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Prof. Dr. Werner Kunz
Institut für Physikalische und Theoretische Chemie

Do we need a solvent?

What matters? Kinetics or thermodynamics?

What are acceptable (green?) solvents?

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Institut für Physikalische und Theoretische Chemie

Monograph *Green Extraction of Natural Products* Wiley-VCH, 2014 (Chemat, Strube, Eds.).

Chapter 6: **Panorama of sustainable solvents for green extraction processes**

- aqueous media
- organic solvents
- aqueous two-phase systems
- supercritical fluids
- Ionic liquids or Deep Eutectic Solvents

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A good solvent must

- ensure a sufficient solubility
- must be stable (chemically inert, not flammable, temperature stable, and of low or best negligible corrosiveness)
- must fulfil economic requirements
- must have a good HSE (health, safety, environment) profile
- must be easily removable

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A green solvent can be

biogenic or not:

the bio-based furfuraldehyde is toxic and carcinogenic,

the petrol-based MMB (3-methoxy-3-methyl-butan-1-ol) is ecofriendly

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SOLUTION CHEMISTRY

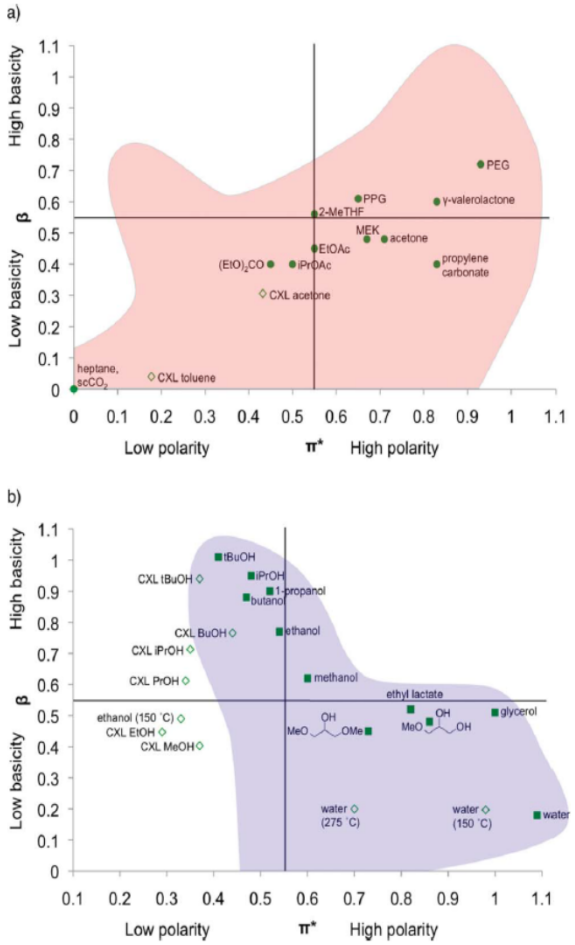

Fig. 4 Plots showing (a) green aprotic solvents and (b) green protic solvents as a function of their π^* (polarity and polarizability) and β (basicity or hydrogen-bond accepting ability) values. Solvents requiring pressure and/or elevated temperatures are shown as hollow symbols. Data was obtained for common solvents,[3–5] glycerol ethers,[15] liquid polymers,[18] valerolactone,[18] ethyl lactate,[18] cyclopentyl methyl ether,[18] 2-methyltetrahydrofuran,[18] $scCO_2$,[19] CXLs (CO_2-expanded liquids at 50 bar, 25 °C)[20] and superheated water[21] from the specified references. The β values for CXLs and glycerol ethers, and the position of isopropyl acetate, are estimates because published data is unavailable. The π^* of heptane is slightly negative. The position of $scCO_2$ depends on the conditions.

P. G. Jessop,
Searching for green solvents,
Green Chemistry (2011) 13,
1391–1398.

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SOLUTION CHEMISTRY

General Green Solvent ranking

NAME	I_{tox}	VOC	Fire	CAS
Cluster II: Weak electron pair donor bases				
Acetone	5	+	R11	67-64-1
N,N-Dimethyloctanamide	4	-	-	1118-92-9
Methyl 5-(dimethylamino) -2-methyl-oxopentanoate	4	-	-	1174627-68-9
2-Pyrrolidone	5	-	-	616-45-5
Cluster III: Aprotic dipolar				
Acetyltributyl citrate	5	-	-	77-90-7
Benzyl benzoate	4	-	-	120-51-4
Butylacetate	4	+	R10	123-86-4
Butyl laurate	5	-	-	106-18-3
1,4-Cineol	4	+	R10	470-67-7
1,8-Cineol	4	+	R10	470-82-6
Cyclopentyl methyl ether	4	+	R11	5614-37-9
Dibutyl sebacate	5	-	-	109-43-3
Diethyl adipate	5	-	-	141-28-6
Diethyl glutarate	4	-	-	818-38-2
Diethyl phthalate	5	-	-	84-66-2
Diethyl succinate	5	+	-	123-25-1
Diisoamylsuccinate	n.f	-	-	818-04-2
Diisobutyl adipate	5	-	-	141-04-8
Diisobutyl glutarate	5	-	-	71195-64-7
Diisobutyl succinate	5	-	-	925-06-4
Diisooctylsuccinate	n.f	-	-	2915-57-3
Dimethyl adipate	4	-	-	627-93-0
Dimethyl glutarate	5	+	-	1119-40-0
Dimethyl phthalate	5	-	-	131-11-3
Dimethyl succinate	5	+	-	106-65-0
N,N-Dimethyldecanamide	4	-	-	14433-76-2
Dimethylisosorbide	5	-	-	5306-85-4
Dioctylsuccinate	n.f	-	-	14491-66-8
1,3-Dioxolane	4	+	R11	646-06-0
Ethyl acetate	5	+	R11	141-78-6
Ethyl laurate	5	-	-	106-33-2
Ethyl linoleate	5	-	-	544-35-4
Ethyl linolenate	6	-	-	1191-41-9
Ethyl myristate	5	-	-	124-06-1
Geranyl acetate	5	-	-	105-87-3
Glycerol triacetate	4	-	-	102-76-1
Glycerol-1,2,3-tributyl ether	n.f	-	-	131570-29-1
Glycerol-1,2,3-triethyl ether	5	+	R10	162614-45-1
Glycerol-1,2,3-trimethyl ether	4	+	R10	20637-49-4
Glycerol-1,3-dibutyl ether	4	-	-	2216-77-5
Isoamyl acetate	6	+	R10	123-92-2
Isobutyl acetate	5	+	R11	110-19-0
Isopropyl acetate	5	-	R11	108-21-4
Isopropyl myristate	6	-	-	110-27-0
Isosorbide dioctanoate	5	-	-	64596-70-4
Methyl abietate	5	-	-	127-25-3
Methyl acetate	5	+	R11	79-20-9
Methyl laurate	4	-	-	111-82-0
Cluster III: Aprotic dipolar (continued)				
Methyl linolenate	5	-	-	112-63-0
Methyl linolenate	5	-	-	301-00-8
Methyl myristate	5	-	-	124-10-7
Methyl oleate	4	-	-	112-62-9
Methyl palmitate	4	-	-	112-39-0
Dimethyl 2-methyl glutarate	4	-	-	14035-94-0
2-Methyltetrahydrofuran	5	+	R11	96-47-9
Menthanyl acetate	5	-	-	58985-18-5
n-Propyl acetate	5	+	R11	109-60-4
Terpineol acetate	5	n.f	-	8007-35-0
Tributyl citrate	5	-	-	77-94-1
Triethyl citrate	5	-	-	77-93-0
Cluster IV: Aprotic highly dipolar				
Dimethyl sulfoxide	5	+	-	67-68-5
2-Furfuraldehyde *	3	+	-	98-01-1
Propylene carbonate	4	-	-	108-32-7
γ-Valerolactone	5	+	-	108-29-2
Cluster V: Apolar				
Butyl myristate	5	-	-	110-36-1
Butyl palmitate	5	-	-	111-06-8
Butyl stearate	6	-	-	123-95-5
Cyclohexane	5	+	R11	110-82-7
p-Cymene	4	+	R10	99-87-6
β-Myrcene	5	+	R10	123-35-3
Decamethylcyclo-pentasiloxane	4	+	-	541-02-6
Dipropyleneglycol	5	-	-	110-98-5
Ethyl oleate	5	-	-	111-62-6
Ethyl palmitate	5	-	-	628-97-7
Isopropyl palmitate	5	-	-	142-91-6
d-Limonene	4	+	R10	5989-27-5
Methyl stearate	5	-	-	112-61-8
Isododecane	5	-	-	31807-55-3
Perfluorooctane	3	+	-	307-34-6
α-Pinene	4	+	R10	80-56-8
β-Pinene	4	+	R10	127-91-3
Terpinolene	4	+	-	586-62-9
Cluster VII: Amphiprotic				
Benzyl alcohol	4	+	-	100-51-6
1-Butanol	4	+	R10	71-36-3
Cyclademol	5	-	-	25225-09-6
1-Decanol	4	-	-	112-30-1
Dihydromyrcenol	4	+	-	18479-58-8
1,3-Dioxolane-4-methanol	5	-	-	5660-53-7
Ethanol	5	+	R11	64-17-5
Ethylhexyllactate	n.f	-	-	6283-86-9
Ethyl lactate	5	+	R10	97-64-3
Geraniol	4	-	-	106-24-1
Glycerol-1,3-diethyl ether	4	-	-	4043-59-8
Cluster VII: Amphiprotic (continued)				
Glycerol-1,2-dibutyl ether	n.f	-	-	91337-36-9
Glycerol-1,2-diethyl ether	n.f	-	R10	4756-20-1
Glycerol-1,2-dimethyl ether	n.f	+	R10	40453-77-8
Glycerol-1,3-dimethyl ether	5	+	R10	623-69-8
Glycerol-1-butyl monoether	5	-	-	624-52-2
Glycerol-1-ethyl monoether	4	-	-	1874-62-0
Glycerol-2-butyl monoether	n.f	-	-	100078-36-2
Glycerol-2-ethyl monoether	n.f	-	R10	22598-16-9
Glycofurol (n=2)	5	-	-	52814-38-7
N,N-Diethyllactamide	5	-	-	136-26-5
Caprylic acid diethanolamide	5	-	-	3077-30-3
Isoamyl alcohol	5	+	R10	123-51-3
Isopropyl alcohol	5	+	R11	67-63-0
Methyl ricinoleate	5	-	-	141-24-2
Menthanol	5	-	-	498-81-7
Nopol	4	-	-	128-50-7
1-Octanol	4	+	-	111-87-5
Oleic acid	6	-	-	112-80-1
Oleyl alcohol	5	-	-	143-28-2
PolyEthyleneGlycol 600	6	-	-	25322-68-3
Solketal	5	+	-	100-79-8
Ricinoleic acid	5	-	-	141-22-0
α-Terpineol	4	-	-	98-55-5
β-Terpineol	5	-	-	138-87-4
Tetrahydrofurfuryllic alcohol	4	+	-	97-99-4
Cluster VIII: Polar protic				
1,3-Dioxan-5-ol	5	+	-	4740-78-7
1,3-Dioxolane-4-methanol	5	+	-	5464-28-8
Ethylene glycol	4	+	-	107-21-1
β-Farnesene	5	-	-	18794-84-8
Furfurylic alcohol *	3	+	-	98-00-0
Glycerol	5	-	-	56-81-5
Glycerol carbonate	5	-	-	931-40-8
Glycerol-1-methyl monoether	4	-	-	623-39-2
Glycerol-2-methyl monoether	5	-	R10	761-06-8
5-(Hydroxymethyl)furfural	4	-	-	67-47-0
3-Hydroxypropionic acid	5	-	-	503-66-2
3-Methoxy-3-methyl-1-butanol	4	-	-	56539-66-3
PolyEthyleneGlycol 200	6	-	-	112-60-7
1,3-Propanediol	4	-	-	504-63-2
Propylene glycol	6	+	-	57-55-6
Cluster IX: Organic acidic compounds				
Acetic acid	4	+	R10	64-19-7
Propionic acid	4	+	-	79-09-4
Cluster X: Polar structured				
Water	6	-	-	7732-18-5
Ionic liquids				
Choline acetate	n.f	-	-	14586-35-7
3-Butyl-1-methylimidazolium tetrafluoroborate	4	-	-	174501-65-6

Laurianne Moity, Morgan Durand, Adrien Benazzouz, Christel Pierlot, Valérie Molinier and Jean-Marie Aubry, Panorama of sustainable solvents using the COSMO-RS approach, Green Chem. 2012, 14, 1132-1145

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SOLUTION CHEMISTRY

Like dissolves (mixes with) Like (Qui se ressemble s'assemble)

What is like? -> From experiment to theory

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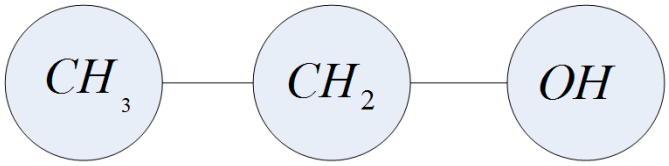
Theoretical approaches:

- **UNIFAC**



- **Hildebrand 1950:** $\delta = (E_{coh}/V_m)^{1/2}$

Cohesion energy density $E_{coh} = \Delta H_{vap} - RT$

Gibbs energy of mixing ΔG_M

$$\Delta G_M = \Phi_1 \Phi_2 V_M (\delta_1 \delta_2)^2 - \Delta(TS)^{ideal}$$

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Theoretical approaches:

- **Hansen Solubility Parameters (HSP)**

$$\delta^2 = \delta^2_D + \delta^2_P + \delta^2_H$$

D: Dispersion P: Permanent Dipole H: Hydrogen Bonding

$$R_a^2 = 4\,(\delta_{D2} - \delta_{D1})^2 + (\delta_{P2} - \delta_{P1})^2 + (\delta_{H2} - \delta_{H1})^2$$

Many Experiments → R_0

the Relative Energy Difference (RED) RED = R_a/R_0

For RED < 1 the compound is alike and will dissolve, for RED = 1, a partial solubility is predicted and for RED > 1 "no" solubility should exist.

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Hansen Solubility Parameters

	δD	δP	δH	R_o
Lignin	21.9	14.1	16.9	13.7

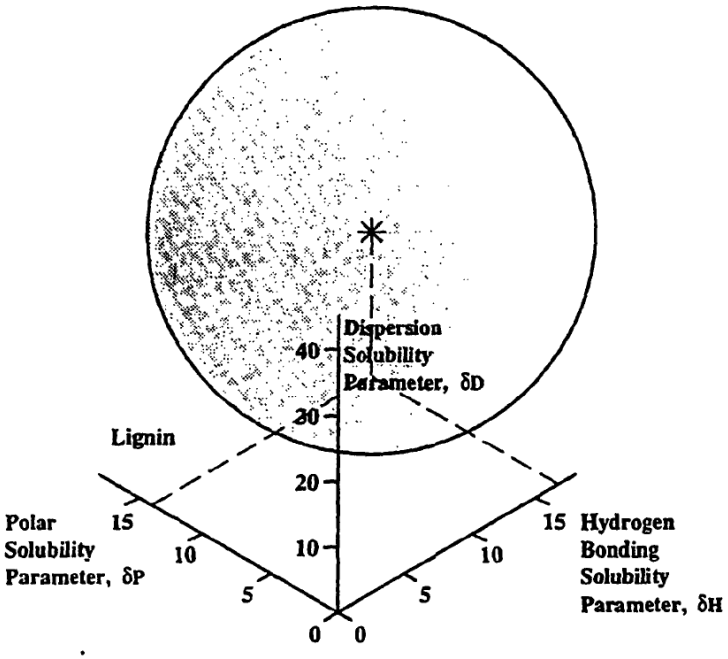

Fig. 1. Sketch of spherical Hansen type correlation for the solubility of lignin, whose parameters must be lower than those of cellulose but perhaps not too different.

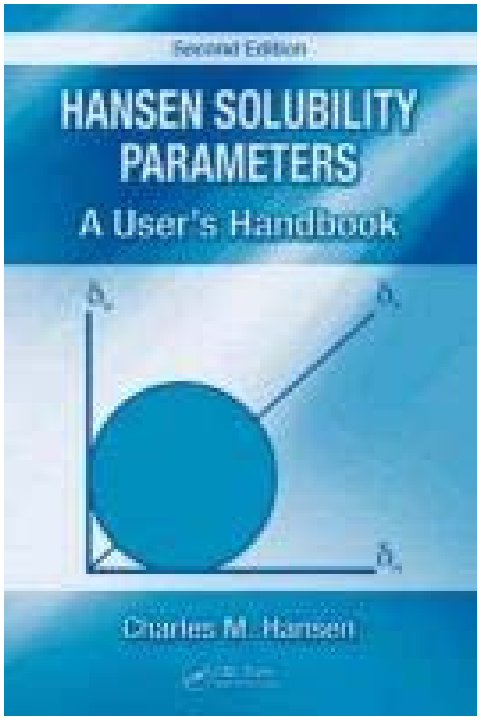

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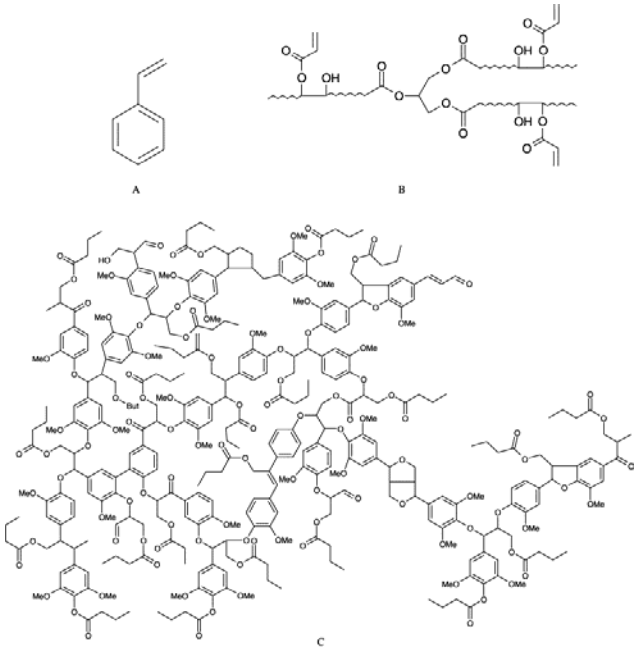
TABLE 15.1
Hansen Solubility Parameter Correlations for Biologically Interesting Materials, $MPa^{1/2}$

Material	δ_D	δ_P	δ_H	Ro	FIT	G/T
DNA	19.0	20.0	11.0	11.0	1.000	6/12
Cholesterol solubility	20.4	2.8	9.4	12.6	1.000	25/41
Lard 37°C solubility	15.9	1.2	5.4	12.0	1.000	29/50
Lard 23°C solubility	17.7	2.7	4.4	8.0	1.000	21/50
Olive oil solubility	15.9	1.2	5.4	12.0	1.000	29/50
Psoriasis scales swelling	24.6	11.9	12.9	19.0	0.927	35/50
Human skin — permeation	17.6	12.5	11.0	5.0	1.000	4/13
Nicotine — calculation	18.8	7.8	6.4	—	—	—
Skatole — calculation	20.0	7.1	6.2	—	—	—
Chlorophyll — solubility	20.2	15.6	18.2	11.1	0.864	7/35
Sinapyl alcohol calculation	19.2	7.3	16.1	—	—	—
Coniferyl alcohol calculation	19.0	7.0	16.3	—	—	—
p-Coumaryl alcohol calculation	19.1	7.0	17.3	—	—	—
Lignin — solubility	21.9	14.1	16.9	13.7	0.990	16/82
Dextran C (= amorphous cellulose) See Chapter 5	24.3	19.9	22.5	17.4	0.999	5/50
Sucrose solubility	23.4	18.4	20.8	16.0	0.981	6/50
N-methyl-morpholine-N-oxide calculation	19.0	16.1	10.2			
Blood serum — swelling	25.5	10.3	22.1	17.8	0.980	4/51
Zein — solubility	22.4	9.8	19.4	11.9	0.964	4/50
Urea — solubility	22.9	14.9	21.3	16.2	0.984	14/50
Water — >1% soluble in	15.1	20.4	16.5	18.1	0.856	88/167
Water — totally miscible	18.1	17.1	16.9	13.0	0.880	47/166
Water — single molecule	15.5	16.0	42.3	—	—	—

Note: The units for the solubility parameters and Ro are $MPa^{1/2}$. G/T represents the number of good liquids (G) and the total number of liquids (T) in the correlation.



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The best: COSMO-RS

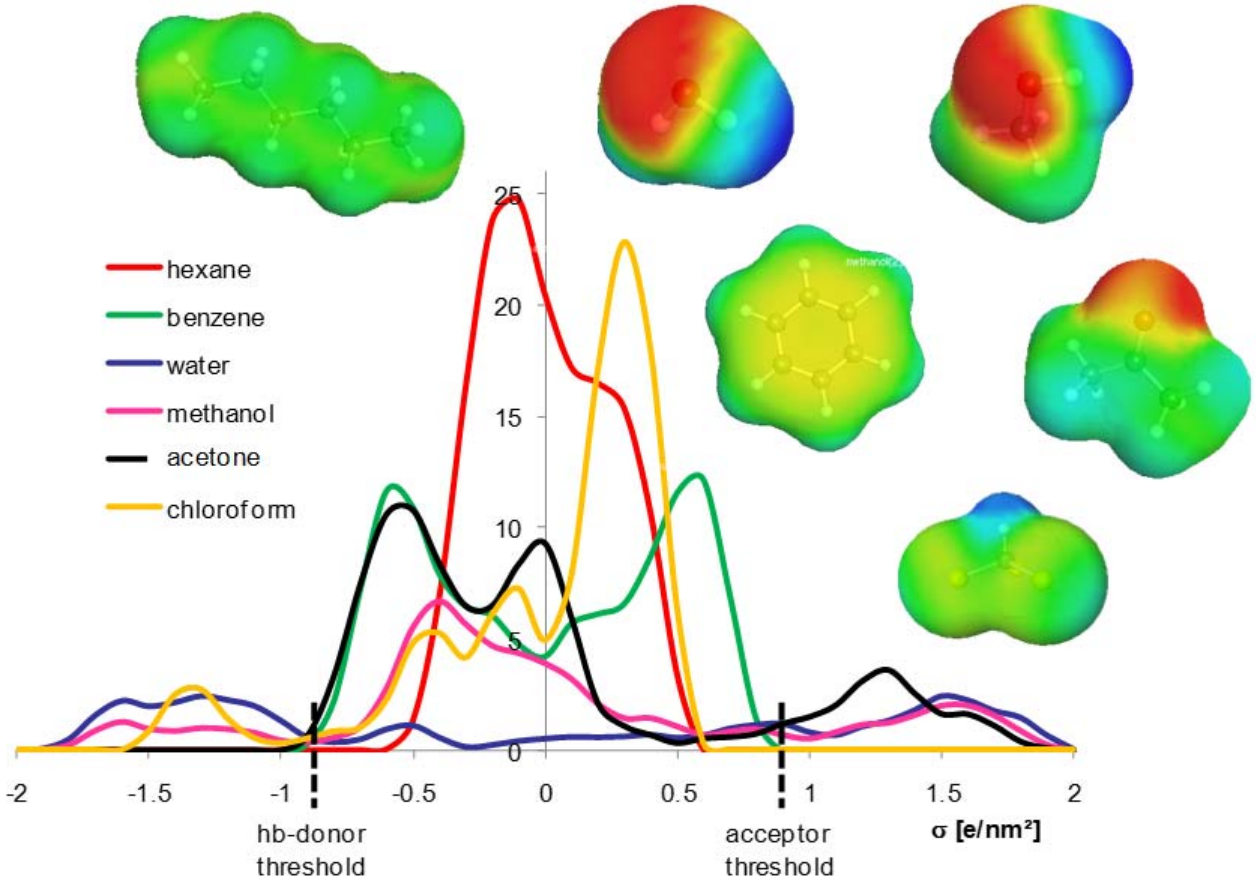

Fig. 2.1.1: σ-surfaces and σ-profiles of 6 representative molecules

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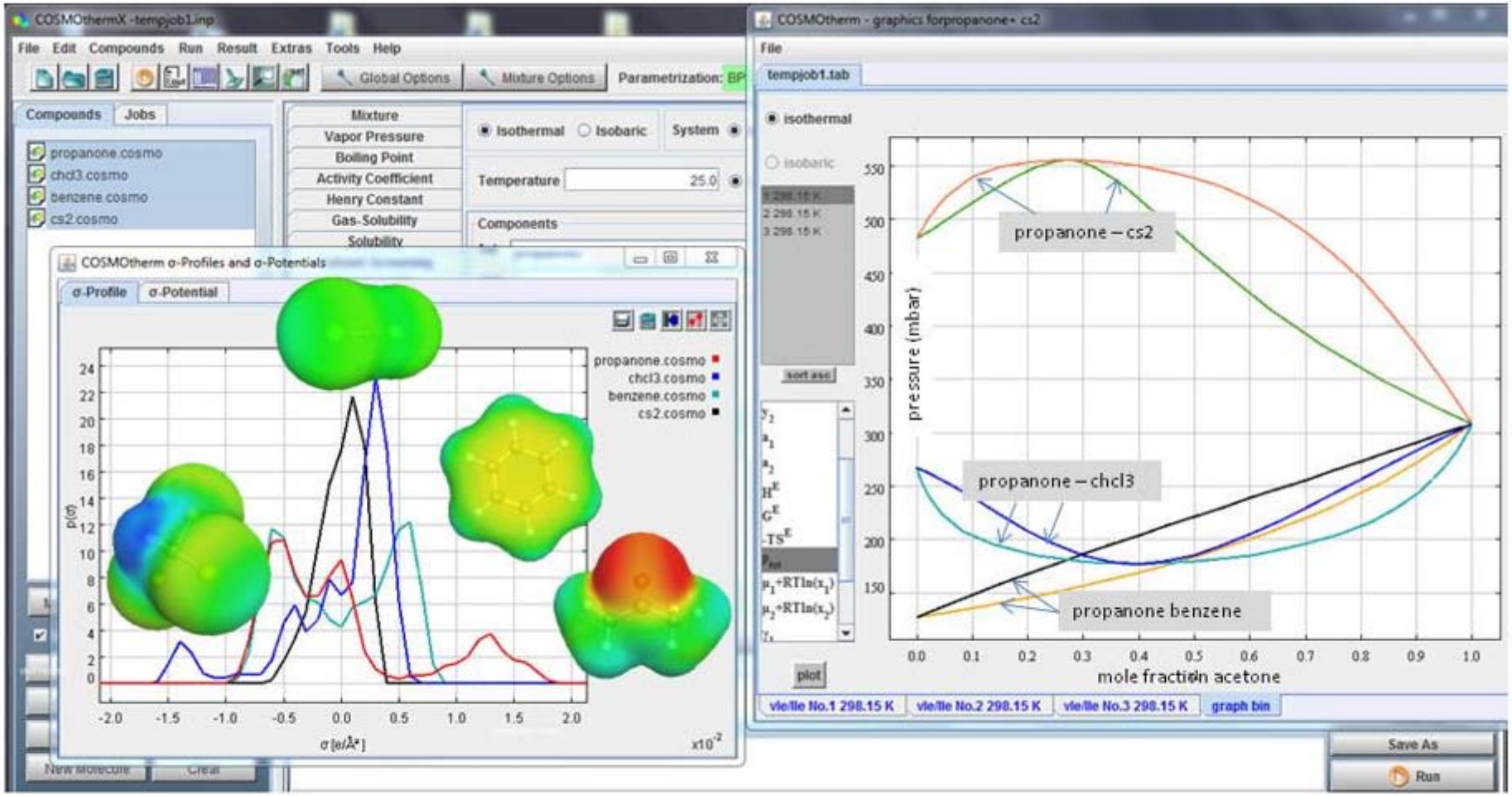

Fig. 2.1.2: Graphical visualization of the COSMOtherm workflow and results for 3

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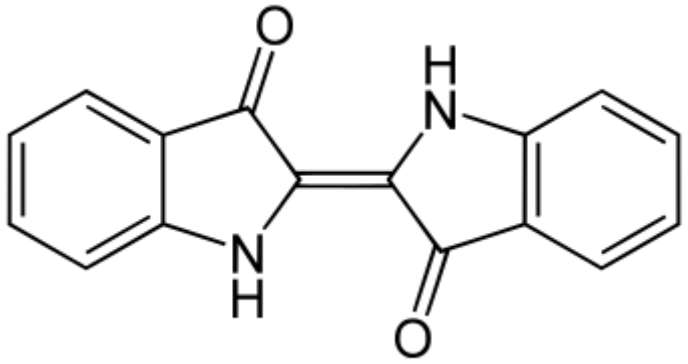
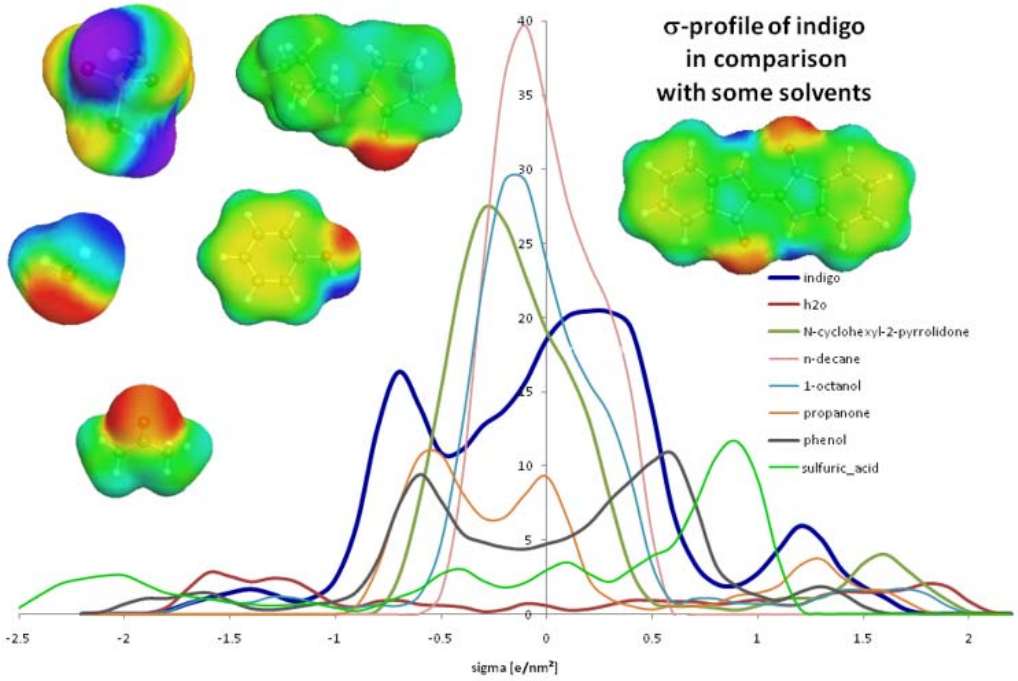
Indigo





Rank	solvent	solubility %-wgt.
1	H_2SO_4	100.0000
2	dimethylsulfoxide	11.9093
3	phenol	10.4013
4	propanone	6.5225
5	pyridine	4.3329
6	pyrrole	4.1934
7	choralhydrate	2.9799
8	n-cyclohexyl-2-pyrrolidone	2.1431
9	aniline	1.7467
10	chloroform	1.6337
11	diethylether	1.4813
12	Acetic acid	1.2209
13	nitrobenzene	0.6988
14	benzene	0.5339
15	camphor	0.4953
16	ethanol	0.4694
17	liquid indigo	0.3500
18	1-pentanol	0.1523
19	1-octanol	0.0742
20	hexane	0.0140
21	n-hexadecane	0.0037
22	water	0.0001

I.1: Results of COSMO-RS solubility screening for indigo