

## Preparation of *Tröger* Base Derivatives by Cross-Coupling Methodologies

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Derivatives of the *Tröger* base are finding increasing application in supramolecular chemistry: they are introduced as rigid scaffolds into synthetic receptors and ‘molecular torsional balances’ to quantify weak intermolecular interactions, and serve as efficient ‘covalent templates’ in the tether-directed remote functionalization of fullerenes. This paper describes the facile synthesis of symmetrically (*Schemes 1* and *2*) and unsymmetrically (*Schemes 4* and *5*) substituted *Tröger* base derivatives starting from the corresponding, readily available dihalo compounds. A variety of metal-catalyzed cross-coupling reactions, including *Suzuki* couplings, palladium-catalyzed cyanation and boronation, and copper-catalyzed amidations are used to achieve these transformations.

**1. Introduction.** – *Tröger* base, ( $\pm$ )-2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b,f*][1,5]diazocine was first synthesized in 1887 [1] and features a rigid tetracyclic structure with a pair of aromatic rings oriented at *ca.* 90° (angle between the planes of the two rings) relative to each other [2][3]. This unusual arrangement has encouraged the use of the *Tröger* base as a scaffold for a variety of interesting molecular designs [4][5]. Thus, the unique arrangement of functional groups tethered to a central *Tröger* base scaffold provided for the creation of a number of supramolecular receptors [6]. ‘Molecular torsional balances’ have been constructed to quantify the energetics of weak intermolecular interactions such as edge-to-face aromatic [7][8] and multipolar C–F  $\cdots$  C=O interactions [9]. Recently, derivatives of the *Tröger* base were introduced as chiral tethers for the regio- and stereoselective tether-directed remote functionalization of fullerenes [10][11]. Many of these increasingly sophisticated scaffolds require intensive synthetic efforts, and, to this end, halogenated derivatives of the *Tröger* base have recently been transformed by metal-catalyzed cross-coupling methodologies to provide a variety of acetylenic and biaryl derivatives [12][13]. We report herein the application of metal-catalyzed cross-coupling methodologies to create two different classes of *Tröger* base derivatives, one bearing identical substituents at the two aryl rings (see **A**) and the other featuring two different substituents at atoms C(2) and C(8) (see **B**) (*Fig.*).

**2. Results and Discussion.** – 2.1. *Symmetrically Substituted Derivatives of the Tröger Base.* Our interest in biaryl-type derivatives of the *Tröger* base arose from their

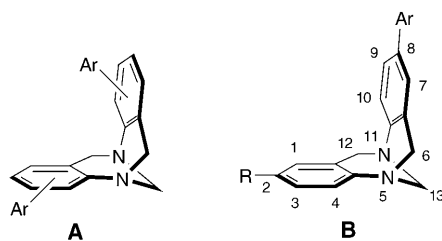


Figure. Derivatives of the Tröger base prepared in this study

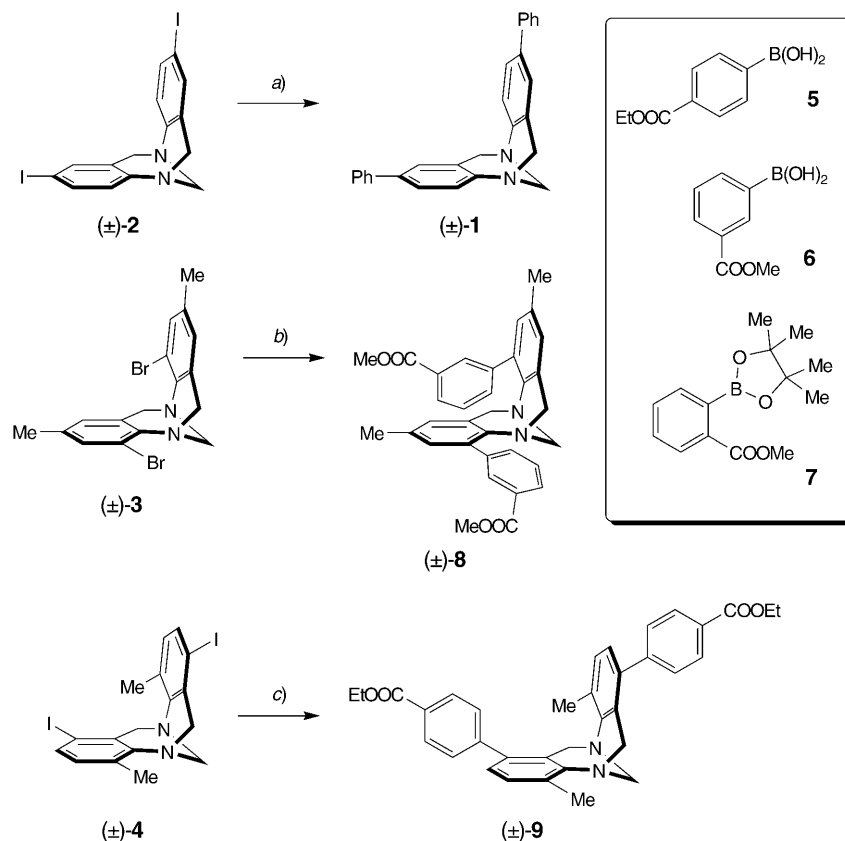
potential as reagents for the tether-directed remote functionalization of fullerenes [10]. In an earlier report, the preparation of 2,8-diphenyl-substituted *Tröger* base ( $\pm$ )-**1** in moderate yield (36%) by direct acid-catalyzed condensation of 4-amino-1,1'-biphenyl with formaldehyde was described [14]. Starting from the readily available diiodo derivative ( $\pm$ )-**2** (obtained by acid-catalyzed condensation of 4-iodoaniline with formaldehyde) [15][16][10b], we developed an efficient alternative approach based on the *Suzuki* cross-coupling reaction (*Scheme 1*). According to a standard protocol for the *Suzuki* coupling [17], diiodo derivative (( $\pm$ )-**2**) was reacted with  $\text{PhB(OH)}_2$  in the presence of  $\text{K}_2\text{CO}_3$  and a catalytic amount of  $[\text{Pd}(\text{PPh}_3)_4]$  in  $\text{PhMe}/\text{H}_2\text{O}/\text{EtOH}$ . Heating the mixture to reflux afforded the expected diphenyl derivative ( $\pm$ )-**1** in 93% yield.

Subsequently, we subjected dihalides ( $\pm$ )-**2**, ( $\pm$ )-**3** [16], and ( $\pm$ )-**4** [10b] under the same conditions to the *Suzuki* cross-coupling with substituted boronic acids **5** and **6** or pinacol boronate **7** [18]. The yields and reaction conditions are summarized in the *Table*. In each case, the diarylated *Tröger* base derivatives ( $\pm$ )-**8**–( $\pm$ )-**13** were isolated in fair-to-excellent yields (54–97%). The ester groups are reasonably stable to hydrolysis under the chosen conditions in spite of the presence of  $\text{H}_2\text{O}$  and base and the relatively high temperature. Neither the identity of the halogen (Br or I) on the *Tröger* base nor the substitution pattern of the boronic acid derivatives seems to play an important role for the outcome of the transformation. Even in the case of the most sterically hindered ( $\pm$ )-**13**, with *ortho*-substituents to the reacting centers in both aryl boronate and *Tröger* base, the reaction proceeds smoothly, rapidly, and in high yield (81%).

For the formation of bis(malonate esters), required for the tether-directed remote functionalization of  $\text{C}_{60}$  by double *Bingel* addition [10], dialkyl esters ( $\pm$ )-**8**, ( $\pm$ )-**10**, and ( $\pm$ )-**11** were subsequently reduced with  $\text{LiAlH}_4$  to give diols ( $\pm$ )-**14**–( $\pm$ )-**16**, respectively, in high yield (*Scheme 2*). The incorporation of these interesting novel scaffolds into new chiral macrocyclic receptors featuring cavities shaped by two *Tröger* base moieties is currently under investigation (for the preparation and binding properties of cyclophane hosts incorporating *Tröger* base scaffolds, see [19]).

**2.2. Differentially 2,8-Substituted Derivatives of the Tröger Base.** *Tröger* base derivatives such as ( $\pm$ )-**17** (*Scheme 3*), which bear two different substituents at C(2) and C(8), were elegantly investigated as ‘molecular torsional balances’ by Wilcox and co-workers in attempts to quantify the energetics of aromatic–aromatic and aromatic–aliphatic interactions [7][8]. The syntheses of these derivatives, which bear

Scheme 1. Synthesis of Symmetrically Substituted Derivatives of the Tröger Base

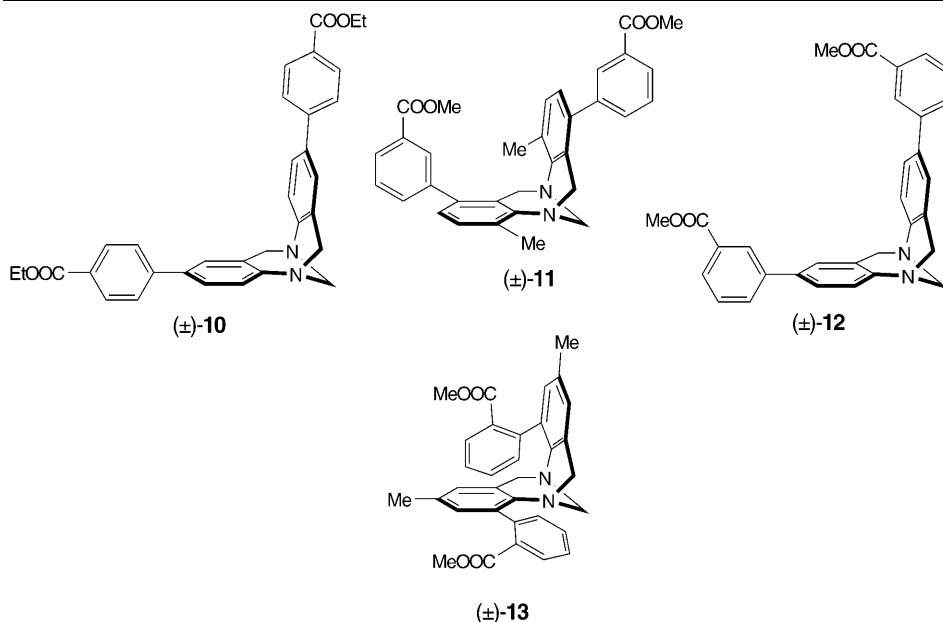


a)  $\text{PhB}(\text{OH})_2$ ,  $[\text{Pd}(\text{PPh}_3)_4]$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{EtOH}/\text{H}_2\text{O}$ ,  $\text{PhMe}$ ,  $110^\circ$ . b) **6**,  $[\text{Pd}(\text{PPh}_3)_4]$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{EtOH}/\text{H}_2\text{O}$ ,  $\text{PhMe}$ ,  $110^\circ$ . c) **5**,  $[\text{Pd}(\text{PPh}_3)_4]$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{EtOH}/\text{H}_2\text{O}$ ,  $\text{PhMe}$ ,  $110^\circ$ . For reaction times and yields, see the Table.

an aryl substituent at C(2) and feature a variety of heteroatomic substitutions at C(8), required the sequential buildup of functionality to create complex linked aniline derivatives (such as **18**, synthesized in eleven steps) before condensation with a formaldehyde equivalent yielded the intact skeleton ((±)-**19**) [20–22]. In support of our own studies with ‘molecular torsional balances’ to quantify the energetics of weak multipolar interactions such as orthogonal  $\text{C}-\text{F}\cdots\text{C}=\text{O}$  interactions [9][23], we reasoned that this route could be significantly shortened by starting from readily available 2,8-dihalogenated Tröger base derivatives [15][16]. The differentiation of 2,8-dibromo-substituted Tröger base by selective mono-lithiation with BuLi had been reported by Wärnmark and co-workers [24], but we found this method difficult to perform on larger scales. We chose instead to pursue differentiation through non-selective reaction of a single halogen substituent by metal-catalyzed cross-coupling reactions.

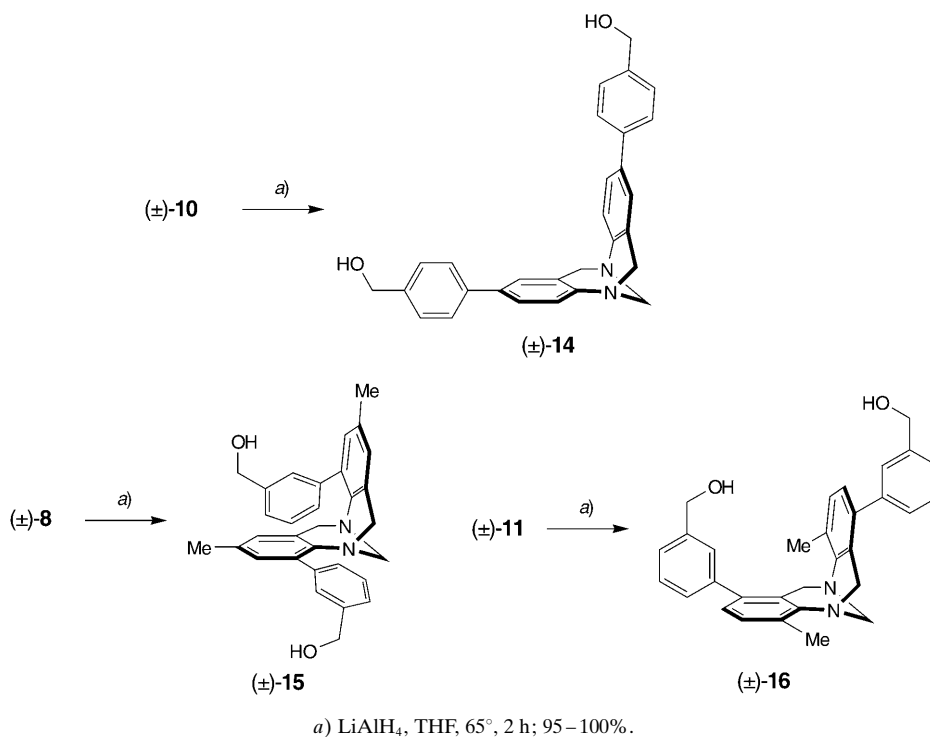
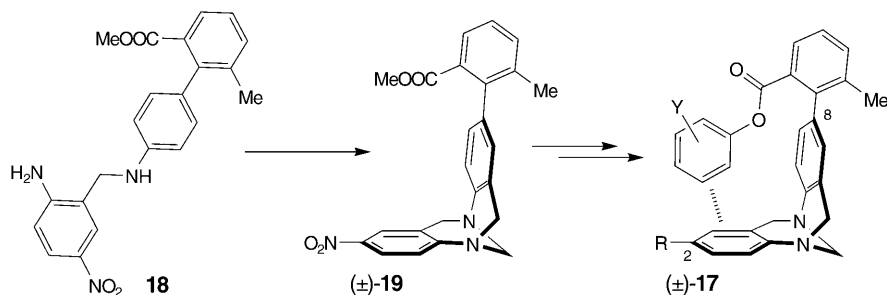
Table. Symmetrically Substituted Diaryl Derivatives of the Tröger Base Obtained by Suzuki Cross-Coupling

Dihalo derivative of Tröger base	Aryl-boron reagent	Product	Reaction time [h]	Yield [%]
(±)- <b>2</b>	PhB(OH) <sub>2</sub>	(±)- <b>1</b>	2	93
(±)- <b>2</b>	<b>5</b>	(±)- <b>10</b>	1.5	81
(±)- <b>2</b>	<b>6</b>	(±)- <b>12</b>	2.5	78
(±)- <b>3</b>	<b>6</b>	(±)- <b>8</b>	5	69
(±)- <b>3</b>	<b>7</b>	(±)- <b>13</b>	6	81
(±)- <b>4</b>	<b>5</b>	(±)- <b>9</b>	3	97
(±)- <b>4</b>	<b>6</b>	(±)- <b>11</b>	6	54



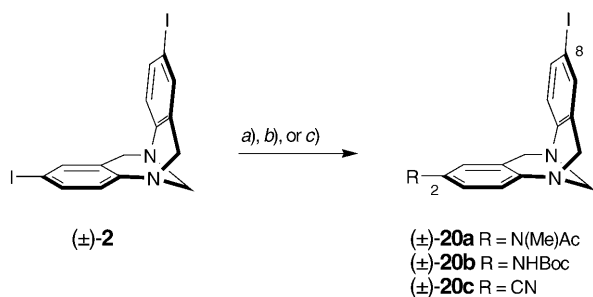
The cross-coupling of 2,8-diiodo derivative (±)-**2** with *N*-methylacetamide (1.2 equiv.) under the catalytic amidation conditions introduced by *Buchwald* and co-workers [25] produced the desired mono-amidated Tröger base (±)-**20a** in 26% yield, along with 54% recovered starting material (±)-**2** (*Scheme 4*). A similar cross-coupling with *tert*-butyl carbamate (BocNH<sub>2</sub>; 1.5 equiv.) afforded the Boc-protected aniline (±)-**20b** in 36–39% yield, along with 30% recovered (±)-**2**. The Pd-catalyzed cyanation of (±)-**2** with CuCN (1.3 equiv.) provided the monocyano derivative (±)-**20c** in 38–45% yield, along with 28–33% recovered (±)-**2**. In each case, separation of products was easily achieved by column chromatography. Although the yields of the desired products are modest, these transformations are fully reproducible, even in larger-scale conversions with up to 5 g of starting material (±)-**2**.

The carbonitrile (±)-**20c** was reduced selectively to aldehyde (±)-**21** in 83% yield with (*i*-Bu)<sub>2</sub>AlH (*Scheme 5*). This aldehyde can be further elaborated in a variety of ways. Conversion to methyl ketone (±)-**22** is achieved by a two-step protocol involving treatment with MeMgCl followed by aqueous workup and immediate oxidation using

Scheme 2. *Synthesis of Diols (±)-14 – (±)-16*Scheme 3. *Synthesis of ‘Molecular Torsional Balances’ Introduced by Wilcox and Co-Workers [20–22]*

$\text{MnO}_2$ . Alternatively, direct oxidation to carboxylic acid (±)-23 is effected in > 95% yield by treatment with  $\text{KMnO}_4$  in  $\text{Me}_2\text{CO}/\text{H}_2\text{O}$ . This result is notable because, in our hands, the direct conversion of cyano compound (±)-20c to carboxylic acid (±)-23 by hydrolysis failed under a variety of acidic and basic conditions.

To achieve rapid access to hindered biaryl derivatives such as those used in the Wilcox ‘torsional balance’, iodide (±)-21 was first converted to pinacol boronate (±)-24 by Pd-catalyzed boronation [18]. The boronate was used without purification in the

Scheme 4. Mono-Transformations of 2,8-Diiodo Derivative ( $\pm$ )-**2** by Cross-Coupling Reactions

a) *N*-Methylacetamide, DMEDA, CuI,  $\text{K}_3\text{PO}_4$ , PhMe,  $110^\circ$ , 48 h; 26%. b) BocNH<sub>2</sub>, DMEDA,  $\text{K}_2\text{CO}_3$ , CuI, DMF,  $100^\circ$ , 20 h; 36%. c) CuCN,  $[\text{Pd}(\text{PPh}_3)_2\text{Cl}_2]$ , DMF,  $100^\circ$ , 20 h; 45%. DMEDA = *N,N*-Dimethylethylenediamine, Boc = (*tert*-butoxy)carbonyl.

subsequent *Suzuki* cross-coupling with aryl iodide **25** [26] to give the hindered biaryl ( $\pm$ )-**26** in 75% yield (Scheme 5). This *Suzuki* coupling benefits greatly from the use of 2-(dicyclohexylphosphino)-1,1'-biphenyl [27] as the ligand: the use of either  $\text{PPh}_3$  or 1,1'-bis(diphenylphosphino)ferrocene (dppf) as ligands under similar conditions provides the desired product in < 50% yield. This two-step route leading from iodide ( $\pm$ )-**21** to ( $\pm$ )-**26** can be generally applied to the production of other hindered biaryl derivatives of the Tröger base.

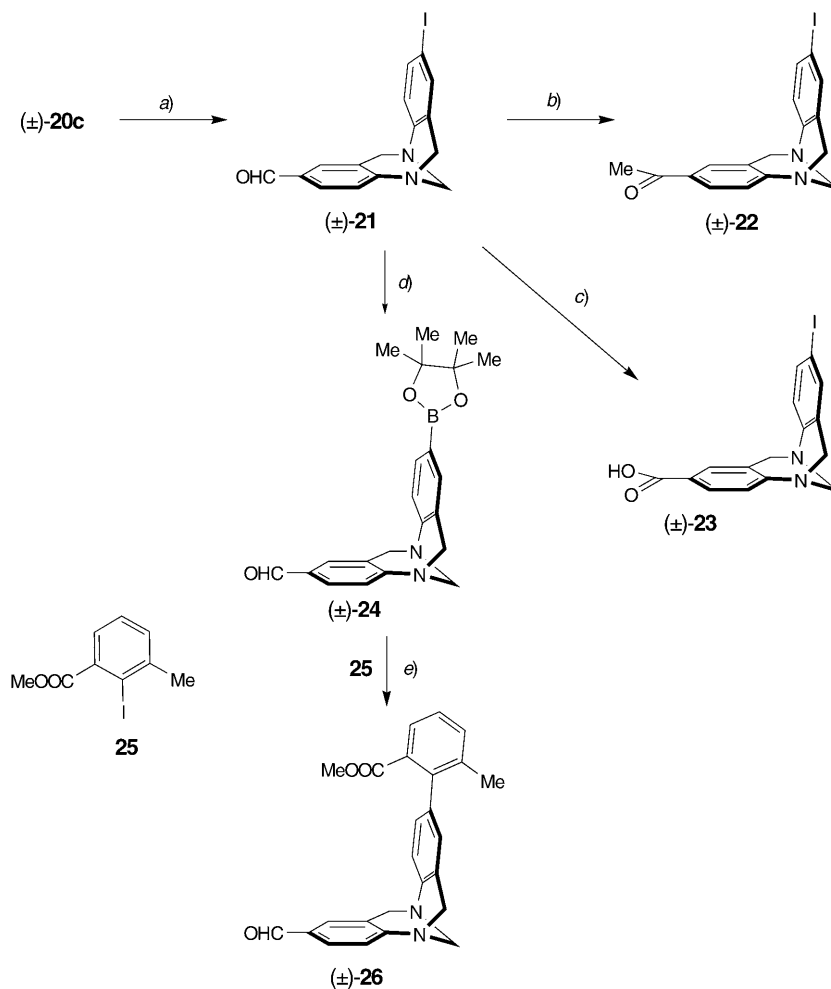
**3. Conclusions.** – In this paper, new synthetic routes to both symmetrically and differentially substituted biaryl-type derivatives of the Tröger base, by various modern metal-catalyzed cross-coupling methodologies, are reported. These methods should provide convenient access to a wide variety of increasingly sophisticated derivatives of Tröger base for supramolecular applications such as molecular recognition or templated synthesis.

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#### Experimental Part

**General.** All reactions were carried out under  $\text{N}_2$  or Ar; solvents and reagents were reagent-grade and used without further purification unless otherwise stated. Anhyd. DMF (< 50 ppm  $\text{H}_2\text{O}$ ) was purchased from *Acros Organics*, and THF and toluene were freshly distilled from sodium before use. The following compounds were prepared according to previously published procedures: ( $\pm$ )-**2** [10b], ( $\pm$ )-**3** [16], ( $\pm$ )-**4** [10b], **7** [18], and **25** [26]. Evaporation *in vacuo* was carried out with a rotary evaporator at a bath temp. of  $40^\circ$ . Flash chromatography (FC): *Fluka*  $\text{SiO}_2$  60 (230–400 mesh, 0.040–0.063 mm). TLC: pre-coated  $\text{SiO}_2$  plates *Alugram UV<sub>254</sub>* (*Macherey-Nagel*), visualization by UV (254 nm). M.p.: *Büchi Melting Point B-540* apparatus; uncorrected. IR Spectra [ $\text{cm}^{-1}$ ]: *Perkin-Elmer 1600 FT-IR*; neat. NMR Spectra: *Varian Gemini 300* at amb. temp., referenced to residual solvent signals. MS ( $m/z$ ): MALDI-MS: *Ion Spec Ultima FT-ICR*, 2,5-dihydroxybenzoic acid (DHB) or 3-hydroxypicolinic acid (3-HPA) as matrix; ESI-MS: *Finnigan TSQ 7000*, positive mode. Elemental analyses were performed by the *Mikrolabor* of the *Laboratorium für Organische Chemie, ETH-Zürich*.

( $\pm$ )-2,8-Diphenyl-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine (( $\pm$ )-**1**). A suspension of  $\text{PhB}(\text{OH})_2$  (187 mg, 1.54 mmol) in EtOH (2 ml) and a soln. of  $\text{K}_2\text{CO}_3$  (885 mg, 6.40 mmol) in  $\text{H}_2\text{O}$  (1 ml) were added to a soln. of ( $\pm$ )-**2** (237 mg, 0.50 mmol) and  $[\text{Pd}(\text{PPh}_3)_4]$  (61 mg, 0.05 mmol) in PhMe (10 ml). The mixture was

Scheme 5. Synthesis of the Sterically Hindered Biaryl Derivative of the Tröger Base (±)-**20c**

a) DIBAL-H, PhMe, 60°, 90 min; 83%. b) MeMgCl, THF, 20°, 1 h; then MnO<sub>2</sub>, Me<sub>2</sub>CO, 20°, 20 h; 71%. c) KMnO<sub>4</sub>, Me<sub>2</sub>CO, H<sub>2</sub>O, 70°, 20 h; > 95%. d) Bis(pinacolato)diboron, AcOK, [Pd(dppf)Cl<sub>2</sub>] · CH<sub>2</sub>Cl<sub>2</sub>, 80°, 20 h; 98%. e) **25**, 2-(Dicyclohexylphosphino)biphenyl, K<sub>3</sub>PO<sub>4</sub>, [Pd<sub>2</sub>(dba)<sub>3</sub>], DMF, 105°, 20 h; 75%. DIBAL-H = Diisobutylaluminium hydride, dppf = 1,1'-bis(diphenylphosphino)ferrocene, dba = dibenzylideneacetone.

heated to reflux for 2 h, then cooled to 20°, and partitioned between CH<sub>2</sub>Cl<sub>2</sub> (100 ml) and H<sub>2</sub>O (50 ml). The org. layer was separated, washed with H<sub>2</sub>O (2 × 50 ml), dried (MgSO<sub>4</sub>), and evaporated *in vacuo*. FC (CH<sub>2</sub>Cl<sub>2</sub>/AcOEt 10:1) afforded (±)-**1** (174 mg, 93%). Colorless solid. *R*<sub>f</sub> (CH<sub>2</sub>Cl<sub>2</sub>/AcOEt 10:1) 0.27. M.p. 205–209.0°. IR: 3025w, 2956w, 2897w, 2842w, 1728w, 1599w, 1578w, 1477s, 1448w, 1438w, 1322m, 1295m, 1237w, 1201m, 1171w, 1152m, 1115s, 1094m, 1043w, 1021w, 958m, 949m, 939s, 867w, 841s, 821m, 797w, 767s, 745m, 734m, 695s. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 4.30 (*d*, *J* = 16.5, 2 H); 4.40 (*s*, 2 H); 4.81 (*d*, *J* = 16.5, 2 H); 7.16 (*d*, *J* = 2.2, 2 H); 7.23 (*d*, *J* = 8.1, 2 H); 7.26–7.51 (*m*, 12 H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 58.9; 67.0; 125.3; 125.5; 126.2; 126.8; 126.9; 128.0; 128.6; 137.0; 140.6; 147.3. ESI-MS: 375.2 (100, *MH*<sup>+</sup>), 397.2 (76, [*M* + Na]<sup>+</sup>). HR-ESI-MS: 375.1861 (*MH*<sup>+</sup>, C<sub>27</sub>H<sub>23</sub>N<sub>2</sub><sup>+</sup>; calc. 375.1861).

((±)-**8**). Prepared as described for ((±)-**1**, from ((±)-**3** (408 mg, 1.00 mmol) and **6** (540 mg, 3.00 mmol). Yield: 355 mg (69%). Colorless solid.  $R_f$  ( $\text{CH}_2\text{Cl}_2$ ) 0.27. M.p. 240–241°. IR: 3003w, 2949w, 2899w, 2842w, 1716s, 1600w, 1460m, 1435m, 1328m, 1285m, 1259s, 1213m, 1194m, 1170m, 1155m, 1113m, 1098m, 1079m, 1042w, 967m, 933m, 905w, 864m, 774m, 751s, 743m.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 2.20 (s, 6 H); 3.48 (d,  $J = 17.1$ , 2 H); 3.96 (s, 6 H); 4.09 (d,  $J = 16.8$ , 2 H); 4.34 (s, 2 H); 6.56 (d,  $J = 1.3$ , 2 H); 6.92 (d,  $J = 1.9$ , 2 H); 7.50 (t,  $J = 7.8$ , 2 H); 7.95 (dt,  $J = 7.8$ , 1.6, 2 H); 8.03 (dt,  $J = 7.8$ , 1.4, 2 H); 8.26 (t,  $J = 1.7$ , 2 H).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 20.8; 52.2; 55.5; 67.5; 127.1; 127.9; 128.0; 128.3; 129.8; 130.2; 130.4; 133.3; 134.1; 135.1; 140.3; 142.4; 167.2. HR-ESI-MS: 519.2269 ( $\text{MH}^+$ ,  $\text{C}_{33}\text{H}_{31}\text{N}_2\text{O}_4^+$ ; calc. 519.2284).

((±)-**9**). Prepared as described for ((±)-**1**, from ((±)-**4** (502 mg, 1.00 mmol) and **5** (484 mg, 2.49 mmol). Yield: 556 mg (97%). Colorless solid.  $R_f$  ( $\text{CH}_2\text{Cl}_2/\text{AcOEt}$  10:1) 0.52. M.p. 246–248°. IR: 2983w, 2941w, 2910w, 1716s, 1708s, 1610m, 1575w, 1471m, 1445w, 1393m, 1365m, 1332w, 1270s, 1212m, 1177m, 1155w, 1119m, 1104s, 1059w, 1021m, 972m, 943m, 839m, 828s, 793w, 772s, 758m.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 1.43 (t,  $J = 7.2$ , 6 H); 2.25 (s, 6 H); 3.81 (d,  $J = 17.1$ , 2 H); 4.35 (s, 2 H); 4.41 (q,  $J = 7.2$ , 4 H); 4.53 (d,  $J = 17.1$ , 2 H); 6.81 (d,  $J = 7.5$ , 2 H); 7.08 (d,  $J = 7.8$ , 2 H); 7.29 (d,  $J = 8.4$ , 4 H); 8.07 (d,  $J = 8.4$ , 4 H).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 14.5; 17.5; 54.3; 61.1; 66.8; 124.8; 125.1; 128.9; 129.0; 129.1; 129.4; 132.5; 137.6; 144.9; 146.1; 166.3. ESI-MS: 547.2 (9,  $\text{MH}^+$ ), 569.2 (100,  $[M + \text{Na}]^+$ ). HR-ESI-MS: 569.2404 ( $[M + \text{Na}]^+$ ,  $\text{C}_{33}\text{H}_{34}\text{N}_2\text{NaO}_4^+$ ; calc. 569.2416).

((±)-**10**). Prepared as described for ((±)-**1**, from ((±)-**2** (948 mg, 2.00 mmol) and **5** (1.076 g, 5.55 mmol). Yield: 835 mg (81%). Colorless solid.  $R_f$  ( $\text{CH}_2\text{Cl}_2/\text{AcOEt}$  5:1) 0.24. M.p. 209–211°. FT-IR: 2956w, 2898w, 1705s, 1606m, 1575w, 1519w, 1485m, 1463w, 1365m, 1349w, 1325w, 1267s, 1212m, 1180s, 1102s, 1073m, 1016m, 962m, 942m, 858m, 834s, 810w, 772s, 747m, 734w, 722m, 701s.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 1.40 (t,  $J = 7.2$ , 6 H); 4.31 (d,  $J = 16.8$ , 2 H); 4.38 (q,  $J = 7.2$ , 4 H); 4.39 (s, 2 H); 4.81 (d,  $J = 16.5$ , 2 H); 7.19 (d,  $J = 1.9$ , 2 H); 7.25 (d,  $J = 8.4$ , 2 H); 7.44 (dd,  $J = 8.4$ , 2.2, 2 H); 7.54 (d,  $J = 8.7$ , 4 H); 8.05 (d,  $J = 8.7$ , 4 H).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 14.5; 58.9; 61.0; 67.0; 125.5; 125.7; 126.3; 126.5; 128.2; 128.9; 129.9; 135.7; 144.8; 148.1; 166.3. HR-ESI-MS: 541.2098 ( $[M + \text{Na}]^+$ ,  $\text{C}_{33}\text{H}_{30}\text{N}_2\text{NaO}_4^+$ ; calc. 541.2103).

((±)-**11**). Prepared as described for ((±)-**1**, from ((±)-**4** (502 mg, 1.00 mmol) and **6** (486 mg, 2.70 mmol). FC ( $\text{CH}_2\text{Cl}_2/\text{AcOEt}$  50:1 → 10:1) afforded ((±)-**11** (279 mg, 54%).  $R_f$  ( $\text{CH}_2\text{Cl}_2/\text{AcOEt}$  20:1) 0.22. M.p. 206–214°. IR: 3023w, 2955w, 1720s, 1602w, 1584w, 1437m, 1298s, 1270m, 1254s, 1241s, 1210m, 1117m, 1084m, 1064m, 968m, 940m, 871w, 828m, 808m, 794w, 752s, 736m, 701m.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 2.25 (s, 6 H); 3.80 (d,  $J = 17.1$ , 2 H); 3.93 (s, 6 H); 4.36 (s, 2 H); 4.54 (d,  $J = 17.1$ , 2 H); 6.81 (d,  $J = 7.8$ , 2 H); 7.07 (d,  $J = 7.8$ , 2 H); 7.40–7.50 (m, 4 H); 7.92 (t,  $J = 1.9$ , 2 H); 8.02 (td,  $J = 1.7$ , 7.5, 2 H).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 17.4; 52.3; 54.4; 66.8; 125.0; 125.3; 128.2; 128.3; 128.9; 130.0; 130.1; 132.3; 133.3; 137.5; 140.5; 146.1; 166.8. ESI-MS: 519.2 (5,  $\text{MH}^+$ ), 541.2 (100,  $[M + \text{Na}]^+$ ). HR-ESI-MS: 541.2089 ( $[M + \text{Na}]^+$ ,  $\text{C}_{33}\text{H}_{30}\text{N}_2\text{NaO}_4^+$ ; calc. 541.2103).

((±)-**12**). Prepared as described for ((±)-**1**, from ((±)-**2** (474 mg, 1.00 mmol) and **6** (540 mg, 3.00 mmol). Yield: 380 mg (78%). Colorless solid.  $R_f$  ( $\text{CH}_2\text{Cl}_2/\text{AcOEt}$  5:1) 0.24. M.p. 156–159°. IR: 2954w, 2889w, 1713s, 1611w, 1586w, 1480m, 1435m, 1315m, 1294m, 1245s, 1209m, 1192m, 1151m, 1109s, 1082m, 1044m, 961m, 942m, 817m, 758s, 745s, 724m.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 3.92 (s, 6 H); 4.31 (d,  $J = 16.5$ , 2 H); 4.40 (s, 2 H); 4.81 (d,  $J = 16.8$ , 2 H); 7.19 (d,  $J = 2.2$ , 2 H); 7.25 (d,  $J = 8.4$ , 2 H); 7.44 (dd,  $J = 2.2$ , 8.4, 2 H); 7.45 (t,  $J = 7.6$ , 2 H); 7.68 (ddd,  $J = 1.2$ , 1.8, 7.8, 2 H); 7.95 (td,  $J = 1.4$ , 7.8, 2 H); 8.17 (t,  $J = 1.7$ , 2 H).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 52.3; 58.9; 67.0; 125.5; 125.6; 126.2; 127.8; 128.0; 128.1; 128.7; 130.5; 131.0; 135.8; 140.7; 147.7; 166.9. HR-ESI-MS: 513.1778 ( $[M + \text{Na}]^+$ ,  $\text{C}_{31}\text{H}_{26}\text{N}_2\text{NaO}_4^+$ ; calc. 513.1790).

((±)-**13**). Prepared as described for ((±)-**1**, from ((±)-**3** (326 mg, 0.80 mmol) and **7** (561 mg, 2.14 mmol). Yield: 338 mg (81%). Colorless amorphous solid.  $R_f$  ( $\text{CH}_2\text{Cl}_2$ ) 0.11. IR: 2948w, 2848w, 1716s, 1599w, 1574w, 1463m, 1435s, 1288s, 1253s, 1214m, 1193m, 1173m, 1159m, 1114s, 1076s, 1044m, 969m, 927s, 857m, 821w, 779m, 757s, 710s.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 2.21 (s, 6 H); 3.22 (d,  $J = 16.5$ , 2 H); 3.67 (s, 6 H); 3.93 (d,  $J = 16.8$ , 2 H); 3.98 (s, 2 H); 6.50 (s, 2 H); 6.94 (s, 2 H); 7.27 (d,  $J = 8.4$ , 2 H); 7.42 (m, 2 H); 7.58 (t,  $J = 7.6$ , 2 H); 7.84 (d,  $J = 7.2$ , 2 H).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 21.0; 51.7; 54.5; 66.4; 126.7; 126.9; 127.4; 128.3; 129.2; 130.9; 131.7; 133.5; 136.0; 139.2; 141.8; 168.4 (1 signal missing due to overlap). HR-ESI-MS: 519.2271 ( $\text{MH}^+$ ,  $\text{C}_{33}\text{H}_{31}\text{N}_2\text{O}_4^+$ ; calc. 519.2284).

((±)-**14**). A soln. of ((±)-**10** (835 mg, 1.6 mmol) in THF (20 ml) was added dropwise to a suspension of  $\text{LiAlH}_4$

(190 mg, 5.0 mmol) in THF (10 ml). The mixture was heated to reflux for 2 h under Ar, then cooled to 0°, and the reaction was carefully quenched by slow addition of H<sub>2</sub>O (0.5 ml). The inorg. precipitate was filtered, and the filtrate was dried (MgSO<sub>4</sub>) and evaporated *in vacuo* to give (±)-**14** (700 mg, quant.). Colorless solid. M.p. 243–245°. IR: 3256w (br.), 2950w, 2899w, 2848w, 1611w, 1479s, 1455m, 1435m, 1320m, 1296m, 1235w, 1205m, 1163w, 1112m, 1095m, 1067m, 1027m, 964s, 941s, 869m, 841s, 764s, 751m, 734s. <sup>1</sup>H-NMR (300 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): 4.23 (d, *J* = 17.1, 2 H); 4.28 (s, 2 H); 4.49 (d, *J* = 5.9, 4 H); 4.70 (d, *J* = 16.8, 2 H); 5.17 (t, *J* = 5.8, 2 H); 7.19 (d, *J* = 8.4, 2 H); 7.25 (d, *J* = 1.9, 2 H); 7.33 (d, *J* = 8.4, 4 H); 7.42 (dd, *J* = 8.4, 2.2, 2 H); 7.50 (d, *J* = 8.4, 4 H). <sup>13</sup>C-NMR (75 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): 58.2; 62.5; 66.2; 124.7; 125.0; 125.1; 125.8; 126.7; 128.3; 135.0; 138.0; 141.0; 147.3. HR-ESI-MS: 435.2061 (*M*H<sup>+</sup>, C<sub>29</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup>; calc. 435.2073).

(±)-[2,8-Dimethyl-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine-4,10-diyl]bis(3,1-phenylene)]dime-thanol ((±)-**15**). Prepared as described for (±)-**14**, from (±)-**8** (353 mg, 0.68 mmol). Yield: 315 mg (quant.). Colorless amorphous solid. FT-IR (neat): 3311w, 2946w, 2921w, 2848w, 1603w, 1582w, 1460s, 1435m, 1359w, 1215m, 1202m, 1144m, 1013m, 971m, 932m, 913m, 889m, 859m, 827m, 793m, 753m, 704s. <sup>1</sup>H-NMR (300 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): 2.13 (s, 6 H); 3.40 (d, *J* = 16.8, 2 H); 4.08 (d, *J* = 16.8, 2 H); 4.31 (s, 2 H); 4.57 (d, *J* = 5.6, 4 H); 5.23 (t, *J* = 5.8, 2 H); 6.54 (d, *J* = 1.6, 2 H); 6.84 (d, *J* = 1.6, 2 H); 7.30 (d, *J* = 7.8, 2 H); 7.39 (t, *J* = 7.5, 2 H); 7.51–7.55 (m, 4 H). <sup>13</sup>C-NMR (75 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): 20.3; 55.2; 62.9; 79.0; 124.8; 126.3; 126.7; 127.2; 127.6; 128.0; 129.3; 132.3; 135.4; 139.3; 142.0; 142.2. HR-ESI-MS: 463.2372 (*M*H<sup>+</sup>, C<sub>31</sub>H<sub>31</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup>; calc. 463.2386).

(±)-[4,10-Dimethyl-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine-1,7-diyl]bis(3,1-phenylene)]dime-thanol ((±)-**16**). Prepared as described for (±)-**14**, from (±)-**11** (261 mg, 0.50 mmol). Yield: 222 mg (95%). Colorless amorphous solid. IR: 3269w, 3028w, 2901w, 1570w, 1470m, 1435m, 1403m, 1393m, 1372m, 1262w, 1210s, 1197m, 1172m, 1109m, 1095m, 1049m, 1026s, 980s, 931m, 915m, 826s, 812m, 782s, 757m, 734m, 706s. <sup>1</sup>H-NMR (300 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): 2.15 (s, 6 H); 3.67 (d, *J* = 16.8, 2 H); 4.33 (s, 2 H); 4.52 (d, *J* = 5.6, 2 H); 4.62 (d, *J* = 17.1, 2 H); 5.20 (t, *J* = 5.6, 4 H); 6.75 (d, *J* = 7.5, 2 H); 7.04–7.15 (m, 6 H); 7.27–7.38 (m, 4 H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 17.5; 54.4; 65.3; 66.8; 125.0; 125.3; 125.5; 127.5; 128.1; 128.3; 128.7; 132.0; 138.4; 140.5; 140.7; 146.1. ESI-MS: 463.2 (11, *M*H<sup>+</sup>), 485.2 (100, [*M* + Na]<sup>+</sup>). HR-ESI-MS: 485.2194 ([*M* + Na]<sup>+</sup>, C<sub>31</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>2</sub><sup>+</sup>; calc. 485.2205).

(±)-N-(8-Iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)-N-methylacetamide ((±)-**20a**). An oven-dried Schlenk tube was charged with (±)-**2** (1.00 g, 2.109 mmol), K<sub>3</sub>PO<sub>4</sub> (891 mg, 4.219 mmol), and CuI (180 mg, 1.051 mmol). The tube was sealed with a septum, evacuated, and refilled with N<sub>2</sub>. DMEDA (84 µl, 0.780 mmol), N-methylacetamide (142 µl, 2.528 mmol), and PhMe (6 ml) were added *via* syringe, and the tube was heated with stirring for 48 h at 110°. The mixture was cooled to 20° and filtered through SiO<sub>2</sub>. The filtrate was washed with Me<sub>2</sub>CO/hexane 1:1 (10 ml) and evaporated *in vacuo* to yield a yellow oil. FC (hexane/Me<sub>2</sub>CO 9:1 → 6:4) provided a first fraction consisting of (±)-**2** (543 mg, 54%), and a second fraction containing (±)-**20a** and traces of N-methylacetamide. A second FC (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 10:0 → 9:1) gave (±)-**20a** (236 mg, 26%). Pale-yellow foam. M.p. 109–111°. IR: 2941w, 2897w, 2841w, 1653s, 1645s, 1491s, 1472s, 1373m, 1319m, 1298m, 1206s. <sup>1</sup>H-NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>): 1.74 (s, 3 H); 3.08 (s, 3 H); 4.09 (d, *J* = 17.0, 1 H); 4.10 (d, *J* = 17.0, 1 H); 4.22 (s, 2 H); 4.61 (d, *J* = 16.8, 1 H); 4.63 (d, *J* = 16.8, 1 H); 6.73 (d, *J* = 2.5, 1 H); 6.87 (d, *J* = 8.5, 1 H); 6.96 (dd, *J* = 2.2, 8.5, 1 H); 7.11 (d, *J* = 8.2, 1 H); 7.24 (d, *J* = 1.9, 1 H); 7.43 (dd, *J* = 1.9, 8.5, 1 H). <sup>13</sup>C-NMR (75 MHz, CD<sub>2</sub>Cl<sub>2</sub>): 22.2; 36.8; 58.1; 58.5; 66.7; 87.1; 125.4; 126.2; 126.3; 127.2; 129.0; 130.7; 135.8; 136.3; 140.5; 147.3; 148.1; 170.1. HR-MALDI-MS (DHB): 420.0558 (*M*H<sup>+</sup>, C<sub>18</sub>H<sub>19</sub>IN<sub>3</sub>O<sup>+</sup>; calc. 420.0567). Anal. calc. for C<sub>18</sub>H<sub>18</sub>IN<sub>3</sub>O (419.26): C 51.57, H 4.33, N 10.02; found: C 51.28, H 4.38, N 9.80.

(±)-N-[(tert-Butoxy)carbonyl]-8-iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-amine ((±)-**20b**). Iodide (±)-**2** (1.00 g, 2.1 mmol), anh. K<sub>2</sub>CO<sub>3</sub> (580 mg, 4.2 mmol), CuI (80 mg, 0.4 mmol), and BocNH<sub>2</sub> (360 mg, 3.2 mmol) were combined in an oven-dried flask that was subsequently evacuated and backfilled with N<sub>2</sub> three times. DMEDA (90 µl, 0.8 mmol) and anh. DMF (15 ml) were added *via* syringe, and the mixture was heated to 100° for 20 h. The mixture was cooled to 20° and filtered through a plug of SiO<sub>2</sub> (1 × 1.5 cm). The filtrate was washed with AcOEt (15 ml) and evaporated *in vacuo*. FC (AcOEt/hexane 1:1 → 7:3) gave (±)-**2** (300 mg, 30%) along with (±)-**20b** (353 mg, 36%). Pale-yellow solid. M.p. 211–214°. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz): 1.47 (s, 9 H); 4.07 (m, 2 H); 4.24 (m, 2 H); 4.59 (d, *J* = 12.6, 1 H); 4.63 (d, *J* = 12.6, 1 H); 6.36 (br. s, 1 H); 6.85 (d, *J* = 8.7, 1 H); 6.98 (m, 2 H); 7.11 (br. s, 1 H); 7.21 (d, *J* = 1.8, 1 H); 7.43 (dd, *J* = 1.8, 8.4, 1 H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 28.5; 58.3; 59.1; 67.0; 80.7; 87.6; 117.0; 118.7; 125.6; 127.2; 128.3; 130.7; 134.7; 135.9; 136.5; 143.0; 148.1; 153.1. HR-ESI-MS: 464.0824 (*M*H<sup>+</sup>, C<sub>20</sub>H<sub>23</sub>IN<sub>3</sub>O<sub>2</sub><sup>+</sup>; calc. 464.0835). Anal. calc. for C<sub>20</sub>H<sub>22</sub>IN<sub>3</sub>O<sub>2</sub> (463.31): C 51.85; H 4.79; N 9.07; found: C 51.85; H 4.87; N 9.12.

(±)-8-Iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine-2-carbonitrile ((±)-**20c**). Iodide (±)-**2** (1.92 g, 4.2 mmol), CuCN (0.48 g, 5.4 mmol), and [Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>] (60 mg, 0.08 mmol) were placed in an oven-dried flask, sealed with a septum, and flushed with N<sub>2</sub> for 15 min. Anh. DMF (30 ml) was added *via*

cannula, and the mixture was heated overnight at 90–100°. The mixture was cooled to 20° and evaporated to dryness *in vacuo*. The residue was taken up in CH<sub>2</sub>Cl<sub>2</sub> (50 ml), and the org. layer was washed with aq. NH<sub>3</sub> soln. (3 × 50 ml) until the blue color had disappeared from the aq. layer, and then washed once with sat. aq. NaCl soln. (50 ml), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated *in vacuo*. FC (hexane/AcOEt 6:4) provided (±)-**2** (540 mg, 28%) along with (±)-**20c** (700 mg, 45%). Pale-yellow solid. M.p. 207–209°. IR: 2959w, 2900w, 2220m, 1602m, 1490m, 1471m, 1416w, 1394w, 1318m, 1296m, 1244w, 1206s, 1151w, 1112m, 1098m, 1072m, 1025w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 4.13 (*d*, *J* = 17.1, 1 H); 4.14 (*d*, *J* = 17.1, 1 H); 4.26 (*d*, *J* = 0.9, 2 H); 4.65 (*d*, *J* = 17.7, 1 H); 4.66 (*d*, *J* = 17.7, 1 H); 6.88 (*d*, *J* = 8.4, 1 H); 7.17 (*d*, *J* = 8.1, 1 H); 7.25 (*m*, 2 H); 7.45 (*m*, 2 H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 58.2; 66.4; 87.8; 107.2; 118.6; 125.7; 127.0; 128.8; 129.7; 131.0; 131.2; 135.6; 136.6; 147.1; 152.4. HR-MALDI-MS (DHB): 374.0145 (*M*H<sup>+</sup>, C<sub>16</sub>H<sub>13</sub>IN<sub>3</sub><sup>+</sup>; calc. 374.0149). Anal. calc. for C<sub>16</sub>H<sub>12</sub>IN<sub>3</sub> (373.19): C 51.49; H 3.24; N 11.26, found C 51.25; H 3.39; N 11.33.

(±)-8-Iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine-2-carbaldehyde ((±)-**21**). To a soln. of (±)-**20c** (800 mg, 2.14 mmol) in anh. PhMe (40 ml), a 1M soln. of DIBAL-H in PhMe (3.2 ml, 3.2 mmol) was added *via* syringe in a dropwise manner, and the mixture was heated to 60° for 90 min. After cooling to 20°, MeOH (4 ml) and H<sub>2</sub>O (4 ml) were added, and the mixture was stirred until a gel precipitate formed (*ca.* 10 min). The precipitate was removed by filtration over *Celite*, and the filtrate was diluted with AcOEt and washed with H<sub>2</sub>O. The org. layer was separated, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to dryness *in vacuo*. FC (CH<sub>2</sub>Cl<sub>2</sub>/AcOEt 4:1) gave (±)-**21** (670 mg, 83%). Pale-yellow solid. M.p. 179–182°. IR: 2953w, 2905w, 2826w, 2736w, 1673s, 1600s, 1565m, 1489w, 1471s, 1431m, 1396w, 1381w, 1327m, 1319m, 1294m, 1259w, 1244m, 1202s, 1175m, 1152m, 1105s, 1091m, 1072m, 1059m, 1007w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 4.18 (*d*, *J* = 16.8, 2 H); 4.26 (*s*, 2 H); 4.66 (*d*, *J* = 16.8, 1 H); 4.71 (*d*, *J* = 16.8, 1 H); 6.88 (*d*, *J* = 8.4, 1 H); 7.22 (*m*, 2 H); 7.42 (*m*, 2 H); 7.66 (*dd*, *J* = 1.8, 8.4, 1 H); 9.82 (*s*, 1 H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 58.4; 58.7; 66.7; 87.9; 125.8; 127.3; 128.4; 129.0; 129.5; 130.3; 132.7; 135.9; 136.8; 147.6; 154.4; 191.3. HR-ESI-MS: 377.0142 (*M*H<sup>+</sup>, C<sub>16</sub>H<sub>14</sub>IN<sub>2</sub>O<sup>+</sup>; calc. 377.0151).

(±)-1-(8-Iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine-2-yl)ethanone ((±)-**22**). Compound (±)-**21** (88 mg, 0.23 mmol) was dissolved in anh. THF (3 ml), and a 3M soln. of MeMgCl in THF (235 µl, 0.70 mmol) was added *via* syringe. After stirring at 20° for 1 h, sat. aq. NH<sub>4</sub>Cl soln. (5 ml), H<sub>2</sub>O (5 ml), and AcOEt (5 ml) were added. The org. layer was separated, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and evaporated to dryness *in vacuo*. The crude benzylic alcohol was taken up in Me<sub>2</sub>CO (15 ml), activated MnO<sub>2</sub> (85%, < 5 µm, 162 mg, 1.6 mmol) was added, and the mixture was stirred for 40 h at 20°. The mixture was filtered over *Celite*, which was washed with excess CH<sub>2</sub>Cl<sub>2</sub> and evaporated to dryness *in vacuo*. FC (AcOEt/hexanes 1:1 → 6:4) gave (±)-**22** (65 mg, 71%). Buff-colored solid. M.p. 173–174°. IR: 3064w, 2993w, 2952w, 2901w, 2844w, 1666s, 1605m, 1562m, 1491w, 1472m, 1434m, 1413m, 1398m, 1348m, 1319m, 1278s, 1267s, 1253m, 1206s, 1171m, 1149m, 1112s, 1096m, 1080m, 1066m, 1018w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 2.50 (*s*, 3 H); 4.17 (*d*, *J* = 16.8, 2 H); 4.27 (*s*, 2 H); 4.66 (*d*, *J* = 16.8, 1 H); 4.72 (*d*, *J* = 16.8, 1 H); 6.88 (*d*, *J* = 8.4, 1 H); 7.16 (*d*, *J* = 8.4, 1 H); 7.22 (*d*, *J* = 1.8, 1 H); 7.44 (*dd*, *J* = 1.8, 8.4, 1 H); 7.54 (*d*, *J* = 1.8, 1 H); 7.75 (*dd*, *J* = 1.8, 8.4, 1 H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 26.5; 58.2; 58.6; 66.6; 87.6; 124.8; 126.9; 127.4; 127.5; 127.6; 130.0; 133.0; 135.5; 136.4; 147.3; 152.5; 196.7. HR-ESI-MS: 391.0307 (*M*H<sup>+</sup>, C<sub>17</sub>H<sub>16</sub>IN<sub>2</sub>O<sup>+</sup>; calc. 391.0307).

(±)-8-Iodo-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine-2-carboxylic Acid ((±)-**23**). To a soln. of (±)-**21** (80 mg, 0.21 mmol) in Me<sub>2</sub>CO (4 ml), KMnO<sub>4</sub> (67 mg, 0.42 mmol) in H<sub>2</sub>O (0.8 ml) was added. The heterogeneous mixture was heated at 80° under ambient atmosphere for 17 h. The mixture was cooled to 20°, diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 ml), and filtered over *Celite*, which was washed with copious amounts of CH<sub>2</sub>Cl<sub>2</sub>/MeOH 1:1. The filtrate was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and evaporated to dryness to provide (±)-**23** (83 mg, quant.; 95% pure by <sup>1</sup>H-NMR). Pale-yellow solid. M.p. 285 ° (dec.). IR: 3207m (br.), 2910w, 2902w, 1673w, 1584s, 1548s, 1473m, 1377s, 1318m, 1301m, 1252w, 1208m, 1174w, 1148w, 1105w, 1089w, 1072w, 1027w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>/CD<sub>3</sub>OD 4:1): 4.04 (*d*, *J* = 16.8, 2 H); 4.18 (br. *s*, 2 H); 4.52 (*d*, *J* = 11.7, 1 H); 4.58 (*d*, *J* = 11.7, 1 H); 6.77 (*d*, *J* = 8.4, 1 H); 6.98 (*d*, *J* = 8.4, 1 H); 7.12 (*s*, 1 H); 7.33 (*d*, *J* = 8.4, 1 H); 7.44 (*s*, 1 H); 7.65 (*d*, *J* = 8.4, 1 H). <sup>13</sup>C-NMR (75 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): 52.8; 59.1; 66.7; 87.7; 123.9; 126.6; 127.8; 128.4; 128.7; 132.0; 135.9; 136.1; 136.9; 148.8; 170.0. HR-MALDI-MS (3-HPA): 393.0090 (*M*H<sup>+</sup>, C<sub>16</sub>H<sub>14</sub>IN<sub>2</sub>O<sub>2</sub><sup>+</sup>; calc. 393.0100).

(±)-8-(4,4,5,5-Tetramethyl[1,3,2]dioxaborolan-2-yl)-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocine-2-carbaldehyde ((±)-**24**). Compound (±)-**21** (605 mg, 1.6 mmol), bis(pinacolato)diboron (450 mg, 1.8 mmol), AcOK (473 mg, 4.8 mmol), and [Pd(dppf)Cl<sub>2</sub>] · CH<sub>2</sub>Cl<sub>2</sub> (26 mg, 0.03 mmol) were combined in an oven-dried flask and flushed with N<sub>2</sub> for 15 min. Anh. DMF (12 ml) was added *via* syringe, and the mixture was heated overnight at 70–80°. The mixture was cooled to 20° and partitioned between PhH (100 ml) and sat. aq. NaCl soln. (50 ml). The org. layer was separated, washed with H<sub>2</sub>O (2 × 25 ml), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to dryness first at rotary evaporator pressure, then under high vacuum (< 0.5 mbar) to remove traces of DMF. The crude dark-brown oil was taken up in pentane and sonicated until a pale brown suspension formed (*ca.* 10 min).

The solid was collected by filtration, washed with excess pentane, and dried to yield ( $\pm$ )-**24** (595 mg, 98%; > 95% pure by  $^1\text{H}$  NMR), which was used without further purification. Pale-brown solid. M.p. 182–185°. IR: 2975w, 2914w, 2727w, 1682s, 1607m, 1568m, 1492w, 1472w, 1437w, 1390m, 1360s, 1332s, 1311m, 1294m, 1284m, 1243m, 1204s, 1178w, 1164m, 1145s, 1110s, 1088s, 1065w.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 1.28 (s, 12 H); 4.29 (m, 4 H); 4.74 (d,  $J = 16.5$ , 2 H); 7.14 (d,  $J = 7.8$ , 1 H); 7.24 (d,  $J = 7.8$ , 1 H); 7.40 (s, 1 H); 7.45 (s, 1 H); 7.60 (d,  $J = 8.1$ , 1 H); 7.66 (dd,  $J = 1.8$ , 8.4, 1 H); 9.82 (s, 1 H).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 25.0; 58.7; 59.0; 66.8; 84.0; 124.6; 125.8; 127.0; 128.7; 128.9; 129.5; 132.5; 134.1; 134.2; 150.7; 154.7; 191.3. HR-ESI-MS: 377.2032 ( $\text{MH}^+$ ,  $\text{C}_{22}\text{H}_{26}\text{BN}_2\text{O}_3^+$ ; calc. 377.2036).

( $\pm$ )-Methyl 2-(8-Formyl-6H,12H-5,11-methanodibenzo[b,f][1,5]diazocin-2-yl)-3-methylbenzoate (( $\pm$ )-**26**). Compound ( $\pm$ )-**24** (300 mg, 0.80 mmol), 2-(dicyclohexylphosphino)biphenyl (28 mg, 0.08 mmol),  $[\text{Pd}(\text{dba})_3]$  (18 mg, 0.02 mmol), anh.  $\text{K}_3\text{PO}_4$  (510 mg, 2.4 mmol), and **25** (240 mg, 0.87 mmol) were combined in an oven-dried flask, which was evacuated and refilled with  $\text{N}_2$  three times. Anh. DMF (5 ml) was added *via* syringe, and the mixture was heated at 105° for 20 h. The mixture was cooled to 20°, and partitioned between PhH (50 ml) and sat. aq. NaCl soln. (25 ml). The org. layer was separated, washed with  $\text{H}_2\text{O}$  ( $2 \times 25$  ml), dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated *in vacuo*. FC (PhMe/ $\text{Me}_2\text{CO}$  9:1  $\rightarrow$  85:15) yielded ( $\pm$ )-**26** (238 mg, 75%). Buff-colored foam. M.p. 80–90°. IR: 2947w, 2905w, 2724w, 1718m, 1680s, 1604m, 1567m, 1490m, 1457w, 1429m, 1406w, 1348m, 1328m, 1292s, 1271m, 1243m, 1204s, 1140s, 1109s, 1090s, 1065m, 1009w.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ , 1:1 mixture of atropisomers): 1.96/2.14 (s, 3 H); 2.87/3.59 (s, 3 H); 4.25–4.45 (m, 4 H); 4.75 (m, 2 H); 6.68/6.70 (s, 1 H); 6.98/7.00 (s, 1 H); 7.1–7.4 (m, 4 H); 7.48 (br. s, 1 H); 7.53/7.61 (d,  $J = 7.5$ , 1 H); 7.66/7.69 (s, 1 H); 9.82/9.84 (s, 1 H).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 21.0; 51.2; 52.1; 58.7; 58.9; 59.1; 59.4; 66.9; 67.3; 124.6; 124.8; 125.5; 125.7; 125.9; 127.1; 127.4; 128.5; 128.7; 128.9; 129.3; 129.4; 129.6; 132.1; 132.5; 132.6; 133.2; 133.3; 136.3; 136.5; 137.1; 137.5; 138.1; 140.8; 141.1; 146.4; 146.5; 154.8; 155.1; 169.1; 169.5; 191.3; 191.5. HR-ESI-MS: 399.1708 ( $\text{MH}^+$ ,  $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_3^+$ ; calc. 399.1709).

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