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THERMODYNAMIC PARAMETERS OF THE SOLUBILITY OF 1-R-2-METHYL-5-PHENYLPYRROLE-3-CARBOXYLIC ACIDS IN METHYL ACETATE AND ETHYL ACETATE

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Using the Paal–Knorr reaction, the following compounds were synthesized: 1-butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid, 1-cyclohexyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid, 2-methyl-5-phenyl-1-(4-tolyl)-1H-pyrrole-3-carboxylic acid, and 1-(furan-2-ylmethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid. The main stages of the synthesis process are described, and the yields of the synthesized compounds are reported. Their identity was confirmed by NMR spectroscopy. An experimental study of the temperature dependence of solubility in ethyl acetate and methyl acetate was carried out gravimetrically over temperature intervals covering the generally accepted reference temperature of 298.15 K or as close to it as possible. The obtained results were processed using the least-squares method and presented in linear form using the Van't Hoff equation. The values of the enthalpy ($\Delta_{sol}H$) and entropy ($\Delta_{sol}S$) of dissolution were calculated based on the coefficients of the linear equations. Since the compounds under study undergo thermo-oxidative degradation during melting, the enthalpy of melting ($\Delta_{fus}H$) was calculated analytically using the melting temperature and a specific value of the entropy change upon melting ($\Delta_{fus}S$) equal to 0.3015±0.0075 J/(g·K), which was determined based on experimental studies of compounds containing an aryl-pyrrole fragment. The calculated molar values of the enthalpy and entropy of melting were corrected to 298.15 K, based on which the entropy ($\Delta_{mix}S$) and enthalpy ($\Delta_{mix}H$) of mixing were calculated. The obtained thermodynamic parameters of the mixing process indicate that the energy required to break the primary bonds in both the solvents and the dissolved substances is lower than the energy released upon the formation of new bonds between the solvent and the solute.

Keywords: polysubstituted pyrrole derivatives, enthalpy of dissolution, enthalpy of mixing, enthalpy of melting, methyl acetate, ethyl acetate, 2-methyl-5-phenylpyrrole-3-carboxylic acid.

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Introduction

For centuries, natural substances derived from plants, animals, or microorganisms have served as a source of treatment for a wide range of diseases. Today, a key objective of medicinal chemistry is the design of compounds with predetermined physicochemical properties, along with optimized pharmacokinetic and pharmacodynamic profiles. One of the strategic approaches involves the use of heterocyclic systems as bioisosteres for the replacement of various functional

groups in order to develop safe and effective drugs exhibiting high affinity toward specific biological targets [1]. This persistent interest in heterocycles is largely due to their widespread presence among known pharmaceutical agents, particularly nitrogen-containing compounds, including pyrrole. Pyrrole derivatives bearing diverse substituents attract considerable attention due to their significant potential for biological activity [2,3].

The study of the mechanisms of action of biologically active substances is largely based on the principle of mimicking natural processes – «deceiving nature» through precise structural modeling. Heterocycles constitute the core of numerous natural compounds, including nucleic acids, amino acids, carbohydrates, vitamins, and alkaloids. Consequently, medicinal chemistry often focuses on designing analogous structural fragments. At the same time, the role of heterocycles in modern organic chemistry extends far beyond pharmaceutical applications. The incorporation of a heterocyclic fragment into a molecular structure enables the targeted modulation of key drug properties, such as efficacy and selectivity through bioisosteric replacement, lipophilicity, polarity, and aqueous solubility [4]. The applications of such compounds are not limited to drugs, they are also successfully used as functional additives in the cosmetics industry and in the development of polymeric materials.

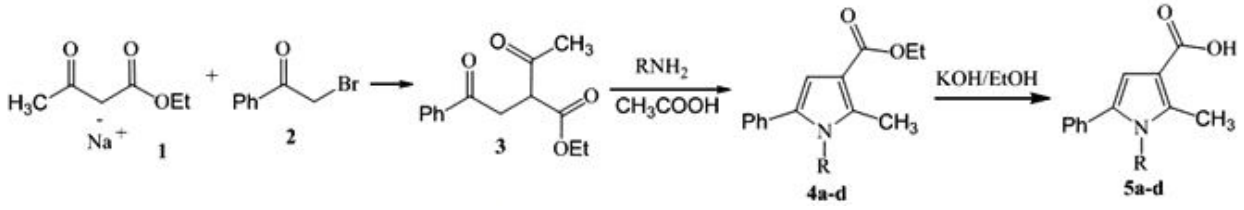
The pyrrole ring is a particularly significant structural fragment, found in numerous natural compounds and biomolecules such as chlorophyll, hemoglobin, myoglobin, cytochromes, vitamin B_{12}, bilirubin, and biliverdin [5]. The synthesis and purification of its derivatives require the use of specific solvents. The choice of solvent for synthesis and recrystallization processes is primarily determined by its chemical inertness toward both the starting materials and the reaction products. High purity of pharmaceutical substances is of critical importance, as it directly affects the quality of the final product. Therefore, the thermodynamic parameters of solvent–solute interactions play a crucial role in solvent selection, as they enable precise calculation of energy balances at the stages of synthesis, purification, and further processing.

The aim of this study was to determine the thermodynamic parameters of solubility of 1-R-2-methyl-5-phenylpyrrole-3-carboxylic acids in methyl acetate and ethyl acetate and to further analyze the obtained results.

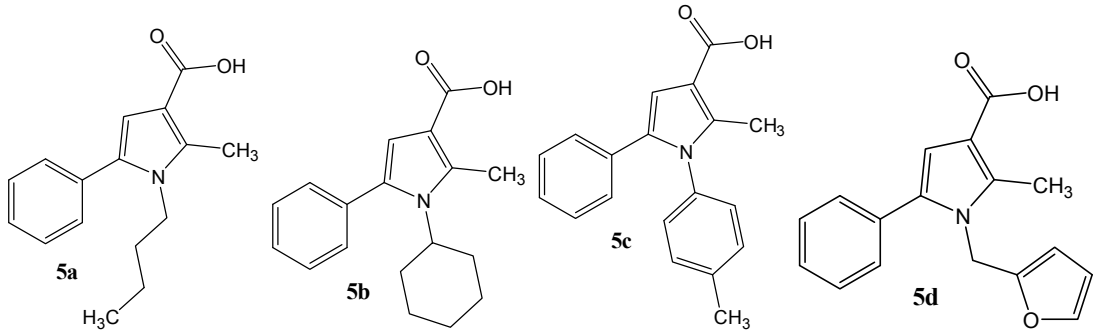
Experimental

The synthesis of carboxylic acids was carried out in a reactor equipped with a thermometer, a stirrer, and a reflux condenser in two stages. At the first stage (Scheme), to a suspension of metallic sodium (0.7 g, 0.03 mol), crushed in 40 mL of toluene, ethyl acetoacetate (3.9 g, 0.044 mol) was gradually added under cooling and vigorous stirring. The mixture was left under stirring at room temperature for three days. After cooling to 10^0C, phenacyl bromide **2** (5.94 g, 0.03 mol) was added to the reaction mixture with continued stirring for 1 h at the same temperature, and then for another 24 h at room temperature. Upon completion of the reaction, the solid residue of sodium bromide was separated by filtration, and the organic solvent (toluene) was removed under reduced pressure (30 mm Hg). The resulting residue was distilled under vacuum and ethyl 2-acetyl-4-oxo-4-phenylbutanoate **3** was obtained. B.p. 175–177^{0}C/2 mm Hg. Yield 6.35 g (86%).

At the second stage, 5.00 g (0.02 mol) of ethyl 2-acetyl-4-oxo-4-phenylbutanoate **3** was dissolved in 30 mL of cooled acetic acid, followed by the addition of 0.02 mol of the corresponding amine. The mixture was refluxed for 2.5 hours. After cooling, the reaction mass was diluted with 100 mL of water, and the resulting viscous oils were extracted with dichloromethane. The organic phase was washed with water and dried over anhydrous sodium sulfate for 2 hours. After removal of the solvent, a solution of KOH (2.24 g, 0.04 mol) in 20 mL of ethanol was added to the crude ester 3. The mixture was heated for 15 min, cooled to room temperature, then 50 mL of water was added and the solution was acidified with diluted hydrochloric acid (1:1). As a result, the target acids **5** were obtained and purified by recrystallization from ethanol. The synthesized compounds are shown in Figure.



Scheme. Synthesis of target compounds **5:** R=$CH_3(CH_2)_3$– (**a**); cyclohexyl (**b**); 4-$CH_3C_6H_4$ (**c**); furfuryl (**d**)



1-R-2-methyl-5-phenyl-pyrrole-3-carboxylic acids **5**

1-Butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid ***5a***

Yield 64%. Mp 163°C. ^{1}H NMR spectra (500 MHz, DMSO-d_6), δ, ppm: 11.70 (br.s, 1H), 7.43 (t, *J*=7.7 Hz, 2H), 7.40–7.29 (m, 3H), 6.36 (s, 1H), 3.89 (t, *J*=7.7 Hz, 2H), 2.54 (s, 3H), 1.41 (quint, *J*=7.5 Hz, 2H), 1.08 (sext, *J*=7.0 Hz, 2H), 0.70 (t, *J*=7.4 Hz, 3H). ^{13}C NMR spectra (126 MHz, DMSO-d_6), δ, ppm: 166.16, 135.97, 132.79, 132.75, 128.85, 128.58, 127.38, 111.81, 109.64, 43.24, 32.03, 19.11, 13.27, 11.21. MS (m/z, ES-API): 258 (M^++1).

1-Cyclohexyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid ***5b***

Yield 68%. Mp 227°C. ^{1}H NMR spectra (500 MHz, DMSO-d_6), δ, ppm: 11.66 (br.s, 1H), 7.43 (t, *J*=7.3 Hz, 2H), 7.37 (t, *J*=7.3 Hz, 1H), 7.30 (d, *J*=7.0 Hz, 2H), 6.27 (s, 1H), 3.98 (tt, *J*=12.7, 3.6 Hz, 1H), 2.66 (s, 3H), 2.03–1.46 (m, 8H), 1.16–1.08 (m, 2H). ^{13}C NMR spectra (126 MHz, DMSO-d_6), δ, ppm: 166.23, 135.47, 133.49, 133.26, 129.61, 128.36, 127.61, 112.37, 110.13, 57.02, 31.69, 25.91, 24.73, 12.80. MS (m/z, ES-API): 284 (M^++1).

2-Methyl-5-phenyl-1-(4-tolyl)-1H-pyrrole-3-carboxylic acid ***5c***

Yield 72%. Mp 229°C. ^{1}H NMR spectra (500 MHz, DMSO-d_6), δ, ppm: 11.93 (br.s, 1H), 7.25 (d, *J*=7.8 Hz, 2H), 7.17 (t, *J*=7.3 Hz, 2H), 7.14–7.08 (m, 3H), 7.05 (d, *J*=6.7 Hz, 2H), 6.65 (s, 1H), 2.33 (s, 3H), 2.28 (s, 3H). ^{13}C NMR spectra (126 MHz, DMSO-d_6), δ, ppm: 166.07, 137.90, 137.45, 135.07, 133.12, 132.12, 129.83, 128.19, 128.14, 127.65, 126.47, 112.70, 109.88, 20.65, 12.15. MS (m/z, ES-API): 292 (M^++1).

1-(Furan-2-ylmethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid ***5d***

Yield 70%. Mp 193°C. ^{1}H NMR spectra (500 MHz, DMSO-d_6), δ, ppm: 11.81 (br.s, 1H), 7.58 (d, *J*=1.9 Hz, 1H), 7.46–7.32 (m, 5H), 6.42 (s, 1H), 6.37 (dd, *J*=3.0, 1.8 Hz, 1H), 6.02 (d, *J*=2.7 Hz, 1H), 5.12 (s, 2H), 2.53 (s, 3H). ^{13}C NMR spectra (126 MHz, DMSO-d_6), δ, ppm: 166.05, 150.31, 142.89, 136.70, 133.25, 132.22, 128.86, 128.63, 127.56, 112.32, 110.61, 109.74, 107.71, 41.06, 11.22. MS (m/z, ES-API): 282 (M^++1).

Solubility studies were conducted in acetates, namely methyl acetate and ethyl acetate. Their selection was based on the similarity of their physicochemical properties and interactions with 1-R-2-methyl-5-phenylpyrrole-3-carboxylic acids. These solvents are aprotic and of medium polarity. Considering the hydrophobic nature of the phenyl and methyl substituents, as well as the presence of a polar carboxyl group, these solvents provide effective interaction with both molecular fragments. The polarity of ethyl acetate is higher, which facilitates better dissolution of derivatives exhibiting more pronounced donor-acceptor properties. Experiments were performed under conditions ensuring the inertness of the solvent toward the dissolved substance, thereby preserving the compound's structure.

Their relative volatility (boiling point of ethyl acetate B.p.=77.1°C, methyl acetate B.p.=56.9°C) and moderate toxicity ensure convenient removal of the solvent after the studies.

The solvents used in the study were supplied by Merck (methyl acetate CAS 79-20-9; ethyl acetate CAS 71-43-2). These solvents are intended for chromatographic analyses, with a purity of the main component ≥99.9%. Identification was performed by measuring the refractive index, which matched the provided literature data and the values indicated in the certificates of analysis. The solvents were used without prior purification.

The temperature dependence of solubility of the studied acids was determined gravimetrically [6–11].

The acids were dissolved in sealed glass round-bottom flasks equipped with a PTFE stirrer, a thermometer, and a sampling port. The flasks were

placed in a thermostat with temperature control accurate to ±0.1 K. The stirring rate was maintained between 30 and 40 rpm. The saturation procedure of the solutions was carried out in two stages: initially 48 hours without stirring, followed by 2 hours with continuous stirring.

To minimize the influence of external factors, experiments were conducted under variable temperature conditions: after increasing the temperature, it was subsequently lowered, and vice versa. This approach allowed confirming the thermodynamic consistency of the data. The absence of hysteresis in the temperature dependence curve of solubility indicated that a state close to thermodynamic equilibrium was achieved.

Sampling was performed in series of three samples, which were immediately transferred into pre-dried and weighed sealed weighing bottles. Further removal of the solvent was carried out in a thermostatted drying oven at 363−373 K. After complete solvent removal, the weighing bottles were hermetically sealed, cooled in a desiccator to room temperature, and weighed. Weighing was performed at 296±2 K on pre-calibrated and certified balances with an accuracy of ±0.0002 g.

Results and discussion

The experimental results are presented in Table 1, where m_1 is the mass of the solvent, m_2 is the mass of the dissolved substance, X_2 is the mole fraction of solubility, and T is the temperature at which solubility was determined. The linear equations obtained from the data are presented in the form of the Van't Hoff equation:

$$\ln X_2 = -\Delta_{sol}H/RT + \Delta_{sol}S/R, \quad (1)$$

where $\Delta_{sol}H$ is the enthalpy of solution; and $\Delta_{sol}S$ is the entropy of solution.

All experimental data processing results presented below were calculated using the Student's t-coefficient at a 0.95 confidence level.

The calculation of the thermodynamic parameters of solubility, namely the enthalpy and entropy of solubility ($\Delta_{sol}H$ and $\Delta_{sol}S$, respectively) presented in Table 2, takes into account the process of solution formation and the transition of solid substances into the liquid phase. In calculating the changes in mixing entropy ($\Delta_{mix}S$) and mixing enthalpy ($\Delta_{mix}H$), the values of the enthalpy ($\Delta_{fus}H$) and entropy ($\Delta_{fus}S$) of melting of the studied compounds were also considered, using either the average solution temperature or the standard value of 298.15 K according to equations (2) and (3):

$$\Delta_{sol}S = \Delta_{fus}S + \Delta_{mix}S, \quad (2)$$

$$\Delta_{sol}H = \Delta_{fus}H + \Delta_{mix}H. \quad (3)$$

The results of the calculation of the enthalpy and entropy of mixing, along with the mole fractions of solubility, are presented in Table 2.

During the investigation of 1-R-2-methyl-5-phenylpyrrole-3-carboxylic acids using a Q-1500 D derivatograph, thermal decomposition of the compounds was observed during melting. Therefore, experimental determination of melting entropy ($\Delta_{fus}S$) and melting enthalpy ($\Delta_{fus}H$) was not possible. Their further calculation was performed using analytical methods described elsewhere [12−14]. Specifically, the specific melting entropy ($\Delta_{fus}S_{Tfus}$) is considered a constant value for organic compounds within the same structural class. For example, the melting entropy values for substances containing pyrazole, pyrrole, and imidazole fragments is $\Delta_{fus}S_{Tfus}$=0.460±0.032 J/(g·K) and it is $\Delta_{fus}S_{Tfus}$=0.323±0.027 J/(g·K) for compounds with arylfuran fragments.

In our case, since the synthesized compounds contain an arylpyrrole fragment, the average specific melting entropy value can be calculated based on published data for structurally related compounds [14,15], as presented in Table 3.

The averaged specific value of the entropy of melting for the given substances is $\Delta_{fus}S$=0.3059±0.0041 J/(g·K).

Using the conversion to the molecular weight of the synthesized substances, the molar entropy of melting was calculated using the following equation:

$$\Delta_{fus}S = (0.3059 \pm 0.0041) \cdot M, \quad (J/(mol \cdot K)). \quad (3)$$

Based on the known relation given in equation (4), the values of the melting enthalpy were calculated using equation (5):

$$\Delta_{fus}S_{Tfus} = \Delta_{fus}H_{Tfus}/T_{fus}, \quad (J/(mol \cdot K)), \quad (4)$$

$$\Delta_{fus}H_{Tfus} = (\Delta_{fus}S) \cdot T_{fus}, \quad (kJ/mol). \quad (5)$$

The values of the enthalpy and entropy of fusion were brought to 298.15 K by recalculating them using the equation given in ref. [13].

The results of the calculation of thermodynamic parameters and their conversion to the standard temperature of 298.15 K are shown in Table 4.

Analysis of the thermodynamic characteristics of the synthesized 1-R-2-methyl-5-phenylpyrrole-3-carboxylic acids indicates a high degree of structural order in the solid state and the stability of their crystal lattices. The obtained values of melting enthalpies and entropies ($\Delta_{fus}H^0_{298}$ and $\Delta_{fus}S^0_{298}$) demonstrate the

Table 1

Temperature dependence of solubility of pyrrole carboxylic acid derivatives in acetates

T, K	m_1, g	m_2, g	$X_2 \cdot 10^3$	T, K	m_1, g	m_2, g	$X_2 \cdot 10^3$	T, K	m_1, g	m_2, g	$X_2 \cdot 10^3$
1	2	3	4	5	6	7	8	9	10	11	12
1-Butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid in methyl acetate **5a**											
278.65	1.4546	0.0439	8.60	290.65	1.6269	0.0725	12.66	296.05	1.6240	0.0892	15.57
278.65	1.2961	0.0391	8.61	290.65	1.7397	0.0778	12.71	300.55	1.6770	0.1060	17.87
278.65	1.6075	0.0488	8.66	291.35	2.3394	0.1116	13.54	300.55	1.0002	0.0636	17.98
285.65	2.0291	0.0790	11.08	291.35	2.0315	0.0970	13.56	300.55	1.1841	0.0754	18.00
285.65	1.6635	0.0648	11.08	291.35	2.1189	0.1013	13.58	301.65	0.6238	0.0415	18.79
285.65	1.4914	0.0583	11.12	294.15	1.4744	0.0776	14.92	301.65	0.1513	0.0101	18.86
286.15	1.3604	0.0533	11.14	294.15	2.1186	0.1120	14.98	301.65	0.2246	0.0150	18.86
286.15	1.4049	0.0550	11.14	294.15	1.9968	0.1061	15.07	302.95	1.1483	0.0790	19.42
286.15	1.3503	0.0538	11.33	296.05	1.9212	0.1038	15.31	302.95	1.2511	0.0862	19.44
290.65	1.7230	0.0767	12.64	296.05	1.7051	0.0933	15.50	302.95	1.7440	0.1203	19.46
$\ln N_2=(5.41\pm0.21)-(2832\pm62)\cdot1/T$											
1-Butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid in ethyl acetate **5a**											
276.65	1.6381	0.0343	7.11	284.15	1.9249	0.0535	9.42	293.15	1.6314	0.0645	13.35
276.65	1.4796	0.0311	7.13	286.15	2.1651	0.0649	10.16	293.15	1.2647	0.0502	13.41
276.65	2.3413	0.0493	7.15	286.15	1.0414	0.0313	10.19	294.15	2.2228	0.0900	13.67
277.05	1.5294	0.0323	7.18	286.15	1.5996	0.0481	10.19	294.15	1.8359	0.0745	13.69
277.05	1.1741	0.0250	7.24	290.95	1.5204	0.0546	12.14	294.15	1.3050	0.0532	13.77
277.05	1.7260	0.0371	7.31	290.95	1.7987	0.0649	12.19	297.55	1.7432	0.0796	15.39
279.15	1.7616	0.0404	7.79	290.95	1.7507	0.0634	12.25	297.55	2.0307	0.0930	15.43
279.15	2.2252	0.0512	7.82	292.15	1.7916	0.0661	12.47	297.55	1.8709	0.0857	15.43
279.15	1.8616	0.0430	7.84	292.15	1.4343	0.0531	12.52	298.15	1.8573	0.0861	15.62
284.15	2.1168	0.0584	9.35	292.15	1.6217	0.0603	12.56	298.15	1.9568	0.0909	15.66
284.15	1.9239	0.0531	9.36	293.15	1.3329	0.0527	13.34	298.15	1.3107	0.0612	15.72
$\ln N_2=(6.06\pm0.23)-(3045\pm72)\cdot1/T$											
1-Cyclohexyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid in methyl acetate **5b**											
278.65	1.1698	0.0277	6.16	294.25	1.5818	0.0576	9.46	301.05	1.7869	0.0775	11.25
278.65	1.5378	0.0370	6.27	294.25	1.4986	0.0562	9.74	301.05	2.3541	0.1028	11.33
278.65	1.2759	0.0314	6.42	294.25	1.8999	0.0721	9.86	301.05	2.0049	0.0876	11.33
284.95	1.1166	0.0317	7.38	295.45	1.6958	0.0663	10.15	302.25	1.5226	0.0702	11.95
284.95	1.0193	0.0289	7.38	295.45	2.2873	0.0895	10.16	302.25	1.5582	0.0721	11.99
284.95	1.5985	0.0469	7.63	295.45	1.8488	0.0728	10.23	302.25	1.5579	0.0722	12.00
289.75	2.1558	0.0708	8.54	297.15	2.0747	0.0819	10.24	303.75	1.0260	0.0490	12.36
289.75	1.8247	0.0602	8.58	297.15	1.9402	0.0770	10.30	303.75	1.0514	0.0503	12.38
289.75	1.3733	0.0458	8.66	297.15	2.0648	0.0820	10.31	303.75	0.9819	0.0470	12.40
290.95	1.8805	0.0632	8.74	298.25	1.7065	0.0690	10.49	304.75	2.1808	0.1064	12.64
290.95	1.6377	0.0556	8.83	298.25	1.2980	0.0525	10.50	304.75	1.6608	0.0826	12.88
290.95	1.6247	0.0554	8.87	298.25	1.9841	0.0805	10.53	304.75	1.9223	0.0958	12.90
$\ln N_2=(3.12\pm0.24)-(2284\pm72)\cdot1/T$											
1-Cyclohexyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid in ethyl acetate **5b**											
278.95	1.6881	0.0532	9.74	284.65	1.1378	0.0420	11.37	293.65	1.6041	0.0740	14.19
278.95	1.8416	0.0585	9.81	284.65	1.6664	0.0616	11.39	294.45	1.1096	0.0521	14.43
278.95	1.7546	0.0561	9.88	286.35	1.1593	0.0450	11.97	294.45	1.5912	0.0748	14.45
280.25	1.3446	0.0437	10.03	286.35	1.0295	0.0403	12.05	294.45	1.3255	0.0625	14.49
280.25	1.4748	0.0479	10.03	286.35	1.2883	0.0505	12.07	297.55	1.3456	0.0693	15.82
280.25	1.5898	0.0518	10.06	287.95	1.8446	0.0725	12.12	297.55	1.4121	0.0730	15.86
281.95	2.8016	0.0958	10.56	287.95	1.6863	0.0664	12.13	297.55	1.2386	0.0645	15.98
281.95	2.1508	0.0742	10.65	287.95	1.5747	0.0625	12.22	299.05	1.8026	0.0957	16.29
281.95	1.8340	0.0633	10.66	293.65	2.3539	0.1085	14.18	299.05	1.1694	0.0622	16.31
284.65	1.2569	0.0463	11.36	293.65	1.9033	0.0878	14.18	299.05	0.9667	0.0516	16.37
$\ln N_2=(2.98\pm0.16)-(2125\pm45)\cdot1/T$											

Continued Table 1

1	2	3	4	5	6	7	8	9	10	11	12
2-Methyl-5-phenyl-1-(4-tolyl)-1H-pyrrole-3-carboxylic acid in methyl acetate **5c**											
291.35	1.6271	0.0217	3.37	296.65	1.3648	0.0220	4.08	299.95	1.7229	0.0320	4.69
291.35	1.3940	0.0186	3.38	296.65	1.6383	0.0265	4.10	302.15	1.6443	0.0322	4.95
291.35	1.9289	0.0260	3.41	297.65	1.1450	0.0193	4.26	302.15	1.4573	0.0288	4.99
292.95	1.8032	0.0253	3.55	297.65	1.4985	0.0252	4.26	302.15	1.2546	0.0251	5.06
292.95	2.0876	0.0295	3.58	297.65	1.2266	0.0209	4.30	303.15	1.1755	0.0243	5.23
292.95	1.6755	0.0238	3.59	298.65	1.1858	0.0207	4.42	303.15	1.2894	0.0267	5.24
295.65	1.2357	0.0192	3.94	298.65	1.6843	0.0298	4.47	303.15	1.6674	0.0350	5.30
295.65	1.3219	0.0206	3.95	298.65	1.3731	0.0244	4.50	308.05	2.1679	0.0527	6.14
295.65	1.0091	0.0159	3.99	299.95	1.3522	0.0246	4.60	308.05	0.9014	0.0220	6.15
296.65	1.2161	0.0196	4.08	299.95	1.5520	0.0284	4.62	308.05	1.3008	0.0320	6.21
$\ln N_2$=(5.48±0.19)–(3254±57)·1/T											
2-Methyl-5-phenyl-1-(4-tolyl)-1H-pyrrole-3-carboxylic acid in ethyl acetate **5c**											
293.65	1.9067	0.0257	4.05	299.65	1.3814	0.0231	5.02	307.15	1.3469	0.0285	6.35
293.65	2.0109	0.0273	4.08	299.65	1.5185	0.0254	5.02	309.65	1.9350	0.0435	6.75
293.65	1.6715	0.0229	4.13	303.15	1.9041	0.0348	5.49	309.65	1.5497	0.0350	6.77
293.65	1.3725	0.0189	4.15	303.15	1.5694	0.0292	5.59	309.65	1.6243	0.0373	6.90
293.65	1.6841	0.0234	4.18	303.15	1.4374	0.0273	5.70	313.15	1.9293	0.0469	7.30
293.65	1.4631	0.0204	4.19	304.15	1.2041	0.0236	5.89	313.15	1.5431	0.0378	7.35
298.15	1.7274	0.0263	4.58	304.15	1.8762	0.0373	5.97	313.15	1.4712	0.0362	7.39
298.15	1.6831	0.0258	4.61	304.15	1.4302	0.0286	6.00	316.15	1.6866	0.0456	8.11
298.15	1.5816	0.0244	4.63	307.15	1.5133	0.0306	6.07	316.15	1.7583	0.0479	8.17
299.65	2.0394	0.0331	4.88	307.15	2.0486	0.0421	6.18	316.15	1.4209	0.0388	8.18
$\ln N_2$=(4.09±0.33)–(2812±99)·1/T											
1-(Furan-2-ylmethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid in methyl acetate **5d**											
277.65	1.4473	0.0396	7.14	284.75	0.9295	0.0310	8.71	291.95	1.8764	0.0746	10.36
277.65	1.3094	0.0359	7.17	284.75	1.3026	0.0438	8.77	298.35	1.2915	0.0605	12.19
277.65	1.4532	0.0400	7.19	286.95	1.0787	0.0382	9.23	298.35	1.5651	0.0737	12.24
282.15	1.6556	0.0495	7.81	286.95	1.1194	0.0398	9.26	298.35	1.6125	0.0762	12.28
282.15	1.6140	0.0485	7.84	286.95	0.8245	0.0298	9.43	301.15	1.7850	0.0889	12.94
282.15	1.1186	0.0337	7.87	288.65	1.7973	0.0662	9.60	301.15	1.6631	0.0832	13.00
283.65	1.7126	0.0535	8.16	288.65	1.3022	0.0480	9.60	301.15	1.9636	0.0987	13.06
283.65	1.2562	0.0396	8.22	288.65	1.6040	0.0592	9.63	303.35	1.2009	0.0631	13.64
283.65	1.6737	0.0529	8.25	291.95	1.9516	0.0771	10.30	303.35	1.6865	0.0889	13.69
284.75	1.8519	0.0614	8.65	291.95	1.7345	0.0686	10.31	303.35	1.1707	0.0622	13.80
$\ln N_2$=(2.86±0.18)–(2169±53)·1/T											
1-(Furan-2-ylmethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid in ethyl acetate **5d**											
274.95	1.4139	0.0127	2.81	281.15	1.5778	0.0165	3.27	289.95	1.7776	0.0232	4.07
274.95	2.0449	0.0185	2.82	281.15	1.1408	0.0120	3.28	289.95	1.9036	0.0249	4.08
274.95	2.3397	0.0214	2.85	281.15	1.6359	0.0175	3.34	289.95	2.3274	0.0305	4.09
280.05	1.6177	0.0167	3.21	285.05	2.2378	0.0259	3.61	292.05	2.2533	0.0311	4.30
280.05	1.6748	0.0174	3.23	285.05	1.9743	0.0229	3.61	292.05	1.0851	0.0151	4.34
280.05	1.6736	0.0174	3.24	285.05	1.7368	0.0202	3.62	292.05	1.1804	0.0166	4.37
280.35	1.4883	0.0155	3.24	289.25	2.2071	0.0278	3.93	292.35	1.1716	0.0165	4.38
280.35	1.8976	0.0198	3.25	289.25	1.8032	0.0229	3.96	292.35	2.0767	0.0292	4.38
280.35	1.9060	0.0199	3.26	289.25	1.6750	0.0214	3.99	292.35	1.4842	0.0210	4.41
$\ln N_2$=(1.36±0.21)–(1987±60)·1/T											

Table 2

Thermodynamic parameters of the process of dissolution of 1-R-2-methyl-5-phenylpyrrole-3-carboxylic acids in methyl and ethyl acetate at 298.15 K

No.	Substance	$X_2 \cdot 10^3$	$\Delta_{sol}H^0$, kJ/mol	$\Delta_{mix}H^0$, kJ/mol	$\Delta_{sol}S^0$, J/mol·K	$\Delta_{mix}S^0$, J/mol·K
Thermodynamic parameters of dissolution of compounds in methyl acetate						
1	1-Butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid **5a**	16.8	23.55±0.52	–2.8±2.7	45.0±1.7	–11.5±6.1
2	1-Cyclohexyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid **5b**	10.7	18.99±0.60	–11.4±3.3	25.9±2.0	–27.5±6.7
3	2-Methyl-5-phenyl-1-(4-tolyl)-1H-pyrrole-3-carboxylic acid **5c**	4.34	27.05±0.47	–4.25±3.3	45.6±1.6	–9.7±6.8
4	1-(Furan-2-ylmethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid **5d**	12.1	18.03±0.44	– 11.37±3.0	23.8±1.6	–33.7±6.6
Thermodynamic parameters of dissolution of compounds in ethyl acetate						
1	1-Butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid **5a**	15.7	25.32±0.60	–1.0±2.7	50.4±1.9	–6.1±6.2
2	1-Cyclohexyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid **5b**	15.8	17.67±0.37	–12.7±3.2	24.8±1.3	–28.6±6.5
3	2-Methyl-5-phenyl-1-(4-tolyl)-1H-pyrrole-3-carboxylic acid **5c**	4.77	23.38±0.82	–7.92±3.4	34.0±2.7	–20.7±7.1
4	1-(Furan-2-ylmethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid **5d**	4.95	16.51±0.50	– 12.89±3.0	11.3±1.7	–46.2±6.6

Table 3

Melting enthalpy of compounds with arylpyrrole fragment

No.	Substance	T_{fus}, K	$\Delta_{fus}H^0{}_{Tfus}$, kJ/mol	$\Delta_{fus}S^0{}_{Tfus}$, J/mol·K
1	3-(1.5-diphenylpyrrole-2-yl)-propanoic acid	442.4	43.6±1.2	0.3383
2	3-(5-phenylpyrrole-2-yl)-propanoic acid	416.5	28.71±0.78	0.3203
3	3-(1-(pyridin-3-yl)-5-phenylpyrrole-2-yl)propanoic acid	438.4	36.5±1.3	0.2848
4	3-(1-(4-methylphenyl)-5-phenylpyrrole-2-yl)propanoic acid	427.9	36.61±0.88	0.2802

Table 4

Recalculation of the thermodynamic parameters of the dissolution of the studied acids in acetates at 298.15 K

No.	Substance	T_{fus}, K	$\Delta_{fus}H^0_{Tfus}$, kJ/mol	$\Delta_{fus}S^0_{Tfus}$, J/mol·K	$\Delta_{fus}H^0_{298}$	$\Delta_{fus}S^0_{298}$
1	1-Butyl-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylic acid **5a**	436.35	34.3±2.4	78.7±5.5	26.3±2.6	56.5±5.9
2	1-Cyclohexyl-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylic acid **5b**	500.75	43.4±3.0	86.7±6.0	30.4±3.2	53.4±6.4
3	2-Methyl-5-phenyl-1-(4-tolyl)-1*H*-pyrrole-3-carboxylic acid **5c**	502.25	44.7±3.1	89.1±6.2	31.3±3.3	54.7±6.6
4	1-(Furan-2-ylmethyl)-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylic acid **5d**	466.65	40.2±2.8	86.0±6.0	29.4±3.0	57.5±6.4

presence of strong intermolecular interactions in the solid phase of all investigated acids, which is indicative of the formation of a stable crystal framework. The high magnitudes of these parameters suggest that significant energy input is required to disrupt the crystal lattice, thus reflecting a high degree of molecular ordering in the solid phase. So more energy is required to break the primary interactions than is gained from the formation of new interactions between the acetates and the dissolved compounds. A comparative evaluation of the standard thermodynamic functions confirms the general trends typical for compounds containing branched aromatic and aliphatic fragments in their molecular structures. Despite variations in the substituents on the pyrrole ring, all the acids exhibit a similar crystallization behavior, as evidenced by the closely related values of the melting entropy ($\Delta_{fus}S^0_{298}$).

The mixing enthalpy values ($\Delta_{mix}H$) obtained in the solvents for this series of compounds are comparable within the margin of calculation error, indicating a uniform solvation nature, primarily due to interactions between the functional groups of the acids and solvent molecules. This suggests the absence of significant steric hindrance or specific intermolecular associations in solution.

The scientific novelty of the study lies in the comprehensive approach to evaluating the thermodynamic stability of a new series of pyrrolecarboxylic acids by recalculating their characteristics to standard conditions (298.15 K), which enables direct comparison of thermal effects for different structural variants.

In particular, it was found that 2-methyl-1-(4-tolyl)-5-phenyl-1H-pyrrole-3-carboxylic acid exhibits the highest melting enthalpy and entropy, which may indicate the special role of steric factors in stabilizing its crystal structure.

By converting thermodynamic functions to standard conditions, the thermal effects of the obtained pyrrolecarboxylic acids can be compared allowing for the characterization of the degree of solid-state stability for each compound.

Conclusions

Nitrogen-substituted 1-R-2-methyl-5-phenylpyrrole-3-carboxylic acids were synthesized via the Paal–Knorr reaction. The thermodynamic properties of the solutions of these compounds in methyl acetate and ethyl acetate were characterized. Enthalpies and entropies of dissolution, mixing, and melting of the solutes were calculated. All obtained values were recalculated to standard conditions. The nature of the solute–solvent interactions was established.

REFERENCES

1. *Bioactive* pyrrole-based compounds with target selectivity / Li Petri G., Spano V., Spatola R., Holl R., Raimondi M.V., Barraja P., Montalbano A. // Eur. J. Med. Chem. – 2020. – Vol.208. – Art. No. 112783.

2. *Heterocyclic* scaffolds: centrality in anticancer drug development / Ali I., Lone M.N., Al-Othman Z.A., Al-Warthan A., Sanagi M.M. // Curr. Drug Targets. – 2015. – Vol.16. – P.711-734.

3. *Insights* into the pharmacology of new heterocycles embedded with oxopyrrolidine rings: DNA binding, molecular docking, and anticancer studies / Ali I., Lone M.N., Alothman Z.A., Alwarthan A. // J. Mol. Liq. – 2017. – Vol.234. – P.391-402.

4. *Gomtsyan A.* Heterocycles in drugs and drug discovery // Chem. Heterocycl. Compd. – 2012. – Vol.48. – P.7-10.

5. *Jones R.A.* Pyrroles: the synthesis and the physical and chemical aspects of the pyrrole ring. – Wiley-Interscience, 1990.

6. *Du C.* The solubility of ethyl candesartan in mono solvents and investigation of intermolecular interactions // Liquids. – 2022. – Vol.2. – No. 4. – P.404-412.

7. *Solubility* measurement, modeling, and solvent effect of m-hydroxyacetophenone in ten pure and binary mixed solvents from T = (289.15−325.15) K / Li Z., Guo J., Hu B., Zhou C., Zheng Y., Zhao H., Li Q. // J. Mol. Liq. − 2022. − Vol.353. − Art. No. 118798.

8. *Maharana A., Sarkar D.* Solubility measurements and thermodynamic modeling of pyrazinamide in five different solvent-antisolvent mixtures // Fluid Phase Equilib. − 2019. − Vol.497. − P.33-54.

9. *Measurement* and correlation of solubility, Hansen solubility parameters and thermodynamic behavior of clozapine in eleven mono-solvents / Huang W., Wang H., Li C., Wen T., Xu J., Ouyang J., Zhang C. // J. Mol. Liq. − 2021. − Vol.333. − Art. No. 115894.

10. *Thermodynamic* parameters of dissolution of 5 nitrophenyl furfural oximes in ethyl acetate / Marshalek A.S., Sobechko I.B., Horak Y.I., Kochubey V.V., Dibrivnyi V.M. // Voprosy Khimii i Khimicheskoi Tekhnologii. − 2017. − No. 1. − P.18-22.

11. *Thermodynamic* properties of solubility of 2-methyl-5-arylfuran-3-carboxylic acids in organic solvents / Sobechko I., Dibrivnyi V., Horak Y., Velychkivska N., Kochubei V., Obushak M. // Chem. Chem. Technol. − 2017. − Vol.11. − No. 4. − P.397-404.

12 *Thermodynamic* properties of 2-methyl-5-arylfuran-3-carboxylic acids chlorine derivatives in organic solvents / Sobechko I., Horak Y., Dibrivnyi V., Obushak M., Goshko L. // Chem. Chem. Technol. − 2019. − Vol.13. − No. 3. − P.280-287.

13. *Synthesis* and thermodynamic parameters of phase transitions of 3-(1-R-5-phenyl-1H-pyrrol-2-yl)propanoic acid derivatives / Shevchenko D., Horak Y., Tyschenko N., Kichura D., Obushak M., Sobechko I. // Chem. Chem. Technol. − 2025. − Vol.19. − No. 3. − P.403-411.

14. Thermodynamic parameters of the solubility of 3-(1,5-diphenylpyrrol-2-yl)propanoic acid in organic solvents / Shevchenko D.S., Horak Y.I., Tischenko N.I., Pyshna D.B., Obushak M.D., Sobechko I.B. // Voprosy Khimii i Khimicheskoi Tekhnologii. − 2025. − No. 2. − P.24-32.

15. *Synthesis* and thermodynamic properties of 3-(5-phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid in condensed and gaseous states / Shevchenko D., Horak Y., Obushak M., Tischenko N., Sobechko I. // Curr. Chem. Lett. − 2025. − Vol.14. − No. 3. − P.559-566.

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ТЕРМОДИНАМІЧНІ ПАРАМЕТРИ РОЗЧИНЕННЯ 1-R-2-МЕТИЛ-5-ФЕНІЛПІРОЛ-3-КАРБОНОВОЇ КИСЛОТИ В МЕТИЛАЦЕТАТІ ТА ЕТИЛАЦЕТАТІ

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За реакцією Пааля-Кнорра синтезовано 1-бутил-2-метил-5-феніл-1*H*-пірол-3-карбонова кислота, 2-метил-5-феніл-1-циклогексил-1*H*-пірол-3-карбонова кислота, 2-метил-1-(4-толіл)-5-феніл-1*H*-пірол-3-карбонова кислота і 2-метил-5-феніл-1-(фуран-2-ілметил)-1*H*-пірол-3-карбонова кислота. Описано основні стадії процесу синтезу та зазначено вихід синтезованих речовин. За даними ЯМР спектроскопії підтверджено їх індивідуальність Експериментальне дослідження температурної залежності розчинності в етилацетаті та метилацетаті проводили гравіметрично в температурних інтервалах, які охоплювали загальноприйняту температуру 298,15 K, або були максимально наближені до неї. Отримані результати обробляли методом найменших квадратів та надавали у лінійній формі рівняння Вант-Гоффа. За величинами коефіцієнтів лінійних рівняння розраховано значення ентальпій ($\Delta_{sol}H$) та ентропій ($\Delta_{sol}S$) розчинення. Оскільки досліджувані речовини у процесі плавлення піддаються термоокисній деструкції, то значення ентальпій ($\Delta_{fus}H$) плавлення розраховано аналітичним методом з використанням температури плавлення та питомої величини зміни ентропії плавлення ($\Delta_{fus}S$), рівної 0,3015±0,0075 Дж/(г·K), яку розраховано за результатами експериментальних досліджень сполук з арил-пірольним фрагментом. Пораховані молярні значення ентальпій та ентропій плавлення приводили до 298,15 K, за яким розраховували величини ентропій ($\Delta_{mix}S$) та ентальпій ($\Delta_{mix}H$) змішування. Отримані значення термодинамічних параметрів процесу змішування вказують на те, що при руйнуванні первинних зв'язків як в розчинниках, так і в розчинених речовинах витрачається менше енергії, ніж виділяється при утворенні нових зв'язків між розчинником та розчиненою речовиною.

Ключові слова: полізаміщені похідні піролу, ентальпія розчинення, ентальпія змішування, ентальпія плавлення, метилацетат, етилацетат, 2-метил-5-фенілпірол-3-карбонова кислота.

THERMODYNAMIC PARAMETERS OF THE SOLUBILITY OF 1-R-2-METHYL-5-PHENYLPYRROLE-3-CARBOXYLIC ACIDS IN METHYL ACETATE AND ETHYL ACETATE

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Using the Paal–Knorr reaction, the following compounds were synthesized: 1-butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid, 1-cyclohexyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid, 2-methyl-5-phenyl-1-(4-tolyl)-1H-pyrrole-3-carboxylic acid, and 1-(furan-2-ylmethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylic acid. The main stages of the synthesis process are described, and the yields of the synthesized compounds are reported. Their identity was confirmed by NMR spectroscopy. An experimental study of the temperature dependence of solubility in ethyl acetate and methyl acetate was carried out gravimetrically over temperature intervals covering the generally accepted reference temperature of 298.15 K or as close to it as possible. The obtained results were processed using the least-squares method and presented in linear form using the Van't Hoff equation. The values of the enthalpy ($\Delta_{sol}H$) and entropy ($\Delta_{sol}S$) of dissolution were calculated based on the coefficients of the linear equations. Since the compounds under study undergo thermo-oxidative degradation during melting, the enthalpy of melting ($\Delta_{fus}H$) was calculated analytically using the melting temperature and a specific value of the entropy change upon melting ($\Delta_{fus}S$) equal to 0.3015 ± 0.0075 J/(g·K), which was determined based on experimental studies of compounds containing an aryl-pyrrole fragment. The calculated molar values of the enthalpy and entropy of melting were corrected to 298.15 K, based on which the entropy ($\Delta_{mix}S$) and enthalpy ($\Delta_{mix}H$) of mixing were calculated. The obtained thermodynamic parameters of the mixing process indicate that the energy required to break the primary bonds in both the solvents and the dissolved substances is lower than the energy released upon the formation of new bonds between the solvent and the solute.

Keywords: polysubstituted pyrrole derivatives; enthalpy of dissolution; enthalpy of mixing; enthalpy of melting; methyl acetate; ethyl acetate; 2-methyl-5-phenylpyrrole-3-carboxylic acid.

REFERENCES

1. Li Petri G, Spano V, Spatola R, Holl R, Raimondi MV, Barraja P, et al. Bioactive pyrrole-based compounds with target selectivity. *Eur J Med Chem*. 2020; 208: 112783. doi: 10.1016/j.ejmech.2020.112783.

2. Ali I, Lone MN, Al-Othman ZA, Al-Warthan A, Sanagi MM. Heterocyclic scaffolds: centrality in anticancer drug development. *Curr Drug Targets*. 2015; 16: 711-734. doi: 10.2174/1389450116666150309115922.

3. Ali I, Lone MN, Alothman ZA, Alwarthan A. Insights into the pharmacology of new heterocycles embedded with oxopyrrolidine rings: DNA binding, molecular docking, and anticancer studies. *J Mol Liq*. 2017; 234: 391-402. doi: 10.1016/j.molliq.2017.03.112.

4. Gomtsyan A. Heterocycles in drugs and drug discovery. *Chem Heterocycl Compd*. 2012; 48: 7-10. doi: 10.1007/s10593-012-0960-z.

5. Jones RA. *Pyrroles: the synthesis and the physical and chemical aspects of the pyrrole ring*. Wiley-Interscience. 1990.

6. Du C. The solubility of ethyl candesartan in mono solvents and investigation of intermolecular interactions. *Liquids*. 2022; 2: 404-412. doi: 10.3390/liquids2040023.

7. Li Z, Guo J, Hu B, Zhou C, Zheng Y, Zhao H, et al. Solubility measurement, modeling, and solvent effect of m-hydroxyacetophenone in ten pure and binary mixed solvents from T = (289.15–325.15) K. *J Mol Liq*. 2022; 353: 118798. doi: 10.1016/j.molliq.2022.118798.

8. Maharana A, Sarkar D. Solubility measurements and thermodynamic modeling of pyrazinamide in five different solvent-antisolvent mixtures. *Fluid Phase Equilib*. 2019; 497: 33-54. doi: 10.1016/j.fluid.2019.06.004.

9. Huang W, Wang H, Li C, Wen T, Xu J, Ouyang J, et al. Measurement and correlation of solubility, Hansen solubility parameters and thermodynamic behavior of clozapine in eleven mono-solvents. *J Mol Liq*. 2021; 333: 115894. doi: 10.1016/j.molliq.2021.115894.

10. Marshalek AS, Sobechko IB, Horak YI, Kochubey VV, Dibrivnyi VM. Thermodynamic parameters of dissolution of 5-nitrophenyl furfural oximes in ethyl acetate. *Voprosy Khimii i Khimicheskoi Tekhnologii*. 2017; (1): 18-22. (*in Ukrainian*).

11. Sobechko I, Dibrivnyi V, Horak Y, Velychkivska N, Kochubei V, Obushak M. Thermodynamic properties of solubility of 2-methyl-5-arylfuran-3-carboxylic acids in organic solvents. *Chem Chem Technol*. 2017; 11(4): 397-404. doi: 10.23939/chcht11.04.397.

12. Sobechko I, Horak Y, Dibrivnyi V, Obushak M, Goshko L. Thermodynamic properties of 2-methyl-5-arylfuran-3-carboxylic acids chlorine derivatives in organic solvents. *Chem Chem Technol*. 2019; 13(3): 280-287. doi: 10.23939/chcht13.03.280.

13. Shevchenko D, Horak Y, Tyschenko N, Kichura D, Obushak M, Sobechko I. Synthesis and thermodynamic parameters of phase transitions of 3-(1-R-5-phenyl-1H-pyrrol-2-yl)propanoic acid derivatives. *Chem Chem Technol*. 2025; / 19(3): 403-411. doi: 10.23939/chcht19.03.403.

14. Shevchenko DS, Horak YI, Tischenko NI, Pyshna DB, Obushak MD, Sobechko IB. Thermodynamic parameters of the solubility of 3-(1,5-diphenylpyrrol-2-yl)propanoic acid in organic solvents. *Voprosy Khimii i Khimicheskoi Tekhnologii*. 2025; (2): 24-32. doi: 10.32434/0321-4095-2025-159-2-24-32.

15. Shevchenko D, Horak Y, Obushak M, Tischenko N, Sobechko I. Synthesis and thermodynamic properties of 3-(5-phenyl-1-(pyridin-3-yl)-1H-pyrrol-2-yl)propanoic acid in condensed and gaseous states. *Curr Chem Lett*. 2025; 14(3): 559-566. doi: 10.5267/j.ccl.2025.3.002.