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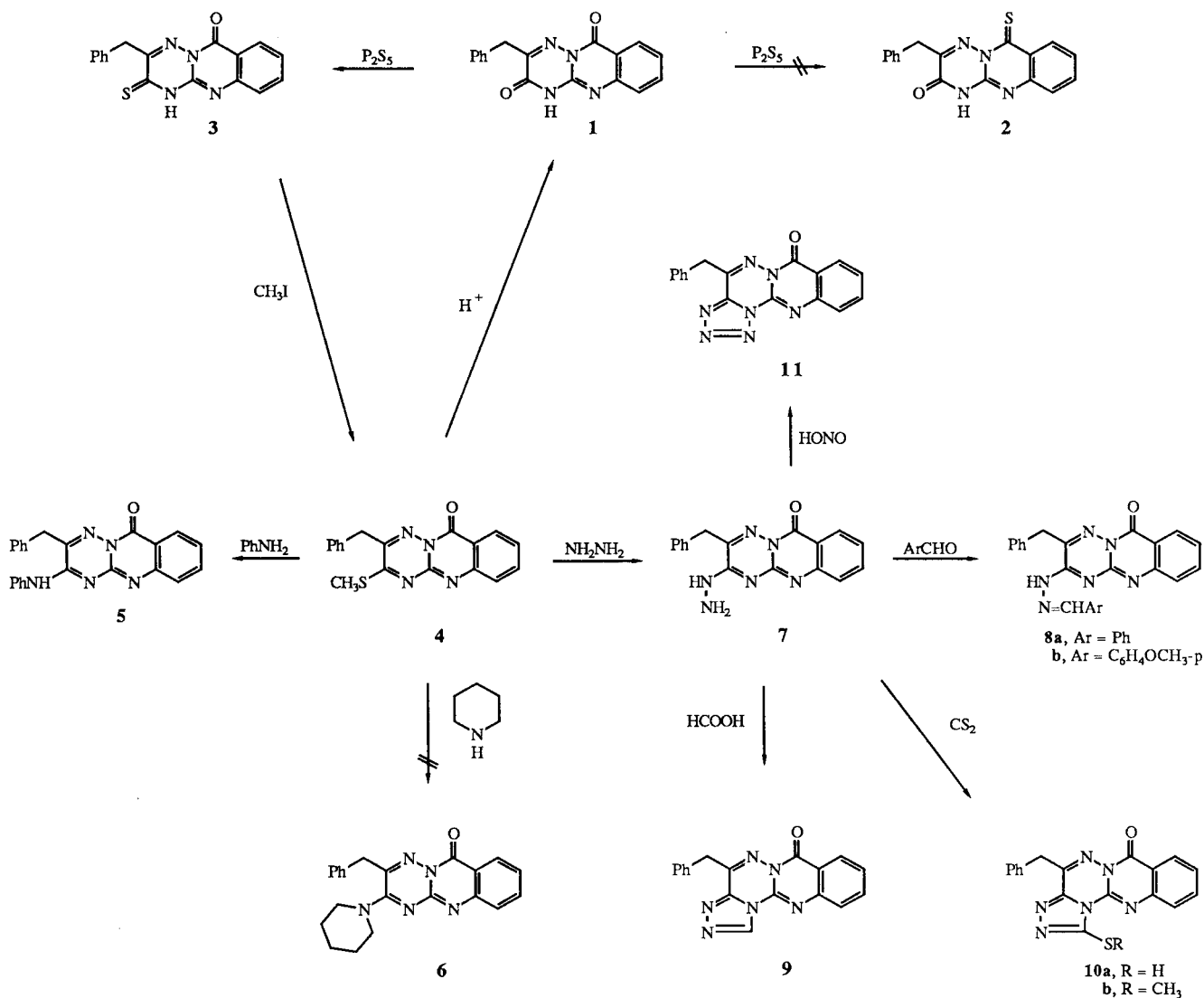
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Thiation of [1,2,4]triazino[3,2-*b*]quinazoline-3,10-dione **1** proceeds selectively to give the 3-thioxo-analog **3**. The latter was converted to the corresponding 3-methylthio derivative **4** which was reacted with aniline and hydrazine to give the corresponding anilino- and hydrazino derivatives **5** and **7**. Compound **7** was converted to the hydrazones **8a,b** and into the novel heterocyclic ring systems [1,2,4]triazolo[4',3':4,5][1,2,4]triazino[3,2-*b*]quinazolin-7-ones **9**, **10a,b** and tetrazolo[1',5':4,5][1,2,4]triazino[3,2-*b*]quinazolin-7-one **11**.

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As a part of a program directed towards condensed 1,2,4-triazines we describe here our results on some reactions of [1,2,4]triazino[3,2-*b*]quinazoline-3,10-dione **1**. The synthesis and structure of compound **1** and its derivatives have recently been described by us [1-3].

In the present study we investigated thiation of compound **1** and its utility in the synthesis of new derivatives of triazinoquinazolines and their condensed systems. Thus, when compound **1** was subjected to thiation with phosphorus pentasulfide in pyridine a selective monothi-



oxo derivative was obtained. Among the two possible monothioxo derivatives, the product was proved to be 3-thioxo[1,2,4]triazino[3,2-*b*]quinazolin-10-one **3** and not the isomeric 10-thioxo[1,2,4]triazino[3,2-*b*]quinazolin-3-one **2**. Assignment of the structure of compound **3** is based on the fact that it readily undergoes methylation in basic medium to afford the corresponding 3-methylthio derivative **4** which was readily hydrolyzed to give the starting dioxotriazinoquinazolinone **1**. The sequence of methylation and hydrolysis is in favor of structure **3** and rules out completely the isomeric structure **2**. Treatment of compound **4** with aniline did afford the corresponding 3-anilino derivative **5**. On the other hand, attempted synthesis of the 3-piperidino derivative **6** by the action of piperidine on compound **4** failed and instead hydrolysis occurred and compound **1** was obtained. Hydrazinolysis of compound **4** did afford the 3-hydrazino derivative **7** which was condensed with benzaldehyde and *p*-methoxybenzaldehyde to give the corresponding hydrazones **8a,b** respectively.

The utility of compound **7** in the synthesis of the tetracyclic systems **9**, **10a,b** and **11** was investigated. Thus, heating compound **7** with formic acid or carbon disulfide in pyridine afforded the corresponding [1,2,4]triazolo[4',3':4,5][1,2,4]triazino[3,2-*b*]quinazolines **9** and **10** respectively, whereas the addition of 1.5 *M* hydrochloric acid to a mixture of **7** and sodium nitrite [4] resulted in a 77% yield of 4-benzyl-7*H*-tetrazolo[1',5':4,5][1,2,4]triazino[3,2-*b*]quinazolin-7-one **11**. Compound **10a** was readily methylated to give the corresponding 1-methylthio derivative **10b**.

## EXPERIMENTAL

All melting points are uncorrected. The ir spectra (potassium bromide) were recorded with a Unicam SP-1200 spectrophotometer. The <sup>1</sup>H-nmr spectra were determined with a Varian EM 390 90 MHz spectrometer. Elemental analyses were carried by the Microanalytical Centre, Cairo University.

**3-Thioxo-2-benzyl-3,4-dihydro-10*H*-[1,2,4]triazino[3,2-*b*]quinazolin-10-one (3).**

A mixture of compound **1** (1.0 g, 3.3 mmoles) and phosphorus pentasulfide (0.75 g) in dry pyridine (10 ml) was heated under reflux for 6 hours. After cooling and acidification with hydrochloric acid (1 *N*), the precipitate formed was collected by filtration, washed with water and crystallized from dimethylformamide as brownish crystals of **3** (1.0 g, 95%), mp 265°; ir: 3200 (NH), 1730 (C=O) cm<sup>-1</sup>.

*Anal.* Calcd. for C<sub>17</sub>H<sub>12</sub>N<sub>4</sub>OS: C, 63.73; H, 3.78; N, 17.49; S, 10.01. Found: C, 63.60; H, 3.70; N, 17.70; S, 10.40.

**3-Methylthio-2-benzyl-10*H*-[1,2,4]triazino[3,2-*b*]quinazolin-10-one (4).**

To a suspension of compound **3** (1.0 g, 3.1 mmoles) in cold methanolic sodium methoxide solution (prepared from 0.07 g of sodium metal and 30 ml of absolute methanol) was added methyl iodide (0.19 ml, 3.0 mmoles). The reaction mixture was stirred for

30 minutes and then refluxed for another 30 minutes. After cooling the precipitate was collected by filtration and recrystallized from dimethylformamide as yellow crystals of **4** (0.7 g, 67%), mp 145°; ir: 1725 (C=O) cm<sup>-1</sup>.

*Anal.* Calcd. for C<sub>18</sub>H<sub>14</sub>N<sub>4</sub>OS: C, 64.65; H, 4.22; N, 16.75; S, 9.59. Found: C, 64.50; H, 4.10; N, 16.50; S, 9.30.

**3-Anilino-2-benzyl-10*H*-[1,2,4]triazino[3,2-*b*]quinazolin-10-one (5).**

A mixture of compound **4** (1.0 g, 3 mmoles) and aniline (2 ml) was heated at 180° (oil bath) for 1 hour. After cooling, ethanol (10 ml) was added and the precipitate formed was collected by filtration and recrystallized from dimethylformamide as orange crystals of **5** (0.9 g, 79%) mp 165°.

*Anal.* Calcd. for C<sub>23</sub>H<sub>17</sub>N<sub>5</sub>O: C, 72.81; H, 4.52; N, 18.46. Found: C, 72.90; H, 4.30; N, 18.60.

**Action of Piperidine on Compound 4.**

A mixture of compound **4** (1.0 g, 3 mmoles) and piperidine (4 ml) was heated under reflux for 6 hours, allowed to cool to room temperature and diluted with water whereupon the precipitate was collected by filtration and recrystallized from dimethylformamide to give compound **1** (0.9 g, 99%) mp 295°. This compound is identical with an authentic sample [1] (mp and mixed mp).

**3-Hydrazino-2-benzyl-10*H*-[1,2,4]triazino[3,2-*b*]quinazolin-10-one (7).**

A mixture of compound **4** (4.0 g, 12 mmoles) and hydrazine hydrate (4 ml, 99%) in isopropyl alcohol (20 ml) was heated under reflux for 8 hours (until methyl mercaptan ceased to evolve). After cooling the precipitate was collected by filtration and recrystallized from dimethylformamide as yellow crystals of **7** (3.5 g, 92%), mp 253° dec.

*Anal.* Calcd. for C<sub>17</sub>H<sub>14</sub>N<sub>6</sub>O: C, 64.14; H, 4.43; N, 26.40. Found: C, 64.30; H, 4.20; N, 26.10.

**Condensation of 7 with Benzaldehyde or *p*-Methoxybenzaldehyde.**

A mixture of compound **7** (0.6 g, 1.9 mmoles) and each of benzaldehyde or *p*-methoxybenzaldehyde (2.1 mmoles) in ethanol (20 ml) was heated under reflux for 1 hour. After cooling, the precipitate was collected by filtration and recrystallized from dimethylformamide or acetic acid to give yellow crystals of **8a** or **8b** respectively.

**3-Benzylidenehydrazino-2-benzyl-10*H*-[1,2,4]triazino[3,2-*b*]quinazolin-10-one (8a).**

This compound had mp 150° and was obtained in 65% yield (0.5 g).

*Anal.* Calcd. for C<sub>24</sub>H<sub>18</sub>N<sub>6</sub>O: C, 70.92; H, 4.46; N, 20.68. Found: C, 70.70; H, 4.60; N, 20.40.

**3-*p*-Methoxybenzylidenehydrazino-2-benzyl-10*H*-[1,2,4]triazino[3,2-*b*]quinazolin-10-one (8b).**

This compound had mp 170° and was obtained in 73% yield (0.6 g).

*Anal.* Calcd. for C<sub>25</sub>H<sub>20</sub>N<sub>6</sub>O<sub>2</sub>: C, 68.80; H, 4.62; N, 19.25. Found: C, 68.50; H, 4.50; N, 19.60.

**4-Benzyl-7*H*-[1,2,4]triazolo[4',3':4,5][1,2,4]triazino[3,2-*b*]quinazolin-7-one (9).**

A mixture of compound **7** (1.0 g, 3.1 mmoles) and formic acid (3 ml, 99%) was heated under reflux for 1 hour. The solid precipitated during reflux was collected by filtration and recrystallized

from dimethylformamide as yellow crystals of **9** in 58% yield (0.6 g), mp 312; ir: 3100, 1700  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  ( $\text{DMSO-d}_6$ ):  $\delta$  4.4 (s, 2H,  $\text{PhCH}_2$ ), 7.1-8.2 (m, 9H, arom), 9.6 (s, 1H, triazole H) ppm.

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{12}\text{N}_6\text{O}$ : C, 65.85; H, 3.68; N, 25.60. Found: C, 65.60; H, 3.50; N, 25.30.

1-Thioxo-4-benzyl-2*H*,7*H*-[1,2,4]triazolo[4',3':4,5][1,2,4]triazino[3,2-*b*]quinazolin-7-one (**10a**).

A mixture of compound **7** (1.0 g, 3.1 mmoles) and carbon disulfide (1 ml) in dry pyridine (10 ml) was heated under reflux for 3 hours. After cooling and acidification with dilute hydrochloric acid, the precipitate obtained was collected by filtration and recrystallized from dimethylformamide as yellow crystals of **10a** in 63% yield (0.7 g), mp 289°; ir: 3190 (NH), 1690 ( $\text{C}=\text{O}$ )  $\text{cm}^{-1}$ .

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{12}\text{N}_6\text{OS}$ : C, 59.99; H, 3.36; N, 23.32; S, 8.90. Found: C, 59.80; H, 3.20; N, 23.20; S, 8.70.

1-Methylthio-4-benzyl-7*H*-[1,2,4]triazolo[4',3':4,5][1,2,4]triazino[3,2-*b*]quinazolin-7-one (**10b**).

To a mixture of compound **10a** (1.0 g, 2.8 mmoles) and sodium methoxide solution (prepared from 0.06 g of sodium metal in 30 ml of absolute methanol) was added methyl iodide (0.2 ml, 3.2 mmoles). The reaction mixture was stirred for 1 hour and left at room temperature overnight. The precipitate formed was collected by filtration and recrystallized from dimethylformamide as yellow crystals of **10b**, mp 278°, yield 67% (0.7 g); ir: 1710  $\text{cm}^{-1}$ ;  $^1\text{H-nmr}$  ( $\text{DMSO-d}_6$ ):  $\delta$ , 2.75 (s, 3H,  $\text{SCH}_3$ ), 4.3 (s, 2H,  $\text{PhCH}_2$ ), 7.25-8.3 (m, 9H, arom) ppm.

*Anal.* Calcd. for  $\text{C}_{19}\text{H}_{14}\text{N}_6\text{OS}$ : C, 60.95; H, 3.77; N, 22.44; S, 8.56. Found: C, 60.80; H, 3.50; N, 22.10; S, 8.30.

4-Benzyl-7*H*-tetrazolo[1',5':4,5][1,2,4]triazino[3,2-*b*]quinazolin-7-one (**11**).

A solution of hydrochloric acid (1.5 *M*, 15 ml) was added dropwise to a stirred suspension of 3-hydrazino-2-benzyl-10*H*-[1,2,4]triazino[3,2-*b*]quinazolin-10-one **7** (0.5 g, 1.6 mmoles) and sodium nitrite (0.7 g, 10 mmoles) in water (5 ml) at room temperature. The mixture was stirred at room temperature for 24 hours, and the precipitate collected by filtration. The solid was recrystallized from ethanol to give 0.4 g (77%) of **11** as yellow needles, mp 168-170° dec; ir: 3110, 3050, 2910, 1710, 1630, 1600, 1560, 1450, 1260, 1140, 780, 740, 700;  $^1\text{H-nmr}$  (deuteriochloroform): 4.5 (s, 2H,  $\text{PhCH}_2$ ), 7.05-8.4 (m, 9H, arom).

*Anal.* Calcd. for  $\text{C}_{17}\text{H}_{11}\text{N}_7\text{O}$ : C, 62.03; H, 3.37; N, 29.79. Found: C, 62.20; H, 3.60; N, 29.90.

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