

A DFT Study of the Chemical Reactivity of Cimetidine A, C and D in Gas, H₂O, MeOH and EtOH solvents.

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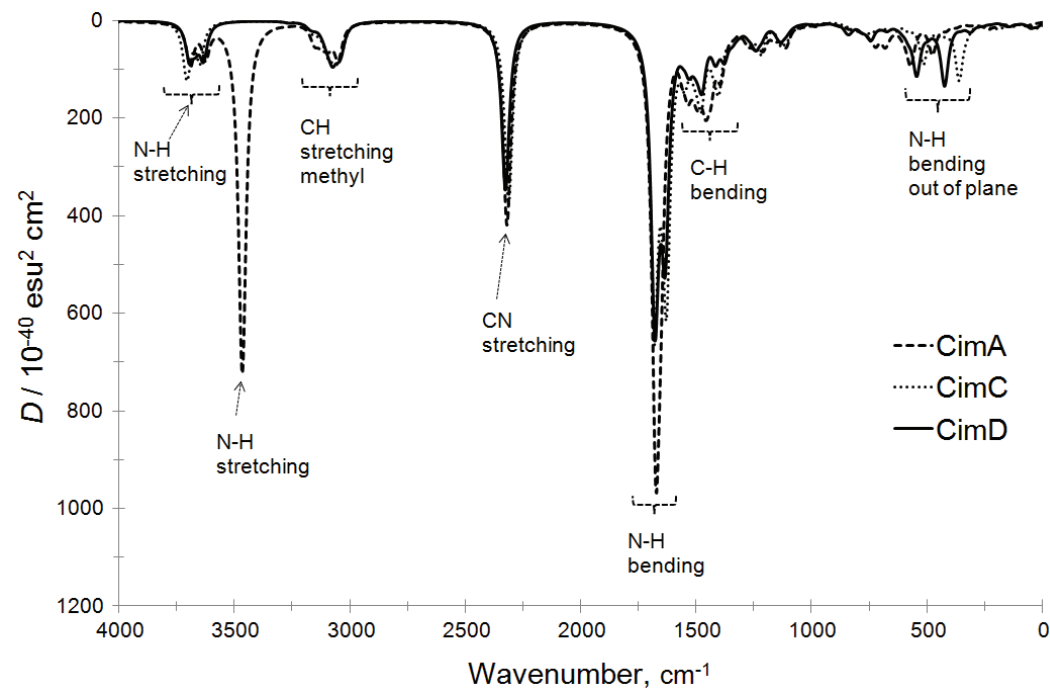
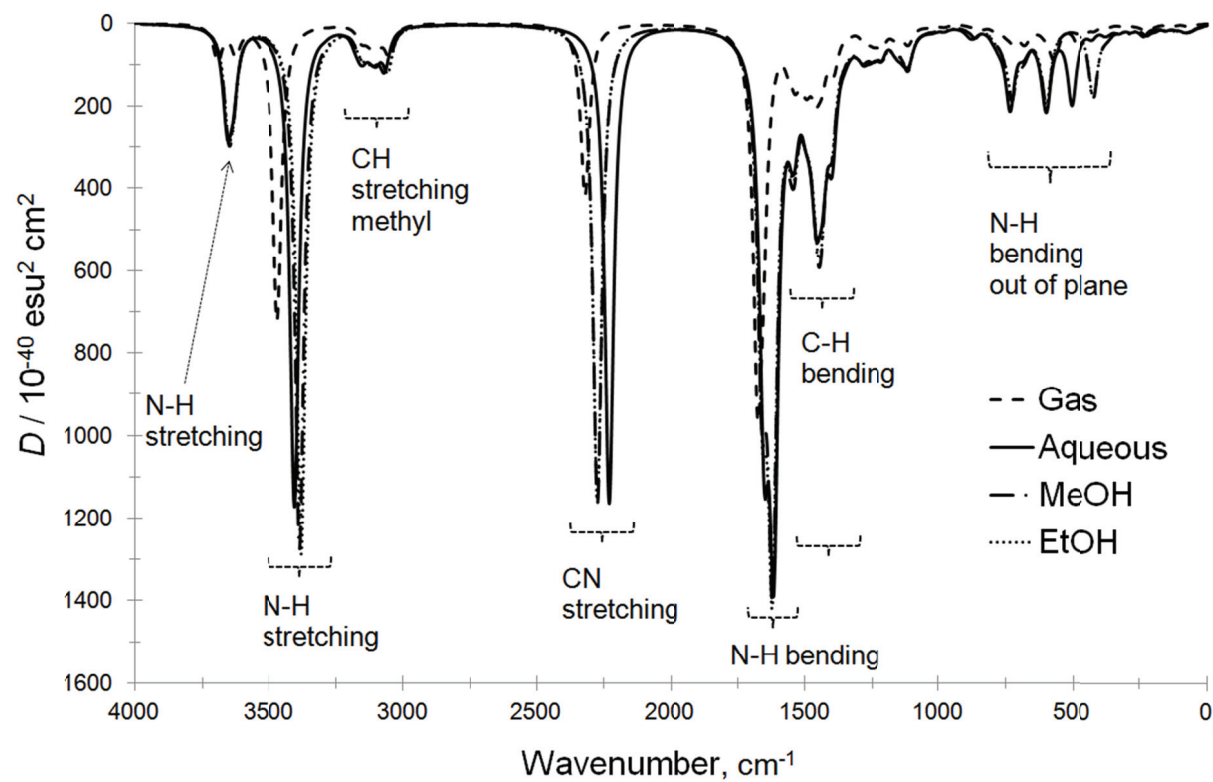


Figure 1S. Theoretical IR spectra of a) CimA, b) CimC and c) CimD obtained at wB97XD/def2TZVP level of theory in the gas phase.



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8 Figure 2S. Theoretical IR spectra of CimA obtained at the wB97XD/def2TZVP level of theory in the different solvents indicated into the Figure.

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11 Table 1S. Electronic energies including the zero-point vibrational energy correction (ZPE) in hartrees (Eh) for CimA, CimC and CimD at the
 12 wB97XD/def2TZVP level of theory.

Solvent	Electronic energy + ZPE / Eh		
	CimA	CimC	CimD
Gas	-1117.18590	-1117.16810	-1117.17586
H ₂ O	-1117.21585	-1117.20897	-1117.21457
MeOH	-1117.22783	-1117.21860	-1117.22364
EtOH	-1117.22900	-1117.21939	-1117.22459

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15 Table 2S. XYZ coordinates for optimized CimA at the wB97XD /def2TZVP level of theory in different solvents.

	Gas			H ₂ O	Y	Z	MeOH			EtOH	y	z
	x	y	z				x	y	z			
S	1.526	2.436	-0.017	1.517	2.447	-0.100	1.494	2.456	-0.146	1.487	2.457	-0.155
N	3.031	-1.928	-0.716	2.943	-1.970	-0.621	3.049	-1.956	-0.584	3.065	-1.952	-0.583
N	1.321	-1.124	0.393	1.342	-1.111	0.607	1.329	-1.075	0.449	1.327	-1.067	0.414
N	-2.292	0.947	0.095	-2.290	0.967	0.273	-2.307	0.958	0.207	-2.311	0.955	0.203
N	-1.654	-1.229	0.579	-1.616	-1.230	0.545	-1.621	-1.235	0.466	-1.622	-1.236	0.463
N	-3.776	-0.849	-0.177	-3.715	-0.820	-0.262	-3.768	-0.834	-0.197	-3.775	-0.839	-0.184
N	-5.517	0.773	-0.865	-5.565	0.698	-0.859	-5.666	0.651	-0.705	-5.676	0.643	-0.690

C	1.769	-2.147	-0.285	1.744	-2.176	-0.046	1.787	-2.145	-0.154	1.793	-2.137	-0.184
C	2.341	-0.199	0.403	2.339	-0.171	0.437	2.354	-0.150	0.404	2.355	-0.147	0.395
C	3.417	-0.681	-0.288	3.346	-0.693	-0.326	3.436	-0.687	-0.239	3.450	-0.686	-0.224
C	4.746	-0.096	-0.603	4.624	-0.121	-0.818	4.775	-0.142	-0.571	4.800	-0.146	-0.521
C	2.176	1.120	1.066	2.235	1.192	1.017	2.204	1.208	0.984	2.198	1.210	0.976
C	-0.030	1.705	-0.568	-0.066	1.697	-0.531	-0.087	1.705	-0.588	-0.094	1.708	-0.596
C	-1.068	1.566	0.544	-1.024	1.569	0.646	-1.047	1.564	0.588	-1.052	1.563	0.581
C	-2.594	-0.373	0.151	-2.541	-0.349	0.170	-2.570	-0.358	0.150	-2.575	-0.360	0.152
C	-1.915	-2.648	0.650	-1.824	-2.660	0.456	-1.841	-2.665	0.436	-1.842	-2.666	0.440
C	-4.696	0.022	-0.537	-4.663	0.019	-0.564	-4.744	-0.014	-0.456	-4.753	-0.022	-0.442
H	3.592	-2.566	-1.251	3.465	-2.642	-1.160	3.618	-2.636	-1.063	3.642	-2.632	-1.052
H	1.229	-3.057	-0.491	1.212	-3.110	-0.130	1.252	-3.069	-0.304	1.257	-3.058	-0.349
H	-3.035	1.540	-0.240	-2.975	1.583	-0.136	-3.029	1.578	-0.120	-3.038	1.575	-0.117
H	-0.675	-0.960	0.602	-0.647	-0.938	0.673	-0.647	-0.942	0.558	-0.647	-0.942	0.542
H	4.869	0.060	-1.677	4.599	0.030	-1.900	4.904	-0.032	-1.651	4.949	-0.016	-1.596
H	5.560	-0.735	-0.255	5.464	-0.781	-0.592	5.570	-0.797	-0.206	5.582	-0.816	-0.155
H	4.850	0.874	-0.120	4.809	0.844	-0.349	4.908	0.840	-0.117	4.933	0.824	-0.045
H	1.539	1.013	1.944	1.664	1.166	1.944	1.608	1.168	1.896	1.600	1.168	1.886
H	0.162	0.738	-1.034	0.107	0.728	-0.999	0.087	0.740	-1.065	0.079	0.743	-1.075
H	-0.401	2.376	-1.344	-0.496	2.356	-1.287	-0.518	2.370	-1.339	-0.527	2.375	-1.344
H	-1.307	2.553	0.943	-1.242	2.555	1.052	-1.270	2.546	1.002	-1.276	2.545	0.997
H	-0.663	0.987	1.375	-0.579	0.990	1.455	-0.600	0.978	1.391	-0.602	0.977	1.383
H	-2.070	-3.088	-0.338	-1.886	-3.002	-0.579	-1.979	-3.036	-0.582	-1.993	-3.041	-0.575
H	-1.057	-3.120	1.128	-0.979	-3.149	0.936	-0.965	-3.144	0.869	-0.959	-3.142	0.863
H	-2.805	-2.845	1.245	-2.733	-2.955	0.978	-2.713	-2.939	1.029	-2.706	-2.939	1.045
H	3.134	1.510	1.410	3.222	1.590	1.253	3.175	1.623	1.253	3.167	1.629	1.249

17 Table 3S. XYZ coordinates for optimized CimC at the wB97XD/def2TZVP level of theory in different solvents.

	Gas			H ₂ O			MeOH			EtOH		
	x	y	z	x	y	Z	x	Y	z	x	y	z
S	-1.130	-0.831	-0.683	1.096	-0.717	0.701	1.108	-0.824	0.675	1.112	-0.874	0.662
N	-5.419	0.609	-0.110	5.455	0.606	0.093	5.465	0.497	0.099	5.447	0.518	0.107
C	-4.084	0.911	0.006	4.162	0.927	-0.231	4.161	0.900	-0.024	4.136	0.901	0.003
N	-4.466	-1.202	0.702	4.429	-1.312	-0.231	4.375	-1.253	-0.657	4.383	-1.224	-0.703
C	-2.081	-0.460	0.835	2.119	-0.510	-0.794	2.050	-0.331	-0.807	2.042	-0.338	-0.812
C	-3.514	-0.225	0.513	3.540	-0.275	-0.432	3.498	-0.200	-0.498	3.489	-0.193	-0.505
C	-5.593	-0.668	0.321	5.565	-0.738	0.079	5.545	-0.792	-0.290	5.547	-0.756	-0.327
N	3.074	1.117	-0.293	-3.200	1.095	0.456	-3.126	1.125	0.277	-3.099	1.127	0.263
N	2.925	-1.157	-0.537	-2.923	-1.180	0.394	-2.940	-1.145	0.490	-2.943	-1.143	0.499
C	0.533	-0.889	0.046	-0.523	-0.872	-0.092	-0.546	-0.886	-0.058	-0.548	-0.912	-0.060
C	3.796	2.156	0.086	-3.914	2.154	0.206	-3.799	2.184	-0.067	-3.757	2.193	-0.090
C	1.571	-1.067	-1.056	-1.592	-1.112	0.964	-1.597	-1.062	1.030	-1.596	-1.073	1.033
C	3.610	-0.069	-0.118	-3.667	-0.105	0.111	-3.657	-0.084	0.105	-3.648	-0.076	0.107
C	-3.508	2.226	-0.385	3.673	2.327	-0.290	3.705	2.267	0.332	3.657	2.248	0.408
N	4.416	3.076	0.422	-4.486	3.153	0.018	-4.331	3.179	-0.350	-4.276	3.192	-0.383
N	4.819	-0.269	0.450	-4.850	-0.292	-0.482	-4.867	-0.291	-0.424	-4.864	-0.271	-0.412
C	5.475	-1.548	0.579	-5.383	-1.583	-0.864	-5.489	-1.588	-0.587	-5.502	-1.562	-0.564
H	-6.557	-1.148	0.336	6.494	-1.241	0.295	6.474	-1.339	-0.291	6.486	-1.287	-0.351
H	-6.135	1.224	-0.450	6.194	1.261	0.292	6.232	1.068	0.417	6.206	1.091	0.441
H	-3.658	2.427	-1.447	3.648	2.780	0.704	3.852	2.468	1.396	3.802	2.414	1.478
H	-3.950	3.047	0.183	4.315	2.945	-0.921	4.251	3.028	-0.229	4.191	3.038	-0.127
H	-2.435	2.227	-0.204	2.663	2.357	-0.697	2.643	2.380	0.114	2.594	2.351	0.193
H	-2.002	-1.301	1.520	2.026	-1.408	-1.404	1.902	-1.086	-1.580	1.903	-1.078	-1.601

H	-1.633	0.418	1.300	1.720	0.334	-1.357	1.641	0.614	-1.167	1.618	0.609	-1.149
H	0.728	0.045	0.572	-0.740	0.045	-0.641	-0.721	0.047	-0.595	-0.712	0.026	-0.592
H	0.588	-1.717	0.755	-0.500	-1.704	-0.799	-0.601	-1.713	-0.769	-0.621	-1.735	-0.773
H	1.378	-1.980	-1.619	-1.413	-2.058	1.473	-1.422	-1.986	1.581	-1.430	-1.998	1.586
H	1.527	-0.229	-1.748	-1.574	-0.323	1.714	-1.550	-0.237	1.741	-1.536	-0.246	1.741
H	3.252	-2.058	-0.246	-3.230	-2.074	0.049	-3.310	-2.064	0.313	-3.326	-2.057	0.332
H	5.314	0.565	0.719	-5.399	0.526	-0.689	-5.399	0.522	-0.686	-5.383	0.546	-0.688
H	4.922	-2.222	1.238	-4.746	-2.077	-1.601	-4.903	-2.233	-1.246	-4.928	-2.216	-1.225
H	6.454	-1.390	1.021	-6.360	-1.425	-1.311	-6.465	-1.438	-1.040	-6.480	-1.403	-1.010
H	5.616	-2.030	-0.391	-5.502	-2.236	0.003	-5.628	-2.088	0.375	-5.639	-2.056	0.401

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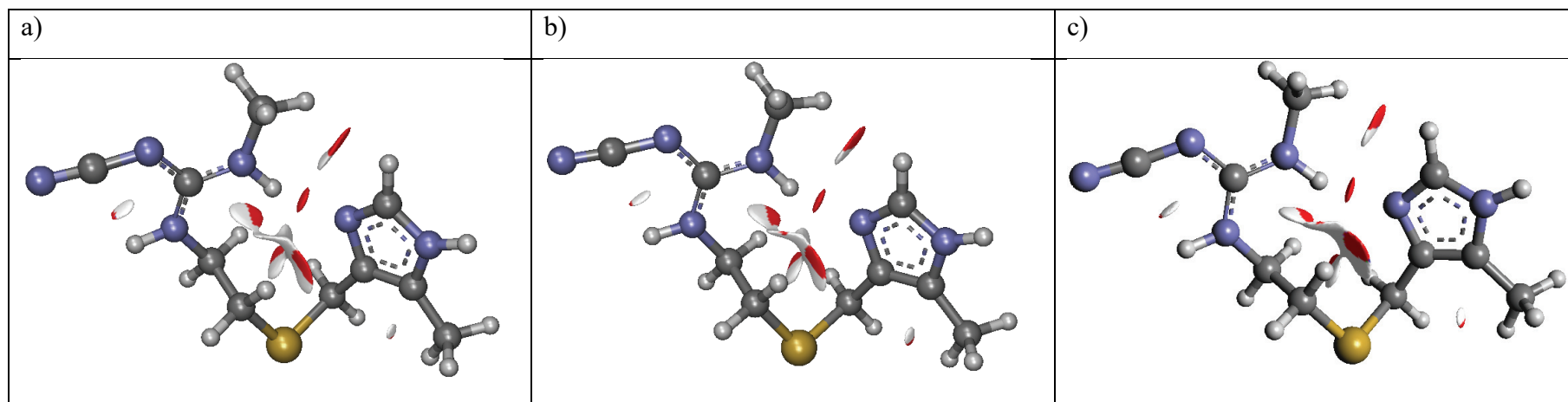
25 Table 4S. XYZ coordinates for optimized CimD at the wB97XD/def2TZVP level of theory in different solvents.

	Gas			H ₂ O			MeOH			EtOH		
	x	y	z	x	y	Z	X	Y	z	x	y	z
S	0.225	-1.868	0.955	0.111	-1.299	1.108	0.409	-1.687	1.043	0.419	-1.705	1.032
N	3.856	0.871	-0.570	4.233	0.313	-0.539	4.155	0.693	-0.682	4.150	0.709	-0.678
N	3.352	-0.802	0.764	3.410	-0.355	1.387	3.625	-0.547	1.050	3.627	-0.550	1.042
N	-1.837	-0.808	-1.217	-2.052	-0.849	-1.220	-1.991	-0.860	-0.996	-1.989	-0.860	-0.988
N	-3.564	-0.035	0.105	-3.703	-0.123	0.209	-3.865	-0.114	0.100	-3.866	-0.112	0.101
N	-1.714	1.323	-0.365	-1.977	1.318	-0.458	-1.967	1.254	-0.102	-1.967	1.255	-0.098
N	-2.712	3.115	1.022	-2.724	3.130	1.037	-2.988	3.130	1.122	-2.990	3.134	1.119
C	4.287	-0.263	0.037	4.489	-0.272	0.649	4.593	-0.176	0.252	4.593	-0.168	0.247
C	2.257	0.020	0.628	2.404	0.211	0.629	2.501	0.118	0.605	2.500	0.115	0.605
C	2.546	1.069	-0.204	2.901	0.636	-0.573	2.815	0.899	-0.475	2.810	0.908	-0.468
C	1.760	2.247	-0.663	2.274	1.302	-1.744	2.012	1.811	-1.332	2.003	1.825	-1.315
C	0.974	-0.249	1.331	1.002	0.293	1.109	1.178	-0.047	1.259	1.178	-0.062	1.259
C	0.350	-1.917	-0.842	0.181	-1.753	-0.638	0.293	-1.809	-0.754	0.295	-1.812	-0.765
C	-0.440	-0.849	-1.596	-0.648	-0.888	-1.580	-0.616	-0.800	-1.442	-0.617	-0.798	-1.442
C	-2.363	0.184	-0.468	-2.573	0.126	-0.458	-2.614	0.109	-0.318	-2.614	0.110	-0.314
C	-4.210	-1.322	0.200	-4.331	-1.423	0.322	-4.608	-1.337	-0.118	-4.608	-1.335	-0.115
C	-2.260	2.267	0.374	-2.407	2.245	0.346	-2.546	2.218	0.549	-2.546	2.221	0.550
H	5.288	-0.645	-0.092	5.474	-0.612	0.924	5.623	-0.494	0.308	5.623	-0.483	0.299
H	4.393	1.466	-1.174	4.903	0.500	-1.267	4.715	1.125	-1.400	4.708	1.149	-1.393
H	1.843	2.381	-1.744	2.072	0.592	-2.549	1.835	1.379	-2.320	1.824	1.400	-2.307
H	0.704	2.121	-0.429	1.331	1.766	-1.457	1.047	2.015	-0.871	1.038	2.023	-0.851
H	0.252	0.538	1.119	0.426	1.009	0.523	0.476	0.712	0.914	0.472	0.696	0.920
H	1.129	-0.284	2.410	0.966	0.616	2.150	1.267	0.060	2.342	1.268	0.037	2.342

H	1.400	-1.852	-1.131	1.220	-1.750	-0.973	1.291	-1.726	-1.190	1.291	-1.726	-1.205
H	0.001	-2.916	-1.115	-0.172	-2.786	-0.675	-0.058	-2.825	-0.944	-0.056	-2.828	-0.961
H	-0.362	-1.043	-2.669	-0.556	-1.296	-2.587	-0.586	-0.997	-2.516	-0.593	-0.989	-2.518
H	-2.302	-1.697	-1.171	-2.498	-1.751	-1.152	-2.474	-1.733	-1.129	-2.474	-1.732	-1.123
H	-0.023	0.137	-1.413	-0.275	0.131	-1.604	-0.258	0.213	-1.286	-0.258	0.213	-1.281
H	-3.917	0.723	0.665	-4.132	0.650	0.690	-4.331	0.638	0.580	-4.330	0.639	0.584
H	-4.497	-1.703	-0.784	-4.729	-1.766	-0.635	-4.742	-1.541	-1.183	-4.740	-1.541	-1.180
H	-5.122	-1.206	0.781	-5.155	-1.336	1.025	-5.590	-1.216	0.331	-5.591	-1.214	0.332
H	2.103	3.168	-0.185	2.927	2.081	-2.141	2.524	2.765	-1.473	2.512	2.782	-1.450
H	-3.575	-2.056	0.705	-3.629	-2.164	0.708	-4.120	-2.192	0.356	-4.121	-2.190	0.360

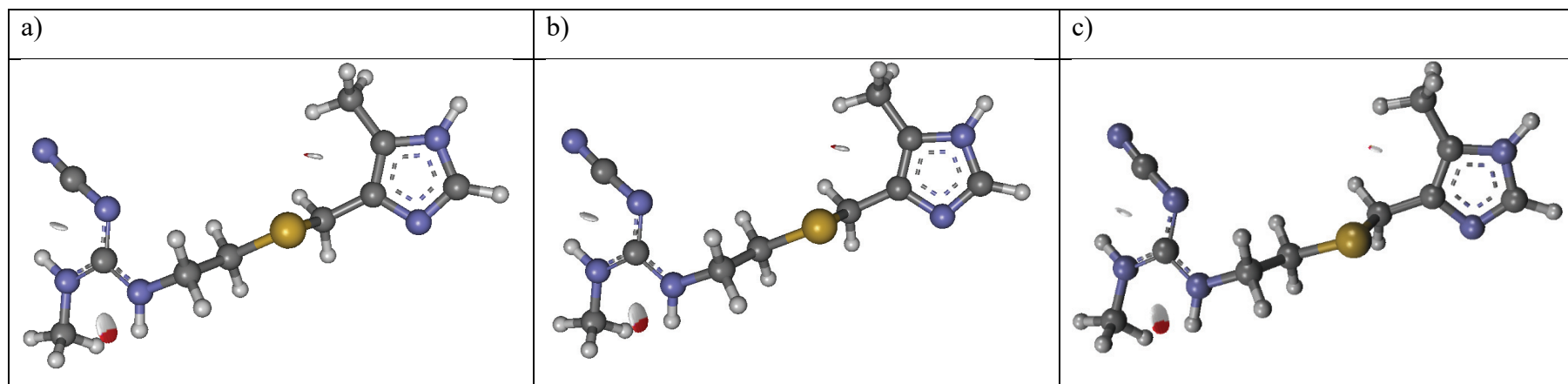
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27 Table 5S. NCI Isosurfaces $\rho=0.3$ for in CimA a) H₂O, b) MeOH and c) EtOH.



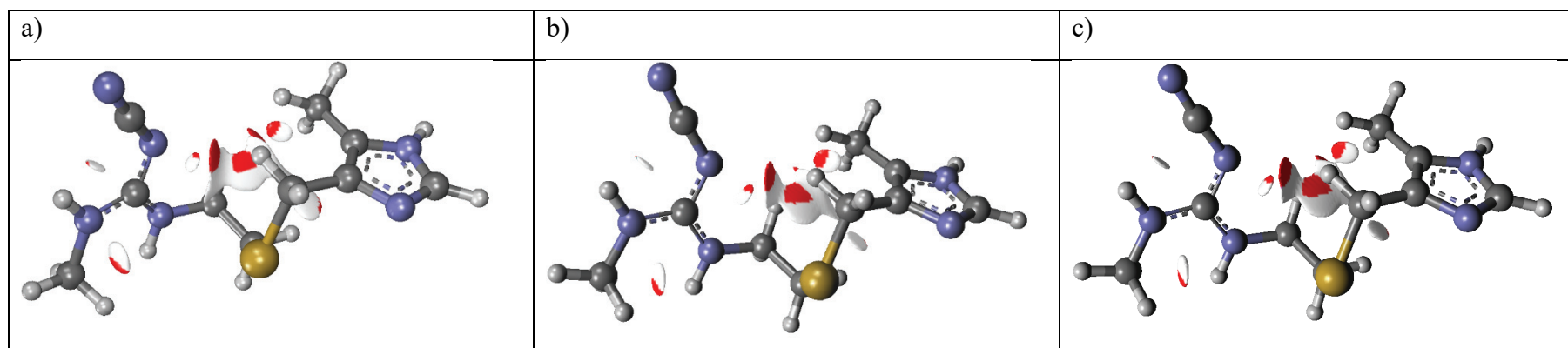
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29 Table 6S. NCI Isosurfaces $\rho=0.3$ for in CimC a) H₂O, b) MeOH and c) EtOH.

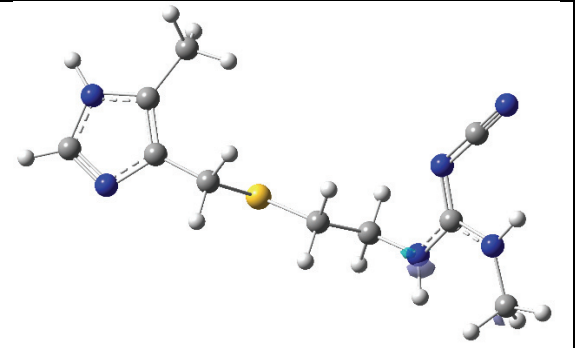
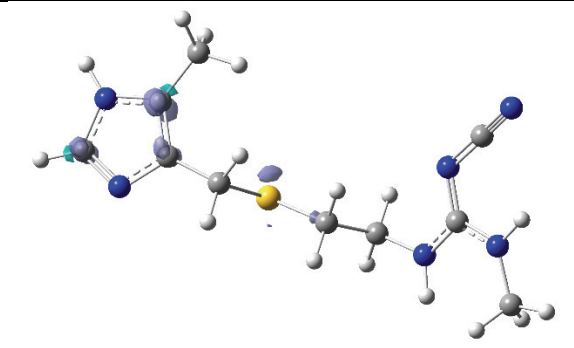
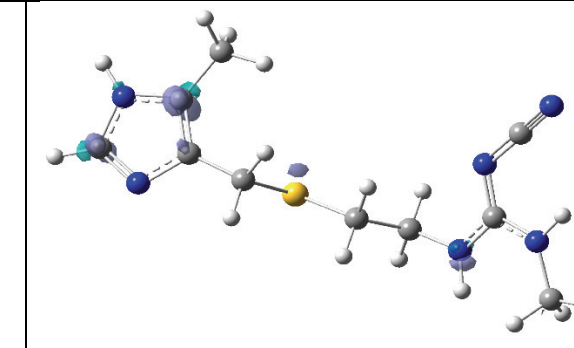
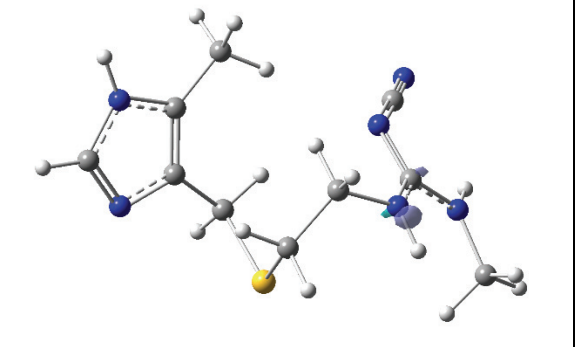
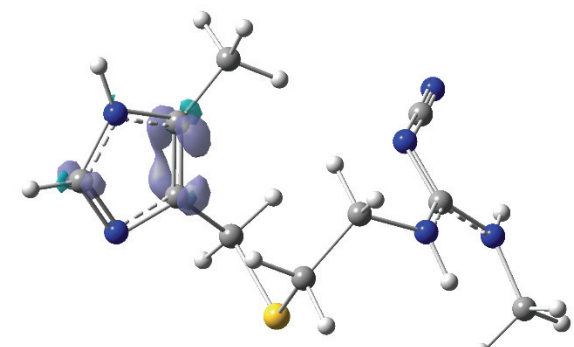
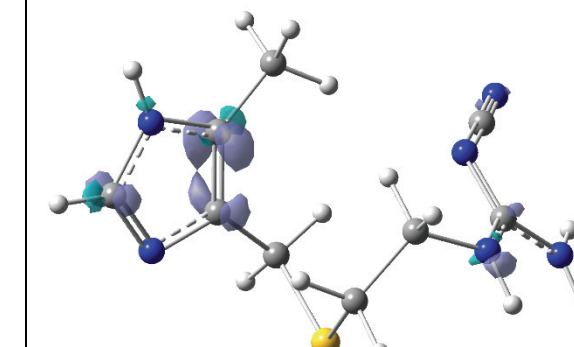


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31 Table 7S. NCI Isosurfaces $\rho=0.3$ for in CimD a) H₂O, b) MeOH and c) EtOH.



32 Table 8S. Local reactivities for CimC and CimD in the gas phase at the wB97XD/def2TZVP level of theory according to equations (6-8).

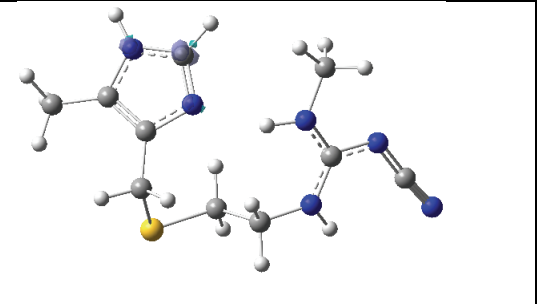
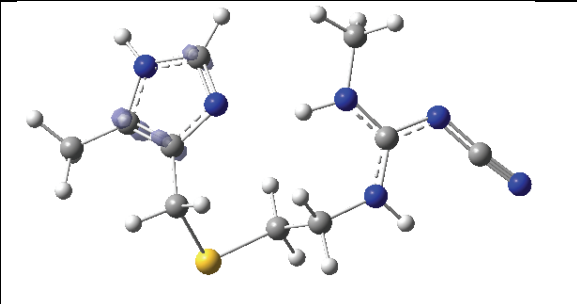
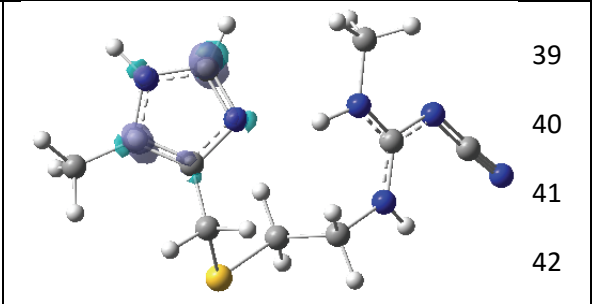
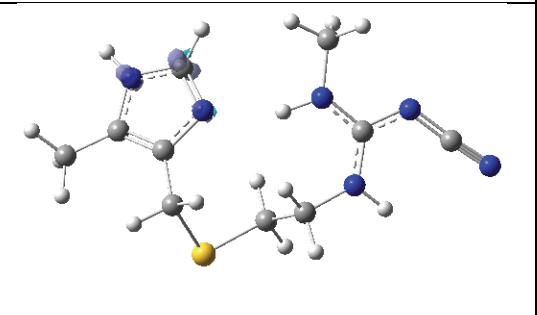
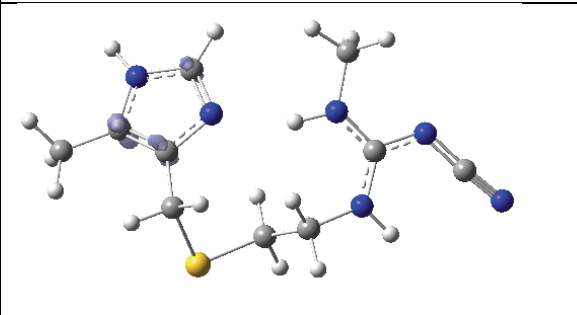
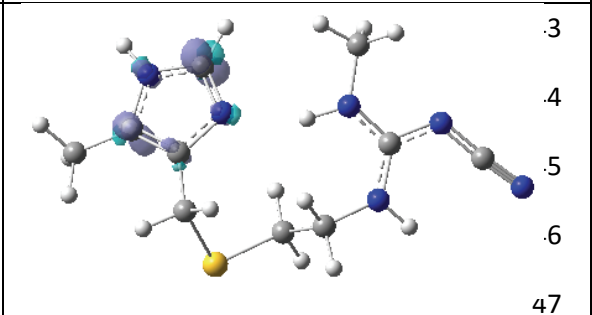
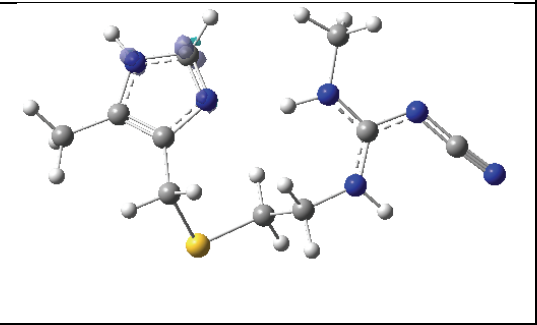
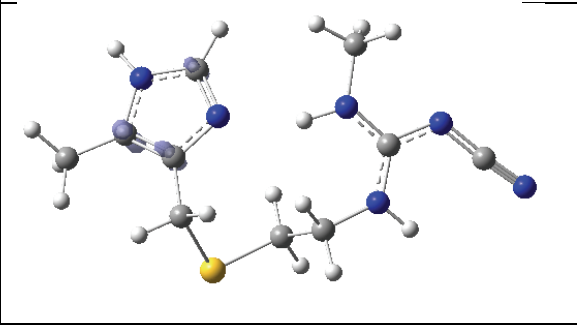
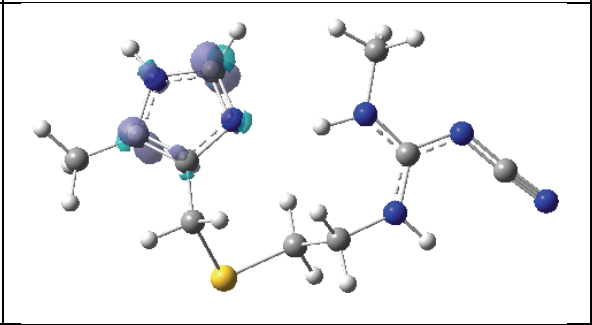
	$f^+(\vec{r})$	$f^-(\vec{r})$	$f^0(\vec{r})$
CimC			
CimD			

33

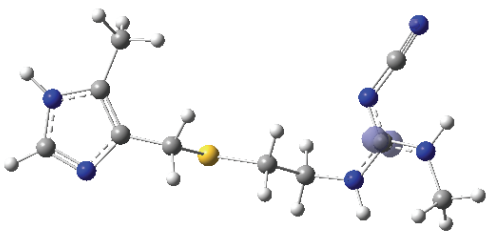
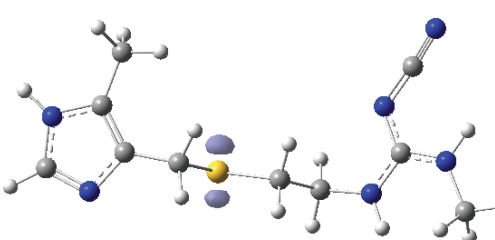
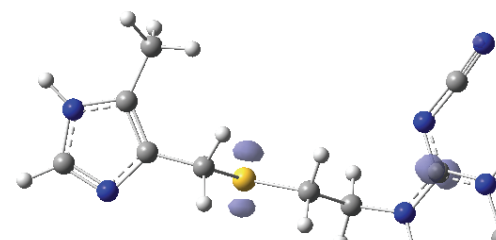
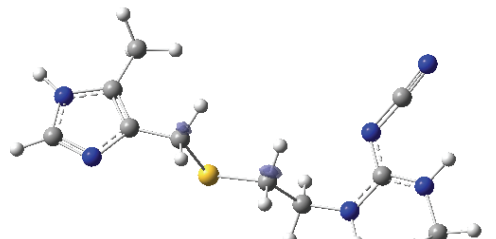
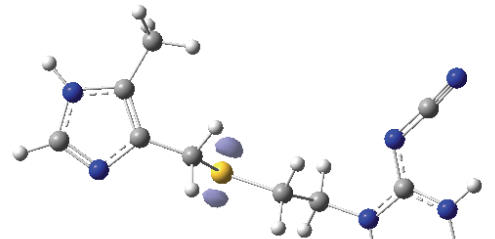
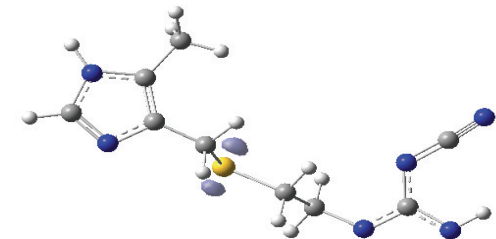
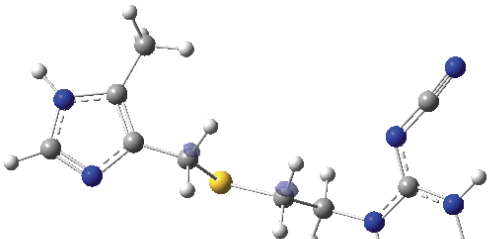
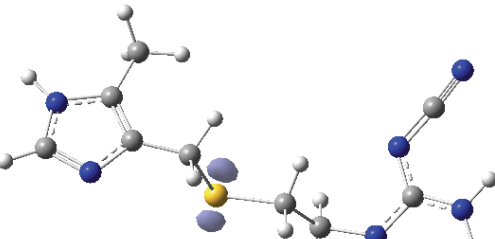
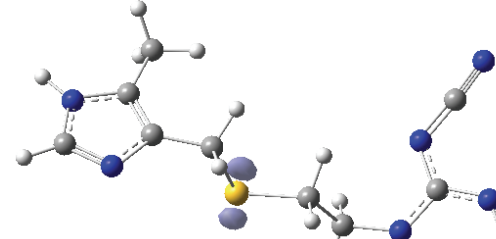
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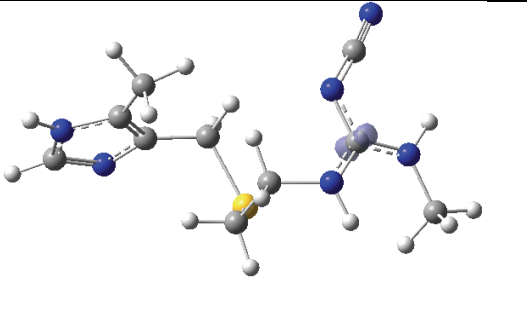
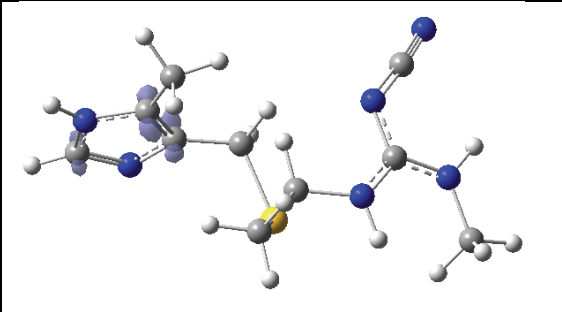
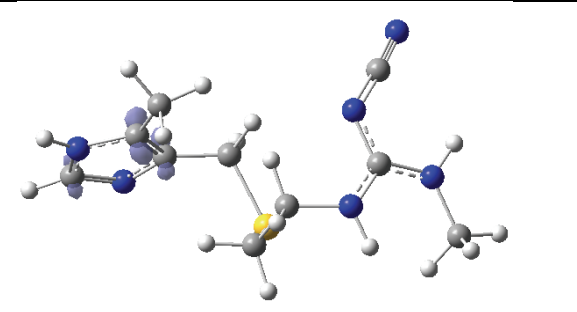
36 Table 9S. Local reactivities for CimA at the wB97XD/def2TZVP level of theory according to equations (6-8) and in different solvents.

	$f^+(r)$	$f^-(r)$	$f^0(r)$	37
				38
H ₂ O				39
				40
				41
				42
MeOH				.3
				.4
				.5
				.6
				47
EtOH				

52 Table 10S. Local reactivities for CimC at the wB97XD/def2TZVP level of theory according to equations (6-8) and in different solvents.

	$f^+(\vec{r})$	$f^-(\vec{r})$	$f^0(\vec{r})$	53
				54
H ₂ O				
MeOH				59 60 61 62
EtOH				

68 Table 11S. Local reactivities for CimD at the wB97XD/def2TZVP level of theory according to equations (6-8) and in different solvents.

	$f^+(\vec{r})$	$f^-(\vec{r})$	$f^0(\vec{r})$
H ₂ O			
MeOH	