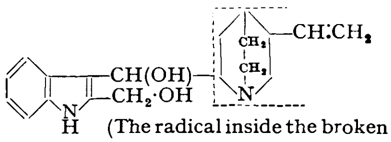
232. *Quinamine. Part IV. Sulphobenzeneazoquinamine and Nitration and Oxidation of Quinamine to 3 : 6 : 8-Trinitro-4-hydroxyquinoline.*

By (Miss) G. Bendz, C. C. J. Culvenor, L. J. Goldsworthy, K. S. Kirby and Sir Robert Robinson.

It has been established that quinamine does not contain an aromatic indole nucleus, since it couples with diazobenzenesulphonic acid to form a compound of methyl-orange type. The strongly acid range for this indicator shows that the N(*a*) of quinamine is very weakly basic. This is apparent also from the electrometric titration of quinamine. The product of the action of nitric acid on the alkaloid, which is obtained in small yield, is found to be 3 : 6 : 8-trinitro-4-hydroxyquinoline. A description of the synthesis of this substance, as well as of related work of a preliminary character is included. *iso*Quinamine exhibits a close resemblance in colour and fluorescence to 4-ketotetrahydroquinoline and must be similarly constituted. The chemistry of quinamine is discussed.

In a previous communication (Part II, *J.*, 1945 528) one of us proposed the formula (I) for quinamine. While the evidence for the quinuclidine portion of the molecule was conclusive, that for the aromatic indole nucleus was based on various colour reactions and the formation of 2 : 3-dimethylindole in degradations at elevated temperature.



(The radical inside the broken line is denoted Qn below.) (I).

It has now been found that quinamine couples in weakly acid solution with diazobenzenesulphonic acid, forming a compound of methyl-orange type, and that several of its derivatives give indications of similar behaviour. It thus appears that the quinamine molecule does not contain an unreduced indole nucleus. In order to confirm this conclusion we have synthesised 2-methyl-3-2′-diethylaminoethylindole, which has a strongly basic group in the side-chain, corresponding to the quinuclidine basic centre in formula (I) for quinamine, and have found that it does not form a methyl-orange with diazobenzenesulphonic acid.

Reduction of the quinamine methyl-orange with stannous chloride and hydrochloric acid gave a substance whose colour reactions were those typical of *p*-aminodialkylanilines.

The indicator change from yellow to red of the methyl-orange takes place between pH 1·5 and pH 0·7. For comparison, the indicator ranges for the methyl-oranges from methylstrychnine and diphenylamine were measured and found to be pH 2·6—1·3 and pH 2·9—1·4, respectively. It is clear that the N(*a*) basic centre of quinamine is extremely weak. We were not surprised, therefore, to find that the electrometric titration curve for quinamine, unlike those for cinchonine and quinine, showed no inflexion at the point corresponding to the neutralisation of the second basic group. It has, however, been found that the curves for tetrahydrostrychnine and strychnidine also show no corresponding inflexion.

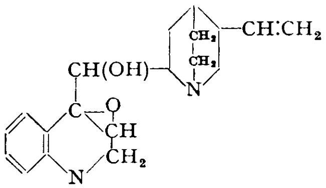
It would appear that the N(*a*) of these substances, known to be present in a hydroindole nucleus, is also very weakly basic indeed, and a 2 : 3-dihydroindole constitution for quinamine is evidently not excluded.

We have observed a very striking resemblance between the colour and fluorescent properties of *iso*quinamine (Part III, *J.*, 1949, 735) and the 4-ketotetrahydroquinoline, which strongly suggests a similarity in structure. Both are bright yellow substances, which give yellow solutions with a vivid green fluorescence in alcohol, and colourless solutions with a violet fluorescence in benzene. With this in mind we have considered (II) as a possible formula for quinamine (Festschrift Paul Karrer, Zürich, 1949), because it was in fair accord with the known chemistry of the alkaloid, including the coupling reaction, and at the same time offered a plausible explanation of the isomeric change to an *iso*quinamine having the tetrahydro-4-quinolone structure (III). Moreover, preliminary work on the infra-red absorption of quinamine by H. W. Thompson showed that a carbonyl group was not present in the molecule.

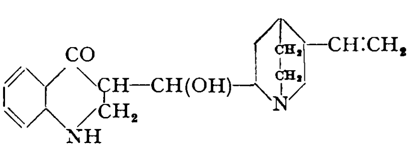
This suggestion was made very provisionally, the phrase actually used being that " we were toying with the idea." We also contemplated the possibility of a hydroindole constitution.

It occurred to us that a closer study of the compound $C_9H_4O_7N_4$, which was obtained by simultaneous nitration and oxidation of quinamine (Part II, *loc. cit.*), might give further information. The dinitronitrosoindole-2-carboxylic acid structure proposed for this substance seemed unsatisfactory for several reasons, and an intriguing possibility was the inversion of the error made in the study of the nitration–oxidation of strychnine.

Dinitrostrycholcarboxylic acid was once thought to be a dinitrodihydroxyquinolinecarboxylic acid. It is actually dinitroindoledicarboxylic acid. Could it be that the quinamine product, thought to be a dinitro-nitroso-indole-carboxylic acid is really a trinitrohydroxyquinoline?



(II.)



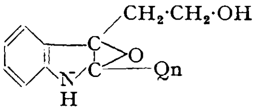
(III.)

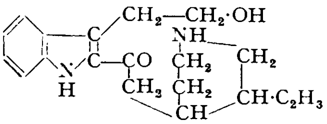
The most likely isomerides of this type were considered to be 4 : 6 : 8-trinitro-3-hydroxyquinoline and 3 : 6 : 8-trinitro-4-hydroxyquinoline and accordingly we undertook the syntheses of these substances. Eventually we succeeded in making the second compound, and found that it was in fact identical with the substance $C_9H_4O_7N_4$ obtained from quinamine.

This work is described below and its outcome appeared at first to strengthen the case for consideration of formula (II). Nevertheless, the quinoline nucleus may have been formed by molecular rearrangement from an indole derivative and a suggestion made to us in a private communication by Professor V. Prelog concerns a constitution which has affinities with (I) and (II) as well as entirely novel features. This formula (IV) is based on highly important fresh evidence that will be disclosed by Professor Prelog in the near future.*

At this stage we may note that it implies the structure (V) for quinamicine and (VI) for *iso*quinamine. The necessary transformation of (IV) into (VI) is of normal type, though the reagent (sodium amyl oxide) is unusual.

(IV.)





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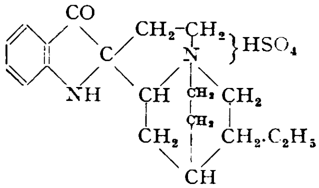
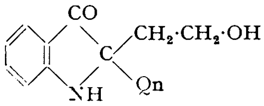


(VII.)

(VI.)



The anhydro*iso*quinamines (Part III, *loc. cit.*) have only been isolated as salts; they are now found to be quaternary salts (VII, for example from dihydro*iso*quinamine) and their solutions give no precipitate on the addition of ammonia. The formula (VI) gives scope for stereoisomeric *iso*quinamines, which have already been isolated (cf. Part III).

According to Prelog, apoquinamine should be (VIII) and this formulation clears up its relation to quinamine very satisfactorily.

In collaboration with Dr. S. G. P. Plant a revision of certain structural formulæ previously advanced for derivatives of tetrahydrocarbazole has been proposed (note submitted to *Nature*). This has involved the recognition that the substance previously regarded as ψ-indoxyl*spirocyclo*pentane (IX) is actually oxindole*spirocyclo*pentane and the so-called 11-hydroxytetrahydrocarbazolenine (Perkin and Plant, *J.*, 1923, **123**, 676) is indeed the indoxyl derivative (IX). These observations removed all difficulties for the formula (VI) for *iso*quinamine.

Both *iso*quinamine and the " hydroxytetrahydrocarbazolenine " (really IX) fail to exhibit the least positive reaction for the groups $-CO{\cdot}CH_2-$ and $-CO{\cdot}CH{:}$ with the sensitive *m*-dinitro-

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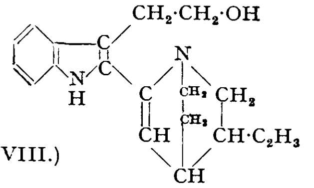
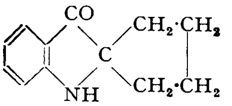
* *Added in proof.* Now published (Goutard, Janot, Prelog, and Taylor, *Helv. Chim. Acta*, 1950, **32**, 150; Taylor, *ibid.*, p. 164).

benzene–alkali test in methanolic solution. The tinctorial and fluorescence properties of these two substances are identical.



(VIII.)



(IX.)

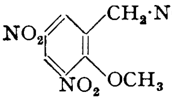
Preparation of Various Nitro-hydroxyquinolines.—The synthesis of the trinitro-3-hydroxyquinoline was first attempted by direct nitration of 3-hydroxyquinoline, but no pure product could be isolated. Nitration of 3-acetamidoquinoline also failed to give the desired product. This substance, which yields a mononitro-derivative on treatment with concentrated sulphuric and fuming nitric acids in the cold (Renshaw and Friedman, *J. Amer. Chem. Soc.*, 1939, **61**, 3320), was for the most part destroyed when the nitration was carried out at 60°, although a very small amount of a mononitrohydroxyquinoline was isolated. More vigorous conditions led to no isolable product.

The use of 3-hydroxy-1 : 2 : 3 : 4-tetrahydroquinoline appeared to offer some advantages, since it was expected that dinitration in the benzene ring would occur with ease, and could be followed by aromatisation of the pyridine ring. However, this substance and its 1-methyl derivative were found to be extremely sensitive to concentrated nitric acid and no homogeneous nitration product could be isolated. It is probable that the hydropyridine ring is opened with subsequent degradation. Since the 1-methyl derivative is very easily prepared by condensation of epichlorohydrin and methylaniline (Lange, G.P. 619,825; Davies and Savige, private communication), it was considered as a precursor of 3-hydroxy-1 : 2 : 3 : 4-tetrahydroquinoline, but attempts to remove the methyl group were unsuccessful. Quinoline was the only substance isolated from thermal decomposition of the hydriodide, while reaction with cyanogen bromide led chiefly to fission of the pyridine ring.

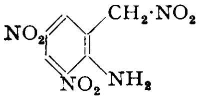
Attempts to replace the halogen of 3-bromo-6 : 8-dinitroquinoline by an amino- or phenoxy-group led to black infusible products. The substance combines with sodium ethoxide to form a nitronium salt, and this reactivity of dinitrobenzene type may well account for the extensive decomposition on treatment with bases.

From 3-bromo-6-nitroquinoline, 3-amino-6-nitroquinoline is readily obtained, but nitration of the acetyl derivative of this base was fruitless.

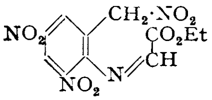
It became clear that 4 : 6 : 8-trinitro-3-hydroxyquinoline could not readily be obtained by nitration procedures; accordingly a synthesis was initiated which involved the closing of the pyridine ring subsequent to the introduction of the three nitro-groups. The intermediate required for this synthesis was 4 : 6-*dinitro-2-nitromethylaniline* (XI), which by condensation with chloral or ethyl glyoxylate might be expected to give the compound (XII) (after subsequent hydrolysis in the case of chloral). Ring closure of (XII) might then give the desired trinitrohydroxyquinoline.



(X.)



(XI.)



(XII.)

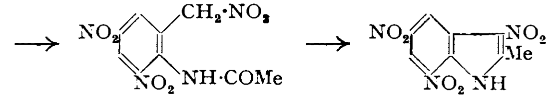
The preparation of (XI) was effected in the following way. 4-Nitro-2-chloromethylanisole, obtained by chloromethylation of *p*-nitroanisole, was converted successively into 4-*nitro-2-iodomethylanisole*, and 4-*nitro-2-nitromethylanisole*. Nitration of the latter yielded 4 : 6-*dinitro-2-nitromethylanisole* (X), which was readily converted by aqueous ammonia into (XI). The position assumed by the second nuclear nitro-group in (X) was proved by nitric acid oxidation of the compound to 3 : 5-dinitro-2-methoxybenzoic acid.

In the reaction of 4-nitro-2-iodomethylanisole with silver nitrite 4-*nitro-2-hydroxymethylanisole* was obtained as a by-product, owing probably to the presence of some silver oxide in the silver nitrite. It was found that (XI) was quite inert towards chloral under neutral or acid conditions and that, although there was a reaction with ethyl glyoxylate, the product could not be isolated.

On treatment with acetic anhydride, (XI) afforded 3 : 5 : 7-*trinitro-2-methylindole* (XIII).

This was not identical with the 3 : *x* : *x*-trinitro-2-methylindole of Mathur and Robinson (*J.*, 1934, 1415) and hence the latter is probably the 3 : 4 : 6-trinitro-derivative.

(XI)



(XIII.)

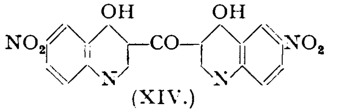
The above synthesis is of interest as an example of the dehydration of an *o*-acylaminotoluene in which a methylene group is activated; the method is capable of extension.

In a final attempt to effect the desired synthesis we treated the anisole derivative (X) successively with potassium and ethyl aminoacetate but although it is probable that the expected products, 4 : 6-dinitro-2-nitromethylanilinoacetic acid and its ethyl ester, were actually formed they were not isolable, and attempted ring-closure with the crude materials was unsuccessful.

Further work on the 3-hydroxyquinoline series was abandoned when our objective was reached by parallel experiments in the 4-hydroxyquinoline series.

In early experiments directed towards the synthesis of 3 : 6 : 8-trinitro-4-hydroxyquinoline, we examined the action of nitric acid on *N*-acyl derivatives of 4-ketotetrahydroquinoline (Clemo and Perkin, *J.*, 1924, **125**, 1608). It was found that the toluene-*p*-sulphonyl and acetyl derivatives of 4-ketotetrahydroquinoline, when heated with concentrated nitric acid in acetic acid solution, gave the same product, a sparingly soluble micro-crystalline compound, $C_{19}H_{10}O_7N_4$, of high melting point and nitrophenolic character. The composition suggests the formula (XIV) though it is extremely difficult to see how it comes about that such a substance is formed under the conditions of the experiment.

4-Hydroxyquinoline, heated with mixed acids, gave a *dinitro*-4-*hydroxyquinoline*, differing in this respect from 2-hydroxyquinoline which forms a trinitro-derivative under the same conditions. Suspecting (wrongly, as it turned out) that the dinitro-derivative was 6 : 8-dinitro-4-hydroxyquinoline, we attempted to establish its constitution synthetically by ring-closure of 5-*nitro*-2-*formamidoacetophenone* (XV) to 6-nitro-4-hydroxyquinoline, followed by nitration of the product. However, treatment of 5-nitro-2-formamidoacetophenone with aqueous-alcoholic sodium hydroxide, under conditions similar to those employed by Camps (*Ber.*, 1901, **34**, 1709) in his synthesis of 4-hydroxyquinoline from *o*-aminoacetophenone, did not give the expected product, but a crystalline substance whose composition suggested that it was 6-*nitro*-2-(5-*nitro*-2-*aminophenyl*)-4-*methylquinoline* (XVI), a dinitro-derivative of *iso*-flavanilin. The formation of this compound might be expected to take place by the action of the alkali in first splitting off the formyl group, and then converting the 5-nitro-2-amino-acetophenone into the dinitro*iso*flavanilin, just as this reagent converts *o*-aminoacetophenone into *iso*flavanilin itself (cf. Camps, *Ber.*, 1899, **32**, 3231). The correctness of this interpretation of the reaction was confirmed by the preparation of the same compound by the action of alkali on 5-nitro-2-aminoacetophenone.



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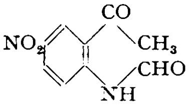

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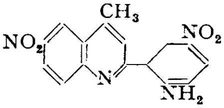


(XVI.)

While this work was in progress a note was published by Adams and Hey (*J.*, 1949, 255), in which they proved that the mononitro-4-hydroxyquinoline, made by nitrating 4-hydroxyquinoline with fuming nitric and sulphuric acids under the conditions described by Gouley, Moersch, and Mosher (*J. Amer. Chem. Soc.*, 1949, **69**, 303), is the 6-nitro-compound. We have prepared 6-nitro-4-hydroxyquinoline by following the procedure described in this note, and have converted it by nitration into the dinitro-derivative which we obtained by the direct nitration of 4-hydroxyquinoline. Although it seemed probable that the second nitro-group would enter the 8-position, it was found that the same dinitro-derivative was formed by the action of fuming nitric acid on 3-nitro-4-hydroxyquinoline, showing that in the nitration of 6-nitro-4-hydroxyquinoline the second nitro-group must have gone into the 3-position. This dinitro-compound, now shown to be 3 : 6-*dinitro*-4-*hydroxyquinoline*, was first prepared by Simpson and Wright (*J.*, 1948, 2023), who were uncertain of its structure, by dinitration of 4-aminoquinoline and replacement of the amino-group by hydroxyl.

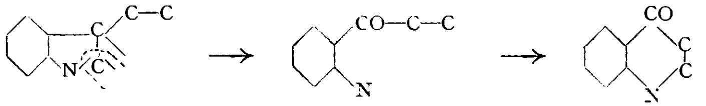
Measurements of the infra-red spectra of our three preparations have been used to demonstrate their identity.

It has long been known that 4-hydroxyquinaldine is nitrated in the 3-position by concentrated nitric acid (Conrad and Limpach, *Ber.*, 1887, **20**, 950), and we find that 4-hydroxyquinoline behaves similarly, giving 3-nitro-4-hydroxyquinoline, mixed with a second product, probably the 6-nitro-compound. 3-Nitro-4-hydroxyquinoline is the sole product when 45% nitric acid is employed. Further nitration of 3-nitro-4-hydroxyquinoline with mixed acid gives a trinitro-derivative, presumably 3 : 6 : 8-*trinitro*-4-*hydroxyquinoline*, m. p. 296° (decomp.), which is much more soluble and tractable than the mono- or the dinitro-4-hydroxyquinolines.

When our specimen of the compound, $C_9H_4O_7N_4$, isolated several years ago, was found to have deteriorated on keeping, the nitration–oxidation of quinamine was repeated (with modification of the final treatment and isolation) and the compound, m. p. 296° (decomp.), obtained in about 3% yield. Its properties were the same as those of 3 : 6 : 8-trinitro-4-hydroxyquinoline, admixture with which caused no depression of the melting point, and the characteristic infra-red spectra of the two compounds were identical.

In view of the above discussion this result is not now interpreted on the hypothesis that quinamine is a quinoline derivative. It seems certain that the quinoline nucleus is produced in the course of the complex processes that must occur in the nitric acid degradation. It is significant that similar nitration–oxidation of *iso*quinamine was found to yield no trace of the trinitrohydroxyquinoline.

The rearrangement of the substituted indoxyl is hardly feasible whereas the skeletal change in quinamine is that shown below.



EXPERIMENTAL.

p-*Sulphobenzeneazoquinamine*.—A cold solution of quinamine (1·56 g.) in N-hydrochloric acid (25 c.c.) was mixed with one of sulphanilic acid (1·86 g.) diazotised in the usual manner. The red pasty precipitate, which separated in a few hours, was collected and dissolved in aqueous sodium carbonate (65 c.c. of 10%), and the solution diluted with water (100 c.c.), filtered, and acidified with hydrochloric acid. The hydrochloride of the methyl-orange gradually separated in long, dark red needles. The free azo-sulphonic *acid* was obtained as a yellow precipitate by adding acetic acid to a solution of the sodium salt. It crystallized from hot water, in which it is very sparingly soluble, as orange-yellow, flat prisms (Found : C, 56·9; H, 5·7; N, 11·1; S, 6·3; loss at 130° in high vacuum over phosphoric anhydride, 4·2%. $C_{25}H_{28}O_5N_4S,1\cdot5H_2O$ requires C, 57·4; H, 5·4; N, 10·7; S, 6·1; $1\cdot5H_2O$, 5·2%).

The indicator ranges of the various sulphobenzene-azo-derivatives were approximately determined by adding solutions of the colouring matters to hydrochloric acid of known pH. Comparable, indeed almost identical, changes of yellow to red occurred as follows: S-B-A-quinamine, pH 1·5 to 0·7; S-B-A-methylstrychnine, pH 2·6 to 1·3; S-B-A-diphenylamine, pH 2·9 to 1·4. Red acid solutions of sulphobenzeneazomethylstrychnine become yellow on keeping, clearly as the result of the formation of sulphobenzeneazomethylstrychninium salts. In the latter N(*a*) is not aminic but amidic and the substance is not an indicator.

Reduction.—The free azo-sulphonic acid (1·2 g.) was shaken with stannous chloride (1·2 g.) and hydrochloric acid (10 c.c. of 1 : 1), and a pale yellow stanno-complex was formed. This was decomposed by the addition of water and zinc, and the filtered solution basified and extracted with ether. The reddish product was taken up in hot water and on cooling separated as a yellow precipitate which was collected and not further purified. The base showed colour reactions of a typical *p*-aminodialkylaniline derivative. With ferric chloride alone the colour produced was reddish-brown, whilst with ferric chloride and dimethylaniline it was blue. Ferric chloride and 2 : 4-diaminotoluene gave a blue-violet coloration, becoming red on warming (eurhodine formation). With ferric chloride and hydrogen sulphide a weak violet colour was developed.

Quinamine methochloride (Part I, *J.*, 1945, 526) also afforded a methyl-orange on coupling with diazobenzenesulphonic acid in an acid medium. This showed the typical indicator change at a low pH.

Electrometric Titration of Weak Bases, including Quinamine.—A solution of aniline hydrochloride has pH about 2 and the titration curve has one inflexion, being relatively flat near pH 4 (Hildebrand, *J. Amer. Chem. Soc.*, 1913, **35**, 859). The dissociation constants of aniline and quinoline are of the same order of magnitude, and the second dissociation constants of cinchonine and quinine are not very different, being one-half to one-third as great.

We have been able to reproduce the results of Schoorl (*Rec. Trav. chim.*, 1922, **41**, 228) who found a double inflexion of the titration curve of quinine, corresponding to neutralisation of basic centres in the regions of pH 6·1 and 3·5. Under similar conditions quinamine is disclosed as a much weaker base than quinine, for, whereas quinine monohydrochloride formed a solution of pH 6·1 (cinchonine sulphate, pH 6·35; cinchonine methochloride, pH 7·1), an equivalent solution of quinamine hydrochloride had pH 2·4. There was no inflexion on the curve (from pH 1·0) corresponding to the neutralisation of a second basic centre. The curve for *iso*quinamine was practically identical, as was also that for quinamine methochloride. The pH of a solution of the pure quinamine methochloride in water was 6·7, the contrast with quinamine hydrochloride being of course due to absence of salt hydrolysis. Cinchonine methochloride (pH 7·1) gave a strong inflexion the centre of which was at pH 3.

These contrasts did not seem to harmonise with the ability of quinamine and its methochloride to couple with diazo-salts which undoubtedly argued a degree of basic strength for N(*a*); but on titrating tetrahydrostrychnine and strychnidine it was found that no indication of the basicity of N(*a*) was observed down to pH 1·0. The flat part of the curve extends from near pH 2·5 to pH 8.

From these results we conclude that a hydroindole nitrogen is much more weakly basic than that of aniline or quinoline, and it would be consistent with these observations if quinamine were found to be a hydro-indole derivative.

2-*Methyl*-3-2′-*diethylaminoethylindole*.—A mixture of 1-diethylaminopentan-4-one (15·7 g.) and phenylhydrazine (10·8 g.), to which 2 drops of glacial acetic acid were added, was kept overnight and then heated on the steam-bath for an hour. A benzene solution of the phenylhydrazone was dried with potassium carbonate, the solvent removed by distillation, and the residue heated with zinc chloride (61 g.) at 180°. The product was steam-distilled, isolated by means of ether, and distilled as a yellow oil, b. p. 172—173°/3 mm., which solidified in contact with ether (Found : C, 78·4; H, 9·4; N, 12·0. $C_{15}H_{22}N_2$ requires C, 78·2; H, 9·6; N, 12·2%). The direction of ring-closure is indicated by the absence of a strong reaction with Ehrlich's reagent.

When a cold solution of the *indole* derivative (1·15 g.) in N-hydrochloric acid (25 c.c.) was added to a suspension of diazobenzenesulphonic acid (0·86 g.), a brown colour developed on long storage, but no methyl-orange was formed.

Nitration of 3-*Substituted Quinolines* (cf. Mills and Watson, *J.*, 1910, **97**, 753; Edinger, *J. pr. Chem.*, 1896, **54**, 358; Renshaw and Friedman, *J. Amer. Chem. Soc.*, 1939, **61**, 3320, for 3-bromoquinoline and 3-aminoquinoline). A solution of 3-acetamidoquinoline (5·5 g.) (Mills and Watson, *loc. cit.*), in concentrated sulphuric acid 25 c.c.) and nitric acid (15 c.c., *d* 1·5), was kept at 60° for ¾ hour, the temperature being maintained by the heat of the reaction, and then heated on the steam-bath with occasional shaking for 1½ hours; the mixture was cooled and added to ice. The brittle red product (1·55 g.) was crystallised several times from alcohol and yielded grey, micro-crystalline material (decomp. 300°) which appeared to be a mononitrohydroxyquinoline (Found : C, 56·8; H, 3·8; N, 14·6. Calc. for $C_9H_6O_3N_2$: C, 56·8; H, 3·2; N, 14·7%). A number of further experiments in this series gave unsatisfactory results and it was deemed necessary to resort to the nitration of 3-substituted hydroquinolines.

3-*Hydroxy*-1 : 2 : 3 : 4-*tetrahydroquinoline*.—Cavallito and Haskell (*J. Amer. Chem. Soc.*, 1944, **66**, 1169) prepared this compound in small amount by hydrogenating 3-hydroxyquinoline, using a palladium sponge catalyst. We have found that the reduction can be effected more easily by sodium and alcohol. Sodium (15 g.) was added to a boiling solution of 3-hydroxyquinoline (4·7 g.) in alcohol (94 c.c.) during 1½ hours. The mixture was diluted with water and concentrated, and the product isolated by means of ether. It crystallised from light petroleum (b. p. 60—80°) in colourless needles (1·6 g.), m. p. 87° (Found : C, 72·35; H, 7·9; N, 8·75. Calc. for $C_9H_{11}ON$: C, 72·5; H, 7·4; N, 9·4%). Cavallito and Haskell give m. p. 93°, but recrystallisation did not raise the m. p. of our specimen. Nitration of this substance under various conditions gave products that could not be purified and appeared to result from more or less profound decomposition.

3-*Hydroxy*-1-*methyl*-1 : 2 : 3 : 4-*tetrahydroquinoline*.—This base was obtained by condensation of epichlorohydrin with methylaniline by the procedure of Lange (*loc. cit.*) with slight modification. By heating the reaction mixture at 140—145° in an atmosphere of nitrogen for 10½ hours, and finally distilling at a lower pressure (1·5 mm. instead of 12 mm.) with a good column, the yield was increased by approx. 25%. The product was an extremely viscous oil, b. p. 130—133°/1·5 mm., which became dark blue on exposure to the air; the picrolonate crystallised from alcohol in clusters of orange needles, m. p. 182—183° (decomp.) (Found : C, 56·1; H, 5·2; N, 16·3. Calc. for $C_{10}H_{13}ON,C_{10}H_8O_5N_4$: C, 56·2; H, 4·9; N, 16·4%). Davies and Savige (private communication) gave m. p. 185° (decomp.). To ensure that the oil was a hydroxyquinoline derivative and not the isomeric ethylene oxide, it was treated with acetyl chloride, which would acetylate the former but add to the latter to form a chloroacetate. The oil (15 g.) was heated at 50° for ½ hour with an excess of acetyl chloride, and the mixture poured into water, neutralised with ammonia, and extracted with ether. The extract gave an oil, b. p. 137°/1 mm. (Found : C, 70·3; H, 7·6; N, 7·2. $C_{12}H_{15}O_2N$ requires C, 70·25; H, 7·3; N, 6·8%. $C_{12}H_{16}O_2NCl$ requires C, 59·6; H, 6·6; N, 5·9%). The substance is probably 3-*acetoxy*-1-*methyl*-1 : 2 : 3 : 4-*tetrahydroquinoline*. The action of nitric acid on this base led to no clear-cut results though a substance, possibly $C_8H_6O_5N_2$, was isolated after treatment first with dilute and then with concentrated nitric acid at 0°.

Attempted Demethylation of 3-*Hydroxy*-1-*methyl*-1 : 2 : 3 : 4-*tetrahydroquinoline*.—(1) A mixture of the base (16·3 g.) and hydriodic acid (30 g., b. p. 126°), after the removal of the excess of acid *in vacuo*, was distilled (bath at 300°). The red oil so obtained was found to consist of unchanged base (picrolonate, m. p. 177—178°) and quinoline (picrate, m. p. 199—200°, undepressed mixed m. p., and analysis) together with hydroquinolines.

(2) A mixture of the base (46 g.) and cyanogen bromide (33 g.) was heated until reaction began. The temperature remained at 40° for an hour, and some gas was evolved. After 12 hours the mixture was shaken with ether and water, and a solid residue (*A*, 6·3 g.) collected. The aqueous layer was extracted with ether, and the extract combined with the ether layer, dried, and distilled, b. p. 107—110°/1 mm. (Found : C, 58·3; H, 5·7; N, 8·1; Br, 25·05%). When kept, the oil rapidly decomposed with loss of hydrogen bromide, becoming dark red. It formed a picrolonate, orange prisms (from alcohol), m. p. 152—153° (decomp.) (Found : C, 50·1; H, 4·0; N, 14·3; Br, 15·8%). The solid (*A*) was halogen-free; it crystallised from alcohol as clusters of silvery needles, m. p. 204° (Found : C, 59·2; H, 6·2; N, 15·2%). It was soluble in dilute acid, reprecipitated by alkali, and very stable to heat.

3-*Bromo*-6 : 8-*dinitroquinoline*.—6 : 8-Dinitroquinoline was prepared from 2 : 4-dinitroaniline following van Dorp (*Rec. Trav. chim.*, 1904, **23**, 310), but using arsenic anhydride in place of arsenic acid (yield, 63%). It was brominated according to the method of Claus and Hartmann (*J. pr. Chem.*, 1896, **53**, 206) by heating the hydrobromide–perbromide in a sealed tube at 155°. The product was purified by passage of its solution in benzene through a column of alumina, on which the compound is visible as a bright orange absorbate. 6 : 8-Dinitroquinoline (32·2 g.) gave 3-bromo-6 : 8-dinitroquinoline (30·2 g.; 69%), which crystallised from alcohol as colourless needles, m. p. 158—159° (Found : C, 37·6; H, 1·6; N, 14·1; Br, 26·9. Calc. for $C_9H_4O_4N_3Br$: C, 36·2; H, 1·3; N, 14·1; Br, 26·85%). Claus and Hartmann (*loc. cit.*) record the m. p. as 120°, which was apparently an error. The compound exhibits very marked triboelectric effects, but only when pure. It forms a deep-red nitronium salt when treated with sodium ethoxide in alcoholic (or benzene) solution. Heating in a sealed tube at 100° for 20 hours with an excess of concentrated aqueous ammonia and a trace of copper sulphate gave an insoluble tar which still contained halogen. Reaction with potassium phenoxide under Ullmann's usual conditions also produced a tar.

3-*Bromo*-6-*nitroquinoline*.—The hydrobromide–perbromide of 6-nitroquinoline (47·3 g.) (prepared by Skraup synthesis as above; yield, 67%) was heated under reflux at 155—160° (oil-bath) for 1 hour. The mass soon liquefied, but after 30 minutes resolidified, some bromine and hydrogen bromide being evolved. The product, after trituration with water, was practically pure 3-bromo-6-nitroquinoline (59 g.), m. p. 164—166°, and, on neutralisation of the washings, 5·4 g. of 6-nitroquinoline were recovered (yield, based on 6-nitroquinoline used, 97%). A specimen of the bromonitroquinoline after passage of its benzene solution through alumina, had m. p. 169—170° (Claus and Hartmann, *loc. cit.*, gave m. p. 166°).

6-*Nitro*-3-*aminoquinoline*.—A mixture of 3-bromo-6-nitroquinoline (2 g.), copper sulphate (0·2 g.), and concentrated aqueous ammonia (8 c.c.) was heated in a sealed tube at 150° for 17 hours. The product was extracted with a large volume of benzene which on concentration deposited bright red needles, m. p. 249—250° (0·95 g., 63%) (Found : C, 57·2; H, 4·0; N, 22·6. $C_9H_7O_2N_3$ requires C, 57·1; H, 3·7; N, 22·3%). The substance is sparingly soluble in benzene and readily soluble in acetone. Refluxing the amine (0·85 g.) in acetic anhydride (4 c.c.) for 5 minutes and pouring the product into water gave the *acetyl* derivative (1·02 g., 98%), pale yellow needles (from water), m. p. 254° (Found : C, 57·1; H, 4·0; N, 17·9. $C_{11}H_9O_3N_3$ requires C, 57·15; H, 3·9; N, 18·2%).

4-*Nitro*-2-*chloromethylanisole*.—The procedure of Quelet (*Bull. Soc. chim.*, 1934, **1**, 539) for the chloromethylation of *p*-nitroanisole, using paraformaldehyde and hydrogen chloride, was found to give a poor yield. The following method is preferable. A mixture of *p*-nitroanisole (50 g.), di(chloromethyl) ether (50 g.), zinc chloride (9 g.), and carbon disulphide (100 c.c.) was refluxed for 9 hours and then cooled, and the organic layer separated (the addition of an equal volume of ether may be necessary since the cooled solution is supersaturated and crystallisation may commence during the working up), washed thoroughly with water, dried, and evaporated. Recrystallisation of the residue from a small volume of methanol yielded 4-nitro-2-chloromethylanisole, m. p. 77—79° (49·1 g., 74%).

4-*Nitro*-2-*iodomethylanisole*.—A solution of 4-nitro-2-chloromethylanisole (68·9 g.) and sodium iodide (57 g.) in acetone (400 c.c.) was refluxed for 20 minutes, cooled, and diluted with a large volume of water. The resulting 4-*nitro*-2-*iodomethylanisole* (96·2 g., 96%) was sufficiently pure for use in the next stage. A specimen was crystallised from alcohol and obtained as long, cream-coloured needles, m. p. 102—104° (Found : C, 33·3; H, 2·9; N, 4·4. $C_8H_8O_3NI$ requires C, 32·8; H, 2·7; N, 4·8%).

4-*Nitro*-2-*nitromethylanisole*.—4-Nitro-2-iodomethylanisole (66·8 g.) in ether (150 c.c.) and benzene (250 c.c.) was treated with powdered silver nitrite (50 g.), and kept at the room temperature for 3 days with occasional shaking. The filtrate from solids was evaporated and crystallisation of the residue from a little methanol gave 4-*nitro*-2-*nitromethylanisole* (39·1 g., 81%) as colourless needles, m. p. 93—94° (Found : C, 45·1; H, 3·6; N, 13·2. $C_8H_8O_5N_2$ requires C, 45·3; H, 3·8; N, 13·2%). Evaporation of the mother-liquor and crystallisation of the residue from benzene yielded 4-*nitro*-2-*hydroxymethylanisole* (5·8 g., 14%), pale yellow needles, m. p. 122—123° (Found : C, 52·4; H, 4·9; N, 7·6. $C_8H_9O_4N$ requires C, 52·6; H, 4·9; N, 7·7%). The use of mercurous nitrite, which is claimed by Neagi and Adhicary (*Z. anorg. Chem.*, 1911, **69**, 270) to give higher yields of phenylnitromethane from benzyl chloride than silver nitrite, resulted in a smaller yield in the present case, the product containing a higher proportion of 4-nitro-2-hydroxymethylanisole. 4-Nitro-2-nitromethylanisole is readily soluble in most organic solvents, insoluble in water, and it may be extracted from benzene or ether solution by dilute alkalis. Acidification of the alkaline solution with hydrochloric or acetic acid precipitates the nitro-, and not the *iso*nitro-compound, as shown by the melting point and absence of a ferric reaction. The nitromethane yields a sodium salt as glistening plates, when dissolved by gently heating with strong sodium hydroxide solution. When heated in a capillary tube over a flame, it explodes violently.

4 : 6-*Dinitro*-2-*nitromethylanisole* (X).—4-Nitro-2-nitromethylanisole (10·5 g.) was added slowly to an ice-cooled mixture of concentrated sulphuric acid (40 c.c.) and nitric acid (20 c.c., *d* 1·5), and the mixture kept at 0° for 45 minutes with intermittent shaking before being poured on ice. The 4 : 6-*dinitro*-2-*nitromethylanisole* (12·6 g., 99%) was precipitated as a solid only when the 4-nitro-2-nitromethylanisole used was quite pure, otherwise as an oil which solidified with difficulty even when seeded. It was very soluble in methanol, acetone, and benzene, somewhat less readily so in ethanol, insoluble in light petroleum, and it crystallised from methanol in colourless prisms, m. p. 65—66° (Found : C, 37·8; H, 2·9; N, 15·9. $C_8H_7O_7N_3$ requires C, 37·4; H, 2·7; N, 16·3%). It explodes violently when quickly heated in a capillary tube. Recrystallisation of a crude specimen was found to be very difficult, and an attempt to effect chromatographic purification was unsuccessful. Purification was best carried out by diffusion in the following way. The crude solid was placed in one arm of an inverted wide V-shaped tube, which was heated in a bath at 55°, and several crystals of the pure material were placed in the other arm, kept at room temperature, the tube being filled with a saturated alcoholic solution. After 24 hours most of the compound was deposited in the cold arm as pure, massive prisms.

The constitution of the compound was confirmed by its oxidation with nitric acid to 3 : 5-dinitro-2-methoxybenzoic acid. A mixture of the pure substance (0·15 g.) and nitric acid (3·5 c.c.; *d* 1·5) was heated in a sealed tube at 160° for 3 hours, then evaporated *in vacuo*, and the residue washed with a little water. The washed residue (2—3 mg.) was almost white, and had m. p. 156—158°, undepressed on admixture with 3 : 5-dinitro-2-methoxybenzoic acid (prepared by permanganate oxidation of 3 : 5-dinitro-2-methoxybenzaldehyde). When the reaction mixture was merely heated under reflux for 2 hours the 4 : 6-dinitro-2-nitromethylanisole was recovered unchanged. The aqueous washings were yellow, the colour being removed by concentrated hydrochloric acid, thus indicating the presence of picric acid.

4 : 6-*Dinitro*-2-*nitromethylaniline* (XI).—A solution of 4 : 6-dinitro-2-nitromethylanisole (1·2 g.) in concentrated aqueous ammonia (15 c.c.) was kept at the room temperature for 3 hours, then diluted with water, filtered, and neutralised with hydrochloric acid. 4 : 6-*Dinitro*-2-*nitromethylaniline* (1·0 g., 91%) separated; it crystallised from ethanol in clusters of golden needles, m. p. 164—166° (Found : C, 35·6; H, 2·6; N, 23·0. $C_7H_6O_6N_4$ requires C, 34·7; H, 2·5; N, 23·1%). The compound is freely soluble in acetone, readily so in alcohol, and sparingly soluble in benzene and ether. It explodes violently when heated in a capillary tube over a flame. 3 : 5 : 7-*Trinitro*-2-*methylindole* (XIII) was obtained when the nitro-amine was refluxed with an excess of acetic anhydride and a trace of sulphuric acid (but not with potassium acetate, which gives rise to a complex tarry product) for 5 minutes, and the product triturated with water. The substance crystallised from aqueous alcohol or dilute acetic acid in glistening plates, m. p. 205—206° (decomp.), consisting of a hydrate (Found, in dried material : C, 40·6; H, 2·2; N, 20·7. $C_9H_6O_6N_4$ requires C, 40·6; H, 2·3; N, 21·1%). Attempted oxidation of the indole to the 2-carboxylic acid (trinitrostrychol) was unsuccessful; it was unaffected by refluxing with selenium dioxide in acetic acid.

Nitration of N-*Toluene*-p-*sulphonyl*-4-*ketotetrahydroquinoline.*—A solution of *N*-toluene-*p*-sulphonyl-4-ketotetrahydroquinoline (0·75 g.) (Clemo and Perkin, *J.*, 1924, **125**, 1608) in acetic acid (5 c.c., 100%) was heated with nitric acid (7·5 c.c.; *d* 1·42) on the steam-bath for 1 hour. After addition to ice, the pale yellow product was collected and washed with water. Crystallisation from ethyl alcohol (240 c.c.) gave microscopic, very pale yellow, flat prisms, m. p. 335° (decomp.) (Found : C, 56·6; H, 3·1; N, 13·7. $C_{19}H_{10}O_7N_4$ requires C, 56·2; H, 2·5; N, 13·8%). The *substance* (XIV ?) gives a bright yellow solution in dilute alkali, from which it is precipitated by acid. It is very sparingly soluble in alcohol, and practically insoluble in boiling benzene.

Nitration of N-*Acetyl*-4-*ketotetrahydroquinoline.*—4-Ketotetrahydroquinoline (0·9 g.) (Clemo and Perkin, *loc. cit.*) was heated with acetic anhydride (2 c.c.) on the steam-bath for 15 minutes. On removal of the excess of acetic acid and acetic anhydride by evaporation under reduced pressure, a pale yellow oil was obtained; this solidified when cooled and rubbed. The *acetyl* derivative crystallised from methanol as thick prisms, m. p. 93° (Found : C, 69·7; H, 6·0; N, 7·2. $C_{11}H_{11}O_2N$ requires C, 69·8; H, 5·8; N, 7·4%).

N-Acetyl-4-ketotetrahydroquinoline (0·6 g.) was added during 45 minutes to a mechanically stirred mixture of concentrated sulphuric acid (0·6 c.c.) and nitric acid (3 c.c.; *d* 1·5) at 0° and the conditions were maintained for a further 45 minutes. After addition of ice the yellow solid was collected, washed, and dried *in vacuo* at room temperature (0·39 g.). The crude product, after crystallisation from ethyl acetate, in which it was easily soluble, had m. p. 110—115°. Recrystallisation from light petroleum (b. p. 60—80°) gave pale yellow prisms of a pure *mononitro*-derivative, m. p. 121° (Found : C, 56·4; H, 4·3; N, 12·0. $C_{11}H_{10}O_4N_2$ requires C, 56·2; H, 4·7; N, 11·5%). Presumably the nitro-group in this compound is in the 6-position. A second experiment was carried out under conditions similar to those employed in the nitration of *N*-toluene-*p*-sulphonyl-4-ketotetrahydroquinolinine. *N*-Acetyl-4-ketotetrahydroquinoline (0·1 g.) in acetic acid (1·0 c.c.) was heated with nitric acid (1·0 c.c.; *d* 1·42) on the steam-bath for 30 minutes. The pale yellow product crystallised from alcohol in nearly colourless, flat prisms, m. p. 335° (decomp.), agreeing in all respects with the compound $C_{19}H_{10}O_7N_4$, which was obtained by nitrating *N*-toluene-*p*-sulphonyl-4-ketotetrahydroquinoline.

Dinitration of 4-*Hydroxyquinoline.*—4-Hydroxyquinoline (Camps, *Ber.*, 1901, **34**, 2709) was conveniently made from 4-hydroxy-3-carboxyquinoline (Gould and Jacobs, *J. Amer. Chem. Soc.*, 1939, **61**, 2890). Decarboxylation was effected by heating the acid in paraffin oil in the manner described by Cavallito and Haskell (*loc. cit.*). 4-Hydroxyquinoline (0·1 g.) was heated with nitric acid (1·0 c.c.; *d* 1·5) and concentrated sulphuric acid (1·0 c.c.) on the steam-bath for an hour. On addition of the mixture to ice, a yellow, microcrystalline precipitate separated, and the substance crystallised from alcohol as very small rectangular prisms, m. p. 345° (decomp.) (Found : C, 45·8; H, 2·0; N, 17·1. $C_9H_5O_5N_3$ requires C, 46·0; H, 2·1; N, 17·9%). As explained in the introduction, this compound is 3 : 6-*dinitro*-4-*hydroxyquinoline*. It is sparingly soluble in all the usual organic solvents.

Nitration of 6-*Nitro*-4-*hydroxyquinoline.*—A mixture of 6-nitro-4-hydroxyquinoline (0·1 g.) (Gouley, Moersch, and Mosher, *J. Amer. Chem. Soc.*, 1947, **69**, 303; Adams and Hey, *J.*, 1949, 255), concentrated sulphuric acid (1·0 c.c.), and nitric acid (1·0 c.c.; *d* 1·5) was heated on the steam-bath for an hour. The product, isolated as usual, proved to be identical with the dinitro-4-hydroxyquinoline described above. Specimens of the two products, recrystallised from acetic acid as very small rectangular prisms, had the same m. p. and mixed m. p. 345° (decomp.), and identical infra-red spectra.

Attempted Synthesis of 6-*Nitro*-4-*hydroxyquinoline. Formation of Dinitro*iso*flavanilin* (XVI).—5-Nitro-2-aminoacetophenone (3 g.) (Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 649) was refluxed with anhydrous formic acid (30 c.c.) for an hour, and the mixture evaporated under reduced pressure. The pale yellow residue of 5-*nitro*-2-*formamidoacetophenone* (XV) crystallised from alcohol in needles, m. p. 149—150° (Found : C, 51·3; H, 3·8; N, 13·3. $C_9H_8O_4N_2$ requires C, 51·9; H, 3·8; N, 13·5%). A solution of the formyl derivative (0·34 g.) in alcohol (2 c.c.) and water (20 c.c.), to which sodium hydroxide (0·12 g.) was added, was refluxed for 3 hours, a yellow precipitate gradually separating. After cooling, this was collected, washed, and dried (0·25 g.). Crystallisation from alcohol (thin yellow prisms) and then from acetic acid gave greenish-white needles, m. p. 301° (block) (Found : C, 58·8; H, 3·5; N, 16·8. $C_{16}H_{12}O_4N_4$ requires C, 59·3; H, 3·7; N, 17·3%). The same 6-*nitro*-2-(5-*nitro*-2-*aminophenyl*)-4-*methylquinoline* was formed by the action of alkali on 5-nitro-2-aminoacetophenone. A solution of the latter (0·11 g.) in alcohol (0·6 c.c.) and water (7 c.c.), to which sodium hydroxide (0·04 g.) was added, was refluxed for an hour. A yellow precipitate was formed, which crystallised from acetic acid in greenish-white needles, m.p. 301° (block), undepressed on admixture with the compound described above.

Nitration of 4-*Hydroxyquinaldine.*—4-Hydroxyquinaldine (2·45 g.) was dissolved in nitric acid

(10 c.c.; *d* 1·5) and concentrated sulphuric acid (20 c.c.) and heated for 4 hours at 100°. Cooling and pouring on ice gave the *dinitro*-derivative (3·0 g.; 78%), which crystallised from acetic acid in colourless very small needles, m. p. 338° (decomp.) (Found: C, 47·8; H, 2·8; N, 16·8. $C_{10}H_7O_5N_3$ requires C, 48·2; H, 2·8; N, 16·9%). The compound is very sparingly soluble in the usual solvents and forms a sparingly soluble sodium salt. It is extensively decomposed on boiling with aqueous sodium hydroxide and it could not be methylated by means of diazomethane.

3-*Nitro*-4-*hydroxyquinoline*.—This compound was prepared from anthranilic acid and methazonic acid by the method of Musajo (*Gazzetta*, 1937, **67**, 222), and also as follows. A mixture of 4-hydroxyquinoline (0·5 g.), nitric acid (4 c.c.; 75% w/w), and water (2 c.c.) was refluxed for 1½ hours and then added to water. The resulting yellow powder (0·35 g.) had m. p. 322° (decomp.); a mixture with the authentic 3-nitro-compound melted at 327° (decomp.). It was methylated by dissolution in water with one molecular proportion of potassium hydroxide and shaking with methyl sulphate; the product crystallised from methanol in needles, m. p. 215—217°, undepressed on admixture with authentic 3-nitro-4-methoxyquinoline. With concentrated nitric acid alone, 4-hydroxyquinoline gave a mixture of the 3-nitro-derivative with a second product (probably the 6-nitro-compound); the crude material had m. p. 285—295°.

Nitration of 3-*Nitro*-4-*hydroxyquinoline*.—A solution of 3-nitro-4-hydroxyquinoline (2 g.) in nitric acid (25 c.c.; *d* 1·5) was refluxed for 8 hours, and then poured into ice-water. The yellow powder (1·92 g.), m. p. 334° (decomp.), crystallised from acetic acid in very small prisms, m. p. 345° (decomp.) undepressed on admixture with specimens of the dinitro-4-hydroxyquinolines prepared from 4-hydroxy- and 6-nitro-4-hydroxy-quinoline. The infra-red absorption spectra of the specimens prepared by the three methods were examined in " Nujol " suspension and found to be identical.*

3 : 6 : 8-*Trinitro*-4-*hydroxyquinoline*.—A solution of 3-nitro-4-hydroxyquinoline (2 g.) in nitric acid (10 c.c.; *d* 1·5) and concentrated sulphuric acid (20 c.c.) was refluxed for 3½ hours, cooled, and added to ice. The washed and dried product (2·1 g., 71%) crystallised from acetone–alcohol as yellow, prismatic needles, m. p. 296° (decomp.) (Found: C, 38·6; H, 1·6; N, 19·6. $C_9H_4O_7N_4$ requires C, 38·6; H, 1·4; N, 20·0%). In contrast to the mono- and di-nitro-4-hydroxyquinolines, this trinitro-compound is readily soluble in acetone and moderately readily soluble in alcohol and ethyl acetate. In common with the mono- and dinitro-compounds, it forms a very sparingly soluble sodium salt, even in contact with sodium hydrogen carbonate solution. The formation of the slender needles of this derivative can be observed microscopically and is characteristic.

Nitrating Oxidation of Quinamine.—The reaction was carried out under the conditions previously employed by one of us (Part II, *loc. cit.*), but the product, before being worked up, was submitted to prolonged treatment with fuming nitric acid with a view to increasing the yield of the compound $C_9H_4O_7N_4$. Quinamine (10 g.) was treated with nitric acid (10 c.c. of 10% and 125 c.c., *d* 1·42), and the solution heated on a steam-bath for 48 hours. The nitric acid was removed by distillation *in vacuo*, and the residual syrup taken up in nitric acid (75 c.c.; *d* 1·5) and heated on a steam-bath for a further 24 hours before the nitric acid was again removed *in vacuo*. The residue was washed with cold water (50 c.c.), then with cold ethyl acetate (50 c.c.), and the residue crystallised from acetone, in which, when hot, it was completely soluble. The aqueous, the ethyl acetate, and the acetone extracts all afforded the same product (total yield, 0·37 g.), the purest sample being that deposited from the aqueous washings on storage (0·11 g.). Recrystallisation from acetone–alcohol gave bright yellow, prismatic needles, m. p. 296° (corr. 307°) (decomp.). The m. p. previously recorded for the compound $C_9H_4O_7N_4$ from quinamine was 303—305° (corr.) (decomp.). A mixture of the compound with 3 : 6 : 8-trinitro-4-hydroxyquinoline had m. p. 296°. The solubilities and reactions of the two substances showed no divergencies, and their infra-red spectra were identical.

Attempted Nitration of iso*Quinamine*.—*iso*Quinamine (1·6 g.) was dissolved in 10% aqueous nitric acid (2 c.c.), and treated with concentrated nitric acid (20 c.c.), and later with fuming nitric acid (15 c.c.), following as closely as possible the procedure used for quinamine. The product after the final evaporation of the reaction mixture was triturated with water, and the residual brown gum was found to be completely soluble in a small volume of cold alcohol. No crystalline material could be isolated, and the amorphous product did not form a sparingly soluble sodium salt. After some days the aqueous washings deposited an amorphous yellow powder (2 mg.) which charred without melting when heated to 360°. We conclude that 3 : 6 : 8-trinitro-4-hydroxyquinoline was not formed in this experiment, even in traces.

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* We are obliged to Dr. J. C. E. Simpson for a specimen prepared by the method of Simpson and Wright (*loc. cit.*). This showed undepressed mixed m. p. with our specimens and had the same infra-red absorption spectrum.