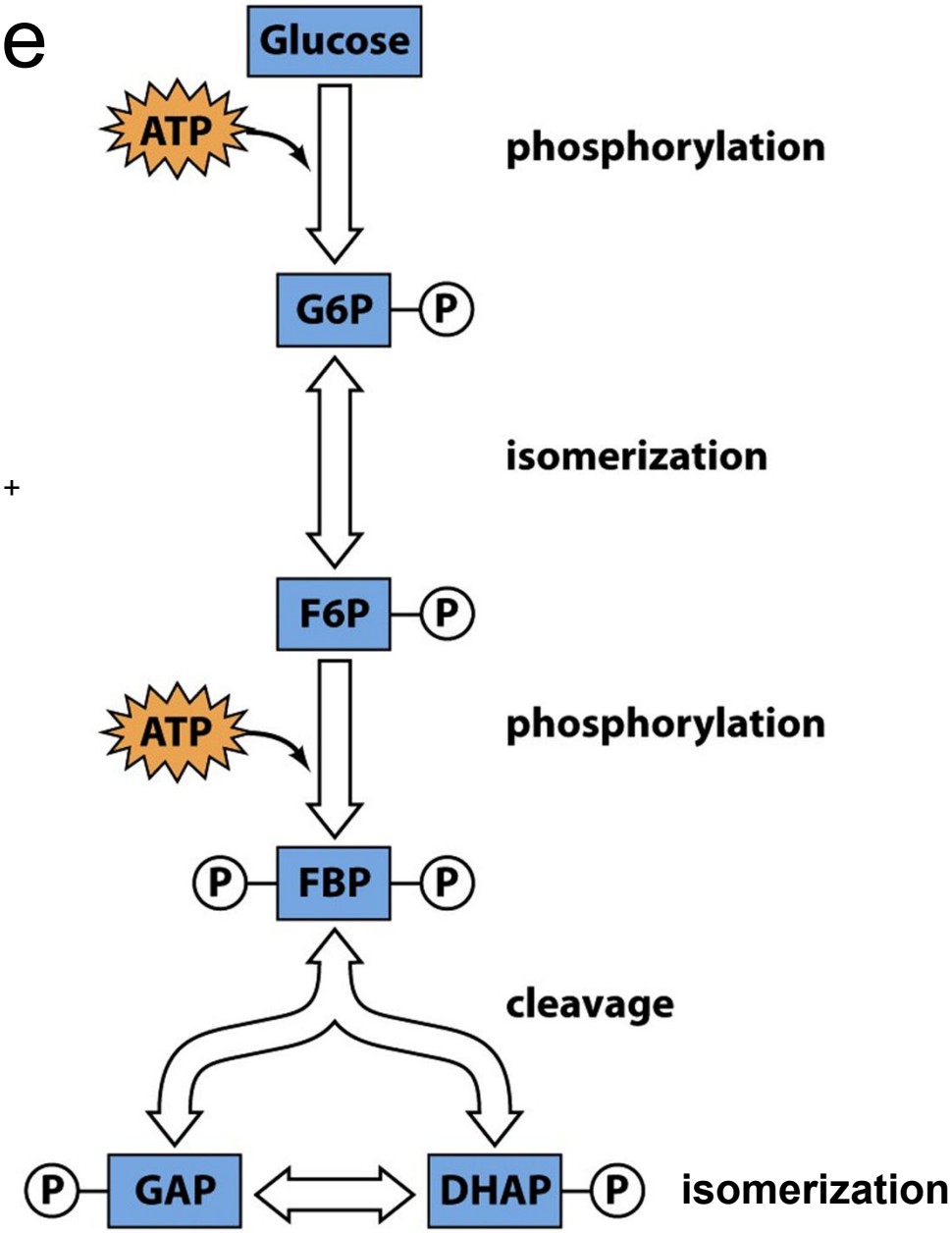
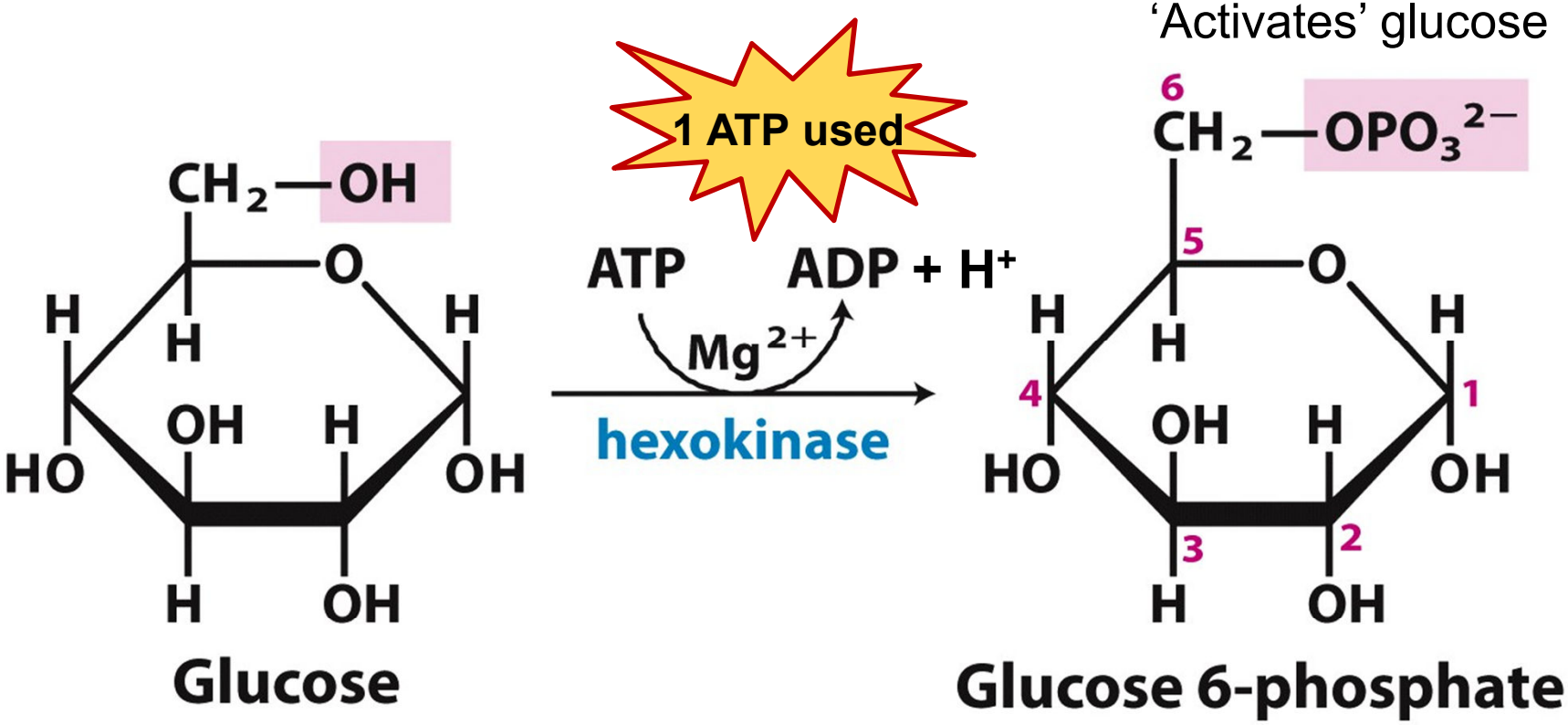
The preparatory phase uses 2 ATP and converts 1 glucose to 2 molecules of GAP

Glucose + 2ATP → 2GAP + 2ADP + $2H^+$



Step 1: Hexokinase catalyzes a phosphoryl transfer from ATP to glucose

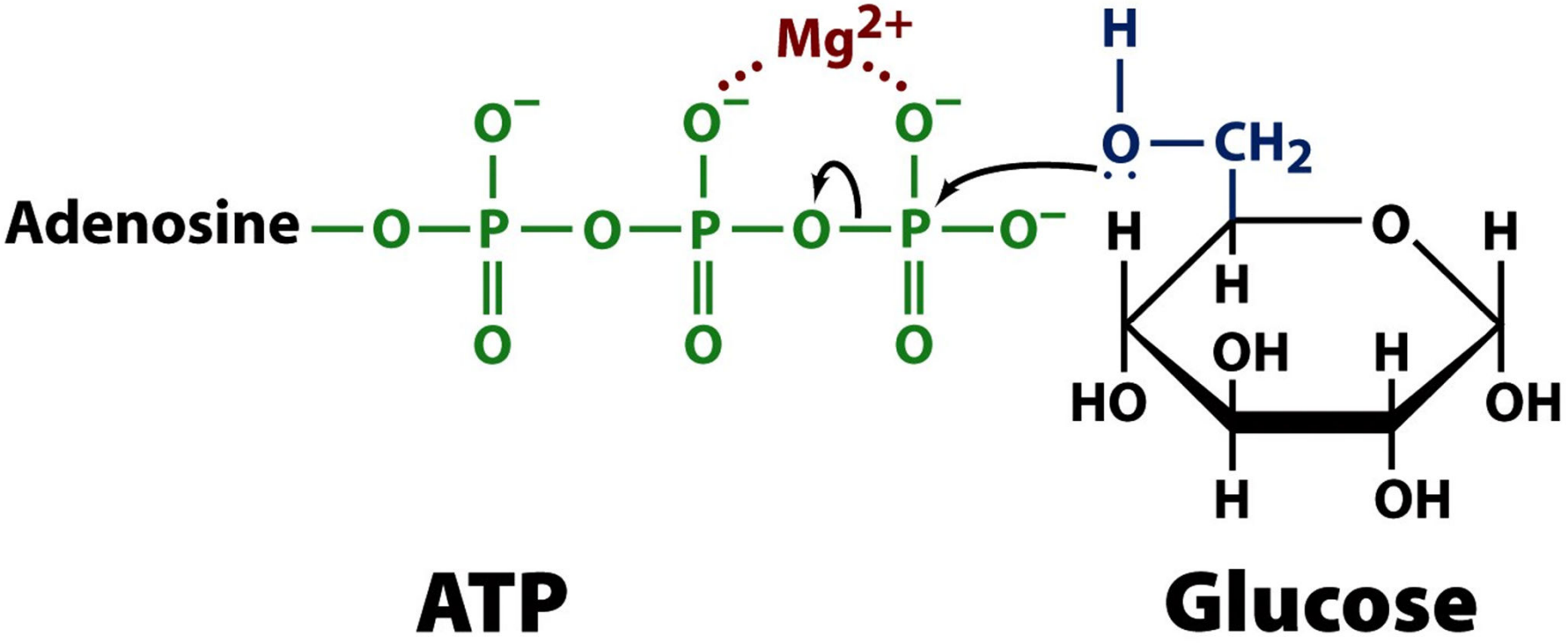
‘Activates’ glucose



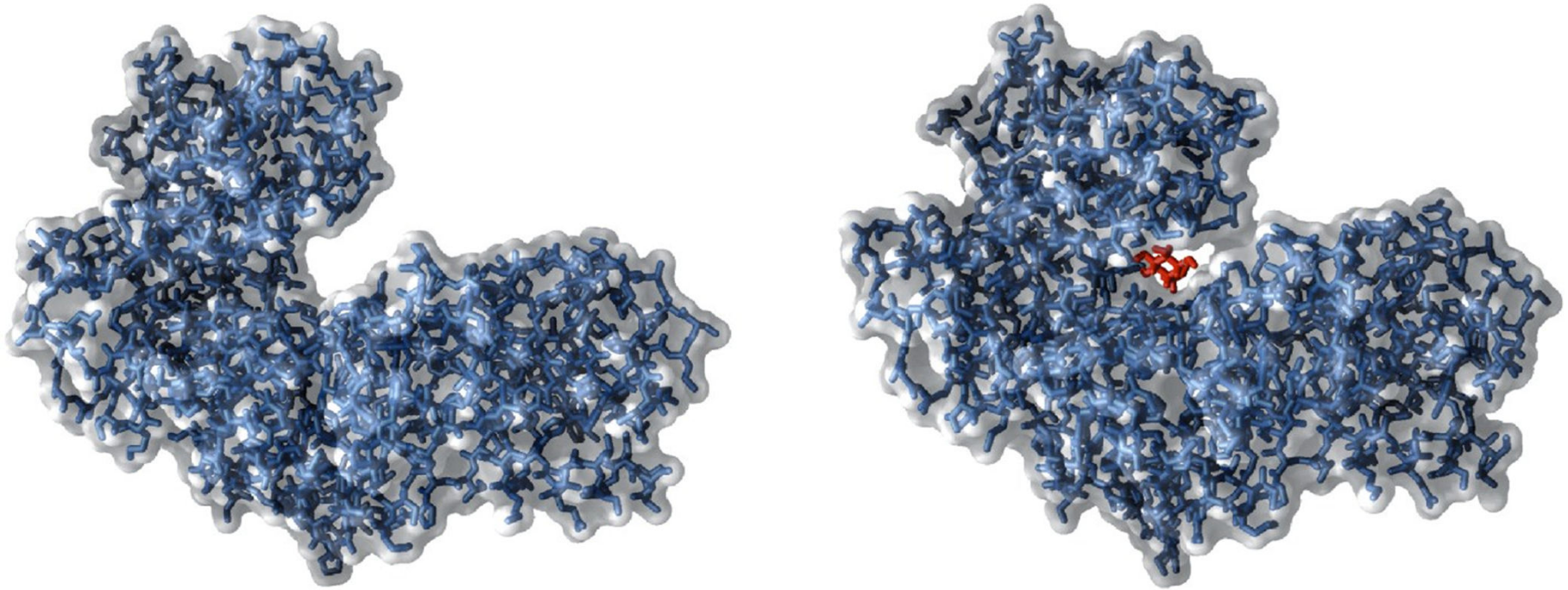
Keeps [glucose] low in the cell, so glucose can always move *down* its gradient into the cell

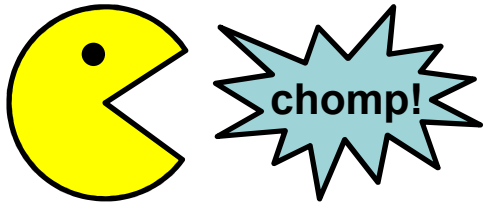
$$\Delta G'^{\circ} = -16.7 \text{ kJ/mol}$$

Mg^{2+} offsets negative charge on phosphates of ATP, allowing nucleophilic attack

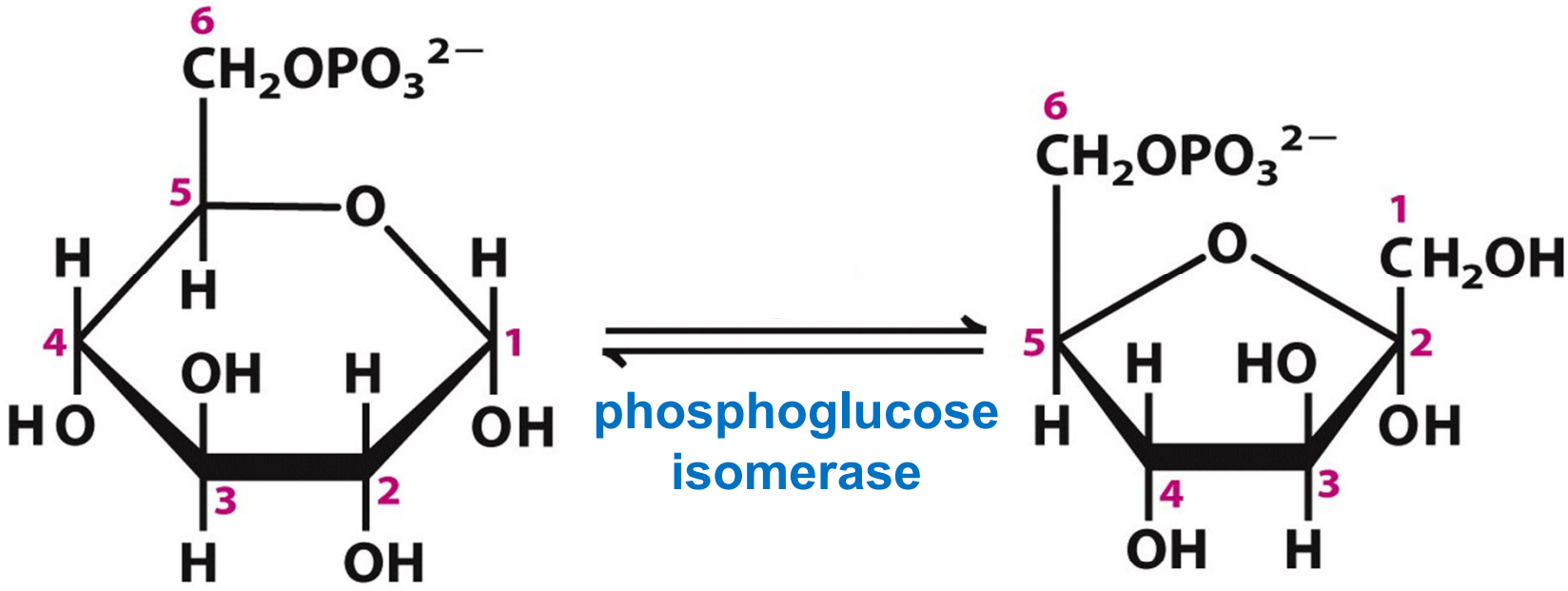


Hexokinase undergoes a conformational change on binding glucose (induced fit)





Step 2: PGI catalyzes the isomerization of the aldose G6P to the ketose F6P

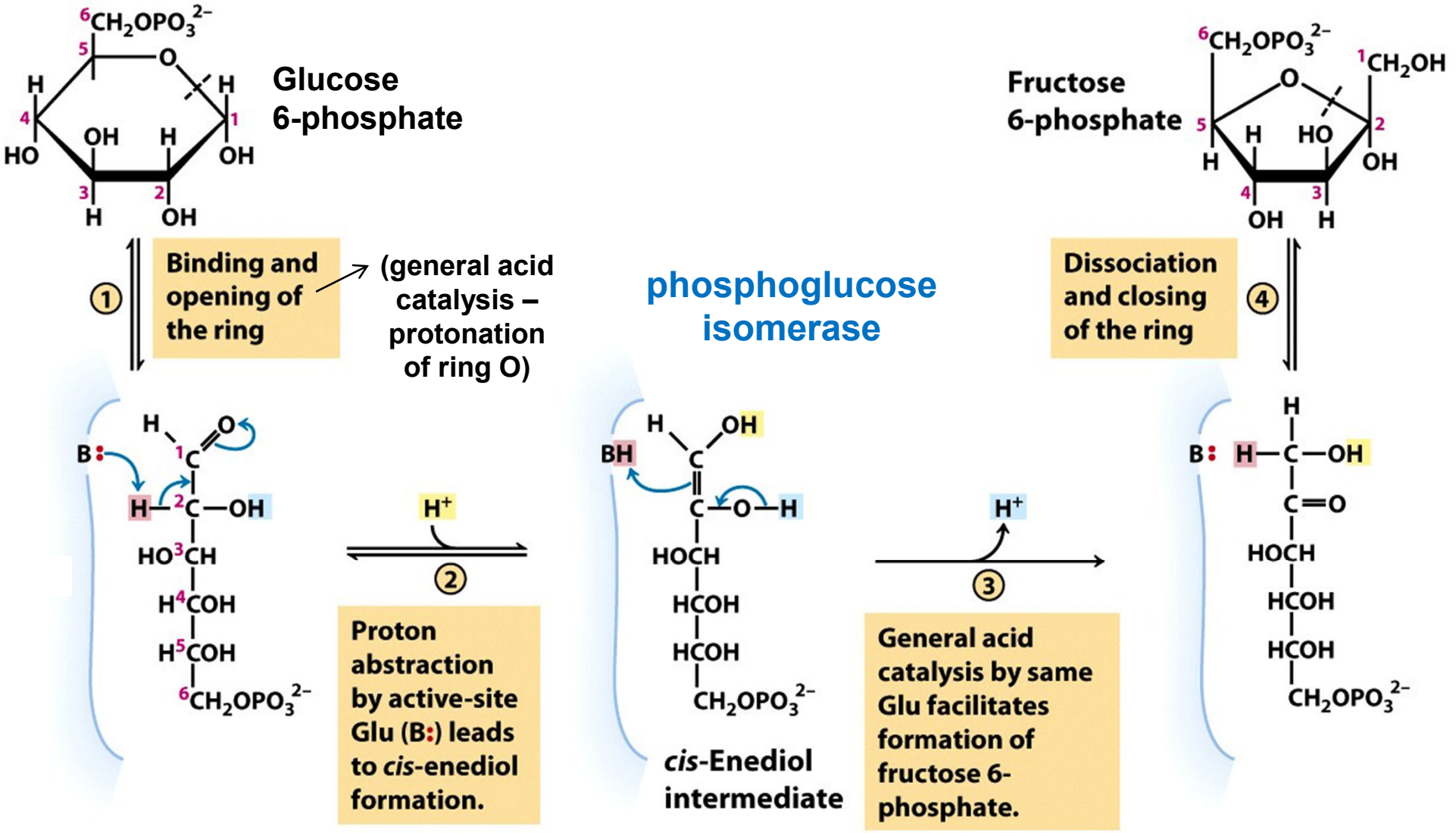


Glucose 6-phosphate **Fructose 6-phosphate**

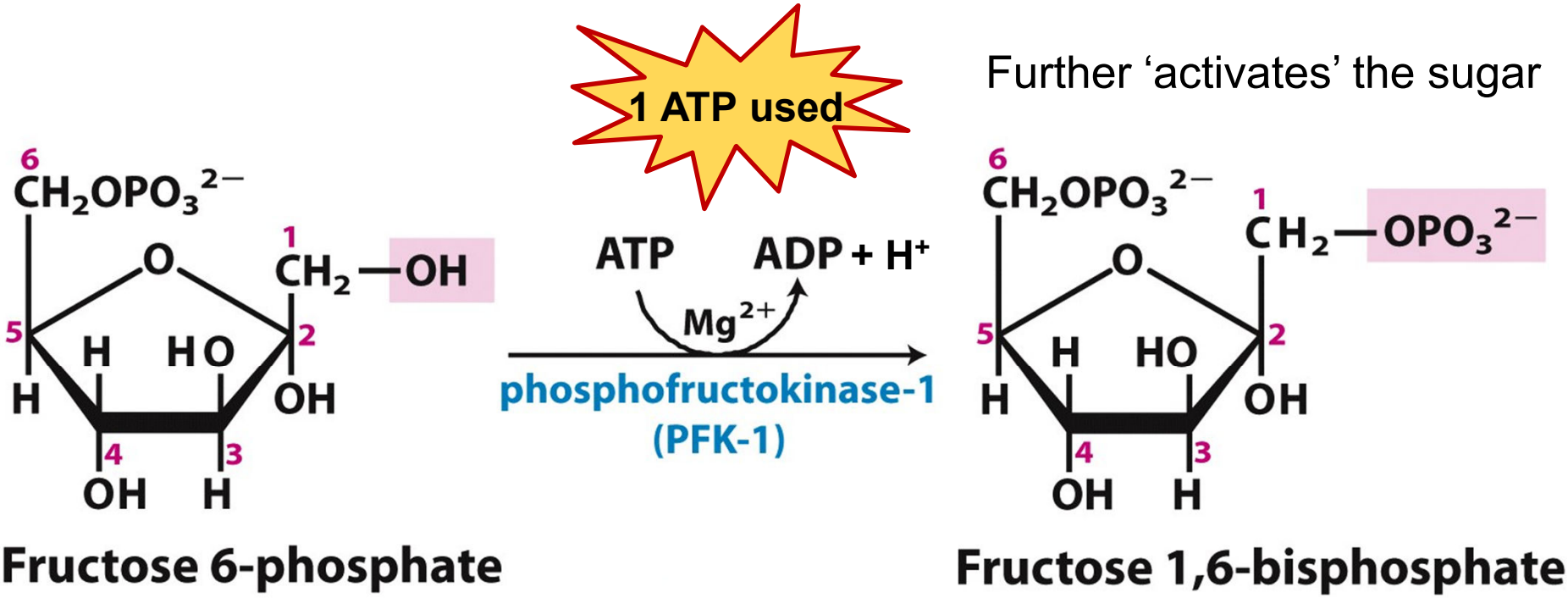
Moving the carbonyl to C2 prepares the molecule for cleavage in step 4

$$\Delta G'^{\circ} = 1.7 \text{ kJ/mol}$$

General acid-base catalysis promotes isomerization via an enediol intermediate



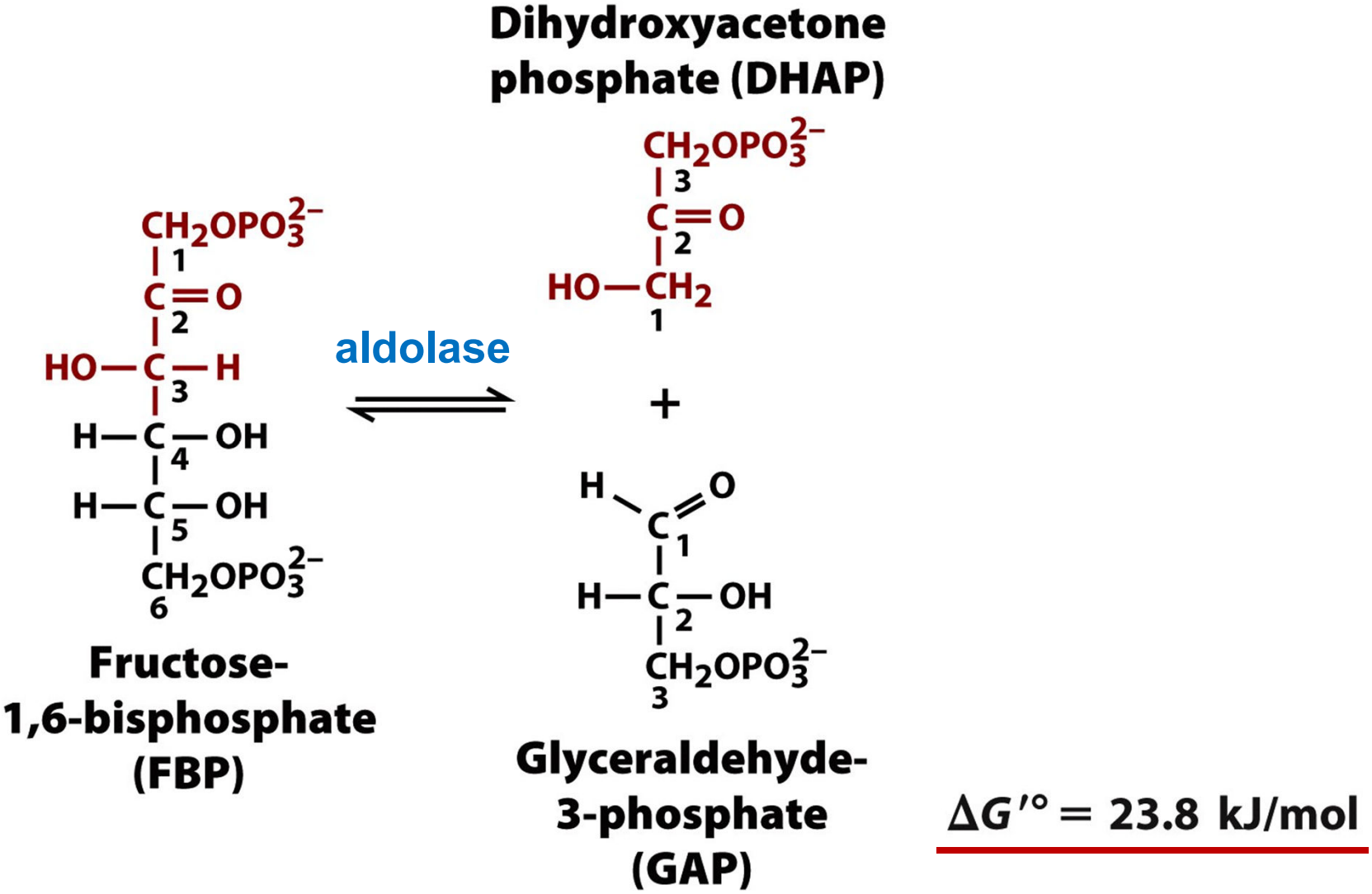
Step 3: PFK catalyzes the second phosphoryl transfer from ATP



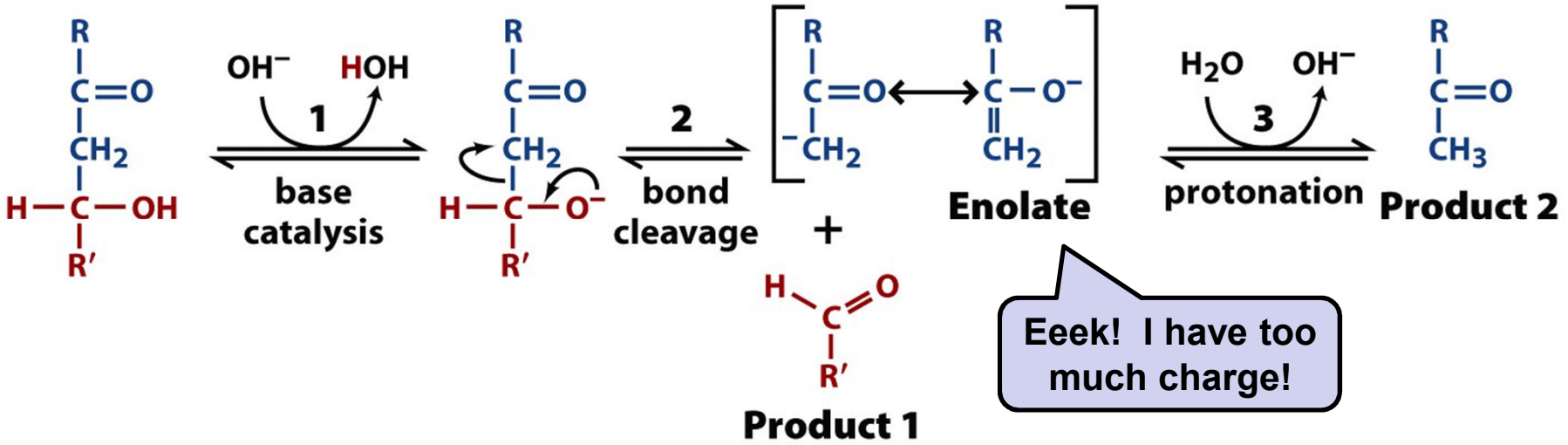
- This step 'commits' the hexose to being broken down
- Phosphorylations become even: at both ends of the molecule

$$\Delta G'^{\circ} = -14.2 \text{ kJ/mol}$$

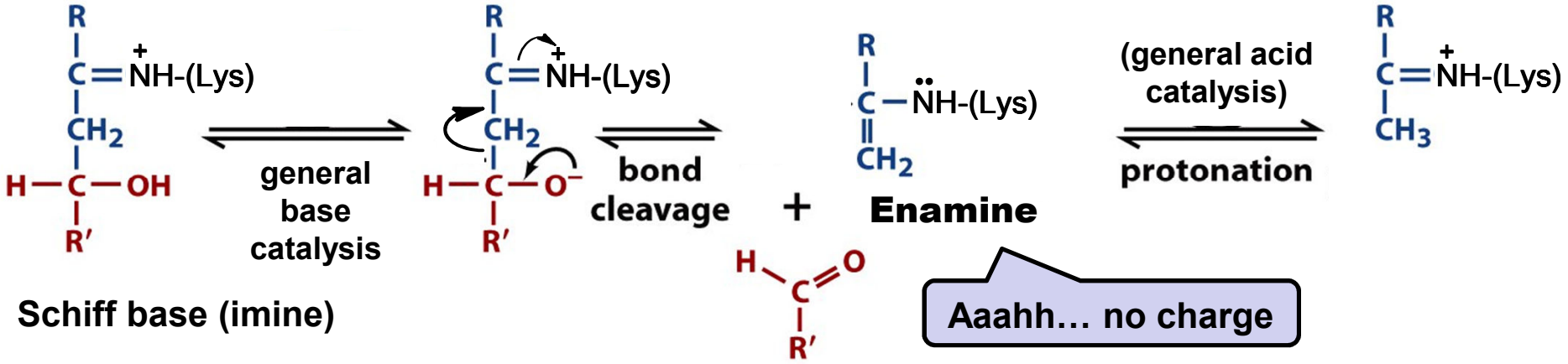
Step 4: Aldolase catalyzes the aldol cleavage of the hexose into 2 trioses



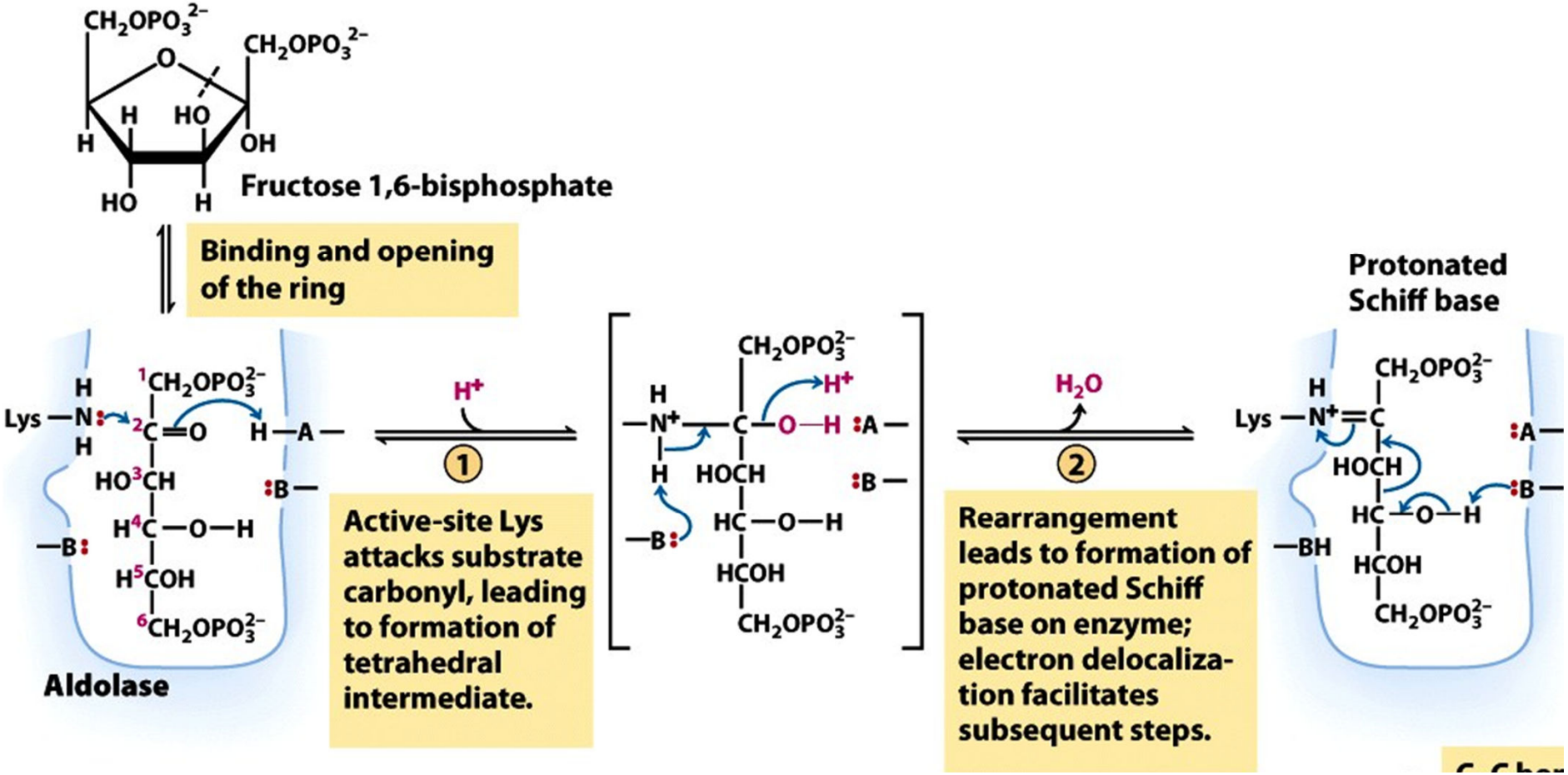
(Non-enzymatic) base-catalyzed aldol cleavage forms an unstable enolate intermediate



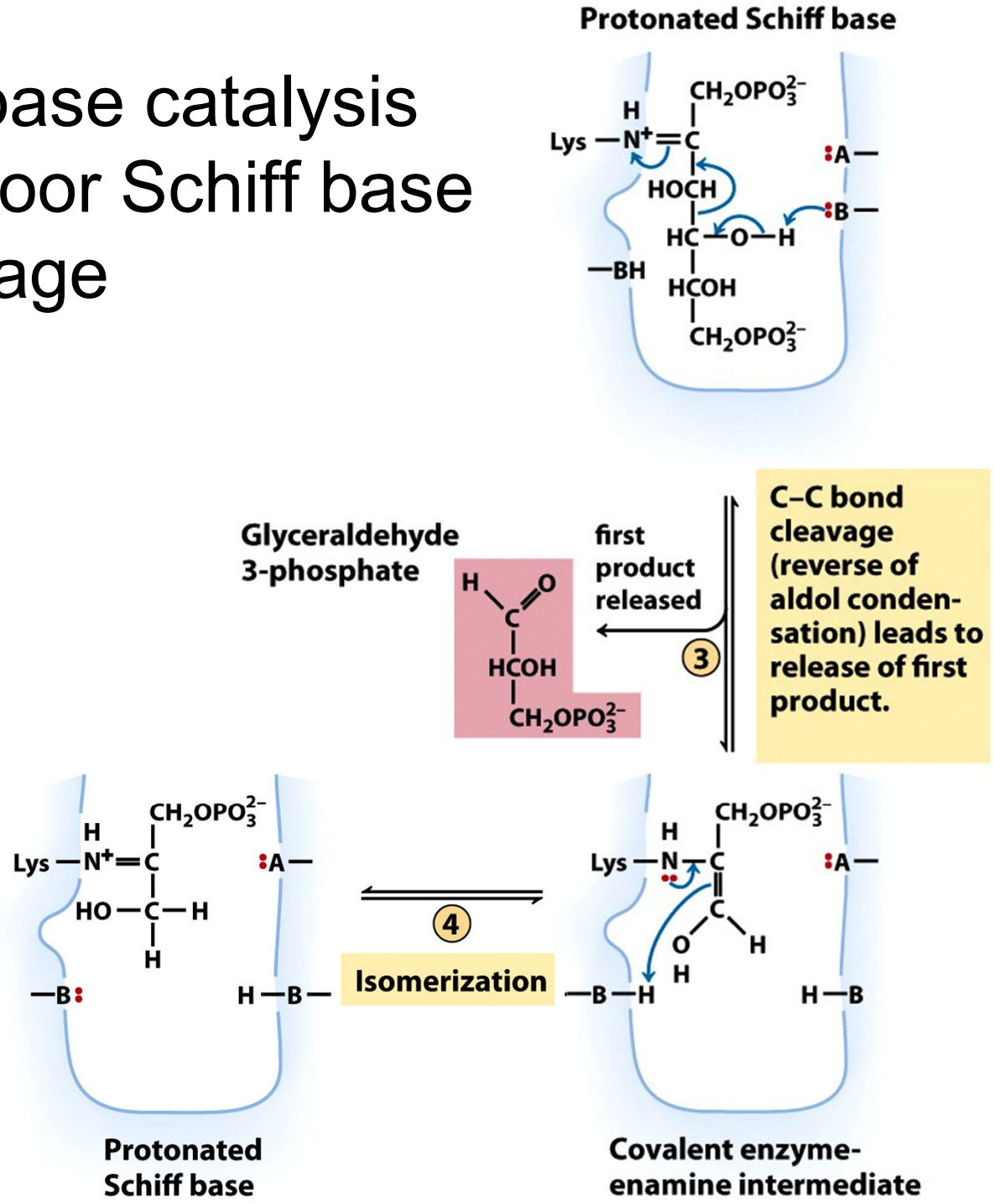
Aldolase promotes the reaction by forming a Schiff base instead:



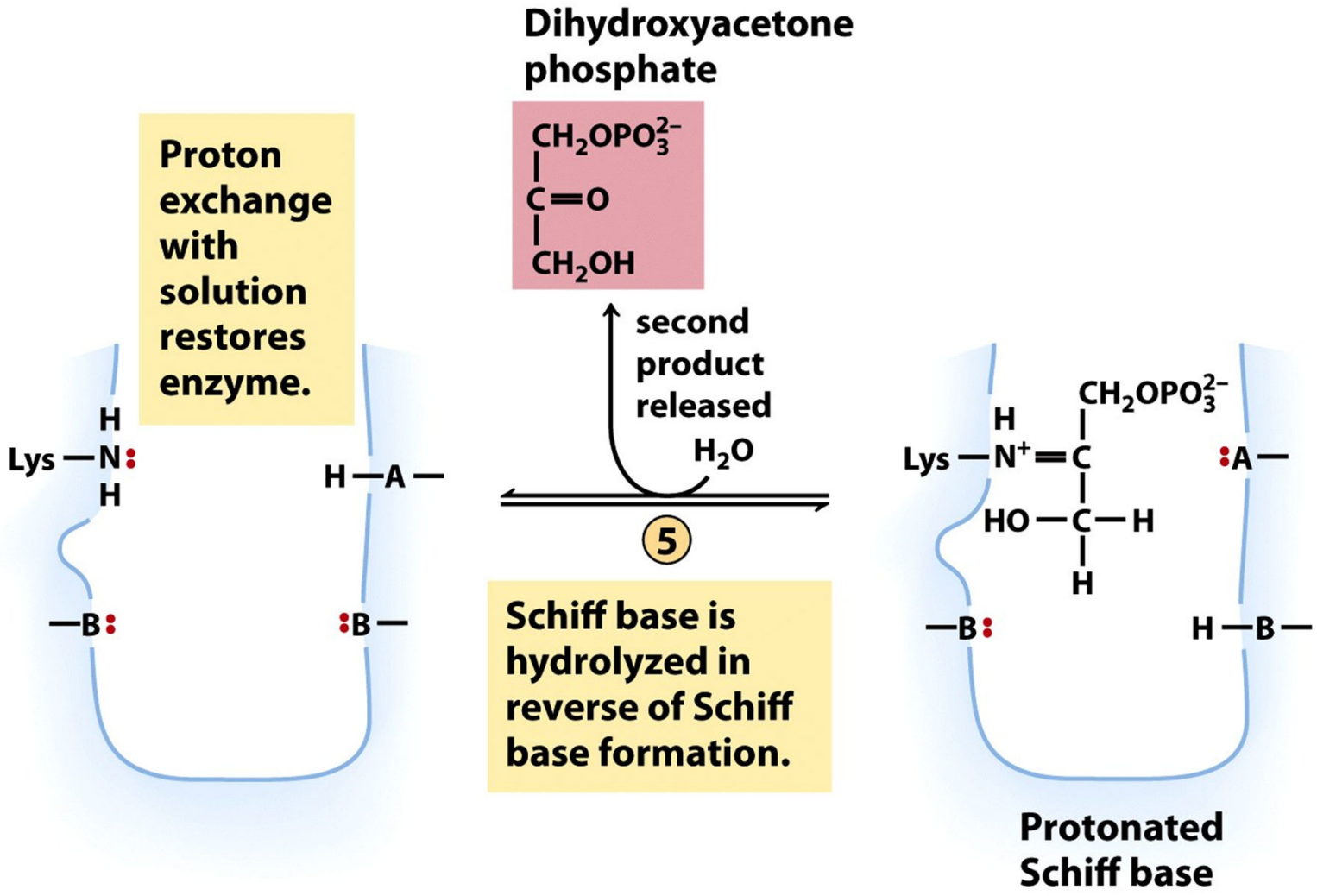
Schiff base formation on aldolase involves covalent and general acid-base catalysis



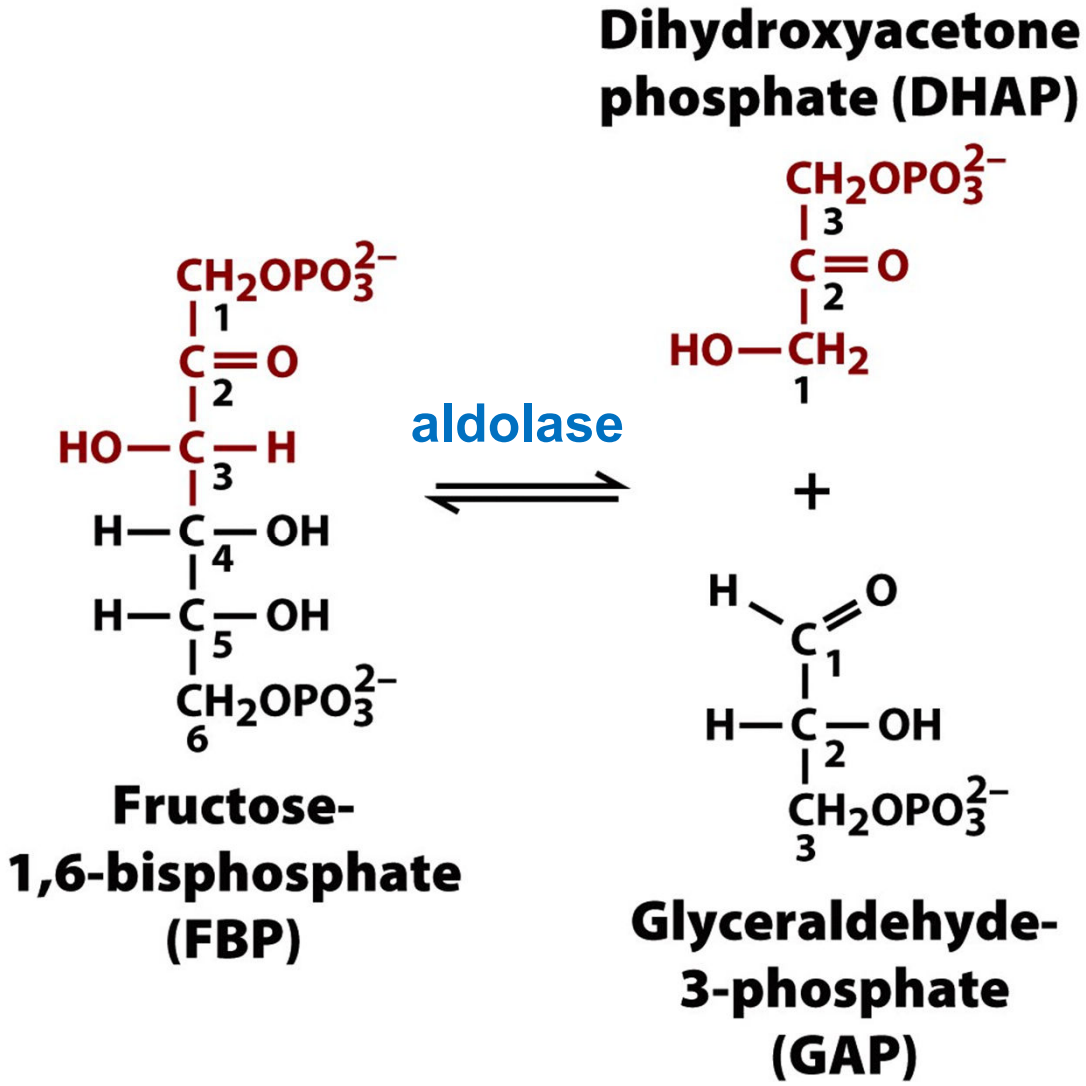
General acid-base catalysis and electron-poor Schiff base promote cleavage



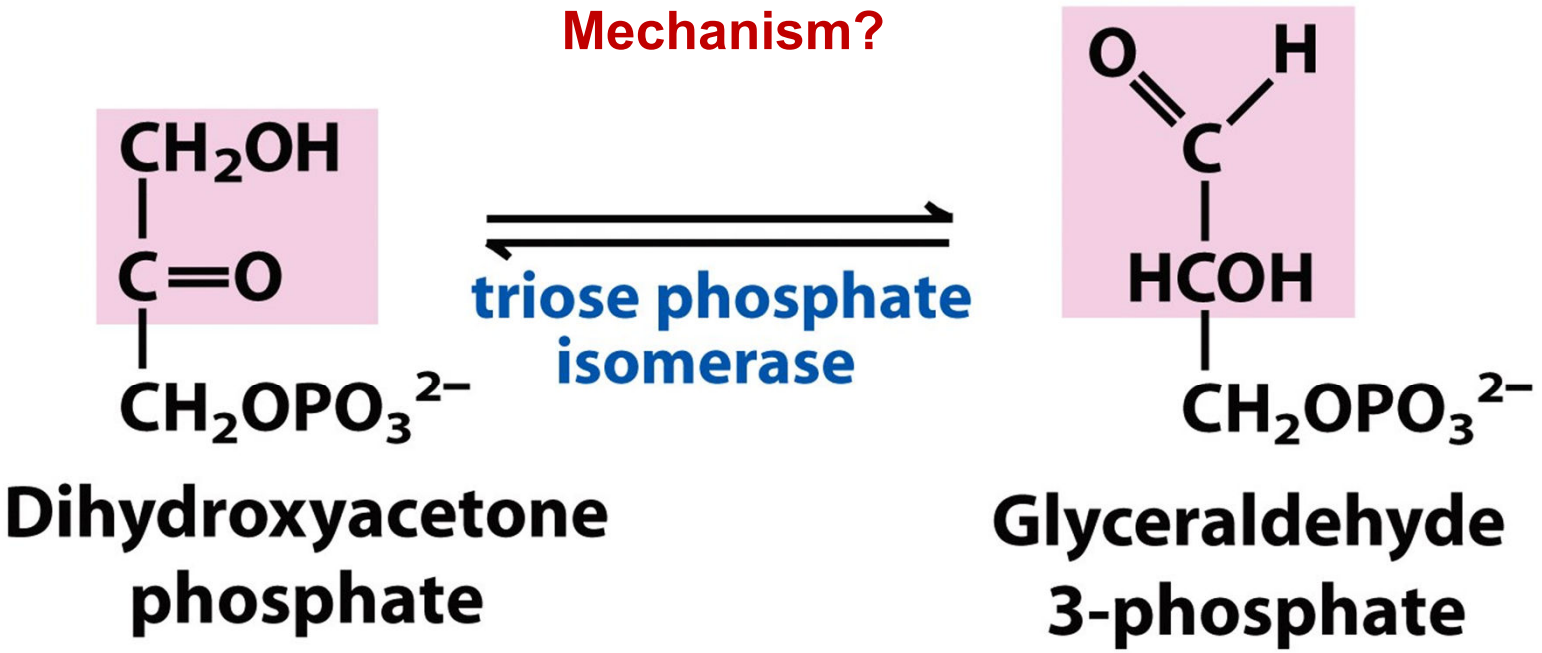
Aldolase releases 2nd product by reversing Schiff-base formation reactions



2 trioses result from aldolase cleavage because hexose carbonyl is at C2



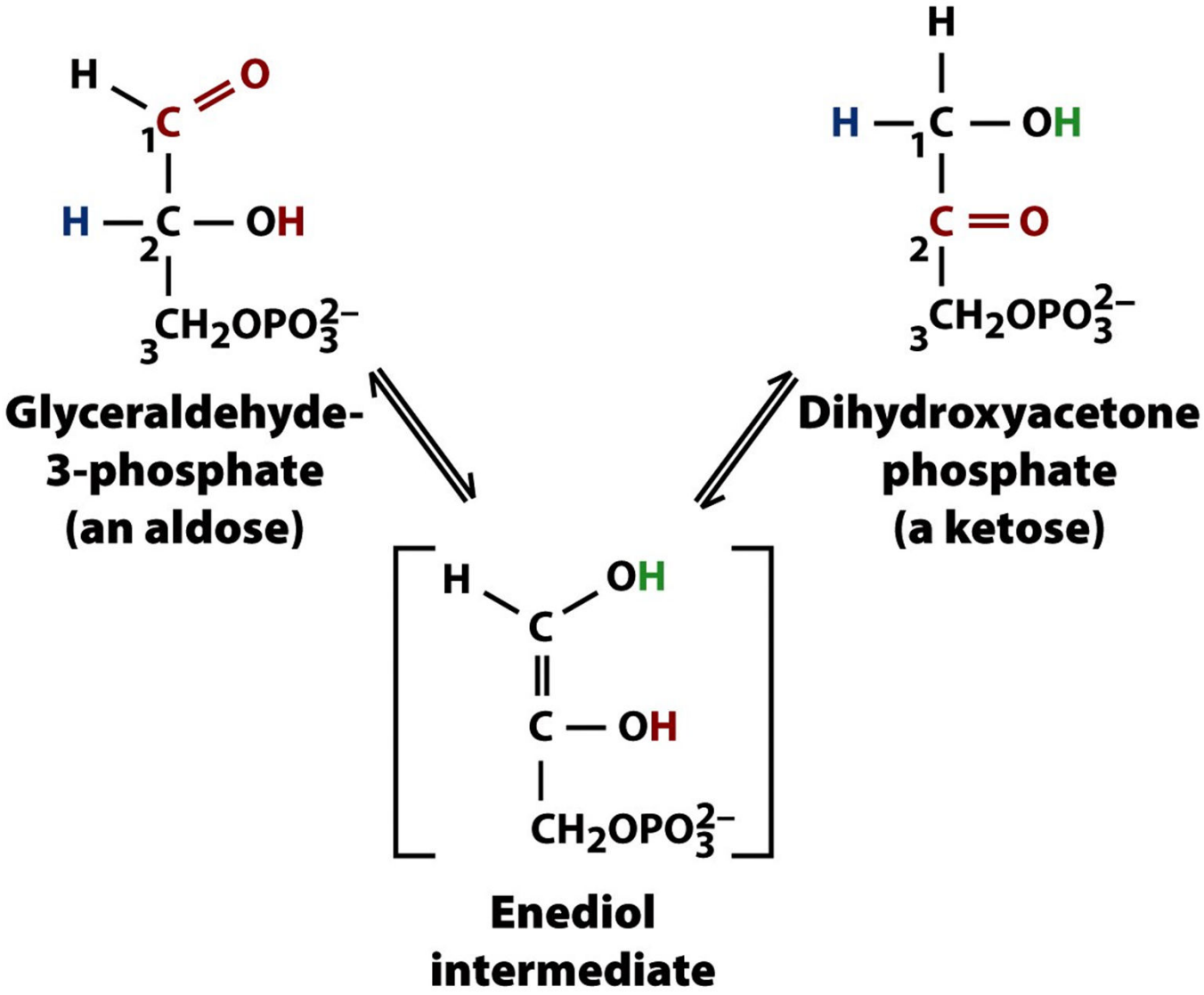
Triose phosphate isomerase interconverts the products of the aldolase reaction



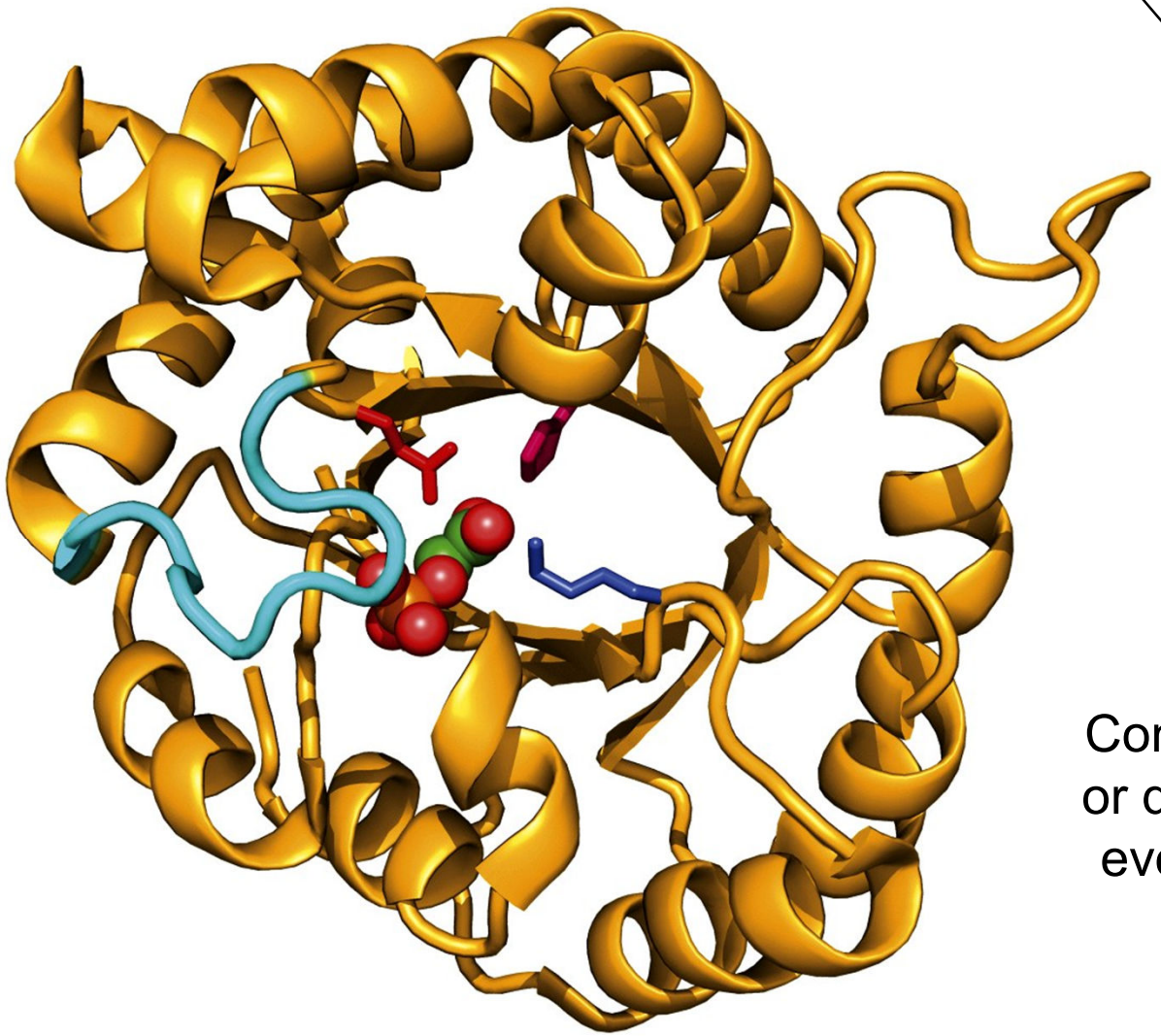
Two of the same molecule can continue through glycolysis: more efficient than two different

$\Delta G'^{\circ} = 7.5$ kJ/mol

Aldose-ketose isomerization occurs through an enediol intermediate



Triose phosphate isomerase (TIM) has a ‘TIM barrel’ fold, as do many other enzymes



Including aldolase, enolase, pyruvate kinase

Convergent or divergent evolution?

The preparatory phase uses 2 ATP and converts 1 glucose to 2 molecules of GAP

Glucose + 2ATP → 2GAP + 2ADP + $2H^+$