989. *Polycyclic Cinnoline Derivatives. Part IX.*[1] *The Bromination of Benzo[c]cinnoline and the Preparation and Ultraviolet Absorption Spectra of Reference Compounds.*

By J. F. Corbett and P. F. Holt.

The electrophilic bromination of benzo[*c*]cinnoline gives 1-bromobenzo[*c*]-cinnoline and the 1,4- or 1,7-dibromo-compound. The preparation of reference compounds involved the use of three routes to benzo[*c*]cinnoline derivatives; three of the four possible bromobenzo[*c*]cinnolines are described, together with some polybromo-derivatives. Lithium aluminium hydride removes bromine atoms from the 1- and the 4-position of benzo[*c*]cinnoline. Bromine atoms in the 4-position prevent *N*-oxidation in the 5(*peri*)-position.

The ultraviolet absorption spectra of the bromobenzo[*c*]cinnolines are recorded. The spectral shifts resulting from the introduction of bromine atoms into benzo[*c*]cinnoline are additive and depend on the position of substitution. Spectra thus provide support for the structure assigned, on chemical evidence, to the dibromo-compound.

Dewar and Maitlis [2] calculated the order of reactivity of the four positions of benzo[*c*]-cinnoline (I) towards electrophilic substitution, to be $1 > 3 > 4 > 2$. Smith and Ruby [3] showed that nitration of benzo[*c*]cinnoline gave the 1-isomer as the major product and

[1] Part VIII, Corbett and Holt, *J.*, 1961, 3695.
[2] Dewar and Maitlis, *J.*, 1957, 2521.
[3] Smith and Ruby, *J. Amer. Chem. Soc.*, 1954, **76**, 5807.

suggested that the minor product was the 3-isomer. We find that the minor isomer is in fact 4-nitrobenzo[*c*]cinnoline.[4] The bromination of benzo[*c*]cinnoline has therefore been studied in order to compare the results with those of nitration.*

There appears to be no report in the literature of the successful bromination of benzo[*c*]cinnoline (I). Ruby used molecular bromine in a variety of solvents, but obtained no bromobenzo[*c*]cinnoline.[5] We confirmed this, an orange-red solid, $C_{12}H_8Br_{1\cdot5-1\cdot7}N_2$, being precipitated when bromine is added to a solution of benzo[*c*]cinnoline in carbon tetrachloride or boiling acetic acid. The solid is stable at room temperature, but resinifies, with the evolution of bromine, at temperatures above 75°. With acetone it gives bromoacetone and benzo[*c*]cinnoline hydrobromide hydrate, and it liberates iodine from aqueous potassium iodide. Iodine in carbon tetrachloride similarly gives a substance $C_{12}H_8I_{1\cdot7}N_2$.

Cheorvas [6] obtained from cinnoline a bromo-compound with similar properties to ours, and Stoermer and Fincke [7] obtained another from 4-phenylcinnoline with bromine in carbon tetrachloride. These products are probably charge-transfer complexes of the type described by Slough and Ubbelohde.[8]

de la Mare, Kiamud-din, and Ridd brominated quinoline in the *Bz*-ring, using bromine in sulphuric acid in the presence of silver sulphate,[9] the active agent being $BrH_2SO_4^+$ or $BrSO_3^+$,[9] Br^+, or $BrOH_2^+$.[10] Bromination of benzo[*c*]cinnoline by this method gave 27% of a monobromo- and 4% of a dibromo-derivative.

There were no reference compounds with which to compare these products. The establishment of their structure by degradation was not attempted, since the reduction of benzo[*c*]cinnoline normally stops at the *NN'*-dihydro-derivative.[11] Scission of the N–N bond has been achieved by catalytic reduction at high pressure,[12] but under such conditions it seemed likely that the bromine atoms would also be reduced. The identity of the monobromo-derivative was established by synthesising three of the four possible bromobenzo[*c*]cinnolines; 1-bromobenzo[*c*]cinnoline was identical with the reaction product.

Determination of the structure of the dibromo-compound by synthesis would have been tedious since there are fourteen isomers and the ten unsymmetrical compounds would have been particularly difficult to prepare. Evidence establishing its structure as 1,7(or 4)-dibromobenzo[*c*]cinnoline was obtained by synthesis of some reference compounds, which eliminated certain isomers, from a consideration of steric hindrance to *N*-oxidation, from a study of the debromination of bromobenzo[*c*]cinnolines by lithium aluminium hydride, and from ultraviolet absorption spectra.

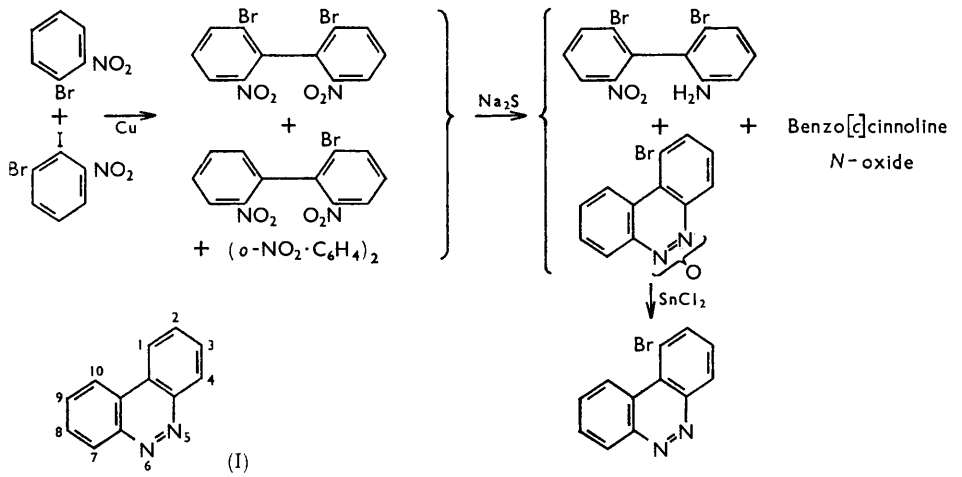
Reduction of the corresponding dinitrobiaryl appeared to be the only route to 1-bromobenzo[*c*]cinnoline. 2-Bromo-6,2'-dinitrobiphenyl can only be formed by a mixed Ullmann reaction from *o*-bromonitrobenzene but the necessary 3-bromo-2-halogenonitrobenzenes are difficult to prepare.[13] A route to 1-bromo-3-methylbenzo[*c*]cinnoline was therefore first worked out starting from the more readily available 3-bromo-4-halogeno-5-nitrotoluenes. 3,4-Dibromo-5-nitrotoluene gave a biphenylene derivative,[14] but the iodo-compound gave mainly 2,2'-dibromo-4,4'-dimethyl-6,6'-dinitrobiphenyl. This compound was

* The failure of molecular-orbital theory to predict the correct orientation for both the nitration and bromination of benzo[*c*]cinnoline will be discussed in a forthcoming paper on the nitration.

[4] Booker, Corbett, and Holt, unpublished work.
[5] Ruby, Ph.D. Thesis, University of Iowa, 1953.
[6] Cheorvas, Thesis, University of California, 1948.
[7] Stöermer and Fincke, *Ber.*, 1909, **42**, 3115.
[8] Slough and Ubbelohde, *J.*, 1957, 918.
[9] de la Mare, Kiamud-din, and Ridd, *J.*, 1960, 561.
[10] Derbyshire and Waters, *J.*, 1950, 572.
[11] Tauber, *Ber.*, 1891, **24**, 197; Wittig and Stichnoth, *Ber.*, 1935, **68***B*, 928; Hata, Tatematsu, and Kubota, *Bull. Chem. Soc. Japan*, 1935, **10**, 425; Kuhn and Erlenmeyer, *Helv. Chim. Acta*, 1955, **38**, 531; Duval, *Bull. Soc. chim. France*, 1910, **7**, 485; Bohlmann, *Chem. Ber.*, 1952, **85**, 390.
[12] Moore and Furst, *J. Amer. Chem. Soc.*, 1957, **79**, 5492; *J. Org. Chem.*, 1958, **23**, 1504.
[13] Körner and Contradi, *Atti R. Acad. Lincei*, 1908, [5], **17**, I, 466.
[14] Corbett and Holt, *J.*, 1961, 4761.

debrominated by lithium aluminium hydride, giving 3,8-dimethylbenzo[*c*]cinnoline, but with sodium sulphide it gave 6-amino-2,2′-dibromo-4,4′-dimethyl-6′-nitrobiphenyl. Although the latter product did not cyclise when refluxed with methanolic sodium hydroxide, cyclisation evidently being hindered by the bulky bromine atoms, a single bromine atom was considered unlikely to inhibit cyclisation.

From these experiments the indicated route to 1-bromobenzo[*c*]cinnoline *N*-oxide was a mixed Ullmann reaction with *o*-bromonitrobenzene and 1-bromo-2-iodo-3-nitrobenzene and reduction of the resulting 2-bromo-6,2′-dinitrobiphenyl with sodium sulphide. The mixed reduction products, rather than the dinitrobiaryls themselves, were separated; the amino-compound was removed by extraction with acid and the sparingly soluble bromobenzo[*c*]cinnoline *N*-oxide was separated from benzo[*c*]cinnoline *N*-oxide by crystallisation from ethanol. The scheme was satisfactory for the preparation of both 1-bromo-3-methylbenzo[*c*]cinnoline *N*-oxide and 1-bromobenzo[*c*]cinnoline *N*-oxide. Reduction of 1-bromo-3-methylbenzo[*c*]cinnoline *N*-oxide with lithium aluminium hydride gave 3-methylbenzo[*c*]cinnoline, but with stannous chloride the bromine was retained. 1-Bromobenzo[*c*]cinnoline *N*-oxide with stannous chloride gave 1-bromobenzo[*c*]cinnoline.



(I)

2-Bromobenzo[*c*]cinnoline 6-oxide was prepared by cyclising 2-amino-5-bromo-2′-nitrobiphenyl. 2,2′-Dinitrobiphenyl was reduced to 2-amino-2′-nitrobiphenyl, the acetyl derivative of which was brominated to give 2-acetamido-5-bromo-2′-nitrobiphenyl. The identity of the latter was proved by its reductive acetylation and subsequent bromination to 2,2′-bisacetamido-5,5′-dibromobiphenyl, previously prepared by Le Fèvre.[15] The acetyl derivative was hydrolysed to the amine which in refluxing methanolic sodium hydroxide gave an almost quantitative yield of 2-bromobenzo[*c*]cinnoline *N*-oxide. This gave 2-bromobenzo[*c*]cinnoline with lithium aluminium hydride.

Oxidation of 2-bromobenzo[*c*]cinnoline with hydrogen peroxide in acetic acid gave the 5- and the 6-oxides, separable by crystallisation.

3-Bromobenzo[*c*]cinnoline was isolated from the mixture obtained by reducing with lithium aluminium hydride the products of a mixed Ullmann reaction between *o*-bromonitrobenzene and 2,5-dibromonitrobenzene. Benzo[*c*]cinnoline was removed with acid; fractional crystallisation of the residue gave 3-bromobenzo[*c*]cinnoline and 3,8-dibromobenzo[*c*]cinnoline. The last compound was also obtained by reducing 4,4′-dibromo-2,2′-dinitrobiphenyl from 2,5-dibromonitrobenzene with lithium aluminium hydride.

Attempts to prepare 4-bromobenzo[*c*]cinnoline from 4-aminobenzo[*c*]cinnoline [4] by a Sandmeyer reaction were unsuccessful.

[15] Le Fèvre, *J.*, 1929, 736.

2,4-Dibromobenzo[*c*]cinnoline was obtained by a method similar to that used for the preparation of the 2-bromo-compound. Bromination of 2-amino-2-nitrobiphenyl gave a dibromo-derivative which on reduction and subsequent bromination gave 3,5,3′,5′-tetrabromo-2,2′-diaminobiphenyl, identical with a specimen formed by the bromination of 2,2′-diaminobiphenyl.[16] The dibromo-compound, which was also obtained by the bromination of 2-amino-5-bromo-2′-nitrobiphenyl, must therefore be 2-amino-3,5-dibromo-2′-nitrobiphenyl. The dibromo-compound, when refluxed with methanolic sodium hydroxide, gave 2,4-dibromobenzo[*c*]cinnoline 6-oxide and this was reduced by stannous chloride to 2,4-dibromobenzo[*c*]cinnoline.

Bromination of 2,2′-diamino-5,5′-dimethylbiphenyl gave its 3,3′-dibromo-derivative which, on oxidation with hydrogen peroxide in acetic acid, gave a quantitative yield of 4,7-dibromo-2,9-dimethylbenzo[*c*]cinnoline.

Structure of the Dibromo-compound obtained by Bromination of Benzo[c]*cinnoline.*—Lithium aluminium hydride removed both bromine atoms from the dibromobenzo[*c*]-cinnoline. To determine from which positions bromine atoms are likely to be abstracted, a number of bromobenzo[*c*]cinnolines were treated with lithium aluminium hydride. The results, given in Table 1, show that bromine atoms in the 1- and the 4-position are always eliminated while those in the 2- and the 3-position are retained and suggest that the dibromo-compound is the 1,10-, 1,4-, 1,7-, or 4,7-isomer. Substitution of 1-bromobenzo-[*c*]cinnoline by a second bromine atom, in the 10-position can, however, be ruled out on the grounds of steric hindrance. Supporting this supposition, the absorption spectrum does not exhibit the loss of fine structure or the " steric bathochromic shift " which is characteristic of 4,5-disubstituted phenanthrenes[17] and of 1,10-disubstituted benzo[*c*]-cinnolines.[18]

TABLE 1.

Debromination of benzo[*c*]cinnolines by lithium aluminium hydride.

Starting benzo[*c*]cinnoline	Benzo[*c*]cinnoline produced
1-Bromo-	Unsubst.
1-Bromo-3-methyl-	3-Methyl-
2,4-Dibromo-	2-Bromo-
2,4,7,9-Tetrabromo-	2,9-Dibromo-
4,7-Dibromo-2,9-dimethyl-	2,9-Dimethyl-
3,8-Dibromo-	(Unchanged)

Oxidation of the dibromo-compound with hydrogen peroxide in acetic acid gave an *N*-oxide. Similar treatment of 1-, 2-, and 3-bromobenzo[*c*]cinnoline resulted in the *N*-oxides, probably mixtures of the 5- and 6-oxides, although both isomers were only isolated in the case of 2-bromobenzo[*c*]cinnoline. Similarly 2,9- and 3,8-dibromobenzo-[*c*]cinnoline gave their *N*-oxides, and 2,4-dibromobenzo[*c*]cinnoline gave its 6-oxide which was identical with that obtained above by the cyclisation of 2-amino-3,5-dibromo-2′-nitrobiphenyl.

No *N*-oxidation occurred when 2,4,7,9-tetrabromobenzo[*c*]cinnoline and 4,7-dibromo-2,9-dimethylbenzo[*c*]cinnoline were treated with hydrogen peroxide in acetic acid. This and the formation of only the 6-oxide from the 2,4-dibromo-compound indicate steric hindrance by the bromine atoms *peri* to the nitrogen atom. It is thus reasonable to suppose that 4,7-dibromobenzo[*c*]cinnoline would also resist *N*-oxidation and that the dibromo-compound obtained by bromination of benzo[*c*]cinnoline is either the 1,4- or the 1,7-isomer, a suggestion which is supported by the ultraviolet absorption spectra.

Of the two possible structures, that of 1,7-dibromobenzo[*c*]cinnoline is preferred;

[16] Corbett and Holt, *J.*, 1961. 3695.

[17] Friedel and Orchin, " Ultra-violet Spectra of Aromatic Compounds," John Wiley & Sons, New York, 1951, p. 23; Friedel, *Appl. Spectroscopy*, 1957, **11**, 13; Johnson, *J. Org. Chem.*, 1959, **24**, 833; Cromartie and Murrell, *J.*, 1961, 2063.

[18] Booker, Corbett, Holt, and Hughes, unpublished work.

the second bromine atom would probably enter the unsubstituted ring, as the substituted ring would be deactivated by the $-I$ effect of the substituent.

The debromination of 1- and 4-bromobenzo[*c*]cinnoline calls for comment since it is unusual for lithium aluminium hydride to reduce aromatic halides. The results do not appear to be explicable in terms of inductive or electromeric effects. Possibly the bromine atom is removed from the 4-position of benzo[*c*]cinnoline during the decomposition of a complex between the cinnoline and aluminium hydride resulting from co-ordination by the lone-pair electrons on the nitrogen atoms. When solutions of benzo[*c*]cinnoline and lithium aluminium hydride in ether are mixed, a green precipitate separates and the yellow colour of the solution disappears. Removal of bromine from the 1-position is possibly due to intramolecular overcrowding which weakens the C–Br bond.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectrum of benzo[*c*]-cinnoline (I) in non-polar solvents consists of four absorption bands. Three are attributed to π–π^* transitions and have been designated group I (λ *ca.* 250 mμ, log ε *ca.* 4·6), group II (λ *ca.* 300 mμ, log ε *ca.* 3·9), and group III (λ *ca.* 350 mμ, log ε *ca.* 3·2), and each exhibits a certain amount of fine structure.[19] These bands correspond, respectively, to the β-, *p*-, and α-bands (Clar's nomenclature [20]) of phenanthrene. The fourth band is a weak, broad absorption band (λ 400—420 mμ, log ε 2·6) and is attributed to an n–π^* transition.[19]

The spectra of the bromobenzo[*c*]cinnolines were determined to provide further evidence for the structure assigned to the dibromo-compound obtained by the bromination of benzo[*c*]cinnoline. The spectra (Table 2) are similar in form to that of benzo[*c*]cinnoline,

TABLE 2.

Absorption spectra ($\lambda_{max.}$) for some bromobenzo[*c*]cinnolines.

	Group I [a]		Group II [b]		Group III	
Subst.		δλ *		δλ *		δλ *
None	251	0	295, 308	0	331, 347, 362	0
1-Bromo-	251	0	306, 319	11	—, 354, 369	7
2-Bromo-	254	3	302, 314	6·5	331,[s] 346, 361	−1
2,9-Dibromo-	257	6	308, 320	12·5	—, 345, 360	−2
3-Bromo-	295	8	295, 308	0	340, 355, 371	9
3,9-Dibromo-	266	15	—, 308	0	349, 362, 380	18
2,4-Dibromo-	258	7	311, 325	16·5	—, 352, 368	5·5
2,4,7,9-Tetrabromo-	265	14	331, 343	35·5	—, —, 373	11
1,7(4?)-Dibromo-	254	3	318, 331	23	—, 359, 375	12·5

* Relative to $\lambda_{max.}$ for benzo[*c*]cinnoline. [s] Shoulder. [a] EtOH as solvent. [b] CCl_4 as solvent.

TABLE 3.

Spectral shifts (mμ) produced by a bromine atom in the various positions in benzo[*c*]cinnoline.

Position	Group I	Group II	Group III
1-	0	11	7
2-	3	6	−1
3-	8	0	9
4-	4	11	6·5

exhibiting a single group I maximum (in ethanol), a group II band having two maxima, and a group III band having three (in carbon tetrachloride), except that, in a number of cases where a large bathochromic shift of one band (relative to that of benzo[*c*]cinnoline) is accompanied by a small shift of the next band, one or more peaks in the latter may be masked or may appear as shoulders.

From Table 2 it can be seen that the shifts produced by the substituents are additive to within 1 mμ, except that the group II shift for the tetrabromo-compound is 2·5 mμ greater than twice the shift for the 2,4-dibromo-compound.

[19] Badger and Walker, *J.*, 1956, 122; Corbett, Holt, and Hughes, *J.*, 1961, 1363.
[20] Clar, " Aromatische Kohlenwasserstoffe," Springer-Verlag, Berlin, 1952.

By estimating the shifts for substitution in the 4-position, on the assumption that the shifts are additive, shifts can be ascribed for substitution by bromine atoms in the four positions of benzo[*c*]cinnoline (Table 3). The spectrum of the 1,7(4?)-dibromo-compound exhibits shifts to be expected for such structures (for the group I, II, and III bands respectively: observed, 3, 23, and 12·5 mμ; estimated 4, 22, and 13·5 mμ).

Experimental

Benzo[c]*cinnoline–Bromine Complexes.*—Bromine was added to a solution of benzo[*c*]-cinnoline [21] in carbon tetrachloride; an orange-red solid separated immediately. The solid was filtered off, washed, and dried in air, at room temperature (Found: C, 47·8; H, 3·0; Br, 40·25; N, 9·3. Calc. for $C_{12}H_8Br_{1\cdot5}N_2$: C, 48·0; H, 2·9; Br, 40·0; N, 9·3%). A similar compound separated as orange-red needles when bromine and benzo[*c*]cinnoline were heated in acetic acid (Found: C, 45·7; H, 2·3; Br, 42·2; N, 9·6. Calc. for $C_{12}H_8Br_{1\cdot66}N_2$: C, 46·0; H, 2·5; Br, 42·5; N, 9·0%.

Recrystallisation of the products from ethanol gave benzo[*c*]cinnoline, m. p. and mixed m. p. 156°, and from acetone gave benzo[*c*]cinnoline hydrobromide hydrate, m. p. 220° [lit.,[22] m. p. 220° (decomp.)].

Benzo[c]*cinnoline–Iodine Complexes.*—Benzo[*c*]cinnoline (0·5 g.) in carbon tetrachloride (5 ml.) was added to a solution of iodine (1·0 g.) in carbon tetrachloride (10 ml.). After 2 hr. at room temperature, the complex was filtered off, washed with a little carbon tetrachloride, and allowed to dry (Found: C, 35·8; H, 2·4; I, 54·9; N, 6·9. Calc. for $C_{12}H_8I_{1\cdot13}N_2$: C, 36·0; H, 2·0; I, 54·9; N, 7·0%).

Bromination of Benzo[c]*cinnoline.*—Benzo[*c*]cinnoline (1·8 g.) in sulphuric acid (5 ml.) was treated with silver sulphate (1·7 g.) and bromine (0·52 ml.) in sulphuric acid (15 ml.). The mixture was shaken for 2 hr. and then filtered. The filtrate was poured into water (500 ml.), and the precipitate was filtered off, washed with water and dried. Basification of the aqueous filtrate gave benzo[*c*]cinnoline (0·75 g., 42%). The mixture of bromo-compounds was a yellow powder, m. p. 140—160° (from ethanol) (0·98 g.). A sample (0·1 g.) was chromatographed on alumina (10 × 0·75 cm.), and the eluate was collected in four fractions: (i) m. p. 146—149°, (ii) m. p. 144—149°, (iii) m. p. 194—199°, (iv) m. p. 197—199°. Recrystallisation of fractions (iii) and (iv) from ethanol gave 1-bromobenzo[*c*]cinnoline (0·06 g.) as bright yellow needles, m. p. 199°; the mixed m. p. with an authentic sample was 198—199° and the absorption spectra of the two samples were identical.

Recrystallisation of fractions (i) and (ii) from benzene gave 1,7(or 4)-*dibromobenzo*[c]*cinnoline* (0·015 g.) as bright yellow needles, m. p. 193° (mixed m. p. with 1-bromobenzo[*c*]cinnoline, 156—160°) (Found: C, 42·6; H, 1·7; Br, 46·5; N, 8·3. $C_{12}H_6Br_2N_2$ requires C, 42·5; H, 1·8; Br, 47·3; N, 8·3%). The mother liquor yielded a further crop of 1-bromobenzo[*c*]cinnoline (0·013 g.).

The remainder of the mixed products was separated qualitatively in a similar fashion.

1,7(or 4)-*Dibromobenzo*[c]*cinnoline* 5(or 6)-*Oxide.*—The dibromocinnoline (20 mg.) in acetic acid (2 ml.) was treated with 80% w/v hydrogen peroxide (0·1 ml.) at 50° for 1 hr. Water was added and the precipitate was filtered off and recrystallised from acetic acid as pale yellow needles, m. p. 241° (Found: C, 40·25; H, 1·7; Br, 45·3; N, 7·9. $C_{12}H_6Br_2N_2O$ requires C, 40·6; H, 1·7; Br, 45·2; N, 7·9%).

Reduction of 6,6′-*Dibromo*-4,4′-*dimethyl*-2,2′-*dinitrobiphenyl.*—*With lithium aluminium hydride.* The biaryl [14] (2 g.) in dry benzene (150 ml.) and dry ether (100 ml.) was treated with lithium aluminium hydride (1 g.) in ether (75 ml.). The mixture was left at room temperature for 2 hr. and warmed on a water bath for 15 min., then cooled. Water was added to decompose the excess of hydride and the mixture was filtered. The filtrate was evaporated and the residue was chromatographed in benzene on alumina; evaporation of the eluate and recrystallisation of the residue from ethanol gave 3,8-dimethylbenzo[*c*]cinnoline (0·8 g., 80%), m. p. and mixed m. p. 186°.

With sodium sulphide. The biaryl (2 g.) in boiling ethanol (100 ml.) was treated with sodium sulphide nonahydrate (2 g.) and sodium hydroxide (0·1 g.) in water (10 ml.), and the mixture was heated under reflux for 4 hr. The mixture was filtered and the filtrate was evaporated

[21] Badger, Seidler, and Thomson, *J.*, 1951, 3207.
[22] Corbett and Holt, *J.*, 1960, 3646.

to low bulk and poured into water. The precipitate was recrystallised four times from benzene to give *2-amino-6,6′-dibromo-4,4′-dimethyl-2′-nitrobiphenyl* as orange rhombs., m. p. 128° (Found: Br, 42·8; N, 6·7. $C_{14}H_{12}Br_2N_2O_2$ requires Br, 42·9; N, 6·7%).

1-Bromo-3-methylbenzo[c]*cinnoline.—The Ullmann reaction.* 3-Bromo-4-iodo-5-nitrotoluene [14] (12 g.) and *o*-bromonitrobenzene (10 g.) were refluxed with copper bronze (15 g.) in dimethylformamide (150 ml.) for 8 hr. The mixture was allowed to cool, then filtered, and the filtrate was poured into water. The precipitate was filtered off, dried, and extracted with boiling benzene. The extract was evaporated and the residue used for the next stage.

Reduction of the biaryls. The oil obtained as above (7·8 g.) in boiling ethanol (150 ml.) was heated with sodium sulphide nonahydrate (12 g.) and sodium hydroxide (2·5 g.) in water (20 ml.) for 4 hr. The mixture was filtered while hot, evaporated to low bulk, and poured into water. The oil which separated was dissolved in benzene and the solution was extracted with 1 : 1 v/v aqueous hydrochloric acid. The benzene solution was washed with water, dried, and chromatographed on alumina to remove tar. Concentration of the yellow eluate gave, on cooling, *1-bromo-3-methylbenzo*[c]*cinnoline N-oxide* (0·4 g., 4%) as pale yellow needles, m. p. 245° (Found: C, 54·45; H, 3·28; Br, 26·95; N, 9·7. $C_{13}H_9BrN_2O$ requires C, 54·0; H, 3·12; Br, 27·6; N, 9·7%). The mother liquor gave benzo[*c*]cinnoline *N*-oxide, m. p. and mixed m. p. 140°. The acid extract was basified and the precipitate filtered off and recrystallised from benzene, to give 2-amino-6,6′-dibromo-4,4′-dimethyl-2′-nitrobiphenyl, m. p. and mixed m. p. 128°.

Reduction of the N-*oxide.* (*a*) The *N*-oxide (0·1 g.) was reduced with lithium aluminium hydride (0·1 g.) as above. The product, which was an oil, was dissolved in ethanol and treated with picric acid. *3-Methylbenzo*[c]*cinnoline picrate* separated as yellow needles, m. p. 176° (Found: C, 54·3; H, 3·1. $C_{19}H_{13}N_5O_7$ requires C, 53·9; H, 3·1%). The picrate, in ethanol, was filtered through a column of alumina; evaporation of the eluate gave 3-methylbenzo[*c*]cinnoline, m. p. 98—100°, which was identical with a sample prepared [4] by reduction of 4-methyl-2,2′-dinitrobiphenyl [23] with lithium aluminium hydride.

(*b*) The *N*-oxide (0·1 g.) was suspended in hydrochloric acid (10 ml.), and a solution of stannous chloride (0·2 g.) in hydrochloric acid (10 ml.) was added. The mixture was kept at 80—90° for 3 hr., water was added, and the solid material was filtered off. *1-Bromo-3-methylbenzo*[c]*cinnoline* formed yellow needles (from ethanol) (0·04 g.), m. p. 154° (Found: C, 57·0; H, 3·2; Br, 29·0; N, 10·15. $C_{13}H_9BrN_2$ requires C, 57·1; H, 3·3; Br, 29·2; N, 10·25%).

1-Bromo-2-iodo-3-nitrobenzene.—2-Bromo-6-nitroaniline [13] (10·5 g.) in cold acetic acid (50 ml.) was added, with stirring, to a solution of sodium nitrite (3·8 g.) in sulphuric acid (50 ml.). The resulting solution was poured into an excess of saturated aqueous potassium iodide. After 15 min., water was added and the solid was filtered off, dissolved in ether, and washed with aqueous sodium metabisulphite and water. The ether solution was dried and the ether evaporated. The residue recrystallised from ethanol, to give 1-bromo-2-iodo-3-nitrobenzene (11·8 g., 72%), m. p. 115° (lit., m. p. 119°).

1-Bromobenzo[c]*cinnoline.*—The mixed Ullmann reaction was carried out, as above, with 1-bromo-2-iodo-3-nitrobenzene (11·8 g.) and *o*-bromonitrobenzene (8 g.). The resulting oil was reduced with sodium sulphide, and the products were separated as described above. *1-Bromobenzo*[c]*cinnoline N-oxide* formed pale yellow needles (0·3 g.), m. p. 225—227° (Found: C, 51·7; H, 2·8; Br, 29·3; N, 9·95. $C_{12}H_7BrN_2O$ requires C, 52·4; H, 2·5; Br, 29·1; N, 10·2%).

The *N*-oxide was reduced with stannous chloride, as above, to give *1-bromobenzo*[c]*cinnoline*, m. p. 199° (Found: C, 55·2; H, 2·6; Br, 31·2; N, 10·75. $C_{12}H_7BrN_2$ requires C, 55·6; H, 2·7; Br, 30·9; N, 10·8%).

2-Amino-5-bromo-2′-nitrobiphenyl.—2-Amino-2′-nitrobiphenyl [24] with acetic anhydride gave 2-acetamido-2′-nitrobiphenyl, m. p. 155—157° (lit.,[25] m. p. 159—160°).

The nitro-amide (2·1 g.) in acetic acid (15 ml.) was treated with bromine (0·42 ml.) in acetic acid (10 ml.). The mixture was left at room temperature for 4 hr. and then poured into water. The precipitate was recrystallised from benzene–light petroleum (b. p. 60—80°), to give 2-acetamido-5-bromo-2′-nitrobiphenyl as colourless needles, m. p. 75°. This product, in ethanol, was refluxed with hydrochloric acid for 3 hr. The solution was evaporated to low bulk, then

[23] Baker, Barton, and McOmie, *J.*, 1958, 2661.
[24] Badger and Sasse, *J.*, 1957, 4.
[25] Purdie, *J. Amer. Chem. Soc.*, 1941, **63**, 2276.

basified, and the precipitate was filtered off and recrystallised from ethanol. *2-Amino-5-bromo-2'-nitrobiphenyl* forms yellow needles, m. p. 133° (Found: C, 48·95; H, 3·19; N, 9·6. $C_{12}H_9BrN_2O_2$ requires C, 49·15; H, 3·07; N, 9·55%).

Reductive Acetylation, and Bromination, of 2-Acetamido-5-bromo-2'-nitrobiphenyl.—The amide (0·5 g.) in acetic acid (20 ml.) was refluxed with zinc dust (2 g.). After 2 hr., acetic anhydride (1 ml.) was added and refluxing was continued for a further 2 hr. Water was added to decompose any excess of anhydride, and the remaining zinc was filtered off. The filtrate was treated with bromine (0·2 ml.), and the solution was warmed on a water bath for 1 hr., concentrated, and allowed to cool. 2,2'-Bisacetamido-5,5'-dibromobiphenyl (0·3 g.) separated as colourless crystals, m. p. 264° (lit., 266—267°). The mixed m. p. with an authentic sample [15] was 264—266°.

2-Bromobenzo[c]*cinnoline 6-Oxide.*—2-Amino-5-bromo-2'-nitrobiphenyl (0·7 g.) in N-methanolic sodium hydroxide (50 ml.) was heated under reflux for 1 hr. (pale yellow needles started to separate after 5 min.). The mixture was cooled and the product (0·59 g., 90%) was filtered off. *2-Bromobenzo*[c]*cinnoline 6-oxide* formed pale yellow needles, m. p. 248° (from ethanol) (Found: C, 52·34; H, 2·63; Br, 29·1; N, 10·16. $C_{12}H_7BrN_2O$ requires C, 52·4; H, 2·54; Br, 29·1; N, 10·2%).

2-Bromobenzo[c]*cinnoline.*—The *N*-oxide (0·3 g.) was suspended in benzene (15 ml.) and ether (20 ml.), and lithium aluminium hydride (0·3 g.) in ether (10 ml.) was added. The mixture was refluxed for 0·5 hr. After the solution had cooled, water was added to decompose the excess of hydride, and the mixture was filtered. The filtrate was dried and evaporated, and the residue was recrystallised from benzene, giving *2-bromobenzo*[c]*cinnoline* (0·27 g., 93%) as yellow needles, m. p. 220° (Found: C, 55·5; H, 2·66; Br, 30·9; N, 10·7. $C_{12}H_7BrN_2$ requires C, 55·6; H, 2·7; Br, 30·9; N, 10·8%).

Oxidation of 2-Bromobenzo[c]*cinnoline.*—The cinnoline was oxidised with hydrogen peroxide in acetic acid as described above. Fractional crystallisation of the product gave the 6-oxide, m. p. and mixed m. p. 248°, and *2-bromobenzo*[c]*cinnoline 5-oxide*, m. p. 230—232° (mixed m. p. with the 6-oxide 220—222°) (Found: C, 52·4; H, 2·54; Br, 29·1; N, 10·2%).

2-Amino-3,5-dibromo-2'-nitrobiphenyl.—(*i*) 2-Amino-2'-nitrobiphenyl (0·52 g.) in acetic acid (8 ml.) was treated with bromine (0·8 g.) in acetic acid (5 ml.). After 2 hr., water was added and the precipitate was filtered off, dried, and recrystallised from ethanol. *2-Amino-3,5-dibromo-2'-nitrobiphenyl* formed orange-yellow needles, m. p. 117° (0·86 g., 94%) (Found: C, 38·0; H, 2·08; Br, 42·7; N, 7·4. $C_{12}H_8Br_2N_2O_2$ requires C, 38·7; H, 2·15; Br, 42·95; N, 7·55%).

(*ii*) 2-Amino-5-bromo-2'-nitrobiphenyl was brominated as above, giving the 3,5-dibromo-compound, m. p. and mixed m. p. 117°.

Reduction and Bromination of 2-Amino-3,5-dibromo-2'-nitrobiphenyl.—The nitro-compound (0·2 g.) in acetic acid was refluxed with zinc dust for 3 hr. The excess of zinc was filtered off, and bromine (0·3 g.) was added to the filtrate. After 1 hr. the solution was concentrated and allowed to cool. 2,2'-Diamino-3,5,3',5'-tetrabromobiphenyl separated as almost colourless crystals, m. p. 170°. The mixed m. p. with an authentic sample [16] was 170°.

2,4-Dibromobenzo[c]*cinnoline 6-Oxide.*—2-Amino-3,5-dibromo-2'-nitrobiphenyl (0·4 g.) in N-methanolic sodium hydroxide (50 ml.) was heated under reflux for 2 hr. After cooling, the product was filtered off and recrystallised from ethanol. *2,4-Dibromobenzo*[c]*cinnoline 6-oxide* formed almost colourless needles (0·38 g., 98%), m. p. 273° (Found: C, 40·4; H, 1·61; Br, 45·15; N, 8·0. $C_{12}H_6Br_2N_2O$ requires C, 40·6; H, 1·69; Br, 45·2; N, 7·9%).

A reaction time of 45 min. gave only 60% of the *N*-oxide.

2,4-Dibromobenzo[c]*cinnoline.* The *N*-oxide (0·2 g.) was reduced with stannous chloride as above. *2,4-Dibromobenzo*[c]*cinnoline* formed yellow needles (from ethanol), m. p. 206° (Found: C, 42·6; H, 1·7; Br, 47·4; N, 8·1. $C_{12}H_6Br_2N_2$ requires C, 42·5; H, 1·8; Br, 47·3; N, 8·3%).

Reduction of the *N*-oxide with lithium aluminium hydride gave 2-bromobenzo[*c*]cinnoline, m. p. and mixed m. p. 220°.

3-Bromobenzo[c]*cinnoline.*—*The mixed Ullmann reaction.* 1,4-Dibromo-2-nitrobenzene (7 g.) and *o*-bromonitrobenzene (5 g.) in dimethylformamide (100 ml.) were refluxed with copper bronze (10 g.) for 8 hr. The mixed products were isolated as above.

Reduction of the mixture of biaryls. The mixed biaryls (4 g.) were reduced with lithium aluminium hydride, as above. The products were dissolved in benzene and the solution was

extracted with 5N-sulphuric acid to remove benzo[*c*]cinnoline (1·2 g.), m. p. and mixed m. p. 154°. The benzene solution was evaporated, and the residue was fractionally recrystallised from ethanol to give 3,8-dibromobenzo[*c*]cinnoline, and 3-*bromobenzo*[c]*cinnoline* (0·2 g.) as a pale yellow powder, m. p. 191° (Found: C, 55·2; H, 2·6; Br, 31·1; N, 10·7. $C_{12}H_7BrN_2$ requires C, 55·6; H, 2·7; Br, 30·9; N, 10·8%).

4,4′-*Dibromo*-2,2′-*dinitrobiphenyl*.—1,4-Dibromo-2-nitrobenzene (14 g.) in dimethylformamide (100 ml.) was refluxed with copper bronze (8 g.) for 6 hr. The mixture was filtered and the filtrate was poured into water. The precipitate was extracted with ethanol, and the extract was concentrated and allowed to cool. The biaryl (7·6 g., 76%) separated as yellow rhombs, m. p. 150° (lit., m. p. 150°).

3,8-*Dibromobenzo*[c]*cinnoline*.—4,4′-Dibromo-2,2′-dinitrobiphenyl (1·4 g.) was reduced with lithium aluminium hydride as above. 3,8-*Dibromobenzo*[c]*cinnoline* (0·87 g., 72%) formed pale yellow needles, m. p. 237° (Found: C, 43·25; H, 1·78; Br, 46·8; N, 8·2. $C_{12}H_6Br_2N_2$ requires C, 42·5; H, 1·79; Br, 47·3; N, 8·3%).

Oxidation of the cinnoline with hydrogen peroxide, as above, gave 3,8-*dibromobenzo*[c]-*cinnoline* N-*oxide* as pale yellow needles, m. p. 263° (Found: C, 40·6; H, 1·74; Br, 45·15; N, 7·8. $C_{12}H_6Br_2N_2O$ requires C, 40·6; H, 1·69; Br, 45·2; N, 7·9%).

2,2′-*Diamino*-3,3′-*dibromo*-5,5′-*dimethylbiphenyl*.—2,2′-Diamino-5,5′-dimethylbiphenyl [26] (1·5 g.) in acetic acid (20 ml.) was treated with bromine (2 g.). The product was precipitated by the addition of water, and recrystallised from ethanol as a white powder, m. p. 139—140°. The crude material was chromatographed in benzene on alumina, to give 2,2′-*diamino*-3,3′-*dibromo*-5,5′-*dimethylbiphenyl* as colourless feathery needles, m. p. 150—152° (Found: C, 45·1; H, 3·9; Br, 43·1; N, 7·4. $C_{14}H_{14}Br_2N_2$ requires C, 45·4; H, 3·8; Br, 43·2; N, 7·6%).

4,7-*Dibromo*-2,9-*dimethylbenzo*[c]*cinnoline*.—2,2′-Diamino-3,3′-dibromo-5,5′-dimethylbiphenyl (0·3 g.) in acetic acid (20 ml.) was treated with 80% w/v hydrogen peroxide (1 ml.), and the mixture was heated on a water bath for 1 hr. On cooling of the solution, 4,7-*dibromo*-2,9-*dimethylbenzo*[c]*cinnoline* (0·26 g., 87%) separated as bright yellow needles, m. p. > 370° (Found: C, 46·2; H, 2·82; Br, 43·3; N, 7·5. $C_{14}H_{10}Br_2N_2$ requires C, 45·9; H, 2·74; Br, 43·7; N, 7·65%).

Debromination of Bromobenzo[c]*cinnolines*.—The cinnoline (0·1 g.) was dissolved in 2 : 1 v/v benzene–ether (25 ml.), and lithium aluminium hydride (0·2 g.) in dry ether (10 ml.) was added. The mixture was refluxed for 1 hr. and then allowed to cool. Water was added to decompose the excess of hydride and the mixture was filtered. The filtrate was dried and evaporated, and the residue was recrystallised from ethanol. The products were identified by mixed m. p.s with authentic samples.

Spectra.—The absorption spectra were determined in carbon tetrachloride (B.D.H. spectroscopic grade), a Unicam S.P. 500 spectrophotometer being used.

The authors are grateful to the Royal Society for the loan of a spectrophotometer.

THE UNIVERSITY, READING. [*Received, June 16th*, 1961.]

[26] Case and Koft, *J. Amer. Chem. Soc.*, 1941, **63**, 510.