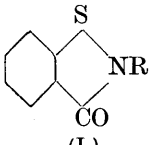
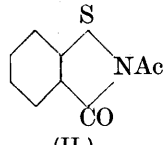
CCVIII.—*The Formation of Thionaphthindole.*

By Ernest Wilson McClelland.

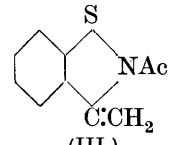
Reaction of 2-keto-1 : 2-dihydrobenz*iso*thiazole (I, R = H) and acetic anhydride under ordinary conditions yields the *N*-acetyl derivative (II) (McClelland and Longwell, J., 1923, **123**, 3310), but it is now shown that in presence of sodium or potassium acetate and at a higher temperature further condensation takes place. The chief product of reaction under these conditions is the methylene derivative (III) evidently formed by loss of carbon dioxide from the primary condensation product (IV).



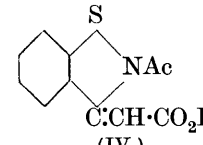
(I.)



(II.)

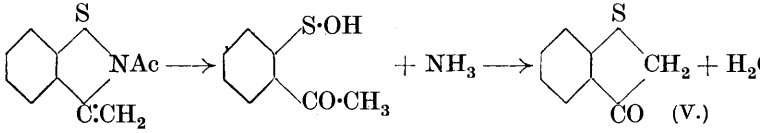


(III.)



(IV.)

The process resembles the formation of methylenephthalide from phthalic anhydride and these reagents (*Ber.*, 1884, **17**, 2522). The structure assigned to this material is supported by the fact that it absorbs bromine instantaneously, yielding eventually a *monobromo*-derivative, and on hydrolysis with acid, ammonia is liberated and 3-oxy-1-thionaphthen (V) is formed. The latter process is similar to the formation of diketohydrindene derivatives from alkylidenephthalides (*Ber.*, 1893, **26**, 951, 2576) and may be formulated thus :

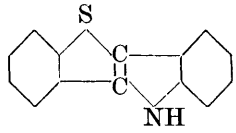


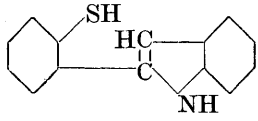
(V.)

During the formation of 1-*acetyl*-2-*methylene*-1 : 2-*dihydrobenz*iso-*thiazole* (III) other substances are produced. From among these

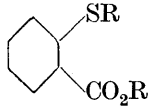
2-acetyl-3-oxy-1-thionaphthen has been isolated, together with a material which is regarded as *o*-thiolacetophenone since it yielded the requisite *semicarbazone* and showed the characteristic behaviour of this ketone with phenylhydrazine. Direct comparison with synthetic *o*-thiolacetophenone was not attained owing to the small amount of the product isolated from the reaction and the instability of this liquid thiol.

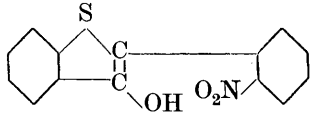
During the comparison of this material with the thiolacetophenone obtained from *o*-aminoacetophenone by Leuckart's method (D.R.-P. 198509) the reaction with phenylhydrazine was studied and it was found that either product did not yield the simple hydrazone under mild conditions but was rapidly converted into the tricyclic indole (VI).

(VI.) 

 (VII.)

The formation of this substance involves the usual indole transformation and subsequent oxidation of the thiol (VII). It shows the usual reactions of the indole group and gives an acetyl derivative. The structure which has been assigned to this compound was further confirmed by synthesis. This was effected from *o*-thiolbenzoic acid through the ester (VIII, R = *o*-$NO_2 \cdot C_6H_4 \cdot CH_2$) to the thionaphthen (IX) (compare *Ber.*, 1913, **46**, 3091); the indole obtained thence by reduction was identical with that prepared from *o*-thiolacetophenone and phenylhydrazine.

(VIII.) 

 (IX.)

Robinson and Robinson (J., 1918, **113**, 639) have pointed out that aldehydes and ketones which tend to exist as enols yield hydrazones which readily undergo the indole transformation; for instance, the hydrazone of phenylacetaldehyde, which exhibits enolic properties, is very easily converted into the indole, whereas the hydrazone of acetophenone, which does not exhibit such properties, requires much more intense conditions (*Ber.*, 1888, **21**, 1072).

The ease with which *thionaphthindole* (VI) is formed by condensation of phenylhydrazine with *o*-thiolacetophenone suggests that the presence of sulphur ortho to carbonyl favours enolisation. This conclusion is supported by the failure to isolate certain di-

substituted derivatives of 3-oxy-1-thionaphthen (Smiles and McClelland, J., 1921, **119**, 1810), which has been attributed to the tendency of the carbonyl group to acquire a tautomeric hydrogen atom (*Ann. Reports*, 1921, 114).

In the *iso*thiazole system (I) a similar tendency to enolise is evident; for instance, 2-keto-1 : 2-dihydrobenz*iso*thiazole (I, R = H) gives a purple coloration with ferric chloride in alcoholic solution. The suggestion that this substance is tautomeric (McClelland and Longwell, J., 1923, **123**, 3310) has recently been confirmed (Reissert, *Ber.*, 1928, **61**, 1308) by the isolation of two isomeric methyl ethers from direct methylation, one of these being identical with the *N*-methyl derivative (I, R = Me) previously obtained (McClelland and Gait, J., 1926, 921; compare *Ber.*, 1928, **61**, 1681).

Since the sulphur in these systems has free valency electrons, it may be considered as a " source " of electrons tending to increase the negative character of the *o*-carbonyl oxygen atom, thus favouring enolisation.

On the assumption that bivalent sulphur functions in this way, substitution of an element having free valency electrons for the sulphur should also give a system exhibiting enolic tendencies, whereas substitution of an element or group lacking free valency electrons might be expected to decrease or suppress enolisation. Indoxyl and 2-keto-1 : 2-dihydrobenz*iso*selenazole (*Ber.*, 1924, **57**, 1077) are representatives of the former type; the latter condition may be attained on substitution of groups such as CH_2 and CO, resulting in substances such as phthalimidine, phthalimide, and hydrindone: these do not appear to have marked enolic tendencies. Moreover, oxidation of the sulphur to the sulphone condition appears to restrain this tendency to enolisation, for the sulphone, *o*-benzoic sulphinide, unlike the corresponding sulphide (I, R = H), does not give a coloration with ferric chloride or other indication of enolic properties.

The reaction of 2-keto-1 : 2-dihydrobenz*iso*thiazole now described is being further investigated.

EXPERIMENTAL.

*Condensation of 2-Keto-1 : 2-dihydrobenziso**thiazole* (I, R = H) *with Acetic Anhydride and Potassium Acetate.*—2-Keto-1 : 2-dihydrobenz*iso*thiazole (J., 1926, 923) (5 g.) was heated with acetic anhydride (30 c.c.) and freshly fused potassium acetate (8 g.) under reflux at 120° for 10 minutes. The cooled product was diluted with water, heated for ½ hour at 100°, and distilled in steam, a yellow volatile oil (A) passing over. The mother-liquor was boiled with charcoal

and filtered hot. 1-*Acetyl*-2-*methylene*-1 : 2-*dihydrobenz*iso*thiazole* (III) (1·6 g.), which crystallised on cooling, separated from ethyl alcohol in colourless plates, m. p. 168—170° (Found : C, 62·3; H, 4·8; N, 7·5; *M*, 195. $C_{10}H_9ONS$ requires C, 62·8; H, 4·7; N, 7·3%; *M*, 191).

Hydrolysis of 1-*Acetyl*-2-*methylene*-1 : 2-*dihydrobenz*iso*thiazole*.—The *iso*thiazole (0·5 g.) was boiled with 2*N*-hydrochloric acid (20 c.c.) under reflux for 1 hour. The mixture was then diluted with water and steam-distilled, 3-oxy-1-thionaphthen passing over. The residual liquor gave ammonia on being made alkaline.

Bromination of 1-*Acetyl*-2-*methylene*-1 : 2-*dihydrobenz*iso*thiazole*.—The compound (0·5 g.), in 30 c.c. of dry chloroform, was gradually treated with a solution of bromine in chloroform (7·4 c.c.; Br = 6·51 g./100 c.c.). After 21 hours, the chloroform was evaporated and the residue crystallised from ethyl alcohol, the *bromo*-compound being obtained in fine white needles, m. p. 201—202° (Found : Br, 29·05. $C_{10}H_8ONBrS$ requires Br, 29·6%).

o-*Thiolacetophenone* (?).—The oil (A) obtained above was extracted from the distillate with ether, and the ethereal solution extracted with dilute aqueous sodium hydroxide. The alkaline extract on acidification gave a substance which was identified as 2-acetyl-3-oxy-1-thionaphthen by its characteristic physical and chemical properties. The ethereal solution was then washed with water, dried over anhydrous sodium sulphate, and evaporated ; the residual oil (B) was used in the subsequent experiments.

Semicarbazone. A solution of semicarbazide hydrochloride (1 g.) and sodium acetate (1·5 g.) in the minimum amount of hot water and an alcoholic solution of the oil (B) (1·3 g.) were mixed and heated on the water-bath for 1 hour. The *semicarbazone*, which crystallised in colourless needles, was purified from ethyl alcohol, in which it was sparingly soluble; m. p. 235° (decomp.) (Found : N, 20·2. $C_9H_{11}ON_3S$ requires N, 20·1%).

Thionaphthindole (VI).—(a) *From the oil* (*B*). A solution of the oil (1·56 g.) in glacial acetic acid (15 c.c.) and phenylhydrazine (2·22 g.) were heated on the water-bath for 10 minutes, crystalline material being deposited. (Condensation takes place readily even at 50°.) When cold, the precipitated *thionaphthindole* was collected, washed with ethyl alcohol, and recrystallised from this solvent, being obtained in colourless plates, m. p. 252—253° (Found : C, 75·7; H, 3·9; N, 6·3; *M*, 228. $C_{14}H_9NS$ requires C, 75·3; H, 4·1; N, 6·3%; *M*, 223).

Thionaphthindole is insoluble in hot and in cold aqueous sodium hydroxide and soluble in most organic solvents. In the presence of concentrated sulphuric acid, it gives an intense blue coloration with

isatin and a red coloration with phenanthraquinone. It is unaffected by boiling concentrated hydrochloric acid and is not readily reduced. It gives an intense yellow colour with concentrated nitric acid and a yellow colour with concentrated sulphuric acid (compare carbazole).

(b) *From o-aminoacetophenone.* *o*-Aminoacetophenone (1·28 g.; 1 mol.), dissolved in *N*-hydrochloric acid (3 mols.), was diazotised with sodium nitrite at 0° and poured into a solution of potassium ethyl xanthate (1·5 g.) in water (50 c.c.) at 0°. The mixture was allowed to attain room temperature with frequent shaking; after 1 hour, it was heated at 70° for ½ hour. The red oily material was extracted with ether, washed with dilute aqueous sodium hydroxide and with dilute hydrochloric acid, and, after removal of the ether, heated on the water-bath for 15 minutes with alcoholic potassium hydroxide (20 c.c. of 5%). The bulk of the alcohol was evaporated, the residue, after acidification with dilute hydrochloric acid, distilled in steam in presence of a little granulated zinc, and the distillate extracted with ether. The residual oil, after removal of the ether, was condensed with phenylhydrazine as in the previous experiment and gave an identical product.

It was not considered advisable to use large quantities in this preparation, as the diazonium xanthate decomposed with explosive violence in one experiment.

(c) *From o-thiolbenzoic acid.* *o*-Thiolbenzoic acid (10 g.) was dissolved in potassium ethoxide solution (potassium, 5 g.; ethyl alcohol, 100 c.c.), and water (4 c.c.) added to dissolve the potassium salt which separated. After the addition of *o*-nitrobenzyl chloride (22 g.) dissolved in ethyl alcohol (50 c.c.), the mixture was heated for 8 hours on the water-bath. The product, which crystallised, was collected, washed with water, dried, and heated on the water-bath with potassium ethoxide (potassium, 2 g., in ethyl alcohol, 100 c.c.) for 2 hours. The alcohol was then removed and water added to the residue. The mixture, after extraction with ether to remove *o*-nitrobenzyl alcohol, was acidified with glacial acetic acid (250 c.c.), and heated to boiling for 1 hour while zinc dust (10 g.) was added. The thionaphthindole, which crystallised from the decanted liquid on cooling, was purified in the usual manner and was identical with the material obtained in the previous experiments.

N-*Acetylthionaphthindole.*—Thionaphthindole (0·2 g.) was boiled with acetic anhydride (5 c.c.) for 1 hour. The excess of acetic anhydride was hydrolysed by warming at 100° with water for ½ hour. The precipitated material crystallised from ethyl alcohol in colourless needles, m. p. 160—161° (Found : C, 72·3; H, 4·1; *M*, 271. $C_{16}H_{11}ONS$ requires C, 72·4; H, 4·1%; *M*, 265).

The author is indebted to Professor Smiles for the interest he has taken in this investigation and to the Research Fund Committee of the Chemical Society for a grant which has defrayed part of the cost of materials.

KING'S COLLEGE, LONDON. [*Received, May 31st,* 1929.]