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ELECTRONIC SUPPLEMENTARY INFORMATION

Adamantane Derivatives of Sulfonamides: Sublimation, Solubility, Solvation and Transfer Processes in Biological Relevant Solvents

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NMR Experiments

N-Adamantan-1-yl-benzenesulfonamide (**I**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 1.28 - 1.62 (m, 6H, AdH), 1.679 (d, $J = 2.79$ Hz, 6H, AdH), 1.91 (br. s., 3H, AdH), 4.58 (s, 1H, NH), 7.37 - 7.60 (m, 3H, ArH), 7.89 (dd, $J = 7.58$, 1.20 Hz, 2H, ArH). Mp 124.3 ± 0.2 °C. Anal. ($C_{16}H_{21}NO_2S$) C, H, N, S.

N-Adamantan-1-yl-4-fluoro-benzenesulfonamide (**II**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 1.47 - 1.77 (m, 6H, AdH), 1.77 - 1.93 (m, 6H, AdH), 2.05 (br. s., 3H, AdH), 4.64 (br. s., 1H, NH), 7.20 (t, $J = 8.84$ Hz, 2H, ArH), 7.83 - 8.09 (m, 2H, ArH). Mp 146.2 ± 0.2 °C. Anal. ($C_{16}H_{20}FNO_2S$) C, H, N, S.

N-Adamantan-1-yl-4-methyl-benzenesulfonamide (**III**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 1.30 - 1.62 (m, 6H, AdH), 1.70 (d, $J = 2.79$ Hz, 6H, AdH), 1.95 (br. s., 3H, AdH), 2.44 (s, 3H, CH_3), 4.62 (s, 1H, NH), 7.16 - 7.35 (d, $J = 7.83$ Hz, 2H, ArH), 7.78 (d, $J = 7.83$ Hz, 2H, ArH). Mp 164.7 ± 0.2 °C. Anal. ($C_{17}H_{23}NO_2S$) C, H, N, S.

N-Adamantan-1-yl-4-chloro-benzenesulfonamide (**IV**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 1.30 - 1.62 (m, 6H, AdH), 1.69 (d, $J = 2.79$ Hz, 6H, AdH), 1.93 (br. s., 3H, AdH), 4.60 (s, 1H, NH), 7.28 - 7.49 (m, 2H, ArH), 7.67 - 7.86 (m, 2H, ArH). Mp 186.8 ± 0.2 °C. Anal. ($C_{16}H_{20}ClNO_2S$) C, H, N, S.

N-(3,5-Dimethyl-adamantan-1-yl)-4-fluoro-benzenesulfonamide (**V**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 0.73 (s, 6H, $2CH_3$), 1.02 (s, 2H, AdH), 1.10 - 1.29 (m, 4H, AdH), 1.31 - 1.53 (m, 4H, AdH), 1.53 - 1.70 (m, 2H, AdH), 1.90 - 2.12 (m, 1H, AdH), 4.70 (br. s., 1H, NH), 6.95 - 7.22 (m, 2H, ArH), 7.78 - 8.03 (m, 2H, ArH).

Mp 137.3 ± 0.2 °C. Anal. ($C_{18}H_{24}FNO_2S$) C, H, N, S.

N-(3,5-Dimethyl-adamantan-1-yl)-4-methyl-benzenesulfonamide (**VI**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 0.77 (s, 6H, $2CH_3$), 1.06 (s, 2H, AdH), 1.12 - 1.32 (m, 4H, AdH), 1.32 - 1.55 (m, 4H, AdH), 1.55 - 1.67 (m, 2H, AdH), 1.98 - 2.11 (m, 1H, AdH), 2.42 (s, 3H, $ArCH_3$), 4.68 (br. s., 1H, NH), 7.16 - 7.35 (d, $J = 7.83$ Hz, 2H, ArH), 7.78 (d, $J = 7.83$ Hz, 2H, ArH). Mp 162.4 ± 0.2 °C. Anal. ($C_{19}H_{27}NO_2S$) C, H, N, S.

N-(3,5-Dimethyl-adamantan-1-yl)-4-chloro-benzenesulfonamide (**VII**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 0.79 (s, 6H, $2CH_3$), 1.08 (s, 2H, AdH), 1.16 - 1.33 (m, 4H, AdH), 1.33 - 1.55 (m, 4H, AdH), 1.73 (br. s, 2H, AdH), 2.02 - 2.18 (m, 1H, AdH), 4.76 (br. s., 1H, NH), 7.46 (d, J = 8.32 Hz, 2H, ArH), 7.84 (d, J = 8.32 Hz, 2H, ArH). Mp 161.8 ± 0.2 °C. Anal. ($C_{18}H_{24}ClNO_2S$) C, H, N, S.

N-(3,5-Dimethyl-adamantan-1-yl)-2,4,6-triisopropyl-benzene-sulfonamide (**VIII**)

^{1}H NMR (200 MHz, $CDCl_3$), δ, ppm: 0.73 (s, 6H, $2AdCH_3$), 0.87 - 1.20 (m, 6H, AdH), 1.22 (d, 6H, J = 7.34 Hz, $HC(C\underline{H}_3)_2$), 1.26 (d, 12H, J = 7.34 Hz, $2HC(C\underline{H}_3)_2$), 1.35 - 1.61 (m, 4H, AdH), 1.73 (br. s, 2H, AdH), 2.00 (br. s, 1H, AdH), 2.68 - 3.01 (m, 1H, $\underline{H}C(CH_3)_2$) 4.20 - 4.58 (m, 2H, $\underline{H}C(CH_3)_2$), 7.06 (s, 2H, ArH), 7.84 (br. s, 1H, NH). Mp 290.5 ± 0.2 °C. Anal. ($C_{27}H_{43}NO_2S$) C, H, N, S.

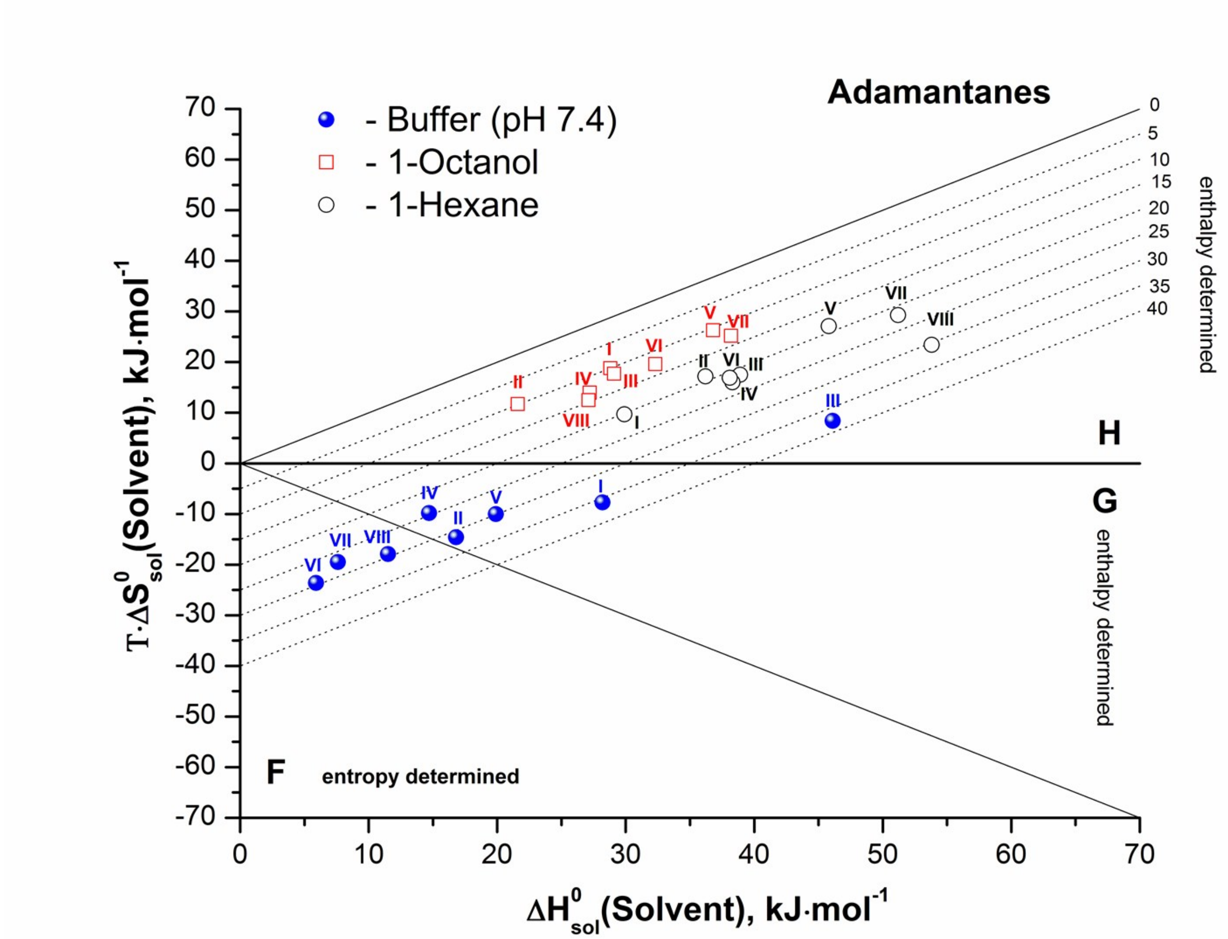

Fig. 1SI Relationship between the thermodynamic functions of dissolution processes of compounds studied in buffer (pH 7.4) (blue cycles), 1-octanol (red square) and 1-hexane (black cycles). The isoenergetic curves of the Gibbs energy are marked by dotted lines. See Figure 1 for numbering of the compounds.

TABLE 1SI
Source, purification and analysis details of the studied samples

N	Chemical name	Provenance	Minimum initial mole fraction purity	Purification method	Final mole fraction purity	Analytical method
I	N-Adamantan-1-yl-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
II	N-Adamantan-1-yl-4-fluoro-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
III	N -Adamantan-1-yl-4-methyl-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
IV	N-Adamantan-1-yl-4-chloro-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
V	N-(3,5-Dimethyl-adamantan-1-yl)-4-fluoro-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
VI	N-(3,5-Dimethyl-adamantan-1-yl)-4-methyl-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
VII	N-(3,5-Dimethyl-adamantan-1-yl)-4-chloro-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
VIII	N-(3,5-Dimethyl-adamantan-1-yl)-2,4,6-triisopropyl-benzenesulfonamide	Synthesis	0.95	Re-crystallization	0.97	NMR
	1-octanol	Sigma Chemical	>0.99	none	-	GC
	1-hexane	RCI Labscan	>0.99	none	-	GC

Table 2SI
Temperature dependencies of saturation vapor pressure of the compounds studied[a]

I[b]		**II**[c]		**III**[d]		**IV**[e]		**V**[f]		**VI**[g]	
t [°C]	*P* [Pa]	t [°C]	*P* [Pa]	t [°C]	*P* [Pa]	t [°C]	*P* [Pa]	t [°C]	*P* [Pa]	t [°C]	*P* [Pa]
93.2	$2.58\cdot10^{-2}$	90.3	$1.60\cdot10^{-2}$	114.3	$4.74\cdot10^{-2}$	105.5	$1.10\cdot10^{-2}$	90.5	$1.87\cdot10^{-2}$	102.0	$4.18\cdot10^{-2}$
94.5	$3.04\cdot10^{-2}$	94.4	$2.40\cdot10^{-2}$	116.4	$5.67\cdot10^{-2}$	108.0	$1.50\cdot10^{-2}$	94.0	$2.75\cdot10^{-2}$	105.0	$5.16\cdot10^{-2}$
95.9	$3.50\cdot10^{-2}$	98.4	$4.00\cdot10^{-2}$	118.6	$7.81\cdot10^{-2}$	113.0	$2.40\cdot10^{-2}$	96.2	$3.60\cdot10^{-2}$	106.5	$6.19\cdot10^{-2}$
97.2	$3.93\cdot10^{-2}$	101.5	$5.40\cdot10^{-2}$	121.5	$1.09\cdot10^{-1}$	117.0	$3.30\cdot10^{-2}$	98.0	$4.23\cdot10^{-2}$	110.0	$8.13\cdot10^{-2}$
98.6	$4.75\cdot10^{-2}$	104.3	$6.60\cdot10^{-2}$	123.1	$1.26\cdot10^{-1}$	120.0	$5.20\cdot10^{-2}$	100.0	$4.98\cdot10^{-2}$	111.0	$9.70\cdot10^{-2}$
101.4	$6.08\cdot10^{-2}$	107.5	$8.70\cdot10^{-2}$	124.8	$1.59\cdot10^{-1}$	126.0	$9.00\cdot10^{-2}$	102.5	$6.11\cdot10^{-2}$	112.0	$1.03\cdot10^{-1}$
102.8	$7.32\cdot10^{-2}$	111.5	$1.34\cdot10^{-1}$	127.1	$2.04\cdot10^{-1}$	128.0	$1.07\cdot10^{-1}$	105.0	$7.73\cdot10^{-2}$	115.5	$1.45\cdot10^{-1}$
104.2	$8.38\cdot10^{-2}$	115.5	$1.96\cdot10^{-1}$	128.2	$2.35\cdot10^{-1}$	131.5	$1.22\cdot10^{-1}$	108.0	$1.02\cdot10^{-1}$	118.0	$1.63\cdot10^{-1}$
105.6	$9.06\cdot10^{-2}$	119.5	$3.13\cdot10^{-1}$	129.4	$2.47\cdot10^{-1}$	136.0	$1.89\cdot10^{-1}$	110.0	$1.37\cdot10^{-1}$	121.0	$2.26\cdot10^{-1}$
107.1	$1.06\cdot10^{-1}$	124.0	$4.18\cdot10^{-1}$	132.4	$3.50\cdot10^{-1}$	138.0	$2.35\cdot10^{-1}$	112.0	$1.54\cdot10^{-1}$	121.5	$2.41\cdot10^{-1}$
108.5	$1.27\cdot10^{-1}$	128.0	$5.98\cdot10^{-1}$	133.9	$4.11\cdot10^{-1}$	143.0	$3.64\cdot10^{-1}$	114.0	$2.01\cdot10^{-1}$	124.0	$2.71\cdot10^{-1}$
110.0	$1.51\cdot10^{-1}$	132.5	$8.85\cdot10^{-1}$	135.6	$5.17\cdot10^{-1}$	146.0	$5.18\cdot10^{-1}$	116.0	$2.38\cdot10^{-1}$	126.0	$3.45\cdot10^{-1}$
111.5	$1.73\cdot10^{-1}$			137.8	$6.77\cdot10^{-1}$	147.5	$5.61\cdot10^{-1}$	118.3	$2.84\cdot10^{-1}$	128.0	$3.76\cdot10^{-1}$
113.0	$1.94\cdot10^{-1}$			139.9	$7.63\cdot10^{-1}$	153.0	$7.70\cdot10^{-1}$				
114.4	$2.27\cdot10^{-1}$			142.3	1.01	155.0	$9.89\cdot10^{-1}$				
116.0	$2.47\cdot10^{-1}$			144.6	1.34	162.0	15.310^{-1}				
117.5	$2.97\cdot10^{-1}$										
119.0	$3.44\cdot10^{-1}$										
120.6	$4.02\cdot10^{-1}$										

[a] Ref [10]

[b]$\ln(P[\mathrm{Pa}]) = (35.5 \pm 0.3) - (14322 \pm 98)/T$; $\sigma = 2.5\cdot10^{-2}$; r = 0.9997; F = 21370; n=19

[c]$\ln(P[\mathrm{Pa}]) = (34.4 \pm 0.4) - (14012 \pm 149)/T$; $\sigma = 4.5\cdot10^{-2}$; r = 0.9993; F = 8836; n=12

[d]$\ln(P[\mathrm{Pa}]) = (42.9 \pm 0.4) - (17808 \pm 151)/T$; $\sigma = 3.4\cdot10^{-2}$; r = 0.9996; F = 13902; n=16

[e]$\ln(P[\mathrm{Pa}]) = (33.7 \pm 0.4) - (14449 \pm 171)/T$; $\sigma = 7.0\cdot10^{-2}$; r = 0.9989; F = 7149; n=16

[f]$\ln(P[\mathrm{Pa}]) = (34.2 \pm 0.5) - (13875 \pm 193)/T$; $\sigma = 4.17\cdot10^{-2}$; r = 0.9986; F = 5182; n=13

[g]$\ln(P[\mathrm{Pa}]) = (31.7 \pm 0.6) - (13089 \pm 217)/T$; $\sigma = 4.19\cdot10^{-2}$; r = 0.9987; F = 3641; n=13

Table 3SI

Thermodynamic characteristics of sublimation and fusion processes of the compounds studied[a]

	I	**II**	**III**	**IV**	**V**	**VI**
ΔG_{sub}^{298} [kJ·mol^{-1}]	59.6	59.8	70.2	65.2	58.2	58.8
ΔH_{sub}^{T} [kJ·mol^{-1}]	119.1 ± 0.8	116.5 ± 1.2	148.1 ± 1.3	120.1 ± 1.4	115.4 ± 1.6	108.8 ± 1.8
ΔH_{sub}^{298} [kJ·mol^{-1}]	123.6 ± 0.8	121.4 ± 1.2	154.4 ± 1.3	126.2 ± 1.4	120.8 ±1.6	115.1 ± 1.8
$C_{p,cr}^{298}$ [J·mol^{-1}·K^{-1}][b]	373.2	389	400.8	392.9	451	462.8
$T \cdot \Delta S_{sub}^{298}$ [kJ·mol^{-1}]	64.0	61.6	84.2	61.0	62.2	56.3
ΔS_{sub}^{298} [J·mol^{-1}·K^{-1}]	215 ± 6	207 ± 6	282 ± 8	205 ± 6	209 ± 7	189 ± 7
ς_{H} [%][c]	65.9	66.3	64.7	67.4	66.0	67.2
ς_{TS} [%][c]	34.1	33.7	35.3	32.6	34.0	32.8
T_m [K]	397.4 ± 0.2	419.3 ± 0.2	437.8 ± 0.2	459.9 ± 0.2	410.4 ± 0.2	435.5 ± 0.2
ΔH_{fus}^{T} [kJ·mol^{-1}]	14.7 ± 0.5	18.8 ± 0.5	25.9 ± 0.5	25.3 ± 0.5	29.8 ± 0.5	29.6 ± 0.5
ΔS_{fus}^{T} [J·mol^{-1}·K^{-1}][d]	37.0	44.8	59.2	55.0	72.6	68.0

[a] Ref [10]

[b] $C_{p,cr}^{298}$ has been calculated by Chikcos additive scheme [14] the error of the calculation procedure corresponds to significant digit;

[c] $\varsigma_{H} = (\Delta H_{sub}^{298} / (\Delta H_{sub}^{298} + T \cdot \Delta S_{sub}^{298})) \cdot 100\%$; $\varsigma_{TS} = (T \cdot \Delta S_{sub}^{298} / (\Delta H_{sub}^{298} + T \cdot \Delta S_{sub}^{298})) \cdot 100\%$

[d] $\Delta S_{fus}^{T} = \Delta H_{fus}^{T} / T_m$

Table 4SI

Thermodynamic transfer functions of the compounds studied from buffer (pH 7.4) to 1-octanol, buffer (pH 7.4) to 1-hexane, and 1-hexane to 1-octanol at 298 K and $p^0 = 0.1$ MPa

	I	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**
				buffer → 1-octanol				
ΔG^0_{tr} / kJ·mol-1	-25.9	-21.5	-26.3	-11.3	-19.4	-16.8	-14.1	-14.8
ΔH^0_{tr} / kJ·mol-1	0.6	4.8	-17.0	12.5	16.9	26.4	30.6	15.6
$T\Delta S^0_{tr}$ / kJ·mol-1	26.5	26.3	9.3	23.8	36.3	43.2	44.7	30.4
$\varsigma_{\mathrm{Htrl}}{}^{a}$ / %	2.2	15.4	64.6	34.4	31.8	37.9	40.6	33.9
$\varsigma_{\mathrm{TStr}}{}^{b}$ / %	97.8	84.6	35.4	65.6	68.2	62.1	59.4	66.1
				buffer → 1-hexane				
ΔG^0_{tr} / kJ·mol^{-1}	-15.7	-12.4	-16.3	-2.2	-11.2	-8.3	-5.2	1.0
ΔH^0_{tr} / kJ·mol^{-1}	1.7	19.4	7.2	23.6	25.9	32.2	43.6	42.3
$T\Delta S^0_{tr}$ / kJ·mol^{-1}	17.4	31.8	9.1	25.8	37.1	40.5	48.8	41.3
$\varsigma_{\mathrm{Htrl}}{}^{a}$ / %	8.9	37.9	44.2	47.8	41.1	44.3	47.2	50.6
$\varsigma_{\mathrm{TStr}}{}^{b}$ / %	91.1	62.1	55.8	52.2	58.9	55.7	52.8	49.4
				1-hexane → 1-octanol				
ΔG^0_{tr} / kJ·mol^{-1}	-10.2	-9.1	-10.0	-9.1	-8.2	-8.5	-8.9	-15.8
ΔH^0_{tr} / kJ·mol^{-1}	-1.1	-14.6	-9.8	-11.1	-9.0	-5.8	-13.0	-26.7
$T\Delta S^0_{tr}$ / kJ·mol^{-1}	9.1	-5.5	0.2	-2.0	-0.8	2.7	-4.1	-10.9
$\varsigma_{\mathrm{Htrl}}{}^{a}$ / %	10.8	72.6	98.0	84.7	91.8	68.2	76.0	71.0
$\varsigma_{\mathrm{TStr}}{}^{b}$ / %	89.2	27.4	2.0	15.3	8.2	31.8	24.0	29.0

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

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