The guanidine-thiourea catalyzed nitro-Michael reaction:

An ab initio study

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Brønstedt-basic, Lewis-acidic bifunctional catalysts are gaining importance in organocatalysis. The possibility of tuning the properties of bifunctional catalysts by modifying the spatial orientation of the two active functional groups is highly attractive for organic chemists. A large number of successive approaches have been reported up to date [1].

Recently, our group and that of Jacobsen reported the first successful application of primary amine-thiourea organocatalysts with the synchronous dual activation of a nucleophile and an electrophile in nitro-Michael addition reactions [2]. Based on this catalyst, a new type of chiral guanidine-thiourea catalyst has been developed in our laboratory. In comparison to literature known thiourea-amine catalysts, the catalyst shows superior activity, but only low enantioselectivity. An extensive DFT study was carried out to rationalize the experimental findings. The study is based on a Model by Hamza et al. [3] for amine thiourea catalysts which had to be extended due to the higher complexity and flexibility of our system. With the computational data we are able to describe the effect of the unique H-bond patterns formed by these types of catalysts and employ them to reproduce the experimental findings. Based on the computational data, we propose an improved catalyst that will be investigated in our laboratories.