

## S1. Details on conformational sampling schemes.

Table S1 shows the steps that were used to generate the COSMO input files using the COSMOconf program. In the SMILES scheme, these correspond to default settings of COSMOconf. In the other schemes, various criteria have been significantly modified to allow a more thorough conformational sampling (at the expense of computing time). In the *SMILES* and *Best/Worst* schemes, the conformer set was generated using the BALLOON\_CONF\_GEN method of COSMOconf. The BALLOON\_CONF\_GEN conformer generation method uses a series of 7 Balloon steps to generate MMFF94 optimized structures. The CLUSTER\_GEOCHECK method was then used to remove the duplicate conformers by comparing the geometries of the conformers. After BP/def-SV(P) level single-point calculations, the chemical potentials of the conformers in a pre-defined set of mixtures were compared using the CLUSTER\_MU method, and conformers with similar chemical potentials were omitted. The COSMOconf program includes additional clustering methods to remove duplicates, but those were not tested here. In the *Systematic* scheme, the conformers were first generated using Spartan'14 and then input to the COSMOconf program. The conformer sampling implemented in Spartan'14 eliminates all of the duplicate conformers, which means that all of the conformers are initially unique. In this scheme, the first clustering steps and low level single-point calculations were skipped to make sure that no important conformers were eliminated. In all of the schemes, the geometries of the remaining conformers were further optimized at two different levels of theory; BP/def-SV(P) and BP/def-TZVP. (The def-SV(P) basis set has two basis functions per valence orbital and polarization functions on nonhydrogen atoms, while def-TZVP has three basis functions per valence orbital and polarization functions on all atoms – calculations with the latter are thus more accurate, but also more time-consuming.) The number of conformers was reduced after each optimization using the CLUSTER\_GEOCHECK and CLUSTER\_MU methods. To reduce the number of conformers even further, additional energy and number cut-offs (REDUCE\_BY\_E\_MAX) were used before each geometry optimization and single-point calculation, using the cut-off values shown in Table S1. Generally, the cut-off energy was set high enough to make the number of conformers the tighter criterion. The final single-point energies were calculated using the same BP functional and a def2-TZVPD basis set (which contains three basis functions per valence orbital, and both polarization and diffuse functions on all atoms) with radii based isosurface cavity (FINE).

**Table S1: The steps in the conformer sampling and COSMO calculations of three different calculation schemes using COSMOconf. All quantum chemical steps include COSMO solvation.**

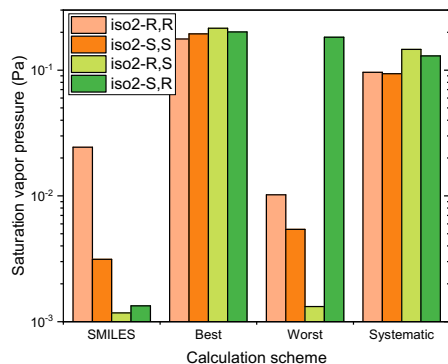
Method	<i>SMILES</i>	<i>Best/Worst</i>	<i>Systematic</i>
BALLOON_CONF_GEN	X	x	-
CLUSTER_GEOCHECK	X	x	-
REDUCE_BY_E_MAX	150 conformers or 2000 kcal/mol (8368 kJ/mol)	-	-
BP-SV_P-COSMO-SP	x	x	-
CLUSTER_MU	x	x	-
REDUCE_BY_E_MAX	50 conformers or 25 kcal/mol (104.6 kJ/mol)	200 conformers or 40 kcal/mol (167.36 kJ/mol)	-
BP-SV_P-COSMO	x	x	x
CLUSTER_GEOCHECK and CLUSTER_MU	x	x	x
REDUCE_BY_E_MAX	12 conformers or 10 kcal/mol (41.48 kJ/mol)	120 conformers or 15 kcal/mol (62.76 kJ/mol)	150 conformers or 15 kcal/mol (62.76 kJ/mol)
BP-TZVP-COSMO	x	x	x
CLUSTER_GEOCHECK and CLUSTER_MU	x	x	x
REDUCE_BY_E_MAX	10 conformers or 6 kcal/mol (25.1 kJ/mol)	100 conformers or 10 kcal/mol (41.48 kJ/mol)	100 conformers or 10 kcal/mol (41.84 kJ/mol)
BP-TZVPD-FINE-COSMO- SP	x	x	x

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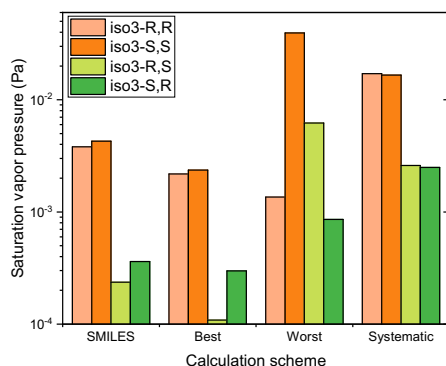
## S2. Vapor pressures for structural isomers 2-6 of C<sub>5</sub>H<sub>12</sub>O<sub>6</sub>

Figure S1: Saturation vapor pressures, at 298.15 K, of different stereoisomers of structural isomer 2 of the dihydroxy dihydroperoxide C<sub>5</sub>H<sub>12</sub>O<sub>6</sub>, at 298.15K, calculated using COSMOtherm version 18 and the BP\_TZVPD\_FINE\_18 parametrization (based on BP/def2-TZVPD//BP/def-TZVP quantum chemical data), using different conformational sampling schemes.



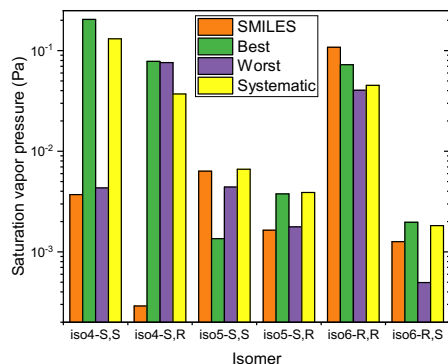
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Figure S2: Saturation vapor pressures, at 298.15 K, of different stereoisomers of structural isomer 3 of the dihydroxy dihydroperoxide C<sub>5</sub>H<sub>12</sub>O<sub>6</sub>, at 298.15K, calculated using COSMOtherm version 18 and the BP\_TZVPD\_FINE\_18 parametrization (based on BP/def2-TZVPD//BP/def-TZVP quantum chemical data), using different conformational sampling schemes.



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Figure S3: Saturation vapor pressures, at 298.15 K, of different stereoisomers of structural isomers 4-6 of the dihydroxy dihydroperoxide C<sub>5</sub>H<sub>12</sub>O<sub>6</sub>, at 298.15K, calculated using COSMOtherm version 18 and the BP\_TZVPD\_FINE\_18 parametrization (based on BP/def2-TZVPD//BP/def-TZVP quantum chemical data), using different conformational sampling schemes.



### S3. Test results on scaling H-bonding parameters in COSMOtherm version 18

Figure S4: Logarithm of the saturation vapor pressure (in units of Pa) computed for the iso1-R,R isomer of ISOP(OOH)<sub>2</sub>, using the ten best conformers identified by the *Systematic* sampling scheme, depending on the values of the three H-bonding parameters s0, c1 and c0. Calculated using COSMOtherm version 18 and the BP\_TZVPD\_FINE\_18 parametrization (based on BP/def2-TZVPD//BP/def-TZVP quantum chemical data).

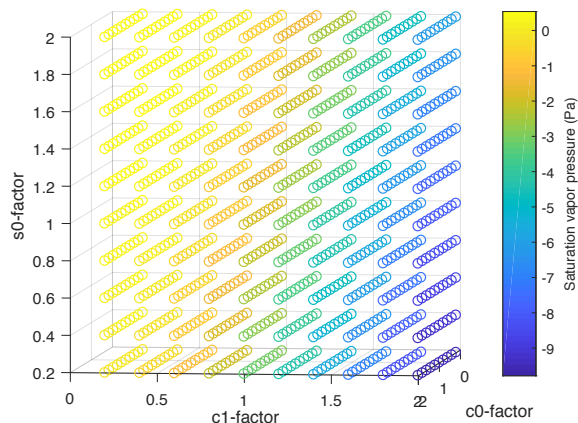
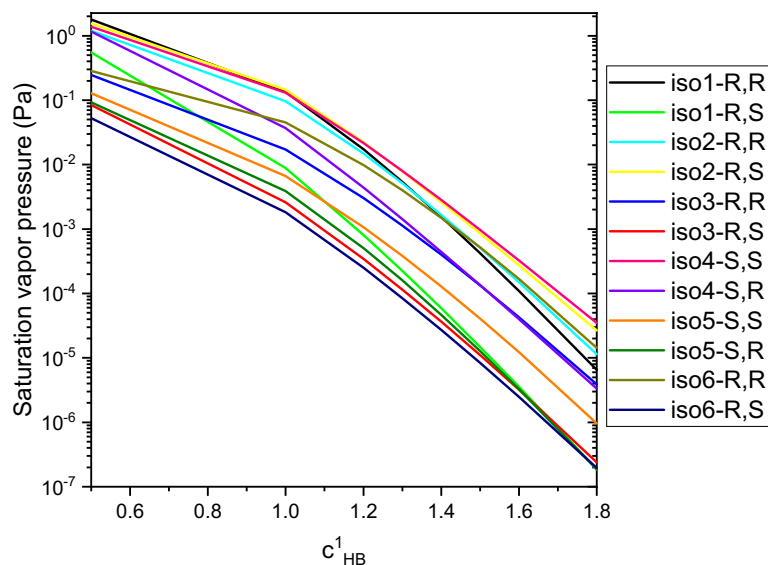


Figure S5: Dependence of the computed saturation vapor pressure, at 298.15 K, for all isomers of ISOP(OOH)<sub>2</sub>, on the scaling factor c1. Calculated using COSMOtherm version 18 and the BP\_TZVPD\_FINE\_18 parametrization (based on BP/def2-TZVPD//BP/def-TZVP quantum chemical data)



#### S4. Selection of COSMO conformers with a certain number of hydrogen bonds

5 The hydrogen bonding information was printed using the pr\_steric option in the global command. The  
pr\_steric option prints hydrogen bonding information of all atoms in the molecule that are available for  
forming intermolecular hydrogen bonds. All OH hydrogens (iele = 8) that have a positive partial charge  
(sighb < 0) are considered as hydrogen bond donors that are not fully hydrogen bonded in that conformer.  
In addition, the hydrogen bonded area (hbarea) was used to determine whether the hydrogen is partially  
hydrogen bonded (hbarea < 5.268) or not bonded (hbarea = 5.268; this is the threshold value for a  
10 completely unbonded hydrogen atom in COSMOtherm version 18). Based on this information, we  
counted the number of full and partial intramolecular hydrogen bonds. The partial intramolecular  
hydrogen bonds are simply all OH hydrogens with a hbarea < 5.268. Since all of our ISOP(OOH)<sub>2</sub> isomers  
have 4 hydrogen bond donors, the number of full intramolecular hydrogen bonds can be counted by  
subtracting the number of partially bonded and non-bonded hydrogens (sighb < 0) from four.

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## S5. Selection of gas-phase conformers with a certain number of hydrogen bonds

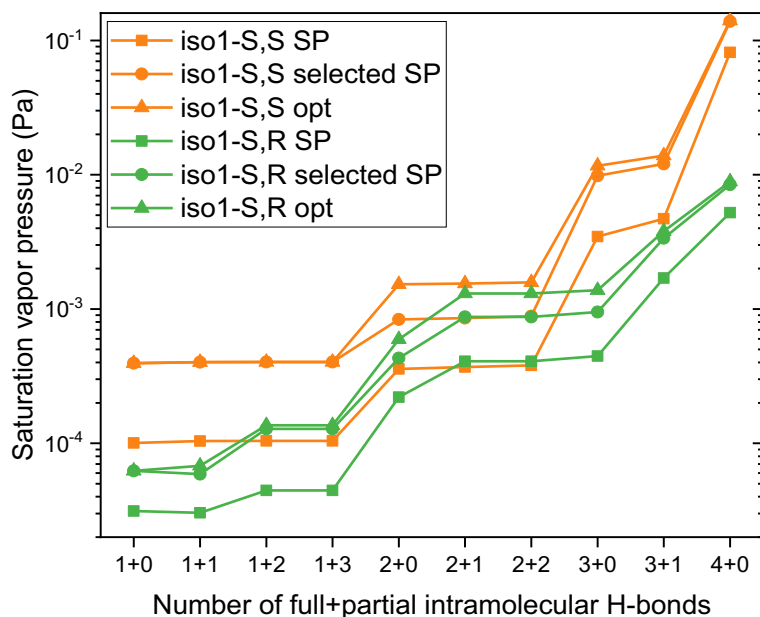
The COSMOconf program for conformer generation maps gas-phase conformers to COSMO conformers (i.e. “liquid-phase” conformers with COSMO solvation), for example to remove possible duplicates. However, the program subsequently reorders and renames the gas-phase conformers by energy. Thus, the *n*:th .energy file (with data on a gas-phase conformer energy) no longer corresponds to the *n*:th .cosmo file (with data on a liquid-phase conformer). This does not affect the results as long as the full set of conformers produced by COSMOconf is used. The .cosmo and .energy files do not contain any data on the mapping, i.e. it is impossible to tell afterwards which .cosmo files match which .energy files. (The mapping information is available in the output of the COSMOconf program, but this output is often not saved for later use, or published even as supplementary data.) However, in our suggested approach, a large part of the .cosmo files are removed, as these contain too many intramolecular H-bonds. Removing the .energy files with the same file numbers would lead to inconsistent results, as they do not correspond to the same structures. Therefore, some extra effort is needed to select the appropriate gas-phase conformers for calculations with a restricted number of intramolecular H-bonds.

We tested three different methods of selecting the gas-phase structures and energies for the COSMOtherm calculations, given a subset of COSMO conformers, selected as described in section S4. Figure S6 shows the saturation vapor pressure of the iso1-S,R and iso1-S,S stereoisomers of ISOP(OOH)<sub>2</sub>, calculated with 100 COSMO conformers (.cosmo files) from COSMOconf, and the following three approaches for selecting the gas phase structures and energies:

- SP: Single-point gas-phase energies calculated at the COSMO geometries were used in the COSMOtherm calculation to ensure that the gas-phase conformers automatically have the same number of H-bonds as the COSMO conformers. The single-point gas phase energies are automatically printed to the .cosmo files by COSMOconf.
- Opt: The COSMO conformers were reoptimized in the gas phase, and the resulting .energy files were used in the COSMOtherm calculation. This option corresponds to the same procedure as used by COSMOconf, but omitting the step where the gas-phase and COSMO conformers are mapped to remove any duplicate gas phase conformers (and subsequently reordered). This ensures that the COSMO and gas-phase conformers are matched in calculations where only certain conformers are selected. However, the gas-phase reoptimization may in some cases lead to an increase in the number of intramolecular H-bonds, and duplicates may also occur.
- Selected SP: In the gas-phase optimization, some of the COSMO conformers converge to a gas-phase minimum that contains a different number of H-bonds. For this reason, the lowest gas-phase energy conformers (within 10 kJ/mol of the lowest-energy optimized gas-phase conformer containing the correct number of H-bonds) were visually checked, and gas-phase conformers that had too many H-bonds were replaced by the single-point gas-phase energy of the corresponding

COSMO conformer. In addition, duplicate gas phase conformers were replaced by the single-point energy.

5 **Figure S6: Saturation vapor pressures for two stereoisomers of ISOP(OOH)<sub>2</sub>, using different methods for selecting gas-phase structures and energies (from an overall set of 100 conformers).**



10 It can be seen from Figure S6 that simply using single-point energies (“SP”; the cheapest option in terms of both human and computer time) can lead to significant underestimation of the saturation vapor pressure, compared both to the more accurate approaches, and (in the  $n=0$  case for iso1-S,R) also the experimental result. This option is thus recommended only for initial test calculations, for example for exploring whether limiting the number of intramolecular H-bonds in a particular system leads to a large difference in results or not. The “opt” and “selected SP” cases are mostly identical, but non-negligible differences can be encountered in cases when the reoptimization of low-energy gas-phase structures leads to an increase in the number of H-bonds. We therefore recommend using the “selected SP” approach whenever feasible.

20 The cut-off of 10 kJ/mol for visual inspection in the “Selected SP” approach (necessary to avoid a potentially enormous unnecessary human effort for large systems with very many conformers) was based on a systematic testing of the effect of replacing a single optimized gas-phase energy by the corresponding single-point energy calculated at the COSMO geometry. We tested this for both diastereomers of iso1 of

ISOP(OOH)<sub>2</sub>, and the set of conformers containing (in the COSMO geometries) one full intramolecular hydrogen bond. The results are shown in Figure S7. For iso1-S,S, the difference between the lowest and the second lowest gas-phase optimized energy is significantly higher than for iso1-S,R, which explains why the effect on the saturation vapor pressure is also larger, if the lowest optimized gas-phase energy is replaced with the corresponding single-point gas-phase energy. In the conformers selected for Figure S7, the energy difference between the optimized and single-point gas phase energies of the same conformer varied between 1 and 23 kJ/mol. Since the change in the saturation vapor pressure is less than 1%, when the relative gas-phase energy of the conformer is higher than 10kJ/mol, we selected 10kJ/mol as a cut-off for visually checking the number of H-bonds in each gas-phase conformer.

**Figure S7: The effect of using a single-point gas-phase energy (at the COSMO geometry) of a single conformer instead of the energy of the optimized gas phase geometry, as a function of the relative gas phase energy of the optimized conformer.  $P_{\text{sat}}$  = Saturation vapor pressure calculated by replacing one of the optimized gas phase conformers with a single-point energy of the same conformer,  $P_{\text{sat},0}$  = Saturation vapor pressure calculated using only the optimized gas-phase energies.**

