some further functionalizations like borylation or protecting group operations.

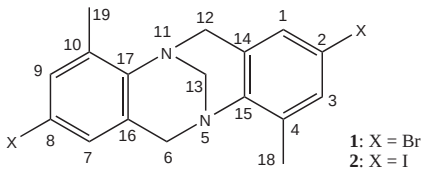

Figure 2 2,8-Dibromo-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (**1**), 2,8-diiodo-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (**2**)

The dimethoxy derivative **3** could already be synthesized by Wilcox in 1988 by condensation of 4-methoxy-2-methylaniline and formaline in acidic ethanol solution, but the yield was only 14%.[14] Treatment of **2** with sodium methoxide under Ullmann conditions gave **3** in almost quantitative yield. Subsequent deprotection of **3** with boron tribromide gave the 2,8-dihydroxy derivative **4** (Scheme 1).

The dialkyne **6**, which contains two ethynyl groups in the 2- and 8-positions of Troeger's base and, therefore, is a very interesting compound with regard to its possible application in building up larger supramolecular aggregates, has already been synthesized through a Corriu–Kumada reaction of **2** and ethynylmagnesium bromide.[8] An alternative route to this molecule is a Sonogashira reaction of **1** or **2** with trimethylsilylacetylene followed by deprotection of the TMS group. This approach offers the possibility to further elaborate the core prior to deprotection or to deprotect the initial Sonogashira product in a stepwise manner in order to differentiate the two terminal groups

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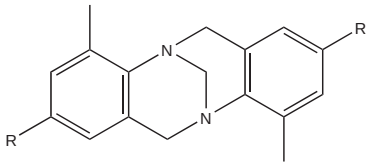
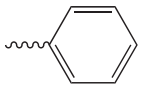
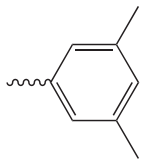
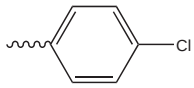
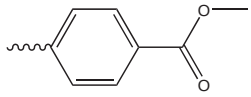
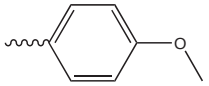
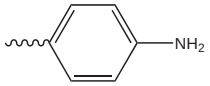
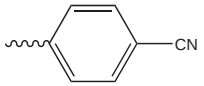
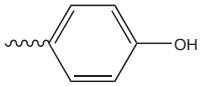
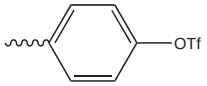
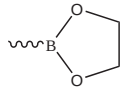
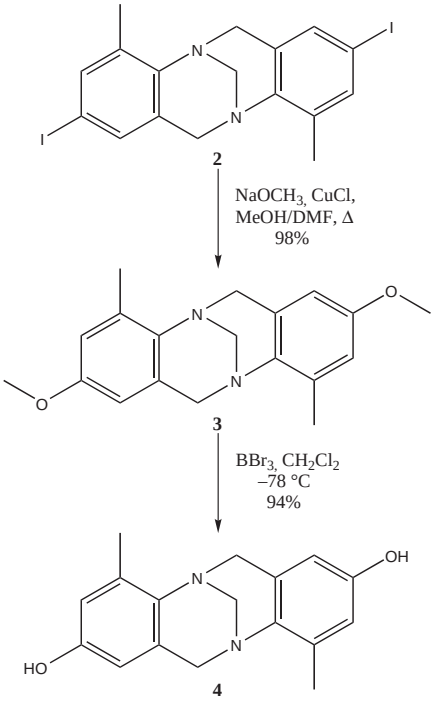
Table 1 2,8-Disubstituted Analogues of Troeger's Base Derived by Transition Metal-Catalyzed Cross-Couplings and Further Functionalizations



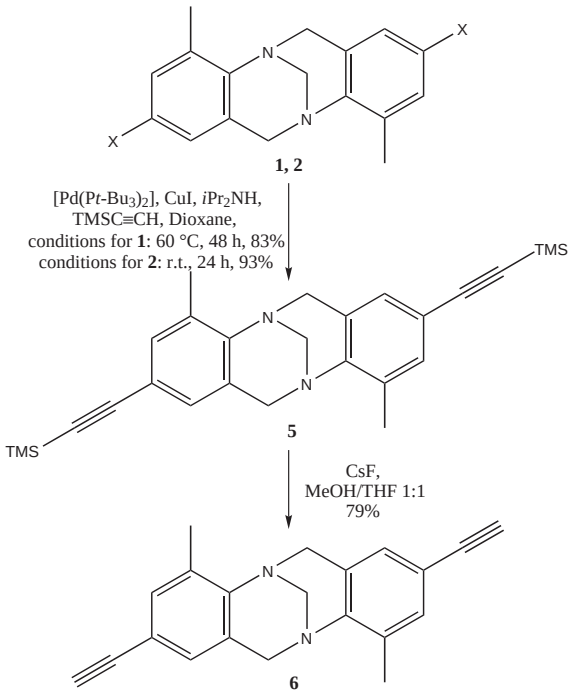
Entry	R	Product
1	OCH_3	**3**
2	OH	**4**
3	C≡CTMS	**5**
4	C≡CH	**6**
5		**7**
6		**8**
7		**9**
8		**10**
9		**11**
10		**12**
11		**13**
12		**14**
13		**15**
14	$B(OH)_2$	**16**
15		**17**



Scheme 1 Ullmann methoxylation of **2** followed by demethylation.

through further functionalization. Recently, a general protocol for the use of **2** in Sonogashira reactions based on a protocol of Fu[15] has been established to introduce several alkyne moieties into the Troeger's base skeleton.[16] Reactions were carried out at room temperature using the highly reactive catalytic system [Pd(P*t*-$Bu_3)_2$], which we were already able to use in other cross-couplings[17] and which is necessary due to the relatively electron-rich character of the benzene rings of the Troeger's base core. We have also applied these conditions to the synthesis of **5**, which could be obtained from both **1** at 60 °C and **2** at room temperature in good to excellent yields. Finally, complete deprotection with cesium fluoride yielded **6** (Scheme 2).

Due to the air and moisture stabilty of boronic acids and their derivatives, the palladium-catalyzed Suzuki reaction is a very versatile and powerful method to form C–C bonds, especially aryl–aryl bonds.[13] So far, there has not been any existing protocol for the Suzuki reaction involving analogues of Troeger's base. The successful Sonogashira cross-couplings of ethynyl derivatives and Troeger's base halides, however, led us to use the same palladium phoshane complex, i.e. [Pd(P*t*-$Bu_3)_2$], in the Suzuki reaction. Thus, a general protocol from Fu and coworkers which also included the use of potassium fluoride as a base and THF as solvent was adapted[18] and first applied to **1**, which we expected to react more reluctantly than **2** due to the much higher reacitivity of iodine compared to bromine in cross-coupling reactions.[19] Compounds **7** and **8** were synthesized this way in good to excellent yields (Table 2).

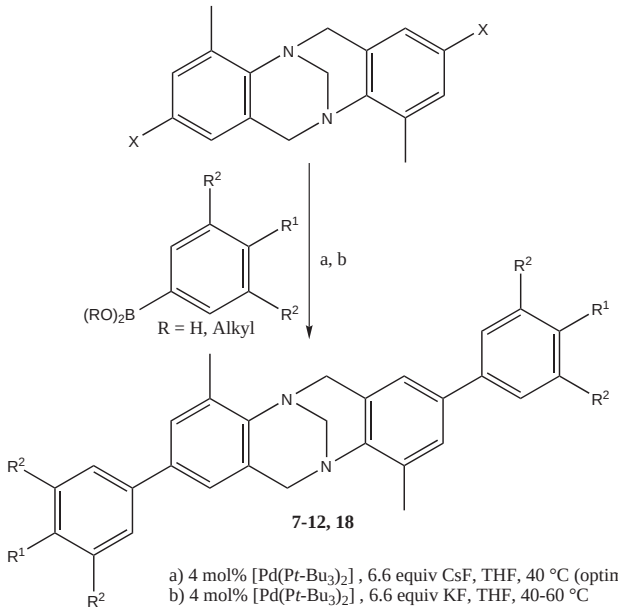


Scheme 2 Sonogashira reaction of **1** and **2** with TMSC≡CH and deprotection of **5** with CsF.

Since $[Pd(Pt\text{-}Bu_3)_2]$ is rather expensive it should be mentioned that we also tested a more conventional and cheaper catalytic system consisting of $[Pd(PPh_3)_4]$ and potassium phosphate in DMF in the synthesis of **8**, but even after two days of refluxing no conversion could be detected. The next logical step was the use of boronic acids substituted with different functional groups.

With respect to the aim to integrate the Troeger's base core into larger (supra)molecular structures, the use of *para*-substituted arylboronic acids is of great interest because a potential *p*-phenylene spacer for larger structures is provided by this strategy. Therefore, our attention was especially turned to the synthesis of *p*-bromo- and *p*-chlorophenyl substituted analogues of Troegers base **18** and **9**, which provide a promising basis for further cross-coupling reactions. Following the protocol for the synthesis of **7** and **8**, the diiodo derivative **2** was chosen as reactant instead of **1** for reactivity reasons. After one day at 60 °C, however, no conversion could be detected in both reactions. Thus, the reaction mixtures were refluxed for another day, which unfortunately led to a complicated mixture of multi-coupling products in case of the 4-bromophenylboronic acid. Nevertheless, **9** could be isolated in 53% yield at least. This result encouraged us to optimize the re-

Table 2 Introduction of Substituted Aryl Moieties into the Troeger's Base Core via Suzuki Reactions

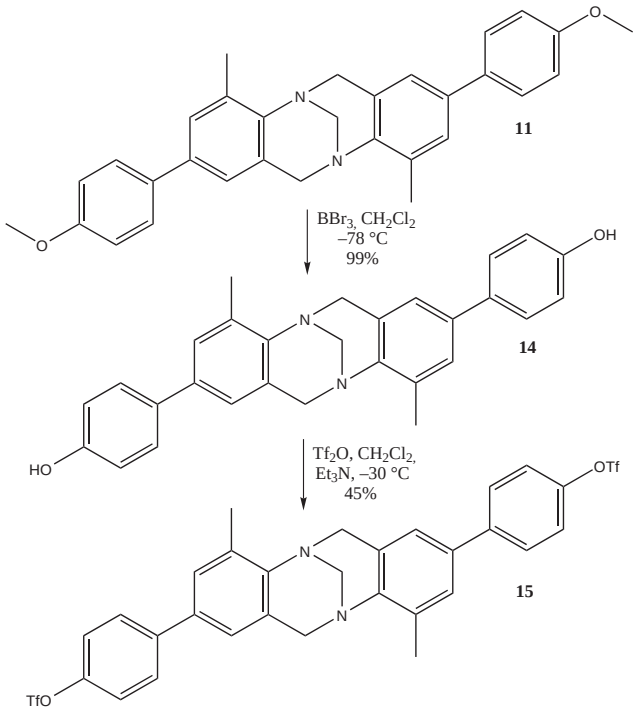


a) 4 mol% $[Pd(Pt\text{-}Bu_3)_2]$, 6.6 equiv CsF, THF, 40 °C (optimized)
b) 4 mol% $[Pd(Pt\text{-}Bu_3)_2]$, 6.6 equiv KF, THF, 40-60 °C

Entry	X	R^1	R^2	Method	Product	Yield (%)
1	Br	H	H	b	7	90
2	Br	H	CH_3	b	8	65
3	I	Cl	H	a	9	97
4	I	CO_2CH_3	H	a	10	85
5	I	OCH_3	H	a	11	93
6	I	Br	H	a	18	–
7	I	NH_2	H	a	12	–

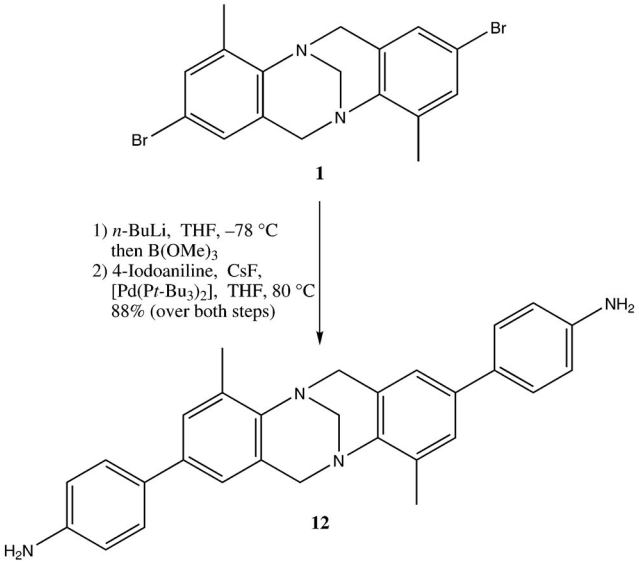
action conditions. Eventually, the change from potassium fluoride to the stronger base cesium fluoride turned out to be very efficient because **9** could now be synthesized in a very smooth reaction at 40 °C in 97% yield (Table 2). Unfortunately, the same polymeric products were obtained again when applying the optimized protocol for the synthesis of **18** probably due to the highly active [Pd(P*t*-$Bu_3)_2$]. Also, the introduction of a *p*-aminophenyl group failed: even after refluxing for 2 days, no conversion could be detected. However, using the same protocol, 4-(methoxycarbonyl)phenyl **10** and 4-methoxyphenyl **11** moieties could be introduced into the Troeger's base core in excellent yields (Table 2).

Triflates do have about the same reactivity as bromides in cross-coupling reactions.[13] Thus, we tried to get access to the corresponding ditriflate as a substitute for the dibromide **18** by deprotection of **11** with boron tribromide to yield **14** and subsequent reaction of the diol with trifluoromethanesulfonic acid anhydride (Tf_2O) (Scheme 3). Following this approach **14** was synthesized in a similiar way as **4** and could be obtained in a quantitative yield from **11**. Surprisingly, the formation of the ditriflate **15** turned out to be problematic since the desired product could only be obtained in a moderate yield of 45%.



Scheme 3 Two-step synthesis of the diftriflate **15** from the dimethoxy derivative **11**

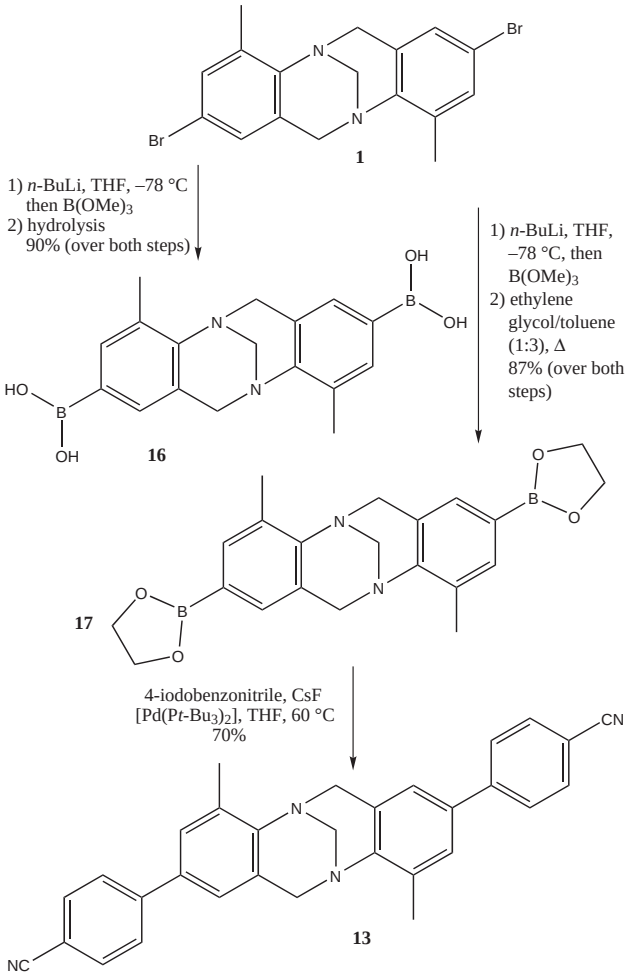
Because the optimized protocol for the Suzuki reaction did not give access to the dianiline analogue **12**, we decided to synthesize it by lithiation of **1** using a published procedure,[20] then forming a diboronic acid derivative in situ by adding trimethyl borate, and finally applying the optimized Suzuki protocol for the reaction with 4-iodoaniline (Scheme 4).



Scheme 4 Bromine–lithium exchange and Suzuki cross-coupling

Since we succeeded to synthesize the diamine **12** by first generating a diboronic acid derivative, the next step was to isolate such a derivative which can be used as a substrate for any of the performed and listed Suzuki cross-couplings. Thus, we performed the bromine–lithium exchange again and the resulting mixture was either hydrolyzed to yield the diboronic acid **16** or concentrated in vacuo followed by heating to reflux in a toluene/glycol mixture (3:1)[21] to give the corresponding diboronic acid ester **17**. The diboronic acid ester **17** was then tested as a substrate in an exemplary Suzuki reaction using the optimized protocol and 4-iodobenzonitrile to obtain **13** in a good yield of 70% (Scheme 5), which proved the principal applicability of **17** in Suzuki reactions.

In conclusion, we have demonstrated that the dibromo (**1**) and the diiodo (**2**) derivatives of Troeger's base are very versatile starting materials for the preparation of elaborated derivatives of Troeger's base. Using cross-coupling conditions, like Ullmann, Sonogashira, or Suzuki-reactions allowed the synthesis of a number of new 2,8-disubstituted analogues and has improved the synthesis of previously known derivatives like **3** and development of an alternative route to diethynylated compound **6**. Furthermore we could show that **1** and **2** as well as some of the cross coupling products could be used for further transfomations involving, for example, the formation of valuable ditriflate **15** and bis(boronic acid) derivatives **16** and **17**. Except for the formation of ditriflate **15** all of these reactions could be performed in very good to excellent yields. These compounds do represent versatile derivatives of Troeger's base that in most cases have elongated rigid V-shaped structures bearing functional groups useful for further elaborations and we are currently trying to use them for the synthesis of ditopic ligands that are thought to form dinuclear helicates.



Scheme 5 Synthesis of **16** and **17**, two substrates for Suzuki cross-couplings as demonstrated exemplarily for the formation of **13**.

All reactions except the synthesis of **6** were performed under argon using standard Schlenk techniques and oven-dried glassware prior to use. TLC was performed on aluminum TLC plates silica gel 60 F_{254} from Merck. Detection was done by UV-light (254 and 366 nm). Products were purified by column chromatography on silica gel 60 (70–230 mesh) from Merck. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 500 spectrometer at 300 K at 500.1 and 125.8 MHz, respectively. ^{19}F NMR spectra were recorded on a Bruker DPX 300 spectrometer at 300 K at 282.4 MHz. ^{1}H NMR chemical shifts are reported on the δ-scale (ppm) relative to residual nondeuterated solvent as internal standard. ^{13}C NMR chemical shifts are reported on the δ-scale relative to deuterated solvent as internal standard. ^{19}F NMR chemical shifts are reported on the δ-scale relative to CCl_3F as external standard. Signals were assigned on the basis of ^{1}H, ^{13}C, H,H-COSY, HMQC, and HMBC NMR experiments. Numbering of the ^{1}H and ^{13}C nuclei was done according to the one shown in Figure 2. Mass spectra were taken on a Finnigan MAT 212 with data system MMS–ICIS (EI, CI, *i*-butane, NH_3) or a Finnigan MAT 95 with data system DEC-Station 5000 (CI, *i*-butane or NH_3; HiRes-CI, *i*-butane or NH_3; FD). Mps were measured with a hot-stage microscope SM-Lux from Leitz and are not corrected. Elemental analyses were carried out with a Fisons Instrument EA1108.

Most solvents were dried, distilled and stored over argon according to standard procedures. *n*-BuLi solutions were purchased from Merck and were titrated prior to use against *N*-pivaloyl-*o*-toluidine.[22] All chemicals were used as received from commercial sources. **1**,[8] **2**,[8] [Pd(P*t*-$Bu_3)_2$][23] and [$Pd(PPh_3)_4$][24] were prepared according to published procedures.

2,8-Dimethoxy-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (3)[14]

Compound **2** (500 mg, 1.0 mmol), NaOMe (290 mg, 5.4 mmol), and CuCl (27 mg, 0.27 mmol) were suspended in a mixture of MeOH (5 mL) and DMF (3 mL) and heated at 80 °C. After 16 h, the suspension was slowly cooled down and a mixture of diisopropyl ether (7 mL), H_2O (15 mL), and 5% aq NH_4Cl solution (10 mL) were added and the resulting solution was stirred at r.t. After 5 h, the solution was filtered over Celite and the filtrate was extracted with CH_2Cl_2 (4 ×). The combined organic layers were washed with aq 5 N NaOH and dried (Na_2SO_4). Concentration in vacuo gave 309 mg (99%) of **3** as a brown solid; mp 129–131 °C (Lit.[14] mp 127–131 °C).

^{1}H and ^{13}C NMR data were in accordance with the literature,[14] where no assignments had been given.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.38 (s, 6 H, H-18, H-19), 3.69 (6 H, OCH_3), 3.90 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –16.5 Hz), 4.30 (s, 2 H, H-13), 4.53 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –16.5 Hz), 6.29 (d, 2 H, H-1, H-7, ^4J = 2.8 Hz), 6.63 (d, 2 H, H-3, H-9, ^4J = 2.8 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.2 (C-18, C-19), 55.3 (OCH_3), 55.5 (C-6, C-12), 68.0 (C-13), 108.4 (C-1, C-7), 115.3 (C-3, C-9), 128.8 (C-14, C-16), 134.3 (C-4, C-10), 139.0 (C-15, C-17), 155.8 (C-2, C-8).

MS (CI, *i*-butane): *m*/*z* = 311.2 ([$C_{19}H_{23}N_2O_2$]$^+$, 100).

2,8-Dihydroxy-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (4)

Compound **3** (100 mg, 0.32 mmol) was dissolved in CH_2Cl_2 (7 mL) and cooled to –78 °C. After addition of 1 M BBr_3 solution in CH_2Cl_2 (1.3 mL, 1.3 mmol) at this temperature, the reaction mixture was allowed to come to r.t. and stirred for 5 h. Aq 2 N NaOH was added until the excess of BBr_3 had been completely hydrolyzed. After addition of EtOAc (10 mL), the solution was neutralized using 6 N HCl and extracted with EtOAc (3 ×). Concentration in vacuo gave 85 mg (94%) of **4** as a yellow solid; mp >300 °C.

^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 2.42 (s, 6 H, H-18, H-19), 3.72 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –16.5 Hz), 4.10 (s, 2 H, H-13), 4.37 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –16.5 Hz), 6.16 (d, 2 H, H-1, H-7, ^4J = 2.8 Hz), 6.44 (d, 2 H, H-3, H-9, ^4J = 2.8 Hz), 8.86 (s, 2 H, OH).

^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 16.7 (C-18, C-19), 54.8 (C-6, C-12), 67.5 (C-13), 109.9 (C-1, C-7), 115.6 (C-3, C-9), 128.9 (C-14, C-16), 133.2 (C-4, C-10), 137.4 (C-15, C-17), 152.9 (C-2, C-8).

MS (CI, *i*-butane): *m*/*z* = 283.1 ([$C_{17}H_{19}N_2O_2$]$^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}N_2O_2$: 282.1369; found: 282.1368.

4,10-Dimethyl-2,8-bis[(trimethylsilyl)ethynyl]-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (5)

Compound **2** (500 mg, 1.0 mmol), [Pd(P*t*-$Bu_3)_2$] (6 mol%, 30.7 mg), and CuI (7.6 mg, 4 mol%) were dissolved in 1,4-dioxane (5 mL). To this solution were added trimethylsilylacetylene (0.56 mL, 4.0 mmol) and *i*-Pr_2NH (0.34 mL, 2.4 mmol). After 20 h, the reaction mixture was quenched with sat. aq NaCl (5 mL) and filtered over Celite. The residue was extracted with CH_2Cl_2. The filtrate was washed with aq sat. $NaHCO_3$ (2 ×), dried (Na_2SO_4), and concentrated in vacuo. Purification by column chromatography (toluene–EtOAc, 20:1 + 0.5% Et_3N, R_f = 0.58) gave 410 mg (93%) of **5** as a yellow solid; mp 67–69 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 0.19 [s, 18 H, $Si(CH_3)_3$], 2.33 (s, 6 H, H-18, H-19), 3.91 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz),

4.27 (s, 2 H, H-13), 4.50 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 6.89 (d, 2 H, H-1, H-7, ^4J = 1.1 Hz), 7.15 (m, 2 H, H-3, H-9).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 0.0 [Si(*C*H$_3$)$_3$], 16.9 (C-18, C-19), 54.8 (C-6, C-12), 67.5 (C-13), 93.1 (C≡*C*TMS), 105.0 (*C*≡CTMS), 118.3, (C-2, C-8), 127.8 (C-14, C-16), 128.1 (C-1, C-7), 132.5 (C-3, C-9), 132.8 (C-4, C-10), 146.3 (C-15, C-17).

MS (CI, *i*-butane): *m*/*z* = 443.2 ([$C_{27}H_{35}N_2Si_2$]$^+$, 100).

HRMS (CI, *i*-butane): *m*/*z* calcd for [$C_{27}H_{35}N_2Si_2$]$^+$: 443.2345; found: 443.2338.

2,8-Diethynyl-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (6)[8]

Compound **5** (200 mg, 0.45 mmol) and CsF (275 mg, 1.8 mmol) were dissolved in MeOH (15 mL) and THF (15 mL). After 16 h, the solution was concentrated in vacuo and the crude product purified by column chromatography (toluene–EtOAc, 20:1 + 0.5% Et_3N, R_f = 0.42) to give 106 mg (79%) of **6**; mp 173–175 °C (Lit.[8] mp 174 °C).

^{1}H and ^{13}C NMR data were in accordance with the literature,[8] where no assignments had been given to the quaternary carbons.

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 16.9 (C-18, C-19), 54.7 (C-6, C-12), 67.3 (C-13), 76.2 (C≡CH), 83.5 (C≡CH), 117.3, (C-2, C-8), 128.0 (C-14, C-16), 128.3 (C-1, C-7), 132.6 (C-3, C-9), 133.1 (C-4, C-10), 146.7 (C-15, C-17).

MS (EI): *m*/*z* = 298.1 ([$C_{21}H_{18}N_2$]$^+$, 100).

2,8-Disubstituted Analogues of Troeger's Base Obtained by Suzuki Cross-Coupling Reactions; General Procedure

To a stirred mixture of either **1** or **2** (1 equiv), KF or CsF (6.6 equiv), [Pd(P*t*-Bu$_3$)$_2$] (4 mol%), and the corresponding boronic acid derivative (2.4 equiv) was added THF (10 mL) with a syringe. The resulting solution was heated (40–80 °C) and the stirring was continued. After 6–48 h, CH_2Cl_2 was added and the mixture was washed with aq sat. solution of Na_2CO_3 (2 ×). The combined aqueous layers were extracted with CH_2Cl_2 (3 ×), and the combined CH_2Cl_2 layers were washed with brine, dried (Na_2SO_4), concentrated in vacuo, and purified by column chromatography.

4,10-Dimethyl-2,8-diphenyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (7)

Following the general procedure compound **1** (200 mg, 0.49 mmol), KF (188 mg, 3.23 mmol), [Pd(P*t*-Bu$_3$)$_2$] (10 mg), and phenylboronic acid (143 mg, 1.18 mmol) in THF were heated for 24 h at 40 °C. Column chromatography (toluene–EtOAc, 5:1 + 0.5% Et_3N, R_f = 0.63) gave 180 mg (91%) of **7** as a white solid; mp 181–183 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.49 (s, 6 H, H-18, H-19), 4.12 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.41 (s, 2 H, H-13), 4.69 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 7.02 (d, 2 H, H-1, H-7, ^4J = 1.6 Hz), 7.27 (dd, 2 H, H-4$_{Ph}$, ^3J = 8.2 Hz, ^4J = 1.1 Hz), 7.30 (d, 2 H, H-3, H-9, ^4J = 1.6 Hz), 7.37 (dd, 4 H, H-3$_{Ph}$, H-5$_{Ph}$, ^3J = 7.7 Hz, ^3J = 8.2 Hz), 7.48 (dd, 4 H, H-2$_{Ph}$, H-6$_{Ph}$, ^3J = 7.7 Hz, ^4J = 1.1 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.3 (C-18, C-19), 55.2 (C-6, C-12), 67.7 (C-13), 123.1 (C-1, C-7), 126.8 (C-3$_{Ph}$, C-5$_{Ph}$,), 126.9 (C-4$_{Ph}$)*, 127.9 (C-3, C-9), 128.6 (C-14, C-16, C-2$_{Ph}$, C-6$_{Ph}$,), 133.3 (C-4, C-10), 136.9 (C-2, C-8)*, 140.8 (C-15, C-17, C-1$_{Ph}$); (*assignment not confirmed).

MS (CI, *i*-butane): *m*/*z* = 403.3 ([$C_{29}H_{27}N_2$]$^+$, 100).

HRMS (CI, *i*-butane): *m*/*z* calcd for [$C_{29}H_{27}N_2$]$^+$: 403.2168; found: 403.2174.

Anal. Calcd for $C_{29}H_{26}N_2$·2/3 *n*-hexane: C, 86.17; H, 7.74; N 6.09. Found: C, 86.47; H, 7.63; N, 5.81.

4,10-Dimethyl-2,8-bis(3,5-dimethylphenyl)-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (8)

Following the general procedure, compound **1** (200 mg, 0.49 mmol), KF (188 mg, 3.23 mmol), [Pd(*t*-Bu$_3$P)$_2$] (10 mg), and 3,5-dimethylphenylboronic acid (177 mg, 1.18 mmol) in THF were heated for 48 h at 60 °C. Column chromatography (toluene–EtOAc 20:1 + 0.5% Et_3N, R_f = 0.37) gave 147 mg (65%) of **8** as a yellowish solid; mp 85 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.35 [s, 12 H, Ar*Me*$_2$], 2.49 (s, 6 H, H-18, H-19), 4.12 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –16.5 Hz), 4.41 (s, 2 H, H-13), 4.69 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –16.5 Hz), 6.94 (s, 2 H, H-4$_{Ph}$), 7.01 (d, 2 H, H-1, H-7′, ^4J = 1.7 Hz), 7.12 (4 H, H-2$_{Ph}$, H-6$_{Ph}$), 7.29 (d, 2 H, H-3, H-9, ^4J = 1.7 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.3 (C-18, C-19), 21.4 (Ar*Me*$_2$), 55.2 (C-6, C-12), 67.7 (C-13), 123.1 (C-1, C-7), 124.8 (C-2$_{Ph}$, C-6$_{Ph}$), 127.9 (C-3, C-9), 128.1 (C-14, C-16), 128.5 (C-4$_{Ph}$), 133.1 (C-4, C-10), 137.0 (C-2, C-8), 138.1 (C-3$_{Ph}$, C-5$_{Ph}$), 140.9 (C-1$_{Ph}$), 145.2 (C-15, C-17).

MS (CI, *i*-butane): *m*/*z* = 459.4 ([$C_{33}H_{35}N_2$]$^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{33}H_{34}N_2$: 458.2724; found: 458.2721.

Anal. Calcd for $C_{33}H_{34}N_2$·2/3H_2O: C, 84.26; H, 7.43; N 6.02. Found: C, 83.96; H, 7.71; N, 5.63.

2,8-Bis(4-chlorophenyl)-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (9)

Following the general procedure, compound **2** (200 mg, 0.40 mmol), CsF (400 mg, 2.63 mmol), Pd(P*t*-Bu$_3$)$_2$ (8.5 mg), and 4-chlorophenylboronic acid (149.5 mg, 0.96 mmol) were heated for 12 h at 40 °C. Column chromatography (toluene–EtOAc, 20:1 + 0.5% Et_3N, R_f = 0.38) gave 185 mg (97%) of **9** as a white solid; mp 205–206 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.49 (s, 6 H, H-18, H-19), 4.10 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.39 (s, 2 H, H-13), 4.68 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 6.97 (d, 2 H, H-1, H-7, ^4J = 1.7 Hz), 7.25 (m, 2 H, H-3, H-9), 7.33 (dd, 4 H, H-3$_{Ph}$, H-5$_{Ph}$, ^3J = 6.9 Hz, ^4J = 2.2 Hz), 7.40 (dd, 4 H, H-2$_{Ph}$, H-6$_{Ph}$, ^3J = 6.9 Hz, ^4J = 2.2 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.3 (C-18, C-19), 55.2 (C-6, C-12), 67.7 (C-13), 122.9 (C-1, C-7), 127.7 (C-3, C-9), 128.0 (C-2$_{Ph}$, C-6$_{Ph}$), 128.3 (C-14, C-16), 128.8 (C-3$_{Ph}$, C-5$_{Ph}$), 133.0 (C-4$_{Ph}$), 133.5 (C-4, C-10), 135.6 (C-2, C-8), 139.2 (C-1$_{Ph}$), 145.5 (C-15, C-17).

MS (CI, *i*-butane): *m*/*z* (%) = 471.1 ([$C_{29}H_{25}{}^{35}Cl_2N_2$]$^+$, 100), 473.1 ([$C_{29}H_{25}{}^{35}Cl^{37}ClN_2$]$^+$, 65).

HRMS (CI, *i*-butane): *m*/*z* calcd for [$C_{29}H_{25}Cl_2N_2$]$^+$, 471.1393 (^{35}Cl); found: 471.1394 (^{35}Cl).

Anal. Calcd for $C_{29}H_{24}Cl_2N_2$·2H_2O·toluene: C, 72.11; H, 6.05; N 4.67. Found: C, 71.85; H, 6.06; N, 4.91.

2,8-Bis[4-(methoxycarbonyl)phenyl]-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (10)

Following the general procedure, compound **2** (246 mg, 0.49 mmol), CsF (493 mg, 2.63 mmol), [Pd(P*t*-Bu$_3$)$_2$] (12 mg), and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaboralan-2-yl)benzoate (308 mg, 1.18 mmol) were heated for 24 h at 40 °C. Filtration over a short column of silica gel 60 (toluene + 0.5% Et_3N, R_f = 0.02) gave 217 mg (85%) of **10** as a yellow solid; mp 240–241 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.49 (s, 6 H, H-18, H-19), 3.91 (s, 6 H, CO_2CH_3), 4.12 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.39 (s, 2 H, H-13), 4.69 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 7.06 (d, 2 H, H-1, H-7, ^4J = 1.1 Hz), 7.33 (d, 2 H, H-3, H-9, ^4J = 1.1 Hz), 7.55 (dd, 4 H, H-2$_{Ph}$, H-6$_{Ph}$, ^3J = 7.4 Hz, ^4J = 1.6 Hz), 8.03 (dd, 4 H, H-3$_{Ph}$, H-5$_{Ph}$, ^3J = 7.4 Hz, ^4J = 1.6 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.3 (C-18, C-19), 52.0 (CO_2CH_3), 55.2 (C-6, C-12), 67.7 (C-13), 123.3 (C-1, C-7), 126.6 (C-2_{Ph}, C-6_{Ph}), 128.0 (C-3, C-9), 128.4 (C-14, C-16), 128.5 (C-4_{Ph}), 130.0 (4C, C-3_{Ph}, C-5_{Ph}), 133.5 (C-4, C-10), 135.4 (C-2, C-8), 145.2 (C-1_{Ph}), 146.2 (C-15, C-17), 167.0 (CO_2Me).

MS (CI, *i*-butane): *m*/*z* = 519.2 ($[C_{33}H_{31}N_2O_4]^+$, 100).

HRMS (CI, *i*-butane): *m*/*z* calcd for $[C_{33}H_{31}N_2O_4]^+$: 519.2294; found: 519.2283.

Anal. Calcd for $C_{33}H_{30}N_2O_4 \cdot 3/4\ H_2O$: C, 74.49; H, 5.97; N 5.26. Found: C, 74.77; H, 6.13; N, 5.13.

2,8-Bis(4-methoxyphenyl)-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (11)

Following the general procedure, compound **2** (400 mg, 0.80 mmol), CsF (798 mg, 5.26 mmol), [Pd(P*t*-$Bu_3)_2$] (17 mg), and 4-methoxyphenylboronic acid (290.5 mg; 1.91 mmol) in THF were heated for 6 h at 40 °C. Filtration over a short column of silica gel 60 (toluene + 0.5% Et_3N, R_f = 0.02) gave 340 mg (92%) of **11** as a white solid; mp 183–184 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.48 (s, 6 H, H-18, H-19), 3.81 (s, 6 H, OCH_3), 4.09 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.39 (s, 2 H, H-13), 4.67 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 6.91 (dd, 4 H, H-3_{Ph}, H-5_{Ph}, ^3J = 6.9 Hz, ^4J = 1.6 Hz), 6.96 (d, 2 H, H-1, H-7, ^4J = 1.1 Hz), 7.25 (d, 2 H, H-3, H-9, ^4J = 1.1 Hz), 7.41 (dd, 4H, H-2_{Ph}, H-6_{Ph}, ^3J = 6.9 Hz, ^4J = 1.6 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.3 (C-18, C-19), 55.2 (C-6, C-12), 55.3 (OCH_3), 67.7 (C-13), 114.4 (C-3_{Ph}, C-5_{Ph}), 122.6 (C-1, C-7), 127.5 (C-3, C-9), 127.8 (C-2_{Ph}, C-6_{Ph}), 128.2 (C-14, C-16), 133.2 (C-4, C-10)*, 133.5 (C-1_{Ph})*, 136.4 (C-2, C-8), 144.8 (C-15, C-17), 158.9 (C-4_{Ph}) (*assignment not confirmed).

MS (CI, *i*-butane): *m*/*z* = 463.3 ($[C_{31}H_{31}N_2O_2]^+$, 100).

HRMS (CI, *i*-butane): *m*/*z* calcd for $[C_{31}H_{31}N_2O_2]^+$: 463.2384; found: 463.2385.

Anal. Calcd for $C_{31}H_{30}N_2O_2 \cdot 1/4\ H_2O$: C, 79.71; H, 6.58; N 6.00. Found: C, 79.51; H, 6.75; N, 5.83.

2,8-Bis(4-aminophenyl)-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (12)

A solution of compound **1** (300 mg, 0.74 mmol) in THF (5 mL) was cooled to –78 °C. At this temperature, *n*-BuLi (1.10 mL of a 1.6 M solution in *n*-hexane, 1.77 mmol) was added dropwise within 5 min. After stirring for 5 min, trimethylborate (0.25 mL, 2.21 mmol) was added instantly and the reaction mixture was allowed to come to r.t. and stirred for another 15 min. This mixture was then added to a solution of 4-iodoaniline (354 mg, 1.62 mmol), CsF (737 mg, 4.85 mmol) and [Pd(P*t*-$Bu_3)_2$] (15 mg) in THF (5 mL). The resulting reaction mixture was refluxed for 48 h. Column chromatography (*n*-hexane–EtOAc, 1:2 + 0.5% Et_3N, R_f = 0.36) gave 280 mg (88%) of **12** as a brown solid; mp 98–100 °C.

^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 2.39 (s, 6 H, H-18, H-19), 4.01 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.25 (s, 2 H, H-13), 4.53 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 5.09 (s, 4 H, NH_2), 6.57 (d, 4 H, H-3_{Ph}, H-5_{Ph}, ^3J = 8.2 Hz), 6.95 (s, 2 H, H-1, H-7), 7.20 (s, 2 H, H-3, H-9), 7.23 (dd, 4 H, H-2_{Ph}, H-6_{Ph}, ^3J = 8.2 Hz).

^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 17.4 (C-18, C-19), 55.1 (C-6, C-12), 67.7 (C-13), 114.6 (C-3_{Ph}, C-5_{Ph},), 121.7 (C-1, C-7), 126.2 (C-3, C-9), 127.2 (C-2_{Ph}, C-6_{Ph},), 127.9 (C-1_{Ph}), 128.7 (C-14, C-16), 132.7 (C-4, C-10), 136.2 (C-2, C-8), 144.3 (C-15, C-17), 148.3 (C-4_{Ph}).

MS (CI, *i*-butane): *m*/*z* = 433.2 ($[C_{29}H_{29}N_4]^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{28}N_4$: 432.2308; found: 432.2313.

Anal. Calcd for $C_{29}H_{28}N_4 \cdot 3/4$ EtOAc: C, 77.08; H, 6.87; N 11.24. Found: C, 76.69; H, 6.87; N, 11.12.

2,8-Bis(4-cyanophenyl)-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (13)

Compound **17** (200 mg, 0.51 mmol), CsF (514 mg, 3.4 mmol), [Pd(P*t*-$Bu_3)_2$] (10.5 mg, 4 mol%), and 4-iodobenzonitrile (282 mg) were dissolved in THF (10 mL) and the resulting solution was refluxed for 20 h. CH_2Cl_2 was added and the reaction mixture was washed with aq sat. solution of Na_2CO_3 (2 ×). The combined organic layers were extracted with CH_2Cl_2 (3 ×), washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (toluene–EtOAc, 20:1 + 0.5% Et_3N, R_f = 0.12) to give 162 mg (70%) of **13** as a white solid; mp 248–250 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.49 (s, 6 H, H-18, H-19), 4.11 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.38 (s, 2 H, H-13), 4.69 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 7.02 (d, 2 H, H-1, H-7, ^4J = 1.6 Hz), 7.30 (d, 2 H, H-3, H-9, ^4J = 1.6 Hz), 7.57 (dd, 4 H, H-2_{Ph}, H-6_{Ph}, ^3J = 7.7 Hz, ^4J = 2.2 Hz), 7.64 (dd, 4H, H-3_{Ph}, H-5_{Ph}, ^3J = 7.7 Hz, ^4J = 2.2 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.3 (C-18, C-19), 55.1 (C-6, C-12), 67.6 (C-13), 110.5 (C-4_{Ph}), 118.9 (CN), 123.3 (C-1, C-7), 127.3 (C-2_{Ph}, C-6_{Ph}), 127.9 (C-3, C-9), 128.6 (C-14, C-16), 132.5 (C-3_{Ph}, C-5_{Ph},), 133.8 (C-4, C-10), 134.6 (2 C-2, C-8), 145.2 (C-1_{Ph}), 146.7 (C-15, C-17).

MS (CI, *i*-butane): *m*/*z* = 453.2 ($[C_{31}H_{25}N_4]^+$, 100).

HRMS (CI, *i*-butane): *m*/*z* calcd for $[C_{31}H_{25}N_4]^+$: 453.2097; found: 453.2079.

Anal. Calcd for $C_{31}H_{24}N_4 \cdot 1/4\ H_2O$: C, 81.46; H, 5.40; N 12.26. Found: C, 81.44; H, 5.48; N, 11.89.

2,8-Bis(4-hydroxyphenyl)-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (14)

Compound **11** (300 mg, 0.65 mmol) was dissolved in CH_2Cl_2 (10 mL) and cooled to –78 °C. After addition of a 1 M BBr_3 solution in CH_2Cl_2 (2.6 mL, 2.6 mmol) at this temperature, the reaction mixture was allowed to come to r.t. and stirred for 16 h. Aq 2 N NaOH was added until the excess of BBr_3 had been completely hydrolyzed. After addition of EtOAc (10 mL), the solution was neutralized using 6 N HCl and extracted with EtOAc (3 ×). Concentration in vacuo gave 275 mg (99%) of **14** as a brown solid, mp 148–149 °C.

^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 2.39 (s, 6 H, H-18, H-19), 4.03 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.26 (s, 2 H, H-13), 4.54 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 6.77 (d, 4 H, H-3_{Ph}, H-5_{Ph}, ^3J = 8.2 Hz,), 6.99 (d, 2 H, H-1, H-7, ^4J = 1.6 Hz), 7.23 (m, 2 H, H-3, H-9), 7.35 (d, 4 H, H-2_{Ph}, H-6_{Ph}, ^3J = 8.2 Hz), 9.40 (s, 2 H, OH).

^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 17.4 (C-18, C-19), 55.1 (C-6, C-12), 67.7 (C-13), 116.0 (C-3_{Ph}, C-5_{Ph},), 122.4 (C-1, C-7), 126.8 (C-3, C-9), 127.8 (C-2_{Ph}, C-6_{Ph},), 128.8 (C-14, C-16), 131.3 (C-1_{Ph}), 132.9 (C-4, C-10), 135.7 (C-2, C-8), 144.8 (C-15, C-17), 157.1 (C-4_{Ph}).

MS (CI, *i*-butane): *m*/*z* = 435.2 ($[C_{29}H_{27}N_2O_2]^+$, 100).

HRMS (CI, *i*-butane): *m*/*z* calcd for $[C_{29}H_{27}N_2O_2]^+$: 435.2081; found: 435.2072.

Anal. Calcd for $C_{29}H_{26}N_2O_2 \cdot 5/4$ EtOAc: C, 74.98; H, 6.66; N 5.14. Found: C, 74.98; H, 6.41; N, 5.58.

2,8-Bis(4-trifluoromethanesulfoxyphenyl)-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocine (15)

Et_3N (1.00 mL) was added to a solution of **14** (500 mg, 1.15 mmol) in CH_2Cl_2 (50 mL) and cooled to – 30 °C. At this temperature, a solution of trifluoromethanesulfonic acid anyhydride (0.78 mL, 4.60

mmol) and CH_2Cl_2 (10 mL) was added dropwise and the resulting reaction mixture was stirred for another hour, then allowed to come to r.t. and stirred for 16 h. This solution was poured into cold H_2O, extracted with CH_2Cl_2 (5 ×), washed with aq sat. solution of $NaHCO_3$, and dried (Na_2SO_4). The crude product was purified by column chromatography (toluene + 0.5% Et_3N, R_f = 0.09) to give 350 mg (45%) of **15** as a white solid; mp 129–131 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.49 (s, 6 H, H-18, H-19), 4.10 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.39 (s, 2 H, H-13), 4.69 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 6.98 (d, 2 H, H-1, H-7, ^4J = 1.1 Hz), 7.26 (m, 2 H, H-3, H-9), 7.27 (dd, 4 H, H-3_{Ph}, H-5_{Ph}, ^3J = 9.0 Hz, ^4J = 2.2 Hz), 7.52 (dd, 4 H, H-2_{Ph}, H-6_{Ph}, ^3J = 9.0 Hz, ^4J = 2.2 Hz).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.3 (C-18, C-19), 55.1 (C-6, C-12), 67.6 (C-13), 118.8 [CF_3, ^1J (C,F) = 322 Hz], 121.5 (C-3_{Ph}, C-5_{Ph}), 123.2 (C-1, C-7), 127.9 (C-3, C-9), 128.4 (C-14, C-16), 128.5 (C-2_{Ph}, C-6_{Ph}), 133.7 (C-4, C-10), 134.9 (C-2, C-8), 141.3 (C-1_{Ph}), 146.0 (C-15, C-17), 148.7 (C-4_{Ph}).

^{19}F (282.4 MHz, $CDCl_3$): δ = –72.8 (CF_3).

MS (CI, *i*-butane): *m*/*z* = 699.1 ($[C_{31}H_{25}F_6N_2O_6S_2]^+$, 100).

HRMS (EI): *m*/*z* calcd for $C_{31}H_{24}F_6N_2O_6S_2$: 698.0989; found: 698.0979.

Anal. Calcd for $C_{31}H_{24}F_6N_2O_6S_2$: C, 53.29; H, 3.46; N 4.01. Found: C, 53.36; H, 3.95; N, 3.96.

2,8-(4,10-Dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*]diazocineylene)diboronic Acid (16)

A solution of **1** (1 g, 2.45 mmol) in THF (10 mL) was cooled to –78 °C. At this temperature, *n*-BuLi (3.65 mL of a 1.6 M solution in *n*-hexane, 5.87 mmol) was added dropwise within 5 min. After stirring for 5 min, trimethylborate (0.83 mL, 7.35 mmol) was added instantly and the reaction mixture was allowed to come to r.t. and stirred for another 15 min. H_2O (15 mL) was added and after extraction with CH_2Cl_2, the aqueous solution was extracted with EtOAc (3 ×) and dried (Na_2SO_4). Concentration in vacuo gave 750 mg (90%) of **16** as a white solid. If necessary, **16** can be recrystallized from acetone; mp >300 °C.

^{1}H NMR (500.1 MHz, DMSO-d_6): δ = 2.33 (s, 6 H, H-18, H-19), 3.93 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –17.0 Hz), 4.24 (s, 2 H, H-13), 4.51 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –17.0 Hz), 7.19 (s, 2 H, H-1, H-7), 7.44 (s, 2 H, H-3, H-9), 7.74 (s, 4 H, OH).

^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 17.3 (C-18, C-19), 54.9 (C-6, C-12), 67.5 (C-13), 127.2 (C-14, C-16), 129.0 (C-2, C-8), 131.0 (C-1, C-7), 131.1 (C-4, C-10), 135.0 (C-3, C-9), 148.1 (C-15, C-17).

MS (CI, *i*-butane): *m*/*z* = 339.2 ($[C_{17}H_{21}B_2N_2O_4]^+$, 100).

HRMS (CI, ammonia): *m*/*z* calcd for $[C_{17}H_{21}B_2N_2O_4]^+$: 356.1971; found: 356.1953.

Anal. Calcd for $C_{17}H_{20}B_2N_2O_4 \cdot 4/3\ H_2O$: C, 56.40; H, 6.31; N 7.74. Found: C, 56.52; H, 6.06; N, 7.62.

2,8-Bis[1,3]dioxa[2]borolane-2-yl-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (17)

A solution of **1** (1 g, 2.45 mmol) in THF (10 mL) was cooled to –78 °C. At this temperature *n*-BuLi (3.65 mL of a 1.6 M solution in *n*-hexane, 5.87 mmol) was added dropwise within 5 min. After stirring for 5 min, trimethylborate (0.83 mL, 7.35 mmol) was added instantly and the reaction mixture was allowed to come to r.t. and stirred for another 15 min. After concentration in vacuo, the residue was dissolved in a mixture of ethylene glycol (10 mL) and toluene (30 mL) and refluxed for 16 h. The toluene layer was separated and concentrated in vacuo to give 830 mg (87%) of **17** as a white solid; mp 183–185 °C.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.39 (s, 6 H, H-18, H-19), 4.03 (d, 2 H, H-6*endo*, H-12*endo*, ^2J = –16.5 Hz), 4.30 (s, 8H, OCH_2CH_2O), 4.32 (s, 2 H, H-13), 4.59 (d, 2 H, H-6*exo*, H-12*exo*, ^2J = –16.5 Hz), 7.23 (s, 2 H, H-1, H-7), 7.48 (s, 2 H, H-3, H-9).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.0 (C-18, C-19), 54.8 (C-6, C-12), 65.9 (OCH_2CH_2O), 67.7 (C-13), 122.3 (C-2, C-8), 127.3 (C-14, C-16), 131.4 (C-1, C-7), 132.2 (C-4, C-10), 135.5 (C-3, C-9), 149.2 (C-15, C-17)

MS (CI, *i*-butane): *m*/*z* = 391.2 ($[C_{21}H_{25}B_2N_2O_4]^+$, 100).

HRMS (CI, *i*-butane): *m*/*z* calcd for $[C_{21}H_{25}B_2N_2O_4]^+$: 391.2000; found: 391.2007.

Anal. Calcd for $C_{21}H_{24}B_2N_2O_4 \cdot 1/4$ toluene: C, 66.15; H, 6.35; N 6.78. Found: C, 65.71; H, 6.58; N, 7.13.

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