TABLE IV
PHYSICAL CONSTANTS AND YIELDS OF 1-ARYL-3-BUTEN-1-OLS

Compound	Index of refraction, $n^{25}D$	Bp (mm), °C	Yield, %	Calcd, % C	Calcd, % H	Formula	Found,[a] % C	Found,[a] % H	Found,[a] % Cl
1-Phenyl-3-buten-1-ol (a)	1.5314[b]	71 (0.75)	41	81.04	8.10	$C_{10}H_{12}O$	81.16	7.92	
1-*p*-Methoxyphenyl-3-buten-1-ol (b)	1.5365	102–103 (0.35)	18	74.13	7.92	$C_{11}H_{14}O_2$	73.53	7.78	
1-*p*-Chlorophenyl-3-buten-1-ol (c)	1.5511	98.5–99 (0.30)	60	65.76	6.07	$C_{10}H_{11}OCl$	65.39	5.91	19.88[d]
1-*o*-Methylphenyl-3-buten-1-ol (d)	1.5313	74 (0.50)	19	81.44	8.70	$C_{11}H_{14}O$	81.24	8.70	
1-*p*-Methylphenyl-3-buten-1-ol (e)	1.5280	74–75 (0.42)	26	81.44	8.70	$C_{11}H_{14}O$	81.80	8.80	
1-*m*-Methylphenyl-3-buten-1-ol (f)	1.5272	79–80 (0.80)	31	81.44	8.70	$C_{11}H_{14}O$	81.88	8.57	
1-*m*-Methoxyphenyl-3-buten-1-ol (g)	1.5372	96–97 (0.30)	18	74.13	7.92	$C_{11}H_{14}O_2$	73.53	7.95	
1-*o*-Chlorophenyl-3-buten-1-ol[c] (h)		83 (0.38)	16	65.76	6.07	$C_{10}H_{11}OCl$	65.43	6.0	19.91[d]
1-*o*-Methoxyphenyl-3-buten-1-ol[c] (i)		96 (0.32)	20	74.13	7.92	$C_{11}H_{14}O_2$	74.52	8.06	

[a] The analytical work was done by M. H. W. Laboratories, Garden City, Mich. [b] Lit.[14] $n^{25}D$ 1.5305. [c] Solids at room temperature. [d] Calcd 19.42%.

excess ether removed by evaporation under vacuum. Distillation yielded 18.4 g of product: bp 71° (0.75 mm); yield 41%; $n^{25}D$ 1.5314 (lit. $n^{25}D$ 1.5305[14]); nmr δ 7.1, 5.1–6.0, 4.6, 2.3, 2.2; ir OH at 3400–3800 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O$: C, 81.0; H, 8.1. Found: C, 81.16; H, 7.92.

Method of Pyrolysis.—The kinetics of pyrolysis were done using a carefully deactivated stainless steel static reactor[8] fitted with a null point gauge and an exterior pressure measuring system. A small sample (0.15–0.25 ml) of alcohol was injected, the reactor sealed, and the pressure followed with time. A pressure at time ∞ (reaction complete) was determined, and a plot of ln $(P_\infty - P_t)$ *vs.* time, where P_t is pressure at time t, was used to determine first-order rate constants. The furnace temperature was monitored to ±0.1° using an iron–constantan thermocouple which had previously been standardized against a Bureau of Standards calibrated platinum resistance thermometer.

Product Analysis.—The pyrolysis products from three or four 0.3-ml injections were collected in a Dry Ice–isopropyl alcohol trap attached directly to the exhaust value in the reaction vessel. To ensure that all products were retained in the trap, the trap was sealed and left in the Dry Ice–isopropyl alcohol slurry before removing from the vacuum line. Since the products from the pyrolysis of 1-aryl-3-buten-1-ols are propene and substituted benzaldehydes, a method was designed to separate the gas by distillation. The propene was distilled into a cold (−72°) mass spectrometer gas cell and analyzed from this directly by mass spectroscopy. The aldehydes were dissolved in deuteriochloroform containing an internal tetramethylsilane standard for nmr analysis.

The products, the stoichiometry, and excellent kinetic data conclusively demonstrated that the pyrolysis in a seasoned reactor of these β-hydroxy olefins followed first-order kinetics to greater than 99% of the reaction in the temperature range studied.

(14) M. Gaudeman, *Bull. Soc. Chim. Fr.*, **5**, 974 (1962).

Registry No.—Table IV—a, 936-58-3; b, 24165-60-4; c, 14506-33-3; d, 24165-62-6; e, 24165-63-7; f, 24165-64-8; g, 24165-65-9; h, 24165-66-0; i, 24165-67-1.

Acknowledgment.—We wish to thank the National Science Foundation, Grant GP 9251, the National Defense Education Act, and the Utah State University Research Council for generous support of this work. We are also indebted to Mr. George Eddington of Electrodynamic Laboratory at Utah State University for the maintenance of the kinetic equipment. Grateful acknowledgment is given to the National Bureau of Standards for the calibration of a platinum resistance thermometer and to the local chapter of Sigma Xi for a small research award to one of us (K. J. V.).

Redox Behavior of α-Tocopherol and Model Compounds. II. Ring Opening of 8a-Hydroxy-2,2,5,7,8-pentamethyl-6-chromanone

M. F. MARCUS AND M. D. HAWLEY

Department of Chemistry, Kansas State University, Manhattan, Kansas 66502

Received October 31, 1969

Double-potential-step chronoamperometry has been used in the study of the kinetics and the mechanisms of the ring opening of 8a-hydroxy-2,2,5,7,8-pentamethyl-6-chromanone, a model of the hemiketal intermediate in the oxidation of α-tocopherol to α-tocopherylquinone. Working curves for the determination of the rate constants were obtained by a digital simulation technique. The system was observed to be both general acid and general base catalyzed. The mechanism proposed for general acid catalysis involves proton transfer from the acid to the oxygen in the 1 position followed by removal of a proton from the hydroxy group in the 8a position by the solvent, water. In the case of general base catalysis, the reaction proceeds by removal of the proton from the hydroxy group by the base and transfer of a proton from the solvent to the oxygen in the 1 position.

The widespread occurrence of chromanols and quinones in nature has led to extensive studies into their possible roles in biological processes.[1-3] The observance of the ready ease with which these compounds enter into redox reactions has led to several proposals relating oxidation–reduction processes to biological activities. Although elucidation of these biological processes must be provided ultimately by studies *in vivo*, the results of chemical studies *in vitro* can provide considerable information regarding intermediates, products, and rates of chemical processes.

(1) G. E. W. Wolstenholme and C. N. O'Connor, Ed., "Quinones in Electron Transport," Little, Brown and Co., Boston, Mass., 1960.

(2) R. A. Morton, Ed., "Biochemistry of Quinones," Academic Press, Inc., New York, N. Y., 1965.

(3) "International Symposium on Recent Advances in Research on Vitamins K and Quinones (Vitamins K, Ubiquinones or Coenzymes Q, Plastoquinones) in Honor of Professor Henrik Dam," in *Vitamins Hormones*, **24**, 291 (1966).

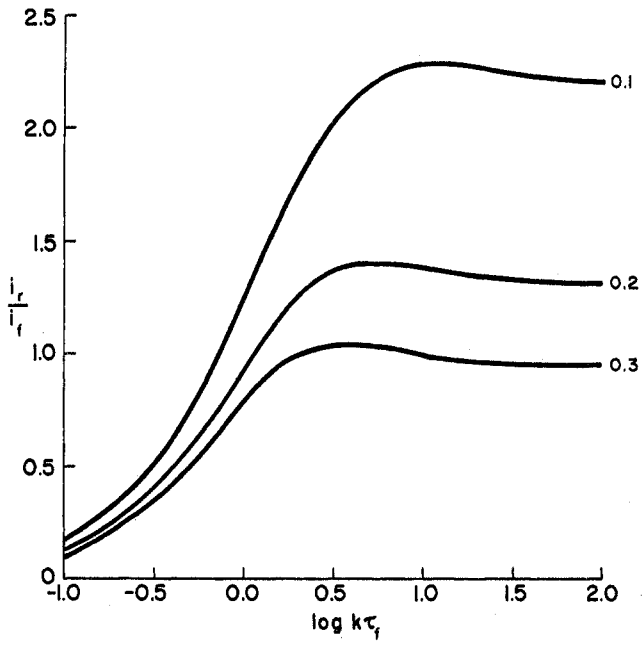
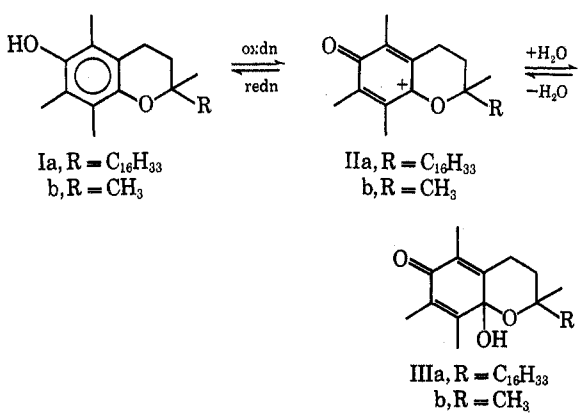


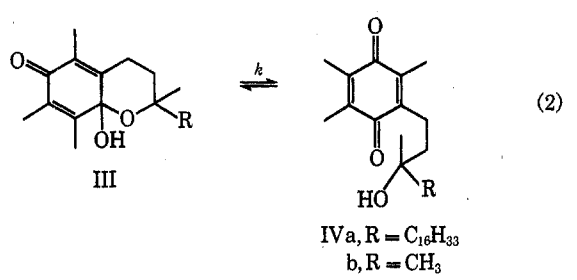
Figure 1.—Theoretical working curves for the double-potential-step chronoamperometric method: A → B + ne; B → C (k); C + ne ⇌ D. The ratios of τ_r/τ_f are indicated on the curves.

In an earlier report from this laboratory[4] it was shown that the predominant pathway for the electrochemical oxidation of α-tocopherol (Ia) and its model compound, 2,2,5,7,8-pentamethyl-6-hydroxychroman (Ib), was *via* a carbonium ion intermediate (eq 1). In the presence



(1)

of nucleophiles, such as water, the carbonium ion II was transformed rapidly into an electroinactive (but chemically reducible) chromanone III. Ring opening of this intermediate then yielded the corresponding quinone IV as the final product of the oxidation (eq 2).



(2)

(4) M. F. Marcus and M. D. Hawley, *Biochem. Biophys. Acta*, **201**, 1 (1970).

The present paper is principally concerned with the mechanism of this last reaction, the conversion of the chromanone into an electroactive quinone.

Experimental Section

Instrumentation.—The cyclic voltammetric and chronoamperometric studies were performed on a transistorized, three-electrode potentiostat–galvanostat described previously.[5] Readout in cyclic voltammetry and long-term chronoamperometry experiments was to a Moseley Model 7030A x–y recorder. For chronoamperometric studies of less than 5-sec duration, readout was to a Tektronix Model 564 oscilloscope equipped with 2A63 and 2B67 plug-ins. Oscilloscope traces were recorded on film using a Dumont Type 302 Polaroid camera. The signal source was a Hewlett-Packard Model 3300–3302 function generator.

Cells and Electrodes.—A planar gold button with a geometric area of 0.33 cm^2 was used as the working electrode in aqueous acetonitrile solutions. A saturated calomel and a platinum foil served as the reference and auxiliary electrodes, respectively. All solutions were deaerated with purified nitrogen to remove traces of oxygen.

Chemicals and Solutions.—2,2,5,7,8-Pentamethyl-6-hydroxychroman was prepared according to a published procedure.[6] The solvent composition was maintained at 25 vol % acetonitrile–75 vol % water. Reagent grade acetonitrile was used as received. Buffer solutions were prepared from reagent grade acids which were neutralized to the appropriate pH with carbonate-free sodium hydroxide. All measurements were made at 23.0 ± 0.1°.

Results

Development of a Working Model.—The calculations of the theoretical working curves for the double-potential-step chronoamperometric method were made by a digital simulation technique described by Feldberg.[7] It is assumed in the model that the oxidation of a chromanol is a two-electron, diffusion-controlled process which gives the corresponding carbonium ion. It is further assumed that the rate constant for the conversion of the carbonium ion to 8a-hydroxy-2,2,5,7,8-pentamethyl-6-chromanone (eq 1) is infinitely large in the presence of a large excess of water. This assumption is justified experimentally since the pseudo-first-order rate constant exceeds 100 sec^{-1} under our reaction conditions.[4]

The kinetically slow step which follows is the conversion of the electroinactive chromanone into an electroactive quinone (eq 2). After a forward electrolysis time, τ_f, the concentration of quinone is studied by stepping the potential cathodically. It is assumed in the model that the reduction of the quinone can be written as a two-electron process. Thus, while the model is compatible with the pathway which produces the corresponding hydroquinone as the reduction product,[4] the model is also compatible with a pathway which produces the recyclized chromanol I.[8] The reaction sequence is summarized in eq 3–5; the chronoamperometric working curves calculated for this sequence are shown in Figure 1.

$$A \longrightarrow B + 2e \quad (3)$$

$$B \xrightarrow{k} C \quad (4)$$

$$C + 2e \rightleftharpoons D \quad (5)$$

(5) J. G. Lawless and M. D. Hawley, *J. Electroanal. Chem.*, **21**, 365 (1969).

(6) L. I. Smith, H. E. Ungnade, H. H. Hoehn, and S. Wawzonek, *J. Org. Chem.*, **4**, 311 (1939).

(7) S. W. Feldberg in "Electroanalytical Chemistry—A Series of Advances," Vol. III, A. J. Bard, Ed., Marcel Dekker, Inc., New York, N. Y., 1969. A copy of the computer program is available upon request from the authors of this paper.

(8) V. D. Parker, *J. Amer. Chem. Soc.*, **91**, 5380 (1969).

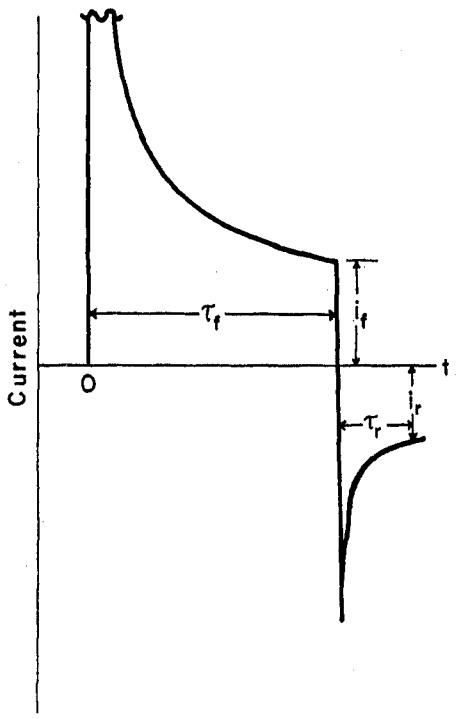


Figure 2.—Anodic–cathodic current–time curves for the model compound, 2,2,5,7,8-pentamethyl-6-hydroxychroman, showing the method of current and time measurements for the double-potential-step chronoamperometric technique. The ratio of τ_r/τ_f shown here is 0.3.

Tests of the Working Model.—Dimensionless working curves (Figure 1) were constructed for several different ratios of the reverse electrolysis time, τ_r, to the forward electrolysis time, τ_f. The method of measuring the forward and reverse currents and the forward and reverse electrolysis times is shown in Figure 2. Each of the working curves confirms the expectation that the ratio of the cathodic current, i_r, to the anodic current, i_f, approaches zero for very small values of $k\tau_f$; *i.e.*, the rate of ring opening of the electroinactive chromanone to produce the electroactive quinone is neglible for small values of $k\tau_f$. For large values of $k\tau_f$, the ratio of i_r/i_f approaches a limit of 2.21 when $\tau_r/\tau_f = 0.1$. This limiting value is predicted for a single redox couple when the anodic and cathodic processes are both diffusion controlled.[9] An experimental test of the model is shown in Figure 3. The linearity of the plot and its extrapolation to the origin confirm the validity of the theoretical model. The slope of the plot yields the rate constant directly.

Effect of pH and Buffer Concentration.—In general, the first-order rate constant for a reaction catalyzed by a single acid–base can be written as

$$k_{obsd} = k_o + k_H[H^+] + k_{OH}[OH^-] + k_{HA}[HA] + k_A[A^-] \quad (6)$$

In order to determine the values of the several catalytic constants, eq 6 can be rewritten in the form

$$k_{obsd} = a[A^-] + b \quad (7)$$

where

$$a = k_{HA}[HA]/[A^-] + k_A \quad (8)$$

and

$$b = k_0 + k_H[H^+] + k_{OH}[OH^-] \quad (9)$$

(9) W. M. Smit and M. D. Wijnen, *Rec. Trav. Chim. Pays-Bas*, **79**, 5 (1960).

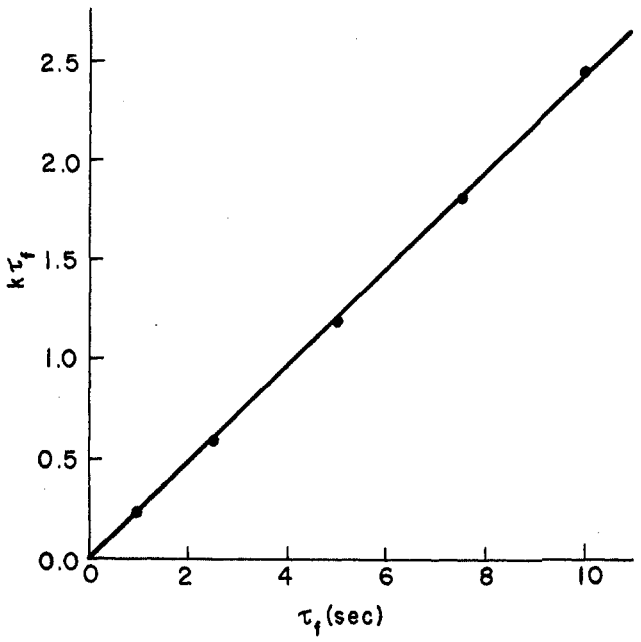


Figure 3.—Plot of $k_{obsd}\tau_f$ *vs.* τ_f for the rearrangement of 8a-hydroxy-2,2,5,7,8-pentamethyl-6-chromanone in 75 vol % water–25 vol % acetonitrile: pH 3.99, 0.5 *M* chloroacetic acid, 0.5 *M* sodium chloroacetate.

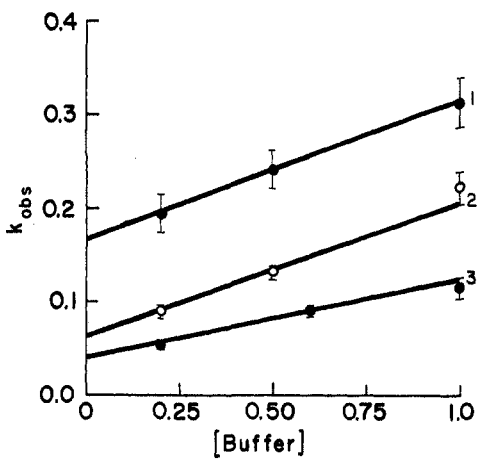


Figure 4.—Dependence of the rate constant for the ring opening of 8a-hydroxy-2,2,2,5,7,8-pentamethyl-6-chromanone on the analytical concentration of the acetic acid buffer and pH: (1) pH 6.24, 90% acetate; (2) pH 5.81, 80% acetate; and (3) pH 5.20, 50% acetate.

Thus, if a constant ratio of $[HA]/[A^-]$ is maintained, a plot of the observed rate constant, k_{obsd}, as a function of the concentration of the conjugate base, A^-, gives values for a and b. The catalytic constants k_{HA} and k_A are then determined either by the solution of the simultaneous equations (eq 8) or (preferably) by a plot of a *vs.* $[HA]/[A^-]$. Values of k_H and k_{OH} are determined in a similar manner from plots of the intercepts, b, as a function of the hydrogen and hydroxyl ion concentrations, respectively. The intrinsic rate constant, k_0, is given by the intercept of either of the latter two plots.

The variation of the observed rate constant as a function of the analytical concentration of acetic acid is shown in Figure 4. Analysis of these data according to the procedure outlined above indicates that the ring-opening reaction is general base catalyzed. The values of the several catalytic constants are summarized

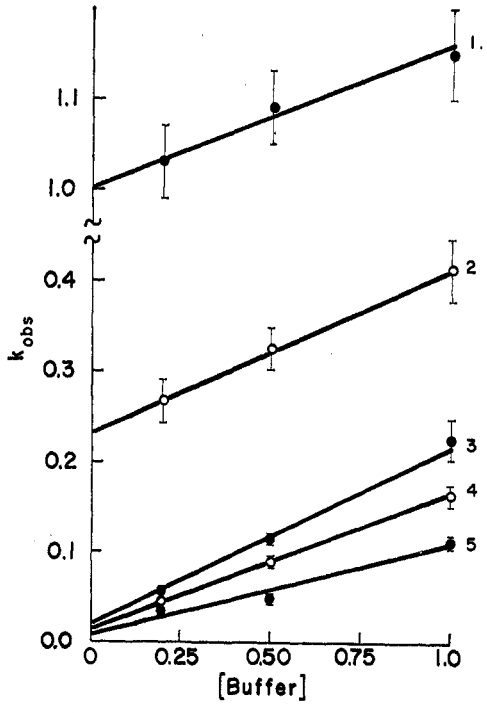


Figure 5.—Dependence of the rate constant for the ring opening of 8a-hydroxy-2,2,5,7,8-pentamethyl-6-chromanone on the analytical concentration of the buffer and pH: (1) pH 2.60, 10% chloroacetate; (2) pH 3.40, 50% chloroacetate; (3) pH 3.99, 80% chlororacetate; (4) pH 4.20, 90% chloroacetate; and (5) pH 4.57, 20% acetate.

in Table I. Although no evidence could be found in this limited pH range (5.20–6.70) to indicate general acid catalysis, its presence would probably not be

TABLE I

CATALYTIC CONSTANTS FOR THE RING OPENING OF 8a-HYDROXY-2,2,5,7,8-PENTAMETHYL-6-CHROMANONE AT 23.0°

Species	k
Intrinsic	4×10^{-3} sec^{-1}
H^+	4×10^{2} M^{-1} sec^{-1}
OH^-	1×10^{7} M^{-1} sec^{-1}
CH_3COO^-	1.6×10^{-1} M^{-1} sec^{-1}

observed if k_{HOAc} were less than 4×10^{2} M^{-1} sec^{-1}.[10] Similarly, no evidence was found to suggest a concerted reaction involving both acetic acid and its conjugate base (acetate ion) in the rate-determining step.

An enhancement in the rate of the reaction with an increase in the buffer concentration was also seen at lower pH (Figure 5). While this result is consistent with catalysis by components of the buffer systems, the addition of an inert salt also causes an increase in the rate constant in this pH range. The data of Table II not only indicate the magnitude of this salt effect, but also indicate a differential salt effect (compare, for example, expt 4 and 5). The occurrence of a marked dependence of the rate constant on the concentration of

(10) This limit is variable, however, and dependent upon the precision of the electrochemical measurements, the concentrations of the several buffer components, and effect of inert salt. The necessity of maintaining an appreciable buffer capacity (protons are involved in both electrochemical redox processes as well as in the addition of water to the carbonium ion, IIb) with respect to the substrate concentration fixes the lower limit for the study of ionic strength effects. Since inert salts undergo varying amounts of ion pairing at these relatively large concentrations, differential salt effects will appear, affecting catalysis in those reactions which are sensitive to changes in ionic strength.

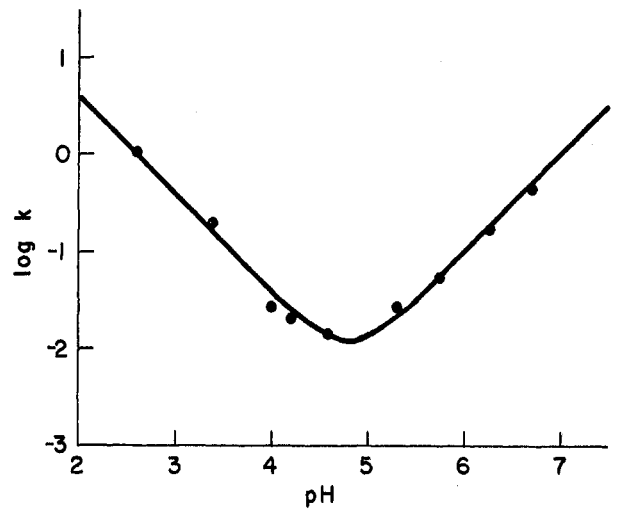


Figure 6.—Plot of log k *vs.* pH for the ring opening of 8a-hydroxy-2,2,5,7,8-pentamethyl-6-chromanone at zero ionic strength and zero buffer concentration. The line is calculated from the data in Table I.

TABLE II

DEPENDENCE OF THE RATE CONSTANT FOR THE RING OPENING OF 8A-HYDROXY-2,2,5,7,8-PENTAMETHYL-6-CHROMANONE ON BUFFER AND INERT SALT CONCENTRATIONS AT 23.0°

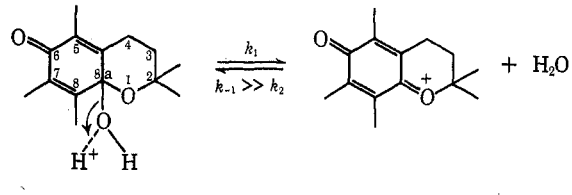
Expt	pH	[HA], M[a]	[A$^-$], M	[NaClO$_4$], M	[NaNO$_3$], M	k_{obsd}, sec^{-1}
1	4.20	0.02	0.18			0.047 ± 0.002
2	4.20	0.05	0.45			0.089 ± 0.005
3	4.20	0.10	0.90			0.162 ± 0.012
4	4.20	0.02	0.18		0.80	0.108 ± 0.007
5	4.20	0.02	0.18	0.80		0.130 ± 0.008
6	4.20	0.05	0.45	0.50		0.166 ± 0.006
7	2.60	0.18	0.02			0.90 ± 0.11
8	2.60	0.18	0.02	1.00		1.12 ± 0.16
9	5.20	0.10	0.10			0.055 ± 0.004
10	5.20	0.10	0.10	0.90		0.051 ± 0.003
11	5.80	0.10	0.10			0.150 ± 0.018
12	5.80	0.10	0.10	0.90		0.248 ± 0.031

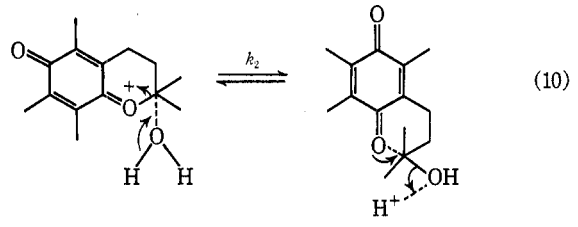
[a] pH 4.20 and 2.60, chloroacetic acid; pH 5.20, acetic acid; pH 5.80, pyridinium perchlorate.

inert salt in slightly more acidic media suggests a change in the mechanism of the rate-determining step. Indeed, there is, as indicated by Figure 6, a minimum in the rate of the reaction near pH 4.8 followed by an increase in the rate with an increase in the hydrogen ion concentration. The slope of the linear plot of log k_{obsd} *vs.* pH is −1 in this region (at zero buffer concentration and zero ionic strength), indicating that the reaction is also specific acid catalyzed. Because of the differential salt effect noted here, it is not possible to determine a rate constant for chloroacetic acid catalysis. For a similar reason, the determination of the effectiveness of chloroacetate ion as a general base is also precluded.

Discussion

The specific acid catalyzed reaction is consistent kinetically with mechanisms 10 and 11. Mechanism

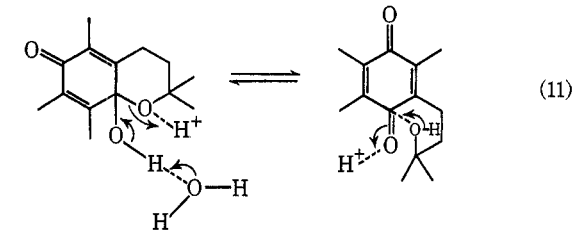




(10)

10, which is probably important in the acid-catalyzed hydrolysis of acetals and ketals,[11,12] can be ruled out on the basis of ^{18}O studies. The chemical oxidation of 2-methoxyphenol[13] and α-tocopherol[14] in the presence of $H_2{}^{18}O$ results in the incorporation of ^{18}O into the quinone nucleus. Since no ^{18}O is incorporated into the hydroxy group of the side chain, the oxidation of Ia and IVa in acidic solution cannot involve dehydration of the 8a-hydroxy-6-chromanone (II) and the subsequent attack of water on the carbon in the 2 position.

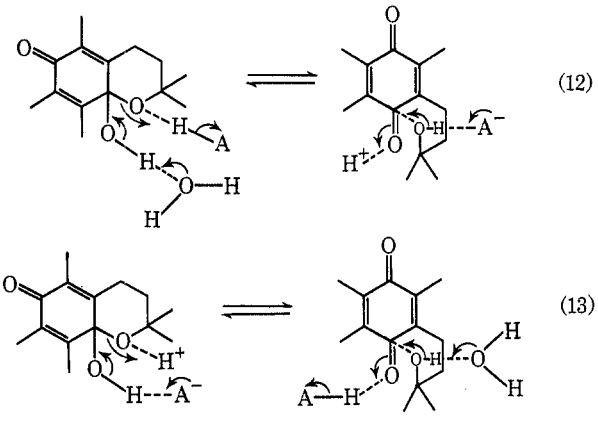
According to mechanism 11, the oxygen in the 1 position is protonated to form the corresponding



(11)

oxonium salt. Removal of the proton from the hydroxy group in the 8a position by the solvent results in the quinone IVb with the ^{18}O derived from the solvent incorporated into the quinone nucleus. Since this mechanism is consistent with the observed kinetics and correctly determines the disposition of the oxygen atom derived from the solvent, it is suggested as the major reaction pathway in solutions of strong acids.

Kinetically, mechanisms 12 and 13 involve catalysis by general acids. Although measurements of the values for the catalytic constants of chloroacetic and



(12)

(13)

acetic acids were precluded by the differential salt effect, there is, nevertheless, considerable evidence for catalysis by general acids. First, when the data of Table II are used to estimate rate constants in the presence of larger amounts of acetic acid (pH 4.57), the calculated rate constants are considerably smaller than the observed rate constants. A catalytic constant for acetic acid which varies from 0.04 to 0.08 M^{-1} sec^{-1} as the analytical concentration of the buffer increases from 0.2 to 1.0 M is required to account for the differences between the calculated and experimental rates. Precedent for catalysis by carboxylic acids is found in the mutarotation of glucose (a ring opening of hemiacetal).[15-17] Although the rate of the ring-opening reaction of IIIb is *ca.* an order of magnitude greater than the mutarotation of glucose, the ratios of k_{OAc^-}/k_{HOAc} are similar in both reactions. Important also from the work of Brønsted and Guggenheim[15] is the result that both chloroacetic acid and chloroacetate anion were only *ca.* one-fifth as effective catalysts on an equimolar basis as acetate anion. In view of the magnitude of the differential salt effect,[18] the presence of general acid catalysis could easily be missed under some of our reaction conditions.

Second, and more compelling, a significant salt effect is anticipated if the ring-opening reaction is general acid catalyzed. In mechanism 12, positive and negative species (the hydronium ion and the anion of the carboxylic acid) are formed from uncharged reactants. According to the theory of Bateman, Church, Hughes, Ingold, and Taher,[19] the effect of salt on the highly polarized transition state complex, and hence on the rate constant k, is given by eq 14. In this equation, μ

$$\log k/k_0 = (9.12 \times 10^{15})\sigma\mu/D^2T^2 \qquad (14)$$

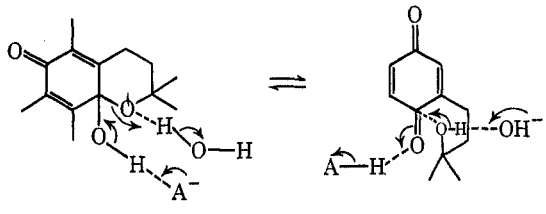
is the ionic strength, D is the dielectric constant, and $\sigma = Z^2d$, which is a measure of the distance of the charge separation in the transition state complex. Although the latter quantity is unknown, a plausible value of $\sigma = 2 \times 10^{-8}$ cm leads to the prediction that a fourfold increase in the rate constant should result from a tenfold increase in the ionic strength. The results reported in Table II (compare expt 1, 4, and 5) are in qualitative agreement with this prediction at pH 4.20. At either lower or higher pH (expt 7–10) the effect of added inert salt is insignificant. This result is anticipated with decreasing pH as the reaction becomes predominately specific acid catalyzed. As seen in eq 11, the pathway involves protonation of the oxygen in the 1 position and loss of a proton from the hydroxy group in the 8a position. Since no additional charged species is either created or destroyed, a neglible salt effect should be observed.[19] For an analogous reason (*vide infra*), the effect of salt also diminishes when the reaction proceeds *via* a base-catalyzed pathway at higher pH.

According to mechanism 13, protonation of the oxygen in the 1 position and the removal of a proton from the hydroxy group in the 8a position by the negatively charged base will behave kinetically as general acid catalysis. Although this mechanism has been

(11) J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure," McGraw-Hill Book Co., New York, N. Y., 1968, p 306.
(12) W. P. Jencks, *Progr. Phys. Org. Chem.*, **2**, 92 (1964).
(13) E. Adler, I. Falkehag, and B. Smith, *Acta Chem. Scand.*, **16**, 529 (1962).
(14) H. Mayer, W. Vetter, J. Metzger, R. Rüegg, and O. Isler, *Helv. Chim. Acta*, **50**, 1168 (1967); P. Schudel, H. Mayer, J. Metzger, R. Rüegg, and O. Isler, *ibid.*, **46**, 333 (1963).
(15) J. N. Brønsted and E. A. Guggenheim, *J. Amer. Chem. Soc.*, **49**, 2554 (1927).
(16) C. G. Swain and J. F. Brown, Jr., *ibid.*, **74**, 2534, 2538 (1952).
(17) C. G. Swain, A. J. Di Milo, and J. P. Cordner, *ibid.*, **80**, 5983 (1958).
(18) For other reports of differential salt effects, see, for example, E. F. J. Duynstee, E. Grunwald, and M. L. Kaplan, *ibid.*, **82**, 5654 (1960); J. F. Bunnett and N. S. Nudelman, *J. Org. Chem.*, **34**, 2038 (1969).
(19) L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, 979 (1940).

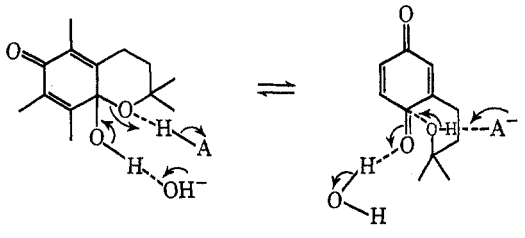
suggested to be important in the acid-catalyzed hydrolysis of a formamidium compound,[20] reaction by this pathway would lead to the prediction that the rate of the ring-opening reaction would decrease significantly with an increase in inert salt concentration.[19] Since this prediction is contradictory to the experimental results, this mechanism cannot be important here.

Little or no effect of salt is predicted and observed (Table II, expt 9 and 10) for the reaction catalyzed by monobasic anions. According to mechanism 15, a



(15)

proton is removed from the hydroxy group by the negatively charged general base, A^-, while a molecule of water functions as the acid. In mechanism 16, a



(16)

proton is transferred from the general acid to the oxygen in the 1 position, while a proton is removed from the hydroxy group in the 8a position by hydroxide ion. This reaction, which proceeds by specific base and general acid catalysis mechanistically, will behave kinetically as catalyzed by general base.

A distinction between the two pathways on the basis of salt effects should be feasible if the general base were unchanged. A change from a negatively to a neutrally charged base leads to the predictions that with an increase in the inert salt concentration the rate constant should increase if the reaction proceeds by mechanism 15 and decrease if the reaction proceeds by mechanism 16. As seen by the results of expt 11 and 12 (Table II), addition of inert salt (sodium perchlorate) to a pyridinium perchlorate–pyridine buffer system results in a marked increase in the experimental rate constant. We conclude from this result that general base catalysis for pyridine proceeds *via* mechanism 15 and suggest that catalysis by carboxylic anions occurs by this reaction pathway also.

It is of final interest to compare the stability of IIIb to that of IIIa.[21] The latter intermediate was reported to exhibit a bell-shaped pH–rate profile with maximum stability at pH 5.5. While maximum stability for IIIb is also noted in this study near this pH, the rate law for the decomposition of IIIb is first order in both hydrogen and hydroxide ions. The apparent difference in the two rate laws probably arises from the different methods used for the preparation of the two intermediates (IIIa,b). In the work of Dürckheimer and Cohen,[21] IIIa was prepared by the chemical oxidation of Ia using N-bromosuccimide as the oxidant. A change in the rate-determining step from the decomposition of IIIa to the oxidation of Ia would satisfactorily account for the observed differences in the rate law.

Registry No.—Ib, 950-99-2; IIIb, 24165-02-4.

Acknowledgment.—These studies were supported by the U. S. Public Health Service Research Grant No. 1 RO1 AM 13258-01.

(20) D. R. Robinson and W. P. Jencks, *J. Amer. Chem. Soc.*, **89**, 7088 (1967). For a complete discussion of carbonyl addition reactions, see ref 11, pp 63–128.

(21) W. Dürckheimer and L. A. Cohen, *ibid.*, **86**, 4388 (1964).

Axially Dissymmetric Molecules. Characterization of the Four 1-Carbethoxy-4-methylspiropentanes

JOSEPH J. GAJEWSKI AND LEO T. BURKA

Contribution No. 1796 from the Department of Chemistry, Indiana University, Bloomington, Indiana 47401

Received January 19, 1970

In order to map the energy surface of various reactions of substituted spiropentanes, the four diastereomers of 1-carbethoxy-4-methylspiropentane were synthesized by methylene addition to *syn*- and *anti*-1-carbethoxy-2-ethylidenecyclopropane. The relative stereochemical configurations of the spiropentane esters were determined by their conversion into the dimethylspiropentanes which were, in turn, synthesized from the spiropentane-1,4-dimethanols, whose configurations were determined by ir hydrogen bonding and nmr studies.

Axially dissymmetric molecules such as allenes and spirans are of historical interest because their synthesis and optical resolution provide experimental confirmation of the predicted geometry of bonds emanating from carbon centers.[1] Spirans with substituents or heteroatoms in each ring having nonsuperimposable mirror images have, in addition, the possibility of existing as diastereomers depending on the nature and point of attachment of the substituents. A few examples of this situation have been reported;[1] however, to our knowledge, the only cases where all possible diastereomers of a disubstituted spiran were separated and characterized are due to Cram[2] and to Applequist[3]

(1) For reviews, see E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 12.

(2) E. Hardegger, E. Maeder, M. Semarne, and D. J. Cram, *J. Amer. Chem. Soc.*, **81**, 2729 (1959).

(3) D. E. Applequist and E. G. Alley, *J. Org. Chem.*, **33**, 2741 (1968).