

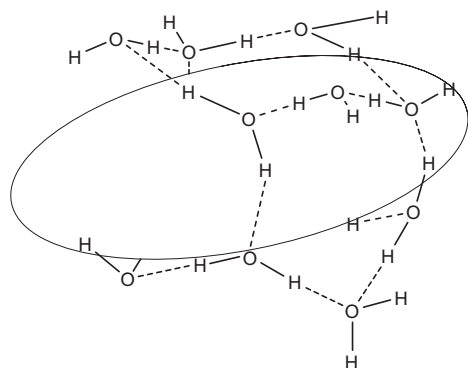
Abstracts

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2 Structure and Properties of Water

S. Otto and J. B. F. N. Engberts

Water is a unique liquid that unites within it an unusually large number of anomalous chemical and physical properties. This review discusses a number of these properties with a special focus on how these impact on the reactivity of neutral and ionic organic molecules in aqueous solution. Both homogeneous and heterogeneous aqueous reaction conditions are discussed.



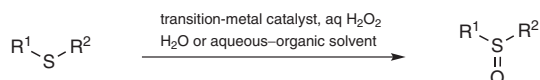
Keywords: water · hydrogen bonding · hydrophobic hydration · hydrophobic interactions · ionic hydration · thermodynamics · transition-state theory · solvent parameters · catalysis · green chemistry

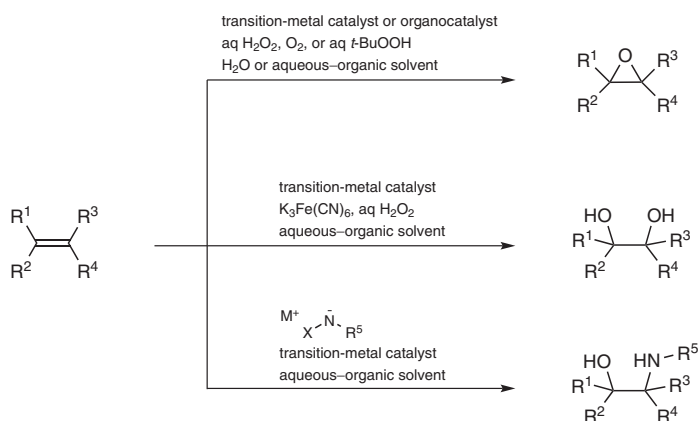
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3.1 Asymmetric Oxidation Reactions: Sulfoxidation, Epoxidation, Dihydroxylation, and Aminohydroxylation

T. Katsuki

The following asymmetric oxidation reactions using transition-metal catalysts or organo-catalysts in water or in aqueous–organic solvent systems are discussed: sulfoxidation, epoxidation, dihydroxylation, and aminohydroxylation. Although various oxidants are available for these oxidation reactions, a particular focus is placed on those processes using aqueous hydrogen peroxide, an atom-efficient and inexpensive reagent. Some examples of how water affects oxidative catalysis with transition-metal complexes are also described.



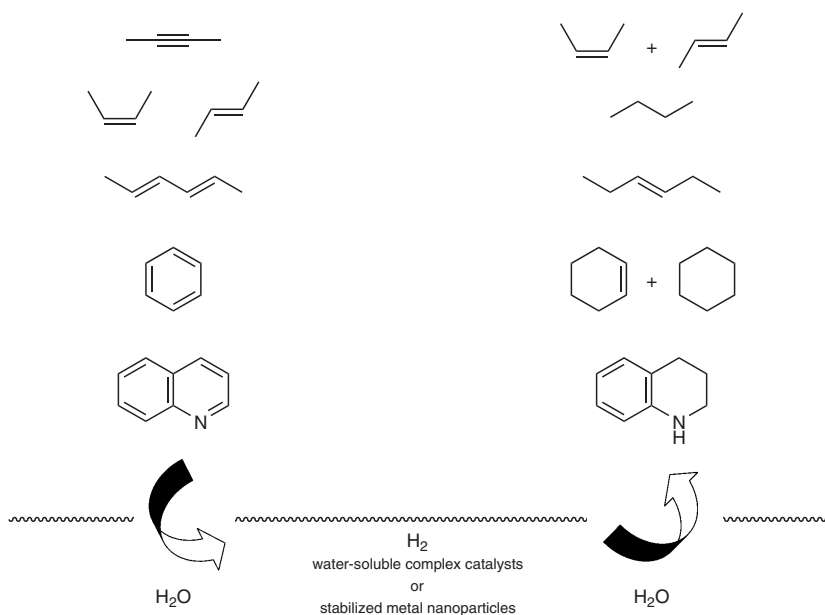


Keywords: aminohydroxylation · aqueous–organic systems · asymmetric catalysis · dihydroxylation · epoxidation · hydrogen peroxide · molecular oxygen · organocatalysis · sulfoxidation · transition-metal catalysis · water

3.2 Hydrogenation of Alkenes, Alkynes, Arenes, and Heteroarenes

F. Joó

Alkenes, alkynes, arenes, and heteroarenes in aqueous systems can be hydrogenated with water-soluble transition-metal complexes as well as with colloidal (nanosize) metal catalysts. In the case of water-insoluble substrates, the reactions proceed in aqueous–organic biphasic mixtures. Several water-soluble ligands (mostly tertiary phosphines) have been developed for the synthesis of soluble metal complex catalysts for hydrogenation. Chiral phosphine complexes are efficient for asymmetric hydrogenation of prochiral alkenes. Selective hydrogenation of dienes to monoenes and alkynes to alkenes has also been developed in aqueous systems; in the latter case, a substantial degree of stereoselectivity for the *Z*- or *E*-alkenes can also be achieved. Hydrogenation of polymers in aqueous emulsions leads to products with improved properties regarding strength and chemical stability. Stabilized metal colloids play a prominent role in the hydrogenation of arenes and heteroarenes in aqueous systems; stable and catalytically highly active colloids can be obtained by using commercially available or easily prepared protective polymers or surfactants.



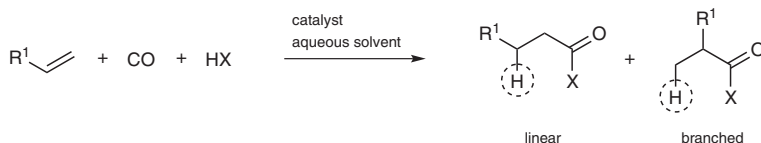
Keywords: alkenes · alkynes · arenes · asymmetric hydrogenation · biodiesel · biphasic · chiral phosphine · colloids · dienes · hetarenes · hydrogenation · polymers · lignin degradation compounds · microemulsion · palladium · poly(butadiene) · rhodium · ruthenium · soybean oil · styrene–butadiene rubber · sulfonated triphenylphosphine

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3.3 Hydroformylation and Related Reactions

L. T. Mika and I. T. Horváth

The activity and selectivity of hydroformylation catalysts can be modified by the presence of phosphorus-, nitrogen-, or sulfur-containing monodentate or polydentate ligands. In addition, functionalization of the ligands with an appropriate number of ionic or hydrophilic solubilizing groups can lead to a very high solubility in water. This chapter describes the hydroformylation of alkenes in aqueous media, with discussion of the ligands and catalysts used, the mechanism, and industrial application. Hydrocarboxylation in water is also discussed.



X = H, OH

Keywords: hydroformylation · phosphine ligands · mechanism · sulfonated phosphines · TPPTS · rhodium catalysts · asymmetric hydroformylation · hydrocarboxylation

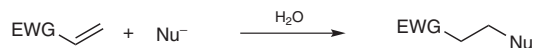
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3.4 Conjugate Addition Reactions

N. Mase

Conjugate addition reactions of H-, C-, N-, O-, and S-nucleophiles, generally called Michael additions, are frequently used in the synthesis of a wide range of β -functionalized com-

pounds from alkenes or alkynes bearing electron-withdrawing groups. The use of water in organic synthesis has been expanding steadily as a result of academic curiosity as well as environmental consciousness. Remarkable progress has been made in aqueous conjugate addition reactions in recent years. In this review, the description of methods for conjugate addition reactions in aqueous media is subdivided on the basis of the various classes of nucleophiles: H-, C-, N-, O-, and S-nucleophiles. In addition, these are further subdivided on the basis of the catalytic reaction conditions: catalyst-free, metal-complex catalyst, and metal-free catalyst (organocatalyst).



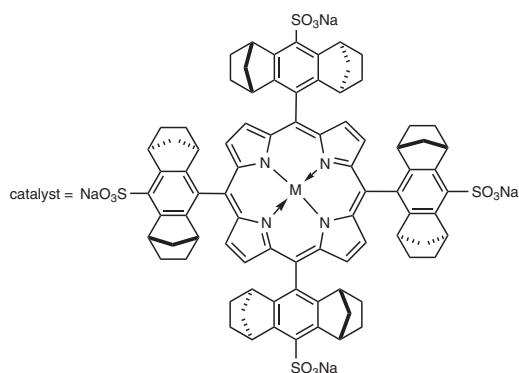
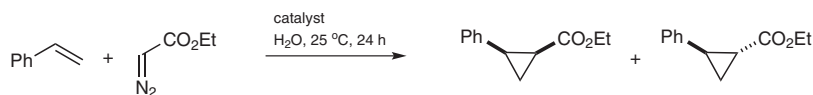
EWG = CHO, COR¹, CO₂R¹, CONR¹₂, CN, NO₂, PO(OR¹)₂, SO₂R¹;
Nu = H, CR²₃, NR²₂, OR², SR²

Keywords: asymmetric synthesis · aza-Michael addition · catalyst-free · conjugate addition · conjugate reduction · metal-complex catalysis · metal-free catalysis · Michael addition · Mukaiyama–Michael addition · organocatalysis · oxa-Michael addition · thia-Michael addition · aqueous conditions

3.5 Cyclopropanation Reactions

G. Simonneaux, P. Le Maux, and S. Chevance

This chapter describes methods for cyclopropanation reactions in water, including transition-metal-mediated reactions of diazo compounds, triphenylarsine-mediated cyclopropanation, and radical reaction of halogenated compounds with zinc. It focuses on the literature published in the period 2000–2010.



M = FeCl, Ru(CO)

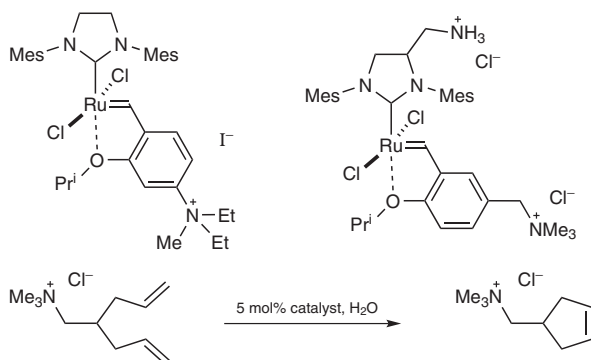
Keywords: cyclopropanes · alkene cyclopropanation · asymmetric cyclopropanation · asymmetric catalysis · chiral complexes · radical cyclization · arsonium ylides

3.6 Metathesis Reactions

C. Torborg, C. Samojłowicz, and K. Grela

Next to the known favorable properties of water itself, such as being cost efficient, non-toxic, and nonflammable, the use of water as a reaction medium for homogeneous alkene metathesis has various advantages. For instance, it allows the modification of biomolecules as well as the mild and convenient synthesis of polymers from cyclic alkenes via emulsion ring-opening polymerization. The catalysts of choice for aqueous alkene metathesis are almost exclusively based on ruthenium, and certain strategies have been developed in order to enhance their stability in aqueous media and provide robust catalytic systems with long active lifetimes. These strategies include various catalyst modifications, immobilization of the catalyst, or working in emulsions.

This chapter focuses on alkene metathesis reactions performed in water or in water-organic solvent mixtures. Both the homogeneous and heterogeneous variants of aqueous metathesis reaction are presented. The stability of common metathesis catalysts in aqueous media is discussed, stressing the exceptionally high stability of ruthenium alkylidene complexes in water. The application of aqueous alkene metathesis in protein modification is presented.

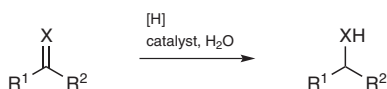


Keywords: alkenes · carbenes · carbon–carbon bonds · carbon–carbon coupling · cross metathesis · emulsion polymerization · ligands · metal–carbene complexes · metathesis · molybdenum catalysts · protein modification · ruthenium catalysts · ruthenium complexes · ring-closing metathesis · ring-opening polymerization · supported catalysis · water

4.1 Reduction of Carbonyl Groups and Imino Groups

X. Wu and J. Xiao

Carbonyl and imino groups appear in countless compounds, and their reduction is one of the most fundamental reactions in synthetic chemistry. This chapter deals with the reduction of carbonyl and imino compounds in water, covering nonasymmetric hydrogenation and transfer hydrogenation of aldehydes, ketones, carbon dioxide, and imino bonds, and asymmetric hydrogenation and transfer hydrogenation of ketones and imino species.



X = O, NR³; [H] = H₂, HCO₂H, HCO₂H, iPrOH

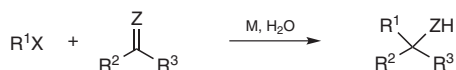
Keywords: ketones · aldehydes · carbon dioxide · imines · iminium salts · alcohols · amines · hydrogenation · transfer hydrogenation · asymmetric catalysis

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4.2 Alkylation, Allylation, and Benzylolation of Carbonyl and Imino Groups

L. Zhao and C.-J. Li

Metal-mediated Barbier–Grignard-type addition of simple alkyl groups, allyl groups, and benzyl groups to carbonyl compounds and imine derivatives in aqueous media, as well as the mechanisms and synthetic applications of such reactions, are reviewed in this chapter.



R^1 = alkyl, allyl, benzyl; Z = O, NR^4

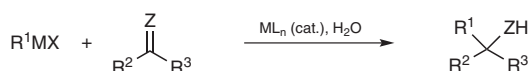
Keywords: aldehyde · allylation · alkylation · Barbier–Grignard-type reactions · benzyla-tion · imines · indium · nucleophilic addition · organic halides · tin · zinc

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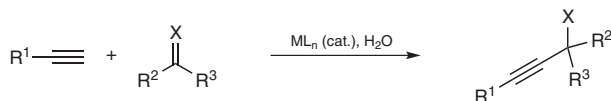
4.3 Arylation, Vinylation, and Alkynylation of Carbonyl and Imino Groups

L. Zhao and C.-J. Li

Metal-mediated and -catalyzed Barbier–Grignard-type addition of aromatic groups, vinyl groups, and alkynyl groups to carbonyl compounds and imine derivatives in aqueous media, as well as the mechanisms and synthetic applications of such reactions, are reviewed in this chapter.



R^1 = aryl, vinyl; Z = O, NR^4



X = O, NR^4

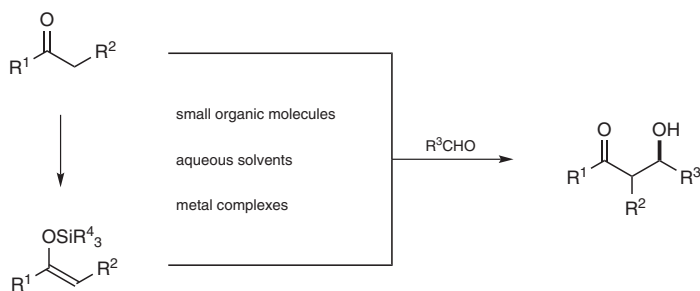
Keywords: aldehydes · alkynes · alkynylation · arylation · Barbier–Grignard-type reactions · copper · gold · imines · nucleophilic addition · rhodium · ruthenium · silver · transition-metal catalysis

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4.4 Aldol Reaction

M. Woyciechowska, O. El-Sepelgy, and J. Mlynarski

This chapter highlights development in aldol-type bond-forming reactions catalyzed by metal complexes and organocatalysts in aqueous media with and without the addition of organic solvents.



Keywords: aldol reaction · Mukaiyama reaction · Lewis acid · aldols · hydroxymethylation · asymmetric synthesis · organocatalysis · water

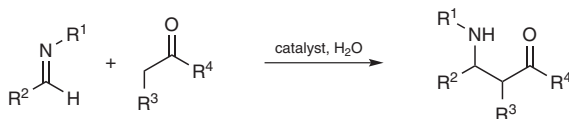
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4.5 Mannich Reaction and Baylis–Hillman Reaction

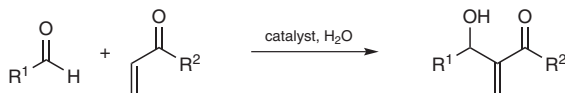
M. Benohoud and Y. Hayashi

Mannich reactions and Baylis–Hillman reactions are C–C bond-forming transformations that give access to highly functionalized compounds. Mannich products, i.e. β-amino carbonyl compounds, are generated from imines and enolizable carbonyl derivatives, whereas Baylis–Hillman products, i.e. α-methylene-β-hydroxy carbonyl compounds, are obtained from aldehydes and α,β-unsaturated carbonyl derivatives. These reactions are catalyzed by metals, organocatalysts, or enzymes, and the development of water-tolerant catalysts has allowed these reactions to be carried out under aqueous conditions. In some cases the use of additives such as surfactants has allowed the complete omission of organic solvents, with the reactions proceeding in the presence of only water. The use of water as a solvent for organic reactions in some cases promotes an acceleration of the rate of the reaction and/or an increase in stereoselectivity. Furthermore, the harmless and environmentally benign character of water makes it an environmentally acceptable solvent. This review covers methods for promoting Mannich reactions and Baylis–Hillman reactions under aqueous conditions (homogeneous solvent mixtures) or in the presence of water (biphasic solvent systems), and the beneficial effect of water is illustrated and explained.

Mannich reaction:



Baylis–Hillman reaction:

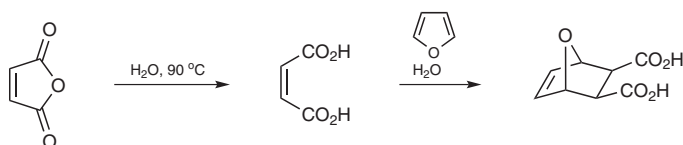


Keywords: Mannich reaction · Baylis–Hillman reaction · imines · enolates · Lewis acid catalysts · Lewis base catalysts · Brønsted acids · Brønsted bases · chiral amines · organometallic catalysts · organocatalysts · enamines · β-amino carbonyl derivatives · α-methylene-β-hydroxy carbonyl derivatives · acrylic compounds · α,β-unsaturated carbonyl derivatives · water · surfactants

5.1 Cycloaddition and Cyclization Reactions

G. Molteni

This chapter is devoted to the systematic discussion of relevant examples of cycloaddition and cyclization reactions that occur in water or aqueous media. In order to broaden the discussion and enhance the relevance, comparisons between water-promoted reactions and the same reactions carried out in organic solvents are presented whenever possible. The organization of the chapter reflects the main kinds of cycloadditions and cyclizations. For the sake of clarity, Diels–Alder, hetero-Diels–Alder, and Lewis acid catalyzed Diels–Alder reactions are presented first, followed by 1,3-dipolar cycloadditions. The latter reactions are arranged according to the 1,3-dipole type, namely nitrile imines, nitrile oxides, diazo compounds, azides, azomethine ylides, and nitrones. A further section of the chapter is devoted to the presentation of water-promoted Barbier-type cyclizations, epoxide-opening cascade cyclizations, and radical cyclizations.

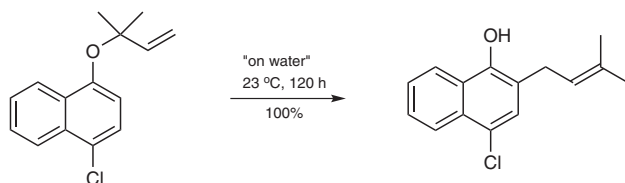


Keywords: Diels–Alder cycloadditions · Lewis acids · 1,3-dipolar cycloadditions · nitrile imines · nitrile oxides · azides · azomethine ylides · nitrones · Barbier cyclizations · epoxide ring opening · radical cyclizations

5.2 Pericyclic Rearrangements: Sigmatropic, Electrocyclic, and Ene Reactions

F. Fringuelli and O. Piermatti

This reviews describes the beneficial effects of aqueous media on both the reactivity and selectivity of sigmatropic rearrangements, electrocyclic reactions, and ene reactions.



Keywords: sigmatropic rearrangements · Claisen rearrangement · Cope rearrangement · electrocyclic reactions · ene reaction

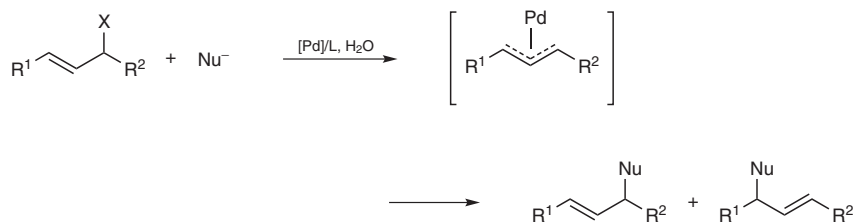
5.3 Allylic and Aromatic Substitution Reactions

Y. Uozumi

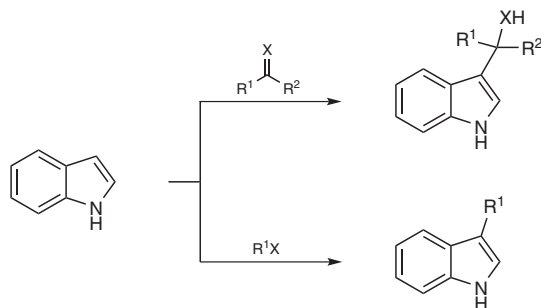
Substitution of allylic alcohols, ethers, and esters with C-, N-, O-, and S-nucleophiles proceeds in water in the presence of water-compatible palladium complexes to give the corresponding substituted products. In addition to these reactions, metal-mediated (e.g. indium or zinc) allylic substitutions, calixarene catalysis, heterogeneous catalysis, as well as asymmetric catalysis are also described.

Indoles and electron-rich aromatics react with carbonyl compounds and electron-deficient alkenes in water to give the corresponding substituted products (e.g., 3-substituted

indoles). These reactions are also discussed in this chapter, together with selected examples of recent progress in nucleophilic aromatic substitution in water.



L = water-compatible ligand



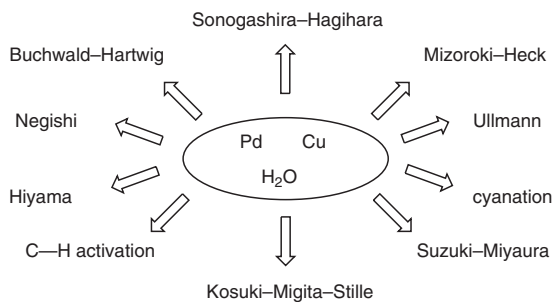
Keywords: allylic substitution · π -allylpalladium · allylic ester · allylic alcohol · indium · zinc · calixarene · amphiphilic polymer · heterogeneous catalysis · asymmetric catalysis · asymmetric substitution · bis(indolyl)methane · 3-substituted indole · Michael addition · haloarene · intramolecular cyclization · scandium(III) tris(dodecyl sulfate) · tungstophosphate · copper—porphyrizine

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5.4 Cross-Coupling and Heck Reactions

D. A. Alonso and C. Nájera

This chapter describes the best available methods to perform palladium- and copper-catalyzed Heck and cross-coupling reactions in neat water. The chapter is divided into two general sections according to the metal catalyst employed. Each section is further subdivided by the type of bond formed and the specific type of coupling which leads to this bond formation. Both homo- and heterogeneous catalysis protocols are considered. The chapter provides the reader with background information, evaluated methods, practical applications, and a detailed overview of the latest trends in palladium- and copper-catalyzed aqueous Heck-type and cross-coupling reactions, covering the literature up to 2011.



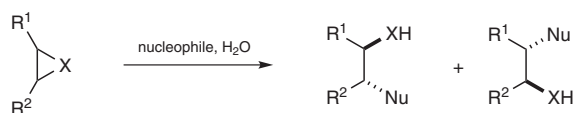
Keywords: aqueous · palladium catalysts · copper catalysts · palladacycles · supported catalysis · Heck reaction · Suzuki coupling · Stille coupling · Sonogashira reaction · Hiyama coupling · Negishi coupling · C–H activation · Buchwald–Hartwig amination · cyanation

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5.5 Ring Opening of Epoxides and Aziridines

C. Ogawa and S. Kobayashi

Epoxides and aziridines are excellent synthetic intermediates, since they are readily converted into other functional groups such as diols, amino alcohols, and diamines. While there are many reports of ring-opening reactions of these cyclic compounds with various nucleophiles in organic solvents, including asymmetric versions, similar reactions in water seem to be difficult, since water may attack these substrates instead of attack of the desired nucleophile. However, because the use of water is attractive not only for the development of green chemistry but also for exploring unique reactivity, significant efforts toward developing these reactions in water have been made. In this chapter, ring-opening reactions of epoxides and aziridines in water as the sole solvent are discussed.



$X = O, NR^3; Nu = OH, OR^4, NR^4R^5, N_3, SR^4$

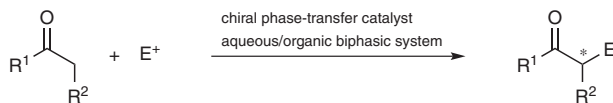
Keywords: amino alcohols · aziridines · diamines · enantioselectivity · epoxides · Lewis acid/surfactant combined catalysts · ring opening · sulfanyl alcohols

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5.6 Asymmetric α -Functionalization of Carbonyl Compounds and Alkylation of Enolates

S. Shirakawa and K. Maruoka

The asymmetric α -functionalization of carbonyl compounds in aqueous media is introduced in this chapter. Representative examples of asymmetric alkylations, alkenylations, and heteroatom functionalizations of various carbonyl compounds under aqueous/organic biphasic phase-transfer conditions are summarized along with detailed experimental procedures. The organocatalyzed asymmetric α -alkylation and α -oxidation reactions of aldehydes in aqueous media are also described.



Keywords: alkylation · alkenylation · alkynylation · oxidation · amination · fluorination · phase-transfer catalysis · organocatalysis · asymmetric synthesis · asymmetric catalysis

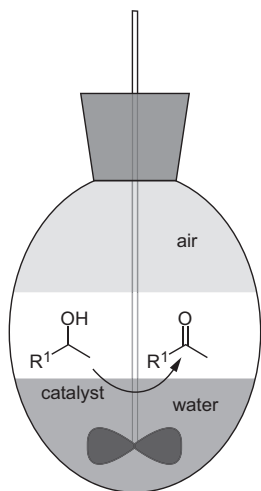
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5.7 Oxidation of Alcohols, Allylic and Benzylic Oxidation, Oxidation of Sulfides

R. A. Sheldon

Catalytic oxidations of alcohols, benzylic and allylic oxidations, and oxidations of sulfides, using the environmentally benign dioxxygen and hydrogen peroxide as the stoichiometric oxidant, in aqueous mono- or biphasic systems in the absence of organic solvents, are reviewed. Other oxidants, such as sodium hypochlorite, receive a cursory mention. There is a marked trend toward the use of relatively simple complexes of inexpensive

and more readily available first-row elements (Fe, Mn, and Cu) rather than noble-metal complexes. Methods using organocatalysts, notably stable *N*-oxyl radicals, are becoming increasingly popular, largely owing to the fact that they are “heavy metal free”. At the same time, noble-metal nanoparticles (particularly Au and Pd) are becoming increasingly popular as quasi-homogeneous catalysts for alcohol oxidations. Enzymatic oxidations in conjunction with dioxygen (oxidases) or hydrogen peroxide (peroxidases) are also reviewed. These various catalytic methodologies constitute green and sustainable alternatives to traditional oxidations employing atom-inefficient and toxic stoichiometric oxidants.



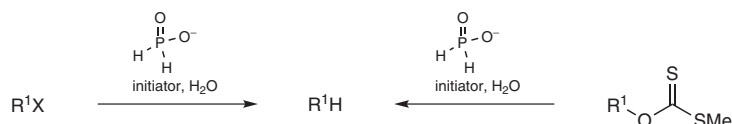
Keywords: green chemistry · catalytic oxidation · stable *N*-oxyl radicals · noble-metal nanoparticles · enzymatic oxidations · cross-linked enzyme aggregates (CLEAs) · Baeyer–Villiger monooxygenases · flavins · laccase · alcohol oxidation · enantioselective sulfoxidation · allylic oxidation · benzylic oxidation

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5.8 Free-Radical Reactions

H. Yorimitsu and K. Oshima

Phosphinate salts play a central role in the radical reduction of organic halides and Barton–McCombie deoxygenation in aqueous media. The phosphinate-mediated reactions are advantageous due to the low cost, low toxicity, and easy removal of phosphorus-based inorganic salts. Water as a reaction medium enhances the efficiency of radical addition to alkenes and imines, atom transfer radical cyclization, and allylation of organic halides.

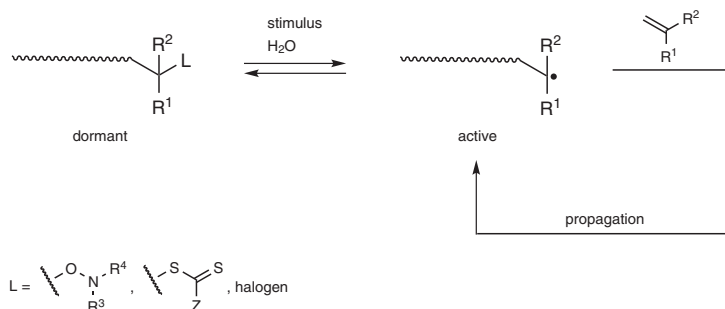


Keywords: radical addition · radical cyclization · radical reaction · reduction · silanes · germanes · phosphinic acids · deoxygenation · boranes · addition · allylation · atom transfer reaction

5.9 Polymerization

M. Ouchi and M. Sawamoto

In this chapter, living (controlled) radical polymerizations using aqueous media are discussed with some selected examples from four typical categories, i.e. mini-emulsion, emulsion, suspension (dispersed or heterogeneous), and homogeneous systems.

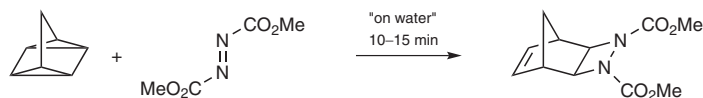


Keywords: living radical polymerization • suspension polymerization • mini-emulsion • emulsion • metal-catalyzed living radical polymerization • atom-transfer radical polymerization • nitroxide-mediated polymerization • reversible addition–fragmentation chain-transfer polymerization

6.1 Organic Synthesis “On Water”

A. Chanda and V. V. Fokin

This chapter surveys reactions that benefit from being performed “on water”: when insoluble reactant(s) are stirred in aqueous emulsions or suspensions without the addition of any organic cosolvents. A considerable rate acceleration is often observed in reactions carried out under these conditions compared to those in organic solvents.



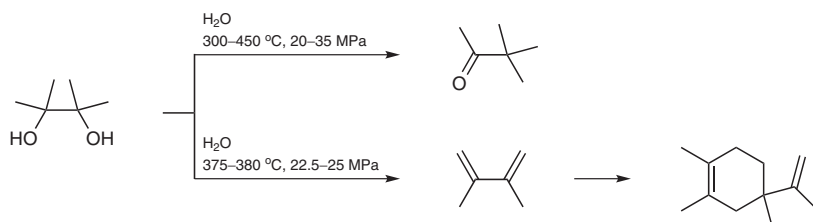
Keywords: on water • Diels–Alder reaction • dipolar cycloaddition • Claisen rearrangement • Passerini reaction • Ugi reaction • ring-opening reaction • nucleophilic substitution • catalysis • coupling reactions • multicomponent reactions • Wittig reaction • bromination • oxidation • reduction

6.2 Sub- and Supercritical Water

A. Kruse and E. Dinjus

The reasons to investigate reactions in sub- and supercritical water (SSCW) lie in the extraordinary properties of this reaction medium. The high ionic product in the subcritical range and the high solubility of compounds in the supercritical range enable a variety of reactions. The most investigated type of reaction is hydrolysis. Here, water is reactant, solvent, and catalyst or catalyst precursor, forming aqueous H^+ or OH^- ions. A very important class of reactions comprises aldol condensation and aldol splitting. In contrast to ambient conditions, these reactions, as well as the Cannizzaro reaction, do not need strong bases as catalysts. Additions and C–C bond-formation reactions are driven by the high pressure

applied in sub- and supercritical water. Here, organometallic reactions such as hydroformylation, Glaser coupling, and especially the Heck reaction are studied. The Diels–Alder reaction can be performed in water at lower temperature, but in the supercritical range the solubility of the components is higher, which leads to high reaction rates and yields. Various rearrangements have also been studied, most of them in the subcritical range to benefit from the high ionic product. The formation of ϵ -caprolactam is of great technical interest, the pinacol rearrangement switches the favored product pathway with reaction conditions, and the Claisen rearrangement gives high yields in a special reactor with low mixing and heating times. Oxidations and reductions are typically catalyzed by heterogeneous (e.g., metal-on-support) catalysts. Here, the challenge is to find a catalyst that survives the reaction conditions and also shows good selectivity. Successful studies with heterogeneous metal catalysts are therefore limited. On the other hand, such reactions are widely used for degradation of biomass. In contrast, oxidations of alkylarenes with manganese(II) bromide as catalyst give high yields of the corresponding carbon acids. Homogeneous reductions with formic acid or its salts are often applied to avoid heterogeneous catalysts in reductions.

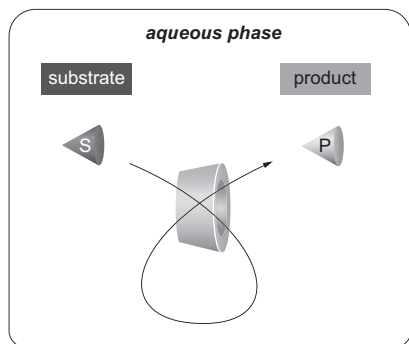


Keywords: subcritical water • supercritical water • ionic product • tunable solvent • hydrolysis • condensation • hydroformylation • Diels–Alder reaction • coupling reactions • rearrangements • oxidation • reduction

6.3 β -Cyclodextrin Chemistry in Water

F. Hapiot and E. Monflier

This chapter highlights the most relevant reactions using cyclodextrins as mass-transfer additives, organocatalysts, solubilizers of organocatalysts, ligands for organometallic complexes, stabilizers of noble-metal nanoparticles, or dispersing agents for catalytically active solids. The emphasis is on reactions where the cyclodextrins are readily available and for which the performance has been demonstrated in terms of activity and selectivity. Throughout this chapter, the modification of cyclodextrins is correlated to the ability to interact with organic guest or to adsorb on the surface of solids.



Keywords: cyclodextrin · mass-transfer additive · organocatalyst · ligand · stabilizer · dispersing agent · organometallic complex · metallic nanoparticle · supported metal

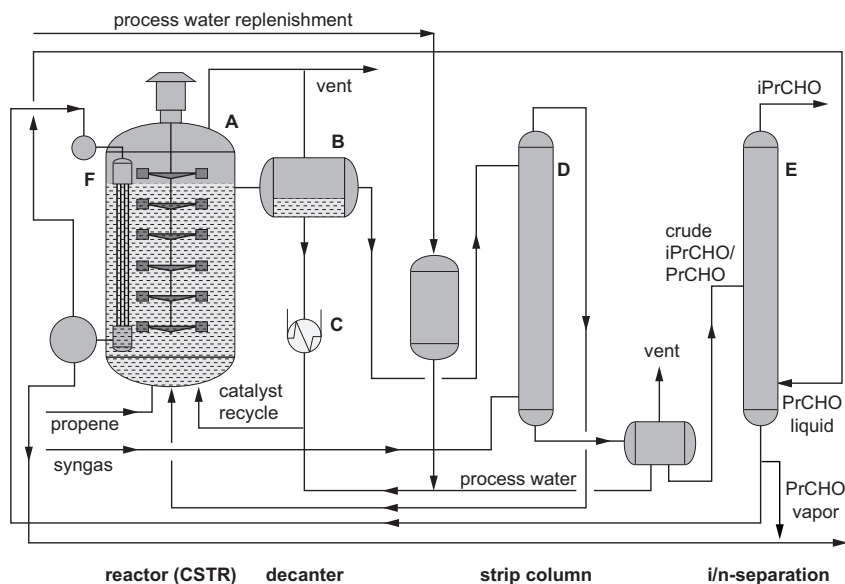
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7.1 Hydroformylation

E. Wiebus, K. Schmid, and B. Cornils

The only large-scale and industrially used version of aqueous–biphasic homogeneous catalysis is Ruhrchemie/Rhône-Poulenc’s hydroformylation process for the manufacture of butanal from propene and syngas, which is the focus of this chapter.

Flow Sheet of the Ruhrchemie/Rhône–Poulenc Process



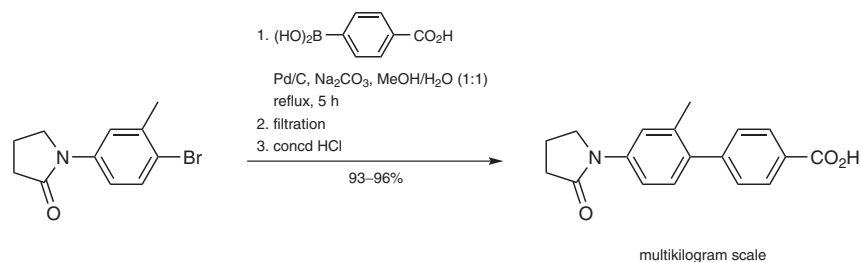
Keywords: hydroformylation · homogeneous catalysis · water-soluble rhodium complexes · aqueous–biphasic process · industrial scale · propene · butanal · catalyst recovery · catalyst recycling · economics

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7.2 Industrial Applications Other than Hydroformylation

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The choice of solvents is an important matter for green chemical processes in industry. In this chapter, industrial applications of organic reactions in water other than hydroformylation are discussed. Classical reactions, metal-catalyzed reactions such as palladium-catalyzed coupling, and enzymatic reactions are highlighted.



Keywords: Aldol reaction • aqueous conditions • Baylis–Hillman reaction • enzyme catalysis • green chemistry • hydration • hydrolysis • kinetic resolution • Lewis acid catalysis • palladium catalysis • phase-transfer catalysis • Suzuki coupling • transition-metal catalysis • water