o-Carbonyl-Assisted Alkaline Hydrolyses of Methyl Benzoates[1,2]

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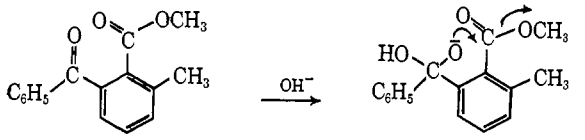
Abstract: The rates of alkaline hydrolysis of methyl 6-methyl-2-benzoylbenzoate, methyl 6-methyl-2-acetylbenzoate, methyl 6-chloro-2-benzoylbenzoate, methyl 6-chloro-2-acetylbenzoate, and the 6-unsubstituted analogs have been measured. The rates are reported in Table II. In each case the 6-substituted esters hydrolyze at rates greater than do the corresponding unsubstituted esters. The results are explained by assuming a rate-controlling intramolecular attack of the anion, formed by adding hydroxyl ion to the ketonic carbonyl group, on the ester grouping which has been forced out of the plane of the aromatic ring by the 6-substituent.

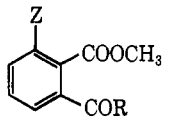
In earlier work, the greater rate of alkaline hydrolysis of methyl 6-methyl-2-benzoylbenzoate as compared to that of methyl 2-benzoylbenzoate was explained[3] by assuming that the hydrolysis of the 6-methyl compound was initiated by attack of a hydroxide ion on the ketonic carbonyl group followed by intramolecular displacement of methoxide ion. The steric acceleration was rationalized by postulating that the 6-methyl group forces the ester grouping to be noncoplanar with the benzene ring to which it is attached and hence better oriented for intramolecular attack by the adjacent negative oxygen.



Large rate increases in hydrolyses of dimethylphosphoacetoin[4] and of methyl 2-formylbenzoate[5] have been explained by postulating attack of hydroxide ion on adjacent acetyl[4] and formyl groups.[5] Later, other examples of increased rates of hydrolysis of esters due to attack of hydroxide on adjacent carbonyl groups have appeared.[6,7]

The magnitude of acceleration of alkaline hydrolysis of all the compounds mentioned[4-7] was considerably greater than the rate increase originally observed here.[3] However, two factors should be mentioned in comparing the results: the compounds having large rate increases[4-7] all involved addition to a formyl or an acetyl group, and in no case was the steric effect of a group adjacent to the ester function studied. Therefore, we decided to determine the rates of hydrolysis of the compounds represented by the general formula A, where Z would be H, CH_3, and Cl and R would be C_6H_5, CH_3, and H.

Unfortunately, we were unable to prepare pure samples of VI and IX so that our objectives were only attained in part. However, the work done shows that



A

I, Z = H; R = C_6H_5
II, Z = H; R = CH_3
III, Z = H; R = H
IV, Z = CH_3; R = C_6H_5
V, Z = CH_3; R = CH_3
VI, Z = CH_3; R = H
VII, Z = Cl; R = C_6H_5
VIII, Z = Cl; R = CH_3
IX, Z = Cl; R = H

there is a steric acceleration when Z is methyl and chloro in the cases where R is methyl and phenyl. The inability to prepare pure VI and IX is unusual as treatment of keto acids with diazomethane gives pure normal ester in all other cases in our experience.

Experimental Section[8]

The normal (I) and pseudo methyl esters of 2-benzoylbenzoic acid used were pure preparations on hand.[9] Methyl 6-methyl-2-benzoylbenzoate (IV), bp 158–159° (0.8 mm),[10] and 6-chloro-2-benzoylbenzoic acid[11] were prepared as described. The melting point behavior of the latter acid was confirmed.[11] Treatment with ethereal diazomethane yielded pure methyl 6-chloro-2-benzoylbenzoate (VII), bp 190–192° (1.2 mm), infrared absorption at 5.75 (1740) and 6.00 μ (1670 cm^{-1}).

Anal. Calcd for $C_{15}H_{11}ClO_3$: C, 65.6; H, 4.0. Found[m]: C, 65.4; H, 4.0.

6-Chloro-2-acetylbenzoic Acid. A finely ground mixture of 10.0 g of 3-chlorophthalic anhydride[11] and 6.7 g of dry malonic acid was heated on a steam bath for 2 hr with 7 ml of dry pyridine.[12] After adding 50 ml of water and 4 ml of concentrated HCl the solution deposited 5.0 g of colorless crystals, mp 124–126°. Recrystallization from benzene yielded 4.1 g (38%) of pure 6-chloro-2-acetylbenzoic acid, mp 128–129°, ir bands at 2.90 (3450) and 5.70 μ (1750 cm^{-1}). From the original aqueous filtrate 4.7 g of 3-chlorophthalic acid, mp 184–186°, was recovered.

Anal. Calcd for $C_9H_7ClO_3$: C, 54.5; H, 3.6; Cl, 17.8. Found[g]: C, 54.3; H, 3.6; Cl, 17.8.

The above structure was confirmed by decarboxylation (Cu powder, quinoline at reflux for 30 min) and oxidation of the result-

(1) This research was supported in part by Grant DA-ARO-D-31-124-G846 of the U. S. Army Research Office, Durham, N. C., and by Grant GP-5552X1 of the National Science Foundation.

(2) This research is reported in greater detail in the Ph.D. thesis of A. L. Leegwater presented to The Ohio State University, 1967.

(3) M. S. Newman and S. Hishida, *J. Am. Chem. Soc.*, **84**, 3582 (1962).

(4) F. Ramirez, B. Hansen, and N. B. DeSai, *ibid.*, **84**, 4588 (1962).

(5) M. L. Bender and M. S. Silver, *ibid.*, **84**, 4589 (1962).

(6) Y. Shalitin and S. A. Bernhard, *ibid.*, **86**, 2292 (1964).

(7) C. N. Lieske, E. G. Miller, Jr., J. J. Zeger, and G. M. Steinberg, *ibid.*, **88**, 188 (1966).

(8) The term "worked up in the usual way" means that an ether–benzene solution of the products was extracted with dilute $NaHCO_3$ solution and/or dilute HCl as needed, washed with saturated salt solution, filtered through anhydrous $MgSO_4$, and concentrated by distillation or on a rotary evaporator. Analyses marked with a superscript g by the Galbraith Microanalytical Laboratories, Knoxville, Tenn., and superscript m by MicroAnalysis, Inc., Wilmington, Del.

(9) M. S. Newman and C. I. Courduvelis, *J. Org. Chem.*, **30**, 1795 (1965).

(10) M. S. Newman and C. D. McCleary, *J. Am. Chem. Soc.*, **63**, 1537 (1941).

(11) M. S. Newman and P. G. Scheurer, *ibid.*, **78**, 5004 (1956).

(12) Compare H. L. Yale, *ibid.*, **69**, 1547 (1947).

ing ketone to *m*-chlorobenzoic acid with sodium hypoiodite. The melting point of 156–158° was not depressed by mixing with an authentic sample.

Esterification of 6-chloro-2-acetylbenzoic acid with diazomethane afforded the pure normal ester VIII (92%), bp 107–109° (0.5 mm), ir bands at 5.78 (1730) and 5.90 μ (1695 cm^{-1}), and with methanolic-HCl for 3 hr, the pseudo ester (69%), mp 79.5–81.0°, ir band at 5.65 μ (1770 cm^{-1}).

Anal. Calcd for $C_{10}H_{19}ClO_3$: C, 56.5; H, 4.3; Cl, 16.7. Found[g] (normal ester): C, 56.4; H, 4.2; Cl, 16.4. Found (pseudo ester): C, 56.5; H, 4.3; Cl, 16.5.

Methyl 2-Acetylbenzoate (II). Treatment of pure 2-acetylbenzoic acid[13] with ethereal diazomethane yielded the pure ester II, bp 134–135° (10 mm), 94–95° (0.6 mm),[14] ir bands at 5.78 (1730) and 5.90 μ (1695 cm^{-1}).

6-Methyl-2-acetylbenzoic Acid. A finely ground mixture of 28.0 of 3-methylphthalic anhydride and 20.8 g of dry malonic acid was heated with 17 ml of dry pyridine for 5 hr on a steam bath.[12] After a work-up similar to that described above for 6-chloro-2-acetylbenzoic acid, 10.2 g (33%) of pure 6-methyl-2-acetylbenzoic acid, mp 126–127°, was obtained. In addition 31% of 3-methylphthalic acid was recovered. By the addition of methylmagnesium iodide to 3-methylphthalic anhydride, there was obtained a 31% yield of 6-methyl-2-acetylbenzoic acid.[15] Esterification with diazomethane yielded pure methyl 6-methyl-2-acetylbenzoate (V), bp 107–108° (0.7 mm), ir bands at 5.75 (1740) and 5.90 μ (1695 cm^{-1}), and with methanolic HCl a 62% yield of pure pseudo methyl ester, mp 72.5–73.5°, ir bands at 5.65 μ (1770 cm^{-1}), nmr peaks at τ 2.75 (3 H, aromatic), 7.01 (3 H, singlet, OCH_3), 7.31 (3 H, singlet, $ArCH_3$), and 8.24 (3 H, singlet, CH_3), waso btained. This compound must be the pseudo ester and is different from the compound, mp 170–180°, previously reported[15] as the pseudo ester.

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.7; H, 6.3. Found[m] (normal ester): C, 68.8; H, 6.4. Found (pseudo ester): C, 68.7; H, 6.4..

Methyl 2-formylbenzoate[16] **(III),** bp 98–100° (1.7 mm), was prepared by treatment of phthalaldehydic acid with diazomethane. Both 6-methyl-2-formylbenzoic and 6-chloro-2-formylbenzoic acids were prepared for the first time. However, we were unable to isolate pure samples of their normal methyl esters as the acids existed mainly in the cyclic form and gave mixtures of normal and pseudo methyl esters on treatment with diazomethane. To our knowledge, these are the first cases in which appreciable amounts of pseudo esters are formed by diazomethane. Treatment of the silver salts with methyl iodide yielded mixtures of normal and pseudo methyl esters which were not readily separated by chromatography.

6-Methyl-2-formylbenzoic Acid. A suspension of 100 g (0.83 mol) of 2,6-dimethylaniline[13] in 250 ml of 48% hydrobromic acid was stirred at 0–5° while a solution of 58 g (0.84 mol) of sodium nitrite in 100 ml of water was slowly added. The resulting solution was added during 30 min to a boiling solution of 66 g of cuprous bromide and 67 ml of 48% hydrobromic acid. The product was steam distilled and worked up in the usual way to afford 70.1 g (46%) of colorless 2,6-dimethylbromobenzene,[17] bp 53–55° (2.3 mm).

Carbonation of the Grignard reagent formed by treatment of 70 g of the bromo compound and 83 g of ethyl bromide in 400 ml of ether with excess magnesium yielded 45 g (79%) of 2,6-dimethylbenzoic acid,[18] mp 118–120°. The methyl ester (diazomethane) boiled at 68–70° (2 mm).

An illuminated (300-W lamp) mixture of 13.4 g of methyl 2,6-dimethylbenzoate and 14.6 g of N-bromosuccinimide in 250 ml of CCl_4 was held at reflux for 2 hr. After removing the succinimide by filtration, the solvent was distilled and the remaining oil treated with 20 ml of methanol and 100 ml of 20% sodium hydroxide at reflux for 20 hr. After acidification and the usual work-up there was obtained 10.1 g (83%) of 7-methylphthalide, mp 83–85°, ir band at 5.71 μ (1750 cm^{-1}). The nmr spectrum (CCl_4) was consistent with the assigned structure.

Anal. Calcd for $C_9H_9O_2$: C, 72.9; H, 5.4. Found[m]: C, 72.6; H, 5.4.

Addition during 30 min of 15.0 g of 3-methylphthalic anhydride to a refluxing suspension of 2.8 g of $LiAlH_4$ in 300 ml of ether followed by 3 hr at reflux afforded 7-methylphthalide in 69% yield. This route does not establish the structure whereas the first route does.

An illuminated (300-W lamp) mixture of 5.5 g of 7-methylphthalide and 6.6 g of N-bromosuccinimide in 150 ml of CCl_4 was held at reflux for 2 hr. After filtration of the succinimide, the solvent was removed on a rotary evaporator. The oily residue was heated for 10 hr with 75 ml of water. Recrystallizations of the crude solid from benzene afforded 2.2 g (36%) of 6-methyl-2-formylbenzoic acid, mp 112.5–114.0°, ir bands at 3.0 (3340) and 5.73 μ (1745 cm^{-1}).

Anal. Calcd for $C_9H_8O_3$: C, 65.9; H, 4.9. Found[g]: C, 65.6; H, 4.8.

6-Chloro-2-formylbenzoic Acid. Reduction of 3-chlorophthalic anhydride[11] with $LiAlH_4$ in ether as described above for 3-methylphthalic anhydride afforded 7-chlorophthalide,[19] mp 146–147°, ir band at 5.70 μ (1755 cm^{-1}), in 44% yield. Bromination, as above described for 7-methylphthalide, followed by hydrolysis yielded 6-chloro-2-formylbenzoic acid, mp 187–189°, ir band at 5.75 μ (1740 cm^{-1}), in 47% yield.

Anal. Calcd for $C_8H_5ClO_3$: C, 52.1; H, 2.7; Cl, 19.2. Found[m]: C, 52.3; H, 2.9; Cl, 18.9.

Measurement of Rates of Hydrolysis of Esters. The hydroxide ion catalyzed hydrolysis of the methyl esters in 70:30 (v/v) water–dioxane at 30° was carried out with a thermostated Beckman DU spectrophotometer. The reaction occurred in a thermostated buffer solution in a 3-ml, glass-stoppered quartz cell. The rate constants were determined by following the increase in carboxylate anion absorption with time at 310 mμ.[20] Experiments with II showed that Beer's law was obeyed in the concentration ranges used.

The pH of the water–dioxane[21] solutions used in this work was determined with a Beckman Model 76 expanded-scale pH meter with a calomel-fiber junction electrode (39170) and a glass electrode (41260, pH 0–14, Type E-2). The pH meter was standardized with aqueous solutions, as recommended.[22] The glass electrode gives the correct pH at the concentration used in the dioxane–water mixtures.[23]

A stock solution of each buffer was prepared from aqueous buffers (μ = 0.15 to 0.19) and the appropriate amount of dioxane. The pH of this stock solution was determined and of the reaction solution after a kinetic run. The pH remained constant within experimental error. After the cell compartment had come to thermal equilibrium, the reaction was initiated by adding 0.2–5 μl of ester (neat) or of a solution of ester in dioxane to the buffer solution. The optical density of the reaction mixture was measured against a blank of the appropriate buffer solution at convenient intervals until the optical density remained unchanged.

The second-order rate expression, k_2[OH^-][ester], was reduced to the expression k_0[ester] since the hydroxide ion concentrations were held constant by buffers in the 7.93–11.58 pH range. Rewritten in terms of optical density measurements the expression below was used to obtain the rate constant.[24]

$$-k_0t/2.303 = \log (OD_\infty - OD_t) - \log OD_\infty$$

A plot of log ($OD_\infty - OD_t$) *vs.* time (in minutes) gave a straight line for several half-lives. The slope (k_0/2.303) of this line was determined by the method of least squares.

Because we do not know the autoprotolysis constant of water in 30% dioxane, the values for the rate constants listed are not strictly accurate. However, since we were interested mainly in relative

(13) Obtained from the Aldrich Chemical Co.

(14) R. Riemschneider, H. G. Kaahn, and L. Horner, *Monatsh. Chem.*, 91, 1040 (1960).

(15) P. R. Jones and P. J. Desio, *J. Org. Chem.*, 30, 4293 (1965).

(16) E. L. Eliel and A. W. Burgstahler, *J. Am. Chem. Soc.*, 71, 2251 (1949), report bp 136–138° (13 mm).

(17) G. Vander Stouw, Ph.D. Dissertation, The Ohio State University, 1964, p 45, reported a 34% yield of 2,6-dimethylbromobenzene, bp 64–67° (5 mm).

(18) B. van Zanten and W. Th. Nauta, *Rec. Trav. Chim.*, 79, 1216 (1960), report mp 116° for the acid, bp 98–100° (12 mm), for the methyl ester, and bp 90–93° (20 mm) for 2,6-dimethylbromobenzene.

(19) S. Biniecki, M. Moll, and L. Rylski, *Ann. Pharm. France*, 16, 421 (1958), report mp 146–147°; J. Tirouflet, *Compt. Rend.*, 238, 2246 (1954), mp 149°.

(20) For an ester of each class studied, the rate was shown to be independent of the wavelength employed.

(21) The *p*-dioxane was purified as described in L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath, New York, N. Y., 1941, p 369.

(22) R. G. Bates, *J. Res. Natl. Bur. Std.*, 66A, 179 (1962).

(23) H. P. Marshall and E. Grunwald, *J. Chem. Phys.*, 21, 2143 (1953).

(24) A. A. Frost and R. T. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1961, p 38

rate constants we did not attempt to determine K_w in 30% dioxane and assumed it to be the same as in pure water.

A typical run is shown in Table I. The constants given in Table II represent the averages of at least two runs.

Table I. Hydrolysis of Methyl *o*-Acetylbenzoate at 30 ± 0.1° in 70:30 Water–Dioxane at pH 9.95 (Borate Buffer)[a]

Time, min	OD_t	$OD_\infty - OD_t$
5	0.242	0.225
10	0.268	0.199
15	0.293	0.174
20	0.314	0.153
25	0.333	0.134
30	0.349	0.118
34	0.362	0.105
40	0.377	0.090
46	0.389	0.078
50	0.396	0.071
56	0.409	0.058
60	0.415	0.052
65	0.419	0.048
70	0.425	0.042
75	0.431	0.036
80	0.435	0.032
90	0.443	0.024

[a] Slope = -0.0114 min^{-1}, $k_0 = 2.63 \times 10^{-2}$ min^{-1}. OD measured at 310 mμ, slit width 0.36; $OD_\infty = 0.567$.

Table II. Summary of Kinetic Data Relative Rate Constants[a]

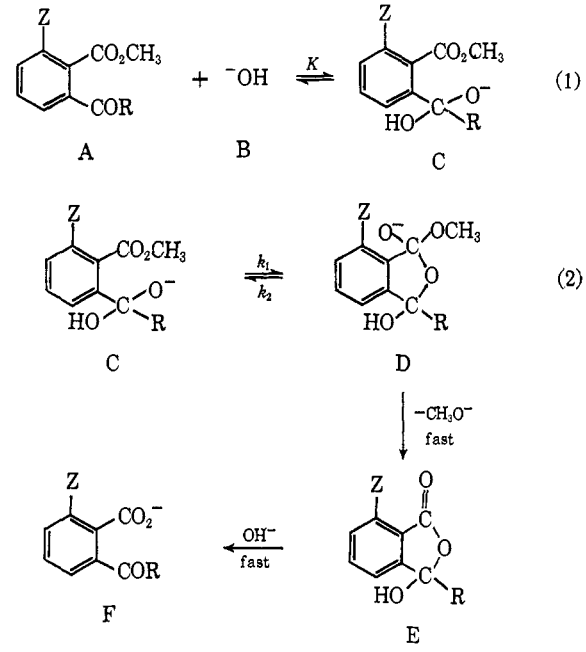
Ester	$k_0 \times 10^4$ sec^{-1} [b]	pH	$k_2K_w \times 10^{14}$ M^{-1} sec^{-1} [c]	k_{rel}
I	2.97 ± 0.20	11.58	0.078	1.0
II	4.50 ± 0.12	9.95	5.05	64.8 (1)
III	2.63 ± 0.02	7.93	310	3970
IV	12.8 ± 0.07	11.58	0.336	4.31
VII	17.3 ± 0.00	10.84	2.51	32.2
V	6.33 ± 0.17	9.95	7.10	91.0 (1.4)
VIII	1.88 ± 0.03	8.70	37.7	483 (7.4)
I (4-benzoyl)	4.33 ± 0.27	11.58	0.114	1.46
I (pseudo ester)	7.28 ± 0.30	11.58	0.192	2.46

[a] At 30.0 ± 0.1° in 70:30 water–dioxane. [b] These rate constants represent the average of two or three determinations. They were obtained from the constants of the type shown in Table I by dividing by 60. [c] If K_w in 30% dioxane is the same as in water, the k_2 values in this column are the true rate constants, k_2.

Discussion of Results

Before discussing the results of hydrolysis, assumptions must be made concerning the various equilibria and rates involved. Hence the following mechanism is proposed (eq 1 and 2).[25]

We assume that the observed rate constant is the product of the rate of cyclization of C (k_1, eq 2) by the equilibrium constant, K, for the reactions indicated in eq 1. If the formation of the anion C were the rate-determining step in the hydrolysis we can see no reason why all of the rates for the 6-substituted esters should be greater than those for the corresponding unsubstituted ester. Furthermore, attack of hydroxide ion on the ester function can also be ruled out as the rate-determining step because the rates for *ortho*-substituted benzoates (in which the substituent cannot participate) would be expected to be slower than the rates for



unsubstituted ester. However, if the cyclization step, illustrated by eq 2, is rate determining then a reason for the rate acceleration by the 6-substituents is apparent, namely, that the 6-substituent forces the carbonyl group of the ester function out of the plane of the ring. In this form, the intramolecular attack by the neighboring anionic oxygen is facilitated.[3,26]

In going from C to D there is undoubtedly some release of strain, but much greater relief is gained by loss of methoxide ion in going from D to E. Hence we rule out the latter as the rate-determining step.

The type of equilibrium shown in eq 1 has not received much study, but analogies exist in the pre-equilibrium involved in the reaction of aldehydes and ketones with hydroxylamine prior to dehyration to form oximes[27] and in the formation of ketimine from acetone and methylamine.[28]

Methyl 2-Benzoylbenzoates. Before discussing the relative rates of hydrolysis of compounds I, IV, and VII, an error in previous work[3] must be corrected. The previously reported[3] rate constant of 3.47×10^2 M^{-1} sec^{-1} for I in 70:30 dioxane–water was in error. Both work here and elsewhere[29] has shown that the rate is higher than reported.[3] The value of 7.8×10^2 M^{-1} sec^{-1} (Table II) has been established for I in 70:30 water–dioxane in this work. The more aqueous solvent was needed in order to dissolve the inorganic buffers. The rates for IV and pseudo methyl 2-benzoylbenzoate were also redetermined in 70:30 water–dioxane and found to agree well with those previously reported[3] in 70:30 dioxane–water. This error in the rate for I does not seriously affect the discussion previously made, but the rate for I in Table II should be used.

Since the rates of hydrolysis of IV and VII are both greater than that for I the 6-methyl and 6-chloro groups

(25) While this work was being finished a similar mechanism was proposed by K. Bowden and G. R. Taylor, *Chem. Commun.*, 112 (1967), but the rate-determining step was considered to be addition of hydroxide ion to the ketonic carbonyl of substituted 2-benzoylbenzoates.

(26) A discussion of the geometry of addition to the carbonyl group is given by M. L. Bender, *Chem. Rev.*, 60, 60 (1960).

(27) W. P. Jencks, *Progr. Phys. Org. Chem.*, 2, 96, 98 (1965),

(28) A. Williams and M. L. Bender, *J. Am. Chem. Soc.*, 88, 2508 (1966).

(29) While this work was in progress Drs. K. Bowden and R. G. Taylor, University of Sussex, England, wrote to us to question our value[3] as they obtained a rate constant of 9.0×10^2 M^{-1} sec^{-1} by a different method in 70:30 dioxane–water.

serve similar functions, namely, to keep the ester carbonyl group out of the plane of the ring to which it is attached. This nonplanarity facilitates the intramolecular nucleophilic attack of the neighboring O^- function in two ways: (a) there is a more favorable orientation,[3] and (b) the carbonyl group carbon of the ester is more electrophilic since there is less distribution of positive charge to the aryl ring. The fact that VII hydrolyzes appreciably faster than IV is explained by the greater inductive effect of Cl as compared to CH_3 on both K and k_1, since the steric effect of each should be about the same.[30]

Methyl 2-Acetylbenzoates. In this series the rates for V and VIII are also greater than that for the unsubstituted ester II but the rate ratios for V (1.4) and VII (7.4) as compared to II are appreciably less than the ratios for IV (4.3) and VII (32.2) as compared to I. The steric explanation for the rate increase is similar to that described for the methyl 2-benzoylbenzoates. However, the fact that there is a greater increase in relative rate for the 2-benzoylbenzoates as compared to the 2-acetylbenzoates is difficult to explain. One would expect the equilibrium constants for addition of hydroxide ion to the acetyl groups involved would be greater than those for the benzoyl group (eq 1). The rates (k_1) of cyclization of the intermediates C to intermediates D may be faster for the benzoyl compounds than for the acetyl compounds because of less freedom of rotation of the former due to the greater steric effect of phenyl as compared to methyl. Also, there may be slightly more release of strain in going from C to D in the benzoyl cases. However, in the absence of further experimental data on rates of hydrolysis at different temperatures, further discussion is not warranted. The most important feature as far as the present work is concerned is that there is a steric facilitation of hydrolysis attributable to the 6-methyl and 6-chloro groups in this series.

Methyl 2-Formyl, 2-Acetyl-, and 2-Benzoylbenzoates. In the three unsubstituted esters, methyl *o*-formylbenzoate (III), methyl *o*-acetylbenzoate (II), and methyl *o*-benzoylbenzoate (I), the alkaline hydrolysis may conceivably proceed *via* two mechanisms: (1) attack of hydroxide ion at the carbonyl function as in the case of the 6-substituted esters, and (2) the normal attack of the hydroxide ion at the carbomethoxy function. Since Bender has shown that III hydrolyzes 10^5 faster than methyl *p*-formylbenzoate the main path undoubtedly involves carbonyl attack.[31] With the unsubstituted benzoyl esters the situation is reversed. Methyl *p*-benzoylbenzoate hydrolyzes 1.46 times faster than I. Thus attack of hydroxide ion on the carbomethoxy group may be the rate-controlling step for I.

The rate of hydrolysis of II is intermediate between that of III and I. Since II and III hydrolyze at so much greater rates than does I, the rate-controlling step may be the forward reaction in eq 1. Unfortunately, we have been unable to find a comparative study involving benzophenone, acetopheone, and benzaldehyde in order to estimate the relative rates of such a reaction.

Methyl 2-Formylbenzoates. Although we were unable to prepare pure samples of the normal methyl esters of 6-methyl- and 6-chloro-2-formylbenzoic acids, mixtures of normal and pseudo esters were obtained. Qualitative tests showed that these esters hydrolyzed more rapidly than did methyl 2-formylbenzoate, but the rates were so rapid that further kinetic work on the ester mixtures was not done. Thus, a steric effect to accelerate the hydrolyses is probably present in these cases also but further work is required before a suitable system for measurement can be found.

Acknowledgment. We thank Professor Jack Hine for valuable discussion concerning the kinetic results.

(30) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1960, p 260, gives 1.80 and 2.0 Å for the van der Waals radii of Cl and CH_3, respectively.

(31) M. L. Bender, J. A. Reinstein, M. S. Silver, and R. Mikulak, *J. Am. Chem. Soc.*, 87, 4545 (1965).

The Hydrolysis of N-Substituted Acetimidate Esters

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Abstract: The hydrolysis of two acetimidate esters (I and II) derived from aniline and α-methylphenethylamine has been studied at 30° in the pH range 0–12. Hydrolysis yields amines and esters in acid solution and amides at alkaline pH, transition between the two sets of products taking place at pH 7.69 and 8.45 for I and II, respectively. At constant pH, bifunctional catalysts (phosphate, bicarbonate, acetic acid) divert the breakdown of tetrahedral intermediates from the formation of amides to the expulsion of amines. The mechanism previously proposed to account for iminolactone hydrolysis seems to hold generally for the hydrolysis of imidates. This mechanism involves the intermediacy of carbinolamine addition compounds whose breakdown is influenced by pH and by general acid–base catalysts. Implications of this work for the mechanism of ester aminolysis are discussed.

Although the mechanism of hydrolysis of acyclic imidate esters attracted attention as early as 1908,[1] few additional studies appeared in the succeeding six

(1) (a) J. Stieglitz, *Am. Chem. J.*, **39**, 29 (1908); (b) I. H. Derby, *ibid.*, **39**, 437 (1908); (c) W. McCracken, *ibid.*, **39**, 586 (1908); (d) H. I. Schlesinger, *ibid.*, **39**, 719 (1908).