to interconversion of II to III (or a similar process from Figure 2 or eq 5). Shiner has observed just such a trend in α-d's for the solvolysis of 1-phenylethyl chlorides.[22a] Although it is unsettling to realize that one can explain practically any trend in mechanistic parameters, it is important to note that this is the case.

Experimental Section

Rates were determined conductimetrically and solvents prepared as described previously.[17] The nondeuterated chlorides were available commercially and were distilled before use. The deuterated chlorides were prepared by reducing the appropriate ketone with lithium aluminum deuteride and then reacting the resulting alcohol with hydrogen chloride.

The error limits reported in Tables I and II are standard deviations of the mean (i.e., standard deviation divided by the square root of the number of determinations; eq 6). The standard

$$s_m = s/n^{1/2} \tag{6}$$

deviations of the mean for functions such as the α-d and the m values are dependent on errors from two sources (e.g., k_H and k_D) as given by eq 7 and 8 which reduce to eq 9 and 10, respectively, for the α-d and the m values.[41]

$$Q = f(a, b, c,...) \tag{7}$$

$$s_{mQ}^2 = \left(\frac{\partial Q}{\partial a}\right)^2 s_{ma}^2 + \left(\frac{\partial Q}{\partial b}\right)^2 s_{mb}^2 + ... \tag{8}$$

$$s_{m,\alpha\text{-}d}^2 = \frac{s_{mH}^2 k_H}{k_D^2} + \frac{s_{mD}^2 k_H^2}{k_D^3} \tag{9}$$

$$s_{mm}^2 = \left(\frac{1}{2.303Yk_2}\right)^2 s_{m2}^2 + \left(\frac{1}{2.303Yk_1}\right)^2 s_{m1}^2 \tag{10}$$

A common-ion rate depression is indicated by a reduction in the instaneous rate constant as the reaction proceeds. For the reactions reported in this work, depression in the rate constants was not observed. Rather, only a very slight random scatter was observed for the measured rate constants as a function of percent reaction.

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Registry No. 1 (X = H; Y = CH_3), 779-14-6; 1 (X = H; Y = H), 90-99-3; 1 (X = H; Y = Cl), 134-83-8; 1 (X = Cl; Y = Cl), 782-08-1.

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Notes

Bromination of Deactivated Aromatics Using Potassium Bromate

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The bromination of aromatic rings containing electron-withdrawing groups has long been an area of concern.[1-7] Currently, methods used for brominating deactivated aromatics such as nitrobenzene (1), include high-temperature ion-catalyzed brominations,[1] brominations involving acid-catalyzed reactions of hypobromous acid,[2-4] bromination using dibromoisocyanuric acid,[5,6] and other methods.[7] Because of our interest in synthesizing m-bromonitrobenzene (2), which is the precursor to (3-aminophenyl)acetylene,[8] we have investigated the reaction of potassium bromate in sulfuric acid with nitrobenzene. Potassium bromate in sulfuric acid is a convenient and powerful brominating agent capable of brominating aromatic rings containing deactivating groups.

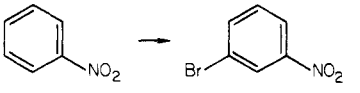
Kraft[9] first reported in 1875 that potassium bromate in sulfuric acid brominated benzene to bromobenzene. Derbyshire and Waters[4] brominated benzoic acid using molecular bromine with potassium bromate as a catalyst. They postulated that bromate functioned by removing bromide ions from the equilibrium (eq 1 and 2) to generate

$$Br_2 + H_2O \rightleftarrows H^+ + Br^- + HOBr \tag{1}$$

$$6H^+ + BrO_3^- + 5Br^- \rightarrow 3Br_2 + 3H_2O \tag{2}$$

hypobromous acids which is a powerful brominating agent in acid solution.[10] Japanese workers[11] reported that potassium bromate brominated benzene in acetic acid in the presence of a catalytic amount of sulfuric acid. Under these conditions, however, nitrobenzene was not brominated. Recently Orban and Körös have reported the bromination of aniline and phenol derivatives using bromate uncatalyzed by metals.[12,13]

Initially, we investigated the bromination of nitrobenzene using the conditions of Derbyshire and Waters.[4] We discovered initially that the bromination reaction (eq 3) was insensitive to the amount of molecular bromine or the amount of potassium bromide used and depended solely on the amount of potassium bromate used.



1 2 (3)

On scale-up, a yield of 88% 3-bromonitrobenzene was obtained after reacting equal molar amounts of potassium bromate and nitrobenzene in 68% sulfuric acid solution

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Table I. Bromination of Aromatics Using Potassium Bromate

aromatic	temp, °C	time, h	product	% yield
nitrobenzene	30	4	*m*-bromonitrobenzene	88
benzoic acid	90	4	*m*-bromobenzoic acid	62
phthalic acid	90	2	4-bromophthalic acid	50
acetophenone	0	16	*o*-bromoacetophenone	10
			m-bromoacetophenone	60
benzene	30	16	bromobenzene	97[a]

[a] GC yield.

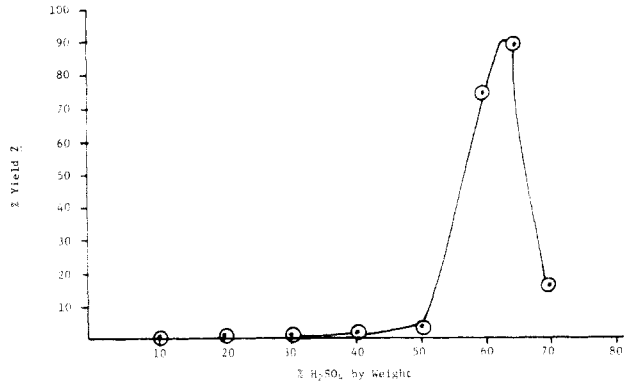

Figure 1. Yield of **2** as a function of percent H_2SO_4 at 30 °C.

(by weight) for 4 h at room temperature (eq 3). Under our reaction conditions, little if any bromine was produced, and control experiments have subsequently shown that bromine did not brominate nitrobenzene.

Acetophenone also reacted with potassium bromate in sulfuric acid to generate a 6:1 mixture of *m*- and *o*-bromoacetophenone. The bromination of acetophenone with bromine occurs normally in the side chain.[14] The formation of *m*- and *o*-bromoacetophenone, in a 6:1 ratio, is identical with the result obtained during the bromination of acetophenone using hypobromous acid in acid solution.[14] This result strongly suggests that hypobromous acid in the presence of sulfuric acid is the active brominating agent in our system also. In support of this assumption, decomposition of potassium bromate (10 mmol) in sulfuric acid in the absence of aromatic produced oxygen (12 mmol), bromine (2.5 mmol), and hypobromous acid (4.5 mmol) (see Tables II and III).

Other aromatics were successfully brominated and these are reported in Table I. No attmept has been made to optimize yield.

The bromination of nitrobenzene was dependent on the concentration of sulfuric acid. Figure 1 is a plot of the yield of *m*-bromonitrobenzene as a function of a concentration of sulfuric acid. *m*-Bromonitrobenzene was produced only above a concentration of 40% *by weight* H_2SO_4. In contrast, reactions of bromate and sulfuric acid with benzene,[9] and with phenol and aniline derivatives,[12] were performed at sulfuric acid concentrations less than 40%. The yield of *m*-bromonitrobenzene increased to about 90% at a H_2SO_4 concentration of 68% and then decreased to 15% at a concentration of 70% H_2SO_4. At acid concentrations of 70%, the decomposition of bromate became uncontrollably rapid. A considerable amount of heat and molecular bromine were produced.

Carbon dioxide (4.6 mmol) was produced during the potassium bromate (10 mmol) bromination of nitrobenzene. Since the only source of carbon in this reaction is the aromatic ring, oxidation of the aromatic ring to CO_2 must be occurring. This is in contrast to the bromate reaction with phenol and aniline derivatives where oxidation products include quinones, quinone imines, and polynuclear aromatic compounds.[15]

In summary, we report that potassium bromate in sulfuric acid successfully brominates a variety of aromatic substrates which contain electron-deactivating substituents. Our data support a mechanism involving hypobromous acid in the presence of sulfuric acid as the brominating agent. This work demonstrates that acid bromate systems are efficient and convenient agents for brominating deactivated aromatics and must be regarded as important reagents for organic synthesis.

Experimental Section

Preparation of *m*-Bromonitrobenzene. Method A. To an 8-L beaker equipped with a mechanical stirrer, thermometer, cooling coil, and cooling bath were added 2.4 L of sulfuric acid, 2.4 L of water, and 306.8 mL of nitrobenzene (3 mol). This was cooled to 25 °C and solid potassium bromate 550 g (3.3 mol) was added in portions at a rate of 50 g every 5 min, while maintaining the temperature between 25 and 35 °C by the rate of addition and by adjusting the cooling bath. After the addition was complete, the reaction was stirred for 3.5 hrs and then filtered. The pale yellow solid was then washed twice with 1.0 L of water and dried under suction overnight. A total of 556 g of product was obtained in 92% yield; mp 48–51 °C. This product by GC consisted of 96% 3-Bromonitrobenzene (lit.[1] mp 51.5–52 °C), 3.6% nitrobenzene, and 0.4% dibromo materials.

Method B. To an 8-L beaker equipped with a mechanical stirrer, thermometer, water-cooling coil, and cooling bath was added 501 g of potassium bromate (3 mol) in 2.1 L of water. To this was added 306.8 mL of nitrobenzene (3 mol). Then over a period of 2 h 2.4 L of concentrated sulfuric acid was added, keeping the temperature between 18 and 28 °C. After the mixture was stirred for an additional 4 h, the product was filtered and washed with 1.0 L of H_2O. A total of 489 g of 3-bromonitrobenzene was recovered, 75% yield, 93% pure by GC.

Preparation of 3-Bromobenzoic Acid. To a three-necked 200-mL flask equipped with a magnetic stirrer, dropping funnel, and thermometer, were added 70 mL of water, 12.3 g of benzoic acid (0.1 mol), and 16.7 g of potassium bromate (0.1 mol). The mixture was heated to 90 °C and 80 mL of concentrated sulfuric acid was added slowly over a period of 70 min. The mixture was then heated further at 90 °C for 2 h. To the product was then added 200 mL of H_2O, and the product was extracted with ether (2 × 100 mL). The ether extract was treated with sodium bisulfite solution then dried over anhydrous magnesium sulfate. The ether was removed in vacuo to give 18.5 g of product. This product consisted of a mixture of 68% 3-bromobenzoic acid and 32% unreacted benzoic acid determined by comparison with authentic sample (GC and NMR comparison); 62% yield.

Preparation of 4-Bromophthalic Acid. To 1.67 g of potassium bromate (0.01 mol) and 1.66 g of phthalic acid (0.01 mol) suspended in 10 mL of water at 90 °C was added 8 mL of concentrated sulfuric acid dropwise with stirring. During the addition, an additional 13 mL of water was added to facilitate stirring. After 2 h at 90 °C, the reaction was cooled and extracted with ethyl ether. The ether extract was dried over anhydrous magnesium sulfate and the ether removed in vacuo. A total of 2.32 g of product was obtained which consisted of 53% 4-bromophthalic acid and 47% unreacted phthalic acid (GC and NMR comparison with authentic samples), 50% yield.

Preparation of 2- and 3-Bromoacetophenone. To a mixture of 8 mL of water and 8 mL of concentrated sulfuric acid was added

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Table II. Oxygen Evolution during the Decomposition of Potassium Bromate in 68% Sulfuric Acid Solution

run	gas evolved,[a,b] mL	atmospheric pressure, KpA	mmol of gas
1	297	96.4	11.7
2	302	98.2	12.1
3	296	98.2	11.9
4	297	99.1	12.1
5	297	98.8	12.0
			av 12.0

[a] Gas obtained by displacement of a volume of mineral oil. [b] 0.01 mol of $KBrO_3$ dissolved in 7 mL of H_2O and reacted with 8 mL of concentrated H_2SO_4 at 0 °C.

Table III. Identification of Products of Decomposition of $KBrO_3$ in 68% Sulfuric Acid

run[a]	Br_2,[b] mmol	HOBr,[c] mmol	BrO_3^-,[d] mmol
1	2.35		
2	2.55		
3		4.45	0.38
4		4.25	0.45
5		4.15	0.48
av	2.45	4.28	0.44

[a] Reaction of 0.01 mol of $KBrO_3$ with 68% sulfuric acid solution at 0 °C. [b] Treatment of CCl_4 extract with excess NaI followed by titration with 0.1 N $Na_2S_2O_3$. [c] Treatment of aqueous phase as in *b* after CCl_4 extraction and after treatment with 0.1 N phenol. [d] Difference before and after 0.1 N phenol treatment calculated as BrO_3^-.

1.2 g of acetophenone (10 mmol). To this was added 1.67 g of potassium bromate (10 mmol) slowly in portions. The reaction mixture became warm and, after addition was complete, was left stirring at room temperature overnight. A total of 1.4 g of product was obtained, 70% yield. Analysis by GC on a 2-ft UCW 952 column at 100 °C indicated that the mixture consisted of *o*- and *m*-bromoacetophenone in a ratio of 1:6 (GC comparison with authentic sample).

Preparation of Bromobenzene. To a solution of 3.33 g of concentrated sulfuric acid and 6.66 g of water was added 0.78 g of benzene. Then 1.67 g of potassium bromate was added in a single portion. The temperature rose slightly from 26 to 30 °C and the mixture was stirred overnight. The product was then diluted with water (50 mL) and extracted with ethyl ether. Analysis on a 2-ft UCW 982 column indicated that bromobenzene in 97% yield was produced (GC comparison with authentic sample).

Reaction of Potassium Bromate with Sulfuric Acid. To 1.67 g of potassium bromate (0.01 mol) in 7 mL of water at 0 °C under nitrogen was added concentrated sulfuric acid dropwise via syringe. After about 5 mL had been added, gas evolution commenced and decomposition of the potassium bromate occurred. A total of 8 mL of H_2SO_4 was added. After the mixture was stirred for 1 h, the total gas volume was measured (Table II) and the gas was anlyzed by mass spectrometry. A total of 12 mmol of oxygen gas was produced which was 98% pure by mass spectrometry. To the remaining solution was then added water (50 mL) and the solution was extracted with carbon tetrachloride (3 × 20 mL) to remove the bromine which produced (Table II). The resulting aqueous solution was then diluted to 100 mL with water and was analyzed for hypobromous acid by treatment with phenol followed by titration.[16] These results are reported in Table III.

A similar experiment was carried out with nitrobenzene present (0.01 mol). The evolved gas (0.0056 mol) was analyzed by mass spectrometry and found to consist of 82% carbon dioxide and 18% oxygen. Identification of the CO_2 was confirmed by reaction with aqueous barium hydroxide solution to form the insoluble barium carbonate.

Acknowledgment. We gratefully acknowledge the technical expertise of Ted Tabacchi.

Registry No. Nitrobenzene, 98-95-3; benzoic acid, 65-85-0; phthalic acid, 88-99-3; acetophenone, 98-86-2; benzene, 71-43-2; *m*-bromonitrobenzene, 585-79-5; 3-bromobenzoic acid, 585-76-2; 4-bromophthalic acid, 6968-28-1; *o*-bromoacetophenone, 2142-69-0; *m*-bromoacetophenone, 2142-63-4; bromobenzene, 108-86-1; potassium bromate, 7758-01-2.

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Effect of the Structure of the Glycon on the Acid-Catalyzed Hydrolysis of Adenine Nucleosides

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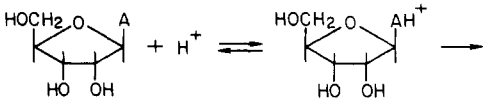
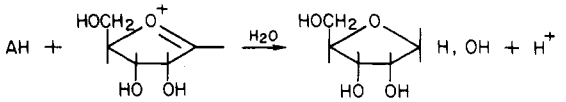
Recent studies[1-6] of the acid-catalyzed hydrolysis of the purine nucleosides support an A1 mechanism, in which the



A = adenine



protonated nucleoside dissociates in the rate-controlling step to a glycosyl carbonium ion and free purine. The glycosyl carbonium ion then extracts a hydroxyl from water to form the sugar. The alternative bimolecular mechanism,[7,9] involving the intermediate formation of a Schiff base, does not have strong experimental support.

The effect of changes in the nucleoside base on the rates of acid-catalyzed hydrolysis has been thoroughly investigated, but a systematic study of the effect of the sugar structure on the lability of the glycosyl–purine bond has not been reported. The acid solvolyses of the β-arabinoside, riboside, and xyloside of adenine have been reported[4] as has that of the 2-deoxyriboside, the dideoxyriboside, and the psicofuranoside.[10] In this paper we report a comprehensive evaluation of the effect of structural changes in the glycon on the rates of hydrolysis of adenosine nucleosides.

In agreement with the reports of others,[4,11] removal of

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