CYCLIC THIOUREAS[1]

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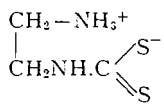
ABSTRACT

1-β-Hydroxyethylimidazolidine-2-thione was prepared from 1-amino-5-hydroxy-3-azapentane and carbon disulphide. Since its properties differ from those claimed by Sergeyev and Kolychev (7) for this compound prepared from ethylene oxide and thiocyanic acid, its structure was confirmed by conversion to 1-β-hydroxyethyl-2-benzylamino-2-imidazoline. The latter compound was prepared for comparison from the known 1-β-hydroxyethyl-2-nitramino-2-imidazoline.

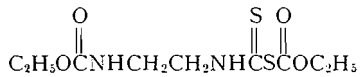
INTRODUCTION

Hofmann (4) found that ethylenediamine combined with carbon disulphide to give an intermediate addition product, which, on being boiled with water, evolved hydrogen sulphide to give ethylene urea. This intermediate was considered to be a dithiocarbamic acid inner salt (I). Later Yakubovich



I

and Klimova (9) proved this assumption to be correct by obtaining compound II from the treatment of the addition product I with alkali and ethylchloro-



II

formate. On the other hand Goldenring (3) found that two mole equivalents of N-phenyltrimethylenediamine combined with one mole of carbon disulphide. This was also observed (2) with N-*p*-tolyltrimethylenediamine. In the present studies 1,3-diaminobutane with carbon disulphide gave an inner salt analogous to that obtained by Hofmann with ethylenediamine. This inner salt was converted by thermal decomposition into 4-methyl-hexahydropyrimidine-2-thione in good yield. Also 1-amino-5-hydroxy-3-azapentane was observed to combine with carbon disulphide to yield a solid addition product. This intermediate when heated in the dry state evolved hydrogen sulphide to give a new product. This new compound melted at 136.5–137.5°C. and gave analytical values in good agreement with the expected 1-β-hydroxyethyl-imidazolidine-2-thione (III). However, Sergeyev and Kolychev (7) previously had claimed to have prepared this compound from ethylene oxide and thiocyanic acid. Their product melted at 168.5°C. with decomposition. Because of this discrepancy in melting points it was considered necessary to confirm

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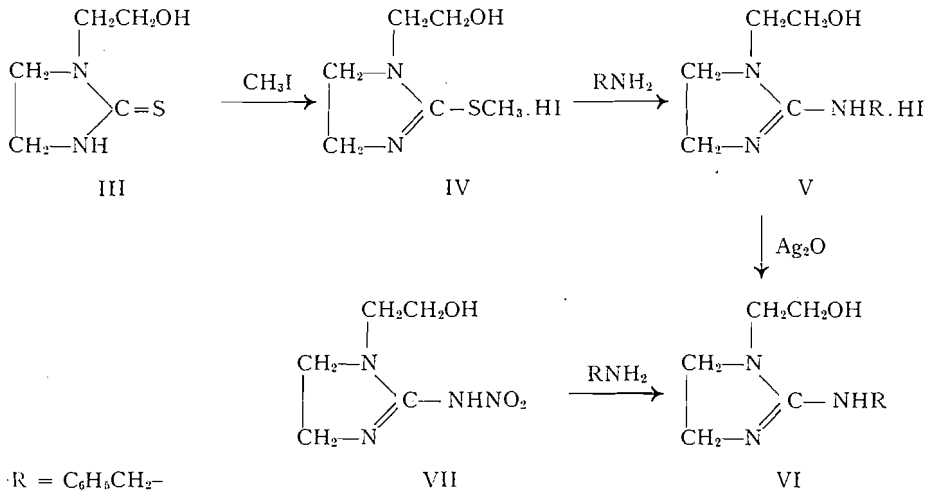
the identity of the compound prepared from 1-amino-5-hydroxy-3-azapentane and carbon disulphide.

1-β-Hydroxyethylimidazolidine-2-thione was converted to 1-β-hydroxyethyl-2-methylmercapto-2-imidazolinium iodide with methyl iodide.



R = $C_6H_5CH_2$–

The iodide (IV) on treatment with benzylamine by the method of Aspinall and Bianco (1) gave the hydrogen iodide salt of 1-β-hydroxyethyl-2-benzylamino-2-imidazoline (V) which was isolated as its picrate. The same compound (VI) was obtained from the known 1-β-hydroxyethyl-2-nitramino-2-imidazoline (VII) (5) and benzylamine. The identity of these two products was established by a mixed melting point determination. The structure of 1-β-hydroxyethyl-2-nitramino-2-imidazoline was established previously (5,6) by nitration and hydrolysis to 1-β-nitroxyethyl-3-nitro-2-imidazolidone which was prepared also by the nitration of the known 1-β-hydroxyethyl-2-imidazolidone (6,8). These chemical reactions confirm the assignment of structure III to the cyclic thiourea from the reaction between aminoethylethanolamine and carbon disulphide.

EXPERIMENTAL[2]

4-Methyl-hexahydropyrimidine-2-thione

A solution of 8.8 gm. (0.1 mole) of 1,3-diaminobutane in 50 cc. of 95% ethanol was added dropwise to a solution of 25 cc. of carbon disulphide in 50 cc. of 95% ethanol. During the addition period the temperature was held below 40°C. with an ice–salt bath. The reaction mixture was allowed to stand at room temperature overnight in an open Erlenmeyer. At this time the viscous white oil had solidified, yield 12.65 gm. (77.2%). One gram of this γ-aminobutyldithiocarbamic acid inner salt was purified by solution in aqueous ammonia. On slow evaporation of ammonia from the solution white crystals separated. These crystals decomposed from 125–160°C. leaving a

[2] *All melting points were determined on a Kofler block. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Illinois.*

residue which then melted at 175–178°C. Calc. for $C_5H_{12}N_2S_2$: C, 36.57; H, 7.32; N, 17.06; S, 39.02%. Found: C, 36.86; H, 7.55; N, 17.00; S, 38.72%.

The remaining inner salt (11.65 gm., 0.088 mole) was placed in an Erlenmeyer and heated in an oil-bath at 130–145°C. until the evolution of hydrogen sulphide ceased. The tan residue was crystallized from ethanol using charcoal for decolorizing the product, yield 8 gm. (87.4%). The melting point of 182–183°C. was increased to 183–184.5°C. after one further crystallization from ethanol. Calc. for $C_5H_{10}N_2S$: C, 46.15; H, 7.69; N, 21.52; S, 24.62%. Found: C, 46.35; H, 7.85; N, 21.88; S, 25.02%.

1-β-Hydroxyethylimidazolidine-2-thione

1-Amino-5-hydroxy-3-azapentane (40.0 gm., 0.38 mole) in 95% ethanol (100 cc.) was added dropwise with stirring into a solution of 100 cc. of carbon disulphide in 100 cc. of 95% ethanol. During the addition period, which required 30 min., the temperature was held below 15°C. The stirring was continued for one half hour after the addition period after which the solid was recovered by filtration, yield 67.0 gm. (96.9% based on formation of inner salt). This solid was heated in an oil bath at 145 ± 5°C. until the evolution of hydrogen sulphide had ceased. The residue was crystallized from 95% ethanol (250 cc.) to give 46.0 gm. (86.3% yield from inner salt) of crystals which melted at 136.5–137.5°C. Calc. for $C_5H_{10}N_2OS$: C, 41.10; H, 6.85; N, 19.16; S, 21.93%. Found: C, 41.34; H, 6.49; N, 19.16; S, 22.30%.

1-β-Hydroxyethyl-2-methylmercapto-2-imidazolinium Iodide

A mixture of 1-β-hydroxyethylimidazolidine-2-thione (14.6 gm., 0.1 mole) and methyl iodide (15.6 gm., 0.11 mole) in 50 cc. of absolute methanol was shaken at room temperature for 40 min., after which all the solid had dissolved. While the vigorous shaking was continued 200 cc. of anhydrous ether was added gradually. A dense white precipitate (m.p. 119–120°C.) was formed, yield 27.3 gm. (95%). This product was brought to a constant melting point of 120–121°C. after one crystallization from absolute ethanol (3.9 cc./gm.). However purification was unnecessary for further chemical reactions. Calc. for $C_6H_{13}IN_2OS$: C, 25.01; H, 4.55; I, 44.10%. Found: C, 25.35; H, 4.67; I, 43.63.

1-β-Hydroxyethyl-2-nitramino-2-imidazoline

1-β-Hydroxyethyl-2-nitramino-2-imidazoline (m.p. 131.5–132°C.) was prepared in 39% yield as previously described (5).

1-β-Hydroxyethyl-2-benzylamino-2-imidazoline

Method A

1-β-Hydroxyethyl-2-methylmercapto-2-imidazolinium iodide (2.5 gm., 0.0087 mole) and benzylamine (1.8 gm., 0.017 mole) were dissolved in 25 cc. water and allowed to stand overnight. The mixture then was heated on a steam bath for one hour after which it was taken to dryness. The residual oil gave no picrate or picrolonate under the usual conditions. This oil was redissolved in 25 cc. water and this solution shaken for one hour with 1.0

gm. (0.0044 mole) of silver oxide. After filtration to remove silver salts, the solution was taken to dryness *in vacuo*. The oil was dissolved in 25 cc. of water, filtered, and the filtrate treated with 200 cc. of 1% aqueous picric acid solution. A crystalline picrate (m.p. 120.5–122.5°C.) was obtained in 64.8% yield (2.48 gm.). One crystallization from absolute alcohol (25 cc.) gave 2.1 gm. of crystalline picrate with a constant melting point of 124–125°C. Calc. for $C_{18}H_{20}N_6O_8$: C, 48.21; H, 4.50; N, 18.74%. Found: C, 48.54; H, 4.26; N, 18.78%.

Method B

One gram (0.0057 mole) of 1-β-hydroxyethyl-2-nitramino-2-imidazoline and 8 cc. of benzylamine were refluxed for one hour in an apparatus protected from carbon dioxide. The excess benzylamine was distilled off under water pump vacuum at 100°C. The residual light yellow oil was dissolved in 30 cc. of 50% aqueous ethanol. One half of this solution was treated with 200 cc., of 1% aqueous picric acid solution. The crude picrate melted at 118–122°C., yield 0.93 gm. (72.4%). Two crystallizations from ethanol raised the melting point to 124–125°C. This melting point was not depressed on admixture with the picrate of 1-β-hydroxyethyl-2-benzylamino-2-imidazoline prepared above by Method A.

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