2.00–2.50 (m, 9 H); MS m/e 124 (M^+); semicarbazone, mp 216–217 °C. Anal. Calcd for $C_9H_{15}ON_3$: C, 59.64; H, 8.34; N, 23.19. Found: C, 59.65; H, 8.30; N, 23.17.

Preparation of δ-Lactones. δ-Lactones **1–9** were prepared by the Baeyer–Villiger oxidation of the corresponding ketones in two methods.

Procedure A. A solution of the ketone and a 20-fold excess of 30% aqueous hydrogen peroxide in acetic acid was stirred at room temperature, and the progress of the reaction was monitored by GLC. The solution was poured into water and extracted with ether, and the ether extract was washed with saturated sodium carbonate solution and brine and dried (Na_2SO_4). The solvent was removed in vacuo, and the residue was distilled under reduced pressure. δ-Lactones **1–9** were obtained in 35–80% yields and purified by preparative GLC.[15]

Procedure B. A solution of the ketone and a 2.5-fold excess of 85% *m*-chloroperbenzoic acid (MCPBA) in chloroform was stirred at room temperature. The solution was washed with saturated sodium sulfite solution and water and dried (Na_2SO_4). The products were isolated as described above (40–90%).

1: IR 1720 cm^{-1}; NMR δ 1.30–2.20 (m, 12 H), 2.30–2.50 (m, 2 H); MS m/e 166 (M^+), 138. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.90; H, 8.78.

2: IR 1720 cm^{-1}; NMR δ 1.00–2.15 (m, 14 H), 2.20–2.50 (m, 2 H); MS m/e 180 (M^+), 152. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.11; H, 9.13.

3: mp 34–36 °C; IR (KBr) 1720 cm^{-1}; NMR δ 1.20–2.20 (m, 16 H), 2.50–2.70 (m, 2 H); MS m/e 194 (M^+), 166. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.92; H, 9.44.

4: IR 1720 cm^{-1}; NMR δ 1.00–2.20 (m, 18 H), 2.50–2.70 (m, 2 H); MS m/e 208 (M^+), 180. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.70; H, 9.74.

5: IR 1720 cm^{-1}; NMR δ 1.50–2.80 (m, 9 H), 4.76 (q, 1 H); MS m/e 126 (M^+), 98.

6: IR 1720 cm^{-1}; NMR δ 1.40 (s, 3 H), 1.40–2.50 (m, 9 H); MS m/e 141 ($M^+ + 1$), 43. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.31; H, 8.72.

7: IR 1720 cm^{-1}; NMR δ 1.24 (s, 3 H), 1.40–2.60 (m, 8 H), 4.32 (q, 1 H); MS m/e 141 ($M^+ + 1$), 99. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.22; H, 8.77.

8: IR 1720 cm^{-1}; NMR δ 0.96 (s, 3 H), 1.14 (s, 3 H), 1.40–2.70 (m, 8 H); MS m/e 155 ($M^+ + 1$), 126. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.05; H, 9.25.

9: IR 1720 cm^{-1}; NMR δ 0.99 (t, 3 H), 1.12 (s, 3 H), 1.50–2.50 (m, 10 H); MS m/e 169 ($M^+ + 1$), 140. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.06; H, 9.98.

Thermal Rearrangement of δ-Lactones 1–9. (a) In Solution. A solution of the δ-lactone in *o*-dichlorobenzene was heated in a sealed tube at 240 °C for 72 h. After evaporation of the solvent in vacuo, the residue was analyzed by GLC (10% FFAP), and the γ-lactones were separated by column chromatography (SiO_2, 10% ether–petroleum ether) and purified by preparative GLC. The results are summarized in Table I.

(b) In the Vapor Phase. A hexane solution of the δ-lactone was passed through a Pyrex column (80 cm) heated at 350 °C in nitrogen stream (contact time ca. 20 s) and collected in a dry ice–acetone trap. Similar workup as above gave a mixture of δ- and γ-lactones. The results are summarized in Table I.

10: IR 1765 cm^{-1}; NMR δ 0.10–0.90 (m, 4 H), 1.40–2.20 (m, 8 H), 2.20–2.50 (m, 2 H); MS m/e 166 (M^+), 111. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.88; H, 8.56.

11: mp 32–34 °C; IR 1765 cm^{-1}; NMR δ 0.15–1.00 (m, 4 H), 1.20–2.20 (m, 10 H), 2.30–2.50 (m, 2 H); MS m/e 180 (M^+). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 72.98; H, 9.03.

12: IR 1765 cm^{-1}; NMR δ 0.10–1.00 (m, 4 H), 1.10–2.20 (m, 12 H), 2.30–2.60 (m, 2 H); MS m/e 194 (M^+), 166. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.33; H, 9.59.

13: IR 1765 cm^{-1}; NMR δ 0.10–1.10 (m, 4 H), 1.10–2.20 (m, 14 H), 2.30–2.60 (m, 2 H); MS m/e 208 (M^+), 180. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H. 9.68. Found: C, 75.13; H, 9.56.

14: IR 1765 cm^{-1}; NMR δ 0.49 (m, 2 H), 0.67 (t, 2 H), 1.10 (s, 3 H), 1.40 (s, 3 H), 1.80–2.60 (m, 4 H); MS m/e 155 ($M^+ + 1$). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.87; H, 9.27.

15: IR 1765 cm^{-1}; NMR δ 0.25–0.68 (m, 4 H), 0.80 (t, 3 H), 1.40 (s, 3 H), 1.50 (q, 2 H), 1.80–2.60 (m, 4 H); MS m/e 169 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.13; H, 9.69.

(15) In the cases of **2**, **8**, and **9**, 10% of **11** and traces of **14** and **15** were also obtained, besides the respective δ-lactones. These may be derived from initially formed δ-lactones by the rearrangement.

Registry No. **1**, 68157-80-2; **2**, 68157-81-3; **3**, 68157-82-4; **4**, 68157-83-5; **5**, 71221-74-4; **6**, 72331-80-7; **7**, 72331-81-8; **8**, 72331-82-9; **9**, 72331-83-0; **10**, 72331-84-1; **11**, 68197-38-6; **12**, 72331-85-2; **13**, 72331-86-3; **14**, 68157-84-6; **15**, 68157-85-7; tetrahydro-3a,6a-ethano-1*H*,4*H*-pentalen-1-one, 5202-23-3; hexahydro-3a,7a-ethano-1*H*-inden-1-one, 42540-17-0; hexahydro-3a,8a-ethano-1*H*,4*H*-azulen-1-one, 70386-90-2; octahydro-3a,9a-ethano-1*H*-cyclopentacyclooctan-1-one, 70386-91-3; bicyclo[3.2.0]heptan-2-one, 29268-42-6; 1-methylbicyclo[3.2.0]heptan-2-one, 50459-43-3; 5-methylbicyclo[3.2.0]heptan-2-one, 50459-35-3; 1,5-dimethylbicyclo[3.2.0]heptan-2-one, 70386-92-4; 1-ethyl-5-methylbicyclo[3.2.0]heptan-2-one, 72331-87-4; 1-ethyl-5-methylbicyclo[3.2.0]heptan-2-one semicarbazone, 72331-88-5; 2-ethyl-3-methylcyclopentenone, 5682-72-4; 2-ethyl-3-methylcyclopentenone semicarbazone, 72331-89-6.

Alkaline Hydrolysis of 7,8-Dimethyl-10-(formylmethyl)isoalloxazine. A Kinetic Study

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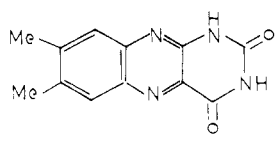
7,8-Dimethyl-10-(formylmethyl)isoalloxazine (**1**) is an important intermediate product in the photolysis of riboflavin (**2**).[2] Marked changes in the distribution of lumichrome (**3**) and lumiflavin (**4**), both major products of the photolysis of **2**, are known to occur in moving from neutral to alkaline media.[3] A possible explanation lies in the alkaline hydrolysis of **1**, formed initially in the photolysis of **2**. A previous study of the side-chain hydrolysis of **1** in the dark reported that **4** was the major product.[4]

1, R = CH_2CHO
2, R = $CH_2(CHOH)_3CH_2OH$
4, R = CH_3



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In the present study, we report kinetic data on the dark hydrolysis of **1** in the pH range 9–12. It is shown that both **3** and **4** are major products and that their relative proportions are pH dependent.

Results and Discussion

The hydrolysis of **1**[5] (10^{-4} M) was carried out in unbuffered solutions at various pH values at 25 ± 1 °C (pH

(1) To whom correspondence should be addressed.
(2) E. C. Smith and D. E. Metzler, *J. Am. Chem. Soc.*, **85**, 3285 (1963).
(3) O. Warburg and W. Christian, *Naturwissenschaften*, **20**, 980 (1932); P. Karrer, H. Solomon, K. Schopp, E. Schlitter, and H. Fritzsche, *Helv. Chim. Acta*, **17**, 1010 (1934).
(4) P. S. Song, E. C. Smith, and D. E. Metzler, *J. Am. Chem. Soc.*, **87**, 4181 (1965).
(5) **1** was prepared as described previously by H. H. Fall and H. G. Petering, *J. Am. Chem. Soc.*, **78**, 377 (1956).

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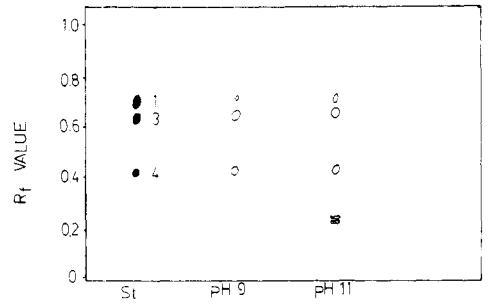

Figure 1. TLC plate (solvent system a), showing hydrolysis products at pHs 9 and 11, after ~90% hydrolysis. St = standards of 1, 3, and 4. All spots show yellow fluorescence under UV light, except 2 (light blue). The plate at pH 11 shows, in addition to 1, 3, and 4, the unknown products (R_f 0.24).

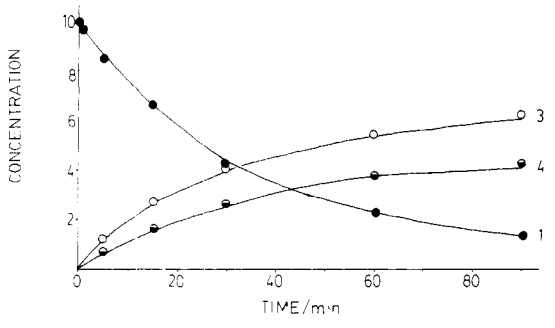

Figure 2. Concentrations ($\times 10^5$ M) of 1, 3, and 4 as a function of time during hydrolysis of 1 at pH 11.0.

Scheme I

was maintained by the addition of 0.1 M NaOH). Examination of the solutions after about 90% hydrolysis by thin-layer chromatography (TLC) showed the presence of 1, 3, and 4 only, in the pH range 9–10.5 (Figure 1). At pH values of 11 and above, some unidentified compounds were observed, in addition to 1, 3, and 4 (Figure 1). The R_f values (where comparable solvent systems were employed) for these unknown compounds were similar to those of the ring-cleavage products of 10-methylisollaxazine, previously reported.[6]

The concentrations of 1, 3, and 4 were determined as a function of time by a multicomponent spectroscopic assay procedure; an example is shown in Figure 2. Typical spectra of the aqueous and "chloroform" layers (see Experimental Section) observed during hydrolysis are shown in Figure 3. These spectra clearly show the absorption of a mixture of 3 (λ_{max} 356 nm) and 4 (λ_{max} 445 nm) in the "chloroform" layer, with 3 being the major component rather than 4 as suggested previously.[4]

The reaction was found to obey pseudo-first-order kinetics[7] with respect to both the disappearance of 1 and the formation of 3 and 4. The results can be rationalized on the basis of the kinetic scheme shown in Scheme I.

The pH dependence of the pseudo-first-order rate constant in Scheme I is shown in Figure 4. Some bimolecular rate constants are also given in Table I. An inflection at

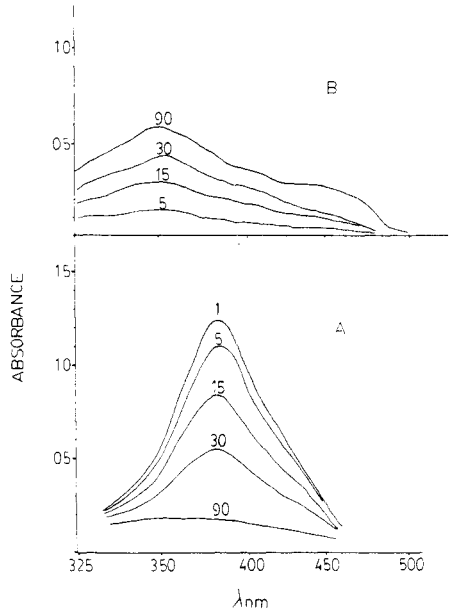

Figure 3. Absorption spectra of (A) the aqueous extracts (pH 2.0) and (B) the "chloroform" extracts[7] (pH 4.5) during the hydrolysis of 1 at pH 11.0. Times indicated are in minutes.

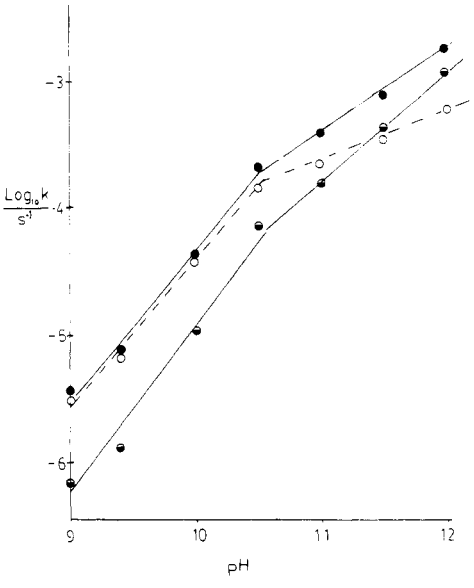

Figure 4. Plot of log k vs. pH for the hydrolysis of 1: (●) 1, (○) 3, (◒) 4. k is equal to the pseudo-first-order rate constant of disappearance of 1 (i.e., $k_1 + k_2$) and formation of 3 (k_1) and 4 (k_2).

Table I. Second-Order Rate Constants (M^{-1} s^{-1}) for the Disappearance of 1 (k') and the formation of 3 (k_1') and 4 (k_2')

pH	k'	k_1'	k_2'
9	0.40	0.348	0.068
12	0.193	0.063	0.132

pH ~10.5 can be seen in Figure 4, for both the disappearance of 1 and the formation of 3 and 4. As the pK_a of 1 is approximately 10.1,[8] this would indicate that the anion of 1 is somewhat less reactive than the neutral form. Finally, it may be pointed out that in the case of the anion

(6) D. A. Wadke and D. E. Guttman, *J. Pharm. Sci.*, **55**, 1088 (1966).
(7) Plots of log $([1]_0/[1]_t)$ vs. time and log $([3]_\infty - [3]_t)$ vs. time (similarly for [4]) were found to be linear in the pH range 9–10.5. At pH 11.0 and above, deviations from linearity were observed after 60% hydrolysis in the plots of 1 but not for 3 or 4. This is due to the presence of ring cleavage products in the aqueous phase.
(8) The pK_a of 1 was determined spectroscopically as previously described for 2;[9] while such measurements were complicated due to the rapid hydrolysis of 1, an estimate of 10.1 ± 0.3 was obtained.
(9) E. J. Land and A. J. Swallow, *Biochemistry*, **8**, 2117 (1969).
(10) I. Ahmad, Ph.D. Thesis, University of London, 1968.

of 1, the rate constant for the formation of 4 exceeds that for 3, in contrast to the neutral form (Figure 4).

Experimental Section

A. Quantitative Analysis. A multicomponent spectrophotometric assay procedure was employed for the determinations of the concentrations of 1, 3, and 4.[10] The hydrolyzed solutions of 1 were buffered to pH 2 (where 1 is completely stable to further hydrolysis). Extraction with chloroform was carried out to remove 3 and 4. The chloroform extract was evaporated to dryness under reduced pressure and the residue redissolved in pH 4.5 acetate buffer. The concentrations of 3 and 4 were then determined by a two-component assay from the absorption at 356 and 445 nm. The concentration of 1 was determined, using the aqueous layer, from its absorption at 385 nm.

B. Thin-Layer Chromatography. TLC was carried out on 250-μm cellulose plates (Whatman CC41) and the following solvent systems were used: (a) 50:30:2:18 1-butanol-1-propanol-acetic acid-water; (b) 40:10:50 (organic phase) 1-butanol-acetic acid-water. TLC was also carried out on silica gel G (Merck) with 70:20:10 1-butanol-ethanol-water as the solvent system. Flavins were detected by their characteristic fluorescence emission under UV (370 nm) excitation.

Registry No. 1, 4250-90-2; 3, 1086-80-2; 4, 1088-56-8.

Isolation and Structure of the Oxidized Diels-Alder Adducts of Certain Styrenes and 1,4-Naphthoquinone

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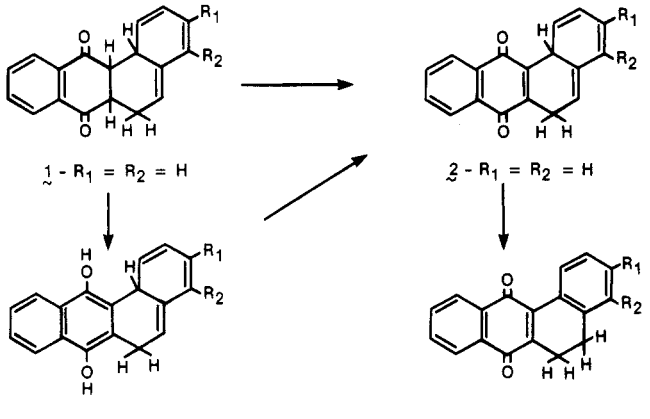
The production of substituted benz[*a*]anthracene-7,12-diones via the Diels-Alder reaction between styrenes and 1,4-naphthoquinones has been demonstrated.[1] The two oxidation steps needed to furnish the benz[*a*]-anthracene-7,12-diones from the Diels-Alder adducts would be "expected" to occur from the intermediates shown below as 1, **1a**, and 2.



1 - $R_1 = R_2 = H$

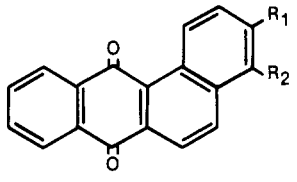
2 - $R_1 = R_2 = H$

1a - $R_1 = R_2 = H$

2a - $R_1 = R_2 = H$
3 - $R_1 = R_2 = OMe$
5 - $R_1 = OMe, R_2 = H$

The type of isomerism of 1 to **1a** has been well documented,[2] and spectral evidence has suggested this in the case of the 4-chloro isomer.[1] The structure of the product of oxidation of 1 or **1a**, however, was not determined. We felt the prolonged heating required to overcome the sluggish styrene reactivity made possible the rearrangement of 2 to the 5,6-dihydro isomer **2a**.

After a toluene solution of 2,3-dimethoxystyrene,[3] 1,4-naphthoquinone, chloranil, and catalytic amounts of trichloroacetic acid[4] was heated at 105 °C for 2 weeks, the product mixture was chromatographed on a silica gel column (benzene/hexane gradient) to yield 5,6-dihydro-3,4-dimethoxybenz[*a*]anthracene-7,12-dione (**3**; mp 173-175 °C, 15%) and 3,4-dimethoxybenz[*a*]anthracene-7,12-dione (**4**; mp 210-211 °C, 12%). Compound **4** was



4 - $R_1 = R_2 = OMe$
6 - $R_1 = OMe, R_2 = H$

identified by its mass spectrum, its IR spectrum, and its complex proton NMR spectrum,[5] which exhibited a doublet (J = 9.7 Hz) at δ 9.49 for H_1[6] and lacked meta coupling (J = 2 Hz). The absence of this meta coupling indicated substitution at the 3-position. Compound **3** was qualitatively identified by its mass spectrum and its proton NMR spectrum which showed an unresolved signal at δ 2.9 whose integral corresponded to four protons. Treatment of compound **3** with oxygen in alcoholic KOH produced **4**, mp 210-211 °C.

When 3-methoxystyrene[3] replaced 2,3-dimethoxystyrene under similar conditions, column chromatography as above afforded 5,6-dihydro-3-methoxybenz[*a*]anthracene-7,12-dione (**5**; mp 148-149 °C, 21%) and 3-methoxybenz[*a*]-anthracene-7,12-dione [**6**; mp 168-169 °C (lit.[7] mp 169-169.5 °C), 19%]. Compound **5** was identified as a dihydro intermediate by its mass spectrum and its proton NMR spectrum which showed an unresolved four-proton resonance signal at δ 2.78. Compound **5** was converted in oxygenated alcoholic KOH to **6**, mp 167.5-169.0 °C.

To determine the structure of the dihydro intermediates, ^{13}C NMR spectra and off-resonance decoupled spectra were taken. Assignment of aromatic resonances was made by single-frequency decoupling. Proton NMR assignments used in the single-frequency decoupling experiments were based on published assignments in 9,10-anthraquinone[5] and benz[*a*]anthracene-7,12-dione.[6] Nonprotonated carbon resonances were identified by their lower intensity. Assignments are shown in Table I.

In both cases the structures such as **2** possess a methylene carbon and methine carbon while the **2a**-like structures contain two methylene carbon atoms. The off-resonance multiplicities for the carbon atoms in the

(1) Manning, W. B.; Tomaszewski, J. E.; Muschik, G. M.; Sato, R. I. *J. Org. Chem.* **1977**, *42*, 3465. Tomaszewski, J. E.; Manning, W. B.; Muschik, G. M. *Tetrahedron Lett.* **1977**, 971.

(2) An early investigation that demonstrated that this isomerization could occur thermally is described by: Bergmann, E.; Bergmann, F. *J. Org. Chem.* **1939**, *3*, 125.

(3) Tagaki, W.; Inoue, I.; Yano, Y.; Okonogi, T. *Tetrahedron Lett.* **1974**, 2487.

(4) Suggested by the fine work of: Wasserman, A. *J. Chem. Soc.* **1942**, 618.

(5) The chemical shifts of H_8, H_9, H_{10}, and H_{11} are based on published assignments in substituted 9,10-anthraquinones found in: Arnone, A.; Fronz, G.; Mondelli, R. *J. Magn. Reson.* **1977**, *26*, 69.

(6) Brown, P. M.; Thomson, R. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 997.

(7) Muschik, G. M.; Tomaszewski, J. E.; Sato, R. I.; Manning, W. B. *J. Org. Chem.* **1979**, *44*, 2150.

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