

## Reduction of 1-alkyl/aryl-3-(4-alkyl-5-alkylimino- $\Delta^2$ -1,2,4-thiadiazolin-3-yl) thioureas: Formation of 1,3,5-triazine-2-thiones

SATISH R. SURVE and SHEENA V. NAIR\*

Department of Chemistry, University of Kerala  
Trivandrum-695 581, India

E-mail: sheenanair2000@yahoo.com

Reduction of 1-alkyl/aryl-3-(4-alkyl-5-alkylimino- $\Delta^2$ -1,2,4-thiadiazolin-3-yl) thioureas in a basic medium yields 1,3-diaryl-4-alkyl/arylimino-6-iminohexahydro-1,3,5-triazine-2-thiones. The structure assigned to these triazines was based on the substituent pattern on the chain formed by the ring opening and its reaction towards alkali.

**Key Words:** Synthesis, Thioureas, Triazines.

### INTRODUCTION

Among the various methods for the synthesis of 1,3,5-triazine thiones the reaction of isothiocyanates with biguanide, dicyandiamide, amidinothiourea or dithiobiuret appears to be quite elegant for the synthesis of 1,3,5-triazine derivatives. In such reactions, the involvement of a labile, extended urea-like chain of more than six atoms with alternate carbon and nitrogen has been invoked. These urea-like chains are reported to undergo rapid eliminative cyclisation yielding 1,3,5-triazine derivatives<sup>1-4</sup>. Similar reactions of 1,3-disubstituted amidinothiourea with isothiocyanates did not appear to be a feasible method since the amidinothioureas as such were found to be very unstable in neutral and basic media. Building up of an amidinothiourea chain of this type was conceived by the reductive ring cleavage of a suitably substituted derivative of 3-amino-4-substituted-5-substituted imino- $\Delta^2$ -1,2,4-thiadiazolines<sup>5,6</sup>. It was expected that the reduction of a product obtained by the condensation of isothiocyanate with a suitably substituted 1,2,4-thiadiazole would give rise to such an extended urea-like chain intermediate and this hence could yield 1,3,5-triazines. Several 1-alkyl/aryl-3-(4-aryl-5-alkyl/arylimino- $\Delta^2$ -1,2,4-thiadiazolin-3-yl) thioureas were therefore synthesized and their reduction products examined. It was observed that depending on the substituents 1,3,5-triazine-2-thiones, 1,3,5-tri-

\*Address for correspondence: 3, Kalpakam, Chedda Nagar, Mumbai-400 089, India.

azine-2,4-dithiones and 1,5-disubstituted amidinothioureas are formed. Since the thiadiazoline derivatives now prepared contain only alkyl substituents, it was of interest to examine the reduction products of these thiocarbamoyl derivatives.

## EXPERIMENTAL

### **Reduction of 1-alkyl/aryl-3-(4-alkyl-5-alkylimino- $\Delta^2$ 1,2,4-thiadiazolin-3-yl) thioureas: Formation of 1,3 dialkyl-4-alkyl/aryl imino-6-imino-hexahydro-1,3,5-triazine-2-thione derivatives with ammoniacal hydrogen sulphide**

A slow stream of hydrogen sulphide was passed through a solution of 1-phenyl-3-(4-benzylimino- $\Delta^2$ -1,2,4 thiadiazolin-3-yl) thiourea in ethanol and ammonium hydroxide for 15 min. The dark green coloured reaction mixture was then heated on a boiling water bath when a product was found to separate. When the reaction mixture turned pale yellow, hydrogen sulphide gas was again passed. When the precipitation of the product appeared complete, it was collected, washed with water and dried. TLC analysis of the product showed it to be a single compound. Crystallization from ethanol gave shining needles of 1,3-dibenzyl-4-phenylimino-6-imino-hexahydro-1,3,5-triazine-2-thione, m.p. 185°C. Analysis: found N, 17.4; S; 7.9;  $C_{23}H_{21}N_5S$  requires N, 17.5; S, 8.0.

Other 1-alkyl/aryl-3-(4-alkyl-5-alkylimino- $\Delta^2$ -1,2,4-thiadiazolin-3-yl) thioureas were also similarly reduced and the products formed are listed in Table-1.

## RESULTS AND DISCUSSION

### **Reduction of 1-alkyl/aryl-3-(4-alkylimino- $\Delta^2$ -1,2,4-thiadiazolin-3-yl) thioureas: Formation of 1,3-dialkyl-4-alkyl/arylimino-6-imino-hexahydro-1,3,5-triazine-2-thiones**

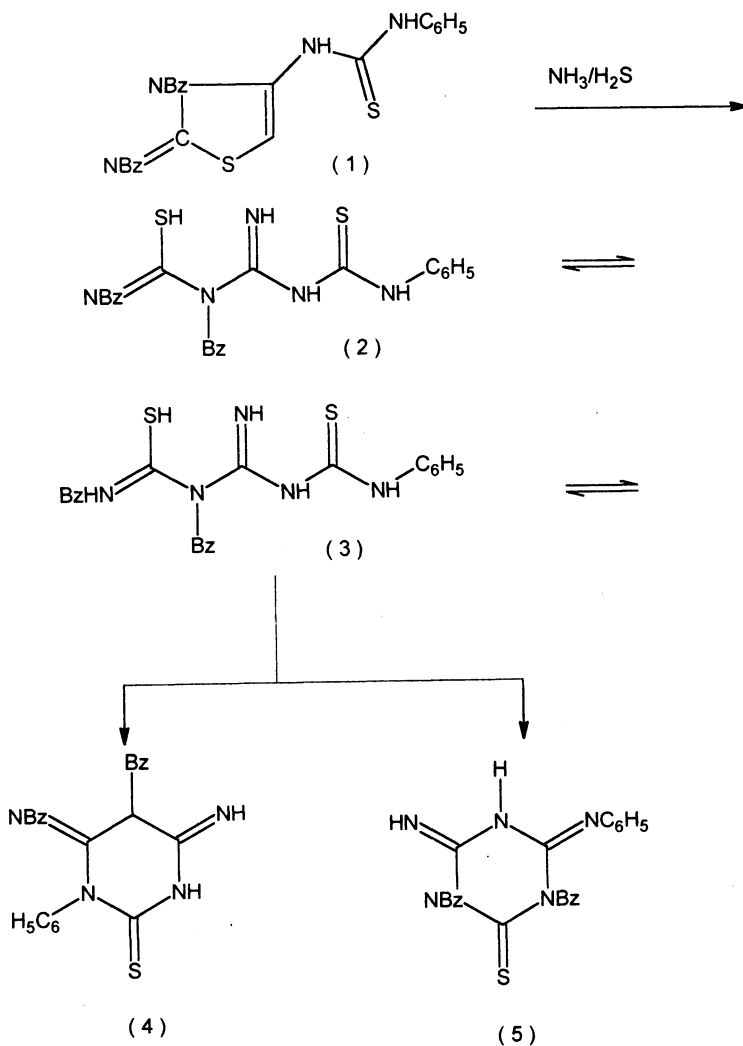
In a typical reaction when hydrogen sulphide is introduced into a hot solution of 1-phenyl-3-(4-benzyl-5-benzylimino- $\Delta^2$ -1,2,4-thiadiazolin-3-yl) thiourea in ammoniacal ethanol, a product was found to be formed whose elemental analysis corresponds to  $C_{23}H_{21}N_5S$ . TLC examination of the product obtained confirmed that only one compound is formed.

The product formed in the above reaction was found to be insoluble in aqueous alkali indicating the absence of an enolizable  $>C=S$  group.

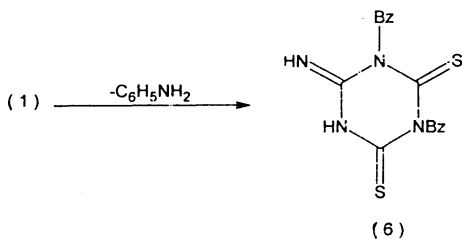
Most of the 3,5-diamino-1,2,4-thiadiazole derivatives are known to undergo ring opening on reduction and yield amidinothioureas<sup>5,6</sup>. The thiadiazol-3-yl thiourea derivative (1) hence was expected to undergo reduction and yield a labile urea-like chain intermediate (2). This could cyclize under the reaction conditions to a 1,3,5-triazine derivative with the elimination of an amine of hydrogen sulphide. Elimination of a molecule of hydrogen sulphide would result in the formation of 1,3,5-triazine derivative with structures (4) or (5) depending upon which (4) or (5) sulphur is involved in the elimination during cyclization.

TABLE I  
1,3-DIALKYL-4-ALKYL/ARYL IMINO-6-IMINO-HEXAHYDRO-1,3,5-TRIAZINE-2-THIONE

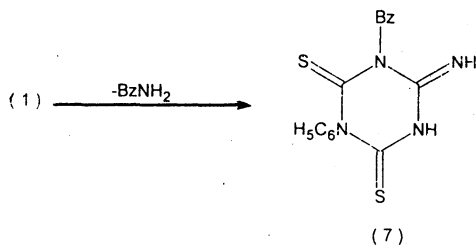
Sl. No.	Substitutions			m.f.	Yield	m.p. (°C)	% S		% N	
	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>				Found	Required	Found	Required
1	Benzyl	Benzyl	Methyl	C <sub>18</sub> H <sub>19</sub> N <sub>5</sub> S	30	255	9.4	9.5	20.7	20.8
2	Benzyl	Benzyl	Ethyl	C <sub>19</sub> H <sub>21</sub> N <sub>5</sub> S	32	257	9.0	9.1	19.9	19.9
3	Benzyl	Benzyl	Propyl	C <sub>20</sub> H <sub>23</sub> N <sub>5</sub> S	34	276	8.7	8.7	19.1	19.2
4	Benzyl	Benzyl	<i>i</i> -Propyl	C <sub>20</sub> H <sub>25</sub> N <sub>5</sub> S	33	245	8.7	8.7	19.1	19.2
5	Benzyl	Benzyl	Butyl	C <sub>21</sub> H <sub>25</sub> N <sub>5</sub> S	30	215	8.3	8.3	18.4	18.5
6	Benzyl	Benzyl	Phenyl	C <sub>23</sub> H <sub>21</sub> N <sub>5</sub> S	30	185	7.9	8.0	17.4	17.5
7	Benzyl	Benzyl	<i>p</i> -Tolyl	C <sub>24</sub> H <sub>23</sub> N <sub>5</sub> S	32	194	7.7	7.8	16.9	16.9
8	Benzyl	Benzyl	<i>o</i> -Phenetyl	C <sub>25</sub> H <sub>25</sub> N <sub>5</sub> OS	31	198	6.7	7.2	14.8	15.8
9	Propyl	Propyl	Methyl	C <sub>10</sub> H <sub>19</sub> N <sub>5</sub> S	32	220	13.0	13.3	28.9	29.0
10	Propyl	Propyl	Ethyl	C <sub>11</sub> H <sub>21</sub> N <sub>5</sub> S	30	238	12.5	12.6	27.5	27.6
11	Propyl	Propyl	Propyl	C <sub>11</sub> H <sub>23</sub> N <sub>5</sub> S	33	240	11.8	11.9	25.6	26.0
12	Propyl	Propyl	<i>i</i> -Propyl	C <sub>12</sub> H <sub>23</sub> N <sub>5</sub> S	32	210	11.8	11.9	25.9	26.0
13	Propyl	Propyl	Butyl	C <sub>13</sub> H <sub>25</sub> N <sub>5</sub> S	30	218	11.2	11.3	24.7	24.7
14	Propyl	Propyl	Phenyl	C <sub>15</sub> H <sub>21</sub> N <sub>5</sub> S	30	179	10.5	10.6	23.0	23.1
15	Propyl	Propyl	<i>p</i> -Tolyl	C <sub>16</sub> H <sub>23</sub> N <sub>5</sub> S	33	160	9.9	10.1	22.0	22.1
16	Propyl	Propyl	<i>p</i> -Phenetyl	C <sub>17</sub> H <sub>25</sub> N <sub>5</sub> OS	30	176	8.3	8.4	18.4	18.5
17	Benzyl	Benzyl	<i>p</i> -Chlorophenyl	C <sub>23</sub> H <sub>18</sub> ClN <sub>5</sub> S	32	195	7.6	7.4	16.2	16.2
18	Benzyl	Benzyl	<i>p</i> -Anisyl	C <sub>24</sub> H <sub>21</sub> N <sub>5</sub> OS	31	169	7.5	7.5	16.3	16.4
19	Butyl	Butyl	Methyl	C <sub>12</sub> H <sub>21</sub> N <sub>5</sub> S	31	180	10.9	11.9	25.9	26.2



Two more possible cyclizations are there. Structure (6) would represent the 1,3,5-triazine derivative formed if elimination of a molecule of  $C_6H_5NH_2$  occurred from the labile intermediate (2) during cyclization.



On the other hand the elimination of a molecule of benzylamine from (1) would give rise to a triazine with structure (7)



Hence the possible structures are (4), (5), (6), (7). But structures (6) and (7) can be ruled out on the basis of the elemental composition data which would not agree with that obtained experimentally. The presence of an enolizable  $>\text{C}=\text{S}$  group in the structure (5) rules out that structure because the product obtained is insoluble in alkali indicating the absence of such a grouping. In the light of the above chemical evidence it can be presumed that structure (5) correctly represents the product formed.

The pmr spectrum of the triazine derivative obtained from the phenyl thioureido derivative of 3-amino-4-benzyl-5-benzylimino- $\Delta^2$ -1,2,4 thiadiazoline shows a broad singlet at  $\delta$  4.7 (1H) due to the exo-imino-NH proton which is more shielded than the endo-NH. The sharp singlets seen at  $\delta$  4.95 (2H) ( $=\text{NBz}$ ) and  $\delta$  5.94 (2H) ( $=\text{N}=\text{Bz}$ ) are assigned to the methylene protons of the benzyl amino and the benzyl group on the endo-nitrogen respectively. The broad multiplets centred between  $\delta$  6.4 and  $\delta$  7.2 (16H) correspond to the protons of the 3-phenyl groups and the endo-amino nitrogen. This data satisfactorily accounts for the 1,3-dibenzyl-4-phenylimino-6-imino-hexahydro-1,3,5-triazine-2-thione structure (5).

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