# Electronic structure and conformational flexibility of D-cycloserine

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# SUPPLEMENTARY MATERIALS

## a) Cycloserine Conformers: Geometry Descriptors

The three-dimensional features of the structures in Figure 1 are defined by:

a) the puckering of the isoxazolidine ring, as described by the sign and the magnitude of the dihedral angle ξ = N(2)-O(1)-C(5)-C(4) (Fig. S1).

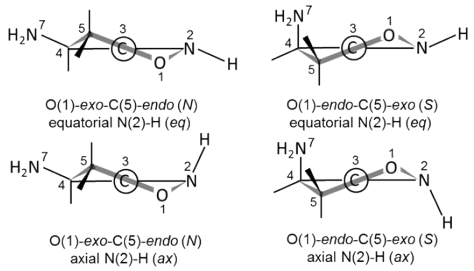


**Fig. S1.** Isoxazolidine ring puckering.

Positive ξ values describe isoxazolidine ring puckering O(1)-*exo*-C(5)-*endo*, relative to the position of the N(7) atom (North conformers denoted with the *N* symbol in Table S1). Instead, negative ξ values refer to ring puckering O(1)-*endo*-C(5)-*exo* (South conformers denoted with the *S* symbol). It is worth noting that in *N*-conformers the N(7)$H_2$ group is equatorially oriented, while it is axially oriented in the *S*-ones.

b) the dihedral angle ω = C(5)-O(1)-N(2)−H (Fig. S1), which describes the orientation of the N(2)−H hydrogen in the isoxazolidine ring. A 130° < $|\omega|$ < 180° value indicates that the N(2)−H hydrogen is equatorially oriented (denoted with the symbol *eq* in Fig. S1 and in Table S1), whereas a 80° < $|\omega|$ < 130° value indicates that the N(2)−H hydrogen is axially oriented (denoted with the symbol *ax* in Fig. S1 and in Table S1);

(c) the torsional angle γ defining the orientation of the N(7)$H_2$ lone pair relative to the C(3) atom. The γ value is calculated by adding 180° to the angle ψ between C(3) and the bisector of the H-N(7)-H angle (Fig. S2a). Depending upon the value of the γ angle, the symbolism illustrated in Fig. S2b is applied in Table S1.

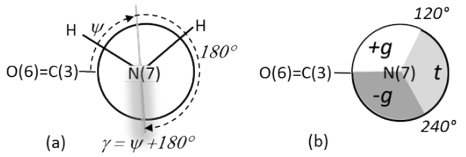


**Fig. S2.** Torsional angle $\gamma$.

Table S1 resumes the results of the **MP2(fc)/6-311++G**** calculations for the 8 most stable conformers reported in Figure 1.

**Table S1.** Structural features, relative energies and relative Boltzmann populations for the 8 most stable conformers of D-cycloserine depicted in Figure 1.

| Conformer (Figure 1) | Dihedral angles | | | MP2/ 6-311++G** | | Boltzmann population[b)] |
|---|---|---|---|---|---|---|
| | ξ | ω | γ | $\Delta^{\circ}H_{395}$[a)] | $\Delta^{\circ}G_{395}$[a)] | |
| **I** | *N* | *eq* | *t* | 0.00 | 0.00 | 1.000 |
| **II** | *N* | *eq* | +*g* | 0.35 | 0.45 | 0.563 |
| **III** | *S* | *eq* | *t* | 0.43 | 0.58 | 0.475 |
| **IV** | *N* | *ax* | +*g* | 0.76 | 0.74 | 0.391 |
| **V** | *N* | *ax* | *t* | 0.92 | 0.66 | 0.434 |
| **VI** | *S* | *ax* | *t* | 1.45 | 1.44 | 0.160 |
| **VII** | *S* | *eq* | +*g* | 1.58 | 1.64 | 0.124 |
| **VIII** | *N* | *eq* | -*g* | 2.82 | 2.73 | 0.031 |

[a)]Relative $\Delta^{\circ}H_{395}$ and $\Delta^{\circ}G_{395}$ (kcal/mol) at T = 395K; [b)] Gibbs free energy Boltzmann populations at T=395K. Only conformers with relative population > 0.100 at T=395K are considered in this work.

# b) D-Cycloserine Conformers: MP2(fc)/6-311++G** Optimized Cartesian Coordinates of Structures I-XII

## Structure I

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 7 | 0 | 0.000000 | 0.000000 | 1.389254 |
| 3 | 8 | 0 | 1.349503 | 0.000000 | 1.863029 |
| 4 | 6 | 0 | 1.989763 | -0.870719 | 0.920857 |
| 5 | 6 | 0 | 1.400381 | -0.462722 | -0.425126 |
| 6 | 7 | 0 | 1.453686 | -1.515679 | -1.421159 |
| 7 | 8 | 0 | -0.954252 | 0.239081 | -0.714097 |
| 8 | 1 | 0 | 0.861231 | -2.290679 | -1.133867 |
| 9 | 1 | 0 | 1.735212 | -1.915405 | 1.145176 |
| 10 | 1 | 0 | 3.061985 | -0.707023 | 1.018093 |
| 11 | 1 | 0 | -0.535899 | 0.706404 | 1.882252 |
| 12 | 1 | 0 | 1.923570 | 0.419930 | -0.811093 |
| 13 | 1 | 0 | 1.077098 | -1.175626 | -2.301550 |

## Structure II

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 7 | 0 | 0.000000 | 0.000000 | 1.385043 |
| 3 | 8 | 0 | 1.343404 | 0.000000 | 1.866481 |
| 4 | 6 | 0 | 1.989470 | -0.850514 | 0.904974 |
| 5 | 6 | 0 | 1.416304 | -0.378258 | -0.428581 |
| 6 | 7 | 0 | 1.377308 | -1.379308 | -1.477697 |
| 7 | 8 | 0 | -0.956907 | 0.198600 | -0.722517 |
| 8 | 1 | 0 | 2.212405 | -1.338389 | -2.051756 |
| 9 | 1 | 0 | 1.709927 | -1.896890 | 1.073309 |
| 10 | 1 | 0 | 3.061150 | -0.698528 | 1.033389 |
| 11 | 1 | 0 | -0.551456 | 0.689062 | 1.884281 |
| 12 | 1 | 0 | 1.899885 | 0.569277 | -0.717407 |
| 13 | 1 | 0 | 0.580086 | -1.192458 | -2.081741 |

## Structure III

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 7 | 0 | 0.000000 | 0.000000 | 1.392525 |
| 3 | 8 | 0 | 1.346137 | 0.000000 | 1.871277 |
| 4 | 6 | 0 | 1.989608 | 0.858665 | 0.912749 |
| 5 | 6 | 0 | 1.418105 | 0.408703 | -0.421762 |
| 6 | 7 | 0 | 2.168128 | -0.725880 | -0.960157 |
| 7 | 8 | 0 | -0.947577 | -0.279714 | -0.708594 |
| 8 | 1 | 0 | 2.214588 | -1.465408 | -0.262625 |
| 9 | 1 | 0 | 3.062416 | 0.692003 | 1.007012 |
| 10 | 1 | 0 | 1.725226 | 1.900352 | 1.127591 |
| 11 | 1 | 0 | -0.535626 | -0.711678 | 1.878663 |

| | | | | | |
|---|---|---|---|---|---|
| 12 | 1 | 0 | 1.383178 | 1.205762 | -1.166747 |
| 13 | 1 | 0 | 1.678478 | -1.109638 | -1.764898 |

## Structure IV

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 7 | 0 | 0.000000 | 0.000000 | 1.382166 |
| 3 | 8 | 0 | 1.326151 | 0.000000 | 1.885928 |
| 4 | 6 | 0 | 2.149323 | -0.385203 | 0.764300 |
| 5 | 6 | 0 | 1.446230 | 0.252266 | -0.429507 |
| 6 | 7 | 0 | 1.707412 | -0.383783 | -1.704653 |
| 7 | 8 | 0 | -0.960376 | -0.176372 | -0.723235 |
| 8 | 1 | 0 | 2.392222 | 0.135667 | -2.241206 |
| 9 | 1 | 0 | 2.150264 | -1.476030 | 0.642204 |
| 10 | 1 | 0 | 3.152135 | -0.013114 | 0.976356 |
| 11 | 1 | 0 | -0.588005 | -0.671324 | 1.865729 |
| 12 | 1 | 0 | 1.610730 | 1.340176 | -0.415289 |
| 13 | 1 | 0 | 0.844762 | -0.414076 | -2.243693 |

## Structure V

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 6 | 0 | 0.000000 | 0.000000 | 1.536981 |
| 3 | 7 | 0 | 1.328779 | 0.000000 | 1.919255 |
| 4 | 8 | 0 | 2.182408 | -0.218573 | 0.805648 |
| 5 | 6 | 0 | 1.323451 | -0.713351 | -0.239211 |
| 6 | 8 | 0 | -0.959912 | -0.018498 | 2.283335 |
| 7 | 7 | 0 | -1.129520 | -0.646598 | -0.631648 |
| 8 | 1 | 0 | -1.289692 | -1.555364 | -0.204614 |
| 9 | 1 | 0 | 1.189494 | -1.800508 | -0.135157 |
| 10 | 1 | 0 | 1.808357 | -0.477911 | -1.185922 |
| 11 | 1 | 0 | 1.614447 | -0.543756 | 2.726920 |
| 12 | 1 | 0 | 0.071019 | 1.036543 | -0.348292 |
| 13 | 1 | 0 | -1.972464 | -0.103952 | -0.467801 |

## Structure VI

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 6 | 0 | 0.000000 | 0.000000 | 1.535645 |
| 3 | 7 | 0 | 1.340091 | 0.000000 | 1.903065 |

| | | | | | |
|---|---|---|---|---|---|
| 4 | 8 | 0 | 2.177934 | 0.269946 | 0.789077 |
| 5 | 6 | 0 | 1.286327 | 0.768242 | -0.234798 |
| 6 | 8 | 0 | -0.942049 | -0.048748 | 2.302830 |
| 7 | 7 | 0 | 0.069437 | -1.335086 | -0.589357 |
| 8 | 1 | 0 | 0.893072 | -1.819539 | -0.239546 |
| 9 | 1 | 0 | 1.758403 | 0.560286 | -1.195134 |
| 10 | 1 | 0 | 1.132464 | 1.845180 | -0.089899 |
| 11 | 1 | 0 | 1.626994 | 0.523344 | 2.724211 |
| 12 | 1 | 0 | -0.886422 | 0.520121 | -0.367032 |
| 13 | 1 | 0 | -0.740584 | -1.881104 | -0.307167 |

## Structure VII

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 7 | 0 | 0.000000 | 0.000000 | 1.386926 |
| 3 | 8 | 0 | 1.339747 | 0.000000 | 1.871421 |
| 4 | 6 | 0 | 2.001881 | 0.841104 | 0.916871 |
| 5 | 6 | 0 | 1.387993 | 0.478814 | -0.430863 |
| 6 | 7 | 0 | 2.043551 | -0.672603 | -1.047742 |
| 7 | 8 | 0 | -0.931152 | -0.305316 | -0.718458 |
| 8 | 1 | 0 | 2.931352 | -0.394614 | -1.455713 |
| 9 | 1 | 0 | 3.066512 | 0.617996 | 0.992584 |
| 10 | 1 | 0 | 1.800552 | 1.892060 | 1.158701 |
| 11 | 1 | 0 | -0.532249 | -0.722068 | 1.861157 |
| 12 | 1 | 0 | 1.287010 | 1.356383 | -1.083078 |
| 13 | 1 | 0 | 1.460941 | -1.027643 | -1.802015 |

## Structure VIII

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 6 | 0 | 0.000000 | 0.000000 | 1.534054 |
| 3 | 7 | 0 | 1.343528 | 0.000000 | 1.916430 |
| 4 | 8 | 0 | 2.153118 | 0.405716 | 0.807759 |
| 5 | 6 | 0 | 1.487450 | -0.250163 | -0.276361 |
| 6 | 8 | 0 | -0.941750 | -0.059368 | 2.293856 |
| 7 | 7 | 0 | -0.992100 | -0.902915 | -0.540333 |
| 8 | 1 | 0 | -0.969194 | -0.910160 | -1.554310 |
| 9 | 1 | 0 | 1.702196 | -1.327678 | -0.251652 |
| 10 | 1 | 0 | 1.865048 | 0.200068 | -1.195041 |
| 11 | 1 | 0 | 1.600492 | 0.541632 | 2.735332 |
| 12 | 1 | 0 | -0.252049 | 1.024492 | -0.302967 |
| 13 | 1 | 0 | -0.848860 | -1.850497 | -0.205894 |

## Structure IX

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 8 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 6 | 0 | 0.000000 | 0.000000 | 1.436012 |
| 3 | 6 | 0 | 1.486841 | 0.000000 | 1.794315 |
| 4 | 6 | 0 | 2.043376 | 0.860705 | 0.647781 |
| 5 | 7 | 0 | 0.996285 | 0.989204 | -0.269232 |
| 6 | 7 | 0 | 2.163616 | -1.291987 | 1.748711 |
| 7 | 8 | 0 | 3.136836 | 1.369130 | 0.536573 |
| 8 | 1 | 0 | 1.921646 | -1.785758 | 0.893493 |
| 9 | 1 | 0 | 1.868270 | -1.870608 | 2.529171 |
| 10 | 1 | 0 | 1.224821 | 0.983316 | -1.258015 |
| 11 | 1 | 0 | 1.697737 | 0.481187 | 2.751735 |
| 12 | 1 | 0 | -0.499344 | 0.908296 | 1.797486 |
| 13 | 1 | 0 | -0.535279 | -0.896347 | 1.751524 |

## Structure X

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.005327 | -0.039775 | -0.000949 |
| 2 | 7 | 0 | -0.002479 | 0.045866 | 1.388425 |
| 3 | 8 | 0 | 1.326402 | 0.053380 | 1.896007 |
| 4 | 6 | 0 | 2.143045 | -0.399817 | 0.800972 |
| 5 | 6 | 0 | 1.455877 | 0.204873 | -0.426334 |
| 6 | 7 | 0 | 1.718018 | -0.328385 | -1.741348 |
| 7 | 8 | 0 | -0.955209 | -0.294325 | -0.695594 |
| 8 | 1 | 0 | 2.709502 | -0.330021 | -1.952785 |
| 9 | 1 | 0 | 2.129103 | -1.498856 | 0.741205 |
| 10 | 1 | 0 | 3.154121 | -0.037353 | 0.993076 |
| 11 | 1 | 0 | -0.580808 | -0.622718 | 1.888573 |
| 12 | 1 | 0 | 1.631537 | 1.288086 | -0.424516 |
| 13 | 1 | 0 | 1.353388 | -1.269668 | -1.842079 |

## Structure XI

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 8 | 0 | -0.093713 | 0.034718 | 0.137449 |
| 2 | 6 | 0 | -0.013005 | 0.019340 | 1.578346 |
| 3 | 6 | 0 | 1.488335 | -0.030174 | 1.848184 |
| 4 | 6 | 0 | 1.942758 | 0.956765 | 0.764374 |
| 5 | 7 | 0 | 1.034055 | 0.793394 | -0.278351 |
| 6 | 7 | 0 | 2.143600 | -1.314057 | 1.629270 |
| 7 | 8 | 0 | 2.887379 | 1.716407 | 0.760369 |
| 8 | 1 | 0 | 1.853381 | -1.706905 | 0.737477 |

| | | | | | |
|---|---|---|---|---|---|
| 9 | 1 | 0 | 1.881264 | -1.972817 | 2.356343 |
| 10 | 1 | 0 | 0.753564 | 1.614136 | -0.806632 |
| 11 | 1 | 0 | 1.764674 | 0.362438 | 2.828162 |
| 12 | 1 | 0 | -0.455562 | 0.941760 | 1.980588 |
| 13 | 1 | 0 | -0.566776 | -0.858490 | 1.915332 |

# Structure XII

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 0.000000 | 0.000000 | 0.000000 |
| 2 | 7 | 0 | 0.000000 | 0.000000 | 1.369630 |
| 3 | 8 | 0 | 1.291003 | 0.000000 | 1.929875 |
| 4 | 6 | 0 | 2.160945 | 0.332617 | 0.828878 |
| 5 | 6 | 0 | 1.462415 | -0.196763 | -0.414576 |
| 6 | 7 | 0 | 1.699382 | -1.623810 | -0.616583 |
| 7 | 8 | 0 | -0.976123 | 0.091983 | -0.723796 |
| 8 | 1 | 0 | 2.627689 | -1.773360 | -1.001573 |
| 9 | 1 | 0 | 3.122718 | -0.137317 | 1.038634 |
| 10 | 1 | 0 | 2.261990 | 1.424435 | 0.768840 |
| 11 | 1 | 0 | -0.680733 | 0.504072 | 1.924134 |
| 12 | 1 | 0 | 1.660903 | 0.435230 | -1.289792 |
| 13 | 1 | 0 | 1.032001 | -1.988355 | -1.291557 |