




The Universality of Acid Catalysis

HKU SCIENCE Distinguished Lectures

 November 4, 2024 (Monday)

 **Reception:** 4:15 - 4:45 pm
Lecture: 4:45 - 6:15 pm
 (incl. Q&A)

 Rayson Huang Theatre,
 Main Campus,
 The University of Hong Kong

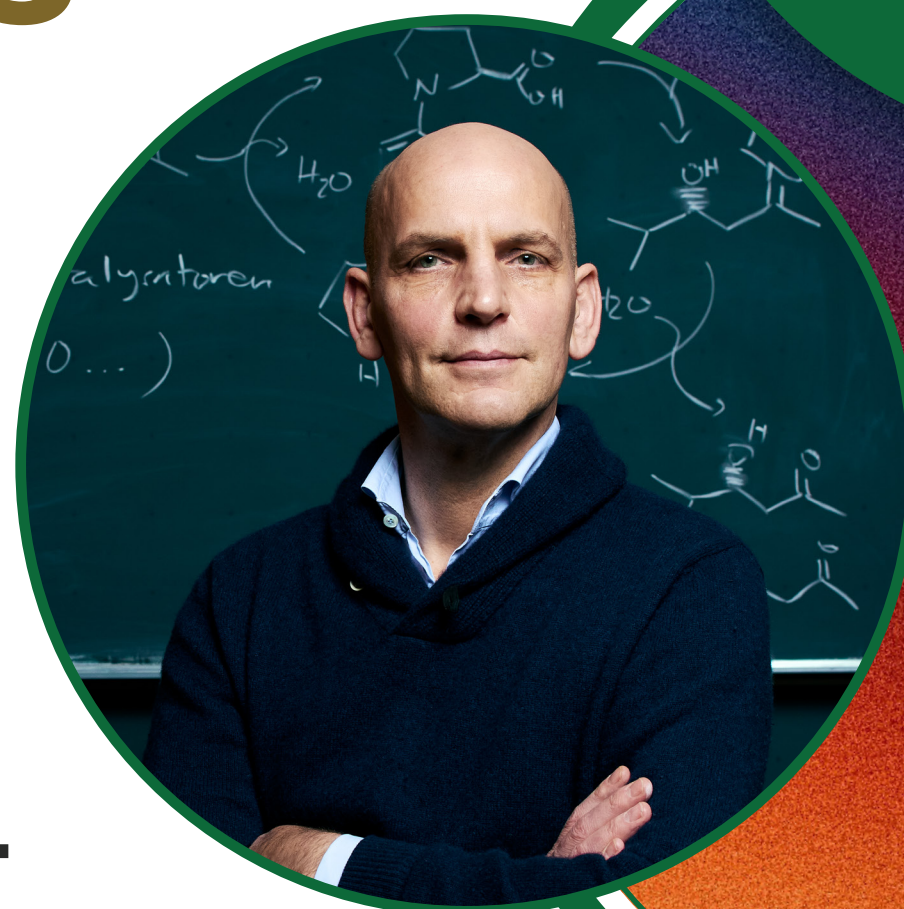
Register at
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For details, please visit:
<https://bit.ly/3XTfgS9>



This is a joint distinguished lecture of the Faculty of Science and the Department of Chemistry.



Professor Benjamin LIST

- Director at Max-Planck-Institut für Kohlenforschung
- 2021 Nobel Prize Laureate in Chemistry

Benjamin List was born in Frankfurt am Main in 1968. He studied chemistry at the Free University of Berlin and received his PhD from the Goethe University in Frankfurt (1997, Prof. G. Mulzer). He worked as a postdoctoral fellow at the Scripps Research Institute in La Jolla/United States from 1997 to 1998 and as an assistant professor from 1999 to 2003. In 2003, he moved to the Max-Planck-Institut für Kohlenforschung in Mülheim/Ruhr as head of a research group and became one of the directors there in 2005. He still holds this position today. He also heads a research group at Hokkaido University in Japan and is an honorary professor at the University of Cologne. List has been awarded dozens of prestigious prizes in the field of chemistry. In 2021, he received the Nobel Prize for his work on asymmetric organocatalysis. Benjamin List lives in Mülheim Ruhr, he is married and father of two grown-up sons.

Abstract

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).

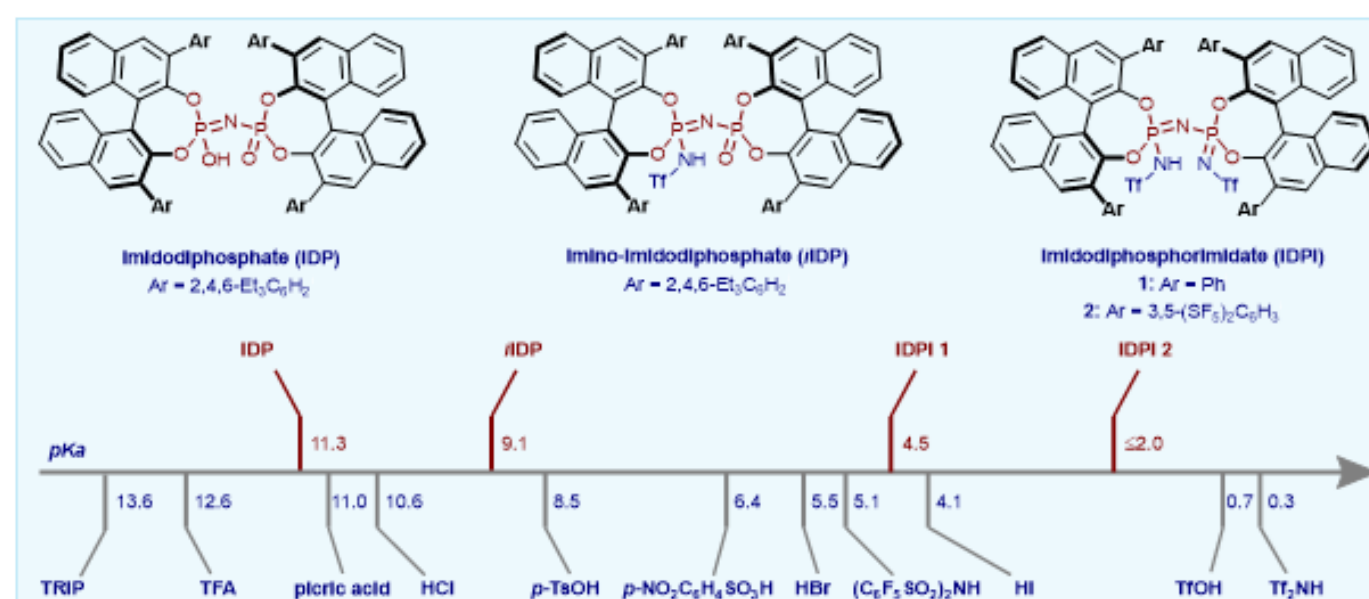


Figure 1. Confined acids cover a broad range of acidity and can be easily fine-tuned.

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.