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SUPPLEMENTARY MATERIAL TO

# The role of non-covalent interactions in the solvation dynamics of metronidazole in water: A theoretical study

SUMIT KUMAR[1]*, NAGENDRA KUMAR[1], RAVINDRA KUMAR[1] and KAMAL K. MISHRA[2]

[1]*PG Department of Chemistry, Magadh University, Bodh Gaya 824234, India and* [2]*University of Kentucky, Lexington, Kentucky-40506, USA*

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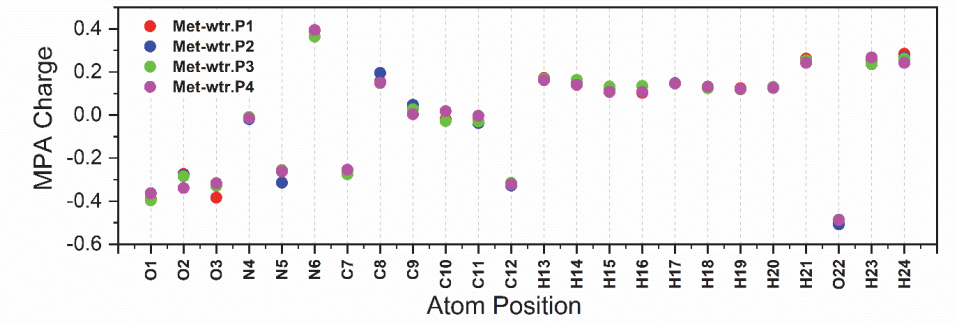


Fig. S-1. Mulliken population analysis (MPA) charge for (a) Met-wtr.P1, (b) Met-wtr.P2, (c) Met-wtr.P3, and (d) Met-wtr.P4.

* Corresponding author. E-mail: sumitkrmgr@gmail.com

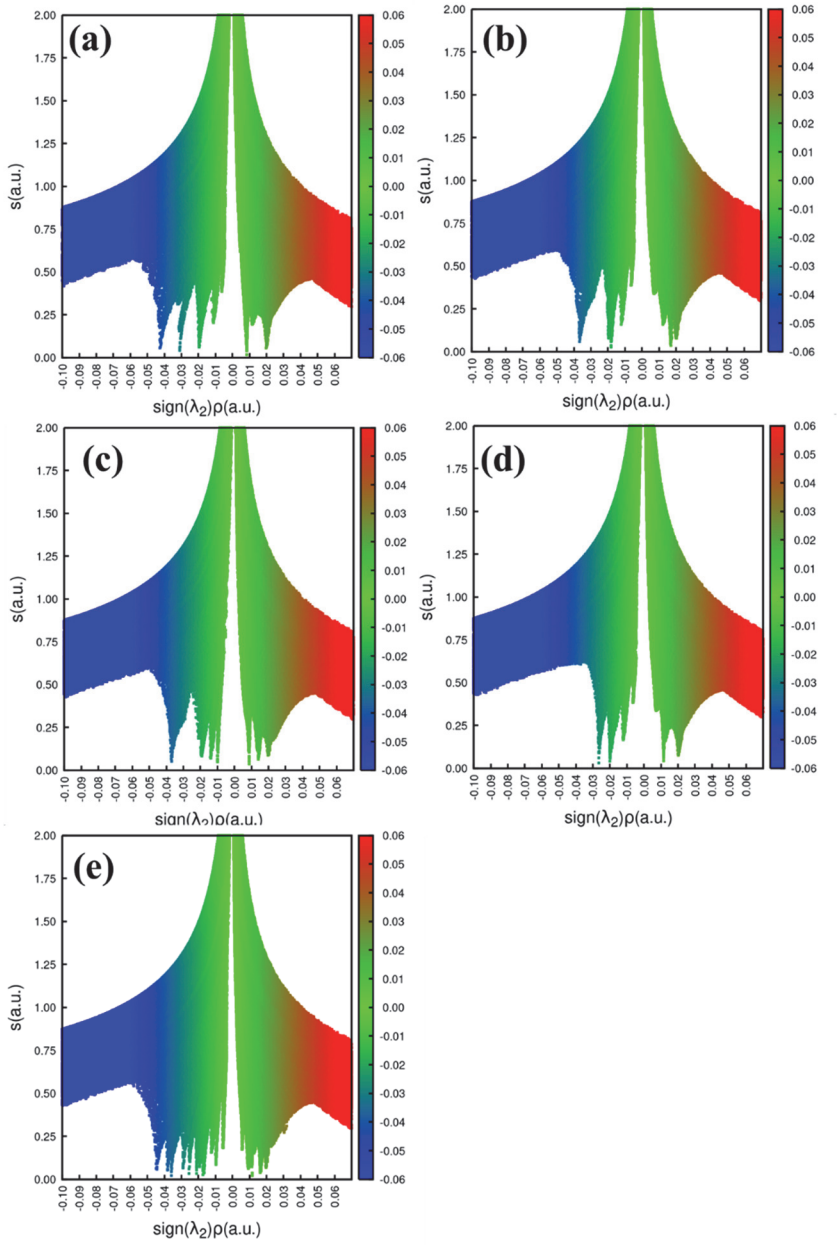


Fig. S-2. RDG plot of NCI analysis of (a) Met-wtr.P1, (b) Met-wtr.P2, (c) Met-wtr.P3, (d) Met-wtr.P4. and (e) Met-wtr.All using the structure optimized at B3LYP/def-TZVP level of theory.

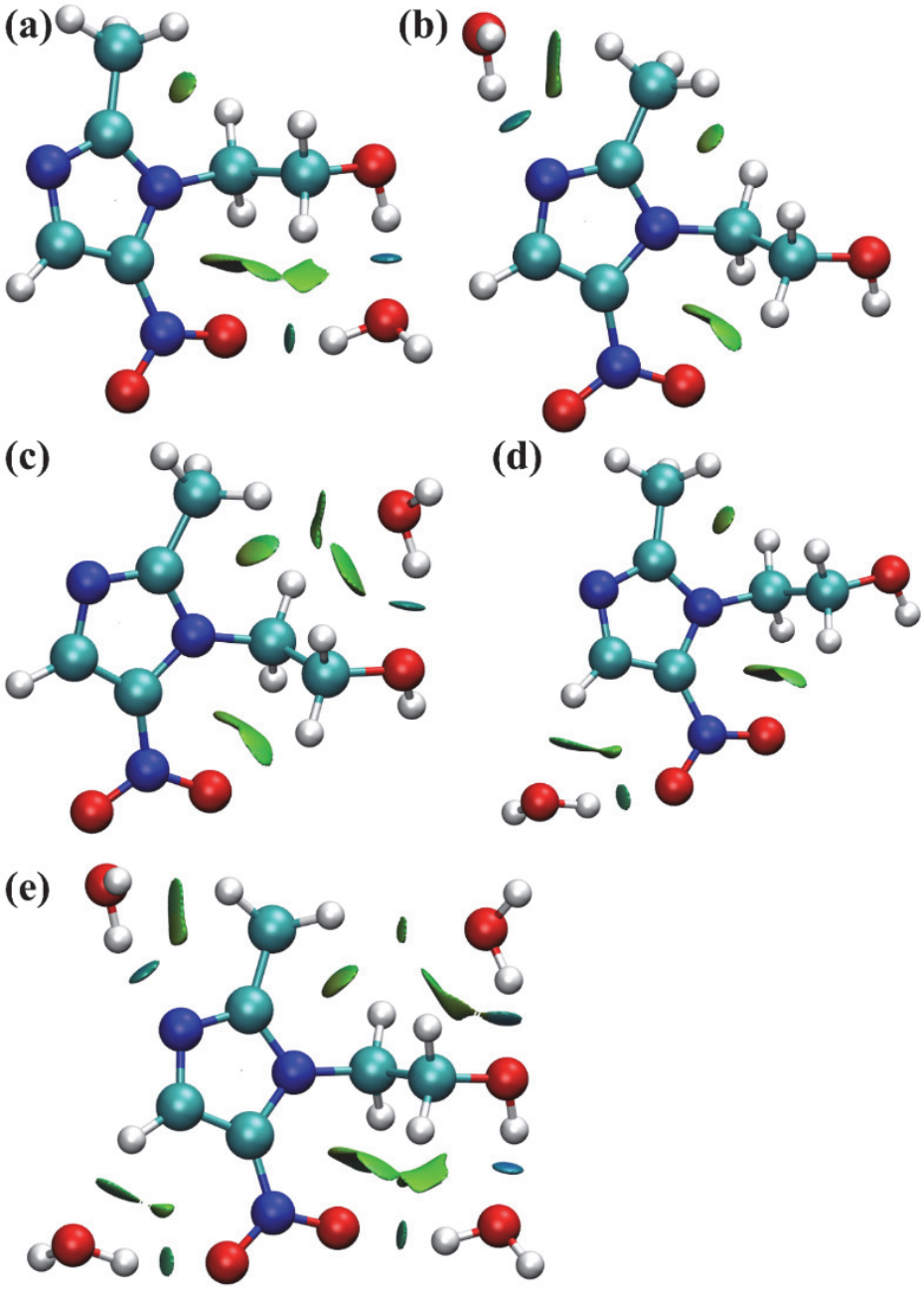


Fig. S-3. Isosurface extractions of RDG plots of NCI analysis of (a) Met-wtr.P1, (b) Met-wtr.P2, (c) Met-wtr.P3, (d) Met-wtr.P4. and (e) Met-wtr.All

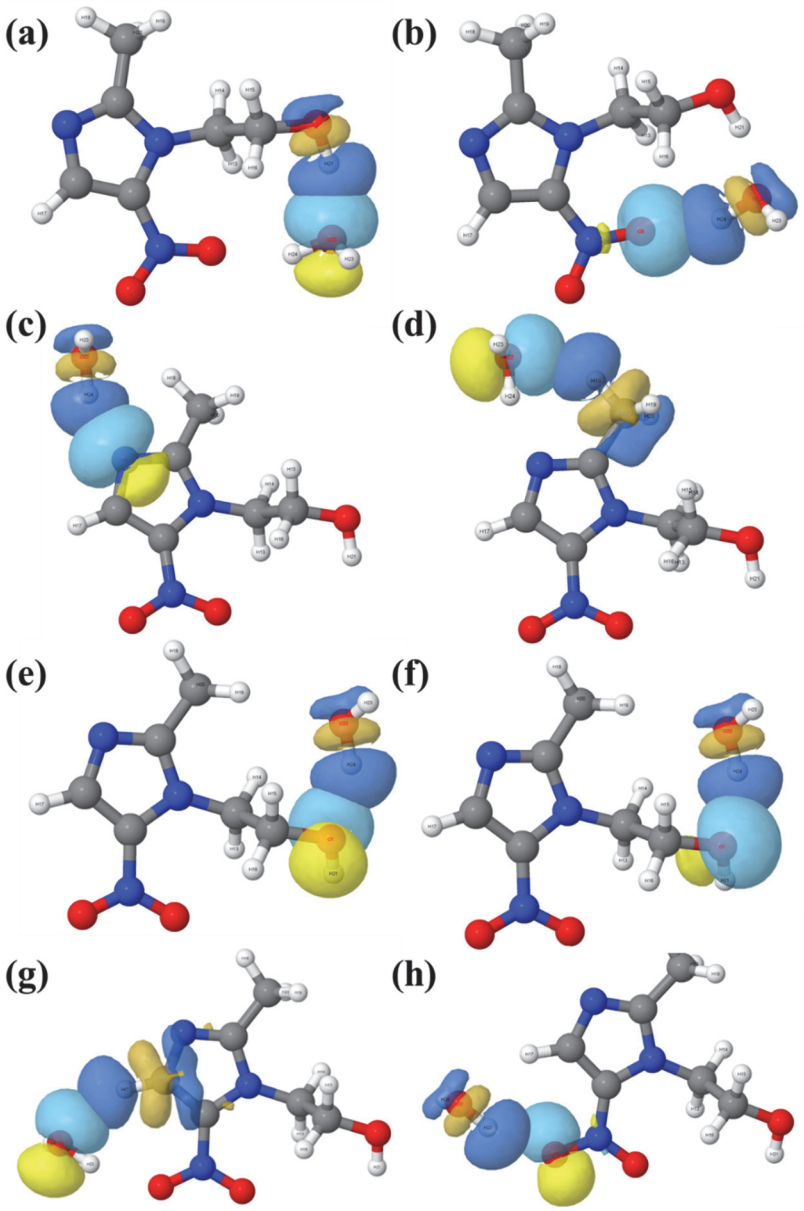


Fig. S-4. NBO interaction of (a) LP(2)O22→BD*(1)O1-H21 and (b) LP(1)O3→BD*(1)O22-H24 for Met-wtr.P1, (c) LP(1)N5→BD*(1)O22-H24 and (d) LP(2)O22→BD*(1)C12-H18 Met-wtr.P2, (e) LP(2)O1→BD*(1)O22-H24 and (f) LP(1)O1→BD*(1)O22-H24 Met-wtr.P3, and (g) LP(2)O22→BD*(1)C11-H17 and (h) LP(2)O2→BD*(1)O22-H23 for Met-wtr.P4.

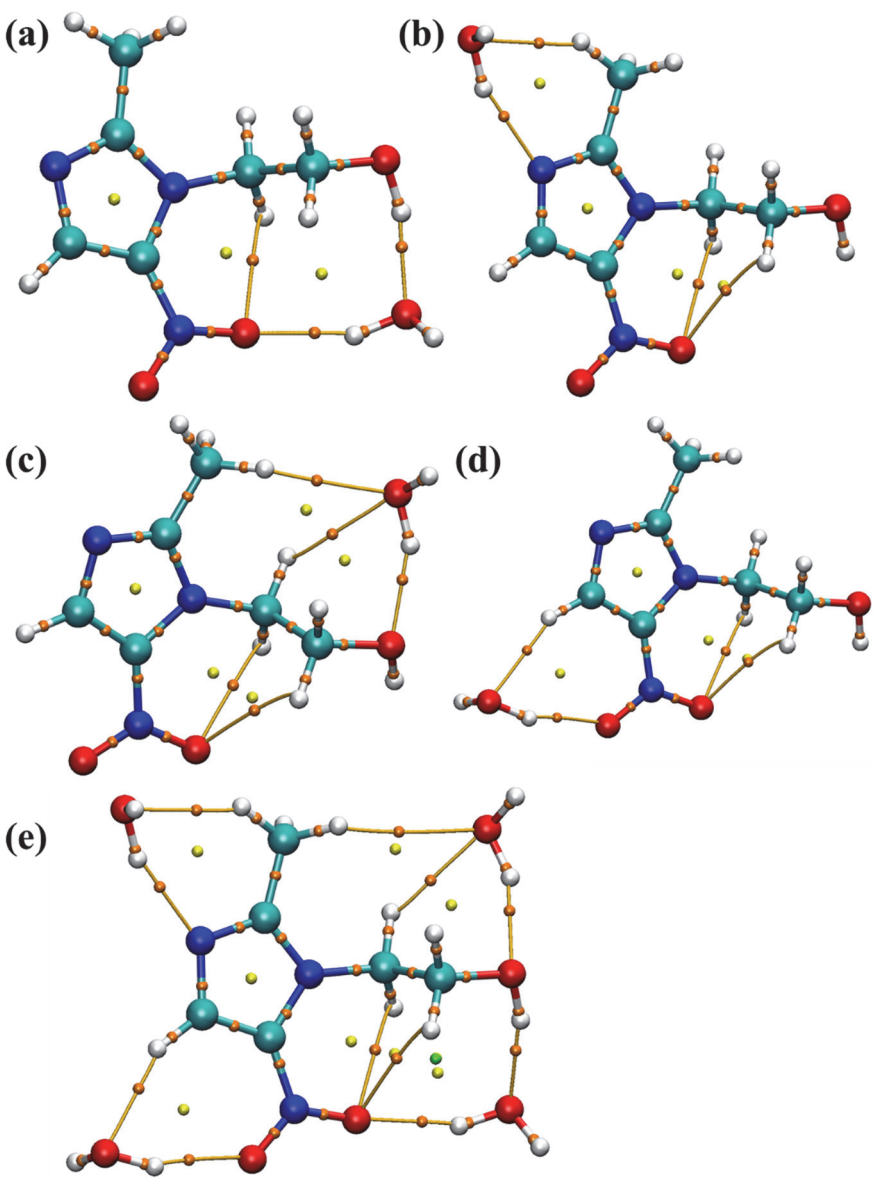


Fig. S-5. AIM study for (a) Met-wtr.P1, (b) Met-wtr.P2, (c) Met-wtr.P3, (d) Met-wtr.P4 and (e) Met-wtr.All.

TABLE S-I. Molecular characteristics of metronidazole, Met-wtr.P1, Met-wtr.P2, Met-wtr.P3, and Met-wtr.P4.

| Molecule | Met | Met-wtr.P1 | Met-wtr.P2 | Met-wtr.P3 | Met-wtr.P4 | Met-wtr.All |
|---|---|---|---|---|---|---|
| LUMO (eV) | -2.441 | -2.716 | -2.664 | -2.351 | -2.699 | -3.045 |
| HOMO (eV) | -7.075 | -7.023 | -7.347 | -6.939 | -7.173 | -7.293 |
| Band gap (eV) | 4.635 | 4.306 | 4.683 | 4.588 | 4.474 | 4.249 |
| Ionisation energy (eV) | 7.075 | 7.023 | 7.347 | 6.939 | 7.173 | 7.293 |
| Electron affinity (eV) | 2.441 | 2.716 | 2.664 | 2.351 | 2.699 | 3.045 |
| Chemical hardness (eV) | 2.317 | 2.154 | 2.342 | 2.294 | 2.237 | 2.124 |
| Electronic chemical potential (eV) | -4.758 | -4.870 | -5.006 | -4.645 | -4.936 | -5.169 |
| Electrophilicity index (eV) | 9.771 | 11.011 | 10.700 | 9.405 | 10.891 | 12.579 |
| Softness (1/eV) | 0.432 | 0.464 | 0.427 | 0.436 | 0.447 | 0.471 |

TABLE S-II. Decomposition of total interaction energy of the solvated metronidazole with water.

| | $\Delta E_{ele}$ | $\Delta E_{ex}$ | $\Delta E_{rep}$ | $\Delta E_{pol}$ | $\Delta E_{disp}$ | $\Delta E_{tot}$ | $\Delta E_{disp}/\Delta E_{ele}$ |
|---|---|---|---|---|---|---|---|
| | kJ mol$^{-1}$ | | | | | | |
| Met-wtr.P1 | -70.29 | -32.55 | 122.63 | -47.15 | -40.29 | -67.66 | 0.57 |
| Met-wtr.P2 | -47.95 | -28.37 | 96.48 | -38.74 | -27.87 | -46.40 | 0.58 |
| Met-wtr.P3 | -46.69 | -21.13 | 87.32 | -38.91 | -35.86 | -55.27 | 0.76 |
| Met-wtr.P4 | -30.96 | -14.69 | 61.63 | -31.46 | -23.14 | -38.62 | 0.74 |
| Met-wtr.All | -199.07 | -98.70 | 372.33 | -154.26 | -128.45 | -208.20 | 0.64 |

TABLE S-III. Solvation model of metronidazole employed at PBE0-D3/def2-TZVP level of theory.

| Solvent | Surface-charge | Charge-correction | Free-energy (cav+disp) | Dielectric constant |
|---|---|---|---|---|
| Water | -28.207 | 0.030 | 4.506 | 80.4 |
| DMSO | -14.465 | 0.022 | -1.829 | 47.2 |
| DMF | -14.471 | 0.022 | -2.932 | 38.3 |
| Acetonitrole | -15.478 | 0.025 | -2.282 | 36.6 |
| Pyridine | -14.501 | 0.021 | -3.906 | 12.5 |
| tetrahydrofuran | -14.531 | 0.020 | -3.774 | 7.3 |
| Chloroform | -16.932 | 0.025 | -2.807 | 4.9 |

TABLE S-IV. Nature bonding orbital (NBO) assay of metronidazole.

| NAOs | Donor NBO (i) | NAOs | Acceptor NBO (j) | $E_{i\rightarrow j}^{(2)}$ (kJ mol$^{-1}$) |
|---|---|---|---|---|
| | **Met-wtr.P1** | | | |
| **24** | **LP(2)O22** | **52** | **BD*(1)O1-H21** | 64.48 |
| **18** | **LP(1)O3** | **76** | **BD*(1)O22-H24** | 16.32 |
| 50 | BD(1)O22-H24 | 55 | BD*(1)O3-N6 | 2.97 |
| 20 | LP(3)O3 | 76 | BD*(1)O22-H24 | 2.18 |
| 29 | BD(1)O3-N6 | 466 | RY(2)H24 | 1.26 |
| 23 | LP(1)O22 | 52 | BD*(1)O1-H21 | 1.13 |
| 24 | LP(2)O22 | 429 | RY(1)H21 | 0.88 |
| 24 | LP(2)O22 | 51 | BD*(1)O1-C10 | 0.46 |
| | **Met-wtr.P2** | | | 0.00 |
| **21** | **LP(1)N5** | **76** | **BD*(1)O22-H24** | 46.65 |
| **24** | **LP(2)O22** | **72** | **BD*(1)C12-H18** | 11.00 |
| 50 | BD(1)O22-H24 | 61 | BD*(1)N5-C11 | 1.88 |
| 35 | BD(1)N5-C11 | 465 | RY(1)H24 | 1.09 |
| 50 | BD(1)O22-H24 | 181 | RY(1)N5 | 0.63 |
| 21 | LP(1)N5 | 467 | RY(3)H24 | 0.59 |
| 50 | BD(1)O22-H24 | 72 | BD*(1)C12-H18 | 0.54 |
| 50 | BD(1)O22-H24 | 414 | RY(1)H18 | 0.54 |
| 41 | BD(1)C9-C11 | 76 | BD*(1)O22-H24 | 0.50 |
| | **Met-wtr.P3** | | | 0.00 |
| **15** | **LP(2)O1** | **76** | **BD*(1)O22-H24** | 24.89 |
| **14** | **LP(1)O1** | **76** | **BD*(1)O22-H24** | 13.81 |
| 24 | LP(2)O22 | 73 | BD*(1)C12-H19 | 4.73 |
| 24 | LP(2)O22 | 65 | BD*(1)C7-H14 | 1.34 |
| 49 | BD(1)O22-H23 | 394 | RY(1)H14 | 0.79 |
| 26 | BD(1)O1-H21 | 466 | RY(2)H24 | 0.71 |
| 24 | LP(2)O22 | 70 | BD*(1)C10-H16 | 0.67 |
| 50 | BD(1)O22-H24 | 52 | BD*(1)O1-H21 | 0.67 |
| | **Met-wtr.P4** | | | 0.00 |
| **24** | **LP(2)O22** | **71** | **BD*(1)C11-H17** | 15.61 |
| **17** | **LP(2)O2** | **75** | **BD*(1)O22-H23** | 13.51 |
| 16 | LP(1)O2 | 75 | BD*(1)O22-H23 | 7.53 |
| 49 | BD(1)O22-H23 | 71 | BD*(1)C11-H17 | 1.13 |
| 49 | BD(1)O22-H23 | 53 | BD*(1)O2-N6 | 1.09 |
| 18 | LP(3)O2 | 75 | BD*(1)O22-H23 | 1.00 |
| 24 | LP(2)O22 | 61 | BD*(1)N5-C11 | 0.46 |
| 49 | BD(1)O22-H23 | 409 | RY(1)H17 | 0.46 |
| | **Met-wtr.All** | | | 0.00 |
| **27** | **LP(2)O22** | **67** | **BD*(1)O1-H21** | **69.91** |
| **25** | **LP(1)N5** | **93** | **BD*(1)O25-H27** | **44.18** |
| **18** | **LP(2)O1** | **97** | **BD*(1)O31-H33** | **25.19** |
| **31** | **LP(2)O28** | **86** | **BD*(1)C11-H17** | **18.03** |
| 17 | LP(1)O1 | 97 | BD*(1)O31-H33 | 15.94 |
| **22** | **LP(1)O3** | **91** | **BD*(1)O22-H24** | **14.06** |
| **20** | **LP(2)O2** | **94** | **BD*(1)O28-H29** | **12.47** |
| **29** | **LP(2)O25** | **87** | **BD*(1)C12-H18** | **9.92** |

| NAOs | Donor NBO (i) | NAOs | Acceptor NBO (j) | $E_{i\rightarrow j}^{(2)}$ (kJ mol$^{-1}$) |
|---|---|---|---|---|
| 19 | LP(1)O2 | 94 | BD*(1)O28-H29 | 6.65 |
| 33 | LP(2)O31 | 81 | BD*(1)C7-H14 | 3.14 |
| 59 | BD(1)O22-H24 | 69 | BD*(1)O3-N6 | 2.72 |
| 61 | BD(1)O25-H27 | 75 | BD*(1)N5-C11 | 1.80 |
| 62 | BD(1)O28-H29 | 86 | BD*(1)C11-H17 | 1.26 |
| 37 | BD(1)O3-N6 | 487 | RY(2)H24 | 1.21 |
| 33 | LP(2)O31 | 88 | BD*(1)C12-H19 | 1.21 |
| 64 | BD(1)O31-H32 | 415 | RY(1)H14 | 1.13 |
| 43 | BD(1)N5-C11 | 522 | RY(1)H27 | 1.09 |
| 26 | LP(1)O22 | 67 | BD*(1)O1-H21 | 1.05 |
| 62 | BD(1)O28-H29 | 68 | BD*(1)O2-N6 | 1.00 |
| 32 | LP(1)O31 | 81 | BD*(1)C7-H14 | 1.00 |
| 65 | BD(1)O31-H33 | 67 | BD*(1)O1-H21 | 0.96 |
| 33 | LP(2)O31 | 85 | BD*(1)C10-H16 | 0.88 |

TABLE S-V. MPA charges of Met-wtr.P1, Met-wtr.P2, Met-wtr.P3, and Met-wtr.P4.

| Atom No | Metronidazole | Met-wtr.P1 | Met-wtr.P2 | Met-wtr.P3 | Met-wtr.P4 |
|---|---|---|---|---|---|
| O1 | -0.364881 | -0.3896 | -0.3629 | -0.3965 | -0.3641 |
| O2 | -0.280926 | -0.2737 | -0.2781 | -0.2837 | -0.3390 |
| O3 | -0.324958 | -0.3833 | -0.3201 | -0.3290 | -0.3163 |
| N4 | -0.013881 | -0.0100 | -0.0190 | -0.0097 | -0.0144 |
| N5 | -0.256843 | -0.2565 | -0.3140 | -0.2576 | -0.2620 |
| N6 | 0.365079 | 0.3928 | 0.3654 | 0.3638 | 0.3946 |
| C7 | -0.253083 | -0.2552 | -0.2548 | -0.2748 | -0.2538 |
| C8 | 0.151093 | 0.1558 | 0.1953 | 0.1480 | 0.1499 |
| C9 | 0.027772 | 0.0301 | 0.0474 | 0.0269 | 0.0041 |
| C10 | 0.018371 | -0.0194 | 0.0178 | -0.0279 | 0.0182 |
| C11 | -0.031026 | -0.0270 | -0.0378 | -0.0301 | -0.0034 |
| C12 | -0.322707 | -0.3220 | -0.3272 | -0.3155 | -0.3221 |
| H13 | 0.162977 | 0.1720 | 0.1641 | 0.1684 | 0.1623 |
| H14 | 0.140126 | 0.1413 | 0.1443 | 0.1626 | 0.1402 |
| H15 | 0.106472 | 0.1155 | 0.1080 | 0.1322 | 0.1075 |
| H16 | 0.106777 | 0.1031 | 0.1060 | 0.1350 | 0.1069 |
| H17 | 0.148904 | 0.1483 | 0.1480 | 0.1475 | 0.1463 |
| H18 | 0.130322 | 0.1293 | 0.1281 | 0.1248 | 0.1318 |
| H19 | 0.121097 | 0.1243 | 0.1214 | 0.1189 | 0.1216 |
| H20 | 0.1261 | 0.1272 | 0.1281 | 0.1295 | 0.1259 |
| H21 | 0.243215 | 0.2616 | 0.2434 | 0.2538 | 0.2428 |
| O22 | | -0.5027 | -0.5073 | -0.4858 | -0.4877 |
| H23 | | 0.2542 | 0.2370 | 0.2377 | 0.2679 |
| H24 | | 0.2839 | 0.2673 | 0.2616 | 0.2426 |

TABLE S-VI. AIM analysis data for Met-wtr.P1

| BCP | ρ(r) | $\nabla^2\rho_{bcp}(r)$ | ELF | LOL |
|---|---|---|---|---|
| C10…H16 | -0.2733 | -0.95299 | 0.989361 | 0.906067 |
| C10…O1 | -0.38933 | -0.71868 | 0.730268 | 0.621999 |
| C11…C9 | -0.35117 | -0.94826 | 0.93623 | 0.793045 |
| C12…C8 | -0.24279 | -0.70858 | 0.957553 | 0.826097 |
| C12…H19 | -0.26594 | -0.90844 | 0.98593 | 0.893312 |
| C7…C10 | -0.20931 | -0.61938 | 0.96297 | 0.836078 |
| C7…H13 | -0.28684 | -1.00942 | 0.990628 | 0.91138 |
| C8…N4 | -0.48341 | -0.94763 | 0.753954 | 0.63644 |
| C9…N6 | -0.38036 | -0.84916 | 0.82946 | 0.688038 |
| H13…O3 | 0.002227 | 0.062306 | 0.045079 | 0.1786 |
| H14…C7 | -0.28096 | -0.981 | 0.989496 | 0.906618 |
| H15…C10 | -0.27718 | -0.97181 | 0.990077 | 0.909023 |
| H17…C11 | -0.29277 | -1.05068 | 0.993018 | 0.922661 |
| H18…C12 | -0.27281 | -0.94355 | 0.988002 | 0.900766 |
| H20…C12 | -0.26418 | -0.90101 | 0.985651 | 0.892359 |
| **H21…O22** | **-0.00364** | **0.111881** | **0.130611** | **0.279395** |
| H24…O22 | -0.64045 | -2.30744 | 0.982795 | 0.883167 |
| N4…C7 | -0.29823 | -0.61289 | 0.793272 | 0.662052 |
| N4…C9 | -0.40694 | -0.88528 | 0.820371 | 0.681242 |
| N5…C11 | -0.49003 | -1.12479 | 0.845012 | 0.700158 |
| N5…C8 | -0.52191 | -1.23904 | 0.862654 | 0.714798 |
| N6…O2 | -0.70453 | -1.24069 | 0.853356 | 0.706948 |
| N6…O3 | -0.6439 | -1.12269 | 0.853679 | 0.707217 |
| O1…H21 | -0.6165 | -2.19996 | 0.979329 | 0.873163 |
| O22…H23 | -0.64558 | -2.30921 | 0.981684 | 0.879839 |
| **O3…H24** | **0.003184** | **0.093755** | **0.04836** | **0.184032** |

TABLE S-VII. AIM analysis data for Met-wtr.P2

| BCP | ρ(r) | $\nabla^2\rho_{bcp}(r)$ | ELF | LOL |
|---|---|---|---|---|
| C10…H16 | -0.27786 | -0.97674 | 0.99053 | 0.910957 |
| C10…O1 | -0.36786 | -0.64682 | 0.707527 | 0.608676 |
| C11…C9 | -0.35802 | -0.96373 | 0.935327 | 0.791809 |
| C12…C8 | -0.24285 | -0.70063 | 0.954394 | 0.820636 |
| C12…H19 | -0.26524 | -0.9031 | 0.985344 | 0.891322 |
| C7…C10 | -0.21386 | -0.63651 | 0.96418 | 0.838428 |
| C7…H13 | -0.28508 | -1.00299 | 0.99059 | 0.911215 |
| C8…N4 | -0.48379 | -0.94725 | 0.752869 | 0.635764 |
| C9…N6 | -0.35902 | -0.83579 | 0.855705 | 0.708911 |
| H13…O3 | 0.002281 | 0.061292 | 0.043683 | 0.176201 |
| H14…C7 | -0.28156 | -0.98496 | 0.989785 | 0.907805 |
| H15…C10 | -0.28073 | -0.98825 | 0.990657 | 0.911508 |
| **H16…O3** | **0.001712** | **0.035909** | **0.022256** | **0.131251** |
| H17…C11 | -0.29334 | -1.05309 | 0.993049 | 0.922821 |
| H18…C12 | -0.27352 | -0.95579 | 0.989566 | 0.906901 |
| H20…C12 | -0.26371 | -0.89756 | 0.985281 | 0.891112 |
| H24…N5 | -0.00042 | 0.080896 | 0.128494 | 0.277542 |
| N4…C7 | -0.29961 | -0.62639 | 0.802227 | 0.668234 |
| N4…C9 | -0.41037 | -0.88324 | 0.813596 | 0.676301 |
| N5…C11 | -0.48078 | -1.09588 | 0.840936 | 0.696916 |
| N5…C8 | -0.52499 | -1.23279 | 0.855268 | 0.708542 |
| N6…O2 | -0.70047 | -1.22994 | 0.852957 | 0.706619 |
| N6…O3 | -0.66796 | -1.1651 | 0.853132 | 0.706763 |
| O1…H21 | -0.65062 | -2.32411 | 0.981498 | 0.879292 |
| **O22…H18** | **0.002167** | **0.048868** | **0.047364** | **0.182471** |
| O22…H23 | -0.63703 | -2.25547 | 0.979283 | 0.873037 |
| O22…H24 | -0.62185 | -2.21723 | 0.979352 | 0.873226 |

TABLE S-VIII. AIM analysis data for Met-wtr.P3

| BCP | ρ(r) | $\nabla^2\rho_{bcp}(r)$ | ELF | LOL |
|---|---|---|---|---|
| C10…H16 | -0.28079 | -0.99146 | 0.991146 | 0.913669 |
| C10…O1 | -0.34585 | -0.57626 | 0.684808 | 0.595808 |
| C11…C9 | -0.35469 | -0.95499 | 0.935358 | 0.791851 |
| C12…C8 | -0.2424 | -0.70367 | 0.9561 | 0.823556 |
| C12…H19 | -0.26977 | -0.93163 | 0.987758 | 0.89985 |
| C7…C10 | -0.21589 | -0.6444 | 0.964839 | 0.839726 |
| C7…H13 | -0.28339 | -0.99537 | 0.990355 | 0.910204 |
| C8…N4 | -0.4728 | -0.92966 | 0.755858 | 0.63763 |
| C9…N6 | -0.36876 | -0.84514 | 0.845898 | 0.700872 |
| H13…O3 | 0.002248 | 0.059883 | 0.042364 | 0.173891 |
| H14…C7 | -0.28444 | -1.00046 | 0.990579 | 0.911165 |
| H15…C10 | -0.28436 | -1.00494 | 0.991207 | 0.913947 |
| H17…C11 | -0.29268 | -1.04967 | 0.992936 | 0.92224 |
| H18…C12 | -0.2714 | -0.93537 | 0.987429 | 0.898633 |
| **H19…O22** | **0.001266** | **0.027317** | **0.030058** | **0.149916** |
| H20…C12 | -0.26214 | -0.89111 | 0.98508 | 0.890443 |
| **H24…O1** | **-0.00012** | **0.10487** | **0.094057** | **0.243763** |
| N4…C7 | -0.30153 | -0.64076 | 0.811153 | 0.674548 |
| N4…C9 | -0.40913 | -0.87978 | 0.813255 | 0.676056 |
| N5…C11 | -0.48154 | -1.11004 | 0.848166 | 0.702701 |
| N5…C8 | -0.52914 | -1.25035 | 0.859496 | 0.712099 |
| N6…O2 | -0.69585 | -1.22127 | 0.853108 | 0.706744 |
| N6…O3 | -0.65964 | -1.14821 | 0.853178 | 0.706801 |
| O1…H21 | -0.64995 | -2.32855 | 0.982151 | 0.88122 |
| **O22…H14** | **0.001707** | **0.034301** | **0.019652** | **0.124183** |
| O22…H23 | -0.64374 | -2.28934 | 0.980303 | 0.875865 |
| O22…H24 | -0.62824 | -2.24433 | 0.98011 | 0.875324 |
| **O3…H16** | **0.001762** | **0.038455** | **0.026051** | **0.140714** |

TABLE S-IX. AIM analysis data for Met-wtr.P4

| BCP | ρ(r) | $\nabla^2\rho_{bcp}(r)$ | ELF | LOL |
|---|---|---|---|---|
| C10...H16 | -0.27781 | -0.97652 | 0.990522 | 0.910921 |
| C10...O1 | -0.36698 | -0.64423 | 0.706789 | 0.608251 |
| C11...C9 | -0.35017 | -0.94333 | 0.935335 | 0.79182 |
| C12...C8 | -0.24243 | -0.7078 | 0.957692 | 0.826342 |
| C12...H19 | -0.26597 | -0.90779 | 0.985781 | 0.892803 |
| C7...C10 | -0.21388 | -0.63664 | 0.964224 | 0.838512 |
| C7...H13 | -0.28477 | -1.00123 | 0.990498 | 0.910818 |
| C8...N4 | -0.47914 | -0.9407 | 0.754895 | 0.637028 |
| C9...N6 | -0.38101 | -0.84889 | 0.828301 | 0.68716 |
| **H13...O3** | **0.002306** | **0.062551** | **0.044259** | **0.177196** |
| H14...C7 | -0.28122 | -0.98248 | 0.989594 | 0.907016 |
| H15...C10 | -0.28069 | -0.98803 | 0.990642 | 0.911441 |
| **H16...O3** | **0.001731** | **0.036398** | **0.021956** | **0.13046** |
| H17...C11 | -0.29327 | -1.06107 | 0.993937 | 0.927578 |
| **H17...O22** | **0.002441** | **0.05554** | **0.051483** | **0.189087** |
| H18...C12 | -0.2729 | -0.9444 | 0.988096 | 0.90112 |
| H20...C12 | -0.26397 | -0.89964 | 0.985527 | 0.891939 |
| **H23...O2** | **0.002546** | **0.079234** | **0.058272** | **0.199293** |
| H24...O22 | -0.63912 | -2.27013 | 0.980044 | 0.875138 |
| N4...C7 | -0.30014 | -0.63286 | 0.806799 | 0.671448 |
| N4...C9 | -0.40448 | -0.87467 | 0.816918 | 0.678711 |
| N5...C11 | -0.484 | -1.11093 | 0.844992 | 0.700142 |
| N5...C8 | -0.52767 | -1.25338 | 0.862861 | 0.714976 |
| N6...O2 | -0.66864 | -1.17122 | 0.85386 | 0.707367 |
| N6...O3 | -0.67251 | -1.178 | 0.853764 | 0.707287 |
| O1...H21 | -0.65048 | -2.32319 | 0.981457 | 0.879173 |
| O22...H23 | -0.64086 | -2.29443 | 0.981297 | 0.878706 |

TABLE S-X. AIM analysis data for Met-wtr.all

| BCP | ρ(r) | $\nabla^2\rho_{bcp}(r)$ | ELF | LOL |
|---|---|---|---|---|
| C10...H16 | -0.27648 | -0.9678 | 0.989922 | 0.908371 |
| C10...O1 | -0.36817 | -0.6578 | 0.716032 | 0.613602 |
| C11...C9 | -0.34761 | -0.9409 | 0.936815 | 0.793851 |
| C11...H17 | -0.29341 | -1.06326 | 0.9941 | 0.928494 |
| C12...C8 | -0.24505 | -0.70261 | 0.952407 | 0.81732 |
| C12...H19 | -0.26795 | -0.92055 | 0.986889 | 0.896676 |
| C7...C10 | -0.21225 | -0.63066 | 0.96387 | 0.837821 |
| C7...H13 | -0.28519 | -1.00098 | 0.990254 | 0.909771 |
| C8...N4 | -0.49678 | -0.96882 | 0.749721 | 0.633811 |
| C9...N6 | -0.39543 | -0.85196 | 0.808 | 0.672296 |
| **H13...O3** | **0.00217** | **0.060194** | **0.042969** | **0.174956** |
| H14...C7 | -0.28588 | -1.00903 | 0.991056 | 0.913268 |
| H14...O31 | 0.002102 | 0.045101 | 0.027781 | 0.144733 |
| H15...C10 | -0.2821 | -0.99407 | 0.990809 | 0.912173 |
| H16...O3 | 0.001665 | 0.036072 | 0.022248 | 0.131228 |
| H17...O28 | 0.002482 | 0.05981 | 0.055658 | 0.195473 |
| H18...C12 | -0.27351 | -0.95436 | 0.989354 | 0.906043 |
| H19...O31 | 0.000693 | 0.014277 | 0.013668 | 0.105648 |
| H20...C12 | -0.26237 | -0.89264 | 0.985207 | 0.890865 |
| H21...O22 | -0.00453 | 0.115585 | 0.137564 | 0.28546 |
| H24...O22 | -0.64182 | -2.3144 | 0.983059 | 0.883974 |
| H27...N5 | -0.0002 | 0.080072 | 0.124589 | 0.274016 |
| H29...O2 | 0.002687 | 0.07602 | 0.054745 | 0.194071 |
| H30...O28 | -0.63978 | -2.27488 | 0.980285 | 0.875814 |
| H33...O1 | -0.00057 | 0.106228 | 0.099273 | 0.24931 |
| N4...C7 | -0.30117 | -0.6116 | 0.786339 | 0.657363 |
| N4...C9 | -0.40026 | -0.87967 | 0.826886 | 0.686093 |
| N5...C11 | -0.49507 | -1.12297 | 0.83671 | 0.693603 |
| N5...C8 | -0.50693 | -1.21287 | 0.866299 | 0.717959 |
| N6...O2 | -0.67572 | -1.18677 | 0.854061 | 0.707533 |
| N6...O3 | -0.65297 | -1.1444 | 0.854186 | 0.707637 |
| O1...H21 | -0.60803 | -2.17217 | 0.979375 | 0.873289 |
| O22...H23 | -0.64747 | -2.32062 | 0.982137 | 0.881179 |
| O25...H18 | 0.002085 | 0.046243 | 0.044681 | 0.177965 |
| O25...H26 | -0.63726 | -2.25667 | 0.979321 | 0.873138 |
| O25...H27 | -0.62357 | -2.22421 | 0.979518 | 0.87368 |
| O28...H29 | -0.64136 | -2.29624 | 0.981354 | 0.878873 |
| O3...H24 | 0.003448 | 0.086886 | 0.041967 | 0.173152 |
| O31...H32 | -0.64402 | -2.28862 | 0.980135 | 0.875392 |
| O31...H33 | -0.62267 | -2.22425 | 0.979913 | 0.874774 |

TABLE S-XI. Cartesian coordinates of Metronidazole

| | | | |
|---|---|---|---|
| O | 3.245939 | 1.738927 | -0.315804 |
| O | -2.61276 | 1.588767 | -0.029273 |
| O | -0.607587 | 2.255099 | 0.376866 |
| N | 0.293796 | -0.387844 | 0.315368 |
| N | -0.95495 | -2.160301 | -0.165808 |
| N | -1.434344 | 1.387593 | 0.1515 |
| C | 1.491219 | 0.385633 | 0.619786 |
| C | 0.256306 | -1.729331 | 0.142129 |
| C | -0.996791 | 0.042053 | 0.088333 |
| C | 2.087146 | 0.997859 | -0.639813 |
| C | -1.744973 | -1.065966 | -0.199515 |
| C | 1.442773 | -2.609422 | 0.295035 |
| H | 1.238333 | 1.162294 | 1.329944 |
| H | 2.209315 | -0.287841 | 1.07476 |
| H | 2.39526 | 0.208996 | -1.321592 |
| H | 1.339262 | 1.612314 | -1.136742 |
| H | -2.793606 | -1.097739 | -0.424129 |
| H | 1.143373 | -3.612492 | 0.01613 |
| H | 2.264387 | -2.291443 | -0.342684 |
| H | 1.795189 | -2.621548 | 1.324744 |
| H | 2.980314 | 2.588193 | 0.041364 |

TABLE S-XII. Cartesian coordinates of Met-wtr.P1

| | | | |
|---|---|---|---|
| O | -2.441894 | -2.07175 | 0.496255 |
| O | 0.366797 | 3.091201 | 0.236281 |
| O | -1.153231 | 1.661836 | -0.276841 |
| N | 0.752805 | -0.387674 | -0.256454 |
| N | 2.915698 | -0.112214 | 0.179035 |
| N | 0.002038 | 1.967313 | -0.011737 |
| C | -0.497775 | -1.096945 | -0.515604 |
| C | 1.961008 | -0.978215 | -0.128314 |
| C | 0.976586 | 0.948291 | 0.005775 |
| C | -1.256579 | -1.374367 | 0.777438 |
| C | 2.315158 | 1.089919 | 0.264091 |
| C | 2.187416 | -2.433142 | -0.31965 |
| H | -1.108583 | -0.513661 | -1.191803 |
| H | -0.24512 | -2.03551 | -0.996091 |
| H | -0.647021 | -1.996556 | 1.430159 |
| H | -1.452785 | -0.432106 | 1.29053 |
| H | 2.835458 | 1.998697 | 0.498432 |
| H | 3.22496 | -2.636887 | -0.084327 |
| H | 1.548922 | -3.026401 | 0.330718 |
| H | 1.993989 | -2.729712 | -1.34869 |
| H | -3.075933 | -1.420948 | 0.163892 |
| O | -3.689197 | 0.304461 | -0.392859 |
| H | -4.521448 | 0.707356 | -0.14477 |
| H | -3.020909 | 0.99452 | -0.329069 |

TABLE S-XIII. Cartesian coordinate of Met-wtr.P2

| | | | |
|---|---|---|---|
| O | 2.746476 | -2.684867 | -0.372409 |
| O | 1.40934 | 3.025247 | -0.146694 |
| O | 2.492091 | 1.206292 | 0.239135 |
| N | 0.087282 | -0.217636 | 0.317412 |
| N | -1.915924 | 0.635819 | -0.087276 |
| N | 1.465169 | 1.834504 | 0.052472 |
| C | 1.103024 | -1.225211 | 0.601887 |
| C | -1.237074 | -0.463038 | 0.21023 |
| C | 0.235127 | 1.129329 | 0.060447 |
| C | 1.767664 | -1.713567 | -0.677732 |
| C | -1.010843 | 1.634146 | -0.179952 |
| C | -1.848559 | -1.800228 | 0.418151 |
| H | 1.841257 | -0.801435 | 1.270134 |
| H | 0.610866 | -2.053763 | 1.098641 |
| H | 1.029364 | -2.195632 | -1.313744 |
| H | 2.18992 | -0.868304 | -1.217301 |
| H | -1.266466 | 2.650218 | -0.409884 |
| H | -2.906379 | -1.724299 | 0.190547 |
| H | -1.390523 | -2.548692 | -0.224433 |
| H | -1.733233 | -2.122147 | 1.451567 |
| H | 3.54038 | -2.241528 | -0.068584 |
| O | -4.708564 | -0.223366 | -0.225499 |
| H | -5.059698 | -0.099542 | -1.10714 |
| H | -3.881948 | 0.281288 | -0.202513 |

TABLE S-XIV. Cartesian coordinate of Met-wtr.P3

| | | | |
|---|---|---|---|
| O | -2.395849 | -2.097383 | -0.328003 |
| O | 3.407385 | -1.068386 | -0.084149 |
| O | 1.537375 | -2.023501 | 0.386013 |
| N | 0.229829 | 0.439628 | 0.244502 |
| N | 1.1788 | 2.369137 | -0.308827 |
| N | 2.214184 | -1.045365 | 0.113045 |
| C | -0.832504 | -0.49754 | 0.582406 |
| C | 0.05166 | 1.764255 | 0.030356 |
| C | 1.570411 | 0.209679 | 0.012788 |
| C | -1.306976 | -1.240889 | -0.657033 |
| C | 2.130481 | 1.412727 | -0.320521 |
| C | -1.256995 | 2.447959 | 0.186007 |
| H | -0.467607 | -1.193442 | 1.327614 |
| H | -1.656955 | 0.075041 | 0.992592 |
| H | -1.68768 | -0.530098 | -1.384177 |
| H | -0.488607 | -1.80395 | -1.097584 |
| H | 3.15896 | 1.601559 | -0.56118 |
| H | -1.152445 | 3.450084 | -0.212215 |
| H | -2.058674 | 1.923208 | -0.327089 |
| H | -1.532447 | 2.516362 | 1.23748 |
| H | -2.068793 | -2.850039 | 0.168151 |
| O | -3.919593 | 0.223371 | 0.102648 |
| H | -4.845255 | 0.336977 | -0.111605 |
| H | -3.731187 | -0.719461 | 0.010884 |

TABLE S-XV. Cartesian coordinate of Met-wtr.P4

| | | | |
|---|---|---|---|
| O | 3.620053 | -1.550636 | 0.509436 |
| O | -2.197102 | -1.604185 | -0.203006 |
| O | -0.146443 | -2.16575 | -0.494758 |
| N | 0.65115 | 0.492604 | -0.29627 |
| N | -0.688412 | 2.212952 | 0.127592 |
| N | -1.014562 | -1.335797 | -0.298309 |
| C | 1.894876 | -0.232145 | -0.525356 |
| C | 0.556187 | 1.826078 | -0.099966 |
| C | -0.640613 | 0.017565 | -0.171226 |
| C | 2.412428 | -0.861284 | 0.760544 |
| C | -1.446708 | 1.098054 | 0.084798 |
| C | 1.719707 | 2.747806 | -0.146277 |
| H | 1.729191 | -0.993898 | -1.276066 |
| H | 2.622571 | 0.478409 | -0.901589 |
| H | 2.636195 | -0.082484 | 1.485371 |
| H | 1.652179 | -1.516214 | 1.181189 |
| H | -2.511288 | 1.098239 | 0.238845 |
| H | 1.365093 | 3.734799 | 0.124784 |
| H | 2.499812 | 2.444817 | 0.548335 |
| H | 2.149965 | 2.790312 | -1.145091 |
| H | 3.416372 | -2.399215 | 0.112584 |
| O | -4.528501 | 0.06212 | 0.58501 |
| H | -3.932056 | -0.665006 | 0.382301 |
| H | -5.224588 | 0.013104 | -0.07031 |

TABLE S-XVI. Cartesian coordinate of Met-wtr.All

| | | | |
|---|---|---|---|
| O | 3.523685 | -0.064457 | 0.749351 |
| O | -1.626322 | -2.804421 | -0.025312 |
| O | 0.464539 | -2.442315 | -0.328819 |
| N | 0.021725 | 0.312857 | -0.353744 |
| N | -1.952639 | 1.287666 | -0.101028 |
| N | -0.684014 | -2.053224 | -0.176168 |
| C | 1.472677 | 0.20582 | -0.480025 |
| C | -0.64943 | 1.479245 | -0.29229 |
| C | -0.93301 | -0.672052 | -0.177135 |
| C | 2.117011 | -0.00923 | 0.884009 |
| C | -2.14475 | -0.041742 | -0.02921 |
| C | -0.009175 | 2.808789 | -0.443476 |
| H | 1.717469 | -0.606009 | -1.152073 |
| H | 1.831096 | 1.13859 | -0.899926 |
| H | 1.885187 | 0.834113 | 1.528997 |
| H | 1.734225 | -0.919959 | 1.342189 |
| H | -3.107196 | -0.497477 | 0.123833 |
| H | -0.744585 | 3.565439 | -0.192886 |
| H | 0.872791 | 2.906806 | 0.184497 |
| H | 0.309365 | 2.95718 | -1.474535 |
| H | 3.736968 | -0.923749 | 0.355344 |
| O | 3.351862 | -2.624826 | -0.363894 |
| H | 3.844804 | -3.436954 | -0.245121 |
| H | 2.419043 | -2.86222 | -0.341898 |
| O | -3.146525 | 3.960401 | 0.072811 |
| H | -3.489659 | 4.082801 | 0.957866 |
| H | -2.966594 | 3.01151 | -0.001122 |
| O | -4.486422 | -2.224553 | 0.593564 |
| H | -3.650716 | -2.677351 | 0.447567 |
| H | -5.10939 | -2.627176 | -0.011678 |
| O | 3.422257 | 2.642236 | 0.098499 |
| H | 4.080201 | 3.2886 | 0.352602 |
| H | 3.796956 | 1.773258 | 0.302102 |