QUANTUM CHEMICAL INVESTIGATION OF THE PREDOMINANT CONFORMATION OF THE ANTIBIOTIC AZITHROMYCIN IN WATER AND DMSO SOLUTIONS: AN INTEGRATED THERMODYNAMIC AND NMR ANALYSIS

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SUPPLEMENTARY MATERIAL

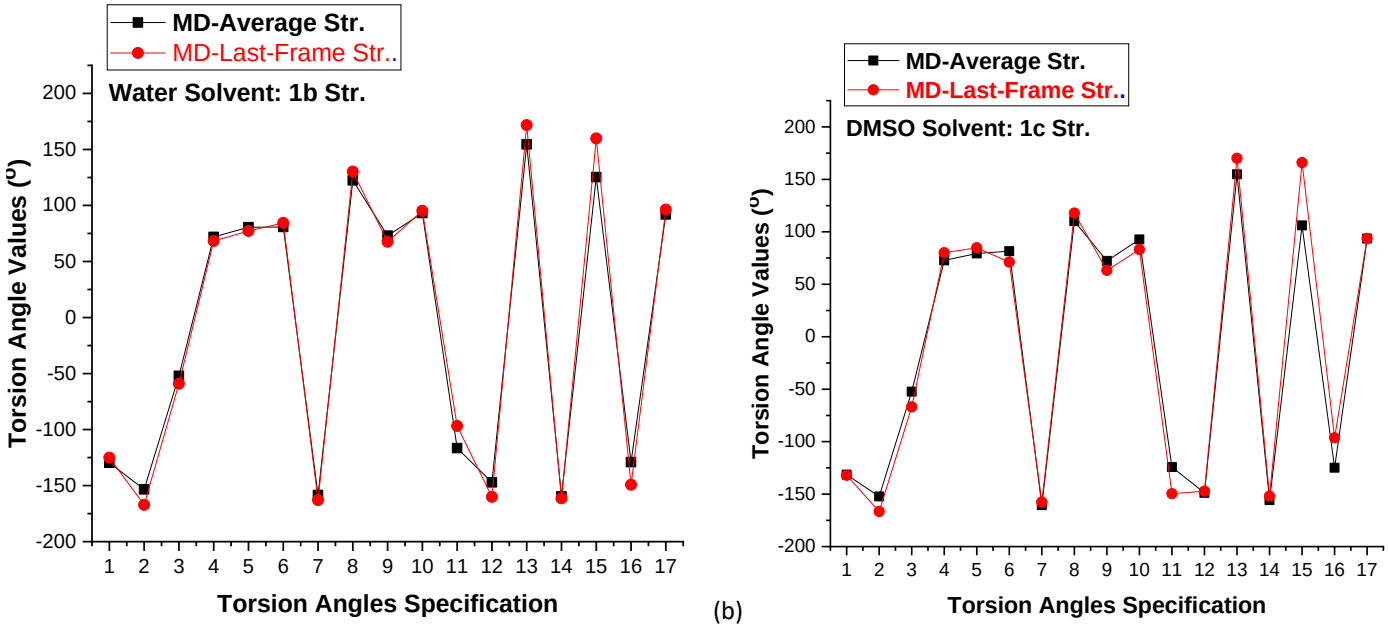


Figure S1. A comparison between average torsion angles and the last structure from the MD trajectory. Selected torsion angle values that fairly represent the AZM conformation are shown.
(a) Structure **1b** (b) Structure **1c**

Definition of dihedral angles.

1	φ_1	[C1'-O-C5-C6]
2	φ_2	[C1''-O-C3-C4]
3	φ_{1a}	[O-C5-C6-C7]
4	φ_{2a}	[O-C3-C4-C5]
5	φ_3	[O-C1'-O-C5]
6	φ_4	[O-C1''-O-C3]
7	$\varphi_{2'}$	[C2-C3-C4-C5]
8	$\varphi_{7'}$	[C1-C2-C3-C4]
9	$\varphi_{1'}$	[C4-C5-C6-C7]
10	$\varphi_{8'}$	[C6-C7-C8-C9]
11	$\varphi_{4'}$	[C12-C13-O-C1]
12	$\varphi_{6'}$	[C9-N-C10-C11]
13	$\varphi_{9'}$	[N-C10-C11-C12]
14	$\varphi_{5'}$	[C10-C11-C12-C13]
15	$\varphi_{10'}$	[C13-O-C1-C2]
16	$\varphi_{3'}$	[O-C1-C2-C3]
17	$\varphi_{11'}$	[C3-C4-C5-C6]

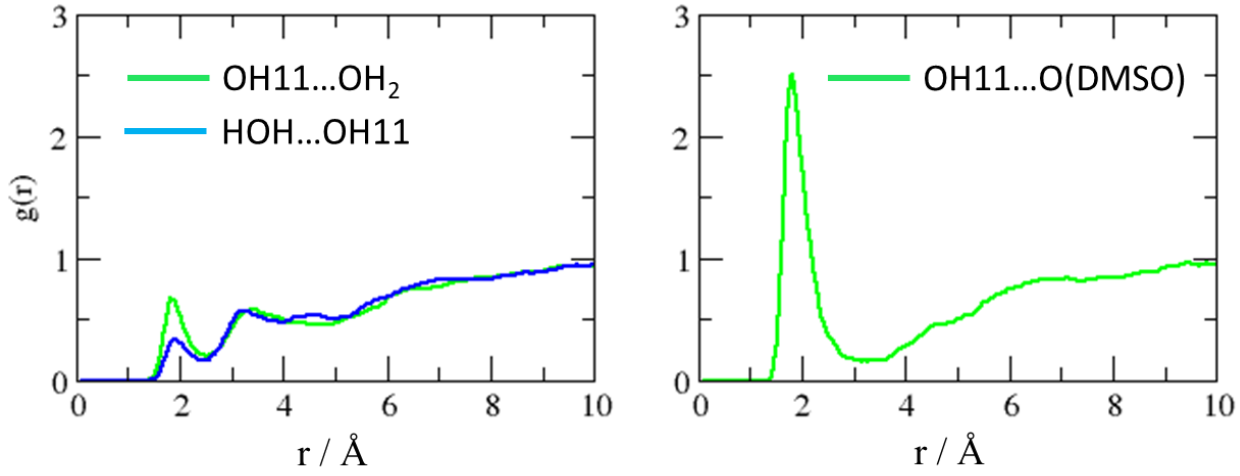


Figure S2. Radial distribution function (g(r)) for OH11 center.

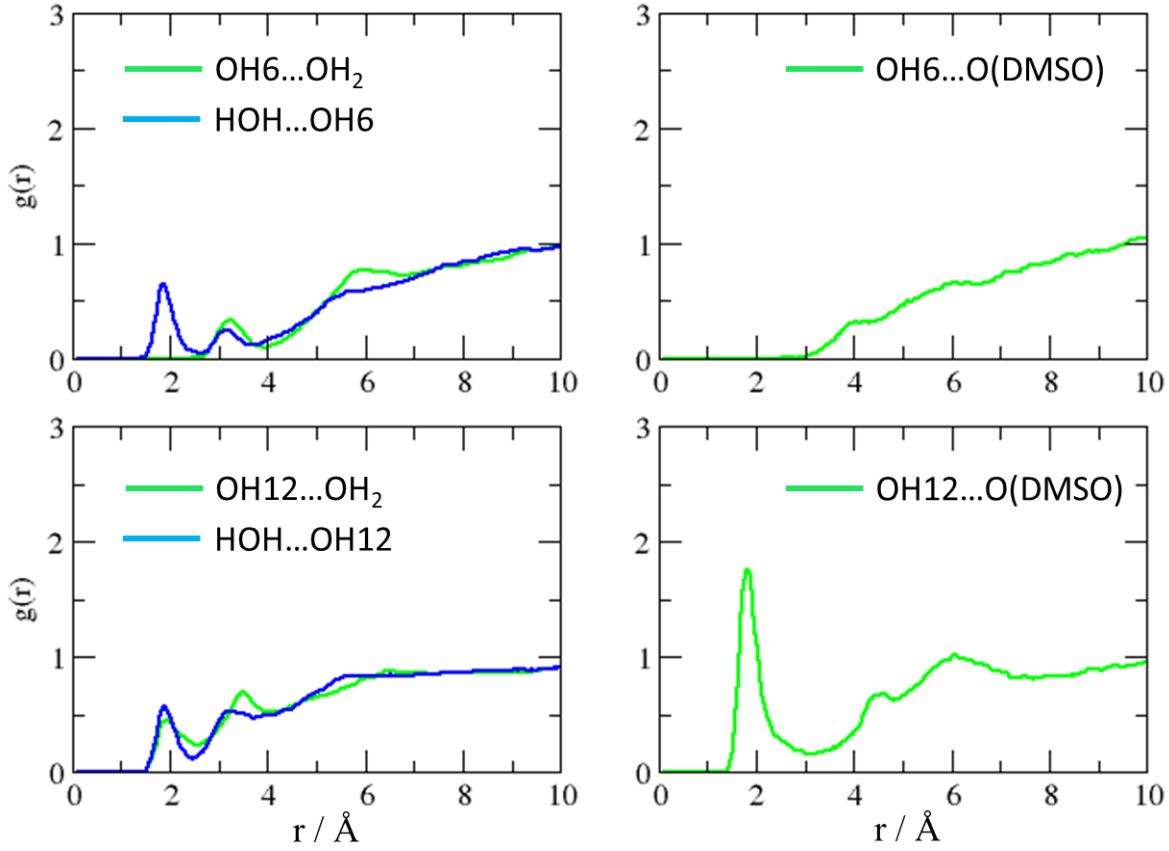
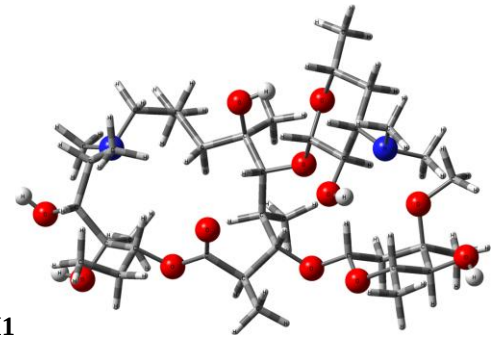
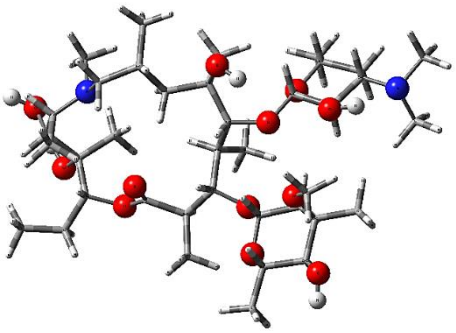


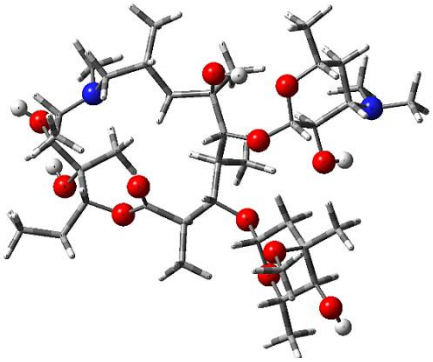
Figure S3. Radial distribution function (g(r)) for OH6 and OH12 centers.



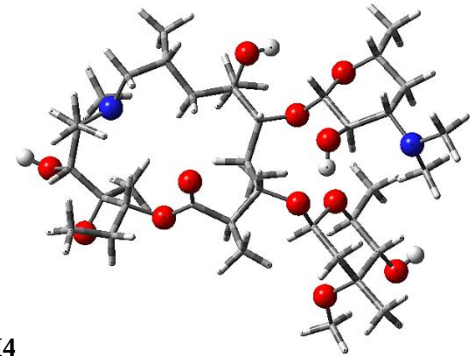
.(a) **M1**



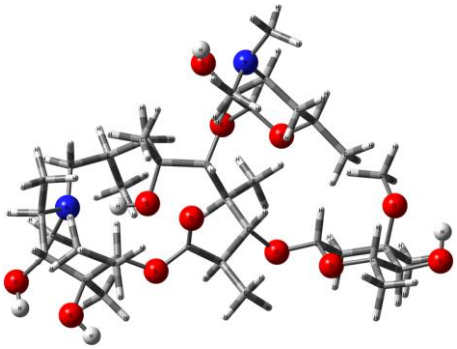
(b) **M2**



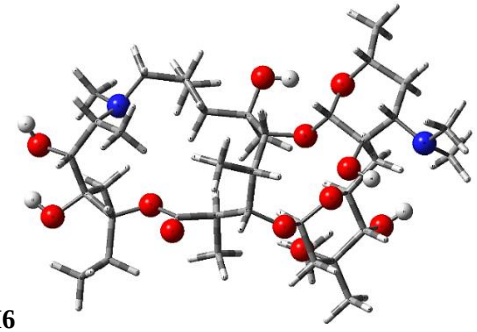
(c) **M3**



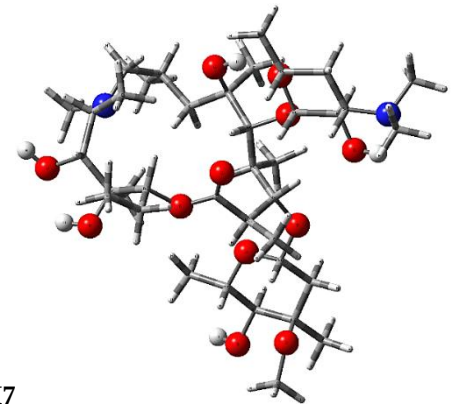
(d) **M4**



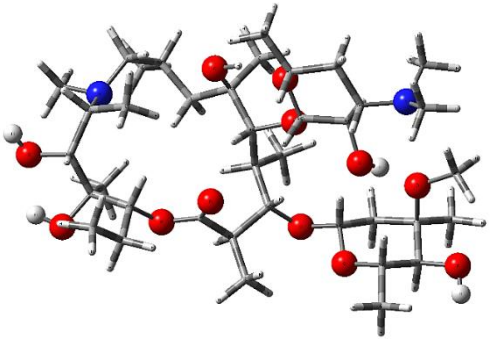
(e) **M5**



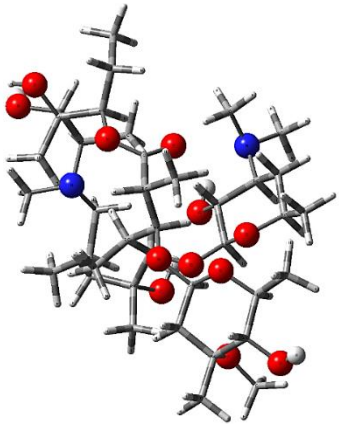
(f) **M6**



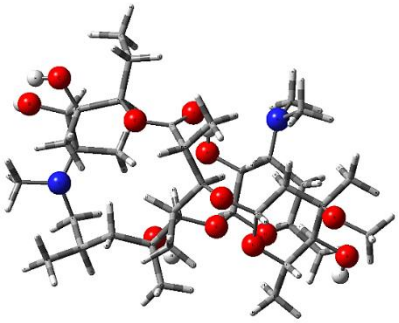
(g) **M7**



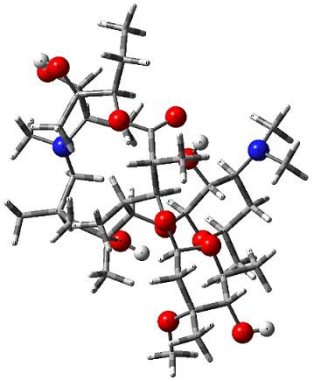
(h) **M8**



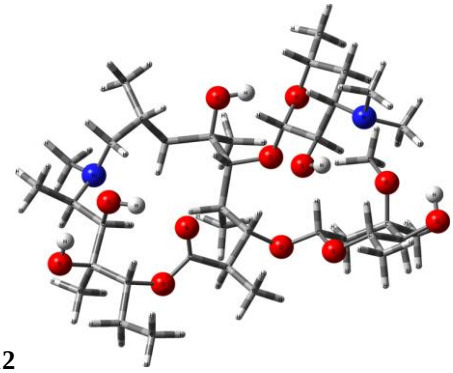
(i) **M9**



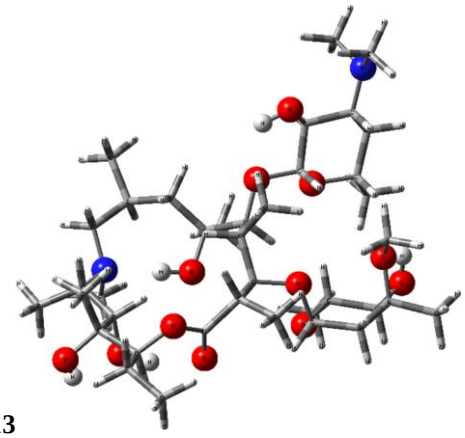
(j) **M10**



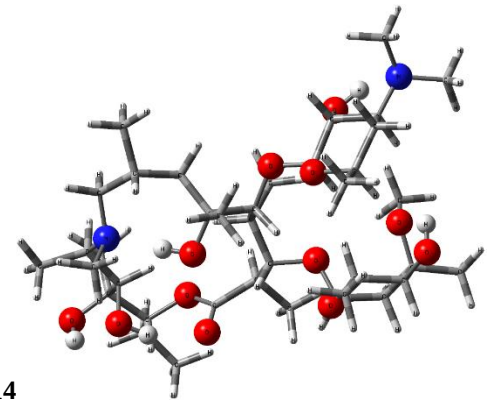
(k) **M11**



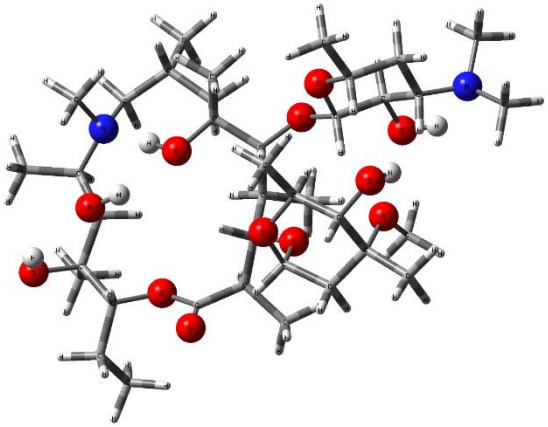
(l) **M12**



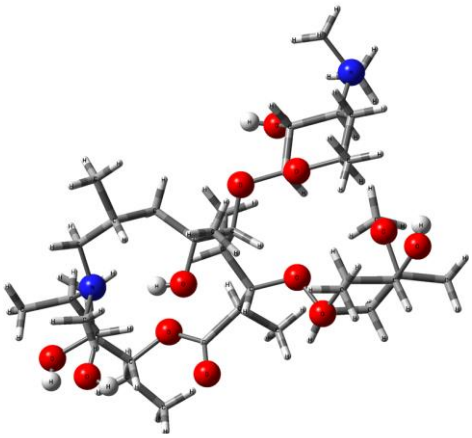
(m) **M13**



(n) **M14**



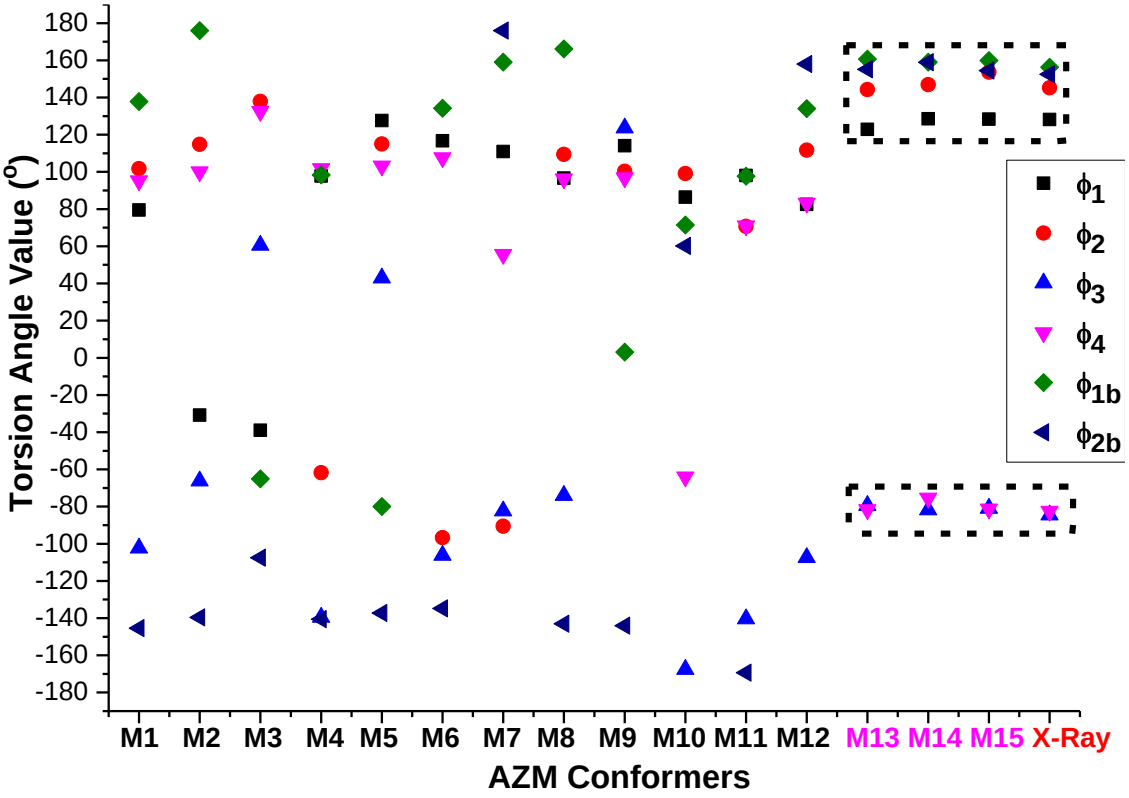
(o) **M15**



(p) **X-Ray**

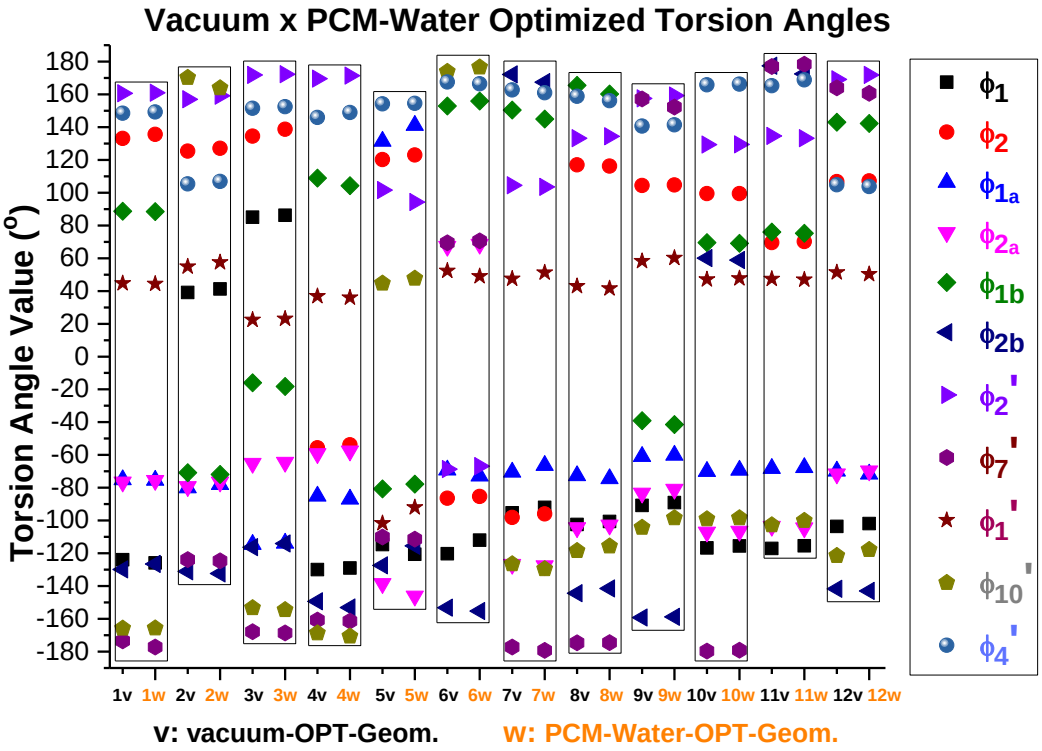
Figure S4. ωB97x-D/6-31G(d,p) optimized structures located on the potential energy surface for azithromycin molecule and **X-Ray** structure [16].

[16] Neglur, R.; Hosten, E.; Aucamp, M.; Liebenberg, W.; Grooff, D. Water and the relationship to the crystal structure stability of azithromycin. J. Therm. Anal. Calorim. 2018, 132, 373–384.

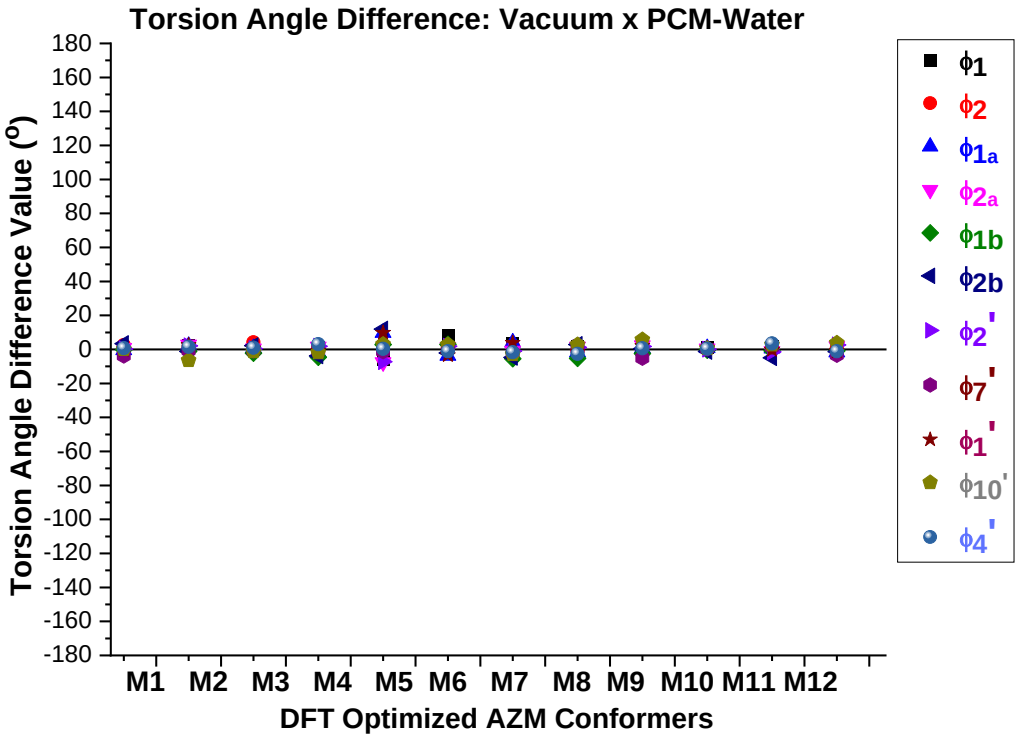


(a)

Figure S5. Selected ωB97X-D/6-31G(d,p) torsion angles (°) defined in Scheme 1 (φ_1, φ_2, φ_3, φ_4, φ_{1b}, φ_{2b}), used in the relaxed scan curves (Figure 1) for all 15 optimized structures of AZM. **X-Ray** [16], **M13, M14,** and **M15** values are highlighted in a dashed rectangle (maximum deviation is 15°, φ_3)

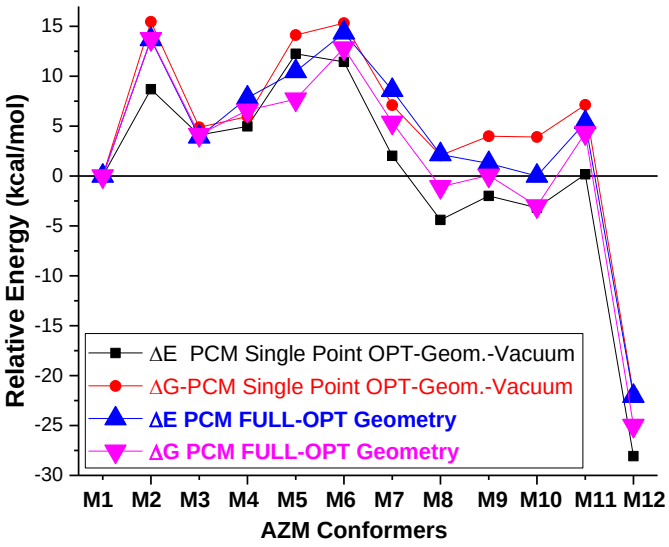


(a)

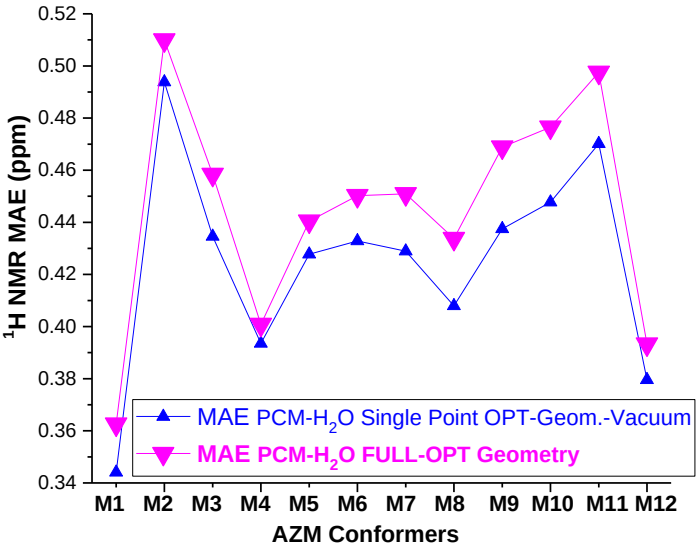


(b)

Figure S6. (a) Main torsion angles (º) defined in Figure 1 for ωB97x-D/6-31G(d,p) optimized structures located on the potential energy surface for azithromycin molecule. A comparison between torsion angle values optimized in the vacuum (1v, 2v, …, 12v) and PCM-Water (1v, 2v, …, 12w) is shown. They are grouped in a rectangle for easy visualization.
(b) Torsion angles difference values (º) between geometries optimized in the vacuum and PCM-Water.



a)



(b)

Figure S7. A comparison between DFT-PCM relative energy (ΔE_{rel} and ΔG_{rel}) and ^{1}H NMR MAE values, using fully optimized DFT-PCM-Water geometries (named PCM-FULL-OPT) and respective structures optimized in the vacuum (named PCM-Single-Point), for optimized structures of azithromycin.
(a) ωB97x-D/6-31G(d,p)-PCM-Water $\mathbf{\Delta E_{rel}}$ and $\mathbf{\Delta G_{rel}}$ relative values (kcal mol^{-1})
(b) B3LYP/6-31G(d,p)-PCM-Water **MAE** values (ppm)

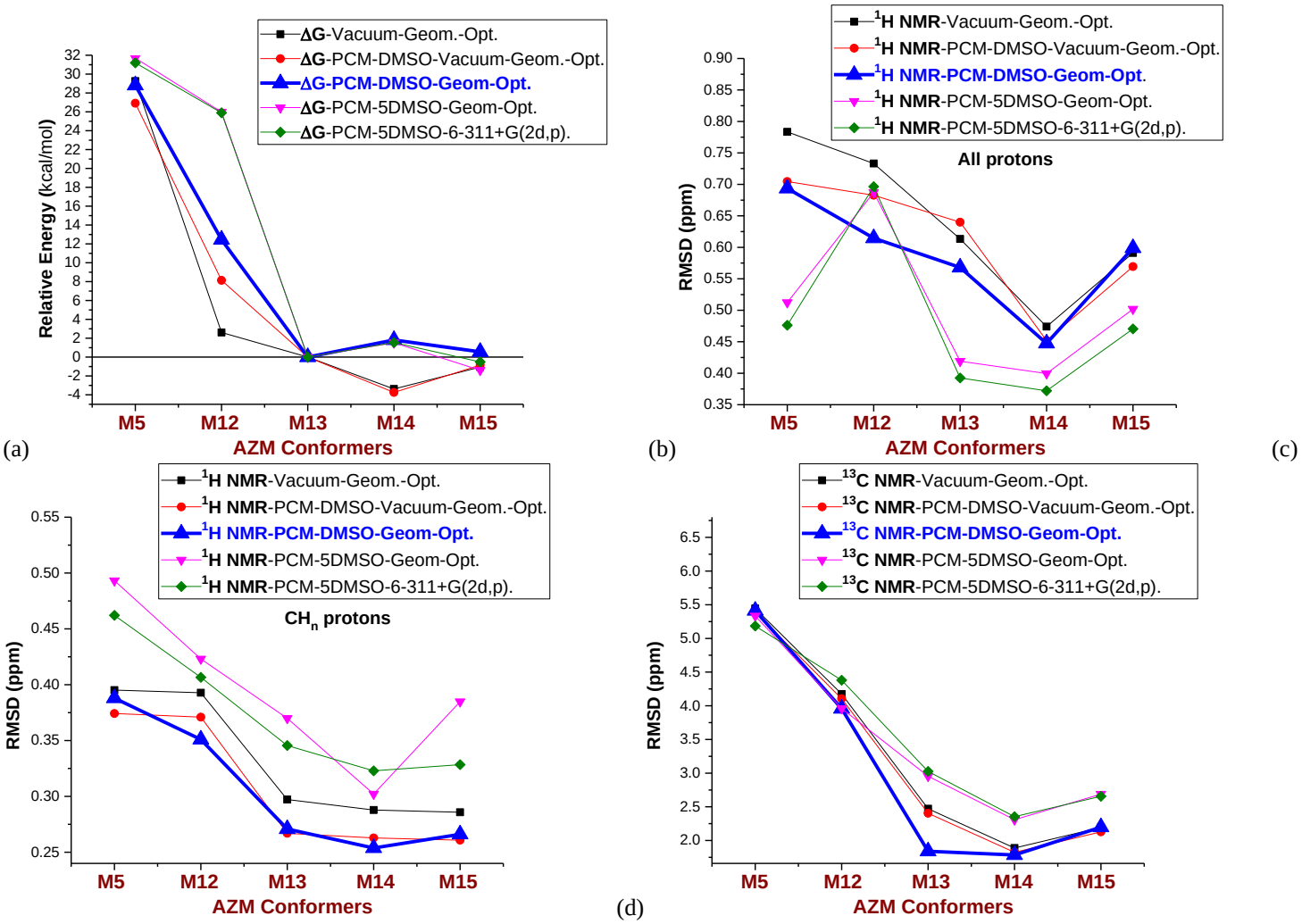


Figure S8. ωB97x-D/6-31G(d,p)-PCM-DMSO relative Gibbs free energy (ΔG_{rel} in kcal mol^{-1}) and NMR B3LYP/6-31G(d,p)-PCM-DMSO RMSD (in ppm) calculated for relevant AZM optimized geometries optimized in the vacuum, using implicit solvent effect model (PCM) and also including five explicit solvent molecules. The effect of increasing the basis set is evaluated with a triple-zeta quality 6-311+G(2d,p) basis set. The PCM-DMSO results, with no inclusion of explicit solvent molecules, are highlighted.

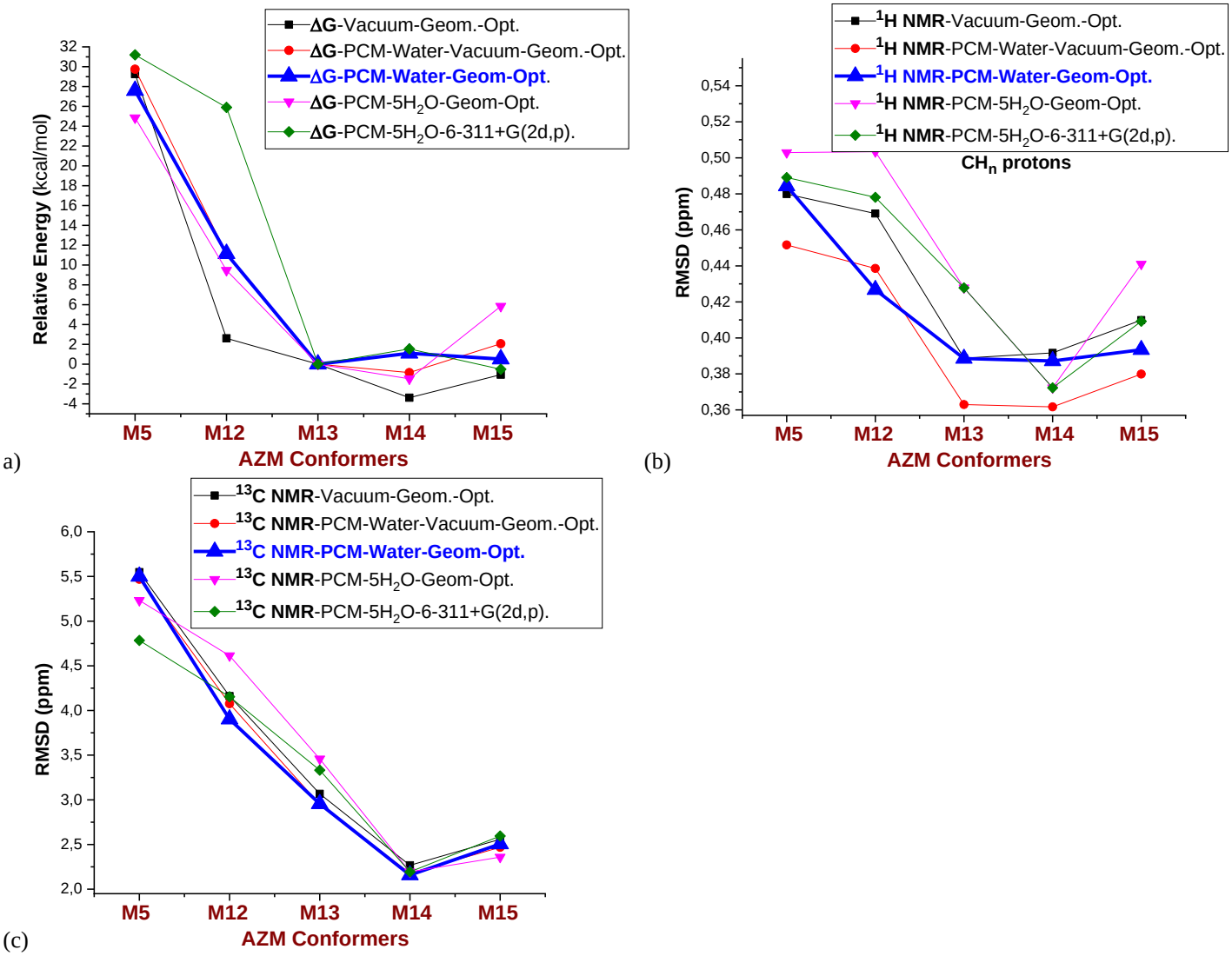


Figure S9. ωB97x-D/6-31G(d,p)-PCM-Water relative Gibbs free energy (ΔG_{rel} in kcal mol^{-1}) and NMR B3LYP/6-31G(d,p)-PCM-Water RMSD (in ppm) calculated for relevant AZM optimized geometries optimized in the vacuum, using implicit solvent effect model (PCM) and also including five explicit solvent molecules. The effect of increasing the basis set is evaluated with a triple-zeta quality 6-311+G(2d,p) basis set. The PCM-Water results, with no inclusion of explicit solvent molecules, are highlighted.

It should be mentioned that harmonic frequencies and geometrical parameters calculated for structures optimized using the implicit solvation model (PCM) were used to generate partition functions for the evaluation of entropy correction to the Gibbs free energy, within the statistical thermodynamics approach, for solvated structures. To eliminate very small imaginary frequencies, present in the PCM-5DMSO optimized structures, associated with low-frequency large amplitude motions of explicit solvent molecules, a very tight convergence criterion in the geometry optimization procedure would be required. This would cause an enormous increase in computation time and is not of practical use. The results shown in Figures S7 to S9 (Supplementary Material) add support to the use of entropic correction evaluated with the PCM model to yield approximate ΔG_{rel} for solvated structures, which exhibit a similar trend predicted by ΔE_{rel} (see Figure 9a,b).

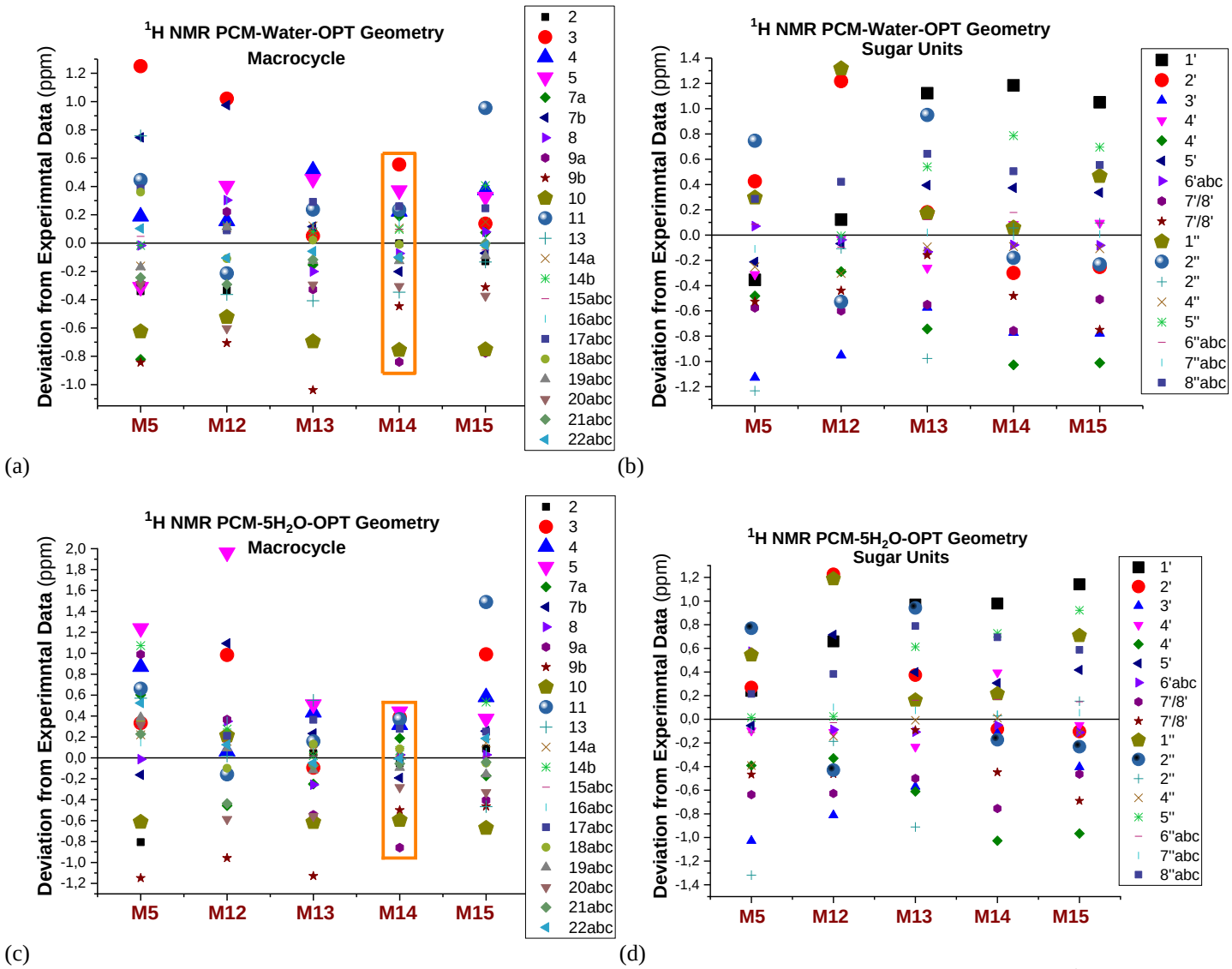


Figure S10. B3LYP/6-31G(d,p)-PCM and PCM-5H$_2$O deviations between calculated and experimental ^{1}H NMR chemical shifts (in ppm) for the most relevant structures of azithromycin. (a,c) Macrocycle and (b,d) sugar units are shown separately.

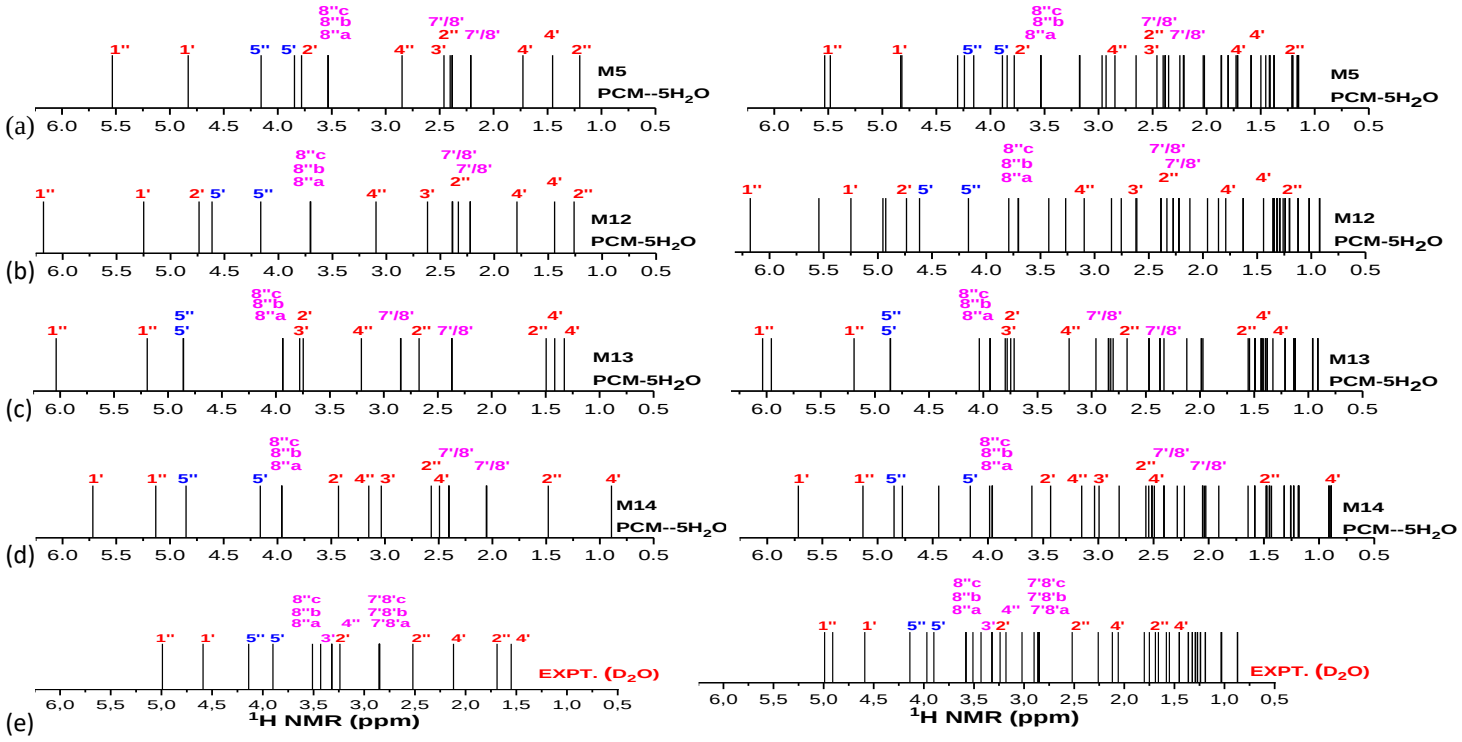


Figure S11. B3LYP/6-31G(d,p)-PCM-Water ^{1}H NMR spectra (CH$_n$ type protons only) for the most relevant structures of azithromycin optimized at the ωB97x-D/6-31G(d,p)-PCM-Water level including five explicit H$_2$O solvent molecules.
(a) **M5**-PCM-5H$_2$O (b) **M12**-PCM-5H$_2$O (c) **M13**-PCM-5H$_2$O (d) **M14**-PCM-5H$_2$O (e) Experimental (D$_2$O)

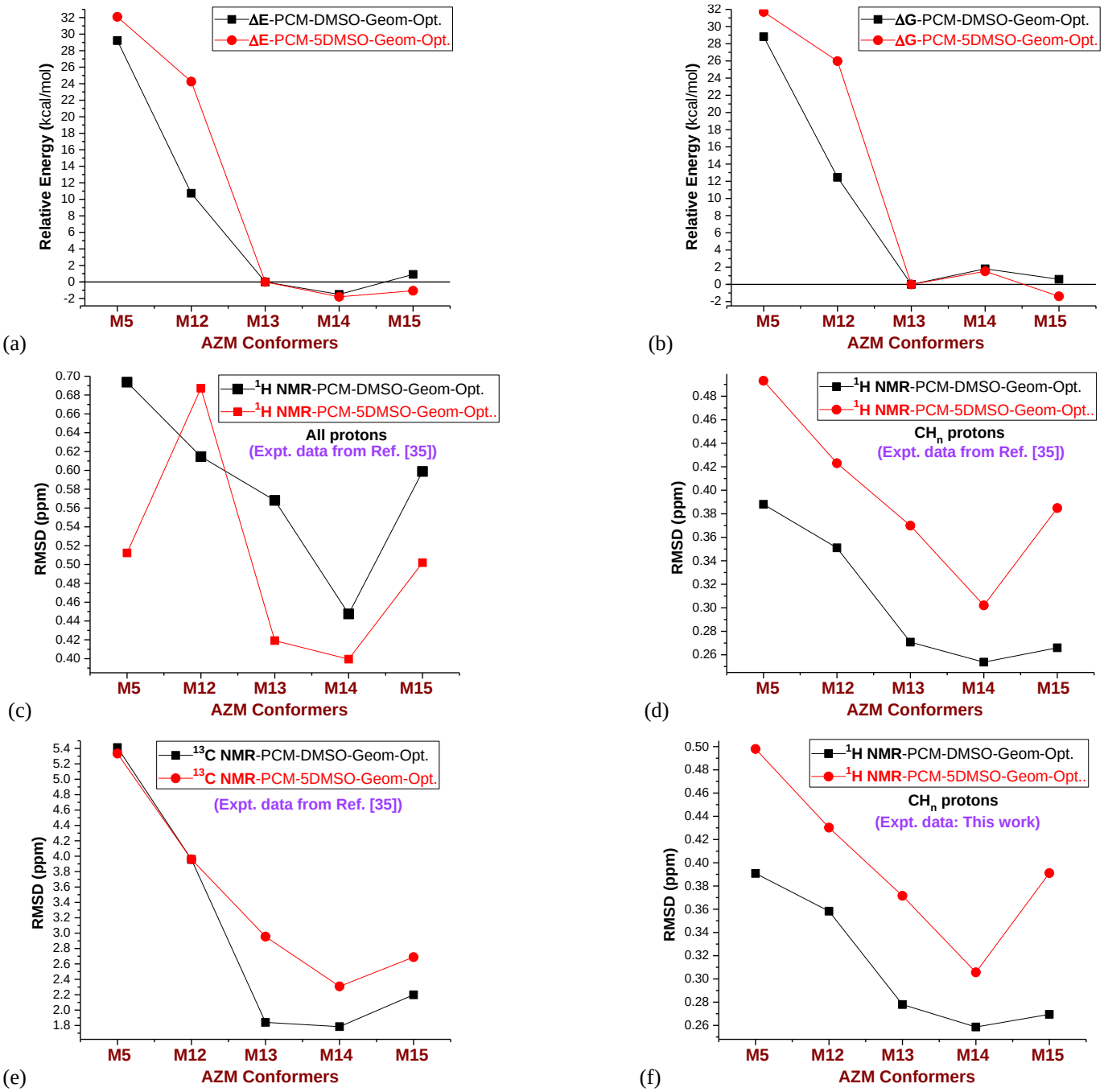


Figure S12. (a) ωB97X-D-PCM/6-31G(d,p) relative energies (ΔG_{rel}, in kcal.mol^{-1}) for selected AZM DFT optimized structures (b) ^{1}H NMR RMSD (all protons included), (c) ^{1}H NMR RMSD (only CH_n protons included), (d) ^{13}C NMR RMSD. NMR chemical shifts were calculated at the B3LYP-PCM/6-31G(d,p) level.

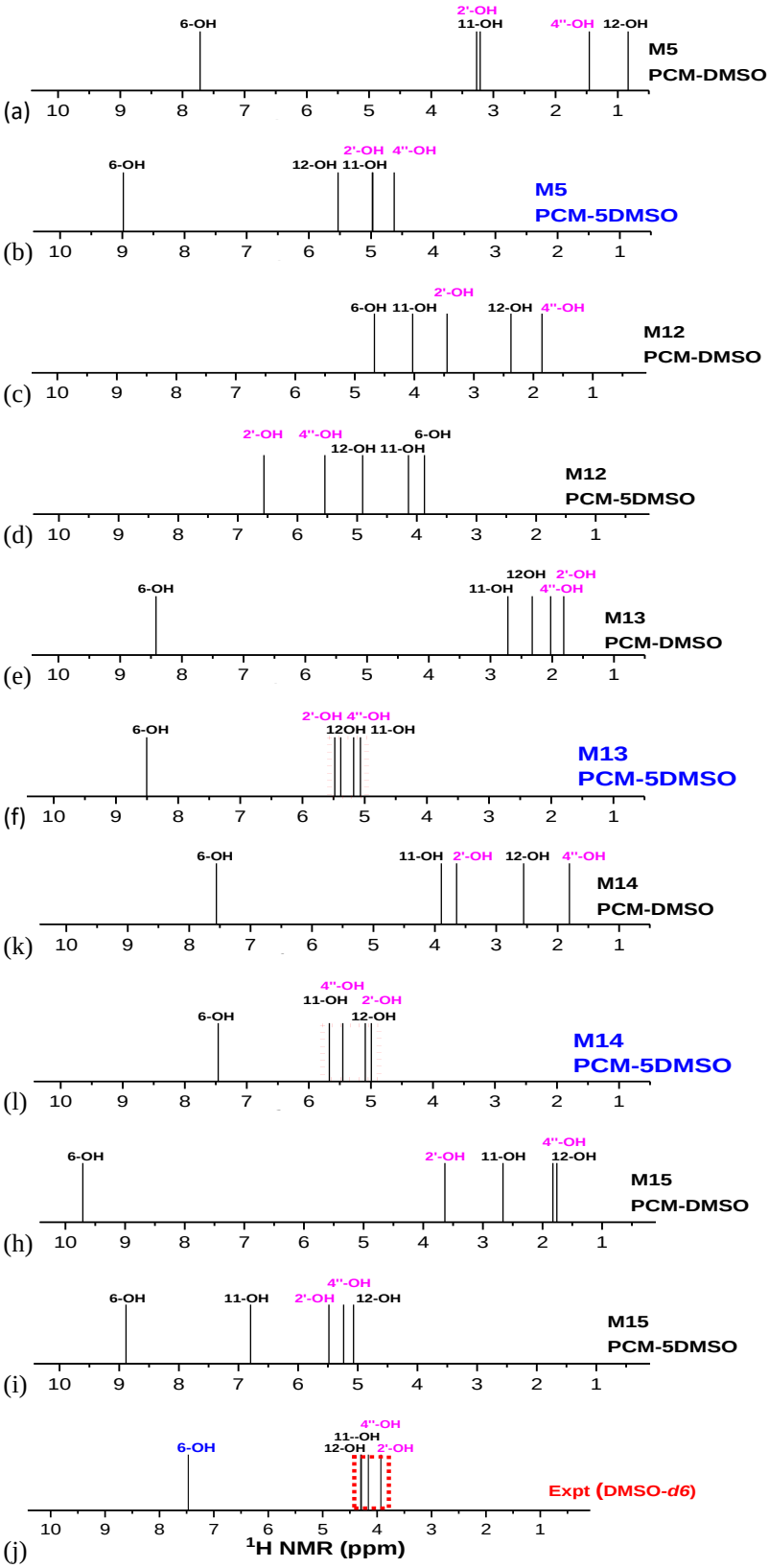


Figure S13. (a-i) B3LYP-PCM/6-31G(d,p) ^{1}H NMR spectra (OH protons only are shown) for relevant structures of AZM optimized at the ωB97X-D-PCM/6-31G(d,p) level (named PCM-DMSO) and also including five explicit DMSO solvent molecules (named PCM-5DMSO). (j) Experimental (in DMDO-*d6*) ^{1}H NMR spectrum. If a small translation of the theoretical spectrum scale is done the agreement with the experiment would be just perfect.

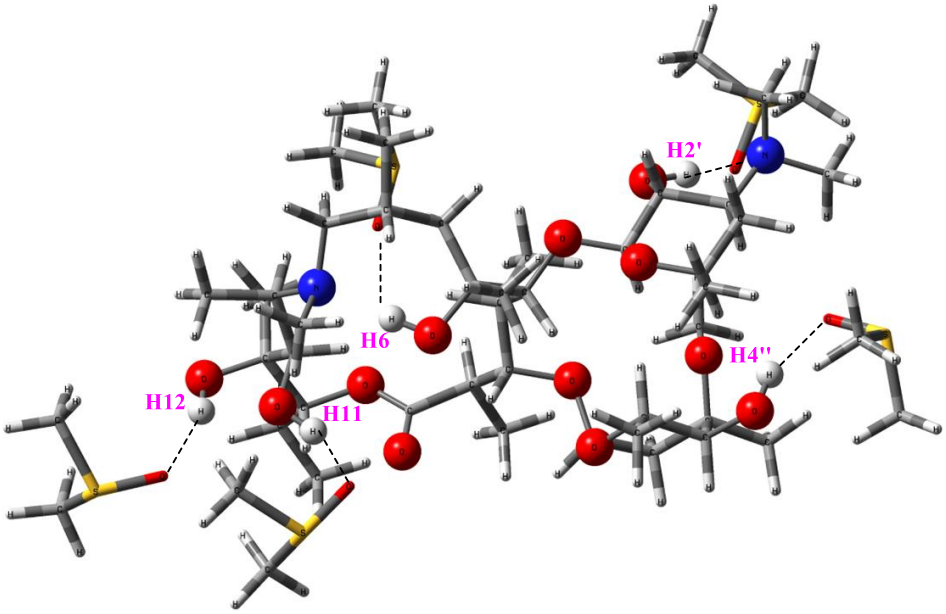


Figure S14. ωB97X-D-PCM/6-31G(d,p) optimized **M14-5DMSO** structure of AZM, most probable to exist in DMSO solution. Solute-solvent H-Bond distances are indicated by dashed lines. AZM-heavy atoms are highlighted for easy visualization.

Table S1. ωB97X-D-PCM/6-31G(d,p) intramolecular O-H…O and O-H…N distances (Å) and AZM-DMSO intermolecular H-bond distances (Å) for AZM structure **M14**.

	Intramolecular Distance (Å)				
	C2'-OH…N	**C4''-OH…O**	**C6-OH…N**	**C11-OH…O**	**C12-OH…O**
PCM-Only	2.05	2.11	1.77	1.92	2.08
PCM-5DMSO	2.30	2.30	1.78	2.65	2.15
	AZM…DMSO Intermolecular Distance (Å)				
	C2'-OH…O=S	**C4''-OH…O=S**	**C6-OH…O=S**	**C11-OH…O=S**	**C12-OH…O=S**
PCM-5DMSO	1.89	1.82	3.46	1.77	1.89

See Figure 1 for the numbering scheme.

Experimental Supporting information

NMR spectra

The azithromycin dehydrate was extracted from a drug capsule (Medquímica) with chloroform, and the excipients were filtered off. Finally, the solvent was removed under reduced pressure yielding 98% of the solid. Thin-layer chromatography (TLC) was performed on TLC plates (silica gel 60 F254) and visualized by an acid solution in ethanol (20%); The ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively. Chemical shifts for ^{1}H and ^{13}C NMR were reported as δ (parts per million - ppm) relative to the signals of DMSO-d_6; at 2.50 ppm (quintet) and 39 ppm (septet); $CDCl_3$ at 7.26 ppm (singlet) and 77 ppm (triplet); CD_3OD at 4.89 (singlet) and D_2O at 4.79 (large singlet). Tetramethylsilane (TMS) was established as the internal reference. NMR chemical shifts are reported employing the following peak abbreviation pattern: br, broad; s, singlet; d, doublet; dd, double doublet; ddd, doublet of doublet of doublet; t, triplet; dt, double triplet; q, quartet; dq; double of quartets; qd, quartet of doublets; dqd, doublet of quartets of doublets; ddq, doublet of doublet of quartets; dtd, doublet of triplet of doublet, and m, multiplet.

Characterization data for Azithromycin

DMSO-d6:

^{1}H NMR (500 MHz, DMSO) δ 4.85 (d, *J* = 4.4 Hz, 1H), 4.75 (d, *J* = 10.0 Hz, 1H), 4.42 (d, *J* = 7.3 Hz, 1H), 4.32 (s, 1H), 4.32 (d, *J* = 8.4 Hz, 1H), 4.31 (s, 1H), 4.20 (d, *J* = 6.6 Hz, 1H), 4.16 (s, 1H), 4.08 (dd, *J* = 8.7, 6.4 Hz, 1H), 3.68 (dt, *J* = 12.2, 6.4 Hz, 1H), 3.52 (d, *J* = 6.8 Hz, 2H), 3.24 (s, 3H), 3.07 (d, *J* = 9.9 Hz, 1H), 3.11 – 3.02 (m, 1H), 3.05 (d, *J* = 7.6 Hz, 1H), 2.93 (d, *J* = 8.4 Hz, 1H), 2.92 (d, *J* = 7.9 Hz, 1H), 2.67 (dt, *J* = 13.5, 6.8 Hz, 2H), 2.48 (d, *J* = 12.0 Hz, 1H), 2.40 (s, *J* = 9.2 Hz, 1H), 2.28 (s, 6H), 2.26 (s, 1H), 2.23 (s, 3H), 2.19 – 2.13 (m, 1H), 1.91 – 1.87 (m, 2H), 1.78 (dt, *J* = 14.6, 8.1 Hz, 1H), 1.63 (d, *J* = 12.6 Hz, 1H), 1.56 – 1.48 (m, 2H), 1.39 (ddd, *J* = 14.5, 7.3, 2.2 Hz, 1H), 1.28 (dd, *J* = 13.5, 7.4 Hz, 1H), 1.24 (s, 2H), 1.19 – 1.14 (m, 9H), 1.12 (s, 1H), 1.11 – 1.08 (m, 6H), 1.02 (s, 3H), 0.96 (d, *J* = 6.9 Hz, 6H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.80 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 177.60, 102.54, 94.96, 83.29, 77.88, 74.09, 73.27, 73.09, 65.29, 49.30, 45.24, 42.10, 40.69, 36.24, 35.13, 30.49, 29.57, 27.95, 26.51, 22.57, 21.90, 21.47, 18.97, 18.19, 15.30, 11.43, 9.51, 7.31.

D_2O:

^{1}H NMR (500 MHz, D_2O) δ 5.49 – 5.43 (m, *J* = 1.2 Hz, 1H), 5.03 (d, *J* = 4.5 Hz, 1H), 4.90 (dd, *J* = 9.9, 1.8 Hz, 2H), 4.51 (d, *J* = 7.6 Hz, 1H), 4.26 – 4.18 (m, 1H), 4.09 (d, *J* = 1.6 Hz, 1H), 3.83 (dd, *J* = 10.8, 5.5 Hz, 1H), 3.72 (s, 1H), 3.63 (d, *J* = 6.7 Hz, 1H), 3.59 (s, 1H), 3.41 (dd, *J* = 10.0, 8.1 Hz, 1H), 3.36 (s, 3H), 3.24 (d, *J* = 9.5 Hz, 1H), 3.08 – 2.97 (m, 3H), 2.85 – 2.77 (m, 1H), 2.65 (d, *J* = 11.2 Hz, 1H), 2.52 (d, *J* = 15.3 Hz, 1H), 2.37 (s, 3H), 2.34 (s, 6H), 2.19 – 2.02 (m, 4H), 1.89 (dd, *J* = 13.3, 3.0 Hz, 1H), 1.85 – 1.78 (m, 2H), 1.70 (dd, *J* = 15.1, 5.1 Hz, 1H), 1.67 (d, *J* = 14.7 Hz, 1H), 1.62 – 1.55 (m, 1H), 1.51 (dd, *J* = 15.5, 7.5 Hz, 1H), 1.34 (s, 3H), 1.33 (s, 2H), 1.29 – 1.22 (m, 7H), 1.17 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 7.3 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H).

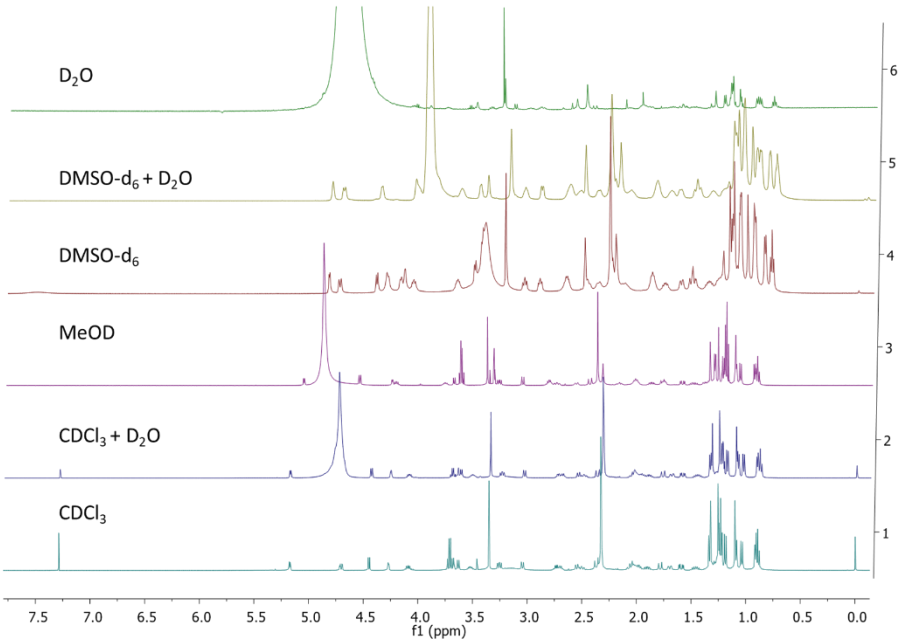


Fig S15 – Azithromycin solution in different solvents

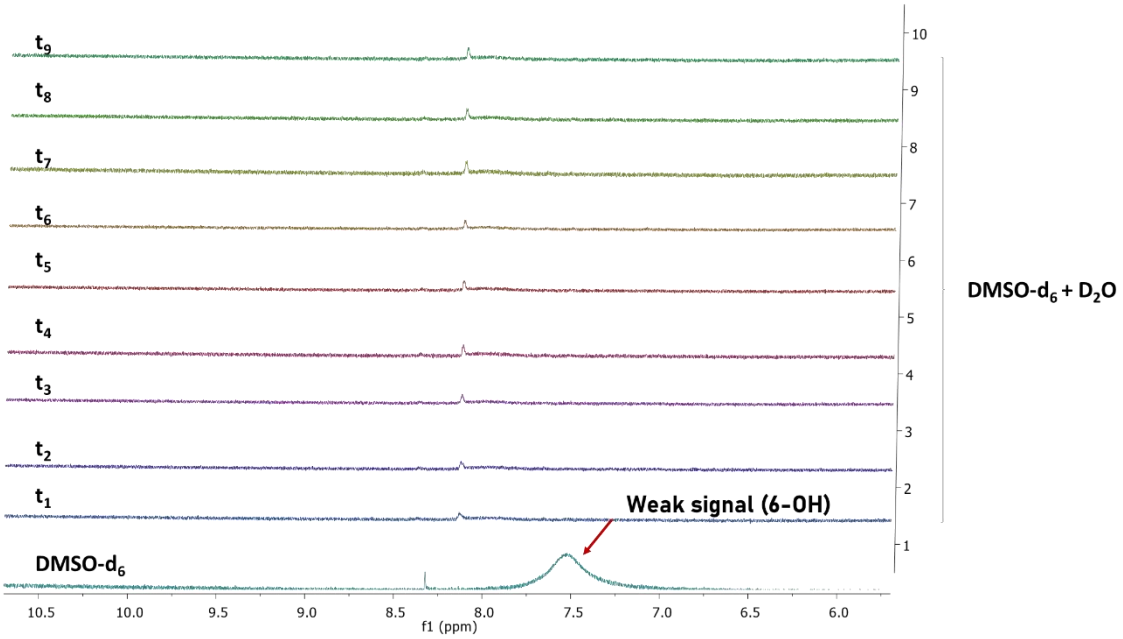


Fig S16 – Expanded signal of 6-OH in DMSO-d_6 and DMSO + D_2O each 10 minutes

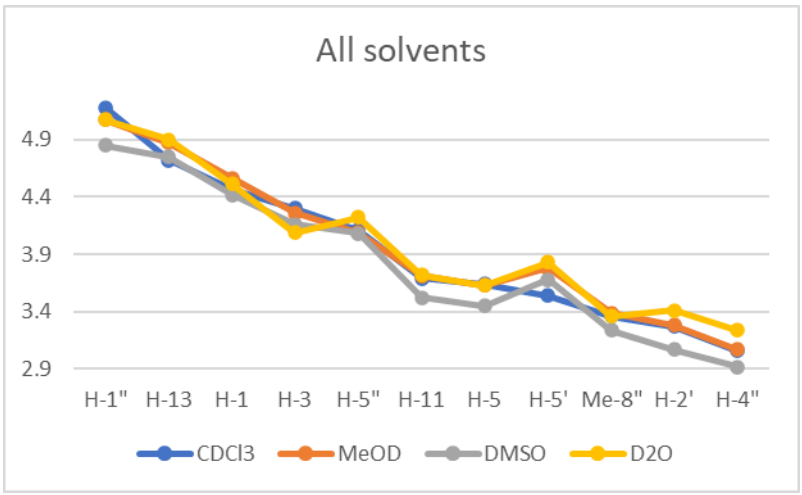


Fig S17 – Oxa-methinic hydrogen atoms in different solvents

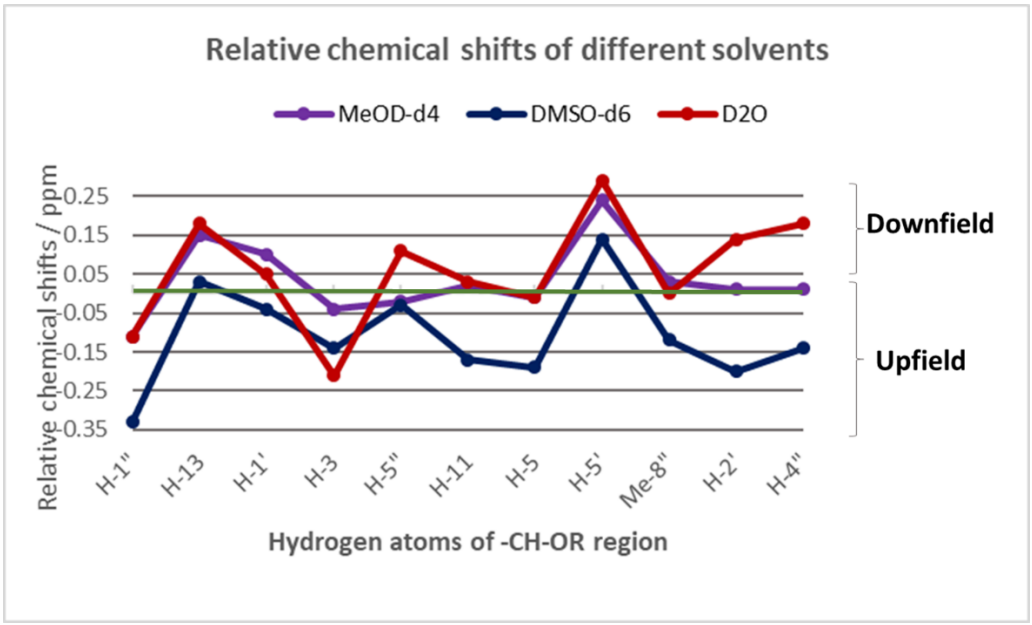


Fig S18 – Relative chemical shifts of oxa-methinic hydrogen atoms in different solvents with $CDCl_3$ (green line)

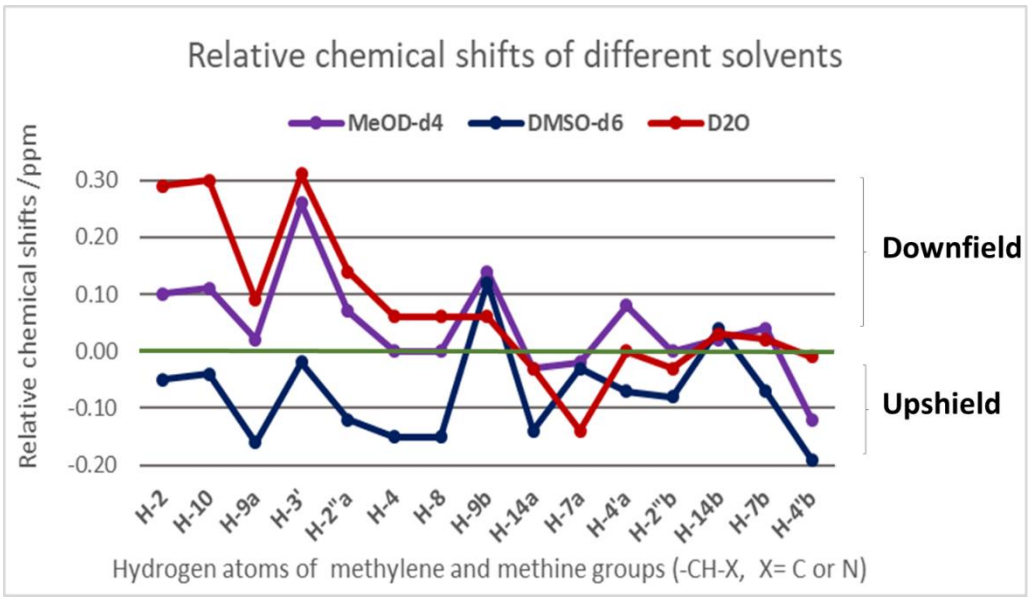
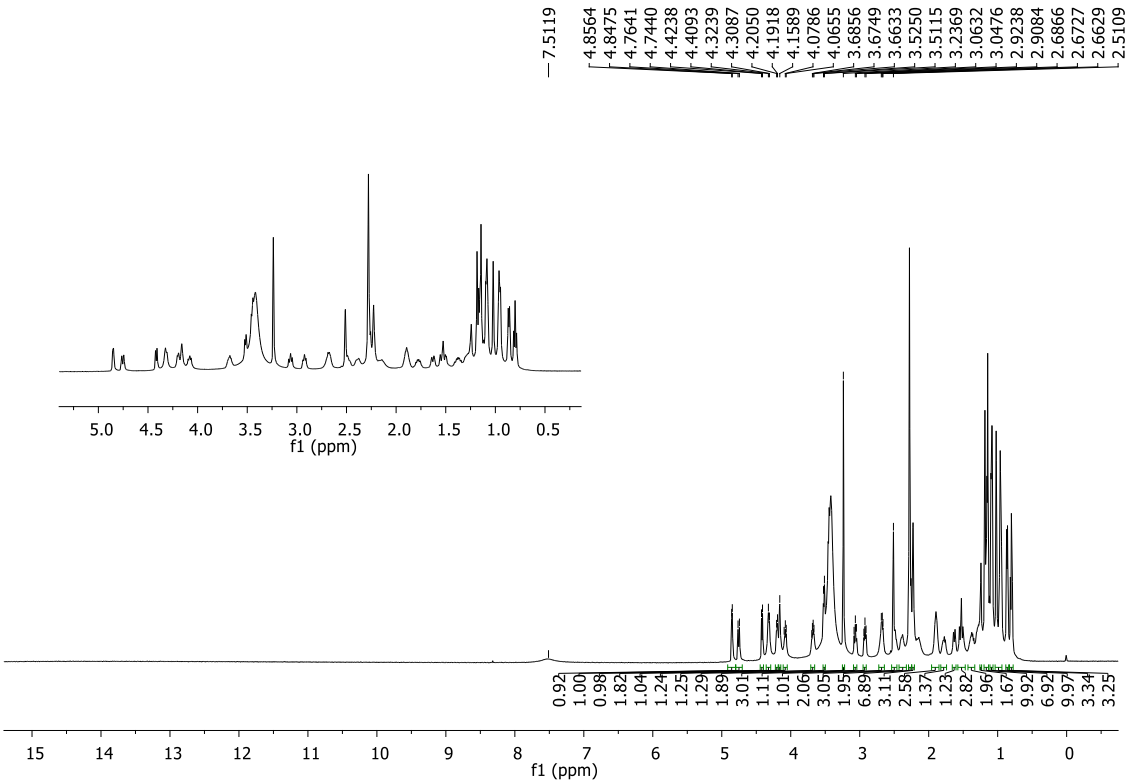
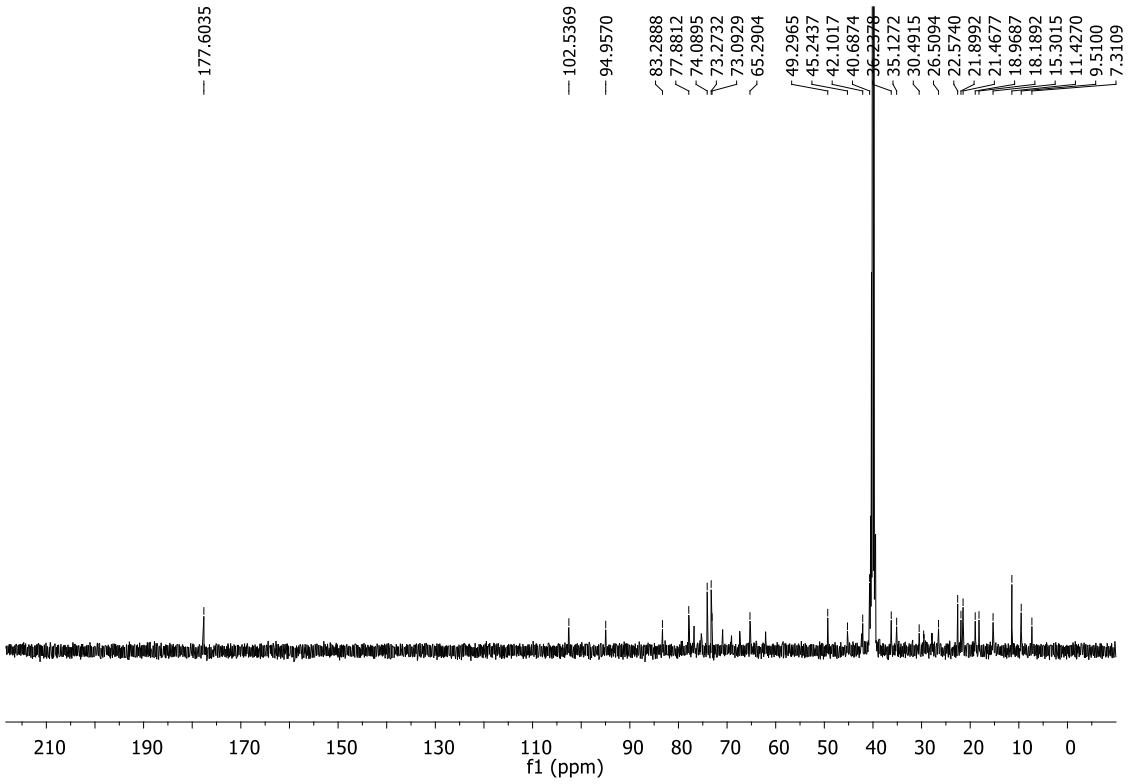


Fig S19 – Relative chemical shifts of methine and methylene hydrogen atoms in different solvents with $CDCl_3$ (green line)

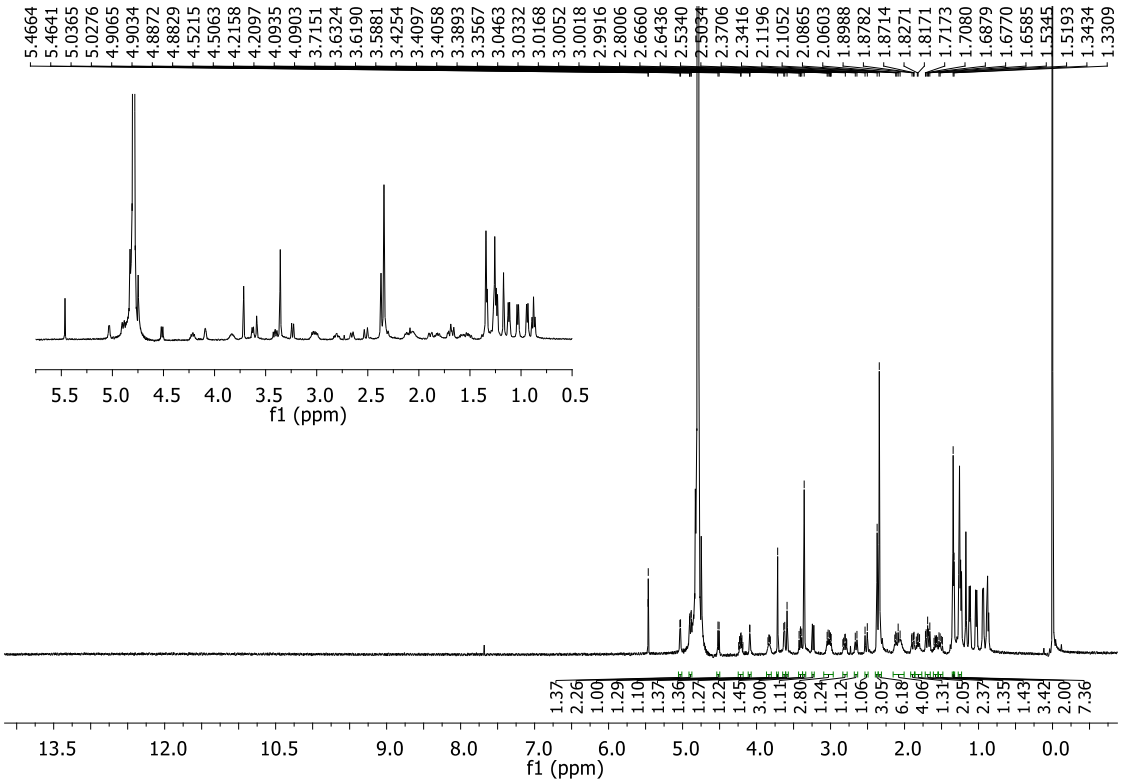
^{1}H, ^{13}C NMR, COSY and NOESY



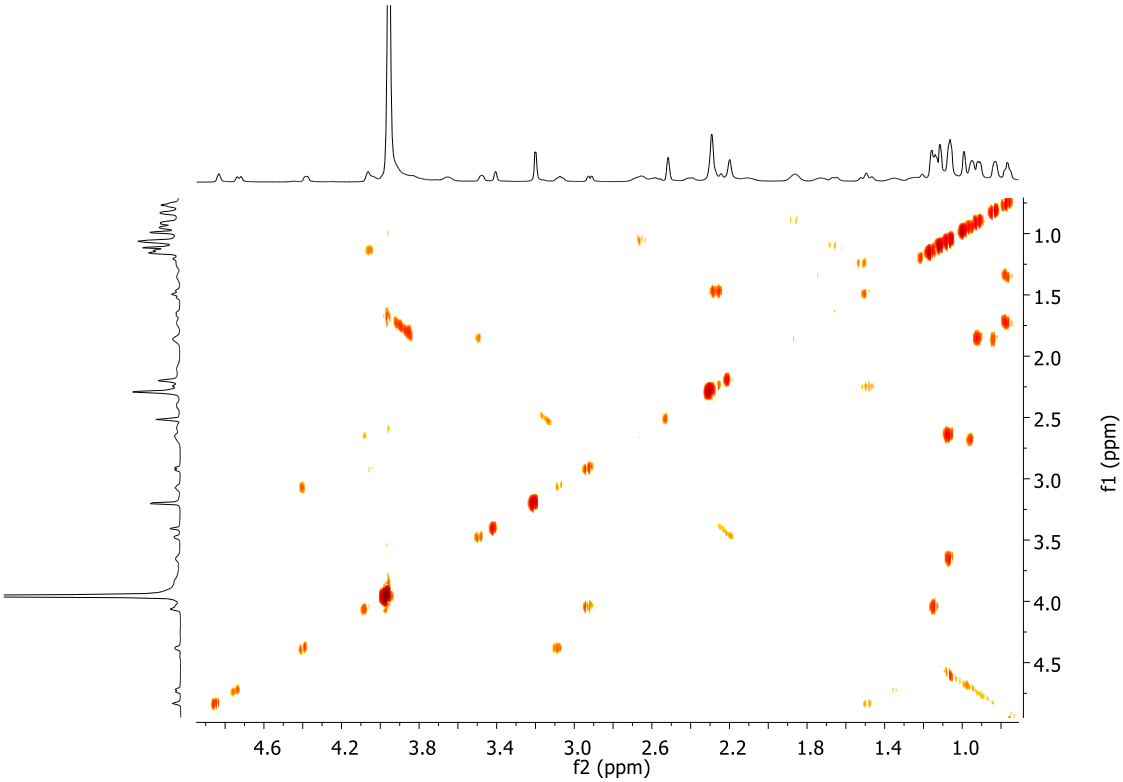
^{1}H NMR spectrum of **Azithromycin** (500 MHz, DMSO-d_6)



^{13}C NMR spectrum of **Azithromycin** (125 MHz, DMSO-d_6)



^{1}H NMR spectrum of **Azithromycin** (500 MHz, D_2O)



COSY contour map of **Azithromycin** in DMSO-*d*$_6$

DFT Optimized Cartesian Coordinates for Relevant Structures

(ωB97X-D/6-31G(d,p)-PCM-Water) – Charge = 0; Spin Multiplicity = 1

Str. M5 - Etot (au) = −2502.92329294

Atomic Number	X	Y	Z
1	-6.163536	-4.531231	1.381989
1	-5.194402	-0.810977	-1.379025
6	-1.347564	2.610864	1.308504
6	2.300247	2.065171	0.690867
1	3.346441	2.227054	0.947523
1	2.214040	1.940141	-0.392840
8	0.979863	0.306029	-1.817902
8	-7.242707	-2.376272	-0.974036
1	3.488470	0.630955	4.408018
1	4.615097	1.314599	2.265469
1	-7.469767	-3.329057	1.441838
6	5.608551	1.218927	0.034288
1	3.452188	-0.004076	-1.203647
6	-5.156847	-2.148247	-3.061872
6	3.506299	-0.863135	-1.874046
6	-4.077426	-2.782632	0.983828
6	3.979717	-2.924927	-0.440815
6	-3.253118	-1.892908	0.074047
8	-3.595497	-2.123524	-1.283924
6	-1.470329	-0.629655	2.422224
6	-5.896514	-2.718501	-0.718068
1	-3.427259	-0.833493	0.308400
1	5.814014	-0.215044	-3.578626
1	5.059200	1.220490	-2.862812
1	4.512400	-2.594682	2.407182
1	5.957684	-2.450754	1.411800
1	5.935840	-1.744317	3.032277
6	5.332758	-1.934411	2.134838
6	3.665797	-0.390125	-3.316090
1	3.629770	-1.262147	-3.973513
1	2.784163	0.218952	-3.526665
8	-1.915309	-2.208809	0.237408
1	-6.206888	-3.348703	2.693930
6	0.060738	-1.790481	-0.977120
6	-1.823067	4.488866	-0.272112
1	-3.842423	-3.825851	0.751174
1	-5.766680	-3.773133	-0.986235
1	0.579694	-2.567794	-0.408389
6	-5.572224	-2.550492	0.775451
1	-1.509762	-0.344733	-0.560402
6	1.130609	-0.859775	-1.512813
8	2.250188	-1.555176	-1.744553
6	-0.722013	3.654268	0.381379
1	-4.916712	-3.193206	-3.276644
1	-6.197976	-1.967380	-3.330259
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1	-4.513932	-1.508276	-3.668133
1	-1.340910	-3.159431	-1.901325
1	0.151922	-2.903184	-2.840534
1	-1.116665	-1.659476	-2.797495
6	-2.805734	3.574036	-0.996972
8	-0.419294	1.782535	1.924662
6	-4.960623	-1.863757	-1.588462
8	-2.271123	1.819364	0.588559
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6	4.926980	0.419779	-3.597024
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6	4.597475	0.302226	2.663037

6	3.264854	0.142498	3.452959
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1	-3.801578	-2.606161	2.027234
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7	4.840569	-0.663126	1.564473
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6	5.846920	-1.158275	-0.745988
1	6.224330	-0.516303	-1.550078
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1	2.119643	1.965063	3.168158
1	1.747057	2.957363	0.993537
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1	6.365230	1.430300	-0.723178
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1	3.404975	-2.486290	0.373227
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1	-1.838349	-1.643631	2.578012
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1	-3.692326	0.909097	-1.333207
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1	0.032791	4.287820	-2.151829
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1	-1.567849	7.516282	-1.711296
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1	-2.508902	7.035246	-0.287424
1	-2.311987	3.038232	-1.814768
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1	-1.859783	3.141528	2.125016
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1	-6.074052	0.342276	2.328529
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1	-5.932710	-1.247310	3.109203
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8	6.825621	-2.158043	-0.501052
1	6.754746	-2.752253	-1.261272
8	5.194643	-2.546857	-2.468531
1	4.591022	-3.237389	-2.757518
8	0.111996	4.504566	1.132366
1	0.138818	5.314450	0.595104
8	2.228905	-0.364970	0.820592
1	3.188625	-0.485107	1.022595

Str. M12 - Etot (au) = −2502.9524638

Atomic Number	X	Y	Z
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1	-6.507786	-0.917807	1.967051
1	-3.873155	-0.285587	1.983012
6	0.409710	2.881382	-2.478013
1	1.423055	2.480033	-2.389698
1	-0.090284	2.388304	-3.308839
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8	6.038813	-2.567911	-0.676772
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1	-3.216910	1.650456	0.832026
1	3.324647	1.030898	-1.969560
1	4.948401	-0.825896	-4.067684
6	-6.687796	1.783143	0.718322
1	-4.478342	-2.278566	1.830057
6	3.994772	-4.083854	0.842124
6	-4.779783	-2.526292	0.809098
6	2.863732	-1.617134	-2.434019
6	-6.238433	-1.703758	-1.098900
6	2.044546	-1.727785	-1.164631
8	2.399235	-2.918286	-0.474811
6	-0.793872	0.037899	-2.679581
6	4.718865	-2.724967	-1.156722
1	2.230146	-0.879117	-0.512967
1	4.873095	1.001017	-2.872535
1	-4.869166	-5.933245	1.455567
1	-4.282442	-4.655670	2.529706
1	-5.899545	2.829886	-2.099377
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1	-4.363749	3.696901	-2.009965
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8	2.692124	2.718962	0.192226
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1	-6.119963	0.864827	-1.127043
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6	-2.524570	3.482366	0.005696
6	-1.828076	3.072476	-1.308956
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1	-1.863129	0.173892	-0.842897
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6	-0.339663	2.731818	-1.150578
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6	-0.250057	-1.247738	-0.588878
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6	5.202705	-1.634197	-3.379511
6	-4.962388	-0.062216	0.404521
1	-4.021550	-0.169832	-0.145197
1	-3.470640	-4.956359	0.989084
1	-1.895307	3.900972	-2.022518
1	0.469688	3.948089	-2.702486
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1	-1.955977	5.551396	-0.104268
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1	-6.963116	-0.952343	-1.412180
1	-6.737561	-2.673610	-1.123235
1	-1.413826	0.822301	-3.113994
1	0.222804	0.128441	-3.065895
1	-1.191107	-0.922008	-3.015698
1	2.815478	3.783881	1.954142
1	3.090892	1.621915	3.166133
6	4.134253	4.567770	0.438112
1	3.376850	5.206476	-0.019374
1	4.726158	5.167134	1.131295
1	4.793985	4.186341	-0.345643
7	4.567485	0.195909	2.998790
6	5.708019	-0.222714	2.192440
1	6.120951	-1.145141	2.605987
1	5.404896	-0.419379	1.161702
1	6.507386	0.533928	2.176301
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1	5.716006	1.374729	4.359919
1	4.134068	0.808668	4.955273
1	5.484959	-0.327004	4.799932
1	5.197913	2.129607	1.002977
1	5.080765	2.975171	2.551748
1	1.232176	1.992583	1.470750
8	2.141196	-0.444122	1.876619
1	3.524869	0.247414	0.495885
1	2.761675	-0.832557	2.515582

Str. M13 - Etot (au) = -2502.96963459

Atomic Number	X	Y	Z
1	6.261897	-1.570365	-3.126649
1	1.158524	3.620976	-0.265833
1	3.833954	-1.955929	0.653452
6	1.938656	1.629048	0.708655
1	-6.507786	-0.917807	1.967051
1	-3.873155	-0.285587	1.983012
6	0.409710	2.881382	-2.478013
1	1.423055	2.480033	-2.389698
1	-0.090284	2.388304	-3.308839
8	-2.378664	-1.286260	1.401751
8	6.038813	-2.567911	-0.676772
1	-1.793790	3.363890	0.810978
1	-3.216910	1.650456	0.832026
1	3.324647	1.030898	-1.969560
1	4.948401	-0.825896	-4.067684
6	-6.687796	1.783143	0.718322
1	-4.478342	-2.278566	1.830057
6	3.994772	-4.083854	0.842124
6	-4.779783	-2.526292	0.809098
6	2.863732	-1.617134	-2.434019
6	-6.238433	-1.703758	-1.098900
6	2.044546	-1.727785	-1.164631
8	2.399235	-2.918286	-0.474811
6	-0.793872	0.037899	-2.679581
6	4.718865	-2.724967	-1.156722
1	2.230146	-0.879117	-0.512967
1	4.873095	1.001017	-2.872535
1	-4.869166	-5.933245	1.455567
1	-4.282442	-4.655670	2.529706
1	-5.899545	2.829886	-2.099377
1	-5.613405	3.992233	-0.786319
1	-4.363749	3.696901	-2.009965
6	-5.142520	3.217094	-1.412833
6	-5.367535	-3.925436	0.797381
1	-6.335283	-3.871965	1.302617
1	-5.554145	-4.232757	-0.235175
8	0.705157	-1.787726	-1.503538
1	5.020788	-2.579699	-3.893855
6	-1.314943	-2.349142	-0.484371
6	3.764337	1.253517	2.381144
1	2.663062	-2.492892	-3.056489
8	-6.838426	-1.377304	1.181375
1	4.678565	-3.661685	-1.724847
8	-4.715311	0.156732	1.790263
8	0.191730	3.711091	-0.254890
1	-1.717214	-2.542263	-1.482804
6	4.358010	-1.568714	-2.112514
1	0.214148	-1.093560	0.390764
6	-2.469287	-1.982016	0.402871
8	-3.589877	-2.571275	-0.012299
6	2.886397	0.610012	1.311275
1	5.009619	-4.046977	1.239995
1	3.286823	-4.144305	1.670108
6	3.486108	3.410360	1.166110
1	6.152469	-1.613474	-0.573633
1	3.890008	-4.980612	0.226162
1	0.140391	-3.948178	-0.503351
1	-1.475265	-4.448888	0.068190
1	-0.403875	-3.492393	1.112681
6	4.501266	2.453064	1.785353
8	1.259227	1.065025	-0.361281
6	3.729908	-2.844722	0.015954

8	2.692124	2.718962	0.192226
6	-0.728319	-3.651661	0.081743
1	-2.358055	2.231849	-1.766317
6	4.404980	0.862498	-1.893104
6	-4.446162	-4.927911	1.483567
1	-6.119963	0.864827	-1.127043
6	-3.675486	2.549335	0.412178
6	-2.524570	3.482366	0.005696
6	-1.828076	3.072476	-1.308956
6	-5.624142	1.179759	-0.203833
1	2.557055	-0.731425	-2.998738
1	-0.563369	1.405669	0.520034
1	-1.863129	0.173892	-0.842897
1	4.801584	1.601292	-1.195726
6	-0.339663	2.731818	-1.150578
6	-0.139595	1.331564	-0.492021
6	-0.811947	0.096593	-1.150454
8	4.702525	-0.406269	-1.340677
1	-4.224427	3.036804	1.237282
7	-4.576868	2.116229	-0.653260
6	-0.250057	-1.247738	-0.588878
6	-5.728171	-1.405205	0.298774
6	5.202705	-1.634197	-3.379511
6	-4.962388	-0.062216	0.404521
1	-4.021550	-0.169832	-0.145197
1	-3.470640	-4.956359	0.989084
1	-1.895307	3.900972	-2.022518
1	0.469688	3.948089	-2.702486
6	-2.875109	4.973494	0.013676
1	-3.554139	5.252204	-0.795368
1	-3.346297	5.257593	0.958787
1	-1.955977	5.551396	-0.104268
1	-7.443348	1.028788	0.944288
1	-7.176332	2.634794	0.240962
1	-6.246026	2.114719	1.658548
1	-5.409440	-1.720115	-1.809358
1	-6.963116	-0.952343	-1.412180
1	-6.737561	-2.673610	-1.123235
1	-1.413826	0.822301	-3.113994
1	0.222804	0.128441	-3.065895
1	-1.191107	-0.922008	-3.015698
1	2.815478	3.783881	1.954142
1	3.090892	1.621915	3.166133
6	4.134253	4.567770	0.438112
1	3.376850	5.206476	-0.019374
1	4.726158	5.167134	1.131295
1	4.793985	4.186341	-0.345643
7	4.567485	0.195909	2.998790
6	5.708019	-0.222714	2.192440
1	6.120951	-1.145141	2.605987
1	5.404896	-0.419379	1.161702
1	6.507386	0.533928	2.176301
6	4.998598	0.538822	4.345605
1	5.716006	1.374729	4.359919
1	4.134068	0.808668	4.955273
1	5.484959	-0.327004	4.799932
1	5.197913	2.129607	1.002977
1	5.080765	2.975171	2.551748
1	1.232176	1.992583	1.470750
8	2.141196	-0.444122	1.876619
1	3.524869	0.247414	0.495885
1	2.761675	-0.832557	2.515582

Str. M14 - Etot (au) = −2502.9721794

Atomic Number	X	Y	Z
8	-3.869944	-2.005674	-1.101399
8	-3.145819	-1.966846	1.033103
8	-5.051444	0.040916	1.476186
1	-4.441519	-0.696104	1.641894
8	-7.059167	-0.436830	-0.246193
1	-6.934577	-0.415545	0.714047
8	0.778390	-2.083145	-0.082780
8	1.337023	1.593441	-0.629362
8	-1.675243	1.141310	1.332016
1	-2.510510	1.573539	1.032792
8	3.147712	0.945964	-2.777909
1	3.989945	0.896079	-3.264962
8	3.082302	1.822365	0.763361
8	3.758488	-2.074360	-0.283232
8	5.036066	-1.700288	2.031553
1	5.175816	-1.399884	1.122993
8	1.376879	-2.059167	2.187731
7	-3.897877	2.617611	0.705483
7	5.796175	1.406375	-2.442781
6	-2.930552	-2.084469	-0.161248
6	-1.576005	-2.398811	-0.742772
1	-1.622036	-2.183458	-1.810664
6	-0.514157	-1.490738	-0.074385
1	-0.819067	-1.306599	0.960852
6	-0.414184	-0.138178	-0.799361
1	-1.445722	0.218470	-0.916359
6	0.346333	0.868091	0.100905
1	0.844267	0.304034	0.897981
6	-0.590084	1.888324	0.806104
6	-1.040899	2.952116	-0.214091
1	-0.123481	3.375937	-0.628113
1	-1.550322	2.446479	-1.045877
6	-1.937963	4.105415	0.283262
1	-1.789595	4.252092	1.358035
6	-3.420557	3.824065	0.029880
1	-3.547566	3.687562	-1.049010
1	-4.023544	4.700496	0.320228
6	-5.004019	1.947609	-0.010662
1	-4.826106	2.159183	-1.068414
6	-4.831832	0.432319	0.126953
1	-3.787135	0.247276	-0.148156
6	-5.741715	-0.443153	-0.773374
6	-5.251894	-1.911576	-0.685195
1	-5.308264	-2.213396	0.363737
6	-4.155205	2.884323	2.121408
1	-4.506164	1.972346	2.600403
1	-3.219871	3.189040	2.596805
1	-4.896028	3.682988	2.265347
6	-1.365374	-3.911403	-0.589644
1	-1.496789	-4.229928	0.445959
1	-2.094971	-4.448449	-1.200953
1	-0.361596	-4.180722	-0.921735
6	-6.388240	2.481292	0.350484
1	-6.660048	2.217302	1.374288
1	-6.397876	3.570571	0.260379
1	-7.142916	2.063107	-0.315932
6	-5.797405	0.046012	-2.210414
1	-6.424228	-0.612216	-2.813990
1	-6.224023	1.048948	-2.259805
1	-4.795080	0.063881	-2.644236
6	-6.024741	-2.908909	-1.527245
1	-7.087253	-2.734495	-1.341281

1	-5.838334	-2.714198	-2.587168
6	-5.637227	-4.344503	-1.184216
1	-5.850324	-4.562928	-0.134129
1	-6.186883	-5.058373	-1.799282
1	-4.566779	-4.506331	-1.348433
6	0.211276	-0.281574	-2.186486
1	0.302567	0.690704	-2.668289
1	1.216164	-0.702807	-2.129525
1	-0.398743	-0.924462	-2.825167
6	0.165975	2.520167	1.975063
1	0.451471	1.734065	2.680739
1	1.075886	3.015626	1.632889
1	-0.468774	3.232120	2.507641
6	-1.560703	5.410563	-0.417023
1	-1.683828	5.308916	-1.500033
1	-2.188465	6.240035	-0.082356
1	-0.517660	5.666586	-0.221126
6	2.642030	1.186010	-0.426218
1	2.700786	0.091031	-0.325670
6	3.520230	1.608662	-1.594320
1	3.420396	2.700232	-1.705050
6	4.969284	1.243269	-1.248279
1	4.969130	0.163660	-1.035254
6	5.389408	1.975451	0.024016
1	6.414725	1.718515	0.306279
1	5.340033	3.060043	-0.123427
6	4.433118	1.579861	1.146378
1	4.557965	0.508388	1.349688
6	4.662277	2.353415	2.428613
1	4.531200	3.424209	2.253905
1	3.949064	2.034655	3.191360
1	5.674681	2.179483	2.797463
6	6.997747	0.588948	-2.405128
1	6.728156	-0.455013	-2.229686
1	7.511450	0.660791	-3.366581
1	7.703734	0.903518	-1.620156
6	6.115947	2.792183	-2.756258
1	6.593447	2.833646	-3.737579
1	5.203479	3.389499	-2.793944
1	6.800412	3.247752	-2.024670
6	1.094721	-2.844814	1.057163
1	0.222330	-3.427051	1.364861
6	2.234921	-3.781461	0.692226
1	2.269556	-4.574486	1.443635
1	2.017290	-4.259122	-0.265559
6	3.616193	-3.122759	0.682115
6	3.788958	-2.368275	2.008844
1	3.783150	-3.087993	2.834004
6	2.630999	-1.376677	2.191386
1	2.663213	-0.678712	1.355105
6	4.704127	-4.173191	0.484211
1	5.687664	-3.701808	0.493293
1	4.663543	-4.914190	1.285646
1	4.569615	-4.694265	-0.466284
6	3.496832	-2.380364	-1.637880
1	4.198277	-3.125595	-2.028653
1	2.468342	-2.727990	-1.771034
1	3.609167	-1.441787	-2.185020
6	2.703952	-0.595013	3.482846
1	3.686416	-0.130781	3.578345
1	1.942017	0.189311	3.486527
1	2.541251	-1.256151	4.336990

Str. M15 - Etot (au) = −2502.9682918

Atomic Number	X	Y	Z
8	-3.723799	-1.880512	-0.924212
8	-2.629924	-3.504582	0.181609
8	-4.170287	0.180692	1.653391
1	-3.210176	0.281759	1.699455
8	-6.608489	-0.709536	0.913314
1	-6.154971	-0.632685	1.762963
8	0.676143	-1.833956	-0.317333
8	1.460204	1.729336	-0.828906
8	-1.707396	1.343781	0.869862
1	-2.538945	1.879873	0.712844
8	3.581842	0.966901	-2.633964
1	4.490866	0.819142	-2.951248
8	2.953223	1.847123	0.849404
8	3.578941	-2.090553	-0.125254
8	4.484900	-1.836197	2.367865
1	4.773582	-1.517513	1.501716
8	0.830771	-2.060426	1.997858
7	-3.880713	2.783463	0.567629
7	6.160958	1.218349	-1.822913
6	-2.651642	-2.630830	-0.661908
6	-1.471380	-2.186024	-1.487576
1	-1.871820	-1.578858	-2.301334
6	-0.586263	-1.251615	-0.589573
1	-1.098988	-1.056002	0.360820
6	-0.343840	0.101702	-1.261316
1	-1.345673	0.486103	-1.484766
6	0.337296	1.062673	-0.252487
1	0.683986	0.472258	0.602681
6	-0.630388	2.107849	0.346503
6	-1.092631	3.092954	-0.747164
1	-0.175301	3.533363	-1.150106
1	-1.552674	2.528521	-1.567895
6	-2.052264	4.240610	-0.364069
1	-1.802888	4.605473	0.637799
6	-3.534026	3.832511	-0.391432
1	-3.751447	3.457087	-1.395799
1	-4.155430	4.727266	-0.231634
6	-5.026641	1.921433	0.174982
1	-5.186572	2.093598	-0.893703
6	-4.565573	0.455832	0.311876
1	-3.701213	0.342064	-0.349688
6	-5.587613	-0.635617	-0.071063
6	-4.859866	-2.005165	-0.046981
1	-4.472590	-2.130190	0.966582
6	-3.926951	3.291399	1.937697
1	-2.953362	3.713492	2.193270
1	-4.687895	4.071492	2.071346
1	-4.127139	2.467073	2.620914
6	-0.718110	-3.375132	-2.077019
1	-1.331122	-3.868680	-2.833289
1	0.212905	-3.043044	-2.538629
1	-0.476302	-4.108568	-1.306197
6	-6.322725	2.260688	0.907462
1	-7.153201	1.689433	0.494683
1	-6.256227	2.012779	1.968355
1	-6.540118	3.326409	0.811474
6	-6.255733	-0.357715	-1.407050
1	-6.766311	0.605940	-1.401955
1	-5.513670	-0.359938	-2.207931
1	-7.000962	-1.125866	-1.616701
6	-5.722942	-3.215866	-0.416539
1	-5.390916	-4.063627	0.185966

1	-6.745438	-2.986123	-0.106080
6	-5.679111	-3.630443	-1.885876
1	-4.677598	-3.965293	-2.165414
1	-6.366599	-4.461249	-2.054358
1	-5.958043	-2.821028	-2.562152
6	0.432834	-0.044422	-2.567629
1	-0.096164	-0.708673	-3.256157
1	0.555511	0.925195	-3.048531
1	1.432050	-0.446387	-2.394971
6	0.062197	2.838030	1.497573
1	0.916684	3.414281	1.141900
1	-0.639877	3.501164	2.009020
1	0.431015	2.103437	2.218969
6	-1.870106	5.412398	-1.332100
1	-0.845920	5.789344	-1.298550
1	-2.079518	5.097038	-2.359606
1	-2.546789	6.235027	-1.087486
6	2.685904	1.241517	-0.404831
1	2.651669	0.145086	-0.302519
6	3.785279	1.600927	-1.394182
1	3.788647	2.696802	-1.504867
6	5.117612	1.124826	-0.801354
1	4.995125	0.049217	-0.606582
6	5.358968	1.810655	0.541761
1	6.290867	1.460910	0.996322
1	5.426596	2.897449	0.420217
6	4.186600	1.479943	1.461291
1	4.184017	0.397346	1.644385
6	4.248908	2.205493	2.788017
1	3.375114	1.959060	3.394566
1	5.148068	1.912636	3.333030
1	4.271802	3.286046	2.629021
6	6.605845	2.580466	-2.085614
1	7.298968	2.573326	-2.928895
1	5.756125	3.212439	-2.350485
1	7.120492	3.030901	-1.224217
6	7.290365	0.355552	-1.513091
1	7.822699	0.670943	-0.601667
1	6.939674	-0.669064	-1.372874
1	8.003323	0.370760	-2.340012
6	0.701463	-2.728563	0.766773
1	-0.259580	-3.249661	0.838954
6	1.827123	-3.725623	0.538153
1	1.699311	-4.541415	1.254222
1	1.738569	-4.157337	-0.461453
6	3.225823	-3.150333	0.770871
6	3.228976	-2.445347	2.136950
1	3.074582	-3.192756	2.923733
6	2.089420	-1.417536	2.205799
1	2.251821	-0.682191	1.414766
6	4.278040	-4.254075	0.711175
1	4.083784	-5.002375	1.482421
1	4.260882	-4.756032	-0.258849
1	5.269869	-3.831253	0.874232
6	3.480645	-2.335687	-1.514102
1	4.138635	-3.152404	-1.830397
1	2.447307	-2.553322	-1.801292
1	3.780127	-1.407135	-2.004812
6	2.013558	-0.700916	3.535124
1	1.236156	0.067513	3.503536
1	1.784947	-1.406071	4.337950
1	2.970616	-0.222823	3.748611