*Yehia A. Ibrahim*, M. M. Eid and S. A. L. Abdel-Hady*

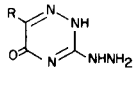
Department of Chemistry, Faculty of Science, University of Cairo, Giza, A. R. Egypt

Received January 17, 1980

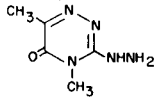
The action of hydrazine on 3-methylmercapto-5-oxo-4-aryl-4,5-dihydro-1,2,4-triazines led to a novel rearrangement and gave 3-arylamino-4-amino-5-oxo-4,5-dihydro-1,2,4-triazines. The mechanism of this rearrangement was discussed.

*J. Heterocyclic Chem.*, **17**, 1733 (1980).

3-Hydrazino-5-oxo-2,5-dihydro-1,2,4-triazines (**1a-c**) are useful starting materials for the synthesis of condensed triazolo (1-5), tetrazolo (3,6,7) and triazino-1,2,4-triazines (6). Previous attempts to synthesize 3-hydrazino-5-oxo-4,6-dimethyl-4,5-dihydro-1,2,4-triazine (**2**) were unsuccessful (4,6).



1



2

a, R=H

b, R=$CH_3$

c, R=$C_6H_5$

In an attempt to synthesize the 4-aryl analogs **4a-d** we studied the reaction of 3-methylmercapto-4-aryl-5-oxo-6-phenyl(or methyl)-4,5-dihydro-1,2,4-triazines (**3a-d**) with hydrazine hydrate. Instead of obtaining the expected 3-hydrazino-4-aryl-5-oxo-6-phenyl(or methyl)-4,5-dihydro-1,2,4-triazines (**4a-d**), the products from this reaction were established to be 3-arylamino-4-amino-5-oxo-6-phenyl(or methyl)-4,5-dihydro-1,2,4-triazines (**7a-d**) (*cf.*, Table) based on the following facts (*cf.*, Scheme 1).

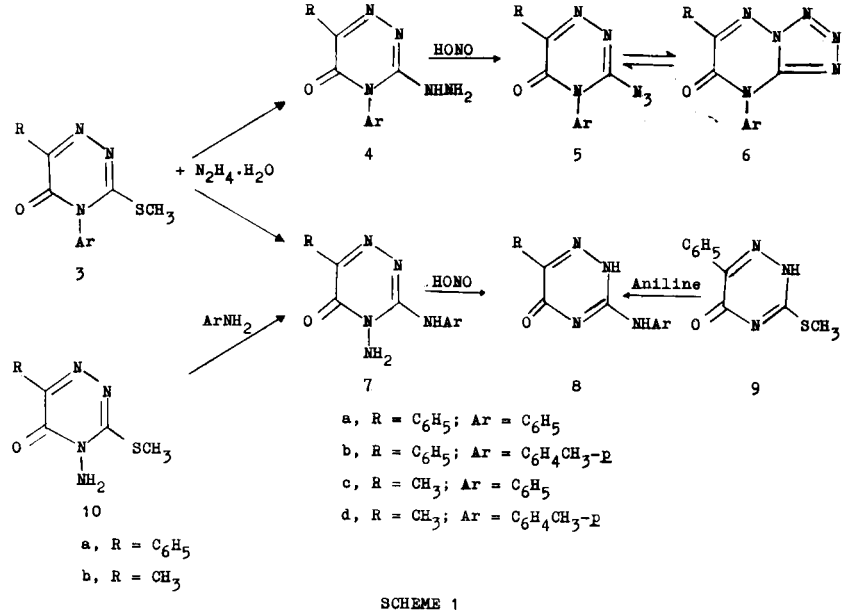
a).

The products **7**, *e.g.*, **7a**, underwent deamination by the action of nitrous acid to give 3-phenylamino-5-oxo-6-phenyl-2,5-dihydro-1,2,4-triazine (**8a**) structure of **8a** was proved by independent synthesis *via* the action of aniline on 3-methylmercapto-5-oxo-6-phenyl-2,5-dihydro-1,2,4-triazine (**9**) (8). On the other hand, azides **5** or tetrazoles **6** would be the expected products if nitrous acid acted upon the 3-hydrazino derivatives **4a-d**.

b).

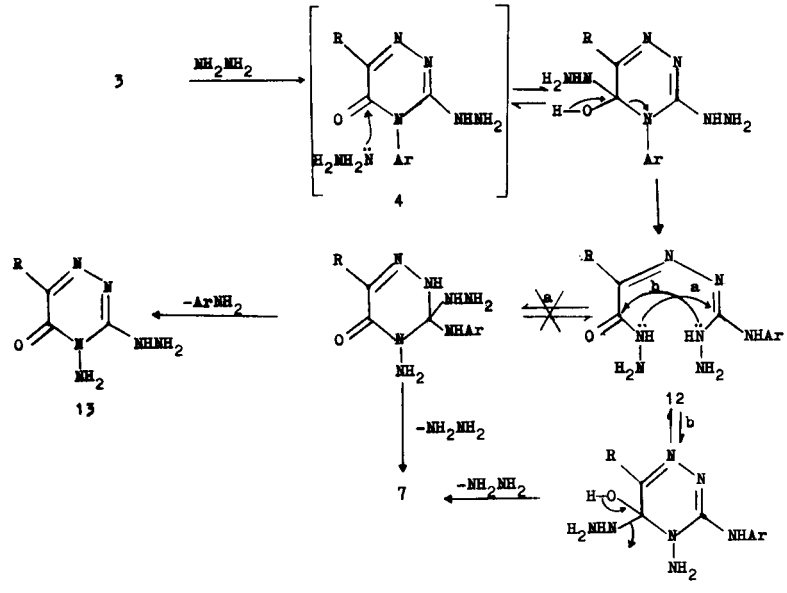
Independent synthesis of compounds **7a-d** have been achieved *via* the action of aromatic amines, namely aniline and *p*-toluidine on 3-methylmercapto-4-amino-5-oxo-6-phenyl(or methyl)-4,5-dihydro-1,2,4-triazines (**10a,b**) (9).

Scheme 2 illustrates the possible mechanism for this novel rearrangement in this class of compounds. The formation of the hydrazine derivatives **4a-d** is probably the first step followed by nucleophilic attack of a second hydrazine molecule on C-5. Apparently, the increased electrophilicity of this carbon atom is due to the presence of the 4-aryl substituents [in cases where there is no 4-aryl




SCHEME 1

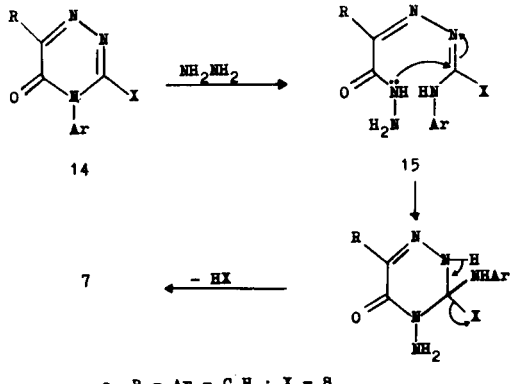
0022-152X/80/081733-03$02.25



SCHEME 2

substituents no such rearrangement was observed (1-3,10,11)]. Intermediate **12** may undergo ring closure according to two possible pathways a and b. However pathway a can be excluded since it can lead to the 3-hydrazino derivatives **13** (by extrusion of $ArNH_2$) as well as compounds **7**.

We studied also the action of hydrazine hydrate on both 3-thioxo-5-oxo **14a,b** and 3,5-dioxo-4-aryl-2,3,4,5-tetrahydro-1,2,4-triazine **14c**. We found that while the former undergoes the same rearrangement to give products **7**, the latter did not (12). This gives an evidence for the formation of a common intermediate **4** from both compounds **3** and **14a,b** but not from **14c** [it is well known that 3-methylmercapto and 3-thioxo-5-oxo but not 3,5-dioxo 1,2,4-triazine derivatives readily undergo hydrazinolysis to the corresponding 3-hydrazino-5-oxo derivatives (1-3, 11,13)]. This also exludes another mechanistic pathway (Scheme 3). Since this mechanism predicts the same final products **7** from any of the starting materials **3**, **14a-c**. In this mechanism the common intermediate **15** arising by the triazine ring opening can cyclize into **7** with extrusion of HX (*i.e.*, methanethiol, hydrogen sulfide and water, respectively).



a, R = Ar = $C_6H_5$; X = S

b, R = $C_6H_5$; Ar = $C_6H_4CH_3$-p; X = S

c, R = Ar = $C_6H_5$; X = O

SCHEME 3

## EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded with a Unicam SP 1200 infrared spectrophotometer. Mass spectrum is obtained on a Mass Spectrometer MAT 112. Elemental analyses were carried out by the Microanalytical Centre, Cairo University.

3-Methylmercapto-4-*p*-tolyl-5-oxo-6-methyl-4,5-dihydro-1,2,4-triazine (**3d**).

To a cold solution of sodium methoxide in methanol (prepared from 0.11 g. of sodium in 15 ml. of anhydrous methanol), was added compound **14** (R = $CH_3$; Ar = $C_6H_4CH_3$-*p*) (1.16 g.) with stirring, until all the solid had dissolved. Then, methyl iodide (0.3 ml.) was added. The reaction mixture was left overnight at room temperature. The precipitated solid was then collected and recrystallized from ethanol as colorless needles of **3d**, m.p. 140° (yield *ca.* 90%); ir (potassium bromide): 3085, 3030, 2950, 1685-1725 and 1655 $cm^{-1}$; ms: $M^+$, m/e 247.

*Anal.* Calcd. for $C_{12}H_{13}N_3OS$: C, 58.27; H, 5.29; N, 16.99; S, 12.96. Found: C, 58.50; H, 5.50; N, 16.90; S, 12.60

3-Arylamino-4-amino-5-oxo-6-phenyl(or methyl)-4,5-dihydro-1,2,4-triazines (**7a-d**).

(a) By the Action of Hydrazine Hydrate on 3-Methylmercapto-5-oxo-4-aryl-4,5-dihydro-1,2,4-triazines (**3a-d**).

General Procedure.

The following exemplifies the procedure. To compound **3a** (0.5 g.) in ethanol (5 ml.), was added hydrazine hydrate (1 ml., 80%). The reaction mixture was heated under reflux for 3 hours, and left to cool. The precipitate was collected and recrystallized from ethanol as colorless needles of **7a**, m.p. 215.5° (yield, *ca.* 80%).

Table

3-Arylamino-4-amino-5-oxo-6-phenyl(or methyl)-4,5-dihydro-1,2,4-triazines (**7a-d**)

| Products (a) | M.p. °C | Yield % (b) | Formula (Molecular Weight) | Analysis % Calcd./Found C | H | N |
|---|---|---|---|---|---|---|
| **7a** | 215 (9) | 80 | $C_{15}H_{13}N_5O$ (279.28) | — | — | — |
| **7b** | 244 | 75 | $C_{16}H_{15}N_5O$ (293.31) | 65.51<br>65.80 | 5.15<br>5.20 | 23.87<br>24.20 |
| **7c** | 235 (9) | 25 | $C_{10}H_{11}N_5O$ (217.21) | — | — | — |
| **7d** | 243 | 25 | $C_{11}H_{13}N_5O$ (231.24) | 57.13<br>57.60 | 5.66<br>6.00 | 30.28<br>30.30 |

(a) Compounds **7a-d**, prepared by different procedures, were found identical (mixed m.p. and ir spectra); **7a**, ir (potassium bromide): 3340, 3280, 3080, 3060, 2950, 1700, 1610, 1570, 1540, 1500, 1480, 1455, 1440, 1310, 1200, 1065, 1030, 900, 885, 850, 790, 750, 700, 695 and 660 $cm^{-1}$; **7b**, ir (potassium bromide): 3330, 3270, 3080, 3060, 2930, 1695, 1610, 1570, 1540, 1520, 1500, 1475, 1440, 1310, 1200, 1070, 1030, 950, 935, 885, 865, 835, 810, 790, 745, 705, 695 and 660 $cm^{-1}$; **7c**, ir (potassium bromide): 3320, 3210, 2935, 1685, 1640, 1595, 1555, 1520, 1500, 1490, 1450, 1390, 1315, 1170, 1120, 1085, 1000, 935, 905, 860, 760, 755, 705, 690 and 670 $cm^{-1}$; **7d**, ir (potassium bromide): 3370, 3350, 3320, 3230, 2940, 1690, 1635, 1590, 1550, 1510, 1385, 1310, 1170, 1115, 1005, 940, 860, 845, 825, 815, 805, 706 and 700 $cm^{-1}$. (b) This yield corresponds to the products obtained from compounds **3a-d** following the general procedure A.

(b) By the Action of Aniline and/or *p*-Toluidine on 3-Methylmercapto-4-amino-5-oxo-6-phenyl- and 6-Methyl-4,5-dihydro-1,2,4-triazines (**10a,b**).

Compounds **7a,c** were obtained by the action of aniline on compounds **10a,b**, respectively, as described by Dornow, *et al.* (9).

Compounds **7b,d** were prepared by heating a mixture of each of compounds **10a,b** (0.5 g.), respectively, with *p*-toluidine (0.5 g.) at 170° (oil bath) for 3 hours. The reaction mixture was cooled triturated with ethanol and recrystallized from ethanol as colorless needles of **7b** (yield 80%) and **7d** (yield 50%), respectively.

(c) By the Action of Hydrazine Hydrate on 3-Thioxo-5-oxo-4-aryl-2,3,4,5-tetrahydro-1,2,4-triazines (**14a,b**).

To each of compounds **14a,b** (0.5 g.) in ethanol (5 ml.) was added hydrazine hydrate (1 ml., 80%). The reaction mixture was heated under reflux for 5 hours, cooled and the precipitate was collected and recrystallized from ethanol into colorless needles of **7a,b**, respectively.

Action of Nitrous Acid on Compound **7a**.

To compound **7a** (0.5 g.) in 2*N* hydrochloric acid (10 ml.) was added aqueous sodium nitrite (5 ml., 5%) at 10°. The precipitate was collected and recrystallized from DMF into colorless needles of **8a**, m.p. 325° (yield, *ca.* 80%). Compound **8a** was found identical with an authentic sample prepared by the action of aniline on 3-methylmercapto-5-oxo-6-phenyl-2,5-dihydro-1,2,4-triazine (**9**) (8); ir (potassium bromide): 3300, 3190 and 1625 $cm^{-1}$.

## REFERENCES AND NOTES

(1) K. Kalfus, *Collect. Czech. Chem. Commun.*, **33**, 2513 (1968).
(2) A. Dornow, W. Abele and H. Menzel, *Chem. Ber.*, **97**, 2179 (1964).
(3) A. Dornow, H. Pietsch and P. Marx, *ibid.*, **97**, 2647 (1964).
(4) J. Daunis, R. Jacquier and P. Villefont, *Bull. Soc. Chim. France*, 2492 (1969).
(5) Ilford Ltd., Belgian Patent 642,615, May 18, 1964; British Application, Jan. 16, 1963; *Chem. Abstr.*, **63**, 18127 (1965).
(6) A. Dornow, H. Menzel and P. Marx, *Chem. Ber.*, **97**, 2185 (1964).
(7) M. M. Goodman and W. W. Paudler, *J. Org. Chem.*, **42**, 1866 (1977).
(8) A. K. Mansour and Y. A. Ibrahim, *J. Prakt. Chem.*, **315**, 221 (1973).
(9) A. Dornow, H. Menzel and P. Marx, *Chem. Ber.*, **97**, 2173 (1964).
(10) J. Lee and W. W. Paudler, *J. Heterocyclic Chem.*, **9**, 995 (1972).
(11) D. Libermann and R. Jacquier, *Bull. Soc. Chim. France*, 383 (1961).
(12) The detailed study of the action of hydrazine hydrate on **14c** and its derivatives will be described in a forthcoming publication.
(13) R. Fusco and S. Rossi, *Tetrahedron*, **3**, 209 (1958).