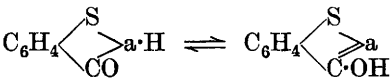
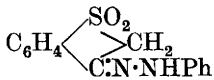
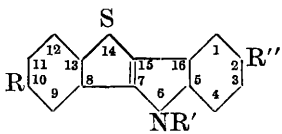
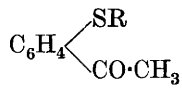
30. *The Formation of Thionaphthindoles. Part III. The Synthesis of Thionaphthindoles from 3-Oxy-1-thionaphthens.*

By Ernest Wilson McClelland and John Leonard D'Silva.

It has been pointed out (Part I; J., 1929, 1589) that oxidation of the sulphur to the sulphone condition in a cyclic system of the type (I) appears to restrain the tendency to enolisation (compare Cohen and Smiles, J., 1930, 408; Levi and Smiles, J., 1931, 523). Aldehydes and ketones readily convertible into enols yield hydrazones which readily undergo the indole transformation (Robinson and Robinson, J., 1918, **113**, 639). Hence the hydrazone of 3-oxy-1-thionaphthen (I; a = CH), in contrast to the hydrazone (II) derived from the corresponding dioxide, might be expected to undergo the indole transformation readily. When 3-oxy-1-thionaphthen is treated with phenylhydrazine in presence of acetic acid, thionaphthindole (III; R, R′, R″ = H) is obtained, whilst the dioxide gives a hydrazone (II) under similar conditions. The hydrazone of the dioxide is recovered unchanged even after prolonged boiling in acetic acid.

(I.)  (II.) 

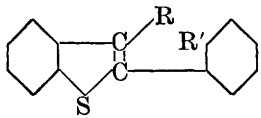
(III.)   (IV.)

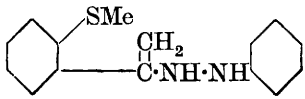
The formation of thionaphthindoles from 3-oxy-1-thionaphthens appears to be of a fairly general nature. Thus *as.*-methylphenylhydrazine, *p*-bromophenylhydrazine, and *p*-tolylhydrazine condense with 3-oxy-1-thionaphthen to give 6-*methylthionaphthindole* (III; R′ = CH_3; R, R″ = H), 2-*bromothionaphthindole* (III; R, R′ = H; R″ = Br), and 2-*methylthionaphthindole* (III; R, R′ = H; R″ = CH_3), respectively, and 5-methyl-3-oxy-1-thionaphthen reacts with phenylhydrazine, giving 10-*methylthionaphthindole* (III; R = CH_3; R′, R″ = H). Methods are thus available for the synthesis of thionaphthindoles substituted in either benzene nucleus. When 3-acetoxy-1-thionaphthen was substituted for 3-oxy-1-thionaphthen in several of these condensations the resulting products were identical, the acetyl group having been eliminated by the phenylhydrazine as previously pointed out (Part II; J., 1931, 2972).

These results suggest that the first stage in the formation of thionaphthindole from 2-thiolacetophenone (IV; R = H) (Part I, *loc. cit.*) is oxidation of the latter to 3-oxy-1-thionaphthen, the hydrazone of which then undergoes the transformation. When oxidation of 2-thiolacetophenone to a cyclic system is prevented by substitution, the normal hydrazone is obtained. Thus 2-*methylthiolacetophenone* (IV, R = CH_3) condenses with phenylhydrazine in acetic acid to give a normal *hydrazone*, which even prolonged heating in acetic acid fails to convert into an indole.

The 2-methylthiolacetophenone required for this investigation was synthesised as follows. 2-Methylthiolbenzoyl chloride was condensed with sodioacetoacetic ester, and the product heated with alcoholic sulphuric acid. The ketone obtained in this way contained an impurity which could not be eliminated by distillation. When the impure material was heated with alkali, 2-methylthiolbenzoic acid was formed in small quantity and the ketone was then easily purified.

According to Robinson's theory of the Fischer indole synthesis (Robinson and Robinson, *loc. cit.*; J., 1924, **125**, 827) the conditions in 3-oxy-1-thionaphthen are particularly favourable to the indole transformation, for its enolic character favours the conversion of its hydrazone into the corresponding hydrazine and the aromatic nature of the thiophen nucleus and the tendency of 3-oxy-1-thionaphthens to form bis-compounds (compare Part II; J., 1931, 2973; Auwers and Thies, *Ber.*, 1920, **53**, 2290) favour the *o*-benzidine rearrangement to the compound (V; R, R′ = NH_2). The tendency of an amino-group in the 3-position in a thionaphthen to be eliminated as ammonia (Friedlaender, *Annalen*, 1907, **351**, 420; Fries and Hemmecke, *ibid.*, 1929, **470**; 7) favours ring closure in this compound. An analogous ring closure with the production of thionaphthindole takes place when the nitrophenyloxythionaphthen (V; R = OH, R′ = NO_2) is reduced (Part I, *loc. cit.*).

(V.) 



(VI.)

When the sulphur of the thionaphthen nucleus is in the sulphone condition as in 3-*oxy*-1-*thionaphthen*-1-*dioxide phenylhydrazone* (II), the enolic tendencies are depressed and consequently the formation of the corresponding hydrazine is not favoured. Further, the absence of free valency electrons in the sulphone condition decreases the aromatic character of the thiophen nucleus, since sextet formation is inhibited (compare *Ann. Reports*, 1928, 120) and the tendency

to the formation of bis-compounds is less marked than in the unoxidised analogues. These two factors will tend to prevent the *o*-benzidine change. The failure of 2-methylthiolacetophenone to give an indole under similar conditions to 3-oxy-1-thionaphthen may be attributed to the lesser tendency of the open-chain compound to enolise or to the fact that the hydrazine (VI), if formed, has not two aromatic nuclei favouring the *o*-benzidine change.

Experimental.

The thionaphthindoles described were prepared by the following general method. The 3-oxy-1-thionaphthen (1 mol.) and the phenylhydrazine (1 mol.) in sufficient acetic acid to keep the reactants in solution were heated at 100° for ½—1 hour. The thionaphthindole crystallised on cooling, and was purified from alcohol (unless otherwise stated). The indoles from 3-oxy-1-thionaphthen were invariably slightly pink owing to the presence of traces of thioindigotin, but were colourless when pure. All the thionaphthindoles described gave a blue coloration with isatin in concentrated sulphuric acid.

Thionaphthindole (III; R, R′, R″ = H), from 3-oxy(or 3-acetoxy)-1-thionaphthen and phenylhydrazine, had m. p. 251—252°, alone or mixed with an authentic specimen.

6-*Methylthionaphthindole* (III; R, R″ = H; R′ = CH_3), from 3-oxy(or 3-acetoxy)-1-thionaphthen and *as*.-methylphenylhydrazine, formed colourless plates, m. p. 172—174° (Found: C, 75·6; H, 4·8. $C_{15}H_{11}NS$ requires C, 75·9; H, 4·7%).

2-*Methylthionaphthindole* (III; R, R′ = H; R″ = CH_3), from 3-oxy-1-thionaphthen and *p*-tolylhydrazine, formed plates, m. p. 257—258° (Found: C, 75·6; H, 5·0; S, 13·4. $C_{15}H_{11}NS$ requires C, 75·9; H, 4·7; S, 13·5%).

10-*Methylthionaphthindole* (III; R′, R″ = H; R = CH_3), from 5-methyl-3-oxy-1-thionaphthen (*Ber*., 1909, **42**, 541) and phenylhydrazine, crystallised from methyl alcohol in colourless plates, m. p. 211° (Found: C, 75·7; H, 5·0. $C_{15}H_{11}NS$ requires C, 75·9; H, 4·7%).

2-*Bromothionaphthindole* (III; R, R′ = H; R″ = Br), from 3-oxy(or 3-acetoxy)-1-thionaphthen and *p*-bromophenylhydrazine, formed plates, m. p. 262—264° (Found: C, 55·2; H, 2·6; Br, 26·8. $C_{14}H_8NBrS$ requires C, 55·6; H, 2·7; Br, 26·5%).

3-*Oxy*-1-*thionaphthen* 1-*Dioxide Phenylhydrazone* (II).—A solution of 3-oxy-1-thionaphthen 1-dioxide (1 mol.) (J., 1931, 2972) in acetic acid and phenylhydrazine (1 mol.) was heated on the water-bath for ½ hour. The *hydrazone*, which separated on cooling, crystallised from alcohol in pale yellow needles, m. p. 245—246°

(decomp.) (Found: C, 62·0; H, 4·7; N, 10·3. $C_{14}H_{12}O_2N_2S$ requires C, 61·7; H, 4·4; N, 10·3%).

2-*Methylthiolacetophenone* (IV; R = CH_3).—A solution of ethyl acetoacetate (10 g.) in dry ether (50 g.) was treated with sodium (1·77 g.) (finely divided by heating under xylene). When the initial reaction had subsided, the mixture was refluxed until all the sodium had reacted. To the suspension of sodioacetoacetic ester, finely powdered 2-methylthiolbenzoyl chloride (McClelland and Warren, J., 1929, 2625) (14·4 g.) in dry ether (28 g.) was added. The mixture was refluxed for 2½ hours, the liquid filtered, and the ether evaporated under reduced pressure. The residual oil was refluxed with alcoholic sulphuric acid (sulphuric acid, 5 g.; alcohol, 50 g.) on the water-bath for 7 hours. The product was diluted with an equal volume of water, and the alcohol removed under reduced pressure. The aqueous solution, after neutralisation with sodium hydroxide, was heated with 2*N*-sodium hydroxide (100 c.c.) on the water-bath for 2 hours and distilled in steam. The distillate was extracted with ether, the ethereal solution washed successively with 2*N*-sodium hydroxide and water, dried over anhydrous sodium sulphate, and evaporated. The 2-*methylthiolacetophenone* thus obtained crystallised from ligroin in colourless needles, m. p. 45—46° (Found: C, 64·7; H, 6·2; S, 19·4; *M*, 184. $C_9H_{10}OS$ requires C, 65·0; H, 6·1; S, 19·3%; *M*, 166).

2-*Methylthiolacetophenonephenylhydrazone*.—A solution of 2-methylthiolacetophenone (2·32 g.) in glacial acetic acid (8 c.c.) and phenylhydrazine (1·26 g.) was heated on the water-bath for 1 hour. The product, which separated on cooling, crystallised from glacial acetic acid (charcoal) in pale yellow needles, m. p. 117—118° (Found: C, 69·8; H, 6·5; N, 10·8; *M*, 251. $C_{15}H_{16}N_2S$ requires C, 70·3; H, 6·3; N, 10·9%; *M*, 256).

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