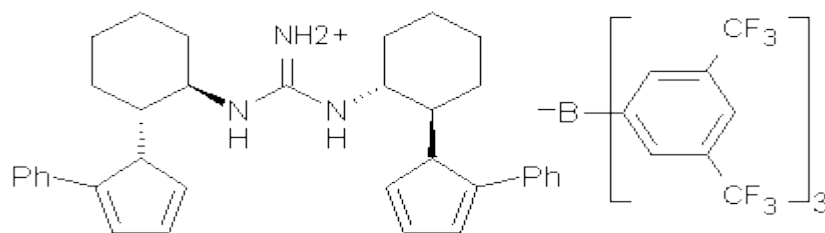
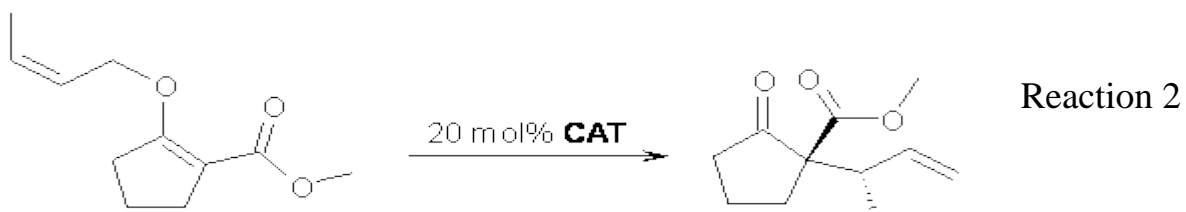
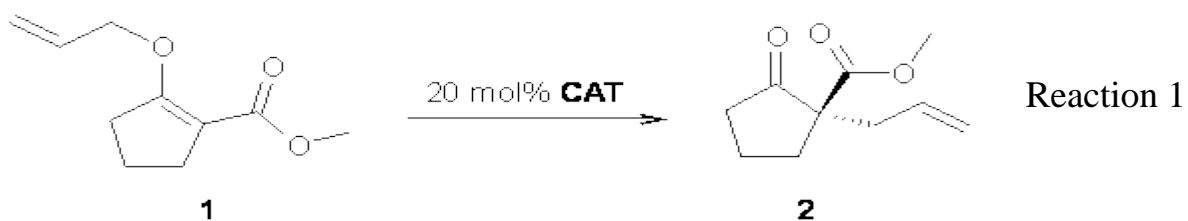


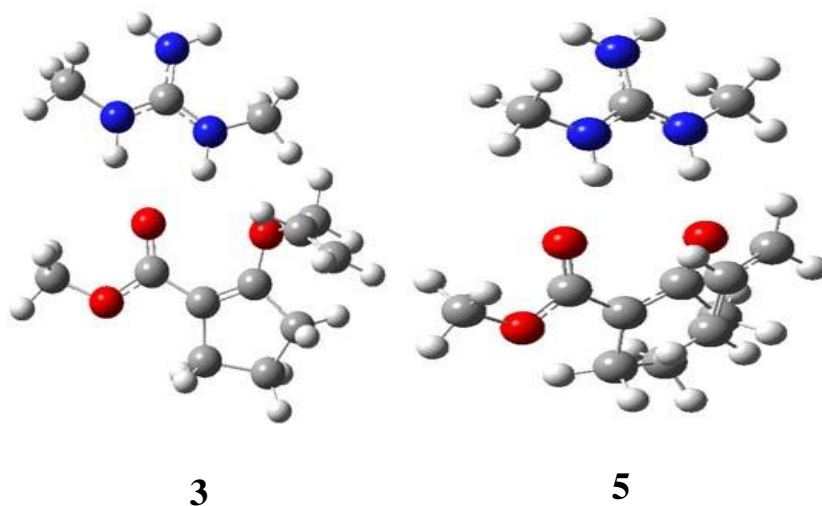
ORGANOCATALYTIC CLAISEN REARRANGEMENTS

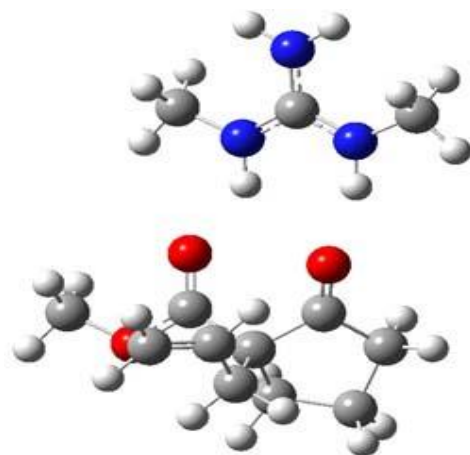
Jacobsen reports another interesting example of organocatalysis, here using a chiral guanadinium salt to catalyze the enantioselective Claisen rearrangement.¹ As an example, Reaction 1 proceeds in 6 days at 30 °C to give 81% yield with an ee of 84%. The system is also diastereoselective, so that Reaction 2, run for 6 days at 40 °C, gives an 82% yield with a diastereomeric ratio of 16:1 and an ee of 81%.



CAT

B3LYP/6-31G(d,p) computations provide some insight. The uncatalyzed reaction of **1** to give **2** is predicted to be exothermic by 16.1 kcal mol⁻¹, with an activation energy of 25.9 kcal mol⁻¹. Using *N,N'*-dimethylguanidinium as a model for the catalyst (and with no counter anion and no treatment of solvent – hexanes in this case), they find a complexation energy of almost 27 kcal mol⁻¹ for forming **3**. **3** exhibits (See Figure 1) three hydrogen bond-like interactions – one N-H bifurcates to interact with the carbonyl oxygen and (a very long interaction) to the other oxygen. The product complex **4** also shows three hydrogen bond-like interactions, with an overall exothermicity of -14.7 kcal mol⁻¹. The complexed transition state **5** has two normal length hydrogen bonds, with an activation energy above **3** of 20.6 kcal mol⁻¹. Thus the complex lowers the barrier by about 5 kcal mol⁻¹, indicating the catalytic effect. They have not however addressed the enantioselectivity.





4

Figure 1. B3LYP/6-31G(d,p) optimized geometries of **3-5**.

Source: <http://comporgchem.com/blog/?p=1341>