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Synthesis and Hydrolysis of a *cis*-Chlorohydrin Derived from a Benzo[*a*]pyrene 7,8-Diol 9,10-Epoxide

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(±)-7β,8α-Dihydroxy-9β,10β-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene (**DE-1**) undergoes reaction with anhydrous HCl in dioxane to yield predominantly (∼94%) a single chlorohydrin. This chlorohydrin was assigned structure **9**, in which the chloro goup at C-10 is located cis to the C-9 hydroxyl group, on the basis of its ^{1}H NMR spectrum. This result is in contrast to the reaction of a diastereomeric benzo[*a*]pyrene 7,8-diol 9,10-epoxide (**DE-2**) with HCl, which yields only *trans*-chlorohydrin **8**. The hydrolysis of *cis*-chlorohydrin **9** in 10:90 dioxane−water solutions yields the same ratio of tetrols (∼89% cis/11% trans) as that formed by acid-catalyzed hydrolysis of **DE-1**. This result again contrasts with the hydrolysis of *trans*-chlorohydrin **8**, which undergoes hydrolysis to give tetrols in a ratio different from that from acid-catalyzed hydrolysis of **DE-2**. A marked common ion rate depression in the hydrolysis of *cis*-chlorohydrin **9** is observed, which shows that hydrolysis proceeds via an intermediate carbocation that has a sufficient lifetime to be trapped by external chloride ion. The observation that **DE-1** reacts with HCl to give mainly the *cis*-chlorohydrin is rationalized by quantum chemical calculations that suggest that the *cis*-chlorohydrin is more stable than the epimeric *trans*-chlorohydrin.

Introduction

The rates[1] and products of the hydrolysis reactions[1−4] of the 7,8-dihydroxy-9,10-epoxide metabolites (**DE-1** and **DE-2**, benzylic 7-hydroxyl group and epoxide oxygen cis and trans, respectively) of the environmental carcinogen benzo[*a*]pyrene have been studied over a wide pH range. At pH < ∼6 for **DE-1** and pH < ∼7.5 for **DE-2** in 10:90 dioxane−water, both diol epoxides react with H^+ to form triol carbocations, which react with water to form mixtures of cis 9,10- and trans 9,10-tetrols. Whereas acid-catalyzed hydrolysis of **DE-1** yields mostly cis tetrol **3** and only a minor amount of trans tetrol **4** (Scheme 1), **DE-2** reacts to form mostly trans tetrol **6** and only a minor amount of cis tetrol **7** (Scheme 2). These marked differences in product distributions are rationalized in terms of axial attack of solvent on individual conformations of the intermediate carbocations **2** and **5**.[5,6]

A most intriguing observation is that the acid-catalyzed hydrolysis of **DE-2** in solutions containing chloride ion, however, yields significantly more cis tetrol (∼35%) than formed from the reaction of **DE-2** in the absence of chloride ion.[7] It was proposed that a *trans*-chlorohydrin **8** is formed as a reactive intermediate and that **8** hydrolyzes to form cis and trans tetrols in a ratio different from that formed from reaction of **DE-2** in the absence of chloride ion (Scheme 2). *trans*-Chlorohydrin **8** was independently synthesized, and a study of its hydrolysis reactions supported the proposal that it is an intermediate in the acid-catalyzed hydrolysis of **DE-2** in solutions containing chloride ion.[8,9] Kinetic and product studies of the reactions of **DE-2** in dioxane−water solutions containing chloride, bromide, and iodide ions showed that in these halide solutions at pH < ca. 5, the reaction of **DE-2** occurs by rate-limiting carbocation formation, followed by capture of the intermediate carbocation by halide ion.[10]

From the observation that the reaction of trans chlorohydrin **8** shows a marked common ion rate depression upon reaction in solutions containing chloride ion, it was concluded that tetrol products from its hydrolysis also

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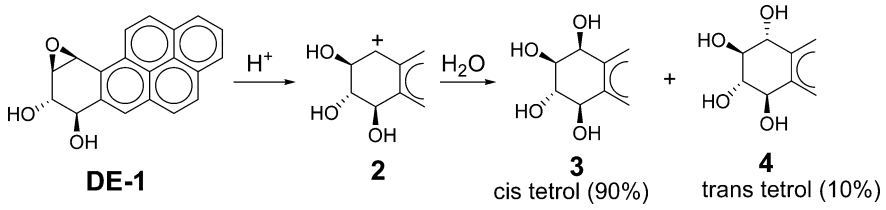

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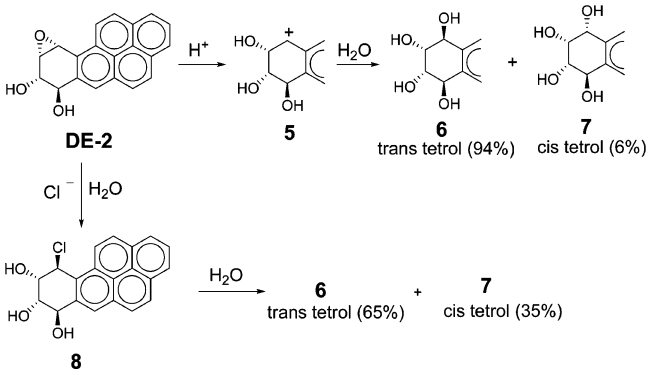

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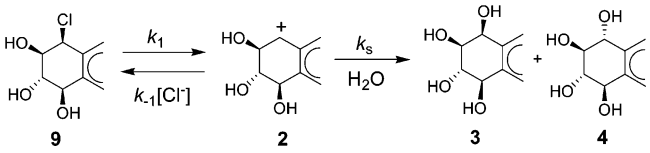

result from reaction of carbocation **5** with water.[11] The observation that diol epoxide and *trans*-chlorohydrin hydrolyze to cis and trans tetrols in different ratios was rationalized by mechanisms in which each reacts via different distributions of two conformations of carbocation **5**, with an energy barrier separating the two conformations that is greater than the energy barrier for reaction of each carbocation conformation with solvent.[11]

trans-Chlorohydrin **8** was first synthesized by the reaction of **DE-2** with LiCl/HOAc in THF.[8,9] This reaction was first thought to specific for the synthesis of *trans*-chlorohydrins from epoxides,[12] and the observation that only *trans*-chlorohydrin **8** was formed from **DE-2** under these conditions appeared to confirm the earlier conclusion that LiCl/HOAc/THF was a reagent specific for synthesis of *trans*-chlorohydrins from epoxides. However, a later study showed that both *cis*- and *trans*-chlorohydrins are formed from the reactions of aryl epoxides with this reagent, and in some cases where the aryl group greatly stabilizes charge at the benzylic position, *cis*-chlorohydrin may even be the major product.[13] The reaction of **DE-2** with HCl in anhydrous THF, a reagent that might also be expected to form both *cis*- and *trans*-chlorohydrins, cleanly yields the *trans*-chlorohydrin **8**.[11] The hydrolysis reactions of **DE-2** to form tetrols and its reaction with HCl to form a chlorohydrin are therefore unusual in that S_N1 addition of a nucleophile to the carbocation formed from reaction of **DE-2** with H^+ yields mostly trans products, the same products expected from concerted S_N2 attack of a nucleophile at the benzylic position of **DE-2**.

In contrast to the observation that the acid-catalyzed hydrolysis of **DE-2** yields mostly trans tetrol (95%), the acid-catalyzed hyrolysis of **DE-1** yields mostly cis tetrol (90%).[1] We now report that the reaction of **DE-1** with HCl in anhydrous THF yields mostly (∼94%) the *cis*-chlorohydrin **9**. The mechanism of hydrolysis of **9** in dioxane−water solutions (cf Scheme 3) is described.

Results and Discussion

Reaction of DE-1 with HCl in Anhydrous THF. The reaction of **DE-1** with HCl in anhydrous THF to yield mostly (∼94%) *cis*-chlorohydrin **9** is in marked contrast to the reaction of **DE-2** with HCl/THF to give **8**, a trans chlorohydrin (>95%). The assignment of cis 9,10-stereochemistry to **9** is based on the vicinal H-C(8)−C(9)-H coupling constant, which is large. In contrast, all of the coupling constants in a 9,10-trans-opened diol epoxide are relatively small.[4] Further confirmation of the cis stereochemistry of **9** is provided by its pH−rate profile in 70:30 dioxane−water. *trans*-Chlorohydrins generally undergo base-catalyzed epoxide formation rather rapidly at pH > 10,[14] which was observed for the *trans*-chlorohydrin **8**.[11] The rate of reaction of **9** remains constant (±2%) from apparent pH 6.5−10.1, and only a very minor increase in rate (∼15%) is observed at apparent pH 11.2.

Quantum chemical calculations of individual conformations of *cis*- and *trans*-chlorohydrins **9** and **8** provide insight on the observation that the predominant product from reaction of **DE-1** with HCl is *cis*-chlorohydrin with conformation **9a**. In Figure 1 are structures of two conformations of the *cis*-9,10-chlorohydrin, **9a** and **9b**, optimized at the B3LYP/6-31G* level of theory. In Figure 2 are two conformations of the *trans*-9,10-chlorohydrin, **10a** and **10b**, optimized at the same level of theory. Other conformations of **9** and **10** with the hydroxyl groups in different orientations were also optimized at lower levels of theory but were calculated to be higher in energy.

The relative energies of **9a**, **9b**, **10a**, and **10b** are calculated to be 0.0, +9.0, +3.1, and +2.5 kcal/mol, respectively. Thus, the *cis*-chlorohydrin conformation **9a** is calculated to be much more stable than cis conformation **9b** and also more stable than either of the two *trans*-chlorohydrin conformations **10a** and **10b**. Although these structures are the result of gas-phase calculations, and therefore the effects of solvation are not accounted for, it seems reasonable to assume that the transition state leading to the more stable cis conformation **9a**, whether

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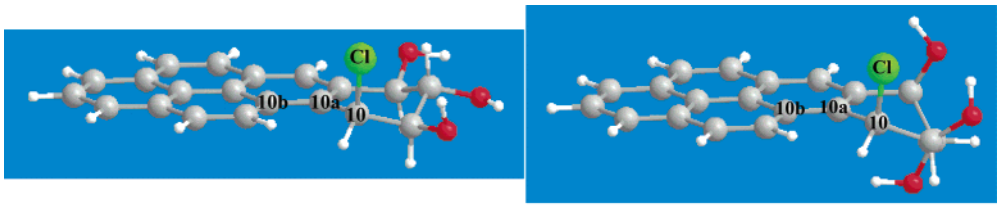
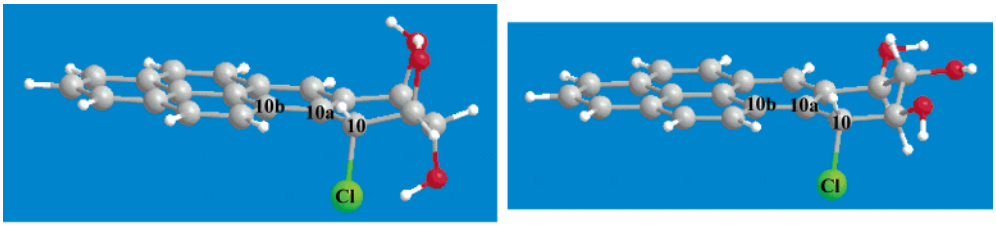


9a 9b

FIGURE 1. Structures of *cis*-9,10-chlorohydrin conformations **9a** and **9b**, calculated at the DFT B3LYP/6-31G* level of theory.



10a 10b

FIGURE 2. Structures of *trans*-9,10-chlorohydrin conformations **10a** and **10b**, calculated at the DFT B3LYP/6-31G* level of theory.

the reaction is concerted or occurs via ion pairs, is simply lower in energy because it reflects the greater stability of the product. A similar argument most likely accounts for the fact that **DE-2** reacts with HCl/THF to give the more stable *trans*-chlorohydrin **8**.[11]

The calculated structures **9a** for *cis*-chlorohydrin and **10a** for *trans*-chlorohydrin are half-chair conformations in which all bonds of the angular ring are staggered and the C−Cl bonds occupy pseudoaxial positions. Structures **9b** and **10b** are significantly distorted from half-chair conformations, however, and there are considerable eclipsing interactions of the C(9) and C(10) groups. The distortions from half-chair conformations are attributed to unfavorable steric interactions between the C(10) chloro group and the bay region C(11)−H if the geometries of **9b** and **10b** were changed into those of half-chair conformations. The Cl−C(10)−C(10a)−C(10b) dihedral angles of **9a**, **9b**, **10a**, and **10b** are calculated to be −75.0°, −78.8°, 72.6°, and 62.6°, respectively.

Hydrolysis of *cis*-Chlorohydrin 9. Chlorohydrin **9** is much too reactive in mostly aqueous solutions for its rate to be measured without using stopped-flow technique. However, its rate in 70:30 dioxane−water is sufficiently slow (half-life ~6 s) to be to conveniently measured. A plot of log k_{obsd} as a function of increasing concentration of sodium chloride at constant ionic strength maintained by addition of sodium perchlorate is provided in Figure 3. These data show a marked common ion rate depression for the reaction of **9**, which is consistent with the mechanism outlined in Scheme 3. This "common ion effect" demonstrates that there is an intermediate in the reaction that is captured by chloride ion and converted back to reactant, thus slowing the reaction. With the assumption that carbocation **2** is a steady-state intermediate in the hydrolysis of **9**, the rate expression for the mechanism of Scheme 3 is given by eq 1. The rate data in Figure 3 were fit to eq 1 and yielded values of 0.115 ± 0.002 s^{-1} and 41.1 ± 2.5 M^{-1} for k_1 and k_{-1}/k_s, respectively. The common ion rate depression data are consistent with a mechanism in which all of the tetrol

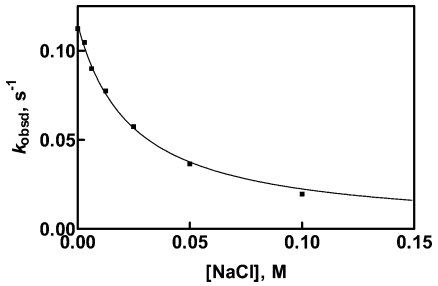


FIGURE 3. Plot of k_{obsd} vs [NaCl] for the reaction of chlorohydrin **9** in 70:30 dioxane−water solutions, 25.0 ± 0.2 °C, μ = 0.1 (maintained with $NaClO_4$).

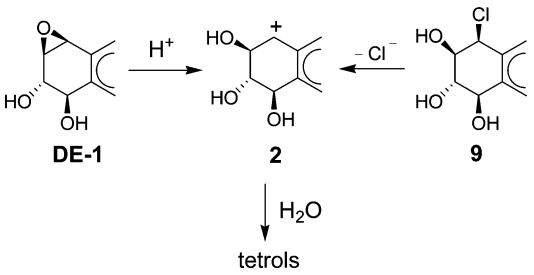
product is formed from capture of an intermediate carbocation by solvent.

$$k_{obsd} = \frac{k_1}{(1 = k_1[Cl^-]/k_s)} \qquad (1)$$

If the minor component of the reaction mixture from treatment of **DE-1** with HCl/THF is the corresponding trans-chlorohydrin, then the reaction of chloride ion with carbocation **2** in water solutions to yield some *trans*-chlorohydrin may also occur. However, at high chloride ion concentrations, the rate-limiting step for the hydrolysis of **9** is attack of solvent on the carbocation. If there are two or more conformations of the cation, then it is expected that they would be at equilibrium when chloride ion concentration is sufficiently high.[11] Thus, the cis/trans tetrol ratio should be independent of the stereochemistry of the chlorohydrin reactant at high chloride concentration.

Comparison of k_{-1}/k_s Values for Hydrolyses of *trans*-Chlorohyrin 8 and *cis*-Chlorohydrin 9. From a study of the acid-catalyzed hydrolysis of diol epoxide **DE-2** in 10:90 dioxane−water solutions containing sodium chloride solutions, a *lower limit* of k_{-1}/k_s for reaction of the *trans*-chlorohydrin intermediate **8** was determined to be 12 M^{-1}.[10] From the common ion rate depression of

SCHEME 4



8 in 50:50 dioxane−water solutions, k_{-1}/k_s was calculated to be 23 M^{-1}.[11] The k_{-1}/k_s value for reaction of *cis*-chlorohydrin **9** in 70:30 dioxane−water (41 M^{-1}) is therefore only slightly larger than that for reaction of *trans*-chlorohydrin **8** in 50:50 dioxane−water. The estimated rate constants (k_s) for reactions of carbocations **5** and **2** with 10:90 dioxane−water solvent are estimated to be 2.0×10^7 and 1.6×10^7 M^{-1} s^{-1}, respectively,[15,16] so they have approximately the same reactivity with water and would be expected to have about the same reactivity with chloride ion. The slightly greater k_{-1}/k_s value for reaction of *cis*-chlorohydrin **9** compared to that for reaction of *trans*-chlorohydrin **8** may partly be due to the fact that the reaction of **8** was carried out in 50:50 dioxane−water and the reaction of **9** was carried out in 70:30 dioxane−water.

Chloride ion is clearly a very reactive nucleophile toward carbocations **2** and **5**. The rate constant for reaction of carbocation **5** with chloride ion (k_{-1}) in 10:90 dioxane−water is estimated to be $>2 \times 10^8$ M^{-1} s^{-1},[10] and the reactivity of carbocation **2** with chloride ion is comparable. This reactivity is within 1 or 2 orders of magnitute of the diffusional limit.

Comparison of the Hydrolyses of DE-1 and *cis*-Chlorohydrin 9. The hydrolysis of chlorohydrin **9** yields the same ratio of cis and trans tetrols as the acid-catalyzed hydrolysis of **DE-1**, both in the absence of added chloride ion and in the presence of added chloride ion. These results are consistent with the mechanism outlined in Scheme 4, in which acid-catalyzed hydrolysis of **DE-1** and solvolysis of chlorohydrin **9** proceed via a common carbocation intermediate **2**. However, carbocation **2** can exist in two conformations (Figure 4), one in which all three hydroxyl groups occupy equatorial positions (**2a**) and a second in which all three hydroxyl groups occupy axial positions (**2b**). It has been suggested that the principal cis tetrol product formed in the acid-catalyzed hydrolysis of **DE-1** is derived from axial attack of solvent on **2a**.[5,6]

To gain insight on the nature of the intermediate, we have calculated structures of carbocation conformations **2a** and **2b** at the B3LYP/6-31G* level of theory. Conformation **2a** with the hydroxyl groups in equatorial positions is calculated to be 3.7 kcal/mol more stable than the triaxial conformation **2b** in the gas phase. Ionization of chlorohydrin **9** from conformation **9a** is expected to yield the more stable carbocation conformation **2a** directly, and energetically favorable axial attack of solvent on this carbocation will yield the major cis tetrol that is observed. The minor trans tetrol (**4**) formed in the hydrolyses of **DE-1** and *cis*-chlorohydrin **9** may also result from attack of solvent on **2a**, although some tetrol from reaction of the less stable carbocation conformation **2b** cannot be ruled out.

The observation that **DE-1** and its *cis*-chlorohydrin **9** both yield the same ratio of cis to trans tetrols (89% cis: 11% trans in 10:90 dioxane−water), both in the absence of and in the presence of chloride ion, is intriguing. In contrast, **DE-2** undergoes acid-catalyzed hydrolysis to a 5:95 ratio of cis and trans tetrols whereas its *trans*-chlorohydrin **8** hydrolyzes to a 21:79 ratio of cis and trans tetrols when chloride ion is absent.[11] However, *at high chloride ion concentrations* **DE-2** and its *trans*-chlorohydrin **8** *both* give a 35:65 ratio of cis to trans tetrols. One possible explanation for the observation that both **DE-1** and chlorohydrin **9** hydrolyze to the same ratio of tetrols is that the "common intermediate" for these reactions (Scheme 4) is the more stable equatorial carbocation conformation **2a**, and that this conformation undergoes attack by water to give a major cis tetrol and a minor trans tetrol. Conformation **2a** might be formed directly from the reaction of H^+ with **DE-1** and from ionization of **9a** and need not be in equilibrium with conformation **2b**. A second possibility is that carbocation conformations **2a** and **2b** undergo conformational interconversion faster than they react with solvent and that a minor yield of tetrols is formed from conformation **2b**. In contrast, **DE-2** and its *trans*-chlorohydrin hydrolyze via two distinct carbocation conformations that do not rapidly interconvert in the absence of chloride ion but do equilibrate faster than they react with solvent at high chloride ion concentrations.[11] If it is assumed that carbocation capture by solvent occurs at approximately the same rate for both conformations, then the product ratio at high chloride ion concentrations will reflect their equilibrium distribution.

The present observations on the hydrolyses of **DE-1** and **DE-2** provide mechanistic insights into related reactions of these DEs with nucleoside derivatives. We recently reported the reactions of **DE-1** and **DE-2** with the exocyclic N^2-amino group of O^6-allyl-3′,5′-di-*tert*-butyldimethylsilyl-2′-deoxyguanosine (O^6-allyl di-TBDMS dG) in trifluroethanol (TFE),[17] a polar solvent that is considerably more acidic as well as less nucleophilic than water. Interestingly, **DE-1** reacts with O^6-allyl di-TBDMS dG to give the N^2 adducts at C(10) in an 85:15 cis/trans ratio, which is very close to the ratio of cis/trans tetrols formed on acid-catalyzed hydrolysis of **DE-1**. This result suggests that the same conformation of the carbocation intermediate from **DE-1** is trapped by O^6-allyl di-TBDMS dG in TFE and by solvent water in the present study. **DE-2** gives the N^2 adducts in a 40:60 cis/trans ratio, which is very similar to the cis/trans tetrol ratio (35:65) formed from its acid-catalyzed hydrolysis at high chloride ion concentration, where the carbocation conformations are in rapid equilibrium.[10] This observation is consistent with the suggestion that the carbocation from **DE-2** undergoes conformational equilibration in TFE faster

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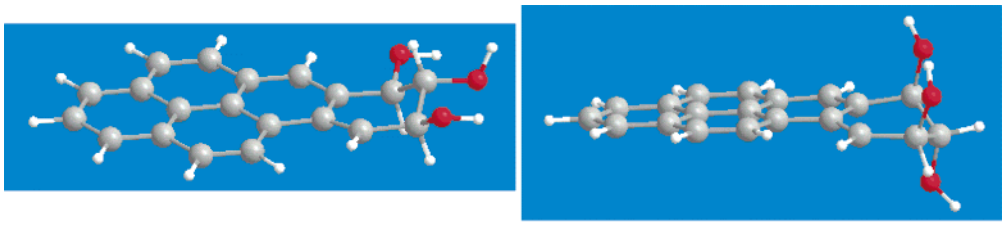


2a 2b

FIGURE 4. Structures of conformations **2a** and **2b** of carbocation **2**, with equatorial and axial hydroxyl groups, calculated at the DFT B3LYP/6-31G* level of theory.

than it is captured by the weakly nucleophilic O^6-allyl di-TBDMS dG.

Conclusions

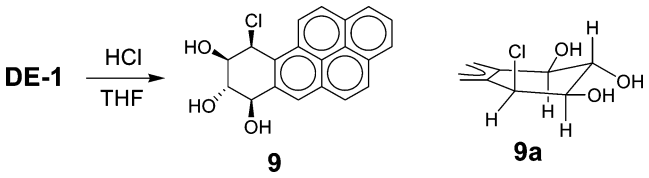
The reaction of **DE-1** with HCl in dioxane yields mostly *cis*-chlorohydrin **9** having conformation **9a**. These results are rationalized with quantum chemical calculations that indicate that the *cis*-chlorohydrin is significantly more stable than the corresponding *trans*-chlorohydrin. The hydrolysis of **9** yields the same cis/trans tetrol ratio as the acid-catalyzed hydrolysis of **DE-1** in the same solvent, both in the absence of added chloride ion and in the presence of added chloride ion. A large common ion rate depression in the hydrolysis of **9** is observed, which demonstrates that an intermediate carbocation occurs along the hydrolysis pathway. It is proposed that axial attack of solvent on a carbocation having conformation **2a** accounts for the major cis tetrol that is formed on hydrolysis of chlorohydrin **9** and also in the acid-catalyzed hydrolysis of **DE-1**.

Experimental Procedures

(±)-7*β*,8α-Dihydroxy-9*β*,10*β*-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene (**DE-1**) was prepared by published procedures.[4] This material may be carcinogenic and should be handled with caution. Dioxane and THF were distilled from sodium prior to use. All other reagents were purchased from commercial sources.

Synthesis of *cis*-Chlorohydrin 9 ((±)-7*β*,8α,9*β*-Trihydroxy-10*β*-chloro-7,8,9,10-tetrahydrobenzo[*a*]pyrene). A solution containing 0.050 mL of 4 M HCl in anhydrous dioxane and 0.2 mL of anhydrous THF was added dropwise to a suspension of 7.3 mg of **DE-1** in 0.8 mL of anhydrous THF while the reaction mixture was swirled. When the HCl solution was added, a clear solution resulted. The solution was allowed to stand at rt for 2 min, and the solvent and excess HCl were removed in vacuo to yield 8.8 mg of residue. The ^{1}H NMR spectrum of the product (see the Supporting Information) indicated that the main product (~94%) was *cis*-chlorohydrin **9**: ^{1}H NMR (THF-d_8) δ 6.34 (d, J = 3.7, H−C(10)), 4.80 (d, J = 8.3 Hz, H−C(7)), 4.21 (dd, J = 10.3, 8.3 Hz, H−C(8)), 4.03 (dd, J = 10.3, 3.7 Hz, H-C(9)). The H-C(7)−C(8)-H coupling constant of 8.3 Hz and the H-C(8)−C(9)-H coupling constant of 10.3 Hz are consistent with trans diaxial arrangements of vicinal hydrogens. The H-C(9)−C(10)-H coupling constant of 3.7 Hz is much too small for the C(10) hydrogen to be axial and trans to the axial C(9) hydrogen and instead supports a structure in which the C(10) hydrogen occupies a pseudoequatorial position and the chloro group occupies a pseudoaxial position, cis to the C(9) hydroxyl group. These coupling constants all indicate that the principal conformation of **9** is the half-chair conformation **9a**, in which the hydrogens on C(7), C(8), and C(9) are in trans, pseudoaxial geometries and the hydrogen on C(10) is pseudoequatorial (Scheme 5).[4,9]

SCHEME 5



A minor unidentified material (~6%), possibly the *trans*-9,10-chlorohydrin, was also present in the product mixture. This material possessed an ^{1}H NMR absorption at δ 6.09 (d, J = 4.0 Hz), presumably due to H(10). The product mixture was used without further purification for kinetic and product studies.

Rates of Hydrolysis of 9. The rates of reaction of **9** in 70:30 dioxane−water as a function of increasing concentrations of NaCl with ionic strength held constant at 0.1 M with $NaClO_4$ were determined. For each kinetic run, approximately 0.05 mL of a stock solution of **9** in dioxane (1 mg/mL) was added to 2.0 mL of 70:30 dioxane−water solution in the thermostated cell compartment (25.0 ± 0.2 °C) of a UV−vis spectrophotometer. Reactions were monitored at 352 nm, and pseudo-first-order rate constants were calculated by nonlinear regression analysis of the absorbance vs time data. The rates of reaction of **9** as a function of apparent pH in 70:30 dioxane−water solutions containing 10^{-3} M MES, HEPES, or CAPS buffer to control pH, but no added NaCl or $NaClO_4$, were also determined. The observed first-order rate constant remained the same within experimental error (0.043 ± 0.001 s^{-1}) from apparent pH 6 to apparent pH > 10. At apparent pH 11.2, the rate increased by about 15%. The rate of reaction of **9** in 0.1 M $NaClO_4$ solution (same solvent, cf. Figure 3) is increased by a factor of ~2.6, which is attributed to a normal salt effect.

Product Studies of the Hydrolysis of Chlorohydrin 9. Aliquots of 15 μL of a stock solution of **9** in dioxane (1 mg/mL) were injected into dioxane−water solutions (~2 mL) containing $NaClO_4$ or NaCl. Each reaction solution was swirled, allowed to stand several minutes at rt, and then analyzed directly by reversed-phase HPLC on a C_{18} column with 60:40 methanol−water as eluting solvent. Products were monitored by UV detection at 265 nm. The relative yields of cis tetrol (retention time 10.6 min) and trans tetrol (retention time 7.3 min) from reaction of **9** in 10:90 dioxane−water solution containing 0.1 M $NaClO_4$, 0.2 M NaCl, and 1.0 M NaCl were determined. The relative yields of cis and trans tetrols from reaction of **9** in each solvent were measured to be 88.6:11.4, 89.3:10.7, and 89.1:10.9, respectively. The relative yields of cis and trans tetrols from reaction of **9** in 0.1 M $NaClO_4$ and 0.5 M NaCl in 50:50 dioxane−water were measured to be 85.7:14.3 and 84.5:15.5, respectively. The similarity in product distributions at these two solvent compositions strongly suggests that the distribution of cis/trans tetrols observed under the kinetic conditions of 70:30 dioxane−water would not be significantly different.

Product Studies of the Hydrolysis of DE-1. Aliquots of 15 μL of a stock solution of **DE-1** in dioxane (1 mg/mL) were injected into dioxane−water solutions (~2 mL) containing

$NaClO_4$ or NaCl at pH 2.75−3.00. Each reaction solution was swirled and allowed to stand several minutes at rt. The pH of the reaction solutions were then adjusted to 5−7 and analyzed by HPLC as indicated above for product studies with chlorohydrin **9**. The relative yields of cis and trans tetrols from reaction of **DE-1** in 10:90 dioxane−water containing 0.1 M $NaClO_4$, 0.2 M NaCl, and 1.0 M NaCl were determined to be 89.7:10.3, 89.4:10.6, and 89.2:10.8, respectively. The relative yields of cis and trans tetrols from reaction of **DE-1** in 0.1 M $NaClO_4$ and 0.5 M NaCl in 50:50 dioxane−water solutions at pH ∼3 were measured to be 83.7:16.3 and 83.9:16.1, respectively.

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Supporting Information Available: H^1 NMR spectrum of chlorohydrin **9**; calculated structures and Cartesian coordinates for optimized structures of *cis*-chlorohydrin **9(a,b)**, *trans*-chlorohydrin **10(a,b)**, and carbocation **2(a,b)**, calculated at the DFT B3LYP/6-31G* level of theory. This material is available free of charge via the Internet at http://pubs.acs.org.

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