Macrozamin. Part IV. Positional and Geometrical Isomerism in Mixed Aliphatic-aromatic Azoxy-compounds.*

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Three of the four possible isomers of representative azoxy-compounds of the type $Ar{\cdot}CH_2{\cdot}(N_2O){\cdot}Ar'$ have been prepared and examined. The two *trans*-isomers were obtained by per-acid oxidation of the azo-compound $Ar{\cdot}CH_2{\cdot}N{:}NAr'$; in the examples studied the *trans*-benzylazoxybenzene, $Ar{\cdot}CH_2{\cdot}N{:}N(O){\cdot}Ar'$, predominated and the *trans*-ω-arylazoxytoluene, $Ar{\cdot}CH_2{\cdot}N(O){:}NAr'$, was the minor product.†

The "hydrazone oxides," *i.e.*, the high-melting products of per-acid oxidation of aromatic aldehyde hydrazones, are *cis*-benzylazoxybenzenes, $Ar{\cdot}CH_2{\cdot}N{:}N(O){\cdot}Ar'$, and have structures the reverse of those proposed by Witkop and Kissman (*J. Amer. Chem. Soc.*, 1953, **75**, 1975) and by Lynch and Pausacker (*J.*, 1953, 2517). These *cis*-compounds are *not* obtained by *careful* oxidation of azo-compounds, but they can be prepared by isomerising the *trans*-benzylazoxybenzenes formed in that reaction. The mechanisms of the isomerisation and of the formation of " oxides " from hydrazones are discussed. Both reactions can be extended beyond the mixed aliphatic-aromatic series, *e.g.*, to the preparation of 4 : 4′-dichloro-*cis*-ω-azoxytoluene.

AMONG unsymmetrically substituted azoxy-compounds studied in connection with the plant poison macrozamin, we have given special attention to those of the type $Ar{\cdot}CH_2{\cdot}(N_2O){\cdot}Ar'$ because of their connection with the problem of " benzaldehyde phenylhydrazone oxide." This compound was obtained by oxidising benzaldehyde phenylhydrazone with perbenzoic acid, and was allotted the improbable structure (I) by Bergmann,

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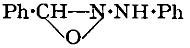
* Part III, *J.*, 1952, 4191.

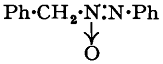
† Unambiguous nomenclature was needed for the asymmetric azoxy-compounds $R{\cdot}N{:}N(O){\cdot}R'$ described in this paper. After consultation with the Editors the following method has been adopted. The compound R′H [where R′ is the residue attached to the N(O) group] is regarded as the parent compound, into which the $R{\cdot}N{:}N(O)$-group is substituted. In conformity with the I.U.P.A.C. name phenylazo (not benzeneazo) for $Ph{\cdot}N{:}N$- (see *J.*, 1952, 5062, 5098), the $R{\cdot}N{:}N(O)$- groups are termed arylazoxy (not areneazoxy) or alkylazoxy (not alkaneazoxy). Arylazoxy- and alkylazoxy-groups, being treated as substituents into the compound R′H, must be listed alphabetically with any other substituents in the R′ moiety. The following examples illustrate the method :

$CH_3{\cdot}N{:}N(O){\cdot}CHMe_2$	2-(methylazoxy)propane
$PhEtCH{\cdot}N{:}N(O){\cdot}CHMe_2$	2-(1-phenyl-1-propylazoxy)propane
$Ph{\cdot}CH_2{\cdot}N{:}N(O){\cdot}C_6H_4Cl$-*p*	*p*-(Benzylazoxy)chlorobenzene
p-$C_6H_4Cl{\cdot}CH_2{\cdot}N{:}N(O){\cdot}Ph$	(4-Chlorobenzylazoxy)benzene
p-$C_6H_4Cl{\cdot}N{:}N(O){\cdot}CH_2{\cdot}Ph$	ω-(*p*-Chlorophenylazoxy)toluene
$Ph{\cdot}N{:}N(O){\cdot}CH_2{\cdot}C_6H_4Cl$-*p*	*p*-Chloro-ω-(phenylazoxy)toluene
p-$C_6H_4Br{\cdot}N{:}N(O){\cdot}CH_2{\cdot}C_6H_4Cl$-*p*	ω-(*p*-Bromophenylazoxy)-*p*-chlorotoluene
p-$C_6H_4Br{\cdot}N{:}N(O){\cdot}CH_2{\cdot}C_6H_4Br$-*p*	*p*-Bromo-ω-(*p*-bromophenylazoxy)toluene

Parentheses are used freely, particularly when it is necessary to avoid confusion with the trivial names for symmetrical azoxy-compounds, such as azoxybenzene for $C_6H_5{\cdot}N{:}N(O){\cdot}C_6H_5$, or with cases where the position of the azoxy-oxygen atom is not known.

Ulpts, and Witte (*Ber.*, 1923, **56**, 679). As mentioned in Part III * we repeated the preparation of this " oxide " a few years ago, because we then expected it to have the structure (II). We had shown that aliphatic azoxy-compounds, obtained by per-acid oxidation of azo-compounds, are characterised by two strong absorption bands in the infra-red near 1500 and 1300 cm.$^{-1}$; the infra-red spectrum of " benzaldehyde phenylhydrazone oxide " contained two such bands and was free from bands near 3300 cm.$^{-1}$ attributable to OH or NH groups. There was thus little doubt that the " oxide " contains an azoxy-group. Nevertheless, a structure exactly analogous to those of the azoxy-compounds described in Part III was in our opinion ruled out by its high melting point (202°) and very sparing solubility in ether and warm light petroleum, solvents in which azoxybenzene (m. p. 36°) and 4 : 4′-dichloro-ω-azoxytoluene (m. p. 107°) are both readily soluble.

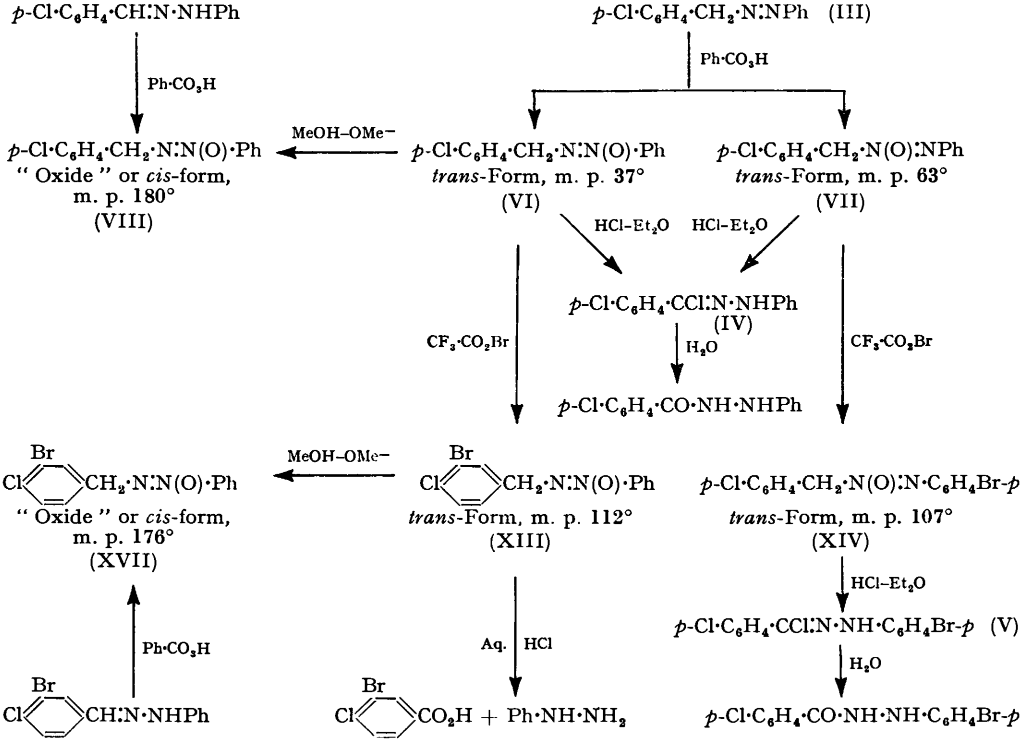
(I) 

 (II)

$$\mathrm{Ph{\cdot}CH_2{\cdot}\underset{\downarrow\atop O}{N}{:}N{\cdot}Ph}$$

These apparently contradictory conclusions showed that further work was needed to settle the structure of the " oxide." Whilst this work was in progress two other groups of workers (Witkop and Kissman, *J. Amer. Chem. Soc.*, 1953, **75**, 1975; Lynch and Pausacker, *J.*, 1953, 2517) reported examinations of " benzaldehyde phenylhydrazone oxide " and some of its analogues; they concluded that the " oxide " has the structure (II). In the present paper we show, first, that the problem is more complex than has formerly been realised, in that the " oxides " differ geometrically from the azoxy-compounds described in Part III; and secondly, that the structure (II), which the American and Australian workers favour, is wrong in respect of the position assigned to the oxygen atom.

Our approach to the problem was to compare the products of perbenzoic acid oxidation of hydrazones with those of the corresponding azo-compounds; *p*-chlorobenzaldehyde phenylhydrazone and the isomeric azo-compound (III) were chosen for initial study, and their more important transformations are set out in the annexed scheme.



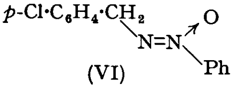
Ethereal perbenzoic acid converted *p*-chlorobenzaldehyde phenylhydrazone into an " oxide " of m.p. 180° with properties similar to those of Bergmann's " oxide." Its infra-red absorption spectrum showed that it was an azoxy-compound; its sparing solubility in ether and light petroleum showed that it was not an analogue of the azoxy-compounds described in Part III.

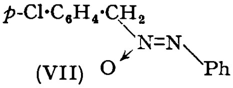
The azo-compound (III) obtained by dehydrogenation of the corresponding hydrazo-compound with aqueous ferric chloride was crystalline; although fairly stable at 0° it isomerised to the hydrazone slowly in methanol at room temperature. On careful oxidation with perbenzoic acid in ether (III) gave only a very small quantity of the " oxide " of m. p. 180°, and it will be clear from the sequel that even this small amount is not a true product of the reaction, but owes its formation to isomerisations of the starting material and of one of the true products. The crude syrupy product left when the " oxide " had been removed was separated by crystallisation into a major product, m. p. 37°, and a minor product, m. p. 63°. Both had the composition $p\text{-Cl·C}_6\text{H}_4\text{·CH}_2\text{·(N}_2\text{O)·Ph}$, and showed the expected absorption bands near 1500 and 1300 cm.$^{-1}$; their low melting points and ready solubility in cold light petroleum showed that they belonged to the same series as the primary aliphatic azoxy-compounds described in Part III.

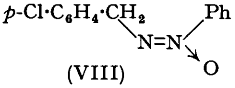
Like the latter, too, they were both hydrolysed cleanly by hot hydrochloric acid, giving ultimately an acid (*p*-chlorobenzoic) and a substituted hydrazine (phenylhydrazine). The behaviour of the closely related compound (XIV) (below) makes it likely that these hydrolyses proceeded through both the intermediates (IV) and *N*-*p*-chlorobenzoyl-*N'*-phenylhydrazine. Hydrogen chloride in ether converted both the azoxy-compounds of m. p. 37° and 63° into (IV), reactions analogous to that in which the same reagent converts an *aci*-nitro-compound into a hydroxamic chloride. The structure of (IV) was shown by its hydrolysis, which gave *N*-*p*-chlorobenzoyl-*N'*-phenylhydrazine and one equivalent of hydrochloric acid; the intervention of substituted hydrazides in the hydrolysis of primary aliphatic azoxy-compounds was demonstrated in Part III (*loc. cit*).

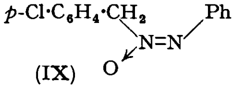
The " oxide " of m. p. 180° behaved quite differently towards ethereal hydrogen chloride; a dark green tar was formed, from which no homogeneous compound could be isolated. Treatment with hot aqueous-ethanolic hydrochloric acid did hydrolyse this " oxide " slowly to give rather poor yields of *p*-chlorobenzoic acid and phenylhydrazine, but much tar was also formed.

The existence of three isomers of the structure $p\text{-Cl·C}_6\text{H}_4\text{·CH}_2\text{·(N}_2\text{O)·Ph}$ shows that geometrical as well as positional isomerism of the azoxy-group is under observation. The isomers of m. p. 37° and 63°, obtained from the azo-compound (III), obviously differ only in the location of the oxygen atom, and belong to the same geometric series. Although the identity of this series cannot yet be decided with complete certainty a tentative assignment must be made here if only for convenience of reference. The azo-compound (III) is very probably, like azomethane, a *trans*-compound (Boersch, *Monatsh.*, **1935**, **65**, 327). Per-acid oxidation of azo-compounds appears to cause no inversion of geometric configuration, since *cis*-azobenzene gives (labile) *cis*-azoxybenzene (Badger, Buttery, and Lewis, *J.*, **1953**, **2143**). The azoxy-compounds of m. p. 37° and 63° may therefore be tentatively assigned to the *trans*-series, with structures (VI) and (VII) (not necessarily respectively); the " oxide " form of m. p. 180° would then be a *cis*-compound, either (VIII) or (IX).


(VI)

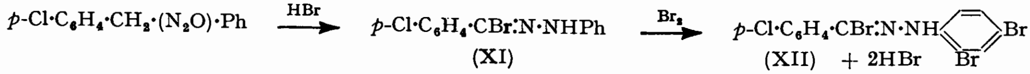

(VII)


(VIII)


(IX)

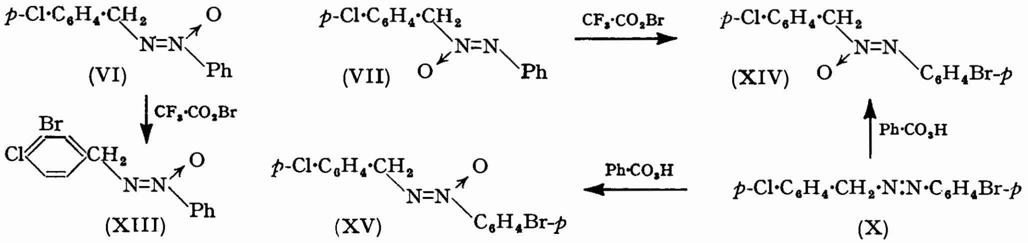
The existence of the three isomeric azoxy-compounds described above is not an isolated case. Oxidation of *p*-chlorobenzaldehyde *p*-bromophenylhydrazone gave a typical " oxide," m. p. 186°. Perbenzoic acid oxidation of ω-(*p*-bromophenylazo)-*p*-chlorotoluene (X) gave two normal *trans*-azoxy-compounds, a major product, m. p. 104°, and a minor product, m. p. 107°; it is noteworthy that no trace of the " oxide " of m. p. 186° was detected as a product.

The key to the structures of all these azoxy-compounds clearly lay in the identification of the *trans*-compounds of m. p. 37° and 63°, preferably by the classical substitution method (Angeli and Valori, *Atti R. Accad. Lincei*, 1912, **21**, 155). However, the more accessible isomer of m. p. 37° did not react with bromine by simple substitution; instead the compound (XII) was isolated. This was no doubt formed by the bromination of the



C-bromo-hydrazone (XI), produced by the action of hydrogen bromide on the azoxy-compound. The structure of (XII) was shown by its formation from *p*-chlorobenzaldehyde phenylhydrazone and bromine (cf. Chattaway and Walker, *J.*, 1925, 1975). Better results than with bromine alone were obtained with bromine and silver trifluoroacetate (bromine trifluoroacetate; Haszeldine and Sharpe, *J.*, 1952, 993). This reagent, used in nitrobenzene at room temperature, substituted azoxybenzene rapidly, giving the same bromo-derivative as that obtained by the action of bromine alone; this and other evidence shows that the reagent is electrophilic, and it could therefore be used instead of bromine for the present purpose. With the azoxy-compound of m. p. 37° in nitrobenzene it reacted slowly, giving only a monobromo-derivative, m. p. 112°, in rather poor yield; the bromo-compound of m. p. 107° obtained from (X) was not detected in the products. Hot hydrochloric acid hydrolysed the azoxy-compound of m. p. 112° cleanly, giving phenylhydrazine and 3-bromo-4-chlorobenzoic acid. The slow substitution of the azoxy-compound of m. p. 37° and the position taken up by the entering bromine atom show that the monosubstituted benzene ring must be deactivated by attachment to the quaternary nitrogen atom of the azoxy-group; that is, the azoxy-compound of m. p. 37° must be (VI), and its bromination product of m. p. 112° (XIII).

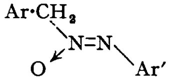
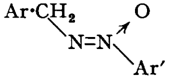
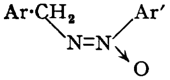
The azoxy-compound of m. p. 63° should therefore be (VII). In agreement, it reacted rapidly with bromine trifluoroacetate, giving in over 50% yield a monobromo-derivative, m. p. 107°, identical with that obtained from oxidation of the azo-compound (X). Its structure follows from this identity, and also from its conversion into the *C*-chloro-hydrazone (V) either by treatment with dry ethereal hydrogen chloride, or by brief interaction with boiling aqueous-ethanolic hydrochloric acid. Hydrolysis of (V) with hot water and alcohol gave *N*-*p*-bromophenyl-*N'*-*p*-chlorobenzoylhydrazine. The rapid formation of the bromo-compound of m. p. 107° from the azoxy-compound of m. p. 63° and the position taken up by the entering bromine atom confirm the structure of the azoxy-compound of m. p. 63° as (VII), and its bromo-derivative of m. p. 107° as (XIV). Hence too, the bromo-compound of m. p. 104° which forms the major product of oxidation of (X) must have the structure (XV), analogous to that of the compound (VI) of m. p. 37°.



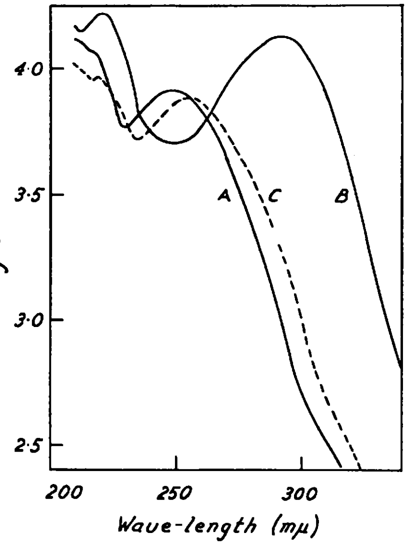
These structures were confirmed by the relevant ultra-violet absorption spectra (Fig. and Table). The azoxy-compound of m. p. 37° and its bromo-analogue of m. p. 104° have their main absorption band near 255 mμ; this is consistent with the structures (VI) and (XV), the chromophores of which resemble that of nitrobenzene ($\lambda_{max.}$ 260 mμ). In the structures (VII) and (XIV) the resonant system is much longer, extending from the oxygen atom through the azo-group to the *p*-position of the benzene ring. Maximal light absorption at wave-lengths considerably longer than 260 mμ would therefore be expected for these compounds and, in fact, the azoxy-compounds of m. p. 63° and 107° both have their main absorption maxima at >290 mμ.

In the products of oxidation of (III), (VI) predominated over (VII) in the approximate ratio 10 : 1. In the products of oxidation of (X) the preponderance of (XV) over (XIV) was even greater. The aromatically bound nitrogen atom of these azo-compounds is therefore attacked much more rapidly than the aliphatically bound nitrogen atom. This is rather surprising, since it might be thought that the latter atom would have the higher electron availability, and perbenzoic acid is almost certainly correctly regarded as an electrophilic reagent.

The structure of the " hydrazone oxides " (or *cis*-azoxy-compounds) may now be considered; the four examined here were derived from the phenylhydrazones of benzaldehyde, *p*-chlorobenzaldehyde, and 3-bromo-4-chlorobenzaldehyde, and from the *p*-bromophenylhydrazone of *p*-chlorobenzaldehyde. Their ultra-violet spectra (Fig. and Table) all show a main absorption maximum near 260 mμ; in this they resemble very closely the *trans*-compounds (VI), (XIII), and (XV), in which the oxygen atom is attached to aromatically bound nitrogen, and they differ markedly from the *trans*-compounds (VII) and (XIV) (oxygen attached to aliphatically bound nitrogen; $\lambda_{max.}$ >290 mμ). It is therefore almost certain that the " oxides " are *cis*-forms in which the oxygen is attached to aromatically bound nitrogen; thus the " oxide " of m. p. 180° from *p*-chlorobenzaldehyde phenylhydrazone is (VIII) and those from *p*-chlorobenzaldehyde *p*-bromophenylhydrazone and 3-bromo-4-chlorobenzaldehyde phenylhydrazone are respectively (XVI) and (XVII).

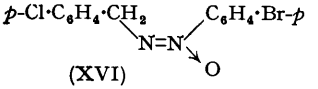
	Compound *	$\lambda_{max.}$ (EtOH) mμ)	$10^{-2}\varepsilon$
	*trans-p*-Chloro-ω-(phenylazoxy)toluene (VII)	292	13·4
	trans-ω-(*p*-Bromophenylazoxy)-*p*-chlorotoluene (XIV)	299·5	18·2
	*trans*-(4-Chlorobenzylazoxy)benzene (VI)	249	13·1
	trans-p-Bromo-(4-chlorobenzylazoxy)benzene (XV)	260·5	17·7
	trans-(3-Bromo-4-chlorobenzylazoxy)benzene (XIII)	249	14·8
	*cis*-(4-Chlorobenzylazoxy)benzene (VIII)	254	12·0
	cis-p-Bromo-(4-chlorobenzylazoxy)benzene (XVI)	264	13·1
	cis-(3-Bromo-4-chlorobenzylazoxy)benzene (XVII)	256	12·4

* For nomenclature see footnote, p. 4069.

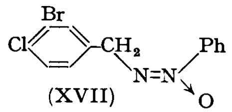


Light absorption of:
A, trans-(*4-chlorobenzylazoxy*)*benzene;*
B, trans-p-*chloro-ω-*(*phenylazoxy*)*toluene; and*
C, "p-*chlorobenzaldehyde phenylhydrazone oxide*" (*all in* EtOH).

It is noteworthy that corresponding *trans*- and *cis*-forms, *e.g.*, (VI) and (VIII), do not show very different absorption intensities; this contrasts with the two azoxybenzenes of which the *cis*-form absorbs considerably less intensely than the *trans*-form. In *cis*-azoxybenzene steric interference between the two benzene rings prevents their coplanarity, and this probably accounts for the reduced intensity of absorption, and possibly also for the inferior stability of the *cis*-form. Steric interference between the methylene group and the phenyl residue in (VIII) is clearly small compared with that in *cis*-azoxybenzene; it is probably little greater than exists between the oxygen atom and the methylene group in (VI), so it is not surprising that (VI) and (VIII) have very similar absorption spectra.

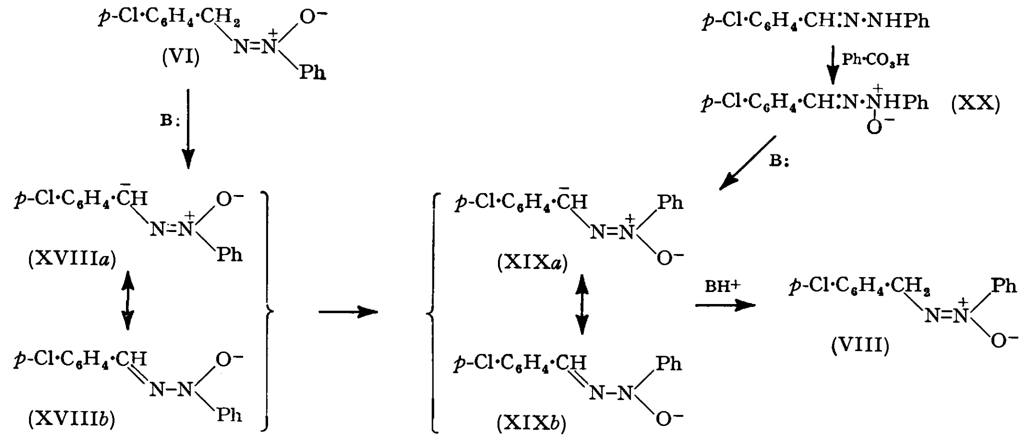


(XVI)



(XVII)

Perhaps the strongest evidence that the " oxides " are *cis*-benzylazoxybenzenes is provided by their formation from the *trans*-benzylazoxybenzenes under very mild conditions. The compound (VI) had to be preserved at —40°, since even in the dark at room temperature the solid slowly isomerised to the " oxide " of m. p. 180° (VIII). The same change took place in solution and was effectively irreversible, although quantitative yields were not obtained owing to partial decomposition. The isomerisation in solution had characteristics which suggested that it took place by removal and replacement of a proton. It was slow in light petroleum, more rapid in methanol; in the latter solvent it was markedly accelerated by 0·01N-sodium methoxide and was almost completely inhibited by 0·01N-toluene-*p*-sulphonic acid. Addition of sodium methoxide to a solution of (VI) in methanol produced an intense yellow colour which was immediately discharged by the addition of acid; this colour is probably due to the resonant anion (XVIII) mentioned below. Similar isomerisations of (XV) to give (XVI), and of (XIII) to give (XVII), were also observed, but they took place much less readily; thus (XV) survived brief heating at 80° in alcohol, and the extent of its isomerisation in absolute ether at 0° during 1 week was very small. These facts have a bearing on the mechanism of formation of the *cis*-compounds by per-acid oxidation of hydrazones. The structural prerequisites for the isomerisation are at present being studied. It is not confined to mixed aliphatic-aromatic azoxy-compounds, since we have found that 4 : 4′-dichloro-*trans*-ω-azoxytoluene (Part III, *loc. cit.*, where it was termed ω-azoxy-*p*-chlorotoluene) is converted into the *cis*-isomer by methanolic sodium methoxide. On the other hand the *trans*-ω-phenylazoxytoluenes such as (VII) did not undergo similar isomerisation.



If the *cis*-azoxy-compound of m. p. 180° is correctly formulated as (VIII), then its formation from the *trans*-isomer (VI) is easily understood as follows. Removal of a proton from the methylene group of (VI) can be effected by a solvent molecule or by an added base because it is assisted by the phenyl residue and by the azoxy-group, the latter stabilising the anion by the resonance (XVIII, $a \longleftrightarrow b$). This resonance would diminish the double-bond character of the link between the two nitrogen atoms and lower the barrier to free rotation, so allowing the change to a resonant ion (XIX, $a \longleftrightarrow b$) of *cis*-configuration; the change would then be completed by return of the proton. No such explanation of the isomerisation could apply if the " oxides " had structures of the type (II) advocated by Witkop and Kissman and by Lynch and Pausacker (*locc. cit.*), for then the change would involve a migration of the oxygen atom as well as a geometrical inversion.

The formation of the " oxides " or *cis*-isomers by per-acid oxidation of hydrazones is also most readily understood if they have structures of the type (VIII). The oxidation probably gives initially an intermediate such as (XX), which would very readily lose a proton to give the resonant ion (XIX, $a \longleftrightarrow b$) which is thus an intermediate in both methods of formation. This mechanism accounts for the fact that it is the more stable *cis*-forms, not the *trans*-forms, which are obtained by oxidising hydrazones.

Witkop and Kissman (*loc. cit.*) assumed that during oxidation hydrazones first isomerise to azo-compounds. Lynch and Pausacker (*J.*, 1954, 1131) showed that in a series of substituted benzaldehyde phenylhydrazones the second-order oxidation reaction velocity was affected more strongly by substituents in the Ph·NH ring than by those in the Ph·CH ring. This they regarded as strong support for the mechanism :

$$\mathrm{Ar{\cdot}CH{:}N{\cdot}NHAr'} \rightleftharpoons \mathrm{Ar{\cdot}CH_2{\cdot}N{:}NAr'} \longrightarrow \mathrm{Ar{\cdot}CH_2{\cdot}N(O){:}NAr'}$$

since in this mechanism alone is the nitrogen atom remote from Ar′ brought under the effective influence of groups situated in that ring. This apparent difficulty arose only because the wrong structure was allotted to the " oxides," and a simpler explanation of the kinetic results is available in terms of our proposed mechanism. In the oxidation step of the latter, it is the aromatically bound nitrogen atom of the phenylhydrazone which undergoes oxidation, and substituents in the benzene ring to which this atom is attached will naturally exert the most strongly marked effect on the reaction velocity. On other grounds, too, the participation of azo-compounds as intermediates in the reaction is unlikely. It would require that the *cis*-forms were not true products of the reaction, but arose from the *trans*-compounds by isomerisation. As mentioned above, some of the *trans*-isomers, *e.g.*, (XIII) and (XV) are rather stable under the conditions of the reaction, and would undoubtedly survive; however, they are not detectable, and instead the *cis*-isomers are obtained.

Witkop and Kissman adopted the structure (II) for " benzaldehyde phenylhydrazone oxide " because they regarded its high melting point and sparing solubility as due to tautomerism of (II) with " salt-like " structures :

$$\text{(II)}\quad \mathrm{Ar{\cdot}CH_2{\cdot}N(O){:}NAr'} \rightleftharpoons \mathrm{Ar{\cdot}\overset{-}{C}H{\cdot}\overset{+}{N}(OH){:}N{\cdot}Ar'} \rightleftharpoons \mathrm{[Ar{\cdot}CH{:}N{:}N{\cdot}Ar']^{+}\quad OH^{-}}$$

it was said that similar tautomeric structures could not be written starting with the structure $\mathrm{Ar{\cdot}CH_2{\cdot}N{:}N(O){\cdot}Ar'}$. Against this it must be observed that infra-red spectroscopy shows the absence of hydroxylic tautomers in the solid state and in solution in chlorinated solvents. Lynch and Pausacker (*J.*, 1953, 2517) claimed that bromine in boiling pyridine converted " benzaldehyde phenylhydrazone oxide " in high yield into a crystalline monobromo-derivative, identical with that obtained by the per-acid oxidation of benzaldehyde *p*-bromophenylhydrazone; such a result would, if substantiated, provide some evidence for structure (II). We have repeated this experiment, but obtained only tars; nor were more favourable results obtained from similar bromination of " *p*-chlorobenzaldehyde phenylhydrazone oxide." With bromine trifluoroacetate the latter gave no well-defined substitution product, but the rate of disappearance of active bromine was, as with the isomer (VI), slow; this favours structure (VIII), not (IX). These and other results described above are not easy to reconcile with Lynch and Pausacker's claim.

EXPERIMENTAL

Infra-red spectra were determined with mulls in hexachlorobutadiene.

cis*(-4-Chlorobenzylazoxy)benzene* (VIII).—To *p*-chlorobenzaldehyde phenylhydrazone (17·8 g.) ethereal 2·75M-perbenzoic acid (29·5 c.c.) was added slowly at 0°; the mixture was diluted with ether (15 c.c.) and kept at 0° for 20 hr., and the precipitated solid collected. Recrystallisation from benzene–alcohol gave the *cis*-azoxy-compound as needles, m. p. 179—180° (decomp.) (Found: C, 63·4; H, 4·4; N, 11·3. Calc. for $C_{13}H_{11}ON_2Cl$: C, 63·3; H, 4·5; N, 11·4%). The asymmetric stretching vibration of the azoxy-group gave a strong absorption band at 1477 cm.$^{-1}$.

N-*4-Chlorobenzyl*-N′-*phenylhydrazine*.—Reduction of *p*-chlorobenzaldehyde phenylhydrazone with 3% sodium amalgam in alcohol by Schlenk's method (*J. pr. Chem.*, 1908, **78**, 50) gave the base *hydrochloride* (80%), m. p. 187—189° (Found: C, 58·0; H, 5·1; N, 10·6. $C_{13}H_{14}N_2Cl_2$ requires C, 58·0; H, 5·2; N, 10·4%). The Schotten–Baumann method gave the N-*benzoyl* derivative, m. p. 124° (from alcohol) (Found: C, 71·6; H, 4·8; N, 8·4. $C_{20}H_{17}ON_2Cl$ requires C, 71·3; H, 5·1; N, 8·3%).

p-*Chloro-ω-(phenylazo)toluene* (III).—Solutions of the above base hydrochloride (12 g. in 1·2 l. of water) and ferric chloride hexahydrate (65 g. in 200 c.c. of water) were mixed and shaken for 10 min. then extracted with light petroleum (2 × 150 c.c.; b. p. 40—60°). The extract was washed with water and evaporated under reduced pressure, giving the almost pure *azo*-compound (8·5 g.) which separated from methanol as yellow prisms, m. p. 57° (Found: C, 67·5; H, 4·8; N, 12·2. $C_{13}H_{11}N_2Cl$ requires C, 67·7; H, 4·8; N, 12·2%). Light absorption in EtOH: max. at 266 and 392 mμ ($10^{-3}\varepsilon$, 12·4 and 0·205).

Perbenzoic Acid Oxidation of p-*Chloro-ω-(phenylazo)toluene*.—The azo-compound (2·75 g.) was treated at 0° with ice-cold ethereal 2·357M-perbenzoic acid (6·02 c.c.); after 3 hr at 0° the mixture was homogeneous; after a further 16 hr. it was diluted with ether (50 c.c.), and the ethereal solutions from three such experiments were united and worked up rapidly below 10° as follows. The solution was added to potassium iodide (3 g.) and acetic acid (5 c.c.) in water (500 c.c.), and the liberated iodine removed by titration with 0·1N-sodium thiosulphate (perbenzoic acid used: 1·02 mols.). The ether layer was washed with sodium hydrogen carbonate solution and then thoroughly with water, and the solvent removed under strongly reduced pressure. The residual pale brown oil dissolved in methanol (60 c.c.) and after 1 hr. at 0° some crude *cis*-(4-chlorobenzylazoxy)benzene (0·3 g.) was removed. The filtrate was seeded at −10° with the corresponding *trans*-isomer and the temperature lowered to −40° during 2 hr. The crystals were collected and recrystallised from methanol giving trans-*(4-chlorobenzylazoxy)-benzene* (VI) (4·2 g.) as needles, m. p. 37° (Found: C, 63·1; H, 4·4; N, 11·3. $C_{13}H_{11}ON_2Cl$ requires C, 63·3; H, 4·5; N, 11·4%). The asymmetric stretching vibration of the azoxy-group gave a strong absorption band at 1484 cm.$^{-1}$.

The mother-liquor from which the above compound originally separated was kept for 16 hr. at −40° and the crystals were collected; more of the same material was obtained by concentrating the solution to 25 c.c. and cooling it to −50°. The combined crystal crops (1·0 g.) were recrystallised from light petroleum (b. p. 40—60°), giving trans-p-*chloro-ω-(phenylazoxy)-toluene* (VII) (0·43 g.) as large prisms, m. p. 63° (Found: C, 63·4; H, 4·4; N, 11·4%). The asymmetric stretching vibration of the azoxy-group gave a strong absorption band at 1495 cm.$^{-1}$.

Hydrolysis of trans- *and* cis-*(4-Chlorobenzylazoxy)benzene*.—A solution of the *trans*-azoxy-compound (726 mg.) in alcohol (15 c.c.) was added to boiling alcohol (75 c.c.) and concentrated hydrochloric acid (25 c.c.), and the solution boiled under reflux for 16 hr., concentrated under reduced pressure to 50 c.c., and heated under reflux for 2 hr. with more concentrated hydrochloric acid (60 c.c.). The cooled solution was then extracted with ether, the ether layer extracted with aqueous sodium hydrogen carbonate, and the extract acidified. The liberated acid was isolated with ether and sublimed under reduced pressure, giving *p*-chlorobenzoic acid (200 mg.), m. p. and mixed m. p. 238—239°. The aqueous acidic phase from the first ether extraction was evaporated to dryness. The residual hydrochloride (418 mg.) was identified as that of phenylhydrazine by interaction with benzoyl chloride and pyridine which gave *NN′*-dibenzoylphenylhydrazine, m. p. and mixed m. p. 176°.

Similar hydrolysis of the *cis*-isomer (500 mg.) required 30 hr. and gave considerable amounts of a black tar, together with *p*-chlorobenzoic acid (70 mg.) which, after sublimation under reduced pressure, had m. p. 238—239°, and impure phenylhydrazine hydrochloride (159 mg.). The latter was purified by sublimation under reduced pressure and identified as described above.

Hydrolysis of trans-p-*Chloro-ω-(phenylazoxy)toluene.*—Similar hydrolysis of this isomer (200 mg.) during 7 hr. gave *p*-chlorobenzoic acid (106 mg.), m p. 238—239°, and phenylhydrazine hydrochloride (100 mg.), identified as *p*-nitrobenzaldehyde phenylhydrazone, m. p. 156—157°.

N-ω : 4-*Dichlorobenzylidene*-N′-*phenylhydrazine* (IV).—(*a*) A solution of *trans*-(4-chlorobenzylazoxy)benzene (102 mg.) in dry saturated ethereal hydrogen chloride (2 c.c.) was kept overnight and then evaporated, giving the pure *product* which separated from alcohol as colourless plates (92 mg.), m. p. 147— 148° (Found: C, 59·0; H, 3·9; N, 10·2; Cl, 26·7. $C_{13}H_{10}N_2Cl_2$ requires C, 58·8; H, 3·8; N, 10·6; Cl, 26·8%).

(*b*) Similar treatment of *trans-p*-chloro-ω-(phenylazoxy)toluene (20 mg.) gave the same product, m. p. 147—148° alone or on admixture with the above material.

N-p-*Chlorobenzoyl*-N′-*phenylhydrazine.*—(*a*) The above dichloro-compound (53 mg.) was heated under reflux for 18 hr. with 40% aqueous alcohol (30 c.c.). The cooled solution deposited the *phenylhydrazide,* which separated from alcohol as needles (39 mg.), m. p. 191—192° (Found: C, 63·1; H, 4·6; N, 11·3. $C_{13}H_{11}ON_2Cl$ requires C, 63·3; H, 4·5; N, 11·4%).

(*b*) Phenylhydrazine (3·2 g.), pyridine (40 c.c.), and *p*-chlorobenzoyl chloride (5·1 g.) were heated together at 100° for 80 min., then kept overnight at room temperature, and poured into dilute sulphuric acid, and the solid was collected and recrystallised from alcohol. The phenylhydrazide (2·9 g.) had m. p. 191—192°, undepressed on admixture with the material prepared as above.

ω-(p-*Bromophenylazo*)-p-*chlorotoluene* (X).—Bromine (1·87 g.) in glacial acetic acid (15 c.c.) was added dropwise during 5 min. to a solution of *N*-benzoyl-*N*-4-chlorobenzyl-*N′*-phenylhydrazine (3·93 g.) in acetic acid (18 c.c.). The solution was poured into crushed ice and water (200 g.), and the crude solid bromo-compound (4·4 g.) collected and dried. It was heated under reflux for 16 hr. with alcoholic hydrogen chloride (80 c.c.; saturated at 15°), the solvent removed, and the residue washed with ether. Recrystallisation from water (charcoal) gave *N-p*-bromophenyl-*N′*-4-chlorobenzylhydrazine hydrochloride as needles (2·3 g.), m. p. 185—186° (decomp.).

To a solution of the hydrochloride (2 g.) in 50% alcohol (400 c.c.) a solution of ferric chloride hexahydrate (10 g.) in water (100 c.c.) was added; the mixture was shaken for 10 min. and then extracted with light petroleum (3 × 150 c.c.; b. p. 40—60°). The extract was washed with water and evaporated under reduced pressure, giving the almost pure *azo*-compound (1·7 g.) which separated from methanol as yellow crystals, m. p. 92—93° (Found: C, 49·9; H, 3·4; N, 9·4. $C_{13}H_{10}N_2ClBr$ requires C, 50·4; H, 3·2; N, 9·0%). Its structure was proved by treating it with warm methanolic hydrogen chloride, which gave *p*-chlorobenzaldehyde *p*-bromophenylhydrazone, m. p. and mixed m. p. 161—162°.

Perbenzoic Acid Oxidation of ω-(p-*Bromophenylazo*)-p-*chlorotoluene.*—After the azo-compound (1·68 g.) had been oxidised with ethereal perbenzoic acid as usual, the crude product was isolated as described for the oxidation of (III) above. It was a solid which dissolved completely in warm light petroleum, showing the absence of *cis*-azoxy-compound. It was triturated with cold methanol (5 × 2·5 c.c.), and the undissolved solid crystallised from ether (30 c.c.) in the temperature range 15° to −40°. The solid was collected and recrystallised from hot light petroleum (40 c.c.; b. p. 60—80°) and finally from warm alcohol, giving trans-p-*bromo-(4-chlorobenzylazoxy)-benzene* (XV) (670 mg.) as prisms, m. p. 103—104° (Found: C, 47·5; H, 3·8; N, 9·1. $C_{13}H_{10}ON_2ClBr$ requires C, 47·9; H, 3·1; N, 8·6%). The asymmetric stretching vibration of the azoxy-group gave a strong absorption band at 1495 (?1473) cm.$^{-1}$.

The ethereal mother-liquor from which the above compound originally separated was evaporated under reduced pressure, and the residue (0·53 g.) crystallised from alcohol (3 c.c.), giving a first crop which consisted of the above azoxy-compound, and a second crop (104 mg.) which had m. p. 75—80° and was shown by ultra-violet spectroscopy to contain about equal amounts of (XV) and of material with maximal absorption at *ca.* 300 mμ. A solution of this material in warm alcohol (3 c.c.) was seeded with the pure material and cooled, giving almost pure ω-(*p*-bromophenylazoxy)-*p*-chlorotoluene (21 mg.) which separated from alcohol as prisms (15 mg.), m. p. 107° alone or on admixture with material prepared as described below.

Action of Bromine on trans-(*4-Chlorobenzylazoxy*)*benzene.*—To a solution of the azoxy-compound (502 mg.) in dry carbon tetrachloride (2 c.c.) containing a trace of iodine (15 mg.) bromine (0·15 c.c.) was added and the solution was kept at 0° for 24 hr. It was then diluted with chloroform and washed successively with aqueous solutions of sodium hydrogen sulphite and sodium hydrogen carbonate and then with water. After the solution had been dried and evaporated the residue was triturated with cold methanol, and the part which did not dissolve was recrystallised from benzene–alcohol, giving N-ω-*bromo*-p-*chlorobenzylidene*-N′-2 : 4-*dibromo*-

phenylhydrazine (XII) (172 mg.) as needles, m. p. 150—151° (Found : C, 33·5; H, 1·9; N, 6·2. $C_{13}H_8N_2ClBr_2$ requires C, 33·4; H, 1·7; N, 6·0%). The same compound was obtained by treating *p*-chlorobenzaldehyde phenylhydrazone in acetic acid with bromine.

Action of Bromine Trifluoroacetate on trans-(*4-Chlorobenzylazoxy*)*benzene*.—To a cooled and agitated solution of the azoxy-compound (493 mg.) in nitrobenzene (1·5 c.c.) a mixture of silver trifluoroacetate (432 mg.) and bromine (314 mg.) in nitrobenzene (4·5 c.c.) was added dropwise. After 2 hr. no active bromine remained; after filtration, the precipitated silver bromide was washed with benzene, and the filtrate and washings were united and washed with aqueous sodium hydrogen sulphite, and then with water. The dried solution was evaporated under strongly reduced pressure, and the last traces of nitrobenzene removed at 35°/10^{-5} mm. The residue crystallised from light petroleum (b. p. 60—80°), giving trans-(*3-bromo-4-chlorobenzylazoxy*)*benzene* (XIII) (110 mg.) as needles, m. p. 112° (Found : C, 48·2; H, 3·4; N, 9·0. $C_{13}H_{10}ON_2ClBr$ requires C, 47·9; H, 3·1; N, 8·6%). The asymmetric stretching vibration of its azoxy-group gave a strong absorption band at 1488 cm.$^{-1}$. Hydrolysis with aqueous-alcoholic hydrochloric acid for 24 hr. gave 3-bromo-4-chlorobenzoic acid, m. p. 214—215°, undepressed on admixture with authentic material (m. p. 216°), and phenylhydrazine, identified as the *p*-nitrobenzylidene derivative, m. p. 156—157°.

Similar bromination of azoxybenzene (510 mg.) gave the same monobromo-derivative (370 mg.), m. p. 72—73°, as that obtained by bromination by Angeli and Valori's method (*loc. cit.*).

Action of Bromine Trifluoroacetate on p-*Chloro*-ω-(*phenylazoxy*)*toluene*.—The azoxy-compound (200 mg.) in nitrobenzene (1·9 c.c.) was brominated with bromine (143 mg.) and silver trifluoroacetate (198 mg.) in nitrobenzene (3 c.c.) in the manner described for the isomer. Reaction was complete within 20 min. and the product, isolated as before, crystallised from light petroleum (b. p. 40—60°), giving trans-ω-(p-*bromophenylazoxy*)-p-*chlorotoluene* (XIV) (147 mg.) as needles, m. p. 107° (Found : C, 47·7; H, 2·9; N, 8·3. $C_{13}H_{10}ON_2ClBr$ requires C, 47·9; H, 3·1; N, 8·6%). The asymmetric stretching vibration of the azoxy-group gave a strong absorption band at 1495 cm.$^{-1}$.

N-p-*Bromophenyl*-N′-ω : 4-*dichlorobenzylidenehydrazine*.—(*a*) The above azoxy-compound (60 mg.) in dry saturated ethereal hydrogen chloride (20 c.c.) was kept overnight, the solution evaporated to dryness under reduced pressure, and the *product* crystallised from alcohol as needles (47 mg.), m. p. 141—142° (Found : C, 45·8; H, 3·0; N, 7·8. $C_{13}H_9N_2Cl_2Br$ requires C, 45·3; H, 2·6; N, 8·1%).

(*b*) The azoxy-compound (39 mg.), alcohol (5 c.c.), and concentrated hydrochloric acid (3 c.c.) were boiled together under reflux for 17 min. The cooled solution deposited crystals which were recrystallised from alcohol (yield, 24 mg.) and then had m.p. 141° alone or when mixed with material prepared as in (*a*) above.

(*c*) Treatment of *N*-*p*-bromophenyl-*N*′-*p*-chlorobenzoylhydrazine with phosphorus pentachloride by von Pechmann and Seeberger's method (*Ber.*, 1894, **27**, 2122) gave a low yield of material, m. p. 141—142° alone or when mixed with material prepared as in (*a*) above.

N-p-*Bromophenyl*-N′-p-*chlorobenzoylhydrazine*.—(*a*) Prepared from *p*-chlorobenzoyl chloride and *p*-bromophenylhydrazine in pyridine in the usual way, the p-*bromophenylhydrazide* separated from alcohol as needles, m. p. 185—186° (decomp.) (Found : C, 47·7; H, 2·9; N, 8·8. $C_{13}H_{10}ON_2ClBr$ requires C, 47·9; H, 3·1; N, 8·6%).

(*b*) *N*-*p*-Bromophenyl-*N*′-ω : 4-dichlorobenzylidenehydrazine (25 mg.) and 40% aqueous alcohol were boiled together under reflux for 18 hr. The product (18 mg.) obtained by cooling the solution and recrystallising the solid from alcohol had m. p. 185—186° (decomp.) alone or when mixed with material from (*a*) above.

Isomerisation of trans-(*4-Chlorobenzylazoxy*)*benzene*.—(*a*) Pure *trans*-azoxy-compound (106 mg.) which had been kept in the dark in an evacuated tube for 11 days had become brown and sticky. Extraction with warm light petroleum left a residue (46 mg.) which crystallised from benzene–alcohol, giving *cis*-(4-chlorobenzylazoxy)benzene, m. p. and mixed m. p. 179—180° (decomp.).

(*b*) The *trans*-azoxy-compound (40 mg.) in dry methanol (2 c.c.) at room temperature started to precipitate the *cis*-isomer after 2 hr., and precipitation was complete in 24 hr. The product (25 mg.) had m. p. 178—179° (decomp.).

(*c*) In a similar experiment in which methanolic 0·01N-sodium methoxide was used in place of pure methanol, separation of the *cis*-isomer began within 30 min. and was markedly faster than in (*b*).

(*d*) The *trans*-isomer (40 mg.) and methanolic 0·01N-toluene-*p*-sulphonic acid were kept together for 27 days at room temperature, then the solution was diluted with ether and the toluene-*p*-sulphonic acid removed. Evaporation under reduced pressure and crystallisation of the residue from methanol at −30° gave unchanged *trans*-isomer, m. p. and mixed m. p. 36°.

cis-(3-*Bromo-4-chlorobenzylazoxy)benzene*.—(*a*) The corresponding *trans*-isomer (33 mg.), treated with methanolic 0·01N-sodium methoxide in the usual way, gave the cis-*compound* (15 mg.) which separated from benzene–alcohol as needles, m. p. 176° (decomp.) (Found: C, 48·0; H, 2·9; N, 8·9. $C_{13}H_{10}ON_2ClBr$ requires C, 47·9; H, 3·1; N, 8·6%). The asymmetric stretching vibration of the azoxy-group gave a strong band at 1470 cm.$^{-1}$.

(*b*) Material identical with that just described was obtained by oxidising 3-*bromo-4-chlorobenzaldehyde phenylhydrazone* [prisms, m. p. 142—143° (Found: C, 50·4; H, 3·3; N, 8·9. $C_{13}H_{10}N_2ClBr$ requires C, 50·4; H, 3·3; N, 9·0%)] with ethereal perbenzoic acid in the usual way. In the mother-liquors from which the *cis*-azoxy-compound had separated a careful chromatographic search was made for the corresponding *trans*-isomer, but none was detected.

cis-p-*Bromo-*(4-*chlorobenzylazoxy)benzene*.—(*a*) The corresponding *trans*-isomer (45 mg.) was dissolved in hot ethanol (2 c.c.), and enough methanolic sodium methoxide added to give a base concentration of 0·001N. Precipitation of the *cis*-isomer commenced at 80° in a few minutes, the mixture was kept at 20° for 3 hr., and the solid (25 mg.) then collected and recrystallised from benzene; it had m. p. 186—187° alone or when mixed with material prepared as described below.

(*b*) p-*Chlorobenzaldehyde* p-*bromophenylhydrazone*, plates (from alcohol), m. p. 162—163° (Found: C, 50·4; H, 3·5; N, 9·1. $C_{13}H_{10}N_2ClBr$ requires C, 50·4; H, 3·3; N, 9·0%), was oxidised with ethereal perbenzoic acid in the usual way, giving the cis-*azoxy*-compound (43%), which separated from benzene–alcohol as needles, m. p. 186—187° (decomp.) (Found: C, 48·2; H, 3·2; N, 8·6%).

4 : 4′-*Dichloro*-cis-ω-*azoxytoluene*.—(*a*) Prepared in the usual way, p-*chlorobenzaldehyde* p-*chlorobenzylhydrazone* had m. p. 105° (decomp.) (Found: C, 59·8; H, 4·7; N, 10·1. $C_{14}H_{12}N_2Cl_2$ requires C, 60·2; H, 4·3; N, 10·0%). A sample (664 mg.), oxidised with ethereal perbenzoic acid in the usual way, gave a small amount (96 mg.) of ether-insoluble material, recrystallisation of which from benzene–alcohol gave the cis-*azoxy*-compound as needles, m. p. 210—211° (decomp.). (Found: C, 57·2; H, 3·9; N, 9·3. $C_{14}H_{12}ON_2Cl_2$ requires C, 57·0; H, 4·1; N, 9·5%). Light absorption in EtOH: max. at 224·5 mμ ($10^{-3}\varepsilon$, 24·7). The infra-red absorption spectrum showed a strong band (asymmetric stretching vibration of the azoxy-group) at 1495 cm.$^{-1}$, whereas that of the *trans*-isomer showed strong bands at 1495 and 1522 cm.$^{-1}$.

(*b*) 4 : 4′-Dichloro-*trans*-ω-azoxytoluene, which has m. p. 107° and not 103° (cf. Part III, *loc. cit.*), when dissolved in methanolic sodium ethoxide, deposited the *cis*-isomer (40%) which after recrystallisation from benzene–alcohol had m. p. 211° (decomp.) undepressed on admixture with material prepared as in (*a*).

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