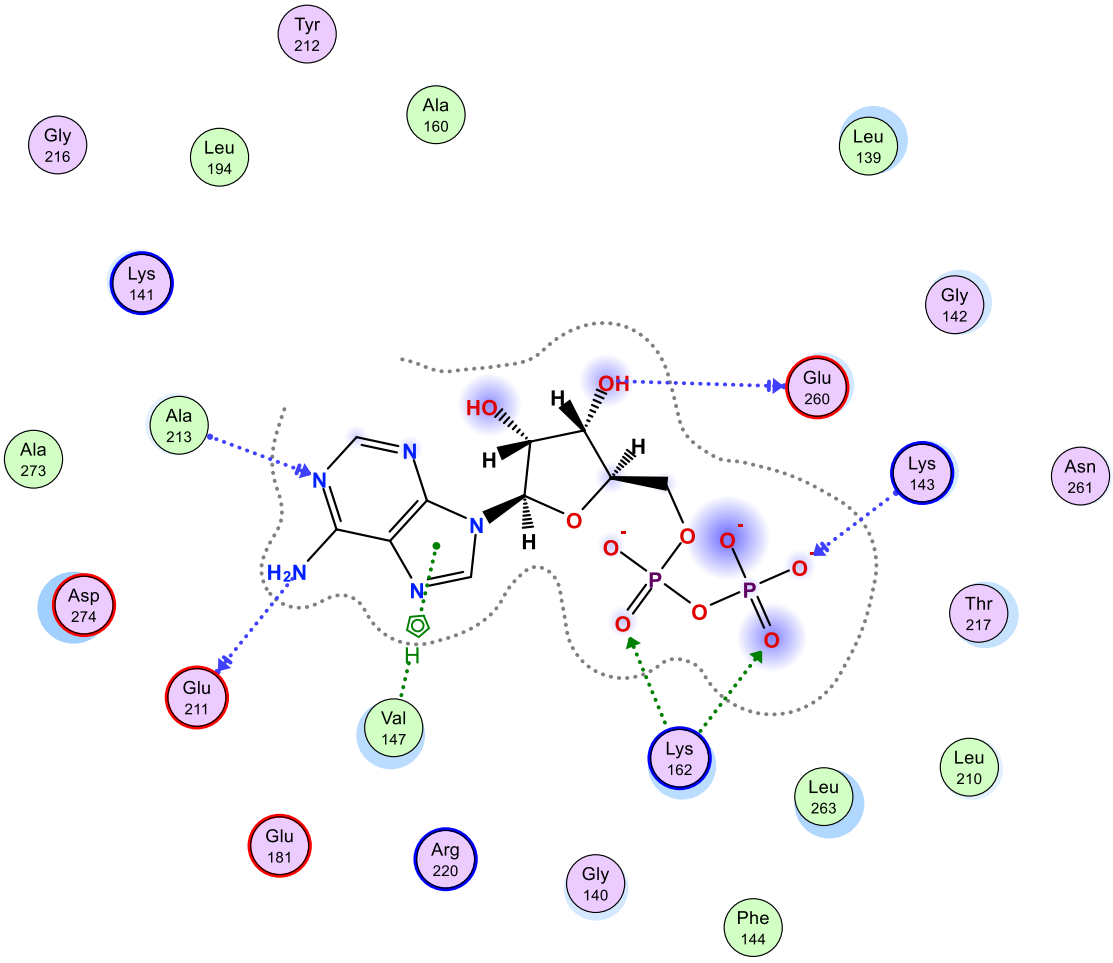
1MQ4 Crystal Structure of Aurora-A Protein Kinase

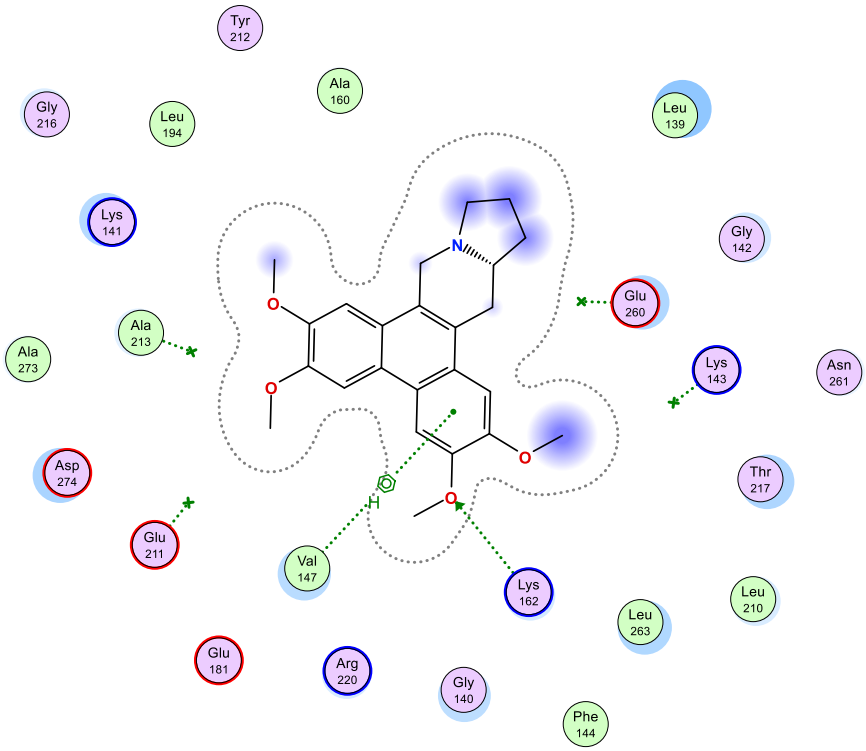
Protein kinases are important drug targets in human cancers, inflammation, and metabolic diseases. This report presents the structures of kinase domains for three cancer-associated protein kinases: ephrin receptor A2 (EphA2), focal adhesion kinase (FAK), and Aurora-A. The expression profiles of EphA2, FAK, and Aurora-A in carcinomas suggest that inhibitors of these kinases may have inherent potential as therapeutic agents. The structures were determined from crystals grown in nanovolume droplets, which produced high-resolution diffraction data at 1.7, 1.9, and 2.3 A for FAK, Aurora-A, and EphA2, respectively. The FAK and Aurora-A structures are the first determined within two unique subfamilies of human kinases, and all three structures provide new insights into kinase regulation and the design of selective inhibitors.

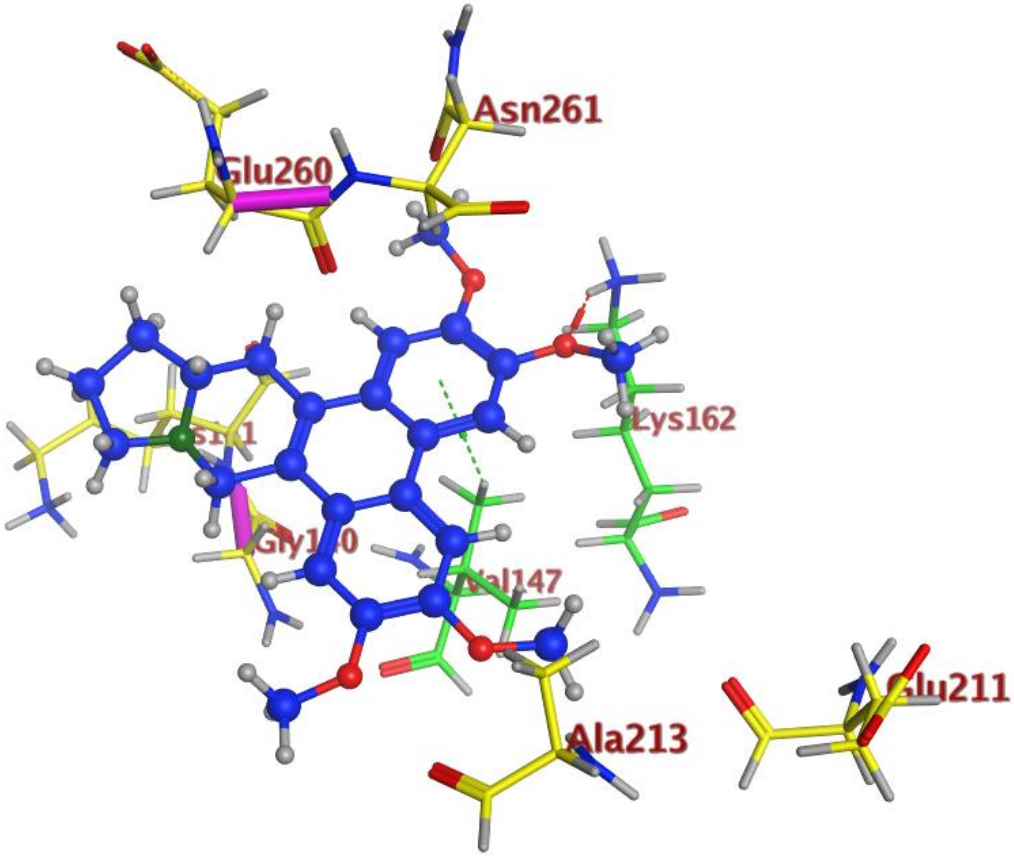
- **Resolution:** 1.90 Å

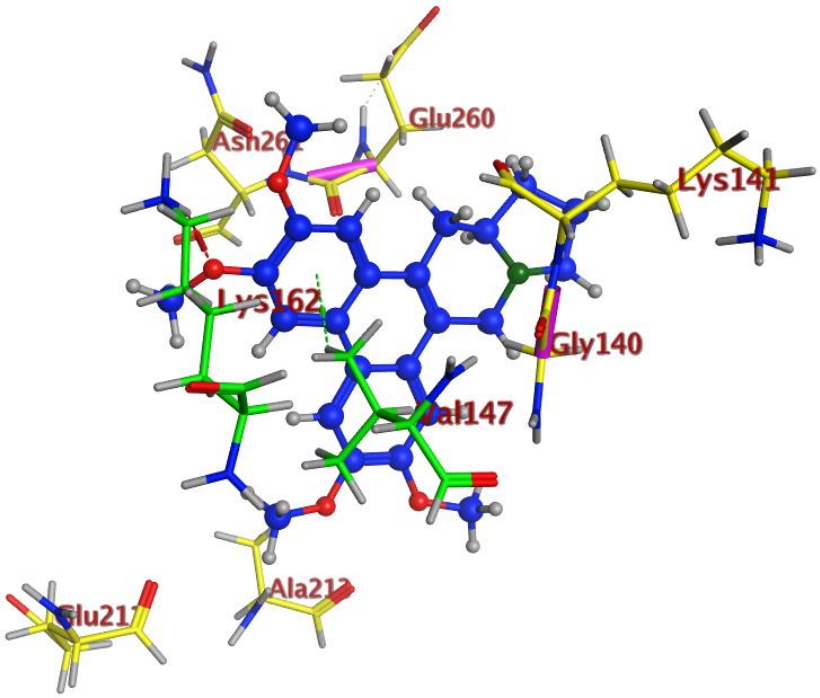
Ligand interactions: Ala213, Val147, Lys143, Lys162, Glu211, & Glu260



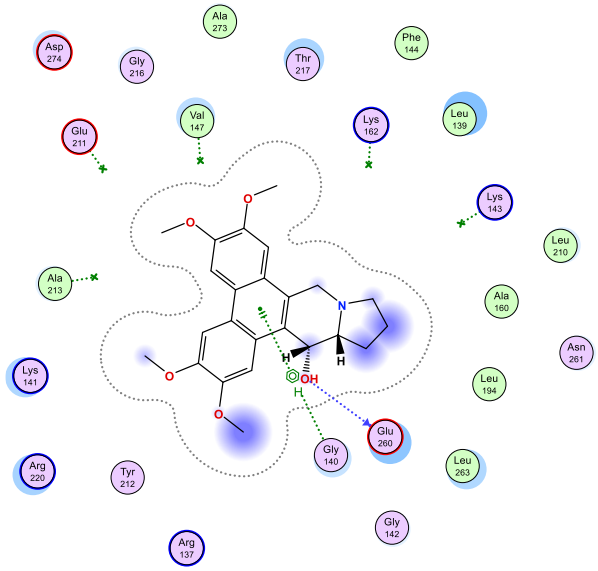
Compound 1: Tylophorine Pose 1 (-7.75664711)

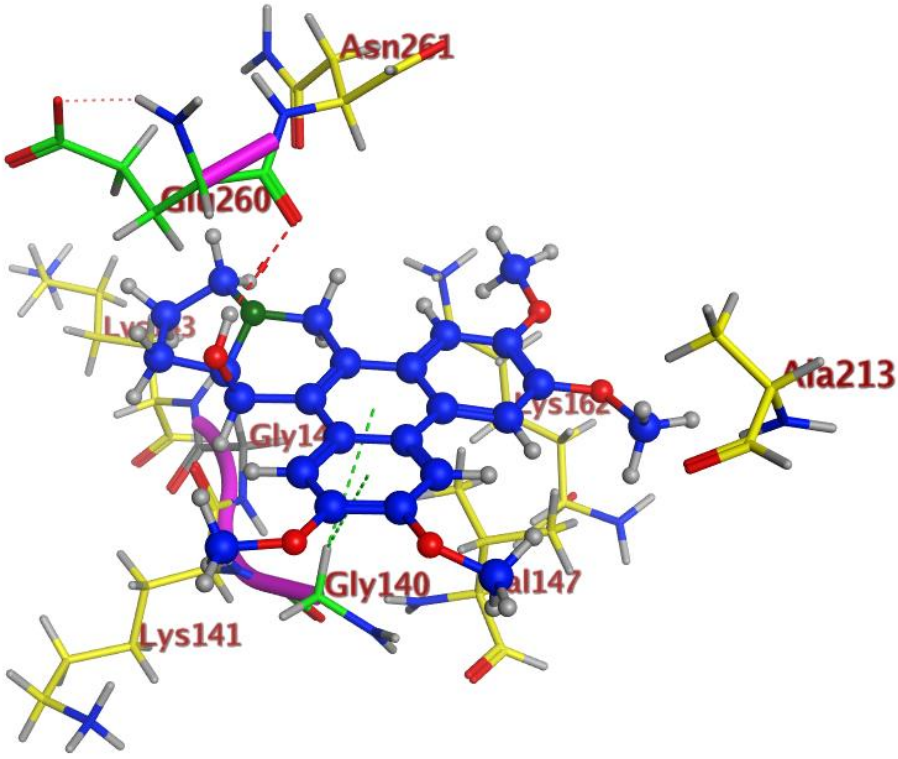




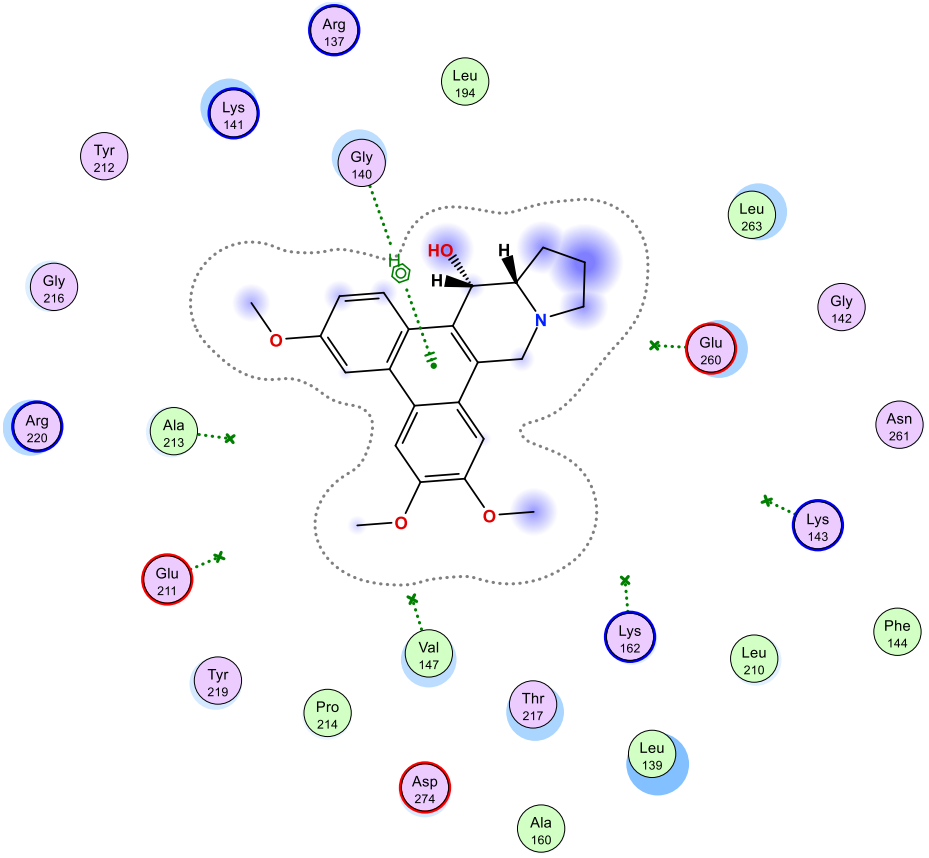

Glu260
Lys141
Lys162
Gly140
Val147
Ala213
Glu211

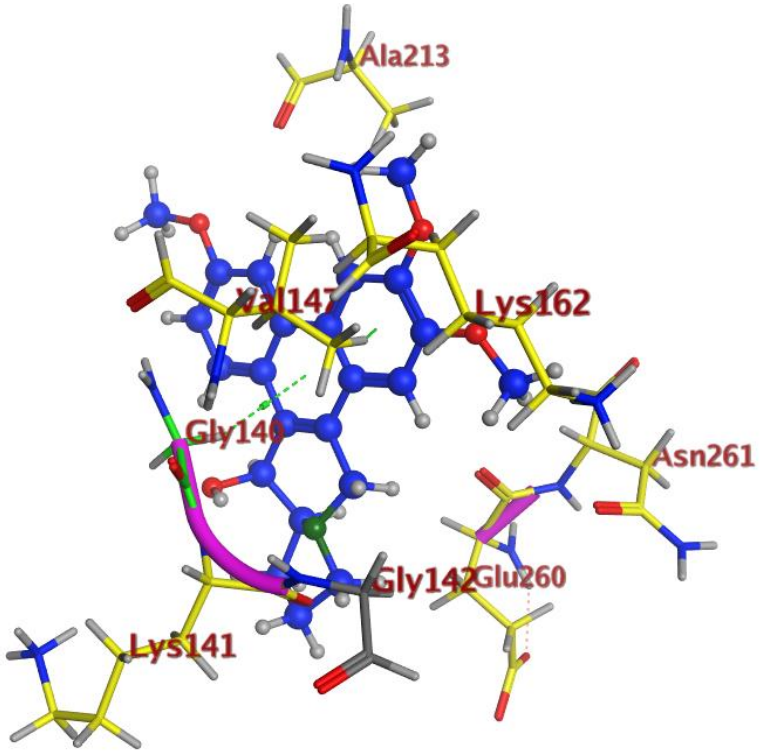
Compound 2: Pose 7 (-7.42515945)



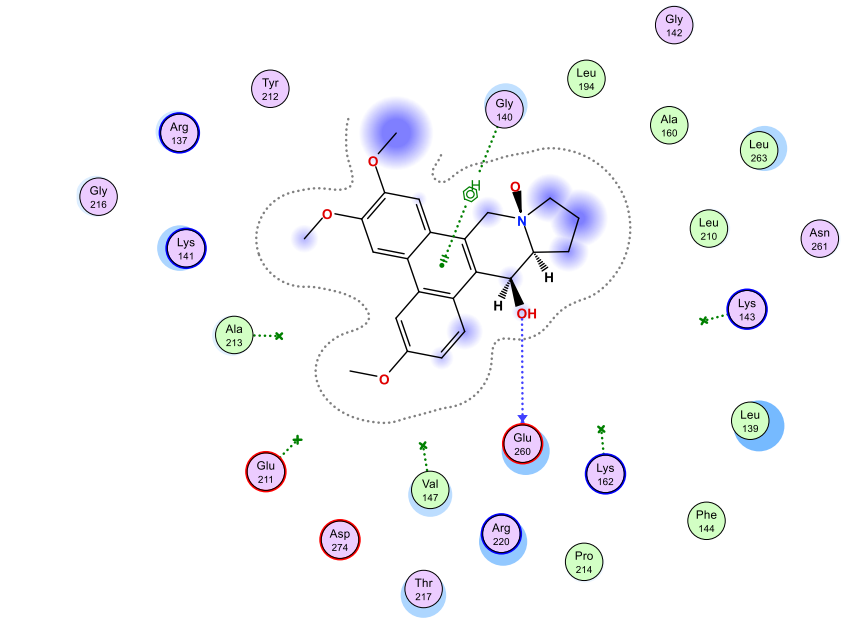


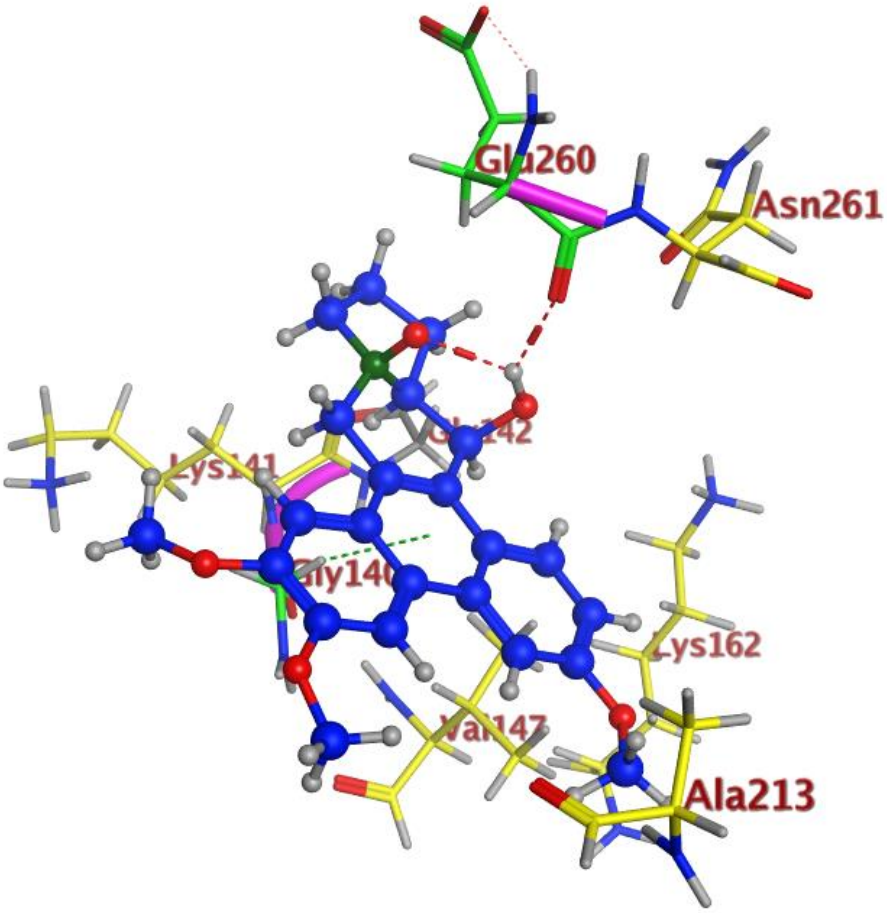
Compound 3: Pose 15 (-6.79220676)





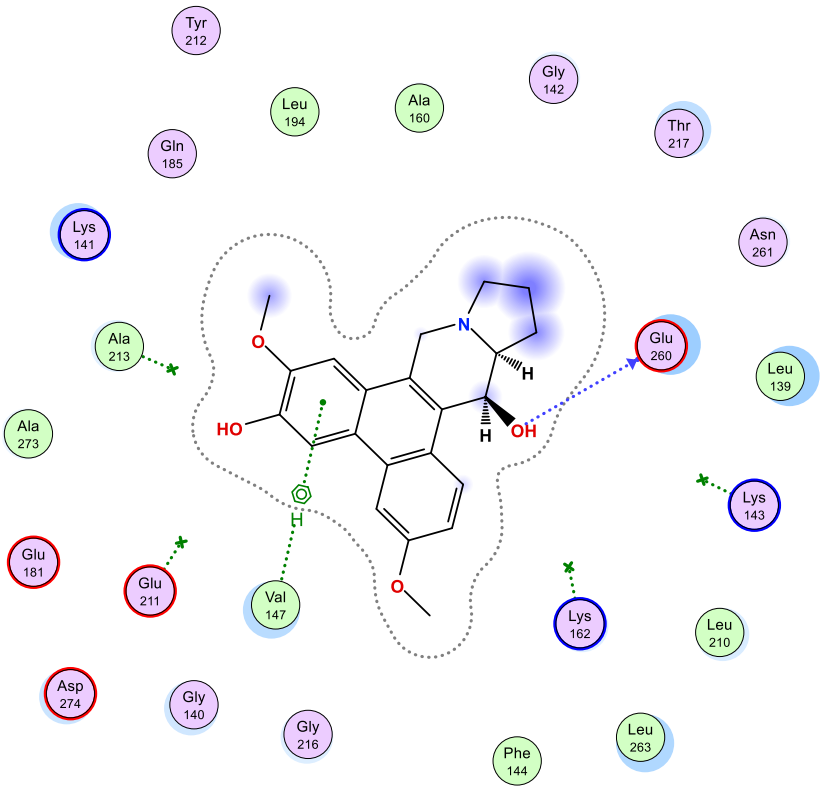
Compound 4 pose 18 (-7.04823351)

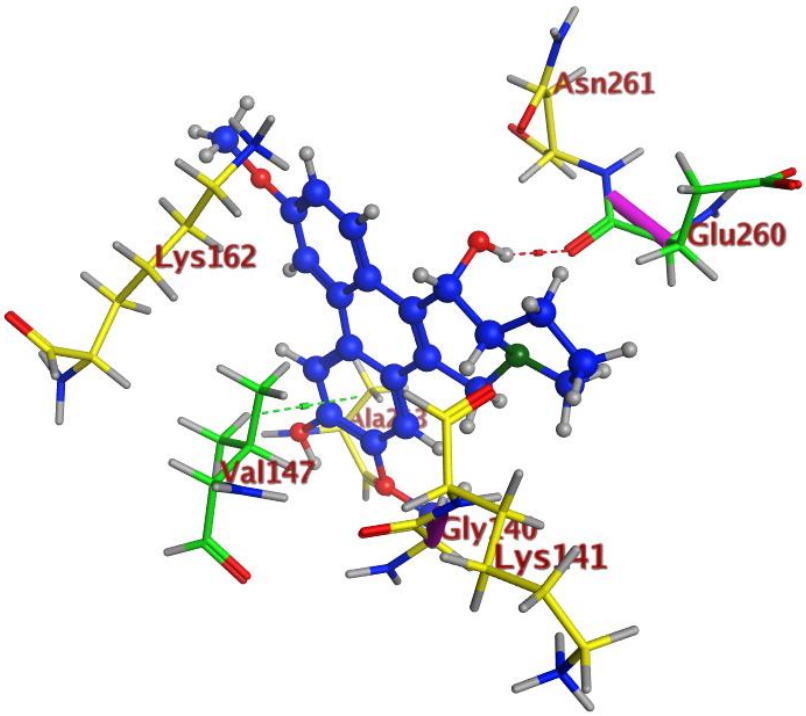




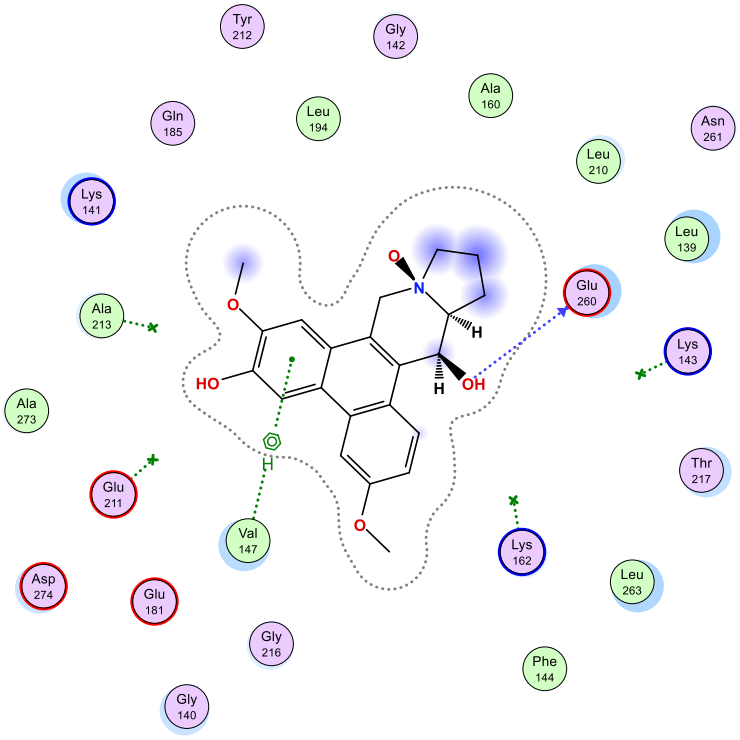
The proton of hydroxy group at C-14 was interacted with the oxygen atom of N-oxide forming intramolecular hydrogen bonding led to stable six membered ring, which might affect the activity.

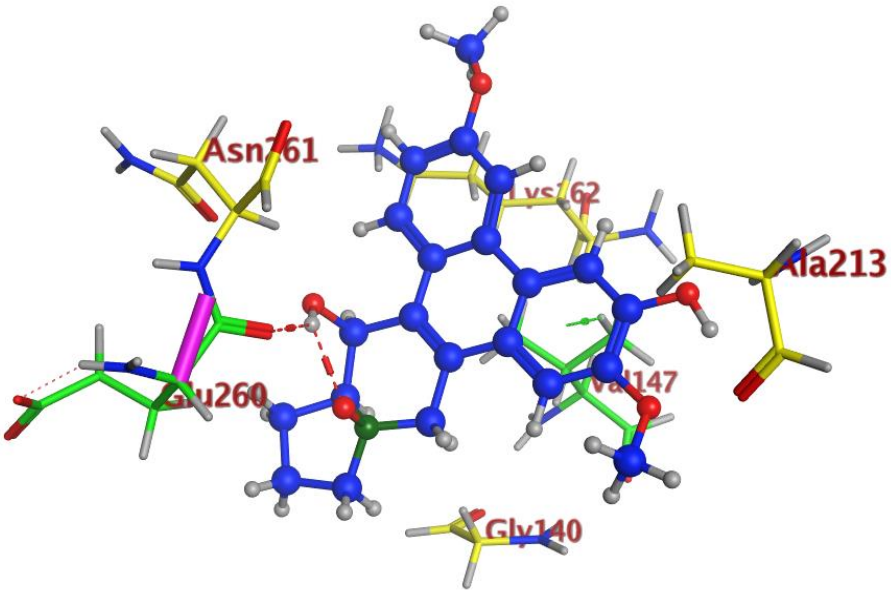
Compound 5 Pose 21 (-7.44532824)





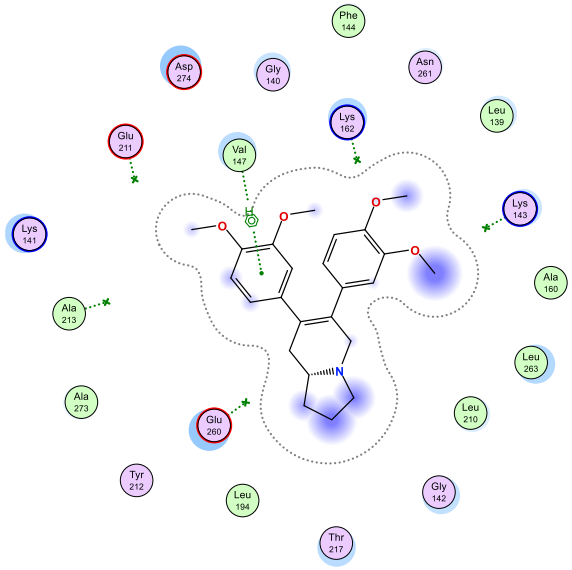
Compound 6 Pose 27 (-7.2439537)

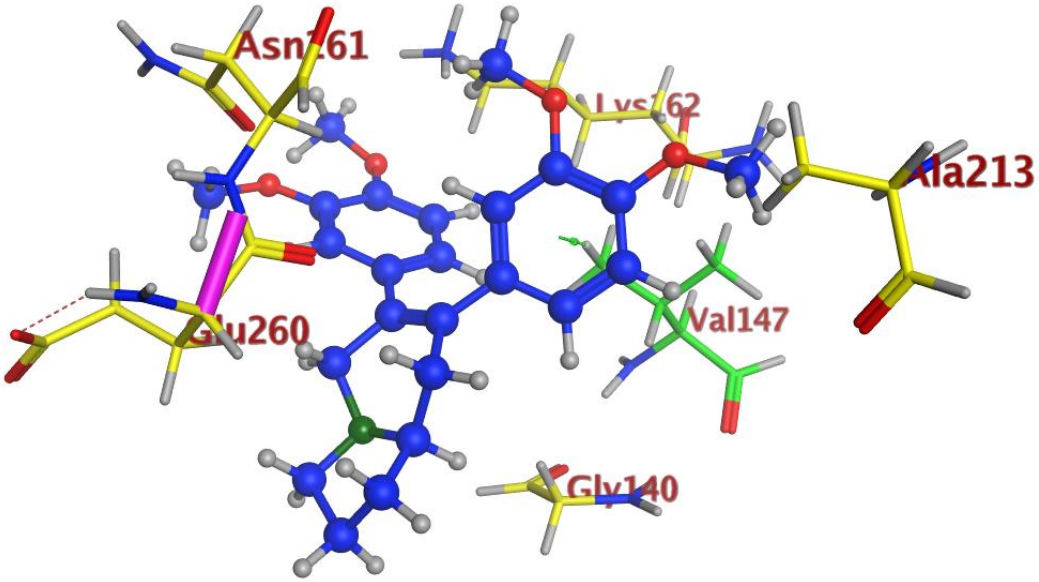




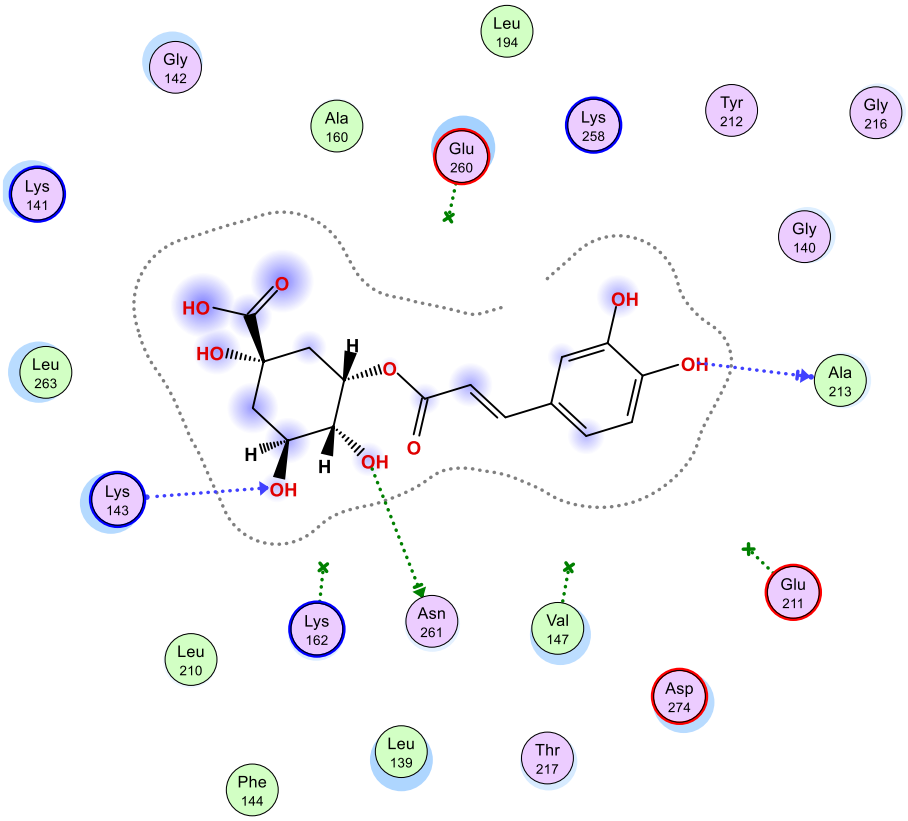
The proton of hydroxy group at C-14 was interacted with the oxygen atom of N-oxide forming intramolecular hydrogen bonding led to stable six membered ring, which might affect the activity.

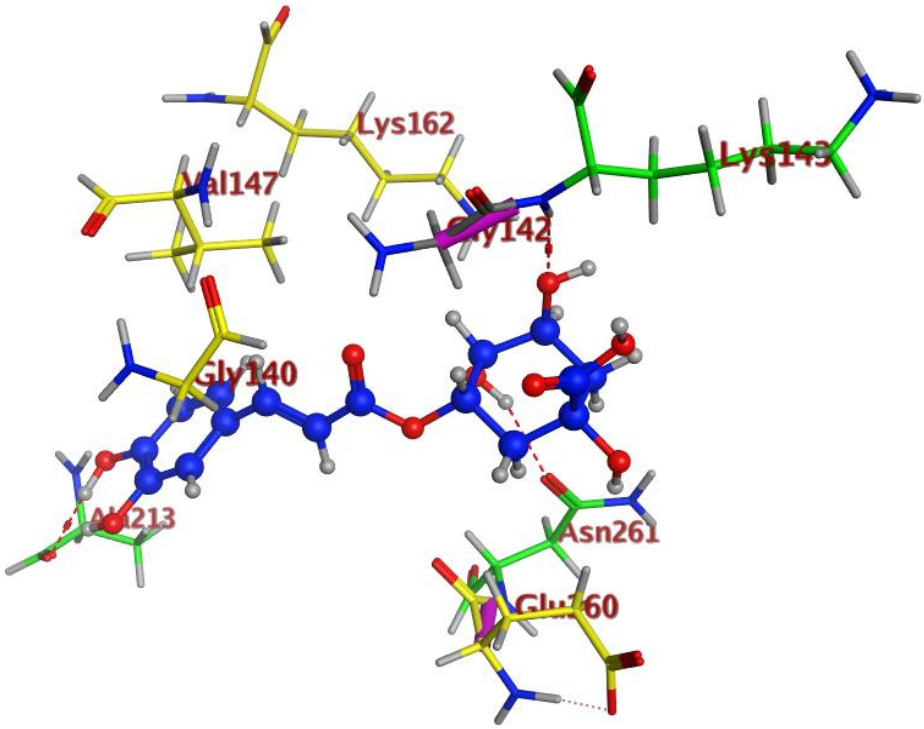
Compound 7 Pose 35 (-7.2439537)





Compound 8 Pose 37 (-6.66843224)





Compound 9 Pose 41 (-7.22312737)