**Thumbsite analysis (keeping D112a as base fragment)**

D1212a

A close-up of a colorful background

Description automatically generated

CC(C=C1)=NC=C1CCNC2=CC=CC=C2

Considering the phenyl ring of the aniline is facing Arg 842, one potential modification to this molecule alone is:



CC(C=C1)=NC=C1CCNC2=CC=NC=C2

A snapshot of d1212a with d0414a below suggests linking the two

A close-up of a molecule

Description automatically generated



C1(NCCC2=CN=C(CCC3=CNN=C3)C=C2)=CC=CC=C1

Though now I feel there is too much conformational flexibility, which may be reduced by looking at D0749a that can be used to argue insertion of sulfonamide ring as below:

A colorful molecule structure with balls and dots

Description automatically generated with medium confidence



O=S(NC1=CC=CC=C1)(CC2=CC=C(CCC3=CNN=C3)C=C2)=O

Or even following:

  
CC(C=C1)=NC=C1CS(NC2=CC=CC=C2)(=O)=O

Analysis with d0283a also suggests growing on pyridine side:

A close-up of a molecule

Description automatically generated



CNS(CCC(C=C1)=CC=C1CCNC2=CC=CC=C2)(=O)=O

Analysis with d0248a is also on the similar lines

A close-up of a molecule

Description automatically generated



O=C(NC(C)(C)O)CCC(C=C1)=CC=C1CCNC2=CC=CC=C2

Analysis with d0174a, also suggested growing in this region

A colorful molecule structure with balls and dots

Description automatically generated with medium confidence



CCS(NCCC(C=C1)=CC=C1CCNC2=CC=CC=C2)(=O)=O

With 5hmx-a (and 5hmw-a)

A close-up of a molecule

Description automatically generated A close-up of a molecule

Description automatically generated



O=C(O)CC1=CC(CC(C=C2)=NC=C2CCNC3=CC=CC=C3)=CC(CC(O)=O)=C1