

A NEW SYNTHESIS OF THIOPHENES AND THIAPYRANS

Part II. Monomethylthionaphthenes and Monochlorothionaphthenes

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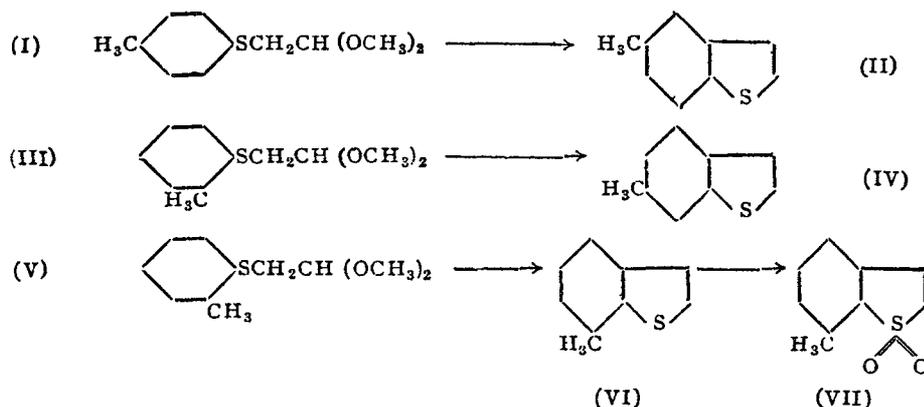
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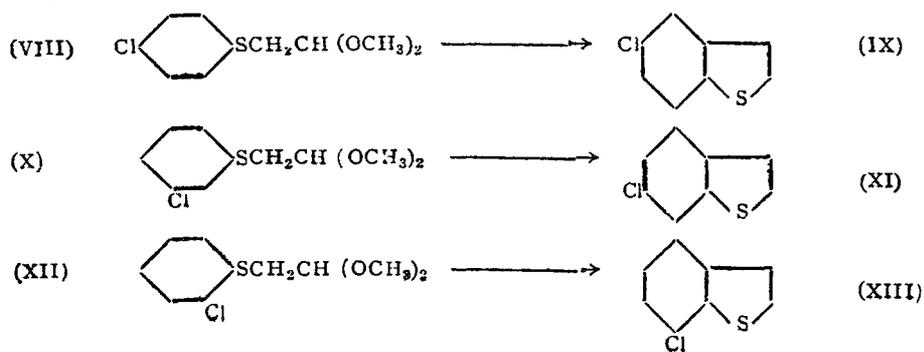
OF the six possible monomethylthionaphthenes, 2-, 3-, 5- and 6-methylthionaphthenes are known. 2-Methylthionaphthene¹ has been prepared by the reduction of 3-hydroxy-2-methylthionaphthene; the latter is obtained from α -(*o*-carboxyphenylmercapto)-propionic acid. 3-Methylthionaphthene has been synthesized recently by Werner² by the cyclization of phenyl acetyl sulphide. 5-Methylthionaphthene³ and 6-methylthionaphthene⁴ have been prepared by the reduction of the corresponding 3-hydroxy-methylthionaphthene. With a view to illustrate the scope of the new synthesis of thionaphthene, 5-methyl-(II) and 6-methylthionaphthene (IV) and the hitherto unreported 7-methylthionaphthene (VI) have been prepared. Another object was to determine the ease of cyclization of *o*-, *m*- and *p*-tolyl ω -dimethoxyethyl sulphides.

5-Methylthionaphthene (II) was prepared by the cyclization of *p*-tolyl ω -dimethoxyethyl sulphide (I). It is a colourless crystalline solid, m.p. 37–38°, whereas Tarbell, *et al.*³ have described the same product as a colourless liquid. Weissgerber⁵ has isolated two methylthionaphthenes, m.p. 36° and m.p. 52°, from crude methylthionaphthalene. On the basis of m.p., these are probably identical with 5-methylthionaphthene (II), m.p. 37–38°, and with 2-methylthionaphthene, m.p. 52°, respectively. 6-Methylthionaphthene (IV), colourless liquid (solidifies on cooling in ice), b.p. 110–115° (bath temp.)/4 mm. (picrate m.p. 114–15°), was prepared by the cyclization of *m*-tolyl ω -dimethoxyethyl sulphide (III). Tarbell and Fukushima⁴ describe (IV) as a colourless solid, m.p. 42–42.5° (picrate 114.5–15.5°). 7-Methylthionaphthene (VI) was obtained by the ring-closure of *o*-tolyl ω -dimethoxyethyl sulphide (V). On oxidation with hydrogen peroxide in acetic acid, (VI) gave 7-methylthionaphthene-1-dioxide (VII). The yields of (II), (IV) and (VI) were 57, 87 and 89% respectively in the crude state and 48.5, 42 and 53% after purification through the picrate. The lower yield of 6-methylthionaphthene (IV) is surprising in view of the activation of the

cyclization position, *p*- to the methyl group in (III). The higher yield, 48.5%, of (II) is also surprising because the cyclization position in (I) is *m*- to the *o*-*p*-directing-methyl group. In view of the considerable difference between the yields of crude and pure (IV), closer examination of crude (IV) obtained after cyclization of (III) will be carried out, to find out if 4-methylthionaphthene is also formed by cyclization of (III).



None of the monohalogenothionaphthenes except 3-bromothionaphthene⁶ has been described so far. 5-Chloro-(IX), 6-chloro-(XI) and 7-chloro-thionaphthenes (XIII) have now been synthesized as an extension of the thionaphthene synthesis and also as intermediates for further syntheses. Cyclization of *p*-chlorophenyl ω -dimethoxyethyl sulphide (VIII), of *m*-chlorophenyl ω -dimethoxyethyl sulphide (X) and of *o*-chlorophenyl ω -dimethoxyethyl sulphide (XII) gave 5-chloro-(IX), 6-chloro-(XI) and 7-chloro-thionaphthenes (XIII) respectively. The yields of (IX), (XI) and (XIII), after purification through the picrate, were 43, 32 and 41% respectively. As in the corresponding 5-methylthionaphthene (II), the yield (43%) of 5-chlorothionaphthene was surprisingly more than 6-chlorothionaphthene (yield, 32%).



EXPERIMENTAL

(M.p. are uncorrected. Microanalyses by Drs. Weiler and Strauss and Mr. T. S. Gore.)

The intermediate sulphides (*S*-arylthioglycolic-aldehyde dimethyl acetals) and the corresponding thionaphthenes obtained by the cyclization of the sulphides have been prepared according to the general procedure outlined earlier.⁷ The sulphides were characterized by the preparation of 2:4-dinitrophenylhydrazones of the parent *S*-arylthioglycolic-aldehydes and the thionaphthenes by the preparation of picrates.⁷ The picrates were obtained in the analytical purity by mixing a solution of the pure thionaphthene and pure picric acid (slight excess over theory for mono-picrate) in absolute alcohol, concentration and cooling.

p-Tolyl ω -dimethoxyethyl sulphide (I)

p-Thiocresol⁸ (13.5 g.), sodium (2.5 g.), bromoacetaldehyde dimethyl acetal (19.8 g.) and absolute alcohol (50 c.c.) were refluxed for 3 hours. The sulphide gave a straw-coloured liquid (15.1 g.; yield 65%). A portion was distilled thrice and finally collected at 170–75° (bath temp.)/15 mm. (Found: C, 61.9; H, 7.5. $C_{11}H_{16}O_2S$ requires C, 62.3; H, 7.6%). 2:4-Dinitrophenylhydrazone gave orange needles from alcohol, m.p. 108–9° (Found: N, 15.9. $C_{15}H_{14}N_4O_4S$ requires N, 16.2%).

5-Methylthionaphthene (II)

The above sulphide (7.8 g.) was added to phosphorus pentoxide (32.0 g.) and phosphoric acid (20.0 c.c.) at 160–70°/2 mm., when a pale yellow liquid was obtained (3.1 g.; yield 57%). On cooling the liquid gave a colourless solid. It was treated with picric acid (7.2 g.) in absolute alcohol and the picrate obtained was decomposed with 2% ammonia. 5-Methylthionaphthene (2.1 g., yield 48.5%) was isolated with ether and gave a white crystalline solid with naphthalene-like odour. It was further purified by distillation, m.p. 37–38°, b.p. 125–35° (bath temp.)/3 mm. (Found: C, 72.6; H, 5.5. Calc. for C_9H_8S : C, 73.0; H, 5.4%). The picrate gave yellow needles from absolute alcohol, m.p. 108–9° (Found: N, 10.4. Calc. for $C_{15}H_{11}N_3O_7S$: N, 11.2%).

m-Tolyl ω -dimethoxyethyl sulphide (III)

m-Thiocresol (7.6 g.), prepared according to Tarbell and Fukushima,⁹ sodium iodide (0.92 g.), bromoacetal (10.4 g.), and absolute alcohol (50 c.c.) were boiled for 2 hours. The sulphide gave a colourless liquid, b.p. 148–150°/6 mm. (9.0 g., yield 69%). A portion was redistilled thrice and finally collected at 135–45° (bath temp.)/5 mm. (Found: C, 62.9; H, 7.7.

$C_{11}H_{16}O_2S$ requires C, 62.3; H, 7.6%. 2:4-Dinitrophenylhydrazone gave lustrous orange needles from alcohol, m.p. 95–96° (Found: N, 16.0. $C_{15}H_{14}N_4O_4S$ requires N, 16.2%).

6-Methylthionaphthene (IV)

The foregoing sulphide (2.6 g.) was added to phosphorus pentoxide (10 g.) and phosphoric acid (6 c.c.) at 175–80°/4 mm. The crude product (1.58 g.) was treated with picric acid, the picrate was decomposed by treatment with 5% sodium hydroxide and 6-methylthionaphthene (0.76 g., yield 42%) was isolated by steam distillation, and purified by two redistillations, when it was obtained as a colourless liquid which solidifies at low temperatures and has naphthalene-like odour; b.p. 110–15° (bath temp.)/4 mm. (Found: C, 73.1; H, 5.7. Calc. for C_9H_8S : C, 73.0; H, 5.4%). The picrate gave felted yellow needles from alcohol, m.p. 114–15° (Found: N, 11.8. Calc. for $C_{15}H_{11}N_3O_7S$: N, 11.2%).

o-Tolyl ω -dimethoxyethyl sulphide (V)

o-Thiocresol (8.6 g.), prepared from *o*-toluidine (*cf.*, preparation of *m*-thiocresol⁹), sodium (1.6 g.), bromoacetal (12.5 g.) and absolute alcohol (50 c.c.) were refluxed for 3 hours. The sulphide gave a colourless liquid (10.2 g., yield 69%), b.p. 155–60° (bath temp.)/6 mm. A portion was redistilled thrice and finally collected at 142–45° (bath temp.)/6 mm. (Found: C, 62.1; H, 7.8. $C_{11}H_{16}O_2S$ requires C, 62.3; H, 7.6%). 2:4-Dinitrophenylhydrazone gave lustrous yellow-orange needles from alcohol, m.p. 123–24° (Found: N, 15.6. $C_{15}H_{14}N_4O_4S$ requires N, 16.2%).

7-Methylthionaphthene (VI)

The foregoing sulphide (6.62 g.) was added to phosphorus pentoxide (27 g.) and phosphoric acid (17 c.c.) at 170–80°/4 mm. when a colourless oil (4.1 g., yield 89%) was obtained. It was treated with picric acid (7.0 g.) in absolute alcohol and the picrate obtained was decomposed by treatment with 2% ammonia. The colourless thionaphthene possessing naphthalene-like odour (2.45 g., yield 53%) was distilled, b.p. 110–15° (bath temp.)/4 mm. (Found: C, 72.5; H, 5.2. C_9H_8S requires C, 73.0; H, 5.4%). The picrate gave elongated golden yellow needles from absolute alcohol, m.p. 144–45° (Found: N, 10.9. $C_{15}H_{11}N_3O_7S$ requires N, 11.2%).

7-Methylthionaphthene-1-dioxide (VII)

The thionaphthene (0.4 g.) was reacted with glacial acetic acid (6 c.c.) and hydrogen peroxide 100 vols. (2 c.c.) on water-bath at 85° for 6 hours. The reaction mixture was poured into crushed ice. After neutralization

with potassium carbonate, 7-methylthionaphthene-1-dioxide (0.21 g.) was isolated by means of ether. It crystallises from aqueous alcohol in colourless flat needles, m.p. 74–75° (Found: C, 60.0; H, 4.5%. $C_9H_8O_2S$ requires C, 60.0; H, 4.4%).

The chlorothiophenols required in the following experiments were prepared from the corresponding chloroanilines by the method used for the conversion of *m*-toluidine to *m*-thiocresol.⁹

p-Chlorophenyl ω -dimethoxyethyl sulphide (VIII)

p-Chlorothiophenol (16.5 g.), sodium (2.7 g.), bromoacetal (21 g.) and absolute alcohol (50 c.c.) were refluxed for 4 hours. The sulphide gave a yellow liquid, b.p. 130–60°/15 mm. (18.5 g.; yield 69%). It was redistilled four times and finally collected at 155° (bath temp.)/12 mm. (Found: C, 51.1; H, 5.2. $C_{10}H_{13}ClO_2S$ requires C, 51.6; H, 5.6%). 2:4-Dinitrophenylhydrazone gave yellow orange needles from ethyl acetate-alcohol, m.p. 138° (Found: N, 14.9. $C_{14}H_{11}ClN_4O_4S$ requires N, 15.3%).

5-Chlorothionaphthene (IX)

The above sulphide (10 g.) was added to phosphorus pentoxide (50 g.) and phosphoric acid (30 c.c.) at 160–80°₁₁₀ mm. and the colourless liquid thionaphthene (3.1 g., yield 43%) obtained was distilled four times. It was steam-distilled and the product was further purified by two redistillations, b.p. 85° (bath temp.)/4 mm. (Found: C, 56.1; H, 3.1. C_8H_5ClS requires C, 57.0; H, 3.0%). The *picrate* crystallized in long yellow needles from absolute alcohol, m.p. 69–70° (Found: N, 10.1. $C_{14}H_8ClN_3O_7S$ requires N, 10.6%).

m-Chlorophenyl ω -dimethoxyethyl sulphide (X)

m-Chlorothiophenol (13.2 g.), sodium (2.25 g.), bromoacetal (17.0 g.) and absolute alcohol (50 c.c.) were boiled for 3 hours. The sulphide gave a yellow liquid, b.p. 100–80°/15 mm. (17.5 g., yield 65%). It was redistilled and the fraction boiling at 173°/44 mm. was collected and further purified by four redistillations, b.p. 170° (bath temp.)/15 mm. (Found: C, 51.3; H, 5.4. $C_{10}H_{13}ClO_2S$ requires C, 51.6; H, 5.6%). 2:4-Dinitrophenylhydrazone gave orange needles from ethyl acetate-alcohol, m.p. 123° (Found: N, 15.1. $C_{14}H_{11}ClN_4O_4S$ requires N, 15.3%).

6-Chlorothionaphthene (XI)

The foregoing sulphide (7.0 g.) was added to phosphorus pentoxide (35 g.) and phosphoric acid (21 c.c.) at 180–200°/15 mm., when a yellow liquid (3.8 g., yield 75%) was obtained. It was treated with picric acid

(5.5 g.), the picrate decomposed by 2% ammonia and the mixture extracted with ether. On removal of ether, the thionaphthene (1.6 g., yield 32%) was obtained as a colourless liquid having naphthalene-like smell. It was redistilled four times and finally collected at 125° (bath temp.)/15 mm. (Found: C, 56.7; H, 3.1. C_8H_5ClS requires C, 57.0; H, 3.0%). The picrate gave yellow needles from absolute alcohol, m.p. 134° (Found: N, 9.8. $C_{14}H_8ClN_3O_7S$ requires N, 10.6%).

o-Chlorophenyl ω -dimethoxyethyl sulphide (XII)

o-Chlorothiophenol (10.4 g.), sodium (2 g.), bromoacetal (15 g.) and absolute alcohol (50 c.c.) were boiled for 4 hours. The sulphide gave a colourless liquid, b.p. 190–200° (bath temp.)/25 mm. (10.4 g., yield 62%). It was redistilled four times and finally collected at 170° (bath temp.)/10 mm. (Found: C, 51.5; H, 5.2. $C_{10}H_{13}ClO_2S$ requires C, 51.6; H, 5.6%). 2:4-Dinitrophenylhydrazone gave yellow orange needles from ethyl acetate-alcohol, m.p. 135–36° (Found: N, 15.2. $C_{14}H_{11}ClN_4S$ requires N, 15.3%).

7-Chlorothionaphthene (XIII)

The above sulphide (7.35 g.) was added to phosphorus pentoxide (37 g.) and phosphoric acid (25 c.c.) at 160–70°/10 mm., when a pale yellow liquid (2.15 g., yield 40%) was obtained. It was redistilled four times and finally collected at 115° (bath temp.)/10 mm. (Found: C, 56.9; H, 3.2. C_8H_5ClS requires C, 57.0; H, 3.0%). The picrate gave long lemon-yellow needles, from absolute alcohol, m.p. 141–42° (Found: N, 10.8. $C_{14}H_8ClN_3O_7S$ requires N, 10.6).

SUMMARY

5-Methyl- (II) and 6-methyl-thionaphthenes (IV) and the hitherto unknown 7-methyl-(VI), 5-chloro-(IX), 6-chloro-(XI) and 7-chloro-thionaphthenes (XIII) were prepared by the new synthesis. 7-Methylthionaphthene-1-dioxide (VII) was also prepared.

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