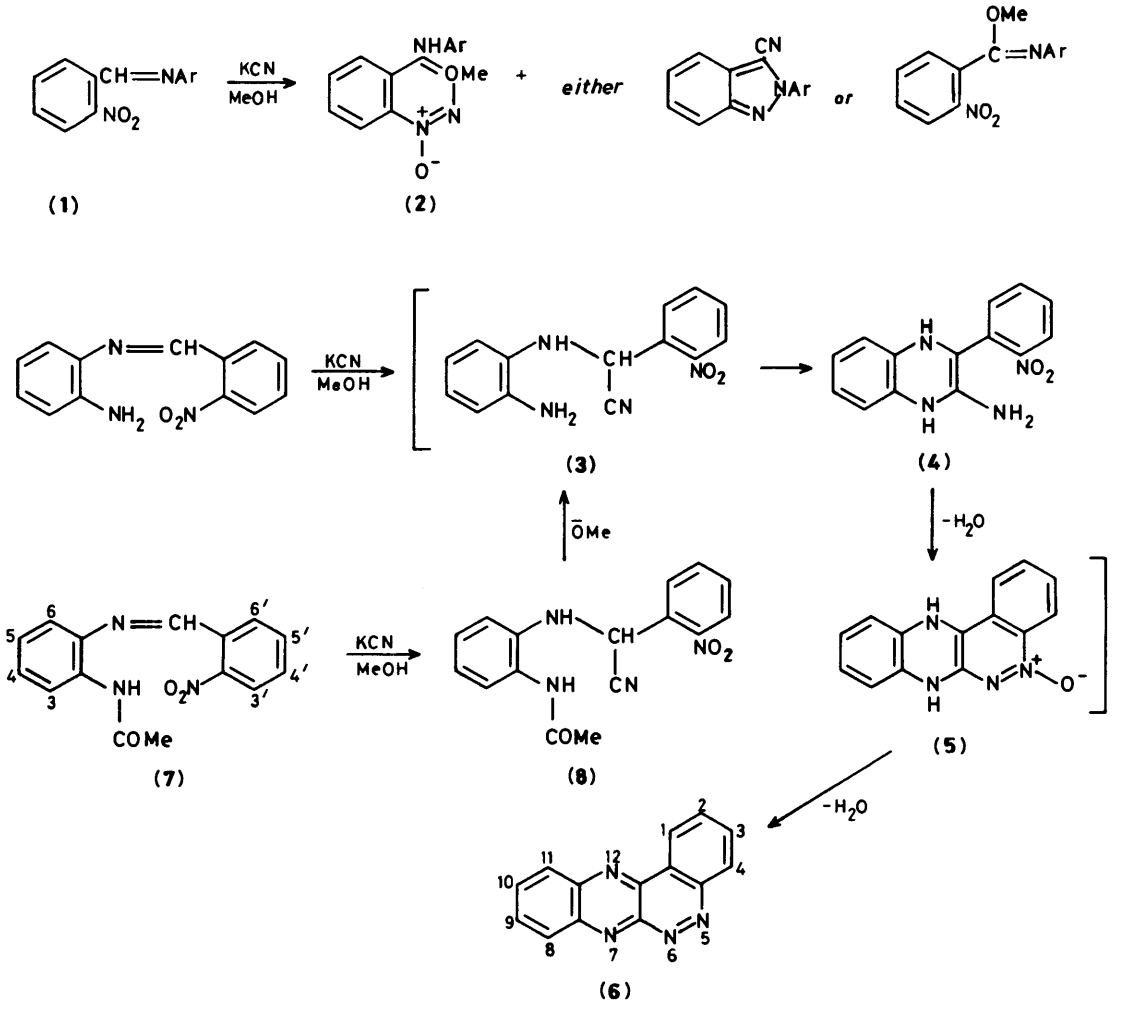
o-Nitrobenzylidene Compounds. Part 4.[1] The Cyanide-induced Cyclisation of o-Acetamido-N-(o-nitrobenzylidene)anilines: an Improved Route to Quinoxalino[2,3-c]cinnolines

Thomas Shepherd and David M. Smith*
Department of Chemistry, University of St. Andrews, Purdie Building, St. Andrews, Fife, KY16 9ST

Cyclisation of *o*-acetamido-*N*-(*o*-nitrobenzylidene)anilines (**7**) with potassium cyanide in methanol (preferably under nitrogen) leads in most cases to quinoxalino[2,3-*c*]cinnolines (**6**) of unambiguous substitution pattern. In some cases, cyclisation appears to be incomplete, and 2-amino-3-(*o*-nitrophenyl)quinoxalines (**11**) are obtained as by-products; in certain cases quinoxalino[2,3-*c*]cinnoline 5-oxides (**10**) are also detected. These by-products are assumed to result from oxidation of intermediates in the cyclisation process (**7**) ⟶ (**6**).

In previous papers[1,2] we have described the synthesis of 4-arylamino-3-methoxycinnoline 1-oxides (**2**) by the cyanide-induced cyclisation of *N*-*o*-nitrobenzylideneanilines (**1**) in methanol solution. Although the co-products differ according to the nature of the substituent(s) in the aniline-derived ring [Ar in (**1**)], the cinnoline oxide (**2**) is usually the major product when this ring is *ortho*-substituted.

When the *ortho*-substituent is an amino-group, however, this can apparently function as an internal nucleophile, adding to the cyano group of the initial adduct (**3**) (Scheme 1a). The resulting aminodihydroquinoxaline (**4**) undergoes base-catalysed cyclisation to the tetracyclic *N*-oxide (**5**), and the latter on dehydration gives the fully conjugated quinoxalino[2,3-*c*]-cinnoline (**6**).[3]

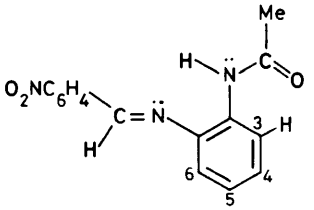


Scheme 1.

We now report that, when the *ortho* substituent in the starting anil is acetamido, as in compound (**7**), reaction with potassium cyanide in methanol leads directly to quinoxalino[2,3-*c*]-cinnoline (**6**). There is evidently no need to remove the protective acetyl group from the amino nitrogen in a separate step: addition of the elements of HCN to the C=N bond of (**7**) requires the concomitant formation of methoxide ion, and it is assumed (Scheme 1b) that methoxide is able to deacetylate the adduct (**8**) in a manner similar to that reported for other acetanilide derivatives.[4] [It should, however, be noted that deacetylation of the anil (**7**) by methoxide is extremely slow.]

The success of this method for the synthesis of quinoxalino-cinnolines makes it possible to resolve a difficulty encountered in the use of the previous method (Scheme 1a). This relates to the use of an unsymmetrically substituted *o*-phenylenediamine in the synthesis of the starting anil, which may give, in principle, a mixture of two anils and thus a mixture of two quinoxalinocinnolines (Scheme 2). 4-Chloro-*o*-phenylenediamine (X = Cl in Scheme 2) is a case in point: condensation with *o*-nitrobenzaldehyde gives a product which is (by high field ^{1}H n.m.r.: see Table 4) a *ca.* 4:1 mixture of the two anils, but cyclisation of this (either crude or recrystallised) gives a single chloroquinoxalinocinnoline isomer.[3] It has not hitherto been possible to distinguish the isomeric anils or the isomeric quinoxalinocinnolines by n.m.r. alone, and the literature is extremely confusing as to the relative nucleophilicities of the two amino groups in 4-chloro-*o*-phenylenediamine: indeed it appears that the order of reactivity may change according to the reaction conditions.[5]

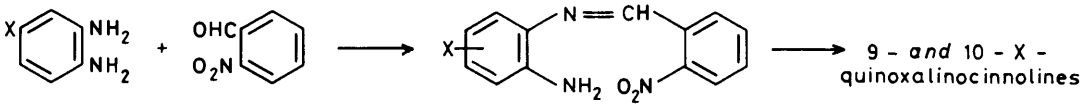
is assumed to be due to the preferred conformation of the acetamido group;[6] it is not unreasonable to suppose that the bulk of the *o*-nitrobenzylideneamino group will encourage the acetamido group to adopt the conformation (**9**) in which 3-H falls within the C=O deshielding zone.



(**9**)

Cyclisation of the anils (**7**) is effected, as described in Part 2,[3] by heating under reflux with 2 mol equiv. of potassium cyanide in methanol. The cyclisations have been carried out under two different sets of conditions: first in air, and then under nitrogen using degassed methanol as the solvent. The results of the cyclisations are collected in Table 3.

In those cases where both sets of conditions have been used, the reaction carried out under nitrogen gives the higher yield of quinoxalino[2,3-*c*]cinnoline. The reaction in the presence of air gives the quinoxalinocinnoline contaminated with two by-products, apparent in the mass spectrum as ions of *m*/*z* 16 and 34 greater than the molecular ion of the quinoxalinocinnoline.



Monoacetyl-*o*-phenylenediamines may be readily prepared by reduction of the corresponding *o*-nitroacetanilides, and the position of other substitutents in the ring is thus unambiguous. Condensation of these *o*-acetamidoanilines with *o*-nitrobenzaldehyde gives in each case a single *o*-acetamido anil (**7**) which in turn yields a quinoxalino[2,3-*c*]cinnoline of known substitution pattern.

Eleven *o*-acetamido-*N*-(*o*-nitrobenzylidene)anilines (**7a**—**k**) have been obtained by this method. Their properties are collected in Tables 1 and 2. It is of interest to note that the proton *ortho*- to the acetamido-group [3-H in formula (**7**)] is considerably deshielded relative to the corresponding proton in the unacetylated analogues (as in Table 4). This deshielding

These by-products, which are usually removable on recrystallisation, are assigned structures of the type (**10**) and (**11**), and they are assumed to arise by atmospheric oxidation of the dihydro compounds (**5**) and (**4**) respectively.

There are several significant features of these results.

(i) The unambiguous synthesis of 9- and 10-chloroquinoxalino[2,3-*c*]cinnolines, described here, leaves no doubt that it is the 9-chloro isomer which is the single product of cyclisation of the anil mixture from 4-chloro-*o*-phenylenediamine and *o*-nitrobenzaldehyde[3] (Scheme 2). It is assumed, therefore, that the major component of this anil mixture is 2-amino-4-chloro-*N*-(*o*-nitrobenzylidene)aniline and that, under the conditions of the initial condensation reaction, it is the amino group *para* to

Table 1. *o*-Acetamido-*N*-(*o*-nitrobenzylidene)anilines (**7**)

Compd. no.	Sub-stituent(s)	Yield (%)	M.p. (°C)[a]	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
(**7a**)		82	124—126	$C_{15}H_{13}N_3O_3$	63.5	4.6	14.9	63.6	4.6	14.8
(**7b**)	5-Cl	82	152—154	$C_{15}H_{12}ClN_3O_3$	56.4	3.7	13.1	56.7	3.8	13.2
(**7c**)	4-Cl	78	162—164	$C_{15}H_{12}ClN_3O_3$	56.5	3.7	13.2	56.7	3.8	13.2
(**7d**)	5,5′-Cl_2	89	206—208	$C_{15}H_{11}Cl_2N_3O_3$	51.2	3.1	11.8	51.2	3.1	11.9
(**7e**)	5-Me	70	133—134	$C_{16}H_{15}N_3O_3$	64.8	5.05	14.15	64.6	5.1	14.1
(**7f**)	5-OMe	77	137—138	$C_{16}H_{15}N_3O_4$	61.3	4.8	13.4	61.2	4.9	13.25
(**7g**)	5′-Cl	74	200	$C_{15}H_{12}ClN_3O_3$	56.7	3.7	13.0	56.7	3.8	13.2
(**7h**)	3,5-Cl_2	83	222—224[b]	$C_{15}H_{11}Cl_2N_3O_3$	51.0	3.1	11.8	51.2	3.1	11.9
(**7i**)	3-Cl	68	195—196[b]	$C_{15}H_{12}ClN_3O_3$	56.8	3.9	13.2	56.7	3.8	13.2
(**7j**)	5-Br	84	166—167	$C_{15}H_{12}BrN_3O_3$	49.4	3.3	11.6	49.7	3.3	11.6
(**7k**)	4-Br	72	165—167	$C_{15}H_{12}BrN_3O_3$	49.6	3.3	11.5	49.7	3.3	11.6

[a] From ethanol unless otherwise stated. [b] From butanone.

Table 2. ^{1}H N.m.r. spectra of the anils (7)*

Compd. no.	3-H	4-H	5-H	6-H	3'-H	4'-H	5'-H	6'-H	CH=N (s)	NH (br s)	$COCH_3$ (s)	Other
(7a)	8.50d	6.9—7.4m			7.5—8.1m				8.85	8.50	2.22	
(7b)	8.47d	7.12—7.20 (with 6-H)		7.12—7.20 (with 4-H)	7.6—8.12m				8.85	8.35	2.32	
(7c)	8.62d		7.05dd	7.20d	7.65—8.15m				8.90	8.50	2.25	
(7d)	8.51d	7.30d		7.20d	8.07d	7.62dd		8.06d	8.91	8.30	2.25	
(7e)	8.46d	7.1—7.3 (with 6-H)		7.1—7.3 (with 4-H)	7.7—8.25m				9.03	8.40	2.27	2.37s (Me)
(7f)	8.47d	6.92dd		6.81d	7.55—8.22m				8.95	8.30	2.25	3.86s (OMe)
(7g)	8.59d	7.1—7.55m			8.05d	7.66dd		8.16d	9.00	8.49	2.25	
(7h)[a]		7.30 or 7.65d		7.65 or 7.30d	7.85—8.32m				8.87	9.70	2.05	
(7i)[a]		7.12[b]	7.37[b]	7.43[b]	7.85—8.3m				8.83	9.62	2.02	
(7j)	8.46d	7.37—7.52 (with 6-H)		7.37—7.52 (with 4-H)	7.67—8.17m				8.90	8.40	2.25	
(7k)	8.82d		7.28dd	7.10d	7.6—8.17m				8.95	8.47	2.25	

* Coupling constants (*J*/Hz): (**7a**) 7.8 (3,4); (**7b**) 8.2 (3,4); (**7c**) 2.5 (3,5) and 8.2 (5,6); (**7d**) 8.6 (3,4 and 3',4') and 2.3 (4,6 and 4',6'); (**7e**) 8.4 (3,4); (**7f**) 8.6 (3,4) and 2.5 (4,6); (**7g**) 8.4 (3,4), 8.8 (3',4'), and 2.4 (4',6'); (**7h**) 2.4 (4,6); (**7i**)[b] 6.5 (4,5), 7.9 (5,6), and 3.1 (4,6); (**7j**) 8.6 (3,4) and 2.2 (4,6); (**7k**) 2.2 (3,5), and 8.6 (5,6).

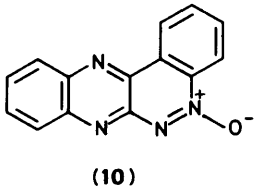
[a] $(CD_3)_2SO$ solution. [b] Non-first order spectrum; chemical shifts and coupling constants obtained by computer simulation.

Table 3. Quinoxalino[2,3-*c*]cinnolines (**6**) obtained by cyclisation of the anils (**7**)

Starting anil	Quinoxalinocinnoline (**6**) obtained	Substituents in (**6**)	Yield (%) [reaction time in brackets] In air	Yield (%) [reaction time in brackets] Under N_2	M.p. (°C; recryst. from DMF)	By-products (detected in mass spectrum)
(7a)	(6a)		40 [3 h]	52 [3 h]	224—226[a]	
(7b)	(6b)	10-Cl	45 [25 min] 25 [1 h] 7.5 [2.5 h]	32 [25 min] 35 [50 min]	246—247[b]	(**10b**), (**11b**), (**6f**)
(7c)	(6c)	9-Cl	54 ([1 h]	62 [25 min]	278[c]	(**10c**)
(7d)	(6d)	2,10-Cl_2	10 [40 min]		288—290[d]	(**10d**), (**11d**)[g]
(7e)	(6e)	10-Me	Trace [by m.s.]	Trace [by m.s.]		At least five products (by t.l.c. including (**6e**)
(7f)	(6f)*	10-OMe		*ca.* 35 [45 min][h] 60 [2 h]	264	(**10f**) None
(7g)	(6g)	2-Cl		*ca.* 20 [50 min][h] 43 [2 h]	260—261[e]	(**10g**)
(7h)	(6h)	8,10-Cl_2		*ca.* 25 [45 min][h]		(**10h**)
(7i)	(6i)	8-Cl		*ca.* 20 [45 min][h]		(**10i**)
(7j)	(6j)	10-Br		50 [1 h]	263—265[f]	
(7k)	(6k)*	9-Br		52 [1 h]	252—254	

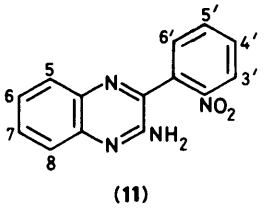
[a] Lit.,[3] 228—230 °C. [b] Lit.,[7] 250—252 °C. [c] Lit.,[3] 274—276 °C. [d] Lit.,[7] 288—290 °C. [e] Lit.,[3] 260—262 °C. [f] Lit.,[7] 261—263 °C [g] Small amount of (**11d**) isolated; m.p. 300 °C. [h] Not obtained pure (see Experimental section).

* Analysis of new compounds: (**6f**) (Found: C, 69.0; H, 3.85; N, 21.6. $C_{15}H_{10}N_4O$ requires C, 68.7; H, 3.8; N, 21.4%). (**6k**) (Found: C, 53.6; H, 2.2; N, 17.9. $C_{14}H_7BrN_4$ requires C, 54.0; H, 2.3; N, 18.0%).



(**10**)

(**10a**—**k**): substituents as in (**6**)



(**11**)

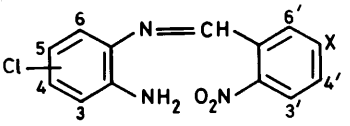
(**11a**): unsubstituted
(**11b**): 6-Cl
(**11d**): 5',6-Cl_2

the chlorine in 4-chloro-*o*-phenylenediamine which is the more reactive. It is similarly assumed that it is this same amino group which condenses preferentially with 5-chloro-2-nitrobenzaldehyde, since the product of cyclisation of this condensation product[3] is undoubtedly 2,9-dichloroquinoxalinocinnoline and not the 2,10-dichloro isomer (**6d**).

The ^{1}H n.m.r. spectra of the anil mixtures are analysed in Table 4.

(ii) The yield of 10-chloroquinoxalino[2,3-*c*]cinnoline (**6b**) obtained by cyclisation of the anil (**7b**) is strongly time-dependent: the longer the reaction time, the lower the yield. The ^{1}H n.m.r. spectrum of (**6b**) shows a small signal at δ 4.15, corresponding to the presence of a methoxy group, and the same is true of the n.m.r. spectrum of the 2,10-dichloro compound (**6d**). These signals are due to methoxyquinoxalinocinnolines, formed by nucleophilic displacement of the chlorine at position 10; the reactions of halogenoquinoxalino[2,3-*c*]cinnolines with nucleophiles will be discussed in detail in a future paper. It should be noted that the 10-bromo analogue (**6j**) is much less reactive towards methoxide than the chloro compounds.

(iii) Cyclisation of the anils (**7f**) and (**7g**), giving 10-methoxy-

Table 4. ^{1}H N.m.r. spectra of 

Compd.	CH=N	3-H	4-H	5-H	6-H	3′-H	4′-H	5′-H	6′-H
†X = H, 4-Cl	8.94	6.74d		•6.69dd	7.04d	7.99dd	——7.55—7.71m——		8.23dd
5-Cl	8.92	•6.69d	7.05dd		7.09d	8.01dd	——7.55—7.71m——		8.21dd
‡X = Cl, 4-Cl	8.96	6.75d		•6.69dd	7.05d	8.00d	7.52dd		8.22d
5-Cl	8.94	•6.69d	7.06dd		7.10d	8.01d	7.54d		8.22d

Coupling constants: $J_{3,4} = J_{5,6}$ 8.4 Hz; $J_{3',4'} = J_{5',6'}$ 7.8 Hz; $J_{3,5} = J_{4,6}$ 2.3 Hz; $J_{3',5'} = J_{4',6'}$ 2.5 Hz.

• Signals coincide. † 360 MHz spectrum. ‡ 100 MHz spectrum.

Table 5. ^{1}H N.m.r. spectra of quinoxalino[2,3-*c*]cinnolines (**6**)* (very dilute solutions in $CDCl_3$)

Compd no.	1-H	2-H	3-H	4-H	8-H	9-H	10-H	11-H	Others
(**6a**)†	9.02—9.22m	——7.90—8.17m—— (with 9-H and 10-H)		8.72—8.93m	8.28—8.63m (with 11-H)	——7.90—8.17m—— (with 2-H and 3-H)		8.28—8.63m (with 8-H)	
(**6b**)	9.14—9.28m	——8.05—8.20m——		8.83—9.00m	8.52dd	7.88dd		8.42dd	
(**6c**)†	9.16—9.27m	——8.03—8.15m——		8.85—8.95m	8.55d		7.99dd	8.30d	
(**6d**)	9.22d		8.10dd	8.90d	8.50dd	8.00dd		8.45dd	
(**6f**)	9.20—9.35m	——8.13—8.25m——		8.95—9.07m	8.50dd	7.74dd		7.64dd	4.14 (OMe)
(**6g**)	9.26dd		8.07dd	8.87dd	8.41—8.62m (with 11-H)	——8.02—8.17m——		8.41—8.62m (with 8-H)	
(**6j**)	9.27—9.45m	——8.20—8.32m——		8.99—9.17m	8.52dd	8.15dd		8.72dd	
(**6k**)	9.35—9.48m	——8.12—8.32m——		9.02—9.15m	8.75dd		8.22dd	8.44dd	

*Coupling constants (*J*/Hz): (**6b**) 9.2 (8,9), 2.4 (9,11), and 0.5 (8,11); (**6c**) 9.2 (10,11) and 2.3 (8,10); (**6d**) 9.2 (8,9), 8.6 (3,4), 2.4 (9,11), 2.2 (1,3), and 0.5 (8,11); (**6f**) 8.8 (8,9), 2.8 (9,11), and 1.2 (8,11); (**6g**) 8.6 (3,4), 2.2 (1,3), and 0.4 (1,4); (**6j**) 9.2 (8,9), 2.0 (9,11), and 0.6 (8,11); (**6k**) 9.2 (10,11), 2.0 (8,10), and 0.6 (8,11).

†From ref. 3

and 2-chloro-quinoxalinocinnoline respectively, is relatively slow.

(iv) Attempts to prepare 10-methylquinoxalinocinnoline (**6e**) by this route have been unsuccessful. [Earlier attempts[8] to prepare a mixture of the 9- and 10-methyl compounds by the method of Scheme 2 had also given very low yields (4%)].

The ^{1}H n.m.r. spectra of the quinoxalinocinnolines (**6**) are collected in Table 5. The data for the chloro and dichloro compounds enable complete assignment of the resonances to be made: in the absence of strongly shielding or deshielding substituents, the deshielding order for the quinoxalinocinnoline protons is 1-H > 4-H > 8-H > 11-H > 2,3,9,10-H. It is not surprising that 1-H is the most deshielded; there is ample precedent in the literature[9] for the deshielding of a proton on the 'inside' of an angularly fused polycyclic system, especially if the proton is in close proximity to a lone pair (on N-12 in this case).* It should be noted, however, that 1-H, 4-H, 8-H, and 11-H are all considerably more deshielded than the corresponding protons in the parent heterocycles, cinnoline and quinoxaline. It should also be noted that, although a bromo substituent is often regarded as having a negligible deshielding effect on benzenoid proton resonances, the *ortho*-deshielding effect[10] is just large enough, in the case of 10-bromoquinoxalinocinnoline (**6j**), to make the deshielding order 1-H > 4-H > 11-H > 8-H.

Of the two types of by-product, (**10**) and (**11**), encountered in the cyclisation of (**7**) to (**6**), the former structure is assigned only on the basis of the mass spectrum [molecular ion 16 mass units higher than the quinoxalinocinnoline (**6**)]. Attempts to deoxygenate the *N*-oxide (**10f**) using phosphorus trichloride have been unsuccessful, as will be described in the following paper, and none of these *N*-oxides has yet been obtained in a pure state.

The 2-amino-3-(*o*-nitrophenyl)quinoxaline structure (**11**) is, however, more firmly based. Some years ago, our colleague Mr. Arshad Ahmad had shown[8] that cyclisation of *N*-*o*-nitrobenzylidene-*o*-phenylenediamine (Scheme 1a) with potassium cyanide in aqueous dimethylformamide (DMF) (instead of methanol) gives (**11a**) in 60% yield. We have shown that cyclisation of the *o*-acetamido anil (**7a**) under the same conditions also yields (**11a**) in comparable amount, and that the corresponding cyclisation of the dichloro analogue (**7d**) gives (**11d**), which is identical in all respects with the by-product referred to in the fourth line of Table 3.

Experimental

^{1}H N.m.r. spectra have been recorded at 80 MHz in $CDCl_3$ solutions unless otherwise indicated.

o-Nitroacetanilide,[11] m.p. 92—93 °C (lit., 92—93 °C); 4-chloro-2-nitroacetanilide,[12] m.p. 100—102 °C (lit., 102 °C); 5-chloro-2-nitroacetanilide,[13] m.p. 118—120 °C (lit., 117—118 °C); 4-methyl-2-nitroacetanilide,[14] m.p. 91—92 °C (lit., 93 °C); 4-methoxy-2-nitroacetanilide,[15] m.p. 114—115 °C (lit., 115 °C); 4,6-dichloro-2-nitroacetanilide,[16] m.p. 188 °C (lit., 188 °C); 6-chloro-2-nitroacetanilide,[4a] m.p. 190—191 °C (lit.,

* A referee has pointed out that the opposite deshielding order, *viz.* 4-H > 1-H, is observed in the ^{1}H n.m.r. spectrum of benzo[*c*]cinnoline.[22] As in our series, however, the presence of a 2-chloro-substituent does not affect the deshielding order; and the ^{1}H n.m.r. spectra of 1- and 3-halogenoquinoxalino[2,3-*c*]cinnolines (to be published in a future paper) provide further confirmation of the deshielding order given above.

194 °C); 4-bromo-2-nitroacetanilide,[17] m.p. 102—103 °C (lit., 103—104 °C); and 5-bromo-2-nitroacetanilide,[18] m.p. 140 °C (lit.,[4b] 144 °C), were all obtained by the published methods.

o-Aminoacetanilide, m.p. 130 °C (lit.,[11] 132—133 °C) was obtained (80% yield) by hydrogenation of *o*-nitroacetanilide in methanol solution over 10% palladium–charcoal. 2-Amino-4-methylacetanilide, m.p. 133—134 °C (lit.,[19] 131—132 °C; yield 90%) and 2-amino-4-methoxyacetanilide, m.p. 147—148 °C (lit.,[19] 155—156.5 °C; yield 91%) were similarly obtained, using ethanol as solvent.

Catalytic hydrogenation of the halogenated *o*-nitroacetanilides led to partial hydrogenolysis of the carbon–halogen bond; these nitro compounds were therefore reduced using iron powder in dilute aqueous acetic acid.[20] 2-Amino-4-chloroacetanilide, m.p. 144—145 °C (lit.,[20] 144 °C; yield 66%), 2-amino-5-chloroacetanilide, m.p. 144—145°C (lit.,[19] 130—132°C; yield 70%), and 2-amino-4-bromoacetanilide, m.p. 162 °C (lit.,[21] 154 °C; yield 44%) were obtainable by this method, as were the following new compounds.

2-*Amino*-6-*chloroacetanilide*: yield 30%, m.p. 138—140 °C (from ethanol), (Found: C, 51.6; H, 4.8; N, 15.0. $C_8H_9ClN_2O$ requires C, 52.0; H, 4.9; N, 15.2%).

2-*Amino*-5-*bromoacetanilide*: yield 46%, m.p. 173—175 °C (from ethanol). (Found: C, 42.0; H, 4.0; N, 12.2. $C_8H_9BrN_2O$ requires C, 41.95; H, 4.0; N, 12.2%).

2-*Amino*-4,6-*dichloroacetanilide*: yield 70%, m.p. 170—172 °C (from ethanol). (Found: C, 43.9; H, 3.7; N, 12.9. $C_8H_8Cl_2N_2O$ requires C, 43.9; H, 3.7; N, 12.8%).

o-*Acetamido*-N-(o-*nitrobenzylidene*)*anilines* (**7**). *General Procedures*.—A. Equimolar quantities of the appropriate *o*-aminoacetanilide and *o*-nitrobenzaldehyde were ground together to form an intimate mixture. A little ethanol was added and the mixture warmed gently in a water-bath to achieve dissolution. After heating for 5—10 min, the solution was cooled and the product filtered off.

B. Equimolar quantities of the reactants were each dissolved in the minimum volume of ethanol: the solutions were mixed and gently warmed, as in A.

Method A was used for the preparation of (**7a**—**e**) and method B for the remainder. A few crystals of toluene-*p*-sulphonic acid were added to the reaction mixture for the preparation of (**7h**). The properties of the products are summarised in Tables 1 and 2.

Quinoxalino[2,3-c]*cinnolines* (**6**).—Suspensions or solutions of the appropriate anil (**7**) (5 mmol) in methanol (100 ml) were heated with potassium cyanide (10 mmol) under reflux for periods of time specified in Table 3. The resulting dark brown solution was cooled to 0 °C, solid product (if any) filtered off, and the filtrate diluted with water to yield a further crop. As indicated in Table 3, the majority of these reactions were carried out under nitrogen; in these cases the methanol was first 'degassed' by boiling while being infused with a stream of dry nitrogen.

The outcome of these reactions, and the ^{1}H n.m.r. spectra of the products, are collected in Tables 3 and 5, respectively. The mass spectra all contain prominent peaks for $M^{+\cdot}$, $(M - N_2)^{+\cdot}$ and, in some cases, $(M - N_2 - HCN)^{+\cdot}$.

In the case of 2- and 8-chloro-, 8,10-dichloro-, and 10-methoxyquinoxalinocinnolines, substantial quantities of the (supposed) *N*-oxides were produced as by-products, and could not be separated from the quinoxalinocinnolines by recrystallisation. For the chloro and dichloro compounds, the yields recorded in Table 3 are estimates based on the further reaction of the crude products with hydrogen chloride (see the following paper), and in the case of the 10-methoxy compound the yield was estimated by ^{1}H n.m.r. spectroscopy.

2-*Amino*-3-(o-*nitrophenyl*)*quinoxaline* (**11a**) (*with Arshad Ahmad*).—(a) *N*-*o*-Nitrobenzylidene-*o*-phenylenediamine (1.2 g, 5 mmol) and potassium cyanide (0.48 g, 7.5 mmol) were dissolved in dimethylformamide (20 ml) and water (3 ml), and the solution stirred at room temperature for 3 h; it was then added to crushed ice. The yellow product (**11a**) was filtered off, washed well with water, sucked dry, and recrystallised from dimethylformamide–ethanol. It had m.p. 260—261 °C (Found: C, 63.0; H, 3.75; N, 21.0. $C_{14}H_{10}N_4O_2$ requires C, 63.2; H, 3.5; N, 20.95%); $\nu_{max.}$(Nujol) 3 460, 3 330, 3 100 (NH_2), 1 515, 1 340 cm^{-1} (NO_2); δ($CDCl_3$) 4.70 (2 H, br, NH_2), 7.61—7.93 (7 H, m), 8.19—8.29 (1 H, m, 3'-H); *m/z* 266.0797 ($M^{+\cdot}$ requires 266.0804), 220.0867 [$(M - NO_2)^+$ requires 220.0875], 132.0554 [$(M - C_7H_4NO_2)^+$ requires 132.0562]; yield 0.8 g (60%).

(b) *o*-Acetamide-*N*-(*o*-nitrobenzylidene)aniline (**7a**) (1.32 g, 4.7 mmol) and potassium cyanide (0.48 g, 7.5 mmol) in dimethylformamide (50 ml) and water (3 ml) similarly gave (**11a**) (0.96 g, 72%).

2-*Amino*-6-*chloro*-3-(5-*chloro*-2-*nitrophenyl*)*quinoxaline* (**11d**), m.p. 300—301 °C (from 45:45:10 dimethylformamide–ethanol–water) was obtained in 68% yield from the anil (**7d**) by procedure (b) above (Found: C, 49.9; H, 2.5; N, 16.6. $C_{14}H_8Cl_2N_4O_2$ requires C, 50.1; H, 2.4; N, 16.8%). Compound (**11d**) was also produced, in small amount, by cyclisation of (**7d**) with potassium cyanide in methanol (*cf.* Table 3); it was more soluble than the quinoxalinocinnoline (**6d**) in methanol, and crystallised slowly from the (diluted) reaction mother-liquor.

Acknowledgements

We thank Mrs. S. Smith for the microanalyses, Mrs. M. Smith (St. Andrews) and Dr. I. H. Sadler (Edinburgh) for the n.m.r. spectra, Mr. C. Millar for the mass spectra, and the University authorities for the award of a research scholarship to T. S.

References

1 Part 3, D. Johnston, D. M. Smith, T. Shepherd, and D. Thompson, *J. Chem. Soc., Perkin Trans. 1*, preceding paper.
2 D. Johnston and D. M. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1976, 399.
3 Arshad Ahmad, F. A. Brand, D. Johnston, and D. M. Smith, *J. Chem. Res. (S)*, 1980, 208.
4 B. M. Wepster and P. E. Verkade, *Recl. Trav. Chim. Pays-Bas*, (*a*) 1949, **68**, 88; (*b*) 1948, **67**, 77; (*c*) 1948, **67**, 425.
5 G. Henseke and R. Jacobi, *Justus Liebigs Ann. Chem.*, 1965, **684**, 146.
6 *cf.* M. Zanger, W. W. Simons, and A. R. Gennaro, *J. Org. Chem.*, 1968, **33**, 3673; J. M. Appleton, B. P. Andrews, I. D. Rae, and B. E. Reichert, *Aust. J. Chem.*, 1970, **23**, 1667.
7 C. Glidewell, T. Shepherd, and D. M. Smith, *Tetrahedron Lett.*, 1983, **24**, 3151; C. Glidewell, T. Shepherd, and D. M. Smith, following paper.
8 Arshad Ahmad, M.Sc. Thesis, University of St. Andrews, 1978.
9 *cf.* J. D. Memory and N. K. Wilson, 'NMR of Aromatic Compounds,' Wiley-Interscience, New York, 1982, pp. 58—61.
10 *cf.* Ref. 9, p. 65.
11 L. F. Fieser and E. L. Martin, *J. Am. Chem. Soc.*, 1935, **67**, 1835.
12 F. D. Chattaway and K. J. P. Orton, *J. Chem. Soc.*, 1901, **79**, 461.
13 R. C. Fuson, R. A. Bauman, E. Howard, and E. N. Marvell, *J. Org. Chem.*, 1947, **12**, 799.
14 H. Green and A. R. Day, *J. Am. Chem. Soc.*, 1942, **64**, 1167.
15 W. C. Lothrop, *J. Am. Chem. Soc.*, 1942, **64**, 1698.
16 H. H. Hodgson and A. Kershaw, *J. Chem. Soc.*, 1929, 2917.
17 D. Britton and W. E. Noland, *J. Org. Chem.*, 1962, **27**, 3218.
18 H. A. Mayes and E. E. Turner, *J. Chem. Soc.*, 1928, 691.
19 K. Tanaka, M. Shimazaki, and Y. Murakami, *Chem. Pharm. Bull.*, 1982, **30**, 2714.
20 J. K. Landquist, *J. Chem. Soc.*, 1956, 2551.
21 M. A. Phillips, *J. Chem. Soc.*, 1931, 1143.
22 J. W. Barton and D. J. Lapham, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1503.

Received 12th February 1986; Paper 6/304