# REGIO- AND STEREOSELECTIVITY IN PREPARATION OF BENZENE BRIDGED BIS- AND TRIS-TRÖGER'S BASES

Martin VALÍK[a1], Bohumil DOLENSKY[a2], Hana PETŘÍČKOVÁ[b] and Vladimír KRÁL[a3,*]

[a] *Department of Analytical Chemistry, Institute of Chemical Technology, Prague, Technická 5, 166 28 Prague 6, Czech Republic; e-mail:* [1] *martin.valik@vscht.cz,* [2] *blbek@seznam.cz,* [3] *kralv@vscht.cz*

[b] *Department of Solid State Chemistry, Institute of Chemical Technology, Prague, Technická 5, 166 28 Prague 6, Czech Republic; e-mail: hana.petrickova@vscht.cz*

Received March 27, 2002
Accepted April 29, 2002

Synthetic strategy for novel multiple Tröger's base derivatives is presented. Compounds were prepared in three steps: *o*-nitrobenzoylation of benzene-1,2- and -1,3-diamines **3** followed by reduction of nitro and amide groups to amino functions and treatment of the obtained tetraamine compounds **6** with formaldehyde lead to simultaneous formation of bis-Tröger's base (bisTB) derivatives **7a**, **7b**. Only products of 1,2,3,4-substituted regioisomers with *anti* conformation were separated from reaction mixtures. The same synthetic procedure was used for preparation of tris-Tröger's base (trisTB) derivative **12b** starting from benzene-1,3,5-triamine (**8**).

**Keywords**: Tröger's bases; Receptors; Tweezers; Amines; Supramolecular chemistry.

One of the leading themes of supramolecular chemistry has been preparation of highly selective receptors. The high selectivity can be achieved by design of suitable scaffold molecule, which support cooperation between single binding units in proper geometrical arrangement. Such synthetic protocol is common for many receptors described to date[1].

One of such scaffolds used for receptor preparation are Tröger's base (TB) derivatives[2]. The TB motif is increasingly attractive in molecular design of receptors for its chirality and rigid V-shaped concave cavity. The TB derivatives have been used for recognition based on the cavity size, *e.g.* α,ω-diamines[3,4], 9-ethyladenine[5] and carboxylic acids[6], or based on chirality, *e.g.* benzyl esters of histidine and lysine[7] or terpenes[8]. Phenantroline[9,10] and acridine[10,11] TB derivatives were reported to interact specifically with DNA (refs[9,11,12]). Very recently, compounds **1** containing two Tröger's base units have been reported[13]. For bisTB systems, *syn* config-

uration (boat-like) is more attractive than *anti* (chair-like) allowing construction of molecular tweezers. Moreover, some regioisomers of oligoTB systems can provide "dish-like" configurations (see **2a** in Fig. 1) resembling calixarenes. The aim of this work is evaluation of possible synthetic approach to oligoTB derivatives and determination of configuration of oligoTBs constructed on the benzene core.

The TBs are usually prepared from *para*-substituted anilines by the reaction with formaldehyde[14], hexamethylenetetramine[8] or dimethoxymethane[15] under acid catalysis and by the reaction with derivatives of isatoic anhydride (3,1-benzoazine-2,4(1*H*)-dione) or 2-nitrobenzoic acid followed by reduction of the product and its cyclization with formaldehyde in acid media[16] (Wilcox procedure). Unsubstituted Tröger's base from aniline was not prepared to date directly even by multistep sequence[16]. From the mechanistic point of view, the main complication of TB formation from aniline is oligomerizations in *para* positions.

The synthetic strategy for our novel bisTB compounds was based on the Wilcox synthetic protocol[16]. Treatment of benzenediamines **3** with 2-nitrobenzoyl chloride gave bisamides **4** (ref.[17] for **4b**) in good yields. Alternative

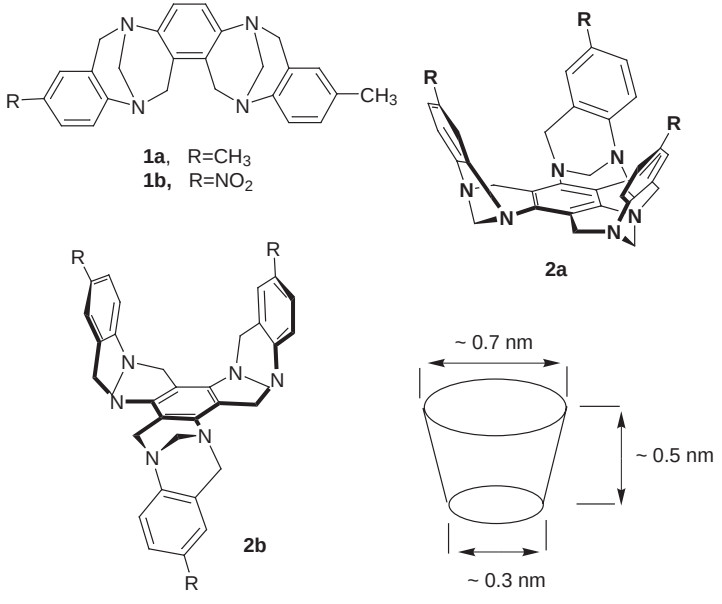
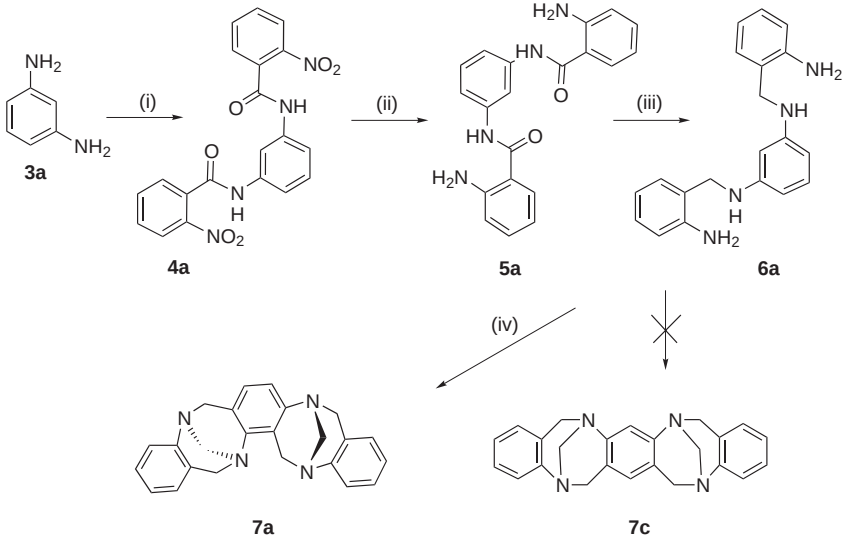



FIG. 1
Structural formulas and configurations of bis- and tris-Tröger's bases **1** and **2**

formation of the bisamides *via* active ester (using DCC) gave mostly monoamides. The reduction of bisamides **4** was performed in two ways. The one-step reduction of bisamides **4** to amines **6** with lithium aluminium hydride (LAH) gave irreproducible results. The reduction of nitro groups by catalytic hydrogenation to aminoamides **5** followed by LAH reduction of amide groups to amines **6** was a more efficient method. The aminoamides **5** can also be prepared by reaction of starting benzenediamines **3** with isatoic anhydride or anthranyloyl chloride. Depending on the reduction method, the overall reaction sequence leading to oligoTB systems involves 3 (simultaneous reduction of nitro and amide groups) or 4 steps. The final treatment of amines **6a** or **6b** with formaldehyde in methanol with hydrochloric acid as catalyst gave bisTB derivative **7a** (Scheme 1) in 4% yield and **7b** (Scheme 2) in 6% yield. Work[13] reported an eight-step synthesis of **1a** in 1% overall yield, while our approach gave in four steps 3% even without *para* substitution. It is important to note that the yields of bisTB **7a** and **7b** are relatively high in comparison with the reported results of multistep synthesis[13].

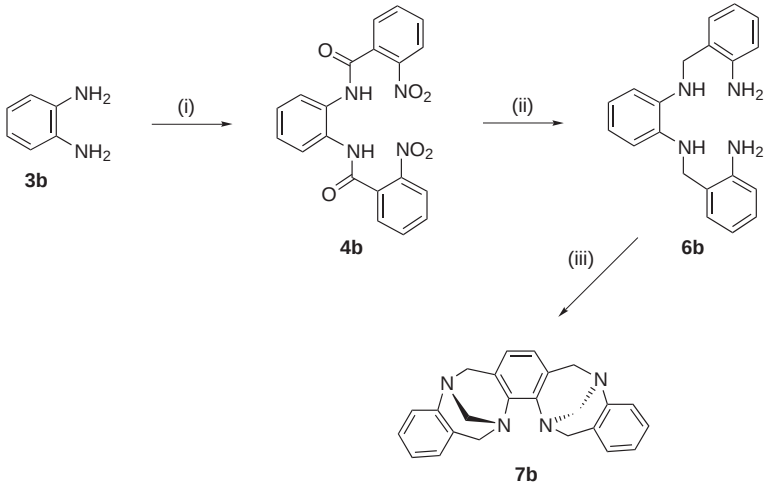



(i) 2-nitrobenzoyl chloride, DMF, pyridine, 12 h, rt; (ii) $H_2$, Pd/C, methanol, DMF, 12 h, rt; (iii) $LiAlH_4$, dioxane, 4 h, reflux; (iv) 36% aq. $CH_2O$, conc. HCl, MeOH, 20 h, rt

SCHEME 1

An interesting regio- and stereoselectivity of these reactions has been observed. In the case of diamine **6a**, two regioisomers **7a** and **7c** can be formed; however, only **7a** was obtained. This result is somewhat surprising

because the substitutions of central benzene ring in positions 1,2,4,5 (structure **7c**) would be preferred to the 1,2,3,4-substitution (structure **7a**) due to steric effects. Based on possible cyclizations (ring-forming positions) of **6a**, the calculated statistic ratio of **7a** and **7c** in the reaction mixture should be 3 : 1; while our experimental data showed the formation of **7a** only. The formation of **7a** can be explained by higher reactivity of the central benzene *meso* position of **6a** towards electrophilic substitution. Furthermore, the same regioselectivity (1,2,3,4-substitution) was observed for bisTB derivatives (**1a**, **1b**) prepared by a stepwise technique[13].




(i) 2-nitrobenzoyl chloride, DMF, pyridine, 12 h, rt; (ii) $LiAlH_4$, dioxane, 48 h, reflux; (iii) 36% aq. $CH_2O$, conc. HCl, MeOH, 20 h, rt

SCHEME 2

Assignments of bisTB regioisomer structures are based on characteristic spin patterns in $^1H$ NMR spectra. In case of compound **7b** just six doublets and one singlet are distinguishable for methylene protons and central benzene ring protons. On the other hand, nonequivalent methylene protons of asymmetric regioisomer **7a** exhibit unresolved multiplets in addition to two doublets of protons of central benzene ring.

As we mentioned before, diastereoselectivity of bisTBs is important for their potential application as building blocks; at that the *syn* configuration being more interesting. However, the X-ray structure analysis (Table I) revealed *anti* configurations for both bisTB derivatives **7a** (Fig. 2) and **7b** (Fig. 3). The same shape was observed for bisTB derivative **1a**. In contrast,

bisTB derivative **1b** was obtained in reverse configuration[13]. The predominant formation of *syn* diastereoisomer **1b** is interpreted by authors by stabilizing π-stacking interaction between the external aromatic rings of different polarity. Hence, it may be concluded that the *anti* configuration of the bisTB skeleton with central benzene ring is probably thermodynamically more stable. Indeed, the thermodynamical stability of *anti*/*syn* configuration of bisTB derivatives depends on the polarity of the substituents on the external aromatic rings.

Another aim of the present work was to prepare trisTB system **2**, unknown to date. We attempted to build up three TB units around the benzene ring (1,2,3,4,5,6-substitution). In the same manner as described above, the starting triamino-1,3,5-benzene[19] (**8**) was treated with 2-nitrobenzoyl chloride giving trisamide **9a**, which was reduced in two steps (through nitroamine **10a**) to amine **11a**. To our disappointment, the reaction of **11a**

TABLE I
Crystal data and structure refinement for structures **7a** and **7b**

| Parameter | **7a** | **7b** |
|---|---|---|
| Formula | $2(C_{24}N_4H_{22})\cdot(CH_3OH)$ | $C_{24}N_4H_{22}$ |
| Formula weight, g mol$^{-1}$ | 764.97 | 366.47 |
| Crystal system | monoclinic | triclinic |
| Space group | $P2_1/c$ | $P\text{-}1$ |
| $a$, Å | 24.824(7) | 8.8315(9) |
| $b$, Å | 15.139(3) | 9.770(1) |
| $c$, Å | 10.716(9) | 11.641(2) |
| α, ° | 90.00(0) | 87.91(1) |
| β, ° | 101.24(4) | 73.79(1) |
| γ, ° | 90.00(0) | 73.50(1) |
| Volume, Å$^3$ | 3 950(4) | 923.7(2) |
| $Z$ | 4 (two in asym. unit) | 2 |
| Absorption coefficient, cm$^{-1}$ | 6.203 | 6.201 |
| Total number of reflections measured | 4 920 | 6 614 |
| Independent reflections, $R_{int}$ | 2 531, 0.056 | 3 356, 0.023 |
| Values of $R$, $R_w$, $S$ | 0.109, 0.100, 1.0705 | 0.0723, 0.038, 1.0197 |

with formaldehyde led to formation of oligomeric products only. The question was if this undesirable process can be suppressed. The successful strategy which allows to eliminate oligo- and polymerization is based on the use of 5-methyl-2-nitrobenzoyl chloride[20] instead of 2-nitrobenzoyl chloride and this sequence gave a novel trisTB **12b** in 4% overall yield (Scheme 3). It is worth noting, that our attempts to prepare trisTB employing the

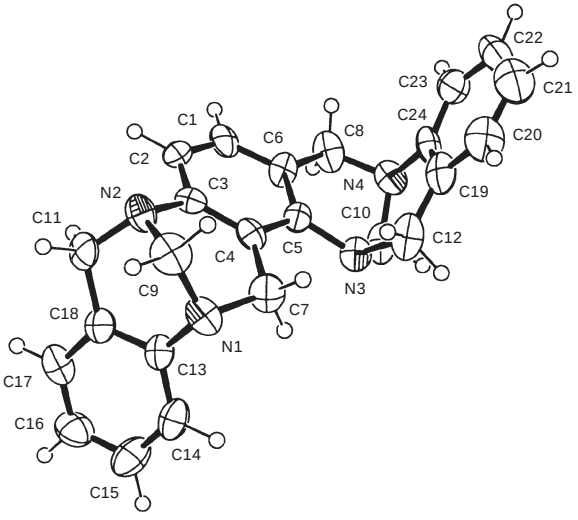



FIG. 2
ORTEP (ref.[18]) drawing of X-ray structure of **7a**

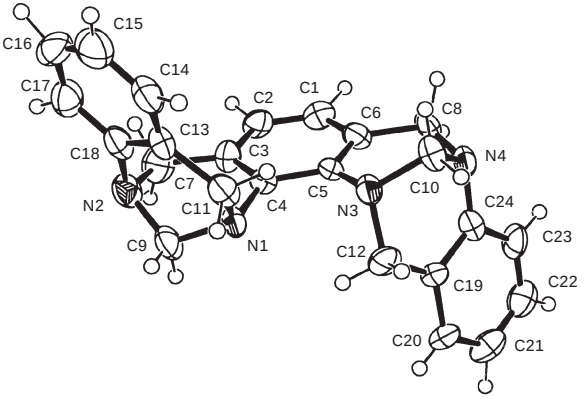
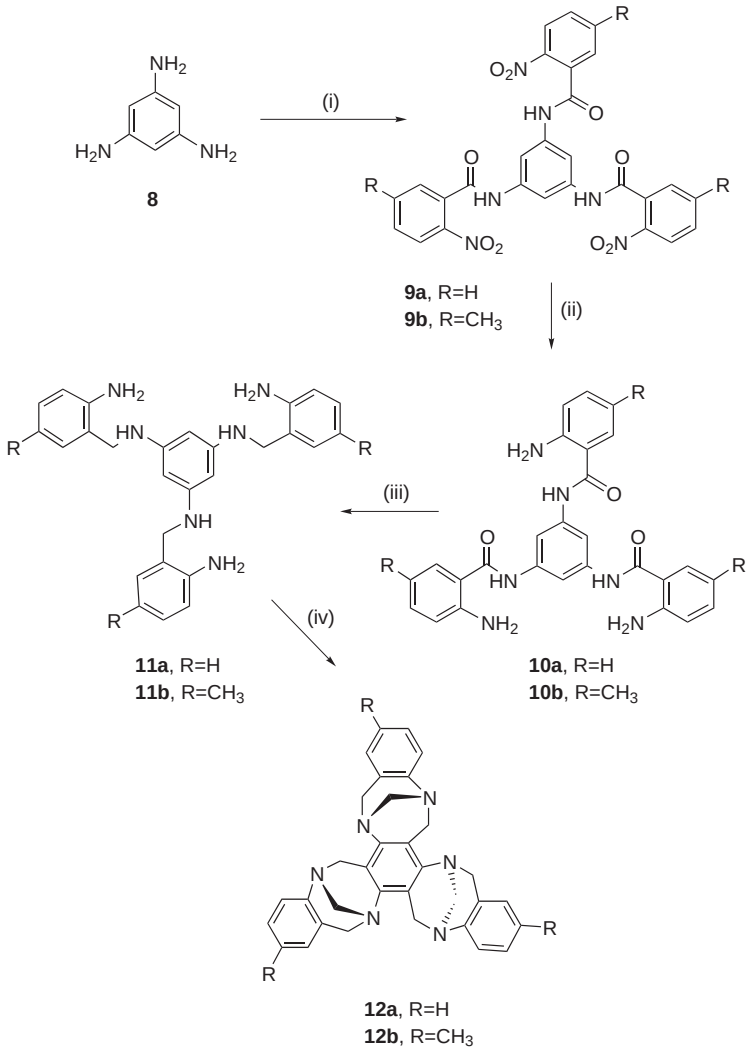



FIG. 3
ORTEP (ref.[18]) drawing of X-ray structure of **7b**

published strategy[16] with nitroisatoic anhydride were unsuccessful due to insolubility of intermediate tris(nitroaminoamides) making their separation as well as reduction impossible.




(i) 2-nitrobenzoyl chloride (for **9a**), 5-methyl-2-nitrobenzoyl chloride (for **9b**), DMF, pyridine, 12 h, rt; (ii) $H_2$, Pd/C, methanol, DMF, 10 h, rt; (iii) $LiAlH_4$, dioxane, 6 h, reflux; (iv) 36% aq. $CH_2O$, conc. HCl, MeOH, 20 h, rt

SCHEME 3

Information about configuration of trisTB **12b** came from analysis of its NMR spectra. There are two possible configurational isomers: highly symmetrical *syn-syn* and *syn-anti* with a lower symmetry. NMR spectra of **12b** are consistent with the latter possible (*cf.* **2b**, Fig. 1). There are three singlets (2.18, 2.24 and 2.26 ppm) corresponding to three nonequivalent methyl groups. Similarly, three distinguishable doublets each of integral intensity 1 H in region of methylene protons and three close aromatic singlets can be observed in $^1$H NMR spectrum as well.

In summary, we prepared novel bisTB and trisTB derivatives with benzene as a central unit. The significant regio- and diastereoselectivity of these novel compounds using a common protocol was observed. For both bisTB derivatives only 1,2,3,4-substituted regioisomers with *anti* conformation were separated from reaction mixtures, which is consistent with Pardo's results[13]. Moreover, our synthetic protocol allowed for the first time to generate systems with three spatially oriented TB units on the benzene core. Other oligoTB systems with a different central aromatic core and their binding properties are currently being investigated.

## EXPERIMENTAL

Commercial solvents for chromatography were purified by distillation. Melting points were determined on a Kofler apparatus and are uncorrected. NMR spectra were obtained with Varian Gemini 300 HC (300.077 MHz for $^1$H NMR and 75.460 MHz for $^{13}$C NMR spectra) at 23 °C in deuteriochloroform $CDCl_3$, deuterated dimethyl sulfoxide DMSO-$d_6$ or deuterioacetonitrile $CD_3CN$. Chemical shifts (δ) are presented in ppm and coupling constants (*J*) in Hz. Infrared spectra (ν in $cm^{-1}$) were recorded on a Nicolet 210 FTIR spectrometer in KBr tablets. Mass spectra were obtained by fast atom bombardment (FAB) with a VG Analytical ZAB-EQ spectrometer. X-Ray data of **7** were measured at 293 K with an Enraf–Nonius CAD4 diffractometer with graphite monochromatized CuKα radiation. CCDC 163116 (**7a**) and CCDC 163115 (**7b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk). Thin-layer chromatography was performed on TLC-sheet (Merck) with UV detection at 254 nm.

*N*,*N*′-(1,3-Phenylene)bis(2-nitrobenzamide) (**4a**)

2-Nitrobenzoyl chloride (4.003 g, 21.33 mmol) in DMF (10 ml) was added to **3a** (0.498 g, 4.62 mmol) in pyridine (20 ml). The reaction mixture was stirred at room temperature for 12 h and than diluted with water (250 ml) and methanol (50 ml). The precipitated product was filtered off and washed with methanol (50 ml) and dichloromethane (50 ml). A second part of the product was obtained by crystallization (methanol–dichloromethane) of the residue after evaporation of the filtrate. Yield of **4a** 1.750 g (93%), m.p. 253–257 °C. $^1$H NMR (300 MHz, DMSO-$d_6$): 7.34 m, 1 H (Ph); 7.78 d, 2 H, *J* = 7.1 (Ph); 7.80 m, 4 H (Ph); 7.88 t,

2 H, *J* = 7.1 (Ph); 8.14 m, 3 H (Ph); 10.74 s, 2 H (CONH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 111.07 (CH), 115.28 (CH), 124.18 (CH), 129.08 (CH), 129.29 (CH), 130.90 (CH), 132.66 (C), 134.06 (CH), 139.20 (C), 146.41 (C), 164.12 (CO). IR: 3 220, 3 142, 3 061, 2 928, 1 648, 1 606, 1 574, 1 546, 1 529, 1 351, 1 431, 1 267, 705, 789. MS: 406 ($M^+$ $C_{20}H_{14}N_4O_6$, requires 406). For $C_{20}H_{14}N_4O_6$ calculated: 59.12% C, 3.47% H, 13.79% N; found: 59.61% C, 3.77% H, 13.89% N.

*N*,*N*′-(1,2-Phenylene)bis(2-nitrobenzamide) (**4b**)

Compound **4b** was prepared in the same way as **4a**. Charges: benzene-1,2-diamine (**3b**) 100 mg (0.93 mmol), 2-nitrobenzoyl chloride 400 mg (2.16 mmol), pyridine 10 ml and DMF 5 ml. Yield of **4b** 368 mg (98%). $^1$H NMR (300 MHz, DMSO-$d_6$): 7.33 m, 2 H (Ph); 7.68–7.90 m, 8 H (Ph); 8.14 d, 2 H, *J* = 7.8 (Ph); 10.12 s, 2 H (CONH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 124.37 (CH), 125.37 (CH), 125.93 (CH), 129.21 (CH), 130.45 (C), 131.17 (CH), 132.36 (C), 134.10 (CH), 146.67 (C), 164.51 (CO). MS: 406 ($M^+$ $C_{20}H_{14}N_4O_6$, requires 406).

*N*,*N*′-(1,3-Phenylene)bis(2-aminobenzamide) (**5a**)

Compound **4a** (1.005 g, 2.46 mmol) and catalyst (5% Pd/C, 100 mg) were added to a mixture of methanol (50 ml) and DMF (6 ml). After removing air the reaction mixture was stirred for 10 h under hydrogen. The catalyst was filtered off under argon and the solvent evaporated. Compound **5a** (810 mg, 95%) was obtained by crystallization (chloroform) of the residue, m.p. 177–180 °C. $^1$H NMR (300 MHz, $CD_3CN$): 5.20–6.20 br s, 4 H ($NH_2$); 6.65 dt, 2 H, *J* = 7.2, 1.1 (Ph); 6.74 dd, 2 H, *J* = 7.1, 1.1 (Ph); 7.22 dt, 2 H, *J* = 7.4, 8.0, 1.7 (Ph); 7.27–7.39 m, 3 H (Ph); 7.57 dd, 2 H, *J* = 8.0, 1.1, 1.6 (Ph); 8.11 t, 1 H, *J* = 1.7, 2.2 (Ph); 8.64 s, 2 H (CONH). $^{13}$C NMR (75 MHz, $CD_3CN$): 118.32 (CH), 120.97 (CH), 121.55 (CH), 121.96 (CH), 133.51 (CH), 134.01 (CH), 137.66 (CH), 144.41 (C), 154.75 (C), 173.14 (C), 176.92 (C). IR: 1 642, 1 612, 1 534, 1 490, 1 450, 1 340, 783, 751. MS: 346 ($M^+$ $C_{20}H_{18}N_4O_2$, requires 346). For $C_{20}H_{18}N_4O_2 \cdot H_2O$ calculated: 65.92% C, 5.53% H, 15.37% N; found: 66.73% C, 5.21% H, 15.53% N.

*N*,*N*′-Bis(2-aminobenzyl)benzene-1,3-diamine (**6a**)

LAH (5 g) was added to **5a** (500 mg, 1.45 mmol) in dioxane (50 ml). The reaction mixture was refluxed for 6 h, cooled and diluted with water (12 ml), 15% solution of NaOH (14 ml) and water (18 ml). The insoluble part was filtered off and washed with diethyl ether (2 × 60 ml). Light brown compound **6a** (420 mg, 91%) was obtained from the filtrate by evaporation and immediately used for preparation of **7a**. $^1$H NMR (300 MHz, $CDCl_3$): 3.70–4.20 br, 6 H (NH + $NH_2$); 4.21 s, 4 H ($CH_2$); 6.09 t, 1 H, *J* = 2.2 (Ph); 6.20 dd, 2 H, *J* = 8.0, 2.2, 1.7 (Ph); 6.75 m, 4 H (Ph); 7.08 t, 1 H, *J* = 8.3, 7.7 (Ph); 7.12–7.30 m, 4 H (Ph). $^{13}$C NMR (75 MHz, $CDCl_3$): 46.95, 98.51, 104.14, 115.85, 118.30, 122.91, 128.85, 130.02, 130.09, 145.74, 149.52. MS: 319 ($MH^+$ $C_{20}H_{23}N_4$, requires 319).

*N*,*N*′-Bis(2-aminobenzyl)benzene-1,2-diamine (**6b**)

Compound **6b** was prepared directly from **4b** in 70% yield. The reaction conditions were same as for reduction of **5a**. Charges: **4b** 500 mg (1.23 mmol), LAH 5 g, dioxane 50 ml; the reaction time was 48 h. $^1$H NMR (300 MHz, DMSO-$d_6$): 3.26 br s, 2 H (NH); 4.03 br s, 4 H

($NH_2$); 4.15 s, 4 H ($CH_2$); 6.64 dd, 2 H, *J* = 7.1, 1.2 (Ph); 6.72 td, 2 H, *J* = 7.5, 1.2 (Ph); 6.82–6.92 m, 4 H (Ph); 7.07–7.14 m, 4 H (Ph). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 46.96, 111.84, 115.73, 118.06, 119.66, 122.62, 128.75, 129.99, 136.98, 145.84.

5α,9β,15β,17α-5,6,9,10,15,16,17,18-Octahydro-5,17:9,15-dimethanodibenzo[*f*,*f*′]benzo-[1,2-*b*:3,4-*b*′]bis[1,5]diazocine (**7a**)

Concentrated HCl (1 ml) and concentrated solution of formaldehyde (0.7 ml) were added to a solution of **6a** (400 mg, 1.26 mmol) in methanol (50 ml). The reaction mixture was stirred at room temperature for 12 h, concentrated by evaporation (to *ca* 5 ml), diluted with water (20 ml), alkalinized with concentrated ammonia solution (2 ml) and extracted with dichloromethane (2 × 30 ml). The combined extracts were dried with anhydrous $MgSO_4$ and evaporated. The residue was dissolved in dichloromethane (5 ml) and filtered through silica gel (10 g, washed with 200 ml of diethyl ether). Product **7a** (20 mg, 4%) was obtained from the filtrate by preparative TLC (20 × 20 cm, dichloromethane–diethyl ether 8 : 2, eluted twice), m.p. 157–161 °C. $^1$H NMR (300 MHz, $CD_3CN$): 3.90–4.28 m, 7 H ($CH_2$); 4.38–4.64 m, 5 H ($CH_2$); 9.72 d, 1 H, *J* = 8.2 (Ph); 6.78 d, 1 H, *J* = 8.2 (Ph); 6.88–7.00 m, 4 H (Ph); 7.08 d, 1 H, *J* = 7.1 (Ph); 7.05–7.18 m, 3 H (Ph). $^{13}$C NMR (75 MHz, $CD_3CN$): 59.47 ($CH_2$), 60.37 ($CH_2$), 62.64 ($CH_2$), 63.25 ($CH_2$), 71.14 ($CH_2$), 71.32 ($CH_2$), 125.01 (CH), 127.05 (C), 127.16 (C), 128.22 (CH), 128.33 (CH), 129.55 (CH), 129.65 (CH), 130.16 (CH), 131.61 (CH), 131.66 (CH), 137.79 (CH), 131.93 (CH), 133.02 (C), 133.13 (C), 149.59 (C), 152.40 (C), 153.17 (C). MS: 367.1910 ($MH^+$ $C_{24}H_{23}N_4$, requires 367.1923).

5α,10β,16β,17α-5,6,9,10,15,16,17,18-Octahydro-5,17:10,16-dimethanodibenzo[*f*,*f*′]benzo-[1,2-*b*:4,3-*b*′]bis[1,5]diazocine (**7b**)

Compound **7b** was prepared in the same way as **7a**. Charges: **6b** 200 mg (0.63 mmol), methanol 50 ml, 36% aqueous formaldehyde 1 ml, concentrated HCl 1 ml. Yield of **7b** 14 mg (6%), m.p. > 220 °C (darkening). $^1$H NMR (300 MHz, $CDCl_3$): 4.10 d, 2 H, *J* = 16.8 ($CH_2$); 4.25 d, 2 H, *J* = 12.6 ($CH_2$); 4.35 d, 2 H, *J* = 12.6 ($CH_2$); 4.53 d, 2 H, *J* = 17.4 ($CH_2$); 4.61 d, 2 H, *J* = 15.9 ($CH_2$); 4.85 d, 2 H, *J* = 17.1 ($CH_2$); 6.53 s, 2 H (Ph); 6.95–7.02 m, 4 H (Ph); 7.10–7.16 m, 4 H (Ph). $^{13}$C NMR (75 MHz, $CDCl_3$): 53.55 ($CH_2$), 58.72 ($CH_2$), 67.10 ($CH_2$), 121.88 (CH), 123.91 (CH), 125.07 (CH), 126.11 (C), 126.94 (CH), 127.15 (CH), 129.41 (C), 141.10 (C), 147.73 (C). MS: 367.1917 ($MH^+$ $C_{24}H_{23}N_4$, requires 367.1923).

*N*,*N*′,*N*″-(Benzene-1,3,5-triyl)tris(2-nitrobenzamide) (**9a**)

Compound **9a** was prepared in the same way as **4a**. Charges: **8** 340 mg (2.76 mmol), 2-nitrobenzoyl chloride 3.192 g (17.07 mmol), pyridine 20 ml and DMF 10 ml. Yield of product **9a** 820 mg (52%), m.p. > 320 °C. $^1$H NMR (300 MHz, DMSO-$d_6$): 7.78–7.92 m, 12 H (Ph); 8.14 d, 3 H, *J* = 7.7 (Ph); 10.82 s, 3 H (CONH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 106.83 (CH), 124.14 (CH), 129.33 (CH), 130.88 (CH), 132.65 (C), 134.05 (CH), 139.35 (C), 146.40 (C), 164.21 (CO). IR: 3 305, 3 107, 3 037, 1 664, 1 617, 1 551, 1 529, 1 480, 1 451, 1 348, 1 296, 856, 789. MS: 571 ($MH^+$ $C_{27}H_{19}N_6O_9$, requires 571). For $C_{27}H_{18}N_6O_9$ calculated: 56.85% C, 3.18% H, 14.73% N; found: 56.50% C, 3.18% H, 14.66% N.

*N*,*N*′,*N*″-(Benzene-1,3,5-triyl)tris(5-methyl-2-nitrobenzamide) (**9b**)

Compound **9b** was prepared in the same way as **4a**. Charges: **8** 362 mg (2.94 mmol), 5-methyl-2-nitrobenzoyl chloride 3.526 g (17.66 mmol), pyridine 10 ml and DMF 10 ml. Yield of product **9b** 1.115 mg (62%), m.p. > 320 °C. $^1$H NMR (300 MHz, DMSO-$d_6$): 2.48 s, 9 H ($CH_3$); 7.53 m, 6 H (Ph); 7.86 s, 3 H (Ph); 8.03 d, 3 H, $J$ = 8.5 (Ph); 10.71 s, 3 H (CONH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 20.85, 106.64, 124.07, 129.43, 130.78, 132.71, 139.18, 143.76, 145.09, 164.16. MS: 613 ($MH^+$ $C_{30}H_{25}N_6O_9$, requires 613). For $C_{30}H_{24}N_6O_9 \cdot H_2O$ calculated: 57.14% C, 4.16% H, 13.33% N; found: 57.28% C, 3.83% H, 13.13% N.

*N*,*N*′,*N*″-(Benzene-1,3,5-triyl)tris(2-aminobenzamide) (**10a**)

Compound **10a** was prepared in the same way as **5a**. Charges: **9a** 400 mg (0.70 mmol), catalyst (5% Pd/C) 50 mg, methanol 30 ml and DMF 5 ml. Yield of product **10a** 330 mg (98%). Analytical sample was obtained by precipitation (chloroform–petroleum ether). $^1$H NMR (300 MHz, DMSO-$d_6$): 6.13 s, 4 H ($NH_2$); 6.65 t, 3 H, $J$ = 7.2, 7.7 (Ph); 6.79 d, 3 H, $J$ = 7.7 (Ph); 7.24 t, 3 H, $J$ = 7.1 (Ph); 7.70 d, 3 H, $J$ = 7.7 (Ph); 7.91 s, 3 H (Ph); 9.87 s, 3 H (CONH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 109.51 (CH), 114.62 (CH), 115.17 (C), 116.29 (CH), 128.79 (CH), 132.02 (CH), 139.01 (C), 149.76 (C), 167.79 (C). MS: 481 ($MH^+$ $C_{27}H_{25}N_6O_3$, requires 481).

*N*,*N*′,*N*″-(Benzene-1,3,5-triyl)tris(2-amino-5-methylbenzamide) (**10b**)

Compound **10b** was prepared in the same way as **5a**. Charges: **9b** 1.050 g (1.71 mmol), catalyst (5% Pd/C) 120 mg, methanol 90 ml and DMF 10 ml. Yield of product **10b** 860 mg (96%). $^1$H NMR (300 MHz, $CDCl_3$): 2.19 s, 9 H ($CH_3$); 4.40–5.80 br s, 6 H ($NH_2$); 6.56 d, 3 H, $J$ = 6.6 (Ph); 7.00 d, 3 H, $J$ = 7.7 (Ph); 7.21 s, 3 H (Ph); 7.67 s, 3 H (Ph); 8.25 s, 3 H (CONH). $^{13}$C NMR (75 MHz, $CDCl_3$): 20.33 ($CH_3$), 108.35 (CH), 116.26 (C), 117.64 (CH), 126.15 (C), 127.47 (CH), 133.50 (CH), 138.71 (C), 146.23 (C), 167.69 (C). MS: 523 ($MH^+$ $C_{30}H_{31}N_6O_3$, requires 523). For $C_{30}H_{30}N_6O_3$ calculated: 68.95% C, 5.79% H, 16.08% N; found: 68.03% C, 5.35% H, 15.25% N.

*N*,*N*′,*N*″-Tris(2-aminobenzyl)benzene-1,3,5-triamine (**11a**)

Compound **11a** was prepared in the same way as **6a**. Charges: **10a** 310 mg (0.65 mmol), LAH 2.5 g and dioxane 50 ml. Yield of product **11a** 260 mg (92%). $^1$H NMR (300 MHz, $CDCl_3$): 3.71 br s, 3 H (NH); 4.16 s, 6 H ($CH_2$); 5.57 s, 3 H (Ph); 6.78 m, 6 H (Ph); 7.13 m, 6 H (Ph). $^{13}$C NMR (75 MHz, $CDCl_3$): 46.94, 89.97, 115.83, 118.27, 123.00, 128.79, 130.01, 145.73, 150.45. MS: 439 ($MH^+$ $C_{27}H_{31}N_6$, requires 439).

*N*,*N*′,*N*″-Tris(2-amino-5-methylbenzyl)benzene-1,3,5-triamine (**11b**)

Compound **11b** was prepared in the same way as **6a**. Charges: **10b** 820 mg (1.57 mmol), LAH 4.2 g and dioxane 120 ml. Yield of product **11b** 700 mg (93%). $^1$H NMR (300 MHz, $CDCl_3$): 2.26 s, 9 H ($CH_3$); 3.20–4.40 br, 6 H (NH + $NH_2$); 4.14 s, 6 H ($CH_2$); 5.59 s, 2 H (Ph); 6.61 d, 3 H, $J$ = 8.3 (Ph); 6.93 m, 6 H (Ph). $^{13}$C NMR (75 MHz, $CDCl_3$): 20.40 ($CH_3$), 46.86 ($CH_2$), 87.72 (CH), 115.87 (CH), 123.04 (C), 127.32 (C), 129.07 (CH), 130.47 (CH), 142.97 (C), 150.30 (C). MS: 481 ($MH^+$ $C_{30}H_{37}N_6$, requires 481).

5α,7α,13α,15β,21β,22α-2,10,18-Trimethyl-5,6,7,8,13,14,15,16,21,22,23,24-dodecahydro-5,23:7,13:15,21-trimethanotribenzo[*f*,*f*′,*f*″]benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]tris[1,5]diazocine (**12b**)

Compound **12b** was prepared in the same way as **7a**. Charges: **11b** 720 mg (1.50 mmol), methanol 500 ml, 36% aqueous formaldehyde 10 ml, concentrated HCl 10 ml. Compound **12b** (67 mg, 8%) was obtained by column chromatography (dichloromethane–diethyl ether 7 : 3) and repurified by preparative TLC (20 × 20 cm, dichloromethane–diethyl ether 7 : 3). $^1$H NMR (300 MHz, $CDCl_3$): 2.18 s, 3 H ($CH_3$); 2.24 m, 3 H ($CH_3$); 2.26 m, 3 H ($CH_3$); 3.60 d, 1 H, *J* = 16.5 ($CH_2$); 3.73 d, 1 H, *J* = 16.8 ($CH_2$); 3.86 d, 1 H, *J* = 16.5 ($CH_2$); 4.00–4.65 m, 15 H ($CH_2$); 6.54 s, 1 H (Ph); 6.70 s, 1 H (Ph); 6.74 s, 1 H (Ph); 6.86–7.14 m, 6 H (Ph). $^{13}$C NMR (75 MHz, $CDCl_3$): 20.88 ($CH_3$), 21.90 ($CH_3$), 20.96 ($CH_3$), 54.39 ($CH_2$), 54.42 ($CH_2$), 55.11 ($CH_2$), 55.17 ($CH_2$), 55.24 ($CH_2$), 56.25 ($CH_2$), 66.59 (2 $CH_2$), 66.85 ($CH_2$), 117.70 (C), 118.13 (C), 118.82 (C), 124.42 (CH), 124.99 (CH), 125.07 (CH), 126.87 (CH), 126.92 (CH), 127.19 (C), 127.35 (2 C), 127.38 (CH), 127.90 (CH), 127.98 (CH), 128.04 (CH), 133.36 (C), 133.38 (C), 133.48 (C), 143.74 (C), 144.03 (C), 144.07 (C), 144.99 (C), 145.09 (C), 145.34 (C). MS: 553.3086 ($MH^+$ $C_{36}H_{37}N_6$, requires 553.3072).

*Financial support from the Howard Hughes Medical Institute (grant No. 75195-541101) and the Grant Agency of the Czech Republic (grant No. 202/02/0933) is gratefully acknowledged. We also thank J. Kroulík, MS for the help in preparation of the manuscript.*

## REFERENCES

1. Atwood J. L., Davies J. E. D., MacNicol D. D., Vögtle F., Lehn J. M.: *Comprehensive Supramolecular Chemistry*, Vol. 2. Pergamon, Oxford 1996.
2. Tröger J.: *J. Prakt. Chem.* **1887**, *36*, 225.
3. a) Crossley M. J., Hambley T. W., Mackay L. G., Try A. C., Walton R.: *J. Chem. Soc., Chem. Commun.* **1995**, 1077; b) Reek J. N. H., Schenning A. P. H. J., Bosman A. W., Meijer E. W., Crossley M. J.: *Chem. Commun.* **1998**, *1*, 11.
4. Hansson A. P., Norrby P. O., Waernmark K.: *Tetrahedron Lett.* **1998**, *39*, 4565.
5. Wilcox C. S., Adrian J. C., Webb T. H., Zawacki F. J.: *J. Am. Chem. Soc.* **1992**, *114*, 10189.
6. Goswami S., Ghosh K., Dasgupta S.: *J. Org. Chem.* **2000**, *65*, 1907.
7. a) Crossley M. J., Mackay L. G., Try A. C.: *J. Chem. Soc., Chem. Commun.* **1995**, 1925; b) Allen P. R., Reek J. N. H., Try A. C., Crossley M. J.: *Tetrahedron: Asymmetry* **1997**, *8*, 1161.
8. Webb T. H., Suh H., Wilcox C. S.: *J. Am. Chem. Soc.* **1991**, *113*, 8554.
9. Yashima E., Akashi M., Miyauchi N.: *Chem. Lett.* **1991**, 1017.
10. Salez H., Wardani A., Demeunynck M., Tatibouet A., Lhomme J.: *Tetrahedron Lett.* **1995**, *36*, 1271.
11. Tatibouet A., Demeunynck M., Andraud Ch., Collet A., Lhomme J.: *Chem. Commun.* **1999**, *2*, 161.
12. Bailly Ch., Laine W., Demeunynck M., Lhomme J.: *Biochem. Biophys. Res. Commun.* **2000**, *273*, 681.
13. Pardo C., Sesmilo E., Gutierrez-Puebla E., Monge A., Elguero J., Fruchier A.: *J. Org. Chem.* **2001**, *66*, 1607.
14. Sucholeiki I., Lynch V., Phan L., Wilcox C. S.: *J. Org. Chem.* **1988**, *53*, 98.

15. Bag B. G., Maitra U.: *Synth. Commun.* **1195**, *25*, 1849.
16. Webb T. H., Wilcox C. S.: *J. Org. Chem.* **1990**, *55*, 363.
17. Black D. S., Rothnie N. E.: *Aust. J. Chem.* **1983**, *36*, 1141.
18. Brueggemann R., Schmidt G.: *ORTEP 3.21*, PC adaptation, Ulm 1991.
19. Lukas A. S., Miller S. E., Wasielewski M. R.: *J. Phys. Chem. B* **2000**, *104*, 931.
20. McNab H., Smith G. S.: *J. Chem. Soc., Perkin Trans. 1* **1984**, 381.