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THERMODYNAMIC PROPERTIES OF 1-[1-(4-METHOXYPHENYL)-2-METHYL-5-PHENYL-PYRROLE-3-YL]ETHANONE SOLUTIONS IN ORGANIC SOLVENTS

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Abstract

Using the Paal-Knorr reaction, 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone was produced. The main stages of synthesis and yield of the target compound are described. The temperature dependence of the solubility of the synthesized compound in the temperature range 275.70–299.40 K was investigated experimentally. The use of the gravimetric method for studying solubility at atmospheric pressure in solvents of different classes is described. Using the Van't Hoff equation, the obtained data were converted to standard molar enthalpies and entropies of dissolution. The enthalpy and entropy of fusion of the obtained substance were determined by the differential thermal method. The equations for converting the research results to standard conditions (298.15 K) are given, and the results are used to calculate the thermodynamic parameters of the mixing and dissolution process of the studied ketone compound with organic solvents. The solubility of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone in all solvents increased with increasing temperature, and these data are in good agreement with the literature data for similar substances. The interaction characteristics of the synthesized substance with solvents of different polarity were established, and the dependencies of the thermal effects of dissolution were obtained. This study of the pyrrole derivative 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone is aimed at optimizing the synthesis processes of this compound, its further purification and processing for various uses.

Keywords: synthesis; IR spectra; intermolecular interaction; solubility; enthalpy of dissolution; enthalpy of fusion; enthalpy of mixing; polysubstituted pyrrole derivatives; 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone.

ТЕРМОДИНАМІЧНІ ВЛАСТИВОСТІ РОЗЧИНІВ 1-[1-(4-МЕТОКСИФЕНІЛ)-2-МЕТИЛ-5-ФЕНІЛ-ПІРРОЛ-3-ІЛ]ЕТАНОНУ В ОРГАНІЧНИХ РОЗЧИННИКАХ

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Анотація

За реакцією Паала-Кнорра синтезований 1-[1-(4-метоксифеніл)-2-метил-5-феніл-пірол-3-іл]етанон. Описані основні етапи синтезу та вихід цільової сполуки. Експериментально досліджена температурна залежність розчинності синтезованої сполуки в діапазоні температур 275.70–299.40 К. Описаний гравіметричний метод дослідження для вивчення розчинності за атмосферного тиску в розчинниках різних класів. За рівнянням Вант-Гоффа отримані дані були переведені в стандартні молярні ентальпії та ентропії розчинення. Диференційно-термічним методом аналізу визначено ентальпію та ентропію плавлення дослідженої речовини та проведений перерахунок ентальпій та ентропій плавлення до стандартних (298.15 К), за якими розраховано термодинамічні параметри процесу змішування та розчинення досліджуваного кетонового замісника з органічними розчинниками. Розчинність 1-[1-(4-метоксифеніл)-2-метил-5-феніл-пірол-3-іл]етанону в усіх розчинниках зростала зі збільшенням температури, і ці дані добре узгоджуються з літературними даними для подібних речовин. Встановлений характер взаємодії синтезованої речовини з розчинниками різної полярності та отримані відповідні залежності теплових ефектів розчинення. Це дослідження похідного піролу 1-[1-(4-метоксифеніл)-2-метил-5-феніл-пірол-3-іл]етанону спрямоване на оптимізацію процесів синтезу, очищення та використання 1-[1-(4-метоксифеніл)-2-метил-5-феніл-пірол-3-іл]етанону та його похідних.

Ключові слова: синтез; ІЧ-спектроскопія; міжмолекулярна взаємодія; розчинність; ентальпія розчинення; ентальпія змішування; полізаміщені похідні піролу; 1-[1-(4-метоксифеніл)-2-метил-5-феніл-пірол-3-іл]етанон.

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Introduction

The current development of the pharmaceutical industry dictates trends in the search for new compounds that have a wide range of therapeutic properties and are not difficult to manufacture.

Heterocycles are one of the most common structural units in medicines. In fact, they can be traced in many small-molecule drugs due to the high prevalence of oxygen-, sulfur- and nitrogen-containing rings in the drug molecule itself. This prevalence is based on the mimicry of nature. The main elements of a wide range of natural products, such as nucleic acids, amino acids, and vitamins, contain heterocyclic fragments, which are modulated by modern pharmaceuticals. Some of the heterocycles, when modelled by strategically incorporating a heterocyclic fragment into a structure, include lipophilicity, polarity, potency and selectivity through bioisosteric substitutions. [1–2]

Thanks to this type of research, as of today, more than 50 % of unique small-molecule drugs contain the nitrogen heterocycle, compared to less impressive percentages for fluorine- and sulfur-containing drugs [3]. The choice of studying pyrrole-containing compounds is not accidental, as pyrrole is a special aromatic heterocycle that occurs in nature as a key component of the 'pigments of life', numerous natural products contain highly functionalised pyrrole fragments as the main rings in their skeleton. [4] Considering that pyrrole derivatives are widely represented in nature as constituents of cofactors and bioactive natural compounds, namely vitamin B_{12}, bile pigments (bilirubin and biliverdin), heme porphyrins, as well as photosynthetic pigments such as chlorophyll, chlorins, bacteriochlorins and porphyrinogens. [5–7] The aromatic structure of the pyrrole molecule allows it to react with various electrophiles to obtain the corresponding derivatives with various biological activities [8].

However, its main application remains in pharmacy. It has already been used to successfully develop and test anti-cancer, anti-viral, and anti-tuberculosis drugs with antibacterial agents. In the development of anti-tumor drugs, pyrole compounds have an advantage due to the simple structure of their ring. On the other hand, condensed pyrroles, in which the structure is complicated by the addition of extra rings, make it harder to develop drugs because of the possible appearance of more chiral centers and functional groups. [3; 9–10]

The growing presence of pyrrole in natural compounds, drugs, and innovative materials is stimulating interest in the chemistry of pyrrole and its derivatives. Today, the synthesis of such compounds has become one of the priority areas in modern chemistry. A significant number of heterocycles are also used as functional additives and modifiers in the cosmetics industry, in the production of polymers, solvents, as well as antioxidants and other active components. [11].

The above-mentioned facts about the growing interest in pyrrole-containing compounds raise another important question about the synthesis and purification of pyrrole derivative structures, namely the choice of solvents. They must be chemically inert to the starting materials and reaction products, and their thermodynamic interaction parameters as a solvent with a dissolved substance must be acceptable and known for calculating energy balances at the stages of synthesis, purification, and processing [12–13].

The purpose of the study. Synthesis of the compound 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone by the Paal-Knorr reaction [14-17], determine the yield of the substance, thermodynamic parameters of interaction with methyl acetate, ethyl acetate, acetonitrile, propan-1-ol, and propan-2-ol.

Experimental

1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone was obtained in a chemical reactor equipped with a mixer and a reflux condenser. The reaction process is shown in Fig.1.

In the first stage, 6 g (0.03 mol) of phenacyl bromide **2** was added in portions to a suspension of 5.4 g (0.044 mol) of sodium acetylacetonate **1** in 30 ml of ethanol with cooling, after which the mixture was stirred at room temperature for 1 day. The reaction mixture was filtered from sodium bromide, the ethanol was distilled off using a rotary evaporator, and the residue was distilled under vacuum, B. p. 443–448 K/2 mm Hg, yield 5.8 g (88 %). Thus, 3-acetyl-1-phenylpentane-1,4-dione **3** was obtained.

In the second stage, 2.46 g (0.02 mol) of 4-anisidine was added to a mixture of 4.36 g (0.02 mol) of 3-acetyl-1-phenylpentane-1,4-dione **3** in 20 ml of absolute ethanol. The mixture was boiled for 16 hours. After cooling, the ethanol was removed using a rotary evaporator, and the residue was recrystallized from hexane. A light yellow precipitate of compound **4** was obtained. Yield 80 % (4.88 g), M.p. 398–399 K. IR spectrum

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(ATR, cm^{-1}): 660, 1597, 1550, 1513, 1445, 1409, 1346, 1298, 1254, 1228, 1169, 1107, 1030, 954, 940, 911, 846, 811, 793, 754, 695, 677, 642, 590, 525, 506, 456, 415. MS (m/z): 306 (M^++1). Calcd. for $C_{20}H_{19}NO_2$ C 78.66; H 6.27; N 4.59; found: C 78.49; H 6.21; N 4.47.

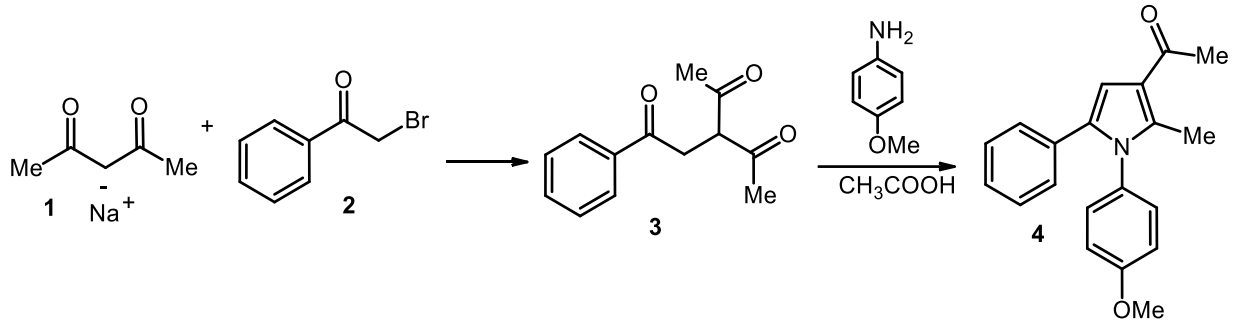

Fig. 1. Scheme of the synthesis of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone 4

The degree of purity of the substance was confirmed by the constant melting point and enthalpy of fusion and vaporization.

Solvents for research were selected according to the following criteria: different classes of compounds; relatively low boiling points; economic feasibility of their use.

Methyl acetate and ethyl acetate solvents can be considered together because they have similar physical and chemical properties, are solvents of medium polarity, have low boiling points (for ethyl acetate T_{boil} = 350.25 K, for methyl acetate T_{boil} = 330.05 K), are low in toxicity to humans, are widely available, and are moderately soluble in water. Ethyl acetate was chosen because of its higher polarity. Substances with more pronounced donor-acceptor properties should dissolve better in it.

Acetonitrile is a polar aprotic solvent. It dissolves compounds with ketone groups, amino groups, and carboxyl groups well [18]. It mixes with water and organic solvents in any proportions, allowing the polarity of the environment to be varied [19]. Its boiling point (T_{boil} = 354.75 K) is relatively low, and it is low-toxic to humans. The presence of a nitrile group (-CN) provides a medium without hydrogen bonds, so interactions between molecules are determined by dipole-dipole and dispersion forces.

Propane-1-ol and propane-2-ol: representatives of lower alcohols, compared to the widespread methanol, are less toxic, although they exhibit similar properties. Their boiling point (for propan-1-ol T_{boil} = 370.25 K, for propan-2-ol T_{boil} = 355.55 K) is relatively low, which makes them easy to remove.

The solvents used were manufactured by Merck: acetonitrile CAS 75-05-8; methyl acetate CAS 79-20-9; ethyl acetate CAS 71-43-2; n-propanol CAS 71-23-8; isopropanol CAS 67-63-0. The content of the main component was ≥99.9%, intended for use in chromatographic studies. The solvents were identified by their refractive index, which matched the data in the substance quality certificate and literature data, allowing us to use them without additional purification.

The physical characteristics of the solvents used, in particular: the values of the donor D_N and acceptor A_N numbers, dielectric permeability ε, and dipole moment μ are given in Table 1 [20].

Table 1

Physical characteristics of selected organic solvents

Solvent	A_N	D_N	ε	μ, D
Methyl acetate	10.7	16.5	6.70	1.69
Ethyl acetate	9.3	17.1	6.40	1.88
Acetonitrile	18.9	14.1	38.80	3.44
Propan-1-ol	37.3	19.8	21.80	1.65
Propan-2-ol	33.5	21.1	19.92	1.59

The temperature dependence of the solubility of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone was determined by the gravimetric method. [21–25].

The solubility of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone was studied in a three-necked round-bottom flask with ground-glass openings into which a thermometer and a stirrer were inserted. The third hole was closed with a ground glass stopper, which served as a sampling tube. The flask was placed in a thermostat that maintained the temperature with

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an accuracy of ±0.1 K. The stirrer speed was 30–40 revolutions per minute. This allowed the solid phase of the solution to be kept in a semi-suspended state. The thermostated solutions were saturated for 48 hours without stirring and for 2 hours with constant stirring. After that, the solutions were additionally settled for 60 minutes. The temperature mode of the thermostat for each series of experiments was constantly changed, raising and lowering the temperature. The absence of a hysteresis loop in the temperature dependence of solubility indicates the establishment of an equilibrium state.

Sampling was carried out in series of three samples with approximately equal masses in one series, which were transferred to pre-weighed sealed flasks. The solvent was removed in a thermal oven at a temperature of 363–373 K. After drying, the flasks were hermetically sealed, cooled in a desiccator to prevent moisture absorption from the air, and reweighed. Weighing was carried out at room temperature (296 ± 2 K) using analytical scales with an accuracy of ±0.0002 g. This method ensured high accuracy of the results, minimizing the influence of external factors.

Differential thermal analysis (DTA) and thermogravimetric analysis (TGA) were performed on a Paulik–Paulik–Erdey Q-1500 D system in dynamic mode in air at a heating rate of 5 K/min and with the following sensitivities: TGA – 100 mg; DTA up to 773 K in a platinum crucible [26–27].

Results and discussion

The enthalpy of fusion ($\Delta_{fus}H$) was calculated using equation (1), taking into account the loss of heat due to the evaporation of the sample:

$$K \cdot S = Q_{fus} + Q_{vap} = m_0 \cdot \Delta_{fus}H + \Delta m_{vap} \cdot \Delta_{vap}H, \quad (1)$$

where K is the heat transfer coefficient of the derivative thermogravimetric analyzer, equal to $8.2023 \cdot 10^{-5} \cdot T_{fus}$, J/(K·s); Q_{fus} and Q_{vap} are the amounts of heat absorbed during melting and evaporation of the sample, respectively, J; $\Delta_{fus}H$ and $\Delta_{vap}H$ are the specific enthalpies of fusion and vaporization of acids, respectively, J/g; m_0 is the mass of the sample corresponding to the temperature of the beginning of its melting Tfus, g; Δm_{vap} – mass loss of the sample (mass of vapor) during the period taken into account when determining the peak area S (K·s) on the DTA curve, g.

The enthalpy of vapour $\Delta_{vap}H$ was determined according to the method described in [25]. Table 2 shows the results of experimental studies of the melting process 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone **4.**

Table 2

Thermodynamic parameters of the melting process of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone

№	m_0, g	Δm_{vap},·10⁴ g	S, K·s	q_{vap}, J	$\Delta_{fus}H$, kJ/mol	$\Delta_{fus}S$, J/mol·K
T_{fus} = 390,15±1.40 K; K=0.03200 J/(K·s)						
1	0,1025	2.91	315.1	0.0822	29.8	76.4
2	0,1058	3.28	333.2	0.0927	30.5	78.2
3	0,1101	4.05	352.6	0.1145	31.0	79.4
				Average value	30.4±1.5	78.0±3.7

Table 3 shows the results of an experimental study of the dissolution of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone in organic solvents. The mass of solvent (m_1), mass of solute (m_2), temperature at which the solubility was studied (T) and mole fraction of solute (X_2) are given.

The linear equations calculated by the least squares method are presented in the form of the Schröder equation (2) and are shown in Table 3:

$$lnX_2 = -\Delta_{sol}H/RT + \Delta_{sol}S/R \quad (2)$$

where: $\Delta_{sol}H$ and $\Delta_{sol}S$ – enthalpy and entropy of solubility.

The significance level of the margin of error for all values is 0.95.

Table 3

Temperature dependence of the solubility of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone in organic solvents

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	$X_2 \cdot 10^3$
Methyl acetate											
276/30	1/4980	0.0749	11.98	284.10	1.0542	0.0683	15.47	287.70	0.9944	0.0716	17.17
276.30	1.1311	0.0568	12.02	284.10	1.0181	0.0661	15.51	287.70	0.8713	0.0629	17.21
276.30	1.1509	0.0582	12.12	284.10	0.8491	0.0554	15.58	287.70	1.1851	0.0860	17.30
278.40	0.8403	0.0452	12.88	286.15	0.5406	0.0368	16.25	290.25	1.0544	0.0820	18.51
278.40	1.2823	0.0697	13.01	286.15	0.8285	0.0565	16.27	290.25	1.1232	0.0877	18.58

Continuation of Table 3

278.40	1.0390	0.0566	13.03	286.15	1.0990	0.0753	16.34	290.25	1.2925	0.1012	18.63
280.60	1.2616	0.0729	13.82	286.55	0.5679	0.0389	16.33	297.80	0.3120	0.0296	22.46
280.60	1.2124	0.0704	13.89	286.55	0.6224	0.0429	16.43	297.80	0.5756	0.0548	22.57
280.60	0.8715	0.0507	13.92	286.55	0.5922	0.0408	16.44	297.80	0.5699	0.0543	22.59
$\ln X_2 = (4.28\pm14)-(2403\pm40)\cdot1/T$											
Ethyl acetate											
278.60	0.7186	0.0392	15.50	283.75	1.1784	0.0739	17.76	288.35	0.6791	0.0476	19.82
278.60	0.8521	0.0467	15.57	283.75	1.0422	0.0657	17.85	288.35	0.7006	0.0494	19.92
278.60	0.8130	0.0448	15.65	283.75	1.1807	0.0744	17.86	288.35	0.5586	0.0397	20.07
280.80	0.7638	0.0443	16.46	285.65	1.0443	0.0688	18.65	290.20	1.3990	0.1034	20.88
280.80	0.8481	0.0494	16.51	285.65	0.6258	0.0413	18.69	290.20	1.2095	0.0894	20.88
280.80	0.8755	0.0510	16.53	285.65	1.0606	0.0704	18.79	290.20	0.7794	0.0578	20.95
281.90	0.8625	0.0513	16.86	286.40	2.0273	0.1361	19.00	291.70	1.1060	0.0845	21.56
281.90	1.2176	0.0727	16.92	286.40	1.1103	0.0752	19.17	291.70	0.8743	0.0670	21.62
281.90	1.4407	0.0864	17.00	286.40	1.5823	0.1073	19.19	291.70	0.4640	0.0356	21.66
$\ln X_2 = (3.19\pm0.11)-(2047\pm33)\cdot1/T$											
Acetonitrile											
275.70	1.1110	0.0353	4.25	282.90	0.9161	0.0378	5.52	290.85	0.7208	0.0391	7.24
275.70	1.1297	0.0360	4.26	282.90	1.0003	0.0413	5.52	290.85	0.8345	0.0453	7.25
275.70	1.2094	0.0386	4.27	282.90	0.8820	0.0367	5.56	290.85	0.6546	0.0359	7.31
277.35	0.7181	0.0244	4.54	285.80	1.0638	0.0494	6.20	294.60	1.2288	0.0763	8.28
277.35	1.2657	0.0431	4.55	285.80	0.7996	0.0372	6.22	294.60	0.7046	0.0444	8.39
277.35	0.7342	0.0250	4.56	285.80	1.0461	0.0487	6.22	294.60	0.8315	0.0525	8.41
278.45	1.0867	0.0382	4.70	289.00	1.0473	0.0537	6.85	299.20	0.8133	0.0598	9.78
278.45	0.8776	0.0309	4.71	289.00	1.0928	0.0561	6.85	299.20	0.8599	0.0635	9.83
278.45	0.9980	0.0354	4.75	289.00	1.0571	0.0543	6.86	299.20	0.8094	0.0599	9.85
$\ln X_2 = (5.05\pm0.12)-(2899\pm33)\cdot1/T$											
Propan-1-ol											
280.60	0.7539	0.0084	2.19	287.90	0.8707	0.0139	3.13	292.60	0.9697	0.0194	3.91
280.60	0.9037	0.0101	2.19	287.90	0.8733	0.0140	3.13	295.00	0.8635	0.0181	4.10
280.60	0.7268	0.0082	2.22	290.15	1.0019	0.0172	3.36	295.00	0.9356	0.0196	4.11
283.80	0.9803	0.0131	2.62	290.15	1.1225	0.0194	3.38	295.00	0.9732	0.0204	4.11
283.80	1.0299	0.0138	2.63	290.15	1.2859	0.0226	3.45	297.75	1.1553	0.0284	4.81
283.80	0.6895	0.0093	2.63	291.30	0.9707	0.0180	3.63	297.75	0.9117	0.0225	4.82
285.35	1.0476	0.0144	2.69	291.30	0.8420	0.0156	3.63	297.75	1.1406	0.0284	4.88
285.35	1.1876	0.0163	2.69	291.30	0.9552	0.0179	3.67	299.40	0.9065	0.0240	5.18
285.35	1.0402	0.0144	2.71	292.60	0.9229	0.0183	3.88	299.40	0.8309	0.0223	5.24
287.90	1.0968	0.0173	3.09	292.60	0.8703	0.0174	3.91	299.40	0.8405	0.0226	5.25
$\ln X_2 = (7.42\pm0.36)-(3800\pm105)\cdot1/T$											
Propan-2-ol											
287.3	0.9378	0.0106	2.22	292.0	0.8405	0.0123	2.87	295.1	1.0621	0.0170	3.13
287.3	0.6268	0.0071	2.22	292.6	0.9697	0.0194	2.91	297.4	1.0118	0.0188	3.63
290.4	1.3635	0.0173	2.49	294.1	0.9313	0.0143	3.01	297.4	1.1253	0.0212	3.69
290.4	0.9979	0.0128	2.51	294.1	0.7569	0.0117	3.02	297.4	0.7237	0.0137	3.71
290.4	1.1745	0.0151	2.52	294.1	0.8461	0.0132	3.06	297.7	1.1553	0.0284	4.81
291.4	0.4848	0.0065	2.63	295.0	0.8635	0.0181	4.10	297.7	0.9117	0.0225	4.82
291.4	1.1202	0.0151	2.64	295.0	0.9356	0.0196	4.11	297.7	1.1406	0.0284	4.88
291.4	0.5850	0.0079	2.65	295.0	0.9732	0.0204	4.11	299.4	0.9065	0.0240	5.18
292.0	0.8110	0.0114	2.76	295.1	1.1676	0.0184	3.08	299.4	0.8309	0.0223	5.24
292.0	0.8349	0.0119	2.80	295.1	1.2602	0.0201	3.13	299.4	0.8405	0.0226	5.25
$\ln X_2 = (9.42\pm0.45)-(4474\pm129)\cdot1/T$											

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Table 4 shows the thermodynamic solubility parameters $\Delta_{sol}H$ and $\Delta_{sol}S$. They take into account the phase transition of solid compounds into solution. The calculation of changes in the enthalpy ($\Delta_{mix}H$) and entropy ($\Delta_{mix}S$) of mixing, which reflect the interaction of components in solution and taking into account the values of the enthalpy ($\Delta_{fus}H$) and entropy ($\Delta_{fus}S$) of fusion of the studied substances at the average temperature of its dissolution, was carried out according to Equations 3 and 4:

$$\Delta_{sol}S = \Delta_{fus}S + \Delta_{mix}S \quad (4)$$

Table 4

Thermodynamic functions of solubility of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone in solvents at 298.15K

Solvent	X_2 (298.15)	$\Delta_{sol}H^o$	$\Delta_{mix}H^o$	$\Delta_{sol}S^o$	$\Delta_{mix}S^o$
		kJ/mol		J/mol·K	
Methyl acetate	0.0228	20.00±0.35	–5.1±1.6	35.6±1.2	–26.8±4.2
Ethyl acetate	0.0252	17.02±0.32	–8.1±1.6	26.1±1.0	–36.3±4.2
Acetonitrile	0.0093	24.10±0.27	–1.0±1.6	42.0±1.0	–20.4±4.2
Propan-1-ol	0.0049	31.59±0.87	6.5±1.7	61.7±3.0	–0.7±5.0
Propan-2-ol	0.0038	37.20±1.10	12.1±1.9	78.3±3.7	15.9±5.4

Since the experimentally determined values of $\Delta_{fus}H$ belong to T_{fus} and the determined thermodynamic parameters of the dissolution process $\Delta_{sol}H$ and $\Delta_{sol}S$ are determined in temperature intervals that are close to or cover the temperature of 298.15 K, in order to generalize the results obtained and calculate the enthalpies and entropies of mixing, it was decided to recalculate $\Delta_{fus}H$ to 298.15 K. In the case when it is not possible to experimentally determine the change in heat capacity during the evaporation process, unified equations are used. The most commonly used methods of recalculation are those proposed in [28–29]. Since in [28], to calculate the change in heat capacity, it is necessary to use group contributions, most of which are estimated approximately for nitrogen-containing compounds, we used the method described in [27], which is much simpler.

According to the methodology presented in [28], $\Delta_{fus}H$ and $\Delta_{fus}S$ were recalculated to 298.15 K using Equations 5 and 6.

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

$$\Delta_{fus}S_T = \Delta_{fus}S_{T_{fus}}\left[1 + 0.74 \cdot \ln\frac{T}{T_{fus}}\right] \quad (6)$$

The calculated values of $\Delta_{fus}S_{298,15}$=62.4±4.0 (J/mol-K); and $\Delta_{fus}H_{298,15}$=25.1±1.6 kJ/mol were used to calculate $\Delta_{mix}H$ and $\Delta_{mix}S$.

The thermodynamic parameters of the interaction between 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone and the solvents used for the study are consistent. Thus, the values of $\Delta_{mix}H$ in methyl acetate, ethyl acetate, and acetonitrile are negative, while those in propan-1-ol and propan-2-ol are positive. This energy distribution is in good agreement with the values of the energies of intermolecular interactions present in the solvents. For example, the values of dipole-dipole and dispersion interactions in acetic acid esters are 3.4 kJ/mol, in acetonitrile the value of such interactions is 16.2 kJ/mol [29; 30]. The energy value of the hydrogen bond formed by hydroxyl groups is 25.4 kJ/mol [29; 30]. Thus, the $\Delta_{mix}H$ of systems where intermolecular interactions in solvents are provided only by dipole-dipole and dispersion interactions are negative, since the energy released during the formation of new bonds between solvents and 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone is sufficient to compensate for the energy expenditure required to destroy the initial interactions both in solvents and in the substance under study. As for the interactions of the dissolved substance with alcohols, no such compensation of energy costs is observed, since the costs of hydrogen bonding destruction are much higher than the costs of dipole-dipole and dispersion interactions destruction. It is also worth while noting that the value of the entropy of mixing ($\Delta_{mix}S^o$) of the solute with propan-2-ol is positive, indicating that the system is in order due to the additional steric effect in propan-2-ol.

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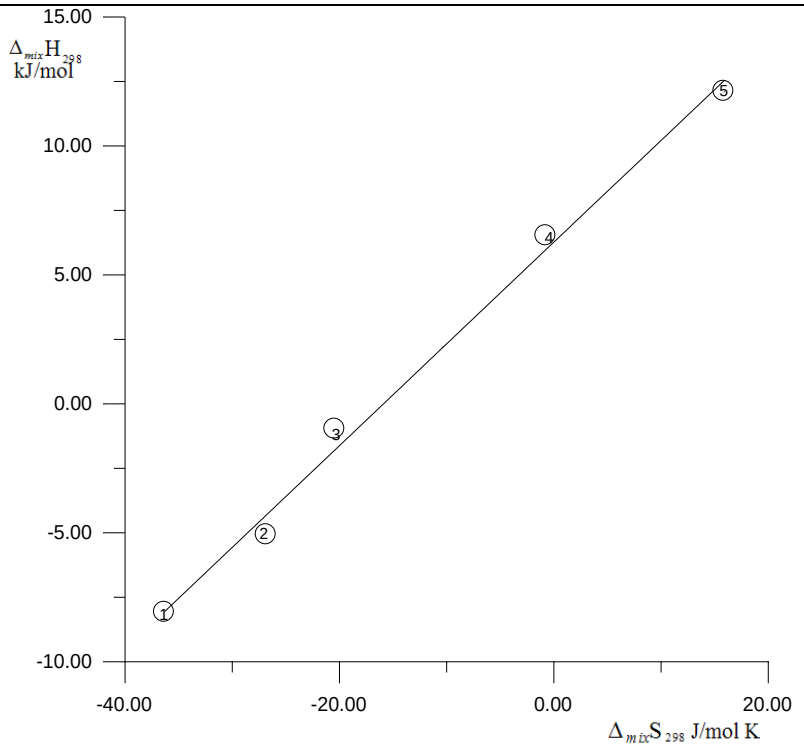

Fig. 2. Dependence of the enthalpy and entropy of mixing 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone in: 1 – Ethyl acetate, 2 – Methyl acetate, 3 – Acetonitrile, 4 – Propan-1-ol,

The presented dependence between $\Delta_{mix}H$ and $\Delta_{mix}S$ demonstrates a clear linear correlation with a high coefficient of approximation, indicating the presence of a compensatory effect (Fig. 2) that arises between the functional groups of the solvent and 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrol-3-yl]ethanone. This behaviour means that changes in enthalpy contribution are accompanied by proportional changes in entropy, so that the free energy of mixing remains relatively constant for all solvents studied. The linearity of the dependence confirms the uniformity of the solvation mechanism and the identical nature of intermolecular interactions between the functional groups of the studied compound and the environment, regardless of the type of solvent, which further emphasises the consistency of the thermodynamic characteristics of the mixing process.

Conclusions

1-[1-(4-Methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone was synthesised by the Paal-Knorr reaction. The temperature dependences of 1-[1-(4-methoxyphenyl)-2-methyl-5-phenyl-pyrrole-3-yl]ethanone in methyl acetate, ethyl acetate, acetonitrile, propan-1-ol and propan-2-ol were determined by the gravimetric method, and the thermodynamic parameters of their solubility and mixing (solvation) were calculated. The enthalpy ($\Delta_{fus}H_{390,15}$ = 30.4 ± 1,4 kJ/mol) and entropy ($\Delta_{fus}S_{390,15}$ = 78.0 ± 3.7 J/mol·K) of fusion at the melting point were obtained using the differential thermal method. The obtained values of enthalpy and entropy of fusion, converted to 298.15 K, are consistent with known data for similar nitrogen-containing aromatic compounds and allow the contribution of the solid phase transition process to be correctly separated from the mixing itself. A comparison of the thermodynamic parameters of solubility in different media shows that the choice of solvent is determined by the competition between the destruction of the initial intermolecular interactions and the formation of new bonds in the solution. The most thermodynamically favorable medium is acetonitrile, where the best balance between the energy costs of dissolution is observed, which is consistent with its high polarity and ability to effectively solvate nitrogen-containing heterocyclic systems.

In general, the study demonstrates clear patterns between the nature of the solvent, the type of intermolecular interactions, and the values of thermodynamic solubility parameters. This allows not only to explain the experimentally obtained values, but also to predict the behavior of structurally related pyrole derivatives in different solvents, which is important for further targeted selection of the environment in synthetic and analytical practice.

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