Journal of Medicinal and Chemical Sciences 6 (2023) 1537-1547

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Synthesis, Characterization and Study Biological Activity of Some 1,2,4-Triazin Heterocyclic Derivatives

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ARTICLE INFO

Article History

Receive: 2022-08-05
Received in revised: 2022-09-29
Accepted: 2022-11-18
Manuscript ID: JMCS-2209-1786
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatimah Ramezani
Editor who approved publication:
Dr. Yasser Fakri Mustafa

DOI:10.26655/JMCHEMSCI.2023.7.6

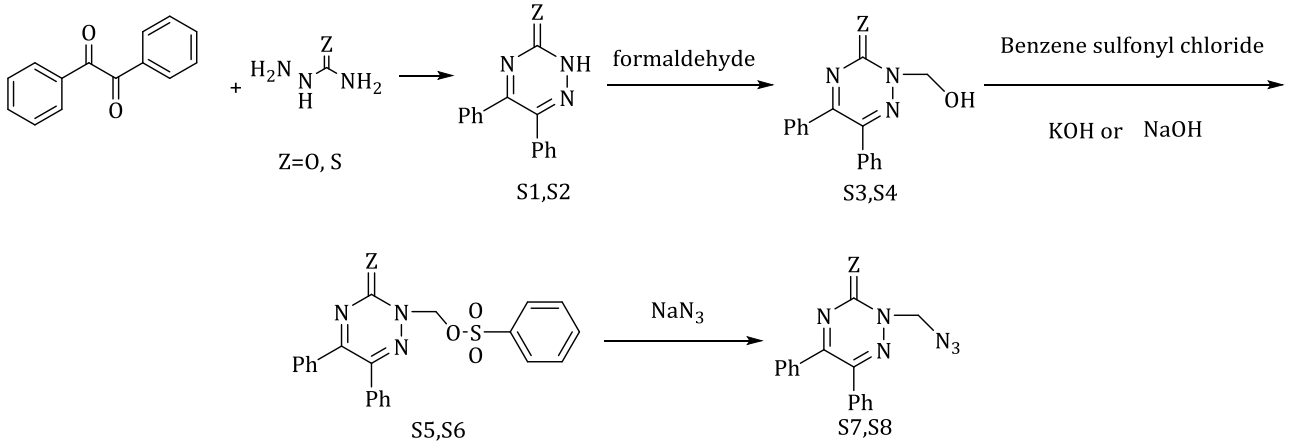
KEYWORDS

Heterocyclic compounds
Benzyl
Triazine derivatives
Quinazoline
Triazole
Tetrazole
Amidazoldine

ABSTRACT

A series of some new heterocyclic compounds containing triazin derivatives have been synthesized in many steps sequence. Triazine derivatives were prepared through reacting benzil with semicarbazide or thiosemicarbazide to form 5,6-diphenyl-1,2,4-triazin-2(3*H*)one,5,6-diphenyl-1,2,4-triazine-2(3*H*)thione, respectively. A hydroxymethylation reaction has been made to the amide group. The hydroxyl group was replaced by azide group. A different substituted triazine rings have been formed using different reagents. The structures of the newly prepared derivatives were identified through more than one technique like (FT-IR, ^{1}H-NMR, and ^{13}C-NMR) for all derivatives.

GRAPHICAL ABSTRACT



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Introduction

Heterocyclic composites play a crucial role in biochemical processes because the side groups of the most prevalent and significant components of living cells are based on heterocyclic [1]. Heterocyclic units can be found in large number of compounds which display manufacturing requests. The activity of the most compounds is mostly dependent on their molecular buildings [2-9]. As an importance of growth of systems suitable for the meeting of molecules containing heterocyclic models continues to be a focus for the attention of both the learning and manufacturing communities [10]. Furthermore, N-heterocyclic compounds exhibit biological properties such herbicidal activity, anti-inflammatory, antibacterial, anti-oxidative, anti-allergic, anti-convulsant, enzyme inhibitors, herbicidal activity, anti-HIV, anti-diabetic, anticancer activity and insecticidal agents [11, 12]. Treatment of infectious diseases brought on by viruses is a challenge regardless of the existence of several antiviral drugs. 1,2,4-triazines and their fused derivatives important in medicinal chemistry due to their high biological activity. Triazine is an aromatic heterocyclic ring analog to benzene in which three carbon atoms are substituted with nitrogen, giving it the chemical formula $C_3H_3N_3$ [13]. According to the location of the nitrogen atoms; namely, 1,2,3-triazine(I), 1,2,4-triazine(II), and 1,3,5-triazine(III) are the three isomeric forms. Due to their great biological activity, 1,2,4-triazines and their fused derivatives are significant compounds in medicinal chemistry [14]. Since compounds with a 1,2,4-triazine nucleus have received the greatest attention in term of their pharmacological and therapeutic potential, some of their derivatives are currently in the final stages of clinical research [15, 16].

Materials and Methods

The entire chemicals were purchased from BDH, Sigma Aldrich, CDH, and Merck. Melting point determinations were performed by the open capillary method using a SMP30 melting point apparatus and are reported uncorrected. The FT-IR spectra (KBr-discs) were recorded with IRAFFINITY-1CE Shimadzu spectrometer. ^{1}H-NMR spectra were recorded on a Jeol-500HZ-NMR spectrophotometer operating at 500MHz for ^{1}H-measurements.

*Synthesis of 5,6-diphenyl-1,2,4-triazine-3-(2H)-one (**S1**) 5 ,6-diphenyl-1,2,4-triazine-3-(2H)-thione (**S2**) [17]*

Benzil (0.5 mmol, 0.10 g) was combined with semicarbazide or thiosemicarbazide (1 mmol, 0.11 g, 0.09 g), respectively, in ethanol for 30 hours. The mixture was refluxed. Under vacuum, the solvent was extracted. These were extracted with dichloromethane, and then the organic layer was washed three times with water (3 × 10 mL), dried over magnesium sulphate, filtered, and the solvent was removed under vacuum to produce the crude products, recrystallization from ethanol.

*Compounds **S1***

IR (KBr) (ν_{max}/ cm^{-1}): 1645(C=O, amide), 3198 (N-H, str), 1635(C=N), 1558 (C=C), 3000 (C-H aromatic), 12000 (N-N), 1026 (C-C), 1369 (C-N). ^{1}H-NMR (500 MHz, DMSO): δ 10.88 (s, H, NH), 7.18-8.38 (m, 5H, C-H aromatic), 13.56 (s, 1H, OH). ^{13}C-NMR (125 MHz, DMSO): δ 153.88 (C=O amide), 128.5-136.23 (Car), 166.88 (C=N).

*Compounds **S2***

IR (KBr) (ν_{max}/ cm^{-1}): 3126 (N-H Str), 1537 (C=C), 1367 (C=N), 1556 (C=S), 3000 (C-H aromatic), 1217 (N-N), 1057 (C-C), 1367(C-N). ^{1}H-NMR (500 MHz, DMSO): δ 10.05 (s, H, NH), 7.19-7.57 (m, 5H, C-H aromatic), 12.13 (s, 1H, SH). ^{13}C-NMR (125 MHz, DMSO): δ 184.22(C-S), 126.84-142.22 (Car), 162.80 (C=N).

*Synthesis of 2-(hydroxy methyl)-5,6-di phenyl-1,2,4-triazin-3(2H)–one (**S3**), 2-(hydroxymethyl)-5,6-di phenyl-1,2,4-triazin-3(2H)-thione (**S4**) [18]*

Equal volume of 37% aqueous solution of formaldehyde was added to a suspension of (1 mmol, 0.24 g, 0.26 g) of compound **S1** and **S2**, respectively, in 3-4 mL of EtOH and the mixture was refluxed during 3-5 min. The product which was crystallized from the formed light red solution was filtered off, washed with cold EtOH

and dried. Analytical-pure compounds were obtained.

*Compound **S3***

IR (KBr) (ν_{max}/ cm^{-1}): 3385 (O-H Stretch), 1658 (C=O, amide), 2900 (C-H alpha), 1084 (C-O, Str), 3000 (C-H aromatic), 1556 (C=C), 1369 (C-N), 1200 (N-N), 1000 (C-C), 1658 (C=N). ^{1}H-NMR (500 MHz, DMSO): δ 5.42 (t, 2H, N-CH_2), 7.09-7.46 (m, 5H, CH aromatic), 4.52 (s, 1H, OH). ^{13}C-NMR (125 MHz, DMSO): δ 155.55 (C=O amide), 75.62 (CH_2 aliphatic), 166.55 (C=N), 128.55-131.49 (C aromatic).

*Compound **S4***

IR (KBr) (ν_{max}/ cm^{-1}): 3360 (O-H, Str), 1057 (C-O, Str), 2978 (C-H alpha), 1489 (C=C), 1599 (C=S), 1114 (N-N), 3061 (C-H aromatic), 1340 (C-N), 1085 (C-C), 1599 (C=N). ^{1}H-NMR (500 MHz, DMSO): δ 4.78 (s, H, OH), 7.20-7.95 (m, 5H, CH aromatic), 5.82 (t, 2H, N-CH_2). ^{13}C-NMR (125 MHz, DMSO): δ 179.59 (C=S), 80.67 (N-CH_2), 126.84-134.79 (C aromatic), 158.59 (C=N).

*Synthesis of (3-oxo-5,6-diphenyl-1,2,4-triazin-2(3H)-yl)methyl benzenesulfonate (**S5**), (5,6-diphenyl-3-thioxo-1,2,4-triazin-2(3H)-yl)methyl benzenesulfonate (**S6**) [18]*

Benzene sulfonyl chloride (5.57 mmol, 0.97 g) was gradually added to a compound (**S3, S4**) (1.85 mmol, 0.50 g, 0.52 g), respectively, in 15 mL of pyridine while stirring at 0 °C. The solution was diluted with 6N. HCl after stirring at 0 °C for 10 hours. With the aid of $CHCl_3$, the reaction mixture was extracted. The extract was washed in brine and dried over anhydrous $MgSO_4$. After the solvent evaporation, chromatography on silica gel (eluent: $CHCl_3$) gave the product.

*Compound **S5***

IR (KBr) (ν_{max}/ cm^{-1}): 1653 (C=O, amide), 1182 (S=O), 2928 (C-H, str), 1050 (C-O), 1489 (C=C), 1691 (C=N), 3063 (C-H aromatic), 1200 (N-N), 1100 (C-C), 1300 (C-N), 1631 (C-S). ^{1}H-NMR (500 MHz, DMSO): δ 5.40 (t, 2H, N-CH_2), 6.53-9.25 (m, 5H, C-H aromatic). C^{13}-NMR (125 MHz, DMSO): δ 158.12 (C=O amide), 77.67 (N-CH_2), 167.59 (C=N), 126.84-134.59 (C aromatic).

*Compound **S6***

IR (KBr) (ν_{max}/ cm^{-1}): 1182 (C-O, Str), 2845 (C-H stretch), 1483 (C=C), 1662 (C=N), 3059 (C-H aromatic), 1125 (S=O), 1506 (C=S), 1097 (C-C), 1211 (N-N), 1330 (C-N). ^{1}H-NMR (500 MHz, DMSO): δ 7.85-9.42 (m, 5H, CH aromatic), 5.53 (t, 2H, N-CH_2).

*Synthesis of 2-(azidomethyl)-5,6-diphenyl-1,2,4-triazin-3(2H)-one (**S7**), 2-(azidomethyl)-5,6-diphenyl-1,2,4-triazine-3(2H)-thione (**S8**) [19]*

The compound (**S5** and **S6**) (1.1 mmol, 0.45 g, 0.477 g), respectively was dissolved in dry DMF (5 mL) and added to a solution of dry DMF (5 mL) and NaN_3 (7.66 mmol, 0.48 g). Prior to use, the solvent has been dried 1 hour on molecular sieves under Argon. The reaction was heated to 100 °C while being stirred beneath a blast shield and heating lasted for 6 hours at 100 °C. The precipitate was removed by filtration through a plug of silica under suction after cooling to room temperature and the solvent was evaporated to dryness. The solid was filtered.

*Compound **S7***

IR (KBr) (ν_{max}/ cm^{-1}): 2123 (N=N=N), 1658 (C=O, amide), 2900 (C-H, str), 1500 (C=C), 1300 (C-N), 3086 (C-H aromatic), 1215 (N-N), 1000 (C-C), 1674 (C=N). ^{1}H-NMR (500 MHz, DMSO): δ 5.77 (S, 2H, N-CH_2), 7.28-7.34 (m, 5H, CH aromatic).

*Compound **S8***

IR (KBr) (ν_{max}/ cm^{-1}): 2114 (N=N=N), 2900 (C-H str), 1500 (C=C), 1301 (C-N), 3000 (C-H ar), 1523 (C=S), 1100 (C-C), 1689 (C=N), 1100(N-N). ^{1}H-NMR (500 MHz, DMSO): δ 5.89 (s, 2H, N-CH_2), 7.45-7.86 (m, 5H, CH aromatic).

*Synthesis of 2-((4-butyl-1H-1,2,3-triazol-1-yl)methyl)-5,6-diphenyl-1,2,4-triazin-3(2H)-one (**S27**), 2-((4-butyl-1H-1,2,3-triazol-1-yl)methyl)-5,6-diphenyl-1,2,4-triazine-3(2H)-thione (**S28**), N-((1-((3-oxo-5,6-diphenyl-1,2,4-triazin-2(3H)-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)-5-((3aR,4R,6aS)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide (**S31**), N-((1-((5,6-diphenyl-3-thioxo-1,2,4-triazin-2(3H)-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)-5-((3aR,4R,6aS)-2-*

*oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide (**S32**) , 2-amino-3-(1-((3-oxo-5,6-diphenyl-1,2,4-triazin-2(3H)-yl)methyl)-1H-1,2,3-triazol-4-yl)propanoic acid (**S33**), 2-amino-3-(1-((5,6-diphenyl-3-thioxo-1,2,4-triazin-2(3H)-yl)methyl)-1H-1,2,3-triazol-4-yl)propanoic acid (**S34**) [20, 21]*

To the mixture of benzyl azide (**S7**, **S8**) (1.00 mmol, 0.30 g, 0.32 g), respectively, and hex-l-yne (1.1 mmol, 0.09 g), biotin alkyne (1.1 mmol, 0.58 g), propargyl-glycine (1.1 mmol, 0.12 g), respectively in THF/water (1:1) were added $CuSO_4$-$5H_2O$ (5 mL, 0.2 mole, 0.04 g) and sodium ascorbate (0.2 mole, 0.03 g) at room temperature. The reaction mixture was stirred at room temperature for 5-6 hours. After completion of the reaction which was monitored by TLC, the reaction mixture was extracted with ethyl acetate (210 mL) and water (5 mL). The organic layer was separated and dried over anhydrous Na_2SO_4, concentrated under reduced pressure and the remaining material was then flash column chromatography purified to provide the desired tri-azole.

*Compound **S27***

IR (KBr) (ν_{max}/ cm^{-1}): 1651 (C=O, amide), 2870 (C-H, str), 1550 (C=C), 1689 (C=N), 2953 (C-H aromatic), 1111 (N-N), 1000 (C-C), 1462 (C-N). ^{1}H-NMR (500 MHz, DMSO): δ 0.65 (t, 3H, CH_3), 1.032-1.34 (m, 4H, CH_2), 7.085-7.136 (m, 5H, C-H aromatic), 2.33 (t, 2H, CH_2), 5.52 (s, 2H, N-CH_2-N).

*Compound **S28***

IR (KBr) (ν_{max}/ cm^{-1}): 1550 (C=C), 2926 (C-H str), 1523 (C=S), 1687 (C=N), 3059 (C-H aromatic, str), 1379 (C-N), 1000 (C-C), 1100 (N-N). ^{1}H-NMR (500 MHz, DMSO): δ 7.233-7.565 (m, 5H, CH aromtic), 0.84 (t, 3H, CH_3), 1.23, 1.65 (t, 4H, CH_2), 2.51 (t, 2H, CH_2), 5.50 (s, 2H, N-CH_2-N).

*Compound **S31***

IR (KBr) (ν_{max}/ cm^{-1}): 3381 (NH), 1653 (C=O, amide), 2922 (C-H, str), 1456 (C=N), 3000 (C-H aromatic), 1500 (C-S), 1136 (N-N), 1369 (C-N), 1000 (C-C), 1600 (C=C). ^{1}H-NMR (500 MHz, DMSO): δ 8.07 (s, H, NH, amide), 7.28-7.37 (m, 5H, C-H aromatic), 5.78 (S, 1H, NH-C=O), 5.57 (s, 2H, N-CH_2-N), 4.23 (d, 2H, CH_2NH), 4.56 (m, 2H, CH-N), 2.76 (d, 4H, CH_2-S), 0.95, 1.25 (m, 6H, CH_2-CH_2-CH_2), 2.25 (t, 2H, O=C-CH_2).

*Compound **S32***

IR (KBr) (ν_{max}/ cm^{-1}): 3383 (NH), 2924 (C-H stretch), 1550 (C=C), 1627 (C=N), 3000 (C-H aromatic), 1653 (C=O, amide), 1525 (C=S), 1126 (N-N), 1000 (C-C), 1516 (C-S), 1300 (C-N). ^{1}H-NMR (500 MHz, DMSO): δ 7.99 (s, H, NH, amide), 5.68 (s, 2H, NH-C=O-NH), 5.57 (s, 2H, N-CH_2-N), 0.95, 1.35 (m, 6H, CH_2–CH_2-CH_2), 2.15 (t, 2H, O=C-CH_2), 4.66 (m, 2H, CH-NH), 7.28-7.96 (m, 5H, CH aromatic), 4.23 (d, 2H, CH_2-NH), 3.27 (d, 4H, CH_2-S).

*Compound **S33***

IR (KBr) (ν_{max}/ cm^{-1}): 2960-3392 (OH, carboxylic acid), 1700 (C=O, Carboxyl), 1635 (C=O, amide), 3298-3200 (NH_2, amine), 1606 (C=C), 1120 (N-N), 1051 (C-C), 1190 (C-N), 2900 (C-H, Str), 3000 (C-H aromatic). ^{1}H-NMR (500 MHz, DMSO): δ 10.71 (S, 1H, OH-carboxylic acid), 5.80 (s, 2H, NH_2, amine), 7.33-7.65 (m, 5H, C-H aromatic), 5.14 (S, 2H, N-CH_2-N), 4.04 (t, H, CH-NH_2), 2.76 (d, 2H, CH_2-C-NH_2).

*Compound **S34***

IR (KBr) (ν_{max}/ cm^{-1}): 2856-3300 (OH, carboxylic acid), 1710 (C=O, Carboxyl), 1640 (C=O, amide), 3184-3200 (NH_2, amine), 2922 (C-H alp), 1066 (C-C), 1286 (N-N), 1516 (C=S), 1379 (C-N), 3055 (C-H aromatic), 1456 (C=C). ^{1}H-NMR (500 MHz, DMSO): δ 11.11 (s, H, OH-carboxylic acid), 5.80 (s, 2H, NH_2, amine), 7.68 CH (1,2,3-triazole), 5.17 (s, 2H, 2H, N-CH_2-N), 4.12 (t, H, CH-NH_2), 7.34-7.99 (m, 5H, C-H aromatic), 2.76 (d, 2H, CH_2-C-NH_2.

*Synthesis of 2-(3-oxo-5,6-diphenyl-1,2,4-triazin-2(3H)-yl)quinazolin-4(3H)-one (**S29**), 2-(5,6-diphenyl-3-thioxo-1,2,4-triazin-2(3H)-yl)quinazolin-4(3H)-one (**S30**) [22]*

Potassium tert-butoxide 1 mmol in 4 mL of DMSO, was added to the mixture of benzyl azide (**S7** and **S8**) (1 mmol, 0.0032 g, 0.0031 g), respectively and isatoic anhydride (1 mmol, 0.006 g). After 4 hours of stirring at 100 °C for 4 hours, and then the reaction mixture was cooled to room temperature, H_2O (4 mL) was added and DCM (2 × 4 mL) was used to extract it.

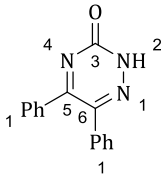
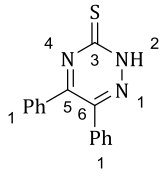
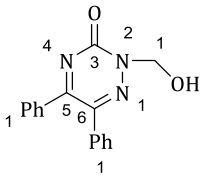
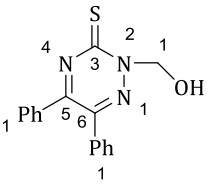
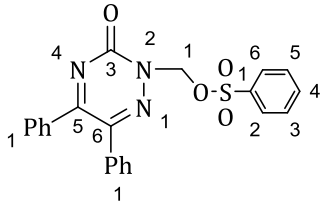
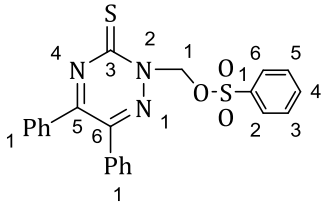
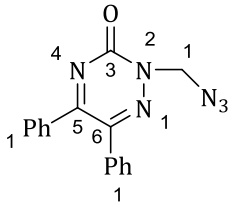
*Compound **S29***

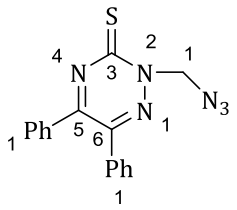
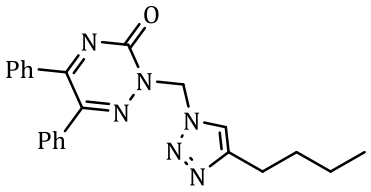
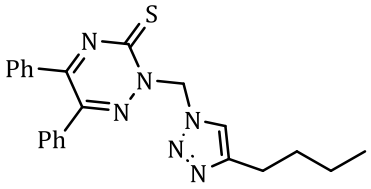
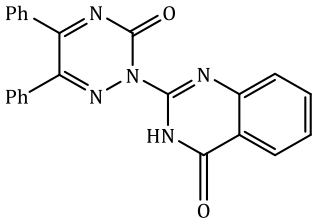
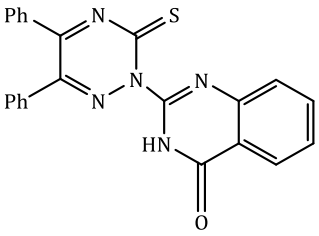
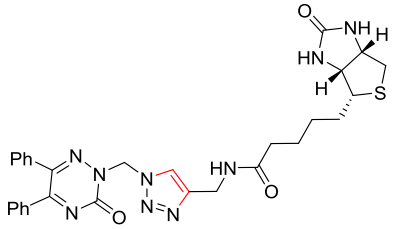
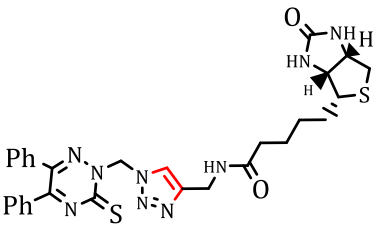
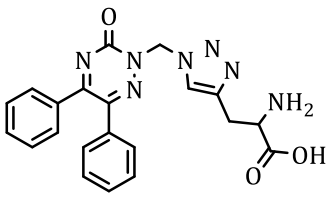
IR (KBr) (ν_{max}/ cm^{-1}): 3392 (NH), 1651 (C=O, amide), 1508 (C=C), 1689 (C=N), 3068 (C-H aromatic), 1238 (N-N), 1381 (C-N), 1000 (C-C). ^{1}H-NMR (500 MHz, DMSO): δ 7.34-8.21 (m, 5H, CH aromatic). ^{13}C-NMR (125 MHz, DMSO): δ 161.17-168.71 (C=O amide), 147.07-152.71 (C=N), 125.98-135.35 (C aromatic).

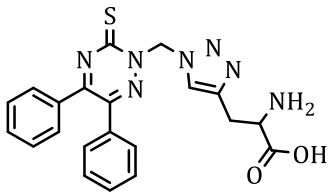
*Compound **S30***

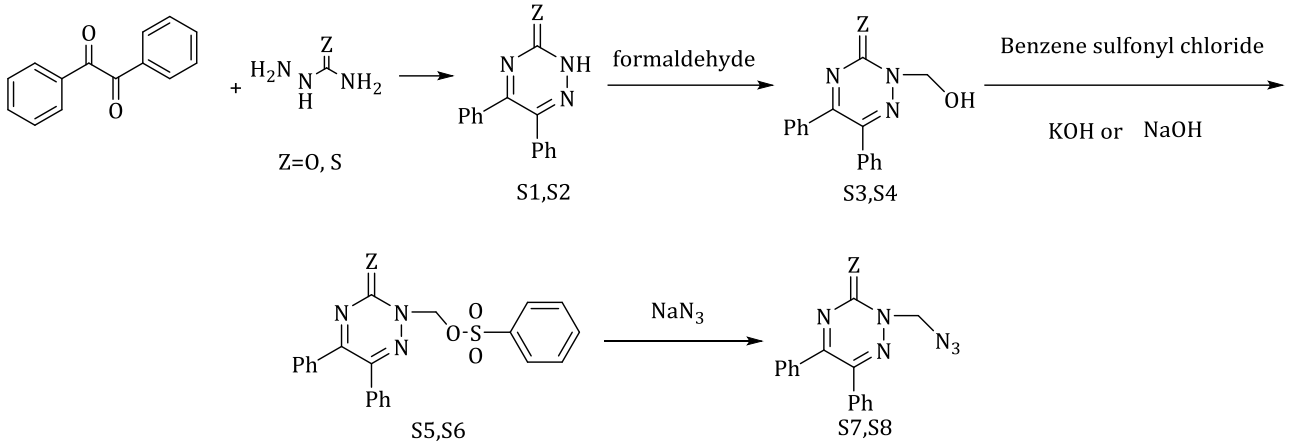
IR (KBr) (ν_{max}/ cm^{-1}): 3389 (NH), 1575 (C=C), 1383 (C-N), 3063 (C-H aromatic), 1516 (C=S), 1257 (N-N), 1026 (C-C), 1689 (C=N), 1610 (C=O), ^{1}H-NMR (500 MHz, DMSO): δ 6.35-7.79 (m, 5H, CH aromatic). ^{13}C-NMR (125 MHz, DMSO): δ 162.81 (C=O, amide), 114.19-150.62 (C aromatic), 164.81 (C=N), 173.81 (C=S).

Table 1: Some physical properties of **S1-S8, S27-S34** compound

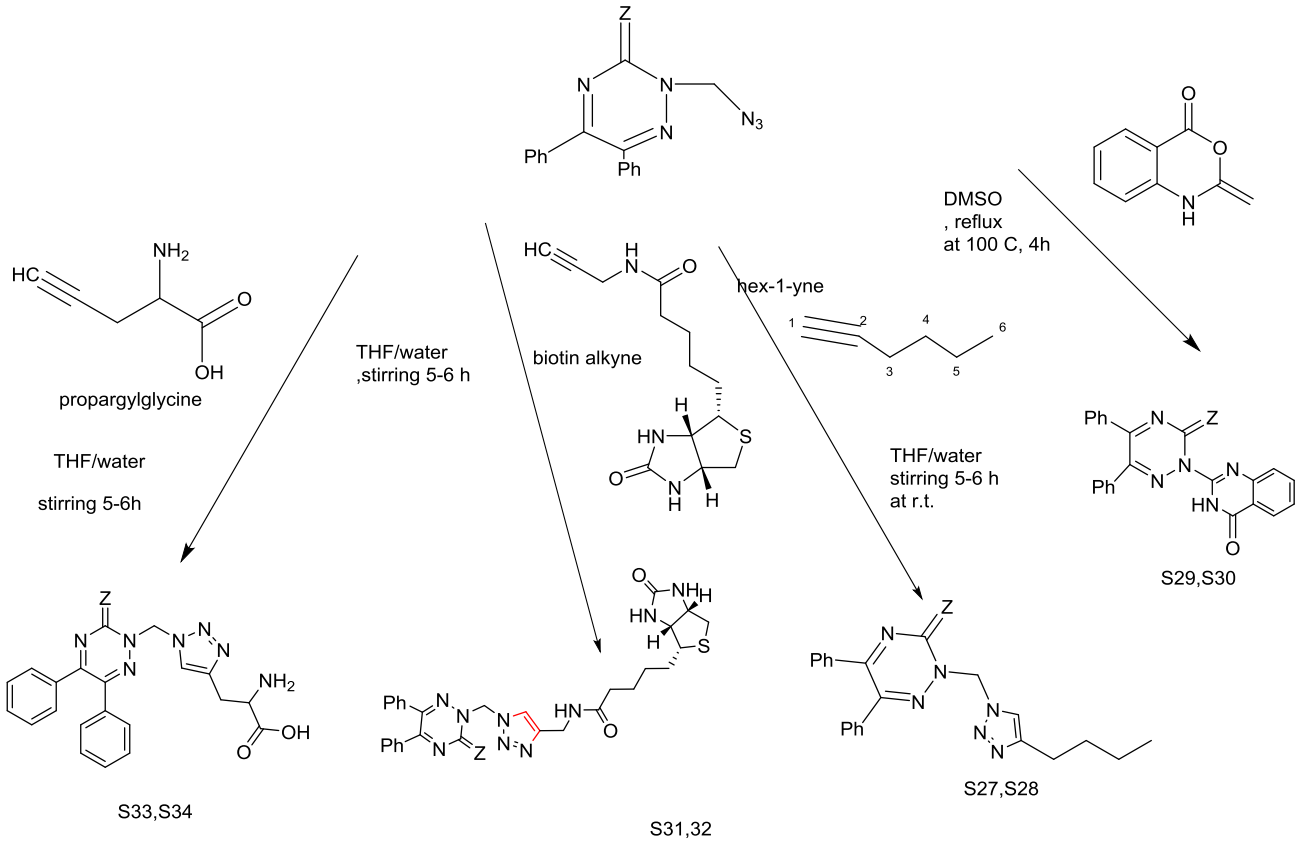
Compound No.	Structural formula	Rf	Yield (%)	Mp (°C)	M.Wt	M. formula
S1		0.40	81.35	219-221	249.07	$C_{15}H_{11}N_3O$
S2		0.43	52.38	215-217	269.09	$C_{15}H_{11}N_3S$
S3		0.50	80	170-172	279	$C_{16}H_{13}N_3O_2$
S4		0.64	72	99-102	295	$C_{16}H_{13}N_3OS$
S5		0.62	80	153-155	419	$C_{22}H_{17}N_3O_4S$
S6		0.70	80.76	124-126	435	$C_{22}H_{17}N_3O_3S_2$
S7		0.72	74.6	271-273	472	$C_{16}H_{12}N_6O$

S8		0.68	78.65	Gumy	488	$C_{16}H_{12}N_6S$
S27		0.81	89.23	283-285	386.19	$C_{22}H_{22}N_6O$
S28		0.76	71	246-248	914.92	$C_{22}H_{22}N_6S$
S29		0.60	90	145-147	393.12	$C_{23}H_{15}N_5O_2$
S30		0.68	8	160-162	409.47	$C_{23}H_{15}N_5OS$
S31		0.40	84	Gumy	585.69	$C_{29}H_{31}N_9O_3S$
S32		0.45	78	Gumy	601.75	$C_{29}H_{31}N_9O_2S_2$
S33		0.74	71	224-226	417.43	$C_{21}H_{19}N_7O_3$

S34		0.96	79	256-258	433.49	$C_{21}H_{19}N_7O_2S$



Scheme 1: Synthesis of compounds **S1-S8**



Scheme 2: Synthesis of compounds **S27-S34**

Results and Discussion

Triazine derivatives were produced as a result of benzil's reaction with smecarbazide or thiosemicarbazide respectively and then with formaldehyde. We first obtained the hydroxymethylation derivative, we carried out multiple reactions to produce the azide compounds, Scheme 1 (S1-S8).

The reaction the azide compounds with different alkynes we obtained the triazole, triazine, quinazoline, imidazoldine derivatives, in the Scheme 2 (S27-S34).

We prepared **S1** by the reaction of benzil with semicarbazid. The IR spectrum of the S1 indicated by disappearance of broad bands at 3309-3433 cm^{-1} of NH_2 group of semicarbazide. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 10.88 ppm of NH group. The ^{13}C-NMR spectrum showed the appearance of peak at 153.88 ppm (C=O, amide) and 166.88 ppm (C=N). Compound **S2** has been identified by IR spectroscopy through the disappearance of bands at 3306 cm^{-1} of NH_2 group of thiosemicarbazid and appearance bands at 3126 cm^{-1} of NH group. Also, the appearance of band at 1367 cm^{-1}related to C=N group, compound **S2** has been identified by ^{1}H-NMR spectroscopy. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 10.05 ppm of NH group. The ^{13}C-NMR spectrum showed the appearance of peak at 184.22 ppm (C=S, thioamide) and 162.80 ppm (C=N). Compound **S3** has been identified by IR spectroscopy through the disappearance of bands at 3198 cm^{-1} of NH group and appearance of bands at 3385 cm^{-1} of OH group and the appearance of band at 2945 related to (C-H alpha). Likewise, the appearance of band at 1367 cm^{-1} related to C=N group. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 10.45 ppm of OH group and appearance of triplet peak at 5.42ppm of N-CH_2. The ^{13}C-NMR spectrum showed the appearance of (C=O) at 155.55 ppm and appearance of (C=N) at 166.55 ppm and appearance of (CH_2) at 75.62 ppm. The IR spectrum of compound **S4** showed the disappearance of bands at 3126 cm^{-1} of NH group and appearance of bands at 3360 cm^{-1} of OH group. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 4.78 ppm of OH group and the appearance of triplet peak at 5.82 ppm to N-CH_2. The infrared spectrum of compound **S5** showed the disappearance of band at 3385 cm^{-1} of OH group. The ^{1}H-NMR spectrum showed the disappearance of triplet peak at 4.52 ppm of OH group and appearance of doublet peak at 5.40 ppm of N-CH_2. The ^{13}C-NMR spectrum showed the appearance of **S5** 158.12 ppm due to (C=O) and appearance of 77.67 ppm due to (N-CH_2). The IR spectrum of compound **S6** showed the disappearance of band at 3360 cm^{-1} of OH group. The ^{1}H-NMR spectrum showed the disappearance of triplet peak at 4.78 ppm of OH group and appearance of doublet peak at 5.53ppm of N-CH_2. The IR spectrum of compound **S7** showed the appearance of band at 2123 cm^{-1} of g (N=N=N) group. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 5.77 ppm to CH_2-N. The IR spectrum of compound **S8** showed the appearance of band at 2114 cm^{-1} of (N=N=N) and the appearance of band at 1674 of (C=N). The ^{1}H-NMR spectrum showed the appearance of singlet peak at 5.89 ppm to CH_2-N. The IR spectrum of compound **S27** showed the disappearance of band at 2123 cm^{-1} of (N=N=N) group. The ^{1}H-NMR spectrum showed the appearance of triplet peak at 0.659 ppm of CH_3 alpha and appearance of multiplet peak at 1.34 ppm to CH_2 and singlet peak at 5.52 ppm of N-CH2-N group. The IR spectrum of compound **S28** showed the disappearance of bands at 2114.05 cm^{-1} of (N=N=N) and appearance of band at (1523 cm^{-1}) of C=S group. The ^{1}H-NMR spectrum of compound S28 showed the appearance of triplet peak at 0.84-0.94 ppm of CH_3 alpha and the appearance of singlet peak at 5.50 ppm to N-CH_2-N. The IR spectrum of compound **S29** showed the disappearance of band at 2123 cm^{-1} of (N=N=N) group and appearance of bands of 3392 cm^{-1} of NH group. The ^{1}H-NMR spectrum of compound **S29** showed the disappearance of singlet peak at 5.77 ppm related to CH_2-N_3. The ^{13}C-NMR spectrum showed the appearance of 161 and 168.71ppm due to (C=O) and appearance of 147,152.71 ppm due to (C=N). The IR spectrum of compound **S30** showed the disappearance of band at 2114 cm^{-1} of (N=N=N) and appearance of band at 3389 cm^{-1} of NH group. The ^{1}H-NMR spectrum showed the disappearance of singlet peak to CH_2-N_3. The ^{13}C-NMR spectrum showed the appearance of 162.8-164.8 ppm due to (C=O) and appearance of 173.8 ppm due to (C=S) and appearance of 147-150.6ppm due to (C=N). The IR spectrum of compound **S31** showed the disappearance of band at 2123 cm^{-1} of (N=N=N) group appearance of band at 3381 cm^{-1} of NH group and 1620 cm^{-1} and 1653 cm^{-1} of amide group. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 8.0 7ppm of NH group and appearance of singlet peak at 5.78 ppm

related to NH-C=O group, and appearance of doublet peak at 3.3 ppm of CH_2-S. The IR spectrum of compound **S32** showed the disappearance of bands at 2114 cm^{-1} of (N=N=N) and appearance of band at 3352cm^{-1} of NH group and 1653 cm^{-1} and 1627cm^{-1} of C=O. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 7.8-7.9 ppm of NH group, and appearance of singlet peak at 5.65 ppm related to NH-C=O and appearance of doublet peak at 3.1-3.2 ppm of CH_2-S. The IR spectrum of compound **S33** showed the appearance of band at 2960 cm^{-1} of OH carboxylic acid group and 3298 and 3392 cm^{-1} of NH_2 group. The ^{1}H-NMR spectrum showed the appearance of doublet peak at 5.8 ppm of NH_2 group and appearance of singlet peak at 10.7 ppm related to OH group and appearance of singlet peak at 5.14 ppm of N-CH_2-N. The IR spectrum of compound **S34** showed the appearance of band at 3318 cm^{-1} of NH_2 group and 2922 cm^{-1} of OH carboxylic acid. The ^{1}H-NMR spectrum showed the appearance of singlet peak at 5.8 ppm of NH_2 group and appearance of singlet peak at 11.11 ppm related to OH group and appearance of singlet peak at 5.17 ppm of N-CH_2-N.

Biological activity

Antibacterial activity

Escherichia coli, and *Staphylococcus aurous*. These bacteria were selected due to the importance in the field of medicine. These types of bacteria caused many diseases. The method used to calculate the inhibitory effect of compounds prepared on these types of bacteria is Agar diffusion method. It includes the following:

1. Work of several drilling in the dishes planted with bacteria.
2. (0.1 mL) of (25 mg/1 mL) of some derivatives prepared in the excavation of cultivars planted with bacteria.
3. Place the dishes in an incubator at a temperature of (37 °C) for 24 hours.
4. The inhibition zone was measured and the results are shown in Table 2.

Table 2: The inhibition of the growth of the bacteria (Inhibition Zone) by some derivatives recorded in millimeter unit

Compound No.	Type of bacteria		
	Escherichia coli	ASP niger	*Staphylococcus aureus*
S1	0	25	0
S2	0	25	0
S3	12	25	15
S4	28	25	30
S5	0	25	0
S6	0	25	0
S7	25	25	25
S8	25	0	30
S27	25	0	25
S28	25	25	25
S29	25	25	25
S30	25	25	25
S31	25	25	25
S32	25	25	25
S33	25	25	25
S34	25		25

These types of bacteria were selected because one of them (*Staphylococcus aurous*) is positive for the Graham stain, while the other (*Escherichia coli*) is negative. The inhibition extent of bacterial growth was studied according to the method of (agar diffusion method), where it was observed that most of the prepared compounds have biological effective as inhibitors to the growth of these two bacteria. Especially the (*Escherichia coli*) trend, where it was shown that the compounds **S4, S8, S7, S27, S28, S29, S30, S31, S32, S33**, and **S34** have a high efficacy towards

inhibiting their growth, and also it was discovered that the compound **S4** and **S8** has a stronger activity preventing the growth of bacteria (*Staph.*) If weighed against the other produced derivatives. Discovered that some additional compounds have a higher level of activity inhibiting *Asp.niger* growth if compared with the rest of the prepared derivatives.

Conclusion

1- New compounds were prepared and identified for the two compounds 5,6-diphenyl-1,2,4-triazine-3-(2*H*)-one and 5,6-diphenyl-1,2,4-triazine-3-(2*H*)-thione.

2- Important heterocyclic compounds such as triazine, triazole, imidazolidine and quinazoline were prepared and diagnosed.

3- Most of the compounds have high stability in weather conditions.

4- The possibility of using some of the prepared compounds as antibacterials as they have high susceptibility to inhibit the growth of bacteria such as *E.coli* and *Staphylococcus aureus* after completing the necessary medical studies.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

The author declared that they have no conflict of interest.

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HOW TO CITE THIS ARTICLE

Safaa Thamer Ahmed, Shireen Ridha Rasool. Synthesis, Characterization and Study Biological Activity of Some 1,2,4-Triazin Heterocyclic Derivatives. *J. Med. Chem. Sci.*, 2023, 6(7) 1537-1547

https://doi.org/10.26655/JMCHEMSCI.2023.x.x

URL: http://www.jmchemsci.com/article_161005.html