Turk J Chem
34 (2010) , 771 – 780.

doi:10.3906/kim-0905-1

Synthesis and characterisations of some new 2,4-dihydro-[1,2,4]-triazol-3-one derivatives and X-ray crystal structures of 4-(3-phenylallylideneamino)-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]triazol-3-one

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Received 04.05.2009

Compounds **2** were synthesised via the reaction of 4-amino-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]-triazol-3-one **(1)** with aldehydes. Compounds **3** and **4** were obtained from compounds **2** with bromo acetophenone and ethyl bromoacetate, respectively. The synthesis of compounds **2**, **3**, and **4** and crystal structure of compound **2a** are being reported. The molecular structures were identified by IR, ^{1}H-NMR, ^{13}C-NMR, MS, and elemental analyses. Compound **2a** crystallises in the monoclinic P 2_1/n space group, with a = 6.565(5) Å, b = 18.278(5) Å, c = 13.8166(18) Å, β = 96.227(5)°, V = 1553.6(14) Å^3, Z = 4.

The newly compounds synthesised were screened for their antibacterial and antifungal properties. Among the compounds, **4d** showed antimicrobial activity against *Candida albicans* ATCC 60193 and *Candida tropicalis* ATCC 13803.

Key Words: 1,2,4-Triazole, aldehydes, ethyl bromoacetate, bromo acetophenone, X-ray crystallography, antimicrobial activity

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Introduction

The 1,2,4-triazole compounds possess important pharmacology activities such as antifungal and antiviral activities. Examples of such compounds bearing 1,2,4-triazole residues are fluconazole, the powerful azole antifungal agent, as well as the potent antiviral N-nucleoside ribavirin.[1,2] The 1,2,4-triazole nucleus is associated with diverse pharmacological activities such as antibacterial, hypoglycemic, antihypertensive, analgesic, and specific magnetic properties.[3,4] In recent years, there has been an increasing interest in the chemistry of thiophenes because of their biological significance. Many of them have been widely investigated for therapeutic uses, especially as antifungal, antibacterial, anti-inflammatory, anticonvulsant, anti-asthmatic, and analgesic agents. They also were known to show anti-HIV, antiproliferative, germicidal, and D2 dopaminergic activities.[5] The azole moiety is an important and frequent insecticidal, agrochemical structural feature of many biologically active compounds such as cytochrome P450 enzyme inhibitors[1] and peptide analogue inhibitors. Recently, much attention has been focused on 1H-1,2,4-triazole derivatives for their broad-spectrum activities, such as fungicidal, herbicidal, anticonvulsant, and plant growth regulatory activities.[6] It was reported that compounds having triazole moieties such as vorozole, anastrozole, and letrozole appear to be very effective aromatase inhibitors very useful for preventing breast cancer.[7–9]

There are antimicrobial agents having different structures that are frequently used in the treatment of microbial infections. However, there is an increasing resistance to these drugs. Moreover, some of azole derivatives used as common antibiotics such as Amphotericin B have a toxic effect on humans as well as their antimicrobial effects.[10] To overcome the development of drug resistance, it is crucial to synthesise a new class of antimicrobials possessing different chemical properties from those used commonly.

In view of these facts, the aim of this present study was to obtain new triazole derivatives (Scheme).

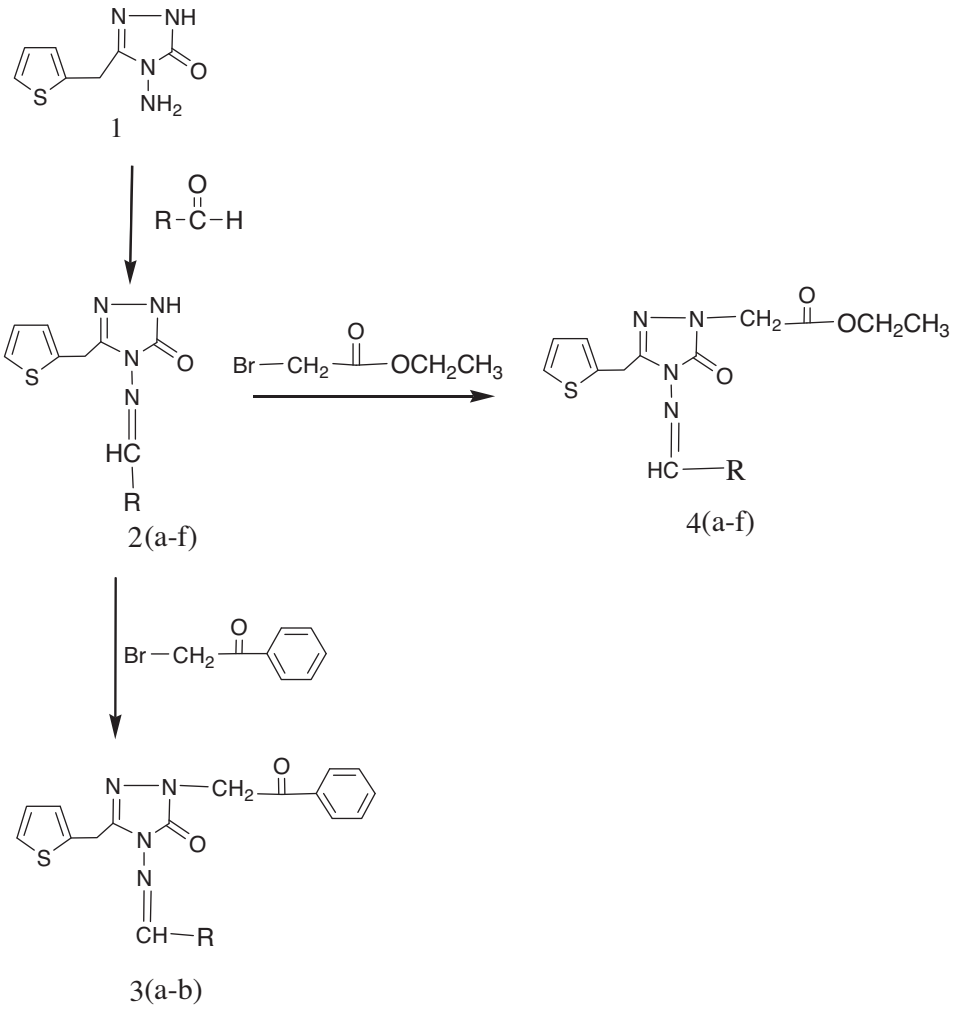
Experimental

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian-Mercury 200 MHz spectrometer. The IR spectra were measured as potassium bromide pellets using a Perkin-Elmer 1600 series FTIR spectrometer. Micromass was determined on a Micromass Quatro LC/ULTIMALC-MS spectrometer. Elemental analyses were carried out on a C,H, N-O rapid elemental analyser Hewlett-Packard 185 for C, H, and N and the results are within 0.4% of the theoretical values. All the chemicals were obtained from Fluka Chemie AG Buchs (Switzerland). Compounds **1** and **2c-f** were synthesised using the published method.[11,12] Compound **3a** is published in Acta Crystallographica.[13]

General method for the synthesis of 4-[arylidene-amino]-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]triazol-3-ones (2a-b): The corresponding 4-amino-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]-triazol-3-one **(1)** (0.01 mol) and aldehydes (0.01 mol) were heated at 160 °C in an oil bath for 2 h. After cooling it to room temperature, a solid appeared and it was crystallised from appropriate solvent to afford the desired compound.

Synthesis of 4-(3-phenylallylideneamino)-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]-triazol-3-one (2a). Recrystallised from ethanol/water (yield: 82.58%). Mp 178-179 °C. IR (KBr) cm^{-1}: 3164 (ν_{NH}), 1696 ($\nu_{C=O}$), 1626 ($\nu_{C=N}$); ^{1}H-NMR (DMSO-d$_6$)δ 4.20 (s, 2H, thiophen-CH$_2$), 6.94-7.11 (m, 2H, arH), 7.31-

7.43 (m, 5H, arH+vinylH), 7.66-7.71 (m, 3H, arH+vinylH), 9.49 (d, 1H, N=CH), 12.01 (s, 1H, NH); ^{13}C-NMR (DMSO-d$_6$)δ 25.60 (thiophen-CH_2), thiophen-C: [125.20 (CH), 126.59 (CH), 126.78 (CH), 137.06 (C), ar-C: [124.70 (CH), 127.53 (CH), 128.78 (CH), 135.17 (C), 129.53 (CH vinyl), 143.52 (CH vinyl)], 145.20 (triazole-C-3), 150.96 (N=CH), 153.96 (triazole-C-5). Analysis (% calculation/ found): C: 61.92/61.97, H: 4.55/4.58, N: 18.05/18.12. MS: m/z 310.99 $(M+1)^+$.



Scheme. Synthesis of compounds **2**, **3**, and **4**.

2, 3, 4	a	b	c	d	e	f
R	—HC=CH—	—	—	—	—	—

4-[(Pyridin-4-ylmethylene)-amino]-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]triazol-3-one (2b). Recrystallised from ethanol (yield: 81.05%). Mp 214-215 °C. IR (KBr) cm^{-1}: 3192 (ν_{NH}), 1718 ($\nu_{C=O}$), 1607 ($\nu_{C=N}$); ^{1}H-NMR (DMSO-d$_6$)δ (ppm) 4.34 (s, 2H, thiophen-CH_2), 6.95-7.07 (m, 2H, arH),

7.41-7.42 (m, 1H, arH), 7.84 (d, 2H, arH, J=5 Hz), 8.76 (d, 2H, arH, J=7.6 Hz), 9.81 (s, 1H, N=CH), 12.18 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6)δ (ppm) 25.46 (thiophen-CH_2), thiophen-C: [125.44 (CH), 126.80 (CH), 127.03 (CH), 137.21 (C)], ar-C: [121.51 (CH), 140.70 (C), 150.50 (CH)], 145.72 (triazole-C-3), 150.75 (N=CH), 150.94 (triazole-C-5). Analysis (% calculation/ found): C: 54.72/54.64, H: 3.89/3.82, N: 24.25/24.31. MS: m/z 285.93 $(M+1)^+$.

General method for the synthesis of 2-(2-oxo-2-phenyl-ethyl)-4-[arylidene-amino]-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4] triazol-3-one (3): The corresponding 4-[arylidene-amino]-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]triazol-3-ones (**2**) (0.01 mol) was refluxed with an equivalent amount of natrium in absolute ethanol for 1 h. Then bromoacetophenon (0.01 mol) was added and refluxed for an additional 5 h. The precipitate was filtered off, washed with H_2O, and recrystallised from appropriate solvent to afford the desired compound.

Synthesis of 2-(2-oxo-2-phenyl-ethyl)-4-[(pyridin-4-ylmethylene)-amino]-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]triazol-3-one (3b). Recrystallised from ethanol/water (1:2) (yield 66.00%). Mp 130-131 °C. IR (KBr) cm^{-1}: 1696 ($\nu_{acetophenonC=O}$), 1719 ($\nu_{triazoleC=O}$), 1589 ($\nu_{C=N}$); ^{1}H-NMR (DMSO-d_6)δ 4.41 (s, 2H, thiophen-CH_2), 5.52 (s, 2H, NCH_2), 6.99-7.10 (m, 2H, arH), 7.43-7.47 (m,1H, arH), 7.58-7.60 (m, 3H, arH), 7.85-7.88 (m, 2H, arH), 9.79 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6)δ 25.52 (thiophen-CH_2), 52.01 (NCH_2), thiophen-C: [125.65 (CH), 126.98 (CH), 127.12 (CH), 136.89 (C)], ar-C: [121.69 (CH), 140.51 (C), 151.41 (CH)], benzene-C: [128.55 (CH), 129.08 (CH), 134.04 (C), 134.36 (CH)], 145.08 (triazole-C-3), 149.99 (N=CH), 150.56 (triazole-C-5), 192.64 (acetophenon-C=O). Analysis (% calculation/ found): C: 62.52/62.58, H: 4.25/4.20, N: 17.36/17.41. MS: m/z 404.06 $(M+1)^+$.

General method for the synthesis of {3-oxo–4-[arylidene-amino]-5-(thiophen-2-ylmethyl)-2,4-dihydro-1,2,4-triazol-2-yl}-acetic acid ethyl ester (4): The corresponding 4-[arylidene-amino]-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]triazol-3-ones **(2)** (0.01 mol) were refluxed with an equivalent amount of natrium in absolute ethanol for 1 h. Then ethyl bromoacetate (0.01 mol) was added and refluxed for an additional 5 h. The precipitate was filtered off, washed with H_2O, and recrystallised from appropriate solvent to afford the desired compound.

Synthesis of {3-oxo–4-[(3-phenylallylidene)amino]-5-(thiophen-2-ylmethyl)-2,4-dihydro-1,2,4-triazol-2-yl}-acetic acid ethyl ester (4a). Recrystallised from ethanol/water (1:2) (yield 81.57%) to afford the desired compound. Mp 116-117 °C. IR (KBr) cm^{-1}: 1744 ($\nu_{ester-C=O}$), 1710 ($\nu_{triazole-C=O}$), 1594 ($\nu_{C=N}$), 1215 (ν_{C-O}); ^{1}H-NMR (DMSO-d_6)δ 1.12 (t, 3H, $OCH_2C\underline{H}_3$, J= 7.0 Hz), 4.13 (q, 2H, $OC\underline{H}_2CH_3$, J= 7.0 Hz), 4.30 (s, 2H, thiophen-CH_2), 4.61 (s, 2H, NCH_2), 6.90-7.12 (m, 2H, arH), 7.35-7.55 (m, 5H, arH+vinylH), 7.60-7.69 (m, 3H, arH+vinylH), 9.63 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6)δ (ppm) 13.96 ($OCH_2\underline{C}H_3$), 25.53 (thiophen-CH_2), 46.48 (NCH_2), 61.34 (OCH_2), thiophen-C: [125.32 (CH), 126.65 (CH), 127.10 (CH), 136.98 (C)], ar-C: [123.78 (CH), 126.59 (CH), 128.44 (CH),133.17 (C), 129.27 (vinyl CH), 144.24 (vinyl CH)], 149.62 (N=CH), 144.97 (triazole-C-3), 154.15 (triazole-C-5), 167.60 (ester-C=O). Analysis (% calculation/ found): C: 60.59/60.51, H: 5.08/5.13, N: 14.13/14.17. MS: m/z 381.05 $(M+1)^+$.

{3-Oxo-4-[(pyridin-4-ylmethylene)-amino]-5-thiophen-2-ylmethyl-2,4-dihydro-[1,2,4] triazole-2-yl}-acetic acid ethyl ester (4b). Recrystallised from ethanol/water (1:2) (yield: 82.86%). Mp 125-126 °C. IR (KBr) (ν, cm^{-1}): 1756 ($\nu_{ester-C=O}$), 1704 ($\nu_{triazole-C=O}$), 1613 ($\nu_{C=N}$), 1209 (ν_{C-O}); ^{1}H-NMR (DMSO-d_6) δ (ppm) 1.20 (t, 3H, $OCH_2C\underline{H}_3$, J= 7.4 Hz), 4.16 (q, 2H, $OC\underline{H}_2CH_3$, J= 7.4 Hz), 4.36 (s, 2H,

thiophen-CH_2), 4.66 (s, 2H, NCH_2), 6.94-7.59 (m, 3H, arH), 7.84 (d, 2H, arH, J=5 Hz), 8.76 (d, 2H, arH, J=5 Hz), 9.81 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6)δ (ppm) 13.87 ($OCH_2\underline{C}H_3$), 25.26 (thiophen-CH_2), 46.30 (NCH_2), 61.22 ($O\underline{C}H_2CH_3$), thiophen-C: [125.71 (CH), 126.80 (C), 127.03 (CH), 137.21 (C)], ar-C: [121.51 (CH), 140.70 (C), 152.50 (C)], 146.86 (N=CH), 144.86 (triazole-C-3), 153.33 (triazole-C-5), 167.46 (ester-C=O). Analysis (% calculation/ found): C: 54.97/54.91, H: 4.61/4.66, N: 18.86/18.81. MS: m/z 372.22 $(M+1)^+$.

{3-Oxo-5-thiophen-2-yl-methyl-4-[(furan-2-ylmethylene)-amino]-2,4-dihydro-[1,2,4] triazole-2-yl}-acetic acid ethyl ester (4c). Recrystallised from ethanol/water (1:1) (yield: 82.00%). Mp 106-107 °C. IR (KBr) (ν, cm^{-1}) 1745 ($\nu_{ester-C=O}$), 1713 ($\nu_{triazole-C=O}$), 1599 ($\nu_{C=N}$), 1221 (ν C-O); ^{1}H-NMR (DMSO-d_6) δ (ppm) 1.19 (t, 3H, $OCH_2C\underline{H}_3$, J= 7.0 Hz), 4.14 (q, 2H, $OC\underline{H}_2CH_3$, J= 7.0 Hz), 4.27 (s, 2H, thiophen-CH_2), 4.63 (s, 2H, NCH_2), 6.72-6.74 (m, 1H, arH), 6.95-7.01 (m, 2H, arH), 7.24-7.28 (m, 1H, arH), 7.38-7.41 (m, 1H, arH), 8.01 (s, 1H, arH), 9.54 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6)δ (ppm) 13.88 ($OCH_2\underline{C}H_3$), 25.23 (thiophen-CH_2), 46.33 (NCH_2), 61.17 ($O\underline{C}H_2CH_3$), thiophen-C: [125.44 (CH), 126.81 (C), 126.98 (CH), 136.50 (C)], ar-C: [112.62 (CH), 118.26 (CH), 143.32 (CH), 144.97 (C)], 144.68 (triazole-C-3), 146.99 (N=CH), 152.06 (triazole-C-5), 167.48 (ester-C=O). Analysis (% calculation/found): C: 53.32/53.39, H: 4.47/4.52, N: 15.55/15.59. MS: m/z 361.08 $(M+1)^+$.

{4[(5-Nitro-thiophen-2-ylmethylene)-amino]-3-oxo-5-thiophen-2-ylmethyl-2,4-dihydro-[1,2,4] triazole-2-yl}-acetic acid ethyl ester (4d). Recrystallised from ethanol/water (1:1) (yield: 76.25%). Mp 184-185 °C. IR (KBr) (ν, cm^{-1}): 1736 ($\nu_{ester-C=O}$), 1709 ($\nu_{triazole-C=O}$), 1598 ($\nu_{C=N}$), 1228 (ν_{C-O}); ^{1}H-NMR (DMSO-d_6) δ (ppm) 1.20 (t, 3H, $OCH_2C\underline{H}_3$, J= 7.0 Hz), 4.15 (q, 2H, $OC\underline{H}_2CH_3$, J= 7.0 Hz), 4.31 (s, 2H, thiophen-CH_2), 4.66 (s, 2H, NCH_2), 6.95-7.05 (m, 2H, arH), 7.42 (m, 1H, arH, J= 5 Hz), 7.83 (d, 1H, arH, J=4 Hz), 8.18 (d, 1H, arH, J=4 Hz), 9.89 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6)δ (ppm) 13.89 ($OCH_2\underline{C}H_3$), 25.27 (thiophen-CH_2), 46.43 (NCH_2), 61.24 ($O\underline{C}H_2CH_3$), thiophen-C: [125.57 (CH), 126.80 (CH), 126.92 (CH), 136.46 (C)], ar-C: [128.21 (CH), 132.87 (CH), 144.43 (C), 147.09 (C)], 144.49 (triazole-C-3), 149.24 (N=CH), 152.56 (triazole-C-5), 167.43 (ester-C=O). Analysis (% calculation/found): C: 45.60/45.64, H: 3.59/3.65, N: 16.62/16.67. MS: m/z 421.99 $(M+1)^+$.

{3-Oxo-5-thiophen-2-yl-methyl-4-[(thiophen-2-ylmethylene)-amino]-2,4-dihydro-[1,2,4] triazole-2-yl}-acetic acid ethyl ester (4e). Recrystallised from ethanol/water (1:1) (yield: 76.86%). Mp 114-115 °C. IR (KBr) (ν, cm^{-1}) 1746 ($\nu_{ester-C=O}$), 1703 ($\nu_{triazole-C=O}$), 1597 ($\nu_{C=N}$), 1217 (ν_{C-O}); ^{1}H-NMR (DMSO-d_6)δ (ppm) 1.17 (t, 3H, $OCH_2C\underline{H}_3$, J= 2.0 Hz), 4.13 (q, 2H, $OC\underline{H}_2CH_3$, J= 2.0 Hz), 4.23 (s, 2H, thiophen-CH_2), 4.61 (s, 2H, NCH_2), 6.91-7.00 (m, 2H, arH), 7.17-7.22 (m, 1H, arH), 7.36-7.38 (m, 1H, arH), 7.70-7.72 (m, 1H, arH), 7.84-7.81 (m, 1H, arH), 9.77 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6)δ (ppm) 13.89 ($OCH_2\underline{C}H_3$), 25.37 (thiophen-CH_2), 46.37 (NCH_2), 61.20 ($O\underline{C}H_2CH_3$), thiophen-C[125.49(CH), 126.80(CH), 126.84(CH), 137.58 (C)], ar-C: [128.28 (CH), 131.45 (CH), 134.39 (CH), 136.61 (C)], 149.56 (triazole-C-3), 144.50 (triazole-C-5), 149.21 (N=CH), 167.49 (ester-C=O). Analysis (% calculation/found): C: 51.05/51.09, H: 4.28/4.32, N: 14.88/14.92. MS: m/z 376.97 $(M+1)^+$.

{4-[(2,4-Dichloro-benzyliden)-amino]-3-oxo-5-thiophen-2-ylmethyl-2,4-dihydro-[1,2,4]triazole-2-yl}-acetic acid ethyl ester (4f). Recrystallised from ethanol (yield: 79.38%). Mp 114-115 °C. IR (KBr) (ν, cm^{-1}): 1751 ($\nu_{ester-C=O}$), 1723 ($\nu_{triazole-C=O}$), 1595 ($\nu_{C=N}$), 1240 (ν_{C-O}); ^{1}H-NMR (DMSO-d_6)δ (ppm) 1.14 (t, 3H, $OCH_2C\underline{H}_3$, J= 7.0 Hz), 4.14 (q, 2H, $OC\underline{H}_2CH_3$, J= 7.0 Hz), 4.34 (s, 2H, thiophen-CH_2), 4.63 (s, 2H, NCH_2), 7.81 (d, 1H, arH), CH_2), 6.96-7.01 (m, 2H, arH), 7.38 (d, 1H, arH), 7.58-7.63 (m, 1H, arH),

8.10 (d, 1H, arH), 10.07 (s,1H, N=CH); ^{13}C-NMR (DMSO-d_6)δ (ppm) 13.90 ($OCH_2\underline{C}H_3$), 25.27 (thiophen-CH_2), 46.33 (NCH_2), 61.26 ($O\underline{C}H_2CH_3$), thiophen-C:[125.48 (CH), 126.82 (CH), 126.90 (CH), 136.86 (C)], ar-C: [127.96 (CH), 128.17 (CH), 129.51 (CH),129.60 (CH),135.17 (CH), 136.61 (C)], 144.84 (triazole-C-3), 148.17 (N=CH), 149.44 (triazole-C-5), 167.73 (ester-C=O). Analysis (% calculation/found): C: 49.21/49.25, H: 3.67/3.74, N: 16.14/16.19. MS: m/z 439.94 $(M+1)^+$.

Crystal structure determination of compound 2a

The data collection was performed at 293(2) K for the compound **2a** on a *Stoe-IPDS–2* diffractometer equipped with a graphite monochromated Mo-$K\alpha$ radiation ($\lambda = 0.71069$ Å). The structure was solved by direct methods using SHELXS–97[14] and refined by a full-matrix least-squares procedure also using SHELXL–97.[14] All hydrogen atoms were placed in idealised locations and refined anisotropically using a riding model. Molecular graphic were prepared using ORTEP3[15] and finally the packing diagram was prepared using PLATON.[16] Details of crystal data, structure solution, and refinement are given in Table 1.

Table 1. Crystallographic data for **2a**.

Chemical formula	$C_{16}H_{14}N_4SO$	h $_{min}$, h_{max}	-7, 8
Formula weight	310.37	k $_{min}$, k_{max}	-16,16
Crystal colour, habit	Colourless, prism	l $_{min}$, l_{max}	-22,22
Crystal system	Monoclinic	θ_{min}	1,9
Crystal dimensions	0.43 × 0.3 × 0.22	θ_{max}	26
Space group	$P2_1/n$	D_{calc}(g/cm^3)	1.327
a(Å)	6.565(5)	(Mo K$_\langle$), (cm^{-1})	0.22
b(Å)	18.278(5)	Measurement reflection	18000
c(Å)	13.024(5)	Unique reflections	3048
α(°), γ(°)	90.000(5)	Observed reflection	1265
(°)	96.227(5)	R	0.090
V(Å^3)	1553.6(14)	Rw	0.301
Z	4	S	0.895

$R = \Sigma$llFol-lFcll/ΣlFol $Rw = [(\Sigma w(1Fo1\text{-}1Fc1)2/\Sigma wFo2)]\,1/2$

Table 2. Selected bond distances an bond angles (Å, °) for **2a**.

Bond Distances	
C1—S1 1.625 (8)	N1—N2 1.380 (6)
C4—S1 1.696 (6)	N3—N4 1.391 (6)
C7—O1 1.241 (6)	
Bond Angles	
C5—C4—S1 122.2 (4)	O1—C7—N3 128.8 (5)
N3—C6—C5 124.0 (5)	C8—N4—N3 118.3 (4)

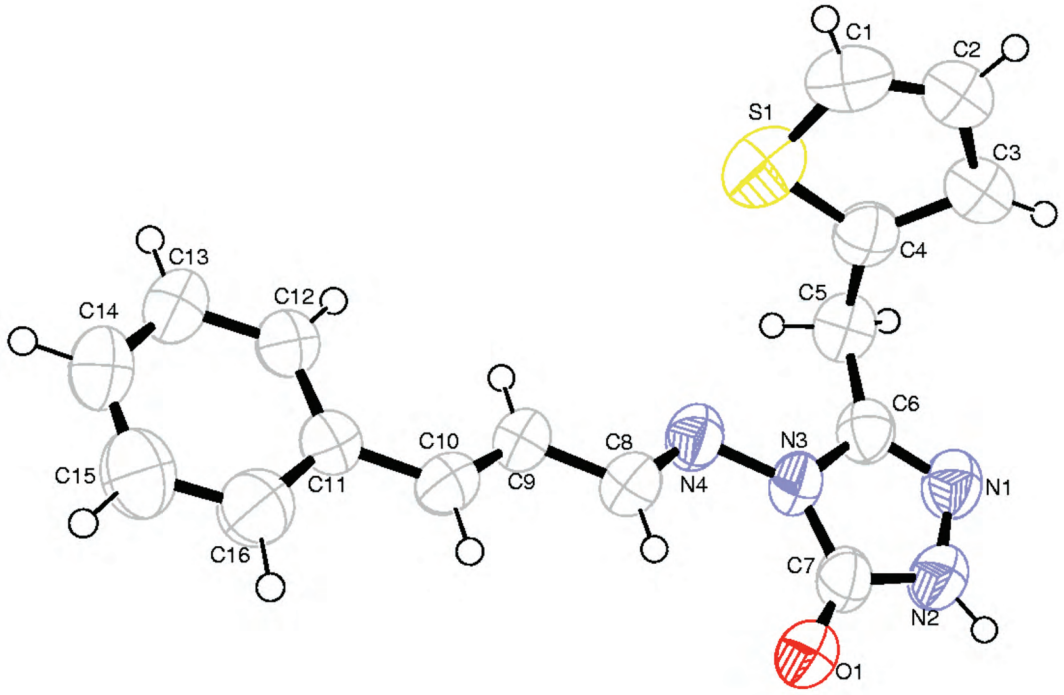


Figure 1. Ortep drawing of the crystal structure of **2a**.

Results and discussion

In this study, compounds **2** was obtained from the reaction with 4-amino-5-thiophen-2-yl-methyl-2,4-dihydro-[1,2,4]-triazol-3-one (**1**) with aldehydes (Scheme 1). In the IR spectra of compounds **2a-b**, one sharp absorption band was seen at 1696 and 1718 cm^{-1}, belonging to the carbonyl function of the triazole ring. While NH_2 was disappeared, N=CH were observed at 9.49 and 9.81 ppm in the ^{1}H-NMR spectra of compounds **2**. Compounds **3** were synthesised via the reaction of compounds **2** with bromo acetophenone. The IR spectra of compounds **3** showed 2 sharp absorption bands, one of which, appearing at 1719 cm^{-1}, was attributed to carbonyl function of 1,2,4-triazole-3-one ring, and the other, observed at 1696 cm^{-1}, was assigned to -C=O stretching frequency corresponding to ketone carbonyl. Compounds **4** were synthesised via the reaction of compounds **2** with ethyl bromoacetate. The IR spectra of compounds **4** showed 2 sharp absorption bands, one of which, appearing at 1702, 1713 cm^{-1}, was attributed to the carbonyl function of 1,2,4-triazol-3-one ring and the other observed at 1736,1746 cm^{-1} was assigned to -C=O stretching frequency corresponding to ester carbonyl. While -NH signal disappeared in the ^{1}H-NMR of compounds 4, the proton signals due to ester group were recorded between 1.17 and 1.20 ppm ($-OCH_2C\underline{H}_3$) integrating for 3 protons, and between 4.13 and 4.15 ppm ($-OC\underline{H}_2CH_3$) integrating for 2 protons. The ^{13}C signals of $-OCH_2\underline{C}H_3$ and $-O\underline{C}H_2CH_3$ were observed at 13.88-13.89 ppm and 61.17-61.24 ppm.

Compound **2a** consist mainly three bonded planar rings, namely a triazole ring (A), a benzene ring (B) and a thiophene ring (C). While triazole and benzene rings are nearly coplanar with each other the thiophene

ring is normal to this plane with the angle 112.35°. The r.m.s. deviation of the molecule is 0.08 Å. Maximum deviation in the mean plane of A and B ring system belong to the C9 atom with -0.081 Å; in ring C this value belongs to the C3 atom with -0.139 Å.

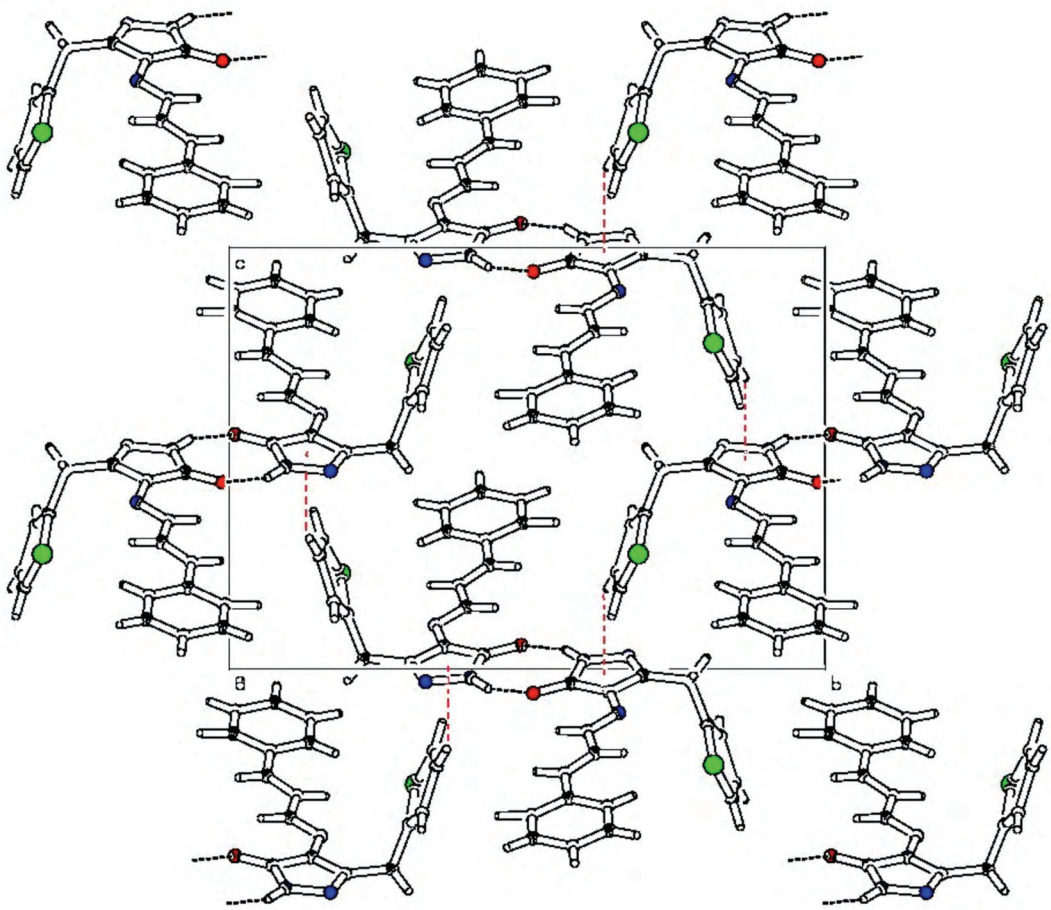


Figure 2. Packing diagram of compound **2a** view along a axis.

The torsion angle S1-C4-C5-C6 (between rings A and C) is -100.2 (5)°. C=N double bond distances are 1.273 Å in the chain and 1.282 Å in the triazole ring and that of the C=O double bond is 1.25(7) Å. The packing of the molecule is shown in Figure 2. Analysis of the crystal packing of compound **2** reveals that the molecule is linked by means of an intermolecular N-H...O type hydrogen bond between N2 and O1 with symmetry code (2-x,1-y,-z) [N.....O = 2.774(7) Å , N-H2A...O1 = 161°] and intramolecular C-H...O type hydrogen bond between C8-H8...O1. In addition to these interactions the crystal structure presents C-H ....π stacking. This C-H ....π interaction occurs between C2-H2 ....Cg2 (Cg2 is the centroid of the triazole ring) with symmetry code (1/2+x, 1/2-y, 1/2+z), with a distance of 3.487(6) Å.

Antimicrobial activity

All test microorganisms were obtained from the Refik Saydam Hıfzıssıha Institute (Ankara, Turkey) and are as follows; Ec: *Escherichia coli* ATCC 25922, Pa: *Pseudomonas aeruginosa* ATCC 10145, Yp: *Yersinia pseudotuberculosis* ATCC 911, Kp: *Klebsiella pneumoniae* ATCC 13883, Ef: *Enterococcus faecalis* ATCC 29212, Sa: *Staphylococcus aureus* ATCC 25923, Bc: *Bacillus cereus* 709 roma, Ca: *Candida albicans* ATCC 60193, Ct: *Candida tropicalis* ATCC 13803. Some the newly compounds were dissolved in dimethylsulphoxide (DMSO) to prepare extract stock solution.

The newly compounds synthesised were screened for their antibacterial and antifungal properties. Among the compounds, **4d** exhibited the highest degree of antimicrobial activity against *Candida albicans* ATCC 60193 and *Candida tropicalis* ATCC 13803.

Acknowledgements

This work was supported by the Research Fund of Karadeniz Technical University. (2004.111.02.11)

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