248. *Benzo*[c]*cinnolines. Part II.*[1] *The Synthesis and Reactions of some Benzo*[c]*cinnoline Oxides.*

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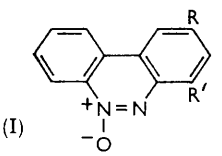
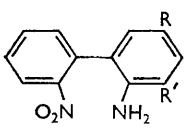
One of the products from the nitration of benzo[*c*]cinnoline oxide is shown to be 4-nitrobenzo[*c*]cinnoline 6-oxide by synthesis of its reduction product, 4-aminobenzo[*c*]cinnoline 6-oxide. Attempts to prepare 4-nitrobenzo[*c*]-cinnoline 6-oxide by the cyclisation of 2-amino-3,2′-dinitrobiphenyl failed, although 2-amino-5,2′-dinitrobiphenyl cyclises readily to give 2-nitrobenzo[*c*]-cinnoline 6-oxide. The preparation of 4-bromobenzo[*c*]cinnoline is described; on *N*-oxidation it gives only the 6-oxide.

In a previous Paper [1] the nitration of benzo[*c*]cinnoline oxide (I; R = R′ = H) with nitric acid was shown to give mainly 2-nitrobenzo[*c*]cinnoline 6-oxide (I; R = NO_2, R′ = H), while with nitric and sulphuric acids a mixture of two different mononitro-oxides was obtained. These were a 1- and a 4-nitrobenzo[*c*]cinnoline oxide, respectively, and the latter is now found to be 4-nitrobenzo[*c*]cinnoline 6-oxide, although Corbett, Holt, and Vickery [2] had assumed it to be the 5-oxide.

Nitration of 2-acetamido-2′-nitrobiphenyl in acetic acid containing acetic anhydride, and subsequent hydrolysis, gave 2-amino-3,2′-dinitrobiphenyl (II; R = H, R′ = NO_2), while nitration with ethyl nitrate in sulphuric acid gave 2-acetamido-5,2′-dinitrobiphenyl which was hydrolysed to the corresponding amine (II; R = NO_2, R′ = H). Deamination of both amines gave 2,3′-dinitrobiphenyl.



(I)



(II)

Muth *et al.*[3] prepared benzo[*c*]cinnoline oxide by the cyclisation of 2-amino-2′-nitrobiphenyl with hot methanolic sodium hydroxide, and the method has been extended to the preparation of 2-bromobenzo[*c*]cinnoline 6-oxide.[1,4] Low yields of 2-nitrobenzo[*c*]-cinnoline 6-oxide could be obtained from 2-amino-5,2′-dinitrobiphenyl by this method, but the product was destroyed on prolonged exposure to the base. With benzyltrimethyl-ammonium hydroxide, however, cyclisation took place smoothly and in high yield. The presence of a nitro-group adjacent to the amino-group apparently inhibits the reaction, for 2-amino-3,2′-dinitrobiphenyl failed to cyclise to 4-nitrobenzo[*c*]cinnoline 6-oxide (I; R = H, R′ = NO_2) under a variety of conditions and with various bases.

Attempts were then made to effect reductive cyclisation of 2-amino-3,2′-dinitrobiphenyl (II; R = H, R = NO_2) to 4-aminobenzo[*c*]cinnoline 6-oxide (I; R = H, R′ = NH_2), a compound obtainable by the selective reduction of (I; R = H, R = NO_2 Reduction of (II; R = H, R′ = NO_2) with hydrazine in the presence of Raney nickel gave 4-aminobenzo[*c*]cinnoline with loss of the oxide function, but reduction with sodium hydrosulphide gave (I; R = H, R′ = NH_2), identical with the compound obtained by reduction of the nitration product, m. p. 259—260°, from benzo[*c*]cinnoline oxide.[1]

In connection with studies of the bromination of benzo[*c*]cinnoline oxide, 4-amino-[*c*]cinnoline 6-oxide has been converted into 4-bromobenzo[*c*]cinnoline 6-oxide (I; R = H, R′ = Br) by the Sandmeyer reaction, a reaction which fails with 4-aminobenzo[*c*]cinnoline

[1] The paper by Barton and Cockett, *J.*, 1962, 2454, is regarded as Part I.
[2] Corbett, Holt, and Vickery, *J.*, 1962, 4384.
[3] Muth, Abraham, Linfield, Wotring, and Pacofsky, *J. Org. Chem.*, 1960, **25**, 736.
[4] Corbett and Holt, *J.*, 1961, 5029.

under these conditions. Reduction of (I; R = H, R′ = Br) with stannous chloride gave 4-bromobenzo[*c*]cinnoline.

Steric inhibition of *N*-oxidation has been observed in benzo[*c*]cinnolines having bromine atoms at positions 4 and 7.[4] The oxidation of 4-bromobenzo[*c*]cinnoline is in keeping with these findings; with hydrogen peroxide in acetic acid the 6-oxide was obtained in high yield.

Experimental

2-*Acetamido*-5,2′-*dinitrobiphenyl*.—A solution of 2-acetamido-2′-nitrobiphenyl (4·25 g.) in sulphuric acid (27 ml.) was cooled and stirred while ethyl nitrate (1·55 ml.) was added dropwise, the temperature being kept below −1°. After 1 hr. the solution was poured into ice–water and the precipitate collected. Chromatography on alumina in benzene–chloroform gave 2-acetamido-5,2′-dinitrobiphenyl (3·0 g., 60%) as pale yellow needles, m. p. 141—142° (from ethanol) (Found: C, 55·8; H, 3·9; N, 14·1. $C_{14}H_{11}N_3O_5$ requires C, 55·8; H, 3·7; N, 13·9%).

2-*Amino*-5,2′-*dinitrobiphenyl*.—A solution of the acetamido-compound (0·2 g.) in hydrochloric acid (5 ml.) and ethanol (5 ml.) was refluxed for 4 hr., then diluted with water, and cooled. The amine (0·15 g., 87%) formed yellow needles (from aqueous ethanol), m. p. 173—174° (lit.,[5] 170°).

2-*Amino*-3,2′-*dinitrobiphenyl*.—2-Amino-2′-nitrobiphenyl (6·3 g.), in acetic acid (6 ml.) and acetic anhydride (12·75 ml.), was warmed on a water-bath for 15 min.; the solution was cooled to 20—25° and stirred while a mixture of nitric acid (2 ml.; *d* 1·5) and acetic acid (2·5 ml.) was added dropwise. After being stirred overnight at room temperature, the solution was poured into ice–water. The crude product separated as an oil and was hydrolysed as for the 5-nitro-isomer above. The resulting oil, in benzene, was chromatographed on alumina, giving the amine (2·5 g., 33%) as deep yellow needles, m. p. 146—148° (from ethanol) (Found: C, 55·9; H, 3·7; N, 15·9. $C_{12}H_9N_3O_4$ requires C, 55·6; H, 3·5; N, 16·2%). Deamination of the amine (0·7 g.), using a method similar to that for the deamination of 4-acetamido-3,4′-dibromobiphenyl,[6] gave 2,3′-dinitrobiphenyl (0·35 g., 53%), m. p. and mixed m. p. 119—120°.

2-*Nitrobenzo*[c]*cinnoline* 6-*Oxide*.—2-Amino-5,2′-dinitrobiphenyl (0·1 g.) in ethanol (3 ml.) was treated with benzyltrimethylammonium hydroxide (2 ml. of a 40% aqueous solution). After 10 min., the precipitate was collected and washed with ethanol; it had m. p. 245—260° (decomp.) (0·085 g., 93%). Recrystallisation from acetic acid gave 2-nitrobenzo[*c*]cinnoline 6-oxide, m. p. 274—276° (decomp.), identical with a sample obtained from the nitration of benzo[*c*]cinnoline oxide.[1]

By similar methods, 2-amino-2′-nitrobiphenyl and 2-amino-5-bromo-2′-nitrobiphenyl gave benzo[*c*]cinnoline oxide and 2-bromobenzo[*c*]cinnoline 6-oxide, in yields of 92 and 96%, respectively.

4-*Aminobenzo*[c]*cinnoline* 6-*Oxide*.—(*a*) A solution of sodium sulphide nonahydrate (0·6 g.) and sodium hydroxide (0·12 g.) in water (1 ml.) was added to a refluxing solution of 2-amino-3,2′-dinitrobiphenyl (0·3 g.) in ethanol (6 ml.). Crystalline material gradually separated, and after 2 hr. the solution was diluted and refrigerated. The precipitate (0·22 g., 90%) yielded 4-aminobenzo[*c*]cinnoline 6-oxide as orange needles (from ethanol), m. p. 222—223° (decomp.) (Found: C, 68·2; H, 4·3; N, 19·9. $C_{12}H_9N_3O$ requires C, 68·3; H, 4·3; N, 19·9%), $\lambda_{max.}$ (in EtOH) 230, 255, 329, 364, 384, and 463 mμ (log ε 4·49, 4·52, 4·35, 4·02, 3·96, and 3·84). The acetyl derivative was obtained as yellow leaflets (from ethanol), m. p. 245—247° (Found: C, 66·3; H, 4·35; N, 16·4. $C_{14}H_{11}N_3O_2$ requires C, 66·5; H, 4·35; N, 16·6%).

(*b*) Reduction of the 4-nitrobenzo[*c*]cinnoline oxide of m. p. 259—260° [1] (2·5 g.), using the method previously described for the reduction of 2-nitrobenzo[*c*]cinnoline 6-oxide to the amino-*N*-oxide,[1] and purification through the acetyl derivative, gave the amine (1·3 g., 59%), m. p. 222—223° (decomp.), identical with that obtained by method (*a*).

4-*Bromobenzo*[c]*cinnoline* 6-*Oxide*.—4-Aminobenzo[*c*]cinnoline 6-oxide (1 g.) in 47% hydrobromic acid (4 ml.) and water (10 ml.) was diazotised with sodium nitrite (0·35 g.) in water (3 ml.). The solution was added to cuprous bromide (5 g.) in 47% hydrobromic acid (10 ml.) at 0°. After 10 min., the resulting brown paste was warmed on a water-bath until the evolution

[5] Corbett, Holt, and Vickery, *J.*, 1962, 4860.
[6] Baker, Barton, and McOmie, *J.*, 1958, 2658.

of nitrogen ceased. The mixture was cooled, neutralised with dilute ammonia, and filtered. The solid was collected and then stirred with several portions of ammonia (*d* 0·88)–water (1 : 1) and benzene. The benzene extracts were concentrated, and diluted with hexane, giving 4-bromobenzo[*c*]cinnoline 6-oxide (0·85 g., 65%), m. p. 230—232°. Vacuum sublimation at 180—200°/15 mm., and recrystallisation from ethanol, gave pale yellow needles, m. p. 234—235° (Found: C, 52·6; H, 2·8; N, 10·2. $C_{12}H_7BrN_2O$ requires C, 52·6; H, 2·55; N, 10·0%), $\lambda_{max.}$ (in EtOH) 244, 250, 258, 289, 298 (infl.), and 350 mμ (log ε 4·59, 4·59, 4·59, 4·26, and 4·18).

4-*Bromobenzo*[c]*cinnoline.*—4-Bromobenzo[*c*]cinnoline 6-oxide (0·5 g.) and stannous chloride dihydrate (1 g.), in hydrochloric acid (10 ml.) and ethanol (10 ml.), were warmed on a water-bath for 30 min. The resultant clear solution was vacuum-evaporated, and the residue was washed with water. Vacuum sublimation at 160°/15 mm. and crystallisation from ethanol gave 4-bromobenzo[*c*]cinnoline (0·37 g., 80%) as yellow needles, m. p. 199—200° (Found: C, 55·5; H, 2·9; N, 10·8. $C_{12}H_7BrN_2$ requires C, 55·6; H, 2·7; N, 10·8%), $\lambda_{max.}$ (in EtOH) 207, 250, 320, and 362 mμ (log ε 4·61, 4·66, 4·26, and 3·53).

Oxidation of 4-*Bromobenzo*[c]*cinnoline.*—4-Bromobenzo[*c*]cinnoline (0·1 g.), acetic acid (1 ml.), and 30% hydrogen peroxide (0·1 ml.) were heated at 80° for 3 hr. On cooling, 4-bromobenzo[*c*]cinnoline 6-oxide crystallised as pale yellow needles (0·094 g., 89%), m. p. 233—235°, identical with that obtained above.

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