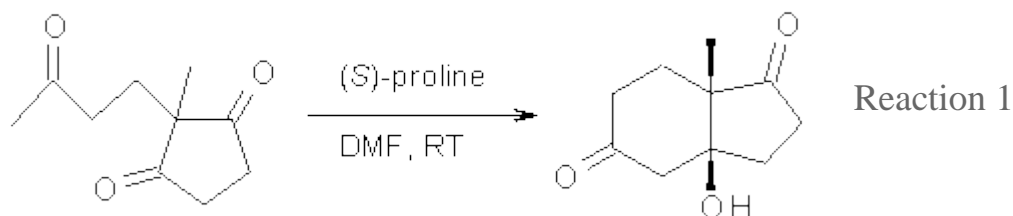


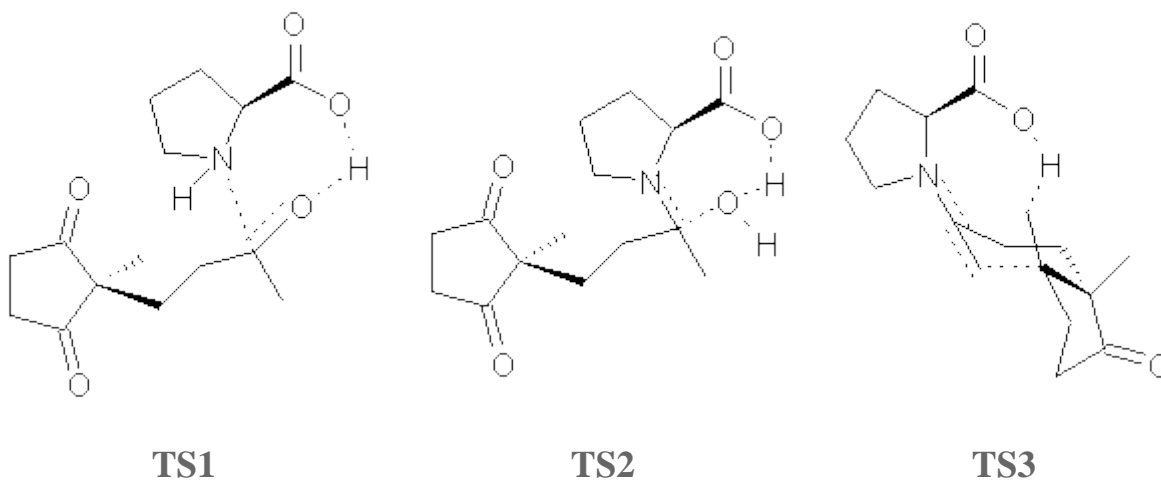
RATE DETERMINING STEP IN THE HAJOS-PARRISH-EDER-SAUER-WIECHERT REACTION

What is the rate determining step in the Hajos-Parrish-Eder-Sauer-Wiechert reaction (reaction 1)? This basic question of the mechanism for the first example of the use of proline as a catalyst remains unanswered, though a recent paper by Meyer and Houk¹ does moves us forward.



Their ¹³C kinetic isotope effect study revealed that only the nucleophilic ketone (the carbonyl of the butyl chain) experiences any significant effect, with a value of about 1.03. B3LYP/6-31G(d,p) computations of the three transition states shown below were performed for both the gas phase and solution using IEF-PCM. Calculations of the transition state for the formation of the C-C bond (**TS3**) predicts no kinetic isotope effect, indicating that it is not the rate limiting step, in conflict with previous² suggestions.

The transition states for the formation of the carbinolamine (**TS1**) and formation of the iminium (**TS2**) both predict an isotope effect comparable with experiment. **TS1** is about 3 kcal mol⁻¹ higher in energy than **TS2**. The authors conclude that a step prior to formation of the C-C is the rate limiting step of the Hajos-Parrish-Eder-Sauer-Wiechert reaction, but cannot discern between the two possibilities examined.



Source: <http://comporgchem.com/blog/?p=121>