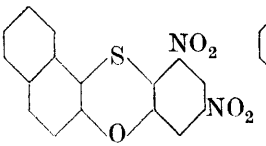
XCVII.—*Syntheses of Thioxins.*

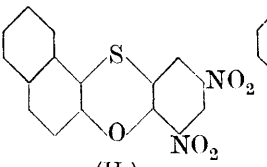
By Herbert A. Stevenson and Samuel Smiles.

During an investigation of the structure of *iso*naphthathioxin progress was hindered by lack of information concerning systematic methods of synthesis in this group. The experiments now described were carried out during the necessary exploration of this field and were made with special reference to mono- and di-naphthathioxins. Two types of method previously known are due to Mauthner (*Ber.*, 1905, **38**, 1411; 1906, **39**, 1340); one of these depends on the reaction of an *o*-hydroxy-mercaptan with picryl chloride in presence of alkali. This process is of limited application, since it is necessarily confined to the production of dinitro-derivatives, and it has the further disadvantage that the structure of the product is indeterminate. Thus 2-hydroxy-1-naphthyl mercaptan and picryl chloride yield a dinitrothioxin which may be represented as either (I) or (II) according as elimination of nitrous acid concerns the hydroxyl (I) or the thiol (II) group. It is now shown that the former is the course taken by the reaction, since the product (I) is identical with that obtained by the action of alkali on the *S*-picryl derivative of 2-acetoxy-1-naphthyl mercaptan.

Mauthner also showed (*loc. cit.*) that dehydration of 2-naphthol 1-sulphide yields αβα′β′-dinaphthathioxin. The method may be extended to derivatives of this sulphide: syntheses of mono-



(I.)



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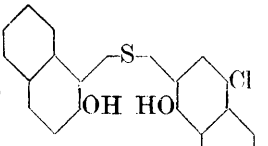
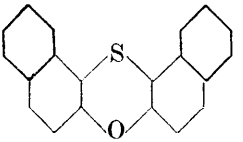


(III.)

and di-bromo-αβα′β′-dinaphthathioxins are now recorded as further examples. It cannot, however, be successfully applied to derivatives of α-naphthol; for instance, 4-chloro-1-naphthol 2-sulphide did not give the desired dichloro-αβα′α′-thioxin, and the αβ-sulphide (III) yielded only a small quantity of the αβα′β′-thioxin (IV), which was evidently produced by fission of the sulphide during the process. Moreover, the dehydration of *o*-hydroxy-sulphoxides, which may be used in the synthesis of dibenzthioxins (Hilditch and Smiles, J., 1911, **99**, 408), is not successful in the naphthalene series.

The method used in the synthesis (J., 1929, 209) of αββ′α′-dinaphthathioxin may be far more widely applied than either of the foregoing processes. This method involves the removal of alkali

halide from a 2′-halogeno-2-hydroxy-sulphide; further examples are now recorded of syntheses of dibenz- and benznaphtha-thioxins, the sulphides of the required type being obtained from the naphthol or phenol by reaction with a chloro-thiol or a suitable disulphoxide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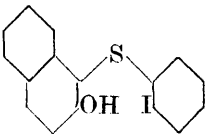
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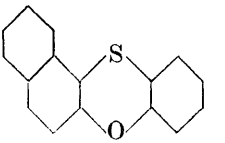
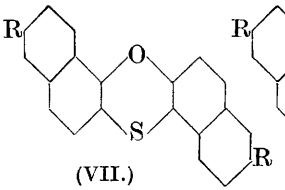

(VI.)

(J., 1926, 1723). Thus the sulphide (V) derived from 2-naphthol gave excellent yields of benznaphthathioxin (VI).

The formation of αββ′α′-dinaphthathioxin (VII; R = H) in high yield from dehydro-2-naphthol 1-sulphide (VIII; R = H) and acetyl iodide has already been recorded (J., 1914, **105**, 1741). It appears that the method may be generally applied to dehydro-*o*-hydroxy-sulphides which contain a sufficiently active quinolic system; the further examples now adduced concern the dehydro-6 : 6′-dibromo-sulphide (VIII; R = Br) and a dehydro-sulphide (IX) obtained by synthesis from 1 : 6-dibromo-2-naphthol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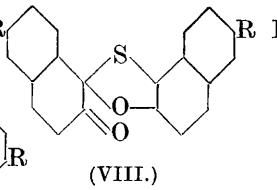
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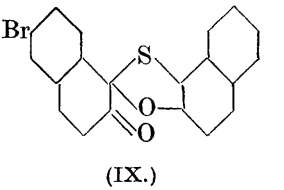
(IX.)

and 1-bromothiol-2-naphthol in presence of pyridine (compare J., 1930, 1740). The process may at present be conveniently regarded as involving the reduction of the dehydro-sulphide and subsequent dehydration of the *iso*-sulphide then formed, and it may be noticed that both operations may be separately effected by hydrogen iodide (Hinsberg, *J. pr. Chem.*, 1914, **90**, 345) and acetic anhydride (Nolan and Smiles, J., 1913, **103**, 340) respectively. These bromo-derivatives are therefore regarded as the 3 : 10- (VII; R = Br) and the 10-substitution products. It has been already recorded (J., 1926, 957) that the action of sulphur on dinaphthyl oxides in presence of iodine or aluminium chloride does not give the satisfactory results obtained in the benzene series.

Experimental.

Hydroxy-sulphides and Derivatives.—(1). 2-*Iodophenyl* 2-*methoxy*-1-*naphthyl sulphide* (as V). *Di*-2-*iodophenyl disulphoxide*, prepared from the sulphinic acid, had m. p. 147° (Found: C, 28·7; H, 1·6.

$C_{12}H_8O_2I_2S_2$ requires C, 28·7; H, 1·6%). This (10 g.) was added to boiling alcohol (300 c.c.) which contained sodium naphthoxide (2·9 g. of 2-naphthol). When reaction was complete (3 hours) the solvent was removed and water was added to the residue, the mixture being rendered alkaline if necessary. The phenolic constituents were liberated by carbonic acid and removed in ether. The residue from this solvent was an oil which was reluctant to crystallise. The required sulphide was therefore brought to analysis as the *methyl* ether, which was obtained from the crude material by methylation (methyl sulphate) in presence of warm aqueous alkali and purified from aqueous acetone; m. p. 162° (Found: C, 51·9; H, 3·3. $C_{17}H_{13}OIS$ requires C, 52·0; H, 3·3%).

(2). 2 : 5-*Dibromophenyl* 2-*hydroxy*-1-*naphthyl sulphide*. (*a*) This was prepared as in the case of (1) from di-2 : 5-dibromophenyl disulphoxide (1 mol.) and sodium 2-naphthoxide (1 mol.) in alcohol. The residue from the ethereal solution solidified and then crystallised from alcohol in needles, m. p. 148° (Found: C, 46·4; H, 2·8. $C_{16}H_{10}OBr_2S$ requires C, 46·8; H, 2·4%).

(*b*) It was more conveniently obtained by the following method. A suspension of di-2 : 5-dibromophenyl disulphide (10 g.) in carbon tetrachloride was treated with chlorine until a clear orange solution of the chlorothiol was obtained. The slight excess of halogen was removed with a current of dry nitrogen, and a suspension of 2-naphthol in the same solvent was added. When reaction was complete the solvent and unchanged naphthol were removed by steam and the required substance was extracted from the residue with alkali and, after liberation, purified from alcohol. The product had m. p. 148° and was identical with that obtained from (*a*).

(3). 2 : 5 : 5′-*Tribromo*-2′-*hydroxydiphenyl sulphide* was obtained as in the case of 2(*b*) by reaction of 4-bromophenol with 2 : 5-dibromo-1-chlorothiolbenzene; the formation of the sulphide was slower (2 days) than with 2-naphthol. The crude product was a viscous oil; it was characterised by conversion into the *methyl* ether. This separated from alcohol (charcoal) in needles, m. p. 142° (Found: C, 34·6; H, 2·1. $C_{13}H_9OBr_3S$ requires C, 34·4; H, 2·0%).

Benznaphthathioxins.—The sodium salts of these hydroxy-sulphides were sparingly soluble in aqueous alkali hydroxide and separated from the warm medium in a liquid phase. They were prepared for conversion into the thioxins by evaporating an alcoholic solution of sodium ethoxide (1 mol.) and the sulphide (1 mol.). The residue, which solidified when kept in a vacuum, was intimately mixed with a little copper sulphate (*ca.* 1 : 20) and heated (1 mm.) to a temperature suited to the particular case; this was lowest (150°) for the iodo-sulphide (1).

The thioxins sublimed in good yield and were purified from suitable solvents.

Benz-αβ-naphthathioxin (VI), from (1), formed bright yellow needles, m. p. 63°, from alcohol (Found: C, 76·5; H, 4·0. $C_{16}H_{10}OS$ requires C, 76·8; H, 4·0%).

10-*Bromobenz-αβ-naphthathioxin*, $C_{10}H_6<\begin{matrix}S\\O\end{matrix}>C_6H_3Br$, from (2), formed pale yellow prisms, m. p. 142°, from alcohol (Found: C, 58·0; H, 2·6. $C_{16}H_9OBrS$ requires C, 58·3; H, 2·7%).

2:8-*Dibromodibenzthioxin*, $C_6H_3Br<\begin{matrix}S\\O\end{matrix}>C_6H_3Br$, from (3), formed needles, m. p. 92°, from alcohol (Found: C, 39·9; H, 1·8. $C_{12}H_6OBr_2S$ requires C, 40·2; H, 1·7%).

9:11-*Dinitrobenz-αβ-naphthathioxin* (I). *N*-Sodium hydroxide (2 mols.) was added to alcohol (25 c.c.) which contained picryl chloride (1·5 g.) and 2-hydroxy-1-naphthyl mercaptan (1 g.). The deep colour at first produced faded as the *dinitro-thioxin* separated in almost theoretical yield. This formed red needles, m. p. 300°, from acetic acid (Found: C, 56·3; H, 2·3; S, 9·5. $C_{16}H_8O_4N_2S$ requires C, 56·5; H, 2·4; S, 9·4%).

The preparation of this substance from the 1-*S*-picryl derivative of 2-acetoxynaphthalene will be described in a subsequent communication. It is most conveniently obtained from 2-naphthol 1-disulphide by reaction with picryl chloride as described.

Dinaphthathioxins.—The dehydration of 2-naphthol 1-sulphide in tetrachloroethane with phosphorus oxychloride, yielding αβα′β′-dinaphthathioxin, has been already described (J., 1912, **101**, 714). The yield obtained by this method may be considerably improved (60—70%) by addition of zinc chloride ($POCl_3 : ZnCl_2 = 1:1$) to the reacting mixture. This process yielded 3:11-*dibromo-αβα′β′-dinaphthathioxin* (compare IV) from 6:6′-dibromo-2-naphthol 1-sulphide, which formed pale yellow needles, m. p. 275°, from tetrachloroethane (Found: C, 52·0; H, 2·2; Br, 34·8. $C_{20}H_{10}OBr_2S$ requires C, 52·4; H, 2·2; Br, 34·9%).

Bromination of the parent thioxin gave (J., 1913, **103**, 907) a dibromo-derivative, m. p. 280°, but this is not identical with the 3:11-derivative, a mixture having m. p. 215—250°.

3-*Bromo-αβα′β′-dinaphthathioxin*, from 6-bromo-2-naphthol 1-sulphide (J., 1930, 1744), formed yellow needles, m. p. 119°, from benzene (Found: C, 63·3; H, 3·1. $C_{20}H_{11}OBrS$ requires C, 3·3; H, 2·9%).

The dehydration of (III) (J., 1926, 957; 1930, 1744) has been more fully investigated. The product insoluble in alkali (10% yield) had m. p. 154—155° after purification from acetic acid and

from its properties was evidently a thioxin; but it contained less than 1% of chlorine (Found: Cl, 0·8. $C_{20}H_{11}OClS$ requires Cl, 10·6%). It was further purified by means of the picrate (J., 1914, **105**, 1741). The latter had m. p. 177—178° and was identical with the picrate of αβα′β′-dinaphthathioxin (IV). The thioxin liberated from this had m. p. 163—164° and was identified with (IV).

3 : 10-*Dibromo*-αββ′α′-*dinaphthathioxin* (VII). The dehydro-derivative of 6-bromo-2-naphthol 1-sulphide (VIII) was more readily obtained from the sulphide by alkaline ferricyanide than by hypobromite (Lesser and Gad, *Ber.*, 1923, **56**, 970). The crude product was thoroughly washed and dried by immersion in alcohol. This material was submitted to reaction with acetyl iodide in acetic anhydride as already described (J., 1914, **105**, 1741) (yield, *ca.* 90%). The required product formed bright yellow needles, m. p. 273°, from tetrachloroethane (Found: C, 52·3; H, 2·3; Br, 35·0. $C_{20}H_{10}OBr_2S$ requires C, 52·4; H, 2·2; Br, 34·9%). It was not identical with the product (m. p. 245°) formed by bromination of *iso*dinaphthathioxin or with the 3 : 11-dibromo-αβα′β′-thioxin (m. p. of mixture 230—245°).

10-*Bromo*-αββ′α′-*dinaphthathioxin* (compare VII). The dehydro-derivative of 6-bromo-2-naphthol 1-sulphide (IX) required was synthesised as follows. Carbon tetrachloride (300 c.c.) which contained 1 : 6-dibromo-2-naphthol (18 g.) was added to a suspension of 1-bromothiol-2-naphthol in the same solvent (25 c.c.). The treatment of this mixture with pyridine and aqueous sodium hydroxide and the isolation of the product from the solution were conducted as described in the case of dehydro-2-naphthol 1-sulphide (J., 1930, 1744). The crude dehydro-sulphide (*ca.* 30%) was very soluble in the usual solvents and was not obtained in the crystalline state. It was converted into the *bromo-thioxin* in the usual manner. The desired product (80—85%) was purified by sublimation (2 mm.) and from acetic acid; it formed yellow needles, m. p. 173° (Found: C, 63·0; H, 2·9. $C_{20}H_{11}OBrS$ requires C, 63·3; H, 2·9%).

In order to obtain further evidence of the character of this synthetical dehydro-sulphide, the oxidation product, obtained as usual from 6-bromo-2-naphthol 1-sulphide (J., 1930, 1744) with ferricyanide, was examined. It is evident that this may be a mixture of two dehydro-sulphides according as the quinolic structure is found in the brominated (IX) or unbrominated nucleus; but in the former case the substance would be identical with the product of synthesis and should furnish an identical bromo-thioxin. The oxidation product, owing to its solubility and reluctance to crystallise, could not be satisfactorily resolved into components; it was therefore

converted into the bromo-thioxin by acetyl iodide. The product, in accordance with theory, proved to be a mixture, from which, after sublimation and fractionation from acetic acid, a thioxin identical with that obtained from the synthetic dehydro-derivative (IX) was isolated. It had m. p. 172—173°, whether alone or mixed with it (Found: C, 62·8; H, 2·9; Br, 20·7. Calc.: C, 63·3; H, 2·9; Br, 21·1%).

In conclusion we wish to thank Dr. L. A. Warren for information concerning the synthesis of dinitrobenznaphthathioxin.

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