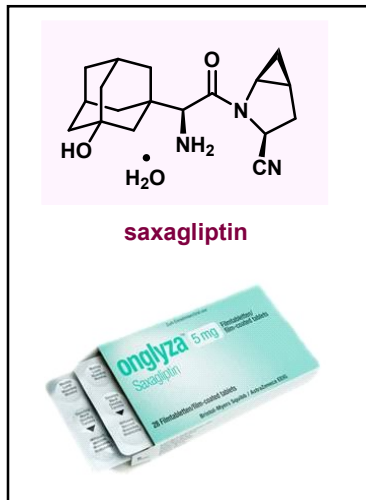


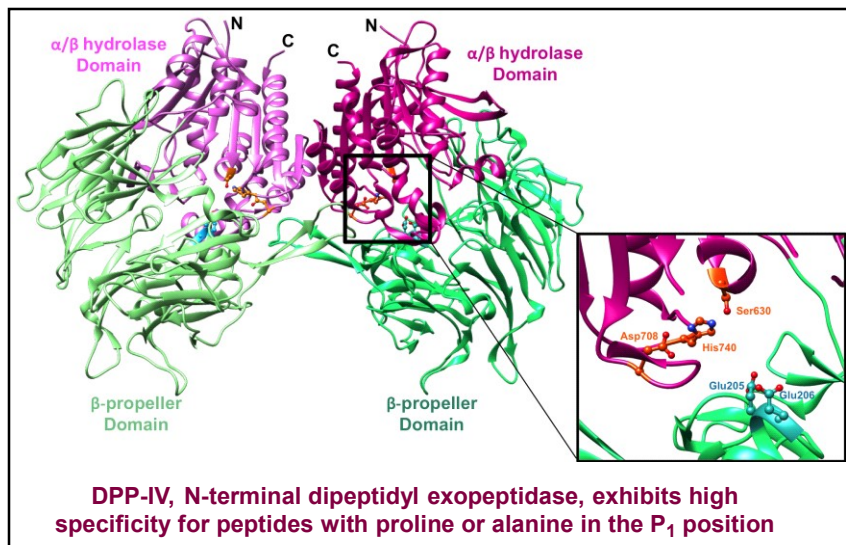
DOTW: Saxagliptin (Onglyza™)



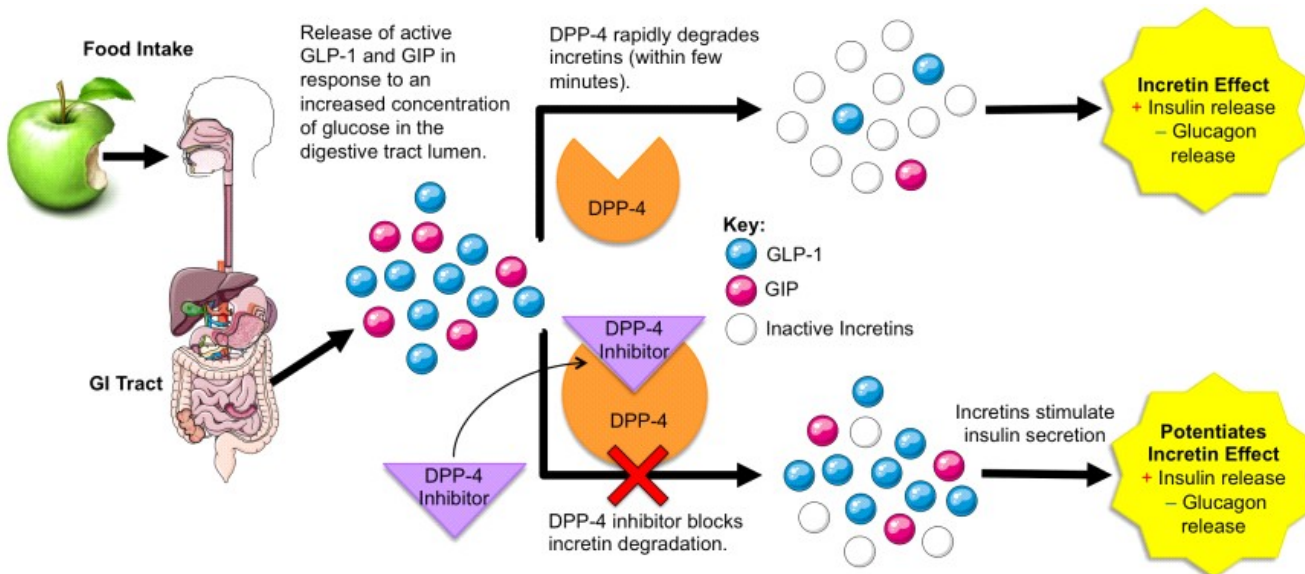
-Dipeptidyl peptidase IV (DPP-IV) inhibitor used in the treatment of type 2 diabetes;
 -Approved by FDA in 2009, soon reached the top 10 highest selling diabetes drugs;
 -Later it was found that it can cause heart failure which prompted a dramatic drop in sales.



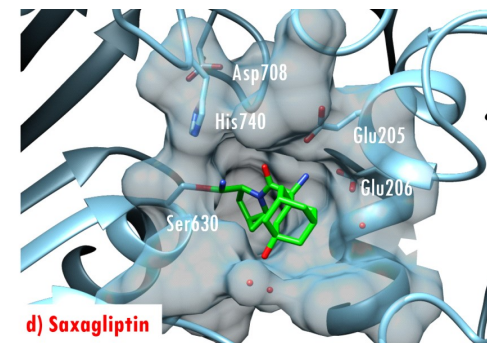
Hamann, *J. Med. Chem.* **2005**, *48*, 5025
 Hanson, *Adv. Synth. Catal.* **2007**, *349*, 1369
 Savage, *Org. Process Res. Dev.* **2009**, *13*, 1169
 Politino, US7741082B2, **2010**



Mechanism of action:

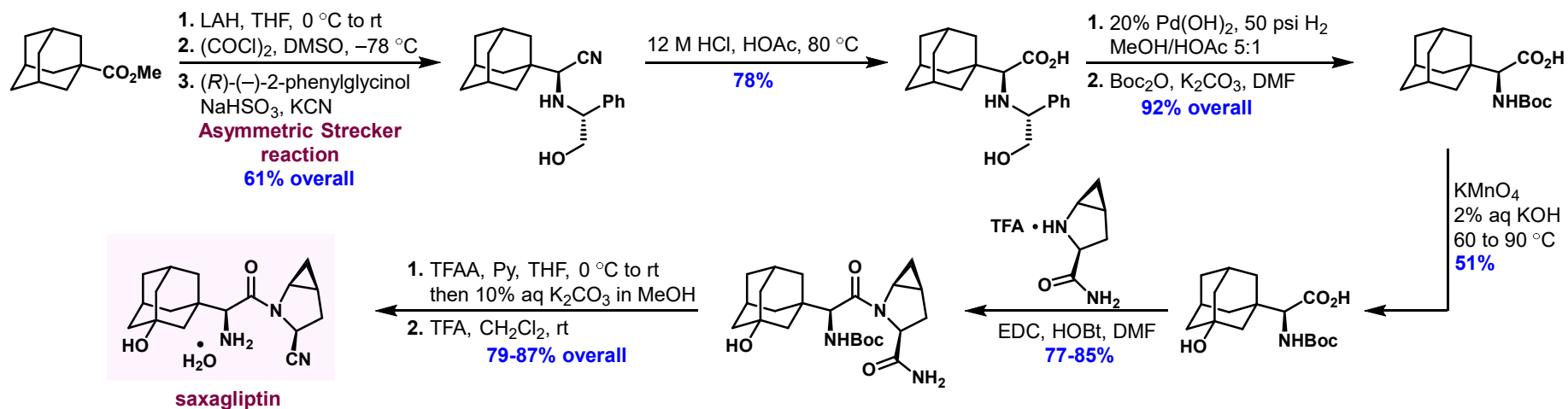


-Glucagon cage-like peptide 1 (GLP-1) regulates insulin secretion following meals;
 -Binding to the GLP-1 receptor on pancreatic β-cells results in increased insulin secretion;
 -DPP-IV truncates GLP-1 on the N-terminal dipeptide His-Ala forming a weak antagonist for the GLP-1 receptor;
 -Inhibitors of DPP-IV lower blood sugar levels, increase glucose tolerance and improve insulin response to oral glucose in patients with type 2 diabetes.



DOTW: Saxagliptin (Onglyza™)

Discovery route:



Process route:

