[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POMONA COLLEGE]

SYNTHESIS OF 6-SUBSTITUTED THIANAPHTHENES[1]

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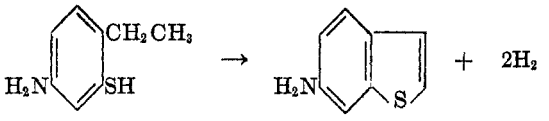
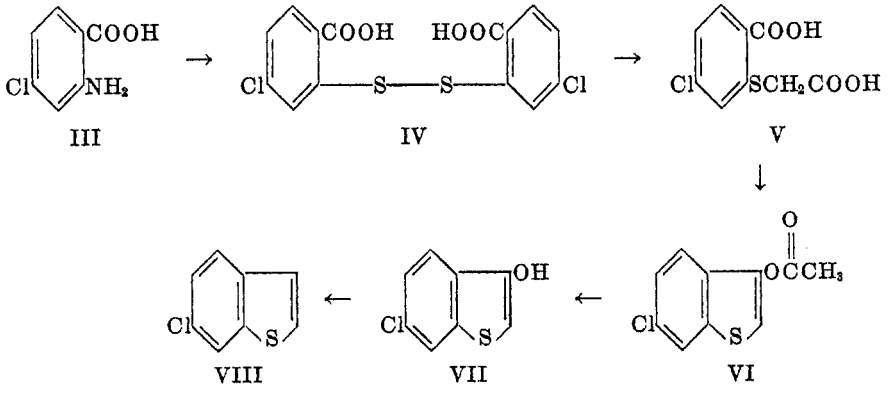
In continuing the study (1) of the synthesis of thianaphthenes by the dehydrocyclization reaction, 2-mercapto-4-aminoethylbenzene was dehydrogenated over a chromium-copper-on-charcoal catalyst under the usual conditions (2) at 445°. The product expected from this reaction was 6-aminothianaphthene according to the following equation:



I II

The product isolated from this reaction possessed the expected properties and gave the correct carbon hydrogen analysis as well as the correct molecular weight. Since 6-aminothianaphthene had not previously been reported it was decided to convert it to 6-chlorothianaphthene which had been reported (3). Tilak and Sunthankar reported that the 6-chlorothianaphthene was a yellow oil boiling at about 125°/15 mm. and giving a picrate of m.p. 134°. The chlorothianaphthene obtained from the diazotization of the catalytically prepared 6-aminothianaphthene melted at 42–43° and gave a picrate of m.p. 75–76°. The two chlorothianaphthenes were obviously different and so it was decided to prepare 6-chlorothianaphthene by an unequivocal method to remove any doubt about the structure of the catalytically prepared 6-aminothianaphthene. The method chosen was that used for the synthesis of thianaphthene (4). 2-Amino-4-chlorobenzoic acid III was prepared by the method of Hunn (5) and then converted to 2,2′-dicarboxy-5,5′-dichlorodiphenyldisulfide (IV) which was



III IV V VI VII VIII

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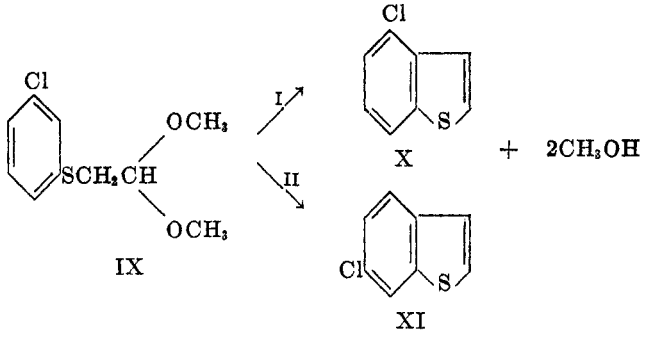
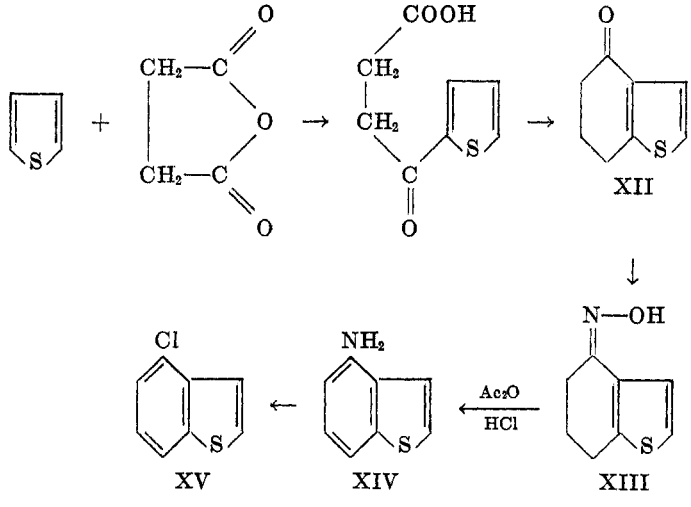
converted to 2-carboxy-4-chlorophenylmercaptoacetic acid (V). Treatment of this with sodium acetate and acetic anhydride followed by hydrolysis and decarboxylation gave 3-hydroxy-6-chlorothianaphthene which on reduction with zinc and acetic acid gave 6-chlorothianaphthene.

6-Chlorothianaphthene prepared this way was identical with that prepared from 6-aminothianaphthene. Both compounds possessed the same melting points. A mixture of the two compounds showed no melting point depression.

Sunthankar and Tilak's (3) chlorothianaphthene therefore is not the 6-substituted one and this is not surprising when one considers the following method used in their synthesis:



Sunthankar and Tilak assume that the above reaction of *m*-chlorophenyl-ω-dimethoxyethylsulfide (IX) with a solution of P_2O_5 in phosphoric acid takes path II rather than I. They base this assumption on the fact that the corresponding methyl compound, *m*-methylphenyl-ω-dimethoxyethylsulfide gave 6-methylthianaphthene (3). To see if the Sunthankar procedure gave 4-chlorothianaphthene instead of the expected 6-derivative, 4-chlorothianaphthene picrate was prepared by the following procedure and found to have the melting point reported by the Indian investigators.



The 4-keto-4,5,6,7-tetrahydrothianaphthene (XII) was prepared from thiophene by the method of Fieser and Kennelly (6). This then was converted to the oxime and the oxime in turn was transformed into the amine hydrochloride by the method used to convert α-tetralone into α-naphthylamine (7). The amine thus obtained gave an acetyl derivative of melting point 134–135°. Fries, *et al.* (8) report the melting point of 4-acetylaminothianaphthene as 134°. The 4-amine then was converted *via* the diazonium salt to 4-chlorothianaphthene of which the picrate was made. This picrate melted at 135–136° which indicates that the picrate reported by Sunthankar and Tilak (m.p. 134°) is very likely that of 4-chlorothianaphthene and not that of 6-chlorothianaphthene.

The only 6-substituted thianaphthene reported in the chemical literature is 6-methylthianaphthene (12). Since the 6-aminothianaphthene is so easily obtained by the dehydrocyclization of 2-mercapto-4-aminoethylbenzene it seems to afford a convenient route to 6-substituted thianaphthenes of various types, therefore, 6-cyano-, 6-hydroxy-, and 6-carboxy-thianaphthene were prepared and characterized in addition to the 6-chlorothianaphthene.

EXPERIMENTAL[2]

6-Aminothianaphthene (II). 2-Mercapto-4-aminoethylbenzene (This substance was prepared by the chlorosulfonation of *p*-nitroethylbenzene and reduction of the sulfonyl chloride with zinc and hydrochloric acid. Details to be published later) was dehydrogenated according to the usual procedure (2) at 445°. From 20 g. of the mercaptan there was obtained, after recrystallization from ether-petroleum ether, 15.9 g. (81%) of 6-aminothianaphthene, m.p. 114–115°.

Anal. Calc'd for C_8H_7NS: C, 64.40; H, 4.80; M.W., 149.
Found: C, 64.60; H, 4.97; M.W., 151.

6-Benzoylaminothianaphthene. This compound was prepared by the Schotten-Baumann procedure using benzoyl chloride and the above amine. It was purified by crystallization from alcohol-water. m.p. 129.5–130°.

Anal. Calc'd for $C_{15}H_{11}NOS$: C, 70.72; H, 4.38.
Found: C, 70.81; H, 4.43.

6-Aminothianaphthene picrate. The picrate formed yellow needles from alcohol and melted with decomposition at 198–200°.

Anal. Calc'd for $C_{14}H_{10}N_4O_7S$: C, 44.45; H, 2.66.
Found: C, 44.73; H, 2.98.

6-Chlorothianaphthene (VIII). In 25 ml. of water and 10 ml. of hydrochloric acid was dissolved 4.37 g. of 6-aminothianaphthene and the mixture was cooled to below 5°. Diazotization then was accomplished with 2.76 g. of sodium nitrite in 5 ml. of water. The diazonium salt was poured into a solution of 8.8 g. of cuprous chloride in 25 ml. of hydrochloric acid and 7.5 ml. of water. To complete the reaction the mixture was heated on a water-bath for ½ hour, then cooled, and extracted with ether. The ether extract was washed with sodium hydroxide solution, water, and finally dried over calcium chloride. Evaporation of the ether gave 3.46 g. of oil which after crystallization from alcohol melted at 42–43°.

Anal. Calc'd for C_8H_5ClS: C, 56.97; H, 2.99.
Found: C, 57.20; H, 3.03.

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[2] The carbon-hydrogen analyses were made by C. F. Geiger, Chaffey College, Ontario, Calif.

6-Chlorothianaphthene picrate. The picrate was formed in alcoholic picric acid solution and after recrystallization from alcohol melted at 74–75°.

Anal. Calc'd for $C_{14}H_8ClN_3O_7S$: C, 42.27; H, 2.02.

Found: C, 42.21; H, 2.21.

6-Hydroxythianaphthene. In a solution of 16 ml. of water and 9 ml. of sulfuric acid there was dissolved 3 g. of 6-aminothianaphthene. Diazotization then was carried out between 1° and 3° with 2 g. of sodium nitrite in 10 ml. of water. The diazonium solution then was added to a refluxing solution of 20 ml. of sulfuric acid and 15 ml. of water. After a few minutes heating the mixture was cooled and extracted with ether. Evaporation of the ether gave 2.8 g. of gummy material only part of which dissolved in 1 to 1 ligroin-benzene. Chromatographing this solution over alumina gave about 0.5 g. of white crystals of m.p. about 96°. Crystallization from acetone followed by sublimation gave a product of m.p. 102–102.5°.

Anal. Calc'd for C_8H_6OS: C, 63.97; H, 4.02.

Found: C, 64.13; H, 4.08.

6-Hydroxythianaphthene p-nitrobenzoate. In a solution of 140 g. of *p*-nitrobenzoyl chloride in 4 ml. of pyridine was dissolved 75 mg. of 6-hydroxythianaphthene and the mixture was refluxed for 1 hr. The reaction mixture then was poured into a bicarbonate solution and was extracted with ether. The ether was washed with dilute HCl, then with bicarbonate solution, and finally with water. Evaporation of the ether gave crystals which on recrystallization from ethanol melted at 149–150°.

Anal. Calc'd for $C_{15}H_9NO_4S$: C, 60.53; H, 3.06.

Found: C, 60.44; H, 3.37.

6-Cyanothianaphthene. 6-Aminothianaphthene (10 g.) was dissolved in 35 ml. of water and 22 ml. of HCl and then cooled to 0°. Diazotization was accomplished with 5.5 g. of sodium nitrite in 15 ml. of water. Then 9.8 g. of cuprous chloride was placed in 15 ml. of water and to this was added 12.4 g. of sodium cyanide in 35 ml. of water. The temperature was kept below 20° during the addition. Next, 50 ml. of toluene was added to the cuprous cyanide solution and the mixture was cooled to 0°. To this cooled solution was added the diazotized 6-aminothianaphthene with stirring, at such a rate that the temperature did not rise above 5°. The mixture was stirred for an hour after the addition was completed and then was heated on a water-bath at 60° for 2 hrs. After cooling, the product was extracted with ether and the ether was washed with dilute sodium hydroxide solution, and water, and then dried over calcium chloride. Distillation gave 3.8 g., b.p. 105–106°/0.1 mm. On standing this light yellow oil crystallized. Recrystallization from acetone-ligroin gave a product of m.p. 41.5–42°.

Anal. Calc'd for C_9H_5NS: C, 67.90; H, 3.17.

Found: C, 67.88; H, 3.31.

6-Carboxythianaphthene. 6-Cyanothianaphthene (0.5 g.) was refluxed for 1½ hrs. with 5 ml. of 75% sulfuric acid. The mixture was cooled, diluted with water, and extracted with ether and the ether solution was extracted with dilute sodium hydroxide. Acidification of the alkaline solution gave a precipitate of 463 mg. of acid which, after crystallization from acetone-ligroin, melted at 215–216°.

Anal. Calc'd for $C_9H_6O_2S$: C, 60.65; H, 3.39.

Found: C, 60.67; H, 3.57.

2,2'-Dicarboxy-5,5'-dichlorodiphenyldisulfide (IV). In 50 ml. of water and 20 ml. of hydrochloric acid there was placed 15.4 g. of 2-amino-4-chlorobenzoic acid (5). After diazotization, at 0°, with 6.9 g. of sodium nitrite in 15 ml. of water the diazonium solution was poured into a solution of 24 g. of $Na_2S{\cdot}9H_2O$ and 3.6 g. of sodium hydroxide in 35 ml. of water. During the addition the temperature was held below 5°. After standing several hours the solution was made strongly acid with HCl and the resulting precipitate was removed by filtration. This product then was dissolved in a boiling sodium carbonate solution, filtered, and reprecipitated by acidification. The yield was 7.82 g. which melted about

300° with decomposition. Recrystallization from alcohol gave a product of m.p. 309–311° with decomposition.

Anal. Calc'd for $C_{14}H_8Cl_2O_4S_2$: C, 44.81; H, 2.14.
Found: C, 45.07; H, 2.39.

2-Carboxy-4-chlorophenylmercaptoacetic acid (V). In a solution of 11.5 g. of anhydrous sodium carbonate and 8.5 g. of $Na_2S_2O_4$ in 85 ml. of water there was dissolved 7 g. of 2,2'-dicarboxy-5,5'-dichlorodiphenyldisulfide. After refluxing this solution for ½ hour, a solution of 8.5 g. of chloroacetic acid in 110 ml. of water previously neutralized with sodium bicarbonate was added, and refluxing was continued for one hour. Cooling and acidification of this reaction mixture gave 7.24 g. of product, m.p. about 190°. After recrystallization from water it melted with decomposition 190–195°. This is the same melting point reported in German Patent 193,724 (9).

Anal. Calc'd for $C_9H_7ClO_4S$: C, 43.86; H, 2.86.
Found: C, 44.30; H, 2.94.

3-Hydroxy-6-chlorothianaphthene (VII). 2-Carboxy-4-chlorophenylmercaptoacetic acid (3 g.) was refluxed with 1.5 g. of anhydrous sodium acetate and 8 ml. of acetic anhydride on an oil-bath for one hour. The reaction mixture then was diluted with ether and washed thoroughly with sodium bicarbonate solution. After drying over sodium sulfate the ether was evaporated leaving 2.14 g. of red oil. This was refluxed for one hour with 50 ml. of 10% sodium hydroxide after which it was acidified with acetic acid and steam-distilled giving 1 g. of 6-chlorothianaphthenol, m.p. about 143°. Friedlander and Sander report (10) m.p. 143°.

6-Chlorothianaphthene (VIII). 6-Chloro-3-hydroxythianaphthene (0.8 g.) was dissolved in 12 ml. of acetic acid and was refluxed with 2 g. of zinc dust for 1 hr. The resulting solution then was made strongly alkaline with sodium hydroxide and steam-distilled. A small amount of oil was collected in 50 ml. of distillate to which was added 1 g. of picric acid and the mixture was heated to boiling. Cooling gave 0.6 g. of picrate which, after crystallization from ethanol, melted at 75–76°. A mixture melting point with the picrate prepared from 6-chlorothianaphthene prepared *via* the diazonium reaction from 6-aminothianaphthene showed no depression. Decomposition of the picrate with sodium hydroxide gave 6-chlorothianaphthene which, after recrystallization from methanol, melted at the same point as the 6-chlorothianaphthene from 6-aminothianaphthene (42–43°). A mixture melting point showed no depression.

4-Keto-4,5,6,7-tetrahydrothianaphthene oxime (XIII). In 25 ml. of pyridine and 25 ml. of absolute ethanol there was placed 5 g. of 4-keto-4,5,6,7-tetrahydrothianaphthene (6) and 5 g. of hydroxylamine hydrochloride. After 8 hrs. refluxing the pyridine and ethanol were removed by heating the solution under a vacuum on a steam-bath. Diluting the residue with water, filtering, and drying gave 4.8 g. of oxime, m.p. about 122°. After recrystallizing from ethanol the oxime melted at 131–132°.

Anal. Calc'd for C_8H_9NOS: C, 57.49; H, 5.43.
Found: C, 57.67; H, 5.51.

4-Aminothianaphthene (XIV). In 25 ml. of acetic acid and 4 ml. of acetic anhydride there was dissolved 3.8 g. of 4-keto-4,5,6,7-tetrahydrothianaphthene oxime. Dry HCl was passed through the solution for ½ hr. and then it was heated to 100° with continued bubbling of the dry HCl for 2 hrs. more. After cooling, it was diluted with water and extracted with ether. The aqueous fraction was made basic with sodium hydroxide and extracted with ether. Evaporation of this ether extract gave 1.1 g. of oil which solidified at about 0°. Acetylation with acetic anhydride (11) gave a white solid, 4-acetylaminothianaphthene, which melted at 133–134° after recrystallization from benzene-ligroin. Fries, *et al.* report a melting point of 134°.

4-Chlorothianaphthene picrate. One gram of the above crude 4-aminothianaphthene was placed in 2 ml. of HCl and 6 ml. of water and was diazotized with 0.6 g. of sodium nitrite. This solution was poured into a solution of 1 g. of cuprous chloride in 5 ml. of HCl and 2 ml. of water. Steam-distillation of this solution gave a light yellow oil which was re-steam-

distilled from sodium hydroxide solution giving 50 ml. of distillate. To this was added 0.5 g. of picric acid and the mixture was heated to boiling. Cooling gave 0.46 g. of picrate which after recrystallization from ethanol melted at 135–136°. The melting point Sunthankar and Tilak report for their chlorothianaphthene picrate is 134°; thus it seems that their compound is the 4-chlorothianaphthene and not the 6-chlorothianaphthene.

Anal. Calc'd for $C_{14}H_8ClN_3O_7S$: C, 42.27; H, 2.02.
Found: C, 42.75; H, 2.27.

SUMMARY

1. It has been established that the dehydrocyclization of 2-mercapto-4-aminoethylbenzene gives 6-aminothianaphthene in 80% yield.

2. 6-Chlorothianaphthene has been prepared by an unequivocal method and found to be different from the compound which Sunthankar and Tilak report as 6-chlorothianaphthene. Their compound appears to be 4-chlorothianaphthene.

3. 6-Cyano-, 6-hydroxy-, and 6-carboxy-thianaphthene have been prepared from 6-aminothianaphthene.

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