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Bromination and Iodination of 6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine: A Convenient Entry to Unsymmetrical Analogs of Tröger's Base

Delphine Didier[a] and Sergey Sergeyev*[a]

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6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine can easily be prepared from aniline and paraformaldehyde. Its reactions with either *N*-bromosuccinimide (NBS) or with iodine monochloride (ICl) in the presence of a suitable activator smoothly afford 2-bromo- and 2-iodo- derivatives, respectively. The combination of these halogenation methods provides access to the 8-bromo-2-iodo derivative, which is an interesting and otherwise inaccessible intermediate for the synthesis of unsymmetrical analogs of Tröger's base. The reported halogenations represent the first examples of electrophilic substitution in 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine.

Introduction

Tröger's base, (±)-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine [(±)-**1a**, Figure 1], was first synthesized in 1887 from *para*-methylaniline and formaldehyde. Tröger's base is a chiral diamine with two stereogenic bridge-head nitrogen atoms. A unique set of structural features (C_2 symmetry and a rigid V-shape geometry with the two aromatic rings nearly perpendicular to each other) has encouraged many elegant applications of Tröger's base derivatives in supramolecular chemistry and molecular recognition.[1] Recently, increasingly sophisticated molecules containing two or more fused methanodibenzodiazocine units were also prepared.[2]

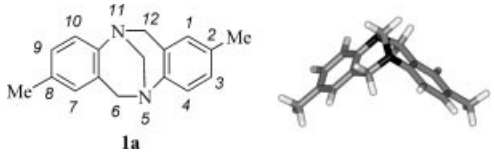
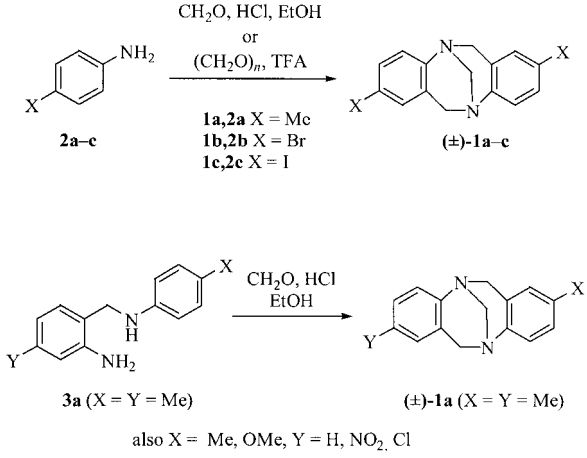


Figure 1. Tröger's base: structural formula with numbering of atoms according to IUPAC rules (left) and optimized geometry of the (*S*,*S*) enantiomer (right).

Generally, symmetrical analogs of Tröger's base (±)-**1** are synthesized by the condensation of anilines **2** with formaldehyde or its synthetic equivalent (Scheme 1).[3] It was accepted for a long time that anilines have to bear an electron-donating substituent in the *para* position to the amino group in order to give Tröger's base analogs in this reaction. However, the synthesis of symmetrical dihalogen analogs of Tröger's base (±)-**1b**,**c** was recently developed by Wärnmark[4,5] and successfully optimized for multigram preparations.[6,7] Dihalides (±)-**1b**,**c** are particularly valuable since they can be converted into a large variety of functional derivatives by metal-catalyzed transformations.[8–10]



Scheme 1. General synthesis for symmetrical (top) and unsymmetrical (bottom) analogs of Tröger's base.

In support of our studies of new building blocks for H-bonded supramolecular assemblies, we are interested in analogs of Tröger's base bearing various substituents in one aromatic ring with another aromatic ring being unsubsti-

[a] Université Libre de Bruxelles (ULB), Laboratoire de Chimie des Polymères,
C. P. 206/01, Boulevard du Triomphe, 1050 Bruxelles, Belgium
Fax: +32-2-6505410
E-mail: sserguee@ulb.ac.be
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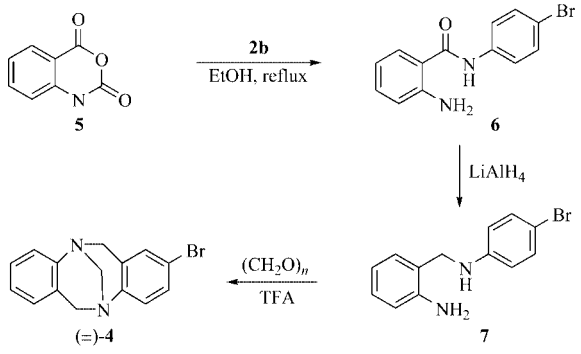
tuted. The corresponding unsymmetrical halogen derivatives of 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine appeared to be attractive intermediates for these molecules. However, known syntheses of such unsymmetrical halogen derivatives still leave room for improvement. Indeed, the approach based on desymmetrization by metal-catalyzed cross-coupling reactions[11] is useful but limited in its scope as it introduces only particular functional groups in one of the aromatic rings. The desymmetrization of a 2,8-dibromo analog of Tröger's base (±)-**1b** by selective monolithiation with *n*BuLi followed by the quenching with a proton source[12] is complicated by the formation of side products, requires very careful temperature control because of the instability of the Li intermediate, and is therefore difficult to reproduce.[11] Therefore, we decided to develop a new, experimentally simple and potentially scalable method for the synthesis of 2-halo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]-diazocines.

Results and Discussion

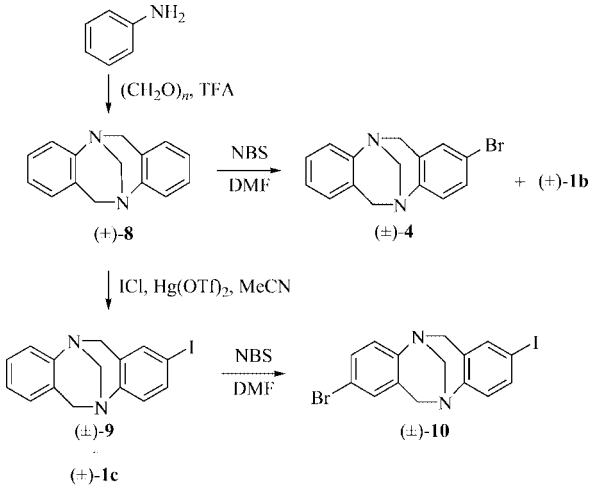
The general method for the synthesis of unsymmetrical Tröger's base analogs bearing different substituents in the 2- and 8-positions relies on the sequential buildup of amine derivatives such as **3a** followed by the condensation with formaldehyde to deliver the intact polycyclic system **1**.[13] All reported examples of this transformation deal with amines **3** bearing electron-donating substituent X (Scheme 1). However, the above-mentioned synthesis of 2,8-dihalogen analogs of Tröger's base clearly demonstrates feasibility of electrophilic substitution in the aromatic ring bearing a halogen atom in the *para* position to the amino group. Therefore, we investigated the possibility to use this approach in the synthesis of bromo derivative (±)-**4** (Scheme 2).



Scheme 2. Synthesis of monobromide (±)-**4** from isatoic anhydride and 4-bromoaniline; TFA = trifluoroacetic acid, CF_3COOH.

The reaction of isatoic anhydride (1*H*-benzo[*d*][1,3]oxazine-2,4-dione, **5**) with 4-bromoaniline (**2b**) afforded amide **6** (45%), which was then reduced to diamine **7** with $LiAlH_4$ in THF (56%). The subsequent condensation of diamine **7** with paraformaldehyde in trifluoroacetic acid (TFA) was expected to deliver bromide (±)-**4** without any problem since the bromo substituted aromatic ring in **7** should be sufficiently activated towards electrophilic substitutions. However, in this crucial step, transformation of **7** into (±)-**4** occurred with a disappointingly poor yield (25%). In addition, the yields of intermediates **6** and **7** were modest, and the separation of **7** from minor amounts of side products, which resulted from the reductive debromination of **6** and the action of $LiAlH_4$ upon **7**, was somewhat tedious. This route to (±)-**4** thus appears to be impractical and we decided to develop an alternative, shorter and more practical synthesis.

To this end, 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (±)-**8** appeared to be an attractive starting point. Indeed, (±)-**8** can be viewed as a structural analog of *N*,*N*-dimethylaniline and should therefore be prone to aromatic electrophilic substitutions. However, to the best of our knowledge, no example of electrophilic substitution on this heterocyclic system has been published earlier. The most straightforward access to (±)-**8** could obviously be granted by a direct condensation of aniline with formaldehyde or its equivalent. However, such a condensation of anilines lacking an electron-donating substituent in the *para* position to the amino group was previously considered not feasible.[3] At the same time, the above-discussed reaction of anilines **2b**,**c** bearing moderately electron-withdrawing halogens with paraformaldehyde in TFA gives fair-to-excellent yields of the halogen analogs of Tröger's base (±)-**1b**,**c** (Scheme 1). As expected, the direct condensation of aniline with paraformaldehyde in TFA gave 78% of (±)-**8**. Pleasantly, we found this reaction to be well reproducible up to a 50-mmol scale (Scheme 3). With this practical synthesis of (±)-**8** in hand, we investigated a few halogenation methods to access 2-bromo- and 2-iodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine [(±)-**4** and (±)-**9**, respectively].



Scheme 3. Synthesis of unsymmetrical dihalogen derivatives of 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine; TFA = trifluoroacetic acid, DMF = *N*,*N*-dimethylformamide, NBS = *N*-bromosuccinimide, Tf = trifluoromethylsulfonyl, CF_3SO_2.

Among the plethora of reagents used for the bromination of arenes, *N*-bromosuccinimide (NBS) seems to remain the most widely used one due to its versatility, low toxicity, and

ease of handling. Bromination of *N*,*N*-dialkylanilines with NBS to give the corresponding 4-bromo derivatives proceeds at room temp. in almost quantitative yield.[14]

When (±)-**8** was treated with 2 equiv. of NBS in DMF, 30% of monobromide (±)-**4** together with 30% of dibromide (±)-**1b** were isolated after 18 h at room temp. These results indicated much lower reactivity of (±)-**8** relative to that of *N*,*N*-dialkylanilines. This is undoubtedly due to poor conjugation between the aromatic ring and the lone pair of electrons of the bridgehead nitrogen atom in (±)-**8**. However, this conjugation is not negligible since substitution occurs exclusively at the 2- and 8-positions of 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine and no isomeric products were isolated. When the amount of NBS was decreased to 1.2 equiv., only traces of dibromide (±)-**1b** were detected, the yield of bromide (±)-**4** was 37%, and 40% of the starting material were recovered. Finally, prolonged reaction times (90 h) resulted in an increase in the yield of (±)-**4** to 57%. In all reactions, (±)-**4** was easily separated from dibromide (±)-**1b** and from starting material (±)-**8** by column chromatography on SiO_2.

Iodide (±)-**9** appears to be an even more appealing synthetic intermediate than bromide (±)-**4** as iodides generally demonstrate superior reactivity in many synthetically useful transformations. At the same time, the direct iodination of aromatic substrates is known to be more challenging due to the poorer electrophilicity of molecular iodine relative to chlorine and bromine. To generate more reactive iodine species, many iodination procedures use harsh conditions and involve strong oxidative agents[15] that are likely incompatible with 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine. In contrast to aromatic bromination and chlorination, catalysis with Lewis acids is less efficient in iodination with molecular iodine. Nevertheless, some softer Lewis acids such as mercury[16] and silver[17] salts have been used in the iodinations of activated substrates with I_2. Recently, interhalogen compounds such as ICl and IBr in combination with various Lewis acids were suggested as a mild, yet highly active, iodination system. In a model study, $Hg(OTf)_2$ was shown to be the most potent activator in the iodination of acetanilide with ICl.[18]

Following the published results with acetanilide, we started experiments on the iodination of (±)-**8** with 1.5 equiv. of ICl in the presence of 0.5 equiv. of $Hg(OTf)_2$. Under these conditions, only 28% of iodide (±)-**9** was isolated together with 53% of the starting material (Table 1, Entry 1). The prolongation of the reaction time to 120 h (Table 1, Entry 2) had nearly no effect on the yield. In an attempt to overcome the low reactivity of (±)-**8** we studied the influence of the amount of catalyst on the yield of iodination products (Table 1, Entries 3–5). The best results in terms of conversion of the starting material were obtained in the presence of 1–2 equiv. of $Hg(OTf)_2$. However, notable amounts of diiodide (±)-**1c** resulting from the iodination of both aromatic rings in (±)-**8** were isolated. A possible explanation to these observations can be that complexation between (±)-**8** and a Hg^{2+} cation may inhibit the catalytic activity of the latter and at least 1 equiv. of $Hg(OTf)_2$ is necessary. This is supported by the fact that iodination of acetanilide required at least 0.5 equiv. of an activating Lewis acid.[18] A further increase in the amount of $Hg(OTf)_2$ was not necessary and resulted in a lower yield of (±)-**9**.

When the iodination of (±)-**8** was conducted with 3 equiv. of ICl in the presence of 2 equiv. of $Hg(OTf)_2$, the complete conversion to diiodide (±)-**1c** (65%) was achieved (Table 1, Entry 6). This transformation is of relatively little preparative value since diiodide (±)-**1c** can be prepared in comparable yield (56–62% on 20 to 100-mmol scale)[7] directly from commercially available 4-iodoaniline (**2c**). However, it is methodologically interesting as a first example of the twofold electrophilic substitution of 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine. On the contrary, when the amount of ICl was decreased to 1.1 equiv. while keeping the amount of $Hg(OTf)_2$ unchanged, iodide (±)-**9** was isolated in an appreciable 55% yield (Table 1, Entry 7). Under these optimized conditions, nearly complete conversion of the starting material was observed and only 7% of twofold iodination product (±)-**1c** was isolated.

Next to $Hg(OTf)_2$, less toxic $In(OTf)_3$ was reported to be a highly efficient activator in the iodination of various electron-rich aromatic substrates upon the action of ICl. However, with the use of the optimized procedure (1.1 equiv. of ICl, 2 equiv. of Lewis acid) and $In(OTf)_3$ in exchange for $Hg(OTf)_2$, only 32% of iodide (±)-**9** was isolated together with 51% of the unreacted starting material. On the other hand, a larger excess of the iodinating reagent resulted in an increase in the yield of (±)-**9** to 51% without

Table 1. Yields of products for the reaction of (±)-**8** (1.0 mmol) with ICl in MeCN (5 mL) at room temp.[a]

Entry	ICl [mmol]	Time [h]	Additive [mmol]	(±)-**8** [%][b]	(±)-**9** [%][b]	(±)-**1c** [%][b]
1	1.5	24	$Hg(OTf)_2$ (0.5)	53	28	traces[c]
2	1.5	120	$Hg(OTf)_2$ (0.5)	51	25	traces[c]
3	1.5	72	$Hg(OTf)_2$ (1.0)	8	48	24
4	1.5	72	$Hg(OTf)_2$ (2.0)	10	47	27
5	1.5	72	$Hg(OTf)_2$ (5.0)	6	34	26
6	3	72	$Hg(OTf)_2$ (2.0)	traces[c]	traces[c]	65
7	1.1	72	$Hg(OTf)_2$ (2.0)	traces[c]	55	7
8	1.1	72	$In(OTf)_3$ (2.0)	43	32	traces[c]
9	2.5	72	$In(OTf)_3$ (1.0)	31	51	traces[c]

[a] No other products were detected by TLC or ^1H NMR spectroscopy. [b] Isolated yield of analytically pure substances. [c] Less than 5%.

detectable formation of diiodide (±)-**1c** (Table 1, Entries 8, 9). Thus, $In(OTf)_3$ appears to be a less potent activator in the iodination of (±)-**8** relative to $Hg(OTf)_2$. Nevertheless, optimized isolated yields of (±)-**9** obtained with both activators were comparable (cf. Table 1, Entries 7 and 9).

In order to eliminate the necessity for toxic metal salts, we decided to test other mild procedures for the iodination of (±)-**8**. For example, nearly quantitative iodination of *N*,*N*-dimethylaniline upon the action of I_2 and pyridine/dioxane was reported.[19] Unfortunately, (±)-**8** was unreactive under these conditions: the starting material was nearly quantitatively recovered after 24 h at room temp. and no iodination products were detected by TLC or ^{1}H NMR spectroscopy of the reaction mixture. This results confirmed the much lower reactivity of (±)-**8** in electrophilic halogenation reactions relative to *N*,*N*-dialkylanilines.

Finally, interesting derivative (±)-**10** bearing bromine and iodine atoms in two different aromatic rings of 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine was prepared in 68% yield by bromination of iodide (±)-**9** with NBS in DMF; this compound is not accessible by other synthetic routes. Both bromine and iodine can serve as leaving groups in many cross-coupling reactions. At the same time, the differences in their reactivity allow selective substitution of iodine and leave bromine intact for subsequent transformations (representative examples: see ref.[20] and references cited therein). Therefore, (±)-**10** can undoubtedly be considered as a very promising intermediate in the synthesis of complex unsymmetrical derivatives of Tröger's base.

Conclusions

We developed convenient methods for the synthesis of 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine [(±)-**8**] and its transformation into unsymmetrical bromo- and iodo derivatives (±)-**4** and (±)-**9**. In our opinion, this is a useful and experimentally simple approach to these valuable synthetic intermediates for many valuable transformations that were earlier reported for symmetrical dihalo analogs of Tröger's base.[8,9,11] Bromide (±)-**4** was prepared in 44% total yield starting from aniline. This can be viewed as a competitive alternative to the known synthesis of (±)-**4** by desymmetrization of dibromide (±)-**1b** (52% starting from 4-bromoaniline).[12] As to iodide (±)-**9** (43% starting from aniline), its synthesis was not described until now, but difficulties in the attempted desymmetrization of diiodide (±)-**1c** were reported.[11] Unsymmetrical derivative (±)-**10** is an even more interesting synthetic intermediate since it allows for the exploration of the different reactivities of bromine and iodine in carbon–carbon or carbon–heteroatom bond formation. In addition, electrophilic halogenation followed by Pd-catalyzed amination[8] can be a very useful iterative strategy in the recently described rational synthesis of "fused tris-Tröger's bases".[21]

The reported halogenation represents the first example of an electrophilic substitution of 6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine. Although our study revealed relatively low reactivity of this heterocyclic system compared to *N*,*N*-dialkylanilines, it clearly demonstrated the feasibility of the perfectly regioselective substitution in the *para* position to the nitrogen atom. Moreover, we showed that such a substitution can be performed in either one or two aromatic rings of the heterocyclic system. Therefore, methanodibenzodiazocine (±)-**8** probably has an even greater synthetic potential as a substrate for other electrophilic substitutions. The preparative utility of (±)-**8** can certainly be limited by its diminished reactivity caused by the poor conjugation between the aromatic ring and the nitrogen atom. Nevertheless, we are currently examining other electrophilic substitutions of (±)-**8** that may result in interesting building blocks and intermediates.

Experimental Section

General: All chemicals were purchased from Aldrich or Acros and used without further purification unless stated otherwise. Technical grade solvents were distilled before use. THF was heated at reflux over sodium and benzophenone until a blue–violet color persisted and then distilled directly into the reaction flask. Iodine monochloride (ICl) was purchased from Aldrich as a 1.0 M solution in dichloromethane. Column chromatography was performed with SiO_2 Kieselgel 60 (Macherey–Nagel, particle size 0.04–0.063 mm). TLC was performed with precoated SiO_2 plates Kieselgel $60F_{254}$ (Merck). ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded with a Bruker Avance 300 spectrometer; chemical shifts (δ) are given in ppm relative to Me_4Si (internal standard); coupling constants (*J*) are given in Hz. Electron impact mass spectra (EIMS) were recorded with a Waters AutoSpec 6F instrument; *m*/*z* with the lowest isotopic mass are reported unless stated otherwise. Melting points were determined with a Nikon Eclipse 80i microscope equipped with a Mettler hot stage. Elemental analyses were carried out at the University of Mainz, Germany.

2-Amino-*N*-(4-bromophenyl)benzamide (6): 4-Bromoaniline (**2b**; 3.44 g, 20 mmol) was added in portions to the suspension of isatoic anhydride (**5**; 13.05 g, 80 mmol) in dry EtOH (160 mL). The mixture was heated to reflux for 24 h, then allowed to reach room temp., filtered, and poured into H_2O (1 L). The precipitated solid was collected by filtration and dissolved in CH_2Cl_2 (100 mL). The resulting solution was filtered, dried with $MgSO_4$, and concentrated in vacuo. Purification of the residue by column chromatography (CH_2Cl_2) afforded **6** (2.61 g, 45%) as a colorless solid. R_f = 0.31 (CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 5.48 (br. s, 2 H, NH_2), 6.68–6.73 (m, 2 H), 7.23–7.28 (m, 1 H), 7.42–7.46 (m, 5 H), 7.75 (s, 1 H, NHCO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 115.7, 116.8, 117.0, 117.6, 121.9 (2 C), 127.1, 131.9 (2 C), 132.9, 136.9, 148.9, 167.4 ppm. HREIMS: calcd. for $C_{13}H_{11}{}^{81}BrN_2O$ $[M]^+$ 292.0034; found 292.0011.

2-Amino-*N*-(4-bromophenyl)benzylamine (7): A solution of amide **6** (291 mg, 1 mmol) in THF (5 mL) was added to the suspension of $LiAlH_4$ (76 mg, 2 mmol) in THF (5 mL). The mixture was heated to reflux for 5 h, allowed to reach room temp., and quenched by the dropwise addition of H_2O (0.2 mL). The resulting mixture was filtered, and the solid on the filter was washed twice with CH_2Cl_2. Combined filtrates were concentrated in vacuo, and the residue was purified by column chromatography (CH_2Cl_2) to give **7** (151 mg, 56%) as a yellow solid. R_f = 0.31 (CH_2Cl_2). ^{1}H NMR (300 MHz,

$CDCl_3$, 25 °C): δ = 3.91 (br. s, 3 H, NH, NH_2), 4.14 (s, 2 H, CH_2), 6.56 and 7.27 (AA′BB′ system, 4 H), 6.68–6.76 (m, 2 H), 7.12–7.16 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 46.4, 109.6, 114.6 (2 C), 115.6, 118.1, 128.6 (2 C), 129.6, 131.6 (2 C), 145.1, 146.8 ppm. HREIMS: calcd. for $C_{13}H_{13}{}^{81}BrN_2$ $[M]^+$ 278.0242; found 278.0229.

(±)-6*H*,12*H*-5,11-Methanodibenzo[*b*,*f*][1,5]diazocine [(±)-8]: Aniline (4.68 g, 50.2 mmol) and then paraformaldehyde (3.06 g, 102 mmol) were added in portions with vigorous stirring to TFA (100 mL) at –15 °C. The resulting mixture was stirred for 20 min at –15 °C. The mixture was allowed to reach room temp., stirred for 48 h, and then slowly added to a stirred mixture of ice and an excess of NH_3 (25% solution in water) at 0 °C. The resulting mixture was extracted with CH_2Cl_2 (3 × 200 mL), dried with $MgSO_4$, and concentrated in vacuo. Purification of the residue by column chromatography (CH_2Cl_2/AcOEt, 95:5) afforded (±)-**8** (4.34 g, 78%). R_f = 0.24 (CH_2Cl_2/AcOEt, 95:5); m.p. 130–131 °C (ref.[22] m.p. 127–128 °C). Spectral data of (±)-**8** were identical to those published earlier.[12]

(±)-2-Bromo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine [(±)-4]: *Method A:* Amine **7** (138 mg, 0.5 mmol) and then paraformaldehyde (30 mg, 1 mmol) were added in portions to TFA (2 mL) at –15 °C. The mixture was allowed to reach room temp., stirred for 72 h, and then slowly added to a stirred mixture of ice and an excess of NH_3 (25% solution in water) at 0 °C. The resulting mixture was extracted with CH_2Cl_2 (3 × 50 mL), dried with $MgSO_4$, and concentrated in vacuo. Column chromatography (SiO_2; CH_2Cl_2/AcOEt, 5:1) afforded (±)-**4** (37 mg, 25%). *Method B:* A solution of NBS (220 mg, 1.24 mmol) in DMF (2.0 mL) was added at 0 °C to a stirred solution of (±)-**8** (227 mg, 1.02 mmol) in DMF (2.0 mL). The resulting mixture was stirred for 15 min at 0 °C, then allowed to reach room temp., and stirred for another 92 h. The reaction mixture was then diluted with CH_2Cl_2 (50 mL), the organic layer was washed with water (3 × 80 mL), dried with $MgSO_4$, and concentrated in vacuo. Purification of the residue by column chromatography (CH_2Cl_2/AcOEt, 95:5) afforded (±)-**4** (175 mg, 57%). Pale yellow solid; R_f = 0.36 (CH_2Cl_2/AcOEt, 5:1); m.p. 119–121 °C (ref.[12] m.p. 123.5–125 °C). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.12 (d, $^2J_{H,H}$ = 16.7 Hz, 1 H), 4.15 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 4.25 (d, $^2J_{H,H}$ = 12.9 Hz, 1 H), 4.32 (d, $^2J_{H,H}$ = 12.9 Hz, 1 H), 4.65 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 4.69 (d, $^2J_{H,H}$ = 16.7 Hz, 1 H), 6.90 (dd, $^3J_{H,H}$ = 6.9 Hz, $^4J_{H,H}$ = 0.9 Hz, 1 H), 6.98 (td, $^3J_{H,H}$ = 7.5 Hz, $^4J_{H,H}$ = 1.6 Hz, 1 H), 7.01 (d, $^3J_{H,H}$ = 8.6 Hz, 1 H), 7.04 (d, $^4J_{H,H}$ = 2.2 Hz, 1 H), 7.12 (td, $^3J_{H,H}$ = 7.5 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H), 7.19 (dd, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H), 7.26 (dd, $^3J_{H,H}$ = 8.6 Hz, $^4J_{H,H}$ = 2.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 58.4, 58.7, 66.7, 116.5, 124.2, 125.0, 126.8, 127.0, 127.5 (2 C), 129.7, 130.0, 130.4, 147.2, 147.7 ppm. HREIMS: calcd. for $C_{15}H_{13}{}^{81}BrN_2$ $[M]^+$ 302.0242; found 302.0247.

(±)-2-Iodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine [(±)-9]: A solution of ICl in CH_2Cl_2 (1.1 mL, 1.1 mmol) was added under an atmosphere of argon to a stirred solution of (±)-**8** (222 mg, 1.0 mmol) and $Hg(OTf)_2$ (997 mg, 2.0 mmol) in dry CH_3CN (5 mL). The resulting reaction mixture was stirred at room temp. for 72 h, and then triethylamine (1.5 mL) was added followed by the addition of a saturated aqueous solution of $Na_2S_2O_3$ until disappearance of the brown color. The resulting mixture was filtered through Celite, which was then additionally washed with CH_2Cl_2 (50 mL). The organic layer was separated and washed with water (3 × 50 mL), dried with $MgSO_4$, and concentrated in vacuo. Purification of the residue by column chromatography (gradient from CH_2Cl_2 to CH_2Cl_2/AcOEt, 95:5) afforded (±)-**9** (192 mg, 55%) as a pale yellow solid. R_f = 0.36 (CH_2Cl_2/AcOEt, 80:20); m.p. 121–123 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.12 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 4.14 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 4.25 (d, $^2J_{H,H}$ = 12.7 Hz, 1 H), 4.32 (d, $^2J_{H,H}$ = 12.7 Hz, 1 H), 4.64 (d, $^2J_{H,H}$ = 16.6 Hz, 1 H), 4.69 (d, $^2J_{H,H}$ = 16.6 Hz, 1 H), 6.88 (d, $^3J_{H,H}$ = 8.5 Hz, 1 H), 6.90 (dd, $^3J_{H,H}$ = 7.6 Hz, $^4J_{H,H}$ = 0.8 Hz, 1 H), 6.99 (td, $^3J_{H,H}$ = 7.6 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H), 7.12 (td, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H), 7.18 (dd, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H), 7.24 (d, $^4J_{H,H}$ = 2.1 Hz, 1 H), 7.44 (dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 58.1, 58.7, 66.7, 87.4, 124.2, 125.0, 127.0, 127.1, 127.53, 127.55, 130.5, 135.7, 136.2, 147.7, 148.0 ppm. HREIMS: calcd. for $C_{15}H_{13}IN_2$ $[M]^+$ 348.0123; found 348.0122. $C_{15}H_{13}IN_2$ (348.0): calcd. C 51.74, H 3.76, N 8.05; found C 51.27, H 3.81, N 7.90.

(±)-2,8-Diiodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine [(±)-1c]: A solution of ICl in CH_2Cl_2 (3.0 mL, 3.0 mmol) was added under an atmosphere of argon to a stirred solution of (±)-**8** (223 mg, 1.0 mmol) and $Hg(OTf)_2$ (997 mg, 2.0 mmol) in dry CH_3CN (5 mL). The resulting mixture was stirred for 72 h at room temp., and then triethylamine (3.0 mL) was added followed by the addition of a saturated aqueous solution of $Na_2S_2O_3$ until disappearance of the brown color. The resulting mixture was filtered trough Celite, which was then additionally washed with CH_2Cl_2 (50 mL). The organic layer was separated and washed with water (3 × 50 mL), dried with $MgSO_4$, and concentrated in vacuo. Purification of the residue by column chromatography (gradient from CH_2Cl_2 to CH_2Cl_2/AcOEt, 95:5) afforded (±)-**1c** (310 mg, 65%) as a pale yellow solid. R_f = 0.54 (CH_2Cl_2/AcOEt, 80:20); m.p. 178.5–180 °C (ref.[4] m.p. 180.5–181.5 °C). Other analytical data were identical with those published earlier.[4]

(±)-8-Bromo-2-iodo-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine [(±)-10]: A solution of iodide (±)-**9** (162 mg, 0.465 mmol) and NBS (91.0 mg, 0.511 mmol) in DMF (2.5 mL) was stirred for 72 h at room temp. The resulting mixture was diluted with CH_2Cl_2 (10 mL). The organic layer was separated, washed with water (3 × 10 mL), dried with $MgSO_4$, and concentrated in vacuo. Purification of the residue by column chromatography (gradient from CH_2Cl_2 to CH_2Cl_2/AcOEt, 95:5) afforded (±)-**10** (134 mg, 68%) as a pale yellow solid. R_f = 0.50 (CH_2Cl_2/AcOEt, 5:1); m.p. 134–136 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.08 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 4.09 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 4.25 (t, $^4J_{H,H}$ = 1.2 Hz, 2 H), 4.62 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 4.63 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H), 6.87 (d, $^3J_{H,H}$ = 8.4 Hz, 1 H), 6.99 (d, $^3J_{H,H}$ = 8.7 Hz, 1 H), 7.05 (d, $^4J_{H,H}$ = 2.1 Hz, 1 H), 7.24 (d, $^4J_{H,H}$ = 2.0 Hz, 1 H), 7.27 (dd, $^3J_{H,H}$ = 8.6 Hz, $^4J_{H,H}$ = 2.2 Hz, 1 H), 7.46 (dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 58.1, 58.3, 66.6, 87.6, 116.8, 126.7, 127.0, 129.67, 129.70, 130.1, 130.6, 135.7, 136.4, 146.8, 147.6 ppm. HREIMS: calcd. for $C_{15}H_{12}{}^{81}BrIN_2$ $[M]^+$ 427.9208; found 427.9196. $C_{15}H_{12}BrIN_2$ calcd. C 42.18, H 2.83, N 6.56; found C 41.96, H 2.92, N 6.48.

Supporting Information (see footnote on the first page of this article)**:** ^1H and ^{13}C NMR spectra of (±)-**4**, (±)-**9**, and (±)-**10**.

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