Tri-(1-naphthyl)-silanol.[7]—When the reaction mixture from 3 g. (0.0071 mole) of tri-(1-naphthyl)-silanol and 40 ml. of formic acid was filtered, 2.04 g. of a product melting over the range 74–140° was obtained. The mother liquor upon concentrating and cooling yielded 0.31 g. of naphthalene melting at 80–81°. No depression was observed in the mixed melting point determination with an authentic specimen. The product melting over the range 74–140° was vacuum-sublimed to give 0.64 g. of naphthalene melting at 80–81.5°. The identity of this product also was confirmed by the method of mixed melting point. The total yield was 1.12 g. (41.4%).

Tri-(*p*-tolyl)-silanol.[8]—From the reaction of 1.0 g. (0.0031 mole) of tri-(*p*-tolyl)-silanol and 15 ml. of formic acid, 0.75 g. of a white precipitate was obtained upon filtration. Recrystallization of this product from a mixture of petroleum ether (b.p. 77–115°) and benzene yielded 0.18 g. of product melting at 226.5–227.5°. By concentrating the mother liquor, 0.20 g. of a product melting at 225–226.5° was obtained. The mixed melting point of the former product with an authentic sample of hexa-(*p*-tolyl)-disiloxane (m.p. 228.5–229.5°) was 228.5–229°. The total yield of hexa-(*p*-tolyl)-disiloxane was 0.38 g. (39.2%).

2-Biphenylyltriphenylsilane.[6]—A sticky, white product was obtained from the filtration of the reaction mixture from 2 g. (0.0049 mole) of 2-biphenylyltriphenylsilane and 25 ml. of formic acid. The recrystallization of this product from a mixture of petroleum ether (b.p. 77–115°) and benzene gave 0.57 g. (28.5% recovery) of 2-biphenylyltriphenylsilane melting at 133–136°. The mixed melting point with an authentic sample melting at 136.5–137.5° was 135–136°.

The distillate from the distillation of the original filtrate upon neutralization and redistillation did not give any fraction which boiled near the boiling point (69.3°) of the benzene–water azeotrope. The residue from the first distillation when neutralized gave a precipitate which when filtered and dried weighed 0.34 g. (m.p. 68–70.5°). Its identity as biphenyl was established by a mixed melting point determination with an authentic specimen. The yield of biphenyl was 45.5%.

Tri-(2-biphenylyl)-silane.[6]—Filtration of the reaction-mixture from the reaction of 4 g. (0.0082 mole) of tri-(2-biphenylyl)-silane and 50 ml. of formic acid gave 4.07 g. of white product melting over the range 164–167°. By recrystallizing the crude product from a mixture of petroleum ether (b.p. 77–115°) and benzene, 2.33 g. (58.4% recovery) of tri-(2-biphenylyl)-silane melting at 170–171° was obtained. The mixed melting point with an authentic sample of tri-(2-biphenylyl)-silane (m.p. 170–171°) was not depressed.

When the original filtrate was neutralized, cooled and filtered 0.34 g. (8.9%) of biphenyl melting at 70–71° was obtained. The identity was confirmed in the usual manner.

Tri-(2-biphenylyl)-chlorosilane.[6]—When the material from the reaction mixture of 4 g. of tri-(2-biphenylyl)-chlorosilane and 50 ml. of formic acid was filtered and dried, 3.85 g. (96.5% recovery) of the starting material melting at 240–240.5° was obtained. The mixed melting point with an authentic sample melting at 240–240.5° was 240–240.5°.

Triphenylsilane.—The clear solution from the reaction of 5 g. (0.02 mole) of triphenylsilane and 50 ml. of formic acid was fractionally distilled. The first fraction which weighed 4.57 g., boiling range 73.5–98.5°, was neutralized with sodium carbonate, diluted with water and redistilled to give a benzene–water azeotrope weighing 0.44 g., boiling range 65–70°. This azeotrope was approximately 0.40 g. in benzene; therefore, the yield was 8.8% assuming cleavage of all the phenyl groups. The benzene was derivatized as *m*-dinitrobenzene. The crude *m*-dinitrobenzene weighing 0.35 g. (m.p. 75–82°), upon recrystallization from a mixture of water and ethanol gave 0.17 g. of pure product melting at 89–90°.

The residue from the distillation was diluted with about 100 ml. of methanol. The methanol was partially separated from the resulting sticky white product by decantation. When a crystallization attempt was carried out with a mixture of methanol and benzene, an oil resulted. This oil crystallized after cooling in a refrigerator at 0° for a month. The product obtained weighed 0.52 g. and melted over the range 175–217°.

Hexaphenyldisiloxane.—Filtration of the mixture from the attempted cleavage of 5 g. of hexaphenyldisiloxane with 50 ml. of formic acid resulted in a recovery of 4.81 g. (96%) of the starting material, m.p. 228–228.5°. Distillation of the filtrate did not give any evidence of benzene.

Tetraphenylsilane.—From the attempted cleavage of 5 g. of tetraphenylsilane with 50 ml. of formic acid, 4.83 g. (96.5% recovery) of tetraphenylsilane melting at 234.5–236.5° was obtained. A mixed melting point with an authentic sample melting at 236.5–237° was 235–237°.

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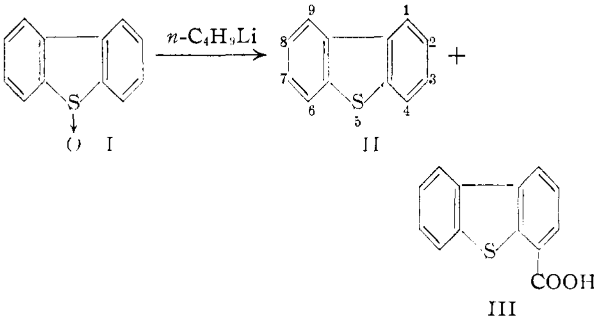
Conversion of Thianthrene-5-oxide to Dibenzothiophene by *n*-Butyllithium

BY HENRY GILMAN AND DHAIRYASHEEL R. SWAYAMPATI

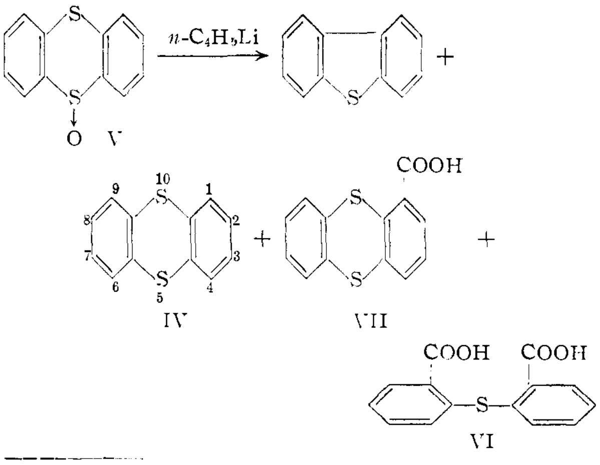
RECEIVED DECEMBER 20, 1954

Metalation of dibenzothiophene-5-oxide (I)[1] at −5 to −15° with 3.2 equivalents of *n*-butyllithium gave a 10.8% yield of dibenzothiophene (II) and a 35.7% yield of dibenzothiophene-4-carboxylic acid (III).



When one equivalent of *n*-butyllithium was used in the above reaction the result was a 56% recovery of dibenzothiophene-5-oxide, a 3.5% yield of dibenzothiophene-4-carboxylic acid and a 4.4% yield of dibenzothiophene.

In the course of a general investigation of the metalation of thianthrene (IV) and its derivatives we found that the treatment of thianthrene-5-oxide (V) with *n*-butyllithium resulted in varying yields of dibenzothiophene, thianthrene and small amounts of acidic materials.



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When thianthrene-5-oxide was metalated with three equivalents of *n*-butyllithium at −40 to −45°, dibenzothiophene was obtained in 34% yield along with a 4% yield of thianthrene. Only traces of acidic material were obtained. Metalation with 1.1 equivalents of *n*-butyllithium at −70° gave a 50% yield of dibenzothiophene, while metalation under the same conditions with three equivalents of *n*-butyllithium gave a 52% yield of dibenzothiophene, a 3.2% yield of thianthrene and a 1% yield of 2,2'-dicarboxydiphenyl sulfide (VI). Metalation at 5–10° with 2 equivalents of *n*-butyllithium gave a 10.4% yield of dibenzothiophene, a 13.2% yield of thianthrene and an 8.1% yield of 1-thianthrenecarboxylic acid (VII). The starting material, thianthrene-5-oxide, was not recovered in any of the experiments.

Schönberg[2] has reported an interesting reaction in which the treatment of diphenyl sulfoxide with sodamide in boiling toluene resulted in 25% yield of dibenzothiophene as a result of cyclization and reduction. Courtot, Chaix and Nicolas[3] used benzene as the solvent in the above reaction and obtained dibenzothiophene in 30–32% yield.

The reaction reported by us differs from the above reaction in that the sulfoxide group is altogether eliminated, but it remains to be determined whether the carbon atoms which were holding the sulfoxide group are those which became linked directly. The conditions of the experiment are much milder in our reaction.

Experimental[4]

Thianthrene-5-oxide.—Fries and Vogt[5] obtained V in 83% yield by the action of dilute nitric acid (sp. gr. 1.2) on thianthrene (IV). We obtained the product in 83% yield in accordance with their method, but the yield was increased to 98% by modifying the method as follows:

To a stirred refluxing solution of 86.4 g. (0.4 mole) of distilled thianthrene[6] in 1400 ml. of glacial acetic acid was added dropwise 150 ml. of the dilute nitric acid over a period of 1.5 hours and the mixture was refluxed for 15 minutes after the addition of nitric acid was complete. The yellow solution was diluted with five liters of ice-water. The product was filtered, washed with water and dried to yield 90.5 g. (98%) of V melting at 143–143.5°.

***n*-Butyllithium.**—In the preparation of *n*-butyllithium[7] it has been found[8] that an 85–92% yield of *n*-butyllithium can be obtained consistently if the internal temperature of the mixture is kept at −30° during the addition of the *n*-butyl bromide solution and for a subsequent period of 2 hours.

Metalation of Thianthrene-5-oxide. Run I.—To a stirred suspension of 18.6 g. (0.08 mole) of V in 200 ml. of anhydrous ether at −40° was added slowly 215 ml. (0.24 mole, 3 equivalents) of an ethereal solution of *n*-butyllithium and the mixture was stirred at −40 to −45° for 5 hours. Subsequently Color Test I[9] was positive and Color Test II[10] was negative.

The olive-green solution was poured jetwise into a stirred slurry of Dry Ice and ether. When all the carbon dioxide had evaporated the mixture was warmed to expel the ether and the dried residue was extracted with benzene in a Soxhlet extractor. The yellow extract was evaporated to dryness and the residue was suction-filtered to remove most of a yellow oily material. The residue was crystallized from 90% acetic acid to give 9.2 g. (50%) of crude dibenzothiophene (II) melting over the range 88–94°. Recrystallization from ethanol, methanol, acetic acid and petroleum ether (b.p. 77–115°) did not raise the melting point. This is probably due to the formation of a mixed crystal system of II and IV. The mixture was sublimed under reduced pressure keeping the oil-bath at 45–50°. The sublimate was recrystallized from methanol to give 5.0 g. (34%) of II melting at 98–99°. The identity was established by the method of mixed melting point and the comparison of the infrared spectra.

The residue from the sublimation was recrystallized from methanol to give 0.7 g. (4%) of IV melting at 156–157°. It gave no depression in melting point when mixed with an authentic specimen of IV.

Run II.—To a stirred suspension of 23.2 g. (0.1 mole) of V in 200 ml. of anhydrous ether at −70° was added slowly 195 ml. (0.3 mole, 3 equivalents) of an ethereal solution of *n*-butyllithium over a period of 30 minutes, and the reaction mixture was stirred at this temperature for 7 hours. Subsequently Color Test I was positive and Color Test II was negative. The olive-green solution was poured jetwise into a stirred slurry of Dry Ice and ether. When all the carbon dioxide had evaporated water was added to the mixture. The ether layer was dried with anhydrous sodium sulfate and evaporated to dryness. The residue was a white crystalline product contaminated with a small amount of a yellow oil. The mixture was suction-filtered and most of the oil was pressed out. The residue was washed once with a small amount of petroleum ether (b.p. 60–70°) to yield 10.1 g. (55%) of crude II melting at 96–98°. Recrystallization of the crude material from methanol gave 9.55 g. (52%) of II melting at 99°.

The aqueous layer was warmed to expel the dissolved ether. A small amount of a white product separated as the ether was removed. The mixture was filtered and the residue was crystallized from methanol to yield 0.7 g. (3.2%) of IV, identified by the method of mixed melting point.

The filtrate from the above was treated with charcoal, filtered, cooled and acidified with 10% hydrochloric acid. The resulting solid was filtered, washed and dried to yield 0.7 g. of a yellow acid. The crude material was crystallized twice from aqueous acetone to yield slightly yellow crystals melting over the range 220–226°. Recrystallization from glacial acetic acid gave 0.28 g. of the acid melting at 229–230°. The neutral equivalent of the acid was found to be 141, 140. The calculated value for the neutral equivalent of 2,2'-dicarboxydiphenyl sulfide (VI) is 137. The acid gave no depression in melting point when it was mixed with an authentic specimen of VI. The identity was established further by comparison of the infrared spectra. The yield of the crude acid was 2.5% and the yield of the pure acid was 1%.

Run III.—This run differed from run II in that 1.1 equivalents of *n*-butyllithium were used for metalation. From the ether layer was obtained 9.2 g. (50%) of II melting at 99–100°. The aqueous layer gave a small amount of acidic material which was not worked up.

Run IV.—This run differed from run II in that the metalation was carried out at 5–10° with 2 equivalents of *n*-butyllithium. The reaction mixture was worked up in the same way to yield 1.91 g. (10.4%) of pure II and 2.85 g. (13.2%) of IV. The aqueous layer was treated with charcoal, filtered, cooled and acidified with 10% hydrochloric acid. The yellow acid was filtered and dissolved in 10% potassium hydroxide solution, given a charcoal treatment, filtered, cooled and acidified with 10% hydrochloric acid. The product was filtered, washed and dried to yield 3.38 g. (13%) of 1-thianthrenecarboxylic acid (VII) melting over the range 205–216°. The acid was crystallized twice from 90% acetic acid to yield 2.1 g. (8.1%) of the pure acid melting at 225–226°. The melting point was not depressed when the acid was mixed with an authentic specimen of VII.

Acknowledgment.—The authors wish to thank the Institute for Atomic Research, Iowa State College, for making available to us the Baird double beam infrared spectrophotometer used in the de-

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(3) C. Courtot, M. Chaix and L. Nicolas, *Compt. rend.*, **194**, 1660 (1932).

(4) All melting points reported are uncorrected. All reactions involving organometallic compounds were carried out in an atmosphere of dry, oxygen-free nitrogen.

(5) K. Fries and W. Vogt, *Ann.*, **381**, 321 (1911).

(6) K. Fleischer and J. Stemmer, *ibid.*, **422**, 267 (1921).

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(9) H. Gilman and F. Schulze, THIS JOURNAL, **47**, 2002 (1925).

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termination of the spectra of the compounds reported.

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Apparent Dissociation Constants of Cysteine Derivatives

BY MELBA A. GRAFIUS AND J. B. NEILANDS

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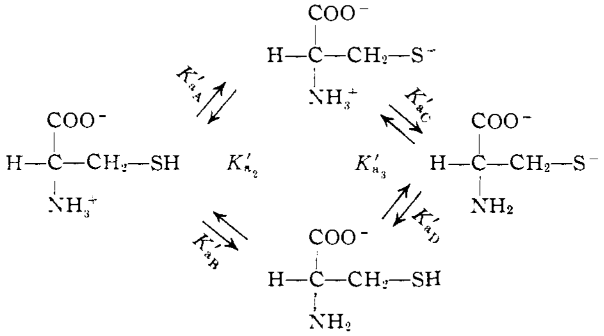
One of the characteristic reactions of the sulfhydryl (–SH) group is the ability to dissociate as a weak acid, $RSH \rightleftarrows RS^- + H^+$. The chemical and biological activity of this group, as it occurs in cysteine (I), coenzymes and proteins, would be expected to vary with the degree of ionization. For this reason, accurate knowledge of the ionization constant of the –SH group is a prerequisite to an understanding of its mechanism of action in both chemical and biological processes.

Inspection of the literature reveals lack of universal agreement concerning the ionization sequence of cysteine.[1] In 1927 Cannan and Knight[2] pointed out that whereas the primary apparent ionization constant (pK'_{a_1}) of cysteine is definitely that of the carboxyl group, a plausible argument could be made for assignment of the pK'_{a_2} and pK'_{a_3} to either the $-NH^+$ or –SH group. Textbooks[3] of protein chemistry list the pK'_{a_2} and pK'_{a_3} values of cysteine as those of the $-NH_3^+$ and –SH groups, respectively. Edsall,[4] on the other hand, regards the secondary and tertiary dissociation constants of cysteine as composite constants which are described by the equilibria



He showed that the individual constants and the two measured values, K'_{a_2} and K'_{a_3}, are related as

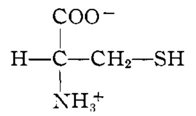
$$K'_{a_2} = K'_{a_A} + K'_{a_B}$$

$$\frac{1}{K'_{a_3}} = \frac{1}{K'_{a_C}} + \frac{1}{K'_{a_D}}$$

$$K'_{a_2}K'_{a_3} = K'_{a_A}K'_{a_C} = K'_{a_B}K'_{a_D}$$

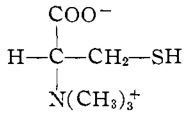
From the experimentally determined values of K'_{a_2} and K'_{a_3} and a probable value of K'_{a_B}, the latter derived from the pK'_{a_2} of 8.60 for S-ethylcysteine,[5] Ryklan and Schmidt[6] have solved for the remaining constants. They found $pK'_{a_A} = 8.66$, $pK'_{a_C} = 10.45$ and $pK'_{a_D} = 10.51$.

In the present investigation we have examined the *alternate* model substance, cysteine betaine (II). This compound contains a permanent positive pole, $-N(CH_3)_3^+$, and the influence of this group on the ionization of the –SH group may be expected to be comparable to that of the $-NH_3$ group of cysteine. For an estimation of K'_{a_B} we have prepared and titrated S-methylcysteine (III), a somewhat closer analog than the S-ethyl derivative.



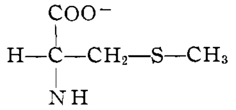
$$\begin{array}{c} COO^- \\ | \\ H-C-CH_2-SH \\ | \\ NH_3^+ \end{array}$$

I



$$\begin{array}{c} COO^- \\ | \\ H-C-CH_2-SH \\ | \\ N(CH_3)_3^+ \end{array}$$

II



$$\begin{array}{c} COO^- \\ | \\ H-C-CH_2-S-CH_3 \\ | \\ NH \end{array}$$

III

Experimental

Cysteine (I).—The Eastman Kodak Co. hydrochloride was used as received.

Cysteine Betaine (II).—The chloride was synthesized according to the method of Schubert.[7] The intermediate cystine betaine was crystallized. The crystalline cysteine betaine chloride contained 1.06 equivalent of –SH (as cysteine[8]). The neutral equivalent, with pH 7 as end-point, was 200.

Anal.[9] Calcd. for $C_6H_{14}O_2NSCl$: C, 36.08; H, 7.06; N, 7.01; S, 16.05. Found: C, 36.42; H, 7.25; N, 7.06; S, 16.30.

S-Methylcysteine (III).—The inner salt was synthesized according to Armstrong and Lewis,[10] m.p. 148° dec. (lit. 147–148° dec.[10]). Exactly one equivalent of alkali was consumed by 136 g. (one mole) over the pH range 6 to 11.

Titration Methods.—Titrations were carried out with standard 1 *N* NaOH in the automatic recording apparatus of Neilands and Cannon.[11] The gas phase was N_2 and the temperature 25°. The solvent was 0.15 *N* NaCl containing 10^{-3} *M* ethylenediaminetetraacetate. The substances were titrated at a concentration of 10 μM per ml. and the pK'_a values read directly from the corrected titration curves.[12]

Results

The measured apparent ionization constants for cysteine, cysteine betaine and S-methylcysteine are recorded in Table I.

TABLE I

APPARENT IONIZATION CONSTANTS OF CYSTEINE, CYSTEINE BETAINE AND S-METHYLCYSTEINE IN 0.15 *N* NaCl AT 25°

	pK'_{a_2}	pK'_{a_3}
Cysteine	8.30	10.40
Cysteine betaine	8.65	. . .
S-Methylcysteine	8.75	. . .

Substituting our pK'_{a_2} values of 8.65 and 8.75 for cysteine betaine and S-methylcysteine, re-

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