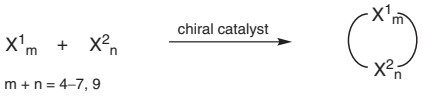
Abstracts

p 7

3.1 [m + n]-Cycloaddition Reactions (Excluding [4 + 2])

G.-J. Jiang, Y. Wang, and Z.-X. Yu

This manuscript covers asymmetric [m + n] cycloadditions for the synthesis of four- to seven-membered rings and nine-membered rings, catalyzed by transition metals or organic molecules using either chiral ligands orchiral catalysts as the chiral sources. These cycloaddition reactions can construct mono-, bi-, or even polycyclic compounds and generate up to four stereocenters in one pot, providing high efficiency in synthesis.



Keywords: asymmetric cycloaddition · [m + n] cycloaddition · C—C bond formation · chiral catalysts · chiral ligands · four-membered rings · five-membered rings · six-membered rings · seven-membered rings · nine-membered rings

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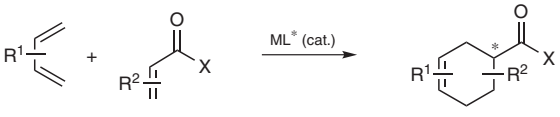
3.2 [4 + 2]-Cycloaddition Reactions

K. Ishihara and A. Sakakura

The Diels–Alder reaction is one of the most powerful organic transformations available and is a versatile tool for the synthesis of many bioactive natural products. Since the discovery of the effective promotion of the Diels–Alder reaction by Lewis acids, stereoselective versions have been extensively investigated. The presence of Lewis acid catalysts bearing chiral ligands allows the Diels–Alder reaction to be conducted under mild conditions, and regio-, diastereo-, and enantioselective reactions can be achieved. In addition, organocatalysis has been successfully applied to the asymmetric Diels–Alder reaction. Various chiral catalysts for the asymmetric hetero-Diels–Alder reactions are also described in this manuscript.



Keywords: asymmetric catalysis · Brønsted acid catalysts · cycloaddition · diastereoselectivity · Diels–Alder reaction · dienes · dienophiles · enantioselectivity · hetero-Diels–Alder reaction · Lewis acid catalysts

p 125

3.3 [m + n + 1]-Carbocyclization Reactions

T. Shibata

In this chapter [2 + 2 + 1]-carbocyclization reactions are discussed and the enantioselective Pauson–Khand reaction, namely a carbonylative alkyne–alkene coupling, is described comprehensively. Reactions catalyzed by chiral titanium, rhodium, iridium, and cobalt complexes are included. The use of aldehydes as a carbon monoxide donor in place of tox-

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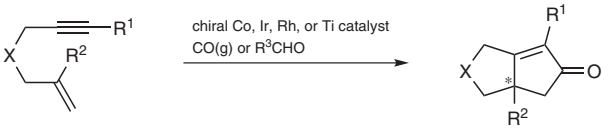
ic carbon monoxide gas is also discussed. Other stereoselective and/or regioselective [m+n+1] carbocyclizations, such as [3+2+1], [4+2+1], and [5+2+1] reactions, are also described.



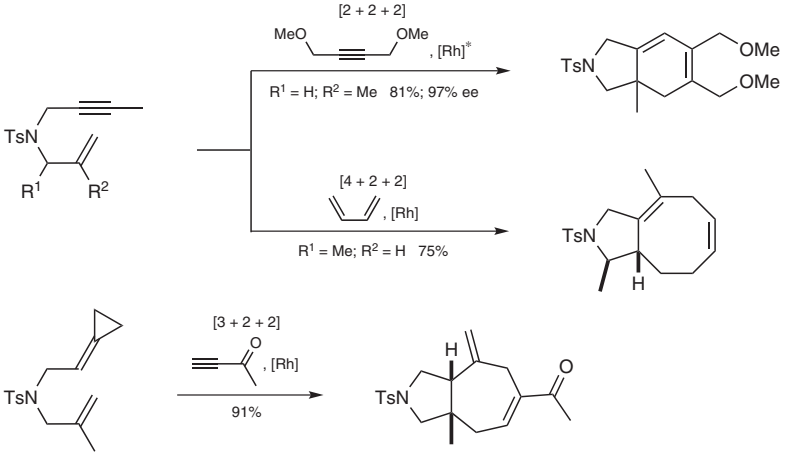
Keywords: aldehydes · alkyne–alkene coupling · bicyclopentenones · carbonylation · carbocyclization · cobalt catalysis · enynes · iridium catalysis · Pauson–Khand reaction · titanium catalysis · rhodium catalysis

p 145

3.4 [m+n+2]-Carbocyclization Reactions

C. Aubert, M. Malacria, and C. Ollivier

The [m+n+2] carbocyclization reactions of unsaturated compounds, which include the [2+2+2], [3+2+2], and [4+2+2] cyclizations, provide a very powerful synthetic tool for the construction of several carbon—carbon bonds in a single chemical transformation. The selection of the transition-metal catalyst, which orchestrates the cyclization reactions, is critical for attaining optimal chemo-, regio-, and stereoselectivity. This review outlines the various factors that govern these important processes using numerous examples to illustrate the synthetic utility.



Keywords: asymmetric catalysis · asymmetric synthesis · chirality · cocyclization · cyclic compounds · [2+2+2] cycloaddition · [3+2+2] cycloaddition · [4+2+2] cycloaddition · cyclotrimerization · diastereoselectivity · enantioselectivity · green chemistry · homogeneous catalysis · transition metals

p 243

3.5 Asymmetric Cycloisomerizations

I. D. G. Watson and F. D. Toste

This chapter will describe topics relating to the asymmetric cycloisomerization reaction. It will summarize some of the most important and recent developments in this area. The chapter will focus primarily on asymmetric C—C bond-forming cycloisomerizations, although some C—X bond-forming reactions (where X = heteroatom) are described. In par-

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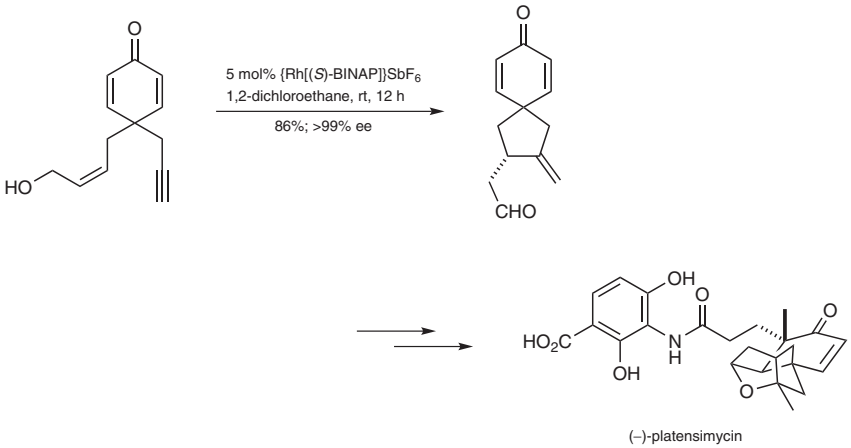
ticular, ene–yne and diene cycloisomerization, carbonyl-ene, Conia-ene, intramolecular hydroacylation and hydrosilation reactions will be discussed.



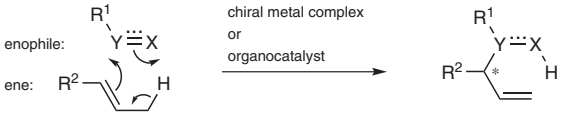
Keywords: Alder–ene reactions • asymmetric cycloisomerization • asymmetric catalysis • atom economy • carbocyclic compounds • carbonyl-ene reactions • C—H activation • Conia-ene reactions • cyclization • hydroacylation • hydrosilylation • intramolecular reactions

p 309

3.6 Ene Reactions

M. Terada

This manuscript focuses on recent achievements in the development of asymmetric ene reactions using chiral metal catalysts and organocatalysts. The contents are divided between intra- and intermolecular reactions, and are further subdivided according to the specific type of enophile used, including aldehydes, ketones, imines, alkynes, alkenes, and heteroatom-containing double bonds.



Keywords: acid catalysts • asymmetric catalysts • C—C bonds • carbonyl additions • chiral compounds • enantioselectivity • ene reactions • homoallylic alcohols • intramolecular reactions • Lewis acid catalysts • organocatalysts • pericyclic reactions

p 347

3.7 Sigmatropic Rearrangements

J. Zeh and M. Hiersemann

This manuscript covers stereoselective sigmatropic rearrangements, i.e. the Claisen, Cope, and [2,3]-Wittig rearrangement. It focuses on examples from natural product syntheses between 2005 and 2009.

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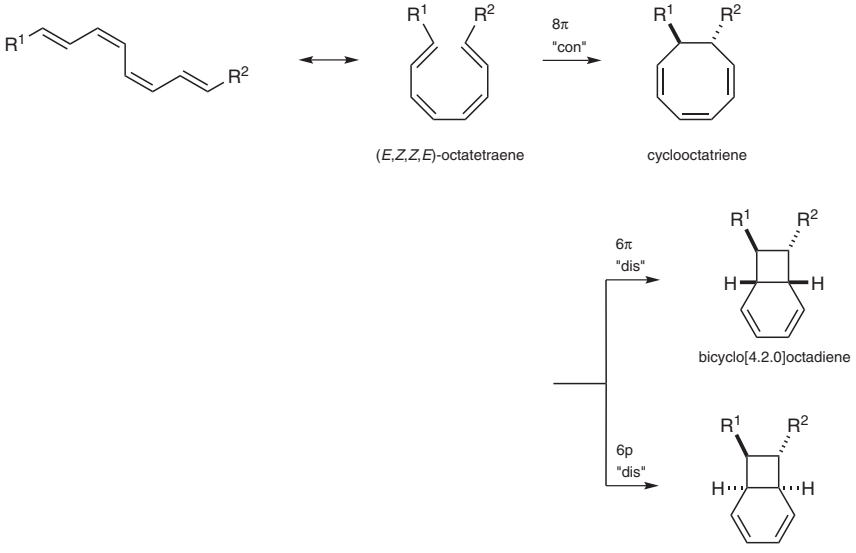
Keywords: asymmetric synthesis · sigmatropic rearrangements · Claisen rearrangement · Ireland–Claisen rearrangement · Cope rearrangement · [2,3]-Wittig rearrangement · carbonyl compounds · C—C bonds · homoallylic alcohols

p 383

3.8 Electrocyclic Reactions

B. Gaspar and D. Trauner

Electrocyclic reactions have provided many classic examples of stereoselectivity governed by orbital symmetry. Herein, we discuss the use in synthesis of electrocyclizations and electrocyclic ring openings involving four, six, and eight π-electrons. Both all-carbon systems and systems with heteratom substitution are presented. The role of electrocyclizations in stereoselective reaction cascades is highlighted.



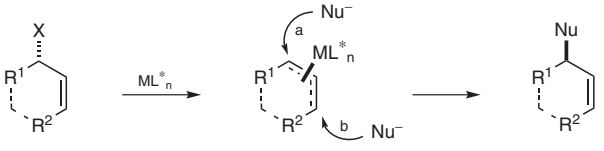
Keywords: asymmetric catalysis · cyclobutenes · cyclohexadienes · cyclooctatrienes · electrocyclization · electrocyclic ring opening · Nazarov cyclizations · Woodward–Hoffmann rules · reaction cascades

p 403

3.9 Allylic Substitution Reactions

M. L. Crawley

The allylic substitution reaction has evolved from a limited process of primarily academic interest to a powerful tool for the asymmetric formation of C—C, C—N, and C—O bonds.



Keywords: allylic substitution · asymmetric allylic alkylation · enantioselective · regioselective · transition-metal catalysis

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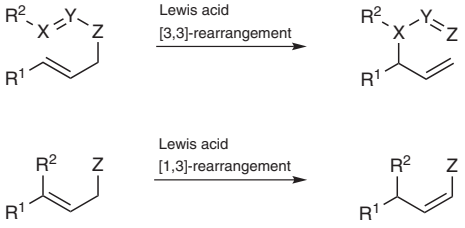
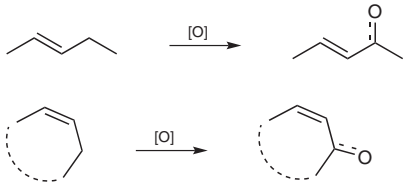
Isomerizations are often attractive reactions since they provide high atom and step economy. This manuscript describes Lewis acid catalyzed or promoted enantioselective isomerizations to form one or more stereogenic centers with a special focus on allylic rearrangements.



Keywords: allylic amines · allylic rearrangement · aza-Claisen rearrangement · aza-phospha-oxa-Cope rearrangement · Carroll rearrangement · Claisen rearrangement · imidates · isomerization · Lewis acid catalysis · Meerwein–Eschenmoser–Claisen rearrangement · palladacycles · sigmatropic rearrangement · thia-Claisen rearrangement · Wagner–Meerwein rearrangement

The selective oxidation of alkenes to give allylic alcohols and their derivatives is commonly performed using selenium dioxide. Conversion of alkenes into allylic esters is also facilitated using a palladium(II) acetate catalyst with benzoquinone and with catalytic copper complexes using perester oxidants. Regio- and stereoselectivity are reliably controlled through proper choice of reagent or additive, and by variation of the metal/ligand combination, but are often dependent on the substrate. Enone formation is promoted by various metal catalysts with *tert*-butyl hydroperoxide, and benzylic oxidation can be achieved using various metal catalysts and oxidants to give benzoyl and benzyl alcohol moieties. Biocatalytic methods have also been developed in a limited number of cases, using catalysts related to metal porphyrin cytochrome P450. C—H activation reactions at the allylic and benzylic position can thus be employed as an efficient approach to the installation of oxygen functionality at a late stage of a multistep synthesis and used as a means to construct enantioenriched starting materials. This section illustrates these transformations and examples are presented which demonstrate high levels of diastereo- and enantioselectivity.



Keywords: alcohol synthesis · allylic oxidation · benzylic oxidation · C—H activation · copper–perester oxidation · enone synthesis · ketone synthesis · palladium–quinone oxidation · selenium dioxide

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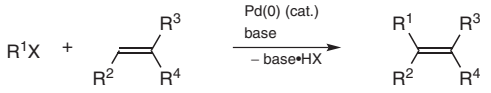
3.12 Mizoroki–Heck Reaction

M. Shibasaki, T. Ohshima, and W. Itano

This manuscript covers both intermolecular and intramolecular Mizoroki–Heck reactions (palladium-catalyzed arylation or alkenylation of alkenes) with brief discussion of the mechanistic aspects relevant for stereoselection.



R^1 = aryl, alkenyl;
X = halide, pseudohalide

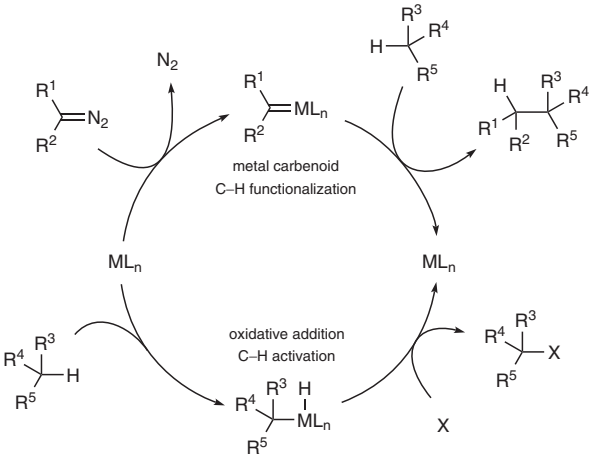
Keywords: alkenylation · arylation · enantioselectivity · palladium catalysts · phosphorus ligands · regioselectivity

p 513

3.13 C—C Bond Formation by C—H Bond Activation

H. M. L. Davies and D. Morton

This manuscript describes the C—C bond-forming reactions that are available via C—H activation. It provides an overview of the many developments in this field, highlighting the most efficient approaches and their application to relevant targets.



Keywords: carbenoids · carbocyclic compounds · C—C bond formation · C—H activation · chiral compounds · diazo compounds · rhodium complexes · rhodium catalysis · palladium complexes · palladium catalysis

p 567

3.14 Cross Coupling

M. Shimizu and T. Hiyama

Transition-metal-catalyzed cross-coupling reactions of organometallic reagents with organic (pseudo)halides have been developed to become one of the most powerful and straightforward methods for C—C bond formation available. This section focuses on those cross-coupling reactions that provide versatile solutions for a variety of stereochemical issues in modern organic synthesis.

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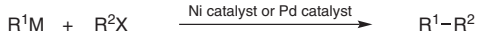


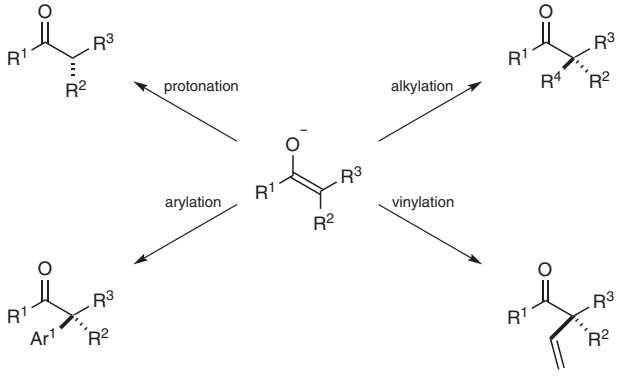
Keywords: alkenylation · alkylation · alkynylation · allylation · asymmetric synthesis · boron compounds · cross-coupling reactions · Grignard reagents · nickel catalysts · palladium catalysts · silicon compounds · tin compounds

p 615

3.15 Protonation, Alkylation, Arylation, and Vinylation of Enolates

B. M. Stoltz and J. T. Mohr

In this manuscript methods for enantioselective functionalization of enolates are reviewed, and strategies for controlling enolate formation, geometry, and steric environment are highlighted. The transformations discussed include protonation, alkylation, arylation, and vinylation of enolates. Enantioselective protonation methods including biocatalytic, stoichiometric, and catalytic processes are discussed. Chiral auxiliaries for alkylation, including acyclic and cyclic enolates, are compared. Other techniques for controlling enolate alkylation, such as chelation of the counterion or generation of transition metal enolates in situ, are analyzed. Enolate arylation with chiral auxiliaries or chiral transition-metal catalysts is reviewed and the processes compared. Vinylation of enolates, including very recent developments, is discussed. The methods covered provide an overview of the available transformations for functionalizing carbonyl compounds via the corresponding enolates. Synthetic applications are highlighted to show the utility of the techniques described.



Keywords: asymmetric catalysis · chiral auxiliaries · chiral ligands · cross coupling · enantioselective alkylation · enantioselective arylation · enantioselective protonation · enantioselective vinylation · enolates · nickel catalysis · palladium catalysis

p 675

3.16 α-Functionalization of Carbonyl Compounds

D. W. C. Macmillan and A. J. B. Watson

Chiral amine organocatalysts enable the facile asymmetric α-functionalization of carbonyl compounds. Under the enamine, SOMO, and photoredox catalysis platforms, C—C and C—X bonds (where X = heteroatom) can be forged, providing access to a broad range of enantioenriched products.

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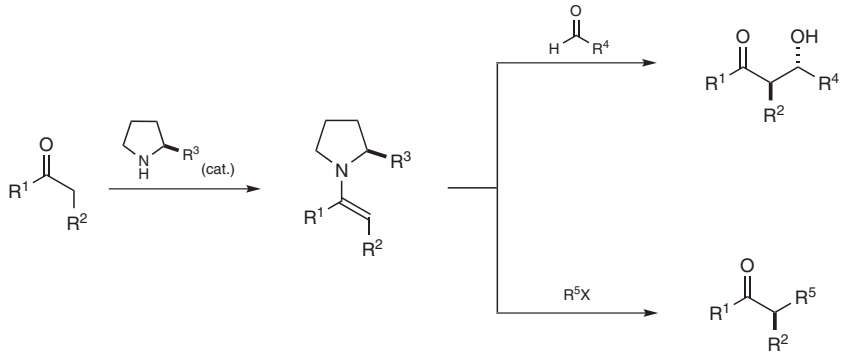


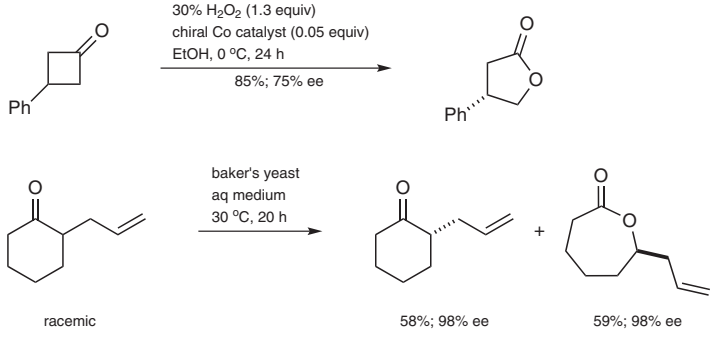
Keywords: aldehydes · asymmetric aldol reaction · alkylation, amine catalysts · asymmetric catalysis · C—C bonds · C—X bonds · chiral compounds · enamines · ketones · asymmetric Mannich reaction · asymmetric Michael reaction · organocatalysis · photoredox catalysis · singly occupied molecular orbital catalysis

p 747

3.17 Baeyer–Villiger Reactions

S. Levinger

Baeyer–Villiger oxidation of chiral and achiral cyclic ketones occuring within the chiral coordination space of metal catalysts or the active site of enzymes leads to the enantioselective formation of lactones accompanied by the kinetic resolution of chiral ketones. Various enzymatic approaches are presented.



Keywords: asymmetric catalysis · Baeyer–Villiger reaction · chiral cyclic ketones · chiral lactones · chiral metal catalysis · enzyme catalysis · kinetic resolution · monooxygenases · oxidation

p 759

3.18 Ring Opening of Epoxides, Aziridines, and Cyclic Anhydrides

J. B. Johnson

Epoxides and aziridines are well established as versatile synthetic intermediates. The electrophilic nature of these compounds dictates their reactivity, and nucleophiles readily attack to open the strained ring and produce 1,2-difunctionalized compounds. Cyclic anhydrides share similar characteristics, as they are also subject to nucleophilic attack and ring opening. Enantioselective ring-opening reactions of these species presents a means of transforming readily available and inexpensive starting materials into a wide range of synthetically viable difunctionalized materials while generating contiguous ste-

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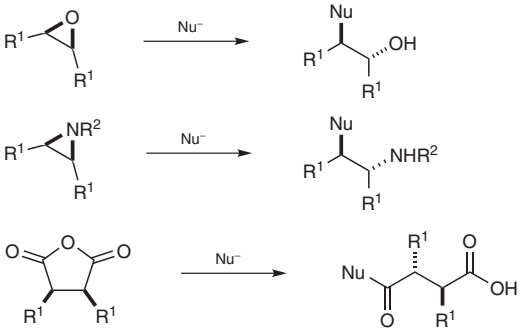
reocenters in a single transformation. The asymmetric addition of nucleophiles to epoxides, aziridines, and cyclic anhydrides has been achieved through enzymatic, main group and transition metal, and organocatalyic methods, presenting numerous means for the generation of a broad range of asymmetric synthons in high yields and enantioselectivities.



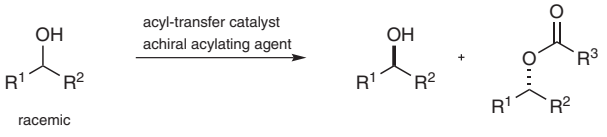
Keywords: asymmetric catalysis · aziridine · cyclic anhydride · epoxide · nucleophilic addition · ring opening · stereoselective synthesis

p 829

3.19 Acylation of Alcohols and Amines

T. Oriyama

Chiral acyl-transfer catalysts catalyze the asymmetric acylation of alcohols and amines. These reactions result in the stereoselective formation of new C—O and C—N bonds.



Keywords: amide synthesis · asymmetric acylation · chiral acyl-transfer catalysts · ester synthesis · kinetic resolution · *meso*-diol desymmetrization · racemic secondary alcohols · racemic amines

p 851

3.20 Asymmetric Fluorination, Monofluoromethylation, Difluoromethylation, and Trifluoromethylation Reactions

V. Gouverneur and O. Lozano

Organofluorine chemistry has established itself as an expanding area of research which benefits agricultural, medicinal, and materials science. With respect to industrial applications, stereoselective fluorination is of great use to medicinal chemists. This chapter presents the most efficient methods developed to date for stereoselective fluorination and fluoroalkylation. The field has progressed rapidly with the development of suitable reagents for direct fluorination as well as mono-, di-, and trifluoromethylation. Asymmetric fluorination is dominated by methods that rely on electrophilic (N—F) fluorinating reagents. Both transition-metal catalysts and organocatalysts have been adopted for the preparation of enantiopure compounds featuring a fluorine substituent on a stereogenic center, and dual activation using these two classes of catalysts simultaneously provides an elegant solution for the fluorination of the least activated substrates. In contrast to direct fluorination, asymmetric fluoroalkylation is more commonly performed using nu-

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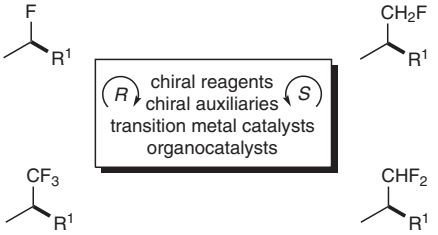
cleophilic reagents, in particular the Ruppert–Prakash reagent ($TMSCF_3$) as well as mono- and difluoro sulfone derivatives. To date, asymmetric catalytic fluoroalkylations are largely outnumbered by asymmetric methods, a notable exception being the photoredox organocatalytic trifluoromethylation of aldehydes with trifluoro(iodo)methane.



Keywords: chiral auxiliaries · chiral reagents · cinchona alkaloids · difluoromethylation · fluorination · fluorine · 1-fluorobis(phenylsulfonyl)methane · monofluoromethylation · *N*-fluorobenzene-1,2-disulfonimide · *N*-fluorobenzenesulfonimide · organocatalysis · Prins cyclization · Ruppert–Prakash reagent · Selectfluor · transition-metal catalysis · trifluoromethylation · Umemoto reagent

p 931

3.21 Stereoselective Polymerization

J.-F. Carpentier and E. Kirillov

This chapter exemplifies methods for stereocontrolled synthesis of several important classes of macromolecular/polymeric materials using organometallic/inorganic precatalysts and initiators. The facile and efficient methods of Ziegler–Natta-type catalytic polymerization and ring-opening metathesis polymerization (ROMP) are selected to provide access to stereoregular polyalkenes and polyalkynes. Stereoselective polymerization of methacrylate monomers, ring-opening polymerization (ROP) of cyclic esters, and syntheses of polycarbonates, polyethers, and polyketones are also featured.

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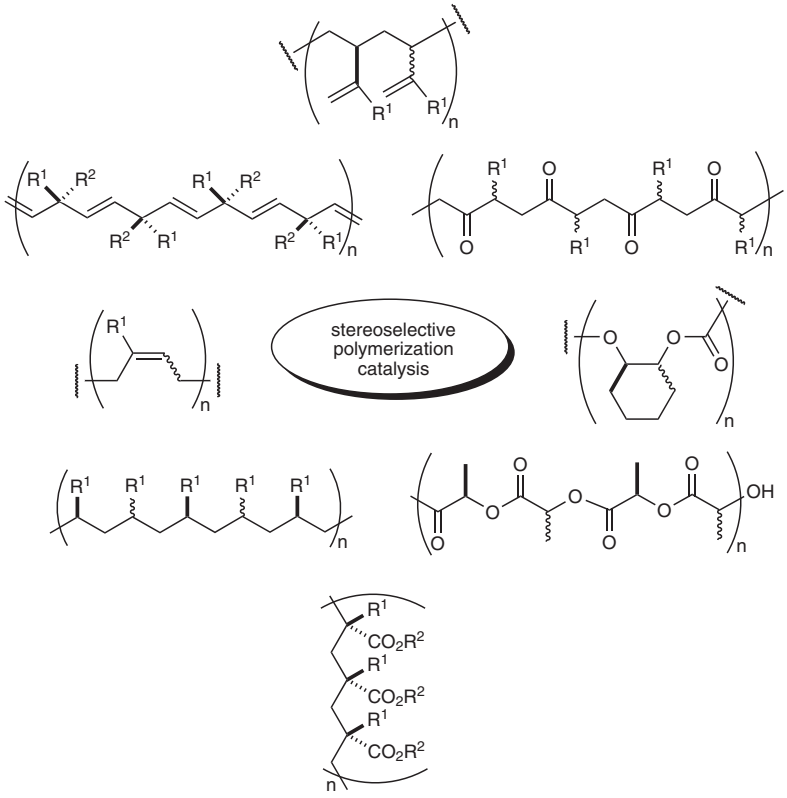

Keywords: catalysis · enantioselectivity · polyalkenes · polycarbonates · polyethers · polyketones · polylactides · polymerization · polymers · polymethacrylates · polyesters · ring-opening polymerization · ring-opening metathesis polymerization · stereoselectivity · tacticity · Ziegler–Natta polymerization

p 973

3.22 Oxidation of Sulfides

A. Lattanzi

This review focuses on the most efficient stoichiometric and catalytic methodologies reported for the highly stereoselective oxidation of sulfides to sulfoxides. The diastereoselective oxidation of sulfides bearing preexisting stereogenic centers by common metal and metal-free achiral oxidants is outlined. The chiral metal based procedures are described according to the metal in the complex used, namely titanium, vanadium, iron, aluminum, niobium, and molybdenum, in conjunction with structurally diverse chiral ligands. A section on metal-free oxidation of sulfides, illustrating the use of chiral oxaziridines and oxaziridinium salts as a mild and recoverable chiral source, is also included. Finally, the oxidation of sulfides with isolated enzymes such as peroxidases, monooxygenases, or more recently discovered whole-cell systems is included. Selected examples of industrial applications of oxidative methodologies for the synthesis of biologically active sulfoxides are also highlighted in the various sections.

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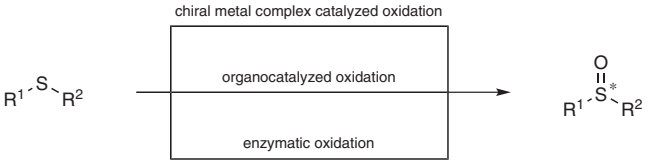

R^1 = alkyl; R^2 = aryl, alkyl, SR^3, NR^3R^4, OR^3

Keywords: sulfides · sulfoxides · sulfones · diastereoselectivity · enantioselectivity · metal-based oxidative systems · metal-free oxidation · titanium(IV) isopropoxide · tartrate esters · hydroperoxides · thiosulfinates · sulfinamides · sulfinates · 1,3-dithianes · 1,3-dithiolanes · kinetic resolution · chiral ligands · oxaziridinium salts · chiral dioxiranes · enzymes

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