

# Ligand Binding Path Sampling Based on Parallel Cascade Selection Molecular Dynamics: LB-PaCS-MD

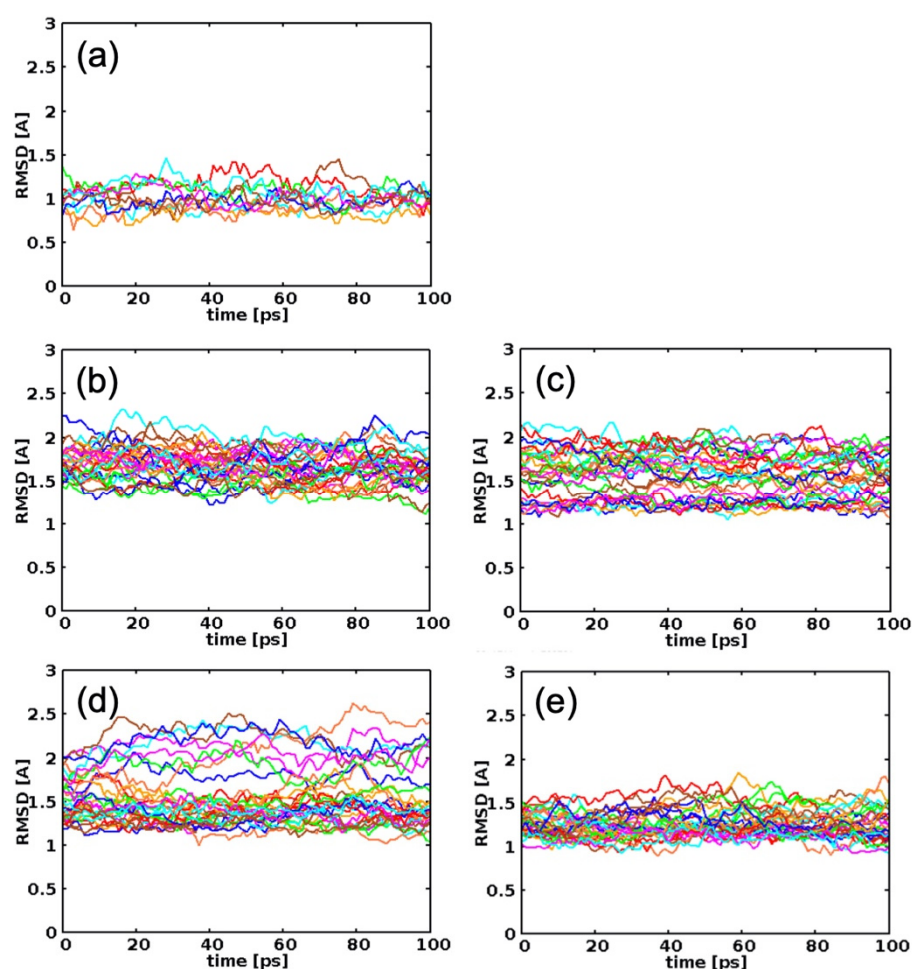
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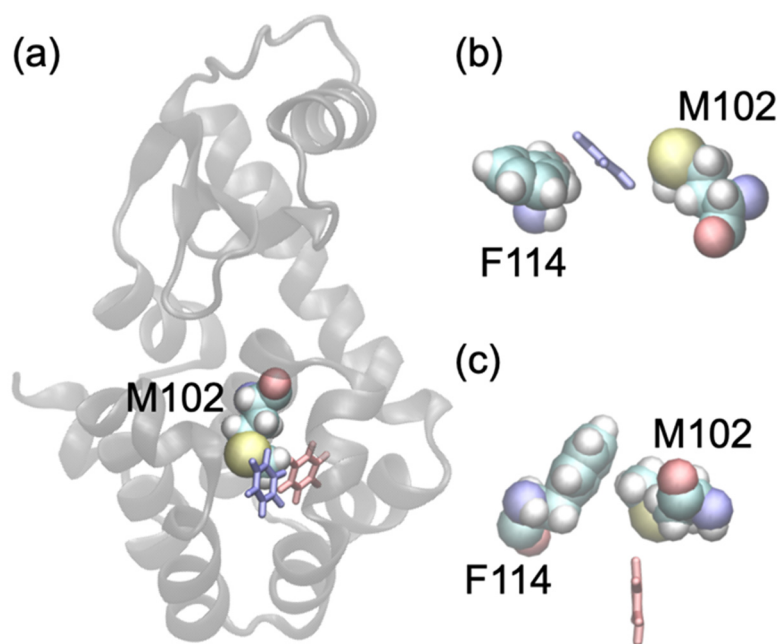
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\* Correspondence: ryuhei@ccs.tsukuba.ac.jp

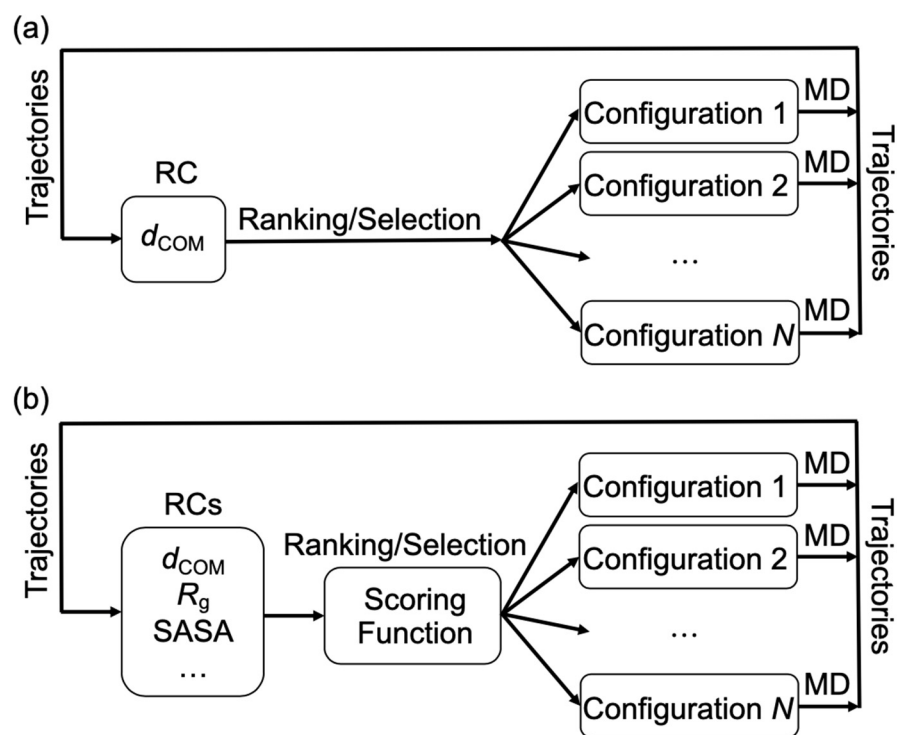
## 1. Supplementary Materials for the T4L and SARS-CoV2 M<sup>pro</sup> Systems



**Figure S1.** Time series of the backbone RMSD of each protein. For each system, the trajectories generated by each final cycle (the 100<sup>th</sup> cycle for T4L and the 50<sup>th</sup> cycle for SARS-CoV2 M<sup>pro</sup>) were used to calculate the backbone RMSD values. For the RMSD calculations, each relaxed configuration (the snapshots after the 200-ps MD simulations from the experimental structures for both systems) was used as each reference. (a) T4L. (b) SARS-CoV2 M<sup>pro</sup> with compound A. (c) SARS-CoV2 M<sup>pro</sup> compound B. (d) SARS-CoV2 M<sup>pro</sup> compound C. (e) SARS-CoV2 M<sup>pro</sup> compound D.



**Figure S2.** (a) Ligand-binding form sampled by LB-PaCS-MD. The key residue (M102) for the ligand-binding process is depicted in vdW representation with each benzene molecule in licorice representation (blue: LB-PaCS-MD, red: the X-ray structure). (b,c) The ligand-binding forms are highlighted around the binding site with a set of key residues (M102 and F114). (top) The benzene molecule sampled by LB-PaCS-MD. (bottom) The benzene molecule in the X-ray structure.



**Figure S3.** Flowchart of selections of initial configurations in LB-PaCS-MD. (a) Selections of initial configurations using a single reaction coordinate (RC) and (b) those using multiple RCs in terms of a pre-defined scoring function.

## 2. Parameter Files for All the Organic Compounds (Benzene, Compound A, B, C, and D)

The followings are the amber prep and frcmod files to perform MD simulations of the organic compounds.

### benzene.frcmod

remark goes here

MASS

BOND

ANGLE

DIHE

IMPROPER

|                                     |     |       |     |                       |
|-------------------------------------|-----|-------|-----|-----------------------|
| ca-ca-ca-ha                         | 1.1 | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |     |       |     |                       |

NONBON

**benzene.prep**

0 0 2

This is a remark line

molecule.res

BNZ INT 0

CORRECT OMIT DU BEG

0.0000

|    |      |    |   |    |    |    |       |         |          |           |
|----|------|----|---|----|----|----|-------|---------|----------|-----------|
| 1  | DUMM | DU | M | 0  | -1 | -2 | 0.000 | .0      | .0       | .00000    |
| 2  | DUMM | DU | M | 1  | 0  | -1 | 1.449 | .0      | .0       | .00000    |
| 3  | DUMM | DU | M | 2  | 1  | 0  | 1.523 | 111.21  | .0       | .00000    |
| 4  | C1   | ca | M | 3  | 2  | 1  | 1.540 | 111.208 | -180.000 | -0.120310 |
| 5  | H1   | ha | E | 4  | 3  | 2  | 1.070 | 24.218  | -179.739 | 0.120310  |
| 6  | C2   | ca | M | 4  | 3  | 2  | 1.397 | 144.319 | 179.930  | -0.120310 |
| 7  | H2   | ha | E | 6  | 4  | 3  | 1.071 | 119.784 | -0.104   | 0.120310  |
| 8  | C3   | ca | M | 6  | 4  | 3  | 1.396 | 120.398 | 179.890  | -0.120310 |
| 9  | H3   | ha | E | 8  | 6  | 4  | 1.070 | 120.087 | -179.580 | 0.120310  |
| 10 | C4   | ca | M | 8  | 6  | 4  | 1.397 | 119.880 | 0.427    | -0.120310 |
| 11 | H4   | ha | E | 10 | 8  | 6  | 1.070 | 120.129 | 179.364  | 0.120310  |
| 12 | C5   | ca | M | 10 | 8  | 6  | 1.395 | 119.643 | -0.660   | -0.120310 |
| 13 | H5   | ha | E | 12 | 10 | 8  | 1.071 | 119.762 | -179.333 | 0.120310  |
| 14 | C6   | ca | M | 12 | 10 | 8  | 1.397 | 120.544 | 0.712    | -0.120310 |
| 15 | H6   | ha | E | 14 | 12 | 10 | 1.070 | 120.127 | 179.464  | 0.120310  |

LOOP

C6 C1

IMPROPER

|    |    |    |    |
|----|----|----|----|
| C6 | C2 | C1 | H1 |
| C1 | C3 | C2 | H2 |
| C2 | C4 | C3 | H3 |
| C5 | C3 | C4 | H4 |
| C6 | C4 | C5 | H5 |
| C5 | C1 | C6 | H6 |

DONE

STOP

**A.frcmod**

remark goes here  
MASS

BOND

ANGLE

DIHE

IMPROPER

|                                     |      |       |     |                       |
|-------------------------------------|------|-------|-----|-----------------------|
| ca-ca-ca-ha                         | 1.1  | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| ca-ca-ca-n                          | 1.1  | 180.0 | 2.0 | Using default value   |
| c -c3-n -ca                         | 1.1  | 180.0 | 2.0 | Using default value   |
| cc-n -c -o                          | 10.5 | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| c -cd-cc-nc                         | 1.1  | 180.0 | 2.0 | Using default value   |
| cc-h4-cd-na                         | 1.1  | 180.0 | 2.0 | Using default value   |
| cd-cd-na-hn                         | 1.1  | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| h5-na-cd-nc                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-h4-ca-nb                         | 1.1  | 180.0 | 2.0 | Using default value   |
| c3-n -c -o                          | 10.5 | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |

NONBON

## A.prep

0 0 2

This is a remark line

molecule.res

LIG INT 0

CORRECT OMIT DU BEG

0.0000

|    |      |    |   |    |    |    |       |         |          |           |
|----|------|----|---|----|----|----|-------|---------|----------|-----------|
| 1  | DUMM | DU | M | 0  | -1 | -2 | 0.000 | .0      | .0       | .00000    |
| 2  | DUMM | DU | M | 1  | 0  | -1 | 1.449 | .0      | .0       | .00000    |
| 3  | DUMM | DU | M | 2  | 1  | 0  | 1.523 | 111.21  | .0       | .00000    |
| 4  | C20  | c3 | M | 3  | 2  | 1  | 1.540 | 111.208 | -180.000 | -0.442270 |
| 5  | H19  | hc | E | 4  | 3  | 2  | 1.096 | 103.783 | 176.498  | 0.096260  |
| 6  | H20  | hc | E | 4  | 3  | 2  | 1.097 | 146.340 | 15.454   | 0.096260  |
| 7  | H21  | hc | E | 4  | 3  | 2  | 1.095 | 50.892  | 74.721   | 0.096260  |
| 8  | C19  | c3 | M | 4  | 3  | 2  | 1.548 | 66.546  | -76.394  | 0.592550  |
| 9  | C21  | c3 | 3 | 8  | 4  | 3  | 1.540 | 108.114 | -158.610 | -0.442270 |
| 10 | H22  | hc | E | 9  | 8  | 4  | 1.096 | 111.825 | -178.432 | 0.096260  |
| 11 | H23  | hc | E | 9  | 8  | 4  | 1.097 | 109.662 | -59.224  | 0.096260  |
| 12 | H24  | hc | E | 9  | 8  | 4  | 1.096 | 111.866 | 59.968   | 0.096260  |
| 13 | C22  | c3 | 3 | 8  | 4  | 3  | 1.547 | 109.323 | 83.904   | -0.442270 |
| 14 | H25  | hc | E | 13 | 8  | 4  | 1.095 | 111.838 | -60.099  | 0.096260  |
| 15 | H26  | hc | E | 13 | 8  | 4  | 1.097 | 110.379 | 59.804   | 0.096260  |
| 16 | H27  | hc | E | 13 | 8  | 4  | 1.095 | 110.911 | 179.524  | 0.096260  |
| 17 | C18  | ca | M | 8  | 4  | 3  | 1.539 | 109.379 | -35.928  | 0.041500  |
| 18 | C23  | ca | B | 17 | 8  | 4  | 1.401 | 122.898 | -119.838 | -0.308670 |
| 19 | C24  | ca | S | 18 | 17 | 8  | 1.396 | 121.389 | -179.791 | -0.071080 |
| 20 | H29  | ha | E | 19 | 18 | 17 | 1.086 | 120.200 | -179.965 | 0.135000  |
| 21 | H28  | ha | E | 18 | 17 | 8  | 1.084 | 120.362 | -0.006   | 0.165670  |
| 22 | C17  | ca | M | 17 | 8  | 4  | 1.406 | 119.990 | 60.026   | -0.308670 |
| 23 | H18  | ha | E | 22 | 17 | 8  | 1.087 | 119.722 | -0.582   | 0.165670  |
| 24 | C16  | ca | M | 22 | 17 | 8  | 1.392 | 121.990 | -179.978 | -0.071080 |
| 25 | H17  | ha | E | 24 | 22 | 17 | 1.084 | 121.026 | 179.219  | 0.135000  |
| 26 | C15  | ca | M | 24 | 22 | 17 | 1.397 | 119.828 | -0.439   | 0.154650  |
| 27 | N1   | n  | M | 26 | 24 | 22 | 1.445 | 121.410 | -178.858 | -0.237230 |
| 28 | C1   | c  | B | 27 | 26 | 24 | 1.385 | 116.041 | -86.544  | 0.471270  |
| 29 | C25  | cc | S | 28 | 27 | 26 | 1.494 | 121.271 | -176.435 | 0.181290  |
| 30 | C26  | cd | B | 29 | 28 | 27 | 1.378 | 121.071 | -169.877 | -0.200760 |
| 31 | N4   | na | B | 30 | 29 | 28 | 1.371 | 105.606 | -177.422 | -0.262270 |
| 32 | C27  | cd | B | 31 | 30 | 29 | 1.368 | 107.510 | 0.333    | 0.072640  |
| 33 | N5   | nc | E | 32 | 31 | 30 | 1.313 | 111.349 | -0.116   | -0.395260 |
| 34 | H31  | h5 | E | 32 | 31 | 30 | 1.082 | 122.610 | 179.701  | 0.159280  |
| 35 | H33  | hn | E | 31 | 30 | 29 | 1.010 | 126.059 | -179.477 | 0.341700  |
| 36 | H30  | h4 | E | 30 | 29 | 28 | 1.078 | 130.888 | 2.110    | 0.220940  |
| 37 | O1   | o  | E | 28 | 27 | 26 | 1.228 | 121.133 | 1.032    | -0.567290 |
| 38 | C2   | c3 | M | 27 | 26 | 24 | 1.471 | 118.479 | 80.006   | -0.026980 |
| 39 | C10  | ca | S | 38 | 27 | 26 | 1.522 | 112.264 | 55.910   | -0.321260 |
| 40 | C11  | ca | B | 39 | 38 | 27 | 1.399 | 119.539 | 95.176   | 0.189540  |
| 41 | C12  | ca | B | 40 | 39 | 38 | 1.394 | 119.451 | -178.845 | -0.517240 |
| 42 | C13  | ca | B | 41 | 40 | 39 | 1.395 | 118.336 | -0.216   | 0.403240  |
| 43 | N3   | nb | S | 42 | 41 | 40 | 1.339 | 123.505 | 0.190    | -0.688890 |
| 44 | C14  | ca | S | 43 | 42 | 41 | 1.338 | 117.374 | 0.148    | 0.501150  |
| 45 | H16  | h4 | E | 44 | 43 | 42 | 1.088 | 115.802 | 179.687  | 0.020300  |

|    |     |    |   |    |    |    |       |         |          |           |
|----|-----|----|---|----|----|----|-------|---------|----------|-----------|
| 46 | H15 | h4 | E | 42 | 41 | 40 | 1.089 | 120.481 | -179.755 | 0.064920  |
| 47 | H14 | ha | E | 41 | 40 | 39 | 1.086 | 121.143 | -179.988 | 0.201900  |
| 48 | H13 | ha | E | 40 | 39 | 38 | 1.088 | 119.564 | 0.703    | 0.086040  |
| 49 | H1  | h1 | E | 38 | 27 | 26 | 1.093 | 105.843 | 171.426  | 0.050770  |
| 50 | C3  | c  | M | 38 | 27 | 26 | 1.555 | 111.431 | -76.704  | 0.887330  |
| 51 | O2  | o  | E | 50 | 38 | 27 | 1.226 | 121.164 | -23.697  | -0.618090 |
| 52 | N2  | n  | M | 50 | 38 | 27 | 1.361 | 115.482 | 161.537  | -0.980760 |
| 53 | H32 | hn | E | 52 | 50 | 38 | 1.011 | 118.688 | -3.542   | 0.387480  |
| 54 | C4  | c3 | M | 52 | 50 | 38 | 1.463 | 123.049 | 172.072  | 0.542290  |
| 55 | H2  | h1 | E | 54 | 52 | 50 | 1.095 | 105.400 | 23.116   | -0.005340 |
| 56 | C5  | c3 | M | 54 | 52 | 50 | 1.536 | 110.399 | 141.067  | -0.161980 |
| 57 | H3  | hc | E | 56 | 54 | 52 | 1.097 | 109.661 | -57.795  | 0.045720  |
| 58 | H4  | hc | E | 56 | 54 | 52 | 1.101 | 109.077 | 58.863   | 0.045720  |
| 59 | C6  | c3 | M | 56 | 54 | 52 | 1.538 | 111.446 | 179.376  | -0.037970 |
| 60 | H5  | hc | E | 59 | 56 | 54 | 1.099 | 109.068 | 65.983   | 0.020740  |
| 61 | H6  | hc | E | 59 | 56 | 54 | 1.097 | 109.823 | -177.644 | 0.020740  |
| 62 | C7  | c3 | M | 59 | 56 | 54 | 1.537 | 111.669 | -54.782  | -0.026140 |
| 63 | H7  | hc | E | 62 | 59 | 56 | 1.098 | 110.113 | 177.378  | 0.014720  |
| 64 | H8  | hc | E | 62 | 59 | 56 | 1.100 | 109.268 | -65.957  | 0.014720  |
| 65 | C8  | c3 | M | 62 | 59 | 56 | 1.536 | 111.216 | 54.798   | -0.037970 |
| 66 | H9  | hc | E | 65 | 62 | 59 | 1.099 | 109.330 | 65.794   | 0.020740  |
| 67 | H10 | hc | E | 65 | 62 | 59 | 1.097 | 110.396 | -177.449 | 0.020740  |
| 68 | C9  | c3 | M | 65 | 62 | 59 | 1.537 | 111.472 | -54.978  | -0.161980 |
| 69 | H11 | hc | E | 68 | 65 | 62 | 1.100 | 109.610 | -65.362  | 0.045720  |
| 70 | H12 | hc | E | 68 | 65 | 62 | 1.095 | 110.787 | 176.764  | 0.045720  |

## LOOP

C15 C24  
 N5 C25  
 C14 C10  
 C9 C4

## IMPROPER

C19 C23 C18 C17  
 C18 C24 C23 H28  
 C23 C15 C24 H29  
 C18 C16 C17 H18  
 C17 C15 C16 H17  
 C24 C16 C15 N1  
 C1 C2 N1 C15  
 C25 N1 C1 O1  
 C1 C26 C25 N5  
 C25 H30 C26 N4  
 C26 C27 N4 H33  
 H31 N4 C27 N5  
 C2 C11 C10 C14  
 C10 C12 C11 H13  
 C11 C13 C12 H14  
 C12 H15 C13 N3  
 C10 H16 C14 N3  
 C2 N2 C3 O2  
 C4 C3 N2 H32

DONE  
STOP

**B.frcmod**

remark goes here  
 MASS

BOND

ANGLE

DIHE

|             |   |       |         |       |                    |
|-------------|---|-------|---------|-------|--------------------|
| ce-cf-ca-ca | 1 | 0.700 | 180.000 | 2.000 | same as X -c2-ca-X |
| ha-cf-ca-ca | 1 | 0.700 | 180.000 | 2.000 | same as X -c2-ca-X |

IMPROPER

|                                     |      |       |     |                       |
|-------------------------------------|------|-------|-----|-----------------------|
| ca-ca-ca-oh                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-ha                         | 1.1  | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| c3-o -c -os                         | 10.5 | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| ce-o -c -os                         | 10.5 | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| c -cf-ce-ha                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ce-cf-ha                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-cf                         | 1.1  | 180.0 | 2.0 | Using default value   |

NONBON

**B.prep**

0 0 2

This is a remark line

molecule.res

LIG INT 0

CORRECT OMIT DU BEG

0.0000

|    |      |    |   |    |    |    |       |         |          |           |
|----|------|----|---|----|----|----|-------|---------|----------|-----------|
| 1  | DUMM | DU | M | 0  | -1 | -2 | 0.000 | .0      | .0       | .00000    |
| 2  | DUMM | DU | M | 1  | 0  | -1 | 1.449 | .0      | .0       | .00000    |
| 3  | DUMM | DU | M | 2  | 1  | 0  | 1.523 | 111.21  | .0       | .00000    |
| 4  | O5   | oh | M | 3  | 2  | 1  | 1.540 | 111.208 | -180.000 | -0.661420 |
| 5  | H13  | ho | E | 4  | 3  | 2  | 0.969 | 32.501  | -71.635  | 0.472560  |
| 6  | C9   | ca | M | 4  | 3  | 2  | 1.380 | 106.335 | 29.256   | 0.229310  |
| 7  | C8   | ca | B | 6  | 4  | 3  | 1.389 | 124.904 | -31.437  | -0.338840 |
| 8  | C5   | ca | S | 7  | 6  | 4  | 1.399 | 119.849 | 179.651  | -0.169490 |
| 9  | H5   | ha | E | 8  | 7  | 6  | 1.086 | 119.417 | -179.765 | 0.173080  |
| 10 | H6   | ha | E | 7  | 6  | 4  | 1.089 | 119.771 | -0.002   | 0.182820  |
| 11 | C7   | ca | M | 6  | 4  | 3  | 1.406 | 114.944 | 148.158  | 0.382290  |
| 12 | O3   | oh | S | 11 | 6  | 4  | 1.364 | 120.336 | 0.047    | -0.631110 |
| 13 | H11  | ho | E | 12 | 11 | 6  | 0.973 | 107.358 | 1.021    | 0.467930  |
| 14 | C4   | ca | M | 11 | 6  | 4  | 1.390 | 119.613 | -179.631 | -0.355470 |
| 15 | H4   | ha | E | 14 | 11 | 6  | 1.086 | 118.417 | -179.536 | 0.226710  |
| 16 | C3   | ca | M | 14 | 11 | 6  | 1.403 | 120.822 | -0.176   | -0.007670 |
| 17 | C1   | c3 | M | 16 | 14 | 11 | 1.515 | 120.614 | -179.407 | -0.026000 |
| 18 | H1   | hc | E | 17 | 16 | 14 | 1.096 | 110.404 | -40.563  | 0.053830  |
| 19 | H2   | hc | E | 17 | 16 | 14 | 1.095 | 109.955 | -158.518 | 0.053830  |
| 20 | C2   | c3 | M | 17 | 16 | 14 | 1.541 | 115.272 | 80.463   | 0.066660  |
| 21 | C6   | c  | B | 20 | 17 | 16 | 1.531 | 112.925 | 55.465   | 0.807380  |
| 22 | O2   | os | S | 21 | 20 | 17 | 1.353 | 109.686 | 63.150   | -0.424070 |
| 23 | C19  | c3 | 3 | 22 | 21 | 20 | 1.438 | 115.086 | 179.479  | -0.158960 |
| 24 | H14  | h1 | E | 23 | 22 | 21 | 1.094 | 110.426 | 61.005   | 0.123560  |
| 25 | H15  | h1 | E | 23 | 22 | 21 | 1.093 | 110.414 | -59.625  | 0.123560  |
| 26 | H16  | h1 | E | 23 | 22 | 21 | 1.090 | 105.584 | -179.253 | 0.123560  |
| 27 | O4   | o  | E | 21 | 20 | 17 | 1.206 | 125.958 | -116.973 | -0.558180 |
| 28 | H3   | h1 | E | 20 | 17 | 16 | 1.095 | 109.519 | 175.068  | 0.075070  |
| 29 | O1   | os | M | 20 | 17 | 16 | 1.426 | 108.308 | -65.794  | -0.441140 |
| 30 | C10  | c  | M | 29 | 20 | 17 | 1.367 | 116.025 | -159.191 | 0.888370  |
| 31 | O6   | o  | E | 30 | 29 | 20 | 1.216 | 122.967 | 4.093    | -0.606440 |
| 32 | C12  | ce | M | 30 | 29 | 20 | 1.470 | 110.405 | -177.056 | -0.527690 |
| 33 | H7   | ha | E | 32 | 30 | 29 | 1.084 | 116.784 | 1.946    | 0.203150  |
| 34 | C13  | cf | M | 32 | 30 | 29 | 1.349 | 119.878 | -178.600 | 0.035410  |
| 35 | H8   | ha | E | 34 | 32 | 30 | 1.089 | 116.001 | 0.192    | 0.123040  |
| 36 | C11  | ca | M | 34 | 32 | 30 | 1.457 | 128.022 | -179.729 | 0.126660  |
| 37 | C14  | ca | M | 36 | 34 | 32 | 1.410 | 118.430 | -179.708 | -0.399590 |
| 38 | H9   | ha | E | 37 | 36 | 34 | 1.089 | 119.469 | -0.072   | 0.203820  |
| 39 | C16  | ca | M | 37 | 36 | 34 | 1.386 | 120.915 | 179.949  | 0.230250  |
| 40 | O7   | oh | S | 39 | 37 | 36 | 1.378 | 124.842 | 179.995  | -0.658900 |
| 41 | H17  | ho | E | 40 | 39 | 37 | 0.968 | 109.803 | -0.663   | 0.476040  |
| 42 | C18  | ca | M | 39 | 37 | 36 | 1.406 | 120.399 | -0.013   | 0.390820  |
| 43 | O8   | oh | S | 42 | 39 | 37 | 1.358 | 120.511 | -179.989 | -0.618420 |
| 44 | H18  | ho | E | 43 | 42 | 39 | 0.972 | 107.586 | -0.186   | 0.468830  |
| 45 | C17  | ca | M | 42 | 39 | 37 | 1.396 | 119.241 | 0.021    | -0.327200 |

|    |     |    |   |    |    |    |       |         |         |           |
|----|-----|----|---|----|----|----|-------|---------|---------|-----------|
| 46 | H12 | ha | E | 45 | 42 | 39 | 1.085 | 118.422 | 179.969 | 0.220410  |
| 47 | C15 | ca | M | 45 | 42 | 39 | 1.390 | 120.320 | -0.046  | -0.210310 |
| 48 | H10 | ha | E | 47 | 45 | 42 | 1.085 | 119.052 | 179.864 | 0.191970  |

LOOP

C3 C5

C15 C11

IMPROPER

C7 C8 C9 O5

C9 C5 C8 H6

C3 C8 C5 H5

C4 C9 C7 O3

C7 C3 C4 H4

C1 C4 C3 C5

C2 O4 C6 O2

C12 O6 C10 O1

C10 C13 C12 H7

C11 C12 C13 H8

C14 C15 C11 C13

C11 C16 C14 H9

C14 C18 C16 O7

C16 C17 C18 O8

C18 C15 C17 H12

C11 C17 C15 H10

DONE

STOP

**C.frcmod**

remark goes here  
 MASS

BOND

ANGLE

DIHE

IMPROPER

|                                     |      |       |     |                       |
|-------------------------------------|------|-------|-----|-----------------------|
| ca-o -no-o                          | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-no                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-ha                         | 1.1  | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| ca-ca-ca-n                          | 1.1  | 180.0 | 2.0 | Using default value   |
| c -ca-n -hn                         | 1.1  | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| ca-n -c -o                          | 10.5 | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| c -ca-ca-ca                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-oh                         | 1.1  | 180.0 | 2.0 | Using default value   |

NONBON

**C.prep**

0 0 2

This is a remark line

molecule.res

LIG INT 0

CORRECT OMIT DU BEG

0.0000

|    |      |    |   |    |    |    |       |         |          |           |
|----|------|----|---|----|----|----|-------|---------|----------|-----------|
| 1  | DUMM | DU | M | 0  | -1 | -2 | 0.000 | .0      | .0       | .00000    |
| 2  | DUMM | DU | M | 1  | 0  | -1 | 1.449 | .0      | .0       | .00000    |
| 3  | DUMM | DU | M | 2  | 1  | 0  | 1.523 | 111.21  | .0       | .00000    |
| 4  | O3   | o  | M | 3  | 2  | 1  | 1.540 | 111.208 | -180.000 | -0.442850 |
| 5  | N2   | no | M | 4  | 3  | 2  | 1.232 | 47.501  | 0.000    | 0.711610  |
| 6  | O4   | o  | E | 5  | 4  | 3  | 1.233 | 124.660 | 180.000  | -0.442850 |
| 7  | C7   | ca | M | 5  | 4  | 3  | 1.464 | 117.618 | -0.000   | -0.010400 |
| 8  | C10  | ca | B | 7  | 5  | 4  | 1.392 | 119.826 | 0.000    | -0.118590 |
| 9  | C5   | ca | S | 8  | 7  | 5  | 1.388 | 119.722 | 180.000  | -0.344720 |
| 10 | H2   | ha | E | 9  | 8  | 7  | 1.080 | 120.795 | 180.000  | 0.232230  |
| 11 | H5   | ha | E | 8  | 7  | 5  | 1.083 | 119.494 | 0.000    | 0.196860  |
| 12 | C9   | ca | M | 7  | 5  | 4  | 1.393 | 118.781 | 180.000  | -0.076980 |
| 13 | H4   | ha | E | 12 | 7  | 5  | 1.082 | 120.181 | -0.000   | 0.187660  |
| 14 | C4   | ca | M | 12 | 7  | 5  | 1.384 | 118.411 | 180.000  | -0.163450 |
| 15 | Cl1  | cl | E | 14 | 12 | 7  | 1.765 | 118.027 | 180.000  | -0.068020 |
| 16 | C1   | ca | M | 14 | 12 | 7  | 1.417 | 122.113 | 0.000    | 0.486820  |
| 17 | N1   | n  | M | 16 | 14 | 12 | 1.392 | 118.462 | 180.000  | -0.601030 |
| 18 | H1   | hn | E | 17 | 16 | 14 | 1.009 | 113.680 | -0.000   | 0.259990  |
| 19 | C3   | c  | M | 17 | 16 | 14 | 1.395 | 128.221 | 180.000  | 0.755950  |
| 20 | O2   | o  | E | 19 | 17 | 16 | 1.220 | 121.892 | 0.000    | -0.526140 |
| 21 | C2   | ca | M | 19 | 17 | 16 | 1.506 | 115.441 | 180.000  | -0.273480 |
| 22 | C8   | ca | S | 21 | 19 | 17 | 1.408 | 122.590 | -0.000   | -0.021530 |
| 23 | H3   | ha | E | 22 | 21 | 19 | 1.083 | 121.575 | -0.000   | 0.164200  |
| 24 | C6   | ca | M | 21 | 19 | 17 | 1.420 | 119.958 | 180.000  | 0.495680  |
| 25 | O1   | oh | S | 24 | 21 | 19 | 1.353 | 120.253 | 0.000    | -0.604380 |
| 26 | H8   | ho | E | 25 | 24 | 21 | 0.971 | 108.433 | 180.000  | 0.451210  |
| 27 | C11  | ca | M | 24 | 21 | 19 | 1.403 | 119.708 | 180.000  | -0.446320 |
| 28 | H6   | ha | E | 27 | 24 | 21 | 1.089 | 118.858 | 180.000  | 0.190230  |
| 29 | C13  | ca | M | 27 | 24 | 21 | 1.387 | 121.748 | -0.000   | 0.087130  |
| 30 | H7   | ha | E | 29 | 27 | 24 | 1.085 | 120.689 | 180.000  | 0.141440  |
| 31 | C12  | ca | M | 29 | 27 | 24 | 1.393 | 118.809 | -0.000   | -0.127610 |
| 32 | Cl2  | cl | M | 31 | 29 | 27 | 1.756 | 119.921 | 180.000  | -0.092640 |

LOOP

C1 C5

C12 C8

IMPROPER

C7 O3 N2 O4

C9 C10 C7 N2

C7 C5 C10 H5

C1 C10 C5 H2

C4 C7 C9 H4

C9 C1 C4 Cl1

|     |     |     |     |
|-----|-----|-----|-----|
| C4  | C5  | C1  | N1  |
| C3  | C1  | N1  | H1  |
| C2  | N1  | C3  | O2  |
| C3  | C8  | C2  | C6  |
| C2  | C12 | C8  | H3  |
| C2  | C11 | C6  | O1  |
| C6  | C13 | C11 | H6  |
| C11 | C12 | C13 | H7  |
| C8  | C13 | C12 | Cl2 |

DONE

STOP

**D.frcmod**

remark goes here  
 MASS

BOND

ANGLE

DIHE

|             |   |       |         |       |                    |
|-------------|---|-------|---------|-------|--------------------|
| ca-ca-cc-cd | 1 | 0.700 | 180.000 | 2.000 | same as X -c2-ca-X |
| ca-ca-cc-c  | 1 | 0.700 | 180.000 | 2.000 | same as X -c2-ca-X |
| cc-cd-os-ca | 1 | 1.050 | 180.000 | 2.000 | same as X -c2-os-X |
| h4-cd-os-ca | 1 | 1.050 | 180.000 | 2.000 | same as X -c2-os-X |

IMPROPER

|                                     |      |       |     |                       |
|-------------------------------------|------|-------|-----|-----------------------|
| c2-c3-c2-c3                         | 1.1  | 180.0 | 2.0 | Using default value   |
| c2-c3-c2-ha                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-oh                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-ha                         | 1.1  | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| ca-ca-ca-cc                         | 1.1  | 180.0 | 2.0 | Using default value   |
| c -ca-cc-cd                         | 1.1  | 180.0 | 2.0 | Using default value   |
| cc-h4-cd-os                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-cc-c -o                          | 10.5 | 180.0 | 2.0 | General improper tor- |
| sional angle (2 general atom types) |      |       |     |                       |
| c -ca-ca-ca                         | 1.1  | 180.0 | 2.0 | Using default value   |
| ca-ca-ca-os                         | 1.1  | 180.0 | 2.0 | Using default value   |

NONBON

## D.prep

0 0 2

This is a remark line

molecule.res

LIG INT 0

CORRECT OMIT DU BEG

0.0000

|    |      |    |   |    |    |    |       |         |          |           |
|----|------|----|---|----|----|----|-------|---------|----------|-----------|
| 1  | DUMM | DU | M | 0  | -1 | -2 | 0.000 | .0      | .0       | .00000    |
| 2  | DUMM | DU | M | 1  | 0  | -1 | 1.449 | .0      | .0       | .00000    |
| 3  | DUMM | DU | M | 2  | 1  | 0  | 1.523 | 111.21  | .0       | .00000    |
| 4  | C19  | c3 | M | 3  | 2  | 1  | 1.540 | 111.208 | -180.000 | -0.442100 |
| 5  | H9   | hc | E | 4  | 3  | 2  | 1.094 | 116.833 | 79.438   | 0.121810  |
| 6  | H10  | hc | E | 4  | 3  | 2  | 1.099 | 10.259  | 113.814  | 0.121810  |
| 7  | H11  | hc | E | 4  | 3  | 2  | 1.099 | 107.197 | -159.252 | 0.121810  |
| 8  | C16  | c2 | M | 4  | 3  | 2  | 1.511 | 101.955 | -42.834  | 0.337910  |
| 9  | C20  | c3 | 3 | 8  | 4  | 3  | 1.512 | 114.399 | -54.449  | -0.442100 |
| 10 | H12  | hc | E | 9  | 8  | 4  | 1.092 | 113.523 | 174.541  | 0.121810  |
| 11 | H13  | hc | E | 9  | 8  | 4  | 1.098 | 110.177 | -64.516  | 0.121810  |
| 12 | H14  | hc | E | 9  | 8  | 4  | 1.099 | 110.791 | 52.853   | 0.121810  |
| 13 | C12  | c2 | M | 8  | 4  | 3  | 1.347 | 120.376 | 127.607  | -0.406140 |
| 14 | H5   | ha | E | 13 | 8  | 4  | 1.088 | 118.268 | -0.431   | 0.200370  |
| 15 | C4   | c3 | M | 13 | 8  | 4  | 1.514 | 128.320 | 178.596  | -0.053590 |
| 16 | H1   | hc | E | 15 | 13 | 8  | 1.097 | 110.805 | 4.975    | 0.094560  |
| 17 | H2   | hc | E | 15 | 13 | 8  | 1.094 | 108.820 | -111.484 | 0.094560  |
| 18 | C2   | ca | M | 15 | 13 | 8  | 1.521 | 112.753 | 126.966  | -0.088300 |
| 19 | C7   | ca | B | 18 | 15 | 13 | 1.398 | 118.084 | -62.924  | 0.178540  |
| 20 | O2   | oh | S | 19 | 18 | 15 | 1.381 | 123.042 | 2.220    | -0.566810 |
| 21 | H15  | ho | E | 20 | 19 | 18 | 0.977 | 108.258 | 33.060   | 0.369990  |
| 22 | C11  | ca | B | 19 | 18 | 15 | 1.404 | 122.107 | -175.742 | 0.351600  |
| 23 | O4   | oh | S | 22 | 19 | 18 | 1.360 | 119.804 | 179.786  | -0.595850 |
| 24 | H16  | ho | E | 23 | 22 | 19 | 0.974 | 106.274 | 2.406    | 0.433580  |
| 25 | C13  | ca | B | 22 | 19 | 18 | 1.391 | 119.363 | -0.321   | -0.345870 |
| 26 | C8   | ca | S | 25 | 22 | 19 | 1.394 | 119.253 | -1.133   | -0.144400 |
| 27 | H3   | ha | E | 26 | 25 | 22 | 1.085 | 119.274 | -177.523 | 0.145020  |
| 28 | H6   | ha | E | 25 | 22 | 19 | 1.085 | 119.241 | -179.533 | 0.217710  |
| 29 | C1   | ca | M | 18 | 15 | 13 | 1.414 | 123.742 | 119.533  | -0.083590 |
| 30 | C3   | cc | M | 29 | 18 | 15 | 1.488 | 122.306 | -3.967   | -0.241960 |
| 31 | C10  | cd | B | 30 | 29 | 18 | 1.356 | 119.893 | 122.316  | 0.185310  |
| 32 | O1   | os | E | 31 | 30 | 29 | 1.351 | 125.794 | 175.209  | -0.346430 |
| 33 | H4   | h4 | E | 31 | 30 | 29 | 1.084 | 123.364 | -4.675   | 0.153410  |
| 34 | C6   | c  | M | 30 | 29 | 18 | 1.470 | 121.911 | -62.493  | 0.807910  |
| 35 | O3   | o  | E | 34 | 30 | 29 | 1.252 | 122.497 | 4.747    | -0.609140 |
| 36 | C5   | ca | M | 34 | 30 | 29 | 1.453 | 115.670 | -175.014 | -0.657450 |
| 37 | C9   | ca | M | 36 | 34 | 30 | 1.409 | 121.093 | -0.117   | 0.572420  |
| 38 | C15  | ca | M | 37 | 36 | 34 | 1.387 | 123.161 | 179.941  | -0.618860 |
| 39 | H7   | ha | E | 38 | 37 | 36 | 1.083 | 121.312 | 179.987  | 0.256940  |
| 40 | C18  | ca | M | 38 | 37 | 36 | 1.399 | 117.608 | -0.188   | 0.629970  |
| 41 | O6   | oh | S | 40 | 38 | 37 | 1.359 | 116.654 | -179.960 | -0.601230 |
| 42 | H18  | ho | E | 41 | 40 | 38 | 0.970 | 109.206 | 179.867  | 0.437430  |
| 43 | C17  | ca | M | 40 | 38 | 37 | 1.401 | 121.681 | 0.089    | -0.705610 |
| 44 | H8   | ha | E | 43 | 40 | 38 | 1.086 | 121.309 | 179.995  | 0.255050  |
| 45 | C14  | ca | M | 43 | 40 | 38 | 1.394 | 119.894 | -0.085   | 0.660370  |

|    |     |    |   |    |    |    |       |         |          |           |
|----|-----|----|---|----|----|----|-------|---------|----------|-----------|
| 46 | O5  | oh | M | 45 | 43 | 40 | 1.339 | 119.249 | -179.977 | -0.609620 |
| 47 | H17 | ho | E | 46 | 45 | 43 | 1.000 | 106.245 | 179.808  | 0.445500  |

LOOP

|     |    |
|-----|----|
| C1  | C8 |
| C9  | O1 |
| C14 | C5 |

IMPROPER

|     |     |     |     |
|-----|-----|-----|-----|
| C12 | C19 | C16 | C20 |
| C16 | C4  | C12 | H5  |
| C4  | C7  | C2  | C1  |
| C2  | C11 | C7  | O2  |
| C7  | C13 | C11 | O4  |
| C11 | C8  | C13 | H6  |
| C13 | C1  | C8  | H3  |
| C2  | C8  | C1  | C3  |
| C6  | C1  | C3  | C10 |
| C3  | H4  | C10 | O1  |
| C5  | C3  | C6  | O3  |
| C6  | C9  | C5  | C14 |
| C5  | C15 | C9  | O1  |
| C9  | C18 | C15 | H7  |
| C15 | C17 | C18 | O6  |
| C18 | C14 | C17 | H8  |
| C5  | C17 | C14 | O5  |

DONE

STOP