(21) G. Carturan, M. Graziani, and U. Belluco, *J. Chem. Soc. A*, 2509 (1971).
(22) N. A. Dunham and M. C. Baird, *J. Chem. Soc., Dalton Trans.*, 774 (1975).
(23) C. P. Casey, C. R. Cyr, and J. A. Grant, *Inorg. Chem.*, **13**, 910 (1974).
(24) K. S. Y. Lau, P. K. Wong, and J. K. Stille, *J. Am. Chem. Soc.*, **98**, 5832 (1976); **96**, 4983 (1974).
(25) J. Tsuji and K. Ohno, *Tetrahedron Lett.*, 2173 (1967).
(26) Y. Becker and J. K. Stille, *J. Am. Chem. Soc.*, submitted.
(27) M. C. Baird, *J. Magn. Reson.*, **14**, 117 (1974).
(28) The program used to analyze the mass spectrum of the perdeuteriophenylethene was supplied by C. A. Bertelo, written by J. Norton, based on a program published by J. Brauman, *Anal. Chem.*, **38**, 607 (1966).
(29) In contrast with these results, the deuterium scrambling observed in the decomposition of dialkyl Pt(II) complexes was shown to take place exclusively by intramolecular hydride elimination-addition mechanism (G. M. Whitesides, J. F. Gaasch, and E. R. Stedronsky, *J. Am. Chem. Soc.*, **94**, 5258 (1972)).
(30) M. Yagupsky and G. Wilkinson, *J. Chem. Soc. A*, 941 (1970).
(31) J. A. Osborn and G. Wilkinson, *Inorg. Synth.*, **10**, 67 (1967).
(32) Assuming that all equilibria in the exchange reaction were established, the extent of tagging in the recovered lithium chloride-^{36}Cl equals that in the product **1***.
(33) R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960).
(34) T. H. Brown and P. J. Green, *J. Am. Chem. Soc.*, **91**, 3378 (1969); **92**, 2359 (1970).
(35) C. A. Tolman, P. Z. Meakin, D. L. Lidmer, and J. P. Jessen, *J. Am. Chem.*, **96**, 2762 (1974).
(36) The detailed x-ray structural analysis will be published elsewhere.
(37) R. Ugo, A. Pasini, A. Fusi, and S. Cenini, *J. Am. Chem. Soc.*, **94**, 7364 (1972).
(38) J. A. Osborn, F. H. Jardine, J. F. Young, and G. Wilkinson, *J. Chem. Soc. A*, 1711 (1966).
(39) K. Kudo, M. Hidai, and Y. Uchida, *J. Organomet. Chem.*, **33**, 393 (1971).
(40) J. K. Kochi and G. S. Hammond, *J. Am. Chem. Soc.*, **75**, 3443 (1953).

Specific Effects of Chloride Ion in the Hydrolysis of a K-Region Arene Oxide

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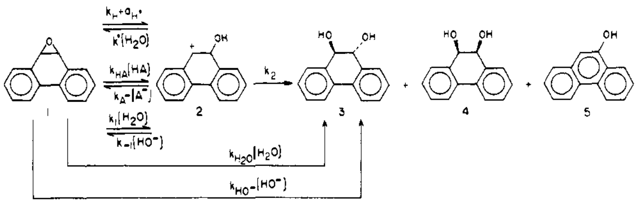
Abstract: The pH-rate profiles for the hydrolysis of phenanthrene 9,10-oxide (**1**) in 1 M KCl, 0.1 M $NaClO_4$, and 1 M $NaClO_4$ solutions in the pH range 4–10 have been determined. The pH-rate profiles indicated that only two mechanisms for hydrolysis of phenanthrene 9,10-oxide in 0.1 M and 1 M $NaClO_4$ solutions are operative in the pH range studied. An acid-catalyzed reaction predominates below pH ~7, and a spontaneous reaction of the epoxide with solvent operates at pH above ~7. The pH-rate profile for the hydrolysis of phenanthrene oxide in 1 M KCl was more complicated, and was explained in part by a specific effect of added chloride ion. A plateau and inflection point in the pH-rate profile were attributed to nucleophilic addition of chloride ion to the epoxide to form an intermediate chlorohydrin. The plateau at pH > 9 results from a reversal of the pH-dependent equilibrium between chlorohydrin and epoxide such that the rate-limiting step becomes the spontaneous reaction of epoxide with solvent. Product analyses throughout the pH range studied were consistent with the mechanism proposed. General acid catalysis in the hydrolysis of **1** by acetic acid and dihydrogen phosphate ion was also studied in $NaClO_4$ and KCl solutions. Variable catalytic constants for general acid catalysis in the hydrolysis of **1** when the solutions were kept at constant ionic strength by KCl were also attributed to specific effects of chloride ion.

K-region arene oxides derived from carcinogenic aromatic hydrocarbons possess both mutagenic[2a,b] and weak carcinogenic activity, and have therefore been implicated as potential causative agents in the carcinogenicity of the parent hydrocarbons.[3] Intermediate arene oxides are further transformed by both enzymatic and nonenzymatic pathways, and knowledge of the solvolytic and nucleophilic reactions of such arene oxides are essential to understanding the more complex processes by which they react under biological conditions.

The elegant kinetic work of Bruice et al.[4] on the hydrolysis of arene oxides throughout the pH range has greatly aided in the understanding of the various mechanisms by which arene oxides can hydrolyze. Many kinetic studies on oxide hydrolyses have been carried out in aqueous solutions containing potassium chloride, and consequently product studies have been carried out in solutions that also contain the same electrolyte.[4,5] We now report that *potassium chloride induces specific effects in the hydrolysis of a typical K-region arene oxide, phenanthrene 9,10-oxide* (**1**).

The pH-rate profile for the hydrolysis of **1** in 1 M KCl solution from pH 3 to 14 has been previously determined.[5b,c] We have verified the kinetic observations reported previously, and the profile for the hydrolysis of **1** in the pH range 4–10 is given in Figure 1. The profile had been interpreted in terms of the general mechanisms outlined in Scheme I. Different rate-limiting steps were assigned to the approximate pH regions 4–5.5, 5.5–7.2, and 8.5–11.5. In the pH region 4–5.5, the dominant reaction is the hydronium-ion-catalyzed process ($k_{H^+}a_{H^+}$). The rate profile in the region 5.5–7.2 was interpreted in terms of general acid catalysis by water ($k_1[H_2O]$), and nucleophilic addition of water to **1** ($k_{H_2O}[H_2O]$) was suggested as being the most reasonable mechanism for hydrolysis at pH 8.5–11.5. An inflection point at pH ~7.2 was attributed to the change in mechanism from general acid catalysis by water to nucleophilic addition of water to **1**.

Scheme I



Although other mechanisms were considered that were consistent with the pH-rate profile, the series of mechanisms presented above were most consistent with the product distributions that were reported throughout the pH range.[5c] Thus, identical product distributions were reported in the pH range ~1-7, which would be consistent with the results expected from specific acid catalysis by H^+ ($k_{H^+}a_{H^+}$) at pH < ~5 and general acid catalysis by water ($k_1[H_2O]$) in the pH range 5.5-7.2. Both mechanisms would generate the same intermediate cation **2**, and therefore identical product distributions would be expected. In the pH range 9-11, however, the *trans*-dihydrodiol **3** was reported to be the principal product (≳92%). Therefore nucleophilic addition of water to **1** was suggested as being the mechanism of hydrolysis of **1** in this pH range. At pH > ~12, the hydrolysis of **1** was catalyzed by ^-OH, and again the predominant product (≳98%) was reported to be the *trans*-dihydrodiol **3**. Therefore nucleophilic addition of hydroxide ion ($k_{OH^-}[^-OH]$) was proposed for the hydroxide-catalyzed term. Additional evidence indicating that water was acting as a nucleophile in the hydrolysis of **1** was provided by a Brønsted plot of the second-order rate constants for addition of ^-OH, CO_3^{2-}, and H_2O to **1**.[6] In this plot, the second-order rate constant for water fell on the line generated by the kinetic parameters for carbonate and hydroxide ions.

Kinetic Studies

In the pH-rate profiles for the hydrolysis of **1** in 0.1 M or 1 M $NaClO_4$ solutions, however, an inflection point at pH 7-8 is not present (Figure 1). The rate data for 0.1 M $NaClO_4$ solutions nicely fit the equation

$$k_{obsd} = k_{H^+}a_{H^+} + k_0 \qquad (1)$$

where k_{H^+} is $(1.15 \pm 0.09) \times 10^2\ M^{-1}\ s^{-1}$ and k_0 is $(2.5 \pm 0.2) \times 10^{-5}\ s^{-1}$.[7] The rate data for hydrolysis of **1** in 1 M $NaClO_4$ solutions were obtained by extrapolating the rates for hydrolysis of **1** in buffered solutions to zero buffer concentration. The extrapolated values thus obtained were also fit to eq 1, and yielded $k_{H^+} = (1.27 \pm 0.16) \times 10^2\ M^{-1}\ s^{-1}$ and $k_0 = (2.8 \pm 0.6) \times 10^{-5}\ s^{-1}$.[7] The more complicated nature of the pH-rate profile for hydrolysis of **1** in 1 M KCl solutions at pH 5.5-8.5 compared to those for hydrolysis of **1** in $NaClO_4$ solutions suggests that potassium chloride induces a specific effect in the hydrolysis of **1**.

Because of the nucleophilic nature of chloride ion, and the susceptibility of **1** to nucleophilic reagents,[6] addition of chloride ion to **1** to yield chlorohydrin **6** in steady-state concentrations (Scheme II) is an attractive mechanism by which the specific effects of chloride ion may be explained. Specific effects of chloride ion have previously been observed in the hydrolysis of indene oxide, and have been attributed to the intermediacy of a chlorohydrin.[8]

An expanded scheme that explains not only the pH-rate profiles for the hydrolysis of **1**, but also the product distributions, is given in Scheme III. Steady-state approximations for intermediates **6** and **7** provide the kinetic expression given in the equation

$$k_{obsd} = k_{H^+}a_{H^+} + \frac{k_2[Cl^-]}{1 + (k_{-2}K_a/k_3a_{H^+})} + k_0 \qquad (2)$$

for the hydrolysis of **1**. The data were fit to eq 2, and yielded values of $k_{H^+} = 1.7 \times 10^2\ M^{-1}\ s^{-1}$, $k_2[Cl^-] = 2.7 \times 10^{-4}\ s^{-1}$, $k_{-2}K_a/k_3 = 10^{-7.0}$ M, and $k_0 = 3.4 \times 10^{-5}\ s^{-1}$. The values of these parameters are in good agreement with the values of similar parameters of an empirical equation from the previous study.[5c]

The pH-rate profile for hydrolysis of **1** in 1 M KCl solutions may therefore be qualitatively interpreted in the following way. In the pH region 4.0-5.5, $k_{H^+}a_{H^+}$ is the dominant term of eq 2, and therefore the hydrolysis of **1** in this pH region is hydronium ion catalyzed. In the pH region 5.5-7.2, nucleophilic addition of chloride ion to **1** to yield **7** becomes competitive with other reaction pathways. Protonation of **7** provides chlorohydrin **6**, which can solvolyze in a first-order process (k_3) to give cation **2**, the same intermediate generated by the acid-catalyzed process.[9] In the pH region 7.2-8.5, however, the pH-dependent equilibrium between **1** and **6** (Scheme III) shifts sufficiently to the left until finally $k_0[\mathbf{1}] > k_3[\mathbf{6}]$. The k_0 term then becomes the dominant term of eq 2, and a plateau is observed in the pH-rate profile at pH > 9.

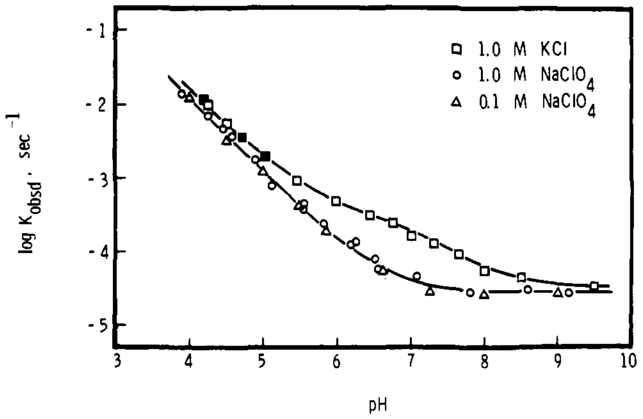
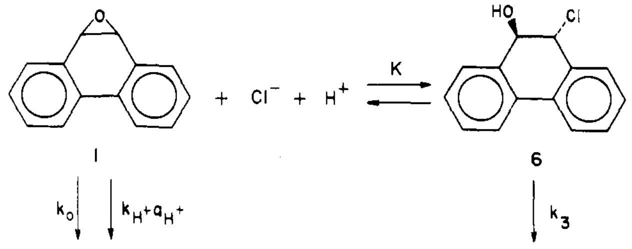
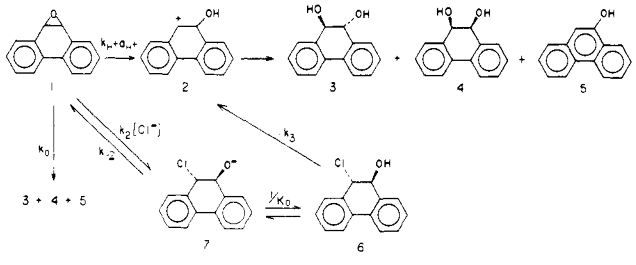


Figure 1. Plots of log k_{obsd} vs. pH for the hydrolysis of phenanthrene 9,10-oxide (**1**) in $NaClO_4$ solutions (10^{-4} M EDTA), 30 °C. All data points were obtained with the aid of a Radiometer pH-stat except for those indicated by ○ and ■, which were obtained from series of buffer solutions at constant pH, extrapolated to zero buffer concentration. The solid lines are theoretical, based on eq 1 for 1 M $NaClO_4$ and eq 2 for 1 M KCl.

Scheme II



Scheme III



Product Studies

Product distributions from the hydrolysis of **1** as a function of pH in 1.0 M KCl and 0.1 M $NaClO_4$ solutions are presented in Table I. Product studies were complicated somewhat because of low solubility of **1** in water, and the fact that **1** rearranges under gas chromatographic conditions to 9-phenanthrol (**5**). When gas chromatography (GLC) was used to analyze product mixtures, therefore, the hydrolysis reactions were carried out for a minimum of 10 half-lives in well-stirred solutions before analyses were conducted. High-pressure liquid chromatography (HPLC) was subsequently utilized to analyze for the product ratios from the hydrolysis of **1** at several pH values. Not only were all of the main products nicely resolved, but also the reactant **1** was stable to the analytical conditions (Figure 2).

Table I. Product Distributions from the Hydrolysis of Phenanthrene 9,10-Oxide (**1**) as a Function of pH in 0.1 M $NaClO_4$ and 1.0 M KCl Solutions at 30 °C[a]

Solvent[b]	pH[c]	*trans*-9,10-Dihydroxy-9,10-dihydrophenanthrene (**3**)	*cis*-9,10-Dihydroxy-9,10-dihydrophenanthrene(**4**)	9-Phenanthrol (**5**)[d]
0.1 M $NaClO_4$	3.2[e]	14	9	77
	4.0	13	7	80
	5.0	17	4	79
	6.0	27	6	67
	6.5	46	2	52
	6.8	58	1	41
	11.0-10.8	66	<1	33
	11.0-10.9[e]	65	2	33
1.0 M KCl	4.0	12	6	82
	5.0	12	6	82
	6.5	11	4	85
	7.0	14	3	83
	11.0-9.6	78	≲1	22
	11.0-10.9[e]	84	2	14

[a] Products were analyzed by gas chromatography (GLC) on a 4.5 ft, 3% Apiezon L column unless otherwise indicated. HPLC analyses of the product mixtures at pH 3.2 (0.1 M $NaClO_4$), 11.0-10.9 (0.1 M $NaClO_4$), and 11.0-10.9 (1 M KCl) indicated the presence of 5-8% total of four to five unidentified materials that were not resolved on GLC. Areas of the three product peaks due to the products listed, excluding any peaks due to unidentified materials, were normalized to 100. [b] All reactions solutions contained 10^{-4} M EDTA. [c] The pH was maintained with a Radiometer pH stat to within ca. ±0.03 pH units of the value listed unless otherwise stated. [d] Significant amounts of phenanthrene-9,10-dione were isolated at pH > 7. The yields of **5** listed correspond to the total amount of **5** and the 9,10-dione. [e] The hydrolysis reaction was carried out with [3-^{3}H]-**1**. Products were separated by HPLC, and analyzed for tritium by liquid scintillation counting.

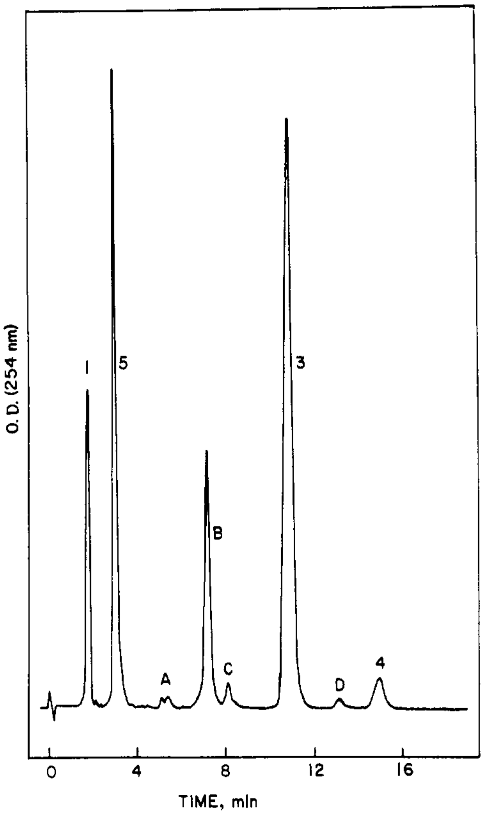
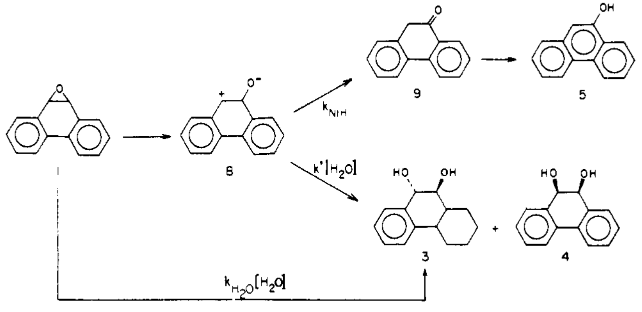


Figure 2. HPLC tracing of the product mixture from hydrolysis of **1** in 1 M KCl solution (pH 11) at 30 °C under argon for 50 h. Peak B is due to phenanthrene-9,10-dione. Peaks labeled A, C, and D are from unidentified products.

Scheme IV



At pH 4-5 in both 0.1 M $NaClO_4$ and 1 M KCl solutions, the hydronium-ion-catalyzed process is the dominant mechanism for the hydrolysis of **1**. The product distribution from hydrolysis of **1** in this pH range in 0.1 M $NaClO_4$ solution was determined by GLC to be 13-17% of **3**, 4-7% of **4**, and 79-80% of **5**. These values agree well with the values of 13% of **3**, 9% of **4**, and 73% of **5** from the hydrolysis of **1** at pH 3.2, determined by HPLC analysis of the product mixture.[10] The product distribution from the hydrolysis of **1** at pH 4-5 in 1 M KCl solution was determined by GLC to be ca. 12% of **3**, 6% of **4**, and 82% of **5**. These values compare with the yields published previously[5c] of 18% of **3**, 7-10% of **4**, and 72-74% of **5** from hydrolysis of **1** under the same conditions.

At pH 11 in 0.1 M $NaClO_4$ solution, the k_0 term (eq 1) is much greater than the $k_{H^+}a_{H^+}$ term. The product distribution from the k_0 mechanism (at pH 11) in 0.1 M $NaClO_4$ solution was determined by HPLC to be 60% of **3**, 2% of **4**, 30% of **5**, and 8% of five unidentified materials. The formation of a significant amount of **5** may result from the intermediacy of a dipolar species **8** (Scheme IV).[4] Hydride migration (k_{NIH}) would lead to 9-phenanthrone (**9**), the precursor of **5**. The large *trans*-*cis*-dihydrodiol ratio from the k_0 process suggests that if *trans*-dihydrodiol **3** is formed mainly from the dipolar intermediate **8**, then collapse of solvent must occur preferentially from the side opposite the negatively charged oxygen in **8**. This mechanism is unlikely, however, since evidence was presented in the earlier paper[5c] that suggested that the k_0 mechanism for hydrolysis of **1** in 1 M KCl solution involved nucleophilic attack of water on neutral substrate. Therefore, direct displacement by water on neutral epoxide ($k_{H_2O}[H_2O]$, Scheme IV), competing with formation of dipolar intermediate **8** (with $k'[H_2O] < k_{NIH}$), is an attractive mechanism for explaining the large *trans*-/*cis*-dihydrodiol ratio from hydrolysis of **1** by the k_0 mechanism in 0.1 M $NaClO_4$ solution.

As reported earlier, the product ratios from hydrolysis of **1** in 1 M KCl solutions in the pH range 4-7 are very similar, although the pH-rate profile (Figure 1) indicates that there

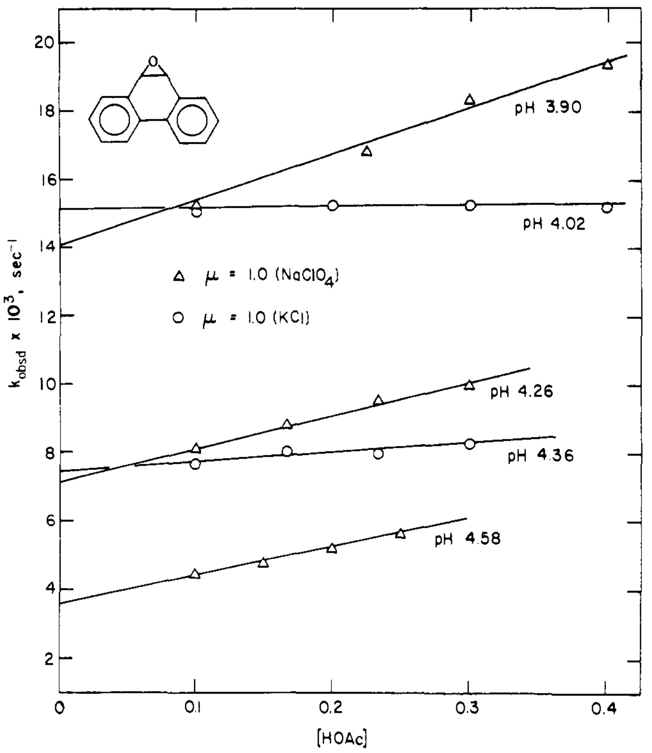


Figure 3. Plots of k_{obsd} vs. [HOAc] for the hydrolysis of phenanthrene 9,10-oxide (1) in water solutions at 30 °C.

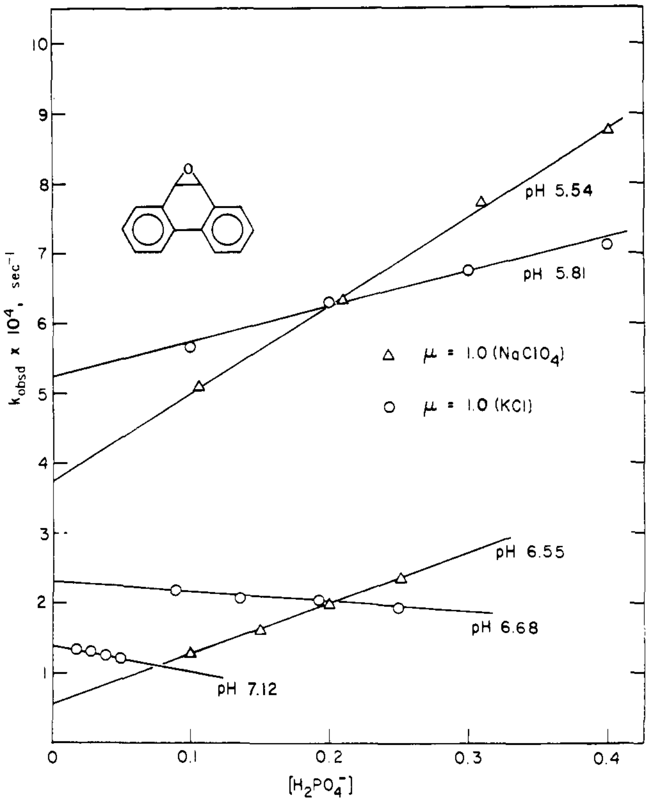


Figure 4. Plots of k_{obsd} vs. [$H_2PO_4^-$] for the hydrolysis of phenanthrene 9,10-oxide (1) in water solutions at 30 °C. The slopes of the NaClO$_4$ lines at pH 5.54 and 6.55 were found to be 1.26×10^{-3} and 0.70×10^{-3} M^{-1} s^{-1}, respectively.

is a change in rate-limiting steps in this region. Scheme III provides a rationale for this observation. As the pH of the reaction solution increases, the rate-limiting step changes from hydronium ion catalysis to nucleophilic addition of chloride ion. Protonation of **7** yields the chlorohydrin **6**, which solvolyzes via a first-order process (k_3) to yield cation **2**, the same intermediate formed via the k_{H^+} process. In the pH range 5-7, (k_3[**6**] + $k_{H^+}a_{H^+}$[**1**]) ≫ k_0[**1**]. Since the k_3 and k_{H^+} processes proceed through a common intermediate **2**, then similar product distributions should result.

The product distribution from the hydrolysis of **1** at pH 11 in 1 M KCl solution was found, by GLC analysis, to contain significant amounts (ca. 20%) of 9-phenanthrol and its oxidation product, phenanthrene-9,10-quinone. At pH 9-11 in 1 M KCl solution, it was originally reported[5c] that only 0-8% of 9-phenanthrol was obtained in the hydrolysis of **1**. The product distributions determined by GLC in the hydrolysis of *1* at pH 9-11 in 1 M KCl solution are uncertain because of the long reaction times (ca. 3 days) required before GLC analyses can be made, and the fact that organic solutions of **3**, **4**, and **5** undergo some decomposition upon standing for several days. To resolve the above uncertainties, the product distribution from hydrolysis of [3-^{3}H]-**1** at pH 11 in 1 M KCl solution was determined by HPLC at times corresponding to 55%, 74%, 87%, and 95% reaction. The product yields determined in this manner were found to be 78-82% of **3**, 1-3% of **4**, 12-16% of **5**, and 3-5% of four unknown materials. The product distribution from the hydrolysis of **1** at high pH determined by HPLC is more reliable than the distribution determined by GLC because the starting material was stable to analytical conditions, several minor products could be resolved, and all products could be separated by HPLC and analyzed for tritium by liquid scintillation counting. The yields reported in Table 1 for 1 M KCl at pH 11 represent the average values observed.

The fact that the k_0 process for hydrolysis of **1** in 1 M KCl solution at pH 11 yields somewhat more phenol product **5** than reported previously does not change significantly the mechanism proposed in the earlier paper for this process, namely nucleophilic addition of solvent to neutral substrate **1** to give *trans*-dihydrodiol **3**, the major product. The minor phenolic product **5** may arise from a competing mechanism that involves formation of a dipolar intermediate (Scheme IV). The yield of 9-phenanthrol (**5**) from the hydrolysis of **1** in 0.1 M NaClO$_4$ solution at pH 11 appears to be greater than the yield of **5** from **1** in 1 M KCl solution at the same pH. Additional work is required to clarify this observation.

General Acid Catalysis

The rates of hydrolysis of **1** were also determined in series of solutions with constant pH values, but varied buffer concentrations. Catalytic constants for buffer catalysis are generally obtained from the slopes of plots of k_{obsd} vs. [HA]. To minimize salt effects, an electrolyte such as KCl is generally added such that the ionic strengths of all solutions are constant. Figures 3 and 4 contain plots of k_{obsd} vs. buffer concentrations for acetic acid and phosphate buffers in which the ionic strengths of the solutions have been maintained at 1.0 by addition of KCl or NaClO$_4$. It is apparent from Figures 3 and 4 that the catalytic constants for buffer catalysis depend markedly on whether the added electrolyte is KCl or NaClO$_4$. In Figure 3, the catalytic constants for buffer catalysis by acetic acid are significantly larger in NaClO$_4$ solutions than in KCl solutions. The fact that the catalytic constants for buffer catalysis are smaller in solutions held at constant ionic strength by KCl indicates that there may be a chloride component in the acid-catalyzed term for hydrolysis of **1**. The slopes of plots of k_{obsd} vs. [HOAc] for hydrolysis of **1** in NaClO$_4$ solutions ($\mu = 1.0$) at the pH values 3.90, 4.26, 4.58, and 4.89 were found to be 0.014, 0.010, 0.0082, and 0.0079 M^{-1} s^{-1}, respectively.

The differences in catalytic constants for buffer catalysis by $H_2PO_4^-$ in KCl and NaClO$_4$ solutions are even more striking. The slopes of the buffer plots of k_{obsd} vs. [$H_2PO_4^-$]

for solutions held at constant ionic strength by $NaClO_4$ are significantly greater than the corresponding slopes for solutions held at constant ionic strength by KCl (Figure 4). In fact, the rates for hydrolysis of **1** at pH 6.68 and 7.12 actually *decreased* with increasing buffer concentration when the added electrolyte was KCl. We attribute the variable slopes of k_{obsd} vs. $[H_2PO_4^-]$ for the KCl solutions to the specific effects of chloride ion. At the higher pH values, as the buffer solutions become more dilute, the rate for hydrolysis of **1** increases because of the chloride term of eq 2. The general acid catalytic constants obtained from hydrolysis of **1** in solutions held at constant ionic strength by KCl, therefore, can be in serious error in those pH regions where specific effects of chloride ion are appreciable.

The presence of a specific effect of potassium chloride on the rates and product distributions from hydrolysis of phenanthrene 9,10-oxide (**1**) reinforces our earlier conclusion[8] that such studies should not be conducted in solutions containing nucleophilic salts such as KCl unless appropriate control experiments are conducted to rule out the presence of specific salt effects. If constant ionic strength is required, a less nucleophilic salt such as $NaClO_4$ should be used.[11] Thus, several of the catalytic constants for general acid catalysis[5c,12] in the hydrolysis of arene oxides determined in solutions kept at constant ionic strength by addition of KCl are subject to error introduced by specific effects of chloride ion.

Experimental Section

Kinetic Studies. A stock solution containing 6 mg of phenanthrene 9,10-oxide[5c] (**1**) in 5.0 mL of dry dioxane was prepared. For each kinetic run, approximately 20 μL of the stock solution of **1** was added to 3.0 mL of reaction solution in the thermostated cell compartment (30.0 ± 0.2 °C) of either a Cary 16K or Gilford 2400 spectrophotometer. The appearance of products was monitored at 255 nm.

The pH-rate profiles were generated from kinetic runs in 0.1 M $NaClO_4$ and 1.0 M KCl solutions containing 10^{-4} M EDTA. The solutions were held at constant pH with a Radiometer pH-stat assembly, and were maintained under a nitrogen atmosphere.

The buffering reagents were available commercially, and were used without further purification. Buffered solutions were generally prepared by adding standard acid or base solutions to base or acid forms of the buffer, respectively. The ionic strengths of the solutions were maintained at 1.0 by addition of either $NaClO_4$[13] or KCl. Second-order rate constants for general acid catalysis were obtained from the slopes of least-squares plots of k_{obsd} vs. [HA]. Generally four solutions of a buffer, at constant pH[14] but varied buffer concentrations, were utilized to obtain each value of a given second-order rate constant.

The pseudo-first-order rate constants (k_{obsd}) were obtained by nonlinear regression analysis of the data, for each kinetic run, by a Wang 700 Calculator-Computer.

Product Studies. The distributions from hydrolysis of **1** were determined in a manner described previously.[5c] A stock solution containing 5.2 mg of **1** in 0.5 mL of dry dioxane was prepared. For the pH range 4–7, an 8-μL aliquot of the stock solution was injected into 10.0 mL of either 1 M KCl or 0.1 M $NaClO_4$ solution maintained at constant pH with a Radiometer pH stat to within ca. ±0.03 pH units of the value listed unless otherwise stated.[15] The solution was stirred and maintained at 30.0 ± 0.1 °C under a nitrogen atmosphere for at least 10 half-lives.

In a typical isolation procedure, the pH of the reaction solution was adjusted to ca. 7 or lower, and the solution was extracted with 2.0 mL of ethyl acetate. The ethyl acetate solution was concentrated and analyzed by gas chromatography on a 5 ft × 1/8 in. diameter, 3% Apiezon L column. The relative yields listed correspond to relative areas due to each product on a GLC tracing, and are subject to some error because of minor overlapping of the GLC peaks. At pH > 7, significant amounts of phenanthrene-9,10-dione were formed from oxidation of 9-phenanthrol. The yields of 9-phenanthrol (**5**) listed in Table I correspond to the total amount of **5** and the 9,10-dione formed in a given reaction.

The product mixtures that were analyzed by high-pressure liquid chromatography were chromatographed on a 7.9 mm × 25 cm Du Pont Zorbax Sil column. The products were eluted with a petroleum ether (88)–dioxane (10)–isopropyl alcohol (2) solvent mixture at 1500 psi, ca. 6 mL/min.

The isotopically labeled [3-^{3}H]-**1**[16] was prepared by previously published procedures. The yields of the hydrolysis products from [3-^{3}H]-**1** were determined by separating the products by HPLC, and analyzing each product for tritium by liquid scintillation counting.

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References and Notes

(1) (a) University of Maryland Baltimore County; (b) National Institutes of Health.

(2) (a) B. N. Ames, P. Sims, and P. L. Grover, *Science*, **176**, 47 (1972); (b) P. G. Wislocki, A. W. Wood, R. L. Chang, W. Levin, H. Yagi, O. Hernandez, P. M. Dansette, D. M. Jerina, and A. H. Conney, *Cancer Res.*, **36**, 3350 (1976); (c) W. Levin, A. W. Wood, H. Yagi, P. M. Dansette, D. M. Jerina, and A. H. Conney, *Proc. Natl. Acad. Sci. U.S.A.*, **73**, 243 (1976).

(3) (a) D. M. Jerina and J. W. Daly, *Science*, **185**, 573 (1974); (b) P. Sims and P. L. Grover, *Adv. Cancer Res.*, **20**, 165 (1974).

(4) (a) G. J. Kasperek and T. C. Bruice, *J. Am. Chem. Soc.*, **94**, 198 (1972); (b) G. J. Kasperek, T. C. Bruice, H. Yagi, and D. M. Jerina, *J. Chem. Soc. Chem. Commun.*, 784 (1972); (c) T. C. Bruice and P. Y. Bruice, *Acc. Chem. Res.*, **9**, 378 (1976), and references cited therein.

(5) (a) D. M. Reuben and T. C. Bruice, *J. Am. Chem. Soc.*, **98**, 114 (1976); (b) P. Y. Bruice, T. C. Bruice, H. G. Selander, H. Yagi, and D. M. Jerina, *ibid.*, **96**, 6814 (1974); (c) P. Y. Bruice, T. C. Bruice, P. M. Dansette, H. G. Selander, H. Yagi, and D. M. Jerina, *ibid.*, **98**, 2965 (1976); (d) J. W. Keller and C. Heidelberger, *ibid.*, **98**, 2328 (1976); (e) J. W. Keller, C. Heidelberger, F. A. Beland, and R. G. Harvey, *ibid.*, **98**, 8276 (1976); (f) D. L. Whalen, *ibid.*, **95**, 3432 (1973); (g) D. L. Whalen and A. M. Ross, *ibid.*, **96**, 3678 (1974).

(6) P. Y. Bruice, T. C. Bruice, H. Yagi, and D. M. Jerina, *J. Am. Chem. Soc.*, **98**, 2973 (1976).

(7) The values for k_{H^+} and k_0 were obtained from a weighted least-squares plot of k_{obsd} vs. a_{H^+}. The activity of hydronium ion was taken to be that measured by the glass electrode.

(8) D. L. Whalen and A. M. Ross, *J. Am. Chem. Soc.*, **98**, 7859 (1976).

(9) The hydrolysis of 1-chloroindan-2-ol takes place by a first-order process from pH 5 to 8.5. See ref 8.

(10) Four other minor products constituting 5% of the product mixture were also observed. These minor products were not resolved on GLC, and may account for some of the minor discrepancies between the GLC and HPLC analyses.

(11) Some difficulties are encountered in measuring the pH of concentrated perchlorate solutions: D. B. Dennison, G. H. Gettys, D. G. Kubler, and D. Shepard, *J. Org. Chem.*, **41**, 2344 (1976).

(12) P. Y. Bruice and T. C. Bruice, *J. Am. Chem. Soc.*, **98**, 2023 (1976).

(13) Because of the difficulties of measuring the pH of concentrated sodium perchlorate solutions (see ref 11), buffer solutions were generally not diluted below a total buffer concentration of ca. 0.1 M. Stable pH readings were obtained on all kinetic solutions.

(14) The pH values of the phosphate buffer solutions of the same buffer ratio but varied buffer concentrations were adjusted to the pH of the most concentrated solution by addition of standard base if the pH range of the series of solutions was more than 0.03 units.

(15) Product determinations in which the concentrations of **1** were greater than that listed presented problems because of the relatively low solubility of **1** in water.

(16) H. Yagi, P. M. Dansette, and D. M. Jerina, *J. Labelled Compd. Radiopharm.*, **12**, 127 (1976).