A. G. Hortmann, *J. Org. Chem.*, **39**, 95 (1974), and references cited therein.
(4) All new materials gave satisfactory spectral data consistant with the assigned structures. Elemental analyses were within acceptable limits for **1**, **2**, **4**, **5**, and the TCNQ salts of **1** and **9**. Compound **3** contained a trace of **1** (mass spectroscopy and analysis) which was retained after repeated chromatography. No analysis of **10** was carried out owing to insufficient material; however see ref 11.
(5) Attempts to carry out the sequence of reactions described in eq 1 with potassium *O*-isopropyldiselenocarbonate have so far been unsuccessful.
(6) The reaction of tetrathiolate salts, **6** and **7**, with transition metal salts to give the corresponding metal dithiolene derivatives will be described in a subsequent paper: R. R. Schumaker, e. M. Engler, and N. Martinez, unpublished work. Solt **6** has previously been prepared by another route (F. Wudl, private communication).
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(8) P. R. Moses and J. Q. Chambers, *J. Am. Chem. Soc.*, **96**, 945 (1974).
(9) Previously, this type of reaction has been carried on the 1,3-dithiole ring system with a carbonyl group (R. Mayer and B. Gebhardt, *Ber.*, **97**, 1298 (1964)) and with a thiocarbonyl group (M. Mizuno, M. P. Cava, and A. F. Garito, *J. Org. Chem.*, **41**, 1484 (1976)).
(10) Thiapen-2-one-5-(dithiomethoxy-1′,3′-dithioliden-2′-yl).
(11) Mass spectrum peak match gave 385.819; calcd for $C_9H_6S_8O$ 385.818.
(12) R. R. Schumaker and E. M. Engler, unpublished work.

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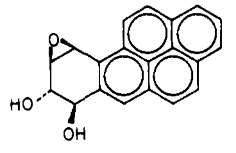
Changes of Mechanisms and Product Distributions in the Hydrolysis of Benzo[*a*]pyrene-7,8-diol 9,10-Epoxide Metabolites Induced by Changes in pH

Sir:

Numerous investigations from several laboratories have indicated that diol epoxides **1** and **2**[1] play a dominant role in



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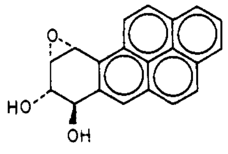

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the cytotoxic, mutagenic,[2] and carcinogenic[3] action of the ubiquitous environmental carcinogen benzo[*a*]pyrene. Thus, a knowledge of the solvolytic reactions of these metabolites[4] assumes a special importance. To date, only product studies with qualitative rate data,[2a,4b,5] and one kinetic study[6] over a very limited pH range (ca. 5-6) in 50% dioxane-water have appeared. In the latter study, kinetic data revealed only the existence of acid-catalyzed mechanisms for the hydrolysis of **1** and **2**, and both isomers were found to possess similar reactivities.[7] The present study reports the pH-rate profiles and product analysis for the hydrolysis of **1** and **2** in water and in dioxane-water mixtures. *This study reveals that the mechanisms for hydrolysis of both* **1** *and* **2** *change from acid-catalyzed processes at low pH to spontaneous reactions with solvent at higher pH in highly aqueous solutions (Figure 1), accompanied by changes in product distributions.* Whereas isomer **2** is about twice as reactive as isomer **1** toward acid-catalyzed hydrolysis, **1** is more than 30 times more reactive than **2** under conditions of spontaneous hydrolysis. The large difference in reactivity between **1** and **2** in the physiological pH range may play a significant role in the relative tumorgenic properties of **1** and **2**.

Table I. Rate Constants for Hydrolysis of **1** and **2** in Water and Dioxane-Water Mixtures at 25 °C[a,b]

Compound	Solvent	k_{H^+}, $M^{-1}\,s^{-1}$	k_0, s^{-1}
1	Water	$5.8 \pm 0.9 \times 10^2$	$1.8 \pm 0.1 \times 10^{-2}$
2		$1.4 \pm 0.2 \times 10^3$	$5.4 \pm 0.8 \times 10^{-4}$
1	10% dioxane-water[c]	$5.1 \pm 0.4 \times 10^2$	$4.2 \pm 0.3 \times 10^{-3}$
2		$1.4 \pm 0.2 \times 10^3$	$1.3 \pm 0.5 \times 10^{-4}$
1	25% dioxane-water[c]	$4.1 \pm 0.1 \times 10^2$	$7.2 \pm 0.3 \times 10^{-4}$
2		$7.9 \pm 0.2 \times 10^2$	

[a] Ionic strength = 0.1 ($NaClO_4$). Rate constants were calculated from weighted least-squares plots of k_{obsd} vs. a_{H^+}. All solutions contained 10^{-4} M ethylenediaminetetraacetic acid (EDTA). Rates were monitored by observing the absorbance change of the reaction solution at 278-279 nm in the thermostated cell compartment (25.0 ± 0.2 °C) of a Gilford 2400 spectrophotometer. [b] Reference 8. [c] v/v.

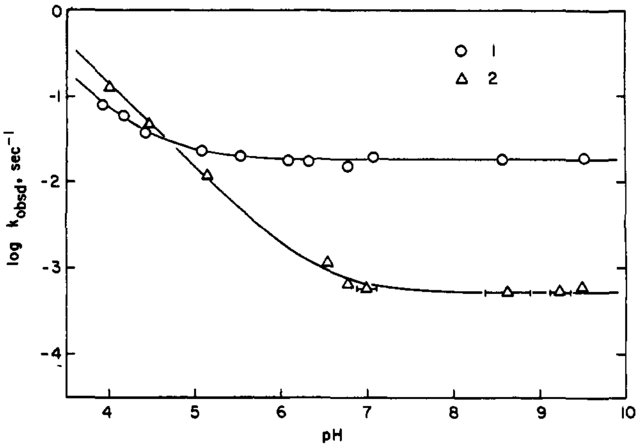


Figure 1. Plots of log k_{obsd} vs. pH for hydrolysis of **1** and **2** in water (0.1 M $NaClO_4$, 10^{-4} M EDTA), 25 °C. The pH range throughout any given run was generally <0.05 pH unit. Several kinetic solutions for **2** underwent a greater pH change in the plateau region, and the ranges are represented by horizontal error bars.

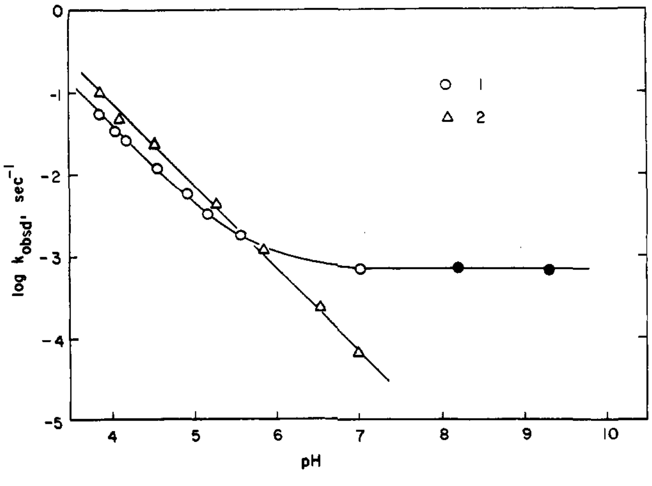


Figure 2. Plots of log k_{obsd} vs. pH for hydrolysis of **1** and **2** in 25% dioxane-water (0.1 M $NaClO_4$, 10^{-4} M EDTA), 25 °C. Several kinetic solutions (●) for **1** contained Tris buffer (total buffer concentration 0.02 M).

The pH-rate profiles for the hydrolysis of **1** and **2** in water and in 25% dioxane-water are given in Figures 1 and 2.[8] The plots of log k_{obsd} vs. pH for **1** and **2** in water exhibited slopes of −1 at low pH, which indicated the predominance of acid-catalyzed mechanisms for hydrolysis. However, at pH > ca. 5 for **1** and 7 for **2**, the profiles leveled out until finally the rates of hydrolysis were independent of pH. These data demonstrate

Table II. Product Distributions from Hydrolysis of **1** in Water and Dioxane-Water Mixtures as a Function of pH[a]

Solvent	pH[b]	**3**, %	**4**, %	**5**, %
Water	3.05-3.15	88	12	<1
	4.00-4.05	89	11	<1
	7.0-7.1[d]	86	10	$\sim$4
	8.1-8.0[d]	86	10	$\sim$4
10% dioxane-water[c]	3.05-3.10	89	11	<1
	4.05-4.10	89	11	<1
	7.10-7.25[d]	85	8	$\sim$7
	8.0-7.9[d]	84	9	$\sim$7
25% dioxane-water[c]	3.05-3.10	87	13	<1
	4.00-4.05	87	13	<1
	8.5-8.4[d]	76	8	$\sim$16

[a] Ionic strength = 0.1 ($NaClO_4$), 25 °C. Products were analyzed by high-pressure liquid chromatography (HPLC) on a Du Pont ODS-Zorbax column. The yields listed correspond to relative areas of each product of a HPLC tracing due to absorption at 280 nm, where **3**, **4**, and **5** have very similar extinction coefficients. The structures of **3**, **4**, and **5** have been established previously (ref 4a, 5). [b] v/v. [c] Measured by the glass electrode. The values listed correspond to initial and final pH readings. [d] The yield of **5** was estimated by analysis of the product after 1 half-life of reaction. This product was slowly transformed to other unidentified materials under the reaction conditions listed. After 10 half-lives, the yield of **5** was reduced by a factor of ca. 3, and additional products, presumably from **5**, were observed. Approximately 10% of unidentified materials, in addition to those mentioned above, was also formed.

Table III. Product Distributions from Hydrolysis of **2** in Water and Dioxane-Water Mixtures as a Function of pH[a]

Solvent	pH[b]	**6**, %	**7**, %
Water	3.05-3.15	19	81
	4.10-4.25	14	86
	7.05-7.20	55	45
	8.05-7.95	58	42
10% dioxane-water[c]	3.05-3.10	8	92
	4.05-4.10	7	93
	7.95-7.80	56	44
	9.0-8.7	51	49
25% dioxane-water[c]	3.05-3.10	4	96
	4.00-4.05	5	95
	6.55-6.53	6	94
	8.95-8.90	60	40

[a] Ionic strength = 0.1 ($NaClO_4$), 25 °C. Products from **2** were analyzed by the same method outlined in Table II, footnote *a*. The structures of **6** and **7** were established previously (ref 4a, 5). [b] Measured by the glass electrode. The values correspond to initial and final pH readings. [c] v/v.

the incursion of mechanisms whereby **1** and **2** undergo spontaneous hydrolysis with the solvent.

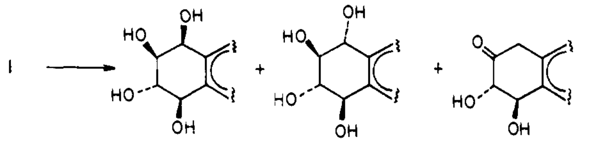
The rate data for hydrolysis of **1** and **2** in water, 10% dioxane-water, and 25% dioxane-water were fit to the equation

$$k_{\text{obsd}} = k_{\text{H}^+}a_{\text{H}^+} + k_0 \tag{1}$$

Values of k_{H^+} and k_0 are summarized in Table I. Although **2** is slightly more than twice as reactive as **1** toward acid-catalyzed hydrolysis in water, **1** is 33 times more reactive than **2** toward spontaneous hydrolysis. The spontaneous hydrolysis rate for **1** is 25 times slower in 25% dioxane-water than in water. Although the k_0 process was readily detected in the hydrolysis of **2** in 10% dioxane-water, no spontaneous reaction of **2** with solvent could be detected in 25% dioxane-water at pH $\sim$7 (Figure 2). If the k_0 mechanism for hydrolysis of **2** were also 25 times slower in 25% dioxane-water than in water, then the half-life for hydrolysis of **2** in 25% dioxane-water would be ca. 9 h. A further reduction of the k_0 rates for **1** and **2** would be expected if hydrolysis were carried out in 50% dioxane-water and readily explains why no spontaneous hydrolysis mechanisms for **1** and **2** were detected in the earlier study.[6]

The products from hydrolysis of **1** and **2** are given in Schemes I and II, and the product distributions as a function of pH are listed in detail in Tables II and III. Isomer **1** undergoes predominantly cis addition of water (ca. 90%) to the epoxide group by both the K_{H^+} and k_0 processes.[9] However, the k_0 mechanism also yields ca. 4% of ketone **5** (presumably via a mechanism involving an "NIH shift") in water, and up to ca. 16% of **5** in 25% dioxane-water. The ketone product **5** could not be detected from hydrolysis of **1** at low pH, where the k_{H^+} mechanism predominates, in any of the solvents listed. The observation that ketone product is formed from **1** by the k_0 process but not by the k_{H^+} process parallels the results previously reported for hydrolysis of indene oxide.[8a]

Scheme I



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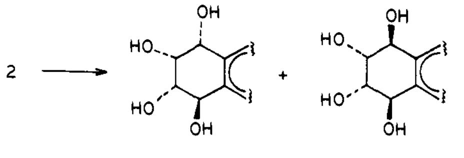
Scheme II



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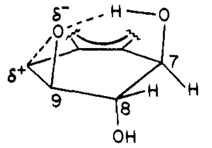
In contrast to the results obtained from **1**, the hydrolysis of **2** by the k_{H^+} mechanism results in predominantly trans addition of water to the epoxide group. The relative amount of trans addition of water to the epoxide group vs. cis addition of water appeared to increase slightly in solvent mixtures containing more dioxane. However, the amount of trans addition of solvent decreases from ca. 80-85% by the k_{H^+} process in water to ca. 40-45% by the k_0 mechanism. No ketone product **5** could be detected throughout the pH range studied.

Models suggest that intramolecular hydrogen bonding between the benzylic hydroxyl group at C-7 and the epoxide oxygen is possible in **1** but not in **2**, although the very similar rates of acid-catalyzed hydrolysis of **1** and **2** suggest that such hydrogen bonding in the ground state may be minimal. However, isomer **1** is considerable more reactive than **2** by the k_0 mechanism. This enhanced reactivity of **1** by the spontaneous mechanism might by attributed to increased hydrogen bonding in the transition state (such as **8**), compared to the ground state, brought about by increased negative charge on the epoxide oxygen.[11] Anchimeric assistance of the benzylic hydroxyl has been postulated to account for an enhanced reactivity of **1** (and structurally related compounds) toward addition of nucleophilic reagents,[12] a reaction type that likewise causes increased negative charge on epoxide oxygen at the transition state.



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Acknowledgment. This investigation was supported by Public Health Service Grant No. CA-17278 from the National Cancer Institute (D.L.W.). Assistance from Angela M. Ross is appreciated.

References and Notes

(1) The complete names of 1 and **2** are (±)-7β,8α-dihydroxy-9β,10β-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene and (±)-7β,8α-dihydroxy-9α,10α-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene, respectively.

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(7) Diol epoxide **2** was reported (ref 6) to be ca. three times more reactive than **1** toward acid-catalyzed hydrolysis in 50% dioxane–water.

(8) Kinetics and product analyses were carried out in solutions that contained 10^{-4} M EDTA, but no other buffering reagents unless indicated. In our experience, the slight buffering effect of the EDTA was sufficient to maintain constant pH in all solutions of Figures 1 and 2 at pH <ca. 7 throughout 4 half-lives. At pH >7, the pH of the reaction solutions remained constant only for those reactions with extremely short half-lives (i.e., <1 min). Several kinetic solutions for **1** (Figure 2) contained dilute Tris buffer. We have observed that certain buffering reagents such as phosphate (pH 6–7) exhibit striking catalysis in the hydrolysis of both **1** and **2.** All solutions were held at constant ionic strength with $NaClO_4$ instead of KCl to exclude any specific effects of chloride ion: (a) D. L. Whalen and A. M. Ross, *J. Am. Chem. Soc.*, **98,** 7859 (1976); (b) D. L. Whalen, A. M. Ross, P. M. Dansette, and D. M. Jerina, *ibid.*, in press.

(9) Acid-catalyzed hydrolyses of indene oxide (ref 8a and references therein) and aryl-substituted cyclohexene oxides (ref 10a,b) also occur with cis addition of water to the epoxide group. However, indene oxide (ref 8a) and 9,10-phenanthrene oxide (ref 8b, 10c) undergo predominantly trans addition of water via the k_0 process. The cis addition of water to 1 via the k_0 process is therefore somewhat surprising, and studies to explain this observation are in progress.

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Enthalpy of Vaporization Measurements by Gas Chromatography[1]

Sir:

Recent studies of reactivity and acidity in the gas phase and comparisons with the corresponding solution properties have provided major insights into the importance of intrinsic properties vs. solvation phenomena in determining solution behavior.[2] Essential to the thermodynamic cycles involved in many such studies are heats of vaporization (evaporation) (ΔH_v^{25}) of organic reactants or products, relatively few of which are presently known with reasonable accuracy.[3]

We now wish to report a simple method for the measurement of heats of vaporization. It has been applied to liquid substances boiling between 100 and 360°, and there is reason to believe that this range could be considerably extended in both directions. It is possibly the easiest method for making such measurements, and, for substances boiling above 150–200°, we believe that this method will prove to be the most accurate available. The equipment required is a gas chromatograph and a solution calorimeter, and the amount of sample used is 200–500 μL.

Table I. Enthalpies of Evaporation of Some Organic Liquids at 25 °C

Compound	Expl ΔH_v[a]	Lit. ΔH_v[b]
2,2,4,4-Tetramethylpentane	9.23	9.12 ± 0.10[c]
tert-Butylbenzene	11.34	11.50 ± 0.05[c]
1-Butanol	12.08	12.27 ± 0.02,[d] 12.19 ± 0.01[e]
2-Pentanone	9.05	9.14 ± 0.05,[c] 9.18[f]
2-Hexanone	10.17	10.1 ± 0.1,[c] 10.25[f]
2-Octanone	12.36	12.38[f]
2-Nonanone	13.48	13.48[f]
3-Pentanone	9.20	9.22[f]
4-Heptanone	11.17	11.16[f]
5-Nonanone	13.16	12.74 ± 0.02,[c] 13.1[f]
2,2,4,4-Tetramethyl-3-pentanone	10.87	10.84 ± 0.01[c]
Methyl octanoate	13.84	13.6 ± 0.4[c]
Tetraethylgermane	10.93	10.7 ± 0.3[c]

[a] kcal/mol. Estimated accuracy ±0.10. [b] kcal/mol. [c] Reference 9. [d] E. M. Arnett and D. Oancea, *J. Chem. Educ.*, **52,** 269 (1975). [e] K. G. McCurdy and K. J. Laidler, *Can. J. Chem.*, **41,** 4867 (1963). [f] D. Ambrose, J. H. Ellender, E. B. Lees, C. H. S. Sprake, and R. Townsend, *J. Chem. Thermodyn.*, **7,** 453 (1975).

The method is derived from reported[4,5] gas chromatographic determinations of $\Delta H(\mathrm{v}\rightarrow\mathrm{S})$, the enthalpy of transfer from vapor to solution:

$$\Delta H(\mathrm{v}\rightarrow\mathrm{S}) = -R\frac{\mathrm{d}\ln V_g}{\mathrm{d}(1/T)}$$

V_g is the retention volume,[6] defined by the equation

$$V_g = \frac{F_c j}{w_t}(t_r - t_a)\frac{273.15}{T_m P_o}(P_o - P_w)$$

where F_c is the carrier gas flow rate at room temperature (T_m) and j is the compressibility factor, w_t is the weight of stationary phase, t_r is the sample retention time, t_a is the retention time of air, P_o is the outlet pressure, and P_w is the vapor pressure of water at room temperature.

Consider a system where F_c, j, w_t, T_m, and P_o are held constant.[7] The specific retention volume would then be given by a constant times the corrected retention time ($\Delta t = t_r - t_a$). If ln Δt is plotted vs. $1/T$ the intercept of the straight line passing through these points will differ from that obtained in the plot of ln V_g vs. $1/T$, but the slope will be unchanged. The resulting enthalpy change will be the same whether Δt or V_g is used.

We have taken advantage of this relationship to obtain enthalpies of transfer from vapor to solution in DC-200 silicone fluid for a number of compounds. The values are corrected from the mean temperature of the range studied to 25 °C using the equation

$$\Delta H^{25}(\mathrm{v}\rightarrow\mathrm{S}) = \Delta H^{T_m}(\mathrm{v}\rightarrow\mathrm{S}) + \int_{T_m}^{298.15}[C_p(\mathrm{l}) - C_p(\mathrm{g})]\,\mathrm{d}t$$

Liquid heat capacities [$C_p(\mathrm{l})$] at 25 °C were calculated by the group contribution method,[8] and the additivity rules of Benson[9] were used to determine gas-phase heat capacities at 25 °C, [$C_p(\mathrm{g})$].

The enthalpy of evaporation is not equal to $-\Delta H(\mathrm{v}\rightarrow\mathrm{S})$