The Consequences of Ipso Attack in Aromatic Nitration. Studies of the Solvolytic Behavior of 4-Nitro-3,4,5-trimethylcyclohexa-2,5-dienyl Acetate[1]

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Abstract: The cis and trans isomers of 4-nitro-3,4,5-trimethylcyclohexa-2,5-dienyl acetate have been prepared by reaction of 1,2,3-trimethylbenzene with acetyl nitrate. The solvolytic rearomatizations of these crystalline adducts have been studied in solvents ranging from aqueous ethanol to concentrated sulfuric acid. In aqueous ethanol and related solvents, the adducts undergo elimination of the elements of nitrous acid to yield 5-acetoxy-1,2,3-trimethylbenzene at rates that correlate with measures of solvent ionizing power but appear independent of variations in concentration of hydronium ion or undissociated acid. These data together with observed common ion rate depressions and small but varying deuterium isotope effects imply an E1-like mechanism passing through intermediate **8**. In aqueous sulfuric acid solution ranging from 50 to 96%, the adducts react rapidly to yield 5-hydroxy-1,2,3-trimethylbenzene and 4-nitro-1,2,3-trimethylbenzene; the yield of nitration product increases steadily over the 50–70% range and then holds near the quantitative mark. No 5-nitro-1,2,3-trimethylbenzene is detected. The results in strong acid solution are taken as evidence of regeneration of the *ipso*-cyclohexadienyl cation that is formally formed by attachment of NO_2^+ at C_2 of 1,2,3-trimethylbenzene. Hence the fate of the ipso ion may be defined by the solvolytic studies described. Problems of transforming isomer proportion data to positional selectivities and the nature of nitro group migrations are discussed.

Addition frequently precedes formation of substitution products in aromatic electrophilic nitration. The numerous reports, particularly from Fischer's laboratory, describing the isolation of labile adducts of the type shown in Figure 1 seem clear evidence of the assertion.[3,4] These adducts have been obtained by conducting conventional aromatic nitration reactions with the use of acetyl nitrate in acetic anhydride followed by nonsolvolytic isolation procedures. The frequency with which these adducts are uncovered and the yields of these adducts leaves little doubt concerning the importance of the addition process when di- and polyalkylbenzenes, particularly those with 1,2- or 1,4-substitution patterns, are subjected to the nitration conditions described.

Further, the available data indicate that adduct formation in acetic anhydride solvent reflects a phenomenon that is general to many aromatic nitration systems.[5] Formation of adducts during nitration is presumably the result of a sequence that begins with bonding of the electrophile to a ring carbon bearing a substituent group. This position has been termed the ipso position.[6] The *ipso*-cyclohexadienyl cation that forms as a consequence of ipso attack appears to be trapped efficiently in media such as acetic anhydride to yield the adduct. In more acidic, less nucleophilic systems a number of alternative carbonium ion processes may stem from the ipso ion. These include nitro group migrations, ring oxidation, side-chain substitution, and dimerization. Since the extent of ipso ion formation is significant in many systems, studies of the chemistry of these ions have mechanistic as well as synthetic importance.

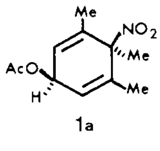
Earlier, we suggested that isolable ipso adducts of acetyl nitrate and alkylbenzenes provided a convenient means to study the chemistry of *ipso*-cyclohexadienyl cations, since the latter could in principle be regenerated by appropriate solvolytic reversion.[7] This approach permits study of the first-formed ipso ion without interference from isomeric cyclohexadienyl cations that are formed concurrently during direct nitration. The initial experimental studies that supported this suggestion have been confirmed and reinforced.[4,8]

The broad outlines of solvolytic chemistry that stem from the ipso adducts or the corresponding ipso ion are known. However, detailed information necessary for precise control and direction of these processes is quite limited. Thus it appeared useful to study a limited number of systems in some depth so that some calibration points could be established. We report here on a study of the solvolytic rearomatizaton reactions of the cis and trans isomers of 4-nitro-3,4,5-trimethylcyclohexa-2,5-dienyl acetate (**1**), an ipso adduct obtained by nitration of 1,2,3-trimethylbenzene.

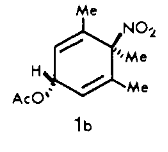
Results

Conventional nitration of 1,2,3-trimethylbenzene with acetyl nitrate in acetic anhydride at 0 °C yields a product mixture containing about 40 mol % dienes. This is easily seen by examination of the ^1H NMR spectrum of the crude reaction mixture, which shows strong vinyl and methine proton bands in addition to absorption bands of the normal nitration products. Two crystalline adducts can be isolated from this reaction mixture if hydrolytic workup is avoided. For reactions of the 0.2-mol scale or less, the solvents and volatile products can be conveniently removed by vacuum evaporation at about 1 Torr or less. The residual oil upon dilution with 1:1 pentane–ether and cooling yields a crystalline crop of the two adducts. Purification can be accomplished by low-temperature fractional crystallization. Additional crystalline product may be recovered from the initial mother liquor by low-temperature chromatography over deactivated alumina.

The spectral and chemical properties of the purified crystalline adducts permit the structure 4-nitro-3,4,5-trimethylcyclohexa-2,5-dienyl acetate (**1**) to be assigned. On the basis of NMR shift reagent studies the higher melting isomer (**1a**) is assigned the cis configuration and the predominant lower melting isomer (**1b**) is assigned the trans configuration.



1a



1b

Both isomers are reasonably stable when pure. The cis isomer is unchanged after a 4-h period of reflux in benzene, although it decomposes in benzene at 120 °C to yield the parent hydrocarbon as a major product with an apparent half-life of 75 min.[9] Both isomers decompose upon attempted gas–liquid

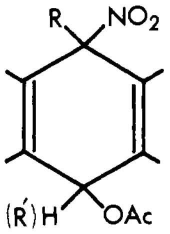


Figure 1. General structure of 1,4 adducts formed upon nitration of alkylbenzenes with acetyl nitrate in acetic anhydride.

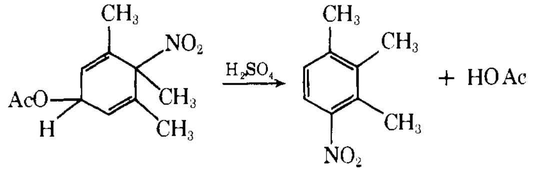
Table I. Solvolysis of **1a**, **1b** and **1a**-d_3 in H_2SO_4 Solutions at 25 °C

Wt % H_2SO_4	% 4-nitro-1,2,3-trimethylbenzene[a] **1a**	**1b**	**1a**-d_3
96.5	98.9		
86.7	96.5	95.0	
76.9	97.2	97.4	
75.0	94.4	95.2	
73.1	90.6	90.8	
68.0	71.2	70.0	72.4
66.0	57.2	56.2	58.0
64.0	41.9	40.5	39.8
62.0	27.0	25.7	
60.0	17.8	15.8	
58.0	10.7	8.9	9.6
56.0	6.4	5.7	
54.0	3.5	3.5	

[a] Calculations based on weighed amounts of adducts and internal standard, *p*-nitrotoluene, and the relative response factors for 4-nitro-1,2,3-trimethylbenzene and the internal standard. Analyses made in at least triplicate. Average std dev was ±0.4%. All std dev are less than ±1.0%. Accuracy is believed to be better than ±2%.

chromatography to yield the parent hydrocarbon and 5-acetoxy-1,2,3-trimethylbenzene as major products.

Both isomers react very rapidly in greater than 75 wt % sulfuric acid at 25 °C to give 4-nitro-1,2,3-trimethylbenzene in essentially quantitative yield.



Careful inspection of chromatographic records reveals no trace of 5-nitro-1,2,3-trimethylbenzene. The yield of the 4-nitro isomer decreases as the sulfuric acid concentration is decreased and becomes negligible below 50 wt %. Yield data accumulated for the solvolysis of **1a**, **1b**, and **1a**-d_3 are presented in Table I and a plot of these data is shown in Figure 2. In addition, studies of the solvolysis of mixtures of **1a** and **1a**-d_3 in 76.9, 64.0, and 56.0% H_2SO_4 revealed no significant change in ratio of labeled to unlabeled nitration product. Normalized intensity ratios for nitration product molecular ions (*m/e* 167:165) were 1.00 (76.9%), 0.99 (64.0%), and 1.01 (56.0%).

When **1a** was solvolyzed in other representative strong acids, the following yields of 4-nitro-1,2,3-trimethylbenzene were obtained: 70 wt % $HClO_4$, 96.7%; trifluoroacetic acid, 90.6%; trifluoromethanesulfonic acid, 98.0%. Again, 5-nitro-1,2,3-trimethylbenzene was not detected as a product in these reactions.

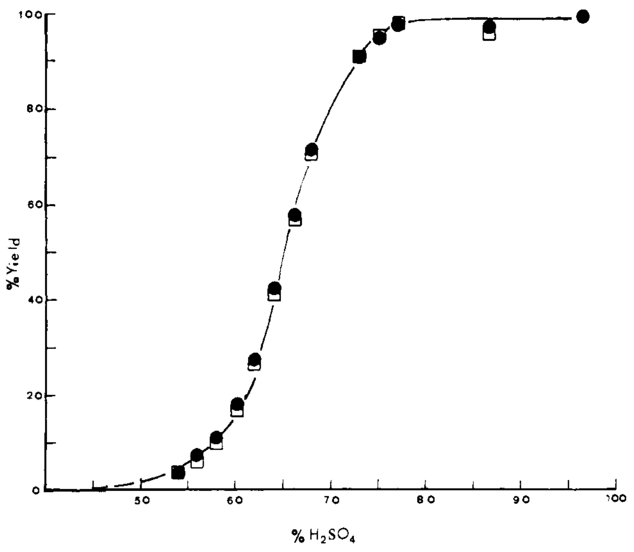


Figure 2. Plot of percent yield of 4-nitro-1,2,3-trimethylbenzene upon reaction of **1a** (●) and **1b** (□) with sulfuric acid solutions of varying strength at room temperature.

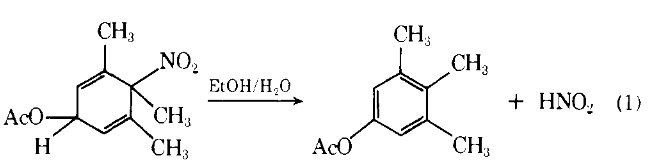
Table II. Solvolysis of **1a** in CH_3NO_2 Containing 96 Wt % H_2SO_4 or 90 Wt % HNO_3[a]

Acid	M	**1a**, M	Rxn time, min	% 4-nitro
H_2SO_4	1.0	1×10^{-2}	30	99
	0.25	4.1×10^{-2}	30	87
	0.10	1×10^{-2}	30	68
	0.10	4×10^{-2}	5	40
	0.10	4×10^{-2}	300	41
HNO_3	2.0	1×10^{-2}	30	84
	1.0	1×10^{-2}	30	60
	0.5	1×10^{-2}	30	33

[a] See footnote *a* of Table I.

An investigation of the solvolytic behavior of the adduct **1a** in nitromethane solutions containing added quantities of 96% sulfuric acid or 90% nitric acid was made. The data shown in Table II reveal that solvolysis is rapid at 25 °C and that quite small molar concentrations of acid are sufficient to direct the reaction toward nitration product.

The solvolytic chemistry of **1** in weakly acidic, aqueous systems is completely different. In aqueous alcohol, aqueous ether, or aqueous acetic acid, **1** solvolyzes to yield 5-acetoxy-1,2,3-trimethylbenzene (eq 1). Rates of this solvolytic elimination of the elements of nitrous acid could be conveniently studied by monitoring the development of the 265-nm band of the product.



Solvolysis of **1a** and **1b** in aqueous ethanol gave clean first-order kinetics over greater than 90% reaction. Reaction rates did not appear to be markedly dependent upon the presence of dilute acids or undissociated acids (see below), but rates increased markedly as the polarity or ionizing power of the solvent increased. Thus, rates of solvolysis increased by about 100-fold upon going from 95% ethanol to 47.5% ethanol. Isomer **1b** solvolyzed about four times more rapidly throughout the solvent range studied. Kinetic data and some derived activation parameters for solvolysis of **1a**, **1b**, **1a**-d_3, and **1b**-d_3 are collected in Table III. It is noted that the more rapid solvolytic elimination of **1b** is due largely to an activation entropy

Table III. Rates of Solvolysis of **1** in Aqueous Ethanol

No.	% EtOH	Temp, °C	$10^4 k$, s^{-1}	
			1a	
1	47.5	11.0	1.16 ± 0.04	
2	47.5	25.0	5.87 ± 0.09	$\Delta H^{\ddagger}_{298}$ = 18.8 ± 0.5 kcal
3	47.5	30.0	10.05 ± 0.15	$\Delta S^{\ddagger}_{298}$ = −10.3 ± 1.8 eu
4	47.5	40.0	27.5 ± 1.0	
5	57	40.0	13.2 ± 0.8	
6	66.5	40.0	6.25 ± 0.5	
7	76	30.0	0.81 ± 0.02	
8	76	40.0	2.82 ± 0.03	
9	95	40.0	0.283 ± 0.006	
			1a-d_3	k_H/k_D
10	47.5	30.0	8.05 ± 0.2	1.25 ± 0.04
11	47.5	40.0	23.5 ± 1.8	1.17 ± 0.13
			1b	
12	38	25.0	46.4	
13	47.5	10.0	3.79 ± 0.09	
14	47.5	25.0	23.8 ± 1.3	$H^{\ddagger}_{298}$ = 20.1 ± 0.5 kal
15	47.5	30.0	42.5 ± 0.3	$S^{\ddagger}_{298}$ = −3.1 ± 1.8 eu
16	57	25.0	9.76 ± 0.3	
17	95	25.0	0.229 ± 0.018	
			1b-d_3	k_H/k_D
18	47.5	25.0	20.5 ± 0.3	1.16 ± 0.07

Table IV. Salt Effects in Solvolysis of **1a** and **1a**-d_3 in Aqueous Ethanol[a]

No.	Temp, °C	Added salt	$10^4 k$, s^{-1}	k_H/k_D
		1a		
19	25	$NaClO_4$, 0.1M	6.50 ± 0.06	
20	25	$NaClO_4$, 0.2 M	7.52 ± 0.06	
21	25	$NaClO_4$, 0.5 M	9.58 ± 0.15	
22	25	$NaNO_2$, 0.1 M	2.93 ± 0.25	
23	25	$NaNO_2$, 0.2 M	3.54 ± 0.30	
24	30	$NaClO_4$, 0.2 M	13.89 ± 0.20	
25	30	$NaNO_2$, 0.2 M	5.6 ± 0.5	
26	40	$NaClO_4$, 0.1 M	31.5 ± 0.8	
27	40	$NaNO_2$, 0.1 M	12.7 ± 1.2	
		1a-d_3		
28	25	$NaNO_2$, 0.2 M	2.58 ± 0.10	1.37 ± 0.13
29	30	$NaClO_4$, 0.2 M	11.95 ± 0.15	1.16 ± 0.02
30	30	$NaNO_2$, 0.2 M	4.3 ± 0.5	1.3 ± 0.2
40	40	$NaNO_2$, 0.1 M	8.66 ± 0.64	1.45 ± 0.14

[a] Composition was 47.5% ethanol in all runs.

that is significantly less negative for **1b** than for **1a**.

A limited study of salt effects on rates of solvolysis of **1a** and **1a**-d_3 in aqueous ethanol was made. The data are collected in Table IV. A positive salt effect was observed upon addition of sodium perchlorate. By contrast, rate depressions are observed upon addition of sodium nitrite. Unfortunately, the quality of the kinetic data that can be obtained in aqueous ethanol with added nitrite ion is limited. The fairly strong absorption bands of nitrite ion in the spectral region observed limit the accuracy of absorbance measurements. More critical, however, are drifting infinite time absorbance values and deviations from first-order kinetics observed under these conditions. Despite the kinetic limitations, the rate depressions and apparent increase in kinetic isotope effect observed with added sodium nitrite seemed sufficiently convincing to warrant a further search for evidence of external return.

A solvolysis of **1a** was conducted in 47.5% ethanol containing added sodium nitrite-^{15}N, 0.1 M. After 1.5 half-lives the reaction mixture was treated with excess cold 80% H_2SO_4 and the resulting 4-nitro-1,2,3-trimethylbenzene was analyzed for nitrogen-15 incorporation by mass spectrometry. The data indicated only 4 ± 2% nitrogen-15 incorporation; poor precision was due to interferences of other components in the product mixture. An alternative approach involved use of **1a**-^{15}N, that had been prepared from nitric acid-^{15}N, and $Na^{14}NO_2$. Solvolysis of the labeled compound was carried out for periods of about 1 and 2 half-lives. The organic products were isolated and the unconsumed diene was solvolyzed in 80% H_2SO_4. The resulting 4-nitro-1,2,3-trimethylbenzene-^{15}N was analyzed for nitrogen-14 incorporation. The results as shown in the Experimental Section indicated a rather small but progressive increase in the nitrogen-14 content of the reactant during the reaction.

Controls of the isomeric integrity of **1a** and **1b** during solvolysis were made by deliberately mixing the isomers and conducting kinetic measurements in 50% ethanol with the mixture. Rate constants and compositions extracted from these data by standard techniques compared well with rate data obtained from pure substances. In addition, large-scale kinetic runs were conducted with **1a**. The unconsumed reactant was isolated after 1 half-life and carefully examined by NMR. Only unconsumed **1a** and 5-acetoxy-1,2,3-trimethylbenzene product could be detected. There was no evidence for contamination by **1b** or the presence of other species.

Rates of solvolysis of **1a** in aqueous acetic acid were also examined. NMR studies of solvolysis of **1a** in acetic-d_3 acid-d_1 and chloroform-d gave no indication of products other than 5-acetoxy-1,2,3-trimethylbenzene, nor were transient intermediates detected. However, first-order rate plots of **1a** in acetic acid solutions gave two distinct slopes; the faster first section spanned slightly more than 1 half-life. A tabulation of these initial rates of solvolysis is collected in Table V. Control studies conducted with sodium nitrite, 5-acetoxy-1,2,3-trimethylbenzene, and mixtures thereof suggest that at least part of the kinetic problem in aqueous acetic acid is associated with

Table V. Initial Rates of Solvolysis of **1a** in Aqueous Acetic Acid at 25 °C

Vol % HOAc	$10^4 k$, s^{-1} [a,b]	Vol % HOAc	$10^4 k$, s^{-1} [a,b]
25	31.1 ± 10	60	3.7 ± 0.7
40	9.6 ± 2.8	70	2.4 ± 0.8
50	6.4 ± 1.0	100	0.85 ± 0.24

[a] Initial rates were determined by computer adjustment of the infinity value to give the best fit to absorbance values spanning the first half-life. [b] Error estimates represent the standard deviation of six or more runs.

further reaction of these products at the concentrations used in these kinetic studies.

A very few kinetic runs were also made in aqueous dioxane solutions. Kinetics were well behaved in these mixtures. At 25 °C, **1a** solvolyzed in 50% dioxane with a rate constant of $1.62 \times 10^{-4} \pm 0.04$ s^{-1}.

Initial studies of the products of strong acid solvolysis of **1** focused on the yield of 4-nitro-1,2,3-trimethylbenzene and only passing attention was given to the essential absence of any other products in the chromatographic record. Later, however, it was determined that 5-acetoxy-1,2,3-trimethylbenzene was relatively stable under simulated reaction conditions with recovery ranging from greater than 90% in 54% H_2SO_4 to 50% in 73% H_2SO_4 after a 1-h reaction period. When the extraction procedure was modified to eliminate the strong base wash, the combined yield of recovered 5-acetoxy- and 5-hydroxy-1,2,3-trimethylbenzene from these control studies was close to quantitative. However, solvolysis of **1a** under these conditions gave, at best, trace indications of the phenol or the acetate derivative. It was found that addition of sodium nitrite to 50% H_2SO_4 solutions of 5-hydroxy-1,2,3-trimethylbenzene led to its complete disappearance and the formation of a mixture of products with very long retention times. 5-Acetoxy-1,2,3-trimethylbenzene was stable under these conditions and could be recovered in good yield. Finally, it was observed that solvolysis of **1a** in 52% H_2SO_4 containing added urea led to an increase in the yield of phenol product, but even at a concentration of 5 M urea, the yield of recovered phenol was not quantitative.

Discussion

A sizable body of qualitative and semiquantitative data supports the view that the solvolytic chemistry of dienes such as **1a** and **1b** is directly relevant to the course of aromatic nitration of the parent arene. Studies reported here permit somewhat more refined discussions of reactivity and mechanism of solvolytic pathways.

Paths of Solvolytic Rearomatization. Two major paths of solvolytic rearomatization of **1a** and **1b** are observed. One path, operative in strong acid media, yields a *single* nitration product, 4-nitro-1,2,3-trimethylbenzene. The second path, dominant in aqueous or mildly acidic media, yields a single ring oxidation product, 5-acetoxy-1,2,3-trimethylbenzene or the related phenol. These results are taken to imply a branch point in the solvolytic scheme that occurs at an early stage. The dienes **1a** and **1b** contain two leaving groups, nitrite and acetate. The conditions of solvolytic rearomatization apparently determine the rates at which these competing leaving groups depart and hence determine the product ratio.

Independent of mechanistic detail, departure of the nitro group as nitrite from the nitro, acetoxy adduct dominates at low acidity while departure of acetate (presumably as acetic acid) dominates in strong acid media. A primitive scheme that accounts for these observations is shown in Chart I, where it is assumed that protonation of the acetate function in strong acid is the step that activates departure of the acetate function as acetic acid. The observation that significant yields of nitration product are obtained from **1a** or **1b** in H_2SO_4 solutions whose H_0 values approach the pK_a of conjugate acids of typical acetate esters seems to qualitatively support this assumption.

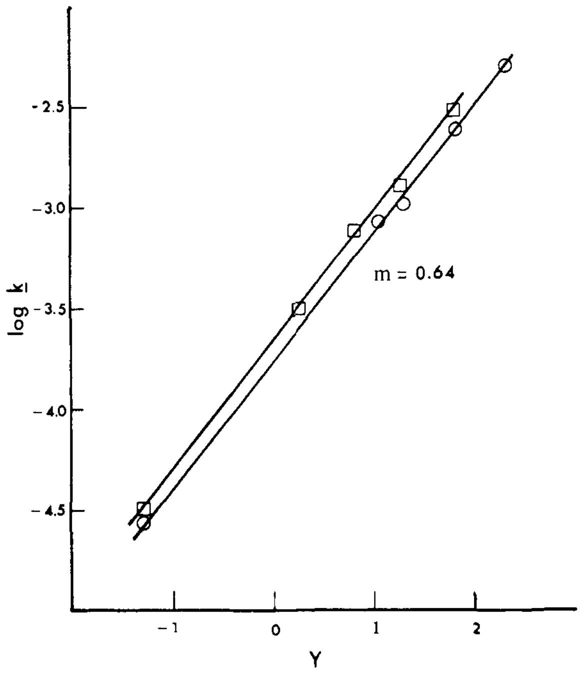
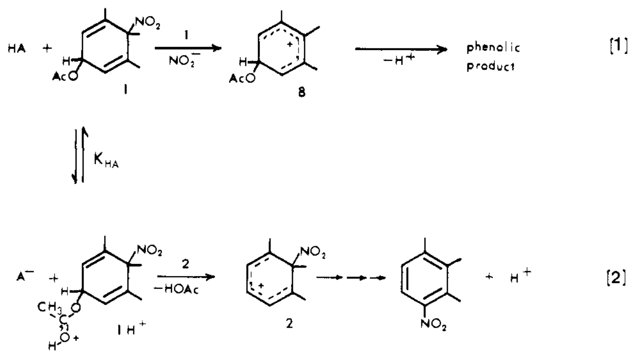


Figure 3. Plot of log k_{obsd} for solvolytic rearomatization of **1a** at 40.0 °C (□) and **1b** at 25.0 °C (○) vs. the Grunwald-Winstein Y parameter.

Chart I



Elimination of Nitrous Acid. The formation of ring oxidation product via path 1 of Chart I has been interpreted as a concerted elimination requiring acid catalysis.[3] Data reported here do not appear consistent with such an assignment. The salient points are these: (1) Rates of formation of 5-acetoxy-1,2,3-trimethylbenzene from **1a** or **1b** correlate with measures of solvent polarity or ionizing power but do not appear to be strongly dependent upon increasing hydrogen ion concentration or the presence of undissociated weak acids. Rates can be predicted on the basis of Y values. For example, from the slope of plots of log k_{obsd} for solvolysis of **1a** and **1b** in aqueous ethanol as shown in Figure 3 and data presented in Table III, one predicts k_{obsd} values for solvolysis in 25, 40, 50, and 60% HOAc at 25 °C to be 26×10^{-4}, 12×10^{-4}, 7.0×10^{-4}, and 3.8×10^{-4} s^{-1}. One finds (Table V) 31×10^{-4}, 9.6×10^{-4}, 6.4×10^{-4}, and 3.7×10^{-4} s^{-1}. (2) Deuterium isotope effects appear too small to be associated with major changes in the force constants of the ring carbon-hydrogen bond in the rate-limiting step. The moderate increase in isotope effect with increases in nitrite ion concentration is also more indicative of a stepwise

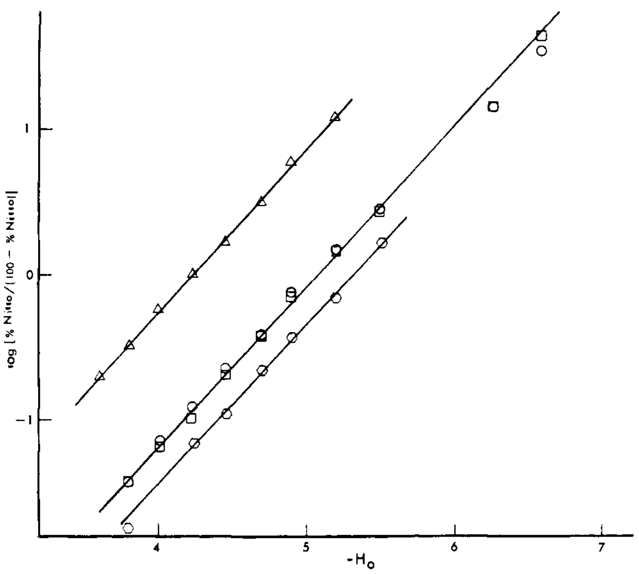


Figure 4. Plots of log [% nitration product/(100 − % nitration product)] vs. $-H_0$ for adducts of *p*-xylene-d_6 (△), **1a** (○), **1b** (□), *o*-xylene (○).

elimination with an increase in return rate relative to proton loss. (3) Common ion rate depression and return data are more consistent with a two-step E1-like elimination of the elements of nitrous acid. Thus, path 1 of Chart I is shown passing through intermediate **8**.

Elimination of Acetic Acid. Solvolysis rates in strong acids are too fast for measurement techniques at our disposal. While rates have not been measured in strongly acidic media, relative rates of formation of nitration product and ring oxidation product may be adduced from yield data collected at various acid concentrations. The data in Table I and Figure 2 indicate a well-behaved transition from predominant formation of nitration product at high acidities to predominant formation of ring oxidation product at low acidities. The point of equapartitioning occurs at about 65% H_2SO_4.

It is not difficult to transform the S-shaped plot of the yield data, Figure 2, into a linear plot that appears relevant to the scheme shown in Chart I. The simplest assumptions that might be made are that steps 1 and 2 control the rates of formation of ring oxidation and nitration product, respectively. This leads directly to the equation

$$\frac{\%\ \text{4-nitro}}{100 - \%\ \text{4-nitro}} = \frac{k_2 a_{1H^+} f_1^{\ddagger}}{k_1 a_1 f_{1H^+}^{\ddagger}} = \frac{1}{K_{HA}} \frac{k_2}{k_1} a_{H^+} \frac{f_1^{\ddagger}}{f_{1H^+}^{\ddagger}} \quad (2)$$

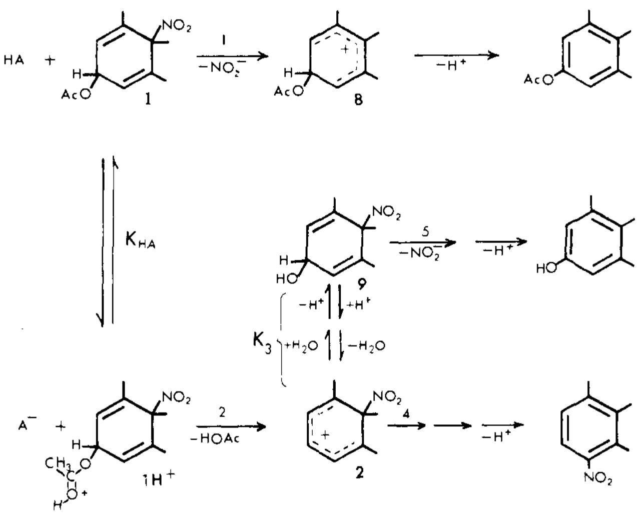
If it is further assumed that **1** behaves as a Hammett base and that activity coefficient terms cancel, eq 2 may be expressed in the familiar form

$$\log\left[\frac{\%\ \text{4-nitro}}{100 - \%\ \text{4-nitro}}\right] = -H_0 + \log\left(\frac{1}{K_{HA}}\frac{k_2}{k_1}\right) \quad (3)$$

Plots of the data collected for **1a** and **1b** in the form shown in eq 3 are found in Figure 4 together with similar plots obtained from studies of related systems.[10] It is to be noted that (1) quite good correlation lines are found, (2) the treatment appears applicable to several related systems, (3) slopes of the correlation lines are rather close to unity.

For several reasons, however, this treatment does not seem to be correct. Most important are two experimental observations. First, the yield data for both **1a** and **1b** are identical within estimated errors. Yet we know that in aqueous ethanol **1b** suffers loss of NO_2^- about four times faster than does **1a**. It seems reasonable that this rate difference would be maintained in aqueous acid solvents. Thus the partitioning scheme shown in Chart I might imply a significantly lower yield of 4-nitro-1,2,3-trimethylbenzene from **1b** than from **1a** in the 55–70% H_2SO_4 range.[11] Such an effect is not seen. Second, the scheme in Chart I implies that 5-acetoxy-1,2,3-trimethylbenzene is the first-formed product of solvolytic elimination of nitrous acid, yet no more than a trace of this product is seen in any of the chromatographic records, even under conditions where phenyl acetate would survive reaction and workup conditions without substantial loss. 5-Hydroxy-1,2,3-trimethylbenzene can, however, be detected, but only if urea is added to suppress its reaction with nitrous acid.

Chart II



Clearly, the reaction scheme requires modification to accommodate these observations. If dienes **1a** and **1b** were rapidly converted via the ipso ion (**2**) to the isomeric dienols (**9a** and **9b**), stereochemical distinctions would be lost and the ring oxidation product would be the phenol, not the corresponding acetate ester. This modified reaction scheme is shown in Chart II, where it is assumed that the rate of step 1 in 50–75% H_2SO_4 is much slower than the rate of the sequence leading to ion **2**.[20]

Should the scheme shown in Chart II give a correlation such as that observed (see eq 3 and Figure 4)? By analogy with the previous treatment, if the product distribution is controlled by two rate constants, k_4 and k_5, and a carbinol equilibrium constant, K_3, the logarithm of the product ratio can be set equal to the terms shown in eq 4. As before, cancellation of activity coefficient terms has been assumed.

$$\log\left[\frac{\%\ \text{4-nitro}}{100 - \%\ \text{4-nitro}}\right] = -H_R + \log\left(\frac{1}{K_3}\frac{k_4}{k_5}\right) \quad (4)$$

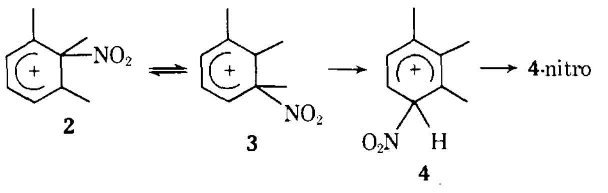
The acidity function appropriate for carbinol ionization equilibria, H_R, proves to be nearly twice the value of the corresponding Hammett acidity function, H_0, in the acid region under discussion.[12] Only the apparent slopes of the plots would change if plotted against this function. Numerous reasons and precedents exist that may account for the deviations of the correlation line slopes from those predicted under conventional assumptions. More detailed information concerning several features of this scheme is required before many of these explanations can be tested.[13] At present, it appears best to summarize by stating that experimental results strongly indicate that solvolytic rearomatization of **1a** and **1b** in strong acid solutions begins with the loss of the acetate function to form the ipso ion **2**. This process is constrained by the data to be faster than direct loss of the nitro group as nitrite ion, since no phenyl acetate product is found in the acid media studied.[20] An interesting and apparently general correlation between the product distribution and the Hammett acidity function has been found, but the underlying significance of this correlation requires further study.

Ipso Ions and Measures of Positional Selectivity in Nitration. The solvolytic data do support the suggestion made previously that adducts such as **1a** and **1b** may be used to regenerate the ipso ion under many conditions that simulate those used in aromatic nitration.[7] Thus it is possible to define the fate of **2** when it is formed during nitration. It should be clear from the data presented in Tables I and II that measurements of the isomer distribution in nitration of 1,2,3-trimethylbenzene in many acidic systems will not yield measures of positional selectivity. The fraction of 4-nitro-1,2,3-trimethylbenzene found is a composite reflecting rates of electrophilic attack at two ipso positions (C_1 and C_2) as well as C_4.

Isomer distributions must be correctly apportioned if they are to be used as indicators of positional selectivity. To do this, two quantities must be known: (1) the fraction of reactant that suffers ipso attack at various substituent positions, and (2) the fraction of ipso ions that undergo intramolecular nitro group shifts. The latter quantity is available from studies of the type reported here. The former is available only by extrapolation. One must measure the extent of ipso attack by trapping reactions, such as those nitrations conducted in acetic anhydride, or by material balance studies conducted under conditions that divert all ipso ions formed to products other than nitro group migration products. Next one must assume that these values are not sensitive to changes in the reaction media.

Schofield, Moodie, and co-workers have presented data for nitration of a variety of methylbenzenes that indicate sizable medium effects on isomer proportions.[8] This creates an obvious dilemma. It appears that the existence of medium effects precludes apportioning a given nitration product yield among the various independent paths of formation until the causes of these medium effects are better defined. At present, it is most unwise to attach positional selectivity significance to isomer distributions in a nitration reaction unless one is confident that ipso ion formation is negligible or unless all ipso ions formed are diverted to products other than nitro group migration products.

Intramolecular Nitro Group Shifts. The details of intramolecular migration of a nitro group are of considerable interest. The results reported here could be rationalized as a formal 1,3 shift of a nitro group. However, a sequence of 1,2 shifts as shown in eq 5 is the preferred representation. Justification for this preference includes analogy with related systems[4] as well as the following evidence.

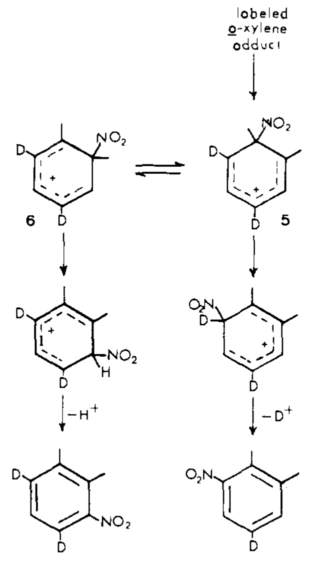


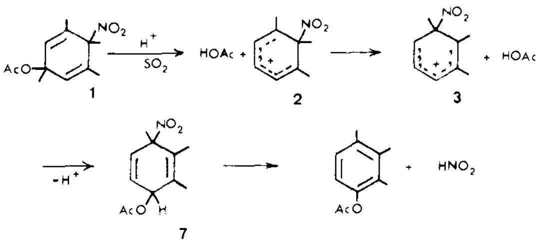
(5)

Labeling studies demonstrate that the ipso ion derived from *o*-xylene undergoes a *formal* 1,3 shift to yield *only* 3-nitro-*o*-xylene at rates that are comparable to the 1,2 shift that also yields 3-nitro-*o*-xylene.[21] These results seem explicable only in terms of a sequence of 1,2 shifts and rapid equilibration of the isotopically isomeric ions **5** and **6**, Chart III.

Solution of **1a** in liquid sulfur dioxide containing adventitious amounts of H_2SO_4 led to rapid decomposition and formation of about 50% 4-nitro-1,2,3-trimethylbenzene, 5% 5-acetoxy-1,2,3-trimethylbenzene, and 45% 4-acetoxy-1,2,3-trimethylbenzene. We interpret this unusual result to indicate trapping of the isomeric ipso ion under the reaction conditions and subsequent rearomatization of the isomeric adduct to yield the 4-acetoxy product, eq 6.

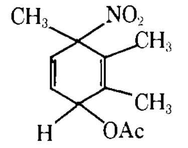
Chart III





(6)

The rapid interconversions of ipso ions by 1,2 shifts of the nitro group may have other implications. It is possible that some fraction of ipso ions trapped as adduct are not first-formed. Thus our failure to isolate or detect isomeric adduct **7** in nitration reaction mixtures may reflect one or a combination of two factors: (1) rapid conversion of the less stable ion, **3**, to **2** with subsequent trapping to yield **1**, (2) relatively fast rate of elimination of the elements of nitrous acid to yield rearomatized product. Evidence available does not permit a clear decision.[14] We hope that studies in progress will provide a more definitive answer.



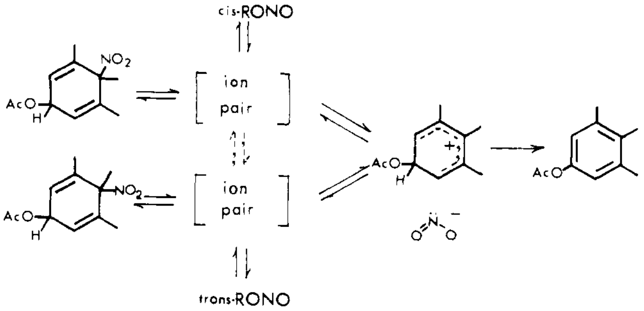
7

It should be noted, however, that variations in rate of elimination of nitrous acid with structure of the adduct, as inferred from stability data, are consistent with the two-step process passing through ionic intermediates analogous to **8**, Chart I.[15] On a more modest scale of structural change, the adducts of *o*-xylene and *p*-xylene exhibit somewhat slower rates of nitrous acid elimination than do the corresponding adducts of 1,2,3-trimethylbenzene, again as expected.

External Return and Common Ion Rate Depressions. Large common ion rate depressions but very small rates of external return serve to illustrate the complexity of a superficially straightforward solvolytic elimination of nitrous acid in aqueous ethanol. At the 0.2 M salt level, a common ion depresses the rate of phenyl acetate formation from reactant **1a** by a factor of about 4. This indicates appreciable return, and this return should be easily measured by appropriate labeling studies. However, measurement of the extent of return, Table VI, by this latter technique indicated that it is quite small. With the use of the simplest model, eq 7

$$\mathbf{1a} \underset{-1}{\overset{1}{\rightleftharpoons}} \mathbf{8} + NO_2^- \xrightarrow{2} H^+ + ArOAc \qquad (7)$$

Chart IV



the ratio k_{-1}/k_2 is estimated to be about 15:1 on the basis of rate depression data but only about 0.1:1 on the basis of nitrogen-15 labeling studies. The model is clearly deficient for at least two reasons. First, external return must yield **1b** as well as **1a**. Second, the ambident character of the nitrite ion requires that return would yield nitrite ester adduct as well as adduct **1**. Data from other systems indicate that nitrite ester adduct formation should be the dominant path of return.[16] These factors appear capable of rationalizing the great discrepancy between the two types of return data, This interpretation also accounts for deviations of kinetics from strict, first-order behavior in solutions containing added nitrite ion. But a complex kinetic scheme is necessary to include these factors. The simplest scheme would involve nine rate constants and three intermediates, two of which cannot be treated by steady-state approximations. The admission of ion pairs, Chart IV, increases the kinetic complexity. Present data are not sufficient to test such a scheme, Chart IV, in detail, The nitrite ester derivatives, structural isomers of **1a** and **1b**, do appear to be obligatory intermediates. The solvolytic reactivities of these intermediates must be much greater than those of **1a** and **1b** to escape detection by direct methods.

Summary

The solvolytic chemistry of adduct **1** has been studied in solvents ranging from aqueous ethanol to concentrated sulfuric acid. Two major paths of solvolytic rearomatization have been identified and characterized in some detail. Evidence has been presented which indicates that **1** undergoes solvolysis in greater than 50% sulfuric acid by loss of acetate to yield the ipso ion **2**. This ion is then partitioned along two paths: one leading to oxidation product (5-hydroxy-1,2,3-trimethylbenzene), the other leading to nitro group migrations by sequential 1,2 shift with eventual formation of 4-nitro-1,2,3-trimethylbenzene. A mechanistic model has been developed that relates this partition ratio to two rate constants and carbinol carbonium ion equilibrium constant.

Studies of the solvolytic behavior of **1** in solvent systems commonly used for aromatic nitration—sulfuric acid, nitromethane containing sulfuric acid or nitric acid, trifluoroacetic acid, and trifluoromethanesulfonic acid—leads to the conclusion that the bulk if not all of ipso ion **2** formed by direct nitration would yield nitro group migration product. With the possible exception of acetic anhydride, all commonly used nitration systems yield isomer distributions that cannot be directly transformed into measures of positional selectivity. Implicit in these results are effective synthetic strategies for controlling the proportion of nitration isomers with variation of reaction conditions.

Data indicate that solvolytic rearomatization of **1** in aqueous or weakly acidic systems results in loss of nitrite ion, formation of ion **8**, and eventual proton loss to yield 5-acetoxy-1,2,3-trimethylbenzene. Detailed studies reveal that the mechanistic scheme may be complicated by external return to nitrite ester isomers of **1**. It has been claimed that this elimination of nitrous acid is not relevant to ipso ion reactions in aromatic nitration.[7] We take a different view. Solvolytic elimination of nitrous acid from **1** to form phenyl acetate should be a rather good model reaction for the less accessible elimination from the nitrodienol, **9**. Studies in progress with the nitroacetate and nitrodienol derived from *p*-xylene support this view.

Experimental Section

Instrumentation. All melting points were taken on a Mel-Temp apparatus and are uncorrected. Routine proton nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrometer. Mass spectra were obtained from a Perkin-Elmer Hitachi RMU-6D instrument. Kinetic studies were made with the use of a Varian-Cary 16K spectrometer. Gas-liquid chromatographic analyses were obtained with the use of a Varian 1200 instrument equipped with a flame ionization detector, disk integrator, and printer.

Reference Substances. 4-Nitro-1,2,3-trimethylbenzene, isolated from nitration reactions, was purified by vacuum distillation followed by low-temperature (−20 °C) recrystallization from *n*-pentane: mp 19 °C (lit.[18] 11–12 °C); NMR ($DCCl_3$) δ 2.14 (s, 3 H), 2.23 (s, 6 H), 6.96 (d, 1 H, J_{AB} = 8.3 Hz, 6-H), 7.36 (d, 1 H, J_{AB} = 8.3 Hz, 5-H); mass spectrum (70 eV) *m/e* (rel intensity) 165 (44), 148 (100), 120 (59), 119 (25), 103 (30), 91 (99), 77 (67).

5-Nitro-1,2,3-trimethylbenzene was isolated from tailing fractions of vacuum distilled nitration product and purified by fractional recrystallization from ethanol: mp 66–67 °C (lit.[18] 64–65 °C); NMR ($DCCl_3$) δ 2.23 (s, 3 H), 2.34 (s, 6 H), 7.79 (s, 2 H); mass spectrum (70 eV) *m/e* (rel intensity) 165 (100), 135 (25), 119 (25), 91 (90), 77 (35).

4-Hydroxy-1,2,3-trimethylbenzene was prepared from the hydrocarbon via the sulfonic acid. Reaction of a stirred mixture of 1,2,3-trimethylbenzene (24 g, 0.20 mol) with concentrated sulfuric acid (18 mL, 0.30 mol) at 75 °C gave the sulfonic acid. The crystalline mass that formed on cooling was diluted with water (40 mL), chilled to −20 °C, collected by suction filtration, and triturated with *n*-pentane. The vacuum dried product, 37.2 g (73%), analyzed for 2,3,4-trimethylbenzenesulfonic acid trihydrate by NMR: mp 115–118 °C after recrystallization from ether–pentane; NMR (D_2O) δ 2.05 (s, 3 H), 2.14 (s, 3 H), 2.61 (s, 3 H), 7.00 (d, 1 H, J_{AB} = 8.0 Hz, 5-H), 7.93 (d, 1 H, J_{AB} = 8.0 Hz, 6-H), 5.67 (s, 7 H, hydroxyl). Neutralization of the sulfonic acid with sodium hydroxide and addition of excess sodium chloride gave 28.6 g of the sodium salt after recrystallization. This material was added in one portion to a 250-mL nickel crucible containing 100 g of potassium hydroxide and 4.2 mL of water preheated to 250 °C. The resulting black slurry was stirred and maintained at 300 °C for 30 min, cooled, and carefully neutralized with hydrochloric acid. The solid collected by filtration was steam distilled to yield 8.64 g, mp 75–78 °C. Recrystallization from *n*-hexane gave 7.91 g of 4-hydroxy-1,2,3-trimethylbenzene: mp 79–80 °C (lit.[19] 76–77 °C); NMR ($DDCl_3$) δ 2.09 (s, 3 H), 2.12 (s, 3 H), 2.13 (s, 3 H), 5.79 (s, 1 H, hydroxyl), 6.50 (d, 1 H, J_{AB} = 8.1 Hz, 5-H), 6.77 (d, 1 H, J_{AB} = 8.1 Hz, 6-H).

4-Acetoxy-1,2,3-trimethylbenzene was prepared by acylation of the corresponding phenol with acetic anhydride-pyridine to give a colorless oil: bp 163–165 °C (16 mm); NMR ($DCCl_3$) δ 2.02 (s, 3 H), 2.06 (s, 3 H), 2.14 (s, 3 H, OAc), 6.65 (d, 1 H, J_{AB} = 8 Hz), 7.03 (d, 1 H, J_{AB} = 8 Hz).

5-Hydroxy-1,2,3-trimethylbenzene was isolated from the crude products of nitration of the parent hydrocarbon. The products from nitration of 16 mL (13.3 mmol) of 1,2,3-trimethylbenzene with 7.5 mmol of nitric acid in 50 mL of acetic anhydride were hydrolyzed in 80 mL of water containing 6 g of urea. The resulting brown oil was extracted with cyclohexane, washed with sodium bicarbonate, and dried to yield 17.1 g of crude product. NMR analysis indicated 37% unconsumed hydrocarbon, 5% 5-nitro-, 29% 4-nitro-, 8% 4-acetoxy-, and 21% 5-acetoxy-1,2,3-trimethylbenzene plus a trace of unconverted diene. Saponification with sodium hydroxide in aqueous methanol at 60 °C for 4 h followed by phase separation and acidification of the aqueous layer gave brown, crystalline product that was steam distilled to yield 2.05 g, mp 95–99 °C. Recrystallization from *n*-hexane gave 1.68 g of colorless, fine needles: mp 108 °C (lit. 106.5–107.5 °C); NMR ($DCCl_3$) δ 2.00 (s, 3 H), 2.16 (s, 6 H), 5.73 (s, 1-H), 6.48 (s, 2 H); mass spectrum (70 eV) *m/e* (rel intensity) 136 (75), 135 (26), 121 (100), 91 (20), 77 (14).

5-Acetoxy-1,2,3-trimethylbenzene was prepared by acylation of the phenol (0.722 g) in excess acetic anhydride–pyridine to yield 0.873 g, mp 55–57 °C. Recrystallization gave 0.724 g: mp 57–58 °C (lit. 59 °C); NMR ($DCCl_3$) δ 2.03 (s, 3 H, methyl), 2.23 (s, 9 H, methyl and acetoxyl), 6.82 (s, 2 H); mass spectrum (70 eV) *m/e* (rel intensity) 178 (18), 136 (100), 135 (17), 121 (63), 91 (23), 71 (10).

1,2,3-Trimethylbenzene-*5-d_1*. 4-Nitro-1,2,3-trimethylbenzene (9.6 g, 58 mmol) was reduced in a low-pressure hydrogenation apparatus with Raney nickel in ethanol. The product was isolated as the hydrochloride salt and recrystallized from methanol–ether, 8.51 g (85%), mp 265–270 °C dec. A portion (7.09 g, 41.3 mmol) of the anilinium hydrochloride was refluxed with 10 mL of D_2O for 48 h. The solvent was removed by vacuum evaporation. The equilibration was repeated three times to yield 7.05 g of the deuterated anilinium salt.

A solution of sodium nitrite (2.89 g, 41 mmol) in 10 mL of water was added dropwise (10 min) to a cooled (−5 °C), stirred solution of the labeled aniline salt in 5 mL of water and 15 mL of 30% hydrochloric acid. Twenty minutes later, 60 mL of precooled (−5 °C) hypophosphorous acid was added to the reaction mixture. Stirring was continued for 3 h, and the mixture was allowed to stand overnight at 0 °C. The dark brown oil that separated was collected and the aqueous phase was extracted with three 15-mL portions of *n*-pentane. The combined extracts were washed sequentially with 20% sodium hydroxide and water and then dried over anhydrous potassium carbonate. Distillation afforded 3.62 g (73%) of 1,2,3-trimethylbenzene-*5-d_1*: bp 71–72 °C (16 mm); NMR ($DCCl_3$) δ 1.73 (s, 3 H), 2.07 (s, 6 H), 6.79 (s, 2 H). Mass spectral examination at 10 eV indicated 98.5% deuteration at C-5.

1,2,3-Trimethylbenzene-*4,5,6-d_3*. Four exchanges of the hydrocarbon (24 g, 0.20 mol, 0.60 equiv) with trifluoroacetic acid-d_1 (92 g, 0.80 equiv) at the reflux temperature gave the ring labeled hydrocarbon. Mass spectral analysis indicated 94.5% deuteration of the ring hydrogen positions.

Reaction of 1,2,3-Trimethylbenzene with Acetyl Nitrate. Isolation of *cis*- and *trans*-4-Nitro-3,4,5-trimethyl-2,5-cyclohexadienyl Acetates (1a and 1b). A solution of acetyl nitrate was prepared by adding nitric acid (9.33 mL, 90%, 0.20 mol) to 50 mL of ice-cold acetic anhydride with efficient stirring and cooling. The solution was allowed to warm to room temperature for about 20 min, cooled again to ice-bath temperature, and added dropwise over 90 min to a magnetically stirred solution of 1,2,3-trimethylbenzene (24 g, 26.8 mL, 0.20 mol) and acetic anhydride (40 mL) cooled in an ice-salt bath. The reaction temperature was held below −5 °C during addition. The solvent and other volatiles were removed at reduced pressure (1 mm, 25 °C, 18 h) to yield 35.5 g of light orange oil. NMR analysis indicated the following product distribution: dienes, 84 mmol (46%); 4- and 5-acetoxy-1,2,3-trimethylbenzene, 27 mmol (15%); 4-nitro-1,2,3-trimethylbenzene, 60 mmol (33%); 5-nitro-1,2,3-trimethylbenzene, 11 mmol (6%); 91% yield overall.

Isomer 1a. The crude product was dissolved in 30 mL of anhydrous ether, diluted with 60 mL of pentane, and stored at −20 °C. The crystalline deposit that had formed after 48 h was collected by suction filtration and triturated with three 15-mL portions of cold (−20 °C) pentane to yield 7.20 g of crude diene. NMR analysis indicated a nearly 1:1 mixture of **1a** and **1b**. Repeated crystallization from ether–pentane afforded 2.1 g of pure **1a** as light, flaky crystals: mp 118–119.5 °C; NMR ($DCCl_3$) δ 1.70 (s, 3 H, 4-Me), 1.75 (m, 6 H, 3,5-Me), 2.09 (s, 3 H, OAc), 5.61 (m, 1 H, 1-H), 5.83 (m, 2 H, 2,6-H); IR (KBr) 1730, 1535, 1435, 970, 940, 846, 797, 742 cm^{-1}.[22]

Isomer 1b. The lower melting isomer could be isolated by careful fractional crystallization of the mother liquors obtained in purification of **1a** with the use of *n*-pentane as solvent. In addition, column chromatography permitted isolation of this isomer from the crude mother liquor obtained in the initial separation. Thus, concentration of this mother liquor gave 28.3 g of dark orange oil. NMR indicated: dienes (mainly **1b**), 48 mmol; 4- and 5-acetoxy-1,2,3-trimethylbenzene, 32 mmol; 4-nitro-1,2,3-trimethylbenzene, 12 mmol; and 5-nitro-1,2,3-trimethylbenzene, 12 mmol. Column chromatography of 6 g of this material over 300 g of deactivated alumina (10% acetic acid) with pentane elution gave 1.23 g of crystalline diene that was greater than 90% **1b**. Fractional crystallization yielded 40 mg of **1a** and 950 mg of **1b**: mp 65–66 °C; NMR ($DCCl_3$) δ 1.76 (m, 9 H, 3,4,5-Me), 2.04 (s, 3 H, OAc), 5.74 (m, 1 H, 1-H), 5.87 (m, 2H, 2,6-H); IR (KBr) 1730, 1538, 1430, 960, 930, 815 cm^{-1}.[22]

Preparation and Isolation of Labeled Dienes 1a and 1b. The ring deuterated samples of **1a** and **1b** were prepared from the appropriately labeled hydrocarbons and isolated by the procedures previously described. Nitrogen-15 adducts were prepared with the use of labeled nitric acid (ca. 100 wt %, 99 atom % ^{15}N) that had been prepared by distillation of 50 wt % $H^{15}NO_3$ from concentrated sulfuric acid at reduced pressure.

Stereochemical Assignments. Stereochemical assignments were made on the basis of NMR spectral shifts observed upon addition of ca. 10-mg portions of Eu(fod)$_3$ to 50-mg samples of **1a** and **1b** in 0.3 mL of $DCCl_3$. It was observed that the 4-methyl singlet of **1a** underwent essentially no shift upon increasing the Eu(fod)$_3$ concentration. Similar measurements for **1b** showed the 4-methyl singlet to be shifted downfield about 0.008 ppm/mg of Eu(fod)$_3$ added.

Preparative Nitration of 1,2,3-Trimethylbenzene in Acetic Anhydride with Sulfuric Acid Workup. A solution of acetyl nitrate was prepared in the usual way from 3.2 mL (68.6 mmol) of 90 wt % nitric acid and 15 mL of acetic anhydride. This solution was added dropwise to a magnetically stirred solution of 1,2,3-trimethylbenzene (10.0 mL, 8.94 g, 74.4 mmol) and 15 mL of acetic anhydride held at ice-bath temperature. After a 1-h reaction period, the mixture was added slowly (20 min) to 100 mL of vigorously stirred 80 wt % sulfuric acid held at −4 to −5 °C. Stirring was continued for 15 min after addition and the dark brown mixture was then poured over ice and the resulting brown oil was extracted with cyclohexane. After washing the cyclohexane extracts with water and aqueous sodium bicarbonate, the dried organic layer was concentrated to yield 10.46 g (92%) of crude product. GLC analysis indicated 78.5% 4-nitro-1,2,3-trimethylbenzene, 8.2% 5-nitro-1,2,3-trimethylbenzene, 5.3% 4-acetoxy-1,2,3-trimethylbenzene, 1% 5-acetoxy-1,2,3-trimethylbenzene, and 7% nitrophenols and nitroacetates. No dinitro-1,2,3-trimethylbenzene (<0.5%) could be detected.

Solvolysis of 1a and 1b in Sulfuric Acid Solutions. Stock solutions were typically prepared by dissolving carefully weighed samples of **1a** or **1b** together with the internal standard, *p*-nitrotoluene, in benzene or chloroform. In many cases the NMR spectrum of the mixture was recorded and carefully integrated to provide an added check on the molar ratio of adduct:standard. (Solutions varied in composition from 1 wt % diene to ca. 15 wt %, but no effect was noted in the product analysis.) Portions of the stock solution (200–20 μL) were added to 2.0-mL portions of sulfuric acid solutions and vigorously mixed by magnetic stirring or with a vortex mixing apparatus. After reaction periods ranging from 30 to 60 min, the solutions were quenched by addition to ice and water and products were extracted with portions of cyclohexane. The extracts were washed with aqueous base and dried over sodium sulfate. Analysis data collected from GLC analysis, corrected for relative response factors, is presented in Table I.

Controls of the procedure included a check of the extraction procedure with the use of 4-nitro-1,2,3-trimethylbenzene and *p*-nitrotoluene. Portions of this mixture were analyzed directly. Other portions were put through the solvolysis isolation procedure. No difference in the area ratio of components was noted. The yield of 4-nitro-1,2,3-trimethylbenzene from **1a** was checked as a function of reaction time. No change in yield (±0.5%) was observed over the time interval 120–2300 s. The stability of 5-acetoxy-1,2,3-trimethylbenzene to the solvolysis and workup procedure was checked. Recoveries of the phenyl acetate after 1-h reaction in sulfuric acid solutions were 50% from 73% H_2SO_4, 74% from 66% H_2SO_4, 86% from 60% H_2SO_4, and 90% from 54% H_2SO_4. Parallel workup procedures with and without extraction with aqueous base showed no significant variation in recovery, but the phenol peak increased and provided a nearly complete material balance.

None of the GC records of solvolysis runs in 50–70% H_2SO_4 showed more than trace quantities of either the phenyl acetate or the corresponding phenol. However, solvolysis of **1a** in 52% H_2SO_4 containing urea (5 M) led to recovery of ca. 50% of 5-hydroxy-1,2,3-trimethylbenzene. The yield of phenol fell off rapidly as the urea concentration was reduced. Further control studies demonstrated that 5-acetoxy-1,2,3-trimethylbenzene is stable in 52% H_2SO_4 containing added sodium nitrite while the corresponding phenol, although stable in 52% H_2SO_4, reacts in 52% H_2SO_4 containing sodium nitrite to yield several products with very long GLC retention times.

Chromatographic analyses were made with the use of a HI-EFF 8BP (cyclohexanedimethanol succinate) column 10 ft × 0.125 in. operated at 200 °C with a 30 mL min^{-1} flow of carrier. Characteristic retention times in minutes (response factors) follow: p-nitrotoluene, 3 (1.0); 4-acetoxy-1,2,3-trimethylbenzene, 4.4 (0.660), 5-acetoxy-1,2,3-trimethylbenzene, 5.1 (0.669); 4-nitro-1,2,3-trimethylbenzene, 7.5 (0.738); 5-nitro-1,2,3-trimethylbenzene, 11 (0.740).

Table VI. Measurement of External Return with Use of **1a**-^{15}N in 47.5% Ethanol and 0.2 M $NaNO_2$-^{14}N

1a-^{14}N[a]/ **1a**-^{15}N	Δ**1a**-^{14}N/ **1a**-^{15}N	(**1a**)[b]/ (**1a**)$_0$	k_{return}[c]/ k_{solv}
0.014		1.00	
0.025	0.011	0.60	0.11
0.038	0.024	0.30	0.10

[a] Determined by conversion of unconsumed **1a** to 4-nitro-1,2,3-trimethylbenzene and measurement of molecular ion ratio, *m/e* 165:*m/e* 166, at 12 eV. [b] Determined by GC analysis of 4-nitro compound with respect to internal standard. [c] Determined from the derived relationship, $k_{return}/k_{solv} = (\Delta(\mathbf{1a}\text{-}^{14}N/\mathbf{1a}\text{-}^{15}N)/[NO_2^-]) \ln(\mathbf{1a}/\mathbf{1a}_0)$.

Solvolysis of 1a in Nitromethane Solutions Containing Added 95 Wt % Sulfuric Acid or 90 Wt % Nitric Acid. The NMR spectrum of **1a** (60 mg, 0.27 mmol) in 0.5 mL of nitromethane was recorded and integrated. To the solution was added 0.1 mL of a 1 M solution of sulfuric acid in nitromethane. The solution turned dark brown immediately and gas evolution was noted. The NMR spectrum showed that the diene had been consumed. Spectral bands attributable to 4-nitro-1,2,3-trimethylbenzene and 1 molar equiv of acetic acid were observed. GLC analysis of the cyclohexane extract obtained by dilution of the reaction mixture with water and extraction revealed only 4-nitro-1,2,3-trimethylbenzene plus a trace (<1%) of 5-acetoxy-1,2,3-trimethylbenzene.

Stock solutions of **1a** in nitromethane with *p*-nitrotoluene as an internal standard were prepared in the usual manner. Aliquots of the stock solution were mixed with solutions of sulfuric acid (95 wt %) in nitromethane. After a 30-min reaction period at room temperature (25 ± 3 °C), the reaction solutions were quenched in water. Organic products were extracted with cyclohexane and subsequently analyzed by GLC. Control studies established that 4-nitro-1,2,3-trimethylbenzene and 5-acetoxy-1,2,3-trimethylbenzene could be recovered quantitatively (with respect to the internal standard) from nitromethane solutions containing 0.1 M sulfuric acid. Reaction time control studies indicated that the product yield was constant as reaction time was varied from 5 min to 3 h. Similar procedures were used for studies involving 90 wt % nitric acid in nitromethane. Yield data for runs are collected in Table II.

Solvolysis Studies in Aqueous Ethanol and Related Solvents. Preliminary experiments indicated that **1a** solvolyzed very rapidly in nearly pure water to yield 5-acetoxy-1,2,3-trimethylbenzene and then slowly underwent a pH dependent hydrolysis to yield 5-hydroxy-1,2,3-trimethylbenzene. Thus, when a stock solution prepared from 31 mg of **1a** in 3 mL of methanol was diluted to 200 mL with aqueous buffer at pH 10.4, the absorption band at 265 nm decreased and a band at 284 nm developed with a half-life of 31 min. When 5-acetoxy-1,2,3-trimethylbenzene was treated in a similar manner, the same spectral changes were observed at essentially the same rate. When a stock solution of **1a** was prepared in the manner described and immediately extracted with methylene chloride, only 5-acetoxy-1,2,3-trimethylbenzene could be detected by chromatographic analysis of the dried extract.

Rates of solvolytic elimination of the elements of nitrous acid to yield the 5-acetoxy-1,2,3-trimethylbenzene could be conveniently followed, however, in aqueous alcohol mixtures containing more than 40 vol % alcohol. The typical procedure involved weighing 3-5 mg of **1a** or **1b** in a capillary tube, dissolving the sample in pure alcohol or purified dioxane (10-40 μL), and injecting 2-5 μL of this stock solution into temperature equilibrated silica cells containing 3-4 mL of the appropriate solvent mixture. The absorbance maxima of 5-acetoxy-1,2,3-trimethylbenzene were monitored as a function of time. Plots of log ($A_\infty - A$) vs. time were linear over 90% of reaction. Final values of rate constants were obtained by least-squares treatment of the data. Collected data are presented in Tables III and IV.

Product analysis of kinetic solutions after more than 9 half-lives revealed only 5-acetoxy-1,2,3-trimethylbenzene. The absence of isomerization of reactants during solvolysis was indicated by conducting kinetic studies using a mixture of **1a** and **1b**. Plots of log ($A_\infty - A$) vs. time indicated two concurrent first-order processes. Conventional treatment of the data afforded rate constants that were in agreement with rate constants obtained from pure samples of **1a** and **1b** in the same solvent mixture.

Test for External Return in Solvolysis of 1a-^{15}N in 47.5% Ethanol. Preliminary tests demonstrated that solvolytic elimination of **1a** could be carried out for 1 half-life in 47.5% ethanol with 90% net recovery of the product-reactant pair by rapid extraction of the ice-chilled, diluted reaction mixture with chloroform. NMR spectral examination revealed only 5-acetoxy-1,2,3-trimethylbenzene and unconsumed **1a**. Isomer **1b** could not be detected in the mixture.

A stock solution containing 52.0 mg of **1a**-^{15}N and 22.0 mg of *p*-nitrotoluene was prepared in 5 mL of absolute ethanol and then transferred to a thermostated (25 °C) flask containing 45 mL of 47.5% ethanol, 0.20 M in $Na^{14}NO_2$. Aliquots were removed after 25 min (10 mL) and 55 min (40 mL). The aliquots were immediately transferred to separatory funnels containing a two- to fourfold excess of ice-cold water plus 5 mL of chloroform. The layers were rapidly separated and a second 5-mL portion of chloroform was added, mixed, and separated. The combined chloroform extracts were extracted once with ice water, dried over sodium sulfate, and evaporated under vacuum. The residual material was treated with 12 mL of 83% sulfuric acid with magnetic stirring for 30 min. Products from the sulfuric acid solvolysis were isolated by dilution with ice and water and extraction with chloroform. After counterextraction of the chloroform with water and sodium bicarbonate solution, the dried (sodium sulfate) chloroform extract was evaporated and the residue was dissolved in *n*-heptane for GLC analysis. The remainder was analyzed by low-voltage (12 eV) mass spectrometry and the *m/e* 166 and 165 peaks were measured. Pertinent data are collected in Table VI.

NMR Study of Solvolysis of 1a in Acetic-d_3 Acid-d_1. A solution composed of **1a** (55 mg, 0.244 mmol), acetic-d_3 acid-d_1 (0.352 g, 5.50 mmol), and chloroform-*d* (0.645 g) was prepared in an NMR tube. Spectra of this reaction were recorded and carefully integrated over a span of 15 days. During this time the characteristic ring methyl and acetoxyl methyl resonance lines of **1a** slowly diminished and lines attributable to 5-acetoxy-1,2,3-trimethylbenzene grew. Only one extra line appeared in the spectrum and this was shown to be the methyl proton resonance line of unlabeled acetic acid formed by transesterification. Otherwise the spectra and integrals conformed to that expected of a mixture of **1a** and the phenyl acetate elimination product. No evidence of isomerization of **1a** to **1b** could be detected, nor could any evidence of the formation of the diacetate be adduced.

After 40% conversion (15 days at 25 ± 4 °C), a portion of the solution (0.645 g) was treated with 10 mL of cold 85% H_2SO_4 containing 0.5 g of urea. Dilution of the acid with water and extraction with chloroform gave 20 mg of brown oil (ca. 80% recovery). NMR and chromatographic analysis revealed 4-nitro-, 5-acetoxy-, and 5-hydroxy-1,2,3-trimethylbenzene in ca. 10:2:5 ratio. Mass spectrometry showed that 25% of the 5-acetoxy derivative contained a trideuterated acyl group. No deuterium incorporation in 4-nitro-1,2,3-trimethylbenzene could be detected.

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References and Notes

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(13) The assumption of an established ipso ion–dienol equilibrium, K_3, of Chart II appears quite reasonable, but the assumption may be open to question.

(14) NMR analysis of crude nitration product indicates that 4-acetoxyl-1,2,3-trimethylbenzene is the predominant phenyl acetate product, but upon decomposition of the diene adducts in the crude mixture in water, the 5-acetoxy isomer is the major phenyl acetate product.

(15) Adducts derived from the tetramethylbenzenes are much more sensitive to decomposition than those derived from the trimethylbenzenes.[3] It seems reasonable to associate this greater liability with more rapid rates of loss of nitrite ion.

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(20) Extrapolation of solvolysis rates of **1b** to pure water implys a half-life of less than 30 s. Assuming that this rate holds in aqueous acid solutions, the rates of formation of **2** from **1a** or **1b** must be considerably faster.

(21) Unpublished work with Aldona Butkus and John Klement.

(22) The spectral properties of isomers designated herein as **1a** and **1b** correspond roughly to those reported in ref 3b and labeled therein as **2a** and **2b**, respectively. The most notable differences are melting points: for the **a** isomer, 118–119.5 °C (lit.[3b] 60 °C), for the **b** isomer, 65–66 °C (lit.[3b] not reported).

Aromatic Substitution in the Gas Phase. On the Mechanism of the Dehalogenation Reactions of Halobenzenes and Dihalobenzenes Promoted by Gaseous Brønsted Acids

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Abstract: The attack of CH_5^+ and $C_2H_5^+$ ions, obtained in the dilute gas state from the γ radiolysis of methane, on halo- and dihalobenzenes causes extensive dehalogenation via two distinct channels, leading respectively to protodehalogenated and methyldehalogenated products, whose relative rate depends primarily on the nature of the leaving halogen. Kinetic and mass spectrometric evidences suggest that direct attack of the Brønsted acid to the halogen substituent leads to formation of the correspondent arylium cation, via hydrogen halide elimination, at a rate which decreases in the order $F \gg Cl \geq Br$. The subsequent electrophilic attack of the arylium cations on CH_4, the bulk constituent of the system, yields methylated arenium ions, and eventually the observed methyldehalogenated products. On the other hand, attack of the Brønsted acid to the aromatic ring of halobenzenes promotes protodehalogenation, at a rate increasing in the order $F \ll Cl < Br$. Direct comparison of the rates of the two dehalogenation processes has been obtained from the study of dihalobenzenes containing different halogens. Furthermore, isolation of a mixture of *m*- and *p*-xylene among the dehalogenation products of *p*-fluorotoluene has provided direct evidence for the isomerization of the *p*-tolyl cation formed from the attack of the gaseous Brønsted acid to the n-type center of the substrate and/or of the xylenium ion formed from the attack of the tolyl ion to methane. The present results, and supporting mass spectrometric evidence, underline the typical ambident behavior of halobenzenes toward charged electrophiles, and allow a unified interpretation of the dehalogenation processes promoted by different Brønsted acids. The gas-phase reactivity of halobenzenes is compared with their behavior in similar processes occurring in solution.

In previous papers[1-4] we reported evidence showing that dehalogenation, a major reaction channel in the gas-phase attack of strong Brønsted acids, such as HeT^+ and D_2T^+, to halobenzenes,[5] occurs via two distinct mechanisms, involving respectively the attack of the electrophile to the halogen substituent (n-type center) and to the aromatic ring (π-type center) of the ambident substrate. In order to obtain a sharper discrimination between the two dehalogenation channels, and to gain further insight into the factors regulating their competition, we have now extended the investigation to a pair of milder electrophiles, the CH_5^+ and $C_2H_5^+$ ions that can be conveniently obtained in the gas phase from the radiolysis of methane, and whose attack to halo- and dihalobenzene has been studied in the dilute gas state.[6]

Experimental Section

Materials. Methane, a research grade product from Matheson Co., with a stated purity of over 99.99 mol %, and oxygen, from SIO Co., with a stated purity of over 99.9 mol %, were used without further purification. Samples of halo- and dihalobenzenes, obtained from Fluka AG, were purified by preparative GLC, until the purity of the recovered fractions, determined by analytical GLC, exceeded 99.99 mol %. A particularly difficult problem was represented by the analysis of *p*-fluorotoluene, necessary to exclude the presence of significant concentrations of the ortho and meta isomers. The resolution of a synthetic mixture of the three isomers required a 30-m Carbowax 20M capillary column, operated at 60 °C. Analysis of the sample revealed the absence of detectable amounts of *o*- and *m*-fluorotoluene.

Procedure. Carefully outgassed 1-L Pyrex bulbs, evacuated to 10^{-5} Torr on a greaseless vacuum line, were filled with a gaseous mixture consisting of CH_4 (760 Torr), O_2 (2 Torr, used as a thermal radical scavenger), and the aromatic substrate (ca. 10 mg, corresponding to 1-2 Torr), and irradiated with the ^{60}Co γ radiation in a 220 Gammacell (Nuclear Canada Ltd.) at the temperature of ca. 34 °C, at a dose rate of 0.4 Mrad h^{-1} to a total dose of 4.8 Mrad, as determined by a Fricke dosimeter. The analysis of the products was carried out using a Model 5700A Hewlett-Packard gas chromatograph, equipped with a FID unit. The following columns were used: 4-m tricresyl phosphate, 4-m diisodecyl phthalate, and 4-m DC 550 silicone oil, all employing acid-washed Chromosorb W as the solid support and N_2 as the carrier gas. The ICR data mentioned in this paper were obtained by bombarding with 15-eV electrons a 10:1 CH_4 (CD_4)-halobenzene