methyl-4,5-dihydroimidazole and 50 cc. of benzene was treated with 22.1 g. (0.1 mole) of *p*-nitrobenzenesulfonyl chloride,[6] fed in slowly at 25°, and the mixture then was refluxed for two hours and cooled. The benzene was decanted and the gummy residue was disintegrated with 150 cc. of water, filtered off and dried at 25° *in vacuo*. The yield was 13.4 g., for the crude substance; m. p. was 125-126°, recrystallized from methanol. This product was very soluble in acetone.

Anal. Calcd. for $C_{10}H_{11}N_3O_4S$: C, 44.6; H, 4.1; N, 15.6; mol. wt., 269. Found: C, 44.6; H, 4.1; N, 15.5; mol. wt., 263.

The material that was insoluble in methanol was purified by solution in dilute alkali, treatment with decolorizing charcoal, and precipitation with dilute acid. It proved to be N,N'-di-(*p*-nitrobenzenesulfonyl)-ethylenediamine; m. p. 278-279°. It did not depress the m. p. of an authentic sample prepared from ethylenediamine.

Hydrolysis of 1-(*p*-Nitrobenzenesulfonyl)-2-methyl-4,5-dihydroimidazole (VII).—The nitro compound (1.0 g.) was dissolved in 7.7 cc. of 0.5 *N* HCl with shaking. After one and one-half hours the crystalline precipitate that had formed was filtered off, washed with water, and dried at 80°. The product (0.45 g.) melted at 150-151° and did not depress the melting point of N-acetyl-N'-(*p*-nitrobenzenesulfonyl)-ethylenediamine.

Acknowledgments.—The author is indebted to Miss G. Pranger and Mrs. J. D. Nevins of the Monsanto Analytical Laboratory for several of the analyses reported.

Summary

The preparation of a 1-acyl-2-hydroxy-tetrahydroimidazole and a 1-acyl-4,5-dihydroimidazole by reaction of aromatic sulfonyl chloride with a 4,5-dihydroimidazole is described.

The 1-arylsulfonyl imidazole derivatives were shown to undergo hydrolysis in dilute acid solution to form N,N'-diacyl-ethylenediamines, the new acyl group being derived from the carbon atom and substituent in the 2-position of the 2-hydroxy-tetrahydroimidazole or dihydroimidazole.

ST. LOUIS 4, MISSOURI RECEIVED FEBRUARY 20, 1945

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[6] Bell, *J. Chem. Soc.*, 2776 (1928).

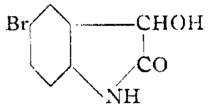
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WESTERN KENTUCKY STATE TEACHERS COLLEGE]

The Structures of the Bromodioxindoles of Baeyer and Knop

BY WARD C. SUMPTER

Monobromo and dibromo derivatives of dioxindole were prepared by Baeyer and Knop[1] through the action of bromine on aqueous solutions of dioxindole (3-hydroxyoxindole). The structures of these derivatives were not determined. The work described in this paper was undertaken in order to determine definitely the structures of these two derivatives.

It was found that both compounds could be prepared more readily through the bromination of aqueous solutions of dioxindole with aqueous bromine–potassium bromide solutions than by the procedure of Baeyer and Knop. It was also found that the same two compounds could be prepared by the reduction of 5-bromoisatin and 5,7-dibromoisatin, respectively. It follows that the two dioxindole derivatives are 5-bromodioxindole (I) and 5,7-dibromodioxindole (II). The identity of the sample of I prepared by the reduction of 5-bromoisatin with that prepared from dioxindole was established by melting point methods and by conversion of both samples to the same acetyl derivative through the agency of acetic anhydride. Similarly the two samples of dibromodioxindole prepared by reduction of 5,7-dibromoisatin and by the bromination of dioxindole were shown to be identical by melting point methods and by conversion to the acetyl derivative.



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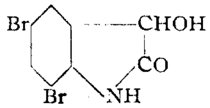

II

Further proof that the two derivatives were 5-bromodioxindole and 5,7-dibromodioxindole was obtained by their conversion to 5-bromoisatin-β-phenylhydrazone and 5,7-dibromoisatin-β-phenylhydrazone, respectively.

Experimental

5-Bromodioxindole (I) A.—By the procedure of Baeyer and Knop.[1] The substance crystallized from hot water as colorless prisms; m. p. 199–200°.[2]

B.—A solution of 8 g. of bromine (0.05 mole) in 25 cc. of water containing 12 g. of potassium bromide was added slowly at room temperature to a solution of 7.45 g. (0.05 mole) of dioxindole in 250 cc. of water. The nearly colorless product which separated almost immediately was collected and purified by crystallization from hot water; colorless prisms, m. p. 199–200°.

C. From 5-Bromoisatin.—5-Bromoisatin (0.01 mole) was suspended in 150 cc. of water and the mixture heated to boiling during the addition of 3 g. of sodium hydrosulfite. The mixture was then heated until all of the material was in solution. The product which separated on cooling was crystallized from hot water; colorless prisms, m. p. 199–200°. Mixtures of the 5-bromodioxindole prepared by procedures A, B and C also exhibited the same m. p.

Anal. Calcd. for $C_8H_6O_2NBr$: N, 6.15. Found: N, 5.90, 5.96.

3-Acetyl-5-bromodioxindole.[3]—A mixture of 3 g. of 5-bromodioxindole with 10 cc. of acetic anhydride was heated for thirty minutes at the reflux temperature. The product which separated on cooling was collected and

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[1] Baeyer and Knop, *Ann.*, **140**, 1 (1866).

[2] Baeyer and Knop, ref. 1, reported 165°.

[3] For evidence that dioxindole and acetic anhydride yield the 3-acetyl derivative see McKenzie and Stewart, *J. Chem. Soc.*, 104 (1935); and Heller and Lauth, *Ber.*, **62B**, 343 (1929).

crystallized from hot water; colorless plates, m. p. 150° Samples of 5-bromodioxindole prepared by procedures A, B and C yielded identical samples of the acetyl derivative (m. p. and mixed m. p. 150°).

Anal. Calcd. for $C_{10}H_8O_3NBr$: N, 5.18. Found: N, 5.12, 5.14.

5-Bromoisatin-β-phenylhydrazone.—A mixture of 2.28 g. of 5-bromodioxindole, 25 cc. of ethyl alcohol and 5 g. of phenylhydrazine was heated at reflux temperature for thirty minutes. The product which separated on cooling was crystallized from ethyl alcohol; orange-yellow needles, m. p. 271–272°. A mixture with an authentic sample of 5-bromoisatin-β-phenylhydrazone exhibited the same m. p.

5,7-Dibromodioxindole (II) A.—By the procedure of Baeyer and Knop.[1] Nearly colorless crystals possessing a slight red tinge, m. p. about 260° (depends on rate of heating).[4]

B.—A solution of 16 g. of bromine (0.1 mole) in 50 cc. of water containing 24 g. of potassium bromide was added slowly to a boiling solution of 7.45 g. (0.05 mole) of dioxindole in 250 cc. of water. The nearly colorless product was crystallized from hot ethyl alcohol from which it separated as colorless microscopic needles which rapidly acquired a reddish tinge on exposure to air. The substance melts at about 260°, the melting point depending on the rate of heating since considerable decomposition takes place below the melting point. The substance is rapidly oxidized to 5,7-dibromoisatin by boiling its solution in glacial acetic acid in contact with air.

C. From 5,7-Dibromoisatin.—5,7-Dibromoisatin (0.02 mole) was suspended in 200 cc. of water and the mixture heated to boiling and 3 g. of sodium hydrosulfite added. The reaction mixture was cooled and the product collected. Nearly colorless microscopic needles were obtained identical with samples prepared by procedures A and B.

Anal. Calcd. for $C_8H_5O_2NBr_2$: N, 4.56. Found: N, 4.60, 4.76.

3-Acetyl-5,7-dibromodioxindole.—A mixture of 2 g. of 5,7-dibromodioxindole with 10 cc. of acetic anhydride was heated at reflux temperature for thirty minutes. The product which separated on cooling was crystallized from glacial acetic acid; colorless microscopic needles, m. p. 226–227°. Mixtures of samples prepared from samples of dibromodioxindole prepared by procedures A, B and C exhibited the same m. p.

Anal. Calcd. for $C_{10}H_7O_3NBr_2$: N, 4.00. Found: N, 4.05, 4.23.

5,7-Dibromoisatin-β-phenylhydrazone.—A solution containing 1.5 g. (0.005 mole) of 5,7-dibromodioxindole and 5 g. of phenylhydrazine in 25 cc. of alcohol was heated at reflux temperature for thirty minutes. The product which separated on cooling was crystallized from glacial acetic acid; orange-yellow needles, m. p. 301–302°. A mixture with an authentic sample of 5,7-dibromoisatin-β-phenylhydrazone exhibited the same m. p.

Acknowledgment.—This work has been supported by a research grant (A. A. A. S.) received through the Kentucky Academy of Science.

Summary

The monobromo and dibromodioxindoles of Baeyer and Knop have been shown to be 5-bromodioxindole and 5,7-dibromodioxindole, respectively.

BOWLING GREEN, KENTUCKY RECEIVED MAY 7, 1945

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[4] Baeyer and Knop, ref. 1, reported 170°.

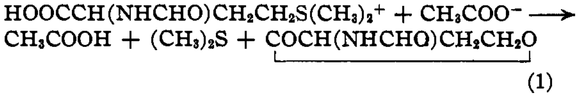
[CONTRIBUTION FROM THE LANKENAU HOSPITAL RESEARCH INSTITUTE]

Methionine Studies. VIII. Regeneration of Sulfides from Sulfonium Derivatives[1]

BY GERRIT TOENNIES AND JOSEPH J. KOLB

Derivatives of methionine containing a sulfonium function have been described.[2] Methionine is distinguished among the known natural amino acids by the capacity to form sulfonium salts, and the possibility of utilizing this distinction for the isolation of methionine from protein hydrolysates seemed worth considering as existing methods are far from satisfactory.[3,4] If in a protein hydrolysate all amino groups were acylated[5] and the resulting mixtures were subjected to the action of a sulfonium-forming reagent, the only cation among the amino acid derivatives should be that of the sulfonium salt formed from the methionine derivative.[6] Isolation of this singular ion as a suitable salt could then serve as a basis for the isolation of methionine if it were possible to regenerate the amino acid from the sulfonium combination. The present paper deals with studies bearing on the question of regeneration.

The potential reversibility of the sulfonium ion forming reaction[7] $R_2S + RX \rightleftharpoons R_3S^+ + X^-$ theoretically permits the derivation of three different sulfides from a methionine sulfonium ion (or of two if a methyl group is the addend). Regeneration of the methionine skeleton would require preferential removal of the added radical (or of a methyl group). Actually, in the case of N-formylmethioninemethylsulfonium acetate, spontaneous removal of the 4-carbon chain, *i. e.*, loss of the methionine skeleton, was observed



$$\mathrm{HOOCCH(NHCHO)CH_2CH_2S(CH_3)_2^+ + CH_3COO^- \longrightarrow CH_3COOH + (CH_3)_2S + COCH(NHCHO)CH_2CH_2O} \quad (1)$$

However, the analogous reaction was not encountered with the corresponding halide salts, nor with acetate or halides of the sulfonium ion with an unsubstituted amino group, although the volatile dimethyl sulfide is a potential product in all these

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[1] Aided by a grant in memory of Emma M. S. Althouse. Original manuscript received June 14, 1944.

[2] Toennies and Kolb, THIS JOURNAL, **67**, 849 (1945).

[3] Toennies and Kolb, *J. Biol. Chem.*, **126**, 367 (1938).

[4] Simmonds, Cohn, Chandler and du Vigneaud, *ibid.*, **149**, 519 (1943).

[5] The amino groups of the α-amino acids, with the exception of some groups of the diamino acids, are readily formylated by formic acid–acetic anhydride mixtures: Kolb and Toennies, *ibid.*, **144**, 193 (1942).

[6] Toennies, *J. Biol. Chem.*, **132**, 455 (1940); **133**, CII (1940).

[7] *Cf.* Ray and Levine, *J. Org. Chem.*, **2**, 267 (1937).