Enzyme Experiments.—All experiments were conducted at 25° and *p*H 7.9 ± 0.1 in aqueous solution 0.02 *M* with respect to the amine component of a tris-(hydroxymethyl)-aminomethane–hydrochloric acid buffer. The methods employed for the experiments with nicotinyl-L-tryptophanamide, $K_S = 2.7 \times 10^{-3}$ *M*,[13] and with methyl hippurate, $K_S' = 8.5 \times 10^{-3}$ *M*,[11] were identical with those described previously for other experiments with these specific substrates. The enzyme preparation was an Armour product, lot no. 90402, and it will be noted that the specific enzyme concentrations E_S' and E_I' for all experiments were such as to satisfy zone A conditions.[13,16,17]

PASADENA 4, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF WASHINGTON]

The Kinetics of the Decarboxylation of 2,4,6-Trihydroxybenzoic Acid in Perchloric Acid Solution

BY W. M. SCHUBERT AND J. D. GARDNER

RECEIVED AUGUST 18, 1952

Both the rate of decarboxylation of 2,4,6-trihydroxybenzoic acid and the ratio $[RCO_2^-]/[RCO_2H]$ were determined by an ultraviolet spectroscopic method in several concentrations of perchloric acid. The value of k_2' in the equation $k_2' = k_{obsd.}([RCO_2^-] + [RCO_2H])/[RCO_2H]$ was found constant in the region of 0.135 to 38.2% perchloric acid. This is consistent with the rate-controlling step being a first order decomposition of RCO_2H (or something proportional to RCO_2H), or the reaction of RCO_2^- with a proton released from the solution to give the products directly. The reaction is solvent dependent.

A study of the decarboxylation of hydroxy aromatic acids was undertaken with the view of determining (1) whether the reactions are acid-catalyzed, and (2) if they are acid-catalyzed, what is the rate controlling step; *i.e.*, is it represented by equation (1), (2) or (3). The acid-catalyzed

$$\overset{+}{R}CO_2H_2 \longrightarrow RH + \overset{+}{C}O_2H, \text{ or } RCO_2H + H^+ \longrightarrow RH + CO_2\overset{+}{H} \quad (1)$$

$$RCO_2^+H_2 + H_2O \longrightarrow RH + CO_2 + H_3O^+ \quad (2)$$

decarboxylation of hindered alkyl benzoic acids is complicated by the occurrence of a side ionization to the acyl ion, $R\overset{+}{C}O$, in at least the higher ranges of sulfuric acid solutions in which it has been studied.[1] It appeared that the decarboxylation of hydroxy aromatic acids could be examined over a range of acid concentration in which ionization to acyl ion does not occur.

In the meantime, Hammick, Brown and Elliot[2a] reported on the kinetics of the decarboxylation of 2,4,6-trihydroxybenzoic acid in 0 to 0.18 *N* HCl. The reaction rate was followed by a titration method. Earlier the kinetics of decarboxylation of this and other hydroxy aromatic acids had been studied in resorcinol as a solvent at higher temperature.[2b] It was concluded that two simultaneous mechanisms applied. The first of these, reaction (3), was pictured as proceeding *via* attack of a solvated proton on the α-carbon of the undissociated acid

$$RCO_2H + H_3O^+ \xrightarrow{k_2} RH + CO_2 + H_3O^+ \quad (3)$$
$$-dc/dt = k_2[H_3O^+][RCO_2H]$$

The second reaction (4) was pictured as the attack of a solvated proton on the carboxylic acid anion, or the decomposition of the undissociated acid with or without the intervention of a molecule of water

$$RCO_2^- + H_3O^+ \xrightarrow{k_3} RH + CO_2 + H_2O \quad (4)$$
$$RCO_2H\ (+H_2O) \xrightarrow{k_4} RH + CO_2\ (+H_2O)$$
$$-dc/dt = k_3\,[H_3O^+][RCO_2^-] = k_4[RCO_2H]$$

Evaluation of k_2 and k_4 from the observed rate constants required a knowledge of the degree of ionization of RCO_2H to RCO_2^-, which was calculated from a value for the ionization constant, *K*, of 2×10^{-2}. On this basis k_2 was determined to be about five times as large as k_4 at 40°.

Since mechanisms (1) and (2) [or (3)] are kinetically indistinguishable in dilute mineral acids, the reaction was studied in these laboratories over a wide range of acid concentrations, from 0 to 58.5% perchloric acid. Perchloric acid was chosen because it is a strong acid for which values of H_0 are known, it is monobasic and is a non-sulfonating medium. It was found that an ultraviolet spectroscopic method could very readily be adapted to following the rate of disappearance of the carboxylic acid, which has limited solubility in aqueous mineral acids. Furthermore, the spectroscopic method could at the same time be used to determine directly the actual concentrations of RCOOH and $RCOO^-$ in the reaction media.

Experimental

Materials.—2,4,6-Trihydroxybenzoic acid prepared by carbonation of phloroglucinol[3] was recrystallized from acetonitrile, m.p. 205–206°. Perchloric acid solutions of desired strength were made by dilution of Baker C.P. 20% acid and Mallinckrodt C.P. 60% acid. The strength of each acid solution was determined by titration of a suitable aliquot against standard alkali.

Apparatus and Kinetic Method.—A stock solution was prepared by dissolving about 20 mg. of 2,4,6-trihydroxybenzoic acid in 100 ml. of water kept at constant temperature. For each kinetic run, 5 ml. of the stock solution was diluted quickly to 50 ml. with perchloric acid of appropriate strength and at constant temperature. A portion of this solution was transferred quickly to a quartz stoppered Beckman cell. This cell and the cell containing the blank solution, made by diluting 5 ml. of water to 50 ml. with the same strength perchloric acid, were placed in a small constant temperature water-bath that had been inserted between the

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(1) W. M. Schubert, THIS JOURNAL, **71**, 2639 (1949).

(2) (a) B. R. Brown, W. W. Elliot and D. Ll. Hammick, *J. Chem. Soc.*, 1384 (1951); (b) B. R. Brown, D. Ll. Hammick and J. B. Scholefield, *ibid.*, 778 (1950).

(3) P. Holmes, D. E. White and I. H. Wilson, *ibid.*, 28 (1950).

monochrometer and photocell compartments of a Model DU Beckman spectrophotometer. The bath had been carefully made impervious to outside light. The thickness of water that the ultraviolet light beam passed through was about 2 mm. on each side of the quartz cell. The maximum fluctuation in bath temperature was 0.05° at 50°.

In runs at 20° and 30°, optical density readings at appropriate times were made at 5 mμ intervals from 240 or 250 mμ to 275 mμ. Due to the speed of the reaction, changes in optical density in the runs at 40° were determined at only 260, 265 and 270 mμ. At 50°, the spectral change was followed at 260 mμ for one run and at 265 mμ for the check run. In Fig. 1 is shown how the spectrum of a particular solution changes with time. In Table I is shown how the spectrum at the end of the reaction in 10.7, 45.7 and 56.6% perchloric acid solutions closely corresponds to that of pure phloroglucinol.

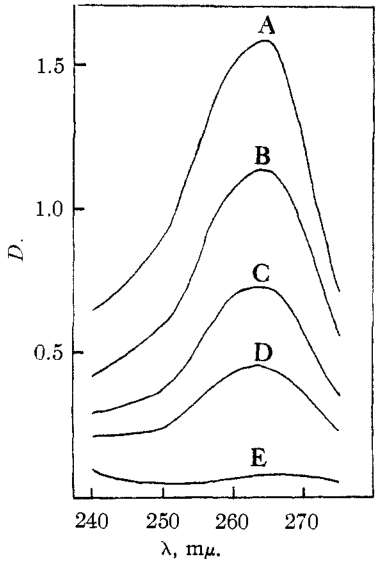

Fig. 1.—Change in optical density with time of 2,4,6-trihydroxybenzoic acid (10^{-4} molar) in 10.7% perchloric acid at 20.0°: A, 0 min., B, 30 min.; C, 60 min.; D, 90 min.; E, 720 min.

TABLE I

COMPARISON OF SPECTRUM AT END OF DECARBOXYLATION, ϵ_∞, WITH SPECTRUM OF PHLOROGLUCINOL, ϵ_P

	HClO$_4$, %					
	56.6		45.7		10.7	
λ, mμ	ϵ_∞	ϵ_P	ϵ_∞	ϵ_P	ϵ_∞	ϵ_P
240	12.64	13.15	..	2.19	0.43	0.48
250	6.82	7.09	1.31	1.25	.00	.00
260	0.43	0.19	0.59	0.33	.17	.11
270	0.34	0.14	0.59	0.35	.27	.22
310	2.05	2.11	..	..	..	.00
320	3.95	4.10	..	..	..	..
330	6.26	6.53	..	..	..	.00
340	7.75	8.11	..	..	..	..
350	6.91	7.23	..	..	..	..
360	4.17	3.86	..	..	..	..

First order rate constants in each concentration of perchloric acid were determined from an average of the slopes of the lines obtained at each wave length in the plot of log $(D - D_\infty)$ against time. A typical first order plot is shown in Fig. 2. Random distribution of points about a line was obtained throughout the entire run in all runs. For any single run deviations in the slope at any wave length were less than 3% from the average slope.

The rate constants obtained in all duplicate runs were within 2% of those obtained in the original runs. See Table II for a summary of the rate constants.

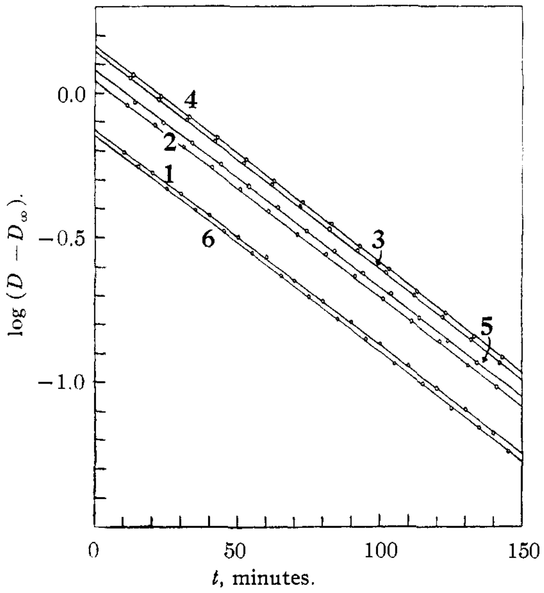

Fig. 2.—First order plot for the decarboxylation of 2,4,6-trihydroxybenzoic acid in 30.6% HClO$_4$ at 30.0°: D, optical density; 1, 250 mμ; 2, 255 mμ; 3, 260 mμ; 4, 265 mμ; 5, 270 mμ; 6, 275 mμ.

TABLE II

VALUES OF k(OBSERVED) AND k_2'(CALCULATED) AT 30.0°

HClO$_4$, %	$k \times 10^4$ sec.$^{-1}$	$k_2' \times 10^4$ sec.$^{-1}$
H_2O	0	..
0.139	0.74, 0.75	2.62
.278	1.07, 1.07	2.59
.556	1.50, 1.51	2.66
1.09	1.91, 1.92	2.73
2.01	2.24, 2.25	2.77
5.70	2.66, 2.66	2.82
10.7	2.79, 2.76	2.78
18.1	2.88, 2.83	2.86
21.5	2.86, 2.85	2.86
26.1	2.88, 2.83	2.86
30.6	2.88, 2.87	2.88
38.2	2.72, 2.76	2.74
45.7	2.37, 2.35	..
56.6	1.11, 1.13	..
21.5[a]	0.92, 0.91	0.92
21.5[b]	8.11, 8.15	8.13
21.5[c]	22.2, 22.2	22.2
75.4% H_2SO_4	0.15	..
CH_3OH[d]	.38	..
CH_3CN[e]	< .09	..

[a] At 20.0°. [b] At 40.0°. [c] At 50.0°. [d] 5 ml. of aqueous stock solution plus 5 ml. of 21.5% HClO$_4$ diluted to 50 ml. with CH_3OH. [e] 5 ml. of CH_3CN stock solution plus 10 ml. of 21.5% HClO$_4$ diluted to 50 ml. with CH_3CN.

Determining the Ratio of RCO_2^- to RCO_2H.—The spectrum at zero time, ϵ_0, of 2,4,6-trihydroxybenzoic acid in various strengths of perchloric acid was calculated from the known total concentration and values of D_0, the optical density at zero time. Values of D_0 were derived from the values of log $(D_0 - D_\infty)$, obtained graphically by extrapolation of the log $(D - D_\infty)$ vs. time plots to zero time. The spectra in most of the acid concentrations also were checked at 10°, where D_0 readings could be obtained without extrapolation. The pertinent data are summarized in Table III, and partially plotted in Fig. 3.

Equation (5) was used to calculate the ratio $[RCO_2^-]/[RCOOH]$ in regions of perchloric acid in which both anion

TABLE III

VALUES OF $\epsilon_0 \times 10^{-3}$ FOR 2,4,6-TRIHYDROXYBENZOIC ACID IN VARIOUS PERCENTAGES OF $HClO_4$

λ, mμ	H_2O	0.139	0.278	0.556	1.09	2.01	5.70	10.7	18.1	38.2	45.7	56.6	75.4% H_2SO_4
240	6.10	5.25	4.79	4.63	4.04	3.74	3.52	3.14	3.09	3.18	3.29	3.31	5.21
245	8.06	7.14	6.70	6.58	5.89	5.67	5.35	5.05	5.01	5.08	5.21	5.20	3.95
250	10.67	9.92	9.57	9.47	8.79	8.60	8.54	8.12	8.05	8.06	8.04	8.04	5.86
255	12.20	11.95	12.00	12.18	11.88	11.99	12.02	11.81	11.84	11.65	11.53	11.43	7.27
260	11.09	12.01	12.62	13.45	13.72	14.26	14.69	14.72	14.92	14.73	14.56	14.44	8.41
265	7.43	9.63	10.81	12.17	13.19	14.13	15.05	15.50	15.77	15.50	15.70	15.71	9.77
270	3.42	5.98	7.24	8.56	9.88	10.84	12.14	12.41	12.61	12.88	13.10	13.98	10.26
275	1.89	3.42	4.10	4.89	5.64	6.14	6.95	7.38	7.42	7.60	8.09	10.13	9.87
280	0.185	...	...	...	...	...	...	...	3.67	3.82	4.18	5.14	8.96
290	0.244	...	...	...	...	...	...	...	2.55	2.52	2.76	2.84	6.48

and undissociated carboxylic acid are present in appreciable amounts

$$\frac{[RCO_2^-]}{[RCO_2H]} = \frac{\epsilon_0 - \epsilon_{RCO_2H}}{\epsilon_{RCO_2^-} - \epsilon_0} \qquad (5)$$

The values of $\epsilon_{RCO_2^-}$ are taken from the spectrum in pure water, for in 10^{-4} molar concentration an acid of the order of strength of 2,4,6-trihydroxybenzoic acid should be practically 100% ionized. Since the zero-time spectrum in 10.7 to 38.2% perchloric acid remained practically constant, without even any noticeable medium effect, the values of ϵ_{RCO_2H} used were taken from ϵ_0 in 10.7% perchloric acid. The ratio of equation (5) was calculated only for 265, 270 and 275 mμ since only at these wave lengths do $\epsilon_{RCO_2^-}$ and ϵ_{RCO_2H} differ sufficiently for reliable values of $[RCO_2^-]/[RCO_2H]$ to be obtained. See Table IV for these values.

TABLE IV

VALUES OF $[RCO_2^-]/[RCO_2H]$ AND OF K IN VARIOUS CONCENTRATIONS OF $HClO_4$

	$[RCO_2^-]/[RCO_2H]$				
$HClO_4$, %	265 mμ	270 mμ	275 mμ	Avg.	$K \times 10^2$ [a]
0.139	2.41	2.51	2.59	2.50	2.72
.278	1.39	1.38	1.48	1.42	2.91
.556	0.71	0.72	0.83	0.76	2.91
1.09	.40	.39	.46	.42	2.79
2.01	.20	.21	.27	.23	2.68
5.70	.06	.03	.11	.06	(2.0)

[a] K calculated on assumption $f_{RCO_2^-} f_{H^+} = f^2_{\pm}$ of HCl at 30°.

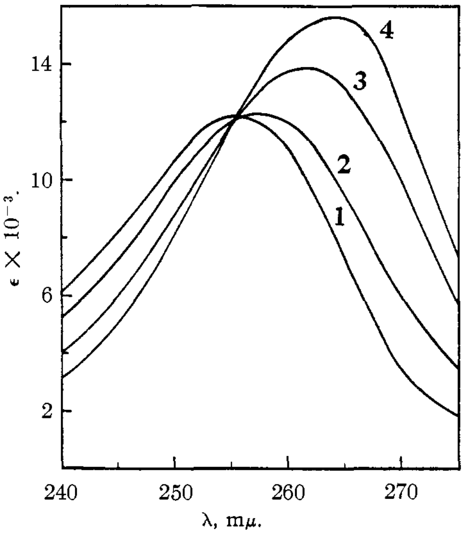

Fig. 3.—Zero-time spectra of 2,4,6-trihydroxybenzoic acid in various percentages $HClO_4$: 1, H_2O; 2, 0.139% $HClO_4$; 3, 1.09%; 4, 10.7%.

Discussion

The observed pseudo-first order rate constant, k_{obsd}, for the decarboxylation of 2,4,6-trihydroxybenzoic acid in perchloric acid solution varies with acid concentration in a manner shown in Table II. In water the rate is practically zero. In water, in the 10^{-4} molar concentrations in which the rates were measured, the carboxylic acid is practically completely ionized to anion. Therefore the rate of unimolecular decomposition of $RCOO^-$, or its reaction with water, is negligible if not zero.[4] Hammick and co-workers[2a] had reached this same conclusion previously. They also concluded that the acid-catalyzed process of equation (3) plays a major role in the decarboxylation in hydrochloric acid. The present work reveals no evidence to indicate any acid catalysis according to equation (3), or (1) or (2) in perchloric acid solution. The change in ϵ_0 from zero to 38.2% perchloric acid indicates only one ionization step for the carboxylic acid in this range (Table III). This ionization must be the equilibrium between RCO_2H and RCO_2^-, since in water the acid is practically completely in the form of its anion. An acid-catalyzed process in the sense of (1), (2) or (3) therefore cannot be playing any appreciable role, for, instead of reaching a maximum near 10.7% perchloric acid, k would continue to rise rapidly. The rise in k would parallel h_0 if mechanism (1) alone applied, or would parallel $[H_3O^+]$ if mechanism (2) or (3) applied.[5] Only in the event that complete or nearly complete ionization to $\overset{+}{RCO_2H_2}$ occurred in 10.7% perchloric acid would a leveling off of k be observable in this region.[6] That 2,4,6-trihydroxybenzoic acid is not a strong enough base to be ionized appreciably to $\overset{+}{RCO_2H_2}$ in this region is not surprising. Despite the added stabilization of the conjugate acid by resonance interaction of the protonated carboxyl group with the ortho and para hydroxyl groups, the hydrogen bond stabilization postulated for the RCO_2H form[7] (structure I) would be largely lost in the conjugate acid.

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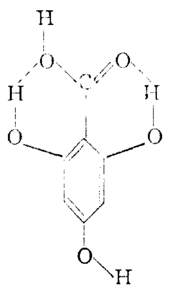
[4] The spectrum of a water solution which was 10^{-4} molar in 2,4,6-trihydroxybenzoic acid declined about 7% overnight at room temperature whereas a 10^{-3} molar solution showed about a 25% decline. If, as seems probable, this difference in rates reflects a change in the concentration of undissociated acid, it could be used as a unique measure in dilute aqueous solution of the ionization constant.

[5] L. P. Hammett and L. Zucker, THIS JOURNAL, **61**, 2791 (1939).

[6] An example of an acid-catalyzed reaction consistent with a mechanism of type (1) in which a leveling off in rate with increasing acid concentration is accountable to appreciable conjugate acid formation is the deacylation of hindered aromatic ketones: W. M. Schubert and H. K. Latourette, *ibid.*, **74**, 1829 (1952).

[7] See L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1942, p. 309.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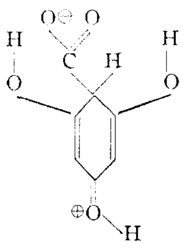
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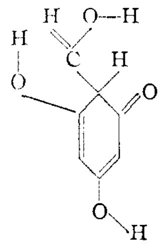
III

Rather than showing acid-catalysis in the usual sense, the data are consistent with a mechanism of either an S_Ni type unimolecular rearrangement of undissociated RCO_2H (equation 7), or a bimolecular transfer of a proton from the solution to the carboxylic acid anion to give the products (equation 8). Equation (8) represents either a single process, such as direct displacement by a proton, or a multistep reaction possibly involving an intermediate such as II or III.

$$RCO_2H \rightleftarrows RCO_2^- + H^+ \qquad (6)$$

$$RCO_2H \xrightarrow{k_2} RH + CO_2 \qquad (7)$$

$$RCO_2^- + H^+ \text{(from the solution)} \xrightarrow{k_3} RH + CO_2 \qquad (8)$$

According to the Brönsted rate equation

$$v = k_2 [RCO_2H]\frac{f_{RCOOH}}{f_{tr}} = k_3 [RCO_2^-][H^+]\frac{f_{RCO_2^-}f_{H^+}}{f_{tr}} = k_3K[RCO_2H]\frac{f_{RCO_2H}}{f_{tr}} \qquad (9)$$

where tr refers to the transition state and K is the equilibrium constant of equation (6). The expression for the observed rate constant, k_{obsd}, is then

$$k_{obsd} = \frac{v}{[RCO_2H] + [RCO_2^-]} = k_2 \frac{[RCO_2H]}{[RCO_2H] + [RCO_2^-]}\frac{f_{RCO_2H}}{f_{tr}} \qquad (10)$$

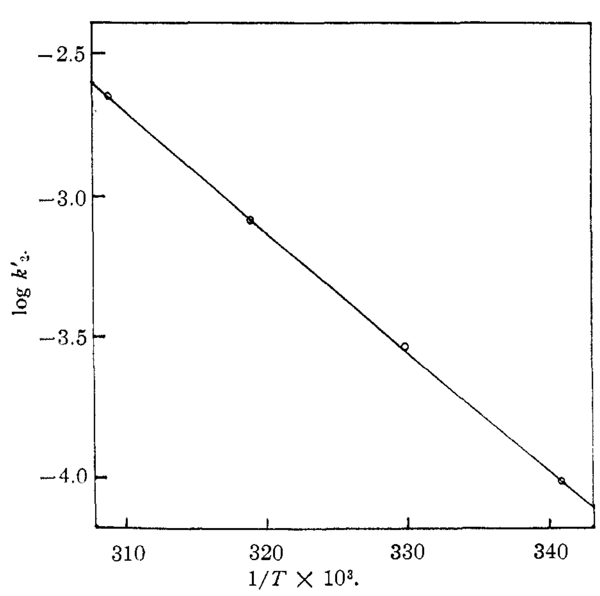

Fig. 4.—Activation energy plot for the decarboxylation of 2,4,6-trihydroxybenzoic acid.

The assumption is made that f_{RCO_2H}/f_{tr} is a constant. Similar assumptions have been made several times,[1,5] and are justified on the basis that they work out and that the species in question (in this case RCO_2H and tr) contain the same elements in similar arrangement, and thus the activity coefficients are likely to be affected in the same way by changes in medium. In this instance, furthermore, both RCOOH and tr have a net charge of zero. If the assumption is justified, then

$$k_2' = k_{obsd}\frac{[RCO_2H] + [RCO_2^-]}{[RCO_2H]} \qquad (11)$$

where k_2' is proportional to k_2. The constancy of k_2' was checked to determine whether mechanism (7) or (8) could apply. The quantity k_{obsd} in equation (11) is, of course, the measured rate constant and the quantity $([RCO_2H] + [RCO_2^-])/[RCO_2H]$ was calculated directly from the zero time spectra at 265, 270 and 275 mμ (Table IV). It can be seen in Table II that k_2' is indeed remarkably constant in 0.135 to 38.2% perchloric acid, including regions in which a measurable amount of RCO_2^- is present (0.139 to 2.01%). Although the reaction is not acid-catalyzed in the sense of mechanisms (1), (2) or (3), but is apparently described by (7) or (8), it can be viewed as an acid-catalyzed decarboxylation of the carboxylate anion.

Mechanisms (12) or (13) appear to be excluded as possibilities since k_4' in equation (14), derived similarly to equation (11), is not nearly so constant with changing perchloric acid strength as is k_2'.

$$RCO_2H + H_2O \xrightarrow{k_4} RH + CO_2 + H_2O \qquad (12)$$

$$RCO_2^- + H_3O^+ \xrightarrow{k_5} RH + CO_2 + H_2O \qquad (13)$$

$$k_4' = k_{obsd}\frac{[RCO_2H] + [RCO_2^-]}{[RCO_2H][H_2O]} \qquad (14)$$

The deviation of k_2' from constancy in 45.7 and particularly in 56.6% perchloric acid may suggest the participation in a polymolecular step of some declining species, or it could be due to a change in f_{RCOOH}/f_{tr}. However, the decline in rate perhaps is more likely due to a lowering of the concentration of reactive species by partial ionization to $RCO_2H_2^+$. This is evidenced by the appearance of increased absorption beyond 270 mμ in the zero-time spectrum of the carboxylic acid in 56.6% perchloric acid. The absorption beyond 270 mμ is even more marked in 75.2% sulfuric acid in which the rate constant is very small (Table II). The product of the reaction, phloroglucinol, apparently is ionized also to the conjugate acid to a large extent in 56.6% perchloric acid (see spectra in Table I). Some ionization of phloroglucinol is also evident in 45.7% perchloric acid. It appears thus to be a somewhat stronger base than 2,4,6-trihydroxybenzoic acid. This may indicate that the conjugate acid of the latter has the proton on a phenolic hydroxyl group rather than on the carboxyl group. If so, the failure of 2,4,6-trihydroxybenzoic acid to decarboxylate by an acid-catalyzed process as do hindered alkylbenzoic acids may be explained.

The decarboxylation reaction is solvent dependent as can be seen from the lowered rate in methanol and the comparatively negligible rate in acetonitrile (Table II). Sufficient aqueous perchloric acid was added to both these media to keep the carboxylic acid practically completely in the undissociated form, as was evidenced by the zero time spectra. Considerably more experimentation will be necessary to determine whether the changes in rate with solvent are due to the participation of solvent species in the rate-controlling step, a change in the ratio $f_{\text{reactants}}/f_{\text{transition}}$, or a change in a preliminary equilibrium (*e.g.*, ketonization to form III as an intermediate).

The activation energy in 10.7% perchloric acid for the decarboxylation, determined over a 40° range, is 19,600 calories (Fig. 4). The value of K, the acid ionization constant of 2,4,6-trihydroxybenzoic acid, was calculated for the several concentrations of perchloric acid for which the degree of ionization had been spectroscopically measured, with the assumption that the mean activity coefficient of RCO_2^- and H^+ is the same as that of hydrochloric acid at the same ionic strength (Table IV).[8] The average value obtained for K (omitting the value in 5.70% perchloric acid, in which the degree of ionization is small) was 2.8×10^{-2}. Ostwald[9] determined K to be 2.1×10^{-2} at 25° by the conductance method, but questioned the validity of the measurement since "the material disappears under one's hands." No doubt decarboxylation occurred during the measurement. Hammick and co-workers[2a] determined K to be $2.0 \pm 0.3 \times 10^{-2}$ by a pH meter method but regarded this value as approximate only.

Acknowledgment.—This work was performed as a joint undertaking of the University of Washington and the Office of Naval Research, U. S. Navy Department, under Contract N8onr-52006, Project NR 055187.

(8) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Ed. 2, Reinhold Publishing Corp., New York, N. Y., 1950, p. 547.

(9) W. Ostwald, *Z. physik. Chem.*, **3**, 253 (1889).

SEATTLE 5, WASHINGTON

[CONTRIBUTION FROM THE NICHOLS CHEMICAL LABORATORIES, NEW YORK UNIVERSITY, UNIVERSITY HEIGHTS]

The Action of Sulfuric Acid on Isocyanic Esters[1]

BY THEODORE I. BIEBER[2]

RECEIVED AUGUST 8, 1952

The action of sulfuric acid on ethyl isocyanate leads to ethylsulfamic acid and carbon dioxide. The reaction of alkyl isocyanates with sulfuric acid appears to offer a convenient route to alkylsulfamic acids. Hexamethylenedisulfamic acid can be prepared from hexamethylenediisocyanate. A related reaction, that of 1,3-dimethylurea with oleum, produces methylsulfamic acid and carbon dioxide. The reaction of phenyl isocyanate with sulfuric acid yields sulfanilic acid and carbon dioxide.

It was shown by Linhard[3] that cyanic acid and 100% sulfuric acid react in ether solution at −60° to give an unstable addition compound, which decomposes into sulfamic acid[4] and carbon dioxide.

$$HNCO + H_2SO_4 \longrightarrow H_2N—SO_3H + CO_2$$

It seemed of interest to study the reaction of organic isocyanates with sulfuric acid, since by analogy monosubstituted sulfamic acids should be formed.

$$R—N{=}C{=}O + H_2SO_4 \longrightarrow RNH—SO_3H + CO_2$$

The Reaction of Aliphatic Isocyanates with Sulfuric Acid.—Ethyl isocyanate, a typical aliphatic isocyanate, was allowed to react with 20% oleum, 5% oleum and concentrated sulfuric acid. In each case carbon dioxide was readily evolved in the cold. The formation of a transitory white solid, which dissolved with gas evolution and which was probably an addition compound of the isocyanate with sulfuric acid, was observed in the course of these reactions. The experiments with 5% and 20% oleum afforded ethylsulfamic acid, which was isolated in about 85% yield. With concentrated sulfuric acid the major product was ethylamine acid sulfate. This was accompanied by a 13% yield of ethylsulfamic acid. The water content of the concentrated sulfuric acid was greater than that required for hydrolysis of all the isocyanate employed. The fact that some ethylsulfamic acid resulted even under these conditions demonstrates that oleum with its powerful sulfonating action is not required for the formation of ethylsulfamic acid. A high yield of ethylsulfamic acid can therefore be expected with 100% sulfuric acid. The proposed synthesis of monosubstituted sulfamic acids has thus been demonstrated with $R = C_2H_5$.

$$C_2H_5—N{=}C{=}O + H_2O + H_2SO_4 \longrightarrow C_2H_5NH_3HSO_4 + CO_2$$

This new preparation of ethylsulfamic acid seems superior to previous ones. The product is easily isolated by pouring the reaction mixture into ether, from which ethylsulfamic acid precipitates as a crystalline solid. Earlier methods involve the reaction of ethylamine with sulfur trioxide in the vapor phase,[5] the reaction of aqueous ethylamine

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(2) Address correspondence concerning this paper to the author at 80-40 Lefferts Blvd., Kew Gardens 15, New York.

(3) M. Linhard, *Ann.*, **535**, 267 (1938).

(4) Sulfamic acid has been shown to be a zwitterion molecule $H_3N^+–SO_3^-$, rather than $H_2N–SO_3H$, at least in the crystalline state [F. A. Kanda and A. J. King, THIS JOURNAL, **73**, 2315 (1951)]. The substituted sulfamic acids mentioned here and in the succeeding paper [T. I. Bieber, *ibid.*, **75**, 1409 (1953)] are no doubt more accurately represented by $RNH_2^+–SO_3^-$ than by $RNH–SO_3H$. For the sake of convenience the formulas showing the proton on the sulfonate group are employed.

(5) F. Beilstein and E. Wiegand, *Ber.*, **16**, 1264 (1883).