

**718.** *Polycyclic Cinnoline Derivatives. Part VIII.<sup>1</sup> Cinnolines and their N-Oxides and oo'-Diaminobiaryls.*

By J. F. CORBETT and P. F. HOLT.

The oxidation of six unsubstituted *oo'*-diaminobiaryls with sodium perborate and with hydrogen peroxide in acetic acid has been studied. The yields of the corresponding cinnolines and their *N*-oxides are poor to moderate. Three substituted derivatives of 2,2'-diaminobiphenyl give excellent yields of the corresponding cinnoline. Evidence for the structure of the *N*-oxides of the unsymmetrical polycyclic cinnolines has been obtained from studies of the competitive oxidation of mixtures of symmetrical polycyclic cinnolines.

POLYCYCLIC cinnolines are generally prepared by reduction of *oo'*-dinitrobiaryls, lithium aluminium hydride usually giving the best yields.<sup>2,3</sup> The method is sometimes inapplicable because substituent groups are removed or reduced; thus nitro-derivatives cannot be prepared by reduction methods, and halogen is sometimes eliminated. Further, some starting materials, particularly unsymmetrical *oo'*-dinitrobiaryls are difficult to prepare.

<sup>1</sup> Part VII, Holt, Hopson-Hill, and McNae, *J.*, 1961, 1404.

<sup>2</sup> Badger, Seidler, and Thomson, *J.*, 1951, 3207; Braithwaite and Holt, *J.*, 1959, 3025.

<sup>3</sup> Corbett and Holt, *J.*, 1960, 3646.

For these reasons a route involving the oxidation of *oo'*-diaminobiaryls has been investigated, such an oxidation, to give a pyridazine ring, having already been used in the synthesis of tetrazapyrene<sup>4</sup> and dibenzo[*c,f*]cinnoline<sup>5</sup> (I).

Peracetic acid,<sup>6</sup> sodium perborate,<sup>7</sup> phenyl iodosoacetate,<sup>8</sup> and lead tetra-acetate<sup>9</sup> oxidise primary aromatic amines to azo-compounds. We have used sodium perborate and hydrogen peroxide in acetic acid to oxidise a number of *oo'*-diaminobiaryls; the results are tabulated below. 2,2'-Diaminobiphenyl, 1-*o*-aminophenyl-2-naphthylamine,

*Oxidation of oo'-diaminobiaryls by sodium perborate in acetic acid.*

Diaminobiaryl	Cinnoline			Carbazole			Overall yield (%) of cinnoline <sup>e</sup>	
	NH <sub>2</sub> Biaryl <sup>a</sup>	Yield (%)	M. p. <sup>b</sup>	Yield (%)	M. p. <sup>b</sup>		A	B
2,2'-Ph <sub>2</sub>	VIII	50	156° (156°)	—	0	—	35 <sup>f</sup>	70 <sup>g</sup>
2,2'-Ph 1-Nap	I	53	156 (157)	Benzo[ <i>c</i> ]	Trace	135° (135°)	14	3 <sup>e</sup>
1,2'-Ph 2-Nap	VI	43	190 (190)	Benzo[ <i>a</i> ]	~5	226 (226)	8 <sup>f</sup>	24 <sup>e</sup>
2,2'-(1-Nap) <sub>2</sub>	II	Trace	269 (270)	—	0	—	1	20 <sup>f</sup>
1,1'-(2-Nap) <sub>2</sub>	IX	5	262 (266)	Dibenzo[ <i>a,i</i> ]	40	216 (216)	3	30 <sup>f</sup>
2,1'-1-Nap 2-Nap	VII	8	185 (185)	Dibenzo[ <i>a,g</i> ]	14	228 (231)	1	9 <sup>e</sup>

<sup>a</sup> Ph = phenyl; Nap = naphthalene or naphthyl. <sup>b</sup> M. p. from the literature in parentheses; the mixed melting points with authentic samples were within  $\pm 2^\circ$  of the figure given. <sup>c</sup> Overall yields from readily available materials: column A, *via* the diaminobiaryl; column B, *via* the dinitrobiaryl. <sup>d</sup> Badger, Seidler, and Thomson, *J.*, 1951, 3207. <sup>e</sup> Corbett and Holt, *J.*, 1960, 3646. <sup>f</sup> Braithwaite and Holt, *J.*, 1959, 3025. <sup>g</sup> These diamines can only be obtained by the reduction of the dinitrobiaryl.

and 2-*o*-aminophenyl-1-naphthylamine gave 43—53% of the corresponding cinnoline, when oxidised with the theoretical amount of sodium perborate in acetic acid. The three diaminobinaphthyls gave less than 10% of the cinnoline in this way. Oxidation with an excess of hydrogen peroxide in acetic acid gave similar yields of the cinnoline *N*-oxides. In all cases an intractable yellow oil was also obtained.

The poor yield of cinnolines from 1,1'-diamino-2,2'-binaphthyl and 2,1'-diamino-1,2'-binaphthyl is, in part, due to the formation of the corresponding carbazoles, as a result of deamination by the solvent. It has been reported previously that *oo'*-diaminobiaryls, in which at least one of the amino-groups is attached to a naphthalene nucleus, readily give carbazoles with acetic acid.<sup>3</sup> Oxidation methods using non-acidic solvents, which will be studied, may give better yields of cinnoline.

Steric hindrance to the adoption of a planar configuration, and thus to the close approach of the two amino-groups, may account for the poor yield of the cinnoline and the absence of carbazole in the oxidation of 2,2'-diamino-1,1'-binaphthyl (III). Some other oxidation process occurs, which results in the formation of a yellow oil, which was not investigated further.

It is apparent from the Table that, as a preparative method for these unsubstituted polycyclic cinnolines, the oxidation of diamines shows no advantage over the reduction of dinitrobiaryls, except in the case of dibenzo[*c,f*]cinnoline (I) where the overall yield from 2-naphthol is 14% in two stages *via* the diamine, compared with 3% from 1-naphthylamine in four stages *via* the dinitro-compound.

Three substituted derivatives of 2,2'-diaminobiphenyl gave excellent yields of the corresponding benzo[*c*]cinnoline. 2,2'-Diamino-5,5'-dibromobiphenyl (IV; X = Br, Y = H) gave a 70% yield of 2,9-dibromobenzo[*c*]cinnoline (V; X = Br, Y = H) on oxidation

<sup>4</sup> Holt and Hughes, *J.*, 1960, 3216.

<sup>5</sup> Badger and Walker, *J.*, 1956, 122; Corbett and Holt, ref. 3.

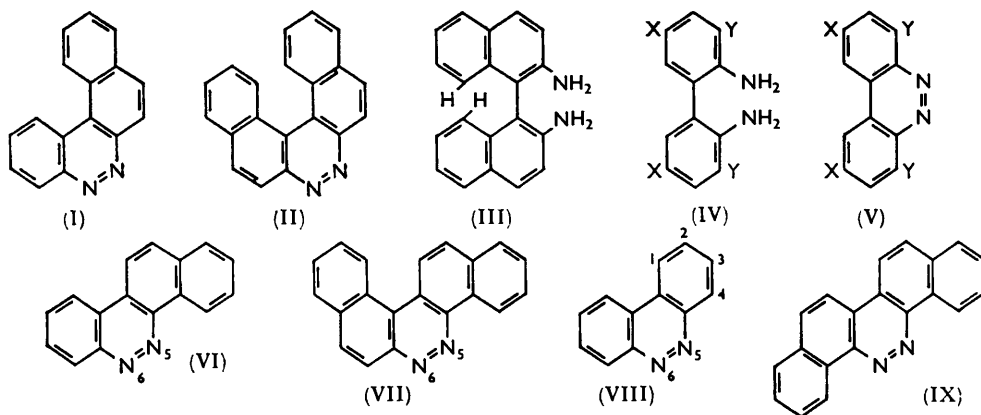
<sup>6</sup> Greenspan, *Ind. Eng. Chem.*, 1947, **39**, 847.

<sup>7</sup> Mehta and Vakildwala, *J. Amer. Chem. Soc.*, 1952, **74**, 563.

<sup>8</sup> Pausacker, *J.*, 1953, 1989.

<sup>9</sup> Pausacker and Scroggie, *J.*, 1954, 4003.

with sodium perborate and an almost quantitative yield of the cinnoline *N*-oxide with excess of hydrogen peroxide in acetic acid.



2,2'-Diamino-3,5,3',5'-tetrabromobiphenyl (IV; X = Y = Br) was obtained by brominating 2,2'-diaminobiphenyl (a specimen was deaminated to 3,5,3',5'-tetrabromobiphenyl which was identical with a sample prepared by the deamination of 3,5,3',5'-tetrabromobenzidine,<sup>10</sup> thus confirming the structure assigned). This diamine gave an excellent yield of 2,4,7,9-tetrabromobenzo[*c*]cinnoline (V; X = Y = Br) on oxidation with sodium perborate or with an excess of hydrogen peroxide in acetic acid. The failure of the tetrabromobenzo[*c*]cinnoline to undergo further oxidation, to an *N*-oxide, can be attributed to steric hindrance by the 4- and 7-bromine atoms and to the strong  $-I$  effect of the four bromine atoms.

2,2'-Diamino-5,5'-dinitrobiphenyl (IV; X = NO<sub>2</sub>, Y = H) gave 2,9-dinitrobenzo[*c*]cinnoline *N*-oxide in high yield, thus providing a route to 2,9-diaminobenzo[*c*]cinnoline (V; X = NH<sub>2</sub>, Y = H) which is formed by catalytic reduction of the dinitro-compound. Arcos, Arcos, and Miller<sup>11</sup> reported that 5-amino-2,2'-dinitrobiphenyl did not give a cinnoline on reduction.

The formation of polycyclic cinnolines by the oxidation of *oo'*-diaminobiaryls presumably occurs by intramolecular condensation of an aminonitrosobiaryl formed by oxidation of one of the amino-groups. Emmons has suggested that the oxidation of primary aromatic amines to azo-compounds, by peracetic acid, occurs by a similar *intermolecular* process.<sup>12</sup>

As expected, the cinnoline *N*-oxides obtained by oxidation of unsymmetrical *oo'*-diaminobiaryls were identical with those obtained by the oxidation of the corresponding cinnolines. In an earlier paper, it was suggested that the *N*-oxides obtained from dibenzo[*c,h*]cinnoline (VI) and benzo[*f*]naphtho[1,2-*c*]cinnoline (VII) were the 6-oxides rather than a mixture of the 5- and 6-oxides.<sup>3</sup> The results of the competitive oxidation of mixtures of symmetrical polycyclic cinnolines with sodium perborate in acetic acid support the contention that, when a ring is fused to the 3,4-position of benzo[*c*]cinnoline (VIII), *N*-oxidation at the 5-nitrogen atom is sterically inhibited. Oxidation of an equimolar mixture of benzo[*c*]cinnoline (VIII) and benzo[*h*]naphtho[1,2-*c*]cinnoline (IX) with one mol. of sodium perborate gave benzo[*c*]cinnoline *N*-oxide as the only oxidation product. Similar treatment of a mixture of benzo[*f*]naphtho[2,1-*c*]cinnoline (II) and benzo[*h*]naphtho[2,1-*c*]cinnoline (IX) gave the *N*-oxide of (II) only. In each case the cinnoline (IX) was recovered as its hemipicrate.

<sup>10</sup> van Roosmalen, *Rec. Trav. chim.*, 1934, **53**, 359.

<sup>11</sup> Arcos, Arcos, and Miller, *J. Org. Chem.*, 1956, **21**, 651.

<sup>12</sup> Emmons, *J. Amer. Chem. Soc.*, 1954, **76**, 3470.

## EXPERIMENTAL

1-*o*-Aminophenyl-2-naphthylamine.—The diamine was obtained by the method of Fuchs and Niszel,<sup>13</sup> but with heating for only 12 hr. This gave a 20% yield (cf. 5%) of the diamine, m. p. 155° (lit., m. p. 156.5—157.5°).

2,2'-Diamino-1,1'-binaphthyl,<sup>14</sup> 1,1'-diamino-2,2'-binaphthyl,<sup>15</sup> 2-*o*-aminophenyl-1-naphthylamine,<sup>16</sup> and 2,1'-diamino-1,2'-binaphthyl<sup>17</sup> were obtained by published methods.

*Oxidation of Diaminobiaryls.*—(i) The diamine (0.1 g.) in acetic acid (2 ml.) was treated with sodium perborate (2 equiv.) in acetic acid, at room temperature. After 2 hr., the solution was poured into water and basified. The precipitate was filtered off and dried, then dissolved in benzene. The solution was chromatographed on alumina and the eluate collected in small fractions. Early fractions contained the carbazole, and later fractions the cinnoline. When the cinnoline fractions contained a yellow oil, the cinnoline was isolated by dissolving the mixture in a small volume of acetone and precipitating the cinnoline as its hydrochloride by bubbling hydrogen chloride through the solution. The cinnoline was recovered from its hydrochloride by treatment with water. The yields of carbazole and cinnoline, m. p.s and mixed m. p.s (cf. ref. 3) are given in the Table.

(ii) The diamine (0.1 g.) in acetic acid (5 ml.) was treated with 80% w/v hydrogen peroxide (0.2 ml.). After 2 hr. at room temperature the solution was poured into water and basified. The precipitate was dried and dissolved in benzene. Chromatography on alumina gave the carbazole in the first portions of eluate and the cinnoline *N*-oxide, together with a yellow oil, in later portions. The cinnoline *N*-oxide was isolated by crystallisation from ethanol.

2,2'-Diamino-5,5'-dibromobiphenyl.—2,2'-Bisacetamidobiphenyl was brominated and the product hydrolysed by Le Fèvre's method.<sup>18</sup> The product formed colourless crystals, m. p. 140° (lit., m. p. 140—141°), from ethanol.

2,9-Dibromobenzo[c]cinnoline.—2,2'-Diamino-5,5'-dibromobiphenyl (0.2 g.) in acetic acid (5 ml.) was treated with sodium perborate (0.185 g.) in acetic acid (8 ml.). The mixture was set aside for 1 hr. at room temperature and then heated, for a further hour, on a water-bath. The solution was poured into water and the precipitate was recrystallised from ethanol. 2,9-Dibromobenzo[c]cinnoline formed pale yellow needles (0.14 g., 70%), m. p. 258° (Found: C, 42.4; H, 1.8; N, 8.2; Br, 46.9. C<sub>12</sub>H<sub>6</sub>Br<sub>2</sub>N<sub>2</sub> requires C, 42.5; H, 1.8; N, 8.3; Br, 47.3%).

2,9-Dibromobenzo[c]cinnoline *N*-Oxide.—2,2'-Diamino-5,5'-dibromobiphenyl (0.2 g.) in acetic acid (10 ml.) was treated with 80% w/v hydrogen peroxide (0.5 ml.), and the mixture heated on a water-bath. After ½ hr., the product separated as a yellow solid. Water was added, and the precipitate recrystallised from acetic acid. 2,9-Dibromobenzo[c]cinnoline *N*-oxide formed pale yellow needles (0.20 g., 98%), m. p. 300° (Found: C, 40.9; H, 2.0; N, 7.6; Br, 45.3. C<sub>12</sub>H<sub>6</sub>Br<sub>2</sub>N<sub>2</sub>O requires C, 40.6; H, 1.7; N, 7.9; Br, 45.2%).

The *N*-oxide was also formed by oxidation of the cinnoline with peracetic acid.

2,2'-Diamino-3,5,3',5'-tetrabromobiphenyl.—2,2'-Diaminobiphenyl (1.0 g.) in acetic acid (20 ml.) was treated with bromine (3.6 g.) in acetic acid (10 ml.). The solution was heated on a water-bath for 1 hr. and then poured into water. The precipitate was filtered off and washed with aqueous sodium metabisulphite and water, then dried. Recrystallisation from ethanol gave 2,2'-diamino-3,5,3',5'-tetrabromobiphenyl as off-white needles, m. p. 170° (Found: C, 29.1; H, 1.5; N, 5.5; Br, 63.7. C<sub>12</sub>H<sub>6</sub>Br<sub>4</sub>N<sub>2</sub> requires C, 28.8; H, 1.6; N, 5.5; Br, 64.0%).

2,4,7,9-Tetrabromobenzo[c]cinnoline.—The diaminotetrabromobiphenyl (0.2 g.) in acetic acid was oxidised with sodium perborate, and with excess of hydrogen peroxide in acetic acid, as described above. Sodium perborate gave 0.11 g. (55%) and peracetic acid 0.185 g. (92%) of 2,4,7,9-tetrabromobenzo[c]cinnoline which crystallised from acetic acid as bright yellow needles, m. p. 300° (Found: C, 29.4; H, 1.2; N, 5.8; Br, 63.8. C<sub>12</sub>H<sub>4</sub>Br<sub>4</sub>N<sub>2</sub> requires C, 29.0; H, 0.8; N, 5.7; Br, 64.4%).

*Deamination of 2,2'-Diamino-3,5,3',5'-tetrabromobiphenyl.*—The diamine was deaminated

<sup>13</sup> Fuchs and Niszel, *Ber.*, 1927, **60**, 209.

<sup>14</sup> Cumming and Howie, *J.*, 1932, 528.

<sup>15</sup> Hodgson and Habeshaw, *J.*, 1947, 77.

<sup>16</sup> Whaley, Meadow, and Robinson, *J. Org. Chem.*, 1954, **19**, 973.

<sup>17</sup> Ward and Pearson, *J.*, 1959, 3378.

<sup>18</sup> Le Fèvre, *J.*, 1929, 736.

as described by van Roosmalen for the deamination of tetrabromobenzidine.<sup>10</sup> 3,5,3',5'-Tetrabromobiphenyl formed almost colourless crystals, m. p. 186° (lit., m. p. 186°). The mixed m. p. with a sample prepared by van Roosmalen's method was 185—186°.

*2,2'-Diamino-5,5'-dinitrobiphenyl*.—2,2'-Bisacetamidobiphenyl was nitrated and the product hydrolysed by Sako's method.<sup>19</sup> The product formed brown-yellow crystals, m. p. 304° (lit., 303°).

*2,9-Dinitrobenzo[c]cinnoline N-Oxide*.—The above diamine (0.2 g.), suspended in hot acetic acid (10 ml.), was treated with 80% w/v hydrogen peroxide (0.5 ml.). The solid dissolved, and later the product separated as yellow needles which were filtered off, washed with acetic acid, and dried. Recrystallisation from aqueous dimethylformamide gave *2,9-dinitrobenzo[c]cinnoline N-oxide* (0.2 g., 97%), m. p. 324° (slight decomp. >300°) (Found: C, 50.4; H, 2.3; N, 19.1. C<sub>12</sub>H<sub>8</sub>N<sub>4</sub>O<sub>5</sub> requires C, 50.4; H, 2.1; N, 19.6%).

*2,9-Diaminobenzo[c]cinnoline*.—The last *N-oxide* (40 mg.) was suspended in ethanol (100 ml.) and shaken with Adams catalyst under hydrogen at 1 atm. After absorption of hydrogen had ceased, the solution was evaporated to small bulk. *2,9-Diaminobenzo[c]cinnoline* separated as yellow needles which decomposed, without melting, at 315° (Found: C, 68.7; H, 4.4; N, 26.65. C<sub>12</sub>H<sub>10</sub>N<sub>4</sub> requires C, 68.6; H, 4.8; N, 26.65%). The diamine gave a yellow solution in dilute hydrochloric acid.

*Competitive Oxidation of Symmetrical Cinnolines*.—(i) Benzo[c]cinnoline (45 mg.) and benzo[h]naphtho[1,2-*c*]cinnoline (70 mg.) in acetic acid (8 ml.) was treated with sodium perborate (38 mg.) in acetic acid (6 ml.). The solution was kept at about 40° for 2 hr., then poured into water and basified with ammonia. The precipitate was filtered off, dried, and dissolved in the minimum amount of ethanol. An excess of picric acid, in ethanol, was added and the cinnoline picrate filtered off (71 mg., 73%); it had m. p. 243—245° (lit., for benzo[h]naphtho[1,2-*c*]cinnoline hemipicrate, m. p. 245°). The ethanolic filtrate was basified with ammonia and extracted with benzene. The benzene extract was dried and evaporated and the residue was recrystallised from ethanol, to give benzo[c]cinnoline *N-oxide* (44 mg., 88%), m. p. 136° (lit., m. p. 141°), mixed m. p. 138—140°.

(ii) The above procedure was repeated, with benzo[f]naphtho[2,1-*c*]cinnoline (70 mg.) and benzo[h]naphtho[1,2-*c*]cinnoline (70 mg.) and sodium perborate (38 mg.). The cinnoline picrate had m. p. 245° (lit., for benzo[h]naphtho[1,2-*c*]cinnoline hemipicrate, m. p. 245°) (yield 65 mg., 67%). The cinnoline *N-oxide* had m. p. 250—252° (lit., for benzo[f]naphtho[2,1-*c*]cinnoline *N-oxide*, m. p. 252.5°) (yield 70 mg., 94%).

THE UNIVERSITY, READING.

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<sup>19</sup> Sako, *Mem. Coll. Eng., Kyushu Univ.*, 1932, 6, 327.