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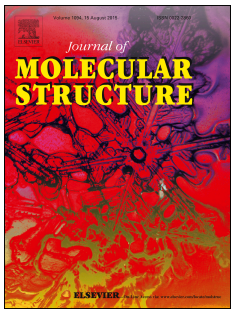

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Katarzyna Wajda-Hermanowicz, Damian Pieniążczak, Robert Wróbel, Aleksandra Zatajska, Zbigniew Ciunik, Sławomir Berski

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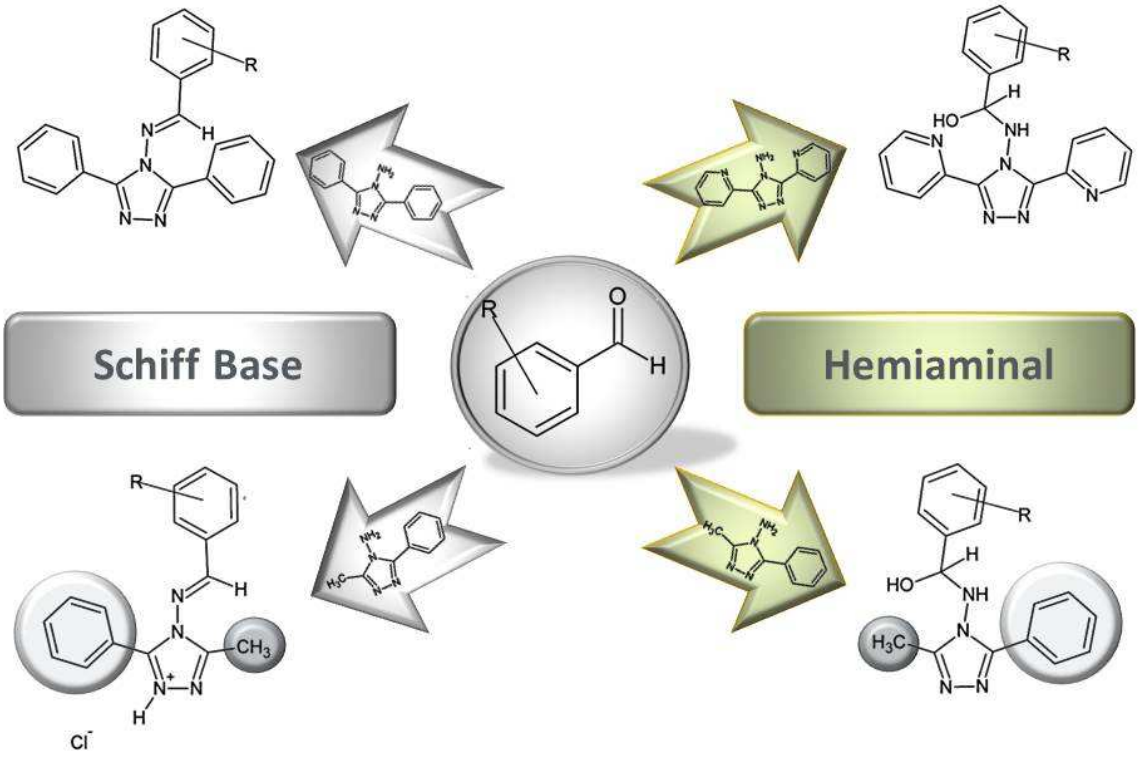

A Study on the Condensation Reaction of Aryl Substituted 4-Amine-1,2,4-triazole with Benzaldehydes: Structures and Spectroscopic Properties of Schiff Bases and Stable Hemiaminals.

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Abstract

A series of stable hemiaminals and Schiff bases containing 3,5-disubstituted 1,2,4-triazole derivatives were synthesized. The structure of the prepared compounds was confirmed by means of ^{1}H NMR, ^{13}C NMR, IR, MS and elemental analysis. The steric and electronic effects of the triazole ring substituents on the hemiaminal formation was also discussed. Single crystal X-ray diffraction studies of hemiaminals obtained from 4-amino-3,5-dipyridyn-2-yl-1,2,4- triazole (**4, 5**) revealed the formation of centrosymmetric dimers linked by strong O-H$^{\cdots}$N$_{1Tr}$ hydrogen bonds. The Schiff bases obtained from the unsymmetrical 3-methyl,5-phenyl-1,2,4-triazole was found to be a different E-conformer which was determined through solution NMR and crystallographic diffraction analysis (**13**). The molecular geometry of the unsymmetrical triazole derivatives: hemiaminal (**12**) and Schiff base (**13**) were also optimized using density functional theory (DFT/M062x) method with the 6-311++G(d,p) basis set in ground state and compared with the experimental data.

Keywords : 4-amino-1,2,4-triazole, chemical reactivity, hemiaminals, Schiff bases ,X-ray structures, DFT.

1. Introduction

Schiff base compounds have been extensively investigated due to their wide range of applications in various fields of science and industry [1-5]. The azomethine groups are present in various natural compounds and the -C=N- linkage is essential for biological activity. In recent years, Schiff bases derivatives of 3(5)-aryl substituted 4-amino-1,2,4-triazole and its complexes were reported to possess antibacterial [6-10], antifungal [11-13], antioxidant and antiradical [14], antitumor [15, 16] and antitubercular [17] activities. Furthemore, the 3,5-diaryl-1,2,4-triazole Schiff bases derivatives upon chelation to metals show photochemical and photophysical properties [18- 20]. One of them, the metallophthalocyanine zinc complex was examined as a photosensitizers for the photocatalytic reactions [21].

Chemical species containing the azomethine group can be synthesized from the primary amine by nucleophilic addition to carbonyl compounds. The reaction creates at first an usually unstable intermediate tetrahedral product called hemiaminal, and then after dehydration the stable imine is formed [22].

In our earlier investigations we have shown that 4-amine-1,2,4-triazole [23, 24] and 4-amine-3,5-dimethyl-1,2,4-triazole [25] can react with benzaldehydes to give stable hemiaminals and Schiff bases. We have examined the effects of the benzaldehyde substituents and reaction conditions on the product distribution and stability [25]. These results prompted us to look at the condensation reaction with the aryl substituted 4-amino-1,2,4-triazoles. The present paper describes the synthesis, spectroscopic and molecular structure study of novel hemiaminals and Schiff bases obtained from 4-amino-3,5-diphenyl-1,2,4-triazole, 4-amino -3,5-dipyridin-2-yl-1,2,4-triazole and 4-amino-3-methyl,5-phenyl-1,2,4-triazole.

2. Experimental

2.1 Materials and Physical Measurements

The reagents and solvents employed were commercially available and used as received without further purification. Elemental analyses were carried out with a CHNS Vario EL III analyzer. The NMR spectra were recorded on a Bruker 300 or 500 MHz spectrometer using solvent as an internal standard. The chemical shifts are reported in ppm and COSY, HMQC and HMBC were routinely used to definitely assign the signals of ^{1}H and ^{13}C. The mass spectra of electrospray ionization (ESI)-MS were obtained on MicrOTOF-Q mass spectrometer. The Fourier transform IR spectra were recorded from KBr pellets in the range of 400-4000 cm^{-1} on a Bruker IFS 66 FT-IR. Flash chromatography was performed on a Sepacore Flash System (Büchi Pump Module C-605, Büchi Pump Manager C-615, Büchi UV Monitor C-630, Büchi Fraction Collector C-660; Büchi Labortechnik, Flawil, Switzerland) using Merck silica gel (0.040–0.063 mm, 230–400 mesh).

2.2 X-ray Crystallography

Single crystal X-Ray diffraction data were collected at a Kuma KM4CCD four-circle diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71073 A ˚) at 100 K using an Oxford Cryosystem adapter [26]. and CC. Data collection and data reduction CrysAlisPro, Agilent Technologies [27] program used. The structures were solved by direct methods with SHELXS and was refined by a full-matrix least squares method using SHELXL97 programs [28]. CCDC 1424617-1424619 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

2.3 Computational Methods

The calculations were carried out using Gaussian09 program [29]. The DFT method with the M062x density functional [30] and 6-311++G(d,p) basis set [31, 32] have been applied. The effect of solvent was simulated using SCRF method [33] with the dielelctric constant for DMSO.

2.4 Preparation of compounds

2.4.1 Synthesis of amines **1-3**

4-amino-3,5-dipyridin-2-yl-4H-1,2,4-triazole (**1**) and *4-amino-3,5-diphenyl-4H-1,2,4-triazole* (**2**) were synthesized in accordance with the published procedure and checked with NMR spectra and elemental analysis [34].

Synthesis of 4-amino-3-methyl-5-phenyl-4H-1,2,4-triazole (**3**) Benzonitrile (2.55 mL, 25 mmol), acetonitrile (2.61 mL, 50 mmol), $NH_2NH_2{\cdot}H_2O$ (80%, 9 mL) and anhydrous ethanol (3 mL) were mixed in a 100 mL Teflon-lined autoclave and heated for 3 days at 120 ^oC. After cooling to room temperature the solvent was removed in vacuum and the residue was washed with benzene (3X3mL). The insoluble part in benzene was recrystallized from 1-propanol to afford a mixture of three products. Pure samples were obtained by the separation method using flash Silica Gel chromatography with 1-propanol as eluent. Three fractions were collected. First it was *4-amino-3,5-dimethyl-4H-1,2,4-triazole* (0.1654 g.). The *4-amino-3-methyl-5-phenyl-4H-1,2,4-triazole* (1.6782 g.) (**3**) was eluted next and the *4-amino-3,5-diphenyl-4H-1,2,4-triazole* (0.5200 g.) (**2**) was collected as a third fraction.

4-amino-3,5-diphenyl-4H-1,2,4-triazole (0.5200 g.) (**2**) Anal. Calc. (%) for $C_{14}H_{12}N_4$: C, 71.17;H, 5.12; N, 23.71. Found: C, 71.20;H, 4.98; N, 23.86. IR (KBr, cm^{-1}): 492w; 604w; 687vs; 700vs; 725w; 763s; 769s; 916m; 928w; 968w; 1074w; 1109vw; 1269vw; 1287w; 1356vw; 1418w; 1454w; 1475s; 1628w; 3045w; 3212w; 3275w; 3362m. MS (ESI, m/z): 237.1 $[M+H]^+$; 259.1 $[M+Na]^+$, 275.1 $[M+K]^+$, 495.2 $[2M+Na]^+$. ^{1}H-NMR (DMSO-d_6, 295 K, ppm, 500 MHz): δ = 8.05 (dd,4H , $J_{2\text{-}3}$ = 8.11 Hz, $J_{2\text{-}4}$ = 1.62 Hz Ph-H_2); 7.55 (m, 6H, Ph-H_3,H_4); 6.29 (s, 2H, NH_2). ^{13}C-NMR (DMSO-d6, 295 K, ppm, 151 MHz): δ = 154.7 (Tr-C), 130.0 (Ph-C_4), 128.9 (Ph-C_3), 128.8 (Ph-C_2), 127.8 (Ph-C_1).

4-amino-3-methyl-5-phenyl-4H-1,2,4-triazole (1.6782 g.) (**3**) Anal. Calc. (%) for $C_9H_{10}N_4$: C, 62.05;H, 5.79; N, 32.16. Found: C, 62.03;H, 5.65; N, 32.27. IR (KBr, cm^{-1}): 473w, 486w, 559s, 642w, 675w, 693vs, 715vs, 722s, 753m, 777s, 921w, 964s, 989s, 1003s, 1057w, 1080w, 1269m, 1288w, 1346m, 1353m, 1363m, 1381w, 1421s, 1446s, 1461m, 1481vs, 1527s, 1536s, 1648s, 2926w, 2991w, 3151m, 3183m, 3253m. MS (ESI, m/z): 175.1 $[M+H]^+$; 197.1 $[M+Na]^+$, 371.1 $[2M+Na]^+$. ^{1}H-NMR (DMSO-d_6, 295 K, ppm, 500 MHz): δ = 8.01 (d,2H , J_{2-3} = 8.01 Hz, Ph-H_2); 7.49 (m, 3H, Ph-H_3,H_4); 6.02 (s, 2H, NH_2); 2.37 (s, 3H, CH_3) . ^{13}C-NMR (DMSO-d6, 295 K, ppm, 126 MHz): δ = 153.2 (Tr-C-CH_3), 152.2 (Tr-C-Ph), 129.2 (Ph-C_4), 128.3 (Ph-C_3), 127.7 (Ph-C_2), 127.6 (Ph-C_1), 9.9 (CH_3).

2.4.2 Synthesis of hemiaminals **4-12**

Compounds **4-6** were synthesized according to the following general procedure. The corresponding aldehyde (0.34 mmol) in acetonitrile (2 mL) was added to a solution of compound **1** (0.34 mmol) in 2.5 ml of acetonitrile and the mixture was then stirred and heated at 50^{o}C for 9 hours. After removing volatile components, raw solid products washed with cold acetonitrile, methanol and dried in air. Crystals of hemiaminals were obtained upon slow evaporation of the solvent from the reaction mixtures.

(4H-3,5-Dipyridin-2-yl-1,2,4-triazole-4-ylamino)(2,4-dinitrophenyl)methanol (**4**) Yield 60 %. Anal. Calc. (%) for $C_{19}H_{14}N_8O_5$: C, 52.78;H, 2.80; N, 25.92. Found: C, 52.63;H, 3.04; N, 25.99. IR (KBr, cm^{-1}): 404m, 448w, 496w, 506w, 599m, 614m, 639w, 674m, 697s, 711s, 736vs, 752m, 791vs, 816vs, 835m, 863m, 892m, 913m, 972m, 992m, 1000m, 1050s, 1088s, 1133m, 1162w, 1184m, 1251w, 1286m, 1349vs, 1423m, 1444vs, 1474s, 1532vs, 1569m, 1594s, 3068m, 3105m. MS (ESI, m/z): 433.1 $[M-H]^+$; 457.1 $[M+Na]^+$. ^{1}H-NMR (DMSO-d6, 295 K, ppm, 500 MHz): δ = 8.75 (d,1H , $J_{(C-H)-(N-H)}$ = 8.24 Hz, N-H); 8.73 (dd, 2H, J_{5-6} = 4.77 Hz, J_{4-6} = 0.60 Hz, Py-H_6); 8.58 (d, 1H, J_{3-5} =2.29 Hz, Ar-H_3); 8.54 (dd, 1H, J_{5-6} =8.70 Hz, J_{3-5} = 2.29 Hz, Ar-H_5); 8.09 (d, 2H, J_{3-4} = 7.78 Hz, Py-H_3);8.03 (dd, 2H, $J_{3,5-4}$ = 7.70 Hz, J_{4-6} = 1.70 Hz, Py-H_4); 7.94 (d, 1H, J_{5-6} = 8.70 Hz, Ar-H $_6$);. 7.59 (m, 2H, $J_{4,-5}$ = 7.66 Hz, J_{5-6} = 4.77 Hz, J_{3-5} = 0.92 Hz, Py-H_5); 7.44 (d, 1H, $J_{(C-H)-(O-H)}$ = 5.49 Hz, O-H); 6.49 (dd, 1H, , $J_{(C-H)-(N-H)}$ = 8.24 Hz , $J_{(C-H)-(O-H)}$ = 5.49 Hz, C-H). ^{13}C-NMR (DMSO-d6, 295 K, ppm, 151 MHz): δ = 152.1 (Tr-C), 149.4 (Py-C_6), 148.8 (Ar-C_2), 148.0 (Ar-C_4), 147.2 (Py-C_2), 141.7 (Ar-C_1), 138.3 (Py-C_4), 132.5 (Ar-C_5), 132.2 (Ar-C_6), 125.4 (Py-C_5), 124.3 (Py-C_3), 122.7 (Ar-C_3), 83.9 (C-OH).

Crystal data ($C_{19}H_{14}N_8O_5$): M=434.38,crystal system: triclinic, space group: P^{-1}, a = 10.414(4) Å, b = 10.596(4) Å, c = 18.168(6) Å, α = 105.31(3)^o, β = 94.61(3)^o, γ = 107.79(3)^o, V = 1812.6(11) Å^3, Z = 4, ρc = 1.592 g cm^{-3}, μ = 0.121 mm, θmax = 36.8^o, reflections: 20420, independent : 10275, R_{int} = 0.0593, R1 =0.0679, wR2 = 0.1738, GoF = 0.995.

(4H-3,5-Dipyridin-2-yl-1,2,4-triazole-4-ylamino)(2-chloro,5-nitrophenyl)methanol (**5**) Yield 60 %. Anal. Calc. (%) for $C_{19}H_{14}ClN_7O_3$: C, 53.85; H, 3.33; N, 23.13;Cl, 8.37. Found: C, 53.83; H, 3.36; N, 23.29; Cl, 8.24. IR (KBr, cm^{-1}):

405w, 464w, 528w, 591m, 607w, 622w, 626w, 633w, 680w, 701m, 711m, 725m, 741vs, 795s, 819m, 831w, 875m, 919w, 946w, 975w, 995w, 999w, 1007w, 1031vs, 1047m, 1079m, 1088m, 1104m, 1138w, 1151w, 1182w, 1193w, 1248m, 1284m, 1343vs, 1434s, 1443s, 1452s, 1463m, 1473m, 1519vs, 1571s, 1590s, 1611m, 3081w, 3132w. MS (ESI,CH_3OH, m/z): 446.1 $[2M+CH_3OH+H_2O]^{+2}$; 477.6 $[2M+Na+CH_3ONa+2H_2O]^{+2}$. ^{1}H-NMR (DMSO-d6, 295 K, ppm, 500 MHz): δ = 8.74 (m, 2H, J_{5-6} = 4.12 Hz, J_{4-6} = 1.83 Hz, J_{3-6} = 0.92 Hz, Py-H_6); 8.54 (d,1H , $J_{(C-H)-(N-H)}$ = 7.92 Hz, N-H); 8.21 (d, 1H, J_{4-6} =2.75 Hz, Ar-H_6); 8.13 (dd, 1H, J_{3-4} =8.70 Hz, J_{4-6} = 2.75 Hz, Ar-H_4); 8.10 (d, 2H, J_{3-4} = 7.78 Hz, Py-H_3);8.04 (m, 2H, J_{4-5} = 7.52 Hz, J_{3-4} = 7.78 Hz, J_{4-6} = 1.83 Hz, Py-H_4); 7.63 (d, 1H, J_{3-4}= 8.70 Hz, Ar-H_3);. 7.59 (m, 2H, J_{4-5} = 7.52 Hz, J_{5-6} = 4.77 Hz, J_{3-5} = 1.40 Hz, Py-H_5); 7.27 (d, 1H, $J_{(C-H)-(O-H)}$ = 5.53 Hz, O-H); 6.36 (dd, 1H, , $J_{(C-H)-(N-H)}$ = 7.92 Hz , $J_{(C-H)-(O-H)}$ = 5.53 Hz, C-H). ^{13}C-NMR (DMSO-d6, 295 K, ppm, 151 MHz): δ = 152.4 (Tr-C), 149.4 (Py-C_6), 147.1 (Py-C_2), 146.9 (Ar-C_5), 139.7 (Ar-C_1), 138.9 (Ar-C_2), 138.2 (Py-C_4), 131.3 (Ar-C_3), 125.3 (Py-C_5), 125.4 (Py-C_5), 125.2 (Ar-C_4), 124.1 (Py-C_3), 81.1 (C-OH).

Crystal data ($C_{19}H_{14}ClN_7O_3$): M=423.82,crystal system: triclinic, space group: P^{-1}, a = 10.131(1) Å, b = 10.223(1) Å, c = 10.312(1) Å, α = 67.54(3)^o, β = 71.38(3)^o, γ = 89.99(3)^o, V = 926.3(3) Å^3, Z = 2, ρc = 1.520 g cm^{-3}, μ = 0.246 mm, θmax = 36.7^o, reflections: 8867, independent : 4497, R_{int} = 0.0760, R1 =0.0589, wR2 = 0.0809, GoF = 0.945.

(4H-3,5-Dipyridin-2-yl-1,2,4-triazole-4-ylamino)(4-chloro,3-nitrophenyl)methanol (**6**) Yield 64 %. Anal. Calc. (%) for $C_{19}H_{14}ClN_7O_3$: C, 53.85; H, 3.33; N, 23.13;Cl, 8.37. Found: C, 53.89; H, 3.16; N, 23.30; Cl, 8.73. IR (KBr, cm^{-1}): 402w, 704m, 743s, 790s, 1049s, 1065m, 1093m, 1156w, 1186w, 1208w, 1267w, 1284w, 1349s, 1433s, 1452s, 1441m, 1466m, 1501w, 1532vs, 1568s, 1590m, 3125m. MS (ESI,CH_3OH, m/z): 446.1 $[M+Na]^+$; 477.6 $[2M+Na+CH_3ONa+CH_3OH]^{+2}$. ^{1}H-NMR (DMSO-d6, 295 K, ppm, 500 MHz): δ = 8.76 (d, 2H, J_{5-6} = 4.12 Hz, Py-H_6); 8.52 (d,1H , $J_{(C-H)-(N-H)}$ = 7.78 Hz, N-H); 8.17 (d, 2H, J_{3-4} =7.78 Hz, Py-H_3); 8.09 (s, 1H, Ar-H_2); 8.06 (dd, 2H, $J_{3,5-4}$ = 7.70 Hz, J_{4-6} = 1.70 Hz, Py-H_4); 7.76 (m, 2H, Ar-$H_{5,6}$);. 7.23 (d, 1H, $J_{(C-H)-(O-H)}$ = 5.49 Hz, O-H); 6.14 (dd, 1H, , $J_{(C-H)-(N-H)}$ = 7.78 Hz , $J_{(C-H)-(O-H)}$ = 5.49 Hz, C-H). ^{13}C-NMR (DMSO-d6, 295 K, ppm, 151 MHz): δ = 152.1 (Tr-C), 149.4 (Py-C_6), 147.5 (Ar-C_3), 147.2 (Py-C_2), 141.4 (Ar-C_1), 138.3 (Py-C_4), 132.5 (Ar-C_6), 132.2 (Ar-C_5), 125.4 (Ar-C_4), 125.3 (Py-C_5), 124.4 (Ar-C_2), 124.1 (Py-C_3), 81.1 (C-OH).

Compounds **7**-**10** were obtained from 4-amino-3,5-dipyridin-2-yl-1,2,4-triazole (**1**) (0.172 mmol) and equimolar amounts of the corresponding aldehyde (0.172 mmol) in hexane (2 mL). The reaction mixture was stirred and heated at 50^{o}C for 9 hours. The solvent was evaporated and the solids were washed two times with acetonitrile and dried in air.

(4H-3,5-Dipyridin-2-yl-1,2,4-triazole-4-ylamino)(2-nitrophenyl)methanol (**7**) Yield 55 %. Anal. Calc. (%) for $C_{19}H_{15}N_7O_3$: C, 58.61; H, 3.88; N, 25.18, Found: C, 58.58; H, 3.81 ;N, 25.10 . . IR (KBr, cm^{-1}): 395w, 404w, 494w, 533w, 603m, 622m, 634w, 672m, 692s, 712s, 737vs, 770m, 789vs, 819m, 855m, 889m, 974m, 999m, 1050s, 1098s, 1153m, 1189m, 1251m, 1282m, 1291m, 1359vs, 1418s, 1443vs, 1473s, 1500m,

1527vs, 1569s, 1592vs, 2923m, 3046s, 3129s, 3198s, 3280s. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 300 MHz): δ = 8.74 (d, 2H, $J_{5\text{-}6}$ = 4.53 Hz, Py-H_6); 8.63 (d,1H , $J_{(C\text{-}H)\text{-}(N\text{-}H)}$ = 8.31 Hz, N-H); 8.12 (d, 2H, J_{3}-$_{4}$ =7.93 Hz, Py-H_3); 8.06 (dd, 2H, $J_{3,5\text{-}4}$ = 7.55 Hz, $J_{4\text{-}6}$ = 1.51 Hz, Py-H_4); 7.79 (m, 1H, Ar-H_5);. 7.75 (m, 1H, Ar-H_6); 7.68 (m, 1H, Ar-H_3);7.60 (m, 2H, $J_{4\text{-}5}$ = 7.55 Hz, $J_{5\text{-}6}$ = 4.53 Hz; $J_{3\text{-}5}$ = 1.32 Hz; Py-H_5); 7.58 (dd, 1H, $J_{3,5\text{-}4}$ = 7.55 Hz, $J_{4\text{-}6}$ = 1.32 Hz; Ar-H_4); 7.14 (dd, 1H, $J_{(C\text{-}H)\text{-}(O\text{-}H)}$ = 5.48 Hz, O-H); 6.39 (dd, 1H, , $J_{(C\text{-}H)\text{-}(N\text{-}H)}$ = 8.31 Hz , $J_{(C\text{-}H)\text{-}(O\text{-}H)}$ = 5.48 Hz, C-H). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 75 MHz): δ = 152.1 (Tr-C), 149.1 (Py-C_6), 148.9 (Ar-C_2), 147.1 (Py-C_2), 138.0 (Py-C_4), 133.4 (Ar-C_1), 133.3 (Ar-C_6), 130.0 (Ar-C_4), 128.4 (Ar-C_3), 125.0 (Py-C_5), 124.0 (Ar-C_5), 123.8 (Py-C_3), 80.7 (C-OH).

(4H-3,5-Dipyridin-2-yl-1,2,4-triazole-4-ylamino)(3-nitrophenyl)methanol (**8**) Yield 63 %. Anal. Calc. (%) for $C_{19}H_{15}N_7O_3$: C, 58.61; H, 3.88; N, 25.18, Found: C, 58.45; H, 3.92 ;N, 25.09. IR (KBr, cm^{-1}): 590w, 631w, 681w, 702m, 714m, 732m, 744m, 792m, 804w, 868w, 922w, 975w, 998w, 1052m, 1061m, 1075m, 1092m, 1152w, 1209w, 1251w, 1302w, 1352s, 1433s, 1449m, 1464s, 1464s, 1481w, 1526vs, 1569m, 1587s, 2924m, 3095m, 3209s. ^{1}H-NMR (DMSO-d6, 298 K, ppm, 300 MHz): δ = 8.78 (d, 2H, $J_{5\text{-}6}$ = 4.08 Hz, Py-H_6); 8.51 (d,1H , $J_{(C\text{-}H)\text{-}(N\text{-}H)}$ = 7.84 Hz, N-H); 8.33(s, 1H, Ar-H_2); 8.18 (d, 2H, J_{3}-$_{4}$ =7.84 Hz, Py-H_3); 8.20 (m, 1H, Ar-H_4); 8.08 (t, 2H, $J_{3,5\text{-}4}$ = 7.53 Hz, Py-H_4); 7.92 (d, 1H, $J_{5\text{-}6}$ = 7.52 Hz, Ar-H_6);. 7.68 (t, 1H, $J_{4,6\text{-}5}$ = 8.00 Hz, Ar-H_6); 7.61 (t, 2H, $J_{4,6\text{-}5}$ = 6.27 Hz, Py-H_5); 7.15 (dd, 1H, $J_{(C\text{-}H)\text{-}(O\text{-}H)}$ = 5.64 Hz, O-H); 6.19 (t, 1H, $J_{(C\text{-}H)\text{-}(N\text{-}H),\ (C\text{-}H)\text{-}(O\text{-}H)}$ = 6.58 Hz, C-H). ^{13}C-NMR (DMSO-d6, 298 K, ppm, 75 MHz): δ = 152.1 (Tr-C), 149.3 (Py-C_6), 148.1 (Ar-C_3), 147.3 (Py-C_1), 142.6 (Ar-C_1), 138.3 (Py-C_4)(Ar-C_5), 133.5 (Ar-C_2), 130.3 (Ar-C_4), 125.3 (Py-C_5), 124.1 (Py-C_3), 121.8 (Ar-C_6), 84.4 (C-OH).

(4H-3,5-Dipyridin-2-yl-1,2,4-triazole-4-ylamino)(4-nitrophenyl)methanol (**9**) Yield 62 %. Anal. Calc. (%) for $C_{19}H_{15}N_7O_3$: C, 58.61; H, 3.88; N, 25.18, Found: C, 58.42; H, 3.83; N, 25.05. IR (KBr, cm^{-1}):403w, 469w, 589m, 623w, 634w, 677w, 694m, 701m, 714m, 737s, 797s, 815s, 856w, 895w, 970w, 999m, 1011w, 1047m, 1072m, 1107w, 1150w, 1198m, 1251w, 1248w, 1325m, 1346vs, 1392w, 1415m, 1435vs, 1466s, 1522vs, 1569m, 1589vs, 2925m, 3220s, 3293s. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 300 MHz): δ = 8.80 (d, 2H, $J_{5\text{-}6}$ = 4.34 Hz, Py-H_6); 8.52 (d,1H , $J_{(C\text{-}H)\text{-}(N\text{-}H)}$ = 8.12 Hz, N-H); 8.23(d, 2H,$J_{2\text{-}3}$ = 8.50 Hz, Ar-$H_{3,5}$); 8.17 (d, 2H, J_{3}-$_{4}$ =8.31 Hz, Py-H_3); 8.08 (dd, 2H, $J_{3,5\text{-}4}$ = 7.74 Hz, $J_{4\text{-}6}$ = 1.70 Hz, Py-H_4); 7.76 (d, 2H, $J_{2\text{-}3}$ = 8.50 Hz, Ar-$H_{2,6}$);. 7.61 (m, 2H, $J_{4\text{-}5}$ = 7.46 Hz, $J_{5\text{-}6}$ = 4.34 Hz, $J_{3\text{-}5}$ = 1.13 Hz, Py-H_5); 7.11 (dd, 1H, $J_{(C\text{-}H)\text{-}(O\text{-}H)}$ = 5.85 Hz, O-H); 6.21 (dd, 1H, $J_{(C\text{-}H)\text{-}(N\text{-}H)}$ = 8.12 Hz, $J_{(C\text{-}H)\text{-}(O\text{-}H)}$ = 5.85 Hz, C-H). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 75 MHz): δ = 152.1 (Tr-C), 149.4 (Py-C_6), 147.5 (Ar-C_4), 147.3 (Py-C_2), 145.3 (Ar-C_1), 138.3 (Py-C_4), 131.1 (Ar-$C_{3,5}$), 128.3.5 (Ar-$C_{2,6}$), 125.2 (Py-C_5), 123.9 (Py-C_3), 84.5 (C-OH).

(4-Cyanophenyl)(4H-3,5-dipyridin-2-yl-1,2,4-triazole-4-ylamino)methanol (**10**) Yield 62 %. Anal. Calc. (%) for $C_{19}H_{15}N_7O_3$: C, 65.03; H, 4.09; N, 26.54, Found: C, 65.17; H, 4.01 ;N, 26.64. IR (KBr, cm^{-1}): 403w, 480w, 556w, 589w, 608w, 635w, 697m, 722w, 747m, 792s, 620m, 843w, 911w, 976w, 995w, 1019w, 1054m, 1060s, 1078m, 1149w, 1159w, 1188w, 1207w, 1249w, 1279w, 1407w, 1435vs, 1448s, 1459m, 1495m, 1568m, 1589s, 1609w, 2226s, 2926m, 3046s, 3075s, 3198s, 3208m. ^{1}H-NMR

(DMSO-d6, 300 K, ppm, 300 MHz): δ = 8.79 (d, 2H, J_{5-6} = 4.15 Hz, Py-H_6); 8.46 (d,1H , $J_{(C-H)-(N-H)}$ = 8.12 Hz, N-H); 8.19 (d, 2H, J_{3-4} =7.93 Hz, Py-H_3); 8.08 (dt, 2H, $J_{3,5-4}$ = 7.74 Hz, Py-H_4); 7.84 (d, 2H,J_{2-3} = 8.12 Hz, Ar-$H_{3,5}$); 7.66 (d, 2H, J_{2-3} = 8.12 Hz, Ar-$H_{2,6}$);. 7.60 (m, 2H, J_{4-5} = 7.41 Hz, J_{5-6} = 4.15 Hz, J_{3-5} = 1.04 Hz, Py-H_5); 7.05 (d, 1H, $J_{(C-H)-(O-H)}$ = 5.67 Hz, O-H); 6.14 (dd, 1H, $J_{(C-H)-(N-H)}$ = 8.12 Hz, $J_{(C-H)-(O-H)}$ = 5.67 Hz, C-H). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 75 MHz): δ = 152.1 (Tr-C), 149.4 (Py-C_6), 147.3 (Py-C_2), 145.7 (Ar-C_1), 138.3 (Py-C_4), 132.7 (Ar-$C_{3,5}$), 127.9 (Ar-$C_{2,6}$), 125.2 (Py-C_5), 124.1 (Py-C_3), 111.5 (Ar-CN), 100.0 (Ar-C_4), 84.5 (C-OH).

(4H-3-Methyl,5-phenyl-1,2,4-triazole-4-ylamino)(2-nitrophenyl)methanol (**11**).
Compound **11** was prepared from 4-amino-3-methyl,5-phenyl-1,2,4-triazole (**3**) (0.040 g, 0.228 mmol) and 2-nitrobenzaldehyde (0.174 g, 1.152 mmol) in acetonitrile (3 mL). The reaction mixture was stirred and heated at 50^{o}C for 6 hours. The solvent was then evaporated and the solid was washed two times with acetonitrile and one time with methanol and dried in air. Yield 57 %. Anal. Calc. (%) for $C_{16}H_{15}N_5O_3$: C, 59.07;H, 4.65; N, 21.53. Found: C, 59.03 ;H, 4.57; N, .21.60. IR (KBr, cm^{-1}): 522w, 562w, 594w, 620w, 653w, 692vs, 709s, 722s, 743s, 770m, 789m, 841vw, 859w, 878w, 899w, 985w, 1007vw, 1029w, 1039w, 1063w, 1073w, 1116m, 1147w, 1158w, 1193w, 1203w, 1262m, 1295m, 1327m, 1342s, 1359s, 1383m, 1410m, 1447m, 1479s, 1523vs, 1557m, 1614w, 2885m, 2926m, 3217s, 3281s. MS (ESI, m/z): 326.1 $[M-H]^+$; 348.1 $[M+Na]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 300 MHz): δ = 7.83 (m, 2H,Ph-H_2); 7.80 (d, 1H, J_{3-4} = 7.93 Hz, Ar-H_3); 7.72 (d, 2H J = 4.15 Hz, Ar-$H_{5,6}$); 7.55 (dt, 1H, $J_{3,5-4}$ = 8.26 Hz, J_{4-6} = 4.27 Hz, Ar-H_4); 7.43 (m, 3H, Ph-$H_{3,4}$); 7.39 (d,1H , $J_{(C-H)-(N-H)}$ = 6.42 Hz, N-H); 6.84 (d, 1H, $J_{(C-H)-(O-H)}$ = 5.48 Hz, O-H); 5.90(t, 1H, , $J_{(C-H)-(N-H),(C-H)-(O-H)}$ = 5.48 Hz, C-H); 2.51 (s, 1H, Tr-CH_3). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 75 MHz): δ = 153.3 (Tr-C(CH_3), 152.0 (Tr-C(Ph), 147.9 (Ar-C_2), 133.6 (Ar-C_1), 133.0 (Ar-C_5), 129.7 (Ar-C_4), 129.1 (Ph-C_4), 128.8 (Ph-C_1), 128.2 (Ph-C_3), 127.5 (Ph-C_2), 123.8 (Ar-C_3, C_6), 78.6 (C-OH), 10.7 (Tr-CH_3).

(4H-3-Methyl,5-phenyl-1,2,4-triazole-4-ylamino)(2,4-dinitrophenyl)methanol (**12**).
Compound was prepared from 4-amino-3-methyl,5-phenyl-1,2,4-triazole (**3**) (0.060 g, 0.345 mmol) and 2,4-dinitrobenzaldehyde (0.067 g, 0.345 mmol) in acetonitrile (4 mL) in the same way as **11**. Yield 60 %. Anal. Calc. (%) for $C_{16}H_{14}N_6O_5$: C, 51.89; H, 3.81; N, 22.69. Found: C, 51.94; H, 3.85; N, .22.74. IR (KBr, cm^{-1}): 488w, 561m, 5598m, 617w, 641w, 693s, 716m, 739s, 770s, 837m, 857m, 920m, 1003m, 1057m, 1076m, 1126w, 1182m, 1246m, 1267m, 1343vs, 1410m, 1446m, 1479s, 1536vs, 1607s, 2730m, 2854m, 3115s, 3210s. MS (ESI, m/z): 393.1 $[M+Na]^+$; 567.2 $[2M-C_6H_3(NO_2)_2CHO+Na]^+$, 763.2 $[2M+Na]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 300 MHz): δ = 8.45 (d, br, 1H, J_{5-6} = 8.50 Hz, Ar-H_5); 8.42 (s,br, 1H, Ar-H_3); 7.82 (d,br, 1H, J_{5-6} = 8.50 Hz, Ar-H_6); 7.69 (d, br, 1H, $J_{(C-H)-(N-H)}$ = 5.48 Hz, N-H); 7.60 (d, br, 1H, J_{2-3}= 7.18 Hz, Ph-H_2); 7.39-7.30 (m, 3H, Ph-$H_{3,4}$); 7.21 (d, br, 1H, $J_{(C-H)-(O-H)}$ = 4.53 Hz, O-H); 6.09(s, br, 1H, C-H); 2.53 (s, 1H, Tr-CH_3). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 75 MHz): δ = 153.4 (Tr-C(CH_3), 152.0 (Tr-C(Ph), 147.23 (Ar-C_2), 147.17 (Ar-C_4), 139.9 (Ar-C_1), 130.3 (Ar-C_6), 129.0 (Ph-C_4), 128.6 (Ph-C_1), 128.0 (Ph-C_3), 127.4 (Ph-C_2), 127.2 (Ar-C_5), 119.4 (Ar-C_3), 77.8 (C-OH), 10.9 (Tr-CH_3).

2.4.3 Synthesis of Schiff bases **13-20**

Compound **13-18** were synthesized according to the general procedure . An equimolar amount of compound **3** and carbonyl compounds (0.344 mmol) in acetonitrile (4.5 mL) in presence of two drops of concentrated HCl was heated under reflux for 5 hours. After solvent removing the solid products washed with acetonitrile and methanol and dried in air.

(N-(2-nitrobenzylidene)- 4H-3-methyl-5-phenyl-1,2,4-triazole-4-amine) hydrochloride (**13**) Yield 80 %. Anal. Calc. (%) for $C_{16}H_{13}N_5O_2 \cdot HCl$: C, 55,90; H, 4,10; N, 20,37; Cl, 10.31. Found: C,55.67; H, 4.12; N, 20.35; Cl, 10.43. IR (KBr, cm^{-1}): 376w, 495w, 593w, 646w, 656m, 692s, 704vs, 743s, 771m, 780m, 792m, 856s, 878w, 896m, 929m, 976s, 1001w, 1141m, 1230m, 1272m,1291m, 1342vs, 1371m, 1409w, 1439w, 1449m, 1527vs, 1568s, 1589m, 1597w, 1653w, 1830s, 2339br,vs, 2918w, 2995w, 3079w. MS (ESI, m/z, M=$C_{16}H_{13}N_5O_2$): 308.1 $[M+H]^+$; 330.1 $[M+Na]^+$, 346.1 $[M+K]^+$. ^{1}H-NMR (DMSO-d6, 295 K, ppm, 500 MHz) [for 1 and (2) isomers]: δ = 9.34 (9.27) (s, 1H, N=CH), 8.26 (8.25) (d, 1H, J_{3-4} = 8.01 Hz, Ar-H_3); 8.10 (d, 1H, J_{5-6} = 7.63 Hz, Ar-H_6); 7.98 (7.97) (t, 1H, $J_{5-4,6}$ = 7.53 (7.63) Hz, Ar-H_5); 7.92 (t, 1H, $J_{3,5-4}$ = 7.06 (8.39) Hz, Ar-H_4); 7.83 (m, 2H, Ph-H_2); 7.58 (m, 3H, Ph-$H_{3,4}$); 2.66 (2.60) (s, 1H, Tr-CH_3). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 75 MHz) [for 1 and (2) isomers]: δ = 167,4 (162.6) (N=CH), 149.8 (150.0) (Tr-C(CH_3), 148.7 (148.7) (Tr-C(Ph), 148.2 (148.0) (Ar-C_2), 134.7 (134.6) (Ar-C_5), 133.7 (133.5) (Ar-C_4), 130.8 (130.4) (Ph-C_4), 129.8 (129.7) (Ar-C_6), 129.0 (128.9) (Ph-C_3), 128.4 (128.2) (Ph-C_2), 126.4 (126.5) (Ar-C_1), 125.1 (125.1) (Ar-C_3), 124.8 (124.2) (Ph-C_1), 10.7 (10.8) (Tr-CH_3).

Crystal data ($C_{16}H_{14}ClN_5O_2$): M=343.77 ,crystal system: orthorhombic, space group: $P2_12_12_1$, a = 7.165(2) Å, b = 10.585(3) Å, c = 20.678(5) Å, α = 90°, β = 90°, γ = 90°, V = 1568.3(7) $Å^3$, Z = 4, ρc = 1.456 g cm^{-3}, μ = 0.264 mm, θmax = 28.6°, reflections: 10428, independent : 3722, R_{int} = 0.0228, R1 =0.0315, wR2 = 0.0886, GoF = 1.013.

(N-(3-nitrobenzylidene)- 4H-3-methyl-5-phenyl-1,2,4-triazole-4-amine) hydrochloride (**14**) Yield 91 %. Anal. Calc. (%) for $C_{16}H_{13}N_5O_2 \cdot HCl$: C, 55,90; H, 4,10; N, 20,37; Cl, 10.31. Found: C,55.58; H, 3.92; N, 20.50; Cl, 10.60. IR (KBr, cm^{-1}): 660w; 675m; 694m; 709s; 737m; 747w; 776m; 788vw; 819w; 854m; 905w; 922w; 943w; 977s; 996 w; 1096w; 1142w; 1237w; 1292m; 1311m; 1332m; 1352vs; 1372m; 1408w; 1451m; 1478m; 1493 ; 1529vs; 1572w; 1591m; 1608s; 1849m; 2321m; 2582w; 2920w. MS (ESI, CH_3OH, m/z, M=$C_{16}H_{13}N_5O_2$): 308.1 $[M+H]^+$; 340.1 $[M+H+CH_3OH]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 500 MHz) [for E and (Z) isomers]: δ = 9.16 (9.10) (s, 1H, N=CH), 8.75 (8.74) (t, 1H, J = 1.91 Hz, Ar-H_2); 8.50 (8.48) (ddd, 1H, J_{4-5} = 8.22 Hz, J_{4-6} = 2.29 Hz, J_{2-4} = 0.96 Hz Ar-H_4); 8.39 (8.37) (d, 1H, J_{5-6} = 8.03 Hz, Ar-H_6); 7.90 ((7.89) (t, 1H, J_{5-6} = 8.01 Hz, Ar-H_5); 7.84-7.87 (7.82-7.86) (m, 2H, Ph-H_2); 7.51-7.59 (7.51-7.55) (m, 3H, Ph-$H_{3,4}$); 2.65 (2.59) (2.60) (s, 1H, Tr-CH_3).). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 126 MHz) (E isomer): δ = 167.0 (N=CH), 149.9 (Tr-C(CH_3), 148.2 (Tr-C(Ph), 148.1 (Ar-C_3), 134.5 (Ar-C_6), 133.1 (Ar-C_1), 131.0 (Ar-C_5), 130.6 (Ph-C_4), 128.9 (Ph-C_3), 128.4 (Ph-C_2), 127.5 (Ar-C_4), 125.2 (Ph-C_1), 124.1 (Ar-C_2), 10.8 (Tr-CH_3).

(N-(4-nitrobenzylidene)- 4H-3-methyl-5-phenyl-1,2,4-triazole-4-amine) hydrochloride (**15**) Yield 75 %. Anal. Calc. (%) for $C_{16}H_{13}N_5O_2 \cdot HCl$: C, 55,90; H, 4,10; N, 20,37; Cl, 10.31. Found: C,55.66; H, 4.12; N, 20.48; Cl, 10.73. IR (KBr, cm^{-1}): 577w; 629w; 634w; 678w; 691m; 698m; 711s; 748m; 780m; 849s; 889vw; 933m; 962w;978m; 1013w; 1025w; 1078vw; 1105w; 1139m; 1177w; 1240w; 1299m; 1334s; 1350vs; 1411w; 1423w; 1449m; 1464w; 1489w; 1524vs; 1580w; 1590m; 1604w; 1857m; 2353m; 2846w; 3032w; 3107w;. MS (ESI, CH_3OH, m/z, M=$C_{16}H_{13}N_5O_2$): 308.1 $[M+H]^+$; 340.1 $[M+H+CH_3OH]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 500 MHz) [for 1 and (2) isomers]: δ =9.14 (9.08) (s, 1H, N=CH), 8.42 (8.42) (d, 2H, J_{2-3} =8.80 Hz, Ar-$H_{3,5}$); 8.20 (8.19) (d, 2H, J_{2-3} = 8.80 Hz, Ar-$H_{2,6}$); 7.83-7.88 (m, 2H, Ph-H_2) (7.84) (d ,2H, J_{2-3} = 7.10 Hz, J_{2-4} = 2.98 Hz, Ph-H_2): 7.51-7.59 (7.50-7.56) (m, 3H, Ph-$H_{3,4}$); 2.66 (2.61) (s, 1H, Tr-CH_3).). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 126 MHz) (isomer 1): δ = 166.9 (N=CH), 150.0 (Tr-C(CH_3), 149.9 (Tr-C(Ph), 148.1 (Ar-C_4), 137.1 (Ar-C_1), 130.6 (Ph-C_4), 130.4 (Ar-$C_{2,6}$), 128.9 (Ph-C_3), 128.4 (Ph-C_2), 125.1 (Ph-C_1), 124.3 (Ar-$C_{3,5}$), 10.8 (Tr-CH_3).

(N-(2,4-dinitrobenzylidene)- 4H-3-methyl-5-phenyl-1,2,4-triazole-4-amine) hydrochloride (**16**) Yield 72 %. Anal. Calc. (%) for $C_{16}H_{12}N_6O_4 \cdot HCl$: C, 49,43; H, 3.37; N, 21,62. Found: C,49.44; H, 3.40; N, 21.63. IR (KBr, cm^{-1}): 703s; 736w; 775m; 836s; 883m; 907w; 924w; 977m; 1059w; 1121w; 1140w; 1200w; 1231w; 1343vs; 1397w; 1450m; 1538vs; 1589s; 1848m; 2319m; 3086w. MS (ESI, m/z, M=$C_{16}H_{12}N_6O_4$): 353.1 $[M+H]^+$; 371.1 $[M+H+H_2O]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 500 MHz) [for 1 and (2) isomers]: δ =9.36 (9.29) (s, 1H, N=CH), 8.88 (8.42) (d, 1H, J_{3-5} =2.29 Hz, Ar-H_3); 8.73 (dd, 1H, J_{5-6} = 8.41 Hz, J_{3-5} = 2.29 Hz Ar-H_5), (8.72) (dd, 1H, J_{5-6} = 8.24 Hz, J_{3-5} = 2.29 Hz, Ar-H_5); 8,34 (d, 1H, J_{5-6} = 8.80, Ar-H_6), (8.33) (d, 1H, J_{5-6} = 8.24, Ar-H_6), 7.84 (dd ,2H, J_{2-3} = 6.12 Hz, J_{2-4} = 2.68 Hz, Ph-H_2) (7.82) (dd ,2H, J_{2-3} = 6. 64 Hz, J_{2-4} = 2.98 Hz, Ph-H_2): 7.56-7.60 (7.53-7.57) (m, 3H, Ph-$H_{3,4}$); 2.66 (2.62) (s, 1H, Tr-CH_3).). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 126 MHz) (1 isomer): δ = 163.5 (N=CH), 150.2 (Tr-C(CH_3), 149.3 (Tr-C(Ph), 148.7 (Ar-C_2), 148.0 (Ar-C_4), 131.7 (Ar-C_1), 131.4 (Ar-C_6), 130.6 (Ph-C_4), 128.9 (Ph-C_3), 128.6 (Ar-C_5), 128.4 (Ph-C_2), 125.4 (Ph-C_1), 120.3 (Ar-C_3), 11.0 (Tr-CH_3).

(N-(4-chloro-3-nitrobenzylidene)- 4H-3-methyl-5-phenyl-1,2,4-triazole-4-amine) hydrochloride (**17**) Yield 78 %. Anal. Calc. (%) for $C_{16}H_{12}ClN_5O_2 \cdot HCl$: C, 50.81; H, 3.46; N, 18.52. Found: C,50.75; H, 3.32; N, 18.49. IR (KBr, cm^{-1}): 374m; 395m; 484w; 495w; 601vw; 689m; 705vs; 740w; 750w; 777m; 789m; 836m; 845w; 899w; 950s; 982s; 1003w; 1048m; 1140m; 1180w; 1205w; 1234w; 1290w; 1365m; 1456s; 1535s; 1589m; 1863m; 2226m; 2855s; 2925s. MS (ESI, m/z, M=$C_{16}H_{12}ClN_5O_2$): 342.1 $[M+H]^+$; 360.1 $[M+H+H_2O]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 500 MHz) [for 1 and (2) isomers]: δ =9.14 (9.08) (s, 1H, N=CH), 8.65 (d, 1H, J_{2-6} =2.29 Hz, Ar-H_2) (8.64) (d, 1H, J_{2-6} =1.83 Hz, Ar-H_2); 8.24 (dd, 1H, J_{5-6} = 8.41 Hz, J_{2-6} = 1.91 Hz Ar-H_6), (8.23) (dd, 1H, J_{5-6} = 8.47 Hz, J_{2-6} = 2.06 Hz, Ar-H_6); 8,02 (d, 1H, J_{5-6} = 8.41, Ar-H_5), (8.02) (d, 1H, J_{5-6} = 8.24, Ar-H_5), 7.87 (dd ,2H, J_{2-3} = 7.46 Hz, J_{2-4} = 2.10 Hz, Ph-H_2) (7.83-7,87) (m ,2H, Ph-H_2): 7.54-7.60 (7.51-7.57) (m, 3H, Ph-$H_{3,4}$); 2.68 (2.63) (s, 1H, Tr-CH_3).). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 126 MHz) (1 isomer): δ = 166.7 (N=CH), 149.7 (Tr-C(CH_3), 148.2 (Tr-C(Ph), 147.8 (Ar-C_3), 133,4 (Ar-C_6), 132.8 (Ar-C_5), 131,7

(Ar-C_4), 130.9 (Ph-C_4), 129,6 (Ar-C_1) 129.0 (Ph-C_3), 128.5 (Ph-C_2), 126.3 (Ar-C_2), 124.6 (Ph-C_1), 10.7 (Tr-CH_3).

(N-(2-chloro-5-nitrobenzylidene)- 4H-3-methyl-5-phenyl-1,2,4-triazole-4-amine) hydrochloride (**18**) Yield 66 %. Anal. Calc. (%) for $C_{16}H_{12}ClN_5O_2 \cdot HCl$: C, 50.81; H, 3.46; N, 18.52; Cl, 18.75. Found: C,50.69; H, 3.22; N, 18.41; Cl, 18.29. IR (KBr, cm^{-1}): 451w; 462w; 480w; 533w; 595m; 698s; 710m; 741s; 776m; 792w; 842m; 908w; 936w; 946w; 967w; 989w; 1031w; 1050m; 1078w; 1118w; 1129w; 1182w; 1197w; 1249m; 1296m; 1348vs; 1374w; 1396m; 1413w; 1449m; 1474m; 1500w; 1529vs; 1610s; 1872m; 2266m; 2863w; 3061w; 3100w; 3164w. MS (ESI, m/z, M=$C_{16}H_{12}ClN_5O_2$): 342.1 $[M+H]^+$; 360.1 $[M+H+H_2O]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 500 MHz) [for 1 and (2) isomers]: δ =9.17 (9.11) (s, 1H, N=CH), 8.78 (d, 1H, J_{4-6} =2.68 Hz, Ar-H_6) (8.77) (d, 1H, J_{4-6} =2,75 Hz, Ar-H_6); 8.45 (dd, 1H, J_{3-4} = 8.80 Hz, J_{4-6} = 2.68 Hz Ar-H_4), (8.44) (dd, 1H, J_{3-4} = 8.93 Hz, J_{4-6} = 2.98 Hz, Ar-H_4); 7.96 (d, 1H, J_{3-4} = 8.80, Ar-H_3), (7,95) (d, 1H, J_{3-4} = 8.70, Ar-H_3), 7.82 (dd ,2H, J_{2-3} = 7.65 Hz, J_{2-4} = 2.29 Hz, Ph-H_2) (7.78-7,82) (m ,2H, Ph-H_2): 7.56-7.60 (7.53-7.59) (m, 3H, Ph-$H_{3,4}$); 2.67 (2.63) (s, 1H, Tr-CH_3).). ^{13}C-NMR (DMSO-d6, 300 K, ppm, 126 MHz) (1 isomer): δ = 163.3 (N=CH), 149.7 (Tr-C(CH_3), 148.6 (Tr-C(Ph), 146.8 (Ar-C_5), 141,2 (Ar-C_2), 132.1 (Ar-C_3), 130.8 (Ph-C_4), 130,4 (Ar-C_1) 129.1 (Ph-C_3), 128.6 (Ph-C_2), 128.4 (Ar-C_4), 125.0 (Ph-C_1), 123,1 (Ar-C_6), 10.7 (Tr-CH_3).

Compounds **19** and **20**- were synthesized according to the following procedure. The corresponding aldehyde (0.846 mmol) in glacial acetic acid (5 mL) was added to a solution of compound **2** (0.846 mmol) in 5 mL of glacial acetic acid and the mixture was then refluxed for 6 hours. After cooling the solution was poured into a beaker containing 50 mL of ice water. The formed solid product was filtered. After drying in vacuum, the product was recrystallized from ethanol.

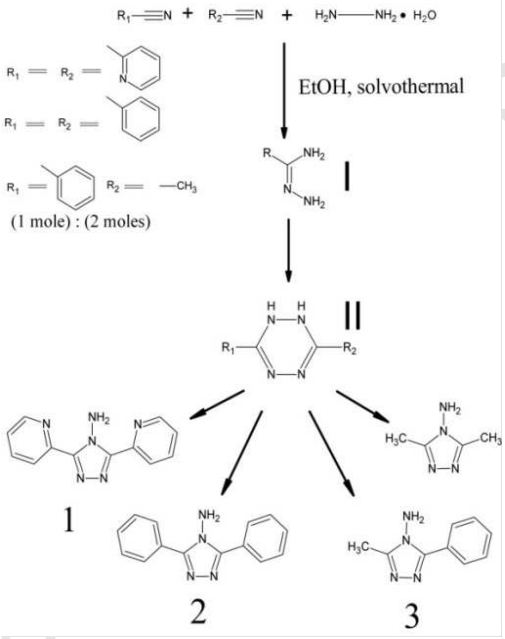
(N-(4-nitrobenzylidene)- 4H-3,5-diphenyl-1,2,4-triazole-4-amine) (**19**) Yield 95 %. Anal. Calc. (%) for $C_{21}H_{15}N_5O_2$: C, 68.28; H, 4.09; N, 18.96. Found: C,67.91; H, 3.91; N, 18.66. IR (KBr, cm-1): 497w; 513w; 611w; 620w; 632w; 677w; 693vs; 701vs; 750w; 773s; 780s; 851m; 860m; 931w; 962w; 981w; 1071w; 1283w; 1320m; 1351vs; 1376w; 1393w; 1446m; 1472s; 1522vs; 1596m; 1620w; 2861w; 3057w. MS (ESI, m/z, M=$C_{21}H_{15}N_5O_2$): 370.1 $[M+H]^+$; 392.1 $[M+Na]^+$, 408.1 $[M+K]^+$, 761.2 $[2M+Na]^+$. ^{1}H-NMR (DMSO-d6, 300 K, ppm, 300 MHz): δ =8.71 (s, 1H, N=CH), 8.31 (d, 2H, J_{2-3} =8.67 Hz, Ar-$H_{3,5}$); 8.00 (d, 2H, J_{2-3} = 8.67 Hz, Ar-$H_{2,6}$); 7.79 (d ,4H, J = 5.07 Hz, Ph-H_2): 7.48 (dd, 4H, J= 5.07, 1.39 Hz, Ph-H_3); 7.48 (d, 2H, J = 1.39 Hz, Ph-H_4). ^{13}C-NMR ($CDCl_3$, 298 K, ppm, 75 MHz): δ = 164.0 (N=CH), 150.8 (Ar-C_4), 150.33(Tr-C(Ph), 136.8 (Ph-C_1), 130.2 (Ar-$C_{2,6}$), 129.6 (Ph-C_4), 129.0 (Ph-C_3), 128.7 (Ph-C_2), 126.3 (Ar-C_1), 124.4 (Ar-$C_{3,5}$).

(N-(2,4-dinitrobenzylidene)- 4H-3,5-diphenyl-1,2,4-triazole-4-amine) (**20**) Yield 96 %. Anal. Calc. (%) for $C_{21}H_{14}N_6O_4$: C, 60.87; H, 3.41; N, 20.28. Found: C,60.66; H, 3.21; N, 20.04. IR (KBr, cm^{-1}): 395w; 439w; 499w; 512w; 590w; 612m; 626s; 667m; 694vs; 710vs; 727m; 739m; 761s; 781vs; 835vs; 843m; 857w; 916s; 925m; 955m; 971w; 979w; 997w; 1010w; 1029w; 1070m; 1124w; 1151w; 1181m; 1202w; 1242m; 1282s; 1310s; 1347vs; 1384s; 1446m; 1471vs; 1536vs; 1596s; 1613s; 3058m; MS (ESI,

m/z, CH_3OH, M=$C_{21}H_{14}N_6O_4$): 415.1 $[M+H]^+$; 437.1 $[M+Na]^+$, 453.1 $[M+K]^+$, 469.1 $[M+Na+ CH_3OH]^+$, 851.2 $[2M+Na]^+$, 883.2 $[2M+Na+CH_3OH]^+$. ^{1}H-NMR (DMSO-d6, 295 K, ppm, 300 MHz): δ =8.92 (s, 1H, N=CH), 8.76 (d, 1H, J_{3-5} =2.31 Hz, Ar-H_3); 8.67 (dd, 1H, J_{5-6} = 8.55 Hz, J_{3-5} = 2.31 Ar-H_5); 8.35 (d ,1H, J_{5-6} = 8.55 Hz, Ar-H_6): 7.80 (d, 4H, J= 5.01 Hz, Ph-H_2); 7.54 (m, 4H, Ph-H_3); 7.53 (m, 2H, Ph-C_4). ^{13}C-NMR (DMSO-d_6, 298 K, ppm, 75 MHz): δ = 165.0 (N=CH), 150.2 (Tr-C(Ph), 148.7(Ar-$C_{2,4}$), 139.3 (Ph-C_1), 131.0 (Ar-C_6), 130.1 (Ph-C_4), 129.0 (Ph-C_3), 128.5 (Ph-C_2), 128.5 (Ar-C_5), 126.0 (Ar-C_1), 120.3 (Ar-C_3).

3. Results and Discussion

The starting 4-amino-1,2,4-triazoles were prepared from nitriles and hydrazine hydrate under solvothermal conditions (**Scheme 1**).

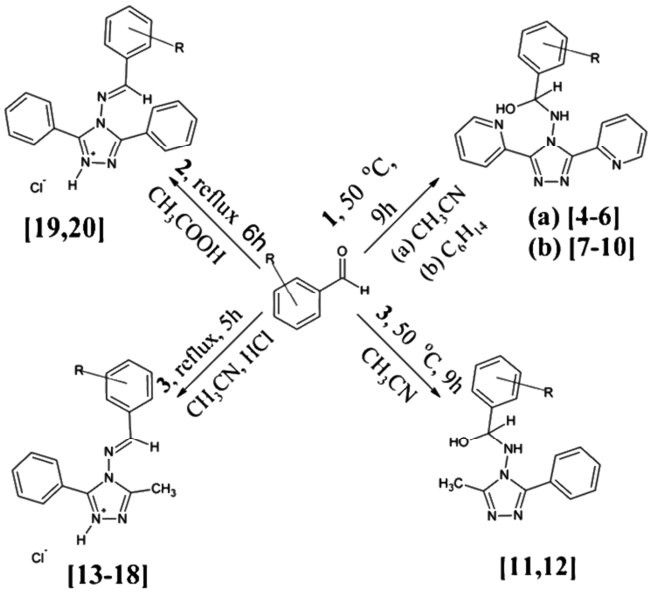


Scheme 1. Preparation of compounds **1**-**3**.

The symmetrically 3,5-disubstituted -4-amino-1,2,4-triazoles can be simply obtained from organonitriles RC≡N and hydrazine in the presence of sulfur or hydrogenesulfide [35], in ethylene glycol [36, 37], dimethylformamide [38] or in one–pot solvothermal conditions [34]. In contrast to that, the unsymmetrical 3,5-disubstituted-4-amino -1,2,4-triazoles were synthesized in a multistep reaction or from other noncommercial reagents as starting materials [39, 40]. When using nitriles only, the 3-ethyl-5-methyl substituted compound was prepared from the equimolar amounts of acetonitrile and propionitrile in the presence of sulfur, but the yield was low [41]. It has been reported previously that in situ solvothermal generation of 4-amino triazoles from hydrazine as a nucleophile to attack various organonitriles takes place by the way of a multi-step process. The reaction involves the initial amidrazone formation (**I**) then the 1,2-dihydrotetrazine (**II**) which undergoes rearrangement to the corresponding 4-

amino-triazole [34]. However to the best of our knowledge, this method to obtain unsymmetrical derivatives is unprecedented. In the condensation of acetonitrile and benzonitrile (molar ratio 2:1 for the higher yield of **3**) with hydrazine hydrate, a mixture of symmetrically 3,5-disubstituted (dimethyl and diphenyl) and 3-methyl,5-phenyl-4-amino-1,2,4-triazole (**3**) was obtained. The separation of products from the reaction mixture was very easy using the normal phase liquid chromatography.

Upon treatment of 4-amino-1,2,4-triazoles (**1**-**3**) with various aromatic aldehydes condensation reaction was expected to take place either to the hemiaminals (**4**-**12**) or Schiff bases (**13**-**20**) (**Scheme 2**).



	-R
4,12,16,20	2,4-$(NO_2)_2$
5,18	2-Cl, 5-NO_2
6,17	3-NO_2, 4-Cl
7,11,13	2-NO_2
8,14	3-NO_2
9,15,19	4-NO_2
10	4-CN

Scheme 2. Synthetic pathway for preparation of compounds **4** to **20.**

3.1 Hemiaminals

Previous experimental and theoretical studies [23-25,42] on the condensation reaction of 4-amino-1,2,4-triazoles with some substituted benzaldehydes showed that the stability of the hemiaminals increased with the increase of electron-withdrawing properties of the aldehyde substituents. Quantum-chemical calculations [42] indicated also that modification of 4-amino-1,2,4-triazole in 3,5 position with almost all small substituents with different electronic effect results in a favorable stabilization of hemiaminal. It was also shown that lack the regularity which was observed for aldehyde substituents. In order to explain how amine structure is affecting the formation and stability of hemiaminals, the aryl substituted 4-amino-1,2,4-triazole derivatives were examined and compared the received data with the previously obtained. The reactions were usually carried out for 9 hours with the reactant ratio 1:1 using acetonitrile or

hexane as solvent at 50° C. Under these conditions, the reaction of 3,5-diphenyl amine (**2**) with substituted benzaldehydes (R= 2-NO_2, 4-NO_2, 2,4-$(NO_2)_2$, 4-Cl,3-NO_2) has not occurred. When the phenyl groups were slightly changed by replacement of a CH in aromatic ring by N , 4-amino-3,5-dipyridyn-2-yl-1,2,4- triazole (**1**) was obtained which was found to be a novel and efficient reagent for stable hemiaminal formation. Similar compounds were also obtained from unsymmetrical 4-aminotriazole substituted by phenyl and methyl groups. Subsequent studies on the effect of the substituents on the selectivity of condensation reaction with 4-amino-triazoles showed that both the steric and electronic effects play an important role in the product formation. The results are summarized in **Table 1.**

Table 1

Substituent effects on the stable hemiaminal formation from 4-amino-3-R_1,5-R_2-1,2,4-triazoles and aromatic aldehydes[a] (Ar-CHO)

Ar	R_1, R_2	Yield (%)		HA/HA+SB (%)
		HA	SB	
2-$NO_2C_6H_4$	R_1=R_2=H	76	2	97
	R_1=R_2=CH_3	27	4	82
	R_1=R_2=2-py	43	7	86
	R_1=CH_3, R_2=Ph	24	35	41
	R_1=R_2=Ph	0	0	0
4-$NO_2C_6H_4$	R_1=R_2=H	70	6	92
	R_1=R_2=CH_3	18	0	100
	R_1=R_2=2-py	34	3	92
	R_1=CH_3, R_2=Ph	0	0	0
	R_1=R_2=Ph	0	0	0
2,4-$(NO_2)_2C_6H_3$	R_1=R_2=H	77	4	92
	R_1=R_2=CH_3	66	0	100
	R_1=R_2=2-py	80	0	100
	R_1=CH_3, R_2=Ph	62	10	86
	R_1=R_2=Ph	0	0	0

a. Reaction were carried out by mixing equimolar amounts of 4-amino-1,2,4-triazole and aldehyde (0.172 mmol) in CH_3CN (2 mL) at 50 °C for 9 hours. Product yields were determined by the ^1H NMR analysis of the crude reaction mixture.

Increasing the steric bulk of the amine groups changes the reactivity of the nitrogen atom. The increase of the size of C-substituents, R_1 and R_2 in the 4-amino-1,2,4-triazoles, reduced the hemiaminal formation in the following order R_1,R_2=H,H; CH_3,CH_3; CH_3,Ph; Ph,Ph. Furthermore, for these substituents the steric effects seem to much more powerful significant than the electronic ones. Isosteric replacement of phenyl substituents by 2-pyridyl results in a significant change in reactivity. Different nucleophilicity of the amine group probably results from electronic effects and from the

fact that in contrast to **2** [43], the H amino atoms of **1** participate in intramolecular H-bonds with the pyridyl N atoms as acceptors [44].

As shown in **Table 2** the reactivity of benzaldehyde substrates with **1** was affected by the number of the electron-withdrawing groups, their position and solvent used. For the mono substituted benzaldehydes, the rate of hemiaminal formation is slower in polar aprotic solvents such as CH_3CN than in apolar aprotic solvents like (hexane), similarly to that observed in the case of 3,5-dimethyl-1,2,4-triazole amine [25].

Table 2

Benzaldehyde substituent and solvent effects on the hemiaminal and Schiff base formation from the 4-amino-3,5-di-2-pyridyl-1,2,4-triazole (**1**)[a].

Ar	solvent	Yield (%)		HA/HA+SB
		HA	SB	(%)
2-$NO_2C_6H_4$	CH_3CN	43	7	86
	Hexane	71	11	87
3-$NO_2C_6H_4$	CH_3CN	25	0	100
	Hexane	46	0	100
4-$NO_2C_6H_4$	CH_3CN	34	3	92
	Hexane	71	6	92
4-CNC_6H_4	CH_3CN	41	9	82
	Hexane	69	4	95
2,4-$(NO_2)_2C6H3$	CH_3CN	80	0	100
3-NO_2,4-ClC_6H_3	CH_3CN	49	0	100
2-Cl,5-$NO_2C_6H_3$	CH_3CN	98	0	100

a. Reactions were carried out by mixing equimolar amounts of **1** and aldehyde (0.172 mmol) in solvent (2 mL) at 50 ^oC for 9 hours. Product yields were determined by the ^1H NMR analysis of the crude reaction mixture.

The formation of hemiaminals was confirmed by FT-IR, MS and NMR. Selected spectral data and their assignments are listed in **Table 3**.

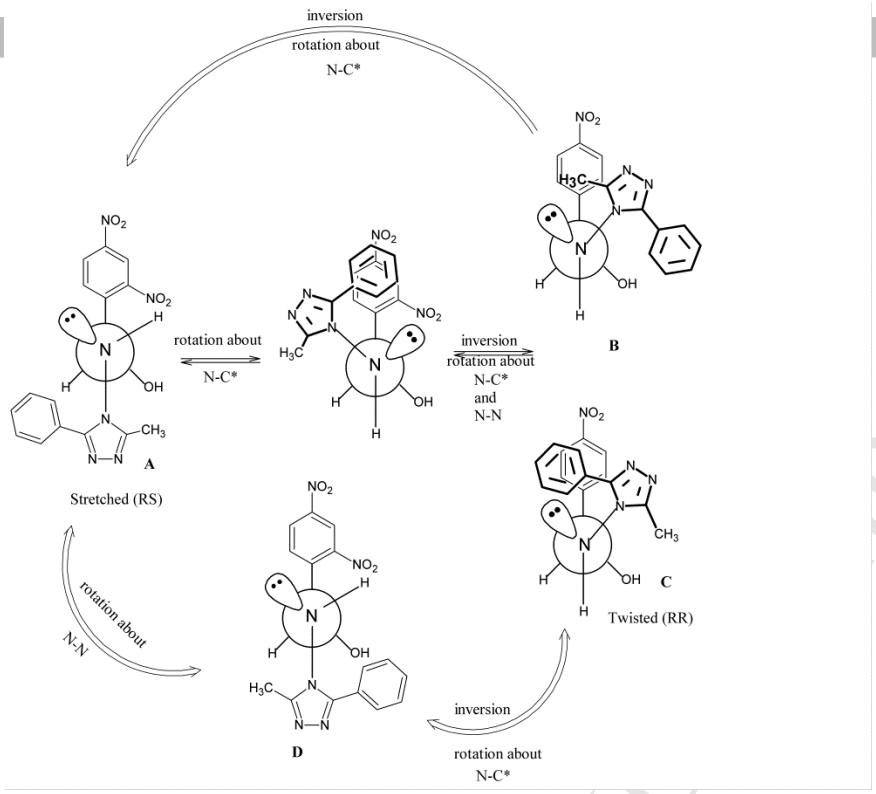
The bands due to NH_2 and C=O groups that were present in the spectra IR of substrates at 3344 cm^{-1}, 3253 cm^{-1} and about 1700 cm^{-1} for di-pyridyl, methyl-phenyl 1,2,4-triazole amine and for benzaldehydes, respectively, disappeared from the infrared spectra of compounds **4**-**12**. The stretching vibrations of –OH and –NH groups were found at 2500-3500 cm^{-1} as broad bands. This indicates that the hemiaminal molecules in the solid state are linked by strong -O-H$\cdots$$N_{Tr}$ and -N-H$\cdots$$N_{py}$ hydrogen bonds. The IR spectra of all hemiaminals show vibrational bands at 1569-1592 and 1418-1473 assigned for C=N and C=C vibrations. The strong bands observed in the IR spectrum of **4**-**9**, **11** and **12** compounds at approximately 1350 and 1520 cm^{-1} can be assigned to the NO_2 group vibrations. The C≡N stretching vibration in **10** was present at 2226 cm^{-1}. The NMR spectra were obtained in the DMSO solution. It is obvious that solute and solvent molecules must interact during the dissolution process. The hydrogen interaction observed for hemiaminals in the solid state must be broken

Table 3
Selected spectral data of hemiaminals $R_1C^*H(OH)NHR_2$

R_1	R_2	vibration frequencies [cm^{-1}]		^1H NMR δ[ppm], J[Hz]					^{13}C NMR [ppm]
		$\nu_{(OH,.NH)}$	$\nu(NO_2)$, $\nu(C\equiv N)$	$\delta_{(NH)}$	$\delta_{(OH)}$	$\delta_{(CH)}$	J_{CH-NH}	J_{CH-OH}	$\delta(C^*)$
2,4-$(NO_2)_2$ C_6H_3 (**4**)	A	3105	1349,1532	8.75	7.44	6.49	8.24	5.49	83.9
2-Cl, 5-NO_2 C_6H_3 (**5**)	A	3132	1343,1519	8.54	7.27	6.36	7.92	5.53	81.1
3-NO_2,4-Cl C_6H_3 (**6**)	A	3125	1349,1532	8.52	7.23	6.14	7.78	5.49	81.1
2-NO_2 C_6H_4 (**7**)	A	3198	1359,1527	8.63	7.14	6.39	8.31	5.48	80.7
3-NO_2 C_6H_4 (**8**)	A	3209	1352,1526	8.51	7.15	6.19	7.84	5.64	84.4
4-NO_2 C_6H_4 (**9**)	A	3220	1346,1522	8.52	7.11	6.21	8.12	5.85	84.5
4-CN C_6H_4 (**10**)	A	3198	2226	8.46	7.05	6.14	8.12	5.67	84.5
2-NO_2 C_6H_3 (**11**)	B	3217	1359,1523	7.39	6.84	5.90	6.42	5.48	78.6
2,4-$(NO_2)_2$ C_6H_3 (**12**)	B	3210	1343,1536	7.69	7.21	6.09	5.48	4.53	77.8

A- 3,5-di-2-pyridyl-1,2,4-triazole, B-3-methyl,5-phenyl-1,2,4-triazole.

and new ones, involving the oxygen atoms of DMSO and acidic protons –OH and -NH were formed [45]. After the condensation reaction, absorptions at 7.82 for **1** and 6.02 for **3** (δNH_2 group) disappeared from the ^1H NMR spectra, and all compounds showed new resonances assigned to the C-NH-N, C-OH and CH-N protons (**Table 3**). The characteristic $\delta(C^*)$ signal for hemiaminals $R_1C^*H(OH)NHR_2$ at 77.8-84.5 ppm was also observed in the ^{13}C NMR. The room temperature ^1H NMR spectrum of **12** is very broad in every region, suggesting the presence of at least two conformers slowly interconverting on the NMR scale. It is known that the vicinal H-H coupling magnitude is a function of the dihedral angle between the protons [46]. Thus, the small coupling constant $^3J_{(CH-NH)}$ for hemiaminal **12** (5.48 Hz) indicates that a transformation of stretched molecule may occur in solution (dihedral angle about 170°) into a twisted one (dihedral angle around 60°). Rotation about N(sp^3) -C*(sp^3) bond and the configuration inversion on the N atom are the steps in that process. **Scheme 3** shows a possible interconversion pathway for **12** in DMSO solution.



Scheme 3. Possible interconversion pathway for **12** in DMSO solution.

Possible mechanism of interconversion for hemiaminal **12** was studied also by means of quantum-chemical calculations (0 K). Relaxed scan of the potential energy surface (PES) was performed for two dihedral angles: N-N-C-C and C-N-N-C. The values of the angles were separately varied from -180 to 180^o with step 6^o. Local minima obtained from the scan of PES were subsequently optimized to minimum of total energy (E_{tot}).

Conformational analysis performed for the N-N-C-C angle and subsequent optimization of geometrical structure yielded two different local minima on PES for -86^o (Min1) and 47^o (Min3). The optimized geometrical structures of both conformers are presented at Figure 1a.

The Min1 conformer is about 5.1 kcal/mol more stable than Min3 conformer. Both conformers are separated by two energy barriers that are local maxima of potential energy with respect to rotation around the N-C single bond. The interconversion from the Min1 to Min3 conformer requires supply of about 6 kcal/mol of energy (the energy barrier for ≈ 0^o) or 12 kcal/mol (the energy barrier for ≈ 130^o). Conformational analysis performed for the C-N-N-C angle showed also two local minima on PES for 97 and -74^o (Min2). The minimum of E_{tot} found for 97^o turned out to be very similar to the Min1 therefore it was not further studied. The Min2 conformer is only 3.9 kcal/mol less stable than the Min1 conformer. The estimated value of the height of energy barrier between Min1 and Min2 is about 9 kcal/mol. Taking into account small differences of the values of E_{tot} between all conformers and small values of the energy barriers our calculations suggest that all three conformers of the hemiaminal may be experimentally observed.

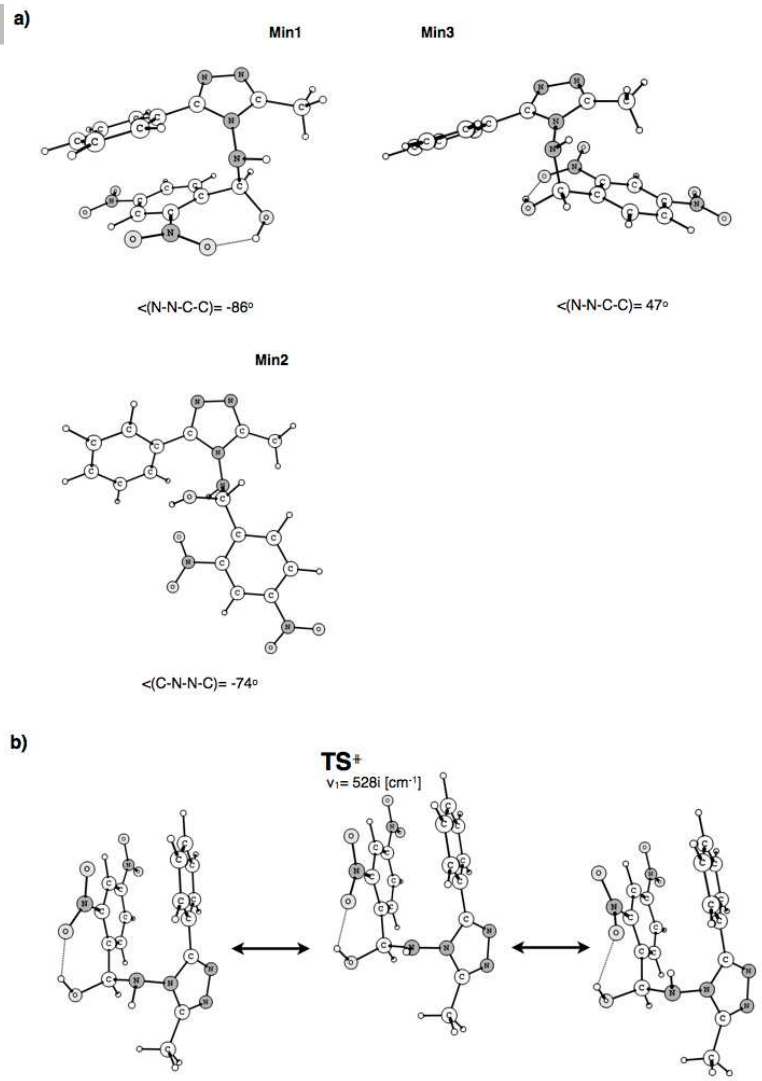


Figure 1. a) Optimised geometrical structures of the molecule of hemiaminal **12** that were selected on the basis of conformational analysis performed for the N-N-C-C (Min1, Min3) and C-N-N-C (Min2) dihedral angles. b) Optimized geometrical structures of transition state (TS) and associated minima of the total energy for a process of interconversion of the chirality of the nitrogen.

The analysis of configuration on the N atom for all points obtained from the relaxed scans of PES for both dihedral angles has shown the interconversion of the chirality of the nitrogen. The geometrical structures of the transition state (TS) and associated local minima on PES obtained from geometry optimization, following the intrinsic reaction coordinate, are shown at Figure 1b. The energy barriers are low (2.94 and 3.25 kcal/mol) and they are smaller than calculated for ammonia using CCSD(T) data (5.06 kcal/mol) [47]. This result suggests that a process of interconversion of the chirality of the nitrogen in hemiaminal **12** is very probable under experimantal conditions.

The hemiaminals **4**-**10** are stable in the solid state for a long time period but in the DMSO solution they decompose mostly to substrates (**Figure 2**).

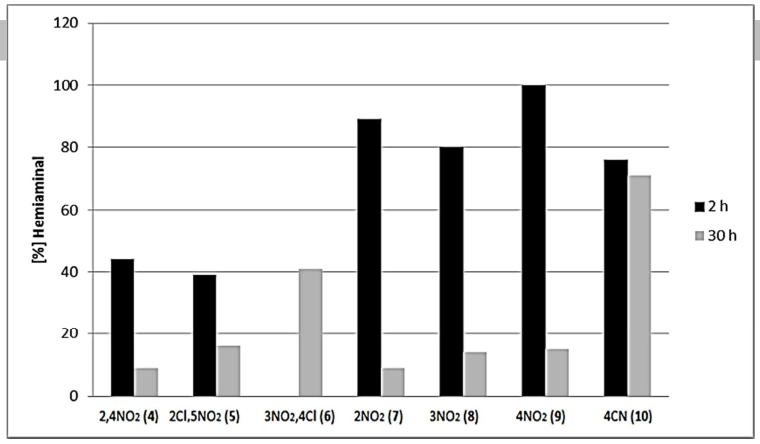


Figure 2. Decomposition of the hemiaminals **4-10** in DMSO solution as the function of time.

In some cases, formation of the Schiff base was observed as a second step of the benzaldehyde and 4-amino-3,5-di-2-pyridyl-1,2,4-triazole condensation, after water elimination from hemiaminal molecules. The compounds **4**, **5**, **6**, **8** and **9** with the phenyl ring substituted by 2,4-$(NO_2)_2$; 2-Cl,5-NO_2; 3-NO_2,4-Cl; 3-NO_2 and 4-NO_2, respectively, were transformed into the Schiff bases with : 5; 3; 37; 12 and 16 % yields, after standing for 30 hours at room temperature in DMSO solution. Also compound **12** is not very stable in DMSO solution (40% of starting hemiaminal after 20 days). The NMR spectra showed also signals corresponding to the -CH=N- Schiff base (δ_H=9.27 and δ_C=161.0 ppm), $-CH(OH)_2$ aldehyde gem-diol (δ_H=6.25 (1H); 7.21(2H) and δ_C=85.1 ppm) groups plus amino-triazole and benzaldehyde signals. The results show also that the replacement of a hydrogen or methyl [25] by a phenyl or a 2-pyridyl group in the triazole ring leads to decrease in the stability of these hemiaminals in DMSO solution.

Single crystals of **4** and **5** suitable for X-ray analysis were obtained from acetonitrile at room temperature by slow solvent evaporation. Molecular views of the compounds are shown in **Figure 3**, and selected geometric parameters are given in **Table 4**.

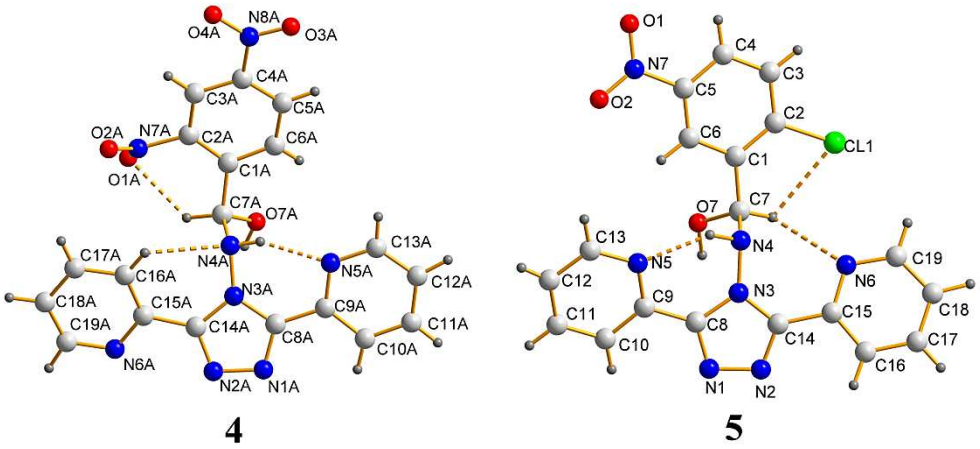


Figure 3. Molecular view of new hemiaminals with atom labeling and intramolecular hydrogen bonding (dashed lines).

Geometry of **4** and **5** displays significant similarities. The molecules are composed of the central 1,2,4,-triazole ring, substituted at the C8 , C14 and N3 atoms by two 2-pyridyl and C_α-hydroxybenzylamino groups. The central heterocyclic ring is planar but in contrast to amine **1** [44], not coplanar with its 2-pyridyl substituents. The pyridyl rings are twisted about the external bond to the 1,2,4-triazole (**Table 4**). The most noteworthy feature of these structures is the dissimilar orientation of the pairs of pyridine rings. While in the molecule of **4** the pyridine nitrogen atoms point in opposite direction, both pyridine nitrogen atoms in the molecule of **5** point away from the N_2 unit of the central five-membered heterocyclic ring.

Table 4
Selected geometric parameters for **4** and **5**.

	4		**5**
	A	**B**	
	Bond lengths [Å]		
C1-C7	1.532(3)	1.526(3)	1,515(4)
C7-N4	1.484(4)	1,485(4)	1,475(5)
N4-N3	1,425(3)	1,417(3)	1,422(4)
C8-C9	1,460(4)	1,477(4)	1,458(5)
C8-N1	1,321(3)	1,319(3)	1,322(4)
C7-O7	1.399(4)	1.400(4)	1.419(4)
N1-N2	1.378(3)	1.381(3)	1.388(3)
	Torsion angle [^{o}]		
C1-C7-N4-N3	-170.5(2)	171.3(2)	173.0(2)
	Dihedral angle [^{o}]		
Phenyl-triazole	21.8(3)	20.5(8)	8,3(5)
Pyridyl (1)-triazole	10.4(3)	23.3(4)	15,1(3)
Pyridyl (2)-triazole	19.3(8)	22.4(3)	22,9(5)

The later conformation was previously observed in most of the 4-substituted 3,5-di(2-pyridyl)-1,2,4-triazoles [48]. The second one was only detected in crystals of 1-(3,5-bis(pyrid-2-yl)-1,2,4-triazol-4-yl)-3-phenylurea [49], 3,5-di(2-pyridyl)-4-(1H-pyrrol-1-yl)-4*H*-1,2,4-triazole and metal complexes [50].

Two aromatic rings, phenyl and triazole are linked through a N3-N4-C7-C1 fragment, central part of molecule. In the hemiaminals, the C7 and N4 atoms are tetrahedral with sp^3 and N3 and C1 are planar with sp^2 hybrydization. The N3-N4-C7-C1 torsion angle is determined by the type of molecules – either stretched or twisted [23]. For **4** and **5** these torsion angles are about 170^o (**Table 4**) and two stretched stereoisomers RS and SR are formed. Structural analysis of **4** and **5** shows that similarly to other hemiaminals derived from 1,2,4-triazoles [23-25], strong intermolecular hydrogen bonds O-H$\cdots$N$_{2Tr}$ exist. This type of almost linear interactions connecting two stretched molecules leads to the formation of centrosymmetric dimers (RS-SR) (**Figure 4**).

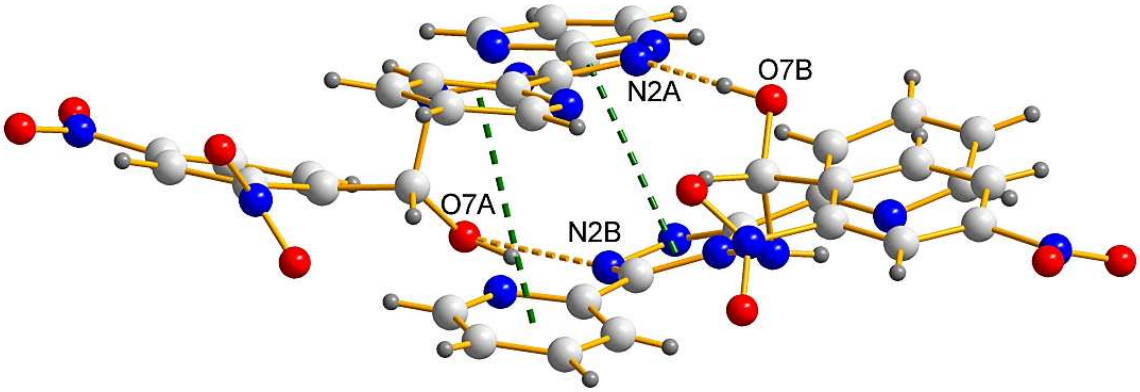


Figure 4. A view of part of the crystal structure of **4** showing the formation of the hydrogen – bonded dimer and π-π interaction between aromatic rings.

The hydrogen bridges between the OH group and the nitrogen N_2 atom of the triazole ring in compounds **4** and **5** (**Table 5**) are comparable to the corresponding bond previously reported for (2,4-dinitrophenyl)(1,2,4-triazole-4-amino)methanol (O-H···N_{Tr} 1.81(2) Å, O·· N_{Tr} 2.744(2) Å , O-H-N_{Tr} angle 168(2)^o) and (2,4-dinitrophenyl)(3,5-dimethyl-1,2,4-triazole-4-amino)methanol (O-H···N_{Tr} 2.00(4) Å, O·· N_{Tr} 2.811(3) Å , O-H-N_{Tr} angle 161(3)^o) dimers [23, 25]. The crystals packing is determined also by the combination of strong N-H···N_{py} intramolecular and C-H···N, C-H···O, C-H···Cl weak intra and intermolecular hydrogen bonds (**Table 5**, **Figure 3**). In addition to these interactions, the crystal structures are stabilized by π-π interaction between aromatic rings. Intermolecular π-π contacts in **4** occur between the two triazole rings (Cg1) (the ring centroids distance from Cg1A to Cg1B is 3.143Å and offset distance is 1.110Å) and pyridine rings (Cg2) (the ring centroids distance from Cg2A to Cg2B is 3.225 with offset of 1.734 Å) (**Figure 4**). The distance between the triazole rings centroids in dimer **5** is 3.275 and the offset is 1.093 Å.

Table 5
Geometry of proposed hydrogen bonds for **4** and **5**

D-H···A [Å]	D-H [Å]	H···A [Å]	D···A [Å]	<D-H···A][°
		4		
O(7B)-H(70B)···N(2A)	0.84(3)	2.15(3)	2.925(3)	154(3)
O(7A)-H(70A)···N(1B)	0.97(3)	2.61(3)	3.412(3)	141(2)
O(7A)-H(70A) ··N(2B)	0.97(3)	1.84(3)	2.787(3)	165(3)
C(5B)-H(5B) ··O(4A)$^{(i)}$	0.95	2.48(3)	3.226(4)	135(3)
C(6B)-H(6B)···O(7B)$^{(ii)}$	0.95	2.50(3)	3.117(4)	123(2)
C(6A)-H(6A)···O(7A)$^{(iii)}$	0.95	2.54(3)	3.283(4)	135(3)

C(13B)-H(13B)···O(4A)$^{(i)}$	0.95	2.50(3)	3.442(3)	171(3)
C(13A)-H(13A)··O(4B)$^{(iv)}$	0.95	2.43(3)	3.225(3)	141(3)
C(18A)-H(18A)···O(4)$^{(v)}$	0.95	2.41(5)	3.297(5)	156(3)
C(19B) -H(19B)···O(1A)	0.95	2.42(3)	3.186(3)	138(3)
C(19A)-H(19A)···O(2B)	0.95	2.42(3)	3.287(3)	152(3)
C(5B) -H(5B)···N(2A)$^{(ii)}$	0.95	2.56(3)	3.379(4)	144(3)
C(5A) -H(5A)···N(1B)$^{(iii)}$	0.95	2.56(3)	3.468(4)	159(3)
C(17A)-H(17A)···N(5A)$^{(vi)}$	0.95	2.61(3)	3.481(4)	152(3)
C(7B) -H(7B)···N(6A)	1.00(3)	2.59(3)	3.311(3)	129(2)
N(4B) -H(40B)···N(5B)	0.83(3)	2.15(3)	2.830(3)	140(3)
N(4A) -H(40A)···N(5A)	0.91(4)	2.00(3)	2.816(3)	150(3)
C(7B) -H(7B)···O(2B)	1.00(3)	2.32(3)	3.004(4)	125(3)
C(7A) -H(7A)···O(1A)	1.00(3)	2.36(3)	3.041(4)	125(3)
C(7A) -H(7A)···N(7A)	1.00(3)	2.61(3)	3.024(4)	105(4)
C(16B) -H(16B)···N(4B)	0.95	2.41(3)	2.994(4)	119(3)
C(16A)-H(16A)···N(4A)	0.95	2.39(3)	3.006(4)	122(2)
		5		
O(7) -H(70)···N(2)$^{(vii)}$	0.84	1.94(3)	2.763(3)	168(2)
C(12) –H(12)…O(1)$^{(viii)}$	0.95	2.59(3)	3.478(4)	155(3)
C(18) -H(18)···Cl(1)$^{(ix)}$	0.95	2.81(3)	3.653(4)	148(2)
N(4) -H(40)···N(5)	0.96(3)	2.07(3)	2.870(5)	139(2)
C(7) -H(7)···Cl(1)	1.00(3)	2.62(3)	3.120(3)	111(2)
C(7) -H(7)··N(6)	1.00(3)	2.58(3)	3.220(5)	122(2)

Symmetry codes: (i) x,y,1+z ; (ii)1-x,1-y,1-z ; (iii)-x,1-y,-z ; (iv)-1+x,-1+y,-1+z ; (v) 2-x,2-y,1-z ; (vi)1-x,1-y,-z ; (vii) 1-x,1-y,-z, (viii) 2-x,1-y,1-z, (ix) -x,-y,1-z

3.2 Schiff bases

The 4-amino-3-methyl-5-phenyl-4H-1,2,4-triazole (**3**) when treated with various substituted benzaldehydes in acetonitrile in presence of hydrochloric acid as a catalyst formed corresponding Schiff base hydrochlorides **13-18.** At the same condition 4-amino-3,5-diphenyl-4H-1,2,4-triazole (**2**) has not reacted with benzaldehydes and imines **19** and **20** could only be obtained after changing the solvent to acetic acid.

The structures of the Schiff bases were in accord with their spectroscopic data. The IR spectra of compound **13-18** showed in the solid state strong, broad absorption bands at 3400- 1800 cm^{-1} which were attributed to the stretching modes of triazolium $C=N^{+}$-H group. Generally, the absorption peaks corresponding to that group occurred at slightly higher frequencies [51]. The appearance of these modes at lower frequencies may be caused by the hydrogen bonding interactions with the chloride ion N^{+}-H··Cl exist (**Table 6**). The spectra of **13-20** display also characteristic azomethine group stretching

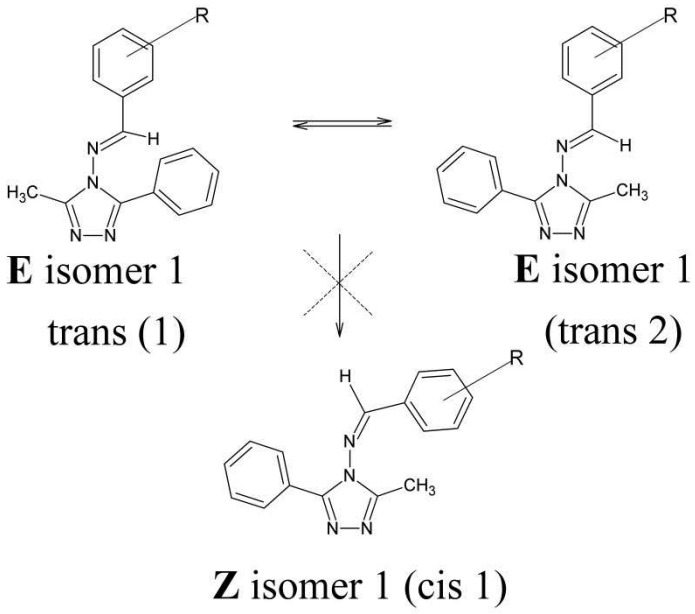
band in the range of 1589-1653 cm^{-1} and strong bands at approximately 1350 and 1530 cm^{-1} which can be assigned to the NO_2 group vibrations.

Table 6
Selected spectral data of Schiff bases R1C*H=NR2.

R_1	R_2	vibration frequencies [cm^{-1}]				NMR δ[ppm], ^1H, (a)		^{13}C,(a)
		$\nu_{(N^+H)}$	$\nu_{(C=N^+)}$	$\nu_{(C^*=N)}$	$\nu(NO_2)$	δ(C*H=N)	δ(CH_3)	δ(C^*)
2-NO_2 C_6H_4 (**13**)	A	2339	1830	1653	1342	(9.34)	(2.66)	(167.4)
					1527	9.27	2.60	162.6
3-NO_2 C_6H_4 (**14**)	A	2582	1849	1608	1352	(9.16)	(2.65)	(167.0)
		2321			1529	9.10	2.59	
4-NO_2 C_6H_4 (**15**)	A	2359	1857	1604	1334	(9.14)	(2.66)	(166.9)
					1524	9.08	2.61	
2,4-$(NO_2)_2$ C_6H_3 (**16**)	A	2319	1848	1589	1343	(9.36)	(2.66)	(163.5)
					1538	9.29	2.62	
4-Cl, 3-NO_2 C_6H_3 (**17**)	A	2226	1863	1589	1365	(9.14)	(2.68)	(166.7)
					1535	9.08	2.63	
2-Cl, 5-NO_2 C_6H_3 (**18**)	A	2266	1872	1610	1348	(9.17)	(2.67)	(163.3)
					1529	9.11	2.63	
4-NO_2 C_6H_4 (**19**)	B			1620	1351	8.71		164.0
					1522			
2,4-(NO2)2 C6H3 (**20**)	B			1613	1347	8.92		165.0
					1536			

A-3-methyl,5-phenyl-1,2,4-triazole, B-3,5-diphenyl -1,2,4-triazole, a- after recrystallization from methanol

The ^1H NMR spectra of compounds **14-18** revealed the presence of two signals belonging to the azomethine CH proton and the methyl triazole CH_3 substituent at 9.08-9.36 and 2.59-2.66 ppm, respectively. The appearance of these protons in the ^1H NMR spectrum of compound **13** as two sets of two singlets can be considered as a proof of the formation of two isomers. It was reported in the literature [52] that compounds possessing the azomethine linkage exhibit E and Z geometrical isomerism around -C=N- double bond (**Scheme 4**). Moreover, the trans-isomers of Schiff bases are more stable and photoinduced cis-isomers return spontaneously and very quickly to the E form [53]. The ^1H NMR signals of the cis and trans isomers of aromatic imines show particularly large differences in their chemical shifts [52, 54]. Our data for compounds **13-18,** and the slight differences observed after recrystallization from methanol allow think that these compounds exist only as a E isomers but in different conformations probably arising from the rotation around N-N single bond (**Scheme 4**).



Scheme 4. Possible conformers of Schiff bases **13**-**18** obtained from 4-amino-3-methyl-5-phenyl-4H-1,2,4-triazole (**3**).

The conformational preference of the Schiff base (shown at Scheme 4) was studied by means of the PES scan with geometry optimization at each point at the M062x/6-311++G(d,p) computational level (0 K) using SCRF method with the dielelctric constant for DMSO. The C-N-N-C dihedral angle was varied between -180 and 180^o with step of 6^o. The evolution of the total energy (E_{tot}) of the Schiff base relative to a value of the C-N-N-C dihedral angle is presented at **Figure 5**. The relationship between values of E_{tot} and dihedral angle was modelled using polynomial regression [55].

Four different local minima (Min1 - Min4) and four local maxima of E_{tot} were observed. The optimized geometrical structures of the conformers are presented at **Figure .5**. The optimized value of the C-N-N-C dihedral angle equals respectively: -146^o (Min1), -50^o (Min2), 47^o (Min3) and 141^o (Min4). The difference of the values of the total energy between the most stable (Min1) and the less stable (Min4) confomer is very small and equals only 1.60 kcal/mol. Similarly, the estimated heights of the energy barrier associated with a rotation about the N-N bond are also very small (< 1.8 kcal/mol). Thus, the single molecule of Schiff base is floppy molecule and presumably can be easily interconverted from one to another conformer.

Additionally conformer Min1 is stabilized by intramolecular C-H....O interaction ($\rho_{(3,-1)}(r)$ = 0.007 e/bohr^3, $\nabla^2\rho_{(3,-1)}(r)$ = 0.026 e/bohr^5) between the methyl and NO_2 groups.

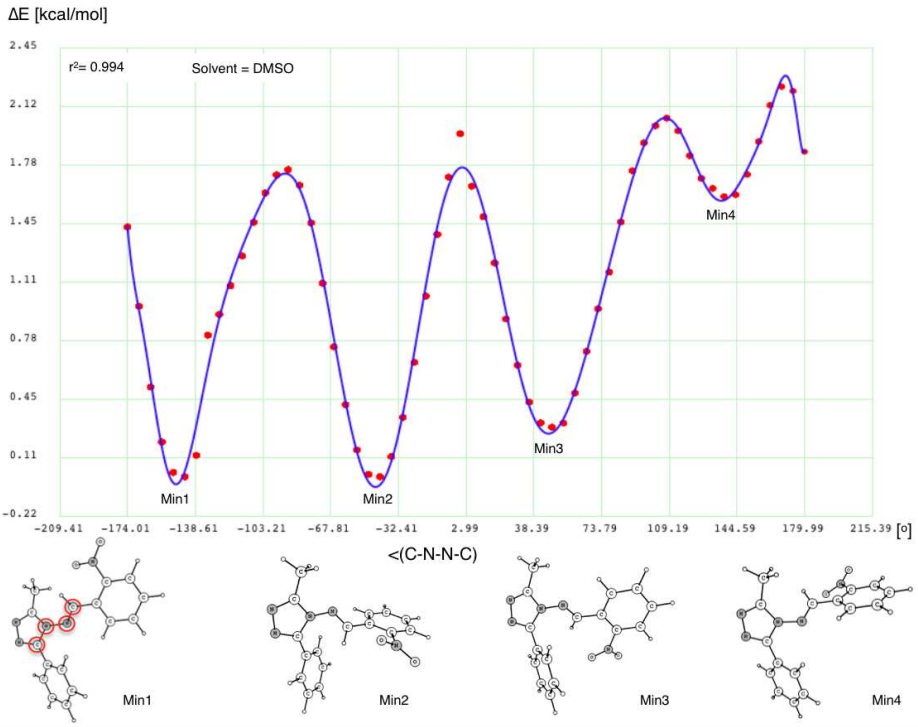


Figure 5. Evolution of the potential energy of the Schiff base relative to a rotation about the N-N bond (the C-N-N-C dihedrial angle denoted by red circles, values in ^{o}) obtained from conformational analysis. The values of the relative energy (in kcal/mol) are calculated in respect to the total energy for Min2. The optimised geometrical structures of the conformers (Min1 - Min4) correspond to four local minima observed in the graph of the potential energy.

Single crystals of **13** were grown by slow evaporation of acetonitrile from the post-reaction mixtures. The X-ray structure of **13** shows the E geometries of the C=N azomethine double bond. The same configuration is expected for all **14-18** because the 3-methyl-5-phenyl-1,2,4-triazole-4-amine moiety is common to all of these compound and the Z configuration would be higher in energy.

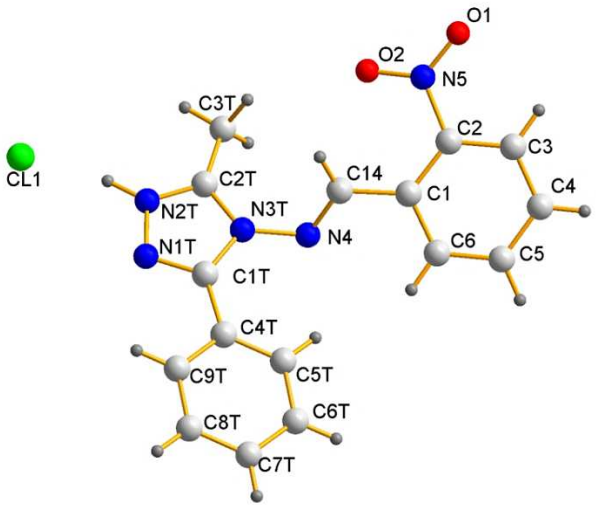


Figure 6. . Molecular view of Schiff base hydrochloride **13** with atom labeling.

The molecular view of compound **13** with atom-numbering scheme is shown in **Figure 6** and selected geometric parameters are given in **Table 7**. The bond lengths and angles are found to have normal magnitudes [56]. In the crystal structure two rings in the phenyl-triazole fragment is not flat and the (N1T-N2T) triazole and (C4T-C9T) phenyl rings make are not coplanar with dihedral angle of 12.5(2)^{o}. The N4=C14 double bond and the C1-C6 aromatic ring are also not coplanar. The C2-C1-C14-N4 torsion angle is equal 152.1(2).

Table 7
Selected geometric parameters for **13**.

Bond lengths [Å]		Bond angles [^{o}]	
C1-C14	1.474(2)	N4-N3-C2T	125.4(2)
C14-N4	1.278(2)	C1-C14-N4	117.3(2)
N4-N3T	1,419(2)	N4-C14-C1	117.2(1)
N2T-C2T	1,317(2)	Torsion angle [^{o}]	
N1T-C1T	1,318(2)	C2-C1-C14-N4	152.1(2)
N1T-N2T	1.361(2)	N3T-N4-C14-C1	176.7(2)
Dihedral angle [^{o}]			
Phenyl-triazole	31.0(2)	Phenyl(T)-triazole	12.5(2)

The dihedral angle between the triazole ring (N1T-N2T) and the phenyl one (C1-C6) indicates that they are twisted from each other (31.0(2)^{o}), which is quite different from that found for (N-(4-nitrobenzylidene)-4H-3,5-Dimethyl-1,2,4-triazole-4-amine) hydrochloride (70.48(2)^{o}) [25]. The differences between these two compounds are mainly due to hydrogen bonding interaction between disordered *orto* CH groups on the C4T-C9T ring and either N1T and N4 atoms (see **Table 8**). The strong N2T-H10T···Cl and weak C-H···O, C-H···Cl intermolecular interactions also occur.

Table 8
Hydrogen bonding geometry for compound **13.**

D-H···A [Å]	D-H [Å]	H···A [Å]	D···A [Å]	<D-H···A][°
N(2T)-H(10T)...Cl(1)	0.98(2)	2.00(2)	2.967(2)	169
C(4)-H(4)...O(1)$^{(i)}$	0.95	2.54	3.206(3)	127
C(6)-H(6)...Cl(1)$^{(ii)}$	0.95	2.77	3.445(2)	128
C(14)-H(14)...Cl(1)$^{(iii)}$	0.95	2.61	3.530(2)	162
C(5T)-H(5T)...N(4)	0.95	2.36	3.030(2)	127
C(9T)-H(9T)...N(1T)	0.95	2.49	2.816(2)	100
C(14)-H(14)...O(2)	0.95	2.82(2)	2.668(2)	101

Symmetry codes: (i) 1-x,-1/2+y,1/2-z; (ii) x,-1+y,z, (iii) 1/2+x,3/2-y,1-z

In addition, the crystal structures are stabilized by π-π interaction between aromatic rings. An intermolecular π-π contacts in **13** occurs between the triazole (Cg1) , phenyl (Cg2) and phenyl(T) (Cg3) rings (the ring centroids distance from Cg1 to Cg2 is 3.432 Å with offset distance 0.964 Å and from Cg2 to Cg3 is 3.982 Å with offset 1.117 Å).

4. Conclusions

In this study the simple one-pot method was established for the synthesis of 4-amino-3-methyl-5-phenyl-1,2,4-triazole (**3**). A series of new hemiaminals were synthesized by introduction of **3** or 4-amino-3,5-dipyridin-2-yl-1,2,4-triazole to aromatic aldehydes. We found that increasing the steric bulk of C- substituents in the 4-amino-1,2,4-triazoles reduced of the hemiaminal formation. Replacement of phenyl substituents into the 2-pyridyl by contrast, result in an increased formation of hemiaminal. The new obtained data suggesting that not only intermolecular O-H…N_{tr} hydrogen bonds but also other factors must be contributing to the hemiaminal isolation. It seems that the additional intramolecular hydrogen bonds and π-π interaction between aryl substituent triazole rings are these factors. The presence of two different substituents in the triazole ring significantly affects the behavior of hemiaminals (**11, 12**) and Schiff Bases (**13**-**18**) which in solution the rotation around the N-N axis can be sufficiently restricted on the NMR time scale at room temperature.

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Conflicts of Interest

The authors declare no conflict of interest.

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Highlights

- One-pot method for the synthesis of 4-amino-3-methyl-5-phenyl-1,2,4-triazole is obtained.
- Hemiaminals and Schiff Bases derived from aryl substituted 4-amino-1,2,4-triazole were synthesized.
- IR, NMR, MS spectroscopy and X-ray diffraction studies were used for the compounds characterization.
- Density Functional Theory (DFT) method with the M062x density functional and 6-311++G(d,p) basis set were used for theoretical studies.