o-Nitrobenzylidene Compounds. Part 3.[1] Formation of 4-Arylamino-3-methoxycinnoline 1-Oxides from *N*-*o*-Nitrobenzylideneanilines, Cyanide Ion, and Methanol: the Intermediacy of 2-Aryl-3-cyano-2*H*-indazole 1-Oxides†

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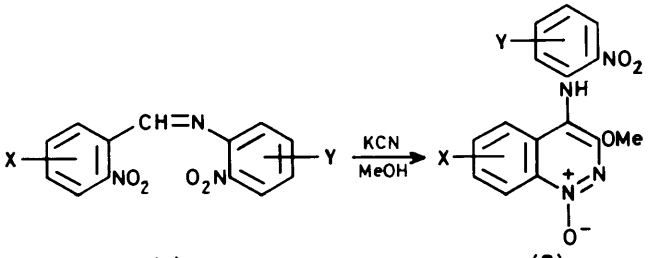
The *N*-*o*-nitrobenzylidene derivatives of variously substituted anilines (**7**) have been cyclised by potassium cyanide in methanol, to give 4-arylamino-3-methoxycinnoline 1-oxides (**9**), the structures of which have been confirmed by independent synthesis of one representative [the *p*-toluidino-compound. (**9b**)]. These cinnoline oxides are the main products (sometimes the only isolated products) when the amine-derived ring in (**7**) is *ortho*-substituted; in other cases the cinnoline oxides are minor products formed along with 2-aryl-3-cyano-2*H*-indazoles (**10**).

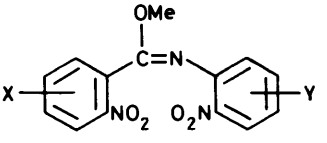
In the latter group of reactions, the primary cyclisation products are 2-aryl-3-cyano-2*H*-indazole 1-oxides (**8**): these have then either been reduced to the indazoles in the basic methanolic medium, or have undergone ring-opening and recyclisation to give the cinnoline oxides (**9**). In the other group, where indazole oxides (**8**) cannot usually be isolated, their intermediacy in cinnoline oxide formation remains a possibility, although other mechanistic pathways can be envisaged.

Some 'borderline' cases are identified and discussed.

We have previously shown[3] that *o*-nitro-*N*-*o*-nitrobenzylideneanilines (**1**) react with potassium cyanide in methanol giving moderate (20—40%) yields of 3-methoxy-4-(*o*-nitroarylamino)cinnoline 1-oxides (**2**), together with smaller amounts (< 15%) of methyl *N*-(*o*-nitroaryl)-*o*-nitrobenzimidates (**3**).



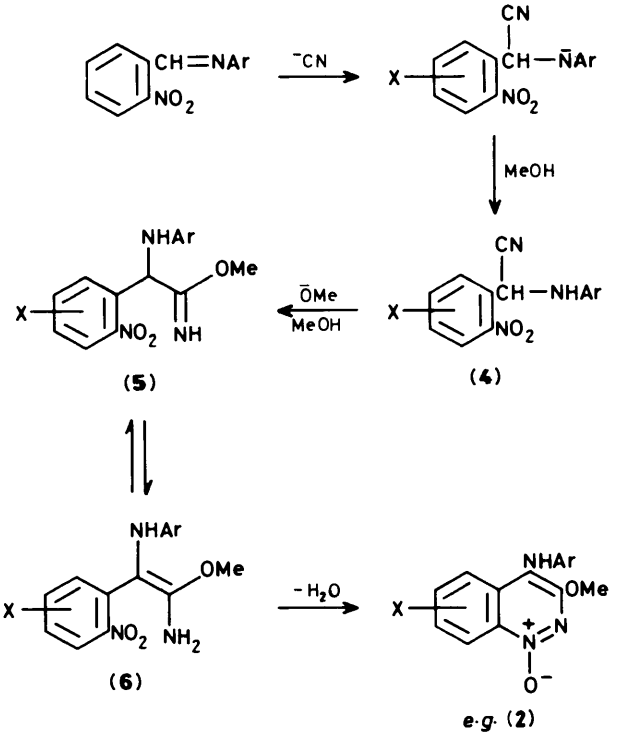
(**1**) + (**2**)



(**3**)

The mechanism proposed[3] for the formation of the cinnoline oxide (**2**) is set out in Scheme 1. Addition of cyanide ion and a (solvent-derived) proton to the Schiff base (**1**) gives the adduct (**4**) and methoxide ion; addition of methanol to the cyano group follows, and the resulting imidate (**5**) or its enamine tautomer (**6**) finally undergoes intramolecular base-catalysed condensation.

It has long been known, of course,[4] that compound (**4**: X = H, Ar = Ph) readily undergoes cyclisation of a different type in the presence of base, to give 3-cyano-2-phenyl-2*H*-indazole 1-oxide (**8a**). This cyclisation occurs under extremely mild conditions and gives good yields, and is the basis of a number of 'one-pot' syntheses of these indazole oxides (Scheme 2).[5–8] The cyclisation step is assumed to involve nucleophilic



(**5**) (**4**) (**6**) *e.g.* (**2**)

Scheme 1

attack by the amino nitrogen on the nitro group, and in our previous paper[3] we suggested that in the case of the *o*-nitroaniline derivatives (**4**: Ar = *o*-$O_2NC_6H_4$) the amino nitrogen may be too weakly nucleophilic, or too sterically hindered (or both), for direct attack on the nitro group to occur.

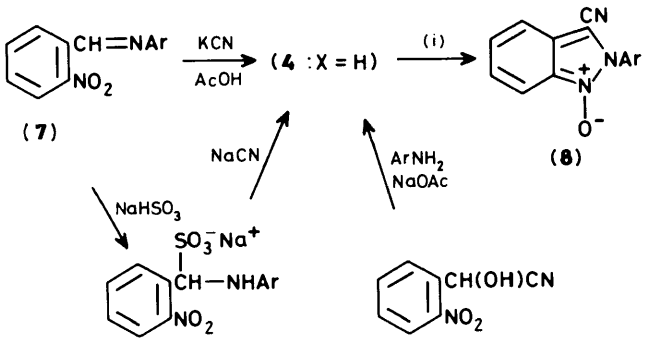
We now report, however, that the formation of cinnoline oxides from *N*-*o*-nitrobenzylideneanilines (**7**), cyanide, and methanol, does not depend on the amino nitrogen of the adduct (**4**) being weakly nucleophilic or sterically hindered. For a wide variety of substituents in the amine-derived ring of (**7**), the 4-

† Part of this work was published in preliminary form.[2]

Table 1. Products from the reaction of *N*-*o*-nitrobenzylideneanilines (7) with potassium cyanide in methanol

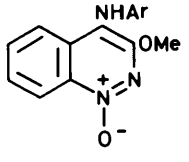
Anil	Substituent(s) in aniline-derived ring	Product yields (%) Cinnoline 1-oxide (9)	Indazole (10)	Others
(7a)	—	11	18	
(7b)	*p*-Me	9	27	
(7c)	*p*-OMe	14	15	†
(7d)	*p*-F	14	34	
(7e)	*p*-Cl	16	30	
(7f)	*p*-Br	15	44	
(7g)	*p*-NO_2	0	0	(12), 31%
(7h)	*o*-Me	5	0	
(7i)	*o*-F	38	3	
(7j)	*o*-Cl	55	0	
(7k)	*o*-Br	45	0	
(7l)	*o*-CO_2Me	15	0	
(7m)	*o*-(SC_6H_4Me-*p*)	12	0	
(7n)	2,6-Me_2	0	0	(7n) recovered (72%)

† In one run, the initially formed precipitate was filtered off and identified as the indazole oxide (8c) (25%). This precipitate, however, redissolves as the reaction proceeds further.

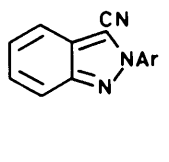


Scheme 2. (i): Na_2CO_3, or NaCN, or NaOAc, or attempted recrystallisation from EtOH. (4a)—(4n), (7a)—(7n), (8a)—(8n): substituents as in the appropriate Tables.

arylamino-3-methoxycinnoline 1-oxide (9) is produced in isolable quantities (Table 1). If the amine-derived ring is *ortho* substituted, the cinnoline oxide (9) is generally the main product (or the only isolable product). If this ring is unsubstituted, or has a *para* substituent, the cinnoline oxide (9) is generally a minor product, the main product in these cases usually being the 2-aryl-3-cyano-2*H*-indazole (10).



(9)



(10)

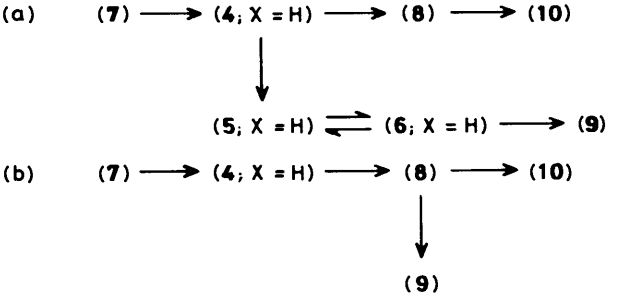
Confirmation of the structures (9) and (10) has been obtained in representative cases by alternative syntheses. 3-Methoxy-4-*p*-toluidinocinnoline 1-oxide (9b) may be prepared from the known[9] 4-chloro-3-methoxycinnoline 1-oxide and sodium *p*-toluidide in benzene; and several indazole derivatives of type (10) have been prepared by reduction of the corresponding *N*-oxides (8) with phosphorus trichloride.

Table 2. Products obtained from the reaction of 2-aryl-3-cyanoindazole 1-oxides (8) with potassium hydroxide and potassium cyanide in methanol

Indazole oxide	Substituent in aryl group	Product yields (%) Cinnoline 1-oxide (9)	Indazole (10)
(8b)	*p*-Me	8	25
(8f)	*p*-Br	15	50
(8h)	*o*-Me	*ca.* 2	0
(8i)	*o*-F	22	Trace (by t.l.c.)

In considering the mechanism for the cyclisation of the anils (7) by cyanide in methanol, we have assumed from the beginning that the indazoles (10) result by initial cyclisation of the anils to indazole oxides (8), as in Scheme 2, followed by reduction of the *N*-oxides in the basic reaction medium. (There is some literature precedent for reductions of this type.[10]) It is thus a reasonable starting hypothesis that those cyclisations which produce no indazole are those in which the initial formation of the indazole oxide is suppressed. Most of the anils which show this reaction behaviour are derived from *ortho*-substituted amines, an observation which gives support to the idea that steric effects may be important in inhibiting the cyclisation (7) ⟶ (8) and thus permitting the alternative mode of cyclisation to the cinnoline oxides (10). It is significant in this connection that previous workers[5] have failed to obtain indazole oxides of the type (8) from the *o*-nitrobenzylidene derivatives of *ortho* substituted amines, and significant also that the only such anil from which we have even detected an indazole is (7i), in which the *ortho* substituent (fluoro-) is small.

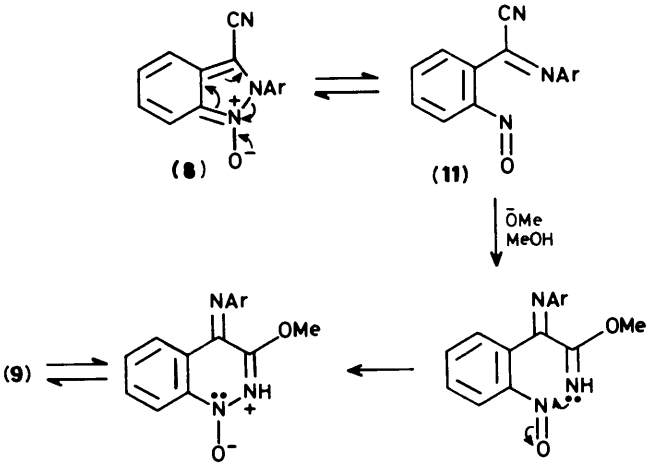
For the other main group of cyclisations, *viz.* those of the anils (7a—f), there are two obvious mechanistic possibilities to be considered. In each of these cases, indazole oxides (8a—f) are obtainable in good yield under extremely mild conditions (Scheme 2), and we have sought to determine whether under our more vigorous conditions, two alternative modes of cyclisation are in competition (Scheme 3a), or whether the indazole oxide serves as a common precursor of both of the observed products (Scheme 3b).



Scheme 3.

All the evidence supports the latter proposal. The indazole oxides (8b) and (8f), on reaction with 1 mol equiv. each of potassium hydroxide and potassium cyanide in methanol, give the corresponding cinnoline oxides, (9b) and (9f), and the indazoles, (10b) and (10f), in almost the same yields (Table 2) as are obtained from the anils (7b) and (7f). It thus appears that these anils are converted, by reaction with methanolic cyanide, essentially quantitatively into the indazole oxides, and that the latter are then further converted into the observed products.

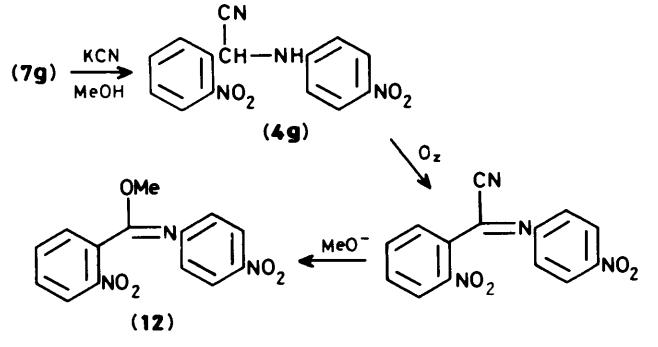
The transformation (**8**) ⟶ (**9**) may be envisaged, as in Scheme 4, in terms of a tautomeric ring-opening of the indazole oxide (**8**) to an α-cyano-*o*-nitrosobenzylideneaniline (**11**), base-catalysed addition of methanol to the cyano group, and recyclisation.



Scheme 4.

The possibility that two distinct reaction mechanisms might operate in these cyclisations has prompted us to seek and investigate some 'borderline' cases. We now report on four of these.

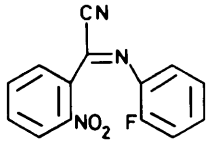
(i) p-*Nitro*-N-o-*nitrobenzylideneaniline* (**7g**). In this case there is no steric factor to inhibit indazole oxide formation, but the amino nitrogen in the adduct (**4**) is weakly nucleophilic (as in the *o*-nitroaniline analogues already described[3]). The reaction of the anil (**7g**) with potassium cyanide in methanol, however, gives neither the indazole nor the cinnoline oxide; the main product (31%) is the imidate ester (**12**), the formation of which is presumably analogous to that of its *o*-nitro counterparts (**3**)[3] (Scheme 5). There is literature precedent[11,12] for all the steps shown in the Scheme.



Scheme 5.

It is assumed that the anil (**7g**) fails to undergo cyclisation because aerial oxidation of the HCN adduct (**4g**) is faster than either of the possible cyclisation sequences.

(ii) o-*Fluoro*-N-o-*nitrobenzylideneaniline* (**7i**). If, as previously suggested, *ortho* substituents in the amine-derived ring of the anils (**7**) sterically hinder the formation of indazole oxides (**8**), then the smaller this *ortho* substituent, the better the chance of this type of cyclisation. The reactions of the *o*-fluoroanil (**7i**) support this suggestion. Unlike the corresponding *o*-chloro- and *o*-nitro-anils, (**7i**) gives a stable HCN adduct (**4i**), and the adduct is in turn cyclised to the indazole oxide (**8i**) in ethanolic sodium carbonate. Admittedly, the cyclisation step is relatively slow, to the extent that aerial oxidation of (**4i**) to the α-cyano anil (**13**) is a competing side-reaction. It is quite likely, however, that the inhibitory effect of the fluorine on the cyclisation in this case is not so much steric as electronic (its $-I$ effect reducing the nucleophilicity of the amino-nitrogen).



(13)

It will be recalled, of course (Table 1), that the reaction of the anil (**7i**) with cyanide in methanol gives mainly the cinnoline oxide (**9i**) and only very little indazole (**10i**). The indazole oxide (**8i**), on reaction with potassium hydroxide and potassium cyanide in methanol, similarly gives mainly (**9i**) together with a small amount of (**10i**) (Table 2). However, *the yield of cinnoline oxide* (**9i**) *obtained from the indazole oxide is considerably smaller than that obtained directly from the anil and cyanide*; it thus appears that the conversion of (**7i**) into (**9i**) does not necessarily involve (**8i**) as an intermediate, and that the cyclisation of (**7i**) probably represents a genuine 'borderline' case where the two reaction mechanisms operate in parallel.

(iii) N-o-*Nitrobenzylidene*-o-*toluidine* (**7h**). In this case, compared with (**7i**), the increased bulk of the *ortho*-substituent is counter-balanced by its electronic ($+I$) effect, which enhances the nucleophilicity of the amino nitrogen. This anil does indeed form an isolable, although rather unstable, HCN adduct (**4h**), and the latter is cyclised to the indazole oxide (**8h**), albeit relatively slowly, by the action of sodium carbonate.

It is impossible to establish, in this case, whether or not the cyclisation of (**7h**) to the cinnoline oxide (**9h**) involves the indazole oxide (**8h**) as an intermediate; the yields of (**9h**) (Tables 1 and 2) obtained from (**7h**) and from (**8h**) are both so low that the difference between them is within the limit of experimental error. The indazole (**10h**), however, is not obtained from either reaction.

(iv) 2,6-*Dimethyl*-N-o-*nitrobenzylideneaniline* (**7n**). In this anil, the C=N group is so hindered that it fails altogether to react with potassium cyanide. Most of the anil is recovered unchanged, the remainder presumably being hydrolysed in the course of the work-up.

It is thus clear that the formation of 4-arylamino-3-methoxycinnoline 1-oxides from *o*-nitrobenzylideneanilines, cyanide ion, and methanol is very far from the simple process depicted in Scheme 1. In certain cases, 2-aryl-3-cyano-2*H*-indazole 1-oxides are, demonstrably, intermediates. In other cases, where the intermediate is not isolated, it is possible that the reaction follows another course (*e.g.* that of Scheme 1); it is also possible, however, that the intermediate is indeed formed, but does not correspond to sufficient of an energy minimum along the reaction pathway to permit its isolation. In an attempt to gain further insight into the mechanisms of these reactons, we are now giving attention to the potential tautomerism of the indazole oxides [(**8**) ⇌ (**11**), as in Scheme 4], and we hope to report on this at a later date.

Experimental

I.r. spectra were recorded for Nujol mulls, u.v./visible spectra for $CHCl_3$ solutions, and ^1H n.m.r. spectra (80 or 100 MHz) for $CDCl_3$ solutions, unless otherwise stated. 'Petroleum' refers to the fraction of b.p. 40—60 °C.

N-o-*Nitrobenzylideneanilines* (**7**).—All the anils except (**7g**) and (**7l**) were prepared by dissolving equimolar quantities of *o*-

nitrobenzaldehyde and the appropriate amine in the minimum volume of warm ethanol, boiling the solution for *ca.* 5 min, and cooling in ice–water. Compounds (**7g**) and (**7l**) were obtained by heating the amine with an excess of *o*-nitrobenzaldehyde (amine:aldehyde = 3:4) in benzene containing toluene-*p*-sulphonic acid as catalyst, and removing the water formed by means of a Dean and Stark trap. The m.p.s. of the anils are collected in Table 3.

N-(α-*Cyano*-o-*nitrobenzyl*)*anilines* (**4**: X = H).—The parent compound (**4a**), m.p. 139—141 °C (from ethanol; lit., 140 °C), was obtained by the method of Reissert and Lemmer,[4] from *N*-*o*-nitrobenzylideneaniline (**7a**), sodium bisulphite, and potassium cyanide, but the yield was low (24%), and so the following method (an adaptation of von Walther and Hübner's procedure[19]) was used for the remainder of the series.

Table 3. *N*-*o*-Nitrobenzylideneanilines (**7**)

Compound No.	Substituent(s) in aniline	M.p., °C (recryst. solvent; lit., m.p.)
(**7a**)	—	68—69 (EtOH; 69.5[13])
(**7b**)	*p*-Me	71—72 (EtOH; 73—74[14])
(**7c**)	*p*-OMe	81—82 (EtOH; 80—81[14])
(**7d**)	*p*-F	84—86 (EtOH; 81–82[15])
(**7e**)	*p*-Cl	90—92 (EtOH; 92.5[14])
(**7f**)	*p*-Br	98—100 (EtOH; 99[14])
(**7g**)	*p*-NO_2	149—150 (C_6H_6–petroleum; 149[16])
(**7h**)	*o*-Me	79—81 (EtOH; 81—81.5[14])
(**7i**)	*o*-F	72—73 (Pr^iOH)†
(**7j**)	*o*-Cl	113—114 (EtOH; 116.5[14])
(**7k**)	*o*-Br	115—117 (EtOH; 118.5—119[14])
(**7l**)	*o*-CO_2Me	80—81 (C_6H_6–petroleum*[17])
(**7m**)	*o*-(SC_6H_4Me-*p*)	133—135 (EtOH*[17])
(**7n**)	2,6-Me_2	56—58 (Pr^iOH; 57[18])

* Analyses for these compounds are given in Part 1.[17] † (Found: C, 64.0; H, 3.7; N, 11.5. $C_{13}H_9FN_2O_2$ requires C, 63.9; H, 3.7; N, 11.5%).

A solution of potassium cyanide (0.65 g, 10 mmol) in water (2 ml) was added dropwise to a stirred suspension or solution of the anil (**7**) (10 mmol) in acetic acid (20 ml) either at room temperature or at 40 °C (see Table 4). Complete solution was usually achieved within a few min, and the product then began to crystallise. At the end of the reaction the mixture was either cooled in ice and the product filtered off directly (work-up A) or it was poured into ice–water and the product then filtered off (work-up B).

The compounds prepared by this method are listed in Table 4. All showed N–H absorption at *ca.* 3 300 cm^{-1} and very weak C≡N absorption at *ca.* 2 200 cm^{-1}.

2-*Aryl*-3-*cyano*-2*H*-*indazole* 1-*Oxides* (**8**).—The 2-phenyl and 2-(*p*-chlorophenyl) compounds (**8a**) and (**8e**) were prepared by Heller and Spielmeyer's method,[5] from *o*-nitromandelonitrile and aniline or *p*-chloroaniline in the presence of sodium acetate. The other members of the series were obtained as follows (in principle the method of Reissert and Lemmer[4]).

The appropriate *N*-(α-cyano-*o*-nitrobenzyl)aniline (**4**) (1 g) was dissolved in ethanol (20 ml) with gentle warming. Aqueous sodium carbonate (0.5 M; 0.3 ml) was added; in most cases an exothermic reaction ensued, and crystallisation of the bright yellow indazole oxide (**8**) began almost immediately. The mixture was allowed to cool slowly to room temperature and the product was filtered off and recrystallised.

The 2-(*o*-tolyl) compound (**8h**) did not crystallise out of the cooled reaction mixture, and was isolated by addition of the latter to ice–water. The 2-(*o*-fluorophenyl) compound (**8i**) required purification by chromatography on silica; the less polar by-product, N-(α-*cyano*-o-*nitrobenzylidene*)-*o*-*fluoroaniline* (**13**), was eluted with ether–petroleum (1:1), and the indazole oxide (**8i**) with ether–methanol (9:1).

[Compound (**13**) was obtained in 15% yield. It crystallised initially from propan-2-ol as fluorescent yellow plates, m.p. 112—113 °C, but subsequent recrystallisations from the same

Table 4. *N*-(α-Cyano-*o*-nitrobenzyl)anilines (**4**:X = H)

Compd. no.	Subst. in aniline	Reaction temp., time, work-up	Yield (%)	M.p. (°C, decomp.) [recryst. solvent]	Formula	Found (%) C	Found (%) H	Found (%) N	Requires (%) C	Requires (%) H	Requires (%) N
(**4b**)	*p*-Me	R.t., 1.5 h, A	61	137—139 [EtOH]*							
(**4c**)	*p*-OMe	R.t., overnight, A	80	129—131 [EtOH]	$C_{15}H_{13}N_3O_3$	63.5	4.5	15.0	63.6	4.6	14.8
(**4d**)	*p*-F	40 °C, 0.5 h, then R.t., overnight, B	70	118—121 [Pr^iOH]	$C_{14}H_{10}FN_3O_2$	62.4	3.7	15.6	62.0	3.7	15.5
(**4f**)	*p*-Br	40 °C, 5 h, A	67	137—139 [EtOH]	$C_{14}H_{10}BrN_3O_2$	50.75	2.8	12.5	50.6	3.0	12.65
(**4h**)	*o*-Me	40 °C, 4 h, B	63	118—122 [Pr^iOH]	$C_{15}H_{13}N_3O_2$	67.25	4.9	15.65	67.4	4.9	15.7
(**4i**)	*o*-F	40 °C, 2 h, then R.t., overnight, B	42	105—107 [Pr^iOH]	$C_{14}H_{10}FN_3O_2$	61.7	3.6	15.3	62.0	3.7	15.5

* Lit.,[16] 135—137 °C.

Table 5. 2-Aryl-3-cyano-2*H*-indazole 1-oxides (**8**)

Compd. no.	2-Subst. (XC_6H_4)	Yield (%)	M.p. (°C) [recryst. solvent]	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
(**8a**)	X = H	53	189—190 [EtOH]*							
(**8b**)	*p*-Me	51	199—201 [EtOH]†							
(**8c**)	*p*-OMe	86	190—191 [EtOH]	$C_{15}H_{11}N_3O_2$	67.9	4.0	15.95	67.9	4.2	15.8
(**8d**)	*p*-F	67	209—210 [AcOH–EtOH]	$C_{14}H_8FN_3O$	66.6	3.2	16.6	66.4	3.2	16.6
(**8e**)	*p*-Cl	60	198—199 [EtOH]¶							
(**8f**)	*p*-Br	76	208—209 [EtOH]‡							
(**8h**)	*o*-Me	74	126—128 [Pr^iOH]	$C_{15}H_{11}N_3O$	72.6	4.3	17.1	72.3	4.45	16.9
(**8i**)	*o*-F	63	175—176 [AcOH–EtOH]	$C_{14}H_8FN_3O$	66.4	3.2	16.6	66.4	3.2	16.6

* Lit.,[5] 190 °C. † Lit.,[5] 198—199 °C. ¶ Lit.,[5] 201 °C. ‡ Lit.,[7] 213—214 °C.

Table 6. 2-Aryl-3-cyano-2*H*-indazoles (**10**)

Compd. no.	2-Subst. (XC_6H_4)	M.p. (°C) [recryst. solvent]	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
(**10a**)	X = H	105—106 [EtOH] *							
(**10b**)	*p*-Me	134—136 [EtOH] †							
(**10c**)	*p*-OMe	153—154 [EtOH]	$C_{15}H_{11}N_3O$	72.5	4.3	16.8	72.3	4.4	16.9
(**10d**)	*p*-F	168—169 [EtOH]	$C_{14}H_8FN_3$	71.0	3.4	17.7	70.9	3.4	17.7
(**10e**)	*p*-Cl	160—161 [EtOH] ¶							
(**10f**)	*p*-Br	162—164 [EtOH]	$C_{14}H_8BrN_3$	56.3	2.5	14.0	56.4	2.7	14.1
(**10h**)	*o*-Me	85—86 [Pr^{i}OH]	$C_{15}H_{11}N_3$	77.2	4.7	18.1	77.2	4.75	18.0
(**10i**)	*o*-F	110 [Pr^{i}OH]	$C_{14}H_8FN_3$	70.7	3.3	17.6	70.9	3.4	17.7

* Lit.,[5] 105 °C. † Lit.,[5] 135 °C. ¶ Lit.,[5] 159 °C.

Table 7. 4-Arylamino-3-methoxycinnoline 1-oxides (**9**)

Compd. no.	4-Subst. (XC_6H_4NH)	M.p. (°C) [from benzene–petroleum unless otherwise indicated]	Formula	Found (%) C	Found (%) H	Found (%) N	Requires (%) C	Requires (%) H	Requires (%) N
(**9a**)	X = H	193—195 (decomp.)	$C_{15}H_{13}N_3O_2$	67.4	4.9	15.7	67.3	5.0	15.4
(**9b**)	*p*-Me	186—188	$C_{16}H_{15}N_3O_2$	68.0	5.2	14.7	68.3	5.4	14.9
(**9c**)	*p*-OMe	193—195	$C_{16}H_{15}N_3O_3$	64.8	5.25	14.05	64.6	5.05	14.1
(**9d**)	*p*-F	204—206 (Pr^{i}OH)	$C_{15}H_{12}FN_3O_2$	63.2	4.2	14.75	63.15	4.2	14.7
(**9e**)	*p*-Cl	219—220	$C_{15}H_{12}ClN_3O_2$	60.1	3.9	13.7	59.7	4.0	13.9
(**9f**)	*p*-Br	209—211	$C_{15}H_{12}BrN_3O_2$	51.9	3.5	12.1	52.0	3.5	12.1
(**9h**)	*o*-Me	196—197 (Pr^{i}OH)	$C_{16}H_{15}N_3O_2$	68.3	5.3	14.9	68.3	5.4	14.9
(**9i**)	*o*-F	194—195 (EtOH)	$C_{15}H_{12}FN_3O_2$	63.1	4.2	14.8	63.15	4.2	14.7
(**9j**)	*o*-Cl	226—228 (decomp.) (AcOH)	$C_{15}H_{12}ClN_3O_2$	60.0	3.9	13.9	59.7	4.0	13.9
(**9k**)	*o*-Br	227—230 (decomp.) (MeOH)	$C_{15}H_{12}BrN_3O_2$	51.7	3.5	12.1	52.0	3.5	12.1
(**9l**)	*o*-CO_2Me	190—191	$C_{17}H_{15}N_3O_4$	62.55	4.7	13.2	62.8	4.6	12.9
(**9m**)	*o*-(SC_6H_4Me-*p*)	198—200	$C_{22}H_{19}N_3O_2S$	68.2	5.1	10.6	67.9	4.9	10.8

solvent gave thick yellow spars, m.p. 127—128 °C (Found: C, 62.1; H, 2.9; N, 15.6. $C_{14}H_8FN_3O_2$ requires C, 62.45; H, 3.0; N, 15.6%); $\nu_{max.}$ 2 210 (C≡N), 1 520 and 1 350 cm^{-1} (NO_2); *m/z* 269.]

The indazole oxides (**8**) all show strong C≡N absorption at *ca.* 2 200 cm^{-1}. Other characteristics are listed in Table 5.

2-*Aryl*-3-*cyano*-2H-*indazoles* (**10**).—Authentic samples of these were obtained in several cases by reduction of the corresponding *N*-oxides (**8**). The *N*-oxide (1 g), dissolved or suspended in chloroform (15 ml), was treated with phosphorus trichloride (2 ml); the mixture was heated under reflux for 1 h and then cooled and added to ice–water. The aqueous layer was basified (NaOH) and chloroform added to extract the organic product. The extract was washed well with water, dried (Na_2SO_4), and evaporated to give the indazole as a colourless solid. Thus were obtained (**10a**), yield 85%; (**10d**), 84%; (**10e**), 80%; (**10f**), 85%; (**10h**), 73%; and (**10i**), 67%. All showed strong C≡N absorptions at *ca.* 2 200—2 250 cm^{-1}, but the only distinguishing features of their ^{1}H n.m.r. spectra were provided by substituents, such as methyl, within the 2-aryl group.

Further details of these compounds are contained in Table 6.

Reactions of the Anils (**7**) *with Potassium Cyanide in Methanol: General Procedure.*—A solution of the anil (10 mmol) and potassium cyanide (1.3 g, 20 mmol) in methanol (200 ml) was heated under reflux for 3 h; the very dark mixture was then either cooled, diluted with water, and extracted with chloroform, or else it was concentrated by distillation and the residue partitioned between chloroform and water. The chloroform solution was dried (Na_2SO_4) and evaporated to small volume; the residue was then chromatographed on silica. The first (colourless) fraction eluted (benzene) contained the indazole (**10**), and the principal coloured fraction [orange-yellow; eluant benzene–ether (1:1)] contained the cinnoline oxide (**9**). A highly polar, tarry residue remained at the top of the column.

The yields of indazoles and cinnoline oxides obtained in these reactions are given in Table 1, and the characteristics of the indazoles in Table 6.

The cinnoline oxides (**9**) were generally of a dull orange (azobenzene-like) colour, with $\lambda_{max.}$ *ca.* 440 nm (log $\varepsilon_{max.}$ *ca.* 4). They showed N–H absorption at *ca.* 3 250 cm^{-1}, and their ^{1}H n.m.r. spectra characteristically contained resonances at δ 4.0—4.1 (OMe), 6.0—6.3 (NH), and (distinct from the other aromatic proton signals) a 1 H multiplet at 8.5—8.6 (8-H of the cinnoline). Details of the individual members of the series are contained in Table 7.

In the case of the 2,6-dimethylanil (**7n**), heating with potassium cyanide in methanol produced no appreciable colour change. Chromatography of the crude product (eluant, benzene) gave only the starting anil (72% recovered) and a trace of 2,6-dimethylaniline (identified by n.m.r.).

In the case of the *p*-nitroanil (**7g**), a very small amount of colourless material was filtered off from the cooled reaction mixture. Analysis of this product (m.p. 287—289 °C) corresponded approximately to an isomer of the starting anil (Found: C, 58.1; H, 3.6; N, 15.3. $C_{13}H_9N_3O_4$ requires C, 57.6; H, 3.3; N, 15.5%) but the compound was almost completely insoluble in all the common solvents, and insufficiently volatile to give a mass spectrum. It was not therefore further characterised.

The methanol-soluble product was precipitated by addition of water; recrystallised from methanol, it had m.p. 132—133 °C. It was identified as *methyl* N-(p-*nitrophenyl*)-o-*nitrobenzimidate* (**12**) (0.93 g, 31%). (Found: C, 55.7; H, 3.6; N, 13.8. $C_{14}H_{11}N_3O_5$

requires C, 55.8; H, 3.65; N, 13.95%); *m/z* 301 (52%, $M^{+\bullet}$), 254 (23), 150 (19), 134 (100), 104 (59); $\nu_{max.}$ 1 680 (C=N), 1 515 and 1 350 cm^{-1} (NO_2); δ 4.09 (3 H, s, OCH_3) and 6.8—8.25 (8 H, m, ArH).

Reactions of 2-*Aryl*-3-*cyano*-2H-*indazole* 1-*Oxides* (**8**) *with Potassium Hydroxide and Potassium Cyanide in Methanol.*—The indazole oxide (10 mmol), potassium hydroxide (0.56 g, 10 mmol), and potassium cyanide (0.65 g, 10 mmol) were heated together in methanol (200 ml), under reflux, for 3 h. The work-up procedure was identical to that described in the preceding section; the yields of indazoles (**10**) and cinnoline oxides (**9**) thus obtained are collected in Table 2.

4-*Chloro*-3-*methoxycinnoline* 1-*Oxide*.—This compound was prepared in 9 stages from ethyl 2-oxocyclohexylacetate, essentially by the published method.[9] The overall yield was *ca.* 2% and the product had m.p. 165—167 °C (from ethanol; lit.,[9] 169—170 °C).

3-*Methoxy*-4-p-*toluidinocinnoline* 1-*Oxide* (**9b**).—Sodium hydride (80% suspension in oil; 40 mg) was added to a solution of *p*-toluidine (200 mg) in dry benzene (10 ml). When the initial effervescence had subsided, the mixture was heated under reflux for 2 h, 4-chloro-3-methoxycinnoline 1-oxide (40 mg) was added, and the resulting mixture was boiled for a further 6 h, cooled, and added to water (50 ml) containing concentrated hydrochloric acid (2 drops). The product was extracted with chloroform, and the extract was dried ($MgSO_4$), clarified with charcoal, and evaporated. Preparative t.l.c. ($CHCl_3$) gave (**9b**) (20 mg, 38%) as the least polar fraction. It had m.p. 186—188 °C (decomp.), and was spectroscopically identical with the sample obtained from the anil (**7b**) and potassium cyanide in methanol.

Acknowledgements

We thank Mr. J. R. Bews, Mrs. S. Smith, and Miss C. Jack for the microanalyses, Mrs. M. Smith for the n.m.r. spectra, and Mr. C. Millar for the mass spectra. We acknowledge the award of a research studentship to D. J. by the (then) Science Research Council, and the award of a Research Scholarship to T. S. by the University authorities.

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Received 12*th February* 1986; *Paper* 6/303