Hydrogen Exchange of Azulenes. IV. The Acid-Catalyzed Detritiation of Azulene-1-t and Guaiazulene-3-t[1]

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The acid-catalyzed detritiation of azulene-1-t and guaiazulene-3-t has been measured in dilute aqueous solutions for a number of general acid catalysts. For azulene-1-t, second-order rate coefficients have been determined for a series of undissociated carboxylic acids, dicarboxylic acid monoanions, and anilinium ions, as well as for hydronium ion and water. For guaiazulene-3-t, second-order rate coefficients have been determined for three undissociated carboxylic acids and for ammonium ion, biphosphate ion, hydronium ion, and water. In addition, the thermodynamic ionization constants have been determined for the conjugate acids of azulene and guaiazulene. The rate data for both azulenes show agreement with a linear Brønsted relation. However, the more complete studies with azulene-1-t show that there are separate Brønsted plots, with differing α-values, for the different classes of acid catalysts. The values for the Brønsted α-parameter exhibited by azulene are larger than that for guaiazulene, in accord with the fact that guaiazulene is the stronger base.

Introduction

The observation that aromatic hydrogen exchange catalyzed by weak acids exhibits general acid catalysis was reported by Kresge and Chiang for the detritiation of trimethoxybenzene-2-t.[2] Similar behavior has been observed for the dedeuteration of azulene-1,3-d_2[3] as well as for the detritiation of azulene-1-t,[4] 2-methylindole-3-t,[5] 1,2-dimethylindole-3-t,[5] and cycl[3.2.2]azine-1-t.[6] These results suggest that general acid catalysis is a normal feature of the aromatic hydrogen exchange process.

Reactions subject to general acid catalysis usually conform to the Brønsted relation.[7,8] The character of the catalysis may be described by the shape of the Brønsted plot and by the value for the Brønsted α-parameter. The results for the detritiation of trimethoxybenzene-2-t are unusual in that for a series of general acids, including water and hydronium ion as well as neutral and positively and negatively charged species, the data are correlated by a single linear Brønsted relation.[2] This behavior is unusual in that Brønsted plots are in general nonlinear if extended over a wide range of acid strength or include water, hydronium ion, and acids of varying charge type. In contrast to the behavior of trimethoxybenzene, the Brønsted plot for the detritiation of 2-methylindole-3-t does not conform to a single, linear Brønsted relation.[5] These observations indicate that, depending upon the aromatic system, varying Brønsted behavior may be observed.

The results of a detailed study for the acid-catalyzed tritium exchange of two closely related aromatic molecules are reported in this paper. The compounds chosen for this study were azulene (I) and guaiazulene (II). Both molecules exhibit proton exchange at the same position in acidic media.[9] In azulene this is the 1- or equivalent 3-position while in guaiazulene it is the 3-position. The detritiation of azulene exhibits general acid catalysis,[4] and guaiazulene is expected to behave similarly. The thermodynamic ionization con-

stant for azulene is known,[4] and that for guaiazulene may be readily determined. Both molecules are suffi-

I   II
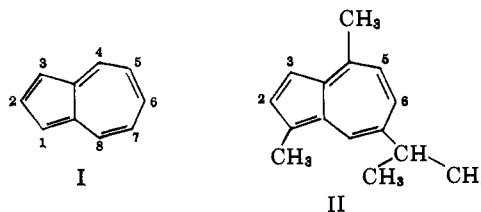
ciently soluble in water to make exchange studies via tritium counting feasible.

Experimental

Materials.—Azulene and guaiazulene were obtained from the Aldrich Chemical Co., Inc., Milwaukee 7, Wis. Azulene was purified by chromatography on alumina followed by vacuum sublimation: m.p. 99.2–99.6°, lit.[10] m.p. 98.5–99.0°. Guaiazulene was purified by chromatography on alumina: m.p. 31.0–31.3°, lit.[11] m.p. 31.5°. Azulene-1-t was prepared by the method of Schulze and Long[4] and purified as indicated above: m.p. 99.2–99.6°. Guaiazulene-3-t was prepared in the same manner: m.p. 30.8–31.8°. Reagent grade acetic acid, formic acid, glycolic acid, maleic acid, sodium chloride, sodium hydroxide, primary potassium phosphate, hydrochloric acid, and perchloric acid were used without further purification. The following compounds were purified by the method indicated until the property being used as a measure of purity was in agreement with the literature value: monochloroacetic acid and iodoacetic acid by recrystallization followed by vacuum sublimation, malonic acid by recrystallization, trimethylacetic acid by vacuum distillation, p-bromoaniline by vacuum sublimation, and aniline, p-anisidine, p-toluidine, m-anisidine, and o-anisidine by vacuum distillation from zinc dust. Aqueous solutions of acetic acid, formic acid, glycolic acid, trimethylacetic acid, oxalic acid, hydrochloric acid, and perchloric acid were standardized by titration. The remaining catalysts were retained in their pure form and solutions were prepared by weight.

Equilibrium Protonation.—The thermodynamic ionization constants for azulene and guaiazulene were determined in perchloric acid solutions at 25° by the conventional spectrophotometric technique.[12] Both molecules were well behaved in that spectral shifts due to changes in medium were absent. The experimental data were obtained on a Cary 14 spectrophotometer and were treated by the method of Long and Paul.[12] The extrapolation to infinite dilution is small, and the pK_a values determined in this manner are -1.76 ± 0.04 for azulene and 1.42 ± 0.01 for guaiazulene. The data for azulene were also plotted in the form of the log indicator ratio vs. the $-H_0$ value[13] of solvent. The slope of this plot is 1.80 ± 0.12.

(1) Work supported by a grant from the Atomic Energy Commission.

(2) A. J. Kresge and Y. Chiang, J. Am. Chem. Soc., **81**, 5509 (1959); **83**, 2877 (1961).

(3) J. Colapietro and F. A. Long, Chem. Ind. (London), 1056 (1960).

(4) J. Schulze and F. A. Long, J. Am. Chem. Soc., **86**, 331 (1964).

(5) B. C. Challis and F. A. Long, ibid., **85**, 2524 (1963).

(6) R. J. Thomas and F. A. Long, unpublished data.

(7) R. P. Bell, "Acid–Base Catalysis," Oxford University Press, New York, N. Y., 1941, pp. 82–95.

(8) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp. 155–182.

(9) J. Schulze and F. A. Long, J. Am. Chem. Soc., **86**, 322 (1964).

(10) P. A. Plattner and A. S. Pfau, Helv. Chim. Acta, **20**, 224 (1937).

(11) K. S. Birrel, J. Am. Chem. Soc., **56**, 1248 (1934).

(12) F. A. Long and M. A. Paul, Chem. Rev., **57**, 1 (1957).

(13) Data from ref. 12 were used to construct a smooth plot to obtain intermediate values of H_0 for perchloric acid solutions.

Detritiation Kinetics.—Aqueous solutions of azulene-1-*t* and guaiazulene-3-*t* were prepared by adding the solid to water and stirring overnight. The excess solid was removed by filtration. Buffered solutions were prepared in volumetric flasks by adding the required amounts of each reagent. The amount of sodium chloride added was such that the ionic strength of each solution was 0.100 after dilution to the mark with aqueous tritiated aromatic solution. Depending upon the rate of detritiation, one of the two sampling techniques was employed. If kinetic points were taken in a period of less than 1 week, the volumetric flask containing the buffered solution of tritiated aromatic was placed directly in the thermostat at 25.0 ± 0.1° and aliquots were pipetted out at appropriate times. If kinetic points were taken over longer periods of time, aliquots were pipetted from the volumetric flask and placed in tubes which were flushed with nitrogen, sealed, and placed in the same thermostat. This was to reduce possible decomposition (of which there was no indication in any run). The rate of detritiation was determined by measuring the loss in tritium activity of the aromatic; the procedure employed was identical, except for aliquot sizes, with that of Schulze and Long.[4] The first-order rate coefficients, k_0, were determined from plots of log ($C - C_\infty$) vs. time, the plots being linear to the maximum per cent reaction followed. Figure 1 is a kinetic plot for the detritiation of azulene-1-*t*-catalyzed by acetic acid and is representative of the experimental accuracy. The treatment for obtaining second-order rate coefficients from k_0 will be discussed in the following section.

Results

Water and Hydroxide Ion Catalysis.—Hydroxide ion is not a catalyst as evidenced by the observation that the rate of detritiation of azulene-1-*t* was the same in 0.001, 0.010, and 0.100 M sodium hydroxide. A similar result was obtained with guaiazulene-3-*t* under identical conditions. In these basic solutions, the loss in activity from azulene-1-*t* was essentially zero, and only an upper limit for the water catalysis could be obtained. The loss in activity from guaiazulene-3-*t* was larger and k_0, the first-order rate coefficient for the water reaction, was obtained in the normal fashion. The k_0 values were converted into second-order rate coefficients, k_{H_2O}, by dividing by 55.5, and these are listed in Tables I and II.

TABLE I

RATE COEFFICIENTS FOR THE DETRITIATION OF AZULENE-1-*t* AT 25°

Acid	k_{HA}, l./mole sec.	Acid	k_{HA}, l./mole sec.
Trimethylacetic	3.14×10^{-4}	*p*-Anisidinium ion	8.0×10^{-4}
Acetic	2.50×10^{-4}	*p*-Toluidinium ion	1.10×10^{-3}
Glycolic	9.58×10^{-4}	Anilinium ion	1.34×10^{-3}
Formic	1.21×10^{-3}	*o*-Anisidinium ion	3.8×10^{-3}
Iodoacetic	4.16×10^{-3}	*m*-Anisidinium ion	4.4×10^{-3}
Chloroacetic	4.57×10^{-3}	*p*-Bromoanilinium ion	7.2×10^{-3}
Oxalate ion	1.76×10^{-3}	H_3O^+	0.181
Malonate ion	9.8×10^{-3}	H_2O	$<2.1 \times 10^{-10}$
Maleate ion	3.3×10^{-3}		

TABLE II

RATE COEFFICIENTS FOR THE ACID-CATALYZED DETRITIATION OF GUAIAZULENE-3-*t* AT 25°

Acid	k_{HA}, l./mole sec.	Acid	k_{HA}, l./mole sec.
H_3O^+	6.1	$H_2PO_4^-$	1.74×10^{-3}
Formic	5.1×10^{-2}	NH_4^+	7.2×10^{-6}
Glycolic	3.6×10^{-2}	H_2O	7×10^{-9}
Acetic	1.38×10^{-2}		

The water reaction for azulene can be neglected for all catalysts while that for guaiazulene is small enough that it can be neglected for all catalysts except ammonium ion and biphosphate ion.

Hydronium Ion Catalysis.—The strong acid catalyzed detritiation of azulene-1-*t* was measured in 0.001, 0.002, and 0.004 M hydrochloric acid. The plot of k_0 vs. hydrochloric acid concentration was linear and passed
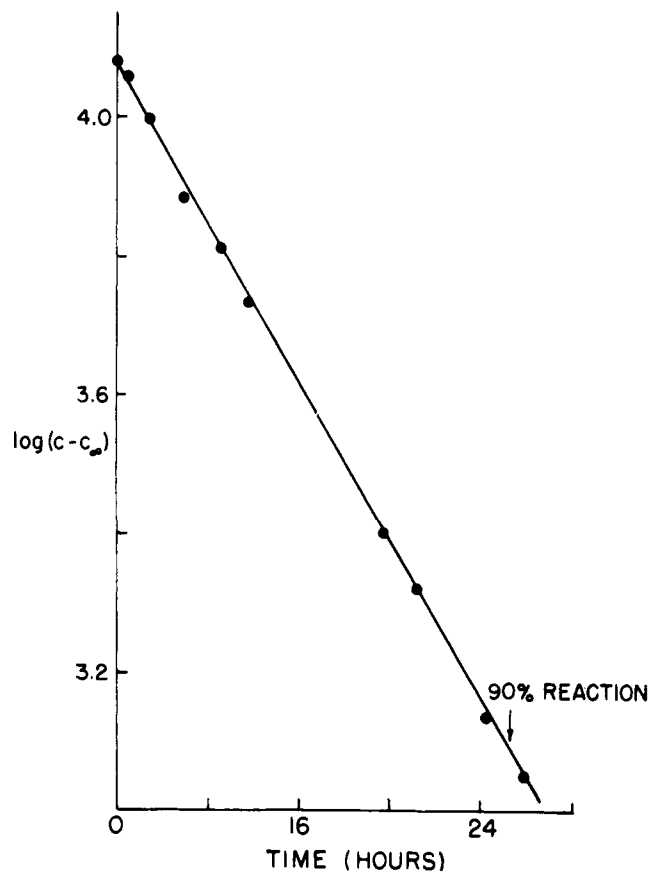

Fig. 1.—The plot of log ($c - c_\infty$) vs. time for the acetic acid-catalyzed detritiation of azulene-1-*t*.

through the origin; the second-order rate coefficient, k_{H^+}, was obtained from the slope of this plot. Guaiazulene-3-*t* is more reactive and k_{H^+} cannot be determined using solutions of strong acids; it was determined from measurements in a series of acetic acid buffers of known hydrogen ion concentration.[14] The value for k_{H^+} was calculated by dividing the value of the intercept from a plot of k_0 vs. undissociated acetic acid concentration by the hydronium ion concentration calculated for this buffer system (see undissociated carboxylic acid catalysis section). The results are listed in Tables I and II.

Acetate Ion Catalyses.—In a buffer system composed of an undissociated monobasic acid, HA, and its anion, A^-, the anion is a potential catalyst for the detritiation process.[7] The anion's catalytic effect may be ascertained as follows. Values for k_0 are determined at several concentrations of undissociated acid while the hydronium ion concentration is held constant. The same measurements are repeated at other hydronium ion concentrations, and plots of k_0 vs. the concentration of undissociated acid are made with the data for each hydronium ion concentration. If the anion has a negligible catalytic effect, these plots will have the same slope, and this was the observed result for azulene-1-*t*. As hydroxide ion also has no catalytic effect, this observation may be generalized to conclude that there is no base catalysis.

Undissociated Carboxylic Acid Catalysis.—The above observations indicate that in buffer systems formed from monobasic acids, the catalysts responsible

(14) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd Ed., Reinhold Publishing Co., New York, N. Y., 1958, p. 676.
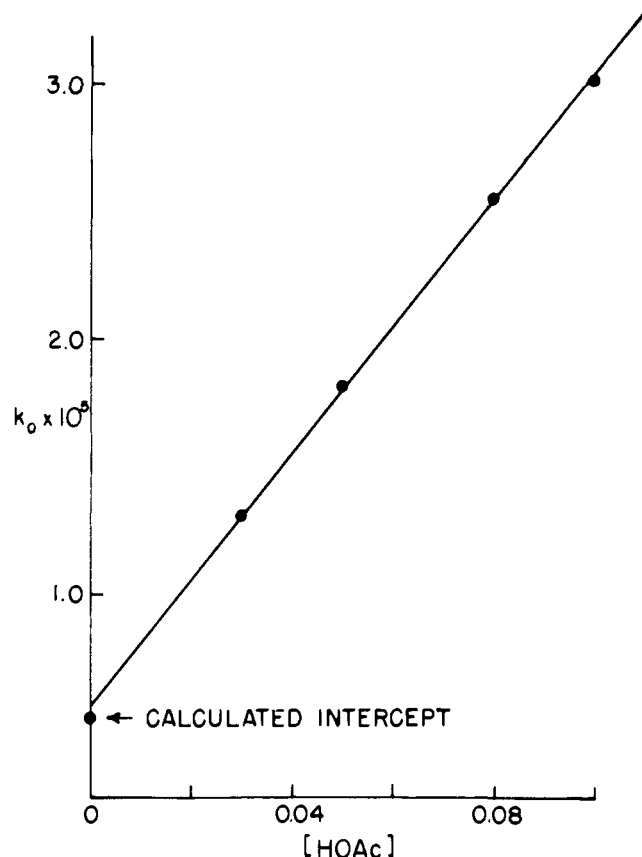
Fig. 2.—The plot of k_0 vs. undissociated acetic acid concentration for the detritiation of azulene-1-t.

for the measured rate of detritiation are hydronium ion and the undissociated acid. Thus, a plot of k_0 vs. the concentration of undissociated acid will be linear with slope equal to the second-order rate coefficient for the undissociated acid, k_{HA}, and with intercept equal to the hydronium ion catalyzed rate. The data for the detritiation of both azulene-1-t and guaiazulene-3-t lead to linear k_0 vs. undissociated acid concentration for all of the carboxylic acids studied. Figure 2 is such a plot for the acetic acid catalyzed detritiation of azulene-1-t and is typical with respect to the linearity and agreement between calculated and observed intercept.[15] The values for k_{HA}, taken from the slopes of these plots, are listed in Tables I and II.

Anilinium Ion Catalysis.—The detriation of azulene-1-t and guaiazulene-3-t catalyzed by anilinium ions also lead to linear k_0 vs. anilinium ion concentration plots. The values for k_{HA}, determined from the slopes of these plots, are listed in Tables I and II. Again the value of the intercepts was in agreement with the calculated value.[16]

Dicarboxylic Acid Monoanion Catalysis.—For detritiation of azulene-1-t catalyzed by a dicarboxylic acid monoanion, HA⁻, the undissociated dicarboxylic acid, H_2A, will also contribute to the catalysis. The catalytic effect of the undissociated dicarboxylic acid may be

(15) An accurate calculated value for the intercept may be obtained only when activity coefficient data are available to allow calculation of the hydronium ion concentration in salt solutions.

(16) It was assumed that the ionization constants for the anilinium ions were the same in 0.1 M salt as at infinite dilution. The justification for this approximation is that the ionization constant for p-nitroanilinium ion increases about 5% in going from infinite dilution to 0.1 M hydrochloric acid.[17]
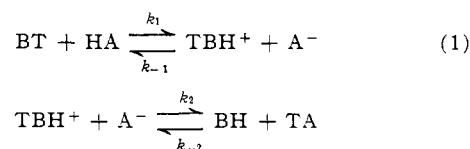
(17) M. A. Paul, J. Am. Chem. Soc., **76**, 3236 (1954).

determined as follows. The same experiments are performed as in the detection of catalysis by the anion of a monobasic acid except that the concentration of dicarboxylic acid monoanion is varied. Plots of k_0 vs. the concentration of dicarboxylic acid monoanion are made with the data obtained at each hydronium ion concentration, and these will have different slopes if catalysis by the undissociated dicarboxylic acid is not negligible. For each of the dicarboxylic acids used, catalysis by the undissociated dicarboxylic acid was observed and the analysis of the data to obtain k_{HA} took cognizance of this catalysis. The values for k_{HA} are listed in Table I.

Ammonium Ion and Biphosphate Ion Catalysis.— These two catalysts were used only with guaiazulene-3-t. In their buffer solutions the hydronium ion concentrations are small enough that no catalysis by hydronium ion was observable. However, the rate of the water reaction was not negligible and appears as the intercept of the plot of k_0 vs. general acid concentration. The data for these two catalysts were in accord with this, and the values for k_{HA} determined from the slope of the k_0 vs. general acid concentration plot are listed in Table II.

Discussion

The acid-catalyzed detritiation of azulene-1-t and guaiazulene-3-t leads to observable general acid catalysis for each acid studied. The result is in accord with the A-SE2 mechanism which predicts a rate-determining proton transfer from the general acid, HA, to the substrate, BT, forming a protonated intermediate, TBH⁺, which then deprotonates to form the product, BH. This mechanism is

$$BT + HA \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} TBH^+ + A^- \qquad (1)$$

$$TBH^+ + A^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} BH + TA$$

In the work presented in this paper, the reverse of the second step may be neglected as the tritium content of BT was at tracer level. The application of steady-state kinetics leads to the following rate law for the detritiation of BT.

$$\text{rate} = k_{HA}[HA][BT]$$
$$= \frac{k_1 k_2}{k_{-1} + k_2}[HA][BT] \qquad (2)$$
$$= k_1 \frac{1}{(1 + k_{-1}/k_2)}[HA][BT]$$

This rate law implies general acid catalysis. Additionally, as the rate coefficients k_2 and k_{-1} are associated with the loss of either tritium or protium from the intermediate, their ratio, k_{-1}/k_2, should be relatively insensitive to moderate changes in the basicity of A⁻. Hence, changes in k_{HA} will reflect changes in k_1, and since this is a slow proton transfer reaction, the k_{HA} values should be correlatable by the Brønsted relation.

The Brønsted plots generated from the data in Tables I and II and are shown in Fig. 3 to 5. The data for azulene-1-t cannot be correlated by a single, linear Brønsted relation.[18] If the data for water and hydronium ion are excluded, and the acids grouped with re-

(18) The normal p,q correction was not applied to the data for the dicarboxylic acid monoanions as this only shifts the curve to the right by 0.3 log units and does not change its slope.
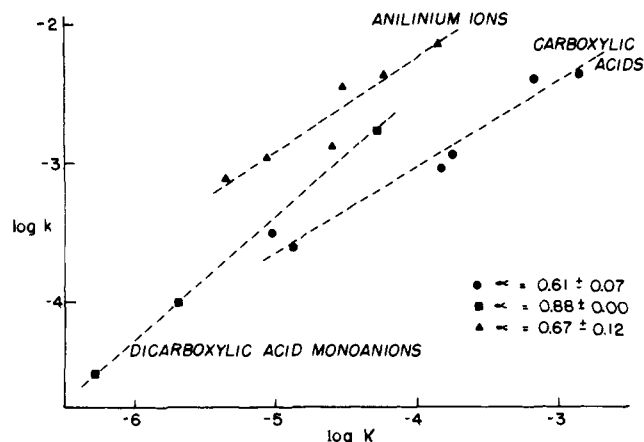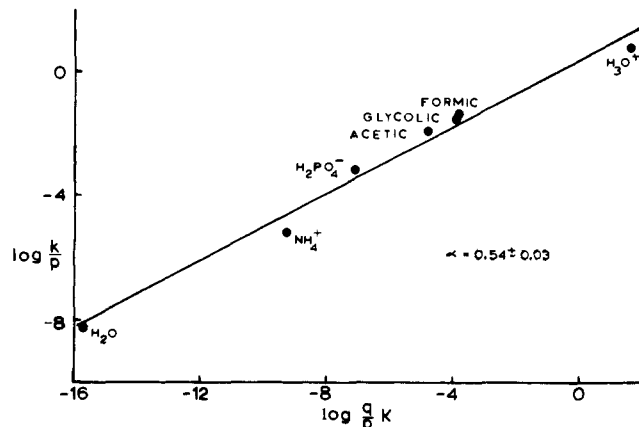
Fig. 3.—Brønsted plot for the detritiation of azulene-1-t.
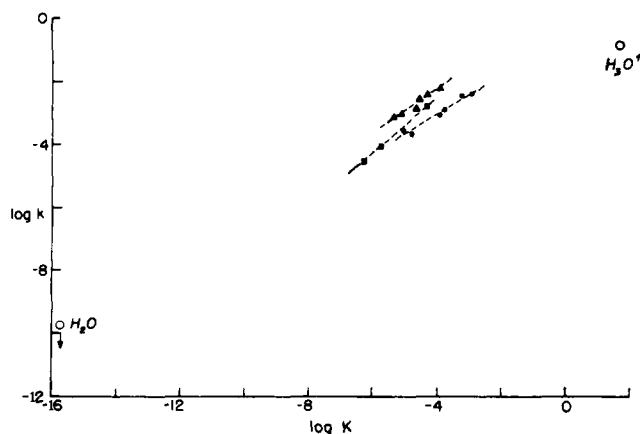
Fig. 4.—Brønsted plot for the detritiation of azulene-1-t.

spect to charge type, the result is three reasonably linear Brønsted plots. The α-values for these lines were obtained by the method of least squares. The data for guaiazulene-3-t, Fig. 5, are approximately correlated by a single, linear Brønsted relation but it should be noted that a smaller number of catalysts was used in this study than was used for azulene.[19] Again the α-value was obtained by the method of least squares.

One may arrive at an expected value for α as follows.[20] Consider the slow proton transfer from HA to BT as a typical acid–base reaction in which the transition state will involve the partial transfer of a proton from the base A$^-$ to the aromatic species being protonated. The value for α should approximately equal the fraction of proton transfer in the transition state. If the fraction of proton transfer is due only to the difference in basicity between the anion and aromatic species, the value for α will be 0.5 when they have equal basicity, larger than 0.5 when the anion is more basic, and less

(19) p, q correction was applied to the H$_2$PO$_4^-$ data.

(20) J. E. Leffler and E. Grunwald, "Rates and Equilibrium of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, pp. 156–159 and 238–241.

Fig. 5.—Brønsted plot for the detritiation of guaiazulene-3-t.

than 0.5 when the aromatic species is more basic. From the known pK_a values for protonated azulene, protonated guaiazulene, and the general acids studied, the value of α should be larger than 0.5. In addition, as guaiazulene is a stronger base than azulene, the value of α for guaiazulene should be smaller than that for azulene. Both of these predictions are in agreement with the observed data. These same considerations imply that the points for water and hydronium ion will fall beneath a Brønsted line determined from acids with pK values between those for water and hydronium ion since the inclusion of hydronium ion should decrease α and inclusion of water should increase it. The data are in general accord with this statement.

A more careful consideration indicates that factors other than differences in basicity must be considered. For example, the data for azulene do not generate a single, linear Brønsted plot. In addition, when the data for azulene are grouped with respect to charge type, there is no trend in the value for α with the catalyst charge type. Finally the values of α for guaiazulene and trimethoxybenzene are 0.54 and 0.52, respectively, while they differ in basicity by at least five pK units. The implication of these results is that there are specific interactions between the catalyzing acids and the aromatic species which lead to deviations from simple Brønsted behavior.

A rationale for the similar α-values for guaiazulene and trimethoxybenzene is that the α-value for trimethoxybenzene is smaller than that predicted from its basicity because of a steric repulsion in the transition state by the neighboring methoxy groups to the catalyzing acid. Similarly a stabilization of the transition state due to interaction of the ionized carboxyl group of a dicarboxylic acid monoanion with the seven-membered ring will result in an α-value larger than that predicted from the acidities of the dicarboxylic acid monoanions. That the anilinium ions and undissociated carboxylic acids generate separate Brønsted plots with similar slopes is probably due to different solvation effects for ionization equilibria of different charge symmetry.