

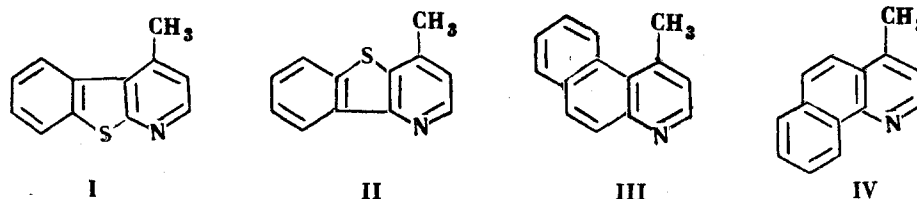
## 4-METHYLTHIONAPHTHENOPYRIDINES

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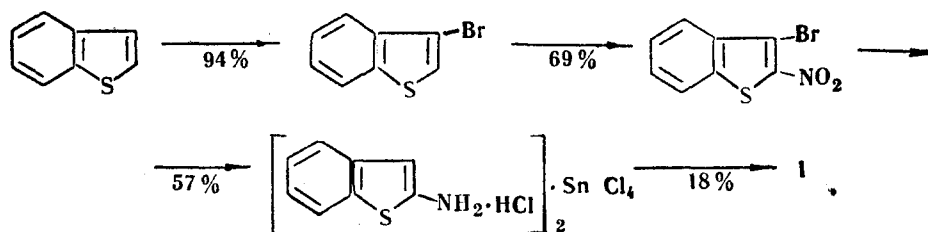
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4-Methylthionaphtheno[2,3-b]pyridine and 4-methylthionaphtheno[3,2-b]pyridine, new organic bases with a condensed thiophene ring, are synthesized. The physical constants of these new heterocyclic bases are quite close to those of the isosteric 4-methylnaphthoquinoline bases.

This paper describes the synthesis of isomeric 4-methylthionaphtheno[2,3-b]pyridines I, II, which are respectively isosteric with 4-methyl- $\beta$ - and - $\alpha$ -naphthoquinolines III, IV:



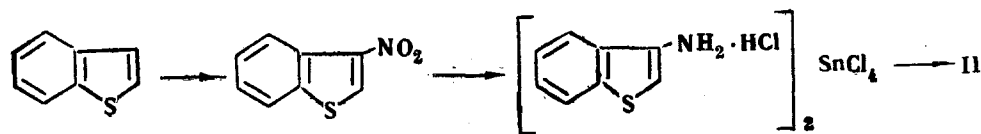
Synthesis of 4-methylthionaphtheno[2,3-b]pyridine was from thionaphthene,



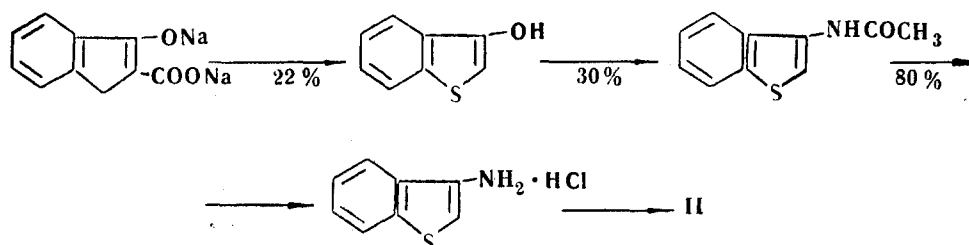
3-Bromothionaphthene was obtained by brominating thionaphthene in chloroform [1]. Action of nitric acid (d 1.5) on 3-bromothionaphthene in glacial acetic acid gives 3-bromo-2-nitrothionaphthene [2]. This is then reduced by heating with tin and hydrochloric acid, when the bromine atom is split off, and the double tin salt with 2-aminothionaphthene formed.

4-Methylthionaphtheno[2,3-b]pyridine (I) is synthesized by the Doebner-Miller reaction from the double tin salt of 2-aminothionaphthene hydrochloride and methylvinylketone, which are heated in alcohol with ferric chloride and anhydrous zinc chloride.

4-Methylthionaphtheno[3,2-b]pyridine is first synthesized from thionaphthene.



Thionaphthene was nitrated with concentrated nitric acid [1] and the resultant 3-nitrothionaphthene reduced by metallic tin the double tin salt of 3-aminothionaphthene hydrochloride [3]. However, as the starting thionaphthene had, in its turn, to be obtained by cyclizing  $\omega$ -phenyldiethoxyethylsulfide, another route was chosen, starting from an alkali melt with 3-hydroxythionaphthene-2-carboxylic acid.



3-Hydroxythionaphthene was prepared by steam-distilling the acidified alkaline melt of 3-hydroxythionaphthene-2-carboxylic acid [4]. Heating 3-hydroxythionaphthene with acetamide in acetic acid gave 3-acetaminothionaphthene,

saponified by an aqueous-alcoholic potassium hydroxide solution to free 3-aminothionaphthene, which with hydrogen chloride gives the corresponding hydrochloride.

The bases synthesized form colorless plates with a characteristic odor. They readily give picrates, methiodides, and ethiodides.

Below are given the melting points of the synthetic bases, and of the isosteric 4-methyl- $\alpha$ - and - $\beta$ -naphthoquinones.

Base	Mp, °C
4-Methylthionaphtheno[2, 3-b]pyridine	101-102
4-Methyl- $\beta$ -naphthoquinoline	100-101 [5]
4-Methylthionaphtheno[3, 2-b]pyridine	53- 54
4-Methyl- $\alpha$ -naphthoquinoline	77- 78 [6]

## EXPERIMENTAL

Thionaphthene is prepared by cyclizing 50 g  $\omega$ -phenyldiethoxyethylsulfide in 1500 ml benzene with 320 g phosphorus pentoxide and 200 ml phosphoric acid. Yield 15.1 g (60.0%). It is purified via the picrate. Colorless plates, mp 30-31°. The literature [7] gives mp 32°.

3-Bromothionaphthene is obtained by the action of a solution of 26 g bromine in 60 ml chloroform on 22 g thionaphthene dissolved in 125 ml chloroform at 20°. Yield 33.1 g (94.5%). Colorless liquid, bp 129-131° (9 mm). The literature [1] gives 136-137° (13 mm).

3-Bromo-2-nitrothionaphthene. 31 g 3-bromothionaphthene in 80 ml glacial acetic acid are treated at 15° with 30 g nitric acid (d 1.5) in 30 ml of the same solvent. Yield 23.8 g (69.4%). Pale yellow needles, mp 159-160° (from alcohol). The literature [2] gives mp 160-161°.

Double tin salt of 2-aminothionaphthene hydrochloride. 4.5 g 3-bromo-2-nitrothionaphthene are suspended in 40 ml concentrated hydrochloric acid, stirred vigorously, and 8 g of tin powder added over 15 min, the temperature being kept at 45-50°. When addition is finished the mixture is stirred for 30 min more, the temperature raised to 55°, and stirring continued until all the tin has dissolved. The mixture is cooled, and the salt which separates out filtered off, washed with ether, and dried in air. Yield 6.3 (57.2%). Slightly yellowish prisms.

Because of the difficulty of carrying out elementary analysis of the double tin salt, it is converted to 2-acetaminothionaphthene.

A solution of 1.1 g acetic anhydride in 2.5 ml ether is added to a suspension of 1.6 g of the double tin salt of 2-aminothionaphthene hydrochloride in 11.5 ml water at 0°, with vigorous stirring. Immediately after adding the acetic anhydride a solution of 2.3 g sodium hydroxide in 3.5 ml water is added dropwise at such a rate that the temperature does not exceed 8-10°. When addition is ended, the mixture is stirred at the same temperature for a further 30 min, then cooled to 1°; the precipitate is filtered off, carefully washed with water and dried in air. Yield 0.38 g (77.5%). Colorless glistening plates, mp 223-224° (benzene). Found: N 7.36%, calculated for C<sub>10</sub>H<sub>9</sub>NOS: N 7.32%. Bromine test negative.

4-Methylthionaphtheno[2, 3-b]pyridine. 42 g methylvinylketone are added over an hour to a well-stirred mixture of 180 g of the double tin salt of 2-aminothionaphthene hydrochloride, 186 g ferric chloride, 10 g fused zinc chloride, and 600 ml dry alcohol at 60-65°. When addition is complete the mixture is boiled for 3 hr, the alcohol distilled off, and the residue in the flask treated with 25% sodium hydroxide solution, with cooling, until alkaline to litmus, and then steam-distilled. The product which separates from the distillate is filtered off, washed with water, and dried over alkali metal hydroxide. Yield 10.7 g (18.7%), mp 101-102° (from petrol ether), colorless plates. Found: N 6.97%, calculated for C<sub>12</sub>H<sub>9</sub>NS: N 7.02%.

Picrate. Light yellow plates, mp 191-192° (from alcohol). Found: N 12.98%, calculated for C<sub>12</sub>H<sub>9</sub>S · C<sub>6</sub>H<sub>2</sub>(NO<sub>2</sub>)<sub>3</sub>-OH: N 13.07%.

Ethiodide. Pale gray prisms, mp 216-217° (from alcohol). Found: N 3.89%, calculated for C<sub>14</sub>H<sub>14</sub>INS: N 3.94%.

Methiodide. Pale yellow prisms, mp 208-209° (from alcohol). Found: N 4.15%, calculated for C<sub>13</sub>H<sub>12</sub>INS: N 4.10%.

3-Nitrothionaphthene. Obtained by treating 20 g thionaphthene in 50 ml glacial acetic acid with 20 g nitric acid (d 1.5) in 20 g of the same solvent, temperature 15°. Yield 10.4 g (38.9%). Pale yellow needles, mp 77-78° (alcohol). The literature [1] gives mp 78°.

Tin-3-aminothionaphthene hydrochloride double salt. Prepared [3] by reducing 6.5 g 3-nitrothionaphthene with 10.8 g tin metal in 65 ml hydrochloric acid at 40-45°, yield 10.8 g (47.6%).

3-Hydroxythionaphthene. 100 g 3-hydroxythionaphthene-2-carboxylic acid [4] is submitted to melting with technical-grade alkali, the product is acidified (to Congo), and then steam-distilled, to give 15.1 g (22.7%) of this compound, forming colorless needles, mp 70-71°; the literature [4] gives mp 71°.

3-Acetaminotionaphthene. Obtained by boiling 12 g 3-hydroxythionaphthene with 20 g acetamide in 60 ml glacial acetic acid. Yield 4.6 g (30%). Colorless glistening plates, bp 168-169° [8].

3-Aminotionaphthene hydrochloride. A mixture of 6.37 g 3-acetaminotionaphthene, 9 g potassium hydroxide, 42 ml alcohol, and 12 ml water is boiled for 4 hr 30 min, cooled, and poured into 250 ml ice water. The solution is extracted a few times with 300 ml ether, the ethereal extracts washed (2 × 200 ml) with water, and dried over potash. The ether is distilled off until the volume remaining is 50 ml, the residual solution cooled, and the precipitate filtered off. Hydrogen chloride is passed through the ether solution, the precipitate is filtered off, washed with ether, and vacuum-dried over sodium sulfate. Yield 4.9 g (80.3%). Light yellow prisms, mp 300° (from alcohol). Found: N 7.43; Cl 19.03%, calculated for  $C_8H_7NS \cdot HCl$ : N 7.54; Cl 19.09%.

#### 4-Methylthionaphtheno[3,2-b]pyridine.

a) 8.5 g methylvinylketone are added over one hour to a mixture of 66.9 g double tin salt of 3-aminotionaphthene hydrochloride, 64.8 g ferric chloride, 2.4 g fused zinc chloride, and 120 ml alcohol, which is well stirred and held at 60-65°. At the end of addition, the mixture is boiled for three hours, the alcohol distilled off, and the residue in the flask is made alkaline to litmus with 25% sodium hydroxide solution, with simultaneous cooling, and then steam-distilled. Next day the precipitate is filtered off, washed with water, and vacuum-dried over solid caustic alkali. Yield 2.7 g (12.7%), mp 53-54° (from petrol ether), colorless plates. Found: N 6.91%, calculated for  $C_{12}H_9NS$ : N 7.02%.

Picrate. Light yellow plates, mp 2.4-2.5° (from alcohol). Found: N 13.01%, calculated for  $C_{12}H_9NS \cdot C_6H_2(NO_2)_3-OH$ : N 13.07%.

Ethiodide. Light gray prisms, mp 227-228° (from alcohol). Found: N 3.99%, calculated for  $C_{14}H_{14}INS$ : N 3.94%.

Methiodide. Light yellow prisms, mp 240-241° (from alcohol). Found: N 4.01%, calculated for  $C_{13}H_{12}INS$ : N 4.10%.

b) 7 g methylvinylketone are added in 30 min to a vigorously stirred mixture of 18.5 g 3-aminotionaphthene hydrochloride, 2 g anhydrous fused zinc chloride, 18.6 g ferric chloride, and 60 ml dry alcohol held at 65-70°. After addition the mixture is boiled for two hours, cooled, 15 g anhydrous zinc chloride added, and boiling continued for two hours more. The rest of the synthesis is carried out as described above. Yield 2.63 g (13.15%).

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