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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 ··· $^{\cdot}N_{1Tr}$ 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.

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. Furthermore 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

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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), $NH_2NH_2H_2O$ (80%, 9 mL) and anhydrous ethanol (3 mL) were mixed in a 100 mL Teflon-lined autoclave and heated for 3 days at 120 °C. After cooling to room temperature the solvent was removed in vacuum and the residue was washed with benzene (3×3mL). 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; 916 m; 928w; 968w; 1074w; 1109vw; 1269vw; 1287w; 1356vw; 1418w; 1454w; 1475s; 1628w; 3045w; 3212w; 3275w; 3362 m. 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, 753 m, 777s, 921w, 964s, 989s, 1003s, 1057w, 1080w, 1269 m, 1288w, 1346 m, 1353 m, 1363 m, 1381w, 1421s, 1446s, 1461 m, 1481vs, 1527s, 1536s, 1648s, 2926w, 2991w, 3151 m, 3183 m, 3253 m. 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, $J_{2\text{-}3}$ = 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 °C for 9 h. 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}): 404 m, 448w, 496w, 506w, 599 m, 614 m, 639w, 674 m, 697s, 711s, 736vs, 752 m, 791vs, 816vs, 835 m, 863 m, 892 m, 913 m, 972 m, 992 m, 1000 m, 1050s, 1088s, 1133 m, 1162w, 1184 m, 1251w, 1286 m, 1349vs, 1423 m, 1444vs, 1474s, 1532vs, 1569 m, 1594s, 3068 m, 3105 m. 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, $J_{(C-H)\text{-}(N-H)}$ = 8.24 Hz, N–H); 8.73 (dd, 2H, $J_{5\text{-}6}$ = 4.77 Hz, $J_{4\text{-}6}$ = 0.60 Hz, Py-H_6); 8.58 (d, 1H, $J_{3\text{-}5}$ = 2.29 Hz, Ar–H_3); 8.54 (dd, 1H, $J_{5\text{-}6}$ = 8.70 Hz, $J_{3\text{-}5}$ = 2.29 Hz, Ar–H_5); 8.09 (d, 2H, $J_{3\text{-}4}$ = 7.78 Hz, Py-H_3); 8.03 (dd, 2H, $J_{3,5\text{-}4}$ = 7.70 Hz, $J_{4\text{-}6}$ = 1.70 Hz, Py-H_4); 7.94 (d, 1H, $J_{5\text{-}6}$ = 8.70 Hz, Ar–H $_6$); . 7.59 (m, 2H, $J_{4,\text{-}5}$ = 7.66 Hz, $J_{5\text{-}6}$ = 4.77 Hz, $J_{3\text{-}5}$ = 0.92 Hz, Py-H_5); 7.44 (d, 1H, $J_{(C-H)\text{-}(O-H)}$ = 5.49 Hz, O–H); 6.49 (dd, 1H,, $J_{(C-H)\text{-}(N-H)}$ = 8.24 Hz, $J_{(C-H)\text{-}(O-H)}$ = 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)°, β = 94.61 (3)°, γ = 107.79 (3)°, V = 1812.6 (11) $Å^3$, Z = 4, ρc = 1.592 g cm^{-3}, μ = 0.121 mm, θmax = 36.8°, 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, 591 m, 607w, 622w, 626w, 633w, 680w, 701 m, 711 m, 725 m, 741vs, 795s, 819 m, 831w, 875 m, 919w, 946w, 975w, 995w, 999w, 1007w, 1031vs, 1047 m, 1079 m, 1088 m, 1104 m, 1138w, 1151w, 1182w, 1193w, 1248 m, 1284 m, 1343vs, 1434s, 1443s, 1452s, 1463 m, 1473 m, 1519vs, 1571s, 1590s, 1611 m, 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, $J_{5\text{-}6}$ = 4.12 Hz, $J_{4\text{-}6}$ = 1.83 Hz, $J_{3\text{-}6}$ = 0.92 Hz, Py-H_6); 8.54