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Supplementary Data

Conformational Preferences of RNase A *C*-Peptide Derivatives Containing A Highly Constrained Analog of Phenylalanine

Destardi Moye-Sherman,[a] Song Jin,[a] Inhye Ham,[a] Dongyeol Lim,[a] J. Martin Scholtz,[b] and Kevin Burgess[a]*

[a] *Texas A & M University, Chemistry Department, P.O. Box 300012, College Station, Texas 77842, and* [b] *Texas A & M University, Department of Biochemistry and Genetics, 426 Reynolds Building, College Station, TX 77843-1114.*

Supplementary Table 1.

Table 1. Determination of Peptide Concentration in CD Studies

Sample	UV	Amino Acid Analysis
RN-24	8.82×10^{-3}	7.81×10^{-3}
3R,3'R-cyclo FiFi	1.39×10^{-2}	1.33×10^{-2}
3S,3'S-cyclo FiFi	6.30×10^{-3}	2.18×10^{-3}

Residue Topology File for Cyclo-FiFi Appended to CHARMm 23.2 (Polar Hydrogens Only)

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MASS  235 CAA  12.01100 C  ! CYCLOPROPANE C Alpha
MASS  236 CA2E 14.02700 C  ! CYCLOPROPANE PRO-S C-BETA CH2
MASS  237 CB2E 14.02700 C  ! CYCLOPROPANE PRO-R C-BETA CH2
MASS  238 CB1E 13.01900 C  ! CYCLOPROPANE PRO-R C-BETA CH1(Mimic of D-AA)
MASS  239 CA1E 13.01900 C  ! CYCLOPROPANE PRO-S C-BETA CH1(Mimic of L-AA)

!3S,3'S-Cyclo-FiFi
RESI CYP    0.00000
GROU
ATOM N   NP    -0.40
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ATOM H   H     0.25
ATOM CA  CAA   0.10
GROU
ATOM CB1  CA1E  0.00
ATOM CG1  C6R   0.00
ATOM CD11 C6RE  0.00
ATOM CD12 C6RE  0.00
GROU
ATOM CE11 C6RE  0.00
ATOM CE12 C6RE  0.00
ATOM CZ1  C6RE  0.00
GROU
ATOM CB2  CB1E  0.00
ATOM CG2  C6R   0.00
ATOM CD21 C6RE  0.00
ATOM CD22 C6RE  0.00
GROU
ATOM CE21 C6RE  0.00
ATOM CE22 C6RE  0.00
ATOM CZ2  C6RE  0.00
GROU
ATOM C   C     0.60
ATOM O   O    -0.55
BOND N   CA     CA  C     C  +N     C  O     N  H
BOND CA  CB1    CB1 CB2   CB2 CA    CB1 CG1   CB2 CG2
BOND CG1 CD11   CG1 CD12   CD11 CE11   CD12 CE12   CE11 CZ1
BOND CE12 CZ1
BOND CG2 CD21   CG2 CD22   CD21 CE21
BOND CD22 CE22   CE21 CZ2   CE22 CZ2
IMPH N   -C  CA  H     C  CA  +N  O     CA  N   C   CB1
IMPH CA  N   C   CB2    CB1 CA  CB2 CG1    CB2 CA  CB1  CG2
IMPH CG1 CD11 CD12 CB1    CG2 CD21 CD22 CB2
IMPH CG1 CD11 CE11 CZ1    CD11 CE11 CZ1 CE12   CE11 CZ1 CE12 CD12
IMPH CZ1 CE12 CD12 CG1    CE12 CD12 CG1 CD11   CD12 CG1 CD11 CE11
IMPH CG2 CD21 CE21 CZ2    CD21 CE21 CZ2 CE22   CE21 CZ2 CE22 CD22
IMPH CZ2 CE22 CD22 CG2    CE22 CD22 CG2 CD21   CD22 CG2 CD21 CE21
DONO H N
ACCE O C
IC  -C  CA  *N  H    0.0000  0.00 180.00  0.00  0.0000
IC  -C  N   CA  C    0.0000  0.00 180.00  0.00  0.0000
IC  N   CA  C   +N   0.0000  0.00 180.00  0.00  0.0000
IC  +N  CA  *C  O    0.0000  0.00 180.00  0.00  0.0000
IC  CA  C   +N  +CA  0.0000  0.00 180.00  0.00  0.0000
IC  N   C   *CA CB1  0.0000  0.00 120.00  0.00  0.0000
IC  N   C   *CA CB2  0.0000  0.00 -120.00 0.00  0.0000
IC  N   CA  CB2 CG2  0.0000  0.00 180.00  0.00  0.0000
IC  CG1 CB1 CA  C    0.0000  0.00 180.00  0.00  0.0000
IC  CB2 CB1 CG1 CD12 0.0000  0.00  90.00  0.00  0.0000
IC  CD11 CB1 *CG1 CD12  0.0000  0.00 180.00  0.00  0.0000
IC  CD11 CG1 CD12 CE12  0.0000  0.00  0.00  0.00  0.0000
IC  CD12 CG1 CD11 CE11  0.0000  0.00  0.00  0.00  0.0000
IC  CG1 CD11 CE11 CZ1   0.0000  0.00  0.00  0.00  0.0000
IC  CB1 CB2 CG2 CD21 0.0000  0.00  90.00  0.00  0.0000
IC  CD21 CB2 *CG2 CD22  0.0000  0.00 180.00  0.00  0.0000
IC  CD21 CG2 CD22 CE22  0.0000  0.00  0.00  0.00  0.0000
IC  CD22 CG2 CD21 CE21  0.0000  0.00  0.00  0.00  0.0000
IC  CG2 CD21 CE21 CZ2   0.0000  0.00  0.00  0.00  0.0000
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IC  CG1  CB1  CB2  CG2   0.0000   0.00 180.00   0.00  0.0000

PATC FIRS YNTE LAST YCTE

!3R,3'R-Cyclo-FiFi
RESI CYPS  0.00000
GROU
ATOM N   NP   -0.40
ATOM H   H     0.25
ATOM CA  CAA   0.10
GROU
ATOM CB1  CA1E  0.00
ATOM CG1  C6R   0.00
ATOM CD11 C6RE  0.00
ATOM CD12 C6RE  0.00
GROU
ATOM CE11 C6RE  0.00
ATOM CE12 C6RE  0.00
ATOM CZ1  C6RE  0.00
GROU
ATOM CB2  CB1E  0.00
ATOM CG2  C6R   0.00
ATOM CD21 C6RE  0.00
ATOM CD22 C6RE  0.00
GROU
ATOM CE21 C6RE  0.00
ATOM CE22 C6RE  0.00
ATOM CZ2  C6RE  0.00
GROU
ATOM C   C     0.60
ATOM O   O    -0.55
BOND N   CA     CA  C     C  +N     C  O     N  H
BOND CA  CB1    CB1 CB2   CB2 CA    CB1 CG1   CB2 CG2
BOND CG1 CD11   CG1 CD12   CD11 CE11   CD12 CE12   CE11 CZ1
BOND CE12 CZ1
BOND CG2 CD21   CG2 CD22   CD21 CE21
BOND CD22 CE22   CE21 CZ2   CE22 CZ2
IMPH N   -C  CA  H     C  CA  +N  O     CA  N   C   CB1
IMPH CA  N   C   CB2   CB1 CA  CB2 CG1   CB2 CA  CB1  CG2
IMPH CG1 CD11 CD12 CB1   CG2 CD21 CD22 CB2
IMPH CG1 CD11 CE11 CZ1   CD11 CE11 CZ1 CE12   CE11 CZ1 CE12 CD12
IMPH CZ1 CE12 CD12 CG1   CE12 CD12 CG1 CD11   CD12 CG1 CD11 CE11
IMPH CG2 CD21 CE21 CZ2   CD21 CE21 CZ2 CE22   CE21 CZ2 CE22 CD22
IMPH CZ2 CE22 CD22 CG2   CE22 CD22 CG2 CD21   CD22 CG2 CD21 CE21
DONO H N
ACCE O C
IC  -C  CA  *N  H    0.0000   0.00 180.00   0.00  0.0000
IC  -C  N   CA  C    0.0000   0.00 180.00   0.00  0.0000
IC  N   CA  C   +N   0.0000   0.00 180.00   0.00  0.0000
IC  +N  CA  *C  O    0.0000   0.00 180.00   0.00  0.0000
IC  CA  C   +N  +CA  0.0000   0.00 180.00   0.00  0.0000
IC  N   C   *CA CB1  0.0000   0.00 120.00   0.00  0.0000
IC  N   C   *CA CB2  0.0000   0.00 -120.00  0.00  0.0000
IC  C   CA  CB1 CG1  0.0000   0.00  0.00    0.00  0.0000
IC  CG2 CB2 CA  N    0.0000   0.00  0.00    0.00  0.0000
IC  CG2 CB2 CA  CA   0.0000   0.00 180      0.00  0.0000
IC  CA  CB1 CG1 CD11 0.0000   0.00  90.00   0.00  0.0000
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IC  CD11 CB1  *CG1 CD12  0.0000   0.00  180.00   0.00  0.0000
IC  CD11 CG1  CD12 CE12  0.0000   0.00   0.00    0.00  0.0000
IC  CD12 CG1  CD11 CE11  0.0000   0.00   0.00    0.00  0.0000
IC  CG1  CD11 CE11 CZ1   0.0000   0.00   0.00    0.00  0.0000
IC  CA   CB2  CG2  CD21  0.0000   0.00  90.00    0.00  0.0000
IC  CD21 CB2  *CG2 CD22  0.0000   0.00  180.00   0.00  0.0000
IC  CD21 CG2  CD22 CE22  0.0000   0.00   0.00    0.00  0.0000
IC  CD22 CG2  CD21 CE21  0.0000   0.00   0.00    0.00  0.0000
IC  CG2  CD21 CE21 CZ2   0.0000   0.00   0.00    0.00  0.0000
IC  CG1  CB1  CB2  CG2   0.0000   0.00  180.00   0.00  0.0000
IC  CA   CB1  *CB2 CG2   0.0000   0.00 -110.00   0.00  0.0000
IC  CA   CB2  *CB1 CG1   0.0000   0.00 -110.00   0.00  0.0000

PATC FIRS YNTE LAST YCTE

! PATCH

PRES NASU       -0.30
! This patch replaces the N-terminal with an succimide group
! This patch will not work with PRO as the first residue
! Apply this patch ONLY after the NTER patch has been applied
GROU
ATOM CT21  CH2E   0.00
ATOM CT22  CH2E   0.00
GROU
ATOM CNT1  C      0.55
ATOM CNT2  C      0.55
ATOM ONT1  O     -0.55
ATOM ONT2  O     -0.55
GROU
ATOM N   NP    -0.40
! change atom type for CA for GLY
ATOM CA  CH1E   .10
DELE ATOM HT1
DELE ATOM HT2
DELE ATOM HT3
BOND CT21  CNT1    CT22  CNT2     CNT1 N      CNT2 N
BOND CNT2  ONT2    CT21  CT22     CNT1 ONT1
ANGL CA  N  CNT1   CA  N  CNT2   CNT1 N  CNT2   N  CNT1 ONT1
ANGL ONT1 CNT1 CT21  ONT2 CNT2 CT22 N  CNT1  CT21  N  CNT1  CT21
ANGL N  CNT2  ONT2  CNT1 CT21 CT22   CT21 CT22 CNT2
DIHE CT21  CNT1  N   CNT2
DIHE CT22  CNT2  N   CNT1
DIHE CT21  CNT1  N   CA
DIHE CT22  CNT2  N   CA
DIHE ONT2  CNT2  N   CNT1
DIHE ONT1  CNT1  N   CNT2
DIHE ONT1  CNT1  N   CA
DIHE ONT2  CNT2  N   CA
DIHE CNT1  N     CA  C
DIHE CNT2  N     CA  C
DIHE CNT1  N     CA  CB
DIHE CNT2  N     CA  CB
IMPH N   CNT1  CA  CNT2
! inverted for new IMPH rules
IMPH CNT1  CT21  ONT1  N
IMPH CNT2  CT22  ONT2  N
```

```
ACCE ONT1 CNT1
ACCE ONT2 CNT2
IC  C   CA    N   CNT1   0.0000   0.00 180.00   0.00  0.0000
IC  C   CA    N   CNT2   0.0000   0.00   0.00   0.00  0.0000
IC  CT21 CNT1 N   CA     0.0000   0.00 180.00   0.00  0.0000
IC  CT22 CNT2 N   CA     0.0000   0.00   0.00   0.00  0.0000
IC  N   CT21 *CNT1 ONT1  0.0000   0.00 180.00   0.00  0.0000
IC  N   CT22 *CNT2 ONT2  0.0000   0.00 180.00   0.00  0.0000
IC  CT21 CT22 CNT2  N     0.0000   0.00   0.00   0.00  0.0000
IC  CT22 CT21 CNT1  N     0.0000   0.00   0.00   0.00  0.0000
IC  CT21 CNT1  N   CNT2  0.0000   0.00   0.00   0.00  0.0000
IC  CT22 CNT2  N   CNT1  0.0000   0.00   0.00   0.00  0.0000
IC  CA  CNT1 *N   CNT2    0.0000   0.00 180.00   0.00  0.0000


!CYCLO-FIFI  NONBOND PARAMETERS
CAA     1.65   -0.0903      1.800   1.65   -0.1   1.75
CA2E    1.77   -0.1142      2.235   1.77   -0.1   1.76
CB2E    1.77   -0.1142      2.235   1.77   -0.1   1.76
CB1E    1.35   -0.0486      2.265   1.35   -0.1   1.76
CA1E    1.35   -0.0486      2.265   1.35   -0.1   1.76
!FINISH CYCLOPROPANE NONBOND PARAMETERS!

! S,S-CYCLO-FIFI DIHEDRAL PARAMETERS
X   NP  CAA X      0.10 3  180.0
X   CAA C   X      0.05 3  180.0
X   CA1E C6R  X      0.10 3   0.0
X   CAA  NT   X      0.50 2  180.0
C   CAA  CB1E C6R     0.16 1   0.0
X   CAA  CB1E X      0.16 3   0.0
NP  CAA  CA1E C6R     0.16 1   0.0
X   CAA  CA1E X      0.16 3   0.0
X   CB1E C6R  X      0.10 3   0.0
C6R  CB1E CA1E C6R     0.16 1  180.0
C6RE C6R  CA1E CB1E    0.40 3   0.0
CAA  CA1E CB1E C6R     0.40 3   0.0
CAA  CB1E CA1E C6R     0.40 3   0.0
!FINISH S,S-CYCLO-FIFI  DIHEDRAL PARAMETERS

! S,S-CYCLO-FIFI  ANGLE PARAMETERS

C   NP  CAA    44.0    117.6
CAA NP  H      23.0    120.8
C   CAA NP     65.0    115.0
CAA C   NP     75.0    120.0
CAA C   O      75.0    121.5
CB1E C6R  C6RE   70.0    122.0
CA1E C6R  C6RE   70.0    122.0
C6R  CB1E CAA    50.0    115.0
C6R  CA1E CAA    50.0    115.0
C6R  CB1E CA1E   50.0    115.0
C6R  CA1E CB1E   50.0    115.0
CAA  CA1E CB1E   45.0     60.0
CAA  CB1E CA1E   45.0     60.0
CB1E CAA  CA1E   45.0     60.0
C   CAA  CA1E   50.0    118.0
C   CAA  CB1E   50.0    118.0
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CA1E CAA  NP    45.0    115.0
CB1E CAA  NP    45.0    115.0
NT   CAA  CB1E  45.0    115.0
NT   CAA  CA1E  45.0    115.0
CAA  C    NT    75.0    120.0
H    NT   CAA   35.0    107.0
NT   CAA  C     70.0    117.0
HC   NT   CAA   35.0    107.0
CAA  C    OC    75.0    121.5

!FINISH S,S-CYCLO-FIFI  ANGLE PARAMETERS

!S,S-CYCLO-FIFI IMPROPER PARAMETERS

CAA  X    X    CA1E   55.0  0  30.75
CAA  X    X    CB1E   55.0  0  -30.75
CB1E X    X    C6R    55.0  0  29.925
CB1E CAA  CA1E C6R    55.0  0  -29.925
CA1E X    X    C6R    55.0  0  -29.925
CA1E CAA  CB1E C6R    55.0  0  -29.925
C6R  C6RE C6RE CB1E   130.0 0   0.00
C6R  C6RE C6RE CA1E   130.0 0   0.00
C    OC   OC   CAA    100.0 0   0.00
X    NP   C    X      55.0  0  35.26439

!FINISH S,S-CYCLO-FIFI  IMPROPER PARAMETERS


! R,R-CYCLO-FIFI ANGLE PARAMETERS

C    NP   CAA    44.0    117.6
CAA  NP   H      23.0    120.8
C    CAA  NP     65.0    115.0
CAA  C    NP     75.0    120.0
CAA  C    O      75.0    121.5
CB1E C6R  C6RE   70.0    122.0
CA1E C6R  C6RE   70.0    122.0
C6R  CA1E CAA    50.0    115.0
C6R  CB1E CAA    50.0    115.0
C6R  CA1E CB1E   50.0    115.0
C6R  CB1E CA1E   50.0    115.0
CAA  CA1E CB1E   45.0     60.0
CAA  CB1E CA1E   45.0     60.0
CB1E CAA  CA1E   45.0     60.0
CA1E CAA  CB1E   45.0     60.0
CAA  CA1E C6RE   50.0    119.9
CAA  CB1E C6RE   50.0    120.4
C    CAA  CA1E   50.0    118.0
C    CAA  CB1E   50.0    118.0
CA1E CAA  NP     45.0    115.0
CB1E CAA  NP     45.0    115.0
CAA  C    NT     75.0    120.0
H    NT   CAA    35.0    107.0
NT   CAA  C      70.0    117.0
HC   NT   CAA    35.0    107.0
CAA  C    OC     75.0    121.5
NT   CAA  CB1E   45.0    115.0
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```
NT  CAA  CA1E   45.0    115.0


!FINISH R,R-CYCLO-FIFI  ANGLE PARAMETERS

!R,R-CYCLO-FIFI  DIHEDRAL PARAMETERS
X   NP   CAA  X      0.10 3   0.0
X   CAA  C    X      0.05 3   0.0
X   C6R  CB1E X      0.10 3   0.0
X   C6R  CA1E X      0.10 3   0.0
C6RE C6R  CB1E CAA     0.10 3   0.0
C6RE C6R  CA1E CAA     0.10 3   0.0
NP   CAA  CA1E C6R     0.16 1   0.0
C    CB1E CAA  NP      0.16 3   0.0
X    CAA  NT   X       0.50 3   0.0
X    CAA  CB1E X       0.16 3   0.0
X    CAA  CA1E X       0.16 3   0.0
X    CB1E C6R  X       0.10 3   0.0
C6RE C6R CA1E CB1E     0.40 3   0.0
CAA  CA1E CB1E C6R     0.40 3   0.0
CAA  CB1E CA1E C6R     0.40 3   0.0

!FINISH R,R-CYCLO-FIFI  DIHEDRAL PARAMETERS

!R,R-CYCLO-FIFI  IMPROPER PARAMETERS

CAA X   X   CB1E   55.0  0  -30.75
CB1E CAA  CA1E C6R    55.0  0  29.925
CA1E CAA  CB1E C6R    55.0  0  29.925
C6R  C6RE C6RE CB1E   130.0 0   0.00
CAA X   X   CA1E   55.0  0  30.75
C6RE CB1E CA1E C6RE   130.0 0  180
C   OC  OC  CAA    100.0 0   0.00
X   NP  C   X      55.0  0  35.26439

!FINISH CYCLOPROPANE IMPROPER PARAMETERS
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