**Figure S3. Ligand fragmentation**

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Diagramed is an example fragmentation of PDB ligand ADP. We pass the ADP SMILES string to PUG SOAP, which returns a list of PubChem compounds that are substructures of the query ligand. These compounds (fragments) are passed to SMSD to generate the atom-to-atom mapping between ADP and the fragments. We then post process the mapping information to produce a fragment list for each heavy atom of ADP. To determine the relevant fragments for a microenvironment, we take the union of the fragment lists for the proximal atoms.