[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Heats of Organic Reactions. XIII. Heats of Hydrolysis of Some Acid Anhydrides

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For the purpose of quantitative estimation of the effect of substitution on the stability of cyclic structures, it would be of interest to compare the heats of hydrolysis of straight-chain acid anhydrides with those of cyclic acid anhydrides. It is necessary to obtain the heat of the reaction

$$\text{Anhydride (g)} + H_2O \text{ (g)} = \text{Acid (g)} + \Delta H \quad (1)$$
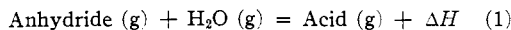
since only in the gas phase, where entropy changes would be very nearly the same for a series of reactions of the type contemplated here, would the ΔH values be a fair measure of stability. Unfortunately no cyclic anhydrides are of sufficient volatility, and no acid anhydrides, whether cyclic or straight-chain, are reactive enough with water to permit application of the technique of gas calorimetry. Nevertheless, as the first step toward obtaining heats of the above reaction 1, we have carried out calorimetric measurements in solution which allow calculation of heats of the following type of reaction

$$\text{Anhydride (s or l)} + H_2O \text{ (l)} = \text{Acid (s or l)} + \Delta H \quad (2)$$
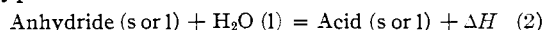
Some of the heats of reaction 2 which we report here can be computed from existing heats of combustion; however, our data cover a wider range of compounds, and we believe that our direct measurements are of greater accuracy than the heats of hydrolysis obtainable from these older combustion data.

Experimental Procedure

The calorimeter used in these measurements has been described in a previous paper of this series.[1] It was used in

(1) Conn, Kistiakowsky and Roberts, THIS JOURNAL, **62**, 1895 (1940).

this work as a single calorimeter. The chemical reaction was carried out in one calorimeter; the other calorimeter was filled with water and allowed to attain its equilibrium temperature due to stirring, thus serving as a reference bath for the main thermel.

An electrical calibration of the calorimeter preceded and followed each chemical run. The procedure was as follows.

The calorimeter was filled and was brought by electrical heating to a suitable temperature somewhat below that of the bath. After waiting fifteen minutes for the attainment of a steady state, observations on the main thermel were made every five minutes for half an hour. A current of approximately 0.4 ampere was then passed through the calorimeter heater for about five minutes. The time interval was measured with an error of less than 0.1% by a chronograph connected with the heater switch. Measurements of the potential across the calorimeter heater and across a 0.1 ohm standard resistance in series with the heater were made frequently during the heating period. Current from the batteries was allowed to pass through a ballast coil of the same resistance as the calorimeter heater for at least half an hour before making a run, and was thrown directly from the ballast coil to the heater. Following the heating period, readings on the main thermel were made frequently until a steady state was reached, then every five minutes for half an hour. From the readings of the half-hour periods before and after the heating period the equilibrium temperature and the cooling constant of the calorimeter and contents were determined. The effective microvolt rise due to electrical heating was then calculated by logarithmic extrapolation of the two cooling curves to the middle of the heating period. The effective microvolt rise, together with the potential readings across the heater and standard resistance gave the calibration constant of the calorimeter and contents in calories per microvolt. In this paper 1 cal. = 4.1833 int. joule. The electrical calibrations before and after the chemical run differed by less than 0.1%.

The method of making the chemical run will now be de-

scribed. After purification, the various compounds were packed in previously weighed thin-walled soft glass sample bulbs whose outside dimensions were about 5×80 mm. Solid compounds were introduced into the sample bulbs in a dry box and sealed off immediately after filling. Sample bulbs were filled with liquid compounds in the absence of air by distillation into special receivers (described below) holding the sample bulbs. The sample bulbs for liquids had capillary tips, and were quickly sealed off after filling and removing from the receiver. The sample bulb was held in place in the calorimeter by four stainless steel strips wired at the bottom, forming a cage for the bulb. At the top the strips were fastened to a stainless steel truncated cone ground to fit the truncated conical sample aperture in the top of the calorimeter.[2] The cone had a threaded hole in its center, into which was screwed a threaded stainless steel rod terminating in a sharp conical tip at its lower end. The upper end of the threaded rod was above the thermostat bath, and was attached to a small reversible motor making it possible to screw the rod up or down. When a sample tube was in place, upon screwing the rod downward the sharp tip on the lower end of the rod drove into the sample bulb and shattered it, allowing the sample to dissolve and react with the alkali. The heat of breaking the sample bulb was determined and was taken into account in calculating the results of the chemical run.

At the beginning of the chemical run the sample bulb was broken, and main thermel readings were made every thirty seconds while the heat evolution was rapid, later at longer intervals, until the cooling constant resumed its normal value. Correction for heat loss during the reaction period was made by numerical computation of the area under a plot of cooling constant $\times$ thermal head against time.

Direct measurement of the heat of hydrolysis of the acid anhydrides in pure water was first attempted, with fair success in the case of acetic anhydride, but the rate of hydrolysis of propionic anhydride proved too slow. The plan was therefore revised, and the hydrolysis was carried out in a slight excess of alkali, so that the sum of the heat of hydrolysis and the heat of neutralization of the acid was measured. Under these conditions the reaction was complete in most cases in about an hour. Heats of neutralization of the acids were subsequently measured. To increase the solubility of some of the compounds studied, the reaction was carried out in a dioxane-water mixture. Heats of dilution of these mixtures were determined.

Preparation of Compounds

Acetic Acid and Anhydride.—Merck Blue Label acetic acid was purified first by partial freezing and then carefully fractionated through Column B.[3] In this and subsequent distillations, the receiver which was to contain the calorimetric sample was specially designed so as to carry within it six previously weighed bulbs. At the conclusion of the distillation, the bulbs were filled by pumping out the receiver and then admitting dry air; as soon as they were full, they were removed and immediately sealed and reweighed. The calorimetric sample was taken in the middle

of the distillation after the head thermometer had been registering a constant temperature for some time (usually an hour). The acetic acid fraction used for calorimetric measurement boiled at $118.03 \pm 0.01°$ (770 mm.)[4] Merck Blue Label acetic anhydride was similarly distilled; the fraction used boiled at $138.70 \pm 0.01°$ (770 mm.).

Propionic Acid and Anhydride.—Eastman Kodak Co. best grade materials were distilled through Column B. The acid boiled at $141.28 \pm 0.01°$ (766 mm.). The anhydride boiled at $166.94 \pm 0.04°$ (777 mm.).

Isobutyric Acid and Anhydride.—Commercial isobutyl alcohol was oxidized to the acid as described by Pierre and Puchot.[5] After preliminary purification, a precision distillation yielded a calorimetric sample boiling at $154.68 \pm 0.02°$ (767 mm.). Isobutyryl chloride was made from the acid by distillation with benzoyl chloride;[6] yield 91%; b. p. 92.8–$92.9°$ (765 mm.). Isobutyric anhydride, prepared from the above chloride and sodium isobutyrate (67% yield), gave a calorimetric sample boiling at $92.41 \pm 0.04°$ (34.1 mm.). It froze at $-56.37°$ with a drift of $0.065°$ to the point where jamming of the stirrer by solid made thermocouple readings unreliable.

Trimethylacetic Acid and Anhydride.—A quantity of trimethylacetic acid was kindly furnished us by Professor P. D. Bartlett of these Laboratories; a further amount was obtained from Eastman Kodak Co. The portion reserved for the calorimeter boiled at $164.18 \pm 0.01°$ (763 mm.). Conversion to the chloride as previously described gave a 96% yield of material boiling at 104.8–$105.0°$ (762 mm.). The anhydride was prepared from the chloride and the dry sodium salt[7]; yield, 78%. The calorimetric sample boiled at $95.00 \pm 0.01°$ (28 mm.) and froze at $-4.24°$ with a drift of $0.03°$ to jamming of the stirrer.

Succinic Acid and Anhydride.—Mallinckrodt Analytical Reagent succinic acid was used for the neutralization measurements. The anhydride was prepared from this acid by phosphorus oxychloride dehydration[8]; yield, 92%. The product was recrystallized from acetyl chloride (m. p. 119–$120°$), and then sublimed in vacuo at $91°$. The sublinator is of all-metal construction; vaporization takes place on a circular plate through the center of which the condenser tube runs. Condensation occurs below the plate; the solid is removed by a rotary scraper, and falls into a series of glass cups carried on a movable tray. The sublimator bell and plate are heated electrically; glass windows in the bell and receiver carriage permit observation of the process. The sublimate, which was in the form of an almost impalpable powder, was preserved in a desiccator over phosphorus pentoxide until transferred to the bulbs.

Maleic Acid and Anhydride.—Eastman Kodak Co. best grade maleic anhydride was recrystallized from acetyl chloride. The best material was sublimed in vacuo; f. p. $52.27°$ with $0.08°$ drift to jamming of the stirrer. Some of the best anhydride was hydrolyzed to the acid.

(2) See ref. 1 for a diagram of the calorimeter.

(3) Column B is described by Kistiakowsky, Ruhoff, Smith and Vaughan, This Journal, **57**, 877 (1935).

(4) This value may be in error in absolute magnitude, inasmuch as the only correction applied to it was for barometric fluctuation. The deviation includes the uncertainty in reading the thermometer used plus the magnitude of the random fluctuations.

(5) Pierre and Puchot, Ann. Chim., (4) **28**, 366 (1873).

(6) Brown, This Journal, **60**, 1325 (1938).

(7) Butlerow, Ann., **173**, 374 (1874).

(8) "Organic Syntheses," Vol. XII, 1932, p. 66.

After two recrystallizations from water, the m. p. was 130–131°, with some decomposition.

Methylenesuccinic (Itaconic) Acid and Anhydride.—Mallinckrodt Analytical Reagent citric acid was converted to methylenesuccinic anhydride as described in "Organic Syntheses." [9] The yield of crude acid anhydride mixture from 4400 g. of citric acid was 45%. The solid acid which separated on standing was systematically recrystallized from water until no further alteration in melting behavior occurred, then twice more; m. p. 162–166°, dec. Some of the best acid was converted to the anhydride by means of acetyl chloride[10]; yield 79%; m. p. 67–68°. It was then sublimed *in vacuo* at 90°.[11]

Methylmaleic (Citraconic) Acid and Anhydride.—Methylmaleic anhydride was prepared by distillation of crude itaconic anhydride[12]; yield 80%; b. p. 119–120° (37 mm.). Precise fractionation through Column B yielded a calorimetric sample with b. p. 110.35±0.01° (28.8 mm.) and f. p. +6.03°, drift, 0.04° to jamming of the stirrer. A sample of the best anhydride was hydrated with a slight excess of water.[12] After prolonged drying in a vacuum desiccator over phosphorus pentoxide, the acid melted at 91–92°.

Methylsuccinic Acid and Anhydride.—Methyl cyanosuccinic ester was prepared from purified ethyl α-bromopropionate (b. p. 80.0–80.1° at 46 mm.) and ethyl cyanoacetate (b. p. 103.0–103.1° at 17.5 mm.).[13] Condensation was carried out in 3.75 mole lots; yield of product boiling flatly at 162.7° (22 mm.), 87%. Hydrolysis of the cyanosuccinic ester (2.5 liters of concentrated hydrochloric acid suffices for 1 kg. of ester) gave 84% yield of methylsuccinic acid; m. p. 112–112.5° after recrystallization from water and absolute ether. The acid was converted to the anhydride by means of phosphorus oxychloride; yield 67%. The calorimetric sample boiled at 135.78±0.02° (24 mm.). The anhydride crystallizes very sluggishly and will remain in the supercooled state almost indefinitely unless it is seeded or strongly cooled in dry-ice.

***dl-* and *meso-α,β*-Dimethylsuccinic Acid; *trans-* and *cis-α,β*-Dimethylsuccinic Anhydride.**—Much confusion exists in the literature as to the configuration of these two acids, and the impression seems to be prevalent that neither of them has ever been resolved,[14] although the resolution of the low melting isomer was carried out by Werner and Basyrin in 1913,[15] and confirmed by Ott in 1928.[16] Thus the "*anti*" acid of Bischoff and Voit[17] and the "*cis*" acid of Bone and W. H. Perkin, Jr.,[18] and of Bone and Sprankling[13] is the *dl-* form and will be so described here; while the "*para*" or "*trans*" acid is *meso-*. The correctness of the

configurations assigned is further indicated by the fact that the lower-melting acid gives the higher-melting anhydride, which would be expected in view of its greater symmetry.

Diethyl α-methyl α'-cyanosuccinate was methylated with purified methyl iodide[13] in 2.5 mole lots. An excess of both sodium and methyl iodide was employed so as to insure completeness of the process; this is necessary since the two esters boil within a few degrees of each other. The yield of product boiling flatly at 161.1° (21 mm.) was 85%. Hydrolysis was effected with concentrated hydrochloric acid (3 liters of acid for 968 g. of ester). The *meso*-acid, which crystallized on cooling, was repeatedly recrystallized from water with intervening treatments with cold acetyl chloride as recommended by Bone and Sprankling.[13] The melting point attained the value 209° given by these workers only on very rapid heating, inasmuch as decomposition to the anhydride is noticeable around 180°, and becomes rapid at 190°. The mother liquor from the *meso*-acid was evaporated to dryness and extracted with boiling acetone, giving the racemic acid contaminated with some of the *meso-* acid (total recovery, 83%). The dry extract was converted to the *trans*-anhydride by refluxing with acetyl chloride and distilling (b. p. 232–233°)[19]; yield, 84%. The *trans*-anhydride was recrystallized from benzene–absolute ether mixture and then sublimed *in vacuo;* m. p. 87–88°. The corresponding *cis*-anhydride was prepared from some of the best *meso*-acid by means of acetyl chloride and subsequent recrystallization from this solvent; m. p. 42°. Owing to its lability when heated, sublimation was not attempted.

Hydration of the best *trans*-anhydride yielded a calorimetric sample of *dl*-acid, m. p. 126°, with some decomposition. The behavior of both the *meso-α,β*-dimethylsuccinic acid and the corresponding *cis*-anhydride in the calorimeter was abnormal; a secondary reaction was indicated by a failure of the calorimeter to return to its normal cooling rate. The only side reaction which would seem to be possible is that of epimerization. The following test was carried out: 1 g. of the best *meso*-acid was dissolved in an excess of c. p. base at room temperature and allowed to stand for nineteen hours. At the end of this time the solution was acidified with c. p. hydrochloric acid, taken to dryness at room temperature *in vacuo* and the residue extracted with c. p. anhydrous ether in a Soxhlet apparatus. The dry extract melted over a wide range of temperature, becoming completely fluid at 184°. Epimerization would thus seem to be established.

α,α-Dimethylsuccinic Acid and Anhydride.—The procedure of Vogel[20] was adopted; the yield of ethyl α-cyanodimethacrylate boiling at 122.9–123.0° (20 mm.) was 52%. Treatment of this ester with sodium cyanide and subsequent hydrolysis with concentrated hydrochloric acid gave a 62% yield of α,α-dimethylsuccinic acid. After three recrystallizations from water the m. p. was 141–142° (dec.). Conversion to the anhydride with acetyl chloride gave an 82% yield; b. p. 222–223°. A precision distillation was unsuccessful because the anhydride solidified in the condenser; likewise sublimation failed because the material condensed as liquid, then froze and jammed the scraper.

(9) "Organic Syntheses," Vol. X1, 1931, p. 70.

(10) Anschütz and Petri, *Ber.*, **13**, 1539 (1880).

(11) The alkaline hydrolysis of methylenesuccinic anhydride pursued an abnormal course, as was shown by the failure of the calorimeter to return to its normal cooling rate after the main reaction was over. The calorimeter liquid was also brownish in color. The abnormality was not observed during neutralization of the acid, nor during hydrolysis of the isomeric methylmaleic anhydride.

(12) "Organic Syntheses," Vol. X1, 1931, p. 28.

(13) Bone and Sprankling, *J. Chem. Soc.*, 839 (1899).

(14) *Cf.* for instance, Whitmore, "Organic Chemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1937, p. 462.

(15) Werner and Basyrin, *Ber.*, **46**, 3229 (1913).

(16) Ott, *ibid.*, **61**, 2134 (1928).

(17) Bischoff and Voit, *ibid.*, **22**, 390 (1889).

(18) Bone and Perkin, Jr., *J. Chem. Soc.*, **69**, 253 (1896).

(19) Any *cis*-anhydride present is converted to the *trans*-form by this process (*cf.* ref. 18).

(20) Vogel, *J. Chem. Soc.*, 2010 (1928).

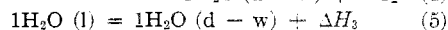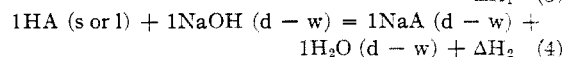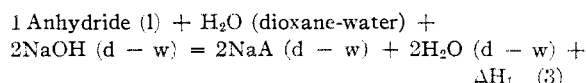It was finally recrystallized from a mixture of anhydrous ether and ligroin.

Tetramethylsuccinic Acid and Anhydride.—As starting material, commercial phorone was used. Neither repeated fractionation through our tall columns nor partial freezing sufficed to obtain a flat boiling fraction.[21] The best sample (1065 g. from 1 gallon) boiled at 103.0–104.2° (35 mm.), began to freeze at 23.4°, and had $n^{20}D$ 1.4912. Following the synthesis of Francis and Willson,[22] the steps were: (1) phorone to phorone tetrabromide, yield, 50%; (2) phorone tetrabromide to dibromophorone, yield, 67%; (3) dibromophorone to 2,2,3,3-tetramethyl-4-bromo-5-hydroxy-Δ^4-cyclopentenone-1, yield of crude product, nearly quantitative; (4) oxidation to α-ketotetramethylglutaric acid, yield, 86%; (5) keto-acid to tetramethylsuccinic acid, quantitative. The crude acid was dissolved in excess acetyl chloride and distilled. The anhydride, b. p. 218–220°, formed a white powder which quickly became sticky and reverted to a waxy mass. That this is not due to hydration has been shown by Auwers and Meyer.[23]

Successive calorimetric runs on this material showed a steadily diminishing heat of hydrolysis. Since this seemed to be due to alteration in crystal form, a portion of the anhydride was left for two weeks in contact with a saturated ether solution of the material, the ether being allowed to evaporate slowly. Large waxy crystals were deposited which underwent no change on standing. This presumably stable form of the solid was used in the calorimeter.

A portion of the best anhydride was dissolved in sodium hydroxide solution, and the acid recovered by acidification. It melted at 200–201° with decomposition (bath preheated to 190°).

Results and Discussion

The experimental results to be presented here are heats of three types of reaction. For the straight-chain anhydrides the three reactions are

1 Anhydride (1) + H_2O (dioxane-water) +
2NaOH (d — w) = 2NaA (d — w) + 2H_2O (d — w) +
$$\Delta H_1 \qquad (3)$$
1HA (s or 1) + 1NaOH (d — w) = 1NaA (d — w) +
$$1H_2O \text{ (d — w)} + \Delta H_2 \qquad (4)$$
$$1H_2O \text{ (1)} = 1H_2O \text{ (d — w)} + \Delta H_3 \qquad (5)$$

In Eqs. 3 and 4 A represents the acid radical. Taking (3) — (2 × (4)) + (5), one obtains

1 Anhydride (1) + 1H_2O (1) = 2HA (s or 1) +
$$\Delta H_1 — 2\Delta H_2 + \Delta H_3 \qquad (6)$$
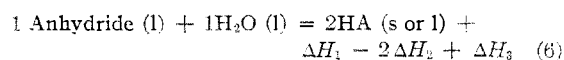
Equation (6) is identical with Eq. 2, in which the heat of hydrolysis is

$$\Delta H = \Delta H_1 — 2\Delta H_2 + \Delta H_3 \qquad (7)$$

For the cyclic anhydrides the equation corresponding to (6) is

1 Anhydride (s or 1) + 1H_2O (1) = H_2A (s or 1) +
$$\Delta H_1 — \Delta H_2 + \Delta H_3 \qquad (8)$$
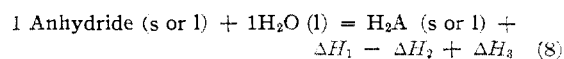
(21) Cf. Auwers and Eisenlohr. J. prakt. Chem., N. F., **84,** 77 (1911).

(22) Francis and Willson, J. Chem. Soc., **103,** 2238 (1913).

(23) Auwers and Meyer, Ber., **23,** 293 (1890).

where ΔH_2 is now the heat of neutralization of one mole of the dicarboxylic acid by two moles of sodium hydroxide.

Table I consists of the heats of hydrolysis and neutralization of the anhydrides. The letters A, B and C in the column headed "Solution" refer to the compositions of the solutions in which the reactions were carried out; these compositions are given in Table III along with the heats of dilution. Table II contains heats of neutralization of the acids. Heats of neutralization are given for some acids for which the heats of hydrolysis and neutralization of the corresponding anhydrides could not be obtained, due to side reactions. These cases were discussed in the section on preparation of materials. In Tables I and II the mean temperatures listed refer to the temperature of the thermostat bath during the reaction. This temperature was measured with a five-junction thermel, one end of which was immersed in ice. This thermel was previously calibrated against a platinum resistance thermometer. The temperature of the calorimeter during reaction in no case differed by more than one degree from that of the bath.

Table I
Heats of Hydrolysis and Neutralization, $- \Delta H_1$

Anhydride	State	Soln.	Mean temp., °C.	$- \Delta H_1$, cal. per mole	$- \Delta H_1$, mean. cal. per mole
Acetic	1	A	30.46	40174	40174
Propionic	1	B	30.44	38703	
		B	30.44	38815	38754
Isobutyric	1	A	30.44	38904	
		A	30.44	38931	38918
Trimethylacetic	1	A	30.45	37048	
		A	30.45	36924	
		A	30.45	37104	37025
Maleic	s	A	30.45	30326	
		A	30.45	30333	
		A	30.63	30310	30323
Methylmaleic	1	A	30.45	31483	
		A	30.45	31430	31457
Succinic	s	A	30.44	30183	
		·A	30.44	30202	30192
Methylsuccinic	1	A	31.04	34035	
		A	31.04	33992	34013
α,α-Dimethyl-succinic	1	A	50.12	32442	
		A	50.12	32456	32449
trans-α,β-Di-methylsuccinic	s	C	50.13	29105	
		C	50.24	29118	29112
Tetramethyl-succinic	s	A	50.12	27737	
		A	50.12	27869	27803

It was hoped that the heat of reaction of equation 1 could be obtained by conversion of the

TABLE II

HEATS OF NEUTRALIZATION, $- \Delta H_2$

Acid	State	Soln.	Mean temp., °C.	$- \Delta H_1$, cal. per mole	$- \Delta H_1$, mean, cal. per mole
Acetic	1	A	30.46	13171	13171
Propionic	1	B	30.44	12655	
		B	30.44	12643	12649
Isobutyric	1	A	30.44	12229	
		A	30.44	12235	
		A	30.44	12232	12232
		A	40.09	12085	12085
Trimethylacetic	s	A	40.03	10882	
		A	40.03	10864	10873
Maleic	s	A	30.44	22159	
		A	30.44	22107	22133
Methylmaleic	s	A	30.44	23488	
		A	30.44	23435	23462
Succinic	s	A	30.45	19143	
		A	30.45	19127	19135
Methylsuccinic	s	A	30.64	21056	
		A	30.81	21008	21032
Methylene- succinic	s	A	30.45	19485	
		A	30.45	19487	19486
α,α-Dimethyl- succinic	s	A	50.12	18899	
		A	50.12	18954	18927
meso-α,β-Di- methylsuccinic	s	A	30.55	22342	
		A	30.55	22319	22330
dl-α,β-Dimethyl- succinic	s	C	50.12	22077	
		C	50.12	22319	22061
		C	30.70	23242	
		C	30.70	23234	23238
Tetramethyl- succinic	s	A	50.12	19492	
		A	50.12	19487	19489

TABLE III

HEATS OF DILUTION, $- \Delta H_3$

Solution	Composition, % dioxane	Temp., °C.	$- \Delta H_3$, cal. per mole
A	45.5	30	136
		50	117
B	30	30	58
C	0	50	1

data of Table IV to the gaseous state by determining heats of vaporization and sublimation. A static all-glass vapor pressure apparatus was constructed which permitted accurate vapor pressure measurements in the range 0.01 to 100 mm. With this equipment measurements on many of the compounds listed in the above tables were made over a range of temperatures, with good results for liquids but with indifferent success in the case of solids. The solid compounds showed extraordinary delays in the establishment of constant vapor pressure. Furthermore, the solid dicarboxylic acids were recrystallized from solvents, and in order to free them from traces of these impurities, sublimation *in vacuo* into the

vapor pressure apparatus was attempted. It was found, however, that at temperatures at which sublimation could be effected with reasonable speed, some decomposition, attended by formation of water, occurred. This work was therefore abandoned and the incomplete data will not be reported here, since no use can be made of them in the following discussion.[24]

Our failure to reduce the data to a common and readily interpretable standard state destroys much of the force of the conclusions to be drawn from Table IV. Nevertheless, some interesting qualitative points can be brought out. In this discussion more weight will be given to values obtained in this investigation than to those determined from heats of combustion, also given in Table IV. The justifications for this choice are: (a) carefully purified materials used by us, and (b) formation of our data of Table IV as rather large differences of relatively small directly determined heat values. We are unable, however, to explain in detail the causes of the discrepancies of the two sets of data of Table IV. It will be noted first of all that methyl substitution in acetic acid has substantially no effect on the heats of hydrolysis of the corresponding anhydrides. The trimethylacetic anhydride is no exception since the heat of fusion of the acid is probably of the order of 1 to 2 kcal.,[25] thus making the heat of the liquid to liquid reaction about 13 to 14 kcal. This is in marked contrast to the well-known effect of methyl groups on the acid strength, demonstrated also by the series of the heats of neutralization given in Table II.

In the series of cyclic anhydrides of Table IV, however, methyl substitution has a very marked and systematic effect. If one allows again 1 to 2 kcal. for the heats of fusion and computes all reactions to the same state of aggregation, one sees that *unsymmetrical* methyl substitution invariably increases the heat of hydrolysis while symmetrical substitution decreases it still more markedly. Even the comparison of the trans-α,β-dimethylsuccinic and the tetramethylsuccinic anhydrides bears out this conclusion. Although we are unable to account for these effects even semiquanti-

(24) The work of F. H. MacDougall on acetic and propionic acids [THIS JOURNAL, **58**, 2585 (1936); **63**, 3420 (1941)] indicates that the very considerable association of the vapors of these acids even at low pressures seriously impairs the calculation of heats of vaporization from vapor pressures of the carboxylic acids.

(25) The heat of fusion of trimethylacetic acid is not recorded in the literature. The heats of fusion of propionic and isobutyric acids are 1.8 and 1.2 kcal., respectively.

TABLE IV

HEATS OF HYDROLYSIS, $-\Delta H$

	Present investigation			From heats of combustion		
	State		$-\Delta H$,	State		$-\Delta H$,
Anhydride	Anhydride	Acid	kcal. per mole	Anhydride	Acid	kcal. per mole
Acetic	1	1	13.96			
Propionic	1	1	13.52			
Isobutyric	1	1	14.59			
Trimethylacetic	1	s	15.12			
Maleic	s	s	8.33			
Methylmaleic	1	s	8.13			
Succinic	s	s	11.20	s	s	12.5[b]
Methylsuccinic	1	s	13.11	1	s	14.6[b]
α,α-Dimethylsuccinic[a]	1	s	13.63	s	s	12.1[b]
trans-α,β-Dimethylsuccinic[a]	s	s	7.06	s	s	7.7[b]
Tetramethylsuccinic[a]	s	s	8.43	s	s	3.1[b]

[a] Reaction carried out at 50°; all others at 30°.   [b] From heat of combustion at 15° given by Verkade and Hartman, Rec. trav. chim., **52**, 945 (1933).

tatively, it is more than probable that interactions are here involved similar to those which show themselves in the heats of hydrogenation of some five-membered carbon ring compounds[26] and which have been interpreted as "steric hindrance" between hydrogen atoms on adjacent carbons. In line with this conclusion is also the difference in the heats of hydrolysis of maleic and of succinic anhydrides, while the conventional view would take maleic anhydride for the more strained of the two five-membered rings, the data actually indicate the reverse, in line with the above-mentioned data on the cyclopentene–cyclopentane relationship.[27]

Finally, the absence of methyl substitution effects in straight-chain anhydrides, where complete freedom of orientation exists, points again to "steric hindrance" as the main if not the sole cause of the observed variations of the heats of hydrolysis. It may be noted in passing that these effects seem to bear no relation to the heats of ionization of the corresponding acids, for which Table II gives a series of relative values.

Without knowledge of the entropy changes concerned, it is rather futile to discuss in detail the relation of the thermal data obtained to the thermodynamic stability of the anhydrides and acids. It may be noted, however, that the increased stability of cyclic, as against the straight-chain, acid anhydrides, can be accounted for by their gen-

erally lower heats of hydrolysis and a probably less positive entropy change caused by a loss of mole numbers in their reaction with water. On the other hand, it is not at all probable that the increasing stability in the series succinic to tetramethylsuccinic anhydrides[28] can be so explained. Possibly some purely rate factors are here of more importance.

Summary

Heats of the hydrolytic reaction: Anhydride (s or 1) + H_2O (1) = Acid (s or 1) computed from heats of reaction in solution are reported here for a number of straight-chain and cyclic (five-membered ring) acid anhydrides.

Acetic, propionic, isobutyric and trimethylacetic anhydrides were found to have the same heat of hydrolysis, showing no effect due to methyl substitution.

Methyl substitution in the ring compounds markedly alters the heat of hydrolysis. Unsymmetrical substitution of methyl groups in succinic anhydride increases the heat of hydrolysis, while symmetrical substitution decreases it. The presence of a double bond in the ring also decreases the heat of hydrolysis.

These effects are qualitatively discussed, and similarities to the trend of heats of hydrogenation of five-membered carbon ring compounds are pointed out.

(26) Dolliver, Gresham, Kistiakowsky and Vaughan, THIS JOURNAL, **59**, 839 (1937).

(27) Some resonance interactions in maleic anhydride are not excluded, although they are unlikely in view of previous results on the heats of hydrogenation of the system —C=C—CO—O—, cf. Dolliver, Gresham, Kistiakowsky, Smith and Vaughan, ibid., **60**, 448 (1938).

(28) Verkade, Rec. trav. chim., **40**, 199 (1921).