

THIOPHENES AND THIAPYRANS

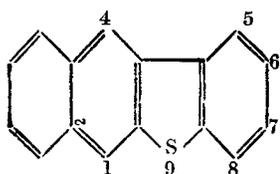
Part X. 1: 2-Benzo-9-thiafluorene and 3:4-Benzo-9-thiafluorene

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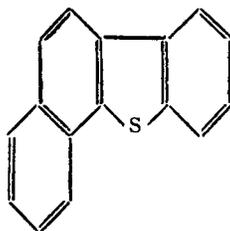
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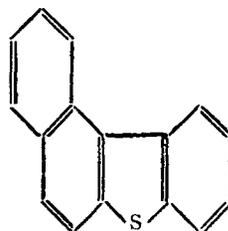
AMONG the three possible benzo-9-thiafluorenes, only the linear isomer 2:3-benzo-9-thiafluorene (I) is known.¹ The other two isomers 1:2-benzo-9-thiafluorene (II) and 3:4-benzo-9-thiafluorene (III) which are angular, have now been synthesized in connection with the study of sulphur isosters of carcinogenic hydrocarbons.² Compound (III) is a thiophene analogue of the carcinogenic hydrocarbon, 3:4-benzphenanthrene. An unsuccessful attempt to synthesize (III) by a modified Pschorr synthesis from phenyl 1-amino-2-naphthyl sulphide has been recently reported.³ The thiophene derivatives (II) and (III) were prepared by the new dibenzothiophene synthesis described earlier.⁴



(I)



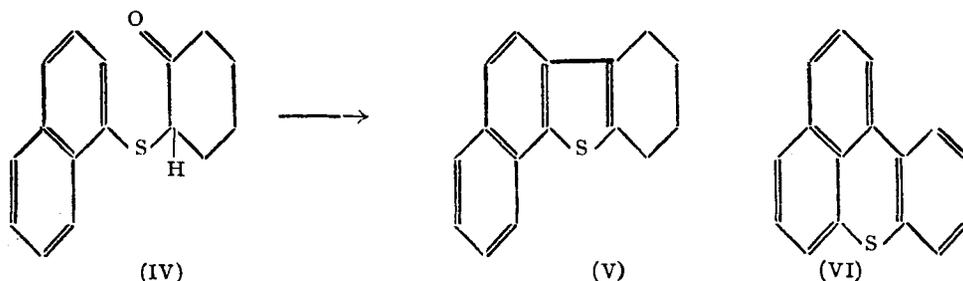
(II)



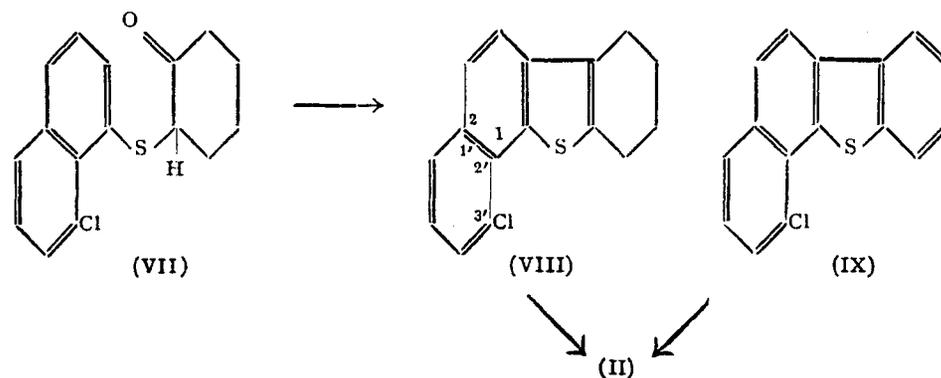
(III)

Condensation of α -thionaphthol with 2-bromocyclohexanone gave 2-(α -naphthylmercapto)cyclohexanone (IV) which on cyclization with phosphorus pentoxide gave (A). It was observed that some (A) was also formed during the purification of (IV) by distillation. Dehydrogenation of (A) by selenium gave the compound (B) which may be represented by the two alternative structures (II) or (VI). The former will be formed if the cyclization of (IV) took place in the β -position in naphthalene and the latter if the cyclization took place in the *peri* position. In view of the isosterism between an aromatic double bond and a divalent sulphur atom,⁵ the compound (II) is an isoster of chrysene. The similarity between the absorption spectra of (B) and chrysene⁶ indicates that (B) is constituted as (II) and the cyclization product (A) is 1:2-benzo-5:6:7:8-tetrahydro-9-thiafluorene (V).

The identity of (B) with (II) has been proved by the unambiguous synthesis of the latter compound by starting from 8-chloro-1-thionaphthol. Condensation of the latter with 2-bromocyclohexanone gave 2-(8'-chloro-1'-naphthylmercapto)cyclohexanone (VII). Cyclization of the latter can only

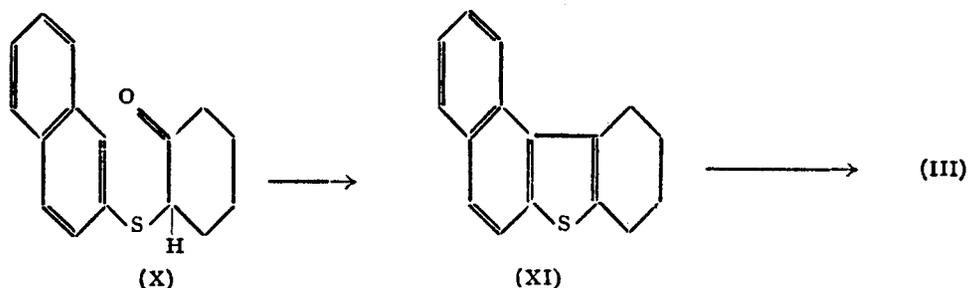


take place in the β -position in the naphthalene nucleus, as the *peri* position is blocked by the chlorine atom. Treatment of (VII) with phosphorus pentoxide, therefore, gave 1:2-(3'-chloro-2':1'-benzo)-5:6:7:8-tetrahydro-9-thiafluorene (VIII). As in the case of (IV), distillation of (VII) also resulted in its cyclization, but in this case the ring-closure was complete as the distilled product did not give a 2:4-dinitrophenylhydrazone. Treatment of (VIII) with selenium⁸ gave 1:2-benzo-9-thiafluorene (II) by simultaneous dehydrogenation and dechlorination.⁷ Although the product obtained in this manner proved to be identical with (B), the removal of chlorine during the dehydrogenation which was carried out at 300–20°, left a doubt as regards the constitution of the dehydrogenation product obtained from (VIII). Due to the possibility of structural changes which may accompany dehydrogenation with selenium, it was necessary to dehydrogenate (VIII) in such a way as to retain the chlorine atom in the molecule. This was achieved by effecting the dehydrogenation with N-bromosuccinimide when 1:2-(3'-chloro-2':1'-benzo)-9-thiafluorene (IX) was obtained.⁷ Dechlorination of the latter by cuprous acetate in pyridine⁹ gave a product which is



unambiguously constituted as 1:2-benzo-9-thiafluorene (II). This proved to be identical with the product (B) obtained by starting from α -thionaphthol. The constitution of (B) is thus conclusively proved.

β -Thionaphthol on condensation with 2-bromocyclohexanone gave 2-(β -naphthylmercapto)cyclohexanone (X) which could not be isolated as it underwent cyclization during distillation in vacuum. Ring-closure of (X) with phosphorus pentoxide gave a product (C) which was identical with that obtained by the distillation of (X) in vacuum. The cyclization of (X) may take place either in the reactive 1-position or the 3-position in the naphthalene nucleus leading to 3:4-benzo-5:6:7:8-tetrahydro-9-thiafluorene (XI) or to 2:3-benzo-5:6:7:8-tetrahydro-9-thiafluorene respectively. Dehydrogenation of the latter compound will lead to (I), whereas (XI) will give (III). The compound actually obtained by dehydrogenation of (C) was different from (I) and is therefore constituted as 3:4-benzo-9-thiafluorene (III). The cyclization product (C) is thus constituted as (XI).



The structures assigned for the benzo-9-thiafluorenes (II) and (III) have been confirmed by Raney nickel desulphurization which led to β -phenylnaphthalene and α -phenylnaphthalene respectively.¹⁰

Although (III) is isosteric with 3:4-benzphenanthrene, the absorption spectrum of (III) showed greater similarity to chrysene than to 3:4-benzphenanthrene.⁶ The similarity of the absorption spectrum of (III) with chrysene rather than 3:4-benzphenanthrene is a matter for further investigation.

EXPERIMENTAL

2-(α -Naphthylmercapto)cyclohexanone (IV)

A mixture of α -thionaphthol (9.2 g.) sodium (1.4 g.), absolute alcohol (50 c.c.) and 2-bromocyclohexanone (11 g.) was refluxed for 6 hours. The condensation product, on isolation by means of ether, gave a brown oil (16.1 g.), most of which distilled at 150–80° (bath temp.)/10 mm. (12.8 g., yield 87%). In further redistillations it was observed that a part of the

product cyclized in each redistillation. The cyclized product distilled at a lower temperature and was separated as an earlier fraction, which gave a picrate but no 2:4-dinitrophenylhydrazone. The higher boiling fraction, which consisted of the condensation product (I) and gave a 2:4-dinitrophenylhydrazone, was a colourless oil, b.p. 215–20°/bath temp./10 mm. (Found: C, 74.3; H, 6.3. $C_{16}H_{16}OS$ requires C, 75.0; H, 6.3%). The 2:4-dinitrophenylhydrazone gave orange needles from alcohol-ethyl acetate, m.p. 186–87° (Found: N, 12.5. $C_{22}H_{20}N_4O_4S$ requires N, 12.8%).

1:2-Benzo-5:6:7:8-tetrahydro-9-thiafluorene (V)

A mixture of (IV) (4.1 g.) and phosphorus pentoxide (12 g.) was heated at 170–80° for 45 minutes. The reaction mixture was poured into ice water and the oil which separated was isolated by means of ether. The dark coloured oil (3.33 g., yield 88%) on distillation gave a colourless liquid, b.p. 160–80° (bath temp.)/10 mm. (2.7 g., yield 70%), which solidified on cooling. Crystallization from alcohol gave cream coloured needles, m.p. 97–98°. The thiafluorene was finally purified through the picrate and crystallized twice from alcohol when it gave needles, m.p. 97–98° (Found: C, 81.1; H, 6.1. $C_{16}H_{14}S$ requires C, 80.7; H, 5.9%). The picrate gave orange needles from alcohol, m.p. 137–38° (Found: N, 8.3. $C_{22}H_{17}N_3O_7S$ requires N, 9.0%).

1:2-Benzo-9-thiafluorene (II)

A mixture of (V) (2.8 g.) and selenium powder (2.16 g.) was heated at 300° for 22 hours. After cooling, the reaction product was extracted with benzene. The brown product (2.46 g., yield 90%) obtained after removal of benzene was twice crystallized from *n*-hexane-benzene when (II) separated as colourless broken plates, m.p. 184–85° (Found: C, 81.9; H, 4.6. $C_{16}H_{10}S$ requires C, 82.1; H, 4.3%). The *sym*-trinitrobenzene derivative gave yellow needles, from benzene, m.p. 176–77° (Found: N, 9.2. $C_{22}H_{13}N_3O_6S$ requires N, 9.4%).

2-(8'-Chloro-1'-naphthylmercapto)cyclohexanone (VII)

8-Chloro-1-thionaphthol (10 g.) was dissolved in 30% aqueous sodium hydroxide (6.85 c.c.), cooled in ice-water and 2-bromocyclohexanone (10 g.) was gradually added under vigorous stirring over 10 minutes. The mixture was stirred for one hour and the product isolated by means of ether. Removal of ether gave a dark thick oil (14.8 g., yield 99%), which on distillation gave a yellow liquid, b.p. 180–200° (bath temp.)/1 mm., which solidified on standing. The distillate gave no dinitrophenylhydrazone, but only a picrate showing complete cyclization of the condensed compound.

The 2:4-dinitrophenylhydrazone prepared from the crude condensation product (VII) could not be purified.

1:2-(3-Chloro-2':1'-benzo)-5:6:7:8-tetrahydro-9-thiafluorene (VIII)

A mixture of the crude condensation product (VII) (6.3 g.) and phosphorus pentoxide (18 g.) was heated at 160–70° for 45 minutes. The reaction product, isolated in the usual manner, was a dark coloured oil (4.4 g., yield 74%), which soon partly solidified. Distillation of the oil gave a colourless liquid, b.p. 180–200° (bath temp.)/2.5 mm., which solidified on standing. Crystallization of the reaction product (3.92 g., 66%), m.p. 93–95° from alcohol-*n*-hexane gave colourless needles, m.p. 95–95.5° of (VIII) (Found: C, 70.6; H, 5.0. C₁₆H₁₃ClS requires C, 70.4; H, 4.8%). The m.p. of (VIII) was not depressed by admixture with the product obtained by the vacuum distillation of (VII). The *sym*-trinitrobenzene derivative gave yellow needles from benzene, m.p. 154–55° (Found: N, 8.5. C₂₂H₁₆ClN₃O₆S requires N, 8.7%).

The dehydrogenation of (VIII) with selenium and N-bromosuccinimide, which has been described in the previous communication, gave (II) and (IX) respectively.⁷

Synthesis of 1:2-benzo-9-thiafluorene (II) by the dechlorination of (IX)

A mixture of (IX) (100 mg.), freshly prepared cuprous oxide (54 mg.), acetic anhydride (40 mg.) and pyridine (200 mg.) were heated at 180–200° for 15 hours. The reaction mixture after cooling was added to dilute ammonia and extracted with benzene. The benzene extract was successively washed with dilute hydrochloric acid, dilute sodium hydroxide and water and dried. Removal of benzene gave a yellow brown product (96 mg.), which on sublimation at 160–80°/0.8 mm. gave pale yellow plates (60 mg., yield 69%), m.p. 170°; raised to 184–85° by recrystallization from *n*-hexane. The m.p. of the purified product which was chlorine-free, was not depressed when mixed with (II), m.p. 184–85°, obtained earlier starting from α -thionaphthol.

2-(β -Naphthylmercapto)cyclohexanone (X)

2-Bromocyclohexanone (10.6 g.) was gradually added to an ice-cooled (20°) solution of β -thionaphthol (9.4 g.) in 35% aqueous sodium hydroxide (6.75 c.c.) during 10 minutes under vigorous stirring. After stirring for 1½ hours the mixture was diluted with water and ether extracted. The ether extract after washing successively with alkali and water was dried. Removal of ether gave (IX) as a dark coloured liquid (14.15 g., yield 93%), which

could not be purified as it underwent cyclization during distillation. Thus whereas the crude product gave a 2:4-dinitrophenylhydrazone, the distilled product gave a picrate but not the hydrazone derivative. The 2:4-dinitrophenylhydrazone from the crude (X) could not be purified by crystallization.

3:4-Benzo-5:6:7:8-tetrahydro-9-thiafluorene (XI)

A mixture of crude (X) (2.85 g.) and phosphorus pentoxide (9 g.) was heated at 170–80° for 30 minutes. Dilution of the reaction mixture with water and ether extraction gave an oil (2.675 g.) which was distilled. The fraction distilling between 190–220° (bath temp.)/5 mm. (1.0 g., yield 38%) solidified on standing and gave colourless needles, m.p. 81.5–82°, of (XI), after crystallization from alcohol (Found: C, 80.3; H, 5.8. $C_{16}H_{14}S$ requires C, 80.7; H, 5.9%).

The cyclization of (X) (1 g.) was also effected by treatment with phosphorus pentoxide (3 g.) in boiling benzene (20 c.c.) for 1 hour. Removal of benzene gave a straw coloured oil (0.764 g., yield 82%), which on dissolution in hot alcohol-*n*-hexane and cooling gave lustrous needles, m.p. 81–82°.

In another experiment crude (X) (3 g.) was distilled and the fraction distilling between 190–230° (bath temp.)/5 mm. (1.2 g., yield 47%) was collected. It solidified on standing and gave, on crystallization from alcohol, a product which was identical with (XI).

The *picrate* from (XI) gave orange needles from alcohol, m.p. 139° (Found: N, 9.2. $C_{22}H_{17}N_3O_7S$ requires N, 9.0%).

3:4-Benzo-9-thiafluorene (III)

A mixture of (XI) (1 g.) and selenium (0.75 g.) was heated at 300–20° for 14 hours. The brown product (0.98 g., yield quantitative) obtained by extraction with benzene crystallized from alcohol in elongated colourless needles, m.p. 102–102.5° (Found: C, 81.7; H, 4.6. $C_{16}H_{10}S$ requires C, 82.1; H, 4.3%). The *picrate* gave orange needles from alcohol, m.p. 147–48° (Found: N, 9.0. $C_{22}H_{13}N_3O_7S$ requires N, 9.4%).

The dehydrogenation of (XI) was also effected under milder conditions using *N*-bromosuccinimide. A mixture of (XI) (250 mg.) *N*-bromosuccinimide (375 g.), benzoyl peroxide (10 mg.) and carbon tetrachloride (15 c.c.) was refluxed for 30 minutes. Potassium acetate (3 g.) and glacial acetic acid (1 c.c.) were added and boiling continued for 30 minutes more. After dilution in aqueous alkali, the mixture was extracted with ether. Removal of the solvents gave a dark coloured oil which fumed in air due to evolution

of hydrogen bromide. The product was sublimed at 150°/1 mm. when it gave a crystalline product (160 mg., yield 65%) which, on crystallization from *n*-hexane, gave colourless needles, m.p. 100°, undepressed when mixed with (III) described above.

SUMMARY

The hitherto unknown angular benzo-9-thiafluorenes, 1:2-benzo-9-thiafluorene (II) and 3:4-benzo-9-thiafluorene (III) have been synthesized. The former was prepared starting from α -thionaphthol and 2-bromocyclohexanone. Condensation of these compounds gave 2-(α -naphthylmercapto)cyclohexanone (IV) which on cyclization and dehydrogenation gave (II). The constitution of (II) was proved by its unambiguous synthesis starting from 8-chloro-1-thionaphthol and 2-bromocyclohexanone. Starting from β -thionaphthol, (III) was prepared by similar steps. The constitution of (III) followed from its non-identity with 2:3-benzo-9-thiafluorene.

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