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The Reactions of Azoxybenzenes in Acids. The Mechanism of the Wallach Rearrangement

G.G.Furin

Data concerning the use of various acids to effect the Wallach rearrangement in the series of azoxybenzenes are analysed and the influence of the chemical nature and position of the substituents on the reactions of azoxybenzenes in the presence of acids, including the Wallach rearrangement and side processes, are examined. Data obtained in the study of the mechanism of the Wallach rearrangement by kinetic and tracer atom methods are discussed and the effect of Lewis acids and UV radiation on azoxybenzenes is considered.
The bibliography includes 63 references.

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I. INTRODUCTION

Organic compounds with a nitrogen-containing functional group play an exceptionally important role in natural and technological processes. Such compounds include medicinal preparations, dyes, pesticides, explosives, etc. The great theoretical and practical importance of these compounds has stimulated the study of the chemical properties of nitrogen-containing functional groups. Among organic nitrogen compounds, azoxybenzenes occupy a special place. As a result of their high thermal and chemical stabilities, all the compounds containing a nitrogen atom attached to the benzene ring can be ultimately converted into azoxybenzenes via oxidation or reduction regardless of the valence state of the nitrogen in the functional group (see, for example, Yandovskii et al.[1]).

On the other hand, the known instances of reversible reactions of azoxybenzenes are fairly few. This has aroused interest in the Wallach rearrangement, discovered more than one hundred years ago, which consists in the conversion of azoxybenzene into 4-hydroxy- and 2-hydroxy-azobenzenes on treatment with concentrated sulphuric acid. The availability of the starting materials and the simplicity of the conditions promoted the wide-scale employment and detailed study of the Wallach rearrangement, which is nowadays included among the principal synthetic methods of organic chemistry. The Wallach rearrangement has been investigated in special detail in relation to azoxybenzene itself: the fundamental features of its occurrence have been discovered and its mechanism has been seemingly elucidated. However, the data obtained in the studies during the last decade have shown that, even when the reaction conditions and the structures of the initial azoxybenzenes are altered only slightly, processes unrelated to the Wallach rearrangement proper begin to occur. Unusual reactions were then observed of the kind which it would perhaps be impossible to predict *a priori* at the present level of development of chemistry. It was also found that the mechanism of the rearrangement is more complex than appeared previously.

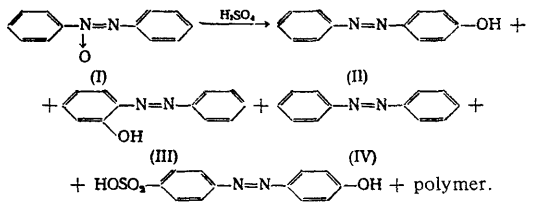
New data require the reconsideration of the accumulated results for a more adequate understanding of the situation which has arisen as regards the study and treatment of the Wallach rearrangement. Analysis of experimental data relevant to the Wallach rearrangement has been frequently carried out in a number of review articles and monographs and both individual aspects of this reaction and the reaction as a whole have been considered.[2-4] Japanese investigators, in Yamamoto's[5,6] and Oae's[7] schools, have made a major contribution to the discovery of the principal features of the Wallach rearrangement and the principal original studies in this field are due to these investigators. The fundamental investigations of Shemyakin's school, carried out by the tracer atom (^{15}N, ^{18}O) methods[8-10] have played a large role in the understanding of the mechanism of the rearrangement.[8-10] Data on the kinetics of the Wallach rearrangement have been obtained.[4,11]

Despite the large number of studies devoted to the mechanism of the Wallach rearrangement, a single view concerning the rearrangement has not so far been elaborated. One of the key questions, concerning the identification of the cationoid species responsible for the rearrangement, has remained unresolved. Olah et al.[12] put forward the hypothesis, shared by many chemists, that this species is a dication generated by the dehydrated diprotonated form of azoxybenzene. The data of the last few years, obtained in the study of the synthetic aspects of the Wallach rearrangement and its mechanism, are analysed in the present review. Earlier investigations are discussed only in those cases where this is required for the understanding of the new data.

II. THE INFLUENCE OF THE NATURE OF THE ACID AND THE ACIDITY FUNCTION OF THE MEDIUM ON THE ACID-CATALYSED REARRANGEMENT OF AZOXYBENZENES

In the course of the study of the behaviour of azoxybenzene in concentrated sulphuric acid, Wallach observed the formation of 4-hydroxyazobenzene together with 2-hydroxyazobenzene and other products (Scheme 1). Somewhat later, this result was confirmed by a number of workers who concluded that its character is general.[2,3]

Scheme 1



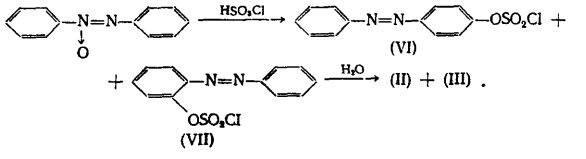
Kinetic data have shown that the rate of the rearrangement depends significantly on the acidity of the medium.[4] Thus, on passing from 75% ($-H_0 = 6.65$) to 99.99% ($-H_0 = 11.9$) sulphuric acid (at 25 °C), the rate constant increases by five orders of magnitude.

At the present time the range of acids used for the Wallach rearrangement is fairly large, starting with sulphuric acid ($-H_0 = 11.93$) and ending with the 1:1 HSO_3F–SbF_5 mixture ($-H_0 = 19.5$). There exist also individual examples of the employment of mixtures of acids (for example, toluene-*p*-sulphonic acid–acetic anhydride). However, these acid systems have no special advantages over sulphuric acid. Sulphuric acid (at a concentration >80%) is employed as a rule for the rearrangement. The product ratio (*ortho* : *para*) is 0.02%. It has been shown[13] that at these sulphuric acid concentrations the solvated proton H_3O^+ is not a sufficiently strong acid to catalyse the reaction considered. Stronger acids (H_2SO_4 and $H_3SO_4^+$) play the role of the catalyst under these conditions.

It has been suggested[11] that the product of the rearrangement of azoxybenzene in concentrated sulphuric acid is azobenzene-4-hydrogen sulphate, whose hydrolysis affords 4-hydroxyazobenzene. Indeed azobenzene-4-hydrogen sulphate hydrolyses in sulphuric acid with formation of 4-hydroxyazobenzene. It has been shown that under these conditions the nitrogen atom of the azo-group is initially protonated, which is followed by the slow protonation of the oxygen atom bound to the benzene ring, and finally the C–S bond is cleaved. The idea of the intermediate formation of 4-substituted esters with their subsequent hydrolysis to 4-hydroxyazobenzene was used to account for the processes occurring in different acids.[3,4]

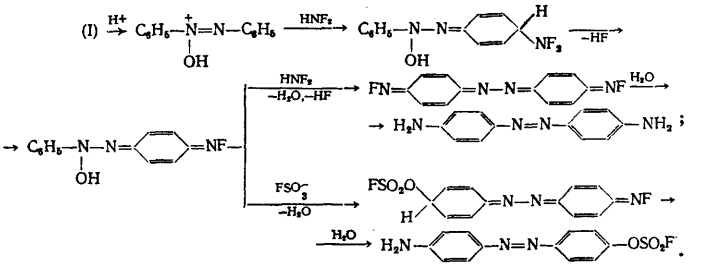
Dissolution of azoxybenzene in HSO_3Cl at −10 °C leads to the formation of its esters (VI) and (VII) (the *ortho* : *para* ratio is 0.51), which are readily hydrolysed by weak alkalis (Scheme 2):[14,15]

Scheme 2



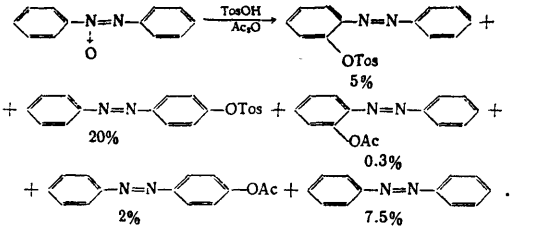
As in concentrated sulphuric acid, the rearrangement in HSO_3F leads to the preferential formation of the *para*-substituted product (II).[15,16]

The presence in the acid system of different anions, whose nucleophilicity has a decisive influence on the character of the products formed, is exceptionally important. For example, when the Wallach rearrangement is carried out in HSO_3F with added HNF_2, the products are 4-fluorosulphonyloxyazobenzene (17–35%), 4,4′-diaminoazobenzene (16–45%), and 4-amino-4′-fluorosulphonyloxyazobenzene (5–20%).[16] The amino-derivatives are formed via the intermediate fluoroimines:



When the Wallach rearrangement is performed in a mixture of acids containing different anions, different products are formed, for example both toluene-*p*-sulphonates and acetates are formed in the toluene-*p*-sulphonic acid–acetic anhydride mixture. This shows that in the second stage of the rearrangement the cationoid species generated from azoxybenzene interacts with the anion of the medium.[17] The *para*-substituted product predominates in this case too (Scheme 3).

Scheme 3



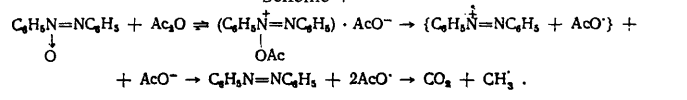
This demonstrates the important role of the second stage of the reaction, which consists in the attack by the nucleophile of the medium on the most electrophilic centre in the intermediate cationoid species responsible for the Wallach rearrangement.

When azoxybenzene is treated with 80% polyphosphoric acid, a mixture of 2-hydroxy- and 4-hydroxy-azobenzenes with an *ortho* : *para* ratio of 1.7 is formed (the yields of products are 26 and 11.8% respectively).[6] In addition 15.1% of azobenzene is produced.

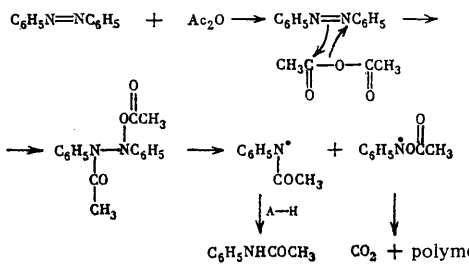
When azoxybenzene is treated with toluene-*p*-sulphonic acid and polyphosphoric acid, azobenzene, the product of the reduction of azoxybenzene, is formed in appreciable amounts, which is extremely unexpected and difficult to explain. It has been shown[18] that azobenzene is the main product resulting from the treatment of azoxybenzene with the (1:1) (HF–SbF_5)–SO_2 mixture at −50 °C (yield 68–72%); the usual product of the Wallach rearrangement, namely 4-hydroxyazobenzene, is obtained in a yield less than 10%, while 2-hydroxyazobenzene is not detected at all. These data show that the nature of the acid used to effect the Wallach rearrangement influences not only the *ortho* : *para* ratio but also the course of the process itself, which is probably due to the difference in the reactivities of the species generated from azoxybenzene under the influence of different acids.

Azoxybenzene does not change in acetic acid at temperatures in the range 20–190 °C, while the addition of acetic anhydride leads to the formation of acetic acid and acetanilide in 70% yield (when the reactants are used in proportions of 1:5). On the other hand, for the equimolar reactant ratio, a complex mixture of products is formed in the system: azobenzene (60%), acetanilide (13%), acetic acid (63%), CO_2 (95%), CO (14%), and CH_4 (2%).[19] The authors suggest the following reaction mechanism (Scheme 4):

Scheme 4



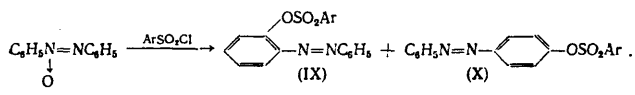
The acetanilide and CO_2 are obtained from azobenzene, which has been demonstrated independently by treating azobenzene with acetic anhydride. It has been suggested that the reaction proceeds as follows:



The usual products of the Wallach rearrangement, namely 2-hydroxy- and 4-hydroxy-azobenzenes, are formed from azoxybenzene in small yields in trichloroacetic acid in the presence of acetic anhydride.[20]

Thus the first feature of an acid system containing electrophilic CH_3CO^+ species is that reduction products and not the products of the Wallach rearrangements are formed, and the second feature is the possibility of catalysis of the Wallach rearrangement not only by H^+ but also by other cationoid species. The first stage under these conditions is attack by the cationoid species on the oxygen atom of the azoxy-group. Indeed, it has been found that, when azoxybenzene is heated with arenesulphonyl chlorides, the arenesulphonic esters (IX) and (X), the products of the Wallach rearrangement, are formed.[21] The *ortho* : *para* ratio then varies as a function of the nature of the arenesulphonyl chloride employed (Scheme 5):

Scheme 5



Ar	(IX) Yield of (IX), %	(X) Yield of (X), %
4-$NO_2C_6H_4$	59.7	24.8
4-BrC_6H_4	28.8	36.8
4-$CH_3C_6H_4$	0.6	61.4
CH_3SO_2Cl	—	63.8

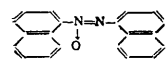
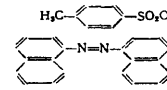
The rearrangement of azoxybenzenes proceeds also on treatment with the anhydrides of benzenesulphonic acids[22] (Table 1). However, the *para*-substituted product is formed exclusively in this case in high yields (Table 2). It has been suggested[22] that the reaction proceeds in accordance with Scheme 6.

The kinetic data (in the presence of an excess of arenesulphonic acid anhydride, the reaction is of pseudo-first order, $E_a = 22.4$ kcal mol^{-1}, and $\Delta S^{\neq} = -14.2$ e.u.) and especially the influence of substituents both in the azoxybenzene ($\rho = -1.5$) and in the arenesulphonic acid anhydride ($\rho = +1.3$) on the rate of reaction show that the overall rate of this reaction is determined by the stage involving the cleavage of the N–C bond.[22]

Table 1. The reactions of azoxybenzene with sulphonic acid anhydrides.[22]

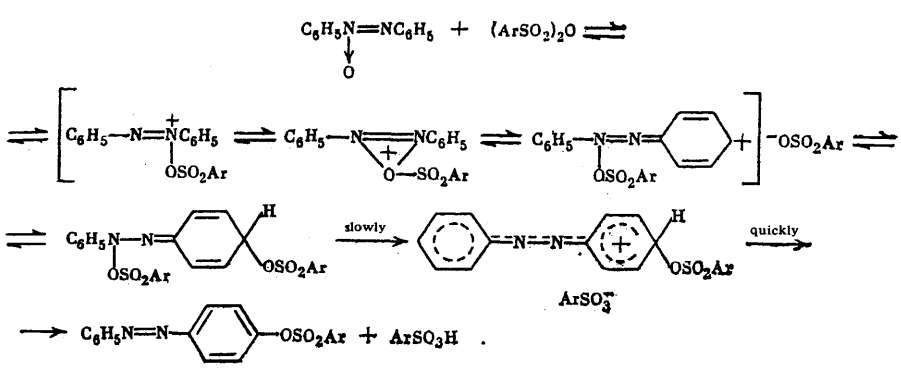
Anhydride	Reaction product	Yield, %
Tos_2O	4-$TosOC_6H_4N{=}NC_6H_5$	92
$(C_6H_5SO_2)_2O$	4-$C_6H_5SO_2OC_6H_4N{=}NC_6H_5$	92
$(4\text{-}BrC_6H_4SO_2)_2O$	4-(4-$BrC_6H_4SO_2O$)$C_6H_4N{=}NC_6H_5$	86

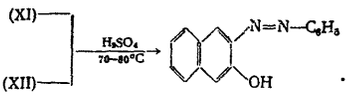
Table 2. The reactions of substituted azoxybenzenes with the anhydride of toluene-*p*-sulphonic acid.[22]

Compound	Product	Yield, %
4-$BrC_6H_4N{=}NC_6H_5$ (O)	4-$BrC_6H_4N{=}N$–$C_6H_3(CH_3)OSO_2C_6H_5$	62
4-$BrC_6H_4N{=}NC_6H_5$ (O)	ditto	75
2-$CH_3C_6H_4N{=}NC_6H_4CH_3$-2 (O)	$C_6H_3(CH_3)_2N{=}N$–$C_6H_3(CH_3)OSO_2C_6H_5$	74
$C_6H_5N{=}NC_6H_4CH_3$-4 (O)	4-$CH_3C_6H_4N{=}N$–$C_6H_3(CH_3)OSO_2C_6H_5$	68
 (O)		70

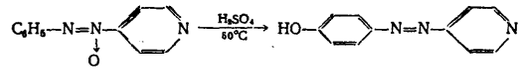
Like azoxybenzene, azoxy-compounds of the naphthalene series undergo the Wallach rearrangement.[23,24] It has been shown that, when 2-naphthyl-*ONN*-azoxybenzene (XI), 2-naphthyl-*NNO*-azoxybenzene (XII), 1,1′-azoxynaphthalene, 1,2′-*ONN*-azoxynaphthalene, and 2,2′-azoxynaphthalene are treated with sulphuric acid (at a concentration in the range 60–93%), the Wallach rearrangement is observed and the corresponding hydroxyazo-derivatives are formed, the site of attack by the nucleophile being the *ortho*-position in the naphthalene nucleus:

Scheme 6





On the other hand, the introduction of the dimethylamino-group into the benzene ring, for example in the case of 2-naphthyl-*ONN*-azoxy(4'-dimethylaminobenzene), prevents the Wallach rearrangement in 70% sulphuric acid (as a result of the protonation of its nitrogen atom).[25] However, at a sulphuric acid concentration of 97–99.9% protonation at the substituent does not prevent the rearrangement.[26] Thus 4-pyridyl-*NNO*-azoxybenzene affords under these conditions 4-(4'-hydroxyphenylazo)-pyridine. However, 4-pyridyl-*ONN*-azoxybenzene does not rearrange under these conditions, which indicates the importance also of the very structure of the azoxy-derivative for the acid-catalysed rearrangement:



Analogous characteristics have been discovered also for the isomeric (α- and β-) 4-(phenylazoxy)pyridine *N*-oxides.[27] Kinetic data for the rearrangement of 4-pyridyl-*NNO*-azoxybenzene have shown that, on passing from 98.46% to 99.91% sulphuric acid, the rate constant increases by two orders of magnitude.[26]

Thus the character of the acid employed has a significant influence on the products of the Wallach rearrangement.

III. THE INFLUENCE OF SUBSTITUENTS ON THE WALLACH REARRANGEMENT

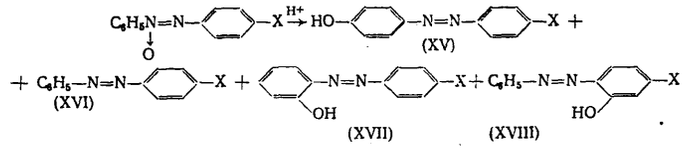
The introduction of electron-accepting substituents in the azoxybenzene molecule reduces the electron-donating capacity of the oxygen atom of the azoxy-group and increases the electron-accepting capacity of the carbon atoms in the benzene rings (Table 3).[28]

Table 3. The basicities of 4-substituted *NNO*-azoxybenzenes.[28]

X	pK_a	X	pK_a
OCH_3	−6.10±0.04	H	−6.45±0.05
OC_2H_5	−6.04±0.03	Br	−7.01±0.04
CH_3	−6.04±0.03	NO_2	−9.83±0.07

For this reason, substituents influence both the rate of the Wallach rearrangement and the nature of the products, so that the study of the influence of the chemical nature and position of the substituent in azoxybenzene on the reactivity and the type of products under the conditions of the Wallach rearrangement is extremely important for the question under consideration. In particular, this applies to those cases where structural factors hinder the Wallach rearrangement and the character of the acid system can promote other processes. Indeed, it will be seen from the data presented below that in many instances unexpected products are formed, which can be explained both from the standpoint of the stabilising influence of the substituent on the cationoid species and on the basis of the character of the electrophilic intermediate generated.

We shall consider in the first place the influence of the halogen in the 2- and 4-positions on the Wallach rearrangement. When 4-halogenoazobenzenes are treated with sulphuric acid, the main products are 4-halogeno-4-hydroxyazobenzenes, i.e. the OH group is in the unsubstituted benzene ring:



The ratio of the products varies little as a function of the structure of 4-halogenoazoxybenzene, i.e. as a function of whether it is the α- or β-isomer [4-halogeno-*ONN*-azoxybenzene (XIII) or 4-halogeno-*NNO*-azoxybenzene (XIV)] (Table 4).[29]

Table 4. The reactions of 4-halogeno-*ONN*-azoxybenzenes with sulphuric acid (92%, 50 °C, 30 min).[29]

X	Yield, %			
	(XV)	(XVI)	(XVII)	(XVIII)
F	54	26	0.5	0.3
Cl	34	46	1.4	0.2
Br	27	55	1.7	0.3
I	5	72	2.0	0.3
Br*	27	52	2.0	0.1

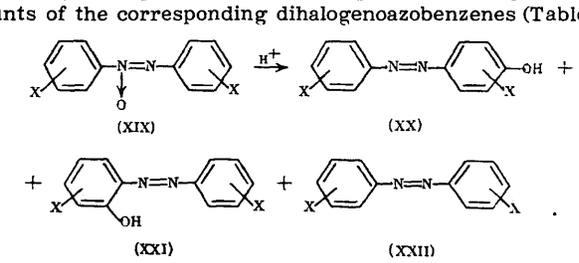
*The β-isomer.

Table 5. The reactions of azoxybenzenes with acids.

X	Reagent*	Amount of product (XIX) recovered, %	Yield, %			Refs.
			(XX)	(XXI)	(XXII)	
2,2'-Br_2	H_2SO_4 (82%)	14.1	62.7	—	33.8	[6]
2,2'-Br_2	HSO_3Cl	41.5	33.4	2.4	20.9	[6]
2,2'-Br_2	H_3PO_4 (80%)	74.3	3.9	3.9	—	[6]
2,2'-Cl_2	H_2SO_4 (82%)	16.2	75.3	—	15.7	[6]
2,2'-Cl_2	HSO_3Cl	51.4	30.5	—	23.7	[6]
2,2'-Cl_2	H_3PO_4 (80%)	68.5	3.2	3.2	5.4	[6]
3,3'-Cl_2	H_2SO_4 (92%)	75	16	1	—	[30]
4,4'-Cl_2	H_2SO_4 (92%)	—	—	13	58	[30]
4,4'-Br_2	H_2SO_4 (92%)	—	—	15	59	[30]
2-Cl	H_2SO_4 (78%)	13.6	35.4	6.9	30.3	[31]
2,2'-Cl_2	H_2SO_4 (78%)	28.4	43.5	0	11.8	[31]
4,4'-Cl_2	H_2SO_4 (78%)	71.6	—	7.3	18.1	[31]
2,2',4,4'-Cl_4	H_2SO_4 (78%)	73.5	0	0.5	17.1	[31]

*The concentration is given in brackets.

In the case of azoxybenzenes where the halogen atoms are in the 2,2'- and 3,3'-positions, treatment with different acids leads to the products of the Wallach rearrangement (4-hydroxydihalogenoazobenzenes) together with appreciable amounts of the corresponding dihalogenoazobenzenes (Table 5):



The Wallach rearrangement takes place selectively in the *para*-position. However, when both *para*-positions in the benzene ring are occupied, it takes place in the *ortho*-position. At the same time detailed study of the products of the reaction of 4,4′-dihalogenoazoxybenzenes in 92% sulphuric acid revealed a number of unexpected substances, among which compounds (XXV), (XXVI), and (XXVIII) were found.[28] The yields of the products are presented in Table 6.

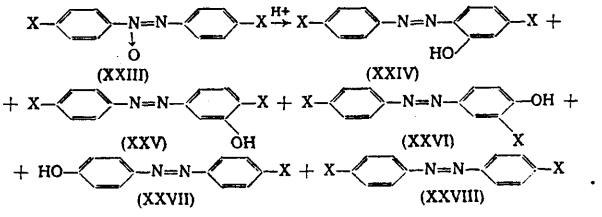
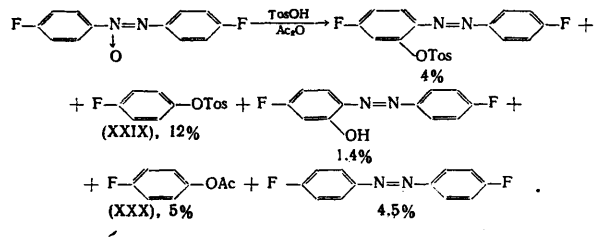


Table 6. The reactions of 4,4′-dihalogenoazoxybenzenes (XXIII) with 92% sulphuric acid (50 °C, 30 min).[29]

X	Composition of reaction mixture, %				
	(XXIV)	(XXV)	(XXVI)	(XXVII)	(XXVIII)
F	0.6	7.4	—	25	40
Cl	12	3.6	2.4	0.2	59
Br	11	—	1.5	0.2	69
I	1	—	—	—	83

The pathways leading to their formation will be examined below. The data in Table 6 illustrate the influence of the nature of the halogen on the character of the products of the reactions of azoxybenzenes in sulphuric acid. In all cases, azobenzenes are formed in appreciable amounts and, when X = F or I, compounds of type (XXVI) are absent from the products. In the case of 4,4′-difluoroazoxybenzene, the influence of the acidity of the medium on the ratio of the reaction products was also observed. Thus, on passing from 85% to 98% sulphuric acid, the yield of the products (XXV) and (XXVIII) increases and the yield of compound (XXVII) falls sharply. Treatment of 4,4′-difluoroazoxybenzene with toluene-*p*-sulphonic acid in the presence of acetic anhydride leads to the products (XXIX) and (XXX) as a result of the interaction of the anions of the medium with the 4-fluorophenyl cation.[17] This presupposes the cleavage of the C–N bond in the protonated form of 4,4′-difluoroazoxybenzene and the subsequent conversion of the 4-fluorobenzenediazonium cation into the 4-fluorophenyl cation:

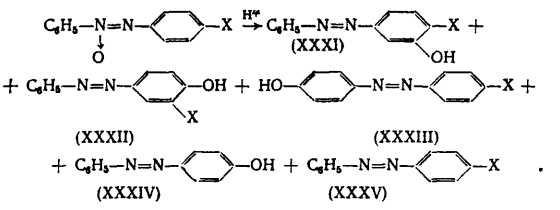


Naturally the formation of these products and their reactions do not take place in the same way in different media. Treatment of 4,4′-dichloroazoxybenzene with the TosOH–Ac_2O acid system at 100 °C leads to a complex mixture of products: 2-tosyloxy-4,4′-dichloroazoxybenzene (3%), 4,4′-dichloroazobenzene (5.5%), 4-chlorophenyl toluene-*p*-sulphonate (0.5%), and 4,4′-dichloro-2′-hydroxyazobenzene (0.5%).

The accumulation of halogen atoms in the benzene ring tends to increase the content of azobenzenes. Thus 59% of 4,4′-dichloroazobenzene is formed from 4,4′-dichloroazoxybenzene in 90% sulphuric acid, while 2,2′,4,4′-tetrachloroazoxybenzene gives rise to 76.8% of 2,2′,4,4′-tetrachloroazobenzene. The exclusive formation of the products of the reduction of 2,2′,4,4′-tetrachloroazoxybenzene is observed also in other acids—chlorosulphonic acid and 80% polyphosphoric acid.[31] However, account must be taken of the role of the nature of the acid in the overall set of reactions of azoxybenzene in acid media. Thus it has been shown[32] that 2,2′,3,3′,5,5′,6,6′-octafluoroazoxybenzene does not undergo the Wallach rearrangement on treatment with HSO_3F, HF, and H_2SO_4, whereas the formation of the products of this rearrangement, namely 4-chlorosulphonyloxy-2,2′,3,3′,5,5′,6,6′-octafluoroazobenzene, is observed in HSO_3Cl, although it is slow. On the other hand, treatment with the very strong 1:1 HSO_3F–SbF_5 acid mixture at 20 °C leads to the formation of only 2,2′,3,3′,5,5′,6,6′-octafluoroazobenzene after hydrolysis. We may note that azoxybenzenes for which the Wallach rearrangement is impossible, for example, decafluoroazoxybenzene and 4,4′-dimethyloctafluoroazoxybenzene, give rise to decafluoroazobenzene and 4,4′-dimethyloctafluoroazobenzene respectively in this acid system.

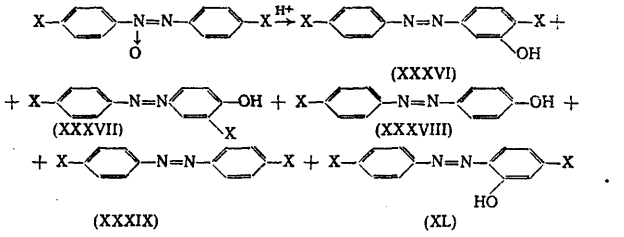
Thus the data presented indicates the importance for the Wallach rearrangement of factors such as the position of the substituent in the benzene ring, the nature of the acid, the presence of active nucleophiles in the system, and the reaction conditions. It is therefore natural to expect that the same features as for the halogeno-substituents will be observed also for other substituents, such as the alkyl, alkoxy-, nitro-, carboxy-, etc. groups.

Indeed, treatment of 4-alkylazoxybenzene with sulphuric acid leads to the formation of both the usual products of the Wallach rearrangement (XXXIII) and the "anomalous" compounds (XXXI), (XXXII), and (XXXIV)[33] and their ratio varies with the character of the alkyl substituent. Thus compound (XXXI) predominates for the CH_3 substituent, whereas compound (XXXIV) is formed exclusively for $CH(CH_3)_2$ and $C(CH_3)_3$. This may be associated with the ability of the group X to be split off in the form of the cationoid species from the product of the addition of the anion in the second stage of the Wallach rearrangement:



The formation of "anomalous" products was to be expected also for 4,4′-dialkylazoxybenzenes. In fact, when such azoxybenzenes are treated with sulphuric acid, compounds (XXXVI), (XXXVII), and (XXXVIII) are formed together with the azo-compounds (XXXIX) and the 2-hydroxyazo-compounds (XL).[30] However, the ratios of these products depend significantly on the character of the alkyl substituents. Thus, on passing from CH_3 to the $C(CH_3)_3$ group, the yield of 4,4′-dialkylazobenzenes increases by a factor of 2 and that of compounds of type (XXXVIII) by a factor of 51. On the other hand, compounds (XXXVI) and (XXXVII) are obtained only in trace amounts from azoxybenzenes containing the $CH(CH_3)_2$ and $C(CH_3)_3$ groups. These features can

be explained by the ability of the alkyl group to form stable carbonium ions:



(XXXVI)

(XXXVII) (XXXVIII)

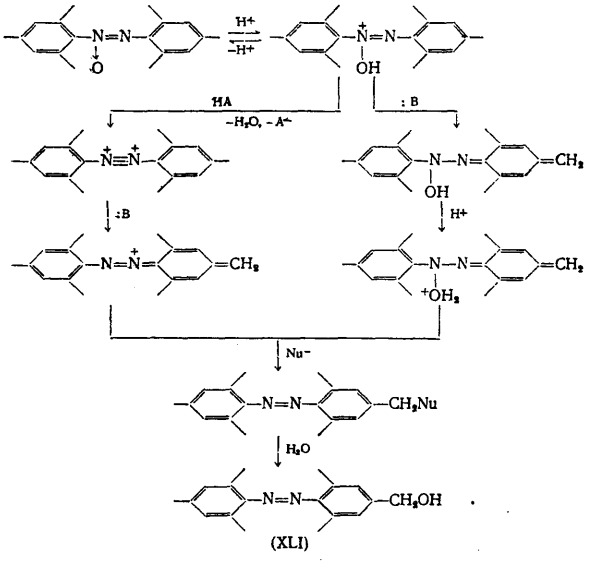
(XXXIX) (XL)

The features which can be accounted for by the ability of the alkyl group to form stable carbonium ions are also manifested here.

The use of a softer acid (trichloroacetic acid), which is used together with acetic anhydride, leads to the formation of the normal products of the Wallach rearrangement from 2,2'-dimethyl- and 4,4'-dimethyl-azoxybenzenes, namely 4-hydroxy- and 2-hydroxy-azobenzenes, in good yields.[5]

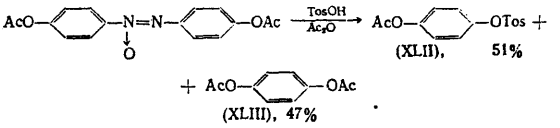
2,2',4,4',6,6'-Hexamethylazoxybenzene, for which the Wallach rearrangement is impossible, rearranges in a different way on treatment with concentrated sulphuric acid, i.e. the OH group is now located at the carbon atom of the methyl group in the *para*-position and 4-(hydroxymethyl)-2,2',4',6,6'-pentamethylazobenzene (XLI) is formed (in 91.5% yield in 85.6% sulphuric acid.[34-36] It has been suggested that the rearrangement proceeds in this case in accordance with Scheme 7.

Scheme 7



(XLI)

It has been found[37] that the reaction of 4,4'-dimethoxyazoxybenzene with the toluene-*p*-sulphonic acid—acetic anhydride mixture at 100 °C affords 3-acetoxy-4,4'-dimethoxyazobenzene (42%), 4,4'-dimethoxy-2-tosyloxyazobenzene (3.5%), and 4,4'-dimethoxyazobenzene (32%). 4-Methoxyazoxybenzene produces 3-acetoxy-4-methoxyazobenzene (38%), 4-methoxy-4'-tosyloxyazobenzene (5.6%), and 4-methoxyazobenzene (42%) in this acid system together with a small amount of the products of the hydrolysis of the esters, for example, 3-hydroxy-4-methoxyazobenzene.[37] Furthermore, the dissolution of 4,4'-diacetoxyazoxybenzene in the same acid system altogether fails to give rise to the product of the Wallach rearrangement and the exclusive formation of the products of 1-*unco*-substitution and the evolution of nitrogen are observed:[17]

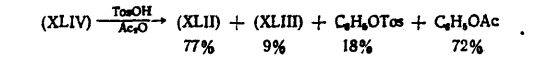


(XLII), 51%

(XLIII), 47%

Similarly, 2,2'-diacetoxyazoxybenzene gives rise to 2-acetoxyphenyl toluene-*p*-sulphonate (41%), 1,2-phenylene diacetate (18%), and 2,2'-diacetoxy-4-tosyloxyazobenzene (16%). We may note that, in the case where the anhydride of toluene-*p*-sulphonic acid in acetonitrile is used, refluxing for 2 h produces compound (XLII) in 16% yield, while in sulphuric acid in the presence of acetic anhydride at 100 °C, compound (XLIII) is formed after 1 h (yield 35%).

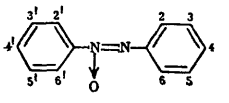
4-Acetoxy-*ONN*-azoxybenzene and 4-acetoxy-*NNO*-azoxybenzene (XLIV) behave in the same way in acetic anhydride (100 °C, 2 h) as in TosOH, the only difference between them being that the β-isomer reacts more slowly:[17]



77% 9% 18% 72%

The behaviour in acids of azoxybenzenes containing electron-accepting substituents in the 4,4'-positions differs from that examined above. Thus treatment of 4,4'-dinitro- and 4,4'-dicarboxy-azoxybenzenes with concentrated sulphuric acid yields the products of the Wallach rearrangement—the corresponding 2-hydroxyazobenzenes.[37] 4,4'-Dinitro-4,4'-dicarboxy-azobenzenes are formed in very low yields. On the other hand, the presence of the CH_3CO group results in the formation of an azo-compound in which the CH_3CO group has been replaced by the OH group.

Table 7. Kinetics of the reaction of azoxybenzene with sulphuric acid (at 30 °C).[42]



X	$10^7 k$, s^{-1}			pK_a
	$[H_2SO_4]$ = 83.6%	$[H_2SO_4]$ = 90%	$[H_2SO_4]$ = 98%	
3,3'-$(NO_2)_2$	—	0.25	18	−8.01
4-NO_2	—	3.5	320	−6.18
3-NO_2	0.28	6.5	684	−6.33
4'-NO_2	—	300	33 300	−6.21
3'-NO_2	9	450	38 000	−6.47
H	200	1 280	9 170	−5.13
3,3'-$(OCH_3)_2$	110	1 350	—	−5.15
4-Br	467	2 920	—	−5.03
4-OH	6120	33 000	—	−5.21

The presence of the NO_2 group in only one benzene ring (the α- and β-isomers) leads to the rearrangement product in which the OH group is in the other benzene ring. Thus 4-hydroxy-4'-nitroazobenzene is formed in 83% yield in 92% sulphuric acid.[6,38] When HSO_3Cl is used, a mixture of products is formed from the α- and β-isomeric 4-nitroazoxybenzenes: 4-hydroxy-4'-nitroazobenzene, 2-hydroxy-4'-nitroazobenzene, and 4-nitroazobenzene.[39] Comparison of these data with the results obtained in concentrated sulphuric acid shows an increase of the *ortho* : *para* ratio for HSO_3Cl.[39]

The presence of a substituent in the 4-position, for example, CH_3CO,[33] AcNH, CH_3COO, and $(CH_3)_2N \rightarrow O$[40] prevents the Wallach rearrangement. Thus azoxybenzene with the $(CH_3)_2N \rightarrow O$ substituent gives rise to a 55.1% yield of

4-hydroxy-4'-dimethylaminoazobenzene in 100% sulphuric acid, which is the first example of the involvement of tertiary amine *N*-oxides in the Wallach rearrangement. If the reactant ratio is 1:1, the overall yield of 2-hydroxy- and 4-hydroxy-4'-dimethylaminoazobenzenes is ~22%, and for the 4:1 ratio, where there is a significant deficiency of acid, the Wallach rearrangement does not take place. In this case the tertiary amine *N*-oxide is reduced with formation of a mixture of α- and β-isomers of 4-dimethylamino-*ONN*-azoxybenzene. A similar reaction in an acid medium has been observed also for *N*-pentafluorophenylpiperidine oxide.[41]

Kinetic data for the influence of the nature and position of the substituent in the benzene ring on the rate of rearrangement indicate its dependence on the acidity function of the medium and the pK_a of the initial azoxybenzene (Table 7).[42]

The electron-accepting properties of the substituent in the 4-position in the benzene ring apparently exert an appreciable influence on the rate of the Wallach rearrangement. According to the results of kinetic studies, the rate of rearrangement is proportion to $[H^+]^2$.[4] Because of this, the presence of an electron-donating group, whose heteroatom is capable of interacting with the proton should lower the rate of rearrangement and should lead to the necessity for the employment of a stronger acid system. Indeed, it has been shown[25] that 4-dimethylamino-1-naphthyl-*ONN*-azoxybenzene does not undergo the Wallach rearrangement in 70% sulphuric acid; only protonation at the dimethylamino-group takes place under these conditions.

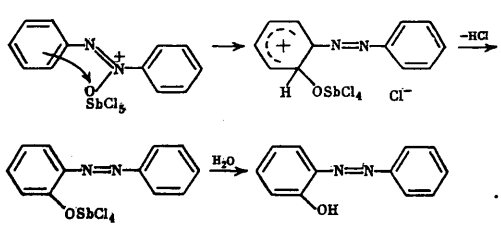
IV. THE EFFECT OF LEWIS ACIDS ON AZOXYBENZENES

The study of the reactions of azoxybenzenes with Lewis acids showed that 1:1 complexes are formed initially, giving rise to azobenzene as the main product on heating. Thus treatment of azoxybenzene with PCl_3 produces a 95% yield of azobenzene.[43] On the other hand, $AlCl_3$ and $FeCl_3$ afford 4-chloroazobenzene in yields of 83 and 63% respectively. If the reaction of $AlCl_3$ is carried out in SO_2Cl_2, then 4,4'-dichloroazobenzene is obtained in 70% yield, while in $SOCl_2$ a mixture of products is formed: 4-chloroazobenzene (3.1%), 4,4'-dichloroazobenzene (5.2%), and azobenzene (75.3%).[43] The reaction in nitromethane gives rise to 65% of 4-chloroazobenzene, 4% of 4,4'-dichloroazobenzene, 6% of 2-chloroazobenzene, 18% of 2,4-dichloroazobenzene, and 48% of 2,4'-dichloroazobenzene.[44]

When the reaction of azoxybenzene with $ZnBr_2$, $FeCl_3$, $AlCl_3$, and $TiCl_4$ is carried out in nitromethane, refluxing affords azobenzene as the main product and its amount increases with increase of the strength of the Lewis acid, the products of the Wallach rearrangement being obtained in trace amounts.[45]

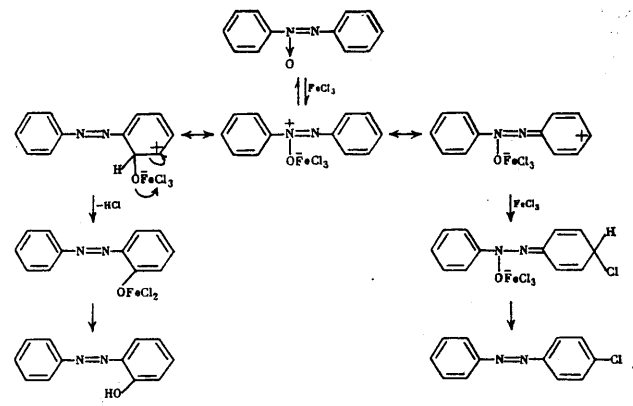
The structure of the reaction products can be influenced decisively by coordination. Thus thermolysis of the complexes of azoxybenzene with $SbCl_5$ leads selectively to an *ortho*-substituted product of the Wallach rearrangement.[45-47] It has been suggested that the reaction proceeds in accordance with Scheme 8:

Scheme 8



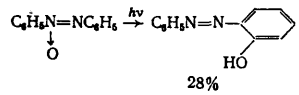
The reactions of substituted azoxybenzenes with $FeCl_3$ [48] or $AlCl_3$ [49] lead exclusively to the formation of reduction products—substituted azobenzenes. 4'-Chloro-2-hydroxyazobenzene and 4-chloroazobenzene have been obtained in proportions of ~1:1 only from 4-chloro-*NNO*-azoxybenzene (β-isomer). The formation of the corresponding chloro-derivatives of azobenzenes is striking and can be accounted for in terms of Scheme 9:

Scheme 9



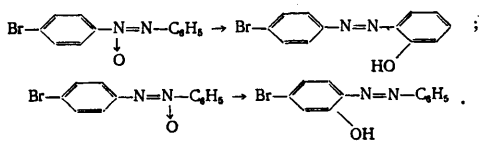
V. THE PHOTO- AND THERMO-INITIATED WALLACH REARRANGEMENT

In 1925 Cumming observed that irradiation of a solution of azoxybenzene in ethanol with UV light from a mercury lamp leads to the formation of 2-hydroxyazobenzene:

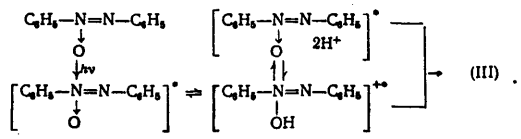


28%

It has been shown[48] that, on exposure of solutions of a number of asymmetrically substituted azoxybenzenes and benzene to sunlight, the oxygen atom of the azoxy-group is transferred to the benzene ring linked to the −N= fragment of the azoxy-group. Since the −N= valence angle is 120°, the oxygen atom is closest to the *ortho*-position of the neighbouring ring. For example, in the rearrangement of α- and β-isomeric 4-bromo-*NNO*-azoxybenzenes, the hydroxy-group is transferred to the benzene ring which in the initial compound was not bound to the NO fragment:



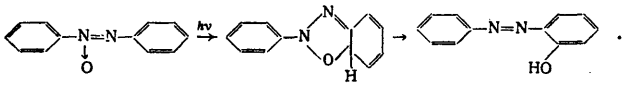
These facts lead to the conclusion that the photoinitiated Wallach rearrangement is intramolecular in character. It has been postulated[49] that it proceeds as follows:



With the aid of azoxybenzene labelled with ^{15}N at the site of the nitrogen atom of the azoxy-group not linked to the oxygen atom, it has been shown[9] that the equalisation of the isotope composition of the nitrogen is not observed for 2-hydroxyazobenzene and the labelled atom is in the benzene ring containing the hydroxy-group. With the aid of ^{18}O-labelled azoxybenzene, it has been demonstrated[8] that the isotope composition of the oxygen of the hydroxy-group in the 2-hydroxyazobenzene produced does not differ from that of the oxygen of the azoxy-group of the initial azoxybenzene. Consequently, in this rearrangement the hydroxy-group of 2-hydroxyazobenzene is formed from the oxygen of the azoxy-group and the reaction is intramolecular. Hence one may conclude that the rearrangement of azoxybenzene to 2-hydroxyazobenzene bypasses the symmetrisation stage and the benzene ring remote from the =N— group is hydroxylated.

On the other hand, when [1-^{14}C]azoxybenzene in ethanol is irradiated, the distribution of the ^{14}C isotope label in the reaction products is inconsistent with an intramolecular rearrangement alone.[21] Thus the specific radioactivity of ^{14}C in the rearranged product is below that of the starting material.[21] This presupposes the simultaneous occurrence of α—β isomerisation and has been indicated also by the results of another study[50] where it was shown that irradiation of α- and β-4-methoxyazoxybenzenes in sulphuric acid results in the formation of 2-hydroxy-4-methoxyazobenzene. The rates of the Wallach rearrangement and α—β isomerisation depend on the character of the substituents in the benzene ring.

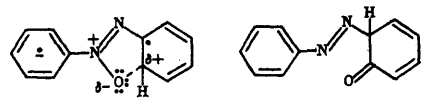
The photochemical reactions of 2,2',6,6'-tetramethyl- and 2,6-dimethyl-*NNO*-azoxybenzenes have been studied in detail;[51] it has been concluded that the nucleophilic attack by the O atom of the azoxy-group on the benzene ring with the intermediate formation of compound (XLV) is more likely than the homolytic abstraction of an H atom from the *ortho*-position with subsequent transfer of the OH group. This conclusion has been confirmed by measurements of the quantum yields of the photochemical reaction and by the study of the isotope effect in the photoisomerisation of [D_{10}]azoxybenzene. The rate-limiting stage of the photochemical reaction of azoxy-compounds is probably the intramolecular migration of an H atom and not the formation of compound (XLV):



(XLV)

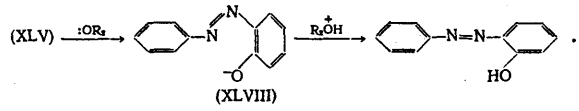
The nature of the substituent and its position in the benzene ring influence significantly the quantum yield of the photochemical reaction of substituted azoxybenzene. Thus the quantum yields in the rearrangements of 4-methyl- and 4-trifluoromethyl-*NNO*-azoxybenzenes are 0.37 and 1.70, while the corresponding yields for 3,5-dimethyl- and 3,5-bis(trifluoromethyl)-*NNO*-azoxybenzenes are 0.80 and 2.5 respectively.[52]

In their discussion of the pathways leading to the formation of compound (XLV), the authors[52] begin with the hypothesis that, on π,π^* excitation of azoxybenzene, the less stable singlet state is converted into the more stable triplet state (XLVI) as a result of the interaction in the electronically excited state of the electrophilic oxygen radical and the electron-enriched remote benzene ring.



(XLVI) (XLVII)

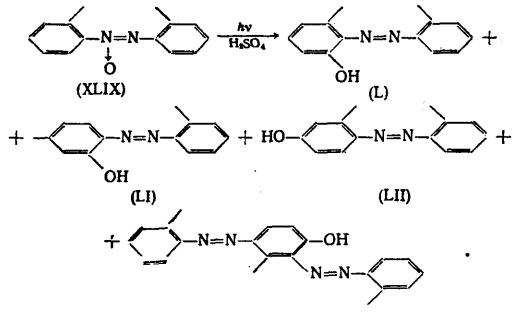
In the presence of moderately basic solvents, for example, ethanol or diethyl ether, compound (XLV) is converted into the reaction product (III) via the anion (XLVIII):



(XLVIII)

The formation of side products of the photochemical reaction has been attributed to the intermediate (XLVII) obtained from compound (XLV) by the intramolecular hydride 1,2-shift. A diazonium ion is formed from compound (XLVII), having been detected by the coupling reaction with β-naphthol.[52] Naturally, the above discussion is general so that one cannot claim to be able to explain many details of the process.

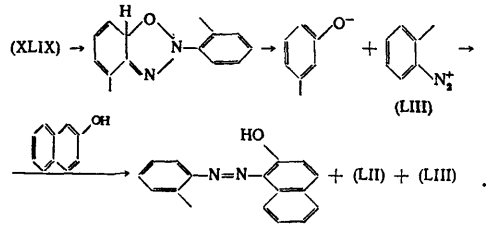
Interesting data have been obtained in the study of the photochemical reaction of 2,2'-dimethylazoxybenzene (XLIX)[53] in which unexpected products are formed:



(XLIX) (L) (LI) (LII)

The authors demonstrated (by adding β-naphthol to the system) the involvement of the arenediazonium cation (LIII) in this reaction (Scheme 10):

Scheme 10



(LIII)

It has been demonstrated[54] that, when 4- and 4'-substituted methoxy- and dimethylamino-derivatives of azoxybenzene are irradiated, 2- and 2'-hydroxyazobenzenes are formed. The authors suggest that the reaction proceeds via the intermediate formation of compounds of type (XLV).

If azoxybenzene is heated to 250 °C, its exothermic decomposition takes place and tarry substances are obtained together with azobenzene; 4-hydroxy- and 2-hydroxy-azobenzenes are formed in insignificant amounts.[55] The thermal reactions of azoxybenzenes have been investigated in detail.[56]

VI. THE MECHANISM OF THE WALLACH REARRANGEMENT

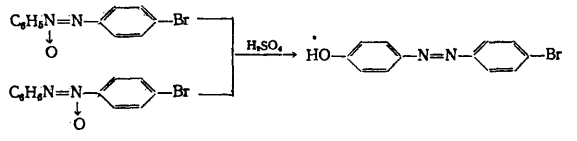
Up to the 1960's, the studies on the Wallach rearrangement were concentrated mainly on its synthetic aspects and virtually no attention was devoted to the mechanism of this

reaction. The hypotheses put forward concerning the mechanism of the Wallach rearrangement were speculative and were not supported by experimental data. Only after the fundamental investigations of Shemyakin's school[8–10] and Buncel's kinetic measurements[4] were the first well-founded ideas concerning the mechanism of the Wallach rearrangement formulated. However, despite the large number of publications on this topic, after the above studies no serious step of any kind was taken towards the understanding of the mechanism of the Wallach rearrangement. On the contrary, a number of experimental data which could not be explained were published. The complexity of the study of the Wallach rearrangement was caused primarily by the possibility of the formation of a multiplicity of intermediates on dissolution of azoxybenzene in acid, each of which can influence the subsequent course of the reaction. The question of which cationoid species determines the rate of the Wallach rearrangement remains unresolved.

In the study of certain acid-catalysed rearrangements, for example the rearrangements of diazoaminobenzenes to phenylhydroxylamines, it was concluded that the mode of substitution in the benzene ring can be used to achieve the understanding of their mechanism. Thus mainly the *para*-substituted products should be formed via the intermolecular mechanism while the intramolecular mechanism gives rise mainly to *ortho*-substituted products. In those cases where 4-hydroxyazobenzenes are formed exclusively from azoxybenzenes, an intermolecular mechanism of the Wallach rearrangement might have been postulated. We shall deal with certain aspects of the mechanism of the Wallach rearrangement.

1. Acid-Catalysed α-β Isomerisation of Azoxybenzenes

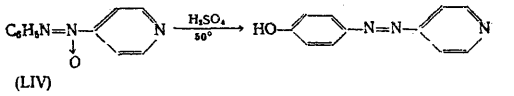
Both the α- and β-isomers of 4-bromoazoxybenzenes undergo an acid-catalysed rearrangement and the same product is formed: 4-bromo-4′-hydroxyazobenzene. Thus the hydroxy-group is in both cases in the *para*-position relative to the unsubstituted benzene ring:



This has also been observed for the α- and β-isomers of 4-methoxyazoxybenzenes. On the other hand, it has been unexpectedly observed that the main product of the reactions of the α- and β-isomers of 4-methylazoxybenzenes corresponds to the migration of the oxygen atom to the *ortho*-position in the unsubstituted benzene ring.[57] In a later study[58] it was shown that the α- and β-isomers of 4-methylazoxybenzene in 80–90% sulphuric acid form only 2-hydroxy-4-methylazobenzene, while the α- and β-isomers of 4-nitroazoxybenzene afford 4-hydroxy-4′-nitroazobenzene. 4-Bromo-*ONN*-azoxybenzene does not undergo the Wallach rearrangement, while 4-bromo-*NNO*-azoxybenzene gives rise to 4-bromo-2-hydroxyazobenzene under these conditions.

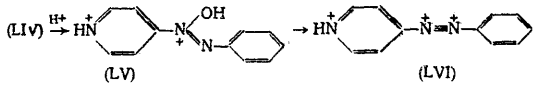
It has been found that the rates of rearrangement of the isomers are different and depend on the character of the substituent in the benzene ring. The use of identical conditions for the rearrangement of the α- and β-isomeric azoxybenzenes showed that the rate of rearrangement of α-isomers is higher for the CH_3 substituent and lower for the NO_2 and Br substituents. The ratio of the rates of rearrangement of α- and β-isomeric azoxybenzenes depends also on the acidity of the medium employed.

An example of an extremely large difference between the rates of rearrangement of the α- and β-isomers has been observed[26] for 4-[benzene-α(β)-azoxy]pyridines (LIV):



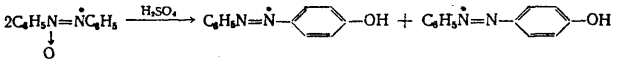
(LIV)

In this case only the β-isomer (LIV) undergoes rearrangement, while the α-isomer remains unchanged, which has been used to isolate it in a pure state. Kinetic measurements showed that the formation of the intermediate species (LVI) (the triprotonated form), as a result of the protonation of the nitrogen atom of the pyridine ring and the azoxy-group, is the rate-determining stage of the reaction:



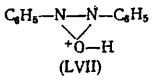
(LV) (LVI)

Whether or not the α–β isomerisation is intramolecular can be elucidated by studying the behaviour in acids of azoxybenzenes labelled at one of the nitrogen or carbon atoms by the ^{15}N or ^{14}C isotopes. These data can also provide an answer to the question which of the benzene rings does the hydroxy-group enter in the Wallach rearrangement. Shemyakin et al.[9] used azoxybenzene labelled with the ^{15}N isotope at one of the nitrogen atoms of the azoxy-group. They found that the formation of 4-azoxyazobenzene is accompanied by the complete equalisation of the isotope compositions of the nitrogen in both positions and they concluded that both benzene rings are hydroxylated to the same extent:



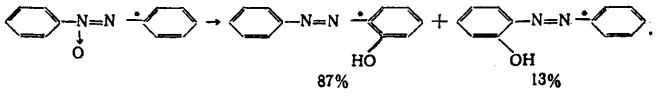
It has been established[9] that the observed equalisation of the distribution of the isotope label takes place during the period of the Wallach rearrangement itself and not before it. It has been demonstrated that the rearrangement of azoxybenzenes is not preceded by reversible isomerisation and that the rearrangement is not coupled with the preliminary conversion of the azoxybenzene to azobenzene, which is then hydroxylated.

The equalisation of the isotope compositions of the nitrogen in the final rearrangement product can indicate that the α–β isomerisation proceeds via a stage involving the formation of a free cation, which exists independently. Shemyakin et al.[9] suggested that this can be the oxonium cation (LVII), which is in fact responsible for the Wallach rearrangement.



(LVII)

These conclusions received some confirmation in a study[59] whose authors used azoxybenzene labelled with ^{14}C at the carbon atom linked to the nitrogen atom of the azoxy-group:



87% 13%

However, the ratio of the products formed is 87 : 13, which throws doubt on the necessity for the intermediate formation of the oxonium cation and its role in the mechanism of the Wallach rearrangement, confirming the possibility of the isomerisation of azoxybenzenes in an acid medium via the corresponding intermediate. Later these results were confirmed on the same object by other workers.[58] There is now no

doubt that the acid catalysed α–β isomerisation is a general property of azoxybenzenes and proceeds independently of the Wallach rearrangement. It may be that this isomerisation takes place via the species (LVII).

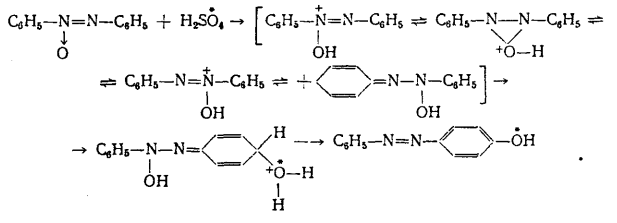
2. Data Obtained By the Tracer Atom (^{15}N, ^{18}O, ^{14}C) Method

An important factor in the understanding of the mechanism of the Wallach rearrangement was the solution of the problem whether it is intermolecular or intramolecular. It has been shown[9] that, in the reaction of azoxybenzene (labelled with the ^{15}N isotope) with acetic anhydride (at 230–240 °C) the formation of only 2-hydroxyazobenzene is observed, in which the distribution of the ^{15}N isotope label is not equalised. This shows that the rearrangement proceeds via an intramolecular mechanism.

4-Bromo-*ONN*-azoxybenzene, 4-nitro-*NNO*-azoxybenzene, and 3,3′-dinitro-azoxybenzene have been used as objects of study in two investigations.[8,10] They were subjected to the Wallach rearrangement in sulphuric acid labelled with the ^{18}O isotope under conditions where it is possible to isolate a certain amount of the initial azoxybenzene which failed to react. The isotope composition of the hydroxy-group in the rearrangement product is the same as that of the oxygen in the acid medium. This demonstrates the intermolecular mechanism of the rearrangement.

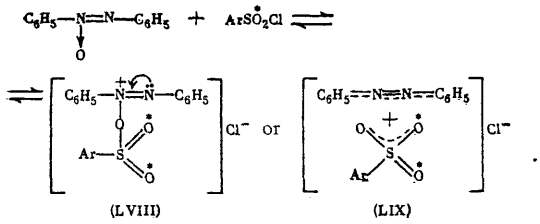
The validity of this conclusion and its independence of the conditions employed, the number of substituents, and their character and positions in the molecule have been confirmed in a study[60] whose authors proposed the mechanism of the Wallach rearrangement illustrated in Scheme 11:

Scheme 11



However, this picture, which is at first sight understandable, becomes much more complex after careful critical analysis. In the first place, the hypothesis that the structure of the monoprotonated form changes in the course of the reaction and even more so the hypothesis that intermediates are formed have not been rigorously proved. Subsequently, the intermolecular mechanism of the Wallach rearrangement was confirmed also for other acid systems. Thus it has been established[22] that, when azoxybenzene is treated with the anhydride of [^{18}O]-labelled benzenesulphonic acid, the oxygen atom of the acid system is found in the hydroxy-group of the final reaction products.

In the reaction of azoxybenzene with [^{18}O]-labelled benzenesulphonyl chloride, which leads to the Wallach rearrangement in the *ortho*-position, the ^{18}O isotope enters the hydroxy-group of the final product.[22] This indicates the intramolecular character of the rearrangement. However, the ^{18}O content in the final product is smaller than its content in benzenesulphonyl chloride, which can be accounted for by the formation of compounds (LVIII) and (LIX). This can also explain the decrease of the ^{18}O content in the *para*-substituted product of the Wallach rearrangement.



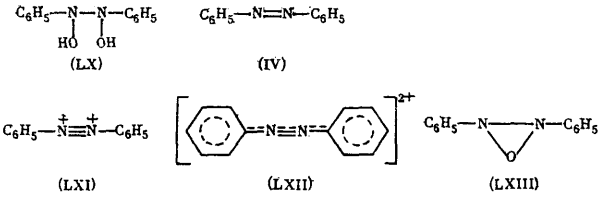
(LVIII) (LIX)

When [^{18}O]-labelled azoxybenzene is used in the Wallach rearrangement, the product is 4-hydroxyazobenzene, in which the ^{18}O content is ~10%.[1] When 4-methyl-*ONN*-azoxybenzene and 2-methyl-*ONN*-azoxybenzene are treated with 80% sulphuric acid, an insignificant amount of ^{18}O is also observed in the product of the Wallach rearrangement.

On the other hand, the study of the rearrangement of 4,4′-dimethylazoxybenzene in concentrated [^{18}O]-labelled sulphuric acid showed that 2-hydroxy-4,4-dimethylazobenzene contains ~70% of ^{18}O.[10] Hence it follows that the product of the Wallach rearrangement of azoxybenzenes is obtained via two mechanisms—intermolecular and intramolecular. Thus the conditions under which the Wallach rearrangement is carried out, the nature of the substituents in the benzene ring, and their positions can influence significantly the ratio of the rates of the process via these two mechanisms. In essence, the problem dealt with here is of central importance for the understanding of the mechanisms of other acid-catalysed rearrangements of nitrogen-containing aromatic compounds. This should be borne in mind in formulating a general mechanism of the Wallach rearrangement.

3. The Generation and Structure of the Intermediate Species When Azoxybenzenes are Treated with Acids

In the first studies of the Wallach rearrangement, it was already suggested that both the initial azoxybenzene and the intermediates formed in the course of the rearrangement may be protonated. On the basis of their own data, according to which the equalisation of the distribution of the ^{15}N label in the final rearrangement product should occur in a symmetrical structure, Shemyakin and co-workers[8] examined the possibility of the formation of compounds (LX)–(LXIII) in the Wallach rearrangement:



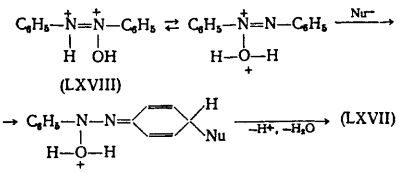
(LX) (IV)

(LXI) (LXII) (LXIII)

The *NN*-diol (LX), proposed by Wohl,[61] apparently cannot be formed under the conditions of the Wallach rearrangement, because the hydration necessary for its formation cannot occur in strong acids such as HSO_3F and HSO_3Cl. Shemyakin and co-workers[9] showed that azobenzene (IV) is not an intermediate in the Wallach rearrangement, because the addition of azoxybenzene containing only the ^{14}N isotope to [^{15}N]azoxybenzene under the conditions of the rearrangement did not lead to the dilution of the isotope label in the reaction product—4-hydroxyazobenzene.[9] The structure of the oxide (LXIII) initially explained satisfactorily the experimental data. However, results were later obtained which are difficult to account for from these standpoints. It was found that an increase of the concentration of sulphuric acid from

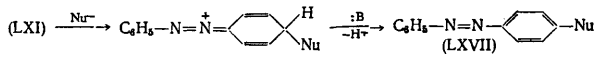
75.3 to 99.99% increases the rate of rearrangement by five orders of magnitude, which indicated an extremely important role of the acidity of the medium. Indeed, kinetic studies of the Wallach rearrangement by Buncel[4] showed that a two proton process takes place. For this reason, the rate-limiting stage of the rearrangement must be the state involving the generation of dicationoid species.

The diprotonated form of azoxybenzene and the dication (LXI) or (LXII), generated by the dehydration of the diprotonated form, are mainly discussed in the literature. The diprotonated form (LXVIII) can be responsible for the Wallach rearrangement, since the reaction of the anion with the medium (or water) results in the formation of the rearrangement product:



(LXVIII)

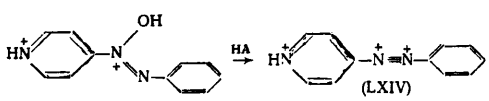
On the other hand, the dication (LXI), generated from the diprotonated form of azoxybenzene by dehydration, also affords the products of the rearrangement (LXVII):



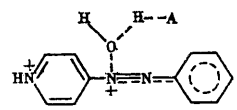
Naturally the question arose which intermediate species are in fact generated in each acid system. The application of ^1H NMR enabled Olah et al.[12] to trace, in relation to azoxybenzene and 4,4'-dichloroazoxybenzene, all the intermediate stages in the Wallach rearrangement—the generation of the mono- and di-protonated forms of azoxybenzene and the formation of a dication of type (LXI). Using ^{19}F and ^{15}N NMR, these intermediate species have been detected analogously[18,63] for decafluoro- and 2,2',3,3',5,5',6,6'-octafluoroazoxybenzenes.

However, one should note that NMR spectroscopy makes it possible to detect only sufficiently long-lived carbonium ions. The data indicated do not therefore necessarily reflect the true picture because the rate-limiting stage may be the generation of a short-lived carbonium ion which is highly reactive. Nevertheless, Olah suggested that a dication of type (LXI) is responsible for the Wallach rearrangement. A number of investigators share this view and the results obtained in the study of the Wallach rearrangement are treated within the framework of Olah's concept. For example, Buncel and Cox[35] invoked the idea of the generation of a cation of type (LXI) to explain the results of the reaction of 2,2',4,4',6,6'-hexamethylazoxybenzene with concentrated sulphuric acid (see Scheme 7).

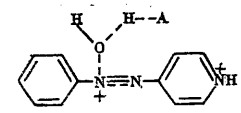
A pathway leading to the rearrangement via the generation of the intermediate trication (LXIV) from the diprotonated form has been put forward.[26] The rate-limiting stage is then the generation process. The authors used this in fact to account for the differences between the rates of rearrangement of the α- and β-isomeric 4-(phenylazoxy)-pyridines. Indeed the formation of the transition state (LXV) from the β-isomer is an energetically favourable process owing to the delocalisation of the charge by the benzene ring, while the transition state derived from the α-isomer (LXIV) is unfavourable from this point of view:[26]



(LXIV)



(LXV)



(LXVI)

The formation of the final product can be readily explained from this standpoint, but the explanation of many other facts encounters difficulties due to the lack of information about the structure of the complexes formed under the real process conditions and about their reactivity. Thus it has been concluded[23] that there is a difference in the pathways leading to the Wallach rearrangement as a function of the acidity of the medium. In relatively weak acids (for example in sulphuric acid at a concentration less than 80%), azoxybenzene is initially protonated at the oxygen atom in the equilibrium stage which is followed by the reversible attack of the nucleophile (probably HSO_4^-) with formation of a substrate of the quinonoid type. Next follows the protonation of this compound at the oxygen atom. In the rate-limiting stage attack by the base takes place (for example by HSO_4^-) with the concerted elimination of water and subsequent rapid hydrolysis, which leads to the final product.

In acids stronger than 80% sulphuric acid, the protonation of the oxygen atom of the azoxy-group is followed by the rate-limiting proton transfer from the undissociated form of the acid (usually acid catalysis) with subsequent elimination of water and the formation of a dication of type (LXV), which is subjected to rapid nucleophilic attack leading to the final product. The claim by Olah et al.[12] that 4-hydroxyazobenzene is formed in the hydrolysis of the dication generated by treating azoxybenzene with $HF-SbF_5-SO$ at −50 °C has been considered as an important argument in support of the formation of a dication of type (LXI). However, the reaction has been studied in detail[18] and it has been found that, under the conditions of the generation of a dication of type (LXI), hydrolysis affords azobenzene in 68–72% yield, while 4-hydroxyazobenzene is formed in small amounts.

We shall quote yet another example of the correction of old experimental data based on a careful analysis of the products of the Wallach rearrangement. It has been reported[57] that treatment of 4-bromoazoxybenzene with with sulphuric acid results in the formation of only 4-bromo-4'-hydroxyazobenzene. However, this study was repeated[29] and it was found that the main product of this reaction is 4-bromoazobenzene, while 4-bromo-4'-hydroxyazobenzene is formed in small amounts.

In contrast to the data of Lukashevich and Kurdyumova,[14] it has been concluded[6] that treatment of azoxybenzene with HSO_3Cl at −10 °C leads to the formation of 26.5% of azobenzene (previously 5% had been found), which appears somewhat strange. We reproduced this reaction and showed that the amount of azobenzene formed is ~5%.[18] Since azobenzene and azobenzene-4-chlorosulphonate have the same R_f, it is difficult to follow by thin-layer chromatography the completeness of the hydrolysis of the sulphate by an aqueous solution of ammonia (as was done by Yamamoto et al.[6]) and the value 26.5% probably refers to a mixture of two substances.

The fact that, as electron-accepting substituents, which reduce the pK_a of azoxybenzenes with a parallel decrease of the capacity of the substrate for diprotonation, are introduced into the benzene ring, the fraction of the azo-compound obtained—the product of the reduction of azoxybenzene—increases, has not so far been explained.

Owing to the probability of the attack by the nucleophile on both benzene rings, in the case of a dication of type (LXI), labelled with ^{14}C in one of the benzene rings, products of the Wallach rearrangement with identical contents of the

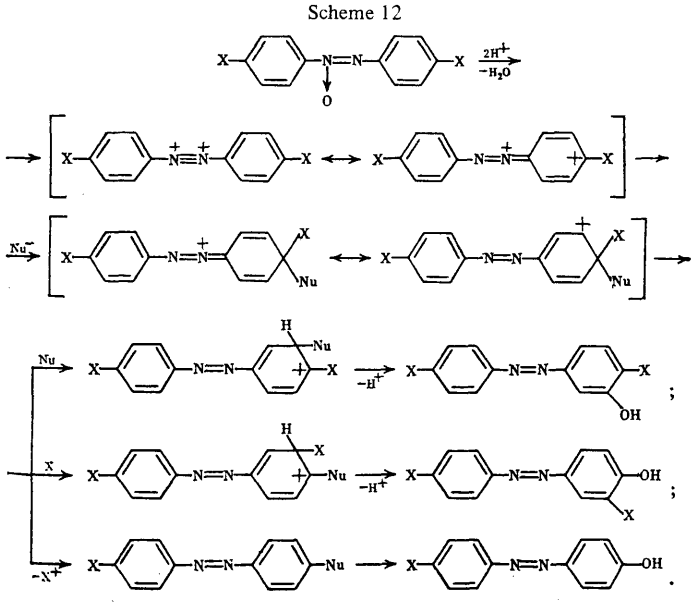
^{14}C label in both rings should be obtained. However, it has been shown for the reaction of [^{14}C]azoxybenzene in sulphuric acid[60] or in the anhydride of benzenesulphonic acid[22] that the ratio of the ^{14}C contents in the benzene rings differs somewhat from 1:1. On the other hand, in the diprotonated form of azoxybenzene the shielding of the carbon atoms of both rings, which parallels the magnitude of the positive charge on the atom, is somewhat different (see the ^{13}C NMR data for the diprotonated form of decafluoroazoxybenzene[18]). The small difference in the shielding of the carbon atom can explain the experimental data for the distribution of the ^{14}C label. These factors can indicate that the true intermediate species determining the course of the Wallach rearrangement is the diprotonated form of azoxybenzene.

Owing to the lack of direct experimental evidence, the above conclusions are to a large extent tentative and hence they do not rule out, in principle, other possible explanations.

4. The Interpretation of the "Anomalous" Processes Accompanying the Classical Wallach Rearrangement

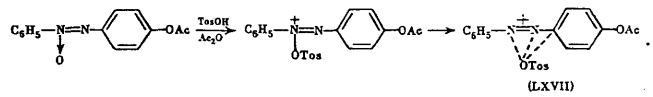
The formation of "anomalous" products on treatment of 4-alkyl- and 4,4′-dialkyl-azoxybenzenes with acids was noted above.[30,33] Assuming the generation of a dication of type (LXI), the appearance of these products can be explained in the following way (Scheme 12):

Scheme 12



The initial diprotonation with subsequent elimination of water leads to the formation of a dication which is attacked by the nucleophile at the carbon atom in the *para*-position. The resulting σ-complex, in which there is a considerable positive charge on C(3), is then converted into the reaction products via several pathways: (a) into 4-hydroxyazobenzene (XXXIII) via the elimination of X^+; (b) into 3-hydroxyazobenzene (XXXI) via a rearrangement with migration of Nu to the 3-position; (c) into 4-hydroxyazobenzene (XXXII) via a rearrangement with migration of X to the 3-position. The ability of X to migrate increases with increase of the electron density at the α-C atom. The group X is readily eliminated if it is able to form a stable carbonium ion [for example, the product (XXXIII) is formed for X = iso-Pr and t-Bu, while the ease of migration of the CH_3 and CH_3CH_2 groups leads to products of type (XXXII)]. The cationoid character of the Wallach rearrangement has been confirmed by these data.

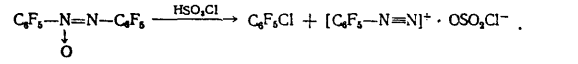
The formation of complex mixtures of products when the Wallach rearrangement is carried out in the toluene-*p*-sulphonic acid–acetic anhydride system can be explained without the concept of the generation of a dication of type (LXI) but via the initial attack of the electrophile from the medium on the oxygen atom of the azoxy-group with subsequent formation of the intermediate (LXVII):[17]



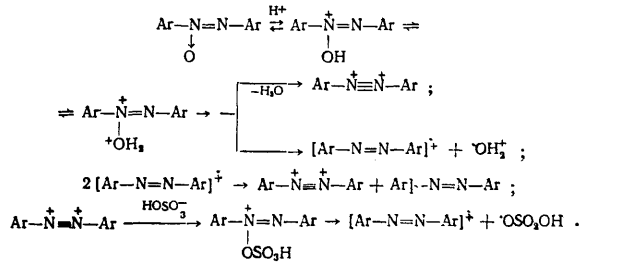
(LXVII)

In the cation (LXVII) there is a possibility of attack also in the *unco*-position. In this case a benzenediazonium cation is formed. Its formation has been confirmed by the reaction with toluene, which yields the corresponding biphenyls. It also affords C_6H_5OAc and C_6H_5OTos via the reaction of the intermediate phenyl cation with the anion of the medium.

It has been demonstrated by spectroscopic methods and by the azo-coupling reaction with dimethylaniline[58] that, when decafluoroazoxybenzene is kept in HSO_3Cl for 200 h, the pentafluorobenzenediazonium cation and chloropentafluorobenzene are formed:



As noted above, the Wallach rearrangement affords in many instances azobenzene, sometimes in predominant amounts. The information about the pathways leading to their formation is fragmentary and frequently contradictory. It has been suggested[19,29] that they are obtained as a result of the disproportionation of the diprotonated form of azoxybenzene, which leads to the azobenzene radical-cation:



By analogy with the reactions of diaryl sulphoxides in sulphuric acid, where the radical-cations of diaryl sulphides were detected by EPR, and the degree of their racemisation was determined using the ^{18}O isotope,[62] Oae and co-workers[19,29] attempted to detect the azobenzene radical-cation but they were unsuccessful. On the other hand, it has been shown for polyfluoroazoxybenzenes[32,63] that azobenzenes are formed only in those cases where dications of type (LXI) are observed, according to ^{19}F and ^{15}N NMR data in the 1:1 HF–SbF_5 or 1:1 HSO_3F–SbF_5 systems.

If the scheme put forward by Oae and co-workers[19,29] is adopted, then after a time one should observe the diprotonated forms of azobenzenes. However, it has been shown[32] that the signal is 13.6 p.p.m., referring to the diprotonated form of decafluoroazobenzene, is not observed for a solution of decafluoroazoxybenzene in the 1:1 HSO_3F–SbF_5 mixture allowed to stand for 20 h at 20 °C, while hydrolysis leads to the formation of decafluoroazobenzene. It has been suggested[32] that the formation of decafluoroazobenzene in this reaction is due to the pronounced oxidising properties of the

type (LXI) dication, which oxidises water to hydrogen peroxide, as a result of which the dication itself is reduced to decafluoroazobenzene.

In all cases of the generation of type (LXI) dications from azoxybenzenes, hydrolysis results in the formation of the corresponding azobenzenes. For example, on treatment with the 1:1 ($HF-SbF_5$)$-SO_2$ mixture of 4,4'-difluoroazoxybenzene (−50 °C, 10 min) and 2,2',4,4'-tetrafluoroazoxybenzene (−10 °C, 30 min), the ^1H NMR spectra revealed the presence of the H_3O^+ cation and the hydrolysis of such solutions results in the formation of 4,4'-difluoro- or 2,2',4,4'-tetrafluoroazobenzene. The diprotonated form of azoxybenzene is incapable of leading to azobenzenes and the starting materials are recovered in all cases. Thus the dissolution of 4,4'-bis(trifluoromethyl)octafluoroazoxybenzene in the 1:1 HSO_3F-SbF_5 or 1:1 $HF-SbF_5$ system leads only to the diprotonated form at 20 °C according to ^1H and ^{19}F NMR spectra, while after 50 h signals due to the protons of the H_3O^+ cation appear in the ^1H NMR spectrum. Hydrolysis of this solution leads only to the starting material.

It has been shown[18] that in superacids, where nucleophiles exhibit a low reactivity, the generation of the diprotonated form of azoxybenzene is an insufficient condition for the occurrence of the Wallach rearrangement; the presence of active nucleophilic species is necessary in addition. Thus, in contrast to the reaction in HSO_3Cl, the Wallach rearrangement has not been observed for 2,2',3,3',5,5',6,6'-octafluoroazoxybenzene in the 1:1 (HSO_3F-SbF_3)$-SO_2ClF$ (at −40 °C) or 1:1 ($HF-SbF_5$)$-SO_2$ (at −60 °C) systems, where the diprotonated form of azoxybenzene is detected.

We believe that the scheme in which azobenzenes are formed via a dication of type (LXI) on treatment of azoxybenzenes with acids, while the product of the Wallach rearrangement is formed as a result of the reaction of the diprotonated form of azoxybenzene with the nucleophile of the medium, is more likely.

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The survey of data on the Wallach rearrangement permits certain general conclusions. Firstly, its mechanism has not yet been ultimately elucidated. Secondly, similar rearrangements are apparently possible in systems having the N → O group and capable of splitting off water on protonation, generating cationoid species. For example, one may expect that the *N*-oxides of tertiary aromatic amines and *CN*-diarylnitrones undergo a rearrangement in acid media which is of the same type as the Wallach rearrangement.

Thus, in order to understand the entire set of processes occurring in the Wallach rearrangement it is still necessary to solve fairly numerous complex problems. The necessity to proceed to a detailed investigation of the mechanism of the Wallach rearrangement has become self-evident. The solution of this problem can only be achieved by a combined method involving the use of modern physical research techniques. It is possible to differentiate two main groups of problems. One is associated with the study by a spectroscopic method of the electronic structures of the electrophilic species generated in the course of the rearrangement. The other concerns the determination of their true role in the Wallach rearrangement, especially in the rate-limiting stage. There is no doubt that further study of the mechanism of the Wallach rearrangement will significantly expand our ideas about molecular rearrangements.

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Novosibirsk Institute of
Organic Chemistry,
Siberian Division of the USSR
Academy of Sciences