349. *Nitrosoacylarylamines. Part V.* The Nitrosation of 3-Acetamido-4-quinolones and -quinaldones.*

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The alleged *O*-alkyl derivatives of substituted 4-hydroxyquinolines described by Colonna (*Gazzetta*, 1937, **67**, 46) are shown to be the corresponding *N*-alkyl derivatives. Whereas 3-amino-1-methyl-4-quinolone and its acetyl derivative are converted into 1-methyl-3-phenyl-4-quinolone by means of the triazen reaction or the nitrosoacetamido-derivative, respectively, the corresponding reactions with 3-amino-4-methoxyquinoline and its acetyl derivative fail. The nitrosation of 3-acetamido-1 : 2-dimethyl-4-quinolone gives a stable nitroso-derivative which is readily converted into 1-methylpyrazolo(4′ : 5′-2 : 3)-4-quinolone. 4-Hydroxy-3-phenylquinaldine is prepared by the cyclisation of ethyl β-anilino-α-phenylcrotonate.

The preparation of 3-phenylquinoline from 3-aminoquinoline by the decomposition in benzene solution of 3-*N*-nitrosoacetamidoquinoline and of 3 : 3-dimethyl-1-3′-quinolyltriazen has been previously described (Adams, Hey, Mamalis, and Parker, *J.*, 1949, 3181). These reactions have now been applied to derivatives of 3-amino-4-hydroxy-quinoline and -quinaldine. A suitable series of 4-alkoxy-derivatives of 3-aminoquinoline appeared to have been prepared by Colonna (*Gazzetta*, 1937, **67**, 46), who obtained them by the action of methyl sulphate or alkyl iodides on 4-hydroxy-3-nitroquinoline followed by reduction.

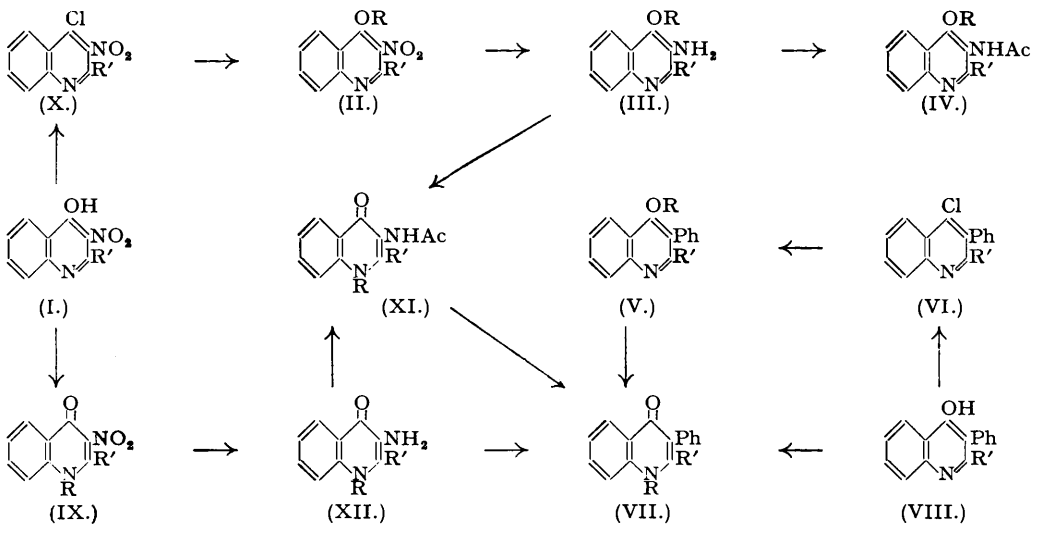
Treatment of 4-hydroxy-3-nitroquinoline (I; R′ = H) with methyl sulphate, as described by Colonna (*loc. cit.*), gave the alleged 4-methoxy-3-nitroquinoline (II; R = Me, R′ = H), which was converted by normal methods into the corresponding 3-amino- (III; R = Me, R′ = H) and 3-acetamido- (IV; R = Me, R′ = H) derivatives. The properties of these compounds were in agreement with those described by Colonna, although the melting point now recorded for the free base is the same as that recorded by Colonna for its hydrochloride, the constitution of which was not supported by analysis and which was reported to lose hydrogen chloride very

* Part IV, *J.*, 1940, 372.

readily. This alleged 3-amino-4-methoxyquinoline was then converted *via* the *N*-nitroso-acetamido-compound and the dimethyltriazen into a compound which gave a correct analysis for the expected 4-methoxy-3-phenylquinoline (V; R = Me, R′ = H) but which was not identical with 4-methoxy-3-phenylquinoline prepared by the action of sodium methoxide on 4-chloro-3-phenylquinoline (VI; R′ = H). The product was, however, identical with the isomeric 1-methyl-3-phenyl-4-quinolone (VII; R = Me, R′ = H) prepared by the action of methyl iodide and sodium methoxide on 4-hydroxy-3-phenylquinoline (VIII; R′ = H). The identity of the two isomeric methyl derivatives of 4-hydroxy-3-phenylquinoline was further confirmed by the conversion of 4-methoxy-3-phenylquinoline (V; R = Me, R′ = H) into 1-methyl-3-phenyl-4-quinolone (VII; R = Me, R′ = H) by heating its methiodide with 10% aqueous sodium hydroxide (cf. Knorr, *Ber.*, 1897, **30**, 922, 929; *Annalen*, 1903, **328**, 81).

This unexpected result necessitated a re-examination of the compounds described by Colonna (*loc. cit.*), since, unless some internal rearrangement had taken place in the course of his series of reactions, his starting materials must have been 1-alkyl-3-nitro-4-quinolones (IX; R′ = H) and not 4-alkoxy-3-nitroquinolines (II; R′ = H). It is known that, whereas alkylation of a 2- or 4-chloroquinoline with sodium alkoxides gives the *O*-alkyl derivative, alkylation of a 2- or 4-hydroxyquinoline with alkyl iodides (or with methyl sulphate) in the presence of alkali gives either an *O*- or an *N*-alkyl derivative, or a mixture of both, depending on experimental conditions and the presence of other substituents in the quinoline nucleus. It has been shown that, with 6- and 8-nitroquinoline and 5- and 8-nitroquinaldine, *O*-methyl derivatives are formed from the 4-chloro-compound, while *N*-methyl derivatives are obtained from the 4-hydroxy-compound (Halcrow and Kermack, *J.*, 1945, 415; Baker, Albisetti, Dodson, and Reigel, *J. Amer. Chem. Soc.*, 1946, **66**, 1532; Simpson and Wright, *J.*, 1948, 1707). In general, *O*-alkyl derivatives have lower melting points, are more soluble in organic solvents, and are less stable than the corresponding *N*-alkyl derivatives, into which they can in most cases be converted by heating, by treatment with alkali, or through the methiodides. The compounds prepared by Colonna could therefore have been either the *O*- or the *N*-alkyl derivatives but were assumed by him to be the former If his assumption is correct his compounds should be identical with the products obtained by the action of sodium alkoxides on 4-chloro-3-nitroquinoline.

4-Methoxy-3-nitroquinoline (II; R = Me, R′ = H), prepared by the action of sodium methoxide on 4-chloro-3-nitroquinoline (X; R′ = H), was not identical with the 4-methoxy-3-nitroquinoline described by Colonna (*loc. cit.*), and had a very much lower melting point and a greater solubility in alcohol. Attempts to prepare the corresponding amino-compound (III; R = Me, R′ = H) by reduction with stannous chloride and hydrochloric acid, as described by Colonna (*loc. cit.*) for his nitro-compound, were unsuccessful. 3-Amino-4-methoxyquinoline (III; R = Me, R′ = H) was, however, obtained by catalytic hydrogenation of the nitro-



compound, and was not identical with the amine described by Colonna (*loc. cit.*), to which this structure was assigned. Acetylation of this amine gave a compound which was identical with

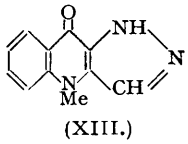
the acetyl derivative of the amine prepared as described by Colonna, and which had been shown to be the *N*-methylquinolone (XI; R = Me, R′ = H). This unexpected transformation to the quinonoid form during acetylation was confirmed when it was shown that acetylation under milder experimental conditions gave 3-acetamido-4-methoxyquinoline (IV; R = Me, R′ = H).

These investigations indicate that the methyl derivatives made by Colonna (*loc. cit.*) are actually 1-methyl-3-nitro-4-quinolone (IX; R = Me, R′ = H), 3-amino-1-methyl-4-quinolone (XII; R = Me, R′ = H), and 3-acetamido-1-methyl-4-quinolone (XI; R = Me, R′ = H), while those prepared in the course of the present work from 4-chloro-3-nitroquinolone are 4-methoxy-3-nitroquinoline (II; R = Me, R′ = H), 3-amino-4-methoxyquinoline (III; R = Me, R′ = H), and 3-acetamido-4-methoxyquinoline (IV; R = Me, R′ = H). Further, 4-ethoxy-3-nitroquinoline (II; R = Et, R′ = H), 3-nitro-4-*n*-propoxyquinoline (II; R = Pr^n, R′ = H), and 4-*n*-butoxy-3-nitroquinoline (II; R = Bu^n, R′ = H) were also prepared by the action of the corresponding sodium alkoxide on 4-chloro-3-nitroquinoline (X; R′ = H). These compounds were low-melting solids, different from those prepared by Colonna which must therefore be assumed to be the corresponding *N*-alkyl derivatives.

3-Amino-1-methyl-4-quinolone (XII; R = Me, R′ = H) was converted into 3 : 3-dimethyl-1-(1-methylquinol-4-on-3-yl)triazen and 1-methyl-3-*N*-nitrosoacetamido-4-quinolone was prepared by the action of nitrosyl chloride on 3-acetamido-1-methyl-4-quinolone (XI; R = Me, R′ = H). Decomposition of both these compounds in benzene solution gave 1-methyl-3-phenyl-4-quinolone (VII; R = Me, R′ = H), identified by comparison with an authentic specimen prepared by the action of methyl iodide on 4-hydroxy-3-phenylquinoline (VIII; R′ = H). Attempts to prepare similar derivatives of 3-amino-4-methoxyquinoline were unsuccessful. Treatment of 3-acetamido-4-methoxyquinoline (IV; R = Me, R′ = H) with nitrosyl chloride resulted in the recovery of unchanged starting material, and the product obtained by the reaction of diazotised 3-amino-4-methoxyquinoline (III; R = Me, R′ = H) with dimethylamine did not possess the properties of a triazen. It was therefore not possible to prepare 4-methoxy-3-phenylquinoline (V; R = Me, R′ = H) from 3-amino-4-methoxyquinoline (III; R = Me, R′ = H).

4-Hydroxy-3-nitroquinaldine (I; R′ = Me), prepared by the nitration of 4-hydroxyquinaldine by a modification of Halcrow and Kermack's method (*loc. cit.*), was converted in almost quantitative yield into 4-chloro-3-nitroquinaldine (X; R′ = Me) by gently warming it with phosphorus oxychloride (cf. Adams and Hey, *J.*, 1949, 3185). In preliminary work on the nitration of 4-hydroxyquinaldine an authentic specimen of the unknown 4-methoxy-6-nitroquinaldine became necessary; a preparation of this is described in the Experimental section. 4-Methoxy-3-nitroquinaldine (II; R = R′ = Me), 3-amino-4-methoxyquinaldine (III; R = R′ = Me), and 3-acetamido-4-methoxyquinaldine (IV; R = R′ = Me) were prepared from 4-chloro-3-nitroquinaldine (X; R′ = Me) as described for the corresponding compounds in the quinoline series. 4-Hydroxy-3-nitroquinaldine (I; R′ = Me) was recovered unchanged after being shaken for 18 hours with methyl sulphate in alkaline solution, but was alkylated by being heated with sodium methoxide and methyl iodide, and the 1 : 2-dimethyl-3-nitro-4-quinolone (IX; R = R′ = Me) was reduced and acetylated to give 3-amino-1 : 2-dimethyl-4-quinolone (XII; R = R′ = Me) and 3-acetamido-1 : 2-dimethyl-4-quinolone (XI; R = R′ = Me), as in the quinoline series.

The action of a solution of nitrosyl chloride in acetic anhydride on 3-acetamido-1 : 2-dimethyl-4-quinolone (XI; R = R′ = Me) gave 1 : 2-dimethyl-3-*N*-nitrosoacetamido-4-quinolone as a pale yellow powder, decomposing, without melting, at 131°, which was found to be unusually stable and could be exposed to the air for several weeks without undergoing decomposition. When a solution of this nitroso-compound in benzene was boiled under reflux there was no darkening and 1-methylpyrazolo(4′ : 5′-2 : 3)-4-quinolone (XIII) separated in almost quantitative yield from the hot solution as a yellow crystalline solid. This compound was also formed during the prolonged nitrosation of 3-acetamido-1 : 2-dimethyl-4-quinolone, thus confirming the non-participation of benzene in the reaction. The formation of this compound by cyclisation involving the nitroso-group and the *o*-methyl group is not unexpected. It is well-known that indazoles are obtained from diazotised *o*-toluidines and from *N*-nitrosoacyl-*o*-toluidines and the known reactivity of the 2-methyl group in the pyridine and quinoline series must render this type of reaction in the heterocyclic series extremely facile.



(XIII.)

The action of nitrosyl chloride on 3-acetamido-4-methoxyquinaldine (IV; R = R′ = Me) gave a yellow oil which did not appear to act normally. The abnormal behaviour of both 3-acetamido-4-methoxy-quinoline and -quinaldine in these reactions is unexpected. That such

behaviour is not entirely due to the *o*-methoxyl group in these benzenoid structures is indicated by the fact that *o*-anisidine reacts normally (as the diazonium salt) with pyridine to give a mixture of *o*-methoxyphenylpyridines in 50% yield (Haworth, Heilbron, and Hey, *J.*, 1940, 358), although in a reaction with 1-*o*-methoxyphenyl-3 : 3-dimethyltriazen and benzene 2-methoxydiphenyl was isolated in only 10% yield.

Although 4-hydroxy-3-phenylquinaldine derivatives could not be obtained by the reaction of derivatives of 3-aminoquinaldine with benzene, 4-hydroxy-3-phenylquinaldine itself (VIII; R′ = Me) was made available in small yield by the ring closure in boiling phenyl ether of ethyl β-anilino-α-phenylcrotonate, obtained by the condensation of ethyl α-phenylacetoacetate with aniline.

Experimental.

1-*Methyl*-3-*nitro*-4-*quinolone* (cf. Colonna, *loc. cit.*).—4-Hydroxy-3-nitroquinoline (Bachmann, Welton, Jenkins, and Christian, *J. Amer. Chem. Soc.*, 1947, **69**, 365) (5 g.) was dissolved in a solution of potassium hydroxide (2 g.) in water (50 c.c.), and methyl sulphate (3·3 g.) was added. The mixture was shaken for 20 minutes and left at room temperature overnight. The precipitated yellow solid was filtered off, washed with aqueous potassium hydroxide and with water, and dried. 1-Methyl-3-nitro-4-quinolone (4·5 g.) was obtained in pale straw-coloured needles, m. p. 219·5—220·5°, after recrystallisation from alcohol. Colonna (*loc. cit.*) who describes this compound as 4-methoxy-3-nitroquinoline, gives m. p. 220°. Since the completion of this work, Price (*Australian J. Sci. Res.*, 1949, *A*, **2**, 272) has reported the preparation of 1-methyl-3-nitro-4-quinolone by the nitration of 1-methyl-4-quinolone. He records m. p. 227—229° (corr.).

3-*Amino*-1-*methyl*-4-*quinolone* (cf. Colonna, *loc. cit.*).—A hot solution of stannous chloride (50 g.) in concentrated hydrochloric acid (50 c.c.) was added with stirring to a suspension of 1-methyl-3-nitro-4-quinolone (10 g.) in glacial acetic acid (100 c.c.). There was an immediate vigorous reaction. The mixture was heated on the water-bath for 1 hour, then left overnight at room temperature. The filtered product was heated with 50% aqueous sodium hydroxide for 10 minutes. The resulting yellow solid was filtered off and washed quickly with cold water. 3-Amino-1-methyl-4-quinolone (8·7 g.) was obtained in yellow needles, m. p. 153—156°, by recrystallisation from benzene or toluene. Colonna (*loc. cit.*) gives m. p. 155° for this compound, which he describes as the hydrochloride of 3-amino-4-methoxyquinoline. Price (*loc. cit.*) records m. p. 234—235° (decomp.) for the picrate of this base.

3-*Acetamido*-1-*methyl*-4-*quinolone* (cf. Colonna, *loc. cit.*).—3-Amino-1-methyl-4-quinolone (8 g.) was boiled under reflux with acetic anhydride (25 c.c.) for 1 hour. The solution was poured into water (100 c.c.) and made alkaline with aqueous sodium hydroxide. Recrystallisation of the precipitated solid from water gave 3-acetamido-1-methyl-4-quinolone (8·4 g.) in white needles, m. p. 214—216°. Colonna, who describes this compound as 3-acetamido-4-methoxyquinoline, gives m. p. 216°.

4-*Methoxy*-3-*nitroquinoline*.—A methanolic solution of 4-chloro-3-nitroquinoline (Albert, Brown, and Duewell, *J.*, 1948, 1288) (3 g.) and sodium methoxide [from sodium (0·33 g.) and methyl alcohol (50 c.c.)] was boiled under reflux for 1 hour, and poured into water (200 c.c.). The solid product was filtered off, washed with water, and dried at 60°. 4-*Methoxy*-3-*nitroquinoline* (2·8 g.) separated from light petroleum (b. p. 40—60°) in long yellow needles, m. p. 99—100° (Found : C, 59·1; H, 4·0. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 3·9%).

3-*Amino*-4-*methoxyquinoline*.—A suspension of 4-methoxy-3-nitroquinoline (3 g.) in methyl alcohol (15 c.c.) was shaken with hydrogen at atmospheric pressure and room temperature in the presence of platinum. When hydrogen uptake (3 moles) ceased, the solution was filtered and the solvent removed under reduced pressure. Crystallisation of the residue gave 3-*amino*-4-*methoxyquinoline monohydrate* (2·4 g.) in brown transparent plates from benzene, or pinkish needles from water. Both forms had m. p. 75—80°, raised to 81° after being dried over phosphoric oxide *in vacuo* for 3 weeks (Found, for specimen dried at 80° at atmospheric pressure : C, 63·2; H, 6·3. $C_{10}H_{10}ON_2,H_2O$ requires C, 62·6; H, 6·3%).

Action of Acetic Anhydride on 3-*Amino*-4-*methoxyquinoline*.—(i) 3-Amino-4-methoxyquinoline (0·5 g.) was heated under reflux with acetic anhydride (5 c.c.) for 1 hour. After removal of half of the excess of solvent by distillation the remaining solution was poured into water (20 c.c.). Addition of aqueous sodium hydroxide precipitated 3-acetamido-1-methyl-4-quinolone as a white solid which crystallised from water in white needles, m. p. 213—214° undepressed on admixture with an authentic specimen prepared as described above.

(ii) Sulphuric acid (3 drops) was added to a mixture of 3-amino-4-methoxyquinoline (0·81 g.) and acetic anhydride (2 c.c.). After 1 hour at room temperature the solution was diluted with water (5 c.c.) and made alkaline with aqueous sodium hydroxide. The precipitated 3-*acetamido*-4-*methoxyquinoline hemihydrate* crystallised from water in white needles (0·77 g.), m. p. 74° after being dried below 50°, raised to 97—101° after being dried for 3 weeks over potassium hydroxide *in vacuo*, and to 105° after being dried for 3 hours over potassium hydroxide *in vacuo* at 100° (Found, for specimen, m. p. 105° : C, 65·9; H, 5·4; N, 13·1. $C_{12}H_{12}O_2N_2$ requires C, 66·7; H, 5·5; N, 13·0%. Found, for specimen, m. p. 74° : C, 64·5; H, 5·8. $C_{12}H_{12}O_2N_2,\frac{1}{2}H_2O$ requires C, 64·0; H, 5·8%).

4-*Ethoxy*-3-*nitroquinoline*.—A mixture of 4-chloro-3-nitroquinoline (2·3 g.) and sodium ethoxide [from sodium (0·26 g.) in dry ethyl alcohol (25 c.c.)] was boiled under reflux for 3 hours. The solution was diluted and the precipitated solid filtered off and dried. 4-*Ethoxy*-3-*nitroquinoline* (1·9 g.) separated from aqueous methyl alcohol or light petroleum in straw-coloured plates, m. p. 57·5° (Found : C, 60·4; H, 4·6. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%). Colonna (*loc. cit.*) gave m. p. 202° for the compound to which this structure was assigned, but which must now be regarded as 1-ethyl-3-nitro-4-quinolone.

3-*Nitro*-4-n-*propoxyquinoline*.—A mixture of 4-chloro-3-nitroquinoline (3·5 g.) and sodium propoxide

[from sodium (0·4 g.) in dry *n*-propyl alcohol (40 c.c.)] was boiled under reflux for 3 hours. After dilution with water, the oil which separated was extracted with ether. The dried (Na_2SO_4) ethereal solution was evaporated and the residue was extracted with light petroleum (b. p. 40—60°). The insoluble residue, after crystallisation from methyl alcohol, had m. p. 119—120° and consisted of unchanged 4-chloro-3-nitroquinoline. Concentration of the light petroleum extract gave 3-*nitro*-4-n-*propoxyquinoline* in pale yellow prisms (2·6 g.), m. p. 42—43° (Found: C, 61·8; H, 5·2. $C_{12}H_{12}O_3N_2$ requires C, 62·1; H, 5·2%). Colonna (*loc. cit.*) gave m. p. 156° for the compound to which this structure was assigned, but which must now be regarded as 3-nitro-1-*n*-propyl-4-quinolone.

4-n-*Butoxy*-3-*nitroquinoline*.—4-Chloro-3-nitroquinoline (2 g.) was added to a solution of sodium butoxide [from sodium (0·22 g.) in *n*-butyl alcohol (25 c.c.)], and the solution was boiled under reflux for 3 hours. The solid obtained on dilution with water was filtered off and dried. 4-n-*Butoxy*-3-*nitroquinoline* separated from light petroleum (b. p. 40—60°) in yellow transparent plates (1·7 g.), m. p. 53—54° (Found: C, 64·1; H, 6·0. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7%). Colonna, *loc. cit.*, gave m. p. 140° for the compound to which this structure was assigned, but which must now be regarded as 1-*n*-butyl-3-nitro-4-quinolone.

1-*Methyl*-3-*phenyl*-4-*quinolone*.—(i) *From* 4-*hydroxy*-3-*phenylquinoline*. Methyl iodide (5 c.c.) was added to a methanolic solution of 4-hydroxy-3-phenylquinoline (0·7 g.) and sodium methoxide [from sodium (0·2 g.) in dry methyl alcohol (15 c.c.)]. The solution was boiled under reflux for 4 hours, and then concentrated and diluted with water (20 c.c.). The precipitated solid was filtered off and dried. 1-*Methyl*-3-*phenyl*-4-*quinolone hemihydrate* was obtained in white needles, m. p. 125—126°, after recrystallisation from aqueous methyl alcohol (Found: C, 78·8; H, 5·6. $C_{16}H_{13}ON,\frac{1}{2}H_2O$ requires C, 78·7; H, 5·7%). It was insoluble in ether and light petroleum, but soluble in hot ethyl alcohol. The *picrate*, long yellow needles from ethyl alcohol, had m. p. 150—151° (Found: C, 56·9; H, 3·9. $C_{16}H_{13}ON,C_6H_3O_7N_3$ requires C, 56·9; H, 3·5%). The methiodide was prepared by heating a methyl alcoholic solution of the base with methyl iodide, followed by concentration and precipitation with ether. It separated in cream-yellow micro-needles, m. p. 156·5—161·5°, but attempted recrystallisation caused decomposition.

(ii) *From* 3 : 3-*dimethyl*-1-(1-*methylquinol*-4-*on*-3-*yl*)*triazen* (cf. Elks and Hey, *J.*, 1943, 441). 3-Amino-1-methyl-4-quinolone (7·2 g.) was dissolved in a mixture of concentrated hydrochloric acid (9·9 c.c.) and water (60 c.c.), and the resulting suspension of hydrochloride stirred vigorously at 0—5° while a solution of sodium nitrite (3·2 g.) in water (20 c.c.) was added slowly. Stirring was continued for 15 minutes after completion of addition. The resulting solution was added to a cooled, stirred mixture of 33% aqueous dimethylamine (6·7 g.) and a solution of anhydrous sodium carbonate (7·6 g.) in water (80 c.c.). After 30 minutes the precipitated 3 : 3-dimethyl-1-(1-methylquinol-4-on-3-yl)triazen was filtered off, washed with water, and dried *in vacuo*. Repeated recrystallisation from benzene gave the triazen as a fawn, crystalline solid, m. p. varying between 100° and 109° with decomposition. An analytically pure specimen could not be obtained. Dry hydrogen chloride was passed through a solution of the triazen (6 g.) in dry benzene (250 c.c.), heated under reflux on a water-bath for 5 hours. The solution was washed with 10% aqueous sodium hydroxide and decanted from the tar. The dried (Na_2SO_4) benzene layer was concentrated by evaporation under reduced pressure. From the residual red oil, by repeated recrystallisation from ethyl alcohol, 1-methyl-3-phenyl-4-quinolone was obtained in white needles, m. p. 118·5—120·5° undepressed on admixture with a specimen prepared as described above. The picrate had m. p. 152°, undepressed on admixture with 1-methyl-3-phenyl-4-quinolone picrate described above.

(iii) *From* 1-*methyl*-3-N-*nitrosoacetamido*-4-*quinolone* (cf. France, Heilbron, and Hey, *J.*, 1940, 369). A 20% solution of nitrosyl chloride in acetic acid (13 c.c.) was added slowly to a stirred mixture of 3-acetamido-1-methyl-4-quinolone (3·8 g.), acetic anhydride (10 c.c.), acetic acid (15 c.c.), phosphoric oxide (0·5 g.), and fused potassium acetate (6 g.), cooled to 0—5°, and stirring was continued for 20 minutes after addition. The yellow solution was poured on crushed ice, and sufficient solid sodium carbonate was added to make the solution alkaline. 1-Methyl-3-*N*-nitrosoacetamido-4-quinolone separated as a brown oil, which gradually solidified. It was filtered off, washed with ice-cold water, dried *in vacuo* (m. p. 50—52° with decomp.), and then added to dry benzene (300 c.c.), which solution was decanted from a small amount of insoluble residue. The solution was maintained at 60° for 7 hours; evolution of nitrogen started at about 40°. Removal of the solvent left a dark-red oil, from which, by recrystallisation from aqueous ethyl alcohol, 1-methyl-3-phenyl-4-quinolone, m. p. 125—126°, was obtained (Found: C, 78·4; H, 5·8. $C_{16}H_{13}ON,\frac{1}{2}H_2O$ requires C, 78·7; H, 5·7%). The picrate separated in bright yellow needles, m. p. 152°, from ethyl alcohol. The melting points of the free base and the picrate were not depressed on admixture with the compounds prepared by methods (i) and (ii) above.

4-*Methoxy*-3-*phenylquinoline*.—4-Chloro-3-phenylquinoline (1 g.) was added to a solution of sodium methoxide [from sodium (0·2 g.) in dry methyl alcohol (10 c.c.)], and the solution was boiled under reflux for 2 hours. The mixture was poured into ice water and the solid which gradually separated was filtered off. 4-*Methoxy*-3-*phenylquinoline* (0·7 g.) crystallised from light petroleum (b. p. 40—60°) in stout prisms, m. p. 82—83° (Found: C, 81·5; H, 5·7. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·3%). It was soluble in cold ether and in ethyl alcohol. The *picrate*, shining yellow micro-needles from ethyl alcohol, had m. p. 157·5—159·5° (Found: C, 56·1, H, 3·3. $C_{16}H_{13}ON,C_6H_3O_7N_3$ requires C, 56·9; H, 3·5%). The methiodide, orange yellow micro-needles, m. p. 151—153°, was prepared by heating a methyl-alcoholic solution of the base with methyl iodide for 5 hours, followed by concentration and precipitation with ether. Attempted recrystallisation caused decomposition. By boiling the methiodide for 1 hour with 10% aqueous sodium hydroxide, 1-methyl-3-phenyl-4-quinolone was obtained, identified by melting point and mixed melting point.

Nitration of 4-*Hydroxyquinaldine* (cf. Halcrow and Kermack, *loc. cit.*).—A mixture of 4-hydroxyquinaldine (33 g.) and concentrated nitric acid (330 c.c.) was heated at 100° for 1 hour. The resultant orange solution was poured into ice and water (1500 c.c.). The precipitated yellow solid was filtered

off, suspended in water, filtered off again, thoroughly washed with water, and dried (25 g.). Extraction of this product with boiling water (2 × 500 c.c.) left 4-hydroxy-3-nitroquinaldine (21·6 g.) as a light yellow powder, m. p. >360°.

1 : 2-*Dimethyl*-3-*nitro*-4-*quinolone*.—A solution of 4-hydroxy-3-nitroquinaldine (6·5 g.) in methyl alcohol (60 c.c.) containing sodium methoxide [from sodium (2 g.)] was heated with methyl iodide (10 c.c.) for 16 hours. More methyl iodide (10 c.c.) was added and heating was continued for a further 8 hours. Excess of solvent was removed and the residue was treated with water (200 c.c.). The precipitated brown solid was filtered off, washed, and dried. 1 : 2-*Dimethyl*-3-*nitro*-4-*quinolone* (3·7 g.) crystallised from ethyl alcohol in pale yellow shining leaflets, m. p. 227—228° (Found : C, 60·3; H, 4·8. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%).

3-*Amino*-1 : 2-*dimethyl*-4-*quinolone*.—A hot solution of stannous chloride (15 g.) in concentrated hydrochloric acid (15 c.c.) was added with stirring to a hot solution of 1 : 2-dimethyl-3-nitro-4-quinolone (2·9 g.) in glacial acetic acid (30 c.c.). There was an immediate vigorous reaction, and after being left at room temperature overnight the precipitated stannichloride was filtered off, washed, and boiled for 15 minutes with 50% aqueous sodium hydroxide (50 c.c.). The solid so obtained was crystallised from hot water. 3-*Amino*-1 : 2-*dimethyl*-4-*quinolone* (2·2 g.) separated in pale yellow needles, m. p. 180·5—181° (Found : C, 69·4; H, 6·5. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4%). Acetylation of 3-amino-1 : 2-dimethyl-4-quinolone (1·9 g.) with acetic anhydride gave 3-*acetamido*-1 : 2-*dimethyl*-4-*quinolone* (1·6 g.) in small white needles, m. p. 255—257°, from water (Found : C, 67·4; H, 6·0. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1%).

4-*Chloro*-3-*nitroquinaldine*.—4-Hydroxy-3-nitroquinaldine (10 g.) was heated gently with phosphorus oxychloride (100 c.c.) until the solid had just dissolved (10 minutes). The resulting solution was added very slowly to a mixture of ammonia solution and crushed ice, so that the solution remained alkaline to phenolphthalein. The precipitated solid was filtered off, washed with dilute ammonia solution and water, and dried *in vacuo* (KOH). 4-Chloro-3-nitroquinaldine (9·8 g., 90%) was obtained as a pale brown, crystalline solid, m. p. 90—93°, after recrystallisation from benzene. Conrad and Limpach (*Ber.*, 1888, **21**, 1981) give m. p. 93—94° for 4-chloro-3-nitroquinaldine prepared from 4-hydroxy-3-nitroquinaldine in only 45% yield.

4-*Methoxy*-3-*nitroquinaldine*.—A solution of 4-chloro-3-nitroquinaldine (9·7 g.) in methyl alcohol (50 c.c.) containing sodium methoxide [from sodium (1 g.)], was heated for 2 hours. Dilution with water precipitated a solid which was filtered off, washed with water, and dried at 50°. 4-*Methoxy*-3-*nitroquinaldine* (6·9 g.) separated from light petroleum (b. p. 40—60°) in deep cream crystals, m. p. 79·5—81° (Found : C, 60·6; H, 4·5. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%).

3-*Amino*-4-*methoxyquinaldine*.—A suspension of 4-methoxy-3-nitroquinaldine (5 g.) in ethyl alcohol containing platinum was shaken with hydrogen at room temperature and atmospheric pressure. When the theoretical quantity of hydrogen had been absorbed the solution was filtered and evaporated. The solid residue was dissolved in hot water and filtered from an insoluble oil. 3-*Amino*-4-*methoxyquinaldine* (3·4 g.) crystallised from the cooled solution in cream needles, m. p. 112—113° (Found : C, 70·2; H, 6·4. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4%). Concentrated sulphuric acid (1 drop) was added to 3-amino-4-methoxyquinaldine (3·3 g.) in acetic anhydride (10 c.c.). After 2 hours at room temperature the solution was diluted with water and made alkaline with aqueous sodium hydroxide, which precipitated a gelatinous mass which became solid on storage. 3-*Acetamido*-4-*methoxyquinaldine* (2·5 g.) separated from water in clusters of white silky needles, m. p. 189° (Found : C, 67·5; H, 6·2. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1%).

Action of Nitrosyl Chloride on 3-*Acetamido*-1 : 2-*dimethyl*-4-*quinolone*.—A 25% solution of nitrosyl chloride in acetic anhydride (8 c.c.) was added slowly to a solution of 3-acetamido-1 : 2-dimethyl-4-quinolone (1·86 g.) in acetic acid (17 c.c.) and acetic anhydride (5 c.c.) containing fused potassium acetate (5 g.) and phosphoric oxide (0·3 g.), stirred at 0—5°. Stirring was continued for 1 hour after the addition was complete, and the resulting solution was poured on crushed ice (50 g.) and made alkaline with aqueous sodium carbonate. The 1 : 2-dimethyl-3-*N*-nitrosoacetamido-4-quinolone (1·5 g.) which separated as a pale yellow powder was filtered off, washed with water, and dried (KOH) *in vacuo*. It decomposed to a brown solid on being heated to 131°, and decomposed with a flash when placed in a flame. 1 : 2-Dimethyl 3-*N*-nitrosoacetamido-4-quinolone (0·5 g.) was dissolved in warm benzene (100 c.c.), and the solution was boiled under reflux for 2 hours. A yellow solid (0·3 g.) separated from the hot solution, and more (0·08 g.) was obtained by evaporation of the benzene solution. 1-*Methylpyrazolo*(4′ : 5′-2 : 3)-4-*quinolone* separated from ethyl alcohol in yellow-fawn micro-needles, m. p. 340—342° (some decomp. >325°) (Found : C, 66·4; H, 4·3; N, 20·9. $C_{11}H_9ON_3$ requires C, 66·4; H, 4·5; N, 21·1%). It was practically insoluble in benzene, only slightly soluble in alcohol, and slightly soluble in hot water, from which solution it separated in pale yellow needles on cooling. Solutions showed an intense violet fluorescence.

4-*Methoxy*-6-*nitroquinaldine*.—4-Chloro-6-nitroquinaldine (0·21 g.) (Kermack and Weatherhead, *J.*, 1939, 566) was added to a solution of sodium methoxide [from sodium (0·02 g.) in dry methyl alcohol (10 c.c.)] and the whole heated under reflux for 2 hours. The solution was diluted with water (30 c.c.), and the precipitated solid was filtered off, washed, and dried. 4-*Methoxy*-6-*nitroquinaldine* was insoluble in light petroleum (b. p. 40—60°) and crystallised from ethyl alcohol in pale fawn needles, m. p. 192—193° (Found : C, 60·2; H, 4·6. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6%).

1-o-*Methoxyphenyl*-3 : 3-*dimethyltriazen* (cf. Elks and Hey, *loc. cit.*).—A solution of *o*-methoxybenzenediazonium chloride, prepared by the slow addition of a solution of sodium nitrite (7·6 g.) in water (50 c.c.) to a solution of *o*-anisidine (12·3 g.) in concentrated hydrochloric acid (24 c.c.) and water (100 c.c.) stirred at 0—5°, was added slowly, with stirring, to a cooled mixture of 33% aqueous dimethylamine (16 g.) and sodium carbonate (18 g.) in water (150 c.c.). The dark red oil which separated was extracted with ether and dried (Na_2SO_4). The residue after removal of solvent was distilled under reduced pressure. 1-o-*Methoxyphenyl*-3 : 3-*dimethyltriazen* (16 g.) was collected at 123—124°/8 mm., or 155°/18 mm. as a pale yellow oil (Found : C, 60·8; H, 7·7. $C_9H_{13}ON_3$ requires C, 60·3; H, 7·3%).

2-Methoxydiphenyl.—A solution of 1-*o*-methoxyphenyl-3 : 3-dimethyltriazen (5 g.) in dry benzene (50 c.c.) was heated on a water-bath while a slow stream of dry hydrogen chloride was passed through it. After 1 hour the reaction mixture was cooled, the precipitated solid was filtered off, and the benzene solution was washed with 10% aqueous sodium hydroxide. Evaporation of the dried ($MgSO_4$) benzene solution left a red oil, which was distilled under reduced pressure. 2-Methoxydiphenyl (0·5 g.) was obtained as a slightly yellow, viscous oil, b. p. 124—128°/3—4 mm. [Borsche and Scholten (*Ber.*, 1917, **50**, 601), give b. p. 159—160°/18 mm.; von Auwers and Harres (*Z. physikal. Chem.*, *A*, 1929, **143**, 14) give b. p. 150°/13 mm.]. Nitration of 2-methoxydiphenyl as described by Borsche and Scholten (*loc. cit.*) gave 2-methoxy-5-nitrodiphenyl, which separated from methyl alcohol in pale yellow needles, m. p. 94—95° (Borsche and Scholten, *loc. cit.*, give m. p. 95—96°).

4-Hydroxy-3-phenylquinaldine.—Ethyl α-phenylacetoacetate was prepared by the hydrolysis of α-phenylacetoacetonitrile as described in *Org. Synth.*, Coll. Vol. II, 1943, 284. The crude ester (42 g.), containing some unchanged nitrile which proved difficult to separate, was added to aniline (20 g.) together with concentrated hydrochloric acid (3 drops). After 24 hours at room temperature the water formed was removed and the dried ($MgSO_4$) oil was added to boiling phenyl ether (250 c.c.), and the solution heated for 1½ hours. The solid which separated on cooling was filtered off, washed thoroughly with light petroleum (b. p. 40—60°), and dried. Recrystallisation from ethyl alcohol gave *4-hydroxy-3-phenylquinaldine* (1·87 g.) in cream needles, m. p. 302—304° (decomp.) (Found: C, 82·2; H, 5·7. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·5%).

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