Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

SUPPLEMENTARY INFORMATION:

THE SOLVATION STRUCTURE OF ALPRAZOLAM

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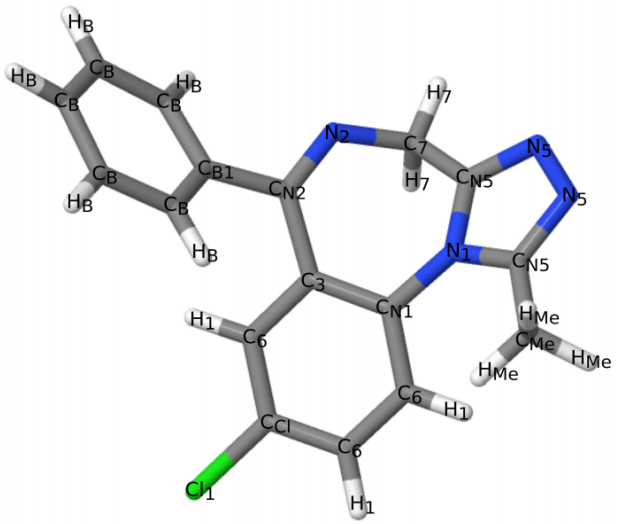
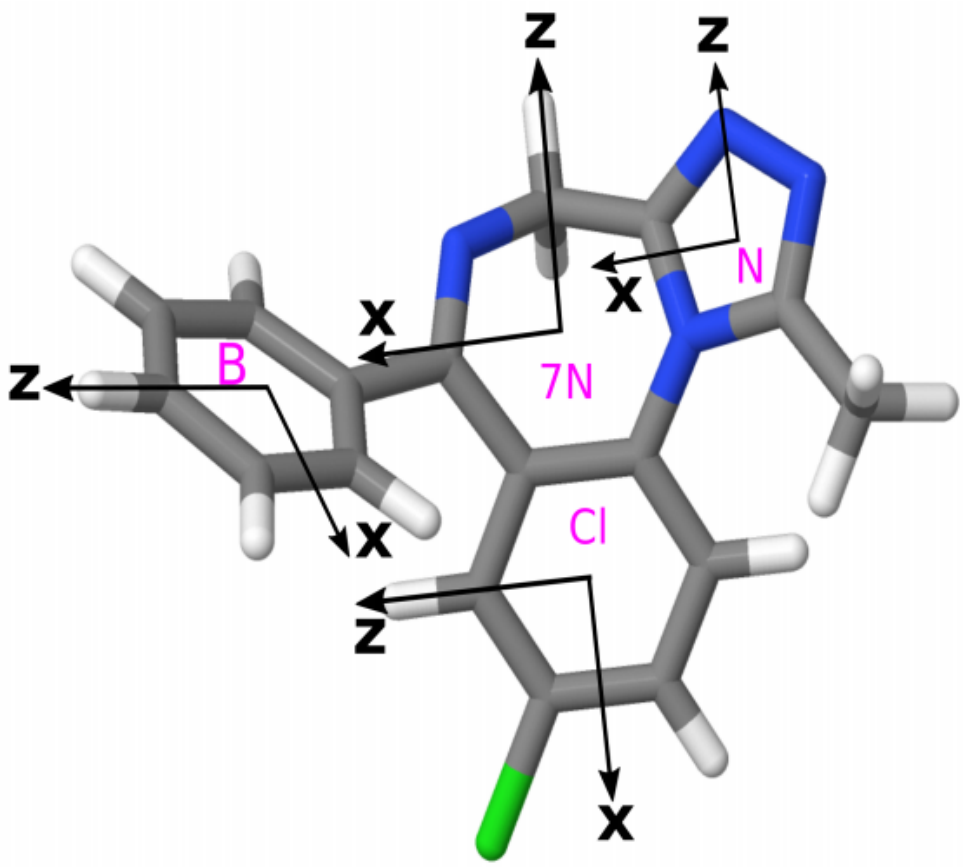
SI Table 1: The seed parameters used in the EPSR simulations of alprazolam/methanol/water. The corresponding labelling scheme for alprazolam is shown in below for convenience.

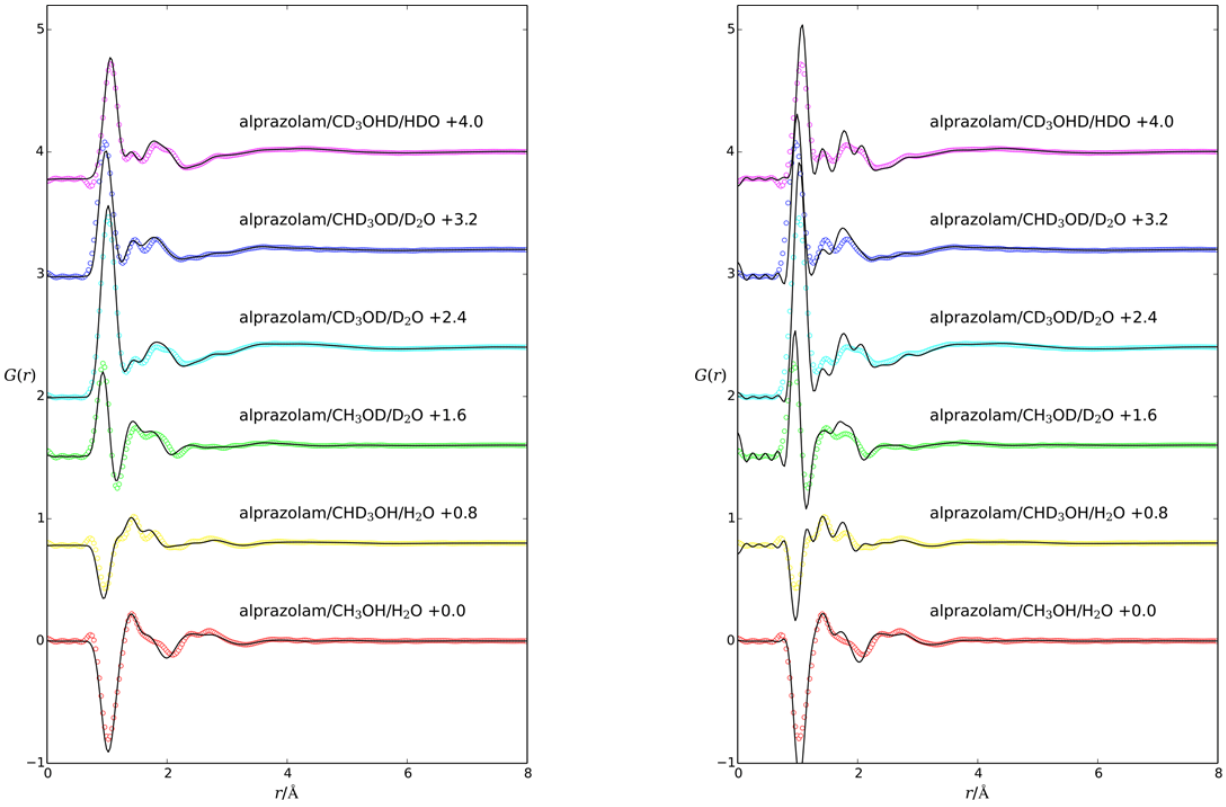
Molecule	Atom Name	σ (Å)	ε (kJ mol^{-1})	*q* (e)
Alprazolam	N5	3.2500	0.71128	-0.3550
Alprazolam	CN5	3.9967	0.35928	0.3650
Alprazolam	N1	3.2500	0.71128	-0.2700
Alprazolam	CMe	3.9967	0.45773	-0.1300
Alprazolam	HMe	2.6495	0.06569	0.0650
Alprazolam	C7	3.9967	0.45773	0.0860
Alprazolam	H7	2.4714	0.06569	0.0890
Alprazolam	N2	3.2500	0.71128	-0.5700
Alprazolam	CN2	3.9967	0.35982	0.5300
Alprazolam	C3	3.9967	0.35982	-0.1800
Alprazolam	CN1	3.9967	0.35982	0.0330
Alprazolam	C6	3.9967	0.35982	-0.1070
Alprazolam	H1	2.5996	0.06276	0.1600
Alprazolam	CCl	3.9967	0.35982	0.0060
Alprazolam	Cl1	3.4709	1.10880	-0.0740
Alprazolam	CB1	3.9967	0.35982	-0.1500
Alprazolam	CB	3.9967	0.35982	-0.1136
Alprazolam	HB	2.5996	0.06276	0.1400
Methanol	Cmeth	3.5000	0.27614	0.1450
Methanol	$H_C$meth	2.5000	0.12552	0.0400
Methanol	Ometh	3.1200	0.71128	-0.6830
Methanol	$H_O$meth	0.0000	0.0000	0.4180
Water	Owat	3.1660	0.6500	-0.8476
Water	Hwat	0.0000	0.0000	0.4238



SI Figure 1. The individual coordinate systems assigned to the four ring structures of alprazolam for the ANGULA analysis of the EPSR simulation.

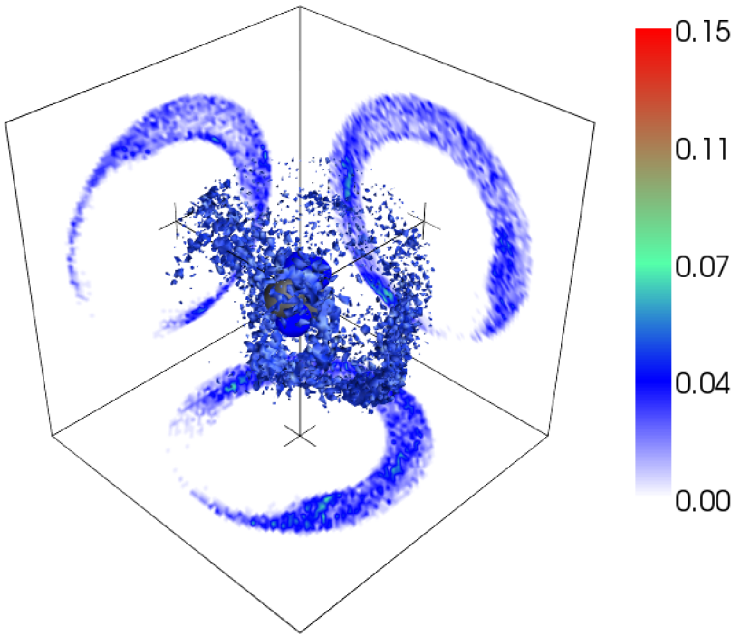


SI Figure 2. Comparison of the scattering functions from EPSR (left) and MD (right) to the measured data in real space obtained through a Fourier transformation of the plots in Figure 2 of the main manuscript. The measured data are plotted as coloured lines while the calculated functions are as black lines.

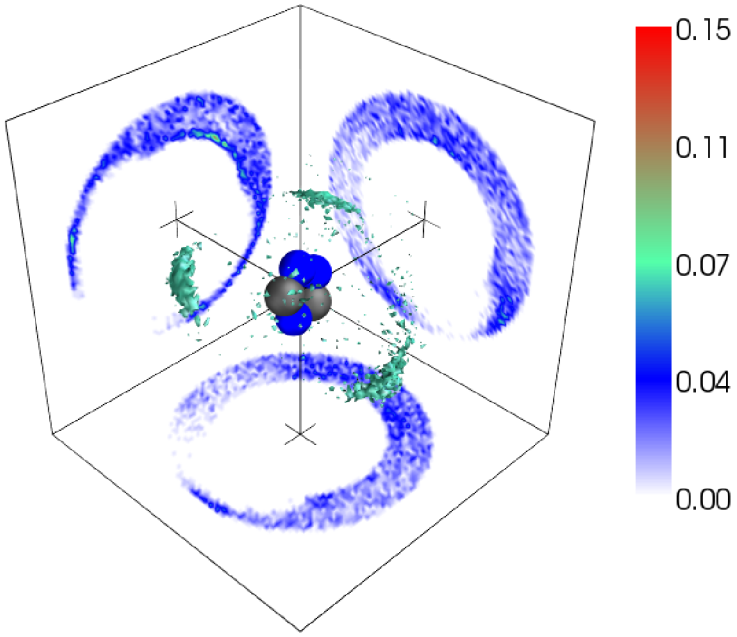


SI Figure 3. Spatial density map (SDM) of (**A**) water and (**B**) methanol in the second solvation shell. The isocontour surfaces enclose the densest 15% of sites. The scale bar shows the local number density of neighbours in $Å^{-3}$.

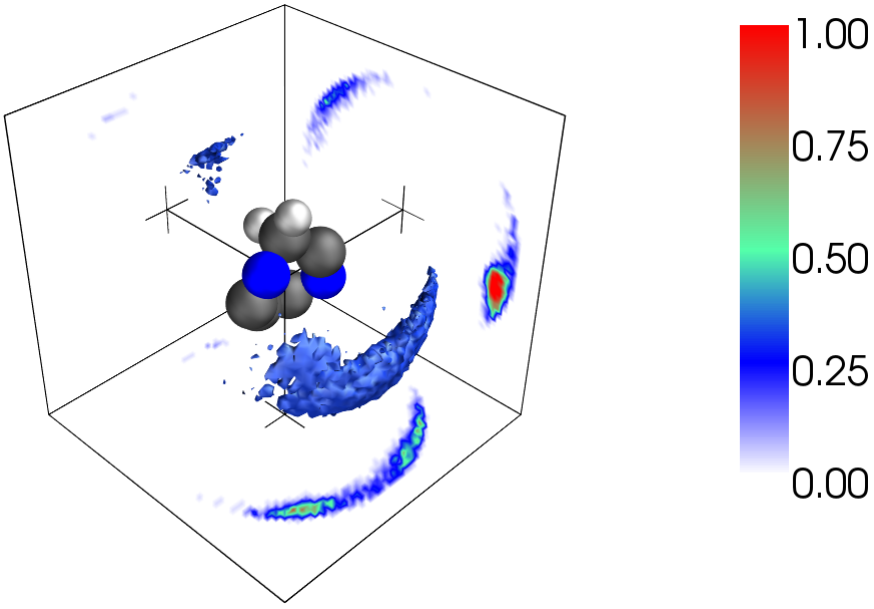
A



B



SI Figure 4. Spatial density map (SDM) of the nearest diazepine rings to a reference diazepine ring from MD simulation. The isocontour surfaces enclose the densest 30% of sites. The scale bar shows the local number density of neighbours in $Å^{-3}$.



SI Figure 5. Occurance through MD simulation trajectory of monomeric, dimeric and trimeric forms of alprazolam. Molecules were considered to be part of a dimer (or trimer) if the center of masses between them was less than 5.5 Å.