Synthesis of Dihalo-Substituted Analogues of Tröger's Base from *ortho*- and *meta*-Substituted Anilines

Anna Hansson,[a] Jacob Jensen,[a] Ola F. Wendt,[b] and Kenneth Wärnmark*[a]

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For the first time, *ortho*- and *meta*-halo-substituted anilines were successfully condensed with formaldehyde to dihalo-substituted analogues of Tröger's base. By using paraformaldehyde and TFA, yields of 2–85% of these potential supramolecular building blocks were obtained. Even the inconceivable achievement of condensing anilines unsubstituted in *para*-position to analogues of Tröger's base was successful. Adding our present results to our previous, makes it now possible to synthesize analogues of Tröger's base halo-substituted in almost any desired position in each of its two aromatic rings. In addition the first X-ray structure of a dihalo-substituted analogue of Tröger's base, 3,9-dibromo-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (**17**), is presented.

Introduction

The C_2-symmetric Tröger's base, 2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, is highly interesting as a supramolecular building block due to its rigid and chiral hydrophobic pocket (Figure 1). Analogues of Tröger's base have so far been used more or less frequently in various applications such as enantioselective recognition,[1] enzyme inhibition,[2] DNA intercalation,[1,3] ligands in asymmetric synthesis,[4,5] and as a molecular torsion balance.[6] However, the use of the Tröger's base motif in the above mentioned areas has been limited by the absence of methods for the synthesis of functionalized analogues of Tröger's base.

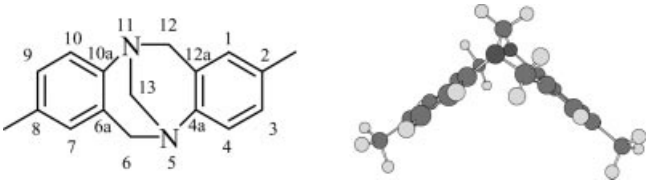
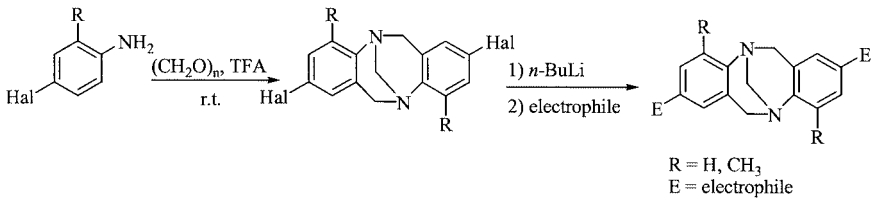


Figure 1. Tröger's base

The reason for the absence of synthetic methods for functionalized analogues of Tröger's base could be traced back to the belief that the Tröger's base condensation, the reaction between an aniline, formaldehyde or its equivalent, and acid, was limited to anilines with certain specific electronic requirements: The anilines should preferably be electron rich and they should also have an inert substituent in *para*-position to the nitrogen.[7,8] However, we recently demonstrated that halogen substituted anilines could undergo the condensation reaction using paraformaldehyde in TFA (trifluoroacetic acid).[9] Accordingly, 2-methyl-4-haloanilines and 4-haloanilines underwent the Tröger's base condensation reaction in yields varying from 41 to 85% (Scheme 1). We further demonstrated that 2,8-dihaloanalogues of Tröger's base constitute the entries to 2,8-disubstituted analogues of Tröger's base in general through halogen−lithium exchanges[10] and cross-coupling reactions.[9,11]

In contrast, general methods for the synthesis of Tröger's base analogues from *ortho*- and *meta*-haloanilines are lacking. For *ortho*-haloanilines, the only example in the literature is 2-iodoaniline, that was treated with paraformaldehyde in TFA to give 6% of an impure Tröger's base analogue, whereas 2-bromoaniline gave only polymerized material.[9] There is one example of a 4,10-dihalo-substituted Tröger's base analogue, dimethyl 4,10-dichloro-1,7-dimethoxy-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine-2,8-dicarboxylate, but it was not synthesized from the corresponding aniline but from methyl-5-chloro-4-(ethoxyoxoacetyl)amino-2-methoxybenzoate.[12] As for the condensation of *meta*-haloanilines, Häring condensed 3-chloro-4-methylaniline to Tröger's base analogues in 60% yield using paraformaldehyde and aqueous HCl in glacial acetic acid. This was confirmed by elemental analysis but no further investigation as to isomeric ratio was made.[7] Kametani et al. gave two examples of 2,8-alkoxy-3,9-dichloro-substi-

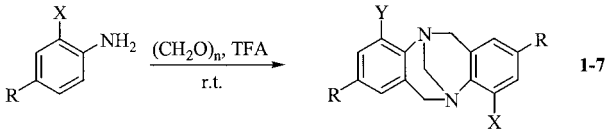
[a] Organic Chemistry 1, Department of Chemistry, Lund University,
P. O. Box 124, 22100 Lund, Sweden
Fax: (internat.) + 46-46/2224119
E-mail Kenneth.Warnmark@orgk1.lu.se
[b] Inorganic Chemistry, Department of Chemistry, Lund University,
P. O. Box 124, 22100 Lund, Sweden



Scheme 1

tuted Tröger's base analogues formed, as it appears, in side reactions in a quest for analgesic oxazolidinones and oxazinones.[13]

Following our success with the synthesis of 2,8-dihalo analogues of Tröger's base from *para*-haloanilines, we now present the synthesis of Tröger's base analogues from anilines substituted with halogens at the *ortho*- and *meta*-position, thus allowing for the until now not feasible synthesis of all possible regioisomers of analogues of Tröger's base monohalo-substituted in each aromatic ring, including analogues not substituted in the 2,8-positions. These results are important because it would allow for, at least in theory, the synthesis of all possible analogues of Tröger's base, monohalo-substituted in each aromatic ring, through halogen−lithium exchanges and cross-coupling reactions in analogy to the 2,8-dihaloanalogues as developed previously by us.[9−11] Specifically, the condensations of 2-halo-4-methylanilines, 3-halo-4-methylanilines, 2-haloanilines, 3-haloanilines, and 3-halo-2-methylanilines with paraformaldehyde in TFA were investigated. The new results presented here would increase the variety and possibilities of new, exciting Tröger's base analogues to be used in for instance supramolecular chemistry.



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Scheme 2

Table 1. The reactions of 2-haloanilines (see Scheme 2)

Analogue of Tröger's Base	R	X	Y	Yield (%)[a]
1	CH_3	Br	Br	85
2	CH_3	Cl	Cl	77
3	CH_3	F	F	75
4a	CH_3	I	I	30
4b	CH_3	I	H	13[b]
−	H	I	I	−[c]
5	H	Br	Br	9
6	H	Cl	Cl	19
7	H	F	F	27

[a] Isolated yields of pure products after CC. [b] Yield after recrystallization. [c] Complicated mixture of presumably polymerized Tröger's base analogues.

Results and Discussion

Since it has been claimed that there must be a substituent in the 4-position of the aniline to obtain successful results in the Tröger's base condensation,[7,8] we launched the investigation using 2-halo-4-methylanilines and 3-halo-4-methylanilines. In addition the methyl group will add some electron density to the benzene ring, facilitating the reaction.

The Condensation of 2-Halo-4-methylanilines

First, 2-bromo-, 2-chloro-, and 2-fluoro-4-methylaniline, respectively, were condensed with paraformaldehyde in TFA resulting in the corresponding 4,10-dihalo-2,8-dimethyl Tröger's base analogues **1−3** (Scheme 2), inherently as one regioisomer, in 75−85% yield (Table 1). The reaction times were optimized by following the progress of the reaction by TLC. Generally, shorter reaction times gave lower yields due to incomplete reaction. Longer reaction times also gave lower yields, most probably due to competing polymerization of the starting materials under the reaction conditions.

The reaction of 2-iodo-4-methylaniline, however, gave after chromatography only 30% yield of the expected product **4a**, and the major side product was the monoiodo compound **4b**. An investigation of the stability of the starting material and the product was undertaken. To prevent an assumed decomposition of the starting material, the reaction was run in the dark. The starting material was found to be stable in TFA in the dark, and a solution of starting material in ethyl acetate exposed to daylight was stable for at least three days. The product **4a** was also stable in TFA, and upon exposure to the reaction conditions, i.e. TFA and paraformaldehyde, no deiodination had taken place after 40 h and only a slight deiodination was noticed after 160 h. Since the reaction time was only 20 h, this could not be the reason for the observed deiodination. We thus conclude that the reductive step probably occurs in one of the intermediate steps of the reaction. This reduction was only observed for the condensation using 2-iodo-substituted anilines. Furthermore, a variation of the reaction time (20−98 h) did not show a significant change of the proportions of diodo- **4a** vs. monoiodo product **4b**. We recently proposed a mechanism for the formation of halo-substituted analogues of Tröger's base, in which the key inter-

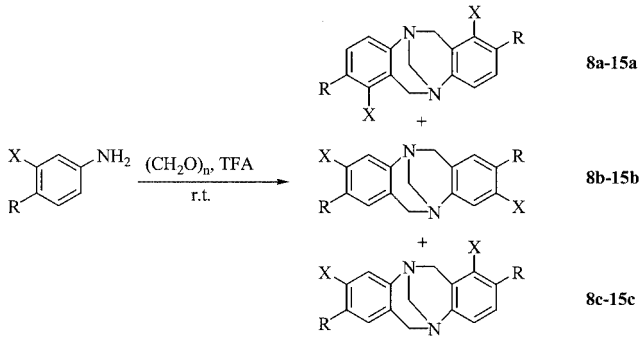
mediate would be a tetrahydroquinazoline that is formed by the reduction of an intermediate dihydroquinazoline by formaldehyde and TFA.[9] We now suggest that the dehalogenation takes place by the reduction of any of the diiododihydroquinazoline or diiodotetrahydroquinazoline intermediates by formaldehyde in TFA.

The Condensation of 2-Haloanilines

Inspired by the results above, we also wanted to synthesize the parent compounds without the methyl substituents in the 2,8-position of the Tröger's base core. In a previous paper from this group,[9] 6% of an impure Tröger's base analogue was isolated from the condensation of 2-iodoaniline, whereas nothing resulted from the reaction with 2-bromoaniline. Contrary to this, we now managed to isolate pure 4,10-dihalo-Tröger's base analogues from the reactions of 2-bromo-, 2-chloro-, and 2-fluoroaniline, respectively (**5**; 9%, **6**; 19%, and **7**, 27%, Table 1, Scheme 2), whereas no product could be isolated from the reaction of 2-iodoaniline. The yields were low and the differences in yields compared to earlier published results, might be due to differences in reaction times. The major products were presumed polymerized material as indicated by TLC-spots with R_f-values close to zero. This assumption was supported by the ^{1}H NMR spectra of the soluble fractions of the crude products, showing broad peaks in both the aromatic region and in the region between δ = 4 and 5 ppm where the methylene protons appear in the ^{1}H NMR spectra of Tröger's base.

The Condensation of 3-Halo-4-methylanilines

When subjecting each of the 3-halo-4-methylanilines to the Tröger's Base reaction conditions, three different regioisomers could be formed; a nonlinear C_2-symmetric one (**a**), a linear C_2-symmetric one (**b**), and an asymmetric one (**c**) (Scheme 3). Based on the analysis of the ^{1}H NMR spectra of the crude products of each reaction it was noted that in the condensation reactions of the iodo-, bromo-, and chloroanilines, all three regioisomers were formed (**8a**,**b**,**c**−**10a**,**b**,**c**), whereas the fluoroaniline gave only the two regioisomers **11b**,**c** (Table 2). A general trend on going from the iodo- to the fluoro analogues (**8**−**11**) was a decreasing amount of the nonlinear C_2-symmetric regioisomer (**a**) formed and an increasing amount of the linear C_2-symmetric regioisomer (**b**).



Scheme 3

Table 2. The reactions of 3-haloanilines (see Scheme 3)

Analogue of Tröger's Base	R	X	Regioisomeric ratio (a/b/c)[a]	Isolated yields (%) (a/b/c)[b]
8	CH_3	I	44:8:48	17:2:3
9	CH_3	Br	39:11:50	24:6:29
10	CH_3	Cl	28:18:54	23:9:26
11	CH_3	F	0:74:26	–[c]
12	H	I	32:17:51	8:2:12
13	H	Br	21:19:60	2:2:18
14	H	Cl	18:28:53	2:5:8
15	H	F	0:66:34	– [c]

[a] As determined by ^{1}H NMR analysis of the crude product. [b] Isolated yields after CC, recrystallization or size exclusion chromatography (SEC). Further details are given in the Exp. Sect. [c] Isolation of the products not possible. Analytical data are given for the mixture.

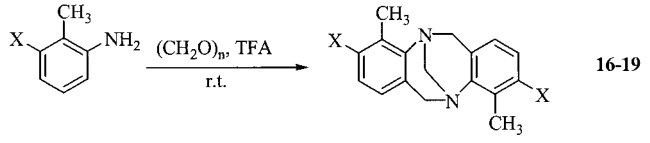
Isolation of the isomers proved to be difficult. The nonlinear C_2-symmetric isomer (**a**) was easily isolated, but the remaining two were only partially separated by CC, thereby the low isolated yields. In some cases, CC was not a sufficient purification method but had to be followed by recrystallization. The different purification methods used make it difficult to compare the yields. In the case of the two resulting fluoro analogues **11b**,**c**, no separation at all was feasible, neither by CC nor by recrystallization and analyzes were consequently made on the mixture of regioisomers. The correct HRMS and elemental analysis on the mixture support the characterization done by ^{1}H and ^{13}C NMR spectroscopy.

The Condensation of 3-Haloanilines

Surprisingly, in contrast to the results for the 2-haloanilines where a methyl substituent in the 4-position was needed to obtain a good yield, 3-iodo-, 3-bromo-, 3-chloro-, and 3-fluoroaniline, respectively (Scheme 3), were condensed with paraformaldehyde in TFA in good yields without the need of a blocked 4-position. Indeed, polymers were formed also in these reactions but not to the degree observed for the 2-haloanilines. A possible reason is the steric effect that the 3-substituent executes on the 4-position. Three regioisomers were formed also in these cases with a distribution of products similar to that of the 3-methyl-4-haloanilines. The iodo-, bromo-, and chloroanilines gave all three regioisomers in the condensation reaction (**12a**,**b**,**c**−**14a**,**b**,**c**) whereas the fluoroaniline gave two regioisomers (**15b**,**c**), just as in the reaction of 3-fluoro-4-methylaniline. As seen from the low isolated yields (Table 2), the same purification problems as for the dimethyl analogues **8**−**10** occurred. The fluoro analogues **15b**,**c** were, as for the dimethyldifluoro analogues **11b**,**c**, not possible to separate and the analyzes were accordingly made on the mixture that demonstrated correct HRMS and elemental analysis supporting again the characterization done by ^{1}H and ^{13}C NMR spectroscopy.

The Condensation of 3-Halo-2-methylanilines

Due to the problems with purification of the different isomers formed when 3-haloanilines were used in the condensation, we thought that using 3-halo-2-methylanilines would give a better view of the reaction with 3-haloanilines than the reaction with 3-halo-4-methylanilines, since only one regioisomer can be formed in this case (Scheme 4). The yields of 32−59% for compounds **16−19** indeed demonstrated that the importance of a 4-substituent is overrated (Table 3). The good isolated yields are not only due to the fact that only one regioisomer can be formed and that the methyl group exerts an electron-donating effect but are also due to our improved purification method: Size exclusion chromatography instead of recrystallization.



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Scheme 4

Table 3. The reactions of 3-halo-2-methylanilines (see Scheme 4)

Analogue of Tröger's Base	X	Yield (%)
16	I	59 [a]
17	Br	41 [b]
18	Cl	48 [b]
19	F	32 [b]

[a] Isolated yields after CC.[b] Isolated yields after CC and size exclusion chromatography (SEC).

X-ray Diffraction Studies of Racemic 17

The crystal structure of 3,9-dibromo-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (**17**) was determined. This is the first X-ray structure of a dihalo-substituted analogue of Tröger's base and it is the first one of an analogue unsubstituted in the 2- and 8-position. A perspective view of the molecular structure is given in Figure 2. A stereoview of the unit cell, containing 4 identical molecules, is given in Figure 3. The mean deviation from the two least-squares planes defined by the atoms in the aromatic rings is 0.007 Å. The most important structural feature of Tröger's base is the angle between the two aromatic planes, defining the chiral cleft. The angle between the planes was found to be 100.9°, which is in the same range as for other Tröger's base analogues. Tröger's base itself has intramolecular dihedral angles of 92.9° and 97.4°, respectively, for each of the two types of molecules in the unit cell.[14] Other analogues have angles that range from 79.3° for a bis-Tröger's base tweezer[15] up to 104.0° for the 2,4,8,10-tetramethyl-Tröger's base analogue.[16]

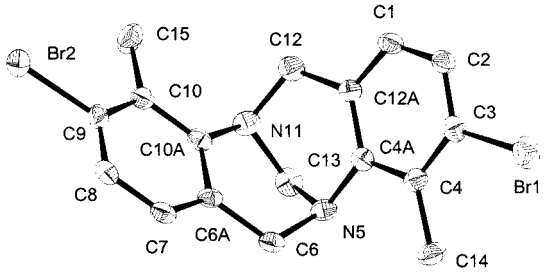

Figure 2. DIAMOND[23] drawing of (**17**). Hydrogen atoms are omitted for clarity. The ellipsoids denote 30% probability

Conclusion

An investigation of the condensation of 2- and 3-halo-substituted anilines to dihalo analogues of Tröger's base was made. We found that, contradictory to earlier work, it is indeed possible to synthesize Tröger's base analogues in moderate to good yields from electron-poor anilines using paraformaldehyde in TFA. Even anilines unsubstituted in the *para*-position undergo the reaction, although in slightly lower yields. Especially the 3-halo-2-methylanilines give good yields since only one regioisomer is formed. It is now possible to synthesize analogues of Tröger's base halo-substituted in almost any desired position in each of the two aromatic rings. It is highly probable that the new analogues synthesized in this work could be further modified to give generally disubstituted Tröger's base analogues with any substitution pattern for instance by halogen-lithium ex-

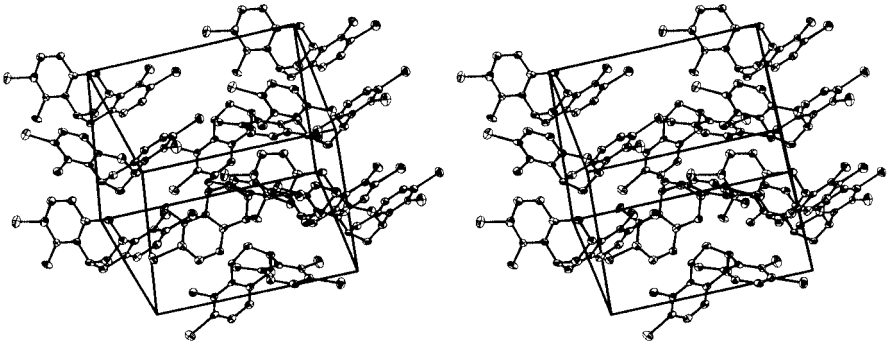

Figure 3. A DIAMOND[23] stereo view of the unit cell of (**17**)

change, just like the case for the 2,8-dihalogen substituted analogues.[10]

Experimental Section

General Remarks: All chemicals were used as received without further purification. 2-Iodo-4-methylaniline, 3-iodo-2-methylaniline, and 3-bromo-2-methylaniline were synthesized according to literature procedures.[17,18] Precoated Merck silica gel 60 F_{254} plates were used for TLC analysis. Flash column chromatography (CC) was performed on Matrex (35−70 μm) silica gel using the indicated eluent. The column dimensions were either 2 × 20 cm (fraction volume 10 mL) or, for the complex product mixtures, 4 × 20 cm (fraction volume 25 mL). Samples with low solubility in the eluent were dissolved in CH_2Cl_2, evaporated onto Matrex (35−70 μm) silica gel and put on the column as a dry powder. In some cases, size exclusion chromatography (SEC) using BioBeads SX-3 (BioRad) were performed on a 2 × 24 cm column using CH_2Cl_2 as an eluent. NMR spectra were recorded on a Bruker ARX300, DRX400, or DRX500 NMR spectrometer in $CDCl_3$ at ambient temperature. Chemical shifts are reported in δ relative to an internal standard of residual chloroform (δ = 7.26 and 7.27 ppm for ^{1}H NMR at 300 and 400 MHz, respectively, and δ = 77.23 ppm for ^{13}C NMR). Assignments of peaks were done using ^{1}H-^{1}H COSY and NOESY and ^{1}H{^{13}C} HMQC and HMBC experiments and C-F coupling constants in relevant cases. Numbering was made according to Figure 1. Melting points were recorded on a Sanyo Gallenkamp Melting Point Apparatus and were corrected or verified using reference substances. Elemental analyses were performed either after CC, SEC, or after recrystallisation by A. Kolbe, Mikroanalytisches Laboratorium, Germany.

General Procedure. Preparation of Dihalo-Substituted Analogues of Tröger's Base: To a stirred mixture of the aniline (1.0 mmol) and paraformaldehyde (60 mg, 2.0 mmol) TFA (2 mL) was added drop wise and the stirring was continued at room temp. until the reaction was finished. TFA was removed in vacuo, 10% NH_4OH (aq.) (2 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried using anhydrous $MgSO_4$, filtered, concentrated in vacuo, and further purified.

4,10-Dibromo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (1): This compound was prepared using 2-bromo-4-methylaniline (187 mg, 1.01 mmol) and paraformaldehyde (62 mg, 2.1 mmol) and stirring for 18 h. CC (5% EtOAc in heptane) gave **1** in 85% yield (175 mg) as a white solid. R_f = 0.29 (10% EtOAc in heptane), m.p. 194.0−194.9 °C (heptane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 6 H, 2 × CH_3), 4.29 (d, J = 17.2 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.36 (s, 2 H, 13-H), 4.55 (d, J = 17.2 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.75 (d, J = 0.8 Hz, 2 H, 1-H and 7-H), 7.28 (d, J = 0.8 Hz, 2 H, 3-H and 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.71 (2 C, 2 × CH_3), 55.59 (2 C, C-6 and C-12), 67.99 (1 C, C-13), 119.72 (2 C, C-4 and C-10), 126.92 (2 C, C-1 and C-7), 130.49 (2 C, C-6a and C-12a), 132.10 (2 C, C-3 and C-9), 135.60 (2 C, C-2 and C-8), 142.18 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): m/z calcd. for $C_{17}H_{16}Br_2N_2$ [M] 405.9680; found 405.9667. $C_{17}H_{16}Br_2N_2$, C 50.03, H 3.95, N 6.86; found C 49.88, H 3.90, N 6.84.

4,10-Dichloro-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (2): This compound was prepared using 2-chloro-4-methylaniline (143 mg, 1.01 mmol) and paraformaldehyde (61 mg, 2.0 mmol) and stirring for 42 h. CC (20% EtOAc in heptane) gave **2** in 77% yield (125 mg) as a white solid. R_f = 0.20 (10% EtOAc in heptane), m.p. 156.8−158.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22 (s, 6 H, 2 × CH_3), 4.27 (d, J = 17.2 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.36 (s, 2 H, H-13), 4.56 (d, J = 17.2 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.70 (d, J = 0.8 Hz, 2 H, 1-H and 7-H), 7.09 (d, J = 0.8 Hz, 2 H, 3-H and 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.84 (2 C, 2 × CH_3), 55.04 (2 C, C-6 and C-12), 68.04 (1 C, C-13), 126.30 (2 C, C-1 and C-7), 128.92 (2 C, C-4 and C-10), 129.06 (2 C, C-3 and C-9), 130.10 (2 C, C-6a and C-12a), 135.11 (2 C, C-2 and C-8), 140.85 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): m/z calcd. for $C_{17}H_{16}Cl_2N_2$ [M] 318.0691; found 318.0678. $C_{17}H_{16}Cl_2N_2$, C 63.96, H 5.05, N 8.78; found C 63.78, H 5.08, N 8.69.

4,10-Difluoro-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (3): This compound was prepared using 2-fluoro-4-methylaniline (127 mg, 1.01 mmol) and paraformaldehyde (61 mg, 2.0 mmol) and stirring for 24 h. CC (20% EtOAc in heptane) gave **3** in 75% yield (110 mg) as a white solid. R_f = 0.20 (20% EtOAc in heptane), m.p. 215.4−217.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 6 H, 2 × CH_3), 4.13 (d, J = 17.1 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.29 (br. s, 2 H, 13-H), 4.55 (d, J = 17.1 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.55 (br. s, 2 H, 1-H and 7-H), 6.75 (br. d, $^3J_{H,F}$ = 11.6 Hz, 2 H, 3-H and 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.06 (2 C, 2 × CH_3), 55.42 (d, $^4J_{C,F}$ = 3 Hz, 2 C, C-6 and C-12), 67.70 (1 C, C-13), 114.78 (d, $^2J_{C,F}$ = 19 Hz, 2 C, C-3 and C-9), 122.86 (d, $^4J_{C,F}$ = 3 Hz, 2 C, C-1 and C-7), 129.86 (d, $^3J_{C,F}$ = 3 Hz, 2 C, C-6a and C-12a), 132.44 (d, $^2J_{C,F}$ = 12 Hz, 2 C, C-4a and C-10a), 134.76 (d, $^3J_{C,F}$ = 8 Hz, 2 C, C-2 and C-8), 156.01 (d, $^1J_{C,F}$ = 246 Hz, 2 C, C-4 and C-10) ppm. HRMS (FAB+): m/z calcd. for $C_{17}H_{16}F_2N_2$ [M] 286.1282; found 286.1268. $C_{17}H_{16}F_2N_2$, C 71.31, H 5.63, N 9.78; found C 71.32, H 5.56, N 9.68.

4,10-Diiodo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (4a) and 4-Iodo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (4b): These compounds were prepared using 2-iodo-4-methylaniline (233 mg, 1.00 mmol) and paraformaldehyde (62 mg, 2.1 mmol) and stirring for 20 h in the dark. CC (gradient 5−20% EtOAc in heptane) gave **4a** in 30% yield (75 mg) as a white solid and **4b** in 54% yield (103 mg) as a beige solid. Recrystallization from EtOAc gave **4b** in 13% yield (25 mg) as a white solid.

4a: R_f = 0.32 (10% EtOAc in heptane), m.p. 228.2−229.8 °C (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (s, 6 H, 2 × CH_3), 4.20 (d, J = 17.3 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.36 (s, 2 H, 13-H), 4.51 (d, J = 17.3 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.79 (d, J = 0.8 Hz, 2 H, 1-H and 7-H), 7.56 (d, J = 0.8 Hz, 2 H, 3-H and 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.55 (2 C, 2 × CH_3), 56.75 (2 C, C-6 and C-12), 68.19 (1 C, C-13), 97.50 (2 C, C-4 and C-10), 127.89 (2 C, C-1 and C-7), 130.38 (2 C, C-6a and C-12a), 136.41 (2 C, C-2 and C-8), 138.49 (2 C, C-3 and C-9), 145.05 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): m/z calcd. for $C_{17}H_{16}I_2N_2$ [M] 501.9403; found 501.9414. $C_{17}H_{16}I_2N_2$, C 40.66, H 3.21, N 5.58; found C 40.34, H 3.17, N 5.51.

4b: R_f = 0.06 (10% EtOAc in heptane), m.p. 133.9−134.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.19 (s, 3 H, C-2-CH_3), 2.24 (s, 3 H, C-8-CH_3), 4.08 (br. d, $^2J_{H,H}$ = 16.7 Hz, 1 H, 12*endo*-H), 4.28 (br. d, $^2J_{H,H}$ = 16.6 Hz, 1 H, 6*endo*-H), 4.29 (dd, $^2J_{H,H}$ = 12.7, $^4J_{H,H}$ = 1.6 Hz, 1 H, 13′-H), 4.39 (dd, $^2J_{H,H}$ = 12.7, $^4J_{H,H}$ = 1.3 Hz, 1 H, 13′′-H), 4.56 (d, $^2J_{H,H}$ = 16.6 Hz, 1 H, 6*exo*-H), 4.60 (d, $^2J_{H,H}$ = 16.7 Hz, 1 H, 12*exo*-H), 6.73 (d, $^4J_{H,H}$ = 0.7 Hz, 1 H, 1-H), 6.78 (br. s, 1 H, 7-H), 6.99 (dd, $^3J_{H,H}$ = 8.2, $^4J_{H,H}$ = 1 Hz, 1 H, 9-H), 7.06 (d, $^3J_{H,H}$ = 8.2 Hz, 1 H, 10-H), 7.55 (d, $^4J_{H,H}$ =

0.7 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.51 (1 C, C-2-*C*H$_3$), 21.08 (1 C, C-8-*C*H$_3$), 56.18 (1 C, C-6), 59.43 (1 C, C-12), 67.74 (1 C, C-13), 97.45 (1 C, C-4), 124.99 (1 C, C-10), 127.55 (1 C, C-7), 127.69 (1 C, C-6a), 127.84 (1 C, C-1), 128.39 (1 C, C-9), 130.47 (1 C, C-12a), 133.99 (1 C, C-8), 136.10 (1 C, C-2), 138.56 (1 C, C-3), 145.31 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{17}IN_2$ [M] 376.0437; found 376.0444. $C_{17}H_{17}IN_2$, C 54.27, H 4.55, N 7.45; found C 54.21, H 4.47, N 7.37.

4,10-Dibromo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (5): This compound was prepared using 2-bromoaniline (173 mg, 1.01 mmol) and paraformaldehyde (60 mg, 2.0 mmol) and stirring for 16 h. CC (10% EtOAc in heptane) gave **5** in 9% yield (17 mg) as a white solid. R_f = 0.40 (20% EtOAc in heptane), m.p. 161.7−163.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.37 (d, *J* = 17.3 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.39 (s, 2 H, 13-H), 4.62 (d, *J* = 17.3 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.91−6.96 (m, 4 H, 1-H, 2-H, 7-H, and 8-H), 7.46 (dd, *J* = 6.7, *J* = 2.6 Hz, 2 H, 3-H and 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.56 (2 C, C-6 and C-12), 67.72 (1 C, C-13), 120.27 (2 C, C-4 and C-10), 125.76 (2 C, C-2 and C-8), 126.47 (2 C, C-1 and C-7), 131.06 (2 C, C-6a and C-12a), 131.69 (2 C, C-3 and C-9), 144.92 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Br_2N_2$ [M] 377.9367; found 377.9375. $C_{15}H_{12}Br_2N_2$, C 47.40, H 3.18, N 7.37; found C 47.55, H 3.25, N 7.28.

4,10-Dichloro-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (6): This compound was prepared using 2-chloroaniline (139 mg, 1.09 mmol) and paraformaldehyde (72 mg, 2.4 mmol) and stirring for 22 h. CC (10% EtOAc in heptane) gave **6** in 19% yield (31 mg) as colourless oil which later solidified. R_f = 0.18 (10% EtOAc in heptane), m.p. 144.8−147.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.35 (d, *J* = 17.6 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.38 (s, 2 H, 13-H), 4.63 (d, *J* = 17.6 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.90 (dd, *J* = 7.7, *J* = 0.8 Hz, 2 H, 1-H and 7-H), 6.99 (t, *J* = 7.7 Hz, 2 H, 2-H and 8-H), 7.27 (dd, *J* = 7.7, *J* = 0.8 Hz, 2 H, 3-H and 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 54.97 (2 C, C-6 and C-12), 67.69 (1 C, C-13), 125.10 (2 C, C-2 and C-8), 125.79 (2 C, C-1 and C-7), 128.49 (2 C, C-3 and C-9), 129.45 (2 C, C-4 and C-10), 130.59 (2 C, C-6a and C-12a), 143.67 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Cl_2N_2$ [M] 290.0378; found 290.0375. $C_{15}H_{12}Cl_2N_2$, C 61.87, H 4.15, N 9.62; found, C 61.74, H 4.07, N 9.57.

4,10-Difluoro-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (7): This compound was prepared using 2-fluoroaniline (124 mg, 1.12 mmol) and paraformaldehyde (74 mg, 2.4 mmol) and stirring for 7 h. CC (5% EtOAc in heptane) followed by a second CC (20% EtOAc in heptane) gave **7** in 27% yield (39 mg) as a white solid. R_f = 0.48 (50% EtOAc in heptane), m.p. 124.1−125.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.23 (d, *J* = 17.1 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.32 (s, 2 H, 13-H), 4.63 (d, *J* = 17.1 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.76 (d, *J* = 7.3 Hz, 2 H, 1-H and 7-H), 6.90−7.00 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.38 (t, $^4J_{C,F}$ = 2 Hz, 2 C, C-6 and C-12), 67.42 (1 C, C-13), 114.06 (d, $^2J_{C,F}$ = 20 Hz, 2 C, C-3 and C-9), 122.54 (d, $^4J_{C,F}$ = 4 Hz, 2 C, C-1 and C-7), 124.54 (d, $^3J_{C,F}$ = 8 Hz, 2 C, C-2 and C-8), 130.30 (d, $^3J_{C,F}$ = 3 Hz, 2 C, C-6a and C-12a), 135.23 (d, $^2J_{C,F}$ = 12 Hz, 2 C, C-4a and C-10a), 156.32 (d, $^1J_{C,F}$ = 247 Hz, 2 C, C-4 and C-10) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}F_2N_2$ [M] 258.0969; found 258.0976. $C_{15}H_{12}F_2N_2$, C 69.76, H 4.68, N 10.85; found C 69.71, H 4.74, N 10.74.

1,7-Diiodo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (8a), 3,9-Diiodo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (8b), and 1,9-Diiodo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (8c): These compounds were prepared using 3-iodo-4-methylaniline (233 mg, 1.00 mmol) and paraformaldehyde (60 mg, 2.0 mmol) and stirring for 98 h in the dark. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (400 MHz, $CDCl_3$) to be **8a/8b/8c**; 44:8:48. CC (gradient 10−20% EtOAc in heptane) gave a crude separation of the regioisomers. Further purifications gave **8a** in 17% yield (44 mg) (recrystallization from EtOAc), **8b** in 1.8% yield (4.7 mg) [SEC followed by CC on a 2 × 5 cm column (5% EtOAc in heptane)], and **8c** in 2.8% yield (7.0 mg) (recrystallization from EtOAc) as white solids.

8a: R_f = 0.60 (50% EtOAc in heptane), m.p. 308.6−310.4 °C dec (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 6 H, 2 × C*H*$_3$), 4.11 (d, *J* = 16.9 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.19 (s, 2 H, 13-H), 4.37 (d, *J* = 16.9 Hz, 2 H, 6*exo*-H and 12*exo*-H), 7.10 (d, J_{AB} = 8.3 Hz, 2 H, 3-H and 9-H), 7.11 (d, J_{AB} = 8.3 Hz, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.49 (2 C, 2 × *C*H$_3$), 66.10 (2 C, C-6 and C-12), 66.30 (1 C, C-13), 105.68 (2 C, C-1 and C-7), 125.08 (2 C, C-4 and C-10), 128.47 (2 C, C-3 and C-9), 130.59 (2 C, C-6a and C-12a), 137.97 (2 C, C-2 and C-8), 147.28 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}I_2N_2$ [M] 501.9403; found 501.9398. $C_{17}H_{16}I_2N_2$, C 40.66, H 3.21, N 5.58; found C 40.47, H 3.16, N 5.43.

8b: R_f = 0.48 (50% EtOAc in heptane), m.p. 258.3−259.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 6 H, 2 × C*H*$_3$), 4.06 (d, *J* = 16.8 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.22 (s, 2 H, 13-H), 4.56 (d, *J* = 16.8 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.78 (s, 2 H, 1-H and 7-H), 7.59 (s, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.49 (2 C, 2 × *C*H$_3$), 58.65 (2 C, C-6 and C-12), 66.95 (1 C, C-13), 98.74 (2 C, C-3 and C-9), 127.81 (2 C, C-1 and C-7), 127.86 (2 C, C-6a and C-12a), 135.24 (2 C, C-4 and C-10), 137.13 (2 C, C-2 and C-8), 147.01 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}I_2N_2$ [M] 501.9403; found 501.9406. $C_{17}H_{16}I_2N_2$, C 40.66, H 3.21, N 5.58; found C 40.74, H 3.25, N 5.66.

8c: R_f = 0.42 (50% EtOAc in heptane), m.p. 182.7−183.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, C-8-C*H*$_3$), 2.37 (s, 3 H, C-2-C*H*$_3$), 4.05 (d, *J* = 17.0 Hz, 1 H, 12*endo*-H), 4.10 (d, *J* = 16.9 Hz, 1 H, 6*endo*-H), 4.18 (d, J_{AB} = 12.8 Hz, 1 H, 13′-H), 4.22 (d, J_{AB} = 12.8 Hz, 1 H, 13′′-H), 4.35 (d, *J* = 17.0 Hz, 1 H, 12*exo*-H), 4.59 (d, *J* = 16.9 Hz, 1 H, 6*exo*-H), 6.77 (s, 1 H, 7-H), 7.05 (d, *J* = 8.2 Hz, 1 H, 4-H), 7.08 (d, *J* = 8.2 Hz, 1 H, 3-H), 7.65 (s, 1 H, 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.50 (1 C, C-8-*C*H$_3$), 28.50 (1 C, C-2-*C*H$_3$), 58.56 (1 C, C-6), 66.07 (1 C, C-12), 66.57 (1 C, C-13), 98.83 (1 C, C-9), 105.89 (1 C, C-1), 124.81 (1 C, C-4), 127.60 (1 C, C-7), 127.83 (1 C, C-6a), 128.36 (1 C, C-3), 130.53 (1 C, C-12a), 135.40 (1 C, C-10), 137.23 (1 C, C-8), 137.88 (1 C, C-2), 147.09 (1 C, C-4a), 147.16 (1 C, C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}I_2N_2$ [M] 501.9403; found 501.9395. $C_{17}H_{16}I_2N_2$, C 40.66, H 3.21, N 5.58; found C 40.46, H 3.18, N 5.50.

1,7-Dibromo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (9a), 3,9-Dibromo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (9b), and 1,9-Dibromo-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (9c): These compounds were prepared using 3-bromo-4-methylaniline (191 mg, 1.03 mmol) and paraformaldehyde (63 mg, 2.1 mmol) and stirring for 72 h. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (400 MHz, $CDCl_3$) to be **9a/9b/9c**; 39:11:50. CC (20% EtOAc in heptane) gave **9a** in 24% yield (50 mg), **9b** in 6% yield (14 mg), and **9c** in 29% yield (60 mg) as white solids.

9a: R_f = 0.54 (50% EtOAc in heptane), m.p. 262.6−264.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 6 H, 2 × CH_3), 4.21 (s, 2 H, 13-H), 4.23 (d, J = 18.0 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.47 (d, J = 18.0 Hz, 2 H, 6*exo*-H and 12*exo*-H), 7.09 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.89 (2 C, 2 × *C*H$_3$), 60.74 (2 C, C-6 and C-12), 66.03 (1 C, C-13), 124.12 (2 C, C-4 and C-10), 125.36 (2 C, C-1 and C-7), 127.70 (2 C, C-6a and C-12a), 129.42 (2 C, C-3 and C-9), 134.02 (2 C, C-2 and C-8), 147.64 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Br_2N_2$ [M] 405.9680; found 405.9693. $C_{17}H_{16}Br_2N_2$, C 50.03, H 3.95, N 6.86; found C 49.79, H 4.11, N 6.81.

9b: R_f = 0.42 (50% EtOAc in heptane), m.p. 239.9−242.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 6 H, 2 × CH_3), 4.07 (d, J = 16.8 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.23 (s, 2 H, 13-H), 4.57 (d, J = 16.8 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.78 (s, 2 H, 1-H and 7-H), 7.31 (s, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 22.41 (2 C, 2 × *C*H$_3$), 58.59 (2 C, C-6 and C-12), 66.97 (1 C, C-13), 123.14 (2 C, C-2 and C-8), 126.89 (2 C, C-6a and C-12 a), 128.64 (2 C, C-4 and C-10), 128.97 (2 C, C-1 and C-7), 133.72 (2 C, C-3 and C-9), 147.07 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Br_2N_2$ [M] 405.9680; found 405.9689. $C_{17}H_{16}Br_2N_2$, C 50.03, H 3.95, N 6.86; found C 50.12, H 4.07, N 6.79.

9c: R_f = 0.33 (50% EtOAc in heptane), m.p. 171.9−173.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, C-8-CH_3), 2.31 (s, 3 H, C-2-CH_3), 4.10 (d, J = 16.7 Hz, 1 H, 6*endo*-H), 4.15−4.27 (m, 3 H, 13-H and 12*endo*-H), 4.44 (d, J = 17.2 Hz, 1 H, 12*exo*-H), 4.59 (d, J = 16.7 Hz, 1 H, 6*exo*-H), 6.77 (s, 1 H, 7-H), 7.02 (d, J = 8.2 Hz, 1 H, 4-H), 7.08 (d, J = 8.2 Hz, 1 H, 3-H), 7.37 (s, 1 H, 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.42 (1 C, C-8-*C*H$_3$), 22.91 (1 C, C-2-*C*H$_3$), 58.48 (1 C, C-6), 60.81 (1 C, C-12), 66.47 (1 C, C-13), 123.18 (1 C, C-9), 123.84 (1 C, C-4), 125.52 (1 C, C-1), 126.86 (1 C, C-6a), 127.70 (1 C, C-12a), 128.79 (1 C, C-7), 128.87 (1 C, C-10), 129.35 (1 C, C-3), 133.79 (1 C, C-8), 133.99 (1 C, C-2), 147.26 (1 C, C-10a), 147.46 (1 C, C-4a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Br_2N_2$ [M] 405.9680; found 405.9670. $C_{17}H_{16}Br_2N_2$, C 50.03, H 3.95, N 6.86; found C 49.95, H 4.08, N 6.87.

1,7-Dichloro-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (10a), 3,9-Dichloro-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (10b), and 1,9-Dichloro-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (10c): These compounds were prepared using 3-chloro-4-methylaniline (143 mg, 1.01 mmol) and paraformaldehyde (62 mg, 2.1 mmol) and stirring for 138 h. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (400 MHz, $CDCl_3$) to be **10a/10b/10c**; 28:18:54. CC (20% EtOAc in heptane) gave **10a** in 23% yield (37 mg), **10b** in 9% yield (15 mg), and **10c** in 26% yield (42 mg) as white solids.

10a: R_f = 0.56 (50% EtOAc in heptane), m.p. 198.3−199.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.28 (s, 6 H, 2 × CH_3), 4.22 (s, 2 H, H-13), 4.28 (d, J = 17.2 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.52 (d, J = 17.2 Hz, 2 H, 6*exo*-H and 12*exo*-H), 7.04 (d, J_{AB} = 8.3 Hz, 2 H, 4-H and 10-H), 7.08 (d, J_{AB} = 8.3 Hz, 2 H, 3-H and 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.90 (2 C, 2 × *C*H$_3$), 58.09 (2 C, C-6 and C-12), 66.01 (1 C, C-13), 123.44 (2 C, C-4 and C-10), 126.03 (2 C, C-6a and C-12a), 129.52 (2 C, C-3 and C-9), 131.96 (2 C, C-2 and C-8), 132.80 (2 C, C-1 and C-7), 147.53 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Cl_2N_2$ [M] 318.0691; found 318.0693. $C_{17}H_{16}Cl_2N_2$, C 63.96, H 5.05, N 8.78; found C 64.07, H 5.06, N 8.65.

10b: R_f = 0.48 (50% EtOAc in heptane), m.p. 227.6−229.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.24 (s, 6 H, 2 × CH_3), 4.08 (d, J = 16.7 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.25 (s, 2 H, 13-H), 4.59 (d, J = 16.7 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.77 (s, 2 H, 1-H and 7-H), 7.12 (s, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.63 (2 C, 2 × *C*H$_3$), 58.53 (2 C, C-6 and C-12), 66.99 (1 C, C-13), 125.38 (2 C, C-4 and C-10), 126.21 (2 C, C-6a and C-12a), 129.16 (2 C, C-1 and C-7), 131.97 (2 C, C-3 and C-9), 133.00 (2 C, C-2 and C-8), 146.93 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Cl_2N_2$ [M] 318.0691; found 318.0690. $C_{17}H_{16}Cl_2N_2$, C 63.96, H 5.05, N 8.78; found C 64.08, H 5.11, N 8.68.

10c: R_f = 0.40 (50% EtOAc in heptane), m.p. 158.8−161.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, C-8-CH_3), 2.27 (s, 3 H, C-2-CH_3), 4.11 (d, J = 16.7 Hz, 1 H, 6*endo*-H), 4.18−4.28 (m, 3 H, 12*endo*-H and 13-H), 4.50 (d, J = 17.3 Hz, 1 H, 12*exo*-H), 4.62 (d, J = 16.7 Hz, 1 H, 6*exo*-H), 6.76 (s, 1 H, 7-H), 6.98 (d, J = 8.2 Hz, 1 H, 4-H), 7.07 (d, J = 8.2 Hz, 1 H, 3-H), 7.18 (s, 1 H, 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.64 (1 C, C-8-*C*H$_3$), 19.92 (1 C, C-2-*C*H$_3$), 58.21 (1 C, C-12), 58.40 (1 C, C-6), 66.49 (1 C, C-13), 123.16 (1 C, C-4), 125.62 (1 C, C-10), 126.05 (1 C, C-12a), 126.19 (1 C, C-6a), 129.02 (1 C, C-7), 129.48 (1 C, C-3), 131.96 (1 C, C-2), 132.02 (1 C, C-8), 132.94 (1 C, C-1), 133.03 (1 C, C-9), 147.13 (1 C, C-10a), 147.36 (1 C, C-4a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Cl_2N_2$ [M] 318.0691; found 318.0688. $C_{17}H_{16}Cl_2N_2$, C 63.96, H 5.05, N 8.78; found C 63.85, H 4.98, N 8.71.

3,9-Difluoro-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (11b): This compound was prepared using 3-fluoro-4-methylaniline (127 mg, 1.01 mmol) and paraformaldehyde (61 mg, 2.0 mmol) and stirring for 23 h. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (400 MHz, $CDCl_3$) to be **11b/11c**: 74:26. Despite several attempts of CC and recrystallization the compound **11b** was not isolated from the 1,9-isomer **11c**. Since it was in excess it could still be analyzed. R_f = 0.16 (30% EtOAc in heptane), m.p. 238.7−241.8 °C (**11b** + **11c**). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.18 (s, 6 H, 2 × CH_3), 4.07 (d, J = 16.4 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.26 (s, 2 H, 13-H), 4.60 (d, J = 16.4 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.70 (d, $^4J_{H,F}$ = 8.3 Hz, 2 H, 1-H and 7-H), 6.78 (d, $^3J_{H,F}$ = 10.8 Hz, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.32 (d, $^3J_{C,F}$ = 3 Hz, 2 C, 2 × *C*H$_3$), 58.37 (2 C, C-6 and C-12), 66.93 (1 C, C-13), 111.19 (d, $^2J_{C,F}$ = 23 Hz, 2 C, C-4 and C-10), 121.21 (d, $^2J_{C,F}$ = 18 Hz, 2 C, C-2 and C-8), 122.98 (d, $^4J_{C,F}$ = 3 Hz, 2 C, C-6a and C-12a), 129.42 (d, $^3J_{C,F}$ = 6 Hz, 2 C, C-1 and C-7), 147.01 (d, $^3J_{C,F}$ = 10 Hz, 2 C, C-4a and C-10a), 160.46 (d, $^1J_{C,F}$ = 244 Hz, 2 C, C-3 and C-9) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}F_2N_2$ [M] 286.1282, found 286.1292 (**11b** + **11c**). $C_{17}H_{16}F_2N_2$, C 71.31, H 5.63, N 9.78; found C 71.26, H 5.58, N 9.86 (**11b** + **11c**).

1,7-Diiodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (12a), 3,9-Diiodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (12b), and 1,9-Diiodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (12c): These compounds were prepared using 3-iodoaniline (227 mg, 1.04 mmol) and paraformaldehyde (63 mg, 2.1 mmol) and stirring for 15 h in the dark. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (300 MHz, $CDCl_3$) to be **12a/12b/12c**; 32:17:51. CC (20% EtOAc in heptane) gave **12a** in 8% yield (20 mg) and **12c** in 12% yield (29 mg) as beige solids. Further purification by SEC followed by CC on a 2 × 5 cm column (20% EtOAc in heptane) gave **12b** in 2% yield (5 mg) as a white solid.

12a: R_f = 0.60 (50% EtOAc in heptane), m.p. 250.1−252.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.06 (d, J = 17.0 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.21 (s, 2 H, 13-H), 4.38 (d, J = 17.0 Hz, 2 H,

6*exo*-H and 12*exo*-H), 6.92 (t, J = 7.9 Hz, 2 H, 3-H and 9-H), 7.19 (dd, J = 7.9, J = 1.0 Hz, 2 H), 7.52 (dd, J = 7.9, J = 1.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.03 (2 C, C-6 and C-12), 66.54 (1 C, C-13), 98.72 (2 C, C-1 and C-7), 125.75 (2 C), 129.22 (2 C, C-3 and C-9), 130.45 (2 C, C-6a and C-12a), 134.98 (2 C), 150.04 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}I_2N_2$ [M] 473.9090, found 473.9095. $C_{15}H_{12}I_2N_2$, C 38.00, H 2.55, N 5.91; found C 37.86, H 2.61, N 5.80.

12b: R_f = 0.56 (50% EtOAc in heptane), m.p. 206.0−207.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.11 (d, J = 16.8 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.23 (t, J = 1.2 Hz, 2 H, 13-H), 4.60 (d, J = 16.8 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.66 (d, J = 8.1 Hz, 2 H, 1-H and 7-H), 7.31 (dd, J = 8.1, J = 1.7 Hz, 2 H, 2-H and 8-H), 7.49 (d, J = 1.7 Hz, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.68 (2 C, C-6 and C-12), 66.57 (1 C, C-13), 91.92 (2 C, C-3 and C-9), 127.54 (2 C, C-6a and C-12a), 128.89 (2 C, C-1 and C-7), 133.34 (2 C, C-2 and C-8), 134.26 (2 C, C-4 and C-10), 149.76 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}I_2N_2$ [M] 473.9090, found 473.9097. $C_{15}H_{12}I_2N_2$, C 38.00, H 2.55, N 5.91; found C 38.08, H 2.58, N 5.85.

12c: R_f = 0.46 (50% EtOAc in heptane), m.p. 248.6−250.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.01 (d, J = 16.9 Hz, 1 H, 12*endo*-H), 4.14 (d, J = 17.0 Hz, 6*endo*-H), 4.09−4.26 (m, 2 H, 13-H), 4.36 (d, J = 16.9 Hz, 1 H, 12*exo*-H), 4.63 (d, J = 17.0 Hz, 1 H, 6*exo*-H), 6.65 (d, J = 8.0 Hz, 1 H, 7-H), 6.91 (t, J = 7.9 Hz, 1 H, 3-H), 7.13 (dd, J = 7.9, J = 0.9 Hz, 1 H), 7.32 (dd, J = 8.0, J = 1.7 Hz, 1 H, 8-H), 7.52 (dd, J = 7.9, J = 0.9 Hz, 1 H), 7.54 (d, J = 1.7 Hz, 1 H, 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.62 (1 C, C-6), 64.91 (1 C, C-12), 66.47 (1 C, C-13), 92.03 (1 C, C-9), 98.93 (1 C, C-1), 125.50 (1 C), 127.51 (1 C, C-6a), 128.73 (1 C, C-7), 129.13 (1 C, C-3), 130.31 (1 C, C-12a), 133.47 (1 C, C-8), 134.36 (1 C, C-10), 134.95 (1 C), 149.76 (1 C), 149.80 (1 C) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}I_2N_2$ [M] 473.9090, found 473.9090. $C_{15}H_{12}I_2N_2$, C 38.00, H 2.55, N 5.91; found C 37.70, H 2.65, N 5.70.

1,7-Dibromo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (13a), 3,9-Dibromo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (13b), and 1,9-Dibromo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (13c): These compounds were prepared using 3-bromoaniline (181 mg, 1.05 mmol) and paraformaldehyde (64 mg, 2.1 mmol) and stirring for 14 h. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (400 MHz, $CDCl_3$) to be **13a/13b/13c**; 21:19:60. CC (20% EtOAc in heptane) gave a crude separation of the regioisomers. Further purifications gave **13a** in 1.8% yield (3.5 mg) (recrystallization from EtOAc), **13b** in 2.2% yield (4.4 mg) [SEC followed by CC on a 2 × 5 cm column (20% EtOAc in heptane)] and **13c** in 18% yield (35 mg) [CC (20% EtOAc in heptane)] as white solids.

13a: R_f = 0.32 (20% EtOAc in heptane), m.p. 231.0−231.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.22 (d, J = 17.0 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.23 (s, 2 H, 13-H), 4.49 (d, J = 17.0 Hz, 2 H, 6*exo*-H and 12*exo*-H), 7.08 (t, J = 7.9 Hz, 2 H, 3-H and 9-H), 7.16 (dd, J = 7.9, J = 1.2 Hz, 2 H), 7.24 (dd, J = 7.9, J = 1.2 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 60.17 (2 C, C-6 and C-12), 66.17 (1 C, C-13), 123.13 (2 C, C-1 and C-7), 124.70 (2 C), 127.64 (2 C, C-6a and C-12a), 128.21 (2 C), 128.75 (2 C, C-3 and C-9), 150.20 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Br_2N_2$ [M] 377.9367; found 377.9381. $C_{15}H_{12}Br_2N_2$, C 47.40, H 3.18, N 7.37; found C 47.15, H 3.10, N 7.18.

13b: R_f = 0.22 (20% EtOAc in heptane), m.p. 201.6−203.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.12 (d, J = 16.8 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.25 (s, 2 H, 13-H), 4.61 (d, J = 16.8 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.80 (d, J = 8.2 Hz, 2 H, 1-H and 7-H), 7.12 (dd, J = 8.2, J = 2.0 Hz, 2 H, 2-H and 8-H), 7.29 (d, J = 2.0 Hz, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.59 (2 C, C-6 and C-12), 66.63 (1 C, C-13), 120.70 (2 C, C-3 and C-9), 126.75 (2 C, C-6a and C-12a), 127.49 (2 C, C-2 and C-8), 128.21 (2 C, C-4 and C-10), 128.68 (2 C, C-1 and C-7), 149.59 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Br_2N_2$ [M] 377.9367; found 377.9370. $C_{15}H_{12}Br_2N_2$, C 47.40, H 3.18, N 7.37; found C 47.28, H 3.13, N 7.28.

13c: R_f = 0.16 (20% EtOAc in heptane), m.p. 190.7−192.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.15 (d, J = 17.0 Hz, 1 H, 6*endo*-H), 4.13−4.28 (m, 3 H, 13-H and 12*endo*-H), 4.47 (d, J = 17.1 Hz, 1 H, 12*exo*-H), 4.64 (d, J = 17.0 Hz, 1 H, 6*exo*-H), 6.78 (d, J = 8.2 Hz, 1 H, 7-H), 7.04−7.13 (m, 3 H), 7.22 (dd, J = 7.6, J = 1.4 Hz, 1 H), 7.35 (d, J = 2.0 Hz, 1 H, 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.51 (1 C, C-6), 60.09 (1 C, C-12), 66.30 (1 C, C-13), 120.71 (1 C, C-9), 123.23 (1 C, C-12a), 124.38 (1 C), 126.69 (1 C, C-6a), 127.51 (1 C), 127.55 (1 C, C-1), 128.13 (1 C), 128.37 (1 C, C-10), 128.49 (1 C, C-7), 128.62 (1 C), 149.65 (1 C, C-4a), 149.98 (1 C, C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Br_2N_2$ [M] 377.9367; found 377.9376. $C_{15}H_{12}Br_2N_2$, C 47.40, H 3.18, N 7.37; found C 47.36, H 3.15, N 7.28.

1,7-Dichloro-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (14a), 3,9-Dichloro-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (14b), and 1,9-Dichloro-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (14c): These compounds were prepared using 3-chloroaniline (132 mg, 1.03 mmol) and paraformaldehyde (63 mg, 2.1 mmol) and stirring for 15 h. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (400 MHz, $CDCl_3$) to be **14a/14b/14c**; 18:28:53. CC (20% EtOAc in heptane) followed by recrystallization gave **14a** in 2% yield (3 mg), **14b** in 5% yield (8 mg) and **14c** in 8% yield (12 mg).

14a: R_f = 0.54 (50% EtOAc in heptane), m.p. 222.6−224.9 °C (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.25 (s, 2 H, 13-H), 4.29 (d, J = 17.3 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.55 (d, J = 17.3 Hz, 2 H, 6*exo*-H and 12*exo*-H), 7.05 (dd, J = 7.5, J = 1.6 Hz, 2 H), 7.10−7.17 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 57.71 (2 C, C-6 and C-12), 66.07 (1 C, C-13), 123.99 (2 C), 124.89 (2 C), 126.08 (2 C, C-6a and C-12a), 128.32 (2 C), 133.01 (2 C, C-1 and C-7), 149.97 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Cl_2N_2$ [M] 290.0378; found 290.0367. $C_{15}H_{12}Cl_2N_2$, C 61.87, H 4.15, N 9.62; found C 61.68, H 4.22, N 9.51.

14b: R_f = 0.44 (50% EtOAc in heptane), m.p. 191.4−192.9 °C (heptane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.14 (d, J = 16.8 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.26 (t, J = 1.1 Hz, 2 H, 13-H), 4.64 (d, J = 16.8 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.85 (d, J = 8.2 Hz, 2 H, 1-H and 7-H), 6.97 (dd, J = 8.2, J = 2.1 Hz, 2 H, 2-H and 8-H), 7.10 (d, J = 2.1 Hz, 2 H, 4-H and 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.52 (2 C, C-6 and C-12), 66.67 (1 C, C-13), 124.63 (2 C, C-2 and C-8), 125.23 (2 C, C-4 and C-10), 126.22 (2 C, C-6a and C-12a), 128.36 (2 C, C-1 and C-7), 132.88 (2 C, C-3 and C-9), 149.32 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Cl_2N_2$ [M] 290.0378; found 290.0376. $C_{15}H_{12}Cl_2N_2$, C 61.87, H 4.15, N 9.62; found C 62.18, H 4.11, N 9.55.

14c: R_f = 0.34 (50% EtOAc in heptane), m.p. 158.0−159.7 °C (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.17 (d, J = 16.7 Hz,

1 H, 6*endo*-H), 4.20−4.29 (m, 3 H, 12*endo*-H and 13-H), 4.52 (d, J = 17.3 Hz, 1 H, 12*exo*-H), 4.66 (d, J = 16.7 Hz, 1 H, 6*exo*-H), 6.85 (d, J = 8.2 Hz, 1 H, 7-H), 6.98 (dd, J = 8.2, J = 2.1 Hz, 1 H, 8-H), 7.03−7.07 (m, 2 H, 2-H and 4-H), 7.12−7.16 (m, 1 H, 3-H), 7.18 (d, J = 2.1 Hz, 1 H, 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 57.71 (1 C, C-12), 58.48 (1 C, C-6), 66.35 (1 C, C-13), 123.72 (1 C), 124.69 (1 C, C-8), 124.87 (1 C), 125.46 (1 C, C-10), 126.06 (1 C, C-12a), 126.20 (1 C, C-6a), 128.25 (2 C, C-3 and C-7), 132.92 (1 C, C-9), 133.10 (1 C, C-1), 149.44 (1 C, C-10a), 149.81 (1 C, C-4a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}Cl_2N_2$ [M] 290.0378; found 290.0377. $C_{15}H_{12}Cl_2N_2$, C 61.87, H 4.15, N 9.62; found C 62.12, H 4.14, N 9.67.

3,9-Difluoro-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (15b): This compound was prepared using 3-fluoroaniline (111 mg, 1.00 mmol) and paraformaldehyde (61 mg, 2.0 mmol) and stirring for 14 h. The regioisomeric ratio of the crude product was determined by ^{1}H NMR (300 MHz, $CDCl_3$) to be **15b/15c**: 66:34. Despite several attempts of CC and recrystallization the compound **15b** was not isolated from the 1,9-isomer **15c**. For elemental analysis a small amount was purified further by SEC followed by CC on a 2 × 5 cm column (5% EtOAc in heptane). R_f = 0.26 (20% EtOAc in heptane), m.p. 171.3−173.8 °C (**15b** + **15c**). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.13 (d, J = 16.4 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.26 (s, 2 H, 13-H), 4.64 (d, J = 16.4 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.71 (dt, J = 8.4, J = 2.4 Hz, 2 H, 2-H and 8-H), 6.80−6.88 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.46 (2 C, C-6 and C-12), 66.73 (1 C, C-13), 111.70 (d, J = 7 Hz, 2 C), 111.91 (d, J = 7 Hz, 2 C), 123.40 (d, $^4J_{C,F}$ = 3 Hz, 2 C, C-6a and C-12a), 128.36 (d, J = 9 Hz, 2 C), 149.61 (d, $^3J_{C,F}$ = 10 Hz, 2 C, C-4a and C-10a), 162.14 (d, $^1J_{C,F}$ = 244 Hz, 2 C, C-3 and C-9) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{15}H_{12}F_2N_2$ (M) 258.0969; found 258.0972 (**15b** + **15c**). $C_{15}H_{12}F_2N_2$, C 69.76, H 4.68, N 10.85; found C 69.92, H 4.81, N 10.81 (**15b** + **15c**).

3,9-Diiodo-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (16): This compound was prepared using 3-iodo-2-methylaniline (237 mg, 1.02 mmol) and paraformaldehyde (69 mg, 2.3 mmol) and stirring for 7 h in the dark. CC (5% EtOAc in heptane) gave **16** in 59% yield (150 mg) as a white solid. R_f = 0.24 (5% EtOAc in heptane), m.p. 214.9−216.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 6 H, 2 × CH_3), 3.87 (d, J = 17.0 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.27 (s, 2 H, 13-H), 4.53 (d, J = 17.0 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.50 (d, J = 8.1 Hz, 2 H, 1-H and 7-H), 7.51 (d, J = 8.1 Hz, 2 H, 2-H and 8-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.03 (2 C, 2 × *C*H_3), 55.39 (2 C, C-6 and C-12), 67.46 (1 C, C-13), 100.51 (2 C, C-3 and C-9), 126.26 (2 C, C-1 and C-7), 128.19 (2 C, C-6a and C-12a), 134.70 (2 C, C-2 and C-8), 136.57 (2 C, C-4 and C-10), 146.75 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}I_2N_2$ [M] 501.9403, found 501.9400. $C_{17}H_{16}I_2N_2$, C 40.66, H 3.21, N 5.58; found C 40.45, H 3.15, N 5.38.

3,9-Dibromo-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (17): This compound was prepared using 3-bromo-2-methylaniline (190 mg, 1.02 mmol) and paraformaldehyde (62 mg, 2.1 mmol) and stirring for 7 h. CC (5% EtOAc in heptane) followed by SEC and CC on a 2 × 5 cm column (5% EtOAc in heptane) gave **17** in 41% yield (86 mg) as a white solid. R_f = 0.44 (20% EtOAc in heptane), m.p. 219.2−221.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48 (s, 6 H, 2 × CH_3), 3.89 (d, J = 16.9 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.28 (s, 2 H, 13-H), 4.54 (d, J = 16.9 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.65 (d, J = 8.2 Hz, 2 H, 1-H and 7-H), 7.23 (d, J = 8.2 Hz, 2 H, 2-H and 8-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.49 (2 C, 2 × *C*H_3), 55.39 (2 C, C-6 and C-12), 67.40 (1 C, C-13), 124.24 (2 C, C-3 and C-9), 125.70 (2 C, C-1 and C-7), 127.15 (2 C, C-6a and C-12a), 128.13 (2 C, C-2 and C-8), 133.23 (2 C, C-4 and C-10), 147.37 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Br_2N_2$ [M] 405.9680, found 405.9690. $C_{17}H_{16}Br_2N_2$, C 50.03, H 3.95, N 6.86; found C 49.97, H 3.90, N 6.81.

3,9-Dichloro-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (18): This compound was prepared using 3-chloro-2-methylaniline (152 mg, 1.07 mmol) and paraformaldehyde (66 mg, 2.2 mmol) and stirring for 7 h. CC (5% EtOAc in heptane) followed by SEC and CC on a 2 × 5 cm column (5% EtOAc in heptane) gave **18** in 48% yield (81 mg) as a white solid. R_f = 0.18 (5% EtOAc in heptane), m.p. 205.9−207.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 6 H, 2 × CH_3), 3.91 (d, J = 16.9 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.29 (s, 2 H, 13-H), 4.57 (d, J = 16.9 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.71 (d, J = 8.2 Hz, 2 H, 2-H and 8-H), 7.05 (d, J = 8.2 Hz, 2 H, 1-H and 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.46 (2 C, 2 × *C*H_3), 55.34 (2 C, C-6 and C-12), 67.38 (1 C, C-13), 124.90 (2 C, C-1 and C-7), 125.22 (2 C, C-2 and C-8), 126.47 (2 C, C-6a and C-12a), 131.43 (2 C, C-3 and C-9), 133.63 (2 C, C-4 and C-10), 147.33 (2 C, C-4a and C-10a) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}Cl_2N_2$ [M] 318.0691, found 318.0704. $C_{17}H_{16}Cl_2N_2$, C 63.96, H 5.05, N 8.78; found C 64.08, H 4.95, N 8.71.

3,9-Difluoro-4,10-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine (19): This compound was prepared using 3-fluoro-2-methylaniline (132 mg, 1.05 mmol) and paraformaldehyde (63 mg, 2.1 mmol) and stirring for 7 h. CC (5% EtOAc in heptane) followed by SEC and CC on a 2 × 5 cm column (5% EtOAc in heptane) gave **19** in 32% yield (49 mg) as a white solid. R_f = 0.14 (5% EtOAc in heptane), m.p. 162.0−163.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (d, $^4J_{H,F}$ = 2.4 Hz, 6 H, 2 × CH_3), 3.94 (d, J = 16.6 Hz, 2 H, 6*endo*-H and 12*endo*-H), 4.29 (s, 2 H, 13-H), 4.57 (dd, J = 16.6, J = 1.5 Hz, 2 H, 6*exo*-H and 12*exo*-H), 6.70−6.75 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.22 (d, $^3J_{C,F}$ = 5 Hz, 2 C, 2 × *C*H_3), 55.11 (2 C, C-6 and C-12), 67.35 (1 C, C-13), 111.16 (d, $^2J_{C,F}$ = 24 Hz, 2 C, C-2 and C-8), 119.94 (d, $^2J_{C,F}$ = 17 Hz, 2 C, C-4 and C-10), 123.41 (d, $^4J_{C,F}$ = 3 Hz, 2 C, C-6a and C-12a), 124.90 (d, $^3J_{C,F}$ = 9 Hz, 2 C, C-1 and C-7), 147.40 (d, $^3J_{C,F}$ = 7 Hz, 2 C, C-4a and C-10a), 160.71 (d, $^1J_{C,F}$ = 242 Hz, 2 C, C-3 and C-9) ppm. HRMS (FAB+): *m*/*z* calcd. for $C_{17}H_{16}F_2N_2$ [M] 286.1282, found 286.1290. $C_{17}H_{16}F_2N_2$, C 71.31, H 5.63, N 9.78; found C 71.22, H 5.70, N 9.86.

X-ray Structural Analysis of Compound 17: Crystallization from EtOAc gave colourless needles (0.4 × 0.06 × 0.06 mm) suitable for X-ray diffraction. Intensity data were collected at 293 K with a Bruker Smart CCD system using ω scans and a rotating anode with Mo-*K*α radiation (λ = 0.71073 Å).[19] The intensity was corrected for Lorentz, polarisation and absorption effects using SADABS (T_{min} = 0.3146, T_{max} = 0.5886).[20] The first 50 frames were collected again at the end to check for decay. No decay was observed. All reflections were merged and integrated using SAINT.[21] The structure was solved by direct methods and refined by full-matrix least-square calculations on F^2 by using SHELXTL5.1.[22] This program was also used for the calculations of least-squares planes. Non-H atoms were refined with anisotropic displacement parameters giving a total of 191 parameters. The hydrogen atoms were constrained to parent sites, using a riding model.

Crystal Data and Collection and Refinement Details: $C_{17}H_{16}Br_2N_2$, M = 408.14, orthorhombic, a = 10.483(2), b = 11.607(2), c = 12.512(3) Å, V = 1522.4(5) Å^3, space group $P2_12_12_1$ (no. 19), Z =

4, μ = 5.319 mm^{-1}, $D_{calcd.}$ = 1.781 g cm^{-3}, θ range 2.39−31.65 deg, 15358 reflections measured, 4741 unique (R_{int} = 0.0395) which were used in all calculations. The final w$R(F^2)$ was 0.0538 and the *S* value 1.008 (all data). The *R*(*F*) was 0.0306 [$I > 2\sigma(I)$]. CCDC 205256 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44−1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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