them.[9] Our results show that they must be attributed to experimental error. The conductance measurements show definitely that the ionization is not greater than 0.1% even in 0.01 *M* solution.

The behavior of mixtures of glycine and alcohol indicates an explanation of the fact that the higher α-amino acids, which may be looked upon as a mixture within a single molecule of glycine and something resembling ethyl alcohol, have osmotic coefficients more nearly unity than that of glycine. The further discussion of these results will be deferred to a later paper.

We take this opportunity to express our thanks to our various colleagues for the materials, use of apparatus and facilities and assistance acknowledged above.

(9) J. Y. Cann, *J. Phys. Chem.*, **36**, 2813 (1932).

Summary

A method is developed for the analytical expression of the thermodynamic functions of dilute solutions of several non-electrolyte components which reduces to a minimum the number of measurements necessary to determine the chemical potential (or activity) of any component in a solution of any composition.

The freezing point depressions of aqueous solutions of glycine, of ethyl alcohol and of two mixtures of them have been determined, and the above method applied to them.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Kinetics of the Saponification of Acetylated Hydroxy Acids*

BY VICTOR K. LA MER AND JOSEPH GREENSPAN

Introduction

Recent developments in the theory of ionic reactions, particularly in relating structure to reaction rate,[1a,2a,3,4] indicated the need for an ionic reaction which would be sufficiently general to permit more extensive studies of such relationships in a series of structurally different ions. The essential requisites of such a reaction, besides general applicability, are a rate suitable for measurement, freedom from side reactions, adherence to a simple kinetic equation over the major part of the reaction, available analytical methods for precise measurement and a constant ionic strength during reaction. Simplicity of experimental procedure and ease in preparation of compounds are desirable, although not essential.

Precise studies of only five more or less general ionic reactions are available at the present time.

$$RCH(X)COO^- + S_2O_3^= \longrightarrow RCH(S_2O_3)COO^= + X^- \quad \text{I}^{2,5,6,7,8b}$$

$$RCH(X)COO^- + SCN^- \longrightarrow RCH(SCN)COO^- + X^- \quad \text{II}^{8b,9,10}$$

$$RCH(X)COO^- + SO_3^= \longrightarrow RCH(SO_3)COO^= + X^- \quad \text{III}^{8}$$

$$RCH(X)COO^- + OH^- \longrightarrow RCH(OH)COO^- + X^-$$
$$\longrightarrow R{=}CHCOO^- + X^- \quad \text{IV}^{11,13}$$

$$R'OOCRCOO^- + OH^- \longrightarrow {}^-OOCRCOO^- + R'OH \quad \text{V}^{3,12}$$

(X represents a halogen atom.)

Reaction I possesses the advantage of high precision in the analytical determination of thiosulfate ion but has a slow rate for long chain compounds (k at 25° is 10^{-3} for α-bromopropionate ion[2b] and still less for γ-bromobutyrate ion[2e]). This reaction is not applicable to benzene ring compounds of the type: $^-OOCC_6H_4Br + S_2O_3^=$. Furthermore, the chemistry of the resultant organic thiosulfate compounds has not been extensively investigated.

(*) This article is based in part upon a dissertation submitted by Joseph Greenspan to the Faculty of Pure Science of Columbia University in partial fulfilment of the requirements for the degree of Doctor of Philosophy, April, 1933.

(1) La Mer, *Chem. Rev.*, **10**, (a) pp. 203–211, (b) p. 210, (c) p. 209, (d) p. 207 (1932).

(2) La Mer and Kamner, THIS JOURNAL, **53**, (a) pp. 2845–2851, (b) p. 2840, (c) p. 2845, (d) pp. 2840–2841, 2846–2849, (e) unpublished results, (f) pp. 2850–2851 (1931).

(3) Ingold, *J. Chem. Soc.*, (a) 1375 (1930); (b) 2170 (1931).

(4) Greenspan, *Chem. Rev.*, **12**, 339 (1933).

(5) Kappana, *J. Ind. Chem. Soc.*, **6**, 45, 419 (1929).

(6) La Mer, THIS JOURNAL, **51**, 3341, 3678 (1929).

(7) Bedford, Mason and Morrell, *ibid.*, **56**, 280 (1934).

(8) Backer and Van Mels, *Rec. trav. chim.*, **49**, (1930), (a) 177, (b) 363, (c) 457.

(9) Holmberg, *Z. physik. Chem.*, **97**, 134 (1921).

(10) La Mer and Greenspan, THIS JOURNAL, **54**, 2739 (1932).

(11) Holmberg, *Z. physik. Chem.*, (a) **79**, 147 (1912); (b) **80**, 573 (1912); (c) **84**, 451 (1913); (d) *Kung. Sven. Vetens. Med.*, **5**, No. 11 (1919).

(12) Ritchie, *J. Chem. Soc.*, 3112 (1931).

(13) Johansson, *Z. physik. Chem.*, **79**, 621 (1912).

Cases II and III, while suitable for precise measurement, have not only all the disadvantages of I to a more pronounced degree but also possess interfering side reactions.

Reaction IV is very general for aliphatic compounds, but, as indicated, usually consists of at least two concurrent reactions.

Case V is applicable to both aliphatic and aromatic ions and capable of precise measurement.[3,12] It possesses, however, the disadvantage of generating a divalent ion; the changing ionic environment thus produced complicates applications of the Brönsted–Debye–Hückel limiting law.

The saponification of acetylated hydroxy and phenolic acids: VI $RCH(OOCCH_3)COO^- + OH^- \longrightarrow RCH(OH)COO^- + C_2H_3O_2^-$ is offered here as a general reaction fulfilling the above requirements.

Two precisely investigated examples of this reaction are available to date, involving acetylglycolic[11c,14] and l-acetylmalic ions.[15] To these, the present work adds rate measurements on the aliphatic acetylmandelic, β-phenyl-α-acetoxypropionic, β-phenyl-β-acetoxypropionic, acetylbenzilic and the aromatic acetylsalicylic ions. Measurements were also attempted on acetylcitric ion.

The comparative rates for α- and β-substituted ions and the velocity–concentration dependence of the reactions have been determined and interpreted on the basis of current theories.[1,16] Further, the end-products have been isolated in every case under the conditions of measurement and their identity established.

Preparation of Materials

Sodium Hydroxide Solution.—A 0.2 *M* stock solution, prepared according to standard methods,[17] was kept in a waxed bottle fitted with an all glass, carbon dioxide guarded delivery system.[18a]

Acetylcitric Acid.—Ninety-six grams of anhydrous citric acid (prepared by keeping the crystals at 120–130° for two and one-half hours) was refluxed with 150 cc. of acetyl chloride[19] for three hours at 60°. Excess acetyl chloride was removed by keeping over potash in a vacuum desiccator. The resultant crystals were purified by dissolving them in acetone and precipitating with carbon tetrachloride, filtering, washing with carbon tetrachloride and drying *in vacuo*. Due to the very rapid saponification of the compound,[20b] its acid equivalent could not be determined.

Acetylmandelic Acid.—Thirty-five grams of mandelic acid was refluxed at room temperature with 51 g. of acetyl chloride until completion of reaction.[21,22] Excess acetyl chloride was distilled off by heating to 100°. The viscous residue was dissolved in 90 cc. of chloroform, cooled by an ice–salt mixture and precipitated in powder form by the careful addition of petroleum ether with continuous stirring. Purification was accomplished by repetition of the above procedure (solution in chloroform, precipitation with petroleum ether), followed by filtration, washing with chloroform–petroleum ether mixture, and air drying for several days; m. p. 80.2° uncorr.; acid equivalent, 0.2371 g. acetylmandelic acid required 25.04 cc. of 0.04886 *M* NaOH; calcd. 25.00 cc.; 0.1093 g. required 25.00, 25.07 cc. 0.02253 *M* NaOH, calcd. 25.00 cc.

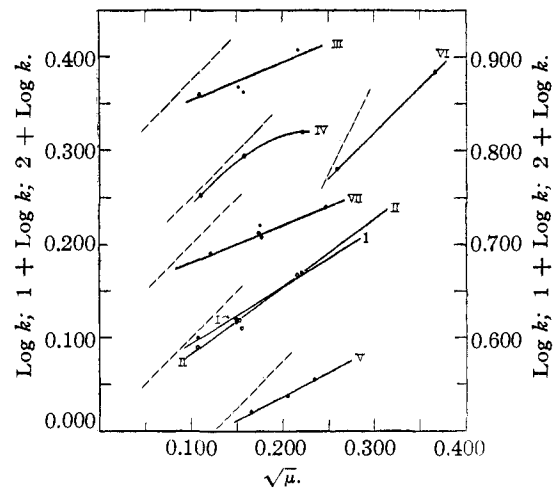

Fig. 1.—I, Acetylmandelic; II, β-acetoxy-β-phenylpropionic; III, acetylsalicylic; IV, α-acetoxy-β-phenylpropionic; V, acetylglycolic; VI, acetyl-*l*-malic; VII, acetylbenzilic. Dotted curves indicate the Brönsted limiting slope.

β-Acetoxy-β-phenylpropionic Acid. Schematic Procedure.—Cinnamic acid $\xrightarrow{HBr}$ β-Bromo-β-phenylpropionic acid $\xrightarrow{H_2O}$ β-Hydroxy-β-phenylpropionic acid $\xrightarrow{Ac_2O}$ β-Acetoxy-β-phenylpropionic acid.

(1) **β-Bromo-β-phenylpropionic Acid.**[23,24]—One hundred and fifty grams of cinnamic acid and 350 cc. of a 30% solution of hydrogen bromide in glacial acetic acid were heated in a sealed flask for one hour at 100° and kept overnight at room temperature. The compound was twice recrystallized from benzene; yield, 84 g.

(2) **β-Hydroxy-β-phenylpropionic Acid.**[25]—Fifty grams of the bromo acid was boiled with 450 cc. water until the

(14) Parts, "Über die Neutralsalzwirkung auf die Geschwindigkeit der Ionenreaktionen," Univ. of Tartu, Esthonia, 1930.

(15) Holmberg, *Ber.*, **45**, 2997 (1912).

(16) Brönsted, *Z. physik. Chem.*, **102**, 169 (1922); **115**, 337 (1925); Monograph in "Contemporary Developments in Chemistry," Columbia University Press, 1927.

(17) Kolthoff, "Volumetric Analysis," Vol. II, 1929 edition, p. 77–78.

(18) Clark, "Determination of Hydrogen Ions," 1928 edition, (a) p. 195, (b) p. 536.

(19) Easterfield and Sell, *J. Chem. Soc.*, **61**, 1003 (1892).

(20) Rath, *Ann.*, **358** (a) 98–125, (b) p. 117 (1908).

(21) "Organic Syntheses," Vol. IV, pp. 1–2.

(22) Anschütz and Böcker, *Ann.*, **368**, 57 (1909).

(23) Anschütz and Kinnicutt, *Ber.*, **11**, 1221 (1878); **12**, 537 (1879).

(24) Cumming, Hopper and Wheeler, "Systematic Organic Chemistry," 1925 edition, p. 333.

(25) Fittig and Binder, *Ann.*, **195**, 138 (1879).

minute droplets of styrene which formed were driven off. Very little cinnamic acid was formed.[25] The solution was extracted several times with 900 cc. of ether and the latter removed; yield, 30 g.

(3) **β-Acetoxy-β-phenylpropionic Acid.**[26]—Thirty grams of hydroxy acid was heated with 35 g. of acetic anhydride for two hours at 100°. Excess anhydride was removed under reduced pressure at 80° and by storage over potash *in vacuo*. When solid, the residue was dissolved in benzene, filtered, cooled with ice–salt mixture and precipitated with petroleum ether. Purification was accomplished by recrystallization from benzene, washing with petroleum ether and air drying; yield 19.5 g.; m. p. 99.5–100.5° uncorr.; acid equivalent, 0.1264 g. acid required 25.00 cc. of 0.02423 *M* NaOH; calcd. 25.05; 0.1216 g. required 24.99, 25.05 cc. of 0.02337 *M* NaOH; calcd. 25.00 cc.

α-Acetoxy-β-phenylpropionic Acid. Schematic Procedure.—Benzyl chloride + Malonic ester $\xrightarrow{NaOC_2H_5}$ Benzylmalonic ester $\xrightarrow{KOH}$ Benzylmalonic acid $\xrightarrow{Br_2}$ Benzyl bromomalonic acid $\xrightarrow{-CO_2}$ α-Bromo-β-phenylpropionic acid $\xrightarrow{H_2O}$ α-Hydroxy-β-phenylpropionic acid $\xrightarrow[\text{chloride}]{\text{Acetyl}}$ α-Acetoxy-β-phenylpropionic acid.

(1) **Benzylmalonic Ester.**[27a,28a]—A yield of 84 g. was obtained from 28 g. of sodium, 360 cc. of absolute alcohol, 192 g. of malonic ester and 150 cc. of benzyl chloride; b. p. 165–180° at 11 mm.

(2) **Benzylmalonic Acid.**[27a,28b]—Saponification of the above yielded 55 g. of material once recrystallized from benzene.

(3) **Benzylbromomalonic Acid.**[27b,28c]—Bromination of the above acid gave 76 g. of crude.

(4) **α-Bromo-β-phenylpropionic Acid**[28d]—Heating the moist bromo acid for three-quarters of an hour at 125–130° yielded a yellow oil.

(5) **α-Hydroxy-β-phenylpropionic Acid.**—(A) The above oil was boiled with 60 g. calcium carbonate and 500 cc. of water[29] for one hour, then acidified (Congo Red) with hydrochloric acid and extracted with ether. After removal of the latter, the oily residue was boiled with several portions of water and the combined water extracts evaporated; 30 g. of impure solid was obtained.

(B) Erlenmeyer[30] prepared this acid by hydrogen cyanide addition to phenylacetaldehyde. A modification was attempted here by use of the bisulfite addition product; 50 g. of commercial 100% phenylacetaldehyde (Ungerer & Co., New York) was treated with a saturated bisulfite solution containing 120 g. of the sodium salt. The precipitate was filtered, made into a paste with water and treated with a saturated solution of sodium cyanide, (23 g. NaCN), stirring constantly. The oil which separated became gummy on standing. The gum was heated for six hours on the steam-bath with 150 cc. of concd. hydrochloric acid, extracted with ether and the latter then removed. The resultant jelly was extracted several times with boiling water and the combined extracts evaporated. A recrystallization of the solid residue from carbon tetrachloride gave 3 g. of the hydroxy acid, m. p. 95–96°. Further treatment of the jelly with hydrochloric acid, as above, yielded an additional 2 g. Although giving a poorer yield, method (B) is simpler and less expensive than (A).

(6) **α-Acetoxy-β-phenylpropionic Acid.**—Thirty grams of impure hydroxy acid (5A above) was refluxed with 50 cc. of acetyl chloride at room temperature.[31b] Excess acetyl chloride was then distilled off under reduced pressure at 90° and the viscous residue kept over potash *in vacuo*. Attempts to induce crystallization by use of various solvents were unsuccessful. Crystals first appeared after several weeks of standing in air and were then freed from impurities by repeated solution in carbon tetrachloride and precipitation with petroleum ether. Evaporation of the combined carbon tetrachloride–petroleum ether extracts yielded the desired product. Final purification was secured by several recrystallizations from toluene, washing with petroleum ether and air drying; yield, 6 g.; m. p. 71–72°; acid equivalent, 0.1303 g. of acid required 25.01 cc. of 0.02504 *M* NaOH; calcd. 25.00 cc.

Acetylsalicylic Acid.—The commercial acid (acid equivalent 25.05 *vs.* 25.00 calcd.) was recrystallized from chloroform; m. p. 133–134°; acid equivalent, 0.1127 g. of acid required 24.99 cc. of 0.02504 *M* NaOH; calcd. 25.00.

Salicylic Acid.—The commercial product was recrystallized from chloroform until an unchanging m. p. was obtained; m. p. 159.1–159.6° corr.; acid equivalent, 0.1193 g. of acid required 34.94, 34.97 cc. of 0.02468 *M* NaOH; calcd. 35.00 cc.

Acetylbenzilic Acid.—Prepared as described by La Mer and Greenspan.[32]

Experimental Procedure and Precision

A. Rate Measurements

1. Standard Sodium Hydroxide.—Sodium hydroxide solution of approximately twice the concentration desired for the run was prepared by diluting the *M*/5 stock alkali. This solution was standardized by titration against 10.00 cc. of standard sulfuric acid in 100–150 cc. of water, using phenolphthalein indicator. Blank titrations were made on 100–150 cc. of water containing only the indicator; the appropriate blank corrections were made in all determinations.

Dilute standard alkali (0.02 *M*) may be preserved for several days without appreciable loss in titer, if kept in a well-stoppered non-sol bottle which is not opened too frequently. One sample gave titer values 29.13 cc. *vs.* 29.15 after a four-day interval; another gave 29.89 *vs.* 29.90 after twelve days. In the measurements described, no standard alkali was used after standing for three days except in the case of acetylbenzilic acid.

2. Velocity Measurements.—50.00-cc. portions of standard alkali were pipetted into several glass-stoppered flasks, which were then suspended in the 25.000 ± 0.005°

(25) Fittig and Slocum, *Ann.*, **227**, 59–60 (1885).

(26) Cohen, "Practical Organic Chemistry," 1924 ed., (a) p. 345, (b) 346.

(27) Fischer, "Introduction to Preparation of Organic Compounds," 1928 ed., (a) p. 78, (b) p. 79, (c) p. 157, (d) p. 158.

(28) Fischer and Zemplén, *Ber.*, **42**, 4891 (1909).

(29) Erlenmeyer, *ibid.*, **13**, 303 (1880).

(30) Anschütz and Motschmann, *Ann.*, **392** (1912); (a) pp. 100–126, (b) p. 110.

(31) La Mer and Greenspan, THIS JOURNAL, **56**, 956 (1934).

thermostat for at least one hour. While temperature equilibrium was being obtained, samples of the acetylated acid sufficient to neutralize exactly half the alkali (*i. e.*, 25.00 cc.) were weighed into small platinum buckets.

A flask was then removed from the thermostat and when the loaded bucket was dropped in, the stop watch was simultaneously started. The flask was stoppered, shaken until the entire sample dissolved (which required almost two minutes for some of the acids) and replaced in the bath.

The reaction was stopped at a desired time by adding 10.00 cc. of the standard sulfuric acid (see above) from a rapid delivery separatory funnel followed by 40 cc. of water. The flask contents were then back titrated with the standardized alkali.

The time required for solution of the samples introduces the largest error of the procedure. In the less concentrated solutions this mixing error decreases but then titration errors become more pronounced. These observations suggest that, for high precision, better titration methods will be necessary in solutions more dilute than here considered (micro-buret[18b] or potentiometric methods[33]) whereas solutions of salts of the compounds will be required to reduce mixing errors in more concentrated regions.

Since the same alkali solution is used for both reaction and back titration, and the same acid for standardization and stopping the reaction, calculation of the bimolecular constant, k, becomes quite simple. In the cases studied, $a = b$ and

$$k = \frac{1}{t} \cdot \frac{1}{a} \cdot \frac{x}{a' - x} \qquad (1)$$

where a = initial concentration of sodium hydroxide in m./l.
b = initial concentration of sodium salt of acetoxy acid in m./l.
t = time in minutes
a' = initial concentration, a, expressed as cc. of standard sodium hydroxide
x = change in concentration of reactants, after time t, expressed in same units as a'

It must be emphasized that the individual measurements in a run were not made on aliquots of one sample, as is usually the case. Each measurement was performed on a separate sample, involving a separate weighing, mixing and timing error. This procedure subjects the constancy of k to a more significant test than does the aliquot procedure.

B. Recovery Experiments

The procedure outlined in A was employed with the following modifications: 200 cc. of the same standard alkali and a corresponding sample were used, and the flask kept in the thermostat for twenty-four hours. The solution, which then reacted neutral to litmus, was acidified with 1.5 cc. of concd. hydrochloric acid and extracted four times with about 700 cc. of ether. The extracts were spontaneously evaporated until the acetic odor disappeared (four to six days), after which the solid residue was transferred to a tared watch glass, weighed and its melting point determined. It was then recrystallized from the appropriate solvent, dried and both the melting point and acid equivalent determined. Even though the procedure is only semi-quantitative in character, about 90% calculated recovery of a not very impure (as judged by the melting point) material was secured.

Data.—A representative reaction velocity table is given.

TABLE I

SODIUM ACETYL MANDELATE $a = b = 0.005763$ m./l.

t	x	$a' - x$	% Conv.	k
30'0"	4.52	20.44	18	1.28
60'	7.47	17.49	30	1.24
90'	9.92	15.04	40	1.27
120'	11.66	13.30	47	1.27
180'	14.16	10.80	57	1.26
300'	17.10	7.86	68	1.26

$k = 1.26 \pm 0.010$.

Discussion of Results

The saponification of acetylated hydroxy acids fulfils the necessary requirements for a study of the relations between structure and reaction velocity in ionic systems. The reactions of the six compounds investigated follow the simple bimolecular rate law over a range of 20–80% conversion as shown by the constancy of k to about $\pm 1\%$ (Table II).

The semi-quantitative recovery of approximately 90% of the resultant hydroxy acids (Table III) further indicates freedom from side reactions. It must be pointed out that each recovery was made after reaction under the conditions of measurement, *i. e.*, in dilute solution at 25°. The customary procedure of isolating end-products in concentrated solution and assuming the same products in dilute solution may lead to error.[11a,26] The reactions investigated permit easy recovery of end-products since the acetic acid produced (on acidification) is volatile, whereas the hydroxy acid is solid.

The analytical method employed for following the reaction over the range 0.005–0.025 molar merely involves an ordinary acid-base titration. For precise work in more dilute solution, however, different methods are indicated.[18b,35]

The velocity of reaction varies, of course, with the particular case. Measurements have been secured by the above simple procedure over a range of half-conversion times extending from 5 to

(33) Kolthoff, "Potentiometric Titrations," 1931 ed., pp. 130–131.

TABLE II

SUMMARY

Compound	Concn., m./l.	$\sqrt{\mu}$	k_{25} ± a. d.	log k	% Conv.	[b] Water hydrolysis,[20,31] k'_{100} c = 0.01852 m./l.
Acetylmandelic	0.005763	0.107	1.26 ± 0.010	0.1004	18–68	
	.01126	.150	1.32 ± .018	.1206	13–78	
	.01129[a]	.150	1.31 ± .012	.1173	13–77	
	.02443	.221	1.48 ± .016	.1703	20–68	0.0027
β-Acetoxy-β-phenylpropionic	.005843	.108	1.23 ± .011	.0899	18–68	
	.01169	.153	1.32 ± .025	.1206	19–73	
	.01212[a]	.156	1.29 ± .022	.1106	19–65	
	.02379	.218	1.47 ± .013	.1673	20–68	.00077
α-Acetoxy-β-phenylpropionic	.006230	.111	0.566 ± .0073	$\bar{1}$.7528	17–69	
	.01252	.158	.622 ± .010	$\bar{1}$.7938	10–70	.0017
	.02456	.222	.662 ± .0063	$\bar{1}$.8209	19–74	
Acetylsalicylic	.006045	.110	7.26 ± .088	0.8609	30–76	
	.01170[a]	.153	7.36 ± .14	.8669	40–80	.013
	.01228	.157	7.29 ± .12	.8627	35–84	
	.02387	.218	8.09 ± .17	.9079	32–82	
Acetylbenzilic	.007620	.123	0.01550 ± .00006	$\bar{2}$.1903	21–58	Sodium salt
	.01537	.175	.01627 ± .00011	$\bar{2}$.2122	23–64	at 25.00°
	.01545	.176	.0166 ± .00021	$\bar{2}$.2201	23–64	k_1 = 44.0 ×
	.01574	.177	.01609 ± .00007	$\bar{2}$.2068	24–64	10^{-6}
	.03054	.247	.01744 ± .00016	$\bar{2}$.2405	21–62	
Acetylglycolic[13,14]	.01381	.166	3.32 ± .022	0.5211	16–76	
	.02119	.206	3.45 ± .053	.5378	37–79	0.0031
	.02762	.235	3.58 ± .035	.5539	23–82	
1-Acetylmalic[15]	.01693	.260	0.191 ± .0025	$\bar{1}$.2810	17–70	
	.03387	.368	.242 ± .0033	$\bar{1}$.3838	14–74	.0071

[a] Preliminary runs on impure material. [b] With the exception of sodium acetylbenzilate, the water hydrolysis constants were obtained[20,31] in aqueous solutions containing only the free acids at a concn. of 0.01852 m./l.

TABLE III

SUMMARY

Compound	Recovery, %	M. p. of impure material, °C.	M. p. of pure material, °C.	M. p. literature, °C.	Acid equivalent calcd. = 25.00
Acetylmandelic	90	104–106	118	118[a]	24.92
β-Acetoxy-β-phenylpropionic	86	86–88	91.5–92.5	92–93[b]	24.96
α-Acetoxy-β-phenylpropionic	100	88–91	97.5	97–98[c]	24.97
Acetylsalicylic	88	154–156	158.6	159[d]	25.03
Acetylbenzilic	97	130–135	149.3–149.6	150[e]	24.88

[a] "I. C. T.," Vol. I, p. 218. [b] Beilstein, Vol. X, p. 249. [c] Fischer and Zemplén, Ref. 29. [d] "I. C. T.," Vol. I, p. 209. [e] "I. C. T.," Vol. I, p. 253.

TABLE IV

ACETYLBENZILIC ACID, $a = b = 0.007620$ m./l.

t, min.	x	$a' - x$	% Conv.	$k \times 10^5$	$k_2 \times 10^5$
1580	5.26	19.74	21	2213	1560
3040	8.61	16.39	34	2268	1540
4380	10.98	14.02	44	2347	1551
7290	14.55	10.45	58	2506	1548

k_2 = 0.01550 ± 0.00006.

240 minutes with an a. d. better than 2% for the most rapid and 1% for the slower reactions.

A possibility of the water hydrolysis, which would yield the same end-products, entering as a side reaction is removed by the data summarized in the last column of Table II. The water reaction in solutions of the free acids is too slow to be significant even at 100°.

In the case of sodium acetylbenzilate, the constants were found to increase with time, as may be seen in Table IV, Column 5. A side reaction was suspected as the cause of the increase; an aqueous solution of sodium acetylbenzilate, initially pink to phenolphthalein, became acid in a few hours. A series of rate measurements on a 0.03054 molar solution of the sodium salt, performed by adding standard alkali after definite time intervals until pink to phenolphthalein, gave a unimolecular constant of 44.0 ± 0.6 × 10^{-6} min.$^{-1}$ (25°) over 11–56% conversion for the water reaction. Thus,

sodium acetylbenzilate decomposes both in a bimolecular and unimolecular fashion, and yields one equivalent of acid per equivalent of sodium salt decomposed by *both* mechanisms.

To correct for such concurrent reactions, the following rate expression must be used

$$-\frac{dC_B}{dt} = k_1(C_B) + k_2(C_A C_B) \qquad (2)$$

If y = change in concentration of sodium acetylbenzilate by unimolecular reaction
z = change in concentration of sodium acetylbenzilate by bimolecular reaction
$a - (y + z)$ = concentration of sodium acetylbenzilate at time t
$b - (y + z)$ = concentration of sodium hydroxide at time t

Then equation (2) becomes

$$-\frac{d(a - (y + z))}{dt} = k_1(a - (y + z)) + k_2(a - (y + z))(b - (y + z)) \qquad (3)$$

However, $y + z = x$, the measured change in alkali concentration and $a = b$ for the cases under discussion, so that equation (3) reduces to

$$-\frac{d(a - x)}{dt} = k_1(a - x) + k_2(a - x)^2 \qquad (4)$$

Integrating[34] and evaluating the constant yields (5)

$$t = \frac{1}{k_1}\left[\ln \frac{a}{a - x}\,\frac{k_1 + k_2(a - x)}{k_1 + k_2 a}\right] \qquad (5)$$

Solving for k_2

$$k_2 = \frac{k_1}{a(a' - x)}\left[\frac{a' - (a' - x)\exp.^{k_1 t}}{\exp.^{k_1 t} - 1}\right] \qquad (6)$$

a' and $a' - x$ have the same meaning as in equation (1). But from equation (1)

$$\frac{1}{a(a' - x)} = \frac{kt}{x} \qquad (1')$$

or, substituting in (6)

$$k_2 = \frac{k_1 k t}{x}\left[\frac{a' - (a' - x)\exp.^{k_1 t}}{\exp.^{k_1 t} - 1}\right] \qquad (7)$$

thus relating the measured bimolecular k and the true bimolecular k_2.

Substitution of the experimentally determined values for k_1 (44×10^{-6}), and the corresponding k, t, x, a' -- x values permit solution of equation (7) for k_2. The last column of Table IV gives k_2 for a typical run, which now exhibits no drift with time.

For ionic reactions between ions of like charge, the Brönsted equation

$$\log k = \log k_0 + Z_A Z_B \sqrt{\mu} \qquad (8)$$

predicts an increasing velocity constant with increasing concentration. This was qualitatively found to be the case for the above reactions. Although they have been investigated only over a five-fold concentration range (0.005–0.025 m), the changes of k with concentration are many times the experimental error (except the two lowest concn. measurements for acetylsalicylic acid). The different ionic strengths were secured solely by changing the initial concentrations of the reactants and not by adding extraneous neutral salts.

The above equation further predicts a slope of $+1$ in the log k *vs.* $\sqrt{\mu}$ graph for the -1, -1 reactions, and a slope of $+2$ for the acetylmalic case. The data of Table II, together with the theoretical slope are plotted in the figure. It should be noted that the experimental data, with one exception (α-acetoxy-β-phenylpropionicion), fall on straight lines which have slopes ranging between four-tenths and seven-tenths that predicted by the Brönsted–Debye theory. This failure of equation (8) may of course be due to the experimentally unavoidable difficulty of having to work in a range of concentrations greater than is permissible for the safe application of the Debye–Hückel limiting law.

However, we favor another interpretation; namely, that the limiting slope now well established for the Debye–Hückel activity coefficient equation is not necessarily applicable in rate equations. It was pointed out in a previous paper[35] that f_x, the activity coefficient of the critical complex, contains kinetic factors (designated by k_j) and thus is not in general a pure thermodynamic activity coefficient. Only in certain special cases is it permissible to substitute the Debye–Hückel limiting law in Brönsted's equation involving f_x.

In considering relations between velocity and separation of reactant group from electrical charge on an ion, La Mer and Kammer[2c] suggested that β-bromopropionic ion should react (as it does) more rapidly than α-bromopropionic ion with the like charged $S_2O_3^=$ due to greater spacial separation of the Br and COO^- groups in the β-compound. Similar results were cited for the same reaction involving[1c] $SO_3^=$ and[10] SCN^- instead of $S_2O_3^=$. Similar results were obtained here for the acetoxy compounds, since β-acetoxy-β-phenylpropionic ion reacted more than twice as rapidly with OH^- than the corresponding α-ion, thus establishing this principle.

It was further suggested[1d,2] that in the absence of charge effects, a reversal of relative velocities

(34) Granville, "Differential and Integral Calculus," 1911 Edition, p. 452, Formula 33.

(35) La Mer, *J. Chem. Phys.*, **1**, 289 (1933).

should occur with the generally more reactive α-position being more readily attacked. Thus, it was found that α-bromopropionic *ester* reacted more rapidly than the β-ester with $S_2O_3^=$. A similar result was found for the water hydrolysis of the acetoxyphenylpropionic acids, the α-compound reacting twice as rapidly as the β-acid. The reversal ($\beta : \alpha > 2$ for alkaline saponification to $\beta : \alpha < {}^1/_2$) is understandable from the proposed electrical picture.

If the water hydrolysis is assumed to occur, for the most part, between the undissociated, and therefore uncharged, molecules of the weak acetoxy acid and the H_2O or OH^- (or between the acid ions present and H_2O) then charge effects between the reactants are absent, and the more reactive α-position is more readily attacked than the β-. For the alkaline hydrolysis, however, reaction occurs between ions, and the negative charge on the COO^- shields the closely situated α-acetoxy group to a much greater extent than the more distant β-acetoxy group from attack by a negative OH^-. Thus, despite the greater reactivity of an α-position, electrical forces between the ions involved may make the β-position comparatively more vulnerable.

It is interesting to note in this connection that the acetylcitric ion is so rapidly attacked by OH^- that a neutralization equivalent cannot be determined.[20b] From the simple electrical picture, this ion with its acetoxy group shielded by *three* negatively charged COO^- groups should possess low reactivity. This serves to emphasize that electrostatic forces alone may not suffice to explain reaction velocity–electrical structure relationships in every case. For ions containing several closely situated charged groups, the external electrostatic forces may become quite negligible compared to distortional and interatomic forces.[3a]

La Mer and Kamner found an increasing k with decreasing concentration for the β-bromopropionic–thiosulfate reaction[2d] whereas the reverse was predicted by the Brönsted equation; a similar result was recently found for the bromosuccinic–thiosulfate case.[7] An explanation based on oriented collision in dilute solution was offered by the authors.[1b,2f] The β-acetoxy-β-phenylpropionic hydroxyl reaction did not exhibit this behavior but followed the Brönsted equation qualitatively (see Curve II).

The velocity constants in the series acetylglycolic, acetylmandelic, acetylbenzilic (*i. e., unsubstituted* acetylglycolic, *monophenyl*acetylglycolic and *diphenyl*acetylglycolic) salts, decrease with increase in the number of substituent phenyl groups. A study of the temperature coefficients of this series is necessary in order to allocate this change in rate to steric factors, critical increment differences or both.

A very interesting comparison was foreseen in the series: *o*-, *m*- and *p*-acetoxybenzoic acids. However, practical and theoretical difficulties were encountered for the last two because the phenolic group of the resultant phenolic acid was acidic and acted as a buffer during reaction and titration. The analytical methods for determining these acids will form the subject matter of a later paper. It was found that salicylic acid, resulting from saponification of the *o*-compound, could be titrated alone or mixed with acetic acid (phenolphth. ind.) without interference from the phenolic group (Compare 38) (k_1 for salicylic acid $\cong 10^{-3}$; [36]$k_2 \cong 10^{-14}$).

Summary and Conclusions

1. The alkaline saponification of acetylated hydroxy acids is offered as a general bimolecular ionic reaction suitable for the investigation of reaction velocity–structure relations. Freedom from side reactions, applicability to aromatic and aliphatic compounds and simplicity of analytic requirements have been demonstrated by precise rate measurements on acetylmandelic, acetylsalicylic and α- and β-acetoxy-β-phenylpropionic ions.

2. The end-products in these reactions have been isolated under the conditions of measurement and identified.

3. The saponification of sodium acetylbenzilate follows a unimolecular and bimolecular course simultaneously. An application of the appropriate rate law for this combination yields the corrected bimolecular constant.

4. A modified method for the preparation of α-hydroxy-β-phenylpropionic acid from phenylacetaldehyde has been given.

5. It has been shown that the β-acetoxy-β-phenylpropionic ion reacts more than twice as rapidly as the corresponding α-acetoxy-β-phenylpropionic ion, a result in agreement with the electrostatic interpretation given by La Mer.

6. The reversal in the comparative rates of the α- and β-compounds for the aqueous hydrolysis

(36) Kolthoff, *Rec. trav. chim.*, **42**, 971–972 (1923).

and the extraordinary reactivity of acetylcitric acid are discussed in the light of this electrostatic theory.

7. The concentration dependence of the rates of these reactions has been studied over the range 0.005-0.025 molar. The salt effect is positive, but only qualitatively in accordance with the Brönsted theory of reaction velocity. The slopes of log k *vs.* $\sqrt{\mu}$ range between two-fifths to two-thirds of that predicted in six of the reactions studied. An explanation based on the kinetic character of the activity coefficient, f_x, of the intermediate has been suggested.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS]

Physical Properties of Methoxymethyl Ethyl Ketone

BY NEIL E. RIGLER, W. A. FELSING AND HENRY R. HENZE

In connection with a study of the general properties of keto ethers we have measured a number of physical properties of methoxymethyl ethyl ketone. This ketone, prepared as previously described by Henze and Rigler,[1] was twice redistilled through a small Vigreux column and the fraction boiling between 133.0 and 133.6° (757 mm.) was preserved over anhydrous potassium carbonate.

The vapor pressures between 24.8 and 134.2° were measured by the static method of Felsing and Thomas,[2] except that calibrated mercury thermometers were employed and a small electric light served to indicate the exact height of the mercury in the short arm of the manometer. The observed vapor pressures were found to be given adequately by the equation $\log p = -1429.5/(t + 205) + 7.11187$ with an average deviation of 0.98% and a maximum deviation of 2.56%, without any definite trend among the deviations. For these measurements the ketone was again fractionated and then distilled under a vacuum directly into the attached apparatus. By use of the equation the normal boiling point of this keto ether was found to be 132.9° and the latent heat of vaporization at this temperature, calculated from these data using the Clausius-Clapeyron equation, is $\Delta H = 9364$ calories. Since $\Delta H/T = 23.06$, this ketone is but slightly associated. The entropy of vaporization calculated by the graphical method of Hildebrand[3] is 28.5, indicating that this ketone is a slightly polar liquid.

The densities were determined over the temperature range 0.01−89.91° by means of the Pyrex pycnometer described by Felsing and Durban,[4] the liquid being introduced by distillation into the evacuated bulb. No correction was required for the small amount of vapor present in the stem above the liquid. The densities were expressed adequately by the formula $d_t = 0.9509 - 0.001018t$. The density at 20° calculated from this equation is 0.9305.

The surface tension was measured by means of Cassel's precision capillarimeter[5] and was found to be 30.10 dynes/cm. The index of refraction was measured by means of the Pulfrich refractomer and was found to be n_D^{20} 1.40454, whence $(MR)_D^{20}$ 26.85; calcd. 26.83. Sugden's parachor[6] is 258.2 compared with 259.0, as determined from the density and surface tension data. The Eötvös constant, using the equation of Walden and Swinne,[7] is 2.117.

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(1) Henze and Rigler, THIS JOURNAL, **56**, 1350 (1934).
(2) Felsing and Thomas, *Ind. Eng. Chem.*, **21**, 1269 (1929).
(3) Hildebrand, "Solubility," The Chemical Catalog Co., Inc., New York, 1924, pp. 93-94.
(4) Felsing and Durban, THIS JOURNAL, **48**, 2885 (1926).
(5) Cassel, *Chem. Ztg.*, **53**, 479 (1929).
(6) Sugden, *J. Chem. Soc.*, **125**, 1178 (1924).
(7) Walden and Swinne, *Z. physik. Chem.*, **82**, 271 (1913).