

CHEMPHYSCHEM

Supporting Information

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Solvent effect on optical rotation: A case study of methyloxirane in water

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Supporting Information

1. Experimental procedure

Optical rotation (α) was measured with an AUTOPOL IV digital polarimeter. Optical rotation of (*S*)-propylene oxide (*Alfa Aesar*) in water and benzene at 0.05 g/mL was measured at six different wavelengths. The specific rotation at a given wavelength $[\alpha]_\lambda$ was calculated using:

$$[\alpha]_l = \frac{\alpha V}{ml}$$

where, α is the optical rotation in degrees, V is the volume (ml) containing a mass m (g) of the optically active substance, and l is the path length (dm).

2. Molecular dynamics simulation setup and procedure

Molecular dynamics (MD) simulations of (*S*) and (*R*)-propylene oxide in a pre-equilibrated box of 2175 water molecules were done in a NPT ensemble using Gromacs

3.1.4.¹ In all simulations a leapfrog integrator was used with a 2-fs time step.² All bonds were constrained to their equilibrium value with the SETTLE algorithm³ for water and the LINCS algorithm⁴ for all other bonds. In all simulations, a DFT/B3LYP/6-311G** optimized fixed geometry of propylene oxide was used. A twin-range cutoff was used for the Lennard-Jones interactions, with interactions within 0.9 nm evaluated every step and interactions between 0.9 and 1.4 nm evaluated every 5 steps. A neighbor list was used and updated every five steps. For electrostatic interactions, a reaction field with a Coulomb cutoff of 1.4 nm was used with dielectric constants of 78.4 for water beyond the cutoff. The pressure was held at 1 bar using the weak-coupling scheme⁵ with a coupling constant of 1.0 ps and an isothermal compressibility of $4.5 \times 10^{-5} \text{ bar}^{-1}$. Each component of the system (i.e. propylene oxide and water) was coupled separately to a temperature bath at 300 K, using the Berendsen thermostat⁶, with a coupling constant of 0.1 ps. The SPC water model was used⁷. The OPLS-AA force field⁸ was used and partial charges on propylene oxide were calculated in Gaussian03⁹ at the DFT/B3LYP level with the 6-31G* basis set and charge partitioning using the chelpg method.¹⁰ Simulations in water were carried out for 40 ns.

3. Calculation of optical rotation

Structures from the MD trajectories were used for optical rotation (OR) calculations. The specific rotation was averaged for 1700 structure snapshots at each wavelength to generate the ORD spectrum of propylene oxide in water. Specific rotations for each structure were calculated according to the equation:

$$[\mathbf{a}]_I = \frac{-1.34229 \times 10^{-4} \text{Tr}[\mathbf{G}'(\omega)] \hbar^2}{3Mw}$$

where $\text{Tr} [\mathbf{G} (\omega)]$ is the trace of frequency dependent electric-dipole magnetic-dipole polarizability tensor, \bar{n} ($=\lambda^{-1}=\omega/2\pi c$) is the radiation wavenumber, and M is the combined molar mass of propylene oxide and the number of solvent molecules in each snapshot. Thus, by including the mass of the water molecules we are properly normalizing $[\alpha]_\lambda$ with respect to the total number of water molecules. $[\alpha]_\lambda$ is an intensive property independent of the number of solvent molecules.

The dipole-length (L) and dipole-velocity (V) formulation of time dependent density functional response theory (TD-DFT) as implemented in Turbomole5.6,¹¹ with B3LYP and BP86 exchange-correlation functional, respectively, was used for the calculation of $[\mathbf{G}' (\omega)]$. Figure S1 shows the computed ORD spectrum of propylene oxide with the first hydration shell, which includes explicit solvent molecules within a cut-off distance of 0.25 nm from methyloxirane oxygen atom. The L and V forms of the TD-DFT results with BP86/aug-cc-pVDZ (or aug-cc-pVTZ) are very similar. Thus we expect the L and V forms of the results with B3LYP/aug-cc-pVDZ (or aug-cc-pVTZ) will also be very similar.

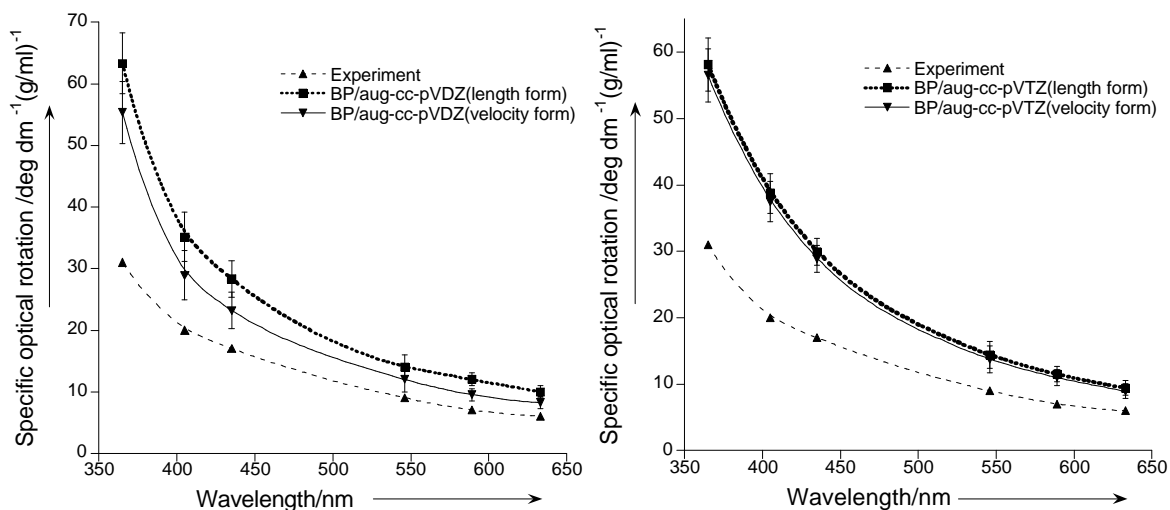


Figure S1. Variation in the dipole-length and dipole-velocity form of calculated optical rotations using TD-DFT/BP86 correlation-exchange functional. The specific rotation was averaged for 1700 structure snapshots from a molecular dynamic simulation to generate the ORD spectrum of propylene oxide in water. The conductor-like screening model (COSMO) was used as the implicit solvent model. The vertical bars show the error estimate of the average optical rotation calculated using the blocking method.^[12]

Figure S2 shows that the computed ORD spectra of (*S*)-methyloxirane with the BP86/aug-cc-pVDZ (or aug-cc-pVTZ) and B3LYP/aug-cc-pVDZ (or aug-cc-pVTZ) analysis are very similar, especially at wavelengths longer than 400 nm. We emphasize that the dipole-length (*L*) form of TD-DFT, as implemented in Turbomole5.6 with the B3LYP exchange-correlation functional, was used to compute the OR. However, the *L*- and dipole-velocity (*V*) forms of the TD-DFT results with BP86/aug-cc-pVDZ (or aug-cc-pVTZ) are very similar (see Figure S1 in the supporting information). Thus, we expect the computed *L*- and *V*-based values with B3LYP/aug-cc-pVDZ (or aug-cc-pVTZ) also to be very similar.

Figure S3 shows the average computed $[\alpha]_D$ value as a function of the number of MD simulation snapshots. Each structure had explicit water molecules within a cut-off distance of 0.40 nm from methyloxirane oxygen atom with a dielectric continuum description based on the COSMO model with the water dielectric constant of 78.4. The average $[\alpha]_D$ value converged to +8.4 as the number of snapshots were increased.

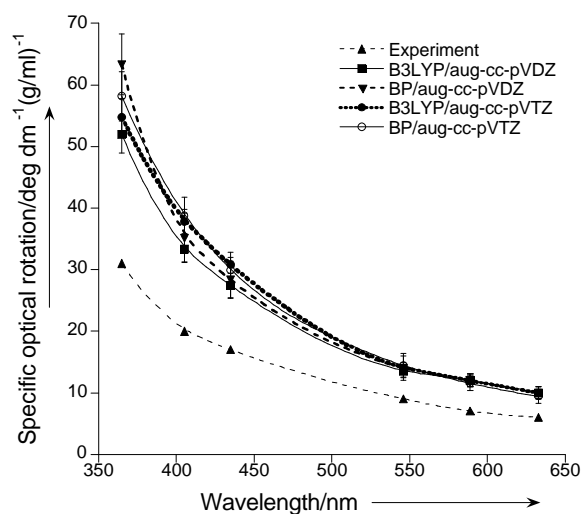


Figure S2. Computed optical rotatory dispersion spectra of (*S*)-methyloxirane with the first explicit hydration shell. Calculations used different combinations of TD-DFT/BP86/B3LYP functionals and aug-cc-pVDZ/aug-cc-pVTZ basis sets as described in the text. The conductor-like screening model (COSMO) was used as the implicit solvent model. The bars indicate error estimates computed using the blocking method.^[12]

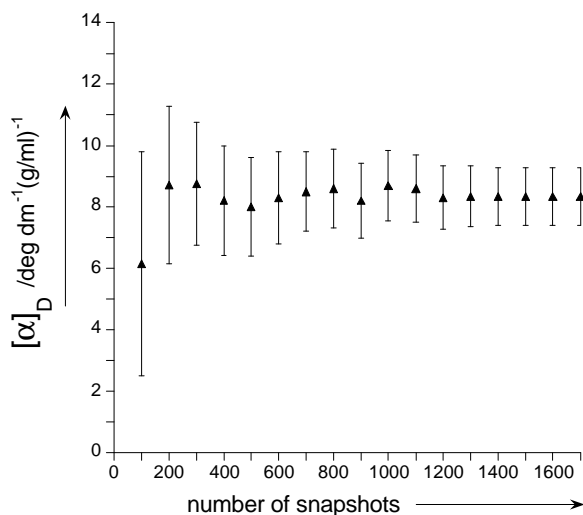


Figure S3. Average optical rotation of (*S*)-methyloxirane at 589 nm, $[\alpha]_D$, as a function of the number of MD simulation snapshots. Calculations used the TD-DFT/BP86 functional and aug-cc-pVDZ basis set. A combination of explicit water molecules (within 0.40 nm of the methyloxirane oxygen atoms) and an implicit solvent model (COSMO) were used in the calculations. The error estimate of the average optical rotation was calculated using the blocking method^[12].

Analysis tool in the Gromacs software^[1] computes and analyzes hydrogen bond geometries. Hydrogen bonds are determined based on cutoffs for the angle (α) acceptor (A) – donor (D) - hydrogen and the distance (r) hydrogen – acceptor as shown below (from the Gromacs manual):

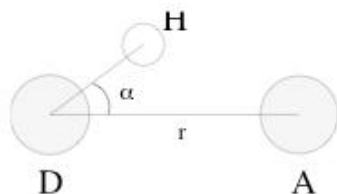
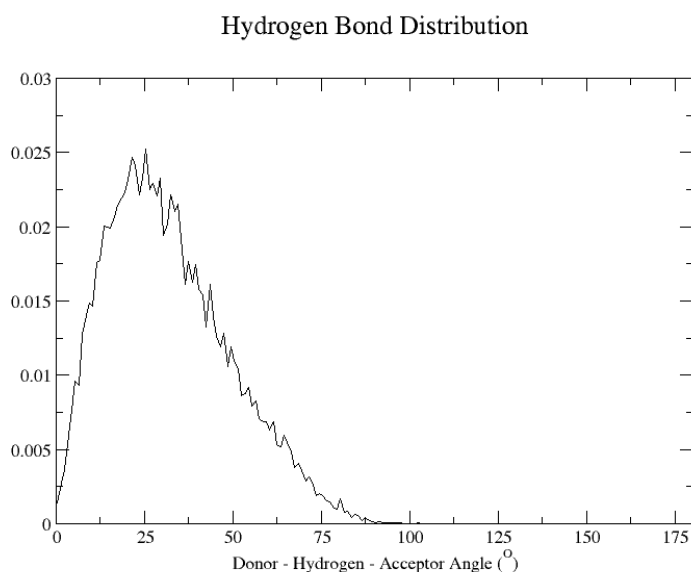


Figure 8.8: Geometrical Hydrogen bond criterion.

D and A are water and methyloxirane oxygen atoms, respectively. Thus, we used gromacs to analyze the angular (α) dependence of the hydrogen bonds of the water molecules in the first hydration shell ($r = 0.25$ nm corresponding to the first minimum in the RDF, Figure 2 of the text). The result is shown in the figure below.



The distribution shows a narrow range of α s. In particular, no hydrogen bonds are formed between water and methyloxirane when $\alpha \geq 90^\circ$, as expected. Thus, the given orientations of the water molecules around the methyloxirane oxygen atom obtained from the MD simulations are reliable. However, using a polarizable force field in the MD simulation should in principle give a better description of the angular distribution of hydrogen bonds between water and methyloxirane, and is beyond the scope of the present work.

The parameter file used in describing the implicit solvent model COSMO (used in the Turbomole program) around the water-methyloxirane adduct is given below:

```
*****
***      radius definition menu      ***
*****
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radius is in Bohr units

Group	type	radius
1	c	3.76
2	h	2.65
3	o	3.36

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