were measured with a Disc integrator. The columns employed were all stainless steel since serious decomposition was noted otherwise. The columns were either 0.125 ft × 6 or 12 ft 15% SF-96 on 60–80 Chromosorb P, 0.125 in. × 6 ft 15% DEGS on 60–80 Chromosorb W, or (for analysis of products from 2-methyl-2-butene) a 150 ft × 0.01 in. Golay column coated with Ucon LB-550-X. Proton magnetic magnetic resonance spectra were obtained on a Varian Associates Model A56/60 spectrometer.

Experimental Procedures. Unless stated in the text, all experimental runs were preformed in an inert Teflon vessel bored out of a Teflon rod. This vessel was thoroughly washed prior to each use, dried in an oven, then cooled in either a stream of dry nitrogen or a desiccator. The appropriate amounts of reagents were added by the indicated methods and the reaction was performed under an aluminum foil cover in a darkened hood. Hydrogen bromide solutions were prepared by dissolving the gas in the appropriate solvent, contained in a previously baked-out bottle, avoiding contact with the atmosphere *via* a suitable venting arrangement. The solution thus obtained was found to be sensitive to trace inpurities, as indicated by slight discoloration, so that any such solution was discarded. The concentration of acid in the solution was determined by titration in a mixed solvent system to a phenolphthalein end point. More accurate determination, when required, was obtained by mixing an aliquot amount of acid solution with an excess of triphenylphosphine in the same solvent, cooling to precipitate the stable triphenylphosphonium bromide salt,[31] filtering, and weighing the dried salt.

The general procedure for HBr addition to alkenes summarized in Table I was to add a solution of hydrogen bromide (15 ml of *ca.* 0.075 *M*) to a solution of 2.0 ml of alkene in 1,1,2-trichlorotrifluoroethane containing the catalyst. The mixture was then stirred 2–6 hr depending on the alkene reactivity. All runs were carried out to less than 10% total conversion to ensure pseudo-first-order behavior in alkene. In addition, an appropriate internal standard was added to determine a material balance. Quantitative conversions (HBr limiting) were generally obtained if allowances for side reactions (as mentioned previously) were made.

Appropriate control experiments in the absence of catalysts were performed under identical conditions free from moisture, light, or surface catalysis. No radical-derived product was observed.

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Kinetics of Bromination of Some Substituted Pyridinium Ions by Hypobromous Acid in Aqueous Perchloric Acid

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The rates of bromination in the 3 and 5 positions of 2-methyl-, 4-methyl-, and 2,4-dimethylpyridine with hypobromous acid have been measured in aqueous perchloric acid at 25.0 ± 0.1°. Reaction occurs through the corresponding pyridinium cations. The rates of bromination of 1,2-dimethyl-, 1,4-dimethyl-, 1,2,6-trimethyl-, 1,2,4-trimethyl-, 1,2,4,6-tetramethyl-, 1-methyl-2-methoxy-, and 1-methyl-2,6-dimethoxypyridinium perchlorates have also been studied. Bromination of the unsubstituted pyridinium cation was not observed; however, the partial rate factor for the bromination of this cation at the 3 position is estimated to be approximately 6 × 10⁻¹³.

The strong deactivation of the pyridinium cation to electrophilic substitution has prevented a detailed kinetic study of these reactions. High temperatures and long reaction times are characteristic of electrophilic halogenation, nitration, and tritiation of the pyridinium cations.[2,3] den

Hertog, van der Does, and Landheer[4] have brominated pyridine at 130° with bromine in fuming sulfuric acid, obtaining a good yield of 3-bromopyridine. 2-Methyl-, 3-methyl-, and 4-methylpyridine have also been brominated in fuming sulfuric acid at 80° and 2,6-dimethylpyridine at

55°.[5] Recently, Abblard, Decoret, Cronenburger, and Pacheco[6] have brominated numerous methylpyridines in fuming sulfuric acid at 50–80° and have concluded, along with van der Does and den Hertog,[5] that the sulfur trioxide pyridine complex is the species that is being brominated. This is similar to the complex proposed by Pearson, Hargrove, Chow, and Suthers[7] resulting from a mixture of aluminium chloride and pyridine, which can be chlorinated with chlorine at 80–130°, and from aluminum chloride and 4-methylpyridine which can be chlorinated at 92°, and brominated at 95°. No kinetic studies of the electrophilic halogenation of methylpyridines have been reported.

Electrophilic nitration of pyridine in concentrated sulfuric acid at high temperatures results in the formation of a low yield of 3-nitropyridine. Methylpyridines can be nitrated under milder comditions and higher yields are obtained; in fact the kinetic nitration of 2,4,6-trimethylpyridine and of the 1,2,4,6-tetramethylpyridinium cation near 100° have been studied.[8] Electrophilic tritiation in sulfuric acid (H_0 = −6.22 to −9.66) of 2,6-dimethylpyridine, 2,4,6-trimethylpyridine, and the 1,2,4,6-tetramethylpyridinium cation at high temperatures resulted in the exchange of the 3 and 5 hydrogen atoms.[9] The variation of the first-order rate constants with H_0, indicated that the exchange involved the pyridinium cations and not the free bases. It is estimated that the pyridinium cation is tritiated 10^{-18} times as rapidly as is benzene. No kinetic electrophilic substitution studies have been made for any methylpyridines at 25°; this complicates the calculation of relative reactivities to other aromatic systems.[10]

The acid-catalyzed bromination by hypobromous acid of deactivated aromatic compounds has been studied by de la Mare and Hilton[11] and also by Gastaminza, Ridd, and Roy.[12] At a given acidity the kinetic form is rate = k_2[ArH][HOBr] but as the acid concentration increases so does the rate. Recently Gilow and Ridd[13] have found that the reaction at low acidites probably occurs through the protonation of a preformed complex of hypobromous acid and the aromatic substrate but, for reaction at high acidities, their arguments do not exclude the conventional reaction path involving a preformed positive brominating agent.

Results

Electrophilic bromination of a number of methylpyridinium cations with hypobromous acid at 25° has been accomplished. A small volume (0.004–0.006 ml) of aqueous hypobromous acid was added to a perchloric acid solution of the aromatic substrate to initiate the reaction. The use of a small volume of aqueous hypobromous acid kept the heat of dilution and consequent decomposition of hypobromous acid to a low level except at concentrations of perchloric acid above 72%. This was not the case when aqueous sulfuric acid was used for the reaction medium.

The formation of the aromatic bromides, in the kinetic brominations, were followed in a thermostated uv spectrometer using at least a tenfold excess of the aromatic substrate. Using these pseudo-first-order conditions eliminates the problem of having to know the exact concentration of hypobromous acid and keeps to a minimum or eliminates disubstitution, two problems encountered when following the reaction under second-order conditions and titrating the excess hypobromous acid. Bromination of the substituted pyridines and pyridinium cations proceeded smoothly following pseudo-first-order kinetics for at least 80% of the reaction provided that the half-life of the reaction was kept relatively short. The resulting first-order rate coefficients were divided by the concentration of the aromatic

Table I
Second-Order Rate Coefficients for the Reaction of Hypobromous Acid and Some Pyridinium Perchlorates in Aqueous Perchloric Acid at 25.0 ± 0.1°

|		$HClO_4$, %	k_2, mol^{-1} sec^{-1} l.
1	1,4,6-Tetramethylpyridinium perchlorate	52.40	0.83
		52.44	0.87
		54.89	2.39
		55.93	4.65
		56.87	7.24
		59.13	22.6
		59.35	23.8
2	1,2,6-Trimethylpyridinium perchlorate	63.12	1.79
		63.66	2.31
		65.20	6.78
		66.53	19.0
3	2,4-Dimethylpyridinium perchlorate	62.45	1.84
		63.77	4.15
		64.62	8.49
		66.01	16.5
4	1,2,4-Trimethylpyridinium perchlorate	62.48	1.66
		63.47	3.57
		64.93	8.16
		66.26	18.0
5	4-Methylpyridinium perchlorate	70.23	2.59
		70.76	2.95
		71.79	8.55
		72.54	16.4
6	1,4-Dimethylpyridinium perchlorate	70.75	4.70
		71.50	9.76
		72.00	15.8
		72.84	29.8
		73.37	50.3
		73.76	82.3
7	2-Methylpyridinium perchlorate	68.54	0.78
		70.21	2.35
		70.23	2.65
		71.32	5.50
		71.63	6.89
		71.62	7.55
		72.09	9.15
		72.15	10.7
8	1,2-Dimethylpyridinium perchlorate	69.69	1.70
		70.77	3.67
		71.80	8.72
9	1-Methyl-2,6-dimethoxypyridinium perchlorate	20.82	4.75
		24.53	8.14
		27.92	14.5
		31.21	26.2
10	1-Methyl-2-methoxypyridinium perchlorate	55.44	1.86
		56.80	3.68
		58.84	9.12
		60.36	20.0
		61.21	35.5

substrate to give the second-order rate coefficients listed in Table I and plotted logarithmically against H_0[14] in Figure 1. The linear plots have slopes close to unity ranging from 1.06 for the 1,2,4,6-tetramethylpyridinium cation to 1.17 for the 2- and 4-methylpyridinium cations. Similar linear plots for unreactive benzene derivatives have slopes which range from 1.16 to 1.48.[11,13] Differences in slopes appear to be due to the nature of the substrate and not due to a change in the mechanism of bromination.

Relative reactivities are shown in Table II determined by a stepwise comparison at the acidities indicated in Figure

Table II
Relative Rates and Partial Rate Factors for the Bromination of Some Pyridinium Salts with Hypobromous Acid
in Perchloric Acid at 25 ± 0.1°

No.	Substrate	Relative rate[a]	f_3	f_5
14	2,4,6-Trimethylpyridinium perchlorate	3.0×10^{-7} [b]	9.0×10^{-7}	
1	1,2,4,6-Tetramethylpyridinium perchlorate	2.3×10^{-7}	6.9×10^{-7}	
13	2,6-Dimethylpyridinium perchlorate	2.8×10^{-9} [b]	8.4×10^{-9}	
2	1,2,6-Trimethylpyridinium perchlorate	2.8×10^{-9}	8.4×10^{-9}	
3	2,4-Dimethylpyridinium perchlorate	4.1×10^{-9}	1.5×10^{-8}	9.8×10^{-9}
4	1,2,4-Trimethylpyridinium perchlorate	3.6×10^{-9}		
5	4-Methylpyridinium perchlorate	3.1×10^{-11}	9.3×10^{-11}	
6	1,4-Dimethylpyridinium perchlorate	4.6×10^{-11}	1.4×10^{-10}	
7	2-Methylpyridinium perchlorate	3.1×10^{-11}	1.0×10^{-10}	8.6×10^{-11}
8	1,2-Dimethylpyridinium perchlorate	3.4×10^{-11}		
9	1-Methyl-2,6-dimethoxypridinium perchlorate	7.8×10^{-3}	2.3×10^{-2}	
10	1-Methyl-2-methoxypyridinium perchlorate	1.8×10^{-7}		
11	Phenyltrimethylammonium perchlorate	2.6×10^{-6} [c]		

[a] Relative rate of $C_6H_6 = 1$. [b] See ref 13. [c] See ref 12.
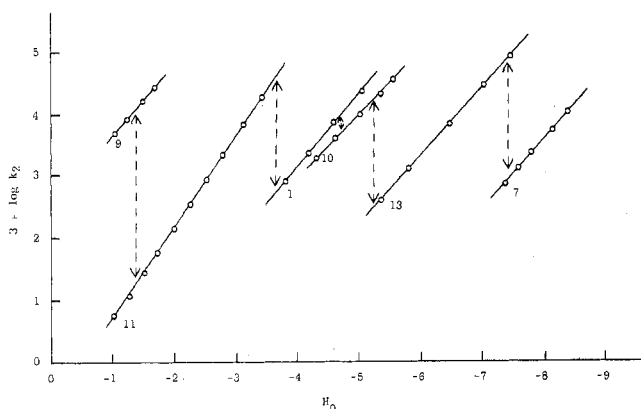
Figure 1. Logarithmic plot of second-order rate coefficients against H_0 for the bromination of phenyltrimethylammonium (11) and some pyridinium cations by hypobromous acid in aqueous perchloric acid. Numbering as in Table II. For clarity some overlapping points and some substrates have been omitted.

1. The relative reactivity of the trimethylanilinium cation for bromination in perchloric acid is that of de la Mare and Hilton[11] to which the other methylpyridinium cations were compared.

In order to establish that the increase in absorbance in the uv was actually due to the formation of the aromatic bromide, the products from the bromination of the 2-methyl-, 2,4-dimethyl-, and 2,6-dimethylpyridinium cations with hypobromous acid under conditions similar to kinetic conditions were isolated. The products were identified by comparison of the known chemical shifts of bromomethylpyridines[6] and product ratios determined by ¹H nmr techniques. Recovery of starting material and products accounted for 72–80% yields. No side products or disubstitution was observed. The relatively low yields are probably due to the fact that it is difficult to extract a small amount of a water soluble pyridine from a relatively large volume of water with an organic solvent.

Bromination of the 2,6-dimethylpyridinium cation gave only a 3-bromo-2,6-dimethylpyridine; the 2,4-dimethylpyridinium cation gave 60% 3-bromo- and 40% 5-bromo-2,4-dimethylpyridine; and the 2-methylpyridinium cation gave 53% 3-bromo- and 47% 5-bromo-2,4-dimethylpyridine. It is somewhat surprising that more 3 than 5 substitution occurs in the case of the 2,4-dimethyl- and 2-methylpyridinium cations but is similar to iodination of the 2-methylpyridium cation in fuming sulfuric acid.[6] These product composi-

tions, in conjunction with the relative reactivities, give the partial rate factors listed in Table II.

Discussion

In principle, the bromination of a C-substituted pyridine could occur through both the neutral molecule and through the conjugate acid but two pieces of evidence suggest that reaction through the neutral molecule can be neglected under the conditions studied here. First, the slopes of the rate profiles for the reaction of the C-substituted pyridines are very similar to those of the corresponding 1-methylpyridinium cations. This is illustrated by the comparison of the rate profiles for the bromination of 2,6-dimethylpyridinium cation and 1,2,6-trimethylpyridinium perchlorate. (Because the rate profiles for two substrates are almost identical only the rate profile for 1,2,6-trimethylpyridinium perchlorate (9) is included in Figure 1.) Secondly, the effect of N-methylation on the reactivity of a given pyridine is very slight (less than a factor of 2). This has also been found to be the case in the nitration[8] and tritiation[9] of 2,4,6-trimethylpyridine and is good evidence that reaction is occurring through the conjugate acid.[10] The partial rate factors listed in Table II are therefore attributed to the pyridinium cations.

From the partial rate factors, it is clear that a methyl group in these pyridinium cations activates the corresponding ortho and para positions by a factor of ca. 100. Using this factor, and starting with the partial rate factors for substitution in the 2-methyl- or 4-methylpyridinium cations, the reactivity of the other C-substituted pyridinium cations can be predicted to well within a factor of 2. This activation by a methyl group is similar to that by a p-methyl group in the trimethylanilinium ion in bromination (a factor of 270)[13] but is not similar to the corresponding activation in the nitration of the trimethylanilinium ion (a factor of 3500).[15]

The results in Table II show also that a second methoxy group activates the aromatic ring by a factor of 4.3×10^4 (9 and 10). A single methoxy group appears, however, to be about equivalent to three methyl groups (1 and 10).

Attempts to calculate the relative reactivity of the pyridinium cation toward electrophilic substitution have been limited by a number of factors. Some of these factors include (a) the kinetic data must be obtained at relatively high temperatures where extrapolation to room temperatures is difficult and at high acidities when a choice of an acidity scale may be a problem,[10] (b) only highly substitut-

Table III
Estimated f_3 for the Bromination of the Pyridinium Cation with Hypobromous Acid in Perchloric Acid

Method of Estimation	f_3
From the known f_3 of 2,4,6-trimethylpyridinium 2,4-dimethylpyridinium, and 4-methylpyridinium cations assuming the additivity principle holds	9×10^{-13}
From the known f_3 of 1-methyl-2,6-dimethoxypyridinium and 1-methyl-2-methoxypyridinium[a] perchlorates assuming the additivity principle holds	1.3×10^{-11}
From the extrapolation of linear plot of Figure 2	6×10^{-13}
From $\log f_3 = \sigma\rho = (2.04)(-6.2) = -12.65$[b]	2×10^{-13}
From the comparison of the f_2 of toluene[c] and the f_3 of 4-methylpyridinium cation with the f of benzene and the f_3 of the pyridinium ion, respectively	1.5×10^{-12}
From the comparison of the f_4 of m-xylene[d] and the f_3 of 2,6-dimethylpyridinium cation with f of benzene and the f_3 of the pyridinium ion, respectively	4×10^{-12}
From the comparison of the f_4 of mesitylene[e] and the f_3 of 2,4,6-trimethylpyridinium cation with f of benzene and the f_3 of the pyridinium cation, respectively	1×10^{-12}
From the comparison of the f_2 of anisole[c] and the f_3 of 1-methyl-2-methoxypyridinium perchlorate with f of benzene and the f_3 of the pyridinium cation, respectively	6.8×10^{-12}

[a] Assuming f_3 and f_5 are equal. [b] See ref 2. [c] See ref 16. [d] Bromination of m-xylene with hypobromous acid with perchloric acid catalyst results in 29% 2-bromo-m-xylene and 71% 4- and 5-bromo-m-xylene by nmr analysis. The amount of 5-bromo-m-xylene formed is considered to be negligible. [e] A better estimate of the relative reactivity $= 1.2 \times 10^5$ than previously published.[13]

ed pyridines can be studied kinetically and therefore extrapolation to the unsubstituted pyridinium ion is difficult, and (c) comparison of the rate of substitution of a pyridine derivative with the corresponding benzene derivative may not be possible because the benzene derivative is reacting at or near the encounter rate.[8] The bromination of monosubstituted pyridinium derivatives with hypobromous acid in perchloric acid proceeds rapidly at 25° and reactive benzene derivatives are not brominated at the encounter rate,[13] thereby overcoming some of the difficulties mentioned in a, b, and c. Estimated values of f_3 for the bromination of the pyridinium cation with hypobromous acid in perchloric acid are listed in Table III. The effect of the N-methyl is ignored in these calculations.

A stepwise comparison of the reactivity of 2,4,6-trimethyl-, 2,4-dimethyl-, and 4-methylpyridinium cations assuming the additivity principle applies, estimates f_3 for the pyridinium cation to be 9×10^{-13}. The chemical shift of the 3 hydrogens of the 1-methylpyridinium derivatives give a linear relation with the $\log f_3$ as indicated in Figure 2. The use of this linear plot for estimating the reactivity of the pyridinium cation results in a value of 6×10^{-13}. (The chemical shifts used are given in the Experimental Section.) These estimated partial rate factors are also consistent with the linear free energy prediction of 2×10^{-13} (Table III). The estimated f_3 of the pyridinium ion toward electrophilic bromination with positive bromine at 25° is about 6×10^{-13}.

Comparison of the f_4 of toluene, m-xylene, mesitylene,
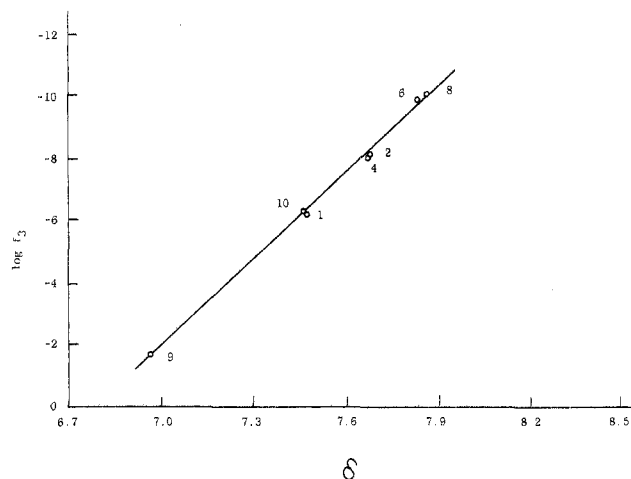
Figure 2. Plot of $\log f_3$ against the chemical shift of the 3 hydrogens of some 1-methylpyridinium perchlorates. Numbering as in Table II. For **4, 8,** and **10** f_3 was calculated on the assumption that the 3 and 5 positions are equally reactive.

and anisole with the f_3 of the 4-methylpyridinium, 2,6-dimethylpyridinium, 2,4,6-trimethylpyridinium, and 2-methoxypyridinium ion, respectively, predicts the f_3 for the pyridinium ion to be somewhat higher than the other methods (Table III). It has been found that substituent effects of more reactive systems may be considerably different than for unreactive systems and therefore this method of estimating the reactivity of the pyridinium cation would be expected to be less reliable. This apparently is also the reason why the comparison of f_3 for 1-methyl-2,6-dimethoxypyridinium and 1-methyl-2-methoxypyridinium cations also predicts f_3 for the pyridinium cation to be somewhat higher.

Bromination of pyridinium and 1-methylpyridinium perchlorate with hypobromous acid was attempted at 25° in perchloric acid up to 77.5% ($H_0 = -10$). No evidence for bromination was observed. There could be a number of reasons for this including (a) the fact that hypobromous acid may decompose at high concentrations of perchloric acid, (b) the relationship of H_0 and $\log k_2$ may no longer be linear, and (c) the pyridinium cation may be less reactive than predicted. It has also been observed that the kinetic bromination of the 3,5-dimethylpyridinium cation can be followed but not the 3-methylpyridinium cation suggesting that (c) is not the most likely explanation.

Experimental Section[18]

Materials. B and A 60% and 70% perchloric acid were ACS grade. Perchloric acid monohydrate (84.8%) was purchased from G. Frederick Smith Chemical Co., Columbus, Ohio. The methyl- and methoxypyridines were reagent grade (Aldrich Chemical Co.) and were purified by distillation through a spinning band column before use: 2,4,6-trimethylpyridine, bp 169° (lit.[9] 169.5–170°); 2,6-dimethylpyridine, bp 143.5° (lit.[19] 144.0°); 2,4-dimethylpyridine, bp 158.5° (lit.[19] 158.4–158.5°); 2-methylpyridine, bp 129° (lit. 129.5°,[19] 129.44° [20]); 4-methylpyridine, bp 145° (lit.[19] 145.2–145.4°); 2,6-dimethoxypyridine, bp 181–182° (lit.[21] 180–182°); and 2-methoxypyridine, bp 142.5° (lit.[22] 141–143°). Aqueous solutions of hypobromous acid were prepared by the method of Derbyshire and Waters.[23]

1,2,4,6-Tetramethylpyridinium perchlorate (1). 2,4,6-Trimethylpyridine and an excess of methyl iodide were refluxed for 3 hr in absolute alcohol.[24] After cooling the crude iodide was isolated by filtration and then dissolved in a minimum of warm water. A saturated solution of aqueous sodium perchlorate was added until no more precipitate formed, then cooled, and filtered. Perchlorate 1 was crystallized from water: mp 204–205° (lit.[25] 204.5–205.5°); ^{1}H nmr spectrum (Varian HA 60 spectrometer) (CF_3CO_2H) δ 7.48 (2, s, ArH), 4.08 (3, s, 1-CH_3), 2.80 (6, s, 2,6-CH_3), 2.57 (3, s, 4-CH_3).

1,2,6-Trimethylpyridinium Perchlorate (2). The above procedure was used to prepare **2** crystallized from 95% alcohol: mp 192.5–193.5° (lit.[25] 192.5–193.5°). ¹H nmr spectrum (CF₃CO₂H) δ 8.18 (1, q, 4-ArH), 7.69 (2, d, 3 ArH), 3.83 (6, s, 2,6-CH₃).

1,2,4-Trimethylpyridinium Perchlorate (4). 2,4-Dimethylpyridine was converted to 1,2,4-trimethylpyridinium iodide as usual. The iodide was converted to the perchlorate by the addition of silver perchlorate following the procedure of Kosower and Klinedinst.[24] Perchlorate **4** was crystallized from absolute alcohol: mp 65.5–66.5°; ¹H nmr spectrum (CF₃CO₂H) δ 8.42 (1, d, 6-ArH), 7.68 (1, s, 3-ArH), 7.63 (1, d, 5-ArH), 4.23 (3, s, 1-CH₃), 2.80 (3, s, 2-CH₃), 2.65 (3, 2, 4-CH₃). *Anal.* for C₈H₁₂ClNO₄: C, 43.35; H, 5.42; N, 6.32. Found: C, 43.50; H, 5.17; N, 6.24.

1,4-Dimethylpyridinium Perchlorate (6). 4-Methylpyridine was converted to perchlorate **6** as described above and crystallized from absolute alcohol: mp 135–136.5° (lit.[26] 130–132°); ¹H nmr spectrum (CF₃CO₂H) δ 8.48 (1, d, 2-ArH), 7.83 (1, d, 3-ArH), 4.39 (3, s, 1-CH₃), 2.70 (3, s, 4-CH₃). *Anal.* for C₇H₁₀NClO₄: C, 40.49; H, 4.86; N, 6.75. Found: C, 40.32; H, 4.93; N, 6.67.

1,2-Dimethylpyridinium Perchlorate (8). 2-Methylpyridine was converted to perchlorate **8** as described and was crystallized from absolute alcohol: mp 154.0–154.5°; ¹H nmr spectrum (CF₃CO₂H) δ 8.62 (1, d, 6-ArH), 8.32 (1, q, 4-ArH), 7.87 (2, m, 3- and 5-ArH), 4.36 (3, s, 1-CH₃), 6.89 (3, s, 2-CH₃). *Anal.* for C₇H₁₀NClO₄: C, 40.49; H, 4.86; N, 6.75. Found: C, 40.63; H, 5.00; N, 6.67.

1-Methylpyridinium Perchlorate. The procedure of Kosower and Klinedinst[24] was used: mp 136.5–137.5° (lit.[24] 135.9–137°); ¹H nmr spectrum (CF₃CO₂H) δ 8.53 (2, d, 2-ArH), 8.68 (1, m, 4-ArH), 8.08 (2, t, 3-ArH), 4.50 (3, s, 1-CH₃).[27]

1-Methyl-2-methoxypyridinium Perchlorate (10). 2-Methoxypyridine was heated (90°) for 1.5 hr with a small excess of dimethyl sulfate. The crude mixture was diluted with absolute alcohol and a solution of sodium perchlorate in absolute alcohol was added until no more precipitate formed. After cooling the crude perchlorate was filtered and crystallized from absolute alcohol: mp 115.5–116°; ¹H nmr spectrum (CF₃CO₂H) δ 8.82–8.20 (2, m, 4,6-ArH), 7.47 (2, m, 3- and 5-ArH), 4.37 (3, s, 2-OCH₃), 4.13 (3, s, 1-CH₃). *Anal.* for C₇H₁₀NClO₅: C, 37.60; H, 4.51; N, 6.26. Found: C, 37.79; H, 4.45; N, 6.25.

1-Methyl-2,6-dimethoxypyridinium Perchlorate (9). 2,6-Dimethoxypyridine was converted to perchlorate **9** following the above procedure. The perchlorate was crystallized from absolute alcohol: mp 171–171.5°; ¹H nmr spectrum (CF₃CO₂H) δ 8.33 (1, t, 4-ArH), 6.97 (2, d, 3-ArH), 4.28 (6, s, 2-OCH₃), 3.89 (3, s, 1-CH₃). *Anal.* for C₈H₁₂ClNO₆: C, 37.88; H, 4.73; N, 5.52. Found: C, 38.03; H, 4.83; N, 5.40.

Kinetic Methods. Solutions of liquid substrates were prepared by weighing a volumetric flask filled with an appropriate concentration of perchloric acid and injecting the substrate into the volumetric flask with a microsyringe and determining the concentration of substrate by weight difference. Substrate concentrations varied from 2 × 10⁻³ to 8 × 10⁻³ M depending on the type of substrate and acid concentration; 3 ml of this solution was pipetted into a 1-cm uv cell and allowed to come to equilibrium for 20 min (25.0 ± 0.1°) in a Coleman 124 spectrometer. The reaction was initiated by the injection of 0.004–0.006 ml of aqueous hypobromous acid of such a concentration so that the final concentration of hypobromous acid in the reaction mixture was ~2 × 10⁻⁴ M. Formation of the pyridinium bromide was followed at a suitable wavelength. The wavelengths used to follow the formation of the pyridinium bromides are for **1**, 290 nm; **2**, 224 nm; **3**, 282 nm; **4**, 280 nm; **5**, 275 nm; **6**, 275 nm; **7**, 224 nm; **8**, 287 nm; **9**, 233; and **10**, 227 nm. Best results are obtained when the half-life of the reaction is kept relatively short (~100 sec). Reactions with relatively long half-lives gave inconsistent infinity readings. The concentration of the perchloric acid was determined by weighing a portion of the reaction mixture, after the reaction was complete, and titrating against standard sodium hydroxide using phenolphthalein as an indicator.

Pseudo-first-order rate coefficients (the aromatic substrate was in at least a tenfold excess) were found graphically by plotting log $(D_\infty - D_t)$ against t which gave a straight line, for about 80% of the reaction, of slope q. D_∞ and D_t are the optical densities at the completion of the reaction and at time t, respectively. Data for a typical kinetic run are given in Table IV. Results are reproducible with errors no greater than 10%.

Product Analysis. To a solution of 2,6-dimethylpyridine (1 × 10⁻³ M) in aqueous perchloric acid (100 ml, 67%) was added an equal molar amount of aqueous hypobromous acid. This was let

Table IV
Example of a Kinetic Run. Bromination of 1,4-Dimethylpyridinium Perchlorate in 71.43% Perchloric Acid at 25.0 ± 0.1° [a]

Time, sec	Optical density, D	
10	0.110	
20	0.171	Slope of log $(D_\infty - D_t)$ *vs.* $t =$
30	0.209	-8.95×10^{-3}
40	0.257	$k_1 = 20.6 \times 10^{-3}$ sec⁻¹
50	0.289	$k_2 = 9.76$ mol⁻¹ sec⁻¹ l.
60	0.314	
70	0.336	
80	0.353	
90	0.367	
100	0.378	
∞	0.428	

[a] [ArH] = 2.11 × 10⁻³ M; [HOBr] = 2 × 10⁻⁴ M.

stand in the dark at room temperature for 2 hr, made basic with sodium carbonate, and extracted three times with chloroform. The chloroform was dried over sodium sulfate and evaporated leaving a product which from the ¹H nmr spectrum contained 18% of the starting material and 82% of a product identified as 3-bromo-2,6-dimethylpyridine from its ¹H nmr (CCl₄) (δ 7.55 (1, d, 4-ArH), 6.74 (1, d, 5-ArH), 2.57 (3, s, 2-CH₃), 2.42 (3, s, 6-CH₃)) which compared favorably with that reported by Abblard, *et al.*[6] The total material isolated (product and starting material) accounted for 78% of the starting material. The presence of starting material may arise because of the oxidation of part of the hypobromous acid to bromine during the mixing of the reactants. These pyridines are soluble in water which may explain why the extraction procedure accounted for only 78% of the starting material.

Bromination of 2,4-dimethylpyridine in 65% perchloric acid by a similar procedure resulted in the isolation of a material which contained 5% starting material; 57% 3-bromo-2,4-dimethylpyridine was identified from its ¹H nmr spectrum (CCl₄) (δ 8.12 (1, d, 6-ArH), 6.83 (1, d, 5-ArH), 2.60 (3, s, 2-CH₃), 2.33 (3, s, 4-CH₃)) and 38% 5-bromo-2,4-dimethylpyridine identified from its ¹H nmr spectrum (CCl₄) (δ 8.37 (1, s, 6-ArH), 6.88 (1, s, 3-ArH), 2.37 (3, s, 2-CH₃), 2.27 (3, s, 4-CH₃)), both of which compare favorably with reported values.[6] Total material isolated accounted for 80% of the starting material.

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Kinetics of Reactions of 1-Substituted 2,4-Dinitrobenzenes with Aniline and Piperidine in Acetone[1]

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The reactions of 1-X-2,4-dinitrobenzenes (X = Cl and F) with aniline and piperidine in acetone were studied. When X = Cl, no base catalysis is found, with k_A = 0.434 $\mp$ 0.011 l. mol^{-1} sec^{-1} (piperidine as nucleophile) and 4.39 $\mp$ 0.25 10^{-5} l. mol^{-1} sec^{-1} (aniline as nucleophile). When X = F the reaction of aniline is catalyzed by aniline and Dabco with linear dependence of k_A on both bases, indicating $k_{-1} \gg k_2 + \sum k_3{}^{\text{Bi}}[\text{B}_i]$.

Primary and secondary amines react with many 1-substituted 2,4-dinitrobenzenes to form 2,4-dinitrophenylamines. Some of these reactions are strongly accelerated by bases, but others are insensitive to base catalysis.[2]

These observations found interpretation in Scheme I.

Scheme I

I
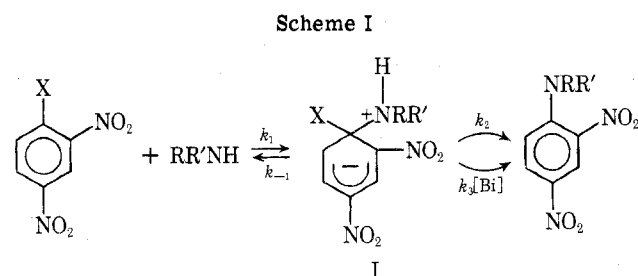
The two-step mechanism was initially proposed by Bunnett.[3] The susceptibility of such a reaction to catalysis by bases depends on the frequency of reversion of intermediate complex I to reactants.[4] According to this mechanism only when expulsion of the leaving group X is at least partially rate determining are reactions of this type subject to catalysis by bases.

Whether or not expulsion of the leaving group is rate limiting depends upon the relative rates of reversion of the intermediate I to reactants and progression to products. Thus base catalysis is observable in those cases where the leaving group is slow to separate from carbon[5] and/or when the amine moiety is easily expelled from the complex.[2a]

In particular, numerous reactions where a secondary amine displaces fluorine from a nitro activated aromatic substrate are base catalyzed ($k_2/k_{-1} \ll 1$) while the analogous displacement of chlorine is not subject to base catalysis[2a] ($k_2/k_{-1} \gg 1$). Even in a nonpolar solvent such as benzene which tends to make all k_2/k_{-1} ratios small compared to more polar solvents, the reaction of piperidine with 1-chloro-4-nitrobenzene[6] or with 1-chloro-2,4-dinitrobenzene[7] is not base catalyzed by piperidine, indicating $k_2/k_{-1} \gg 1$.

For these reasons a report by Bamkole, *et al.,*[8] in which the reaction of piperidine with 1-chloro-2,4-dinitrobenzene

Table I
Reactions of 1-Chloro-2,4-dinitrobenzene with Piperidine and Aniline in Acetone

A. With piperidine at 25.0 $\mp$ 0.1° [a,b]

Piperidine, M	k, 10^3 sec^{-1}	k_A, l. mol^{-1} sec^{-1}
0.00202	0.869	0.430 $\mp$ 0.010
0.00500	2.23	0.442 $\mp$ 0.012
0.0101	4.40	0.436 $\mp$ 0.012
0.0149	6.55	0.438 $\mp$ 0.010
0.0202	8.89	0.440 $\mp$ 0.010
0.202	84.8	0.419 $\mp$ 0.030
		Av 0.434 $\mp$ 0.011

B. With aniline at 50.0 $\mp$ 0.1° [b,c]

Aniline, M	k, 10^6 sec^{-1}	k_A, 10^5 l. mol^{-1} sec^{-1}
0.099	4.48	4.53 $\mp$ 0.20
0.149	6.67	4.47 $\mp$ 0.10
0.198	8.60	4.34 $\mp$ 0.15
0.295	12.42	4.21 $\mp$ 0.30
		Av 4.39 $\mp$ 0.25

[a] Substrate 4.87 × 10^{-5} M. [b] Rate constants are average of two or three determinations, average deviation is given. [c] Substrate 3.20 × 10^{-4} M.

is strongly catalyzed by piperidine in the polar solvent acetone, has been regarded with considerable skepticism.[2a]

We report here a reinvestigation of this and some other reactions studied in the same laboratory. Our results not only fail to confirm the earlier report of piperidine catalysis in the reaction of piperidine with 1-chloro-2,4-dinitrobenzene in acetone, they are also at variance with a similar report on the reaction of aniline with the same substrate and with 1-fluoro-2,4-dinitrobenzene.

Results and Discussion

A. 1-Chloro-2,4-dinitrobenzene. In the reaction of piperidine with this substrate (Table I, A) a 1000-fold increase in the concentration of the base causes no increase in the second-order rate constant, k_A. Similar behavior is