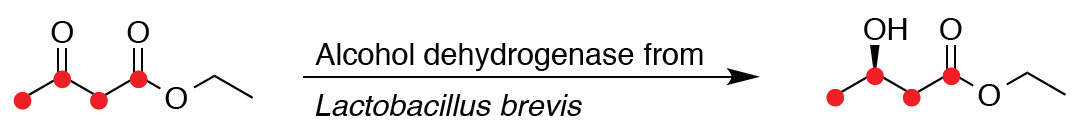
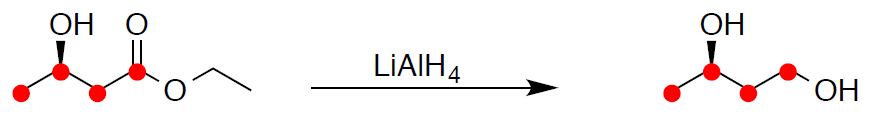
**SDC 1. Description of stable isotope preparation and synthesis.**

The two tetra-13C-labelled KME used was synthesised from a total of 47 g of ethyl acetoacetate-1,2,3,4-13C4 purchased form Cambridge Isotope Laboratories, USA.

*Synthesis of ethyl (R)-3-hydroxybutyrate-1,2,3,4-13C4:* The synthesis of the first component of the 13C-labelled KME, ethyl (*R*)-3-hydroxybutyrate-1,2,3,4-13C4, was carried out using the asymmetric reduction catalysed by alcohol dehydrogenase derived from lactobacillus (ADH-LB), from the starting reagent ethyl acetoacetate-1,2,3,4-13C4 (reaction 1).

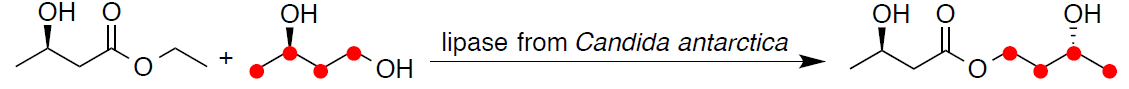
*Reaction 1*

*Synthesis of (R)-butane-1,3-diol-1,2,3,4-13C4:* Half of the product prepared by the ADH-LB reduction (ethyl ester reaction 1 above) was used to synthesise the second component of the 13C-labelled KME, (*R*)-butane-1,3-diol-1,2,3,4-13C4. This reduction was carried out using LiAlH4 as a suspension in anhydrous THF (reaction 2).

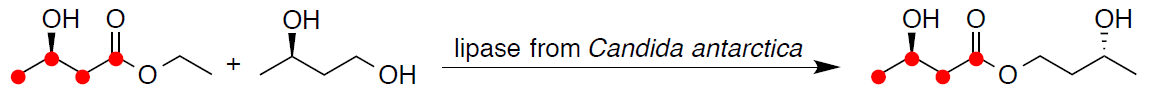
*Reaction 2*

Finally, both *(R)-butane-1,3-diol-1,2,3,4-13C4, and ethyl (R)-3-hydroxybutyrate-1,2,3,4-13C4* from reactions 1 and 2were transferred to Sterling Pharmaceutical solutions Ltd (Northumberland, UK) for final KE transesterification under GMP grade conditions.

Breifly, KME was prepared from 13C-labelled (*R*)-butane-1,3-diol using an excess of unlabelled ethyl (*R*)-3-hydroxybutyrate (reaction 3). The reaction was carried out at 20–25 °C under reduced pressure (approx. 2 mbar) for 5 h in order to distil off the ethanol and drive the reaction forward. The product was subsequently purified by short-path distillation in two batches using Kugelrohr apparatus.

Reaction 3

KME was prepared from 13C-labelled ethyl (*R*)-3-hydroxybutyrate using an excess of unlabelled (*R*)-butane-1,3-diol (reaction 4). The reaction was carried out at 20–25 °C for 4 h at ~5 mbar and then for 3.5 h at ~2 mbar. Again, the product was purified by short-path distillation using Kugelrohr apparatus.

Reaction 4

Equal aliquots of the final products of both reactions 3 and 4 (>98% purity) were incorporated with the native (unlabelled) KME during drink preparation to achieve a final drink 13C enrichment of approximately 25%.