Synthesis of New Bis-1,2,4-Triazole Derivatives

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Abstract: A series of new 1,2/1,3-bis[o-(N-methylidenamino-3-aryl-5-phenyl-4H-1,2,4-triazole-4-yl)phenoxy]ethane/propane derivatives 4 were prepared in good yields by treatment of 4-amino-3-aryl-5-phenyl-4H-1,2,4-triazoles 2 with certain bis-aldehydes 1. Compounds 4 were reduced with NaBH₄ to afford the corresponding 1,2/1,3-bis[o-(N-methylamino-3-aryl-5-phenyl-4H-1,2,4-triazole-4-yl)phenoxy]ethane/propane derivatives 5. All new compounds were characterized by IR, ¹H-NMR, ¹³C-NMR and mass spectral data.

Keywords: 4-Amino-4H-1,2,4-triazoles, bis-1,2,4-triazoles, bis-Schiff bases, bis-aldehydes

Introduction

1,2,4-triazoles and their derivatives are found to be associated with various biological activities such as anticonvulsant [1-2], antifungal [3-5], anticancer [6-9], antiinflammatory [10-12] and antibacterial properties [13-16]. Several compounds (Figure 1) containing 1,2,4-triazole rings are well known as drugs. For example, fluconazole is used as an antimicrobial drug [17], while vorozole, letrozole and anastrozole are non-steroidal drugs used for the treatment of cancer [18] and loreclezole is used as an anticonvulsant [19].
Furthermore, in recent years some Schiff base derivatives of 1,2,4-triazoles and their reduced derivatives have been also found to possess pharmacological activities [20-26]. These biological data prompted us to synthesize some new bis-1,2,4-triazole derivatives, and in the present study, a novel series of bis-Schiff base derivatives resulting from the reaction of 4-amino-3-aryl-5-phenyl-4H-1,2,4-triazoles with bis-aldehydes and their corresponding reduced derivatives were synthesized and characterized by IR, $^1$H-NMR, $^{13}$C-NMR and mass spectral data.

**Results and Discussion**

The syntheses of the 1,2/1,3-bis[o-(N-methylidnamino-3-aryl-5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]ethane/propane derivatives 4 were accomplished according to the reactions shown in Schemes 1-3. First, bis-aldehydes 1 were synthesized using a published method [27], as indicated in Scheme 1. 3-Aryl-5-phenyl-4-amino-4H-1,2,4-triazoles 3 were obtained from the reaction of ethyl benzoate benzoylhydrazone derivatives 2 with hydrazine using the published method shown in Scheme 2 [28]. Finally reactions of compounds 1 and 3 afforded the desired compounds 4 (Scheme 3). In general, reduction of imine type compounds is possible [26, 29], but attempts to reduce imines such as 4 may also lead to a reduction of the heterocyclic ring. For this reason, the selective reduction of the imino group present in compounds 4 without affecting the heterocyclic ring was another aim of the study. Thus, a general and convenient method using NaBH$_4$ as a selective reducing agent was employed for the synthesis in good yields of the 1,2/1,3-bis[o-(N-methylamino-3-aryl,5-phenyl-4H-1,2,4-triazole-4-yl)phenoxy]ethane/propane derivatives 5 (Scheme 3).
In the IR spectra of compounds 4 the characteristic C=N absorption bands appeared at 1597 cm$^{-1}$. The $^1$H-NMR signals for the -N=CH group were observed at $\delta$ 8.23-8.70 ppm. The $^{13}$C-NMR signals for the –N=CH- group were recorded at $\delta$ 164 ppm. Reduced compounds 5 showed IR absorption bands around 3245-3290 cm$^{-1}$ ($\nu_{NH}$). The $^1$H-NMR signals for the -NH-CH$_2$- group of these compounds were observed as a doublet or strong singlet at around $\delta$ 3.55-3.75 ppm and the proton signals of –NH-CH$_2$- groups were recorded as a triplet or strong singlet between $\delta$ 6.95-7.08 ppm. The NH-CH$_2$- carbon signals of compounds 5 were recorded at $\delta$ 48 ppm in the $^{13}$C-NMR. In addition to this, in the $^{13}$C-NMR the triazole C3 and C5 of the bis-Schiff base derivatives 4 were observed between $\delta$ 148-149 ppm and the triazole C3 and C5 signals of the reduced compounds 5 were observed between $\delta$ 152-153 ppm.
Conclusions

In this study, a convenient method was established for the synthesis in good yields of bis[o-(N-methylenediamino-3-aryl-5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy] alkane derivatives 4a-f and bis[o-(N-methylamino-3-aryl-5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy] alkane derivatives 5a-f. The twelve new bis-(4H-1,2,4-triazole) derivatives synthesized in the study are expected to exhibit some biological activities and these results will be reported in due course.

Experimental

General

Melting points were determined on a Barnstead Electrothermal melting point apparatus and are uncorrected. $^1$H-NMR and $^{13}$C-NMR spectra (δ, ppm) were recorded on a Varian-Mercury 200 MHz spectrophotometer using tetramethylsilane as the internal reference. The IR spectra (υ, cm$^{-1}$) were obtained with a Perkin-Elmer 1600 FTIR spectrometer in KBr pellets. The mass spectra were recorded on a MicroMass Quattro LC-MS/MS (70 eV) spectrometer. The necessary chemicals were purchased from Merck and Fluka.

Synthesis of bis-aldehydes 1a-b

Salicylaldehyde (0.01 mol) was dissolved in hot ethanolic KOH (prepared by dissolving 0.01 mol of KOH in 100 mL of absolute ethanol) and the solvent was then removed in vacuo. The residue was dissolved in DMF (25 mL) and the appropriate dihalide (0.005 mol) was added. The reaction mixture was refluxed for 5 minutes, during which KCl separated out. The solvent was then removed in vacuo and the remaining material was washed with water and crystallized from an appropriate solvent to give compounds 1a-b.

1,2-Bis(o-formylphenoxy)ethane (1a). Yield 68%; m.p. 129-130 °C (from ethanol; lit. [27] m.p. 129 °C).

1,3-Bis(o-formylphenoxy)propane (1b). Yield 70%; m.p. 99-100 °C (from ethanol; lit. [27] m.p. 99 °C).

Synthesis of hydrazones 2a-c

A solution of an appropriate hydrazide (0.01 mol) in absolute ethanol (25 mL) was added to a solution of iminoester hydrochloride (0.01 mol) in absolute ethanol (25 mL). The mixture was stirred for 6 h at 0-5 °C and subsequently for 2 h at room temperature. The reaction mixture was then poured into a beaker containing cold water (40 mL) and ice (10 g). The precipitate formed was washed with ice-water (50 mL), dried and the product was recrystallized from from 2:1 benzene-petroleum ether to give compounds 2a-c.
Ethyl benzoate benzoylhydrazone (2a). Yield 79%; m.p. 120-121 °C (lit. [28] m.p. 121°C).

Ethyl p-methylbenzoate benzoylhydrazone (2b). Yield 84%; m.p. 77-78 °C (lit. [26] m.p. 78 °C).

Ethyl p-chlorobenzoate benzoylhydrazone (2c). Yield 72%; m.p. 80-81 °C; IR: 3199 (N-H), 1637 (C=O), 1613 (C=N), 702, 730, 839 (aromatic ring); 1H-NMR (DMSO-d6) δ (ppm): 1.37 (t, 3H, CH3), 4.09 (q, 2H, CH2), 7.44-7.75 (m, 5H, Ar-H), 8.07 (m, 4H, Ar-H), 10.79 (s, 1H, NH).

Synthesis of amino compounds 3a-c

Compounds 2 (0.005 mol) were added to a solution of hydrazine hydrate (0.01 mol) in 1-propanol (50 mL) and the mixture was refluxed for 24 h. On cooling, a precipitate was formed. This product was filtered and, after drying, was washed with benzene (20 mL). The product was then recrystallized from an appropriate solvent to give compounds 3a-c.

4-Amino-3,5-diphenyl-4H-1,2,4-triazole (3a). Yield 80%; m.p. 264-265 °C (from 1-propanol; lit. [28], m.p. 265 °C).

4-Amino-3-p-tolyl-5-phenyl-4H-1,2,4-triazole (3b). Yield 85%; m.p. 283-284 °C (from 1-propanol; lit. [26], m.p. 284 °C).

4-Amino-3-p-chlorophenyl-5-phenyl-4H-1,2,4-triazole (3c). Yield 68%; m.p. 284-285 °C (from ethyl acetate; lit. [28], m.p. 285 °C).

Synthesis of bis-Schiff bases 4a-f

The corresponding bis-aldehyde (0.01 mol) was added to a solution of compound 3 (0.005 mol) in glacial acetic acid (20 mL) and the mixture was refluxed for 16 h. After cooling, the mixture was poured into a beaker containing ice-water (100 mL). The precipitate formed was filtered. After drying in vacuo, the product was recrystallized from 1:2 benzene-petroleum ether to give the desired compound.

1,2-Bis[o-(N-methylidenoaminio-3,5-diphenyl-4H-1,2,4-triazole-4-yl)-phenoxyjethane (4a). Yield 70%; m.p. 212-213 °C; IR: 1598 (C=N), 693, 770 cm⁻¹ (aromatic ring); 1H-NMR (DMSO-d6) δ (ppm): 3.98 (s, 4H, OCH2), Ar-H: [6.89-7.04 (m, 4H), 7.33 (m, 10H), 7.70 (m, 6H), 7.44-7.56 (m, 4H), 7.92-8.06 (m, 4H)], 8.23 (s, 2H, CH); 13C-NMR (DMSO-d6) δ (ppm): 164.44 (2C, N=CH), 149.87 (2C, triazole C3), 149.87 (2C, triazole C5), Ar-C: [158.20 (2C), 134.75 (2C), 129.55 (2C), 128.76 (8C), 128.27 (8C), 126.88 (4C), 126.23 (4C), 121.33 (2C), 119.39 (2C), 113.48 (2C), 66.86 (2C, OCH2); LC-MS/MS, m/z (I, %) for C44H34N8O2 (m.w.: 706.81 g/mol): 729.26 [M+Na]^+ (50), 707.25 [M+H]^+ (30), 221.97 (100), 103.86 (60).
1,3-Bis[o-(N-methylidenamino-3,5-diphenyl-4H-1,2,4-triazole-4-yl)-phenoxy]propane (4b). Yield 72%; m.p. 189-190 °C; IR: 1595 (C=N), 694, 754 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 1.65 (q, 2H, -CH₂-), 3.77 (t, 4H, OCH₂), Ar-H: [6.97-7.16 (m, 6H), 7.51 (m, 12H), 7.80 (m, 8H), 7.97 (m, 2H)], 8.67 (s, 2H, CH); ¹³C-NMR (DMSO-d₆) δ (ppm): 164.73 (2C, N=CH), 150.00 (2C, triazole C₃), 150.00 (2C, triazole C₅), Ar-C: [158.53 (2C), 134.93 (2C), 129.60 (8C), 128.66 (8C), 128.23 (8C), 126.95 (4C), 126.48 (4C), 120.97 (2C), 119.29 (2C), 112.93 (2C)], 64.29 (2C, OCH₂), 27.75 (C, CH₂); LC-MS/MS, m/z (I, %) for C₄₅H₃₆N₈O₂ (m.w.: 720.83 g/mol): 743.18 [M+Na⁺]⁺ (25), 721.23 [M+1]⁺ (60), 500.16 (12), 221.96 (100), 114.83 (28), 103.82 (32).

1,2-Bis[o-(N-methylidenamino-3-p-tolyl-5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]ethane (4c). Yield 72%; m.p. 271-272 °C; IR: 1597 (C=N), 696, 721, 757, 823 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 2.52 (s, 6H, CH₃), 4.00 (s, 4H, OCH₂), Ar-H: [7.12 (m, 8H), 7.32 (bs, 6H), 7.49-7.68 (m, 10H), 7.94 (m, 2H)], 8.25 (s, 2H, CH); ¹³C-NMR (DMSO-d₆) δ (ppm): 164.34 (2C, N=CH), 149.90 (2C, triazole C₃), 149.72 (2C, triazole C₅), Ar-C: [158.45 (2C), 139.30 (2C), 134.72 (2C), 129.50 (2C), 129.16 (4C), 128.56 (4C), 128.09 (4C), 128.00 (4C), 126.93 (2C), 126.31 (2C), 123.42 (2C), 121.36 (2C), 119.50 (2C), 113.56 (2C)], 66.86 (2C, OCH₂), 20.73 (2C, CH₃); LC-MS/MS, m/z (I, %) for C₄₆H₃₈N₈O₂ (m.w.: 734.86 g/mol): 757.18 [M+Na⁺]⁺ (100), 735.14 [M+1]⁺ (70), 555.17 (22), 503.05 (14), 288.99 (98), 251.00 (35), 104.75 (27).

1,3-Bis[o-(N-methylidenamino-3-p-chlorophenyl-5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]propane (4d). Yield 62%; m.p. 229-230 °C; IR: 1597 (C=N), 697, 723, 765, 822 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 2.51 (s, 6H, CH₃), 1.69 (q, 2H, -CH₂-), 3.78 (t, 4H, OCH₂), Ar-H: [6.98-7.13 (m, 4H), 7.24 (m, 4H), 7.49 (m, 10H), 7.78 (m, 3H), 7.98 (m, 2H)], 8.69 (s, 2H,CH); ¹³C-NMR (DMSO-d₆) δ (ppm): 164.65 (2C, N=CH), 149.90 (2C, triazole C₃), 149.72 (2C, triazole C₅), Ar-C: [158.33 (2C), 139.25 (2C), 134.90 (2C), 129.52 (2C), 129.20 (4C), 128.62 (4C), 128.17 (4C), 128.11 (4C), 126.96 (2C), 126.54 (2C), 123.61 (2C), 120.94 (2C), 119.31 (2C), 112.88 (2C)], 64.26 (2C, OCH₂), 27.72 (C, CH₂), 20.68 (2C, CH₃); LC-MS/MS, m/z (I, %) for C₄₇H₄₀N₈O₂ (m.w.: 748.89 g/mol): 771.20 [M+Na⁺]⁺ (55), 749.24 [M+1]⁺ (40), 475.31 (42), 235.88 (15), 155.88 (26), 148.83 (32), 117.86(100).

1,2-Bis[o-(N-methylidenamino-3-p-chlorophenyl-5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]ethane (4e). Yield 75%; m.p. 213-214 °C; IR ν (cm⁻¹): 1598 (C=N), 695, 723, 758, 834 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 4.02 (s, 4H, OCH₂), Ar-H: [7.01-7.10 (m, 3H), 7.30-7.37 (m, 6H), 7.42-7.55 (m, 10H), 7.64-7.73 (m, 3H), 7.81 (d, 3H), 7.94 (m, 1H)], 8.30(s, 2H, CH); ¹³C-NMR (DMSO-d₆) δ (ppm): 164.68 (2C, N=CH), 149.85 (2C, triazole C₃), 149.10 (2C, triazole C₅), Ar-C: [158.47(2C), 134.85 (2C), 134.46 (2C), 129.74 (4C), 129.56 (4C), 128.74 (4C), 128.57 (4C), 128.17 (2C), 127.01 (2C), 126.07 (2C), 125.11 (2C), 119.35 (2C), 113.51 (2C)], 66.87 (2C, OCH₂); LC-MS/MS, m/z (I, %) for C₄₄H₃₂Cl₂N₈O₂ (m.w.: 775.70 g/mol): 798.11 [M+Na⁺]⁺ (18), 775.13 [M⁺]⁺ (10), 166.84 (15), 164.84 (43), 134.83(100).

1,3-Bis[o-(N-methylidenamino-3-p-chlorophenyl-5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]propane (4f). Yield 77%; m.p. 189-190 °C; IR: 1597 (C=N), 690, 723, 757, 833 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 1.69 (bs, 2H, -CH₂-), 3.80 (bs, 4H, OCH₂), Ar-H: [6.99-7.14 (m, 6H), 7.44-7.56
(m, 12H), 7.83-7.99 (m, 8H), 8.70 (s, 2H, CH); \(^{13}\)C-NMR (DMSO-d\text{6}) \(\delta\) (ppm): 163.88 (2C, N=CH), 149.08 (2C, triazol C\text{3}), 148.21 (2C, triazol C\text{5}), Ar-C: [157.41 (2C), 133.99 (2C), 133.47 (2C), 128.89 (4C), 127.78 (4C), 127.66 (4C), 127.24 (4C), 126.03 (2C), 125.35 (2C), 124.35 (2C), 124.23 (2C), 119.99 (2C), 118.25 (2C), 111.91 (2C)], 63.31 (2C, OCH\text{2}), 26.79 (CH\text{2}); LC-MS/MS, m/z (I, %) for C\text{45}H\text{34}Cl\text{2}N\text{8}O\text{2} (m.w.: 789.72 g/mol): 811.19 [M+Na\text{+}] \text{+} (60), 789.31 [M\text{+}] \text{+} (56), 559.18 (13), 256.03 (53), 134.93 (84), 104.86 (100).

Synthesis of reduced compounds 5\text{a-f}

The corresponding compound 4\text{a-f} (0.005 mol) was dissolved in dried methanol (50 mL) and NaBH\text{4} (0.01 mol) was added in small portions to this solution. The mixture was refluxed for 20 min and then allowed to cool. After evaporation at 30-35 °C under reduced pressure, the solid residue was washed with cold water. After drying \textit{in vacuo}, the solid product was recrystallized from an appropriate solvent (1:1 ethanol-water, unless otherwise noted) to afford the desired compound.

\textit{1,2-Bis\{o-(N-methylamino-3,5-diphenyl-4H-1,2,4-triazole-4-yl)-phenoxy\}ethane (5\text{a})}. Yield 85%; m.p. 242-243 °C; IR: 3245 (NH), 1600 (C=N), 690, 720, 756 cm\textsuperscript{-1} (aromatic ring); \(^{1}\)H-NMR (DMSO-d\text{6}) \(\delta\) (ppm): 3.63 (d, 4H, -NH-CH\text{2}), 3.86 (s, 4H, OCH\text{2}), 6.95 (t, 2H, NH), Ar-H: [6.70 (d, 6H), 7.09-7.16 (m, 2H), 7.42 (m, 12H), 7.85-7.90 (m, 8H); \(^{13}\)C-NMR (DMSO-d\text{6}) \(\delta\) (ppm): 153.57 (2C, triazole C\text{3}), 153.57 (2C, triazole C\text{5}), Ar-C: [156.20 (2C), 130.02 (2C), 129.47 (4C), 129.05 (2C), 128.29 (8C), 127.68 (8C), 126.97 (4C), 124.31 (2C), 120.11 (2C), 111.47 (2C)], 65.96 (2C, OCH\text{2}), 48.78 (2C, CH\text{2}-NH); LC-MS/MS, m/z (I, %) for C\text{44}H\text{38}N\text{8}O\text{2} (m.w.: 710.84 g/mol): 733.22 [M+Na\text{+}] \text{+} (15), 711.22 [M\text{+}] \text{+} (35), 490.18 (8), 269.02 (11), 221.96 (28), 147.85 (100).

\textit{1,3-Bis\{o-(N-methylamino-3,5-diphenyl-4H-1,2,4-triazole-4-yl)-phenoxy\}propane (5\text{b})}. Yield 74%; m.p. 216-217 °C; IR: 3253 (NH), 1601 (C=N), 694, 717, 745 cm\textsuperscript{-1} (aromatic ring); \(^{1}\)H-NMR (DMSO-d\text{6}) \(\delta\) (ppm): 1.88 (q, 2H, -CH\text{2}), 3.55 (bs, 4H, OCH\text{2} + 4H, -NH-CH\text{2}), 7.04 (m, 2H, 2NH + 2H, Ar-H), Ar-H: [6.66 (m, 4H), 7.47 (bs, 14H), 7.94 (bs, 8H); \(^{13}\)C-NMR (DMSO-d\text{6}) \(\delta\) (ppm): 153.65 (2C, triazole C\text{3}), 153.65 (2C, triazole C\text{5}), Ar-C: [156.24 (2C), 130.02 (2C), 129.47 (4C), 129.07 (2C), 128.34 (8C), 127.76 (8C), 127.07 (4C), 123.31 (2C), 119.81 (2C), 111.09 (2C)], 63.90 (2C, OCH\text{2}), 48.87 (2C, CH\text{2}-NH), 28.17 (CH\text{3}); LC-MS/MS, m/z (I, %) for C\text{45}H\text{40}N\text{8}O\text{2} (m.w.: 724.87 g/mol): 747.26 [M+Na\text{+}] \text{+} (95), 725.28 [M+1\text{+}] \text{+} (100), 272.98 (52), 234.97 (100), 104.86 (16).

\textit{1,2-Bis\{o-(N-methylamino-3-p-tolyl,5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy\}ethane (5\text{c})}. Yield 79%; m.p. 192-193 °C; IR: 3261(NH), 1601(C=N), 690, 729, 748, 820 cm\textsuperscript{-1} (aromatic ring); \(^{1}\)H-NMR (DMSO-d\text{6}) \(\delta\) (ppm): 2.29 (s, 6H, CH\text{3}), 3.64 (d, 4H, -NH-CH\text{2}-), 3.88 (s, 4H, OCH\text{2}), 6.92 (t, 2H, NH), Ar-H: [6.72 (d, 4H), 7.22 (d, 4H), 7.37-7.43 (m, 10H), 7.78-8.77 (m, 8H); \(^{13}\)C-NMR (DMSO-d\text{6}) \(\delta\) (ppm): 153.51 (2C, triazole C\text{3}), 153.47 (2C, triazole C\text{5}), Ar-C: [156.23 (2C), 130.02 (2C), 129.47 (4C), 128.89 (4C), 128.23 (4C), 127.71 (4C), 127.53 (4C), 127.05 (2C), 124.20 (2C), 123.48 (2C), 120.14 (2C), 111.48 (2C)], 65.98 (2C, OCH\text{2}), 48.76 (2C, CH\text{2}-NH), 28.17 (CH\text{3}); LC-MS/MS, m/z (I, %) for C\text{46}H\text{42}N\text{8}O\text{2} (m.w.: 748.87 g/mol): 740.30 [M+2\text{+}] \text{+} (55), 739.23 [M+1\text{+}] \text{+} (100), 414.95 (12), 370.13 (15), 216.93 (16), 156.88 (38).
1,3-Bis[(N-methylamino-3-p-tolyl,5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]propane (5d). Yield 78%; m.p. 181-182 °C; IR: 3249 (NH), 1601 (C=N), 692, 729, 749, 823 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 2.33 (s, 6H, CH₃), 1.89 (q, 2H, -CH₂-), 3.76 ( bs, 4H, OCH₂ + 4H, -NH-CH₂), 7.04 (t, 2H, NH), Ar-H: [6.63-6.74 (m, 6H), 7.11-7.16 (m, 2H), 7.26-7.37 (m, 5H), 7.45 (m, 5H), 7.82-7.93 (m, 8H)]; ¹³C-NMR (DMSO-d₆) δ (ppm): 153.57 (2C, triazole C₃), 153.48 (2C, triazole C₅), Ar-C: [156.25 (2C), 159.27 (2C), 129.97 (2C), 129.44 (2C), 129.05 (2C), 128.94 (4C), 128.28 (4C), 127.77 (4C), 127.62 (4C), 127.12 (2C), 124.29 (2C), 123.37 (2C), 119.82 (2C), 111.06 (2C)], 63.93 (2C, OCH₂), 28.19 (C, CH₂), 48.82 (2C, CH₂-NH), 20.83 (2C, CH₃); LC-MS/MS, m/z (I, %) for C₄₇H₄₄N₈O₂ (m.w.: 752.85 g/mol): 775.23 [M+Na]+ (65), 753.33 [M+1]+ (100), 235.94 (5), 105.02 (5).

1,2-Bis[(N-methylamino-3-p-chlorophenyl,5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]ethane (5e). Yield 69%; m.p. 219-220 °C (from 1:2 ethanol-water); IR: 3249 (NH), 1601 (C=N), 689, 729, 749, 833 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 3.63 (bs, 4H, -NH-CH₂-), 3.89 (bs, 4H, -OCH₂), 6.99 (bs, 2H, NH), Ar-H: [6.71 (bs ,6H), 7.14 (bs, 2H), 7.45 (bs, 10H), 7.88 (m, 8H); ¹³C-NMR (DMSO-d₆) δ (ppm): 153.81 (2C, triazole C₃), 152.65 (2C, triazole C₅), Ar-C: [156.21 (2C), 134.27 (2C), 130.20 (2C), 129.65 (2C), 129.35 (4C), 128.41 (4C), 128.30 (4C), 127.66 (2C), 126.79 (2C), 125.78 (2C), 123.29 (2C), 120.14 (2C), 111.40 (2C)], 65.95 (2C, OCH₂), 48.79 (2C, CH₂-NH); LC-MS/MS, m/z (I, %) for C₄₄H₃₆Cl₂N₈O₂ (m.w.: 778.24 g/mol): 801.12 [M+Na]⁺ (48), 779.15 [M+1]+ (18), 747.26 (21), 725.22 (20), 214.93 (13), 164.84 (43), 134.83 (100).

1,3-Bis[(N-methylamino-3-p-chlorophenyl,5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]propane (5f). Yield 72%; m.p. 126-127 °C (from 1:2 ethanol-water); IR: 3291(NH), 1601(C=N), 690, 734, 754, 835 cm⁻¹ (aromatic ring); ¹H-NMR (DMSO-d₆) δ (ppm): 1.89 (bs, 2H, -CH₂-), 3.75 ( bs, 4H, OCH₂ + 4H, -NH-CH₂ ), 7.08 ( m,2H, 2NH + 2H, Ar-H ), Ar-H: [6.65(m, 6H), 7.50 (m, 10H), 7.93 (m, 8H)]; ¹³C-NMR (DMSO-d₆) δ (ppm): 153.81 (2C, triazole C₃), 152.78 (2C, triazole C₅), Ar-C: [156.21 (2C), 134.29 (2C), 130.11 (2C), 129.68 (2C), 129.44 (4C), 129.15 (2C), 128.45 (4C), 128.30 (4C), 127.69 (2C), 126.79 (2C), 125.69 (2C), 123.29 (2C), 120.14 (2C), 111.40 (2C)], 64.20 (2C, OCH₂), 48.82 (2C, CH₂-NH); LC-MS/MS, m/z (I, %) for C₄₅H₃₈Cl₂N₈O₂ (m.w.: 792.25 g/mol): 815.26 [M+Na]⁺ (100), 793.15 [M+1]+ (18), 747.26 (21), 725.22 (20), 214.93 (13), 164.84 (43), 134.83 (100).

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