

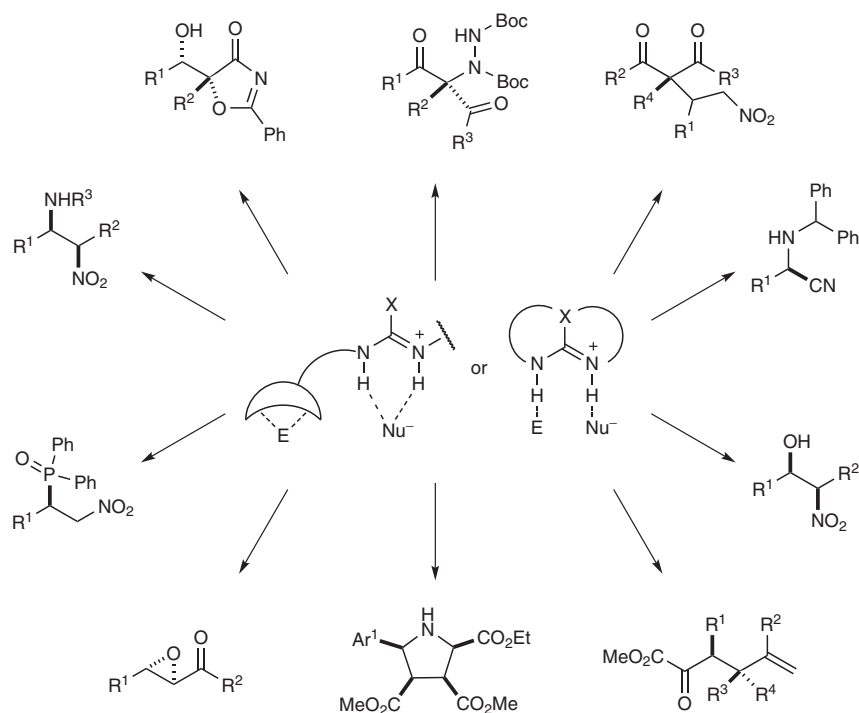
Abstracts

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2.1.1 Chiral Guanidine and Amidine Organocatalysts

K. Nagasawa and Y. Sohtome

Guanidines and amidines are relatively strong Brønsted bases owing to the stability of their conjugate acids. The corresponding guanidinium and amidinium salts are able to serve as double hydrogen bond donors and play key roles in controlling the three-dimensional geometries of transition states. This review describes the development of useful general strategies for catalytic asymmetric transformations using chiral guanidines and amidines or their salts. Special emphasis is given to the key requirements for the design of guanidine and amidine organocatalysts and to reaction protocols employed.



Keywords: guanidines · amidines · guanidinium salts · amidinium salts · 2-aminoacetonitriles · alcohols · amines · nitroalkanes · epoxy ketones · hydrazines · phosphonates · phosphine oxides · δ -lactones · pyrrolidines · α -keto esters · Strecker · nitroaldol · Henry · aldol · nitro-Mannich · Mannich · Michael · epoxidation

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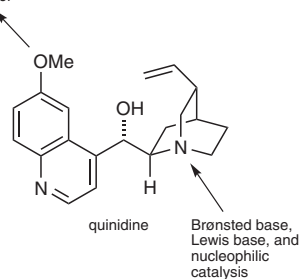
2.1.2 Cinchona Alkaloid Organocatalysts

R. P. Singh and L. Deng

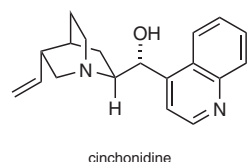
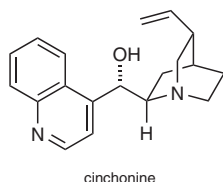
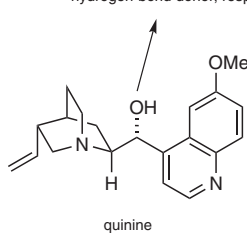
Cinchona alkaloid derivatives have emerged as one of the most powerful classes of chiral catalysts in asymmetric synthesis. At a fundamental level, this development resulted from the key mechanistic discovery that modified cinchona alkaloids could serve as efficient and general base catalysts to promote highly enantioselective asymmetric reactions

via the activation of a broad range of nucleophiles. Moreover, this mode of asymmetric catalysis has been successfully coupled with various modes of catalysis centered on the activation of electrophiles, such as acid and iminium catalysis, thereby leading to the development of highly efficient and general cooperative catalysis based on organic catalysts. Importantly, this powerful strategy, proven to be among the most generally applicable in asymmetric catalysis, has been extended to multifunctional catalysis, which promotes and controls multiple stereoselective steps involving distinct transition states. In this review, we highlight the practice of these newly emerged concepts as a widely applicable strategy for the development of an extremely broad range of stereoselective transformations.

conversion to OH or thiourea makes it an acid or hydrogen-bond donor



conversion to amines or thioureas helps in amino catalysis or works as a hydrogen-bond donor, respectively

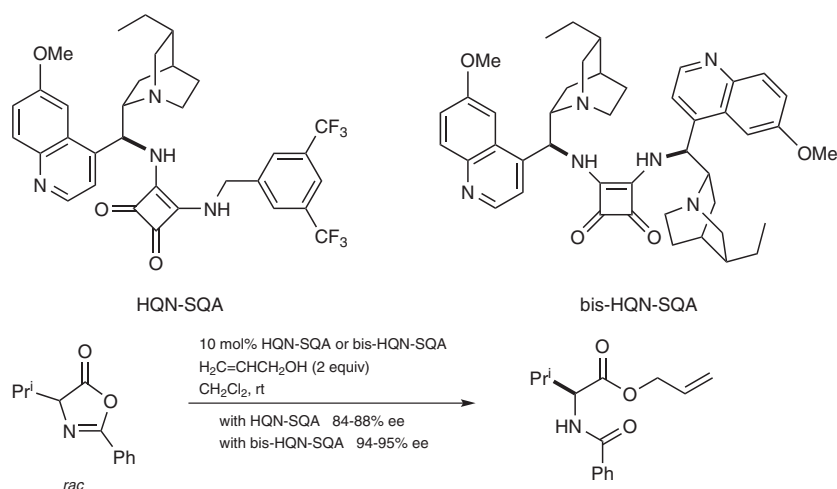


Keywords: cinchona alkaloids • enantioselective catalysis • acid–base bifunctional catalysis • base–iminium catalysis • Friedel–Crafts alkylations • kinetic resolution • organo-catalyst • cooperative catalysis • bifunctional catalysts • cycloadditions • conjugate addition

2.1.3 Bifunctional Cinchona Alkaloid Organocatalysts

H. B. Jang, J. S. Oh, and C. E. Song

This chapter presents the current state of the art in the development of cinchona alkaloid based bifunctional catalysts in organocatalysis. In the last few years, cinchona alkaloid based bifunctional catalysts have been shown to catalyze an outstanding array of enantioselective chemical reactions by a dual activation mechanism, often with remarkable stereoselectivity. Although the bifunctionality of the catalysts has enabled cooperative catalysis to be achieved, it has also been identified as a potential source of self-aggregation of the catalysts which will have to be addressed in the coming years.



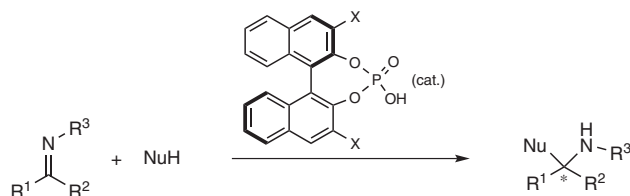
Keywords: organocatalysis · asymmetric catalysis · cooperative catalysis · bifunctional chiral catalysts · cinchona alkaloids · enantioselectivity · self-association

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2.2.1 Phosphoric Acid Catalyzed Reactions of Imines

T. Akiyama

Chiral phosphoric acids derived from 1,1'-bi-2-naphthols catalyze nucleophilic addition reactions, cycloaddition reactions, and transfer hydrogenation reactions to imines, giving rise to chiral nitrogen-containing compounds with excellent enantioselectivities.



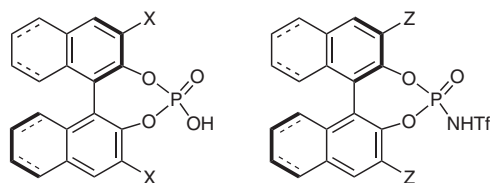
Keywords: amines · asymmetric catalysis · asymmetric synthesis · Brønsted acids · chiral compounds · cycloaddition · Friedel–Crafts alkylation · hetero-Diels–Alder reaction · imines · indoles · Mannich reaction · nucleophilic addition · phosphoric acids · transfer hydrogenation · reduction

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2.2.2 Phosphoric Acid Catalysis of Reactions Not Involving Imines

M. Terada and N. Momiyama

Chiral phosphoric acid derivatives, in particular phosphoric acids and phosphoramides derived from 3,3'-disubstituted 1,1'-bi-2-naphthols, are highly effective catalysts for a diverse range of enantioselective reactions, including cycloadditions, ene reactions, ring-opening reactions, Friedel–Crafts reactions, Michael additions, aldol reactions, epoxidations, and various rearrangements. This chapter presents the state of the art of the rapidly developing field of reactions involving catalysis by chiral phosphoric acid derivatives, with the exception of transformations using imines as electrophiles.



X = Ph, 4-*t*-BuC₆H₄, 4-PhC₆H₄, 2,4,6-*i*Pr₃C₆H₂, 2,4-*i*Pr₂-4-*t*-BuC₆H₂, SiPh₃, 9-anthryl, 9-phenanthryl, etc; Z = bulky aryl group, SiPh₃

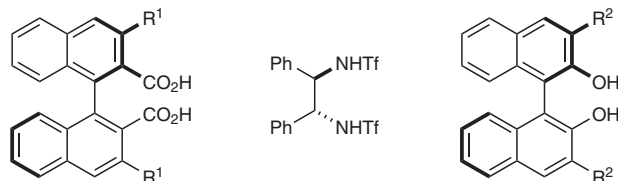
Keywords: asymmetric catalysis · Baeyer–Villiger oxidation · binaphthols · chiral phosphoric acids · chiral phosphoramides · conjugate addition · cycloaddition · ene reaction · epoxidation · Friedel–Crafts reaction · Michael addition · Nazarov cyclization

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2.2.3 Brønsted Acid Catalysts Other than Phosphoric Acids

T. Hashimoto

The decade 2001–2010 has witnessed the remarkable development of chiral Brønsted acid or hydrogen-bond donor catalysis, both in terms of the emergence of structurally diverse catalysts and applications in various novel synthetic transformations. As for the source of the hydrogen bond donor, the research has mainly relied on the use of weak acids such as diols and (thio)ureas, and strong acids, typically phosphoric acids. This chapter summarizes asymmetric reactions promoted by other chiral Brønsted acids, the acidity of which ranges from moderate to strong.



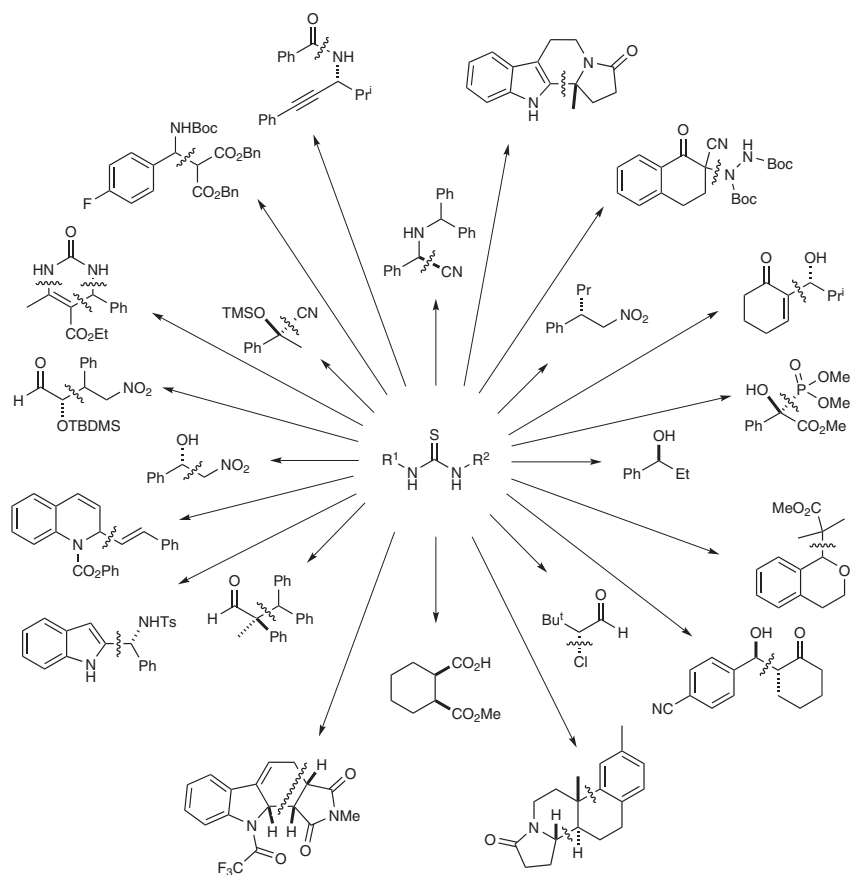
Keywords: acid catalysts · alkenylation · alkynylation · allylation · amines · arylation · asymmetric catalysis · aziridination · boron compounds · Brønsted acids · carboxylic acids · conjugate addition · diazo compounds · hydrazones · imines · Mannich reaction · Mukaiyama reaction · nitroso compounds · sulfonamides

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2.2.4 Hydrogen-Bonding Catalysts: (Thio)urea Catalysis

K. Hof, K. M. Lippert, and P. R. Schreiner

This chapter reviews the application of thiourea organocatalysts in asymmetric synthesis, and the development and current status quo of the field. The chapter is then classified according to reaction type, focusing on: Michael reactions including phospho-Michael and nitrocyclopropanations; Mannich reactions including acyl- and *anti*-Mannich, vinyl-ogous Mannich, and nitro-Mannich (aza-Henry) reaction; Henry (nitro-aldol) and aldol/vinylogous aldol reactions, and vinylogous Mukaiyama–aldol reactions; (aza-)Morita–Baylis–Hillman reactions; Strecker reactions; cyanosilylations; hydrophosphonylations; Friedel–Crafts reactions; desymmetrization; kinetic resolutions; cycloadditions, including the Diels–Alder reaction and 1,3-dipolar cycloadditions; Pictet–Spengler reactions, including acyl- and protio- variants; Biginelli reactions; Petasis-type reactions; transfer hydrogenations; reduction of ketones; aminations; alkylations; chlorinations; cationic polycyclization; and additions to oxocarbenium ions.



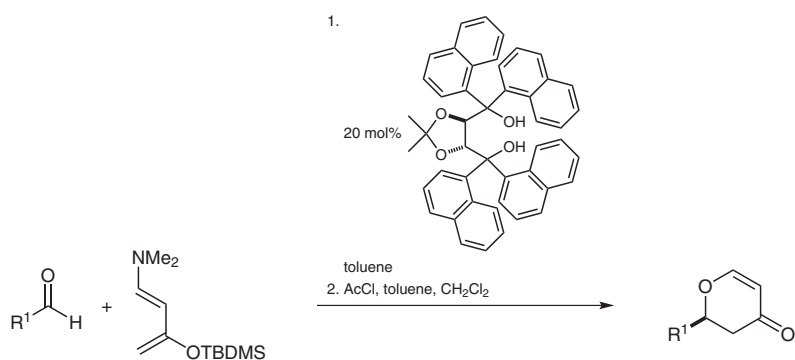
Keywords: thiourea · kinetic resolution · cycloaddition · Petasis reaction · transfer hydrogenation · addition · Henry reaction · Mannich reaction · chlorination · Morita–Baylis–Hillman reaction · reduction · alkylation · amination · Friedel–Crafts reaction · Pictet–Spengler reaction · polycyclization · cyanocyclization · Michael reaction · Biginelli reaction · hydrophosphonylation · aldol · desymmetrization · Strecker reaction

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2.2.5 Hydrogen-Bonding Catalysts Other than Ureas and Thioureas

D. Uraguchi and T. Ooi

Asymmetric catalyses of weakly acidic chiral molecules featuring hydrogen-bonding donor capabilities are summarized in this section. Besides the reactions catalyzed by chiral diols, as representative nonionic Brønsted acids, enantioselective transformations under the influence of chiral ionic Brønsted acids are mainly described.



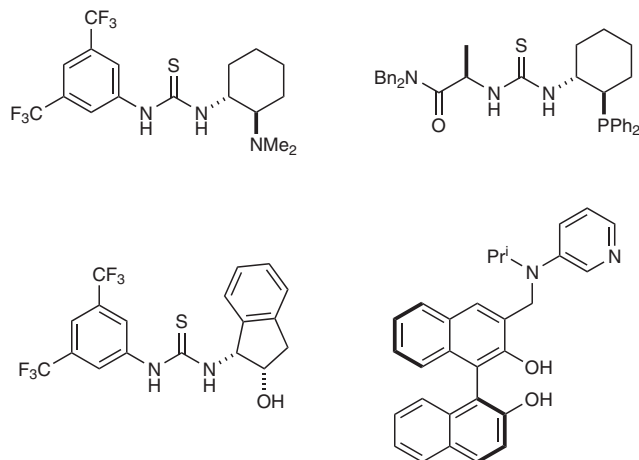
Keywords: diol · guanidinium salt · amidinium salt · aminophosphonium salt · pyridinium salt · Diels–Alder reaction · Mannich-type reaction · aldol reaction · Michael addition · Henry reaction · Claisen rearrangement

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2.2.6 Bifunctional (Thio)urea and BINOL Catalysts

T. Inokuma and Y. Takemoto

Chiral bifunctional (thio)ureas and 1,1'-bi-2-naphthol derivatives (BINOLS) bearing amine, alcohol, phosphine, sulfinamide, or pyridine substituents have been developed. These catalysts can activate both a nucleophile and an electrophile simultaneously and promote a wide range of 1,2- and 1,4-nucleophilic additions with ketones, imines, nitroalkenes, enones, and α,β -unsaturated carboxylic acid derivatives in a highly stereoselective manner.



Keywords: α -amino acids · β -amino acids · γ -amino acids · 1,2-diamines · pyrrolidines · piperidines · Michael addition · aza-Morita–Baylis–Hillman reaction · Mannich Reaction · aza-Henry reaction · cyanation · [3+2] cycloaddition

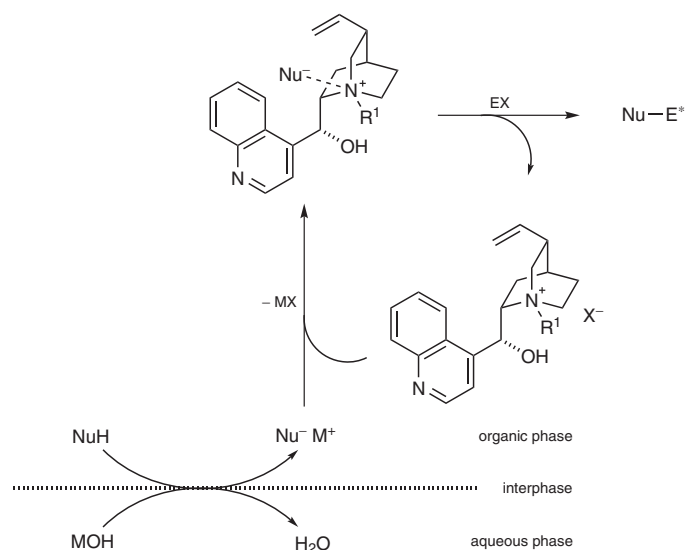
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2.3.1 Phase-Transfer Catalysis: Natural-Product-Derived PTC

H.-g. Park

Natural-product-derived chiral quaternary ammonium salts generate ionic complexes with nucleophilic anions under phase-transfer catalytic conditions. Reaction of these

complexes with electrophiles results in the stereoselective formation of chiral compounds.



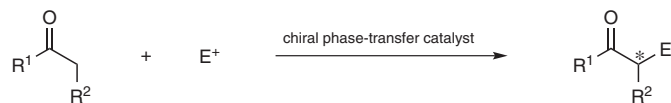
Keywords: asymmetric phase-transfer catalytic reaction • enantioselective synthesis • chiral quaternary ammonium salts • cinchona alkaloid • tartrate

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2.3.2 Phase Transfer Catalysis: Non-Natural-Product-Derived PTC

S. Shirakawa and K. Maruoka

This chapter focuses on the progress of asymmetric reactions with various types of non-natural-product-derived chiral phase-transfer catalysts, showcasing the variations of their molecular designs and synthetic applications.



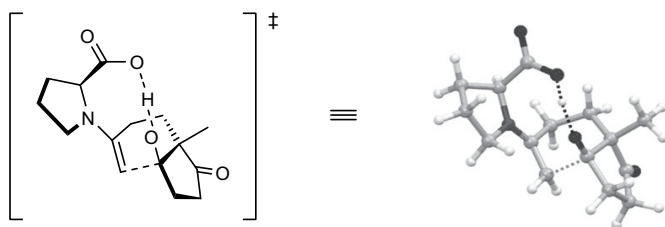
Keywords: phase-transfer catalysis • organocatalysis • asymmetric synthesis • asymmetric catalysis • alkylation • amino acids • Michael addition • aldol reaction • amination • epoxidation

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2.3.3 Computational and Theoretical Studies

I. Pápai

Thorough computational investigations, employing reliable electronic structure methods and realistic molecular models, provide valuable insight into the origin of catalysis and stereoselectivity of organocatalytic transformations. This knowledge can be effectively utilized in new synthetic developments.



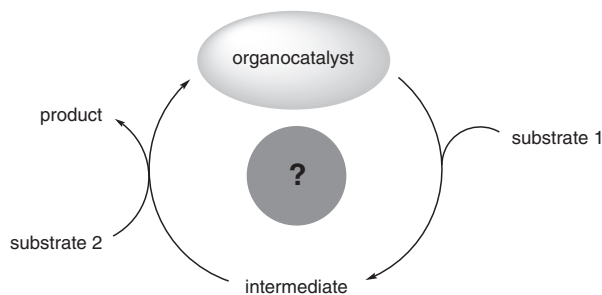
Keywords: reaction mechanism · density functional theory · transition states · mechanistic models · stereoselectivity · hydrogen bonding · activation modes · C–C bond formation

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2.3.4 Mechanism in Organocatalysis

M. Klussmann

The dramatic rise of asymmetric organocatalysis in recent years is certainly due, to a large extent, to the increased awareness of its generality, based on an understanding of its reaction mechanisms. In the first part of this chapter, a short overview of methods that have been used for the investigation of reaction mechanisms in organocatalysis is given, illustrated by selected examples of their application. In the second part of the chapter, the beneficial interplay of different methods in bringing about a full mechanistic picture is demonstrated by discussing two selected types of well-investigated organocatalytic reactions: enamine and iminium catalysis. The emphasis of this chapter is to highlight the information that can be retrieved from the various experimental methods and to guide the experimentalist in choosing the right experiments that can provide answers to their mechanistic questions.



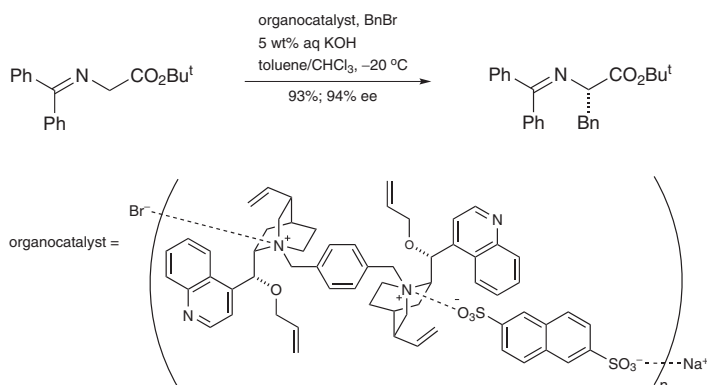
Keywords: asymmetric catalysis · enamine catalysis · iminium catalysis · kinetics · spectroscopy · reaction mechanism

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2.3.5 Supported Organocatalysts

S. Itsuno and N. Haraguchi

Polymer-immobilized chiral organocatalysts have been prepared and successfully used in various asymmetric reactions. An ionically immobilized chiral quaternary ammonium sulfonate polymer catalyzes the asymmetric alkylation of glycine derivatives with high enantioselectivity.



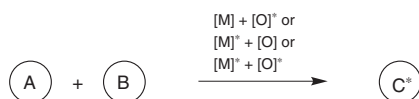
Keywords: chiral organocatalyst • polymer-immobilized catalyst • enantioselective methanolysis • ketene dimerization • aldol reaction • Michael addition • alkylation • epoxidation • Diels–Alder reaction • allylation

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2.3.6 Organocatalysis Combined with Metal Catalysis or Biocatalysis

Z.-Y. Han, C. Wang, and L.-Z. Gong

This review describes recent developments in reactions catalyzed by binary catalytic systems consisting of an organocatalyst and a metal complex. The two catalysts may drive the reaction in a cooperative manner or sequentially.



[M] = metal catalyst; [O] = organocatalyst

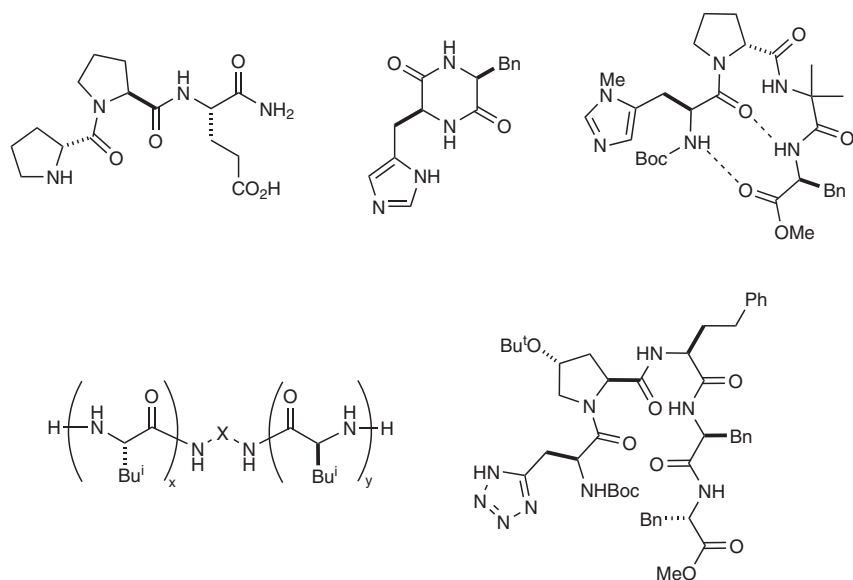
Keywords: alkaloids • alkynes • α -amino acids • asymmetric catalysis • Brønsted acids • hydrogenation • Lewis base catalysts • tandem reaction • transfer hydrogenation • transition metals

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2.3.7 Peptide Catalysis

J. Duschmalé, Y. Arakawa, and H. Wennemers

Peptides have been developed as excellent asymmetric catalysts for numerous reactions. This manuscript summarizes the range of different reactions that are effectively catalyzed by peptides and highlights special features of peptidic catalysts.



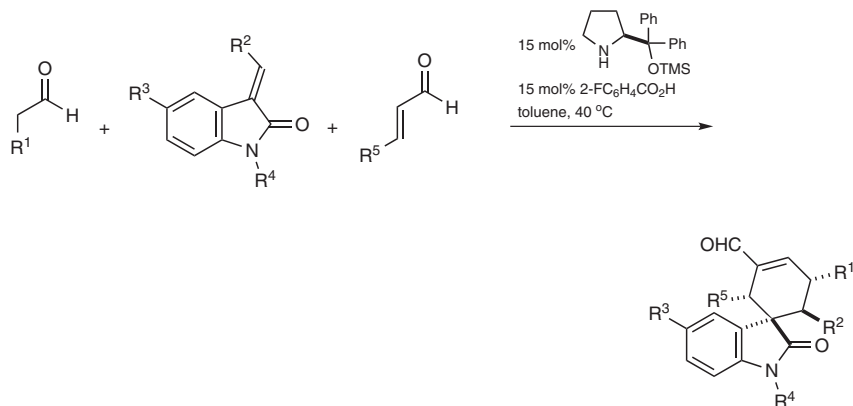
Keywords: peptides · asymmetric catalysis · epoxidation · oxidation · acylation · phosphorylation · sulfonylation · kinetic resolution · C–C bond forming reaction · aldol reaction · hydrocyanation · conjugate addition reaction · Stetter reaction · Morita–Baylis–Hillman reaction · acylation equivalents · bromination · protonation

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2.3.8 Organocatalytic Cascade Reactions

Y.-C. Chen and H.-L. Cui

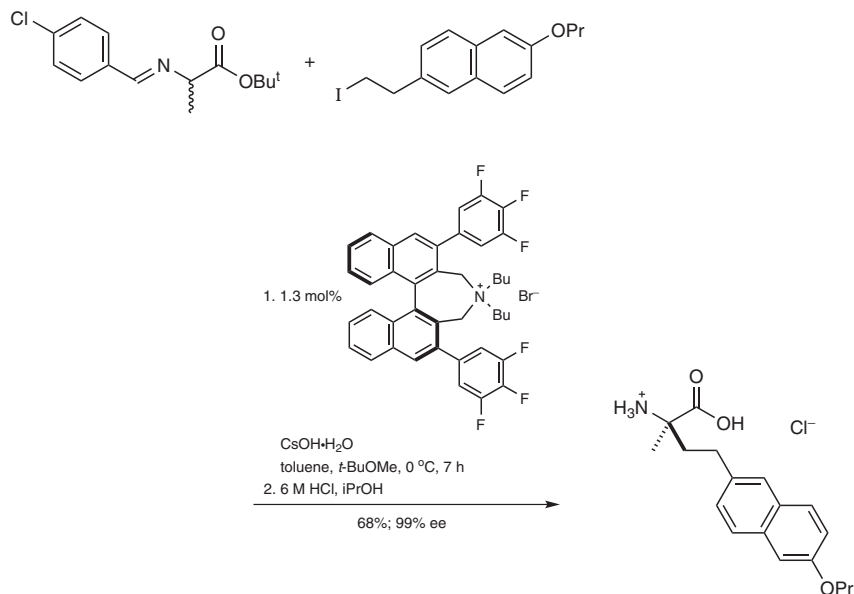
This section focuses on organocatalytic cascade reactions, which enable the enantioselective assembly of complex molecules and efficient formation of multiple bonds in one step. The well-known activation modes of organocatalysis, such as enamine activation, iminium activation, SOMO activation, Brønsted acid catalysis, hydrogen-bonding activation, and homoenolate activation, or combinations of these, may be implemented to complete various cascade transformations.



Keywords: organocatalysts · cascade reactions · enamine activation · iminium activation · SOMO activation · Brønsted acid catalysis · hydrogen-bonding activation · homoenolate activation

2.3.9 Industrial Applications*K. Izawa, T. Torii, T. Nishikawa, and H. Imai*

This review describes recent progress in asymmetric organocatalyzed reactions particularly focusing on industrial applications, although some of the reactions cited here have not yet been performed on an industrial scale.



Keywords: kinetic resolution · desymmetrization · bifunctional thiourea-type organocatalyst · alkylation · α -alkylated amino acids · cross-aldol reactions · Mannich reaction · maraviroc · Michael reaction · (-)-oseltamivir · Shi epoxidation · aza-Henry reaction · β -amino acid · enantioselective Friedel–Crafts reaction · hydrocyanation · Strecker reaction