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Electronic Supplementary Information

Impact of structural modification of 1,2,4-thiadiazole derivatives on thermodynamics of solubility and hydration processes

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Table S1. Temperature dependencies of solubility, X_2 (mol. fraction), of the compounds **I–VI** in buffer pH 7.4

	I[d]	**II**[d]	**III**[d]	**IV**[e]	**V**[e]	**VI**[e]
T, K	$x_2 \cdot 10^5$	$x_2 \cdot 10^5$	$x_2 \cdot 10^5$	$x_2 \cdot 10^6$	$x_2 \cdot 10^5$	$x_2 \cdot 10^5$
293.2	7.56	3.47	0.75	2.57	6.01	1.03
298.2	9.05	3.95	1.79	3.11	6.13	1.38
303.2	10.31	4.36	2.00	3.62	6.23	2.15
310.2	12.34	5.22	2.47	4.38	6.38	3.20
315.2	14.63	5.60	2.87	5.40	6.51	4.23
A[a]	-0.3 ± 0.3	-3.2 ± 0.2	-2.3 ± 0.3	-2.2 ±0.3	-8.6 ±0.2	9.1 ± 0.9
B[a]	2684 ± 95	2060 ± 62	2577 ± 86	3121 ± 79	329 ± 44	6040 ± 259
R[b]	0.998	0.998	0.998	0.999	0.974	0.997
$\sigma \cdot 10^2$[c]	2.68	1.37	1.66	1.50	0.85	4.96

[a]Parameters of the correlation equation: $\ln X_2 = A - B/T$;
[b]R– pair correlation coefficient;
[c]σ– standard deviation;
[d]Data taken from ref. 12;
[e]Data taken from ref. 13.

Table S2. Thermodynamic solubility and solvation functions of the compounds **I-VI** in buffer 7.4 at 298 K

	x_2^{298}	$\Delta_{sln}G^0$ kJ·mol^{-1}	$\Delta_{sln}H^0$ kJ·mol^{-1}	$T\Delta_{sln}S^0$ kJ·mol^{-1}	$\Delta_{sln}S^0$ J·mol^{-1}·K^{-1}	ς_{Hsln}[a] [%]	ς_{TSsln}[b] [%]	$\Delta_{hyd}G^0$ kJ·mol^{-1}	$\Delta_{hyd}H^0$ kJ·mol^{-1}	$T\Delta_{hyd}S^0$ kJ·mol^{-1}	$\Delta_{hyd}S^0$ J·mol^{-1}·K^{-1}	ς_{Hhyd}[c] [%]	ς_{TShyd}[d] [%]
I[e]	$9.05\cdot10^{-5}$	23.1	22.3 ± 0.8	-0.8	-2.7 ± 2	96.5	3.5	-35.2	-101.5	-66.2	-222	60.5	39.5
II[e]	$3.95\cdot10^{-5}$	25.1	17.1 ± 0.5	-8.0	-27 ± 2	68.1	31.9	-37.4	-124.9	-87.5	-294	58.8	41.2
III[e]	$1.79\cdot10^{-5}$	27.1	21.4 ± 0.7	-5.7	-19 ± 2	79.0	21.0	-33.1	-131.4	-98.3	-330	57.2	42.8
IV[f]	$3.09\cdot10^{-6}$	31.5	25.9 ± 0.7	-5.6	-19 ± 1	82.2	17.8	-27.1	-133.7	-106.6	-358	55.6	44.4
V[f]	$6.13\cdot10^{-5}$	24.0	2.7 ± 0.4	-21.3	-71 ± 11	11.3	88.8	-35.1	-122.1	-86.9	-291	58.4	41.6
VI[f]	$1.45\cdot10^{-5}$	27.6	50.2 ± 2.1	22.6	76 ± 5	69.0	31.0	-44.3	-87.8	-43.5	-146	66.9	33.1

[a] $\varsigma_{Hsol} = (|\Delta H^0_{sol}| / (|\Delta H^0_{sol}| + |T\Delta S^0_{sol}|)) \cdot 100\%$; [b] $\varsigma_{TSsol} = (|T\Delta S^0_{sol}| / (|\Delta H^0_{sol}| + |T\Delta S^0_{sol}|)) \cdot 100\%$;

[c] $\varsigma_{Hhyd} = (|\Delta H^0_{hyd}| / (|\Delta H^0_{hyd}| + |T\Delta S^0_{hyd}|)) \cdot 100\%$; [d] $\varsigma_{TShyd} = (|T\Delta S^0_{hyd}| / (|\Delta H^0_{hyd}| + |T\Delta S^0_{hyd}|)) \cdot 100\%$.

[e] Data taken from ref. 12;

[f] Data taken from ref. 13.

Table S3. Thermodynamic characteristics of sublimation process of the compounds studied

	I[b]	**II**[b]	**III**[b]	**IV**[c]	**V**[c]	**VI**[c]
$\Delta_{sub}G^0$, kJ·mol^{-1}	58.3	62.5	60.2	58.6	59.1	71.9
$\Delta_{sub}H^T$, kJ·mol^{-1}	121.4 ± 1.1	139.3 ± 1.6	149.6 ± 2.2	157.2 ± 2.1	122.0 ± 0.9	133.3 ± 0.8
$\Delta_{sub}H^0$, kJ·mol^{-1}	123.8 ± 1.1	142.0 ± 1.6	152.8 ± 2.2	159.6 ± 2.1	124.8 ± 0.9	138.0 ± 0.8
$C_{p,cr}^{298}$, J·mol^{-1}·K^{-1}[a]	288.6	316.2	392.9	349.0	304.4	348.7
$T_{ref}\cdot\Delta_{sub}S^0$, kJ·mol^{-1}	65.5	79.5	92.6	101.0	65.6	66.1
$\Delta_{sub}S^0$, J·mol^{-1}·K^{-1}	220 ± 6	267 ± 8	311 ± 7	339 ± 11	220 ± 6	222 ± 8
	VII[d]	**VIII**[d]	**IX**[d]	**X**[d]	**XI**[d]	**XII**[d]
$\Delta_{sub}G^0$, kJ·mol^{-1}	60.8	62.6	64.5	60.2	60.4	57.6
$\Delta_{sub}H^T$, kJ·mol^{-1}	126.1 ± 2.1	116.3± 2.5	128.9± 2.5	134.8 ± 1.9	112.4 ± 2.1	98.9± 1.5
$\Delta_{sub}H^0$, kJ·mol^{-1}	129.0 ± 2.1	120.7 ±2.5	132.6 ± 2.5	137.3 ± 1.9	115.6 ± 2.1	101.9 ±1.5
$C_{p,cr}^{298}$, J·mol^{-1}·K^{-1}[a]	366.0	344.9	308.3	316.2	308.3	344.9
$T_{ref}\cdot\Delta_{sub}S^0$, kJ·mol^{-1}	68.2	58.1	68.1	77.1	55.2	44.3
$\Delta_{sub}S^0$, J·mol^{-1}·K^{-1}	229 ± 8	195 ± 8	228± 9	259 ± 8	185 ± 7	149 ± 5

[a] $C_{p,cr}^{298}$ has been calculated by additive scheme[S1];

[b]Data taken from ref. 12;
[c]Data taken from ref. 13;
[c]Data taken from ref. 14.

References

S1 J. S. Chickos, W. E. Acree Jr. *J. Phys. Chem. Ref. Data.* 2002, **31**, 537 − 698.

Table S4. Numerical values of HYBOT physicochemical descriptors used for correlation with the hydration Gibbs energy

Compound	$\sum(C_{ad})$	α	$\sum(C_{ad})/\alpha$
I	8.36	25.451	0.328
II	8.39	27.286	0.307
III	9.07	29.395	0.308
IV	8.29	27.013	0.307
V	8.31	25.360	0.328
VI	11.38	29.758	0.382
VII	9.06	27.560	0.329
VIII	8.41	29.214	0.288
IX	8.35	27.379	0.305
X	8.31	27.286	0.305
XI	8.34	27.379	0.305
XII	8.48	29.214	0.290