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Full Paper

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 $NaBH_4$ 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, ^{1}H-NMR, ^{13}C-NMR and mass spectral data.

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

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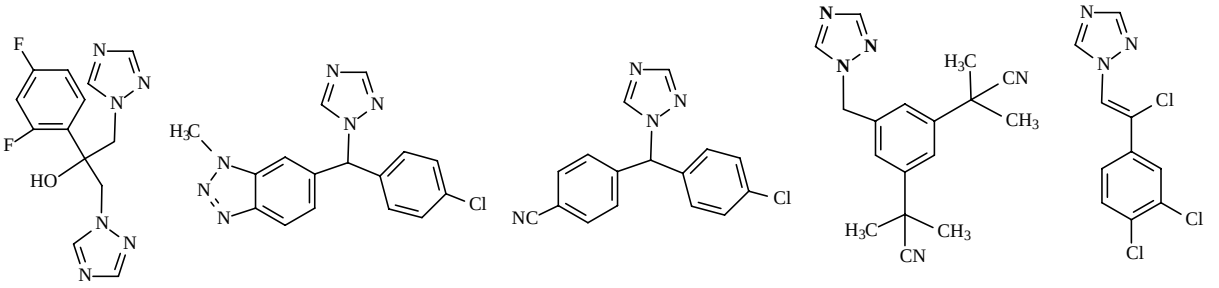
Introduction

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 threatment of cancer [18] and loreclezole is used as an anticonvulsant [19].

Figure 1



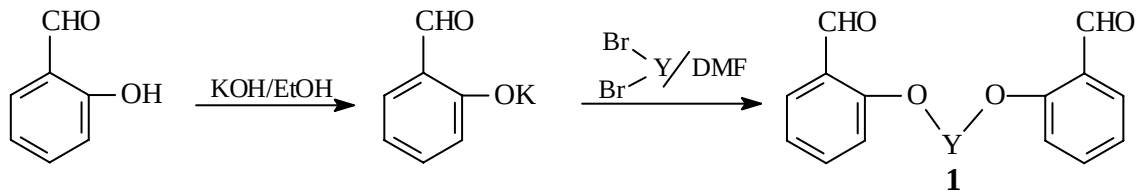
Fluconazole **Vorozole** **Letrozole** **Anastrozole** **Loreclezole**

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 **3** with bis-aldehydes **1** and their corresponding reduced derivatives were synthesized and characterized by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral data.

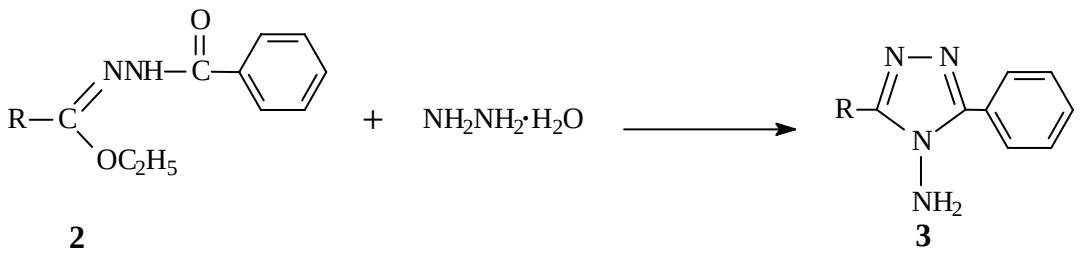
Results and Discussion

The syntheses of the 1,2/1,3-bis[o-(N-methylidenamino-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).

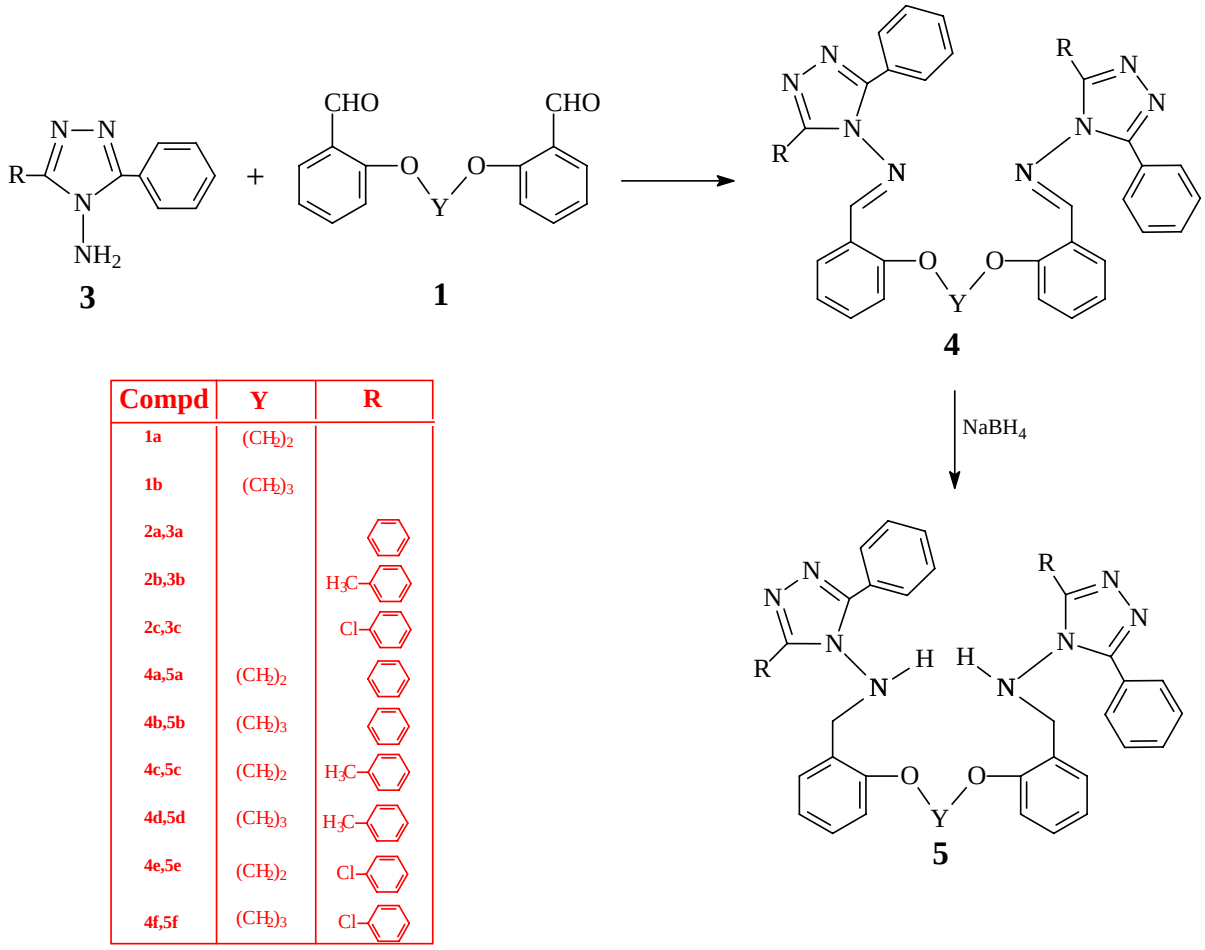
Scheme 1



Scheme 2



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=C<u>H</u> group were observed at δ 8.23-8.70 ppm. The ^{13}C-NMR signals for the –N=<u>C</u>H- group were recorded at δ 164 ppm. Reduced compounds **5** showed IR absorption bands around 3245-3290 cm^{-1} (υ_{NH}). The ^{1}H-NMR signals for the -NH-C<u>H</u>$_2$- group of these compounds were observed as a doublet or strong singlet at around δ 3.55-3.75 ppm and the proton signals of –N<u>H</u>-CH$_2$- groups were recorded as a triplet or strong singlet between δ 6.95-7.08 ppm. The NH-<u>C</u>H$_2$- carbon signals of compounds **5** were recorded at δ 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 δ 148-149 ppm and the triazole C3 and C5 signals of the reduced compounds **5** were observed between δ 152-153 ppm.

Conclusions

In this study, a convenient method was established for the synthesis in good yields of bis[o-(N-methylidenamino-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, 759, 839 (aromatic ring); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.37 (t, 3H, CH_3), 4.10 (q, 2H, CH_2), 7.44-7.75 (m, 5H, Ar-H), 8.13 (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-methylidenamino-3,5-diphenyl-4H-1,2,4-triazole-4-yl)-phenoxy]ethane (**4a**). Yield 70%; m.p. 212-213 °C; IR: 1598 (C=N), 693, 770 cm^{-1} (aromatic ring); ^{1}H-NMR (DMSO-d_6) δ (ppm): 3,98 (s, 4H, OCH_2), 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); ^{13}C-NMR (DMSO-d_6) δ (ppm): 164.44 (2C, N=CH), 149.87 (2C, triazole C_3), 149.87 (2C, triazole C_5), 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, OCH_2); LC-MS/MS, m/z (I, %) for $C_{44}H_{34}N_8O_2$ (m.w.: 706.81 g/mol): 729.26 $[M+Na]^+$ (50), 707.25 $[M+1]^+$ (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); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1,65 (q, 2H, -CH_2-), 3,77 (t, 4H, OCH_2), 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); ^{13}C-NMR (DMSO-d_6) δ (ppm): 164.73 (2C, N=CH), 150.00 (2C, triazole C_3), 150.00 (2C, triazole C_5), Ar-C: [158.36 (2C), 134.93 (2C), 129.60 (2C), 128.66 (8C), 128.23 (8C), 126.95 (4C), 126.48 (4C), 120.97 (2C), 119.29 (2C), 112.93 (2C)], 64.29 (2C, OCH_2), 27.75 (C, CH_2); LC-MS/MS, m/z (I, %) for $C_{45}H_{36}N_8O_2$ (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); ^{1}H-NMR (DMSO-d_6) δ (ppm): 2,52 (s, 6H, CH_3), 4,00 (s, 4H, OCH_2), 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); ^{13}C-NMR (DMSO-d_6) δ (ppm): 164.34 (2C, N=CH), 149.90 (2C, triazole C_3), 149.72 (2C, triazole C_5), 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, OCH_2), 20.73 (2C, CH_3); LC-MS/MS, m/z (I, %) for $C_{46}H_{38}N_8O_2$ (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-tolyl-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); ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.51 (s, 6H, CH_3), 1,69 (q, 2H, -CH_2-), 3,78 (t, 4H, OCH_2), Ar-H: [6.98-7.13 (m, 4H), 7.24 (m, 4H), 7.49 (m, 10H), 7.78 (m, 3H), 7.82 (m, 3H), 7.98 (m, 2H)], 8.69 (s, 2H,CH); ^{13}C-NMR (DMSO-d_6) δ (ppm): 164.65 (2C, N=CH), 150.04 (2C, triazole C_3), 149.87 (2C, triazole C_5), 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, OCH_2), 27.72 (C, CH_2), 20.68 (2C, CH_3); LC-MS/MS, m/z (I, %) for $C_{47}H_{40}N_8O_2$ (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 υ (cm^{-1}): 1598 (C=N), 695, 723, 758, 834 cm^{-1} (aromatic ring); ^{1}H-NMR (DMSO-d_6) δ (ppm): 4,02 (s, 4H, OCH_2), 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); ^{13}C-NMR (DMSO-d_6) δ (ppm): 164.68 (2C, N=CH), 149.85 (2C, triazole C_3), 149.10 (2C, triazole C_5), 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), 121.36 (2C), 119.35 (2C), 113.51 (2C)], 66.87 (2C, OCH_2); LC-MS/MS, m/z (I, %) for $C_{44}H_{32}Cl_2N_8O_2$ (m.w.: 775.70 g/mol): 798.11 $[M+Na]^+$ (20), 775.13 $[M]^+$ (18), 255.93 (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-triazol-4-yl)-phenoxy]propane (**4f**). Yield 77%; m.p. 189-190 °C; IR: 1597 (C=N), 690, 723, 757, 833 cm^{-1} (aromatic ring); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1,69 (bs, 2H, -CH_3-), 3,80 (bs, 4H, OCH_2), 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_6) δ (ppm): 163.88 (2C, N=CH), 149.08 (2C, triazol C_3), 148.21 (2C, triazol C_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_2), 26.79 (CH_2); LC-MS/MS, m/z (I, %) for $C_{45}H_{34}Cl_2N_8O_2$ (m.w.: 789.72 g/mol): 811.19 $[M+Na]^+$ (60), 789.31 $[M]^+$ (56), 559.18 (13), 256.03 (53), 134.93 (84), 104.86 (100).

Synthesis of reduced rompounds **5a-f**

The corresponding compound **4a-f** (0.005 mol) was dissolved in dried methanol (50 mL) and $NaBH_4$ (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 *in vacuo*, the solid product was recrystallized from an appropriate solvent (1:1 ethanol-water, unless otherwise noted) to afford the desired compound.

1,2-Bis[o-(N-methylamino-3,5-diphenyl-4H-1,2,4-triazole-4-yl)-phenoxy]ethane (**5a**). Yield 85%; m.p. 242-243 °C; IR: 3245 (NH), 1600 (C=N), 692, 720, 756 cm^{-1} (aromatic ring); ^{1}H-NMR (DMSO-d_6) δ (ppm): 3.63 (d, 4H, -NH-CH_2), 3.86 (s, 4H, OCH_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_6) δ (ppm): 153.57 (2C, triazole C_3), 153.57 (2C, triazole C_5), Ar-C: [156.20 (2C), 130.02 (2C), 129.47 (4C), 129.05 (2C), 128.29 (8C), 127.68 (8C), 126.97 (4C), 123.41 (2C), 120.11 (2C), 111.47 (2C)], 65.96 (2C, OCH_2), 48.78 (2C,CH_2-NH); LC-MS/MS, m/z (I, %) for $C_{44}H_{38}N_8O_2$ (m.w.: 710.84 g/mol): 733.22 $[M+Na]^+$ (15), 711.22 $[M+1]^+$ (35), 490.18 (8), 269.02 (11), 221.96 (28), 147.85 (100).

1,3-Bis[o-(N-methylamino-3,5-diphenyl-4H-1,2,4-triazole-4-yl)-phenoxy]propane (**5b**). Yield 74%; m.p. 216-217 °C; IR: 3253 (NH), 1601 (C=N), 694, 717, 745 cm^{-1} (aromatic ring); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.88 (q, 2H, -CH_2-), 3.55 (bs, 4H, OCH_2 + 4H, -NH-CH_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_6) δ (ppm): 153.65 (2C, triazole C_3), 153.65 (2C, triazole C_5), Ar-C: [156.24 (2C), 129.96 (2C), 129.54 (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_2), 48.87 (2C, CH_2-NH), 28.17 (CH_2); LC-MS/MS, m/z (I, %) for $C_{45}H_{40}N_8O_2$ (m.w.: 724.87 g/mol): 747.26 $[M+Na]^+$ (95), 725.28 $[M+1]^+$ (100), 272.98 (52), 234.97 (100), 104.86 (16).

1,2-Bis[o-(N-methylamino-3-p-tolyl,5-phenyl-4H-1,2,4-triazole-4-yl)-phenoxy]ethane (**5c**). Yield 79%; m.p. 192-193 °C; IR: 3261(NH), 1601(C=N), 690, 729, 748, 820 cm^{-1} (aromatic ring); ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.29 (s, 6H, CH_3), 3.64 (d, 4H, -NH-CH_2-), 3.88 (s, 4H, OCH_2), 6.92 (t, 2H, NH), Ar-H: [6.72 (d, 4H), 7.22 (d, 4H), 7.37-7.43 (m, 10H), 7.78-7.87 (m, 8H); ^{13}C-NMR (DMSO-d_6) δ (ppm): 153.51 (2C, triazole C_3), 153.47 (2C, triazole C_5), Ar-C: [156.23 (2C), 139.15 (2C), 130.03 (2C), 129.40 (2C), 129.04 (2C), 128.92 (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_2), 48.76 (2C, CH_2-NH), 20.80 (2C, CH_3); LC-MS/MS, m/z (I, %) for $C_{46}H_{42}N_8O_2$ (m.w.: 738.65 g/mol): 740.30 $[M+2]^+$ (55), 739.23 $[M+1]^+$ (100), 414.95 (12), 370.13 (15), 216.93 (16), 156.88 (38).

1,3-Bis[o-(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); ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.33 (s, 6H, CH_3), 1.89 (q, 2H, -CH_2-), 3.76 (bs, 4H, OCH_2 + 4H, -NH-CH_2), 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)]; ^{13}C-NMR (DMSO-d_6) δ (ppm): 153.57 (2C, triazole C_3), 153.48 (2C, triazole C_5), Ar-C: [156.25 (2C), 139.22 (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, OCH_2), 28.19 (C, CH_2), 48.82 (2C, CH_2-NH), 20.83 (2C, CH3); LC-MS/MS, m/z (I, %) for $C_{47}H_{44}N_8O_2$ (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[o-(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); ^{1}H-NMR (DMSO-d_6) δ (ppm): 3.63 (bs, 4H, -NH-CH_2-), 3.89 (bs, 4H, -OCH_2), 6.99 (bs, 2H, NH), Ar-H: [6.71 (bs ,6H), 7.14 (bs, 2H), 7.45 (bs, 10H), 7.88 (m, 8H); ^{13}C-NMR (DMSO-d_6) δ (ppm): 153.81 (2C, triazole C_3), 152.65 (2C, triazole C_5), Ar-C: [156.21 (2C), 134.27 (2C), 130.20 (2C), 129.65 (2C), 129.35 (4C), 129.17 (4C), 128.41 (4C), 128.30 (4C), 127.66 (2C), 126.79 (2C), 125.69 (2C), 123.29 (2C), 120.14 (2C), 111.40 (2C)], 65.95 (2C, OCH_2), 48.79 (2C, CH_2-NH); LC-MS/MS, m/z (I, %) for $C_{44}H_{36}Cl_2N_8O_2$ (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[o-(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); ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.89 (bs, 2H, -CH_2-), 3.75 (bs, 4H, OCH_2 + 4H, -NH-CH_2), 7.08 (m,2H, 2NH + 2H, Ar-H), Ar-H: [6.65(m, 6H), 7.50 (m, 10H), 7.93 (m, 8H)]; ^{13}C-NMR (DMSO-d_6) δ (ppm): 153.81 (2C, triazole C_3), 152.78 (2C, triazole C_5), 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 (4C), 126.90 (2C), 125.78 (2C), 123.17 (2C), 119.78 (2C), 110.94 (2C)], 64.20 (2C, OCH_2), 48.82 (2C, CH_2-NH), 28.19 (C, CH_2); LC-MS/MS, m/z (I, %) for $C_{45}H_{38}Cl_2N_8O_2$ (m.w.: 792.25 g/mol): 815.26 $[M+Na]^+$ (100), 793.25 $[M+1]^+$ (45), 563.18 (28), 283.10 (12), 34.93 (15).

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