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Synthesis of Some 5-Substituted-1,2,4-triazole-3-thiones, Containing Thiourea, Arylidenamino and Morpholin-4-yl methyl Fragments

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In this study, first 4-amino-5-(pyridine-4yl)-4*H*-1,2,4-triazole-3-thione (**1**) and 4-amino-5-(2-hydroxyphenyl)-4*H*-1,2,4-triazole-3-thione (**2**) were synthesized. In the second step (**1**) and (**2**) compounds undergo reaction with aryl isothiocyanates in dry C_6H_6 to give corresponding N-substituted thiourea derivatives (**3a-d** and **4a-d**). In addition, in the another reaction (**1**) and (**2**) compounds were reacted with some aromatic aldehyde in anhydrous ethanol to give corresponding arylidenamino compounds (**5a-d** and **6a-d**). In the third step, aminomethylation derivatives (**7a-d** and **8a-d**) were obtained by the Mannich reactions of arylidenamino compounds (**5a-d** and **6a-d**), with formaldehyde/morpholine in ethanol. The structures of all the synthesized compounds were confirmed by elemental analyses, FT-IR, ^{1}H and ^{13}C NMR spectra.

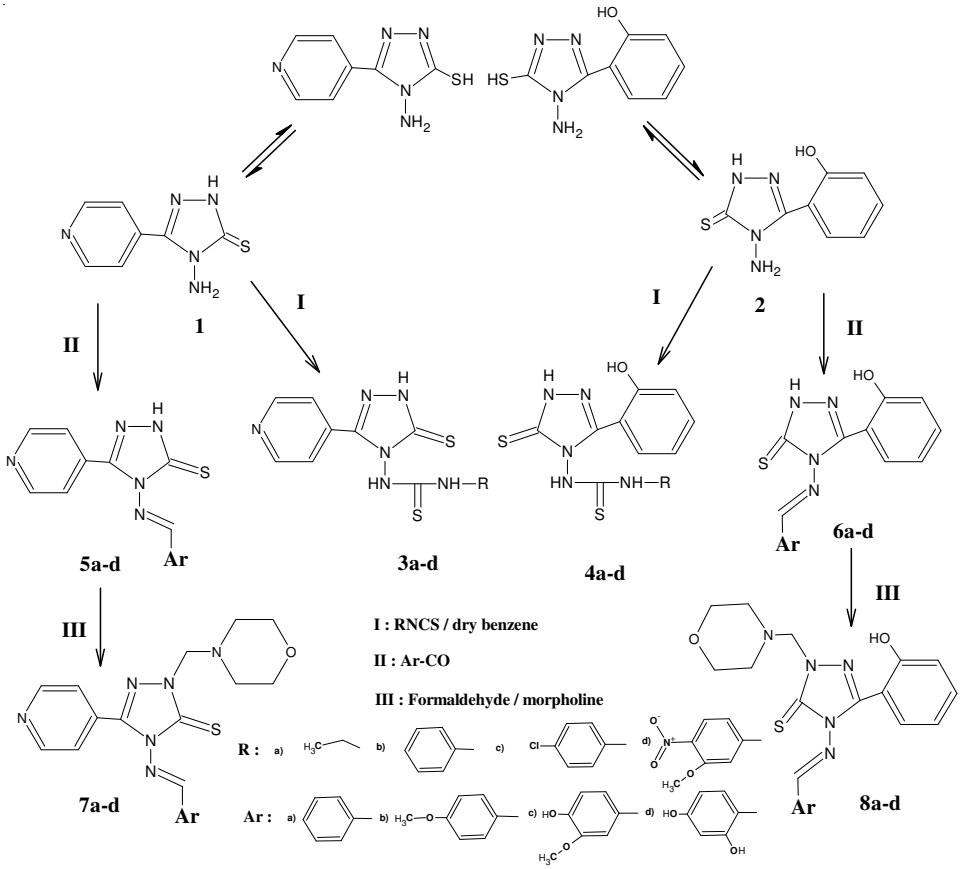
Key Words: 1,2,4-Triazole, Mannich bases, Thiourea, Arylidenamino.

INTRODUCTION

Triazoles and their derivatives have been proved to be effective bactericides, pesticides and fungicides[1-3]. Derivatives of 1,2,4-triazole are known to exhibit antiinflammatory, antiviral, analgesic, antimicrobial, anticonvulsant, and antidepressant activity, the latter being usually explored by the forced swim test[4-14]. 4,5-Substituted products containing 1,2,4-triazole and thiourea functions in their molecules seem to be suitable candidates for further chemical modifications and might be of interest as pharmacologically active compounds and ligands useful in coordination chemistry[15]. In addition there are some studies on electronic structures and thiol-thione tautomeric equilibrium of heterocyclic thione derivatives[16-18]. Thiouracil moieties play a vital role in many biological processes and are used as intermediates for the synthesis of drugs[19,20]. It is well known that derivatives of thiourea compounds exhibit anti HIV activity[21,22].

Many Schiff base complexes with metals have also provoked wide interest because they possess a diverse spectrum of biological and pharmaceutical activities, such as antitumour, antioxidative, antiviral, antimicrobial activities[23-26] and so on.

We now report the synthesis of 24 original compounds derived from 4-amino-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione **1** and 4-amino-5-(2-hydroxyphenyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione **2** with the purpose of considering their possible antibacterial and antifungal activity in the future. The new derivatives were prepared following the reaction sequences depicted in **Scheme-I**.



Scheme-I

EXPERIMENTAL

Melting points were determined in open capillary tubes on a digital Gallenkamp melting point apparatus and are uncorrected. Elemental analyses (C, H, N) were caried out using LECO-932 CHNSO by Technical and Scientific Research Council of Turkey, Tubitak. The IR spectra were recorded for KBr disks with a Mattson 1000 FT-IR spectrometer. ^{1}H NMR spectra were recorded on a Varian-Mercury-Plus 400 MHz ^{1}H NMR, 100 MHz ^{13}C NMR spectrometer in DMSO-d_6 and $CDCl_3$ with TMS as an internal standard. Starting materials was obtained from Fluka or Aldrich.

General procedure for the preparation of compounds (1,2): (**1, 2**) Compounds were prepared following literature procedures[18,27], respectively.

General procedure for the preparation of compounds (3a-d) and (4a-d): A mixture of (0.01 mol) of compounds **1** (or **2**) and substituted isothiocyanate (0.01 mol) in dry C_6H_6 was refluxed for 6 h, the solid material obtained on cooling was filtered off and recrystallized from suitable solvent to give compounds, respectively (**3a-d**) and (**4a-d**).

N-Ethyl-N'-(3-pyridin-4-yl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)thiourea (3a): Yield (86 %), m.p. 267-268 ºC; IR (KBr, ν_{max}, cm^{-1}): 3235 (NH), 1615 (C=N), 1329 (C=S); ^{1}H NMR (ppm): δ 10.78-9.79 (m, 2H, 2xNH), 8.74 (s, 1H, NH), 8.73 (s, dd *J* = 6.23, 1.47, 2H, pyridine H_3, H_5), 7.99 (dd, *J* = 6.23, 1.47, 2H, pyridine H_2, H_6), 3.39 (q, 2H, -$\underline{CH_2}CH_3$), 1.22 (t, 3H, -$CH_2\underline{CH_3}$); ^{13}C NMR (ppm): δ 154.60, 153.77, 150.89, 139.92, 138.31, 122.65, 39.11, 15.38; Anal. calcd. (%) for $C_{10}H_{12}N_6S_2$: C 42.84, H 4.31, N 29.97, S 22.87; found: C 42.82, H 4.31, N 29.95, S 22.86.

N-Phenyl-N'-(3-pyridin-4-yl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)thiourea (3b): Yield (71 %), m.p. 250-251 ºC; IR (KBr, ν_{max}, cm^{-1}): 3280 (NH), 1611 (C=N), 1328 (C=S); ^{1}H NMR (ppm): δ 11.27 (s, 2H, 2xNH), 9.11-7.01 (m, 10H, Ar-H and NH); ^{13}C NMR (ppm): δ 155.60, 152.76, 150.88, 151.01, 131.50, 138.75, 128.40, 122.60, 121.99, 115.97; Anal. calcd. (%) for $C_{14}H_{12}N_6S_2$: C 51.20, H 3.68, N 25.59, S 19.53; found: C 51.18, H 3.67, N 25.60, S 19.54.

N-(4-Chlorophenyl)-N'-(3-pyridin-4-yl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)thiourea (3c): Yield (60 %), m.p. 261-262 ºC; IR (KBr, ν_{max}, cm^{-1}): 3278 (NH), 1625 (C=N), 1330 (C=S); ^{1}H NMR (ppm): δ 10.97 (s, 3H, 3xNH), 8.69-7.23 (m, 4H, Ar-H, pyridine), 7.16-6.54 (m, 4H, Ar-H, phenyl); ^{13}C NMR (ppm): δ 154.58, 153.75, 150.83, 151.01, 139.55, 138,75, 128.90, 124.63, 122.85, 116.98; Anal. calcd. (%) for $C_{14}H_{11}N_6S_2Cl$: C 46.34, H 3.06, N 23.16, S 17.67; found: C 46.31, H 3.07, N 23.16, S 17.65.

N-(4-Nitrophenyl)-N'-(3-pyridin-4-yl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)thiourea (3d): Yield (69 %), m.p. 254-255 ºC; IR (KBr, ν_{max}, cm^{-1}): 3228 (NH), 1627 (C=N), 1325 (C=S); ^{1}H NMR (ppm): δ 11.01 (s, 3H, 3xNH), 8.71-7.28 (m, 4H, Ar-H, pyridine), 8.75-6.59 (m, 4H, Ar-H, phenyl); ^{13}C NMR (ppm): δ 156.17, 155.59, 154.76, 151.01, 139.55, 139.21, 138.75, 125.80, 123.01, 112.71; Anal. calcd. (%) for $C_{14}H_{11}N_7O_2S_2$: C 45.03, H 2.97, N 26.26, S 17.17; found: C 44.99, H 2.96, N 26.24, S 17.19.

N-Ethyl-N'-[3-(2-hydroxyphenyl)-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl]thiourea (4a): Yield (88 %), m.p. 358-359 ºC; IR (KBr, ν_{max}, cm^{-1}): 3355 (OH), 3235 (NH), 1622 (C=N), 1323 (C=S); ^{1}H NMR (ppm): δ 11.22 (s, 1H, Ar-$\underline{OH}$), 10.83-9.99 (br, 3H, 3xNH), 8.79-6.99 (m, 4H, Ar-H), 3.38 (q, 2H, -$\underline{CH_2}CH_3$), 1.23 (t, 3H, -$CH_2\underline{CH_3}$); ^{13}C NMR (ppm): δ 162.20, 153.35, 152.76, 133.37, 130.70, 121.85, 117.85, 114,49, 39.52, 12.98; Anal. calcd. (%) for $C_{11}H_{13}N_5OS_2$: C 44.73, H 4.44, N 23.71, S 21.71; found: C 44.82, H 4.43, N 23.70, S 21.69.

N-[3-(2-Hydroxyphenyl)-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl]-N'-phenyl thiou rea (4b): Yield (61 %), m.p. 324-325 ºC; IR (KBr, ν_{max}, cm^{-1}): 3360 (OH), 3299 (NH), 1628 (C=N), 1327 (C=S); ^{1}H NMR (ppm): δ 11.23 (s, 1H, Ar-OH), 10.84-10.08 (br, 3H, 3xNH), 8.65-7.05 (m, 9H, Ar-H); ^{13}C NMR (ppm): δ 161.45, 153.98, 153.71, 149.21, 132.60, 130.71, 127.81, 125.10, 123.92, 121.05, 117.55, 113.85; Anal. calcd. (%) for $C_{15}H_{13}N_5OS_2$: C 52.46, H 3.82, N 20.39, S 18.67; found: C 52.44, H 3.79, N 20.38, S 18.69.

N-(4-Chlorophenyl)-N'-[3-(2-hydroxyphenyl)-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl]thiourea (4c): Yield (65 %), m.p. 302-303 ºC; IR (KBr, ν_{max}, cm^{-1}): 3390 (OH), 3285 (NH), 1623 (C=N), 1320 (C=S); ^{1}H NMR (ppm): δ 11.18 (s, 1H, Ar-OH), 10.88-9.98 (br, 3H, 3xNH), 8.78-6.84 (m, 8H, Ar-H); ^{13}C NMR (ppm): δ 161.45, 153.98, 153.71, 149.21, 143.99, 132.60, 130.77, 128.81, 124.10, 122.92, 121.65, 118.55, 114.85; Anal. calcd. (%) for $C_{15}H_{12}N_5OS_2Cl$: C 47.68, H 3.20, N 18.53, S 16.97; found: C 47.67, H 3.22, N 18.52, S 16.99.

N-[3-(2-Hydroxyphenyl)-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl]-N'-(4-nitrophen yl)thiourea (4d): Yield (69 %), m.p. 341-342 ºC; IR (KBr, ν_{max}, cm^{-1}): 3410 (OH), 3295 (NH), 1614 (C=N), 1318 (C=S); ^{1}H NMR (ppm): δ 11.08 (s, 1H, Ar-OH), 10.84-10.01 (br, 3H, 3xNH), 8.91-6.44 (m, 8H, Ar-H); ^{13}C NMR (ppm): δ 161.46, 153.98, 153.76, 149.23, 145.99, 142.81 133.60, 131.77, 124.81, 121.10, 120.92, 115.85; Anal. calcd. (%) for $C_{15}H_{12}N_5OS_2Cl$: C 47.68, H 3.20, N 18.53, S 16.97; found: C 47.67, H 3.22, N 18.52, S 16.99.

General procedure for the preparation of compounds (5a-d) and (6a-d): A mixture of **1** (or **2**) (0.01 mol) of compounds and the corresponding aryl aldehyde (0.01 mol) in ethanol (25 mL) was treated with concentrated HCl (0.5 mL) and refluxed for 2 h. The reaction mixture on cooling was filtered and recrystallized from ethanol to give compounds respectively (**5a-d**) and (**6a-d**).

4-(Benzylideneamino)-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (5a): Yield (70 %), m.p. 121-122 ºC; IR (KBr, ν_{max}, cm^{-1}): 3280 (NH), 1612 (C=N), 1329 (C=S); ^{1}H NMR (ppm): δ 14.06 (br, 1H, SH), 9.81-7.63 (m, 10H, Ar-H and N=CH); ^{13}C NMR (ppm): δ 160.23, 156.01, 150.23, 149.92, 135.45, 132.21, 130.70, 127.85, 125.03; Anal. calcd. (%) for $C_{10}H_{12}N_6S_2$: C 59.77, H 3.94, N 24.89, S 11.40; found: C 59.75, H 3.90, N 24.90, S 11.46.

4-[(4-Methoxybenzylidene)amino]-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (5b): Yield (75 %), m.p. 116-117 ºC; IR (KBr, ν_{max}, cm^{-1}): 3331 (NH), 1618 (C=N), 1330 (C=S); ^{1}H NMR (ppm): δ 14.05 (br, 1H, SH), 9.69-7.07 (m, 9H, Ar-H and N=CH), 3.86 (s, 3H, O-CH_3); ^{13}C NMR (ppm): δ 160.79, 159.80, 155.01, 149.96, 149.67 133.43, 131.14, 125.20, 114.32, 55.23; Anal. calcd. (%) for $C_{15}H_{13}N_5OS$: C 57.86, H 4.21, N 22.49, S 10.30; found: C 57.85, H 4.20, N 22.48, S 10.30.

4-[(4-Hydroxy-3-methoxybenzylidene)amino]-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (5c): Yield (68 %), m.p. 229-230 ºC; IR (KBr, ν_{max}, cm^{-1}): 3465 (OH), 3280 (NH), 1618 (C=N), 1328 (C=S); ^{1}H NMR (ppm): δ 14.06

(br, 1H, SH), 10.21 (s, 1H, Ar-OH), 9.49-6.87 (m, 8H, Ar-H and N=CH), 3.87 (s, 3H, O-CH_3); ^{13}C NMR (ppm): δ 166.18, 159.81, 158.24, 156.34, 150.25, 150.01, 137.86, 131.14, 125.41, 113.47, 109.80, 101.66; Anal. calcd. (%) for $C_{15}H_{13}N_5O_2S$: C 55.03, H 4.00, N 21.39, S 9.80; found: C 54.98, H 3.99, N 21.37, S 9.78.

4-[(2,4-Dihydroxybenzylidene)amino]-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (5d): Yield (55 %), m.p. 327-328 ºC; IR (KBr, ν_{max}, cm^{-1}): 3405 (OH), 3285 (NH), 1637 (C=N), 1324 (C=S); ^{1}H NMR (ppm): δ 14.06 (br, 1H, SH), 11.81 (br, 1H, Ar-OH), 10.19 (s, 1H, Ar-OH), 9.01-6.77 (m, 8H, Ar-H and N=CH); ^{13}C NMR (ppm): δ 159.79, 154.30, 150.11, 150.01, 149.55, 131.11, 129.01, 126.56, 125.21, 115.55, 112.01, 55.03; Anal. calcd. (%) for $C_{14}H_{11}N_5O_2S$: C 53.66, H 3.54, N 22.35, S 10.23; found: C 53.66, H 3.56, N 22.37, S 10.22.

4-(Benzylideneamino)-5-(2-hydroxyphenyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (6a): Yield (66 %), m.p. 207-208 ºC; IR (KBr, ν_{max}, cm^{-1}): 3455 (OH), 3211 (NH), 1622 (C=N), 1321 (C=S); ^{1}H NMR (ppm): δ 14.01 (s, 1H, SH), 11.90 (s, 1H, Ar-OH), 10.04 (s, 1H, N=CH), 9.57-6.88 (m, 9H, Ar-H); ^{13}C NMR (ppm): δ 159.82, 159.21, 155.01, 154.22, 135.46, 133.85, 132.11, 130.01, 128.12, 118.01, 115.06, 108.75; Anal. calcd. (%) for $C_{15}H_{12}N_4OS$: C 60.76, H 4.08, N 18.91, S 10.82; found: C 60.74, H 4.07, N 19.00, S 10.82.

4-[(4-Methoxybenzylidene)amino]-5-(2-hydroxyphenyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (6b): Yield (79 %), m.p. 200-201 ºC; IR (KBr, ν_{max}, cm^{-1}): 3402 (OH), 3281 (NH), 1625 (C=N), 1360 (C=S); ^{1}H NMR (ppm): δ 14.03 (s, 1H, SH), 10.02 (s, 1H, Ar-OH), 9.86 (s, 1H, N=CH), 9.34-6.87 (m, 8H, Ar-H), 3.81 (s, 3H, O-CH_3); ^{13}C NMR (ppm): δ 161.01, 159.83, 159.11, 155.01, 149.15, 133.40, 133.03, 132.74, 128.96, 118.57, 114,11, 109.65, 55.21; Anal. calcd. (%) for $C_{16}H_{14}N_4O_2S$: C 58.88, H 4.32, N 17.17, S 9.82; found: C 58.84, H 4.31, N 17.15, S 9.79.

4-[(4-Hydroxy-3-methoxybenzylidene)amino]-5-(2-hydroxyphenyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (6c): Yield (77 %), m.p. 235-236 ºC; IR (KBr, ν_{max}, cm^{-1}): 3490 (OH), 3251 (NH), 1623 (C=N), 1358 (C=S); ^{1}H NMR (ppm): δ 14.02 (s, 1H, SH), 11.71 (s, 1H, Ar-OH), 10.48 (s, 1H, N=CH), 10.36 (s, 1H, Ar-OH), 9.23-7.94 (m, 4H, Ar-H), 7.55-6.90 (m, 3H, Ar-H), 3.76 (s, 3H, O-CH_3); ^{13}C NMR (ppm): δ 160.82, 159.20, 154.65, 154.20, 133.04, 132.88, 128.75, 125.60, 118.01, 115.07, 112.08, 108.98, 55.39; Anal. calcd. (%) for $C_{16}H_{14}N_4O_3S$: C 56.13, H 4.12, N 16.36, S 9.37; found: C 56.14, H 4.11, N 16.35, S 9.39.

4-[(2,4-Dihydroxybenzylidene)amino]-5-(2-hydroxyphenyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (6d): Yield (74 %), m.p. 265-266 ºC; IR (KBr, ν_{max}, cm^{-1}): 3467 (OH), 3213 (NH), 1621 (C=N), 1328 (C=S); ^{1}H NMR (ppm): δ 14.02 (s, 1H, SH), 11.40-11.35 (br, 1H, Ar-OH), 10.90 (s, 1H, Ar-OH), 10.46 (s, 1H, N=CH), 10.03-6.33 (m, 7H, Ar-H); ^{13}C NMR (ppm): δ 165.11, 159.77, 158.95, 156.75, 154.20, 136.88, 133.11, 131.84, 118.01, 116.25, 114.75, 110.25, 108.80, 101.92; Anal. calcd. (%) for $C_{15}H_{12}N_4O_3S$: C 54.87, H 3.68, N 17.06, S 9.77; found: C 54.86, H 3.66, N 17.05, S 9.79.

General procedure for the preparation of compounds (7a-d) and (8a-d): A slurry consisting (0.002 mol) of **5a-d** (or **6a-d**), ethanol (10 mL) and (0.03 mol) 37 % formaline was made. To this (0.002 mol) morpholine was added drop wise, with cooling and shaking. The reaction mixture was allowed to stand at room temperature for 1 h, with occasional shaking after which it was warmed on a steam bath for 0.5 h, at the and of period the contents were cooled and the product obtained was recrystallized from suitable solvent to give compounds respectively (**7a-d**) and (**8a-d**).

4-(Benzylideneamino)-2-(morpholin-4-ylmethyl)-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (7a): Yield (78 %), m.p. 318-319 ºC; IR (KBr, ν_{max}, cm^{-1}): 1631 (C=N), 1318 (C=S); ^{1}H NMR (ppm): δ 9.78-9.06 (m, 2H, pyridine, N-CH-), 8.99-7.98 (m, 2H, pyridine, CH), 7.42 (s, 1H, N=CH), 7.39-6.95 (m, 4H, Ar-H), 5.16 (s, 2H, N-CH_2), 3.71-3.11 (m, 4H, morpholine, OCH_2), 2.73-2.45 (m, 4H, morpholine, N-CH_2); ^{13}C NMR (ppm): δ 154.40, 150.95, 148.99, 137.50, 135.11, 134.01, 128.01, 127.90, 125.91, 123.80, 67.11, 65.98, 47.91; Anal. calcd. (%) for $C_{19}H_{20}N_6OS$: C 59.98, H 5.30, N 22.09, S 8.43; found: C 59.97, H 5.29, N 22.10, S 8.42.

4-[(4-Methoxybenzylidene)amino)]-2-(morpholin-4-ylmethyl)-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (7b): Yield (75 %), m.p. 326-327 ºC; IR (KBr, ν_{max}, cm^{-1}): 1629 (C=N), 1327 (C=S); ^{1}H NMR (ppm): δ 9.72-9.05 (m, 2H, pyridine, N-CH-), 8.98-8.00 (m, 2H, pyridine, CH), 7.42 (s, 1H, N=CH), 7.39-6.96 (m, 4H, Ar-H), 5.13 (s, 2H, N-CH_2), 3.87-3.09 (m, 7H, O-CH_3 and morpholine, OCH_2), 2.74-2.48 (m, 4H, morpholine, CH_2); ^{13}C NMR (ppm): δ 154.40, 159.42, 153.47, 150.01, 146.99, 135.01, 13.6, 130.80, 125.01, 115.01, 67.08, 65.25, 55.17, 48.38; Anal. calcd. (%) for $C_{20}H_{22}N_6O_2S$: C 58.52, H 5.40, N 20.47, S 7.81; found: C 58.52, H 5.39, N 20.46, S 7.82.

4-[(4-Hydroxy-3-methoxybenzylidene)amino]-2-(morpholin-4-ylmethyl)-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (7c): Yield (81 %), m.p. 360-361 ºC; IR (KBr, ν_{max}, cm^{-1}): 3388 (OH), 1617 (C=N), 1318 (C=S); ^{1}H NMR (ppm): δ 11.13 (S, 1H, Ar-OH), 9.43-9.06 (m, 2H, pyridine, N-CH-), 8.77-7.89 (m, 2H, pyridine, CH), 7.49 (s, 1H, N=CH), 7.38-6.94 (m, 3H, Ar-H), 5.11 (s, 2H, N-CH_2), 3.85-3.69 (m, 7H, O-CH_3 and morpholine, OCH_2), 2.54-2.48 (m, 4H, morpholine, CH_2); ^{13}C NMR (ppm): δ 153.35, 150.11, 148.55, 146.99, 145.11, 135.18, 134.01, 128.61, 125.52, 115.55, 112.01, 67.08, 65.01, 55.31, 48.33; Anal. calcd. (%) for $C_{20}H_{22}N_6O_3S$: C 56.32, H 5.20, N 19.70, S 7.52; found: C 56.32, H 5.19, N 19.69, S 7.51.

4-[(2,4-Dihydroxybenzylidene)amino]-2-(morpholin-4-ylmethyl)-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (7d): Yield (80 %), m.p. 390-391 ºC; IR (KBr, ν_{max}, cm^{-1}): 3446 (OH), 1637 (C=N), 1318 (C=S); ^{1}H NMR (ppm): δ 10.03 (s, 2H, Ar-OH), 9.07-8.95 (m, 2H, pyridine, N-CH-), 8.07-8.01 (m, 2H, pyridine, CH), 7.60 (s, 1H, N=CH), 7.48-6.99 (m, 3H, Ar-H), 5.19 (s, 2H, N-CH_2), 3.87-3.09 (m, 4H, morpholine, OCH_2), 2.86-2.18 (m, 4H, morpholine, CH_2); ^{13}C NMR (ppm): δ 165.01, 158.21, 152.37, 150.95, 145.87, 136.86, 134.15, 124.50, 114.01, 110.01, 100.85, 67.01, 66.01, 48.35; Anal. calcd. (%) for $C_{19}H_{20}N_6O_3S$: C 55.33, H 4.89, N 20.38, S 7.77; found: C 55.32, H 4.88, N 20.39, S 7.76.

4-(Benzylideneamino)-5-(2-hydroxyphenyl)-2-(morpholin-4-ylmethyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (8a): Yield (77 %), m.p. 338-339 ºC; IR (KBr, ν_{max}, cm^{-1}): 3400 (OH), 1617 (C=N), 1321 (C=S); ^{1}H NMR (ppm): δ 10.11 (s, 1H, Ar-OH), 9.28 (s, 1H, N=CH), 8.92-6.97 (m, 9H, Ar-H), 5.15 (s, 2H, N-CH_2), 3.59-3.31(m, 4H, O-CH_2), 2.73-2.46 (m, 4H, N-CH_2); ^{13}C NMR (ppm): δ 164.01, 160.77, 154.01, 135.11, 135.04, 132.53, 130.01, 123.12, 120.11, 116.17, 110.93, 67.01, 65.98, 47.99; Anal. calcd. (%) for $C_{20}H_{21}N_5O_2S$: C 60.74, H 5.35, N 17.71, S 8.11; found: C 60.74, H 5.37, N 17.69, S 8.12.

4-[(4-Methoxybenzylidene)amino]-5-(2-hydroxyphenyl)-2-(morpholin-4-ylmethyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (8b): Yield (76 %), m.p. 333-334 ºC; IR (KBr, ν_{max}, cm^{-1}): 3410 (OH), 1614 (C=N), 1338 (C=S); ^{1}H NMR (ppm): δ 10.09 (s, 1H, Ar-OH), 9.29 (s, 1H, N=CH), 8.66-6.89 (m, 8H, Ar-H), 5.13 (s, 2H, N-CH_2), 3.81 (s, 3H, O-CH_3), 3.57-3.32(m, 4H, O-CH_2), 2.74-2.48 (m, 4H, N-CH_2); ^{13}C NMR (ppm): δ 163.99, 161.77, 160.48, 153.54, 135.21, 133.01, 132.11, 130.16, 128.88, 120.55, 117.01, 115.05, 110.34, 67.11, 66.01, 54.30, 48.44; Anal. calcd. (%) for $C_{21}H_{23}N_5O_3S$: C 59.28, H 5.45, N 16.46, S 7.54; found: C 69.28, H 5.47, N 16.45, S 7.52.

4-[(4-Hydroxy-3-methoxybenzylidene)amino]-5-(2-hydroxyphenyl)-2-(morpholin-4-ylmethyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (8c): Yield (74 %), m.p. 360-361 ºC; IR (KBr, ν_{max}, cm^{-1}): 3424 (OH), 1625 (C=N), 1324 (C=S); ^{1}H NMR (ppm): δ 12.77-11.98 (br, 1H, Ar-OH), 10.47-10.04 (br, 2H, Ar-OH and, N=CH), 9.79-6.89 (m, 7H, Ar-H), 5.19 (s, 2H, N-CH_2), 3.82-3.18 (m, 7H, O-CH_3, and O-CH_2), 3.06-2.45 (m, 4H, morpholine N-CH_2); ^{13}C NMR (ppm): δ 163.06, 161.87, 153.41, 148.60, 146.35, 135.13, 132.14, 130.10, 127.53, 124.01, 119.94, 117.94, 114.98, 112.00, 111.34, 67.08, 66.11, 55.49, 47.96; Anal. calcd. (%) for $C_{21}H_{23}N_5O_4S$: C 57.13, H 5.25, N 15.86, S 7.26; found: C 57.11, H 5.27, N 15.85, S 7.26.

4-[(2,4-Dihydroxybenzylidene)amino]-5-(2-hydroxyphenyl)-2-(morpholin-4-ylmethyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (8d): Yield (75 %), m.p. 341-342 ºC; IR (KBr, ν_{max}, cm^{-1}): 3409 (OH), 1618 (C=N), 1324 (C=S); ^{1}H NMR (ppm): δ 12.89-12.73 (br, 3H, Ar-OH), 10.16 (s, N=CH), 9.96-6.84 (m, 7H, Ar-H), 5.18 (s, 2H, N-CH_2), 3.86-3.06 (m, 4H, O-CH_2), 3.04-2.58 (m, 4H, morpholine N-CH_2); ^{13}C NMR (ppm): δ 165.11, 163.06, 161.88, 157.21, 154.05, 145.50, 136.99, 135.01, 131.94, 120.12, 116.95, 114.76, 110.11, 100.37, 68.09, 48.40; Anal. calcd. (%) for $C_{20}H_{21}N_5O_4S$: C 56.19, H 4.95, N 16.38, S 7.50; found: C 56.17, H 4.95, N 16.35, S 7.49.

RESULTS AND DISCUSSION

The characterization data of compounds (**1** and **2**), are given in the literature procedures[18,27], respectively and that of the other compounds synthesized is summarized in experimental section. All the newly synthesized compounds gave satisfactory analyses for the proposed structures, which were confirmed on the basis of their IR and ^{1}H NMR spectral data. The IR spectra of these compounds showed moderately strong bands around 3467-3355, 3331-3211, 1637-1611 and 1360-1318 cm^{-1}, charac-

teristic of the OH, NH, C=N and C=S groups, respectively. In the ^{1}H NMR spectra, a characteristic signal due to the -N-CH_2- protons appeared at 5.11-5.19. Compounds (**5a-d** and **6a-d**), exist as thiol-thione tautomers as indicated by their ^{1}H NMR spectra, wich showed a signal due to the SH protons appeared at 14.01-14.06. The signal due to the aromatic protons appeared as multiplets at 10.03-6.33. While is observed that thione-thiole tautomers exist in solution of related substances through the spectroscopic analysis of (**1, 2**), (**3a-d, 4a-d, 5a-d**) and (**6a-d**) compounds, it is ascertained that there are only thione tautomer in pure and solid forms. The data of all the compounds are given in the experimental section.

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