Supplementary material

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

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

|  |  |  |  |
| --- | --- | --- | --- |
| Solvent | Electronic energy + ZPE / Eh | | |
|  | CimA | CimC | CimD |
| Gas | -1117.18590 | -1117.16810 | -1117.17586 |
| H2O | -1117.21585 | -1117.20897 | -1117.21457 |
| MeOH | -1117.22783 | -1117.21860 | -1117.22364 |
| EtOH | -1117.22900 | -1117.21939 | -1117.22459 |

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

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Gas |  |  | H2O |  |  | MeOH |  |  | EtOH |  |
|  | x | y | z | x | 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 |

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

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Gas |  |  | H2O |  |  | 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 |

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

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Gas |  |  | H2O |  |  | 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 |

Table 5S. Local reactivities for CimA at the wB97XD/def2TZVP level of theory according to equations (6-8) and in different solvents.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| H2O |  |  |  |
| MeOH |  |  |  |
| EtOH |  |  |  |

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

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| H2O |  |  |  |
| MeOH |  |  |  |
| EtOH |  |  |  |

Table 7S. Local reactivities for CimD at the wB97XD/def2TZVP level of theory according to equations (6-8) and in different solvents.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| H2O |  |  |  |
| MeOH |  |  |  |
| EtOH |  |  |  |