What we are reminded of here is important: “the mechanism of action begins… [with]… hydroxide deprotonating one of the SH bonds” — SH bonds have a pKa of ~10, while OH bond are ~16. If the Cys$^{300}$ is replaced by a Ser$^{300}$, then there is presumably an OH in the hydrogen bonded network that is not as readily deprotonated as the SH was. If that does not occur, then the mechanism is not operating. There are other options: perhaps it is deprotonated but it is so much more basic that it deprotonates another critical group, such as the His$^{132}$. The one experiment is important for identifying a key residue, but working of the details of the exact mechanistic effect takes doing a lot more science!

The $^{1}$° C-I is an excellent electrophile for $S_N$2 reactions, and an uncharged or anionic sulfur atom is an excellent nucleophile for $S_N$2. The reagent will irreversibly alkylate the S and render the active site inactive.
The Glu to Asp mutation shortens the chain length by 1 CH$_2$ unit; the carboxylate can no longer reach the substrate and so the reaction fails.
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Chapter 18
18.03

Diagram showing a sequence of chemical reactions involving Ser$^{540}$, Tyr$^{552}$, His$^{324}$, and SCoA.