Acid-Catalyzed Hydrolysis of 1-Arylcyclopropyl Acetates. Electrophilic Cyclopropane Ring Cleavage

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Eight 1-arylcyclopropyl acetates **5** were prepared and subjected to hydrolysis with 0.1 *N* hydrochloric acid in 50 wt % aqueous dioxane at 40, 55, and 70°. With the exception of the hydrolyses at 40° of those acetates substituted with electron-withdrawing groups, all compounds gave nonlinear first-order plots (production of acetic acid) which could be analyzed in terms of normal A'2 hydrolysis to cyclopropanol **6** in competition with ring opening to an unstable intermediate which breaks down to propiophenone **7**. The structure of the intermediate was tentatively assigned as hydroxyacetate **8** on the basis of the product study and rate meaurements on model compounds.

Although the acid-catalyzed opening of various substituted cyclopropanols is now well documented,[2,3] the extent to which such a reaction might intervene during the acidic hydrolysis of a simple cyclopropyl carboxylate has not been previously determined and should be of considerable interest. In view of the often quoted similarity between the cyclopropane ring and a double bond, it is of interest to note that the preferred path for acid hydrolysis of enol esters involves slow addition of water across the double bond followed by alkyl–oxygen cleavage,[4] a result which suggest that ring cleavage during the hydrolysis of cyclopropyl esters might be important.

In the following study eight 1-arylcyclopropyl acetates have been prepared and the rates of acid-catalyzed hydrolysis measured at several temperatures.

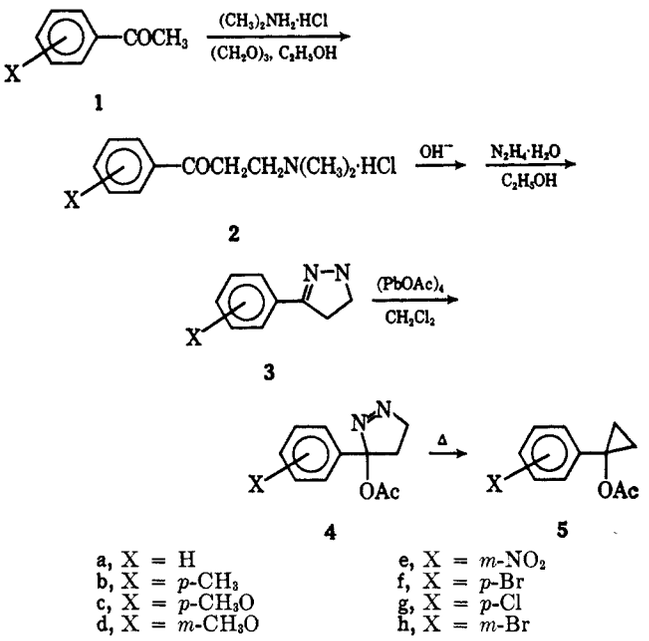
Results

All the cyclopropyl esters of general structure **5** were synthesized from the substituted acetophenones **1** according to the general procedure described by Freeman[5] and outlined in Scheme I.

Kinetic measurements of the hydrolyses of acetates **5** with *ca.* 0.1 *N* hydrochloric acid in 50 wt % aqueous dioxane were carried out at several temperatures by following the rate of production of acetic acid. At 40° all the substituted esters except acetates **5b** and **5c**, in which an electron donor is located in the *para* position, followed good pseudo-first-order kinetics (Table I). A simple extrathermodynamic relationship between log (relative rate) and the Hammett σ values was found and exhibited a slope of -0.108.[6,7]

Acetates **5b** and **5c** at 40, 55, and 70°, and all other acetates at temperatures above 40° (except **5e** at 55°) displayed non-first-order behavior as indicated in Figure 1 for the *p*-tolyl ester **5b** at 70°. A rational kinetic scheme capable of explaining these results consists of a direct hydrolysis path k_2, involving the normal acyl–oxygen cleavage step, in competition with a two-step sequence which results in initial cleavage of the cyclopropane ring to intermediate A which undergoes hydrolysis. A similarity in the values for k_2 and k_3 results in the type of behavior indicated in Figure 1. Assumption that the three steps are essentially irreversible under the reaction conditions (see Discussion) and

SCHEME I



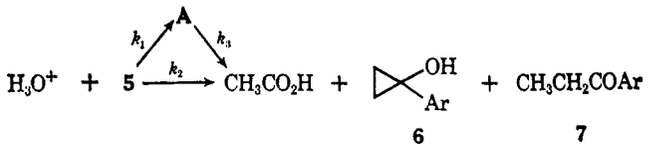
a, X = H
b, X = *p*-CH_3
c, X = *p*-CH_3O
d, X = *m*-CH_3O
e, X = *m*-NO_2
f, X = *p*-Br
g, X = *p*-Cl
h, X = *m*-Br

TABLE I

RATE DATA FOR THE ACID HYDROLYSES OF 1-ARYLCYCLOPROPYL ACETATES IN 50 WT % AQUEOUS DIOXANE[a] AT 40°

Substituent	No. of runs	$k(H^+) \times 10^6$ [b,c]	$k \times 10^5$ [b,d]	Rel rate
H (**5a**)	4	4.69	4.79	1.000
m-CH_3O (**5d**)	3	4.56	4.49	0.937
p-Cl (**5g**)	2	4.43	4.35	0.908
p-Br (**5f**)	3	4.41	4.33	0.904
m-Br (**5h**)	3	4.57	4.08	0.852
m-NO_2 (**5e**)	5	3.87	3.98	0.831
	4[e]	15.58[e]	15.53[e]	...

[a] *Ca.* 0.1 *N* in hydrochloric acid. [b] Average deviation for several runs is ±1% except for *m*-NO_2 (**5e**) for which it is ±1.5%. [c] Units of sec^{-1}. [d] Units of mol $l.^{-1}$ sec^{-1}. [e] 55°.



(1) Taken from the Ph.D. Dissertation of W. L. B. Support of this work by a grant from the University of Kansas General Research Fund is gratefully acknowledged.

(2) (a) C. H. DePuy, F. W. Breitbeil, and K. P. DeBruin, *J. Amer. Chem. Soc.*, **88**, 3347 (1966); (b) C. H. DePuy and F. N. Breitbeil, *ibid.*, **85**, 2176 (1963).

(3) P. S. Wharton and T. I. Bair, *J. Org. Chem.*, **31**, 2480 (1966).

(4) J. A. Landgrebe, *ibid.*, **30**, 2997 (1965).

(5) (a) J. Freeman, *ibid.*, **28**, 885 (1963); (b) *ibid.*, **29**, 1379 (1964).

(6) The Hammett relationship for acid-catalyzed hydrolysis of benzyl acetates in 60% acetone in water at 40° has a ρ value of -0.053.[7]

(7) E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, 1801 (1938).

solution of the appropriate differential equations leads to the following expression in which x is the fraction of reaction.

$$x = 1 + \frac{1}{k_1 + k_2 - k_3}\left[(k_3 - k_2)e^{-(k_1+k_2)t} - k_1 e^{-k_3 t}\right] \quad (1)$$

Values of k_1, k_2, and k_3 were chosen by a GE-625 computer so as to obtain the best possible fit of the equation to the actual plot of the raw data. The χ^2 function minimized by the computer was found to be rather sensitive to variations in k_2 and k_3 but insensitive to k_1; thus, values for k_2 and k_3 became constant after only 5–10 iterations while values for k_1 continued to fluctuate markedly even after 40 iterations. Computed values of k_2 and k_3 are listed in Table II.

TABLE II

COMPUTED RATE CONSTANTS FOR THE HYDROLYSES OF 1-ARYLCYCLOPROPYL ACETATES WITH 0.1 N HYDROCHLORIC ACID IN 50 WT % AQUEOUS DIOXANE

Substituent	No. of runs	Temp, °C	Second-order constants[a] $k_2 \times 10^4$	Second-order constants[a] $k_3 \times 10^4$	Average deviation (±) $k_2 \times 10^4$	Average deviation (±) $k_3 \times 10^4$	Rel rates (70°) k_2	Rel rates (70°) k_3
p-CH_3O (5c)	2	70	8.65	8.65	0.14	0.14	1.14	1.01
	2	55	4.60	4.48	0.19	0.32	...	...
p-CH_3 (5b)	2	70	7.90	7.90	0.12	0.12	1.04	1.01
	3	40	1.02	1.02	0.08	0.08	...	...
H (5a)	5	70	7.60	7.82	0.22	1.00	1.00	1.00
m-CH_3O (5d)	2	70	8.19	8.40	0.10	0.11	1.08	1.07
p-Cl (5g)	2	70	6.32	5.73	0.08	0.51	0.83	0.73
p-Br (5f)	5	70	7.43	7.92	0.33	0.62	0.98	1.01
m-Br (5h)	3	70	5.98	5.98	0.11	0.11	0.79	0.77
m-NO_2 (5e)	3	70	6.92	7.40	0.40	0.61	0.91	0.95

[a] Units of l. mol^{-1} sec^{-1}.

Although there is some scatter in a plot of log k_2 *vs.* Hammett σ for the data at 70°, the slope lies between the extreme limits of −0.06 and −0.24.

Activation parameters calculated for k_2 from the data in Tables I and II are listed in Table III.

TABLE III

ACTIVATION PARAMETERS FOR k_2[a]

Substituent	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
p-CH_3O (5c)	16.9	−23
p-CH_3 (5b)	13.9	−32
H (5a)	19.0	−18
m-CH_3O (5d)	20.0	−14
p-Cl (5g)	18.4	−19
p-Br (5f)	19.5	−16
m-Br (5h)	18.4	−19
m-NO_2 (5e)	19.7	−15

[a] Determined from data at 40 and 70° except for 5c for which data at 55 and 70° were used.

Products identified after partial hydrolysis of several 1-arylcyclopropyl acetates at two temperatures are listed in Table IV.

Discussion

The data of Table I clearly indicate that at 40° those 1-arylcyclopropyl acetates substituted with electron-withdrawing groups undergo hydrolysis in complete accord with the classical $A'2$ mechanism.[8] That electrophilic ring cleavage was unimportant under these circumstances was confirmed by the absence of propiophenone 7 among the products (Table IV).

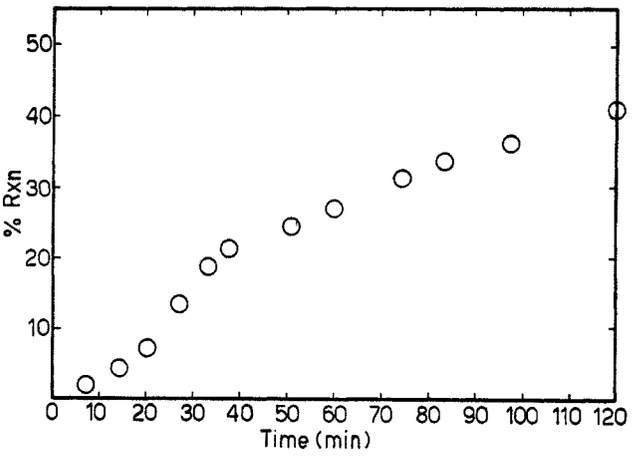


Figure 1.—Hydrolysis of 1-(*p*-tolyl)cyclopropyl acetate with 0.1 N hydrochloric acid in 50 wt % aqueous dioxane at 70°.

TABLE IV

PRODUCTS DETECTED AFTER ACID HYDROLYSIS OF 1-ARYLCYCLOPROPYL ACETATES IN 50 WT % AQUEOUS DIOXANE FOR 4.5 HALF-LIVES[a]

Substituent	Temp, °C	Nonlinear first-order plot	Cyclopropanol 6	Propiophenone 7
p-CH_3O (5c)	70	+	+	+
	40	+	+	+
H (5a)	70	+	+	+
	40	−	+	?
p-Cl (5g)	40	−	+	−
m-Br (5h)	70	+	+	+
m-NO_2 (5e)	40	−	+	−

[a] Residual starting material was detected in all experiments.

For acetates 5b and 5c in which an electron donor was present on the aromatic ring or for all esters at elevated temperatures, the kinetic behavior illustrated in Figure 1 was observed and could be analyzed by the scheme previously presented in which a dual path for the production of acetic acid was envoked. An important observation consistent with the propsed kinetic scheme was that only under circumstances which resulted in nonlinear first-order kinetics was the presence of ketone 7 noted among the products (Table IV).

Although the electrophilic opening of cyclopropanol 6 might conceivably account for the production of a portion of ketone 7,[9-11] this process does not affect the rate of production of acetic acid and is therefore not directly related to the observation of unusual kinetic behavior. The proposed path k_1,k_2 not only accounts for the observed rate data but demands the presence of ketone 7 as a product.

The nature of intermediate A must be deduced indirectly since it does not accumulate under the reaction conditions. Acid-catalyzed opening of the ring of

(8) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1963, p 319.

(9) Ring opening of 1-(*p*-tolyl)cyclopropanol with 5 N perchloric acid in 60:40 (v/v) dioxane–water at 50° occurs with a rate constant of 1.01×10^{-5} sec^{-1}.[10] Thus, it seems unlikely that under the conditions for the product study on 5b at 40°, more than a small fraction of the propiophenone could have been accounted for by ring opening of the alcohol.

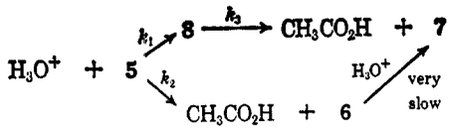
(10) R. A. Klein, Ph.D. Dissertation, Iowa State University, 1965.

(11) 1-(*p*-Chlorophenyl)cyclopropanol and 1-(*p*-methoxyphenyl)cyclopropanol prepared from the corresponding acetates by reduction with lithium aluminum hydride, when subjected to hydrolysis under the conditions used in the product study, produced only a trace of the corresponding propiophenones.

acetate **5** with subsequent or simultaneous attack by water would result in the formation of hydroxyacetate **8**, or *via* an elimination reaction, enol acetate **9**. A

8 **9**

model enol acetate, 1-*p*-anisyl-1-acetoxypropene, was prepared from the corresponding ketone and found to undergo acid-catalyzed hydrolysis (55°) in aqueous dioxane with a rate constant one-fourth that of the k_3 hydrolysis constant of 1-(*p*-anisyl)cyclopropyl acetate under the same conditios. This result implies that intermediate A is probably the labile hydroxyacetate **8**.[12,13] The over-all kinetic scheme is summarized below.



It should be noted that the small relative rate range for the k_2 values is associated with a substantial compensation of activation enthalphy and entropy values (Table III).[14]

Experimental Section[15]

1-Arylcyclopropyl acetates (**5**) were prepared from the corresponding acetophenone *via* the Mannich reaction,[16] followed by neutralization of the resulting β-dimethylaminopropiophenone hydrochloride with 1 *N* sodium hydroxide, treatment of the crude amine with 90–100% hydrazine hydrate,[17] oxidation of the pyrazoline with lead tetraacetate,[5,18] and thermal decomposition to the cyclopropane.[5] The crude intermediate pyrazoline was isolated by crystallization and rapid filtration under nitrogen. Those 1-arylcyclopropyl acetates obtained as solids were crystallized from *n*-pentane.

It was noted that 3-*p*-anisyl-Δ^2-pyrazoline was quite air sensitive. Exposure to air resulted in a vigorous exothermic reaction.

If precautions were not taken to neutralize the hydrochloride of β-dimethylamino-*m*-nitropropiophenone with a layer of ether present, considerable polymeric material formed. The ether solution of free amine was used directly in the next step. Total polymerization could not be avoided during the neutralization of the hydrochloride of β-dimethylamino-*p*-nitropropiophenone consistent with observation by Knott[19] and Nobles and Burckhalter.[20]

Physical constants and analytical data for the cyclopropyl acetates are presented in Table V. Spectral data are summarized in Table VI.

TABLE V

PHYSICAL CONSTANTS AND ANALYSES OF 1-ARYLCYCLOPROPYL ACETATES

		Calcd, %			Found, %		
Substituent	Mp, °C	C	H	N	C	H	N
H (**5a**)	Oil[a]	...	...	...	...	...	...
p-CH_3 (**5b**)	34–35.5	75.76	7.42	...	75.98	7.48	...
p-CH_3O (**5c**)	36.8–37.7	69.88	6.84	...	70.23	7.06	...
m-CH_3O (**5d**)	Oil[b]	69.88	6.84	...	70.88	7.00	...
m-NO_2 (**5e**)	84.3–86.3	59.72	5.01	6.33	59.66	5.05	6.38
p-Br (**5f**)	57.5–59.5	51.79	4.35	...	52.09	4.51	...
p-Cl (**5g**)	67.0–69.4	62.72	5.26	...	63.03	5.30	...
m-Br (**5h**)	Oil[c]	51.79	4.35	...	51.59	4.34	...

[a] Bp 63–70° (0.40–0.45 mm); lit.[5] bp 68–70° (0.4 mm). [b] Bp 98° (0.40 mm) and 109° (0.75 mm). [c] Bp 100° (0.68 mm).

TABLE VI

SPECTRAL DATA ON 1-ARYLCYCLOPROPYL ACETATES[a]

Substituent	
H (**5a**)	Nmr: 2.57–2.90, m, 5 H; 8.12, s, 1 H; 8.75–8.92, m, 4 H Infrared: 3033, 1748, 1369, 1243, 1204, 1026, 990
p-CH_3 (**5b**)	Nmr: 2.67–3.11, m, 4 H; 7.73, s, 3 H; 8.12, s, 3 H; 8.80–9.00, m, 4 H Infrared: 3029, 1747, 1370, 1349, 1240–1180, 1100, 988
p-CH_3O (**5c**)	Nmr: 2.52–3.38, m, 4 H; 6.26, s, 3 H; 8.11, s, 3 H; 8.83–9.03, m, 4 H Infrared: 3010, 2950, 2840, 1750, 1613, 1517, 1368, 1349, 1300, 1246, 1204, 1175, 1030, 986
m-CH_3O (**5d**)	Nmr: 2.71–3.44, m, 4 H; 6.33, s, 3 H; 8.12, s, 3 H; 8.79–8.95, m, 4 H Infrared: 3006, 2941, 2837, 1755, 1605, 1587, 1457, 1370, 1234, 1205, 1047, 1026
m-NO_2 (**5e**)	Nmr: 1.77–2.68, m, 4 H; 8.00, s, 3 H, 8.60–8.80, m, 4 H Infrared: 3090, 1759, 1532, 1354, 1369, 1242, 1207
p-(Br (**5f**)	Nmr: 2.50–2.92, m, 4 H; 8.08, s, 3 H, 8.72–8.90, m, 4 H Infrared: 3015, 1751, 1495, 1368, 1240, 1204, 1097, 1026, 1010
p-Cl (**5g**)	Nmr: 2.75, s, 4 H; 8.06, s, 3 H, 8.75–8.95, m, 4 H Infrared: 3017, 1753, 1499, 1370, 1241, 1203, 1100, 1026, 1015, 997
m-Br (**5h**)	Nmr: 2.41–2.97, m, 4 H; 8.10, s, 3 H; 8.68–8.90, m, 4 H Infrared: 3024, 1741, 1566, 1480, 1451, 1411, 1366, 1338, 1240–1190, 1070, 1024, 990

[a] Nmr data indicate the chemical shift (τ scale), multiplicity, and integrated area. Infrared absorptions are expressed in cm^{-1}.

1-(*p*-Anisyl)cyclopropanol was prepared from 1-*p*-anisylcyclopropyl acetates by treatment of the acetate in ether with excess lithium aluminum hydride followed by an aqueous work-up. The nmr spectrum of the alcohol, mp 62–63°, showed a complex multiplet at 3.07 (4 H), a singlet at 6.28 (3 H), a broad singlet at 6.68 (1 H), and a complex multiplet at 9.06 (4 H), Infrared peaks occurred at 3600, 3500–3150, 3002, 2952, 2833, 1614, 1516, 1247, 1220, 1178, 1038, 1011, and 827–734 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37; O, 19.48. Found: C, 72.92; H, 7.41; O, 19.68.

1-(*p*-Chlorophenyl)cyclopropanol, mp 68–69°, was prepared from the acetate in the manner described above. The nmr spectrum showed a complex multiplet at 2.83 (4 H), a broad singlet at 6.30 (1 H), and a complex multiplet at 9.00 (4 H). Significant peaks in the infrared spectrum occurred at 3600,

(12) Newman and Smith,[13] having formed the carbonyl addition product of *n*-butylmagnesium bromide and acetic anhydride at −70°, were unable to isolate any hydroxy ester even though the salt was carefully hydrolyzed at −10°.

(13) M. S. Newman and A. S. Smith, *J. Org. Chem.*, **13**, 592 (1948).

(14) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, p 315.

(15) Melting points, taken on a Thomas–Hoover capillary melting point apparatus, are corrected. Boiling points are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn., or on an F & M Model 185 C,H,N-Analyzer. All infrared spectra were obtained in *ca.* 10% carbon tetrachloride solution in a 0.05-mm sodium chloride cell on a Beckman IR-8 double-beam recording spectrometer with a 6101-cm^{-1} peak from polystyrene *vs.* air as a calibration point. Nuclear magnetic resonance spectra were obtained on a Varian A-60 or A-60A as a solution in carbon tetrachloride containing tetramethylsilane. Chemical shifts are designated by the τ scale.

(16) C. E. Maxwell, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 305.

(17) S. G. Beech, J. H. Turnbull, and W. Wilson, *J. Chem. Soc.*, 4686 (1952).

(18) The use of temperatures in excess of 25° or the presence of acetic anhydride in the lead tetraacetate greatly reduced the yield of **4**.

(19) E. D. Knott, *J. Chem. Soc.*, 1190 (1947).

(20) L. N. Nobles and J H. Burckhalter, *J. Amer. Pharm. Soc., Sci. Educ.*, **47**, 77 (1958).

3530–3130, 3091, 3010, 1498, 1222, 1100, 1013, 866, and 820–734 cm^{-1}.

Anal. Calcd for C_6H_9ClO: C, 64.11; H, 5.38. Found: C, 63.94; H, 5.33.

1-*p*-Anisyl-1-acetoxypropene was prepared by passing ketene through molten *p*-methoxypropiophenone (100 g, 0.61 mol, Aldrich) for 15.5 hr with 10 drops of concentrated H_2SO_4 as catalyst. Two washings with aqueous base and several with water followed by an ether work-up gave a viscous brown liquid which was distilled on a 14-in. wire, spiral column to give a high-boiling fraction, bp 115–150° (0.4 mm), which was recrystallized twice from *n*-pentane and twice from ethanol. The product, mp 49–50°, gave an nmr spectrum which showed a complex multiplet at 2.98 (4 H), a quartet at 4.36 (1 H, J = 7 cps), a singlet at 6.28 (3 H), a singlet at 7.73 (3 H), and a doublet at 8.36 (3 N, J = 7 cps). Significant peaks in the infrared spectrum were found at 3000, 2936, 2838, 1760, 1611, 1509, 1465, 1441, 1368, 1313 (sh), 1307, 1282, 1247, 1206, 1175, 1111, 1040 (sh), 1027, 834, and 814 cm^{-1}.

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; O, 23.27. Found: C, 69.61; H, 6.78; O, 23.50.

Acid hydrolysis (0.1 N HCl) at 55° in 50 wt % aqueous dioxane resulted in a pseudo-first-order constant of 1.086×10^{-4} sec^{-1}.

1-*p*-Anisyl-1-acetoxypropane.—1-*p*-Anisyl-1-propanol (21 g, 0.126 mol), prepared by the addition of *p*-methoxyphenylmagnesium bromide to propionaldehyde, and dimethylaniline (45.9 g, 0.378 mol, Eastman) in ether (150 ml) were stirred at 5° while acetyl chloride (29.7 g, 0.378 mol) was added dropwise. The solution was maintained at reflux for 62 hr and worked up in the usual manner with ether and water to give the desired product, bp 94–96° (0.31 mm). The nmr spectrum showed a complex multiplet at 2.74–3.31 (4 H), a triplet at 4.43 (1 H, J = 7 cps), a singlet at 6.32 (3 H), a singlet at 8.07 (3 H), a multiplet at 8.05–8.43 (2 H), and a triplet at 9.17 (3 H, J = 7 cps).

Acid hydrolysis (0.1 N HCl) at 40° in 50 wt % aqueous dioxane resulted in a pseudo-first-order constant of 1.025×10^{-3} sec^{-1}.

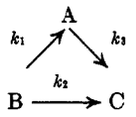
Kinetic Procedure. At 40°.—Approximately 0.001 or 0.002 mol of ester weighed to the nearest 0.0001 g was placed into a clean, dry 25-ml volumetric flask to which an acid solution (25 ml), *vide infra*, was introduced with a volumetric pipet, and the total volume was estimated to the nearest 0.01 ml *via* calibration marks on the neck of the volumetric flask. Corrected acid and ester concentrations were calculated at 40°, and the stoppered flask was immersed in a constant temperature bath. Aliquots (*ca.* 1 ml) of known volume to 0.0001 ml were withdrawn at intervals of 1 hr, diluted with 25.00 ml of distilled water and titrated with a standardized solution of sodium methoxide in methanol to a phenophthalein end point.

At 55 and 70°.—When the ester and acid had been combined, *ca.* 1.4-ml portions were sealed in 100-mm test tubes packed in ice and the sealed tubes were then immersed in a constant temperature bath. At the appropriate time interval a tube was removed from the bath, cooled for several minutes in water, and broken. An accurate aliquot was treated as previously indicated. Intervals of 7.5–30 min were used.

The acid solution was prepared by the addition of the appropriate volume of dry hydrogen chloride to equal weights of *p*-dioxane (purified by passage through Woelm, acid-washed alumina (I) and distillation from sodium) and water so as to give an *ca.* 0.1 M acid solution. Standardization was accomplished with a solution of sodium methoxide (Matheson Coleman and Bell) in anhydrous methanol. The latter was standardized with potassium hydrogen phthalate.

All titrations were performed with a 5-ml self-filling buret (readable to 0.001 ml) with a stoppered reservoir. Three drops of a solution of 1 g of phenolphthalein in 50 ml of ethanol and 50 ml of water were used. The polyurethane insulated constant temperature bath was maintained at ±0.01° with a solid-state electronic thermostating circuit.

Calculations.—The derivation of eq 1 is given below. If we let cyclopropyl ester = B, intermediate ester = A, and acetic acid = C, the differential equations which describe the indicated kinetic system are as follows.



$$\frac{dB}{dt} = -(k_1 + k_2)B \quad (2)$$

$$\frac{dA}{dt} = k_1B - k_3A \quad (3)$$

$$\frac{dC}{dt} = k_2B + k_3A \quad (4)$$

Integration of eq 2 and introduction of the initial conditions that $B = B_0$ at $t = 0$ gives

$$B = B_0e^{-(k_1+k_2)t}$$

Substitution of this value for B into eq 3, application of the integrating factor e^{k_3t}, and introduction of the condition that $A = 0$ at $t = 0$ leads to the following solution to the linear differential equation.

$$A = [B_0k_1/(k_3 - k_1 - k_2)]\,[e^{-(k_1+k_2)t} - e^{-k_3t}]$$

Substitution of the values for A and B into eq 4, separation of variables, integration, and introduction of the condition that $C = 0$ at $t = 0$ gives

$$C = B_0 + [B_0/(k_1 + k_2 - k_3)]\,[(k_3 - k_2)\,e^{-(k_1+k_2)t} - k_1e^{-k_3t}]$$

The fraction of reaction, $X = C/B_0$ is then equal to eq 1.

Typical pseudo-first-order rate data are given in Table VII for the hydrolysis of 1-(*m*-bromophenyl)cyclopropyl acetate in 50 wt % aqueous dioxane at 40.00 ± 0.02° in the presence of 0.1119 M hydrochloric acid. The initial ester concentration was 0.05302 M. All pseudo-first-order runs were followed to *ca.* 25% reaction except for 1-(*m*-nitrophenyl)cyclopropyl acetate which was only followed to *ca.* 15% reaction.

TABLE VII

Time, sec	Titer, ml[a]	Ln [a/(a − x)]	Time, sec	Titer, ml[a]	Ln [a/(a − x)]
3,600	3.220	0.0200	25,200	3.365	0.1231
7,440	3.240	0.0336	28,931	3.380	0.1343
11,140	3.268	0.0530	32,500	3.404	0.1527
14,400	3.292	0.0699	39,600	3.442	0.1824
18,000	3.314	0.0856	43,290	3.461	0.1976
21,680	3.332	0.0987	46,860	3.488	0.2196
			64,800	3.580	0.2985

[a] 0.03399 N sodium methoxide in methanol; $k = 4.016 \times 10^{-5}$ sec^{-1}.

Typical non-first-order data are given in Table VIII for the hydrolysis of 1-(*p*-tolyl)cyclopropyl acetate in 50 wt % aqueous dioxane at 40.00 ± 0.02° in the presence of 0.12026 M hydrochloric acid. The initial ester concentration was 0.06646 M.

TABLE VIII

Time, sec	Titer, ml[a]	% hydrolyzed	Time, sec	Titer, ml[a]	% hydrolyzed
3,624	3.437	0.79	32,370	4.062	33.89
7,326	3.530	5.71	39,630	4.122	37.01
10,940	3.700	14.70	43,200	4.140	39.67
14,420	3.844	22.31	46,950	4.178	39.97
18,096	3.920	26.33	50,400	4.203	41.29
21,560	3.958	28.34	54,110	4.244	43.46
25,215	3.995	30.30	57,600	4.266	44.63
28,770	4.030	32.15			

[a] 0.03405 N sodium methoxide in methanol.

Registry No.—**5a,** 16031-49-5; **5b,** 16031-50-8; **5c,** 16031-51-9; **5d,** 16109-33-4; **5e,** 15973-63-4; **5f,** 16031-52-0; **5g,** 16031-53-1; **5h,** 15973-64-5; 1-(*p*-anisyl)cyclopropanol, 15973-65-6; 1-(*p*-chlorophenyl)cyclopropanol, 16031-54-2; 1-*p*-anisyl-1-acetoxypropene, 16031-56-4; 1-*p*-anisyl-1-acetoxypropane, 16031-55-3.