QM/MM STUDY OF THE INACTIVATION OF B$_{12}$-DEPENDENT DEHYDRATASES BY SUBSTRATE GLYCEROL

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Some bacteria are able to grow in anaerobic conditions, using alcohols as source of carbon. First step of fermentation is dehydration of alcohol:

\[
\text{R-CH}_2\text{OH} \rightarrow \text{R-CHO} + \text{H}_2\text{O} \quad (R = -\text{H, CH}_3, -\text{CH}_2\text{OH})
\]

This reaction is catalysed by two enzymes, glycerol dehydratase (GDH) and diol dehydratase (DDH).\(^1\)

Both of these enzymes use coenzyme B$_{12}$ as an essential cofactor.\(^1\) As with most B$_{12}$-dependent reactions, the mechanism of action of these two enzymes involves the formation of radical intermediates. It is known that both enzymes undergo mechanism based inactivation by their substrate glycerol, the rate of which being higher for DDH than for the GDH.\(^2\)

The results of computational study of glycerol dehydration catalysed by GDH and DDH are reported. We present and discuss energy profiles of mechanism of action and inactivation, and explain the mechanism of this unusual suicidal inactivation.

\(^2\)W. W. Bachovchin, R. G. Eagar, Jr., K. W. Moore, J. H. Richards, Biochemistry, 16, 1082 (1977)