849. *Polycyclic Cinnoline Derivatives. Part XII.*[1] *The Nitration of Benzo*[c]*cinnoline, its Oxide, and Some Methyl Derivatives.*

By J. F. Corbett, P. F. Holt, and (Mrs.) M. L. Vickery.

Benzo[*c*]cinnoline and 1-nitrobenzo[*c*]cinnoline yield the same 1,10-dinitrobenzo[*c*]cinnoline. Mononitration of benzo[*c*]cinnoline 5-oxide gives two isomeric 4-nitro-derivatives (probably the 5- and the 6-oxide) as the major products and the 1 nitro-derivative as minor product. 3,8-Dimethylbenzo[*c*]cinnoline 5-oxide gives only the 4-nitro-5-oxide, and 2,9-dimethylbenzo[*c*]cinnoline 5-oxide gives only the 1-nitro-5-oxide. Amines corresponding to these nitro-compounds are described.

Mononitration of benzo[*c*]cinnoline gives the 1-nitro-derivative as the major and the 4-nitro-derivative as the minor isomer.[1] Treating benzo[*c*]cinnoline with an excess of nitric acid in sulphuric acid at room temperature yielded a dinitrobenzo[*c*]cinnoline, m. p. 270°, as the main product together with a small amount of 4-nitrobenzo[*c*]cinnoline (identified by reduction to the known 4-amine). Apparently the dinitration of benzo[*c*]-cinnoline yields the 1- and the 4-nitro-isomer initially and further nitration affects the 1-nitro-isomer exclusively, giving a 1,10-dinitrobenzo[*c*]cinnoline. This was confirmed when 4-nitrobenzo[*c*]cinnoline was not further nitrated under the same conditions, while the 1-nitro-compound gave this 1,10-dinitrobenzo[*c*]cinnoline. The structure of the dinitro-derivative follows from its reduction to 1,10-diaminobenzo[*c*]cinnoline, identified by its ultraviolet absorption spectra.

King and King [2] treated benzo[*c*]cinnoline 5-oxide with fuming nitric acid at 80—90° and obtained two products, which they converted into aminocarbazoles. They concluded

[1] Part XI, *J.*, 1962, December issue.
[2] King and King, *J.*, 1945, 824.

that the major product was 2-nitro- and the minor 3-nitro-oxide. Calderbank and Le Fèvre [3] found, however, that the dipole moment of the major isomer pointed to 3-nitrobenzo[*c*]cinnoline 6-oxide. Arcos, Arcos, and Miller [4] found that the substance contained 19·4% of nitrogen which, they stated, corresponded to a dinitrobenzo[*c*]cinnoline dioxide. However this value corresponds more nearly to a mono-oxide (N, 19·6%) than a dioxide (N, 18·5%).

By reducing the minor product we obtained 4-aminobenzo[*c*]cinnoline, so the minor product must be 4-nitrobenzo[*c*]cinnoline 5-oxide. Since the major product, the dinitro-compound, is evidently formed by the further nitration of this product and has a dipole moment equivalent to that of 3-nitrobenzo[*c*]cinnoline 5-oxide, it must be 1,7(or 2,4)-dinitrobenzo[*c*]cinnoline 6(or 5)-oxide. Orientation of the nitro-groups in the 1,7-positions is more probable since the second nitro-group would probably enter the unsubstituted ring.

Arcos, Arcos, and Miller [4] also mononitrated benzo[*c*]cinnoline 5-oxide with nitric acid in sulphuric acid at 70—80°. The resulting nitro-oxide was reduced to the 4-amine. We found that the crude nitration product, on reduction, gave also a small amount of the 1-amine (in the ratio 1 : 8). Use of fuming nitric acid gives a (?1,7-)dinitro-derivative as major product and 4-nitrobenzo[*c*]cinnoline oxide as minor product. The latter was separated into two isomers, presumably the 5- and the 6-oxide.

Mononitration of 3,8-dimethylbenzo[*c*]cinnoline gives only the 4-nitro-derivative.[1] Under similar conditions, 3,8-dimethylbenzo[*c*]cinnoline 5-oxide gave a single product, which was reduced to the 4-amine; the nitration product must then be 3,8-dimethyl-4-nitrobenzo[*c*]cinnoline 5-oxide.

2,9-Dimethylbenzo[*c*]cinnoline gives only the 1-nitro-derivative on mononitration. The oxide under similar conditions gave 2,9-dimethyl-1-nitrobenzo[*c*]cinnoline 5-oxide, identified by reduction to the known 1-amine.

The results suggest that the activation by *N*-oxygen is greater in the 4- or 7-position of benzo[*c*]cinnoline than the 1- or 10-position and is accentuated by 3- and 8-methyl groups; but 2- and 9-methyl groups activate positions 1 and 10.[1] Evidently activation by methyl groups is greater than by *N*-oxygen since 2,9-dimethylbenzo[*c*]-cinnoline 5-oxide is nitrated at position 1.

Experimental

Nitration of Benzo[c]*cinnoline.*—Benzo[*c*]cinnoline (0·6 g.) was dissolved in 1 : 1 nitric acid (*d* 1·5)–sulphuric acid (15 ml. each) and left at room temperature for 24 hr., then poured on ice. The product was dissolved in benzene and filtered through alumina. Crystallisation gave a brown powder, m. p. 209°, which, after repeated crystallisation from ethanol gave green-yellow crystals of 1,10-*dinitrobenzo*[c]*cinnoline* (0·52 g.), m. p. 270° (Found: C, 53·3; H, 2·2; N, 20·7. $C_{12}H_6N_4O_4$ requires C, 53·4; H, 2·2; N, 20·7%). Evaporation of the mother-liquor and recrystallisation of the product gave a substance, m. p. 220—225°, which could not be further purified by recrystallisation. It was shaken in ethanol (100 ml.) with platinum oxide (0·1 g.) and hydrogen at atmospheric pressure and room temperature until gas ceased to be absorbed, and then filtered. Evaporation gave a product which was dissolved in benzene, filtered through alumina, and crystallised. Recrystallisation from ethanol gave an amine (5 mg.), m. p. 197—199°, which gave a blue colour with 0·1M-hydrochloric acid, as does 4-aminobenzo[*c*]cinnoline (m. p. 198—200°).

The dinitrobenzo[*c*]cinnoline (0·4 g.) was similarly reduced and the product purified, giving an amine (0·26 g.), m. p. 217—218°, which in ethanol and 0·1M-hydrochloric acid gave spectra identical with those given by 1,10-diaminobenzo[*c*]cinnoline, m. p. 217—221°.

Nitration of 1-*Nitrobenzo*[c]*cinnoline.*—1-Nitrobenzo[*c*]cinnoline (0·1 g.) was kept in 1 : 1 nitric acid (*d* 1·5)–sulphuric acid (2·5 ml. each) at room temperature for 24 hr. The solid product

[3] Calderbank and Le Fèvre, *J.*, 1951, 649.
[4] Arcos, Arcos, and Miller, *J. Org. Chem.*, 1956, **21**, 651.

obtained by pouring the solution on ice was recrystallised twice from ethanol, to give 1,10-dinitrobenzo[*c*]cinnoline (84 mg.), m. p. and mixed m. p. 270°.

Attempted nitration of 4-nitrobenzo[*c*]cinnoline as described above gave only recovered starting material.

Mononitration of Benzo[c]*cinnoline Oxide.*—The oxide (2·0 g.) in sulphuric acid (20 ml.) was treated with nitric acid (*d* 1·42; 0·65 ml.) in sulphuric acid (7·5 ml.). The solution was kept at 60—70° for 2 hr. and then poured on ice. The product was washed, dried, and recrystallised from benzene (500 ml.). The first crop of crystals was recrystallised twice from dimethylformamide to give 4-*nitrobenzo*[c]*cinnoline 5-oxide*, m. p. 255° (Found: C, 58·6; H, 2·8; N, 17·3. $C_{12}H_7N_3O_3$ requires C, 59·7; H, 2·9; N, 17·4%). Catalytic reduction as above gave 4-aminobenzo[*c*]cinnoline, m. p. and mixed m. p. 198°. Evaporation of the mother-liquor followed by repeated recrystallisation from pyridine–ethanol gave a product, m. p. 210—214°. All crops of this impure material were mixed and catalytically reduced as above to a product which, on fractional crystallisation, gave 4-, m. p. and mixed m. p. 198°, and 1-aminobenzo[*c*]-cinnoline, m. p. and mixed m. p. 167°.

Nitration of Benzo[c]*cinnoline 5-Oxide with an Excess of Nitric Acid.*—The oxide (2·5 g.) in nitric acid (*d* 1·5; 15 ml.) was heated to 80° for 3 hr., then poured into water, and the solid product recrystallised from acetic acid (300 ml.) to give a yellow powder, m. p. 245—250°. Recrystallisation from aqueous dimethylformamide gave a (?1,7)-*dinitrobenzo*[c]*cinnoline 5-oxide* as pale yellow needles, m. p. 278—279° (Found: C, 50·15; H, 2·2; N, 19·5. $C_{12}H_6N_4O_5$ requires C, 50·4; H, 2·1; N, 19·6%). The acetic acid was evaporated from the mother-liquor, and the residue recrystallised from ethanol to give a 4-nitrobenzo[*c*]cinnoline oxide, m. p. 230—231° (King and King give m. p. 226° for their " 2-isomer "). Catalytic reduction gave 4-aminobenzo[*c*]cinnoline, m. p. and mixed m. p. 196—198°.

Catalytic reduction of the dinitro-compound gave a diaminobenzo[*c*]cinnoline, m. p. 242—243° (picrate m. p. 265°) (King and King give m. p. 243°, picrate m. p. 265°, for their " 3-isomer ").

Nitration of 2,9-*Dimethylbenzo*[c]*cinnoline 5-Oxide.*—This oxide (0·2 g.) was left in nitric acid (*d* 1·5; 56 mg.) and sulphuric acid (10 ml.) at room temperature for 30 min., then poured on ice, and the product was recrystallised from benzene and then from acetone to give 2,9-*dimethyl*-1-*nitrobenzo*[c]*cinnoline 5-oxide* (0·17 g.), m. p. 213°, as pale yellow needles (Found: C, 62·1; H, 4·3; N, 15·7. $C_{14}H_{11}N_3O_3$ requires C, 62·5; H, 4·1; N, 15·6%). Catalytic reduction gave 1-amino-2,9-dimethylbenzo[*c*]cinnoline, m. p. and mixed m. p. 242—243° (pink colour with 0·1M-hydrochloric acid).

Nitration of 3,8-*Dimethylbenzo*[c]*cinnoline 5-Oxide.*—This oxide (0·2 g.) was treated as described above for the 2,9-dimethyl isomer; it gave pale yellow 3,8-*dimethyl*-4-*nitrobenzo*[c]-*cinnoline 5-oxide* (0·15 g.), m. p. 282° (Found: C, 62·6; H, 4·2; N, 15·0%). Catalytic reduction gave 4-amino-3,8-dimethylbenzo[*c*]cinnoline, m. p. and mixed m. p. 173—174° (blue colour in 0·1M-hydrochloric acid).

One of the authors (M. V.) acknowledges a grant from Imperial Chemical Industries Limited, Paints Division. The spectrophotometer was purchased with a grant from the Department of Scientific and Industrial Research.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
READING, BERKS.

[*Received, April 9th,* 1962.]