Aromatic Azo-compounds. Part VII. The Synthesis and Absorption Spectra of Some Azoquinolines.*

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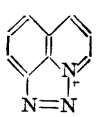
Five azoquinolines have been synthesised for comparison with the carcinogenic 2 : 2′-azonaphthalene. The absorption spectra have been compared with those of the azonaphthalenes and phenylazonaphthalenes.

2 : 2′-AZONAPHTHALENE is of interest in cancer research as it produces liver tumours in mice but is inactive or only very weakly active in rats (Cook *et al.*, *Amer. J. Cancer*, 1940, **40**, 62; Badger, Lewis, and Reid, *Nature*, 1954, **173**, 313), thus contrasting with 4-dimethylaminoazobenzene which is active in rats but relatively inactive in mice. Synthesis of a number of azoquinolines was accordingly undertaken.

6 : 6′-Azoquinoline was obtained by Knueppel (*Annalen*, 1900, **310**, 75) in small yield as a by-product in the reduction of 6-nitro- to 6-amino-quinoline by iron powder and calcium chloride. Our attempts to improve the yield by using other methods of reduction failed, so an alternative synthesis was sought, especially as Macey and Simpson (*J.*, 1952, 2602) have suggested that Knueppel was mistaken in the identity of his compound.

Azonaphthalenes have been synthesised by sulphite reduction of diazotised naphthylamines (Cohen and Oesper, *Ind. Eng. Chem. Anal.*, 1936, **8**, 306). This method, applied to 6-aminoquinoline, gave 6 : 6′-azoquinoline in 80% yield. The product was identical with that prepared by Knueppel's method. 7 : 7′- and 5 : 5′-Azoquinoline were similarly prepared. The method, however, failed with the diazonium derivatives of 3- and 8-aminoquinoline; the former failure is difficult to understand; but with 8-aminoquinoline the reduction of the diazonium compound is evidently prevented by the formation of the cyclic compound (I) (cf. G.P. 576,119; Cook *et al.*, *J.*, 1943, 404).



(I)

Many other attempts to prepare 8 : 8′-azoquinoline were without success, including reduction of 8-nitroquinoline, oxidation of 8-aminoquinoline, condensation of 8-nitroquinoline with 8-aminoquinoline (cf. Martynoff, *Bull. Soc. chim. France*, 1951, 214; Faessinger and Brown, *J. Amer. Chem. Soc.*, 1951, **73**, 4606), a double Skraup synthesis with 2 : 2′-diaminoazobenzene, and Bucherer-type reaction with 8-hydroxyquinoline, hydrazine hydrate, and hydrazine sulphite (cf. Franzen, *Ber.*, 1905, **38**, 266). Many similar attempts to prepare 3 : 3′-azoquinoline were also fruitless and these two azoquinolines are still unknown.

2 : 2′-Azoquinoline was obtained by Marckwald and Meyer (*Ber.*, 1900, **33**, 1885) by oxidation of the hydrazo-compound formed as a by-product in the preparation of 2-quinolylhydrazine from 2-chloroquinoline and hydrazine hydrate. Some improvements have been effected in this method which has also been adapted to the preparation of 4 : 4′-azoquinoline from 4-chloroquinoline.

* Part VI, *J.*, 1954, 2243.

The ultraviolet absorption spectra of the azonaphthalenes show three main regions of absorption, I, IA, and II (Badger and Buttery, *J.*, 1953, 2156). The spectra of the azoquinolines can also be divided into similar regions (see Table). Region I contains a peak

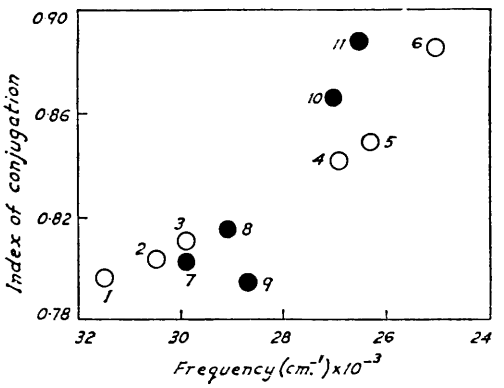
Absorption maxima (Å) *and* log ε (*in parentheses*) *for the azoquinolines in ethanol.*

			Region II	
Azoquinoline	Region I	Region IA	*K*-Band	*R*-Band
2 : 2′-	2200 (4·43)	2600 (4·43)	3480 (4·45)	4640 (2·78)
		—		
		—		
4 : 4′-	2240 (4·52)	2640 (4·21)	3700 (3·92)	—
		—		
		—		
5 : 5′-	2300 (4·69)	—	3780 (4·27)	4700 (3·01)
		—		
		2920 (3·63)		
6 : 6′-	2200 (4·45)	2680 (4·47)	3340 (4·51)	4460 (3·07)
		2840 (4·43)		
		2960 (4·30)		
7 : 7′-	2220 (4·29)	2640 (4·36)	3440 (4·54)	4520 (2·96)
		—		
		2900 (4·22)		

of high intensity at about 2200 Å, similar to that found in the spectra of the azonaphthalenes in this region. Region IA is also similar to that for the azonaphthalenes in that it contains 1—3 peaks at about 2650, 2750, and 2900 Å. Region II contains the *K*- and *R*-bands

Relation between the frequency of the K*-absorption band and the sum of the self-polarisabilities of the positions to which the* N : N *group is attached.*

1, Azobenzene.
2, 2-Phenylazonaphthalene.
3, 2 : 2′-Azonaphthalene.
4, 1-Phenylazonaphthalene.
5, 1 : 2′-Azonaphthalene.
6, 1 : 1′-Azonaphthalene.
7, 6 : 6′-Azoquinoline.
8, 7 : 7′-Azoquinoline.
9, 2 : 2′-Azoquinoline.
10, 4 : 4′-Azoquinoline.
11, 5 : 5′-Azoquinoline.



characteristic of aromatic azo-compounds, the *R*-band being more prominent than with the azonaphthalenes.

With the azonaphthalenes and phenylazonaphthalenes, Badger and Buttery (*loc. cit.*) found a remarkable correlation between the observed frequency of the *K*-band and the conjugating abilities of the position to which the azo-group is attached. The " index of conjugation " was estimated by summing the self-polarisabilities (calculated by the method of molecular orbitals) of the two positions. This comparison has now been extended to the azoquinolines, using the self-polarisabilities for the different positions in the quinoline ring system as calculated by Sandorfy and Yvan (*Bull. Soc. chim. France*, 1950, 131). All the results to date are summarised in the Figure, in which the phenylazonaphthalenes and azonaphthalenes are shown with open circles, and the azoquinolines by black points. The correlation is seen to be less good with the heterocyclic compounds.

Experimental

6 : 6′-*Azoquinoline*.—A solution of 6-aminoquinoline (5 g.) in concentrated sulphuric acid (15 c.c.) and water (100 c.c.) was diazotised at 0° with sodium nitrite (2·5 g.) in water (20 c.c.). Then sodium acetate (50 g.) in water (200 c.c.) was added with stirring, followed by sodium sulphite (5 g.) in water (40 c.c.). The mixture was heated on a water-bath, and then filtered. **6 : 6′**-Azoquinoline (4·0 g.) formed, after recrystallisation from xylene, orange needles, **m. p.**

248—248·5° (Found : C, 76·0; H, 4·4; N, 19·4. Calc. for $C_{18}H_{12}N_4$: C, 76·1; H, 4·3; N, 19·7%). Knueppel (*Annalen*, 1900, **310**, 75) gives m. p. 248°.

5 : 5′-*Azoquinoline*.—5-Aminoquinoline (5 g.), treated as above, yielded 5 : 5′-*azoquinoline* (2 g.), red needles, m. p. 256·5—257° (Found : C, 75·8; H, 4·3; N, 19·6%).

7 : 7′-*Azoquinoline* (2 g. from 3 g. of 7-aminoquinoline) formed orange needles, m. p. 245·5—246° (Found : C, 76·3; H, 4·3; N, 19·4%).

2 : 2′-*Azoquinoline*.—The following method proved superior to that described by Marckwald and Meyer (*Ber.*, 1900, **33**, 1885). 2-Chloroquinoline (19 g.) and 100% hydrazine hydrate (5·7 g.) was heated under reflux at 140° for 4 hr. The resulting solid was washed with water and then taken up in 50% acetic acid (500 c.c.). Oxides of nitrogen, obtained by the action of nitric acid (*d* 1·40) on copper, were passed through the solution until it became deep red. After the addition of aqueous ammonia the product was collected (10 g.; m. p. 228—229°). Recrystallisation from benzene gave 2 : 2′-azoquinoline as orange needles, m. p. 232—233°. Marckwald and Meyer give m. p. 230—231°.

4 : 4′-*Azoquinoline*.—4-Chloroquinoline (2 g.) and 100% hydrazine hydrate (0·6 g.) were heated at 140° in a sealed tube for 2 hr. After cooling, the product was dissolved in 50% acetic acid (50 c.c.) and oxides of nitrogen were then passed through the solution until it became deep red. The solution was cooled, and the red solid collected and dried. The resulting 4 : 4′-*azoquinoline* (0·7 g.; m. p. 200—202°), crystallised from benzene–light petroleum (b. p. 40—100°), formed orange needles, m. p. 201·5—202° (Found : C, 76·4; H, 4·3; N, 19·7%).

Absorption Spectra.—These were determined in absolute ethanol with a Hilger Uvispek spectrophotometer.

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