## [1945] King and Beer: New Potential Chemotherapeutic Agents. Part I. 791

## **206.** New Potential Chemotherapeutic Agents. Part I. Derivatives of Aminoquinoxalines.

By F. E. KING and R. J. S. BEER.

Starting from 3:4:5-triaminoanisole, a quinoxaline analogue (I,  $R = \cdot CH_2 \cdot CH_2 \cdot NEt_2$ ) of pamaquin has been synthesised (cf. Gawron and Spoerri, *J. Amer. Chem. Soc.*, 1945, **67**, 514). Attempts to prepare a benzquinoxaline from 1:2:4-triaminonaphthalene gave amorphous products, but the acetyltriamine was successfully converted to 7-acetamido-5:6-benzquinoxaline (II, R = COMe). During experiments on the preparation of 4-acylamino-1:2-diaminonaphthalenes the quinone (IV) was obtained, from which 3- $\beta$ -diethylaminoethylamino-1:2-benzphenazine (V,  $R = \cdot CH_2 \cdot CH_2 \cdot NEt_2$ ) was synthesised. Experiments with 8-amino-6-methoxyquinoline have given the 8- $\beta$ -cyanoethylamino and 8-guanidino derivatives.

RECENTLY Gawron and Spoerri (J. Amer. Chem. Soc., 1945, 67, 514) have recorded the synthesis of 5-amino-7-methoxyquinoxaline (I; R = H) and of its N-diethylaminoethyl and N-diethylaminopropyl derivatives. We have been engaged in synthetical investigations in this field, and in the course of our work have also prepared the quinoxaline (I; R = H) and (I;  $R = CH_2 \cdot CH_2 \cdot NEt_2$ ). The methods we have used, though similar to those employed by the American chemists, differ from them in many respects. We therefore present this detailed account of our experiments, which were carried out during 1942—1943 and cover other relevant substances not hitherto described.

Both syntheses use 3:5-dinitro-4-aminoanisole which Gawron and Spoerri obtained in five stages from p-aminophenol. In our preparation of this dinitroamine, p-anisidine is the starting point, and details are given for the first time of the nitration of 4-p-toluenesulphonamidoanisole, whereby the 3:5-dinitro derivative (Reverdin, *Ber.*, 1909, 42, 1523) is obtained. Hydrolysis of the toluenesulphonyl group with cold sulphuric acid afforded the required 3:5-dinitro-4-aminoanisole, which on catalytic reduction yielded 3:4:5-triamino-anisole. This rapidly oxidisable base, characterised by the 2:3-diphenylquinoxaline it gave with benzil, readily condensed with glyoxal under approximately neutral conditions and the resulting aminomethoxy-quinoxaline and its acetyl derivative are identical with the compounds since described by Gawron and Spoerri.



The American authors, being unable to obtain a pure product from the action of  $\beta$ -chloroethyldiethylamine on the aminoquinoxaline, alkylated the quinoxaline-*p*-toluenesulphonamide. By means of high-vacuum distillation, however, it is not difficult to isolate from the direct alkylation product the desired amine (I;  $R = CH_2 CH_2 NEt_2$ ), which is an oil characterised by its crystalline monopicrate and hydrochloride.

In order to obtain amino substituted benzquinoxalines, e.g. (II; R = H), numerous attempts were made, at various hydrogen-ion concentrations and with exclusion of air, to condense glyoxal and 1:2:4-triaminonaphthalene (Fieser and Fieser, J. Amer. Chem. Soc., 1934, 56, 1565). These experiments, unlike those with triaminobenzenes (v. supra and also Hinsberg, Ber., 1886, 19, 1254), invariably gave amorphous products, evidently from intermolecular reactions. This difficulty was obviously unlikely to arise if the synthesis of (II; R = H) were attempted through the 4-nitro- or 4-acylamino-diaminonaphthalenes and attempts were therefore made to prepare these compounds. Preliminary experiments on the partial reduction of 2:4-dinitronaphthylamine were not encouraging and were abandoned, but the mononitration of 4-amino-1-p-toluenesulphonamidonaphthalene (III; R = R' = H) followed by reduction, appeared to offer a simple route to an intermediate of the second type. The necessary amine (III; R = R' = H) was obtained by Raney nickel reduction of either 4-nitro-1-p-toluenesulphonamidonaphthalene or of 4-benzeneazo-1-p-toluenesulphonamidonaphthalene (cf. Morgan and Grist, J., 1921, 119, 605), but the chief product of the action of nitric acid on its acetyl derivative was 4-p-toluenesulphonamido-1: 2-naphthaquinone (IV), and only small amounts of 2- (or 3-) nitro-1-acetamido-4-p-toluenesulphonamidonaphthalene were obtainable. It proved impossible to condense the quinone (IV) with ethylenediamine and thus use it for the synthesis of (II;  $R = \rho - SO_2 C_6 H_4 Me$ ), but its reaction with o-phenylenediamine afforded 3-p-toluenesulphonamido-1: 2-benzphenazine (V, R = p- $SO_2 \cdot C_6H_4 \cdot Me$ ). After alkylation in alcoholic sodium ethoxide, and removal of the toluenesulphonyl group with sulphuric acid,  $3-(\beta-diethylaminoethylamino)-1: 2-benzphenazine was obtained and characterised by$ its monopicrate and brilliant red dihydrochloride.

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Having failed to find a convenient synthesis of the 4-toluenesulphonamidodiaminonaphthalene, the corresponding 4-acetamido compound already described by Panizzon-Favre (Gazzetta, 1924, 54, 826) was prepared. Some improvements in the reduction stages of this synthesis from 1-amino-4-benzeneazonaphthalene are recorded in the experimental section. By the action of glyoxal, 1:2-diamino-4-acetamidonaphthalene gave 7-acetamido-5: 6-benzquinoxaline (II; R = Ac), which after treatment with sodamide was condensed with  $\beta$ -chlorethyldiethylamine. Subsequently, 7- $\beta$ -diethylaminoethylacetamido-5: 6-benzquinoxaline was isolated as a monopicrate, but owing to the formation of other products the desired amine is difficult to obtain and further work in this direction was discontinued.

Some new derivatives of the readily available 8-amino-6-methoxyquinoline (VI; R = H) were prepared with the intention of synthesising their quinoxaline analogues should the quinolines possess therapeutic properties. 8- $\beta$ -Cyanoethylamino-6-methoxyquinoline (VI;  $R = -CH_2 \cdot CH_2 \cdot CN$ ), which was required for the preparation of related amidines, was obtained by the alkylation of the aminoquinoline (VI; R = H) with  $\beta$ -chloroethyl cyanide or  $\beta$ -iodoethyl cyanide. Some unsuccessful experiments on the synthesis of the lower homologue (VI;  $R = -CH_2 \cdot CN$ ) by the Strecker method led to what is regarded as the 8 : 8'-diaminomethylene compound, which rearranged in acid to di-(8-amino-6-methoxy-5)-quinolylmethane. Finally, the hydrochloride and hydriodide of 8-guanidino-6-methoxyquinoline (VI;  $R = -C(:NH)NH_2$ ) were prepared from the appropriate salts of 8-amino-6-methoxyquinoline and cyanamide in boiling ethanol.

## EXPERIMENTAL.

3: 5-Dinitro-4-p-toluenesulphonamidoanisole (cf. Reverdin, loc. cit.).—A mixture of p-anisidine (60 g.) and p-toluene-sulphonyl chloride (95 g.) in pyridine (125 c.c.) was heated at 100° for 3 hours. The product precipitated by water and crystallised from aqueous acetic acid formed nearly colourless needles, m. p. 114° (114 g., 95%). The cautious addition of nitric acid (65 c.c., d 1·4) to a cooled suspension of the toluenesulphonamide (30 g.) in alcohol (150 c.c.), afterwards warmed if precessary led to a vigorous reaction which was completed by refusing on a charm beth for addition of mute acid (65 c.c., a 1.4) to a cooled suspension of the follomesuphonamide (30 g.) in alcohol (150 c.c.), afterwards warmed if necessary, led to a vigorous reaction which was completed by refluxing on a steam-bath for 1 hour. The precipitated solid was collected and crystallised from aqueous acetic acid, the pure *dinitro* derivative (20.5 g., 53%) separating in long pale yellow needles, m. p. 204° (Found : C, 45.9; H, 3.8; N, 11.3.  $C_{14}H_{13}O_7N_3S$ requires C, 45.8; H, 3.5; N, 11.4%). 3 : 4 : 5-*Triaminoanisole*...3 : 5-Dinitro-4-p-toluenesulphonamidoanisole (100 g.) dissolved in cold sulphuric acid (250 c.c. of 90%) was left overnight and the solution poured on to ice (200 g.). The dinitroanisidine precipitated by aqueous ammonia (18%) and crystallised from acetic acid\_water formed red prisms with a green reflex (5.8 g. 0.90%)

(250 c.c. of 90%) was left overnight and the solution poured on to ice (200 g.). The dinitroanisidine precipitated by aqueous ammonia (18%) and crystallised from acetic acid-water formed red prisms with a green reflex (5.8 g., 98%), m. p. 161—162° (literature, 163°). A suspension of the dinitroanine (25 g.) in alcohol (300 c.c.) was hydrogenated at  $50-60^\circ/50$  atms. over Raney nickel. When this was freed from catalyst, concentrated hydrochloric acid (21 c.c.) was added and the solution evaporated under reduced pressure until crystallisation began. The triamine hydrochloride, which is very soluble in water but less soluble in alcohol, separated in pale pink needles (20 g., 76%) which were washed with ether and stored in an evacuated desiccator. The free base, which crystallised from alcohol in bronze plates, m. p. ca. 150° rapidly origined and the water but less of the water bare of the pressure of a 5.5 ° rapidly or disconter the pressure of ca. 150°, rapidly oxidised, and it was characterised as 5-amino-7-methoxy-2: 3-diphenylquinoxaline, prepared from the base hydrochloride and benzil in boiling alcohol containing sodium acetate. The derivative precipitated by water and recrystallised from methanol consisted of brownish-yellow needles, m. p. 174—175° (Found: C, 76.5; H, 5.2.

 $C_{21}H_{17}ON_3$  requires C, 77.1; H, 5.2%). 5-Amino-7-methoxyquinoxaline (I; R = H).—The triamine hydrochloride (4 g.) dissolved in water (25 c.c.) and neutralised with aqueous sodium carbonate was warmed to 60° with a saturated solution of glyoxal bisulphite (5 g.) The pure quinoxaline separated in bright yellow needles, m. p.  $94-96^{\circ}$  (Found : C, 61.6; H, 5.2. Calc. for C<sub>9</sub>H<sub>9</sub>ON<sub>3</sub>: C, 61.7; H, 5.1%). Gawron and Spoerri, *loc. cit.*, give m. p.  $95^{\circ}$  (corr.). Using the amine hydrochloride, as in the synthesis of 5-aminoquinoxaline (Hinsberg, *loc. cit.*), instead of the free base, gave only chocolate-coloured amorphous synthesis of 5-annhoquinoxaline (rinsberg, *loc. cit.*), instead of the free base, gave only chocolate-coloured amorphous products. The quinoxaline (0.4 g.) suspended in water (5 c.c.) was dissolved by warming with acetic anhydride (0.5 c.c.). The product obtained on cooling was 5-acetamido-7-methoxyquinoxaline which crystallised from aqueous acetic acid in very pale yellow needles, m. p. 174° (Found : C, 60.5; H, 5.0. Calc. for  $C_{11}H_{11}O_2N_3$ : C, 60.8; H, 5.1%). Gawron and Spoerri record m. p. 175—176° (corr.).  $5-(\beta-Diethylaminoethylamino)-7-methoxyquinoxaline (I, R = CH_2 CH_2 \cdot NEt_2).$ —A solution of 5-amino-7-methoxy-quinoxaline (4 g.) in alcohol (20 c.c.) containing  $\beta$ -chloroethyldiethylamine hydrochloride (King, J., 1928, 2436) (2 g.) and fused sodium acetate (I g.) was refluxed on a steam-bath. After 5 hours and again after 10 hours further similar

and fused sodium acetate (I g.) was refluxed on a steam-bath. After 5 hours and, again, after 10 hours, further similar amounts of the last two reactants were added and the heating continued for a total of 22 hours. Continuous extraction amounts of the last two reactants were added and the heating continued for a total of 22 hours. Continuous extraction with ether of the liquid basified with sodium carbonate gave a dark viscous oil which was distilled at low pressure. The fraction (2 g.) of b. p. 100—130°/0·01 mm. was 8-amino-6-methoxyquinoxaline (mixed m. p.); the reddish oil (1·1 g., 35%, allowing for the aminoquinoxaline recovered), b. p. 130—140°/0·01 mm., consisted of 5-( $\beta$ -diethylamino-ethylamino)-7-methoxyquinoxaline, and was identified by its *monopicrate*, precipitated on slowly mixing alcoholic solutions of picric acid and the base, which formed orange-yellow prisms, m. p. 139°, when recrystallised from ethanol (Found : C, 50·4; H, 4·9. C<sub>18</sub>H<sub>22</sub>ON<sub>4</sub>, C<sub>6</sub>H<sub>3</sub>O, N<sub>4</sub> requires C, 50·1; H, 5·0%). Excess picric acid gave a red crystalline precipitate, presumably the dipicrate described by Gawron and Spoerri. This insoluble salt was also formed during attempts to recover the quinoxaline base from the purified monopicrate with acid. Consequently, the monopicrate was decomposed with dilute sodium hydroxide; the alkali-washed ether extract, dried and treated with hydrogen chloride, vielded a pale lilac deliquescent *monohydrochloride*, m. p., after

extract, dried and treated with hydrogen chloride, yielded a pale lilac deliquescent monohydrochloride, m. p., after three crystallisations from ethanol-ether, 169–171° (Found: C, 57.3; H, 7.5.  $C_{15}H_{22}ON_4$ , HCl requires C, 58.0; H, 7.4%).

4-Amino-1-p-toluenesulphonamidonaphthalene (III; R = R' = H).—A suspension of 4-nitro-1-p-toluenesulphon-amidonaphthalene (3.6 g.) (Hodgson and Walker, J., 1934, 180) in ethanol (50 c.c.) hydrogenated over Raney nickel at 60°/40 atm. gave the 4-amino compound as colourless tablets, m. p. 182—184°. It was identical with the product (28.5 g., 84%) from the reduction of 4-benzeneazo-1-*p*-toluenesulphonamidonaphthalene (45 g.) under similar conditions (cf. Morgan and Grist, *loc. cit.*). Acetylation of the base with acetic anhydride at 100° gave the *acetyl* derivative, crystallising from aqueous acetic acid in soft fluffy needles, m. p. 265–267° (Found : C, 64.6; H, 5.1  $C_{19}H_{18}O_3N_2S$ requires C, 644; H, 5·1%). 4-p-Toluenesulphonamido-1: 2-naphthaquinone (IV).—A solution of nitric acid (4 c.c., d 1·42, 4 mol.) in acetic acid

(50 c.c.) was gradually stirred into a suspension of 4-acetamido-1-*p*-toluenesulphonamidonaphthalene (5 g.) in acetic acid (150 c.c.) at room temperature. Addition of water to the resulting clear solution gave 4-p-tolenesulphonamido-1: 2-naphthaquinone which crystallised from ethanol in yellow plates, m. p. 140—160° (decomp.) (Found: C, 62.5; H, 4.3; N, 4.3.  $C_{17}H_{13}O_4NS$  requires C, 62.4; H, 4.0; N, 4.3%). With considerably smaller quantities of acetic acid, a resinous product was obtained but from the reaction mixture separated small amounts of 2 (or 3)-nitro-4-acet-amido-1-p-toluenesulphonamidonaphthalene, crystallising from ethanol in pale yellow needles, m. p. 218° (Found: C, 57.5; H, 4.5,  $C_{17}H_{12}O_4NS$  requires C, 57.1; H, 4.3%).

and, a result was obtained but non the reaction inverte separated small anothers of 2 (of 5)-min-4-action amido-1-p-toluenesulphonamidonaphthalene, crystallising from ethanol in pale yellow needles, m. p. 218° (Found : C, 57.5; H, 4.5.  $C_{19}H_{17}O_5N_3S$  requires C, 57.1; H, 4.3%). The quinone reacted easily with ethylenediamine in aqueous alcohol, less readily in acetic acid, but the products were deeply coloured and amorphous. Oxidation with alcoholic ferric chloride or potassium ferricyanide gave black insoluble material.

3-p-Toluenesulphonamido-1:2-benzphenazine (V; R = p-SO<sub>2</sub>·C<sub>6</sub>H<sub>4</sub>·Me).—o-Phenylenediamine (1·9 g.) was added to a hot solution of the toluenesulphonamidoquinone (5·5 g.) in the minimum quantity of boiling alcohol and then heated on a steam-bath for 20 minutes. The separated red solid (3·2 g.) gave on crystallisation from acetic acid the toluenesulphonamidophenazine as yellow tablets, m. p. 274—276° (decomp.) (Found : C, 68·8; H, 4·4. C<sub>23</sub>H<sub>17</sub>O<sub>2</sub>N<sub>3</sub>S requires C, 69·2; H, 4·3%).

C, 69·2; H, 4·3%). 3-( $\beta$ -Diethylaminoethylamino)-1: 2-benzphenazine (V, R = ·CH<sub>2</sub>·CH<sub>2</sub>·NEt<sub>2</sub>).—The bright scarlet solution of the above toluenesulphonamidophenazine (2 g.) in alcohol (20 c.c.) containing sodium (0·22 g.) was heated under reflux with  $\beta$ -chloroethyldiethylamine hydrochloride (0·86 g.) for 25 hours. After basifying with 2× sodium hydroxide, the product was removed by several ether extractions, giving a dark red partly crystalline material from which the alkylated sulphonamide was isolated in the form of pink needles (1·55 g.), m. p. 85—90°, by hot ligroin (b. p. 80—100°). This product (1·2 g.) was dissolved in ice-cold sulphuric acid (10 c.c. of 90%), and, after 21 hours at 0—2°, the deep emerald green solution and separated solid were added to crushed ice. The bright red liquid was basified with dilute aqueous sodium hydroxide and the liberated oil collected in ether. From the dried solution, anhydrous hydrogen chloride precipitated the *dihydrochloride*, separating after 2 crystallisations from alcohol-ether in bright vermilion needles (0·75 g.), m. p. (evac. capillary) 250°, with shrinking and darkening at *ca*. 230° (Found after drying at 80° in a high vacuum : C, 61·8; H, 6·4; N, 12·9; Cl, 16·9. C<sub>22</sub>H<sub>24</sub>N<sub>4</sub>.2HCl,  $\frac{1}{2}$ H<sub>2</sub>O requires C, 62·0; H, 6·3; N, 13·1; Cl, 16·7%). The *picrate* crystallised from ethanol in glistening deep orange blades, m. p. *ca*. 220° (decomp.) (Found : C, 58·6; H, 5·0. C<sub>22</sub>H<sub>23</sub>N<sub>4</sub>.C<sub>6</sub>H<sub>4</sub>O<sub>2</sub>N<sub>3</sub> requires C, 58·6; H, 4·7%).

 $\Gamma_{02}H_{24}N_{4}C_{6}H_{3}O_{7}N_{3}$  requires C, 58.6; H, 4.7%). 1:4-Diaminonaphthalene.—1-Amino-4-benzeneazonaphthalene (80 g.) suspended in ethanol (600 c.c.) was hydrogenated at 50° and 70 atms. over Raney nickel. The product was isolated from the resulting solution after filtration by addition to a mixture of sulphuric acid (40 c.c.) and water (1000 c.c.), the yield of precipitated diamine sulphate being quantitative. The amine was characterised by its diacetyl derivative (Panizzon-Favre, *loc. cit.*) (Found : N, 11·2. Calc. for  $C_{14}H_{14}O_{2}N_{2}$ : N, 11·6%). 7-Acetamido-5: 6-benzquinoxaline (II; R = Ac).—2-Nitro-1: 4-diacetamidonaphthalene was prepared from 1: 4-dicontentior with blane but in interior with 500 mixing acid (Hadron and Filicitt I 1026, 1764), and the larget from 1: 4-di-

7-Acetamido-5: 6-benzquinoxaline (II; R = Ac).—2-Nitro-1: 4-diacetamidonaphthalene was prepared from 1: 4-diacetamidonaphthalene by nitration with 50% nitric acid (Hodgson and Elliott, J., 1936, 1764), and the 1-acetyl group removed by warm sulphuric acid (Panizzon-Favre, *loc. cit.*). Reduction with iron and aqueous acetic acid as described by Panizzon-Favre is unsatisfactory, and the nitro compound (2 g.) suspended in methanol (100 c.c.) was hydrogenated over Raney nickel at 60°/75 atms. 1: 2-Diamino-4-acetamidonaphthalene was isolated by concentration of the filtered solution. Glyoxal bisulphite (0.5 g.) shaken with a suspension of the diamine (0.34 g.) in boiling water (150 c.c.) caused the precipitation of 7-acetamido-5: 6-benzquinoxaline which was collected after heating for 1 hour. The product (0.3 g.) crystallised from ethanol in pale yellow needles, m. p. 252—253° (Found : C, 71·1; H, 4·9; N, 17·5. C<sub>14</sub>H<sub>11</sub>ON<sub>8</sub> requires C, 70·9; H, 4·6; N, 17·7%). 7-( $\beta$ -Diethylamino-ethylacetamido)-5: 6-benzquinoxaline.—A toluene solution (20 c.c.) of  $\beta$ -chloroethyldiethylamine, prepared from the hydrochloride (1 g.), containing 7-acetamidobenzquinoxaline (1·2 g.) and powdered sodamide (0·2 g.), was refluxed for 6 hours. When cold, the liquid was washed with a little water and then with 0·1N hydrochloric acid, from which, by treatment with alkali and ether extraction, the alkylated acetamidobenzquinoxaline was isolated as

7- $(\beta$ -Diethylamino-ethylacetamido)-5 : 6-benzquinoxaline.—A toluene solution (20 c.c.) of  $\beta$ -chloroethyldiethylamine, prepared from the hydrochloride (1 g.), containing 7-acetamidobenzquinoxaline (1·2 g.) and powdered sodamide (0·2 g.), was refluxed for 6 hours. When cold, the liquid was washed with a little water and then with 0·1N hydrochloric acid, from which, by treatment with alkali and ether extraction, the alkylated acetamidobenzquinoxaline was isolated as a light brown viscous oil. An attempt was made to hydrolyse the acetyl group by heating on a steam-bath with 10% hydrochloric acid. The product did not give a crystalline hydrochloride, and a solution of the base in alcohol was treated with an alcoholic solution of picric acid. A red gum was precipitated and, on standing, yellow needles separated which after repeated crystallisation from ethanol had m. p. 195–197° (decomp.) after sintering at *ca*. 185°. The product is evidently the monopicrate of a residue of unhydrolysed 7-( $\beta$ -diethylaminoethylacetamido)-5 : 6-benzquinoxaline (Found : C, 55·7; H, 4·8; N, 17·6, 17·7. C<sub>20</sub>H<sub>24</sub>ON<sub>4</sub>, C<sub>5</sub>H<sub>3</sub>O<sub>7</sub>N<sub>3</sub> requires C, 55·2; H, 4·8; N, 17·4%). The red gum was an unresolvable mixture containing at least 2 other salts.  $8-\beta$ -Cyanoethylamino-6-methoxyquinoline (VI; R = ·CH<sub>3</sub>·CH<sub>3</sub>·CN).—A solution of 8-amino-6-methoxyquinoline (4 g., 2 mols.) and  $\beta$ -chloroethyl cyanid (1 g., 1 mol.) in ethanol (20 c.c.) was heated under pressure for 15 hours at 120°.

8-β-Cyanoethylamino-6-methoxyquinoline (VI;  $R = \cdot CH_2 \cdot CH_2 \cdot CN$ ).—A solution of 8-amino-6-methoxyquinoline (4 g., 2 mols.) and β-chloroethyl cyanide (1 g., 1 mol.) in ethanol (20 c.c.) was heated under pressure for 15 hours at 120°. The base, liberated by aqueous ammonia after evaporation of the alcohol, was extracted in ether and distilled. The principal fraction, b. p. 131°/0·15 mm., was the unchanged aminomethoxyquinoline, but an oil (0·25 g.) of b. p. 160–170°/0·04 mm. was identified as 8-β-cyanoethylamino-6-methoxyquinoline by the monopicrate which crystallised from alcohol in minute vermilion-coloured needles, m. p. 188–189° (Found : C, 50·0; H, 3·6.  $C_{13}H_{13}ON_3, C_6H_3O_7N_3$  requires C, 50·0; H, 3·5%). Slightly improved yields (ca. 17%) of the amine were obtained from β-iodoethyl cyanide. This was prepared by refluxing for 6 hours a solution of the chloro-cyanide (16 g.) and sodium iodide (33 g.) in acetone (200 c.c.). Evaporation and washing with thiosulphate solution gave an oil of which the fraction (16·6 g.), b. p. 101°/23 mm., consisted of β-iodoethyl cyanide (Found : I, 69·0.  $C_3H_4NI$  requires I, 70·2%), ca. 8 g. of the chloro compound being recovered. The deliquescent solid (imino-ester hydrochloride?) obtained from the cyanoethylaminoquinoline by keeping it for several days in alcoholic hydrogen chloride, gave an unidentified oily base, not apparently the aminine, when treated with alcoholic mmonia in the usual way.

Di-( $\dot{s}$ -amino-6-methoxy-5)-quinolylmethane.—The condensation of 8-amino-6-methoxyquinoline hydrochloride, formalin and sodium bisulphite gave only red, insoluble polymerised compounds (cf. Brahmachari *et al., J. Ind. Chem. Soc.,* 1931, **8**, 305). Using the free base (0.6 g.), which was heated for 7 hours on a steam-bath with formaldehyde bisulphite (0.7 g.) containing excess formaldehyde, an uncrystallisable brownish-yellow solid, m. p. *ca.* 120°, was obtained, probably the 8 : 8'-diaminomethylene compound. After dissolving in warm hydrochloric acid, the product separated in microscopic vermilion-coloured needles, m. p. 250° (decomp.), and in view of the well-known rearrangement of dianilinomethylene compounds it is regarded as di-(8-amino-6-methoxy-5)-quinolylmethane *hydrochloride* (Found : C, 55.7; H, 5.3. C<sub>21</sub>H<sub>20</sub>O<sub>2</sub>N<sub>4</sub>,2HCl,H<sub>2</sub>O requires C, 55.9; H, 5.3%). The orange solid, m. p. >250°, liberated from the salt with alkalis could not be crystallised.

8-Guanidino-6-methoxyquinoline [VI;  $R = -C(:NH)\cdot NH_2$ ].—A suspension of 8-amino-6-methoxyquinoline hydrochloride (2·9 g.) in ethanol (30 c.), containing cyanamide (2·8 g.) was heated under reflux for 10 hours. The solid obtained on evaporation and treatment of the residue with ether was crystallised from ethanol-ether, 8-guanidino-6-methoxyquinoline hydrochloride separating in almost colourless needles (1·6 g.), m. p. 238—240° (Found : C, 52·3; H, 5·2.  $C_{11}H_{12}ON_4$ , HCl requires C, 52·3; H, 5·1%). The amine hydroidide, similarly prepared, crystallised from Hodgson and Ward: The Preferential Reduction of

water in colourless microscopic tablets, m. p. 250–252° (Found : C, 38.5; H, 4.0.  $C_{11}H_{12}ON_4$ , HI requires C, 38.4; H, 3.8%).

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