Electronic Supplementary Material (ESI) for CrystEngComm.

Supplementary Information

Thermodynamic solubility of celecoxib in organic solvents

Vivek Verma[1*], Rodrigo Soto[1,2], Shayon Bhattacharya[3], Damien Thompson[3], Kevin M. Ryan[1], Luis Padrela[1]

[1]SSPC Research Centre, Department of Chemical Sciences, Bernal Institute, University of Limerick V94 T9PX, Ireland.

[2]Department of Chemical Engineering and Analytical Chemistry. University of Barcelona. Marti i Franquès 1-11, 08028. Barcelona. Spain.

[3]Department of Physics, Bernal Institute, University of Limerick, Limerick V94 T9PX, Ireland

*Corresponding author email: vivek.verma@ul.ie

Table S1. Numerical values of the Abraham, Hansen and Catalan parameters used in this work for the thermodynamic model described by Eq. 6. These values are taken from Ref 1.

	Abraham		*Hansen*	*Catalan*			
Solvent	**e**	**s**	δ_D	**SP**	**SdP**	**SA**	**SB**
Methanol	0.33	-0.71	15.1	0.61	0.9	0.61	0.55
Acetonitrile	0.08	0.33	11.59	0.65	0.97	0.04	0.29
isopropanol	0.34	-1.05	15.8	0.63	0.81	0.28	0.83
butanol	0.4	-1.01	16	0.67	0.66	0.34	0.81
ethyl acetate	0.37	-0.45	15.8	0.66	0.6	0	0.54
Toluene	0.53	-0.72	18	0.78	0.28	0	0.13

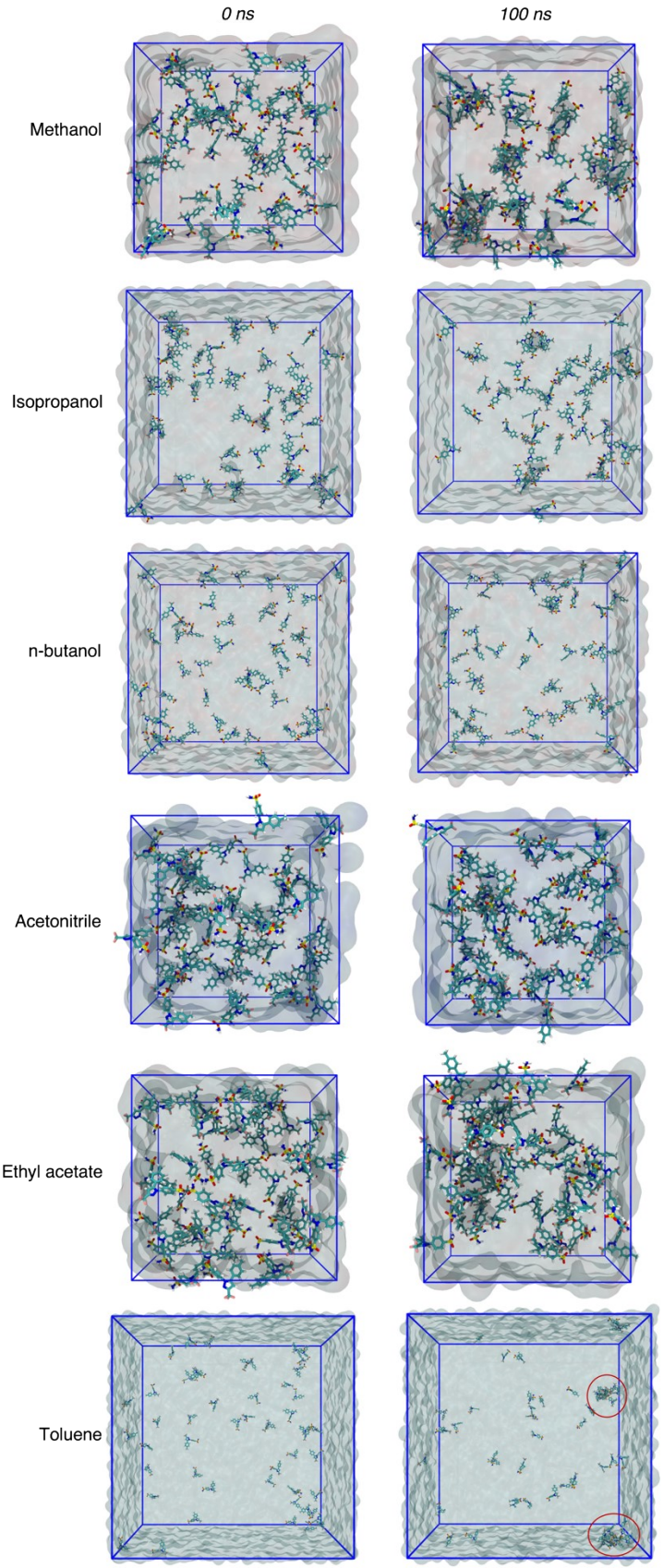

Fig. S1. The starting and final computed structures of 50 Celecoxib (CEL) molecules in bulk solvent boxes of six different pure organic solvents, after 100ns of fully equilibrated unconstrained room temperature molecular dynamics. The CEL clusters formed in toluene (TOL) are circled in red.

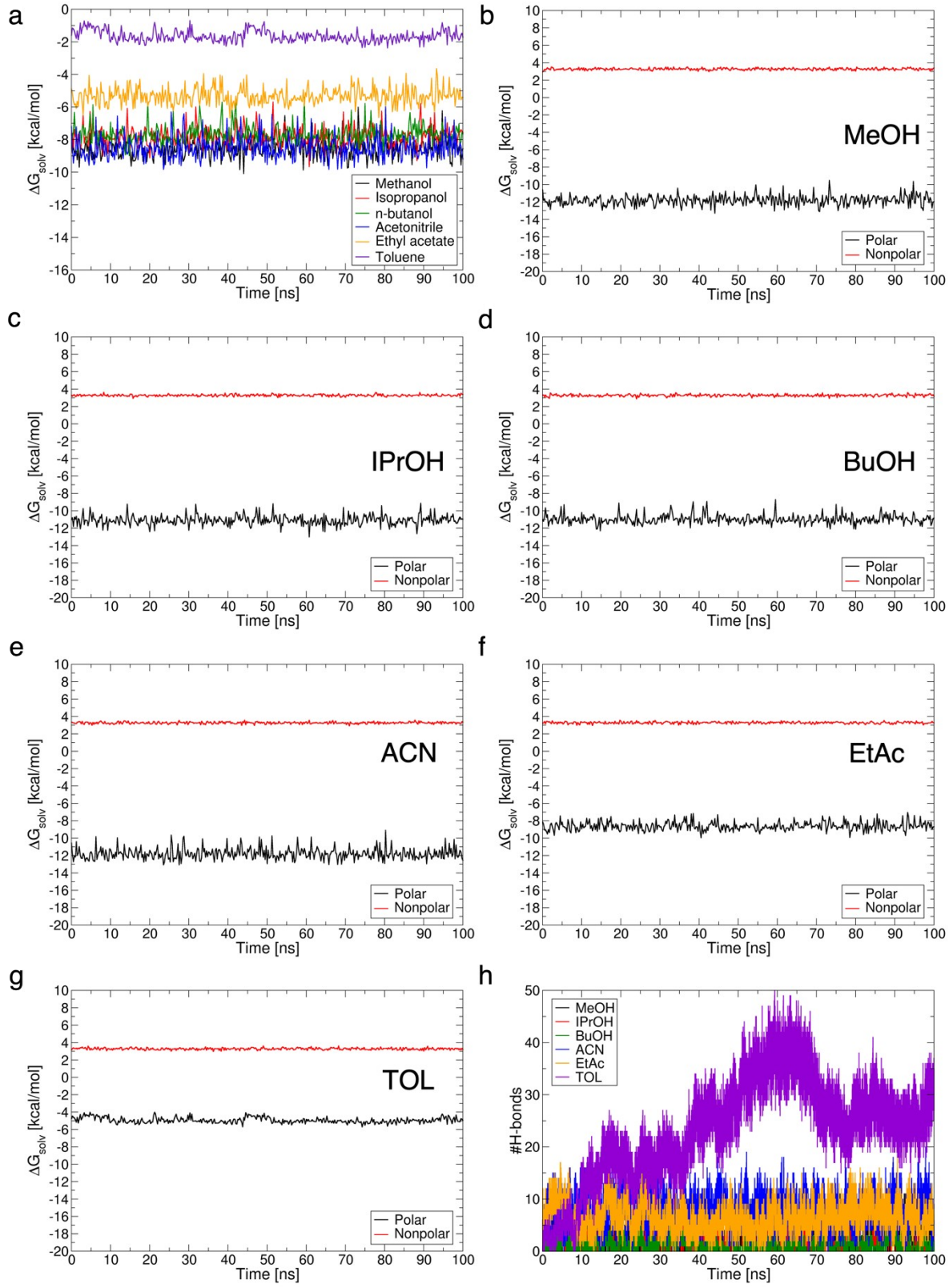

Fig. S2. (a) Free energy of solvation (ΔG_{solv}) of Celecoxib (CEL) in different solvents as a function of simulation time. **(b) – (g)** Timelines of ΔG_{solv} of CEL decomposed into their respective polar and non-polar components in the different solvents. **(h)** Timelines of the evolution of CEL–CEL hydrogen bond populations (#H-bond) between 50 CEL molecules in different solvents.

Table S2. Details of the MD simulation systems with 50 Celecoxib (CEL) molecules and the corresponding dielectric constants of solvents.

Solvent	Number of solvent molecules (per 50 molecules of CEL)	Density of solvent (kg.m^{-3})	Box volume (nm^3)	Dielectric constant of solvent (at 298 K)
Methanol (MeOH)	1923	792	175.6	32.70
Isopropanol (IPrOH)	5000	786	729	19.92
n-butanol (BuOH)	6250	810	1000	17.51
Acetonitrile (ACN)	1057	786	140.6	37.50
Ethyl acetate (EtAc)	555	902	125	6.02
Toluene (TOL)	24996	867	4451.4	2.38

Reference:

1. Jouyban, A.; Rahimpour, E.; Karimzadeh, Z. A new correlative model to simulate the solubility of drugs in mono-solvent systems at various temperatures. J. Mol. Liq. 2021, 343, 117587