

# The synthesis of 1,5:3,7-dimethano-1,3,5,7-benzotetrazonine

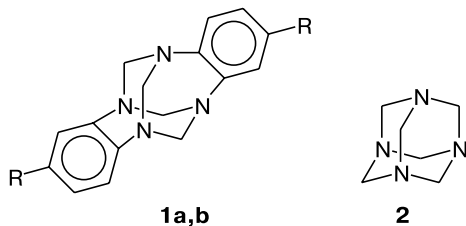
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A three-component condensation of formaldehyde, *o*-phenylenediamine, and ammonia gave a novel 1,5:3,7-dimethano-1,3,5,7-benzotetrazonine. Its structure was determined by X-ray diffraction analysis. An analogous condensation of formaldehyde, ammonia, and 1,2-diamino-4-methylbenzene yielded 9-methyl-1,5:3,7-dimethano-1,3,5,7-benzotetrazonine.

**Key words:** *o*-phenylenediamine, 1,2-diamino-4-methylbenzene, ammonia, formaldehyde, X-ray diffraction analysis.

It is known<sup>1–3</sup> that a condensation of formaldehyde with *o*-phenylenediamine and 1,2-diamino-4-methylbenzene gives 5,12:7,14-dimethanodibenzo[*d,i*][1,3,6,8]-tetrazecine (**1a**) and its dimethyl homolog, 2,9-dimethyl-5,12:7,14-dimethanodibenzo[*d,i*][1,3,6,8]tetrazecine (**1b**). A condensation of formaldehyde with ammonia produces 1,3,5,7-tetraazatricyclo[3.3.1.1<sup>3,7</sup>]decane (hexamethylenetetramine, or urotropin) (**2**).

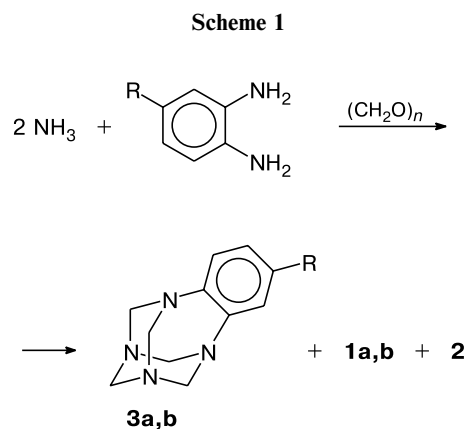


R = H (**a**), Me (**b**)

Our study showed that a reaction of formaldehyde with a mixture of ammonia and *o*-phenylenediamine yields, along with the known products **1a** and **2** of two-component condensations, an earlier unknown product of a three-component condensation, namely, 1,5:3,7-dimethano-1,3,5,7-benzotetrazonine (**3a**) (Scheme 1).

An analogous three-component condensation of formaldehyde with a mixture of ammonia and 1,2-diamino-4-methylbenzene gave 9-methyl-1,5:3,7-dimethano-1,3,5,7-benzotetrazonine (**3b**); its structure was confirmed by elemental analysis, <sup>1</sup>H NMR spectroscopy, and mass spectrometry.

To compare the spectroscopic data for new compounds **3a,b** with the data for their analogs **1a,b**, we synthesized 5,12:7,14-dimethanodibenzo[*d,i*][1,3,6,8]tetrazecine (**1a**) and 2,9-dimethyl-5,12:7,14-dimethanodibenzo[*d,i*]-



R = H (**a**), Me (**b**)

[1,3,6,8]tetrazecine (**1b**) according to modified procedures.

Neutral base **3a** was converted into salts. Addition of HCl to a solution of compound **3a** in isopropyl alcohol gave stable 1,5:3,7-dimethano-1,3,5,7-benzotetrazonine hydrochloride (**3a**·HCl). The action of methyl iodide on compound **3a** in heptane afforded 3-methyl-1,5:3,7-dimethano-1,3,5,7-benzotetrazonin-3-ium iodide (**3a**·MeI).

The structure of compound **3a** was determined by X-ray diffraction analysis (Fig. 1). A comparison of its geometrical parameters with those for compounds **1a** (see Refs 4, 5) and **2** (see Refs 6, 7) showed that the C—C bond lengths in the benzene ring of compounds **3a** and **1a** are virtually equal (1.383 and 1.390 Å, respectively). The average C<sub>sp3</sub>—N bond length in structure **3a** (1.464 Å) approaches that in urotropin **2** (1.475 Å). The N—C—N angles are 111.6(6)°–116.4(7)° (the average value

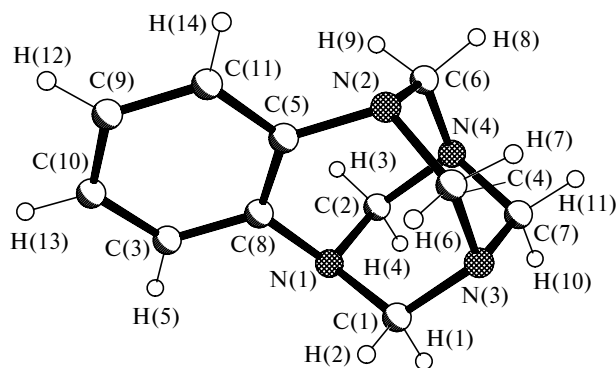


Fig. 1. Structure **3a**.

is  $115.1^\circ$ ); the C—N—C angles range from  $107.1^\circ$  to  $113.6(5)^\circ$  (the average value is  $110.8^\circ$ ) and are comparable with those in hexamethylenetetramine **2** (the average C—N distance is  $1.478 \text{ \AA}$ , the average N—C—N and C—N—C angles are  $113.3^\circ$  and  $107.5^\circ$ , respectively).

Compounds **3a,b** belong to a specific group of aromatic amines in which the lone electron pairs on the N atoms bound to the benzene ring cannot efficiently interact with the electronic system of the benzene ring because of steric hindrances. A relation to urotropin and a sufficient solubility in water make them potential biologically active compounds.

## Experimental

$^1\text{H}$  NMR spectra were recorded on a Bruker WM-250 spectrometer (250.13 MHz) for 2–3% solutions of the compounds under study in  $\text{CDCl}_3$ . Mass spectra were recorded on a Finnigan MRT-90 instrument (direct inlet probe, voltage 5.0 kV, cathode emission current 100  $\mu\text{A}$ , ionizing electron energy 70 eV, ionization chamber temperature  $200^\circ\text{C}$ ). Perfluorokerosene was used as a standard. The resolution was  $M/\Delta M = 10000$ . The injector temperature was  $20^\circ\text{C}$ .

The course of the reactions was monitored and the purity of the products was checked by TLC on Silufol UV-254 plates. Spots were visualized with iodine vapor in a moist chamber or under UV light.

**5,12:7,14-Dimethanodibenzo[*d,i*][1,3,6,8]tetrazecine (1a).** Paraformaldehyde (3.0 g, 100 mmol) was added in small portions for 15 min to a hot and stirred solution of *o*-phenylenediamine (5.4 g, 50 mmol) in isopropyl alcohol (20 mL). The reaction mixture was heated to homogenization and concentrated. The residue was recrystallized from acetone. The yield of compound **1a** was 4.48 g (68%), white crystals, m.p.  $144\text{--}146^\circ\text{C}$  (cf. Refs 1, 2: m.p.  $142\text{--}144^\circ\text{C}$ ).  $^1\text{H}$  NMR,  $\delta$ : 4.40 (s, 8 H, 4  $\text{NCH}_2\text{N}$ ); 7.70 (s, 8 H,  $(\text{C}_6\text{H}_4)_2$ ). MS,  $m/z$  ( $I_{\text{rel}}$  (%)): 264 [ $\text{M}]^+$  (35), 134 (18), 133 (75), 132 (84), 131 (100), 104 (55), 92 (21), 78 (44), 77 (52), 51 (44).

**2,9-Dimethyl-5,12:7,14-dimethanodibenzo[*d,i*][1,3,6,8]-tetrazecine (1b).** Paraformaldehyde (1.45 g, 49 mmol) was added in small portions for 15 min to a hot and stirred solution of

1,2-diamino-4-methylbenzene (3.0 g, 24 mmol) in isopropyl alcohol (15 mL). The reaction mixture was heated to homogenization and then cooled. The resulting precipitate was filtered off and recrystallized from toluene. The yield of compound **1b** was 2.8 g (78%), white crystals, m.p.  $192\text{--}193^\circ\text{C}$  (cf. Refs 1, 2: m.p.  $193\text{--}194^\circ\text{C}$ ).  $^1\text{H}$  NMR,  $\delta$ : 2.35 (s, 6 H,  $\text{Me}_2$ ); 4.40 (s, 8 H, 4  $\text{NCH}_2\text{N}$ ); 7.00 (m, 6 H,  $(\text{C}_6\text{H}_3)_2$ ). MS,  $m/z$  ( $I_{\text{rel}}$  (%)): 292 [ $\text{M}]^+$  (9), 147 (51), 146 (82), 145 (100), 131 (11), 118 (30), 91 (52), 77 (15), 65 (34).

**1,5:3,7-Dimethano-1,3,5,7-benzotetrazonine (3a).** *o*-Phenylenediamine (5.4 g, 50 mmol) was added to a 20% aqueous solution of ammonia (32 mL, 350 mmol). The mixture was heated to homogenization. Paraformaldehyde (7.5 g, 250 mmol) was added in small portions with vigorous stirring for 20 min at such a rate as to maintain the reaction temperature not above  $40^\circ\text{C}$ . After the paraformaldehyde was completely dissolved, the reaction mixture was refluxed for an additional 30 min and filtered hot. The filtrate was left at  $-20^\circ\text{C}$  for 12 h. The precipitate that formed was filtered off and recrystallized successively from water and isopropyl alcohol. The yield of compound **3a** was 4.6 g (45%), white crystals, m.p.  $150\text{--}151^\circ\text{C}$  (subl.). Found (%): C, 64.47; H, 7.03; N, 27.40.  $\text{C}_{11}\text{H}_{14}\text{N}_4$ . Calculated (%): C, 65.33; H, 6.97; N, 27.70.  $^1\text{H}$  NMR,  $\delta$ : 4.55 (dd, 8 H, 4  $\text{NCH}_2\text{N}$ ,  $^2J = 13.0 \text{ Hz}$ ); 4.70 (s, 2 H,  $\text{NCH}_2\text{N}$ ); 7.15 (s, 4 H,  $\text{C}_6\text{H}_4$ ). MS,  $m/z$  ( $I_{\text{rel}}$  (%)): 202 [ $\text{M}]^+$  (79), 174 (63), 159 (57), 133 (78), 132 (80), 131 (100), 119 (59), 78 (44), 77 (56), 71 (48), 70 (45), 51 (41).

**9-Methyl-1,5:3,7-dimethano-1,3,5,7-benzotetrazonine (3b).** 1,2-Diamino-4-methylbenzene (3.0 g, 24 mmol) was added to a 20% aqueous solution of ammonia (20 mL, 220 mmol) and the mixture was heated to homogenization. Paraformaldehyde (3.68 g, 123 mmol) was added in small portions with vigorous stirring for 10 min. The reaction mixture was heated for an additional 20 min to homogenization and filtered hot. The product was extracted with hot toluene ( $3 \times 30 \text{ mL}$ ). The extract was concentrated *in vacuo* and the residue was recrystallized successively from water and isopropyl alcohol. The yield of compound **3b** was 2.5 g (47%), white crystals, m.p.  $162\text{--}163^\circ\text{C}$  (subl.). Found (%): C, 66.25; H, 7.29; N, 26.39.  $\text{C}_{12}\text{H}_{16}\text{N}_4$ . Calculated (%): C, 66.63; H, 7.45; N, 25.90.  $^1\text{H}$  NMR,  $\delta$ : 2.30 (s, 3 H, Me); 4.30 (s, 2 H,  $\text{NCH}_2\text{N}$ ); 4.55 (dd, 8 H, 4  $\text{NCH}_2\text{N}$ ,  $^2J = 13.0 \text{ Hz}$ ); 7.00 (m, 3 H,  $\text{C}_6\text{H}_3$ ). MS,  $m/z$  ( $I_{\text{rel}}$  (%)): 216 [ $\text{M}]^+$  (24), 188 (21), 173 (26), 147 (55), 146 (89), 145 (100), 133 (32), 118 (33), 91 (35), 43 (44).

**1,5:3,7-Dimethano-1,3,5,7-benzotetrazonine hydrochloride (3a·HCl).** Hydrochloric acid (0.02 g, 0.5 mmol) was added to a stirred solution of 1,5:3,7-dimethano-1,3,5,7-benzotetrazonine (**3a**) (0.1 g, 0.5 mmol) in isopropyl alcohol (10 mL). The precipitate that formed was filtered off, washed with hot isopropyl alcohol (10 mL), and dried on filter paper. The yield of compound **3a·HCl** was 0.09 g (82%), white crystals, m.p.  $136\text{--}137^\circ\text{C}$ . Found (%): C, 55.35; H, 6.42; Cl, 14.90; N, 23.53.  $\text{C}_{11}\text{H}_{15}\text{ClN}_4$ . Calculated (%): C, 55.31; H, 6.32; Cl, 14.90; N, 23.45.

**3-Methyl-1,5:3,7-dimethano-1,3,5,7-benzotetrazonin-3-ium iodide (3a·MeI).** A solution of methyl iodide (0.35 g, 2.5 mmol) in dry heptane (5 mL) was added to a stirred solution of 1,5:3,7-dimethano-1,3,5,7-benzotetrazonine (**3a**) (0.5 g, 2.5 mmol) in dry heptane (10 mL). The precipitate that formed was filtered off, washed with heptane (10 mL), and dried in a vacuum desiccator. The yield of compound **3a·MeI** was 0.6 g

**Table 1.** Crystallographic parameters of structure **3a** and a summary of data collection

Parameter	Value
Molecular formula	C <sub>11</sub> H <sub>14</sub> N <sub>4</sub>
M	202.26
Crystal size/mm	0.23×0.17×0.07
Crystal system	Orthorhombic
Space group	<i>Pbca</i>
Unit cell parameters	
<i>a</i> /Å	7.3520(10)
<i>b</i> /Å	16.017(3)
<i>c</i> /Å	17.371(3)
$\alpha$ /deg	90
$\beta$ /deg	90
$\gamma$ /deg	90
<i>V</i> /Å <sup>3</sup>	2045.6(6)
<i>Z</i>	8
$\rho_{\text{calc}}$ /g cm <sup>-3</sup>	1.314
$\mu_{\text{Mo}}$ /mm <sup>-1</sup>	0.084
<i>F</i> (000)	864
Diffractometer	Enraf—Nonius CAD-4
Temperature/K	293
Radiation ( $\lambda$ /Å)	Mo-K $\alpha$ (0.71073)
	graphite monochromator
Scan mode	$\omega$
$\theta$ range/deg	2.54–24.75
Ranges of <i>hkl</i> indices	0 < <i>h</i> < 8, 0 < <i>k</i> < 18, –20 < <i>l</i> < 20
Total number of reflections	652
Number of independent reflections	430 ( <i>R</i> <sub>int</sub> = 0.0194)
Number of reflections with <i>I</i> ≥ 2 $\sigma$ ( <i>I</i> )	137
GOOF on <i>F</i> <sup>2</sup>	0.870
<i>R</i> ( <i>I</i> ≥ 2 $\sigma$ ( <i>I</i> ))	<i>R</i> <sub>1</sub> = 0.0402, <i>wR</i> <sub>2</sub> = 0.0978
Extinction coefficient	0.0039(14)
Residual electron density (max/min)/e Å <sup>-3</sup>	0.129/–0.109

(70.5%), white crystals, m.p. 130–131 °C. Found (%): C, 42.06; H, 5.09; I, 36.90; N, 16.85. C<sub>12</sub>H<sub>17</sub>IN<sub>4</sub>. Calculated (%): C, 41.87; H, 4.97; I, 36.86; N, 16.27.

**X-ray diffraction analysis.** Crystallographic parameters and a summary of data collection for structure **3a** are given in Table 1. The structure was solved by the direct method and refined by the least-squares method in the full-matrix anisotropic approximation for all non-hydrogen atoms. The H atoms were located geometrically and refined in the rider model with fixed isotropic thermal parameters (*U*<sub>iso</sub> = 0.08 Å<sup>2</sup>). The calculations were performed with the SHELXS86 (see Ref. 8) and SHELXS93 programs.<sup>9</sup> Atomic coordinates have been deposited with the Cambridge Crystallographic Data Center.

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