

**Mechanism of Oxidative Debenzylation in Isodithiobiuret System :
Preparation of some new 5-Diaryl/Arylalkylamino-3-Aryl/
Alkyl-Imino-1,2,4-Dithiazolines by the Oxidative Debenzylation of
1,1,5,-Trisubstituted-2-S-Benzyliso-4-Thiobiurets**

V. K. Verma

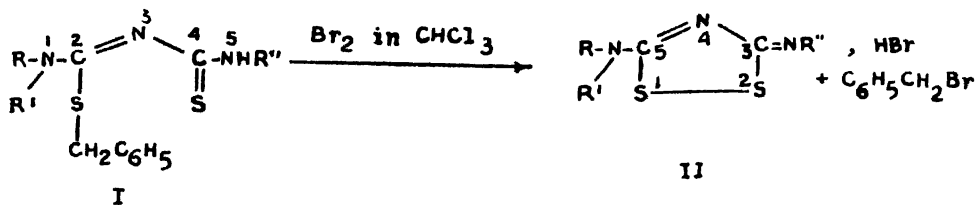
Preparation of 5-ethylphenylamino-3-*p*-Cl-phenylimino-, 5-ethylphenylamino-3-*p*-tolylimino-, 5-ethyl-phenylamino-3-benzylimino-, 5-diphenylamino-3-*p*-Cl-phenylimino, 5-diphenylamino-3-benzylimino-1, 2, 4-dithiazolines has been described by the oxidative debenzylation of the corresponding 1, 1, 5-trisubstituted-2-S-benzyliso-4-thiobiurets. Mechanism of the reaction has been discussed.

In continuation to the earlier studies on this subject,¹⁻³ this communication describes the synthesis of some new 5-disubstituted amino-3-substitutedimino-1, 2, 4-dithiazolines (II) by the oxidative debenzylation of the related 1, 1, 5-trisubstituted-2-S-benzyliso-4-thiobiurets¹.

The condensation of the appropriate 1-disubstituted-2-S-benzylisothiocarbamides with the required aryl/alkylisothiocyanates afforded the desired isodithiobiurets (I) which on oxidation with bromine in chloroform afforded the related 1, 2, 4-dithiazolines (II). The structure of (II) was confirmed by their preparation by the direct oxidation of the related 1, 1, 5-trisubstituted-2, 4-dithiobiurets, which were obtained by the reductive debenzylation of the respective isodithiobiurets (I) with hydrogen sulphide in pyridine-triethylamine (vide Experimental Tables 1, 2 and 3) and also by the reduction of (II) to the corresponding 1, 1, 5-trisubstituted-2,4-dithiobiurets.

The oxidative debenzylation reaction can be represented

as follows :

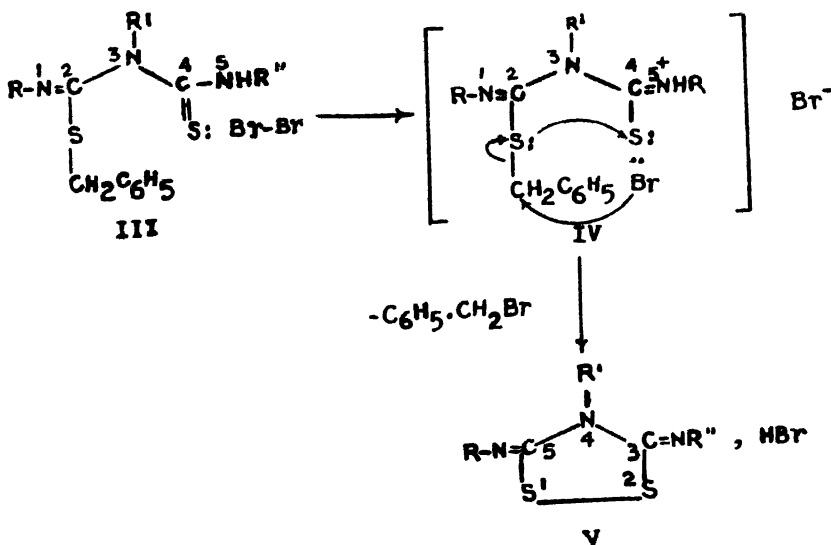


where R, R' & R'' = aryl or alkyl or hydrogen

1. C. P. Joshua and V. K. Verma, *Jour. Indian Chem. Soc.*, 1961, **38**, 988.
2. V. K. Verma, *J. Sci. industr. Res.*, 1962, **21B**, 491.
3. V. K. Verma, *Indian J. Chem.*, 1963, **1**, 116.

Mechanism : The initial step appears to be the attack of the oxidant (bromine or iodine) on the sulphur atom of the $>C=S$ group in position 4- of the isodithiobiurets (III).

This sulphur of the thiocarbonyl group is a strong nucleophile ($H_2N-C(=S)N=C(=O)R$) and offers a suitable site for attack by an electrophilic reagent such as the Br^+ available from the oxidant, forming a sulphenyl bromide (IV) intermediate which eliminates benzylbromide and forms a dithiazolidine/dithiazoline salt (V). Thus :



EXPERIMENTAL

1, 1, 5-trisubstituted-2-S-benzyliso-4-thiobiurets (I) : The required 1-disubstitutedthiocarbamides were benzylated following Werner's procedure⁴ and the benzene solution of the related 2-S-benzylisothiocarbamides thus obtained treated with the required aryl/alkylisothiocyanate (1 : 1 mole) on waterbath for about 30 min. The semisolid product, on washing with petroleum ether followed by treatment with ethanol, afforded the expected 1, 1, 5-trisubstituted-2-S-benzyliso-4-thiobiurets as crystalline products. These were recrystallised from ethanol except 1, 1-diphenyl-5-benzyl-2-S-benzyl-isothiobiuret which was purified by dissolving in chloroform and reprecipitation with petroleum ether (Table 1).

5-disubstitutedamino-3-substitutedimino-1, 2, 4-dithiazolines (II) :

(i) *Oxidative debenylation of 1, 1, 5-trisubstituted-2-S-benzyliso-4-thiobiurets with Bromine in chloroform* : Details of a typical experiment are as follows : To a warm solution of 1-ethyl-1-phenyl-5-benzyl-2-S-benzyliso-4-thiobiuret (3 g) in chloroform (8 ml.) was added molecular bromine (1 ml) with brisk stirring until the colour of bromine persisted. Expulsion of benzylbromide was evident by its lachrymatory fumes; to complete the reaction, the mixture was allowed to stand for 30 min. The semisolid product on treatment

4. E. A. Werner, *J. Chem. Soc.*, 1890, 57, 295.

TABLE 1

1, 1-diaryl/arylalkyl-5-aryl-2-S-benzyliso-4-thiobiurets

2-S-benzyliso-thiocarbamide	Reactants		1, 1, 5-trisubstituted-2-S-benzyliso-4-thiobiurets formed (mol. formula)	Yield %	M.P. °C	Nitrogen %	
	Isothiocyanate					Found	Reqd.
1-ethyl-1-phenyl-	<i>p</i> -Cl-phenyl-		1-ethyl-1-phenyl-5- <i>p</i> -Cl-phenyl- (C ₂₃ H ₂₂ N ₃ S ₂ Cl)	68.9	164	9.01	9.55
1-ethyl-1-phenyl-	<i>p</i> -tolyl-		1-ethyl-1-phenyl-5- <i>p</i> -tolyl- (C ₂₄ H ₂₅ N ₃ S ₂)	59.0	138	9.87	10.02
1-ethyl-1-phenyl-	benzyl-		1-ethyl-1-phenyl-5-benzyl- (C ₂₄ H ₂₅ N ₃ S ₂)	62.8	136	9.74	10.02
1-diphenyl-	<i>p</i> -Cl-phenyl		1, 1-diphenyl-5- <i>p</i> -Cl-phenyl- (C ₂₇ H ₂₂ N ₃ S ₂ Cl)	51.7	154	8.32	8.61
1-diphenyl-	benzyl-		1, 1-diphenyl-5-benzyl- [*] (C ₂₈ H ₂₅ N ₃ S ₂)	49.1	167	8.81	8.99

^{*}This isodithiobiuret was purified by dissolving in minimum amount of chloroform and reprecipitating with petroleum ether.

with a small quantity of ethanol afforded a crystalline solid which was filtered out and washed thoroughly with ethanol followed by ether. On recrystallisation from ethanol the hydrobromide of II, m.p. 185° was obtained. The hydrobromide on treatment with ammonia afforded the free base, which was also recrystallised from ethanol, m.p. 154°. These experiments are summarised in Table 2.

TABLE 2

5-diaryl/arylalkylamino-3-aryl/alkylimino-1, 2, 4-dithiazolines

2-S-benzyliso-4-thiobiurets oxidised	5-diaryl/arylalkylamino-3-aryl/alkylimino-1, 2, 4-dithiazoline formed. (mol. formula)	Yield %	M.P. °C	Dithiazoline Analysis		M.P. °C	Hydrobromide Equivalent Wt.	
				Found	reqd.		Found	Reqd.
1-ethyl-1-phenyl-5- <i>p</i> -Cl-phenyl-	5-ethylphenylamino-3- <i>p</i> -Cl-phenylimino- (C ₁₆ H ₁₄ N ₃ S ₂ Cl)	84.2	123 N S:	11.82 17.70	12.08 18.41	161	417.6	428.5
1-ethyl-1-phenyl-5- <i>p</i> -tolyl-	5-ethylphenylamino-3- <i>p</i> -tolylimino- (C ₁₇ H ₁₇ N ₃ S ₂)	90.7	149 N:	12.59	12.84	167	—	—
1-ethyl-1-phenyl-5-benzyl-	5-ethylphenylamino-3-benzylimino- (C ₁₇ H ₁₇ N ₃ S ₂)	79.0	154 N:	12.73	12.84	185	399.6	408.0
1, 1-diphenyl-5- <i>p</i> -Cl-phenyl-	5-diphenylamino-3- <i>p</i> -Cl-phenylimino- (C ₂₀ H ₁₄ N ₃ S ₂ Cl)	88.5	186 N: S:	10.20 15.21	10.61 16.18	215	468.3	476.5
1, 1-diphenyl-5-benzyl-	5-diphenylamino-3-benzylimino- (C ₂₁ H ₁₇ N ₃ S ₂)	72.6	162 N: S:	10.88 16.33	11.20 17.06	225	415.9	456.0 ¹

(ii) *Oxidation of 1, 1, 5-trisubstituted-2, 4-dithiobiurets with Bromine in dilute ethanol*: The 2, 4-dithiobiurets listed in Table 3 were oxidised with bromine in ethanolic solution and ether added when the hydrobromides of the respective dithiazolines precipitated. Free bases were obtained by treating these with ammonia. The hydrobromides and bases were crystallised from ethanol. No depression in the mixed melting points were observed when mixed with the respective 5-di-substituted-amino-3-substituted-imino-1, 2, 4-dithiazolines recorded in Table 2.

(i) *1, 1-diaryl arylalkyl 5-aryl-2, 4-dithiobiurets: Reduction of (I) with hydrogensulphide in pyridine-triethylamine medium*: The isodithiobiurets (I) were reduced with hydrogensulphide (for 4 hr.) in pyridine-triethylamine (6:1) medium⁵. The reaction mixture on pouring over crushed ice and acidification with hydrochloric acid, afforded the related 2,4-dithiobiurets which were filtered out and crystallised from ethanol (Table 3).

TABLE 3

1, 1-diaryl/arylalkyl-5-arylalkyl-2, 4-dithiobiurets: Reduction of 2-S-benzyliso-4-thiobiurets (Table 1) in pyridine-triethylamine with hydrogen sulphide

2-S-benzyliso-4-thiobiurets reduced	1, 1-diaryl/arylalkyl-5-aryl/alkyl-2, 4-dithiobiurets formed (mol. formula)	Yield %	M.P. °C	Nitrogen % Found	% Req'd.
1-ethyl-1-phenyl-5- <i>p</i> -Cl-phenyl-	1-ethyl-1-phenyl-5- <i>p</i> -Cl-phenyl- (C ₁₆ H ₁₆ N ₃ S ₂ Cl)	76.1	104	11.69	12.01
1-ethyl-1-phenyl-5- <i>p</i> -tolyl-	1-ethyl-1-phenyl-5- <i>p</i> -tolyl- (C ₁₇ H ₁₉ N ₃ S ₂)	74.3	114	11.92	12.76
1-ethyl-1-phenyl-5-benzyl-	1-ethyl-1-phenyl-5-benzyl- (C ₁₇ H ₁₉ N ₃ S ₂)	57.9	126	12.33	12.76
1, 1-diphenyl-5- <i>p</i> -Cl-phenyl-	1, 1-diphenyl-5- <i>p</i> -Cl-phenyl- (C ₂₀ H ₁₆ N ₃ S ₂ Cl)	65.0	141	10.31	10.56
1, 1-diphenyl-5-benzyl-	1, 1-diphenyl-5-benzyl (C ₂₁ H ₁₉ N ₃ S ₂)	72.3	116	10.74	11.14

(ii) *Reduction of 1,2,4-dithiazolines (II) with ethanolic ammoniacal hydrogen sulphide*: The dithiazolines (II) (Table 2) were dissolved in hot, ethanolic, ammoniacal hydrogen sulphide and hydrogen sulphide passed for about 45 min. On dilution and acidification, the expected 2, 4-dithiobiuret was obtained. These were crystallised from aq. ethanol. No depression in m.p. was observed when mixed with the respective 2, 4-dithiobiurets recorded in Table 3.

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Chemistry Section,
Institute of Technology,
Banaras Hindu University,
Varanasi-5.

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