

# SYNTHESIS AND STRUCTURE ELUCIDATION OF 1,2,4-TRIAZINO [4,3-b] 1,2,4-TRIAZINES, 1,2,4-TRIAZINO [3,4-c] 1,2,4-TRIAZINES AND 1,2,4-TRIAZINO [4,3-d] 1,2,4-TRIAZINES

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## Abstract

Reaction of 6-Methyl-3-methylmercapto-1,2,4-triazine-5(2H)-one (9) with phenacyl bromide yielded 3-methylmercapto-2-phenacyl-1,2,4-triazin-5-one (10) which was treated with hydrazine hydrate to yield 7-Methyl-3-phenyl-4H-1,2,4-triazino [4,3-b] 1,2,4-triazin-8 (1H)-one (1;  $R_1=Me$ ;  $R_2=Ph$ ). Reaction of 3-Hydrazino-1,2,4-Triazin-5 (2H) - one (3;  $R=H$  or  $Me$ ) with  $\alpha$ - haloketones afforded substituted 4H-1,2,4-triazino [3,4-c] 1,2,4-triazin-6 (1H)-ones (2;  $R^1=H$  or  $Me$ ;  $R^2=ph$ ,  $p-BrC_6H_4-$ ) one of which (2;  $R^1=H$ ;  $R^2=P-BrC_6H_4-$ ) was brominated to yield 7-bromo-3-bromophenyl-4H-1,2,4-triazino [3,4-c] 1,2,4-triazin-6 (1H)-one (2;  $R^1=Br$ ;  $R^2=P-BrC_6H_4$ ). Interaction of 2,6-dimethyl-3-hydrazino-1,2,4-triazin-5-one (6) with phenacyl bromide gave 7,9-dimethyl-3-phenyl-4H-1,2,4-triazino [3,4-c] 1,2,4-triazin-6-one (7). 5-Hydrazino-6-methyl-1,2,4-triazin-3(4H) -one (18;  $R^1=Me$ ) was synthesized by treatment of 6-methyl-5-methylmercapto-1,2,4-triazin-3 (4H)- one (17;  $R^1=Me$ ) with hydrazine hydrate and reaction of the compound (18;  $R^1=Me$ ) with phenacyl bromide and subsequent treatment of the intermediate hydrazone (20;  $R^1=Me$ ;  $R^2=Ph$ ) with base afforded 9-methyl-3-phenyl-4H-1,2,4-triazino [4,3-d] 1,2,4-triazin-6 (1H)- one (21;  $R^1=Me$ ;  $R^2=Ph$ ) as the first representative of the 1,2,4-triazino [4,3-d] 1,2,4-triazine system.

## Introduction

A broad spectrum of pharmacological properties and chemical reactivities have been demonstrated with 1,2,4-triazine nucleus [1-4]. A series of 1,2,4-triazino [4,3-b] 1,2,4-triazines have been reported to have potential

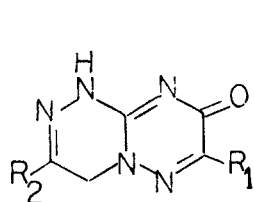
**Keywords:** Triazinotriazines; 1,2,4- Triazines

antineoplastics activity [5].

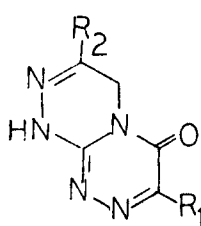
During a study of some bicyclic compounds derived from 1,2,4-triazine we became interested in the synthesis and structural study of two previously reported heterocyclic system substituted 1,2,4-triazino [4,3-b] 1,2,4-triazines (1) and 1,2,4-triazino [3,4-c] 1,2,4-

triazines (2).

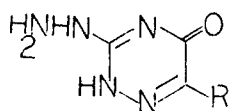
In 1964 Dornow and coworkers [6] reported the first triazino-triazine with the [b] configuration. These authors claimed [7] the synthesis of the 7-methyl-3-phenyl-4H-1,2,4-triazino [4,3-b] 1,2,4-triazin-8(1H)-one (1;  $R^1=Me$ ;  $R^2=ph$ ) from the reaction between 6-methyl-3-hydrazino-1,2,4-triazin-5 (2H)-one (3;  $R=Me$ ) and phenacyl bromide. In this reaction cyclization could proceed at nitrogen 4 of the triazine leading to the formation of another isomer 7-methyl-3-phenyl-4H-1,2,4-triazino [3,4-c] 1,2,4-triazin-6 (1H)-one (2;  $R^1=Me$ ;  $R^2=ph$ ).



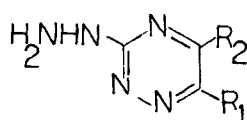
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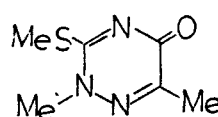
Lempert and his group reported the synthesis of several triazines [8]. Hadacek claimed the synthesis of a few triazino 3,4 c-1,2,4-triazine 9 from 3-hydrazino-1,2,4-triazin (3;  $R=Me$ ) by using butane-2,3-dione and pyruvic acid. It has been reported that the reaction of 3-hydrazino-5,6-diphenyl-1,2,4-triazine (4;  $R^1, R^2=ph$ ) with  $\alpha\beta$ -bifunctional compounds gives a variety of 1,2,4-triazino [4,3-b]-1,2,4-triazines [10-11]. However, so far no strong and firm evidence has been given for the structure of the possible isomers obtained.

### Results and Discussion

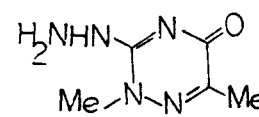
It is clear from the introduction that very little reliable work in the field of triazinotriazines has been published so far. The uncertain results as well as the report of being potentially antineoplastics prompted us to attempt to achieve some reliable results in the field of

triazinotriazine.

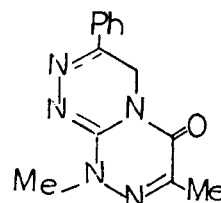
Already prepared and well authenticated 2,6-dimethyl-3-methyl-mercapto-1,2,4-triazin-5-one (5) [12-13] was treated with hydrazine hydrate to afford 2,6-dimethyl-3-hydrazino-1,2,4-triazin-5-one (6). The latter was reacted with phenacyl bromide to yield 7,9-dimethyl-3-phenyl-4H-1,2,4-triazino [3,4-c] 1,2,4-triazin-6-one (7). This reaction showed that nitrogen 4 in the triazine ring can be reactive in the formation of triazinotriazines as nitrogen 2 had already been blocked by the methyl group.



(5)



(6)

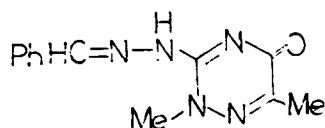


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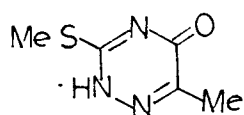
The 3-hydrazino 1,2,4-triazine (3;  $R=Me$ ) was also reacted with phenacyl bromide to give a single crystalline product. Spectroscopic evidence demonstrated that the compound could be triazino [4,3-b] 1,2,4-triazine (1;  $R^1=Me$ ;  $R^2=ph$ ) or a 1,2,4-triazino [3,4-c] 1,2,4-triazine (2;  $R^1=Me$ ;  $R^2=ph$ ). To establish the correct structure for the compound, 2,6-dimethyl-3-hydrazino-1,2,4-triazine (6) was condensed with benzaldehyde to yield the hydrazone (8). The ultraviolet spectrum of the latter was not similar to ultraviolet spectrum of the compound which resulted from the reaction of 3-hydrazino-1,2,4-triazine (3;  $R=Me$ ) and phenacyl bromide. The triazinotriazine therefore could not be the [4,3-b] compound (1;  $R^1=Me$ ;  $R^2=ph$ ). If it were, its ultraviolet spectrum would be similar to that of hydrazone (8) because it features a similar cross

conjugated bond system in the triazine ring. This result contradicted Dornow's finding. The formation of the [b] configuration through the reaction of 3-hydrazino-1,2,4-triazine (3; R=Me) and phenacyl bromide was completely disproved when it was prepared by an independent synthesis.

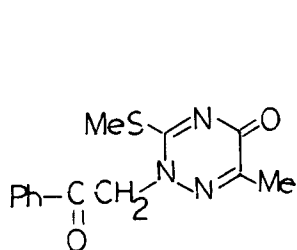
Reaction of 6-methyl-3-methylmercapto-1,2,4-triazin-5(2H)-one (9) [12] with phenacyl bromide in the presence of triethylamine gave a crystalline compound which could have any one of three possible structures (10), (11) or (12).



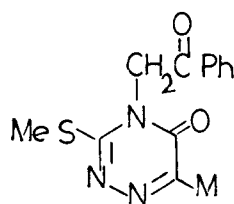
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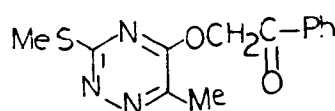
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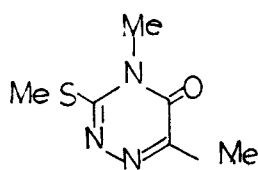
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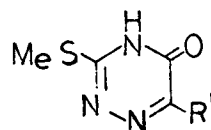


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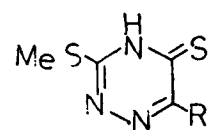
The infrared spectrum of the compound showed two different bands at  $1700\text{ cm}^{-1}$  which is characteristic of a ketone carbonyl group and at  $1620\text{ cm}^{-1}$  which is characteristic of an amide carbonyl group. This ruled out the possibility of the formation of the ether (12). Comparison of the  $^{13}\text{C-NMR}$  spectrum of the condensed product with those of 5 and 9 revealed that amide

carbonyl group had been retained intact. This ruled out the possibility of the formation of ether.

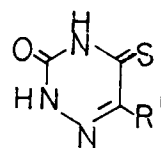
The structure for a 4 N-condensed product (11) was ruled out when the ultraviolet spectrum of the resulting compound was compared with 5 and 4,6-dimethyl 1,2,4-triazine. The ultraviolet spectrum of the condensed product was similar to that of 5 and different from that of 4,6-dimethyl-1,2,4-triazine. These results showed that the reaction between the 3-methylmercapto-1,2,4-triazine and phenacyl bromide gives 6-methyl-3-methylmercapto-2-phenacyl-1,2,4-triazin-5-one (10). Treatment of 10 with hydrazine hydrate afforded a compound which could only be 7-methyl-3-phenyl-4H-1,2,4-triazino [4,3-b] 1,2,4-triazin-8 (1H) -one (1;  $R^1 = \text{Me}$ ;  $R^2 = \text{ph}$ ). This compound has a different melting point and different infrared, ultraviolet and  $^1\text{H-NMR}$  spectra from the compound which was isolated from the reaction of 3-hydrazino-1,2,4-triazine (3; R= Me) and phenacyl bromide. We could therefore assume that the above reaction gave the isomeric 1,2,4-triazino [3,4-c] 1,2,4-triazine (2;  $R^1 = \text{Me}$   $R^2 = \text{Ph}$ ). The structure elucidation of the triazinotriazines led to the preparation of a series of 1,2,4-triazines (2;  $R^1 = \text{H}$  or Me;  $R^2 = \text{Ph}$  or  $\text{P-BrC}_6\text{H}_4$ -).



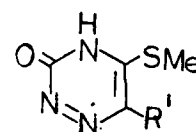
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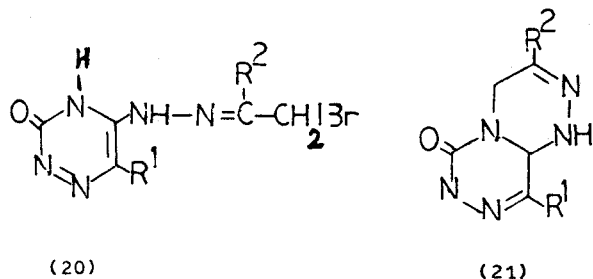
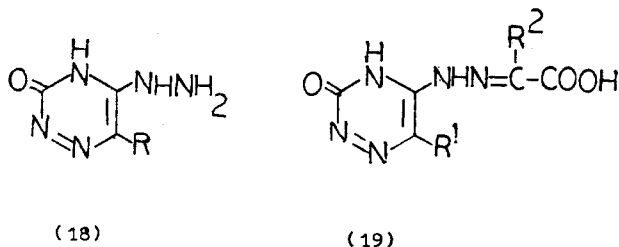
(17)

Treatment of (2;  $R^1 = \text{H}$ ;  $R^2 = \text{ph}$ ) with bromine gave a dibromo compound. The  $^1\text{H-NMR}$  of this compound showed that the proton of the triazine ring and one of the protons in the phenyl group had been replaced by bromine to afford 7-bromo-3-p-bromophenyl-4H-1,2,4-

triazino [3,4-c] 1,2,4-triazin-6(1H) - one (2;  $R^1 = \text{Br}$ ;  $R^2 = p\text{-BrC}_6\text{H}_4$ ). The position of the bromine atom in the phenyl group was confirmed by treating the *P*-bromophenyl derivative (2;  $R^1 = \text{H}$ ;  $R^2 = p\text{BrC}_6\text{H}_4$ ) with bromine.

Only a small number of 1,2,4-triazine-5-thiones (15 and 16) were known [14]. Treatment of 6-methyl-3-methylmercapto 1,2,4-triazin-5 (4H)- one (14;  $R^1 = \text{Me}$ ) [15] with phosphorus pentasulphide in pyridine gave 6-methyl-3-methylmercapto- 1,2,4-triazin- 5 (4H)- thione (15;  $R^1 = \text{Me}$ ). The latter was treated with hydrochloric acid to obtain 6-methyl 1,2,4-triazin-3 (2H)-one-5 (4H)- thione (16;  $R^1 = \text{Me}$ ).

Treatment of (16;  $R^1 = \text{Me}$ ) with methyl iodide gave the methyl mercapto derivative (17;  $R^1 = \text{Me}$ ). Reaction of the latter with hydrazine hydrate yielded 5-hydrazino-6-methyl- 1,2,4-triazin-3 (4H)- one (18;  $R^1 = \text{Me}$ ). The latter was reacted with glyoxalic acid and pyruvic acid to afford the corresponding hydrazones (19;  $R^1 = \text{Me}$ ,  $R^2 = \text{H}$  or  $\text{Me}$ ). The hydrazones (19) were treated with thionyl chloride, concentrated sulphuric acid and sodium ethoxide to obtain the desired 1,2,4-triazino [4,3-d] 1,2,4-triazines, but in most cases the starting material was recovered.

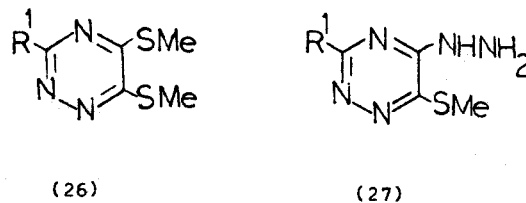
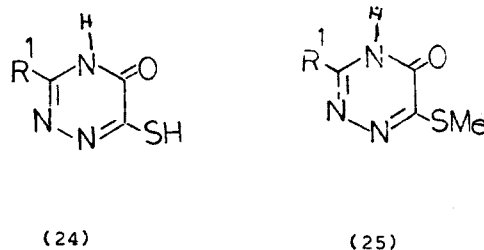
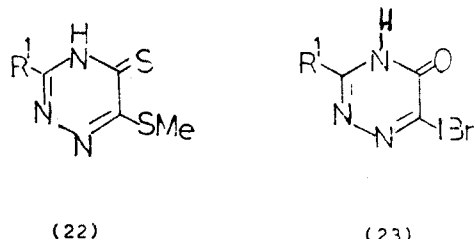


Reaction of the 5-hydrazino derivative (18;  $R = \text{Me}$ ) with phenacyl bromide afforded the hydrazone (20;  $R^1 = \text{Me}$ ;  $R^2 = \text{Ph}$ ) which was refluxed in a mixture

of propan-2-ol and triethylamine for a long period of time. The product, 9-methyl-3-phenyl-4H- 1,2,4-triazino [4,3-d] 1,2,4-triazin-6 (1H)- one (21;  $R^1 = \text{Me}$ ;  $R^2 = \text{Ph}$ ) was the first representative of the 1,2,4-triazino [4,3-d] 1,2,4-triazine system to be synthesized.

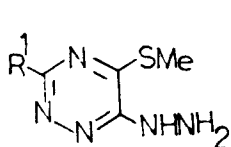
It was decided to prepare other-5-hydrazino-1,2,4-triazines in order to condense them with  $\alpha\beta$  bifunctional compounds and cyclize the product to the desired 1,2,4-triazino [4,3-d] 1,2,4-triazines .

6-Methylmercapto-3-morpholino-1,2,4-triazine-5 (4H) thione (22;  $R^1 = \text{morpholino}$ ) was prepared by the following reaction sequence. Treatment of the readily available 6-bromo-3-morpholino-1,2,4-triazin-5 (4H) -one (23;  $R^1 = \text{morpholino}$ ) [16] with sodium hydrogen sulphide gave 3-morpholino-1,2,4-triazin-5 (4H) -one-6-thione (24;  $R^1 = \text{morpholine}$ ) [17] which was methylated by methyl iodide to yield 6-methylmercapto derivative (25;  $R^1 = \text{morpholino}$ ). Treatment of (25;  $R^1 = \text{morpholino}$ ) with phosphorus pentasulphide afforded (22;  $R^1 = \text{morpholino}$ ).

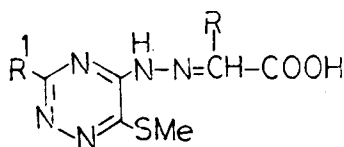


Methylation of the compound (22;  $R^1 = \text{morpholino}$ ) was afforded 5,6-

dimethylmercapto-3-morpholino-1,2,4-triazine (26;  $R^1 = \text{morpholino}$ ). The latter was treated with hydrazine hydrate. Spectroscopic data showed only one of the methylmercapto group had been replaced by hydrazine to give either the 5-hydrazino (27;  $R^1 = \text{morpholino}$ ) or 6-hydrazino derivative (28;  $R^1 = \text{morpholino}$ ). The same compound was obtained from the compound (22;  $R^1 = \text{morpholino}$ ) when it was treated with hydrazine hydrate showing that the methyl-mercapto group in 5-position of triazine ring is more susceptible toward nucleophilic attack, therefore the compound obtained was actually (27;  $R^1 = \text{morpholino}$ ). The latter was reacted with glyoxalic acid and pyruvic acid to afford the corresponding hydrazones (29;  $R^1 = \text{morpholino}$ ;  $R^2 = \text{H or Me}$ ). All attempts to cyclize the hydrazones (29) failed.



(28)



(29)

### Experimental Section

Melting points (uncorrected) were obtained on a Kofler Hot Stage Apparatus. The IR spectra were obtained using the Nujol mull technique on a Perkin-Elmer 297 Double Beam Spectrometer. The  $^1\text{H-NMR}$  spectra were recorded on a Perkin-Elmer B32/90MHz model at normal temperature, using tetramethylsilane as an internal standard. Mass spectra were run on an AEI MS 902S, mass spectrometer. The UV spectra were recorded on a Unicam SP800 double beam visible spectrometer. Microanalysis was done by Butterworth Laboratories Ltd. Teddington, Middlesex, England.

#### 6-Methyl-3-methylmercapto-2-phenacyl-1,2,4-triazin-5-one (10)

6-Methyl-3-methylmercapto-1,2,4-triazin-5 (2H) -one (16g) and phenacyl bromide (20g) were refluxed in a mixture of methanol (300 ml) and triethylamine (10 ml) for 2hrs. The solvent was evaporated to dryness, the

residue was dissolved in water (200 ml) and extracted with chloroform (3x100 ml). The combined extracts were dried over  $\text{MgSO}_4$  and evaporated to dryness. The residue was crystallized from ethyl acetate (60%) and light petroleum (b.p. 60-80, 40%) to afford the **title compound**, (10.5g; 37%), m.p. 159-160 [Found; C, 56.76; H, 4.73; N, 15.19;  $M^+$  (mass spectrum), 275.  $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}_3\text{S}$  requires; C, 56.71 H, 4.75; N, 15.26,]  $M$ , 275;  $^1\text{H-NMR}$ ; DMSO- $d_6$  2.1 (S, 3H, Me), 2.45 (S 3H, Me, 5.71, S, 2H,  $\text{CH}_2$ ), 7.9 (m, SH, Ph); UV ( $\text{H}_2\text{O}$ ) $_{\text{max}}$  247nm.

#### 7-Methyl-3-phenyl-4H-1,2,4-triazino [4,3-b] 1,2,4-triazin-8(1H) -one(1)

6-Methyl-3-methylmercapto-2-phenacyl-1,2,4-triazin-5-one (1g) and hydrazine hydrate (1.5 ml) were refluxed in propan-2-ol (100 ml) for 4 hrs. The solution was cooled to room temperature and evaporated to dryness. The residue was suspended in water (10 ml) and left in an ice bath overnight. The precipitated bright yellow solid was filtered off, washed with water and dried to afford the **title compound** (0.6g; 64%) m.p. 285-286 $^\circ$  (decomp) (from dimethyl-formamide) [found; C, 59.7; H, 4.73; N, 29.14;  $M^+$  (mass spectrum), 241,  $\text{C}_{12}\text{H}_{11}\text{N}_5\text{O}$  requires; C, 59.74; H, 4.95; N, 29.03]  $M$ , 241.  $^1\text{H-NMR}$  DMSO- $d_6$  2.14 (S, 3H, Me), 5.5 (S, 2H,  $\text{CH}_2$ ), 7.6 (m, 5H, Ph), 16.34 br (S, 1H\*, NH).

#### 4H-1,2,4-triazino [3,4-c] 1,2,4-triazin-6 (1H) -one (2)

The appropriate 3-hydrazino- 1,2,4-triazin-5 (4H) -one (0.01 mole) and appropriate  $\alpha$  -halo ketones (0.01 mole) were refluxed in propan-2-ol (200 ml) for 2hrs. The solution was cooled to room temperature and the precipitated solid was filtered off. The solid was washed with sodium carbonate solution and subsequently with water dried and crystallized from appropriate solvent. Melting point yields, halides used and elemental analysis are reported in Table 1.

#### 7-Bromo-3-P-bromophenyl-4H- 1,2,4-triazino [3,4-c]

1,2,4-triazin-6 (1H) -one (2;  $R^1 = \text{Br}$ ,  $R_2 = \text{P-C}_6\text{H}_4$ -) 3-P-bromophenyl-4H- 1,2,4-triazino [3,4-c] 1,2,4-triazin-6 (1H) -one (2g) was suspended in water (100 ml)

Table 1

R <sup>1</sup>	R <sup>2</sup>	halide used	yield m.p.(C°)		Crystn. solvent	Found %			Requires %		
						C	H	N	C	H	N
H	Ph.	BrCH <sub>2</sub> COPh	65%	252 decomp	DMF +H <sub>2</sub> O	58.26	4.07	4.42	58.15	3.99	3.85
H	C <sub>6</sub> H <sub>4</sub> Br	BrCH <sub>2</sub> COC <sub>6</sub> H <sub>4</sub>	60%	270 decomp	DMF +H <sub>2</sub> O	40.62	2.70	22.58	40.84	2.74	23.81
Me	Ph	BrCH <sub>2</sub> COPh	75%	295-296	DMF	59.73	4.74	29.15	59.74	4.95	29.03
Me	C <sub>6</sub> H <sub>4</sub> Br	BrCH <sub>2</sub> COC <sub>6</sub> H <sub>4</sub>	55%	213-214	DMF +H <sub>2</sub> O	M	319.0067		M	319.0069	

and bromine (4.16g) was added dropwise. The reaction mixture was stirred at room temperature for 48 hrs. The solid was filtered off and stirred in cold water (25 ml) for 10 min. The solid was filtered off washed with water and dried to yield the **title compound** (2.1g; 83%) m.p. 237 (decomp) (from aqueous dimethylformamide). [Found; C, 34.50; H, 2.07 N, 18.37; M<sup>+</sup>(mass spectrum), 383 C<sub>11</sub>H<sub>9</sub>N<sub>5</sub>Br<sub>2</sub> requires C, 34.31; H, 1.83; N, 8.19] M, 383. <sup>1</sup>H-NMR, (DMSO- d<sub>6</sub>) 5.86 (S, 2H, CH<sub>2</sub>) 7.65 (S, 4H, C<sub>6</sub>H<sub>4</sub>) 13.15br (S, 1H, NH).

#### 7,9-Dimethyl-3-phenyl-4H-1,2,4-triazino [3,4-c] 1,2,4-triazin-7-one (7)

2,6-Dimethyl-3-hydrazino-1,2,4-triazin-5-one (1g) and phenacyl bromide (1.15g) were refluxed in propan-2-ol (100 ml) for 2hrs. The solution was cooled to room temperature and the pale yellow solid filtered off and dried to yield the **title compound** (0.8g; 50%) m.p. 229-230<sup>o</sup> (from ethanol) [Found; C, 61.10; H, 4.98; N, 27.51; M<sup>+</sup>(mass spectrum), 255.C<sub>13</sub>H<sub>13</sub>N<sub>5</sub>O requires; C, 61.17; H, 5.13; N, 27.43, M 255]. <sup>1</sup>H-NMR (DMSO- d<sub>6</sub>) 2.29 (S, 3H, Me), 3.79 (S, 3H, Me) 4.99 (S, 2H, CH<sub>2</sub>), 7.6 and 7.35 (m, 5H, Ph).

#### The hydrazone from 2,6-dimethyl-3-hydrazino-1,2,4-triazin-5 (2H) one and benzaldehyde

Compound 6 (1g) was dissolved in propan-2-ol and benzaldehyde (1.2g) was added. The reaction mixture was

refluxed for 2hrs. and cooled to room temperature. The pale yellow solid was filtered off and dried to give the product (0.9g; 56%) m.p. 216-217<sup>o</sup> (from ethanol) [Found. C, 59.23; H, 5.38; N 28.87; M<sup>+</sup>(mass spectrum), 243.C<sub>12</sub>H<sub>13</sub>N<sub>5</sub>O requires; C, 59.25; H, 5.38; N, 28.79;] M, 243. <sup>1</sup>H-NMR (DMSO- d<sub>6</sub>) 2.01 (S, 3H, Me) 3.48 (S, 3H, Me) 7.35 and 7.85 (m, 5H, Ph), 8.25 (S, 1H, CH).

#### 6-Methyl-3-methylmercapto-1,2,4-triazin-5 (4H) -Thione (15)

To 6-methyl-3-methylmercapto- 1,2,4-triazin-5 (2H) -one (10g), phosphorus pentasulphide (8g) and dry pyridine (200 ml) were added. The reaction mixture was refluxed for 4hrs. and then cooled to room temperature. The red solution was decanted and evaporated to dryness. The residue was taken up in water (100 ml) and the aqueous solution was adjusted to a pH value of 9 by addition of 2 N sodium hydroxide and treated with charcoal. The solution was filtered and the filtrate was acidified to a pH of 3 with 2N hydrochloric acid. The orange solid was filtered off washed with water and crystallized from water to give the **title compound** (6.2g; 56%), m.p. 180-181<sup>o</sup> [Found; C, 34.69; H, 4.15; N, 24.04 M<sup>+</sup>(mass spectrum), 173, C<sub>5</sub>H<sub>7</sub>N<sub>3</sub>S<sub>2</sub> requires, C, 34.66; H, 4.07; N, 25.25;] M, 173. <sup>1</sup>H-NMR (DMSO- d<sub>6</sub>) 2.35 (S, 3H, Me), 2.59 (S, 3H, Me).

**5-Hydrazino-6-methyl-1,2,4-triazin-3(4H)-one (18)**

Compound 15 (2g) was dissolved in propan-2-ol and hydrazine hydrate (5 ml) was added. The reaction mixture was heated under reflux for 2 hrs. and allowed to cool to room temperature. The precipitated white solid was filtered off, washed with water and dried to afford the **title compound** (1.2g; 67%), m.p. 285-288<sup>o</sup> (from water).

**The hydrazone from 5-hydrazino-6-methyl-1,2,4-triazin-3(4H)-one with phenacyl bromide**

Compound 18 (R<sup>1</sup>CH<sub>3</sub>, 9.5g) 5-Hydrazino-6-methyl-1,2,4-triazin-3(4H)-one and phenacyl bromide (0.8g) were refluxed in propan-2-ol (25 ml) for 2 hrs. The solution was cooled down to room temperature and the precipitated pale yellow solid was filtered off to give compound 20 (R=CH<sub>3</sub>, R<sup>2</sup>=ph) (0.7g 61%) m.p. 235-237<sup>o</sup> (decomp) (from propan-2-ol). [Found; C, 44.72; H, 3.82; N, 21.57; M<sup>+</sup> (mass spectrum), 321, C<sub>12</sub>H<sub>12</sub>N<sub>5</sub>OBr requires; C, 44.74, H, 3.76, N, 21.73] M, 321. <sup>1</sup>H-NMR (DMSO- d<sub>6</sub>): 2.2 (S, 3H, Me) 4.78 (S, 2H, CH<sub>2</sub>), 7.45, 8.25 (m, 5H, Ph), 13.51 (brs, 1H, NH).

**9-Methyl-3-phenyl-4H-1,2,4-triazino [4,3-d] 1,2,4-triazin-6(1H)-one (21)**

The above hydrazone (0.5g) was dissolved in propan-2-ol (15 ml) and triethylamine (2 ml) was added. The reaction mixture was refluxed for 24 hrs. and the solvent was evaporated to dryness. The residue was stirred in cold water (10 ml) for 5 min. and the solid was filtered off, washed with water and dried to give the **title compound** (0.2g 54%) m.p. 256-258<sup>o</sup> [Found; C 59.71; H, 4.66; N, 29.05; M<sup>+</sup> (mass spectrum), 214, C<sub>12</sub>H<sub>11</sub>N<sub>5</sub>O requires; C, 59.74; H, 4.59; N, 29.03]; M 241. <sup>1</sup>H-NMR (DMSO- d<sub>6</sub>) 2.11 (S, 3H, Me), 4.59 (S, 2H, CH<sub>2</sub>); 7.45, 7.85 (m, 5H, Ph), 13.34 (br S, 1H, NH).

**The hydrazone from 5-hydrazino-6-methyl-1,2,4-triazin-3(4H)-one and glyoxalic acid**

Compound (18) (R<sup>1</sup>=CH<sub>3</sub> 0.5 g) was dissolved in hot water (15 ml) and glyoxalic acid (0.3g) in water (5 ml) was added dropwise. The reaction mixture was stirred at

room temperature for 2 hrs. and subsequently chilled in an ice bath for a further hour. The precipitated solid was filtered off, washed with water and dried to give compound 19 (R<sup>1</sup>=CH<sub>3</sub>, R<sup>2</sup>=H) (0.4g; 57%) m.p. 249-250, from aqueous dimethylformamide [Found; C, 36.64, H, 3.57; N, 35.6; M<sup>+</sup> (mass spectrum) 197, C<sub>6</sub>H<sub>7</sub>N<sub>5</sub>O<sub>3</sub> requires; C, 36.55; H, 3.58 N, 35.52] M. 197. <sup>1</sup>H-NMR: (DMSO- d<sub>6</sub>): 2.12 (S, 3H, Me), 7.65 (S, 1H, CH) 13.11 (br S, 1H, \*NH).

**3-Morpholino-6-methylmercapto-1,2,4-triazin-5(4H)-one (25)**

3-Morpholino-1,2,4-triazin-5(4H)-one-6-thione (5.5g) was dissolved in sodium carbonate solution [anhydrous sodium carbonate (3g) in water (100 ml)] and methyl iodide (4.1g) was added. The reaction mixture was shaken at room temperature for 2 hrs. The white solid was filtered off, washed with water and dried to give the **title compound** (4.0 g; 68%), mp 300 (decomp) (from aqueous dimethyl formamide [Found; C; 42.08; H, 5.39; N, 24.80; M<sup>+</sup> (mass spectrum), 228, C<sub>8</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>S requires; C, 42.09; H, 5.30; N 24.54, M, 228] <sup>1</sup>H-NMR: (DMSO- d<sub>6</sub>): 2.29 (S, 3H, Me) 6.60 (d, 8H, C<sub>4</sub>H<sub>8</sub>), 12.35 (br S, 1H, NH)

**3-Morpholino-6-methylmercapto-1,2,4-triazine-5(4H) thione (22)**

The above compound (4g) and phosphorus pentasulphide (4g) were refluxed in dry pyridine (150 ml) for 3 hrs. The pyridine was distilled under reduced pressure, the residue was dissolved in 2N sodium hydroxide (100 ml) treated with active charcoal and filtered. The filtrate was adjusted to a pH of 3 with diluted hydrochloric acid, the precipitated solid was filtered off, washed with water and dried to afford the **title compound** (2.5g; 58%), m.p. 239-240<sup>o</sup> (from ethanol) Found; C 39.60; H, 4.79; N, 22.51, M<sup>+</sup> (mass spectrum) 224. <sup>1</sup>H-NMR: (DMSO- d<sub>6</sub>): 2.23 (S, 3H, Me) 3.3 and 3.63 (2S, 8H, C<sub>4</sub>H<sub>8</sub>), 11.85 (br S, 1H, NH).

**5-Hydrazino-6-methylmercapto-3-morpholino-1,2,4-triazine (27)**

The above compound (4g) was dissolved in ethanol (100 ml) and hydrazine hydrate (4.4g) was added. The

reaction mixture was refluxed for 2 hrs. and cooled to room temperature. The solvent was evaporated off and the residue was crystallized from water to afford the **title compound** (3.74g 85%), m.p. 123-124<sup>o</sup> [Found; C, 39.69; H, 5.96; N, 34.73; M<sup>+</sup> (mass spectrum) 242, C<sub>8</sub>H<sub>14</sub>N<sub>6</sub>O<sub>5</sub> requires; C, 39.65; H, 5.83; N; 34.65;] M<sup>+</sup> 242 <sup>1</sup>H-NMR: (DMSO- d<sub>6</sub>): 2.36 (s, 3H, Me), 3.42 (brs, 2H, NH<sub>2</sub>), 3.61 and 3.69 (2d, 8H, C<sub>4</sub>H<sub>8</sub> ).

**The hydrazone from 5-hydrazino-6-methylmercapto-3-morpholino-1,2,4-triazine with glyoxalic acid**

The above compound (1g) was dissolved in hot water and glyoxalic acid (0.4g) in water (10 ml) was added dropwise. The reaction mixture was stirred at room temperature for 2 hrs. and subsequently chilled in an ice bath for 1 hr. The precipitated solid was filtered off washed with water and dried to yield the **title compound** (0.8g; 65%) m.p. 232-233<sup>o</sup>.

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