

# Month 2018 Synthesis and Acaricidal Activity of Some New 1,2,4-Triazine Derivatives

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A new series of 1,2,4-triazine derivatives were designed, synthesized, and identified on the basis of IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, and EI-MS spectral data. The potent acaricidal activity of 1,2,4-triazine derivatives against eggs and adult female of *Tetranychus urticae* (Koch) was assessed compared with pyridaben under laboratory conditions. Structure acaricidal activity relationships of the promising 1,2,4-triazine derivatives were analyzed for eggs and adult female; the nature and position of the substituents were important in demonstration of the activities.

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### **INTRODUCTION**

Triazine derivatives are widely utilized in different fields as pharmaceuticals, herbicides, pesticides, dyes, and agriculture. So that is great concern, is paid us to the synthesis of trains as the result of its importance as biological agents in medical and agricultural fields [1,2]. The 1,2,4-triazin has two competing reactive sites at both the amino and thiol groups that can be used for the synthesis of binary and/or fused triazines [3]. Twospotted spider mite, Tetranychus urticae (Koch), is considered to be highly polyphagous species of the Tetranychidae, causing economic injuries to cotton, vegetables, fruits, and several other agricultural crops [4]. The primary method used for controlling this pest is the chemical control using of different synthetic acaricides to protect the crops and reduce the crops yield losses [4,5]. The intensive use of many conventional acaricides to control this pest population lead to very rapidly mite pesticide resistant [6]. Therefore, there is a continuous need for development and application of new synthetical acaricides with new biochemical modes of action, to prevent the development of mite resistance [6,7]. The present study is directed to the synthesis and evaluates the acaricidal activity of some 1,2,4-triazine derivatives against eggs and adult females of two-spotted spider mite, T. urticae (Koch).

# **RESULTS AND DISCUSSION**

**Chemistry.** A great attention has been directed to the synthesis of fused 1,2,4-triazines with ring junction nitrogen systems because they constitute an important class of natural products and exhibit many useful

biological activities. 4-Amino-6-benzyl-3-mercapto-1,2,4-triazin-5(4*H*)-one (**3**) acts as a building block for the synthesis of fused heterocyclic rings incorporating 1,2,4-triazines ring junction nitrogen. Compound **3** was prepared as previously reported in the literature from 4-benzylidene-2-methyloxazol-5(4*H*)-one (**1**) and thiocarbohydrazide (**2**) [8,9]. While, in our case, when attempting preparation of **3** following the literature procedure, **3** was separated on hot from the reaction mixture as a major product besides a minor product of thiocarbohydrazide acetic acid salt **4** (Scheme 1).

Triazine 3 has two competing reactive sites at both the thiol and amino groups, which can be used for the synthesis of nitrogen ring junction triazines [3]. Heterocyclic fused ring systems consisting of 1,2,4triazolo, 1,3,4-thiadiazole, and 1,3,4-thiadiazine represent a class of compounds that possesses a broad spectrum of biological activities such as anti-inflammatory, antiviral, antimicrobial, and antitumor activity [10–14]. Consequently, in view of the myriad biological activities of these ring systems and as a part of an ongoing investigation into biologically more active and less toxic substances, we focused our attention on the synthesis of a series of new 1,2,4-triazolo[5,1-c]1,2,4-triazin, 1,3,4thiadiazolo[2,3-c]1,2,4-triazin-4-ones, and 1,2,4-triazolo[3,4b]1,3,4-thiadiazines in order to investigate their acaricidal activity. Thus, cyclocondensation reaction of triazine 3 with phenyl isothiocyanate [15] in DMF afforded 3-benzyl-8phenyl-7-thioxo-7,8-dihydro-1,2,4-triazolo[5,1-c]1,2,4-

triazin-4(6*H*)-one (5). The structure of compound 5 was established by its spectral analysis. Thus, the IR spectrum of 5 showed a band at 3192 cm<sup>-1</sup> for NH, which appeared at  $\delta = 10.87$  ppm in its <sup>1</sup>H-NMR. Also, triazine 3 was refluxed with mono chloroacetic acid in phosphorus oxychloride (POCl<sub>3</sub>) [16] and afforded the corresponding



3-benzyl-7-(chloromethyl)-4*H*-[1,3,4]thiadiazolo[2,3-*c*] [1,2,4]triazin-4-one (**6**). The <sup>1</sup>H-NMR showed new peaks at  $\delta = 4.82$  ppm attributed to CH<sub>2</sub>Cl, indicating that the

carboxylic group of the acids used was reacted with SH and  $NH_2$  groups to afford 1,3,4-thiadiazolo[2,3-*c*]1,2,4-triazin-4-ones **6**. Also, <sup>13</sup>C-NMR spectra of compound **6** 





showed signals at  $\delta = 58.43$  ppm attributed to CH<sub>2</sub>Cl. Additionally, refluxing **6** with benzoimidazole-2-thiol in EtOH afforded 7-((1*H*-benzo[*d*]imidazol-2-ylthio)methyl)-3-benzyl-4*H*-1,3,4-thiadiazolo[2,3-*c*]1,2,4-triazin-4-one

(7). The IR spectrum of compound 7 revealed the appearance of the NH group at 3144 cm<sup>-1</sup>, and its <sup>1</sup>H-NMR spectrum showed singlet signals at  $\delta = 4.98$  and 12.81 ppm for CH<sub>2</sub>-S and NH protons, respectively (Scheme 2).

Alkylation of compound **3** with chloroacetonitrile in dioxin [17] in the presence of Et<sub>3</sub>N produced 2-((4-amino-6-benzyl-5-oxo-4,5-dihydro-1,2,4-triazin-3-yl)thio) acetonitrile (**8**) in 53% yield and 7-amino-3-benzyl-4*H*,8*H*-1,2,4-triazino[3,4-*b*]1,3,4-thiadiazin-4-one (**9**) in 41% yield. Compound **8** was obtained *via* direct attack of 4-amino group to the nitrile bond followed by isomerization of the imino group to the amino group (Scheme 2).

The IR spectrum of compound **8** showed bands at 3445, 3320 and 2249 cm<sup>-1</sup> for NH<sub>2</sub> and CN groups, respectively. The <sup>1</sup>H-NMR spectrum of compound **8** showed singlet signals at  $\delta = 6.48$  ppm for NH<sub>2</sub> protons and at  $\delta = 5.48$  ppm attributed to CH<sub>2</sub>-S protons, which also verified by appearance at  $\delta = 17.10$  ppm in its <sup>13</sup>C-NMR spectrum, indicating that the thiol group reacted with a chloro atom of choloroacetonitrile beside the presence of CN group at  $\delta = 114.37$  ppm. In addition, the IR spectrum of compound **9** showed the disappearance of CN group and presence of bands at 3445, 3320 cm<sup>-1</sup> for NH<sub>2</sub>. Also, its <sup>1</sup>H-NMR spectrum showed singlet signals at  $\delta = 4.13$  and 4.78 ppm attributed to CH<sub>2</sub>-S and NH<sub>2</sub> protons, respectively.

Once more, stirring of 3 with halo compounds such as methyl iodide and ethyl bromoacetate [18,19] at room temperature furnished the respective triazine derivatives **10** (major) and/or **11** (minor) (Scheme 2).

Thus, alkylation of triazine **3** with either methyl iodide or ethyl bromoacetate afforded a higher ratio of *S*-alkyl versus *N*-alkyl-1,2,4-triazine derivatives 4-amino-6benzyl-3-(methylthio)-1,2,4-triazin-5(4*H*)-one (**10a**) and ethyl-2-(4-amino-6-benzyl-5-oxo-4,5-dihydro-1,2,4-

triazin-3-ylthio)acetate (10b) and 4-amino-6-benzyl-2-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2*H*)-one

(11a) and ethyl-2-(4-amino-6-benzyl-5-oxo-3-thioxo-4,5dihydro-1,2,4-triazin-2(3*H*)-yl)acetate (11b). Compound 10a [R=CH<sub>3</sub>] was prepared as previously reported in the literature (method a) [18]. But in our case, when attempting preparation of 10a under the same condition (method a) and/or under condition (method b) afforded both 10a and 11a. The structures of 1,2,4-triazines 10a,b and 11a,b were established on the basis of their spectral analyses.

The IR spectrum of S-alkyl triazine **10a** [R=CH<sub>3</sub>] showed bands at 3308, 3260 and 1687 cm<sup>-1</sup> for (NH<sub>2</sub>)

and (C=O amide), respectively. Also, the IR spectrum of *N*-alkyl triazine **11a** [R=CH<sub>3</sub>] displayed bands at 3330, 3298 (NH<sub>2</sub>), 1669 (C=O amide), and 1162 cm<sup>-1</sup> for (C=S), and its mass spectrum showed a molecular ion peak at m/z = 248 (M<sup>+</sup>, 77.32) and a base peak at m/z = 91 (100.0%) corresponding to the molecular formula C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>OS.

In addition, the IR spectrum of *S*-alkyl triazine **10b** [R =  $-CH_2$ -COOEt] appeared bands at 3323, 3258 (NH<sub>2</sub>) and 1739 cm<sup>-1</sup> (-OOC), and its <sup>1</sup>H-NMR showed signals at  $\delta$  = 1.30 (t, 3H, CH<sub>3</sub>), 3.99 (s, 2H, CH<sub>2</sub>-Ph), 4.06 (s, 2H, CH<sub>2</sub>), 4.28 (q, 2H, CH<sub>2</sub>-CH<sub>3</sub>), and 4.82 ppm (s, 2H, NH<sub>2</sub>). Also, the IR spectrum of *N*-alkyl triazine **11b** displayed bands at 3310, 3219 (NH<sub>2</sub>), 1742 (COO), and 1177 cm<sup>-1</sup> for (C=S), and its <sup>1</sup>H-NMR showed signals at  $\delta$  = 1.20 (t, 3H, CH<sub>3</sub>), 4.19 (q, 2H, CH<sub>2</sub>-CH<sub>3</sub>), and 5.17 ppm (s, 2H, N-CH<sub>2</sub>), while its <sup>13</sup>C-NMR spectrum displayed signals at  $\delta$  = 13.92, 59.05, 61.33, 145.78, 166.57, and 168.65 ppm for (CH<sub>3</sub>-CH<sub>2</sub>), (-OCCH<sub>2</sub>), (CH<sub>2</sub>-CH<sub>3</sub>), (C<sub>6</sub>), (C=O), and (COO-), respectively.

Reaction of hydrazine hydrate with **10b** ( $R = CH_2COOC_2H_5$ ) furnished 3-benzyl-7-hydrazinyl-4*H*,8*H*-1,2,4-triazino[3,4-*b*]1,3,4-thiadiazin-4-one (**12**) in 35% yield besides the 4-amino-6-benzyl-3-hydrazinyl-1,2,4-triazin-5(4*H*)-one (**13**) in 57% yield (Scheme 2).

The IR spectrum of compound **12** showed bands at 3330, 3282, and 1686 cm<sup>-1</sup> related to NH<sub>2</sub>, NH, and (C=O amide) groups. In addition, its <sup>1</sup>H-NMR spectrum showed singlet signals at  $\delta = 3.81$ , 3.92, 5.51, and 6.06 ppm for CH<sub>2</sub>–Ph, S–CH<sub>2</sub>, NH<sub>2</sub>, and NH protons, respectively. <sup>13</sup>C-NMR also revealed signals at  $\delta = 35.52$  and 36.40 ppm for S–CH<sub>2</sub> and CH<sub>2</sub>–Ph, respectively, which indicated the formation of compound **12**.

Furthermore, the assignment of the structure for compound **13** was based on its spectroscopic analysis. Thus, IR spectrum of **13** showed the disappearance of the ester group and a presence of new hydrazinyl group bands at 3330, 3283, 3226 cm<sup>-1</sup> for (2NH<sub>2</sub>) and 3184 cm<sup>-1</sup> for NH groups, respectively. Its mass spectrum revealed a molecular ion peak at m/z = 232 (M<sup>+</sup>, 25.35) corresponding to the molecular formula  $C_{10}H_{12}N_6O$  and a base peak at m/z = 50 (100.0%).

In addition, the reaction of **3** with cyanoacetic acid in acetic anhydride yielded *N*-(6-benzyl-5-oxo-3-thioxo-2,5-dihydro-1,2,4-triazin-4(3*H*)-yl)acetamide (**14**) *via* a pathway **a** which confirmed by its spectral analysis (Scheme 2). The <sup>1</sup>H-NMR spectrum of **14** showed signals at  $\delta = 1.99$ , 10.94, and 13.79 ppm attributable to CH<sub>3</sub>, NH-C=O, and NH<sub>triazine</sub> protons, respectively.

The nucleophilic displacement reaction of compound **3** with 4,4'-diselanediyldianiline yielded 3,3'-((diselanediylbis(4,1-phenylene))bis(azanediyl))bis(4-amino-6-benzyl-1,2,4-triazin-5(4*H*)-one (**15**). The structure of this compound was established by its spectral analysis. The <sup>1</sup>H-NMR

spectrum of compound **15** indicates singlet signals at  $\delta = 5.35$  and 8.28 ppm for 2NH<sub>2</sub> and 2NH protons, respectively.

The reaction of 4-amino-6-benzyl-3-mercapto-1,2,4-triazin-5(4*H*)-one (**3**) with various aldehydes [20] under reflux in ethanol in the presence either of conc.  $H_2SO_4$  and/or conc. HCl resulted in the formation of the corresponding imines 6-benzyl-4-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyleneamino)-3-mercapto-1,2,4-triazin-5(4*H*)-one (**16a**) and 6-benzyl-4-((2-hydroxynaphthalen-1-yl)methyleneamino)-3-mercapto-1,2,4-triazin-5(4*H*)-one (**16b**). These compounds were characterized by their

spectroscopic data. The <sup>1</sup>H-NMR of **16a,b** showed the methine (=CH) proton at  $\delta = 8.26$  and 9.54 ppm, which supported the condensation products and not the cyclized structure **16**` (Scheme 3).

Once more, stirring of **16a** with halo compounds [21] such as methyl iodide and/or ethyl bromoacetate at room temperature under three different solvent such as EtOH/DMF in presence of  $Et_3N$  gave solely the corresponding 6-benzyl-4-((1,3-diphenyl-1*H*-pyrazol-4-yl) methyleneamino)-3-(methylthio)-1,2,4-triazin-5(4*H*)-one (**17**) and ethyl 2-(6-benzyl-4-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyleneamino)-5-oxo-4,5-dihydro-1,2,4-triazin-3-

ylthio)acetate (18) in high yield while in sodium methoxide solution or EtOH/DMF in presence of fused sodium acetate, afforded triazines 17 and 18 in low yield [R = -N=CH-Ar] (Scheme 3). The structures of 1,2,4-

triazines **17** and **18** were established on the basis of their spectral analyses. The <sup>1</sup>H-NMR spectrum of *S*-alkyl triazine **17** showed signals at  $\delta = 2.61$ , 8.64, and 9.11 ppm attributed to CH<sub>3</sub>, CH—pyrazole, and ==CH protons, respectively. Also, the IR spectrum of *S*-alkyl triazine **18** demonstrated bands at 1739 cm<sup>-1</sup> for (-OOC), and its <sup>1</sup>H-NMR showed signals at  $\delta = 1.16$  (t, 3H, CH<sub>3</sub>), 4.09 (s, 2H, CH<sub>2</sub>), 4.11 (q, 2H, CH<sub>2</sub>--CH<sub>3</sub>), 9.10 (s, 1H, CH<sub>pyrazole</sub>), and 9.13 ppm (s, 1H, =CH).

Furthermore, compound 16a was reacted with either allyl bromide or 1,2-bis(bromomethyl)benzene only in the presence of Et<sub>3</sub>N to vield 3-(allvlthio)-6-benzvl-4-((1.3diphenyl-1H-pyrazol-4-yl)methyleneamino)-1,2,4-triazin-5(4H)-one (19) and 3,3'-((1,2-phenylenebis(methylene))) bis(sulfanediyl))bis(6-benzyl-4-(((1,3-diphenyl-1H-pyrazol-4-yl)methylene)amino)-1,2,4-triazin-5(4H)-one) (20).respectively (Scheme 3). An assignment of the structure of compounds 19 and 20 was based on their spectroscopic analyses. Therefore, compound 19 showed signals at  $\delta = 3.89$  (d, 2H, S–CH<sub>2</sub>=CH), 5.01 (dd, 2H, CH<sub>2</sub>=CH), 6.02 (m, 1H, CH), 8.63 (s, 1H, CH<sub>pyrazole</sub>), and 9.09 ppm (s, 1H, =CH) in its <sup>1</sup>H-NMR spectrum. Also, <sup>1</sup>H-NMR of compound **20** displayed singlet signals at  $\delta = 4.64$ , 8.51, and 9.067 ppm corresponding to (CH2-S), CHpyrazole and =CH protons. Furthermore, the mass spectrum of compound 19 showed an ion peak at m/z = 505 (M+1, 24.2) (1.00) and a base peak at m/z = 50 (100.0%) corresponding to the molecular formula C<sub>36</sub>H<sub>27</sub>N<sub>7</sub>O<sub>4</sub>S.

Scheme 3. Synthetic pathways of 1,2,4-triazines derivatives 16-20. [Color figure can be viewed at wileyonlinelibrary.com]



ticit	Table 1	y of 1,2,4-triazines derivatives against adult females of T. urticae after 24 h and 72 h of treatment.
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	$ccc$ Slope ± SE $\delta$ Slope ± SE $70.65$ $1.402 \pm 0.402$ $1.70.65$ $1.278 \pm 0.396$ $2 E + 2$ $0.672 \pm 0.157$ $4 E + 2$ $0.672 \pm 0.157$ $4 E + 2$ $1.409 \pm 0.300$ $88.42$ $0.637 \pm 0.198$ $8.42$ $0.637 \pm 0.198$ $4.1E + 5$ $0.603 \pm 0.174$ $7.7E + 4$ $1.104 \pm 0.216$	<b>Toxicity</b> index 19.53 19.36 100.00 62.11 6.52 16.35	LC <sub>50</sub> (ppm) and confidence limits at 95% 122.24 45.126 203.029 511.68 206.53 3570.03 7.55 0.50 2.2.47 74.16 37.16 120.72 956.81 415.36 6198.24 252.31 270.99 1950.18	LC% (ppm) and confidence limits at 95% [1302.06 691.94 5780.17 128975.14 128975.14 128975.14 128975.14 10554.27 8305.61 E + 5 709.99 267.51 6890.21 947.14 537.36 2357.10 80755.46 991.83 3617.9 E + 4 9991.83 3617.9 E + 4	Slope ± SE 1.247 ± 0.230 0.534 ± 0.154 0.650 ± 0.163 1.159 ± 0.184	<b>Toxicity</b> index 6.18 1.48 10.000 10.18 0.79 1.37
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	$\delta$ Slope $\pm$ SE           170.65         1.402 $\pm$ 0.402           1.70.65         1.278 $\pm$ 0.396           2 E + 2         0.672 $\pm$ 0.157           4 E + 2         0.672 $\pm$ 0.157           88.42         0.637 $\pm$ 0.198           1.1E + 5         0.603 $\pm$ 0.174           7.7E + 4         1.104 $\pm$ 0.216	index 19.53 19.36 100.00 62.11 6.52 16.35 16.35	limits at 95% 122.24 45.126 203.029 511.68 206.53 3570.03 7.55 0.50 2.2.47 74.16 37.16 120.72 956.81 415.36 6198.24 552.31 270.99 1950.18	limits at 95% 1302.06 691.94 5780.17 128975.14 10554.27 8305.61 E + 5 709.99 267.51 6890.21 947.14 537.36 2357.10 80755.46 9991.83 3617.9 E + 4 9991.83 3617.9 E + 4 34879.06 5487000000000000000000000000000000000000	Slope ± SE 1.247 ± 0.230 0.534 ± 0.154 0.650 ± 0.163 1.159 ± 0.184	index 6.18 6.18 1.48 10.00 10.18 0.79 1.37
3       1522.87       12498.35         5       1536.63       3623.32       902870.65         5       1536.63       3623.32       902870.65         6       297.45       3574.77       50745.2 E + 2         6       297.45       3574.77       50745.2 E + 2         8       143.88       821.99       13901.24       1759.4 E + 2         8       320.11       810.25       1781.54       23188.42         9       478.88       387.65       3887.65         9       478.04       3887.65       457.55         9       478.05       1781.54       23188.42         9       476.02       5333737.12       24718.39       46782.54         10       819.05       3305.307       17436.00       241737.7E + 4         10       634.42       39053.07       17436.00       241737.7E + 4         10       812.07       2310.74       86713.99       175.48         13       634.42       39053.07       17436.00       241737.7E + 4         10       817.66       23188.42       362.77       13574.33E + 3         16       1718.24       1836.37       34781.02       34781.02	$\begin{array}{c} 1.402 \pm 0.402 \\ 2.10.65 \\ 2.11.278 \pm 0.396 \\ 4.12.72 \pm 0.157 \\ 4.12.72 \pm 0.157 \\ 1.409 \pm 0.300 \\ 88.42 \\ 0.637 \pm 0.198 \\ 1.112 \pm 5 \\ 0.603 \pm 0.174 \\ 7.7E \pm 4 \\ 1.104 \pm 0.216 \end{array}$	19.53 19.36 100.00 62.11 6.52 16.35 16.35	$\begin{array}{c} 122.24 \\ 45.126 \\ 511.68 \\ 511.68 \\ 206.53 \\ 3570.03 \\ 7.55 \\ 0.50 \\ 37.16 \\ 120.72 \\ 37.16 \\ 120.72 \\ 956.81 \\ 415.36 \\ 6198.24 \\ 552.31 \\ 270.99 \\ 1950.18 \end{array}$	1302.06           691.94         5780.17           128975.14           10554.27         8305.61 E + 5           709.99           267.51         6890.21           947.14           537.36         2357.10           80755.46           9991.83         3617.9 E + 4           9991.83         3617.9 E + 4	$1.247 \pm 0.230$ $0.534 \pm 0.154$ $0.650 \pm 0.163$ $1.159 \pm 0.184$	6.18 1.48 100.00 10.18 0.79 1.37
<ul> <li>861.62 8033.40 3623.32 902870.65</li> <li>1536.63 15659.07 3574.77 50745.2 E+2</li> <li>297.45 15659.07 3574.77 50745.2 E+2</li> <li>297.45 2397.45 24083.14</li> <li>143.88 821.99 13901.24 17759.4 E+2</li> <li>9 478.88 231.99 13901.24 17759.4 E+2</li> <li>9 478.88 231.99 13901.24 17759.4 E+2</li> <li>9 478.88 233737.12 24718.39 670094.1E+5</li> <li>10 a 1819.18 24 467825.54</li> <li>10 a 634.42 39053.07 17436.00 241737.7E+4</li> <li>10 b 634.03 380.72 3210.74 86713.99</li> <li>13 17.76 25530.44 386.37 17436.03</li> <li>16 a 1316.70 34781.02</li> <li>16 b 634.03 1380.71 13574.33E+3</li> <li>16 b 637.08 14704.21 5564.59 794820.6 E+2</li> <li>16 b 638.011 22665.88</li> </ul>	$(70.65)$ $2 E + 2$ $4 E + 2$ $1.278 \pm 0.396$ $4 E + 2$ $1.409 \pm 0.300$ $88.42$ $0.637 \pm 0.198$ $1.1E + 5$ $0.603 \pm 0.174$ $7.7E + 4$ $1.104 \pm 0.216$	19.36 100.00 62.11 6.52 16.35	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	691.94 5780.17 128975.14 10554.27 8305.61 E + 5 709.99 267.51 6890.21 947.14 537.36 2357.10 80755.46 9991.83 3617.9 E + 4 34879.06 51 3700 E + 3 6105 51 3700 E + 3	$0.534 \pm 0.154$ $0.650 \pm 0.163$ $1.159 \pm 0.184$	1.48 100.00 10.18 0.79 1.37
<ul> <li>5 1536.63 15659.07 3574.77 50745.2 E + 2</li> <li>6 297.45 15659.07 3574.77 50745.2 E + 2</li> <li>8 297.45 24083.14</li> <li>8 297.45 24083.14</li> <li>9 478.88 21.99 13901.24 17759.4 E + 2</li> <li>8 320.11 810.25 1781.54 23188.42</li> <li>9 4560.94 467825.54</li> <li>9 4560.94 467825.54</li> <li>1230.85 533737.12 24718.39 670094.1E + 5</li> <li>10 a 1819.18 245242.43</li> <li>1230.85 533737.12 24718.39 670094.1E + 5</li> <li>13 1230.85 533737.12 24718.39 670094.1E + 5</li> <li>10 b 634.03 3053.07 17436.00 241737.7E + 4</li> <li>10 b 634.03 3053.07 17436.00 241737.7E + 4</li> <li>10 b 634.03 3053.07 17436.00 241737.7E + 4</li> <li>11 b 634.03 380.72 3210.74 86713.99</li> <li>13 17.76 25530.44 386.37 13574.33E + 3</li> <li>16 a 1316.70 34781.02</li> <li>13 180.11 2564.59 794820.6E + 2</li> <li>16 b 180.11 22665.88</li> </ul>	$\begin{array}{c} 2 \ \mathrm{E} + 2 \\ 2 \ \mathrm{E} + 2 \\ 4 \ \mathrm{E} + 2 \\ 1.409 \pm 0.300 \\ 88.42 \\ 0.637 \pm 0.198 \\ 1.1\mathrm{E} + 5 \\ 0.603 \pm 0.174 \\ 7.7\mathrm{E} + 4 \\ 1.104 \pm 0.216 \end{array}$	19.36 100.00 62.11 6.52 16.35 16.35	$\begin{array}{c} 511.68\\ 206.53& 3570.03\\ 7.55\\ 0.50& 22.47\\ 74.16\\ 37.16& 120.72\\ 956.81\\ 415.36& 6198.24\\ 552.31\\ 270.99& 1950.18\end{array}$	128975.14 10554.27 8305.61 E + 5 709.99 267.51 6890.21 947.14 537.36 2357.10 80755.46 9991.83 3617.9 E + 4 9991.83 3617.9 E + 4 34879.06	$0.534 \pm 0.154$ $0.650 \pm 0.163$ $1.159 \pm 0.184$	1.48 100.00 10.18 0.79 1.37
767.36       15659.07       3574.77       50745.2 E+2         297.45       297.45       24083.14         297.45       24083.14       1759.4 E+2         8       478.88       3887.65         9       478.88       3887.65         9       476.094       13901.24       1759.4 E+2         9       478.88       3887.65       3887.65         9       4560.94       1781.54       23188.42         9       4560.94       467825.54       45783.42         10       819.18       810.25       1781.54       23188.42         10       1230.85       533377.12       24718.39       670094.1E+5         10       634.42       39053.07       17436.00       241737.7E+4         10       634.03       0353.07       17436.00       24137.7E+4         10       812.76       23053.07       17436.00       241737.7E+4         10       834.22       1380.72       3210.74       86713.99         13       1718.24       1836.37       17436.03       34781.02         16       1316.70       25530.44       382.77       13574.33E+3         16       1380.11       2564.59       794820.6E+2<	$2 E + 2$ $4 E + 2$ $1.409 \pm 0.300$ $88.42$ $0.637 \pm 0.198$ $1.1E + 5$ $0.637 \pm 0.198$ $1.1E + 4$ $1.104 \pm 0.216$	100.00 62.11 6.52 16.35 46.91	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	10554.27 8305.61 E + 5 709.99 267.51 6890.21 947.14 537.36 2357.10 80755.46 9991.83 3617.9 E + 4 34879.06 34879.06 51 3700 E + 3	$0.650 \pm 0.163$ 1.159 $\pm 0.184$	100.00 10.18 0.79 1.37
6         297.45         24083.14           143.88         821.99         13901.24         17759.4 E + 2           8         478.88         821.99         13901.24         17759.4 E + 2           9         478.88         3887.65         3887.65           9         4560.94         46782.54         23188.42           9         4560.94         46782.554         24578.24           10         1819.18         24718.39         670094.1E + 5           10         1819.18         245542.43         245542.43           10         1319.10         17436.00         241737.7E + 4           634.42         39053.07         17436.00         241737.7E + 4           10         534.03         39053.07         17436.00         241737.7E + 4           13         1718.24         180.72         3210.74         86713.99           13         1718.24         1836.37         13574.33E + 3           16         1357.08         14704.21         5564.59         794820.6 E + 2           16         1380.11         22655.88         2056.57         2056.57	$\begin{array}{c} 4 \ \mathrm{E} + 2 \\ 4 \ \mathrm{E} + 2 \\ 1.409 \pm 0.300 \\ 88.42 \\ 8.42 \\ 0.637 \pm 0.198 \\ 1.1\mathrm{E} + 5 \\ 0.603 \pm 0.174 \\ 7.7\mathrm{E} + 4 \\ 1.104 \pm 0.216 \end{array}$	100.00 62.11 6.52 16.35 46.91	7.55 0.50 22.47 74.16 37.16 120.72 956.81 415.36 6198.24 552.31 270.99 1950.18	709.99 267.51 6890.21 947.14 537.36 2357.10 80755.46 9991.83 3617.9 E + 4 34879.06 34879.06	$0.650 \pm 0.163$ $1.159 \pm 0.184$	100.00 10.18 0.79 1.37
143.88       821.99       13901.24       17759.4 E + 2         8       478.88       3887.65       3887.65         9       478.09       13901.25       1781.54       23188.42         9       4560.94       467825.54       23188.42         10       1230.85       533737.12       24718.39       670094.1E + 5         10       1230.85       533737.12       24718.39       670094.1E + 5         10       634.42       39053.07       17436.00       241737.7E + 4         10       634.42       39053.07       17436.00       241737.7E + 4         10       634.42       1380.72       3210.74       86713.99         13       1718.24       183.6.37       13554.33       4376.39         16       1316.70       25530.44       386.2.77       13574.33E + 3         16       1356.30       14704.21       5564.59       794820.6 E + 2         16       1380.11       22655.88       2000.000000000000000000000000000000000	$\begin{array}{c} 4 \ E + 2 \\ 88.42 \\ 88.42 \\ 0.637 \pm 0.198 \\ 4.1E + 5 \\ 0.603 \pm 0.174 \\ 7.7E + 4 \\ 1.104 \pm 0.216 \end{array}$	62.11 6.52 16.35 46.91	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	267.51 6890.21 947.14 537.36 2357.10 80755.46 9991.83 3617.9 E + 4 34879.06 *106.51 3700 E + 3	$1.159 \pm 0.184$	10.18 0.79 1.37
8         478.88         3887.65           9         478.88         3887.65           9         4560.94         810.25         1781.54         23188.42           9         4560.94         467825.54         467825.54           10 a         1819.18         242542.43         670094.1E + 5           10 a         1819.18         242542.43         67004.1E + 5           10 a         1819.18         242542.43         9175.48           10 b         634.42         39053.07         17436.00         241737.7E + 4           10 b         634.03         39073.07         17436.00         241737.7E + 4           11 b         634.03         39073.07         17436.00         241737.7E + 4           13 ft         234.03         3176.54         3867.17         1356.37           13 ft         817.76         25530.44         3862.77         1356.37         34781.02           16 b         1380.11         5564.59         794820.6 E + 2         2056.58           16 b         1880.11         2056.58         2056.58         2056.58	$88.42   1.409 \pm 0.300   88.42   0.637 \pm 0.198   1.1E + 5   0.603 \pm 0.174   7.7E + 4   1.104 \pm 0.216   1.104 $	62.11 6.52 16.35 46.91	74.16 37.16 120.72 956.81 415.36 6198.24 552.31 270.99 1950.18	947.14 537.36 2357.10 80755.46 9991.83 3617.9 E + 4 34879.06 610.6 51 3700 E + 3	$1.159 \pm 0.184$	10.18 0.79 1.37
320.11         810.25         1781.54         23188.42           9         4560.94         467825.54         2458.53           10 a         11230.85         533737.12         24718.39         670094.1E + 5           10 a         1819.18         242542.43         242542.43           10 a         1819.18         242542.43         247542.43           10 b         634.42         39053.07         17436.00         241737.7E + 4           10 b         634.03         317436.00         241737.7E + 4           13         384.22         1380.72         3210.74         86713.99           13         1718.24         1836.37         13574.33E + 3         34721.02           16 a         1316.70         34721.02         34731.02         34731.02           16 b         1380.11         5564.59         794820.6 E + 2         366.37	$88.42 \\ 0.637 \pm 0.198 \\ 1.1E + 5 \\ 0.603 \pm 0.174 \\ 7.7E + 4 \\ 1.104 \pm 0.216 \\ 1.004 \pm 0.204 $	6.52 16.35 46.91	37.16 120.72 956.81 415.36 6198.24 552.31 270.99 1950.18	537.36 2357.10 80755.46 9991.83 3617.9 E + 4 34879.06 610.6 51 3770.0 E + 3		0.79 1.37
9         4560.94         467825.54           10 a         1230.85         533737.12         24718.39         670094.1E + 5           10 a         1819.18         242542.43         5377.7E + 4           10 b         634.42         39053.07         17436.00         241737.7E + 4           10 b         634.03         39053.07         17436.00         241737.7E + 4           10 b         634.03         39053.07         17436.00         241737.7E + 4           11 b         634.03         39053.07         17436.00         241737.7E + 4           13         384.22         1380.72         3210.74         86713.99           13         1718.24         18366.37         13574.33E + 3           16 a         1316.70         34721.02         34781.02           16 b         5564.59         794820.6 E + 2         2055.58	$\begin{array}{c} 0.637 \pm 0.198 \\ 1.1E + 5 \\ 0.603 \pm 0.174 \\ 7.7E + 4 \\ 1.104 \pm 0.216 \end{array}$	6.52 16.35 46.91	956.81 415.36 6198.24 552.31 270.99 1950.18	80755.46 9991.83 3617.9 E + 4 34879.06 6 1 3700 E + 3		0.79 1.37
1230.85       533737.12       24718.39       670094.1E + 5         10 a       1819.18       242542.43         10 b       634.42       39053.07       17436.00       241737.7E + 4         10 b       634.42       39053.07       17436.00       241737.7E + 4         10 b       634.03       39053.07       17436.00       241737.7E + 4         11 b       634.03       39053.07       17436.00       241737.7E + 4         12 334.22       1380.72       3210.74       86713.99         13       1718.24       1836.37       1836.37         13       1718.24       18366.37       13574.33E + 3         16 a       1316.70       34731.02       34781.02         16 b       1380.11       5564.59       794820.6 E + 2         16 b       1880.11       2665.88       20045.665.88	$\begin{array}{c} 1.1 \mathrm{E} + 5 \\ 0.603 \pm 0.174 \\ 7.7 \mathrm{E} + 4 \\ 1.104 \pm 0.216 \end{array}$	16.35 46.91	415.36 6198.24 552.31 270.99 1950.18	9991.83 3617.9 E + 4 34879.06 6106 61 3070 E + 3	$0.665 \pm 0.170$	1.37
10 a         1819.18         242542.43           634.42         39053.07         17436.00         241737.7E + 4           10 b         634.42         39053.07         17436.00         241737.7E + 4           384.22         33053.07         17436.00         241737.7E + 4           13         634.03         3015.48         86713.99           13         1718.24         18366.37         13574.33E + 3           16 a         1316.70         34781.02         34781.02           16 b         537.08         14704.21         5564.59         794820.6 E + 2           16 b         530.01         1201.02         5564.59         794820.6 E + 2	$0.603 \pm 0.174$ 7.7E + 4 1.104 \pm 0.216	16.35 46.91	552.31 270.99 1950.18	34879.06 6106.51 3070.0 E ± 3		1.37
634.42         39053.07         17436.00         241737.7E + 4           10 b         634.03         9175.48         9175.48           384.22         1380.72         3210.74         86713.99           13         1718.24         18366.37         13574.33E + 3           16 a         1316.70         3862.77         13574.33E + 3           16 b         637.08         14704.21         5564.59         79482.06 E + 2	7.7E + 4 1.104 ± 0.216	46.91	270.99 1950.18	$610651$ $3070.0 E \pm 3$	$0.712 \pm 0.166$	
10 b         634.03         9175.48           13         384.22         1380.72         3210.74         86713.99           13         1718.24         18366.37         13574.33E + 3           16 a         1316.70         3862.77         13574.33E + 3           16 b         1316.70         34781.02         34781.02           16 b         1880.11         22665.88         2000.000000000000000000000000000000000	$1.104 \pm 0.216$	46.91		01700,01 ULV ULV ULV ULV		
384.22         1380.72         3210.74         86713.99           13         1718.24         18366.37         1356.37           817.76         25530.44         3862.77         13574.33E + 3           16 a         1316.70         34781.02         34781.02           637.08         14704.21         5564.59         794820.6 E + 2           16 b         2000.11         20065.88         2000.10			22.43	1848.97	$0.669 \pm 0.155$	33.67
13         1718.24         18366.37           13         817.76         25530.44         3862.77         13574.33E + 3           16 a         1316.70         34781.02         34781.02           16 b         637.08         14704.21         5564.59         794820.6 E + 2           16 b         1880.11         22665.88         2000.000000000000000000000000000000000	13.99		4.23 51.65	624.51 23375.71		
817.76 25530.44 3862.77 13574.33E + 3 16 a 1316.70 34781.02 637.08 14704.21 5564.59 794820.6 E + 2 16 b 2000.11 22665.88	$1.246 \pm 0.399$	17.31	57.70	4007.74	$0.696 \pm 0.152$	13.09
<b>16 a</b> 1316.70 34781.02 637.08 14704.21 5564.59 794820.6 E + 2 <b>16 b</b> 1880.11 22665.88	33E + 3		19.65 116.85	1221.08 61646.70		
637.08 14704.21 5564.59 794820.6 E + 2 <b>16 b</b> 1880.11 22665.88	$0.901 \pm 0.288$	22.59	543.03	13660.49	$0.915 \pm 0.264$	1.39
<b>16 b</b> 1880.11 22665.88	1.6 E + 2		300.70 1612.06	3247.73 19356.07 E + 2		
	$1.185 \pm 0.365$	15.82	159.76	8354.93	$0.746 \pm 0.156$	4.73
07.8600/86 C1.828.1 20311./0 4828.13 98/0098.20	698.26		78.22 326.86	2323.73 14987.5 E + 1		
17 857.31 5603.68	$1.572 \pm 0.506$	34.70	738.13	47716.23	$0.708 \pm 0.222$	1.02
504.63 5516.62 1743.43 818573.91	573.91		266.24 21445.37	4250.20 91425.0 E + 4		
<b>18</b> 1458.22 24082.45	$1.052 \pm 0.340$	20.40	776.67	41589.81	$0.741 \pm 0.174$	0.97
674.49 22760.43 4258.44 41313.4 E + 3	4 E + 3		374.22 3236.19	7170.42 41455.0 E + 2		
<b>19</b> 796.20 17730.42	$0.951 \pm 0.306$	37.36	662.16	57693.00	$0.661 \pm 0.203$	1.14
322.22 16114.75 2597.19 604112.8E + 3	2.8E + 3		252.48 12090.41	5141.07 70871.0 E + 4		
Pyridaben 670.21 8182.54	$1.179 \pm 0.315$	44.38	119.74	1307.28	$1.235 \pm 0.268$	6.31
343.30 4276.62 1916.98 755943.21	43.21		78.73 198.56	561.53 9500.72		

Compound	LC <sub>50</sub> (ppm) and confidence limits at 95	% LC <sub>90</sub> (ppm) and confidence limits at 95%	Slope ± SE	Toxicity index		
3	626.03	4382.83	$1.516 \pm 0.190$	3.08		
	521.05 748.96	2913.78 8415.70				
5	1899.00	12465.36	$1.568 \pm 0.221$	1.02		
	1478.18 2826.25	6704.14 36624.21				
6	1548.34	16059.88	$1.262 \pm 0.390$	1.25		
	1004.06 6921.27	4581.85 24744.8 E + 2				
8	14335.87	680094.08	$0.765 \pm 0.191$	0.14		
0	5700.43 191426.74	78354.19 346831.6 E + 3	0.400	- 0		
9	380.64	27001.65	$0.692 \pm 0.187$	5.07		
10 -	15/.82 56/.4/	/350.55 1/1//90.61	2.052 . 0.221	6.09		
10 a	317.38 266.19 274.92	1006 15 2027 54	$2.055 \pm 0.251$	0.08		
10 h	1639 50	1000.15 2057.54	$0.872 \pm 0.103$	1 18		
10.0	1173 68 2613 61	19843 63 196961 60	$0.072 \pm 0.105$	1.10		
13	1285 59	8489 56	$1.563 \pm 0.213$	1.50		
	1020.30 1770.99	4883.21 21533.92				
16 a	420.34	1684.16	$2.126 \pm 0.251$	4.59		
	352.22 496.90	1262.76 2603.36				
16 b	3635.46	207969.41	$0.729 \pm 0.093$	0.53		
	2274.19 7520.87	61213.97 1558421.68				
17	4742.98	71726.12	$1.086 \pm 0.179$	0.41		
	3417.17 8325.57	28203.40 433781.21				
18	701.40	5741.72	$1.404 \pm 0.263$	2.75		
	523.72 940.08	3115.06 20354.85				
19	11015.69	126830.85	$1.208 \pm 0.239$	0.18		
<b>D</b>	6271.33 36596.40	37738.58 19072.10 E + 2	1 105 0 005	100.00		
Pyridaben	19.29	265.58	$1.125 \pm 0.325$	100.00		
	1.37 42.41	1/2.19 /58.46				

 Table 2

 Toxicity of 1.2.4-triazines derivatives against 24 h old eggs of *T. urticae*.

\*Pyridaben was used as reference acaricide in the tests

Acaricidal activity. The acaricidal properties of the new series of 1,2,4-triazine derivatives against eggs and adult females of T. urticae using the leaf-dip technique are shown in Tables 1 and 2. Comparing the toxicity indexes at LC50 values for adult females after 24 h of exposure (Table 1), the tested compounds can be classified according to their toxic action into two main groups: the first group included the most toxic compounds in the series, 6, 8, and 10b and then the standard pyridaben and the second group included the least active compounds 19, 17, 16a, 18, 3, 5, 13, 10a, 16b, and 9. Of the tested 13 compounds that significantly showed adulticide activity on the basis of toxicity index against T. urticae after 72 h of exposure, four (6, 10b,13, 8, and then the standard pyridaben) followed by nine less active compounds 3, 16b, 5, 16a, 10a, 19, 17, 18, and 9.

The susceptibility of 24 h old egg stage of *T. urticae* (Table 2) to the same series of synthesized compounds showed that the standard **pyridaben** exhibited a high degree of efficiency followed by **10a**, **9**, **16a**, **3**, **18**, **13**, **6**, **10b**, **5**, **16b**, **17**, **19**, and **8**, the lowest activity. The LC<sub>50</sub> values of compounds were 43.36, 317.58, 380.64, 420.34, 626.03, 701.40, 1285.59, 1548.34, 1639.50, 1899.00, 3635.46, 4742.98, 11,015.69, and 14,335.87, respectively.

The analysis of the relationships of 1,2,4-triazines derivatives structures to its effects as miticidal properties revealed that the nature and position of the substituents were important. Compound **6** was superior to the standard **pyridaben**; also, compounds **8** and **10b** were the most significantly toxic than the standard one against adult females after 24 h of treatment. This may be attributed to the fused and/or infused mercapto 1,2,4-triazines active methylene, which appear in each active previously mentioned compound. Moreover, the presence of electron-withdrawing groups found to enhance the pesticidal activity [22]. So, the active methylene component with chlorine substitution **6** was the most potent, followed by the cyano substitution **8** and then the acetate substitution **10b**.

The structure/ovicidal activity relationships differed somewhat from those obtained by the adulticidal one. The ovicidal properties were remarkably observed in mercapto 1,2,4-triazines containing (N–NH<sub>2</sub> group) such as compounds **10a** and **3**, also compounds containing imino group **9** and (N–NH– group) **16a** in addition to unfused 1,2,4-triazines containing (N–NH<sub>2</sub> and hydrazine groups) **13** [22].

The results obtained from these laboratory studies have shown the acaricidal properties of 1,2,4-triazines derivatives compared with pyridaben against *T. urticae*. Three of these compounds may be investigated practically in the field after its toxicity application to mammalians.

### CONCLUSIONS

Design and synthesis of 1,2,4-triazine derivatives had a great demand because of their biological interest, especially as pesticides. The results showed significant achievements in the synthesis of a new series of 1,2,4-triazine derivatives and its investigations as acaricides against *T. urticae* (Koch). Structure–activity relationship of the most effective 1,2,4-triazine derivatives was analyzed and laid pillars to structure modification of more new 1,2,4-triazine derivatives.

# EXPERIMENTAL

Gallenkamp electric melting point apparatus. General. Elemental analyses were carried out at Micro Analytical Center, Faculty of Science, Cairo University. IR spectra were recorded (KBr), ( $\circ$  cm<sup>-1</sup>) on a Mattson 5000 FTIR Spectrophotometer at Micro Analytical Center Faculty of Science, Mansoura University. The <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were measured on a Varian Spectrophotometer at 300 and 75 MHz, respectively. Using TMS as an internal reference and DMSO- $d_6$  as solvent at Chemistry Department, Faculty of Science, Cairo University. The chemical shifts ( $\delta$ ) are reported in parts per million and were referenced to the residual solvent peak. Mass spectra were recorded on (Kratos, 70 eV) MS equipment and/or a Varian MAT 311A Spectrometer, at Micro Analytical Center, Faculty of Science, Cairo University. Reaction mixtures were monitored by thinlayer chromatography (TLC) using EM science silica gel coated plates with visualization by irradiation with ultraviolet lamp. Pyridaben 20% WP (2-tert-butyl-5-(4-tertbutyl-benzylthio)-4-chloropyridazin-3(2*H*)-one) was obtained in a formulated form, and the dosages were calculated on the basis of parts per million of active ingredient. All melting points are in degree centigrade (uncorrected) and were determined on.

Synthesis of target compounds. Synthesis of 4-amino-6-benzyl-3-mercapto-1,2,4-triazine-5(4H)-one (3). *Method a.* A mixture of azalactone 1 (1.87 g, 10 mmol) in warm aq. ethanol 50% (18 mL) and thiocarbohydrazide 2 (1.06 g, 10 mmol) in warm water (18 mL) was refluxed for 4 h. A binary solid mixture was separated upon cooling by filtration and further purified by column chromatography (petroleum ether/ethyl acetate 4:1) to afford 3 and 4.

*Method b.* A solution of phenyl pyruvic acid **3c** (1.64 g, 10 mmol) in ethanol (20 mL) was dropwise

added to a solution of thiocarbahydrazide 2 (1.06 g, 10 mmol) in warm water (30 mL). The reaction mixture was refluxed on a water bath for 1 h. The solid that precipitated on hot was filtered off, dried, and recrystallized in ethanol to afford pure compound 3.

### 4-Amino-6-benzyl-3-mercapto-1,2,4-triazine-5(4H)-one

(3). White crystals (1.9 g, 85%); m.p 205–206°C (lit. yield 78%), (lit. m.p 204–205 [8], 195–198°C [9]); R<sub>f</sub> = 0.37 ]pet. ether/ethyl acetate (4:1)[. IR (KBr): v/cm<sup>-1</sup> = 3298, 3209 (NH<sub>2</sub>), 1686 (C=O amide). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) = 2.51 (s, 1H, SH), 3.91 (s, 2H, CH<sub>2</sub>-Ph), 6.57 (s, 2H, NH<sub>2</sub>), 7.22–7.32 (m, 5H, H–Ar). <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) = 36.34 (1C, CH<sub>2</sub>Ph), 127.11 (1C, C<sub>Ar</sub>), 128.88 (2CH, C<sub>Ar</sub>), 129.67 (2CH, C<sub>Ar</sub>), 136.83 (1C, C=O). <sup>13</sup>C-NMR (DEPT-135, DMSO-*d*<sub>6</sub>)  $\delta$  = 35.54 (1C, CH<sub>2</sub>). Elemental analysis: found: C, 51.25; H, 4.01; N, 23.94%. Calcd for C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>OS (234.06): C, 51.27; H, 4.30; N, 23.92%.

Thiocarbohydrazide acetic acid (4). White crystals (0.25 g, 15%); m.p 230–232°C.  $R_f = 0.45$  ]pet. ether (60:80)/ethyl acetate (4:1)[; IR (KBr): v/cm<sup>-1</sup> = 3271, 3177 (NH<sub>2</sub>), 3098 (NH), 1715 (COOH). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>) δ (ppm) = 2.24 (s, 3H, CH<sub>3</sub>), 3.33 (s, 4H, 2NH<sub>2</sub>), 5.5 (s, 2H, 2NH), 8.4 (S, 1H, OH). <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>) δ (ppm) = 10.39 (1C, CH<sub>3</sub>), 149.10 (C=O), 165.37 (C=S); MS (EI, 70 eV) *m*/*z* (%) = 166 (4.1), 165 (10.1), 150 (9.3), 149 (9.7), 135 (7.2), 133 (10.9), 121 (12.1), 106 (5.3), 90 (20.3), 89 (20.4), 78 (24.1), 62 (14.5), 46 (36.4), 45 (82.4). Elemental analysis: found: C, 21.66; H, 6.05; N, 33.73%. Calcd for C<sub>3</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S (166.06): C, 21.68; H, 6.07; N, 33.71%.

**3-Benzyl-8-phenyl-7-thioxo-7,8-dihydro-1,2,4-triazolo[5,1***c*]**1,2,4-triazin-4(6***H***)-one (5). A mixture of triazine <b>3** (0.5 g, 2.1 mmol) and phenyl isothiocyanate (0.37 mL, 3.15 mmol) in DMF 10 mL with  $K_2CO_3$  (0.6 g) was stirred overnight. The reaction mixture was cooled and then poured onto crushed ice. The formed precipitate was collected by filtration and recrystallized in ethanol/dioxan (1:2) to afford **5**.

White powder (0.67 g, 93%); m.p 260–262°C.  $R_f = 0.24$ [pet. ether (60:80)/ethyl acetate (4:2)]. IR (KBr): v/cm<sup>-1</sup> = 3192 (NH), 1675 (C=O amide). <sup>1</sup>H-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 4.12 (s, 2H, CH<sub>2</sub>-Ph), 7.10–7.61 (m, 10H, H—Ar), 10.87 (s, 1H, NH). MS (EI, 70 eV) *m/z* (%) = 336 (M<sup>+</sup> + 1, 1.6), 260 (4.3), 161 (11.1), 152 (2.5), 150 (2.44), 136 (25.0), 117 (24.7), 104 (24.1), 91 (70.3), 77 (99.4), 53 (16.8), 50 (100.0). Elemental analysis: found: C, 60.85; H, 3.94; N, 20.90%. Calcd for C<sub>17</sub>H<sub>13</sub>N<sub>5</sub>OS (335.08): C, 60.88; H, 3.91; N, 20.88%.

**3-Benzyl-7-(chloromethyl)-4H-[1,3,4]thiadiazolo[2,3-***c*] [1,2,4]triazin-4-one (6). A mixture of triazine 1 (0.5 g, 2.14 mmol) and mono chloroacetic acid (0.2 mL, 2.14 mmol) in phosphorus oxychloride (7.5 mL) was refluxed for 12 h over a water bath. The reaction mixture was cooled and poured onto crushed ice. The resulting solid was filtered off and washed with aqueous (2%) sodium bicarbonate solution till neutralize at pH 7 and then water (30 mL). It was dried and recrystallized in ethanol to yield **6**.

Yellow powder (0.5 g, 80%); m.p 225–227°C.  $R_f = 0.45$ ] pet. ether (60:80)/ethyl acetate (4:1)[. IR (KBr): v/cm<sup>-1</sup> = 1697 (C=O). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm): 4.327 (s, 2H, CH<sub>2</sub>—Ph), 4.823 (s, 2H, CH<sub>2</sub>—Cl), 7.259–7.486 (m, 5H, H—Ar). <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  36.264 (1C, CH<sub>2</sub>Ph), 58.437 (1C, CH<sub>2</sub>Cl), 126.110 (1CH, C<sub>Ar</sub>), 128.781 (2CH, C<sub>Ar</sub>), 129.016 (2CH, C<sub>Ar</sub>), 142.850 (1C, C<sub>Ar</sub>), 152.810 (1C, C-3), 153.705 (1C, C-6), 160.842 (1C, C-3), 165.467 (1C, CO); MS (EI, 70 eV) *m/z* (%) = 292/294 (M<sup>+</sup>, 100.0/83.7), 217 (23.8), 117 (61.5), 91 (54.3), 78 (8.5), 77 (57.1), 76 (18.5), 75 (13.4), 52 (10.9), 50 (22.4). Elemental analysis: found: C, 49.22; H, 3.08; N, 19.13%. Calcd for C<sub>12</sub>H<sub>9</sub>ClN<sub>4</sub>OS (292.02): C, 49.24; H, 3.10; N, 19.14%.

**7-((1***H***-benzo[***d***]imidazol-2-ylthio)methyl)-3-benzyl-4***H***-<b>1,3,4-thiadiazolo[2,3-***c***]1,2,4-triazin-4-one (7).** A mixture of **6** (0.5 g, 2.14 mmol) and 1*H*-benzo[*d*]imidazole-2-thiol (0.1 g, 2.14 mmol) in ethanol (15 mL) was refluxed for 6 h; the precipitate that formed on hot was separated by filtration and recrystallized in ethanol to afford 7.

Yellow powder (0.8 g, 92%); m.p 191–192°C.  $R_f = 0.15$ [pet. ether (60:80)/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 3144 (NH), 1714 (C=O amide). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) = 4.13 (s, 2H, CH<sub>2</sub>-Ph), 4.98 (s, 2H, CH<sub>2</sub>-S), 7.15–7.60 (m, 9H, H–Ar), 12.81 (s, 1H, NH). MS (EI, 70 eV) *m/z* (%) = 406 (M<sup>+</sup>, 20.07), 373 (1.5), 346 (1.0), 289 (5.6), 266 (4.1), 257 (16.8), 219 (67.3), 209 (0.57), 207 (12.5), 199 (12.1), 187 (29.2), 175 (9.1), 164 (1.05), 162 (27.9), 131 (27.7), 123 (100.0), 110 (3.5), 77 (50.01), 65 (86.9), 51 (70.8). Elemental analysis: found: C, 56.11; H, 3.49; N, 20.66%. Calcd for C<sub>19</sub>H<sub>14</sub>N<sub>6</sub>OS<sub>2</sub> (406.48): C, 56.14; H, 3.47; N, 20.68%.

**2-((4-Amino-6-benzyl-5-oxo-4,5-dihydro-1,2,4-triazin-3-yl) thio)acetonitrile (8)** and 7-amino-3-benzyl-4*H*,8*H*-1,2,4-triazino[3,4-*b*]1,3,4-thiadiazin-4-one (9). A mixture of triazine **3** (0.5 g, 2.14 mmol) and chloroacetonitrile (0.2 mL, 3.16 mmol) in dioxan (15 mL) was refluxed for 5 h in the presence of TEA (0.6 mL, 8.30 mmol), cooled to room temperature, and poured onto crushed ice. The precipitate that formed the two components was separated by PTLC silica gel (eluent:petroleum ether/ethyl acetate 4:1).

**Compound 8.** Brown powder (0.30 g, 53%); m.p 290–293°C.  $R_f = 0.30$  [pet. ether (60:80)/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 3445, 3320 (NH<sub>2</sub>), 2249 (CN), 1687 (C=O amide). <sup>1</sup>H-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 3.94 (s, 2H, CH<sub>2</sub>-Ph), 5.48 (s, 2H, CH<sub>2</sub>-S), 6.48 (s, 2H, NH<sub>2</sub>), 7.21–7.32 (m, 5H, H-Ar). <sup>13</sup>C-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 17.10 (1C, CH<sub>2</sub>-S), 35.75 (1C,

CH<sub>2</sub>—Ph), 114.36 (CN), 126.50 (1C, C<sub>Ar</sub>), 128.98 (2CH, C<sub>Ar</sub>), 129.05 (2CH, C<sub>Ar</sub>), 135.59 (1C, C<sub>Ar</sub>), 146.68 (1C, C<sub>6</sub>), 147.38 (1C, C<sub>3</sub>), 168.13 (1C, C=O); MS (EI, 70 eV) m/z (%) = 273 (M<sup>+</sup>, 62.2), 257 (24.3), 233 (14.2), 219 (2.7), 217 (8.7), 201 (8.9), 198 (11.1), 175 (6.0), 160 (5.3), 146 (7.5), 144 (26.4), 117 (100.0), 104 (11.9), 103 (61.5), 91 (95.9), 65 (9.8), 53 (7.9), 51 (45.0). Elemental analysis: found: C, 52.70; H, 4.09; N, 25.60%. Calcd for C<sub>12</sub>H<sub>11</sub>N<sub>5</sub>OS (273.31): C, 52.73; H, 4.06; N, 25.62%.

**Compound 9.** Gray powder (0.24 g, 41%); m.p 91– 92°C.  $R_f = 0.22$  [pet. ether/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 3445, 3320 (NH<sub>2</sub>), 1679 (C=O amide). <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  (ppm) = 3.93 (s, 2H, CH<sub>2</sub>-Ph), 4.13 (s, 2H, CH<sub>2</sub>-S), 4.78 (S, 2H, NH<sub>2</sub>), 7.22–7.39 (m, 5H, H-Ar). MS (EI, 70 eV) *m/z* (%) = 273 (M<sup>+</sup>, 48.7), 257 (2.7), 233 (1.5), 188 (34.9), 118 (8.9), 117 (37.0), 91 (100.0), 76 (54.2), 53 (7.1), 50 (25.3). Elemental analysis: found: C, 52.71; H, 4.03; N, 25.59%. Calcd for C<sub>12</sub>H<sub>11</sub>N<sub>5</sub>OS (273.31): C, 52.73; H, 4.06; N, 25.62%.

Synthesis of S-alkyl and N-alkyl triazines 10a,b and 11a,b. General procedure. *Method a.* Triazine 3 (10 mmol) was dissolved in cold methanolic sodium methoxide solution [prepared from sodium metal (0.23 g, 10 mmol) and 10-mL methanol], and then, either methyl iodide (10 mmol) or ethyl bromoacetate (10 mmol) was added. The reaction mixture was stirred at room temperature. The precipitate obtained was collected by filtration, washed with water, and dried at room temperature to give 10a,b and 11a,b.

*Method b.* A mixture of triazine **3** (0.5 g, 2.14 mmol), methyl iodide (0.13 mL, 2.14 mmol), or ethyl bromoacetate (0.24, 2.14 mmol) in EtOH/DMF mixture (1:1) (10 mL) in the presence of either fused sodium acetate (0.3 g, 3.21 mmol) or Et3N (0.45 mL, 3.21 mmol) was stirred at room temperature. The reaction mixture was monitored by TLC and then poured into cold water. The precipitate that formed was filtered off, washed with water (10 mL), and dried at room temperature to give **10a,b** and **11a,b**.

# 4-Amino-6-benzyl-3-(methylthio)-1,2,4-triazin-5(4H)-one (10a). RX=CH\_3I

White crystal (0.39 g, 75%); m.p 195–196°C [lit. m.p. 196–198°C [18]].  $R_f = 0.24$  [pet. ether/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 3308, 3260 (NH<sub>2</sub>), 1687 (C=O).

# 4-Amino-6-benzyl-2-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2H)-one (11a). $RX=CH_3I$

White crystal (0.06 g, 12%); m.p 110°C. Rf = 0.15 [pet. ether/ethyl acetate (4:1)]. IR (KBr):  $v/cm^{-1}$  = 3305, 3258 (NH2), 1687 (C=O amide), 1162 (C=S); MS (EI, 70 eV) m/z (%) = 248 (M+, 77.3), 231 (19.4), 230 (28.1), 221 (2.6), 204 (2.1), 188 (11.1), 173 (1.2), 160 (4.2), 149 (10.9), 145 (10.9), 131 (3.7), 117 (13.9), 116 (28.1), 103

# (9.1), 102 (12.8), 91 (100.0), 77 (13.8), 53 (3.4), 50 (6.8). Elemental analysis: found: C, 53.19; H, 4.90; N, 22.53%. Calcd for C11H12N4OS (248.07): C, 53.21; H, 4.87; N, 22.56%.

# Ethyl-2-(4-amino-6-benzyl-5-oxo-4,5-dihydro-1,2,4-triazin-3-ylthio)acetate (10b). RX=Br-CH<sub>2</sub>-COOEt

White flakes (0.65 g, 82%); m.p  $130-131^{\circ}$ C [ethanol]. Rf = 0.26 [pet. ether/ethyl acetate (4:2)]. IR (KBr): v/cm<sup>-1</sup> = 3323, 3258 (NH2), 1739 (COO), 1691 (C=O amide). <sup>1</sup>H-NMR (CDCl3)  $\delta$  (ppm) = 1.30 (t, 3H, CH3), 3.99 (s, 2H, CH2–Ph), 4.06 (s, 2H, CH2), 4.28 (q, 2H, CH2–CH3), 4.82 (s, 2H, NH2), 7.19–7.40 (m, 5H, H–Ar). MS (EI, 70 eV) *m/z* (%) = 321 (M<sup>+</sup> + 1, 26.9), 305 (2.1), 292 (1.0), 275 (16.7), 259 (2.1), 247 (33.7), 230 (13.2), 219 (14.7), 198 (1.3), 174 (3.6), 160 (2.7), 144 (18.8), 130 (49.8), 119 (13.5), 117 (45.9), 102 (32.8), 91 (100.0), 77 (40.9), 73 (27.4), 53 (10.1), 50 (41.3), 45 (77.1). Elemental analysis: found: C, 52.52; H, 5.06; N, 17.46%. Calcd for C14H16N4O3S (320.09): C, 52.49; H, 5.03; N, 17.49%.

## Ethyl-2-(4-amino-6-benzyl-5-oxo-3-thioxo-4,5-dihydro-1,2,4-triazin-2(3*H*)-yl)acetate (11b). RX=Br-CH<sub>2</sub>-COOEt

Pale yellow powder (0.1 g, 15%); m.p 152-153°C. [Separated by pet. ether].  $R_f = 0.5$  [pet. ether (60:80)/ ethyl acetate (4:1.5)]. IR (KBr):  $v/cm^{-1} = 3310, 3219$ (NH<sub>2</sub>), 1742 (COO), 1687 (C=O amide), 1177 (C=S). <sup>1</sup>H-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 1.20 (t, 3H, CH<sub>3</sub>), 3.97 (s, 2H, CH<sub>2</sub>-Ph), 4.19 (q, 2H, CH<sub>2</sub>-CH<sub>3</sub>), 5.17 (s, 2H, CH<sub>2</sub>), 6.63 (s, 2H, NH<sub>2</sub>), 7.23–7.29 (m, 5H, Ar–H). <sup>13</sup>C-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 13.92 (1C, CH<sub>3</sub>-CH<sub>2</sub>), 35.85 (1C, CH<sub>2</sub>Ph), 59.05 (1C, CH<sub>2</sub>-COO), 61.33 (1C, CH<sub>2</sub>-CH<sub>3</sub>), 126.73 (1CH, C<sub>Ar</sub>), 128.27 (2CH, C<sub>Ar</sub>), 128.81 (2CH, CAr), 135.87 (1C, CAr), 145.78,147.15 (1C, C<sub>6</sub>), 147.15 (1C, C<sub>3</sub>), 166.53 (1C, C=O), 168.68 (1C, COO–). MS (EI, 70 eV) m/z (%) = 321 (M<sup>+</sup> + 1, 1.0), 320 (2.7), 260 (1.0), 244 (1.0), 218 (4.6), 117 (16.1), 116 (24.3), 105 (61.8), 104 (27.2), 103 (31.4), 91 (100.0), 88 (4.4), 87 (2.1), 78 (12.3), 77 (82.7), 74 (3.3), 73 (2.3), 68 (15.5), 62 (15.6), 61 (5.7), 58 (11.3), 55 (12.4), 53 (6.5), 51 (23.3), 50 (11.7), 45 (18.7), 43 (42.9). Elemental analysis: found: C, 52.46; H, 5.00; N, 17.51%. Calcd for C<sub>14</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>S (320.09): C, 52.49; H, 5.03; N, 17.49%.

**Formation of hydrazinyl-1,2,4-triazine derivatives 12** and **13**. A solution of compound **10b** (0.46 g, 1 mmol) in ethanol (50 mL) and hydrazine hydrate 98% (0.2 mL, 4 mmol) was added. The reaction mixture was refluxed for 1 h. The precipitate, which formed on hot, was separated by filtration and recrystallized to afford **12**, and the filtrate was cooled to afford **13**.

### 3-Benzyl-7-hydrazinyl-4H,8H-1,2,4-triazino[3,4-b]1,3,4-

thiadiazin-4-one (12). Pale yellow (0.24 g, 35%); m.p 295–297°C. [DMF:EtOH (2:1)].  $R_f = 0.33$  [pet. ether/ethyl acetate (4:3)]. IR (KBr): v/cm<sup>-1</sup> = 3330, 3282

(NH<sub>2</sub>), 3184 (NH), 1686 (C=O). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ (ppm) = 3.81 (s, 2H, CH<sub>2</sub>-Ph), 3.92 (s, 2H, CH<sub>2</sub>), 5.55 (s, 2H, NH<sub>2</sub>), 6.06 (s, 1H, NH), 7.19–7.28 (m, 5H, Ar-H); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) = 35.52 (1C, CH<sub>2</sub>-S), 36.40 (1C, CH<sub>2</sub>-Ph), 126.13 (1CH, C<sub>Ar</sub>), 128.15 (2CH, C<sub>Ar</sub>), 128.69 (2CH, C<sub>Ar</sub>), 137.31 (1C, C<sub>Ar</sub>), 147.48 (1C, C<sub>6</sub>), 148.55 (1C, C<sub>3</sub>), 168.142 (1C, C=O). MS (EI, 70 eV) *m/z* (%) = 288 (M<sup>+</sup>, 3.1), 257 (5.6), 230 (6.4), 232 (16.5), 218 (26.8), 219 (10.9), 215 (10.9), 188 (32.7), 185 (18.6), 172 (20.1), 171 (36.7), 161 (47.5), 158 (7.0), 145 (14.6), 115 (100.0), 104 (19.0), 97 (43.6), 94 (35.7), 72 (23.3), 71 (6.3), 59 (23.8). Elemental analysis: found: C, 49.96; H, 4.24; N, 29.18%. Calcd for C<sub>12</sub>H<sub>12</sub>N<sub>6</sub>OS (288.08): C, 49.99; H, 4.20; N, 29.15%.

**4-Amino-6-benzyl-3-hydrazinyl-1,2,4-triazin-5(4***H***)-one (13). White needles (0.84 g, 85%); m.p 265–266°C [lit. m. p 254–255°C [23]]. [ethanol]. R\_f = 0.14 [pet. ether (60:80)/ ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 3330, 3283, 3226 (2NH<sub>2</sub>), 3184 (NH), 1685 (C=O amide). MS (EI, 70 eV) m/z (%) = 232 (M<sup>+</sup>, 25.3), 216 (3.8), 185 (1.6), 186 (5.8), 117 (24.1), 91 (96.7), 76 (67.4), 53 (27.6), 50 (100.0). Elemental analysis: found: C, 51.70; H, 5.24; N, 36.22%. Calcd for C\_{10}H\_{12}N\_6O(232.11): C, 51.72; H, 5.21; N, 36.19%.** 

*N*-(6-benzyl-3-mercapto-5-oxo-1,2,4-triazin-4(3*H*)-yl) acetamide (14). *Method a.* A warm solution of cyanoacetic acid (2 g, 2.14 mmol) in acetic anhydride (2 mL) was left at 50°C for 5 min, followed by the addition of triazine **3** (0.5 g, 2.14 mmol). The temperature of the reaction mixture was raised to  $85^{\circ}$ C and left for 2 h. The precipitate, which formed on hot, was separated by filtration, washed with hot ethanol (10 mL, threefold), and recrystallized in DMF to afford 14.

*Method b.* A mixture of triazine **3** (0.5 g, 2.14 mmol), acetic anhydride (2 mL), and acetic acid (2 mL) was refluxed for 2 h over a water bath. The precipitate, which formed on hot, was separated by filtration, washed with hot ethanol (10 mL, threefold), and recrystallized in DMF to afford **14**.

White crystals (0.54 g, 92%); m.p 230–232°C.  $R_f = 0.15$ [pet. ether/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 3227 (NH), 1717 (C=O), 1686 (C=O amide), 1174 (C=S). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) = 1.99 (s, 3H, CH<sub>3</sub>), 3.89 (s, 2H, CH<sub>2</sub>—Ph), 7.23–7.33 (m, 5H, H—Ar), 10.94 (s, 1H, NH—C=O), 13.79 (s, 1H, NH<sub>triazine</sub>). MS (EI, 70 eV) *m/z* (%) = 277 (M<sup>+</sup> + 1, 33.9), 260 (1.4), 242 (4.5), 235 (76.8), 218 (2.7), 217 (11.5), 188 (7.5), 175 (4.6), 160 (6.5), 145 (7.6), 130 (57.53), 117 (15.2), 102 (20.6), 91 (100.0), 76 (41.1), 59 (84.9), 52 (8.3), 50 (57.6). Elemental analysis: found: C, 52.14; H, 4.35; N, 20.30%. Calcd for C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>S (276.31): C, 52.16; H, 4.38; N, 20.28%.

**3,3'-((Diselanediylbis(4,1-phenylene))bis(azanediyl))bis(4-amino-6-benzyl-1,2,4-triazin-5(4H)-one (15)**. A mixture of triazine **3** (0.5 g, 2.14 mmol) and 4,4'-

diselanediyldianiline (1.5 g, 4.28 mmol) in DMF was refluxed for 30 h, cooled, and poured onto crushed ice. The obtained solid was filtered off, washed with hot ethanol (10 mL, threefold), and recrystallized in EtOH–DMF (1:2) to afford **15**.

Brown powder (0.37 g, 23%); m.p >300°C.  $R_f = 0.21$  [ethyl acetate/pet. ether (60:80) (4:2.5)]. IR (KBr): v/cm<sup>-1</sup> = 3339, 3305 (NH<sub>2</sub>), 3212 (NH), 1669 (C=O amide). <sup>1</sup>H-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 3.90 (s, 2H, CH<sub>2</sub>-Ph), 5.35 (s, 4H, 2NH<sub>2</sub>), 7.11–7.53 (m, 18H, H-Ar), 8.28 (s, 2H, 2NH). MS (EI, 70 eV) *m/z* (%) = 746 (M<sup>+</sup> + 2, 1.0), 451 (1.0), 371 (1.0), 159 (24.7), 157 (29.0), 155 (28.0), 130 (16.8), 116 (41.7), 103 (17.3), 91 (31.2). 76 (100.0), 53 (9.3), 50 (61.8). Elemental analysis: found: C, 51.73; H, 3.83; N, 18.84%. Calcd for C<sub>32</sub>H<sub>28</sub>N<sub>10</sub>O<sub>2</sub>Se<sub>2</sub> (744.07): C, 51.76; H, 3.80; N, 18.86%.

Preparation of Schiff's bases 16a,b. General procedure. A mixture of triazine 3 (0.5 g, 2.14 mmol) and aldehyde derivatives (2.14 mmol) in either ethanol/conc.  $H_2SO_4$  (20 mL:5 drops) or ethanol/HCl (15 mL:5 mL) was boiled under reflux for 6 or 10 h, respectively. The precipitate, which formed on hot, was separated by filtration and recrystallized to afford 16a,b.

**6-Benzyl-4-((1,3-diphenyl-1***H***-pyrazol-4-yl)methyleneamino)-3-mercapto-1,2,4-triazin-5(4***H***)-one (16a). The aldehyde used was 1,3-diphenyl-1***H***-pyrazole-4-carbaldehyde.** 

Yellow powder (0.84 g, 85%); m.p  $215-217^{\circ}$ C. [Toluene].  $R_{\rm f} = 0.4$  [pet. ether (60:80)/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 1699 (C=O amide), 1177 (C=S). <sup>1</sup>H-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 3.91 (s, 2H, CH<sub>2</sub>—Ph), 7.29– 8.05 (m, 15H, H—Ar), 8.67 (s, 1H, CH<sub>pyrazole</sub>), 8.26 (s, 1H, =CH), 13.73 (s, 1H, NH, D<sub>2</sub>O exchangeable). MS (EI, 70 eV) *m/z* (%) = 464 (M<sup>+</sup>, 2.1), 433 (2.1), 378 (2.6), 328 (2.1), 287 (2.9), 261 (2.1), 246 (71.7), 245 (18.1), 219 (21.6), 217 (8.3), 187 (7.5), 168 (3.6), 141 (11.0), 132 (3.5), 127 (2.3), 117 (19.3), 104 (18.4), 91 (20.2), 77 (100.0), 76 (18.2), 52 (17.1), 50 (23.9). Elemental analysis: found: C, 67.20; H, 4.32; N, 18.07%. Calcd for C<sub>26</sub>H<sub>20</sub>N<sub>6</sub>OS (464.14): C, 67.22; H, 4.34; N, 18.09%.

**6-Benzyl-4-((2-hydroxynaphthalen-1-yl)methyleneamino)-3-mercapto-1,2,4-triazin-5(4***H***)-one (16b). The aldehyde used was 2-hydroxy-1-naphthaldehyde.** 

Yellow powder (0.69 g, 83%); m.p 250–253°C. [Ethanol].  $R_{\rm f} = 0.4$  [pet. ether/ethyl acetate (4:1.5)]. IR (KBr): v/cm<sup>-1</sup> = 3143 (OH), 1690 (C=O amide), 1176 (C=S). <sup>1</sup>H-NMR (DMSO- $d_6$ )  $\delta$  (ppm) = 3.96 (s, 2H, CH<sub>2</sub>-Ph), 7.29–8.69 (m, 11H, H-Ar), 9.54 (s, 1H, =CH), 11.70 (s, 1H, OH), 13.84 (s, 1H, NH). MS (EI, 70 eV) m/z (%) = 388 (M<sup>+</sup>, 17.9), 334 (1.0), 220 (17.6), 219 (59.1), 201 (1.2), 186 (2.3), 170 (21.8), 169 (100.0), 148 (2.5), 140 (28.3), 127 (13.4), 117 (14.1), 114 (42.7), 91 (72.6), 76 (6.5), 53 (1.6), 51 (4.2). Elemental analysis: found: C, 64.95; H, 4.12; N, 14.40%. Calcd for  $C_{21}H_{16}N_4O_2S$  (388.10): C, 64.93; H, 4.15; N, 14.42%.

Synthesis of S-alkyl triazines 17–20. General procedure for synthesis of compounds 17 and 18. *Method a.* Triazine 16a (2.14 mmol) was dissolved in cold methanolic sodium methoxide solution [prepared from sodium metal (0.23 g, 10 mmol) and 10-mL methanol], and then either methyl iodide (0.13 mL, 2.14 mmol) or ethyl bromoacetate (0.24, 2.14 mmol) was added. The reaction mixture was stirred at room temperature. The precipitate obtained was collected by filtration, washed with water, and dried at room temperature to give 17 and 18.

*Method b.* A mixture of triazine **16a** (2.14 mmol), methyl iodide (0.13 mL, 2.14 mmol), or ethyl bromoacetate (0.24, 2.14 mmol), in EtOH–DMF mixture (1:1) (10 mL) in the presence of either fused sodium acetate (0.3 g, 3.21 mmol) or  $Et_3N$  (0.45 mL, 3.21 mmol), was stirred at room temperature. The reaction mixture was monitored by TLC and then poured into cold water. The precipitate that formed was filtered off, washed with water (10 mL), and dried at room temperature to give **17** and **18**.

**6-Benzyl-4-((1,3-diphenyl-1***H***-pyrazol-4-yl)methyleneamino)-3-(methylthio)-1,2,4-triazin-5(4***H***)-one (17)**. White powder (0.88 g, 86%); m.p 228–230°C. [Ethanol].  $R_f = 0.26$  [pet. ether/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 1668 (C=O amide). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm) = 2.61 (s, 3H, CH<sub>3</sub>), 4.17 (s, 2H, CH<sub>2</sub>-Ph), 7.27–7.85 (m, 15H, H–Ar), 8.64 (s, 1H, CH<sub>pyrazole</sub>), 9.11 (s, 1H, =CH). MS (EI, 70 eV) *m/z* (%) = 478 (M<sup>+</sup>, 1.3), 463 (1.9), 362 (1.1), 349 (1.0), 322 (1.1), 259 (3.5), 245 (100.0), 233 (32.7), 217 (7.8), 203 (3.2), 186 (1.7), 165 (1.9), 155 (7.3), 131 (25.6), 117 (18.6), 104 (16.9), 91(14.2), 52 (12.4), 47 (6.2). Elemental analysis: found: C, 67.79; H, 4.95; N, 17.53%. Calcd for C<sub>27</sub>H<sub>22</sub>N<sub>6</sub>OS (478.16): C, 67.76; H, 4.63; N, 17.56%.

Ethyl-2-(6-benzyl-4-((1,3-diphenyl-1*H*-pyrazol-4-yl) methyleneamino)-5-oxo-4,5-dihydro-1,2,4-triazin-3-ylthio) acetate (18). White powder (1 g, 85%); m.p 183–184°C. [Ethanol]. R<sub>f</sub> = 0.37 [pet. ether/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 1740 (OC=O), 1680 (C=O amide). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ (ppm) = 1.20 (t, 3H, CH<sub>3</sub>), 3.78 (s, 2H, CH<sub>2</sub>-Ph), 4.01 (s, 2H, CH<sub>2</sub>), 4.11 (q, 2H, CH<sub>2</sub>-CH<sub>3</sub>), 7.25–7.95 (m, 15H, H-Ar), 9.10 (s, 1H, CH<sub>pyrazole</sub>), 9.13 (s, 1H, =CH). MS (EI, 70 eV) *m/z* (%) = 550 (M<sup>+</sup>, 2.8), 120 (2.8), 117 (7.8), 94 (2.2), 91 (11.7), 87 (2.2), 78 (13.4), 76 (6.1), 52 (12.8), 50 (8.4). Elemental analysis: found: C, 65.41; H, 4.79; N, 15.24%. Calcd for  $C_{30}H_{26}N_6O_3S$  (550.18): C, 65.44; H, 4.76; N, 15.26%.

General procedure for synthesis of compounds 19 and 20. 6-Benzyl-4-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyleneamino)-3-(prop-1-enylthio)-1,2,4-triazin-5(4*H*)-one (19). A mixture of triazine 16a (0.5 g, 2.14 mmol), allyl bromide (0.2 mL, 2.14 mmol), or 1,2-bis (bromomethyl) benzene (0.6 g, 2.14 mmol) and Et<sub>3</sub>N (0.45 mL, 3.21 mmol) in EtOH– DMF mixture (1:1) (10 mL) was stirred at room temperature for 5 min for allylbromide and overnight for 1,2bis(bromomethyl)benzene. The reaction mixture was poured into cold water; the precipitate that formed was filtered, washed with water, dried, and recrystallized to afford **19** and **20**, respectively, whereas, repeating the same reaction, but using fused sodium acetate instead of  $Et_3N$  or in cold methanolic sodium methoxide solution, no reaction occurred.

White powder (1.3 g, 83%); m.p 177–178°C. [Ethanol].  $R_f = 0.4$  [pet. ether/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 1674 (C=O amide). <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  (ppm) = 3.89 (d, 2H, S–CH<sub>2</sub>=CH), 4.21 (s, 2H, CH<sub>2</sub>=Ph), 5.08 (dd, 2H, CH<sub>2</sub>=CH), 6.02 (m, H, CH), 7.27–7.84 (m, 15H, H–Ar), 8.63 (s, 1H, CH<sub>pyrazole</sub>), 9.09 (s, 1H, =CH). MS (EI, 70 eV) m/z (%) = 505 (M<sup>+</sup> + 1, 4.2), 259 (17.0), 246 (35.1), 245 (92.0), 244 (85.6), 150 (14.4), 142 (18.6), 127 (13.8), 117 (11.7), 115 (17.6), 114 (21.3), 104 (21.3), 94 (4.7), 91 (38.8), 77 (100.0), 52 (13.3), 50 (39.4). Elemental analysis: found: C, 69.06; H, 4.77; N, 16.68%. Calcd for C<sub>29</sub>H<sub>24</sub>N<sub>6</sub>OS (504.17): C, 69.03; H, 4.79; N, 16.65%.

3,3'-((1,2-Phenylenebis(methylene))bis(sulfanediyl))bis(6benzyl-4-(((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)amino)-1,2,4-triazin-5(4*H*)-one) (20). White powder (2.2 g, 73%); m.p 165–167°C. [Ethyl acetate]. R<sub>f</sub> = 0.15 [pet. ether (60:80)/ethyl acetate (4:1)]. IR (KBr): v/cm<sup>-1</sup> = 1678 (C=O amide). <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  (ppm) = 4.15 (s, 2H, CH<sub>2</sub>-Ph), 4.64 (s, 2H, CH<sub>2</sub>-S), 7.18–7.76 (m, 15H, H-Ar), 8.51 (s, 1H, CH<sub>pyrazole</sub>), 9.06 (s, 1H, =CH). Elemental analysis: found: C, 69.91; H, 4.47; N, 16.00%. Calcd for C<sub>60</sub>H<sub>46</sub>N<sub>12</sub>O<sub>2</sub>S<sub>2</sub> (1030.33): C, 69.88; H, 4.50; N, 16.30%.

Acaricidal activity assay. Test pest. Two-spotted spider mite, *T. urticae* (Koch), colonies were laboratory reared by the same procedure previously described by Dittrich [24]. A pure culture of the spider mite was maintained on castor oil leaf plants under laboratory conditions  $(25^{\circ}C \pm 2^{\circ}C \text{ and } 60\% \pm 5\% \text{ R.H})$  at Plant Protection Research Institute branch, Dakahlia Governorate.

Assessment of acaricidal activity. Laboratory experiments are conducted to evaluate the acaricidal activity of tested 1,2,4-triazine derivatives against eggs and adult females of *T. urticae* using the leaf-dip technique [25].

All tested compounds were formulated as an emulsion in water containing 0.3% triton X-100 and 5% ethanol as solvent [22]. The emulsions were used immediately after preparation to minimize any decomposition. Serial five concentrations of each compound were prepared for each tested stage.

Castor oil leaf discs (2-cm diameter) were dipped in each concentration for 10 s and left to dry. Discs were placed onto cotton wool pads in petri-dishes (12 cm in diameter). Ten *T. urticae* individuals of the same age were transferred to treated castor oil leaf disc, which was

replicated three times, in addition, to control and were left under laboratory condition. Controls were dipped in the solvent mixture minus the tested extract. Mortality was taken after 24 and 72 h of exposure [24].

Ten adults females of *T. urticae* were transferred from the sensitive laboratory culture to castor oil leaf discs (3 cm in diameter), placed on moist cotton wool pads in petri-dishes. Adult females were removed after 24 h, as it deposits their eggs of 1 day old. The toxic effect of tested compounds was evaluated by dipping these castor oil leaf discs in a series of diluted concentrations for 10 s. Discs with the same age of eggs were dipped in the emulsion mixture minus the tested extracts as a control. Three replicates of leaf discs for each concentration as well as control were used. Discs with treated eggs were placed onto pads of wet cotton in petri-dishes and kept under laboratory conditions until hatching ( $25^{\circ}C \pm 2^{\circ}C$  and  $60\% \pm 5\%$  R.H). After complete hatching of control eggs, the number of unhatched eggs of different concentrations was counted, and the percentage of unhatchability was determined [26].

### STATISTICAL ANALYSIS

Mortality was recorded for adult females after 24 and 72 h of treatment and for eggs after complete hatching of control eggs. This mortality was corrected according to Abbott's formula [27] and statistically analyzed to estimate  $LC_{50}$ ,  $LC_{90}$ , and slope values utilizing LDP line probit analysis program version 1.0 according to Finney [28].

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