Supporting Information

Modeling the solubility of monoterpenoids with hybrid and predictive thermodynamic tools

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Section S1 – Experimental

Analytical procedures for the solubility experiments

The solubilities of (1R)-(+)-camphor and thymol in the studied organic solvents were determined by UV-vis spectroscopy (T70, PG Instruments) at 287 nm and 275.5 nm, respectively. Calibration curves ($R^2 > 0.999$) were built using at least seven standards independently prepared using ethanol/water (50:50 in mass proportion) as the solvent. At least two independent readings were carried out for each sample collected from the saturated solutions.

For (-)-borneol and L-(-)-menthol, the solubilities were quantified by gas chromatography using the internal standard method (with linalool as the internal standard and acetonitrile as the solvent). The GC (Varian, CP3800) was equipped with a split/splitless injection unit and a flame-ionization detector (FID), and fitted with a SUPELCOWAX® 10 capillary column (L x I.D. 30 m x 0.25 mm, df 0.25 μm) coupled to a deactivated fused silica pre-column (L x I.D. 30 m x 0.25 mm). The GC operating conditions were performed using the following parameters: injector and detector were kept at 523.2 K; helium was used as the carrier gas at a flow rate of 1.2 $ml \cdot min^{-1}$; the injection volume was 1 μl with a split ration of 1:60; the oven temperature was initially maintained at 393.2 K for 20-25 min, followed by a temperature ramp of 50 $K \cdot min^{-1}$ up to 503.2 K, and an isothermal step at 503.2 K for 5 min. Calibrations curves ($R^2 > 0.9999$) for each solute were built using at least seven independent standards.

Section S2 – Results and discussion

Table S1. Experimental solubilities (in mole fraction) of the monoterpenoids in water measured at 298.2 K and 313.2 K.

Monoterpenoid	**$10^5\ x_{terpene}$**		**source**
	298.2 K	**313.2 K**	
(–)-borneol	9.909 ± 0.366	10.722 ± 0.100	this work
(1R)-(+)-camphor	13.65	4.371	[1]
L-(–)-menthol	4.419		[1]
thymol	11.80	16.89	[2]

Table S2. Experimental activity coefficients (γ_i) of the monoterpenoids in water and organic solvents at 298.2 K and 313.2 K

Solvent	**(–)-borneol**		**(1R)-(+)-camphor**		**L-(–)-menthol**	**thymol**	
	298.2 K	313.2 K	298.2 K	313.2 K	298.2 K	298.2 K	313.2 K
acetonitrile	6.03	4.27	0.72	0.66	1.83	0.84	0.92
1-butanol	0.87	0.96	0.93	0.89	1.04	0.89	1.00
ethanol	0.91	1.02	1.11	0.92	1.14	0.90	0.99
ethyl acetate	1.15	1.13	0.72	0.68	1.09	0.84	0.96
hexane	3.07	2.34	0.81	0.87	1.07	1.76	1.01
R-(+)-limonene	1.89	1.47	0.67	0.70	1.07	1.24	1.03
1,2-propanediol	2.20	2.13	4.72	4.11	1.20	0.85	0.98
water	2746	3109	3093	10928	16757	5039	4927

Table S3. Overview of the available solubility data of the monoterpenoids for the binary systems addressed in this work.

Solute	Solvent	Temperature range (K)	Reference
(±)-borneol	Ethanol	297.1 – 348.7	[3]
(–)-borneol		298.2 – 313.2	this work
borneol[b]	water	298.2	[4c]
borneol[b]		288.2 -298.2	[5]
(–)-borneol		298.2 -313.2	this work
(±)-camphor	ethanol	303.2 – 343.2	[3]
(1R)-(+)-camphor		298.2 – 313.2	this work
camphor[b]	ethyl acetate	298.2	[6]
(1R)-(+)-camphor		298.2 – 313.2	this work
camphor[b]	hexane	298.2	[6]
(1R)-(+)-camphor		298.2 – 313.2	this work
camphor[b]	1,2-propanediol	298.2	[6]
(1R)-(+)-camphor		298.2 -313.2	this work
thymol	acetonitrile	279.2 – 313.2	[7]
		298.2 – 313.2	this work
	1-butanol	279.2 – 313.2	[7]
		298.2 – 313.2	this work
	ethanol	279.2 – 313.2	[7]
		304.1 – 316.2	[8]
		298.2 – 313.2	this work
	R(+)-limonene	304.1 – 316.2	[8]
		298.15 -313.15	this work

[a] Number of experimental data points. [b]No information regarding the main isomeric form. [c]The solubility data from the literature were converted from the original unit (volume basis) to g/100 moles of solvent.

Table S4. Abraham descriptors for the studied monoterpenoids available in literature and the obtained ARD (%) in the description of the solubility data measured in this work, at 298.2 K.

Compound	***E***	***S***	***A***	***B***	***V***	**ARD(%)**	**Reference**
borneol	0.510	0.520	0.280	0.680	1.3591	31	[9]
	0.757	0.714	0.158	0.653	1.3591	19	[10]
	0.659	0.635	0.203	0.632	1.3591	40	[11]
camphor	0.500	0.690	0	0.710	1.3161	81	[9]
	0.506	0.829	0	0.671	1.3161	79	[10]
	0.579	0.850	0	0.642	1.3161	72	[11]
menthol	0.400	0.500	0.230	0.580	1.4677	65[a]	[9]
thymol	0.822	0.840	0.440	0.430	1.3387	54[b]	[12]

[a]The solubilities in 1-butanol and ethanol were excluded from the predicted set since $x_i^{calc} > 1$ was found for those systems.

[b]The solubilities in 1-butanol, ethanol and ethyl acetate were excluded from the predicted set since $x_i^{calc} > 1$ was found for those systems.

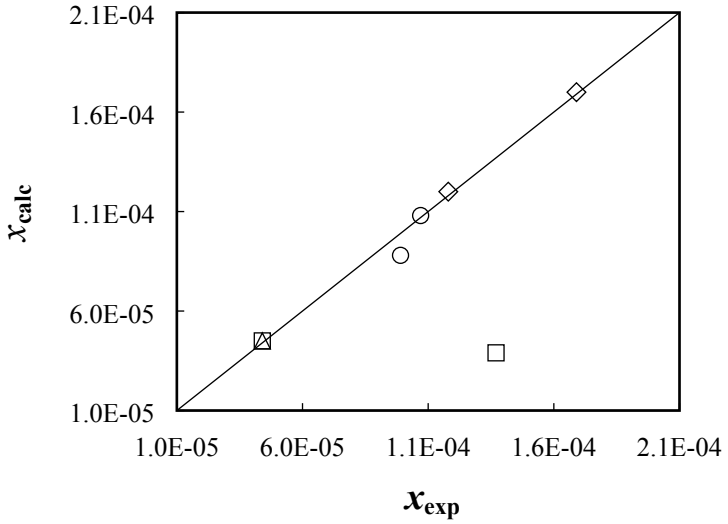


Figure S1. Comparison of the mole fraction water-solubilities calculated by NRTL-SAC with the experimental values.[1,2] Symbols correspond to: ○ - borneol, □ - camphor, △ - L-(–)-menthol, and ◇ - thymol.

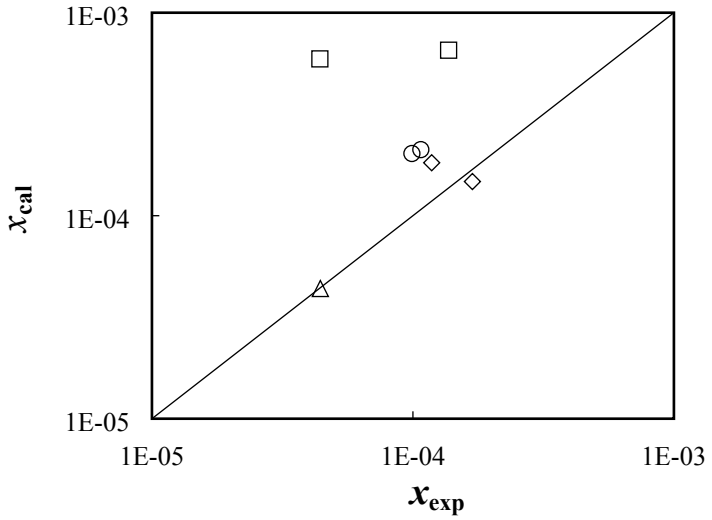
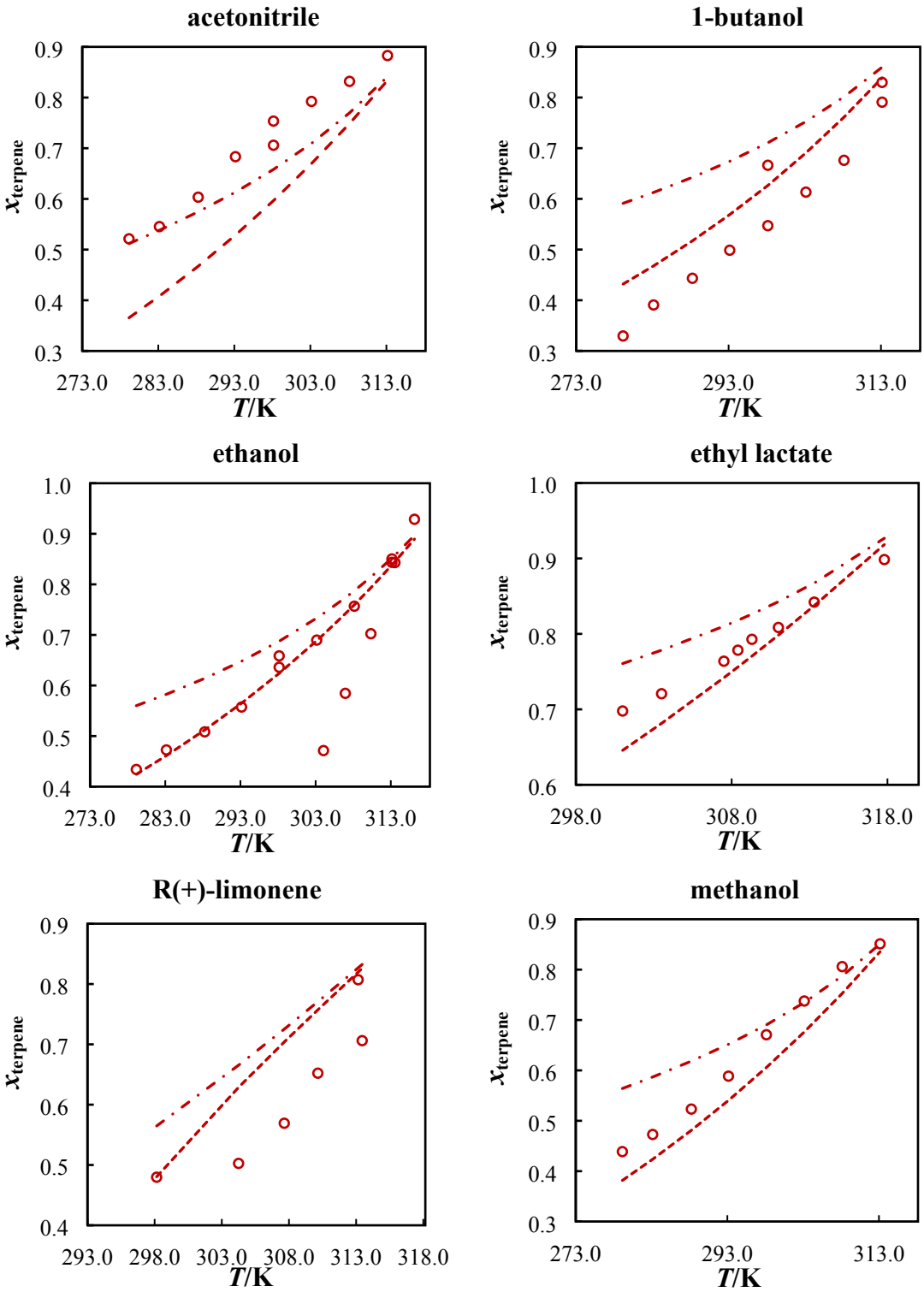


Figure S2. Comparison of the mole fraction water-solubilities calculated by COSMO-RS with the experimental values.[1,2] Symbols correspond to: ○ - borneol, □ - camphor, △ - L-(–)-menthol, and ◇ - thymol.


acetonitrile
1-butanol
ethanol
ethyl lactate
R(+)-limonene
methanol
$x_{terpene}$
T/K

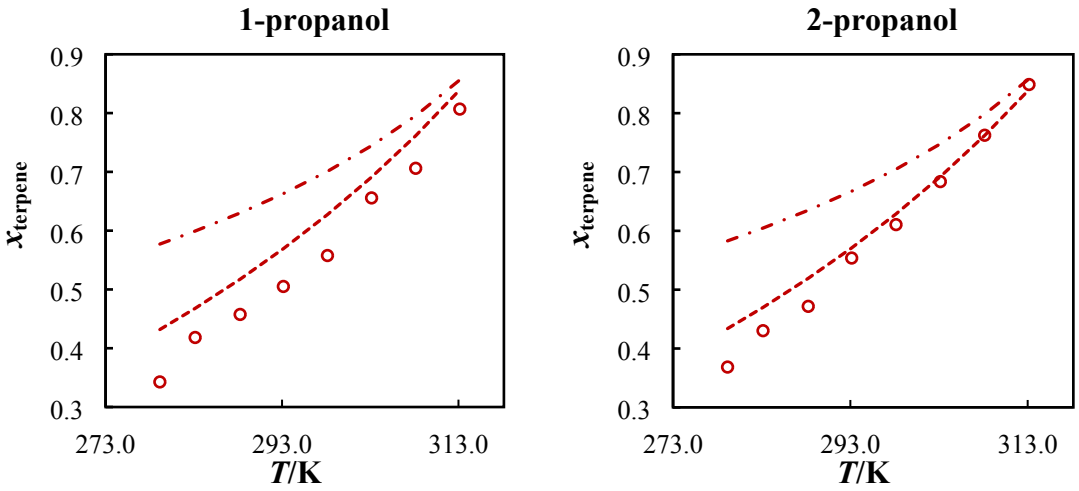


Figure S3. Comparison of the calculated solubility curves of thymol with the experimental data measured in this work and reported in literature.[7,8,13] Circles (○) correspond to the experimental data, dashed lines represent the NRTL-SAC predictions, and the dot-dash line represented the COSMO-RS predictions.

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