Advanced in silico drug design

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Training: Scoring

Task:

preparation of protein-ligand system for binding energy calculations, such as MM/GBSA or FEP

Target:

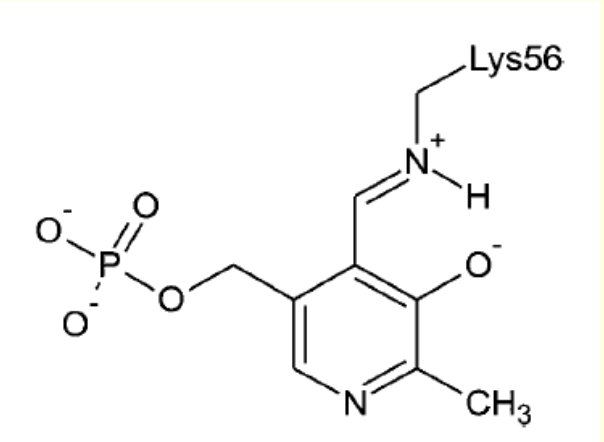
human serine racemase (hSR)

pharmaceutical target for human neuropathies, e.g. epilepsy

Detailed Protein Preparation

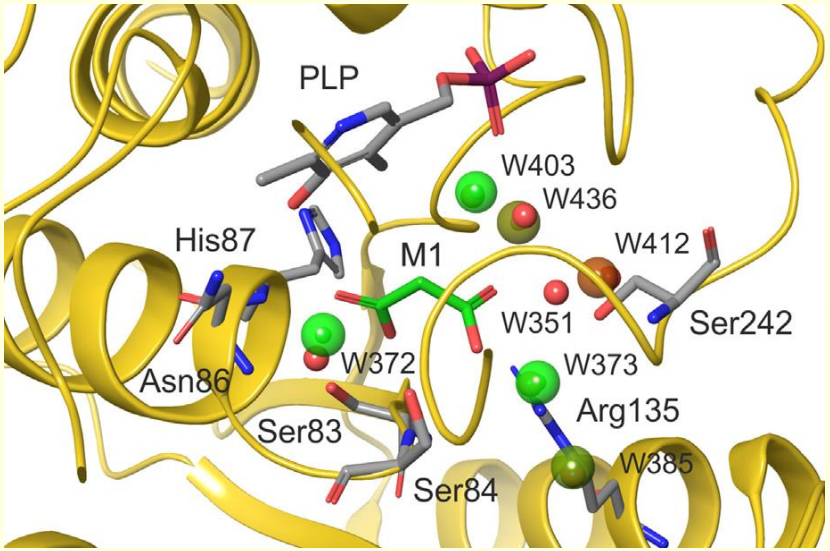
- Schrodinger Maestro 10.4 (2015-4)
- Project: SaveAs hSR.prj
- hSR/MAL complex
- GetPDB – 3L6B
- PrepWizard
- Problems: Overlapping Atoms – How to Solve?
- Refine: Optimize – Clash Removed
- Review and Modify, Analyze Workspace

DETAILED LIGAND PREPARATION



- PLP: Schiff base
- Delete – Atoms (O)H
- Build: Increment Bond Order C=N

- Mn2+
- MLI (=malonate)
- Waters
- Display H-bonds
- Contacts: Ugly
- Measure: Distance
- Delete: W351



- Interactive H-bond Optimizer, Analyze Network
- Restrained Minimization, Hydrogens Only

Summary

Need to care about details, such as protonation, interactions, clashes

Better spend more time in the beginning than be sorry later on