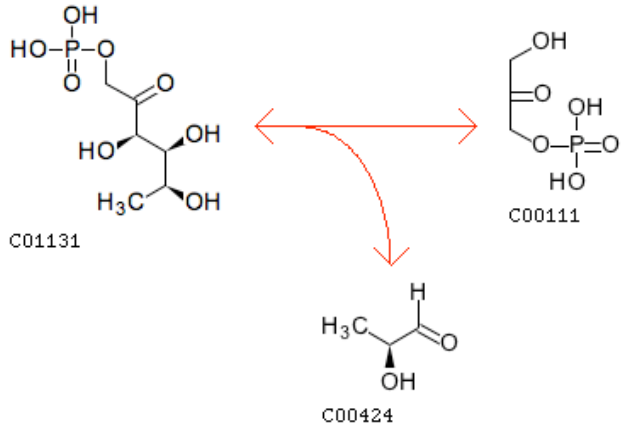
A.



B.

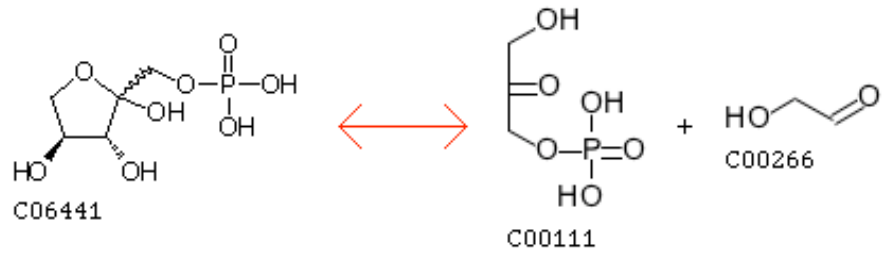


Figure S2. An example of an enzyme annotated in KEGG with a single EC number (EC 4.1.2.19) and two reactions that are dissimilar (catalytic promiscuity) and with dissimilar substrates (substrate promiscuity). *E. coli* b3902 (rhaD).

A) KEGG ID R02263

L-Rhamnulose 1-phosphate <=> Glycerone phosphate + (S)-Lactaldehyde

B) KEGG ID R01785

L-Xylulose 1-phosphate <=> Glycerone phosphate + Glycolaldehyde

EC numbers = 1; Reactions = 2; ${}^{1}\sigma(R_A) \neq {}^{1}\sigma(R_B)$; ${}^{0\text{-}3}\sigma(R_A) \neq {}^{0\text{-}3}\sigma(R_B)$.

In this case, both reactions have different signatures and process different substrates.