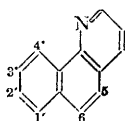


116. *The Orientation of Some Substitution Products of 7 : 8-Benzoquinoline.*

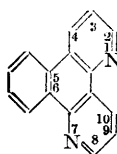
By J. A. BARLTROP and K. E. MACPHEE.

Nitration of 7 : 8-benzoquinoline yields four mononitro-derivatives, the structures of three of which have been proved by comparison with synthetic specimens of known orientation. The nature of the fourth isomer is established by inference.

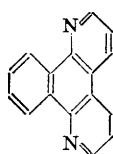
THE mono-nitration of 7 : 8-benzoquinoline (I) has been investigated sporadically for half a century. Claus and Imhoff (*J. pr. Chem.*, 1898, **57**, 68) isolated two nitro-derivatives, m. p. 151° (nitrate, m. p. 178°) and m. p. 138° (nitrate, m. p. 173°), and suggested that these were 5- and 6-nitro-7 : 8-benzoquinoline respectively. Haid (*Monatsh.*, 1906, **27**, 141), by a laborious fractionation, obtained four mononitro-7 : 8-benzoquinolines, m. p. 230°, 175°, 166°, and 155°.



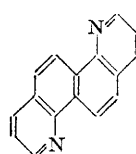
(I)



(II)



(III)



(IV)

He proved that the two most abundant isomers, of m. p. 230° and 175°, were substituted in the benzo-ring by reducing them to the corresponding amines and oxidising these to quinoline-7 : 8-dicarboxylic acid. Utermohlen and Hamilton (*J. Amer. Chem. Soc.*, 1941, **63**, 156), having performed a Skraup reaction on 4- and 5-nitro-1-naphthylamine, obtained 6- and 1'-nitro-7 : 8-benzoquinoline, m. p. 149° and 175° respectively, and suggested, without experimental evidence, that the latter was identical with Haid's isomer, m. p. 175°.

Data concerning the monoamino-7 : 8-benzoquinolines are rather more complete. I. G. Farbenind. (Fr. P. 796 601; *Chem. Abs.*, 1936, **30**, 6208) prepared 5-, 6-, 1'-, and 2'-amino-7 : 8-benzoquinoline from the corresponding 1-naphthylaminesulphonic acids by Skraup reactions followed by two-stage replacements of the sulphonic acid residues by amino-groups, and Schenkel and Schenkel (*Helv. Chim. Acta*, 1944, **27**, 1456) prepared 4'-amino-7 : 8-benzoquinoline by a similar method.

These data, collected in the table, lead to no certain conclusion as to the orientation of the nitration products of 7 : 8-benzoquinoline. The only apparent correlation is that between Haid's isomer, m. p. 175°, and 1'-nitro-7 : 8-benzoquinoline, but even this seems illusory since Haid reduced his product to an amine, m. p. 175°, whereas 1'-amino-7 : 8-benzoquinoline is reported to possess m. p. 192°.

In order to remove this obscurity, we set out to compare the four nitration products of (I) with synthetic specimens.

Ref.	M. p. of mononitro-isomers	M. p. of monoamino-isomers,		Ref.
		from NO ₂ -compound	by Skraup reaction	
1	{ 151° 138		{ 5-NH ₂ , 146° 6-NH ₂ , 118	4
2	{ 230 175 166 155	{ → 151° → 175°	{ 1'-NH ₂ , 192 2'-NH ₂ , ? 4'-NH ₂ , 85—86	
3	{ 6-NO ₂ , 149 1'-NO ₂ , 175			5

Refs.: (1) Claus and Imhoff, (2) Haid, (3) Utermohlen and Hamilton, (4) I. G. Farbenind., (5) Schenkel and Schenkel, *loc. cit.*

^a Ref. 2.

7 : 8-Benzoquinoline was nitrated according to Haid's directions (*loc. cit.*), but the isomers were separated by chromatography on alumina in ultra-violet light, the total yield of the mononitrobenzoquinolines being thus raised to 92%.

3-Nitro-1-naphthylamine (Hodgson, *J.*, 1943, 318) behaved anomalously under the conditions of the Skraup reaction: the only product isolated was 5 : 6-benzo-1 : 7-phenanthroline (II).

A Skraup reaction on 4-nitro-1-naphthylamine under the conditions described by Utermohlen and Hamilton (*loc. cit.*) and chromatographic analysis of the product gave 5 : 6-benzo-4 : 7-phenanthroline (III) and 6-nitro-7 : 8-benzoquinoline, m. p. 155°, identical with Haid's product of the same m. p. The ultra-violet absorption spectra of the two specimens also agree moderately well (see Fig. 1)—the deviations are probably caused by contamination of the synthetic compound by a minute amount of the phenanthroline (III). Reduction of the nitration product gave an amino-7 : 8-benzoquinoline, m. p. 117—118°. According to I. G. Farbenind. (*loc. cit.*), 6-amino-7 : 8-benzoquinoline has m. p. 118°.

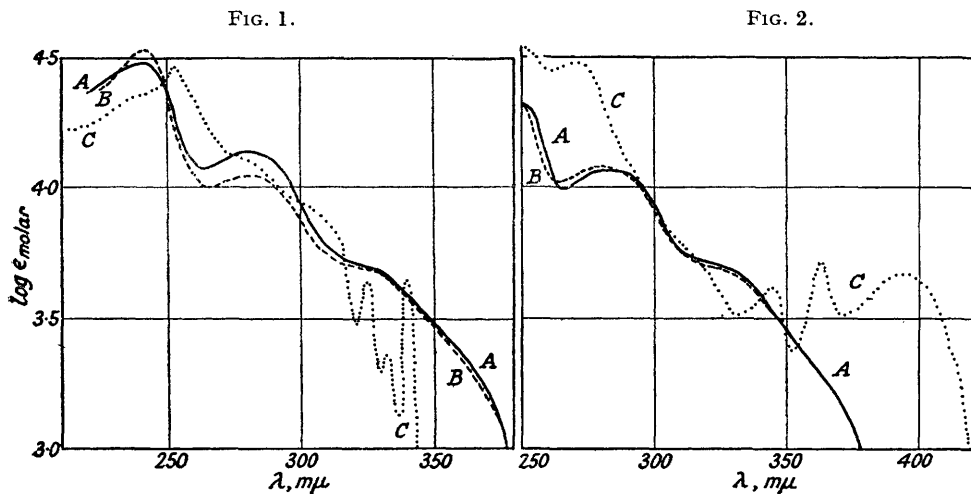


FIG. 1. A, Nitration product, m. p. 155°; B, 6-nitro-7 : 8-benzoquinoline; C, 5 : 6-benzo-4 : 7-phenanthroline (III). (Solvent, methanol.)

FIG. 2. A, Nitration product, m. p. 174°; B, 1'-nitro-7 : 8-benzoquinoline; C, quinolino(8' : 7'-7 : 8)quinoline (IV). (Solvent, methanol.)

Utermohlen and Hamilton (*loc. cit.*) report the preparation of 1'-nitro-7 : 8-benzoquinoline from 5-nitro-1-naphthylamine by a Skraup reaction. We were unable to repeat their experiment, but, under modified conditions, obtained quinolino(8' : 7'-7 : 8)quinoline (IV) and 1'-nitro-7 : 8-benzoquinoline, m. p. 174°. The latter was found to be identical with Haid's product, m. p. 174° by a mixed melting-point determination and by ultra-violet absorption spectra (Fig. 2). Reduction of the nitration product gave 1'-amino-7 : 8-benzoquinoline, m. p. 167—168° (Haid gives m. p. 175° and I. G. Farbenind. m. p. 192°).

2'-Nitro-7 : 8-benzoquinoline, synthesised from 6-nitro-1-naphthylamine, was found not to be identical with any of the nitration products; no fluorescent tetracyclic compound was formed with it.

For the synthesis of 3'-nitro-7 : 8-benzoquinoline, 8-nitro-2-naphthylamine (Saunders and Hamilton, *J. Amer. Chem. Soc.*, 1932, 54, 636) was diazotised and converted into 1 : 7-dinitronaphthalene (Vesely and Dvorak, *Bull. Soc. chim.*, 1923, 33, 319), then reduced to 7-nitro-1-naphthylamine, and subject to a Skraup reaction. 3'-Nitro-7 : 8-benzoquinoline, m. p. 224—225°, was isolated and found to be identical, by a mixed melting-point determination and ultra-violet spectra (Fig. 3), with Haid's main nitration product, m. p. 230°, which we find to possess m. p. 225°. Reduction gave 3'-amino-7 : 8-benzoquinoline, m. p. 146—147°.

In spite of repeated attempts, we were unable to isolate any 4'-nitro-7 : 8-benzoquinoline from the products of a Skraup reaction with 8-nitro-1-naphthylamine, although Schenkel and Schenkel (*loc. cit.*) were successful with the analogous 1-naphthylamine-8-sulphonic acid.

The structures of three of the four mono-nitration products of (I) have thus been established. Since it is extremely unlikely that the heterocyclic ring would be nitrated under the conditions used and since the fourth isomer (m. p. 166°) is not identical with 6-, 1'-, 2'-, or 3'-nitro-7 : 8-benzoquinoline described above (cf. Fig. 4), it follows that this substance must be either 5- or 4'-nitro-7 : 8-benzoquinoline. Furthermore, the isomer, m. p. 166°, on reduction, affords an amino-7 : 8-benzoquinoline of m. p. 140° and, since 4'-amino-7 : 8-benzoquinoline is reported to have m. p. 85—86° while the 5-amino-derivative has m. p. 146°, it follows that this fourth nitration product must be 5-nitro-7 : 8-benzoquinoline. Collateral evidence in support of this is provided (*a*) by the fact that phenanthrene, through steric hindrance, is resistant to substitution at C₍₄₎ which corresponds

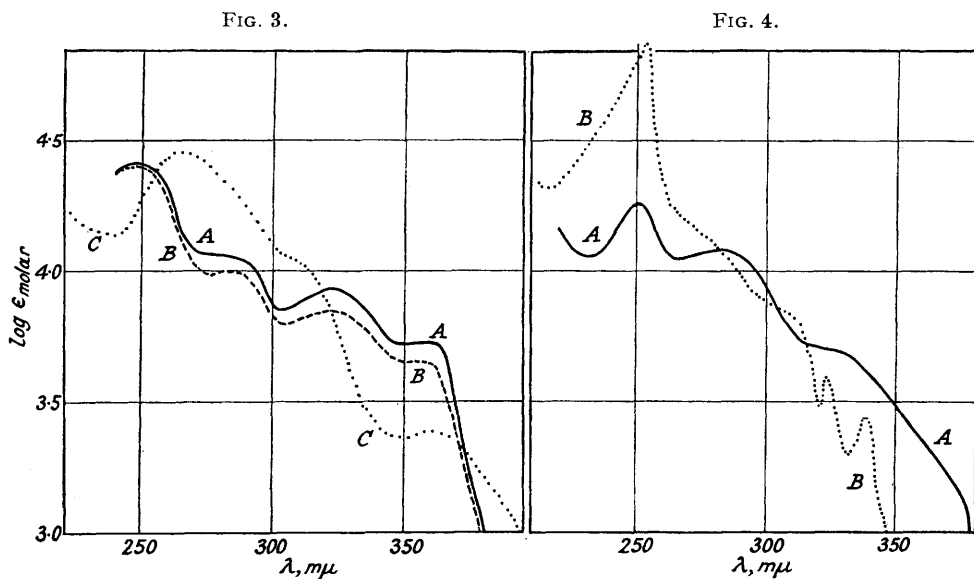


FIG. 3. A, Nitration product, m. p. 225°; B, 2'-nitro-7 : 8-benzoquinoline; C, 3'-nitro-7 : 8-benzoquinoline. (Solvent, methanol.)

FIG. 4. A, Nitration product, m. p. 166°; B, 5 : 6-benzo-1 : 7-phenanthroline (II). (Solvent, methanol.)

to C₍₄₎ in (I), and (*b*) by Longuet-Higgins and Coulson's calculations (*J.*, 1949, 971). These authors computed the electron density at the various carbon atoms of (I) and showed that the highest densities are located at C₍₃₎, C₍₁₎, C₍₅₎, and C₍₆₎ in this order of diminishing negative charge. Although it may be objected that the entity existing in the nitration mixture is the salt of (I), whereas the calculations of electron density are given only for the uncharged form of (I), nevertheless, the fact that we find that the nitration products of (I) in order of decreasing abundance are the 3'-, 1'-, and 6-nitro-7 : 8-benzoquinolines in agreement with the calculated order of decreasing electron density, justifies, we feel, our citing these calculations in support of the suggestion that the fourth isomer is 5-nitro-7 : 8-benzoquinoline.

EXPERIMENTAL

(M.p.s are uncorrected. Analyses are by Drs. Weiler and Strauss and by Mr. F. C. Hall.)

7 : 8-Benzoquinoline.—A mixture of 1-naphthylamine (50 g.), glycerol (110 g.), concentrated sulphuric acid (200 g.), and arsenic pentoxide (50 g.) was heated at 140—150° for 4 hours and then poured into water (1 l.). Next morning, the solid (A) was collected and washed with water and sodium hydroxide solution. The filtrate was basified with concentrated sodium hydroxide

solution, and the precipitated tar collected and added to the solid (A), which was then boiled under reflux with benzene (400 c.c.) for 2 hours. The benzene extract, after being dried and distilled, gave 7 : 8-benzoquinoline (20 g.), b. p. 210—225°/47 mm., m. p. 51°.

Nitration of 7 : 8-Benzoquinoline (cf. Haid, *loc. cit.*).—7 : 8-Benzoquinoline (20 g.), dissolved in concentrated sulphuric acid (50 g.), was nitrated at 0—5° with a mixture of nitric acid (8 g.; *d* 1.5), and concentrated sulphuric acid (24 g.). After 1 hour, the mixture was poured into water (2 l.) and the precipitated nitro-7 : 8-benzoquinolines were collected, washed with water, dried, and extracted twice with boiling benzene (total vol., 2 l.). The benzene-insoluble material crystallised from ethanol in bright yellow needles (7 g.), m. p. 225° (Haid gives m. p. 230°). The benzene extract was chromatographed on four alumina columns (4 × 30 cm.) in parallel and the chromatogram developed with benzene in ultra-violet light until the lowest band had been washed through. The columns were then extruded and cut up in ultra-violet light, and the individual bands were extracted with hot ethanol. The benzene eluate and ethanol extracts, on concentration, yielded yellow solids, which on crystallisation from ethanol gave pure specimens of the isomeric nitro-7 : 8-benzoquinolines. Yields were: m. p. 225°, 11.6 g. (46.5%); m. p. 174°, 9.3 g. (37%); m. p. 166°, 0.6 g. (2.5%); m. p. 155°, 1.5 g. (6%); total yield, 23 g. (92%). Haid (*loc. cit.*) records m. p. 230°, 175°, 166°, 155°, and a total yield of 54%.

The product of m. p. 166°, which has not been orientated, behaves as a single substance when chromatographed on alumina; the 6- and the 1'-nitro-isomer are easily separated in this way. Further, a fusion diagram of the 6- and the 1'-nitro-isomer shows no sign of separation of a compound of m. p. 166°.

Attempted Preparation of 5-Nitro-7 : 8-benzoquinoline.—3-Nitro-1-naphthylamine (5 g.), glycerol (11 g.), concentrated sulphuric acid (20 g.), and arsenic pentoxide (5 g.) were heated together for 5 hours at 130—140°, poured into water (600 c.c.), heated to 100°, and filtered hot. The filtrate was basified with ammonia, and the green solid collected, washed with water, and dried. The solid, dissolved in benzene, was chromatographed on alumina. A yellow substance (0.9 g.), fluorescing blue in ultra-violet light, was isolated. Crystallisation from ethanol gave 5 : 6-benzo-1 : 7-phenanthroline, pale yellow needles, m. p. 163—164° (Found: C, 84.0; H, 4.6; N, 11.8. $C_{16}H_{10}N_2$ requires C, 83.5; H, 4.35; N, 12.15%).

6-Nitro-7 : 8-benzoquinoline (cf. Utermohlen and Hamilton, *J. Amer. Chem. Soc.*, 1941, **63**, 156).—Reaction of 4-nitro-1-naphthylamine (5 g.) as above and working up similarly gave a solid which was washed with water, dried, taken up in benzene, and chromatographed on alumina. 6-Nitro-7 : 8-benzoquinoline (0.3 g.), crystallised from ethanol, formed yellow needles, m. p. 155°, alone or when mixed with the nitration product, m. p. 155° (Found: C, 70.0; H, 3.5; N, 13.0. Calc. for $C_{13}H_8O_2N_2$: C, 69.6; H, 3.6; N, 12.5%). Utermohlen and Hamilton (*loc. cit.*) record m. p. 149°. Another product, apparently 5 : 6-benzo-4 : 7-phenanthroline, gave a blue fluorescence in ultra-violet light and crystallised from ethanol in pale yellow prisms, m. p. 159—160° (Found: C, 83.1; H, 4.4; N, 12.3%). Marckwald (*Annalen*, 1893, **274**, 365) reports m. p. 160°.

6-Amino-7 : 8-benzoquinoline.—The nitration product, m. p. 155° (0.3 g.), dissolved in hot acetic acid (20 c.c.), was treated with a hot solution of stannous chloride dihydrate (1.2 g.) in concentrated hydrochloric acid (2.5 c.c.). The solution became orange and, on its cooling, a solid separated, which was collected, triturated with concentrated sodium hydroxide solution, collected again, washed with water, and dried. Crystallisation from ethanol gave 6-amino-7 : 8-benzoquinoline as light brown platelets, m. p. 117—118° (Found: C, 79.9; H, 5.1; N, 14.4%). I. G. Farbenind. (*loc. cit.*) give m. p. 118°.

1'-Nitro-7 : 8-benzoquinoline.—5-Nitro-1-naphthylamine (5 g.) gave, by a Skraup reaction as above, a product which was extracted with hot ethanol (2 × 300 c.c.). The extract was concentrated to small volume, diluted with water (200 c.c.), and basified with ammonia. The precipitated solid was collected, washed with water, and dried. The combined solids were extracted with benzene and chromatographed on alumina. 1'-Nitro-7 : 8-benzoquinoline (0.3 g.) was obtained as a yellow solid, which crystallised from ethanol in pale yellow needles, m. p. 174° alone or mixed with a specimen of the nitration product, m. p. 174° (Found: C, 69.6; H, 3.8; N, 12.2%). Utermohlen and Hamilton (*loc. cit.*) give m. p. 175°. Another product (0.3 g.), which gave a blue fluorescence in ultra-violet light and appears to be quinolino-(8' : 7' : 7 : 8) quinoline, crystallised from ethanol in bright yellow needles, m. p. 216° (Found: C, 83.0; H, 4.4; N, 12.0. Calc. for $C_{16}H_{10}N_2$: C, 83.5; H, 4.35; N, 12.15%). Finger and Spitz (*J. pr. Chem.*, 1909, **79**, 445) give m. p. 217°.

1'-Amino-7 : 8-benzoquinoline.—The nitration product, m. p. 174°, when reduced in the same manner as 6-nitro-7 : 8-benzoquinoline gave 1'-amino-7 : 8-benzoquinoline, which crystallised

from ethanol in pale yellow platelets, m. p. 167—168° (Found : C, 79.9; H, 5.2; N, 14.7%). Haid (*loc. cit.*) gives m. p. 175° and I. G. Farbenind. (*loc. cit.*) give m. p. 192°. 1'-Acetamido-7 : 8-benzoquinoline separated from ethanol in needles, m. p. 205° (Found : C, 75.9; H, 5.1; N, 11.6). $C_{15}H_{12}ON_2$ requires C, 76.3; H, 5.1; N, 11.9%.

2'-Nitro-7 : 8-benzoquinoline.—A Skraup reaction, as above, with 6-nitro-1-naphthylamine (5 g.) gave, after chromatography, 2'-nitro-7 : 8-benzoquinoline (0.4 g.), which crystallised from ethanol in pale yellow needles, m. p. 200—201° (Found : C, 69.2; H, 3.4; N, 12.2%).

3'-Nitro-7 : 8-benzoquinoline.—7-Nitro-1-naphthylamine (4.1 g.) similarly gave 3'-nitro-7 : 8-benzoquinoline (0.3 g.) as fluffy, yellow needles (from ethanol), m. p. 224—225° alone or mixed with a specimen of the nitration product, m. p. 225° (Found : C, 69.9; H, 3.9; N, 12.4%).

3'-Amino-7 : 8-benzoquinoline.—The above compound was reduced in the same manner as 6-nitro-7 : 8-benzoquinoline. The aminobenzoquinoline crystallised from ethanol in light brown platelets, m. p. 146—147° (Found : C, 80.2; H, 5.3; N, 14.4%). Haid gives m. p. 151° for the amine derived by reducing the nitration product, m. p. 225°. 3'-Acetamido-7 : 8-benzoquinoline crystallised from ethanol in pale pink needles, m. p. 183° (Found : C, 75.8; H, 5.2; N, 11.9%).

Attempted Preparation of 4'-Nitro-7 : 8-benzoquinoline.—8-Nitro-1-naphthylamine (Morgan and Jones, *J. Soc. Chem. Ind.*, 1923, 42, 341r) (5 g.) was subjected to a Skraup reaction under the conditions recorded above but only traces of starting material could be isolated. Variations in the reaction conditions brought no success.

Reduction of Nitration Product of *M. p.* 166°.—The substance was reduced under the conditions described above. α -Amino-7 : 8-benzoquinoline crystallised from ethanol in orange needles, m. p. 140° (decomp.). The acetyl derivative separated from ethanol in pale yellow needles, m. p. 194—195° (Found : C, 75.8; H, 4.9; N, 12.3%).

We are grateful to Dr. F. Strauss for determining the ultra-violet absorption spectra.

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