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Synthesis of Some Novel N^7-tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one Compounds as Potential Antimicrobial Agents

Susan M. El-Badry and Mamdouh A. M. Taha†,*
Physical and Chemistry Department, Faculty of Education, Alexandria University, Alexandria, Egypt.
†Chemistry Department, Faculty of Science, Fayoum University, Fayoum 63514, Egypt.
**E-mail: mamdouhamtaha@yahoo.com*
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ABSTRACT. A series of new N^7-tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one derivatives **4–16** were designed and synthesized from **3** with different reagents. The newly prepared compounds were characterized by spectral data and screened for their antimicrobial activities against various bacteria and fungi strains.

Key words: Tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one, Synthesis, Structure elucidation, Biological assay

INTRODUCTION

The tetrazole nucleus of several compounds has been published of different heterocyclic rings.[1–8] Numerous biological properties have been reported for tetrazolo-heterocycles, such as being useful due to their antibacterial,[3,5,6,9] antiproliferation,[10] anticancer,[10] and anticonvulsant[11] activities. Various reviews.[12–14] dealing with the synthesis of condensed 1,2.4-triazine moiety plays a vital role in many biological activities including antiviral,[15] antihypertensive,[15,16] blood-platelet aggregation inhibitory,[16,17] analogesic,[18] and antibacterial properties,[19,20] as well as some of new anti-HIV and anticancer agents.[21] In report here high yield synthetic procedures for the preparation of the title compounds and their full characterization data.

EXPERIMENTAL

Melting points were determined in open glass capillaries on a Buchi-530 melting point apparatus an are uncorrected. Spectroscopic data were recorded on the following instruments: Infrared (IR) spectra (KBr, γ cm^{-1}) Perkin Elimer 1240 spectrophtotomer, nuclear magnetic resonance (^{1}H NMR) spectra (Chemical shift, δ ppm) varion Mercury (300 MHz) spectrometer using TMS as internal standard and electron impact. Mass spectra (El-Ms) GC-MS (QP/000EX) Shimadzu spectrometer at an ionizing voltage of 70 ev. Reaction progress and purity of the compounds wer checked by TLC, making use of Silica Gel plates F254 on Aluminum sheets. Elemental analyses were performed by the Microanalytical center of Cairo University.

N^7-Potassium salt tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 3

Compound **2**, 2 mmol was disolvesed in 20 cm^3 of abs. ethanol and treated with alcoholic potassium hydroxide solution (0.12 g, 2 mmol). The mixture was stirred for 2 h and the potassium salt **3** was filtered washed with abs. ethanol and dried, yield: 0.28 g (73%); m.p. >300 °C.

N^7-[(2-Oxopropyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 4

A mixture of (**3**, 2 mmol) and cholroacetone (2 mmol) in dimethylformanide (15 cm^3) was refluxed for 3 h. The reaction mixture was filtered under hot, concentrated and the obtained solid was crystallized from abs. ethanol, and dried, yield: 0.22 g (66%); m.p. 180–182 °C; IR (KBr): γ = 1750 (CO), 1680 (CO, aromatic), 1620 (CN) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ = 8.22 (s, 1H, CH triazine ring), 5.21 (s, 2H, CH_2), 1.62 (s, 3H, CH_3) ppm; MS: *m/z* (%) = 194 (M^+, 20). Anal. Calcd. for $C_6H_6N_6O_2$ (194): C: 37.11; H, 3.09; N, 43.29. Found: C, 37.15; H, 3.21; N, 42.99.

N^7-[(Ethoxycarbonylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 5

Compound **5** was prepared from (**3**, 2 mmol) and ethylchloroacetate (2 mmol) as just described for the preparation of 4. It was crystallized from abs. ethanol, and dried, yield: 0.29 g (76%); m.p. 151–152 °C IR (KBr): γ = 1765 (CO), 1685 (CO, aromatic), 1620 (CN) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ = 8.44 (s, 1H, CH triazine ring), 5.20 (s, 2H, CH_2), 4.21 (q, 2H, CH_2CH_3), 1.31 (t, 3H, CH_2CH_3) ppm; MS: *m/z* (%) = 225 (M^+ + 1, 30). Anal. Calcd. for $C_7H_8N_6O_3$ (224): C,

37.50; H, 3.57; N, 37.50. Found: C, 37.32; H, 4.11; N, 37.92.

N^7-[(Hydrazinocarbonylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 6

To a solution of (**5**, 1 mmol) in abs. ethanol (30 cm^3), hydrazine hydrate (1 mmol) was added and the reaction mixture was heated under stirring for 2 h. After cooling the separated product was filtered and crystallized from abs. ethanol, and dried, yield: 0.21 g (75%); m.p. 170–172 °C; IR (KBr): γ = 3310, 3270 (NH_2), 3210 (NH), 1680 (CO, aromatic), 1660 (CO, amidic), 1620 (C=N) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 10.20 (s, 1H, NH, exchangeable with D_2O), δ = 8.40 (s, 1H, CH triazine ring), 5.01 (s, 2H, CH_2) 4.40 (s, 2H, NH_2, exchangeable with D_2O) ppm; MS: *m/z* (%) = 212 (M^+ + 2, 28). Anal. Calcd. for $C_5H_6N_8O_2$ (210): C: 28.57; H, 2.85; N, 53.33. Found: C, 28.61; H, 3.02; N, 53.22.

N^7-[(3,5-Dimethylpyrazol-1-ylcarbonylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 7

A mixture of (**6**, 1 mmol) and acetylacetone (1 mmol) in abs. ethanol (15 cm^3) was heated at 90 °C on water-bath for 3 h. The reaction mixture was cooled, poured onto water and the formed precipitate was filtered and crystallized from ethanol, and dried, yield: 0.28 g (71%); m.p. 210–211 °C; ^1H NMR (DMSO-d_6): δ = 8.25 (s, 1H, CH triazine ring), 6.40 (s, 1H, CH pyrazole ring) 5.31 (s, 2H, CH_2), 2.50, 1.72 (s, 3H each, 2 CH_3) ppm. Anal. Calcd. for $C_{10}H_{10}N_8O_2$ (274): C: 43.79; H, 3.64; N, 40.87. Found: C, 44.21; H, 4.02; N, 40.44.

N^7-[(3-Methyl-5-oxopyrazolidin-1-ylcarbonylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 8

The title compound **8** was prepared from hydrazide (**6**, 1 mmol) and ethyl acetoacetate (1 mmol) as previously described for the preparation of **7**. It was crystallized from abs. ethanol, and dried yield: 0.22 g (56%); m.p. 260–262 °C; IR (KBr): γ = 1720 (CO, pyrazole ring), 1680 (CO aromatic), 1675 (CO amidic) cm^{-1}; MS: *m/z* (%) = 277 (M^+ + 1, 2.23). Anal. Calcd. for $C_9H_8N_8O_3$ (276): C: 39.13; H, 2.89; N, 40.57. Found: C, 38.66; H, 3.02; N, 40.31.

N^7-[(1-Phenylthiocarbamoylhydrazinocarbonylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 9

Compound (**6**, 1 mmol) and phenylisothiocyanate (1 mmol) in abs. ethanol was heated under reflux for 1 h. After cooling the precipitated was collected and crystallized from abs. ethanol, and dried, yield: 0.35 g (72%), m.p. 200–202 °C; IR (KBr): γ = 3280, 3210, 3108 (3 NH), 1690 (CO, triazine ring), 1670 (CO, side chain) and 1180 (CS) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 11.94, 11.82, 11.64 (3s, 3NH, exchangeable with D_2O), 8.30 (s, 1H, CH triazine ring), 7.60–7.20 (m, 5H, *A*rH), 5.20 (s, 2H, CH_2) ppm. MS: *m/z* (%) = 346 (M^+ + 1, 11), 345 (M^+, 7). Anal. Calcd. for $C_{12}H_{11}N_9O_2S$ (345): C: 41.73; H, 3.18; N, 36.52. Found: C, 42.22; H, 3.52; N, 36.41.

N^7-[(-5-Thioxo-4-phenyl-4*H*-1,2,4-triazol-3-ylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 10

The thiocarbamate (**9**, 1 mmol) was refluxed in (15 cm^3) of sodium hydroxide (0.34 g) solution for 2 h, filtered after coohing and acidified with 2 N hydrochloric acid. The precipitated of the crude product was filtered, washed several times with cold water and crystallized from abs. ethanol, and dried, yield: 0.20 g (71%); m.p. 215–217 °C; IR (KBr): γ = 3230 (NH), 1685 (CO, aromatic), 1200 (CS) cm^{-1}, ^1H NMR (DMSO-d_6): δ = 10.82 (s, 1H, NH, exchangeable with D_2O), 8.25 (s, 1H, CH triazine ring), 7.50–7.20 (m, 5H, *A*rH), 5.10 (s, 2H, CH_2) ppm; MS: *m/z* (%) = 327 (M^+, 23). Anal. Calcd. for $C_{12}H_9N_9OS$ (327): C: 44.03; H, 2.75; N, 38.53. Found: C, 43.98; H, 3.21; N, 38.67.

N^7-[(5-Phenylamino-1,3,4-thiadiazol-2-ylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 11

To an ice-cold stirred solution of thiocarbamate (**9** 1 mmol) in abs. ethanol (10 cm^3), concentrated sulphuric acid (10 cm^3), was added over a period of 1 h, the strirring was maintained at ambient temperature for an additional for hours. Then, the reaction mixture was poured onto ice-water. The solid was filtered off and recrystallized from abs. ethanol dried, yield: 0.19 g (67%); m.p. 190–192 °C. IR (KBr): γ = 3187 (NH) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 10.22 (s, 1H, NH, exchangeable with D_2O), 8.62 (s, 1H, CH triazine ring), 5.31 (s, 2H, CH_2) ppm; MS: m/z(%) = 327 (M^+, 10). Anal. Calcd. for $C_{12}H_9N_9OS$ (327): C: 44.03; H, 2.75; N, 38.53. Found: C, 44.07; H, 2.66; N, 38.22.

General Procedure for the Synthesis of Arylbenzylidenes 12a–c

A mixture of the acetic acid hydrazide (**6**, 1 mmol) and an appropriate aromatic aldehyde (1 mmol) namely, benzaldehyde, p-methylbenzaldehyde or p-nitrobenzaldehyde was refluxed in 20 cm^3 abs. ethanol for 3 h. After cooling the reparated solid was collected by filtration, dried and crystallized from absolute ethanol. The physico-chemical and spectral data of **12a–c** the following:

N^7-[(2-Benzylideneacetohydrazide)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 12a:

Yield: 0.33 g (78%); m.p.: 175–177 °C; IR (KBr): γ =

3188 (NH), 1680 (CO, aromatic), 1665 (CO, amidic), 1615 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6): δ = 9.30 (s, 1H, NH, exchangeable with D_2O), 9.22 (s, 1H, CH=N), 8.11–7.20 (m, 6H, CH triazine ring + 5 *ArH*), 5.10 (s, 2H, CH_2) ppm.; MS: *m/z* (%) = 299 (M^+ + 1, 17). Anal. Calcd. for $C_{12}H_{10}N_8O_2$ (298): C: 48.32; H, 3.35; N, 37.58. Found: C, 47.81; H, 3.41; N, 37.88.

N^7-[(2-p-Methylbenzylideneacetohydrazide)]tetrazolo [5,1-*f*]-1,2,4-triazin-8-(7H)-one 12b:

Yield: 0.22 g (52%); m.p. 153–155 °C; ^1H NMR (DMSO-d_6): δ = 9.35 (s, 1H, NH, exchangeable with D_2O), 9.20 (s, 1H, CH=N), 8.20–7.97 (m, 5H, CH + 4 *ArH*), 7.12 (s, 1H, CH triazine ring) 5.20 (s, 2H, CH_2), 2.33 (s, 3H, CH_3) ppm; MS: *m/z* (%) = 312 (M^+, 12). Anal. Calcd. for $C_{13}H_{12}N_8O_2$ (312): C: 50.00; H, 3.84; N, 35.89. Found: C, 49.81; H, 4.22; N, 36.32.

N^7-[(2-p-Nitrobenzylideneacetohydrazide)]tetrazolo [5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 12c:

Yield: 0.35 g (83%); m.p. 178–180 °C; IR (KBr): γ = 3180 (NH), 1690 (CO, aromatic), 1660 (CO, amidic), 1620 (C=N) cm^{-1}; MS: *m/z* (%) = 344 (M^++1, 10). Anal. Calcd. for $C_{12}H_9N_9O_4$ (343): C: 41.98; H, 2.62; N, 36.73. Found: C, 42.22; H, 2.55; N, 36.51.

General Procedure for the Synthesis of 5-Aryl-1,3,4-oxadiazoles 13a–c

A mixture of the appropriate (**12a–c**, 1 mmol) and acetic anhydride (15 cm^3) were heated under reflux for 4 h. The reaction mixture was cooled, poured onto ice-water and allowed to stand at ambient temperature. The solid product formed was collected and recrystallized from abs. ethanol to afford the product. The physico-chemical and spectral data of **13a–c** the following:

N^7-[(4-Acetyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-ylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 13a:

Yield: 0.27 g (79%); m.p. 167–169 °C; IR (KBr): γ = 1760 (CO), 1680 (CO, aromatic), 1620 (C=N) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 8.16–7.15 (m, 6 H, CH triazine ring + 5 *ArH*), 5.12 (s, 2H, CH_2), 2.08 (s, 1H, CH oxadiazole ring), 2.29 (s, 3H, CH_3) ppm; MS: *m/z* (%) = 340 (M^+, 7). Anal. Calcd. for $C_{14}H_{12}N_8O_3$ (340): C: 49.41; H, 3.52; N, 32.94. Found: C, 49.24; H, 3.11; N, 33.21.

N^7-[(4-Acetyl-5-p-methylphenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl methyl)]tetrazolo [5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 13b:

Yield: 0.19 g (55%); m.p.: 140–142 °C; IR (KBr): γ = 1760 (CO), 1680 (CO, aromatic), 1625 (C=N) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 8.12–7.30 (m, 5H, CH triazine ring + 4 *ArH*), 5.14 (2, 2H, CH_2), 2.10 (s, 1H, CH oxadiazole ring), 2.30, 2.12, (2s, 3H each, $2CH_3$) ppm; MS: *m/z* (%) = 355 (M^+ + 1, 10). Anal. Calcd. for $C_{15}H_{14}N_8O_3$ (354): C: 50.84; H, 3.95; N, 31.63. Found: C, 51.22; H, 4.24; N, 31.42.

N^7-[(4-Acetyl-5-p-nitrophenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl-methyl)]tetrazolo [5,1-*f*]-1,2,4-triazin-8-7*H*)-one 13c:

Yield: 0.32 g (86%); m.p.: 162–164 °C; IR (KBr): γ = 1740 (CO), 1690 (CO, aromatic), 1620 (C=N) cm^{-1}; MS: *m/z* (%) = 385 M^+, 22). Anal. Calcd. for $C_{14}H_{11}N_9O_5$ (385): C: 43.63; H, 2.85; N, 32.72. Found: C, 44.01; H, 3.11; N, 32.42.

N^7-[(2-Thioxo-2,3-dihydro-1,3,4-oxadiazol-5-ylmethyl)] tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 14

To a mixture of (**6**, 1 mmol) in abs. ethanol (15 cm^3) was added of potassium hydroxide (0.10 g) in abs. ethanol (20 cm^3). Then, carbon disulfide (10 cm^3) was added portion wise and the reaction mixture was refluxed till no color of hydrogen sulphide evolved. The solid prouduct obtained after cooling and acidification with dilute hydrochloric acid was collected by filteration and recrystallized from abs. ethanol (yellow color), dried, yield: 0.27 g (75%); m.p. 152–154 °C, IR (KBr): γ = 3295 (NH), 1690 (CO, aromatic), 1220 (CS) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 10.86 (s, 1H, NH, exchangeable with D_2O), 8.50 (s, 1H, CH triazine ring), 5.29 (s, 2H, CH_2) ppm; MS: *m/z* (%) = 252 (M^+, 12). Anal. Calcd. for $C_6H_4N_8OS$ (252): C: 28.57; H, 1.58; N, 44.44. Found: C, 28.34; H, 2.01; N, 44.49.

N^7-[(4-Amino-5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-ylmethyl)]tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 15

A mixture of (**14**, 1 mmol) and hydrazine hydrate (1 mmol) in 15 cm^3 abs. ethanol was refluxed for 2 h. The solvents were removed under reduced pressure, the residue was washed with ether then recrystallized from abs. ethanol, and dried, yield: 0.18 g (58%), m.p. 144–146 °C; IR (KBr): γ = 3300, 3290 (NH_2), 3230 (NH), 1680 (CO, aromatic) cm^{-1}; ^1H NMR (DMSO-d_6): *d* = 11.20 (s, 1H, NH exchangeable with D_2O), 8.30 (s, 1H, CH triazine ring), 5.29 (2, 2H, NH_2, exchangeable with D_2O), 4.95 (s, 2H, CH_2) ppm; MS: *m/z* (%) = 266 (M^+, 10). Anal. Calcd. for $C_6H_6N_{10}OS$ (266): C: 27.06; H, 2.25; N, 52.63. Found: C, 27.22; H, 2.44; N, 52.41.

General Procedure for the Synthesis of Schiff's Bases 16a–c

A mixture of (**15**, 1 mmol) and an appropriate aromatic aldchyde (1 mmol) namely, benzenaldehyde, p-methylbenzenaldehy, or p-nitrobenzenaldehyde (1 mmol) was refluxed in 20 cm^3 abs. ethanol for 3 h. After cooling the separated solid was collected by filteration, dried and crystallized from abs. ethanol. The physico-chemical and spectra data of **16a–c** the following:

N^7-[(4-Benzylideneamino)-5-thioxo)-4,5-dihydro-1*H*-1,2,4-triazol-3-yl-methyl)]-tetrazolo-[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 16a:

Yield: 0.29 g (74%); m.p. 160–162 °C; IR (KBr): γ = 3195 (NH), 1675 (CO, aromatic) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ = 10.95 (s, 1H, NH, exchangeable with D_2O), 9.51 (s, 1H, CH=N), 8.52–8.30 (m, 5H, *ArH*), 8.20 (s, 1H, CH triazine ring), 4.85 (s, 2H, CH_2) ppm; Ms: *m/z* (%) = 355 (M^+ + 1, 13). Anal. Calcd. for $C_{13}H_{10}N_{10}OS$ (354): C: 44.06; H, 2.82; N, 39.54. Found: C, 45.21; H, 3.01; N, 39.42.

N^7-[(4-p-Methylbenzylidenoamino)-5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl-methyl)]-tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 16b:

Yield: 0.24 g (58%); m.p. 135–137 °C; IR (KBr): γ = 3220 (NH), 1680 (CO, aromatic) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ = 10.90 (s, 1H, NH, exchangeable with D_2O), 8.90 (s, 1H, CH=N), 8.50–8.15 (m, 4H, *ArH*), 7.30 (s, 1H, CH triazine ring), 4.79 (s, 2H, CH_2), 2015 (s, 3H, CH_3); MS: *m/z* (%) = 368 (M^+, 7). Anal. Calcd. for $C_{14}H_{12}N_{10}OS$ (368): C: 45.65; H, 3.26; N, 38.04. Found: C, 45.71; H, 3.42; N, 38.21.

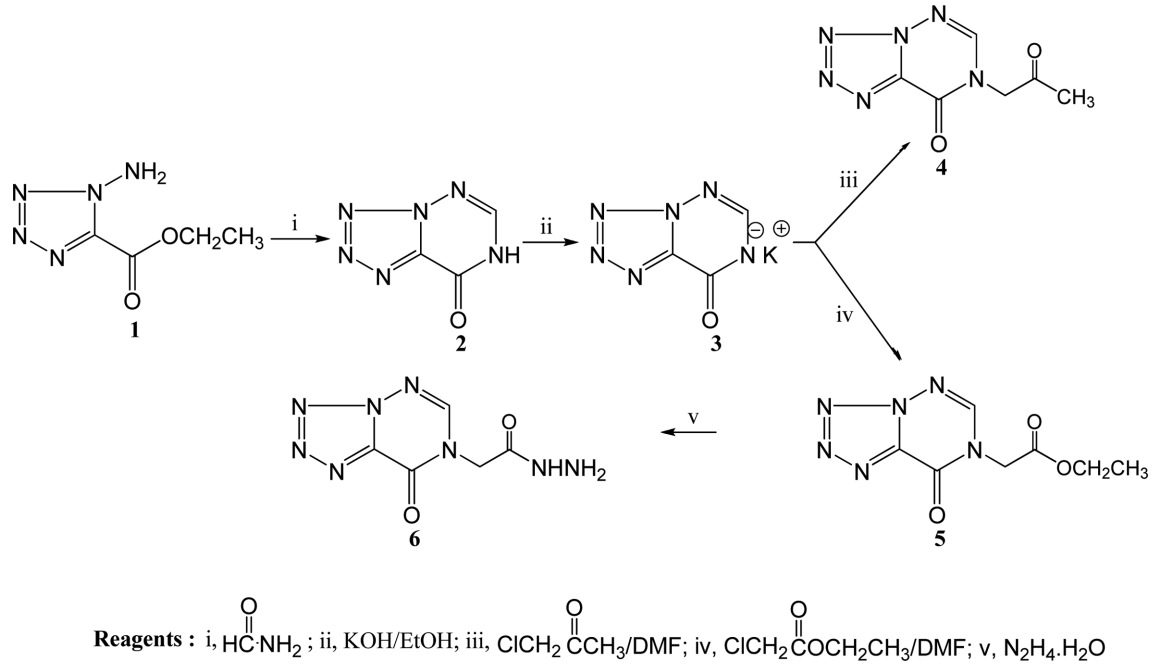
N^7-[(4-p-Nitrobenzylideneamino)-5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl-methyl)]-tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one 16c:

Yield: 0.39 g (86%); m.p. 177–178 °C; IR (KBr): γ = 3240 (NH), 1690 (CO, aromatic) cm^{-1}; MS: *m/z* (%) = 400 (M^+ + 1, 12). Anal. Calcd. for $C_{13}H_9N_{11}O_3S$ (399): C, 39.09; H, 2.25; N, 38.59. Found: C, 39.22; H, 2.44; N, 38.24.

RESULTS AND DISCUSSION

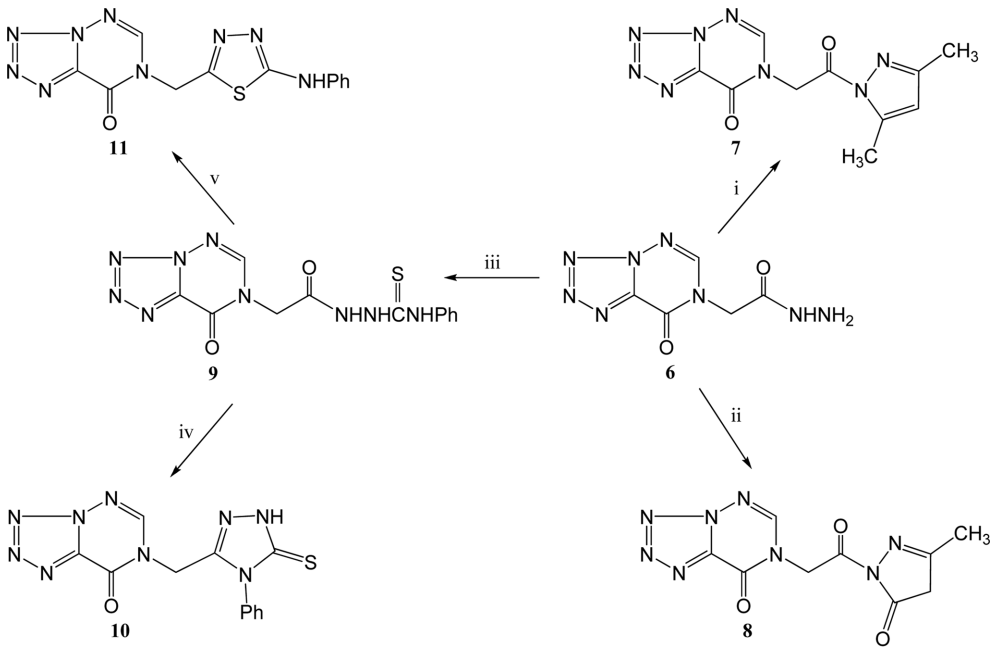
The structure of the prepared compounds was elucidated using IR, ^{1}H NMR, and mass spectroscopic methods besides elemental analyses. The pathways leading to the products obtained have been depicted in *Schemes* 1, 2, and 3.

Ethyl 1-aminotetrazole-5-carboxylate [2] (**1**) was reacted with formamide yielded tetrazolo[5,1-*f*]-1,2,4-triazin-8-(7*H*)-one [2] (**2**) which upon treatment with potassium hydroxide afforded the potassium salt **3**. Reaction of **3** with chloroacetone and ethyl chloroacetate in dimethylformamide afforded N^7-oxopropyl and N^7-ethyloxycarbonyl-methyl derivatives **4** and **5**, respectively. N^7-Hydrazinocarbonylmethyl **6** was synthesized from the ester **5** with hydrazine hydrate in ethanol. The hydrazide **6** revealed



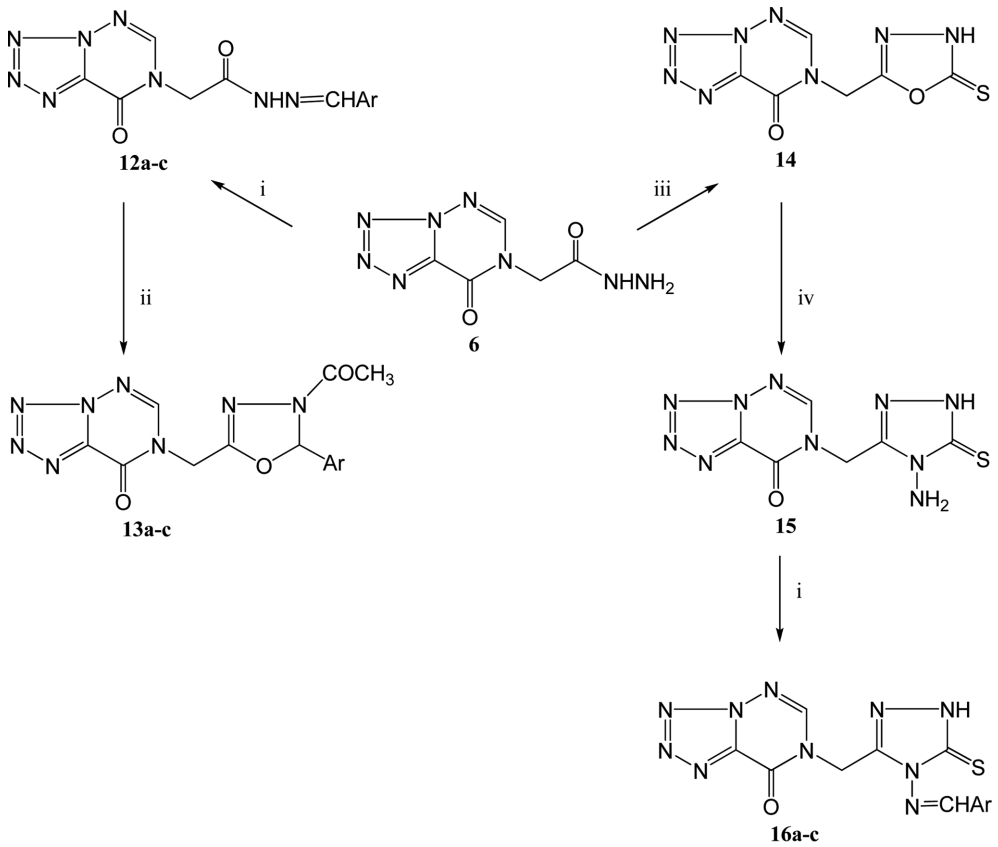
Reagents : i, $HC(=O)NH_2$; ii, KOH/EtOH; iii, $ClCH_2C(=O)CH_3$/DMF; iv, $ClCH_2C(=O)OCH_2CH_3$/DMF; v, $N_2H_4.H_2O$

***Scheme* 1.**



Reagents: i, $(CH_3CO)_2CH_2$; ii, $CH_3COCH_2COCH_2CH_3$; iii, PhNCS; iv, NaOH/HCl; v, H_2SO_4

***Scheme* 2.**



Reagents : i, ArCHO; ii, $(CH_3CO)_2O$; iii, CS_2/KOH; iv, $N_2H_4.H_2O$

Ar = a = C_6H_5; b = C_6H_4-CH_3(p) ; c = C_6H_4-NO_2(p)

***Scheme* 3.**

absorption bands at γ = 3310, 3270, 3210, 1680 and 1660 cm^{-1} corresponding to $NHNH_2$ and two CO groups. The ^1H NMR spectrum of compound **6** showed δ = 10.20 (s, 1H, NH exchangeable with D_2O), 8.40 (s, 1H, CH triazine ring), 5.10 (s, 2H, CH_2CO) and 4.40 (s, 2H, NH_2 exchangeable with D_2O) ppm.

Reaction of the acid hydrazide **6** with acetylacetone and ethyl acetoacetate gave pyrazolyl and pyrazolidinyl structures **7** and **8**, respectively. The ^1H NMR spectrum of **7** exhibited, CH pyrazolyl ring and two methyl signals. The IR spectrum of **8** showed characteristic absorption bands at γ =1720, 1680 and 1675 cm^{-1} corresponding to three carbonyl amides of pyrazole, triazine and side chain, respectively.

Compound **6** was refluxed with phenylisothiocyanate, the expected N^7-phenyl-thiocarbamoylhydrazinocarbonylmethyl derivative **9** was resulted, which ^1H NMR spectrum contained characteristic signals to three NH exchangeable with D_2O and aromatic protons. Alkaline cyclization of the thiocarbamate **9** using sodium hydroxide solution furnished the corresponding 1,2,4-triazolyl nucleus **10**, which IR region displayed the disappearance of the two NH and CO absorptions in side chain. The mass spectrum of **10** revealed the molecular ion peak at *m/z* = 327. Also, the thiosemicarbazide **9** was cyclized with cold concentrated sulphuric acid caused in the formation of the corresponding 1,3,4-thiadiazolyl derivative **11**. The ^1H NMR spectrum of compound **11** showed signals for assigned NH (exchangeable with D_2O), CH (triazine ring), aromatic protons, and CH_2 group.

Additionally, the condensation of the acetic acid hydrazide **6** with variety of aromatic aldehydes namely, benzaldehyde, p-methylbenzaldehyde and p-nitrobenzaldehyde in absolute ethanol leading to the benzylidenes **12a–c**. The ^1H NMR spectra of the latter products showed the methylidene proton signals and the correct mass spectra. Condensation cyclization of benzylidene structures **12a–c** with acetic anhydride afforded the 4-acetyl-5-aryl-1,3,4-oxadiazole congeners **13a–c**. The IR spectra of the latter compounds showed the presence of the absorption bands for carbonyl groups at 1760 or 1740 cm^{-1} and devoid any bands corresponding NH groups and lacked any NH signals in ^1H NMR spectra.

Cyclocondensation reaction of **6** with carbon disulfide in alcoholic potassium hydroxide, by heating under reflux yielded 1,3,4-oxadiazolyl derivative **14**, which showed in IR spectrum NH, CO (aromatic) and CS absorptions and lacked $NHNH_2$ and CO (amidic) absorptions characteristic of the parent compound **6**. The mass spectrum of **14** revealed a peak corresponding to its molecular ion peak at *m/z* = 252. The structure of **14** was inferred chemically its reaction with hydrazine hydrate afforded the amino-1,2,4-triazole derivative **15**. The IR spectrum of **15** showed a characteristic absorption bands corresponding to NH_2, NH and CO groups, whereas its mass spectrum showed a peak exhibited to its molecular ion at *m/z* = 266.

Furthermore, condensation of **15** with various of aromatic aldehydes namely, benzaldehyde, p-methylbenzaldelye and p-nitrobenzaldehyde in absolute ethanol afforded the corresponding the expected Schiff's bases **16a–c** which possessed IR absorption characteristic of NH group and lacked NH_2 group. The ^1H NMR spectra of **16a–c** revealed signals for assigned NH (exchangeable with D_2O), methine (CH=N), aromatic protons, CH (triazine ring) and CH_2 group.

The antimicrobial activity of the newly synthesized compounds **4–6**, **8–10**, **12a,c**, **13a,c** and **14–16a–c** were evaluated

***Table* 1.** Minimal inhibitory concentration (*MIC*/μg cm^{-3}) of compounds **4–6, 8–10, 12a,c, 13a,c** and **14–16a,c**

Compound	*B. subtitis*	*S. aureus*	*K. pneumoniae*	*E. coli*	*A. niger*	*C. albican*
4	100	>200	100	>200	100	100
5	50	100	100	100	100	100
6	100	50	100	50	100	25
8	100	50	100	50	100	25
9	>200	50	100	100	100	100
10	100	100	>200	100	100	100
12a	100	100	100	100	100	100
12c	100	>200	100	>200	100	100
13a	50	50	100	50	100	25
13c	100	100	50	100	25	100
14	100	50	50	50	25	100
16a	100	100	100	100	100	100
16c	50	100	100	100	100	100
Ampicillin	12.5	12.5	25	25	–	–
Clotrimazole	–	–	–	–	12.5	12.5

against Gram-positive (*Bacillus subtitis* and *Staphylococcus aureus*) and Gram-negative (*Klebsiella pneumoniae* and *Escherichia coli*) bacteria strains and (*Aspergillums niger* and *Condida albican*) fungi strains. The minimal inhibitory concentration (*MIC*/mg) cm^{-3} [22] is displayed in *Table* 1, showing that **5**, **13a** and **16c** exhibit an antimicrobial activity against *B. substitis* (25%); **6**, **8**, **9**, **13a** and **14** against *S. aureus* (25%); **13c** and **14** against *K. pneumoniae* (50%); **6**, **8**, **13a** and **14** against *E. coil* (50%) comparable to that of ampicillin. Furthermore, **13c**, **14**, possessed an antimycotic activity against *A. niger* (50%) and **6**, **8** and **13a** against *C. albican* (50%) cormparable to that of clotrimazole.

ANTIMICROBIAL SCREENING

Solutions of the test compounds, ampicillin trihydrate and clotrimazole were prepared in *DMSO* at a concentration of 100 μg/cm^3. Twofold dilution of the compounds were prepared (800, 400, ….. 6.25 g/cm^3). The microorganism suspensions at 10^6 Colony Formin Unit 1 cm^3 (*CFU*/cm^3) concentration were inoculate to the corresponding wells. Plates were incubated at 36 °C for 24 to 28 h the incubation chamber. The minimal inhibitory concentration (*MIC*) were determined. Controls with *DMSO* and infected media were also investigated.

CONCLUSION

In this paper, the synthesis of some novel N^7-tetrazolo [5,1-*f*]-1,2,4-triazin-8-(7*H*)-one compounds **4**–**16** through potassium salt **3** are described. The antimicrobial activities against various bacteria and fungi strains are screened.

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