



A REVIEW ON THE SYNTHESIS AND COMPUTATIONAL STUDIES OF KETOSIS

Alison Michael Ebiekpi^{1*}, Mohammed Isiaka¹ and Ibrahim Adebayo Oladosu¹

Department of Chemistry, University of Ibadan

*Corresponding author: alisonebiekpi@gmail.com

Abstract

Ketosis is a metabolic condition characterised by the oxidation of fatty acids to generate ketone bodies. The ketone bodies are primarily acetoacetate, β -hydroxybutyrate and acetone which function as alternative energy sources in the absence of carbohydrates. In addition to their physiological functions, ketone bodies contain reactive carbonyl and β -hydroxy functional groups that facilitate significant transformations in organic synthesis. Recent developments in synthetic chemistry have facilitated the synthesis of modified ketone derivatives to investigate stability, acidity and biological activity providing pathways to new therapeutic agents. Complementary computational methods, such as density functional theory, quantum simulations and molecular docking offer mechanistic insights into ketogenesis. Ketolysis involves proton exchange dynamics and the interactions of ketone bodies with proteins associated with obesity.

This dual perspective combines experimental and in silico methodologies, highlighting opportunities for the targeted design of synthetic ketogenic compounds to address dietary compliance challenges and enhance metabolic outcomes. This review integrates historical, biochemical, synthetic and computational insights on ketosis, emphasising its chemical basis and potential applications in managing metabolic, neurological and degenerative diseases.

Keywords: Ketosis, ketone bodies, chemical synthesis, computational chemistry, metabolic disorders.

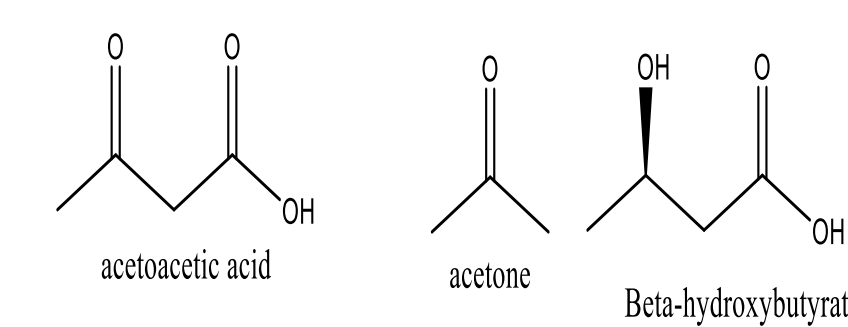


Fig. 1: Ketone Bodies

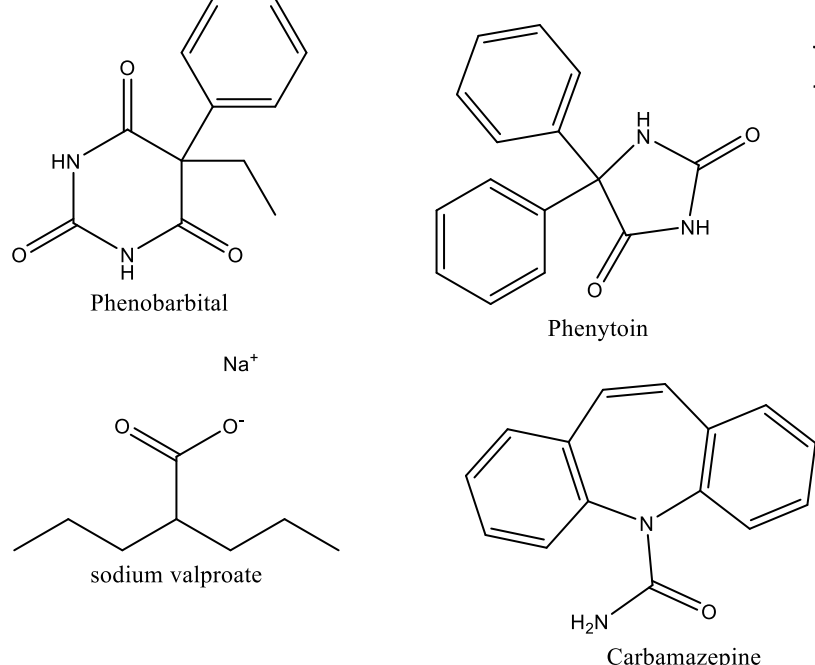


Fig. 2: Some Anticonvulsant Medication

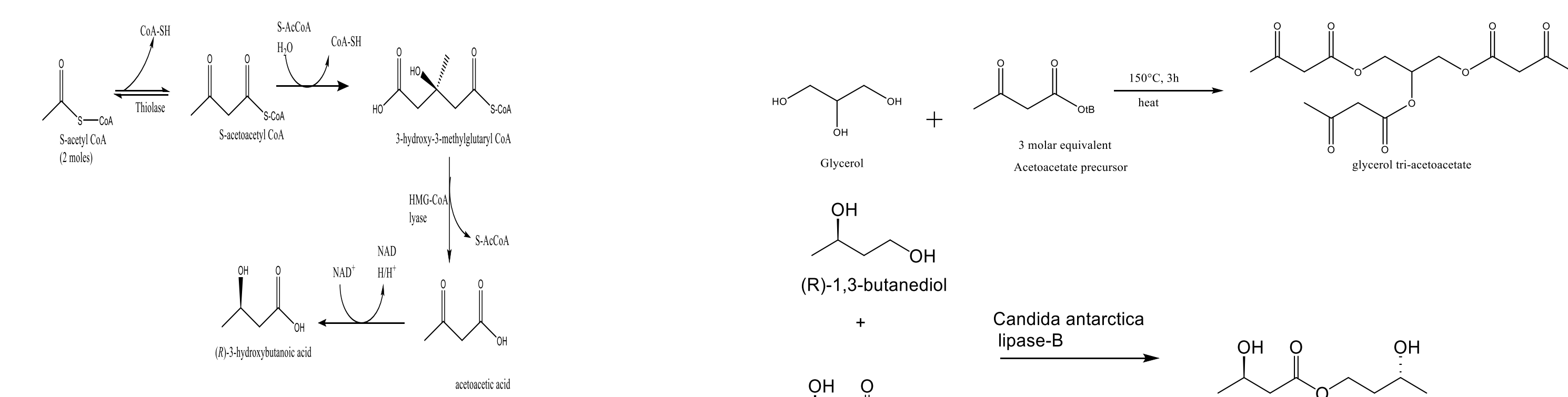


Fig 3: Ketogenesis Of Ketone Bodies From S-acetyl CoA

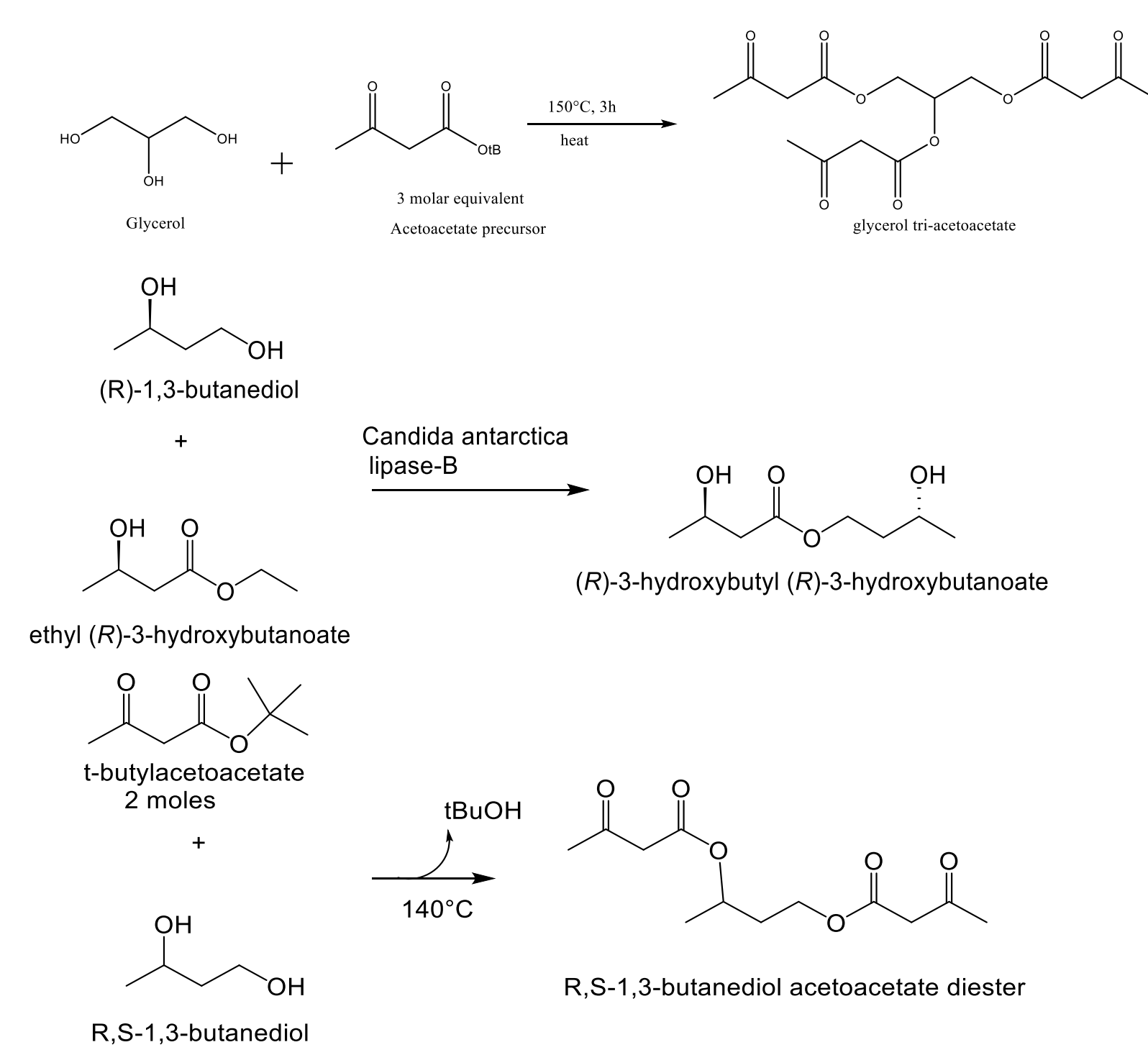


Fig. 4: Synthesis Of Some Ketogenic Compounds

COMPUTATIONAL STUDIES ON KETOSIS

- Computational studies reveals that proton release during ketosis is as a result of covalent modifications and not acid dissociation/association
- The studies indicate that ketone bodies, especially beta-hydroxybutyrate (BHB) can effectively bind to essential metabolic proteins with certain interactions comparable to or exceeding those of conventional anti-obesity medications such as orlistat and cetilistat.

Conclusion

- Synthetic ketogenic compounds, including glycerol tri-acetoacetate, *R,S*-1,3-butanediol acetoacetate diester and (*R*)-3-hydroxybutyl (*R*)-3-hydroxybutanoate, illustrate the potential to induce ketosis without dietary restrictions
- Computational analyses challenge the conventional perspective of ketone bodies as potent metabolic acids, instead uncovering complex proton-exchange dynamics influenced by covalent modifications.
- Docking studies indicate that β -hydroxybutyrate and related compounds interact with metabolic proteins at affinities similar to those of approved anti-obesity drugs.

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