

Synthesis and thermodynamic properties of 3-(5-phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid in condensed and gaseous states

Dmytro Shevchenko^a, Yuriy Horak^b, Mykola Obushak^b, Nadiia Tischenko^c and Iryna Sobeckho^{a*}

^aDepartment of Physical, Analytical and General Chemistry, Lviv Polytechnic National University, S. Bandery St. 12, Lviv 79013, Ukraine

^bDepartment of Organic Chemistry, Ivan Franko National University of Lviv, Kyryla and Mefodiya St. 6, Lviv 79005, Ukraine

^cChemistry and Technology of Nanotextured Ceramics and Nanocomposite Materials, National Academy of Sciences of Ukraine, Krzhizhanovskoho St. 3, Lviv 03142, Ukraine

CHRONICLE

Article history:

Received October 15, 2024

Received in revised form

November 1, 2024

Accepted March 14, 2025

Available online

March 14, 2025

Keywords:

Enthalpy of formation

Enthalpies of phase

transitions

Analytical calculations

Pyrrole derivatives

N-substituted 3-(5-phenylpyrrol-2-yl)propanoic acids

ABSTRACT

A combined experimental and theoretical study of the fundamental thermodynamic parameters of 3-(5-phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid was carried out for the first time. The enthalpies of combustion, formation in the condensed state, fusion, and vaporization were determined using high-precision equipment. Based on the experimentally obtained results, the enthalpies of sublimation and formation in the gaseous state at 298.15 K were calculated using two methods. The possibility of applying analytical methods of Domalski, Joback and quantum chemical calculations to determine the enthalpy of formation in the gas phase is analysed.

© 2025 by the authors; licensee Growing Science, Canada.

1. Introduction

The pharmaceutical market is full of drugs that include biologically active compounds with fragments of heterocycles with a nitrogen atom in their structure.¹ Some of them are polysubstituted pyrrole derivatives, particularly arylpyrroles. These compounds are characterized by antitumor, antibacterial, analgesic, antioxidant, and anti-inflammatory effects.²⁻⁵ The possibility of diversification of biological activity due to substituents in the ring is explained by the ability of pyrrole to react with various electrophiles, which is caused by the aromatic nature of the ring.⁶ For the chemical industry, pyrrole-based derivatives are valuable in the production of optoelectronic materials, electrically conductive materials, corrosion inhibitors, organic catalytic components, and plant protection.⁷⁻¹⁰

These compounds have significant potential for use as drug components. Thus, the share of low-molecular weight drugs containing at least one nitrogen-containing heterocycle in the US market is about 75%, and the number of such drugs is expected to increase further.¹¹ Consequently, this motivates the scientific community to develop new ways of synthesizing. Among a number of such arylpyrrole derivatives is 3-(5-phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid. The lack of fundamental thermodynamic parameters (enthalpies of combustion, formation, fusion and vaporization) motivated us to determine them experimentally in this work. The availability of these will make it possible to optimize the processes of synthesis, processing, transportation, and storage of this substance. In addition, if necessary, information on the calorific value will be required when the substance is disposed of by combustion in boilers with the subsequent use of the released

* Corresponding author

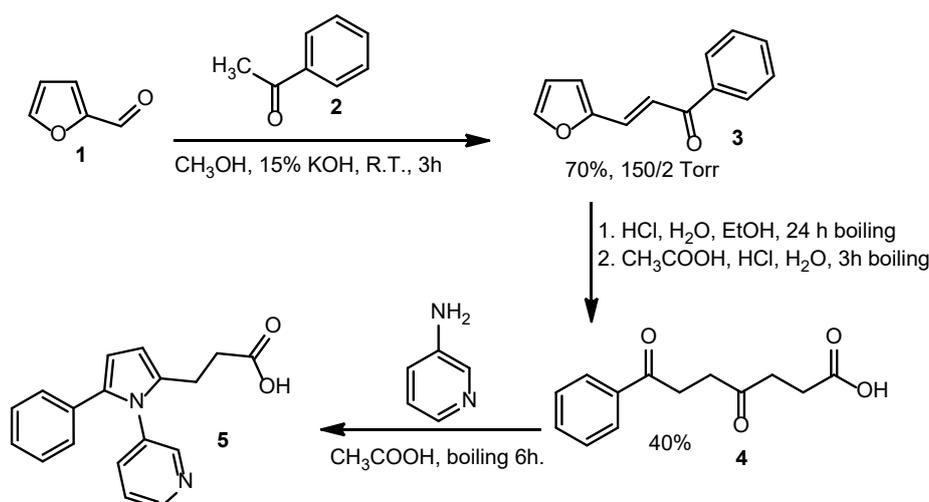
E-mail address iryna.b.sobeckho@lpnu.ua (I. Sobeckho)

energy in heat exchange processes, which is one of the simplest methods of ecological disposal of pharmaceutical substances containing carbon, hydrogen, oxygen, and nitrogen atoms.¹²

The purpose of this work is to determine the fundamental thermodynamic parameters of 3-(5-phenyl-1-(pyridin-3-yl)-1*H*-pyrrol-2-yl)propanoic acid. Determine the combustion energy of the acid under study using the bomb calorimetry method and calculate the standard enthalpy of combustion and formation in the condensed state. Determine the thermodynamic parameters of phase transitions based on the results of derivatographic studies. Recalculate the obtained values of the phase transition parameters to the generally accepted temperature 298.15 K and calculate the enthalpy of formation in the gaseous phase. Conduct a theoretical calculation of the enthalpy of formation using analytical calculations methods of Domalski, Joback and quantum chemical calculations.

2. Results and Discussion

The synthesis of 3-(5-phenyl-1-(pyridin-3-yl)-1*H*-pyrrol-2-yl)propanoic acid **5** was carried out according to the reaction scheme shown in **Scheme 1**:



Scheme 1. Preparation of 3-(5-phenyl-1-(pyridin-3-yl)-1*H*-pyrrol-2-yl)propanoic acid **5**

The calculation of the combustion energy $\Delta_c U$ of the studied acid under the combustion process conditions was carried out according to Eq. (1):

$$-\Delta_c U = \frac{W \cdot \Delta T - Q_{fuser} - Q_{HNO_3} + Q_{carb}}{m_{comp}} \quad (1)$$

where W is the energy equivalent of the calorimetric system, J/V; ΔT is true temperature increase in a calorimetric experiment; m_{comp} is the mass of the substance that burned during the experiment, g; Q_{fuser} , Q_{HNO_3} and Q_{carb} are the amount of heat released during the combustion of cotton thread (16704.2 J/g)¹³, the formation of nitric acid solution (59 J/g)¹³, and the formation of soot (32800 J/g)¹³, respectively.

The reliability of the calorimetric system was checked by burning a secondary standard. We chose biphenyl as a secondary standard, for which the thermodynamic parameters have been repeatedly determined¹⁴. The experimentally determined values of the heat of combustion ($\Delta_c H_{298}^0 = -6249.2 \pm 2.0$ kJ/mol) and the heat of formation in the condensed state ($\Delta_f H_{298}^0 = -97.9 \pm 2.0$ kJ/mol) are in good agreement within the error of the experiment and calculations with the published values in the scientific literature.

Table 1 shows the data of the experimental determination of the combustion energy of the studied acid **5** according to Eq. (1), as well as the combustion completeness (%). The value of combustion completeness was given as the ratio of the amount of carbon dioxide determined by gas analysis to the amount of carbon dioxide calculated from the stoichiometric Eq. (2) of the acid combustion reaction:



Table 1. Experimental data of combustion energy determination of 3-(5-Phenyl-1-(pyridin-3-yl)-1*H*-pyrrol-2-yl)propanoic acid **5**.

m_{comp} , g	ΔT , V	Q_{fuser} , J	Q_{HNO_3} , J	Q_{carb} , J	$-\Delta_c U$, J/g	Combustion completeness, %
0.29092	0.88378	89.0	8.9	36.1	31224	99.53
0.22736	0.69254	76.8	3.5	25.3	31279	99.38
0.21916	0.66651	79.8	5.3	33.1	31234	99.00
0.23510	0.71367	73.5	5.0	32.8	31218	99.87
0.27460	0.83457	90.5	9.4	38.9	31228	99.64
0.20098	0.61312	94.4	6.8	29.2	31210	99.81
0.28531	0.86494	85.4	5.3	44.1	31207	99.89

$$\Delta_c U = -31229 \pm 16 \text{ J/g}$$

Taking into account¹³ the Washburn correction π and the correction for the expansion work ΔnRT , the mean value of combustion energy $\Delta_c U$ was used to calculate the standard enthalpy of combustion $\Delta_c H_{298}^0$. The following values of formation energies (kJ/mol) were used to calculate the standard enthalpy of formation $\Delta_f H_{298}^0$ in the condensed state for the acid under study: CO_2 (g) = 393.5±0.1,¹⁵ H_2O (l) = 285.8±0.1,¹⁵ O_2 (g) = 0¹⁵. **Table 2** shows the determined value of the energy of combustion under standard conditions, the Washburn correction, the correction for expansion work, and the standard enthalpies of combustion and formation in the condensed state of the acid under study.

Table 2. Standardized calorimetry values of 3-(5-Phenyl-1-(pyridin-3-yl)-1*H*-pyrrol-2-yl)propanoic acid combustion.

$\Delta_c U_{298.15}^0$, kJ/mol	π	ΔnRT	$\Delta_c H_{298.15}^0$, kJ/mol	$\Delta_f H_{298.15}^0$ (cr), kJ/mol
-9129.3±4.6	-6.0	-4.96	-9140.2±4.6	-229.6±4.6

To verify the reliability of the derivatographic equipment and the methodology for processing the results of experimental studies, a series of derivatographic studies of biphenyl were performed. Based on the results of differential thermal analysis (DTA), the melting point $T_{fus} = 343.45 \pm 0.55$ K and $\Delta_{fus} H_{T_{fus}} = 18.6 \pm 1.4$ kJ/mol were calculated. According to the results of the thermogravimetric (TG) method of analysis in the temperature range from 370.0 to 469.4 K, the enthalpy of vaporization was calculated $\Delta_{vap} H_{419.7} = 57.3 \pm 1.5$ kJ/mol. The determined thermodynamic parameters of phase transitions under the conditions of the study are consistent with the values given in the published literature¹⁴. Based on the experimental results of DTA and TG methods, the enthalpy of vaporization and the enthalpy of fusion of the acid under study were calculated. The results are presented in **Tables 3** and **4**. In **Table 3** $T_1 - T_2$ is temperature range for which the enthalpy of vaporization is calculated, K; $\Sigma \Delta m$ is complete loss of sample mass in the specified temperature range, g.

Table 3. Thermodynamic parameters of the evaporation process of the acid under study

Sample number	$T_1 - T_2$, K	$\Sigma \Delta m \cdot 10^3$, g	A	$-B$, K	$\Delta_{vap} H$, kJ/mol
1	545.6–575.8	4.51	14.03	12336	106.2
2	520.7–585.0	17.2	14.56	12398	106.7
3	534.2–581.3	14.6	13.98	12305	105.9
Mean value:					106.3±1.0

Table 4. Thermodynamic parameters of the melting process of the acid under study

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
$T_{fus} = 438.40 \pm 1.50$ K;						
1	0.0960	0.0003	338.2	0.0958	35.96	36.7
2	0.1017	0.0005	361.4	0.1817	35.96	36.8
3	0.1059	0.0007	367.6	0.2543	35.96	35.8
Mean value:						36.4 ± 1.3

Calculation of the enthalpy of sublimation at 298.15 K requires recalculation of thermodynamic parameters to 298.15 K in order to standardize the results of experimental studies. For this purpose, the Kirchoff equation (**Eq. 3**) is used:

$$\Delta H_{298.15}^0 = \Delta H_{T_1}^0 - \int_{298.15}^{T_1} \Delta C_p dT, \quad (3)$$

where ΔC_p is change in heat capacity, with a corresponding phase transition. It is determined experimentally using precision equipment or analytical calculation methods. In recent years, more and more attention has been paid^{16,17} to the use of analytical methods of calculation ΔC_p . For instance, to calculate the change in heat capacity at the corresponding phase transition, authors in work¹⁶ considered the use of a linear equation and the value of heat capacity at the corresponding

aggregate state, which was calculated by group contributions. In other work¹⁷, it was proposed that the specific value of the change in the heat capacity of the evaporation process is a constant value in the range of 4–6%. Thus, we decided to use the equations given in work¹⁷ to recalculate the enthalpies of vaporization.

The recalculation of $\Delta_{vap}H$ to 298.15 K of the acid under study was performed using equation (4) from the average temperature of the interval (T_{av}) at which the study was performed. The calculation of $\Delta_{fus}H_{298.15}^0$ was carried out from T_{fus} according to equation (5)¹⁸. The results of the calculations are shown in **Table 5**.

$$\Delta_{vap}H_{298.15} = \Delta_{vap}H_{T_m} + (0.591 \pm 0.024) \cdot M \cdot (T_{av} - 298.15), \quad (4)$$

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

$$\Delta_{fus}H_{298.15} = \Delta_{fus}H_{T_{fus}} \left[1 + \frac{298.15 - T_{fus}}{1.35 \cdot T_{fus}} \right] \quad (5)$$

The calculation of the enthalpy of sublimation $\Delta_{sub}H_{298.15}^0$ from the values of $\Delta_{vap}H$ and $\Delta_{fus}H$ determined by the derivatographic method was performed using two methods of recalculation. The first method recalculates the value of the enthalpy of fusion from T_{fus} to 298.15 K and the value of enthalpy of vaporization from T_{av} , at which $\Delta_{vap}H$ is determined, to T_{fus} by Eq. (6).

$$\Delta_{sub}H_{298.15}^0 = \left(\Delta_{vap}H_{T_{av}} + \Delta_{vap}Cp_{298.15}(T_{av} - T_{fus}) + \Delta_{fus}H_{T_{fus}} \left[1 + \frac{298.15 - T_{fus}}{1.35 \cdot T_{fus}} \right] \right) \quad (6)$$

In order to reduce the steps of recalculation, it was assumed in the second method that the $\Delta_{vap}H$ values were calculated in the temperature range, the minimum value of which is very close to the T_{fus} of the substance. Since T_{fus} corresponds to the temperature of the triple point, when a substance is simultaneously in three aggregate states, it can be assumed that the calculated value of $\Delta_{vap}H$ at T_{av} will be the same as at T_{fus} . Therefore, to calculate the enthalpy of sublimation, we used Eq. (7) and considered that the heat of phase transitions specified in the equation belong to T_{fus} .

$$\Delta_{sub}H_{T_{fus}} = \Delta_{vap}H_{T_{fus}} + \Delta_{fus}H_{T_{fus}} \quad (7)$$

In this case, the enthalpy of sublimation was recalculated using equation (8) from T_{fus} to 298.15 K.

$$\begin{aligned} \Delta_{sub}H_{298.15}^0 &= \Delta_{sub}H_{T_{fus}} + \Delta_{sub}Cp_{298.15}(T_{fus} - 298.15) = \\ &= \Delta_{sub}H_{T_{fus}} + (0.261 \pm 0.035) \cdot M \cdot (T_{fus} - 298.15) \end{aligned} \quad (8)$$

The results of $\Delta_{sub}H_{298.15}^0$ calculations are also shown in **Table 5**.

Table 5. Thermodynamic parameters of the enthalpies of phase transitions of the investigated acid at 298.15 K, kJ/mol.

$\Delta_{fus}H_{298.15}^0$	$\Delta_{vap}H_{298.15}^0$	$\Delta_{sub}H_{298.15}^0$	
		Method 1	Method 2
27.9±1.9	150.3±2.8	154.0±3.4	153.5±3.6

Thus, the values of the enthalpy of formation of 3-(5-phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid in the gaseous state $\Delta_f H_{298.15}^0(g)$ at 298.15 K according to the first and second methods are -75.7 ± 5.7 kJ/mol and -76.1 ± 5.8 kJ/mol, respectively.

In this work, experiments to determine the main thermodynamic parameters of the compound require the use of high-precision equipment and qualified researchers. This makes them expensive and complicated. In this context, attention should be paid to alternative approaches to determining thermodynamic parameters. In order to determine the enthalpy of formation in the condensed and gas phases, there are analytical calculation methods, including Domalski,¹⁹ Joback,²⁰ Benson,²¹ Salmon,²² and quantum chemical. These methods generally provide good reproducibility of results for compounds with simple structures. During our analytical calculations, we did not use the Benson and Salmon methods, since the first one has a limited number of group contributions of nitrogen-containing groups, and the second one gives²³ significant deviations for a compound of similar structure. To perform quantum chemical calculations, we used method known as T1 recipe²⁴ described by W. S. Olinger et al. **Table 6** presents all the necessary group contributions for calculating the enthalpy of formation of the acid under study in the condensed and gaseous states by the Domalski and Joback methods.

Table 6. Group contributions of Domalski and Joback analytical calculation method, kJ/mol

Group	$\Delta_f H_{298.15}^0$		Group	$\Delta_f H_{298.15}^0$	
	(cr)	(g)		(cr)	(g)
Domalski group contributions					
$C_b - (C_b)_2(H)$	6.53	13.81	$C - (C)(C_d)(H)_2$	-21.6	-18.92
$C_b - (C_d)(C_b)_2$	20.27	24.17	$C - (C)(CO)(H)_2$	-27.9	-21.84
$C_d - (C_b)(C_d)(N)$	-3.95	-5.74	$CO - (C)(O)$	-153.6	-137.24
$C_d - (C_d)_2(H)$	17.53	28.28	$O - (CO)(H)$	-282.15	-254.3
$N - (C_d)_2(C_b)$	88.92	120.64	$C_b - (C_b)(N)(H)$	6.53	13.81
$C_b - (C_b)_2(N)$	9.75	-1.3	$N - (C_b)_2$	57.00	69.00
$C_d - (C_d)(C)(N)$	-3.95	-5.74	Pyrrole ring	-17.84	-30.48
Joback group contributions					
=C- (ring)	-	2.09	-COOH (acid)	-	-426.72
=C< (ring)	-	46.43	>N-	-	123.34
-CH₂-	-	-20.24	-N= (ring)	-	55.52

According to the Domalski method, the enthalpies of formation in the solid and gaseous states are $\Delta_f H_{298.15}^0(cr) = -241.2$ kJ/mol and $\Delta_f H_{298.15}^0(g) = -80.9$ kJ/mol, respectively. The deviations of the values obtained by the Domalski method from the experimental ones for $\Delta_f H_{298.15}^0(cr)$ is 11.6 kJ/mol and $\Delta_f H_{298.15}^0(g)$ are 5.2 kJ/mol and 4.8 kJ/mol, correspondingly. As for the Joback method, the calculated value of the enthalpy of formation in the gaseous state is $\Delta_f H_{298.15}^0(g) = -12.1$ kJ/mol. The Joback method shows a noticeable deviation from the values $\Delta_f H_{298.15}^0(g)$ calculated by the two methods, which are 63.6 kJ/mol and 64.0 kJ/mol, respectively. Such deviations between the values of the analytical calculation method and the experimental ones can be explained in terms of the spatial structure of the acid under study and the tensions arising in the molecule. One of the factors may also be the presence of phenyl and pyridine substituents in the fifth and first positions of the pyrrole ring. Their presence can cause tension in the molecule itself and prevent the formation of intra- and intermolecular interactions. This, in turn, has a significant impact on the thermodynamic properties of individual substances, which analytical calculation methods might not take into account.

Based on the results of quantum chemical calculations using the method of T1 recipe to calculate the enthalpy of formation in the gas state, the following value was obtained $\Delta_f H_{298.15}^0(g) = -50.1$ kJ/mol. The obtained value deviates from the values of $\Delta_f H_{298.15}^0(g)$, calculated earlier by the two methods, by 25.6 kJ/mol and 26.0 kJ/mol, respectively. Judging by the obtained results, the error of the analytical methods of calculation according to Domalski are within 5–6 kJ/mol. The other methods give larger errors.

3. Conclusions

The following fundamental thermodynamic parameters for 3-(5-phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid were determined as a result of our studies. By experimental combustion calorimetry, the energy of combustion of the acid was determined with the subsequent calculation of the standard enthalpies of combustion ($\Delta_c H_{298.15}^0 = -9140.2 \pm 4.6$ kJ/mol) and formation in the condensed state ($\Delta_f H_{298.15}^0(cr) = -229.6 \pm 4.6$ kJ/mol). According to the data of the differential thermal analysis method, the melting point was calculated ($T_{fus} = 438.40 \pm 1.50$ K) and the value of the standard enthalpy of fusion ($\Delta_{fus} H_{298.15}^0 = 27.9 \pm 1.9$ kJ/mol). Based on the results of the thermogravimetric method of analysis, the standard enthalpy of vaporization was calculated ($\Delta_{vap} H_{298.15}^0 = 150.3 \pm 2.8$ kJ/mol). The standard enthalpies of sublimation (154.0 ± 3.4 kJ/mol and 153.5 ± 3.6 kJ/mol) and formation in the gaseous state (-75.7 ± 5.7 kJ/mol and -76.1 ± 5.8 kJ/mol) of the acid under study were calculated using the two methods described previously.

The analytical methods of Domalski, Joback, and quantum chemical calculations were applied to determine the enthalpy of formation in the gas phase. The smallest deviations of values obtained by analytical calculation methods from the experimentally determined in this study were observed using the Domalski (5.2 kJ/mol and 4.8 kJ/mol).

Acknowledgements

This work was financially supported by the Ministry of Education and Science of Ukraine and the Simons Foundation (Award No. 1290588).

4. Experimental

4.1. Materials and Methods

^1H and ^{13}C NMR spectra were recorded on Bruker Avance 500 (500 and 126 MHz, respectively). Mass spectral analyses were performed using an Agilent 1100 LC/MSD with API-ES/APCI mode. The Shimadzu IRSpirit-T apparatus was used to obtain data on the infrared spectrum.

According to the established method,^{13,22} the combustion energy of 3-(5-phenyl-1-(pyridin-3-yl)-1*H*-pyrrol-2-yl)propanoic acid was measured using a precision calorimeter B-08-MA with an isothermal shell (± 0.003 K) and a static calorimetric bomb. The energy equivalent for this calorimetric installation was determined and is as follows $W = 10347 \pm 7$ J/V. It was determined using reference benzoic acid (main component content 99.995 ± 0.01 mol%) with an accuracy of $\pm 0.06\%$.

The acid under study exists in a solid aggregate state under normal conditions. A sample of the acid was first pressed into tablets using a press mold, tied with cotton thread, placed in a platinum cup, and placed in a calorimeter bomb. To the bomb 1 ml of distilled water was added. During the experiment, the samples were ignited by discharging capacitors through a nichrome wire, which set the cotton thread on fire. The initial pressure of oxygen in the calorimetric bomb, pre-purified from combustible impurities, carbon dioxide and water, was 30 atmospheres. The temperature at the beginning of all experiments was 298.15 K.

At the end of each combustion experiment, procedures for quantitative analysis of combustion by-products were carried out to detect the presence of mono- and dioxide, soot and nitric acid. To perform gas analysis of the produced carbon dioxide after the combustion process, the Rossini method²⁵ was used with an accuracy of $\pm 2 \cdot 10^{-4}$ g. Additionally, the carbon monoxide content was measured in individual experiments using indicator tubes with an accuracy of $\pm 5 \cdot 10^{-6}$ g. The reliability of the gas analysis was confirmed by numerous experiments on the combustion of reference benzoic acid. The resulting nitric acid solution in a calorimetric bomb was analysed by titration with 0.1N KOH. The amount of soot formed on the walls of the platinum cup after acid combustion was determined by weighing with an accuracy of $\pm 5 \cdot 10^{-6}$ g.

In the study, the derivatograph Q-1500 D of the Paulik-Paulik-Erdey system was used to perform differential thermal analysis and thermogravimetric analysis of 3-(5-phenyl-1-(pyridin-3-yl)-1*H*-pyrrol-2-yl)propanoic acid. Derivatographic studies were conducted in a dynamic mode in the air atmosphere. The heating rate was 5 K/min with the following sensitivities on the scales: TG – 100 mg; TA up to 773 K using a platinum crucible. The enthalpy of vaporization ($\Delta_{vap}H$) was determined from the temperature dependence of the vaporization rate $V = \Delta m / \Delta \tau$ in the temperature range when the acid under study was in a liquid aggregate state, before the thermo-oxidative degradation processes began.

According to the experimentally obtained results of TG analysis, the rate of acid evaporation was determined by plotting the integral curve of sample mass loss with its subsequent differentiation every 30 s. The data on the temperature dependence of the evaporation rate were approximated by the linear form of the Arrhenius Eq. (9):

$$\ln V = A - \frac{B}{T} \quad (9)$$

where: $B = E_{act}/R$.

During the calculations, it was assumed that the process of vapor condensation in the presence of a liquid phase occurs with practically no energy loss. Therefore, according to Eq. (10), the values of the enthalpy of vaporization and activation energy (E_{act}) are equal.

$$\Delta_{vap}H_{T_{fus}} = E_{act} + RT_{fus} \quad (10)$$

The heat of vaporization absorbed during the mass loss of the sample was taken into account in Eq. (11) when calculating the enthalpy of fusion ($\Delta_{fus}H_{T_{fus}}$):

$$K \cdot S = Q_{fus} + Q_{vap} = m_0 \cdot \Delta_{fus}H_{T_{fus}} + \Delta m_{vap} \cdot \Delta_{vap}H_{T_{fus}} \quad (11)$$

where K is the heat transfer coefficient of the derivatograph Q-1500 D, which was determined using biphenyl, silver nitrate, adipic acid, benzoic acid $K-1$ and was $8.2023 \cdot 10^{-5} \cdot T_{fus}$, J/(K·s); Q_{fus} and Q_{vap} are the amount of heat absorbed during the melting or evaporation processes of the sample, respectively, J; $\Delta_{fus}H$ and $\Delta_{vap}H$ are specific values of the enthalpies of fusion and vaporization of the acid sample under study, respectively, J/g; m_0 is mass of the sample corresponding to the temperature of its melting point T_{fus} , g; Δm_{vap} is the loss of sample mass (vapor mass) over the period taken into account when determining the peak area S (K·s) on the differential thermal analysis curve, g.

4.2. Synthesis

Furfurylidene acetophenone 3. To the reaction mixture of furfural **1** (38.4 g, 0.4 mol), acetophenone **2** (48 g, 0.4 mol) in 100 ml methanol was added solution of KOH (1.4 g, 0.025 mol) under vigorous stirring. The temperature of the reaction mixture was maintained in the range of 20–25°C. After stirring for 3 h, the reaction mixture was neutralised with acetic acid, diluted with water (200 ml), extracted with dichloromethane, and washed with water. The organic layer was separated and dried with sodium sulfate. After distillation of the solvent, the residue was distilled in vacuum to obtain 56.2 g (71 %) furfurylidene acetophenone **3**. Bp 137–138°C /1 mm Hg.

4,7-Dioxo-7-phenylheptanoic acid 4. A mixture of 39.6 g (0.2 mol) furfurylidene acetophenone **3**, 300 ml ethanol, 90 ml of con. 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, 400 ml of water were added to this mass and 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 decanted from the residual resin, filtered, washed three times with water and recrystallized from ethanol. 18.7 g (40%), mp 186–187°C.

3-(5-Phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid 5. A mixture of 4,7-dioxo-7-phenylheptanoic acid **4** (5.85 g, 0.025 mol), pyridine-3-amine (2.35 g, 0.025 mol) and 50 ml of glacial acetic acid was refluxed for 6 h. Under stirring cooled reaction mixture was transferred to a beaker with 100 ml cold water. The resulting precipitate was filtered off after 20 min, washed with water and recrystallized from EtOH/DMF mixture. Yield 5.55 g (76%). ¹H NMR spectra (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). ¹³C NMR spectra (126 MHz, CDCl₃), 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).

References

- Heravi M. M., and Zadsirjan, V. (2020). Prescribed Drugs Containing Nitrogen Heterocycles: An Overview. *RSC Adv.*, 10 (72), 44247–44311 (DOI: 10.1039/d0ra09198g)
- Masci D., Hind C., Islam M. K., Toscani A., Clifford M., Coluccia A., Conforti I., Touitou M., Memdouh S., Wei X., La Regina G., Silvestri R., Sutton J. M., and Castagnolo D. (2019). Switching on the Activity of 1,5-Diaryl-Pyrrole Derivatives against Drug-Resistant ESKAPE Bacteria: Structure-Activity Relationships and Mode of Action Studies. *Eur. J. Med. Chem.*, 178 (1), 500–514 (DOI: 10.1016/j.ejmech.2019.05.087).
- Romagnoli R., Oliva P., Maria Kimatrai Salvador, Manfredini S., Padroni C., Brancale A., Ferla S., Hamel E., Ronca R., Maccarinelli F., Ruga F., Mariotto E., Viola G., and Bortolozzi, R. (2021). A Facile Synthesis of Diaryl Pyrroles Led to the Discovery of Potent Colchicine Site Antimitotic Agents. *Eur. J. Med. Chem.*, 214, 113229–113229 (DOI: 10.1016/j.ejmech.2021.113229).
- Li Petri G., Spanò V., Spatol, R., Holl R., Raimondi M., Barraja P., and Montalbano, A. (2020). Bioactive Pyrrole-Based Compounds with Target Selectivity. *Eur. J. Med. Chem.*, 208, 112783 (DOI: 10.1016/j.ejmech.2020.112783).
- Ganesh B., Raj A., Aruchamy B., Nanjan P., Drago C., and Ramani P. (2023). Pyrrole: A decisive scaffold for the development of therapeutic agents and structure-activity relationship. *ChemMedChem*, 19 (1) (DOI: 10.1002/cmdc.202300447).
- Ji Ram V., Sethi A., Nath M., and Pratap R. (2019). Five-Membered Heterocycles. *The Chemistry of Heterocycles*, 149–478 (DOI: 10.1016/b978-0-08-101033-4.00005-x)
- Zhao Y., Li Y., Ou X., Zhang P., Huang Z., Bi F., Huang R., and Wang Q. (2008). Synthesis, Insecticidal, and Acaricidal Activities of Novel 2-Aryl-Pyrrole Derivatives Containing Ester Groups. *J. Agric. Food Chem.*, 56 (21), 10176–10182 (DOI: 10.1021/jf802464d)
- El Mahdy A., Halim S., and Taha H. (2018). DFT and TD-DFT Calculations of Metallotetraphenylporphyrin and Metallotetraphenylporphyrin Fullerene Complexes as Potential Dye Sensitizers for Solar Cells. *J. Mol. Struct.*, 1160, 415–427. (DOI: 10.1016/j.molstruc.2018.02.041).
- Bulumulla C., Gunawardhana R., Gamage P., Miller J., Kularatne R., Biewer M., and Stefan, M. (2020). Pyrrole-containing semiconducting materials: Synthesis and applications in organic photovoltaics and organic field-effect transistors. *ACS Appl. Mater. Interfaces*, 12 (29), 32209–32232 (DOI: 10.1021/acsami.0c07161).
- Rebbah B., El Haib A., Lahmady S., Forsal I., Gouygou M., Mallet-ladeira S., Medaghri-alaoui A., Rakib E., and Hannioui A. (2024). Synthesis, characterization, and inhibition effects of a novel eugenol derivative bearing pyrrole functionalities on the corrosion of mild steel in a hcl acid solution. *RSC Adv.*, 14 (20), 14152–14160 (DOI: 10.1039/d4ra01337a)
- Kerru N., Gummidi L., Maddila S., Gangu K. K., and Jonnalagadda S. (2020). A review on recent advances in nitrogen-containing molecules and their biological applications. *Molecules*, 25 (8), 1909 (DOI: 10.3390/molecules25081909)
- Zhuang X., Song Y., Zhan H., Yin X., and Wu C. (2019). Synergistic Effects on the Co-Combustion of Medicinal Biowastes with Coals of Different Ranks. *Renewable Energy*, 140, 380–389 (DOI: 10.1016/j.renene.2019.03.070)

13. Sobechko B., Dibrivnyi V., and Gorak Yu. (2022). Enthalpy of formation and combustion of 5-(4-nitrophenyl)furan-2-carbaldehyde and its 2-methyl and 2-oxomethyl derivatives in the condensed state. *Chemistry, technology and application of substances*, 5 (2), 30–36 (DOI: 10.23939/ctas2022.02.030).
14. P.J. Linstrom and W.G. Mallard, Eds., NIST Chemistry WebBook, NIST Standard Reference Database Number 69, National Institute of Standards and Technology, Gaithersburg MD, 20899, (DOI: 10.18434/T4D303)
15. Electronic resource: <http://www.codata.info/resources/databases/key1.html> (Accessed on Jan 22, 2025)
16. Acree W., and Chickos J. (2016). Phase Transition Enthalpy Measurements of Organic and Organometallic Compounds. Sublimation, Vaporization and Fusion Enthalpies From 1880 to 2015. Part 1. C1–C10. *J. Phys. Chem. Ref. Data*, 45, 033101 (DOI: 10.1063/1.4948363).
17. Sobechko I. (2016). Calculation Method of Heat Capacity Change during Organic Compounds Vaporization and Sublimation. *Chem. Chem. Technol.*, 10 (1), 27–33 (DOI: 10.23939/chcht10.01.027).
18. Sobechko I., Horak Y., Dibrivnyi V., Obushak M., Goshko L. (2019). Thermodynamic Properties of 2-Methyl-5-Arylfuran-3 Carboxylic Acids Chlorine Derivatives in Organic Solvents. *Chem. Chem. Technol.*, 13 (3), 280–287 (DOI: 10.23939/chcht13.03.280).
19. Domalski, E. and Hearing, E. (1993). Estimation of the thermodynamic properties of C-H-N-O-S-halogen compounds at 298.15 K. *J. Phys. Chem. Ref. Data*, 22 (4), 805–1159 (DOI: 10.1063/1.555927)
20. Joback K. and Reid R. (1987). Estimation of pure-component properties from group-contributions. *Chem. Eng. Commun.*, 57 (1-6), 233–243 (DOI: 10.1080/00986448708960487).
21. Benson S. (1965). III-bond energies. *J. Chem. Educ.*, 42 (9), 502. (DOI: 10.1021/ed042p502)
22. Salmon A. and Dalmazzone D. (2007). Prediction of enthalpy of formation in the solid state (at 298.15 K) using second-order group contributions – part 2: Carbon-hydrogen, carbon-hydrogen-oxygen, and carbon-hydrogen-nitrogen-oxygen compounds. *J. Phys. Chem. Ref. Data*, 36 (1), 19–58 (DOI: 10.1063/1.2435401).
23. Shevchenko D., Horak, Y., Tischenko, N., Pyshna, D., and Sobechko, I. (2024). Thermodynamic properties of 3-(1,5-diphenylpyrrol-2-yl)-Propanoic acid. *Chemistry, technology and application of substances*, 7 (1), 8–14. (DOI: 10.23939/ctas2024.01.008).
24. Ohlinger W. S., Klunzinger P. E., Deppmeier B. J., Hehre W. J. (2009). Efficient Calculation of Heats of Formation. *J. Phys. Chem. A*, 113 (10), 2165–2175. (DOI: 10.1021/jp810144q).
25. Rossini F. D. (1956) Experimental Thermochemistry. *Interscience Publishers. N. Y.; London*, Vol. 2. P. 326.



© 2025 by the authors; licensee Growing Science, Canada. This is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license (<http://creativecommons.org/licenses/by/4.0/>).