

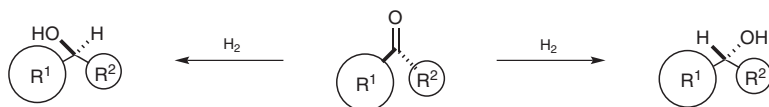
Abstracts

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2.1 Reduction of Carbonyl Groups: Hydrogenation

N. Arai and T. Ohkuma

In the first part of this review, diastereoselective hydrogenation of ketones, controlled mainly by steric interaction, with or without chelated metal intermediates, is discussed. This section includes a comparison of the stereoselectivity in the hydrogenation of 4-*tert*-butylcyclohexanone with heterogeneous and homogeneous catalysts, and 1,2- or 1,3-chiral induction in the reaction of ketones bearing a functional group, such as an amino or hydroxy group, that is capable of coordination. The second part of the review covers the enantioselective hydrogenation of various types of ketones and is further categorized into hydrogenation of functionalized ketones and that of nonfunctionalized simple ketones. Selected examples are provided in each section to illustrate practical methods for the preparation of a wide range of optically active secondary alcohols. Generally accepted catalytic cycles and explanations for the enantiofacial discrimination are also provided.



Keywords: alcohols · catalysts · diastereoselectivity · enantioselectivity · hydrogenation · ketones

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2.2 Reduction of Carbonyl Groups: Transfer Hydrogenation, Hydrosilylation, Catalytic Hydroboration, and Reduction with Borohydrides, Aluminum Hydrides, or Boranes

M. Zaidlewicz and M. M. Pakulski

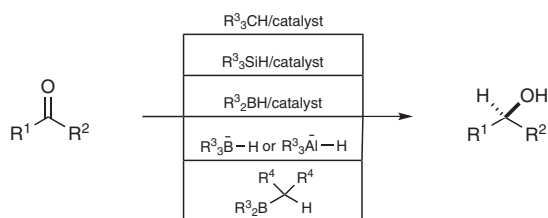
The stereoselective reduction of ketones and functionalized ketones by the following methods, leading to products with high selectivity, is described:

Transfer hydrogenation: diastereoselective and enantioselective Meerwein–Ponndorf–Verley reduction; asymmetric transfer hydrogenation with propan-2-ol and formic acid/triethylamine, catalyzed by group 8 and 9 metal complexes in organic solvents and in water; immobilized catalysts and biomimetic reductions.

Hydrosilylation: asymmetric hydrosilylation, catalyzed by rhodium, titanium hydride, and copper hydride complexes; organocatalytic asymmetric hydrosilylation.

Catalytic hydroboration: asymmetric hydroboration with borane and catecholborane, catalyzed by oxazaborolidines, (aminoalkoxy)boranes, and aminoborates.

Reduction with borohydrides, aluminum hydrides, and boranes: stoichiometric asymmetric reduction with hydridoaluminates and boranes, such as *B*-isopinocampheyl-9-borabicyclo[3.3.1]nonane, chlorodiisopinocampheylborane, and derivatives; diastereoselective and enantioselective reduction with borohydrides.



$R^1 = \text{alkyl, aryl}; R^2 = \text{alkyl, aryl}$

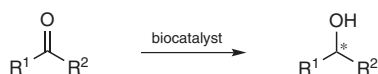
Keywords: asymmetric reduction • transfer hydrogenation • hydrosilylation • hydroboration • borohydrides • aluminum hydrides • boranes • (aminoalkoxy)boranes • aminoborates

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2.3 Enzymatic Reduction of Carbonyl Groups

S. De Wildeman and N. Sereinig

Enzyme-mediated carbonyl reductions have been studied for many decades and have been introduced in several industrial processes for the production of various chiral alcohols. The earlier hurdle of expensive cofactors has been overcome by the development of highly efficient cofactor-regeneration methods that are easily implemented in chemical laboratories. Screening and testing of alcohol dehydrogenases attracts a growing community of chemists looking for shortcuts or competitive technologies in route-scouting of fine chemicals, while the robustness of the technology allows penetration into bulk chemicals business. The growing number of suitable and accessible dehydrogenases is demonstrated in substrate-categorized tables throughout the chapter, indicating that these enzymes often show high stereospecificity and activity on an impressive set of ketone substrates.



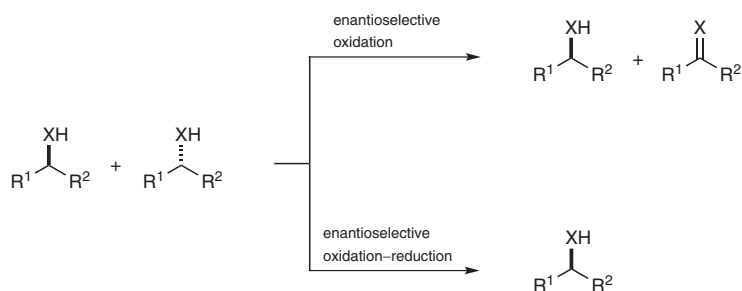
Keywords: alcohol dehydrogenases • ketoreductases • biocatalysts • enzyme catalysis • chiral compounds • alcohols • ketones • cofactor • cofactor regeneration • enzyme screening • whole cells • microorganisms

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2.4 Oxidative Deracemization

B. Stoltz, D. C. Ebner, and N. Park

The oxidative deracemization of alcohols and amines is described. This procedure generates enantioenriched alcohols and amines from the corresponding racemates by enantioselective oxidation. Methods involving kinetic resolution and oxidation–reduction coupled processes are presented. Kinetic resolution of alcohols can be accomplished by transfer hydrogenation, aerobic metal-catalyzed enantioselective oxidation, oxidation with nitroxyl radical based catalysts, manganese catalysts, and biocatalysts. Kinetic resolution with biocatalysts can also provide enantioenriched amines and amino acids. Enantioselective alcohol oxidation coupled with reduction can also afford enantioenriched alcohols via chemical systems, chemoenzymatic processes, microbial deracemizations, and multi-enzymatic systems. Enantioenriched amines and amino acids are also provided in deracemizations involving enantioselective enzymatic oxidation and chemical or enzymatic reductions.



X = O, NH

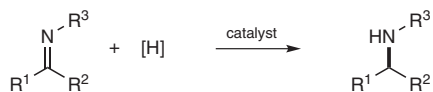
Keywords: alcohols · amines · kinetic resolution · ketones · imines · oxidation · reduction · catalysts · biocatalysts · enzyme catalysis · stereoselectivity

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2.5 Stereoselective Reduction of Imino Groups

L. Xu, X. Wu, and J. Xiao

This chapter presents a wide range of efficient methods for enantio- and diastereoselective reduction of isolated and in situ formed imino compounds, including hydrogenation with hydrogen gas and transfer hydrogenation with an organic hydrogen source.



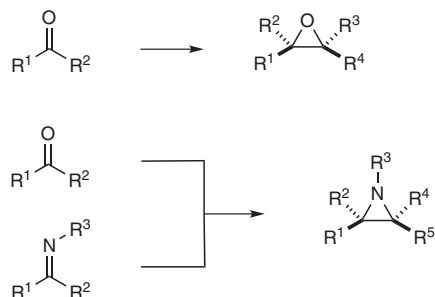
Keywords: imines · amines · hydrogenation · transfer hydrogenation · hydroboration · hydrosilylation · reductive amination · asymmetric reduction

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2.6 Epoxidation and Aziridination of Carbonyl Groups and Imines

V. K. Aggarwal, E. M. McGarrigle, and M. A. Shaw

Aldehydes and ketones can be stereoselectively transformed into epoxides in one step. Aziridines can be synthesized stereoselectively in one step from either aldehydes or imines. Selected diastereoselective and enantioselective methods are reviewed and sample procedures are given.

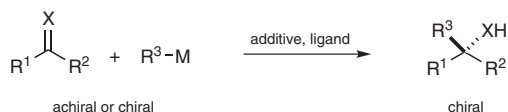


Keywords: aldehydes · asymmetric catalysis · asymmetric synthesis · aziridines · diazo compounds · epoxides · imines · ketones · Lewis acids · rhodium catalysts · sulfur ylides · ylides

2.7 Alkylation of Carbonyl and Imino Groups

D. J. Ramón and M. Yus

In this section, different protocols for the diastereoselective addition of alkylmetal reagents to aldehydes, ketones, and imines using chiral reagents are presented, as well as the related enantioselective addition of alkylmetal reagents to carbonyl derivatives using chiral ligands.



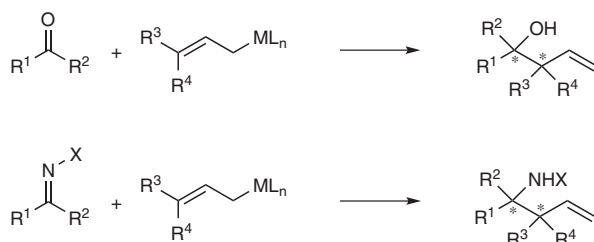
X = O, NR⁴

Keywords: nucleophilic alkylation · ketones · imines · aldehydes · alcohols · amines · enantioselectivity · diastereoselectivity

2.8 Allylation of Carbonyl and Imino Groups

A. Buitrago Santanilla and J. L. Leighton

Aldehydes, ketones, aldimines, and ketimines may all be allylated with high levels of enantioselectivity by the addition of allylmetal (or allylmetaloid) reagents. Preformed chiral allylmetal reagents, preformed achiral allylmetal reagents in combination with a chiral catalyst, and chiral allylmetal reagents formed catalytically in situ have all been employed with significant success. The reactions stereoselectively form a C—C bond and one or two stereocenters and provide access to a variety of homoallylic alcohols and amines.

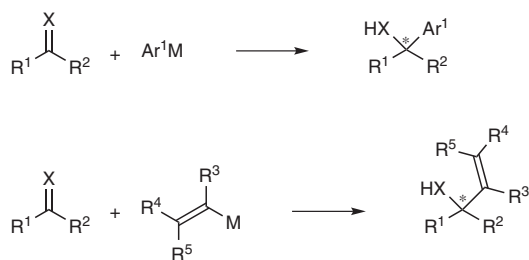


Keywords: allylation · crotylation · cinnamylation · aldehydes · ketones · aldimines · ketimines · allylboranes · allylboronates · allylsilanes · allylzincs · allylindiums

2.9 Arylation and Alkenylation of Carbonyl and Imino Groups

M. C. Kauffman and P. J. Walsh

Enantioenriched benzylic and allylic alcohols and amines are important synthetic intermediates and are present in many natural products and target molecules in medicinal chemistry. The most direct and efficient route to these compounds is the addition of an aryl or vinyl nucleophile to a carbonyl compound or imine. This review highlights the most important synthetic methods for the arylation and alkenylation of aldehydes, ketones, and imines.



X = O, NR⁶

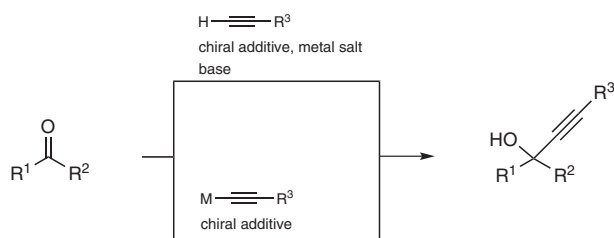
Keywords: aldehydes · alkenylation · allylamines · allylic alcohols · arylation · hydroboration · benzylic compounds · ketones · imines · transmetalation · vinylation · zinc catalysts

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2.10.1 Enantioselective Addition of Acetylide Nucleophiles to Carbonyl Compounds

E. M. Carreira and D. E. Frantz

A survey of state-of-the-art methods for the alkynylation of carbonyl compounds is presented. Electrophiles that are described include aldehydes and ketones, which react with alkynyl nucleophiles to afford the corresponding secondary and tertiary alcohols. The collection of stereoselective methods prescribe the use of stoichiometric and substoichiometric quantities of chiral additives and metal salts or reagents. Special attention is given to methods that are practical and general.



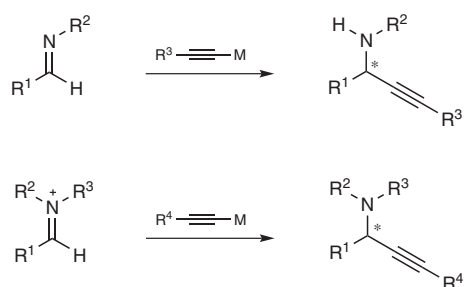
Keywords: alkynylation · propargyl alcohols · metal acetylides · aldehyde/ketone additions · enantioselectivity

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2.10.2 Enantioselective Addition of Metal Alkynylides to Imino Groups

E. M. Carreira and P. Aschwanden

Advances in catalytic, enantioselective additions of alkynylides to imines are described. The selected methods represent the state of the art in this rapidly evolving area.



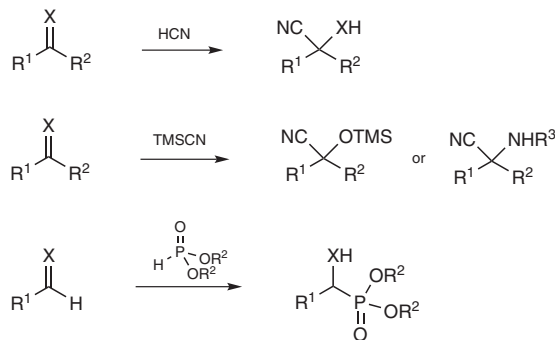
Keywords: asymmetric catalysis · imines · alkynylides · copper · propargylamines

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2.11 Hydrocyanation, Cyanosilylation, and Hydrophosphonylation of Carbonyl and Imino Groups

E. Bergin

This review describes practical methods for the asymmetric hydrocyanation, cyanosilylation, and hydrophosphonylation of carbonyl and imino groups. The applications of metal-based catalysis, organocatalysis, and enzymatic reactions are all discussed.



X = O, NR³

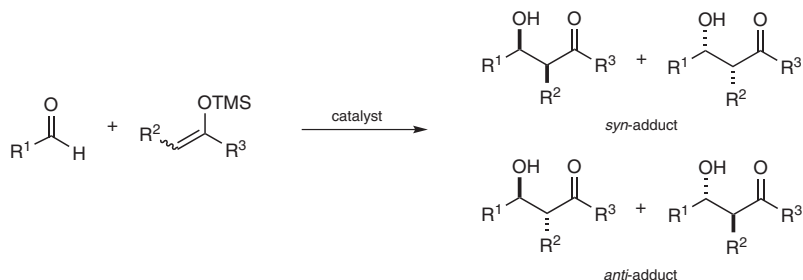
Keywords: hydrocyanation · cyanosilylation · hydrophosphonylation · Strecker synthesis · asymmetric catalysis · cyanohydrins · aminonitriles · hydroxyphosphonates

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2.12 Asymmetric Mukaiyama Aldol Reaction

L. Liu, D. Wang, and C.-j. Li

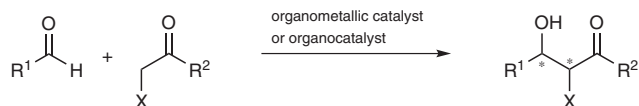
Asymmetric Mukaiyama aldol reactions proceed smoothly under Lewis acid catalysis, Lewis base catalysis and organocatalysis to afford chiral aldol adducts, which have been widely applied in organic syntheses. The employment of the asymmetric Mukaiyama aldol reaction leads to regioselective and stereoselective formation of new carbon–carbon bonds.



Keywords: asymmetric Mukaiyama aldol reaction · chiral aldol adduct · diastereoselectivity · enantioselectivity · Lewis acid catalysis · Lewis base catalysis · organocatalysis · regioselectivity · silyl enol ethers

2.13 Direct Aldol Reaction*S. M. Yliniemelä-Sipari and P. M. Pihko*

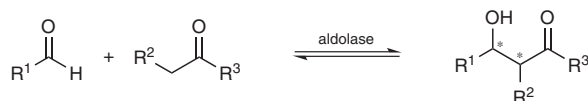
This review discusses synthetic methods for the enantioselective, catalytic direct aldol reaction between enolizable carbonyl compounds or aliphatic nitro compounds and aldehydes or ketones as acceptors, and is presented from a practical, preparative standpoint, illustrated with selected examples from the literature. The scope and limitations of the protocols are discussed. Approaches using metal-based catalysts and organocatalysts are included.



Keywords: direct aldol reaction · asymmetric synthesis · direct nitroaldol reaction · organometallic catalysis · organocatalysis

2.14 Enzymatic Direct Aldol Additions*P. Clapés and W.-D. Fessner*

Direct aldol additions catalyzed by aldolases are finding increasing acceptance in chemical research and production for the synthesis of asymmetric compounds due to the high selectivity and efficacy of the process. Carbonylating enzymes offer a unique tool to perform asymmetric carbon–carbon bond formation in a sustainable, environmentally benign fashion. In this section, the different methodologies and procedures used for enzymatic carbon–carbon bond formation are described. These include the asymmetric catalytic aldol additions of dihydroxyacetone phosphate (DHAP), 1-hydroxyalkan-2-ones (i.e., dihydroxyacetone, hydroxyacetone, and hydroxybutanone), pyruvate, glycine, acetaldehyde, and glycolaldehyde as the nucleophilic components to a variety of electrophilic aldehyde structures.



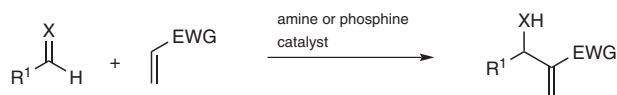
R^1 = alkyl, aryl, etc.; R^2 = H, F, OH, NH_2 ; R^3 = H, Me, Et, OH, CH_2OH , CO_2H , $\text{CH}_2\text{PO}_4^{2-}$

Keywords: asymmetric carbon–carbon bond formation · aldol additions · DHAP-dependent aldolases · D-fructose 6-phosphate aldolase from *E. coli* (FSA) · DHAP mimics · transketolases · pyruvate aldolases · glycine aldolases · self- and cross-aldol additions of aldehydes · 2-deoxy-D-ribose 5-phosphate aldolase · dihydroxyacetone phosphate (DHAP) · dihydroxyacetone (DHA) · hydroxyacetone (HA) · hydroxybutanone (HB) · pyruvate · glycine · glycolaldehyde · alkylaldehydes · hydroxyaldehydes · aminoaldehydes

2.15 Asymmetric Morita–Baylis–Hillman Reaction and Its Aza Analogue*G. Masson and J. Zhu*

The development of the asymmetric Morita–Baylis–Hillman reaction has evolved dramatically over the past few years and remains an important and highly active research field in organic chemistry. This section summarizes recent mechanistic insights and advances in

the design and synthesis of small organic molecules for the enantioselective Morita–Baylis–Hillman reaction and its aza counterpart.



X = O or NZ (Z = electron-withdrawing group)

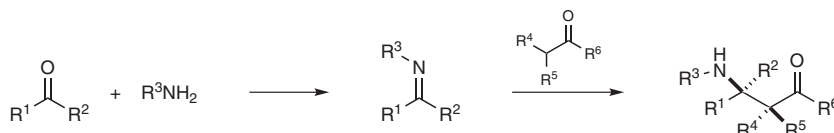
Keywords: asymmetric synthesis • Brønsted acids • Lewis bases • organocatalysis • reaction mechanisms • tertiary amines • tertiary phosphines • bifunctional catalysts • Morita–Baylis–Hillman reaction • aza–Morita–Baylis–Hillman reaction

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2.16 Mannich Reaction

N. Z. Burns and E. N. Jacobsen

This chapter focuses on modern methods for the stereoselective formation of a C–C bond between an enolate or enolate equivalent and a C=N bond: the Mannich reaction. The majority of such processes utilize asymmetric catalysis. The chapter is organized according to the type of Mannich base produced and includes β -amino ester/amide products, β -amino ketone products, products from the addition of β -dicarbonyl nucleophiles, β -amino aldehyde products, the vinylogous Mannich reaction, the nitro-Mannich reaction, the synthesis of 1,2-diamines, and additions to nitrogen-containing heterocycles.



Keywords: aldimines • β -amino acids • β -amino aldehydes • β -amino amides • β -amino esters • β -amino ketones • aza-Henry reaction • Brønsted acids • carbolines • cinchona alkaloid catalysis • hydrogen bonds • isoquinolines • ketimines • Lewis acid catalysts • Mannich bases • Mannich reaction • nitro-Mannich reaction • phase-transfer catalysis • sulfinyl compounds

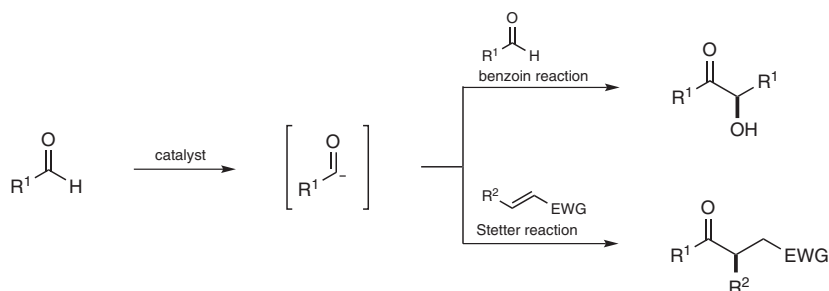
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2.17 Asymmetric Benzoin and Stetter Reactions

D. A. DiRocco and T. Rovis

N-Heterocyclic carbenes and metallophosphites have proven to be efficient and selective catalysts for the asymmetric benzoin and Stetter reactions. Enzymes are also useful catalysts for the benzoin reaction. These catalysts allow the stereoselective synthesis of a variety of 1,2- and 1,4-functionalized compounds in a mild and unconventional manner. Utilizing “umpolung” reactivity, aldehydes and aldehyde surrogates can be transformed efficiently into the corresponding ketone products without the use of the traditional harsh, forcing conditions. Aldehydes react in homobenzoin reactions catalyzed by N-heterocyclic carbenes and enzymes to yield the corresponding α -hydroxy ketones in good yield and high enantioselectivity. Heterobenzoin reaction products can also be synthesized efficiently in a cross silyl-benzoin reaction using aldehydes and acylsilanes, as well as by enzyme catalysis with the corresponding aldehydes. The Stetter reaction allows an entry into the stereoselective synthesis of 1,4-functionalized compounds by coupling aldehydes with a variety of Michael acceptors. Intra- and intermolecular Stetter reactions can be catalyzed highly efficiently and stereoselectively by N-heterocyclic carbenes. Similarly, met-

alophosphites are shown to catalyze the reaction of acylsilanes with Michael acceptors efficiently and highly enantioselectively.



Keywords: benzoin reaction · Stetter reaction · triazolium salts · thiazolium salts · enzymes · aldehydes · metallophosphites · acylsilanes · imines · ketones · cyclization · desymmetrization · cyclohexadienones · glyoxamide · alkylidenemalonates · nitroalkenes · acylation · amides

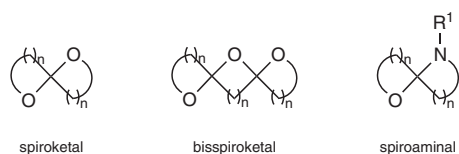
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2.18 Asymmetric Synthesis of Spiroketal, Bisspiroketal, and Spiroacetal

R. G. Carter and D. L. Kuiper

The spiroketal group consists of two intersecting rings connected via a spiro linkage in which each ring has one oxygen bonded to the central spiro carbon. This structural motif is found widely in many natural products. Although a wide array of ring sizes are theoretically possible, the three most common examples are spiroketals containing combinations of five- and six-membered rings (5,5-, 5,6-, and 6,6-spiroketal). Bisspiroketal contains two spiroketal moieties that share a common central ring system. Spiroaminals are spiroketals in which one of the oxygen atoms is replaced by a nitrogen atom.

This review focuses particularly on the asymmetric synthesis of spiroketals and spiroaminals in the context of natural product synthesis.



Keywords: spiro compounds · cyclization · natural products · acetalization · ketals · diastereoselectivity · acid catalysts · anomeric effect

