finding also suggests that the attack of the amines is the rate-determining step.

(3) Both the attack of water and the reactions of the amines with benzhydrylidenedimethylammonium ion and other cationic benzophenone Schiff bases (Results) are subject to general base catalysis. This finding is consistent with and support for rate-determining amine attack. It is, of course, quite possible to account for general base catalysis of the aminolysis reactions by a specific base–general acid catalyzed decomposition of the *gem*-diamine intermediate (in the reverse reaction, this corresponds to general base catalysis of the attack of dimethylamine on the unprotonated oxime), or by a general base-catalyzed decomposition of the protonated *gem*-diamine intermediate (general acid catalysis of the attack of dimethylamine on the oxime in the reverse direction).

(4) No evidence has been found, despite a reasonably careful search, for the accumulation of a detectable amount of the *gem*-diamine intermediate in the reactions of the benzophenone Schiff bases with weakly basic amines. This finding is consistent with rate-determining attack since only in the case of rate-determining *gem*-diamine decomposition would the intermediate accumulate.

In summary, the similarity of the effect of alteration of the structure of either the amine or carbonyl component of the Schiff bases on reaction rates for the attack of water and for the reactions with the amines, together with the finding that these reactions have similar catalytic pathways available to them, suggests that the attack of the amines is rate determining.

The above conclusions are consistent with data obtained for the acid-catalyzed interconversions of oximes and semicarbazones. Third-order rate constants for the acid-catalyzed formation of semicarbazones from benzaldehyde oximes and for the acid-catalyzed formation of oximes from benzaldehyde semicarbazones are correlated by Hammett σ-constants with identical ρ-values of -1.7 (Fig. 4). According to the above arguments, the attack of semicarbazide on the oximes should be rate determining rather than *vice versa*. Since the observed ρ-value of -1.7 must be the sum of ρ-values for oxime protonation and for semicarbazide attack on the protonated substrate, it follows that the ρ-value for the protonation of benzaldehyde oximes must have a value more negative than -1.7 since the ρ-value for the attack reaction is certainly positive. The observed ρ-value of -1.9 for the dissociation constants of protonated benzaldehyde oximes is consistent with this expectation.

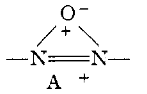
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO]

cis-Azoxybenzenes. I. Synthesis and Structure

BY D. L. WEBB AND H. H. JAFFÉ

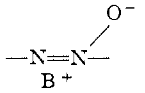
RECEIVED JANUARY 17, 1964

Nuclear magnetic resonance spectra are used to establish the configuration of the *cis*-azoxy group and to show the existence of two isomers in the monosubstituted compounds of this class. All the known monosubstituted and disubstituted *p*-methylazo and azoxy compounds were prepared and the chemical shifts of the methyl peaks, in c.p.s. downfield from tetramethylsilane, were obtained. In the compound *cis-p,p'*-dimethylazoxybenzene two methyl peaks were seen (at 112.7 and 105.2 c.p.s.), clearly eliminating the possibility of a symmetrical structure A and strongly indicating the structure B for the *cis*-azoxy group, analogous to the known configuration of the corresponding *trans* isomers. This contention is further strengthened by the spectral evidence for two isomeric *cis*-azoxybenzenes from the oxidation of *cis-p*-methylazobenzene. Two methyl peaks of approximately the same intensity were seen (at 112.6 and 105.4 c.p.s.). Only the compound whose methyl resonance occurred at 112.6 c.p.s. was isolated, and on decomposition formed α-*trans-p*-methylazoxybenzene (I, X = CH_3). Two other *cis* monosubstituted compounds were isolated from the oxidation of *p*-bromo- and *p*-chloroazobenzene, respectively. We believe these to be the first reported examples of monosubstituted *cis*-azoxybenzenes.



$$\overset{\mathrm{O}^-}{\overset{/\;+\;\backslash}{-\mathrm{N}{=}\mathrm{N}-}}$$

A +

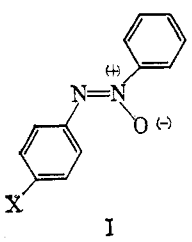


$$-\mathrm{N}{=}\overset{\qquad\mathrm{O}^-}{\overset{\qquad/}{\mathrm{N}}}-$$

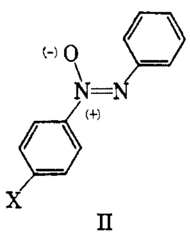
B +

The chemistry and the configuration of the *trans*-azoxybenzenes have been known for several years. Angeli[1] and co-workers have shown that the monosubstituted and the dissymmetrically substituted compounds exist in two isomeric forms, designated as "α" (I), and "β" (II), which differ only in the relative position of the oxygen atom. These results have recently been corroborated by the independent, unequivocal synthesis of each of the isomeric forms of *trans-p*-bromo- and *-p*-ethoxyazobenzene.[2]

However, reports of the geometric *cis* isomers have been scarce and pertain only to the unsubstituted or the symmetrically disubstituted compounds.[3] To our knowledge no *cis* monosubstituted azoxybenzenes have been reported. This paper presents a general synthetic method for the preparation of these compounds, albeit in small yields, and reports a preliminary study of their structure.



I



II

---

(1) A. Angeli and L. Alessandri, *Atti. Accad. Lincei*, **20I**, 896 (1911); **20II**, 170 (1911); A. Angeli and B. Valori, *ibid.*, **21I**, 155, 729, 794 (1912); A. Angeli and D. Bigiavi, *ibid.*, **6**, 5, 819 (1927).

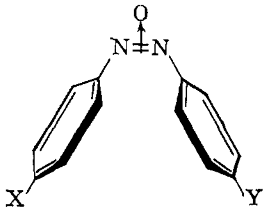
(2) I. C. Behr, *J. Am. Chem. Soc.*, **76**, 3672 (1954).

(3) K. E. Calderbrink and R. J. W. LeFèvre, *J. Chem. Soc.*, 1949 (1948); A. H. Cook, *ibid.*, 876 (1938); A. H. Cook and D. G. Jones, *ibid.*, 1309 (1939).

The method chosen was successful for the preparation of two symmetrically disubstituted and three monosubstituted compounds (Table I) in *ca.* 2% yields. It requires the oxidation of a mixture of *cis-* and *trans*-azobenzenes by an anhydrous mixture of peracetic acid and hydrogen peroxide in chloroform. When pure *cis-p*-methylazobenzene was used, and the temperature reduced to 0°, the yield increased to 48% of the theoretical. This fact, and the behavior of the spectral solutions of the *cis*-azoxy compounds, suggests that the *in situ cis* → *trans* rearrangement is strongly inhibited by depressed temperatures. Badger, Buttery, and Lewis[4] have shown that rate of oxidation of *cis*-azo compounds is more rapid than that of the corresponding *trans* isomers and that log k_c/k_t is fairly constant between 20 and 30°. Hartley and LeFèvre[5] have shown that an equilibrium mixture of about 80% *trans*–20% *cis* is obtained by irradiation of *trans*-azobenzene. The low yields we obtained in reactions at room temperature indicate extensive rearrangement of the *cis* compound during the oxidation.

TABLE I

cis-AZOXYBENZENES[a]

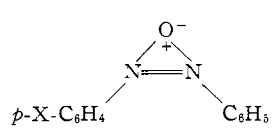


X	Y	M.p., °C.	λ_1, mμ	ϵ_{max}	λ_2, mμ	ϵ_{max}
H–	H–	69-71	239	11,200	327	3900
CH_3–	CH_3–	73–73.5	241	14,800	338	4100
Br–	H–	83.5	242	14,900	332	5100
Cl–	H–	81.5–82	241	20,600	330	6600
CH_3–	H–	83.5–84.5	240	12,900	339	3800

[a] The NO bond is localized but not located.

Results and Discussion

In the oxidation of the monosubstituted *cis*-azo compounds only one product was isolated from each of the reactions. Since similar reaction of the corresponding *trans* isomers produced two azoxy compounds, the following explanations were considered: (A) The single product had a symmetrical structure of the type

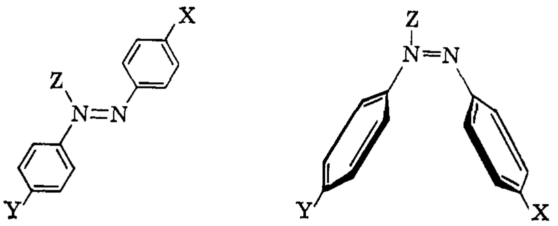


(B) The orienting effect of the substituent group caused a preferential oxidation of one of the nitrogen atoms. (C) Both possible isomers were formed, one of which decomposed during the isolation procedure.

To resolve this question the entire series of mono- and dimethyl substituted azo- and azoxybenzenes were prepared and their nuclear magnetic resonance spectra were obtained (Table II). The change of chemical shift of the methyl protons was found to demonstrate the spatial configuration of the phenyl rings, *cis* or *trans*, and to indicate the position of the oxygen atom.

TABLE II

CHEMICAL SHIFT OF THE METHYL GROUP



X	Y	Z	δ^a	X	Y	Z	δ^a
CH_3–	H–	..	124.8	CH_3–	H–	..	115.5
CH_3–	CH_3–	..	124.6	CH_3–	CH_3–	..	115.5
CH_3–	H–	O	124.6	CH_3–	H–	O	112.6
H–	CH_3–	O	117.4	H–	CH_3–	O	105.4
CH_3–	CH_3–	O	124.5, 118.4	CH_3–	CH_3–	O	112.9, 105.8

[a] All chemical shifts are reported in c.p.s. downfield from TMS.

The spectra of both *cis-* and *trans-p,p'*-dimethylazobenzene showed a single methyl resonance, as expected; the spectra of both *cis-* and *trans-p,p'*-dimethylazoxybenzene show two methyl peaks, each separated by *ca.* 7 c.p.s. Hence, it is apparent that the methyl groups of the two latter compounds exist in different magnetic environments, and the possibility of the symmetrical NNO link, shown above under A, is eliminated.

Careful oxidation of *cis-p*-methylazobenzene at 0° and isolation of the *cis*-azoxy compounds at that temperature by absorption chromatography produced a material which showed two methyl resonances at 112.6 and 105.5 c.p.s. downfield from TMS. These correspond exactly to the two methyl peaks produced by *p,p'*-dimethylazoxybenzene and indicate the presence of two *cis* isomers. When the solution of these compounds was allowed to rise to room temperature there appeared two additional peaks at 124.4 and 118.3 c.p.s. which correspond to the "α"- and "β"-*trans* isomers, respectively. On further standing, the higher field signals disappeared altogether and the lower field signals showed a corresponding increase in intensity. The rate of disappearance of the peak at 105 c.p.s. was much more rapid than that of the peak at 112 c.p.s.

Since the methyl resonance of the "α"-*trans* isomer occurs at lower field than that of the "β"-, the methyl resonances of the *cis* isomers were assigned following the same order; *i.e.*, the "α" occurs at 112.6 c.p.s. and the "β" at 105.5 c.p.s. Further analogy is obtained from Freeman's work in a similar system of aliphatic azoxy compounds.[6] Having made this assignment, the thermal rearrangement of the *cis* isomers was found to take place with no change in the ratio total α/total β during and after the rearrangement. This behavior strongly indicates that the rearrangement takes place without migration of the oxygen, since decomposition of either of the isomers to a mixture of *trans* isomers would lead to a change in the α/β ratio during the rearrangement.

Interpretation of Chemical Shifts.—The n.m.r. results are consistent if one takes the methyl resonance of *trans-p*-methylazobenzene as a standard and assumes that any further substitution, oxidation, or change of configuration will affect the chemical shift according to the degree of perturbation of the system. Thus we find that the addition of a methyl group to the unoccupied *p*-position causes no change of chemical shift.

---

(4) G. M. Badger, R. G. Buttery, and G. E. Lewis, *J. Chem. Soc.*, 2143 (1953)

(5) G. S. Hartley and R. J. W. LeFèvre, *ibid.*, 531 (1939).

(6) J. P. Freeman, private communication.

CHART I

CHANGE OF CHEMICAL SHIFT OF THE METHYL GROUP BY PERTURBATION OF *p*-METHYLAZOBENZENE

Perturbation	Effect, c.p.s.	Compound	A	B	C	Total	δ_{Calcd}	δ_{Found}
A, *trans–cis*	−9	(1) Azo (*trans*)	0	0	0	0	(124.6)	124.6
		(2) Azo (*cis*)	−9	0	0	− 9	(115.6)	115.5
		(3) "α" (*trans*)	0	0	0	0	(124.6)	124.6
B, Oxidation-*cis* (steric)	−3	(4) "α" (*cis*)	−9	−3	0	−12	(112.6)	112.6
		(5) "β" (*trans*)	0	0	−7	− 7	(117.6)	117.4
C, Oxidation (electronic)	−7	(6) "β" (*cis*)	−9	−3	−7	−19	(105.6)	105.4

This is not unexpected since the steric and inductive effects of this group will be negligible at such a distance, and the resonance effect is a low order effect in n.m.r. spectroscopy.

When the configuration is changed to *cis* there is an upfield shift of almost 10 c.p.s. Molecular models show that in such a configuration, if the rings were to remain coplanar, there would be considerable overlap of the adjacent *o*-hydrogens. X-Ray studies on crystalline *cis*-azobenzene indicate also that the rings are not coplanar, and, in the solid, are at an angle of 56° to the plane of the N=N bond.[7] This arrangement makes possible an interaction of the π-systems of the rings with an increase in paramagnetic shielding and a consequent decrease of the chemical shift of the methyl protons. Addition of a second methyl groupi n this system is again seen to have no effect.

In the *trans* compound oxidation of the nitrogen atom nearer the substituent causes an upfield shift of about 7 c.p.s., while oxidation of the farther nitrogen does not affect the chemical shift. The same difference (7 c.p.s.) is seen in the *cis*-azoxy pair. Apparently the effect is a field effect rather than a formal electronic interaction, since the conformation of the rings has been shown to be different in the two systems. In the *trans*-" α" isomer the effect is passed only into the unsubstituted ring and there is no change of chemical shift of the methyl group.

It may be shown by molecular models that oxidation of the *cis*-azo group decreases the angle between the two phenyl rings and thereby increases the ring–ring interaction. Therefore, the *cis*-"α" isomer shows a slight upfield shift of 3 c.p.s. The *cis*-"β" isomer, by a combination of ring–ring interaction and field effect, shows the greatest upfield shift. There is no apparent transmission of the field effect to the substituted ring by ring–ring interaction in the *cis*-"α" isomer. Chart I shows the proposed effects and the consistency of the model compounds in demonstrating them.

These data permit reasonable assurance for the assignment of structure for the methyl compounds, but do not allow analogous assignments in the case of the bromo or the chloro products, since the Hammet σ-constants of the latter two are similar to each other but are opposite in sign to that of the methyl group. Also unresolved is the observed lesser thermal stability of the *cis*-"β" isomer.

Ultraviolet Spectra.—The ultraviolet spectra of the *cis* compounds were obtained and the spectral values are reported in Table I. The spectra are similar to the *cis*-stilbene spectra, an analogy that has already been drawn in the comparison of the *trans* series. That is, there are two, apparently uncomplicated, absorptions; the long wave length absorption corresponding to a lengthwise polarization of the molecule is considerably reduced in intensity, whereas the short wave length absorption is greatly increased.

Experimental

Preparation of the Oxidizing Mixture.—Becco 98% hydrogen peroxide (3.0 ml., 124 mmoles) and glacial acetic acid (7.0 ml.) were mixed and allowed to stand overnight. The mixture was extracted with 3 × 10 ml. of $CHCl_3$, dried over $CaSO_4$, and filtered. The solution was used without titration.

Preparation of *cis*-Azoxybenzenes.—The general procedure for the preparation may be shown by using the example of the *p*-bromo compound.

p-Bromoazobenzene (1.0 g., 3.9 mmoles) in 10 ml. of $CHCl_3$ was irradiated with a Hanovia ultraviolet lamp (type 16200) for 2 hr. A previously prepared solution of hydrogen peroxide–acetic acid–peracetic acid in 25 ml. of $CHCl_3$ (oxidizing mixture) was added, and the reaction mixture was placed *ca.* 20 in. from a GE 200-watt heat lamp for 3 hr. At the end of this time the solution was poured into 100 ml. of H_2O and the organic phase was removed, washed with two 50-ml. portions of H_2O, once with 50 ml. of 10% Na_2CO_3 solution, and again with 50 ml. of H_2O. The $CHCl_3$ layer was then dried over $CaSO_4$, filtered, and blown dry under a current of dry air, leaving a yellow-orange solid. This was taken up in 12 ml. of redistilled 40–60° ligroin and placed on a 12 × 150 mm. column of 200 mesh silicic acid. The unreacted *trans* starting material and the *trans*-azoxy products were eluted with ligroin followed by a 2% (vol.) Et_2O–ligroin mixture. There remained behind a bright yellow-green material which was eluted with 10% Et_2O-ligroin. As this material was removed, it was held at 0° and kept under a current of air. When the solvent had been removed, there remained a yellow-green solid which was washed with cold ligroin until the washings were colorless; yield 22 mg. (0.1 mmole, 2%), m.p. 85.5°.

Oxidation of *cis-p*-Methylazobenzene.—*cis-p*-Methylazobenzene (1.00 g., 5.27 mmoles) was prepared by irradiating 6.0 g. of *trans-p*-methylazobenzene in ligroin for 4 hr., followed by chromatographic separation on an alumina column. The *trans* material was eluted with ligroin; the *cis* with Et_2O. The eluted *trans* was concentrated and re-irradiated. This process was repeated until sufficient *cis* material had been prepared. It was taken up in 5 ml. of $CHCl_3$, and 50 ml. of oxidizing solution was added. The mixture was placed in an enameled black flask in a dewar flask at 0° and kept there or 6 hr. The work-up of the product was performed as above, save that all solutions used in washing were precooled to −5°, and the column used for chromatographic separation was kept at 0 ± 3°; yield 541 mg. (2.54 mmoles, 48%); n.m.r. spectra showed no *trans*-azo or azoxy impurities and no *cis*-azo impurities.

Ultraviolet Spectra.—All spectral solutions were made by preparing a 10^{-2} *M* solution in EtOH and diluting to 10^{-4} *M* with EtOH. Spectra were taken on a Cary Model 11.

N.m.r. Spectra.—All spectra were taken on a Varian Model A-60 in benzene solution. The chemical shifts are reported in c.p.s. downfield from TMS as an internal standard. The chemical shifts were obtained by audio oscillating side-band technique.

It was found that the change of chemical shift of the methy group in *p,p'*-dimethylazobenzene was negligible between concentrations of 1 to 5 × 10^{-3} *M*. Therefore, all n.m.r. values are reported without extrapolation to infinite dilution.

Acknowledgment.—Support of this work by the American Cancer Society is gratefully acknowledged. The authors wish to express appreciation to Dr. F. Kaplan of this university and to Dr. J. H. Collins of the Procter and Gamble Co. for their helpful discussions.

---

(7) G. C. Hampson and J. M. Robertson, *J. Chem. Soc.*, 409 (1941).