

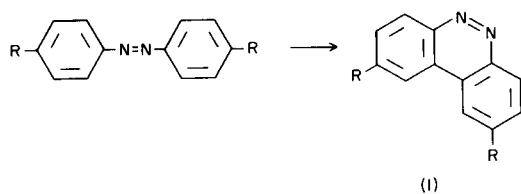
The Conversion of Azobenzenes to Phenazines: A New Molecular Rearrangement

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When azobenzenes are heated with ferrous oxalate or with a fused mixture of aluminum chloride and sodium chloride the corresponding phenazines are formed in low yield. Azobenzene itself is exceptional in giving benz[*c*]cinnoline with $\text{AlCl}_3\text{-NaCl}$. Azoxybenzenes and ferrous oxalate give azobenzenes and some phenazines, while azoxybenzene itself also gives 2-hydroxyazobenzene *via* a Wallach-type rearrangement. The rearrangements are thought to occur at the surfaces of the reagent. No rearrangement to the phenazines occurs in the absence of the reagent.

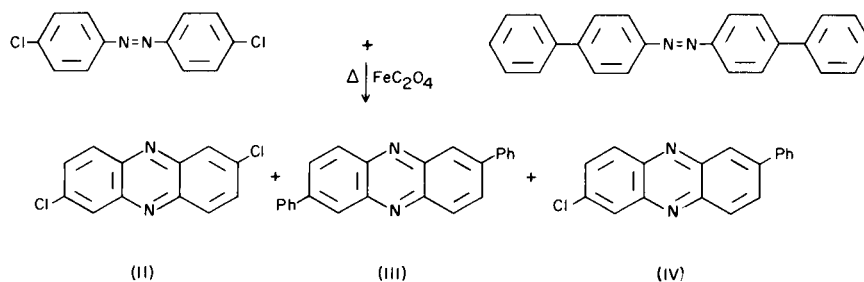
Azobenzenes have been reported to undergo photo-induced cyclization and dehydrogenation in acid solution to the corresponding benz[*c*]cinnoline (1) (1), and there has been one report of the thermal cyclization of azobenzene itself to 1($R=H$) using a fused mixture of aluminum chloride-sodium chloride (2). A study of the pyrolysis of azobenzene alone at 460° gave numerous products: benzene, aniline, biphenyl, diphenylamine, anthracene, phenanthrene, ammonia, hydrogen cyanide and nitrogen (3).



In an earlier paper (4), it was reported that the reaction of simple aromatic nitro-compounds with transition-metal oxalates gave mainly azobenzene derivatives together with traces of phenazines. Three mechanisms were envisioned for the formation of phenazines: (i) Dimerization of a nitrene ($R\text{-C}_6\text{H}_4\text{-N}$) to a 9,10-dihydrophenazine, followed by dehydrogenation, a process for which there was one precedent (5). Another has recently been reported (6). (ii) Ring-closure of an *o*-nitrodiphenylamine derivative with ferrous oxalate. The formation of *o*-nitrodiphenylamine was, however, considered to be rather unlikely. (iii) Rearrangement of the azobenzene first formed to a

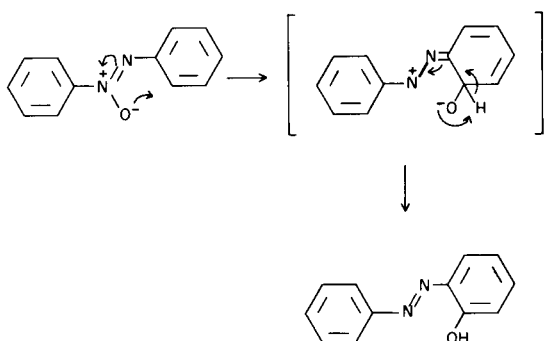
dihydrophenazine in the presence of ferrous oxalate. This latter possibility forms the subject of the present investigation.

When azobenzenes are heated with ferrous oxalate at $280\text{-}300^\circ$, phenazines are obtained in yields usually lower than 15%. In many cases, the primary amines were also isolated, and invariably considerable amounts of tar. Recovery of starting material was usually poor, suggesting that strong complexes were formed with the iron compounds (probably decomposition products of the oxalate). Formation of primary amines shows that the azo-linkage is broken at some stage (reduction by hydrogen transfer to the hydrazo-state is also possible followed by cleavage of the NH-NH bond; no hydrazobenzene derivative was ever detected, however). On the other hand, cross-over experiments indicate a *predominantly* intramolecular rearrangement. Thus, when a mixture of 4,4'-dichloroazobenzene and 4,4'-diphenylazobenzene was heated with ferrous oxalate, 2,7-dichloro- (II), 2,7-diphenyl- (III) and 2-chloro-7-phenylphenazine (IV) were obtained in the ratio of 60:120:1. Since no reaction at all occurs in the absence of ferrous oxalate, it is suggested that the rearrangement occurs at the surface of the oxalate or its decomposition products. The yields of products are summarized in Table I. In one case of the rearrangement of 4,4'-dichloroazobenzene, acetone was used in the extraction procedure. An additional product of molecular weight 506 (mass spectrum) was isolated under these conditions. The pattern of isotopic clusters in the parent ion indicated the presence of three chlorine atoms in the molecule and this, together with analytical and fragmentation data, confirmed the molecular formula, $\text{C}_{27}\text{H}_{21}\text{Cl}_3\text{N}_4$. The NMR spectrum



showed the presence of one NH group and two methyl groups. The latter undoubtedly arise from the condensation of a primary amino group with the acetone used in the extraction process to give a Schiff's base. The infrared and ultraviolet absorption spectra were consistent with the presence of azobenzene and diphenylamine-type moieties in the molecule. When, however, the compound was boiled with concentrated hydrochloric acid for 8 hours, most of it was recovered unchanged and only tars were formed. A similar type of product was not isolated in any of the other reactions with other azocompounds, nor could any of the primary amine precursors of the compound be isolated in the absence of acetone.

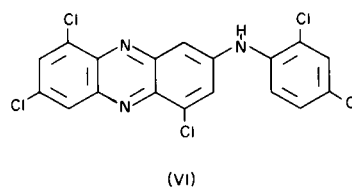
When azoxybenzenes are heated with ferrous oxalate, the major product is, as expected, the corresponding azo-compound in good yield. Phenazines are byproducts, and are presumably formed in secondary reactions of the azo-compounds, although rearrangement of the azoxy-compounds to the phenazine *N*-oxide followed by deoxygenation cannot be ruled out. Azoxybenzene itself behaves exceptionally, in that, in addition to azobenzene (60%), phenazine (0.2%) and a trace of aniline, it also gives 2-hydroxyazobenzene (3%). The latter most probably results from a Wallach-type rearrangement (7).



In contrast to the behaviour of azobenzenes, benzylidene aniline only gave a trace of acridine on heating with ferrous oxalate, and no anthracene or phenazine.

Several mechanisms can be envisioned for the rearrangement of azobenzenes to phenazines and these are depicted in Scheme I. Intramolecular heterolytic (path *a*) or homolytic (path *b*) routes as well as an intermolecular pathway (*c*) involving nitrenes, are conceivable. The isolation of primary amines and the observation of crossover products (albeit in minute yields) appear to favour the nitrene pathway. As has already been pointed out, there are precedents for the dimerization of nitrenes to dihydrophenazines (5,6). Dehydrogenation of V could occur with ferrous oxalate (8) or by hydrogen abstraction by a nitrene intermediate, which would account for some of the primary amine formed. It is also conceivable that dihydrophenazines could arise by a "double" semidine-type rearrangement of an intermediate hydrazobenzene, but there is no evidence for the formation of dihydrophenazines in the normal benzidine rearrangement. Such a pathway could also perhaps account for the formation of primary amines.

When 2,2',4,4'-tetrachloroazobenzene and 2,4-dichloroaniline were heated with ferrous oxalate, a product, $\text{C}_{18}\text{H}_8\text{Cl}_5\text{N}_3$, identical with compound A obtained from the reaction of 2,4-dinitrochlorobenzene with ferrous oxalate (4) was obtained. This is either 1,6,8-trichloro-3-(2,4-dichloroanilino)-phenazine (VI) or the isomer in



which the anilino-residue is at the 1-position (4). The same compound was obtained when 2,2',4,4'-tetrachloroazoxybenzene and 2,4-dichloroaniline were heated with ferrous oxalate.

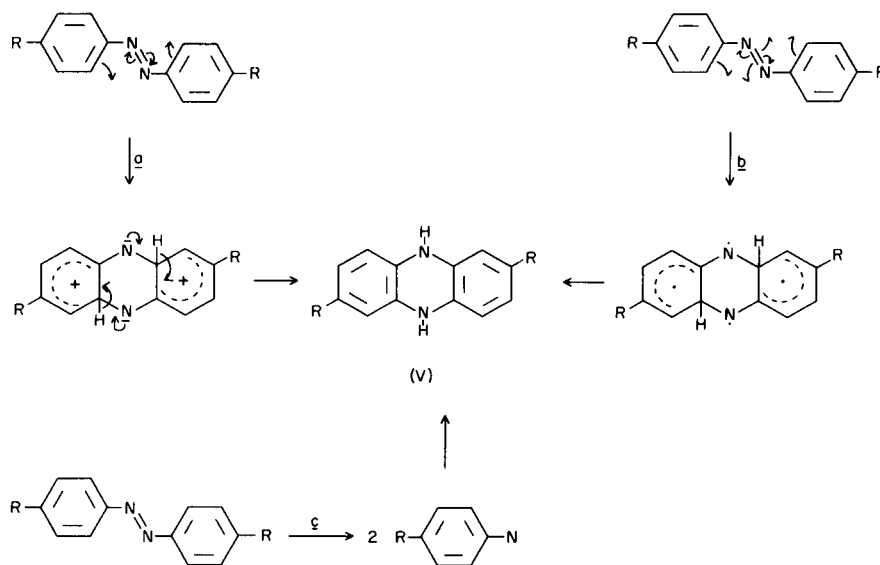
TABLE I
Reaction Conditions and Product Yields for the Reactions of Azo Compounds with Ferrous Oxalate

Run	Azo Compound (g.)	Oxalate (g.)	Reaction Time (min.)	Reaction Temp. (°C)	Azo Cpd. Recovered (g.)	Yield of Phenazine		Yield of Amine	
						%*	m.p. (ref)	Grams	Eluent(f)
1	azobenzene (5.0)	10.0	40	220-260	4.0	5.0	170 (12)	C	
2	4,4'-dichloro- (5.0)	5.0	45	270	2.8	0.14	268-269 (9)	B	
3	4,4'-dichloro- (5.0)	10.0	80	300	0.95	0.27	268-269 (9)	B	1.10
4	4,4'-dichloro- (5.0)	15.0	60	280-300	2.1	0.17	268-269 (9)	B	0.56
5	4,4'-dichloro- (5.0)	0.0	90	270	5.0	0			
6	4,4'-dichloro- (5.0)	5.5	35	245-255	4.2	0			
7	4,4'-dichloro- (4.2)	8.4	60	280-300	1.6	0.25	268-269 (9)	B	0.53
8	4,4'-dichloro- (2.5)	3.5	50	260-290	1.3	0.12	268-269 (9)	B	0.16
9	2,2',4,4'-tetrachloro- (0.5)	2.0	40	240-280	0.09	0.05	223-224 (13)	A	
10	4,4'-diphenyl- (0.65)	0.9	60	270-310	0.08	0.085	270-272	D	
11	4,4'-dimethoxy- (1.98)	1.3	40	260-290	1.34	0.05	246.5-247 (14)	D	0.11
12 (a)	4,4'-dichloro- (0.68) and 4,4'-diphenyl- (0.90)	1.08	40	280-310	trace (e)	0.06 (b)	268-269 (b)		
13	4,4'-dichloro- (0.41) and 2,2',4,4'-tetrachloro- (0.52)	0.80	50	260-290	0.40 0.35	0.001 (c) 0.12 (d)	271-272 (d) 268 (b)		
14 (h)	4,4'-dichloro- (0.36) and 2,2',4,4'-tetrachloro- (0.46)	0.70	180	290	0.34 0.3 (both azo cpds.)	0.004 (g) 0.003 (g)	210-213 (f) 222-223 (g) (13) 222-224 (g)		

(a) Detected by thin-layer chromatography but not isolated were *p*-chloroaniline (R_f 0.20) and 4-aminobiphenyl (R_f 0.09). (b) 2,7-Dichlorophenazine. (c) 2-Chloro-7-phenylphenazine. (d) 2,7-Diphenylphenazine. (e) 4-Chloro-4'-phenylazobenzene. (f) 1,3,6-Trichlorophenazine. (g) 1,3,6,8-Tetrachlorophenazine. (h) Reaction carried out in hexadecane solution. (i) A, light petroleum; B, light petroleum-benzene (4:1); C, light petroleum-benzene (3:1); D, light petroleum-benzene (2:1).

* Taking into account recovered azobenzene.

SCHEME I



The cyclization of azobenzene to benz[*c*]cinnoline with fused aluminum chloride-sodium chloride mixture (2) has been confirmed. In contrast, when the oxidative cyclization was carried out with substituted azo-compounds the products were the phenazines rather than the benz[*c*]cinnolines. The yields of rearranged products were again low as was the overall recovery of organic material (Table II). It is not clear why ring substitution should affect the mode of cyclization. No primary amines were detected when $\text{AlCl}_3\text{-NaCl}$ melts were used, which suggests a mechanism for the cyclizations involving an intramolecular heterolytic attack by nitrogen complexed with aluminum chloride upon the opposing aryl nucleus. No crossover experiments have been carried out.

EXPERIMENTAL

Melting points are uncorrected. Light petroleum refers to the fraction, b.p. $36\text{-}56^\circ$.

A. Reactions of Aromatic Azo Compounds with Ferrous Oxalate Dihydrate.

Reaction of 4,4'-Dichloroazobenzene.

4,4'-Dichloroazobenzene (5 g.) was heated with ferrous oxalate (10 g.) at 300° for 80 minutes. The black reaction mixture was extracted with hot benzene, the solvent evaporated and the residue chromatographed on a column of alumina. Elution with light petroleum gave unreacted 4,4'-dichloroazobenzene (0.95 g.), 2,7-Dichlorophenazine (0.27 g.), m.p. $268\text{-}269^\circ$ [reported (9) m.p. 265.5°], was eluted with light petroleum-benzene (4:1). With the same eluent *p*-chloroaniline (1.1 g.), m.p. $70\text{-}71^\circ$, was obtained. Melting points were undepressed on admixture with authentic samples.

In an earlier run, in which acetone was used as well as benzene in the extraction procedure, elution of the column with light petroleum-benzene (3:1) gave an orange-red compound (0.14 g.), m.p. $197.5\text{-}198.5^\circ$. Infrared spectrum (potassium bromide disc): $3270(\text{m})$, (NH), $2970(\text{w})$, $2920(\text{w})$, $1622(\text{m})$, (C=N?), $1598(\text{s})$, $1572(\text{s})$, $1531(\text{s})$, $1488(\text{s})$, $1317(\text{s})$, $1298(\text{s})$, $1123(\text{m})$, $1082(\text{s})$, $1007(\text{m})$, $820(\text{s})$, and 784 cm^{-1} (m). U. V. λ_{max} (95% ethanol), 470 (ϵ , 690), 367 (ϵ , 24,000), 277 (ϵ , 21,600), and $211\text{ m}\mu$ (ϵ , 34,200); NMR spectrum (deuteriochloroform), $1.62\text{ }\tau$ (NH) (1 H singlet, removed by exchanging with deuterium oxide); $2.71\text{ }\tau$ (5 H singlet), $2.77\text{ }\tau$ (4 H quartet), $3.01\text{ }\tau$ (4 H quartet), $3.48\text{ }\tau$ (1 H singlet) and $8.52\text{ }\tau$ [$(\text{CH}_3)_2\text{C}=\text{}$] (6 H singlet).

Anal. Calcd. for $\text{C}_{27}\text{H}_{21}\text{Cl}_3\text{N}_4$: C, 63.90; H, 4.18; N, 11.04; Cl, 20.96; M. W. (for 3^{35}Cl), 506. Found: C, 64.07; H, 4.32; N, 10.97; Cl, 20.95; M. W. (mass spec.) 506.

Reaction of 2,2',4,4'-Tetrachloroazobenzene in the Presence of 2,4-Dichloroaniline.

2,2',4,4'-Tetrachloroazobenzene (0.5 g.), 2,4-dichloroaniline (0.75 g.), and ferrous oxalate (2.0 g.) were heated at $240\text{-}280^\circ$ for 40 minutes. The reaction mixture was extracted with boiling benzene, the solvent was distilled and the residue washed with 5% hydrochloric acid; 2,4-dichloroaniline (0.65 g.) was recovered. The material insoluble in the dilute acid was chromatographed on a column of alumina. In addition to the products obtained in the absence of 2,4-dichloroaniline (Table I), elution with light petroleum-benzene (3:1) gave compound A (0.005 g.) (4), m.p. and mixed m.p. $255\text{-}256^\circ$.

Reaction of a Mixture of 4,4'-Diphenylazobenzene and 4,4'-Dichloroazobenzene.

A mixture of 4,4'-dichloroazobenzene (0.68 g.), 4,4'-diphenylazobenzene (0.90 g.), and ferrous oxalate (1.08 g.) was heated at $280\text{-}310^\circ$ for 40 minutes. The products were extracted with benzene and chromatographed on alumina. Elution with light petroleum gave unchanged 4,4'-dichloroazobenzene (0.60 g.). Further elution with a variety of solvents did not lead to good

TABLE II
Reaction Conditions and Product Yields for the Reactions of Azo Compounds with Fused AlCl_3 -NaCl Mixture

Run	Azo Compound (g.)	AlCl_3 -NaCl (g.)	Reaction Time (min.)	Reaction Temp. ($^{\circ}\text{C}$)	Azo Compd. Recovered (g.)	Yield of Phenazine	
						Grams	%
1	4,4'-dichloro- (1.25)	12.4; 2.5	4	230-240	0.32	0.11	11.8
2	4,4'-dichloro- (1.0)	10.0; 2.0	4	100	0.70	—	0
3	4,4'-dichloro- (0.6)	10.0; 2.0	25	100	0.48	—	0
4	azobenzene (0.5)	10.0; 2.0	4	230-240	0.07	0.06 (a)	14.0 (a)
5	4-chloro-4'-phenyl- (0.4)	10 ; 2	5	230-240	0.04	0.002	0.6
6	4,4'-diphenyl- (0.5)	10 ; 2	4	230	—	0.01	2.0
7 (b)	4,4'-diphenyl- (2.3)	5.5; 1.1	3	240	0.15	0.07	3.2

(a) In this case only, the product is a benz[c]innoline, rather than phenazine. (b) The procedure was modified in that the product mixture was heated on a water-bath for 30 min. with concentrated (12M) hydrochloric acid before being chromatographed on alumina. (c) Same eluents as in Table I.

product resolution. The remaining products were therefore washed off the column and resolved by preparative thin layer chromatography on silica gel (1 mm. plate thickness) using benzene containing 1% formic acid as the developer. In this way the following products were detected: 4,4'-diphenylazobenzene (0.40 g.), 4-chloro-4'-phenylazobenzene (R_f 0.93, quantity too small to permit isolation), *p*-chloroaniline (R_f 0.20, quantity too small to permit isolation), 4-aminobiphenyl (R_f 0.09, quantity too small to permit isolation), 2,7-dichlorophenazine (0.06 g.) R_f 0.13, m.p. 268-269 $^{\circ}$, 2-chloro-7-phenylphenazine (1 mg.), R_f 0.12, m.p. 184-186 $^{\circ}$ [reported (10) m.p. 186 $^{\circ}$], and 2,7-diphenylphenazine (0.12 g.), R_f 0.05, m.p. 271-272 $^{\circ}$. All melting points of isolated compounds were undepressed on admixture with authentic samples.

Reaction of Benzylidene Aniline.

Benzylidene aniline (5 g.), ferrous oxalate (10 g.) and lead shot (10 g.) were heated at 260 $^{\circ}$ for 30 minutes and then at 290-300 $^{\circ}$ for 150 minutes. The reaction mixture was continuously extracted with benzene, the solvent was distilled, and the residue chromatographed on alumina. Elution with light petroleum-benzene (4:1) gave a mixture (1.0 g.) of unreacted benzylidene aniline and benzaldehyde. Light petroleum benzene (1:3) gave aniline (0.06 g.). Ether eluted 4,4'-diaminotriphenylmethane (0.4 g.), m.p. 139-140 $^{\circ}$, undepressed on admixture with an authentic sample (11) and acridine (0.005 g.), m.p. 108-109 $^{\circ}$, which were resolved by preparative TLC on 1 mm. silica gel plates using benzene-ethyl acetate (1:1).

B. Reaction of Azoxy Compounds with Ferrous Oxalate.

Reaction of 4,4'-Dichloroazoxybenzene.

4,4'-Dichloroazoxybenzene (1.24 g.) was heated with ferrous oxalate (1.28 g.) at 260-265 $^{\circ}$ for 55 minutes. The reaction mixture was worked up and chromatographed as usual. Elution with light petroleum-benzene (4:1) gave 4,4'-dichloroazobenzene (0.80 g.). Unreacted azoxy compound (0.01 g.) was eluted with light petroleum-benzene (3:1). 2,7-Dichlorophenazine (0.01 g.), m.p. 266-267.5 $^{\circ}$, was eluted with light petroleum-benzene (2:1).

Reaction of Azoxybenzene.

Azoxybenzene (2.0 g.) was heated with ferrous oxalate (2.2 g.) at 220-235 $^{\circ}$ for 25 minutes and the reaction mixture worked up. Elution of the alumina with light petroleum gave azobenzene (1.10 g.), m.p. 65-66 $^{\circ}$. Elution with light petroleum-benzene (4:1) gave unreacted azoxybenzene (0.52 g.). 2-Hydroxyazobenzene (0.03 g.), m.p. 82 $^{\circ}$, undepressed on admixture with an authentic sample (15), was eluted with light petroleum-benzene (1:2). Elution with light petroleum-benzene (1:1) gave phenazine (0.003 g.), m.p. 170 $^{\circ}$, undepressed on admixture with an authentic sample.

C. Reaction of Azo Compounds with Fused Aluminum Chloride-Sodium Chloride Mixture.

Reaction of 4,4'-Dichloroazobenzene.

Aluminum chloride (12.5 g.) and sodium chloride (2.5 g.) were mixed and heated to 150 $^{\circ}$. 4,4'-Dichloroazobenzene (1.25 g.) was added in portions and the temperature then raised to 230-240 $^{\circ}$ rapidly and held there for 4 minutes. Crushed ice was added to the cooled reaction mixture followed by 5% hydrochloric acid (10 ml.). The mixture was filtered and the residue chromatographed on a column of alumina. Unreacted azo-compound (0.32 g.) was recovered by elution with light petroleum. Elution with petroleum ether-benzene (4:1) afforded 2,7-dichlorophenazine (0.11 g.), m.p. and mixed m.p. 263.5-264.5 $^{\circ}$.

The reaction conditions and product yields for other reactions in this series are summarized in Table II.

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