In recent years, much interest has been shown in the use of multi-enzyme cascades as a tool in organic synthesis. Such enzymatic cascades can provide added value to a synthetic scheme by starting from cheaper raw materials or making more valuable products. Additionally, they can be used to help shift the equilibrium of otherwise thermodynamically unfavourable reactions to give a higher conversion of the target product. By coupling an energetically unfavourable reaction with a more favourable one, the multi-enzyme cascade mimics the approach taken in nature in metabolic pathways. Nevertheless, it can be challenging to combine several engineered enzymes in vitro for the conversion of non-natural substrates. In this mini-review we focus on enzyme coupling reactions as a tool to alleviate thermodynamic constraints in synthetically useful biocatalytic reactions. The implications of thermodynamic parameters such as the equilibrium constant on the multienzyme cascades and the conventional methods of equilibrium shifting are also discussed in addition to methods used to estimate such values.