the preparation of 3,5-dimethyl-1,4-thiazan, b.p. 88–92° (10 mm.).

Anal. Calcd. for $C_7H_{15}NS$: N, 9.7. Found: N, 9.7.

The *p*-toluenesulfonamide derivative melted at 139–141°.

Anal. Calcd. for $C_{14}H_{21}NO_2S_2$: C, 48.1; H, 7.1. Found: C, 47.7; H, 7.3.

Bis-(2-hydroxy-*s*-butyl) Sulfide.—2,3-Butylene chlorohydrin (43.4 g., 0.4 mole) was added to 50 g. of sodium sulfide nonahydrate (0.21 mole) contained in 500 ml. of boiling ethanol. Carbonization occurred during the concentration of the product which resulted in considerable loss, b.p. 113–117° (0.5 mm.), yield 19 g. (72%).

Anal. Calcd. for $C_8H_{18}O_2S$: C, 50.4; H, 10.1. Found: C, 50.3; H, 10.5.

Bis-(2-chloro-*s*-butyl) Sulfide.—The procedure described for bis-(2-chloro-*n*-propyl) sulfide was the method of choice. The colorless chlorosulfide distilled at 123–127° (17 mm.).

Anal. Calcd. for $C_8H_{16}Cl_2S$: S, 14.9. Found: S, 14.6.

2,3,5,6-Tetramethyl-1,4-thiazan (X).—The procedure which was previously described for 3,5-dimethyl-1,4-thiazan was used to cyclize the above chloro sulfide. The mobile colorless product distilled at 94–98° (10 mm.).

Anal. Calcd. for $C_8H_{17}NS$: N, 8.8. Found: N, 8.6.

The *p*-toluenesulfonamide derivative melted at 138°.

Anal. Calcd. for $C_{15}H_{24}N_2O_2S_2$: C, 54.8; H, 7.3. Found: C, 54.5; H, 7.7.

BROOKLYN 1, NEW YORK

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Some 1-Substituted Dibenzothiophene Derivatives

BY HENRY GILMAN AND GENE R. WILDER

RECEIVED JANUARY 16, 1954

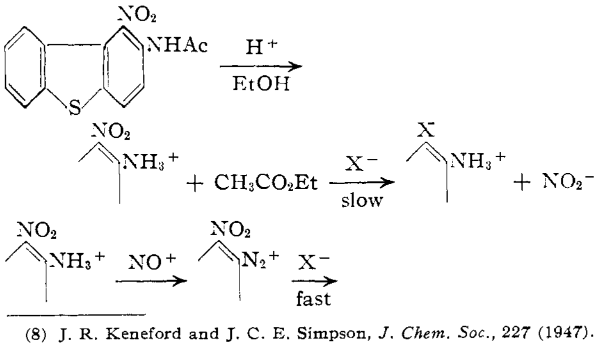
2-Acetamidodibenzothiophene reacts with nitric acid affording 1-nitro-2-acetamidodibenzothiophene which reacts with ethanolic hydrobromic or ethanolic hydrochloric acid yielding 1-bromo- and 1-chlorodibenzothiophene, respectively; however, ethanolic hydriodic acid affords only the nitroamine. 1-Nitro-2-acetamidodibenzothiophene may be diazotized in ethanol using sulfuric acid without the displacement of the nitro group, thus yielding 1-nitrodibenzothiophene.

Confirmed substitutions in the 1-position of dibenzothiophene have previously been made by electrophilic attack on a 4-substituted dibenzothiophene nucleus containing an activating group.[1] A nitro-2-acetamidodibenzothiophene has been obtained by the action of fuming nitric acid on 2-acetamidodibenzothiophene. This compound, upon treatment with ethanolic hydrochloric acid in an attempt to obtain the corresponding nitroamine, gave a compound which contained no nitrogen, and during the course of the reaction an odor resembling acetaldehyde was noticeable.[1]

1-Bromodibenzothiophene has been prepared by the action of 30% hydrobromic acid in ethanol on the above-mentioned nitro-2-acetamidodibenzothiophene and its structure has been established by the method of mixed melting points with an authentic specimen of 1-bromodibenzothiophene prepared in this Laboratory by a different method.[1] The very similar nature of the infrared spectra given by the product obtained by the ethanolic hydrochloric acid treatment of nitro-2-acetamidodibenzothiophene and that of 1-bromodibenzothiophene indicates that the compound is 1-chlorodibenzothiophene. Treatment of nitro-2-acetamidodibenzothiophene with either ethanolic hydriodic acid or ethanolic sodium hydroxide yields only the corresponding nitro-2-aminodibenzothiophene, which also gives rise to 1-bromo and 1-chloro derivatives when treated with ethanolic HBr or HCl, respectively.

Displacements of nitro groups during diazotization are to be found in the literature.[2-9] Recently[10-12] it has been shown that a chain reaction occurs with certain nitroamines initiated by displacement of a nitro group by halide ion from the conjugate acid of the nitroamine, the nitrite ion displaced then diazotizes more nitroamine which in turn gives rise to a more rapid displacement of nitrite ion by halide ion. It has been found[13] that in compounds of a similar nature the addition of a small amount of nitrite greatly accelerates the rate at which the diazonium salt is formed, thus indicating that one of the slow steps in the reaction is the displacement of nitrite from the conjugate acid of the nitroamine.

From the above observations and the fact that acetaldehyde was evolved during the reactions of the ethanolic HBr and HCl on nitro-2-acetamidodibenzothiophene and that when naphthol-2 was added to the reaction mixture coupling took place, it apears quite evident that nitration of 2-acetamidodibenzothiophene gave as a product 1-nitro-2-acetamidodibenzothiophene and the sequence of reactions for the formation of 1-chloro and 1-bromodibenzothiophene may be illustrated as



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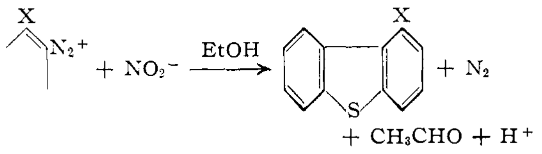
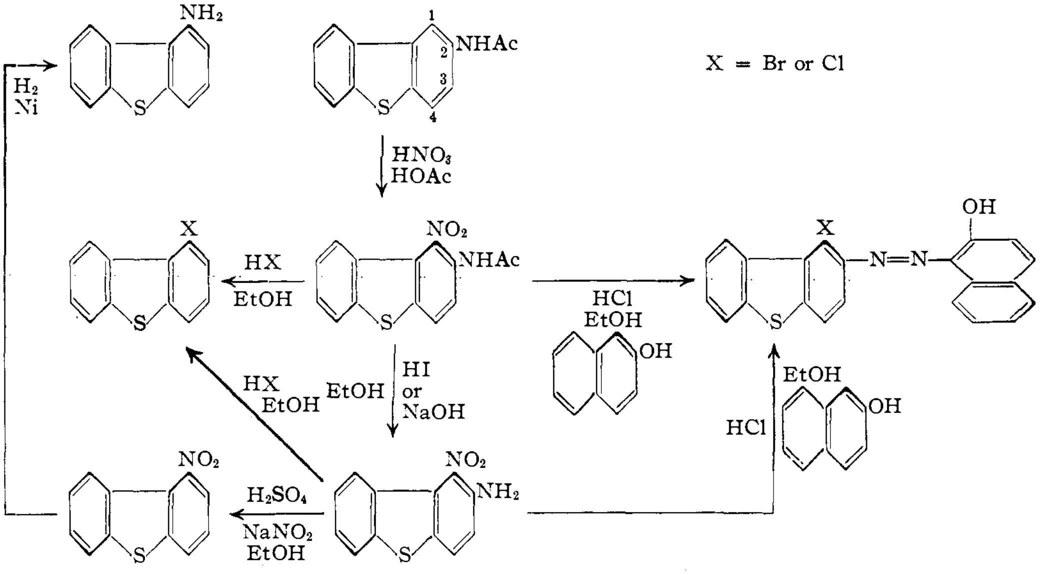
[13] Unpublished studies of this Laboratory.



The formation of the 1-chloro coupling product when naphthol-2 was added to the reaction mixture is easily explained by the consideration of the high concentration of chloride in the reaction mixture, displacement of nitrite takes place more rapidly than does coupling and coupling takes place more readily than reduction of the diazonium ion by ethanol.

Fortunately no displacement of nitrite occurs when 1-nitro-2-acetamidodibenzothiophene is diazotized in ethanol by sulfuric acid and sodium nitrite, thus it affords a convenient method for the synthesis of 1-nitrodibenzothiophene and products derived from it.



Experimental[14]

1-Nitro-2-acetamidodibenzothiophene.[15]—Into a three-necked liter round-bottom flask equipped with a mechanical stirrer and a reflux condenser were added 15 g. (0.0623 mole) of 2-acetamidodibenzothiophene and 650 ml. of glacial acetic acid. To the stirred reaction mixture was added over a period of 0.5 hour, 13 ml. of fuming nitric acid (90%), not allowing the temperature of the reaction mixture to rise over 30°. The reaction mixture became homogeneous after the addition of the nitric acid, whereupon, in a short time, crystals of product precipitated out of solution. The mixture was stirred for one hour subsequent to the addition of the nitric acid at which time the crude product was filtered and then recrystallized from a methanol–water pair to yield 13.0 g. (73%) of 1-nitro-2-acetamidodibenzothiophene melting at 209–210°.

Anal. Calcd. for $C_{14}H_{10}N_2O_3S$: C, 58.71; H, 3.52; N, 9.79; S, 11.20. Found: C, 58.59, 58.76; H, 3.53, 3.56; N, 9.68, 9.85; S, 11.09, 11.19.

1-Nitro-2-aminodibenzothiophene (a).—Into a 125-ml. erlenmeyer flask equipped with a reflux condenser were placed 0.5 g. (0.00175 mole), 1-nitro-2-acetamidodibenzothiophene, 20 ml. of 30% HI and 20 ml. of absolute ethanol. The reaction mixture was allowed to reflux for a period of 2 hours during which time the mixture became homogeneous and upon cooling a precipitate formed. The crude material was recrystallized from a methanol–water pair to yield 0.41 g. (95.5%) of 1-nitro-2-aminodibenzothiophene (orange needles) melting at 162–163°.

(b).—Into a 125-ml. erlenmeyer flask equipped with a reflux condenser were placed 0.5 g. (0.00175 mole) of 1-nitro-2-acetamidodibenzothiophene, 20 ml. of absolute ethanol and 20 ml. of 15% NaOH. The reaction mixture was allowed to reflux for one hour, cooled in an ice-bath and filtered. The crude material was recrystallized from a methanol–water pair to yield 0.40 g. (94%) of 1-nitro-2-aminodibenzothiophene melting at 162–163° and gave no depression by method of mixed melting points with a sample obobtained from the HI hydrolysis of 1-nitro-2-acetamidodibenzothiophene.

Anal. Calcd. for $C_{12}H_8N_2O_2S$: N, 11.47. Found: N, 11.04, 11.07.

1-Bromodibenzothiophene (a).—Into a 125-ml. erlenmeyer flask equipped with a reflux condenser were placed 1.0 g. (0.0035 mole) of 1-nitro-2-acetamidodibenzothiophene, 40 ml. of 30% HBr and 40 ml. of absolute ethanol. The reaction mixture was refluxed for one hour at which time 50 ml. of water was added to the system and allowed to cool. The resulting mixture was filtered and recrystallized from a methanol–water pair using Norit A to yield 0.43 g. (46.8%) of 1-bromodibenzothiophene melting at 84°. This compound gave no depression with an authentic sample of 1-bromodibenzothiophene[1] by method of mixed melting point.

(b).—Into a 125-ml. erlenmeyer flask equipped with a reflux condenser were placed 0.43 g. (0.00175 mole) of 1-nitro-2-aminodibenzothiophene, 20 ml. of 30% HBr and 20 ml. of absolute ethanol. The reaction mixture was allowed to reflux for one hour at which time 50 ml. of water was added to the system and the mixture allowed to cool in an ice-bath. The residue was collected by filtration and recrystallized from a methanol–water pair using Norit A to yield 0.13 g. (28.2%) of 1-bromodibenzothiophene melting at 83° and gave no depression with an authentic sample of 1-bromodibenzothiophene by the method of mixed melting points.

1-Chlorodibenzothiophene (a).—Into a 125-ml. erlenmeyer flask equipped with a reflux condenser and a gas outlet tube at the top of the condenser in series with a gas washing-bottle filled with 20% KOH were placed 0.5 g. (0.00175 mole) of 1-nitro-2-acetamidodibenzothiophene, 20 ml. of concd. HCl and 20 ml. of absolute ethanol. The mixture was refluxed for 1.5 hours during which time the reaction mixture became homogeneous and then an oil separated out of solution. During the course of the reaction there was evolved from the mixture a gas which was not soluble in the KOH solution. Concurrently, the odor of acetaldehyde could be detected. A small amount of the

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[14] All melting points are uncorrected.

[15] It has been found that comparable yields may be obtained using glacial acetic acid instead of acetic anhydride as a solvent for this reaction.

reaction mixture was collected by distillation which gave a positive Schiff test and also a positive test with 2,4-dinitrophenylhydrazine.

The reaction mixture was cooled and the mixture subsequently filtered. The crude material was recrystallized from a methanol–water pair to yield 0.13 g. (34.0%) of 1-chlorodibenzothiophene melting at 88°.

The infrared spectrum of this compound was almost identical with the spectra obtained from 1-bromodibenzothiophene.

Anal. Calcd. for $C_{12}H_7ClS$: C, 65.89; H, 3.23; Cl, 16.21; S, 14.66. Found: C, 65.93, 66.01; H, 3.23, 3.39; Cl, 16.29, 16.15; S, 14.51, 14.67.

(b).—Into a 125-ml. erlenmeyer flask equipped with a reflux condenser were placed 0.43 g. (0.00175 mole) of 1-nitro-2-aminodibenzothiophene, 20 ml. of concd. HCl and 20 ml. of absolute ethanol. The reaction mixture was refluxed for 1.5 hours at which time the reaction mixture was cooled, filtered and the residue recrystallized from a methanol–water pair to yield 0.11 g. (28.8%) of 1-chlorodibenzothiophene melting at 88° and which did not give a depression with the sample obtained from the treatment from 1-nitro-2-acetamidodibenzothiophene with concd. HCl and ethanol by the method of mixed melting points.

1-Chloro-2-(2-hydroxy-1-naphthaleneazo)-dibenzothiophene.—Into a 125-ml. erlenmeyer flask equipped with a reflux condenser were placed 0.8 g. (0.0028 mole) of 1-nitro-2-acetamidodibenzothiophene, 0.8 g. (0.0056 mole) of 2-naphthol, 40 ml. of absolute ethanol and 30 ml. of concd. HCl. The mixture was refluxed for a period of 20 min., allowed to cool, filtered and then recrystallized from glacial acetic acid twice to yield 0.41 g. (38.0%) of long, red needles melting at 257–258°.

Anal. Calcd. for $C_{22}H_{12}ClN_2OS$: Cl, 9.14; N, 7.22. Found: Cl, 8.95, 9.10; N, 7.09, 7.16.

1-Nitrodibenzothiophene.—To a suspension of 2.4 g. (0.0099 mole) of 1-nitro-2-aminodibenzothiophene in 40 ml. of absolute ethanol was added slowly 13 ml. of fuming sulfuric acid (15% SO_3). The reaction mixture was heated to approximately 80° at which time 6.0 g. of $NaNO_2$ was added over a period of 15 minutes. The mixture was allowed to cool, filtered and the resulting precipitate recrystallized from an ethanol–water pair, using Norit A to yield 1.21 g. (53.8%) of 1-nitrodibenzothiophene melting at 97°.

Anal. Calcd. for $C_{12}H_7NO_2S$: N, 6.11; S, 13.99. Found: N, 6.01, 6.02; S, 13.53, 13.57.

1-Aminodibenzothiophene.—Into a 125-ml. hydrogenation bottle were placed 1.21 g. (0.0053 mole) of 1-nitrodibenzothiophene, 30 ml. of absolute ethanol and approximately 0.4 g. of Raney nickel. The material was hydrogenated with an initial pressure of 50 p.s.i. for one hour in a mechanical shaker. The material was then filtered, the solution concentrated and finally recrystallized from an ethanol–water pair to yield 0.60 g. (57.0%) of 1-aminodibenzothiophene melting at 96°. This compound gives a depression in melting point of over 20° when admixed with 1-nitrodibenzothiophene.

Anal. Calcd. for $C_{12}H_9NS$: N, 7.03. Found: N, 6.62, 6.73.

1-Acetamidodibenzothiophene.—Into a 50-ml. erlenmeyer flask equipped with a reflux condenser were placed 0.40 g. (0.0020 mole) of 1-aminodibenzothiophene, 15 ml. of benzene and 1.0 ml. of acetic anhydride. The reaction mixture was refluxed for 10 minutes, allowed to cool, filtered and recrystallized from an ethanol–water pair to yield 0.40 g. (83.5%) of 1-acetamidodibenzothiophene melting at 227°.

Anal. Calcd. for $C_{14}H_{11}NO_2S$: C, 69.67; H, 4.60. Found: C, 69.73, 69.60; H, 4.79, 4.71.

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AMES, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF BOTANY, CORNELL UNIVERSITY]

The Detection, Isolation and Identification of L(−)Pipecolic Acid in the Non-protein Fraction of Beans (*Phaseolus vulgaris*)[1,2]

BY R. M. ZACHARIUS,[3a] J. F. THOMPSON[3b] AND F. C. STEWARD[3c]

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The isolation and identification of pure (−)pipecolic acid from the green bean by procedures using chromatography and ion exchange resins is described. The wide occurrence of pipecolic acid in plants is recognized, though it occurs in quantity in the bean. The possible metabolic role of pipecolic acid is discussed.

The isolation of (−)pipecolic acid from beans (*Phaseolus vulgaris*) has already been reported in brief form.[4] This paper gives the complete account of the detection and isolation of pipecolic acid and presents the critical proof of its identity.

Detection and Isolation of Pipecolic Acid

Following the application of two-directional partition chromatography on paper[5] to the examination of the non-protein nitrogen compounds of the potato tuber by Dent, Stepka and Steward,[6] a survey was made of these compounds in a number of plant materials. This survey[7] revealed the frequent occurrence of a number of known, naturally occurring, amino acids and a number of ninhydrin-reacting compounds whose identity was not then known. Some of the results of this survey have been summarized by Steward and Thompson[7] by means of a map which records the position of the various substances that occur on two-directional chromatograms (phenol and collidine–lutidine) together with a key which describes the characteristics and occurrence of the unidentified compounds.

Prominent among the unidentified substances was one which is particularly abundant in the fruit of the common bean (*Phaseolus vulgaris*) and designated unknown 1 by Steward and Thompson.[7]

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(1) This work began at the University of Rochester and was supported in part by a grant to one of us (F.C.S.) from the Nutrition Foundation. The completion of the work at Cornell University was supported by the Grasselli Grant to Cornell University for work directed by one of us (F.C.S.).

(2) Based on a portion of the dissertation presented by R. M. Zacharius in partial fulfillment of the requirements for the degree of Ph.D. at the University of Rochester, Rochester, N. Y.

(3) (a) General Cigar Co., Inc., Research Laboratory, Lancaster, Pa.; (b) U. S. Plant, Soil and Nutrition Laboratory, Ithaca, N. Y.; (c) Dept. of Botany, Cornell University, Ithaca, N. Y.

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