シンポジウム | アジア国際シンポジウム：アジア国際シンポジウム—有機化学ディビジョン/環境・安全化学・グリーンケミストリー・サステイナブルテクノロジーディビジョン—

📅 2024年3月19日(火) 13:00 ~ 15:40 🏛 A1422(14号館 [2階] 1422)

[A1422-2pm] アジア国際シンポジウム—有機化学ディビジョン/環境・安全化学・グリーンケミストリー・サステイナブルテクノロジーディビジョン—

座長、シンポジウム関係者：石原 一彰、大嶋 孝志

🏷 英語 🏷 Invited Lecture
13:00 ~ 13:30
[A1422-2pm-01]
キラルビスホスフィンオキシドのLewis/Brønsted塩基協奏触媒作用を利用したエナンチオ選択的ブロモ環化反応

○山下 賢二[1] (1. 静岡県大薬)

🏷 英語 🏷 Keynote Lecture
13:30 ~ 14:00
[A1422-2pm-02]
Anion-encapsulating sodium alkoxide clusters (X@RONa): structure and function as multi-functional Lewis acid catalysts

○Zhi Li[1] (1. ShanghaiTech University)

14:00 ~ 14:20
休憩

🏷 英語 🏷 Invited Lecture
14:20 ~ 14:50
[A1422-2pm-03]
計算科学主導によるジフルオロカルベンを用いるフルオロアルキル化反応の開発

○林 裕樹[1,2] (1. 北大WPI-ICReDD、2. 北大JST-ERATO)

🏷 英語 🏷 Asia Special Lecture
14:50 ~ 15:30
[A1422-2pm-04]
Asymmetric Carbene-Transfer Reactions Catalyzed by Low Coordination State Rhodium(I)

○Ming-Hua Xu[1] (1. Southern University of Science and Technology, China)

15:30 ~ 15:40
閉会挨拶

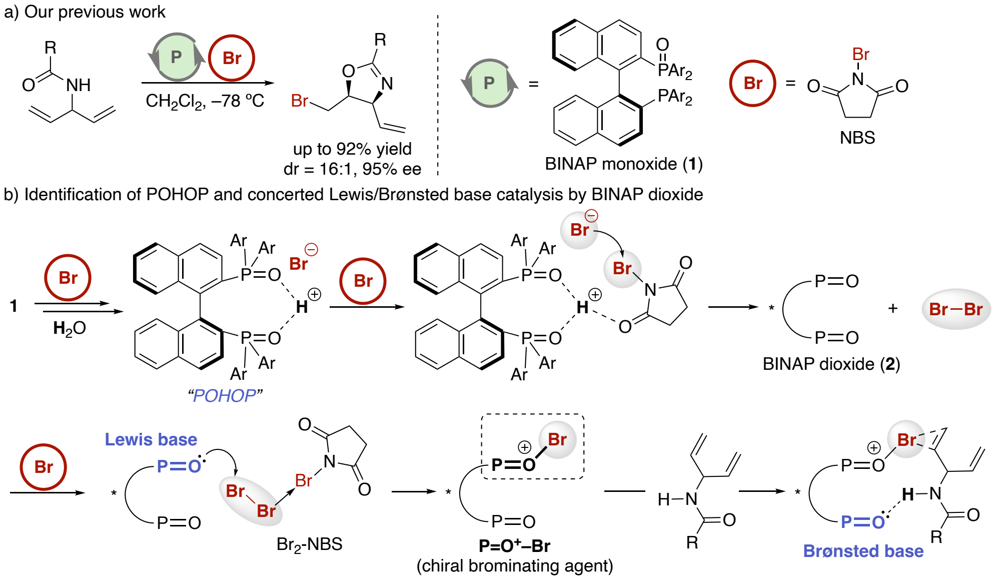
Enantioselective Bromocyclization Reactions Enabled by Lewis/Brønsted Base Concerted Catalysis of Chiral Bisphosphine Oxide

(1. *School of Pharmaceutical Sciences, University of Shizuoka*) ○Kenji Yamashita[1]

Keywords: Organocatalyst; Halogenation; Asymmetric Reaction; Lewis Base; Brønsted Base

Electrophilic halo-functionalizations of carbon–carbon unsaturated bonds are one of the most synthetically attractive transformations that allow for simultaneous incorporation of two heteroatom functionalities across these unsaturated bonds. In this context, we recently reported the desymmetrization of bisallylic amides via an enantioselective bromocyclization using (*S*)-BINAP monoxide (**1**) (Scheme 1a).[1] However, the catalytic role of **1** has remained elusive. Then, the catalytic mechanism of the above reaction was examined in detail by several control experiments, X-ray analysis, NMR studies, and CryoSpray MS analysis. **1** was transformed to a key catalyst precursor, proton-bridged bisphosphine oxide complex "POHOP" (Scheme 1b). The thus-formed POHOP further reacts with *N*-bromosuccinimide (NBS) to afford BINAP dioxide (**2**) and molecular bromine (Br_2) simultaneously. While the resulting Br_2 is activated by NBS through halogen bonding interaction to form a more reactive brominating reagent (Br_2-NBS),[2] **2** serves as a bifunctional catalyst, acting as both a Lewis base that reacts with Br_2-NBS to form a chiral brominating agent (**P=O$^+$–Br**), and also as a Brønsted base for activating the substrate.[3]

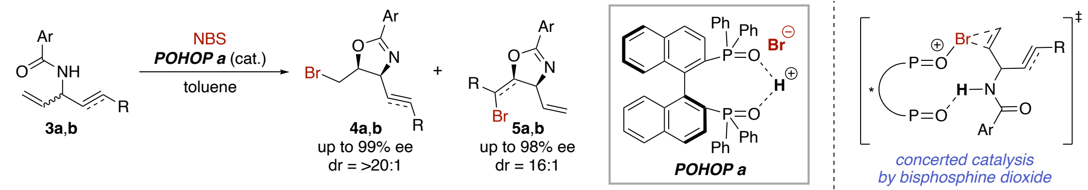
Scheme 1. Bifunctional Catalysis of Chiral Bisphosphine Oxide



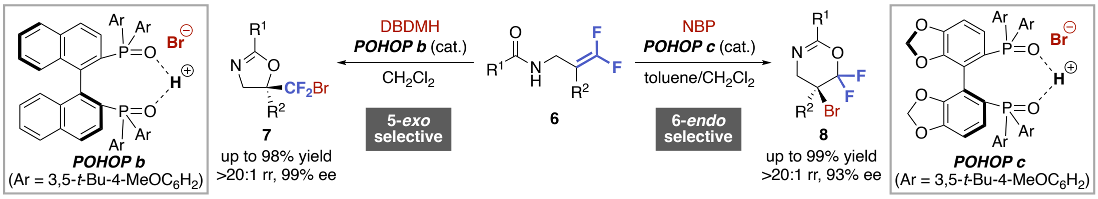
This novel catalysis of the chiral bisphosphine oxide was applicable to various highly challenging asymmetric bromocyclization reactions. For example, we have successfully developed *regiodivergent* parallel kinetic resolution (PKR) of racemic allylic amides **3a** via bromocyclization (Scheme 2a).[3] When **3a** having two different alkenes was employed as a substrate, **3a** was transformed into two distinct cyclization products (**4a** and **5a**) in a highly stereoselective manner via concurrent resolution processes. The catalysis could also promote *chemodivergent* PKR of racemic ene-yne **3b** to provide the corresponding products (**4b** and **5b**), regardless of the electronic difference between alkene and alkyne. To our knowledge, these are the first examples of *regio-* and *chemodivergent* PKRs via halocyclization. Furthermore, regio- and enantioselective bromocyclizations of difluoroalkenes **6**[4] were also demonstrated (Scheme 2b).[5] Owing to the extremely high electrophilicity of **P=O$^+$–Br** species, the cyclization of less reactive **6** proceeded smoothly even at low temperature. A particularly noteworthy feature is that regio- and enantioselectivity were greatly influenced by the solvent, the catalyst structure, and the brominating reagent. Consequently, both the 5-*exo* and 6-*endo* selective bromocyclizations became feasible, providing the corresponding oxazolines **7** or oxazines **8** bearing a tetrasubstituted difluoromethylated stereocenter in high yield with excellent enantioselectivity. Moreover, a gram-scale synthesis of chiral oxazoline **7** was also achieved with as little as 1 mol% of the catalyst, highlighting the synthetic utility of our protocol.

Scheme 2. Enantioselective Bromocyclizations Using POHOP as a Catalyst Precursor

a) *Regio-* and *chemodivergent* Parallel Kinetic Resolution (PKR) via bromocyclization



b) Regio- and enantioselective bromocyclization of difluoroalkenes



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Anion-encapsulating sodium alkoxide clusters (X@RONa): structure and function as multi-functional Lewis acid catalysts

([1]*School of Physical Science and Technology, ShanghaiTech University*) ○Zhi Li[1]

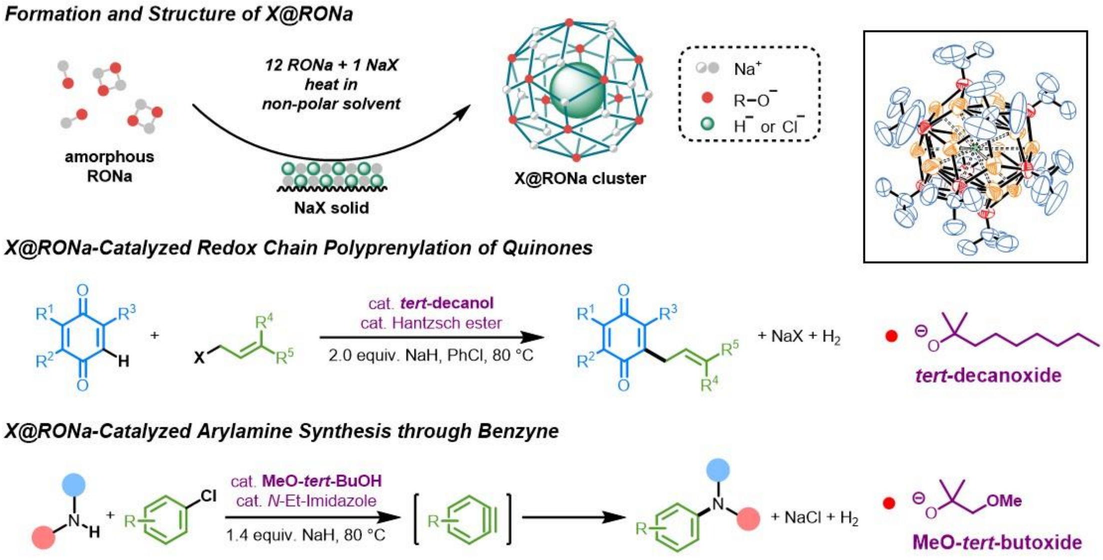
Keywords: sodium alkoxide clusters; benzyne; aryl amines; polyprenylquinones; Lewis acid catalysis

Sodium salts are able to aggregate into various types of polymeric or molecular substances depending on anions. We discovered that sodium *tert*-butoxide formed thermodynamically favored dodecameric anion-encapsulating molecular clusters $(NaO\textit{t}\text{-}Bu)_{12}NaX$, or X@*t*-BuONa, where X is the encapsulated anion. The synthesis could be as simple as heating NaO*t*-Bu and fine powder of NaCl together in a non-polar solvent. The structures of these substances were studied by X-ray crystallography and NMR. Unlike their well-known oligomeric clusters or amorphous ionic polymers, its structure consists of 12 alkoxide anions located at vertices of an icosahedron, a halide or other anion at the center, and 13 sodium cations dynamically distributed at 13 of the 20 faces.

The multi-level composition of these clusters allowed us to design clusters by changing the *tert*-butoxide to other alkoxide ligand RO as X@RONa, thus enabling their catalytic activities. The RO ligand, encapsulated X, and substrates coordinated to Na were all Lewis basic ligands that interacting with the cluster as well as each other, thus we consider the X@RONa as a new type of Lewis acid catalyst. The catalytic activity will be illustrated in the following two cases.

First, X@RONa was able to promote transition-metal-free polyprenylation of quinones through redox chain mechanism we discovered earlier.[1] Many biologically important polyprenylquinones were synthesized from corresponding parent quinone and polyprenyl halide as precursors and NaH as base in one step and high yield.

Second, X@RONa was applied in catalytic transition-metal-free C-N bond formation. Aryl amines are usually synthesized from transition metal-catalyzed cross coupling or C-H activations from aryl halides, triflates, or arenes. Although these methods are effective, the costs of precursors, reagents and catalysts are often too high for them to be applied in large scale synthesis. We recently discovered that X@RONa was capable of catalytically promoting benzyne formation from simple aryl chlorides, as well as the subsequent arylation of amines. From very simple and cheap aryl chlorides, alkyl amines and NaH, aryl amines can be easily synthesized in large scale. This is also a very rare case of large-scale application of benzyne.



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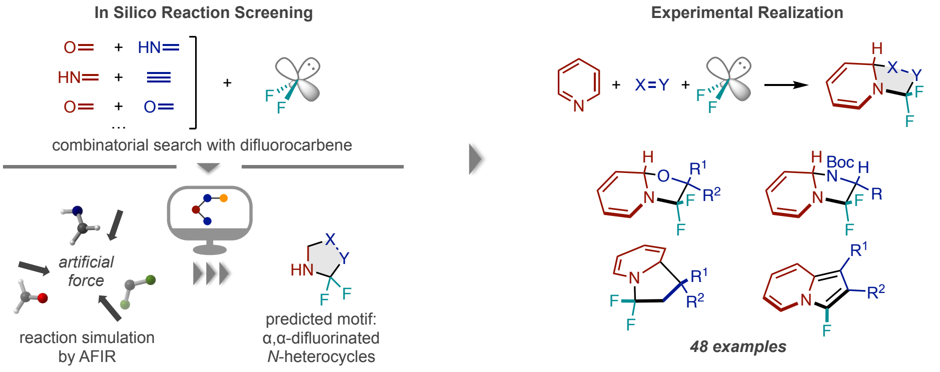
Computation-based Strategy for the Development of Fluoroalkylation Reactions with Difluorocarbene

(*WPI-ICReDD, Hokkaido University & JST-ERATO*) ○Hiroki Hayashi

Keywords: Quantum Chemical Calculations; Reaction Development; Fluoroalkylation; Difluorocarbene; Dearomatization

Quantum chemical calculations have been an indispensable tool in synthetic methodology development. The progress of computational methods as well as computer technology has enabled the systematic exploration of reaction pathways, and their current primary role is to gain the mechanistic insight into established reactions. In this context, our group has developed an artificial force induced reaction (AFIR) method, an automated reaction path search algorithm that can explore the possible reaction pathways from single input structure. This method can create reaction path networks comprising computationally estimated reaction intermediates and products without any prior knowledge of organic transformations, showcasing its ability to predict even unknown chemical processes.[1]

Here, we report a strategy that leverages computational reaction simulations for the development of three-component reactions with difluorocarbene using the AFIR method. Difluorocarbene, an electrophilic carbene species useful not only for incorporating the difluoromethylene unit into organic molecules but also in the calculations due to its relatively small character, is used for in silico combinatorial reaction screening with two unsaturated compounds containing C=O, C=N, C=C, or C≡C bonds. These simulations suggested that the less explored three-component cycloaddition of methanimine, difluorocarbene, and the other unsaturated component would proceed preferentially to furnish α,α-difluorinated *N*-heterocyclic skeletons. Based on the computational results, we realized the identified reaction mode experimentally, leading to a diverse dearomative cycloaddition of pyridines with difluorocarbene and a series of unsaturated compounds (aldehydes, ketones, imines, alkenes, and alkynes).[2]



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Asymmetric Carbene-Transfer Reactions Catalyzed by Low Coordination State Rhodium(I)

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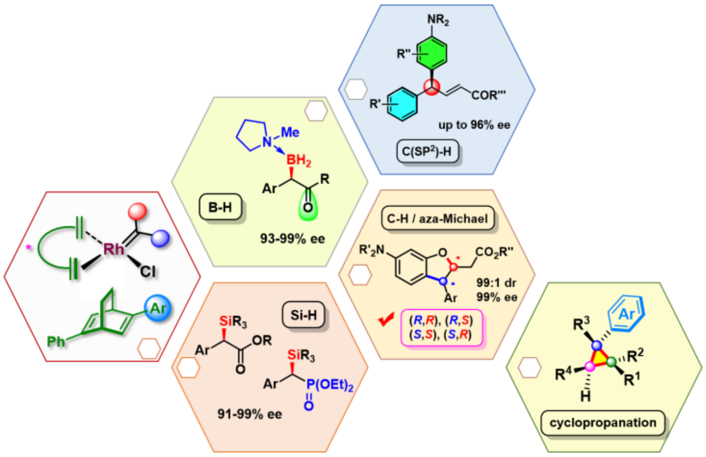
Keywords: Asymmetric Catalysis; Carbene-Transfer; Rhodium(I); Chiral Diene; Carbene Insertion

Transition metal-catalyzed asymmetric carbene insertion reactions have been recognized as one of the most powerful methods for the construction of C-C or C-heteroatom bonds. In recent years, our group has been interested in Rh(I)−carbene chemistry, and achieved the first asymmetric metal−carbene insertion into B−H and Si-H bonds using Rh(I)/C_1-symmetric diene complexes as catalysts.[1] With the established Rh(I)−carbene chemistry, we also discovered that C-H insertion reaction of styryldiazoacetates with aniline derivatives could be achieved in a highly region- and enantio-selective manner.[2] Moreover, the rhodium(I)/chiral diene catalytic system also enables efficient asymmetric Rh(I)-carbene-directed S-H, C(sp^3)-H, N-H, O-H insertions, as well as intramolecular cyclopropanations.[3] In this presentation, these results together with some new achievements will be described.



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