A NEW SYNTHESIS OF THIOPHENES AND THIAPYRANS

Part VII. Bromothionaphthenes and 5-Nitrothionaphthene

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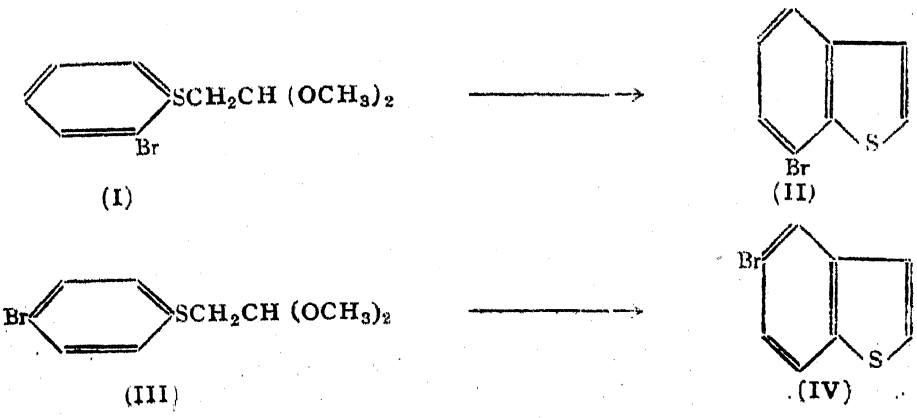
THE synthesis of 5-chloro, 6-chloro, and 7-chlorothionaphthenes have been described by us recently.[1] Of the other monohalogenothionaphthenes, only the 3-bromo derivative has been reported in the literature.[2] We have recently described briefly the synthesis of 7-bromothionaphthene[3] (II). This compound is now fully described in addition to the hitherto unreported 5-bromothionaphthene (IV).

o-Bromothiophenol was condensed with bromoacetaldehyde dimethyl acetal to give *o*-bromophenyl ω- dimethoxyethyl sulphide (I). Cyclization of (I) with a mixture of phosphorus pentoxide and phosphoric acid gave (II) in 75% yield.

p-Bromothiophenol was condensed with bromoacetaldehyde dimethyl acetal to give *p*-bromophenyl ω-dimethoxyethyl sulphide (III). When (III) was cyclized with phosphorus pentoxide and phosphoric acid in the usual way, most of the sulphide (III) distilled over unchanged along with a very small quantity of the thionaphthene (IV). The quantities of phosphorus pentoxide and phosphoric acid were then doubled, and the sulphide added to the phosphorus pentoxide-phosphoric acid mixture kept at 130–40°/10 mm. The sulphide (III) does not distil under these conditions, whereas the thionaphthene (IV) distills over. The crude thionaphthene was purified by steam distillation (yield 13%).

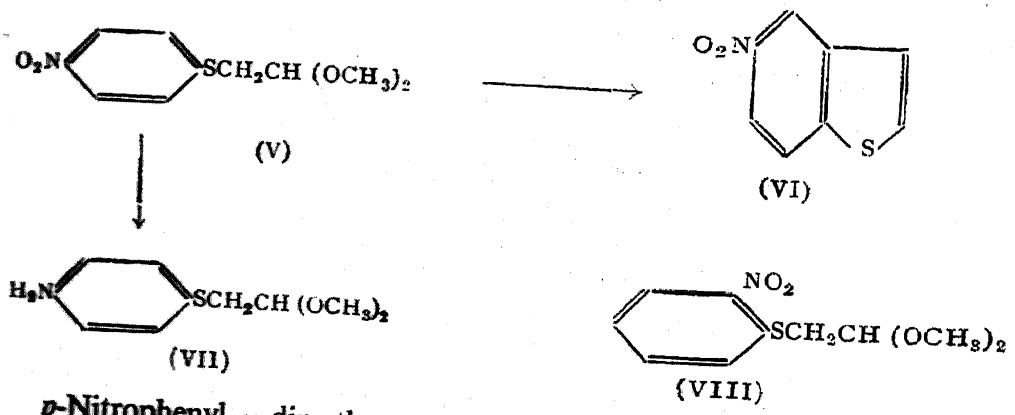


(I) (II)

(III) (IV)

Syntheses of substituted thionaphthenes by the cyclization of ary ω-dimethoxyethyl sulphides where the aryl group is phenyl in which *o*-, *p*-directing groups such as methyl, methoxy, ethoxy, chlorine or bromine are present, have been described in the present and previous communications.[4] It was of interest to synthesize nitrothionaphthenes by the ring-closure of nitrophenyl ω-dimethoxyethyl sulphides, although the cyclization of the latter was likely to prove difficult.

Of the six possible mononitrothionaphthenes, 3-, 4- and 5-nitrothionaphthenes are known. 3-Nitrothionaphthene[5] is obtainable by direct nitration of thionaphthene in acetic acid. Nitration with potassium nitrate in sulphuric acid leads to a mixture of dinitro and trinitrothionaphthenes from which the 3:4-dinitroderivative is separated by crystallization. A solution of the latter in alcoholic ammonia on treatment with hydrogen sulphide gives 4-nitrothionaphthene,[6] although the method does not appear to be unambiguous. 5-Nitrothionaphthene[7] is obtained synthetically starting from 2-chloro-5-nitrobenzaldehyde.



p-Nitrophenyl ω-dimethoxyethyl sulphide (V) was prepared by the condensation of bromoacetaldehyde dimethyl acetal with *p*-nitrothiophenol. Cyclization of (V) proved to be difficult in the initial experiments but success was achieved by employing the special conditions given in the experimental part. Several attempts to effect the cyclization of (V) under milder conditions with phosphorus pentoxide and phosphoric acid and with sulphuric acid of different strengths in presence of glacial acetic acid proved unsuccessful. The nitrothionaphthene (VI) was characterized by reduction with hydrogen in presence of Raney nickel to the known 5-aminothionaphthene[6] and by the preparation of 5-acetaminothionaphthene from the latter.

Catalytic reduction of (V) with hydrogen in presence of Raney nickel gave *p*-aminophenyl ω-dimethoxyethyl sulphide (VII) which in preliminary experiments failed to cyclize by the usual method.

Condensation of *o*-nitrothiophenol with bromoacetaldehyde dimethyl acetal gave *o*-nitrophenyl ω-dimethoxyethyl sulphide (VIII) as an oil which partially decomposes during vacuum distillation. An analytical specimen of (VIII) could not therefore be prepared but it was characterized by preparation of 2:4-dinitrophenylhydrazone of the parent *S*-(*o*-nitrophenyl)thioglycolic-aldehyde. Ring-closure of (VIII) to 7-nitrothionaphthene by the usual method however proved unsuccessful, the only product isolated being 2:2′-dinitrodiphenyl disulphide.

EXPERIMENTAL

The condensation of bromothiophenols and nitrothiophenols with bromoacetaldehyde dimethyl acetal and the characterization of the resulting sulphides as 2:4-dinitrophenylhydrazones of the parent *S*-arylthioglycolic-aldehyde have been carried out according to the general method outlined earlier.[8]

O-Bromophenyl ω-dimethoxyethyl sulphide (I)

O-Bromothiophenol (14·2 g.), sodium (1·9 g.), bromoacetaldehyde dimethyl acetal (13 g.) and absolute alcohol (50 c.c.) were refluxed for 5 hours. The sulphide (19·6 g.) after distillation gave a colourless oil (16·2 g., yield 78%), b.p. 130–31° (bath temp.)/7 mm. (Found: C, 43·7; H, 4·7. $C_{10}H_{13}BrO_2S$ requires C, 43·3; H, 4·7%). 2:4-*Dinitrophenylhydrazone* gave fine orange-yellow needles from alcohol-ethyl acetate, m.p. 136° (Found: N, 13·1. $C_{14}H_{11}BrN_4O_4S$ requires N, 13·6%).

7-Bromothionaphthene (II)

The sulphide (I) (9·5 g.) was added to phosphorus pentoxide (38 g.) and phosphoric acid, sp. gr. 1·75 (23 c.c.) at 170–80°/10 mm. 7-Bromothionaphthene (5·45 g., yield 75%), which distilled over, on purification through the picrate, gave a colourless oil (2·8 g., yield 39%), b.p. 108–9° (bath temp.)/10 mm. (Found: C, 45·7; H, 2·5. C_8H_5BrS requires C, 45·0; H, 2·3%). The *picrate* crystallized in yellow needles from alcohol, m.p. 144–45° (Found: N, 9·9. $C_{14}H_8BrN_3O_7S$ requires N, 9·5%).

p-Bromophenyl ω-dimethoxyethyl sulphide (III)

p-Bromothiophenol (23·2 g.), sodium (3 g.), bromoacetaldehyde dimethyl acetal (22·7 g.) and absolute alcohol (100 c.c.) were refluxed for 4 hours. The crude sulphide (31 g.) on distillation gave a colourless oil (24·5 g., yield 72%), b.p. 142–44° (bath temp.)/10 mm. (Found: C, 43·1; H, 4·8. $C_{10}H_{13}BrO_2S$ requires C, 43·3; H, 4·7%). 2:4-*Dinitrophenylhydrazone* gave yellow needles from ethyl alcohol, m.p. 140–41° (Found: N, 13·6. $C_{14}H_{11}BrN_4O_4S$ requires N, 13·6%).

5-Bromothionaphthene (IV)

The sulphide (III) (5 g.) was gradually added to a mixture of phosphorus pentoxide (40 g.) and phosphoric acid (48 c.c.) at 130–40°/10 mm. The thionaphthene, which distilled over, was dissolved in ether and the ethereal solution shaken with aqueous sodium hydroxide to remove some *p*-bromothiophenol which was formed in the cyclization. After removal of ether, the residue was steam distilled. A yellow oil distilled over which soon solidified (0·5 g., yield 13%). On redistillation it gave a colourless oil, b.p. 105–7° (bath temp.)/10 mm., which solidified on cooling. The product gave colourless plates from alcohol, m.p. 47–47·5° (Found: C, 45·0; H, 2·6. C_8H_5BrS requires C, 45·0; H, 2·3%). The thionaphthene did not give a picrate.

p-Nitrophenyl ω-dimethoxyethyl sulphide (V)

p-Nitrothiophenol[9] (15·5 g.), prepared from *p*-nitrochlorobenzene, sodium (2·3 g.), bromoacetaldehyde dimethyl acetal (18 g.) and absolute alcohol (100 c.c.) were refluxed for 12 hours. After distillation of alcohol, the mixture was diluted with water and the sulphide which separated as a red orange precipitate was extracted with ether. The ether extract was washed with 10% caustic soda solution, then with water, dried over sodium sulphate and ether removed. The sulphide (16·5 g., 68%) was crystallized from benzene-*n*-hexane when it gave orange-yellow needles, m.p. 55° (Found: C, 49·2; H, 5·0; N, 6·2. $C_{10}H_{13}NO_4S$ requires C, 49·4; H, 5·3; N, 5·7%). 2:4-*Dinitrophenylhydrazone* crystallized from *n*-hexyl alcohol in orange needles, m.p. 185° (Found: N, 18·4; $C_{14}H_{11}N_5O_6S$ requires N, 18·6%).

5-Nitrothionaphthene (VI)

Phosphoric acid (25 c.c.) was added to a mixture of the sulphide (V) (5·5 g.) and phosphorus pentoxide (30 g.) and the mixture was immediately heated in an oil bath for 5 minutes at 130° and then added to crushed ice. Extraction of the mixture with benzene and removal of the solvent, gave the thionaphthene (2·5 g.) as an oil. It was redissolved in benzene and the solution was passed through a column of activated alumina. Removal of the solvent from the percolate gave a dark brown oil (1·2 g.), which after distillation and sublimation in vacuum gave needles (0·5 g.). Crystallization from benzene-*n*-hexane gave 5-nitrothionaphthene as pale yellow needles, m.p. 149° (Literature,[6] m.p. 150°) (Found: C, 53·6; H, 2·8. Calc. for $C_8H_5NO_2S$: C, 53·6; H, 2·7%).

5-Aminothionaphthene

A mixture of the thionaphthene (VI) (0·5 g.), Raney nickel (0·1 g.) and absolute alcohol (25 c.c.) was shaken in a Parr hydrogenator with

hydrogen for 8 hours at 42 lb./sq. inch. Removal of Raney nickel and evaporation of the alcoholic extract, gave 5-aminothionaphthene as a brown oil (0·4 g.), b.p. 145° (bath temp.) 2 mm. After crystallization from benzene-*n*-hexane, the thionaphthene gave, m.p. 70°. Acetylation of the amine gave 5-acetamidothionaphthene which crystallized from benzene-*n*-hexane in white flakes, m.p. 108°. M.p.s. quoted[6] for the amine and its N-acetyl derivative are 72° and 107° respectively.

p-Aminophenyl ω-dimethoxyethyl sulphide (VII)

A mixture of the sulphide (V) (2 g.), Raney nickel (0·1 g.) and absolute alcohol (30 c.c.) was shaken in a Parr hydrogenator with hydrogen for 6 hours at 42 lb./sq. inch. Removal of Raney nickel and evaporation of alcohol, gave *p*-aminophenyl ω-dimethoxyethyl sulphide, b.p. 200–5° (bath temp.)/25 mm. (1·58 g., yield 90%). After four redistillations it was finally collected at 185° (bath temp.)/4 mm. (Found: C, 56·3; H, 7·0; N, 6·7. $C_{10}H_{15}NO_2S$ requires C, 56·3; H, 6·8; N, 6·6%).

o-Nitrophenyl ω-dimethoxyethyl sulphide (VIII)

o-Nitrothiophenol (8 g.), prepared from *o*-nitrochlorobenzene,[10] sodium (1·2 g.), bromoacetaldehyde dimethyl acetal (9 g.) and absolute alcohol (50 c.c.) were boiled for 12 hours on water-bath. After removal of alcohol and dilution with water, a dark red oil was obtained, which was extracted with ether. Removal of ether gave a dark brown oil which on distillation gave yellow liquid, b.p. 140–80° (bath temp.)/4 mm. (yield, 6·0 g.). The sulphide does not give a sharp b.p. and partially decomposes during distillation. 2:4-*Dinitrophenylhydrazone* crystallized from hexyl alcohol in yellow needles, m.p. 180° (Found: C, 45·0; H, 3·3; N, 18·2. $C_{14}H_{11}N_5O_6S$ requires C, 44·6; H, 2·9; N, 18·6%).

Summary

5-Bromothionaphthene and 7-bromothionaphthene were prepared by the cyclization of *p*-bromophenyl ω-dimethoxyethyl sulphide and *o*-bromophenyl ω-dimethoxyethyl sulphide respectively.

The new synthesis of thionaphthene may also be extended to negatively substituted thionaphthenes as shown by the synthesis of 5-nitrothionaphthene (VI) by the ring-closure of *p*-nitrophenyl ω-dimethoxyethyl sulphide (V). *o*-Nitrophenyl ω-dimethoxyethyl sulphide could not be cyclized by the usual method. 5-Aminothionaphthene and *p*-aminophenyl ω-dimethoxyethyl sulphide were obtained by the reduction of (VI) and (V) respectively.

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