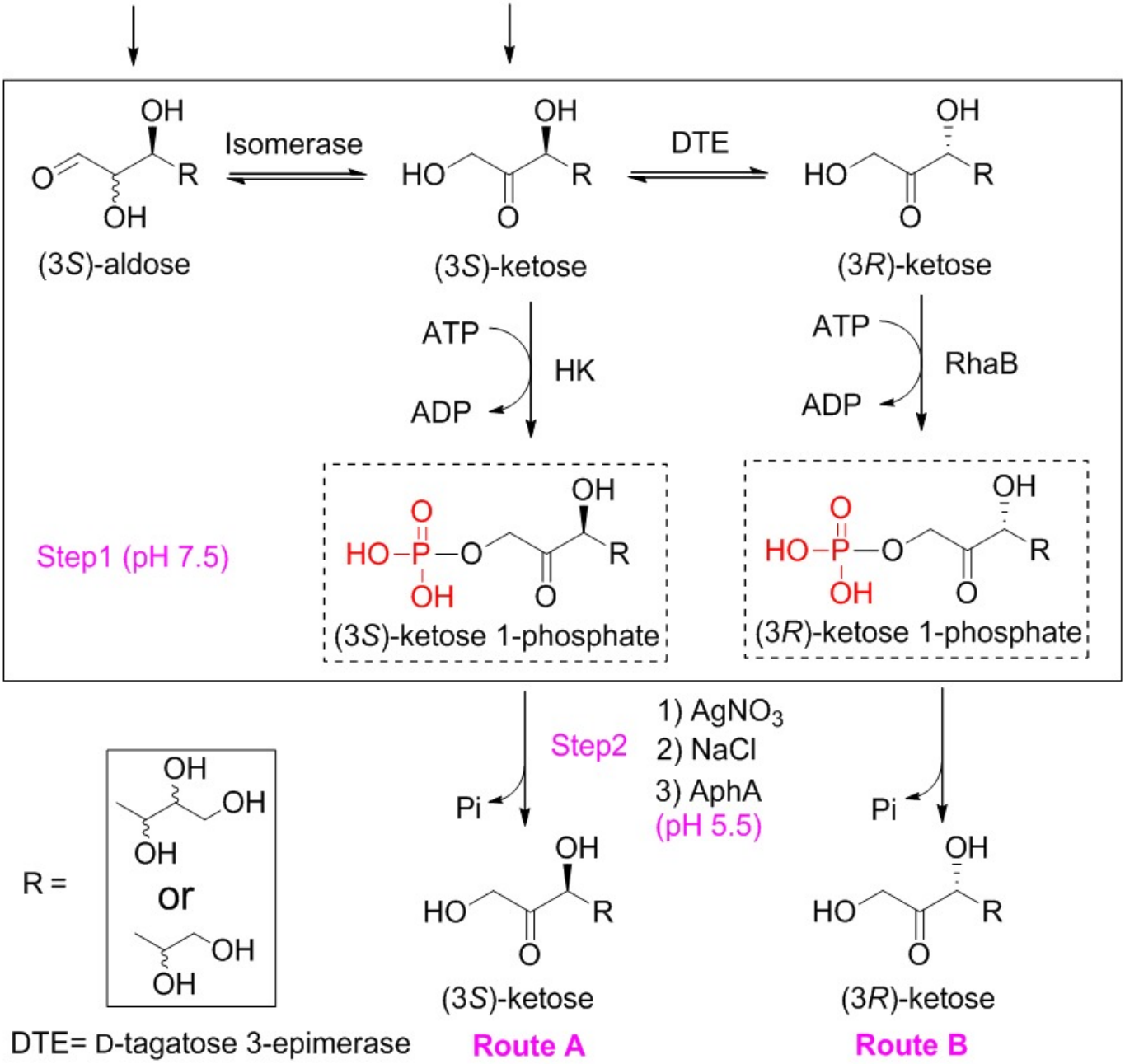
Facile enzymatic synthesis of ketoses

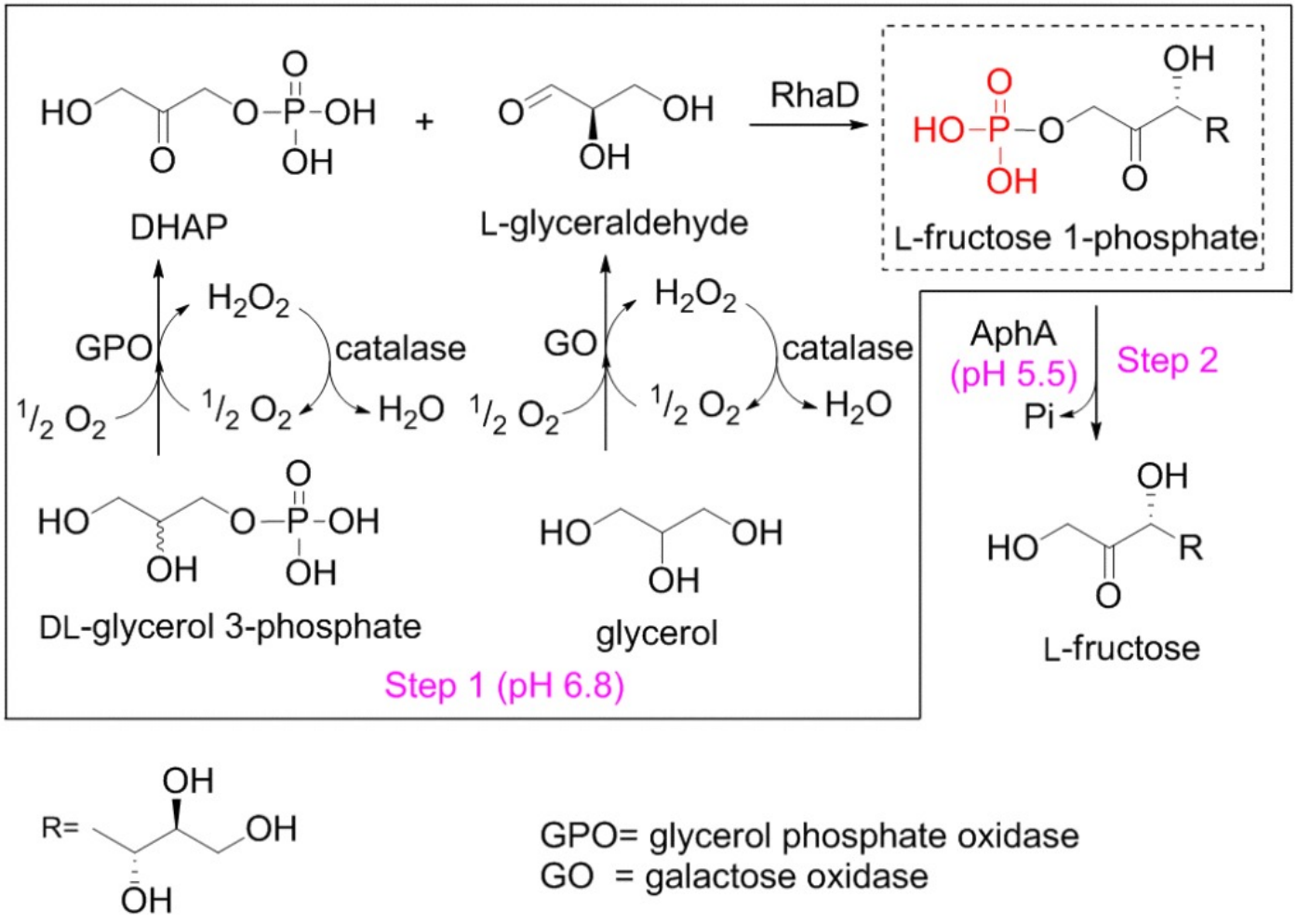
Over the past decades, 11 rare ketopentoses and ketohexoses have been successfully synthesized by scientist. However, all the reported processes suffer from complicated purification steps, low yield, or expensive starting materials. Studies of rare ketoses have been hampered by the lack of efficient preparation methods.



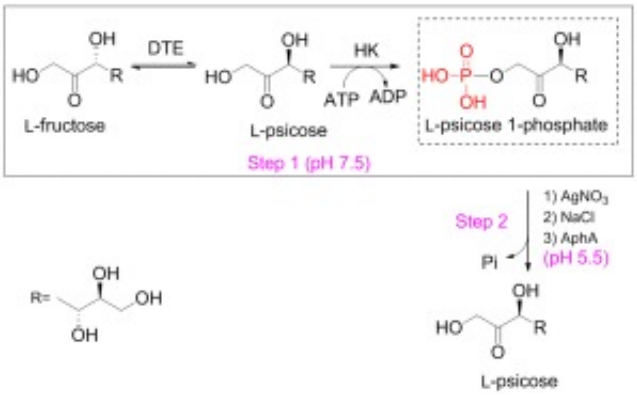
Scheme 1. One-pot two-step enzymatic synthesis of L-ribulose, D-xylulose and D-tagatose (Route

A), and L-xylulose, D-ribulose, D-sorbose, D-psicose and L-tagatose (Route B) from L-arabinose, D-xylose, D-galactose, D-fructose and L-sorbose

At this point, a convenient, efficient and cost-effective platform undergoing “phosphorylation®de-phosphorylation” cascade reaction for the facile synthesis of ketoses is described by which all non-readily available ketopentoses and ketohexoses were prepared from common and inexpensive starting materials with high yield and purity without having to undergo a tedious isomer separation step.



Scheme 2. One-pot multienzyme reaction for the synthesis of L-fructose from glycerol and DL-glycerol 3-phosphate



Scheme 3. One-pot multienzyme reaction for the synthesis of L-psicose from L-fructose.

In the first reaction step of Scheme 1, we combined thermodynamically unfavorable bioconversions of common (3*S*)-sugars to the desired (3*S*)-ketoses (route A) or (3*R*)-ketoses (route B) with phosphorylation reactions by substrate-specific kinases (Fructokinase (HK) from humans in route A, L-rhamnulose kinase (RhaB) from *Thermotoga maritima* MSB8 in route B). In the second reaction step, phosphate adenosines (ATP and ADP) were selectively removed by a convenient method called silver nitrate precipitation. Then, acid phosphatase (AphA) was added to hydrolyze the phosphate groups to produce the desired ketoses. Notably, both reaction steps can be performed in a one-pot fashion. Scheme 2 was designed to prepare L-fructose from DL-glycerol 3-phosphate and glycerol relying on the aldol condensation reaction using rhamnulose bisphosphate aldolase (RhaD). L-psicose was further prepared from L-fructose using the targeted phosphorylation strategy shown in Scheme 3.

Publication

Facile Enzymatic Synthesis of Ketoses.
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