[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Synthesis of Thienothianaphthene Derivatives by Ring Formation with Sulfur[1]

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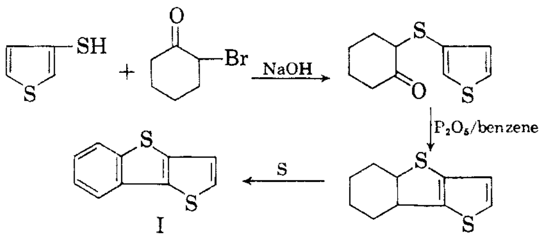
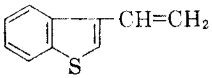
The syntheses of 3-phenylthieno[3,2-b]thianaphthene and 3-phenylthieno[2,3-b]thianaphthene from thianaphthene are described. Their structures are confirmed by synthesis, using alternate unambiguous routes.

Tilak and co-workers[2] in a series of recent papers have prepared two of the three possible thiophthenes, together with a number of their benzo derivatives. Their synthetic routes are based on the reaction of an α-bromoketone with a 2-, or 3-, mercapto-thiophene or -thianaphthene, cyclodehydration of the resulting β-ketosulfide, and finally dehydrogenation to a fully aromatised structure, equation 1.

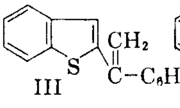


Horton[3] has described the reaction of sulfur, at 340°, with hydrocarbons as a means of thiophene ring formation, while Harper[4] has evidence for the production of two sulfur-containing rings at the same time by treating a diaryl olefin with sulfur at 200°.

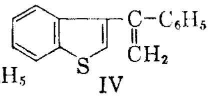
It was of interest to investigate the scope of the use of sulfur as a means of producing, by an alternative route, ring structures related to those prepared by Tilak *et al.*[2] The preparations of II, III and IV were therefore undertaken with a veiw to their conversion to the corresponding thienothianaphthenes.



II



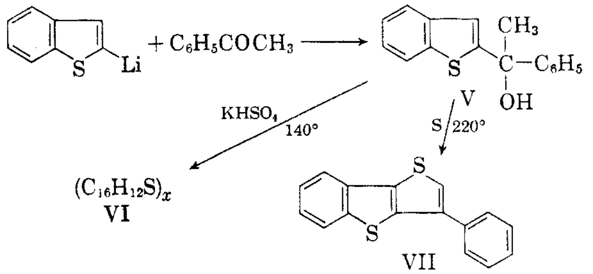
III



IV

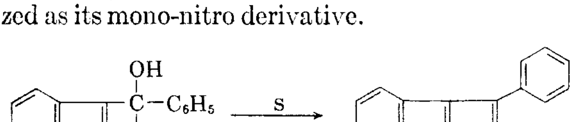
3-Vinylthianaphthene (II), prepared by dehydration of 2(3′-thianaphthenyl)ethanol,[5] on treatment with sulfur at 220° for four hours yielded, on distillation, a bright orange oil. Chromatography of the oil on alumina gave only a series of orange-yellow oils, instead of the expected crystalline thieno[2,3-b]thianaphthene.[2b]

1-Phenyl-1(2′-thianaphthenyl)ethylene III was obtained as a colorless oil, slowly polymerising at room temperature to a brown gum, by dehydration under mild conditions (iodine-benzene) of the tertiary alcohol V. The latter was prepared, in high yield, by the reaction of acetophenone with 2-thianaphthenyl lithium (cf. Shirley and Cameron[6]).



The dehydration of V with potassium bisulfate under more vigorous conditions produced only a white amorphous solid (VI) of indefinite melting point.

In view of the instability of the olefin III further investigations were confined to the alcohol V. The latter was treated with sulfur under varying conditions of time and temperature. Under the least vigorous conditions (220° for four hours) 3-phenylthieno[3,2-b]thianaphthene (VII) was isolated as a white crystalline solid. The latter was characterized as its mono-nitro derivative.



The isomeric tertiary alcohol VIII was prepared by reaction of the Grignard reagent derived from 3-bromothianaphthene with acetophenone. Direct treatment of the alcohol with sulfur gave a 33% yield of the expected 3-phenylthieno[2,3-b]thianaphthene (IX).

The fact that ring closure in both cases occurred to form a thienothianaphthene derivative rather than the corresponding thianaphthenylthianaphthene was confirmed by the synthesis in each case of

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(1) This work was supported by the Office of Ordnance Research, U. S. Army, Contract No. DA-11-022-Ord-571.

(2) (a) V. V. Ghaisas and B. D. Tilak, *J. Sci. Ind. Research* **16B**, 345 (1957), cf. Chemical Abstracts **52**, 5370 (1958). (b) R. B. Mitru, L. J. Pandya, and B. D. Tilak, *J. Sci. Ind. Research*, 348, cf. Chemical Abstracts **52**, 5371 (1958). (c) V. V. Ghaisas and B. D. Tilak, *Proc. Ind. Acad. Sci.* **22**, 184 (1953).

(3) A. W. Horton, *J. Org. Chem.*, **14**, 760 (1949).

(4) E. T. Harper, Ph.D. thesis, University of Minnesota 1959.

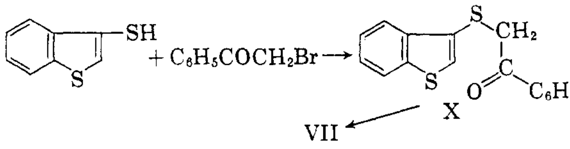
(5) W. Davies, Q. N. Porter, and J. R. Wilmshurst, *J. Chem. Soc.*, 3366 (1957).

(6) D. A. Shirley and M. D. Cameron, *J. Am. Chem. Soc.*, **74**, 664 (1952).

TABLE I

Experiment	Temp.	Time (hr.)	% Yield of VII	By-products
1	310	16	0	Polymeric material of indefinite m.p.
2	245	15	7.5	—
3	200–250	16	17	18% of $(C_{16}H_{10}S)_x$
4	220	1.5	16	—
5	200	16	0	yellow oils

an authentic specimen. This was achieved by a route similar to that of Tilak *et al.*[2] 3-Mercaptothianaphthene,[2a] prepared from 3-iodothianaphthene, was treated with phenacyl bromide and the resulting β-ketosulfide (X) was treated with phosphorus pentoxide in refluxing benzene to yield 3-phenylthieno[3,2-b]thianaphthene, identical in every respect with that derived from V.



Similarly, the reaction of 2-mercaptothianaphthene, prepared from 2-thianaphthenyl lithium,[2b] with phenacyl bromide, and subsequent cyclodehydration of the derived β-ketosulfide gave 3-phenylthieno[2,3-b]thianaphthene, identical in every respect with the product obtained from VIII.

EXPERIMENTAL[7]

The reaction of 3-vinylthianaphthene with sulfur. A mixture of 3-vinylthianaphthene[5] (6.5 g., 0.039 mol.) and sulfur (2.6 g., 0.081 mol.) was heated at 220° for 3 hr. The resulting black oil was distilled to give a bright orange distillate (2 g.), b.p. 110–130°/0.5 mm. Elution of the latter from 100 g. of alumina with petroleum–benzene gave only unreacted sulfur and a series of red-yellow oils.

Methylphenyl-2-thianaphthenylcarbinol V. Thianaphthene (17.9 g., 0.133 mol.), dissolved in dry ether (40 ml.), was added at −10° to a solution of butyllithium, prepared from butyl bromide (29.5 g., 0.217 mol.) and lithium (3.61 g., 0.535 mol.), in ether (100 ml.), followed by the addition of a solution of acetophenone (16.0 g., 0.33 mol.) in ether (40 ml.) at room temperature. The mixture was stirred for 1 hr. and then hydrolyzed by pouring onto iced ammonium chloride. The ethereal extracts (2 × 100 ml.) were combined, dried over magnesium sulfate and distilled to give methylphenyl-2-thianaphthenylcarbinol, (26.15 g., 77%) b.p. 168–170°/0.1 mm. n_D^{27} 1.6466. The distillate slowly crystallized and an analytical sample, recrystallized from petroleum, melted at 56.5–58°.

Anal. Calcd. for $C_{16}H_{14}OS$: C, 75.57; H, 5.55; S, 12.62. Found: C, 75.64; H, 5.60; S, 12.90.

The dehydration of methylphenyl-2-thianaphthenylcarbinol. (a) *With iodine-benzene.* A solution of methylphenyl-2-thianaphthenylcarbinol (1.0 g., 4 m. mol.) and iodine (0.2 g.) in benzene (200 ml.) was boiled under reflux for 2 hr., washed with a 10% aqueous solution of sodium sulfite (two 20-ml. portions), dried magnesium sulfate and the solvent was then evaporated to leave a dark brown oil (0.5 g.). The latter was eluted from a column of alumina (40 g.) with petroleum and the solvent evaporated to leave the olefin as a colorless mobile oil (0.3 g.) (n_D^{25} 1.6809). The infrared spectrum had a strong band at 895 cm.$^{-1}$, indicative of a terminal methylene group.

Anal. Calcd. for $C_{16}H_{12}S$: C, 81.34; H, 5.12; S, 13.54. Found: C, 81.15; H, 5.14; S, 13.37.

(b) *With potassium bisulfate.* A mixture of the carbinol V (5.0 g.) and freshly fused potassium bisulfate (1.0 g.) was heated on an oil bath at 140° for 20 min. The cold residue was extracted with ether (two 50-ml. portions) and the combined extracts were washed with 10% aqueous sodium carbonate (50 ml.) and a saturated sodium chloride solution (50 ml.), dried potassium carbonate, and the solvent then evaporated to leave a viscous oil (4.7 g.). The latter was distilled to give a semi-solid glass (b.p. *ca.* 185°/4 mm.). The distillate was extracted with petroleum and recrystallized from the same solvent to give a white amorphous solid (0.45 g.) m.p. 170–180°. Further recrystallization of this solid had no effect on the melting point.

Anal. Calcd. for $C_{16}H_{12}S$: C, 81.34; H, 5.12; S, 13.54. Found: C, 81.19; H, 5.68; S, 13.11.

The reaction of methylphenyl-2-thianaphthenylcarbinol with sulfur. The carbinol V (5.0 g., 0.02 mol.) and sulfur (2.0 g., 0.062 mol.) were mixed and heated in an atmosphere of nitrogen, under the conditions stated in Table I.

The residual dark oil was dissolved in the minimum quantity of benzene and placed on a column of alumina (150 g.). Unchanged sulfur was eluted first with 10% benzene-petroleum ether, followed in later fractions by 3-phenylthieno[3,2-b]thianaphthene melting at 90–100°. Recrystallization of these fractions from benzene–petroleum gave a solid m.p. 103.5–104.5°. A mixed melting point with an authentic sample of 3-phenylthieno[3,2-b]thianaphthene (see later) showed no depression.

Experiment 2 was modified in that the carbinol V (10.0 g.) was treated with a solution of iodine in benzene, as described above, and the crude product (7.4 g.) was then treated with sulfur (3.0 g.).

In experiment 3, elution of the chromatographic column with a 30% benzene-petroleum mixture, after removal of 3-phenylthieno[3,2-b]thianaphthene asd escribed, yielded 0.95 g. (18%) of a white solid (m.p. 200–201.5°) corresponding to the formula $(C_{16}H_{10}S)_x$.

Anal. Calcd. for $C_{16}H_{10}S$: C, 82.04; H, 4.30; S, 13.66. Found: C, 81.87; H, 4.29; S, 13.47.

Methylphenyl-3-thianaphthenylcarbinol (VIII). A solution of 3-bromothianaphthene (40.25 g., 0.188 mol.) and methyl iodide (26.8 g., 0.188 mol.) in ether (150 ml.) was added to a stirred suspension of magnesium (9.2 g., 0.376 mol.) in ether (50 ml.) and the mixture was boiled under reflux for 1.5 hr. Acetophenone (45 g., 0.376 mol.), dissolved in ether (100 ml.) was then added slowly. The mixture was stirred at room temperature for 30 min. and then hydrolyzed by pouring onto ice-ammonium chloride. The ethereal layer was separated and the aqueous phase extracted with ether (two 200-ml. portions). The combined ethereal solutions were dried magnesium sulfate, the solvent was evaporated under reduced pressure and the mixture then heated on a steam bath at 1.5 mm. pressure for 30 min. The solid obtained on cooling the residue was recrystallized from benzene-petroleum to yield methylphenyl-3-thianaphthenylcarbinol (29.4 g., 61.5%) m.p. 118.5–120.5°.

Anal. Calcd. for $C_{16}H_{14}O$: C, 75.57; H, 5.55; S, 12.62. Found: C, 75.77; H, 5.59; S, 12.60.

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[7] Petroleum denotes petroleum ether of b.p. 60–68°.

The reaction of methylphenyl-3-thianaphthenylcarbinol with sulfur. A mixture of methylphenyl-3-thianaphthenylcarbinol (5.0 g., 0.02 mol.) and sulfur (2.0 g., 0.062 mol.) was heated at 240° for 4 hr. The residual oil was dissolved in a minimum of methylene chloride and placed on a column of alumina (previously activated by heating at 200° for 4 hr.). Development of the column with petroleum (500 ml.) separated unchanged sulfur. Elution with a 10% solution of methylene chloride-petroleum (350 ml.) yielded a colorless oil (2.05 gm.) which subsequently became crystalline. Recrystallization of this solid from petroleum ether and finally from methanol gave 3-phenylthieno[2,3-b]thianaphthene (1.73 g., 33%) as needles m.p. 75–77.5°. An analytical sample melted at 76.5–77.5°.

Anal. Calcd. for $C_{16}H_{10}S_2$: C, 72.18; H, 3.79; S, 24.04. Found: C, 72.53; H, 3.64; S, 24.09.

Phenacyl-3-thianaphthenyl sulfide (X). Phenacyl bromide (16.1 g., 0.081 mol.) was added, during 10 min., to a solution of 3-mercaptothianaphthene[22] (13.2 g., 0.08 mol.) dissolved in 20 g. of 20% aqueous sodium hydroxide and cooled to 20°. The mixture was stirred for a further 2 hr., diluted with water and then extracted with ether (three 100-ml. portions). The ethereal extracts were dried (magnesium sulfate) and the solvent evaporated. The residue was recrystallized from ethanol to yield phenacyl-3-thianaphthenyl sulfide (13.75 g., 57%) m.p. 82–85°. An analytical sample melted at 85.5–86.5°.

Anal. Calcd. for $C_{16}H_{12}OS_2$: C, 67.60; H, 4.26; S, 22.51. Found: C, 67.62; H, 4.38; S, 22.51.

The *2,4-dinitrophenylhydrazone* (orange needles from ethyl acetate) melted at 183–183.5°.

Anal. Calcd. for $C_{22}H_{16}N_4O_4S_2$: C, 56.90; H, 3.47; N, 12.07. Found: C, 57.04; H, 3.47; N, 11.77.

3-Phenylthieno[3,2-b]thianaphthene (VII). Phosphorus pentoxide (50 g.) was added to a solution of phenacyl-3-thianaphthenyl sulfide (12.65 g., 0.045 mol.) in benzene (200 ml.) and the mixture was separated and the residue washed with further benzene (two 100-ml. portions). The solvent was evaporated from the combined benzene solutions to leave a light yellow semi-crystalline residue. The latter was dissolved in a minimum quantity of benzene and placed on a column of alumina (150 g.). Elution of the column with 30% benzene–petroleum (400 ml.) yielded 3-phenylthieno[3,2-b]thianaphthene (3.70 g., 35%) m.p. range 93–100°. An analytical sample melted at 104–105°.

Anal. Calcd. for $C_{16}H_{10}S_2$: C, 72.18; H, 3.79; S, 24.04. Found: C, 72.12; H, 3.91; S, 23.94. λ^{241}_{max} ϵ30,110, λ^{269}_{max} ϵ16,490, λ^{293}_{max} ϵ10,090; $\lambda^{306}_{inf.}$ ϵ7,223, λ^{319}_{max} ϵ5,042.

The product was found to be identical (mixed melting point—no depression, infra-red spectrum) with the product derived from methylphenyl-3-thianaphthenylcarbinol.

Further elution of the column with 70% benzene-petroleum yielded some unchanged phenacyl-3-thianaphthenyl sulfide (1.50 g.) m.p. 80–84°.

2-Nitro-3-phenylthieno[3,2-b]thianaphthene. To a solution of 3-phenylthieno[3,2-b]thianaphthene (2.45 g., 9.2 m. mol.) in acetic anhydride (25 ml.) at −10° was added 2 ml. of a solution prepared from nitric acid (3 ml. d. 1.42) and acetic anhydride (10 ml.). The mixture was stirred at 0° for 40 min. then poured onto ice and ammonium bicarbonate and the resulting yellow solid extracted with benzene. The benzene extract was evaporated to leave a yellow solid. The latter was placed on a column of alumina (150 g.). Elution of the column with 60% benzene–petroleum (1200 ml.) yielded 2-nitro-3-phenylthieno[3,2-b]thianaphthene as a bright yellow solid, m.p. 215–216°. An analytical sample (needles from benzene-petroleum) melted at 215.5-217°.

Anal. Calcd. for $C_{16}H_9NO_2S_2$: C, 61.74; H, 2.91; N, 4.50. Found: C, 61.78; H, 3.05; N, 4.40.

Phenacyl-2-thianaphthenyl sulfide (XI). Phenacyl bromide (17.1 g., 0.086 mol.) was added, during 10 min., to a solution of 2-mercaptothianaphthene[2b] (14.2 g., 0.086 mol.) and sodium hydroxide (3.5 g.) in water (20 ml.), cooled to 20°. The mixture was stirred for 1 hr., diluted with water and extracted with ether (three 100-ml. portions). The ethereal extracts were dried (magnesium sulfate) and the solvent evaporated. The solid residue was recrystallized from methanol to give phenacyl-2-thianaphthenyl sulfide as white needles (15.6 g., 64%), m.p. 53–55.5°. An analytical sample melted at 55–56°.

Anal. Calcd. for $C_{16}H_{12}OS_2$: C, 67.60; H, 4.26; S, 22.51. Found: C, 67.90; H, 4.13; S, 22.77.

3-Phenylthieno[2,3-b]thianaphthene (IX). Phosphorus pentoxide (40 g.) was added to a solution of phenacyl-2-thianaphthenyl sulfide (10.0 g.) in chlorobenzene (150 ml.) and the mixture boiled under reflux for 3 hr. The chlorobenzene layer was separated, and the residue was cautiously dissolved in water and then extracted with benzene (two 100-ml. portions). The combined organic solutions were washed with water, dried and (magnesium sulfate), solvent was evaporated on a steam bath at reduced pressure to leave a brown crystalline residue. The latter was dissolved in a minimum of benzene, placed on a column of activated alumina (200 g.), and eluted with 15% benzene–petroleum to yield 3-phenylthieno[2,3-b]thianaphthene (4.90 g., 52%), m.p. 74–77°. Recrystallization of the product from methanol gave the pure material of m.p. 76.5–77.5°.

The above product was found to be identical (mixed melting point—no depression, infrared spectrum) with the product obtained from methylphenyl-3-thianaphthenylcarbinol VIII.

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