

Internuclear Cyclisation. Part VIII. Naphth[3 : 2 : 1-cd]oxindoles.*

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The condensation of *o*-nitrobenzaldehyde with oxindole gives 3-*o*-nitrobenzylideneoxindole, which on successive reduction, diazotisation, and decomposition of the diazonium solution with copper powder gives naphth[3 : 2 : 1-*cd*]oxindole. This sequence of reactions is further exemplified by the use of (a) benzo-substituted oxindoles, (b) substituted *o*-nitrobenzaldehydes, and (c) *N*-phenyloxindole. An attempt to apply the same reaction to thio-oxindole gave 3-*o*-mercaptophenylcarbostyryl. Condensation of quinoline-2-aldehyde with oxindole gives the same product as is obtained from isatin and quinaldine, and similar condensation reactions of isatin with α -picoline, 4-hydroxy-quinaldine, and 3-nitroquinaldine are reported. An improved general method for the preparation of oxindoles is described.

AMONG tetracyclic structures which lend themselves to a method of synthesis involving internuclear cyclisation by means of the Pschorr reaction or one of its modifications is the naphth[3 : 2 : 1-*cd*]oxindole system.† The parent substance (III), which appears to be the only known representative of this series, was prepared by Pschorr and Popovici (*Ber.*, 1906, **39**, 3120; see also Kishi, *J. Pharm. Soc. Japan*, 1926, **532**, 475), who reduced *o*-nitro- α -*o'*-nitrophenylcinnamic acid (I), obtained by condensation of *o*-nitrobenzaldehyde with *o*-nitrophenylacetic acid, to 3-*o*-aminobenzylideneoxindole (II), which was then diazotised and decomposed with copper powder to give naphth[3 : 2 : 1-*cd*]oxindole (III). The structure assigned by Pschorr to this compound is not free from ambiguity because the precise stereochemistry of this reduction of *o*-nitro- α -*o'*-nitrophenylcinnamic acid is uncertain. If his amine possessed the structure (II) the identity of his product, m. p. 229°, as naphth[3 : 2 : 1-*cd*]oxindole (C₁₅H₉ON) is clearly established; but if a geometrical isomerisation occurred during the reduction, his amine would have the structure (V) derived from the diamine (IV), and this could lead under similar experimental conditions to 3-phenylcarbostyryl (VI) (C₁₅H₁₁ON), m. p. 228.5°, the small difference in hydrogen content being barely adequate to permit an unequivocal decision between the two. Borsche, Wagner-Roemmich, and Barthenheier (*Annalen*, 1942, **550**, 160) prepared an amine identical in physical properties with that of Pschorr and Popovici (*loc. cit.*) by reduction of 3-*o*-nitrobenzylideneoxindole. This amine was converted into quinindoline (VIII) by the action of heat. Quinindoline can be obtained from the amine (V) as well as from (VII), and in view of the results obtained in the thio-oxindole series (p. 1703), there was a possibility that this amine was 3-*o*-aminophenylcarbostyryl (V) and not 3-*o*-aminobenzylideneoxindole (VII).

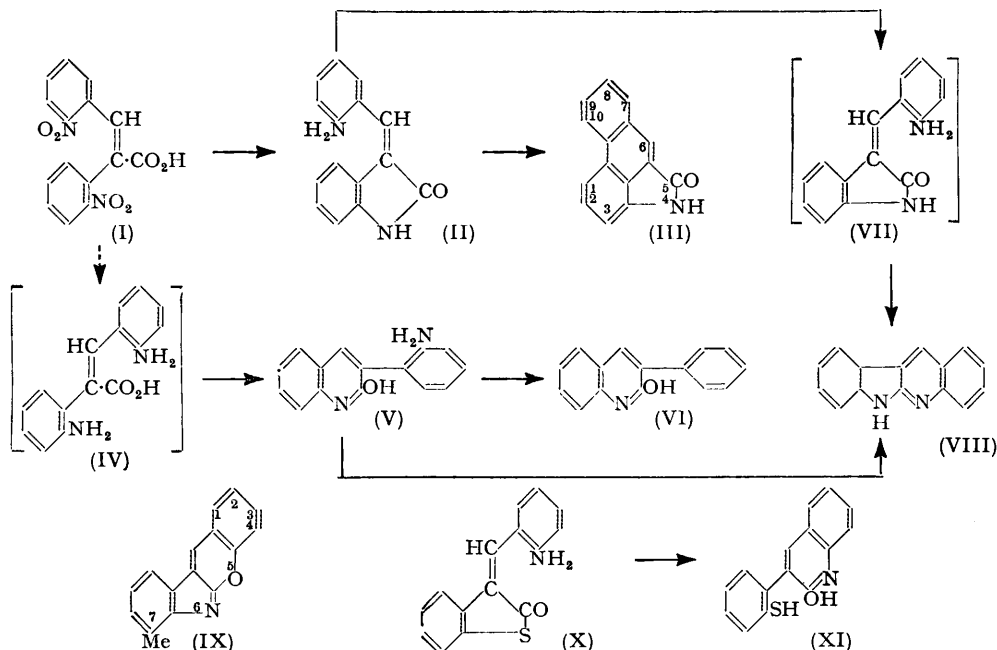
It thus became necessary to establish the structure of Pschorr's naphthoxindole and its amine precursor beyond doubt, and for this purpose it was prepared by the more straightforward route from oxindole by means of 3-*o*-nitrobenzylideneoxindole and 3-*o*-aminobenzylideneoxindole, a general method which was subsequently used for the preparation of further members of the series. The product obtained in this manner was isolated in the form of yellow prisms, m. p. 229°, whereas 3-phenylcarbostyryl, m. p. 228.5°, is colourless. A mixed melting point showed a marked depression to 180—185°.

The identity of Pschorr's naphthoxindole and 3-*o*-aminobenzylideneoxindole being established, the general method outlined above was then applied to the synthesis of 3-methyl-, 1-bromo-, 8 : 9-dimethoxy-, 8 : 9-methylenedioxy-, 8-chloro-, and 4-phenyl-naphth[3 : 2 : 1-*cd*]oxindole. These reactions include examples with a substituent in turn in each of the three ring systems present in the aminobenzylideneoxindole. In addition, an attempt to prepare 1 : 3-dibromonaphth[3 : 2 : 1-*cd*]oxindole led unexpectedly to 3-bromonaphth[3 : 2 : 1-*cd*]oxindole.

For the preparation of oxindoles used as starting compounds an improved method was developed which involved heating the chloroacetanilide in a molten mixture of aluminium

* Part VII, *J.*, 1953, 3. † The method of numbering used in this paper is based on the Ring Index.

chloride and sodium chloride. The reaction is complete within two minutes and gives more satisfactory results than that of Stollé (*J. pr. Chem.*, 1930, **123**, 1). Reduction of the nitrobenzylideneoxindoles was carried out with a solution of stannous chloride in glacial acetic acid containing hydrogen chloride under mild conditions in order to minimise geometric isomerisation. The products from the internuclear cyclisation reaction were worked up with the aid of chromatographic adsorption which revealed a number of by-products.



The decomposition of the diazonium sulphate prepared from 3-*o*-aminobenzylidene-7-methyloxindole gave, in addition to 3-methylnaphth[3:2:1-*cd*]oxindole, an isomeric compound considered to be 7-methylbenzopyrano[2:3-*b*]indolenine (IX) (cf. Täuber, *Ber.*, 1891, **24**, 197; Täuber and Halberstadt, *Ber.*, 1892, **25**, 2745; Cullinane, Davey, and Padfield, *J.*, 1934, 716), and believed to have arisen from partial *cis-trans*-isomerisation of the aminobenzylidenemethyloxindole, and its ultra-violet absorption shows a band at about 320 $m\mu$, which is absent in the naphthoxindoles. That such isomerisation occurs during the preparation of the amine salt prior to diazotisation is indicated by the fact that if higher temperatures were allowed to develop the yield of the benzopyranoindolenine was increased. In the decomposition with copper powder of the diazonium sulphate prepared from 3-*o*-aminobenzylidene-5:7-dibromo-oxindole one bromine atom was removed and the product proved to be 3-bromonaphth[3:2:1-*cd*]oxindole, together with 7-bromo-3-*o*-hydroxybenzylideneoxindole; a similar decomposition effected by the action of heat gave the latter phenol only. Decomposition of the diazonium salt prepared from 3-*o*-aminobenzylidene-5-bromo-oxindole gave 1-bromonaphth[3:2:1-*cd*]oxindole, which was different from that prepared from the dibromo-derivative which must therefore be 3-bromonaphth[3:2:1-*cd*]oxindole. It is assumed that the same bromine atom is eliminated during the formation of the phenol.

The decomposition of the diazonium sulphate prepared from 3-6'-aminoveratrylideneoxindole gave, in addition to 8:9-dimethoxynaphth[3:2:1-*cd*]oxindole, 3-veratrylideneoxindole, m. p. 161—162°, which probably has a *cis*-configuration. It is different from the 3-veratrylideneoxindole, m. p. 210—211°, prepared from oxindole and veratraldehyde, but was converted into it on recrystallisation from acetone.

In an attempt to extend this synthetic route to include the preparation of aza-

derivatives of naphth[3 : 2 : 1-*cd*]oxindole attention was directed to the possible use of isatin, in place of oxindole. It is known that isatin undergoes condensation reactions at the 3-position with compounds containing active methylene groups. In preliminary work it was shown that reaction between α -picoline and isatin in the presence of fused zinc chloride gave 3- α -picolinylideneoxindole. Similar reactions were carried out successfully with quinaldine, 3-nitroquinaldine, and 4-hydroxyquinaldine, the product obtained with quinaldine being identical with that obtained by condensation of quinoline-2-aldehyde with oxindole.

The availability of thio-oxindole by the method of Glauert and Mann (*J.*, 1952, 2127) suggested its use for the preparation of naphthothio-oxindoles. Condensation with *o*-nitrobenzaldehyde gave 3-*o*-nitrobenzylidene-thio-oxindole, but reduction of the latter with stannous chloride gave 3-*o*-mercaptophenylcarbostyryl (XI), which can arise from a *cis-trans*-isomerisation coupled with the opening of the five-membered ring followed by re-cyclisation to form the quinoline ring (X) \rightarrow (XI).

The data for the absorption spectra of three of the foregoing compounds are given in the accompanying table.

Naphth[3 : 2 : 1- <i>cd</i>]oxindole				3-Methylnaphth[3 : 2 : 1- <i>cd</i>]-oxindole				7-Methylbenzopyrano[2 : 3- <i>b</i>]-indolenine			
λ_{\max} . (m μ)	$10^{-3}\epsilon$	λ_{\max} . (m μ)	$10^{-3}\epsilon$	λ_{\max} . (m μ)	$10^{-3}\epsilon$	λ_{\max} . (m μ)	$10^{-3}\epsilon$	λ_{\max} . (m μ)	$10^{-3}\epsilon$	λ_{\max} . (m μ)	$10^{-3}\epsilon$
203	37.8	290	18.6	202	31.6	290	20.3	206	23.5	258	51.8
207	42.6	353	5.47	205	33.7	353	6.3	224	50.2	319	22.0
220	49.7	365	5.65	209	34.4	365	6.5				
257.5	40.6	368	5.75	223	37.9	368	6.55				
				260	37.6						

EXPERIMENTAL

Alumina used for chromatography was supplied by Peter Spence & Sons, Ltd., as Activated Alumina Type H, 100/200 Mesh.

Preparation of Oxindoles.—The improved general method employed is exemplified by the preparation of oxindole. ω -Chloroacetanilide (10 g.) was added to a fused mixture of anhydrous aluminium chloride (50 g.) and sodium chloride (10 g.) at 140° and the temperature was raised rapidly to 220°. Brisk effervescence with evolution of hydrogen chloride took place. The melt was kept at 220–230° for 2 min. and then allowed to cool. The product was decomposed with crushed ice and a little dilute hydrochloric acid. Oxindole separated in an almost colourless crystalline form. It was collected, washed with a small volume of cold water, and recrystallised from water (with charcoal). Oxindole (5 g.) separated in colourless needles, m. p. 126–127°. The optimum temperature for the reaction, which varies with different chloroacetanilides, is recognised by brisk effervescence with evolution of hydrogen chloride.

*Naphth[3 : 2 : 1-*cd*]oxindole.*—A solution of 3-*o*-aminobenzylideneoxindole (1.5 g.), prepared by the method of Borsche, Wagner-Roemmich, and Barthenheier (*loc. cit.*), in concentrated sulphuric acid (6 c.c.), was diluted with water (50 c.c.), and the resultant suspension was stirred and diazotised at 0° by slow addition of 5*N*-sodium nitrite (5 c.c.). After 1½ hours' stirring at 0° the mixture was diluted with water (150 c.c.) and filtered, and the residue washed with water. Urea (0.5 g.) was added to the combined filtrates, and freshly prepared copper powder (cf. Gattermann, *Ber.*, 1890, 23, 1219) (1.5 g.) was added to the solution stirred at room temperature. Nitrogen was evolved and stirring was continued for 48 hr. to complete the reaction. The mixture was extracted with chloroform and then with ether, and the combined extracts were dried (MgSO₄) and evaporated. The residual solid (1 g.) was passed in alcohol-ether (1 : 2 v/v) through a column of alumina (40 g.). Elution with the same solvent gave naphth[3 : 2 : 1-*cd*]oxindole (0.4 g.) in prisms, m. p. 229°, from alcohol (Found : C, 81.9; H, 4.1. Calc. for C₁₅H₉ON : C, 82.1; H, 4.1%). Further elution with alcohol gave a brown tar (0.6 g.). Pschorr and Popovici (*loc. cit.*) record m. p. 230° for this compound prepared from *o*-nitro- α -*o'*-nitrophenylcinnamic acid.

7-Methyloxindole.—7-Methyloxindole was prepared from ω -chloroacet-*o*-toluidide by the general method outlined above and also by the method of Stollé *et al.* (*J. pr. Chem.*, 1930, 128, 4), modified by the use of double the quantity of aluminium chloride, but repeated crystallisation from benzene and purification by adsorption on silica gel gave needles, m. p. 175–182° (Found : C, 73.5; H, 6.1; N, 9.55. Calc. for C₉H₉ON : C, 73.4; H, 6.2; N, 9.5%). The benzylidene derivative had m. p. 224–225° (Found : C, 81.3; H, 5.6. Calc. for C₁₆H₁₅ON : C, 81.7;

H, 5.5%). Stollé records m. p. 200° for 7-methyloxindole, and Wahl and Faivret (*Ann. Chim.*, 1926, 5, 349) m. p. 204° for 7-methyloxindole and m. p. 224° for the benzylidene derivative.

3-Methylnaphth[3 : 2 : 1-cd]oxindole.—A mixture of 7-methyloxindole (1.75 g.) and *o*-nitrobenzaldehyde (1.85 g.) was heated to 130° in an oil-bath and kept at this temperature until evolution of water vapour ceased. The cooled product was extracted with boiling glacial acetic acid and filtered. On cooling, 7-methyl-3-*o*-nitrobenzylideneoxindole (1.8 g.) separated, which crystallised from the same solvent (charcoal) in orange globules, m. p. 232° (Found : C, 68.0; H, 4.3. $C_{16}H_{12}O_3N_2$ requires C, 68.5; H, 4.7%). The nitro-compound (1 g.) was dissolved in the stannous chloride reagent (10 c.c.) (prepared from 9 g. of $SnCl_2 \cdot 2H_2O$ in 15 c.c. of glacial acetic acid, saturated with hydrogen chloride and made up to 20 c.c. with the same solvent; Thiele and Dimroth, *Annalen*, 1899, 305, 114) by warming and then set aside overnight. The stannic chloride complex was decomposed with concentrated aqueous sodium hydroxide, the temperature being kept below 40°. The yellow solid was collected, washed well with dilute aqueous sodium hydroxide and with water, and then dried. Recrystallisation from methanol gave 3-*o*-aminobenzylidene-7-methyloxindole (0.6 g.) in golden-yellow needles, m. p. 222—223° (Found : C, 76.5; H, 5.6. $C_{16}H_{14}ON_2$ requires C, 76.8; H, 5.6%). The same compound was also obtained but in lower yield by the condensation of *o*-aminobenzaldehyde with 7-methyloxindole in alcohol containing a few drops of piperidine. 3-*o*-Aminobenzylidene-7-methyloxindole (1.5 g.) was diazotised and the resulting diazonium salt was decomposed with copper powder as described in the previous example. The product was isolated as before, but the alumina column was first eluted with benzene. Evaporation of the benzene solution left a white crystalline residue (0.15 g.), which on recrystallisation from light petroleum (b. p. 40—60°) gave 7-methylbenzopyrano[2 : 3-b]indolenine in rosettes of needles, m. p. 143—144° (Found : C, 82.6; H, 4.5; N, 6.15; *M*, 221. $C_{16}H_{11}ON$ requires C, 82.4; H, 4.85; N, 6.0%; *M*, 233). Subsequent elution with alcohol-ether (1 : 2) gave 3-methylnaphth[3 : 2 : 1-cd]oxindole (0.4 g.), which crystallised from benzene in yellow needles, m. p. 275—276° (Found : C, 82.7; H, 4.7. $C_{16}H_{11}ON$ requires C, 82.4; H, 4.85%). When precautions were not taken to minimise the rise in temperature during the preparation of the solution of the amine salt for diazotisation, the benzopyranindolenine became the main product.

Derivatives of 5 : 7-Dibromo-oxindole.—This compound, m. p. 260°, was prepared by the bromination of oxindole as described by Sumpter, Miller, and Hendrick (*J. Amer. Chem. Soc.*, 1945, 67, 1657). When boiled under reflux with two drops of piperidine, 5 : 7-dibromo-oxindole (1 g.) and benzaldehyde (1 c.c.) gave the 3-benzylidene derivative (0.8 g.) in yellow needles, m. p. 223—225° (from alcohol) (Found : C, 47.7; H, 2.6. $C_{15}H_9ONBr_2$ requires C, 47.5; H, 2.4%). In the same manner 5 : 7-dibromo-3-*o*-nitrobenzylideneoxindole (1.3 g.) was obtained from the dibromo-oxindole (1 g.) and *o*-nitrobenzaldehyde (0.75 g.) and crystallised from glacial acetic acid in orange needles, m. p. 257.5° (Found : C, 42.4; H, 1.9. $C_{15}H_8O_3N_2Br_2$ requires C, 42.45; H, 1.9%). Reduction of the nitro-compound (1 g.) with the stannous chloride reagent (10 c.c.) as described above gave 3-*o*-aminobenzylidene-5 : 7-dibromo-oxindole (0.91 g.), which crystallised from glacial acetic acid in needles, m. p. 251—252° (Found : Br, 40.5. $C_{15}H_{10}ON_2Br_2$ requires Br, 40.6%).

Decomposition of the Diazonium Sulphate prepared from 3-*o*-Aminobenzylidene-5 : 7-dibromo-oxindole.—(i) A cooled solution of the oxindole (1 g.) in concentrated sulphuric acid (6 c.c.) was diluted with water (25 c.c.) and diazotised at 0—5° with a solution of sodium nitrite (1.5 g.) in water (5 c.c.). After 1 hr. the mixture was diluted with water (150 c.c.) and filtered, the residue being washed with water. After the addition of urea (1 g.) to the combined filtrates, the red solution was boiled under reflux for 1 hr. The yellow precipitate (0.69 g.) separated from nitrobenzene and gave 7-bromo-3-*o*-hydroxybenzylideneoxindole, m. p. 248—250° (Found : C, 57.5; H, 3.0; Br, 25.6. $C_{15}H_{10}O_2NBr$ requires C, 57.0; H, 3.2; Br, 25.3%).

(ii) The diazonium sulphate was prepared from the base (1.5 g.) as described under (i). After the addition of urea to the filtered diazonium solution, copper powder (1.6 g.) was slowly added to the vigorously stirred solution at room temperature. After 44 hr. evolution of nitrogen had ceased and the precipitated solid was extracted with chloroform (3 × 250 c.c.) and then with ether (2 × 150 c.c.). The combined extracts were dried ($MgSO_4$) and evaporated to 50 c.c., which solution was passed down a column of alumina (70 g.; $6\frac{1}{2}'' \times 1''$). Elution with benzene gave an oil (0.02 g.) and then with alcohol gave a yellow solid, which was reabsorbed on alumina and eluted with benzene. The resulting yellow solid (0.11 g.) gave 7-bromo-3-*o*-hydroxybenzylideneoxindole, m. p. 248—250°, as in method (i), but subsequent elution with ether gave 3-bromonaphth[3 : 2 : 1-cd]oxindole (0.2 g.), m. p. 185—186°, from ether (Found : Br, 27.3. $C_{15}H_8ONBr$ requires Br, 26.85%).

Derivatives of 5-Bromo-oxindole.—5-Bromo-oxindole (0.5 g.), prepared by the method of Sumpter, Miller, and Hendrick (*loc. cit.*), and benzaldehyde (0.25 c.c.) heated at 135° gave 3-benzylidene-5-bromo-oxindole (0.4 g.) in yellow needles, m. p. 197—199°, from ethanol (Found : Br, 26.2. $C_{15}H_{10}ONBr$ requires Br, 26.6%). In similar manner, 5-bromo-oxindole (1 g.) and *o*-nitrobenzaldehyde (0.75 g.) gave 5-bromo-3-*o*-nitrobenzylideneoxindole (1.45 g.) in red-orange clusters, m. p. 228—230°, from glacial acetic acid (Found : Br, 22.4. $C_{15}H_9O_3N_2Br$ requires Br, 23.2%). Reduction of the nitro-compound (1 g.) with the stannous chloride reagent (10 c.c.), as described above, gave 3-*o*-aminobenzylidene-5-bromo-oxindole (0.55 g.) in yellow crystals from methanol, which partially melted at 205° and finally at 310—320°, probably owing to the formation of a high-melting quinindoline derivative (Found : Br, 25.0. $C_{15}H_{11}ON_2Br$ requires Br, 25.4%).

1-Bromonaphth[3 : 2 : 1-cd]oxindole.—A fine suspension of 3-*o*-aminobenzylidene-5-bromo-oxindole (1.5 g.) in a mixture of concentrated hydrochloric acid (15 c.c.) and water (30 c.c.) was diazotised at 0—5° with sodium nitrite (2 g.) in water (10 c.c.). After 1 hr. water (150 c.c.) was added, and the solution filtered, the residue being washed with water. Urea (1 g.) was added to the combined filtrates, followed by copper powder (1.5 g.). Nitrogen was immediately evolved, and after being kept overnight the suspension was extracted with chloroform (2 × 250 c.c.) and then with ether (2 × 150 c.c.). The combined dried ($MgSO_4$) extracts were concentrated to about 50 c.c. and passed through an alumina column (70 g.). Elution with ether gave first an orange-coloured oil (0.16 g.) and then 1-bromonaphth[3 : 2 : 1-cd]oxindole (0.4 g.), which crystallised from benzene in pale yellow needles, m. p. 278—279° (Found : C, 60.7; H, 2.9. $C_{15}H_8ONBr$ requires C, 60.4; H, 2.7%).

Derivatives of 3-Veratrylideneoxindole.—Oxindole (1.3 g.) and veratraldehyde (1.66 g.) heated at 125° gave in almost quantitative yield 3-*veratrylideneoxindole*, which separated from acetone in golden-yellow needles, m. p. 212.5—213.5° (Found : C, 72.6; H, 5.5; N, 5.05. $C_{17}H_{15}O_3N$ requires C, 72.6; H, 5.3; N, 5.0%). In similar manner, oxindole (1.47 g.) and 6-nitroveratraldehyde (2.11 g.), heated at 130—140° with the addition of one drop of piperidine, gave 3-6'-nitroveratrylideneoxindole (3.0 g.), which separated from glacial acetic acid in orange-red needles, which sintered at 222° and finally melted at 235—236° (Found : C, 62.15; H, 4.6; N, 8.05. $C_{17}H_{14}O_5N_2$ requires C, 62.6; H, 4.3; N, 8.6%). Borsche, Wagner-Roemmich, and Barthenheier (*Annalen*, 1942, 550, 172) reported m. p. 261° for this compound. Reduction of the nitro-compound (0.35 g.) with the stannous chloride reagent (5 c.c.), as described in the previous examples, gave 3-6'-aminoveratrylideneoxindole (0.3 g.), which separated from methanol in orange-red plates, m. p. 213—214° on rapid heating (Found : C, 68.5; H, 5.6; N, 8.9. $C_{17}H_{14}O_3N_2$ requires C, 68.9; H, 5.4; N, 9.5%). When slowly heated the amine partially melted at 214°, resolidified, and finally melted at 261—264°. Borsche, Wagner-Roemmich, and Barthenheier (*loc. cit.*) were unable to purify this compound and record m. p. 110—115° for the crude product.

8 : 9-Dimethoxynaphth[3 : 2 : 1-cd]oxindole.—A suspension of 3-6'-aminoveratrylideneoxindole (1.5 g.) in a mixture of concentrated sulphuric acid (8.25 c.c.) and water (25 c.c.) was diazotised at 0—5° with sodium nitrite (2 g.) in water (5 c.c.). After 1 hr. at 0° the suspension was diluted with water (150 c.c.) and filtered, and the residue (0.4 g.) washed with water. Urea (1 g.) was added to the filtrate, which was then stirred for 24 hr. at room temperature after the addition of copper powder (1.5 g.), a further quantity (1 g.) being added after 15 hr. The product was extracted with chloroform and ether, and the extracts were concentrated and passed through alumina as in previous examples. Benzene eluted a yellow oil (0.05 g.), after which benzene-ether (1 : 2 by vol.) eluted *cis*-3-*veratrylideneoxindole* (0.14 g.), m. p. 161—162°, in orange-yellow crystals from light petroleum (b. p. 40—60°) (Found : C, 72.3; H, 4.9; N, 4.5. $C_{17}H_{15}O_3N$ requires C, 72.6; H, 5.3; N, 5.0%). Recrystallisation from acetone gave *trans*-3-*veratrylideneoxindole* in yellow plates, m. p. 210—211°, undepressed on admixture with the product from the action of veratraldehyde on oxindole. Further elution of the column with alcohol gave 8 : 9-dimethoxynaphth[3 : 2 : 1-cd]oxindole (0.6 g.), which separated from methanol in pale yellow micro-crystals which melted partially at 278° and finally at 296—297° (Found : C, 72.7; H, 4.7. $C_{17}H_{13}O_5N$ requires C, 73.1; H, 4.7%).

Derivatives of 3-Piperonylideneoxindole.—Oxindole (1 g.) and piperonaldehyde (1.05 g.) at 125—130° gave in quantitative yield 3-*piperonylideneoxindole*, which separated from alcohol in yellow needles, m. p. 210—211° (Found : C, 72.2; H, 3.8. $C_{16}H_{11}O_3N$ requires C, 72.5; H, 4.15%). In similar manner oxindole (0.67 g.) and 6-nitropiperonaldehyde at 125—130°, with a drop of piperidine, gave 3-6'-nitropiperonylideneoxindole (1.23 g.) in orange needles from glacial acetic acid which darkened at 245° and partially melted at 254° (Found : C, 61.85; H,

3-6. $C_{16}H_{10}O_5N_2$ requires C, 61.9; H, 3.2%). Reduction of the nitro-compound (1 g.) with the stannous chloride reagent (10 c.c.) (p. 1700) gave 3-6'-aminopiperonylideneoxindole (0.9 g.) in orange-red needles from alcohol, which melted partially at 226°, as recorded by Armit and Robinson (*J.*, 1925, 127, 1612), who obtained it from oxindole and 6-aminopiperonaldehyde.

8: 9-Methylenedioxyaphth[3:2:1-cd]oxindole.—A suspension of 3-6'-aminopiperonylideneoxindole (1.5 g.) in a mixture of concentrated hydrochloric acid (12 c.c.) and water (30 c.c.) was diazotised at 0° with sodium nitrite (1.75 g.) in water (10 c.c.). The resulting diazonium chloride, after the addition of urea (1 g.), was decomposed with copper powder, and the product worked up as in the preceding examples. Elution with benzene gave a yellow oil (0.03 g.), after which elution with ether gave 8:9-methylenedioxyaphth[3:2:1-cd]oxindole (0.67 g.), which separated from ethanol in yellow plates which darkened at 280° and melted at 298—300° (decomp.) (Found: C, 72.4; H, 3.4; N, 5.4. $C_{16}H_8O_3N$ requires C, 73.0; H, 3.4; N, 5.3%).

Derivatives of 3-m-Chlorobenzylideneoxindole.—Oxindole (0.5 g.) and *m*-chlorobenzaldehyde (0.5 g.) at 130° gave 3-*m*-chlorobenzylideneoxindole (0.3 g.) after purification by adsorption on alumina. It separated from benzene-light petroleum (b. p. 40—60°) in yellow needles, m. p. 164° (Found: C, 70.8; H, 4.1. $C_{16}H_{10}ONCl$ requires C, 70.5; H, 3.9%). In similar manner oxindole (0.67 g.) and 5-chloro-2-nitrobenzaldehyde (0.92 g.), prepared by the method of Alford and Schofield (*J.*, 1952, 2105), at 110—115°, gave 3-(5-chloro-2-nitrobenzylidene)oxindole (1.5 g.) in orange needles from glacial acetic acid, m. p. 247—248° (Found: Cl, 12.0. $C_{16}H_8O_3N_2Cl$ requires Cl, 11.8%). Reduction of the nitro-compound (1 g.) with the stannous chloride reagent (12 c.c.) (see above) gave 3-(2-amino-5-chlorobenzylidene)oxindole (0.85 g.), which separated from methanol in yellow needles, m. p. 218—219° after sintering at 211° (Found: C, 66.3; H, 4.1. $C_{16}H_{11}ON_2Cl$ requires C, 66.55; H, 4.1%).

8-Chloronaphth[3:2:1-cd]oxindole.—A suspension of 3-(2-amino-5-chlorobenzylidene)oxindole (1.5 g.) in concentrated hydrochloric acid (13 c.c.) and water (30 c.c.) was diazotised at 0—5° with sodium nitrite (1.7 g.) in water (10 c.c.), the diazonium solution was decomposed with copper powder (1.5 g.), and the product worked up as in the preceding examples. Elution with ether gave 8-chloronaphth[3:2:1-cd]oxindole (1.2 g.), which separated from alcohol in pale yellow needles which darkened at 285—286° and finally melted at 305—306° (decomp.) (Found: C, 70.5; H, 3.3; Cl, 13.7. $C_{15}H_8ONCl$ requires C, 71.0; H, 3.2; Cl, 14.0%).

Derivatives of *N*-Phenyloxindole.—*N*-Phenyloxindole (2 g.; m. p. 121.5°), prepared by the general method above, and *o*-nitrobenzaldehyde (1.5 g.) with one drop of piperidine at 125—130° gave 3-*o*-nitrobenzylidene-*N*-phenyloxindole (2.1 g.) in orange needles, m. p. 215—216°, from glacial acetic acid (Found: C, 73.3; H, 3.8. $C_{21}H_{14}O_3N_2$ requires C, 73.7; H, 4.1%). Reduction of the nitro-compound (4 g.) by the method described in previous examples gave 3-*o*-aminobenzylidene-*N*-phenyloxindole, m. p. 125—130°, in almost quantitative yield, probably as a mixture of geometrical isomerides. Recrystallisation from methanol gave the *cis*-isomeride (2.1 g.) in hard needles, m. p. 161° (Found: C, 81.0; H, 5.2; N, 8.7. $C_{21}H_{16}ON_2$ requires C, 80.7; H, 5.1; N, 9.0%).

4-Phenylnaphth[3:2:1-cd]oxindole.—Diazotisation of 3-*o*-aminobenzylidene-*N*-phenyloxindole (2.1 g.) in dilute hydrochloric acid and subsequent decomposition with copper powder gave a yellow solid which was extracted with chloroform (2 × 150 c.c.); the extract was dried ($MgSO_4$), diluted with benzene (30 c.c.), and concentrated to about 50 c.c. Chromatographic adsorption on alumina (70 g.) and elution with benzene gave 4-phenylnaphth[3:2:1-cd]oxindole (0.56 g.) in pale yellow needles, m. p. 178—179°, from alcohol (Found: C, 85.35; H, 4.5. $C_{21}H_{13}ON$ requires C, 85.4; H, 4.4%).

3- α -Picolinylideneoxindole.—A mixture of isatin (7 g.), α -picoline (10 c.c.), and fused zinc chloride (8 g.) was heated under reflux for 1 hr. and then poured into ice-water. The dark product was dissolved in glacial acetic acid, the solution filtered, and the product precipitated with ammonia, the whole operation being repeated a second time. After being washed well with water and dried *in vacuo*, 3- α -picolinylideneoxindole (6 g.) was obtained as a brick-red amorphous powder, m. p. 154—155° after sintering at 110°, which was only sparingly soluble in most organic solvents and could not be recrystallised (Found: N, 12.5. $C_{14}H_{10}ON_2$ requires N, 12.6%).

3-Quinaldinylideneoxindole.—(a) Quinaldine (7.15 g.), isatin (7.35 g.), and fused zinc chloride (8 g.) were heated at 170° (air-condenser). When the vigorous reaction had subsided the dark red mass was extracted first with boiling water and then with boiling alcohol. Recrystallisation of the residue from benzene gave 3-quinaldinylideneoxindole (4 g.) in yellow needles, m. p. 229—230° (Found: C, 79.3; H, 4.4. $C_{18}H_{12}ON_2$ requires C, 79.4; H, 4.4%). (b) A solution of quinoline-2-aldehyde (0.78 g.) (Kaplan, *J. Amer. Chem. Soc.*, 1941, 63, 2655) and oxindole

(0.67 g.) in alcohol (5 c.c.) containing one drop of piperidine was boiled under reflux for 30 min. The orange-yellow product which separated was collected, washed with a little cold alcohol, and recrystallised from benzene. 3-Quinaldinylideneoxindole (1.1 g.) was obtained in yellow needles, m. p. 225—266°, undepressed on admixture with the product prepared by method (a) above.

3-4'-Hydroxyquinaldinylideneoxindole.—A mixture of isatin (7.4 g.), 4-hydroxyquinaldine (7.95 g.), fused sodium acetate (10 g.), glacial acetic acid (50 c.c.), acetic anhydride (2 c.c.), and fused zinc chloride (8 g.) was boiled under reflux for 5 hr. The dark solution was poured into water, and the precipitate collected. A further precipitate was obtained on addition of ammonia to the filtrate. The combined solid product (2 g.) proved to be very sparingly soluble in most organic solvents, but recrystallisation from a large volume of methyl alcohol gave *3-4'-hydroxyquinaldinylideneoxindole* as a fluffy yellow solid, m. p. above 300° (Found: C, 74.6; H, 4.2. $C_{18}H_{12}O_2N_2$ requires C, 75.0; H, 4.2%).

3-Nitroquinaldine.—A solution of toluene-*p*-sulphonhydrazide (3.7 g.) (Albert and Royer, *J.*, 1949, 1150) in warm chloroform (100 c.c.) was added to a solution of 4-chloro-3-nitroquinaldine (4.4 g.) (Adams and Hey, *J.*, 1951, 1526) in chloroform (50 c.c.). After this had stood for 6 days, dry hydrogen chloride was passed into the suspension for 10 sec., and it was then left overnight. The *3-nitro-4-toluene-p-sulphonhydrazinoquinaldine hydrochloride* which separated in almost quantitative yield was collected and washed with a small volume of cold chloroform. A sample recrystallised from 95% ethyl alcohol by partial evaporation in a current of air to avoid decomposition was obtained in yellow translucent crystals, m. p. 176—178° (Found: C, 49.6; H, 5.3. $C_{17}H_{16}O_4N_4S.HCl$ requires C, 49.9; H, 5.2%). The hydrochloride (20 g.) was added slowly to sodium carbonate (40 g., anhyd.) in water (400 c.c.) at 65°. The mixture, which became purple as the solid decomposed with evolution of nitrogen, was heated under reflux on a boiling-water bath for 15 min. and then boiled for 100 min. Steam-distillation of the resulting mixture gave *3-nitroquinaldine* (1.1 g.) in colourless needles, m. p. 110—111° (Found: C, 63.8; H, 4.6. $C_{10}H_8O_2N_2$ requires C, 63.8; H, 4.25%).

3-3'-Nitroquinaldinylideneoxindole.—*3-Nitroquinaldine* (1 g.), isatin (0.8 g.), and fused sodium acetate (1 g.) in acetic anhydride (0.2 c.c.) and glacial acetic acid (6 c.c.) were boiled under reflux for 5 hr. When cold, *3-3'-nitroquinaldinylideneoxindole* (0.5 g.) separated; it crystallised from glacial acetic acid in brick-red needles, m. p. 235—236° (Found: C, 68.1; H, 3.5. $C_{18}H_{11}O_3N_3$ requires C, 68.1; H, 3.5%).

3-o-Nitrobenzylidenethio-oxindole.—(a) A mixture of thio-oxindole (0.37 g.), prepared as described by Glauert and Mann (*loc. cit.*), and *o*-nitrobenzaldehyde (0.37 g.) was heated to 130° with one drop of piperidine. After 20 min. the oil was triturated with alcohol, and the solid product was collected, washed with cold alcohol and ether, and recrystallised from glacial acetic acid. *3-o-Nitrobenzylidenethio-oxindole* (0.56 g.) was obtained in mustard-yellow needles, m. p. 147° (Found: C, 63.2; H, 2.8; N, 4.7. $C_{15}H_9O_3NS$ requires C, 63.4; H, 3.2; N, 4.95%). (b) The same product was obtained when a solution of thio-oxindole (1 g.) and *o*-nitrobenzaldehyde (1 g.) in ethyl alcohol (5 c.c.) was boiled under reflux for 10 min. with two drops of piperidine. The product (1.6 g.) separated in a pure crystalline form.

Reduction of 3-o-Nitrobenzylidenethio-oxindole.—Reduction of the nitro-compound (1 g.) with the stannous chloride reagent (10 c.c.), as described above for the nitrobenzylidene-oxindoles gave, on decomposition of the stannichloride complex, *3-o-mercaptophenylcarbostyryl* (0.7 g.), which separated from ethyl alcohol in needles, m. p. 200—201° (Found: C, 70.6; H, 4.5; N, 5.9. $C_{15}H_{13}ONS$ requires C, 71.1; H, 4.35; N, 5.5%). The same product (1.22 g.; m. p. 200—201°) was obtained on heating under reflux for 45 min. thio-oxindole (1.5 g.) and *o*-aminobenzaldehyde (1.2 g.) in ethyl alcohol (7 c.c.) containing two drops of piperidine. Refluxing of an alcoholic solution of 2 : 4-dinitrochlorobenzene and the thiol in alcoholic sodium hydroxide gave the 2 : 4-dinitrophenylthio-derivative, which crystallised from dioxan in greenish-yellow needles, m. p. 227—228° (Found: C, 59.8; H, 3.3. $C_{21}H_{13}O_5N_3S$ requires C, 60.1; H, 3.1%).

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