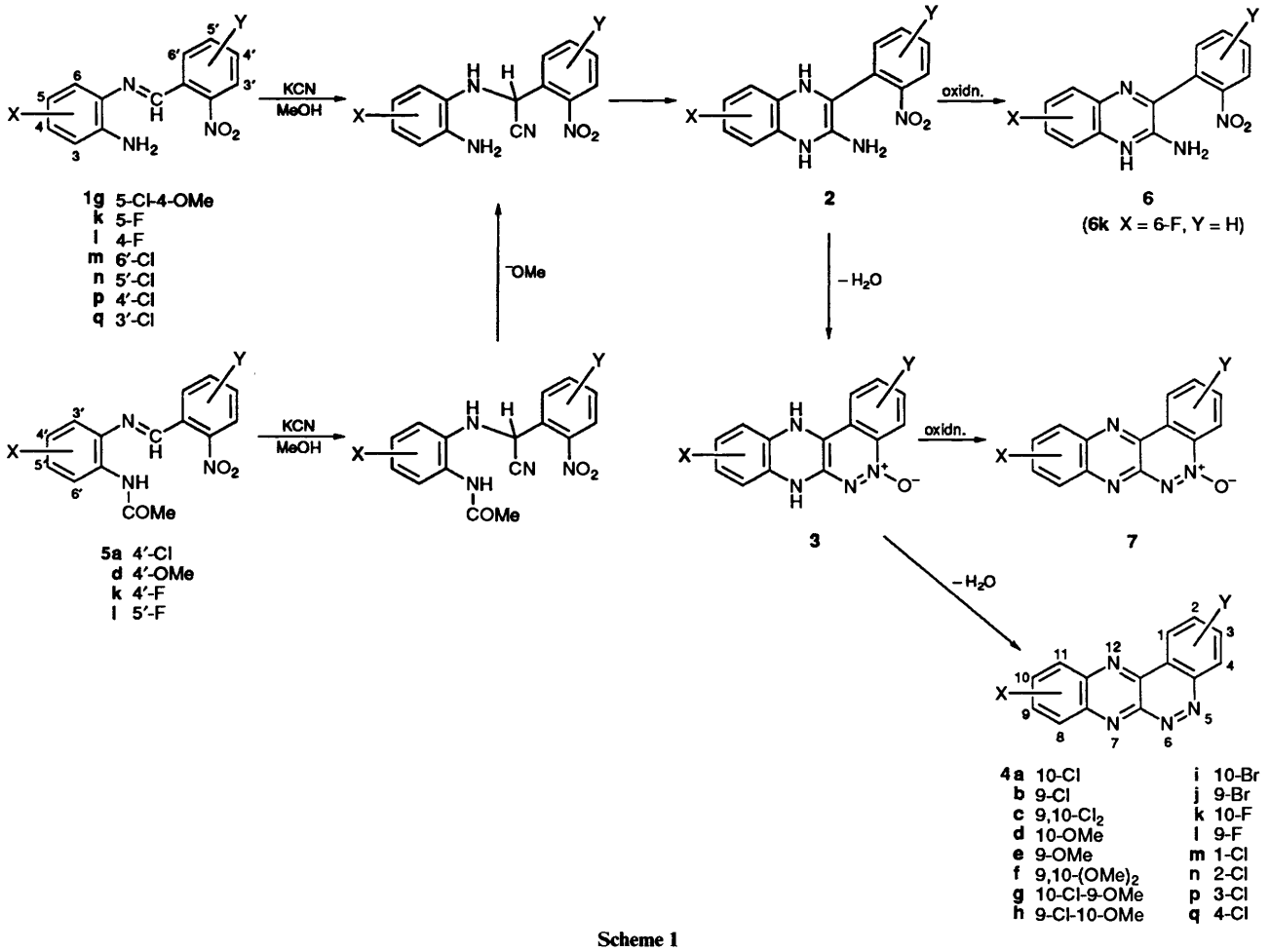
# Polyaza Heterocycles. Part 2.[1] Nucleophilic Substitution of Halogens in Halogenoquinoxalino[2,3-*c*]cinnolines

**Arshad Ahmad, Linda J. Dunbar, Iain G. Green, Ian W. Harvey, Thomas Shepherd, David M. Smith* and Robert K. C. Wong**
*School of Chemistry, University of St. Andrews, Purdie Building, St. Andrews, Fife KY16 9ST, UK*

10-Chloroquinoxalino[2,3-*c*]cinnoline readily undergoes methoxydechlorination when treated with sodium methoxide. The 1-, 2-, 3-, 4- and 9-chloro isomers are unreactive towards this reagent, but the 9,10-dichloro derivative undergoes substitution of both chlorines (the 10-position being much the more reactive). The 9- and 10-bromo analogues are both unreactive towards sodium methoxide, but the 9- and 10-fluoro analogues are both highly reactive, to the extent that it has not been possible even to isolate the 10-fluoro compound. Routes to 9- and 10-piperidinoquinoxalino[2,3-*c*]-cinnolines are described.

Some years ago[2] we described the synthesis of quinoxalino-[2,3-*c*]cinnoline and some of its simple derivatives by the reaction of *N*-(2-nitrobenzylidene)-*o*-phenylenediamines, **1**, with potassium cyanide in methanol. The individual steps in the reaction sequence were formulated as in Scheme 1: (i) initial addition of HCN to the azomethine group, with the concomitant formation of methoxide ions; (ii) intramolecular nucleophilic attack by the primary amino-nitrogen on the cyano group, giving the aminodihydroquinoxaline **2**; (iii) a second intramolecular nucleophilic attack, this time by the primary amino-nitrogen of **2** on the nitro group, leading to the fused cinnoline oxide **3**; and (iv) dehydration of the latter, giving the fully conjugated quinoxalino[2,3-*c*]cinnoline **4**.

The formation of the anils (Schiff bases) **1** is easily achieved by treatment of equimolar quantities of the appropriate diamine and 2-nitrobenzaldehyde, sometimes, if necessary, in the presence of an added acidic catalyst (such as toluene-*p*-sulfonic acid). The reaction of an unsymmetrically substituted *o*-phenylenediamine with 2-nitrobenzaldehyde can, in principle, give either of two isomeric Schiff bases (or a mixture of both), and there is thus a possible ambiguity in the position of the substituent(s) in the derived quinoxalinocin-




Scheme 1

noline(s). In a second paper, however,[3] we showed that cyclisation of 2'-(2-nitrobenzylideneamino)acetanilides, **5**, using potassium cyanide in methanol, was equally effective in producing quinoxalino[2,3-*c*]cinnolines, thus allowing the synthesis of unambiguously substituted derivatives of this ring system. Two types of by-product sometimes encountered in these cyclisations were the 2-amino-3-(2-nitroaryl)quinoxaline **6** and the quinoxalinocinnoline 5-oxide **7**; these were presumed to arise from atmospheric oxidation of the intermediates **2** and **3** respectively. If these by-products constituted major impurities in any particular cyclisation, it was advantageous to carry out the reaction under nitrogen.

In the course of this work it was noted that the yield of 10-chloroquinoxalino[2,3-*c*]cinnoline **4a**, obtained by cyclisation of the Schiff base **5a**, was strongly time-dependent: the longer the reaction time, the lower the yield. The $^1$H NMR spectrum of compound **4a** showed a small signal at $\delta$ 4.15, corresponding to the presence of a methoxy group, and suggesting that substitution of chlorine by methoxy might be occurring at some stage in the reaction sequence; the mass spectrum of the crude product also suggested the presence of a methoxyquinoxalinocinnoline impurity.

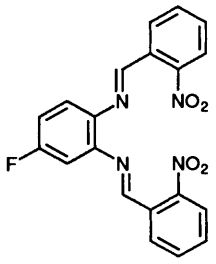
Renewed investigation of this reaction confirms these earlier indications. 10-Chloroquinoxalino[2,3-*c*]cinnoline, **4a**, when heated with sodium methoxide in methanol (with dimethylformamide as co-solvent to promote solubility) is converted, in good yield (82%), into the 10-methoxy analogue **4d**. The product is identical with that obtained by cyclisation of the anil **5d**,[3] and so the reaction may be regarded as a normal nucleophilic aromatic substitution. There is no evidence for the formation of any cine-substitution product.

Under these reaction conditions, 9-chloroquinoxalino[2,3-*c*]-cinnoline **4b** is completely unreactive: even prolonged treatment (up to 10 h) with sodium methoxide leaves this compound unaffected. Not surprisingly, therefore, 9,10-dichloroquinoxalino[2,3-*c*]cinnoline **4c** readily undergoes replacement of one chlorine (attached to C-10),[1] but prolonged reaction with sodium methoxide also effects the replacement of the second chlorine and the formation of the 9,10-dimethoxyquinoxalinocinnoline **4f**. 10-Chloro-9-methoxyquinoxalino[2,3-*c*]cinnoline **4g**, on the other hand, is highly reactive towards methoxide ions, to the extent that attempts to prepare it from the anil **1g** have led directly to the dimethoxyquinoxalinocinnoline **4f**.

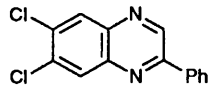
It is well-established that bromine is generally a somewhat poorer leaving group than chlorine in aromatic nucleophilic substitution, especially when the nucleophile is anionic and the nucleophilic atom is from the first row of the Periodic Table.[4] However, 10-bromoquinoxalino[2,3-*c*]cinnoline, **4i**, is very much less susceptible towards methoxydechlorination than its 10-chloro counterpart. Even after 10 h with boiling sodium methoxide the extent of substitution, according to the mass spectrum of the product, is very small. As expected, the 9-bromo isomer **4j** is just as unreactive as the 9-chloro compound.

On the other hand, fluorine is by far the best of all the halogen leaving groups in aromatic nucleophilic substitution,[4] and all attempts to isolate 10-fluoroquinoxalino[2,3-*c*]cinnoline, **4k**, from the cyclisation of the anil **5k** have so far been unsuccessful. Compound **4k** can be detected by mass spectrometry, but it is so reactive that the main product of this reaction, even after only short reaction times, is the 10-methoxy compound **4d**. Even 9-fluoroquinoxalinocinnoline, **4l**, is highly reactive towards methoxide, and its successful isolation requires that the cyclisation of the anil **1l** be conducted under very mild conditions (at room temperature). (It is interesting to note that the reaction of 4-fluoro-*o*-phenylenediamine with 2-nitrobenzaldehyde gives the anil **11** rather than the isomeric anil **1k**; as with the corresponding chloro diamine,[2] it is the amino group *para* to the halogen which is apparently the more nucleophilic under these conditions.[5,6] It is also interesting to note that the formation of the anil **1l**, like its cyclisation, requires unusually mild reaction conditions: otherwise the bis-2-nitrobenzylidene compound **8** is formed.)

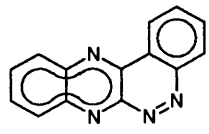
The reactivity of the halogens in these compounds is remarkable by virtue of the fact that the corresponding reactions in simple quinoxalines are unknown. In 6,7-dichloro-2-phenylquinoxaline **9**, which we had hoped to use as a model




**8**




**9**




**11**

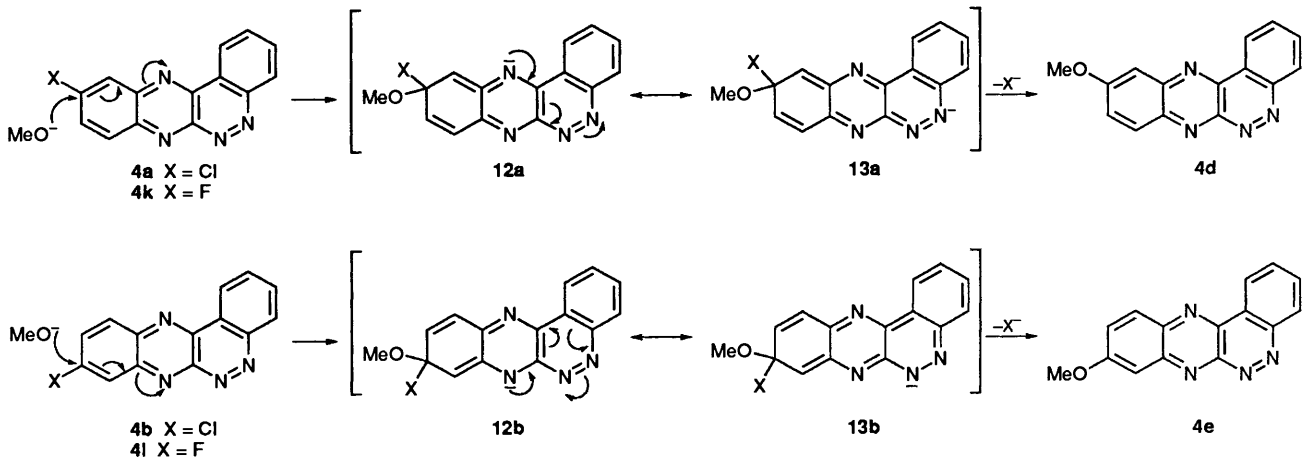
for 9,10-dichloroquinoxalinocinnoline, neither chlorine is displaceable by the action of methoxide, and what little is known of quinoxalines containing a fluoro substituent in the carbocyclic ring suggests that even these undergo nucleophilic substitution only under forcing conditions.[6,7]

Since the reactivity in the quinoxaline portion of the fused-ring system **4** is clearly different from that of simple quinoxalines, it was also of interest to discover if there was also a difference in reactivity between halogens in the cinnoline portion of **4** and those in a simple cinnoline. (As far as we are aware, nucleophilic substitution of halogens from 5-, 6-, 7- or 8-halogenocinnolines is unknown.) Accordingly the synthesis of quinoxalino[2,3-*c*]cinnolines substituted by chlorine in the cinnoline portion have been undertaken.

These require as starting materials the appropriate chloro-2-nitrobenzaldehydes, of which only one (the 5-chloro isomer) is commercially available. 4-Chloro-2-nitrobenzaldehyde is relatively easily obtained, however, by oxidation of the commercially available 4-chloro-2-nitrobenzyl alcohol using pyridinium chlorochromate[8] in dichloromethane. The other two isomers, **10a** and **10b**, are made from the corresponding chloronitrotoluenes by Kröhnke oxidation.[9] 3-Chloro-2-nitrotoluene itself is made in four stages from 4-methyl-3-nitroaniline; the final stage of this sequence is an unusual 'one-pot' reaction in which diazotisation of 4-methyl-2,3-dinitroaniline is followed by nucleophilic aromatic substitution of the 2-nitro substituent by chlorine, and subsequently by deamination with ethanol as the hydrogen donor. The overall yield in the synthesis of **10b** is low (*ca.* 4%); however, the materials required for the synthesis are all relatively inexpensive and a low yield is therefore acceptable.

The cyclisation of *N*-(5-chloro-2-nitrobenzylidene)-*o*-phenylenediamine **1n** to 2-chloroquinoxalino[2,3-*c*]cinnoline **4n** has already been described.[2] The formation of the anils **1m**, **1p** and **1q** from *o*-phenylenediamine and the other three chloronitrobenzaldehydes, and their subsequent cyclisation to 1-, 3- and 4-chloroquinoxalino[2,3-*c*]cinnolines **4m**, **4p** and **4q**, respectively, follow similar lines. None of these chloroquinoxalinocinnolines shows any reaction when heated with sodium methoxide.

MNDO calculations suggest that the delocalisation of the π-electrons in the quinoxalino[2,3-*c*]cinnoline ring system is best represented by means of the structure **11**, in which systems containing 10π- (quinoxaline), 6π- (benzene) and 2π-electrons (azo) are separated by bonds of low order.[1] There is, appar-




Scheme 2

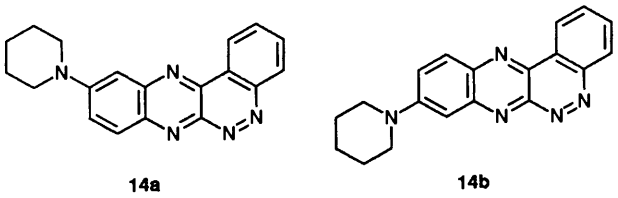
ently, no tendency for the isolated π-electron systems to interact, giving a completely delocalised 18π-electron system. On this basis, it is perhaps not surprising that the 1-, 2-, 3- and 4-chloroquinoxalinocinnolines are not susceptible to nucleophilic substitution any more than, for example, chlorobenzene. It is conceivable that nucleophilic attack at C-2 or C-4 could generate a negative charge on the ring system which could be delocalised as far as N-6 without destroying the integrity of the quinoxaline 10π-system; but this is, apparently, not observed.

However, the exceptional reactivity of the 10- relative to the 9-halogenoquinoxalinocinnolines, and the apparent reactivity of both relative to simple quinoxalines, remain to be explained. The very fact that there is this increase in reactivity when the cinnoline system is fused to the quinoxaline implies that the cinnoline portion of the fused tetracyclic system has a facilitating role in the substitution process, and a possible rationalisation of the observed facts is shown in Scheme 2.

The negative charge resulting from nucleophilic attack at C-10 may be delocalised as far as N-12 (structure **12a**), giving a structure retaining an intact 10π- (cinnoline) system, and as far as N-5 while still retaining an intact 6π- (benzene) system (structure **13a**). If the nucleophilic attack occurs at C-9, delocalisation of the negative charge may extend to N-7 (structure **12b**), without disruption of the cinnoline, but delocalisation beyond C-12a (*e.g.* as far as N-6: *cf.* structure **13b**) requires loss even of the benzenoid 6π-system, and this reaction pathway is therefore likely to be less energetically favourable.

One feature of these reactions which is still unexplained, however, is the replaceability of both chlorines in 9,10-dichloroquinoxalinocinnoline. While rapid substitution of the 10-chloro substituent is to be expected, giving the 9-chloro-10-methoxy compound **4h**, it is surprising that the 9-chloro substituent is then also displaced, albeit slowly, given the complete lack of reactivity of 9-chloroquinoxalinocinnoline **4b** towards methoxide. Indeed the electronic effect of the *o*-methoxy substituent might be expected to inhibit nucleophilic substitution at C-9 in **4h** relative to **4b**.

A preliminary investigation has been carried out into the nucleophilic substitution of 9- and 10-halogenoquinoxalino-[2,3-*c*]cinnolines using piperidine. 10-Chloroquinoxalinocinnoline **4a** reacts directly with piperidine (as both solvent and reagent) giving a dark purple solid which, although not analytically pure, has $^1$H NMR and mass spectra which are consistent with its formulation as 10-piperidinoquinoxalino-[2,3-*c*]cinnoline **14a**. Reaction of compound **14a** with increasingly concentrated hydrochloric acid in acetone solution leads to an interesting series of colour changes, from deep reddish-purple ($\lambda_{max}$ *ca.* 510 nm) through blue ($\lambda_{max}$ *ca.* 605 nm) to purple again ($\lambda_{max}$ *ca.* 560 nm). The significance of these colour changes remains to be investigated.




9-Piperidinoquinoxalino[2,3-*c*]cinnoline, **14b**, is accessible by the reaction of the anil **5l** with potassium cyanide in a methanol–piperidine mixture. In this reaction 9-fluoroquinoxalinocinnoline is the presumed primary product, and this is then expected to react *in situ* with piperidine rather than with the less nucleophilic methanol. In our preliminary experiment, the mass spectrum indicates, not surprisingly, that 9-methoxyquinoxalinocinnoline is also obtained as a by-product; nevertheless this approach opens up possible new synthetic routes to a variety of substituted derivatives of what has proved so far to be a fascinating ring system.

## Experimental

The IR spectra were recorded as Nujol mulls. Unless otherwise stated, $^1$H NMR spectra were recorded at 360 MHz for quinoxalinocinnolines, and at 80 MHz for other compounds, in $CDCl_3$ with tetramethylsilane ($\delta_H$ 0) as reference; $^{19}$F NMR spectra were recorded at 75.3 MHz, with $CFCl_3$ ($\delta_F$ 0) as reference. *J* Values are given in Hz. Ether refers to diethyl ether.

The following quinoxalino[2,3-*c*]cinnolines have been described in previous papers: 10-chloro- **4a**,[3] m.p. 250–252 °C; 9-chloro-**4b**,[2,3] m.p. 278 °C; 9,10-dichloro-**4c**,[1] m.p. 257–258 °C; 10-methoxy- **4d**,[3] m.p. 264 °C; 9-chloro-10-methoxy- **4h**,[1] m.p. 242–243 °C; 10-bromo-**4i**,[3] m.p. 263–265 °C; 9-bromo-**4j**,[3] m.p. 252–254 °C; and 2-chloro- **4n**,[2] m.p. 260–262 °C.

4-*Chloro*-2-*nitrobenzaldehyde*.—A solution of 4-chloro-2-nitrobenzyl alcohol (1.87 g, 10 mmol) in dichloromethane (20 cm$^3$) was added rapidly at room temperature to a well-stirred suspension of pyridinium chlorochromate (3.23 g, 15 mmol) in dichloromethane (15 cm$^3$). After 2 h the black mixture was diluted with dry ether (175 cm$^3$); the ethereal solution was decanted and the residue washed twice with more ether. The combined ethereal solutions were filtered through Celite and

concentrated, giving the crude aldehyde [1.05 g, 57%; $\nu_{max}$/cm$^{-1}$ 1690 (C=O), 1510 and 1340 ($NO_2$); $\delta_H$ 7.75–8.25 (3 H, m, ArH), 10.56 (1 H, s, CHO)], m.p. *ca.* 50–60 °C (lit.,[10] 67–68 °C). This was used directly for the preparation of the anil **1p**.

2-*Chloro*-6-*nitrobenzaldehyde* **10a**.—2-Chloro-6-nitrotoluene (30.5 g), was brominated using *N*-bromosuccinimide and benzoyl peroxide in carbon tetrachloride according to the literature method.[11] The resulting 2-chloro-6-nitrobenzyl bromide was converted, without purification, into the pyridinium salt by reaction with dry pyridine in ethanol at room temperature, and the latter condensed with *N*,*N*-dimethyl-4-nitrosoaniline in presence of aqueous sodium hydroxide. The resulting nitrone was filtered off and then hydrolysed by reaction with dilute hydrochloric acid at room temperature. The aldehyde (24.3 g, 75%), m.p. 69–71 °C (lit.,[11] 70–71 °C) was adjudged sufficiently pure by NMR spectroscopy for use in the preparation of the anil **1m**; $\nu_{max}$/cm$^{-1}$ 1690 (C=O), 1510 and 1340 ($NO_2$); $\delta_H$ 7.75 (1 H, t, $J_{4,5}$ 7.9, 4-H), 7.94 (1 H, dd, $J_{3,4}$ 7.9, $J_{3,5}$ 2.5, 3-H), 8.13 (1 H, dd, 5-H) and 10.60 (1 H, s, CHO).

3-*Chloro*-2-*nitrotoluene*.—4′-Methyl-3′-nitroacetanilide, m.p. 143–144 °C (lit.,[12] 144.5 °C) was prepared (yield, 64%) by acetylation of 4-methyl-3-nitroaniline.

4′-Methyl-3′-nitroacetanilide (30.0 g, 0.155 mol) was added portionwise to well-stirred fuming nitric acid (*d* 1.5; 120 cm$^3$) so that the temperature was maintained below 20 °C. After the addition was complete, stirring was continued for 45 min, and the mixture then poured gradually into cold water (1 dm$^3$). The yellow product was filtered off, washed with water, and recrystallised (twice) from acetic acid, giving the almost colourless 4′-methyl-2′,3′-dinitroacetanilide (20.0 g, 54%), m.p. 172 °C (lit.,[13] 174.5 °C).

4′-Methyl-2′,3′-dinitroacetanilide (35.4 g, 0.15 mol) was hydrolysed in aqueous sulfuric acid,[14] giving 4-methyl-2,3-dinitroaniline (27.7 g, 96%), m.p. 123–124 °C (from ethanol; lit.,[14] 124 °C). This amine (27.7 g, 0.115 mol) was diazotised in a mixture of concentrated hydrochloric acid and ethanol, according to the literature procedure:[15] the mixture was then slowly heated to 70 °C and the product steam distilled, giving 3-chloro-2-nitrotoluene (13.0 g, 54%) as a yellow oil (lit.,[15] m.p. 22 °C). This was not purified further but was used directly in the next step.

3-*Chloro*-2-*nitrobenzaldehyde* **10b**.—A mixture of 3-chloro-2-nitrotoluene (13.0 g, 76 mmol), *N*-bromosuccinimide (13.5 g, 76 mmol), benzoyl peroxide (0.2 g, 8 mmol) and carbon tetrachloride (25 cm$^3$) was heated at 80 °C under UV light for 30 h. A further two portions of benzoyl peroxide (0.2 g each) were added, after 8 and 20 h. The mixture was then cooled and filtered, and the solid washed with carbon tetrachloride and discarded. The carbon tetrachloride solution was then evaporated under reduced pressure and the crude 3-chloro-2-nitrobenzyl bromide (a pale brown oil) was converted directly into *N*-(3-chloro-2-nitrobenzyl)pyridinium bromide by the addition, at 0 °C, of a mixture of dry pyridine (5.0 cm$^3$) and dry ethanol (5 cm$^3$). The reaction mixture was stirred for 1 h at room temperature and then cooled to 0 °C; after 4 h the pyridinium salt was filtered off and recrystallised from ethanol to give the pure product (5.71 g, 22% overall), m.p. 201–203 °C (lit.,[16] 205 °C).

A stirred solution of *N*-(3-chloro-2-nitrobenzyl)pyridinium bromide (5.71 g, 17 mmol) and *freshly prepared*[17] *N*,*N*-dimethyl-4-nitrosoaniline (3.44 g, 23 mmol) in ethanol (85 cm$^3$) was cooled to 0 °C, and aqueous sodium hydroxide (1 mol dm$^{-3}$; 50 cm$^3$) was then added dropwise so that the temperature was maintained below 2 °C. The mixture was stirred at room temperature for 4 h, then diluted with water (40 cm$^3$) and chilled in ice. The brown nitrone was filtered off and washed with water. The crude product was recrystallised from acetone to give the pure *nitrone*, m.p. 178–179 °C (3.20 g, 58%) (Found: C, 56.1; H, 4.0; N, 13.5. $C_{15}H_{14}ClN_3O_3$ requires C, 56.35; H, 4.4; N, 13.1%).

The nitrone (4.0 g, 12.5 mmol) was stirred with sulfuric acid (6 mol dm$^{-3}$; 70 cm$^3$) at room temperature for 1.5 h, then the mixture was heated at 50 °C for 50 min and finally at 100 °C for 5 min. After cooling, the mixture was extracted with chloroform (3 × 50 cm$^3$) and the combined extracts were washed with water, dried ($Na_2SO_4$), and then the solvent evaporated to give the crude *aldehyde* as a pale brown oil (2.12 g, 91%; lit.[16] m.p. 62 °C), which was used without further purification.

N-(2-*Chloro*-6-*nitrobenzylidene*)-o-*phenylenediamine* **1m**.—A solution of *o*-phenylenediamine (1.08 g, 0.01 mol) and 2-chloro-6-nitrobenzaldehyde (1.85 g, 0.01 mol) in the minimum volume of ethanol was heated to boiling for 3 min, then cooled to 0 °C and a little ice added. The oily product was separated and triturated with propan-2-ol (10 cm$^3$). The *anil* **1m** was then filtered off, and a second crop was obtained by concentrating the mother-liquors (total yield 2.00 g, 72%), m.p. 113–115 °C (from acetone–water) (Found: C, 56.7; H, 3.6; N, 15.0. $C_{13}H_{10}ClN_3O_2$ requires C, 56.6; H, 3.7; N, 15.2%); $\delta_H$ 3.95 (2 H, s, $NH_2$), 6.70–6.95 (2 H, m), 7.10–7.35 (2 H, m), 7.50–7.80 (3 H, m) and 8.98 (1 H, s, CH=N); *m*/*z* 275/277 ($M^{+\cdot}$).

N-(4-*Chloro*-2-*nitrobenzylidene*)-o-*phenylenediamine* **1p**.—A mixture of *o*-phenylenediamine (1.08 g) and 4-chloro-2-nitrobenzaldehyde (1.85 g) in the minimum volume of ethanol was heated to boiling for 2 min and then cooled, whereupon the bright red anil crystallised out. The product was recrystallised from ethanol to give pure *anil* **1p** (2.29 g, 83%), m.p. 92–94 °C (Found: C, 56.7; H, 3.55; N, 15.3. $C_{13}H_{10}ClN_3O_2$ requires C, 56.6; H, 3.7; N, 15.2%); $\delta_H$ 4.08 (2 H, br s, $NH_2$), 6.7–7.0 (2 H, m), 7.1–7.4 (2 H, m), 7.78 (1 H, dd, $J_{5,6}$ 8.5, 5-H), 8.13 (1 H, d, $J_{3,5}$ 2.5, 3-H), 8.40 (1 H, d, 6-H) and 9.10 (1 H, s, CH=N); *m*/*z* 275/277 ($M^{+\cdot}$).

N-(3-*Chloro*-2-*nitrobenzylidene*)-o-*phenylenediamine* **1q**.—The impure 3-chloro-2-nitrobenzaldehyde, prepared above (2.12 g, 11.5 mmol) and *o*-phenylenediamine (1.29 g, 12 mmol) were dissolved separately in the minimum volume of ethanol. The solutions were combined, a few crystals of toluene-*p*-sulfonic acid were added, and the mixture heated under reflux for 15 min and then cooled and concentrated under reduced pressure. The crude product was recrystallised from propan-2-ol to give pure *anil* **1q** (3.03 g, 95%) (Found: C, 56.6; H, 3.4; N, 15.2. $C_{13}H_{10}ClN_3O_2$ requires C, 56.6; H, 3.65; N, 15.2%) $\nu_{max}$/cm$^{-1}$ 3420 and 3330 ($NH_2$), 1530 and 1330 ($NO_2$); $\delta_H$(300 MHz) 4.20 (2 H, br s, $NH_2$), 6.65–6.75 (2 H, m), 7.10–7.25 (2 H, m), 7.47 (1 H, t, $J_{4',5'} = J_{5',6'}$ 7.2, 5′-H), 7.53 (1 H, dd, $J_{4',6'}$ 1.8, 4′-H), 7.73 (1 H, d, 6′-H) and 8.37 (1 H, s, CH=N).

3′-*Chloro*-4′-*methoxyacetanilide*.—1,2-Dichloro-4-nitrobenzene (40 g) was added to a solution of sodium methoxide [from sodium (5.8 g)] in methanol (250 cm$^3$); the mixture was heated under reflux for 2 h, cooled, and then the crystalline 2-chloro-4-nitroanisole was filtered off (33.0 g, 84%), m.p. 92–94 °C (from ethanol; lit.,[18] 95 °C).

Iron powder (17.0 g) and 2-chloro-4-nitroanisole (20.0 g) were added to water (140 cm$^3$) containing acetic acid (1 cm$^3$), and the mixture was heated under reflux for 3 h and then diluted with water (700 cm$^3$), basified using aqueous sodium carbonate (2 mol dm$^{-3}$), and filtered hot through Celite. 3-Chloro-4-methoxyaniline crystallised from the cooled solution, and a second crop was obtained by concentration of the filtrate to *ca.* 200 cm$^3$ and saturating it with sodium chloride. The

combined crops were recrystallised from light petroleum (b.p. 60–80 °C) to give 3-chloro-4-methoxyaniline (15.0 g, 89%), m.p. 60–62 °C (lit.,[18] 62 °C).

Acetic anhydride (30 $cm^3$) was added to a solution of 3-chloro-4-methoxyaniline (20.0 g) in acetic acid (30 $cm^3$), the mixture was heated at 100 °C for 15 min, and then poured slowly into ice–water (200 $cm^3$). The product on recrystallisation from toluene gave 3'-chloro-4'-methoxyacetanilide (25.0 g, 80%), m.p. 92–94 °C (lit.,[18] 94 °C).

*5-Chloro-4-methoxy-o-phenylenediamine.*—3'-Chloro-4'-methoxyacetanilide (14.0 g) was added portionwise, with stirring, to concentrated sulfuric acid (14 $cm^3$) at room temperature. When complete dissolution was achieved (*ca.* 2 h), the deep violet solution was added dropwise to a well-stirred mixture of concentrated nitric acid (*d* 1.38; 4.8 $cm^3$) and concentrated sulfuric acid (4.8 $cm^3$) at 0 °C. The colour faded and a yellow product was precipitated; the mixture was added to crushed ice and the product was filtered off. 5'-Chloro-4'-methoxy-2'-nitroacetanilide was recrystallised from ethanol to give the pure compound (12.4 g, 73%), m.p. 157–159 °C (lit.,[19] 159 °C); $\delta_H$ 2.30 (3 H, s, MeCO), 3.97 (3 H, s, MeO), 7.71 (1 H, s, 3-H) and 8.88 (1 H, s, 6-H).

Hydrolysis of the acetamido group was achieved by heating 5'-chloro-4'-methoxy-2'-nitroacetanilide (12.0 g) with hydrochloric acid (5 mol $dm^{-3}$; 65 $cm^3$) under reflux for 1 h. The mixture, which contained a black tarry residue, was filtered hot; the tarry residue was extracted with a second portion of hot hydrochloric acid (10 $cm^3$) containing charcoal, and this extract also filtered hot through Celite. The combined (orange) acidic solutions were cooled to give 5-chloro-4-methoxy-2-nitroaniline (5.7 g, 57%), m.p. 135–137 °C (lit.,[19] 139 °C).

The nitroamine (5.0 g) and sodium dithionite (15 g) were added, simultaneously, in small portions to gently boiling water (100 $cm^3$), and heating continued, with slow stirring, until the solution was decolourised. The solution was filtered hot, then cooled to 0 °C and the residue filtered off and dried under reduced pressure to give 5-chloro-4-methoxy-*o*-phenylenediamine (1.5 g, 35%), m.p. 120 °C (decomp.) (lit.,[20] 126.5 °C); $\delta_H$ 3.27 (4 H, br s, 2 × $NH_2$), 3.83 (3 H, s, Me), 6.42 (1 H, s, 3-H) and 6.78 (1 H, s, 6-H).

*2-Amino-5-chloro-4-methoxy-*N*-(2-nitrobenzylidene)aniline* **1g**.—This was prepared by the standard method, *viz.* reaction of equimolar quantities of 5-chloro-4-methoxy-*o*-phenylenediamine and 2-nitrobenzaldehyde in the minimum volume of warm ethanol; in this case it was advisable to conduct the reaction under nitrogen. The *anil* **1g** was obtained in a yield of 71%, m.p. 130–132 °C (Found: C, 54.75; H, 4.0; N, 13.8. $C_{14}H_{12}ClN_3O_3$ requires C, 55.0; H, 4.2; N, 13.7%); $\delta_H$ 3.85 (3 H, s, OMe), 4.10 (2 H, br s, $NH_2$), 6.38 (1 H, s, 3-H), 7.30 (1 H, s, 6-H), 7.45–7.75 (2 H, m, 4'- and 5'-H), 7.90–8.02 (2 H, m, 3'- and 6'-H) and 8.89 (1 H, s, CH=N); *m/z* 305/307 ($M^{+\bullet}$).

*4'-Fluoro-2'-(2-nitrobenzylideneamino)acetanilide* **5k**.—4'-Fluoroacetanilide, m.p. 152–154 °C (from water; lit.,[21] 153.1–153.3 °C), was prepared (yield, 59%) by acetylation of 4-fluoroaniline. Concentrated nitric acid (*d* 1.42; 4 $cm^3$) was added dropwise to a solution of 4'-fluoroacetanilide (7.65 g, 0.05 mol) in concentrated sulfuric acid (85 $cm^3$), with the temperature of the mixture kept in the range 0–5 °C. When the addition was complete the mixture was added to crushed ice, and the product filtered off, washed with aqueous sodium hydrogen carbonate and recrystallised from aqueous ethanol to give 4'-fluoro-2'-nitroacetanilide (5.50 g, 56%), m.p. 68–70 °C (lit.,[22] 69.5–70.5 °C).

*2'-Amino-4'-fluoroacetanilide.* (*a*) A solution of 4'-fluoro-2'-nitroacetanilide (2.0 g, 10 mmol) in ethanol (80 $cm^3$) was hydrogenated over 5% palladium–charcoal (0.25 g). When hydrogenation was complete and the catalyst removed, the solution was concentrated to approximately 10 $cm^3$ and the grey–green precipitate (0.82 g) filtered off and dried to give the product, m.p. 250–255 °C (decomp.) (lit.,[23] for 2'-amino-4'-fluoroacetanilide 95–97 °C); however it had the correct mass spectrum, and was therefore presumed to be a salt (the hydrofluoride?) of the required amine.

(*b*) 4'-Fluoro-2'-nitroacetanilide (2.0 g, 0.01 mol) was added slowly to a suspension of iron powder (1.8 g, 0.032 mol) in acetic acid (0.2 $cm^3$) and water (12 $cm^3$) kept in the temperature range 65–80 °C. When the addition was complete, the temperature was held at 80 °C for a few min, and then calcium carbonate (0.5 g) was added to neutralise the mixture. After 10 min the hot mixture was filtered and the filtrate concentrated under reduced pressure to give the impure amine (1.30 g, 77%), m.p. 117–119 °C (lit.,[23] 95–97 °C); $\delta_H$ 2.18 (3 H, s, Me), 3.52 (2 H, br s, $NH_2$), 6.7–6.85 (2 H, m), 7.10–7.30 (1 H, m) and 7.60 (1 H, v br, N*H*Ac); *m/z* 168 (39%, $M^{+\bullet}$), 127 (14), 126 (100), 125 (39), 111 (34), 110 (12), *etc.*

The hydrofluoride of 2'-amino-4'-fluoroacetanilide (1.10 g, 6 mmol) and 2-nitrobenzaldehyde (0.90 g, 6 mmol) were each dissolved in ethanol (6 $cm^3$) and warmed gently on a water bath for a few min. The solutions were then mixed and a few drops of saturated aqueous sodium hydrogen carbonate were added. The mixture was then allowed to cool and the yellow precipitate filtered off to give the *anil* **5k** (1.28 g, 71%), m.p. 162–164 °C (from ethanol) (Found: C, 59.45; H, 4.1; N, 14.2. $C_{15}H_{12}FN_3O_3$ requires C, 59.8; H, 4.0; N, 13.95%); $\delta_H$ 2.26 (3 H, s, Me), 6.85–8.80 (8 H, unresolved, ArH and NH) and 9.00 (1 H, s, CH=N).

*2'-Amino-5'-fluoroacetanilide.*—5'-Fluoro-2'-nitroacetanilide[24] (4.70 g, 24 mmol), dissolved in ethanol (750 $cm^3$), was hydrogenated in the presence of 5% palladium–charcoal (0.6 g). When the uptake of hydrogen was complete, the catalyst was filtered off and the red filtrate was evaporated to dryness to give a dark solid (3.4 g), m.p. 89–100 °C. Attempts to purify this solid were unsuccessful and the crude material was therefore used for the next stage.

*5'-Fluoro-2'-(2-nitrobenzylideneamino)acetanilide* **5l**.—Solutions of crude 2'-amino-5'-fluoroacetanilide (1.50 g, 9 mmol) and of 2-nitrobenzaldehyde (1.35 g, 9 mmol), each in ethanol (15 $cm^3$), were mixed a few crystals of toluene-*p*-sulfonic acid were added, and the mixture heated under reflux for 15 min and then cooled in ice. The bright yellow precipitate was filtered off and recrystallised from propan-2-ol to give *anil* **5l** (2.15 g, 79%) (Found: C, 59.4; H, 4.0; N, 14.0. $C_{15}H_{12}FN_3O_3$ requires C, 59.8; H, 4.0; N, 13.95%); $\nu_{max}/cm^{-1}$ 3350 (NH), 1670 (CO), 1510 and 1360 ($NO_2$); $\delta_H$(300 MHz) 2.25 (3 H, s, Me), 6.75 (1 H, 8 lines, $J_{3',4'}$ 9.0, $J_{4',F}$ 8.0, $J_{4',6'}$ 2.7, 4'-H), 7.20 (1 H, dd, $J_{3',F}$ 5.7, 3'-H), 7.6–7.8 (2 H, dt, $J_{4'',5''}$ 5, $J_{4'',6''}$ 1.2*, 4''-, 5''-H), 7.90 (1 H, dd, 6''-H), 8.02 (1 H, dd, $J_{3'',4''}$ 8.4, $J_{3'',5''}$ 1.5*, 3''-H), 8.30 (1 H, dd, $J_{6',F}$ 10.5, 6-H), 8.57 (1 H, br s, NH) and 8.80 (1 H, s, CH=N); $\delta_F$ −110.5.

*1-Chloroquinoxalino*[2,3-c]*cinnoline* **4m**.—A mixture of the anil **1m** (1.37 g, 5 mmol) and potassium cyanide (0.65 g, 10 mmol) in methanol (100 $cm^3$) was heated under reflux for 3 h and then cooled to 0 °C, and the *quinoxalinocinnoline* **4m** (0.37 g, 28%) filtered off, m.p. 255–259 °C (from dimethylformamide) (Found: C, 63.1; H, 2.5; N, 21.1. $C_{14}H_7ClN_4$ requires C, 63.1; H, 2.6; N, 21.0%); $\delta_H$ 8.01 (1 H, t, $J_{2,3}$ 8.0, $J_{3,4}$ 8.0, 3-H), 8.02–8.11 (2 H, symm. m, 9- and 10-H), 8.12 (1 H, dd, $J_{2,4}$ 1.3, 2-H),

* Non-first-order spectrum for the 2-nitrobenzylidene group.

8.44–8.48 and 8.52–8.56 (2 H, 2 m, 8- and 11-H), and 8.89 (1 H, dd, 4-H); *m/z* 266/268 ($M^{+\bullet}$) and 238/240 [$(M - N_2)^{+\bullet}$].

3-*Chloroquinoxalino*[2,3-c]*cinnoline* **4p**.—The title compound, m.p. 264–265 °C (from dimethylformamide), was similarly prepared (59%) from the anil **1p** (Found: C, 63.1; H, 2.55; N, 21.1. $C_{14}H_7ClN_4$ requires C, 63.1; H, 2.6; N, 21.0%); $\delta_H$ 8.00–8.11 (2 H, m, 9- and 10-H), 8.02 (1 H, dd, $J_{1,2}$ 8.4, $J_{2,4}$ 2.1, 2-H), 8.37–8.41 (1 H, m, 11-H), 8.53–8.56 (1 H, m, 8-H), 8.87 (1 H, dd, 4-H) and 9.20 (1 H, dd, 1-H); $J_{1,4}$ 0.3; *m/z* 266/268 ($M^{+\bullet}$) and 238/240 [$(M - N_2)^{+\bullet}$].

4-*Chloroquinoxalino*[2,3-c]*cinnoline* **4q**.—Methanol (120 $cm^3$) was heated under reflux in a nitrogen atmosphere for 45 min. *N*-(3-Chloro-2-nitrobenzylidene)-*o*-phenylenediamine **1q** (2.50 g, 9 mmol) and potassium cyanide (1.2 g, 18.5 mmol) were added to it, and the mixture then heated under reflux, in a nitrogen atmosphere, for 4 h. The product obtained after cooling was filtered off; recrystallisation from dimethylformamide gave the *quinoxalinocinnoline* **4q** (1.20 g, 50%), m.p. 323–325 °C (Found: C, 62.9; H, 2.3; N, 20.9. $C_{14}H_7ClN_4$ requires C, 63.05; H, 2.65; N, 21.0%); $\delta_H$ 8.03 (1 H, t, $J_{1,2}$ 7.8, $J_{2,3}$ 7.8, 2-H), 8.04–8.16 (2 H, 2 × 8 lines, 9- and 10-H), 8.18 (1 H, dd, $J_{1,3}$ 1.3, 3-H), 8.42–8.47 (1 H, m, 11-H), 8.58–8.63 (1 H, m, 8-H) and 9.26 (1 H, dd, 1-H).

*Treatment of Chloroquinoxalino*[2,3-c]*cinnolines with Sodium Methoxide*.—1-Chloroquinoxalino[2,3-*c*]cinnoline **4m** (0.20 g) was dissolved in a boiling solution of sodium methoxide [prepared from sodium (0.05 g) in methanol (25 $cm^3$) with the subsequent addition of dimethylformamide (15 $cm^3$)]. The solution was heated under reflux for 5 h and then set aside overnight; unchanged chloroquinoxalinocinnoline crystallised out from the cooled reaction mixture. The recovery was 0.18 g (90%).

Under similar reaction conditions, and with reaction times in certain cases of up to 10 h, 2-, 3-, 4- and 9-chloro- and 9-bromoquinoxalino[2,3-*c*]cinnoline were recovered in yields greater than 85%; no other products were detected.

*Treatment of* 10-*Chloroquinoxalino*[2,3-c]*cinnoline* **4a** *with Sodium Methoxide*.—10-Chloroquinoxalino[2,3-*c*]cinnoline **4a** (0.23 g, 0.86 mmol) was dissolved in a boiling solution of sodium methoxide [prepared from sodium (0.05 g) in methanol (25 $cm^3$) with the subsequent addition of dimethylformamide (10 $cm^3$)]. The solution was heated under reflux for 1 h and then set aside overnight; the crystalline product was filtered off, washed with water, and recrystallised from dimethylformamide to give 10-methoxyquinoxalino[2,3-*c*]cinnoline **4d** (0.185 g, 82%), m.p. 262–264 °C, spectroscopically identical with an authentic sample.

*Treatment of* 10-*Bromoquinoxalino*[2,3-c]*cinnoline* **4i** *with Sodium Methoxide*.—10-Bromoquinoxalino[2,3-*c*]cinnoline **4i** (0.155 g, 0.5 mmol) was heated with sodium methoxide solution [from sodium (40 mg) in methanol (40 $cm^3$)], as previously described, for 10 h. The starting compound was recovered in a yield of 90%; only a trace of the methoxy compound was detected in the mass spectrum.

*Treatment of* 9,10-*Dichloroquinoxalino*[2,3-c]*cinnoline* **4c** *with Sodium Methoxide*.*—9,10-Dichloroquinoxalino[2,3-*c*]-cinnoline **4c** (0.25 g, 0.83 mmol) was dissolved in sodium methoxide solution [from sodium (0.10 g) in methanol (40 $cm^3$)]; the solution was heated under reflux for 1 h and then diluted with water and the solid product filtered off and dried (0.22 g, 90%). The $^1H$ NMR spectrum of the product was identical with that of 9-chloro-10-methoxyquinoxalino[2,3-*c*]-cinnoline **4h**. The mass spectrum, however, revealed the presence of a trace of a dimethoxy derivative, and so the crude material was heated with another portion (40 $cm^3$) of the above sodium methoxide solution for a further 1.5 h. The product obtained by dilution at this stage (0.21 g) consisted of compound **4h** and the 9,10-dimethoxy compound **4f** in a ratio of *ca.* 6:4; and when this was subjected to renewed treatment with a third portion of sodium methoxide for 7.5 h, the relative proportions of the two compounds were *ca.* 5:1 in favour of **4f**. The progressive conversion of **4h** into **4f** is also shown by the mass spectra of the mixture (see Table 1).

**Table 1** Mass spectra of the product mixture from the reaction of **4c** with NaOMe: relative intensities of molecular ions

| Reaction time ($t$/h) | Relative intensity: $M^{+\bullet}$ of **4h** 298 | $M^{+\bullet}$ of **4h** 296 | $M^{+\bullet}$ of **4f** 292 |
|---|---|---|---|
| 1 | 20 | 60 | 20 |
| 2.5 | 7 | 20 | 32 |
| 10 | 5 | 16 | 60 |

9-Chloro-10-methoxy compound **4h**: $\delta_H$ 4.27 (3 H, s, Me), 7.67 (1 H, s, 11-H), 8.06–8.21 (2 H, m, 2- and 3-H), 8.57 (1 H, s, 8-H), 8.87–9.00 (1 H, m, 4-H) and 9.15–9.30 (1 H, m, H-1). 9,10-Dimethoxy compound **4f**: $\delta_H$ 4.22 and 4.26 (2 × 3 H, 2 s, 2 × Me), 7.65 (1 H, s, 11-H), 7.78 (1 H, s, 8-H), 8.08–8.26 (2 H, m, 2- and 3-H), 8.92–9.10 (1 H, m, 4-H) and 9.25–9.40 (1 H, m, 1-H).

*Attempted Preparation of* 10-*Chloro*-9-*methoxyquinoxalino*-[2,3-c]*cinnoline* **4g**.—When the anil **1g** (140 mg, 0.5 mmol), potassium cyanide (65 mg, 1 mmol) and methanol (10 $cm^3$) were heated under reflux for 3 h, the only product isolated (60 mg, 44%) was impure 9,10-dimethoxyquinoxalino[2,3-*c*]cinnoline **4f** (Found: $M^{+\bullet}$, 292.0954. $C_{16}H_{12}N_4O_2$ requires *m/z* 292.0960).

4-*Fluoro*-o-*phenylenediamine*.—5-Fluoro-2-nitroaniline[25] (1.50 g, 9.6 mmol), dissolved in ethanol (120 $cm^3$), was hydrogenated over 5% palladium–charcoal (0.2 g). When hydrogen uptake was complete and the catalyst removed by filtration, the dark red solution was evaporated to dryness to give the diamine (1.17 g, 96%), m.p. 87–89 °C (lit.,[26] 88–89 °C).

2-*Amino*-4-*fluoro*-N-(2-*nitrobenzylidene*)*aniline* **1l**.—Solutions of 4-fluoro-*o*-phenylenediamine (0.50 g, 4 mmol) and 2-nitrobenzaldehyde (0.59 g, 3.9 mmol), each in the minimum volume of ethanol, were mixed and a few crystals of toluene-*p*-sulfonic acid were added, and the mixture then set aside at room temperature for 48 h. The bronze-coloured product was filtered off and recrystallised from ethanol to give *anil* **1l** (0.73 g, 71%), m.p. 130–132 °C (Found: C, 60.0; H, 3.8; N, 16.1. $C_{13}H_{10}FN_3O_3$ requires C, 60.2; H, 3.9; N, 16.2%); $\nu_{max}/cm^{-1}$ 3480 and 3390 ($NH_2$), 1520 and 1340 ($NO_2$); $\delta_H$(300 MHz)† 4.50 (2 H, br s, $NH_2$), 6.42–6.53 (2 H, m), 7.14 (1 H, d), 7.55–7.77 (2 H, m), 8.01 (1 H, dd), 8.27 (1 H, dd) and 8.95 (1 H, s, CH=N). $\delta_F$† −113.6.

When the reaction was carried out under reflux, as for the other anils, the product was a viscous red oil, the mass

* This has been described, in part, in Part 1.[1]

† Neither the $^1H$ nor the $^{19}F$ spectrum is first-order.

spectrum of which (found, *m/z* 392) indicated the presence of the *N,N'*-bis(2-nitrobenzylidene) compound **8**.

*Attempted Preparation of* 10-*Fluoroquinoxalino*[2,3-c]*cinnoline* **4k**.—4'-Fluoro-2'-(2-nitrobenzylideneamino)acetanilide **5k** (1.20 g, 4 mmol), potassium cyanide (0.52 g, 8 mmol) and methanol (80 $cm^3$) were heated together, under reflux, for 35 min and then cooled to 0 °C and the product filtered off. Recrystallisation from dimethylformamide gave 10-methoxyquinoxalino[2,3-*c*]cinnoline **4d** (0.17 g, 16%), m.p. 263–265 °C, spectroscopically identical with an authentic sample. The mother-liquor on dilution with water gave a second crop, the mass spectrum of which showed, in addition to the peaks for compound **4d**, small peaks at *m/z* 250 and 284. These are attributed, respectively, to the molecular ions of the expected 10-fluoroquinoxalino[2,3-*c*]cinnoline **4k** and 2-amino-6-fluoro-3-(2-nitrophenyl)quinoxaline **6k**.

9-*Fluoroquinoxalino*[2,3-c]*cinnoline* **4l**.—(*a*) Potassium cyanide (0.52 g, 8 mmol) was added to a mixture of 5'-fluoro-2'-(2-nitrobenzylideneamino)acetanilide **5l** (1.20 g, 4 mmol) and methanol (80 $cm^3$), and the mixture then heated under reflux for 35 min, cooled in ice, and the golden yellow product filtered off. This was identified as 9-methoxyquinoxalino[2,3-*c*]cinnoline **4e** (0.64 g, 61%) (see below). A trace of the required 9-fluoro compound **4l** was detected in the mass spectrum (found, *m/z* 250).

(*b*) Potassium cyanide (0.50 g, 8 mmol) was added to a mixture of 2-amino-4-fluoro-*N*-(2-nitrobenzylidene)aniline **1l** (1.00 g, 3.9 mmol) and methanol (75 $cm^3$), and the reaction carried out as in (*a*), above. The product isolated was again 9-methoxyquinoxalino[2,3-*c*]cinnoline **4e** (40%), and again a trace of the 9-fluoro-compound was detected by mass spectrometry.

(*c*) Method (*a*) was repeated but the reaction time was shortened to 10 min. The precipitate filtered off was a mixture of the 9-methoxy and the 9-fluoro compounds in the ratio of *ca.* 3:2 (by NMR); the combined yield was *ca.* 40%. The methanolic mother-liquor was evaporated to dryness and the residue was partitioned between chloroform and water. The chloroform layer was dried and evaporated. This gave a similar mixture of the 9-methoxy and 9-fluoro compounds, together with unchanged anil **5l**.

(*d*) Anil **5l** (1.00 g, 3.3 mmol) and potassium cyanide (0.43 g, 6.6 mmol) were stirred together in methanol (100 $cm^3$) at room temperature. After 20 min a golden yellow precipitate appeared in the red solution; after a further 15 min at room temperature, the mixture was chilled in ice for 45 min, and the precipitate (0.20 g) filtered off. This was identified as slightly impure 9-*fluoroquinoxalino*[2,3-c]*cinnoline* **4l** (24%) (Found: C, 66.3; H, 2.65; N, 22.4. $C_{14}H_7FN_4$ requires C, 67.2; H, 2.8; N, 22.4%); $\delta_H$ 7.7–7.8 (1 H, 8 lines, $J_{10,11}$ 9.7, $J_{10,F}$ 8.7, 10-H), 8.05–8.20 (3 H, m, $J_{8,F}$ 8.7, 2-, 3- and 8-H), 8.41 (1 H, dd, $J_{11,F}$ 5.7, 11-H), 8.90 (1 H, m, 4-H) and 9.23 (1 H, m, 1-H); $\delta_F$ −103.7 (8 lines); *m/z* 250 ($M^{+\bullet}$, 35%), 222 [$(M - N_2)^{+\bullet}$, 35], 195 [$(M - N_2 - HCN)^{+\bullet}$, 31] *etc.* The impurity, as revealed by the mass spectrum (found, *m/z* 266), was probably the 5-oxide of **4l**.

The methanolic mother-liquor from the original reaction was evaporated to dryness and the residue treated as in method (*c*). This residue consisted of a mixture of the 9-methoxy compound and unchanged anil.

9-*Methoxyquinoxalino*[2,3-c]*cinnoline* **4e**.—The crude product from reaction (*a*), above, (0.40 g) was heated under reflux with sodium methoxide [from sodium (0.2 g)] in methanol (10 $cm^3$) for 8 h. The solution was then cooled and the solvent evaporated under reduced pressure; the residue was washed with water and recrystallised from dimethylformamide, giving 9-*methoxyquinoxalino*[2,3-c]*cinnoline* (0.33 g, 48% overall from the anil **5l**), m.p. 285–286 °C (decomp.) (Found: C, 69.1; H, 3.8; N, 21.5. $C_{15}H_{10}N_4O$ requires C, 68.7; H, 3.8; N, 21.5%); $\delta_H$ 4.10 (3 H, s, Me), 7.66 (1 H, d, $J_{8,10}$ 2.4, $J_{8,11}$ 0.6, 8-H), 7.69 (1 H, dd, $J_{10,11}$ 9.4, 10-H), 8.05–8.17 (2 H, m, 2- and 3-H), 8.22 (1 H, dd, 11-H), 8.85–8.95 (1 H, m, 4-H) and 9.17–9.25 (1 H, m, 1-H).

6,7-*Dichloro*-2-*phenylquinoxaline* **9**.—A mixture of 4,5-dichloro-*o*-phenylenediamine (0.88 g, 5 mmol), phenylglyoxal (0.67 g, 5 mmol) and methanol (10 $cm^3$) was stirred at 50–60 °C for 30 min, then cooled. The solid product was filtered off and recrystallised from light petroleum (b.p. 100–120 °C) to give 6,7-*dichloro*-2-*phenylquinoxaline* **9** (1.0 g, 73%), m.p. 152–154 °C (Found: C, 61.3; H, 2.8; N, 10.1. $C_{14}H_8Cl_2N_2$ requires C, 61.1; H, 2.9; N, 10.2%); $\delta_H$ 7.52–7.60 (3 H, m, 3-, 4- and 5-H of Ph), 8.15–8.25 (2 H, m, 2- and 6-H of Ph), 8.22 and 8.26 (2 H, 2 s, 5- and 8-H) and 9.30 (1 H, s, 3-H); *m/z* 274/276/278 ($M^{+\bullet}$).

*Attempted Reaction of* 6,7-*Dichloro*-2-*phenylquinoxaline* **9** *with Sodium Methoxide*.—The quinoxaline (0.27 g, 1 mmol) was added to sodium methoxide [from sodium (0.23 g, 1 mmol)] in methanol (20 $cm^3$) and the mixture was heated under reflux. When boiling commenced, dioxane (5 $cm^3$) was added to ensure complete solution, and the mixture was then heated under reflux for 2 h. Evaporation of the solvent followed by addition of water led only to the recovery of the starting material.

9-*Piperidinoquinoxalino*[2,3-c]*cinnoline* **14b**.—Potassium cyanide (0.43 g, 6.6 mmol) was added to a mixture of anil **5l** (1.00 g, 3.3 mmol), methanol (30 $cm^3$) and piperidine (30 $cm^3$), and the mixture was then heated under reflux for 6 h. (Within the first 5 min the colour of the solution changed from orange to crimson and finally purple.) The mixture was then cooled and evaporated under reduced pressure; the residue was triturated with ice–water, and the solid (0.93 g), m.p. 98–102 °C, filtered off. Attempts to purify the product were unsuccessful, but the spectroscopic properties were consistent with its formulation as 9-piperidinoquinoxalino[2,3-*c*]cinnoline: on this basis the yield was 88%. $\delta_H$ 1.90 (6 H, br, 3 × $CH_2$), 3.59 (4 H, br, 2 × $CH_2$), 7.50 (1 H, d, $J_{8,10}$ 3.0, 8-H), 7.87 (1 H, dd, $J_{10,11}$ 9.5, 10-H), 7.95–8.05 (2 H, symm. m, 2- and 3-H), 8.15 (1 H, d, 11-H), 8.80–8.87 (1 H, m, 4-H) and 9.11–9.18 (1 H, m, 1-H); *m/z* 315 ($M^{+\bullet}$), 287 [$(M - N_2)^{+\bullet}$], 231 $(M - piperidino)^+$ *etc.*; also 262 ($M^{+\bullet}$ for 9-methoxyquinoxalino[2,3-*c*]cinnoline).

10-*Piperidinoquinoxalino*[2,3-c]*cinnoline* **14a**.—10-Chloroquinoxalino[2,3-*c*]cinnoline **4a** (0.80 g, 3 mmol) and piperidine (90 $cm^3$) were heated together at 100 °C for 1.5 h and then cooled, and the mixture filtered to remove piperidine hydrochloride. The piperidine was then evaporated under reduced pressure, ethanol–water (1:1) was added to the residue, and this solvent evaporated until solid material began to be precipitated. The mixture was then chilled in ice, and the product was obtained as a dark crimson solid (0.82 g, 87%), m.p. 119–121 °C. As in the case of the 9-piperidino isomer, further purification was difficult, and assignment of the 10-piperidinoquinoxalinocinnoline structure is based only on spectroscopic characteristics; $\delta_H$ 1.75 (6 H, br, 3 × $CH_2$), 3.60 (4 H, br, 2 × $CH_2$), 7.26 (1 H, d, $J_{9,11}$ 2.8, 11-H), 7.73 (1 H, dd, $J_{8,9}$ 9.7, 9-H), 7.90–8.06 (2 H, symm. m, 2- and 3-H), 8.22 (1 H, d, 8-H), 8.75–8.81 (1 H, m, 4-H) and 9.08–9.13 (1 H, m, 1-H); *m/z* 315 ($M^{+\bullet}$).

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