

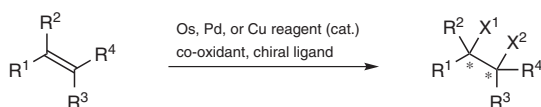
Abstracts

p 5

1.1 Dihydroxylation, Aminohydroxylation, Diamination, and Dibromination of Carbon–Carbon Double Bonds

K. Muñiz

Direct oxidative transformation of alkenes into the corresponding 1,2-difunctionalized derivatives represents a powerful tool for the introduction of heteroatoms. The formation of the two new C–X bonds can occur either within a concerted process or within stepwise transformations. In this review, standard procedures for oxidative alkene transformation, including dihydroxylation, ketohydroxylation, aminohydroxylation, and diamination, will be presented. Emphasis is placed on synthesis, and mechanistic details are only given in order to underline the conceptual background of a given transformation.



$X^1/X^2 = \text{OH/OH}, \text{OR}^5/\text{NHR}^6, \text{Br/Br}, \text{NR}^5_2/\text{NR}^6_2$

Keywords: alkenes · dihydroxylation · ketohydroxylation · dibromination · aminohydroxylation · diamination · 1,2-diols · β -amino alcohols · 1,2-diamines · osmium · oxidation · palladium · transition-metal catalysis · cinchona alkaloid ligands

p 69

1.2 Epoxidation of Carbon–Carbon Double Bonds

K. Matsumoto, T. Katsuki, and I. W. C. E. Arends

Catalytic enantioselective epoxidation of C=C bonds, including allylic alcohols and nonfunctionalized alkenes, using chiral transition-metal catalysts and organocatalysts as well as enzymes are reviewed in this chapter.



Keywords: alkenes · allylic alcohols · asymmetric catalysis · epoxidation · epoxy compounds · oxiranes · enzyme catalysis

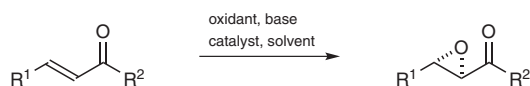
p 123

1.3 Epoxidation of Enones by Nucleophilic Oxidation

S. Colonna and D. Perdicchia

Efficient asymmetric techniques for the epoxidation of α,β -unsaturated ketones, in the presence of hydrogen peroxide, hypochlorite, or an organic peroxide as an oxygen source under basic conditions, are described. Considerable attention has been paid to asymmet-

ric variants of this epoxidation reaction using chiral metal-based or organic catalysts. The epoxidation of enones using nucleophilic oxidants is one of the most important reactions in organic synthesis because the corresponding enantiomerically enriched epoxides can be converted into a variety of useful enantioenriched intermediates.



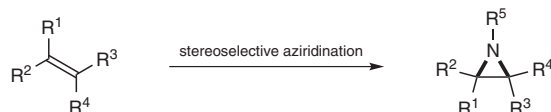
Keywords: epoxidation of enones · α,β -unsaturated ketones · hydrogen peroxide · alkyl peroxides · Weitz–Scheffer reaction · Julià–Colonna epoxidation · poly(amino acids) · enantioselectivity · diastereoselectivity · phase-transfer catalysis · scale-up · mechanistic considerations · chiral-ligand metal peroxide systems · organocatalyzed epoxidation · cinchona alkaloid based catalyst · chiral dioxiranes

p 155

1.4 Aziridination

H. Muchalski and J. N. Johnston

Aziridines are the smallest carbocycles containing one nitrogen atom. Due to their angle strain, they exhibit a synthetically useful balance between stability and reactivity. Thus, they are often employed as versatile intermediates. This chapter focuses on stereoselective synthesis of aziridines from alkenes using a variety of methods that include both stoichiometric and catalytic reactions.



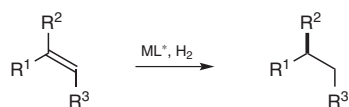
Keywords: asymmetric catalysis · alkenes · azides · aziridination · aziridines · bis(4,5-dihydrooxazole) ligands · chiral auxiliaries · metal complexes · diastereoselectivity · enantioselectivity · heterocycles · iminoiodinanes · nitrenes · nitrogen heterocycles · sulfonamides · three-membered rings · zeolites · organocatalysis · heterogeneous catalysis

p 185

1.5 Hydrogenation of Carbon–Carbon Double Bonds

D. Ager

The asymmetric hydrogenation of C=C bonds is an extremely powerful method to introduce a stereogenic center with high enantioselectivity. Although there is no general catalyst system, many types of functionalized and some nonfunctionalized alkenes can be reduced. The method has been used at industrial scale, as exemplified by the production of α - and β -amino acid derivatives, and 2-substituted alkanolic acids. There are many catalyst systems available allowing for this green approach to be applied to a wide range of substrates.

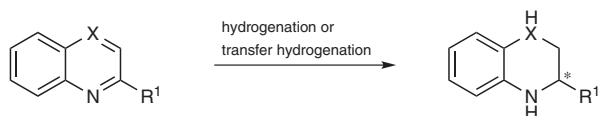


Keywords: α -amino acids · β -amino acids · asymmetric catalysis · amides · carboxylic acids · hydrogenation · rhodium catalysts · ruthenium catalysts · iridium catalysts

1.6 Hydrogenation of Arenes and Hetarenes

S.-M. Lu and Y.-G. Zhou

Methods for the asymmetric hydrogenation/transfer hydrogenation of aromatic and heteroaromatic compounds, including quinolines, isoquinolines, furans, protected indoles, activated pyridines, pyrroles, and quinoxalines, are presented in eight sections. In each section, the methods are organized further on the basis of the catalysts used. Asymmetric hydrogenation of bicyclic heteroaromatic compounds is easier than the simple monocyclic heteroaromatic compounds; thus, there are more effective methods that demonstrate excellent activity and enantioselectivity. The very limited methods available for asymmetric hydrogenation of simple monocyclic heteroaromatic compounds, such as furans, pyrroles, and pyridines, are also presented.

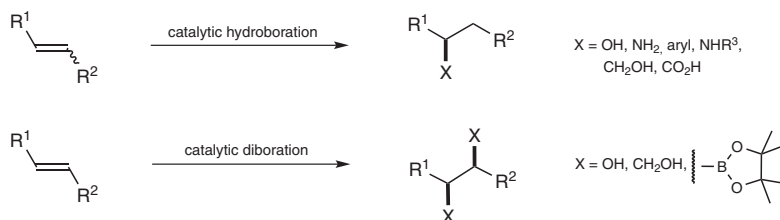


Keywords: asymmetric hydrogenation · transfer hydrogenation · arenes · hetarenes · quinolines · isoquinolines · furans · indoles · pyridines · pyrroles · quinoxalines · chiral cyclic compounds

1.7 Stereoselective Hydroboration and Diboration of Carbon–Carbon Double Bonds

J. M. Brown and B. N. Nguyen

This chapter covers all recent aspects of the stereoselective addition of boranes to C=C unsaturation. In reflecting the literature, most emphasis is placed here on catalytic hydroboration, and related reactions. This affords the ability to prepare secondary alcohols from a wide range of substrates in good to high enantiomeric purity through oxidation of the intermediate borane. Both catecholborane and pinacolborane can be used. Variations on this procedure can lead to amines, homologous alcohols, or further products of catalytic coupling. Catalytic diboration is a more recent discovery, based on vicinal addition of dicaticholdiborane or dipinacoldiborane to alkenes. This opens up a range of additional possibilities for the stereocontrolled introduction of functional groups. Diboron additions to electrophilic or conjugated alkenes can lead directly to the product of β -hydroboration in high enantiomeric purity.



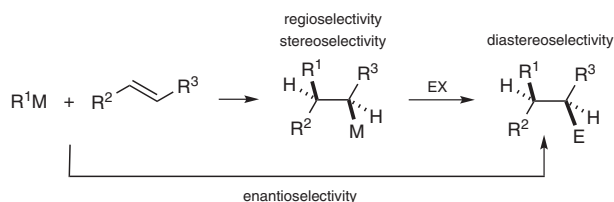
...and more elaborate variations

Keywords: hydroboration · diboration · conjugate addition · diphosphine ligands · phosphinamine ligands · catecholborane · pinacolborane · dipinacoldiborane · rhodium · iridium · copper · hydrogen peroxide · hydroxylamine-*O*-sulfonic acid · (dichloromethyl)-lithium

1.8 Carbometalation of Carbon–Carbon Double Bonds

I. Marek and A. Basheer

Although the functionalization of a double bond has been the focus of intense research in the last few decades (i.e., hydrocyanation, hydrosilylation, hydroboration, hydroformylation, dihydroxylation, epoxidation, cyclopropanation, aziridination, aminohydroxylation, etc.), the diastereo- and enantioselective bis-alkylation of nonactivated alkenes has not yet fulfilled its potential. The addition of organometals to such nonactivated C=C bonds (carbometalation) is an efficient way to create bis-alkylated linear or cyclic substructures if the organometallic thus formed can react diastereoselectively with electrophiles. The latest developments of this approach provide a route to nonracemic metalated structures from common organometallics (R^1Li , R^1_3Al , R^1MgX), either by transmetalation with asymmetrically ligated transition metals (as Zr complexes) or simply by coordination with chiral amines (as Li species). However, the simplicity of the protocols, once the right conditions are found, certainly warrants increasing efforts in its development for organic synthesis.



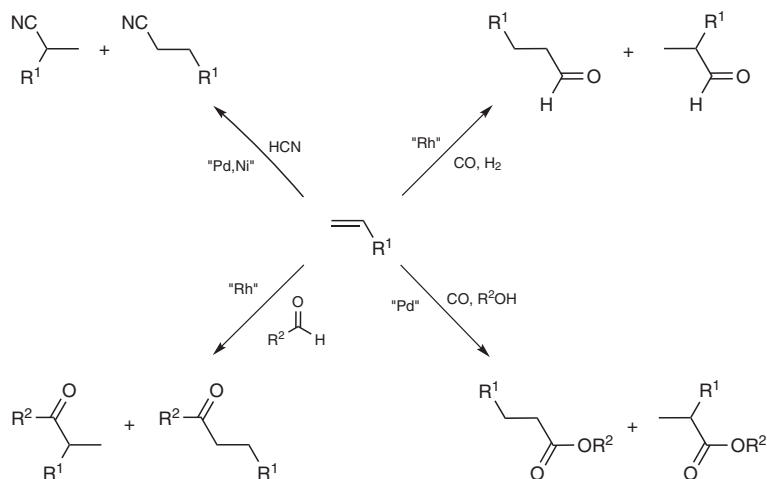
Keywords: carbometalation · diastereoselectivity · enantioselectivity · regioisomer · carbolithiation · 5-*exo-trig* cyclization · cyclopentylmethyl lithium · lithium–iodine exchange · lithium–tin exchange · epimerization · anionic cyclization · lithium–ene cyclization · lithium–selenium exchange · lithium–hydrogen exchange · (–)-sparteine · reductive lithiation · hydroamination · hydrazone · carbomagnesiation · magnesium–ene reaction · *syn*-addition · carbozincation of alkenes · radical chain cyclization · zinc–ene–allene carbocyclization · zinc–ene carbocyclization · zinc-promoted Brook rearrangement–carbocyclization · α -amino zinc enolate cyclization · allylzincation of alkenylmetals · bismetalated adducts · zinccyclopropane · zinc azaenolate · carbocupration reaction · cyclopropenes · zirconium-catalyzed enantioselective alkylaluminum

1.9 Hydroformylation, Hydrocarbonylation, Hydrocyanation, and Hydroacylation of Carbon–Carbon Double Bonds

P. W. N. M. van Leeuwen

The following catalytic reactions are discussed: hydroformylation, carbonylation, hydrocyanation, and hydroacylation. The literature data in this area is reported in a different way to that of organic synthesis, and many reports are concerned with simple, bulk-chemical compounds, rather than advanced organic materials. Yet, the usefulness of these reactions in organic synthesis is beyond doubt. In this context, the general considerations of the catalytic processes were regarded as important, perhaps more so than the inclusion of a large number of specific examples. The understanding of the factors important to a successful catalytic conversion, together with the examples given, will help in the design of a reaction for a substrate of interest. Catalysis research in general focuses on turnover numbers and turnover frequencies rather than on isolated yields, as one would prefer in high-standard organic synthesis literature. The procedures reported in de-

tail are those of the best methods encountered. Enantioselective examples have been included for all four reactions, although for several reactions the number of successful reactions is limited and enantiomeric excesses are not extremely high; purification steps of the enantiomeric products are often needed. Only for hydrocyanation has this actually been practiced; for the other reactions only chromatographic, analytic separations have been reported.



Keywords: hydroformylation · carbonylation · rhodium-catalyzed hydroformylation · palladium-catalyzed carbonylation · methoxycarbonylation of alkenes · methoxycarbonylation of alkynes · hydroxycarbonylation · hydrocyanation of alkenes · intramolecular hydroacylation · intermolecular hydroacylation · asymmetric catalysis

1.10 Hydrovinylation and Hydroarylation of Carbon–Carbon Double Bonds

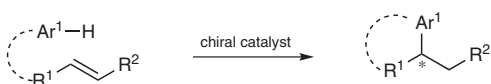
G. Franciò, W. Leitner, and P. L. Alsters

This chapter covers methods for the enantioselective inter- and intramolecular addition of a compound containing an sp²-C–H group to a C=C bond, catalyzed by transition-metal catalysts or organocatalysts. The sp²-C–H group can be part of an alkene (Sections 1.10.1–1.10.2) or an aromatic compound (Sections 1.10.3–1.10.4). These transformations are often referred to as hydrovinylation and hydroarylation, respectively, and allow a stereoselective assembly of carbon skeletons with perfect atom economy.

inter- and intramolecular hydrovinylation:



inter- and intramolecular hydroarylation:



Keywords: hydrovinylation · cycloisomerization · heterodimerization · intermolecular dimerization · intramolecular dimerization · hydroarylation · all-carbon quaternary cen-

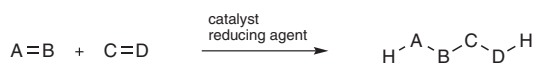
ter · nickel catalyst · cobalt catalyst · rhodium catalyst · phosphoramidites · phosphines · phosphorus ligands · hemilabile coordination · weakly coordinating anions · alkenes · vinyl arenes · linear dienes · 1,2-addition · 1,4-addition · diallyl malonates · aryl ketimines · imidazoles · indoles

p 521

1.11 Reductive Coupling and Cyclization of Carbon–Carbon Multiple Bonds

K. D. Schleicher and T. F. Jamison

Transition-metal-catalyzed reductive couplings and cyclizations have attracted significant recent interest for their potential to rapidly increase molecular complexity starting from simple precursors. This broad class of reactions most frequently involves the union of two or more π -systems with the aid of a reducing agent. Highly substituted double bonds, heterocycles, contiguous stereocenters, and numerous other functional-group arrays may be prepared using these methods, frequently from achiral, readily accessible substrates. For many of these multicomponent processes, the precise mechanism remains undefined. As new research on reductive coupling continues to unfold, this chapter provides a selection of the methods currently available to the chemist engaged in stereoselective synthesis.



catalyst = Ni-, Rh-, Ir-, Co-based catalysts

Keywords: reductive coupling · reductive cyclization · C–C bond formation · metallacycles · multicomponent reactions · catalysis · nickel · rhodium · cobalt · iridium · hydrogen · triethylborane · alkynes · aldehydes · alkenes · alcohols · regioselective · enantioselective

p 571

1.12 Conjugate Addition Reactions

B. N. Nguyen, K. K. Hii, W. Szymański and D. B. Janssen

1,4-Addition of various nucleophiles to activated C=C bonds is reviewed. Various methodologies effective for achieving high stereoselectivity in these processes are described, including the use of chiral auxiliaries, as well as metal catalysts and bio- and organocatalysis. The sections are organized according to the type of nucleophile and/or acceptor used.



X = electron-withdrawing group

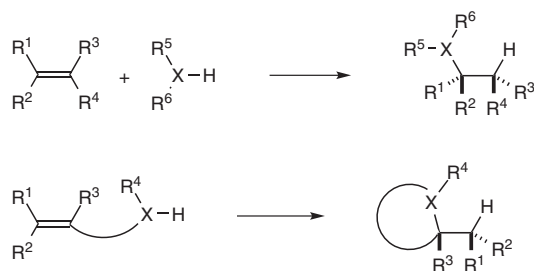
Nu⁻ = C-, N-, O-, S-, P-, Si-, or B-nucleophile

Keywords: asymmetric catalysis · asymmetric synthesis · biocatalysis · chiral auxiliaries · conjugate addition · carbon–carbon bonds · carbon–heteroatom bonds · Michael acceptors · Michael donors · nucleophilic addition

1.13 Hydroamination, Hydrophosphination, Hydrophosphinylation, and Hydrophosphonylation of Carbon–Carbon Double Bonds

A. L. Reznichenko and K. C. Hultsch

The direct addition of amine N–H or phosphine (or phosphonate or phosphonite) P–H bonds across an unsaturated carbon–carbon linkage gives fast and highly atom-economical access to amines and phosphines. This chapter provides an overview of the most effective stereoselective methods using alkali- and transition-metal-based catalyst systems. Except for a few sporadic examples in the 20th century, this field has evolved primarily since 2000. Some catalyst systems have reached enantioselectivities exceeding 90% ee for certain substrate classes.



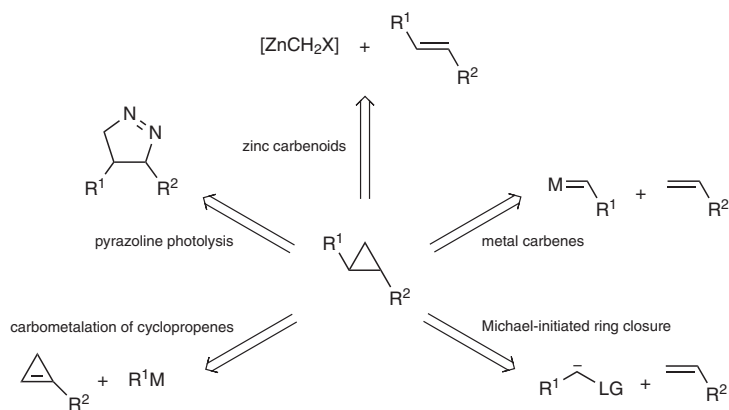
X = N, P

Keywords: hydroamination · hydrophosphination · hydrophosphinylation · hydrophosphonylation · hydroboration/amination · hydrozirconation/iodination · hydroamination/reduction · hydroamination/hydrosilylation · kinetic resolution · pyrrolidines · piperidines · azacycles · amines · lithium · rare earth metals · zirconium · palladium · iridium · rhodium · gold

1.14 Cyclopropanation Reactions

M.-N. Roy, V. N. G. Lindsay, and A. B. Charette

This chapter describes the most important stereoselective methods since 1995 to generate substituted, enantiomerically enriched cyclopropane derivatives. The first part of the chapter describes the stereoselective addition of zinc carbenoid reagents to alkenes. The following sections focus on the reaction of chiral metal carbenes obtained from chiral catalysts derived from transition metals. A review of various other methodologies involving ring closing and ring contracting processes is then presented. Finally, other more specific methodologies that have not been included in the previous sections are highlighted. The cyclopropanation derived from carbometallation of cyclopropenes is not discussed in this chapter.

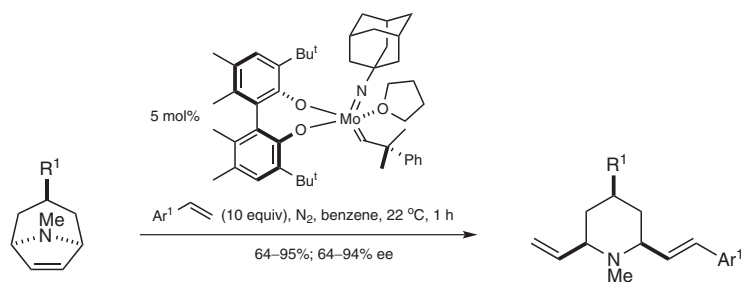


Keywords: asymmetric cyclopropanation • Corey–Chaykovsky cyclopropanation • cyclopropane • cyclopropane functionalization • Fischer–carbene complexes • Kulinkovich cyclopropanation • nucleophilic alkylidene transfer • ring-closure cyclopropanation • ring-contraction cyclopropanation • Simmons–Smith reaction • transition-metal-catalyzed cyclopropanation • zinc carbenoids

1.15 Enantioselective and Diastereoselective Alkene Metathesis

S. K. Collins

Enantioselective or diastereoselective alkene metathesis is a powerful method for stereocontrolled synthesis in that it allows the formation of C=C bonds under relatively mild reaction conditions. Many of the current efforts in catalyst design are aimed at developing solutions to long-standing problems in the fields of enantioselective or diastereoselective metathesis, since these challenges require catalysts that display high levels of efficiency, selectivity, and/or alkene stereoselectivity. Enantioselective and diastereoselective processes are now found in all metathesis related transformations including ring-closing metathesis, ring-opening metathesis, cross metathesis, enyne metathesis, polymerization reactions, and tandem processes involving one or more of the aforementioned transformations.



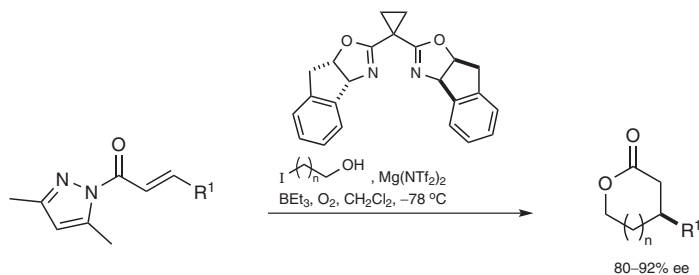
$R^1 = \text{H, OTBDMS}; \text{Ar}^1 = \text{Ph, 4-MeOC}_6\text{H}_4, \text{4-F}_3\text{CC}_6\text{H}_4, \text{2-BrC}_6\text{H}_4$

Keywords: alkene metathesis • chirality • resolution • asymmetric synthesis • asymmetric catalysis • ruthenium catalysts • desymmetrization • ring closure • ring opening • enynes • cross metathesis

1.16 Addition of Free Radicals to Carbon–Carbon Multiple Bonds

S. Hata and M. P. Sibi

In this chapter details of stereoselective radical reactions are provided. In the first half, diastereoselective radical reactions that include both inter- and intramolecular reactions are discussed. The stereochemistry in these reactions is controlled either by a resident chiral center or by the use of a chiral auxiliary. Conjugate additions, atom-transfer reactions, tandem reactions, and cyclizations are discussed in detail. The application of radical reactions as key steps in the total synthesis of natural products is also included. The second half of the chapter details enantioselective radical reactions, which include a wide variety of bond-forming processes. Chiral Lewis acid catalyzed and organocatalyzed reactions are included.

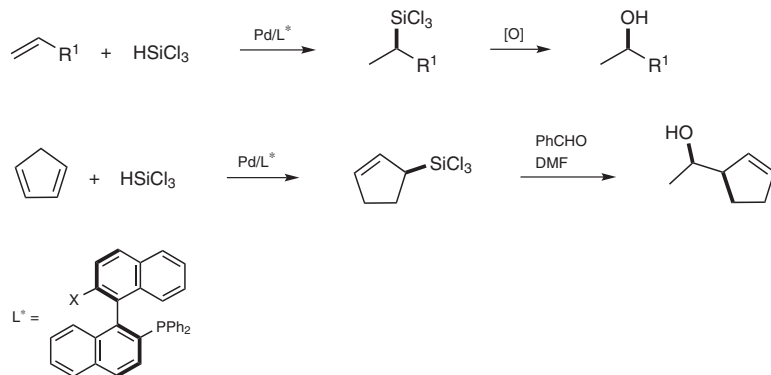


Keywords: asymmetric synthesis · hydrogen-atom transfer · tin hydrides · radical addition · chiral auxiliaries · oxazolidinones · radical cyclization · annulation reactions · tandem reactions · triethylborane · chiral Lewis acid · bis(4,5-dihydrooxazoles) · enantioselectivity · organocatalysts

1.17 Asymmetric Hydrosilylation of Carbon–Carbon Double Bonds

J. W. Han and T. Hayashi

Palladium complexes coordinated with chiral monodentate phosphine ligands catalyze the formation of enantiomerically enriched organosilicon compounds from alkenes and trichlorosilane. The chiral organosilanes can be further transformed into versatile intermediates for asymmetric synthesis.



Keywords: amines · asymmetric hydrosilylation · carbon–carbon double bonds · carbon–silicon bond formation · chiral monodentate ligands · chiral organosilanes · dienes · palladium catalysts