New Chiral Molecular Tweezers with a Bis-Tröger's Base Skeleton†

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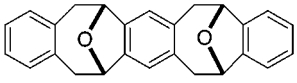
A convenient synthesis of 5α,8α,14α,17α-5,17:8,14-dimethano-5,8,14,17-tetraaza-5,6,7,8,13,14,17,-18-octahydrodibenzo[*e*,*e*′]benzo[1,2-*a*:3,4-*a*′]dicyclooctene derivatives is described, and the compounds have been fully characterized by NMR; in some cases, the molecular structure has been determined by X-ray crystallography. These compounds represent the first examples of a new class of molecular tweezers.

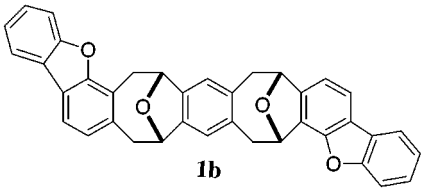
Introduction

Recognition of planar molecules based on noncovalent interactions is of interest in host−guest chemistry. Molecular tweezers[1] containing two aromatic chromophores connected by a spacer unit are suitable receptors for aromatic guests since they can hold the guest by the two aromatic arms through π-stacking interactions. Harmata et al.[2] have described molecular tweezers derived from Kagan's ether, both achiral **1a** and chiral **1b**. Recently, Fukazawa et al.[3] have reported the synthesis of **2** and related compounds formed by units of dioxa[2.2]-*o*-cyclophane with an arrangement of the two terminal aromatic rings in a face-to-face orientation in the syn conformation. The lateral aromatic rings act as tweezers toward π-electron-deficient compounds when at least one of the terminal aromatic rings, Ar or Ar′, is larger than benzene.

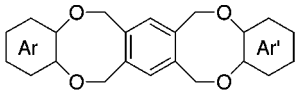
Tröger's base **3**, first synthesized by Tröger in 1887,[4] is a concave chiral molecule, the chirality of which results from the blocked configuration of the stereogenic nitrogen atoms. Tröger's base and its analogues have been described as "fascinating molecules",[5] and they provide relatively rigid chiral armatures for the construction of chelating and biomimetic systems, which were essentially developed thanks to the efforts of Wilcox and co-workers.[6] Tröger's base and its analogues show a perpendicular



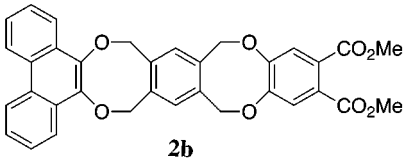
1a



1b



2a



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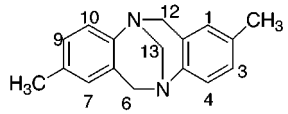

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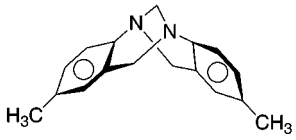

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†Dedicated to Professor José Luis Soto on the occasion of his 70th birthday.

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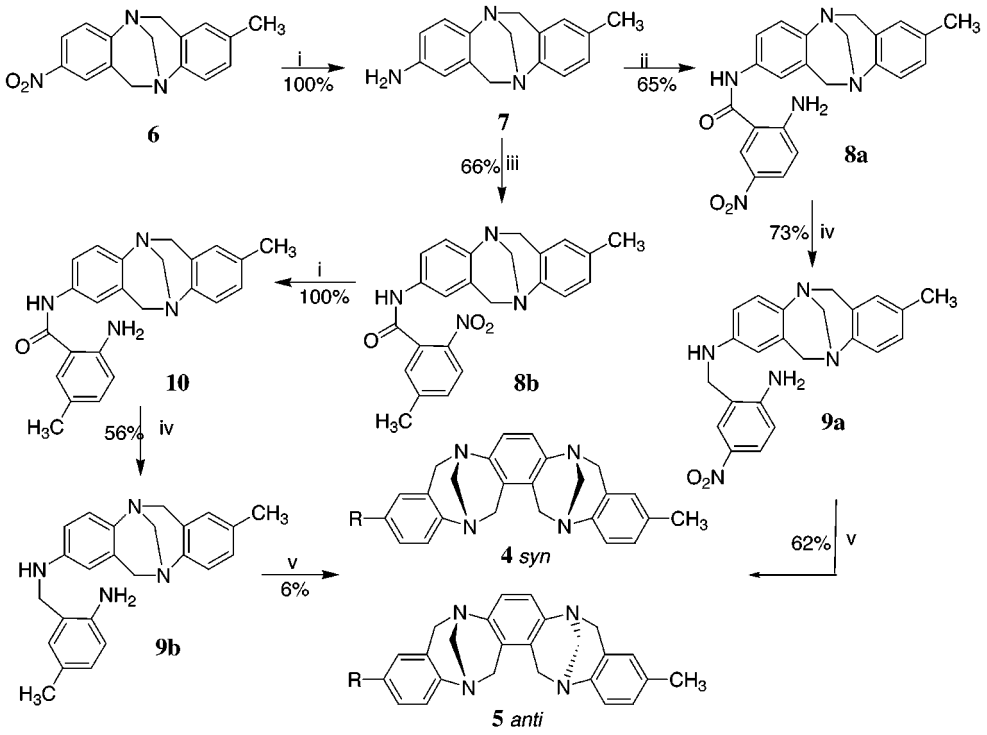
Scheme 1[a]



[a] Key: (i) H_2/Pd 10%(C), $CHCl_3$/EtOH, rt, 3 h; (ii) 6-nitroisatoic anhydride, THF, reflux, 3 h; (iii) 5-methyl-2-nitrobenzoic acid, DCC, DMF, rt, 5 h; (iv) BH_3−THF, reflux, 1 h; (v) 37% aqueous CH_2O, 95% EtOH, 36% HCl, 90 °C, 24 h.

arrangement of the two aromatic rings,[6a] as in Kagan's ether, and could serve as starting compounds in the synthesis of chiral molecular tweezers. Tröger's base analogues are mostly derived from the reaction of formaldehyde with simple para-substituted anilines, but in the past few years, new Tröger's base analogues derived from heterocyclic compounds, such as phenanthroline,[7] porphyrin,[6h,8] azolyl-substituted anilines,[9] acridines,[10] benzophenanthroline,[10] and various aminoheterocycles,[11] have been reported, and some of them have been shown to interact with DNA.[7,10] In the course of our work on the development of analogues of Tröger's bases, we report in this paper the first example of molecular tweezers with a bis-Tröger's base skeleton.

Results and Discussion

We have synthesized the bis-Tröger's base analogues **4** and **5** (Scheme 1) starting from the unsymmetrical Tröger's base **6** and following a synthetic pathway similar to the procedure established by Wilcox et al. for the synthesis of unsymmetrically substituted Tröger's bases.[12]

Base **6**[12] was catalytically hydrogenated over 10% palladium on charcoal, yielding amine **7** in almost quantitative yield. The reaction of **7** with 6-nitroisatoic anhydride[13] in anhydrous THF afforded amide **8a** in 65% yield. Amide **8b** was prepared in 66% yield by reaction of **7** with 5-methyl-2-nitrobenzoic acid and dicyclohexylcarbodiimide (DCC) in anhydrous DMF and was then hydrogenated over 10% palladium on charcoal, yielding the amino derivative **10** in almost quantitative yield. Amides **8a** and **10** were reduced with BH_3−THF in anhydrous THF to the corresponding amines **9a** and **9b** in 73% and 56% yields, respectively. All attempts to reduce **8b** to **9b** in only one step using Ti_4Cl/BH_3 in dimethoxyethane or in THF,[14] conditions in which amides and nitro compounds are reduced in high yields to secondary and primary amines, respectively, failed. Finally, cyclization of amines **9** by reaction with aqueous formaldehyde in 95% ethanol and concentrated hydrochloric acid at 90 °C for 24 h yielded the corresponding bis-Tröger's bases **4** and **5**.

Compound **9a** affords, in a 63% yield, a 4:1 mixture of stereoisomers **4a** and **5a**, which were separated by chromatography. The reaction of cyclization to form the

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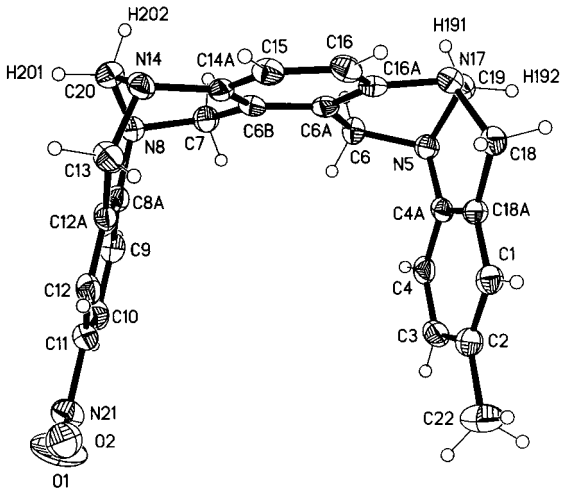


Figure 1. X-ray structure of **4a**: ORTEP view.

new Tröger's base skeleton is stereo- and regioselective and only one of the two possible regioisomers, as mixture of the syn/anti stereoisomers **4a** and **5a**, was obtained and their structure was established by ^{1}H NMR. In the ^{1}H NMR spectra of both stereoisomers, the aromatic protons of the central ring form an AB system with a coupling constant of 8 Hz, corresponding to a J_{ortho}. The syn configuration of the major stereoisomer **4a** was determined by X-ray crystallography (Figure 1). When the minor isomer **5a** was placed in the above cyclization conditions, an identical mixture (4:1) of **4a** and **5a** was obtained. Therefore, the syn isomer is thermodynamically more stable than the anti isomer, either because π-stacking interaction between the lateral aromatic rings, which are parallel, or due to differences in solvation between the two isomers. The X-ray structure (Figure 1) shows that the aromatic arms lie almost parallel with each other (23.1°), with a distance between its centroids of 4.368(5) Å. The central phenyl ring is almost orthogonal to the external aromatic arms (*p*-methyl, 88.6°; *p*-nitro, 79.3°). The molecular packing shows that in the **c** direction every two molecules are intercalated each other in such a way that the nitro-arm of one molecule is located between the two arms of the front molecule with the nitro group pointed to the central aromatic ring in an edge-to-face interaction**.** The UV−vis spectrum of **4a** in chloroform shows a weak broad band at 700 nm that we tentatively assign to a donor−acceptor interaction between the external aromatic rings. In general, the formation of Tröger's bases is sensitive to the steric hindrance and the less hindered regioisomers are favored.[15] The transformation of **9a** into the Tröger's bases **4a** and **5a** requieres two molecules of formaldehyde, one for the N−CH_2−N bridge and the other to create the N−CH_2−C(Ar) bond. The formation of the *gem*-diamine bridge is reversible as the isomerization **5a** to **4a** proved (the facile racemization of Tröger's bases has the same explanation).[6a] Since it is difficult to know in which order these two reactions took place, we will assume that the bridge N−CH_2−N is already present before the deciding C−C bond formation occur. There are four transition states, that should resemble the intermediates depicted in Figure 2, two correspond to an attack at the ortho position, **I1** and **I2**, and two to an attack at the para position, **I3** and **I4**. The formation of bis-Tröger's bases **11** and **12** was not observed, although they seem to be less hindered than regioisomer **4a**. We propose that the formation of the major isomer **4a** corresponds to the stabilizing π-stacking present in a transition state close to **I1** while in that corresponding to **I3** the external aromatic rings are too far apart to π stack. The anti isomer **5a** results from an equilibration of **4a** in the reaction conditions.

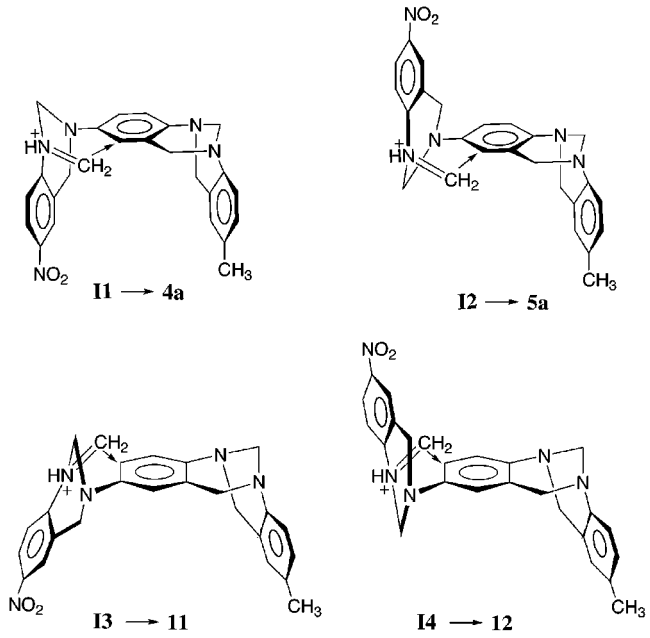
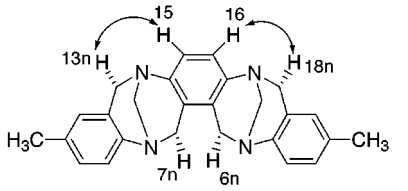


Figure 2.



4b/5b

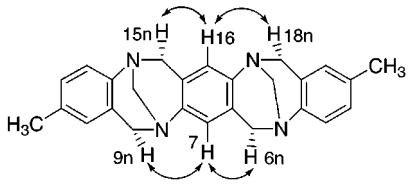


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Figure 3.

Compound **9b**, in the same reaction conditions, afforded a complex reaction mixture from which a significant quantity of **9b** was recovered, and a sole stereoisomer of the bis-Tröger's base was obtained in very low yield. The reaction is also regioselective, and the assignment of the structure as the more hindered regioisomer **5** was made on the basis of its ^{1}H NMR spectrum. The protons in the central aromatic ring are chemically equivalent but NOE and NOESY experiments showed that they are spatially close to the methylene protons H-13n (H-18n) but not to H-6n (H-7n) (Figure 3). The other pair of regioisomers, **13**, should show NOE interac-

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tions between the central aromatic protons H-7 (H-16) and both pairs of endo protons H-9n (H-18n) and H-6n (H-15n) (Figure 3).

The assignment of the structure to the anti stereoisomer **5b** was established by X-ray crystallography. The central aromatic ring is also orthogonal to both external aromatic rings (*p*-methyl, 83.4°; *p*-nitro, 75.6°) and the planes defined by the external rings form an angle of 23.4°, similar to base **4a**. The molecular packing shows that the molecules are stacked along the **c** direction. The low yield obtained in the cyclization reaction may be due to the absence of stabilizing π-stacking interactions between the external phenyl rings. Note that, contrary to **4a**, the lateral phenyl rings in **5b** are identically polarized.

Conclusion

The successful synthesis of compounds **4a** and **5a**,**b** opens the way to the preparation of supramolecular boxes and channels by addition of successive Tröger's bases, by using larger spacers (phenantrenes instead of benzenes) or by linking them through polyethylenoxy bridges (bis-Trögerophanes). All these approches are under way in our group.

Experimental Section

Melting points are uncorrected. ^{1}H spectra were recorded at 250, 300, and 400 MHz, and ^{13}C NMR spectra were recorded at 63, 75, and 100 MHz. ^{1}H and ^{13}C chemical shifts were measured in ppm relative to internal Me_4Si, and coupling constants are expressed in Hz.

General Procedure for the Hydrogenation of Nitro Compounds. A solution of 1 mmol of the corresponding nitro compound in 10 mL of chloroform and 40 mL of ethanol was hydrogenated over 90 mg of Pd 10% (C) at 2 atm and room temperature during 3 h. The reaction mixture was filtered through Celite, the Celite was washed with ethyl acetate, and the filtrate and washes were evaporated under reduced pressure. The residual solid was dissolved in 30 mL of chloroform, successively washed with 2 × 30 mL of 5% aqueous NaOH and 30 mL of water, and then dried over anhydrous $MgSO_4$. The solvent was eliminated under reduced pressure, and the almost pure amine was utilized without further purification.

8-Amino-2-methyl-5,11-methano-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,5]diazocine (7): yield 99%; mp 210−212 °C; IR (KBr) ν 3398, 3325, 3207, 1614, 1497, 1207, 831 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.23 (s, 3H), 4.04 (d, 1H, J = 16.6), 4.05 (d, 1H, J = 16.6), 4.30 (s, 2H), 4.61 (d, 1H, J = 16.6), 4.62 (d, 1H, J = 16.6), 6.22 (d, 1H, J = 2.7), 6.52 (dd, 1H, J = 8.5, 2.7), 6.72 (bs,1H,), 6.94 (d, 1H, J = 8.5), 6.97 (dd, 1H, J = 8.3, 1.5), 7.03 (d, 1H, J = 8.3); ^{13}C NMR δ 20.81, 58.60, 58.75, 67.18, 112.53, 114.99, 124.71, 125.77, 127.29, 127.62, 128.02, 128.63, 133.37, 139.30, 142.68, 145.44.

***N*-(2-Amino-5-methylbenzoyl)-8-amino-2-methyl-5,11-methano-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,5]diazocine (10):** yield 98%; mp 158−160 °C; IR (KBr) ν 3449, 3356, 1655, 1491, 1205, 829 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 2.23 (s, 3H), 2.26 (s, 3H), 4.121 (d, 1H, J = 16.4), 4.171 (d, 1H, J = 16.8), 4.32 (s, 2H), 4.67 (d, 1H, J = 16.8), 4.69 (d, 1H, J = 16.6), 5.24 (bs, 2H), 6.63 (d, 1H, J = 8.3), 6.72 (bs, 1H), 6.97 (dd, 1H, J = 8.3, 1.7), 7.03 (d, 1H, J = 8.3), 7.07 (d, 1H, J = 2.0), 7.12 (d, 1H, J = 8.1), 7.20, 7.24, 7.26; ^{13}C NMR ($CDCl_3$) δ 20.33, 20.80, 58.69, 58.76, 67.03, 116.41, 117.70, 119.00, 120.16, 124.72, 125.47, 126.07, 127.16, 127.21, 127.32, 128.20, 128.50, 133.53, 133.53, 133.69, 144.47, 145.20, 146.47, 167.43.

***N*-(2-Amino-5-nitrobenzoyl)-8-amino-2-methyl-5,11-methano-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,5]diazocine (8a).** To a stirred solution of 6-nitroisatoic anhydride[13] (1.000 g, 4.81 mmol) in anhydrous THF (9.2 mL), at room temperature under argon, was added portionwise amine **7** (0.891 g, 3.55 mmol), and the resulting mixture was refluxed for 3 h until amine **7** disappeared, the progress of the reaction being followed by TLC (eluent: hexane/ethyl acetate 3:7). The reaction mixture was then cooled to room temperature and poured into water; the mixture was extracted with ethyl acetate (3 × 50 mL), the combined extracts were dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude product was then purified by flash chromatography over silica gel. Elution with hexane/dichloromethane (6/4) yielded pure **8a** in 65% yield as an orange solid: mp 250−253 °C; IR (KBr) ν 3385, 1655, 1622, 1589, 1537, 1497, 1327 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.24 (s, 3H), 4.15 (d, 1H, J = 16.1), 4.19 (d, 1H, J = 16.8), 4.35 (s, 2H), 4.70 (d, 1H, J = 16.6), 4.72 (d, 1H, J = 16.8), 6.47 (bs, 2H), 6.67 (d, 1H, J = 9.3), 6.74 (bs, 1H), 6.99 (dd, 1H, J = 8.3, 1.7), 7.07 (d, 1H, J = 8.3), 7.18 (d, 1H, J = 8.6), 7.27, 7.29 (dd, 1H, J = 2.4), 7.83 (bs, 1H), 8.11 (dd, 1H, J = 9.3, 2.4), 8.44 (d, 1H, J = 2.4); ^{13}C NMR (DMSO-d_6) δ 20.54, 58.43, 58.58, 66.66, 113.75, 115.99 119.28, 120.43, 124.62, 124.80, 126.34, 127.19, 127.71, 127.81, 127.86, 128.18, 132.48, 134.15, 135.08, 144.40, 145.63, 155.29, 165.91. Anal. Calcd for $C_{23}H_{21}N_5O_3$: C, 66.49; H, 5.09; N, 16.86. Found: C, 66.58; H, 4.85; N, 17.01.

***N*-(5-Methyl-2-nitrobenzoyl)-8-amino-2-methyl-5,11-methano-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,5]diazocine (8b).** To a stirred suspension of amine **7** (0.276 g, 1.10 mmol) and 5-methyl-2-nitrobenzoic acid (0.199 g, 1.10 mmol) in anhydrous DMF (1.2 mL), at 0 °C under argon, was added slowly DCC (0.272 g, 1.32 mmol). The resulting mixture was stirred at 0 °C for 15 min and then allowed to warm to room temperature, and finally 0.25 mL of DMF was added. The mixture was stirred at room temperature for 2.5 h, 0.25 mL of DMF was added, and the stirring was continued for additional 2.5 h. The dicyclohexylurea precipitate was filtered off and washed with dichloromethane. The combined organic filtrate and CH_2Cl_2 wash were successively washed with saturated aqueous $NaHCO_3$ (3 × 50 mL) and water (10 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$, evaporated under reduced pressure, and flash chromatographed over silica gel. Elution with hexane/ethyl acetate (4/6) afforded pure **8b** in 66% yield as a pale yellow solid: mp 220−222 °C; IR (KBr) ν 3227, 3171, 3061, 1639, 1551, 1512, 1491, 1341, 837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.24 (s, 3H), 2.44 (s, 3H), 4.11 (d, 1H. J = 17.1), 4.15 (d, 1H, J = 17.0), 4.30 (s, 2H), 4.67 (d, 2H, J = 16.6), 6.73 (bs, 1H), 6.98 (bd, 1H, J = 8.1), 7.04 (d, 1H, J = 8.1), 7.10 (d, 1H, J = 8.6), 7.19 (dd, 1H, J = 8.6, 2.2), 7.30, 7.32, 7.57 (bs, 1H), 7.94 (d, 1H, J = 9.0); ^{13}C NMR (DMSO-d_6) δ 20.55, 20.95, 58.44, 58.57, 66.64, 117.89, 119.19, 124.44, 124.63, 125.05, 127.19, 127.76, 127.87, 128.46, 129.58, 131.06, 132.50, 133.10, 134.47, 144.30, 144.31, 145.35, 145.59, 164.08. Anal. Calcd for $C_{24}H_{22}N_4O_3$: C, 69.55; H, 5.35; N, 13.52. Found: C, 69.47; H, 5.28; N, 13.61.

General Procedure for the Reduction of Amides. To a stirred solution of the corresponding amide (2.84 mmol) in anhydrous THF (9.87 mL), at 0 °C under argon, was added dropwise a 1.0 M solution of BH_3−THF (14.20 mmol). The mixture was refluxed for 1 h and then cooled to room temperature. HCl (6 N, 9.70 mL) was added dropwise, and the resulting mixture was stirred at room temperature for 1 h, basified with 6 N NaOH (pH = 9), poured into water (50 mL), and extracted with chloroform (3 × 30 mL). The organic extracts were dried over anhydrous $MgSO_4$, evaporated under reduced pressure, and flash chromatographed over silica gel.

***N*-(2-Amino-5-nitrobenzyl)-8-amino-2-methyl-5,11-methano-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,5]diazocine (9a).** Elution with hexane/ethyl acetate (1/9) yielded amide **8a** (25%) and pure **9a** in 73% yield: mp 150−152 °C; IR (KBr) ν 3368, 3223, 1618, 1585, 1493, 1313, 831, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.24 (s, 3H), 4.07 (d, 1H, J = 17.1), 4.10 (d, 1H, J = 17.1), 4.18 (s, 2H), 4.32 (s, 2H), 4.65 (d, 2H, J = 16.6), 5.01 (bs, 2H), 6.28 (d, 1H, J = 2.7), 6.59 (dd, 1H, J = 8.0, 2.7), 6.63 (dt, 1H, J = 9.3, 1.7), 6.99 (dd, 1H, J = 8.1, 2.0), 7.04 (d, 1H, J = 8.6), 7.05 (d, 1H, J = 8.1), 8.03 (1H, dd, J = 2.5), 8.06; ^{13}C NMR ($CDCl_3$) δ 20.83, 47.57, 58.60, 58.88, 67.16, 111.33, 114.30, 114.35, 121.48, 124.77, 125.56, 125.94, 126.28, 127.31, 127.52,

128.11, 128.78, 133.50, 138.59, 140.05, 144.07, 145.39, 152.31. Anal. Calcd for $C_{23}H_{23}N_5O_2$: C, 68.81; H, 5.77; N, 17.44. Found: C, 68.92; H, 5.61; N, 17.39.

***N*-(2-Amino-5-methylbenzyl)-8-amino-2-methyl-5,11-methano-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,5]-diazocine (9b).** Elution with hexane/ethyl acetate (3/7) yielded amide **10** (13%), amine **7** (15%), and pure **9b** in 56% yield: mp 173−175 °C; IR (KBr) ν 3402, 1618, 1541, 1491, 1261, 1205, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.25 (s, 6H), 3.74 (bs, 2H), 4.08 (d, 1H, J = 16.6), 4.11 (s, 2H), 4.12 (d, 1H J = 16.6), 4.32 (s, 2H), 4.65 (d, 1H, J = 16.6), 4.66 (d, 1H, J = 16.6), 6.25 (d, 1H, J = 2.4), 6.57 (dd, 1H, J = 8.5, 2.4), 6.62 (d, 1H, J = 8.0), 6.74 (bs, 1H), 6.94 (bs, 1H), 6.97 (d, 1H), 6.99 (bd, 1H, J = 8.1), 7.02, 7.06 (d, 1H, J = 8.1); ^{13}C NMR ($CDCl_3$) δ 20.30, 20.78, 47.36, 58.55, 58.88, 67.20, 110.50, 113.74, 115.99, 122.93, 124.72, 125.73, 127.29, 127.49, 127.50, 128.03, 128.52, 129.29, 130.56, 133.38, 138.88, 133.19, 145.03, 145.39. Anal. Calcd for $C_{24}H_{26}N_4$: C, 77.80; H, 7.07; N, 15.12. Found: C, 77.63; H, 6.99; N, 15.21.

General Procedure of Formation of Bis-Tröger's Bases. To a stirred suspension of the corresponding amine **9** (4.47 mmol) in 95% ethanol (9.4 mL), at room temperature under argon, were successively added 35−40% aqueous formaldehyde (2.4 mL) and 36% HCl (2.3 mL). The mixture was stirred at 90 °C for 24 h, cooled to room temperature, and basified with concentrated ammonia solution (pH = 9). The alkaline solution was extracted with methylene chloride (3 × 50 mL) and the combined organic extracts were successively washed with saturated aqueous solutions of $NaHCO_3$ (100 mL) and NaCl (100 mL). The organic layer was dried over anhydrous $MgSO_4$, evaporated under reduced pressure, and flash chromatographed over silica gel.

2-Methyl-11-nitro-5α,8α,14α,17α-5,17:8,14-dimethano-5,8,14,17-tetraaza-5,6,7,8,13,14,17,18-octahydrodibenzo-[*e*,*e*′]benzo[1,2-*a*:3,4-*a*′]dicyclooctene (4a). Elution with ethyl acetate/dichloromethane (7/3) yielded the isomer **5a** in 12% yield and then pure **4a** in 50% yield.

4a: mp >230 °C dec; IR (KBr) ν 1610, 1582, 1512, 1495, 1475, 1340, 1215, 941, 744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.17 (s, 3H), 3.87 (d, 1H, J = 17.0), 3.94 (d, 1H, J = 16.8), 4.09 (d, 1H, J = 16.7), 4.18 (d, 1H, J = 16.9), 4.19 (dd, 1H, J = 12.5, 1.5,), 4.21 (dd, 1H, J = 12.7, 1.1), 4.24 (dd, 1H, J = 12.5, 1.2), 4.26 (dd, 1H, J = 12.7, 1.6), 4.40 (d, 1H, J = 17.0), 4.48 (d, 1H, J = 16.8), 4.64 (d, 1H. J = 16.7), 4.69 (d, 1H, J = 16.9), 6.69 (d, 1H, J = 1.8), 6.94 (dd, 1H, J = 8.1, 1.8), 7.00 (d, 1H, J = 8.1), 7.01 (d, 1H, J = 8.7), 7.04 (d, 1H, J = 8.7), 7.20 (d, 1H, J = 8.9), 7.80 (d, 1H, J = 2.6), 7.99 (dd, 1H, J = 8.9, 2.6). ^{13}C NMR ($CDCl_3$) δ 20.78, 55.79, 56.17, 57.75, 57.84, 66.34, 66.06, 122.85, 122.90, 124.17, 124.19, 124.72, 124.90, 125.11, 125.72, 127.04, 127.62, 128.14, 128.97, 133.61, 142.85, 143.72, 144.29, 145.59, 155.08; HRMS (EI) calcd for $C_{25}H_{23}N_5O_2$ 425.18516, found 425.18521.

5a: mp 185−187 °C; IR (KBr) ν 1610, 1580, 1514, 1474, 1333, 1221, 939, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.25 (s, 3H), 3.87 (d, 1H, J = 16.7), 3.95 (d, 1H, J = 16.7), 4.12 (d, 1H, J = 16.8), 4.15 (dd, 1H, J = 12.5, 1.7), 4.20 (s, 2H), 4.23 (d, 1H, J = 16.8), 4.25 (dd, 1H, J = 12.5, 1.5), 4.34 (d, 1H, J = 16.7), 4.42 (d, 1H, J = 16.7), 4.63 (d, 1H, J = 16.8), 4.69 (d, 1H, J = 16.8), 6.75 (bs, 1H), 7.01 (dd, 1H, J = 8.3, 1.7), 6.99 (d, 1H, J = 8.7), 7.02 (d, 1H, J = 8.7), 7.05 (d, 1H, J = 8.3), 7.25 (d, 1H, J =8.9), 7.87 (d, 1H, J = 2.6), 8.06 (dd, 1H, J = 8.9, 2.6), ^{13}C NMR ($CDCl_3$) δ 20.88, 55.79, 56.20, 58.08, 58.17, 66.02, 66.28, 122.82, 123.05, 128.87, 124.40, 124.82, 124.64, 124.88, 125.58, 127.36, 128.30, 134.13, 143.01, 143.72, 143.86, 144.93, 154.94; HRMS (EI) calcd for $C_{25}H_{23}N_5O_2$ 425.18516, found 425.18514.

2,11-Dimethyl-5α,8*β*,14*β*,17α-5,17:8,14-dimethano-5,8,-14,17-tetraaza-5,6,7,8,13,14,17,18-octahydrodibenzo[*e*,*e*′]-benzo[1,2-*a*:3,4-*a*′]dicyclooctene (5b). Elution with hexane/ethyl acetate (1/9) yielded impure **5b** that was again flash chromatographed; elution with dichloromethane/ethyl acetate (6/4) yielded pure **5b** in **6**% yield: mp 278−80 °C; IR (KBr) ν 1497, 1474, 1261, 1094, 827, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.25 (s, 3H), 3.86 (d, 1H, J = 16.6), 4.11 (d, 1H, J = 16.8), 4.14 (dd, 1H, J = 13.2, 1,5), 4.26 (d, 1H, J = 13.2), 4.33 (d, 1H), 4.63 (d, 1H, J = 16.8), 6.74 (bs, 1H), 6.99 (s, 1H), 7.00 (dd, 1H, J = 8.3, 1.7), 7.06 (d, 1H, J = 8.3). ^{13}C NMR ($CDCl_3$) δ 20.88, 55.83, 58.15, 66.27, 124.31, 124.86, 127.32, 127.40, 128.24, 133.96, 143.51, 145.14; HRMS (EI) calcd for $C_{26}H_{26}N_4$ 394.21573, found 394.21451.

Crystal Structures of Compounds 4a and 5b. Crystal of both compounds **4a** and **5b** were obtained from saturated solutions in chloroform/96% ethanol. Those crystals showing well-defined faced were mounted on a Bruker-Siemens Smart diffractometer equipped with normal focus, 2.4 kW sealed tube X-ray source (Molybdenum radiation, λ = 0.710 67 Å) operating at 50 kV and 20 mA. Compound **5b** crystallized with a disordered molecule of ethanol whose electron density has been included in the crystal structure resolution. Data for each crystal were collected over a quadrant, by combination of two exposure sets, respectively. Each exposure of 10 s covers 0.3° in ω. The unit cell dimensions were determined by least-squares refinement using reflections with $I > 20\sigma$ and $3° < \theta < 27°$ and $3° < \theta < 32°$ for compounds **4a** and **5b**, respectively. The crystal-to-detector distance was 4.5 cm. The first 50 frames were recollected at the end of the data collection to monitor crystal decay. The intensities were corrected for Lorentz and polarization effects. Scattering factors for neutral atoms were taken from the *International Tables for X-ray Crystallography*.[16] The structure was solved by Multan and Fourier methods. Full-matrix least-squares refinement was carried out minimizing $w(F_o^2 - F_c^2)$.[17] The hydrogen atoms were in both cases located in Fourier synthesis and refined isotropically. Refinement on F^2 for all reflections. Weighted factors (R_w) and all goodness of fit S are based on F^2; conventional R factors (R) are based on F.

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Supporting Information Available: ^1H NMR spectra of compounds **4a**, **5a**, and **5b**. ORTEP structure of compound **5b**. Molecular packing in the crystal structure for compounds **4a** and **5b**. Crystal data and structure refinement for compounds **4a** and **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, 1974; Vol. IV, pp 78−98.

(17) SHELTXTL, Siemens Energy & Automation, Inc., Analytical Instrumentation, 1996.