

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, NORTHWESTERN UNIVERSITY, EVANSTON, ILL., AND ILLINOIS INSTITUTE OF TECHNOLOGY, CHICAGO 16, ILL.]

Acylium Ion Formation in the Reactions of Carboxylic Acid Derivatives. IV. The Acid-catalyzed Hydrolysis of Methyl 4-Substituted-2,6-dimethylbenzoates¹

BY MYRON L. BENDER² AND MARK C. CHEN

RECEIVED JULY 11, 1962

The kinetics of hydrolysis of four methyl 4-substituted-2,6-dimethylbenzoates in 9.70 *M* sulfuric acid were determined. Electron-donating 4-substituents accelerate the hydrolysis. The Hammett ρ -constant for the hydrolysis is -3.22 , obtained from a plot employing σ^+ -constants. The substituent effect is considered to be mainly operative in the rate-determining heterolysis of the protonated ester. In conjunction with other evidence, the substituent effects in this hydrolysis strongly suggest a mechanism involving an acylium ion intermediate. Comparison of the Hammett ρ -values of a series of hydrolytic reactions and the relative rates of a series of reactions of benzoic acid and mesitoic acid derivatives indicates that hindered benzoic acid derivatives may react via two distinct pathways: (1) a bimolecular pathway which shows considerable steric hindrance to reaction and is facilitated by electron-withdrawing substituents and (2) a unimolecular pathway which is facilitated by steric hindrance and by electron-donating substituents.

Introduction

The hydrolysis of methyl mesitoate in concentrated sulfuric acid solution is the classical example of a mechanism involving an acylium ion intermediate. A number of different experimental approaches gives a consistent picture of this mechanism. The cryoscopic behavior of methyl mesitoate in 100% sulfuric acid,³ the proportionality between the rate constant of hydrolysis and h_0 in moderately concentrated sulfuric acid,⁴ the positive entropy of activation⁵ and the lack of oxygen exchange⁵ all indicate that the reaction proceeds by a unimolecular heterolysis. In the previous paper in this series,⁶ a different criterion was developed for the delineation of a mechanism involving the formation of an acylium ion intermediate, namely, the use of substituent effects in 4-substituted-2,6-dimethylbenzoic acid derivatives. The applicability of this mechanistic criterion is tested here by investigating the effect of substituents on the rates of hydrolysis of methyl 4-substituted-2,6-dimethylbenzoates in 9.70 *M* sulfuric acid. Substituent effects in the alkaline hydrolysis of this set of compounds had previously been determined.⁷ Therefore, it was possible in this investigation to compare substituent effects on the rates of acid-catalyzed ester hydrolysis with those of the base-catalyzed ester hydrolysis which has been shown to proceed through a mechanism involving a tetrahedral intermediate^{7,8} and with those of neutral and acid-catalyzed hydrolysis of the corresponding acid chlorides which have been shown to proceed through a mechanism involving an acylium ion intermediate.⁶ This comparison should provide a good test for the validity of the acylium ion mechanism in the acid-catalyzed hydrolysis of hindered esters, and should secondarily provide a test for the applicability of the mechanistic criterion of substituent effects in the reactions of hindered substrates.

Experimental

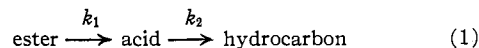
Materials.—The sulfuric acid solutions of desired molarity were diluted from commercial concentrated sulfuric acid (B. and A. quality, C.P. reagent grade). Diluted aliquots of the stock solutions were standardized by titration with standard sodium hydroxide. The methyl 4-substituted-2,6-dimethylbenzoates were prepared from the 4-substituted-2,6-dimethylbenzoyl chlorides whose preparation was described in the previous paper,⁶ in the following manner. The acid chloride was added dropwise,

with stirring, to an ice-cooled solution containing a 30% excess of anhydrous methanol (Baker, reagent grade) and a few drops of pyridine (Baker, reagent grade, stored over potassium hydroxide). After refluxing for half an hour, pyridine, methanol and the gaseous by-products were removed under vacuum. The residue, the methyl ester, was dissolved in methylene chloride (Matheson, Coleman and Bell), washed with a 5% sodium carbonate solution and dried overnight over anhydrous sodium sulfate. Methyl 2,6-dimethylbenzoate was distilled under vacuum; b.p. 52° (2 mm.), lit.⁷ b.p. 109° (19 mm.). Methyl mesitoate distilled at 113–114° (11 mm.), n_D^{25} 1.5045; lit.⁷ b.p. 113–113.5° (11 mm.), n_D^{20} 1.5085.⁷ Methyl 4-methoxy-2,6-dimethylbenzoate was recrystallized from aqueous methanol, m.p. 56.5°.

Anal. Calcd. for C₁₁H₁₄O₃: C, 68.0; H, 7.22. Found: C, 67.95; H, 7.11.

Methyl 4-bromo-2,6-dimethylbenzoate was recrystallized from aqueous methanol; m.p. 55°, lit.⁷ m.p. 54°.

Kinetic Measurements.—The spectrophotometric method for the determination of the kinetics of hydrolysis has been described in the previous paper.⁶ The hydrolysis of the hindered benzoate esters in 9.70 *M* sulfuric acid is in some instances followed by the acid-catalyzed decarboxylation of the corresponding benzoic acid produced in the reaction. The spectrophotometric measure-



ments will lead to the rate constant for hydrolysis only if k_2 is much smaller than k_1 . In the hydrolysis of methyl mesitoate, k_2 is 30-fold less than k_1 in 5.78 *M* sulfuric acid, and 70-fold less in 11.7 *M* sulfuric acid.⁴ Furthermore, in 9.70 *M* sulfuric acid, 2,6-dimethylbenzoic acid and 4-bromo-2,6-dimethylbenzoic acid have been shown to be stable during the time necessary for the determination of the kinetics of hydrolysis of the corresponding esters. Typical kinetic runs are shown in Fig. 1. However, 4-methoxy-2,6-dimethylbenzoic acid is not stable during the time necessary for measurement of the kinetics of hydrolysis. In this case the rate constant of the decarboxylation reaction, k_2 , was determined independently starting with the acid itself, and the rate constant of the hydrolysis was obtained in the following way. The system in eq. 1 consists of two consecutive first-order reactions. From the expression for the concentrations of ester (A), acid (B) and hydrocarbon (C),⁹ and the fact that the absorbance of the system must be the sum of the absorbances of the three species, it may be shown that

$$D_t = \epsilon_a A_0 e^{-k_1 t} + \epsilon_b A_0 k_1 \frac{(e^{-k_1 t} - e^{-k_2 t})}{k_2 - k_1} + \epsilon_c A_0 \left[1 + \frac{1}{k_1 - k_2} (k_2 e^{-k_1 t} - k_1 e^{-k_2 t}) \right] \quad (2)$$

where ϵ_a , ϵ_b , ϵ_c are the molar absorptivities of A, B and C, and D_t is the absorbance at time t . Here $\epsilon_a A_0$ is the absorbance at zero time and $\epsilon_c A_0$ is the absorbance at infinite time. If the term containing $\epsilon_b A_0$ is eliminated in the conventional way from two simultaneous equations employing D_1 at time t_1 and D_2 at time t_2 , then D can be expressed as an exponential equation involving k_1 , k_2 , t_1 , t_2 , $\epsilon_a A_0$ and $\epsilon_c A_0$. In this equation all quantities but k_1 are known. Therefore k_1 can be obtained analytically from the exponential equation, knowing k_2 and the numerical values of D at time t , at zero time and at infinite time.

Results

The kinetics of hydrolysis in 9.70 *M* sulfuric acid of a series of methyl 4-substituted-2,6-dimethylbenzoates in

(9) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 153.

(1) This research was supported by grants from the National Science Foundation and the U. S. Atomic Energy Commission.

(2) Alfred P. Sloan Foundation Research Fellow; present address, Northwestern University.

(3) M. S. Newman, H. G. Kuivila and A. B. Garrett, *J. Am. Chem. Soc.*, **67**, 704 (1945), and references cited therein.

(4) C. T. Chmiel and F. A. Long, *ibid.*, **78**, 3326 (1956).

(5) M. L. Bender, H. Ladenheim and M. C. Chen, *ibid.*, **83**, 123 (1961).

(6) M. L. Bender and M. C. Chen, *ibid.*, **85**, 30 (1963).

(7) H. L. Goering, T. Rubin and M. S. Newman, *ibid.*, **76**, 787 (1954).

(8) M. L. Bender and R. S. Dewey, *ibid.*, **78**, 317 (1956).

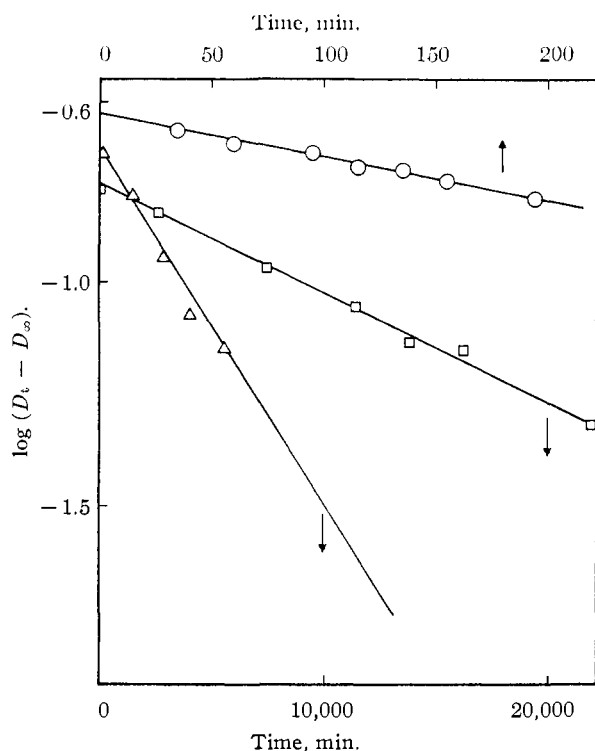


Fig. 1.—Kinetics of the hydrolysis of methyl 4-X-2,6-dimethylbenzoates in 9.70 M H_2SO_4 at 25°: X = CH_3 , O; H, Δ ; Br, \square .

9.70 M sulfuric acid at 25° are shown in Table I. Since the hydrolysis of methyl 4-methoxy-2,6-dimethylbenzoate in 9.70 M sulfuric acid does not follow simple first-order kinetics because of the subsequent decarboxylation reaction, the rate constant of this hydrolysis was calculated by means of the numerical analysis described in the Experimental section. In 9.70 M sulfuric acid solution, the first-order rate constant for the decarboxylation of 4-methoxy-2,6-dimethylbenzoic acid is $4.0 \times 10^{-4} \text{ sec.}^{-1}$. Comparison of this value with that of the hydrolytic constant of the ester under comparable conditions shown in Table I indicates that the rate constants of the two consecutive reactions of hydrolysis and decarboxylation are very similar and must be treated according to eq. 2. It is interesting to note that while k_1 (hydrolysis) and k_2 (decarboxylation) are comparable to one another in 9.70 M sulfuric acid, k_1 is much greater than k_2 in 11.50 M sulfuric acid, indicating that the hydrolysis reaction is much more sensitive to sulfuric acid concentration than is the decarboxylation reaction.

The Hammett plots of the logarithms of the rate constants versus σ and σ^+ values are shown in Fig. 2. The plot utilizing σ -values yields a curved line, whereas the plot utilizing σ^+ -values results in a straight line with a slope of -3.22 .

TABLE I

THE KINETICS OF THE HYDROLYSIS OF METHYL 4-SUBSTITUTED-2,6-DIMETHYLBENZOATES IN 9.70 M SULFURIC ACID^a

Substituent	$k \times 10^4, \text{ sec.}^{-1}$	Substituent	$k \times 10^4, \text{ sec.}^{-1}$
CH_3O	5.0	H	0.033
CH_3	0.37 ^b	Br	0.01

^a 25.0°. ^b 9.80 M sulfuric acid at 24.2°. ^c Average of at least two runs.

Discussion

In moderately concentrated sulfuric acid solutions the hydrolysis of methyl mesitoate can be reasonably assumed to proceed by way of an $A_{AC}1$ mechanism¹⁰;

(10) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 767.

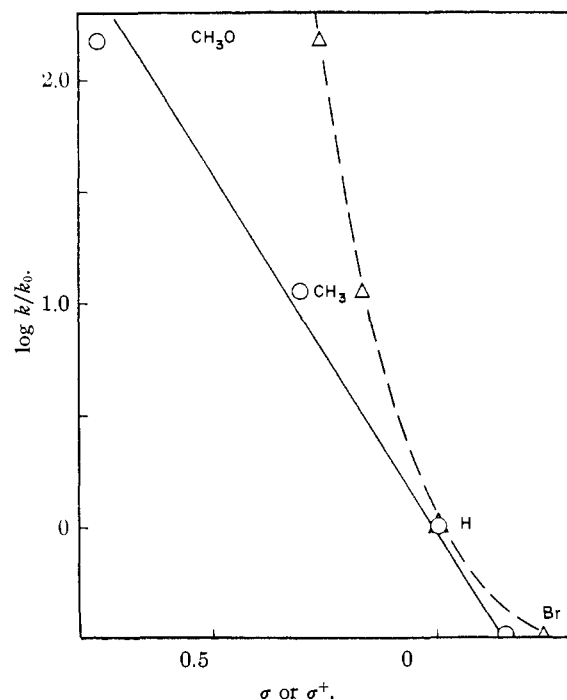


Fig. 2.— $\log k/k_0$ for the rates of hydrolysis of methyl 4-X-2,6-dimethylbenzoates in 9.70 M H_2SO_4 at 25° vs. σ^+ or σ : O, σ^+ ; Δ , σ .

that is a mechanism involving the rate-determining formation of an acylium ion. This hypothesis is based on cyroscopic measurements in 100% sulfuric acid which indicate the formation of an acylium ion,⁸ on the much faster rate of hydrolysis of methyl mesitoate than methyl benzoate in concentrated sulfuric acid solution (although the opposite is true in dilute acid solution),⁴ and on the correlation between the logarithm of the hydrolytic rate constant and H_0 .⁴ The last mechanistic argument has been subject to much criticism in recent years and certainly cannot be used as definitive evidence.¹² The acylium ion mechanism for the hydrolysis of methyl mesitoate is further supported by the observation of positive values of the entropy of activation in this reaction.⁵ This result is considerably different from the entropy of activation of an ordinary acidic hydrolysis such as that of methyl acetate, for example, which exhibits an entropy of activation of -21.3 entropy units.^{11,12}

The absence of carbonyl oxygen exchange of methyl mesitoate during its hydrolysis in a number of sulfuric acid solutions has been reported.⁶ The acylium ion mechanism explains the inability of exchange to occur. However, as mentioned previously, it is *a priori* impossible to state whether this lack of exchange is due to the formation of an acylium ion intermediate rather than a tetrahedral intermediate whose reversion to reactants is less than its decomposition to products.

Although all of the above pieces of experimental evidence are self-consistent, many of the individual pieces of evidence are ambiguous. This is a common occurrence in mechanistic arguments. In such a situation the best that can be done is to collect a large number of pieces of evidence using different approaches to see if any piece is inconsistent with the proposed hypothesis. One aspires to obviate such difficulties by finding a definitive experiment which will prove the mechanism unequivocally. The present experiment was directed to this goal. At best, the present experiment can

(11) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **74**, 5372 (1952); R. W. Taft, Jr., E. L. Purlee, P. Riesz, and C. A. DeFazio, *ibid.*, **77**, 1584 (1955).

(12) N. C. Deo and C. Perizzolo, *ibid.*, **79**, 1345 (1957).

TABLE II
HAMMETT ρ -VALUES FOR THE HYDROLYSIS OF SUBSTRATES

Reaction	Sigma	ρ -Value			Ref.
		Pre-equil.	Rate-determ.	Over-all	
Benzamide + H ⁺ (dil. sulfuric acid)	σ	-0.93	1.05	0.12	17
Benzamide + H ⁺ (99% sulfuric acid)	σ^+	-1.8 to -3.4	-1.8 to -3.4	16
Methyl benzoates + H ⁺ (99% sulfuric acid)	σ^+	-3	-3	15
Methyl-4-subst.-2,6-dimethylbenzoates + H ⁺	σ^+	0 to -0.9	-2.3 to -3.2	-3.22	^a
4-Subst.-2,6-dimethylbenzoyl chlorides	σ^+	-3.85	-3.85	6
4-Subst.-2,6-dimethylbenzoyl chlorides + H ⁺	σ^+	-3.73	-3.73	6
4-Subst.-2,6-dimethylbenzoyl chlorides + Me ₄ N ⁺ OH ⁻	σ	1.20	1.20	6
Methyl 4-subst.-2,6-dimethylbenzoates + NaOH	σ	1.26	1.2	7

^a This investigation.

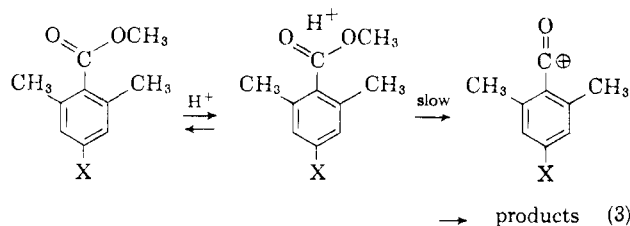
furnish an unequivocal proof of the mechanism; otherwise it can add one further experimental criterion to the other pieces of information listed above.

The rates of reaction involving the formation of carbonium ion intermediates adjacent to a benzene ring are greatly increased by electron-donating substituents in the *p*-position. For example, the ρ of the solvolysis of *m*- and *p*-substituted phenyldimethylcarbinyl chlorides is highly negative.¹³ Furthermore ordinary σ -constants would not correlate the rate data, leading to the definition of a new set of electrophilic substituent constants, σ^+ . The σ^+ -values reflect a higher degree of resonance interaction between the substituent and the positively charged reaction center than do σ -values. Therefore two substituent effect criteria exist for a mechanism involving an acylium ion intermediate, a ρ which is highly negative and a correlation with σ^+ -constants rather than σ -constants. There are limitations to the use of the latter criterion, however. σ^+ -Values differ from σ -values only for highly electron-donating substituents such as *p*-methyl and *p*-methoxyl groups. In addition, some electrophilic reaction series are not adequately correlated by σ^+ -values^{13,14} and the value may vary of the order of tenfold, depending on the reaction series.¹⁴

The present results indicate that the hydrolysis of methyl 4-substituted-2,6-dimethylbenzoates in 9.70 *M* sulfuric acid has a ρ of -3.22 and that a correlation between the logarithms of the rate constants and σ^+ -constants is found. In the hydrolysis of six ethyl 3,4,5-substituted-benzoates in 99.9% sulfuric acid at 45°, although weakly electron-withdrawing substituents on the benzene nucleus retard the rate of hydrolysis, there are successive increases in rate with stronger electron-withdrawing substituents.¹⁵ On the other hand, electron-withdrawing substituents retard the rate of hydrolysis of similarly substituted methyl benzoates in 99.9% sulfuric acid solution. These results led to the conclusion that in 99.9% sulfuric acid all methyl esters hydrolyze with the A_{AC}1 mechanism, while the ethyl esters hydrolyze with either an A_{AC}1 or an A_{AL}1 mechanism, depending upon the substituent. The Hammett plots of the rates of hydrolysis of the methyl esters yields a ρ -value of -3 utilizing σ^+ , very similar to the present results. Furthermore, the hydrolysis of substituted benzamides in 98-100% sulfuric acid yields a ρ -value of -1.8 to -3.4, again a value very similar to the results obtained in the present experiments.¹⁶

An analysis of the meaning of the Hammett ρ -constant found in the present investigation is complicated by the fact that the acid-catalyzed hydrolysis of an ester proceeding through an acylium ion intermediate involves a pre-equilibrium protonation before

the rate-determining step. A substituent can affect both the pre-equilibrium and the rate-determining step, and therefore the question arises as to what the Hammett ρ -constant means in such an instance. Leisten¹⁷



encountered this problem when analyzing substituent effects in the hydrolysis of substituted benzamides in moderately concentrated acid. He was successful in separating the substituent effects of the two steps according to the equation

$$\rho_{\text{over-all}} = \rho_{\text{pre-equil.}} + \rho_{\text{rate-determ. step}} \quad (4)$$

In the benzamide system it is possible to determine each ρ independently, $\rho_{\text{over-all}}$ from reaction in dilute sulfuric acid, $\rho_{\text{rate-determ. step}}$ from reactions in moderately concentrated sulfuric acid and $\rho_{\text{pre-equil.}}$ from measurements of the pK_a 's of the benzamides. All the ρ 's thus found were completely consistent with eq. 4. In 100% sulfuric acid, substituted benzamides and methyl benzoates are fully protonated and one therefore measures the ρ of the rate-determining step. The question may, however, be asked as to what step the ρ determined in the present investigation pertains. The basicity constants of substituted benzoic acids, substituted benzaldehydes and substituted acetophenones have been determined by Stewart and co-workers.¹⁸⁻²⁰ Their data yield values of ρ of -2.7, -1.85 and -0.9 for the protonation of acetophenones, benzaldehydes and benzoic acids, respectively, using σ^+ -constants in the correlation. The protonation of the hindered benzoate esters used in this study are probably less susceptible to substituent effects than are the closest analogs above, the benzoic acids, because of steric inhibition of resonance. Therefore we shall assume that the ρ of the pre-equilibrium step in the present reaction is less than -0.9 and possibly very close to zero. On this basis, the ρ of the rate-determining step of the reaction is -3.22 to -2.3. The comparison of the ρ 's of a number of acid-catalyzed hydrolyses is shown in Table II.

The Hammett ρ -values for the rate-determining steps of the reactions in Table II can be grossly divided into those which have a value of +1 and those which have a value of -3 to -4. The former values are characteristic of nucleophilic attack at a carboxylic acid derivative. The latter values are characteristic

(13) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **79**, 1913 (1957); **80**, 4979 (1958).

(14) N. C. Deno and W. L. Evans, *ibid.*, **79**, 5804 (1957).

(15) D. N. Kershaw and J. A. Leisten, *Proc. Chem. Soc.*, 84 (1960)

(16) J. A. Duffy and J. A. Leisten, *J. Chem. Soc.*, 853 (1960).

(17) J. A. Leisten, *ibid.*, 1572 (1956).

(18) R. Stewart and K. Yates, *J. Am. Chem. Soc.*, **80**, 6355 (1958).

(19) R. Stewart and K. Yates, *ibid.*, **82**, 4059 (1960).

(20) K. Yates and R. Stewart, *Can. J. Chem.*, **37**, 664 (1959).

TABLE III: COMPARISON OF REACTIVITY OF BENZOIC ACID AND MESITOIC ACID DERIVATIVES

R ^{vac}	Reactions	Catalyst	Solvent	Temp., °C.	k _{benzoic}	k _{mesitoic}	k _B /k _M	Ref.
1	ArCO ₂ H + MeOH	Satd. HCl soln. ^a	MeOH	18	92 ^{b,c}	No react. ^c	>>1	39, 22
2	ArCO ₂ H + MeOH	0.1 M HCl	MeOH	25	2.04 × 10 ⁻⁴ l./mole. sec.	No react. ^d	>>1	23
3	ArCO ₂ H + PhCH ₂ OH	ArCO ₂ H	PhCH ₂ OH	100	4.19 × 10 ⁻⁷ l./mole. sec.	7.41 × 10 ⁻¹⁰ l./mole. sec.	570	24
4	ArCO ₂ H + H ₂ O ¹⁸	0.07 M HCl	H ₂ O	80	1.61 × 10 ⁻⁴ l./mole. sec.	1.48 × 10 ⁻⁷ l./mole. sec.	1100	25
5	ArCO ₂ Me + OH ⁻	0.06 M OH ⁻	33% (vol.) dioxane-water	25	23.2 × 10 ⁻³ l./mole. sec.	2.2 × 10 ⁻¹ l./mole. sec. ^e	>>1	8, 26
6	ArCO ₂ Me + H ₂ O	HClO ₄ 0.98 M 1.93 3.82	H ₂ O	90	18.7 × 10 ⁻⁸ sec. ⁻¹ 36.6 × 10 ⁻⁴ sec. ⁻¹ 74.5 × 10 ⁻⁸ sec. ⁻¹	7.3 × 10 ⁻⁷ sec. ⁻¹ 42 × 10 ⁻⁷ sec. ⁻¹ 560 × 10 ⁻⁷ sec. ⁻¹	256 87 13	4
7	ArCONH ₂ + OH ⁻	0.08-0.1 M OH ⁻	H ₂ O	109	2.63 × 10 ⁻³ l./mole. sec.	No hydrolyt. ^f	>>1	27, 28
8	ArCOCH ₃ + PhNHNH ₂	HOAc	Concd. HOAc	Heat		No react.	>>1	29
9	ArCOCH ₃ + H ₂ NOH	OH ⁻				No react.	>>1	30
10	ArCHO + HSO ₄ ⁻	Satd. soln. of NaHSO ₄	H ₂ O	25	>90 ^g	46 ^{h,i}	>>1	31
11	Steric strain						Large	32
12	ArCOCl + H ₂ O				1-2 kcal./mole ⁱ	≥ 17 kcal./mole ⁱ	1/44	33
13	ArCOCl + MeOH				7.71 × 10 ⁻⁵ sec. ⁻¹	3.35 × 10 ⁻³ sec. ⁻¹	1/61	34, 35
14	ArCO ₂ Me + H ₂ SO ₄	100% H ₂ SO ₄			2.63 × 10 ⁻⁶ sec. ⁻¹	1.58 × 10 ⁻³ sec. ^{-1k}	>>1	36
15	ArCOCl + H ₂ O				~0 ^{h,i}	Too fast	>>1	37, 38
16	ArCOCl + H ₂ O	1.09 × 10 ⁻² M HClO ₄	95% (vol.) dioxane	25	1.3 × 10 ⁻⁶ /sec.	4.45 × 10 ⁻³ /sec.	2.82 × 10 ⁻⁴	6
17	ArCOCl + H ₂ O	1.49 × 10 ⁻³ M Me ₄ N ⁺ OH ⁻	95% (vol.) acetone	15	1.2 × 10 ⁻⁶ /sec.	58.4 × 10 ⁻³ /sec.	2.06 × 10 ⁻¹	6
			MeOH	0	1.32 × 10 ⁻³ /sec.	45.8 × 10 ⁻³ /sec.	2.88 × 10 ⁻¹	6
			100% H ₂ SO ₄	25				
			99% (v./v.) aq. CH ₃ CN	25				
			99% (v./v.) aq. CH ₃ CN	25				
			99% (v./v.) aq. CH ₃ CN	25				

^a *Circa* 44% alc. HCl. ^b % product. ^c After 12 hours. ^d Ar = 2,5-dimethyl-C₆H₃. ^e 126°, 60% (vol.) dioxane-water, 0.05 M OH⁻. ^f 195°, 0.27 molal OH⁻ in ethylene glycol. ^g Ar = *p*-methyl-C₆H₄, isolated after 2 min. ^h After 3 weeks. ⁱ For 1,2,3-trimethylbenzene. ^j 1-*tert*-Butyl-2,6-dimethylbenzene. ^k 0.2°. ^l After 2 min.

of reactions involving a transition state which has a high degree of cationic character. These reactions which include the reaction studied in the present investigation possess ρ -values which are quite similar to those of many carbonium ion reactions²¹ and are thus reasonably described as reactions involving acylium ion intermediates. The structural reasons leading to this mechanism have been discussed in detail previously.⁵

A comparison of the reactivity of sterically hindered and unhindered benzoic acid derivatives, as represented by mesitoic and benzoic acid derivatives, is shown in Table III. In Table III two distinct patterns emerge. Reactions 1-10 include processes in which the benzoic acid derivative reacts considerably more rapidly than the mesitoic acid derivative. Reactions 12-17, on the other hand, show exactly the opposite behavior. Two separate mechanisms may be assigned to these two categories of behavior, the two mechanisms being bimolecular and unimolecular, respectively. In dilute acid or alkaline solution, the rate of reaction of the mesitoic acid derivatives is always much slower than that of the benzoic acid derivatives, with the exception of the acid chloride reactions. Apparently steric hindrance occurs in all reactions of mesitoic acid derivatives in dilute acid or alkaline solutions which proceed by a bimolecular mechanism. The anomalous behavior of the reaction of mesitoyl chloride (k_B/k_M is much less than one) implies that this compound reacts *via* a different mechanism which is not adversely affected by steric hindrance. The fact that k_B/k_M decreases with an increase in the concentration of perchloric acid in the acid-catalyzed hydrolysis of methyl benzoate and mesitoate (reaction 6) is presumably due to the increasing incursion of the unimolecular mechanism. This presumption is further supported by the results of the hydrolysis in 100% sulfuric acid (reaction 14), in which methyl mesitoate hydrolyzes much faster than methyl benzoate by a mechanism involving acylium ion formation.

Thus the comparison of the Hammett ρ -values of a series of hydrolytic reactions in Table II and the relative rates of the series of reactions of benzoic acid and mesitoic acid derivatives in Table III indicates that hindered benzoic acid derivatives may react *via* two distinct pathways: (1) a bimolecular pathway which shows considerable steric hindrance to reaction and is facilitated by electron-withdrawing substituents and (2) a unimolecular pathway which is facilitated by steric hindrance and by electron-donating substituents.

Acknowledgment.—The authors gratefully acknowledge valuable discussions with Dr. H. Ladenheim.

- (21) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4986 (1958).
- (22) V. Meyer and J. J. Sudborough, *Ber.*, **27**, 1580 (1894).
- (23) H. A. Smith and R. B. Hurley, *J. Am. Chem. Soc.*, **72**, 112 (1950).
- (24) C. N. Hinshelwood and A. R. Legard, *J. Chem. Soc.*, 587 (1935).
- (25) M. L. Bender, R. R. Stone and R. S. Dewey, *J. Am. Chem. Soc.*, **78**, 319 (1956).
- (26) M. L. Bender and R. J. Thomas, *ibid.*, **83**, 4189 (1961).
- (27) L. Tsai, T. Miwa and M. S. Newman, *ibid.*, **79**, 2530 (1957).
- (28) M. L. Bender and R. D. Ginger, *ibid.*, **77**, 348 (1955).
- (29) F. Baum, *Ber.*, **28**, 3207 (1895).
- (30) E. Feith and S. H. Davies, *ibid.*, **24**, 3546 (1891).
- (31) L. I. Smith and J. Nichols, *J. Org. Chem.*, **6**, 489 (1941).
- (32) H. C. Brown, *et al.*, *J. Am. Chem. Soc.*, **75**, 1-20 (1953).
- (33) C. A. Bunton and T. A. Lewis, *Chemistry & Industry*, 180 (1956).
- (34) D. A. Brown and R. F. Hudson, *J. Chem. Soc.*, 883 (1953).
- (35) D. A. Brown and R. F. Hudson, *ibid.*, 3352 (1953).
- (36) J. F. Norris and H. H. Young, *J. Am. Chem. Soc.*, **57**, 1420 (1935).
- (37) M. S. Newman, *ibid.*, **63**, 2431 (1941).
- (38) A. Bradley and M. E. Hill, *ibid.*, **77**, 1575 (1955).
- (39) "International Critical Tables," E. W. Washburn, ed., McGraw-Hill Co., New York, 1928, Vol. III, p. 264.