due to the vinyl protons of the triene **14** were roughly proportional to the yield as determined by uv.

Table II summarizes the results of extending the foregoing procedure to other active methylene compounds. All reactions were exothermic (6–9° temperature increase) and proceeded to neutrality in less than 5 min. In some cases (especially the enolizable diketones) extraneous stable uv absorption, presumably from starting materials or enol ethers, interfered with the satisfactory estimation of triene. In these instances, when no nmr evidence for triene was detectable, yields were considered to be less than 5%. In two cases (**22** and **25**) triene nmr absorption could be detected only by integration in the expected range. Yields of 5–10% therefore were assigned to this borderline area. All other yields listed in Table II are based on the uv data, assuming ϵ = 24,000 for all trienes involved in this work.

Tri-*p*-tolylmethyl Fluoroborate. To a stirred solution of 15.12 g (0.05 mol) of tri-*p*-tolylmethanol in 50 ml of acetic anhydride, cooled to 3°, was added dropwise 8 ml (0.068 mol) of 48% fluoroboric acid. The temperature was not allowed to rise above 10°. After addition was complete, 120 ml of cold, dry ether was added to the dark green solution. Solvent was drawn off from the resulting precipitate through a sintered-glass filter tube, and fresh cold ether (50 ml) was added and again drawn off. After two more such washings with ether, the wet residue was partially dried with a stream of dry nitrogen and finally by evacuation (1 mm) for several hours. The yellow-brown product weighed 16.7 g and was used without further purification.

Reaction of Tri-*p*-tolylmethyl Fluoroborate with Sodiodipivaloylmethane. 4-(Tri-*p*-tolylmethyl)-2,2,6,6-tetramethyl-3,5-heptanedione (5). To a stirred solution of 0.00625 mole of sodiodipivaloylmethane (procedure A) in 20 ml of dimethylformamide (under nitrogen) was added 2.60 g (0.007 mol) of the crude tri-*p*-tolylmethyl fluoroborate. The temperature rose from 24 to 30° and the reaction mixture became neutral. Suitable dilution of a 2-ml sample with methanol followed by scanning of the uv spectrum in the 250–400-mμ region showed that less than a 3% yield of a cross-conjugated triene could have formed (assuming uv$_{\max}$ 305–315 mμ with ϵ 24,000). The reaction mixture was poured into water and extracted with ether. Washing with water followed by drying ($MgSO_4$) and removal of the ether by distillation gave a yellow glassy product (2.57 g) which was taken up in pentane (20 ml) and cooled at −25° for several days. Colorless prisms (0.48 g, 16%, mp 154–156°) that formed were removed by filtration and recrystallized from isopropyl alcohol (10 ml) to give pure **5**: mp 156–157°; ir ($CHCl_3$) 1675 (C=O) and 1712 cm^{-1} (C=O); nmr ($CDCl_3$), δ 7.25 (d, 6, J = 8 Hz, ArH), 7.05 (d, 6, J = 8 Hz, ArH), 6.25 (s, 1, COCHCO), 2.30 (s, 9, ArCH_3), and 1.07 ppm (s, 18, CCH_3).

Anal. Calcd for $C_{33}H_{40}O_2$: C, 84.57; H, 8.60. Found: C, 84.51; H, 8.57.

Application of the foregoing procedure to the dilactone **35** (in place of **26**) resulted in an exothermic (6°) neutralization reaction. However, uv analysis indicated less than 2% triene formation, and no other product could be isolated.

Acknowledgments. We are indebted to Dr. Peter Beak, University of Illinois, for the mass spectra and for helpful suggestions, to Mr. Russel Kriese and Mrs. Ruth Stanaszak for the nmr spectra, to Mr. W. H. Washburn for the infrared spectra, to Mr. Orville Kolsto and Mr. Victor Rauschel for the microanalyses, and to Miss Evelyn Schuber and Mr. Robert Hallas for the preparation of several intermediates.

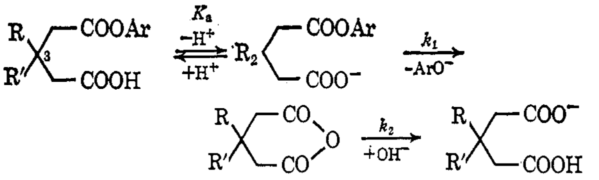
The *gem* Effect. IV.[1] Activation Parameters Accompanying the Increased Steric Requirements of 3,3′ Substituents in the Solvolysis of Mono-*p*-bromophenyl Glutarates

Thomas C. Bruice and William C. Bradbury[2]

Contribution from the Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106. *Received January 29, 1968*

Abstract: The kinetics for the solvolyses of 11 *p*-bromophenyl 3-R- and 3,3′-R,R′-glutarate monoesters with R and R′ groups of differing steric requirements have been studied at several temperatures. The values of $\Delta H^{\ddagger}$ have been found, within experimental error, to be independent of the nature of R and R′ so that steric acceleration is reflected in $T\Delta S^{\ddagger}$. The values of $T\Delta S^{\ddagger}$ are in accord with intramolecular nucleophilic displacement of *p*-bromophenoxide by the carboxyl anion. An explanation is offered for the observed change of mechanism from intramolecular nucleophilic attack when a cyclic anhydride can be formed to intramolecular general base assisted attack of water when the cyclic anhydride cannot be formed.

In previous studies[1] we concluded that substituents in the 3 and 3,3′ positions of mono-*p*-bromophenyl glutarate esters increase the rate of hydrolysis by decreasing the population of extended conformations and thus bring the carboxylate and carbo-*p*-bromophenoxy moieties closer together. No special *gem* effect was noted and the logs of the rate constants for 3-R,3′-R-disubstituted esters were generally calculable from the sum of the log k_1 values for the 3-R- and 3′-R′-monosubstituted esters.



(1)

In the case of phenyl substituents, two different steric parameters were required depending upon whether the second substituent was large or small. This variable steric requirement of the phenyl group has found recent verification in another system.[3] In contrast to the kinetic data, the values of pK_a' for the 3-R- and 3,3′-

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[1] For previous papers in this series see: (a) T. C. Bruice and W. C. Bradbury, *J. Amer. Chem. Soc.*, 87, 4838 (1965); (b) *ibid.*, 87, 4846 (1965); (c) *ibid.*, 87, 4851 (1965).

[2] Postdoctoral Fellow, Department of Chemistry, University of California at Santa Barbara, Santa Barbara, Calif.

[3] S. Sicsic and Z. Welvart, *Chem. Commun.*, 499 (1966).

Table I. Temperature and pH Dependence of the Observed Pseudo-First-Order Rate Constants (min^{-1}) for Monoester Hydrolysis

T = 39.7°		T = 30.0°		T = 19.9°	
pH	10^2k_{obsd}	pH	10^2k_{obsd}	pH	10^2k_{obsd}
		R = R′ = H			
5.90	0.427	5.67	0.119		
6.10_5	0.544	5.98	0.168		
6.40	0.680	6.17	0.214		
6.53	0.761	6.46	0.261		
6.66_5	0.846	6.50	0.264		
		6.58	0.290		
		6.66	0.274		
		6.74	0.283		
		6.78	0.302		
		R = H, R′ = Me			
5.93	1.73	5.70	0.501	5.94	0.199
6.14	2.42	5.80	0.606	6.30_5	0.312
6.20	2.76	6.01	0.782	6.52	0.361
6.40	2.84	6.24	1.01_5	6.57_5	0.381
6.41	3.14	6.50	1.18		
6.44	2.92	6.91	1.43		
6.50	3.26				
		R = H, R′ = *n*-Pr			
5.63	2.26	5.66	1.07	6.02	0.613
5.97	4.37	5.84	1.50	6.45_5	0.990
6.21	5.85	5.99	1.85	6.59	1.13
6.33_5	6.84	6.09	1.91	6.82_5	1.28_5
6.47_5	7.76	6.34	2.69		
		6.45	2.95		
		6.68	3.37		
		6.88	3.68		
		6.88	3.79		
		R = H, R′ = *i*-Pr			
5.58_5	4.77	5.66	2.18	6.12	1.39
5.91	8.40	5.97	3.71	6.31	1.64
6.18_5	12.4	6.20	4.99	6.32	1.67
6.27	13.6	6.71	8.00	6.68	2.28
6.40	16.2	6.85	9.20	6.87_5	2.72
		R = Me, R′ = Me			
5.60	3.02	5.98	2.36	5.48	0.312
5.95	5.65	6.21	3.33	5.75_5	0.542
6.18_5	7.72	6.51	4.72	6.00	0.754
6.39	10.2_8	6.77	5.67	6.29	1.10
6.78	13.7	6.97	6.33	6.30_5	1.06
				6.70	1.64
				6.72	1.57
				6.99	2.09
		R = Me, R′ = Phenyl			
5.53	4.32	5.47	1.70	5.79	0.766
5.86_5	8.16	5.50	1.74	5.98	1.08
6.33_5	15.0	5.68	2.55	6.33	1.72
		5.69	2.52	6.62	2.37
		5.99	4.05	6.86	2.99
		5.99	4.16		
		6.23	5.60	T = 10.0°	
		6.39	6.83	6.68_5	0.796
		6.47	6.86	6.72_5	0.805
		6.73	8.41	6.92	0.867

T = 30.0°		T = 19.9°		T = 10.0°	
pH	10^2k_{obsd}	pH	$10^2k^2_{\text{obsd}}$	pH	$10k_{\text{obsd}}$
		R = Me, R′ = *i*-Pr			
5.28	3.84	5.89	3.45	6.15_5	1.78
5.59	7.46	6.28	7.02	6.37_5	2.28
5.80	11.0	6.60	12.8	6.49_5	2.64
6.06	17.6	6.62	11.5	6.66_5	3.02
6.41	31.5	6.83	15.9	6.92	4.07
6.63	38.3	6.97	18.6		
6.86	52.9				
		R = R′ = Et			
5.51	4.48	5.80	1.87	5.83_5	0.556
5.75	6.77	5.96	2.54	6.33	1.46
6.01	11.5	6.31_5	5.30	6.39	1.76
6.25	16.9	6.60	7.85	6.68	2.60
6.56	27.2	6.82_5	10.5	6.89	3.50
6.76	35.2			6.92_5	3.77
6.92	40.7				
		R = Et, R′ = Phenyl			
5.46	5.75	5.70_5	2.29	5.77	0.79
5.72	10.2_6	6.30	6.51	6.12	1.56
5.98	15.7	6.31	7.31	6.46	2.60
6.22	24.8	6.61	12.2	6.67	3.36
6.23	23.0	6.66	10.8	6.92	4.23
6.75	45.6	6.70	12.2		
6.96	54.4	6.86	14.6		
		R = R′ = *n*-Pr			
5.26	1.76	5.39	0.672	6.07	0.797
5.48	3.08	5.76	1.50	6.39	1.42
5.97	8.50	5.98	2.24	6.62	1.96
6.19	11.6	5.99	2.35	6.63	2.12
6.24	13.9	6.15	3.28	6.98	3.14
6.39	17.7	6.26	4.07		
6.47	20.3	6.46	5.31		
6.60	26.6	6.46	5.85		
6.72	30.4	6.69	8.30		
6.74	27.6				
6.77	30.5				
6.82	32.4				
		R = R′ = Phenyl			
5.39	6.14	5.77_5	3.14	5.85	1.00
5.45	7.02	6.04_5	5.25	6.07	1.51
5.74	12.2_7	6.25_5	7.78	6.34_5	2.39
6.00	20.0	6.58	11.8	6.70_5	3.85
6.21	28.3	6.59	11.6	6.92_5	4.74
6.46	43.0	6.77	14.0		
6.72	53.0				
6.91	66.7				

R,R′-substituted glutaric acids exhibited a marked *gem* effect. Thus, monosubstitution does not alter the values of pK_a' but disubstitution has a marked effect on the pK_a' values. A rationale for this observation was offered based on the Kirkwood–Westheimer equation,[4] and anticipated conformational changes.

The purpose of the present investigation has been to determine how $\Delta H^{\ddagger}$ and $T\Delta S^{\ddagger}$ for phenol release are changed when $\Delta F^{\ddagger}$ is decreased by increasing the steric requirements of substituents in the 3 and 3,3′ positions of *p*-bromophenyl hydrogen glutarate.

Experimental Section

Compounds, apparatus, and kinetic procedures employed in this study are identical with those provided in parts II and III.[1c,d] The determined values of the pseudo-first-order rate constants (k_{obsd}) for *p*-bromophenol and *p*-bromophenolate ion release from the *p*-bromophenyl glutarate esters as a function of pH and temperature are recorded in Table I.

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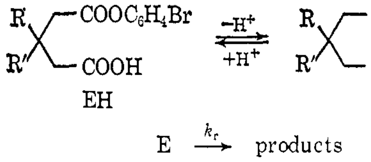
(4) J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506, 513 (1938).

Results

The mono-*p*-bromophenyl glutarate esters studied herein have previously been shown to hydrolyze *via* eq 2. In the pH range employed, alkaline hydrolysis



(2)

of the esters is not important so that the appearance of *p*-bromophenol and *p*-bromophenolate ion can be expressed kinetically as in eq 3, where E_T is the total

$$\frac{dP}{dt} = k_r\left[\frac{K_{app}}{K_{app} + a_H}\right]E_T \tag{3}$$

ester concentration (*i.e.*, $E_T = EH + E$), K_{app} is the kinetically apparent acid dissociation constant for the carboxyl group, and a_H is the hydrogen ion activity as determined with the glass electrode. At constant pH, the pseudo-first-order rate constant (k_{obsd}) for appearance of phenol and phenolate is provided by eq 4, which on rearrangement provides eq 5. From eq 5 it is seen that plots of k_{obsd} *vs.* $k_{obsd}a_H$ should be linear with slopes equal to $-1/K_{app}$ and intercepts equal to k_r. The hydrolysis of the esters of this investigation followed eq 5 at the various temperatures employed. Sample plots for three esters have been provided previously in part II[1b] of this study. In Table I are provided the values of k_{obsd}, the temperatures employed, and the pH values employed for the hydrolysis of each ester. In Table II are recorded the values of pK_{app}, log k_r (k_r in min^{-1}), and the correlation coefficients derived from the data of Table I when plotted according to eq 5.

$$k_{obsd} = k_r\left[\frac{K_{app}}{K_{app} + a_H}\right] \tag{4}$$

$$k_{obsd} = k_r - \left[\frac{k_{obsd}a_H}{K_{app}}\right] \tag{5}$$

Inspection of the values of log k_r for R, R′ = Et, Et; Me, *i*-Pr; *n*-Pr, *n*-Pr; Ph, Et; and Ph, Ph at each temperature reveals that they differ by an average of 2.8 (10), 2.5 (19.9), and 1.96% (30°). Thus, for these disubstituted monoesters the same value of $\Delta H^{\ddagger}$ (19.4 ± 0.3 kcal mol^{-1}) pertains within experimental error. Because the values of $\Delta H^{\ddagger}$ and $\Delta F^{\ddagger}$ (*i.e.*, log k_r) are so alike for these five esters, any calculated variation in $T\Delta S^{\ddagger}$ would be meaningless ($T\Delta S^{\ddagger}$ at 25° = −0.6 ± 0.7).

In Table III are presented the values of $\Delta H^{\ddagger}$ and $T\Delta S^{\ddagger}$ calculated from the data of Table II. For R = R′ = H the values of $\Delta H^{\ddagger}$ and $T\Delta S^{\ddagger}$ have been reported by Gaetjens and Morawetz[5] to be 20.2 and −3.1 kcal mol^{-1}, respectively.

Table II. Derived Values of k_r (min^{-1}) and pK_{app} for the Solvolysis of Mono-*p*-bromophenyl Esters of 3- and 3,3′-R,R′-Glutaric Acids

	R	R′	*T*, °C	pK_{app}	log k_r + 3	r^a
1.	H	H	39.7	6.01 ± 0.12	1.01	0.989
			30.0	5.95 ± 0.02	0.530	0.989
2.	H	Me	39.7	6.05 ± 0.10	1.635	0.840
			30.0	6.04 ± 0.02	1.21	1.00
			19.9	6.14 ± 0.03	0.716	0.998
3.	H	*n*-Pr	39.7	6.29 ± 0.01	2.11	0.990
			30.0	6.14 ± 0.03	1.64	0.990
			19.9	6.24 ± 0.02	1.21	1.00
4.	H	*i*-Pr	39.7	6.27 ± 0.02	2.44	0.990
			30.0	6.29 ± 0.03	2.05	1.00
			19.9	6.28 ± 0.05	1.515	0.975
5.	Me	Me	39.7	6.30 ± 0.02	2.265	1.00
			30.0	6.34 ± 0.01	1.89	1.00
			19.9	6.28 ± 0.04	1.35	0.995
6.	Me	Ph	39.7	6.26 ± 0.03	2.44	0.990
			30.0	6.21 ± 0.02	2.04	0.990
			19.9	6.41 ± 0.03	1.59	0.990
			10.0	6.10	0.998	
7.	Me	*i*-Pr	30.0	6.55 ± 0.03	2.87	0.990
			19.9	6.78 ± 0.05	2.48	0.970
			10.0	6.45 ± 0.07	1.71	0.960
8.	Et	Et	30.0	6.63 ± 0.03	2.78	0.990
			19.9	6.78 ± 0.04	2.30	0.990
			10.0	6.91 ± 0.04	1.86	0.980
9.	Et	Ph	30.0	6.53 ± 0.03	2.86	0.990
			19.9	6.69 ± 0.06	2.39	0.960
			10.0	6.61 ± 0.01	1.80	1.00
10.	*n*-Pr	*n*-Pr	30.0	6.77 ± 0.04	2.78	0.970
			19.9	6.83 ± 0.06	2.28	0.925
			10.0	6.90 ± 0.05	1.77	0.980
11.	Ph	Ph	30.0	6.54 ± 0.02	2.96	0.990
			19.9	6.56 ± 0.03	2.36	0.995
			10.0	6.64 ± 0.01	1.86	1.00

[a] Correlation coefficient.

Table III. Activation Parameters for Carboxyl Group Catalyzed Hydrolysis of 3-Mono- and 3,3′-Disubstituted *p*-Bromophenyl Hydrogen Glutarates[a]

R	R′	kcal mol^{-1} $\Delta H^{\ddagger}$	kcal mol^{-1} $T\Delta S^{\ddagger}$
Et	Et	19.4 ± 0.3	−0.6 ± 0.7
Me	*i*-Pr		
n-Pr	*n*-Pr		
Ph	Et		
Ph	Ph		
Me	Me	18.7	−3.0
Ph	Me	18.8	−2.6
i-Pr	H	18.9	−2.6
n-Pr	H	18.4	−3.5
Me	H	18.8	−3.8
H	H	20.2	−3.1

[a] Values of E_a were determined from plots of log k_r *vs.* $1/T$; $\Delta H^{\ddagger} = E_a - RT$; $\Delta F^{\ddagger} = RT2.303 \log (Kt/k_rh)$; $-T\Delta S^{\ddagger} = \Delta F^{\ddagger} - \Delta H^{\ddagger}$. Concentrations in moles and time in seconds. $\Delta S^{\ddagger}$ calculated at 25°: A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1953, pp 95–101.

Discussion

The solvolysis of monophenyl esters of dicarboxylic acids has been shown to proceed through intermediate formation of anhydride (eq 1). Thus, for esters in which $k_1 \gg k_2$ the value of k_1 can be determined from the time course for liberation of phenol + phenoxide ion (spectrophotometrically) and the value of k_2 determined from the following rate of uptake of OH$^-$ (pH-Stat) or change of absorbance with time. By this means it has been established that the hydrolysis of the monoaryl esters, (a) mono-*p*-methoxyphenyl maleate, (b) mono-*p*-methoxyphenyl hydrogen 3,6-endoxo-Δ^4-tetrahydrophthalate,[6] and (c) monophenyl hydrogen

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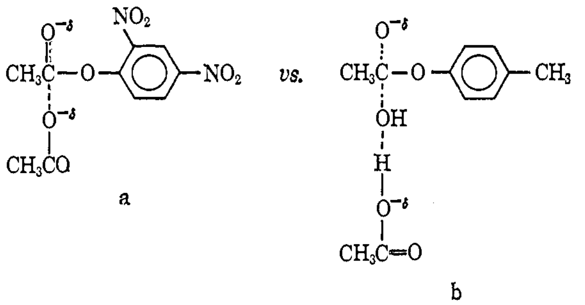
(5) E. Gaetjens and H. Morawetz, *J. Amer. Chem. Soc.*, **82**, 5328 (1960).

(6) T. C. Bruice and U. K. Pandit, *ibid.*, **82**, 5858 (1960).

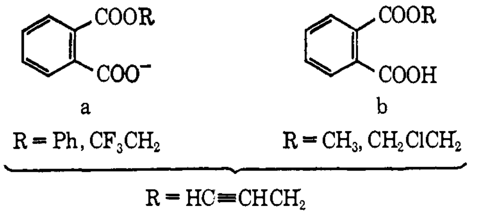
phthalate,[7] proceeds through formation of a cyclic anhydride *via* liberation of a phenoxide species (eq 1). Numerous other examples of neighboring carboxyl group participation in the hydrolysis of phenyl esters of dicarboxylic acids have been investigated in which $k_1 \ll k_2$, so that a cyclic anhydride could not be kinetically established as an intermediate.[1b,c,5-7] For these cases we can only assume the mechanism of eq 1 to pertain. This assumption would appear eminently reasonable on the basis that the kinetic data fit linear free energy plots[1] and provide no evidence for a change in mechanism.

Oakenfull, Riley, and Gold[8] have shown that the acetate ion catalyzed hydrolysis of phenyl esters is nucleophilic (6a) if the departing phenolate ion is of comparable basicity to the attacking acetate ion (*e.g.*, 2,4- and 2,6-dinitrophenyl acetate), but of a general base nature (6b) if the phenolate departing group is strongly basic (phenyl acetate, *p*-methylphenyl acetate).



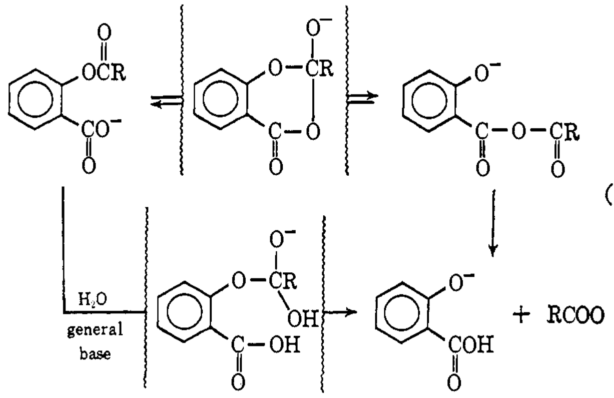
(6)

For general base catalyzed hydrolysis of phenyl acetate and *p*-nitrophenyl acetate by acetate anion (6b),[9,10] the values of $\Delta H^{\neq}$ and $T\Delta S^{\neq}$ (25°) were determined to be 16.6, 15.7, −9.3, and −8.5 kcal mol^{-1}, respectively.[8] A comparison of these values to those for intramolecular carboxyl group catalysis of the hydrolysis of the corresponding monoglutarate esters (for *p*-nitrophenyl ester $\Delta H^{\neq} = 19.1$ and $T\Delta S^{\neq} = -1.8$ kcal mol^{-1}) led to the conclusion by Bruice and Benkovic[11] that a change of mechanism from general base to nucleophilic catalysis occurred on conversion of bimolecular to intramolecular catalysis. This conclusion is supported by the change of the Hammett ρ value from +1.1 to +2.5 in converting the bimolecular carboxyl group catalysis to an intramolecular reaction. Comparison of the role of the carboxyl group in the intramolecular hydrolysis of monophenyl esters of dicarboxylic acids to that of the acetate carboxyl groups in the intermolecular catalysis of phenyl acetate hydrolysis establishes that the carboxyl group in the former acts as a much stronger nucleophile (*i.e.*, is capable of directly displacing leaving groups of much greater basicity).[1b,c,6,7] In addition to direct nucleophilic displacement of leaving groups and general base assistance to the departure of leaving groups by the carboxyl anion, general acid catalysis is possible. It has been established that the hydrolysis of monohydrogen phthalate esters changes from dependence on the mole fraction of base species (7a) to dependence on the mole fraction of ester with undissociated carboxyl group (7b) when the leaving groups become very strong bases.



(7)

Recently, Fersht and Kirby[9] have presented rather compelling evidence that the classical case of acetyl salicylate hydrolysis does not involve the neighboring carboxyl group as a nucleophile, as previously thought,[12] but as a general base. The values of $\Delta H^{\neq}$ and $T\Delta S^{\neq}$ for the intramolecular carboxyl group catalyzed and the intermolecular acetate catalyzed hydrolysis of acetyl salicylate were determined to be 18.4, −6.7 and 17.4, −9.15 kcal mol^{-1}, respectively. The values of $T\Delta S^{\neq}$ for both processes are comparable to those for general base acetate ion catalyzed hydrolysis of phenyl acetate. This and other evidence including the values of ρ for the hydrolysis of substituted acetyl salicylates provided the basis for their conclusion. Presumably intramolecular general base catalysis in the case of acetyl salicylate is due to the fact that the leaving phenolate ion does not depart but remains in a position to be reesterified by the anhydride moiety. This allows favorable competition by the alternate path of general base catalysis.



(8)

Our objective in this study has been twofold: (a) to determine if the increase in rate of hydrolysis on increase of the steric demand of the 3 and 3,3′ substituents is due to an increase in $T\Delta S^{\neq}$ reflecting proposed conformational changes,[1d] and (b) by comparing activation parameters to those determined by Fersht and Kirby[9] for acetyl salicylate to determine if any evidence exists for a switch in mechanism from nucleophilic to general base catalysis with decreasing steric requirements at the 3 and 3,3′ positions.

Inspection of Table III reveals that the value of $\Delta H^{\neq}$ for the hydrolysis of the 11 monoesters averages 19.0 ± 0.4 kcal mol^{-1} with a maximum deviation of 1.2 kcal mol^{-1} for R = R′ = H. Neglecting the unsubstituted *p*-bromophenyl glutarate ester, since the kinetic data are not ours, the average value of $\Delta H^{\neq}$

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[7] J. W. Thanassi and T. C. Bruice, *J. Am. Chem. Soc.*, **88**, 747 (1966)

[8] D. G. Oakenfull, T. Riley, and V. Gold, *Chem. Commun.*, 385, (1966).

[9] A. R. Fersht and A. J. Kirby, *J. Amer. Chem. Soc.*, **89**, 4853 (1967).

[10] A. R. Butler and V. Gold, *J. Chem. Soc.*, 1334 (1962).

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is 18.8 ± 0.2 with a maximum deviation of 0.6 kcal mol^{-1}. Clearly within experimental error $\Delta H^{\ddagger}$ is the same for all esters investigated. Inspection of the values of $T\Delta S^{\ddagger}$ in Table III reveals that the largest value of $\Delta(T\Delta S^{\ddagger})$ is 3.2 kcal mol^{-1} which compares favorably to the largest value of $\Delta\Delta F^{\ddagger}$ of 3.0 kcal mol^{-1} (at 25° $\Delta F^{\ddagger}$ = 20.3 kcal mol^{-1} for R, R′ = Ph, Ph; Me, *i*-Pr; and Ph, Et and $\Delta F^{\ddagger}$ = 23.3 kcal mol^{-1} for R = R′ = H). These considerations lead to the conclusion that changes in $\Delta F^{\ddagger}$ are, within experimental error, primarily attributed to steric effects on $T\Delta S^{\ddagger}$. The relative constancy of the values of $\Delta H^{\ddagger}$ compared to the steric dependence of $T\Delta S^{\ddagger}$ is as anticipated if one assumes that the former reflects potential energy and the latter kinetic energy parameters.[13]

A comparison of the values of $T\Delta S^{\ddagger}$ for the hydrolysis of the 11 mono-*p*-bromophenyl glutarate esters (Table III) to the values established for carboxyl general base catalyzed reactions reveals that the former are greater by ~5 kcal mol^{-1}. The smaller values of $T\Delta S^{\ddagger}$ for the general base mechanisms are as expected for the inclusion of water molecules in the transition state. No evidence exists, therefore, that general base catalysis is an important mechanism for the hydrolysis of phenyl glutarates. It should be noted that care should be taken in assigning mechanisms on the basis of $T\Delta S^{\ddagger}$ values alone since it is an established fact that these values are not only a function of steric effects but are markedly dependent on the electronic nature of the leaving phenolate anion.[5,11] In this study the leaving group has been held constant.

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[13] This is a certain oversimplification since $\Delta H^{\ddagger}$ possesses both potential and kinetic energy terms, whereas $\Delta S^{\ddagger}$ is composed of only kinetic energy terms. See R. W. Taft, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, pp 556–675.

Carbonyl Participation in the Solvolysis of Ketone Derivatives. The Observation and Isolation of Intermediates[1]

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Abstract: The solvolyses of γ- and δ-keto-*p*-bromobenzenesulfonates in formic or trifluoroacetic acid proceed with participation of the carbonyl through intermediates which have been directly observed by nmr. The rates of formation of these intermediate oxonium ions (**1** and **13**) have been measured for 4-(*p*-bromobenzenesulfonoxy)-butyrophenone (1.9×10^{-2} sec^{-1}, 30°) and 5-(*p*-bromobenzenesulfonoxy)valerophenone (4.9×10^{-4} sec^{-1}, 30°). The hexachloroantimonate salt of **1** has been isolated and found to be stable to 120°. The relative shifts in the nmr spectra of these intermediate ions compared to model compounds indicate that most of the positive charge resides on oxygen. Intermediates have not been observed for β- or ε-keto-*p*-bromobenzenesulfonates.

There has been much concern in the recent literature about the intramolecular effect of nonbonding and π-bonding electron pairs on the formation of carbonium ions. Examples of this effect include the participation of olefinic bonds[2] and of carbonyl oxygen[3–5] in solvolytic reactions of halides and sulfonates. The evidence for participation commonly includes an acceleration in the solvolysis rate, when compared to a similar system where such participation cannot occur, and the observation of rearranged products which would result from the interaction of the neighboring group with the potential charge center. For example, the solvolyses of several halo ketones have been shown to proceed faster than the normal alkyl halides,[3,4] even though the carbonyl group would be expected to inductively retard the reaction. In addition, in the same systems, rearranged products which could arise from participation have been observed.[4] The results of these studies, by Oae[3] and by Pasto and Serve,[4] are summarized in Table I.

Table I. Relative Rates of Solvolysis of Halo Ketones

	Relative rate	
	Cl[a]	Br[b]
n-Butyl halide	1.00	1.00
Phenacyl halide	1.3	0.055
3-Halopropiophenone	7.9	0.31
4-Halobutyrophenone	759.0	71.1
5-Halovalerophenone	21.3	
6-Halocapriophenone	2.7	

[a] The reaction of chloro ketones with silver perchlorate in 80% aqueous ethanol at 56.2°.[4] [b] The reaction of bromo ketones with mercuric nitrate in weakly acidic dioxane at 40.05°.[3]

The most striking facet of these data is that the 4-halobutyrophenones are by far the most reactive of both series. Both research groups suggested that there is a participation of the carbonyl oxygen which assists

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[1] Parts of this work were published as a preliminary communication: H. R. Ward and P. D. Sherman, Jr., *J. Am. Chem. Soc.*, **89**, 4222 (1967).

[2] See P. D. Bartlett, S. Bank, R. J. Cranford, and G. H. Schmid, *ibid.*, **87**, 1288 (1965).

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