A NEW SYNTHESIS OF THIOPHENES AND THIAPYRANS

Part V. 6 : 7-Benzothionaphthene and 9-Chloronaphtho-(1′ : 8′-*bc*)-thiapyran

By V. K. Dikshit and B. D. Tilak

(Department of Chemical Technology, University of Bombay)

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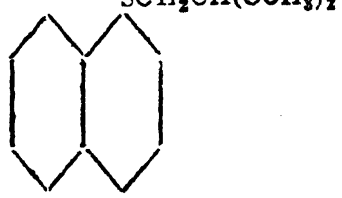
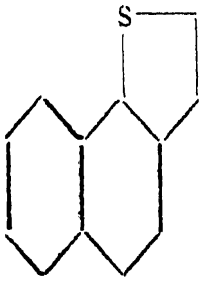
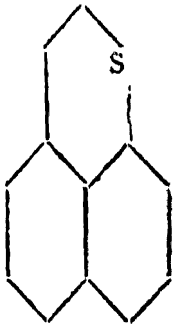
The product obtained by the cyclization of α-naphthyl ω-dimethoxyethyl sulphide (I), described in the previous communication, may be constituted either as 6 : 7-benzothionaphthene (II) or as naphtho-(1′ : 8′-*bc*)-thiapyran (III) depending on cyclization in the β- or the *peri*-positions. Unambiguous syntheses of (II) and (III) were therefore undertaken.



(I)

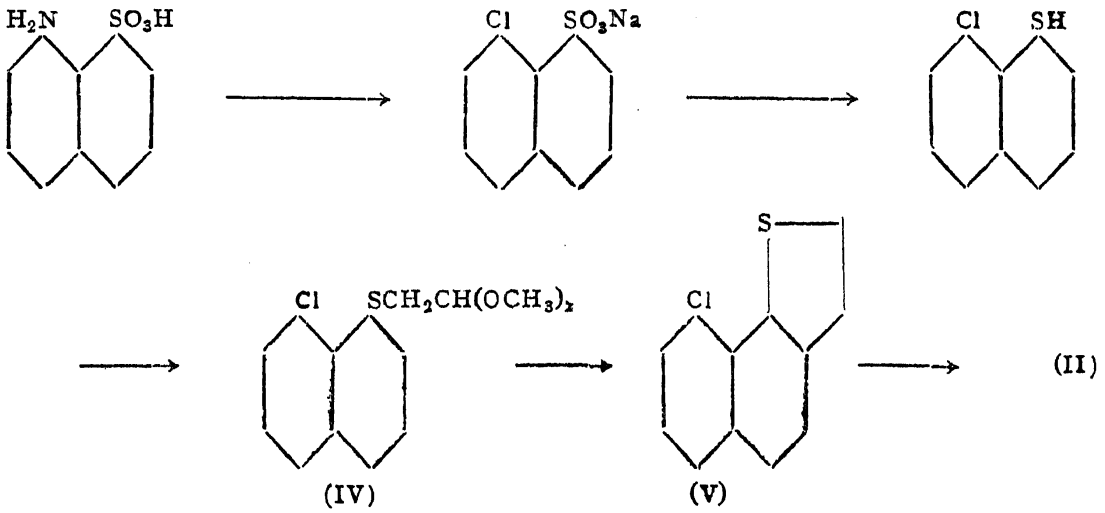


(II)



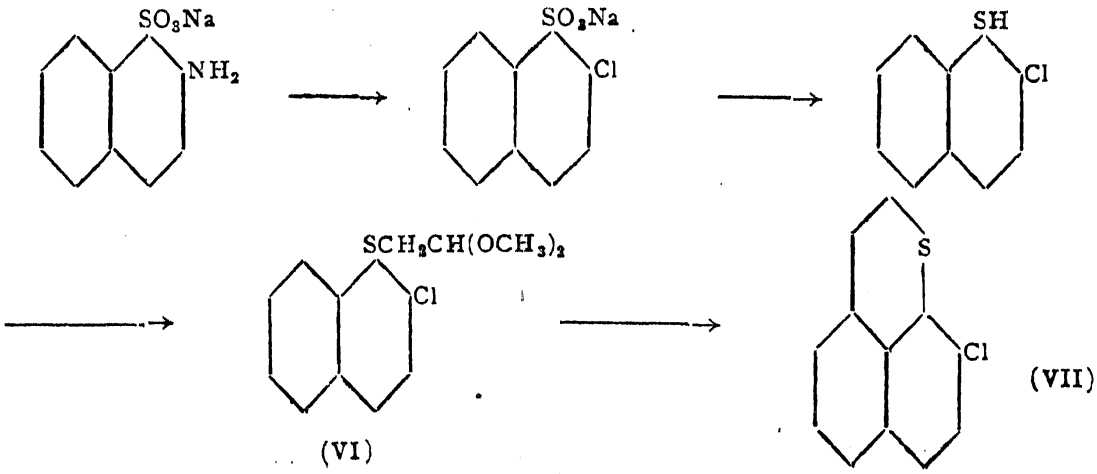
(III)

Sodium 8-chloronaphthalene-1-sulphonate, obtained in 80% yield by Sandmeyer reaction on 1-naphthylamine-8-sulphonic acid (*peri*-acid), was converted to 8-chloro-1-thionaphthol in 86% yield by the reduction of the intermediate 8-chloronaphthalene-1-sulphonyl chloride which was not isolated. Condensation of the thiol with bromoacetaldehyde dimethyl acetal gave 8-chloro-1-naphthyl ω-dimethoxyethyl sulphide (IV) in 70% yield and the latter on cyclization gave 3′-chlorobenzo-(1′ : 2′, 6 : 7)-thionaphthene (V) in 82% yield. Dechlorination of (V) yielded 6 : 7-benzothionaphthene (II), a pale straw-coloured liquid, b.p. 140–42° (bath temp.)/10 mm. (picrate: brick-red needles, m.p. 140–41°), which is different from the product, lemon-yellow liquid, b.p. 150–55° (bath temp.)/1·5–2 mm. (picrate: olive-brown needles, m.p. 177–78°), obtained by the ring-closure of (I) (*vide* previous communication). The latter product is therefore constituted as naphtho-(1′ : 8′-*bc*)-thiapyran (III).



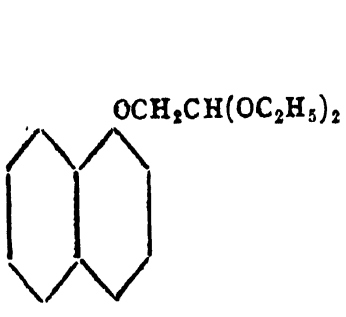
While the present work was in progress, Szmuszkovicz and Modest[1] have reported the synthesis of (II) by the Diels-Alder addition of maleic anhydride to 1-(2′-thienyl)-cyclohexene followed by dehydrogenation and decarboxylation of the adduct.

Synthesis of (III) starting from sodium 2-naphthylamine-1-sulphonate (salt of Tobias acid) was then undertaken. Sodium 2-chloronaphthalene-1-sulphonate was prepared by Sandmeyer reaction on Tobias acid. It is essential to treat the diazo salt from Tobias acid with cuprous chloride in concentrated hydrochloric acid to prevent the formation of 2-naphthol-1-sulphonic acid. 2-Chloro-1-thionaphthol was prepared from the sulphonic acid through the sulphonyl chloride, which was not isolated. The yield of the thiol starting from Tobias acid was 54%. Condensation of the thiol with bromoacetaldehyde dimethyl acetal, gave 2-chloro-1-naphthyl ω-dimethoxyethyl sulphide (VI) in good yield (71%), but due to the low yield (11%) of 9-chloronaphtho-(1′:8′-*bc*)-thiapyran (VII) during cyclization of (VI), the dechlorination of (VII) to (III) could not be carried out.

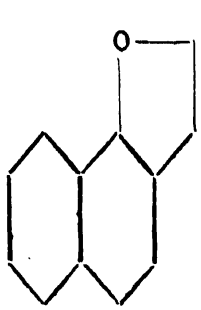


It is of interest to study the cyclization of α-substituted naphthalene derivatives. α-Naphthylacetic acid gives 9-keto-9:10-dihydroacenaphthene by *peri*-ring-closure.[2] Similarly β-1-naphthyl-propionic acids and γ-(5-methoxy-1-naphthyl)-butyric acid cyclize in the *peri*-positions.[3] Ingham *et al.*[4] cyclized α-naphthoxyacetyl chloride and obtained an isomer of 6:7-benzocoumaranone,[5] the properties of which suggested that it is probably the naphthopyrone obtained by *peri*-cyclization. Anand and Venkataraman[6] have, however, established the constitution of the cyclization product from α-naphthoxyacetic acid as 6:7-benzocoumaranone. Whereas the cyclization of β-thionaphthoxyacetic acid has been reported,[7] the ring-closure of α-thionaphthoxyacetic acid has not been recorded. 3-Hydroxynaphtho-(1′:8′-*bc*)-thiapyran and 3-hydroxy-6:7-benzothionaphthene which would result by the peri- or β-cyclization of α-thionaphthoxyacetic acid have been synthesized by Friedländer and Woroschzow[7] from *S*-8-carboxy-1-naphthyl thioglycolic acid and *S*-2-carboxy-1-naphthylthioglycolic acid respectively. Harley-Mason and Mann[8] experienced difficulty in the *peri*-cyclization of 2-chloro- and 2-acetamido-1-thionaphthoxyacetic acid. Whereas the *peri*-cyclization of α-thionaphthoxy derivatives is difficult and low yields of such cyclization products are to be expected, it is not impossible in view of the synthesis of (III) and (VII). Cyclization of α-thionaphthoxyacetic acid is of interest and is being studied.

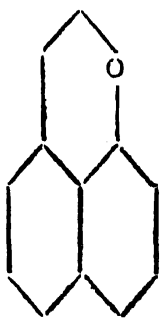
Stoermer[9] has constituted the cyclization product of α-naphthoxyacetaldehyde diethyl acetal (VIII) as 6:7-benzocoumarone (IX), without adducing evidence of β-cyclization. The cyclization of α-naphthoxyacetic acid in the β-position,[6] supports the structure (IX) assigned by Stoermer. In view, however, of the *peri*-ring-closure of the sulphur analogue (I), the alternative naphthopyran structure (X) for the cyclization product cannot be ruled out. Unambiguous syntheses of (IX) and (X) have been undertaken.



(VIII)



(IX)



(X)

Experimental

The preparations of sodium 8-chloronaphthalene-1-sulphonate and sodium 2-chloronaphthalene-1-sulphonate from the corresponding amino

sulphonic acids have been described as convenient laboratory methods for the preparation of these acids are not available. Similarly, the syntheses of 8-chloro-1-thionaphthol and 2-chloro-1-thionaphthol from the above acids are also described.

The condensation of the chlorothionaphthols with bromoacetaldehyde dimethyl acetal and the isolation of the sulphides (IV) and (VI) were carried out according to the general procedure outlined earlier.[10] The sulphides being viscous oils, were dissolved in dry benzene and the benzene solution was added to a hot mixture of phosphorus pentoxide and phosphoric acid under the general conditions described earlier.[10]

The sulphides (*S*-arylthioglycolic-aldehyde dimethyl acetals) were characterized by the preparation of 2:4-dinitrophenylhydrazones of the parent *S*-arylthioglycolic-aldehydes, and the cyclized products were characterized as picrates.

Sodium 8-chloronaphthalene-1-sulphonate.—Commercial *peri*-acid (28 g.; 85% purity) was extracted with a hot suspension of magnesium oxide (3 g.) in water (175 c.c.) at 95° C. and the solution of the magnesium salt of the acid, after cooling to room temperature (25°) by addition of ice, was treated with 30% sulphuric acid (75 g.) under stirring. The finely divided suspension of the acid was diazotized at room temperature by addition of an aqueous solution of sodium nitrite (10 g. in 25 c.c.). The nitrite solution was added gradually in two hours below the surface of the liquid. After leaving overnight under stirring, the diazo salt which precipitated was filtered and washed with a little ice-cold water, made into a slurry with water and then added gradually to freshly prepared cuprous chloride [from copper sulphate (19·0 g.), sodium chloride (11·2 g.) and sodium sulphite (11·2 g.)] and concentrated hydrochloric acid (8 c.c.) at 30–35°. After the completion of the reaction (no colour with an alkaline solution of R-salt), the mixture was warmed to 55° and the precipitated naphthasultone was filtered. The filtrate was made alkaline and the precipitated copper salts filtered using 'supercel' filter-aid. Sodium 8-chloronaphthalene-1-sulphonate was salted out by adding 25 g. of salt per 100 c.c. of the solution, collected and washed with saturated brine and dried (26 g. of 95% pure sodium salt; yield 87%). Concentration of the mother liquor gave a second crop of the impure salt.

8-*Chloro*-1-*thionaphthol.*—A mixture of sodium 8-chloronaphthalene-1-sulphonate (15 g.), phosphorus pentachloride (16 g.) and dry chloro benzene (127 g.) was heated at 78–80° under stirring till the evolution of hydrogen chloride ceased. After cooling to 10°, 30% sulphuric acid (110 g.) was added followed by zinc dust (23 g.), keeping the temperature below 30°,

The mixture was raised to 70° in 30 minutes and maintained at this temperature for one hour. Chlorobenzene was steam distilled, the residue cooled and poured into ice. The crude thiol was filtered, extracted with peroxide-free ether, and the thiol (9·0 g., yield 86%), m.p. 106–108°, recovered by removal of the solvent.

8-*Chloro*-1-*naphthyl ω-dimethoxyethyl sulphide* (*IV*).—The above thiol (8·75 g.), sodium (1·1 g.), bromoacetal (9 g.) and absolute alcohol (50 c.c.) were refluxed for 6 hours. The crude sulphide (8·9 g.; yield 70%) on repeated distillation gave a viscous brown oil, b.p. 164–66° (bath temp.)/6 mm., which however did not give correct elementary analysis. The sulphide gave 2:4-*dinitrophenylhydrazone* of the parent *S*-(8-chloro-1-naphthyl)-thiolglycolic-aldehyde. The hydrazone crystallized from ethyl acetate in yellow needles, m.p. 179·5° (Found: C, 51·4; H, 3·0; Cl, 7·8, N, 13·4. $C_{18}H_{13}ClN_4O_4S$ requires C, 51·8; H, 3·1; Cl, 8·5; N, 13·4%).

3′-*Chlorobenzo*-(1′:2′, 6:7)-*thionaphthene* (*V*).—A solution of the sulphide (IV) (5 g.) in benzene (20 c.c.) was added gradually to a mixture of phosphorus pentoxide (25 g.) and phosphoric acid (15 c.c.) at 200°/8–10 mm. A small amount of cyclized product distilled over, but the major portion was recovered by ether extraction of the phosphoric acid mixture after dilution with water. The combined product (4·23 g.), m.p. 76–78°, was treated with a saturated solution of picric acid (5 g.) and the picrate was decomposed with 1% ammonia, and the thionaphthene was recovered by extraction with ether. Evaporation of the solvent, gave the purified thionaphthene (3·2 g.; yield 82%), m.p. 81–82°, raised to 83° by recrystallization from aqueous alcohol, when it gave pale straw-coloured needles (Found: C, 65·7; H, 3·3. $C_{12}H_7ClS$ requires C, 65·8; H, 3·2%). The *picrate* gave orange-yellow needles from alcohol, m.p. 160° (Found: N, 9·4. $C_{18}H_{10}ClN_3O_7S$ requires N, 9·4%).

6:7-*Benzothionaphthene* (*II*).—The above chlorobenzothionaphthene (0·65 g.), magnesium turnings (1·3 g.), a drop of methyl iodide and absolute methyl alcohol (50 c.c.) were refluxed for ten hours, when most of magnesium reacted. After distillation of alcohol, the residue was acidified with 5% hydrochloric acid (200 c.c.) and the mixture extracted three times with ether (30 c.c. each time). The combined ether extract after drying (sodium sulphate) and removal of solvent gave an oil (0·52 g.) which on fractional distillation in a bulb-tube gave 6:7-benzothionaphthene (II), light straw-coloured liquid (0·24 g.), b.p. 140–45° (bath temp.)/10 mm. and unreacted (V), pale yellow solid (0·25 g.), m.p. 75–77°, b.p. 155–60° (bath temp.)/10 mm. The yield of (II) taking into account the recovered (V) is 71%. Redistillation

of crude (II) gave light straw-coloured liquid, b.p. 140–42° (bath temp.)/10 mm. (Found: C, 78·8; H, 4·7. $C_{12}H_8S$ requires C, 78·3; H, 4·3%). The *picrate* gave orange-red needles from alcohol, m.p. 140·5–41·5° (Found: C, 51·8; H, 2·7; N, 10·8. $C_{18}H_{11}N_3O_7S$ requires C, 52·3; H, 2·7; N, 10·2%).

Sodium 2-chloronaphthalene-1-sulphonate.—An aqueous solution of sodium salt of Tobias acid (43·5 g. in 150 c.c.) was decolourized (Norit), acidified with acetic acid (30 c.c.) and 50% sulphuric acid (100 c.c.), the mixture cooled to 5° and an aqueous solution of sodium nitrite (15 g. in 25 c.c.) was gradually added under stirring. The mixture was diazotized for one hour below 10° and the insoluble diazo salt was filtered, washed with a little ice-cold water and gradually added to a solution of freshly prepared cuprous chloride (from 40 g. copper sulphate) in hydrochloric acid (100 c.c.), keeping the temperature below 15°. After working for one hour, the mixture was warmed to 55° and filtered. The filtrate was made alkaline to precipitate copper salts, and the mixture filtered through a bed of supercel filter-aid. The filtrate was concentrated to half the bulk, cooled, and the crude sodium 2-chloronaphthalene-1-sulphonate collected and dried in vacuum at 60° (yield 40 g., the crude salt contains some sodium chloride). Evaporation of the mother liquor gave a further crop of the impure product.

2-*Chloro*-1-*thionaphthol.*—The thiol was prepared as in the case of 8-chloro-1-thionaphthol starting from crude sodium 2-chloronaphthalene-1-sulphonate (20 g.), phosphorus pentachloride (21·5 g.) and chlorobenzene (36 g.). The crude thiol (8 g., yield 54% on the basis of the Tobias salt) was crystallized three times from aqueous alcohol, when it gave pale yellow crystals, m.p. 65·5°. Dosser and Richter[11] give m.p. 66·5° (Found: C, 61·2; H, 3·7. $C_{10}H_7ClS$ requires C, 61·7, H, 3·6%). Oxidation of the thiol with alcoholic ferric chloride, gave the disulphide which crystallized from *n*-hexane in pale yellow diamond-shaped crystals, m.p. 138°. Dosser and Richter[11] give m.p. 134° (Found: C, 61·4; H, 2·9. $C_{20}H_{12}Cl_2S_2$ requires C, 62·0; H, 3·1%). Condensation of the thiol with chloroacetic acid in alkaline solution gave the corresponding thioglycolic acid, which crystallized from water in colourless needles, m.p. 98·5°. Harley-Mason and Mann[12] give, m.p. 95–97° (Found: C, 57·0; H, 3·5. $C_{12}H_9ClO_2S$ requires C, 57·0; H, 3·6%).

2-*Chloro*-1-*naphthyl ω-dimethoxyethyl sulphide* (*VI*).—2-Chloro-1-thionaphthol (9 g.) was condensed with bromoacetal (9 g.) as in the preparation of (IV). The crude sulphide (9·35 g., yield 71·5%) after four distillations gave a colourless oil, b.p. 163–68° (bath temp.)/5–6 mm. (Found: C, 60·1; H, 6·1. $C_{14}H_{15}ClO_2S$ requires C, 59·5; H, 5·3%). 2:4-*Dinitrophenyl*-

hydrazone crystallized in yellow needles from *n*-hexyl alcohol, m.p. 165° (Found: N, 13·5. $C_{18}H_{13}ClN_4O_4S$ requires N, 13·4%).

9-*Chloronaphtho*-(1′: 8′-*bc*)-*thiapyran* (*VII*).—The sulphide (VI) (5 g.) was cyclized with a mixture of phosphorus pentoxide (25 g.) and phosphoric acid (15 c.c.) as in the preparation of (V). The crude thiapyran (0·43 g., yield 11%) was crystallized from *n*-hexane, then distilled at 190–200° (bath temp.)/11 mm. and finally purified by crystallization from *n*-hexane, when it gave stout yellow needles, m.p. 121° (Found: C, 65·4; H, 3·5. $C_{12}H_7ClS$ requires C, 65·8; H, 3·2%). The *picrate* crystallized from alcohol in greenish black needles, m.p. 169°.

Summary

8-Chloro-1-thionaphthol, prepared from *peri*-acid, was condensed with bromoacetaldehyde dimethyl acetal to give 8-chloro-1-naphthyl ω-dimethoxyethyl sulphide (IV). Ring-closure of (IV) gave 3′-chlorobenzo-(1′: 2′, 6: 7)-thionaphthene (V), which on dechlorination gave 6: 7-benzothionaphthene (II). The cyclization product from α-naphthyl ω-dimethoxyethyl sulphide (I) reported in the previous communication being different from (II) is therefore naphtho-(1′: 8′-*bc*)-thiapyran (III).

9-Chloronaphtho-(1′: 8′-*bc*)-thiapyran (VII) was prepared from Tobias acid in a manner similar to (V), but dechlorination of (VII) to (III) could not be carried out due to the low yields of (VII) in the cyclization of 2-chloro-1-naphthyl ω-dimethoxyethyl sulphide (VI).

The literature on the cyclization of certain related α-substituted naphthyl, naphthoxy and thionaphthoxy derivatives is discussed.

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