Synlett C.-H. Tan, B. List Cluster

Cluster Preface: Asymmetric Brønsted Base Catalysis

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Choon-Hong Tan is a professor at the Division of Chemistry and Biological Chemistry, Nanyang Technological University, Singapore. He received his BSc (Hons) First Class from the National University of Singapore (NUS) and his Phd from the University of Cambridge. He underwent postdoctoral training at the Department of Chemistry and Chemical Biology, Harvard University and the Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School. He began his independent career at the Department of Chemistry, National University of Singapore in 2003. Choon Hong has focused on the development of organocatalytic Brønsted base reactions that can be catalyzed with chiral guanidines. He has also demonstrated that pentanidiums (conjugated guanidiniums) are efficient phase-transfer catalysts. Recently, he described the use of chiral organic cations such as bisguanidiniums to modulate and activate anionic metallic salts.
Benjamin List has been a director at the Max-Planck-Institut für Kohlenforschung since 2005. He obtained his Ph.D. in 1997 (Frankfurt). From 1997 until 1998 he conducted postdoctoral research at The Scripps Research Institute in La Jolla (USA) and became an assistant professor there in January 1999. In 2003 he joined the Max-Planck-Institut für Kohlenforschung. He has been an honorary professor at the University of Cologne since 2004. Ben List's research focuses on organic synthesis and catalysis. He has contributed fundamental concepts to chemical synthesis including aminocatalysis, enamine catalysis, and asymmetric-counteranion-directed catalysis (ACDC). His latest work deals with chiral counteranions in asymmetric catalysis. This remarkably general strategy for asymmetric synthesis has recently found widespread use in organocatalysis, transition-metal catalysis, and Lewis acid catalysis.

Most, if not all, organocatalysts initiate catalytic cycles by either donating or removing electrons or protons. They can therefore be classified as Lewis bases, Lewis acids, Brønsted bases, or Brønsted acids.[1] Since the early years of this century, hundreds of groups have been working on Lewis base and Brønsted acid catalysis, but the community has been somewhat slower in warming up to Lewis acid and Brønsted base organocatalysis. This cluster on 'Asymmetric Brønsted Base Catalysis' now provides a snapshot of state-of-the-art approaches towards organic Brønsted base catalyzed reactions with the aim of convincing the readers of the great potential this area holds.

There are a several strategies for realizing catalytic asymmetric Brønsted base catalyzed reactions. One obvious approach involves the use of catalysts that are comprised of neutral organic Brønsted bases such as tertiary amines, guanidines, amidines, and imidazoles.[2] When the Tan group was formed in 2003, they realized that simple organic Brønsted bases can catalyze many carbon–carbon bond-forming reactions such as aldol, Henry, Michael, and Strecker reactions, and Claisen condensations. This group then spent close to a decade developing and describing Brønsted base catalyzed reactions of readily deprotonated substrates by using chiral guanidines as a powerful catalyst platform.[3] More recently, there has been a surge in the number of attempts to make use of only weakly acidic substrates. Toward this goal, dual activation modes using a combination of two different catalysts have been successfully implemented as one strategy. Examples of this approach include new methods that combine a Lewis acid catalyst with a Brønsted base catalyst, or an iminium ion activation-type Lewis base catalyst with a Brønsted base catalyst. Bifunctional Brønsted base/hydrogen bonding catalysis is also an area of increasing importance and has led to several industrial applications. Finally, the development of chiral superbases, which can efficiently distribute positive charge over their conjugate acid through conjugation, has also attracted significant attention lately. Some of these recent advances are summarized in a cluster account (Choon-Hong Tan, Recent Advances in Enantioselective Brønsted Base Organocatalytic Reactions) presented right after this cluster preface.[4]

In this SYNLETT Cluster, we have contributions from Takemoto et al.[5] as well as from Chen and Huang et al.,[6] illustrating the power of bifunctional hydrogen bonding/Brønsted base catalysts in the catalysis of highly enantioselective aldol reactions; Odagi and Nagasawa et al.[7] use beautiful guanidine–bisurea bifunctional organocatalysts for enantioselective hydroxylations of β-keto esters, while Ooi et al.[8] describe chiral 1,2,3-triazolium salts as phase-transfer catalysts that also catalyze highly enantioselective hydroxylations; Kobayashi et al.[9] use an elegant cation-binding catalysis strategy to mediate enantioselective conjugate additions to simple α,β-unsaturated amides; Zhao and Jiang et al.[10] also demonstrate remarkably enantioselective and diastereoselective 1,4-additions, followed by a protonation, on the basis of yet another type of amine–urea bifunctional catalyst; Wennemers et al.[11] continue their studies on powerful peptide catalysts for enamine catalysis and describe conjugate additions to benzylidenemalononitriles; and last but not least, Berkessel et al.[12] use another class of bifunctional chiral base/H-bonding catalysts, squaramide organocatalysts, to catalyze kinetic resolutions towards β^2-amino acids.

Clearly, asymmetric Brønsted base organocatalysis is currently being established not only as a powerful approach to constructing valuable enantiopure compounds but also as one of the four fundamental pillars of organocatalysis. In this cluster, we highlight a number of new developments and hope to encourage colleagues all over the world to contribute to this exciting area, especially by providing solutions to remaining challenges.

References and Notes

(1) (a) Seayad, J.; List, B. *Org. Biomol. Chem.* **2005**, *3*, 719. (b) *Asymmetric Organocatalysis*; List, B., Ed.; Springer-Verlag: Berlin Heidelberg, **2009**. (c) *Asymmetric Organocatalysis*; List, B.; Maruoka, K., Eds.; Georg Thieme Verlag KG: Stuttgart, New York, **2012**.
(2) For reviews of organobase-catalyzed reactions, see: (a) *Superbases for Organic Synthesis: Guanidines, Amidines, Phosphazenes and Related Organocatalysts*; Ishikawa, T., Ed.; John Wiley & Sons Ltd: Chichester, UK, **2009**. (b) Palomo, C.; Oiarbide, M.; Lopez, R. *Chem. Soc. Rev.* **2009**, *38*, 632.
(3) (a) Leow, D.; Tan, C. *Chem. Asian J.* **2009**, *4*, 488. (b) Leow, D.; Tan, C. *Synlett* **2010**, *11*, 1589.
(4) Teng, B.; Lim, W. C.; Tan, C.-H. *Synlett* **2017**, *28*, 1272.
(5) March, T.; Murata, A.; Kobayashi, Y.; Takemoto, Y. *Synlett* **2017**, *28*, 1295.
(6) Wang, F.; Chen, J.; Huang, Y. *Synlett* **2017**, *28*, 1300.
(7) Odagi, M.; Hosoya, K.; Yamamoto, Y.; Nagasawa, K. *Synlett* **2017**, *28*, 1305.
(8) Ohmatsu, K.; Ando, Y.; Ooi, T. *Synlett* **2017**, *28*, 1291.
(9) Yamashita, Y.; Igarashi, R.; Suzuki, H.; Kobayashi, S. *Synlett* **2017**, *28*, 1287.
(10) Zhang, G.; Yin, Y.; Zhao, X.; Jiang, Z. *Synlett* **2017**, *28*, 1310.
(11) Schnitzer, T.; Wennemers, H. *Synlett* **2017**, *28*, 1282.
(12) Eröksüz, S.; Neudörfl, J.; Berkessel, A. *Synlett* **2017**, *28*, 1278.