124. *The Preparation and Properties of Thionaphthindoles.*

By Charles E. Dalgliesh and Frederick G. Mann.

The condensation of various thioindoxyls with phenylhydrazine and substituted phenylhydrazines has been investigated. This condensation gives thionaphthindoles very readily by the Fischer indole reaction. It is now found, however, that the formation of the thionaphthindoles is apparently completely inhibited by 4-substituents in the thioindoxyls and by ortho-substituents in the phenylhydrazines. The significance of these results is discussed.

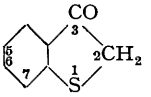
Several thionaphthindoles having additional fused rings have been synthesised: these compounds resemble in general molecular structure certain carcinogenic polycyclic aromatic hydrocarbons, and their therapeutic properties are therefore under investigation.

It has been shown by McClelland and D'Silva (*J.*, 1932, 227) that when thioindoxyl (I) is warmed with phenylhydrazine in acetic acid solution, the intermediate phenylhydrazone very readily undergoes the Fischer indole reaction with the formation of thionaphthindole (II),* the structure

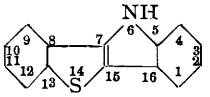
* The numbering of (II) is that used by McClelland and D'Silva (*loc. cit.*) and differs from that adopted in " The Ring Index " (Patterson and Capell, 1940).

of which had been proved by McClelland (*J.*, 1929, 1588). It was found that 5-methylthioindoxyl similarly gave 10-methylthionaphthindole, and that the reaction also proceeded readily when thioindoxyl was treated with certain substituted phenylhydrazines. These authors concluded therefore that the reaction was general. Subsequently 5-chlorothioindoxyl was found to give 10-chlorothionaphthindole (Fowkes and McClelland, *J.*, 1941, 187). No application of this reaction to thioindoxyls other than the above three has been recorded.

We have investigated the nature and scope of this reaction for two reasons. First, Dalgliesh and Mann (*J.*, 1945, 893) have condensed a number of substituted thioindoxyls (as I) with



(I.)



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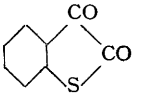
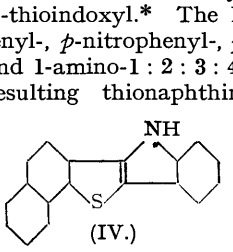


(III.)

similar thionaphthenquinones (as III) to ascertain the factors which determined whether the methylene group of the thioindoxyls condensed with the α(or 2)-carbonyl group of the quinones to form a thioindigo, or with the β(or 3)-carbonyl group to form a thioindirubin. In the majority of the condensations studied, the β-carbonyl group of the thionaphthenquinone reacted, but such a condensation appeared to be inhibited almost invariably by a 4-substituent in thionaphthenquinone. The reasons why these 4-substituted quinones thus gave solely thioindigos by α-carbonyl condensation were discussed, and evidence was adduced that steric hindrance by the 4-substituent was probably the main cause. In McClelland's thionaphthindole synthesis, the intial reaction is necessarily the condensation of the reactive amino-group of the phenylhydrazine with the 3-carbonyl group of the thioindoxyl (as such or in its enol form), and it was of some interest therefore to determine whether this reaction was also markedly affected by the presence of 4-substituents.

Secondly, it is clear that the use of various benzthioindoxyls and of naphthylhydrazines should result in thionaphthindoles containing additional fused rings, and these polycyclic derivatives would bear a structural resemblance to polycyclic hydrocarbons known to possess carcinogenic properties (*vide infra*). The synthesis of such compounds was therefore investigated.

We found that the following thioindoxyls readily gave the corresponding thionaphthindoles: thioindoxyl, and 5-chloro-7-methyl-, 6-ethoxy-, 6 : 7-benz-, 5 : 6-benz-, 5-methyl-, 7-methyl-, and 7-chloro-thioindoxyl.* The hydrazines used for condensation with these thioindoxyls included phenyl-, *p*-nitrophenyl-, *p*-tolyl-, *m*-tolyl-, 1-phenyl-2-methyl-, and 1-phenyl-2-ethyl-hydrazine, and 1-amino-1 : 2 : 3 : 4-tetrahydroquinoline. These reactions proceeded so readily that the resulting thionaphthindoles formed excellent crystalline derivatives for the



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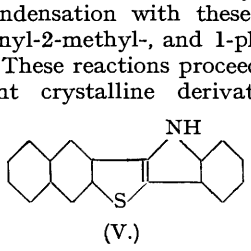


(V.)

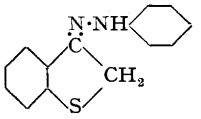
characterisation of the parent thioindoxyls. The use of 6 : 7- and 5 : 6-benzthioindoxyl gave two new ring systems, 11 : 12- (IV) and 10 : 11-*benzthionaphthindole* (V). The new ring systems obtained by the use of the aminoquinoline are described later.

It is noteworthy that no thionaphthindole could be detected in the reaction products of the following pairs: (A) phenylhydrazine with 6-chloro-4-methyl-, 4 : 5-benz-, 4-chloro-, and 4 : 7-dichloro-thioindoxyl; (B) thioindoxyl with 2 : 4-dinitrophenyl-, *o*-tolyl- and α-naphthyl-hydrazine, or 6 : 7-benzthioindoxyl with *o*-tolylhydrazine. Each pair in class (A) includes a thioindoxyl carrying a 4-substituent, whereas each in class (B) includes a phenylhydrazine carrying an ortho-substituent. All these reaction products appeared to be complex, and usually tarry, mixtures and were in striking contrast to the highly crystalline thionaphthindoles which resulted from the earlier reactions.

The mechanism of the formation of thionaphthindoles from thioindoxyls has been discussed by McClelland and D'Silva (*loc. cit.*), who pointed out that the properties of the thioindoxyl molecule are peculiarly favourable for indolisation of the hydrazone to occur by the mechanism of the Fischer indole reaction proposed by Robinson and Robinson (*J.*, 1918, **113**, 639; 1924,

* For purpose of comparison, these thioindoxyls are cited throughout this paper in the order given by Dalgliesh and Mann (*loc. cit.*).

125, 827). This mechanism in the present case would involve the isomerisation of the hydrazone (VI) to the hydrazino-compound (VII), followed by an *o*-benzidine rearrangement to give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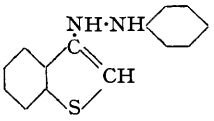
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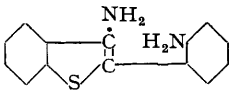
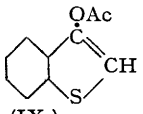

(VIII.)

the diamine (VIII), which would finally lose ammonia, possibly by the mechanism suggested by Allen and Wilson (*J. Amer. Chem. Soc.*, 1943, **65**, 611), to form the thionaphthindole (II).

It is clear therefore that at least one stage of this mechanism must be inhibited by 4-substituents in the thioindoxyl and by ortho-substituents in the phenylhydrazine. If the effect of the 4-substituent were solely steric, it would be expected that this critical stage would be the initial formation of the hydrazone (VI). This is not so, however, because we find that all our thioindoxyls react readily in the cold with 2 : 4-dinitrophenylhydrazine to give the corresponding 2 : 4-dinitrophenylhydrazones. The latter compounds, when derived from a 4-substituted thioindoxyl, therefore possess both types of substituents which inhibit the complete indolisation.

It is possible that the thioindoxyls always react in the enol form with hydrazines to give the hydrazides of type (VII) without intermediate formation of a true hydrazone of type (VI). This receives some support from the fact that 3-acetoxythionaphthens of type (IX) also react readily with phenylhydrazine to form thionaphthindoles (McClelland and D'Silva, *loc. cit.*). Furthermore, these authors state that 1 : 1-dioxythioindoxyl (X) gives a phenylhydrazone which cannot be indolised : they consider that the free valency electrons of the sulphone group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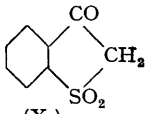
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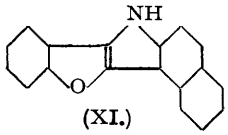

(XI.)

decrease (or possibly entirely suppress) the enolisation of (X) which therefore forms a true hydrazone, which in turn cannot tautomerise to the hydrazide; hence the indolisation process is arrested. It is difficult, however, to adduce any steric or electronic reason why a 4-substituent in thioindoxyl should suppress enolisation: we have used only methyl, chloro- and 4 : 5-benz-groups; the effect of a 4-nitro-group, having an opposite and much stronger electronic influence than the methyl and chloro-group, would repay investigation.

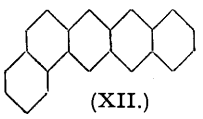
Parallel examples of the inhibiting effect of an ortho-substituent in the phenylhydrazine are known. Thus McClelland and Smith (*J.*, 1945, 408) have shown that although 3-hydroxy-2-acetylthionaphthen reacts readily with *m*- and *p*-nitrophenylhydrazine to give thionaphthenopyrazoles, the reaction with *o*-nitro- and 2 : 4-dinitro-phenylhydrazine goes no further than the formation of the corresponding nitrophenylhydrazones. Similarly Cawley and Plant (*J.*, 1938, 1216) have shown that although coumaranone reacted readily with β-naphthylhydrazine to form coumarono-(2′ : 3′ : 1 : 2)-β-naphthindole (XI), the reaction with both *o*- and *m*-nitrophenylhydrazines stopped at the nitrohydrazone stage. Finally Barclay and Campbell (*J.*, 1945, 530) found that *cyclo*hexanone *o*-tolylhydrazone decomposed rapidly even at room temperature without detectable conversion into a tetrahydrocarbazole : this was in striking contrast to the ready formation of the carbazole from the unsubstituted phenylhydrazone.

Since our work has shown that either a methyl or a nitro-group (groups opposite in their electronic effects) in the ortho-position in phenylhydrazine inhibits indolisation, it would appear that this result must be steric rather than electronic. Cawley and Plant's result with *m*-nitrophenylhydrazine is exceptional, and deserves fuller investigation.

The reaction of thioindoxyl with *m*-tolylhydrazine can theoretically give rise to 1- or 3-*methylthionaphthindole*. It is possible that our product, although of sharp m. p. and apparently homogeneous, may be a mixture of these isomerides, for *cyclo*hexanone *m*-nitrophenylhydrazone on cyclisation gives a mixture (probably equimolecular) of 5- and 7-nitrotetrahydrocarbazoles which also has a sharp m. p. (Plant, *J.*, 1936, 899; Barclay and Campbell, *loc. cit.*).

It is known that if a polycyclic aromatic hydrocarbon possesses carcinogenic properties, a corresponding compound in which one of the aromatic rings has been replaced by a similar heterocyclic ring may also possess these properties. For example, the carcinogenic properties

of 1 : 2 : 6 : 7-dibenzanthracene (XII) (Barry, Cook, *et al.*, *Proc. Roy. Soc.*, 1935, *B*, **117**, 318) appear also in 1 : 2 : 7 : 8-dibenzacridine. Carcinogenic properties are also shown by certain polycyclic sulphur compounds, such as 4 : 9-dimethyl-5 : 6-benzthiophanthrene (Sandin and Fieser, *J. Amer. Chem. Soc.*, 1940, **62**, 3098). There is an obvious similarity in general molecular outline between the dibenzanthracene (XII) and 11 : 12-benzthionaphthindole (IV). We have



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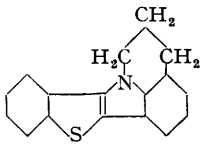

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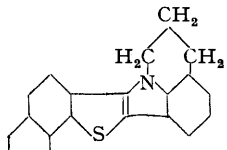

(XIV.)

consequently synthesised a number of these thionaphthindoles having additional rings, for therapeutic tests. In particular, the reaction of thioindoxyl with 1-amino-1 : 2 : 3 : 4-tetrahydroquinoline (mentioned above) readily furnished 4 : 6-*trimethylenethionaphthindole* (XIII), whereas the use of 6 : 7- and 5 : 6-benzthioindoxyls gave 4 : 6-*trimethylene*-11 : 12-*benzthionaphthindole* (XIV) and its 10 : 11-*benz*-isomeride. These three compounds represent new heterocyclic types. It is noteworthy that thionaphthindole (II) reacted readily with vinyl cyanide to form 6-(2-*cyanoethyl*)*thionaphthindole*, which on hydrolysis gave 6-(2-*carboxyethyl*)-*thionaphthindole*. Attempts to convert the latter into the corresponding acid chloride and then, by cyclisation with aluminium chloride, to obtain an independent synthesis of the ring system of (XIII) failed.

The thionaphthindoles all gave crystalline *picrates*, but it is noteworthy that the parent indole (II) and those of its derivatives having only four unsaturated rings all gave monopicrates, whereas those derivatives with five such rings all gave dipicrates. This further emphasises the resemblance between the thionaphthindoles and the polycyclic aromatic hydrocarbons.

Several of these thionaphthindoles containing additional fused rings are now being examined by Dr. A. L. Walpole in the Biological Laboratories of Imperial Chemical Industries Ltd., Blackley, Manchester. Preliminary tests indicate that certain of them may possess growth inhibitory action on experimental tumours; the results of carcinogenic tests are not yet available.

Towards certain reagents, the >NH group in thionaphthindole (II) and that in 11 : 12-benzthionaphthindole (IV) showed a striking difference in reactivity. This group in the parent indole (II), in addition to its ready combination with vinyl cyanide, could also be acetylated, whereas the same group in (IV) would undergo neither this cyanoethylation nor acetylation. This marked effect upon the reactivity of the >NH group by the remote extra ring is striking. Both compounds did, however, give N-*nitroso*-derivatives, which were too unstable even for recrystallisation.

The thioindoxyl 2 : 4-dinitrophenylhydrazones described above and tabulated later were all too insoluble for recrystallisation, and their isolation in the pure state was therefore dependent upon the use of pure thioindoxyls, free in particular from traces of the corresponding thioindigos which they form so readily by atmospheric oxidation. We have therefore purified the thioindoxyls by sublimation in a vacuum, after which they usually showed m. p.s markedly higher than previously recorded values.

We have been unable to effect indolisation by heating thio-oxindole with phenylhydrazine in acetic acid solution. Had indolisation occurred, a thionaphthindole isomeric with (II), but having the >S and >NH in the *cis*- instead of the *trans*-position, should have resulted.

Experimental.

The preparation of various thionaphthindoles from the thioindoxyls is described first, followed by the reactions of certain of these compounds. The properties of the pure thioindoxyls and of their 2 : 4-dinitrophenylhydrazones are tabulated subsequently.

The names of solvents used for recrystallisation are given in parenthesis after the compounds concerned.

Preparation of Thionaphthindoles.—1. *From thioindoxyl.* (i) Phenylhydrazine (11·2 c.c.) was added to a stirred solution of thioindoxyl (15 g.) in acetic acid (100 c.c.) at 40°; the temperature soon rose to 105° as the indole separated. The stirred mixture was maintained at 95—100° for 30 minutes. The thionaphthindole (II) was then collected from the cold mixture, washed with alcohol and water, and dried; 19·8 g.(89%).

It readily furnished a *monopicrate*, reddish-brown needles (alcohol), m. p. 171° (decomp.) (Found : N, 12·3. $C_{14}H_9NS,C_6H_3O_7N_3$ requires N, 12·4%); a *monostyphnate*, brick-red needles (alcohol), m. p. 175—176° (decomp.) (Found : N, 11·9. $C_{14}H_9NS,C_6H_3O_8N_3$ requires N, 11·9%); a *picrolonate*, yellow needles (alcohol), m. p. 188° (decomp.) (Found : N, 14·3. $C_{14}H_9NS,C_{10}H_8O_5N_4$ requires N, 14·4%).

(ii) Solutions of *p*-nitrophenylhydrazine (2·9 g.) and thioindoxyl (2·8 g.), each in acetic acid (20 c.c.), were mixed, whereupon a red product, presumably the hydrazone, immediately separated, but subsequently redissolved with deposition of the indole, when the mixture was heated at 100° for 30 minutes. The 2-*nitrothionaphthindole* when collected and recrystallised (xylene) formed yellow needles: owing to their low solubility they were further purified by sublimation at 0·1 mm. (jacket temperature, 260°); m. p. 350—352° (decomp.) (Found: C, 62·5; H, 2·9; N, 10·7. $C_{14}H_8O_2N_2S$ requires C, 62·7; H, 3·0; N, 10·5%).

(iii) *m*-Tolylhydrazine similarly gave 1 (or 3)-*methylthionaphthindole*, colourless leaflets (alcohol), m. p. 256° (Found: C, 76·4; H, 4·9. $C_{15}H_{11}NS$ requires C, 76·0; H, 4·6%); the *monopicrate* formed brown crystals, m. p. 185° (decomp.) (Found: N, 12·1. $C_{15}H_{11}NS,C_6H_3O_7N_3$ requires N, 12·0%).

(iv) 1-Amino-1 : 2 : 3 : 4-tetrahydroquinoline was prepared by Holliman and Mann's method (*J.*, 1942, 737). A solution of the sulphate (4 g.) in acetic acid (40 c.c.) and one of thioindoxyl (3 g.) and anhydrous sodium acetate (2 g.), also in acetic acid (40 c.c.), were mixed and refluxed for 30 minutes. When cold, the 4 : 6-*trimethylenethionaphthindole* (XIII) [3·3 g. (63%)] was collected, washed with alcohol and hot water, and recrystallised (alcohol); colourless leaflets, m. p. 139° (Found: C, 77·2; H, 5·6; N, 5·1. $C_{17}H_{13}NS$ requires C, 77·6; H, 4·9; N, 5·3%). It gave a *monopicrate*, bluish-black needles (alcohol), m. p. 149° (Found: N, 11·7. $C_{17}H_{13}NS,C_6H_3O_7N_3$ requires N, 11·4%).

2. *From* 5-*chloro*-7-*methylthioindoxyl*. (i) *p*-Tolylhydrazine hydrochloride, with sodium acetate and the thioindoxyl, readily gave 10-*chloro*-2 : 12-*dimethylthionaphthindole*, pale-brown crystals (alcohol) m. p. 241° (Found: C, 67·5; H, 4·5. $C_{16}H_{12}NClS$ requires C, 67·3; H, 4·2%); the *monopicrate* formed deep bronze leaflets (alcohol containing picric acid), m. p. 201° (decomp.) (Found: N, 11·1. $C_{16}H_{12}NClS,C_6H_3O_7N_3$ requires N, 10·9%).

(ii) 1-Phenyl-2-ethylhydrazine and the thioindoxyl, refluxed together in acetic acid solution, readily gave 10-*chloro*-12-*methyl*-6-*ethylthionaphthindole*, pale purple leaflets (alcohol), m. p. 165° (Found: C, 68·0; H, 4·8; N, 4·7. $C_{17}H_{14}NClS$ requires C, 68·1; H, 4·7; N, 4·7%); the *monopicrate* formed ruby-red needles, m. p. 129° (Found: N, 11·5. $C_{17}H_{14}NClS,C_6H_3O_7N_3$ requires N, 11·3%).

Both the above indoles were considerably more soluble in alcohol than most of the other indoles isolated in this investigation.

3. *From* 6-*ethoxythioindoxyl*. Phenylhydrazine gave 11-*ethoxythionaphthindole*, white needles (alcohol), m. p. 243° (Found: C, 72·3; H, 5·2. $C_{16}H_{13}ONS$ requires C, 71·9; H, 4·9%).

4. *From* 6 : 7-*benzthioindoxyl*. (i) Phenylhydrazine gave 11 : 12-*benzthionaphthindole* (IV), white crystals (alcohol), m. p. 325—326° (Found: C, 79·3; H, 4·3. $C_{18}H_{11}NS$ requires C, 79·1; H, 4·0%); the *dipicrate* formed bronze-coloured leaflets (alcohol containing picric acid), m. p. 178—180° (decomp.) (Found: N, 13·4. $C_{18}H_{11}NS,2C_6H_3O_7N_3$ requires N, 13·4%). The indole was unaffected by 1 hour's refluxing with acetic anhydride.

(ii) *p*-Nitrophenylhydrazine by the usual treatment and isolation gave 2-*nitro*-11 : 12-*benzthionaphthindole*, purified by vacuum sublimation, orange-brown crystals, m. p. 380—382° (Found: C, 67·7; H, 3·0; N, 8·8. $C_{18}H_{10}O_2N_2S$ requires C, 67·9; H, 3·1; N, 8·8%).

(iii) *p*-Tolylhydrazine gave 2-*methyl*-11 : 12-*benthionaphthindole*, colourless crystals (alcohol), m. p. 318° (Found: C, 79·6; H, 4·8. $C_{19}H_{13}NS$ requires C, 79·4; H, 4·5%); the *dipicrate* formed purple-brown needles, m. p. 186—187° (decomp.) (Found: N, 13·1. $C_{19}H_{13}NS,2C_6H_3O_7N_3$ requires N, 13·1%).

(iv) 1-Phenyl-2-methylhydrazine gave 6-*methyl*-11 : 12-*benzthionaphthindole*, silvery plates (alcohol), m. p. 226° (Found: C, 79·5; H, 4·6. $C_{19}H_{13}NS$ requires C, 79·4; H, 4·5%); the *dipicrate* formed deep brown needles (alcohol), m. p. 165° (Found: N, 12·9. $C_{19}H_{13}NS$, $2C_6H_3O_7N_3$ requires N, 13·1%).

(v) 1-Amino-1 : 2 : 3 : 4-tetrahydroquinoline gave 4 : 6-*trimethylene*-11 : 12-*benzthionaphthindole* (XIV), silvery crystals by vacuum sublimation, m. p. 237° (Found: C, 80·4; H, 5·2; N, 4·6. $C_{21}H_{15}NS$ requires C, 80·5; H, 4·8; N, 4·5%); the *dipicrate* formed chocolate needles (toluene), m. p. 184° (Found: N, 12·6. $C_{21}H_{15}NS,2C_6H_3O_7N_3$ requires N, 12·7%).

5. *From* 5 : 6-*benzthioindoxyl*. (i) Phenylhydrazine gave 10 : 11-*benzthionaphthindole*, (V), very pale green plates (toluene), m. p. 358° (Found: C, 79·0; H, 4·3; N, 4·9. $C_{18}H_{11}NS$ requires C, 79·1; H, 4·0; N, 5·1%).

(ii) 1-Amino-1 : 2 : 3 : 4-tetrahydroquinoline gave 4 : 6-*trimethylene*-10 : 11-*benzthionaphthindole*, pale yellow needles by vacuum sublimation, m. p. 195—197° (Found: C, 80·8; H, 4·4. $C_{21}H_{15}NS$ requires C, 80·5; H, 4·8%).

6. *From* 5-*methylthioindoxyl*. (i) *p*-Tolylhydrazine gave 2 : 10-*dimethylthionaphthindole*, pale brown needles (alcohol), m. p. 304° (Found: C, 76·6; H, 5·6. $C_{16}H_{13}NS$ requires C, 76·5; H, 5·2%).

7. *From* 7-*methylthioindoxyl*. (i) Phenylhydrazine gave 12-*methylthionaphthindole*, colourless leaflets (alcohol), m. p. 202° (Found: C, 76·3; H, 4·8. $C_{15}H_{11}NS$ requires C, 76·0; H, 4·6%); the *monopicrate* formed deep brown needles (alcohol), m. p. 186—188° (decomp.) (Found: N, 12·2. $C_{15}H_{11}NS,C_6H_3O_7N_3$ requires N, 12·0%).

8. *From* 7-*chlorothioindoxyl*. (i) Phenylhydrazine gave 12-*chlorothionaphthindole*, colourless leaflets (acetic acid, then alcohol), m. p. 223° (Found: C, 65·4; H, 3·0. $C_{14}H_8NClS$ requires C, 65·3; H, 3·1%); the *monopicrate* formed reddish-bronze needles (alcohol containing picric acid). m. p. 178° (decomp.) (Found: N, 11·5. $C_{14}H_8NClS,C_6H_3O_7N_3$ requires N, 11·5%).

Reactions of Thionaphthindole.—(1) *Formylation.* A mixture of the indole (2 g.), formic acid (98—100%, 40 c.c.), and acetic anhydride (10 c.c.) was refluxed for 2·5 hours, cooled, and poured into water. The precipitated material when crystallised (alcohol) furnished colourless needles of 6-*formylthionaphthindole*, m. p. 145° (Found: C, 71·9; H, 3·9. $C_{15}H_9ONS$ requires C, 71·7; H, 3·6%); the *picrate* formed brown needles (alcohol), m. p. 148—150° (decomp.) (Found: N, 11·8. $C_{15}H_9ONS,C_6H_3O_7N_3$ requires N, 11·7%).

(2) *Nitrosation.* An aqueous solution of sodium nitrite (1·5 g.) was added slowly with stirring to a solution of the indole (1·5 g.) in cold acetic acid (350 c.c.). The precipitated yellow needles of the 6-*nitrosothionaphthindole* were collected, washed with alcohol and water, and dried; m. p. 151—153° (decomp.) (Found: C, 67·1; H, 3·1; N, 11·0. $C_{14}H_{18}ON_2S$ requires C, 66·7; H, 3·2; N, 11·1%). Attempted recrystallisation of this compound from alcohol regenerated the indole.

(3) *Cyanoethylation.* A mixture of the indole (1·5 g.), vinyl cyanide (10 c.c.), dioxan (10 c.c.), and a trace of sodium methoxide was refluxed for 1·5 hours, and then poured into water (400 c.c.). The precipitate when recrystallised (alcohol) furnished 6-(2-*cyanoethyl*)*thionaphthindole*, pale yellow crystals, m. p. 167° (Found: C, 73·7; H, 4·7; N, 10·1. $C_{17}H_{12}N_2S$ requires C, 73·9; H, 4·5; N, 10·1%); 1·6 g. (86%).

For hydrolysis, a mixture of the cyanide (2·76 g.), potassium hydroxide (2 g.), alcohol (65 c.c.), and water (10 c.c.) was refluxed for 3·5 hours. The cyanide dissolved during the first 15 minutes' boiling, and the clear solution then deposited colourless crystals which subsequently redissolved. The final solution was poured into water (400 c.c.), and next day the small precipitate was removed, and the filtrate acidified with hydrochloric acid. The precipitated 6-(2-*carboxyethyl*)*thionaphthindole* [2·45 g. (83%)] gave colourless needles (50% aqueous alcohol), m. p. 168° (Found: C, 69·2; H, 4·7. $C_{17}H_{13}O_2NS$ requires C, 69·2; H, 4·4%). It is essential that the pure cyanide is used for this hydrolysis.

For attempted cyclisation, thionyl chloride (1·3 c.c., 1·5 mols.) was added to the above acid (3·6 g.) in dry benzene (35 c.c.) and the mixture refluxed until hydrogen chloride evolution ceased (*ca.* 1 hour). Powdered aluminium chloride (3 g.) was then added, and the refluxing continued for 3 hours more; considerable tar was produced. After addition of water, the benzene was removed in steam, and the dried residue then extracted (Soxhlet) with light petroleum (b. p. 60—80°). Evaporation of the extract gave only a minute residue.

Reactions of 11 : 12-*Benzthionaphthindole.*—(1) *Nitrosation.* This process, performed as in (2) above, furnished 6-*nitroso*-11 : 12-*benzthionaphthindole*, yellow needles, m. p. 164—165° (decomp.) (Found: N, 8·9. $C_{18}H_{10}ON_2S$ requires N, 9·2%). The compound decomposed on attempted recrystallisation.

(2) *Attempted cyanoethylation.* When a mixture of the indole (1·3 g.), vinyl cyanide (5 c.c.), dioxan (8 c.c.), and a trace of sodium methoxide was refluxed for 1·5 hours, and the solvents were then removed under reduced pressure, recrystallisation of the residue afforded only unchanged indole.

Formation of the Thioindoxyl 2 : 4-*Dinitrophenylhydrazones.*—Since these *compounds* could not be recrystallised without decomposition, they were prepared from purified thioindoxyls. For this purpose, thioindoxyl was distilled in steam, but the substituted thioindoxyls were sublimed at *ca.* 0·2 mm., jacket-temperature approximating to m. p. of the thioindoxyl. For the hydrazone formation, an alcoholic solution of 2 : 4-dinitrophenylhydrazine hydrochloride was added to a cold alcoholic solution of the pure thioindoxyl: the hydrazone rapidly separated, and was ultimately collected, washed with alcohol and ether, and dried. The properties of the thioindoxyls and their hydrazones are given in the following Table.

Thio-indoxyl.	Properties of purified thioindoxyl.	Properties of 2 : 4-dinitro-phenylhydrazones.	Formula.	Nitrogen (%). Found.	Required.
Unsubst.		Scarlet, m. p. 230° with darkening above 175°.	$C_{14}H_{10}O_4N_4S$	17·0	17·0
6-Cl-4-Me	Pale yellow needles, m. p. 106—108°.	Brick red, m. p. 217—218°.	$C_{15}H_{11}O_4N_4ClS$	14·6	14·8
5-Cl-7-Me	Cream crystals, m. p. 102—103°.	Scarlet, m. p. 216—218°, darkening above 195°.	$C_{15}H_{11}O_4N_4ClS$	14·9	14·8
6-EtO	Pale yellow crystals, m. p. 123—124°.	Scarlet, m. p. 217—219°, darkening above 185°.	$C_{16}H_{14}O_5N_4S$	15·2	15·0
4 : 5-Benz	Yellow crystals, m. p. 122—123°.	Scarlet, m. p. 199—200°.	$C_{18}H_{12}O_4N_2S$	14·8	14·7
6 : 7-Benz	Orange crystals, m. p. 142—143°.	Scarlet, m. p. 235—237°, darkening above 200°	$C_{18}H_{12}O_4N_2S$	15·0	14·7
4-Cl	Yellow needles, m. p. 113—114°.	Orange, m. p. 205°.	$C_{14}H_9O_4N_4ClS$	15·4	15·4
4 : 7-Dichloro	Yellow crystals, m. p. 140—141°.	Orange, m. p. 210°.	$C_{14}H_8O_4N_4Cl_2S$	14·3	14·0
5-Me	(Not sublimed)	Deep red, m. p. 227—228°, darkening above 190°.	$C_{15}H_{12}O_4N_4S$	16·6	16·3
7-Cl	Pale orange needles, m. p. 136—140°.	Orange, m. p. 242—243°.	$C_{14}H_9O_4N_4ClS$	15·6	15·4

All the above hydrazones are new, all melt with decomp., and all are microcrystalline.

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