2,3-dibromo-2,3-dihydrobenzofuran, 36739-96-5; 3-bromo-6-chlorobenzofuran, 36739-97-6; 2-hydroxy-4-chlorophenylacetylene, 36739-98-7; 5-chloro-2,3-dibromo-2,3-dihydrobenzofuran, 36826-29-6; 3-bromo-5-chlorobenzofuran, 36739-99-8; 4-bromo-5-methoxybenzofuran, 36826-30-9; 2,3,4-tribromo-5-methoxy-2,3-dihydrobenzofuran, 36740-00-8; 3,4-dibromo-5-methoxybenzofuran, 36826-31-0; 1,(4-bromo-5-methoxy-3-benzofuryl)ethanol, 36740-01-9; ethyl 6-methoxy-2-carboxybenzofuran-3-carboxylate, 28238-33-7; ethyl 4-methoxy-2-carboxybenzofuran-3-carboxylate, 36748-73-9; ethyl 6-methoxybenzofuran-3-carboxylate, 36748-74-0; 6-methoxybenzofuran-3-carboxylic acid, 29822-97-7; 6-methoxy-3-acetylbenzofuran, 36748-76-2.

Confirmation of Concurrent General Acid, General Base Catalysis in the Lactonization of 2-(Hydroxymethyl)benzoic Acid

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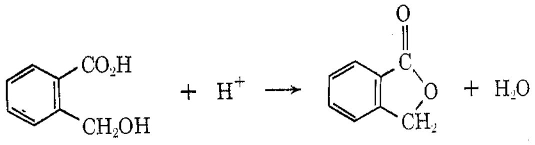
An earlier report that lactonization of 2-(hydroxymethyl)benzoic acid in water is general acid and general base catalyzed (by formic acid and formate ion, respectively) is confirmed, and for the first time substantiating experimental details are presented.

Although *intra*molecular general base catalysis of the reactions of carboxylic acids and esters is fairly common,[1] *inter*molecular general acid catalysis has been observed in only a few cases.[1]

In 1969, Milstien and Cohen[2a] reported in a preliminary communication that the lactonizations of 2-(hydroxymethyl)benzoic acid (**1**) and some phenolic acids in water are subject to concurrent general acid and general base catalysis by formate, acetate, and several other buffers. A subsequent full paper[2b] reported details of their study in respect to the phenolic acids, but details concerning lactonization of **1** have not appeared. Inasmuch as catalysis of the lactonization of **1** was of special interest to us, we undertook a reexamination of the rates of lactonization of **1** in formic acid–formate ion buffers at 60°. Our results confirm the report[2a] that the reaction is catalyzed by both the acidic and basic constituents of the buffer.



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Results and Discussion

The rates of lactonization of **1** in formic acid buffers were studied under pseudo-first-order conditions identical with those used by Milstien and Cohen,[2a] that is, 60.0° and an ionic strength, μ, of 0.30. Although previous studies[3,4] were available on the hydrogen ion catalyzed lactonization at 60° under slightly different conditions, we also determined this rate constant at 60.0° and μ 0.30 using two different hydrochloric acid concentrations. Also, the apparent ionization constants (K_a's) of **1** and of formic acid were measured under the reaction conditions.

A composite rate law[1] was found for the lactonization in formic acid buffers, as set forth in eq 1, where

$$k_\psi = \alpha(k_0 + k_{H^+}[H^+] + k_{HA}[HA] + k_{A^-}[A^-]) \qquad (1)$$

k_ψ is the pseudo-first-order rate coefficient, α is the fraction of substrate undissociated at a particular pH, k_0 and k_{H^+} are the water and hydrogen ion catalyzed components of the rate, and k_{HA} and k_{A^-} are the rate constants for catalysis by the buffer acid and its conjugate base, respectively.

Since the buffer components are present in large excess over the substrate, α can be calculated for each buffer without knowledge of the actual pH, provided that the relative pK_a's of the buffer acid and the substrate are known under the reaction conditions. The determination of these ionization constants is described in the Experimental Section; the observed values are pK_a = 3.66, formic acid, and pK_a = 3.79, **1**. These values compare with pK_a = 3.77 at 30° and μ 0.3 for formic acid, reported by Milstien and Cohen,[2b] and pK_a = 3.84 at room temperature and μ <0.01, reported[4] for **1**. From these experimental pK_a's, α was evaluated for each buffer and used to calculate the corrected pseudo-first-order rate coefficients, $k_\psi' = k_\psi/\alpha$.

In order to simplify determination of the several rate constants, two sets of buffer experiments were performed. The first set consisted of eight kinetic runs at a constant buffer ratio of $[HA]/[A^-] = 1$ but with variation of the total buffer concentration. Under these conditions eq 1 simplifies to eq 2, where

$$k_\psi' = k_0 + k_{H^+}K_{HA} + (k_{HA} + k_{A^-})[HA] \qquad (2)$$

K_{HA} is the ionization constant of formic acid. A plot of k_ψ' *vs.* [HA] for these runs (Table I, runs 1–8) is shown in Figure 1; the slope is ($k_{HA} + k_{A^-}$) and the intercept ($k_0 + k_{H^+}K_{HA}$).

In the second set of experiments the concentration of formate ion was held constant at 0.30 *M* while five different formic acid concentrations were employed (runs 8, 12–15). For these conditions eq 3 applies.

$$k_\psi' = k_0 + k_{A^-}[A^-] + (k_{H^+}K_{HA}/[A^-] + k_{HA})[HA] \qquad (3)$$

The anticipated linear plot of k_ψ' *vs.* [HA] was obtained; it is not shown. Since the intercept is $k_0 + 0.30\ k_{A^-}$,

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[1] S. L. Johnson, *Advan. Phys. Org. Chem.*, **5**, 237 (1967).

[2] (a) S. Milstien and L. A. Cohen, *J. Amer. Chem. Soc.*, **91**, 4585 (1969); (b) *ibid.*, **92**, 4377 (1970).

[3] J. Tirouflet, *Bull. Soc. Chim. Fr.*, 799 (1954).

[4] J. F. Bunnett and C. F. Hauser, *J. Amer. Chem. Soc.*, **87**, 2214 (1965).

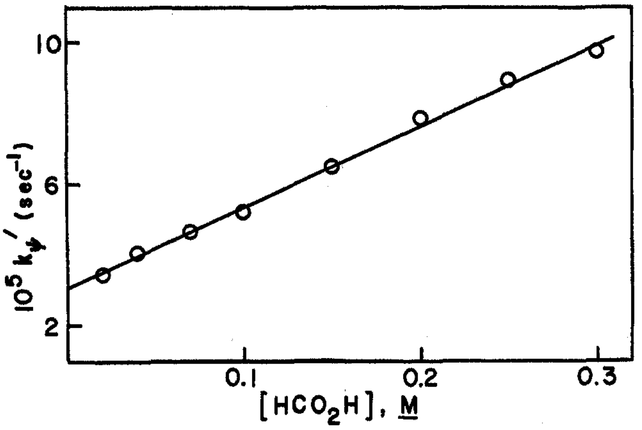

Figure 1.—Plot of pseudo-first-order rate coefficients *vs.* formic acid concentration, $[HCO_2H]/[HCO_2^-] = 1$.

TABLE I

PSEUDO-FIRST-ORDER RATE COEFFICIENTS FOR THE LACTONIZATION OF 2-(HYDROXYMETHYL)BENZOIC ACID IN WATER AT 60.0° [a]

Run	$[HCO_2H]$, *M*	$[HCO_2Na]$, *M*	$10^5 k_\psi$, sec^{-1}	$10^5 k_\psi'$,[b] sec^{-1}
1	0.020	0.020	1.98	3.45
2	0.040	0.040	2.32	4.04
3	0.070	0.070	2.69	4.68
4	0.100	0.100	2.99	5.21
5	0.150	0.150	3.74	6.51
6	0.200	0.200	4.50	7.84
7	0.250	0.250	5.15	8.96
8	0.300	0.300	5.60	9.75
9	0.020	0.020	1.94	3.38
10[c]	0.020	0.020	1.98	3.45
11[d]	0.020	0.020	1.92	3.34
12	0.100	0.300	2.28	7.35
13	0.150	0.300	3.45	8.56
14	0.600	0.300	11.0	15.1
15	0.900	0.300	15.7	18.5
16	0.001[e]		6.61	7.69
17	0.002[e]		13.9	15.0

[a] μ 0.30 with added NaCl; substrate concentration 5.0×10^{-4} *M*. [b] $k_\psi' = k_\psi/\alpha$; see text. [c] Added salt was $NaNO_3$. [d] Added salt was $NaClO_4$. [e] Acid was HCl.

k_{HA} and k_{A^-} can now be evaluated, provided that k_0 can be determined.

The value of k_0 was evaluated from the intercept of Figure 1, by subtracting from it $k_{H^+}K_{HA}$ (*cf.* eq 2), experimentally determined values of k_{H^+} and K_{HA} being used. The rate constant for hydrogen ion catalyzed lactonization, k_{H^+}, was determined by measuring the pseudo-first-order coefficients at 60° and μ 0.30 at two HCl concentrations, 1.0×10^{-3} and 2.0×10^{-3} *M* (runs 16 and 17). Under these conditions the rate law is $k_\psi = \alpha(k_0 + k_{H^+}[H^+])$. Also, α equals $[H^+]/([H^+] + K_a)$, where K_a is the ionization constant of the substrate. Assuming that $[H^+] = [HCl]_{st}$, we calculated k_{H^+} as 7.3×10^{-2} M^{-1} sec^{-1}. This value is in good agreement with 7.2×10^{-2} M^{-1} sec^{-1} found by Tirouflet[3] for the reaction in water and 6.9×10^{-2} M^{-1} sec^{-1} reported by Bunnett and Hauser[4] for lactonization in 9% (v/v) ethanol–water.

An alternative method[4] of reckoning k_{H^+}, which allows for the small increase in $[H^+]$ due to ionization of the substrate, gave the same value as the above method. Multiplication of k_{H^+} by 2.2×10^{-4} *M*, the ionization constant of formic acid, gives $k_{H^+}K_{HA} = 1.6 \times 10^{-5}$ sec^{-1}. Subtraction from the intercept of Figure 1 gives $k_0 = 1.45 \times 10^{-5}$ sec^{-1}.

Subtraction of this k_0 from the intercept of a plot of k_ψ' *vs.* [HA], based on the data of runs 8 and 12–15 of Table I (*cf.* eq 3), provided an evaluation of k_{A^-} as 1.54×10^{-4} M^{-1} sec^{-1} for formate ion catalysis. Furthermore, subtraction of this value from the slope of Figure 1 (*cf.* eq 2) afforded $k_{HA} = 7.6 \times 10^{-5}$ M^{-1} sec^{-1} for formic acid catalysis of the lactonization reaction.

These results compare with the corresponding values reported by Milstien and Cohen,[2a] namely, 1.54×10^{-4} M^{-1} sec^{-1} for k_{A^-} and 3.45×10^{-5} M^{-1} sec^{-1} for k_{HA}. The agreement between the values of k_{A^-} is perhaps fortuitous and, in view of the numerous arithmetic operations required to obtain the rate coefficients, the discrepancy between the values of k_{HA} is not disturbing. On the contrary, it serves to emphasize the difficulties involved in obtaining precise data in systems such as this one, in which sizable corrections for equilibria are involved. The problem is particularly acute at temperatures very different from ambient.

Although our results appeared to confirm the earlier work, there remained the (unlikely) possibility that the variation in rate in runs 1–8 was due to a specific salt effect arising from the replacement of chloride ion by formate ion. Salomaa, Kankaanperä, and Lahti[5] observed specific salt effects in the hydrolysis of acetals and ortho esters when buffer experiments of this type were carried out in mixed aqueous solvents, and Bunton and coworkers[6] found similar effects in other types of reactions. To test this possibility, three runs (runs 9–11, Table I) were carried out simultaneously at the lowest buffer concentration employed, with formic acid and formate ion both 0.02 *M*, with three different added electrolytes used to bring the ionic strength to 0.30. The electrolytes chosen, NaCl, $NaNO_3$, and $NaClO_4$, were those shown by Salomaa and coworkers[5] to give very different slopes in their buffer experiments and widely divergent rate coefficients at low buffer concentration. Our results provide no indication of such a specific salt effect in this system and assure that the variation in rate with buffer concentration is in fact due to buffer catalysis. Table II summarizes the kinetic data.

TABLE II

SUMMARY OF KINETIC DATA

k_0, sec^{-1}	k_{H^+}, M^{-1} sec^{-1}	k_{HA},[a] M^{-1} sec^{-1}	k_{A^-},[b] M^{-1} sec^{-1}
1.45×10^{-5}	7.3×10^{-2}	7.6×10^{-5}	1.54×10^{-5}

[a] HA = formic acid. [b] A^- = formate ion.

Experimental Section

Material.—Phthalide, mp 72–74° (lit.[7] mp 72–73°), was an old sample prepared by Dr. C. F. Hauser.[4] Formic acid, sodium hydroxide, sodium chloride, sodium nitrate, and sodium perchlorate were analytical reagent grade materials and were used without further purification. Ordinary distilled water was distilled from potassium permanganate solution before use.

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(5) P. Salomaa, A. Kankaanperä, and M. Lahti, *J. Amer. Chem. Soc.*, **93**, 2084 (1971).

(6) C. A. Bunton, T. W. Del Pesco, A. M. Dunlop, and K.-U. Yang, *J. Org. Chem.*, **36**, 887 (1971).

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pK_a Determinations.—The apparent pK_a's of formic acid and 2-(hydroxymethyl)benzoic acid were measured at 60 ± 1° and 0.3 M sodium chloride using a Model E 300B Metrohm pH meter, equipped with scale expander and temperature calibration. The electrode used was the Metrohm EA-120X combination electrode and the meter was calibrated at 60° using commercial standard buffers.

Standard (0.01 M) solutions of the sodium salts of the acids were prepared [the sodium salt of 2-(hydroxymethyl)benzoic acid was prepared by heating phthalide with a slight excess of sodium hydroxide[4]], made up to μ 0.30 with sodium chloride, and titrated with standard 0.1 N HCl solution (Titrisol). The pH's of the solutions were measured after every 5% neutralization from 10 to 90% neutralization, and the pK_a for each point was calculated using the equation

$$pK_a = pH + \log\{([HA]_{st} - [H^+])/([A^-]_{st} + [H^+])\}$$

where pH is the value read from the pH meter and [H$^+$] is calculated therefrom. Values of pK_a in the region of 30–70% neutralization agreed very well and were averaged to determine the final pK_a value. Owing to instrument drift and instability at the temperature used, the absolute values of the pK_a's are probably less reliable than the relative values, which were determined consecutively as rapidly as possible. The effect of a small error in the absolute value of the pK_a of I on the value of k_{H^+} is not appreciable.

The pK_a value of 1 was 3.79 ± 0.01, while that of formic acid was 3.66 ± 0.01.

Kinetic Procedures.—The rates of lactonization of 1 were determined under pseudo-first-order conditions by measuring absorbance due to the hydroxy acid reactant and the lactone product of aliquots of the reaction solution kept in sealed ampoules immersed in an oil bath at 60.00 ± 0.05°. The absorbances at 254 and 276 nm, respectively, were calculated from transmittance values measured on a Hitachi Perkin-Elmer Model 139 spectrophotometer.

A standard solution of the sodium salt of 1 (5×10^{-3} M) was prepared by saponification of the phthalide. In a typical experiment, 10 ml of the standard was combined with appropriate amounts of standard formic acid, sodium hydroxide, and sodium chloride solutions and diluted to the mark in a 100-ml volumetric flask. Aliquots (10 ml) of this solution were then transferred to 10-ml glass ampoules (Kimble Neutraglas), and the ampoules were sealed and immersed in the constant-temperature bath. At appropriate intervals samples were removed from the bath and quenched in ice; the sample was then transferred to a quartz cuvette and the transmittance was recorded. Six to eight points were obtained over a period of *ca.* 2 half-lives; infinity values were recorded at 10 or more half-lives.

The observed pseudo-first-order rate coefficients (k_ψ) were reckoned by a least-squares plot of log ($A_\infty - A$) *vs.* time on an Olivetti-Underwood Programma 101 programmable calculator. Correlation coefficients (r) were 0.999 or better and were typically 0.9999. Agreement between the two rate constants as determined by reactant decrease and product increase was excellent, although the latter generally gave better r values. The k_ψ values reported in Table I are those of product increase. The slopes and intercepts of Figure 1 and of the plot of k_ψ' *vs.* [HA] according to eq 3 (plot 2) were also evaluated by least-squares analysis and the results are summarized in Table III.

TABLE III

EVALUATION OF KINETIC PARAMETERS

Plot	Runs	Slope, M^{-1} sec^{-1}	Intercept, sec^{-1}	r
1	1–8	2.30×10^{-4}	3.05×10^{-5}	0.998
2	8, 12–15	1.42×10^{-4}	6.06×10^{-5}	0.995

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Acknowledgments.—This research was supported in part by the National Science Foundation. N. Tomoto expresses his thanks for a fellowship from the Japanese Ministry of Education.

Solution Photochemistry. X. A Study of the Effects of Double-Bond Geometry and of Increasing Double-Bond Separation on the Photochemical Reactions of Acyclic Nonconjugated Dienes[1,2]

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The triplet-sensitized photochemical reactions of the geometric isomers of the homologous dienes **2a–c**, **3a–c**, **5a–c**, and **6a–c** have been investigated. In the case of the 1,5 dienes **2a–c**, irradiation using acetone as the triplet energy sensitizer leads to cis,trans isomerization and, at a similar rate, to internal "crossed" [2 + 2] cycloaddition to give adducts **7** and **8** in a ratio of 65:35. Similar excitation of the 1,6 dienes **3a–c** causes concurrent geometric isomerism and "straight" [2 + 2] cyclization yielding adducts **9** and **10** (ratio of 3:1). Based on the stereochemistries of the adducts and on the triplet nature of these processes, these cyclizations are interpreted as occurring *via* two-step mechanisms involving the intermediacy of 1,4 diradicals. The specificity observed in the direction of initial bond formation (straight *vs.* crossed) is discussed in terms of excited states **15** and **16** which bond in accordance with strain and entropy effects. Final 1,4-diradical closure is shown to be kinetically controlled and possible explanations for the product ratios are advanced. Triplet excitation of the 1,8 and 1,9 dienes **5a–c** and **6a–c** leads only to geometric isomerism. Since previous work showed that the corresponding 1,7 dienes in this series undergo straight cyclization, the limit of double-bond separation for cyclization has been reached. Direct irradiation studies on trans,trans dienes **2a** and **3a** reveal that α,β to β,γ double-bond migration is an important process; geometric isomerism and internal cyclization are also observed in these cases.

The photochemistry of acyclic nonconjugated dienes has been a subject of continuing interest.[4] Apart from 1,4 dienes, which commonly undergo the di-π-methane rearrangement,[5] the major pathways by which these molecules react upon absorption of a photon of light are cis,trans isomerization and intramolecular [2 + 2] cycloaddition.[6] This latter process can lead to two

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[2] Portions of this work have appeared as preliminary communications: J. R. Scheffer and R. A. Wostradowski, *Chem. Commun.*, 144 (1971); J. R. Scheffer, R. A. Wostradowski, and K. C. Dooley, *ibid.*, 1217 (1971).

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[5] H. E. Zimmerman and P. S. Mariano, *ibid.*, **91**, 1718 (1969).

[6] In addition, substituted 1,5 dienes are occasionally observed to undergo 1,3-allyl shifts from their singlet excited states. For examples, see R. C. Cookson and J. E. Kemp, *Chem. Commun.*, 385 (1971), and references therein.