**DFT, molecular docking and ADME prediction of tenofovir drug as a promising therapeutic inhibitor of SARS-CoV-2 Mpro**

Siyamak Shahaba,b,c\*, Masoome Sheikhid, Maksim Khancheuskia, Hooriye Yahyaeie, Hora Alhosseini Almodarresiyehf, Sadegh Kavianig

a Belarusian State University, ISEI BSU, Minsk, Republic of Belarus

b Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus,13 Surganov Str., Minsk 220072

c Institute of Chemistry of New Materials, National Academy of Sciences of Belarus, 36 Skarina Str., Minsk 220141

d Independent Researcher, Gonbad-e-Kavoos, Iran

e Department of Chemistry, Zanjan Branch, Islamic Azad University, Zanjan, Iran

f Department of Materials Science and Engineering, School of Engineering, Meybod University, 89616-99557, Meybod, Yazd, Iran

g Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran.

\*Corresponding author Email address: [siyamak.shahab@yahoo.com](mailto:siyamak.shahab@yahoo.com)

**Table S1**

Mulliken andnatural charge charges (e) of the tenofovir molecule.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Mulliken | | | |  | NBO | | | |
| Atom | Charge | Atom | Charge |  | Atom | Charge | Atom | Charge |
| C1 | 0.114 | O18 | -0.539 |  | C1 | -0.004 | O18 | -0.983 |
| C2 | 0.647 | C19 | -0.459 |  | C2 | 0.380 | C19 | -0.720 |
| N3 | -0.729 | H20 | 0.184 |  | N3 | -0.547 | H20 | 0.227 |
| C4 | 0.430 | H21 | 0.322 |  | C4 | 0.237 | H21 | 0.411 |
| N5 | -0.711 | H22 | 0.330 |  | N5 | -0.530 | H22 | 0.413 |
| C6 | 0.679 | H23 | 0.213 |  | C6 | 0.423 | H23 | 0.245 |
| N7 | -0.705 | H24 | 0.205 |  | N7 | -0.750 | H24 | 0.269 |
| N8 | -0.702 | H25 | 0.208 |  | N8 | -0.482 | H25 | 0.267 |
| C9 | 0.437 | H26 | 0.185 |  | C9 | 0.199 | H26 | 0.249 |
| N10 | -0.755 | H27 | 0.189 |  | N10 | -0.377 | H27 | 0.243 |
| C11 | -0.079 | H28 | 0.196 |  | C11 | -0.290 | H28 | 0.258 |
| C12 | 0.095 | H29 | 0.421 |  | C12 | 0.041 | H29 | 0.486 |
| O13 | -0.621 | H30 | 0.430 |  | O13 | -0.530 | H30 | 0.482 |
| C14 | 0.046 | H31 | 0.178 |  | C14 | -0.508 | H31 | 0.249 |
| P15 | 0.371 | H32 | 0.172 |  | P15 | 2.093 | H32 | 0.245 |
| O16 | -0.428 | H33 | 0.173 |  | O16 | -1.005 | H33 | 0.241 |
| O17 | -0.504 |  |  |  | O17 | -0.936 |  |  |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table S2**  Significant donor–acceptor interactions and second order perturbation energies of the tenofovir molecule. | | | | | | |
| Donor (i) | Occupancy | Acceptor (j) | Occupancy | E(2)a  kcal/mol | E(j)-E(i)b  a.u. | F(i , j)c  a.u. |
| π(C1-C2) | 1.64406 | π\*(N3-C4) | 0.42013 | 10.83 | 0.25 | 0.047 |
|  |  | π\*(N5-C6) | 0.48441 | 30.16 | 0.26 | 0.081 |
|  |  | π\*(N8-C9) | 0.33284 | 14.54 | 0.27 | 0.056 |
| π(N3-C4) | 1.81214 | π\*(C1-C2) | 0.47896 | 24.87 | 0.32 | 0.086 |
|  |  | π\*(N5-C6) | 0.48441 | 6.61 | 0.30 | 0.043 |
| π(N5-C6) | 1.67416 | π\*(C1-C2) | 0.47896 | 9.30 | 0.30 | 0.049 |
|  |  | π\*(N3-C4) | 0.42013 | 42.95 | 0.27 | 0.099 |
| π(N8-C9) | 1.88378 | π\*(C1-C2) | 0.47896 | 17.10 | 0.31 | 0.072 |
| σ(C1-C2) | 1.97267 | σ\*(C1-C6) | 0.03763 | 4.16 | 1.27 | 0.065 |
| σ(C1-C6) |  | σ\*(C1-C2) | 0.03622 | 3.87 | 1.27 | 0.063 |
|  |  | σ\*(C1-N8) | 0.02281 | 2.44 | 1.18 | 0.048 |
| σ(C1-N8) | 1.97602 | σ\*(C1-C6) | 0.03763 | 2.36 | 1.31 | 0.050 |
|  |  | σ\*(C2-N3) | 0.02352 | 3.14 | 1.26 | 0.056 |
|  |  | σ\*(C9-H23) | 0.01497 | 4.69 | 1.24 | 0.068 |
| σ(N3-C4) | 1.98547 | σ\*(C2-N3) | 0.02352 | 2.07 | 1.33 | 0.047 |
|  |  | σ\*(C2-N10) | 0.03670 | 7.46 | 1.27 | 0.087 |
| σ(N8-C9) | 1.98770 | σ\*(C1-C6) | 0.03763 | 5.54 | 1.39 | 0.079 |
|  |  | σ\*(C1-N8) | 0.02281 | 1.21 | 1.29 | 0.035 |
|  |  | σ\*(C9-H23) | 0.01497 | 0.76 | 1.32 | 0.028 |
|  |  | σ\*(N10-C11) | 0.02706 | 1.37 | 1.15 | 0.036 |
| σ(C14-P15) | 1.95762 | σ\*(P15-O16) | 0.10764 | 4.29 | 0.82 | 0.054 |
|  |  | σ\*(P15-O17) | 0.25431 | 4.60 | 0.69 | 0.053 |
|  |  | σ\*(P15-O18) | 0.20783 | 6.11 | 0.74 | 0.063 |
|  |  | σ\*(O17-H29) | 0.00794 | 1.47 | 0.88 | 0.032 |
| n1(N3) | 1.81593 | π\*(C1-C2) | 0.47896 | 7.36 | 0.91 | 0.076 |
|  |  | σ\*(C2-N10) | 0.03670 | 2.47 | 0.81 | 0.042 |
|  |  | σ\*(C4-N5) | 0.02127 | 9.42 | 0.88 | 0.085 |
|  |  | σ\*(C4-H20) | 0.01984 | 2.34 | 0.85 | 0.042 |
| n1(N5) | 1.91150 | σ\*(C1-C6) | 0.03763 | 8.18 | 0.90 | 0.077 |
|  |  | σ\*(N3-C4) | 0.03106 | 12.30 | 0.85 | 0.092 |
|  |  | π\*(N5-C6) | 0.48441 | 51.58 | 0.27 | 0.110 |
| n1(N8) | 1.93358 | σ\*(C1-C2) | 0.03622 | 5.28 | 0.92 | 0.063 |
|  |  | σ\*(C9-N10) | 0.03737 | 8.27 | 0.79 | 0.073 |
| n1(N10) | 1.53740 | π\*(C1-C2) | 0.47896 | 45.31 | 0.26 | 0.097 |
|  |  | π\*(N8-C9) | 0.33284 | 46.83 | 0.25 | 0.100 |
| n1(O13) | 1.96564 | σ\*(C12-H26) | 0.02265 | 3.42 | 1.04 | 0.053 |
|  |  | σ\*(C14-H27) | 0.02305 | 2.72 | 1.01 | 0.047 |
| n2(O13) | 1.90784 | σ\*(C11-C12) | 0.03453 | 3.93 | 0.63 | 0.045 |
|  |  | σ\*(C12-C19) | 0.02130 | 4.55 | 0.66 | 0.050 |
|  |  | σ\*(C14-P15) | 0.17597 | 9.49 | 0.45 | 0.060 |
|  |  | σ\*(C14-H27) | 0.02305 | 3.02 | 0.70 | 0.042 |
| n1(O16) | 1.97989 | σ\*(C14-P15) | 0.17597 | 0.66 | 0.93 | 0.023 |
| n2(O16) | 1.78857 | σ\*(C14-P15) | 0.17597 | 14.37 | 0.40 | 0.068 |
|  |  | σ\*(P15-O18) | 0.20783 | 26.18 | 0.40 | 0.092 |
| n1(O17) | 1.96405 | σ\*(C14-P15) | 0.17597 | 1.73 | 0.85 | 0.035 |
|  |  | σ\*(P15-O18) | 0.20783 | 1.30 | 0.85 | 0.031 |
| n2(O17) | 1.90658 | σ\*(C11-H24) | 0.01750 | 1.49 | 0.76 | 0.031 |
|  |  | σ\*(P15-O16) | 0.10764 | 11.05 | 0.56 | 0.071 |
|  |  | σ\*(P15-O18) | 0.20783 | 9.31 | 0.48 | 0.062 |
| n1(O18) | 1.95374 | σ\*(C14-P15) | 0.17597 | 2.29 | 0.79 | 0.039 |
|  |  | σ\*(P15-O16) | 0.10764 | 2.76 | 0.87 | 0.044 |
|  |  | σ\*(P15-O18) | 0.20783 | 1.13 | 0.79 | 0.028 |
| n2(O18) | 1.88380 | σ\*(C14-P15) | 0.17597 | 5.40 | 0.46 | 0.045 |
|  |  | σ\*(P15-O17) | 0.25431 | 17.96 | 0.42 | 0.080 |
| a E(2) Energy of hyperconjucative interactions,  b Energy difference between donor and acceptor i and j NBO orbitals,  c F(i, j) is the Fock matrix element between i and j NBO orbitals. | | | | | | |