Electronical Supplementary Information

Phenolic Hydrogen Bond Donors as the Key to the Formation of Non-Ionic Deep Eutectic Solvents: The Quest for Type V DES

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Experimental Details

The SLE phase diagram of the mixture menthol + thymol was determined by Differential Scanning Calorimetry (DSC). First, mixtures were prepared in the full range of compositions using an analytic balance Mettler Toledo XP205. Samples were heated under stirring until a homogenous liquid was formed and stirred in the liquid state for 30 minutes. After cooling at room temperature, samples of 2 – 5 mg were hermetically sealed in aluminium pans and weighed in a micro-analytical balance AD6 (PerkinElmer, precision = 0.002 mg). A Hitachi DSC7000X working at atmospheric pressure was used to acquire the thermal events at 5 K/min and 2 K/min for cooling and heating, respectively. The equipment was previously calibrated with several standards with weight fraction purities higher than 99%. Thermal transitions were taken as the peak temperature.

The melting temperature of potential Type V deep eutectic solvents were measured, for a given composition, using the methodology described above.

The melting properties of R-Camphor were measured in this work using DCS as described above. The melting temperature obtained was 450.4 K and the corresponding melting enthalpy was 5.28 kJ/mol.

Computational Details

Thermodynamic Framework

Since the mixtures analysed in this work are of the eutectic type, their components solidify into a pure form and no solid-solid transitions are present, the solid-liquid equilibrium lines of each component were described in this work using the equation[1–3]:

$$\ln\left(x_i \cdot \gamma_i\right) = \frac{\Delta_m h_i}{R} \cdot \left(\frac{1}{T_{m,i}} - \frac{1}{T}\right) \tag{S1}$$

where x_i is the mole fraction of component i, γ_i its activity coefficient, $\Delta_m h_i$ its melting enthalpy and $T_{m,i}$ its melting temperature, whilst R is the ideal gas constant and T is the temperature of the system. The melting properties used in this work are reported in Table S1.

The ideal liquid phase model considers the liquid phase of the system to be thermodynamically ideal. That is, the activity coefficients of both components are set to unit ($\gamma_i = 1$) and the solid-liquid equilibrium curve of each components is estimated through:

$$\ln\left(x_i\right) = \frac{\Delta_m h_i}{R} \cdot \left(\frac{1}{T_{m,i}} - \frac{1}{T}\right) \tag{S2}$$

COSMO-RS

COSMO-RS, short for Conductor like Screening Model for Real Solvents, is a thermodynamics model based on quantum chemistry that can predict the chemical potential (and, thus, the activity coefficient) of individual components in a liquid mixture[4,5]. To use it, each molecule needs to be optimized using the COSMO solvation model and its sigma surface (a map of the polarity of the molecule) created. Then, the model considers pair-wise interactions between all area segments of all molecules in the system and computes the corresponding chemical potential and activity coefficient.

In this work, the software COSMOtherm[6,7] was used to apply the model COSMO-RS, along with the parametrization BP_TZVP_C30_1701. Each molecule was optimized using the TmoleX interface of TURBOMOLE[8], adopting a DFT with the B-P86 functional, a def-TZVP basis set and the COSMO solvation model (continuum with infinite permittivity).

Energies of Interaction

The molecular pairs presented in Figure 2 were optimized, as described above for each single molecule (def-TZVP basis set, B-P86 DFT and COSMO solvation model), from an initial pair-wise contact given by COSMOtherm as the most probable. The energy of interaction was taken as the difference between the energy of the pair and the energy of each single molecule previously optimized.

Tables

Table S1. Experimental solid-liquid equilibria data (x_{Thymol}, T_m) for the system thymol-menthol, obtained through differential scanning calorimetry at atmospheric pressure, including glass transitions (T_g). The activity coefficients (Υ) of thymol or menthol were obtained as per Equation 1 using the melting properties reported in Table S2.

x_{Thymol}	T_m /K	T_g /K	Υ_{Thynol}	x_{Thymol}	T_m /K	T_g /K	$\Upsilon_{Menthol}$

0.503	——	214.5	——	0.105	304.4	210.8	0.933
0.537	265.4	212.0	0.377	0.200	295.5	213.3	0.895
0.602	278.3	210.4	0.507	0.300	272.4	217.9	0.655
0.700	281.3	209.2	0.477	0.352	263.9	214.0	0.588
0.799	308.3	211.3	0.873	0.401	——	211.6	——
0.899	317.9	210.9	0.977				

Table S2. Substances experimentally used in this work, along with their melting properties and acidity constants.

Substance	CAS Number	T_m /K	$\Delta_m h$ /kJ·mol^{-1}	*pKa*
Thymol	89-83-8	323.5[9]	19.65[9]	10.62[10]
Coumarin	91-64-5	342.3[11]	18.63[11]	
Hydroquinone	123-31-9	445.1[12]	27.33[12]	10.85[13]
(-)-Menthol	2216-51-5	315.7[9]	12.89[9]	
R-Camphor	464-49-3	450.4[a)]	5.28[a)]	
4-Nitrophenol	100-02-7	387.0[14]	18.25[14]	7.15[10]
Salicylic Acid	69-72-7	432.5[15]	23.05[15]	2.97[10]
Butylated Hydroxytoluene	128-37-0	341.7[16]	19.85[16]	

Figures

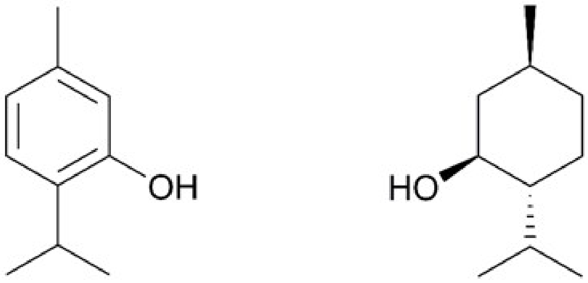


Figure S1. Chemical structure of thymol (left) and of (-)-menthol (right).

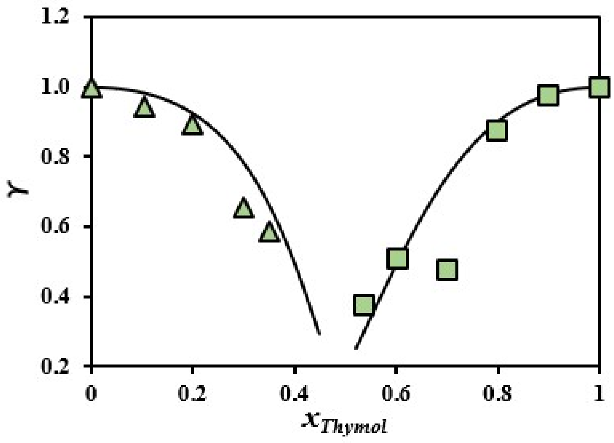


Figure S2. Activity coefficients for the system thymol/menthol (🟩 for thymol and △ for menthol) calculated from experimental solid-liquid equilibrium data (measured in this work using DSC). The prediction by COSMO-RS (full line) is included.

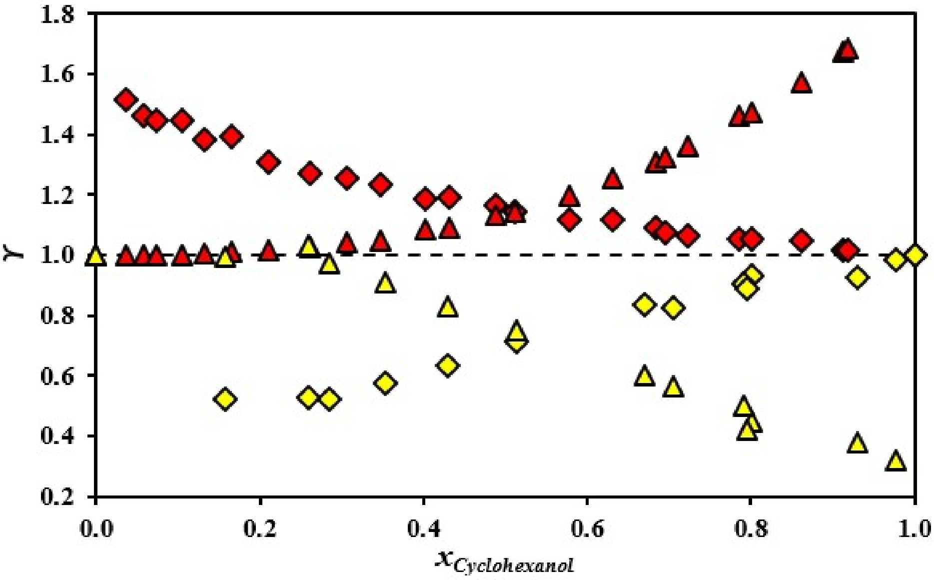


Figure S3. Activity coefficients of phenol (△) and cyclohexanol (◇) in the phenol/cyclohexanol system[17] and of benzyl alcohol (▲) and cyclohexanol (◆) in the benzyl alcohol/cyclohexanol system[18]. The dashed line represents ideal thermodynamic behaviour (activity coefficient equal to unity).

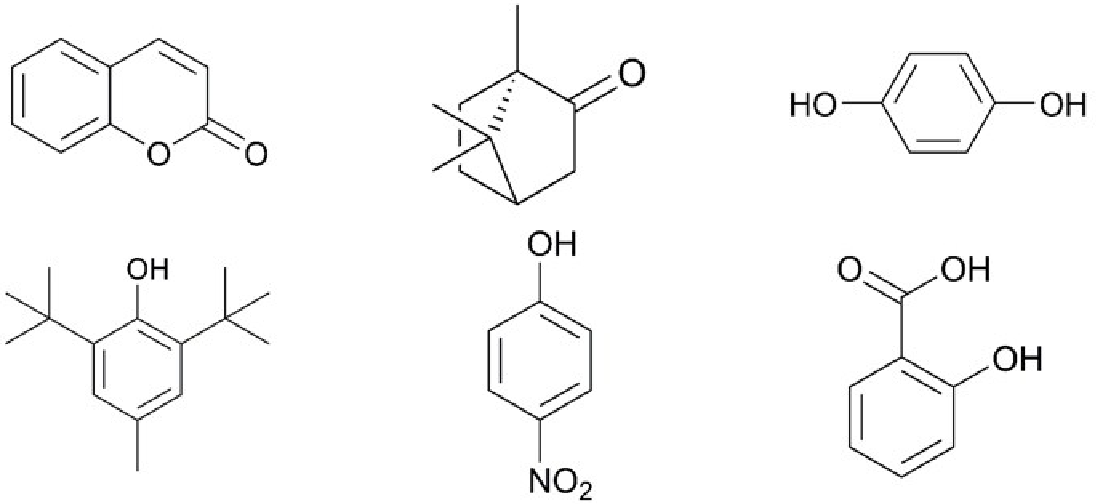
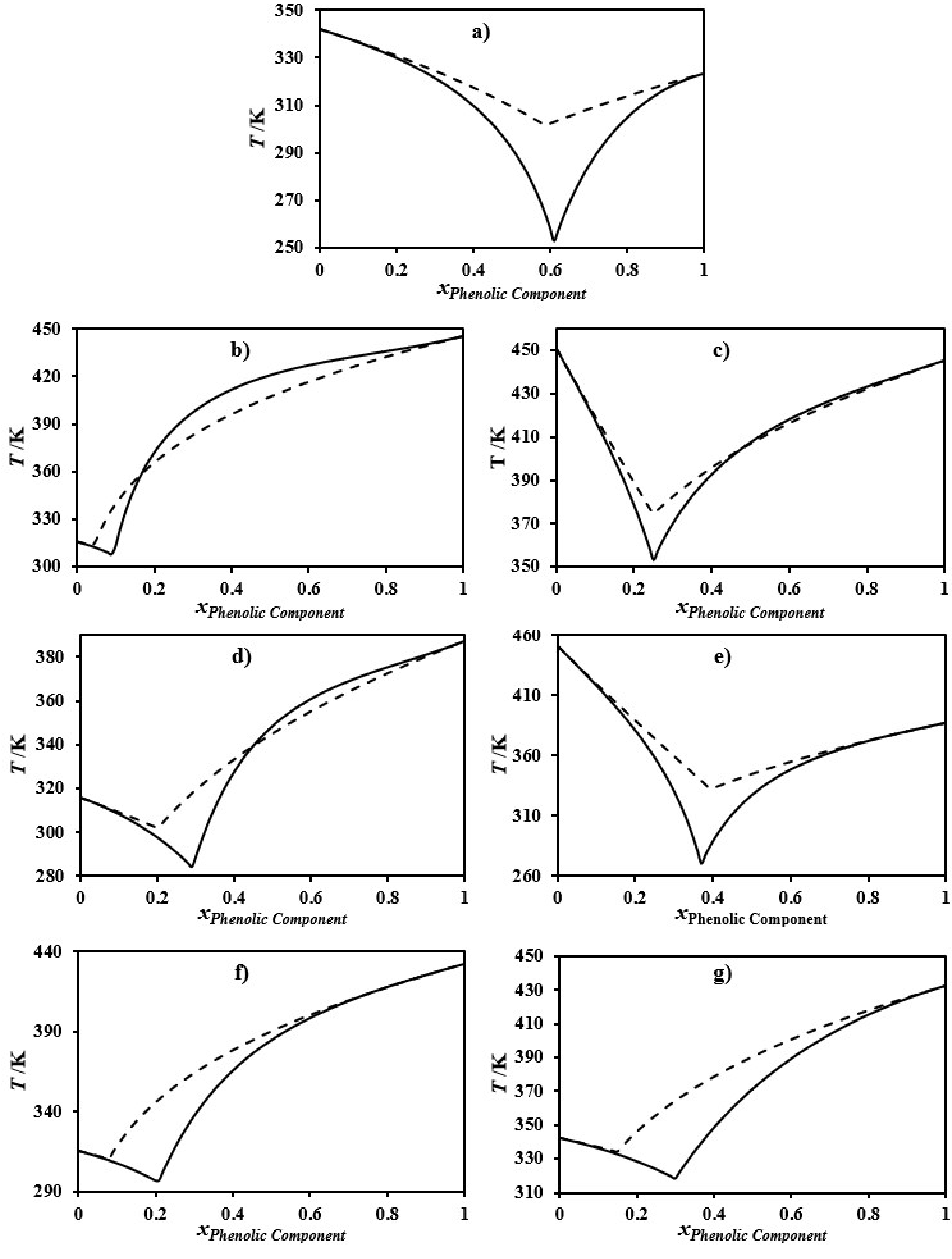


Figure S4. Chemical structures of the substances used to prepare new type V DES. From left to right: coumarin, R-camphor, hydroquinone, BHT, 4-nitrophenol and salicylic acid.


a)
350
330
310
290
270
250
T /K
0
0.2
0.4
0.6
0.8
1
$x_{Phenolic\ Component}$
b)
450
420
390
360
330
300
T /K
0
0.2
0.4
0.6
0.8
1
$x_{Phenolic\ Component}$
c)
450
430
410
390
370
350
T /K
0
0.2
0.4
0.6
0.8
1
$x_{Phenolic\ Component}$
d)
380
360
340
320
300
280
T /K
0
0.2
0.4
0.6
0.8
1
$x_{Phenolic\ Component}$
e)
460
410
360
310
260
T /K
0
0.2
0.4
0.6
0.8
1
$x_{\text{Phenolic Component}}$
f)
440
390
340
290
T /K
0
0.2
0.4
0.6
0.8
1
$x_{Phenolic\ Component}$
g)
450
430
410
390
370
350
330
310
T /K
0
0.2
0.4
0.6
0.8
1
$x_{Phenolic\ Component}$

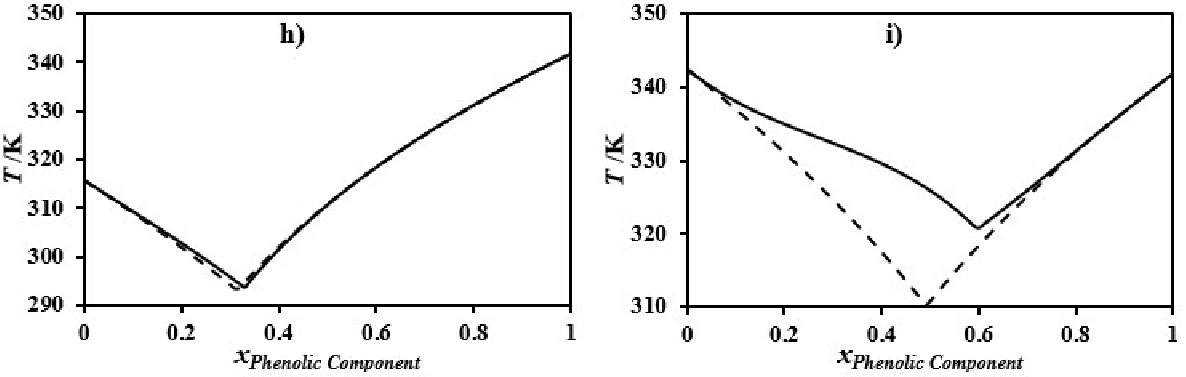


Figure S5. Solid-liquid equilibrium phase diagrams predicted by the ideal liquid phase model (dashed lines) and by COSMO-RS (full lines) for the systems a) thymol/coumarin, b) hydroquinone/menthol, c) hydroquinone/camphor, d) 4-nitrophenol/menthol, e) 4-nitrophenol/camphor, f) salicylic acid/menthol, g) salicylic acid/coumarin, h) BHT/menthol and i) BHT/coumarin.

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