257. *Geometrical Isomerism of Azo-compounds.*

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cis-2 : 2′- and -3 : 3′-Azopyridine have been prepared and their properties studied. Unsuccessful attempts to isolate the *cis*-forms of other azopyridine derivatives are reported. Methods of characterisation included determination of eutectic points with selected second components by means of contact preparations (Kofler, see below), *X*-ray powder photographs, and measurements of dipole moments. Numerous cases of polymorphism are recorded. The thermal behaviour of *cis*-azobenzene is quite different from that of a mixture of azoxybenzene and hydrazobenzene (cf. Hodgson, *J.*, 1948, 1102).

The evidence from several laboratories is overwhelmingly in favour of the unstable form of azobenzene being *cis*-azobenzene. Hodgson (*J.*, 1948, 1102) does not accept this, however, and states " a double compound of azoxybenzene and hydrazobenzene exhibits far more convincingly many of the reactions of *cis*-azobenzene." Hodgson's objections have been refuted by Le Fèvre (*Chem. and Ind.*, 1948, **26**, 158), Waters (*ibid.*, p. 301), Bright, Carson, and Dyson (*Research*, 1950, **3**, 185), and Tetlow (*ibid.*, p. 187). In particular Le Fèvre and Souter (*J.*, 1949, 1595) reported that hydrazobenzene and azoxybenzene form a simple eutectic below 20° and this is in agreement with Hyrnakowski's statement (*Atti* 10*th Congr. Intern. Chim.*, 1939, **3**, 197) that azoxybenzene and hydrazobenzene form a mechanical mixture. We have confirmed these findings by comparing the melting behaviour on microscope slides of *cis*-azobenzene films in contact along an edge with films of (*a*) azoxybenzene and (*b*) hydrazobenzene, using Kofler's method of contact preparations (Kofler and Kofler, " Mikromethoden zur Kennzeichnung organischen Stoffe und Stoffgemische," Universitätsverlag, Innsbruck, 1949). We found that azoxybenzene and hydrazobenzene do not form a molecular compound, but give a eutectic at 31·5°. *cis*-Azobenzene forms eutectics with hydrazobenzene and azoxybenzene at 58° and 19° respectively. On the other hand *cis*-azobenzene when repeatedly melted and cooled is gradually converted into the stable *trans*-isomer with which it forms a eutectic (40°). The individuality of the unstable isomer was further demonstrated by *X*-ray powder photographs (Unicam 9-cm. camera, Cu-$K\alpha$ radiation), a unique set of spacings being found. Mixtures of azoxybenzene and hydrazobenzene on the other hand, whether melted together or crystallised together from a solvent, gave only those spacings characteristic of the separate components. These results strongly suggest that the unstable azobenzene is the *cis*-isomer.

Le Fèvre (*J.*, 1951, 1814) obtained evidence for the existence of *cis*-2 : 2′-azopyridine. We have isolated the *cis*-compound by irradiating solutions of 2 : 2′-azopyridine with light from a mercury-vapour lamp and separating the products on a column of silica gel. *cis*-2 : 2′-Azopyridine exists as deep-red needles, m. p. 87°, and forms a eutectic with the *trans*-compound at 56°. When the substance is repeatedly heated and cooled, the m. p. falls to 55—57°, and then increases to 83°. The substance then shows no m. p. depression when mixed with a sample of the pure *trans*-isomer.

Absorption spectra also confirm the *cis-trans*-isomerism of 2 : 2′-azopyridine and closely parallel those of *cis*- and *trans*-azobenzene. The azopyridine absorbs at two wavelengths, *trans*- at 314 mμ (log ε 3·97) and 450 mμ (log ε 2·53), and *cis*- at 284 mμ (log ε 3·87) and 446 mμ (log ε 3·03). The comparable figures for azobenzene are : *trans*- 320 mμ (log ε 4·2) and 450 mμ (log ε 2·5), and *cis*- 305 mμ (log ε 3·4—3·5) and 440 mμ (log ε 3·2) (Winkel and Siebert, *Ber.*, 1941, **74**, 675; Le Fèvre and Wilson, *J.*, 1949, 1106; cf. Le Fèvre and Worth, *J.*, 1951, 1814). No great accuracy is claimed for the *cis*-azopyridine curve as the measurements had to be carried out as rapidly as possible owing to the mobility of the *cis-trans*-equilibrium under the influence of ultra-violet light. About the main features of the curve, however, there is no doubt.

3 : 3′-Azopyridine was likewise obtained both in the *cis-* and the *trans*-form, but here the melting points of the two forms—82° (*cis*) and 140° (*trans*)—differ considerably. The *cis-* is converted into the *trans*-form much more rapidly than with the 2 : 2′-compound. *X*-Ray powder photographs again showed that each *cis*-isomer possessed characteristic spacings.

Unsuccessful attempts were made to isolate the *cis*-forms of 4 : 4′-azopyridine, 3-phenylazopyridine, 2- and 3-*o*-chlorophenylazopyridine, 4 : 4′-dimethyl-2 : 2′-azopyridine, and 5-bromo-2-phenylazopyridine.

Further evidence for the occurrence of *cis*-isomers was obtained from dipole moments, determined with an apparatus described by Henderson and Taylor (*Trans. Faraday Soc.*, 1953, **49**, 92). The values (see Table) for the 2 : 2′- and 3 : 3′-compounds are parallel to those for azobenzene (zero for *trans*, 3 D for *cis*; Le Fèvre and Hartley, *J.*, 1939, 531) and azoxybenzene (1·7 D for *trans*, 4·7 D for *cis*; Gehrckens and Müller, *Annalen*, 1933, **500**, 296). For the other compounds, since the pure *cis*-isomers could not be isolated, only the approximate change in dipole moment after illumination in benzene solution could be evaluated. Le Fèvre and Vine's procedure (*J.*, 1937, 1805) was used, a constant value 0·26 being assumed for β, this being the mean value for eleven solutions of the *cis-* and *trans*-2 : 2′- and -3 : 3′-compounds. [In their equations for the dipole moment, β is defined by $d = d_1(1 + \beta w_2)$ where d and d_1 are the densities of solution and solvent respectively, and w_2 is the weight fraction of the solute.] The individual values of β varied from 0·20 to 0·31, but since all the compounds in the Table are of similar type and since errors in β have only minor importance in the calculation of the dipole moment, the direction of change of the latter after illumination is considered significant. The changes are consistent with *cis*-isomer formation, except possibly for 4-phenylazopyridine and 4 : 4′-azopyridine. However, simple calculations using structures based on the analogous azobenzenes (Robertson and Hampson, *J.*, 1941, 409) show that in these cases a fall in dipole moment on *cis*-isomer formation may in fact be expected owing to the opposing effects of the azo- and ring nitrogen atoms.

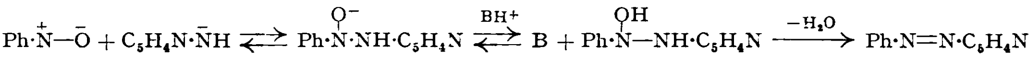
Pyridine derivative	Dipole moment (D)		Change in μ after ultra-violet illumination
	trans	*cis*	
2 : 2′-Azo	1·77	4·0	—
3 : 3′-Azo	2·40	2·85	—
2-Phenylazo	2·2	—	+0·6
3-Phenylazo	2·3	—	+0·2
4-Phenylazo	2·7	—	−0·1
4 : 4′-Azo	2·0	—	−0·3
4-Methyl-2-phenylazo	2·7	—	+0·4
5-Bromo-2-phenylazo	2·6	—	+0·2
3 : 5-Dibromo-2-phenylazo	1·8	—	+0·2
2-*o*-Chlorophenylazo	2·1	—	+0·8
3-*o*-Chlorophenylazo	2·4	—	+0·3

A number of our compounds were found to be polymorphous, monotropy greatly predominating over enantiotropy (cf. Campbell, Henderson, and Taylor, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 376). Depending on the stability of the polymorphs, such compounds when examined by the Kofler technique may show several melting points (and eutectic points when in contact with a second component) and this greatly assisted characterisation of the compounds. As second components in the contact preparations, azobenzene, benzil, *p*-nitrophenol, phenylacetic acid and phenacetin were particularly useful. Contact preparations with pairs of azo-compounds revealed many instances of solid solutions, but none involving *cis*-components. With *trans*-components, great similarity of molecular size and configuration was necessary, the methyl groups in the case of 4-methyl-2-phenylazopyridine + 4 : 4′-dimethyl-2 : 2′-azopyridine being enough to disturb the continuous series of solid solutions obtained with the unmethylated compounds.

A general method for the preparation of aromatic azo-compounds is the condensation of nitrosobenzenes with primary aromatic amines in glacial acetic acid. Attempts to condense nitrosobenzene with 2-aminopyridine in this way failed, but syntheses were successful with an alkaline condensing agent. This suggests that these reactions are of the aldol type (cf. Schönberg and Michaelis, *J.*, 1937, 627; Bergmann, *ibid.*, p. 1628).

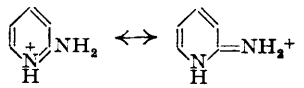
The failure of 2(and 4)-aminopyridine to condense with nitrosobenzene in an acid medium can be attributed to the addition of a proton to the ring-nitrogen atom (see, *e.g.*, Steck and Ewing, *J. Amer. Chem. Soc.*, 1948, **70**, 3397; Mann and Watson, *J. Org. Chem.*, 1948, **13**, 502). This results in a positive charge on the 2-amino-nitrogen atom, as in (I), so that interaction with the cation $C_6H_5\cdot\overset{+}{N}\cdot OH$ is impossible. Such a reason cannot be advanced to explain the inertness of 3-aminopyridine in acid solution. It is known, however, that in contrast to its isomers 3-aminopyridine forms dihydrochlorides, etc. Consequently in acid media the amino-nitrogen atom is positively charged, as in (II), and thus does not condense with nitrosobenzene.

$$C_5H_4N\cdot NH_2 + B \rightleftharpoons C_5H_4N\cdot NH^- + BH^+$$

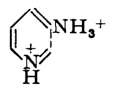


$$Ph\cdot\overset{+}{N}-\overset{-}{O} + C_5H_4N\cdot\overset{-}{N}H \rightleftharpoons Ph\cdot\overset{O^-}{N}\cdot NH\cdot C_5H_4N \overset{BH^+}{\rightleftharpoons} B + Ph\cdot\overset{OH}{N}-NH\cdot C_5H_4N \xrightarrow{-H_2O} Ph\cdot N{=}N\cdot C_6H_4N$$

(B is a base).



(I)



(II)

EXPERIMENTAL

All the thermal data (m. p.s, eutectic points, etc.) were obtained by means of the Kofler hot-stage microscope (Kofler and Kofler, *op. cit.*).

Preparations of Azopyridines.—(a) Oxidation of aminopyridines by sodium hypochlorite (Kirpal and Reiter, *Ber.*, 1927, **60**, 664) can be used when there is no danger of nuclear chlorination. We confirmed that oxidation of 2-aminopyridine by this method gives 2 : 2′-azopyridine and a little 5-chloro-2 : 2′-azopyridine (Kirpal, *Ber.*, 1934, **67**, 70) by purifying the oxidation product by partition chromatography on silica gel. The chloro-compound, m. p. 136°, was quickly washed out, leaving the pure 2 : 2′-azopyridine at the top. This was eluted with ether–ethanol and crystallised from light petroleum (b. p. 60—80°) in deep red needles, m. p. 85—86°. The method was used to prepare the following substances from the appropriate substituted aminopyridines. 5 : 5′-Dibromo-2 : 2′-azopyridine, orange needles (from benzene–light petroleum), m. p. 260° (Found: C, 35·0; H, 1·5; N, 16·3; Br, 47·3. Calc. for $C_{10}H_6N_4Br_2$: C, 35·1; H, 1·8; N, 16·4; Br, 46·7%). Bystrikskaya and Kirsanov (*Chem. Abs.*, 1941, **35**, 4023) give m. p. 235° (decomp.). 3 : 3′ : 5 : *5′-Tetrabromo-2* : *2′-azopyridine* (23% yield) was purified by passing a benzene solution down a column of alumina and separated from benzene in orange needles, polymorphous, m. p. of stable form 103° (Found : C, 24·3; H, 1·7; N, 11·0; Br, 63·0. $C_{10}H_4N_4Br_4$ requires C, 24·0; H, 0·8; N, 11·2; Br, 64·0%). 3 : 3′-Dinitro-2 : 2′-azopyridine (23% yield), red rhombs (from benzene), m. p. 230° (Found : C, 43·9; H, 2·3; N, 30·5. $C_{10}H_6O_4N_6$ requires C, 43·8; H, 2·2; N, 30·7%). 5 : *5′-Dinitro-2* : *2′-azopyridine* (41% yield), brownish-red needles (from benzene), m. p. 220° (Found : C, 44·0; H, 2·7; N, 30·9%). 3 : 3′-Azopyridine, orange needles (from light petroleum), m. p. 140°. 4 : 4′-Azopyridine (41% yield), orange needles, m. p. 108—109°, after purification on alumina and crystallisation from light petroleum (Found : C, 64·6; H, 4·7; N, 30·2. Calc. for $C_{10}H_8N_4$: C, 65·2; H, 4·4; N, 30·4%). den Hertog and Combe (*Rec. Trav. chim.*, 1951, **70**, 588) give m. p. 104—105°.

(b) *Reduction of nitropyridines by alkaline arsenious oxide.* This method gave 2 : 2′-azopyridine, m. p. 85—86° (20% yield); 4 : *4′-dimethyl-2* : *2′-azopyridine* (65% yield), orange needles (from light petroleum), m. p. 149—151°, after purification on alumina (Found : C, 68·0; H, 5·7; N, 26·0. $C_{12}H_{12}N_4$ requires C, 67·9; H, 5·7; N, 26·4%); and 3 : 3′-azopyridine (62%), m. p. 138—140°.

(c) *Condensation of nitrosobenzenes and aminopyridines.* 2-Aminopyridine (5 g.) was added to a warm 50% sodium hydroxide solution (50 ml.) which was then gently heated, and benzene (3 ml.) was added. Nitrosobenzene (6 g.) was added during 10 minutes, with shaking, and the mixture warmed for a further 10 minutes. Extraction with benzene (3 × 100 ml.) gave a solution which was heated with charcoal, filtered, and concentrated under reduced pressure to 100 ml. The concentrate was passed down a column of alumina, development of which with benzene gave a lower zone of nitrosobenzene and azoxybenzene, and an orange-red zone which was extracted with benzene. Evaporation afforded 2-*phenylazopyridine* (8 g.), red needles (from light petroleum, b. p. 40—60°), m. p. 32—34° (Found: C, 72·1; H, 4·7; N, 22·4. $C_{11}H_9N_3$ requires C, 72·1; H, 4·9; N, 22·9%). Similarly nitrosobenzene and the appropriate aminopyridine gave the following: 5-*bromo*-2-*phenylazopyridine* (86% yield based on the amine), scarlet diamonds, polymorphous, m. p. of stable form 115° (Found: N, 15·8; Br, 30·3. $C_{11}H_8N_3Br$ requires N, 16·0; Br, 30·5%), 3 : 5-*dibromo*-2-*phenylazopyridine* (84%), crimson plates, polymorphous, m. p. of stable form 112° (Found: N, 12·4; Br, 46·8. $C_{11}H_7N_3Br_2$ requires N, 12·3; Br, 46·9%), 4-*methyl*-2-*phenylazopyridine* (68%), red prisms, polymorphous, m. p. of stable form 55° (Found: C, 73·1; H, 5·5; N, 21·1. $C_{12}H_{11}N_3$ requires C, 73·1; H, 5·6; N, 21·3%), 3-*phenylazopyridine* (60%), orange leaflets, polymorphous, m. p. of stable form 52—53° (Found: C, 73·3; H, 4·7; N, 22·4%), and 4-phenylazopyridine (69%), orange leaflets, m. p. 98° (Found: C, 71·6; H, 5·0; N, 23·1%). *o*-Chloronitrosobenzene likewise gives 2-o-*chlorophenylazopyridine* (48%), red needles, m. p. 54—55° (Found: N, 18·8; Cl, 15·8. $C_{11}H_8N_3Cl$ requires N, 19·3; Cl, 16·3%), and 3-o-*chlorophenylazopyridine* (47%), red needles, polymorphous, m. p. of stable form 60° (Found: N, 19·7; Cl, 16·8%). The method fails with aminonitropyridines and 2 : 6-diaminopyridine.

Conversion of trans- *into* cis-*Isomers.*—The *trans*-compounds were dissolved in sodium-dried solvents and irradiated by a Hanovia mercury-vapour lamp. Clamping the reaction flask 18 in. from, and 8 in. above, the lamp gave a slight heating effect which mixed the liquid. In a typical experiment azobenzene (5 g.) was irradiated for 12 hours in benzene (250 ml.). The solution was then chromatographed on alumina (diam. 3 in., depth 1½ in.). The chromatogram was developed with benzene until the strongly adsorbed *cis*-layer was separated from the *trans*-compound. Extraction with benzene containing acetone (20 : 1) and evaporation of the extract at low pressure and temperature gave *cis*-azobenzene, rhombic plates (from light petroleum, b. p. 40—60°), m. p. 71° (*lit.*, 71·4°). A sample when melted and cooled afforded broad, flat needles of *cis*-azobenzene followed by smaller needles of the eutectic mixture, m. p. 40°, penetrating in all directions. Alternate heating and cooling caused the temperature of "final melting" (disappearance of last crystals in the melt) to decrease and then rise again, while the melting began consistently at 40°. In this way the final m. p. decreased from 71° to 51° then rose to 66°. The final solidified melt under the microscope showed the absence of eutectic crystals, and the material gave no m. p. depression with a sample of *trans*-azobenzene, m. p. 68°.

cis-*m*-Nitroazobenzene, m. p. 69—71° (*lit.*, 70°) was repeatedly melted and cooled. The final m. p. sank to 60°, then rose to 94—95°, which was not altered when the substance was admixed with the *trans*-isomer, m. p. 96°. The latter is polymorphic.

cis-*p*-Iodoazobenzene separated from light petroleum (b. p. 40—60°) in red leaflets, m. p. 74—76°. Repeated melting and cooling caused the m. p. to fall to 62·5° (eutectic point) and then to rise to 99°, which was unaltered when the substance was mixed with pure *trans*-isomer, m. p. 104°. It is suggested that the substance cited in the literature as the *cis*-compound, m. p. 62° (Cook and Jones, *J.*, 1939, 1309) is in fact the eutectic mixture of *cis*- and *trans*-isomers.

Solid *cis*-*p*-iodoazobenzene is stable and showed no lowering of m. p. after 3 months in the dark.

cis-2 : 2′-*Azopyridine.*—*trans*-2 : 2′-Azopyridine (2 g.) was irradiated in dry benzene–light petroleum (50 ml.) for 12 hours, then shaken with water, and the non-aqueous solution passed down a column of silica gel (30—40 g. of SiO_2 + 53% of its weight of water in a column 2—5 cm. wide) made up with the same solvent mixture. Development with benzene–light petroleum washed down the *cis*-band, leaving the *trans* as a dull orange layer. The *cis*-solution was evaporated at low temperature and yielded cis-2 : 2′-*azopyridine* (0·25 g.), deep red needles (from light petroleum, b. p. 40—60°), m. p. 87° (Found: C, 65·6; H, 4·3; N, 30·1. $C_{10}H_8N_4$ requires C, 65·2; H, 4·4; N, 30·4%). It forms a mixture with the *trans*-compound, eutectic temperature 56°. Repeated heating and cooling gave the following results:

Disappearance of last crystal (° c)	87	77	80	78	68	67	55	57	75	77	82	84	83	84	83	83	83
Initial melting		75	56	55	50	50	50	38	35	35	35	35	60	55	55	55	

At the final stage the eutectic mixture had practically all disappeared, and the substance showed no m. p. depression when mixed with a sample of pure *trans*-compound. The eutectic value of 35° in some observations can be explained by the assumption that there is a tendency towards polymorphism in either or both the *cis*- and the *trans*-compound.

cis-2 : 2′-Azopyridine is almost insoluble in water whereas the *trans*-compound is extremely soluble (cf. Kirpal, *Ber.*, 1934, **67**, 70). It is suggested that the insolubilitv of the *cis* is due to effective screening of the nitrogen atoms in this configuration. The *trans*-compound gives a deep blue colour with ferrous salts, but the *cis*-compound does not. The *trans*-compound in ethanol gives green and white precipitates with copper sulphate and silver nitrate respectively.

cis-3 : 3′-*Azopyridine.*—*trans*-3 : 3′-Azopyridine (1 g.) was irradiated as above and the solution passed down a silica gel column (30 × 2 cm.). Development with water-saturated benzene–light petroleum resulted in rapid passage of the *trans*-compound, m. p. 139° (*lit.*, 142°) down the column. The residual orange zone was eluted with benzene–methanol (100 : 1), evaporation of which at low temperature and pressure gave cis-3 : 3′-*azopyridine*, scarlet rhombs (from light petroleum), m. p. 82° (Found : C, 65·1 ; H, 4·5 ; N, 29·9%). Heating the compound above 100° causes small groups of laths to appear. These grow as the temperature is raised until no liquid is left and then melt at 142°, undepressed when the substance is admixed with the *trans*-compound. Clearly the *cis*- is more quickly converted into the *trans*-compound than is the corresponding 2 : 2′-compound.

4-*Methyl*-2-*nitropyridine.*—2-Amino-4-methylpyridine was oxidised by hydrogen peroxide and sulphuric acid (Kirpal and Bohm, *Ber.*, 1932, **65**, 680) to 4-methyl-2-nitropyridine (36% yield), leaflets (from light petroleum, b. p. 60—80°), m. p. 65·5—66·5° (Found : C, 55·2; H, 4·1; N, 20·4. Calc. for $C_6H_6O_2N_2$: C, 52·2; H, 4·4; N, 20·3%). Wiley and Hartman (*J. Amer. Chem. Soc.*, 1951, **73**, 494) give m. p. 61—62°.

Thanks are expressed to the D.S.I.R. for a maintenance grant (to A. W. H.), to Imperial Chemical Industries Limited for a Fellowship (to D. T.), and to the Anglo-Iranian Oil Co. Ltd. and Moray Endowment Fund for grants for chemicals and apparatus.

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[*Received, January* 12*th*, 1953.]