Design and Synthesis of Chiral Organic Molecules for Asymmetric Synthesis

Department of Life and Coordination-Complex Molecular Science
Division of Complex Catalysis

MOMIYAMA, Norie
Associate Professor
[momiyama@ims.ac.jp]

Education
2000 B.S. Nagoya University
2005 Ph.D. The University of Chicago

Professional Employment
2005 Postdoctoral Fellow, Harvard University
2006 Assistant Professor, Tohoku University
2014 Associate Professor, Institute for Molecular Science
Associate Professor, The Graduate University for Advanced Studies

Awards
2003 The Elizabeth R. Norton Prize for Excellence in Research in Chemistry, University of Chicago
2004 Abbott Laboratories Graduate Fellowship
2005 Damon Runyon Cancer Research Foundation Post Doctoral Research Fellowship
2008 Thieme Chemistry Journals Award

Member
Secretary
WATANABE, Yoko

Keywords Organic Synthesis, Molecular Catalyst, Non-Covalent Interaction

The field of molecular catalysis has been an attractive area of research to realize efficient and new transformations in the synthesis of functional molecules. The design of ligands and chiral molecular catalysts has been recognized as one of the most valuable strategies; therefore, a great deal of effort has been dedicated to the developments. In general, "metal" has been frequently used as the activation center, and conformationally rigid, and C_2- or pseudo C_2 symmetry has been preferably components for the catalyst design. To develop new type of molecular catalysis, we have focused on the use of hydrogen and halogen atom as activation unit, and have utilized conformationally flexible components in the molecular design of catalyst, which had not received much attention until recently. We hope that our approach will open the new frontier in chiral organic molecules from chiral molecular chemistry to chiral molecular science.

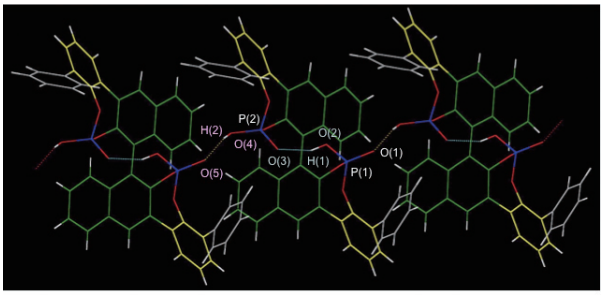

Figure 1. Hydrogen bonding network in chiral bis-phosphoric acid catalyst derived from (*R*)-3,3'-di(2-hydroxy-3 -arylphenyl)binaphthol. Hydrogen bond acts as activation unit for the substrate in asymmetric reaction space and controls atropisomeric behavior in naphthyl–phenyl axis.

Selected Publications

- T. P. Yoon and E. N. Jacobsen, *Science* **299**, 1691–1693 (2003).
- N. Momiyama and H. Yamamoto, "Brønsted Acid Catalysis of Achiral Enamine for Regio- and Enantioselective Nitroso Aldol Synthesis," *J. Am. Chem. Soc.* **127**, 1080–1081 (2005).
- N. Momiyama, H. Tabuse and M. Terada, "Chiral Phosphoric Acid-Governed Anti-Diastereoselective and Enantioselective Hetero-Diels–Alder Reaction of Glyoxylate," *J. Am. Chem. Soc.* **131**, 12882–12883 (2009).
- N. Momiyama, T. Konno, Y. Furiya, T. Iwamoto and M. Terada, "Design of Chiral Bis-Phosphoric Acid Catalyst Derived from (*R*)-3,3'-Di(2-hydroxy-3-arylphenyl)binaphthol: Catalytic Enantioselective Diels–Alder Reaction of α,β-Unsaturated Aldehydes with Amidodienes," *J. Am. Chem. Soc.* **133**, 19294–19297 (2011).

1. Brønsted Acid Catalyzed Asymmetric 1,3-Alkyl Migration of 1,2,2-Substituted Butenyl Amines: Asymmetric Synthesis of Linear Homoprenylamines

Allylation of imines with allylic metal reagents has been one of the most valuable tools to synthesize enantioenriched homoallylic amines. Due to the inherent nature of allylic metal reagent, however, regioselectivity has been a long-standing subject in this area. To develop the synthetic reaction for enantioenriched linear homoprenylic amines, we discovered chirality transferred 1,3-alkyl migration of 1,2,2-substituted butenyl amines in the presence of trifluoromethyl acetic acid, and developed it as synthetic method for variety of enantioenriched linear homoprenylic amines.[1] In sharp contrast, Ollis *et al.* previously reported that chirality was significantly dropped in 1,3-alkyl migration of *N*,*N*-dimethyl-1-substituted-3-buten-1-amine.[2] To the best our knowledge, our discovery is the first example of chirality transferred 1,3-alkyl migration and the new entry of the synthetic methodology for the linear enantioenriched homoallylic amines.

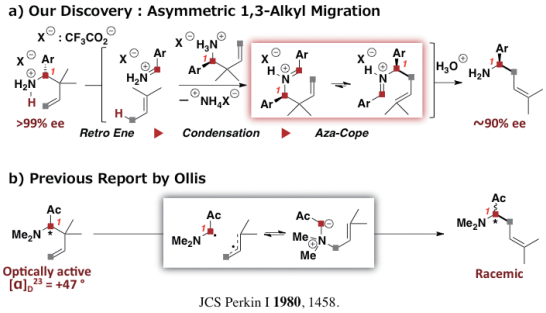

Figure 2. 1,3-Alkyl migration of 1-substituted-3-buten-1-amine. a) Our discovery, b) Previous report by Ollis *et al.*

2. Design of C_1 Symmetric Chiral Bis-Phosphoric Acid: Catalytic Enantioselective Diels–Alder Reaction of Acrolein with Amidodienes

We recently developed (*R*)-3,3'-di(2-hydroxy- 3-arylphenyl) binaphthol derived pseudo-C_2 symmetric chiral bis-phosphoric acid which efficiently catalyzed enantioselective Diels–Alder reaction of α,β-unsaturated aldehydes with amidodienes.[3] Two cyclic phosphoric acid motifs introduced between the $C_{Naph}(2)$ and $C_{Ar}(2)$ positions and between the $C_{Naph}(2')$ and $C_{Ar}(2)$ positions represents a characteristic feature of our catalysts. On the basis of our early hypothesis and recent results, the intramolecular hydrogen bonding between two acidic moieties seems to be deeply related to control an atropisomeric behavior of catalyst structure; however, none of systematic study have been employed with respect to the importance of hydrogen bond in the molecular design of chiral catalysts.

We designed a new C_1 symmetric chiral bis-phosphoric acid that possesses an electron-withdrawing group at the $C_{Naph}(3')$–$C_{Ar}(3)$, $C_{Ar}(5)$.[4] We found that (i) the stereodynamic behavior of atropisomeric biaryls was controlled by the intervention of hydrogen bond, (ii) the requisite catalyst activity was served by the electronic effect at the $C_{Naph}(3')$–$C_{Ar}(3)$, and (iii) the precise distinction of asymmetric reaction space was realized by the different substitution at the $C_{Naph}(3)$–$C_{Ar}(3)$ and the $C_{Naph}(3')$–$C_{Ar}(3)$.

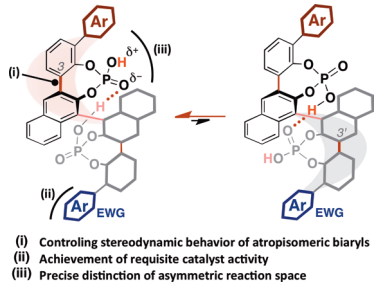

Figure 3. Molecular design of chiral C_1 symmetric bis-phosphoric acid.

3. Halogen Bond Donor Catalyzed Allylation Reaction of Isoquinoline with Allylsilatrane

Halogen bonds are attractive non-covalent interactions between terminal halogen atoms in compounds of the type R–X (X = Cl, Br, I) and Lewis bases LB. It has been known that strong halogen bonds are realized when "R" is highly electronegative substituents such as perfluorinated alkyl or aryl substituents. We recently developed synthetic methodology for perfluorinated aryl compounds, and applied it for the development of chiral Brønsted acid catalysts. On the basis of our achievements, we have examined it to develop halogen bond donor catalyzed allylation reaction.

We found that pentafluoroiodebenzene was able to catalyze the allylation reaction of isoquinoline with allylsilatrane to give the corresponding product in good yield.[5]

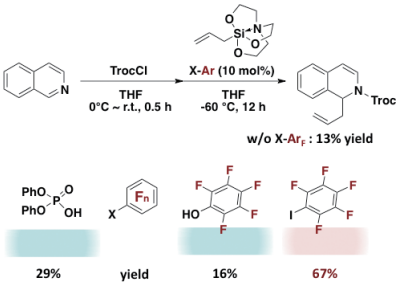

Figure 4. Halogen bond donor catalyzed allylation reaction. Comparison with Brønsted acid/hydrogen bond donor catalyst.

References

1) N. Momiyama, C. Kanai, A. Takei and M. Terada, Manuscript in preparation.
2) R. W. Jemison, T. Laird, W. D. Ollis and I. O. Sutherland, *J. Chem. Soc. Perkin Trans. 1* 1458–1461 (1980).
3) N. Momiyama, T. Konno, Y. Furiya, T. Iwamoto and M. Terada, *J. Am. Chem. Soc.* **133**, 19294–19297 (2011).
4) N. Momiyama, K. Funayama, H. Noda, M. Yamanaka, N. Akasaka, S. Ishida, T. Iwamoto and M. Terada, Manuscript in preparation.
5) N. Momiyama, H. Nishimoto, Y. Kamata and M. Terada, Manuscript in preparation.