Novel Bis(2-(5-((5-phenyl-1*H*-tetrazol-1-yl)methyl)-4*H*-1,2,4-triazol-3-yl) phenoxy)Alkanes: Synthesis and Characterization

Aamer Saeed,* Muhammad Qasim, and Majid Hussain

Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan
*E-mail: aamersaeed@yahoo.com

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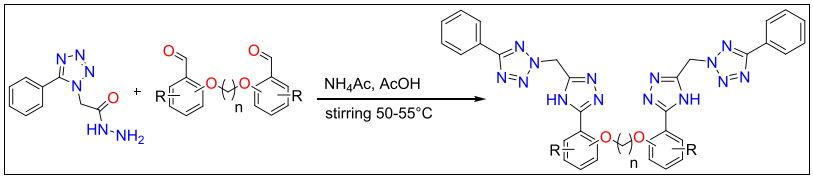

In this study, 10 different substituted aromatic bis-benzaldehydes were synthesized by treating hydroxy benzaldehydes with various dihaloalkanes. Bis aldehydes **5a–j** were treated with 2-(5-phenyl-1*H*-tetrazole-1-yl) acetohydrazide **(4)** in acidic medium and in the presence of ammonium acetate to yield a series of new isomeric bis(2-(5-((5-phenyl-1*H*-tetrazol-1-yl)methyl)-4*H*-1,2,4-triazol-3-yl)phenoxy)alkanes **(6a–j)** in excellent to good yield. The newly synthesized compounds were characterized by the available spectroscopic analysis.

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INTRODUCTION

An azole is a class of five-membered nitrogen heterocyclic ring compounds, which have attained a valuable scope over the last decade due its broad range of applications in pharmaceutical, agrochemical, and material science.

Tetrazole, a subclass of azoles is such a unique nucleus, which possesses both energetic and medicinal applications. Polynitrogen compounds are used as a propellant [1,2] due to their use for high-energy density materials (HEDM), whose crucial characteristic from an energetic point of view is the ratio between the energy released in a fragmentation reaction and the specific weight. The formation of nitrogen molecule only in such processes renders nitrogen clusters as eco-caring HEDMs. In medicinal chemistry, tetrazole derivatives are used as an antihypertensive [3], antimycobacterial [4], anti-inflammatory [5], anticonvulsant [6], hypoglycemic [7], antibacterial [8], and antifungal [9] agents.

On the other hand, 1,2,4-triazole is equally important nucleus in competition with tetrazoles based on its applications. 1,2,4-Triazole ring with various pharmacological effects has been reported as therapeutic agents. Compounds bearing triazole moieties such as anastrozole, vorozole, and letrozole appear to be very effective aromatase inhibitors for preventing breast cancer. It strongly interacts with the heme iron and aromatic substituents in the active site of aromatase [10]. This nucleus not only possesses antimicrobial [11], antitumor [12], antimalarial [13], anti-inflammatory [14], and antifungal [15] but also corrosion inhibitory [16] activities. Additionally, substituted 1,2,4-triazoles also have attracted substantial notice in coordination chemistry due to their rich and versatile coordination properties. Their iron (II) complexes show intriguing spin-crossover properties for potential use in molecular electronics, as information storage and switching materials [17–19].

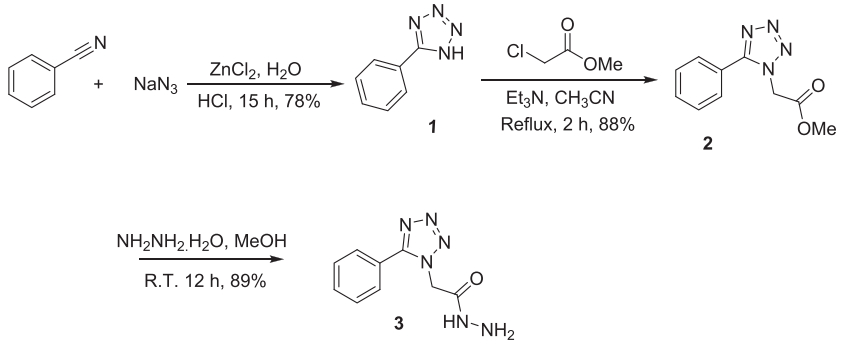
Keeping in view the immense biological importance of these two nuclei and in continuation of our interest on the synthesis of biologically active heterocycles [19,20], herein, we describe the construction of molecules with these biolabile rings together in a single molecular frame work by molecular hybridization.

RESULTS AND DISCUSSION

Synthesis of the easily accessible 2-(5-phenyl-1*H*-tetrazole-1-yl)acetohydrazide was carried out according to Scheme 1. Thus, 5-phenyl-1,2,3,4-tetrazole **1** was synthesized by the cycloaddition reaction of benzonitrile with sodium azide in the presence of zinc chloride as a catalyst in aqueous medium. An improved synthesis of 2-(5-phenyl-1*H*-tetrazole-1-yl)acetate (**2**) was achieved by use of triethylamine and high dielectric solvent acetonitrile followed by recrystallization from *n*-hexane. In FTIR, the presence of vibrational stretching at 1756 cm^{-1} confirmed the attachment of ester moiety. In ^{1}H NMR, the two protons singlet at 5.94 ppm was assigned to methylene protons, whereas a three-proton singlet appeared at 3.75 ppm for ester methyl group. In ^{13}C NMR spectrum, the signal at 167.11 ppm was observed for ester carbonyl carbon.

Reaction of ester **2** with slight excess of hydrazine hydrate in dry methanol at 45–50°C afforded the acetohydrazide **3**. In FTIR, the stretchings at 3132 (–NH) and 3307 ($–NH_2$) cm^{-1} confirmed the conversion of ester into hydrazide. In ^{1}H NMR spectrum, the singlet at

Scheme 1. Synthesis of 2-(5-Phenyl-1*H*-tetrazole-1-yl) acetohydrazide (**3**).



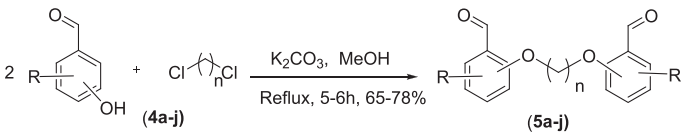
4.46 ppm was assigned to (NH_2) and that at 9.65 ppm to (–NH) proton, respectively. In ^{13}C NMR spectrum, upfield shift of carbonyl signal at 164.6 ppm confirmed conversion of ester into hydrazide.

A variety of bis aldehydes were synthesized according to route illustrated in Scheme 2. Anhydrous potassium carbonate was used to abstract the acidic proton of different isomeric hydroxybenzaldehydes **4a–j**. The resulting phenoxide ions were reacted with different dihaloalkanes ($n = 3,4,6$) to afford a series of bis aldehydes **5a–j**. In FTIR, the absence of broad band of hydroxyl group and the presence of stretching frequency at 1185 cm^{-1} confirmed the formation of ether linkage, see Scheme 3.

Finally, the cyclization of 2-(5-phenyl-1*H*-tetrazole-1-yl)acetohydrazide **(3)** with aromatic bis aldehydes **4a–j** was carried out in acidic medium in the presence of an excess of ammonium acetate to furnish **6a–j**. Mechanistically, the initial reaction of **3** with bis aldehydes **4a–j** may lead to the formation of Schiff bases. Subsequent attack of the hydrazide moiety to the electrophilic carbon of the Schiff bases followed by heterocyclization in the presence of ammonia from ammonium acetate affords the 1,2,4-triazoles.

In FTIR, the absence of carbonyl stretching in all synthesized compounds and the presence of absorption in the region of 3428–3435 cm^{-1} attributed to N–H of

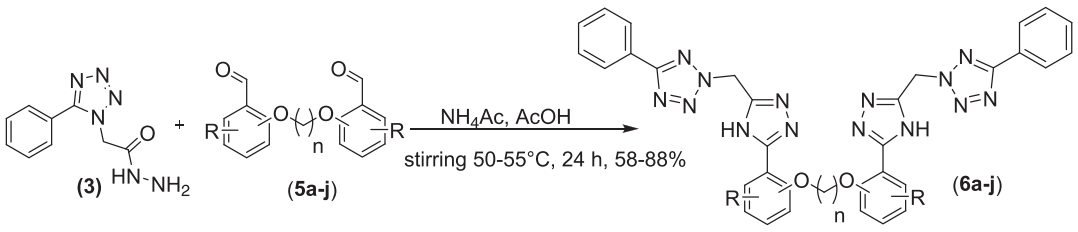
Scheme 2. Synthesis of 2,2′-(alkane-1,3-diylbis(oxy))dibenzaldehydes (**5a–j**).



4a-c; OH=ortho, R=H
4d-f; OH=meta, R=H
5g-i; OH=para, R=H
5j; OH=para, R=3-OMe

5a-c; n=3, 4, 6, R=H
5d-f; n=2, 4, 6, R=H
5g-i; n=3, 4, R=H
5j; n=6, R=3-OMe

Scheme 3. Bis(2-(5-((5-phenyl-1*H*-tetrazol-1-yl)methyl)-4*H*-1,2,4-triazol-3-yl)phenoxy)alkanes (**6a–j**).



6a-c; n= 3, 4, 6, R= H
6d-f; n= 2, 4, 6, R= H
6g-i; n= 3, 4, 6, R= H
6j; n= 6, R= 3-OMe

triazole ring confirms the functional group interconversion. ^{1}HNMR reveals the presence of signal at 11–11.5 ppm and the absence of signals of NH_2 of hydrazide indicated the formation of 4*H*-1,2,4-triazole. In ^{13}C NMR spectrum, the absence of characteristic signal of carbonyl carbon of aldehydes at 210 ppm and the presence of signal at 158–165 ppm for carbons of triazole ring is another strong evidence for the formation of 1,2,4-triazole. In GC-MS spectral analysis, the molecular ion peak was observed in almost all compounds. The base peak was observed at $m/z = 196$.

CONCLUSION

In the present study, the molecular hybridization of triazole and tetrazole followed by their connection via phenoxy ether linkage leading to symmetrical molecules with four rings has been carried out. The new scaffold incorporates biologically important pharmacophores in a single molecular frame work, and the possibility of introduction of different substituents in the aromatic ring as well as variable spacer chain length indicates their potential diversity leading to molecules for use in drug discovery.

EXPERIMENTAL

Melting points were recorded using a digital Gallenkamp (SANYO, Loughborough, UK) model MPD BM 3.5 apparatus and were uncorrected. ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$ at 300 and 75 MHz, respectively, using Bruker AM-300 spectrophotometer (Billerica, Middlesex, MA, USA). FT-IR spectra were recorded using Rad Excalibur FTS 3000 MX spectrophotometer (Madison, WI, USA). Mass spectra (EI, 70 eV) were recorded on a GC–MS instrument (Agilent Technologies 1200 series, Santa Clara, CA, USA), and elemental analyses were carried out with a LECO-183 CHNS analyzer (LECO Corporation, St Joseph, MI, USA).

Synthesis of 5-phenyl tetrazole (1). 5-Phenyl tetrazole was synthesized by a one of the most convenient routes reported by Sharpless et al. [21]. A mixture of sodium azide (3 mmol), benzonitrile (2 mmol), and zinc (II) chloride (3 mmol) was suspended in H_2O (16 mL). The reaction mixture was heated under reflux for 15 h. After consumption of nitriles, the mixture was cooled at room temperature and filtered. In continuation of workup, the solid residue was treated with 3 N HCl (4 mL) to afford pure product. White solid, yield: 78%; mp = 216°C [17]; ^{1}H-NMR (DMSO-d_6, δ/ppm) 7.59–7.62 (m, 3H, Ar–H), 8.02–8.06 (m, 2H, Ar–H), ^{13}C NMR (DMSO-d_6, δ/ppm) 124.55–131.73 (Ar), 155.79 (tetrazole ring carbon).

Synthesis of methyl 2-(5-phenyl-1*H*-tetrazole-1-yl)acetate (2). Methyl chloroacetate was refluxed (0.523 mL, 6 mmol) in 15 mL of acetonitrile. Then a stirred mixture of 5-phenyl tetrazole (**1**) (0.438 g, 3 mmol), triethylamine (1.674 mL, 12 mmol), and acetonitrile (25 mL) was added dropwise. The reaction mixture was heated on oil bath for 2 h keeping the temperature 82°C. The reaction was monitored by TLC. Acetonitrile was removed under reduced pressure and product was recrystallized in *n*-hexane to get pure methyl 2-(5-phenyl-1*H*-tetrazole-1-yl)acetate. White crystalline solid, yield: 88%; mp = 98–100°C:. IR (neat) cm^{-1}: 1281 (N═N–N), 1547 (Ar–C═C), 1606 (C═N), 1756 (C═O), 2854 (CH_3), 3067 (Ar–C–H); ^{1}H-NMR (DMSO-d_6, δ/ppm) 3.75 (s, 2H, CH_3), 5.93 (s, 2H, CH_2), 7.56–7.59 (m, 3H, Ar–H), δ 8.06–8.10 (m, 2H, Ar–H). ^{13}C NMR (DMSO-d_6, δ/ppm) 53.43, 53.83 ($\underline{CH_2}$C═O, OCH_3), 126.85–131.28 (Ar), 164.85 (tetrazole ring carbon), 167.11 (C═O).

Synthesis of 2-(5-Phenyl-1*H*-tetrazole-1-yl)acetohydrazide (3). To a solution of tetrazole-ester **(2)** (0.218 g, 1.0 mmol) in 10 mL of dry distilled methanol was added hydrazine hydrate (2 mmol). The reaction mixture was stirred at room temperature for 12 h. The reaction was monitored by TLC. The precipitates obtained were filtered, washed with methanol to obtain tetrazole-hydrazide **(3)**. White crystalline solid, yield: 89%; mp = 212°C:. IR (neat) cm^{-1}: 1280 (N═N–N), 1549 (Ar-C═C), 1608 (C═N), 1659 (C═O), 3057 (Ar–C–H), 3132 (N–H), 3307 (NH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 4.46 (s, 2H, NH_2), 5.45 (s, 2H, CH_2), 7.55–7.61 (m, 3H, Ar–H), 8.05–8.08 (m, 2H, Ar–H), 9.65 (s, 1H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 54.14 ($\underline{CH_2}$C═O), 126.78–131.12 (Ar), 163.99 (tetrazole ring carbon), 164.62 (C═O).

General procedure for the synthesis of bis aldehydes (5a–j). Suitable substituted hydroxybenzaldehydes (**4a–j**) (0.2 mmol) were refluxed with different dihaloalkanes (0.1 mmol) using anhydrous potassium carbonate (0.1 mmol) in dry acetone for 4–5 h. The completion of reaction was checked by TLC. On completion, the reaction mixture was filtered and the residue was washed with dry hot acetone. Filtrate was evaporated to afford pure crystalline products (**5a–j**) in each case in 80–86% yields.

2,2′-(Propane-1,3-diylbis(oxy))dibenzaldehyde (5a). IR (neat) cm^{-1}: 1553 (Ar–C═C), 1725 (C═O), 3052 (Ar–C–H), 2903 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 2.18–2.27 (m, 2H, CH_2), 4.02 (t, $J = 11.93$ Hz, 4H, CH_2), 7.23–8.28 (m, 8H, Ar–H), 9.13 (s, 1H, CHO).

2,2′-(Butane-1,4-diylbis(oxy))dibenzaldehyde (5b). IR (neat) cm^{-1}: 1561 (Ar–C═C), 1734 (C═O), 3098 (Ar–C–H), 2909 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.53–1.69 (m, 4H, CH_2), 4.32–4.41 (t, $J = 11.82$ Hz, 4H, CH_2), 6.23 (s, 4H, CH_2), 7.21–8.34 (m, 8H, Ar–H), 9.76 (s, 1H, CHO).

2,2′-(Hexane-1,6-diylbis(oxy))dibenzaldehyde (5c). IR (neat) cm^{-1}:1575 (Ar–C═C), 1745 (C═O), 3043 (Ar–C–H), 2921 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.32–1.64 (m, 8H, CH_2), 4.01–4.12 (t, $J = 11.67$ Hz, 4H, CH_2), 7.32–8.76 (m, 8H, Ar–H), 9.53 (s, 2H, CHO).

3,3′-(Ethane-1,2-diylbis(oxy))dibenzaldehyde (5d). IR (neat) cm^{-1}: 1563 (Ar–C═C), 1774 (C═O), 3093 (Ar–C–H), 2903 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 4.31–4.42 (t, $J = 11.73$ Hz, 4H, CH_2), 7.65–8.89 (m, 8H, Ar–H), 9.74 (s, 2H, CHO).

3,3′-(Butane-1,4-diylbis(oxy))dibenzaldehyde (5e). IR (neat) cm^{-1}:1541 (Ar–C═C), 1723 (C═O), 3052 (Ar–C–H), 2906 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.63–1.73 (m, 4H, CH_2), 4.32–4.63 (t, $J = 11.82$ Hz, 4H, CH_2), 7.34–8.89 (m, 8H, Ar–H), 9.78 (s, 1H, CHO).

3,3′-(Hexane-1,6-diylbis(oxy))dibenzaldehyde (5f). IR (neat) cm^{-1}: 1585 (Ar–C═C), 1745 (C═O), 3081 (Ar–C–H), 2907 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.51–1.62 (m, 8H, CH_2), 4.20–4.32 (t, $J = 11.74$ Hz, 4H, CH_2), 7.22–8.95 (m, 8H, Ar–H), 9.62 (s, 2H, CHO).

4,4′-(Propane-1,3-diylbis(oxy))dibenzaldehyde (5g). IR (neat) cm^{-1}: 1543 (Ar–C=C), 1767 (C=O), 3061 (Ar–C–H), 2903 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 2.06–2.17 (m, 2H, CH_2), 4.01 (t, J = 11.86 Hz, 4H, CH_2), 7.15–8.34 (m, 8H, Ar–H), 9.32 (s, 1H, CHO).

4,4′-(Butane-1,4-diylbis(oxy))dibenzaldehyde (5h). IR (neat) cm^{-1}:1556 (Ar–C=C), 1727 (C=O), 3067 (Ar–C–H), 2901 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.61–1.71 (m, 4H, CH_2), 4.21–4.67 (t, J = 11.82 Hz, 4H, CH_2), 7.21–8.34 (m, 8H, Ar–H), 9.72 (s, 1H, CHO).

4,4′-(Hexane-1,6-diylbis(oxy))dibenzaldehyde (5i). IR (neat) cm^{-1}: 1563 (Ar–C=C), 1732 (C=O), 3054 (Ar–C–H), 2904 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.48–1.57 (m, 8H, CH_2), 4.19–4.24 (t, J = 11.74 Hz, 4H, CH_2), 7.10–8.76 (m, 8H, Ar–H), 9.45 (s, 2H, CHO).

4-((6-(4-Formyl-2-methoxyphenoxy)hexyl)oxy)-2-methoxybenzaldehyde (5j). IR (neat) cm^{-1}: 1535 (Ar–C=C), 1756 (C=O), 3082 (Ar–C–H), 2911 (CH_2); ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.43–1.64 (m, 8H, CH_2), 3.32 (s, 6H, OCH_3), 4.75–4.89 (t, J = 11.81 Hz, 4H, CH_2), 6.81–8.72 (m, 6H, Ar–H), 7.83 (s, 2H, CHO).

General procedure for the synthesis of bis(2-(5-((5-phenyl-1*H*-tetrazol-1-yl)methyl)-4*H*-1,2,4-triazol-3-yl)phenoxy)alkanes (6a–j). About 0.2 mol of 2-(5-phenyl-1*H*-tetrazol-1-yl) acetohydrazide (**3**) and 0.1 mol of bisaldehydes (**5a–j**) was dissolved in glacial acetic acid followed by the addition of a pinch of ammonium acetate, and resulting mixture was stirred for 24 h at room temperature. The reaction mixture was then neutralized with liquid ammonia solution, and the resulting precipitates were filtered and then washed with excess of water to obtain the pure product (**6a–j**) in 58–88% yields.

1,3-Bis(2-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)propane (6a). Yield: 78%; mp = 275–280°C: *Anal*. Calcd for $C_{35}H_{30}N_{14}O_2$: C, 61.94; H, 4.46; N, 28.89; Found C, 61.95; H, 4.47; N, 28.90; IR (neat) cm^{-1}: 3430 (N–H), 3161 (NCH), 3053 (ArCH), 1631 (C=N), 1567 (–N=N), 1131 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 2.28 (m, 2H, CH_2), 4.30 (t, J = 10.8 Hz, 4H, –OCH_2), 6.1 (s, 4H, NCH_2N), 7.01–8.63 (m, 18H, Ar–H), 11.96 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 29.21 (CH_2), 54.33 (NCH_2N), 65.16 (OCH_2), 113.15–141.28 (Ar), 157.46, 164.59 (triazole ring carbons), 166.47 (tetrazole ring carbon). MS, *m/z* (%): 678 $[M]^+$ (69), 196 (100), 315 (32), 357 (44), 476 (64).

1,4-Bis(2-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)butane (6b). Yield: 68%; mp = 292–297°C: *Anal*. Calcd for $C_{36}H_{32}N_{14}O_2$: C, 63.32; H, 5.03; N, 27.21; Found C, 63.36; H, 5.06; N, 27.22; IR (neat) cm^{-1}: 3428 (N–H), 3154 (NCH), 3043 (ArCH), 1623 (C=N), 1571 (–N=N), 1122 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.56–1.84 (m, 8H, CH_2), 4.10 (t, J = 10.50 Hz, 4H, –OCH_2), 6.11 (s, 2H, CH_2), 6.69–8.45 (m, 18H, Ar–H), 11.96 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 25.59, 29.08 ($2CH_2$), 54.36 (NCH_2N), 68.30 (OCH_2), 113.17–141.23 (Ar), 157.68, 164.58 (triazole ring carbons), 166.50 (tetrazole ring carbon). MS, *m/z* (%): 692 $[M]^+$ (69), 196 (100), 315 (43), 399 (67), 518 (23).

1,6-Bis(2-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)hexane (6c). Yield: 72%; mp = 310–314°C: *Anal*. Calcd for $C_{38}H_{36}N_{14}O_2$: C, 63.32; H, 5.03; N, 27.21; Found C, 63.36; H, 5.06; N, 27.22; IR (neat) cm^{-1}: 3428 (N–H), 3154 (NCH), 3043 (ArCH), 1623 (C=N), 1571 (–N=N), 1122 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.56–1.84 (m, 8H, CH_2), 4.10 (t, J = 10.50 Hz, 4H, –OCH_2), 6.11 (s, 2H, CH_2), 6.69–8.45 (m, 18H, Ar–H), 11.96 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 25.59, 29.08 ($2CH_2$), 54.36 (NCH_2N), 68.30 (OCH_2), 113.17–141.23 (Ar), 157.68, 164.58 (triazole ring carbons), 166.50 (tetrazole ring carbon). MS, *m/z* (%): 720 $[M]^+$ (69), 196 (100), 315 (43), 399 (67), 518 (23).

1,2-Bis(3-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)ethane (6d). Yield: 68%; mp = 265–270°C: *Anal*. Calcd for $C_{34}H_{28}N_{14}O_2$: C, 61.44; H, 4.25; N, 29.50; Found C, 61.45; H, 4.28; N, 29.52; IR (neat) cm^{-1}: 3431 (N–H), 3152 (NCH), 3043 (ArCH), 1627 (C=N), 1563 (–N=N), 1123 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 4.10 (4H, –OCH_2), 6.13 (s, 2H, CH_2), 7.09–8.55 (m, 18H, Ar–H), 11.96 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 54.36 (NCH_2N), 68.38 (OCH_2), 113.25–142.23 (Ar), 157.78, 164.58 (triazole ring carbons), 166.50 (tetrazole ring carbon). MS, *m/z* (%): 664 $[M]^+$ (75), 196 (100), 315 (27), 343 (41), 462 (66).

1,4-Bis(3-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)butane (6e). Yield: 79%; mp = 285–289°C: *Anal*. Calcd for $C_{36}H_{32}N_{14}O_2$: C, 61.44; H, 4.25; N, 29.50; Found C, 61.45; H, 4.28; N, 29.52; IR (neat) cm^{-1}: 3431 (N–H), 3152 (NCH), 3043 (ArCH), 1627 (C=N), 1563 (–N=N), 1123 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.98 (m, 4H, CH_2), 4.15 (t, J = 11.2 Hz, 4H, –OCH_2), 6.1 (s, 4H, NCH_2N), 7.29–8.68 (m, 18H, Ar–H), 11.99 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 25.95 (CH_2), 54.34 (NCH_2N), 68.17 (OCH_2), 113.10–141.15 (Ar), 157.60, 164.59 (triazole ring carbons), 166.50 (tetrazole ring carbon). MS, *m/z* (%): 692 $[M]^+$ (75), 196 (100), 315 (27), 343 (41), 462 (66).

1,6-Bis(3-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)hexane (6f). Yield: 58%; mp = 320–324°C: *Anal*. Calcd for $C_{38}H_{36}N_{14}O_2$: C, 61.44; H, 4.25; N, 29.50; Found C, 61.45; H, 4.28; N, 29.52; IR (neat) cm^{-1}: 3431 (N–H), 3152 (NCH), 3043 (ArCH), 1627 (C=N), 1563 (–N=N), 1123 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.58–1.94 (m, 8H, CH_2), 4.15 (t, J = 10.70 Hz, 4H, –OCH_2), 6.11 (s, 2H, CH_2), 6.69–8.45 (m, 18H, Ar–H), 11.96 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 27.59, 30.08 ($2CH_2$), 54.36 (NCH_2N), 69.30 (OCH_2), 113.17–141.43 (Ar), 157.7, 164.6 (triazole ring carbons), 166.59 (tetrazole ring carbon). MS, *m/z* (%): 720 $[M]^+$ (75), 196 (100), 315 (27), 343 (41), 462 (66).

1,3-Bis(4-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)propane (6g). Yield: 68%; mp = 245–248°C: *Anal*. Calcd for $C_{35}H_{30}N_{14}O_2$: C, 61.94; H, 4.46; N, 28.89; Found C, 61.96; H, 4.48; N, 28.91; IR (neat) cm^{-1}: 3427 (N–H), 3154 (NCH), 3043 (ArCH), 1626 (C=N), 1572 (–N=N), 1125 (C–N). ^{1}H-NMR (DMSO-d_6, δ/ppm) 2.28 (m, 2H, CH_2), 4.30 (t, J = 10.8 Hz, 4H, –OCH_2), 6.1 (s, 4H, NCH_2N), 7.01–8.63 (m, 18H, Ar–H), 11.88 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 29.21 (CH_2), 54.33 (NCH_2N), 66.92 (OCH_2), 115.31–145.22 (Ar), 160.4, 164.6 (triazole ring carbons), 166.4 (tetrazole ring carbon). MS, *m/z* (%): 678 $[M]^+$ (69), 196 (100), 315 (22), 357 (43), 476 (73).

1,4-Bis(4-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)butane (6h). Yield: 69%; mp = 272–276°C: *Anal*. Calcd for $C_{36}H_{32}N_{14}O_2$: C, 62.42; H, 4.66; N, 28.31; Found C, 62.39; H, 4.54; N, 28.29; IR (neat) cm^{-1}: 3429 (N–H), 3159 (NCH), 3049 (ArCH), 1628 (C=N), 1568 (–N=N), 1127 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.85 (m, 4H, CH_2), 4.20 (t, J = 11.6 Hz, 4H, –OCH_2), 6.1 (s, 4H, NCH_2N), 7.56–8.48 (m, 18H, Ar–H), 11.99 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 25.95 (CH_2), 54.54 (NCH_2N), 68.37 (OCH_2), 113.58–141.65 (Ar), 157.60, 164.59 (triazole ring carbons), 166.55 (tetrazole ring

carbon). MS, *m/z* (%): 692 $[M]^+$ (69), 196 (100), 315 (78), 371 (33), 490 (24).

1,6-Bis(4-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy)hexane (6i). Yield: 58%; mp = 302–306°C: *Anal*. Calcd for $C_{38}H_{36}N_{14}O_2$: C, 63.32; H, 5.03; N, 27.21; Found C, 63.33; H, 5.04; N, 27.39; IR (neat) cm^{-1}: 3431 (N–H), 3150 (NCH), 3060 (ArCH), 1628 (C═N), 1561 (-N═N), 1124 (C–N). ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.76, 1.84 (m, 8H, CH_2), 4.16 (t, J = 10.54 Hz, 4H, –OCH_2), 6.11 (s, 2H, CH_2), 6.69–8.65 (m, 18H, Ar-H), 11.96 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 26.59, 29.88 (2x CH_2), 54.96 (NCH_2N), 68.30 (OCH_2), 113.17–141.23 (Ar), 158.68, 164.78 (triazole ring carbons), 166.58 (tetrazole ring carbon): 720 $[M]^+$ (69), 196 (100), 315 (50), 399 (62), 518 (31).

1,6-Bis(2-methoxy-4-(5-((5-phenyl-1H-tetrazol-1-yl)methyl)-4H-1,2,4-triazol-3-yl)phenoxy) hexane (6j). Yield: 88%; mp = 331–336°C: *Anal*. Calcd for $C_{40}H_{40}N_{14}O_4$: C, 61.53; H, 5.16; N, 25.11; Found C, 61.56; H, 5.18; N, 25.13; IR (neat) cm^{-1}: 3432 (N–H), 3149 (NCH), 3048 (ArCH), 1629 (C═N), 1565 (–N═N), 1126 (C–N), ^{1}H-NMR (DMSO-d_6, δ/ppm) 1.48, 1.76 (m, 8H, CH_2), 3.79 (–OMe), 4.01 (t, J = 11.4 Hz, 4H, –OCH_2), 6.14 (s, 2H, CH_2), 6.99–8.09 (m, 18H, Ar–H), 11.87 (s, 2H, NH), ^{13}C NMR (DMSO-d_6, δ/ppm) 25.72, 29.06 ($2CH_2$), 54.44 (NCH_2N), 56.04 (–OMe), 68.61 (OCH_2), 109.35–149.67 (Ar), 150.68, 164.60 (triazole ring carbons), 166.43 (tetrazole ring carbon). MS, *m/z* (%): 780 $[M]^+$ (69), 196 (100), 345 (59), 429 (74), 578 (41).

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