Convenient Preparation of 3,3-Dibromo-1,3-dihydroindol-2-ones† and Indole-2,3-diones (Isatins)† from Indoles

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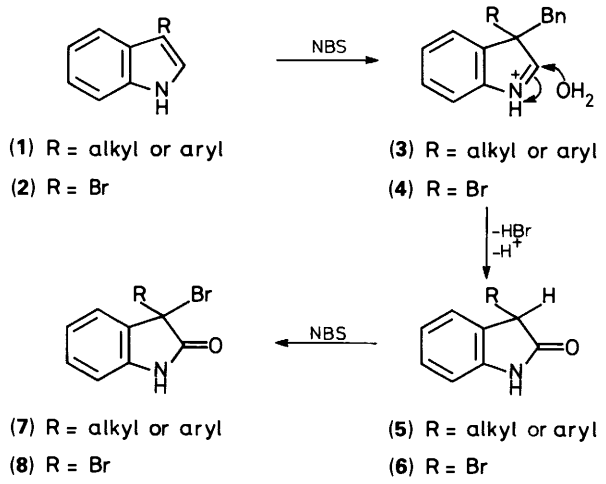
3,3-Dibromo-1,3-dihydroindol-2-ones, useful precursors of indole-2,3-diones, are readily formed by the reaction of either 3-bromoindoles or indoles with 2 or 3 mol equiv. of *N*-bromosuccinimide, respectively, in aqueous t-butyl alcohol. Some bromination of the 6-membered ring may occur and 3,5,6-tribromoindole-4,7-dione is a product from 3-bromo-4,7-dimethoxy-indole. Similar reactions with indole-3-carbaldehyde and 1*H*-pyrrolo[2,3-*b*]pyridine give 3,3-dibromo-1,3-dihydroindole-2-one and 3,3-dibromo-1*H*-pyrrolo[2,3-*b*]pyridin-2-one analogue, respectively, the latter yielding the corresponding 2,3-dione only with difficulty.

The closely related compounds indole and isatin† have been known for many years and although their individual chemistries have been explored extensively[1,2] to our knowledge there are no efficient and widely applicable methods available for the conversion of indoles into the corresponding isatins. A method that has been used is the oxidation of chromium trioxide in acetic acid of an indole[3] or 2,3-dihydroindole[4] but these conditions may cause modification of the substituents and yields are generally poor, particularly when the indole is unsubstituted at the nitrogen atom. We have sought a method which utilises mild conditions and is applicable to a wide range of indole derivatives.

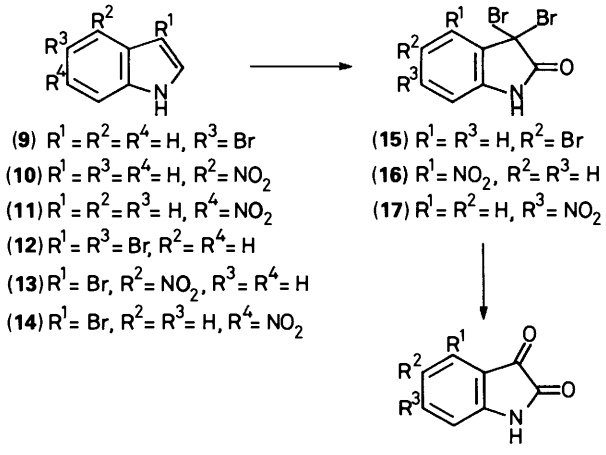
Our attention was attracted to the use of bromine and bromine-containing reagents because, although the reactions of these reagents with indoles have been studied extensively,[5] there appeared to be the opportunity to optimise their use in the particular conversion we wished to achieve. A search of the literature revealed that treatment of a 4,7-disubstituted indole gave a 4,7-disubstituted-5-bromo-isatin in unspecified yield by the action of bromine in acetic acid and in the presence of nitrobenzene.[6] However, it seemed that a two-step approach involving oxidation of the indole to the corresponding 3,3-dibromo-oxindole† and subsequent hydrolysis of the latter to the isatin was more likely to be successful. Bromine in acetic acid is reported to produce this type of conversion[7,8] but in low yield and with unwanted nuclear bromination.[7] More promising were the reports that *N*-bromosuccinimide (NBS) in aqueous acetic acid converted 3-methylindole into 5-bromo-3-methyloxindole[9] and that 3-alkyl (or aryl)-indoles (**1**) were oxidised to the corresponding 3-substituted oxindoles (**5**) upon treatment with NBS (1 molar equiv.) in aqueous t-butyl alcohol *via* the intermediate (**3**).[10] Particularly noteworthy was that 3-substituted-3-bromo-oxindoles (**7**) were formed when NBS (2 molar equiv) was used under mild conditions because the oxindoles (**5**) were brominated *in situ* (Scheme 1). It seemed likely that application of this reaction to 3-bromoindoles (**2**) would yield the corresponding 3,3-dibromo-oxindole (**8**) and hence the isatins in two mild reaction steps. We report details of an investigation of this idea[11] and the extension of the idea to the reactions of indole-3-carbaldehyde and 1*H*-pyrrolo[2,3-*b*]pyridine.

The oxidation of 3-bromoindole (**2**) with NBS (2 mol) under the mild reaction conditions used by Hinman and Beaumann[10] gave 3,3-dibromo-oxindole (**8**) (69%) and subsequent hydrolysis of (**8**) in aqueous methanol yielded isatin (98%). The presence of



(**1**) R = alkyl or aryl
(**2**) R = Br
(**3**) R = alkyl or aryl
(**4**) R = Br
(**7**) R = alkyl or aryl
(**8**) R = Br
(**5**) R = alkyl or aryl
(**6**) R = Br

Scheme 1.



(**9**) $R^1 = R^2 = R^4 = H$, $R^3 = Br$
(**10**) $R^1 = R^3 = R^4 = H$, $R^2 = NO_2$
(**11**) $R^1 = R^2 = R^3 = H$, $R^4 = NO_2$
(**12**) $R^1 = R^3 = Br$, $R^2 = R^4 = H$
(**13**) $R^1 = Br$, $R^2 = NO_2$, $R^3 = R^4 = H$
(**14**) $R^1 = Br$, $R^2 = R^3 = H$, $R^4 = NO_2$
(**15**) $R^1 = R^3 = H$, $R^2 = Br$
(**16**) $R^1 = NO_2$, $R^2 = R^3 = H$
(**17**) $R^1 = R^2 = H$, $R^3 = NO_2$
(**18**) $R^1 = R^3 = H$, $R^2 = Br$
(**19**) $R^1 = NO_2$, $R^2 = R^3 = H$
(**20**) $R^1 = R^2 = H$, $R^3 = NO_2$

certain substituents in the six-membered ring of the indole did not affect the course of the reaction. For instance 5-bromo- (**9**), 4-nitro- (**10**), and 6-nitro-indole (**11**) were converted into their

† In the discussion, isatin and oxindole are used, for convenience, to refer to indole-2,3-dione -1,3-dihydroindole-2-one respectively.

Table 1. Preparation of 3,3-dibromo-1,3-dihydroindol-2-one from indoles by the action of NBS in t-butyl alcohol

	Reaction conditions								
Indole	Molar ratio NBS: indole	Temp. (°C)	Time (h)	Isol'n procedure[a]	Oxindole	Crys'n solvent	Yield (%)	M.p. (°C)	Lit. M.p. (°C)
Indole	3:1	20	3	A	(**8**)	CCl_4	73	164—165	165[24]
(**2**)	2:1	20	3	A	(**8**)	CCl_4	67	164—165	165[24]
(**12**)	2:1	20	6	A	(**15**)	CCl_4	96	247—260	250—260[24]
(**13**)	2:1	20	3	A	(**16**)	LP	71	214—216	
(**14**)	2:1	20	3	A	(**17**)	LP	71	193—195	
(**21**)	3:1	0	3	B	(**23**)		28	185—186 (decomp.)	
	3:1	20	3	B	(**22**)		45	195—197 (decomp.)	
	3.2:1	20	3	C	(**22**)		42	195—197 (decomp.)	
					(**23**)		30	185—186 (decomp.)	
(**26**)	2:1	20	3	D	(**22**)[b]		23	195—197 (decomp.)	
(**29**)	2:1	20	3	E	(**6**)		38	160—161	161—16 225
					(**8**)		43	163—165	16 524
	3:1	20	5	F	(**6**)		14		
					(**15**)		26		
	4:1	20	5	A	(**15**)	CCl_4	53		
(**30**)	4:1	0	4	D	(**31**)		78	Decomp. > 170	
(**37**)	2:1	20	3	A	(**38**)	AcOEt	92	198—199	198—200[12]

[a] Isolation procedures included (A) crystallisation of the solid from the solvent indicated, or flash chromatography on silica gel using (B) chloroform, (C) benzene–ethyl acetate (5:1), (D) light petroleum (b.p. 40—60 °C)–diethyl ether (1:4), (E) chloroform–ethyl acetate (9:1), or (F) cyclohexane–ethyl acetate (4:1). [b] In addition, 3,5,6-tribromoindole-4,7-dione and 5,6-dibromo-4,7-dimethoxyindole-2,3-dione were isolated and characterised (see the Experimental Section for details). [c] LP = light petroleum (b.p. 60—80 °C).

Table 2. M.p.s and elemental analyses for the 1,3-dihydroindol-2-ones

			Elemental analysis					
			Found (%)			Requires (%)		
Oxindole	Cryst'n solvent*	M.p. (°C)	C	H	N	C	H	N
(**16**)	A	214—216	28.8	1.25	7.8	28.6	1.20	8.34
(**17**)	A	193—195 (decomp.)	28.35	1.15	7.8	28.6	1.20	8.34
(**22**)	B	195—197	28.2	1.9	3.4	27.9	1.86	3.26
(**23**)	B	185—186	34.0	2.8	4.2	34.2	2.56	3.99
(**31**)	B	170 (decomp.)	31.75	1.65	7.1	31.4	1.20	6.66

* A = Light petroleum (b.p. 40—60 °C)–diethyl ether and B = Light petroleum (b.p. 60—80 °C)–chloroform.

corresponding 3-bromo derivatives (**12**), (**13**), and (**14**) respectively, and these were smoothly oxidised with NBS (2 mol) in t-butyl alcohol in good yield to the corresponding dibromo-oxindoles (**15**), (**16**), and (**17**) (Tables 1 and 2). The isatins (**18**), (**19**), and (**20**) were then obtained readily by hydrolysis (Table 3).

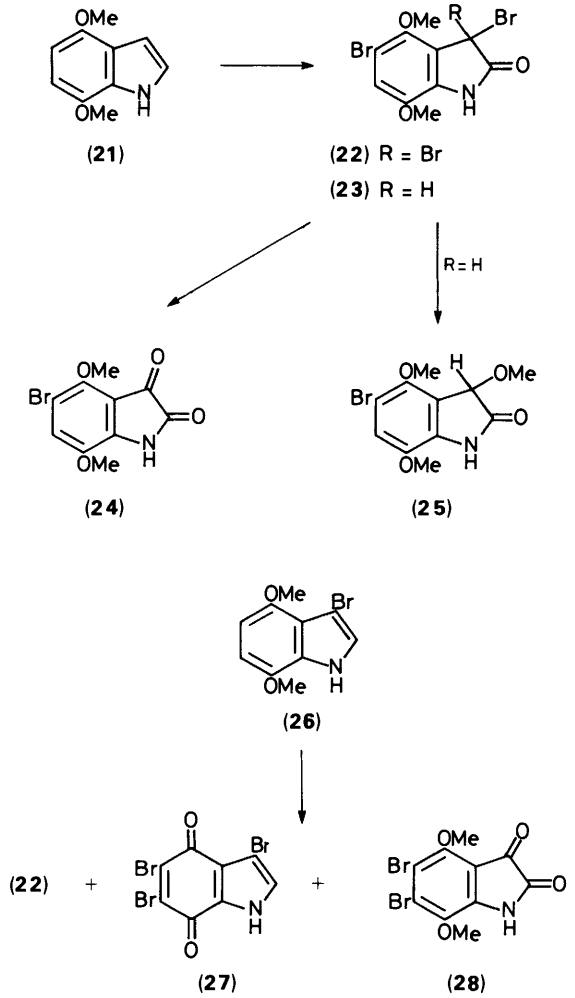
Up to this stage of our investigations, the 3-bromoindoles had been prepared from the indoles by the action of pyridine perbromide hydrobromide, a source of positive bromine. It seemed possible that the manipulative procedures might be simplified by combining the 3-bromination of indole and the subsequent oxindole formation by using the action of 3 molar equiv. of NBS on the indole in a one-pot reaction. This was shown to be possible by the conversion of indole into 3,3-dibromo-oxindole in a one-pot process in a marginally higher yield (73%) than we had obtained from 3-bromoindole. Thus, a two-step high-yield process for the conversion of indoles into isatins was achieved.[11]

Treatment of 4,7-dimethoxyindole (**21**) with 3 mol equiv. of NBS at room temperature gave 3,3,5-tribromo-4,7-dimethoxy-oxindole (**22**) as the major product. Mild hydrolysis of (**22**) gave 5-bromo-4,7-dimethoxyisatin (**24**) which was also obtained by bromination of 4,7-dimethoxyisatin. A similar reaction conducted at 0 °C gave 3,5-dibromo-4,7-dimethoxyoxindole (**23**). Thus it appeared that 3-bromination of (**23**) occurred less readily than 3-bromination of the indole. The availability of (**23**) and re-examination of the reaction at room temperature showed that both (**22**) and (**23**) were present in the product and both were isolated. Treatment of (**23**) with aqueous methanol gave 5-bromo-3,4,7-trimethoxyoxindole (**25**).

In an attempt to find conditions which would allow the formation 3,3-dibromo-4,7-dimethoxyoxindole unsubstituted in the 5-position, the preparation of 3-bromo-4,7-dimethoxy-indole (**26**) and its oxidation by NBS in t-butyl alcohol were investigated. The 3-bromo compound (**26**) was readily formed from (**21**) by the action of pyridine perbromide hydrobromide, though (**26**) decomposes above 60 °C. The oxidation of (**26**) with 2 mol equiv. of NBS in t-butyl alcohol gave at least six products. The major components, 3,3,5-tribromo-4,7-dimeth-oxyoxindole (**22**) was isolated as were two other products. A red solid (7% yield) was shown by elemental analysis and mass spectrometry to have a molecular formula of $C_8H_2Br_3NO_2$ and by ^1H n.m.r. to have one exchangeable hydrogen atom. The absence of methyl groups together with the presence of absorptions at 1 640 and 1 650 cm^{-1} in the i.r. spectrum indicated the presence of an indole-4,7-quinone rather than an isatin which would have been expected to show carbonyl stretching

Table 3. Spectroscopic properties of the 1,3-dihydroindole-2-ones

	I.r. spectra $\nu_{max.}$(KBr) cm^{-1}		^1H N.m.r. spectra	
	NH str.	CO str.	Solvent	Chemical shifts (δ, p.p.m.)
(16)	3 200	1 750	$(CD_3)_2SO$	11.65 (1 H, br s, exchanged with D_2O, NH), 7.82 (1 H, d, *J* 9 Hz, 7-H), 7.61 (1 H, dd, $J_{6,7}$ 9 Hz, $J_{5,6}$ 9 Hz, 6-H), and 7.30 (1 H, d, *J* 9 Hz, 5-H)
(17)	3 190	1 760	$(CD_3)_2SO$	11.6 (1 H, br s, exchanged with D_2O, NH), 8.0 (1 H, d, *J* 9 Hz, 4-H), 7.81 (1 H, d, *J* 9 Hz, 5-H), and 7.58 (1 H, s, 7-H)
(22)	3 200	1 730	$(CD_3)_2CO$	10.2 (1 H, br s, exchanged with D_2O, NH), 7.30 (1 H, s, 6-H), 4.13 (3 H, s, OCH_3), and 3.97 (3 H, s, OCH_3)
(23)	3 200	1 730	$(CD_3)_2CO$	10.12 (1 H, br s, exchanged with D_2O, NH), 7.30 (1 H, s, 6-H), 5.68 (1 H, s, 3-H), 4.02 (3 H, s, OCH_3), 3.97 (3 H, s, OCH_3)
(31)	3 375	1 755 1 725	$(CD_3)_2SO$	12.23 (1 H, br s, exchanged with D_2O, NH), 7.98 (2 H, m, 5- and 8-H), 7.73 (2 H, m, 6- and 7-H)



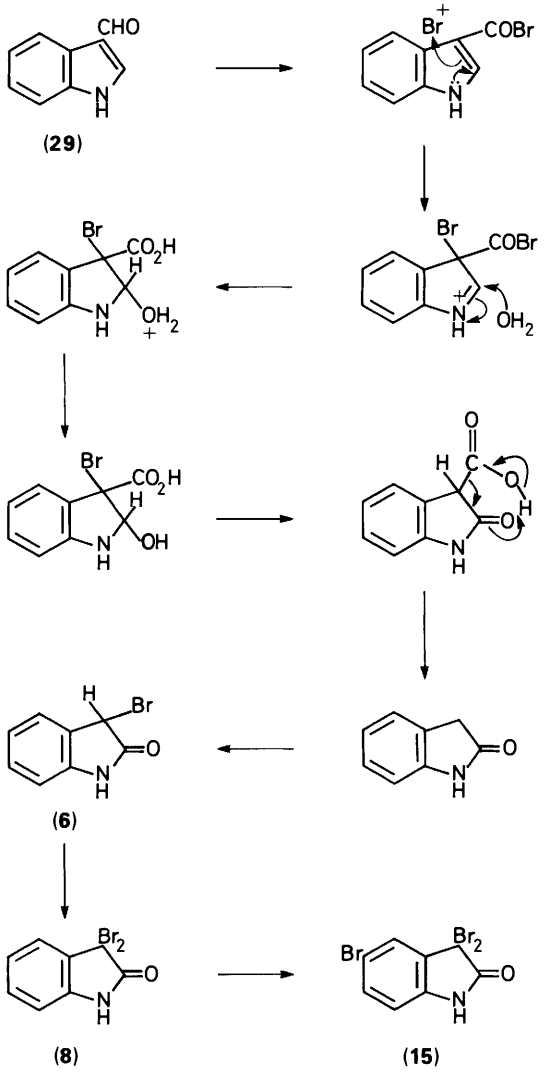
absorption bands at *ca.* 1 740 and 1 760 cm^{-1}. Bromine atoms are expected in the 3 and 5 positions but further bromination has occurred. The one remaining non-acidic proton showed at δ_H 7.28 which was thought likely to be the 2-H signal, and so the compound was tentatively assigned structure (**27**). The third product was red and had a molecular formula, $C_{10}H_7Br_2NO_4$, and showed the presence of two methyl groups and one acidic hydrogen in its ^1H n.m.r. spectrum. The i.r. spectrum showed peaks at 1 740 and 1 760 cm^{-1} typical of an isatin. The compound was thought to be 5,6-dibromo-4,7-dimethoxyisatin (**28**). The assignment of the position of the bromine substituents in this case is unambiguous and lends some support to structure (**27**).

The oxidation of (**26**) gave a more complex reaction product than was found for other cases investigated. This may have been due to the relative instability of (**26**), a higher than usual proportion of water in the reaction mixture, or to unusually highly acidic conditions. However, this was the only aberrant reaction we met in this work but it is worthy of note that very recently Marfat and Carta[12] have used the general procedure we described[11] to obtain dibromo-oxindoles as intermediates for the formation of oxindoles. They found pyridine perbromide hydrobromide to be a more reliable reagent than NBS.

The reaction of NBS with indole-3-carbaldehyde (**29**) in aqueous t-butyl alcohol provided some unexpected results and of particular interest was the ready deformylation process. It was found that (**29**) was converted into 3,3-dibromo-oxindole (43%) and 3-bromo-oxindole (**6**) (38%) in the presence of 2 mol equiv. of NBS. 3,3,5-Tribromo-oxindole (**15**) and 3-bromo-oxindole (**6**) were isolated when 3 mol equiv. of NBS were used, while 4 mol equiv. of NBS yielded (**15**) (53%) as the only isolated product. These results indicate that deformylation occurred before 3-bromo-oxindole formation, 5-bromination was the last bromination step, and that further bromination of 3,3-dibromo-oxindole occurred rapidly. The suggested reaction process is shown in Scheme 2. NBS is known[13] to convert arenecarbaldehydes into the corresponding carboxylic acid bromide in a photochemically initiated reaction in carbon tetrachloride solution. Oxindole-3-carboxylic acid would be expected to undergo ready decarboxylation as a β-carbonyl acid. Some additional evidence for the reaction scheme proposed was obtained in the observation of a component corresponding to oxindole in the t.l.c. analysis of the reaction mixture obtained when 2 mol equiv. of NBS were used.*

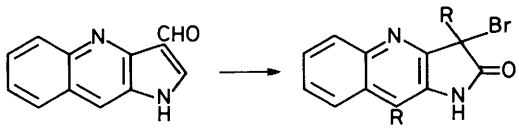
In a similar way, pyrrolo[3,2-*b*]quinoline-3-carbaldehyde (**30**) on treatment with 3 mol equiv. of NBS gave a major product which showed the presence of an amide system in its i.r. spectrum (peaks at 3 375 and 1 750 cm^{-1}) and had elemental analysis and a mass spectrum in agreement with the molecular formula, $C_{11}H_5Br_3N_2O$. Comparison of the ^1H n.m.r. spectrum of the tribromo compound with that for (**30**) showed the expected absence of the peaks for the aldehyde group and the 2-H but the peaks for the 5- and 8-H and the 6- and 7-H present. Significantly the tribromo compound did not show the singlet at 8.77 p.p.m. assigned to 9-H in the spectrum of the aldehyde. The product was thought to be 3,3,9-tribromo-2,3-dihydropyrrolo-[3,2-*b*]quinolin-2-one (**31**). Two minor components of the

* A referee has suggested that a possible alternative mechanism is the conversion of (**29**) into 3-formyloxindole followed by decarbonylation to oxindole, and then as given above.



(29) (6) (8) (15)

Scheme 2.

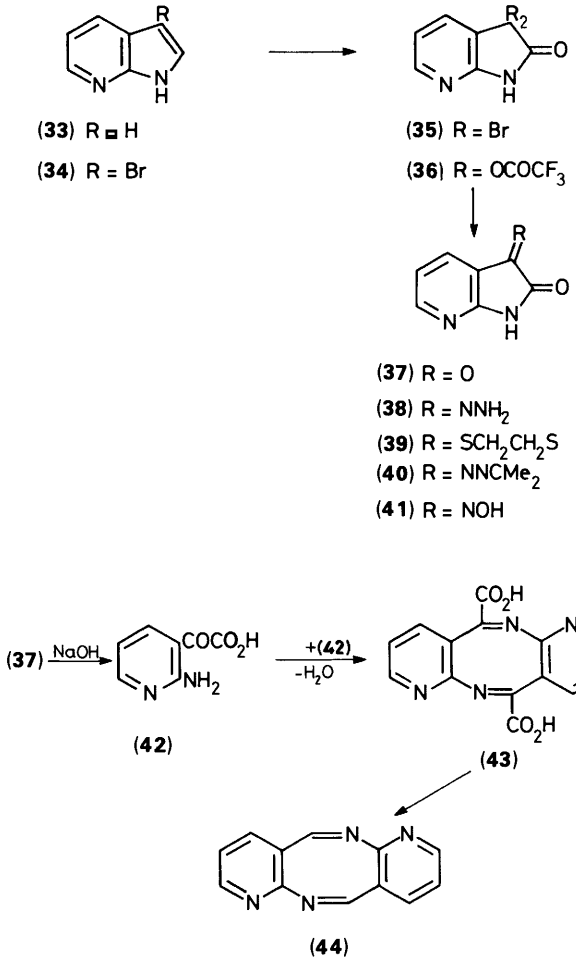


(30) (31) R = Br (32) R = H

reaction mixture could not be separated but the mass spectrum of this mixture showed molecular ion peaks of equal intensity at 262 and 264 Daltons corresponding to the molecular formula, $C_{11}H_7BrN_2O$. One of the components of the mixture is likely to be (**32**) corresponding to (**6**) in the reaction indole-3-carbaldehyde (Scheme 2).

The simpler pyrrolopyridine (azaindole) systems are of interest[14] because of their relationship with both the biologically important indoles and purines but few azaoxindoles are accessible in quantity and only the 7-azaisatin is known.[15] Thus, oxidation of 7-azaindole (**33**) is of interest as a possible route to 7-azaisatin.

The conversion of 7-azaindole (**33**) into the stable 3-bromo-7-azaindole (**34**) was accomplished by a known procedure[16] and this when treated with 2 mol equiv. of NBS gave 3,3-di-bromo-7-



(33) R = H (34) R = Br (35) R = Br (36) R = $OCOCF_3$ (37) R = O (38) R = NNH_2 (39) R = SCH_2CH_2S (40) R = $NNCMe_2$ (41) R = NOH (42) (43) (44)

azaoxindole (**35**) (97%). However, in marked contrast to the indole series, we were unable to isolate and characterise 7-azaisatin (**37**) from the hydrolysis of the oxindole (**35**) with aqueous methanol. In each case a red solid was obtained but all attempts to obtain a sample having a satisfactory i.r. and ^1H n.m.r. spectrum were unsuccessful. Treatment of (**35**) with silver trifluoroacetate[17] in acetonitrile gave a reaction product which was presumed to be (**36**) but the compound was not isolated. Mild hydrolysis of the reaction mixture and extraction of the aqueous phase with methylene dichloride gave 7-azaisatin, though in poor yield. Neutralisation of the aqueous phase and work up yielded sodium 2-amino-3-pyridylglyoxylate (**42**) and this, on acidification, gave the corresponding acid. The electron impact mass spectrum of (**42**) showed a molecular ion peak m/z = 208 Daltons which is consistent with (**44**) formed by dehydrative cyclisation of two molecules of (**42**) to give (**43**) followed by decarboxylation to (**4**).

The ring opening of isatins in the presence of alkali is well known[2] and is the basis of the Pfitzinger synthesis of quinolines; the presence of electron-withdrawing substituents in the 5- or 7-positions promotes the ring-opening process. In these cases the isatin is reformed on acidification of the 2-aminophenylglyoxylic acid. A similar cyclisation reaction did not occur with (**42**), presumably due to the low nucleophilicity of the 2-amino group on the pyridine ring which is further reduced by protonation of the pyridine nitrogen atom in acid solution.

The sum of the yields of 7-azaisatin and 2-amino-3-pyridylglyoxylic acid represents a high conversion of 3,3-dibromo-azaoxindole (**35**) but it was hoped to obtain a higher yield of the isatin (**37**). Other methods for the conversion of (**35**) into (**37**) were explored. The 3-hydrazone (**38**) and the ethane-3,3-

Table 4. Formation of indole-2,3-diones by hydrolysis of 3,3-dibromo-1,3-dihydroindol-2-ones

3,3-Dibromo-1,3-dihydroindol-2-on	Reaction time (h)	Product substituent	Cryst'n solvent	Yield (%)	M.p. (°C)	Lit. m.p. (°C)
(**8**)	3	—	MeOH	98	198—200	200—201[26]
(**15**)	0.5	5-Bromo	Aq. MeOH	99	260—261	255—256[27]
(**16**)	6	4-Nitro	MeOH	50	235—237	245[28]
(**17**)	6	6-Nitro	MeOH	49	290—291	288—290[29]
(**22**)	0.25	5-Bromo-4,7-dimethoxy-	$CHCl_3$	98	269—270[a]	

[a] *5-Bromo-4,7-dimethoxyindole-2,3-dione* gave purple needles (Found: C, 41.75; H, 3.05; N, 4.51. $C_{10}H_8BrNO_4$ requires C, 41.98; H, 2.82; N, 4.90%); $\nu_{max.}$ 3 200 (NH) and 1 760 and 1 740 cm^{-1} (CO); $\delta[(CD_3)_2CO]$ 10.21 (1 H, br s, disappeared on addition of D_2O, NH), 6.93 (1 H, s, 6-H), 3.93 (3 H, s, OCH_3), and 3.79 (3 H, s, OCH_3).

dithiol derivative (**39**) were readily obtained from (**35**) but we were unable to generate the azaisatin (**37**) from them: treatment of (**38**) with an excess of acetone yielded (**40**) but the reaction did not proceed further to yield (**37**) as expected,[18] and treatment of (**39**) with thallium(III) nitrate was unsuccessful.[19] However, the reactive dibromo-oxindole was readily converted into its oxime (**41**) (65%) and, since the oxime has been converted into the isatin (**37**) *via* the amine in a 78% overall yield, this represents a formal conversion of 7-azaindole into the corresponding isatin in 42% overall yield but in five steps.

Experimental

3-Bromoindole[20] and 3-bromo-7-1*H*-pyrrolo[2,3-*b*]pyridine[16] were obtained by literature methods. Both 4- and 6-nitroindole were prepared from ethyl pyruvate *m*-phenylhydrazone by the three-step literature route[21] but the isomers were separated by dry flash-column chromatography (alumina, diethyl ether) at the ethyl nitroindole-2-carboxylate stage. Additionally, 6-nitroindole was obtained from indole.[22] Pyrrolo[3,2-*b*]quinoline-3-carbaldehyde[23] had $\delta[(CD_3)_2SO]$ 12.66 (1 H, br s, exchanged with D_2O, NH), 10.20 (1 H, s, CHO), 8.77 (1 H, s, 9-H), 8.10 (2 H, 5- and 8-H), and 7.67 (2 H, m, 6- and 7-H).

I.r. spectra were recorded for KBr discs on a Unicam SP200 spectrometer and the n.m.r. spectra were obtained on either a Varian T-60 or CFT-20 spectrometer with $SiMe_4$ as an internal standard. Low-resolution data were provided by the S.E.R.C's Physicochemical Measurements Unit.

3,5-*Dibromoindole* (**12**).—A cold solution of pyridinium hydrobromide perbromide (3.2 g, 10 mmol) in pyridine (15 cm^3) was added dropwise to a stirred solution of 5-bromoindole (2 g, 10 mmol) in pyridine (10 cm^3) at such a rate that the temperature did not rise above 2 °C. After a further 0.5 h the mixture was poured into cold diethyl ether. The insoluble material was filtered off and the filtrate washed successively with dilute hydrochloric acid, dilute aqueous sodium hydroxide and water and then dried ($MgSO_4$) and evaporated to yield a solid which was crystallised from cyclohexane as 3,5-*dibromoindole* (2.0 g, 75%), m.p. 85—86 °C (decomp.) (Found: C, 34.9: H, 1.95; N, 5.25. $C_8H_5Br_2N$ requires C, 34.9; H, 1.82; N, 5.10%); $\nu_{max.}$ 3 425 cm^{-1} (NH); $\delta(CDCl_3)$ 8.10 (1 H, br s, disappeared on addition of D_2O, NH), 7.74 (1 H, s, 4-H), and 7.3—7.2 (3 H, m, 2-, 6- and 7-H); *m/z* 277 (50%, M^+ when $^{81}Br_2$), 275 (100), and 273 (50).

Similarly, the following 3-bromo derivatives were prepared from the corresponding indole 3-*Bromo-4-nitroindole* (**13**). Yellow needles (72%) from light petroleum–diethyl ether, m.p. 115—117 °C (decomp.) (Found: C, 39.5; H, 2.4; N, 11.55. $C_8H_5BrN_2O_2$ requires C, 39.9; H, 2.09; N, 11.62%); $\nu_{max.}$ 3 270 cm^{-1} (NH); $\delta[(CD_3)_2SO]$ 12.18 (1 H, br s, disappeared on addition of D_2O, NH), 7.95—7.57 (3 H, m, 2-, 5- and 7-H), and 7.27 (1 H, dd, 6-H); *m/z* 242 (100%, M^+ when ^{81}Br), 240 (100), 212 (15), 210 (17), 196 (47), and 194 (41).

3-*Bromo-6-nitroindole* (**14**). Yellow needles (41%) from light petroleum (b.p. 40—60 °C), m.p. 175—177 °C (Found: C, 39.9; H, 2.45; N, 11.4. $C_8H_5BrN_2O_2$ requires C, 39.9; H, 2.09; N, 11.62%); $\nu_{max.}$ 3 260 cm^{-1} (NH); $\delta[(CD_3)_2SO]$ 12.08 (1 H, br s, disappeared on addition of D_2O, NH), 8.33 (1 H, s, 7-H), 7.90 (1 H, d, *J* 9 Hz, 5-H), 7.33 (1 H, s, 2-H), and 7.55 (1 H, d, *J* 9 Hz, 4-H); *m/z* 242 (100%, M^+ when ^{81}Br), 240 (100), 212 (13), 210 (14), 196 (34), and 194 (36).

3-*Bromo-4,7-dimethoxyindole* (**26**). Obtained as colourless needles (2.5 g, 96%), m.p. 69—70 °C (decomp.) [ex. diethyl ether–light petroleum (b.p. 40—60 °C)] (Found: C, 46.9; H, 4.2; N, 5.25. $C_{10}H_{10}BrNO_2$ requires C, 46.9; H, 3.91; N, 5.47%); $\nu_{max.}$ 3 400 cm^{-1} (NH); $\delta(CDCl_3)$ 8.38 (1 H, br s, disappeared on addition of D_2O, NH) 7.0 (1 H, m, 6-H), 6.65—6.35 (2 H, m, 2- and 5-H), 3.92 (3 H, s, OCH_3), and 3.82 (3 H, s, OCH_3).

3,3-*Dibromo-1,3-dihydroindol-2-one: General Method.*—The indole or 3-bromoindole was dissolved in aqueous t-butyl alcohol (95%). *N*-Bromosuccinimide (crystallised from water before use) was added portionwise over a period of 30 min with stirring under a nitrogen atmosphere. The mixture was set aside and the progress of the reaction was monitored by t.l.c. At the completion of the reaction, the mixture was concentrated at room temperature under reduced pressure and the precipitated succinimide was filtered off. The solid was washed with cold ether and the combined ethereal and alcoholic solution was evaporated to dryness and then treated as indicated in Table 1 to yield the 3,3-dibromo-1,3-dihydroindol-2-one (Table 2).

In addition to the corresponding 3,3-dibromo-1,3-dihydroindol-2-one these experiments yielded other indole derivatives from 4,7-dimethoxyindole as indicated in Table 1. These compounds are described below.

3,3,5-*Tribromo-4,7-dimethoxy-1,3-dihydroindol-2-one* (**22**). Obtained as yellow needles, m.p. 195—197 °C (decomp.) (Found: C, 28.2; H, 1.9; N, 3.4. $C_{10}H_8Br_3NO_3$ requires C, 27.9; H, 1.86; N, 3.26%); $\nu_{max.}$ 3 200 (NH) and 1 730 cm^{-1} (CO); $\delta[(CD_3)_2CO]$ 10.20 (1 H, br s, disappeared on addition of D_2O, NH), 7.30 (1 H, s, 6-H), 4.13 (3 H, s, OCH_3), and 3.97 (3 H, s, OCH_3); *m/z* 433 (2%, M^+ when ^{81}Br), 431 (4), 429 (4), 427 (2), and 43 (100).

3,5,6-*Tribromoindole-4,7-dione* (**27**). Formed red prisms, m.p. 266—267 °C (decomp.) (Found: C, 25.1; H, 0.65; N, 3.75. $C_8H_2Br_3NO_2$ requires C, 25.0; H, 0.52; N, 3.65%); $\nu_{max.}$ 3 150 (NH) and 1 650 cm^{-1} (CO); $\lambda_{max.}$(EtOH) 213 (log ε 4.0), 227 (4.02), 287 (3.91), and 348 nm (3.06); $\delta[(CD_3)_2CO]$ 10.25 (1 H, br s, disappeared on addition of D_2O, NH) and 7.28 (1 H, s, 2-H); *m/z* 387 (13%, M^+ when $^{81}Br_3$) 385 (37), 383 (37), 381 (13), and 43 (100).

5,6-*Dibromo-4,7-dimethoxyindole-2,3-dione* (**28**). Obtained as red prisms, m.p. 260—261 °C (Found: C, 32.9, H, 2.2; N, 3.95.

$C_{10}H_7Br_2NO_4$ requires C, 32.9; H, 1.91; N, 3.83%); $\nu_{max.}$ 3 200 (NH), 1 760, and 1 740 cm^{-1} (CO); δ[$(CD_3)_2CO$] 10.48 (1 H, br s, disappeared on addition of D_2O, NH), 4.08 (3 H, s, OCH_3), and 3.83 (3 H, s, OCH_3); *m/z* 367 (6%, M^+ when $^{81}Br_2$), 365 (12), 363 (6), and 43 (100).

5-*Bromo*-3,4,7-*trimethoxy*-1,3-*dihydroindol*-2-*one* (**25**). A solution of 3,5-dibromo-4,7-dimethoxy-1,3-dihydroindol-2-one (0.1 g) in aqueous methanol (70%; 20 cm^3) was boiled under reflux for 2 h and then evaporated to dryness. The red solid was dissolved in benzene and purified by flash column chromatography (silica gel, benzene–ethyl acetate, 4:1) to give the *title compound* (0.8 g, 89%), m.p. 134—135 °C (Found: M^+, 300.9943. $C_{11}H_{12}NO_4{}^{79}Br$ requires 300.9950); $\nu_{max.}$ 3 200 (NH) and 1 740 cm^{-1} (CO) δ[$(CD_3)_2SO$] 11.16 (1 H, br s, disappeared on addition of D_2O, NH), 7.29 (1 H, s, 6-H), 5.13 (1 H, s, 3-H), 3.80 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), and 3.28 (3 H, s, 3-OCH_3); *m/z* 303 (100%, M^+ when ^{81}Br), 301 (100), 260 (54), and 258 (55).

Hydrolysis of 3,3-*Dibromo*-1,3-*dihydroindol*-2-*one: General Method.*—A solution of the 3,3-dibromo-1,3-dihydroindol-2-one (typically 1 mmol) in aqueous methanol (50%; 40 cm^3) was boiled under reflux. The solution was evaporated and the residue crystallised (Table 3).

1H-*Pyrrolo*[2,3-b]*pyridine*-2,3-*dione and 2-Amino*-3-*pyridylglyoxylic Acid.*—A mixture of 3,3-dibromo-1,3-dihydropyrrolo[2,3-*b*]pyridin-2-one (0.7g, 2 mmol), silver trifluoroacetate (0.9 g, 4 mmol), water (2 cm^3), and acetonitrile (30 cm^3) was boiled under reflux in the dark for 1 h. The silver bromide was filtered off from the cold mixture and the filtrate evaporated to dryness. Addition of water and extraction with dichloromethane of the latter gave, after evaporation of the organic extract, a solid which was crystallised from the methanol to give the yellow title dione (0.1 g, 25%), m.p. 220—230 °C (decomp.) [lit.,[15] m.p. 225—230 (decomp. from 220 °C].

An ethyl acetate extract of the neutralised aqueous layer from the above experiment yielded yellow sodium 2-amino-3-pyridylglyoxylate (0.4 g, 67%). Addition of acetic acid to an aqueous solution of the sodium salt gave a solid which crystallised from ethanol as 2-amino-3-pyridylglyoxylic acid, m.p. 200—204 °C (decomp.) (lit.,[15] m.p. 197—199 °C); $\nu_{max.}$ 3 475 and 3 350 (NH_2) and 1670 cm^{-1} (CO); δ[$(CD_3)_2SO$] 8.37 (1 H, dd, 6-H) 7.97 (1 H, dd, 4-H), 7.78 (1 H, br s, disappeared on addition of D_2O, OH), 6.80 (1 H, dd, 5-H), and 6.28 (2 H, br s, disappeared on addition of D_2O, NH_2).

1H-*Pyrrolo*[2,3-b]*pyridine*-2,3-*dione* 3-*Hydrazone* (**38**).—A mixture of the parent dione (0.58 g, 2 mmol), hydrazine hydrate (2 g, 6 mmol), and ethanol (50 cm^3) was boiled under reflux for 0.5 h. The insoluble material was removed and the solution evaporated to dryness. Purification of the product by flash chromatography [silica gel, light petroleum (b.p. 40—60 °C)–diethyl ether (1:1)] gave the yellow *title compound* (0.24, 50%), m.p. 237—238 °C (Found: C, 51.8; H, 3.86; N, 34.63. $C_7H_6N_4O$ requires C, 51.85; H, 3.70; N, 34.57%); $\nu_{max.}$ 1 680 cm^{-1} (CO); δ[$(CD_3)_2SO$] 11.30 (1 H, br s, disappeared on addition of D_2O, NH), 10.58 and 10.00 (2 H, 2 × br s, disappeared in addition of D_2O, NH_2 having 1 H intramolecularly H-bonded), 8.15 (1 H, dd, 6-H), 7.72 (1 H, dd, 4-H), and 7.03 (1 H, dd, 5-H); *m/z* 162 (70%, M^+) and 134 (22).

1H-*Pyrrolo*[2,3-b]*pyridine*-2,3-*dione*-3-*oxime* (**41**).—A mixture of the parent dione (0.6 g, 2 mmol), hydroxylamine hydrochloride (0.6 g, 8 mmol), triethylamine (0.6 g, 6 mmol), and ethanol (30 cm^3) was boiled under reflux for 8 h and then evaporated. The residue was chromatographed (silica gel, 230—400 mesh, chloroform–ethyl acetate, 1:1) to give the *oxime* (0.15 g, 45%), m.p. 250—252 °C (decomp.) (lit.,[15] m.p. 252—254 °C); $\nu_{max.}$ 3 300 (OH) and 1 740 cm^{-1} (CO).

1H-*Pyrrolo*[2,3-b]*pyridine*-2,3-*dione* 3,3-*Dithioketal* (**39**).—Solutions of the parent dione (3 g, 0.01 mmol) in dry benzene (100 cm^3) and ethane-1,2-dithiol (0.94 g, 0.01 mmol) in dry benzene (100 cm^3) were added separately but at the same rate to a boiling solution of trimethylamine (2.2 g, 22 mmol) in dry benzene (500 cm^3) under reflux and in the presence of molecular sieve (4A). The mixture was refluxed for a further 2 h after completion of the addition. The red solid was filtered off and crystallised from methanol to give [7,7′-bi-1*H*-pyrrolo[2,3-*b*]pyrridine]-2,2′,3,3′-tetraone (0.9 g, 33%), m.p. decomp. from 300 °C (Found: M^+, 264.0646. $C_{14}H_8N_4O_2$ requires M^+, 264.0647); $\nu_{max.}$ 1 700 cm^{-1} (CO); δ[$(CD_3)_2SO$)] 11.60 (2 H, br s, disappeared on addition of D_2O, 2-NH), 10.10 (2 H, dd, 6- and 6′-H), 8.41 (2 H, dd, 4- and 4′-H), and 7.84—7.48 (2 H, m, 5- and 5′-H; *m/z* 264 (100%, M^+), 236 (22), 222 (9), 220 (5), 209 (3), 208 (4), 165 (7), 100 (8), and 89 (5).

The filtrate was evaporated and the residue dissolved in chloroform and subjected to flash chromatography [silica gel; ethyl acetate–chloroform (1:9)] to give the *title compound* (1.6 g, 65%), m.p. 184—185 °C (decomp.) (Found: C, 48.2; H, 3.5; N, 12.4. $C_9H_8N_2OS_2$ requires C, 48.2; H, 3.57; N, 12.50%); $\nu_{max.}$ 3 150 (NH) and 1 720 cm^{-1} (CO); δ[$(CD_3)_2SO$] 12.24 (1 H, br s, disappeared on addition of D_2O, NH), 8.11 (1 H, dd, $J_{5,6}$ 10 Hz, $J_{4,6}$ 2 Hz, 6-H), 7.73 (1 H, dd, $J_{4,5}$ 9 Hz, $J_{4,6}$ 2 Hz, 4-H), 7.01 (1 H, dd, $J_{4,5}$ 9 Hz, $J_{5,6}$ 10 Hz, 5-H), and 3.38 (4 H, s, 2 × CH_2).

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