**The Universality of Acid Catalysis**

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Acid catalysis only requires the presence of electron density in its substrates and one can therefore argue that it is the most general approach to catalysis there is.

The concept of using chiral, enantiomerically pure Brønsted acids has led to a breakthrough in selective catalysis and suggests vast potential. Early asymmetric Brønsted catalysis, for example with proline or BINOL-derived phosphoric acids, has operated in a bifunctional mode, where a base-co-catalyst accompanies the acid.

By tuning the acidity, chemists know very well how to control the reactivity of their acid catalysts and ever more acidic catalysts are currently being developed. While BINOL-derived phosphates are frequently used, their reactivity and ability to activate less basic substrates is limited. For example, the popular phosphoric acid TRIP has a pKa of 13.6 in acetonitrile. This acidity is certainly sufficient to catalyze various additions to imines and also to certain oxygenous substrates. However, to enable activation of simple aldehydes, for example, requires much stronger acids. Similarly, olefin activation *via* protonation has been beyond reach of this catalyst class.

Another major challenge is to make acid catalysis selective, even with small and unbiased substrates. This requires a good control over the ionic intermediates and transition states.

In 2012, we have introduced a new catalyst design, in which two phosphates are bridged *via* an imido nitrogen group. The resulting imidodiphosphate (IDP) catalysts, because of the now four substituents in the corresponding 3- and 3’-positions, all pointing toward the active site, create significant confinement, while still displaying relatively strong acidity (pKa = 11.3, CH3CN). By carefully choosing appropriate substituents, the confinement can be easily fine-tuned. Furthermore, successive replacement of oxygen atoms with NTf-groups, can massively enhance the acidity. The resulting imino imidodiphosphates (iIDP) and imidodiphosphorimidates (IDPi) display pKa’s of around 9 and 4.5. With fluorinated substituents, the acidity can be further enhanced reaching a level displayed by common “magic acids” such as triflic acid and triflimide (Figure 1).



**Figure 1.** Confined acids cover a broad range of acidity and can be easily fine-tuned.

With these three catalyst classes in hand, and even more acidic catalysts under development, we feel in a good position to tackle important challenges of contemporary selective catalysis, including the activation of unreactive and unbiased, small substrates.