CVII.—*Strychnine and Brucine. Part XII. The Constitution of Dinitrostrycholcarboxylic Acid.*

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THE application of a Curtius transformation to dinitrostrycholcarboxylic acid (Tafel, *Annalen*, 1898, **301**, 285) was described in Part X (J., 1930, 830) and the degradation of the resulting urethane to picric acid and to dinitroisatin clearly excluded all formulæ for Tafel's acid based on *iso*quinoline.

The conclusion was drawn that the substance must be a derivative of quinoline and as the possibility of its being a 2 : 4-dihydroxyquinoline had already been eliminated (Ashley, Perkin, and Robinson, J., 1930, 382), synthetical experiments in the 2 : 3- and the

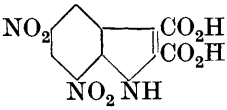
3 : 4-dihydroxyquinoline series were instituted. An account of these will, it is hoped, be submitted in a short time, but it may be stated at once that they afforded no confirmation of our views and we accordingly had to modify our previous conclusion.

At a much earlier stage of this investigation the possibility that dinitrostrycholcarboxylic acid is a dicarboxylic acid was contemplated, but in view of the great stability of dinitrostrychol the idea was set aside; it seemed incompatible with experience that any indolecarboxylic acid should remain undecomposed as does dinitrostrychol in contact with water at 210° in a sealed tube or when boiled with quinoline, glycerol, or diphenylmethane. In returning to the examination of this aspect of our problem we again made use of the Curtius transformation, which is one of the very few diagnostic reactions for carboxylic acids capable of distinguishing these from isomeric phenols the acidity of which is enhanced by nitroxyl substituents.

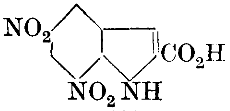
Dinitrohydrazinodeoxystrychol (Part X, *loc. cit.*) readily yields an *azide* which can be crystallised unchanged from boiling alcohol but is slowly converted under these conditions into a *urethane* : the change of composition is that involved in the normal transformation, $RCON_3 \longrightarrow RNH \cdot CO_2Et$.

Trinitrostrychol also yields a *methyl* ester, *hydrazide*, *azide*, and *urethane*, and the last can be obtained by nitration of the urethane from dinitrostrychol. In this case the decomposition of the azide was facile, a matter of a few seconds. Therefore dinitrostrychol and trinitrostrychol are carboxylic acids and, taking into consideration the degradation to dinitroisatin and the composition of the substances, it is now certain that dinitrostrycholcarboxylic acid is 5 : 7-dinitroindole-2 : 3-dicarboxylic acid (I).

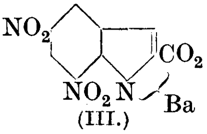
Dinitrostrychol is very probably 5 : 7-dinitroindole-2-carboxylic acid (II), because (*a*) indole-3-carboxylic acid suffers decarboxylation very much more readily than indole-2-carboxylic acid, (*b*) nitration of the indole nucleus is known to occur in position 3 and trinitrostrychol is thus accommodated, (*c*) the barium salt can be formulated as (III).



(I.)



(II.)



(III.)

Leuchs (*Ber.*, 1930, **63**, 3184) has made it very probable that strychnine contains the group $\vdots N(a) \cdot CH_2 \cdot$, and if this is confirmed it will be apparent that (I) must be produced by ring closure at some stage in a complex series of reactions.

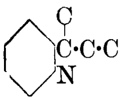
The formulæ which we have proposed (Part X, *loc. cit.*) are, therefore, not excluded by the present development but, if there is a methylene group at C-2 (compare formula VIII on p. 833, *loc. cit.*), then C-12 should be joined to C-3 or C-4, and in both cases the formulæ can be completed in one way only if rings of fewer than five members are not admitted.

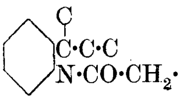
Very recently, Professor Leuchs, in an appendix to a memoir (*Ber.*, 1931, **64**, 462), has expressed the view that strychnine is a dihydroindole derivative and consequently dinitrostrycholcarboxylic acid is either not a derivative of quinoline or is produced by ring enlargement.

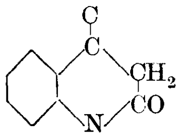
We can illustrate our general views of the chemistry of strychnine in formulæ based on dihydroindole (and hexahydrocarbazole), but we cannot reconcile our views on this basis with the occurrence of the group $\vdots N(a){\cdot}CH_2{\cdot}$ in tetrahydrostrychnine.

Apart from such speculations it is now established that strychnine contains the group (IV), and, taking benzylidenestrychnine into account, this may be developed to (V), or, much less probably, to (VI).

Synthetical work in the dinitroindole group is in progress.


(IV.)


(V.)


(VI.)

EXPERIMENTAL.

Dinitrohydrazinodeoxystrychol (5 : 7-*Dinitroindole*-2-*carboxyhydrazide*).—The yellow by-product previously obtained (*loc. cit.*) is the result of contamination of the dinitrostrychol employed with dinitrostrycholcarboxylic acid; it was probably 5 : 7-*dinitro*-3-*carbomethoxyindole*-2-*carboxyhydrazide* (Found : C, 41·1; H, 2·7; N, 21·3; MeO, 9·5. $C_{11}H_9O_7N_5$ requires C, 40·8; H, 2·8; N, 21·7; 1MeO, 9·7%).

O-Methyldinitrostrychol (1·5 g.) was suspended in boiling methyl alcohol (75 c.c.), and hydrazine hydrate (8 c.c. of 90—95%) added. The boiling was continued for one minute after a clear solution was obtained and, on cooling, the pure hydrazide (1·2 g.) separated in orange-yellow needles.

O-Methyldinitrostrychol was recovered unchanged after being heated with an excess of methyl-alcoholic ammonia in a sealed tube at 100° for 7 hours, and also after being boiled with *p*-toluidine.

5 : 7-*Dinitroindole*-2-*carboxyazide*, $(NO_2)_2C_6H_2{:}C_2NH_2{\cdot}CON_3$.—The

finely powdered hydrazide (2·3 g.) was stirred with acetic acid (60 c.c.), a colourless acetate separating; the addition of aqueous sodium nitrite (1·5 g. in 150 c.c.) then produced a caseous precipitate of the *azide*, which was collected after the addition of 5% hydrochloric acid and stirring (yield, theoretical). The substance crystallised from ethyl alcohol, in which it was sparingly soluble, in long colourless needles which melted with sudden decomposition at 160° (Found: N, 30·2. $C_9H_4O_5N_6$ requires N, 30·5%). This azide is much more stable than its mononitro-derivative.

5 : 7-*Dinitro-α-indolylurethane*, $(NO_2)_2C_6H_2{:}C_2NH_2{\cdot}NH{\cdot}CO_2Et$.—The crude azide (from 2·3 g. of the hydrazide) was refluxed with alcohol (1000 c.c.) for 5 hours, giving an orange solution. Most of the solvent was then removed by distillation; golden-orange spangles (1·5 g.) separated on cooling and a further quantity (0·1 g.) was obtained from the mother-liquor. The substance is rather readily soluble in alcohol, but it crystallises very well from benzene, in which it is sparingly soluble to a yellow solution, in deep orange, prismatic needles (or on quick cooling in kite-shaped and dagger-shaped plates and needles), m. p. 194° (Found: C, 45·0; H, 3·5; N, 18·9; EtO, 15·1. $C_{11}H_{10}O_6N_4$ requires C, 44·9; H, 3·4; N, 19·1; 1EtO, 15·3%).

The passage of hydrogen chloride into a benzene solution of this *urethane* mixed with *p*-dimethylaminobenzaldehyde gives a carmine coloration, not destroyed on the addition of water. This typical Ehrlich reaction is difficult to observe in aqueous or alcoholic solutions.

Methyl 3 : 5 : 7-*Trinitroindole*-2-*carboxylate* (O-*Methyltrinitrostrychol*).—A solution of trinitrostrychol (0·5 g.) in methyl alcohol (50 c.c.) and sulphuric acid (5 c.c.) was refluxed for 7 hours; the *ester* then crystallised from the solution, the yield being almost quantitative. Recrystallised from acetic acid, it formed colourless needles, m. p. 212° (Found: C, 38·8; H, 2·0; N, 17·9; MeO, 10·1. $C_{10}H_6O_8N_4$ requires C, 38·7; H, 1·9; N, 18·1; 1MeO, 10·0%).

The related *hydrazide* was readily obtained in the usual manner in methyl-alcoholic solution (the amount of hydrazine used must not greatly exceed the theoretical quantity). It crystallised from ethyl alcohol in bunches of short, yellow, microscopic needles, m. p. 209—210° (decomp.) (Found: C, 36·9; H, 3·4; N, 23·3. $C_9H_6O_7N_6,C_2H_6O$ requires C, 37·1; H, 3·4; N, 23·6%). The alcohol of crystallisation was detected by the iodoform reaction after distillation of a sample with dilute sulphuric acid.

3 : 5 : 7-*Trinitro-α-indolylurethane*.—The conversion of 3 : 5 : 7-trinitroindole-2-carboxyhydrazide into the azide was carried out in the usual manner. The colourless chalky precipitate could not

in this instance be recrystallised. When it was boiled with alcohol there was a rapid evolution of nitrogen and a new crystalline substance separated. More alcohol was added in order to dissolve this in the boiling liquid: the filtered solution deposited slender, pale yellow needles, m. p. 218—219° (decomp.) (Found: C, 39·0; H, 2·7; N, 20·5; EtO, 13·3. $C_{11}H_9O_8N_5$ requires C, 38·9; H, 2·6; N, 20·6; 1EtO, 13·3%). The same substance was obtained by nitration of the urethane from dinitrostrychol by means of an excess of cold nitric acid (*d* 1·48); after a few hours the substance separated in prismatic needles, and after recrystallisation from much alcohol was obtained in pale yellow needles, m. p. 218—219°, alone or mixed with the specimen from trinitrostrychol. When it was heated with concentrated sulphuric acid, carbon dioxide was evolved, and on dilution and addition of ammonia a trinitroamino-indole was precipitated, but this substance has not yet been further examined. The urethane does not develop a coloration with *p*-dimethylaminobenzaldehyde under any conditions.

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