1305. *Polycyclic Cinnoline Derivatives. Part XVI.*[1] *Nitration of Benzo*[h]*naphtho*[1,2-c]*cinnoline*

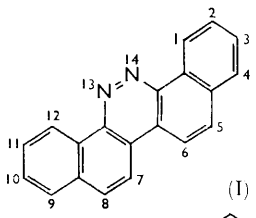
By P. F. Holt and A. E. Smith

Nitration of benzo[*h*]naphtho[1,2-*c*]cinnoline gives the 1,10- and 1,12-dinitro-derivatives. Corresponding diamines and a dibromo-derivative were prepared. The positions of substitution were determined by infrared and ultraviolet spectroscopy. The cyclisation of 3,3′-dibromo-2,2′-azonaphthalene gives 2,5-dibromobenzo[*f*]naphtho[2,1-*c*]cinnoline. The attempted cyclisation of some dinitro-2,2′-azonaphthalenes and some dinitro- and dibromo-1,1′-azonaphthalenes is reported. The mechanism of cyclisation of azo-compounds with aluminium chloride is discussed.

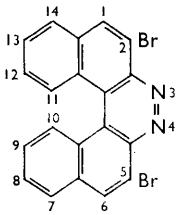
Braithwaite and Holt [2] isolated one dinitro-derivative as a product of nitration of benzo[*h*]naphtho[1,2-*c*]cinnoline (I) but they did not determine the positions of the nitro-groups. As products of the nitration of the cinnoline (I) with fuming nitric acid at room temperature we have isolated two dinitro-derivatives. The minor product crystallises

[1] Part XV, P. F Holt and A. E. Smith, *J.*, 1964, 6095.
[2] R. S. W. Braithwaite and P. F. Holt, *J.*, 1959, 3025.

first from the nitration mixture. That which separates later appears to be identical with the dinitro-compound obtained by Braithwaite and Holt.



(I)



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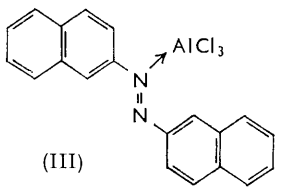

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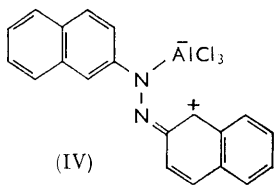

(IV)

These two dinitro-compounds have been reduced to diamines one of which was converted by a Sandmeyer reaction into the dibromo-compound.

Braithwaite and Holt deduced that nitration of the cinnoline (I) occurred in the outer rings. The protonated azo-group would deactivate positions 2, 4, 5, 8, 9, and 11 towards attack by the nitronium ion and, on these grounds, the positions 1, 3, 6, 7, 10, and 12 must be regarded as possible sites of attack.

Chemical evidence and ultraviolet and infrared absorption spectra allow the structures of these dinitro-compounds to be established as 1,10-dinitro-, identical with the derivative described by Braithwaite and Holt, and 1,12-dinitro-benzo[*h*]naphtho[1,2-*c*]cinnolines.

TABLE 1

Spectra ($\nu_{max.}$ in cm.$^{-1}$) for some benzo[*h*]naphtho[1,2-*c*]cinnoline derivatives and a benzo[*f*]naphtho[2,1-*c*]cinnoline

Compound	1 900—800	2 860—800	3 810—770	4 770—735
Benzo[*h*]naphtho[1,2-*c*]cinnoline	—	810s	—	747s
,, *N*-oxide	—	810s	—	747s
1,10-(β)-$(NO_2)_2$	—	832s	805s	757m (nitro?)
1,10-(β)-$(NH_2)_2$	—	820s	787s	—
1,10-(β)-Br_2	—	833m, 820m	807m, 790m	—
1,12-(α)-$(NO_2)_2$	—	808s	—	758m (nitro?)
1,12-(α)-$(NH_2)_2$	—	830m	800s, 790m	—
2,5-Dibromobenzo[*f*]naphtho[2,1-*c*]cinnoline	885m	—	—	750s

Infrared spectra. The spectra of dibromo- and diamino-compounds (Table 1) derived from the two dinitro-derivatives showed no prominent peaks in the region 770—735 cm.$^{-1}$ (4 adjacent CH groups). Strong absorption peaks in this region are features of the spectra of the cinnoline (I) and its oxide and there are peaks due to nitro-groups in the spectra of the dinitro-derivatives. In these compounds, therefore, both the outer rings are substituted. The three possible orientations are then 1,10, 3,10, and 1,12.

Both dinitro-compounds and their derivatives show absorption peaks in the region 860—800 (2 adjacent CH groups) and 810—770 (3 adjacent CH groups), but not in the region 900—860 cm.$^{-1}$ (lone CH groups). This eliminates the 3,10-derivatives which have only lone and paired adjacent methine groups.

Ultraviolet spectra. The spectrum of the cinnoline (I) in ethanol has the usual group I, II, and III bands and a long-wavelength band of lower intensity due to n–π^* transitions.

The spectra of the two diamines in ethanol (Table 2) are similar to one another but differ from that of the parent cinnoline in that a bathochromic shift of the group I band obliterates the group II band. The long-wavelength bands attributed to n–π^* transitions

TABLE 2

Values of $\lambda_{max.}$ (mμ) and (log ε) for some diaminobenzo[*h*]naphtho[1,2-*c*]cinnolines in various solvents

Amino-groups	Solvents			Group I				Group II	Group III	Long wavelength band
			β′				α′			
None	Ethanol	236s (4·6)	242 (4·7)	250 (4·8)	283s (4·6)	288 (4·7)	312 (4·2)	350 (4·2)	373s (3·7)	405
	2N-HCl	—	—	248 (4·6)	—	298 (4·5)	—	441 (4·0)		—
1,12-$(NH_2)_2$	Ethanol	238 (4·5)	—	257 (4·6)	275 (4·3)	306 (4·4)	—	—	—	414 (3·5)
	0·1N-HCl	230 (4·4)	—	263 (4·3)	—	294 (4·5)	304s (4·4)	337 (3·8)	—	—
	80% H_2SO_4	236 (4·4)	249 (4·3)	261s (4·5)	—	300 (4·4)	308s (4·0)	401 (4·0)	433 (3·6)	—
1,10-$(NH_2)_2$	Ethanol	—	—	271 (4·5)	—	305 (4·2)	—	—	—	408 (3·7)
	0·1N-HCl	—	243s (4·5)	250 (4·5)	—	287 (4·4)	309s (4·1)	360 (3·9)	—	415 (3·3)
	80% H_2SO_4	—	243s (4·5)	248 (4·5)	—	299 (4·5)	—	448 (4·0)	—	—

s = Shoulder.

occur at 414 and 408 mμ for the 1,12- and 1,10-diamines, respectively, as compared with 405 mμ for the parent cinnoline. The spectra of both diamines in 80% sulphuric acid (Figure 1) are similar in that they show peaks near the region 250—260 mμ and the group I band at 300 mμ. These values are similar to those given by the parent cinnoline in 2N-hydrochloric acid. The group II band of the 1,10-diamine in 80% sulphuric acid is similar in position and shape to that of the cinnoline (I) in 2N-hydrochloric acid. That of the 1,12-diamine occurs at a much shorter wavelength, the hypsochromic shift being −47 mμ.

Protonation of the diaza-group in other polycyclic cinnolines results in large bathochromic shifts of the group II band; for example protonation of benzo[c]cinnoline results in a shift of +48 mμ and of benzo[*f*]naphtho[2,1-*c*]cinnoline of +71 mμ. Protonation of benzo[*h*]naphtho[1,2-*c*]cinnoline results in a shift in the group II band of +91 mμ. It would appear, then, that the diaza-group of the 1,10-diamine of the cinnoline (I) is protonated and that of the 1,12-diamine is not protonated in 80% sulphuric acid. The reason for this is obvious from a comparison of molecular models. Amino-groups in the 1 and 12 positions, even if unprotonated, leave no room for an additional proton on the diaza-group. The 1,10-diamine can be protonated at position 13 only.

The spectrum of 1,10-diaminobenzo[*h*]naphtho[1,2-*c*]cinnoline in 0·1N-hydrochloric acid (Figure 2) closely resembles that of the 1,12-diamine in 80% sulphuric acid; the 1,10-derivative in 0·1N-hydrochloric acid must then be diprotonated at the amine groups and the diaza-group is not protonated. 1-Amino-, 2-amino-, 3-amino-, 4-amino-, 1,10-diamino-, 2,9-diamino-, and 3,8-diaminobenzo-[*c*]cinnoline [3] and 2,7-diaminobenzo[*c*]cinnoline [4] in 0·1N-hydrochloric acid have been shown to be protonated at the diaza-group and not at the amine groups. 1,12-Diaminobenzo[*h*]naphtho[1,2-*c*]cinnoline in 0·1N-hydrochloric acid is presumably monoprotonated at one amine group since the absorption curve differs from that of the diamine in ethanol and in 80% sulphuric acid. The spectrum of the monoprotonated 1,12-diamine shows shifts in the group I and II bands, relative to

[3] J. F. Corbett, P. F. Holt, A. N. Hughes, and M. Vickery, *J.*, 1962, 1812.
[4] R. Oakland, private communication.

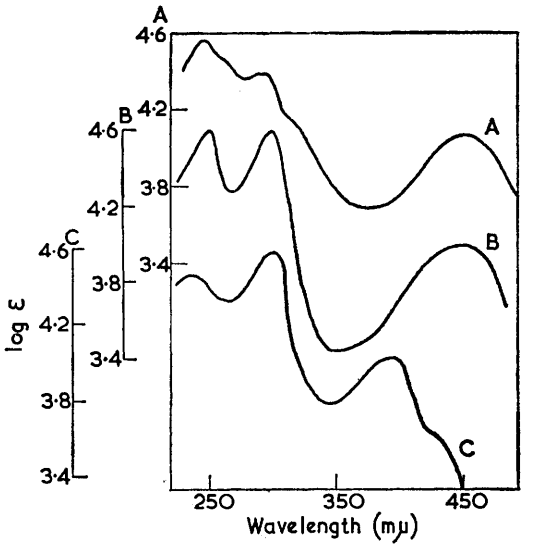

FIGURE 1. Ultraviolet spectra of benzo[*h*]-naphtho[1,2-*c*]cinnoline (A) and its 1,10-diamino- (B) and 1,12-diamino-derivatives (C) in 80% sulphuric acid

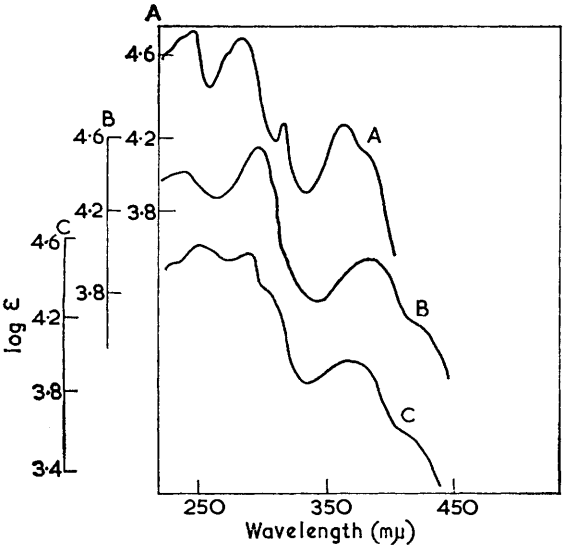

FIGURE 2. Ultraviolet spectra of benzo[*h*]-naphtho[1,2-*c*]cinnoline (A) and its 1,12-diamino- (B) and 1,10-diamino-derivatives (C).

Solvents: (A) ethanol, (B) 80% sulphuric acid, (C) 0·1N-hydrochloric acid

the cinnoline (I), of 6 and 27 mμ, respectively; the corresponding shifts of the diprotonated diamine have approximately double these values (12 and 51 mμ, respectively).

Dinitro-derivatives. The spectra of the two dinitro-derivatives are very similar in shape, but deviate slightly in the positions of the peak (Table 3). The group I band is shifted hypsochromically by 10 and 12 mμ in the 1,12- and 1,10-derivatives, respectively, relative to that of the cinnoline (I). This band is broadened and decreased in intensity.

TABLE 3

Values of $\lambda_{max.}$ (mμ) and (log ε) for some benzo[*h*]naphtho[1,2-*c*]cinnoline derivatives in chloroform

Subst.	Group I		δλ	Group II			δλ	Group III			δλ
None	285s (4·65)	290 (4·7)	—	314 (4·2)	350 (4·2)	369s (4·1)	—	—	—	378	—
N-Oxide	285s (4·65)	290 (4·75)	0	314 (4·25)	352 (4·15)	369s (4·0)	0	378 (3·4)	402 (3·4)	426 (3·4)	48
1,12-$(NO_2)_2$ ...	—	280 (4·6)	−10	334s (4·25)	350 (4·3)	366 (4·1)	−2	—	—	—	—
1,10-$(NO_2)_2$ ...	—	278 (4·6)	−12	331 (4·25)	346 (4·3)	—	−4	—	—	—	—
1,10-Br_2.....	—	294 (4·65)	4	317 (4·1)	355 (4·15)	372 (4·05)	3	—	—	—	—

The group II band is also broadened and increased slightly in intensity. There is a hypsochromic shift of 2 mμ in the case of the 1,12-derivative and this band shifts by 4 mμ hypsochromically in the 1,10-derivative. The group III band disappears under the broadening of the group II band in both cases.

The dibromo-derivative. The 1,10-dibromo-derivative of compound (I) gives small bathochromic shifts of group I and II bands which is usually the case with bromo-derivatives of benzo[*c*]cinnoline [3] and benzo[*f*]naphtho[2,1-*c*]cinnoline.[1]

Chemical evidence of structure. Almost all cinnolines yield *N*-oxides when dissolved in acetic acid containing hydrogen peroxide. Neither 1,10-dinitro- nor 1,12-dinitro-benzo-[*h*]naphtho[1,2-*c*]cinnoline forms an oxide, indicating steric hindrance. Although models and spectral evidence indicate that there is distortion,[5] the *N* oxide of the cinnoline (I) has been prepared.

The very low solubility of both dinitro-derivatives in acetic and hydrochloric acids is probably due to the shielding of the diaza-groups by the nitro-groups. The 1,12-dinitro-compound is precipitated first from a nitration mixture even though formed in smallest yield, in agreement with the more efficient shielding of the diaza-group.

The smaller yield of the 1,12-dinitro-compound is in keeping with a sequence in which the nitrogen in position 13 is first protonated followed by nitration at position 1. Because of the proton at position 13, nitration at position 12 is hindered and nitration at position 10 occurs more readily.

Because of the inaccessibility of the parent cinnoline, and low yields of interaction products it was possible to obtain only small amounts of the nitro- and amino-derivatives. Slight contamination with tar could account for discrepancies in the analyses which were usually carried out on minimal amounts.

Cyclisation of azo-compounds. An attempt was made to prepare di-substituted derivatives of the cinnoline (I) by the cyclisation of corresponding disubstituted 1,1′-azonaphthalenes with aluminium chloride. No derivatives of 1,1′-azonaphthalene could be cyclised although 1,1′-azonaphthalene itself yields 10% of the cinnoline (I).[7] Only tars and green material were formed when 4,4′-dinitro-, 5,5′-dinitro-, 4,4′-dibromo-, and 5,5′-dibromo-1,1′-azonaphthalenes were treated with aluminium chloride. The method was also applied to several derivatives of 2,2′-azonaphthalene. 3,3′-Dibromo-2,2′-azonaphthalene gave 2,5-dibromobenzo[*f*]naphtho[2,1-*c*]cinnoline (II) but no cinnolines were isolated when the following were treated with aluminium chloride: 1,1′-dinitro-, 5,5′-dinitro-, 6,6′-dinitro-, and 8,8′-dinitro-2,2′-azonaphthalene.

Before cyclisation, an azo-compound must attain the *cis*-configuration. Badger, Drewer, and Lewis [6] found that the initial step in the cyclisation of azobenzene in sulphuric acid by irradiation was the conversion of *trans*- into *cis*-azobenzene, an equilibrium being established under the influence of light in which 45% of the azo-compound was in the *cis*-form. Cyclisation under the influence of aluminium chloride could involve resonance forms such as (III) and (IV), the latter permitting rotation about the diaza-link. Badger, Drewer, and Lewis isolated equal amounts of cinnoline and benzidine as reaction products in the cyclisation of azobenzene, the benzidine being derived from hydrazobenzene. 2,2′-Hydrazonaphthalene is unstable in acid conditions but we isolated a red substance which was shown by its infrared spectrum to have N–H links. It seems likely that the second stage in this cyclisation may also involve disproportionation; it cannot be the only mechanism, however, as yields up to 70% of the cinnoline have been obtained by this method.[7]

When cyclisation is induced with aluminium chloride using methylene chloride as solvent, hydrogen chloride is copiously evolved. This suggests that the reaction involves separation of a hydrogen atom from the α-position of the naphthalene ring which subsequently reacts with a methylene chloride molecule.

It seems likely that cyclisation occurs readily once the *cis*-form has been established. Under certain conditions which will probably give initially some of the *cis*-form of the azo-compound, some cinnoline derivative is formed: thus, 2-nitronaphthalene reduced with zinc dust and sodium hydroxide [8] gave benzo[*f*]naphtho[2,1-*c*]cinnoline as well as 2,2′-azonaphthalene and 2,2′-diamino-1,1′-binaphthyl, and reduced with sodium sulphide in

[5] J. F. Corbett, P. F. Holt, and A. N. Hughes, *J.*, 1961, 1363.
[6] G. M. Badger, R. J. Drewer, and G. E. Lewis, *Austral. J. Chem.*, 1963, **16**, 1042.
[7] P. F. Holt and C. W. Went, *J.*, 1963, 4099.
[8] J. Meisenheimer and K. Witte, *Ber.*, 1903, **36**, 4153.

sodium hydroxide it gave the cinnoline *N*-oxide and 2,2′-azoxynaphthalene. 1-Bromo-3-nitronaphthalene reduced with lithium aluminium hydride in ether gave [1] 1,6-dibromobenzo[*f*]naphtho[2,1-*c*]cinnoline as well as 4,4′-dibromo-2,2′-azonaphthalene.

Experimental

Nitration of benzo[h]*naphtho*[1,2-c]*cinnoline.* The cinnoline (I) (0·5 g.) was added in small amounts to ice-cold fuming nitric acid (5 ml.) and the solution was set aside. After a week a light yellow precipitate was collected and recrystallised from acetic acid. It was shown to be 1,12-*dinitrobenzo*[h]*naphtho*[1,2-c]*cinnoline* (50 mg.), m. p. >360° (Found: C, 63·2; H, 2·85; N, 15·6. $C_{20}H_{10}N_4O_4$ requires C, 64·6; H, 2·7; N, 15·0%). Succeeding crops of solid removed from the nitrating mixture were almost pure 1,10-dinitrobenzo[*h*]naphtho[1,2-*c*]-cinnoline (0·25 g.), m. p. >360°. Both isomers form yellow solutions in concentrated sulphuric acid.

Both dinitro-derivatives were reduced to the corresponding diamines with stannous chloride in concentrated hydrochloric acid. The 1,12-dinitro-isomer (100 mg.) gave 1,12-diaminobenzo-[*h*]naphtho[1,2-*c*]cinnoline (15 mg.); and the 1,10-dinitro-isomer (0·2 g.) gave 1,10-diamino-benzo[*h*]naphtho[1,2-*c*]cinnoline (0·1 g.), m. p. 261°.

Both amines form green-yellow solutions in concentrated sulphuric acid. The 1,12-diamino-derivative was not prepared in large enough quantity to permit a recrystallisation and analysis.

The 1,10-diamino-derivative was diazotised according to the method of Hodgson and Walker [9] to yield yellow plates from dimethylformamide of 1,10-*dibromobenzo*[h]*naphtho*[1,2-c]-*cinnoline* (15 mg.), m. p. 252° (Found: Br, 38·6. $C_{20}H_{10}Br_2N_2$ requires Br, 36·4%). This analysis was carried out on 2·2 mg. This compound forms a green solution in concentrated sulphuric acid.

Preparation of 2,5-*dibromobenzo*[f]*naphtho*[2,1-c]*cinnoline.* 3,3′-Dibromo-2,2′-azonaphthalene (0·5 g.) was cyclised in dry boiling methylene chloride (200 ml.) containing anhydrous aluminium chloride (5 g.) for 2 hr. according to the method of Holt and Went.[7] The reaction products were dissolved in chloroform, the resulting solution was passed through an alumina column. On elution with chloroform the first (orange) band was found to be starting material. The second yellow band was 2,5-*dibromobenzo*[f]*naphtho*[2,1-c]*cinnoline* (35 mg.), m. p. 287°, yellow crystals from dimethylformamide. Starting material (0·2 g.) was also obtained even though the reaction time was extended to 2 hr. (Found: C, 53·5; H, 2·55; Br, 36·6; N, 6·4. $C_{20}H_{10}Br_2N_2$ requires C, 54·9; H, 2·35; Br, 36·4; N, 6·4%). This compound forms a red-brown solution in concentrated sulphuric acid going to yellow on dilution.

The ultraviolet spectrum of compound (II) in chloroform showed the following peaks: Group I, 282 (ε 4·32), 321 (4·39); group II 339 (4·12); group III, 389 (3·30), 413 mμ (3·27).

The ultraviolet spectra were recorded on an Optica C.F.4 and the infrared spectra by a Perkin-Elmer Infracord, 137.

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The University, Reading, Berkshire. [*Received, May 19th,* 1965.]

[9] H. H. Hodgson and J. Walker, *J.*, 1933, 1620.