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NEW HETEROCYCLIC DERIVATIVES FROM THE ACTION OF VARIETY ELECTROPHILES ON 4-AMINO-5-BENZYL-4*H*-1,2,4-TRIAZOLE-3-THIOL AND EVALUATION OF THEIR ANTIBACTERIAL ACTIVITY

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Abstract: The title compound, 4-amino-5-benzyl-4*H*-1,2,4-triazole-3-thiol **(1)**, was found to be a useful starting material for the synthesis of some new heterocyclic derivatives. New heterocycles **2**, **4- 13** containing 1,2,4-triazole ring were synthesized by the reaction of **1** with different electrophilic reagents such as, triethyl orthoformate, phenyl isothiocyanate, chalcone, benzoin, thiocarbonyl-bis-thioglycolic acid, aromatic anhydrides and sulfonyloxy-derivatives of cyclic imides. The chemical structures of the synthesized compounds **2, 4- 13** were characterized by their elemental analyses, FT-IR, ^{1}H ^{13}C NMR and mass spectra. Investigation of the antimicrobial activity of these compounds was done by the paper disc technique. Some of the tested compounds showed high and favorable antimicrobial activity.

Keywords: Antibacterial activity, 1,2,4-triazoles, acetylation, thiadiazole, anhydrides.

Introdution

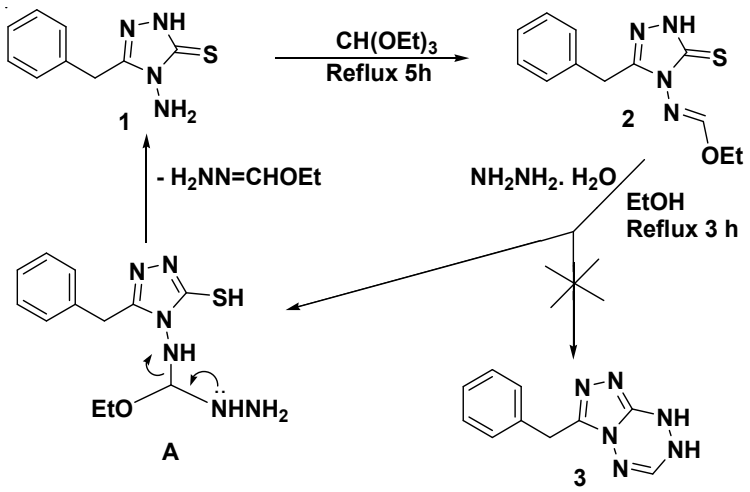
During the last few decades, the chemistry of 1,2,4-triazoles and their fused heterocyclic derivatives constitutes an important class of organic compounds with their diverse pharmacological properties such as, anti-inflammatory [1-3], antibacterial [4-7], antitubercular [8, 9], antifungal [10-12], anticonvulsant [13-15], antiviral [16, 17], antioxidant [18], antitumor [19, 20], anthelmintic [21], analgesic [22-24] and antidepressant [25] activities. In addition, the triazole derivatives have attracted considerable attention in fields, such as medicinal and agrochemical research [26].

Consequently, in light of the above facts, the objective of this work is to synthesize new heterocyclic compounds derived from 4-amino-5-benzyl-4*H*-1,2,4-triazole-3-thiol (**1**), and to investigate their possible antibacterial activity.

Results and discussion

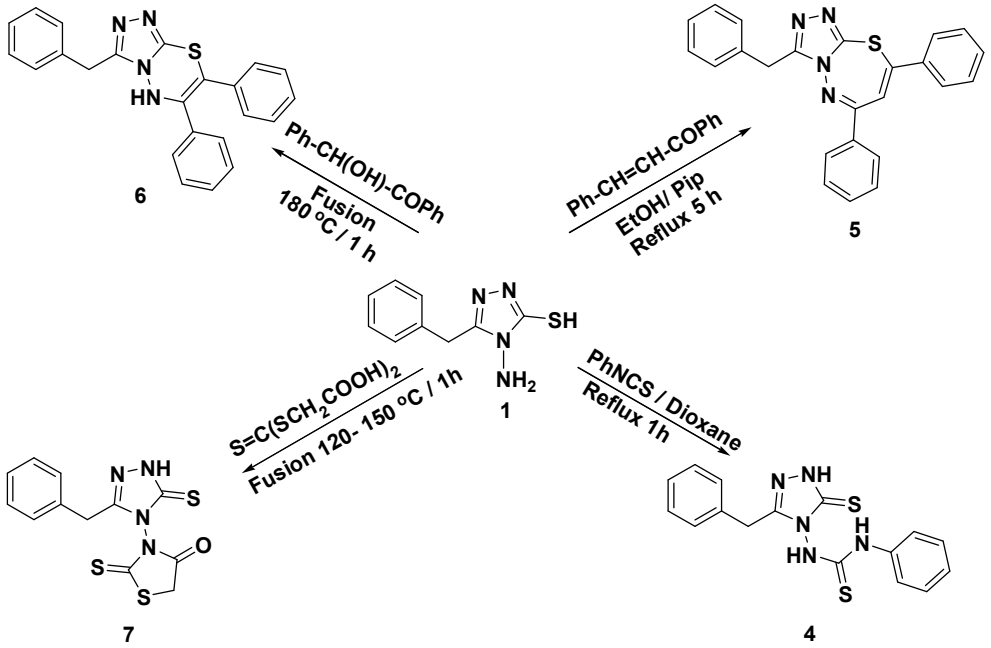
In continuation of the previous study [27], the present study aimed at investigation of the reactivity of the titled compound upon the action of variety of electrophilic reagents. Compound **1** was previously prepared either by fusion of phenylacetic acid with thiocarbohydrazide [28], or by treatment of phenylacetic acid hydrazide with carbon disulfide in ethanolic potassium hydroxide, and then treatment the resulting salt with hydrazine hydrate [29, 30]. In the present work, boiling of compound **1** with triethyl orthoformate gave the ethoxymethylenamine derivative **2**, which was recovered to the start **1** (mp., mix. mp and *TLC*) on treatment with hydrazine hydrate in ethanol instead of the expected tetrazine **3** (Scheme 1). The formation of **1** from the reaction of **2** with hydrazine hydrate was assumed to proceed via the addition of hydrazine at the imino function group to form the unstable

intermediate **A**, followed by the elimination of ethyl formate hydrazone [31]. Elucidation of the chemical structure of compounds **2** based on its spectroscopic data. The ^{1}H NMR spectrum of compound **2** exhibited a singlet proton at δ 10.08 ppm corresponding to (NH), singlet at δ 8.79 ppm for the proton of azomethine linkage (N=CH), multiplets at δ 7.45-7.20 ppm for (Ar'H), singlet at δ 5.15 ppm for the two protons of ($\underline{CH_2}$Ph) , quartet at δ 4.35 ppm and triplet at δ 1.3 ppm for the ethyl group. The mass spectrum of compound **2** showed molecular ion peak at *m/z* 262, which in agreement with the assigned structure.



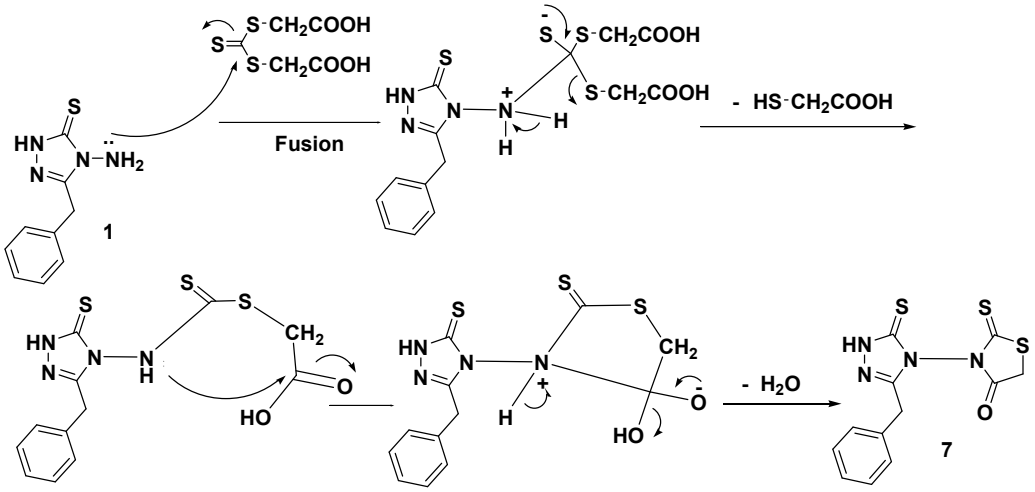
Scheme 1: Reaction of compound **1** with triethylorthoformate to give compound **2** and *vice-versa*.

When compound **1** was heated with phenyl isothiocyanate in dioxane during 1 hour, compound **4** assigned as 1-(3-benzyl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)-3-phenylthiourea was obtained without detecting its cyclized derivative [32] (Scheme 2). The absorption bands in its IR spectrum showed bands at 3210- 3173 for (NH's), 2850 for (CH_2) group, and at 1293 cm^{-1} for the (C=S) group. The ^{1}H NMR spectrum of **4** showed three singlets at δ 13.63, 10.51 and 10.07 for the three (NH) groups, multiplets at 7.43-7.21 for the ten aromatic protons and singlet at δ 4.16 for the two protons of ($\underline{CH_2}$Ph). A series of triazolothiadiazepines were synthesized by cyclocondensation of substituted 2-mercapto-4-amino triazoles and substituted chalcones [33, 34]. Analogously, condensation of the triazole **1** with the chalcone (1,3-diphenyl-propenone) in ethanolic piperidine solution followed by acidification of the reaction mixture using acetic acid then further heating for 3 hours afforded the corresponding triazolothiadiazepine **5**. The structure of **5** was confirmed from its spectral data. The ^{1}H NMR spectrum showed multiplets at δ 7.99-7.07 ppm corresponding to the aromatic protons, singlet at δ 6.42 ppm for the thiadiazepine proton and singlet at δ 4.02 ppm for the two protons of ($\underline{CH_2}$Ph). The mass spectrum showed molecular ion peak at *m/z* 394 corresponding to the formula ($C_{24}H_{18}N_4S$). The cycloaddition of compound **1** with benzoin afforded the corresponding triazolothiadiazine derivative **6**, whose elemental analysis and spectroscopic data are consistent with its assigned structure.



Scheme 2: Reaction of compound **1** with phenyl isothiocyanate, chalcone, benzoin and thiocarbonyl-bis-thioglycolic acid

Fusion of compound **1** with thiocarbonyl-bis-thioglycolic acid at 160 ^{o}C afforded the corresponding thiazolidin-4-one derivative **7** (Scheme 2). The structure of compound **7** was in agreement with its spectral data and elemental analysis [Experimental part]. The conversion of compound **1** to compound **7** may proceed *via* elimination of thioglycolic acid moiety followed by cyclic condensation through losing of water according to the proposed mechanism (Scheme 3).

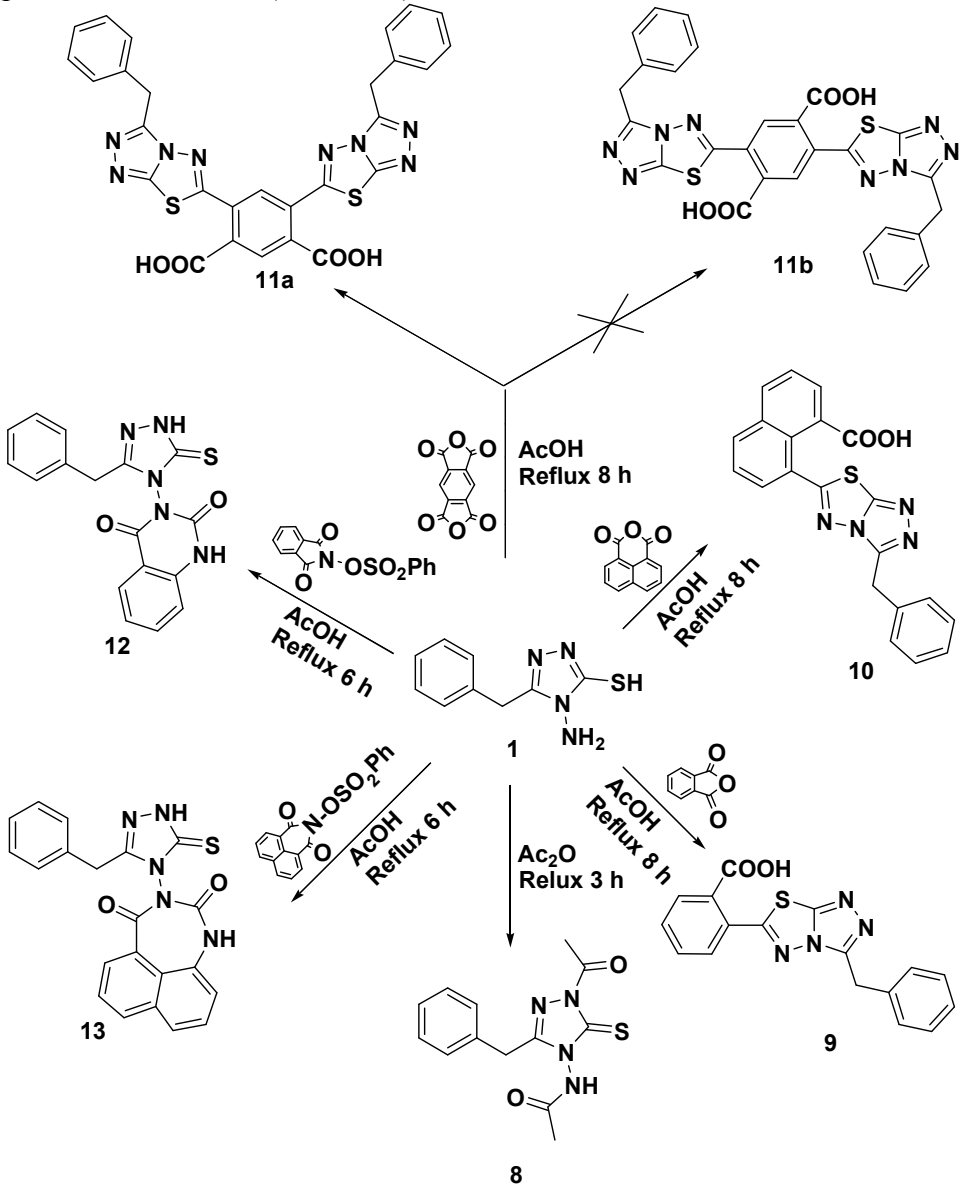


Scheme 3: The suggested reaction mechanism of **1** to give thiazolidin-4-one derivative **7**.

Acetylation of the thione **1** with excess acetic anhydride proceeded with participation of the amino group and the $N_{(2)}$ atom of the triazole ring to afford only the diacetyl derivative **8**. It is worth mentioning that the acetylation of other aminotriazoles gave mono-, di- and triacetyl derivatives [35, 36]. The mass spectrum of compound **8** showed a molecular ion peak at *m/z* 290 corresponding to the formula ($C_{13}H_{14}N_4O_2S$). The ^{1}H NMR spectrum showed the

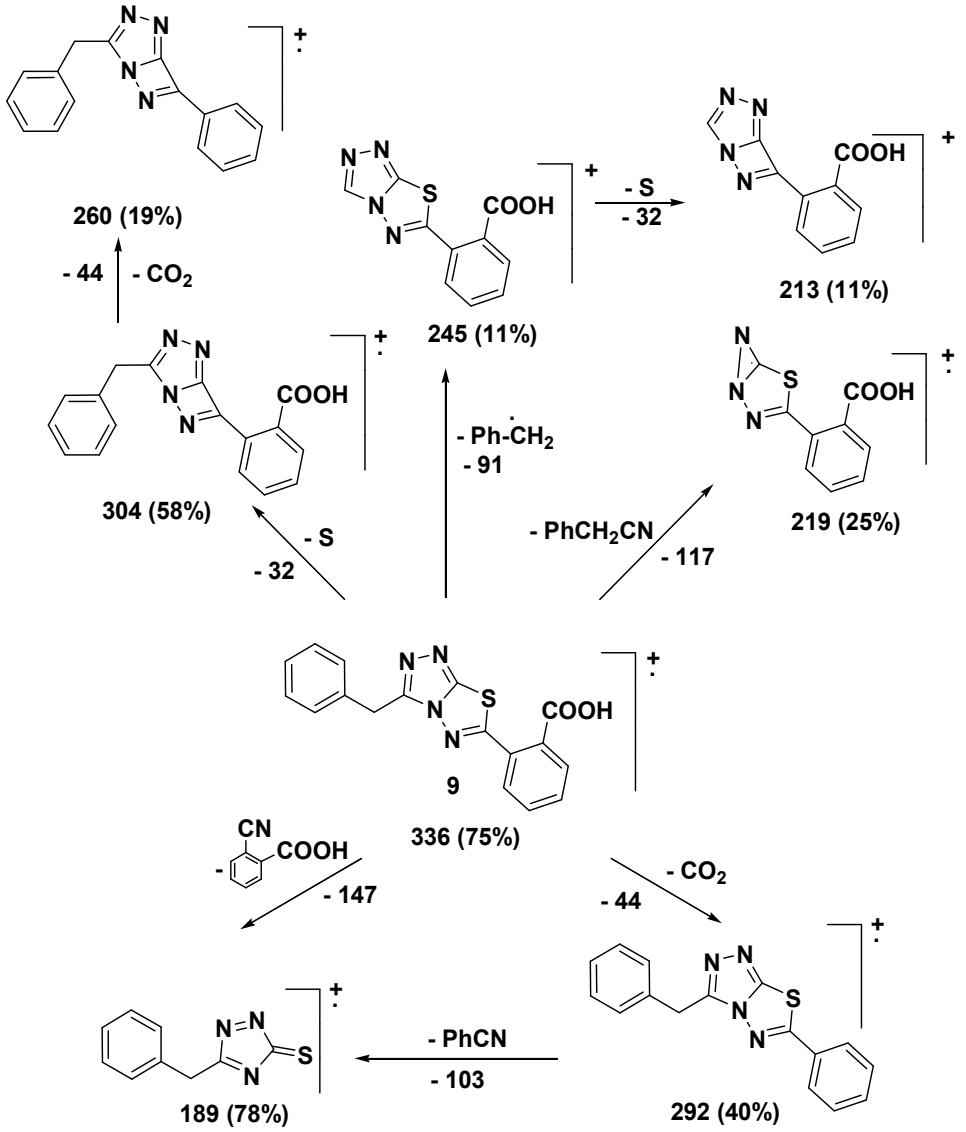
presence of the (NH) at δ 11.14 ppm and two different methyles protons at δ 2.04 ppm and δ 1.91 ppm, which indicates that the acetylation was occurred on both (NH) triazole and the amino group. Also, the ^{13}C NMR spectrum of compound **8** showed eleven different signals for eleven different carbon atoms, which confirms the proposed structure (Scheme 4).

It was reported that cyclic imides containing 1,2,4-triazole ring were synthesized by reacting substituted 4-amino-1,2,4-triazole-2-thiols with different anhydrides *via* multistep synthesis [32, 37]. On the contrary, refluxing of the thione **1** with aromatic anhydrides namely, phthalic anhydride, 1,8-naphthalic anhydride and pyromellitic dianhydride in glacial acetic acid for 8 hours afforded the corresponding 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazole derivatives **9**, **10** and **11a** through a nucleophilic ring opening of the anhydride followed by intramolecular nucleophilic cyclization to give the fused triazolothiadiazole moiety. Two possible isomeric structures were expected from the reaction of compound **1** with pyromellitic dianhydride. However, monitoring the reaction mixture using *TLC* revealed the formation of one product, which was the isophthalic isomer **11a** without detecting of the other terephthalic isomer **11b** (Scheme 4).



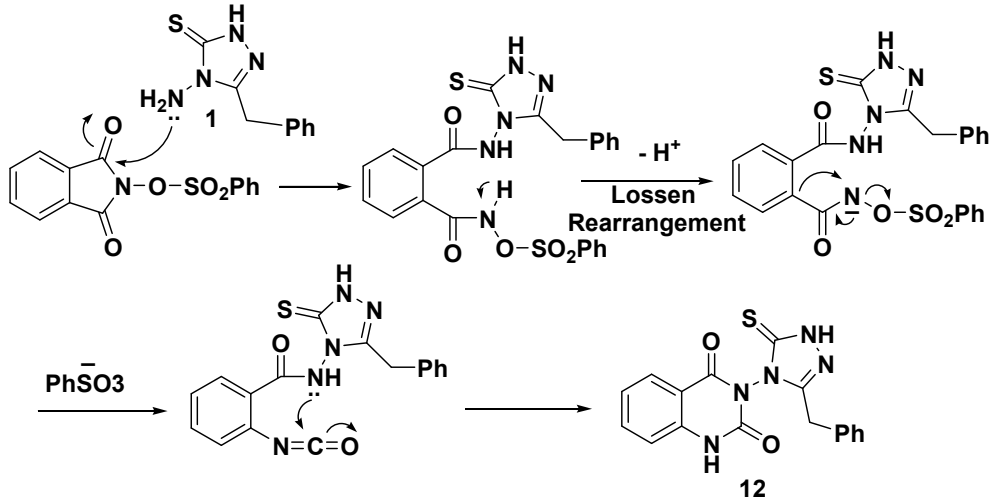
Scheme 4: Reactions of **1** with different anhydrides and *N*-sulphonyloxy-imides

The chemical structures of **9, 10** and **11a** have been established from their spectral data, which were found to be completely fit with the proposed structures**.** The IR spectra absorption bands of compounds **9**, **10** and **11a** showed the presence of the carboxylic C=O at 1761, 1736 and 1763 cm^{-1} and the carboxylic OH at 3545, 4495 and 3450 cm^{-1}, respectively. The ^{1}H NMR spectra showed signals at δ 14.27, 14.31 and 14.38 ppm for the (carboxylic-OH) protons of compounds **9**, **10** and **11a**, respectively. Moreover, the ^{1}H NMR spectrum of the isophthalic isomer **11a** indicates the presence of two singlets for the two different benzene protons at δ 8.82 and at δ 7.95, respectively. The ^{13}C NMR spectrum of compound **9** showed fifteen different signals for fifteen different carbon atoms and for **11a** showed thirteen different signals for thirteen different carbon atoms, which adds additional confirmation for the proposed structures [Experimental part]. The mass spectra showed molecular ion peak at *m/z* 336 (75%) for compound **9**, at *m/z* 386 (41%) for compound **10** and at *m/z* 594 (47%) for compound **11a**. Scheme (5) shows the fragmentation pattern for compound **9**, which confirms its structure.



Scheme 5: Mass fragmentation pattern of compound **9**.

Other electrophilic reagents such as *N*-sulphonyloxypthalimide and *N*-sulphonyloxynaphthalimide were reacted with the triazole **1** in acetic acid/ sodium acetate mixture to give the corresponding quinazoline-2,4-dione derivative **12** and diaza-cyclohepta-naphthalene-8,10-dione derivative **13** through "*Lossen rearrangement*", according to the following mechanism in scheme (6).



Scheme 6: The suggested reaction mechanism of **1** with *N*-sulphonyloxypthalimide.

The structures of compounds **12** and **13** were deduced from the respective spectral data. The IR spectra showed absorption bands at 3180- 3110 cm^{-1} and 1795, 1761 cm^{-1} for NH and C=O groups of compound **12**; and at 3300- 3100 cm^{-1} and 1740, 1689 cm^{-1} for NH and C=O groups of compound **13**. The elemental analyses and the mass spectra data of **12** and **13**, which showed molecular ion peak at *m/z* 351 and at m/z 401, led to the assignment of the molecular formula $C_{17}H_{13}N_5O_2S$ and $C_{21}H_{15}N_5O_2S$, respectively. The ^{13}C NMR spectrum of compound **13** showed nineteen different signals for nineteen different carbon atoms, which confirms the assigned structure [Experimental part].

Antibacterial activity: The antibacterial activity of the synthesized compounds **2, 4- 13** were carried out on the growth of two pathogenic bacteria (*E. Coli* and *Enterococcus faecalis*). The data obtained in Table (1) indicate that 6/13 of these compounds have a clear effect on *E. Coli* bacteria, the greater inhibition was observed by the diaza-cyclohepta-naphthalene-8,10-dione derivative **13** (12 mm). The thiazolidinone **7**, Triazolo[3,4-b][1,3,4]thiadiazole derivatives **9**, **10**, **11a** and the quinazoline-2,4-dione derivative **12** showed high inhibition (8- 9 mm). The inhibition effect was decreased on *Enterococcus faecalis* and only 5/13 of the tested compounds have a clear effect, the thiazolidinone **7** showed high inhibition (9 mm) and compounds **9**, **10**, **12** and **13** showed moderate inhibition effect (7 mm). It can be seen from Table (1) that the compounds **2**, **4**, **5**, **6** and **8** had no effect against both kinds of bacteria.

Table 1: Effect of the synthesized compounds (**2, 4- 13**) on bacterial growth (mm).

	Bacterial growth inhibition zone diameter (*mm*)	
	Gram (-*ve*) Bacteria	**Gram (+*ve*) Bacteria**
Sample No.	***E. Coli***	***Enterococcus faecalis***
2	**-----**	**-----**
4	**-----**	**-----**
5	**-----**	**-----**
6	**-----**	**-----**
7	**8**	**9**
8	**-----**	**-----**
9	**8**	**7**
10	**8**	**7**
11a	**8**	**-----**
12	**9**	**7**
13	**12**	**7**
***Choramphenicol* 30 *µg* (Control)**	**18**	**18**
(--) No bacterial growth inhibition zone.		

Conclusion

In summary, 4-amino-5-benzyl-4*H*-[1,2,4]triazole-3-thiol (**1**) was used as a precursor to synthesize some new heterocyclic compounds **2, 4- 13**, their structures were confirmed by IR, ^{1}H ^{13}C-NMR, mass spectra and elemental analyses, which were found to be completely fit with the assigned structures. The examination of antibacterial activity data of the synthesized compounds reveals that the compounds **7**, **9**, **10**, **11a**, **12** and **13** are found more active against gram (-*ve*) and gram (+*ve*) bacteria. It can be stated that half of the tested compounds are promising new antimicrobial agents.

Experimental

Melting points (uncorrected) were recorded on an Electrothermal melting apparatus. The IR spectra were recorded on a Shimadzu FT-IR 8101 PC spectrometer. The ^{1}H and ^{13}C NMR spectra were determined in DMSO-d_6 at 300 MHz on a Varian Mercury VX 300 NMR spectrometer; Chemical shifts are reported in ppm with TMS as an internal standard and are given in δ units. Electron impact mass spectra were obtained at 70 eV using a GCMS-QP 1000 EX spectrometer. Elemental analyses, mass and NMR spectra were carried out at the Microanalytical Center of Cairo University.

4-Ethoxymethylendenamino-5-benzyl-3,4-dihydro-2*H*-1,2,4-triazole-3-thione (**2**). A mixture of compound **1** (2 g, 10 mmol) and 3 ml triethylorthoformate was refluxed for 5 h. After cooling, the solid formed was filtered off and crystallized from ethanol as yellow crystals. Yield 1.7 g (65%); mp 234- 236 °C; ir (KBr), *v*, cm^{-1}: 3197 (NH), 3030 (CH-aromatic), 2890 (CH-aliphatic), 1589 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 10.08 (s, 1H, NH), 8.79 (1H, s, N=C-H), 7.40-7.20 (5H, m, Ar'H), 4.35 (2H, q, CH_2), 3.46 (2H, s, CH_2Ph), 1.30 (3H, t, CH_3); ms: *m/z* (*I rel*, %):262 [M^{+}] (31), 229 (14), 206 (28), 191 (25), 118 (4), 91(6). *Anal*. Calcd. for $C_{12}H_{14}N_4OS$: C, 54.94; H, 5.38; N, 21.36; S, 12.22. Found: C, 54.77; H, 5.23; N, 21.49; S, 12.41.

1-(3-benzyl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)-3-phenylthiourea (4). A mixture of compound **1** (2 g, 10 mmol) and phenylisothiocyanate (1.3 ml, 10 mmol) in 20 ml dioxane was refluxed for 1 h. After cooling, the solid formed was filtered off and recrystallized from ethanol as yellow crystals. Yield 2.9 g (85%); mp 208- 210 °C; ir (KBr), *v*, cm^{-1}: 3210- 3173 (NH's), 3028 (CH-aromatic), 2850 (CH_2), 2360 1593 (C=N), 1293 (C=S); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 13.63 (1H, s, NH), 10.51 (1H, br, Ph-NH-CS), 10.07 (1H, s, N-NHCS), 7.50-7.09 (10H, m, Ar'H), 4.02 (2H, s, CH_2Ph); ms: *m/z* (*I rel*, %): 341 [M$^+$] (0.3), 307 (3), 274 (0.4), 223 (2), 205 (13), 91 (95). *Anal*. Calcd. for $C_{16}H_{15}N_5S_2$: C, 56.28; H, 4.43; N, 20.51; S, 18.78. Found: C, 56.37; H, 4.29; N, 20.48; S, 18.86.

3-Benzyl-6,8-diphenyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazepine (5). A mixture of compound **1** (2 g, 10 mmol) and 1,3-diphenyl-propenone (2 g, 10 mmol) in 20 ml ethanol in presence of few drops of piperidine was heated under reflux for 5 h., and then 1 ml of acetic acid was added. The refluxing was continued for another 3 hrs. The reaction mixture was allowed to stand overnight at room temperature. The solid formed was filtered, dried and crystallized from ethanol/ chloroform (2: 1) as yellow crystals. Yield 2.45 g (62%); mp 116- 118 °C; ir (KBr), *v*, cm^{-1}: 3023 (CH-aromatic), 2951 (CH_2), 1595 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 7.99-7.07 (15H, m, Ar'H), 6.42 (1H, s, H-thiadiazepine), 4.02 (2H, s, CH_2Ph); ms: *m/z* (*I rel*, %): 394 [M$^+$] (3), 363 (17), 292 (24), 207 (57), 177 (33), 105 (100). *Anal*. Calcd. for $C_{24}H_{18}N_4S$: C, 73.07; H, 4.60; N, 14.20; S, 8.13. Found: C, 73.18; H, 4.67; N, 14.12; S, 8.03.

3-Benzyl-6,7-diphenyl-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazine (6). A mixture of compound **1** (2 g, 10 mmol) and benzoin (2.12 g,10 mmol) was fused in an oil bath at 120- 150 ^{o}C for 1 h. The color of the reaction mixture changed to yellow and after cooling the residue was trituration with petroleum ether then water. The solid formed was collected by filtration and crystallized from ethanol/ water (1: 1) as yellow crystals. Yield 2.6 g (68%); mp 110- 112 °C; ir (KBr) , *v*, cm^{-1}: 3414 (NH), 3062 (CH-aromatic), 2935 (CH_2), 1592 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 8.01-7.27 (15H, m, Ar'H), 5.96 (1H, s, NH), 4.06 (2H, s, CH_2Ph); ms: *m/z* (*I rel*, %): 382 [M$^+$] (67), 353 (77), 328 (55), 286 (74), 260 (75), 157 (100). *Anal*. Calcd. for $C_{23}H_{18}N_4S$: C, 72.22; H, 4.74; N, 14.65; S, 8.38. Found: C, 72.30; H, 4.69; N, 14.71; S, 8.30.

3-(3-benzyl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)-2-thioxo-1,3-thiazolidin-4-one (7). A mixture of compound **1** (2 g, 10 mmol) and thiocarbonyl-bis-thioglycolic acid (2.26 g, 10 mmol) was fused in an oil bath at 160 ^{o}C for 1 h. The color of the reaction mixture changed to red and after cooling the residue was trituration with petroleum ether then water. The solid formed was collected by filtration and crystallized from ethanol as red crystals. Yield 1.9 g (59%); mp 196-198 °C; ir (KBr), *v*, cm^{-1}: 3219 (NH), 2957 (CH_2), 1741 (C=O), 1590 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 10.09 (1H, s, NH), 7.33-7.20 (5H, m, Ar'H), 4.61 (2H, s, SCH_2CO), 3.96 (2H, s, CH_2Ph); ms: *m/z* (*I rel*, %): 322 [M$^+$] (14), 278 (1), 262 (99), 228 (6), 172 (7), 95 (49). *Anal*. Calcd. for $C_{12}H_{10}N_4OS_3$: C, 44.70; H, 3.13; N, 17.38; S, 29.83. Found: C, 44.61; H, 3.08; N, 17.45; S, 29.90.

***N*-(1-acetyl-3-benzyl-5-thioxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)acetamide (8)**. Compound **1** (2 g, 10 mmol) was refluxed in 20 ml acetic anhydride for 3 h. The reaction mixture was allowed to stand two days at room temperature. The crystals formed were filtered, dried and recrystallized from ethanol as white crystals. Yield 2.1 g (72%); mp 200- 202 °C; ir (KBr), *v*, cm^{-1}: 3195 (NH), 3050 (CH-aromatic), 2936 (CH- aliphatic), 1705 (C=O), 1576 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 11.14 (1H, s, NH), 7.34-7.21 (5H, s, Ar'H), 3.85 (2H, s, CH_2Ph), 2.04 (3H, s, COCH_3), 1.91 (3H, s, COCH_3); ^{13}C NMR spectrum (75 MHz, DMSO-*d6*), δ, ppm 20.42

(CH$_3$), 21.23 (CH$_3$), 28.49 (CH$_2$Ph), 122.87, 127.59, 128.30, 135. 68 (Ar-C), 160.67 (N=C-N), 162.42 (C=S)166. 25 (C=O), 167.76 (C=O) and; ms: *m/z* (*I rel*, %): 290 [M$^+$] (0.04), 248 (7), 205 (41), 190 (2), 91 (100). *Anal*. Calcd. for $C_{13}H_{14}N_4O_2S$: C, 53.78; H, 4.86; N, 19.30; S, 11.04. Found: C, 53.62; H, 4.80; N, 19.46; S, 11.10.

General procedure for the reaction of compound 1 with aromatic anhydrides. A mixture of compound **1** (2 g, 10 mmol) and an aromatic anhydride, namely, phthalic anhydride, 1,8-naphthalic anhydride and pyromellitic dianhydride (10 mmol) in 30 ml glacial acetic acid was heated under reflux and monitored using TLC for about 8 h., the starting materials had disappeared and the reaction mixture was left to cool overnight. The solid formed was filtered off, dried and crystallized from acetic acid to give **9, 10** and **11a**.

2-(3-Benzyl-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)benzoic acid (9). This compound was obtained as yellowish white crystals, Yield 2.56 g (76%); mp 222- 224 °C; ir (KBr), *ν*, cm^{-1}: 3545 (carboxylic-OH), 3057 (CH-aromatic), 2948 (CH-aliphatic), 1761 (C=O), 1578 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 14.27 (1H, s, OH), 8.09-7.21 (9H, m, Ar'H), 4.12 (2H, s, CH$_2$Ph); ^{13}C nmr (75 MHz, DMSO-*d6*), δ, ppm 28.59 (CH$_2$Ph), 122.03, 127.47, 128.48, 128.91, 133.20, 133.67, 134.22, 135. 03, 135.27, 135. 84 (Ar-C), 151.67 (N=C-N, triazole), 160.20 (N=C-N), 160.96 (N=C-S) and 166. 28 (C=O); ms: *m/z* (*I rel*, %): 336 [M$^+$] (75), 304 (58), 292 (40), 260 (19), 245 (11), 219 (25), 213 (11), 189 (78). *Anal*. Calcd. for $C_{17}H_{12}N_4O_2S$: C, 60.70; H, 3.60; N, 16.66; S, 9.53. Found: C, 60.83; H, 3.67; N, 16.54; S, 9.45.

8-(3-benzyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)naphthalene-1-carboxylic acid (10). This compound was obtained brown crystals, Yield 3.15 g (81%); mp 226- 228 °C; ir (KBr) , ν, cm^{-1}: 4495 (carboxylic–OH), 3070 (CH-aromatic), 1736 (C=O), 1581 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 14.31 (1H, s, OH), 8.57-7.89 (11H, m, Ar'H), 4.05 (2H, s, CH$_2$Ph); ms: *m/z* (*I rel*, %): 386 [M$^+$] (41), 324 (1), 290 (32), 275 (99), 249 (35), 136 (43). *Anal*. Calcd. for $C_{21}H_{14}N_4O_2S$: C, 65.27; H, 3.65; N, 14.50; S, 8.30. Found: C, 65.35; H, 3.58; N, 14.57; S, 8.22.

4,6-di(3-benzyl-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)-1,3-dicarboxylic acid (11a). This compound was obtained as yellow crystals, Yield 4.22 g (71%); mp > 300 °C; ir (KBr), *ν*, cm^{-1}: broad band at 3450 (carboxylic–OH), 3017 (CH-aromatic), 2930 (CH$_2$), 1763 (C=O), 1579 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 14.38 (2H, s, 2OH), 8.82 (1H, s, benzene-H), 7.95 (H, s, benzene-H), 7.32-7.24 (10H, m, Ar'H), 4.15 (4H, s, 2CH$_2$Ph); ^{13}C nmr (75 MHz, DMSO-*d6*), δ, ppm 29.55 (CH$_2$Ph), 120.72, 127.19, 128.58, 134.00, 134. 12, 134.82, 135. 14, 135. 38 (Ar-C), 151.71 (N=C-N, triazole), 160.91 (N=C-N), 161.35 (N=C-S) and 166. 32 (C=O); ms: *m/z* (I *rel*, %): 594 [M$^+$] (4), 554 (2), 397 (10), 340 (7), 279 (99), 193 (28). *Anal*. Calcd. for $C_{28}H_{18}N_8O_4S_2$: C, 56.56; H, 3.05; N, 18.84; S, 10.78. Found: C, 56.50; H, 3.13; N, 18.93; S, 10.68.

General procedure for the reaction of compound 1 with *N*-sulphonyloxy-pthalimide and *N*-sulphonyloxy-naphthaimide. A mixture of compound **1** (2 g, 10 mmol) and *N*-sulphonyloxy-pthalimide and/or *N*-sulphonyloxy-naphthaimide (10 mmol) in 30 ml glacial acetic acid in presence of anhydrous sodium acetate (0.82 gm, 10 mmol) was refluxed for 6 h. The reaction mixture was allowed to stand overnight at room temperature. The solid formed was filtered, washed with water, dried and crystallized from acetic acid to give **12** and/or **13,** respectively.

3-(3-Benzyl-5-mercapto-[1,2,4]triazol-4-yl)-1*H*-quinazoline-2,4-dione (12). This compound was obtained as light brown crystals, Yield 2.32 g (66%); mp 194- 196 °C; ir (KBr), *ν*, cm^{-1}: 3180- 3110 (NH's), 3057 (CH-aromatic), 2948 (CH$_2$), 1795, 1761 (C=O's),1578 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 14.26 (1H, s, NH), 10.07 (1H, s, NH), 8.10-7.18 (9H, m, Ar'H),

4.13 (2H, s, $\underline{CH_2}$Ph); ms: *m/z* (*I rel*, %): 351 [M$^+$] (49), 305 (38), 277 (24), 144 (10), 106 (43), 91 (99). *Anal*. Calcd. for $C_{17}H_{13}N_5O_2S$: C, 58.11; H, 3.73; N, 19.93; S, 9.13. Found: C, 58.21; H, 3.64; N, 19.97; S, 9.07.

9-(3-Benzyl-5-thioxo-1,5-dihydro-[1,2,4]triazol-4-yl)-7*H*-7,9-diaza-cyclohepta[*de*] naphthalene-8,10-dione (13). This compound was obtained as brown crystals, Yield 2.8 g (69%); mp 214- 216 °C; ir (KBr), *v*, cm^{-1}: 3300- 3100 (NH's), 3070- 3030 (CH-aromatic), 2905 (CH_2), 1740, 1689 (C=O's), 1585 (C=N); ^{1}H nmr (300 MHz, DMSO-*d6*), δ, ppm 13.37 (1H, s, NH), 10.72 (1H, s, NH), 8.54-7.69 (11H, m, Ar'H), 4.12 (2H, s, $\underline{CH_2}$Ph)); ^{13}C nmr (75 MHz, DMSO-*d6*), δ, ppm 28.03 ($\underline{C}H_2$Ph), 116.20, 120.72, 122.33, 127.19, 127.69, 128.02, 128.35, 128.58,133.10, 133.57, 134.22, 135. 27, 135.74, 137.92 (Ar-C), 152.07 (N=$\underline{C}$-N), 162. 36 ($\underline{C}$=O), 162.68 ($\underline{C}$=S), 166.55 ($\underline{C}$=O) and; ms: *m/z* (*I rel*, %):401 [M$^+$] (1), 384 (1), 297 (99), 256 (17), 228 (16), 152 (21). *Anal*. Calcd. for $C_{21}H_{15}N_5O_2S$: C, 62.83; H, 3.77; N, 17.45; S, 7.99. Found: C, 62.76; H, 3.80; N, 17.60; S, 7.87.

The study of biological activity. The used Bacterial strains were gram negative bacteria including *E. Coli* (ATCC 25922) and gram positive bacteria *Enterococcus faecalis* (ATCC 29212). Mueller-Hinton Agar was used as culture media (gl^{-1}) [38]: Beef extract, 3.0; Peptone, 17.5; Starch, 1.5; Agar, 17, pH= 7.3 ± 0.1. The plates were incubated at 37 ºC for 24– 48 hrs.

Paper disc technique: Antibacterial activity was determined against the above strains using the paper disc assay method [39]. Whatman number 1 filter paper disc of 6.0 mm diameter was sterilized by autoclaving for 20 min at 121 °C. The sterile discs were impregnated with 50 µl of compounds **2, 4- 13** in concentration of each (50 µg/ ml) The impregnated discs were placed on Muller-Hinton medium, suitably spaced apart and plates were incubated at 37 °C for 24- 48 hrs [40]. Chloramphenicol 30 µg/ml was used as a positive control. Diameter of the growth inhibition halos caused by the tested compounds were measured and expressed in millimeter. All the assays were carried out in triplicate.

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