"Click" Synthesis of Isomeric Compounds for Assessing the Efficiency of Bifurcated Br···NO_2 Synthon

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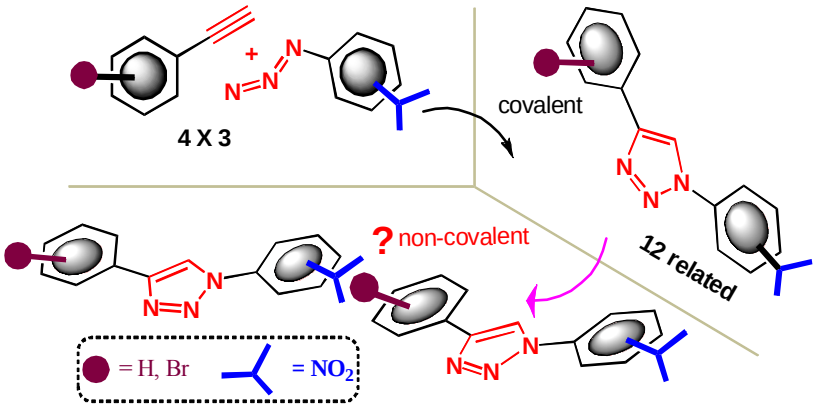

Experimental

General Methods: All solvents were dried according to the standard methods prior to use. Commercial reagents were used without purification. Column chromatography was carried out by using Spectrochem silica gel (60–120 mesh). ^{1}H and ^{13}C NMR spectroscopy measurements were carried out on Bruker AC 200 MHz or Bruker DRX 400 MHz spectrometers, and TMS was used as internal standard. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm downfield from tetramethylsilane and coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Elemental analysis data were obtained on a Thermo Finnigan Flash EA 1112 Series CHNS Analyser.

General procedure for cycloaddition reactions with 2/4-nitroflurobenzenes (2, 4):
Fluoronitrobenzene (100 mg, 0.71 mmol) was mixed with bromophenylacetylene (128 mg, 0.71 mmol)/ phenyl acetylene (72 mg, 0.71 mmol) in 9:1 DMSO:H_2O (10 mL). To the mixture were added L-proline (16 mg, 0.142 mmol), Na_2CO_3 (15 mg, 0.142 mmol), NaN_3 (55 mg, 0.852 mmol), sodium ascorbate (14 mg, 0.071 mmol), and $CuSO_4.5H_2O$ (9 mg, 0.036 mmol). The mixture was stirred for 24-48 h at 70 °C (bath temperature) and then the mixture was poured into 30 mL of ice-cold water. The solid residue was filtered and crystallized from appropriate solvent systems to procure white to yellow crystalline solids in (57-83%) yield.

General procedure for cycloaddition reactions with 3-azidobenzene (3):
A mixture of 3-Azidonitrobenzene (116 mg, 0.71 mmol), bromophenylactylene (128 mg, 0.71 mmol)/ phenyl acetylene (72 mg, 0.71 mmol) was taken in 9:1 DMSO:H_2O (10 mL) in a round bottom flask and L-proline (16 mg, 0.142 mmol), Na_2CO_3 (15 mg, 0.142 mmol), sodium ascorbate (14 mg, 0.071 mmol), and $CuSO_4.5H_2O$ (9 mg, 0.036 mmol) were added to that mixture and the complete reaction mixture was heated at 70 ºC (bath temperature) for 24 h with stirring. The reaction mixture was cooled to room temperature and diluted with 30 mL of water and combined water layer was thoroughly extracted with

ethyl acetate (3 x 50 mL). Organic layer was dried over sodium sulphate and concentrated under vacuum. The crude solid was purified by column chromatography over 230-400 silica using ethyl acetate-light petroleum (1:4) to obtain white to yellow solids (65-77%). This solid was crystallized from appropriate solvent system.

1-(2-Nitrophenyl)-4-phenyl-1H-1,2,3-triazole (8, P2NPT): MP: 140-141 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.42-7.56 (m, 3H), 7.83-8.01 (m, 5H), 8.26 (dd, *J* = 1.1, 8.5 Hz, 1H), 9.20 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$). 120.8 (d), 125.6 (d), 126.0 (d), 127.9 (d), 128.7 (d), 129.0 (d), 129.8 (s), 130.4 (s), 130.6 (d), 133.7 (d). Anal. Calcd for $C_{14}H_{10}N_4O_2$ **:** C, 63.15; H, 3.79; N, 21.04; O, 12.02; Found: C, 62.99; H, 3.67; N, 21.19.

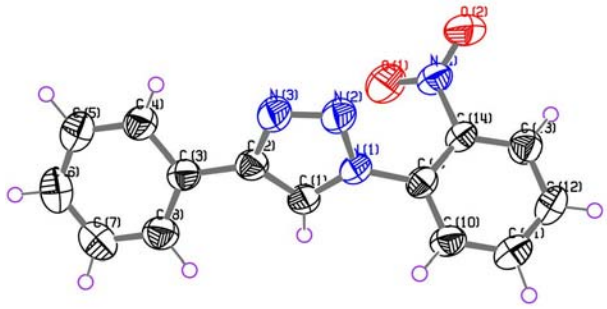

Figure 1. *The molecular structure of compound **8***

4-(2-Bromophenyl)-1-(2-nitrophenyl)-1H-1,2,3-triazole (9, 2BP2NPT): MP: 125 °C. ^{1}H (400 MHz, $CDCl_3$) δ 7.24 (dt, *J* = 1.7, 7.8 Hz, 1H), 7.46 (dt, *J* = 1.2, 7.8 Hz, 1H), 7.68 (dd, *J* = 1.0, 8.1 Hz, 1H), 7.73 (br. s, 1H), 7.75 (br. s, 1H), 7.83 (dt, *J* = 1.6, 8.1 Hz, 1H), 8.12 (dd, *J* = 1.5, 8.2 Hz, 1H), 8.24 (dd, *J* = 1.8, 7.8 Hz, 1H), 8.56 (s, 1H).^{13}C (100 MHz, $CDCl_3$) 121.3 (s), 124.3 (d), 125.7 (d), 127.4 (s), 127.8 (d), 128.1 (s), 129.7 (d), 130.7 (d), 130.9 (d), 133.7 (d), 142.0 (s), 145.9 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$ **:** C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.98; H, 2.39; Br, 23.19; N, 16.51.

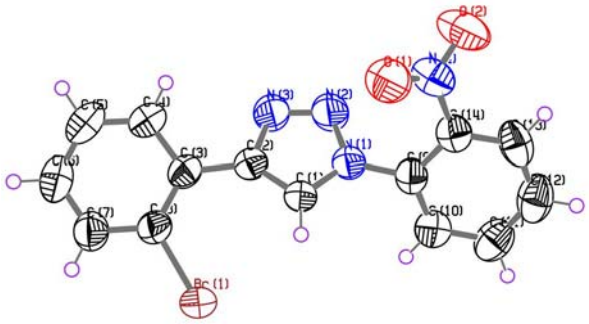

Figure 2. *The molecular structure of compound* ***9***

4-(3-Bromophenyl)-1-(2-nitrophenyl)-1H-1,2,3-triazole (10, 3BP2NPT): MP: 101 °C. ^{1}H (400 MHz, $CDCl_3$) δ 7.02-7.44 (m, 3H), 7.58-7.82 (m, 4H), 7.94-8.04 (m, 2H). ^{13}C (100 MHz, $CDCl_3$) 121.4 (d), 123.1 (s), 124.5 (d), 125.7 (d), 126.9 (d), 127.90 (d), 129.0 (d), 130.5 (d), 130.8 (d), 131.5 (d), 131.8 (s), 133.8 (d), 144.4 (s), 146.9 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$ **:** C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.76; H, 2.52; Br, 23.42; N, 16.11.

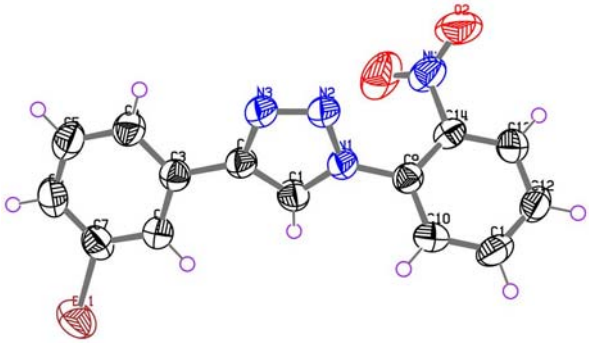

Figure 3. *The molecular structure of compound* ***10***

4-(4-Bromophenyl)-1-(2-nitrophenyl)-1H-1,2,3-triazole (11, 4BP2NPT): MP: 136-137 °C. ^{1}H (400 MHz, $CDCl_3$) δ 7.40-7.50 (m, 1H), 7.57 (dt, J = 2.2, 8.7 Hz, 1H), 7.65-7.88 (m, 5H), 8.06 (s, 1H), 8.06-8.22 (m, 1H). ^{13}C (100 MHz, $CDCl_3$) 121.0 (d), 122.7 (s), 125.6 (d), 127.5 (d), 127.9 (d), 129.8 (d), 130.8 (d), 132.2 (d), 132.4 (d), 133.8 (d), 144.4 (s), 147.4 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$ **:** C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.44; H, 2.40; Br, 23.11; N, 16.41.

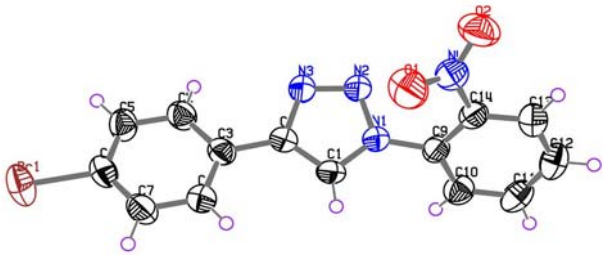

Figure 4. *The molecular structure of compound* ***11***

1-(3-Nitrophenyl)-4-phenyl-1H-1,2,3-triazole (12, P3NPT): MP: 204-205 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.40-7.50 (m, 3H), 7.78 (t, *J* = 8.21 Hz, 1H), 7.91-7.93 (m, 2H), 8.25-8.33 (m, 2H), 8.30 (s, 1H), 8.65 (t, *J* = 2.20 Hz, 1H). ^{13}C NMR (50 MHz, $DMSOd_6$) 115.0 (d), 120.4 (d), 123.5 (d), 125.8 (d), 126.3 (d), 128.9 (d), 129.5 (d), 130.2 (s), 132.0 (d), 137.5 (s), 148.1 (s), 148.9 (s). Anal. Calcd for $C_{14}H_{10}N_4O_2$ **:** C, 63.15; H, 3.79; N, 21.04; Found: C, 63.06; H, 3.88; N, 20.89.

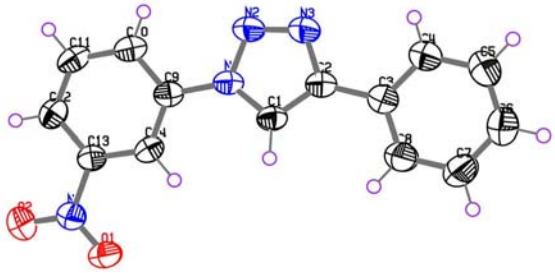

Figure 5. *The molecular structure of compound* ***12***

4-(2-Bromophenyl)-1-(3-nitrophenyl)-1H-1,2,3-triazole (13, 2BP3NPT): MP: 131-132 °C. ^{1}H (400 MHz, $CDCl_3$) δ 7.25 (ddd, *J* = 1.8, 7.4, 9.2 Hz, 1H), 7.46 (dt, *J* = 1.3, 7.8 Hz, 1H), 7.69 (dd, *J* = 1.1, 8.1 Hz, 1H), 7.78 (t, *J* = 8.2 Hz, 1H), 8.20 (dd, *J* = 1.8, 7.8 Hz, 1H), 8.27 (ddd, *J* = 1.0, 2.1, 8.2 Hz, 1H), 8.33 (ddd, *J* = 1.0, 2.1, 8.2 Hz, 1H), 8.66 (t, *J* = 2.1 Hz, 1H), 8.79 (s, 1H). ^{13}C (100 MHz, $CDCl_3$) 115.3 (d), 120.6 (d), 121.3 (s), 123.2 (d), 126.0 (d), 127.9 (d), 129.9(d), 130.4 (s), 130.8 (d), 131.0 (d), 133.7 (d), 137.8 (s), 146.6 (s), 149.1 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$ **:** C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 49.00; H, 2.81; Br, 23.42; N, 16.11.

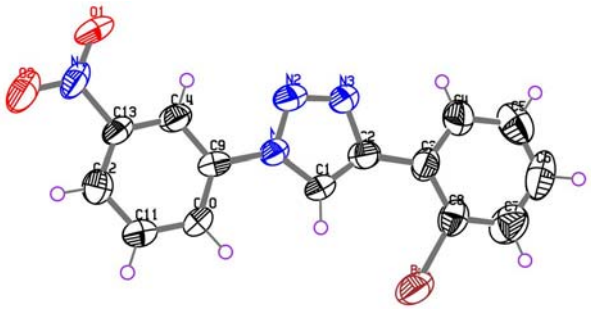

Figure 6. *The molecular structure of compound* ***13***

4-(3-Bromophenyl)-1-(3-nitrophenyl)-1H-1,2,3-triazole (14, 3BP3NPT): MP: 195-196 °C. ^{1}H (400 MHz, DMSO-D_6) δ 7.37-7.54 (m, 2H), 7.84-7.99 (m, 2H), 8.14 (t, *J* = 1.6 Hz, 1H), 8.32 (dd, *J* = 1.6, 8.3 Hz, 1H), 8.46 (dd, *J* = 1.6, 8.3 Hz, 1H), 8.86 (t, *J* = 2.0 Hz, 1H), 9.58 (s, 1H). ^{13}C (100 MHz, DMSO-D_6) 112.7 (d), 118.5 (d), 120.7 (s), 121.1 (d), 122.4 (d), 123.8 (d), 126.4 (d), 129.1 (d), 129.2 (d), 129.6 (d), 130.6 (s), 135.6 (s), 144.8 (s), 146.9 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$: C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.91; H, 2.83; Br, 23.09; N, 16.06.

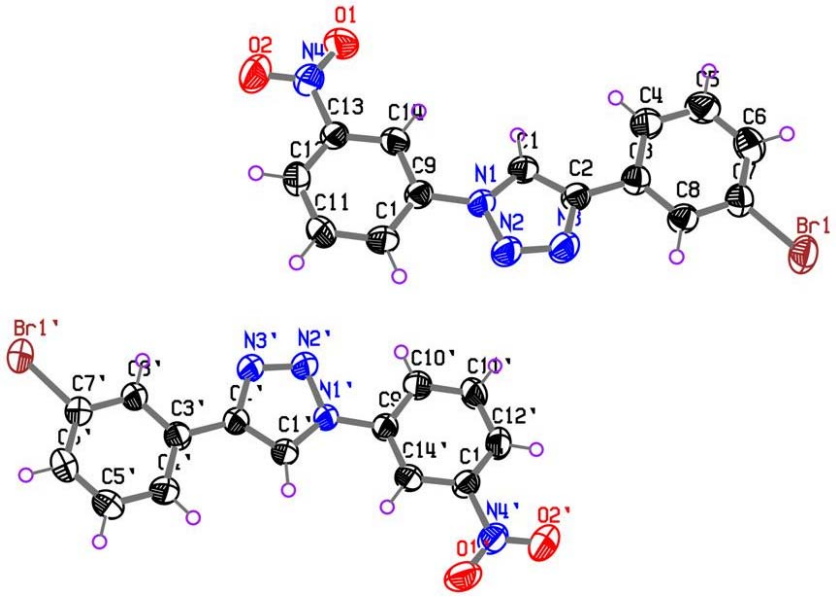

Figure 7. *The molecular structure of compound* ***14***

4-(4-Bromophenyl)-1-(3-nitrophenyl)-1H-1,2,3-triazole (15, 4BP3NPT): MP: 230-231 °C. ^{1}H (400 MHz, DMSO-D_6) δ 7.46 (br. s, 1H), 7.50 (br. s, 1H), 7.71-7.78 (m, 3H), 8.18 (dd, *J* = 2.1, 8.1 Hz, 1H), 8.30 (dd, *J* = 2.5, 8.2 Hz, 1H), 8.68 (t, *J* = 2.1 Hz, 1H), 9.35 (s,

1H). ^{13}C (100 MHz, DMSO-D_6) 112.8 (d), 118.2 (d), 120.0 (s), 121.2 (d), 123.9 (d), 125.1 (d), 125.6 (d), 127.5 (s), 127.7 (d), 129.7 (d), 130.1 (d), 135.7 (s), 145.3 (s), 146.9 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$: C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.75; H, 2.81; Br, 23.23; N, 16.30.

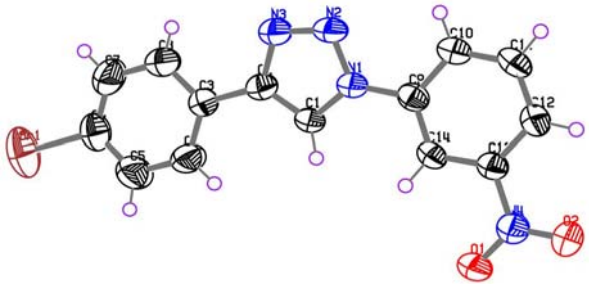

Figure 8. *The molecular structure of compound* ***15***

1-(4-Nitrophenyl)-4-phenyl-1H-1,2,3-triazole (16, P4NPT): MP: 236-238 °C (d). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.41-7.56 (m, 3H), 7.93-7.98 (m, 2H), 8.23-8.28 (m, 2H), 8.47-8.51 (m, 2H), 9.48 (s, 1H). ^{13}C NMR (125 MHz, DMSO-D_6) 120.0 (d), 120.6 (d), 125.5 (d), 125.7 (d), 128.7 (d), 129.2 (d), 129.8 (s), 140.9 (s), 146.8 (s), 147.9 (s). Anal. Calcd for $C_{14}H_{10}N_4O_2$: C, 63.15; H, 3.79; N, 21.04; O, 12.02; Found: C, 63.31; H, 3.53; N, 20.91.

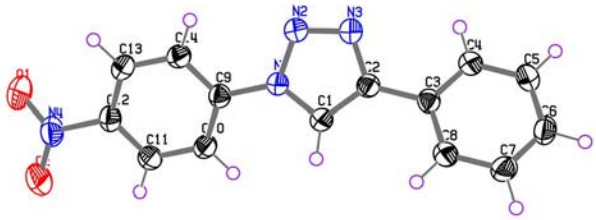

Figure 9. *The molecular structure of compound* ***16***

4-(2-Bromophenyl)-1-(4-nitrophenyl)-1H-1,2,3-triazole (17, 2BP4NPT): MP: 170-171 °C. ^{1}H (400 MHz, $CDCl_3$) 7.26 (ddd, *J* = 1.8, 7.4, 9.2 Hz, 1H), 7.47 (dt, *J* = 1.2, 7.8 Hz, 1H), 7.69 (dd, *J* = 1.2, 7.9 Hz, 1H), 8.04 (t, *J* = 2.6 Hz, 1H), 8.09 (t, *J* = 2.6 Hz, 1H), 8.2 (dd, *J* = 1.6, 7.8 Hz, 1H), 8.42 (t, *J* = 2.6 Hz, 1H), 8.47 (t, *J* = 2.6 Hz, 1H), 8.79 (s,

1H). ^{13}C (100 MHz, $CDCl_3$) 120.5 (d), 121.3 (s), 124.1 (d), 124.9 (d), 125.6 (d), 127.9 (d), 130.0 (d), 130.2 (d), 130.8 (d), 131.9 (s), 133.8 (d), 141.1 (s), 146.7 (s), 147.3 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$: C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.57; H, 2.90; Br, 22.89; N, 16.12.

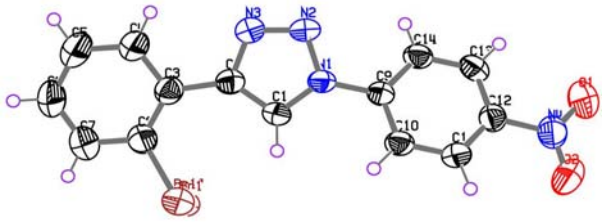

Figure 10. *The molecular structure of compound* ***17***

4-(3-Bromophenyl)-1-(4-nitrophenyl)-1H-1,2,3-triazole (18, 3BP4NPT): MP: 217-218 °C. ^{1}H (400 MHz, DMSO-D_6) 7.36-7.54 (m, 2H), 7.96 (dt, *J* = 1.8, 7.6 Hz, 1H), 8.14 (t, *J* = 1.6 Hz, 1H), 8.26, 8.31, 8.45, 8.51 (4br. m, 4H), 9.47 (s, 1H). ^{13}C (100 MHz, DMSO-D_6) 118.6 (d), 120.8 (d), 122.6 (s), 123.8 (d), 124.1 (d), 126.5 (d), 127.4 (d), 129.1 (d), 129.4 (d), 130.5 (s), 139.3 (s), 145.0 (s), 145.1 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$: C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.63; H, 2.88; Br, 23.29; N, 16.48.

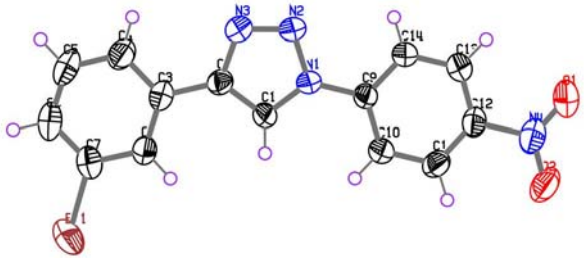

Figure 11. *The molecular structure of compound* ***18***

4-(4-Bromophenyl)-1-(4-nitrophenyl)-1H-1,2,3-triazole (19, 4BP4NPT): MP: 149-150 °C. ^{1}H (400 MHz, DMSO-D_6) 7.59 (t, *J* = 2.2 Hz, 1H), 7.64 (t, *J* = 2.2 Hz, 1H), 7.77 (t, *J* = 2.2 Hz, 1H), 7.82 (t, *J*=2.2 Hz, 1H), 8.01 (t, *J* = 2.2 Hz, 1H), 8.06 (t, *J* = 2.2 Hz, 1H), 8.28 (t, *J* = 2.2 Hz, 1H), 8.44 (t, *J* = 2.2 Hz, 1H), 8.48 (t, *J* = 2.2 Hz, 1H). ^{13}C (100 MHz, DMSO-D_6) 118.2 (d), 118.5 (d), 119.9 (s), 123.7 (d), 125.5 (d), 127.3 (s), 130.1

(d), 139.1 (s), 144.9 (s), 145.2 (s). Anal. Calcd for $C_{14}H_9BrN_4O_2$: C, 48.72; H, 2.63; Br, 23.15; N, 16.23; Found: C, 48.70; H, 2.40; Br, 23.43; N, 16.01.

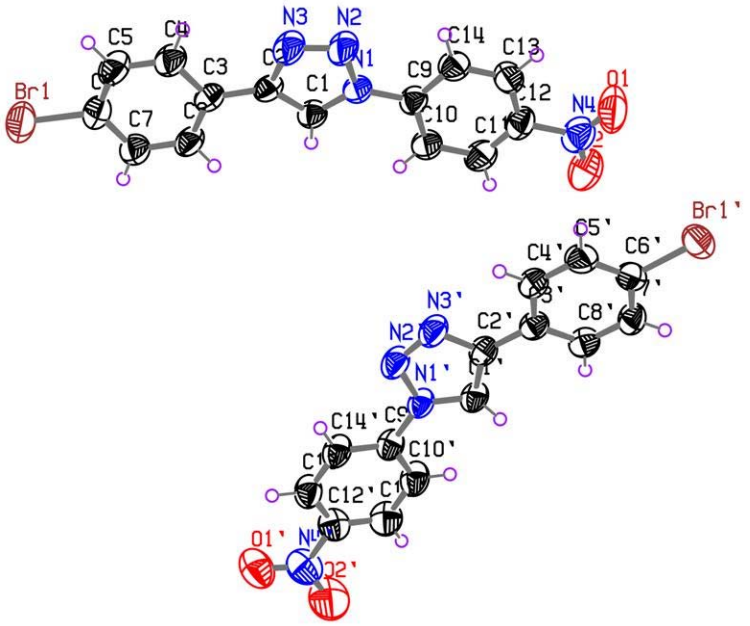

Figure 12. *The molecular structure of compound* ***19***