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SYNTHESIS AND EXPERIMENTAL CHARACTERIZATION OF SOME NEW [1,2,4]TRIAZOLO[3,4-*b*][1,3,4]THIADIAZOLE DERIVATIVES

ABSTRACT

In this study, salicylic and izonicotinic acid hydrazide was converted into 4-amino 5-substituted-4*H*-1,2,4-triazole-3-thiol **1a,b**. A series of [1,2,4]triazolo[3,4-b] [1,3,4]thiadiazole-6(5*H*)-thione **2a,b** were prepared from aminomercaptotriazoles. The reaction of aminomercaptotriazole compounds **2a,b** with aromatic carboxylic acid and phosphorus oxychloride afforded the newly synthesized 3-substituted-[1,2,4]triazolo[3,4-b] [1,3,4]thiadiazole derivatives **3a-h** in good yields. In addition, the structures of synthesized compounds were confirmed by IR, ^{1}H-NMR and ^{13}C-NMR spectra.

Keywords: 1,2,4-triazole, Aminomercaptotriazoles, Thiadiazole, Hydrazide, Phosphorus Oxychloride.

BAZI YENİ [1,2,4]TRIAZOLO[3,4-*b*][1,3,4]TİYADİAZOL TÜREVLERİNİN SENTEZİ VE DENEYSEL KARAKTERİZASYONU

ÖZET

Bu çalışmada, salisilik ve izonikotinik asit hidrazit bileşikleri 4-amino 5-substitüe-4*H*-1,2,4-triazol-3-tiyole **1a,b** dönüştürüldü. [1,2,4] triazolo[3,4-b] [1,3,4]tiyadiazol-6(5*H*)-tiyon **2a,b** bileşik serisi aminomerkaptotriazollerden **1a,b** sentezlendi. Aminomerkaptotriazol bileşikleri **2a,b** ile aromatic karboksilik asit ve fosfor oksiklorürün reaksiyonundan iyi verimle yeni 3-substitüe-[1,2,4]triazolo[3,4-b] [1,3,4]tiyadiazol türevleri **3a-h** sentezlendi. Sentezlenen bileşiklerin yapıları IR, ^{1}H-NMR and ^{13}C-NMR spektro-fotometreleri kullanılarak aydınlatıldı.

Anahtar Kelimeler: 1,2,4-triazol, Aminomerkaptotriazoller, Tiyadiazol, Hidrazit, Fosfor Oksiklorür

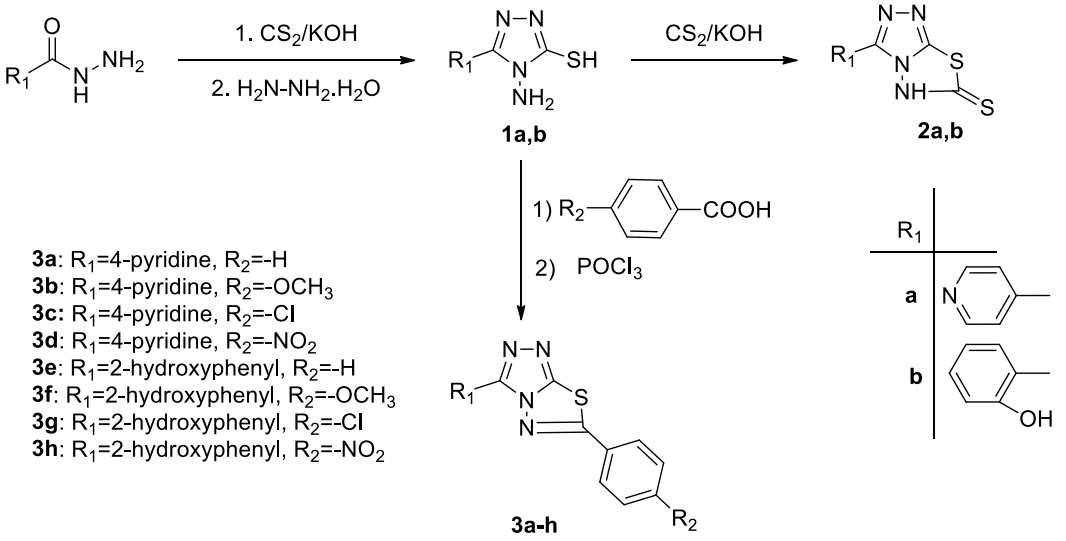
1. INTRODUCTION (GİRİŞ)

Triazoles and thiadiazoles fused with six-membered ring systems are found to possess diverse applications in the field of medicine, agriculture and industry. The literature survey reveals that there are not many examples of triazoles fused with thiadiazines.

Aromatic heterocycles are very important motifs in medicinal chemistry researches. In recent years increasing number of methods have been developing for the formation and elaboration of heterocycles. Electron-rich oxygen, sulfur and nitrogen heterocycles themselves are proper reactants for different synthetic variations and express effective biological activities [1].

Various 5-substituted 4-amino-3- mercapto-1,2,4-triazoles and their heterocyclic derivatives have been reported to possess antibacterial, antifungal, anticancer, antiviral, anti-inflammatory, herbicidal and plant growth regulatory effects [2 and 5]. Among these heterocycles, the mercapto and thione substituted 1,2,4-triazole ring systems represent one of the most biologically active classes of compounds, possessing a wide spectrum of activities including antibacterial, antifungal, antiviral, anti-inflammatory, anti convulsant, antidepressant, anti-tubercular, antihypertensive, analgesic, diuretic, and hypoglycemic properties [7 and 12].

In addition to these important biological applications, mercapto-1,2,4-triazoles are also of great utility in preparative organic chemistry, for example, in the present of various reagents, undergo different types of reaction to yield other heterocyclic compounds, e.g., thiazolotriazoles, triazolothiadizoles, triazolo thiazepines and triazolothiadiazines. The amino and mercapto groups of these compounds serve as readily accessible nucleophilic centers for the preparation of N-bridged heterocyclic. Also, there are some studies on electronic structures and thiol-thione tautomeric equilibrium of heterocyclic thione derivatives. [13 and 14]. In the X-ray single crystallographic analysis of 1,2,4-triazole compounds have been reported in the literature by N-H...S hydrogen bonds, forming dimers which are linked into a chain by N-H...N hydrogen bonds. [15 and 16]. Furthermore, there are known drugs containing the 1,2,4-triazole group e.g. Triazolam [17], Alprazolam [18], Etizolam [19] and Furacylin [20].



Scheme 1. Chemical structures for the synthesized compounds
(Şema 1. Sentezlenen bileşiklerin kimyasal yapıları)

2. RESEARCH SIGNIFICANCE (ÇALIŞMANIN ÖNEMİ)

Aromatic heterocycles are very important motifs in medicinal chemistry researches. In recent years increasing number of methods has been developing for the formation and elaboration of heterocycles Synthesis of novel triazole compounds is an important issue since they are key compounds used in pharmacology and already present in many medicinal preparations. Most are compounds that are synthesized triazole because of their pharmacologic effects. These compounds show different synthetic variations and express effective biological activities. Therefore, recently triazole derivatives gain great interest in pharmaceutical and organic chemistry; many studies have been concentrated on synthesis of these compounds

3. EXPERIMENTAL METHOD (DENEYSEL ÇALIŞMA)

Melting points (mp) were determined on a Perkin-Elmer DSC-4000 apparatus and were uncorrected. The IR spectra were recorded with a Perkin-Elmer 100 FT-IR spectrophotometer. All ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian-Mercury-Plus 400/100 MHz spectrometer, in DMSO-d_6 and $CDCI_3$ with TMS as an internal standard. Starting materials was obtained from Merck or Aldrich.

3.1 General Procedure for The Synthesis of 5-substituted 4-amino-2,4-dihydro-4*H*-1,2,4-triazole-3-thione (1a,b) ((5-substitüe-4-amino-2,4-dihidro-4*H*-1,2,4-triazol-3-tiyonun Genel Sentez Yöntemi) (1a,b))

A solution of potassium hydroxide (0.015 mole, 8.40 g), 100 mL of absolute ethanol and substituted hydrazide (0.01 mole) was treated to the addition of carbon disulfide (0.015 mole, 0.91 mL). This mixture was diluted with 50 mL of absolute ethanol and agitated for 14 h. It was then diluted with 200 mL of dry diethyl ether and vacuum dried at 70 ^{0}C. A suspension of potassium salts, 0.03 mole of 98 % hydrazine hydrate (15 mL) and 2 mL of water was refluxed with stirring for 2-3 h. The color of reaction mixture changed to green, hydrogen sulfide was evolved, and a homogeneous solution resulted. Dilution with 100 mL of cold water and acidification with concentrated hydrochloric acid precipitated a white solid. The product was filtered, washed with 5x10 mL portions of cold water, and recrystallized from ethanol to analytical purity. The characterizations of these compounds are given in findings parts.

3.2. General Procedure for The Synthesis of [1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazole-6(5*H*)-thione (2a,b)((3-substitüe-[1,2,4]triazolo[3,4-*b*] [1,3,4]tiyadiazol-6(5H)-tiyonun Genel Sentez Yöntemi)(2a,b))

A mixture of aminomercaptotriazole 1 (2 mmol), equivalents KOH, and CS_2 (2 mL) in absolute EtOH (50 mL) was refluxed for 12 h. The solvent was removed by evaporation and the filtrate acidified with diluted HCI. İt was filtered, washed with cold water and recrystallized from suitable solvent. The characterizations of these compounds are given in findings parts.

3.3. General Procedure for The Synthesis of 3-substituted-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole derivatives((3a,h) ([1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazole türevlerinin Genel Sentez Yöntemi (3a,h))

To a mixture of aminomercaptotriazole 1 (2 mmol) and aromatic carboxylic acid (4 mmol) phosphorus oxychloride (30 mL)was added and

the contents refluxed for 5 h. in a water bath. Excess of phosphorus oxychloride was then removed under reduced pressure and ice water, dilute $NaHCO_3$ was added to the residue and the solid product was collected by filtration. It recrystallized from a mixture of dioxane and dimethylformamide. The characterizations of these compounds are given in findings parts.

4. FINDINGS (BULGULAR)

4.1. 4-amino-5-pyridine-2,4-dihydro-4*H*-1,2,4-triazole-3-thione (1a)(4-amino-5-piridine-2,4-dihidro-4*H*-1,2,4-triazol-3-tiyo (1a))

mp:250 ^{0}C, yield:82%, color: white, recrystallized solvent: EtOH, IR (KBr): υ 33760-3190 (NH_2), 3095-3010 (ArCH), 2925-2762-2560,1250-1265 (S-H) cm^{-1}; ^{1}H-NMR (400 MHz,DMSO-d_6): δ 14.02 (br, 1H, SH), 8.72 (dd, *J*=6.26, 1.49, 2H, pyridyl H_3, H_5), 7.98 (dd, *J*=6.25, 1.49, 2H, pyridyl H_2, H_6), 5.80 (br, 2H, NH_2) ppm; ^{13}C-NMR (DMSO-d_6): δ 167.2, 151.2, 148.4, 134.0, 121.9 ppm.

4.2. 4-amino-5-(2-salicyl)-2,4-dihydro-4*H*-1,2,4-triazole-3-thion (1b)(4-amino-5-(2-salisil)-2,4-dihidro-4*H*-1,2,4-triazol-3-tiyon (1b))

mp:217-218 ^{0}C, yield:74%, color: yellowish, recrystallized solvent: EtOH,; IR (KBr): υ 3472-3176 (OH, NH_2), 3080-3010 (ArCH), 2925 2762-2560, 1250-1265 (S-H) cm^{-1}; ^{1}H-NMR (400 MHz,DMSO-d_6): δ 14.00 (br, 1H, SH), 8.79 (br, 1H, OH), 7.40 (dd, *J*=7.72, 1.85, 1H), δ 7.36 (t, *J*=7.70, 1H), 6.98 (d, *J*=7.72, 1H), 6.93 (dt, *J*=7.72, 1.85, 1H), 5.61 (br, 2H, NH_2) ppm; ^{13}C-NMR (100 MHz,DMSO-d_6): δ 165.7, 156.7, 149.8, 132.8, 131.5, 119.8, 116.9, 113.7 ppm.

4.3. (3-pyridin-4-yl)-[1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazole-6(5*H*)-thione (2a)((3-piridin-4-il)-[1,2,4]triazolo[3,4-*b*] [1,3,4]tiyadiazol-6(5*H*)-tiyon (2a))

mp:225.8 °C, yield:80%, color: brownish, recrystallized solvent: EtOH-dioxane (3:1), IR (KBr): υ 3360-3240 (NH), 3165-3042 (ArCH), 1620-1590(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.6 (br, 1H, SH/NH), 8.23 (dd, J=6.25, 1.47, 2H, prC-CH), 8.80 (d, J=5.94, 2H, prN-CH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 168,4 160.2, 150.1, 148.3, 134.2, 121.8 ppm.

4.4. 3-(2-hydroxyphenyl)-[1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazole-6(5*H*)-thione (2b)(3-(2-hidrokifenil)-[1,2,4]triazolo[3,4-*b*] [1,3,4]tiyadi azol-6(5*H*)-tiyon (2b))

mp:183-184 °C, yield:68 %, color: whitish, recrystallized solvent: EtOH-dioxane (2:1), IR (KBr): υ 3460-3340 (OH),3350-3275 (NH), 3105-3010 (ArCH), 1622-1593(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.6 (br, 1H, SH/NH), 8.60 (br, 1H, OH), 7.40 (dd, *J*=7.72, 1.84, 1H), 7.36 (t, *J*=7.72, 1H), 6.98 (d, *J*=7.72, 1H), 6.93 (dt, *J*=7.72, 1.84, 1H), ppm; ^{13}C-NMR (100 MHz,DMSO-d_6): δ 168.2, 161.7, 152.6, 149.1, 133.5, 131.2, 120.1, 116.3, 114.4 ppm.

4.5. 6-phenyl-3-pyridin-4-yl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole (3a)(6-fenil-3-piridin-4-il[1,2,4]triazolo[3,4-*b*][1,3,4]tiyadi azol (3a))

mp:222-224 °C, yield:70%, color: yellowish, recrystallized solvent: dimethylformamide, IR (KBr): υ 3140-3042 (Ar CH), 1620-1594(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.07 (d, J=7.08, 2H,o-ArCH) 7.62-7.72 (m, 3H,m,p-ArCH), 8.24 (dd, J=6.25, 1.47, 2H, prC-CH), 8.80 (d, J=5.94, 2H, prN-CH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 168.30,

151.52, 143.67, 134.08, 133.06, 131.12, 130.20, 130.13, 127.80, 120.20 ppm.

4.6. 6-(4-methoxyphenyl)-3-(pyridin-4-yl)[1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazole (3b)(6-(4-metoksifenil-3-(piridin-4-il)[1,2,4]triazolo[3,4-*b*] [1,3,4]tiyadiazol (3b))

mp:290-291 °C, yield:72%, color: brownish, recrystallized solvent: EtOH-dimethylformamide(1:1), IR (KBr): υ 3140-2910 (Ar/Al CH), 1612-1591(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.05 (s, 3H, OCH_3), 7.24 (d, J=7.08, 2H, ArCH) 7.82 (d, J=7.08, 2H, ArCH), 8.22 (dd, J=6.25, 1.47, 2H, prC-CH), 8.80 (d, J=6.12, 2H, prN-CH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 168.20, 156.52, 154.18, 143.60, 133.98, 133.06, 133.02, 130.22, 130.10, 127.81, 62.04 ppm.

4.7. 6-(4-chlorophenyl)-3-(pyridin-4-yl)[1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazole (3c)(6-(4-klorfenil-3-(piridin-4-il)[1,2,4]triazolo[3,4-*b*] [1,3,4]tiyadiazol (3c))

mp:241-243 °C, yield:70%, color: light brown, recrystallized solvent: EtOH-dimethylformamide(2:1), IR (KBr): υ 3140-3010 (Ar CH), 1612-1590(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.36 (d, J=7.08, 2H, ArCH) 7.90 (d, J=7.08, 2H, ArCH), 8.21 (dd, J=6.25, 1.47, 2H, prC-CH), 8.78 (d, J=6.12, 2H, prN-CH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 168.78, 156.60, 143.60, 133.98, 133.06, 133.16, 130.22, 129.09, 125.41, 110.60 ppm.

4.8. 6-(4-chlorophenyl)-3-(pyridin-4-yl)[1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazole (3d)(6-(4-klorfenil-3-(piridin-4-il)[1,2,4]triazolo[3,4-*b*] [1,3,4]tiyadiazol (3d))

mp:333-334 °C, yield:65%, color: dark brown, recrystallized solvent: EtOH-dioxane(2:1), IR (KBr): υ 3140-3010 (ArCH), 1612-1590(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.36 (d, J=7.08, 2H, ArCH) 7.90 (d, J=7.08, 2H, ArCH), 8.21 (dd, J=6.25, 1.47, 2H, prC-CH), 8.78 (d, J=6.12, 2H, prN-CH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 165.01, 155.60, 142.60, 133.65, 133.43, 131.14, 128.26, 123.12, 119.11, 108.20 ppm.

4.9. 2-(6-phenyl-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-3-yl) phenol (3e)(2-(6-fenil-[1,2,4]triazolo[3,4-*b*][1,3,4]tiyadiazol-3-il) fenol (3e))

mp:186-187 °C, yield:74%, color: yellowish, recrystallized solvent: dimethylformamide, IR (KBr): υ 3422-3340 (OH), 3180-3020 (ArCH), 1620-1587(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.58 (br, 1H, OH),7.17-7.90 (m, 9H, ArCH)ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 166.20, 152.01, 141.21, 137.19, 132.06, 131.12, 130.94, 130.08, 126.80, 124.45 ppm.

4.10. 2-(6-(4-methoxyphenyl)-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadi azol-3-yl) phenol(3f)(2-(6-(4-metoksifenil)-[1,2,4]triazolo[3,4-*b*][1,3,4]tiyadi azol-3-il) fenol (3f))

mp:284-286 °C, yield:63%, color: yellowish, recrystallized solvent: EtOH-dioxane(2:1) IR (KBr): υ 3420-3342 (OH), 3180-2960 (Ar/AlCH), 1612-1590(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.60 (br, 1H, OH),7.07-8.10 (m, 8H, ArCH),4.10 (s,3H, CH_3)ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 166.24, 151.10, 141.42, 137.46, 131.66, 131.04, 130.94, 130.08, 126.62, 123.40, 62.08 ppm.

4.11. 2-(6-(4-chlorophenyl)-[1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazol-3-yl)phenol(3f)(2-(6-(4-klorfenil)-[1,2,4] triazolo[3,4-*b*] [1,3,4]tiyadiazol -3-il) fenol (3f))

mp:>350 °C, yield:66%, color: yellow, recrystallized solvent: EtOH-dioxane(1:1) IR (KBr): υ 3420-3320 (OH), 3180-3040 (Ar/CH), 1618-1590(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.54 (br, 1H, OH),7.05-8.12 (m, 8H, ArCH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.10, 152.11, 140.40, 135.22, 131.69, 131.02, 131.00, 128.14, 123.66, 111.40 ppm.

4.12. 2-(6-(4-nitrophenyl)-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-3-yl)phenol (3f)(2-(6-(4-nitrofenil)-[1,2,4] triazolo[3,4-*b*] [1,3,4]tiyadi azol-3-il) fenol (3f))

mp:>350 °C, yield:51%, color: brown, recrystallized solvent: dimethylformamide); IR (KBr): υ 3430-3315 (OH), 3140-3010 (Ar/CH), 1608-1581(C=C, C=N)cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.50 (br, 1H, OH),7.02-8.10 (m, 8H, ArCH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ 162.15, 152.98, 144.21, 135.43, 131.65, 131.12, 130.85, 128.19, 123.60, 109.20 ppm.

5. CONCLUSION AND RECOMMENDATIONS (SONUÇ VE ÖNERİLER)

The synthetic reactions of synthesized compounds are summarized in **Scheme 1**. The Melting points, solvents for recrystallization and characterization data of the compounds **1a,b**, **2a,b** and **3a-h** are given in the experimental section. The disappearance of the signal at 1670-1680 cm^{-1} (C=O stretching bands), disappearance of the signal at δ 5.80 (broad NH_2) band in ^{1}H-NMR spectrum and observed C=S stretching bands at 1250-1265 confirmed structure formation **1a,b**. The signal SH proton (br, 1H) was too weak to be recorded presumably due to the extensive thiol-thione tautomerism and shows appear 14.02 ppm. The disappearance of this signal of mercapto triazoles in ^{1}H-NMR spectrum and the appearance of the signal at δ 150-170 due to C=N, C=S of the 1,3,4-thidiazol ring **2a,b**, **3a-h** in ^{13}C-NMR spectrum. In conclusion, the structure of all synthesized compounds was established on the basis of their spectroscopic data.

NOTICE (NOT)

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REFERENCES (KAYNAKLAR)

1. Cansiz, A., Orek, C., Koparir, M., Koparir, P., and Cetin, A., (2012). 4-Allyl-5-pyridin-4-yl-2,4-dihydro-3H-1,2,4-triazole-3-thione: Synthesis, Experimental and Theoretical Characterization, Spectrochimica Acta Part A-Molecular and Bimolecular Spectroscopy, 91, 136-145.
2. Holla, B.S., Poojary, K.N., Rao, B.S., and Shivananda, M.K., (2002). New Bis-aminomercaptotriazoles and Bistriazolo Thiadiazoles as Possible Anticancer Agents, Eur. J. Med. Chem.,37, 511-517.
3. Holla, B.S. and Kalluraya, B., (1988). Synthesis of some substituted 4-(5-nitro-2-furfurylidenamino)-5-mercapto-1,2,4-triazoles and 7*H*-6-(5-nitro-2-furyl)-*s*-triazolo[3,4-*b*] [1,3,4] thiadiazines, Indian Journal of Chemistry, 27B, 683-685.
4. Zhang, Z.Y. and Xiao-Wen, S., (1998). Heterocycles, 48, 561-584.
5. Pandeya, S.N., Sriram, S., Nath, G., and DeClercq, E., (2000). Syntehesis, Antibacterial, Antifungal and Anti-HIV Evaluation of

Schiff and Mannich Bases of Isatin and Its Derivatives with Triazole, Arzneim.-Forsch./Drug Res., 50,55-59.
6. Cansiz, A., Cetin, A., Orek, C., Karatepe, M., Sarac, K., Kus, A., and Koparir, M ., (2012). 6-Phenyl-3-(4-pyridyl)-1,2,4-triazolo-[3,4-b][1,3,4]thiadiazole: Synthesis, Experimental, Theoretical Characterization and Biological Activities, Spectrochimica Acta Part A-Molecular and Biomolecular Spectroscopy, 97, 606-615.
7. Menegola, E., Broccia, M. L., Di Renzo, F., and Giavini, E., (2001). Reproductive Toxicology, 15, 421.
8. Abbas, A.A. and Khalil, N.S.A.M., (2005). Nucleosides, Nucleotides, and Nucleic Acids, 24, 1353.
9. Holla, B. S., Sarojini, B. K., Gonsalves, R., (1998), II Farmaco, 53, 395.
10. Ram, V.J., Mishra, L., Pandey, N.H., Kushwaha, D.S., Pieters, L. A.C., and Vlietinck, A.J., (1990). J. Heterocycl. Chem., 27, 351.
11. Koparır, M., Çetin, A., and Cansız, A., (2005). Molecules, 10, 475.
12. Yale, H.L. and Piala, J.J.J., (1966). Med. Chem., 9, 42.
13. Coyanis, E.M., Vedova, D.C.O., Has, A., and Winter, M., (2002). J. of Fluorine Chem., 117, 185.
14. Cansiz, A., Çetin, A., Kutulay, P., and Koparır, M., (2009). Asian Journal of Chem., 21, 617.
15. Dege, N., Andaç, O., Çetin, A., Cansiz, A., Sekerci, M., and Dincer, M., (2005). 5-(Furan-2-yl)-4-(p-tolyl)-2,4-dihydro-1,2,4-triazole-3-thione, Acta Cryst. E61, O17.
16. Dege, N., Ozdemir, N., Cansiz, A., Çetin, A., Sekerci, M., and Dincer, M., (2004). 4-Ethyl-5-(2-hydroxyphenyl)-2H-1,2,4-triazole-3(4H)-thione, Acta Cryst., E60, O1405.
17. Brucato, A., Coppola, A., Gianguzza, S., and Provenzano, P.M., (1978). Bull. Soc. Ital. Biol. Sper., 54, 1051.
18. Coffen, D.L. and Fryer, R.I., (1975). US Patent 3(849): 434, Chemical Abstracts, 82, 730044v.
19. Shiroki, M., Tahara T., and Araki, K., (1975). Japanese Patent No. 75100096, Chemical Abstracts, 84, 59588k.
20. Povelitsa, F.D. and Gural, A.G., (1973). "Antibiotiki" Moscow, Chemical Abstracts, 78, 93044.