

Abstracts

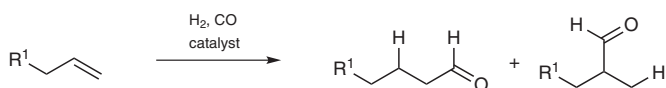
p 23

1.1.1 Hydroformylation of Alkenes

R. P. J. Bronger, P. C. J. Kamer, and D. Vogt

Hydroformylation of alkenes is a mild and clean method for the functionalization of hydrocarbons and has grown to be among the most important homogeneously catalyzed reactions in industry. It is a 100% atom-economic reaction to prepare aldehydes that are important synthons for organic synthesis, and has wide functional group compatibility.

In this review the focus is on the effects of various catalysts on the selective hydroformylation of both functionalized and unfunctionalized alkenes to produce high-value aldehydes. In particular, rhodium catalysts have undergone a remarkable development, while cobalt catalysts have remained more or less unchanged over the years, and palladium has recently been recognized as a suitable transition metal for hydroformylation.



Keywords: hydroformylation · homogeneous catalysis · aldehydes · phosphorus ligands · ligand design · rhodium · cobalt · palladium · platinum

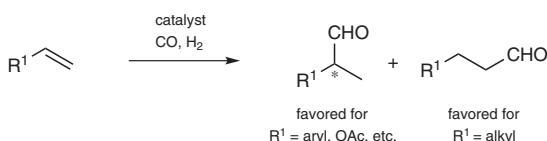
p 63

1.1.2 Asymmetric Hydroformylation of Alkenes

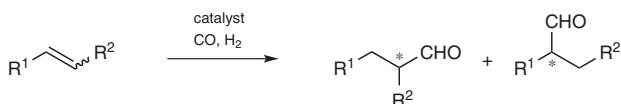
C. Godard, B. F. Perandones, and C. Claver

Asymmetric hydroformylation is a very promising catalytic reaction that produces chiral aldehydes from inexpensive feedstocks (alkenes and syngas) in a single step under essentially neutral reaction conditions. Asymmetric hydroformylation offers a great potential for the fine chemical industry since enantiomerically pure or enriched aldehydes can be obtained through hydroformylation of a variety of substrates using the appropriate chiral-phosphorus-modified rhodium catalyst. This chapter presents the successful transformations of benchmark and specific substrates, organized according to the substitution pattern.

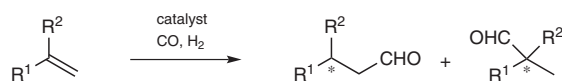
monosubstituted alkenes



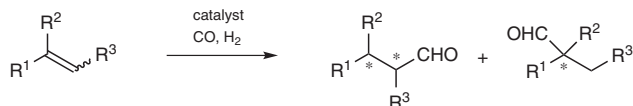
1,2-disubstituted alkenes



1,1-disubstituted alkenes



trisubstituted alkenes



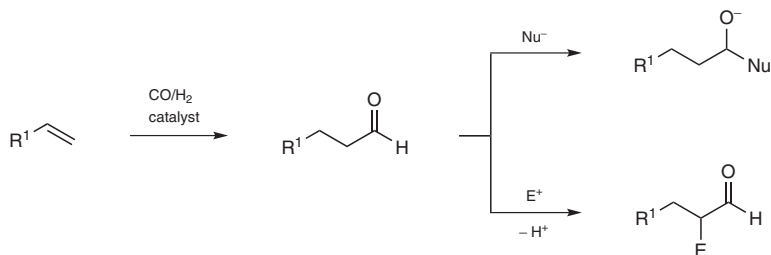
Keywords: asymmetric catalysis · hydroformylation · rhodium · chirality · phosphorus ligands · aldehydes

p 107

1.1.3 Tandem Hydroformylation of Alkenes

I. Fleischer and E. Mejía

This overview encompasses the most recent developments in the field of tandem hydroformylation reactions up to late 2012. The combination of the hydroformylation of alkenes and a subsequent transformation of the corresponding aldehydes gives access to a broad range of functionalities, relevant for both academy and industry. The chapter is subdivided according to the type of functionalization following the hydroformylation step.



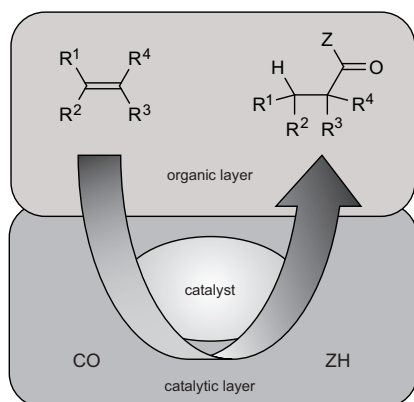
Keywords: acetalization · aldehydes · aldol reaction · alkenes · amines · C—C bonds · carbon—heteroatom bonds · homogeneous catalysis · hydroformylation · metal carbonyl complexes · rhodium catalysts · tandem reactions · domino reactions · Wittig reaction · reductive amination

p 165

1.1.4 Nonconventional Reaction Media: Hydroformylation, Carbonylation, and Hydroxycarbonylation of Alkenes

A. Mortreux, M. Sauthier, E. Monflier, and S. Tilloy

This chapter focuses on catalytic reactions involving the use of carbon monoxide and alkenes together with tertiary substrates such as hydrogen, alcohols, amines, or water where the catalyst recovery and recycling has been emphasized via the use of biphasic media. These atom-economical catalytic reactions result in the synthesis of aldehydes, esters, amines, and carboxylic acids, as well as polyketones, where the activity and regioselectivity concerns have been addressed.



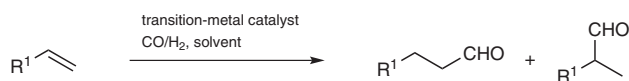
Keywords: hydroformylation · hydroesterification · carbonylation · hydroxycarbonylation · carbon monoxide · biphasic catalysis · ionic liquid · water-soluble ligands · phosphines · cyclodextrins · recycling · regioselectivity

p 193

1.1.5 Hydroformylation of Alkenes: Industrial Applications

J. G. de Vries

Alkenes can be converted into aldehydes using a highly atom-efficient hydroformylation reaction in which carbon monoxide and hydrogen are added across the double bond. In this chapter industrial hydroformylation processes are described. Catalysts are based on cobalt with or without trialkylphosphine ligands, or rhodium with triarylphosphine ligands or monodentate or bidentate triaryl phosphite ligands. The products are raw materials for plasticizers and solvents.



Keywords: alcohols · aldehydes · alkenes · carbonyl complexes · cobalt catalysts · diols · hydroformylation · isomerization · rhodium catalysts · phosphine oxides · phosphines · phosphites

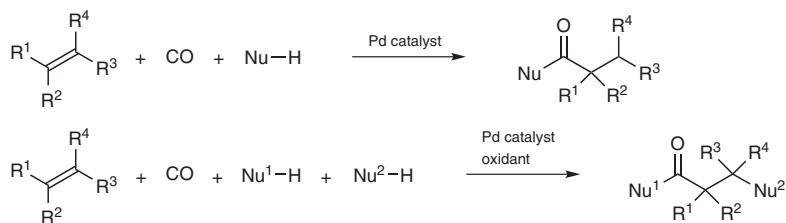
p 229

1.1.6 Carbonylation of Alkenes

M. L. Clarke and J. A. Fuentes

This chapter provides a concise overview of metal-catalyzed additions to alkenes that involve carbon monoxide and another nucleophilic species, such as water or an alcohol. This is an important area of research in terms of several commodity chemical targets, with many papers devoted to the evolution and mechanistic interrogation of catalysts that are viable for industry. This chapter demonstrates that this class of reaction is synthetically useful for a wide range of possible target molecules. Such reactions include the formation of carboxylic acids, including the “profen” family of drugs by hydroxycarbonylation of vinylarenes, in which it is now possible to control both regioselectivity and, to a lesser degree, enantioselectivity. The alkoxy carbonylation of alkenes primarily refers to what is more strictly a hydroalkoxy carbonylation, where hydride and carbon monoxide are added across an alkene and then terminated with an alcohol. Both intermolecular and intramolecular variants of this reaction are discussed. Other variants of alkene carbonylation are those where a nucleophile attacks an alkene, with the other terminus be-

ing functionalized with a carboxylic acid derivative derived from carbon monoxide. A few examples are highlighted with typical experimental procedures that should aid the non-specialist in conducting these reactions.



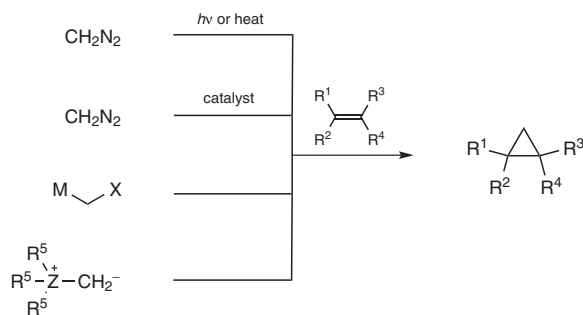
Keywords: alkoxyacylation · hydroalkoxyacylation · hydroesterification · hydroxycarbonylation · hydrocarbonylation · cyclization · asymmetric synthesis · carbon monoxide · carboxylic acids · carboxylic acid esters · chiral phosphines · large-scale processes · atom efficiency · green chemistry

p 259

1.1.7 Cyclopropanation of Alkenes with C-1

T. R. Belderrain and M. C. Nicasio

Cyclopropanation of alkenes is a direct route for the synthesis of cyclopropanes. This can be achieved by various methodologies. Specifically, this chapter is intended to provide an overview of the use of one-carbon reagents in cyclopropanation; thus, only synthetic methodologies regarding the use of methylene-transfer reagents are discussed.



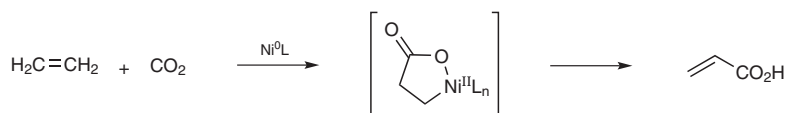
Keywords: alkenes · cyclopropanes · diazomethane · carbenes · transition-metal catalysis · dihalomethanes · zinc reagents · ylides

p 281

1.1.8 Addition of Carbon Dioxide to Alkenes and Other Unsaturated Hydrocarbons

J. Takaya and N. Iwasawa

Various transition-metal complexes promote C–C bond-forming reactions of carbon dioxide with acyclic unsaturated hydrocarbons including alkenes, alkynes, 1,3-dienes, and allenes. These reactions provide efficient methods for the synthesis of carboxylic acids and their derivatives.



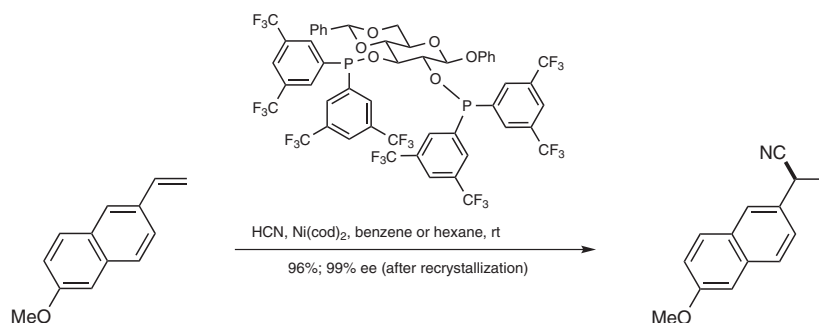
Keywords: carbon dioxide · carboxylic acids · esters · lactones · pyrones · C—C bond formation · transition metals · alkenes · 1,3-dienes · alkynes · allenes

p 309

1.1.9 Hydrocyanation of Alkenes

M. E. Tauchert

Hydrocyanation of alkenes is an atom-economical reaction to install a functionalized C-1 building block into a molecule. The reaction can be run to yield either the linear or the branched nitrile product. Branched nitriles can be produced in moderate to good enantiomeric excess. A detailed overview of the mechanism of nickel-catalyzed hydrocyanation is provided to help assess the scope and limitations of this reaction.



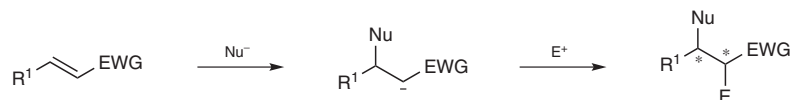
Keywords: styrene · vinylarenes · dienes · hydrocyanation · alkenes · nitriles · nickel · palladium

p 341

1.1.10 Stereoselective Conjugate Addition of Methyl and Cyanide

B. Goldfuss

Conjugate additions of methyl and cyanide nucleophiles to Michael acceptors are powerful methods for stereoselective homologation. New ligands and a variety of copper sources today enable highly enantioselective nucleophilic 1,4-methylations. Besides Grignard reagents, methylzinc reagents and trimethylaluminum are well established as nucleophilic methyl sources. Enantioselective cyanations of alkenes, aldehydes, or imines can be accomplished with metal catalysts (e.g., based on nickel, aluminum, or titanium) or organocatalysts, mostly employing silyl cyanides or acetone cyanohydrin as the cyanide source.

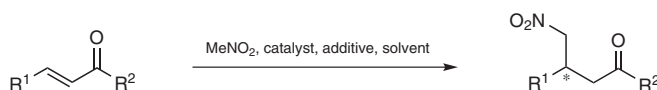


Nu = Me, CN

Keywords: copper catalysts · methyl Grignard reagents · methylaluminum reagents · cyanide · asymmetric catalysis · asymmetric synthesis · conjugate addition · C—C bonds · carbon—heteroatom bonds · Michael acceptors · nucleophilic addition

1.1.11 Enantioselective Conjugate Addition of Nitromethane*R. Ballini and M. Petrini*

The enantioselective conjugate addition of nitromethane to electron-poor alkenes is a powerful synthetic strategy allowing the introduction of a single carbon linked to a nitrogen atom in its higher oxidation state. The installation of a newly generated stereocenter in enantioenriched form and the subsequent reduction of the nitro group to an amino functionality represents a flexible gateway to the preparation of optically active amino-containing compounds. Organocatalytic methods are the most exploited procedures for this purpose and may involve activation of the carbonyl group in the corresponding enones and enals by optically active secondary amines (iminium ion catalysis). Activation of nitromethane using thiourea derivatives is also a viable approach to attain the corresponding adducts with high enantioselectivity. Chiral complexes of lanthanum, aluminum, and copper are also successfully used for this purpose and are substantially based on the activation of both nitromethane and the Michael acceptor.

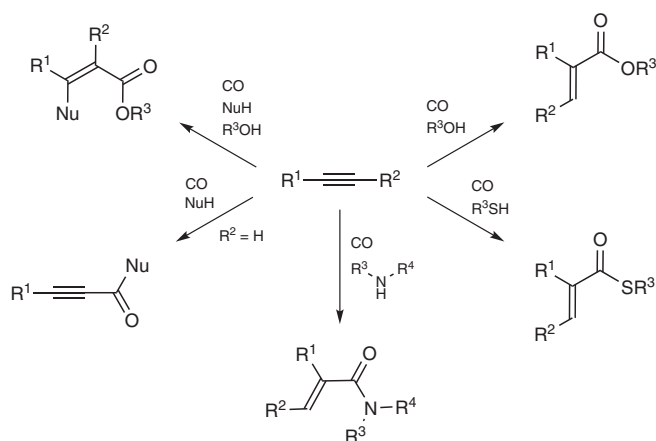


R¹ = alkyl, aryl; R² = H, alkyl, aryl, OR³

Keywords: conjugate addition · iminium ion · nitromethane · organocatalysis · metal catalysis · pyrrolidines · thioureas · unsaturated aldehydes · unsaturated ketones · unsaturated esters

1.2.1 Carbonylation of Alkynes*M. L. Clarke and J. A. Fuentes*

This chapter provides a concise overview of metal-catalyzed additions to alkynes that involve carbon monoxide and a nucleophilic species, such as water, an alcohol, a thiol, or an amine. Alkynes undergo very efficient hydroalkoxyesterifications of the type extensively studied in alkene carbonylation chemistry, but in this case giving unsaturated esters and seemingly by a different mechanism that allows for a wider range of reaction pathways. In this chapter, examples are presented where relatively subtle changes in substrate structure or competing pathways lead to a range of products; nucleophiles can add to alkynes in an intramolecular fashion prior to carbonylation, or external nucleophiles attack an alkyne to initiate a carbonylation. The carbonylation events can also be terminated in several different ways, especially under oxidative conditions. Several representative experimental procedures are given for the main classes of carbonylation covered.



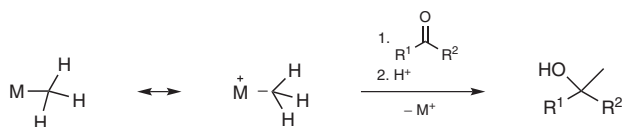
Keywords: alkoxyesterification · hydroalkoxycarbonylation · hydroesterification · hydroxycarbonylation · cyclization · asymmetric synthesis · carbon monoxide · alkynes · atom efficiency

p 415

1.3.1 Stereoselective (Nucleophilic) Methylation of Ketones and Aldehydes

B. Goldfuss

Direct nucleophilic 1,2-methylations of aldehydes or ketones with polar methylmetal systems (e.g., methyllithium or Grignard reagents) are rarely (enantio)selective, due to fast background reactions. However, procedures with special chiral additives or even catalytic versions based on methylzinc or methyltitanium intermediates enable high and reliable selectivities with many substrates. Most modern are nickel and rhodium catalysts in cooperation with trimethylaluminum, providing catalytic and highly stereoselective methylations of aldehydes and ketones.



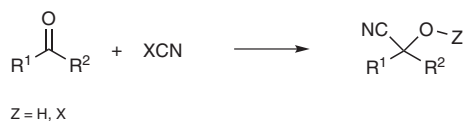
Keywords: methylations · enantioselectivity · catalysis · aldehydes · ketones · methyllithium · methyl Grignard reagents · dimethylzinc · trimethylaluminum · methylnickel species · methylrhodium species · methylchromium species · methyltitanium species

p 445

1.3.2 Cyanation of Ketones, Aldehydes, and Imines

L. L. Lin, X. H. Liu, and X. M. Feng

The synthesis of various cyanohydrins and α -aminonitriles is achieved through the cyanation of aldehydes, ketones, aldimines, and ketimines using different cyanide sources and is catalyzed by chiral or achiral organic or metallic catalysts.





PG = protecting group; Z = H, X

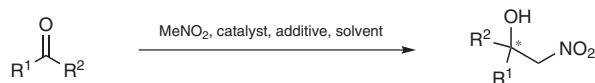
Keywords: cyanohydrins · α -aminonitriles · cyanation · cyanide sources · asymmetric synthesis · catalysts

p 507

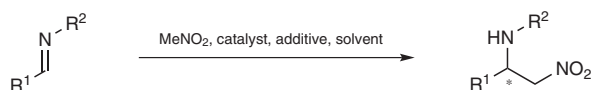
1.3.3 Stereoselective Addition of Nitromethane

R. Ballini and M. Petrini

Nitromethane readily adds to carbonyl derivatives in a process known as the nitroaldol or Henry reaction. The enantioselective addition onto prochiral carbonyl groups can be carried out under asymmetric catalysis, mainly using copper and zinc complexes. Organocatalytic methods find only limited applications in nitroaldol reactions, being especially applied in diastereoselective processes and in the addition of nitromethane to activated ketone derivatives. The asymmetric aza version of the nitroaldol reaction (the aza-Henry reaction) with nitromethane is also possible using highly reactive *N*-acylaldimino derivatives. The latter electrophilic species can be freshly prepared before their utilization or generated in situ from suitable precursors. Finally, addition of nitromethane to *N*-sulfonylimines and optically active *N*-sulfinylketimines readily provides an efficient entry to enantioenriched nitro amino compounds bearing a quaternary stereocenter.



R¹ = alkyl, aryl; R² = H, CO₂R³



R¹ = alkyl, aryl; R² = CO₂R³, SO₂R³, S(O)R³

Keywords: aldehydes · bis(dihydrooxazoles) · diamines · cinchona alkaloids · keto esters · *N*-acylimines · *N*-sulfonylimines · nitromethane · nucleophilic addition · organocatalysis · metal catalysis · thioureas