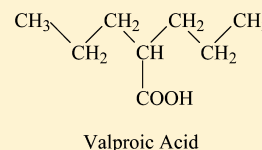


Vaporization Enthalpy and Vapor Pressure of Valproic Acid by Correlation Gas Chromatography

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ABSTRACT: The vaporization enthalpy of valproic acid (2-propylpentanoic acid) is reported, and the vapor pressures of a series on aliphatic carboxylic acids are used to evaluate its vapor pressure as a function of temperature. The vaporization enthalpy was derived by correlation-gas chromatography. This resulted in a vaporization enthalpy, $\Delta H_{\text{vap}}(298.15 \text{ K})$ of $(74.8 \pm 2.4) \text{ kJ}\cdot\text{mol}^{-1}$. Vapor pressures from $T/\text{K} = 298.15$ to boiling temperature of valproic acid are also reported. A normal boiling temperature of $T/\text{K} = 492.8$ (lit., 494–5 K) and a vapor pressure of $(2.2 \pm 0.3) \text{ Pa}$ has been evaluated for valproic acid at $T/\text{K} = 298.15$. This compares favorably with an Environmental Protection Agency estimate of 6.1 Pa.



INTRODUCTION

Valproic acid, 2-propylpentanoic acid, Figure 1, and its sodium salt, also marketed under various trade names including,

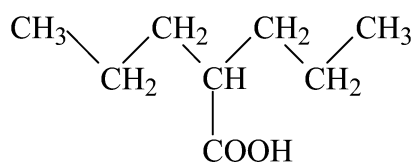


Figure 1. Structure of valproic acid.

Valparin, Depakote, Depakote ER, Depacon, and Stavzor, has been used clinically in the treatment of bipolar disorder, epilepsy, other mood disorders, and for neuropathic pain and fibromyalgia.^{1,2} It has also been of recent interest in HIV treatment³ although further studies found no long-term benefits from its use.⁴ Valproic acid may also have implications in the treatment of various cancers.^{5,6} Despite the fact that valproic acid has been in use in various therapies for over 30 years, there is very little information available regarding its thermochemical properties in the literature. The Environmental Protection Agency (EPA), for example, cites a vapor pressure of 6.1 Pa at $T/\text{K} = 298$, and this is an estimated value.⁷ Similarly, for its vaporization enthalpy, an estimated value of $(50.3 \pm 6.0) \text{ kJ}\cdot\text{mol}^{-1}$ is predicted by ACD Laboratories software as cited by SciFinder Scholar.⁸ Another simple equation for the estimation of vaporization enthalpies of singly substituted alkanes such as valproic acid is given by eq 1:

$$\begin{aligned} \Delta H_{\text{vap}}(298\text{K})/\text{kJ}\cdot\text{mol}^{-1} \\ = 4.69(n_{\text{C}} - n_{\text{Q}}) + 1.3n_{\text{Q}} + 3 + b_i \end{aligned} \quad (1)$$

where n_{C} identifies the total number of carbon atoms, n_{Q} refers to the number of quaternary sp^3 carbons atoms, and b_i is the contribution of the functional group, in this case the carboxylic acid.⁹ Using the group value for a carboxylic acid, 38.8, results in a vaporization enthalpy of $79.3 \text{ kJ}\cdot\text{mol}^{-1}$ for valproic acid, a significantly different estimation. This article reports the vapor pressure of valproic acid from (298.15 to 492.8) K, the boiling

temperature at 101.325 kPa, and the vaporization enthalpy at $T/\text{K} = 298.15$, both derived by correlation-gas chromatography.

The measurement of vaporization enthalpy and liquid vapor pressure by correlation-gas chromatography is a relatively simple experiment. The method is applicable to both liquids and solids provided appropriate standards are available with reliable vaporization enthalpies and liquid vapor pressures. The technique is particularly well suited for measuring vaporization enthalpies and vapor pressures of homologous series.^{10,11} For valproic acid, the *n*-alkanoic acids from pentanoic to undecanoic acid were used as standards. The vaporization enthalpies of these acids have been reported numerous times.¹² We have used the work of DeKruif et al.¹³ who has reviewed literature vapor pressure data and has reported both vaporization enthalpies and vapor pressures of all the acids used as standards with the exception of pentanoic acid. The vaporization enthalpy reported by Verevkin was used for pentanoic acid.¹⁴ Since not all of the vaporization enthalpies are available at a common temperature, eq 2 was used to adjust these values to $T/\text{K} = 298.15$.¹⁵ The $C_p(l, 298 \text{ K})$ term in eq 2 refers to the heat capacity of the liquid and was estimated by group additivity.¹⁶ The vaporization enthalpies of the standards and their adjustment to a common temperature, $T/\text{K} = 298.15$, are reported in Table 1.

$$\begin{aligned} \Delta H_{\text{vap}}(298.15\text{K})/(\text{kJ}\cdot\text{mol}^{-1}) \\ = \Delta H_{\text{vap}}(T_{\text{m}})/(\text{kJ}\cdot\text{mol}^{-1}) \\ + [(10.58 + 0.26C_p(1, 298 \text{ K})/(\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1})) \\ (T_{\text{m}}/\text{K} - 298.15)]/1000 \end{aligned} \quad (2)$$

In the protocol that was followed, the standards were injected simultaneously with the target substance along with a nonretained analyte, which measured elution time. The vapor pressure of each analyte governs its movement on the column.

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Table 1. Vaporization Enthalpies and Estimated Heat Capacities of the Standards and Their Temperature Adjustment to $T/K = 298.15$

	$\Delta H_{\text{vap}}(T_m)$	T_m	$C_p(l, 298 \text{ K})$	$\Delta C_p \Delta T^a$	$\Delta H_{\text{vap}}(298.15 \text{ K})$	ref
	$\text{kJ}\cdot\text{mol}^{-1}$	K	$\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$	$\text{kJ}\cdot\text{mol}^{-1}$	$\text{kJ}\cdot\text{mol}^{-1}$	
pentanoic acid	63.0 ± 0.5	298.15	218		63.0 ± 0.5	14
hexanoic acid	69.2 ± 0.9	298.15	249.9		69.2 ± 0.9^b	14
hexanoic acid	64.9 ± 0.1	352.4	249.9	4.10 ± 0.9	69.0 ± 0.9^b	13
octanoic acid	81.0 ± 0.6	298.15	313.7		81.0 ± 0.6^c	14
octanoic acid	80.0 ± 0.2	290	313.7	-0.75 ± 0.1	79.3 ± 0.2^c	13
decanoic acid	88.6 ± 2.0	313.8	377.5	1.70 ± 0.3	90.3 ± 2.0	13
undecanoic acid	90.7 ± 1.3	322.8	409.4	2.88 ± 0.4	93.6 ± 1.4	13

^aCalculated using the second term of eq 2. ^bAn average value of (69.1 ± 0.9) was used in subsequent correlations. ^cAn average value of (80.1 ± 0.9) was used in subsequent correlations.

Measurement of the amount of time each analyte spends on the column, t_a , is inversely proportional to its vapor pressure off the column. The adjusted retention time, t_a' , is evaluated as the difference between the retention time of each analyte and that of a nonretained reference. The temperature dependence of t_a provides a convenient measure of the analyte's vapor pressure and interaction with the column. A plot of $\ln(t_o/t_a)$ versus $1/T$ run isothermally, usually over a 30 K range, results in a linear relationship with a slope equal to the negative of the enthalpy of transfer of the analyte from the column's stationary phase to the gas phase, $\Delta H_{\text{tm}}(T)$, divided by the gas constant.¹⁷ The term t_o refers to a reference time, 1 min. The following thermodynamic relationship relates the analyte's enthalpy of transfer to its vaporization enthalpy, $\Delta H_{\text{vap}}(T_m)$:

$$\Delta H_{\text{tm}}(T_m) = \Delta H_{\text{vap}}(T_m) + \Delta H_{\text{intr}}(T_m) \quad (3)$$

where the term $\Delta H_{\text{intr}}(T_m)$ is a measure of the enthalpy of interaction of each analyte with the column at some mean temperature, T_m . The enthalpy of transfer, $\Delta H_{\text{tm}}(T_m)$, has been found to correlate linearly with $\Delta H_{\text{vap}}(T)$ even though temperature T differs from T_m . Temperature T usually refers to $T/K = 298.15$. A study of how the magnitude of $\Delta H_{\text{tm}}(T_m)$ compares with $\Delta H_{\text{vap}}(T_m)$ both derived at T_m suggests that the $\Delta H_{\text{vap}}(T_m)$ makes the largest contribution to $\Delta H_{\text{tm}}(T_m)$.¹⁷ The quality of data available for the standards and appropriate selection of standards usually governs the quality of the correlations. Additional details regarding the relationships between $\Delta H_{\text{tm}}(T_m)$, $\Delta H_{\text{vap}}(T_m)$, and $\Delta H_{\text{intr}}(T_m)$ are available.¹⁷

Similarly, vapor pressures can be evaluated by correlating $\ln(p/p_o)$ with $\ln(t_o/t_a)$ of the standards as a function of temperature. In this instance, reliable vapor pressures are available for all but one of the alkanolic acids used as standards from $T/K = 298.15$ to their respective boiling temperatures at $p/\text{Pa} = 101.325$.¹³ Although the vapor pressure of pentanoic acid is available over a narrow temperature range near ambient temperatures,¹⁴ this compound was also treated as an unknown and used as a test subject to evaluate the reliability of the correlations as discussed below.

MATERIALS AND METHODS

The origin of the carboxylic acids used in this study and their purities are described in Table 2. Additionally, they were also analyzed by gas chromatography. Their purities were consistent with Table 2. Unlike other studies where thermochemical properties are highly dependent on purity, all were analyzed as mixtures, separated by the chromatography. All experiments were performed on an HP 5890 Gas Chromatograph equipped with

Table 2. Suppliers of the Acids of This Study

	supplier	purity wt %
valproic acid	Sigma	pharmaceutical grade
pentanoic acid	SAFC St. Louis MO	99 %
hexanoic acid	SAFC St. Louis MO	98 %
octanoic acid	Sigma	98+ %
decanoic acid	SAFC St. Louis MO	98+ %
undecanoic acid	Eastman White Label	99 %

a flame ionization detector and run at a split ratio of approximately 100/1. Retention times were recorded on an HP Chemstation. The compounds were run isothermally on a 0.32 mm ID, 30 m J&W FFAP column. Column temperatures were monitored independently using a Fluke digital thermometer. The temperature maintained by the gas chromatograph was constant to ± 0.1 K. Helium was used as the carrier gas. Methylene chloride was used as the solvent, and at the temperatures of these experiments, it also served as the nonretained reference. The nonretained reference can be identified since its retention time increases slightly with temperature due to an increase in the viscosity of the carrier gas. The enthalpies of transfer measured depend both on the nature of the column and various instrumental parameters used such as flow rate and temperature. The results following the correlation with the vaporization enthalpies, however, remain independent of the experimental conditions.

Adjusted retention times, t_a' , were calculated by the difference between the retention time of the analyte and that of the nonretained reference. This was repeated over a 30 K range at 5 K intervals. The slope of the line obtained multiplied by the gas constant resulted in $-\Delta H_{\text{tm}}(T_m)$.

Correlation of the vaporization enthalpies of the standards with the enthalpies of transfer resulted in a linear relationship from which the vaporization enthalpy of the target could be evaluated. In a similar fashion, the vapor pressures of the standards, $\ln(p/p_o)$, were correlated with $\ln(t_o/t_a)$. This also resulted in a linear relationship from which $\ln(p/p_o)$ of the target was evaluated as described below. This procedure was repeated at 10 K intervals from $T/K = 298.15$ to the boiling temperature of the most volatile standard.

An uncertainty of $16 \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$ was used for the uncertainty in the $C_p(l)$ term of eq 2.¹² The uncertainties in the slope and intercept of the equations listed at the bottom of each respective run were used to calculate the values listed in the last column of Table 4. These uncertainties are a measure of the precision of the measurements. Although the results obtained from the correlations are highly reproducible, we have found that experiments conducted at different times can not be

Table 3. Experimental Retention Times (min) of Valproic Acid and Standards

Run 1 T/K	435.4	440.4	445.2	450.1	455.0	460.0	465.0
	t/min						
CH ₂ Cl ₂	1.219	1.223	1.227	1.242	1.226	1.254	1.243
pentanoic acid	2.292	2.141	2.013	1.917	1.809	1.761	1.685
hexanoic acid	2.890	2.637	2.427	2.265	2.100	2.007	1.895
valproic acid	3.650	3.259	2.939	2.689	2.450	2.299	2.140
octanoic acid	5.164	4.496	3.955	3.527	3.141	2.875	2.624
decanoic acid	10.274	8.589	7.252	6.202	5.309	4.652	4.089
undecanoic acid	14.78	12.148	10.08	8.465	7.119	6.116	5.282
Run 2 T/K	435.2	440.2	445.2	450.1	455.1	460.1	465.1
	t/min						
CH ₂ Cl ₂	1.203	1.218	1.22	1.232	1.242	1.249	1.254
pentanoic acid	2.274	2.131	2.00	1.904	1.823	1.753	1.694
hexanoic acid	2.874	2.629	2.415	2.251	2.116	2.001	1.904
valproic Acid	3.641	3.261	2.935	2.679	2.471	2.299	2.155
octanoic acid	5.158	4.498	3.949	3.515	3.164	2.877	2.640
decanoic acid	10.284	8.606	7.256	6.188	5.342	4.669	4.121
undecanoic acid	14.792	12.163	10.081	8.442	7.154	6.135	5.318

Table 4. Results of the Correlations Obtained Between Enthalpies of Transfer Measured From $\ln(t_o/t_a)$ vs $1/T$ Plots and Literature Vaporization Enthalpies

run 1	slope ^a T		ΔH_{tm} (450 K)	ΔH_{vap} (298 K) (lit)	ΔH_{vap} (298 K) (calcd)
	K	intercept ^a	kJ·mol ⁻¹	kJ·mol ⁻¹	kJ·mol ⁻¹
pentanoic acid	-5674.8	12.972	47.177	63.0	63.1 ± 2.4
hexanoic acid	-6178.1	13.684	51.362	69.1	69.2 ± 2.4
valproic acid	-6640.2	14.369	55.204		74.7 ± 2.5
octanoic acid	-7076.1	14.886	58.828	80.1	79.9 ± 2.6
decanoic acid	-7881.5	15.904	65.524	90.3	89.6 ± 2.7
undecanoic acid	-8269.9	16.393	68.753	93.6	94.3 ± 2.8

run 2	slope T		ΔH_{tm} (450 K)	ΔH_{vap} (298 K) (lit)	ΔH_{vap} (298 K) (calcd)
	K	intercept	kJ·mol ⁻¹	kJ·mol ⁻¹	kJ·mol ⁻¹
pentanoic acid	-5287.1	12.092	43.95	63.0	62.8 ± 2.0
hexanoic acid	-5885.8	13.021	48.93	69.1	69.4 ± 2.1
valproic acid	-6381.4	13.781	53.05		74.9 ± 2.2
octanoic acid	-6867.5	14.413	57.09	80.1	80.3 ± 2.2
decanoic acid	-7703.9	15.503	64.05	90.3	89.6 ± 2.4
undecanoic acid	-8106.1	16.024	67.39	93.6	94.0 ± 2.5

^aThe slope and intercept of the line obtained by plotting $\ln(t_o/t_a)$ against $1/T$.

$$\Delta H_{\text{vap}}(298.15 \text{ K})/\text{kJ}\cdot\text{mol}^{-1} = (1.44 \pm 0.03)\Delta H_{\text{tm}}(450 \text{ K}) - (4.97 \pm 1.83) \quad r^2 = 0.9986 \quad (4)$$

$$\Delta H_{\text{vap}}(298.15 \text{ K})/\text{kJ}\cdot\text{mol}^{-1} = (1.33 \pm 0.03)\Delta H_{\text{tm}}(450 \text{ K}) - (4.12 \pm 1.6) \quad r^2 = 0.9987 \quad (5)$$

combined. The enthalpies of transfer measured can vary substantially from day to day for various reasons. It is therefore important that all the data for each correlation be obtained sequentially over a reasonably short period of time and under identical conditions. Variations in flow rate, column aging, and temperature reproducibility from day to day are some causes responsible. The absolute uncertainty in our vaporization enthalpies have generally been within $\pm 4 \text{ kJ}\cdot\text{mol}^{-1}$.^{10-12,15-17}

Retention Times. The experimental retention times for duplicate runs are reported in Table 3. Both runs were conducted at a mean temperature of $T_m/\text{K} = 450$.

RESULTS

The results of the correlations between $\ln(t_o/t_a)$ vs $1/T$ are provided in Table 4, for runs 1 and 2. Figure 2 also provides a visual assessment of the quality of the correlation for run 1. Equations 4 and 5 located below each run in Table 4 define the equation of the line obtained by correlating the vaporization enthalpies of the standards at $T_m/\text{K} = 298.15$ with their corresponding enthalpies of transfer measured at $T_m/\text{K} = 450$ by linear regression.

In this instance, there are no other experimental results in the literature for comparison. As noted above, the vapor pressures of most of the compounds used as standards have been previously evaluated by DeKruif et al.¹³ as a function of temperature. While the only vapor pressure available for valproic acid is an EPA estimate, an alternate method of validating the results reported in Table 4 is to evaluate the vapor pressures of valproic acid as a function of temperature and then to use the results to estimate its boiling temperature. The experimental boiling temperature of valproic acid has been previously reported.

Vapor Pressures. The vapor pressures of the alkanolic acids from hexanoic to octadecanoic acid in the literature evaluated by DeKruif et al.¹³ have been fit by these authors to the equation of Clarke and Glew,¹⁸ eq 6. Values for the thermodynamic parameters used in eq 6 are provided in Table 5.

$$R \cdot \ln(p/p_o) = -\Delta G^\circ(\theta)/\theta + \Delta H^\circ(\theta)(1/\theta - 1/T) + \Delta C_p(\theta)\{\theta/T - 1 + \ln(T/\theta)\} \quad (6)$$

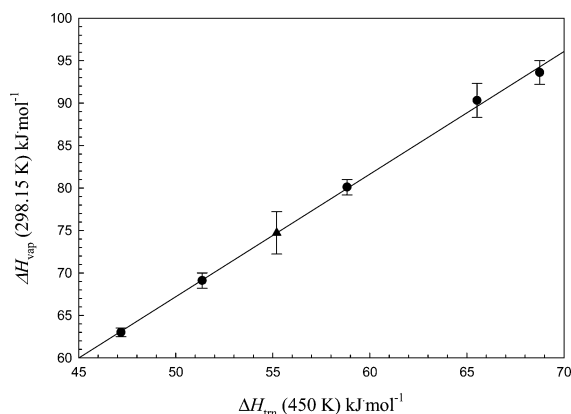


Figure 2. Plot of $\Delta H_{\text{vap}}(298.15 \text{ K})$ against $\Delta H_{\text{tm}}(450 \text{ K})$ of the standards (●) for run 1 (Table 4). Uncertainties of the standards are experimental values. The line was calculated by a linear regression, eq 4. The triangle (▲) represents the value and uncertainty associated with vaporic acid calculated from the correlation.

The terms $\Delta G^\circ(\theta)$ and $\Delta H^\circ(\theta)$ refer to the Gibbs energy and enthalpy difference between the vapor and condensed phase, θ refers to a reference temperature and is the average temperature of the experimental results while p_o is a reference pressure, 1 Pa, and R is the universal gas constant. Prior to use, the vapor pressures calculated from eq 6 for each standard were divided by p_{atm} where $p_{\text{atm}}/\text{Pa} = 101\,325$ and then converted to the natural logarithm, $\ln(p/p_{\text{atm}})$.

Vapor pressure data over an extended temperature range are not available for pentanoic acid, and therefore, this substance was also treated as an unknown along with valproic acid. Results for pentanoic acid could then be used as an additional means of evaluating the quality of the vapor pressures calculated by this correlation. Table 6 provides an example of how the vapor pressures of pentanoic and valproic acid were evaluated. Using the results from Table 4, run 1, calculated values of $\ln(p/p_{\text{atm}})$ of the standards were correlated against $\ln(t_o/t_a)_{\text{std}}$, both at $T_m/\text{K} = 298.15$. Figure 3 illustrates the results of these correlations. Correlation eq 7 of the standards listed below Table 5 was used to evaluate the vapor pressures of both acids at this temperature. Similar correlations between $\ln(p/p_{\text{atm}})_{\text{std}}$ and $\ln(t_o/t_a)_{\text{std}}$ were repeated at 10 K intervals from $T/\text{K} = (298.15 \text{ to } 480)$, the boiling temperature of the lowest standard, hexanoic acid. This set of correlations was also repeated using the results of the second run. The correlation coefficient, r^2 , exceeded 0.999 over the entire range of temperature for all correlations between $\ln(p/p_{\text{atm}})_{\text{std}}$ and $\ln(t_o/t_a)_{\text{std}}$ for both runs. The resulting $\ln(p/p_{\text{atm}})$ values for both pentanoic and valproic acid calculated from the correlation equations of the standards were then fit to a third order polynomial, eq 8. The coefficients of eq 8 for both acids treated as unknowns are provided in Table 7.

Table 5. Thermodynamic Properties of the Carboxylic Acid Standards Used in eq 6^a

	θ	$-\Delta G^\circ(\theta)$	$\Delta H^\circ(\theta)$	$-\Delta C_p(\theta)$	$p(\theta)$
	K	J·mol ⁻¹	J·mol ⁻¹	J·mol ⁻¹ ·K ⁻¹	Pa
hexanoic acid	352.36	17740 ± 20	64890 ± 50	75 ± 3	427 ± 3
octanoic acid	370.18	17070 ± 20	72300 ± 60	96 ± 3	256 ± 2
decanoic acid	389.39	17160 ± 20	78920 ± 40	111 ± 2	200 ± 1
undecanoic acid	395.80	16660 ± 10	82180 ± 30	122 ± 1	158 ± 1

^aFrom reference 13.

Table 6. Correlation of $\ln(t_o/t_a)$ with Experimental $\ln(p/p_{\text{atm}})$ Values at $T/\text{K} = 298.15^a$

	slope T/K	intercept	$\ln(t_o/t_a)$	$\ln(p/p_{\text{atm}})$ lit	$\ln(p/p_{\text{atm}})$ calcd
pentanoic acid	-5674.77	12.972	-6.062		-8.32
hexanoic acid	-6178.12	13.684	-7.038	-9.631	-9.54
valproic acid	-7076.13	14.886	-7.902		-10.70
octanoic acid	-7881.54	15.904	-8.848	-11.946	-11.96
decanoic acid	-8269.92	16.393	-10.53	-14.207	-14.21
undecanoic acid	-6640.23	14.369	-11.345	-15.292	-15.30

$$^a \ln(p/p_{\text{atm}})_{\text{calcd}} = (1.316 \pm 0.011) \ln(t_o/t_a) - (0.344 \pm 0.107) \quad r^2 = 0.9999 \quad (7)$$

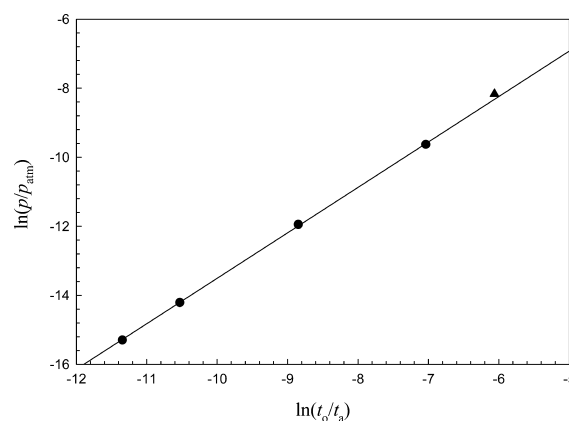


Figure 3. Plot of $\ln(p/p_o)$ against $\ln(t_o/t_a)$ of the standards (●) at $T/\text{K} = 298.15$ for run 1 (Table 4). The literature value of pentanoic acid (▲) at $T/\text{K} 298.15^{14}$ was not used in evaluating the line obtained by linear regression, eq 8.

Table 7. Coefficients of eq 8 for Pentanoic and Valproic Acids from Runs 1 and 2

	run	$A \times 10^{-5}$	$B \times 10^{-3}$	C	D
pentanoic acid	1	1406	-1698	-888.5	8.454
	2	1506	-1782	-553.6	8.012
valproic acid	1	2840	-2943	1481	6.739
	2	1655	-2048	-751.8	8.577

$$\ln(p/p_{\text{atm}})_{\text{calcd}} = A(T/\text{K})^{-3} + (BT/\text{K})^{-2} + (CT/\text{K})^{-1} + D \quad (8)$$

The coefficients reported in Table 7 for pentanoic acid were derived by using calculated data from (298.15 to 460) K, 460 K

Table 8. Summary of the Vaporization Enthalpy and Vapor Pressure of Valproic Acid

	run	$\Delta H_{\text{vap}}(298 \text{ K})$	boiling temperature/K		$p(298.15 \text{ K})/\text{Pa}$	
		$\text{kJ}\cdot\text{mol}^{-1}$	calcd	exptl ^a	calcd	lit
pentanoic acid	1		461.9	459–461 ^a	21.2 ± 4	27.3 ^c
	2		462.3		27.5 ± 2	
valproic acid	1	74.7 ± 2.5	492.8	494–495, ^a 492.7 ^b	2.2 ± 0.4	6.1 ^d
	2	74.9 ± 2.2	492.7		2.2 ± 0.1	
average		74.8 ± 2.4	492.8		2.2 ± 0.3	

^aReference 21. ^bReference 7. ^cReference 14. ^dReference 7.

being the highest 10 K interval at which $\ln(p/p_{\text{atm}})$ remained negative. For valproic acid, vapor pressures calculated up to $T/\text{K} = 480$ were used, the highest temperature at which $\ln(p/p_{\text{atm}})_{\text{std}}$ of all the standards remained negative. The boiling temperature was then calculated by extrapolating eq 7 until $\ln(p/p_{\text{atm}})$ for valproic acid changed signs. Equation 8 has been found previously to extrapolate well with temperature.^{10,11,19,20}

SUMMARY

Table 8 summarizes the results of this study. A vaporization enthalpy of $(74.8 \pm 2.4) \text{ kJ}\cdot\text{mol}^{-1}$ has been measured, which varies substantially from the estimated value of $(50.29 \pm 6.0) \text{ kJ}\cdot\text{mol}^{-1}$ using the ACD Laboratories software as cited by SciFinder Scholar.⁸ The value calculated by eq 1, $79.3 \text{ kJ}\cdot\text{mol}^{-1}$, is in better agreement with the experimental value. The boiling temperatures calculated for both pentanoic acid valproic acids are within the various experimental boiling temperatures. Similarly, the vapor pressure evaluated for pentanoic acid at $T/\text{K} = 298.15$ is within a few Pascals of the literature value reported for pentanoic acid,¹⁴ and the value derived for valproic acid agrees well with the EPA estimate.⁷

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Notes

The authors declare no competing financial interest.

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