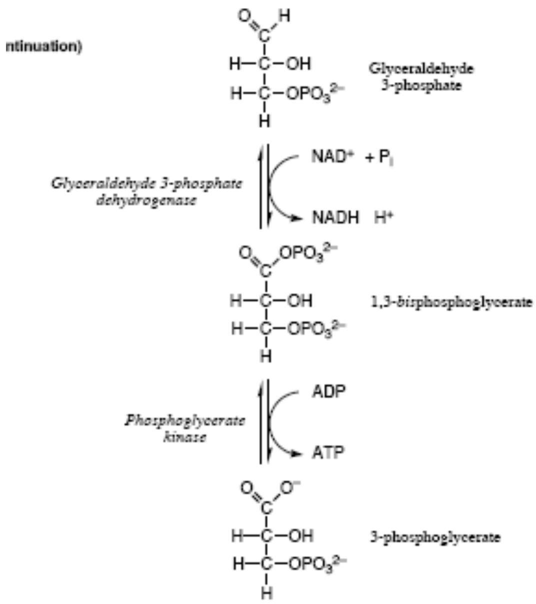
## Glycolysis Stage 2

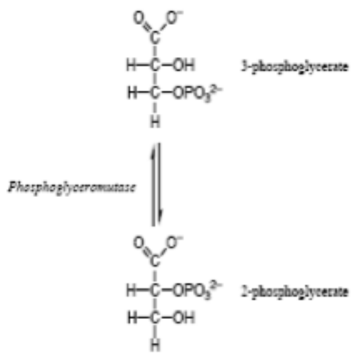
The first two steps of stage 2 generate ATP.




- The 1st reaction, catalysed by glyceraldehdye 3-phosphate dehydrogenase (GAPDH) makes 1, 3 bis phosphoglycerate (1, 3BPG) which has lot of trapped energy; phosphoglycerate kinase harvests this energy to generate ATP.
- GAPDH uses NAD+ to help add phosphate to the C1 of G3P to generate 1, 3BPG
- 1, 3BPG contains an acyl phosphate and has an even higher phosphate transfer potential than ATP itself
- Phosphoglycerate kinase uses this power to transfer the phosphate to ADP and so create ATP.
- Since 2 G3P molecules enter stage 2 for every glucose starting stage 1, the 2 ATPs per glucose generated have paid the cost of stage 1.
- BUT, NAD+ was used and NAD+ is essential for glycolysis to continue so it must be replenished.



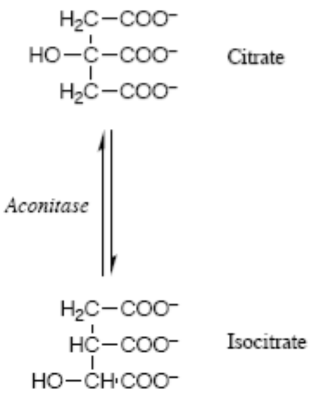
The first two reactions in stage 2 used a theme of making a compound that is slightly unstable, but has high potential energy, in the first step and letting the second step collect that energy. But the phosphates need to be in the correct place.




- The last step created 3-phosphoglycerate; 2-phosphoglycerate would've been better.
- Phosphoglyceromutase catalyses an intramolecular re-arrangement that moves the phosphate from C3 to C2 and so sets the scene for taking more energy from the trioses.
- Dehydration - removal of water - from 2-phosphoglycerate makes it possible to squeeze a little more energy out of the pathway.

Aconitase

- Moves a hydroxyl group from the 2-position to the ideal 3-position.
- Catalyses a two-step isomerisation reaction.
- It dehydrates citrate to yield cis-aconitate (hence the name of the enzyme).
- Cis aconitate is then re-hydrated to yield isocitrate.
- An –OH and an –H have been interchanged.
- All the functional groups are now in the correct place for the subsequent enzymes to work optimally. Note, too, that isocitrate is not a symmetrical molecule.

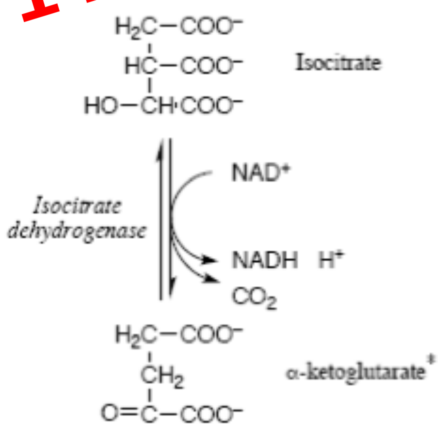



**Phase 2: Collecting Energy**

The citric acid cycle collects energy form electrons with high transfer potential using oxidation-reduction reactions. The first of these is catalysed by isocitrate dehydrogenase.

Isocitrate dehydrogenase

- Catalyses a two-step process.
- Creates an unstable intermediate...
- … And generates NADH + H+: the first high transfer potential electron carrier.
- The unstable 'oxalosuccinate' degrades.
- α-ketoglutarate is produced and CO2 is released (* α-ketoglutarate is also known as 2-oxoglutarate).
- This is a key regulatory step in the TCA cycle. The enzyme is exquisitely sensitive to the 'energy charge' of the cell. It is inhibited by NADH and by ATP and activated by ADP.




The next step follows a similar design, forming an unstable intermediate with a high energy thioester bond whose cleavage drives the reaction forward.