rivative from 20 g. (0.085 mole) of 1-bromo-6-methoxynaphthalene which was allowed to react with an equimolar amount of β-carbomethoxypropionyl chloride[7] and the synthesis was conducted in the usual fashion. The crude keto ester was saponified with alcoholic potassium hydroxide and the resulting β-(6-methoxy-1-naphthoyl)-propionic acid recrystallized from methanol; m.p. 153.7–154.6°, yield 9.6 g. (44%).

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 69.55; H, 5.34.

B. By the Inverse Grignard Reaction.—1-Iodo-6-methoxynaphthalene was prepared in 65% yield by the method of Wilds and Close,[9] purified by vacuum distillation (b.p. 145–155° at 0.5 mm.) and subsequently recrystallized from methanol, m.p. 34–35°.[4,14]

A solution of 28.5 g. (0.1 mole) of the iodide and 10.5 g. (7.3 ml., 0.096 mole) of ethyl bromide in 75 ml. of dry thiophene-free benzene was added dropwise over the period of 80 minutes to 4.9 g. (0.2 mole) of magnesium turnings and 50 ml. of dry ether in a nitrogen atmosphere. Refluxing was continued for one hour after all the reagent had been added. The Grignard reagent was diluted with 100 ml. of dry benzene and added during 15 minutes to a vigorously stirred suspension of 20 g. (0.2 mole) of succinic anhydride[8] in 120 ml. of 1:2 ether–benzene. The mixture was refluxed for two hours and the yellow complex that formed was decomposed with ice and acidified to congo red with 6 *N* hydrochloric acid. The keto acid produced was extracted with 10% sodium carbonate solution. The crude brown colored acid obtained upon acidification was collected by filtration, washed with water to remove any acidic material produced by the Grignard carrier, dried over potassium hydroxide and weighed; 13.4 g. (52%), m.p. 135–138°. After two recrystallizations from methanol 10.7 g. (41%) of the white crystalline acid was obtained, m.p. 153.5–154.3°.

(14) A. Butenandt and G. Schramm, *Ber.*, **68**, 2083 (1935).

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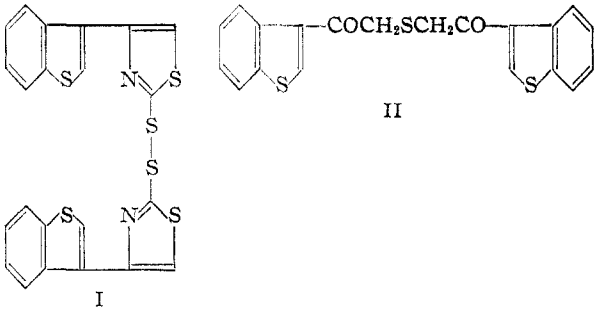
4-(3′-Thianaphthyl)-2-mercaptothiazole

BY WILLIAM S. EMERSON

When 3-chloroacetylthianaphthene was treated with ammonium dithiocarbamate in ethanol suspension, according to the procedure used for the preparation of 4-(2′-thienyl)-2-mercaptothiazole,[1] the product isolated was 69% of 4-(3′-thianaphthyl)-2-thiazolyl disulfide (I). Only 2% of the desired 4-(3′-thianaphthyl)-2-mercaptothiazole was obtained. However, treatment with zinc and acetic acid converted the disulfide to the mercaptan quantitatively.



I

II

In a preparation in which the ammonium dithiocarbamate was of poor quality, the principal product isolated was bis-(3-thianaphthacyl) sulfide (II). The identity of this compound was shown by a separate preparation from 3-chloroacetylthianaphthene and sodium sulfide and by oxidation to the corresponding sulfone.

(1) Emerson and Patrick, *J. Org. Chem.*, **13**, 722 (1948).

Experimental

3-Chloroacetylthianaphthene.—A stream of chlorine was introduced into a vigorously stirred solution of 50 g. of 3-acetylthianaphthene (Jefferson Chemical Co.) in 100 cc. of chloroform and 100 cc. of carbon tetrachloride initially at room temperature. No cooling bath was used. After 20 minutes the chlorine flow was stopped and the reaction mixture was cooled in ice. The white crystals were separated by filtration, washed with hexane and dried to give 40 g. (67% yield) of 3-chloroacetylthianaphthene, m.p. 137–140°.[2] An analytical sample was recrystallized twice from a mixture of benzene and hexane, m.p. 139.5–140.5°.

Anal.[3] Calcd. for $C_{10}H_7OSCl$: C, 57.0; H, 3.32. Found: C, 57.4; H, 3.46.

4-(3′-Thianaphthyl)-2-thiazolyl Disulfide.—A suspension of 21 g. of 3-chloroacetylthianaphthene and 77 g. of ammonium dithiocarbamate in 325 cc. of ethanol was allowed to stand with occasional shaking for eight days. Then the mixture was cooled in ice, diluted with 325 cc. of water and filtered. The precipitate was washed three times with water and sucked as dry as possible. It then was suspended in benzene which was boiled for 13 hours while the evolved water was collected in a Dean and Stark trap. The resulting suspension was heated to boiling and filtered hot. When the filtrate was chilled, crystals appeared. These were separated by filtration, washed with benzene and dried to give 0.5 g. (2%) of crude 4-(3′-thianaphthyl)-2-mercaptothiazole, m.p. 212–214°. One recrystallization from a mixture of benzene and ethanol raised the melting point to 221–223°. Dilution of the original filtrate with hexane precipitated 4.5 g. of crude 4-(3′-thianaphthyl)-2-thiazolyl disulfide, m.p. 109–117°. The solid which had been filtered from the original hot benzene suspension was crystallized from a mixture of ethanol and dioxane. Two crops were collected: I, 10.5 g., m.p. 126–127° and II, 2.0 g., m.p. 116–120°. The total yield of crude 4-(3′-thianaphthyl)-2-thiazolyl disulfide was 17 g. (69%). When a sample of fraction I was crystallized successively from benzene, ethanol and dioxane, and benzene and ethanol, the melting point remained the same.

Anal. Calcd. for $C_{22}H_{12}N_2S_6$: C, 53.2; H, 2.42. Found: C, 53.5; H, 2.24.

4-(3′-Thianaphthyl)-2-mercaptothiazole.—Excess powdered zinc was added to a solution of 6 g. of 4-(3′-thianaphthyl)-2-thiazolyl disulfide in 200 cc. of glacial acetic acid. After boiling for one hour, the solution was filtered hot and the funnel was washed with boiling acetic acid. The filtrate was diluted to 1 l. with water containing 25 cc. of concd. hydrochloric acid. The precipitate was separated by filtration, washed four times with water and crystallized from a mixture of ethanol and benzene. The essentially quantitative yield of 4-(3′-thianaphthyl)-2-mercaptothiazole was collected in two crops: I, 5 g., m.p. 221–223°, and II, 1 g., m.p. 220–222°.

Anal. Calcd. for $C_{11}H_7NS_3$: C, 53.0; H, 2.81. Found: C, 52.9; H, 2.82.

Bis-(3-thianaphthacyl) Sulfide.—A suspension of 21 g. of 3-chloroacetylthianaphthene and 12 g. of sodium sulfide nonahydrate in 200 cc. of ethanol was shaken occasionally and allowed to stand overnight. The mixture, now dark brown, was cooled in ice and diluted with 200 cc. of water. The crude product was separated by filtration and crystallized from a mixture of benzene and ethanol (Norit) to yield 10.5 g. (55%) of bis-(3-thianaphthacyl) sulfide in three crops, m.p. 149.5–150.5°, 149–150° and 149.0–149.5°.

Bis-(3-thianaphthacyl) sulfide also was isolated from a 3-chloroacetylthianaphthene–ammonium dithiocarbamate reaction in which the carbamate was of poor quality. The product was leached five times with boiling ethanol, crystallized from a benzene–hexane mixture and then from a benzene–ethanol mixture, m.p. 149–150°. An analytical sample was recrystallized from benzene–hexane, m.p. 150–151°.

(2) All of the melting points are uncorrected.

(3) Microanalyses by Mr. P. J. Adams and Mr. Donald Stoltz of this Laboratory and by the Micro-Tech Laboratories, 8000 Lincoln Avenue, Skokie, Illinois.

Anal. Calcd. for $C_{20}H_{14}O_2S_3$: C, 62.9; H, 3.67. Found: C, 63.0; H, 3.70.

When a sample of this material, m.p. 148–150°, was mixed with the first crop obtained by the other method, m.p. 149.5–150.5°, the melting point of the mixture was 148.0–149.5°.

Bis-(3-thianaphthacyl) Sulfone.—To a suspension of 2.0 g. of bis-(3-thianaphthacyl) sulfide in 40 cc. of glacial acetic acid held at 70–85° was added over a ten-minute period a solution of 1.8 cc. of 30% hydrogen peroxide in 4 cc. of glacial acetic acid. After ten more minutes an additional 0.2 cc. of hydrogen peroxide in 3 cc. of acetic acid was added. After ten more minutes at 70–85° the mixture was cooled and diluted with water. The precipitate was separated by filtration, washed with water and dried to yield 0.3 g. (14%) of crude bis-(3-thianaphthacyl) sulfone. An analytical sample was crystallized three times from a mixture of toluene and ethanol, m.p. 236–237°.

Anal. Calcd. for $C_{20}H_{14}O_4S_3$: C, 58.0; H, 3.38. Found: C, 58.6; H, 3.70.

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The Synthesis of L-Lyxonic Acid

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D-Lyxonic acid has been reported several times, but L-lyxonic acid apparently has not been synthesized. D-Lyxonic acid has been obtained as a sirup by the oxidation of the readily available D-lyxose[1,2] and also by the epimerization of D-xylonic acid.[3] The application of these two methods for the preparation of L-lyxonic acid is obvious. However, both L-lyxose and L-xylose are not easily obtained starting compounds.

L-Xylonic acid was prepared by the oxidative degradation[4] of 2-keto-L-gulonic acid. The L-xylonic acid was separated as the cadmium bromide double salt[5,6] which was resolved to the L-xylonic acid and characterized as the 1,4-anhydro-L-xylobenzimidazole derivative. L-Xylonolactone was epimerized to L-lyxonic acid which was characterized as its benzimidazole derivative.

L-Lyxose was prepared by a modified Ruff reaction[7] from calcium L-galactonate and was oxidized by iodine[8] in an alkaline methanol solution. This gave L-lyxonic acid which was separated as the barium salt and subsequently freed of barium ion. The L-lyxonic acid was again obtained as an uncrystallized sirup and was identified as the benzimidazole derivative.

Experimental

Cadmium-L-xylonate-cadmium Bromide Dihydrate.[4,5,6]—Fifty grams of 2-keto-L-gulonic acid was treated with 15 g. of sodium carbonate in 300 ml. of water. The solution was cooled, and 32 ml. of 30% hydrogen peroxide dropped in at 0° over a period of 1 hour. Then a slight excess of concd. HCl was added (foaming), and the solution concentrated to a sirup. The sirup was then diluted to 300 ml. and digested with about 25 g. of powdered cadmium carbonate. The excess cadmium carbonate was removed by filtration after complete reaction and 40 g. of cadmium bromide added. On cooling and with the addition of alcohol to turbidity, 23.5 g. of crude complex separated. The complex was purified by solution in 100 ml. of water, decolorized and on cooling separated by crystallization as a colorless, crystalline compound. Concentration of the mother liquor gave a further small yield; $[\alpha]^{26}D$ −10.5° (*c*, 1, H_2O). The analogous D-complex has been reported to have rotations of $[\alpha]D$ +7.4°[9] and $[\alpha]^{20}D$ +8.8°.[10]

Anal. Calcd. for $Cd(C_6H_9O_6)_2CdBr_2 \cdot 2H_2O$: C, 16.0; H, 2.9; Br, 21.3. Found: C, 15.7; H, 2.9; Br, 21.3.

1,4-Anhydro-L-xylobenzimidazole.—In 500 ml. of hot water 2.5 g. of cadmium-L-xylonate-cadmium bromide dihydrate was dissolved, and hydrogen sulfide was passed in until all of the cadmium had been precipitated. The clarified solution was concentrated to 10 ml. and treated with 1.5 g. of *o*-phenylenediamine as described for the D-isomer.[8] The product was purified by extraction with ice-water five times, using 5 ml. of water for each extraction, to remove soluble salts. The residue was recrystallized from about 10 ml. of water containing ammonia; yield 0.8 g. (50%); m.p. 224–226° (uncor.), $[\alpha]^{25}D$ −63° (*c*, 0.6, 5% citric acid).

Anal. Calcd. for $C_{11}H_{12}O_3N_2$: N, 12.7. Found: N, 12.8.

After completion of our work this compound was reported[11] having been synthesized from *o*-phenylenediamine and 2,5-anhydro-L-xylonic acid. The benzimidazole was reported, m.p. 225–228°; $[\alpha]^{25}D$ −64.6° (5% citric acid soln.).

The corresponding D-compound[5,12] has a m.p. 224°; $[\alpha]^{25}D$ +64.8° (5% citric acid soln.).

L-Lyxonic Acid from L-Xylonic Acid.[3]—Cadmium-L-xylonate-cadmium bromide dihydrate (20 g.) was dissolved in 300 ml. of water and 55 ml. of 1 *N* HCl acid was added. To this solution was added 1200 ml. of pyridine, and the solution was heated in an autoclave under nitrogen (500 lb.) at 140–145° for 3.5 hours. The pyridine was removed by distillation, and then the residue dissolved in 200 ml. of water and digested with 10 g. of cadmium carbonate. The excess cadmium carbonate was removed by filtration, and the solution concentrated to 50 ml. On cooling, 5.35 g. of the unepimerized cadmium xylonate complex separated. Further concentration gave only traces of the complex salt. The viscous solution was diluted to 500 ml., the cadmium removed by hydrogen sulfide, and the halides by silver oxide. Concentration to a sirup and dehydration using ethanol gave 4.4 g. of crude sirup (60%). This material did not crystallize.

2-(L-Lyxotetrahydroxybutyl)-benzimidazole.—Crude L-lyxonic acid sirup (2 g.) was treated with *o*-phenylenediamine according to Link's procedure[8] for D-lyxonic acid. The recovered product was purified as described above for the xylo derivative; yield 0.7 g. (24%); m.p. 188–189°; $[\alpha]^{25}D$ +11.3° (*c*, 1, 5% citric acid soln.).

Anal. Calcd. for $C_{11}H_{14}O_4N_2$: N, 11.8. Found: N, 11.5.

The corresponding D-form has been reported[8]: m.p. 189°; $[\alpha]^{25}D$ −12.8°.

L-Lyxonic Acid from L-Lyxose.—L-Lyxose (4 g.) was obtained as a sirup from calcium-L-galactonate by a modified Ruff procedure,[7] and was converted into the barium salt in the manner described for D-lyxonic acid[8]; yield 3.7 g. This amorphous salt was dissolved in 100 ml. of hot water and the barium precipitated by the addition of a solution of 1.3 g. of oxalic acid hydrate in 10 ml. of water. After filtration, the excess oxalic acid was removed by silver oxide, and the L-lyxonic acid liberated by hydrogen sulfide. The solution of L-lyxonic acid was concentrated to a sirup which could not be induced to crystallize. The benzimidazole derivative was prepared as described above; m.p. 188–189°; $[\alpha]^{25}D$ +11.0°; mixed m.p. with 2-(L-lyxotetrahydroxybutyl)-benzimidazole prepared from L-lyxonic acid obtained by epimerizing L-xylonic acid; m.p. 187–188°. This confirms the generality of both methods for the preparation of L-lyxonic acid.

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