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THERMODYNAMIC PROPERTIES OF 2-METHYL-5-ARYLFURAN-3-CARBOXYLIC ACIDS CHLORINE DERIVATIVES IN ORGANIC SOLVENTS

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Abstract. The temperature dependences of the solubility of 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid and 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid in acetonitrile, dimethyl ketone, isopropanol and ethyl acetate have been experimentally determined. The enthalpies of fusion of the investigated substances, as well as their enthalpies and entropies of mixing at 298 K have been calculated. The dependence of the saturated solution concentration on the values of enthalpy and entropy of solubility at 298 K has been determined. The compensating effect of mixing the investigated acids with all solvents containing the carbonyl group has been established.

Keywords: enthalpy, entropy of solubility, mixing, melting, 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid, 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid.

1. Introduction

Functionalized aryl derivatives of five-membered heterocycles belong to a class of substances that attract researchers' attention from the standpoint of studying their valuable properties and various modifications of their structure. In particular, the compounds with an arylfuran fragment have become widely used as the modifying agents in the synthesis of polymeric materials [1, 2] and biologically active compounds, since they exhibit a wide spectrum of biological activity [3] and are less toxic than those containing only a functionalized fragment of furan [4]. The compounds with this fragment have begun to be used in therapeutic practice for the treatment of neurodegenerative diseases [5], the treatment of genetic diseases [6], the creation of drugs for the treatment of tobacco dependence in order to reduce the need for nicotine and remove abstinence symptoms [7] and in the treatment of HIV-1 infection as a component of antiretroviral therapy [8]. It should ne noted that polymeric materials with arylfuran fragments are also biologically active [9]. The chitosan polymers modified with chlorine- and nitro-containing arylfurans showed significantly higher antimicrobial activity than unmodified chitosans [10, 11]. Thus, the search for promising reactions involving arylfuran fragments and the need for a deeper understanding of their biochemical functions requires the study of their thermodynamic properties. Naturally, the scientific researches appeared in which thermodynamic properties of individual organic compounds with an arylfuran fragment were examined. The determined values may contribute to solve practical problems concerning the optimization processes of their synthesis and purification. Since most reactions occur in solutions, the optimization of synthesis and purification of compounds with an arylfuran fragment is impossible without the determination of thermodynamic parameters of solubility. Some works regarding the thermodynamic properties of compounds with arylfuran fragment have appeared in recent years [12-17]. The presented work is the continuation of the previous research. Its purpose is to study the thermodynamic properties of 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid and 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid solubility in organic solvents of different polarity.

2. Experimental

2.1. Materials

2-Methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid (I) and 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid (II) were synthesized according to Scheme 1 by two stages:

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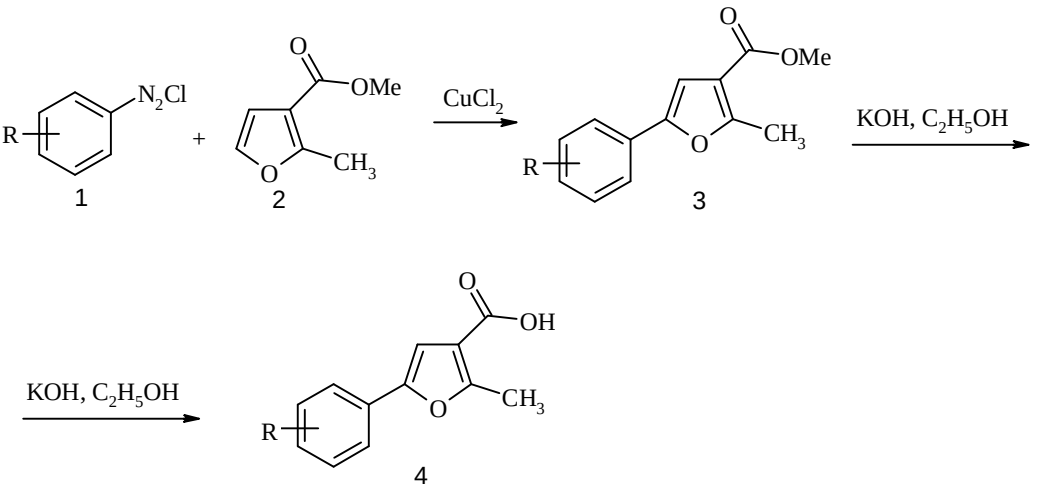


where R = 2-Cl-5-CF_3 (a) and 2,5-Cl_2 (b)

Scheme 1. Synthesis of investigated acids

Arylfuran-containing acids under normal conditions are white crystalline compounds with a molecular weight of 304.7 g/mol (compound I) and 517.6 g/mol (compound II).

At the first stage, methyl esters of 5-aryl-2-methyl-3-furan carboxylic acids (**3a** and **3b**) were synthesized. For this purpose 28 g (0.2 mol) of methyl ester of 2-methyl-3-furan carboxylic acid, 2 g of copper(II) chloride and 80 ml of acetone were added to the three-necked reactor equipped with a stirrer, dropping funnel and bubble counter. A solution of arendiazonium chloride **1**, obtained by diazotization of 0.21 mol of the corresponding amine, was added under vigorous stirring. After nitrogen was released, the product was filtered (compound **3b**) or distilled under vacuum (compound **3a**) and recrystallized from ethanol. At the second stage 5-aryl-2-methyl-3-furancarboxylic acids (**4a** and **4b**) were obtained by saponification of the synthesized esters **3a** and **3b** in the following way. A hot ethanolic solution of potassium hydroxide (4.2 g, 0.075 mol) was gradually added to the hot solution of the corresponding ester (0.05 mol) in ethanol. The mixture was left overnight. After acidification with hydrochloric acid, the precipitate was filtered off, washed with water and repeatedly recrystallized from ethanol. The samples after 4-fold recrystallization were used for research.

Identification of acids was performed using NMR spectroscopy. ^{1}H NMR spectra were recorded by the Bruker DRX 500 (500 MHz, DMSO-d6). Chemical shifts (δ, ppm) are given in relation to the DMSO signal (2.50 ppm).

2-Methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid: ^{1}H NMR (500 MHz, DMSO) δ 2.67 (3H, s, CH_3); 7.36 (1H, s, 4-H-furan); 7.60 (1H, dd, J_1 = 8.4, J_2 = 1.6, 4-H6CH3); 7.74 (1H, d, J = 8.4, 3-H C_6H_3); 8.05 (1H, s, 6-H C_6H_3); 12.60 (1H, s, COOH).

2-Methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid: ^{1}H NMR (500 MHz, DMSO) δ 2.62 (3H, s, CH_3); 7.31 (1H, s, 4-H furan); 7.44 (1H, dd, 4-H, C_6H_3); 7.59 (1H, d, 3-H, C_6H_3); 7.83 (1H, s, 6-H, C_6H_3); 12.83 (1H, s, COOH).

The compounds purity was determined using a high-performance liquid chromatograph Agilent 1100 HPLC equipped with a diode matrix with a selective detector on a Zorbax SB-C18 column, 4.6×15 mm, eluent A acetonitrile-water with 0.1% TFA (95: 5). No admixtures were found in the samples.

For solubility studies, commonly used organic solvents with a high volatility and sufficiently low boiling point were used: acetonitrile, dimethyl ketone, ethyl acetate and isopropanol (Merck, Germany). A content of the main component was not less than 99.0 wt %. Before use, the solvents were purified by a fractional distillation followed by identification relative to the refractive index (n_D^{20}) and boiling point (T_{boil}). The content of the main component was determined using a gas-liquid chromatograph LXM-8D with a thermal conductivity detector (TCD). Chromatograph columns with a diameter of 0.4 cm and a length of 2 m were filled with a solid phase Chromator N-AW (0.20–0.25 mm) containing 10 % polyethylene glycolidipinate + 1% orthophosphoric acid. Gas carrier was helium. The column temperature was 423 K, the evaporator temperature was 493 K, TCD current was 120 mA.

The determined values differed from those given in the literature by no more than the value of experimental error, and the content of the main component was not less than 99.8 wt% (Table 1).

Table 1

Physicochemical properties of solvents

Solvents	*M*, g/mol	n_D^{20}		T_{boil}, K		Content of the main component, wt %
		determ.	lit.	determ.	lit.	
Acetonitrile	41.05	1.3443	1.3442 [10]	354.6	354.8 [10]	99.9
Dimethyl ketone	58.08	1.3590	1.3591 [10]	329.2	329.3 [10]	99.8
Ethyl acetate	88.11	1.3722	1.3724 [10]	349.9	350.2 [10]	99.9
Isopropanol	60.10	1.3776	1.3776 [10]	355.1	355.3 [10]	99.8

2.2. Solubility

The temperature dependence of the solubility of the investigated acids was determined by gravimetric method, the same as in previous studies [12-17].

The dissolution of the acids was carried out in a sealed glass vessel with a Teflon stirrer, a thermometer and an aperture for sampling. The stirrer speed was 40□50 rpm. The accuracy of thermostatting was ±0.1 K. Saturation of solutions was carried out for not less than 48 h under constant stirring at the experimental temperature. Experiments were carried out at different temperatures. The absence of a hysteresis loop on the solubility curve confirmed the achievement of a state close to equilibrium.

Samples were selected in series of two or three samples and transferred to a pre-weighed sealed weighing bottle, followed by removal of the solvent and re-weighing at the temperature of 333–343 K. The accuracy of the weighing was ±0.0002 g.

2.3. Differential Thermal Analysis

Derivatographic studies of acids were carried out using Q-1500 D derivatograph (Paulik-Paulik-Erday) under a dynamic mode in an atmosphere of air. Heating rate was 5 K/min; platinum crucible was used.

3. Results and Discussion

The experimental results are given in Tables 2 and 3, where m_1 and m_2 are the weights of the solvent and the solute, respectively, and T is the temperature at which solubility was determined. The experimental data were processed using the least squares method and presented in a linear form (1).

$$\ln x_2 = -\frac{\Delta_{sol}H}{RT} + \frac{\Delta_{sol}S}{R} \quad (1)$$

where $\Delta_{sol}H$ and $\Delta_{sol}S$ are partial molar enthalpy and entropy of solubility. Here and below the errors of all values are given for the significance level of 0.95.

The thermodynamic parameters of solubility $\Delta_{sol}H$ and $\Delta_{sol}S$ can be represented by the sum of the corresponding phase transition parameters of crystalline 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid and 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acids in the liquid phase with the parameters of their mixing with the solvent (Eqs. (2) and (3)).

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

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

To determine the change in enthalpy ($\Delta_{mix}H$) and entropy ($\Delta_{mix}S$) of mixing, it is necessary to consider the enthalpy ($\Delta_{fus}H$) and entropy ($\Delta_{fus}S$) of fusion of the investigated compounds at the average experimental temperature. It is impossible to determine the enthalpy and entropy of acid fusion using the differential thermal analysis due to their increased ability to thermooxidative degradation. Derivatograms show a significant weight loss of acid samples immediately after the melting point has reached (Fig. 1). Therefore, the thermodynamic parameters of solubility were determined by the approximate method of calculation [19, 20]. These works show the constancy of the change in the specific entropy of fusion $\Delta_{fus}S$ (J/g·K) at the melting point for more than 100 organic compounds of different classes. Then $\Delta_{fus}H$ (J/g) is calculated according to the known Eq. (4).

$$\Delta_{fus}H = T_{fus} \cdot \Delta_{fus}S \quad (4)$$

To evaluate the specific entropy of fusion of the investigated acids, we used the experimental results [13-20] obtained by a derivatographic method for arylfurans (Table 4).

The average value of the specific entropy of fusion for derivatives of arylfurans presented in Table 4, is 0.319 ± 0.027 J/g·K). Then, the values of molar entropy and enthalpy of fusion for 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid can be evaluated as $\Delta_{fus}S$ = 97.2 ± 8.2 J/mol·K, $\Delta_{fus}H_{517.6}$ = 50.3 ± 4.2 kJ/mol; for 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid $\Delta_{fus}S$ = 86.5 ± 7.3 J/mol·K, $\Delta_{fus}H_{556.7}$ = 48.1 ± 4.1 kJ/mol.

Table 2

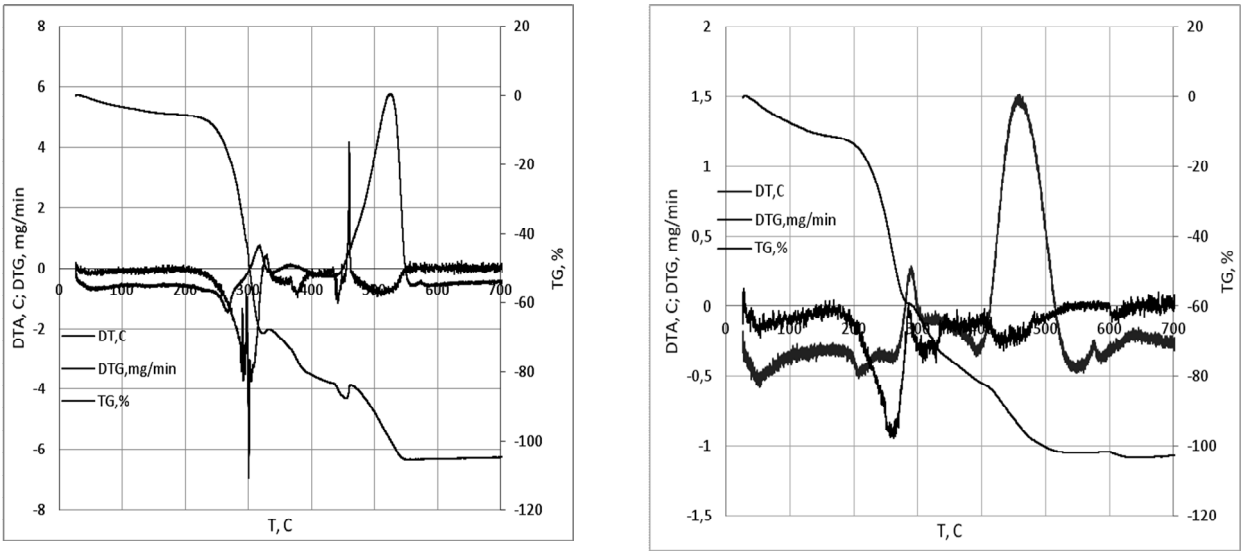
Temperature dependence of 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid in organic solvents

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	$x_2 \cdot 10^3$
Acetonitrile											
287.8	1.5972	0.0020	0.17	304.0	1.6718	0.0038	0.31	317.6	1.0579	0.0045	0.56
287.8	2.2961	0.0027	0.16	306.5	1.0005	0.0026	0.35	317.6	1.6170	0.0067	0.57
297.9	0.6311	0.0011	0.25	306.5	1.0093	0.0026	0.35	321.4	0.2190	0.0010	0.62
297.9	1.3606	0.0025	0.25	306.5	1.3974	0.0036	0.35	321.4	0.3726	0.0017	0.63
297.9	1.4730	0.0028	0.26	307.5	1.5766	0.0045	0.38	321.4	0.4511	0.0021	0.63
298.5	1.4068	0.0027	0.26	307.5	1.6851	0.0047	0.38	321.5	1.0791	0.0050	0.62
298.5	1.4563	0.0027	0.25	312.1	0.7054	0.0022	0.43	321.5	1.3964	0.0067	0.65
298.5	1.6833	0.0032	0.26	312.1	1.6105	0.0055	0.46	321.5	2.1091	0.0098	0.63
302.5	0.5314	0.0011	0.29	312.1	1.6162	0.0053	0.44	322.5	0.6668	0.0032	0.65
302.5	1.5940	0.0032	0.27	316.4	0.8819	0.0032	0.49	322.5	1.7365	0.0087	0.68
302.5	2.2415	0.0048	0.29	316.4	1.5886	0.0060	0.51	322.5	2.3690	0.0117	0.67
304.0	1.4387	0.0034	0.32	316.4	2.0771	0.0076	0.50	326.0	1.7918	0.0106	0.80
304.0	1.4455	0.0034	0.32	317.6	0.8318	0.0033	0.54	326.0	1.9125	0.0111	0.79
$\ln x_2 = (4.46 \pm 0.32) - (3804 \pm 96) \cdot 1/T$											
Dimethyl ketone											
294.4	0.5663	0.0085	2.85	304.3	0.4794	0.0100	3.98	312.9	0.3626	0.0098	5.12
294.4	0.6290	0.0088	2.68	305.5	0.4379	0.0089	3.86	312.9	0.4436	0.0118	5.05
297.0	0.7068	0.0111	2.99	305.5	0.5542	0.0111	3.82	312.9	0.49825	0.0140	5.33
297.0	0.8928	0.0141	3.01	305.5	0.5879	0.0126	4.07	315.8	0.2935	0.0085	5.49
297.0	0.5204	0.0084	3.07	308.4	0.4479	0.0106	4.51	315.8	0.4579	0.0134	5.55
297.5	0.5837	0.0096	3.13	308.4	0.5572	0.0133	4.53	315.8	0.8215	0.0244	5.63
297.5	0.4294	0.0069	3.08	308.7	0.3662	0.0092	4.77	320.0	0.3700	0.0128	6.55
297.5	0.4671	0.0075	3.07	308.7	0.4870	0.0122	4.75	320.0	0.4315	0.0146	6.41
299.4	0.5117	0.0095	3.55	308.7	0.5076	0.0119	4.47	320.0	0.6311	0.0217	6.53
299.4	0.5849	0.0109	3.56	311.1	0.4388	0.0110	4.76	322.9	0.2179	0.0078	6.82
304.3	0.3658	0.0079	4.10	311.1	0.5027	0.0124	4.70	322.9	0.4877	0.018	6.99
304.3	0.3972	0.0082	3.94	311.1	0.6387	0.0168	4.99	322.9	0.5324	0.0195	6.93
$\ln x_2 = (4.40 \pm 0.39) - (3025 \pm 119) \cdot 1/T$											
Ethyl acetate											
300.8	0.4210	0.0048	3.29	308.5	0.5978	0.0087	4.19	315.8	0.7298	0.0135	5.32
300.8	0.7449	0.0086	3.33	311.2	0.4783	0.0074	4.48	315.8	0.8266	0.0151	5.26
300.9	0.4801	0.0054	3.24	311.2	0.5197	0.0080	4.43	315.9	0.8431	0.0158	5.41
300.9	0.6917	0.0080	3.33	311.2	0.5767	0.0090	4.49	315.9	1.1951	0.0221	5.33
300.9	0.8809	0.0101	3.32	311.6	1.0630	0.0164	4.44	318.5	0.4338	0.0090	6.00
304.4	0.6576	0.0082	3.59	311.6	1.0684	0.0164	4.42	318.5	0.4751	0.0100	6.08
304.4	0.7460	0.0092	3.55	313.0	0.4077	0.0069	4.87	318.5	0.5155	0.0108	6.02
304.4	0.7920	0.0095	3.48	313.0	0.4807	0.0080	4.79	323.5	0.4687	0.0118	7.23
307.0	0.7857	0.0107	3.92	313.0	0.5851	0.0098	4.82	323.5	0.4846	0.0122	7.26
307.0	0.8963	0.0122	3.94	313.6	0.5731	0.0102	5.12	323.5	0.5622	0.0136	6.95
307.0	0.9086	0.0123	3.92	313.6	0.6294	0.0114	5.23	327.5	0.4230	0.0118	8.04
308.5	0.4489	0.0062	3.98	313.6	0.7089	0.0129	5.24	327.5	0.5032	0.0139	7.95
308.5	0.5767	0.0080	4.00	315.8	0.7111	0.0130	5.26	327.5	0.5647	0.0157	8.00
$\ln x_2 = (5.47 \pm 0.41) - (3376 \pm 129) \cdot 1/T$											
Isopropanol											
302.7	0.4111	0.0041	1.96	312.4	0.3827	0.0062	3.19	318.0	0.4092	0.0082	3.96
302.7	0.8314	0.0083	1.97	312.4	0.4612	0.0075	3.20	318.0	0.4713	0.0095	3.98
302.7	0.6382	0.0064	1.97	312.4	0.5483	0.0089	3.19	318.0	0.6676	0.0137	4.03
305.0	0.3983	0.0045	2.22	313.5	0.4097	0.0070	3.36	318.4	0.3741	0.0079	4.15
305.0	0.7478	0.0083	2.19	313.5	0.5072	0.0085	3.30	318.4	0.4456	0.0095	4.18
305.0	0.7564	0.0082	2.13	313.5	0.7026	0.0121	3.38	318.4	0.4479	0.0090	3.95
308.6	0.3938	0.0054	2.70	316.2	0.4073	0.0075	3.62	320.9	0.3668	0.0085	4.55
308.6	0.4269	0.0058	2.67	316.2	0.4185	0.0078	3.66	320.9	0.4458	0.0105	4.60
308.6	0.4996	0.0068	2.68	316.2	0.4662	0.0087	3.67	320.9	0.4735	0.0111	4.63
309.8	0.5238	0.0074	2.78	317.1	0.4233	0.0086	4.01	325.5	0.4017	0.0117	5.74
309.8	0.5293	0.0076	2.82	317.1	0.4843	0.0095	3.88	325.5	0.6713	0.0201	5.87
309.8	0.5313	0.0078	2.89	317.1	0.4992	0.0096	3.80	325.5	0.7425	0.0217	5.73
$\ln x_2 = (8.78 \pm 0.35) - (4543 \pm 110) \cdot 1/T$											

Table 3

Temperature dependence of 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid in organic solvents

T, K	m_1, g	m_2, g	$x_2 \cdot 10^4$	T, K	m_1, g	m_2, g	$x_2 \cdot 10^4$	T, K	m_1, g	m_2, g	$x_2 \cdot 10^4$
Acetonitrile											
304.1	1.7584	0.0005	0.43	314.0	4.0253	0.0018	0.68	326.5	2.9971	0.0023	1.16
304.1	1.8033	0.0005	0.42	318.1	1.7062	0.0009	0.80	326.5	3.3645	0.0027	1.22
304.1	3.0456	0.0009	0.45	318.1	1.8319	0.0010	0.83	330.4	2.9830	0.0029	1.47
307.9	1.4604	0.0005	0.52	318.1	2.2592	0.0012	0.80	330.4	3.1800	0.0031	1.48
307.9	1.8749	0.0007	0.53	320.5	2.1442	0.0014	0.99	330.4	3.6235	0.0036	1.50
307.9	1.9603	0.0007	0.54	320.5	2.2392	0.0014	0.95	331.5	2.8957	0.0028	1.46
311.3	2.3067	0.0009	0.59	320.5	2.7723	0.0017	0.93	331.5	3.1059	0.0031	1.51
311.3	2.6456	0.0011	0.63	322.5	1.7379	0.0011	0.96	331.5	3.4128	0.0034	1.51
311.3	2.8480	0.0012	0.64	322.5	1.9867	0.0013	0.99	335.5	2.3662	0.0027	1.73
314.0	2.6318	0.0012	0.69	322.5	2.2074	0.0015	1.03	335.5	2.6048	0.0029	1.69
314.0	2.7298	0.0012	0.67	326.5	2.6295	0.0021	1.21	335.5	3.1141	0.0036	1.75
$\ln x_2 = (4.90 \pm 0.38) - (4546 \pm 123) \cdot 1/T$											
Dimethyl ketone											
298.4	0.7363	0.0014	4.22	309.1	0.7198	0.0021	6.40	317.9	0.9182	0.0041	9.67
298.4	0.8695	0.0017	4.31	309.1	0.9384	0.0027	6.16	317.9	1.1962	0.0050	8.95
300.7	0.4267	0.0009	4.52	312.9	0.3561	0.0013	8.12	318.5	0.6722	0.0030	9.71
300.7	0.5979	0.0012	4.30	312.9	0.4697	0.0017	7.45	318.5	0.7778	0.0034	9.49
300.7	0.7235	0.0015	4.44	312.9	0.5483	0.0020	7.81	318.5	1.0268	0.0045	9.48
305.1	0.3205	0.0008	5.34	313.3	0.9008	0.0031	7.49	322.4	0.4674	0.0023	10.5
305.1	0.3450	0.0009	5.59	313.3	0.9656	0.0034	7.65	322.4	0.7638	0.0039	10.9
305.1	0.5816	0.0015	5.52	313.3	0.9734	0.0034	7.59	322.4	1.1164	0.0054	10.5
308.7	0.4072	0.0012	6.31	313.6	0.8663	0.0033	8.28	323.4	0.4976	0.0026	11.2
308.7	0.4840	0.0014	6.41	313.6	1.0496	0.0038	7.85	323.4	0.7291	0.0040	10.9
309.1	0.6145	0.0018	6.27	317.9	0.7403	0.0030	8.67	323.4	0.8057	0.0043	10.5
$\ln x_2 = (5.33 \pm 0.49) - (3918 \pm 153) \cdot 1/T$											
Ethyl acetate											
301.9	1.6540	0.0023	4.52	316.8	1.5951	0.0039	8.04	324.1	1.2017	0.0039	10.5
301.9	1.6751	0.0023	4.46	316.8	1.6465	0.0041	8.09	324.1	1.3336	0.0043	10.5
301.9	2.7724	0.0038	4.45	316.8	2.0522	0.0052	8.23	324.1	1.7066	0.0057	10.8
304.8	1.4656	0.0022	4.99	318.1	1.2866	0.0033	8.33	327.6	1.6734	0.0060	11.6
304.8	1.7084	0.0026	4.94	318.1	1.8164	0.0048	8.58	327.6	1.8576	0.0067	11.7
304.8	2.0557	0.0031	4.90	318.1	2.1476	0.0057	8.62	327.6	2.3365	0.0085	11.8
312.1	1.1236	0.0023	6.65	321.1	1.5380	0.0045	8.50	331.0	1.6803	0.0069	13.3
312.1	1.9614	0.0040	6.62	321.1	2.0603	0.0060	9.46	331.0	1.8667	0.0076	13.2
312.1	2.5448	0.0053	6.76	321.1	2.7656	0.0082	9.63	331.0	2.0869	0.0085	13.2
316.4	2.9336	0.0071	7.86	321.9	1.3308	0.0039	9.52	332.3	1.0041	0.0044	14.2
316.4	2.9757	0.0071	7.75	321.9	1.8228	0.0055	9.80	332.3	2.0169	0.0088	14.2
316.4	3.2686	0.0081	8.05	321.9	2.4157	0.0072	9.68	332.3	2.2388	0.0098	14.2
$\ln x_2 = (4.84 \pm 0.34) - (3791 \pm 110) \cdot 1/T$											
Isopropanol											
296.9	2.4509	0.0026	2.35	308.5	2.6075	0.0055	4.67	325.5	2.3500	0.0105	9.94
296.9	2.4984	0.0028	2.48	311.3	0.8232	0.0019	5.11	325.5	2.9287	0.0128	9.72
296.9	2.9357	0.0032	2.42	311.3	1.6908	0.0040	5.24	329.8	1.7107	0.0085	11.1
300.5	0.8686	0.0012	3.06	311.3	2.3636	0.0056	5.25	329.8	1.8791	0.0099	11.7
300.5	1.1662	0.0015	2.85	315.2	1.8976	0.0055	6.42	329.8	1.9543	0.0104	11.8
300.5	1.9272	0.0026	2.99	315.2	3.0420	0.0085	6.19	332.2	1.7855	0.0107	13.3
305.6	2.0011	0.0036	3.78	315.2	3.3571	0.0095	6.27	332.2	1.8194	0.0112	13.6
305.6	2.0313	0.0036	3.99	320.5	2.6229	0.0093	7.85	332.2	2.0900	0.0123	13.0
305.6	2.0539	0.0035	3.93	320.5	2.6394	0.0099	8.05	335.5	1.5851	0.0110	15.4
308.5	1.3292	0.0027	4.50	320.5	2.6542	0.0096	8.31	335.5	1.8269	0.0126	15.3
308.5	2.0353	0.0042	4.57	325.5	1.7651	0.0076	9.545	335.5	2.3993	0.0171	15.8
$\ln x_2 = (7.52 \pm 0.39) - (4697 \pm 123) \cdot 1/T$											



a) b)

Fig. 1. Derivatograms of 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid (a) and 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid (b)

Table 4

Thermodynamic parameters of arylfurans

Compound	*Mw*, g/mol	T_{fus}, K	$\Delta_{fus}H$, kJ/mol	$\Delta_{fus}S$	
				J/mol·K	J/g·K
2-Methyl-5-phenylfuran-3-carboxylic acid	202.2	458.1±0.5	32.4±1.8	70.7±1.9	0.350
2-Methyl-5-(4-methylphenyl)-furan-3-carboxylic acid	216.2	507.2±1.2	32.7±1.0	64.5±1.5	0.299
5-(2-Nitrophenyl)-furan-2-carboxylic acid	235.2	491.6±1.0	33.59±0.22	68.3±1.0	0.291
3-[5-(2-Nitrophenyl)-furan-2-]-acrylic acid	259.2	447.6±1.0	25.00±0.66	55.9±1.2	0.216
5-(2-Nitrophenyl)-furan-2-oxime	232.2	411.1±1.0	20.1±1.3	48.9±1.6	0.211
5-(3-Nitrophenyl)-furan-2-oxime	232.2	444.9±1.0	26.75±0.48	60.1±1.1	0.259
5-(4-Nitrophenyl)-furan-2-oxime*	232.2	451.1±1.2	22.30±0.17	49.4±1.5	0.213
5-(2- Nitrophenyl)-furan-2-carbaldehyde	217.2	368.3±1.0	33.39±0.70	90.7±1.2	0.417
5-(3- Nitrophenyl)-furan-2-carbaldehyde	217.2	428.6±1.0	36.31±0.44	84.7±1.1	0.390
5-(4- Nitrophenyl) furan-2-carbaldehyde	217.2	479.8±1.0	39.86±0.69	83.1±1.2	0.383
5-(2-Nitro-4-methylphenyl)-furan-2-carbaldehyde	231.2	379.2±1.2	28.10±0.10	74.1±1.2	0.321
5-(2-Nitro-4-oxymethylphenyl)-furan-2-carbaldehyde	247.2	372.0±1.0	35.89±0.07	96.5±1.0	0.390
5-(2-Methyl-4-nitrophenyl)-furan-2-carbaldehyde	231.2	440.4±1.3	34.7±1.1	78.8±1.7	0.341
5-(2-Oxymethyl-4-nitophenyl)-furan-2-carbaldehyde	247.2	490.9±1.5	36.93±0.13	75.2±1.5	0.304
Ethyl-4-(5-formylfuran-2-yl)-benzoate	244.3	386.1±1.5	33.5±1.5	86.7±2.1	0.355
2-Cyano-[3-(4-phenyl)-2-furan]-acrylic acid ethyl ester	267.3	391.5±1.0	34.6±1.8	88.4±2.1	0.331
2-Cyano3-[4-(4-methylphenyl)-2-furan]-acrylic acid ethyl ester	281.3	387.7±1.0	26.8±3.0	69.1±3.2	0.246
2-Cyano-3-[5-(2-nitrophenyl)-2-furan]-acrylic acid ethyl ester	312.3	437.0±1.0	34.93±1.0	79.9±1.3	0.256
2-Cyano-3-[5-(3-nitrophenyl)-2-furan]-acrylic acid ethyl ester	312.3	487.3±1.5	58.7±2.3	120.4±2.7	0.385
2-Cyano-3-[5-(4-nitrophenyl)-2-furan]-acrylic acid ethyl ester	312.3	523.8±1.5	76.6±3.4	146.2±3.7	0.468
2-Cyano-3-[4-(4-methyl-3-nitrophenyl)-2-furan]-acrylic acid ethyl ester	326.3	427.2±1.0	40.9±1.2	95.7±1.6	0.293
2-Cyano-3-[5-(phenyl)-2-furyl]-2-propenamide	238.3	480.8±1.5	37.6±1.7	78.2±2.3	0.328
2-Cyano-3-[5-(4-methylphenyl)-2-furyl]-2-propenamide	252.3	461.0±1.1	40.3±1.6	87.4±2.1	0.346
2-Cyano-3-[5-(2-nitrophenyl)-2-furyl]-2-propenamide	283.2	513.9±1.1	37.43±0.76	72.8±1.3	0.257
2-Cyano-3-[5-(2-nitro-4-methylphenyl)-2- фурил]-2-propenamide	297.2	481.6±1.0	45.3±1.0	94.1±1.4	0.316

Note: * the ratio of *anti*:*sin* isomers is 9:41 (~1:4.55).

Table 5

Thermodynamic parameters of solubility, melting and mixing of investigated compounds in organic solvents at 298 K

Solvent	$\Delta_{fus}H$	$\Delta_{sol}H$	$\Delta_{mix}H$	$\Delta_{fus}S$	$\Delta_{sol}S$	$\Delta_{mix}S$
	kJ/mol			J/mol·K		
2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid						
Acetonitrile	34.5±4.6	31.63±0.80	-2.9±4.7	57.4±8.9	37.1±2.7	-20.3±9.3
Dimethyl ketone		25.15±0.95	-9.4±4.7		36.6±3.2	-20.8±9.5
Ethyl acetate		28.1±1.1	-6.4±4.7		45.5±3.4	-11.9±9.5
Isopropanol		37.77±0.92	3.3±4.7		73.0±2.9	15.6±9.4
2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid						
Acetonitrile	31.6±4.4	37.8±1.0	6.2±4.5	46.5±7.9	40.7±3.2	-5.8±8.5
Dimethyl ketone		32.6±1.3	1.0±4.6		44.3±4.1	-2.2±8.9
Ethyl acetate		31.52±0.91	-0.1±4.5		40.2±2.8	-6.3±8.4
Isopropanol		39.1±1.0	7.5±4.5		62.5±3.2	16.0±8.5

Calculated values of enthalpy and entropy of fusion (Table 5) were recalculated relative to a generally accepted temperature of 298 K according to Eqs. (5) and (6) [19].

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

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

where $\left(\frac{\Delta_{fus}S^0}{\Delta_{fus}Cp^0}\right)_{T_{fus}} = \left(\frac{\Delta_{fus}H^0}{T_{fus}\cdot\Delta_{fus}Cp^0}\right)_{T_{fus}} = 1.35 \pm 0.11.$

According to Table 5, the mixing of saturated solutions of both investigated acids in ethyl acetate occurs with negative deviations from the ideal solution ($\Delta_{mix}H < 0$), and the mixing in isopropanol – with positive ones ($\Delta_{mix}H > 0$). Mixing in acetonitrile and methyl ketone occurs with different signs of deviation. The saturated solutions of 2-methyl-5-(2-chloro-5-trifluoromethyl-phenyl)-furan-3-carboxylic acid are mixed with negative, and saturated solutions of 2-methyl-5-(2,5-dichloro-phenyl)-furan-3-carboxylic acid – with positive deviations from the ideal solution.

We also managed to establish the compensatory effect of the mixing process for the acids (Eq. (8)) using organic solvents except acetonitrile (Fig. 2). A similar dependence was observed in our previous studies [13] for 2-methyl-5-phenylfuran-3-carboxylic acid (Eq. (9)) and 2-methyl-5-(4-methylphenyl)-furan-3-carboxylic acid (Eq. (10)).

The location of 1–4 points outside the straight lines can be explained by the formation of hydrogen bond of various types between acids and solvents. An intermolecular hydrogen bond with oxygen is formed between acids and dimethyl ketone, ethyl acetate and isopropanol due to the carbonyl and hydroxyl groups; in the acetonitrile molecules the hydrogen bond is formed between the hydrogen atoms of the hydroxyl group and nitrogen of the nitrile group.

$$\Delta_{mix}H_{298} = 0.350\cdot\Delta_{mix}S_{298} - 2.17 \quad (7)$$

$$\Delta_{mix}H_{298} = 0.346\cdot\Delta_{mix}S_{298} + 1.94 \quad (8)$$

$$\Delta_{mix}H_{298} = 0.414\cdot\Delta_{mix}S_{298} + 6.40 \quad (9)\ [13]$$

$$\Delta_{mix}H_{298} = 0.409\cdot\Delta_{mix}S_{298} + 1.59 \quad (10)\ [13]$$

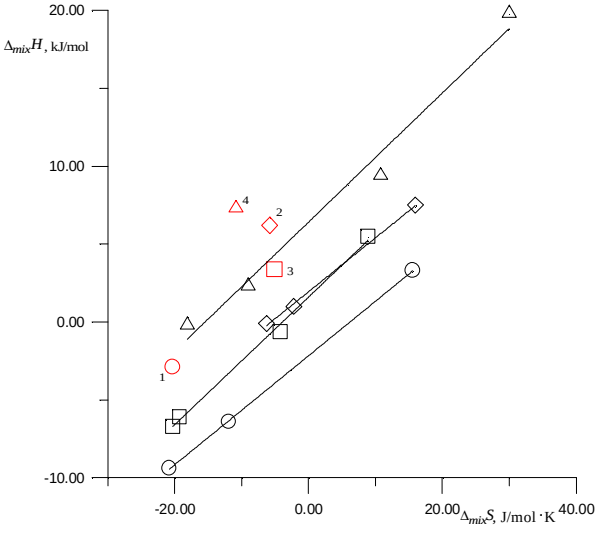


Fig. 2. Dependence between the enthalpy and the entropy of mixing for acids in organic solvents: 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid (○); 2-methyl-5-(2,5-dichlorophenyl)-furan-3-carboxylic acid (◊); 5-methyl-5-(4-methylphenyl)-furan-3-carboxylic acid [13] (□) and 5-phenyl-2-methyl-3-furancarboxylic acid [13] (Δ); points 1–4 refer to solutions of investigated compounds in acetonitrile

4. Conclusions

The thermodynamic properties of 2-methyl-5-(2-chloro-5-trifluoromethylphenyl)-furan-3-carboxylic acid and 2-methyl-5- (2,5-dichlorophenyl)-furan-3-carboxylic acids solubility in organic solvents were determined. The established compensatory effect of mixing acids with solvents shows the same type of their intermolecular interaction with the formation of a hydrogen bond with oxygen between the carbonyl and hydroxyl groups. The mixing of acids with acetonitrile occurs *via* another mechanism (without compensatory effect) to form a hydrogen bond between hydrogen atoms the hydroxyl group and nitrogen of the nitrile group. The obtained results may be used for optimization of synthesis and purification of investigated acids.

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ТЕРМОДИНАМІЧНІ ВЛАСТИВОСТІ РОЗЧИНІВ ХЛОРПОХІДНИХ 2-МЕТИЛ-5-АРИЛФУРАН-3-КАРБОКСИЛЬНИХ КИСЛОТ В ОРГАНІЧНИХ РОЗЧИННИКАХ

Анотація. *Експериментально визначено температурні залежності розчинності 2-метил-5-(2-хлор-5-трифторметилфеніл)-фуран-3-карбонової та 2-метил-5-(2,5-дихлорфеніл)-фуран-3-карбонової кислот в ацетонітрилі, диметилкетоні, ізо-пропанолі та етилацетаті. Розраховані ентальпії плавлення досліджених речовин та їх ентальпії та ентропії змішування за 298 К. Встановлено рівняння зв'язку концентрації насиченого розчину з величинами ентальпії і ентропії розчинності за 298 К. Виявлений компенсаційний ефект змішування досліджених кислот зі всіма розчинниками, що містять карбонільну групу.*

Ключові слова: *ентальпія, ентропія розчинності, змішування і плавлення, 2-метил-5-(2-хлор-5-трифторметилфеніл)-фуран-3-карбонова кислота, 2-метил-5-(2,5-дихлорфеніл)-фуран-3-карбонова кислота.*