The Acid-Catalyzed Nitramine Rearrangement. VI. Diversion of the Rearrangement[1-3]

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The aromatic nitramine rearrangement produced lowered yields of nitroanilines and more aromatic amine and nitrous acid in the presence of a variety of reducing agents (iodide and thiocyanate ions, sulfur dioxide, thiourea, aromatic amines, and phenols). The rate was not affected by the presence of the reductant, indicating that diversion of the reaction occurs after the rate-determining step. The effect of the concentration of the diverting agent was unusual and can be interpreted by a mechanism in which the protonated nitramine undergoes N-N bond cleavage to produce a pair of caged radicals which can rebond to form precursors of the nitrated products or can undergo reversible dissociation to free radicals capable of being reduced.

It was recognized very early in the study of the aromatic nitramine rearrangement that, under certain conditions, a portion of the nitramine could be diverted from the isomerization pathway. For example, although N-nitro-2,4-dichloroaniline was converted principally into 2-nitro-4,6-dichloroaniline by nitric, sulfuric, hydrochloric, or perchloric acid,[4] a quantitative yield of 2,4-dichlorobenzenediazonium bromide was formed in the presence of hydrobromic acid.[5] The product of reaction of N-2,4-trinitro-N-methylaniline with concentrated sulfuric acid was 2,4,6-trinitro-N-methylaniline unless *p*-xylene was added to the reaction mixture. In the latter instance, 2,4-dinitro-N-methylaniline resulted.[6] Seldom does the rearrangement of a nitramine produce a quantitative yield of nitroaniline. The systematic study of the effect of apparently extraneous substances on the course of nitramine rearrangement reported in this paper leads to important conclusions about the course of the reaction.

Results and Discussion

Nature of Diverting Agents.—A cursory survey of the influence of various compounds on the course of the rearrangement of N-nitro-N-methylaniline was made. This was accomplished by comparison of the absorbances of the product mixtures from reactions to which various concentrations of different reagents had been added. The absorbance at 410 mμ was utilized for the comparison, since the maximum absorption of the combined nitroaniline products (and also of *p*-nitro-N-methylaniline) occurs at this point. The results are summarized in Table I.

TABLE I

EFFECTS OF ADDED SUBSTANCES ON THE YIELDS OF REARRANGEMENT PRODUCTS FROM N-NITRO-N-METHYLANILINE[a]

Substance	M	A^b	Substance	*M*	A^b
None	. . .	0.642	Sulfamic acid	0.5	0.644
$LiClO_4$	2.0	0.665	Thiourea	0.05	0.436
$LiNO_3$	1.0	0.660	*N*-Methylaniline	0.01	0.533
LiCl	1.0	0.659	*p*-Toluidine	0.01	0.526
LiBr	1.0	0.622	Phenol	0.01	0.558
NaSCN	1.0	0.475	*p*-Cresol	0.005	0.507
NaI	0.01	0.417	2,4-Xylenol	0.005	0.488
$NaHSO_3$	0.05	0.468	Resorcinol	0.05	0.475
SO_2	0.5	0.475	1-Naphthol	0.001	0.443
H_3PO_2	0.03	0.616	Hydroquinone	0.001	0.430

[a] $HClO_4$ = 0.503 *M*, T = 40.0°. [b] Absorbance of reaction mixture after treatment with ammonium sulfamate and dilution with acetate buffer.

The data in Table I indicate that the lowered yields of nitroanilines cannot be associated with the nucleophilicity of the added substance. Thus, bromide ion, which is a good nucleophile, was much less effective in diverting rearrangement than was *p*-cresol, which is a poor nucleophile. The ability of a reagent to scavenge nitrous acid also seems insignificant as a determinant. Thus the effect of sulfamic acid, which reacts selectively and readily with nitrous acid, was much different from that of iodide ion or phenol. The single common feature of the reagents that were effective in diverting the nitramine rearrangement is that they are easily oxidized, *i.e.*, they are reducing agents.

Products of the Diverted Reaction.—Quantitative determination of the products formed in the presence of diverting agents proves that reduction occurs. The proportions of N-methylaniline and nitrite ion were increased, while the amounts of *o*- and *p*-nitro-N-methylaniline decreased (Table II). Nitrite ion and N-methylaniline involve a lower oxidation state for the nitrogen atoms than do N-nitro-N-methylaniline or *o*- or *p*-nitro-N-methylaniline.

TABLE II

PRODUCTS OF REARRANGEMENT OF N-NITRO-N-METHYLANILINE[a] IN THE PRESENCE OF DIVERTING AGENTS (PER CENT YIELD)

	Diverting agent			
Product	None	*p*-HO-$C_6H_4OH^b$	α-$C_{10}H_7OH^c$	NaI^d
o-Nitro-N-methylaniline	49	38	39	. . .
p-Nitro-N-methylaniline	32	18	18	. . .
N-Methylaniline	10	41	40	43
Nitrite ion	13	41	. . .	. . .

[a] $HClO_4$ = 0.503 *M*, *T* = 40.0°. [b] 0.001 *M* hydroquinone. [c] 0.001 *M* α-naphthol. [d] 0.01 *M* NaI.

Influence of Diverting Agents on Rates.—The formation of aromatic amine and nitrous acid could occur

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(1) Previous papers in this series: (a) W. N. White, D. Lazdins, and H. S. White, *J. Amer. Chem. Soc.*, **86**, 1517 (1964); (b) W. N. White, C. Hathaway, and D. Huston, *J. Org. Chem.*, **35**, 737 (1970); (c) W. N. White and J. R. Klink, *ibid.*, **35**, 965 (1970); (d) W. N. White, J. T. Golden, and D. Lazdins, *ibid.*, **35**, 2048 (1970).

(2) Part of this work has been reported in a preliminary form: W. N. White, J. R. Klink, D. Lazdins, C. Hathaway, J. T. Golden, and H. S. White, *J. Amer. Chem. Soc.*, **83**, 2024 (1961).

(3) This work was supported by Grants G-7345 and GP-1970 from the National Science Foundation.

(4) K. J. P. Orton, *Chem. News*, **106**, 236 (1912).

(5) K. J. P. Orton, *Brit. Assoc. Advan. Sci. Rep.*, 115 (1908).

(6) E. D. Hughes and G. T. Jones, *J. Chem. Soc.*, 2678 (1950).

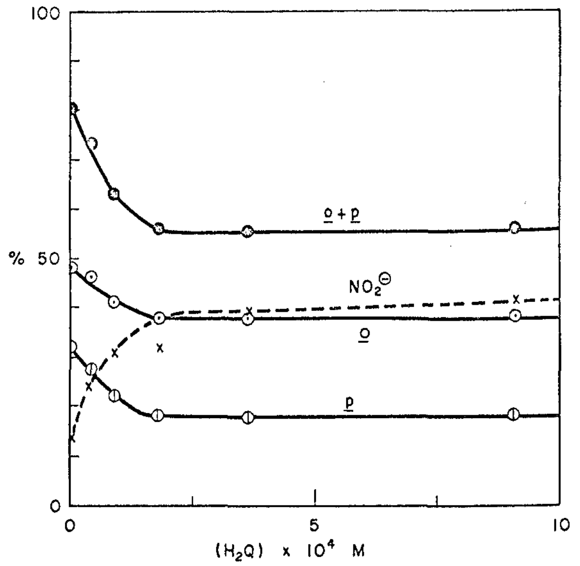

Figure 1.—Percentages of *o*- and *p*-nitro-N-methylaniline and nitrite ion formed in the rearrangement of N-nitro-N-methylaniline in the presence of varying amounts of hydroquinone (H_2Q) (40°, 0.503 *M* $HClO_4$): ⊙, per cent of *o*-nitro-N-methylaniline; ⦶, per cent of *p*-nitro-N-methylaniline; ●, sum of percentages of *o*- and *p*-nitro-N-methylaniline; and ×, per cent of nitrite ion.

through direct reduction of the nitramine by the diverting agent. In such a case there would be two kinetic pathways for disappearance of the nitramine (rearrangement and reduction) compared with one (rearrangement) under normal conditions, and thus the reaction should be faster in the presence of diverting reagents. However, it was found that the rate of reaction of N-nitro-N-methylaniline was unaffected by added reducing agents (Table III). This indicates that the incursion of the diverting agent occurs after the rate-determining step, which normally leads to rearrangement. Thus there is a common route and common intermediates for rearrangement and diversion.

Table III
Rate of Rearrangement of N-Nitro-N-methylaniline[a] in the Presence of Diverting Agents

Diverting agent	*M*	10^3k, sec^{-1}
None	...	1.06 ± 0.06
Hydroquinone	0.001	1.00 ± 0.02

[a] $HClO_4$ = 0.503 *M*, *T* = 40.0°.

Effect of the Concentration of Diverting Agent.—The influence of the concentration of the reducing agent on the product composition was very helpful in defining the mechanism of the nitramine rearrangement. As the concentration of hydroquinone was increased from 0 to *ca.* 0.00015 *M*, the percentages of *o*- and *p*-nitro-N-methylaniline formed from N-nitro-N-methylaniline decreased. Thus a bimolecular process involving the diverting agent and the nitramine or an intermediate derived from it was occurring. However, increasing the hydroquinone concentration above 0.00015 *M* caused no further effect on yield. The amount of nitrite ion produced behaved in about the same way except that it first increased before becoming constant at higher reducing agent concentrations. These results are presented graphically in Figure 1.

These findings indicate that the diverting agent is not reacting with the free or protonated nitramine, nor with the intermediate resulting directly from the rate-determining step. Any of these processes would involve direct competition between the pseudo-first-order rearrangement and second-order diversion, so that increasing the concentration of reducing agent should eventually decrease the yields of nitroanilines to zero. The species being reduced must not be on the rearrangement pathway, but must be in equilibrium with an intermediate that is. Furthermore, the kinetic effect of diverting agent (*vide supra*) shows that this latter intermediate is one that is formed after the rate-limiting step.

The situation is reminiscent of that found for the scavenging of α-isobutyronitrile radicals formed in the decomposition of azobisisobutyronitrile,[7] and an analogous interpretation appears appropriate. Substituent-effect studies[1c] suggested that the protonated nitramine undergoes N–N bond cleavage to form an anilinium radical and nitrogen dioxide. These species are undoubtedly held in a solvent cage for a short period of time, during which they may combine to form nitroanilines. Alternatively, dissociation to free radicals may occur. These radicals may reassociate to the caged pair and lead to nitrated products or they may react with a hydrogen donor to yield nitrous acid and amine. Caged species are ordinarily inert to scavengers. As the concentration of reducing agent is increased, more of the dissociated radicals are reduced and fewer return to the solvent cage and produce nitroanilines. Finally, a point is reached at which all of the free radicals formed are being reduced and a further increase in the amount of diversion is not possible. If the rate of rebonding of the caged radicals is similar to the rate of dissociation, then rearrangement and diversion will occur simultaneously and it will be impossible to completely eliminate rearrangement by increasing the reducing agent concentration. The mechanism implied by these findings and considerations is indicated in Chart I.

The nitrated product from rearrangement of N-nitro-N-methylaniline in the presence of 0.00015 *M* or more hydroquinone arises from caged radicals formed directly and entirely from protonated nitramine (Chart I, step 2 followed only by steps 3*o* and 3*p*). The proportion of *o*- and *p*-nitroanilines produced under these conditions is different from that obtained under normal circumstances in the absence of reductant (step 2 followed by steps 3*o*, 3*p*, 4f, and 4r). This implies that the isomer ratio resulting from free-radical reassociation (step 4r followed by steps 3*o* and 3*p*) is different from that derived from the directly formed caged radicals (step 2 followed by steps 3*o* and 3*p*). It is possible to estimate the proportions of isomers formed in each sequence. The results are listed in Table IV and suggest that the "structure" or average configuration of the caged radical pair differs depending on its source (step 2 or step 4r).

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[7] G. S. Hammond, J. N. Sen, and C. E. Boozer, *J. Amer. Chem. Soc.*, **77**, 3244 (1955).

CHART I

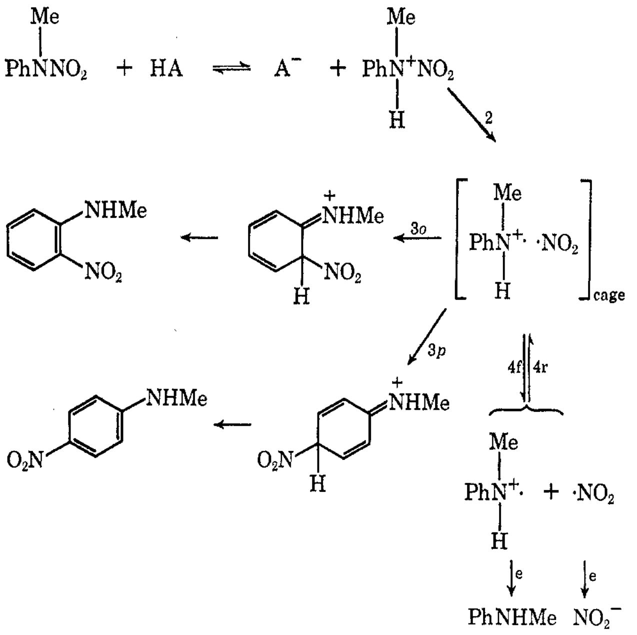

TABLE IV

COMPOSITION OF REARRANGEMENT PRODUCT FROM DIFFERENT MECHANISTIC SEQUENCES (PER CENT YIELD)

Product	Sequence of steps[a] 2 + 3o, 3p	Sequence of steps[a] 4r + 3o, 3p
o-Nitro-N-methylaniline	68	31
p-Nitro-N-methylaniline	32	69

[a] See Chart I.

Since radical reassociation (step 4r) is an equilibrium process, the resulting caged pair probably possesses the lowest energy, most stable average configuration. The product composition in this case is therefore due to the operation of ordinary electronic and steric effects. The much larger amount of *ortho* isomer in the product formed directly from the nitramine (step 2 followed by steps 3*o* and 3*p*) might result if recombination of the radicals is very rapid and occurs before the nitro group has had an opportunity to migrate far from its origin.

The results of this study of the diversion of the aromatic nitramine rearrangement by reducing agents add considerable detail to the mechanism of the isomerization process and support the previously proposed radical mechanism[1c] (Chart I)

Experimental Section

N-Nitro-N-methylaniline.—This compound was prepared by alkaline nitration of aniline followed by methylation of the resulting N-nitroaniline without isolation of the latter substance.[8]

Rearrangement Conditions.—A 2.00-ml aliquot of a solution of N-nitro-N-methylaniline in dioxane was added to a previously thermostatted (40.0 ± 0.5°) solution of 5.00 ml of 5.03 *M* perchloric acid, diverting agent (if present), and *ca.* 40 ml of water in a 50-ml volumetric flask. The contents of the flask were made up to volume with water at 40° and the mixture was shaken and thermostatted at 40.0 ± 0.5° for 60 min. Aliquots of this solution were then analyzed for absorbance at 410 mμ, the percentage of *o*- and *p*-nitro-N-methylaniline present, the nitrous acid content, and/or the amount of N-methylaniline using the following procedures.

Total Absorbance.—A 5.00-ml aliquot of the rearrangement solution was heated with 5.00 ml of 5% ammonium sulfamate solution in a 25-ml volumetric flask at 80° for 30 min. The solution was cooled and acetate buffer (15.0 g of sodium acetate trihydrate, 50.0 ml of water, and 50.0 ml of acetic acid) was added to bring the volume to 25.0 ml. The mixture was shaken and its absorbance at 410 mμ was determined.

Determination of *o*- and *p*-Nitromethylaniline.—Spectrophotometric determination of these components of the reaction mixture was accomplished by the procedure described previously.[1a]

Determination of Nitrous Acid.—Nitrous acid was assayed by a colorimetric method.[1a]

Determination of N-Methylaniline.—^{14}C-labeled nitramine was rearranged as described above. The percentage of N-methylaniline formed was determined by isotope dilution analysis.[1a]

Rates of Rearrangement.—The methods described in previous papers[1b,c] in this series were utilized to determine the kinetic constants for the acid-catalyzed rearrangement of N-nitro-N-methylaniline in the presence and absence of diverting agents.

Registry No.—N-Nitro-N-methylaniline, 7119-93-9.

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(8) W. N. White, E. F. Wolfarth, J. R. Klink, J. Kindig, C. Hathaway, and D. Lazdins, *J. Org. Chem.*, **26**, 4124 (1961).