Thermochemistry of Biologically Important Compounds

Heats of Combustion of Five Organic Acids

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Standard heats of formation, calculated from measured heats of combustion of citraconic acid, itaconic acid, α-ketoglutaric acid, *trans*-aconitic acid, and *cis*-aconitic acid, are reported for the anhydrous compound in the solid state.

THIS REPORT presents additional results on the measurement of heats of combustion of organic compounds of biochemical importance. The apparatus used, the experimental technique, and the calculation procedures were all similar to those described in a previous paper (*5*).

EXPERIMENTAL

Materials. Most samples used in the heat of combustion measurements were obtained by further purification either of commercially available materials or of samples synthesized in the laboratory. Itaconic acid, sample A was purified by sublimation at low pressure, and the *cis*-aconitic acid was used as received. Other samples were purified by recrystallization from various solvents. A brief summary of the source and method of purification is given in Table I. Table I also lists the procedure used to remove the recrystallizing solvent and the results of certain purity tests which were described in the previous report (*5*). The equivalent weights reported in Table I were the average of three or four determinations, and in all cases the difference between the highest and lowest values was less than 1 part in 5000. All samples were given a final drying, just before being used in a combustion experiment, by heating to 50° C. in vacuum for about 1 hour.

Sample purity was also tested by paper chromatography and by solvent extraction. Experiments were done to ascertain the value of these techniques in determining sample purity as well as to obtain additional information about samples used in the present series of measurements. The eluting solvent used in the paper chromatography was a mixture of 3 parts (by volume) of benzyl alcohol, 1 part *tert*-butyl alcohol, 1 part isopropyl alcohol, 1 part water, and 0.06 part formic acid. After elution, the paper was heated in an oven at 125° C. for 1 hour to remove the solvent, and then sprayed with an aqueous solution of Brom Phenol Blue, previously adjusted to a pH of 7, to develop the spots. A number of tests with known mixtures of acids were made to determine the limit of impurities which could be detected by this method. In most cases, it was difficult to detect impurities present in amounts less than about 2%, and in some cases even this amount could not be detected. The samples of *cis*- and *trans*-aconitic acids gave two spots on the paper chromatogram while all other samples used in the combustion experiments gave only one spot. The reasons for the two spots with the *cis*- and *trans*-aconitic acid have not been determined with certainty, and the authors' were not able to prepare samples which gave only one spot. It seems most likely that the aconitic acid samples were contaminated with impurities of the opposite isomer, and the R_f values of the spots obtained in the paper chromatography were consistent with this interpretation. It is also possible that the *cis*-aconitic acid contained citric acid as an impurity.

Several of the samples were analyzed by a 30-tube, Craig-type countercurrent distribution apparatus using water and *n*-butanol as the liquid phases. At the end of the extraction, the amount of acid in each tube was determined by titration with standard sodium hydroxide. This technique gave evidence of impurities in the starting samples of citraconic and *trans*-aconitic acids but not in the final samples obtained after recrystallization. Countercurrent distribution probably has value as a method for testing purity, but at least 100 tubes are needed to obtain the desired resolution.

Specific volumes of the solid acids as a function of temperature were determined by the dilatometric technique described previously (*5*). These results, along with the coefficient of expansion and the pressure coefficient of internal energy used to correct the heats of combustion to the standard state, are listed in Table II. It was assumed this pressure correction is the same for *cis*- and *trans*-aconitic acids.

Calorimetry. Heats of combustion were measured with an adiabatic bomb calorimeter previously described (*5*). One additional calibration run with N.B.S. benzoic acid sample 39h gave the heat capacity of the empty calorimeter as 24441.0 cal. ohm^{-1}. Since this was the same as the previous value of 24441.0 cal ohm^{-1} (obtained after making a small change resulting from minor repairs on the calorimeter), this value was used in calculating the values reported here. The energy unit used in these data is the defined thermochemical calorie (4.184 abs. joules), and molecular weights are based on the 1961 atomic weight scale.

DISCUSSION

The average of measured values of heats of combustion at 25° C. are reported in Table III. The values of 2σ (σ = standard deviation from the mean) listed there were calculated from the individual experimental values and include the effect of uncertainty in calibration. The values of s_a were calculated by the computer from estimates of uncertainties in experimental measurements, as previously described. These represent estimates of the uncertainties owing to calorimetric errors. The two samples of citraconic acid and of itaconic acid appeared to have the same heat of combustion so that both samples A and B were averaged

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Table I. Preparation and Properties of Samples

Sample	Starting Material	Recrystallizing Solvents	Final Treatment In Vacuum	Melting Range, °C.	Observed – Calculated: Equiv. wt.	Observed – Calculated: % C	Observed – Calculated: % H
Citraconic acid, A	Synthesized (2)	None	Over P_2O_5 room temp. 2 days, then at 55° for 1 day	83.0– 83.5	–0.006		
Citraconic acid, B	Synthesized (2)	Ether–petroleum ether then ethyl acetate–cyclohexane	Over P_2O_5 room temp. 1 week	82.5– 83.5	0.002	0.18	–0.10
Itaconic acid, A	Nutritional Biochem. Corp., No. 3058	None	Sublime at 110–120° and 10 microns	164.6–165.6	0.027	–0.06	–0.06
Itaconic acid, B	Nutritional Biochem. Corp., No. 3058	Twice dioxane	Room temp. 3 days, then 60° for 2 days	165.7–166.0	0.017		
α-Ketoglutaric acid, A	Nutritional Biochem. Corp., No. 6397	Acetone–benzene then ethyl acetate–benzene	Room temp. 2 days, 40° for 4 days	117.2–118.2	0.047	0.22	0.00
α-Ketoglutaric acid, B	Nutritional Biochem Corp., No. 6397	Twice from ethyl acetate	Room temp. 1 week, then 52° for 6 hours	115.0–115.6	0.326		
trans-Aconitic acid, A	Synthesized (*1*)	Twice from water	60° for 16 hours	182.5–182.7[a]	–0.479		
trans-Aconitic acid, B	Nutritional Biochem. Corp., No. 6545	Twice from glacial acetic acid	Over NaOH room temp. 1 week, then at 50° for 2 days	183.2–183.4	0.006	0.06	0.02
cis-Aconitic acid	Cal. Corp. for Biochem. Research, No. 1130	No further treatment			0.178	–0.01	0.01

[a] Decomposition temperature.

Table II. Coefficients in the Specific Volume Formula, $V = a + bt + ct^2$ (V in ml. gram^{-1} and t in °C.), Coefficient of Expansion, and Coefficient of Internal Energy for the Organic Acids

Compound	Temp. Range, °C.	a	$b \times 10^4$	$c \times 10^6$	$(\partial V/\partial T)_p \times 10^4$, Ml. G.$^{-1}$ Deg.$^{-1}$ at 25° C.	$(\partial E/\partial p)_T \times 10^3$, Cal. G.$^{-1}$ Atm.$^{-1}$ at 25° C.
Citraconic acid	10–31	0.7415	5.168		5.168	–3.73
Itaconic acid	33–85	0.6689	1.627	0.060	1.657	–1.20
α-Ketoglutaric acid	7–85	0.6047	1.776	–0.092	1.730	–1.25
trans-Aconitic acid	25–85	0.6256	1.596	0.246	1.719	–1.24

Table III. Average Heats of Combustion

Compound	Samples	Number of Measurements	Average $-\Delta E_c^\circ$ Cal. G.$^{-1}$	2σ	s_a
Citraconic acid	A, B	8	3677.6	2.66	0.61
Itaconic acid	A, B	8	3646.9	1.09	0.60
α-Ketoglutaric acid	A	4	2947.2	2.86	0.76
α-Ketoglutaric acid	B	4	2939.7	0.56	0.95
α-Ketoglutaric acid	A, B (corr.)	8	2946.8	1.41	0.59
trans-Aconitic acid	A	3	2713.4	2.48	0.96
trans-Aconitic acid	B	4	2731.1	2.42	0.68
cis-Aconitic acid		4	2742.3	6.8	0.67

Table IV. Heats of Formation from Elements in Their Standard States at 25° C.

Compound	Molecular Weight	Heat of Formation, $-\Delta H_f^\circ$, Kcal. Mole^{-1} Experimental	Other data (*4*)
Citraconic acid	130.10	197.04 ± 0.35	195.8
Itaconic acid	130.10	201.03 ± 0.14	199.6
α-Ketoglutaric acid	146.10	245.35 ± 0.21	
trans-Aconitic acid	174.11	294.63 ± 0.6	294.2
cis-Aconitic acid	174.11	292.7 ± 1.8	

together in Table III. These averages were used to calculate the data in Table IV for these two compounds. However, the heat of combustion of the two samples of *trans*-aconitic acid were noticeably different. Table I shows that sample A has a lower equivalent weight and lower melting point than does sample B. It seems likely that sample A contains some impurity, and only the data for sample B were used in calculating the heat of formation of *trans*-aconitic acid in Table IV.

The heats of combustion of the two samples of α-ketoglutaric acid are also significantly different. Table I shows that the equivalent weight of sample B is higher than the theoretical value for pure α-ketoglutaric acid. If it is assumed that this high equivalent weight is due to the presence of water in the sample, a correction can be applied to the heat of combustion. This corrected value for sample B is −2946.3 cal. gram^{-1} which differs from sample A by not much more than the calorimetric uncertainty. Therefore this seems to be the correct interpretation and the values listed in Table III as A, B (corr.) were obtained by adding 6.6 to each of the individual values of Sample B and then averaging the values for A and B together. This result was used to calculate the value for α-ketoglutaric acid in Table IV.

Because of its instability, rigorous drying conditions were not used for *cis*-aconitic acid, and it is possible that these samples contained some water. The high equivalent weight shown in Table I indicates this. On this basis, the corrected heat of combustion of *cis*-aconitic acid is −2745.1 cal. gram^{-1}. However, since there was no way to check this result, and since the size of the correction is less than the experimental uncertainty, the original uncorrected value was retained in calculating the value in Table IV. Purity tests described earlier indicate that both the *cis*- and *trans*-aconitic acids were contaminated with the other isomer. However the difference in heats of combustion of these two isomers is only 11 cal. gram^{-1}, and a significant error in the data could be produced only by a large amount of impurity.

The standard state heats of formation at 25° C. which are listed in Table IV were calculated from the experimental data of Table III using the N.B.S. values (*3*) of the heats of formation of carbon dioxide and liquid water with appropriate corrections to the 1961 atomic weight scale. The uncertainties were based on the values of 2σ listed in Table III. The uncertainties for *cis*- and *trans*-aconitic acids were increased by 50% to allow for the possible effect of impurities in these samples. The literature values shown in Table IV for comparison were obtained by recalculating the experiemntal data of Stohman (*4*) in terms of modern units and atomic weights.

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Heats of Mixing of Some Alcohol-Hydrocarbon Systems

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Heats of mixing at 30° and 45° C. are reported for the liquid binary systems made up of ethanol with *n*-hexane and *n*-nonane, *n*-propanol with *n*-heptane, *n*-butanol with *n*-heptane, *n*-pentanol with *n*-hexane, and *n*-octanol with *n*-heptane and *n*-nonane.

AS PART of a continuing and comprehensive study of thermodynamic properties of alcohol-hydrocarbon systems, extensive experimental measurements were made of heats of mixing of the following alcohol-normal hydrocarbon binary systems at 30° and 45° C.: ethanol-*n*-hexane, ethanol-*n*-nonane, *n*-propanol-*n*-heptane, *n*-butanol-*n*-heptane, *n*-pentanol-*n*-hexane, *n*-octanol-*n*-heptane, and *n*-octanol-*n*-nonane. The measurements were made with an isothermal dilution calorimeter similar to that described by Mrazek and Van Ness (*4*). However, many modifications and refinements in detail have been incorporated into the present version of this calorimeter. The purpose here is exclusively the disclosure of data.

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