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Dedicated to the memory of
Professor Ioan Silaghi-Dumitrescu (1950 – 2009)

NEW *N*-SUBSTITUTED POLYAMINES. SYNTHESIS, CHARACTERIZATION AND CRYSTAL AND MOLECULAR STRUCTURE OF 2-[{$C_6H_4(CO)_2NCH_2CH_2$}$_2$$NCH_2$]$C_6H_4Br$

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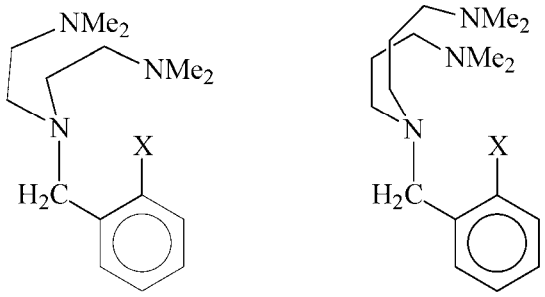
New branched polyamines starting from diethylenetriamine, *i.e.* ($Me_2NCH_2CH_2)_2NCH_2C_6H_5$ (**9**) and 2-[$(Me_2NCH_2CH_2)_2NCH_2$]C_6H_4X [X = Cl (**10**), Br (**11**)], were prepared by a multi-step procedure. Both the branched polyamines and the corresponding intermediates were characterized by multinuclear NMR spectroscopy in solution. The crystal and molecular structure of the intermediate 2-[{$C_6H_4(CO)_2NCH_2CH_2$}$_2$$NCH_2$]$C_6H_4Br$ (**5**) was established by single-crystal X-ray diffraction.

INTRODUCTION

Recent developments in main group organometallic chemistry provided evidences that aryl ligands with pendant arms containing nitrogen atoms, *e.g.* 2-$(Me_2NCH_2)C_6H_4$,[1-7] 2-$(Et_2NCH_2)C_6H_4$,[8,9] 2-[$E(CH_2CH_2)_2NCH_2$]C_6H_4 (E = O, NMe),[10,11] 2,6-$(Me_2NCH_2)_2C_6H_3$,[3,12-17] 2,6-[$MeN(CH_2CH_2)_2NCH_2]_2C_6H_3$,[18] are efficient in protecting the metal centre not only sterically, but also through intramolecular N→M coordination, thus bringing increased stabilisation of unusual species.

In an attempt to design new compounds which can provide useful organic ligands with several nitrogen atoms available for coordination to metal centres in organometallic compounds we have decided to prepare aromatic derivatives with branched pendant arms (Scheme 1).



X = H, Cl, Br

Scheme 1

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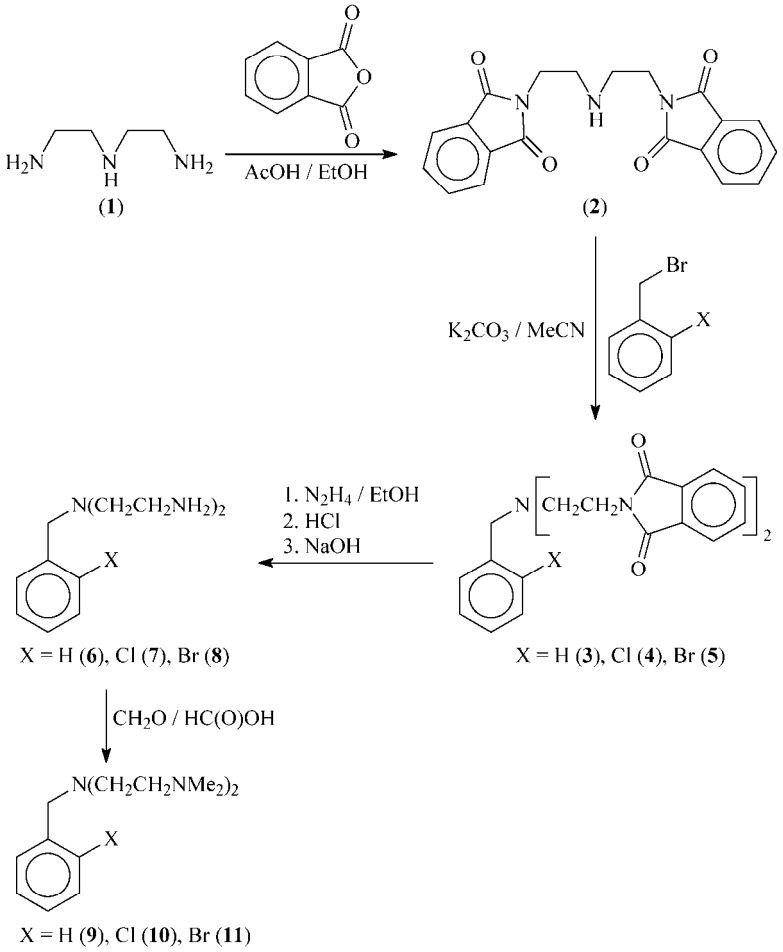
We report here on the synthesis and the solution NMR characterization of the new branched polyamines starting from diethylenetriamine, *i.e.* $(Me_2NCH_2CH_2)_2NCH_2C_6H_5$ (**9**) and 2-$[(Me_2NCH_2CH_2)_2NCH_2]C_6H_4X$ [X = Cl (**10**), Br (**11**)], as well as of some of the corresponding intermediates. The crystal and molecular structure of the intermediate 2-$[\{C_6H_4(CO)_2NCH_2CH_2\}_2NCH_2]C_6H_4Br$ (**5**) is also reported.

RESULTS

Three new branched polyamines derived from diethylene triamine, *i.e.* $(Me_2NCH_2CH_2)_2NCH_2C_6H_5$ (**9**) and 2-$[(Me_2NCH_2CH_2)_2NCH_2]C_6H_4X$ [X = Cl (**10**), Br (**11**)], were obtained using a multi-step procedure as shown in Scheme 2.



Scheme 2

The starting material used was commercial available diethylenetriamine. In a first step the terminal primary amine functions were protected by phthaloyl groups (compound **2**), using the method reported by R. Guilard and co-workers for dipropylenetriamine,[19] which is more simple by comparison to the procedure given by D. G. Rowe and co-workers for diethylenetriamine.[20] The internal amine was then benzylated (compounds **3**–**5**)[21] and the phthalimide groups removed by hydrazinolysis to give intermediates **6**–**8**.[22] Finally, the N-benzylated diethyletriamines **6**–**8** were permethylated by reductive methylation using a mixture of paraformic aldehyde and formic acid to give the desired compounds **9**–**11**.

The compounds **2**–**5** were isolated as white solids, while compounds **6**–**11** were obtained as yellow oils. Details of the preparations are given in the Experimental section.

All compounds were characterized using multinuclear (^1H, ^{13}C) NMR spectroscopy. The solution NMR spectra of the isolated products, recorded in $CDCl_3$ or DMSO-d_6 (for **3**) are consistent with the formation of the title

compounds, exhibiting the expected resonances in the alkyl as well as in the aryl regions.

Single crystals of the intermediate **5** were grown from acetonitrile and the molecular structure was established by X-ray diffraction. The crystal contains discrete monomers, with no unusual intermolecular distances shorter than the sum of the van der Waals radii between heavy atoms. Selected bond distances and angles are listed in Table 1. Figure 1 shows the ORTEP-like view of the molecular structure of **5**, with the atom numbering scheme.

Table 1

Selected interatomic distances (Å) and angles (deg) in [2-{1',2'-$C_6H_4(CO)_2NCH_2CH_2\}_2NCH_2$]$C_6H_4Br$ (**5**)

Br(1)–C(1)	1.904(3)			
N(1)–C(7)	1.463(4)		N(1)–C(8)	1.461(4)
N(1)–C(18)	1.469(4)			
N(2)–C(9)	1.446(4)		N(3)–C(19)	1.457(4)
N(2)–C(10)	1.390(4)		N(3)–C(20)	1.391(4)
N(2)–C(17)	1.397(4)		N(3)–C(27)	1.392(4)
O(1)–C(10)	1.213(4)		O(3)–C(20)	1.208(4)
O(2)–C(17)	1.206(4)		O(4)–C(27)	1.200(4)
C(7)–N(1)–C(8)	112.9(2)		C(7)–N(1)–C(18)	111.0(2)
C(8)–N(1)–C(18)	112.2(2)			
C(9)–N(2)–C(10)	122.6(3)		C(19)–N(3)–C(20)	123.2(3)
C(9)–N(2)–C(17)	125.2(3)		C(19)–N(3)–C(27)	124.4(3)
C(10)–N(2)–C(17)	112.1(3)		C(20)–N(3)–C(27)	112.2(3)
O(1)–C(10)–C(11)	129.0(3)		O(3)–C(20)–C(21)	129.0(3)
O(1)–C(10)–N(2)	124.7(3)		O(3)–C(20)–N(3)	125.1(3)
C(11)–C(10)–N(2)	106.4(3)		C(21)–C(20)–N(3)	105.9(3)
O(2)–C(17)–C(16)	129.3(3)		O(4)–C(17)–C(26)	129.3(3)
O(2)–C(17)–N(2)	125.4(3)		O(4)–C(17)–N(3)	125.3(3)
C(16)–C(17)–N(2)	105.3(3)		C(26)–C(17)–N(3)	105.5(3)

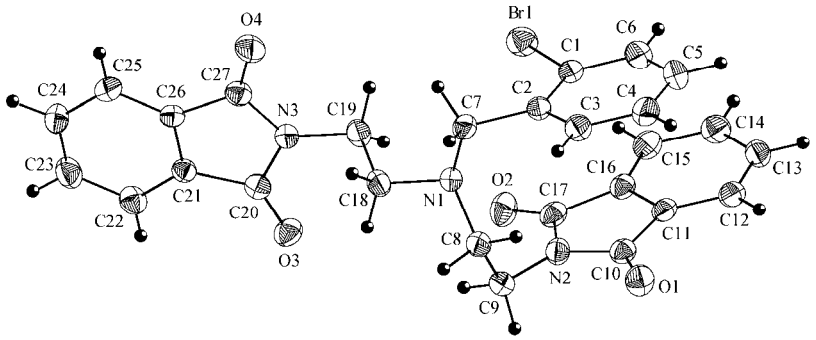


Fig. 1 – ORTEP plot of [2-{1',2'-$C_6H_4(CO)_2NCH_2CH_2\}_2NCH_2$]$C_6H_4Br$ (**5**).
The atoms are drawn with 30% probability ellipsoids.

DISCUSSION

Polyamines containing terminal or secondary amine functions are important starting materials for synthesis of polyaza- or peraza-crowns as well as ligands with linear or branched structure containing potential nitrogens as donor atoms.[23,24] The bis-phthalimido intermdiate **2** can be obtained using a Gabriel synthesis, *i.e.* by reacting $HN(CH_2CH_2X)_2$ and potassium phthalimide.[25] We have used an alternative procedure starting from diethylenetriamine, resulting in the isolation of **2** in a quite good yield. The coupling between **2** and benzyl bromide or 2-halobenzyl bromides was performed using conventional procedures. The use of hydrazine hydrate hydrolysis of an imide[26] instead of acidic hydrolysis is well known to give better results in the preparation of the

corresponding amines and, therefore, it was applied in the synthesis of compounds **6**–**8**. Alternatively, we have also tried to prepare benzyl-bis(2-aminoethyl)amine (**6**) using the method of Tweeedle and co-workers,[27] using the reaction between benzylamine and acrylamide to form the bisamide intermediate that can be converted to the desired compound using a Hofmann amide degradation, but the general yield was lower.

Solution behavior

The solution NMR spectra of the intermediates **2**–**5** do not exhibit unusual resonances and splitting patterns. The main difference, in addition to the new resonances corresponding to benzyl and *ortho*-halo substituted benzyl groups, is the lack of the N*H* resonance in the spectra of the derivatives **3**–**5**. For the intermediates **7** and **8** and the corresponding permethylated compounds **10** and **11** the multiplicity of the resonances for the NCH_2CH_2N protons of the branched arms suggests some asymmetry induced by the presence of the halogen atom in the *ortho* position of the aromatic ring.

Solid state structure

The molecule of **5** (Fig. 1) exhibits three basically planar fragments: two phthalimido-containing $C_6H_4(CO)_2NC$ fragments and the CC_6H_4Br group. As a result, the NC_3 cores including the N(2) and N(3) atoms are planar, with different nitrogen-carbon distances, *i.e.* two shorter N-C(sp^2) bonds (ca. 1.39 Å) from the aromatic phthalimido moiety and a longer N-C(sp^3) bond (ca. 1.45 Å). The third NC_3 core around the N(1) of the pendant arm is, as expected, distorted *pseudo*-tetrahedral, with N-C(sp^3) bond distances of about 1.46 Å. An interesting feature of the molecule of **5** is that one of the arms bearing a phthalimido group is twisted to bring the planar $C_6H_4(CO)_2NC$ fragment almost parallel to the CC_6H_4Br fragment [$C_6H_4(CO)_2N(2)C$ / CC_6H_4Br dihedral angle 3.6º], a behavior which might be due to some π-π interaction between the two aromatic systems. The second arm is twisted on opposite direction with its $C_6H_4(CO)_2NC$ fragment almost orthogonal to the previous two planar sytems [$C_6H_4(CO)_2N(3)C$ / $C_6H_4(CO)_2N(2)C$ and $C_6H_4(CO)_2N(3)C$ / CC_6H_4Br dihedral angles of 88.1º and 84.8º, respetively].

A closer check of the crystal structure revealed that the molecules are associated into chain polymers (Fig. 2) through intermolecular O(3)···H(25a) (2.41 Å) contacts shorter than the sum of van der Waals radii for the corresponding atoms [cf. Σr_{vdW}(O,H) ca. 2.60 Å].[28] These chain polymers are further associated into layers through additional weaker, intermolecular contacts which involve the same oxygen atoms [O(3a')···H(14) 2.52 Å] (Fig. 3). No further inter-layer contacts are established.

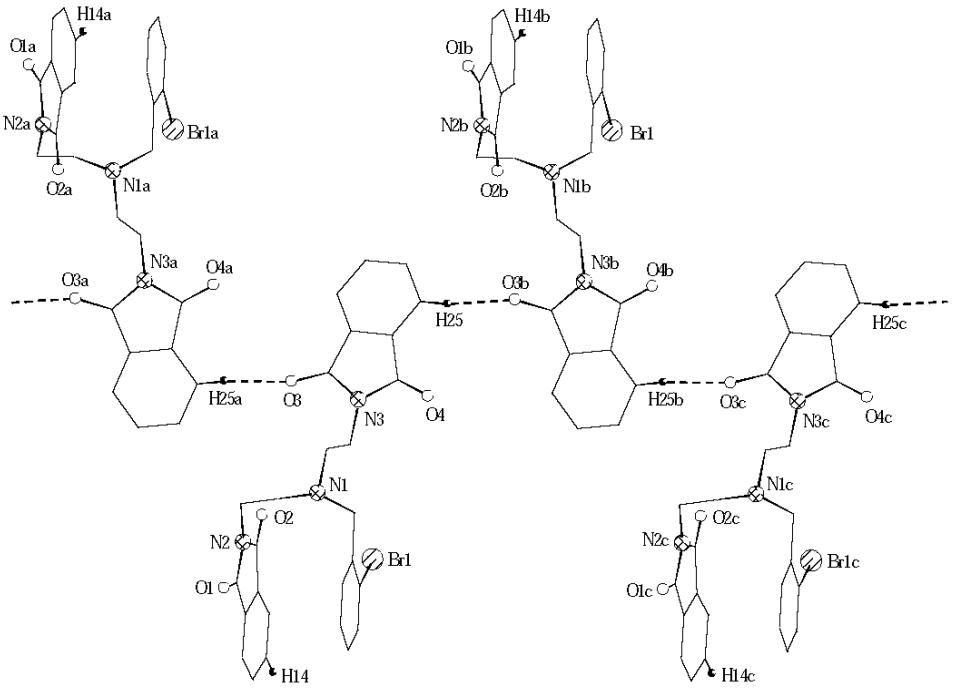


Fig. 2 – View of the chain polymer association in the crystal of 5 based on intermolecular O···H contacts (only hydrogens involved in such contacts are shown) [symmetry equivalent atoms (x, 2.5 – y, 0.5 + z), (x, 2.5 – y, –0.5 + z), and (x, y, –1 + z) are given by ''a'', "b" and "c"].

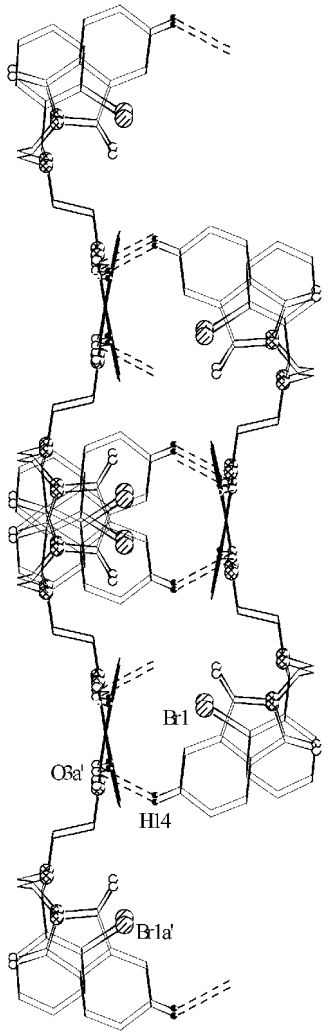


Fig. 3 – View along *c* axis of the association between chain polymers in the crystal of **5** based on intermolecular O···H contacts (only hydrogens involved in such contacts are shown) [symmetry equivalent atoms (1 – *x*, –0.5 + *y*, 1.5 – *z*) are given by ''prime a'']

EXPERIMENTAL

The reactions were monitorized by TLC, using silica gel plates and toluene as eluent. The plates were developed with iodine. ^{1}H and ^{13}C spectra, including 2D experiments, were recorded on Bruker Avance 300, BRUKER AVANCE DRX 400 and Bruker Avance III 500 instruments using solutions in $CDCl_3$ or DMSO-d_6. The chemical shifts are reported in δ units (ppm) relative to the residual peak of the deuterated solvent (ref. $CHCl_3$: ^{1}H 7.26, ^{13}C 77.0 ppm; DMSO-d_6: ^{1}H 2.50, ^{13}C 39.43 ppm) for ^{1}H and ^{13}C NMR spectra. Melting points are uncorrected. Diethylenetriamine (**1**), phtalic anhydride, benzyl bromide, 2-chlorobenzyl bromide and 2-bromoobenzyl bromide were commercial products.

Synthesis of bis(2-phthalimidoethyl)amine, $[C_6H_4(CO)_2NCH_2CH_2]_2NH$ (**2**)

Diethylenetriamine (**1**) (29.2 g, 0.28 mol) was added to a solution of phthalic anhydride (92 g, 0.62 mol) in glacial acetic acid (500 mL). The mixture was refluxed for one hour, then the solvent was removed *in vacuo*. The residue was solved in ethanol (500 mL) and refluxed for an additional one hour. The reaction mixture was cooled and the solid formed was filtered, washed with ethanol and water, and dried *in vacuo*. Yield: 77 g (75%). M.p. = 178-180 °C (lit. 180 °C;[19] 182-183 °C[29]). ^{1}H NMR (300 MHz, $CDCl_3$): 2.00s (1H, N*H*), 3.00t [4H, $(CH_2CH_2)_2NH$, $^{3}J_{HH}$ = 6.0 Hz], 3.81t [4H, $(CH_2CH_2)_2NH$, $^{3}J_{HH}$ = 6.0 Hz], 7.71m (8H, C_6H_4). ^{13}C NMR (75.5 MHz, $CDCl_3$): 37.47s [$(CH_2CH_2)_2NH$], 45.15s [$(CH_2CH_2)_2NH$], 123.10s, 123.20s (*C*H, C_6H_4), 133.80s [*C*(CO)N], 158.50s (*C*=O).

Synthesis of benzyl-bis(2-phthalimidoethyl)amine, $[C_6H_4(CO)_2NCH_2CH_2]_2NCH_2C_6H_5$ (**3**)

A suspension of **2** (36.3 g, 0.1 mol), benzyl bromide (22.6 g, 0.13 mol) and anhydrous potassium carbonate (41.4g, 0.3 mol) in acetonitrile (300 mL) was refluxed for 48 hours. After cooling, the inorganic salts were filtered off and the solvent was removed *in vacuo*. The residue was dissolved in methylene dichloride and the organic phase was washed with water, dried over magnesium sulfate, filtered and the solvent was removed *in vacuo*. The compound was isolated as a white solid.[21] Yield: 27 g (60%). M.p. = 128 °C (lit. 130-132.5 °C[22]). Anal. Calc. for $C_{27}H_{23}N_3O_4$: C, 71.50, H, 5.11, N, 9.27. Found: C, 71.65, H, 5.43, N, 9.44. ^{1}H NMR (300 MHz, DMSO-d_6): 2.62t [4H, $(CH_2CH_2)_2NCH_2$, $^{3}J_{HH}$ = 5.6 Hz], 3.58s (2H, $NCH_2C_6H_5$), 3.60t [4H, $(CH_2CH_2)_2NCH_2$, $^{3}J_{HH}$ = 5.7 Hz], 6.83t (2H, C_6H_5-*meta*, $^{3}J_{HH}$ = 7.5 Hz), 6.96d (2H, C_6H_5-*ortho*,

$^3J_{HH}$ = 7.1 Hz), 7.01t (1H, C_6H_5-*para*, $^3J_{HH}$ = 7.3 Hz), 7.65m (4H, C_6H_4), 7.81m (4H, C_6H_4). ^{13}C NMR (75.5 MHz, DMSO-d_6): 35.27s [(CH_2CH_2)$_2$NCH$_2$], 51.36s [(CH$_2$$CH_2$)$_2NCH_2$], 57.16s (NCH$_2C_6H_5$), 122.90s (*C*H, C$_6H_4$), 126.75s ($C_6H_5$-*para*), 127.88s ($C_6H_5$-*meta*), 128.65s ($C_6H_5$-*ortho*), 131.87s (*C*H, C$_6$H$_4$), 134.30s [*C*(CO)N], 138.99s (C_6H_5-*ipso*), 167.90s (*C*=O).

Synthesis of 2-[di(2'-phthalimidoethyl)aminomethyl]phenyl chloride,
2-[{C_6H_4(CO)$_2$NCH$_2$CH$_2$}$_2$NCH$_2$]C_6H_4Cl (**4**)

Compound **4** was prepared using a similar procedure as indicated for compound **3**, starting from **2** (36.3 g, 0.1 mol), 2-chlorobenzyl bromide (27.1 g, 0.13 mol) and anhydrous K_2CO_3 (41.4 g, 0.3 mol), in acetonitrile (300 mL). Yield: 30 g (61%). M.p. = 137-139 °C (lit. 138-139 °C[22]). Anal. Calc. for: $C_{27}H_{22}ClN_3O_4$: C, 66.46, H, 4.54, N, 8.60. Found: C, 66.63, H, 4.30, N, 8.44. ^{1}H NMR (300 MHz, $CDCl_3$): 2.85t [4H, (CH$_2$CH_2)$_2$NCH$_2$, $^3J_{HH}$ = 6.3 Hz], 3.75s (2H, NCH_2C$_6$H$_4$Cl), 3.77t [4H, (CH_2CH$_2$)$_2$NCH$_2$, $^3J_{HH}$ = 6.3 Hz], 6.72m (1H, H_5, C$_6$H$_4$Cl), 6.82m (1H, H_4, C$_6$H$_4$Cl), 7.05m (1H, H_3, C$_6$H$_4$Cl), 7.20m (1H, H_6, C$_6$H$_4$Cl), 7.69m (8H, C$_6$H$_4$). ^{13}C NMR (75.5 MHz, $CDCl_3$): 34.00s [(*C*H$_2$CH$_2$)$_2$NCH$_2$], 50.24s [(CH$_2$*C*H$_2$)$_2$NCH$_2$], 56.64s (N*C*H$_2$C$_6$H$_4$Cl), 122.89s (*C*H, C$_6$H$_4$), 124.00s (C_4, C$_6$H$_4$Cl), 126.80s (C_5, C$_6$H$_4$Cl), 128.00s (C_6, C$_6$H$_4$Cl), 130.10s (C_3, C$_6$H$_4$Cl), 132.00s (*C*H, C$_6$H$_4$), 132.40s [*C*(CO)N], 133.55s (C_1, C$_6$H$_4$Cl), 137.80s (C_2, C$_6$H$_4$Cl), 168.00s (*C*=O).

Synthesis of 2-[di(2'-phthalimidoethyl)aminomethyl]phenyl bromide, *2-[{C_6H_4(CO)$_2$NCH$_2$CH$_2$}$_2$NCH$_2$]C_6H_4Br* (**5**)

Compound **5** was prepared using a similar procedure as indicated for compound **3**, starting from **2** (36.3 g, 0.1 mol), 2-bromobenzyl bromide (32.9 g, 0.13 mol) and anhydrous K_2CO_3 (41.4 g, 0.3 mol), in acetonitrile (300 mL). Yield: 32 g (60%). M.p. = 138-139 °C. Anal. Calc. for: $C_{27}H_{22}BrN_3O_4$: C, 60.9, H, 4.17, N, 7.89. Found: C, 61.20, H, 4.53, N, 7.54. ^{1}H NMR (300 MHz, $CDCl_3$): 2.87t [4H, (CH$_2$CH_2)$_2$NCH$_2$, $^3J_{HH}$ = 6.3 Hz], 3.77s (2H, NCH_2C$_6$H$_4$Br), 3.79t [4H, (CH_2CH$_2$)$_2$NCH$_2$, $^3J_{HH}$ = 6.3 Hz], 6.75ddd (1H, H_5, C$_6$H$_4$Br, $^3J_{HH}$ = 7.4, $^4J_{HH}$ = 1.2 Hz), 6.89ddd (1H, H_4, C$_6$H$_4$Br, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.8 Hz), 7.10dd (1H, H_3, C$_6$H$_4$Br, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.7 Hz), 7.24dd (1H, H_6, C$_6$H$_4$Br, $^3J_{HH}$ = 7.4, $^4J_{HH}$ = 1.2 Hz), 7.71m (8H, C$_6$H$_4$). ^{13}C NMR (75.5 MHz, $CDCl_3$): 35.47s [(*C*H$_2$CH$_2$)$_2$NCH$_2$], 51.20s [(CH$_2$*C*H$_2$)$_2$NCH$_2$], 57.20s (N*C*H$_2$C$_6$H$_4$Br), 122.97s (*C*H, C$_6$H$_4$), 124.45s (C_1, C$_6$H$_4$Br), 126.87s (C_4, C$_6$H$_4$Br), 128.23s (C_5, C$_6$H$_4$Br), 130.73s (C_3, C$_6$H$_4$Br), 132.18s (*C*H, C$_6$H$_4$), 132.43s (C_6, C$_6$H$_4$Br), 133.57s [*C*(CO)N], 137.88s (C_2, C$_6$H$_4$Br), 168.05s (*C*=O).

Synthesis of benzyl-bis(2-aminoethyl)amine,
(H_2NCH$_2$CH$_2$)$_2$NCH$_2$C$_6$H$_5$ (**6**)

A mixture of **3** (45.3 g, 0.1 mol) and hydrazine hydrate (10.5 g, 0.3 mol) in ethanol (500 mL) was heated under reflux for 4 h. At boiling temperature the solid first dissolved and after short time the phthaloylhydrazide salt of the amine precipitated. The solvent was removed *in vacuo* and the remaining solid was partially solved in water (500 mL), treated with concentrated HCl (40 mL) and the resulting mixture was then stirred at 50 °C for 0.5 h. The solid phthaloylhydrazide was filtered off and the remaining solution was concentrated *in vacuo*, when a second crop of phthaloylhydrazide was isolated. The trihydrochloride was dissolved in water and the solution brought to pH 14, at 0-5 °C, usig 20% NaOH aqueous solution. The aqueous solution was extracted with methylene chloride (7x50 mL) and the organic phase was separated and dried on anhydrous $MgSO_4$. After filtration, the solvent was removed to dryness *in vacuo*, when the title compound was isolated as an yellow oil, which was used without further purification (lit. b.p. 156-158 °C / 10 mm Hg[22]). Yield: 12.5 g (65%). Anal. Calc. for: $C_{11}H_{19}N_3$: C, 68.35, H, 9.91, N, 21.74. Found: C, 68.54, H, 10.04, N, 22.00. ^{1}H NMR (300 MHz, $CDCl_3$): 2.62m [4H, (H$_2$NCH$_2$CH_2)$_2$NCH$_2$], 2.75m [4H, (H$_2$NCH_2CH$_2$)$_2$NCH$_2$], 3.62s (2H, NCH_2C$_6$H$_5$), 7.05m (3H, C_6H_5-*meta*+*para*), 7.14m (2H, C_6H_5-*ortho*). ^{13}C NMR (75.5 MHz, $CDCl_3$): 34.25s [(H$_2$N*C*H$_2$CH$_2$)$_2$NCH$_2$], 50.80s [(H$_2$NCH$_2$*C*H$_2$)$_2$NCH$_2$], 56.35s (N*C*H$_2$C$_6$H$_5$), 123.50s (C_6H_5-*para*), 124.82s (C_6H_5-*meta*), 128.44s (C_6H_5-*ortho*), 129.28s (C_6H_5-*ipso*).

Synthesis of 2-[bis(2'-aminoethyl)aminomethyl]phenyl chloride,
2-[(H_2NCH$_2$CH$_2$)$_2$NCH$_2$]C_6H_4Cl (**7**)

Compound **7** was prepared using a similar procedure as indicated for compound **6**, starting from **4** (48.75 g, 0.1 mol) and hydrazine hydrate (10.5 g, 0.3 mol), in ethanol (500 mL). The reaction mixture was worked up as described for **6**, the title compound being isolated as an yellow oil, which was used without further purification (lit. b.p. 153-157 °C / 3 mm Hg[22]). Yield: 13.6 g (60%). Anal. Calc. for: $C_{11}H_{18}ClN_3$: C, 58.00, H, 7.97, N, 18.45. Found: C, 57.83, H, 8.12, N, 18.63. ^{1}H NMR (300 MHz, $CDCl_3$): 2.62m [4H, (H$_2$NCH$_2$CH_2)$_2$NCH$_2$], 3.35m [4H, (H$_2$NCH_2CH$_2$)$_2$NCH$_2$], 3.62s (2H, NCH_2C$_6$H$_4$Cl), 7.05m (1H, H_3, C$_6$H$_4$Cl), 7.15m (1H, H_4, C$_6$H$_4$Cl), 7.25m (1H, H_5, C$_6$H$_4$Cl), 7.45m (1H, H_6, C$_6$H$_4$Cl). ^{13}C NMR (75.5 MHz, $CDCl_3$): 35.00s [(H$_2$N*C*H$_2$CH$_2$)$_2$NCH$_2$], 51.22s (N*C*H$_2$C$_6$H$_4$Cl), 54.20s [(H$_2$NCH$_2$*C*H$_2$)$_2$NCH$_2$], 123.28s (C_4, C$_6$H$_4$Cl), 124.00s (C_5, C$_6$H$_4$Cl), 128.20s (C_6, C$_6$H$_4$Cl), 129.87s (C_3, C$_6$H$_4$Cl), 130.34s (C_1, C$_6$H$_4$Cl), 131.00s (C_2, C$_6$H$_4$Cl).

Synthesis of 2-[bis(2'-aminoethyl)aminomethyl]phenyl bromide,
2-[(H_2NCH$_2$CH$_2$)$_2$NCH$_2$]C_6H_4Br (**8**)

Compound **8** was prepared using a similar procedure as indicated for compound **6**, starting from **5** (53.2 g, 0.1 mol) and hydrazine hydrate (10.5 g, 0.3 mol), in ethanol (500 mL). The reaction mixture was worked up as described for **6**, the title compound being isolated as an yellow oil, which was used without further purification. Yield: 15 g (55%). Anal. Calc. for: $C_{11}H_{18}BrN_3$: C, 48.54, H, 6.67, N, 15.44. Found: C, 48.61, H, 6.82, N, 15.07. ^{1}H NMR (500 MHz, $CDCl_3$): 2.72m [4H, (H$_2$NCH$_2$CH_2)$_2$NCH$_2$], 2.90m [4H, (H$_2$NCH_2CH$_2$)$_2$NCH$_2$], 3.78s (2H, NCH_2C$_6$H$_4$Br), 4.55s,br [4H, (H_2NCH$_2$CH$_2$)$_2$NCH$_2$], 7.12ddd (1H, H_4, C$_6$H$_4$Br, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.5 Hz), 7.29ddd (1H, H_5, C$_6$H$_4$Br, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.0 Hz), 7.46dd (1H, H_3, C$_6$H$_4$Br, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.5 Hz), 7.53dd (1H, H_6, C$_6$H$_4$Br, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 1.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 35.44s [(H$_2$NCH$_2$CH$_2$)$_2$NCH$_2$], 52.00s [(CH$_2$*C*H$_2$)$_2$NCH$_2$], 55.43s (N*C*H$_2$C$_6$H$_4$Br), 123.15s (C_1, C$_6$H$_4$Br), 123.80s (C_4, C$_6$H$_4$Br), 124.40s (C_5, C$_6$H$_4$Br), 127.90s (C_3, C$_6$H$_4$Br), 129.67s (C_6, C$_6$H$_4$Br), 131.34s (C_2, C$_6$H$_4$Br).

Synthesis of benzyl-bis(2-dimethylaminoethyl)amine,
(Me_2NCH$_2$CH$_2$)$_2$NCH$_2$C$_6$H$_5$ (**9**)

Compound **6** (10.8 g, 0.056 mol) was added, under stirring and external cooling with ice, into a flask (500 mL) that contains 99% formic acid (21.6 g, 0.47 mol) and then a suspension of paraformaldehyde (23.4 g, 0.45 mol) in water (290 mL) was added. The resulting mixture was warmed on an oil bath to 90-100 °C. Carbon dioxide evolution ceased after a few minutes (the flask is taken out from the oil bath). Subsequently the flask is put again into the oil bath and the solution refluxed overnight. After cooling the solution was

made alkaline with a 20% KOH aqueous solution and the reaction product extracted with toluene (7x50 mL). The organic layer was separated, dried on anhydrous $MgSO_4$, and the solvent evaporated *in vacuo*, when pure **9** was obtained pure as an oil. Yield: 6.4 g (65%). Anal. Calc. for: $C_{15}H_{27}N_3$: C, 72.24, H, 10.91, N, 16.85. Found: C, 72.44, H, 11.23, N, 16.72. ^{1}H NMR (300 MHz, $CDCl_3$): 2.10s (12H, NMe_2), 2.23m [4H, $(Me_2NCH_2CH_2)_2NCH_2$], 2.49m [4H, $(Me_2NCH_2CH_2)_2NCH_2$], 3.49s (2H, $NCH_2C_6H_5$), 6.63m (2H, C_6H_5-*ortho*), 7.12m (3H, C_6H_5-*meta*+*para*). ^{13}C NMR (75.5 MHz, $CDCl_3$): 45.60s (NMe_2), 51.00s [$(Me_2NCH_2CH_2)_2NCH_2$], 56.20s [$(Me_2NCH_2CH_2)_2NCH_2$], 60.10s ($NCH_2C_6H_5$), 127.32s (C_6H_5-*para*), 128.51s (C_6H_5-*meta*), 129.00s (C_6H_5-*ortho*), 135.40s (C_6H_5-*ipso*).

Synthesis of 2-[bis(2'-dimethylaminoethyl)aminomethyl]phenyl chloride, 2-[(Me$_2$NCH$_2$CH$_2$)$_2$NCH$_2$]C$_6$H$_4$Cl (**10**)

Compound **10** was prepared using a similar procedure as indicated for compound **9**, starting from **7** (12.7 g, 0.056 mol), 99% formic acid (21.6 g, 0.47 mol) and a suspension of paraformaldehyde (23.4 g, 0.45 mol) in water (290 mL). The reaction mixture was worked up as described for **9**, the title compound being isolated pure as an oil. Yield: 9.5 g (60%). Anal. Calc. for: $C_{15}H_{26}ClN_3$: C, 63.50, H, 9.23, N, 14.80. Found: C, 53.73, H, 9.30, N, 14.63. ^{1}H NMR (400 MHz, $CDCl_3$): 2.16s (12H, NMe_2), 2.38m [4H, $(Me_2NCH_2CH_2)_2NCH_2$], 2.61m [4H, $(Me_2NCH_2CH_2)_2NCH_2$], 3.69s (2H, $NCH_2C_6H_4Cl$), 7.11dd (1H, H_4, C_6H_4Cl, $^3J_{HH}$ = 7.3 Hz), 7.19dd (1H, H_5, C_6H_4Cl, $^3J_{HH}$ = 7.4 Hz), 7.27d (1H, H_3, C_6H_4Cl, $^3J_{HH}$ = 8.1 Hz), 7.50d (1H, H_6, C_6H_4Cl, $^3J_{HH}$ = 7.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 45.61s (NMe_2), 51.00s [$(Me_2NCH_2CH_2)_2NCH_2$, overlapped with $NCH_2C_6H_4Cl$], 56.31s [$(Me_2NCH_2CH_2)_2NCH_2$], 126.60s (C_4, C_6H_4Cl), 128.62s, 129.00s (C_5 and C_6, C_6H_4Cl), 130.31s (C_3, C_6H_4Cl), 134.22s (C_1, C_6H_4Cl), 136.40s (C_2, C_6H_4Cl).

Synthesis of 2-[bis(2'-dimethylaminoethyl)aminomethyl]phenyl bromide, 2-[(Me$_2$NCH$_2$CH$_2$)$_2$NCH$_2$]C$_6$H$_4$Br (**11**)

Compound **11** was prepared using a similar procedure as indicated for compound **9**, starting from **8** (15.2 g, 0.056 mol), 99% formic acid (21.6 g, 0.47 mol) and a suspension of paraformaldehyde (23.4 g, 0.45 mol) in water (290 mL). The reaction mixture was worked up as described for **9**, the title compound being isolated pure as an oil. Yield: 12 g (65%). Anal. Calc. for: $C_{15}H_{26}BrN_3$: C, 54.81, H, 7.98, N, 12.80. Found: C, 55.03, H, 8.25, N, 12.67. ^{1}H NMR (300 MHz, $CDCl_3$): 2.21s (12H, NMe_2), 2.42m [4H, $(Me_2NCH_2CH_2)_2NCH_2$], 2.55m [4H, $(Me_2NCH_2CH_2)_2NCH_2$], 3.72s (2H, $NCH_2C_6H_4Br$), 7.08ddd (1H, H_4, C_6H_4Br, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.7 Hz), 7.28ddd (1H, H_5, C_6H_4Br, $^3J_{HH}$ = 7.3, $^4J_{HH}$ = 1.2 Hz), 7.51dd (1H, H_3, C_6H_4Br, $^3J_{HH}$ = 7.9, $^4J_{HH}$ = 1.2 Hz), 7.56dd (1H, H_6, C_6H_4Br, $^3J_{HH}$ = 7.7, $^4J_{HH}$ = 1.6 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$): 45.86s (NMe_2), 52.83s [$(Me_2NCH_2CH_2)_2NCH_2$], 57.47s [$(Me_2NCH_2CH_2)_2NCH_2$], 58.96s ($NCH_2C_6H_4Br$), 125.21s (C_1, C_6H_4Br), 127.12s (C_4, C_6H_4Br), 128.13s (C_5, C_6H_4Br), 130.43s (C_3, C_6H_4Br), 132.45s (C_6, C_6H_4Br), 138.92s (C_2, C_6H_4Br).

Crystal structure determination

A colorless block crystal of 2-[{1',2'-$C_6H_4(CO)_2NCH_2CH_2\}_2NCH_2]C_6H_4Br$ (**5**) was mounted on a cryoloop. Data collection and processing was carried on a Bruker SMART APEX system (Babes-Bolyai University, Cluj-Napoca) using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å). Cell refinement gave cell constants corresponding to monoclinic cell (space group $P2_1/c$), whose dimensions are given in Table 2 along with other experimental parameters.

Table 2

Crystallographic data for [2-{1',2'-$C_6H_4(CO)_2NCH_2CH_2\}_2NCH_2]C_6H_4Br$ (**5**)

Molecular formula	$C_{27}H_{22}BrN_3O_4$	F(000)	1088
M	532.39	μ(Mo-Kα)/mm^{-1}	1.753
Crystal system	Monoclinic	Crystal size (mm^3)	0.26 x 0.20 x 0.14
Space group	$P2_1/c$	θ range for data collection (º)	1.90 to 26.37
Temperature (K)	297(2)	Reflections collected	19014
a/Å	11.175(3)	Independent reflections	4897 [R_{int} = 0.0623]
b/Å	15.423(4)	Absorption correction	Multi-Scan[31]
c/ Å	14.516(4)	Maximum and minimum transmissions	0.7914 and 0.6586
α/º	90	Data / restraints / parameters	4897 / 0 / 316
β/º	106.469(6)	Goodness-of-fit on F^2	1.054
γ/º	90	Final R indices [$I>2\sigma(I)$][a]	R_1 = 0.0561 wR_2 = 0.0995
V/Å^3	2399.2(12)	R indices (all data)[a]	R_1 = 0.0882 wR_2 = 0.1097
Z	4	Largest difference peak and hole (e Å-^{3})	0.278 and –0.353
D_{calc}/gcm^{-3}	1.474		

[a] Definition of the R values: $R_1 = (\Sigma||F_o| - |F_c||)/\Sigma|F_o|$; $wR_2 = \{[w\Sigma(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$ with $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$.

The structure was refined with anisotropic thermal parameters. The hydrogen atoms were refined with a riding model and a mutual isotropic thermal parameter. For structure solving and refinement the software package SHELX-97 was used.[30] The drawings were created with the Diamond program.[32]

Supplementary material

Crystallographic data for the structural analysis of 5 have been deposited with the Cambridge Crystallographic Data Centre (CCDC no. 769844). Copies of the information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033;

e-mail: deposit@ccdc.cam.ac.uk or www: http:// www.ccdc.cam.ac.uk).

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