Enantioselective Hydrogenation with Chiral Frustrated Lewis Pairs

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The development of transition metal catalyzed asymmetric hydrogenation could be stated as the cradle of modern enantioselective catalysis. Since the early asymmetric hydrogenation example from Knowles and Sabacky in 1968, the method has been rapidly advanced over the years into an important tool in academia and chemical industry. In general, for these transformations the development of effective transition-metal complexes having chiral ligands was a basic prerequisite. However, since the pioneering work of Stephan and co-workers in 2006,[1] the field of homogenous hydrogenation was extended to the possibility of metal-free hydrogenation based on the utilization of frustrated Lewis pairs (FLPs) for hydrogen activation. Combinations of the strong Lewis acid tris(perfluorophenyl)borane (B(C₆F₅)₃) with a variety of sterically encumbered Lewis bases were able to activate hydrogen at ambient conditions (Scheme 1).[2]

Scheme 1: Hydrogen activation with Frustrated Lewis Pairs (FLPs).

Furthermore, these chemical peculiarities rapidly found application in catalytic hydrogenation reactions. Some of the FLPS were found to serve as catalysts for the hydrogenation of imines, nitriles, and functionalized alkenes.[3-5] In the absence of bulky Lewis bases also imine substrates could adopt the function of the FLP-partner and B(C₆F₅)₃ was discovered to be sufficient as catalyst for their hydrogenation.[6] Additionally, recent mechanistic investigations and preparative experiments corroborated the assumption that for asymmetric transformations, the element of chirality has to be favorably incorporated into the Lewis acid structure. In early experiments employing a-pinene-derived chiral borane, asymmetric reduction of imines were achieved, albeit with low enantioselectivity (13% ee).[6]
Based on this concept, the first examples of highly enantioselective imine hydrogenations with chiral FLPs are demonstrated and detailed spectroscopic and computational investigations elucidating the underlying mechanism are presented (Scheme 2).[7]

Scheme 2: Asymmetric imine hydrogenation with chiral Frustrated Lewis Pairs.

References: