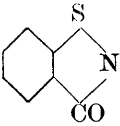
CCCCXII.—*The Formation of Thionaphthindoles. Part II.*

By ERNEST WILSON MCCLELLAND and JOHN LEONARD D'SILVA.

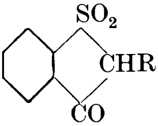
THE products from the condensation of 2-keto-1 : 2-dihydrobenz*iso*thiazole (I) with potassium acetate in the presence of acetic anhydride (Part I; J., 1929, 1588) have been further investigated. The unstable oil (B) (*loc. cit.*) which, with phenylhydrazine, gave thionaphthindole, and formed a semicarbazone with the requisite nitrogen for the semicarbazone of 2-thiolacetophenone, was not definitely identified. It is now shown that this material (B) is converted to 3-oxy-1-thionaphthen by bases such as aniline and methylamine and also by sodium hydroxide solution, in which it is sparingly soluble. It is oxidised by potassium ferricyanide to thioindigotin and by hydrogen peroxide to 3-oxy-1-thionaphthen 1-dioxide (II; R = H) (Lanfry, *Compt. rend.*, 1912, **154**, 1517). 2 : 2′-Dithioacetophenone could not be obtained from it by oxidation.

These properties suggested that the substance was a derivative of 3-oxy-1-thionaphthen and not 2-thiolacetophenone, or a derivative thereof. This conclusion was confirmed when, by heating the material with aniline, 3-oxy-1-thionaphthen and acetanilide were obtained, indicating that the substance was an acetyl oxythionaphthen. Comparison with 3-acetoxy-1-thionaphthen, prepared by heating *o*-carboxyphenylthiolacetic acid (IV; R = H) with acetic anhydride (compare *Annalen*, 1907, **351**, 406), showed identical behaviour in the reactions enumerated. Further, the semicarbazones derived from (B) and from 3-acetoxy-1-thionaphthen were identical with the semicarbazone of 3-oxy-1-thionaphthen (Auwers and Thies, *Ber.*, 1920, **53**, 2292).

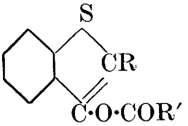
In some experiments, indications of the presence of traces of another material were obtained, but it is concluded that the oil (B) is mainly 3-acetoxy-1-thionaphthen (III; R = H; R′ = CH_3) and that it is this substance which gives rise to thionaphthindole, as described in Part I, p. 1591. It is evident that the formation of thionaphthindole from 3-acetoxy-1-thionaphthen is preceded by deacetylation by the phenylhydrazine. The 3-oxy-1-thionaphthen thus formed then reacts with the phenylhydrazine to give a hydrazone which undergoes the indole transformation.



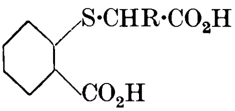
(I.)



(II.)



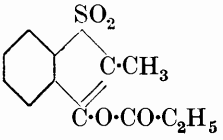
(III.)



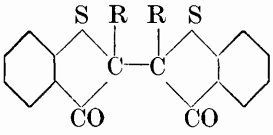
(IV.)

To confirm these results, the interaction of 2-keto-1 : 2-dihydrobenz*iso*thiazole (I) with sodium propionate and propionic anhydride was next investigated. The chief product of the reaction is the methyl oxythionaphthen derivative (III; $R = CH_3$, $R' = C_2H_5$). The formation of this substance, a homologue of 3-acetoxy-1-thionaphthen, is in agreement with the conclusions as to the nature of the oil (B). The structure assigned to this derivative of methyloxythionaphthen was confirmed by synthesis. This was effected by heating α-*o*-carboxyphenylthiolpropionic acid (IV; $R = CH_3$) (Auwers, *Annalen*, 1912, **393**, 376) with propionic anhydride; ring closure and propionylation then took place with the formation of an identical product.

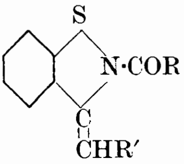
The presence of a methyl group in the 2-position appears to increase the stability of an oxythionaphthen. For instance, oxidation of 3-acetoxy-1-thionaphthen (III; $R = H$, $R' = CH_3$) is accompanied by loss of the acetyl group, as in most of its reactions, whereas oxidation of 3-*propionoxy*-2-*methyl*-1-*thionaphthen* (III: $R = CH_3$, $R' = C_2H_5$) yields the *sulphone* (V), from which the *substance* (II; $R = CH_3$) is obtained by hydrolysis.



(V.)



(VI.)



(VII.)

Hydrolysis of 3-propionoxy-2-methyl-1-thionaphthen yields an oil, evidently 3-oxy-2-methyl-1-thionaphthen, since the product is readily oxidised to the *bis-compound* (VI; $R = CH_3$). Unlike the analogous phenyl derivative (VI; $R = Ph$), this substance does not dissociate (Kalb and Bayer, *Ber.*, 1913, **46**, 3879). Further oxidation of the bis-compound (VI; $R = CH_3$) by hydrogen peroxide yields a *disulphone* (VI; $R = CH_3$, $S = SO_2$) in contrast to thioindigotin, which gives resinous products (Lanfry, *loc. cit.*).

During the formation of 3-propionoxy-2-methyl-1-thionaphthen (III; $R = CH_3$, $R' = C_2H_5$), another *substance* is produced in small quantity. This material ($C_{12}H_{13}ONS$) is probably a homologue of the compound, previously obtained (*loc. cit.*), to which the structure (VII; $R = CH_3$, $R' = H$) was assigned. On theoretical grounds it seems probable that substances of the type (VII) may undergo intramolecular rearrangement, and they are being further investigated.

EXPERIMENTAL.

The oil (B) used in the following experiments was prepared as described in Part I (J., 1929, 1591).

(a) The oil (2·3 g.) was heated with 2*N*-sodium hydroxide (30 c.c.) until dissolved. The alkaline mixture, after extraction with ether, was acidified, and distilled in steam, and 3-oxy-1-thionaphthen separated from the distillate.

3-Oxy-1-thionaphthen was also obtained when an alcoholic solution of the oil (B) was treated with methylamine.

(b) The oil (1·6 g.) and aniline (1·2 g.) were heated together at 100° for 1 hour. The cooled product was treated with dilute aqueous sodium hydroxide, and the mixture extracted with ether. From the ethereal solution, after being washed successively with sodium hydroxide and hydrochloric acid, acetanilide was obtained. The alkaline solution gave 3-oxy-1-thionaphthen on acidification.

(c) The oil (1 g.) in acetic acid (8 c.c.) and hydrogen peroxide (2 c.c.; 90/100 vol.) was set aside for several days. The solution was then filtered and diluted with water. The precipitate, after purification, had m. p. 135°, alone or mixed with authentic 3-oxy-1-thionaphthen 1-dioxide (Lanfry, *loc. cit.*).

3-*Propionoxy*-2-*methyl*-1-*thionaphthen* (III; $R = CH_3$, $R' = C_2H_5$).—(a) *From* 2-*keto*-1 : 2-*dihydrobenz*iso*thiazole* (I). The *iso*thiazole (5 g.) was heated with propionic anhydride (30 c.c.) and sodium propionate (8 g.) under reflux at 145—150° for 15 minutes. The excess of propionic anhydride was hydrolysed by heating the mixture with water at 100°, the product distilled in steam, the distillate extracted with ether, and the ethereal solution washed successively with dilute aqueous sodium hydroxide and water, dried over anhydrous sodium sulphate, and evaporated. 3-*Propionoxy*-2-*methyl*-1-*thionaphthen* thus obtained crystallised from aqueous alcohol in colourless plates, m. p. 75° (Found : C, 65·2; H, 5·7; S, 14·4. $C_{12}H_{12}O_2S$ requires C, 65·4; H, 5·5; S, 14·5%).

The mother-liquor from the above steam distillation was boiled with charcoal and filtered. The *product*, which crystallised on cooling, was purified from water, forming colourless needles, m. p. 152—153° (Found : C, 65·8; H, 6·2; S, 14·3. $C_{12}H_{13}ONS$ requires C, 65·7; H, 6·0; S, 14·6%).

(b) *From* α-o-*carboxyphenylthiolpropionic acid* (IV; $R = CH_3$). The acid (5 g.) was refluxed with propionic anhydride (10 g.) for ½ hour. The mixture was diluted with water, heated on the water-bath for a short time, and distilled in steam. The distillate was extracted with ether, and the extract washed with alkali and water and dried. The material obtained on evaporation of the ether had, after crystallisation from aqueous alcohol, m. p. 75—76°, alone or mixed with 3-propionoxy-2-methyl-1-thionaphthen obtained in the previous experiment.

3-*Propionoxy*-2-*methyl*-1-*thionaphthen* 1-*Dioxide* (V).—A solution of 3-propionoxy-2-methyl-1-thionaphthen (1 g.) in acetic acid (7 c.c.) and hydrogen peroxide (3 c.c.; 90/100 vol.) was heated for 1 hour at 100°. The material (0·7 g.) which separated on addition of water crystallised from aqueous acetic acid in colourless needles, m. p. 109—110° (Found: C, 56·7; H, 4·7; S, 12·6. $C_{12}H_{12}O_4S$ requires C, 57·1; H, 4·8; S, 12·7%). 3-*Propionoxy*-2-*methyl*-1-*thionaphthen* 1-*dioxide* is insoluble in cold aqueous sodium hydroxide (2*N*).

3-*Oxy*-2-*methyl*-1-*thionaphthen* 1-*Dioxide* (II; R = CH_3).—The preceding dioxide (1 g.) was refluxed with alcoholic sulphuric acid (20 c.c.; 10%) for 2 hours. The product was diluted with water (20 c.c.), and the alcohol removed on the water-bath. On cooling, a material separated, which crystallised from water (charcoal) in colourless needles, m. p. 110—111°. A mixed melting point with 3-propionoxy-2-methyl-1-thionaphthen gave a large depression (Found: C, 55·3; H, 4·3; S, 16·2. $C_9H_8O_3S$ requires C, 55·1; H, 4·1; S, 16·3%). 3-*Oxy*-2-*methyl*-1-*thionaphthen* 1-*dioxide* is soluble in cold aqueous sodium hydroxide (2*N*).

2 : 2′-*Bis*-(3-*oxy*-2-*methyl*-1-*thionaphthen*) (VI; R = CH_3).—3-Propionoxy-2-methyl-1-thionaphthen (1 g.) was refluxed with alcoholic sodium hydroxide (20 c.c.; 10%) for 1 hour. On cooling, a solid separated; sufficient water was added to redissolve this material. Potassium ferricyanide (1·6 g.) in water (10 c.c.) was gradually added, and the mixture heated on the water-bath for ¼ hour. The *product* which separated, after being washed with water and dried, crystallised from alcohol in pale yellow needles, m. p. 151—153° (Found: C, 65·7; H, 4·5; *M*, ebullioscopic in benzene, 323. $C_{18}H_{14}O_2S_2$ requires C, 66·2; H, 4·3%; *M*, 326).

2 : 2′-*Bis*-(3-*oxy*-2-*methyl*-1-*thionaphthen* 1-*dioxide*) (VI; R = CH_3; S = SO_2).—A solution of the preceding compound (1 g.) in acetic acid (7 c.c.) and hydrogen peroxide (5 c.c.; 90/100 vol.) was heated at 100° for 1½ hours. The solution was diluted with water, the precipitate collected and dried, and the process repeated. The *product* separated from acetic acid in very small, colourless plates, m. p. above 300° (Found: C, 55·2; H, 3·6; S, 16·0. $C_{18}H_{14}O_6S_2$ requires C, 55·3; H, 3·6; S, 16·4%).

We wish to thank the Department of Scientific and Industrial Research for a grant to one of us (J. L. D'S.) whilst this work was in progress.

KING'S COLLEGE, LONDON. [*Received, September 12th*, 1931.]