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SYNTHESIS AND THERMODYNAMIC PARAMETERS OF PHASE TRANSITIONS OF 3-(1-R-5-PHENYL-1*H*-PYRROL-2-YL) PROPANOIC ACID DERIVATIVES

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Abstract. A series of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl)propanoic acids (R = H, Ar, Alk, Hetaryl) was obtained via the reaction of 4,7-dioxo-7-phenylheptanoic acid with amines. The enthalpies of vaporization and fusion of eight compounds were experimentally determined using differential thermal and thermogravimetric methods of analysis for the first time. Based on the experimentally determined thermodynamic parameters of the melting process, an analytical method for calculating the enthalpy of fusion from the specific value of the entropy of fusion for substances with an arylpyrrole fragment is proposed. Calculating methods for the enthalpies of sublimation using the data of derivatographic studies are analyzed. Recalculation of the enthalpies of phase transitions to 298.15 K was performed.

Keywords: synthesis, enthalpy of sublimation, enthalpy of fusion, enthalpy of vaporization, pyrrole derivatives; N-substituted 3-(5-phenylpyrrol-2-yl) propanoic acids.

1. Introduction

Heterocyclic compounds with a nitrogen atom are widespread in nature, since they are involved in many biological processes.[1] Among them there are compounds with a pyrrole fragment which are found in alkaloids, chlorophyll, vitamin B_{12}, hemoglobin, and cytochromes.[2,3] Due to its aromatic nature, pyrrole exhibits the ability to react with electrophilic reagents, which allows it to be used for synthesizing a wide range of substances with predetermined pharmacophore properties.[4,5] Thus, pyrrole derivatives, which in addition to the pyrrole ring contain one or more aryl fragments, are capable of exhibiting antitumor, antibacterial, antioxidant, and analgesic effectts.[6–8] Apart from being used in pharmaceuticals, substances with a pyrrole fragment are also used in the chemical industry for the synthesis of catalysts, materials with increased electrical conductivity, corrosion inhibitors, dyes, and plant protection products.[9,10] Considering the mentioned properties and the industries where they are actively used, there is a need for the availability of thermodynamic parameters related to phase transitions, in particular, the enthalpies of fusion, vaporization, and sublimation.

The obtained thermodynamic parameters of phase transitions will serve for the development and optimization of existing processes of synthesis, processing, storage, and transportation of substances of this class. The values of enthalpies of vaporization allow to refine the Hansen parameters for the dissolution process to improve the accuracy of solubility prediction.[11] In particular, the value of the enthalpy of sublimation estimates the volatility of a substance to maintain optimal storage conditions, since substances with a low value of the enthalpy of sublimation are subject to faster mass loss.[12] The enthalpy of fusion is used to determine the thermosdynamic parameters of the dissolution process, which allows to quantify the present intermolecular interactions.[13] The thermodynamic parameters of the melting process also affect the active pharmaceutical ingredients (APIs), which are a key factor in drug development.[14]

The enthalpies of vaporization and sublimation are related to the enthalpies of evaporation, which are experimentally determined by direct and indirect methods. Direct (calorimetric) methods of experimental determination allow determining the enthalpies of evaporation under standard

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conditions directly at a temperature of 298.15 K.[15] However, this method is applicable for substances with a high value of saturated vapor pressure, which causes the ability of the substance to sublimate/evaporate at low temperatures. Taking into account the modern needs of the chemical and pharmaceutical industries, newly synthesized substances are usually polyfunctional with a high molecular weight, the structures of which, on the contrary, cause low values of saturated vapor pressure. In such cases, indirect methods are used to calculate the enthalpies of evaporation from the temperature dependence of saturated vapor pressure or mass loss of a sample per unit time, followed by the Clapeyron equation[16,17] for evaporation processes. In recent years, along with the Knudsen diffusion method, which determines the temperature dependence of saturated vapor pressure, the thermogravimetric method of analysis has been used. The advantage of this method is the use of a small amount of the test substance, the ability to conduct the experiment in a wide temperature range, and a shorter process time.[18–20] As for the experimental enthalpies of fusion determination, the differential thermal method or the method of differential scanning calorimetry is usually used.

Considering the above, arylpyrrole derivatives, namely some 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl)propanoic acids, were studied for the experimental determination of the thermodynamic parameters of phase transitions. For this class of substances, a wide range of biological activity has been established, which makes it possible to use them as drug components.[21] This study is a continuation of the experimental determination of the thermodynamic properties of biologically active substances.[22,23]

The purpose of this work is to experimentally determine and recalculate to 298.15 K the enthalpies of phase transitions of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl) propanoic acids.

2. Experimental

2.1. Synthesis of the studied compounds

The synthesis of the 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl) propanoic acid **5**–**12** derivatives studied in this work was carried out according to the reaction scheme shown in Fig. 1. 3-(Furan-2-yl)-1-phenylprop-2-en-1-one (furfurylidene acetophenone) **3** was obtained using the Claisen-Schmidt condensation of furfural **1** with acetophenone **2**. This reaction, as well as the opening of the furan ring to form 4,7-dioxo-7-phenylheptanoic acid **4**, was carried out using methods similar to those described previously.[24–26] The yields of compounds **3** and **4** are comparable to those reported in these articles. At the same time, we have somewhat simplified the procedures for the isolation and purification of the compounds without using column chromatography for this purpose. Pyrroles **5**–**12** were prepared by the reaction of 4,7-dioxo-7-phenylheptanoic acid **4** with amines.[25–27] We have shown that a wide range of aromatic, aliphatic, and heterocyclic amines can be used in this method.

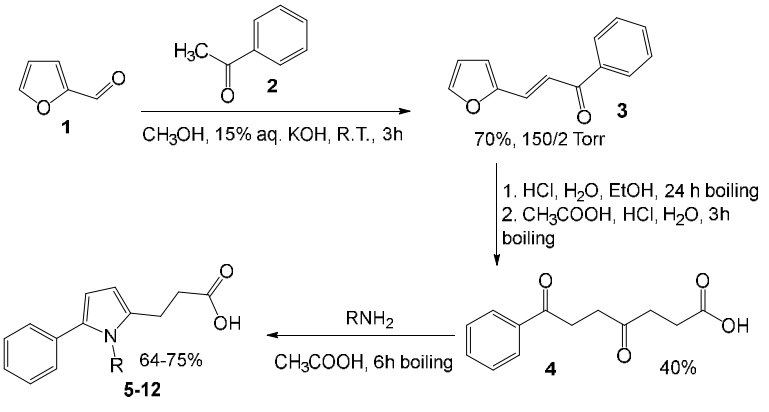


Fig. 1. Synthesis scheme of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl)propanoic acid derivatives:
R = H (**5**); C_6H_5 (**6**); 4-$CH_3C_6H_4$ (**7**); 4-$OCH_3C_6H_4$ (**8**); *n*-Bu (**9**); 2-Furylmethyl (**10**); 3-Pyridyl (**11**); Allyl (**12**)

3-(Furan-2-yl)-1-phenylprop-2-en-1-one 3. The KOH solution (1.7 g, 0.03 mol) was added to the reaction mixture of furfural **1** (48 g, 0.5 mol), acetophenone **2** (60 g, 0.5 mol), and methanol (120 mL) under vigorous stirring. The temperature of the reaction mixture was controlled in the range of 20–25°C. After stirring for 3 h, the reaction mixture was neutralized with acetic acid, diluted with 250 mL of water, extracted with dichloromethane, and washed with water. The organic layer was separated and dried using sodium sulfate. After solvent removal, the residue was distilled in a vacuum to obtain 69.3 g of furfurylidene acetophenone **3**. B.p. 137°C/1 mm Hg.

4,7-Dioxo-7-phenylheptanoic acid 4. A mixture of furfurylidene acetophenone **3** (39.6 g, 0.2 mol), 300 mL of ethanol, 90 mL of conc. HCl and 15 mL of water were refluxed for 24 h. The alcohol was distilled off, and a black,

viscous mass was obtained. Then 200 mL of conc. HCl, 200 mL of glacial acetic acid, and 400 mL of water were added, and the mixture was heated under reflux for the next 3 hours. After cooling, the formed light yellow crystalline precipitate of 4,7-dioxo-7-phenylheptanoic acid **4** was separated from the residual resin, filtered, washed three times with water, and recrystallized from ethanol. M.p. 110–112°C.

3-(1-R-5-Phenyl-1*H*-pyrrol-2-yl)propanoic acids 5–12. A mixture of 4,7-dioxo-7-phenylheptanoic acid **4** (0.025 mol, 5.85 g), 0.025 mol of the corresponding amine, and 50 mL of glacial acetic acid was refluxed for 6 h. After cooling, the reaction mixture was transferred under stirring to a beaker with 100 mL of cold water. After 20 min, the resulting precipitate was filtered off, washed with water, and recrystallized from ethanol/water or EtOH/DMF mixtures.

2.2. Identification of synthesized substances

The structure of the synthesized 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl)propanoic acids **5-12** for our studies was confirmed by NMR and IR spectroscopy (Table 1). ^{1}H and ^{13}C NMR spectra were recorded using a Bruker Avance 500 spectrometer (500 and 126 MHz, respectively) in DMSO-*d*6 solutions. The infrared spectra of the synthesized compounds were obtained using Shimadzu IRSpirit-T (compounds **9**, **11**, **12**) and Spectrum Two (PerkinElmer) (compounds **5–8**, **10**) in the range from 400 to 4 000 cm^{-1}. The mass spectra were recorded on an Agilent 1100 LC/MSD instrument with API-ES/APCI mode.

2.3. Differential thermal and thermogravimetric analysis

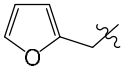
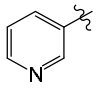
For the differential thermal analysis (DTA) and thermogravimetric analysis (TG), a Q-1500 D derivatograph Paulik-Paulik-Erdey was used. Derivatographic studies were carried out in a dynamic mode in an air atmosphere with a heating rate of 5 K/min and sensitivities according to the scales: TG – 100 mg; TA up to 773 K in a platinum crucible.

The enthalpies of vaporization ($\Delta_{vap}H$) were determined from the temperature dependence of the vaporization rate $V=\Delta m'/\Delta\tau$ in the temperature interval when the substance was in the liquid aggregate state, before the thermo-oxidative processes began. To determine the evaporation rate, the integral curve of the sample mass loss obtained from the TG analysis was differentiated every 30 s. The temperature dependence of the evaporation rate of a substance was approximated by the linear form of the Arrhenius equation $lnV = A - B/T$, where: $B = E_a/R$.

Table 1. Yields and spectral data of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl)propanoic acids **5-12**

№	R	Yield, %	Spectral data
1	2	3	4
5	H	64	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 12.15 (br.s, 1H), 10.95 (s, 1H), 7.56 (d, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.09 (br.s, 1H), 6.29 (br.s, 1H), 5.83 (t, *J* = 3.0 Hz, 1H), 2.82 (t, *J* = 7.7 Hz, 2H), 2.57 (t, *J* = 7.7 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6), δ, ppm: 173.9, 133.1, 132.73, 129.9, 128.6, 125.0, 122.9, 106.3, 105.5, 33.8, 22.8. IR (ATR, cm^{-1}): 3 439 cm^{-1}, 2 921 cm^{-1}, 1 692 cm^{-1}. MS (m/z, ES-API): 216 (M^{+}+1).
6	C_6H_5	75	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 12.14 (br.s., 1H), 7.49–7.37 (m, 3H), 7.21 (d, *J* = 7.3 Hz, 2H), 7.13 (t, *J* = 7.5 Hz, 2H), 7.06 (t, *J* = 7.3 Hz 1H), 7.00 (d, *J* = 7.2 Hz, 2H), 6.33 (d, *J* = 3.6 Hz, 1H), 6.07 (d, *J* = 3.6 Hz, 1H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.43 (t, *J* = 7.7 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6), δ, ppm: 173.94, 138.9, 135.0, 133.8, 133.3, 129.6, 128.9, 128.4, 128.3, 127.5, 126.1, 109.1, 106.7, 33.0, 22.5. IR (ATR, cm^{-1}): 2 924 cm^{-1}, 1 701 cm^{-1}. MS (m/z, ES-API): 292 (M^{+}+1).
7	4-$CH_3C_6H_4$	74	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 12.13 (s, 1H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 2H), 7.05–7.01 (m, 3H), 6.98 (d, *J* = 7.6 Hz, 2H), 6.28 (d, *J* = 3.6 Hz, 1H), 6.02 (d, *J* = 3.6 Hz, 1H), 2.57 (t, *J* = 7.6 Hz, 2H), 2.40 (t, *J* = 7.6 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6), δ, ppm: 174.0, 137.6, 136.4, 135.1, 133.8, 133.4, 130.1, 128.6, 128.4, 127.5, 126.1, 109.0, 106.6, 33.1, 22.6, 21.1. IR (ATR, cm^{-1}): 2 920 cm^{-1}, 1 709 cm^{-1}. MS (m/z, ES-API): 306 (M^{+}+1).
8	4-$CH_3OC_6H_4$	77	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 12.14 (br.s., 1H), 7.18–7.11 (m, 4H), 7.07 (t, *J* = 7.0 Hz, 1H), 7.03 (d, *J* = 7.7 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.30 (d, *J* = 3.6 Hz, 1H), 6.03 (d, *J* = 3.8 Hz, 1H), 3.78 (s 3H), 2.58 (t, *J* = 7.6 Hz, 2H), 2.43 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6), δ, ppm: 173.6, 158.5, 134.8, 133.6, 133.1, 131.2, 129.6, 128.1, 127.2, 125.6, 114.3, 108.4, 106.1, 55.3, 32.7, 22.1. IR (ATR, cm^{-1}): 2 912 cm^{-1}, 1 707 cm^{-1}. MS (m/z, ES-API): 322 (M^{+}+1).

Table 1. (Continuation).

1	2		3	4
9	*n*-Bu		70	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 12.22 (s, 1H), 7.43–7.36 (m, 2H), 7.34 (d, *J* = 7.7 Hz, 2H), 7.32–7.26 (m, 1H), 5.98 (d, *J* = 3.5 Hz, 1H), 5.85 (d, *J* = 3.7 Hz, 1H), 3.88 (t, *J* = 7.6 Hz, 2H), 2.83 (t, *J* = 7.6 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 1.41 (quintet, *J* = 7.6 Hz, 2H), 1.09 (hex, *J* = 7.2 Hz, 2H), 0.72 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ, ppm: 173.8, 133.9, 133.1, 132.8, 128.4, 128.3, 126.5, 107.8, 105.2, 43.0, 32.7, 21.6, 19.2, 13.3. IR (ATR, cm^{-1}): 2 960 cm^{-1}, 1 697 cm^{-1}. MS (m/z, ES-API): 272 (M^++1).
10			66	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 7.43–7.23 (m, 6H), 6.29 (d, *J* = 2.9 Hz, 1H), 6.18 (d, *J* = 3.8 Hz, 1H), 6.03 (d, *J* = 3.7 Hz, 1H), 5.95 (d, *J* = 3.4 Hz, 1H), 5.04 (s, 2H), 2.97 (t, *J* = 7.6 Hz, 2H), 2.72 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6), δ, ppm: 178.97, 151.5, 142.3, 135.2, 133.6, 132.9, 129.3, 128.5, 127.2, 110.6, 108.4, 107.4, 106.1, 41.8, 33.0, 21.8. IR (ATR, cm^{-1}): 2 919 cm^{-1}, 1 688 cm^{-1}. MS (m/z, ES-API): 296 (M^++1).
11			76	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 12.19 (s, 1H), 8.61–8.57 (m, 1H), 8.40 (d, *J* = 2.5 Hz, 1H), 7.74–7.70 (m, 1H), 7.50 (dd, *J* = 8.1, 4.8 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 6.97 (d, *J* = 7.6 Hz, 2H), 6.37 (d, *J* = 3.6 Hz, 1H), 6.13 (d, *J* = 3.6 Hz, 1H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.46 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*), δ, ppm: 173.4, 149.0, 148.7, 136.1, 135.2, 134.8, 133.9, 132.5, 128.2, 127.7, 126.1, 124.0, 109.3, 106.9, 32.6, 22.0. IR (ATR, cm^{-1}): 2 922 cm^{-1}, 1 706 cm^{-1}. MS (m/z, ES-API): 293 (M^++1).
12	CH_2=$CHCH_2$–		72	^{1}H NMR (500 MHz, DMSO-d_6), δ, ppm: 12.20 (s, 1H), 7.41–7.31 (m, 4H), 7.28–7.24 (m, 1H), 6.09 (d, *J* = 3.5 Hz, 1H), 5.97 (ddt, *J* = 17.4, 10.5, 4.0 Hz, 1H), 5.92 (d, *J* = 3.6 Hz, 1H), 5.14 (dd, *J* = 10.4, 1.8 Hz, 1H), 4.67 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.50 (dt, *J* = 4.3, 2.2 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ, ppm: 173.8, 135.6, 133.4, 133.4, 133.3, 128.4, 128.0, 126.5, 115.2, 107.7, 105.4, 45.8, 32.6, 21.3. IR (ATR, cm^{-1}): 2 904 cm^{-1}, 1 703 cm^{-1}. MS (m/z, ES-API): 256 (M^++1).

Given that vapour condensation in the presence of a liquid phase is an almost non-activation process, the activation enthalpy will be equal to $\Delta_{vap}H$ of the substance, taking into account the correction for the expansion work (Eq. 1):

$$E_a + RT_{fus} = \Delta_{vap}H \quad (1)$$

The calculation of the enthalpy of fusion ($\Delta_{fus}H$) was carried out according to equation (2), taking into account the loss of heat due to the evaporation of the sample:

$$K \cdot S = Q_{fus} + Q_{vap} = m_0 \cdot \Delta_{fus}H + \\ + \Delta m_{vap} \cdot \Delta_{vap}H \quad (2)$$

where K is the heat transfer coefficient of the derivatograph, which was determined by the results of DTA analysis of reference samples of biphenyl, silver nitrate, adipic and benzoic (K-1) acids, and was equal to $8.2023 \cdot 10^{-5} - T_{fus}$, J/(K·s); Q_{fus} and Q_{vap} are the amount of heat absorbed during sample melting or evaporation, respectively, J; $\Delta_{fus}H$ and $\Delta_{vap}H$ are the specific enthalpies of fusion and vaporization of studied acids, respectively, J/g; m_0 is the mass of the sample corresponding to the temperature of its melting point T_{fus}, g; Δm_{vap} is the loss of sample mass (vapour mass) over the period, taken into account when determining the peak area S (K·s) on the DTA curve, g.

3. Results and Discussion

The results of the experimental determination of the sample mass loss during the differential thermal and thermogravimetric methods of analysis are shown in Table 2, namely: T_1-T_2 are the temperature interval at which the sample mass loss rate was analysed; $S\Delta m'$ are total mass loss of the sample in the given temperature range; *A* and *B* are the coefficients of the linear equation (1) and the calculated value of $\Delta_{vap}H$.

Experimental results of the $\Delta_{fus}H$ determination of the acids under study are shown in Table 3.

Table 2. Enthalpies of vaporization of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl)propanoic acid derivatives in temperature intervals

Sample number	T_1-T_2, K	$\sum \Delta m' \cdot 10^3$, g	A	$-B$, K	$\Delta_{vap}H$, kJ/mol
3-(5-phenylpyrrol-2-yl)propanoic acid **5**					
1	451.6–470.1	0.154	13.99	11553	99.5
2	485.4–540.1	3.43	13.30	11447	98.6
3	440.4–540.8	7.13	14.37	11605	99.9
Mean value:					99.3±1.0
3-(1,5-diphenylpyrrol-2-yl)propanoic acid **6**					
1	522.6–600.8	35.7	24.08	12445	107.10
2	511.2–593.8	11.2	23.10	12414	106.90
Mean value:					107.00±0.14
3-(1-(4-methylphenyl)-5-phenylpyrrol-2-yl)propanoic acid **7**					
1	450.7–463.0	0.005	15.08	12427	106.9
2	514.3–581.9	5.95	14.32	12591	108.2
3	524.2–594.0	20.6	14.77	12414	106.8
Mean value:					107.3±1.8
3-(1-(4-methoxyphenyl)-5-phenylpyrrol-2-yl)propanoic acid **8**					
1	529.5–584.7	4.11	16.40	14016	120.3
2	528.9–580.0	13.6	16.35	13896	119.3
3	532.2–598.3	14.1	16.41	13677	117.5
Mean value:					119.0±3.3
3-(1-butyl-5-phenylpyrrol-2-yl)propanoic acid **9**					
1	490.1–580.5	37.1	13.34	11022	94.78
2	491.0–572.3	28.6	13.82	11246	96.64
3	488.6–568.3	25.2	13.18	11200	96.30
Mean value:					95.9±2.3
3-(1-(furan-2-ylmethyl)-5-phenylpyrrol-2-yl)propanoic acid **10**					
1	495.6–578.8	19.8	15.38	12455	106.9
2	536.3–582.8	16.2	16.85	12315	105.7
3	499.2–564.5	14.1	12.43	12495	107.2
Mean value:					106.6±1.8
3-(1-(3-pyridyl)-5-phenylpyrrol-2-yl)propanoic acid **11**					
1	545.6 –575.8	4.51	14.03	12336	106.20
2	520.7–585.0	17.2	14.56	12398	106.72
3	534.2–581.3	14.6	13.98	12305	105.95
Mean value:					106.3±1.0
3-(1-allyl-5-phenylpyrrol-2-yl)propanoic acid **12**					
1	502.3–577.3	27.3	11.76	10234	88.31
2	498.2–565.4	29.5	10.94	10175	87.82
3	506.0–572.1	25.4	11.42	10198	88.02
Mean value:					88.05±0.56

Table 3. Enthalpies of fusion of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl)propanoic acid derivatives **5–12** at melting point

Sample number	m_0, g	Δm_{vap}, g	S, K×s	q_{vap}, J	$K \cdot 10^3$, J/K×s	$\Delta_{fus}H$, kJ/mol
1	2	3	4	5	6	7
(**5**) T_{fus} = 416.45±1.50 K;						
1	0.0746	0.0003	306.9	0.1428	3.574	29.28
2	0.0740	0.0003	306.7	0.1406	3.808	28.25
3	0.1012	0.0004	399.1	0.1818	31.04	28.60
Mean value:						28.71±0.78
(**6**) T_{fus} = 442.40±1.50 K;						
1	0.1009	0.0013	436.9	0.4813	36.28	44.4
2	0.1096	0.0013	456.9	0.4621	36.28	42.8
Mean value:						43.6 ± 1.2

Table 3. (Continuation).

1	2	3	4	5	6	7
(**7**) T_{fus} = 427.90±1.50 K						
1	0.0612	0.0004	1930.9	0.1525	3.888	36.67
2	0.0740	0.0003	2266.0	0.0618	4.001	36.95
3	0.1026	0.0004	350.1	0.1248	35.09	36.21
Mean value:						36.61±0.88
(**8**) T_{fus} = 454.45±1.60 K						
1	0.0749	0.0003	2639.1	0.1048	3.732	41.8
2	0.1001	0.0002	348.6	0.0643	37.28	41.5
3	0.1027	0.0003	362.2	0.1054	37.28	42.6
Mean value:						42.0±1.3
(**9**) T_{fus} = 377.85±1.65 K;						
1	0.1022	0.0003	393.1	0.0901	30.99	32.2
2	0.1023	0.0004	398.1	0.1314	30.99	32.4
3	0.0936	0.0001	369.5	0.03445	30.99	33.1
Mean value:						32.6 ± 1.1
(**10**) T_{fus} = 398.35±1.50 K;						
1	0.1022	0.0006	374.8	0.2300	32.68	34.8
2	0.1056	0.0008	385.2	0.2894	32.68	34.4
3	0.1002	0.0005	370.5	0.1809	32.68	35.2
Mean value:						34.8 ± 1.0
(**11**) T_{fus} = 438.40±1.50 K;						
1	0.0960	0.0003	338.2	0.0958	35.96	36.73
2	0.1017	0.0005	361.4	0.1817	35.96	36.84
3	0.1059	0.0007	367.6	0.2543	35.96	35.79
Mean value:						36.5 ± 1.3
(**12**) T_{fus} = 388.45±1.00 K;						
1	0.1029	0.0003	362.7	0.0935	31.86	28.44
2	0.1032	0.0004	374.9	0.1384	31.86	29.21
3	0.0992	0.0002	342.4	0.0692	31.86	27.90
Mean value:						28.5 ± 1.5

3.1. Analytical calculation of enthalpies of fusion at melting point.

The generalization of the thermodynamic parameters of the melting process determined in this work was carried out using specific values rather than the more conventional molar values, since the intermolecular forces that are decisive in this process are provided by all the atoms in the molecule. Particularly, when generalised, it was found that the values of the entropies of fusion ($\Delta_{fus}S_{T_{fus}}$), calculated by the Eq. (3), are similar within the error of the experimental determination (Table 4).

$$\Delta_{fus}S_{T_{fus}} = {}^{\Delta_{fus}H_{T_{fus}}}\Big/_{T_{fus}} \qquad (3)$$

Table 4. Thermodynamic parameters of the melting process of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl) propanoic acid derivatives at the melting point

Substance	*M*, g/mol	T_{fus}, K	$\Delta_{fus}S_{T_{fus}}$,		$\Delta_{fus}H_{T_{fus}}$, kJ/mol		
			J/mol·K	J/g·K	Exp.	Calc.	Δ
5	215.252	416.45	68.9±1.7	0.3203	28.71±0.78	27.1±2.4	1.6
6	291.350	442.40	98.6±1.9	0.3383	43.6±1.2	38.9±3.2	4.7
7	305.377	427.90	85.6±1.7	0.2802	36.61±0.88	39.5±3.4	-2.9
8	321.376	454.45	92.4±2.0	0.2876	42.0±1.3	44.1±3.5	-2.1
5	271.360	377.85	86.3±1.9	0.3179	32.6±1.1	31.0±3.0	1.6
10	295.338	398.35	87.4±1.8	0.2958	34.8±1.0	35.5±3.2	-0.7
11	292.338	438.40	83.3±2	0.2848	36.5±1.3	38.7±3.2	-2.2
12	255.317	388.45	73.4±2.1	0.2874	28.5±1.5	30.0±2.8	-1.5

where *M* are molecular masses of substances.

The averaged value of $\Delta_{fus}S_{T_{fus}}$, which is 0.3015±0.0075 J/g·K, makes it possible to calculate $\Delta_{fus}H_{T_{fus}}$ for thermally unstable substances with an arylpyrrole fragment whose melting process is accompanied by thermo-oxidative destruction. For comparison, Table 4 shows $\Delta_{fus}H_{T_{fus}}$ calculated from the established average specific value $\Delta_{fus}S_{T_{fus}}$ and experimentally determined. The difference between them is acceptable. Such an analytical approach to calculate $\Delta_{fus}H_{T_{fus}}$ was used in our work[13] where we studied the thermodynamic parameters of substances with an arylfuran fragment.

3.2. Recalculation of enthalpies of phase transitions to 298.15 K.

To summarize the results of experimental studies and calculate the enthalpy of sublimation at 298.15 K, it becomes necessary to recalculate the thermodynamic parameters to 298.15 K, for which the Kirchhoff equation (Eq. 4) is used:

$$\Delta H^0_{298.15} = \Delta H^0_{\mathrm{T}} - \int_{298.15}^{T} \Delta C_p dT, \quad (4)$$

where ΔC_p is the change in heat capacity at the corresponding phase transition, which is determined experimentally using precision equipment or analytically.

However, in recent years, analytical methods have been increasingly used to calculate ΔCp.[28,29]. Thus, in work[28] a linear equation and the value of heat capacity at the corresponding aggregate state, which is calculated by group contributions, are used to calculate the change in heat capacity at the corresponding phase transition, and in work[29] the specific value of the change in heat capacity of the vapour formation process is considered to be a constant value within 4–6%. Therefore, it was decided to use the equations given in work.[29] In this work, the recalculation of $\Delta_{vap}H$ to 298.15 K of the studied acids was carried out according to equation (5) from the average temperature of the interval (T_{av}) in which the study was carried out. The calculation of $\Delta_{fus}H_{298.15}$ was carried out from T_{fus} according to equation (6)[13], the results of the calculations are shown in Table 5.

$$\Delta_{vap}H_{298.15} = \Delta_{vap}H_{T_m} + (0.591 \pm 0.024) \cdot \cdot M \cdot (T_{av} - 298.15) \quad (5)$$

where M is the molecular mass of the substance, g/mol.

$$\Delta_{fus}H_{298.15} = \Delta_{fus}H_{T_{fus}} \left[1 + \frac{298.15 - T_{fus}}{1.35 \cdot T_{fus}}\right] \quad (6)$$

To calculate the sublimation enthalpies $\Delta_{sub}H_{298.15}$ using the values $\Delta_{vap}H$ and $\Delta_{fus}H$ determined by the derivatographic method, two calculation methods can be applied.

Using the first method, the value of $\Delta_{fus}H$ is recalculated from T_{fus} value to 298.15 K, and $\Delta_{vap}H$ from T_{av} from which $\Delta_{vap}H$ is determined to T_{fus} (Eq. 7).

$$\Delta_{sub}H_{298.15} = \left(\Delta_{vap}H_{T_{av}} + \Delta_{vap}Cp_{298.15}(T_{av} - -T_{fus}) + (\Delta_{\mathrm{fus}}\mathrm{H}_{\mathrm{T_{fus}}}\left[1 + \frac{298.15 - \mathrm{T_{fus}}}{1.35 \cdot \mathrm{T_{fus}}}\right]\right) \quad (7)$$

Using the second method, in order to reduce the number of recalculation steps, it was assumed that the $\Delta_{vap}H$ values were calculated in temperature intervals where the minimum value is very close to the T_{fus} of the substance. Since T_{fus} is nothing more than the temperature of the triple point, where the substance is simultaneously in three aggregate states: liquid, solid, and gaseous, it can be assumed that the calculated value of $\Delta_{vap}H$, according to T_{av}, will be the same as at T_{fus}. Thereby, to calculate $\Delta_{sub}H$, we can use this equation $\Delta_{sub}H_{T_{fus}} = \Delta_{vap}H_{T_{fus}} + \Delta_{fus}H_{T_{fus}}$, considering that the heat of phase transitions specified in the equation belongs to T_{fus}, and recalculate it according to Eq. (8) from T_{fus} to 298.15 K.

$$\Delta_{sub}H_{298.15} = \Delta_{sub}H_{T_{fus}} + + \Delta_{sub}Cp_{298.15}(T_{fus} - 298.15) = = \Delta_{sub}H_{T_{fus}} + (0.261 \pm 0.035) \cdot M \cdot \cdot (T_{fus} - 298.15) \quad (8)$$

The results of the calculation of $\Delta_{sub}H_{298.15}$ are shown in Table 5.

Table 5. Thermodynamic parameters of the enthalpies of phase transitions of 3-(1-R-5-phenyl-1*H*-pyrrol-2-yl) propanoic acid derivatives at 298.15 K, kJ/mol

Substance	$\Delta_{fus}H_{298.15}$	$\Delta_{vap}H_{298.15}$	$\Delta_{sub}H_{298.15}$	
			Method 1	Method 2
5	22.7±1.1	125.7±2.5	133.3±2.7	134.7±3.0
6	33.1±1.7	151.4±2.6	159.7±3.1	161.6±3.4
7	28.4±1.3	147.8±3.3	152.8±3.5	154.3±3.8
8	31.3±1.9	168.1±4.3	169.7±4.7	174.1±4.9
5	27.5±1.6	133.9±3.4	148.6±3.8	134.1±4.0
10	28.3±1.4	148.7±3.2	159.5±3.5	149.1±3.8
11	27.9±1.9	150.3±2.8	154.0±3.4	153.5±3.6
12	23.6±2.1	124.2±2.5	134.2±3.3	122.6±3.4

According to the calculation results of $\Delta_{sub}H_{298.15}$ by the two proposed methods, for most of the studied compounds, the values are similar within the errors of the calculation methods, but in our opinion, the values obtained by the first proposed calculation method are more reliable, since using this method we conduct a stepwise calculation of $\Delta_{vap}H$ from T_{av} to T_{fus}, and $\Delta_{fus}H$ from T_{fus} to 298.15 K, covering the entire temperature range at which the thermodynamic studies were carried out, in contrast to the second method, where we do not take into account the values of the temperature intervals of the evaporation process.

4. Conclusions

It has been shown that by the reaction of 4,7-dioxo-7-phenylheptanoic acid with amines, it is possible to obtain derivatives of 3-(5-phenyl-1*H*-pyrrol-2-yl)propanoic acid with various substituents in position 1. Considering the results of the experimental study, the use of differential thermal and thermogravimetric methods of analysis is quite acceptable for determining the enthalpies of phase transitions. The generalized analysis of the $\Delta_{fus}H_{T_{fus}}$, determined in this study, makes it possible to calculate analytically $\Delta_{fus}H_{T_{fus}}$ for thermally unstable arylpyrrole derivatives. The calculation of the enthalpies of phase transitions at 298.15 K, namely the enthalpies of evaporation, will make it possible to estimate the energies of intra- and intermolecular interactions in macromolecules, and will also allow optimizing the processes of synthesis, processing, storage and transportation of substances.

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СИНТЕЗ І ТЕРМОДИНАМІЧНІ ПАРАМЕТРИ ФАЗОВИХ ПЕРЕХОДІВ ПОХІДНИХ 3-(1-R-5-ФЕНІЛ-1*H*-ПІРОЛ-2-ІЛ)ПРОПАНОВИХ КИСЛОТ

Анотація. *Отримано реакцією 4,7-діоксо-7-феніл-гептанової кислоти з амінами ряд 3-(1-R-5-феніл-1H-пірол-2-іл)пропанових кислот (R = H, Ar, Alk, Hetaryl). Уперше експериментально визначено ентальпії випаровування та плавлення восьми похідних 3-(1-R-5-феніл-1H-пірол-2-іл)пропанових кислот з використанням диференційно-термічного та термогравіметричного методів аналізу. На основі експериментально визначених термодинамічних параметрів процесу плавлення запропоновано аналітичний метод розрахунку ентальпії плавлення за питомим значенням ентропії плавлення для речовин з арилпірольним фрагментом. Проаналізовано методи розрахунку ентальпій сублімації за даними дериватографічних досліджень. Проведено перерахунок ентальпій фазових переходів до 298,15 K.*

Ключові слова: *синтез, ентальпія сублімації, ентальпія плавлення, ентальпія випаровування, похідні піролу, N-заміщені 3-(5-фенілпірол-2-іл)пропанові кислоти.*