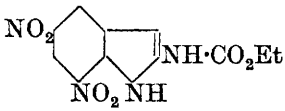
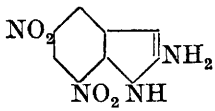
101. *Strychnine and Brucine. Part XVIII. Final Stages of the Degradation of Dinitrostrychol and an Account of some Nitrohydroxyquinoline Derivatives.*

By KOTTIAZATH NARAYANA MENON and ROBERT ROBINSON.

IN Part XII (J., 1931, 773) it was shown that dinitrostrychol is a carboxylic acid, probably 5 : 7-dinitroindole-2-carboxylic acid, and the application of the Curtius reaction to the acid led to the formation of 5 : 7-dinitro-2-indolylurethane (I). This substance has now been hydrolysed to 5 : 7-*dinitro*-2-*aminoindole* (II).


(I.)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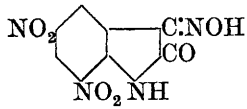

(III.)

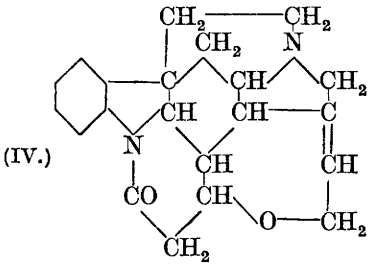
The action of nitrous acid on the salts of this base yields 5 : 7-*dinitroisatin*-3-*oxime* (III), which can also be obtained from dinitroisatin (Part X; J., 1930, 830) by the action of hydroxylamine. The oxime can be hydrolysed to dinitroisatin.

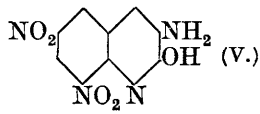
We have previously stated (Part XII; *loc. cit.*) that our views on the course of the permanganate oxidation (Leuchs) could be brought into line with the recognition that dinitrostrycholcarboxylic acid is 5 : 7-dinitroindole-2 : 3-dicarboxylic acid and symbolised in a constitutional formula. This was not actually put forward, because it seemed at the time that the evidence for the existence of the group $\cdot N(a) \cdot CH_2 \cdot$ was not to be set aside.

But Professor Leuchs (private communication) has now been able to arrive at a satisfactory explanation of the nature of the product obtained by oxidising tetrahydrostrychnine with chromic acid without such an assumption. Consequently full weight can be attached to the ascertained constitution of dinitrostrycholcarboxylic acid.

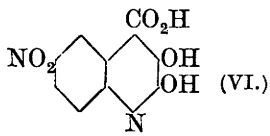
The formula which we had in mind is (IV); it contains carbazole and tryptophan skeletons and a blocked dihydroindole structure.

(IV.)





(V.)



(VI.)

The expression also accommodates the arguments mentioned in the Bakerian Lecture of 1930 (*Proc. Roy. Soc.*, 1931, *A*, **130**, 431) with the exception of those based on the supposed presence of a quinoline nucleus.

The model of the skeleton of dihydrostrychnine on this basis is entirely strainless and the bridge-ring and seven-membered ring fit in very conveniently. It is also a remarkably symmetrical arrangement in space.

A number of substances prepared in the course of synthetical work in this group are described in the experimental section.

Carbostyril-3-carboxylic acid was nitrated with formation of 6 : 8-*dinitrocarbostyril*-3-*carboxylic acid*, and the Curtius reaction then applied to the substance. In this way 6 : 8-*dinitro*-3-*amino*-2-*hydroxyquinoline* (V) has been obtained. The conversion into 6 : 8-dinitro-2 : 3-dihydroxyquinoline, an isomeride of dinitrostrychol, has not yet been accomplished in spite of many attempts.

Ethyl 2 : 3-dihydroxyquinoline-4-carboxylate could be nitrated with formation of 6-*nitro*-2 : 3-*dihydroxyquinoline*-4-*carboxylic acid* (VI), but up to the present all attempts to introduce a second nitro-group have been fruitless.

Experimental.

5 : 7-*Dinitro*-2-*aminoindole* (II).—A solution of 5 : 7-dinitro-2-indolylurethane (0·1 g.) (*loc. cit.*) in concentrated sulphuric acid (3 c.c.) was gently heated over a free flame until the evolution of gas ceased. The cooled solution was added to water (15 c.c.) and neutralised with ammonia. The brick-red precipitate was collected and dried; the *amine* crystallised from nitrobenzene, or xylene, in bright red, microscopic needles, m. p. 265° (Found: C, 43·5; H, 2·8; N, 25·0. $C_8H_6O_4N_4$ requires C, 43·2; H, 2·7; N, 25·2%). This red base is very sparingly soluble in most organic solvents; it forms nearly colourless salts and gives rise to a diazonium salt which couples with β-naphthol to a crimson azo-compound.

5 : 7-*Dinitroisatin*-3-*oxime* (III).—The diluted sulphuric acid solution of the base, obtained as described above, was not neutralised by ammonia but diazotised at — 10° by means of sodium nitrite (2 mols.). More water (5 c.c.) was added and the mixture was boiled until nitrogen was no longer evolved and then filtered hot (charcoal). On cooling, the *oxime* separated in long, light yellow, woolly needles, m. p. 252° (Found: C, 38·3; H, 1·9; N, 21·9. $C_8H_4O_6N_4$ requires C, 38·1; H, 1·6; N, 22·2%).

The same substance was readily obtained from dinitroisatin by the action of hydroxylamine hydrochloride and sodium carbonate in aqueous-alcoholic solution. The product had m. p. 252° and a mixture of the two specimens also melted at this temperature.

The oxime (prepared from strychnine) was hydrolysed to dinitroisatin by 6 hours' boiling with a large excess of a mixture of equal volumes of concentrated hydrochloric acid and 40% formaldehyde solution: the process was slow but gave good results. The dinitroisatin was identified with an authentic specimen.

6 : 8-*Dinitrocarbostyril*-3-*carboxylic Acid*.—A mixture of carbostyril-3-carboxylic acid (10 g.), concentrated sulphuric acid (50 c.c.), and nitric acid (50 c.c.; *d* 1·52) was heated for an hour in a boiling water-bath and then poured into water. The precipitate crystallised from acetic acid in microscopic prisms, m. p. 240° (yield, theoretical) (Found: C, 43·0; H, 2·2; N, 14·8. $C_{10}H_5O_7N_3$ requires C, 43·0; H, 1·8; N, 15·0%).

The positions of the nitro-groups in this compound were determined by heating the dinitro-acid with 10 times its weight of water in a sealed tube at 200° for 4 hours: complete decarboxylation was effected and the product, after crystallisation from acetic acid, melted at 218°, the m. p. of 6 : 8-dinitrocarbostyril (Kaufmann and Petherd, *Ber.*, 1917, **50**, 336).

Ethyl 6 : 8-*Dinitrocarbostyril*-3-*carboxylate*.—6 : 8-Dinitrocarbostyril-3-carboxylic acid was refluxed for 12 hours with a large excess

of 20% ethyl-alcoholic sulphuric acid. The acid itself is not soluble in alcohol to any great extent, but it is gradually replaced by the *ethyl* ester, which separates from the hot solution in needles. Recrystallised from acetic acid, the ester had m. p. 210° (Found: C, 46·9; H, 3·0; N, 13·8; EtO, 15·1. $C_{12}H_9O_7N_3$ requires C, 46·9; H, 2·9; N, 13·7; 1EtO, 14·7%).

6 : 8-*Dinitrocarbostyril*-3-*carbohydrazide and Azide.*—The ethyl ester failed to react with hydrazine hydrate in the presence of a solvent and after a large number of trials the following procedure was adopted.

The ester (1 g.) was finely powdered and stirred with hydrazine hydrate (3 c.c., 90—95%): a deep red solution was formed with evolution of heat and when heated on the steam-bath for 5 minutes the whole solidified to a yellow mass. This was extracted with a large volume of water, and washed with boiling water till the washings were no longer coloured. The hydrazide (m. p. 255°) was very sparingly soluble in all solvents and could not be purified for analysis.

A solution of 1 g. in hot 10% hydrochloric acid (250 c.c.) was filtered, cooled, and treated with sodium nitrite (1 g.) in 10 c.c. of water. The azide that separated was collected and dried on a porous plate (m. p. 95°, decomp.).

6 : 8-*Dinitro*-2-*hydroxyquinolyl*-3-*urethane.*—A suspension of the azide (3 g.) in alcohol (150 c.c.) was refluxed on a steam-bath. Solution was effected with evolution of nitrogen and after a short time the *urethane* separated. More alcohol was added and the boiling continued for an hour. The urethane crystallised from acetic acid in yellow needles, m. p. 239° (Found: C, 44·6; H, 3·4; N, 17·6. $C_{12}H_{10}O_7N_4$ requires C, 44·7; H, 3·1; N, 17·4%).

6 : 8-*Dinitro*-3-*amino*-2-*hydroxyquinoline* (V).—The urethane (0·5 g.) was boiled for ½ hour with 10% aqueous sodium hydroxide (300 c.c.), and the solution cooled and acidified with acetic acid. The *base* crystallised from acetic acid in coppery plates, m. p. 239° (Found: C, 43·4; H, 2·6; N, 22·1. $C_9H_6O_5N_4$ requires C, 43·2; H, 2·4; N, 22·4%). It can be diazotised and then couples with β-naphthol to a crimson azo-compound. The base is soluble in concentrated mineral acids, but separates on dilution.

3-*Nitroindole*-2-*carboxylic Acid.*—Indole-2-carboxylic acid (2 g.) was gradually added to nitric acid (10 c.c.; *d* 1·42), kept at 0—5°, with good stirring. The reaction mixture was kept at the room temperature for 3 hours with intermittent stirring. The solid that separated was collected, washed first with concentrated nitric acid, then with dilute nitric acid, and finally with water. It crystallised from water in pale yellow needles, m. p. 232° (Found: C, 52·6; H, 2·6; N, 13·7. Calc. for $C_9H_6O_4N_2$: C, 52·4; H, 2·9; N, 13·6%).

The same nitro-acid was obtained by Angelico and Velardi (*Atti R. Accad. Lincei*, 1904, **13**, i, 241) by the oxidation of 3-nitro-2-methylindole. 3-Nitroindole-2-carboxylic acid could not be nitrated to give either a di- or a tri-nitro-compound. Experiments in this direction always resulted in the formation of degradation products.

6-*Nitro*-2-*hydroxy*-4-*ethoxyquinoline*-3-*carboxylic Acid*.—A mixture of 2-hydroxy-4-ethoxyquinoline-3-carboxylic acid (5 g.) and nitric acid (50 c.c.; *d* 1·42) was gently refluxed for 15 minutes and then diluted with water. The *product* crystallised from acetic acid in needles, m. p. 285° (decomp.) (Found: C, 51·9; H, 3·8; N, 10·0. $C_{12}H_{10}O_6N_2$ requires C, 51·8; H, 3·6; N, 10·1%). The substance is very resistant towards the further action of nitrating agents.

6-*Nitrocoumarin*-3-*carboxylic Acid*.—Coumarin-3-carboxylic acid (5 g.) was slowly added to nitric acid (100 c.c.; *d* 1·52), cooled in running water. The mixture was kept at room temperature for 60 hours and then poured into water; the *nitro*-compound soon crystallised in plates. Recrystallised from acetic acid, it melted at 234° and decomposed at 260° (Found: C, 51·4; H, 1·8; N, 6·2. $C_{10}H_5O_6N$ requires C, 51·1; H, 2·1; N, 5·9%).

The position of the nitro-group was determined by decarboxylation. The acid was recovered unchanged after treatment with ammonia under different conditions.

6-*Nitro*-2 : 3-*dihydroxyquinoline*-4-*carboxylic Acid* (VI).—Ethyl 2 : 3-dihydroxyquinoline-4-carboxylate (Wislicenus and Bubeck, *Annalen*, 1924, **436**, 122) (2 g.) was added in one portion to nitric acid (10 c.c.; *d* 1·42). The temperature was maintained below 50° by appropriate cooling and the mixture was later stirred until the temperature fell to 18°. It was then slowly heated to 100°, maintained at that temperature for 15 minutes, and poured into water; the solid obtained crystallised from acetic acid in needles, m. p. 212° (decomp.) (Found: N, 10·9. $C_{10}H_6O_6N_2$ requires N, 11·2%). The *nitro*-acid is recovered unchanged from boiling fuming nitric acid or from a mixture of equal parts of nitric acid (*d* 1·42) and concentrated sulphuric acid at 100°.

The behaviour of the 4-carboxylic ester towards nitric acid is in striking contrast to that of 2 : 3-dihydroxyquinoline, which has not yielded any definite nitro-compound under a variety of experimental conditions.

THE UNIVERSITY OF OXFORD.
UNIVERSITY COLLEGE, LONDON. [*Received, January 21st*, 1932.]