LII.—*Strychnine and Brucine. Part IX. Preparation of Some Isomerides of Dinitrostrychol and Trinitrostrychol.*

By Julius Nicholson Ashley, (the late) William Henry Perkin, jun., and Robert Robinson.

In 1898, Tafel (*Annalen*, **301**, 336) showed that, when strychnine was heated first with dilute and then with concentrated nitric acid, the base was nitrated and subsequently degraded, with the formation

of oxalic and picric acids, together with a compound, $C_{10}H_5O_8N_3$, considered to be $C_9NH_2(OH)_2(NO_2)_2 \cdot CO_2H$ and termed dinitrostrycholcarboxylic acid.

The carboxyl group could be eliminated, or displaced by nitroxyl, dinitrostrychol, $C_9NH_3(OH)_2(NO_2)_2$, and trinitrostrychol, $C_9NH_2(OH)_2(NO_2)_3$, respectively being produced.

From the properties of these substances and of dinitrostrychol monomethyl ether, Tafel concluded that the hypothetical strychol is either a dihydroxyquinoline or a dihydroxy*iso*quinoline; he further considered that one of the hydroxyl groups is in proximity to a nitro-group and is responsible for the formation of the yellow neutral alkali-metal salts of dinitrostrychol and that the other hydroxyl exhibits a carbostyril-like character and functions in the formation of the red alkaline-reacting salts. Finally, Tafel stated (*loc. cit.*, p. 300) that attempts to transform dinitrostrychol derivatives to known substances had been unsuccessful, and that synthetical experiments also had been fruitless; the details of the latter have not been published.

The work recorded in the present communication was completed in 1926, before there was any suggestion (Fawcett, Perkin, and Robinson, Part VII, J., 1928, 3082) that dinitrostrychol might be an *iso*quinoline derivative,* and, at that time, we followed Tafel in regarding strychnine as a derivative of quinoline. It appeared highly improbable that the benzene ring of dinitrostrycholcarboxylic acid is not the original benzene ring of strychnine; brucine gives quite different products and nitric acid would not be expected to dehydrogenate the reduced rings of the alkaloid. The same argument applies to the picric acid which is formed alongside the dinitrostrycholcarboxylic acid. But the first action of nitric acid on strychnine is to nitrate it to dinitrostrychnine hydrate, which must then break down into picric acid and the strychol derivative. It follows from these considerations that the nitro-groups in dinitrostrychnine hydrate and dinitrostrycholcarboxylic acid are in the *m*-relation to each other.

On the assumption that dinitrostrychol is a dinitrodihydroxyquinoline, we can proceed a step further and restrict attention to the 6 : 8-dinitrodihydroxyquinolines, since the quinoline nitrogen atom would certainly be replaced by hydroxyl in the course of the reactions leading to the formation of picric acid from dinitrostrychnine hydrate. The same orientation follows from a consideration of analogies in connexion with the original nitration of strychnine; the

* We have now a definite proof that the substance is a quinoline derivative. A communication on this subject will shortly be submitted to the Society.—R. R.

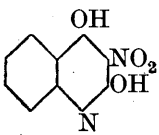
nitro-groups would, doubtless, enter the *op*-positions with respect to the nitrogen atom attached to the nucleus.

The positions 6 and 8 are therefore not possible situations for the hydroxyl groups of dinitrostrychol, and strychol might be 2 : 3-, 2 : 4-, 2 : 5-, 2 : 7-, 3 : 4-, 3 : 5-, 3 : 7-, 4 : 5-, 4 : 7-, or 5 : 7-dihydroxyquinoline.

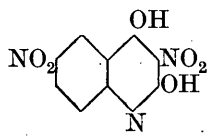
Very little was known of the nitro-derivatives of such dihydroxyquinolines, and in order to study their properties we have synthesised some typical members of this group, selecting those representatives which had the best claim to be considered in connexion with the strychol problem.

The outcome has been to exclude the 2 : 4-, 2 : 5-, and 2 : 7-formulæ with certainty, and the 4 : 7-formula on somewhat less definite grounds. Of the remaining possibilities, all but the 2 : 3-, 3 : 4-, and 4 : 5-formulæ are highly improbable.

The first stage in the nitration of 2 : 4-dihydroxyquinoline was studied by Gabriel (*Ber.*, 1918, **51**, 1500), who obtained 3-nitro-2 : 4-dihydroxyquinoline (I), and this substance has been found to yield 3 : 6(or 8)-*dinitro*-2 : 4-*dihydroxyquinoline* (II, 3 : 6) on further nitration in sulphuric acid solution. The introduction of a third nitro-group presented great difficulties, which were only surmounted after many unsuccessful experiments. The acetyl derivative of (II) was treated under special conditions with a mixture of 10% oleum and potassium nitrate, and the product was 3 : 6 : 8-*trinitro*-2 : 4-*dihydroxyquinoline* (III), an isomeride of trinitrostrychol.



(I.)



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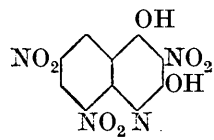


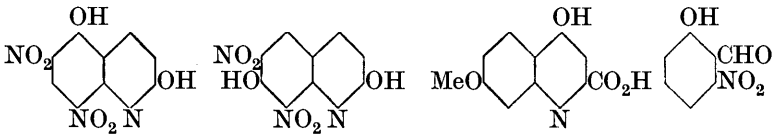
(III.)

The constitution of the substance is proved by its conversion into picric acid by means of boiling nitric acid, and this reaction constitutes one of the distinctions from trinitrostrychol, which cannot be similarly degraded. Attempts to effect the ring closure of *ethyl* 3 : 5-*dinitro*-2-*acetamidobenzoate*, which would have afforded 6 : 8-dinitro-2 : 4-dihydroxyquinoline, were not successful.

6 : 8-*Dinitro*-2 : 5-*dihydroxyquinoline* (IV) and 6 : 8-*dinitro*-2 : 7-*dihydroxyquinoline* (V) were obtained from the corresponding aminocarbostyrils by diazotisation, decomposition, and nitration without isolation of intermediate stages.

Neither of these substances was identical with dinitrostrychol; they did not yield trinitro-compounds but suffered degradation on boiling with nitric acid and gave rise to styphnic acid.

Compound (IV) was much more stable than (V), and the yield of the trinitroresorcinol was poor; the reaction is of interest in that it confirms the view that the quinoline nitrogen atom is replaced by hydroxyl in all such nitration–oxidation processes.



(IV.) (V.) (VI.) (VII.)

A synthesis of 4-*hydroxy*-7-*methoxyquinoline*-2-*carboxylic acid* (VI) has been effected, and the results obtained on nitrating this substance were not in agreement with the view that strychol is 4 : 7-dihydroxyquinoline.

Further, in some preliminary experiments on the synthesis of 4 : 5-dihydroxyquinoline derivatives, the Tiemann–Reimer reaction was applied to *m*-nitrophenol, and 6-*nitrosalicylaldehyde* (VII) obtained in 3% yield. The orientation of this substance follows from the facts that it is not a *p*-hydroxybenzaldehyde, being volatile in steam, and that its methyl ether yields an indigotin derivative on treatment with acetone and sodium hydroxide.

EXPERIMENTAL.

Dinitrostrycholcarboxylic Acid and Dinitrostrychol.—The method of Tafel (*loc. cit.*) was modified in that the mixture of strychnine and 20% nitric acid was heated on the steam-bath for 120 hours; losses by evaporation were compensated by the addition of 20% nitric acid. Strychnine nitrate (115 g.), nitric acid (900 g., *d* 1·42), and water (3600 c.c.) gave ultimately 10·3 g. of pure dinitrostrychol-carboxylic acid.

A large number of analyses of dinitrostrycholcarboxylic acid, of dinitrostrychol and its methyl ether have been carried out, and Tafel's view of the composition of these substances is unquestionably correct.

Dinitrostrychol crystallises best from acetic acid, in very pale yellow needles, m. p. 282° (Tafel, *loc. cit.*, crystallised the substance from alcohol or nitric acid, and gives the m. p. 284°).

When dinitrostrychol is reduced in alcoholic solution with zinc dust and hydrochloric acid, the resulting colourless solution exhibits a strong bluish-violet fluorescence; it becomes discoloured rapidly, and, on dilution with water and the addition of ferric chloride, develops a deep red coloration, changing to reddish-brown.

Attempts to reduce only one nitro-group of dinitrostrychol were unsuccessful.

Complete degradation, without formation of picric or styphnic acid, resulted when dinitrostrychol (0·5 g.) was heated in a sealed tube at 200° with nitric acid (4 c.c., *d* 1·5) for 4½ hours. With the same quantities, heated at 120—125° for 2 hours, the product was pure trinitrostrychol.

Dinitrostrychol monomethyl ether (Tafel, *loc. cit.*, p. 345) was obtained by heating the dry monopotassium salt of dinitrostrychol (2 g.) with methyl iodide (5 c.c.) in a sealed tube at 155° for 2½ hours, or by refluxing a mixture of the monopotassium salt (4 g.), purified methyl sulphate (5 c.c.), and xylene (150 c.c.) for 1½ hours (yield, 70—75%; m. p. 194—195°).

The conditions for the hydrolysis of the methyl ether by aqueous sodium hydroxide have been studied, and the following experiments are typical. (1) The finely powdered methyl ether (0·2 g.) was triturated with cold aqueous sodium hydroxide (10 c.c. of 1%); very little material passed into solution. On heating at 40° for 2 minutes, an orange-red solution was obtained, and this was filtered and acidified, yielding dinitrostrychol free from its methyl ether. (2) The finely powdered methyl ether (0·2 g.), when triturated with cold aqueous sodium hydroxide (10 c.c. of 8%), was converted into a deep red, insoluble sodium salt. This was collected and treated with dilute sulphuric acid, yielding the original methyl ether, m. p. 192°. It is evident that the monomethyl ether possesses very weak acidic character, and is hydrolysed by aqueous alkalis with special facility.

Tafel (*loc. cit.*) made the very interesting observation that dinitrostrychol behaves as a dibasic acid towards baryta, since, although the potassium salt, stable in the presence of water, has the composition $C_9H_4O_6N_3K$, the barium salt under similar conditions appears to be $C_9H_3O_6N_3Ba$. This suggested to us that the hydroxyl groups are probably in the ortho- or peri-positions with respect to each other, and we attempted to confirm this view by the preparation of an ethylene ether or an oxalyl derivative of dinitrostrychol. The disodium salt (5 g.) was refluxed for 50 hours with ethylene dibromide (4 c.c.) and absolute alcohol (100 c.c.). Apart from unchanged dinitrostrychol, a relatively very small amount of a sparingly soluble substance, crystallising from alcohol in pale brown needles, m. p. 186—187° (Found : N, 15·0, 14·8%), was isolated. This substance exhibited the behaviour of dinitrostrychol monomethyl ether towards 1% sodium hydroxide solution and was probably the corresponding monoethyl ether (N, 15·1%).

The dipotassium salt of dinitrostrychol (2·9 g.) was mixed with oxalyl chloride (2 c.c.) (Staudinger, *Ber.*, 1908, **41**, 3563) and pure toluene (10 c.c.); the initial reaction was controlled by cooling in

water and, after 12 hours, the mixture was heated on the steam-bath for 2 hours. The filtered liquid was evaporated under diminished pressure; the pale yellow residue, after being lixiviated with water, crystallised from toluene in very pale yellow, irregular prisms, m. p. 161° (Found : N, 19·5, 19·5%). Unfortunately, the yield was poor, so that a full examination was not possible, but it is clear that the action of the oxalyl chloride must have removed either carbon or oxygen or both from the dinitrostrychol molecule (dinitrostrychol, $C_9H_5O_6N_3$, requires N, 16·8%).

The substance was insoluble in cold aqueous sodium carbonate, but, on boiling, it dissolved to an orange solution; it was immediately soluble in cold dilute aqueous sodium hydroxide to an orange-red solution. On boiling with nitric acid (*d* 1·42, boiled), oxidation occurred and the evaporated liquid gave, with a little water, long, pale yellow rods, m. p. 278—279° (decomp.) (Found : N, 15·3%, a provisional figure in the absence of a duplicate). This substance was readily soluble in cold dilute sodium carbonate to a deep orange solution.

It is very difficult to explain these remarkable results, and the subject merits further investigation.

Trinitrostrychol was found to be more readily obtainable by the nitration of dinitrostrychol than from dinitrostrycholcarboxylic acid (Tafel). It sufficed to heat a mixture of dinitrostrychol (0·5 g.) and nitric acid (5 c.c., *d* 1·5) on the steam-bath for 1 hour. On the addition of water (15 c.c.), the trinitrostrychol separated in pale yellow, microscopic needles, m. p. 218°. No trace of picric or styphnic acid was produced. The pale yellow solution in dilute aqueous sodium hydroxide rapidly darkened on heating and became deep brown. This characteristic behaviour is exhibited by traces of trinitrostrychol, and advantage has been taken of this fact in showing that certain synthetic products do not contain the substance.

2 : 4-*Dihydroxyquinoline and Derivatives.*—According to Camps (*Arch. Pharm.*, 1899, **237**, 688), the action of sodium on methyl acetylanthranilate (Mehner, *J. pr. Chem.*, 1901, **64**, 83) gives a 60% yield of crude 2 : 4-dihydroxyquinoline, but we find that the yield of pure substance barely exceeds 40%. Other methods, however, including those of Erdmann (*Ber.*, 1899, **32**, 3570) and of D.R.-P. 11767, were still less satisfactory. Camps's method was slightly modified. Dry powdered methyl acetylanthranilate (50 g.) was added to granulated sodium (6 g.) suspended in toluene (200 c.c.). Reaction occurred and the yellow liquid boiled spontaneously. The mixture was finally refluxed (oil-bath) until it became viscous. After cooling, the solid was collected, freed as far as possible from toluene, and dissolved in water (800 c.c.) at 70—80°. The solution

was just acidified to litmus, and the precipitated dihydroxyquinoline collected (Found : N, 8·7. Calc. : N, 8·7%).

Further addition of acid to the filtrate precipitated acetylanthranilic acid in a crystalline condition.

4(or 2)-*Hydroxy*-2(or 4)-*acetoxyquinoline* was obtained when 2 : 4-dihydroxyquinoline (1 g.) was heated with acetic anhydride (20 c.c.) and three drops of pyridine on the steam-bath for ¾ hour. The derivative crystallised from alcohol in needles, m. p. 214—215° (Found : C, 65·1; H, 4·5; N, 6·6. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·5; N, 6·9%), readily soluble in acetic acid and acetone, moderately readily soluble in methyl alcohol, chloroform, ethyl acetate, and benzene, sparingly soluble in ether and light petroleum.

4(or 2)-*Hydroxy*-2(or 4)-p-*nitrobenzyloxyquinoline* possesses similar solubility properties and was prepared by refluxing a mixture of 2 : 4-dihydroxyquinoline (4 g.), alcohol (250 c.c.), *p*-nitrobenzyl bromide (6 g.), and potassium hydroxide (2 g.) for 2 hours. Yellow crystals separated from the filtered solution, and this substance crystallised from alcohol in pale yellow plates, m. p. 247° (decomp.) (Found : C, 64·8; H, 4·3; N, 9·7. $C_{16}H_{12}O_4N_2$ requires C, 64·9; H, 4·1; N, 9·5%).

3-Nitro-2 : 4-dihydroxyquinoline (I) was prepared by Gabriel's method (*Ber.*, 1918, **51**, 1500) in 85% yield, and also by nitration in sulphuric acid solution in somewhat inferior yield. A clear proof of the constitution of this derivative does not appear to have been recorded, but we have now observed that a small amount of aniline is formed on distillation with soda-lime.

The *monoacetyl* derivative was obtained under the conditions described above for the acetylation of 2 : 4-dihydroxyquinoline. It formed yellow needles, m. p. 194° (decomp.), from alcohol (Found : C, 53·6; H, 3·6; N, 11·1. $C_{11}H_8O_5N_2$ requires C, 53·2; H, 3·3; N, 11·3%).

Attempts to obtain a methyl ether of 2 : 4-dihydroxyquinoline were unsuccessful, but the action of diazomethane was not tried.

3 : 6-*Dinitro*-2 : 4-*dihydroxyquinoline* (II).—Powdered potassium nitrate (16 g.) was added during 1 hour to a solution of 2 : 4-dihydroxyquinoline (10 g.) in sulphuric acid (100 c.c.) with stirring and cooling to below 5°. Nitric acid (20 c.c.) was then introduced in four portions, and the stirring continued at room temperature for 2½ hours. The brown liquid was added to crushed ice, and the yellow solid isolated and dissolved in hot aqueous sodium carbonate. On cooling, the *sodium* salt separated in glistening, slender, yellow needles (Found : Na, 8·2. $C_9H_4O_6N_3Na$ requires Na, 8·4%). The regenerated nitrophenol was almost colourless and crystallised from acetic acid in long needles, m. p. 200° (decomp.) (yield, 60%)

(Found : C, 43·5; H, 2·2; N, 16·8. $C_9H_5O_6N_3$ requires C, 43·1; H, 2·0; N, 16·7%).

3 : 6-*Dinitro*-2 : 4-*dihydroxyquinoline* is moderately readily soluble in the simple alcohols, acetone and hot water, but is very sparingly soluble in ether, light petroleum, benzene, ethyl acetate, and chloroform. It does not dissolve readily in cold aqueous sodium carbonate, but with sodium hydroxide an orange-red disodium salt is produced. The stability of this substance towards alkali is remarkable; 1 gram was heated with 15 c.c. of 10% sodium hydroxide solution in a sealed tube at 145° for 10 hours without suffering any decomposition.

A completely reduced acid solution became deep blue, quickly changing to reddish-brown, on the addition of ferric chloride.

The *monoacetyl* derivative was obtained by heating a mixture of the dinitrodihydroxyquinoline (1 g.) and acetic anhydride (20 c.c.), with stirring, just to the boiling point. The yellow solution deposited almost colourless plates, m. p. 190° (decomp.) after recrystallisation from acetic acid (Found : C, 45·3; H, 2·6; N, 14·2. $C_{11}H_7O_7N_3$ requires C, 44·9; H, 2·4; N, 14·3%).

3 : 6 : 8-*Trinitro*-2 : 4-*dihydroxyquinoline* (III).—Finely powdered potassium nitrate (11 g.) was gradually added with shaking to a solution of 3 : 6-dinitrohydroxyacetoxyquinoline (5 g.) in 10% oleum (50 c.c.), and the yellow liquid stirred at 85° for 3 hours and then at 90—95° for 4 hours, the temperature having been raised very gradually. The product was slowly added to water (200 c.c.) with stirring. The pale brown solid obtained crystallised from acetic acid in pale yellow leaflets, m. p. 192—193° (decomp.) (yield, 65%) (Found : C, 36·9; H, 1·6; N, 18·4. $C_9H_4O_8N_4$ requires C, 36·6; H, 1·4; N, 18·9%).

This *trinitrodihydroxyquinoline* is fairly readily soluble in water, alcohol and ethyl acetate and readily soluble in acetone; it is sparingly soluble in most other organic solvents.

The solution in aqueous sodium carbonate is golden-yellow. In aqueous sodium hydroxide the compound gives a deep yellow solution, from which a sparingly soluble sodium salt separates almost immediately; there is no change on boiling : this behaviour is in marked contrast with that of trinitrostrychol.

The *monoacetyl* derivative was prepared by heating the trinitrodihydroxyquinoline with acetic anhydride for 5 minutes; it crystallised in colourless elongated plates, m. p. 158° (decomp.) (Found : C, 38·8; H, 1·9. $C_{11}H_6O_9N_4$ requires C, 39·1; H, 1·8%).

The oxidation and nitration of the trinitrodihydroxyquinoline (1 g.) afforded a proof of its constitution and was effected by heating the substance with a mixture of acetic acid (10 c.c.) and nitric acid (10 c.c., *d* 1·5) for ½ hour on the steam-bath and, after addition of

water (10 c.c.), refluxing the solution for ½ hour and concentrating it to a syrup. The picric acid formed was isolated as its sodium salt and characterised by its m. p., undepressed by admixture with an authentic specimen, and by other properties.

2-*Chloro*-3 : 5-*dinitrobenzoyl Chloride*.—2-Chloro-3 : 5-dinitrobenzoic acid (Purgotti and Contardi, *Gazzetta*, 1902, **32**, i, 526) was treated with phosphorus pentachloride; the *chloride* (mentioned by Barnett, *Ber.*, 1925, **58**, 1610, without properties or analysis) crystallised from ether–benzene in white needles, m. p. 62° (Found : Cl, 26·7. $C_7H_2O_5N_2Cl_2$ requires Cl, 26·8%). Attempts to condense the chloride with ethyl sodioacetoacetate and to hydrolyse the product were fruitless.

3 : 5-*Dinitro*-2-*methoxybenzoyl Chloride*.—The acid was obtained in 85% yield by following Ullmann's directions (*Annalen*, 1909, **366**, 85), and in 95% yield by nitrating *o*-methoxybenzoic acid (20 g.) with a mixture of sulphuric acid (100 c.c.) and nitric acid (30 c.c., *d* 1·5) for ½ hour at room temperature.

The *chloride* crystallised in plates when the crude product was washed with light petroleum; it had m. p. 37—38° (Found : Cl, 13·8. $C_8H_5O_6N_2Cl$ requires Cl, 13·6%). Condensations with the sodium derivatives of ethyl acetoacetate and ethyl malonate led to no satisfactory outcome.

Methyl 3 : 5-*Dinitro*-2-*acetamidobenzoate*.—Salkowski (*Annalen*, 1874, **173**, 46) obtained methyl 3 : 5-dinitroanthranilate by the action of ammonia on methyl dinitroethoxybenzoate, and recorded the m. p. 166°. Esterification of 3 : 5-dinitroanthranilic acid (Purgotti and Contardi, *loc. cit.*) by means of 5% methyl-alcoholic sulphuric acid gave the same derivative, m. p. 165—166°, in 71% yield (Found : C, 39·6; H, 3·1. Calc. for $C_8H_7O_6N_3$: C, 39·8; H, 2·9%). The corresponding ethyl ester had m. p. 136°.

Acetylation of the methyl ester (2·5 g.) was carried out by means of acetic anhydride (25 c.c.) and a drop of sulphuric acid. The *acetyl* derivative crystallised from the solution after a few minutes and separated from benzene in long colourless rods, m. p. 172—173° (Found : C, 42·3; H, 3·4. $C_{10}H_9O_7N_3$ requires C, 42·4; H, 3·2%). The related *ethyl* ester could be obtained by the use of acetic anhydride without a catalyst; it crystallised from benzene in clusters of needles, m. p. 174° (Found : C, 44·9; H, 3·7; N, 14·2. $C_{11}H_{11}O_7N_3$ requires C, 44·5; H, 3·7; N, 14·1%). Ring closure of these esters was attempted under a variety of conditions, but it could not be effected and thus a long series of attempts to prepare 6 : 8-dinitro-2 : 4-dihydroxyquinoline failed.

6 : 8-*Dinitro*-2 : 5-*dihydroxyquinoline* (IV).—5-Aminocarbostyril has been prepared by Claus and Setzer (*J. pr. Chem.*, 1896, **53**, 392),

but the method was modified in some details. 5-Nitrocarbostyril (10 g.) was mixed with hydrated stannous chloride (36 g.) and concentrated hydrochloric acid (70 g.). After boiling for a few minutes, the solution was concentrated, then diluted, and tin eliminated as sulphide. The filtrate was again concentrated until crystals separated from the hot liquid. After cooling and keeping, the hydrochloride was isolated (6·5 g.); it crystallised in long colourless rods and gave a deep brownish-red coloration with ferric chloride in aqueous solution.

Sodium nitrite (4 g.), dissolved in water (10 c.c.), was gradually added to a stirred solution and suspension of 5-aminocarbostyril hydrochloride (9 g.) in water (100 c.c.) and nitric acid (20 c.c., *d* 1·42) cooled to 0°. The mixture was kept at 0° for 1 hour and then heated on the steam-bath for 2 hours; nitrogen was evolved at about 70°. An almost black, resinous substance which separated was collected and dissolved in acetic acid; the solution deposited crystals and, after several recrystallisations, 6 : 8-*dinitro*-2 : 5-*dihydroxyquinoline* was obtained in pale yellowish-brown prisms, m. p. 260° (decomp.). A small additional amount was obtained from the reaction mother-liquor and had m. p. 261° (decomp.) (Found : C, 43·2; H, 2·3. $C_9H_5O_6N_3$ requires C, 43·0; H, 2·0%). The substance is moderately readily soluble in alcohol, acetone, ethyl acetate, and water and sparingly soluble in chloroform, benzene, ether, and light petroleum. The aqueous solution is golden-yellow, and the solution in cold aqueous sodium carbonate is yellow. With aqueous sodium hydroxide, a deep red salt is produced; this dissolves to an orange-red solution on heating.

When the substance was refluxed with fifteen times its weight of nitric acid (*d* 1·5) for 3 hours, a small amount of styphnic acid, m. p. 175°, was produced.

The reduced acid solution is not fluorescent and develops a bright red colour on the addition of ferric chloride.

The derivative obtained on acetylation with boiling acetic anhydride for 10 minutes crystallised from alcohol in clusters of very pale yellow needles, m. p. 178°.

6 : 8-*Dinitro*-2 : 7-*dihydroxyquinoline* (V).—Decker (*J. pr. Chem.*, 1901, **64**, 99) recorded meagre details of his preparation of 7-nitrocarbostyril and did not state the yield. Following his method as closely as possible, we found this to be 23%; under the following conditions, the yield is about 60%.

A solution of 7-nitroquinoline (22 g.) in water (1600 c.c.), boric acid (160 g.), and sulphuric acid (5 c.c.) was added to water (4400 c.c.) and heated on the steam-bath until a clear solution resulted. Fresh bleaching powder (200 g.) was digested with water (900 c.c.)

for 24 hours, and the filtered solution added to the nitroquinoline solution. After 24 hours, the precipitate was collected and boiled for 5 minutes with a solution of sodium hydroxide (14 g.) in water (1100 c.c.). Acidification of the alkaline filtrate afforded a voluminous precipitate of the carbostyril. The reduction was carried out like that of the isomeride (above), and the diazotisation, decomposition and simultaneous nitration were also similar to those already described. Here, however, the black resin yielded nothing, and the filtrate from it, after being heated for a further period, was cooled and kept. The yellow solid that separated was collected, washed, and dried; it then crystallised from benzene in glistening yellow plates that gradually darkened on heating and had m. p. 207—208° (decomp.), exploding a few degrees higher. The results of analyses indicated a composition midway between that of a mono- and of a di-nitro-derivative. Accordingly, the product (1 g.) was dissolved in sulphuric acid (5 c.c.), and potassium nitrate (2 g.) added slowly with stirring. The mixture was poured into water (25 c.c.), and the precipitate crystallised several times from aqueous acetic acid, giving glistening, pale orange parallelipipeds, which darkened on heating but did not melt below 310°. At higher temperatures, explosion occurred, and for this reason no analysis by combustion could be performed. By using a very large excess of copper oxide, a Pregl–Dumas estimation of nitrogen could be carried out (Found : N, 16·6. $C_9H_5O_6N_3$ requires N, 16·7%).

The substance is soluble in hot water to a yellow solution, and in this respect and in other solubility properties and colour reactions with alkalis it resembles the dinitro-2 : 5-dihydroxyquinoline described above.

The decomposition to styphnic acid was more facile than with the isomeride and could be effected by boiling the substance (0·5 g.) under reflux with nitric acid (5 c.c., *d* 1·5), acetic acid (5 c.c.), and water (5 c.c.) for ½ hour. The liquid was evaporated to dryness, and the residue extracted with ether; the resulting styphnic acid had m. p. 174—175°. This treatment does not change dinitro-2 : 5-dihydroxyquinoline to any appreciable extent.

3-*Nitroanisic Acid and Derivatives.*—The conditions for the nitration of *p*-tolyl carbonate (D.R.-P. 206,638) were modified.

A mixture of nitric acid (102 g., *d* 1·5) and sulphuric acid (265 g.) was gradually added to a stirred solution of *p*-tolyl carbonate (181 g.) in sulphuric acid (1200 c.c.) kept below 20°. After 5 hours, the product was isolated and hydrolysed; the yield of the nitrocresol was 75%.

3-Nitroanisic acid has been obtained by Simonsen and Rau (J., 1917, **111**, 235) by a series of reactions from 2-nitroanisic acid.

It can also be prepared by oxidation of 2-nitro-*p*-tolyl methyl ether in 35% yield. 2-Nitro-*p*-tolyl methyl ether (100 g.) was refluxed with a solution of potassium permanganate (120 g.) in water (2500 g.), further quantities of permanganate (180 g.) being introduced in the course of 5 hours and the boiling continued for 2 hours more. The acid, isolated in the known manner, crystallised from acetic acid in white hexagonal prisms, m. p. 195—196° (Found : C, 48·6; H, 3·9. Calc. for $C_8H_7O_5N$: C, 48·7; H, 3·6%).

Hydrogen chloride was the catalyst used in the preparation of the *ethyl* ester, which crystallised from alcohol in colourless plates, m. p. 71—72° (Found : C, 53·2; H, 5·0. $C_{10}H_{11}O_5N$ requires C, 53·3; H, 4·9%).

The *chloride* was obtained by boiling the acid (50 g.) for 3 hours with pure thionyl chloride (140 c.c.). The yield was 53 g. and the derivative crystallised from light petroleum in small white tablets, m. p. 56° (Found : C, 44·3; H, 2·9. $C_8H_6O_4NCl$ requires C, 44·5; H, 2·8%).

2-*Nitro*-4-*methoxybenzoylpyruvic Acid*,

$$NO_2\cdot C_6H_3(OMe)\cdot CO\cdot CH_2\cdot CO\cdot CO_2H.$$

—2-Nitroanisoyl chloride was brought into reaction with an equimolecular quantity of ethyl sodioacetoacetate in dry ethereal solution and suspension; the mixture was refluxed for 1 hour. The oily product gave a *potassium* salt which crystallised from alcohol in bright yellow leaflets (Found : K, 11·0. $C_{14}H_{14}O_7NK$ requires K, 11·2%). The regenerated ester (25 g.) was refluxed for 8 hours with a mixture of sulphuric acid (50 g.) and water (100 c.c.), and about 6 g. of 2-nitro-4-methoxyacetophenone were isolated from the mixture as a yellowish-brown oil. This ketone (5 g.) and then ethyl oxalate (7 g.) were added with shaking and cooling to a solution of sodium (3 g.) in alcohol (100 c.c.). After 24 hours, water (500 c.c.) was introduced, and the filtered liquid acidified with hydrochloric acid. On keeping, a pale brown, flocculent substance was deposited which crystallised from benzene–light petroleum in almost colourless, feathery needles, m. p. 161° (yield, 65%) (Found : C, 49·4; H, 3·6. $C_{11}H_9O_7N$ requires C, 49·4; H, 3·4%).

The *acid* is readily soluble in most organic solvents with the exception of light petroleum. It gives a bright yellow solution in aqueous sodium hydroxide and a deep reddish-brown ferric chloride reaction in alcoholic solution. Reduction with alkaline hydrosulphite, followed by oxidation, gave a bluish-green precipitate of dimethoxyindigotin.

4-*Hydroxy*-7-*methoxyquinoline*-2-*carboxylic Acid* (7-Methoxykynurenic Acid) (VI).—A hot solution of crystallised ferrous sulphate (40 g.) in water (80 c.c.) was slowly added to one of 2-nitro-4-meth-

oxybenzoylpyruvic acid (10 g.) in water (100 c.c.) and aqueous ammonia (60 c.c., *d* 0·880). The liquid was heated for ½ hour on the steam-bath and filtered hot, and the precipitate washed with boiling dilute aqueous sodium carbonate. The combined filtrates were acidified, and the whole process was repeated on the isolated solid. The crude acid was boiled with acetic acid (50 c.c.), and the residue crystallised from a much larger volume of the same solvent, affording microscopic needles (2 g.), m. p. 278° (decomp.) (Found : C, 60·0; H, 3·8. $C_{11}H_9O_4N$ requires C, 60·3; H, 4·1%). The *acid* is extremely sparingly soluble in the usual organic solvents. Its solution in sulphuric acid is yellow, and in alkaline solution it couples with benzenediazonium chloride to a red azo-compound.

3(or 8)-*Nitro*-7-*methoxykynurenic Acid*.—A solution of 7-methoxykynurenic acid (0·5 g.) in nitric acid (5 c.c., *d* 1·5) was stirred for 15 minutes, heated at 30° for 10 minutes, cooled, and poured into water. The derivative crystallised from acetic acid in clusters of almost colourless needles, m. p. 250° (decomp.) (Found : N, 10·5; MeO, 11·3. $C_{11}H_8O_6N_2$ requires N, 10·6; 1MeO, 11·7%). The *acid* is soluble in alcohol, moderately readily soluble in acetone, chloroform and ether, and very sparingly soluble in other organic solvents of low b. p. It gives bright yellow alkaline solutions.

3 : 6 : 8-*Trinitro*-7-*methoxykynurenic Acid*.—A solution of 7-methoxykynurenic acid (0·5 g.) in nitric acid (5 c.c., *d* 1·5) was refluxed for 1 hour and then evaporated to dryness on the steam-bath; the residue crystallised from acetic acid in colourless, nearly rectangular prisms, which darkened but did not melt below 310° (Found : N, 15·8; MeO, 8·8. $C_{11}H_6O_{10}N_4$ requires N, 15·8; 1MeO, 8·8%). This *trinitromethoxykynurenic acid* is moderately readily soluble in alcohol, acetone, or ethyl acetate, but is almost insoluble in other usual solvents. The solution in aqueous sodium carbonate is pale yellow, and the yellow solution in cold aqueous sodium hydroxide almost immediately deposits a yellow sodium salt.

A number of experiments were made on the exhaustive nitration of decarboxylated 7-methoxykynurenic acid and specimens undoubtedly containing 3 : 6 : 8-trinitro-7-methoxyquinoline were obtained. These did not show the characteristic behaviour of trinitrostrychol towards hot aqueous sodium hydroxide, and we are convinced that the trinitro-4 : 7-dihydroxyquinoline derivatives are more stable than trinitrostrychol.

6-*Nitrosalicylaldehyde* (VII).—Chloroform (24 c.c.) was added to a solution of *m*-nitrophenol (30 g.) in water (200 c.c.) and sodium hydroxide (40 g.), and the mixture refluxed for 1 hour. After removal of the excess of chloroform, the solution was acidified with sulphuric acid and distilled in steam. The pale yellow solid (yield,

3%) in the distillate crystallised from light petroleum or methyl alcohol in pale yellow prisms, m. p. 54—55° (Found : N, 8·6. $C_7H_5O_4N$ requires N, 8·4%). The sodium salt was orange-red, and the ferric chloride coloration in alcoholic solution was reddish-brown. The salicylaldehyde configuration was confirmed by applying Dakin's reaction, a substance giving pyrocatechol-type reactions being obtained in small yield.

Methylation by means of methyl sulphate and sodium hydroxide yielded the *methyl* ether, which crystallised from carbon tetrachloride in colourless plates or needles, m. p. 111° (Found : C, 52·9; H, 3·9. $C_8H_7O_4N$ requires C, 53·0; H, 3·9%). This methoxy-*o*-nitrobenzaldehyde gave a bulky, deep blue precipitate of dimethoxyindigotin (dark brownish-purple lustre) when cold aqueous sodium hydroxide was added to its solution in acetone.

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