Unusual Reaction of Azoxybenzenes with *p*-Toluenesulfonic Acid in Acetic Anhydride

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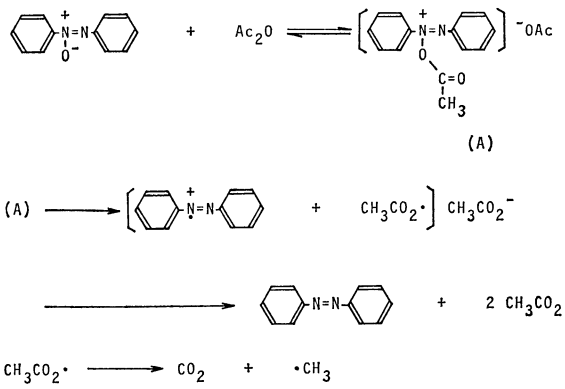
Treatment of azoxybenzene with *p*-toluenesulfonic acid in acetic anhydride gave tosylates of 4- and 2-(phenylazo)phenols, and the corresponding acetates as by-product, besides azobenzene. However, a similar reaction of 4,4′-difluoroazoxybenzene gave 2-tosyloxy-4,4′-difluoroazobenzene as rearrangement product, besides 4-fluorophenyl tosylate and 4-fluorophenyl acetate. Meanwhile, the reaction of 4,4′-diacetoxyazoxybenzene afforded 4-acetoxyphenyl tosylate and hydroquinone diacetate in high yields. These unique reactions involve C–N bond cleavage, and may proceed through a pathway involving formation of benzenediazonium ion as the key intermediate.

In the Wallach rearrangement of azoxybenzenes, concentrated sulfuric acid has generally been used.[1] Meanwhile, treatment of azoxybenzene with chlorosulfuric acid[2] yielded chlorosulfate of *p*-hydroxyazobenzene. Similarly, in the reaction with fluorosulfuric acid,[3] the corresponding fluorosulfate of *p*-hydroxyazobenzene was obtained. Recently, the reaction of azoxybenzene with arenesulfonyl chloride[4] and tosyl anhydride[5] have also been found to give the arenesulfonates of *o*- and *p*-hydroxyazobenzene.

In the ordinary Wallach rearrangement of azoxybenzene with sulfuric acid, hydrogen sulfate ester of *p*-hydroxyazobenzene is formed as the rearrangement product, which is then rapidly hydrolyzed to give *p*-hydroxyazobenzene as the final product.[6] However, the sulfonic acid esters of hydroxyazobenzene do not hydrolyze under the reaction conditions. Recently, Yamamoto *et al.* reported that the treatment of azoxybenzene with trichloroacetic acid in acetic anhydride afforded hydroxyazobenzene,[7] *via* forming the corresponding ester, which is however unstable and hydrolyzed during the isolation of the reaction product.

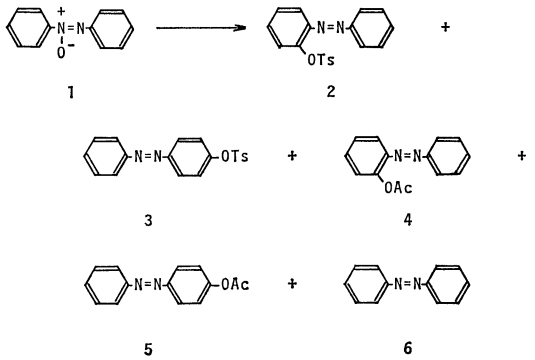
Earlier, we reported that azoxybenzene reacts with an equimolar amount of acetic anhydride only upon heating at such a high temperature as 190 °C for a long hour, affording a mixture of azobenzene, acetanilide and acetic acid along with carbon dioxide, carbon monoxide and methane.[8] We then suggested that the initial slow step is the acetylation to give the *N*-acetoxyazobenzene, which undergoes homolytic fission of N–O bond shown below.



Since acetylation of *N*-oxides or sulfoxides is markedly accelerated by acid catalysis, it was anticipated that the reaction of azoxybenzene with acetic anhydride would proceed under mild conditions in the presence of a strong acid such as *p*-toluenesulfonic acid, and gives the rearranged ester, because water is absent under the conditions and hence the esters would not be hydrolyzed. Indeed the reaction between azoxybenzene and a mixture of acetic anhydride and *p*-toluenesulfonic acid was found to proceed smoothly even at 100 °C, and gave both tosyl and acetyl esters of hydroxyazobenzene. This paper is concerned with the reaction of some azoxybenzenes with *p*-toluenesulfonic acid in acetic anhydride.

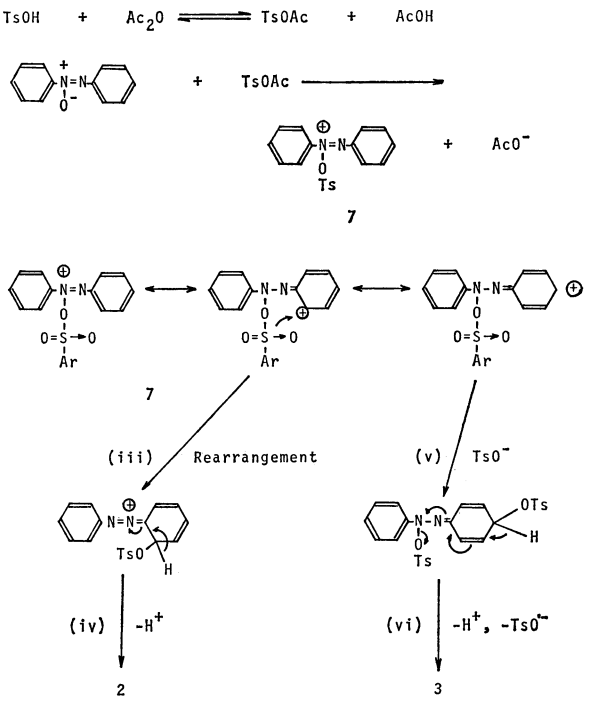
Results and Discussion

Treatment of azoxybenzene (**1**) with excess *p*-toluenesulfonic acid (TsOH) in excess acetic anhydride at 100 °C for 12 h gave 2-tosyloxyazobenzene (**2**) (5%) and 4-isomer (**3**) (20%), 2-acetoxyazobenzene (**4**) (0.3 %) and 4-isomer (**5**) (2%) as rearrangement products, along with azobenzene (**6**) (7.5%).

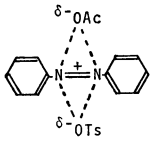


These rearrangement products may be formed through a mechanistic pathway similar to that proposed for the reaction of **1** with arenesulfonyl chloride,[3] as illustrated in the following sequential scheme: (i) Formation of the mixed acid anhydride, (ii) reaction of **1** with TsOAc to form *O*-tosylated intermediate (**7**), (iii) migration of tosyloxyl group to *o*-position, (iv) deprotonation to give eventually **2**, or (v) nucleophilic attack of tosylate ion (or acetate ion) at *p*-position of **7**, and (vi) subsequent elimination of tosyloxyl group bonded to azo nitrogen and deprotonation

to give **3** (or **5**).



In the step (iii), the intermediate, **7**, may dissociate to form an intimate ion pair (**8**), prior to migration. When acetoxyl group migrates to the *o*-position, compound **4** is formed, though the yield is so low. In addition, there might be an alternative pathway to form a dication intermediate directly by cleavage of tosylate ion from **7**.



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Here again, the formation of azobenzene may be rationalized in terms of incipient formation of azobenzene cation radical similarly as in the reaction of azoxybenzene with acetic anhydride at 190 °C.

The ratio of *o*-rearrangement to *p*-rearrangement is higher (1:4) than that of the reaction of **1** with sulfuric acid (*o*:*p*=1:26).[9] Probably, unlike the rearrangement in polar sulfuric acid, in which dissociation of water from azo group is more complete and hence the intermolecular migration to *p*-position predominates, that of the intermediate, **7**, in less polar acetic anhydride is more prone to proceed intramolecularly to *o*-position (step iii). This may be the reason why the *o*/*p* product ratio is a little higher in the reaction with acetic anhydride–TsOH system than with sulfuric acid.

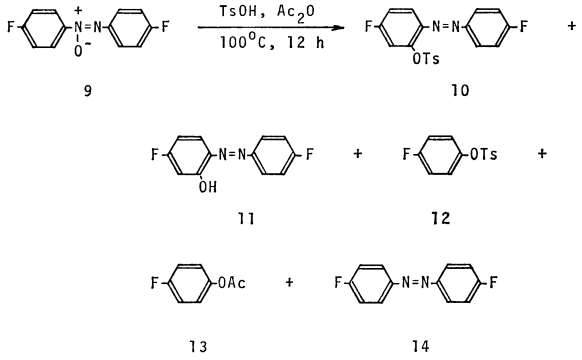
The yield of acetate, **5**, was low, despite more nucleophilic character of acetate ion than tosylate ion. However, in the presence of TsOH, acetate ion, if formed, would be completely protonated to form acetic acid which is no longer nucleophilic enough to compete with tosylate ion to attack the *p*-position. The ester exchange reaction between tosylate, **3**, and acetate, **5**, was not observed under the above reaction conditions.

Table 1. Reaction of 4-bromo-ONN- and 4-bromo-NNO- azoxybenzenes

Compound	Yield/%					
	16	**17**	**18**	**19**	Acetate[a]	Recovery
15α	4.0	2.5	1.3	0.7	1.3	80
15β	4.8	3.3	1.6	0.8	1.3	73

a) 4-(*p*-Bromophenylazo)phenyl acetate contaminated by small amounts of the 2-isomer.

Treatment of 4,4′-difluoroazoxybenzene (**9**) with a mixture of TsOH and acetic anhydride gave in poor yield, ortho rearrangement product, 2-tosyloxy-4,4′-difluoroazobenzene (**10**) (yield 4%) and 2-(*p*-fluorophenylazo)-5-fluorophenol (**11**) (yield 1.5%) which is undoubtedly formed by hydrolysis of 2-acetoxy-4,4′-difluoroazobenzene during the isolation process of the reaction products. However, *p*-fluorophenyl tosylate (**12**) (yield 12%) and *p*-fluorophenyl acetate (**13**) (yield 5%) formed by the cleavage[16] of azoxy N and phenyl C bond were obtained, besides 4,4′-difluoroazobenzene (**14**) (yield 4.5%).

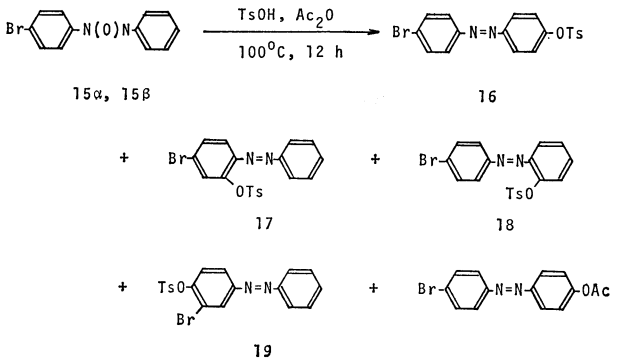


The reaction of 4,4′-dichloroazoxybenzene with a mixture of TsOH and acetic anhydride was relatively slow, and only after heating at 100 °C for 50 h, 2-tosyloxy-4,4′-dichloroazobenzene (3%), 2-(*p*-chlorophenylazo)-5-chlorophenol (0.4%), *p*-chlorophenyl tosylate (0.5%), and 4,4′-dichloroazobenzene (5.5%) were obtained.

Meanwhile, the reaction of 4,4′-dichloroazoxybenzene with sulfuric acid yielded abnormal rearrangement products, *e.g.* 2-chloro-4-(*p*-chlorophenylazo)phenol and 4-(*p*-chlorophenylazo)phenol, in which chlorine is migrated or lost.[10] However, these abnormal products were not observed at all in the reaction of 4,4′-dichloroazoxybenzene with a mixture of TsOH and acetic anhydride. The *O*-tosylated intermediate, **7**, did not accept the nucleophilic attack of tosylate ion at ipso position but preferentially rearranged to form the ester of *o*-hydroxyazobenzene. In addition, the formation of dicationic intermediate (Ar–$\overset{+}{N}\equiv\overset{+}{N}$–Ar) may be suppressed by low acidity under this reaction conditions. Consequently, the ipso attack of tosylate ion did not occur.

The reaction of 4-bromo-ONN-azoxybenzene (**15α**) and the NNO-isomer (**15β**) with a mixture of TsOH and acetic anhydride gave 4-(*p*-bromophenylazo)phen-

yl tosylate (**16**), 2-(phenylazo)-5-bromophenyl tosylate (**17**), 2-(*p*-bromophenylazo)phenyl tosylate (**18**), and 2-bromo-4-(phenylazo)phenyl tosylate (**19**) (Table 1).



Azophenol tosylates, **16**—**19**, could not be isolated in this reaction. Therefore, the mixture was analyzed by gas chromatography. The mixture was hydrolyzed further with sodium hydroxide solution to isolate the corresponding azophenols.

The reaction products obtained from α-isomer of 4-bromoazoxybenzene (**15α**) were practically similar to those formed from the β-isomer (**15β**). It appears that the reaction proceeds *via* a common intimate ion pair intermediate (**20**). The product, **19**, is considered to be formed by rearrangement accompaning the migration of bromine. The similar rearrangement was observed in the reaction of 4,4'-dibromoazoxybenzene with sulfuric acid.[10] Thus, the rearrangement may be interpreted by the following mechanistic scheme in which the intimate ion pair, **20**, is the common intermediate in the rearrangement to both *o*- and *p*-positions and also in the migration of bromine, similar to that proposed previously.

The reaction of 4,4'-diacetoxyazoxybenzene(**21**)

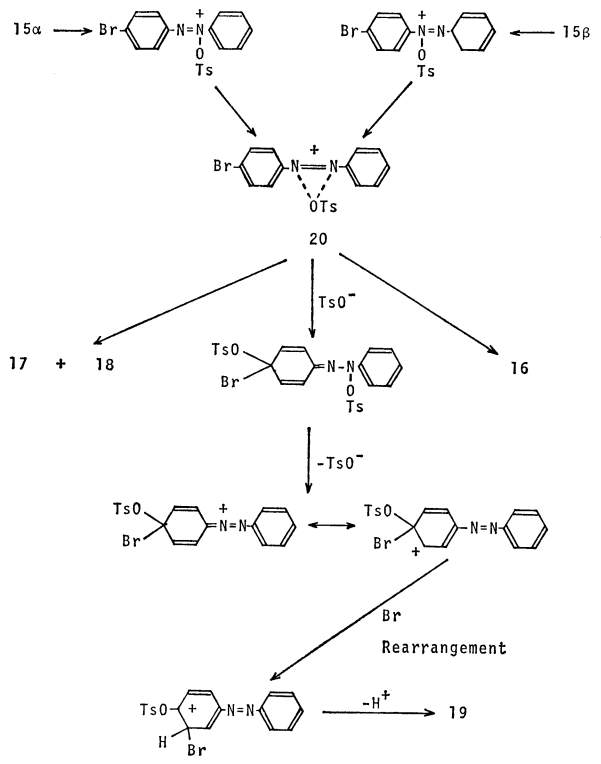
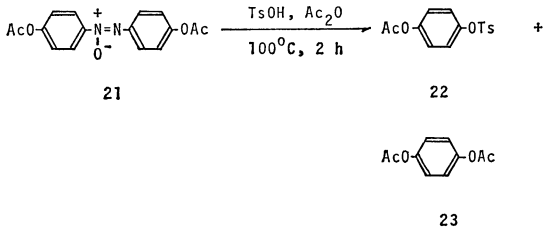


Table 2. Reaction of 4-acetoxyazoxybenzenes with TsOH in acetic anhydride (100 °C, 2 h)

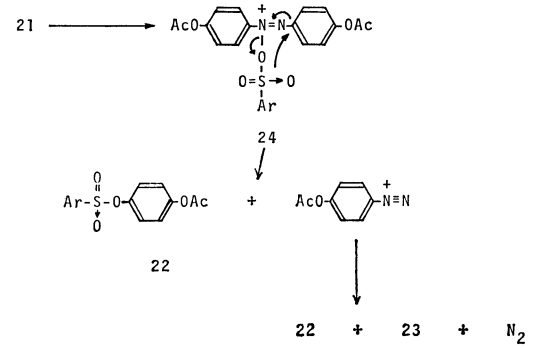
Compound	Yield/%				
	22	**23**	**26**	**27**	**25β**
25α	77	9	18	72	
25β	33	4	8	30	60

gave mainly unique 1-ipso substitution products, *i.e.* 4-acetoxyphenyl tosylate (**22**) (yield 51%) and hydroquinone diacetate (**23**) (yield 47%), in high yield with evolution of nitrogen. The expected rearrangement products (the corresponding azophenol esters) were not obtained.



The reaction may be nicely explained by the following mechanistic scheme: (i) The initial formation of *O*-tosylated azoxybenzene (**24**), (ii) cleavage of the C–N bond and simultaneous attack to the tosyloxy oxygen (*i.e.* formation of **22** and the diazonium ion), (iii) decomposition of the diazonium ion to form **22** and **23** with evolution of nitrogen. Step (ii) may be attributed to the resonance effect of acetoxyl group to facilitated the cleavage of C–N bond. In this process, there might be a possibility that tosyloxyl group is alternated to acetoxyl group to give **23**.

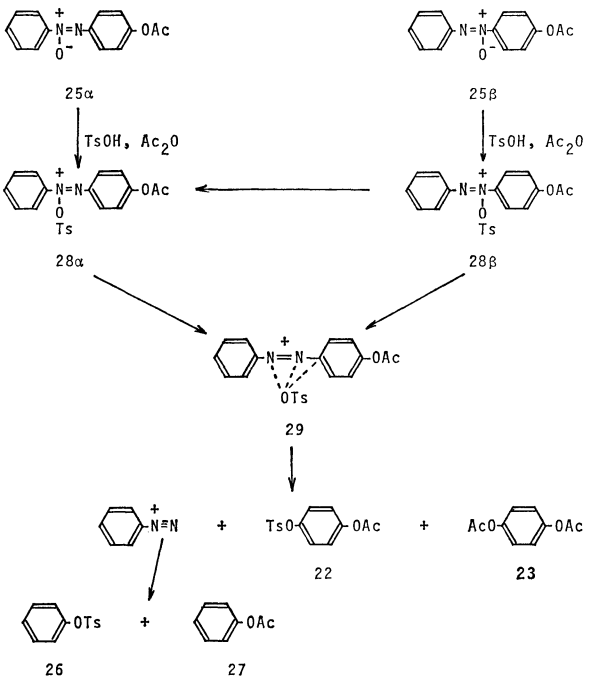
In analogy with the reaction, when a solution of **21** and tosyl anhydride in acetonitrile was refluxed for 2 h, **22** was obtained in yield of 16%. Also the reaction of **21** with sulfuric acid in acetic anhydride (100 °C, 1 h) afforded **23** (yield 35%).



On the other hand, 2,2'-diacetoxyazoxybenzene gave also 2-acetoxyphenyl tosylate (41%), cathecol diacetate (18%), and 2,2'-diacetoxy-4-tosyloxyazobenzene (16%). In this reaction, the rearrangement product was obtained to a considerable extent.

The C–N bond cleavage was also found to occur in the reaction of 4-acetoxyazoxybenzene. Compounds, **22** and **23**, as well as, phenyl tosylate (**26**) and phenyl acetate (**27**) were obtained in the reaction of 4-acetoxy-ONN-azoxybenzene (**25α**) and 4-acetoxy-

NNO-azoxybenzene (**25β**). The results are shown in Table 2.

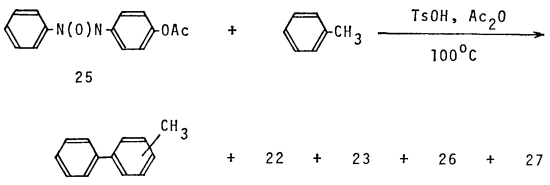


The α-isomer (**25α**) was found to react more rapidly than the β-isomer (**25β**). Accordingly, when the mixture of α- and β-isomers was used, the β-isomer was isolated as recovered material. Thus this procedure can be applied to prepare the β-isomer.

Both **25α** and **25β** gave the products nearly in the same ratio. Therefore, the reaction is presumed to proceed *via* a same common transient intermediate, perhaps a symmetrical ion pair (**29**). Alternatively, there is a possibility that **28β** rearranges to **28α** before undergoing the C–N bond cleavage.

The yield of tosylate, **22**, was higher than that of acetate, **23**, and while the yield of **27** was higher than that of **26**. Therefore, the first C–N bond cleavage would occur on the carbon atom of benzene ring having *p*-acetoxyl group, to give benzenediazonium ion and **22** (and **23**). In this step, tosyloxyl oxygen attacks the C_1 atom of benzene ring in preference to acetoxyl oxygen, since acetoxyl group would be completely protonated and lack enough nucleophilicity to attack ipso C_1. Benzenediazonium ion thus formed is reactive and hence would react readily with acetoxyl group present in a large exess.

In the presence of toluene, the reaction of **25** (α- and β-isomer) with TsOH and acetic anhydride afforded methylbiphenyl (yield 9%), as well as **22**, **23**, **26**, and **27**. Gas chromatographic analysis showed



that the isomer distribution of methylbiphenyl was *o*: 57%, *m*: 21%, *p*: 22%. This ratio is close to that obtained by the reaction of toluene with benzenediazoniom ion in the presence of TsOH (*o*: 61%, *m*: 16%, *p*: 23%). The formation of methylbiphenyl demonstrates the participation of benzenediazonium ion as the intermediate.

Formation of arenediazonium ion from azoxyarene is not entirely unprecedented. The photo-rearrangement of 2,2′-dimethylazoxybenzene was reported to give a diazonium ion as an intermediate which eventually yielded abnormal by-product.[11]

Similarly, 4-chloro-4′-acetoxyazoxybenzene (a mixture of α- and β-isomer) yielded **22** (52%), **23** (5%), *p*-chlorophenyl tosylate (13%), and *p*-chlorophenyl acetate (45%). The recovered azoxy compound (37%) was almost 4-(*p*-chlorophenylazoxy)-NNO-phenyl acetate (β-isomer).

Experimental

Melting points are uncorrected. GLC analyses were performed on a Shimadzu GC-6A (column: 1.5% Silicone OV-17, 1 m or 2% Silicone OV-225, 3 m). Other instruments used are the same as those previously described.[10]

The reaction products were identified by comparison with samples prepared independently.

Material. 4,4′-Difluoro- and 4,4′-dichloro-azoxybenzenes and *p*-bromoazoxybenzenes were prepared according to the method given in the previous paper.[10] 4,4′-Diacetoxyazoxybenzene (**21**) was obtained as described by Jeonard and Curry,[12] mp 169—170 °C (from benzene). 2,2′-Diacetoxyazoxybenzene, *p*-acetoxyazoxybenzene, and *p*-acetoxy-*p*′-chloroazoxybenzene were prepared by oxidation of the corresponding azo compound with 30% H_2O_2 in AcOH. 2,2′-Diacetoxyazoxybenzene, mp 115—116 °C. Found: C, 61.35; H, 4.60; N, 8.72%. Calcd for $C_{16}H_{14}N_2O_5$: C, 61.14; H, 4.50; N, 8.91%. 4-Acetoxyazoxybenzene was a mixture of α-isomer 61% and β-isomer 39% (GLC). 4-Acetoxy-4′-chloroazoxybenzene was a mixture of α-isomer 57% and β-isomer 43% (HPLC). 4-Phenylazoxy-ONN-phenyl acetate (**25α**) and its NNO-isomer (**25β**) were prepared by acetylation of the corresponding phenylazoxyphenol with acetic anhydride and pyridine, **25α**, mp 93—95 °C (lit,[13] 89—90 °C), **25β**, mp 80—81 °C (lit,[13] 79—80 °C).

Reaction of Azoxybenzene (1). *p*-Toluenesulfonic acid (TsOH) monohydrate (5.0 g) was heated at 140 °C under reduced pressure to remove the crystalline water. To a solution of TsOH in acetic anhydride (12.5 ml) was added **1** (0.5 g). The solution was heated at 100 °C for 12 h. The reaction mixture was poured into cold water, and extracted with benzene. The extract was washed with $NaHCO_3$ solution, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (benzene). Each fraction was analyzed by GLC. First fraction was a mixture of azobenzene (**6**) (0.034 g) and **1** (0.156 g). Second fraction was a mixture of 2-tosyloxyazobenzene (**2**) (0.045 g) and 4-tosyloxyazobenzene (**3**) (0.178 g). Third fraction was a mixture of 2-acetoxyazobenzene (**4**) (1.7 mg) and 4-acetoxyazobenzene (**5**) (12 mg).

Reaction of 4,4′-Difluoroazoxybenzene (9). Compound, **9**, (0.2 g) was treated with a mixture of TsOH and Ac_2O similarly, and worked up according to the procedure described above. The reaction product was chromatographed on silica gel (benzene). First fraction was a mixture o 4,4′-difluoroazobenzene (**14**) (9 mg) and **9** (82 mg). Second fraction was distilled under reduced pressure to give 4-fluorophenyl acetate (**13**) (7 mg), and the residue was chromato-

graphed on alumina.[15] Elution with benzene gave a mixture of 4-fluorophenyl tosylate (**12**) (27 mg) and 2-tosyloxy-4,4′-difluoroazobenzene (**10**) (13 mg). Recrystallization from hexane gave **10**, mp 116—117 °C, and the mother liquor was evaporated and distilled *in vacuo* to give **12**, mp 56—58 °C) from hexane). The residue on alumina column was eluted with EtOH–H_2O to give 2-(*p*-fluorophenylazo)-5-fluorophenol (**11**), mp 126 °C (from hexane).

*Reaction of 4,4′-Diacetoxyazoxybenzene (**21**).* TsOH monohydrate (5.0 g) was dehydrated at 140 °C under reduced pressure. A solution of **21** (0.5 g) and TsOH in Ac_2O (12.5 ml) was then heated at 100 °C for 2 h. The solution was poured into cold water. The precipitate was filtered off and purified by column chromatography on silica gel (benzene) to give 4-acetoxyphenyl tosylate (**22**) (0.50 g), mp 77.5—78 °C (from hexane–benzene). The mother liquor was extracted with benzene. The extract gave hydroquinone diacetate (**23**) (0.29 g), mp 122—123 °C (from hexane).

Reaction of 2,2′-Diacetoxyazoxybenzene. 2,2′-Diacetoxyazoxybenzene (0.2 g) was treated with a mixture of TsOH and Ac_2O similarly according the method described above. The reaction product was chromatographed on silica-gel column (benzene). First fraction was 2-acetoxyphenyl tosylate (0.16 g), mp 90—91 °C (from hexane). Second fraction was cathecol diacetate (0.044 g), mp 61—62 °C (from hexane). Third fraction (0.05 g) gave 2,2′-diacetoxy-4-tosyloxyazobenzene, mp 97—98 °C (from EtOH). Found: C, 59.02; H, 4.37; N, 6.00%. Calcd for $C_{23}H_{20}N_2O_7S$: C, 58.97; H, 4.30; N, 5.98%. The authentic sample was prepared by acetylation of 2,2′-dihydroxy-4-tosyloxyazobenzene (mp 223—225 °C).

*Reaction of 4-Acetoxyazoxybenzene (**25**).* 4-Acetoxyazoxybenzene (0.5 g) was treated with a similar mixture of TsOH and Ac_2O at 100 °C for 1 h according to the procedure described above. The reaction mixture was poured into cold aqueous $NaHCO_3$ solution, and then extracted with ether. The extract was distilled to give phenyl acetate (0.09 g). The residue was chromatographed on silica gel (benzene). First fraction gave phenyl tosylate (0.06 g), mp 94—95 °C (from hexane). Second fraction was the unchanged azoxy compound (0.16 g) (α-isomer 13.5% and β-isomer 86.5%). Third fraction gave 4-acetoxyphenyl tosylate (0.29 g) mp 79—80 °C (from hexane–benzene). Fourth fraction gave hydroquinone diacetate (0.019 g), mp 122—123 °C.

Authentic Sample of Tosylate Derivatives. The corresponding phenol was treated with tosyl chloride and pyridine by conventional method. **2**, mp 84—85 °C (lit,[4] 85—86 °C). **3**, mp 164—165 °C (lit,[4] 159—160 °C). 2-Tosyloxy-4,4′-dichloroazobenzene, mp 136—138 °C (from benzene–hexane). Found: C, 54.22; H, 3.14; N, 6.39%. Calcd for $C_{19}H_{14}Cl_2N_2O_3S$: C, 54.16; H, 3.33; N, 6.65%. **10**, mp 115—116 °C (from EtOH). Found: C, 58.88; H, 3.50; N, 7.22%. Calcd for $C_{19}H_{14}F_2N_2O_3S$: C, 58.76; H, 3.63; N, 7.21%. **16**, mp 157—159 °C. Found: C, 53.22; H, 3.33; N, 6.71%. **17**, mp 132—133 °C. Found: C, 52.83; H, 3.47; N, 6.75%. **18**, mp 123—124 °C. Found: C, 53.14; H, 3.40; N, 6.63%. **19**, mp 78—79 °C. Found: C, 52.63; H, 3.51; N, 6.52%, (from benzene–hexane). Calcd for $C_{19}H_{15}BrN_2O_3S$: C, 52.91; H, 3.51; N, 6.50%.

12, mp 58—59 °C (from hexane), Found: C, 58.45; H, 3.98%. Calcd for $C_{13}H_{11}FO_3S$: C, 58.64; H, 4.16%. *p*-Chlorophenyl tosylate, mp 68—70 °C, (from hexane). Found: C, 55.22; H, 3.92%. Calcd for $C_{13}H_{11}ClO_3S$: C, 55.23; H, 3.96%. **22**, mp 76.5—77.5 °C (from hexane–benzene). Found: C, 58.94; H, 4.83%. Calcd for $C_{15}H_{14}O_5S$: C, 58.81; H, 4.61%. 2-Acetoxyphenyl tosylate, mp 91—92 °C. Found: C, 58.65; H, 4.78%. Calcd for $C_{15}H_{14}O_5S$: C, 58.81; H, 4.61%. **26**, mp 94—95 °C (lit,[14] 94—95 °C).

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15) In this process, aryl acetate was hydrolyzed to give the corresponding phenol.

16) The resonance effect of fluorine is more suitable on the C–N bond cleavage than that of chlorine, however, acetoxyl group serves more effectively on the cleavage reaction than fluorine.