Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Unbinding of Fluorinated Oxime Drug from AChE Gorge in Polarizable Water: A Well-Tempered Meta Dynamics Study

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1. Generalized AMBER Force field parameters for the drugs

(A) OBI

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[ atom types ]
;name   bond_type     mass     charge   ptype   sigma         epsilon
 oh       oh          0.00000  0.00000   A     3.06647e-01   8.80314e-01
 ho       ho          0.00000  0.00000   A     0.00000e+00   0.00000e+00
 n2       n2          0.00000  0.00000   A     3.25000e-01   7.11280e-01
 ce       ce          0.00000  0.00000   A     3.39967e-01   3.59824e-01
 ca       ca          0.00000  0.00000   A     3.39967e-01   3.59824e-01
 ha       ha          0.00000  0.00000   A     2.59964e-01   6.27600e-02
 h4       h4          0.00000  0.00000   A     2.51055e-01   6.27600e-02
 na       na          0.00000  0.00000   A     3.25000e-01   7.11280e-01
 c3       c3          0.00000  0.00000   A     3.39967e-01   4.57730e-01
 os       os          0.00000  0.00000   A     3.00001e-01   7.11280e-01
 h2       h2          0.00000  0.00000   A     2.29317e-01   6.56888e-02

[ atoms ]
;   nr  type  resi  res  atom  cgnr     charge      mass
     1   oh     1   OBI    O3    1     0.1428     16.00000
     2   ho     1   OBI   H32    2     0.3119      1.00800
     3   n2     1   OBI    N4    3    -0.3009     14.01000
     4   ce     1   OBI   C14    4    -0.6436     12.01000
     5   ca     1   OBI   C11    5     0.0293     12.01000
     6   ca     1   OBI   C12    6    -0.1862    12.01000
     7   ha     1   OBI   H12    7     0.2752      1.00800
     8   ca     1   OBI   C13    8    -0.1437     12.01000
     9   h4     1   OBI   H13    9     0.1798      1.00800
    10   ca     1   OBI   C10   10     0.4319    12.01000
    11   ha     1   OBI   H10   11     0.3230      1.00800
    12   ca     1   OBI    C9   12    -0.0549     12.01000
    13   h4     1   OBI    H9   13     0.1784      1.00800
    14   na     1   OBI    N3   14     0.2645     14.01000
    15   c3     1   OBI    C8   15    -0.5683     12.01000
    16   os     1   OBI    O2   16     0.0216     16.00000
    17   c3     1   OBI    C7   17    -0.3621     12.01000
    18   na     1   OBI    N2   18     0.2534     14.01000
    19   ca     1   OBI    C5   19    -0.1499     12.01000
    20   h4     1   OBI    H5   20     0.1866      1.00800
    21   ca     1   OBI    C6   21    -0.3915     12.01000
    22   ha     1   OBI    H6   22     0.2706      1.00800
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    23   ca     1   OBI    C4   23    -0.4299     12.01000
    24   h4     1   OBI    H4   24     0.2213      1.00800
    25   ca     1   OBI    C3   25     0.7984     12.01000
    26   ha     1   OBI   H31   26     0.3204      1.00800
    27   ca     1   OBI    C2   27     0.1513     12.01000
    28   ce     1   OBI    C1   28    -0.6434     12.01000
    29   n2     1   OBI    N1   29    -0.3035     14.01000
    30   oh     1   OBI    O1   30     0.1422     16.00000
    31   ho     1   OBI   H15   31     0.3121      1.00800
    32   h4     1   OBI  HC14   32     0.2288      1.00800
    33   h2     1   OBI  HC82   33     0.2229      1.00800
    34   h2     1   OBI  HC83   34     0.2179      1.00800
    35   h2     1   OBI  HC72   35     0.1931      1.00800
    36   h2     1   OBI  HC73   36     0.2695      1.00800
    37   h4     1   OBI   HC1   37     0.2310      1.00800

[ bonds ]
;   ai     aj funct   r             k
     1      2   1    9.7400e-02    3.0928e+05 ;     O3 - H32
     1      3   1    1.3940e-01    3.4828e+05 ;     O3 - N4
     3      4   1    1.2790e-01    5.0191e+05 ;     N4 - C14
     4      5   1    1.4720e-01    3.0627e+05 ;    C14 - C11
     4     32   1    1.0916e-01    2.8267e+05 ;    C14 - HC14
     5      6   1    1.3870e-01    4.0033e+05 ;    C11 - C12
     5     10   1    1.3870e-01    4.0033e+05 ;    C11 - C10
     6      7   1    1.0870e-01    2.8811e+05 ;    C12 - H12
     6      8   1    1.3870e-01    4.0033e+05 ;    C12 - C13
     8      9   1    1.0880e-01    2.8694e+05 ;    C13 - H13
     8     14   1    1.3500e-01    3.9355e+05 ;    C13 - N3
    10     11   1    1.0870e-01    2.8811e+05 ;    C10 - H10
    10     12   1    1.3870e-01    4.0033e+05 ;    C10 - C9
    12     13   1    1.0880e-01    2.8694e+05 ;     C9 - H9
    12     14   1    1.3500e-01    3.9355e+05 ;     C9 - N3
    14     15   1    1.4560e-01    2.8008e+05 ;     N3 - C8
    15     16   1    1.4390e-01    2.5230e+05 ;     C8 - O2
    15     33   1    1.1000e-01    2.7313e+05 ;     C8 - HC82
    15     34   1    1.1000e-01    2.7313e+05 ;     C8 - HC83
    16     17   1    1.4390e-01    2.5230e+05 ;     O2 - C7
    17     18   1    1.4560e-01    2.8008e+05 ;     C7 - N2
    17     35   1    1.1000e-01    2.7313e+05 ;     C7 - HC72
    17     36   1    1.1000e-01    2.7313e+05 ;     C7 - HC73
    18     19   1    1.3500e-01    3.9355e+05 ;     N2 - C5
    18     23   1    1.3500e-01    3.9355e+05 ;     N2 - C4
    19     20   1    1.0880e-01    2.8694e+05 ;     C5 - H5
    19     21   1    1.3870e-01    4.0033e+05 ;     C5 - C6
    21     22   1    1.0870e-01    2.8811e+05 ;     C6 - H6
    21     27   1    1.3870e-01    4.0033e+05 ;     C6 - C2
    23     24   1    1.0880e-01    2.8694e+05 ;     C4 - H4
    23     25   1    1.3870e-01    4.0033e+05 ;     C4 - C3
    25     26   1    1.0870e-01    2.8811e+05 ;     C3 - H31
    25     27   1    1.3870e-01    4.0033e+05 ;     C3 - C2
    27     28   1    1.4720e-01    3.0627e+05 ;     C2 - C1
    28     29   1    1.2790e-01    5.0191e+05 ;     C1 - N1
    28     37   1    1.0916e-01    2.8267e+05 ;     C1 - HC1
    29     30   1    1.3940e-01    3.4828e+05 ;     N1 - O1
    30     31   1    9.7400e-02    3.0928e+05 ;     O1 - H15

[ pairs ]
;   ai     aj    funct
     1      5      1 ;     O3 - C11
     1     32      1 ;     O3 - HC14
     2      4      1 ;    H32 - C14
     3      6      1 ;     N4 - C12
     3     10      1 ;     N4 - C10
     4      7      1 ;    C14 - H12
     4      8      1 ;    C14 - C13
     4     11      1 ;    C14 - H10
     4     12      1 ;    C14 - C9
     5      9      1 ;    C11 - H13
     5     13      1 ;    C11 - H9
     5     14      1 ;    C11 - N3
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     6     11      1 ;    C12 - H10
     6     12      1 ;    C12 - C9
     6     15      1 ;    C12 - C8
     6     32      1 ;    C12 - HC14
     7      9      1 ;    H12 - H13
     7     10      1 ;    H12 - C10
     7     14      1 ;    H12 - N3
     8     10      1 ;    C13 - C10
     8     13      1 ;    C13 - H9
     8     16      1 ;    C13 - O2
     8     33      1 ;    C13 - HC82
     8     34      1 ;    C13 - HC83
     9     12      1 ;    H13 - C9
     9     15      1 ;    H13 - C8
    10     15      1 ;    C10 - C8
    10     32      1 ;    C10 - HC14
    11     13      1 ;    H10 - H9
    11     14      1 ;    H10 - N3
    12     16      1 ;     C9 - O2
    12     33      1 ;     C9 - HC82
    12     34      1 ;     C9 - HC83
    13     15      1 ;     H9 - C8
    14     17      1 ;     N3 - C7
    15     18      1 ;     C8 - N2
    15     35      1 ;     C8 - HC72
    15     36      1 ;     C8 - HC73
    16     19      1 ;     O2 - C5
    16     23      1 ;     O2 - C4
    17     20      1 ;     C7 - H5
    17     21      1 ;     C7 - C6
    17     24      1 ;     C7 - H4
    17     25      1 ;     C7 - C3
    17     33      1 ;     C7 - HC82
    17     34      1 ;     C7 - HC83
    18     22      1 ;     N2 - H6
    18     26      1 ;     N2 - H31
    18     27      1 ;     N2 - C2
    19     24      1 ;     C5 - H4
    19     25      1 ;     C5 - C3
    19     28      1 ;     C5 - C1
    19     35      1 ;     C5 - HC72
    19     36      1 ;     C5 - HC73
    20     22      1 ;     H5 - H6
    20     23      1 ;     H5 - C4
    20     27      1 ;     H5 - C2
    21     23      1 ;     C6 - C4
    21     26      1 ;     C6 - H31
    21     29      1 ;     C6 - N1
    21     37      1 ;     C6 - HC1
    22     25      1 ;     H6 - C3
    22     28      1 ;     H6 - C1
    23     28      1 ;     C4 - C1
    23     35      1 ;     C4 - HC72
    23     36      1 ;     C4 - HC73
    24     26      1 ;     H4 - H31
    24     27      1 ;     H4 - C2
    25     29      1 ;     C3 - N1
    25     37      1 ;     C3 - HC1
    26     28      1 ;    H31 - C1
    27     30      1 ;     C2 - O1
    28     31      1 ;     C1 - H15
    30     37      1 ;     O1 - HC1

[ angles ]
;   ai     aj     ak    funct   theta         cth
     1      3      4      1    1.1348e+02    5.9789e+02 ;     O3 - N4     - C14
     2      1      3      1    1.0274e+02    4.2317e+02 ;    H32 - O3     - N4
     3      4      5      1    1.2072e+02    5.7329e+02 ;     N4 - C14    - C11
     3      4     32      1    1.2152e+02    4.3823e+02 ;     N4 - C14    - HC14
     4      5      6      1    1.2066e+02    5.4292e+02 ;    C14 - C11    - C12
     4      5     10      1    1.2066e+02    5.4292e+02 ;    C14 - C11    - C10
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     5      4     32      1    1.1686e+02    3.9087e+02 ;    C11 - C14    - HC14
     5      6      7      1    1.2001e+02    4.0551e+02 ;    C11 - C12    - H12
     5      6      8      1    1.1997e+02    5.6216e+02 ;    C11 - C12    - C13
     5     10     11      1    1.2001e+02    4.0551e+02 ;    C11 - C10    - H10
     5     10     12      1    1.1997e+02    5.6216e+02 ;    C11 - C10    - C9
     6      5     10      1    1.1997e+02    5.6216e+02 ;    C12 - C11    - C10
     6      8      9      1    1.2109e+02    4.0367e+02 ;    C12 - C13    - H13
     6      8     14      1    1.1834e+02    5.8752e+02 ;    C12 - C13    - N3
     7      6      8      1    1.2001e+02    4.0551e+02 ;    H12 - C12    - C13
     8     14     12      1    1.2009e+02    5.6049e+02 ;    C13 - N3     - C9
     8     14     15      1    1.2436e+02    5.2844e+02 ;    C13 - N3     - C8
     9      8     14      1    1.1465e+02    4.3413e+02 ;    H13 - C13    - N3
    10     12     13      1    1.2109e+02    4.0367e+02 ;    C10 - C9     - H9
    10     12     14      1    1.1834e+02    5.8752e+02 ;    C10 - C9     - N3
    11     10     12      1    1.2001e+02    4.0551e+02 ;    H10 - C10    - C9
    12     14     15      1    1.2436e+02    5.2844e+02 ;     C9 - N3     - C8
    13     12     14      1    1.1465e+02    4.3413e+02 ;     H9 - C9     - N3
    14     15     16      1    1.0906e+02    5.9639e+02 ;     N3 - C8     - O2
    14     15     33      1    1.0766e+02    4.2066e+02 ;     N3 - C8     - HC82
    14     15     34      1    1.0766e+02    4.2066e+02 ;     N3 - C8     - HC83
    15     16     17      1    1.1245e+02    5.2208e+02 ;     C8 - O2     - C7
    16     15     33      1    1.0858e+02    4.2543e+02 ;     O2 - C8     - HC82
    16     15     34      1    1.0858e+02    4.2543e+02 ;     O2 - C8     - HC83
    16     17     18      1    1.0906e+02    5.9639e+02 ;     O2 - C7     - N2
    16     17     35      1    1.0858e+02    4.2543e+02 ;     O2 - C7     - HC72
    16     17     36      1    1.0858e+02    4.2543e+02 ;     O2 - C7     - HC73
    17     18     19      1    1.2436e+02    5.2844e+02 ;     C7 - N2     - C5
    17     18     23      1    1.2436e+02    5.2844e+02 ;     C7 - N2     - C4
    18     17     35      1    1.0766e+02    4.2066e+02 ;     N2 - C7     - HC72
    18     17     36      1    1.0766e+02    4.2066e+02 ;     N2 - C7     - HC73
    18     19     20      1    1.1465e+02    4.3413e+02 ;     N2 - C5     - H5
    18     19     21      1    1.1834e+02    5.8752e+02 ;     N2 - C5     - C6
    18     23     24      1    1.1465e+02    4.3413e+02 ;     N2 - C4     - H4
    18     23     25      1    1.1834e+02    5.8752e+02 ;     N2 - C4     - C3
    19     18     23      1    1.2009e+02    5.6049e+02 ;     C5 - N2     - C4
    19     21     22      1    1.2001e+02    4.0551e+02 ;     C5 - C6     - H6
    19     21     27      1    1.1997e+02    5.6216e+02 ;     C5 - C6     - C2
    20     19     21      1    1.2109e+02    4.0367e+02 ;     H5 - C5     - C6
    21     27     25      1    1.1997e+02    5.6216e+02 ;     C6 - C2     - C3
    21     27     28      1    1.2066e+02    5.4292e+02 ;     C6 - C2     - C1
    22     21     27      1    1.2001e+02    4.0551e+02 ;     H6 - C6     - C2
    23     25     26      1    1.2001e+02    4.0551e+02 ;     C4 - C3     - H31
    23     25     27      1    1.1997e+02    5.6216e+02 ;     C4 - C3     - C2
    24     23     25      1    1.2109e+02    4.0367e+02 ;     H4 - C4     - C3
    25     27     28      1    1.2066e+02    5.4292e+02 ;     C3 - C2     - C1
    26     25     27      1    1.2001e+02    4.0551e+02 ;    H31 - C3     - C2
    27     28     29      1    1.2072e+02    5.7329e+02 ;     C2 - C1     - N1
    27     28     37      1    1.1686e+02    3.9087e+02 ;     C2 - C1     - HC1
    28     29     30      1    1.1348e+02    5.9789e+02 ;     C1 - N1     - O1
    29     28     37      1    1.2152e+02    4.3823e+02 ;     N1 - C1     - HC1
    29     30     31      1    1.0274e+02    4.2317e+02 ;     N1 - O1     - H15
    33     15     34      1    1.0919e+02    3.2635e+02 ;   HC82 - C8     - HC83
    35     17     36      1    1.0919e+02    3.2635e+02 ;   HC72 - C7     - HC73

[ dihedrals ] ; propers
; treated as RBs in GROMACS to use combine multiple AMBER torsions per quartet
;    i      j      k      l   func    C0         C1         C2         C3         C4         C5
     1      3      4      5      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     O3-    N4-   C14-   C11
     1      3      4     32      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     O3-    N4-   C14-  HC14
     2      1      3      4      3   26.77760    0.00000  -26.77760    0.00000    0.00000
0.00000 ;    H32-    O3-    N4-   C14
     3      4      5      6      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     N4-   C14-   C11-   C12
     3      4      5     10      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     N4-   C14-   C11-   C10
     4      5      6      7      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C12-   H12
     4      5      6      8      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C12-   C13
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     4      5     10     11      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C10-   H10
     4      5     10     12      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C10-    C9
     5      6      8      9      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C12-   C13-   H13
     5      6      8     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C12-   C13-    N3
     5     10     12     13      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C10-    C9-    H9
     5     10     12     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C10-    C9-    N3
     6      5      4     32      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;    C12-   C11-   C14-  HC14
     6      5     10     11      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C12-   C11-   C10-   H10
     6      5     10     12      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C12-   C11-   C10-    C9
     6      8     14     12      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C12-   C13-    N3-    C9
     6      8     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C12-   C13-    N3-    C8
     7      6      5     10      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H12-   C12-   C11-   C10
     7      6      8      9      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H12-   C12-   C13-   H13
     7      6      8     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H12-   C12-   C13-    N3
     8      6      5     10      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C13-   C12-   C11-   C10
     8     14     12     10      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C13-    N3-    C9-   C10
     8     14     12     13      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C13-    N3-    C9-    H9
     8     14     15     16      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;    C13-    N3-    C8-    O2
     8     14     15     33      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;    C13-    N3-    C8-  HC82
     8     14     15     34      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;    C13-    N3-    C8-  HC83
     9      8     14     12      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    H13-   C13-    N3-    C9
     9      8     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    H13-   C13-    N3-    C8
    10      5      4     32      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;    C10-   C11-   C14-  HC14
    10     12     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C10-    C9-    N3-    C8
    11     10     12     13      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H10-   C10-    C9-    H9
    11     10     12     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H10-   C10-    C9-    N3
    12     14     15     16      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C9-    N3-    C8-    O2
    12     14     15     33      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C9-    N3-    C8-  HC82
    12     14     15     34      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C9-    N3-    C8-  HC83
    13     12     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     H9-    C9-    N3-    C8
    14     15     16     17      3    1.60247    4.80742    5.43920   -6.40989    0.00000
0.00000 ;     N3-    C8-    O2-    C7
    15     16     17     18      3    1.60247    4.80742    5.43920   -6.40989    0.00000
0.00000 ;     C8-    O2-    C7-    N2
    15     16     17     35      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C8-    O2-    C7-  HC72
    15     16     17     36      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C8-    O2-    C7-  HC73
    16     17     18     19      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     O2-    C7-    N2-    C5
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    16     17     18     23      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     O2-    C7-    N2-    C4
    17     16     15     33      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C7-    O2-    C8-  HC82
    17     16     15     34      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C7-    O2-    C8-  HC83
    17     18     19     20      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C5-    H5
    17     18     19     21      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C5-    C6
    17     18     23     24      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C4-    H4
    17     18     23     25      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C4-    C3
    18     19     21     22      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C5-    C6-    H6
    18     19     21     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C5-    C6-    C2
    18     23     25     26      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C4-    C3-   H31
    18     23     25     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C4-    C3-    C2
    19     18     17     35      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C5-    N2-    C7-  HC72
    19     18     17     36      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C5-    N2-    C7-  HC73
    19     18     23     24      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C5-    N2-    C4-    H4
    19     18     23     25      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C5-    N2-    C4-    C3
    19     21     27     25      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C5-    C6-    C2-    C3
    19     21     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C5-    C6-    C2-    C1
    20     19     18     23      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     H5-    C5-    N2-    C4
    20     19     21     22      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H5-    C5-    C6-    H6
    20     19     21     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H5-    C5-    C6-    C2
    21     19     18     23      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C6-    C5-    N2-    C4
    21     27     25     23      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C6-    C2-    C3-    C4
    21     27     25     26      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C6-    C2-    C3-   H31
    21     27     28     29      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     C6-    C2-    C1-    N1
    21     27     28     37      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;     C6-    C2-    C1-   HC1
    22     21     27     25      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H6-    C6-    C2-    C3
    22     21     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H6-    C6-    C2-    C1
    23     18     17     35      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C4-    N2-    C7-  HC72
    23     18     17     36      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C4-    N2-    C7-  HC73
    23     25     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C4-    C3-    C2-    C1
    24     23     25     26      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H4-    C4-    C3-   H31
    24     23     25     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H4-    C4-    C3-    C2
    25     27     28     29      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     C3-    C2-    C1-    N1
    25     27     28     37      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;     C3-    C2-    C1-   HC1
    26     25     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H31-    C3-    C2-    C1
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    27     28     29     30      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     C2-    C1-    N1-    O1
    28     29     30     31      3   26.77760    0.00000  -26.77760    0.00000    0.00000
0.00000 ;     C1-    N1-    O1-   H15
    30     29     28     37      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     O1-    N1-    C1-   HC1

[ dihedrals ] ; impropers
; treated as propers in GROMACS to use correct AMBER analytical function
;    i      j      k      l   func   phase     kd      pn
     5      8      6      7      1   180.00   4.60240   2 ;    C11-   C13-   C12-   H12
     5     12     10     11      1   180.00   4.60240   2 ;    C11-    C9-   C10-   H10
     5     32      4      3      1   180.00   4.60240   2 ;    C11-  HC14-   C14-    N4
     6      9      8     14      1   180.00   4.60240   2 ;    C12-   H13-   C13-    N3
     6     10      5      4      1   180.00   4.60240   2 ;    C12-   C10-   C11-   C14
     8     12     14     15      1   180.00   4.60240   2 ;    C13-    C9-    N3-    C8
    10     13     12     14      1   180.00   4.60240   2 ;    C10-    H9-    C9-    N3
    17     19     18     23      1   180.00   4.60240   2 ;     C7-    C5-    N2-    C4
    19     27     21     22      1   180.00   4.60240   2 ;     C5-    C2-    C6-    H6
    21     20     19     18      1   180.00   4.60240   2 ;     C6-    H5-    C5-    N2
    21     25     27     28      1   180.00   4.60240   2 ;     C6-    C3-    C2-    C1
    23     27     25     26      1   180.00   4.60240   2 ;     C4-    C2-    C3-   H31
    25     24     23     18      1   180.00   4.60240   2 ;     C3-    H4-    C4-    N2
    27     37     28     29      1   180.00   4.60240   2 ;     C2-   HC1-    C1-    N1
```

(B) OBIF

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[ atom types ]
;name   bond_type     mass     charge   ptype   sigma         epsilon
 oh       oh          0.00000  0.00000   A     3.06647e-01   8.80314e-01
 ho       ho          0.00000  0.00000   A     0.00000e+00   0.00000e+00
 n2       n2          0.00000  0.00000   A     3.25000e-01   7.11280e-01
 ce       ce          0.00000  0.00000   A     3.39967e-01   3.59824e-01
 ca       ca          0.00000  0.00000   A     3.39967e-01   3.59824e-01
 f        f           0.00000  0.00000   A     3.11815e-01   2.55224e-01
 h4       h4          0.00000  0.00000   A     2.51055e-01   6.27600e-02
 ha       ha          0.00000  0.00000   A     2.59964e-01   6.27600e-02
 na       na          0.00000  0.00000   A     3.25000e-01   7.11280e-01
 c3       c3          0.00000  0.00000   A     3.39967e-01   4.57730e-01
 os       os          0.00000  0.00000   A     3.00001e-01   7.11280e-01
 h2       h2          0.00000  0.00000   A     2.29317e-01   6.56888e-02

[ atoms ]
;   nr  type  resi  res  atom  cgnr     charge      mass
     1   oh     1   OBI    O3    1     0.1518    16.00000
     2   ho     1   OBI   H32    2     0.3137      1.00800
     3   n2     1   OBI    N4    3    -0.3106     14.01000
     4   ce     1   OBI   C14    4    -0.4548     12.01000
     5   ca     1   OBI   C11    5     0.4968     12.01000
     6   ca     1   OBI   C12    6    -0.8190     12.01000
     7    f     1   OBI    F2    7    -0.1165     19.00000
     8   ca     1   OBI   C13    8     0.2461     12.01000
     9   h4     1   OBI   H13    9     0.2349      1.00800
    10   ca     1   OBI   C10   10     0.3531     12.01000
    11   ha     1   OBI   H10   11     0.3259      1.00800
    12   ca     1   OBI    C9   12    -0.0769     12.01000
    13   h4     1   OBI    H9   13     0.1846      1.00800
    14   na     1   OBI    N3   14     0.2366     14.01000
    15   c3     1   OBI    C8   15    -0.5219      12.01000
    16   os     1   OBI    O2   16     0.0207     16.00000
    17   c3     1   OBI    C7   17    -0.3979      12.01000
    18   na     1   OBI    N2   18     0.2457     14.01000
    19   ca     1   OBI    C5   19     0.2080     12.01000
    20   h4     1   OBI    H5   20     0.2409      1.00800
    21   ca     1   OBI    C6   21    -0.9735     12.01000
    22    f     1   OBI    F1   22    -0.1143     19.00000
    23   ca     1   OBI    C4   23    -0.5312     12.01000
    24   h4     1   OBI    H4   24     0.2199      1.00800
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    25   ca     1   OBI    C3   25     0.8431     12.01000
    26   ha     1   OBI   H31   26     0.3251      1.00800
    27   ca     1   OBI    C2   27     0.5801     12.01000
    28   ce     1   OBI    C1   28    -0.4724     12.01000
    29   n2     1   OBI    N1   29    -0.3124     14.01000
    30   oh     1   OBI    O1   30     0.1504     16.00000
    31   ho     1   OBI   H15   31     0.3136      1.00800
    32   h4     1   OBI  HC14   32     0.2553      1.00800
    33   h2     1   OBI  HC82   33     0.2138      1.00800
    34   h2     1   OBI  HC83   34     0.2209      1.00800
    35   h2     1   OBI  HC72   35     0.1934      1.00800
    36   h2     1   OBI  HC73   36     0.2725      1.00800
    37   h4     1   OBI   HC1   37     0.2545      1.00800

[ bonds ]
;   ai     aj funct   r             k
     1      2   1    9.7400e-02    3.0928e+05 ;     O3 - H32
     1      3   1    1.3940e-01    3.4828e+05 ;     O3 - N4
     3      4   1    1.2790e-01    5.0191e+05 ;     N4 - C14
     4      5   1    1.4720e-01    3.0627e+05 ;    C14 - C11
     4     32   1    1.0916e-01    2.8267e+05 ;    C14 - HC14
     5      6   1    1.3870e-01    4.0033e+05 ;    C11 - C12
     5     10   1    1.3870e-01    4.0033e+05 ;    C11 - C10
     6      7   1    1.3440e-01    3.0443e+05 ;    C12 - F2
     6      8   1    1.3870e-01    4.0033e+05 ;    C12 - C13
     8      9   1    1.0880e-01    2.8694e+05 ;    C13 - H13
     8     14   1    1.3500e-01    3.9355e+05 ;    C13 - N3
    10     11   1    1.0870e-01    2.8811e+05 ;    C10 - H10
    10     12   1    1.3870e-01    4.0033e+05 ;    C10 - C9
    12     13   1    1.0880e-01    2.8694e+05 ;     C9 - H9
    12     14   1    1.3500e-01    3.9355e+05 ;     C9 - N3
    14     15   1    1.4560e-01    2.8008e+05 ;     N3 - C8
    15     16   1    1.4390e-01    2.5230e+05 ;     C8 - O2
    15     33   1    1.1000e-01    2.7313e+05 ;     C8 - HC82
    15     34   1    1.1000e-01    2.7313e+05 ;     C8 - HC83
    16     17   1    1.4390e-01    2.5230e+05 ;     O2 - C7
    17     18   1    1.4560e-01    2.8008e+05 ;     C7 - N2
    17     35   1    1.1000e-01    2.7313e+05 ;     C7 - HC72
    17     36   1    1.1000e-01    2.7313e+05 ;     C7 - HC73
    18     19   1    1.3500e-01    3.9355e+05 ;     N2 - C5
    18     23   1    1.3500e-01    3.9355e+05 ;     N2 - C4
    19     20   1    1.0880e-01    2.8694e+05 ;     C5 - H5
    19     21   1    1.3870e-01    4.0033e+05 ;     C5 - C6
    21     22   1    1.3440e-01    3.0443e+05 ;     C6 - F1
    21     27   1    1.3870e-01    4.0033e+05 ;     C6 - C2
    23     24   1    1.0880e-01    2.8694e+05 ;     C4 - H4
    23     25   1    1.3870e-01    4.0033e+05 ;     C4 - C3
    25     26   1    1.0870e-01    2.8811e+05 ;     C3 - H31
    25     27   1    1.3870e-01    4.0033e+05 ;     C3 - C2
    27     28   1    1.4720e-01    3.0627e+05 ;     C2 - C1
    28     29   1    1.2790e-01    5.0191e+05 ;     C1 - N1
    28     37   1    1.0916e-01    2.8267e+05 ;     C1 - HC1
    29     30   1    1.3940e-01    3.4828e+05 ;     N1 - O1
    30     31   1    9.7400e-02    3.0928e+05 ;     O1 - H15

[ pairs ]
;   ai     aj    funct
     1      5      1 ;     O3 - C11
     1     32      1 ;     O3 - HC14
     2      4      1 ;    H32 - C14
     3      6      1 ;     N4 - C12
     3     10      1 ;     N4 - C10
     4      7      1 ;    C14 - F2
     4      8      1 ;    C14 - C13
     4     11      1 ;    C14 - H10
     4     12      1 ;    C14 - C9
     5      9      1 ;    C11 - H13
     5     13      1 ;    C11 - H9
     5     14      1 ;    C11 - N3
     6     11      1 ;    C12 - H10
     6     12      1 ;    C12 - C9
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     6     15      1 ;    C12 - C8
     6     32      1 ;    C12 - HC14
     7      9      1 ;     F2 - H13
     7     10      1 ;     F2 - C10
     7     14      1 ;     F2 - N3
     8     10      1 ;    C13 - C10
     8     13      1 ;    C13 - H9
     8     16      1 ;    C13 - O2
     8     33      1 ;    C13 - HC82
     8     34      1 ;    C13 - HC83
     9     12      1 ;    H13 - C9
     9     15      1 ;    H13 - C8
    10     15      1 ;    C10 - C8
    10     32      1 ;    C10 - HC14
    11     13      1 ;    H10 - H9
    11     14      1 ;    H10 - N3
    12     16      1 ;     C9 - O2
    12     33      1 ;     C9 - HC82
    12     34      1 ;     C9 - HC83
    13     15      1 ;     H9 - C8
    14     17      1 ;     N3 - C7
    15     18      1 ;     C8 - N2
    15     35      1 ;     C8 - HC72
    15     36      1 ;     C8 - HC73
    16     19      1 ;     O2 - C5
    16     23      1 ;     O2 - C4
    17     20      1 ;     C7 - H5
    17     21      1 ;     C7 - C6
    17     24      1 ;     C7 - H4
    17     25      1 ;     C7 - C3
    17     33      1 ;     C7 - HC82
    17     34      1 ;     C7 - HC83
    18     22      1 ;     N2 - F1
    18     26      1 ;     N2 - H31
    18     27      1 ;     N2 - C2
    19     24      1 ;     C5 - H4
    19     25      1 ;     C5 - C3
    19     28      1 ;     C5 - C1
    19     35      1 ;     C5 - HC72
    19     36      1 ;     C5 - HC73
    20     22      1 ;     H5 - F1
    20     23      1 ;     H5 - C4
    20     27      1 ;     H5 - C2
    21     23      1 ;     C6 - C4
    21     26      1 ;     C6 - H31
    21     29      1 ;     C6 - N1
    21     37      1 ;     C6 - HC1
    22     25      1 ;     F1 - C3
    22     28      1 ;     F1 - C1
    23     28      1 ;     C4 - C1
    23     35      1 ;     C4 - HC72
    23     36      1 ;     C4 - HC73
    24     26      1 ;     H4 - H31
    24     27      1 ;     H4 - C2
    25     29      1 ;     C3 - N1
    25     37      1 ;     C3 - HC1
    26     28      1 ;    H31 - C1
    27     30      1 ;     C2 - O1
    28     31      1 ;     C1 - H15
    30     37      1 ;     O1 - HC1

[ angles ]
;   ai     aj     ak    funct   theta         cth
     1      3      4      1    1.1348e+02    5.9789e+02 ;     O3 - N4     - C14
     2      1      3      1    1.0274e+02    4.2317e+02 ;    H32 - O3     - N4
     3      4      5      1    1.2072e+02    5.7329e+02 ;     N4 - C14    - C11
     3      4     32      1    1.2152e+02    4.3823e+02 ;     N4 - C14    - HC14
     4      5      6      1    1.2066e+02    5.4292e+02 ;    C14 - C11    - C12
     4      5     10      1    1.2066e+02    5.4292e+02 ;    C14 - C11    - C10
     5      4     32      1    1.1686e+02    3.9087e+02 ;    C11 - C14    - HC14
     5      6      7      1    1.1895e+02    5.6492e+02 ;    C11 - C12    - F2
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     5      6      8      1    1.1997e+02    5.6216e+02 ;    C11 - C12    - C13
     5     10     11      1    1.2001e+02    4.0551e+02 ;    C11 - C10    - H10
     5     10     12      1    1.1997e+02    5.6216e+02 ;    C11 - C10    - C9
     6      5     10      1    1.1997e+02    5.6216e+02 ;    C12 - C11    - C10
     6      8      9      1    1.2109e+02    4.0367e+02 ;    C12 - C13    - H13
     6      8     14      1    1.1834e+02    5.8752e+02 ;    C12 - C13    - N3
     7      6      8      1    1.1895e+02    5.6492e+02 ;     F2 - C12    - C13
     8     14     12      1    1.2009e+02    5.6049e+02 ;    C13 - N3     - C9
     8     14     15      1    1.2436e+02    5.2844e+02 ;    C13 - N3     - C8
     9      8     14      1    1.1465e+02    4.3413e+02 ;    H13 - C13    - N3
    10     12     13      1    1.2109e+02    4.0367e+02 ;    C10 - C9     - H9
    10     12     14      1    1.1834e+02    5.8752e+02 ;    C10 - C9     - N3
    11     10     12      1    1.2001e+02    4.0551e+02 ;    H10 - C10    - C9
    12     14     15      1    1.2436e+02    5.2844e+02 ;     C9 - N3     - C8
    13     12     14      1    1.1465e+02    4.3413e+02 ;     H9 - C9     - N3
    14     15     16      1    1.0906e+02    5.9639e+02 ;     N3 - C8     - O2
    14     15     33      1    1.0766e+02    4.2066e+02 ;     N3 - C8     - HC82
    14     15     34      1    1.0766e+02    4.2066e+02 ;     N3 - C8     - HC83
    15     16     17      1    1.1245e+02    5.2208e+02 ;     C8 - O2     - C7
    16     15     33      1    1.0858e+02    4.2543e+02 ;     O2 - C8     - HC82
    16     15     34      1    1.0858e+02    4.2543e+02 ;     O2 - C8     - HC83
    16     17     18      1    1.0906e+02    5.9639e+02 ;     O2 - C7     - N2
    16     17     35      1    1.0858e+02    4.2543e+02 ;     O2 - C7     - HC72
    16     17     36      1    1.0858e+02    4.2543e+02 ;     O2 - C7     - HC73
    17     18     19      1    1.2436e+02    5.2844e+02 ;     C7 - N2     - C5
    17     18     23      1    1.2436e+02    5.2844e+02 ;     C7 - N2     - C4
    18     17     35      1    1.0766e+02    4.2066e+02 ;     N2 - C7     - HC72
    18     17     36      1    1.0766e+02    4.2066e+02 ;     N2 - C7     - HC73
    18     19     20      1    1.1465e+02    4.3413e+02 ;     N2 - C5     - H5
    18     19     21      1    1.1834e+02    5.8752e+02 ;     N2 - C5     - C6
    18     23     24      1    1.1465e+02    4.3413e+02 ;     N2 - C4     - H4
    18     23     25      1    1.1834e+02    5.8752e+02 ;     N2 - C4     - C3
    19     18     23      1    1.2009e+02    5.6049e+02 ;     C5 - N2     - C4
    19     21     22      1    1.1895e+02    5.6492e+02 ;     C5 - C6     - F1
    19     21     27      1    1.1997e+02    5.6216e+02 ;     C5 - C6     - C2
    20     19     21      1    1.2109e+02    4.0367e+02 ;     H5 - C5     - C6
    21     27     25      1    1.1997e+02    5.6216e+02 ;     C6 - C2     - C3
    21     27     28      1    1.2066e+02    5.4292e+02 ;     C6 - C2     - C1
    22     21     27      1    1.1895e+02    5.6492e+02 ;     F1 - C6     - C2
    23     25     26      1    1.2001e+02    4.0551e+02 ;     C4 - C3     - H31
    23     25     27      1    1.1997e+02    5.6216e+02 ;     C4 - C3     - C2
    24     23     25      1    1.2109e+02    4.0367e+02 ;     H4 - C4     - C3
    25     27     28      1    1.2066e+02    5.4292e+02 ;     C3 - C2     - C1
    26     25     27      1    1.2001e+02    4.0551e+02 ;    H31 - C3     - C2
    27     28     29      1    1.2072e+02    5.7329e+02 ;     C2 - C1     - N1
    27     28     37      1    1.1686e+02    3.9087e+02 ;     C2 - C1     - HC1
    28     29     30      1    1.1348e+02    5.9789e+02 ;     C1 - N1     - O1
    29     28     37      1    1.2152e+02    4.3823e+02 ;     N1 - C1     - HC1
    29     30     31      1    1.0274e+02    4.2317e+02 ;     N1 - O1     - H15
    33     15     34      1    1.0919e+02    3.2635e+02 ;   HC82 - C8     - HC83
    35     17     36      1    1.0919e+02    3.2635e+02 ;   HC72 - C7     - HC73

[ dihedrals ] ; propers
; treated as RBs in GROMACS to use combine multiple AMBER torsions per quartet
;    i      j      k      l   func    C0         C1         C2         C3         C4         C5
     1      3      4      5      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     O3-    N4-   C14-   C11
     1      3      4     32      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     O3-    N4-   C14-  HC14
     2      1      3      4      3   26.77760    0.00000  -26.77760    0.00000    0.00000
0.00000 ;    H32-    O3-    N4-   C14
     3      4      5      6      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     N4-   C14-   C11-   C12
     3      4      5     10      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     N4-   C14-   C11-   C10
     4      5      6      7      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C12-    F2
     4      5      6      8      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C12-   C13
     4      5     10     11      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C10-   H10
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     4      5     10     12      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C14-   C11-   C10-    C9
     5      6      8      9      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C12-   C13-   H13
     5      6      8     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C12-   C13-    N3
     5     10     12     13      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C10-    C9-    H9
     5     10     12     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C11-   C10-    C9-    N3
     6      5      4     32      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;    C12-   C11-   C14-  HC14
     6      5     10     11      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C12-   C11-   C10-   H10
     6      5     10     12      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C12-   C11-   C10-    C9
     6      8     14     12      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C12-   C13-    N3-    C9
     6      8     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C12-   C13-    N3-    C8
     7      6      5     10      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     F2-   C12-   C11-   C10
     7      6      8      9      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     F2-   C12-   C13-   H13
     7      6      8     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     F2-   C12-   C13-    N3
     8      6      5     10      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    C13-   C12-   C11-   C10
     8     14     12     10      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C13-    N3-    C9-   C10
     8     14     12     13      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C13-    N3-    C9-    H9
     8     14     15     16      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;    C13-    N3-    C8-    O2
     8     14     15     33      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;    C13-    N3-    C8-  HC82
     8     14     15     34      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;    C13-    N3-    C8-  HC83
     9      8     14     12      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    H13-   C13-    N3-    C9
     9      8     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    H13-   C13-    N3-    C8
    10      5      4     32      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;    C10-   C11-   C14-  HC14
    10     12     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;    C10-    C9-    N3-    C8
    11     10     12     13      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H10-   C10-    C9-    H9
    11     10     12     14      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H10-   C10-    C9-    N3
    12     14     15     16      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C9-    N3-    C8-    O2
    12     14     15     33      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C9-    N3-    C8-  HC82
    12     14     15     34      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C9-    N3-    C8-  HC83
    13     12     14     15      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     H9-    C9-    N3-    C8
    14     15     16     17      3    1.60247    4.80742    5.43920   -6.40989    0.00000
0.00000 ;     N3-    C8-    O2-    C7
    15     16     17     18      3    1.60247    4.80742    5.43920   -6.40989    0.00000
0.00000 ;     C8-    O2-    C7-    N2
    15     16     17     35      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C8-    O2-    C7-  HC72
    15     16     17     36      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C8-    O2-    C7-  HC73
    16     17     18     19      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     O2-    C7-    N2-    C5
    16     17     18     23      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     O2-    C7-    N2-    C4
```

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    17     16     15     33      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C7-    O2-    C8-  HC82
    17     16     15     34      3    1.60387    4.81160    0.00000   -6.41547    0.00000
0.00000 ;     C7-    O2-    C8-  HC83
    17     18     19     20      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C5-    H5
    17     18     19     21      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C5-    C6
    17     18     23     24      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C4-    H4
    17     18     23     25      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C7-    N2-    C4-    C3
    18     19     21     22      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C5-    C6-    F1
    18     19     21     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C5-    C6-    C2
    18     23     25     26      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C4-    C3-   H31
    18     23     25     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     N2-    C4-    C3-    C2
    19     18     17     35      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C5-    N2-    C7-  HC72
    19     18     17     36      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C5-    N2-    C7-  HC73
    19     18     23     24      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C5-    N2-    C4-    H4
    19     18     23     25      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C5-    N2-    C4-    C3
    19     21     27     25      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C5-    C6-    C2-    C3
    19     21     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C5-    C6-    C2-    C1
    20     19     18     23      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     H5-    C5-    N2-    C4
    20     19     21     22      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H5-    C5-    C6-    F1
    20     19     21     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H5-    C5-    C6-    C2
    21     19     18     23      3    2.51040    0.00000   -2.51040    0.00000    0.00000
0.00000 ;     C6-    C5-    N2-    C4
    21     27     25     23      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C6-    C2-    C3-    C4
    21     27     25     26      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C6-    C2-    C3-   H31
    21     27     28     29      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     C6-    C2-    C1-    N1
    21     27     28     37      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;     C6-    C2-    C1-   HC1
    22     21     27     25      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     F1-    C6-    C2-    C3
    22     21     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     F1-    C6-    C2-    C1
    23     18     17     35      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C4-    N2-    C7-  HC72
    23     18     17     36      3    0.00000    0.00000    0.00000    0.00000    0.00000
0.00000 ;     C4-    N2-    C7-  HC73
    23     25     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     C4-    C3-    C2-    C1
    24     23     25     26      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H4-    C4-    C3-   H31
    24     23     25     27      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;     H4-    C4-    C3-    C2
    25     27     28     29      3   21.33840    0.00000  -21.33840    0.00000    0.00000
0.00000 ;     C3-    C2-    C1-    N1
    25     27     28     37      3   55.64720    0.00000  -55.64720    0.00000    0.00000
0.00000 ;     C3-    C2-    C1-   HC1
    26     25     27     28      3   30.33400    0.00000  -30.33400    0.00000    0.00000
0.00000 ;    H31-    C3-    C2-    C1
    27     28     29     30      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     C2-    C1-    N1-    O1
```

```
    28     29     30     31      3   26.77760    0.00000  -26.77760    0.00000    0.00000
0.00000 ;     C1-    N1-    O1-   H15
    30     29     28     37      3   34.72720    0.00000  -34.72720    0.00000    0.00000
0.00000 ;     O1-    N1-    C1-   HC1

[ dihedrals ] ; impropers
; treated as propers in GROMACS to use correct AMBER analytical function
;    i      j      k      l   func   phase     kd      pn
     5      8      6      7      1   180.00   4.60240   2 ;    C11-   C13-   C12-    F2
     5     12     10     11      1   180.00   4.60240   2 ;    C11-    C9-   C10-   H10
     5     32      4      3      1   180.00   4.60240   2 ;    C11-  HC14-   C14-    N4
     6      9      8     14      1   180.00   4.60240   2 ;    C12-   H13-   C13-    N3
     6     10      5      4      1   180.00   4.60240   2 ;    C12-   C10-   C11-   C14
     8     12     14     15      1   180.00   4.60240   2 ;    C13-    C9-    N3-    C8
    10     13     12     14      1   180.00   4.60240   2 ;    C10-    H9-    C9-    N3
    17     19     18     23      1   180.00   4.60240   2 ;     C7-    C5-    N2-    C4
    19     27     21     22      1   180.00   4.60240   2 ;     C5-    C2-    C6-    F1
    21     20     19     18      1   180.00   4.60240   2 ;     C6-    H5-    C5-    N2
    21     25     27     28      1   180.00   4.60240   2 ;     C6-    C3-    C2-    C1
    23     27     25     26      1   180.00   4.60240   2 ;     C4-    C2-    C3-   H31
    25     24     23     18      1   180.00   4.60240   2 ;     C3-    H4-    C4-    N2
    27     37     28     29      1   180.00   4.60240   2 ;     C2-   HC1-    C1-    N1
```

2. Convergence of Well-Tempered Metadynamics Runs

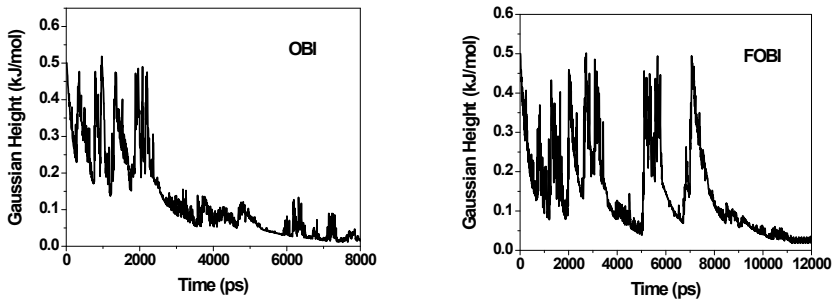

Fig. S1: The heights of the Gaussians as a function of number of hills added (at an interval of 5 ps) during the course of well-tempered metadynamics runs for OBI and FOBI in polarizable water. As a signature of the convergence of the well-tempered metadynamics, heights of added Gaussians can be seen to approach a value close to zero and remain there for a long time as the simulation progresses.

3. Snapshots of cation-π interactions

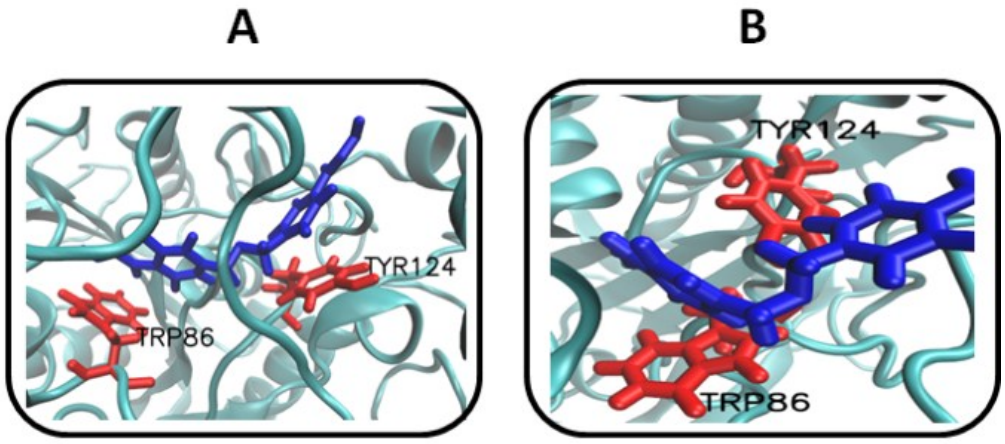

Fig. S2: Cation-π interactions in a typical bound state of the drug molecules with Trp86 and Tyr124 aromatic residues are shown for (A) fluorinated obidoxime and (B) obidoxime. As it can be seen in this figure, that both the pyridinium rings of FOBI are more in-plane with the aromatic rings of either of these two residues than that in the case of OBI. This also explains the larger cation-π interaction parameters for FOBI than that for OBI molecule.

4. Snapshots of the basins and barriers

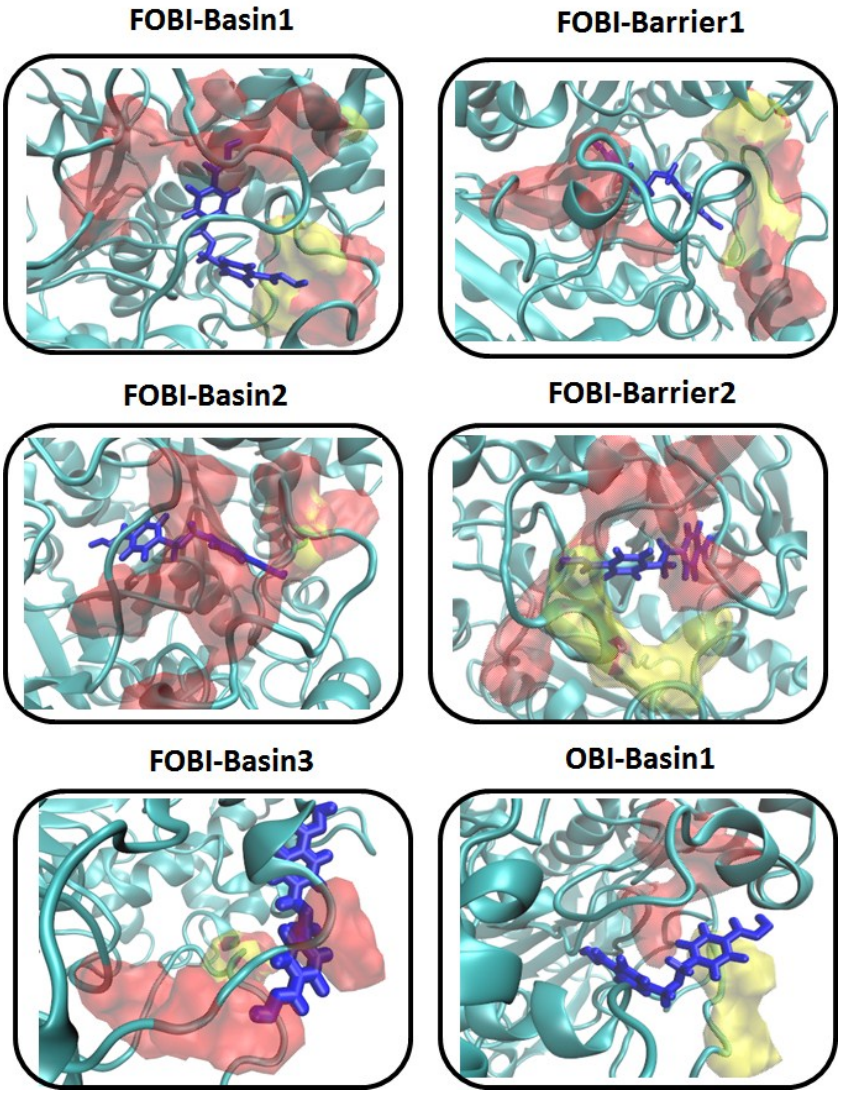

Fig. S3: Snapshots of the basins and barriers (marked in Fig. 2, main text) along the unbinding pathway of obidoximes (blue colour) are shown. The hydrogen bond and water bridge forming residues are shown by red and yellow colour surface representations, respectively. The respective residues responsible for these interactions are mentioned in Table 2 and 3 (main text).