

Carbohydrates

Metabolism: Citric Acid Cycle

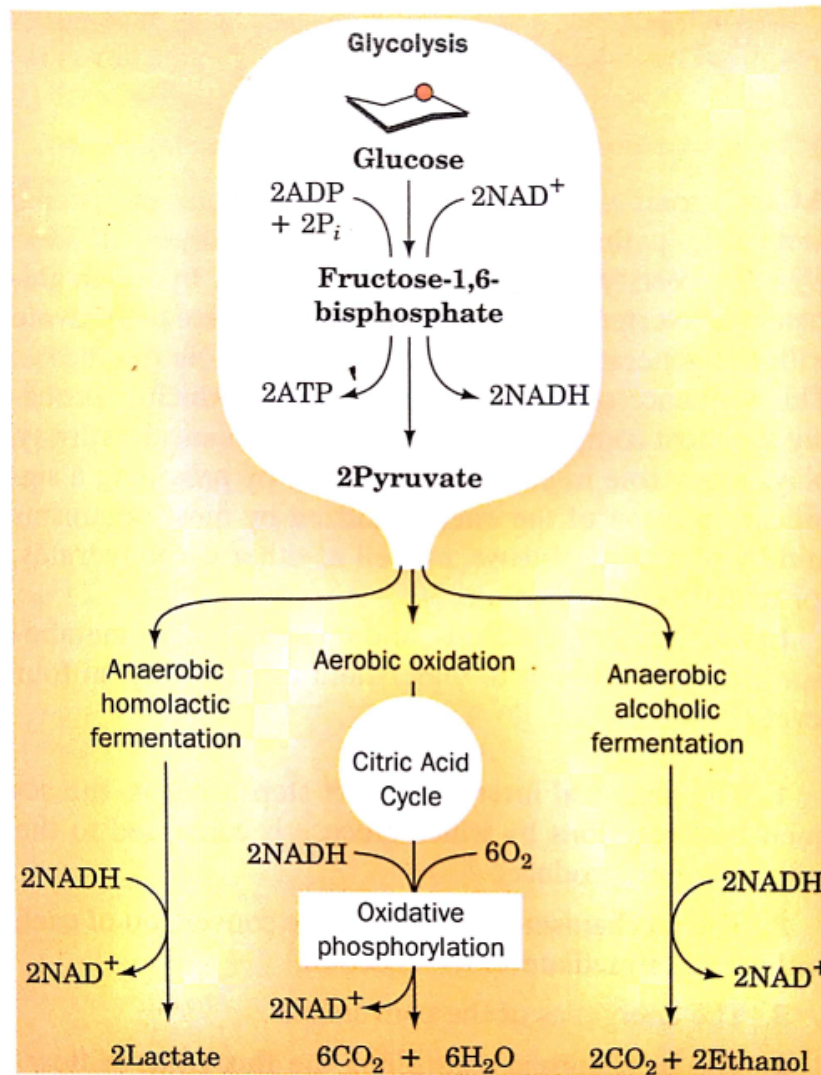


FIGURE 17-1 Glycolysis. Glycolysis converts glucose to pyruvate while generating two ATPs. Under anaerobic conditions, alcoholic fermentation of pyruvate occurs in yeast, whereas homolactic fermentation occurs in muscle. Under aerobic conditions, pyruvate is oxidized to H₂O and CO₂ via the citric acid cycle (Chapter 21) and oxidative phosphorylation (Chapter 22).

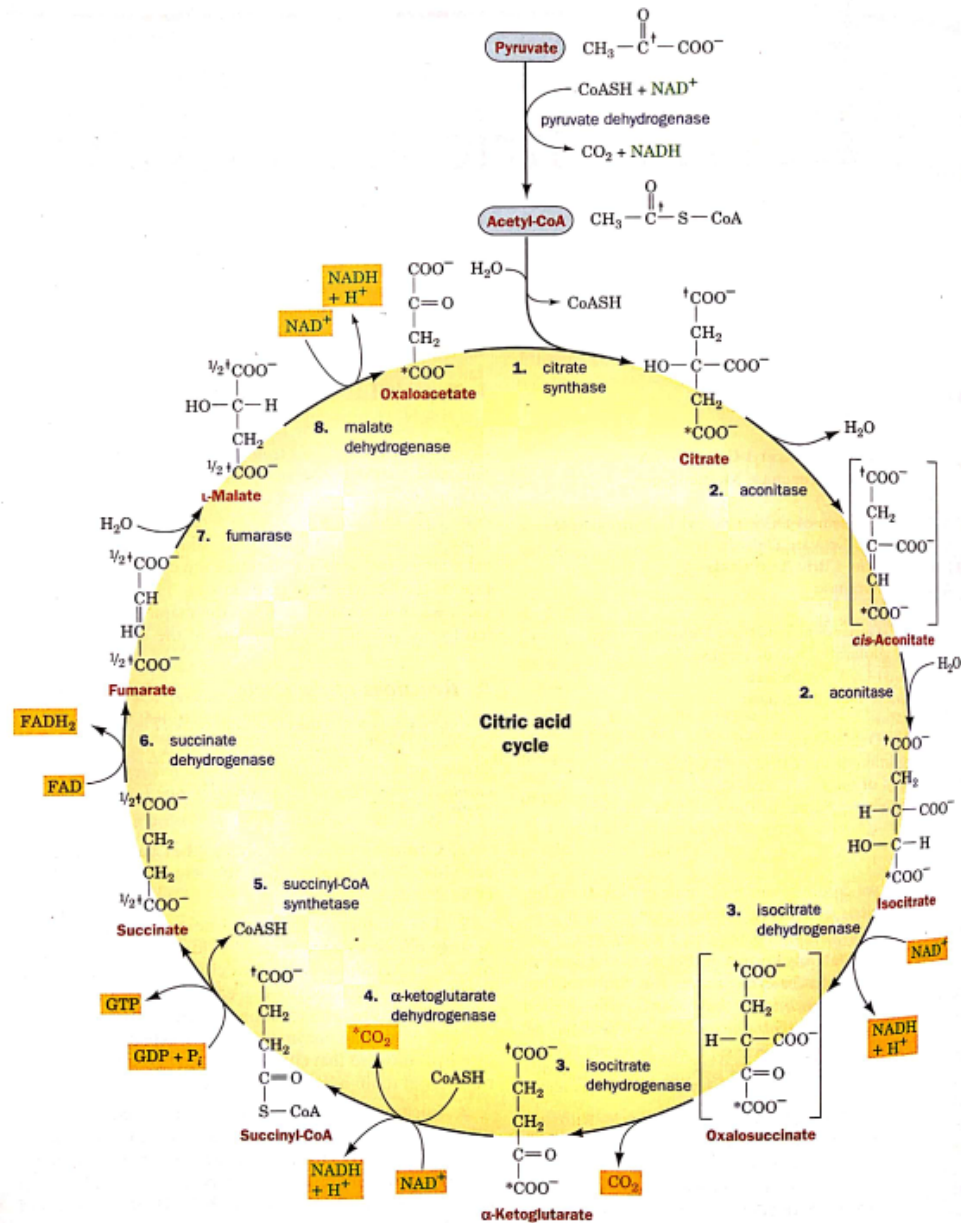


FIGURE 21-1 Reactions of the citric acid cycle. The reactants and products of this catalytic cycle are boxed. The pyruvate \rightarrow acetyl-CoA reaction (top) supplies the cycle's substrate via carbohydrate metabolism but is not considered to be part of the cycle. The bracketed compounds are enzyme-bound

intermediates. An isotopic label at C4 of oxaloacetate (*) becomes C1 of α -ketoglutarate and is released as CO_2 in Reaction 4. An isotopic label at C1 of acetyl-CoA (†) becomes C5 of α -ketoglutarate and is scrambled in Reaction 5 between C1 and C4 of succinate (1/2‡). See the Animated Figures

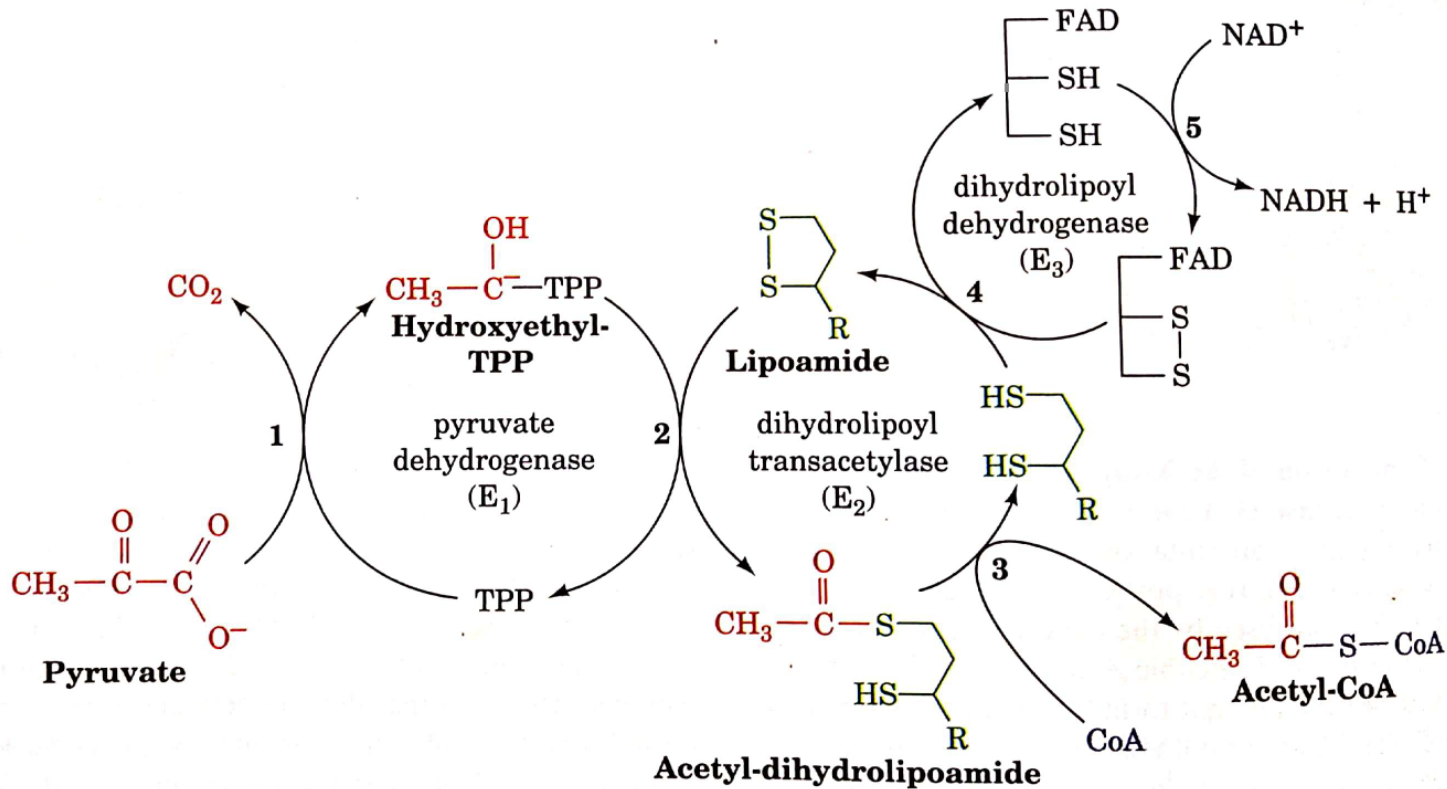
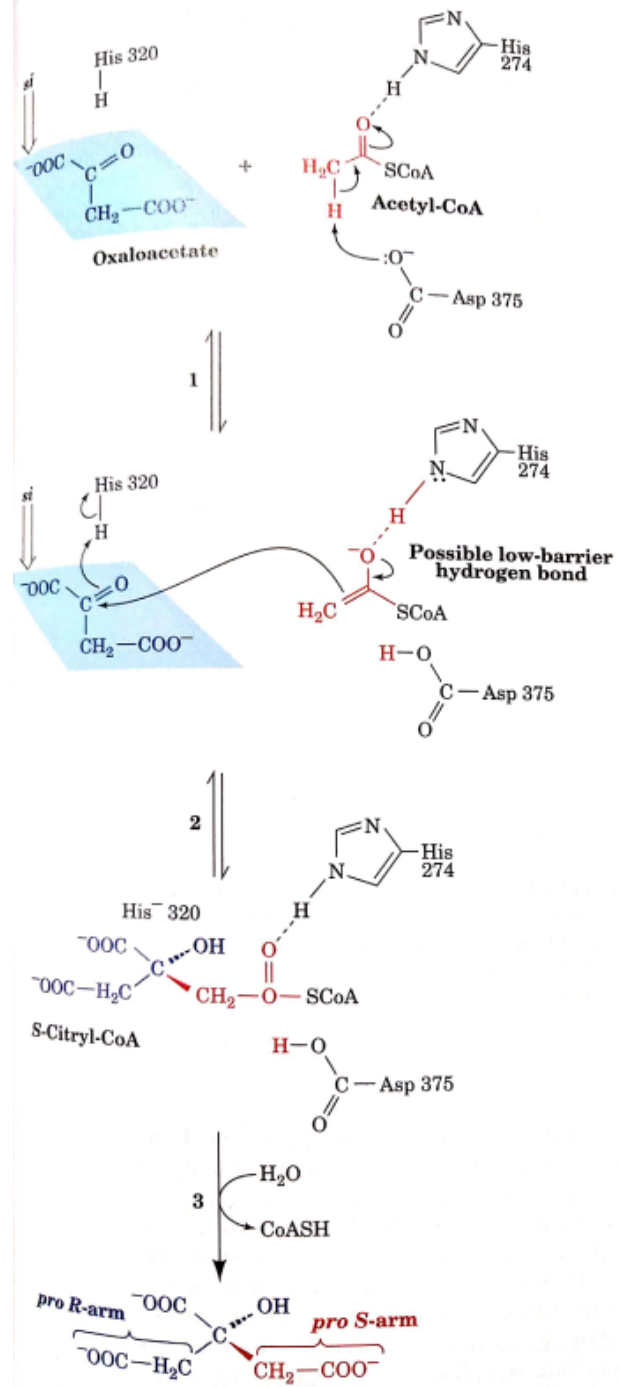


FIGURE 21-6 The five reactions of the PDC. E₁ (pyruvate dehydrogenase) contains TPP and catalyzes Reactions 1 and 2. E₂ (dihydrolipoyl transacetylase) contains lipoamide and

catalyzes Reaction 3. E₃ (dihydrolipoyl dehydrogenase) contains FAD and a redox-active disulfide and catalyzes Reactions 4 and 5.



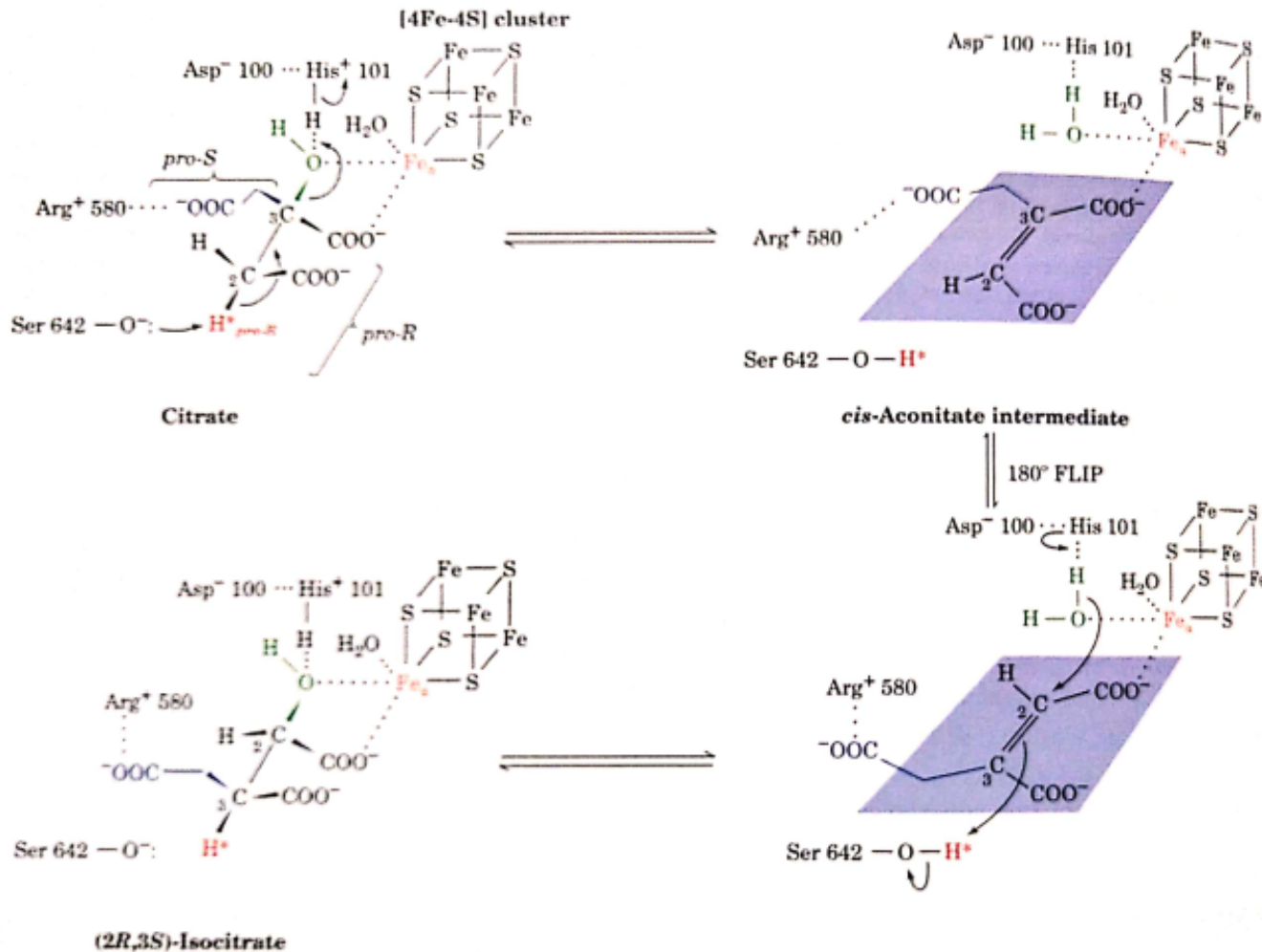


FIGURE 21-20 Mechanism and stereochemistry of the aconitase reaction. Fe₂ of the enzyme's [4Fe-4S] cluster coordinates the citrate hydroxyl and central carboxyl groups; Arg 580 forms a salt bridge with the *pro-S* carboxyl group; Ser 642, in its alkoxide form, acts as a general base; and the Asp 100-polarized His 101 acts as a general acid in the elimination

of water to form *cis*-aconitate. Note the unusual 180° FLIP that *cis*-aconitate apparently undergoes, possibly while remaining bound to the active site; thus rehydration takes place on the opposite face of the substrate from which dehydration occurred, thereby yielding (2*R*,3*S*)-isocitrate.

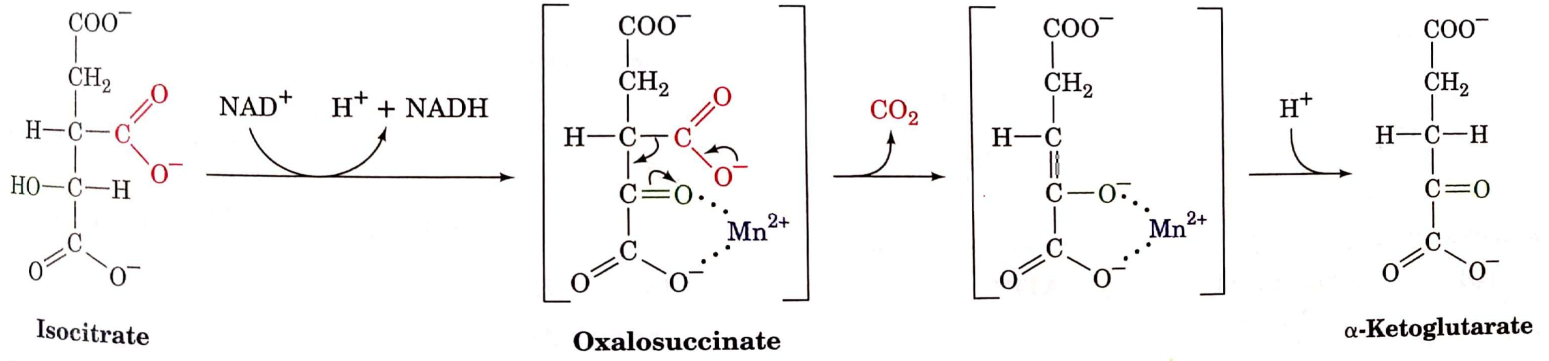


FIGURE 21-21 Probable reaction mechanism of isocitrate dehydrogenase. Oxalosuccinate is shown in brackets because it does not dissociate from the enzyme.

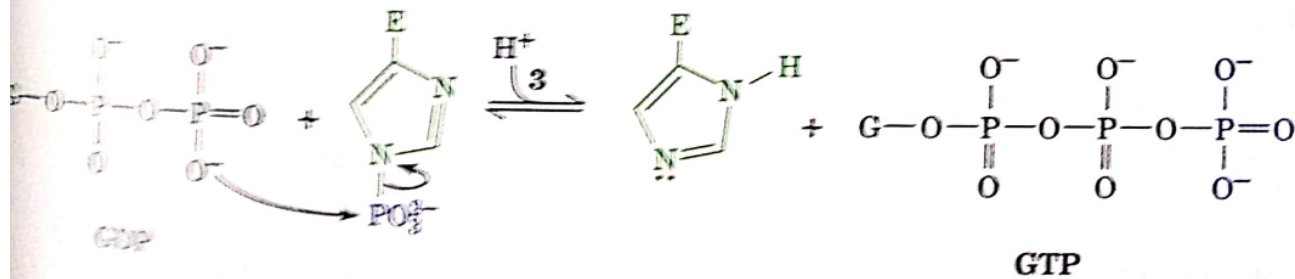
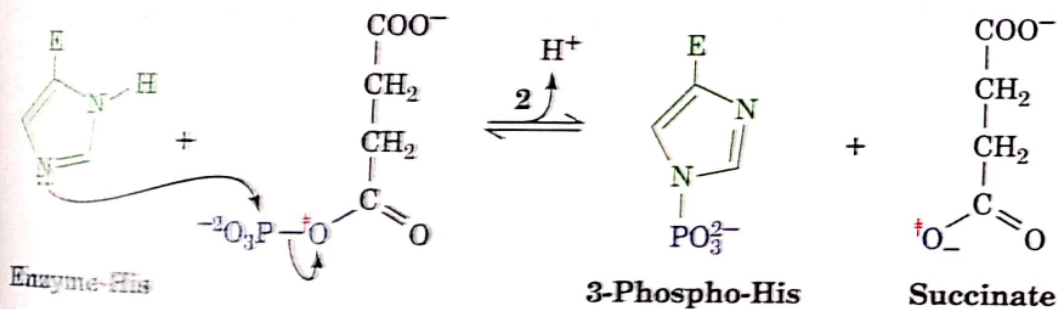
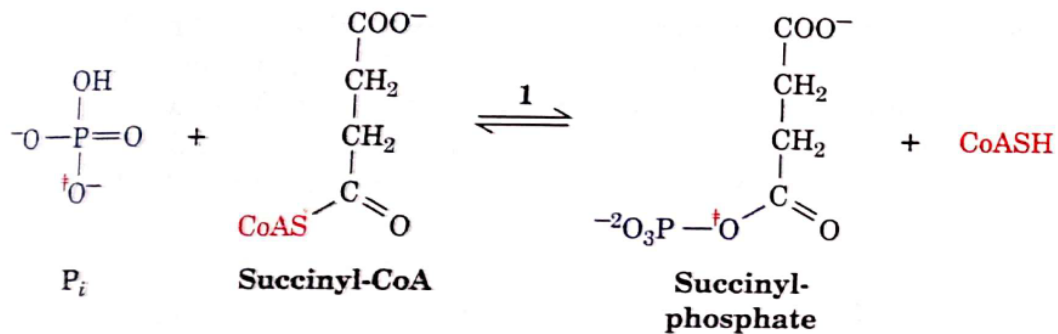
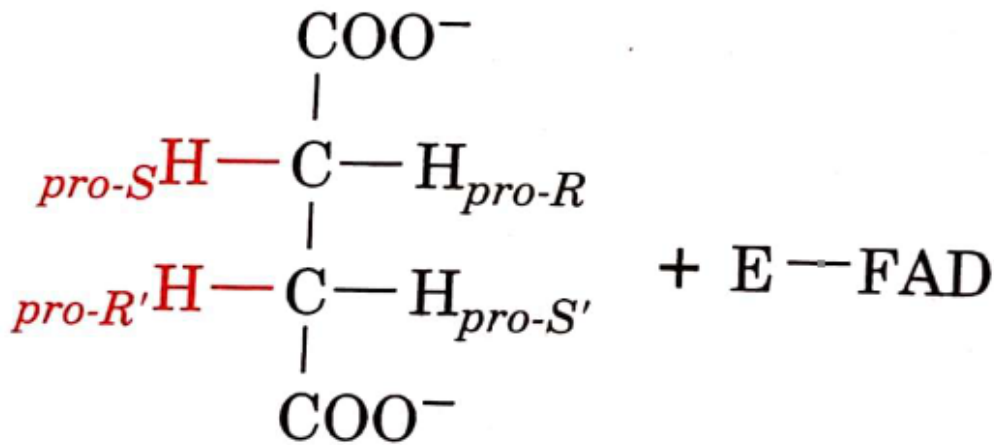
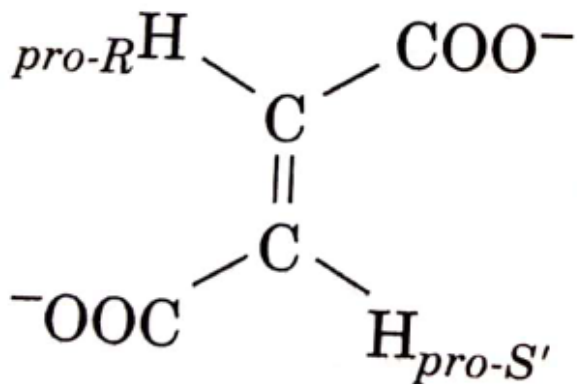


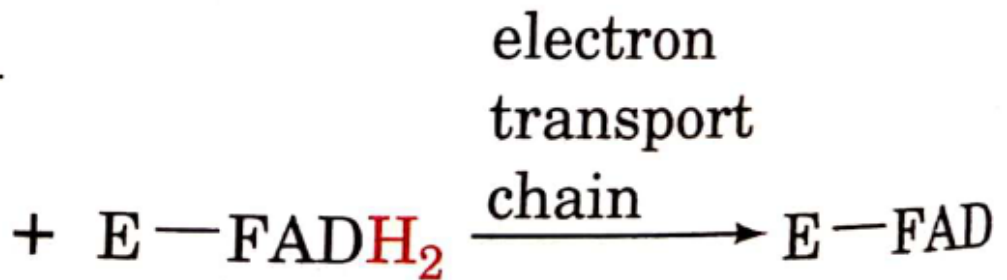
FIGURE 21-22 Reactions catalyzed by succinyl-CoA synthetase. (1) Formation of succinyl phosphate, a “high-energy” mixed anhydride. (2) Formation of phosphoryl-His, a “high-energy” intermediate. (3) Transfer of the phosphoryl group to GDP, forming GTP. The symbol † represents ¹⁸O in isotopic labeling reactions.



Succinate



Fumarate



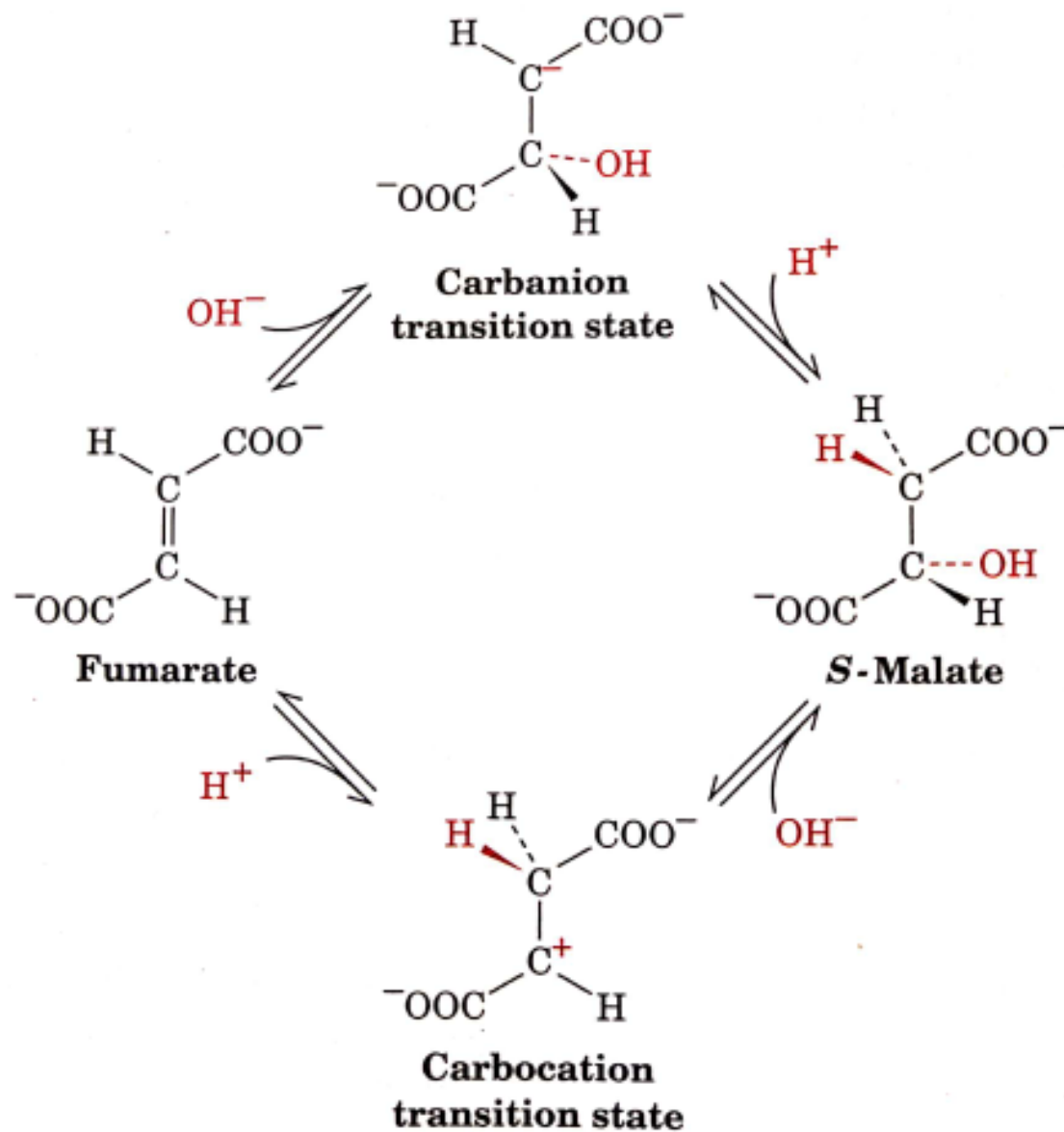
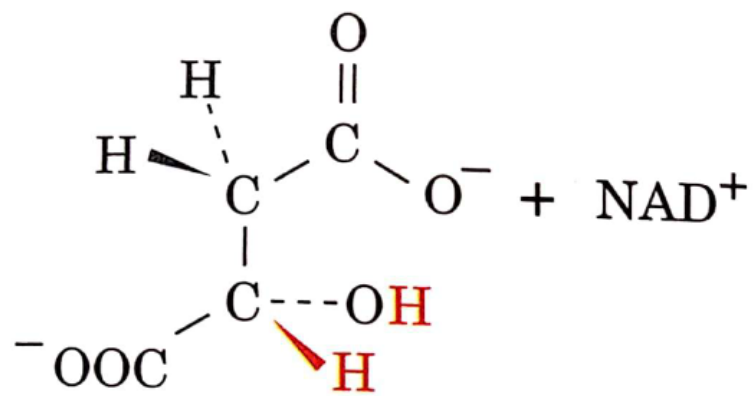
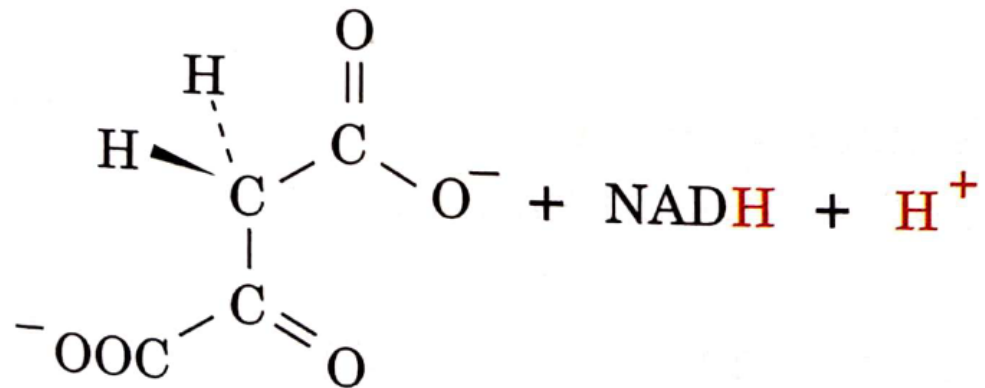


FIGURE 21-24 Possible mechanisms for the hydration of fumarate as catalyzed by fumarase.



S-Malate



Oxaloacetate

