"Systems Biocatalysis" is a term describing multi-enzyme processes in vitro for the synthesis of chemical products. Unlike in-vivo systems, such an artificial metabolism can be controlled in a highly efficient way in order to achieve a sufficiently favourable conversion for a given target product on the basis of kinetics. However, many of the most interesting non-natural chemical reactions which could potentially be catalysed by enzymes, are thermodynamically unfavourable and are thus limited by the equilibrium position of the reaction. A good example is the enzyme ω-transaminase, which catalyses the transamination of a pro-chiral ketone into a chiral amine (interesting in many pharmaceutical applications). Here, the products are often less energetically stable than the reactants, meaning that the reaction may be thermodynamically unfavourable. As in nature, such thermodynamically-challenged reactions can be altered by coupling with other reactions. For instance, in the case of ω-transaminase, such a coupling could be with alanine dehydrogenase. Herein, the aim of this work is to identify thermodynamic bottlenecks within a multi-enzyme process, using group contribution method to calculate the Gibbs free energy change, View the MathML source ΔG^0, of the overall cascade. The findings show that unfavourable reactions in the cascade can be improved by coupling to a favourable reaction giving more energetically stable products.