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THE MECHANISM OF 2-ARYLIMINOTHIAZOLIDINE FORMATION BY THE NOVEL ELIMINATION OF DIMETHYL DISULFIDE

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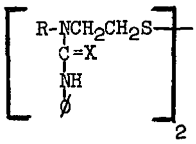
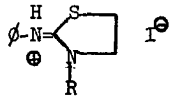
2-Aryliminothiazolidines (II) are formed by treatment of 1-(2-hydroxylethyl)thioureas with mineral acids;[1,2] by reaction of 1,3-disubstituted thioureas with ethylene bromide;[3-5] and from arylisothiocyanates and β-aminoethylphosphites.[6] In this connection, we wish to report that reaction of 1-substituted 1-(2-dithiobis)ethyl-3-phenyl-bis-thioureas (Ia,b)[7] with excess methyl iodide in refluxing ethanol affords 2-phenylimino-3-substituted-thiazolidinium hydroiodides (II) in yields of 61 and 66% when R = benzyl (m.p. 177.5-179.5°) and phenethyl (m.p. 216-218°), respectively. Compounds IIa and IIb were identified by elemental analysis [(found, R = benzyl): C, 48.26; H, 4.36; N, 6.91; I, 32.01; S, 8.11; calcd. for $C_{16}H_{17}N_2IS$: C, 48.49; H, 4.33; N, 7.07; I, 32.03; S, 8.09] and [(found, R = phenethyl): C, 49.64; H, 4.52; N, 6.77, I, 31.24; S, 7.85; calcd. for $C_{17}H_{19}N_2IS$: C, 49.76; H, 4.67; N, 6.83; I, 30.93; S, 7.81], by IR-spectrum (absorption in accordance with the presence of $C = \overset{\oplus}{N}H$), and by NMR-spectrum (correct ratio of aromatic:aliphatic protons).



I

a, $R = C_6H_5CH_2$; $X = S$
b, $R = C_6H_5CH_2CH_2$; $X = S$
c, $R = C_6H_5CH_2CH_2$; $X = O$



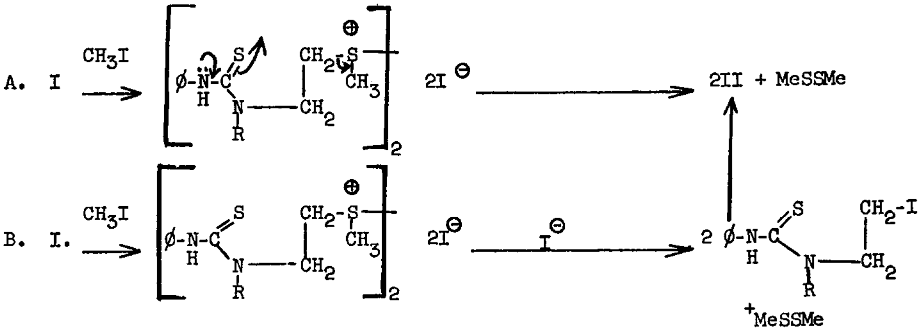
II

a, $R = C_6H_5CH_2$
b, $R = C_6H_5CH_2CH_2$

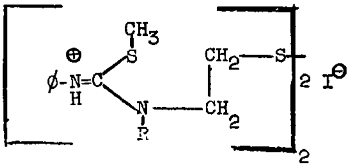
This conversion appears unique to thioureas having a disulfide substituent. The reactio of 1-[(2-dithiobis)ethyl]-1-(phenethyl)-3-phenyl-bis-urea (Ic)[8] and methyl iodide was carried out and only unchanged starting material was recovered. Similarly the mercaptan corresponding to Ib (1-benzyl-1-(2-mercaptoethyl)-3-phenylthiourea) gave no product on treatment with excess methyl iodide in boiling ethanol.

That dimethyl disulfide was present during the reaction was evidenced by gas chromatographic studies using a Porapak Q column and comparison of retention time with an authentic sample. The presence of dimethyl disulfide during the conversion of I to II was confirmed by mass spectrometry of the vapors above the reaction mixtures. Abundant ions were observed at m/e = 94 (M^+), m/e = 64 (S_2^+), and m/e = 30 ($C_2H_6^+$) which were also predominant in the mass spectrum of an authentic sample of dimethyl disulfide.

The data cited are thus consistent for the conversion of I to II with the concomitant evolution of dimethyl disulfide. Two mechanisms (A and B) consistent with these observations are depicted below.



The observation that dimethyl disulfide is evolved as the major by-product of the transformation precludes the possibility that the reaction proceeds via an intermediate S-methylisothiouronium salt (III).



III

In either mechanism A or B methylation at the disulfide linkage gives an intermediate having a positively charged sulfur. A redistribution of electron density as shown in mechanism A results in elimination of dimethyl disulfide and formation of II. In mechanism B, iodide ion displaces dimethyl disulfide with the formation of a 2-iodoethyl thiourea intermediate which cyclizes to II. If mechanism B were operating one would not expect to isolate the reactive intermediate; however the corresponding 1-phenyl-3-(2-iodoethyl)urea from Ic and methyl iodide should be isolable. Since only starting materials were obtained from Ic and methyl iodide, we tend to favor mechanism A for this transformation.

Further studies of this novel dimethyl disulfide elimination are being conducted.

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7. The bis-thioureas were prepared by passage of air through the appropriate N-monosubstituted-2-mercaptoethylamine in refluxing ethanol for three days, and subsequent reaction with two equivalents of phenylisothiocyanate. Elemental analyses of these compounds for C, H, N, and S were satisfactory. The molecular weights of these compounds were determined ebulliomertically in N,N-dimethylformamide and were in excellent agreement with theory.
8. The compound was prepared as described in 7. Dry benzene was used as the solvent. Elemental analyses for C, H, N, and S were satisfactory. The molecular weight was determined by ebulliometric means (N,N-dimethylformamide solvent) and was in excellent agreement with theory
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