Perchloric Acid and Its Salts: Very Powerful Catalysts in Organic Chemistry†

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1. Introduction

The first reported perchlorate compound was called by von Stadion "oxygenated potassium chlorate".[1] It was a water-insoluble residue from a mixture of potassium chlorate and sulfuric acid. From this new salt an "oxygenated chloric acid" was distilled off, collecting vapors from a mixture with its own weight of sulfuric acid diluted 1/3 (w/w) with water. Actually, a 70% water solution of perchloric acid was obtained. In 1830, Serullas synthesized ammonium perchlorate and a number of metal perchlorates and first introduced the term "perchlorate" to name them.[2−4] Anhydrous perchloric acid was obtained only in 1862.[5]

The explosive nature of certain perchlorates pushed their production to the maximum levels during World War I and II, but research activity continues strong to this day. Perchlorate is used as solid fuel for rockets and missiles and in air bag inflators, lubricating oils, leather finishing, electroplating, rubber manufacture, and other manufacturing processes.[6] Indeed, the use of perchlorates has found a renaissance in organic chemistry in the last years.

Preparation and properties of perchloric acid and many perchlorates have been covered by Schilt in 2003.[7] Perchloric acid is a colorless, odorless, oily liquid that is very hygroscopic. It is one of the strongest and most corrosive mineral acids. Its strength depends, obviously, on

† Dedicated to prof. M. Tiecco in University of Perugia on the occasion of his retirement.

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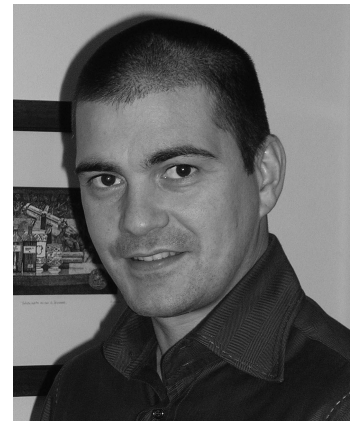
Renato Dalpozzo graduated from the University of Bologna in 1981 with a Laurea in Industrial Chemistry under the supervision of Professor Bartoli. He was Researcher of Organic Chemistry at University of Bologna (Italy) from 1983. In 1992, he moved to the University of Calabria (Italy) as Associate Professor and now is Full Professor of Environmental and Cultural Heritage Chemistry. His research interests include studies on the reactivity of organometallic compounds with aromatic systems, the use of dianions derived from enamino carbonyl compounds, the stereoselective reduction of various classes of ketones, the development of new Lewis acid systems, and the chemistry of mimicry of social insects.

Giuseppe Bartoli graduated from the University of Bologna in 1967 with a Laurea in Industrial Chemistry. He was Assistant Professor of Organic Chemistry at the University of Bari (Italy) from 1968, moving to the University of Bologna (Italy) as Associate Professor and then to the University of Camerino in 1986 as Full Professor. In 1993, he returned to the University of Bologna, where he is currently Professor of Organic Chemistry. From 2001 to 2006, he has held the position of Head of the Department of Organic Chemistry "A. Mangini", and now he is chairman of the Industrial Chemistry degree course. His research interests include studies on the reactivity of organometallic compounds with aromatic systems, the use of dianions derived from enamino carbonyl compounds, the stereoselective reduction of various classes of ketones, and the development of new Lewis acid systems. Now he is interested in enantioselective organocatalysis.

the basicity of the solvent in which it is dissolved. In water, it is completely dissociated up to a concentration of about 4 M. In organic solvents, it behaves as highly ionized, but not necessarily dissociated, acid. Perchloric acid finds significant application in acid-catalyzed organic reactions such as esterification reactions, cationic polymerization, isomerization, and rearrangement. Moreover, very recently, perchloric acid has found new applications, when its intrinsic hazardousness is reduced by dispersion on silica.[8] The good thermal and mechanical stabilities of this supported reagent make it easy to handle. Moreover, being a heterogeneous catalyst, it is easily separable from the reaction mixture through filtration. The feasibility of reuse makes it suitable for

Letizia Sambri graduated from the University of Bologna in 1993 with a Laurea in Industrial Chemistry, and she obtained her Ph.D. degree in 1998 in the group of Prof. G. Bartoli. During her thesis, she spent a research period at the University of Nijmegen (NL) in the group of Prof. Zwanenburg. Since 2000, she has been Assistant Professor at the Department of Organic Chemistry, University of Bologna. During 2009, she spent four months as visiting scientist in the group of Prof. L. De Cola at the University of Münster (D). Her research interests included the application of Lewis acid activators in organic reactions and the development of new methods for the synthesis of useful intermediates. Currently her research interests focus on the synthesis and the properties of organic materials for molecular electronics. In particular, she works on the development of new ligands for neutral and charged metal complexes to be employed in organic electronics and on the study of new hydro- and organogelators.



Professor Melchiorre, born in 1973 in Camerino, Italy, studied Chemistry at the University of Bologna where he graduated in 1999. After a brief stint in the biology research program at Bologna University, he began his doctoral studies in Chemistry working in the area of asymmetric catalysis under the guidance of Professor Achille Umani-Ronchi. Before obtaining his Ph.D. degree in 2003, he spent 10 months in Denmark working with Professor Karl Anker Jørgensen at the "Centre for Catalysis", Århus University, where his studies centred on asymmetric organocatalysis. Afterwards, he worked as a postdoctoral associate at the Industrial Chemistry Faculty of the Bologna University. There he began his studies on the development of novel organocatalytic asymmetric transformations. In October 2007, he took a permanent position as an Assistant Professor at Bologna University. In September 2009, together with his wife Lorna and their two kids Niccolò and Anita, he moved to Catalonia as an ICREA Research Professor at the Institute of Chemical Research of Catalonia (ICIQ) in Tarragona, Spain, and ICIQ Group Leader. Professor Melchiorre's research focuses on the discovery and mechanistic understanding of stereoselective organic reactions catalyzed by chiral organic molecules. He was recently the recipient of the 2007 "G. Ciamician" Medal, awarded by the Italian Chemical Society, and the 2009 Thieme Journal Prize. He was also nominated Liebig Lecturer 2008 by the Organic Division of the German Chemical Society.

meeting the requirement of green chemistry, minimizing undesirable waste causing environmental pollution. These reactions will be covered in this review from discovery to early 2009.

Also perchlorate salts are of great chemical interest and importance, because they possess several unique properties, behaving as problem-solving reagents and enabling new and unusual chemistry. They have a large degree of ionic character; the perchlorate ion, in fact, has a very high electronegativity, which corresponds to high solvation energy. This is a major factor in the high solubility of most of perchlorates in water and in a large number of nonaqueous solvents. Another consequence of the high ionic character is the weak tendency of perchlorate ion to coordinate metal ions, which favors its use in studies on coordination power of many ligands. Moreover, they show an exceedingly weak basicity that enhances the Lewis acid power of the metal counterions, so metal perchlorates find applications very close to those of perchloric acid, in particular when a Brønsted acid is not tolerated. The counterions are, in fact, capable of strongly coordinating electron donors, especially chelating compounds such as 1,3-dicarbonyl substrates and bidentate ligands. Metal perchlorates are powerful and selective catalysts that can usually be employed under mild reaction conditions, at relatively low temperatures, and several functional groups are generally well tolerated. In several cases, metal perchlorates prove to be much more active than other commonly used Lewis acids, such as triflates, while at the same time being much less expensive. Some perchlorate salts can be employed in their hydrate form and can frequently be recovered and reused without loss of activity. Moreover, they are extraordinarily stable to air in aqueous solutions and are used to provide a constant ionic environment in otherwise reactive solutions. Perchlorates have long half-lives with transition metal complexes such as $[Ti(H_2O)_6]^{3+}$ (0.17 year) and $[V(H_2O)_6]^{2+}$ (53 years).[9]

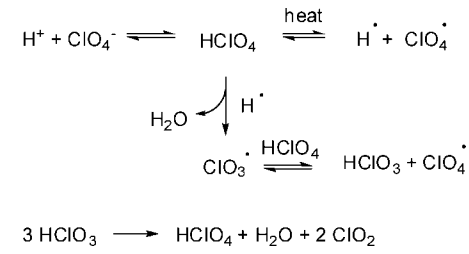
As well as $HClO_4$, also $LiClO_4$ has been dispersed on silica and found interesting applications, compared with solid salt or LPDE (5 M $LiClO_4$ in diethyl ether). In past years, some partial reviews on the synthetic use of perchlorate appeared in the literature, in particular about ferric perchlorate,[10] LPDE,[11,12] and magnesium perchlorate.[13] We address the reader to them for other information on this topic; in this review, the application of metal perchlorates as Lewis acids or catalysts appearing in the literature mainly from 2000 to early 2009 will be covered.

2. Hazard and Safety

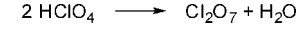
In 2002, Long affirmed that "the mistaken association of perchlorate salts with the oxidizing potential of perchloric acid and the pyrotechnic performances of ammonium perchlorate has severely compromised the objective consideration of perchlorates in commercial processes".[14] Today, much information on properties and preparation of perchloric acid and perchlorates has been collected, and fortunately many hazards in their chemistries can be anticipated and addressed.[15–17]

The oxidative properties of perchloric acid depend on its concentration. When hot and concentrated, its oxidizing power can become dangerously vigorous, but it can serve as a highly efficient oxidant for destruction of organic matter. Working with diluted cold perchloric acid solution (up to 73% concentration) is not hazardous and is suitable for use in many redox reactions, but above room temperature, continued application of heat could drive off water vapor, affecting the oxidizing power of the perchlorate ion. When hot, perchloric acid solution begins to exhibit oxidative power at about 50% concentration.[14]

Scheme 1. The First Steps of Perchloric Acid Decomposition



Scheme 2



Perchloric acid is more unstable than perchlorate ion, and the degree of dissociation of aqueous perchloric acid solutions can be taken as a measure of its stability: the dissociation constant (10^{14}) is the greatest among the common inorganic acids. Therefore, perchloric acid can survive only in highly concentrated solution, where it can interact with hydrogen atoms (e.g., from homolytical thermal cleavage of perchloric acid itself), followed by loss of water and formation of chlorate radical. The ClO_3 radical is a trap for electrons by electron transfer. Having trapped an electron, it is transformed into ClO_3^- ion, which is in turn an efficient proton trap. Chloric acid then decomposes rapidly, since it is very unstable. Chlorine oxides formed in the decomposition of chloric acid catalyze the decomposition of perchloric acid (Scheme 1).[18] The situation described in Scheme 1 is markedly complicated by the presence of organic or metal ions that can enhance electron transfer processes. Finally, anhydrous perchloric acid is postulated to decompose to the extremely unstable chlorine heptoxide (Scheme 2).[14]

In conclusion, commercially available perchloric acid solutions are stable if stored properly and away from organic or flammable materials, best inside secondary containment; dilution of perchloric acid must be done by adding acid to water not the reverse; perchloric acid waste must not be mixed with any other waste; fume hoods for perchloric acid require particular materials and construction and a vapor trap apparatus.[19]

Lithium and magnesium perchlorates are dangerous if heated over their decomposition temperatures (300−500 °C)[14,20] in the presence of oxidizable materials or under highly acidic conditions. Actually, they can be dried at 160 °C without any accident. The National Fire Protection Association ranks magnesium perchlorate as barely hazardous for health and as an oxidizing product but not as an explosive one.[21,22] Suppliers inform us that common metal perchlorates are stable under ordinary conditions of use and storage but that contact with heat and reducing agents must be avoided.[23,24]

On the other hand, ammonium perchlorate is highly explosive. It is manufactured in large quantities primarily for use as an oxidizer in solid rocket propellants. It is also used in fireworks, batteries, and automobile air bags. Its properties in general and particularly its thermal decomposition have been a subject of many reviews.[18,25,26]

The toxicity of perchlorate salts and perchloric acid have received prominent attention recently in some reviews.[27,28] Initially identified as a groundwater contaminant associated primarily with rocket fuel spillage or poor disposal practices, perchlorate ion is now found to be ubiquitous, when detected in groundwater of regions with no historical potential anthropogenic sources, and its presence in rain and snow

samples has led to the suspicion that perchlorate ion is formed atmospherically. Actually, Dasgupta demonstrated perchlorate formation by a number of atmospheric processes and concluded that a natural perchlorate background of atmospheric origin should exist.[29]

Widespread human exposure to both anthropogenic and naturally occurring perchlorate occurs primarily via ingestion. Concern about potential human health risks from perchlorate in food and drinking water results from the observation that perchlorate has a great affinity for the sodium (Na^+)/iodide (I^-) symporter, the protein responsible for transporting iodide into the thyroid gland for the purpose of synthesizing thyroid hormones. As a result of that affinity, perchlorate ion can block the transport of iodide into thyroid follicular cells.[30] On the other hand, it can find use as a medical treatment for Graves' disease (hyperthyroidism).

The 2005 National Academy of Sciences report, evaluating human health risks from perchlorate, recommends an exposure limit considered to be without adverse effects over a lifetime of oral exposure, or reference dose (RfD), of 0.0007 mg/(kg·day).[31] That RfD was adopted by US EPA in February 2005 as the no observed effect level, while a RfD of 0.5 mg/(kg·day) was adopted as the low observed effect level,[17] but the health impact of perchlorate at low doses is unresolved. Chemists must therefore handle perchloric acid and perchlorate using full body protection, goggles or face shield, gloves, and apron.

Removing of perchlorates from the environment has recently received attention from chemists,[9,32] and complete information can be also obtained on the Web.[33]

Perchlorate can be removed from water using an ion exchange (IX) technique, but the final recovered water is too corrosive for use in water distribution systems without restoring water hardness. Disposing the resulting IX brines can be problematic because the perchlorate is concentrated but not destroyed.[34] A commercially available IX treatment process includes also a module that uses high-temperature and rare-earth metals for perchlorate reduction to chloride.

Bioremediation of perchlorate-contaminated waters is promising.[35] Bacteria capable of perchlorate degradation appear to be widely distributed in nature at concentrations ranging from one to thousands of bacteria per gram of water, wastewater, sediment, and soil. Perchlorate is used as an electron acceptor by these bacteria for cellular respiration, and it is completely degraded to chloride ion. The reason these bacteria are so widely distributed in the environment and can grow so quickly using perchlorate is unknown. Biodegradation of perchlorate in engineered systems offers the greatest potential for inexpensive and complete perchlorate degradation. In this field, recently proteomic studies by mass spectrometry on perchlorate (and chlorate) reductase and chlorite dismutase proteins, the two central enzymes in the perchlorate (or chlorate) reduction pathways, have appeared in the literature.[36]

3. Applications to Carbohydrate Chemistry

3.1. Glycosylation

Glycosides are very common compounds in nature, for example, oligosaccharides, glycolipids, and glycoproteins are glycosides. Glycoconjugates play important roles in numerous biological processes; that is, they mediate cell adhesion and communication and they are the characteristic determinants of the human blood group system and of so-called "tumor-associated" antigens.

To synthesize a glycoside, in general, a suitably protected glycosyl donor, which carries a leaving group "X" at the anomeric center, is activated by means of a promoter to give rise to a reactive intermediate, for instance, a glycosyl cation, which is then trapped by a glycosyl acceptor to give the desired glycoside. Moreover, *O*-alkyl-protected glycosyl donors display a higher reactivity than the analogous compounds carrying *O*-acyl groups ("armed/disarmed" concept).[37] In addition, while benzyl ethers do not influence the steric course of the glycosylation reactions, acyl blocking functions display marked neighboring group assistance. They shield one of the diastereotopic faces of the intermediately formed glycosyl cation, and thereby, in general, they induce the formation of 1,2-*trans*-glycosides. On this basis, a variety of glycosidation methods have been developed since the first use of the classical Koenigs−Knorr reaction.[38]

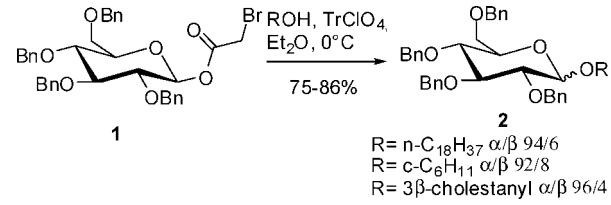
Trityl perchlorate is one of the first derivatives introduced as the promoter of the glycosylation reaction. Good yields and stereoselectivity are obtained from 1-*O*-bromoacetyl sugars, when they react with simple alcohols (Scheme 3).[39]

An interesting feature is observed with ribofuranosides, that is, $LiClO_4$ drastically influences the stereochemistry. In fact, 1-*O*-acetyl-β-D-ribose (**3**) exclusively leads to the β-riboside in the presence of free alcohol and $TrClO_4$ owing to acid anomerization. Isomerization can be suppressed by addition of a basic additive (molecular sieves 4 Å and $LiClO_4$) (Scheme 4).[39]

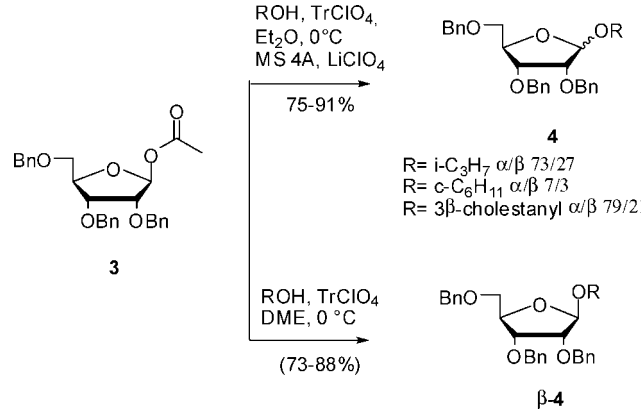
In the same manner, α-ribofuranosides are stereoselectively prepared in high yields by the reaction of 1-*O*-haloacetyl-β-D-ribose with silylated nucleophiles by the promotion of the combined use either of a catalytic amount of $SnCl_4$ and $Sn(OTf)_2$ with a stoichiometric amount of $LiClO_4$[40] or of a catalytic amount of $AgClO_4$ with a 3 M $LiClO_4$ solution.[41]

The introduction of the perchlorate salt is supposed to increase the acidity of the Lewis acid to promote the abstraction of the acetoxy group from the donor. In fact,

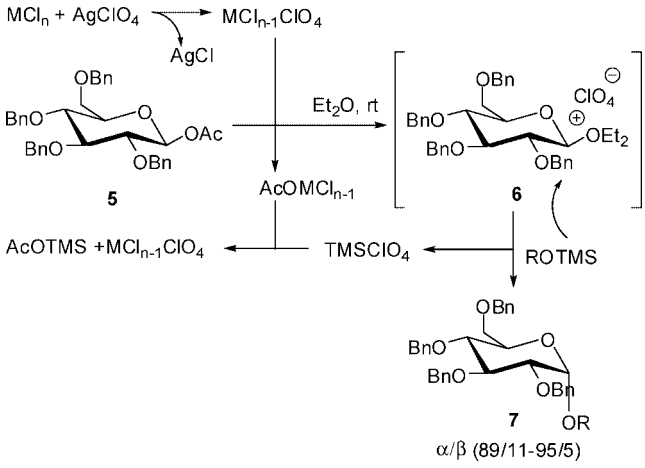
Scheme 3



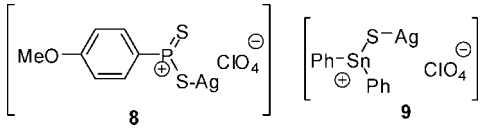
Scheme 4



Scheme 5



Scheme 6



simple Sn salts, as well as Ge, Si, Ga, In, and Hf chlorides, are unable to promote glycosidation at all.

Interestingly, while metallocenes[42–45] and metals of groups 4 and 13[46] show the best reactivity with 1:2 Lewis acid/perchlorate salt ratio, group 14 metals give the expected glycosides in better yields at 1:1 ratio. The active catalytic species are supposed to be $MCl_{n-2}(ClO_4)_2$ and $MCl_{n-1}(ClO_4)$, respectively.

The α-selectivity is assured by the complex ether−perchlorate anion, which blocks the *β*-side of the anomeric carbon (**6**). Finally the catalytic cycle is closed by reaction by $TMSClO_4$ and acetate (Scheme 5). Actually increase in stability of the metal−acetate bond decreases yields, because the catalytic loop is prevented.[46]

A similar stereochemical outcome is observed with glucopyranosyl 1-*O*-carbonate in the presence of the $SnCl_4-AgClO_4$ catalytic system. In diethyl ether the cyclohexylmethylglycoside is obtained in 78% yield and 92/8 α-selectivity. Conversely, switching the solvent to CH_2Cl_2 causes a decrease in selectivity (82/14). Analogous results are obtained with a $Cp_2HfCl_2-2AgClO_4$ catalytic system.[47]

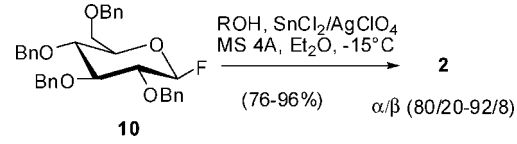
This reaction is interesting because it involves the linkage of two sugar moieties using a carbonate as a connector, which acts as the leaving group for one sugar moiety and as the protecting group for the other. Then removal of the internal carbon dioxide by the aid of a Lewis acid provides the glycosyl bond.

Accordingly with above-reported methods, a mixture of tin tetrachloride or Cp_2HfCl_2 and silver perchlorate are found to be the best catalytic mixture for this decarboxylation reaction. A good α-selectivity is observed, especially in Et_2O. On the other hand, selectivity can be efficiently reversed to the *β*-isomer, combining $AgClO_4$ and Lawesson's reagent or diphenyltin sulfide, starting from 1-haloacetyl or C-1 free furanose.[41]

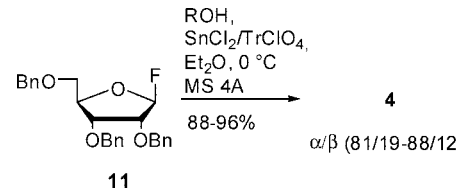
In fact, the proposed catalytic species **8** and **9** do not shield the cationic intermediate, and the thermodynamically more stable *β*-isomers are formed (Scheme 6).

Finally, whereas trityl perchlorate can couple free alcohols with acetyl ribosides or TMS ethers with anomeric free

Scheme 7



Scheme 8



furanoses, it is inefficient when both partners have free hydroxyl functions. The reaction can be exploited by other trityl derivatives, but interestingly addition of $LiClO_4$ still reverses the stereochemistry.[48]

The reaction is then extended in good yields to *C*- and *N*-ribosides by using $Sc(ClO_4)_3$ and the appropriate silyl nucleophile. Stereoselectivity is significantly higher versus α-ribosides, ranging from 8:2 to almost exclusive.[49]

Moreover, 1-*O*-acetyl sugars serve as efficient glycosyl donors in the O → C glycoside rearrangement approach to *C*-aryl glycosides of 2-deoxy-glycosyl acetates promoted by $Cp_2HfCl_2-AgClO_4$.[50]

Recently, the sulfonamido-glycosylation of simple methyl glycosides of benzyl-protected ribose, 2-deoxyribose, 2-deoxyglucose, and 2-deoxygalactose in the presence of perchloric acid immobilized on silica gel was performed to afford the corresponding sulfonamido glycosides with 78−95% yields with minimal workup and short reaction times, except for very sterically hindered sulfonamides.[51]

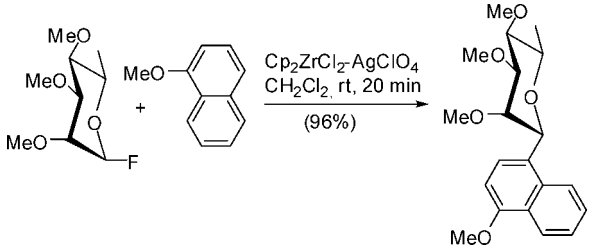
Among glycosyl donors, glycosyl halides (fluorides, chlorides, and bromides) in combination with Lewis acids belong to well-established and reliable techniques of carbohydrate chemistry. Among halides, one of the notable advantages of the glycosyl fluoride as a glycosyl donor is its high thermal and chemical stability as compared with the other glycosyl halides.[52]

Pioneer studies on perchlorate salts as promoters have been conducted by Mukayiama since 1981, when the glycosylation of glucopyranosyl fluoride **10** was obtained in the presence of a mixture of $AgClO_4/SnCl_2$ in good yields and moderate selectivity (Scheme 7).[53]

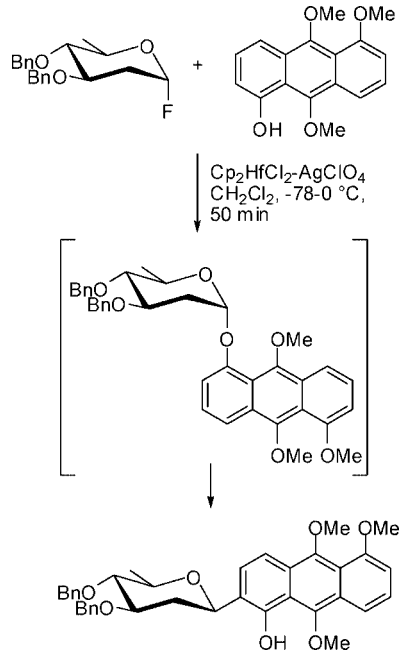
Under the same experimental conditions, furanosyl fluorides react smoothly but lead to *β*-ribofuranosides that are poorly interesting products. However when the perchlorate partner is changed to trityl perchlorate, various ribofuranosides are synthesized in 88−96% yields and 81/19 to 88/12 α-selectivity (Scheme 8).[54]

$AgClO_4$ combined with metallocenes has been known as an activator of glycosyl fluorides for more than 20 years. Systematic work is not present in the literature, but many single examples are reported.[42–44,55] Among them, two different types of aryl *C*-glycosylations with electron-rich aromatic compounds using $Cp_2ZrCl_2-AgClO_4$ are reported. One is a Friedel−Crafts-type reaction (Scheme 9),[56] and another is the C-glycosylation of naphthol derivatives via the O → C migration pathway (Scheme 10) already mentioned above with *O*-acyl sugars.[50,57] The thermodynamic products, that is, the aryl *β*-glycosides, are generally obtained in high yields and excellent stereoselectivity.

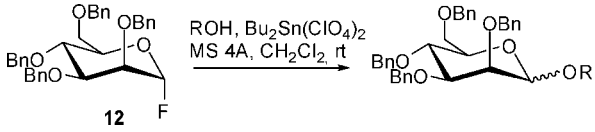
Scheme 9



Scheme 10



Scheme 11



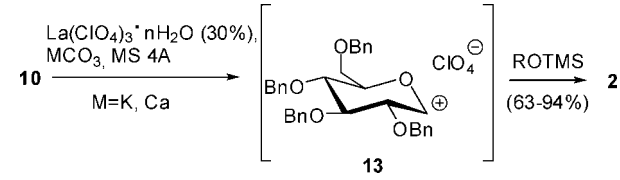
Furthermore, Suzuki also reported the combined use of $Bu_2SnCl_2-AgClO_4$, which gives $Bu_2Sn(ClO_4)_2$ as the active species, as an effective promoter for the glycosidation of totally benzylated α-mannopyranosyl fluoride and several alcohols (Scheme 11).[58]

More recently, from the basic idea that the rare earth metal−fluorine bond has a large bond dissociation energy, that is, they form tight pair, a method that uses a catalytic amount of a rare earth perchlorate, glycosyl fluorides, and glycosyl trimethylsilyl ethers as acceptors has been developed.[59]

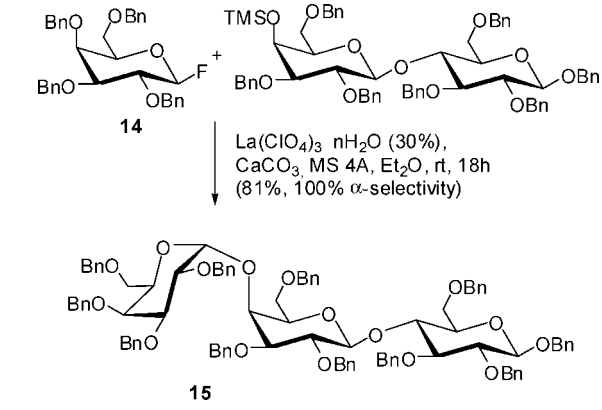
Many rare earth perchlorates were tested, and the use of 30 mol % of hydrated $La(ClO_4)_3$, $Ce(ClO_4)_3$, or $Pr(ClO_4)_3$, in the presence of K_2CO_3 (4 mol equiv) and MS 4 Å, was found to be most effective.

On the other hand, the glycosidation does not proceed in the presence of hydrated perchlorate of Gd, Ho, Yb, or Y, suggesting that only rare earth metals with a certain range of ionic radii are effective for this type of glycosidation. Mechanistic investigation of the reaction suggests that the interaction of the glycosyl fluoride with the rare earth perchlorate produces an oxonium cation intermediate (**13**), which then reacts with the trimethylsilyl ether to form the

Scheme 12



Scheme 13



glycoside **2**, trimethylsilyl fluoride, and rare earth perchlorate, thereby making possible the catalytic cycle (Scheme 12).

The reactions are found to proceed quite smoothly, affording only the glycosides in good to excellent yields (63−94%). Noteworthy, the predominance or exclusive formation of the β-isomer is observed in CH_2Cl_2 as the solvent and K_2CO_3 as the base, while the α-isomer prevails with the diethyl ether/$CaCO_3$ system, and its exclusive formation is obtained in the reaction of 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl fluoride with (trimethylsilyloxy)-cyclohexane.

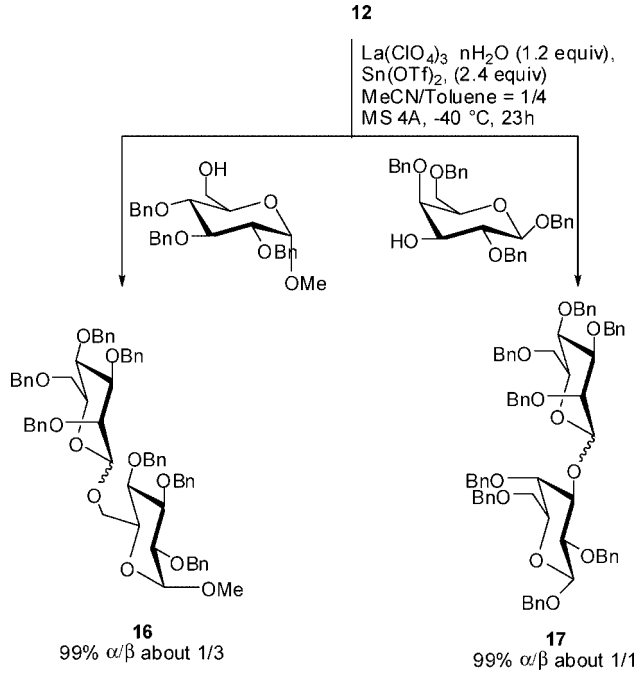
The reaction can be applied in the synthesis of the trisaccharide **15** in 81% yield (Scheme 13), an intermediate leading to globotriaosyl ceramide, a glycosphingolipid of considerable biological significance within the area of cellular recognition. According to the reaction course, the procedure using diethyl ether/$CaCO_3$ has to be employed, being that an α-linkage is required.

The reaction can be performed also in the presence of free alcohols as glycosyl acceptors, even if a mixture of rare earth triflate and barium perchlorate is required.[60]

Rare earth perchlorates allow partial solving of one of the most important problems in carbohydrate chemistry, the direct construction of 1,2-β-D-mannopyranosides, which possess the stereoelectronically disfavored anomeric equatorial C−O linkage. A combination of $Sn(OTf)_2$ and $La(ClO_4)_3 \cdot nH_2O$ as an activator, in fact, succeeds in β-mannosylation coupling with the primary C-6 position of sugars, albeit in poor selectivity (**16**, 3:1, Scheme 14).[61] No selectivity is found upon coupling with secondary C-4 or C-3 positions (**17**).

Waldmann et al. have reported a number of glycosidation reactions under essentially neutral conditions,[37,62,63] using lithium perchlorate as the promoter and fluorides as the donors. $LiClO_4$ is certainly less expensive and more common than rare earth perchlorates; therefore a glycosidation reaction that employs this salt is certainly well-accepted. The design of new glycosidation reactions can start from the idea that the detachment of the anomeric leaving group might be supported by an appropriate solvent capable of stabilizing

Scheme 14



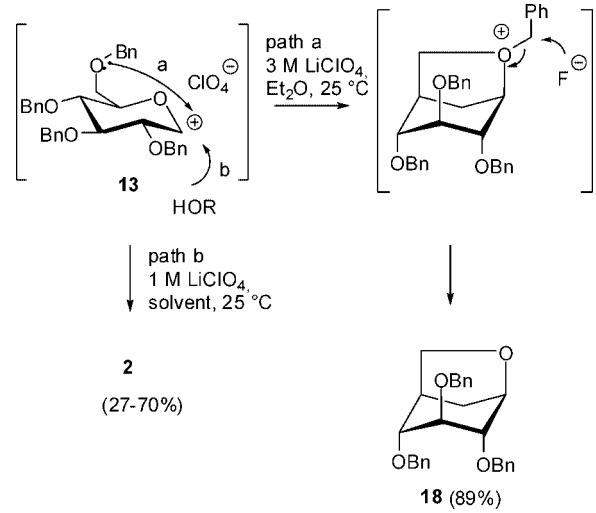
the formation of a glycosyl cation like **13**. Since $LiClO_4$ in organic solvents is well-known to be able to stabilize polar and ionic transition states and intermediates, it represents a valuable candidate in glycosidation reactions.[64] Moreover, the choice of the solvent can influence the stereochemical outcome of the reaction. The use of CH_2Cl_2 is ineffective either on the magnitude or on the direction of the stereoselectivity. On the other hand, solvents such as Et_2O may behave as a nucleophile, thereby generating an intermediate that is preferentially approached by the alcohols from the axial α-direction, thus affecting the anomeric ratio. Acetonitrile, however, is able to stabilize glycosyl cations by complexation at their α-face,[65] so in this solvent, the *β*-anomer predominates.

Glycosyl fluorides react advantageously with different alcohols to give the respective glycosides in moderate to acceptable yields (27−70%)[37] in 1 M solutions of $LiClO_4$, whereas higher concentrations (the classical 5.0 or 3.0 M $LiClO_4$ in Et_2O mixture (LPDE))[12] favor the formation of 1,6-anhydro-*β*-D-glucose derivative **18** (Scheme 15). These findings can advantageously be applied to the construction of fucosyl glycosides **20** under neutral conditions (Scheme 16).[66]

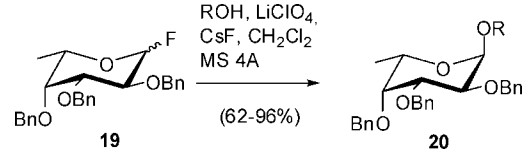
Cesium fluoride has to be added as an acid scavenger. The reaction conditions are then adjusted, because part of the salt remains undissolved in the reaction mixture. A 0.07 M solution of $LiClO_4$ gives a homogeneous solution without substantial modification of yield and stereoselectivity, and the acid scavenger can be omitted.[67] Under these conditions, fucosyl tri- and tetrasaccharides are synthesized in good yields.

As mentioned above, an acetyl blocking group shows marked neighboring effect (intermediate **22**, Scheme 17), leading to orthoesters (like **24**), through a well-known side reaction. They arise from a competitive attack of the alcohol to be glycosylated at the carbonyl group of the acyl blocking function at O-2 instead of at the anomeric center.[37,62] It is worth noting that, conversely from classical glycosidation in which the initial formed orthoesters are then rearranged

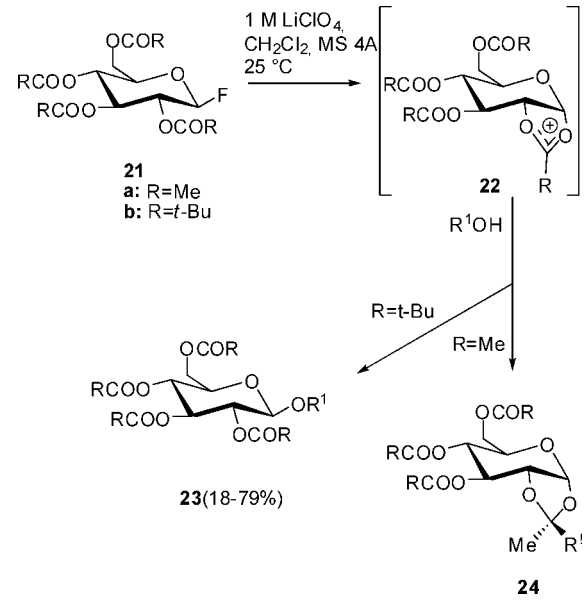
Scheme 15



Scheme 16



Scheme 17



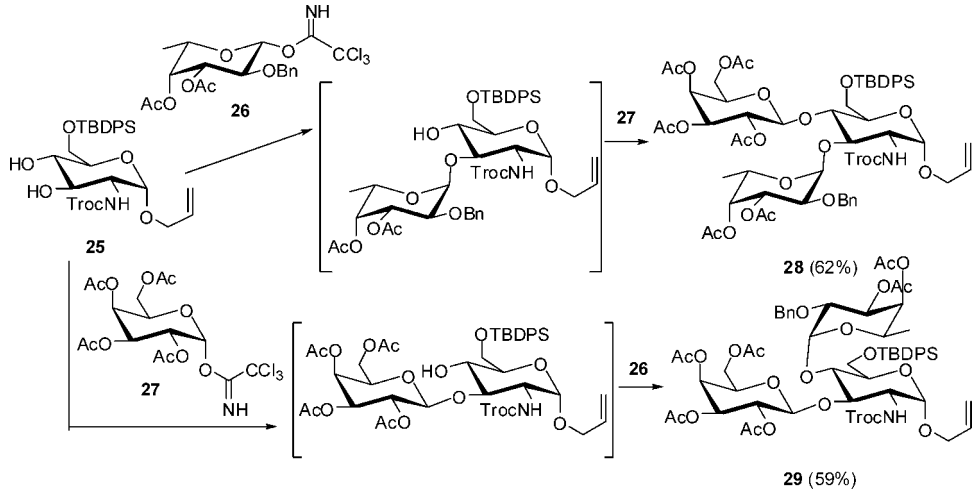
by the Lewis acid to glycoside, $LiClO_4/CH_2Cl_2$ solutions are so mild that the acid-labile orthoesters **24** remain stable.

The use of the sterically hindered pivaloyl protecting group minimizes the formation of orthoesters and *β*-per-*O*-pivaloylglucosyl fluoride (**21b**) is converted into the desired *β*-*O*-glycosides **23** stereospecifically and in high yields for simple alcohols but in unsatisfactory yield with more complex alcohols.

As an alternative to halides, other glycosyl donors such as trichloroacetimidates, thioglycosides, glycosyl phosphites, and glycosyl phosphates have been developed.

Under Waldmann's conditions, however, trichloroacetimidates give worse results with respect to fluoride,[68] so glycosylation procedures are studied only after the discovery of the $HClO_4-SiO_2$ system.[8] A series of acetyl-protected

Scheme 18



glycosyl tricholoroacetimidate donors are used for glycosylation reactions with a series of primary and secondary alcohol acceptor substrates in good-to-excellent yields (55−94%) with this catalyst in CH_2Cl_2 or DCE solution.[69] The strategy is also effective for deoxy and pentose sugars and for the preparation of complex trisaccharides, such as Le^X (**28**) and Le^A (**29**) trisaccharide derivatives (Scheme 18).

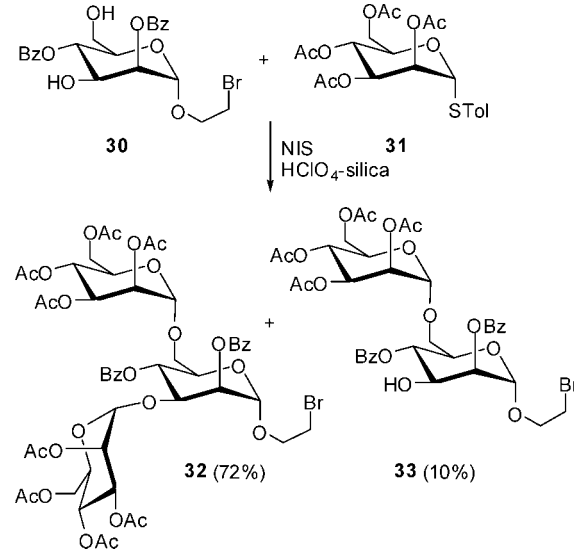
In order to ensure the correct selectivity, the synthesis of **28** is conducted in DCE/Et_2O (2:1) mixture as the solvent. This result is consistent with the solvent effect of Et_2O already observed in the glycosidation reaction with fluorides.[59] The same procedure is extended to a practical "on-column" synthesis. Since the reaction essentially involves reagents and silica, authors considered the addition of the reagents to a chromatography column filled with flash silica gel and topped with a band of perchloric acid−silica. After charging onto the column, the donor and the acceptor were dissolved in dry CH_2Cl_2 and left for 30 min; the column is then eluted, and the desired disaccharide is obtained in yield comparable to that obtained in the corresponding solution phase reaction.[69]

The reaction is further scaled up to 100 g of donor and to a variety of hydroxyl protecting groups such as benzylidene, *tert*-butyldimethylsilyl, benzoyl, allyl, trityl, and benzyl groups without substantial detriment of yields and selectivity.[70] The mild reaction conditions, experimental simplicity, low cost, excellent yields, and environmentally benign nature are major advantages of this new approach compared with other classical Lewis acid promoters of glycosylations.

Thioglycosides, particularly stable and easily handled donors, require a strong acid to be activated. Typically triflic acid in conjunction with *N*-iodosuccinimide (NIS) is the reagent of choice.[71] However, $HClO_4$−silica is much easier to handle and store than triflic acid,[72] so a series of NIS/$HClO_4$−silica promoted reactions have been investigated with representative thioglycoside donors and glycosyl acceptors with excellent results, providing the expected 1,2-*trans*-linked disaccharides in 74−87% isolated yields. The reaction can be extended to one-pot double glycosylation synthesis of trimannoside (**32**) in 72% yield, along with 10% of the 1,6-linked disaccharide **33** (Scheme 19).

Other examples of the same reaction are reported by Misra et al.[73] The yields are comparable to those in the earlier report. Then the authors turned their attention to the conversion of pyranose structures to the corresponding

Scheme 19

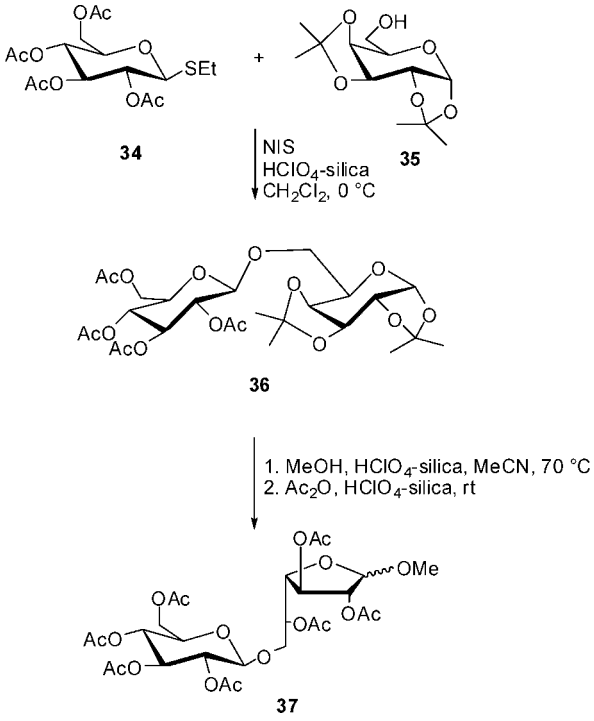


furanose. The rearrangement of the galactopyranose ring into galactofuranose in oligosaccharides can be exploited by $HClO_4$−silica at elevated temperature (Scheme 20), starting from di- and trisaccharides containing a di-*O*-isopropylidene-α-D-galactopyranose moiety at the reducing end.

A series of compounds were converted into galactofuranoses as their methyl glycosides in excellent yield (70−78%). Interestingly, if per-acetyl protection is needed, acetylation with acetic anhydride can be obtained with $HClO_4$−silica as the catalyst again,[74] thus allowing a three-step synthesis fully catalyzed by a unique catalyst.

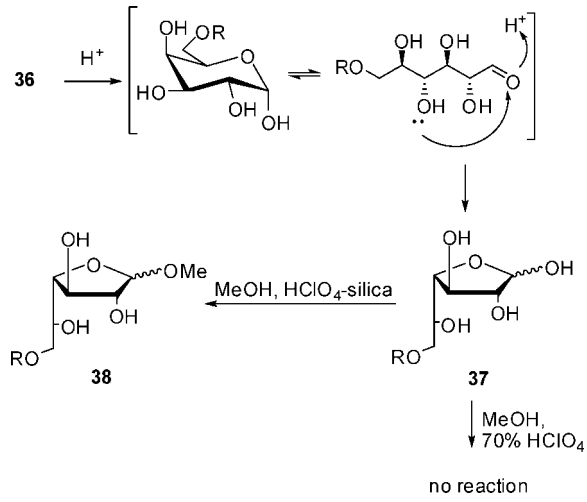
The consumption of the starting material and the formation of a more polar compound were observed during the reaction course. Therefore a mechanism involving first the acidic hydrolysis of the isopropylidene groups of **36**, followed by five-membered ring closure, was supposed. Finally methanol formed the new glycosidic bond at the reducing end (**38**, Scheme 21). This mechanism was supported by the use of 70% $HClO_4$, under which conditions no formation of furanosidic glycoside was observed, owing to the presence of water in the 70% $HClO_4$ leading to the formation of the hemiacetal **37** only. Conversely, use of $HClO_4$−SiO_2 maintained the anhydrous reaction conditions, and furanosidic glycosides were obtained.

Scheme 20



34 35 36 37

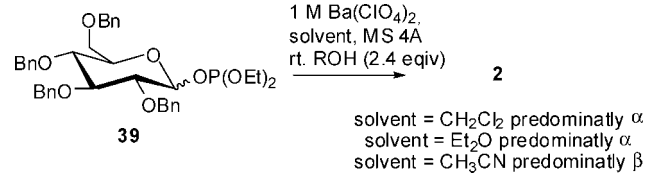
Scheme 21



38 37

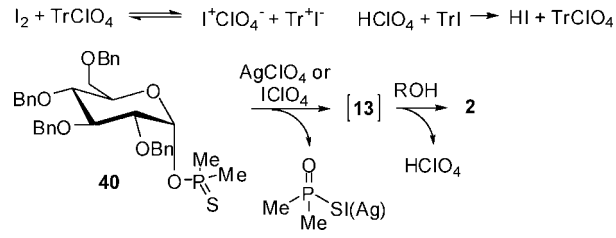
Glycosyl derivatives with phosphorus-based leaving groups are another class of donors, although they are considered to be not as reactive as halides or imidates. Waldmann carried out reactions with β- and α-configured benzyl- and acetyl-protected glycosyl phosphates under his conditions, but treatment with 1 M solutions of $LiClO_4$ in CH_2Cl_2 or Et_2O gave the glycosides in moderate yields.[37,62] On the other hand, diethyl phosphites in the presence of $Ba(ClO_4)_2$ significantly improved yields of glycosides (61−95%).[75] The reaction followed the well-known and already above-described stereochemistry pattern, that is, the α-anomers were formed predominantly in ether and dichloromethane, whereas the β-anomers prevailed in acetonitrile (Scheme 22). The improved yields with barium instead of the classical $LiClO_4$ may be rationalized by the fact that it is a much larger and softer Lewis acid. Consequently the soft and relatively weak phosphorus atom of the phosphite is better coordinated, thereby being activated.

Scheme 22



39 2

Scheme 23



40

Phosphorodithioates are other easily accessible, efficient, and versatile glycosylating reagents, which, depending on the mode of activation, can be used in the synthesis of β- as well as α-glycosides.[76] Among them, silver perchlorate in acetonitrile in the presence of *sym*-collidine is able to activate 2-deoxy-α-glycosylphosphorodithioates leading to pure 2-deoxy-α-glycosides and α-disaccharides in high yields (80−92%). 1-*O*-Dimethylphosphinothioyl sugars like **40** were also found to be valuable glycosyl donors when activated by $TrClO_4/I_2$ or $AgClO_4$ (Scheme 23). The reaction has been deeply studied on various substrates for the synthesis of both *O*- and *C*-glycosides.[77−84]

From Inzazu's work, some features can be obtained: the reaction proceeds mainly through a S_N1 mechanism, via perchlorate cation **13** after leaving of the dimethylphosphinothioyl group by interaction of the iodonium or silver cation with the sulfur atom,[79] the corresponding S_N2 mechanism, previously hypothesized,[83] being discarded by subsequent evidence; α-isomers are mainly obtained with gluco, manno, rhamno, and fuco derivatives.[79,81]

β-Mannosides can be obtained by reducing the $TrClO_4$ amount from 50 to 5 mol %, demonstrating that an adequate amount of promoters is required to prevent the isomerization to the more stable α-anomer. Only for this reaction, a stable mannosyl iodide is proposed as the donor.[81]

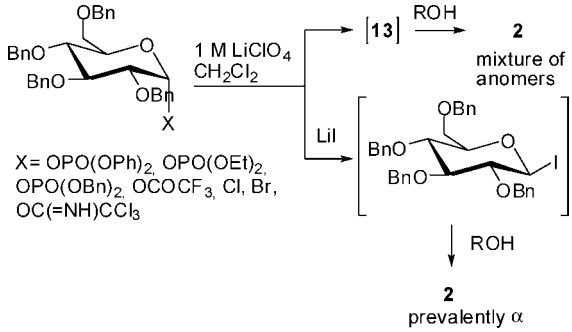
N-(Phenyl)imidazolium perchlorate has shown extremely high reactivity as promoter for the condensation of a nucleoside phosphoramidite and a nucleoside in a liquid phase. The azolium salt has allowed smooth and high-yield condensation of the nucleoside phosphoramidite and a 5′-*O*-free nucleoside. However, azolium triflates work better in the solid-phase synthesis of oligodeoxyribonucleotides and oligoribonucleotides.[85]

C-Glycosidation (Friedel-Crafts-like reaction) was also attempted, but it was unsuccessful except with the highly activated 1,3,5-trimethoxybenzene.[77]

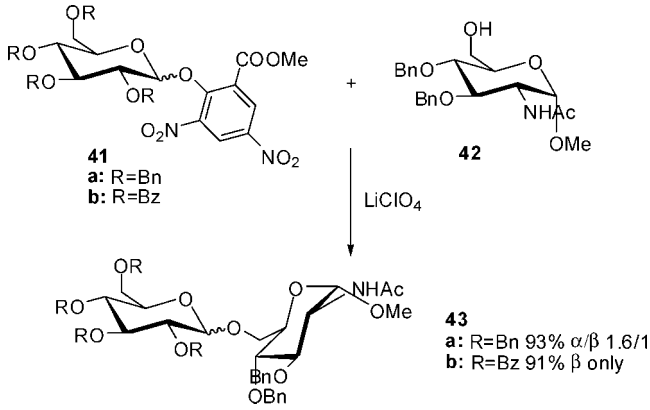
Another glycosyl donor, the 1-*C*-methyl-α-D-glucopyranosyl derivative, was expected to be highly reactive, because the electron-donating effect of the methyl group would stabilize the tertiary anomeric glycosyl cation intermediate, and actually, glycosidation smoothly proceeded to afford the 1-*C*-methyl-D-glucopyranosides in good yields (82−88%) with high α-stereoselectivities, the little amount of β-form being attributed to the S_N2-like reaction mechanism.[82]

Conversely from Inazu's mechanistic hypothesis, Waldmann postulates glycosyl iodides as advantageous but

Scheme 24



Scheme 25



unstable in glycosylation reactions under neutral conditions (1 M solutions of $LiClO_4$ in CH_2Cl_2 in the presence of LiI).[86] Iodides can be generated from different leaving groups at the anomeric center, and then an S_N2 mechanism leads to the product. A lower ratio of anomers in the absence of LiI is presented as supporting evidence of the mechanism. In fact, oxonium ions **13** may be attacked from both the axial and equatorial direction (Scheme 24), since no dichloromethane perchlorate anion complex can block one side of the anomeric carbon, conversely from ether (see above).[63]

Recently, methyl 3,5-dinitrosalicylate glycosides were introduced as glycosyl donors. Among numerous promoters suggested, $LiClO_4$ was a competent one. Protective groups followed the "armed−disarmed" theory; that is, benzyl-protected donors gave predominantly the α-glycosides, whereas the benzoyl-protected donors in general gave *β*-glycosides (Scheme 25).[87]

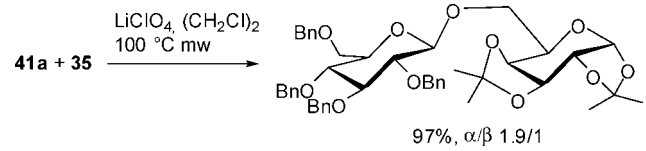
By this protocol, disaccharides were prepared in up to 93% and 82% yield for the (1→6)- and (1→4)-linkages, respectively, in solution, as well as in good to moderate yields in solid-phase synthesis. The reaction is then extended to the synthesis of tetra- and hexa-saccharides, optimal glycosylations being obtained at room temperature in the presence of Bu_4NI in $LiClO_4$,[88] and to the synthesis of interesting phenazine glycosides, in $LiClO_4$ in nitromethane.[89]

Methyl 3,5-dinitrosalicylate glycosides are also employed for fast, high-temperature glycosylations using precise microwave heating for classical glucosides (Scheme 26),[90] variously protected glucosamine derivatives,[91] and directed mannosylation.[92]

3.2. Ferrier Rearrangement

2,3-Unsaturated glycosides obtained by Ferrier rearrangement of glycals are versatile chiral intermediates in the synthesis of modified carbohydrates and nucleosides with important pharmacological properties. This class of compounds can be transformed into 2-deoxy and 2,3-dideoxy sugars, which are building blocks for the total synthesis of many antibiotics. However, the requirement for an acid catalyst precludes the use of acid-sensitive protecting groups, and the development of a nonacidic alternative would extend the scope of the reaction. Chemists have attempted to overcome this drawback employing among others some perchlorate derivatives and mainly perchloric acid supported on silica.

Scheme 26



For example, Ferrier-type reactions can be carried out under nonacidic but oxidative conditions by treating 3-*n*-pentenoyl glycals with iodonium dicollidinium perchlorate (IDCP). The terminal double bond is chemoselectively activated to furnish an allylic oxo-carbenium ion, which reacts at the anomeric position with monosaccharide alcohols to afford 2,3-unsaturated disaccharides in fairly good yields (Scheme 27).[93]

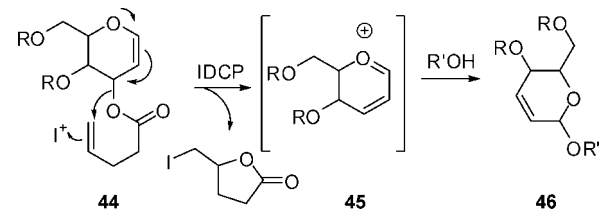
This oxidative modification of the Ferrier rearrangement allows the reaction to take place with fairly unreactive secondary and tertiary hydroxy groups of monosaccharides. It should be noted that the vinyl ether of **44** should be more reactive toward an iodonium ion than the isolated pentenyl double bond, but C-3 ester functions sufficiently disarm the glycal double bond inverting chemoselectivity.

Treatment of tri-*O*-acetyl glucal (**47a**) and other acetyl glycals with acetyl perchlorate provides an efficient dimerization leading to good yields of the corresponding *C*-disaccharides (**48**) with a high degree of stereocontrol at the new C−C bond (Scheme 28). First the loss of the 3-*O*-acyl group generates an allylic oxo-carbenium ion (**45a**), and then a second equivalent of the starting glycal adds to the double bond. The process is terminated by capture of this species by an acetate anion. On the other hand, the more nucleophilic tri-*O*-benzyl-D-glucal (**47b**) results in a rearrangement via a 1,6-hydride shift, leading to the bicyclic acetal **49** (about 40% yield). The formation of this product can be rationalized by trapping of the bicyclic oxo-carbenium with the (initially formed) benzyl alcohol. This rearrangement is peculiar to the benzyl group. In fact even substituted benzyl groups (e.g., *p*-methoxybenzyl) inhibit the reaction.[94]

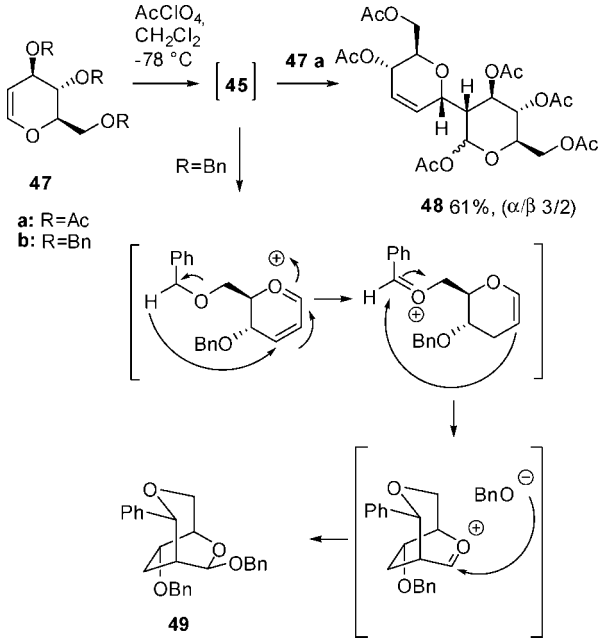
Interestingly the reactivity pattern differs also between tri-*O*-acetyl-D-galactal and **47a** in LPDE medium. In fact, glucal gives Ferrier rearrangement, whereas galactal does double bond addition to 2-deoxyglycoside (Scheme 29).[95]

Very likely, the 4-*O*-acetyl group provides anchimeric assistance in the *trans*-biaxial conformation of glucal,

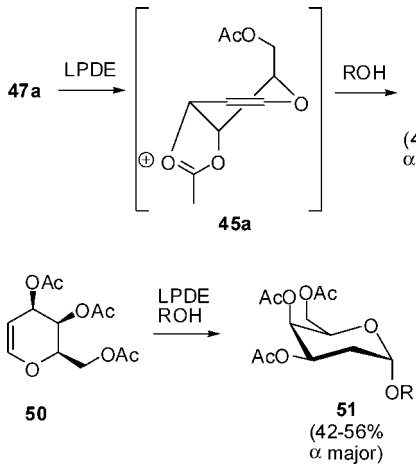
Scheme 27



Scheme 28



Scheme 29



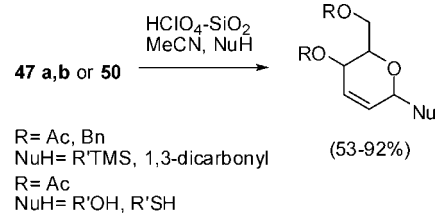
undergoing Ferrier rearrangement to the 2,3-unsaturated glucosides. Conversely, in the galactal the 3-OAc and 4-OAc are *cis* to each other and no anchimeric assistance is possible. Addition of the alcohol to the enol ether double bond takes precedence, leading to 2-deoxy sugar.

Perchloric acid supported on silica is the most widely and recently studied catalyst for performing Ferrier rearrangement. There are several advantages in the use of this catalyst: high yields of products, simplicity in operation, cleaner reaction profiles, short reaction times, exceptionally high selectivity, no additives, no stringent reaction conditions, and no need for special precautions in either handling the catalyst or excluding moisture from the reaction medium (Scheme 30).

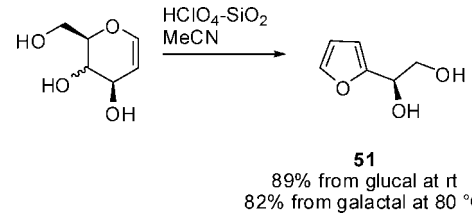
$HClO_4-SiO_2$ catalyzes allylic rearrangement of acylated and alkylated glycals with silylated C-nucleophiles and active methylene compounds,[96] producing excellent yield of 2,3-unsaturated *C*-glycosides, prevalently α form.

Moreover only acetylglycals can be converted into 2,3-unsaturated *O*- and *S*-glycosides.[97,98] *N*-Glycosyl sulfonamides are prepared via Ferrier sulfonamido-glycosylation of D-glycals.[99] Prevalent α selectivity is maintained, and

Scheme 30



Scheme 31



important disaccharides can be obtained by using hydroxy sugars. As in the glycosylation reaction,[57] C-glucosylation of naphthol derivative is obtained via the O → C migration pathway of the corresponding O-glucoside.[97]

Interestingly, another feature resembles glycosylation chemistry. $HClO_4-SiO_2$ catalyzes ring rearrangement of free glucal and galactal to the furanoid skeleton **51**, which is a component of many biologically important natural products (Scheme 31). As in the above-described chemistry,[73] galactal rearrangement needs heating, while glucal rearranges at room temperature. Moreover in the present reaction dehydration occurs, whereas in glycosylation conditions it does not.[97]

During these reactions, some racemization occurs, but supported $HClO_4$ remains the best promoter for this purpose among all of the reagents reported so far.

Finally alkyl and aryl 2,3-unsaturated glycosides have been prepared in acetonitrile, at room temperature, in the presence of a catalytic amount of magnesium perchlorate, by the reaction of 3,4,6-tri-*O*-acetyl-D-glucal with alcohols, thiols, or silyl nucleophiles in excellent yields with high α-selectivity.[100]

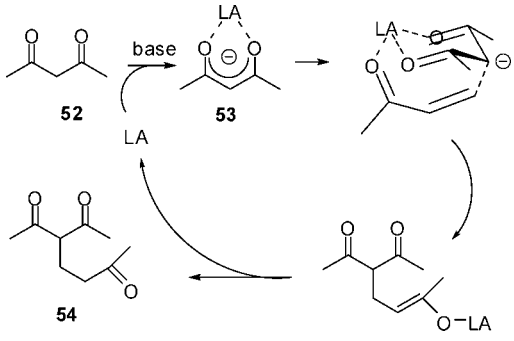
4. Conjugate Additions

Conjugate additions of nucleophiles to α,β-unsaturated carbonyl compounds are typically acid-catalyzed organic reactions. The metal ions are able to activate carbonyl groups by coordination to the lone pair of electrons on the oxygen of the carbonyl moiety in organic substrates and thereby activate them to undergo transformations due to their Lewis acidity. The Michael addition is among the most important C−C bond-forming reactions, and often it is catalyzed by Lewis acids. As originally defined, the Michael addition is the addition to the β carbon of an α,β-unsaturated carbonyl compound of an enolate of a ketone or aldehyde. Now this name means the 1,4-addition of every nucleophile to an α,β-unsaturated carbonyl compound and a prefix indicating the nucleophilic species is added (e.g., thia- or aza- for sulfur and nitrogen nucleophiles, respectively).

4.1. Michael Addition

In this section, we include carbon nucleophiles as in the classical definition. Stable carbon nucleophiles such as β-ketoesters and malonates give rise to compounds with a highly useful 1,5-dioxygenated pattern. The Michael reaction

Scheme 32



often needs double catalysis, a basic catalyst to deprotonate the nucleophile and an acid one to activate the carbonyl moiety (Scheme 32).[101] After coordination to the metal ion of the acetylacetonate metal complex (**53**), the carbonyl group of the unsaturated ketone is activated by metal Lewis acidity. Then, it undergoes the conjugate addition, and the release of the Lewis acid completes the catalytic cycle. Metal perchlorates obviously play an important role as Lewis acids.

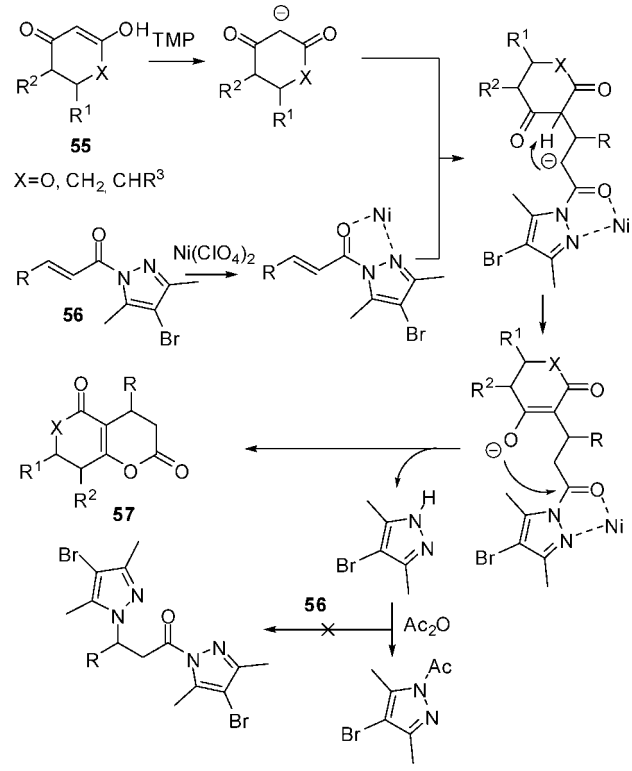
The use of LPDE in Michael additions in the past century has been extensively reviewed, and we refer the reader there for more details.[11] However, recently, solid $LiClO_4$ has found use in this reaction. The interesting difference in behavior of LPDE and solid $LiClO_4$ is attributed to the Lewis acidity of the lithium ion. In a coordinating solvent such as diethyl ether, the Lewis acidity of lithium ion is moderated and lower than that under solventless conditions. When the reaction is carried out under solvent-free conditions, a small amount of catalyst ($LiClO_4/Et_3N$, 5 mol %) is needed for the coupling of a wide range of structurally different compounds with an active methylene group and α,β-unsaturated ketones, esters, nitriles, and nitro-olefins, affording the corresponding Michael products in almost quantitative yield. The simplicity of the workup procedure, the high purity, and the short reaction time, without the use of any organic solvent, are merits of the reaction.[102]

Ferric perchlorate in only 0.35 mol % is an interesting catalyst. It catalyzes Michael reaction of β-ketoesters with methyl vinyl ketone and methyl acrylate, to give the products in 99% yields after removal of the catalyst by simple filtration. It should be noted that $FeCl_3 \cdot 6H_2O$ does not require a stoichiometric amount of base, since, unique among all other metals, it is able to give the dionato chelate complex (**53**) without prior deprotonation and even in Brønstedt acidic media.[101]

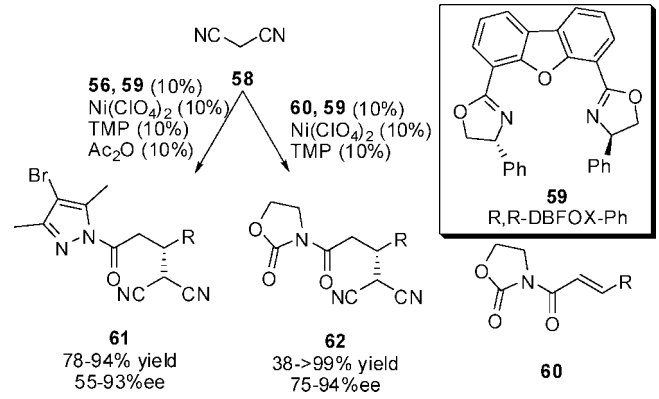
Other perchlorates have been used, partially covered in our microreview[13] and extensively resumed here. Reactions of cyclic 1,3-dicarbonyl compounds (**55**) with 1-(2-alkenoyl)-4-bromo-3,5-dimethylpyrazoles (**56**), 3-(2-alkenoyl)-2-oxazolidinones (**60**), and 1-(2-alkenoyl)-3,5-dimethylpyrazoles (**63**) under the double catalytic activation conditions (10 mol % each of $NiClO_4 \cdot 6H_2O$ and TMP) provide a new direct synthetic route to enol lactones (**57**).[103] Among the three Michael acceptors, **55** works in 41−85% yields (Scheme 33).[104]

In order to set up an enantioselective version of the Michael additions to unsaturated ketones, Kanemasa and coworkers have examined (*R*,*R*)-4,6-dibenzofurandiyl-2,2′-bis(4-phenyloxazoline) (**59**, *R*,*R*-DBFOX-Ph) in mixtures with many perchlorate salts. Although the magnesium and zinc complexes show satisfactory catalytic activity, the enantioselectivities observed are relatively poor, while metal

Scheme 33



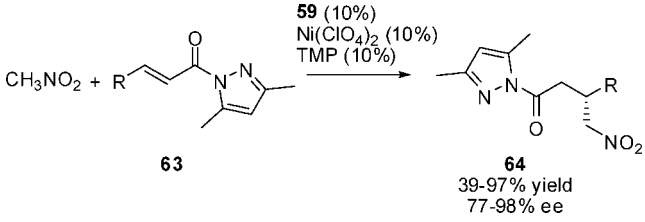
Scheme 34



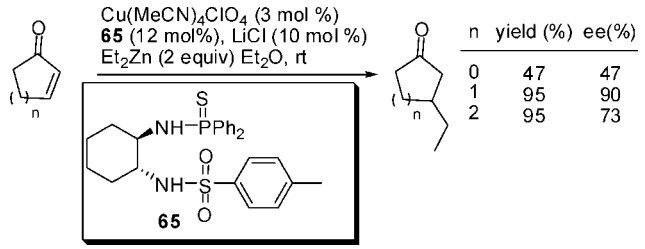
complexes prepared from the perchlorates of copper(II), iron(II), and manganese(II) show only a low catalytic activity. From this screening, the couple **59** and $Ni(ClO_4)_2 \cdot 3H_2O$ is found to be the most effective catalytic system, exploiting under double catalysis with TMP the asymmetric Michael addition of malononitrile (**58**) to **56** or to **60**, leading to adducts **61** and **62**, respectively, in high chemical yields and with satisfactory enantioselectivities (Scheme 34).[105] Moreover, the same reaction is obtained also with substituted malononitriles but employing more polar solvents.[106]

The same *R*,*R*-DBFOX-Ph/$Ni(ClO_4)_2 \cdot 3H_2O$ mixture is successfully applied for the enantioselective synthesis of **57**. Moreover the addition of acetic anhydride, to prevent the undesired pyrazole competitive attack to the substrate **55**, allows the catalytic loadings to be minimized to 2 mol % with yield increased up to almost quantitative and enantioselectivity up to 99% ee (Scheme 33).[103] The same catalytic mixture exploits then the enantioselective Michael addition of nitromethane to **63** (Scheme 35). The nitro adducts **64**

Scheme 35



Scheme 36



are generally obtained in very satisfactory yields and enantioselectivities except for those with crowded double bonds.[107]

Together with stabilized nucleophiles, simple organometallic reagents can add to α,β-unsaturated carbonyl compounds in a 1,4-fashion. Original syntheses have recently appeared in literature, where the use of perchlorates and chiral auxiliaries are coupled in order to enantioselectively exploit this C−C bond formation.

For example, $Cu(CH_3CN)_4ClO_4$ (3 mol %) and a chiral sulfonamide−thiophosphoramide ligand (**65**, 12 mol %) in Et_2O at room temperature in the presence of LiCl (10 mol %) as an additive shows high catalytic activity and chiral induction ability in the enantioselective 1,4-conjugate addition of diethylzinc to cyclic enones (Scheme 36).[108] The catalytic system allows the efficient and moderate to high enantioselective functionalization of six- and seven-membered cyclic enones, but it is not as effective for five-membered ones. The chiral ligand has the advantage to be quite stable and can be recovered and reused without loss of catalytic ability and enantioselectivity.

LPDE is a very good medium for the 1,4-conjugate addition of organolithium reagents to α,β-unsaturated amides. Particularly, diastereoselective conjugate addition without any 1,2-addition byproduct takes place with amides bearing (*R*)-phenylethylamine as a chiral auxiliary under these conditions. Diastereomeric ratios are between 91/9 and 59/41, in yields exceeding 90%. Hydrolysis of the chiral auxiliary leads to enantiopure acids.[109]

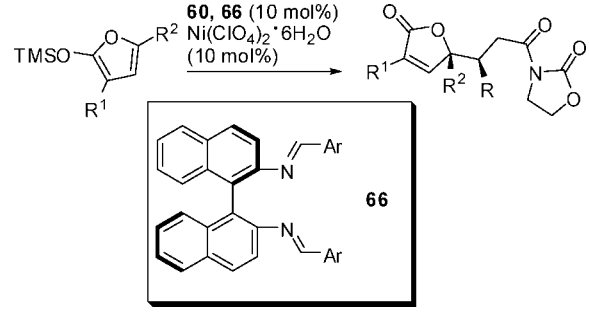
Finally, Suga and co-workers report a catalyst consisting of $Ni(ClO_4)_2 \cdot 6H_2O$ and chiral binaphthyldiimine ligands (**66**), indicating high levels of asymmetric induction for Michael additions between 2-silyloxyfurans and **60** (up to 95% yield and 97% ee) to obtain 5,5-disubstituted furan-2(5*H*)-ones (Scheme 37).[110]

The conjugate addition of indoles can be considered as an addition of a carbanion to α,β-unsaturated carbonyl compounds, but also a Friedel−Crafts reaction, so it will be reviewed in section 5.2.

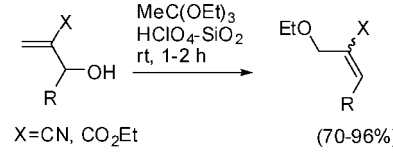
4.2. Conjugate Addition of Alcoholates or Thiols (Thia-Michael)

Only one example of alcoholate conjugate addition catalyzed by perchlorate has been found in the literature.

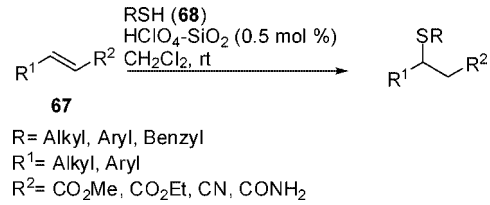
Scheme 37



Scheme 38



Scheme 39



3-Hydroxy-2-methylenealkanoates and 3-hydroxy-2-methylenealkanenitriles on treatment with triethyl orthoacetate in the presence of $HClO_4-SiO_2$ afford the corresponding allyl ethyl ethers in 70−96% yield via conjugate addition to the α,β-unsaturated ester (nitrile) followed by formal elimination of water (Scheme 38).[111]

The addition of thiols to α,β-unsaturated carbonyl compounds is a very important process in carbon−sulfur bond formation. By this process, the olefinic double bond of a conjugated carbonyl compound can selectively be protected, and deprotection can be easily done either by copper-induced elimination or by oxidation followed by thermolytic elimination. Moreover thia-Michael addition products are very important building blocks in organic synthesis.

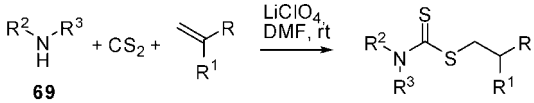
Among catalysts exploited for this reaction, $HClO_4/SiO_2$ is efficient and valuable for addition to α,β-unsaturated ketones, carboxylic esters, nitriles, and amides (Scheme 39).[112]

Supported perchloric acid performs the reaction with better yields and shorter reaction times than aqueous $HClO_4$ (95% vs 82% yield and 10 min vs 1 h respectively). Moreover, nonaqueous workup and involvement of inexpensive reusable catalyst are other significant advantages. The scope and limitations of this reaction have been studied by Chakraborti.[113] The rate of the reaction was found to be dependent on the electronic and steric factors of the α,β-unsaturated ketones and the thiols and these features can be utilized for selective reactions.

Another effective solid catalyst is $LiClO_4$. In fact, a wide range of α,β-unsaturated olefins are converted into the corresponding Michael adduct with good to high yields (65−97%).[114]

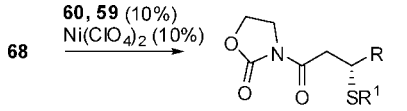
As well as thiols, dithiocarbamate anion can be added to α,β-unsaturated olefins by solid lithium perchlorate catalysis.[115] In fact, primary or secondary amines can react with carbon disulfide and olefins carrying electron-withdrawing

Scheme 40



R= Alkyl, Benzyl
R^1= H, Alkyl
R^2= CO_2Me, COMe, CN, $CONH_2$
R^3= H, Me

Scheme 41



(26->99% y, 78-95% ee)

groups in one pot and in good to high yields (85−95%) except for highly hindered carbonyl compounds (Scheme 40).

Zinc perchlorate is as effective as $LiClO_4$ catalyst except for crowded unsaturated compounds and, moreover, the addition of aryl thiols occurs more rapidly than that of alkyl ones, showing also a dependence of the reaction on electronic factors. On the other hand, $Zn(ClO_4)_2$ is needed in catalytic amounts (1 mol %), while solid $LiClO_4$ is required in more than stoichiometric amounts.[116]

Kanemasa and co-workers report also an enantioselective version of this reaction, that is, the enantioselective thiol conjugate additions to 3-(2-alkenoyl)-2-oxazolidinone **60** catalyzed by DBFOX-Ph/$Ni(ClO_4)_2 \cdot 3H_2O$ (Scheme 41).[117]

4.3. Conjugate Addition of Amines (Aza-Michael)

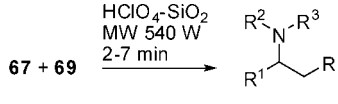
No catalyst is generally required in aza-Michael reactions with amines or lithium amides as nucleophiles. Meanwhile, Lewis and Brønsted acidic catalysts have been employed with less reactive aza-nucleophiles.

Among Brønsted acids, $HClO_4-SiO_2$ catalyzes the aza-Michael addition of several primary and secondary amines to α,β-unsaturated compounds providing, with low cost of the catalysts, β-amino esters, ketones, amides, and nitriles, which are remarkably interesting products since some of them are precursors of β-amino acids. Aromatic amines show poor reactivity (50−85% yield) compared with aliphatic amines (90−96% yield), but no side products or double additions are ever observed by using excess amines.[118] Microwave irradiation lowers reaction times without affecting yields (Scheme 42).[119]

The literature reports many Lewis acidic metal perchlorates as catalysts for aza-Michael reactions. Solid $LiClO_4$ in a stoichiometric amount, for example, promotes the conjugate addition under solvent-free conditions, and it can be easily recovered and reused after reactivation.[120]

Poor nucleophilic carbamates add to enones as a nitrogen nucleophile in the presence of many metal salts. Among the tested salts, $Fe(ClO_4)_3 \cdot 9H_2O$ is the most efficient catalyst together with $PtCl_4$ in dichloromethane at room temperature,

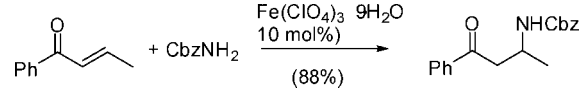
Scheme 42



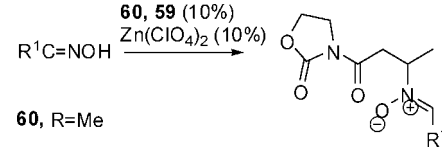
(78-98%)

R=R^2=R^3=H, Alkyl
R^1= CO_2Me, CO_2Et, CN, $CONH_2$

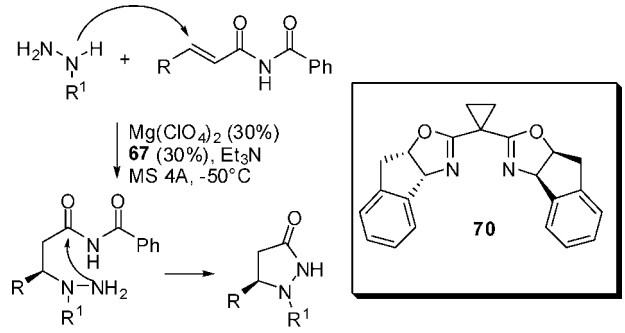
Scheme 43



Scheme 44



Scheme 45



(61-92% y, chemosel >90%, 37-99% ee)

since it is partially soluble in the solvent and it dissolves to some extent after adding the substrates (Scheme 43).[121]

Asymmetric versions of previously reported conjugate additions of aza-nucleophiles to electron-poor acceptors are also reported. As well as (*R*)-phenylethylamine as the chiral auxiliary for conjugate addition of organolithiums to amides (see section 4.1), (*S*)-2-methyl-1-butanol is found to be the best chiral auxiliary (diastereomeric ratios between 90/10 and 75/25) for the conjugate addition of different primary and secondary amines to esters in the presence of solid $LiClO_4$. Interestingly, without solid $LiClO_4$, the reactions do not take place.[122]

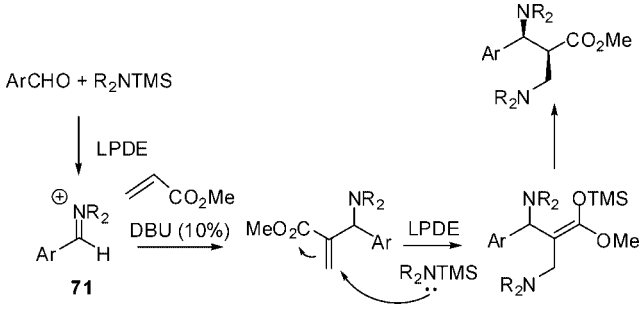
Notwithstanding a lack of bibliographic data on enantiocatalysis of conjugate amine addition to unsaturated carbonyl compounds promoted by perchlorate salt complexes, some papers describe the addition of other nitrogen nucleophiles.

Kanemasa uses his *R*,*R*-DBFOX/Ph as the successful ligand of $Zn(ClO_4)_2 \cdot 6H_2O$ to perform addition of oximes to crotonyloxazolidinones and imidazolidinones.[123] The nitrones are produced in high yields in short reaction times when 10 mol % of the catalyst is used. The aqua complex derived from *R*,*R*-DBFOX/Ph and $Zn(ClO_4)_2 \cdot 6H_2O$ is found to be more effective in its catalytic activity, but enantioselectivity does not exceed 64% (Scheme 44).

Hydroxylamines and hydrazines can provide direct access to small-ring heterocycles, by double addition to unsaturated amides. Magnesium perchlorate is very effective as a Lewis acid in conjunction with chiral cyclopropane bisoxazoline **70** to give high levels of enantioselectivity. Hydroxylamines need no chemoselectivity control, since nitrogen is a better nucleophile than oxygen.[124] On the other hand, low temperature favors the reaction to discriminate between the nucleophilicity of the hydrazine nitrogens. Thus the more nucleophilic and bulky nitrogen adds selectively to the β-carbon (Scheme 45).[125]

An interesting multistep reaction is the reaction of aldehydes with (trimethylsilyl)dialkylamines followed by electrophilic addition with methyl acrylate and finally conjugate

Scheme 46



addition of a second molecule of (trimethylsilyl)dialkylamine in LPDE. Actually the reaction is carried out by mixing a 2-fold excess of (trimethylsilyl)dialkylamine and aldehyde; then a catalytic amount of a tertiary amine and methyl acrylate are added in the same pot to afford only the *syn*-diastereomer of the diamine (Scheme 46). The reactions are clean and the products are obtained in high yield (65−95%) except for the reaction with 2-methylpropanal or enolizable aldehydes perhaps due to the formation of enamines as side products.[126]

4.4. Radical Conjugate Additions

A Lewis acid can promote radical conjugate additions to esters and amides, and the presence of a chiral ligand renders the reaction enantioselective. The pioneering work of Kanemasa has found that chiral Lewis acid complexes of DBFOX/Ph do not provide sufficient substrate activation in terms of conjugate radical additions onto his classical oxazolidinones **60** and pyrazoles **56**. A less electron-donating ligand such **70** reaches high levels of enantioselectivity, but the requirement of multiple equivalents of radical precursors remains unresolved owing to the low inherent reactivity of compounds **56** and **60** toward carbon radicals.[127,128] More recently, however, β-substituted α-amino acid by radical conjugate addition on α,β-unsaturated α-nitroesters and amides have been obtained by DBFOX/Ph ligand combined with $Mg(NTf_2)_2$ or $Mg(ClO_4)_2$.[129]

Moreover, the same salts combined with cyclopropyl bisoxazoline ligands like **70** exploit the enantioselective radical addition to α,β-disubstituted unsaturated imides for the synthesis of *anti*-propionate aldols in a reaction that is the radical counterpart of the first step of Scheme 45.[130]

5. Friedel−Crafts Reactions

The Friedel−Crafts alkylation and acylation reactions are among the most fundamental transformations in organic chemistry. The alkylation reaction proceeds in the presence of a catalytic amount of Lewis acid, while, in its classical formulation, the acylation requires more than stoichiometric amounts of a Lewis acid as the promoter ($AlCl_3$), due to consumption by coordination to the produced aromatic ketone. In both cases, however, the Lewis acid cannot be recovered and reused, owing to its instability in aqueous media. To obviate this problem, several approaches based on the employment of catalytic amounts of water-stable Lewis acid have been developed. Perchlorates find use in two main research fields, in addition to other Lewis acids or alone. In the former case, they act as promoters that accelerate the process and increase the yields. In the following subsections, these two lines will be reviewed.

5.1. Perchlorates as Friedel−Crafts Acylation Promoters

Continuing their studies on Lewis acid mixtures, in 1991 Kobayashi and Mukaiyama proposed $AgClO_4/GaCl_3$ for the Friedel−Crafts acylation of activated arenes,[131] as a natural extension of the couple $AgClO_4/SnCl_4$ used in the glycosylation reaction (see section 3.1).[46] Moreover, as shown in that section, glycosyl cation from fully protected glucopyranosyl phosphinothioate is able to exploit Friedel−Crafts alkylation of highly activated benzenes.[77] The same authors use the couple $AgClO_4/SiCl_4$ (in 4:1 or 3:1 ratio and 20% mol with respect to the reagents) as the source of active cationic species from carboxylic acids or their trimethylsilyl esters. These cationic species react with *p*-trifluoromethylbenzoic anhydride to form *in situ* the corresponding mixed anhydrides.

Then the catalytic Friedel−Crafts acylation reaction between initially formed mixed anhydrides and aromatic compounds smoothly proceeds at room temperature to afford the corresponding aromatic ketones in 68−100% yields.[132,133]

Finally, the acylation of 1,2-dimethoxybenzene with Ac_2O was investigated in the presence of $AgClO_4$ (5 mol %)/$NbCl_5$(2.5 mol %) at 80 °C in nitromethane to give the acylated product in 93% yield.[134] The proposed catalytic cycle resembles Scheme 42, obviously replacing triflate with chloride and lithium with silver ion.

However lithium perchlorate has found use as the most valuable cocatalyst in various Friedel−Crafts acylation reactions in conjunction with various Lewis acids, especially triflates.[135]

Lithium perchlorate is demonstrated to form a stable acylium cation (**72**) when mixed with an acylating agent. Then this acylium perchlorate reacts in the presence of triflate salts with aromatic compounds to afford the corresponding aromatic ketone (Scheme 47).

The acceleration effect often depends on the amount of $LiClO_4$, and yields are improved with excess up to 10 equiv (Table 1). Finally it is worth noting that these mixtures can be easily recovered and reused without loss of activity.

5.2. Perchlorates as Friedel−Crafts Reaction Catalysts

For many years, the action of $LiClO_4$ has seemed to be limited to enhance the efficiency of the metal triflate catalyst; in fact it has been reported that the reaction does not work in the presence of $LiClO_4$ alone,[139,143] despite its well-known Lewis acid character.

Recently,[145] in solventless conditions, the formation of a complex with a strong electrophilic character between $LiClO_4$ and Ac_2O was demonstrated by NMR spectroscopy to be formed. This complex is able to give the desired product in good to excellent yields and high regioselectivity. Unfortu-

Scheme 47

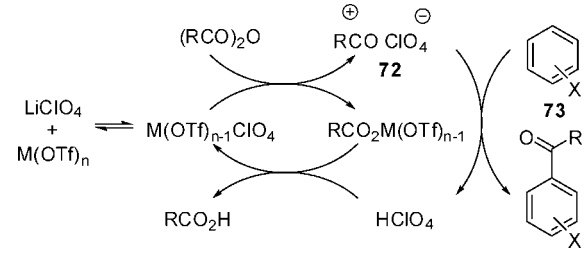
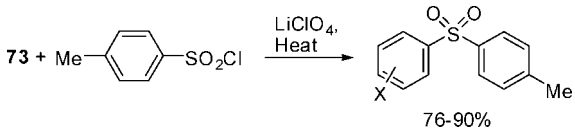


Table 1. Representative Examples of Friedel−Crafts Acylation of Arenes Promoted by Lewis Acids and Lithium Perchlorate

substrate	product	catalyst	T (°C), [t (min)]	Y (%)	ref
anisole	pentyl (4-methoxyphenyl) ketone	$SbCl_5$ (4 mol %), $LiClO_4$ (1 equiv)	40, [30]	92	136
anisole	4-methoxyacetophenone	$Hf(OTf)_4$ (5 mol %), $LiClO_4$ (6 equiv)	rt, [360]	95	137, 138
m-xylene	2,4-dimethylacetophenone	$Yt(OTf)_3$ (0.2 equiv), $LiClO_4$ (6 equiv)	50, [60]	83	139, 135
m-xylene	2,4-dimethylacetophenone	$Sc(OTf)_3$ (0.2 equiv), $LiClO_4$ (10 equiv)	50, [60]	89	
2-methoxy-naphthalene	2-acetyl-6-methoxynaphthalene	$Sb(OTf)_3$ (10 mol %), $LiClO_4$ (6 equiv)	50, [240]	93	140
3-methyl-2(3*H*)-benzoxazolone	bis(3-methyl-2(3*H*)-benzoxazolon-6-yl) ketone	$AlCl_3$ (4 equiv), $LiClO_4$ (6 equiv)	rt, [120]	47	141
acetanilide	4-(acetylamino)acetophenone	$Ga(OTf)_3$ (10 mol %), $LiClO_4$ (15 equiv)	50, [720]	93	142
anisole	4-methoxyacetophenone	$In(OTf)_3$ (1 mol %), $LiClO_4$ (1 equiv)	rt, [2400]	99	143
p-methylanisole	2-methoxy-5-methylacetophenone	$Ce(OTf)_3$ (5 mol %), $LiClO_4$ (16 equiv)	100, [25]	98	144

Scheme 48



nately, 2 equiv of $LiClO_4$ is required, because the side product AcOH can compete with Ac_2O in complexing $LiClO_4$, thus decreasing conversion of staring material and lowering the reaction rate. Nitromethane, the typical solvent of reaction reported in Table 1, analogously decreases the catalytic power of $LiClO_4$, since it competes with Ac_2O in complexing the $LiClO_4$ as well. The usefulness of this reaction has found many applications in recent years.[146,147]

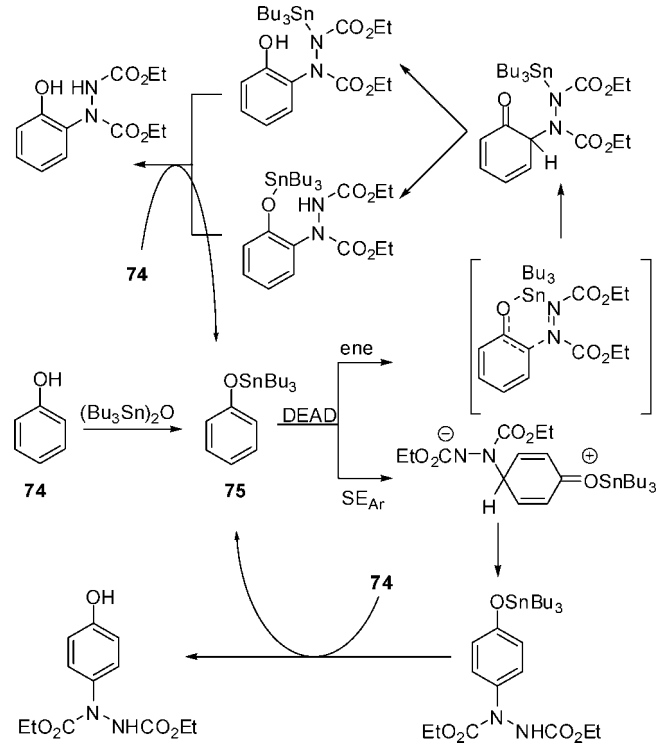
Besides acylation the catalytic activity of lithium perchlorate was demonstrated for the sulfonylation of various aromatics with *p*-toluenesulfonyl chloride under reflux conditions to give the corresponding sulfones in good to excellent yields (Scheme 48).[148]

Also magnesium (79−94% yield)[149] and sodium perchlorate (73−88% yield)[150] are found as efficient catalysts for sulfonylation of activated, inactivated, and heterocyclic aromatics under almost neutral conditions with exclusive *para*-selectivity.

Leblanc and co-workers have shown that electron-rich arenes react with the bis(2,2,2-trichloroethyl)azodicarboxylate derivative in 3 M lithium perchlorate−diethyl ether or acetone solutions to produce *para*-substituted arylhydrazide.[151] The arylhydrazides can be easily converted in high yields to their corresponding anilines by reduction with zinc dust in acetic acid; hence this reaction provides a means for introducing the amino group into an aromatic ring under very mild conditions. The reaction might be extended to phenols.[152] Phenols do not react with azodicarboxylates under these conditions, but the use of O-metalation to enhance the rate of electrophilic substitution in the ring is a familiar process. Indeed the reactions occur equally with 10 mol % of tributyltin oxide thus avoiding the need to prepare quantitatively the tin phenoxide.[153] Under these conditions, bis(2,2,2-trichloroethyl)azodicarboxylate adds to tin phenoxides in 5 M solution of $LiClO_4$ in diethyl ether at room temperature. The reaction can be extended to DEAD,[153] but bis(2,2,2-trichloroethyl) may sometimes lead to better results than diethyl azodicarboxylate (for example, with 2-methylphenol and 2,6-dimethoxyphenol, which do not react with DEAD). Both reactions are mild methods for the preparation of aminophenols.

The mechanism of the reaction is argued to follow a metalloene or a conventional electrophilic aromatic substitution pathway (Scheme 49). The product distribution provides evidence for the SE_{Ar} mechanism when azodicarboxylates are involved, since only this mechanism explains *para*-

Scheme 49

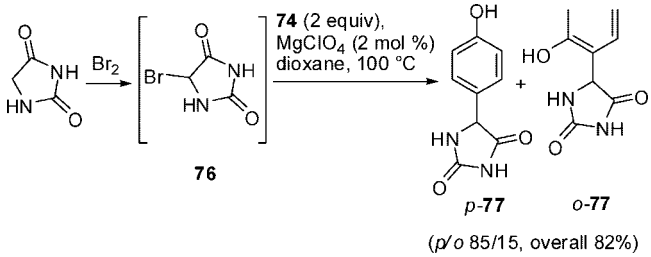


substituted products. On the other hand, diethyl acetylenedicarboxylate seems to follow the metalloene mechanism, because only products from vinylation in the *ortho* position are recovered. In fact, the reaction usually gives pairs of *ortho*-substituted vinylphenols and phenyl vinyl ethers, but for the reaction of tributyl-(2,6-dimethoxyphenoxy)tin, only the formation of ethers is observed.[154] It is worth noting that exclusively tin phenoxides can give ring alkylated products (in fact sodium phenoxides give only phenyl vinyl ethers) supporting evidence of a stabilization of tin in the intermediate by coordination to anionic centers.[155]

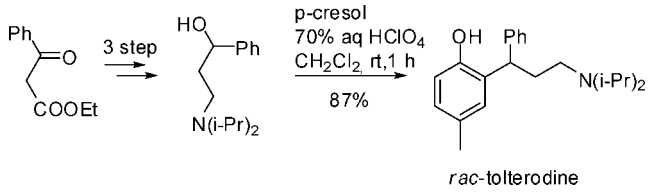
Different Lewis acids are able to promote the Friedel−Crafts reaction between 5-bromohydantoin (**76**) and aromatic compounds to give 5-arylhydantoins (Scheme 50), important intermediates in the enzymatic production of (*R*)-2-arylglycines. In particular, 5-(4-hydroxyphenyl)hydantoin (*p*-**77**) is used in the preparation of semisynthetic penicillins and cephalosporins. Among the tested Lewis acids, $Mg(ClO_4)_2$ (2 mol %) leads to the best *ortho*/*para* selectivity (15/85, 82% yield), although YCl_3 (2 mol %) gives the best overall yield (93%, *o*/*p* 24/76).

In this case phenol does not need to be transformed into its salt. $Mg(ClO_4)_2$ catalysis can be extended to anisole with total selectivity for 5-(4-methoxyphenyl)hydantoin, but the yield is lower than in the case of phenol (67%). However

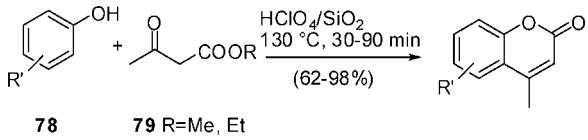
Scheme 50



Scheme 51



Scheme 52



taking into account the *para* isomers (the only ones pharmacologically important), the yields obtained from phenol and anisole are very similar.[156]

A recent synthesis of tolterodine, the drug of choice for most patients for the treatment of urinary urge incontinence, is reported to use aqueous perchloric acid in the last Friedel−Crafts step of the reaction (Scheme 51).[157] The presence of two electron-donating groups, competing in coordinating metal ions, prevents, in fact, the use of metal Lewis acid catalysts.

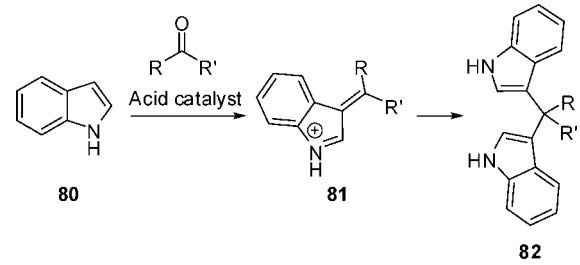
Another alkylation of phenols catalyzed by silica-supported perchloric acid allows the synthesis of coumarins via the Friedel−Crafts modification called Pechmann condensation.[158] Both ethyl and methyl acetoacetate (**79**) undergo condensation under solvent-free conditions to produce the coumarins in excellent yields, 65−98% (Scheme 52). The method presents all the environmentally benign advantages typical of this heterogeneous catalyst.

Regioselective Friedel−Crafts alkylation at the 3-position of indoles represents one of the most straightforward methods for the synthesis of many naturally occurring alkaloids. For example, the acid-catalyzed reaction of indoles with aromatic or aliphatic aldehydes and ketones produces azafulvenium salts (**81**), which in turn can undergo further addition with a second indole molecule to afford bis-indolylmethanes (**82**). Compounds **82** are of paramount importance in biological and pharmacological chemistry in view of their versatile activities (Scheme 53). Both protic and Lewis acids are able to catalyze this reaction.

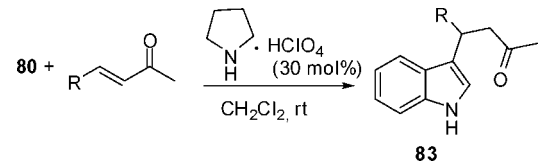
Triphenylphosphonium perchlorate ($PPh_3 \cdot HClO_4$), an inexpensive and readily available reagent, which retains its activity even in the presence of water and protic substrates,[159] and aqueous $HClO_4$ (5 mol %)[160] can catalyze the electrophilic substitution of substituted benzaldehyde at room temperature, leading to bis-indolylmethanes in good yield, but other carbonyl compounds do not give any product.

On the other hand, $HClO_4-SiO_2$ (0.01 mmol) is able to catalyze the reaction of a variety of carbonyl compounds

Scheme 53



Scheme 54



with indoles to produce bis-indolylmethanes in high to excellent yields (88−95%).[160] Electronic and steric effects on the carbonyl partner do not show any effects except longer reaction time with ketones. The generality of the protocol can be extended to 2-methylindole or to sugar-derived aldehydes, providing a powerful and versatile method for the preparation of bis-indolylglycoconjugates.

LPDE or 10% lithium perchlorate in acetonitrile are also mild and highly efficient catalysts for the preparation of bis-indolylmethanes under neutral reaction conditions (79−95% and 75−92% yield, respectively).[161] However, these conditions always take longer reaction times with respect to supported perchloric acid; the electron deficiency and the nature of the substituents on the aromatic ring show some effects on this conversion. Finally, reactions with sugar aldehydes were not mentioned.

$PPh_3 \cdot HClO_4$ is also used to catalyze the acetylation of indoles with acetic anhydride to give 3-acetyl indoles.[159]

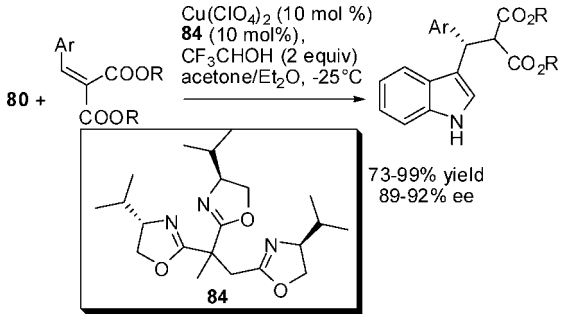
An elegant method for the synthesis of 3-alkylated indoles involves the conjugate addition of indoles to α,β-unsaturated compounds in the presence of protic acids. From the unsaturated carbonyl derivative point of view, this reaction can be considered as an addition of a carbanion to α,β-unsaturated carbonyl compounds (Michael reaction, section 4), but we prefer to consider it a Friedel−Crafts reaction, so it is reviewed in this section.

Pyrrolidine−$HClO_4$ salt in dichloromethane was found to be an efficient catalytic system for this transformation (Scheme 54).[162] The reaction is quite general and afforded exclusively 3-alkylated products in 69−92% yield, without substantial differences with different ketones or 1-substituted, 2-substituted, and/or 1,2-disubstituted indoles.

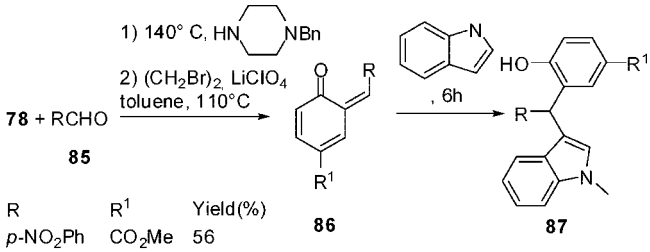
Recently, **83** have been obtained in the presence of solid $LiClO_4$ in moderate to good yields and relatively short reaction times. The electronic properties of the aromatic ring seem to have an effect on the rate of the reaction: the reaction is accelerated by an indole bearing an electron-donating group.[114]

Enantioselective addition of indoles to alkylidene malonates is exploited in the presence of trisoxazoline **84**/$Cu(ClO_4)_2 \cdot 6H_2O$ complex as the chiral Lewis acid.[163] Arylidene malonates with indole work well to afford the desired products in excellent yields with high ee (Scheme 55). The addition of 2 equiv of hexafluoroisopropanol greatly improves the reactivity, while a decrement of the reaction temperature increased enantiomeric excess.

Scheme 55

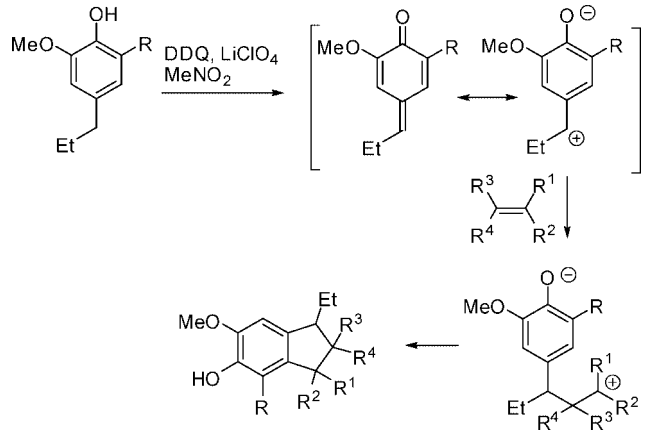


Scheme 56



R	R^1	Yield(%)
p-NO_2Ph	CO_2Me	56
p-MeOPh	Me	72

Scheme 57

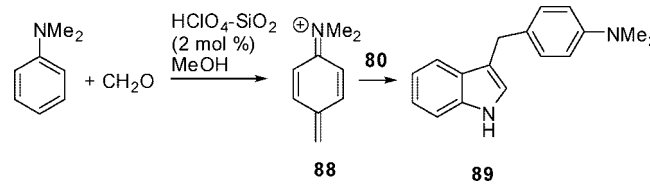


ortho-Quinone methides (**86**) are a particular class of α,β-unsaturated compounds, which can be obtained from adducts of phenols, aldehydes, and *N*-benzylpiperazine, which is a Friedel−Crafts reaction from phenol point of view, followed by the quartenarization of the amine with 1,2-dibromoethane and $LiClO_4$ (10 mol %) in refluxing toluene. Finally the complex between Lewis acid and **86** is trapped with methylindole (Scheme 56).[164]

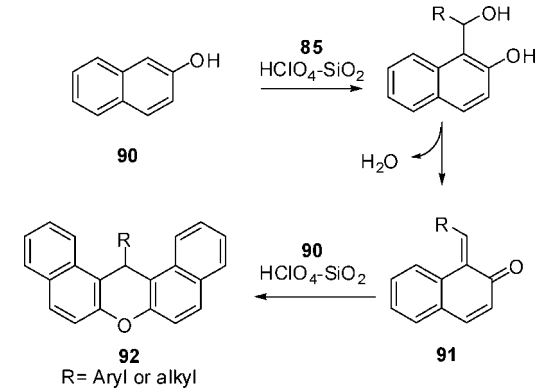
The isomeric *para*-quinone methides, efficiently generated by the DDQ oxidation of corresponding 4-alkylphenols, add to aliphatic alkenes in highly concentrated (3 or 6 M) lithium perchlorate in nitromethane in 53−99% yields. Lithium perchlorate is expected to stabilize the *in situ* generated zwitterions, which are equivalent to *para*-quinone methides. The reaction proceeds by the initial intermolecular carbon−carbon bond formation between the benzyl carbon of the zwitterion and the alkene, followed by Friedel−Crafts alkylation by the *in situ* generated carbocation to alkylindanes, most of them difficult to obtain in good yields through other methods (Scheme 57).[165]

As well as phenols, anilines can undergo the same reaction, by using silica-dispersed $HClO_4$. The reaction is operationally simple and offers 68−88% yields of the 3-[(4-aminoaryl)-methyl]indoles (**89**). The mechanism is supposed to generate an *N*-methyl-*N*-(4-methylenecyclohexa-2,5-dienylidene)methanaminium (**88**), which on addition of indole gives the desired product (Scheme 58).[166]

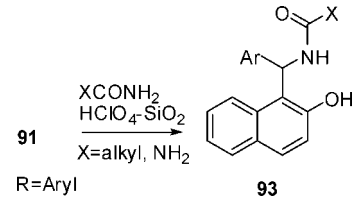
Scheme 58



Scheme 59



Scheme 60

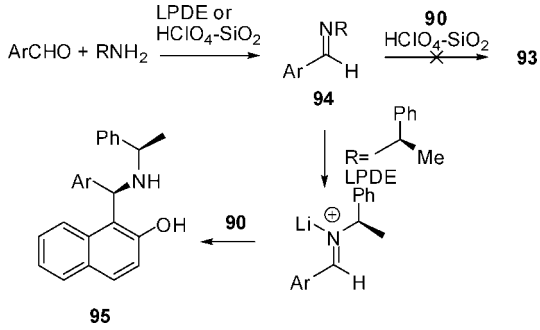


The reaction of 2-naphthol with aromatic aldehydes in the presence of an acid catalyst allowed the formation of the corresponding *ortho*-quinone methides (**91**),[167,168] without the intervention of quaternary amines as the leaving group. Then, **91** *in situ* reacts with nucleophiles. For example, 2-naphthol, in the presence of silica-supported $HClO_4$ after the mixture is stirred for 3−6 h at 100 °C[169] or few minutes at 125 °C[170] in the absence of solvent, leads to 14-aryl- or 14-alkyl-14*H*-dibenzo[*a*,*j*]xanthenes (**92**) in 77−93% or 88−96% yield, respectively (Scheme 59).

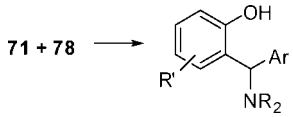
Independently two Iranian research groups directed by Mahdavinia[167] and Shaterian[171] and the Indian group directed by Das[169] reported the reaction between aryl aldehydes, 2-naphthol, and amides in the presence of supported $HClO_4$. Aqueous $HClO_4$ was once more found to be less efficient than the supported one, leading to the products in longer times and lower yield (Scheme 60).

Among these reports, the only significant difference is that Shaterian's reactivity (0.6 mol % catalyst at 110 °C)[171] is enhanced by microwave irradiation and it is applied only to acetamide and acetonitrile, while the other ones (1 mol % catalyst at 125 °C)[167,169] can be applied to different amides and ureas. Under these conditions, in all cases, aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups react successfully and give

Scheme 61



Scheme 62



the products in high yields (75−94%, 90−96%, and 68−93%, respectively). The reaction with aliphatic aldehydes is instead sluggish.[167]

The reaction of aniline instead of acetamide with 2-naphthol and benzaldehyde in the presence of the same catalyst is unsuccessful.[171] The experiment shows that the mechanism is quite different, because the Schiff base (**94**), the first intermediate, is unable to add to naphthol, which is recovered quantitatively (Scheme 61).

On the other hand, lithium perchlorate solution in diethyl ether (LPDE) provides an efficient, straightforward aminoalkylation of naphthols.[172] In particular the use of enantiopure (*R*)-1-phenylethylamine leads to aminoalkylated products in 55−78% yield with good to high diastereomeric ratio (75−99% in favor of the *R*,*R* stereoisomer of **95**, Scheme 61). The same reaction applies to 1-naphthol, giving lower diastereomeric ratio and yield.

The same author reported an extension of this reaction to other electron-rich aromatic compounds, such as 1- or 2-naphthol, 1,5-dihydroxynaphthol, indole, *N*-methylindole, 7-hydroxycoumarin, 2,4-dimethylphenol, or 6-hydroxyisoquinoline, by three-component reaction with aldehydes and (trimethylsilyl)dialkylamines.[173] The reaction proceeds through the same iminium ion intermediate **71** as in Scheme 46 in 1−6 h at room temperature in good to moderate yields (35−95%, Scheme 62).

Friedel−Crafts reactions of 1,2-thiazinylium salts with arenes are also performed and will be reviewed in section 9.4, together with nucleophile addition to the same salt.

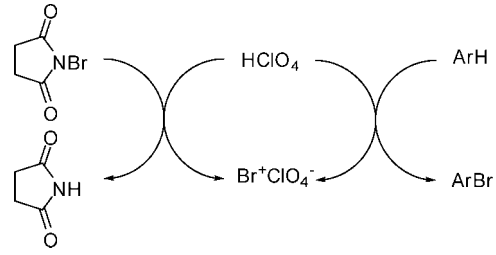
5.3. Miscellaneous Electrophilic Reactions

In this section, reactions that are not Friedel−Crafts reactions but that involve the reaction of electrophilic species with aromatic compounds and with double bonds will be reviewed.

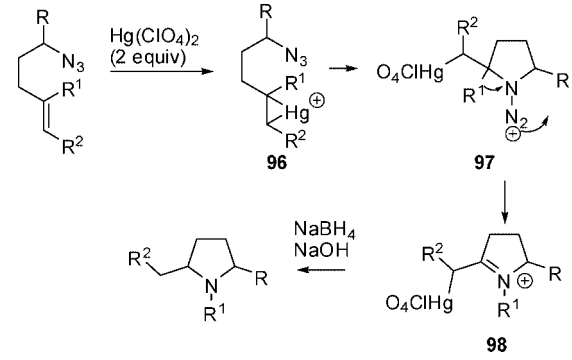
For example, a regioselective electrophilic aromatic halogenation of activated aromatics and heteroaromatics with *N*-halosuccinimide (Cl or Br) is catalyzed by 70% perchloric acid (mostly 1 mol %) in high yields (72−99%). The reactive species is supposed to be a halonium perchlorate (Scheme 63).[174]

The same reaction is also catalyzed by $LiClO_4$ dispersed in silica. All of the substrates examined undergo clean electrophilic aromatic bromination (not chlorination) to afford

Scheme 63



Scheme 64



the corresponding bromoarenes under neutral conditions in excellent yield, except thiophenol,where oxidation to the corresponding disulfide was exclusively obtained.[175]

The electrophilic nitrogen of an azide group adds to activated double bonds of a suitably disposed alkene, when treated with either mercuric perchlorate or mercuric triflate. A mercuronium ion intermediate (**96**) is formed, which is captured by the azide to produce an aminodiazonium ion (**97**), which undergoes a 1,2-shift to give an iminium ion (**98**), which is then reduced to an amine (Scheme 64). The reaction has some advantages over the protic version such as no limitation on the substitution of alkenes, milder conditions allowing the presence of acid-sensitive functionality, and no carbocation rearrangement. Yields are moderate (37−73%).[176]

6. Protection and Deprotection Reactions

The single greatest obstacle to complex molecule synthesis is represented by the presence of many functional groups that are either promiscuously reactive or stubbornly inert. The entire control has the potential to ravel an entire strategic design. Often chemists' chemoselective control is unable to reproduce a skill that nature has practiced deftly for billions of years. Therefore during the multistep synthesis of natural products, the efficiency of the employed synthetic protocol often depends largely on protection and deprotection of the functional groups involved. To this end, protecting groups have played a crucial role during the synthesis of complex natural products. Many protecting groups have been invented in natural product chemistry, and often the introduction or the cleavage of these functions is carried out under acidic conditions. Perchlorates, therefore, find great use in this chemistry. The metal ions of perchlorates are, in fact, hard Lewis acids due to the high delocalization of the negative charge in the perchlorate anion. The metal ion coordinates to the lone pair of electrons on the oxygen or on the nitrogen of functional groups containing these atoms and thereby activates them to undergo selective transformation due to its mild Lewis acidity.

6.1. Alcohols

6.1.1. Esters

Esterifications and transesterifications are very important reactions in synthetic organic chemistry laboratories for the preparation of natural products from alcohols and acids. An ester, however, can also be seen as a protecting group both of the alcohol and of the acid functions, and therefore, these reactions are reviewed in this section. The use of ferric perchlorate alone or supported on chromatographic grade silica gel in esterification reactions has been already extensively reviewed.[10]

Among the various protecting groups used for the hydroxyl group, acetyl is one of the more common. This is due to its facile introduction, because it is stable in the acid reaction conditions, and also because it is easily removed by mild alkaline hydrolysis. A variety of perchloric acid derivatives catalyze acetylation of alcohols with acetic anhydride generally in solvent-free conditions. In fact, the acetic anhydride−alcohol mixture gives rise to a homogeneous solution, and only in the case of some solid alcohols is a solvent needed.

A summary of the acetylation of alcohols by these catalysts is provided in Table 2. Reaction conditions are very similar, but copper(II) perchlorate seems to be the most efficient, since very low amounts are charged and reaction is practically immediate. It should be noted that no Fries rearranged products are ever detected under these reaction conditions, even if an acylium perchlorate (**72**, Scheme 46) has been invoked as the reactive species. As already discussed above, competitive Friedel−Crafts acylation on aromatic substrates occurs only with 200 mol % $LiClO_4$ as catalyst,[145] and reactions on phenols are restricted to very strange electrophiles.

Extensive studies have found that perchlorates with higher values of the charge-size function of the metal ion exhibit better catalytic activity following the order $Zn(ClO_4)_2 > Mg(ClO_4)_2 > Ba(ClO_4)_2 > LiClO_4$.[177] Moreover, acylation is influenced by the steric and electronic factors of the anhydrides and follows the order $Ac_2O > (PhCO)_2O > (EtCO)_2O > (i\text{-}PrCO)_2O > (t\text{-}BuCO)_2O \gg (ClCH_2CO)_2O$.[178] Therefore, some acylation reactions are extended to anhydrides other than acetic.[179–181] When attempted, selective acetylation of polyols failed, and peracetylated products were always recovered.

Prompted by these results, carbohydrate chemists successfully have extended the $HClO_4-SiO_2$ (25 mg/mmol of free sugar),[185] as well as $LiClO_4$ (10 mol %),[186] catalyzed acetylation for the per-O-acetylation of monosaccharides, disaccharides, and trisaccharides. The former reaction is complete within a few (3−20) minutes in high yield (85−96%) under solvent-free conditions.[185] The latter needs 40 °C, but very high yields (90−99%) are obtained, and the reaction is extended both to β-cyclodextrin and to saccharides containing internal acetonide, Boc, and *t*-butyl protecting groups.[186] In an earlier report, 60% $HClO_4$ catalyzed the peracetylation reaction using a large excess of acetic anhydride at extended reactions times.[187]

It should be noted that the same $HClO_4-SiO_2$ amount that allows the per-acetylation reaction at 0 °C is able to selectively deprotect the anomeric acetyl group at 70 °C in acetonitrile. Under these conditions, both α- and β-acetates and even anomeric benzoyl groups could be removed in excellent yield (80−95% yield). Interglycoside linkages remained unaffected.[188]

Interestingly supported perchloric acid is able to catalyze almost the entire synthetic pathway, sugar → peracetylated sugar[185] → anomeric deprotection to hemiacetal[188] → tricholoroacetimidate synthesis [the only step that uses basic (K_2CO_3) activation] → glycosylation reaction,[69,70] with only little modification of the reaction conditions.

A variety of primary alcohols are converted to the corresponding benzoates (73−87% yield) using equimolecular amounts of benzoyl chloride in the presence of catalytic $LiClO_4$ (20 mol %) in THF at 25 °C. Primary alcohols can be selectively benzoylated in the presence of secondary or tertiary alcoholic or phenolic OH's that are unreactive.[148] It should be noted that reactions with both acetic and benzoic anhydride are reported to be unsuccessful, but they occur with low amounts of $LiClO_4$.[182] The comparison between the two protocols makes us think that the amount of anhydride or the presence of a solvent are the critical parameters. In fact, the reaction conditions (temperature and time) are almost identical.

A series of diverse polymer-bound β-ketoesters have been prepared using a transesterification reaction between methyl or ethyl β-ketoesters and a hydroxybutyl functionalized JandaJel resin and lithium perchlorate (20 mol %) as the catalyst.[189]

Various esters (87−98% yield) have been obtained by Goossen through a decarboxylative esterification of alkyl and aryl carboxylic acids with dialkyl pyrocarbonates at room temperature in the presence of 1 mol % of $Mg(ClO_4)_2$. In most cases only volatile byproducts are released, so the purification of the products becomes particularly easy, and many sensitive functionalities are tolerated.[190] However, the synthesis of esters is restricted to frameworks arising from commercially available dicarbonates. Recently we have given a rationale to this reaction, since we have found that the strength of the Lewis acid influences the reaction course. Strong Lewis acids, such as magnesium perchlorate, mainly decompose dicarbonate, and the alcohol that arose from it rapidly increases its concentration, making very favorable its attack to the anhydride intermediate (**102**, Scheme 65, path a). A large excess of dicarbonate is therefore required, since "path a" prevails over "path b". Weaker Lewis acids, magnesium chloride, for example, instead, mainly form **102** (Scheme 65, path b), and **99** is not decomposed, so the released alcohol concentration is always low. As a consequence the addition to **102** of slight excess of every primary or secondary alcohol and phenol is preferred, especially when the bulk *t*-butyl framework is released from dicarbonate.[191]

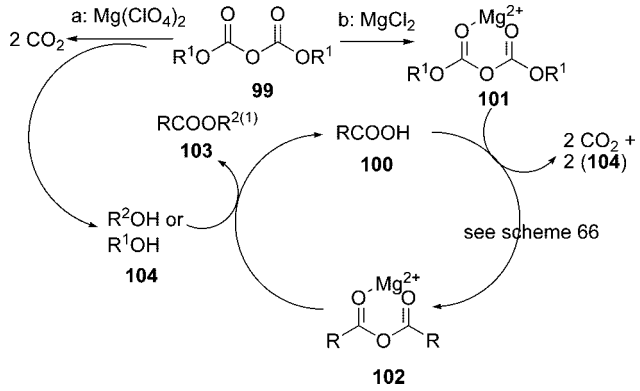
Interestingly, the prevalence of carboxylic acid attack onto the carbonyl of dicarbonate suggests that the reaction rate depends on the acidity of the starting compound rather than

Table 2. Representative Examples of Acetylation of Alcohols Catalyzed by Perchlorates

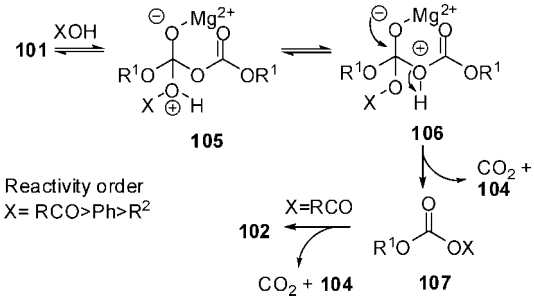
catalyst	(anhydride/alcohol), *T* (°C)	time	yield (%)	ref
$LiClO_4$ (10 mol %)	(2−10:1),[b] 25−40	4−48 h	85−100	182
$HClO_4/SiO_2$ (1 mol %)	(1:1),[b] rt	5−60 min	80−100	8
$Zn(ClO_4)_2$ (0.1 mol %)	(1:1), rt	10−270 min	90−100	179
$Mg(ClO_4)_2$ (1 mol %)	(1:1), rt	15 min-6 h	92−100	180
$BiOClO_4$ (1 mol %)	(1:1),[b] rt	10−120 min	79−100	181
$Cu(ClO_4)_2$ (0.05 mol %)[c]	(1:1),[b] rt	1−10 min	97	183
$Fe(ClO_4)_3$ (0.25 mol %)	(2.5:1),[a] rt	15−24 h	87−96	184

[a] Acetic acid instead of anhydride used. [b] Polyols give peracetylated products. In these cases, reagent ratio refers to each hydroxyl. [c] Comparable results with $Mn(ClO_4)_2$, $Co(ClO_4)_2$, and $Ni(ClO_4)_2$.

Scheme 65



Scheme 66



its nucleophilicity (Scheme 66). Actually this evidence is confirmed by the reaction of phenols with diethyldicarbonate, which react faster than the less acidic and more nucleophilic aliphatic alcohols.[192]

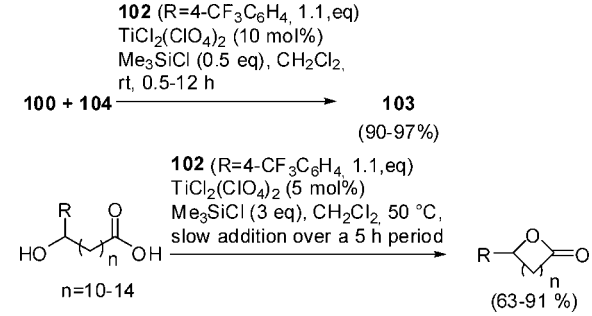
This evidence allows setting up a new, mild, general, and efficient synthesis of aryl ethyl carbonates from diethyldicarbonate under solvent-free conditions promoted by magnesium perchlorate. The best reaction conditions require 10 mol % of the catalyst at 40 °C and yields range from 80% to 100% in a few hours. The reaction between almost equimolecular amounts of a carboxylic acid and an alcohol is a highly atom-economic process. In Table 2, $LiClO_4$ is shown as an efficient catalyst, but only for acetylation.[182]

Since 1992, an efficient synthesis of esters[193] or lactones[194] starting from silyl carboxylates and alkyl silyl ethers via the active intermediary mixed anhydrides prepared *in situ* from silyl carboxylates with 4-(trifluoromethyl)benzoic anhydride using a catalytic amount of a Lewis acid, in particular $TiCl_2(ClO_4)_2$ has been reported. The method was extended to the reaction between nearly equimolar amounts of free carboxylic acids and alcohols[195] or ω-hydroxycarboxylic acids[196] under similar reaction conditions together with chlorotrimethylsilane, but the use of silyl derivatives of carboxylic acids and of alcohols seems to be essential for the completion of the esterification reaction at room temperature (Scheme 67).[197]

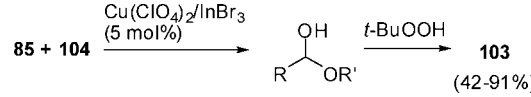
Later a detailed study appeared, and high yields were obtained without silyl derivative employing 3,5-bis(trifluoromethyl)benzoic anhydride.[197] It is noteworthy that bulky pivalic acid esters are also obtained in high yields. The synthesis of naturally occurring macrocycles (*R*)-ricinelaidic acid lactone and (*R*)-ricinoleic acid lactone from labile *seco*-acids was reported to smoothly occur in 92% and 83% yield, respectively.

We have found that $Zn(ClO_4)_2 \cdot 6H_2O$ efficiently catalyzes esterification (65−96% yield) between nearly equimolar amounts of every carboxylic acid and alcohol when used at

Scheme 67



Scheme 68



80−100 °C under solvent-free conditions in the presence of $MgSO_4$ as water scavenger. The catalyst can be filtered off, regenerated, and reused without loss of activity, various functionalities are tolerated by the reaction conditions, and the procedure can be scaled up to 100 mmol.[198] This procedure is highly economic and completely free from byproducts.

An even more convenient and clean procedure of esterification was reported, very recently,[199] by direct condensation of equimolar amounts of carboxylic acids with alcohols catalyzed by $HClO_4-SiO_2$. The direct condensation of many acids and alcohols has been achieved in 59−98% yields. Chiral alcohol and *N*-t-Boc protected chiral amino acid also resulted in ester formation without competitive deprotection and detrimental effect on the optical purity of the product. The reaction was also applied to the synthesis of ibuprofen and a few commercial flavoring agents. $HClO_4$ was proven to be more effective than other protic acids adsorbed on silica gel, and silica was more effective than other solid supports.

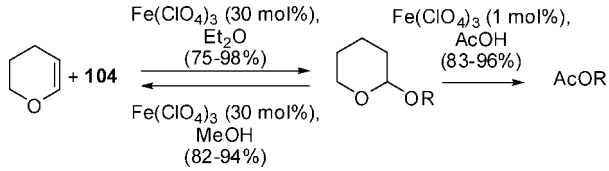
Oxidative esterification of aldehydes generally requires long reaction time and high temperature and often the presence of a carbonyl directing group in the β-position, despite the corresponding oxidative amidation proceeding under mild conditions. The catalytic system $Cu(ClO_4)_2 \cdot 6H_2O-InBr_3$ (5 mol %) was found to perform oxidation of aldehydes to esters using *t*-butyl hydroperoxide as the oxidant of the intermediate hemiacetal (Scheme 68).[200]

Both aliphatic and aromatic aldehydes are compatible with the reaction conditions, and a large excess of the alcohol is not required. However, sterically hindered alcohols and the presence on the substrates of functional groups that readily oxidize diminish the effectiveness of the reaction.

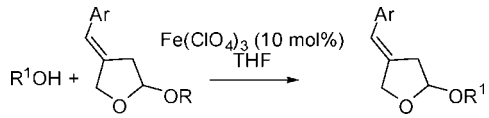
Finally, metal perchlorates catalyzed some one-pot changes of protecting group. In particular, lithium perchlorate acts as an efficient catalyst for selective transesterification of β-keto esters. In a different manner from that above, the directing β-keto group is essential for the occurrence of the reaction. In fact α-keto esters, γ-keto esters, and normal esters fail to undergo transesterification reaction. Various alcohols (primary, secondary, and benzylic) undergo smooth transesterification reactions (67−93% yield). Crowded and less reactive trityl alcohol gives the reaction in 57% yield, and allylic and propargylic alcohols do not undergo decarboxylative rearrangement.[201]

Moreover, $Fe(ClO_4)_3$ (1 mol %) can directly and selectively deprotect and acetylate THP ethers using inexpensive acetic acid in 83−96% yield (Scheme 69).[202]

Scheme 69



Scheme 70



6.1.2. Ethers

Ethers are among the most used protective groups in organic synthesis and vary from the simplest, the most stable methyl ether, to the most elaborate, substituted ethers developed for use in nucleotide synthesis. Ethers are formed and removed under a wide variety of conditions.

THP ethers, for example, can be easily prepared from a variety of hydroxyl-containing compounds by reaction with (2*H*)-3,4-dihydropyran. Deprotection of THP ethers for regeneration of hydroxyl compounds usually entails rather harsh acidic conditions, which are rarely compatible with sensitive substrates.

Primary, secondary, tertiary, benzylic, allylic, and propargylic alcohols are easily converted to THP ethers by the treatment of dihydropyran with catalytic amounts of ferric perchlorate in Et_2O at ambient temperature. The deprotection of THP ethers in turn can be carried out under similar mild reaction conditions and with the same ease as the protection process in methanol as transetherification solvent (Scheme 69).[203] As above-reported, lower amounts of the same catalyst are able to directly convert THP ethers into acetates.[202]

Previously,[204] LPDE has been reported to be a reaction medium for the protection of alcohols as THP ethers as efficient as $Fe(ClO_4)_3$ but in much longer reaction times (8−17 h vs 1−3 h).

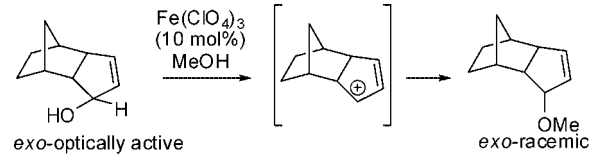
Also, supported perchloric acid (1 mol %) smoothly converts a large variety of primary and secondary alcohols and phenols to the corresponding THP ether (80−97% yield) within 5 min under solvent-free conditions.[205] It is worthwhile to mention that this protocol is faster than other perchlorate-catalyzed methods, but it does not provide a method for deprotection.

Ferric perchlorate (10 mol %) catalyzes the transacetalization of 2-alkoxy-4-benzylidenetetrahydrofurans, heterocycles very close to THP ethers, with alcohols. $Fe(ClO_4)_3$ is found to be superior to zinc and magnesium perchlorates (Scheme 70). The transacetalization proceeds smoothly (64−85% yield) with a wide range of alcohols, but no reactions occur with phenol (less nucleophilicity) or *t*-butanol (steric constraints). When H_2O is used as a nucleophile, a large amount of $Fe(ClO_4)_3$ is needed, probably because the catalyst is deactivated by water.[206]

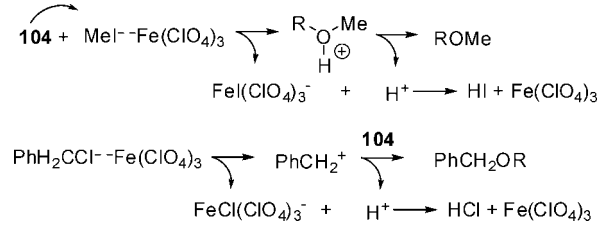
Moreover $Fe(ClO_4)_3$ provides an efficient (78−98% yield) and selective method for the conversion of allylic and benzylic alcohols into their corresponding ethers under solvolytic conditions at reflux. The results obtained from optically active allylic alcohols show that a carbocation is formed during the course of the reaction (Scheme 71).[207]

The same catalyst (5 mol %) provides a synthesis of methyl and benzyl ethers starting from alcohol and benzyl

Scheme 71



Scheme 72



chloride at 100 °C under solvent-free conditions or a methylation of alcohols using methyl iodide at room temperature. Etherification is completed within 25−120 min in high yields of the products (82−97%), except for phenols, which do not react at all. Diols can be selectively monoprotected at the less hindered position, using exact molar ratio between the halide and hydroxyl function.[208] The authors propose that iron activates methyl iodide and then the alcohol oxygen lone pair attacks the activated methyl, followed by abstraction of the proton, providing the methyl ether. With more stable cations (benzyl) an S_N1 mechamism is not *a priori* excluded (Scheme 72).

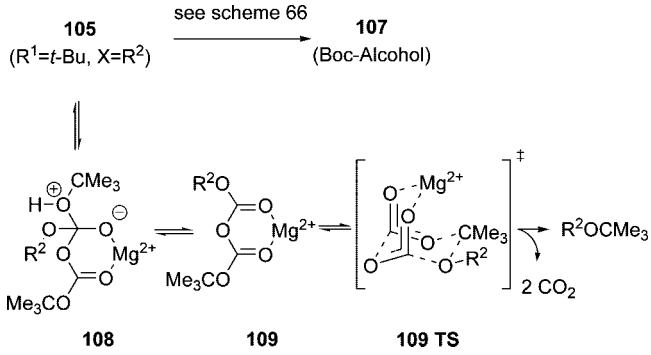
Etherification of aromatics is a typical acid-catalyzed reaction and in particular etherification of 2-naphthol with methanol to produce the industrially important 2-naphthyl methyl ether is carried out in the presence of homogeneous $HClO_4$ solutions. Recently, a detailed report on 2-naphthyl methyl ether selectivity depending on molar ratio of 2-naphthol/methanol, acid concentration, temperature, and inert atmosphere has appeared in the literature.[209]

The *t*-butyl ether is a much underused alcohol protecting group, although it is one of the few ethers stable under strongly basic conditions. Its scarce employment in organic synthesis is probably due to the conditions required for its formation and removal. Most of the known methodologies involve the formation of a *t*-butyl carbocationic intermediate, thus avoiding the application, for example, to the protection of aromatic alcohols, which predominantly undergo a Friedel−Crafts alkylation.

We have found that primary, secondary, benzylic, allylic, and homoallylic alcohols and, notably, a large variety of phenols can be easily converted (65−95% yield) to the corresponding *t*-butyl ether by *t*-butyl dicarbonate (Boc_2O) in the presence of anhydrous $Mg(ClO_4)_2$.[210] Only tertiary alcohols failed to give the desired ether.

Moreover, Boc alcohol or *t*-butyl ether formation is mainly tuned by the anionic part of the Lewis acid catalyst. Perchlorates and triflates, anions with highly delocalized negative charge, give prevalent or exclusive ether formation. On the other hand, Boc alcohols are the main or exclusive products with undelocalized isopropoxide or low-delocalized acetate ions.[211] The proposed explanation is that highly nucleophilic anions do not dissociate from their metal counterpart, and as a consequence, **105** (Schemes 66 and 73) has high anionic character, so it is more prone to restore the carbon−oxygen double bond, favoring elimination of the good leaving group carbonate monoester and

Scheme 73



leading to the exclusive formation of carbonate **107** (Scheme 66). On the other hand, "naked" metal ions, such as those of perchlorates and triflates, tightly bind to the oxygen anion of **105** and allow equilibrium between **105** and **108** to be established (Scheme 73). The *t*-butyl alcohol becomes the best leaving group, leading to the mixed carbonate carbonic anhydride **109**, which decomposes through a synchronous mechanism in a "six-ring" transition state (**109TS**). On the other hand the bad leaving group ethanol does not allow this pathway, and formation of carbonate results in the only pathway that can be followed.[192]

Finally, both $Mg(ClO_4)_2$ and $Sc(OTf)_3$ behave as comparably efficient catalysts in the synthesis of aromatic *t*-butyl ethers, but the former allows decomposition of the product for long reaction times. *t*-Butyl ethers can be then efficiently deprotected by a $CeCl_3$/NaI system.[212]

Trimethylsilylation of organic compounds having labile hydrogen atoms such as alcohols, phenols, and carboxylic acids is a frequently used protection method in several chemical conversions and synthesis of natural products due to the enhanced stability under a variety of conditions, solubility in nonpolar solvents, thermal stability, and ease of removal of the protecting group, which is simply accomplished by acid- or base-induced hydrolysis giving only unreactive siloxane as byproduct.

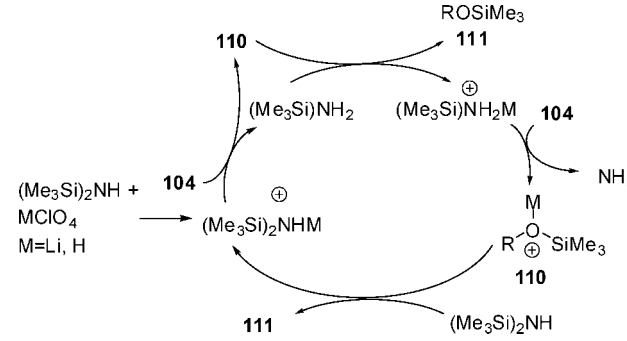
Among silylation reagents, hexamethyldisilazane (HMDS) is an inexpensive, easy-to-handle, and commercially available reagent. Its workup is not time-consuming, because the byproduct of the reaction is ammonia. However, its low silylation power is the main drawback to its application.

Solid lithium perchlorate (50 mol %, solvent-free)[213] or $LiClO_4/SiO_2$ (1:2 w/w ratio, 1.0 g/10 mmol alcohol in CH_2Cl_2)[214] readily provides transformation of allylic, benzylic, and hindered primary alcohols, unhindered secondary, tertiary, and acid-sensitive alcohols, and phenols into their corresponding trimethylsilyl ethers in 80−99% and 84−96% yield, respectively (Scheme 74).

Supported lithium perchlorate is not selective toward hydroxyl groups, and in the case of diol and dihydroxyphenols, only bis(silylated) product is formed, but it is selective in the presence of an amino group.

The trimethylsilylation of hydroxyl groups is also easily carried out at room temperature in the presence of supported perchloric acid on both silica[215] and alumina.[216] Alcohol/HMDS/$HClO_4-SiO_2$ (1:0.8:0.05) in acetonitrile are the best conditions, and silylated products are obtained in excellent isolated yields (85−98%) in very short times. Trimethylsilylation of aldoxime and ketoxime also produces the corresponding trimethylsilylated compounds at these conditions. Thiols and amines remained unaffected. This method is

Scheme 74



shown to be highly selective for primary alcohols in the presence of secondary and tertiary alcohols and phenols and for secondary ones in the presence of tertiary hydroxyls.

Among deprotection reactions of ethers, the cleavage of trityl ethers from the primary position of sugars, catalyzed by supported perchloric acid, should be mentioned.[217] CH_3OH acts as a nucleophile to trap the generated trityl cation, and free alcohols are recovered in 85−92% yield. Under these conditions, several other protecting groups, such as benzoyl, *p*-nitrobenzoyl, tosyl, *t*-butyldimethylsilyl, allyl, *p*-methoxyphenyl, thiophenyl, and *p*-methoxybenzyl remain unaffected.

6.2. Carbonyls

6.2.1. Acetals

The protection of the carbonyl functional group as an acetal, oxathiolane, or thioacetal is an important and useful synthetic transformation. There are some differences among the three functional groups: *O*,*O*-acetals are the easiest to remove, the *O*,*S*-acetals can serve as valuable starting materials for enantioselective syntheses, and *S*,*S*-acetals often serve as masked acyl anions. Among the plethora of known methodologies, some of them involve perchlorate derivatives.

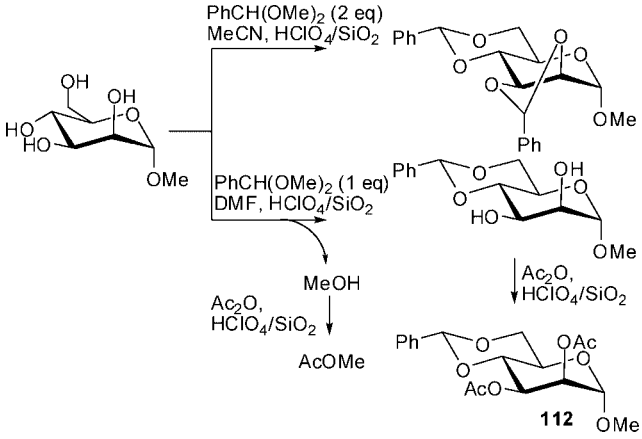
No acetal formation obviously takes place in aqueous $HClO_4$, but the acetal formation is effective after treatment of aldehydes and ketones with trimethyl- or triethyl-orthoformate and $HClO_4-SiO_2$ at room temperature under neat conditions (80−95% yield).[218]

For aldehydes bearing substituents that are capable of coordination with the metal ion or where electrophilicity is lowered by resonance, the acetal formation proceeds better using MeOH or EtOH, respectively, as solvent, affording excellent yields (80−96%). The role of the solvent can be explained by initial reaction of the aldehydes with MeOH/EtOH and formation of a hemiacetal, which undergoes nucleophilic attack on orthoformate complexed with $HClO_4-SiO_2$.

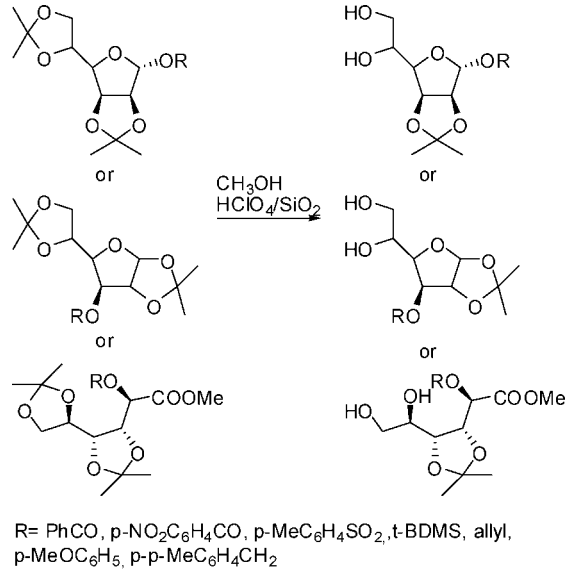
Acetal formation is used in carbohydrate chemistry. Pyranosides react with equimolar amounts of benzaldehyde dimethylacetal in dry acetonitrile in the presence of $HClO_4-SiO_2$ to give the benzylidene acetal derivative. This compound is not isolated, but 4 equiv of acetic anhydride is added, and the corresponding per-acetylated product is isolated (72−86% yield).[219] The excess of acetic anhydride is necessary to trap the moles of methanol liberated by benzaldehyde dimethylacetal upon formation of the acetal (Scheme 75).

It should be noted that mannopyranoside treated with equimolar benzaldehyde dimethylacetal gives a mixture of

Scheme 75



Scheme 76



R= PhCO, p-$NO_2C_6H_4CO$, p-$MeC_6H_4SO_2$,t-BDMS, allyl, p-$MeOC_6H_5$, p-p-$MeC_6H_4CH_2$

mono- and dibenzylidene derivatives in acetonitrile and only mono adduct in DMF. However, with 2 equiv in acetonitrile, the bis-benzylidene derivative is obtained in 93% yield. The same one-pot acetal/acetylation procedure is applied for the preparation of isopropylidene ketal derivatives without difficulty (80−92% yield).

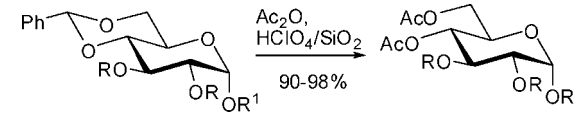
Supported perchloric acid is also explored for regeneration the carbonyl compounds from the acetals. Dimethyl or diethyl acetals treated with MeOH or EtOH−H_2O (1:1) in the presence of $HClO_4$−SiO_2 (0.5 mol %) at room temperature are deprotected after 10 min to 1 h in 80−95% yields. The deprotection also takes place using aqueous $HClO_4$.[218]

Terminal isopropylidene groups are deprotected by $HClO_4$−SiO_2 (1:1 w/w) in 83−95% yields (Scheme 76). Deprotection of the isopropylidene group is based on transacetalization with methanol used as the solvent. Under these conditions, several functional groups remain unaffected, and the reactions can be performed at relatively large scale.[217]

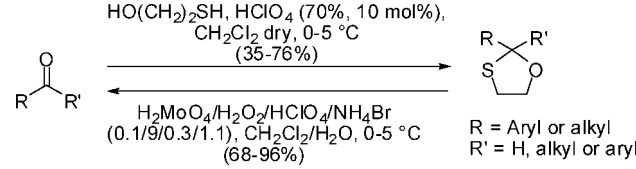
Rapid deprotection of sugar benzylidene (like **110**) or 4-methoxybenzylidene acetals is also performed (2.5 mol % of $HClO_4$−SiO_2) in commercial CH_3CN at room temperature in a few minutes in 90−96% yields.[220]

A series of anomeric protecting groups and interglycosidic linkages remain intact under the reaction conditions, so the reaction can be extended to benzylidene-containing di- and trisaccharide derivatives. Moreover, a sequential deprotection

Scheme 77



Scheme 78



of benzylidene acetal and acetylation of the diol generated *in situ* following a one-pot protocol can be achieved with acetic anhydride (5.0 equiv) (Scheme 77)

Oxathioacetals can be easily protected (35−76% yield) using a catalytic amount of perchloric acid and then deprotected to the parent carbonyl compounds (68−96% yield) by involving molybdic acid, ammonium bromide, hydrogen peroxide, and perchloric acid (Scheme 78).[221]

It is significant to note that neither the allylic position nor the aromatic ring is brominated by the deprotection mixture, notwithstanding that the oxidizing condition allows the *in situ* formation of bromine. Actually, more recently silica-supported $HClO_4$ (1 mol %) was found to be more effective in terms of reaction time (10−60 vs 20−90 min) and yield (65−90%) as the catalyst for oxathioacetal formation.[205]

Highly chemoselective dithioacetalization of aldehydes and acetals is achieved in an LPDE medium or with $LiClO_4$ and has been already reviewed.[11,12]

Various aromatic, heteroaromatic, and alicyclic aldehydes and ketones, bearing functional groups such as hydroxyl, alkoxy, halogen, cyano, or nitro, were reported independently by Khan[205] and Chakraborti[222] to undergo dithioacetalization under the same experimental conditions: $HClO_4$−SiO_2 (1 mol %) under solvent-free conditions at room temperature, with comparable reaction times (1−30 min) and yields (81−98% vs 75−100%). Interestingly, 4-nitrobenzaldehyde is protected in 61% yield in 30 min and 85% yield in 5 min and cyclohexanone in 93% yield in 30 min and 95% yield in 1 min by Khan and Chakraborti, respectively.

6.2.2. Acylals

Acylals are synthetically useful protecting groups for aldehydes due to their stability toward aqueous acids and bases. On the other hand, 1,1-diacylals of ketones are found to be very unstable under acidic conditions, and they cannot be isolated except rare lucky cases.[223] The low stability of the product is the reason authors generally found no reaction or very low yields with ketones, and the boasted high stereoselectivity toward aldehydes is actually a drawback of the applicability of the reaction. Various catalysts have been reported for the synthesis of aldehyde acylals.

Aqueous $HClO_4$ (0.5 mol %) has been used to catalyze acylal formation from aldehydes.[224,225] It requires a larger excess of Ac_2O and longer reaction time than silica-supported acid perhaps due to the presence of water in the reaction medium.

Perchlorates are instead among the more versatile, inexpensive, and mild catalysts. A summary of the catalyzed acetylation of aldehydes is provided in Table 3. Both

Table 3. Representative Examples of Acetylation of Aldehydes Catalyzed by Perchlorates

catalyst	(anhydride/aldehyde), T (°C)	time	yield (%)	ref
$LiClO_4$ (200 mol %)	(1.7:1), 60	15−40 min[a]	80−92	226
$HClO_4/SiO_2$ (0.5 mol %)	(2:1), rt	2−10 min	85−98	227
$HClO_4/SiO_2$ (2.5 mol %)	(1.5:1), rt	2−15 min	85−96	228
$HClO_4/SiO_2$ (0.1 mol %)	(1:1), rt	1−30 min	90−99	229
$Zn(ClO_4)_2 \cdot 6H_2O$ (1 mol %)	(1.5:1), rt	2−45 min	86−98	230
$Mg(ClO_4)_2$ (5 mol %)	(3:1), rt	20−210 min	85−95	231
$Cu(ClO_4)_2$ (0.05 mol %)[b]	(1:1), rt	1−45 min	92−98	183
$Fe(ClO_4)_3 \cdot 6H_2O$ (5 mol %)	not reported	not reported	efficient	10

[a] Ten hours for peracetylation of 4-hydroxybenzaldehyde. [b] Comparable results with $Mn(ClO_4)_2$, $Co(ClO_4)_2$, and $Ni(ClO_4)_2$.

aromatic and aliphatic aldehydes are efficiently acetylated, and peracetylated products are generally recovered in molecules containing two or more types of acylatable groups. *N*,*N*-Diethylaminobenzaldehyde, due to strong deactivation of the carbonyl group by virtue of the conjugation, does not give any reaction under any catalytic system.

Interestingly, LPDE does not afford acylation of aldehydes. This difference in behavior of LPDE and solid $LiClO_4$ can be referred to the Lewis acidity of the lithium ion, moderated in a coordinating solvent, such as ether.[226]

Zinc(II) perchlorate is reported to give other 1,1-dicarboxylate formation (84−95% yield), and the reactivity order is as follows: $Ac_2O > (i\text{-}PrCO)_2O > (t\text{-}BuCO)_2O > (PhCO)_2O$, and no 1,1-dicarboxylate formation takes place with $(ClCH_2CO)_2O$ and $(F_3CO)_2O$.[230]

It is worth noting that three papers appeared during one year reporting $HClO_4-SiO_2$ as the catalyst. The oldest one is the only report on the topic that does not mention peracetylation of hydroxyl aldehydes, and even it reports selective acetylation of 4-hydroxy- and 2-hydroxy-5-bromobenzaldehyde.[228] The middle one points out the mildness of the reaction conditions, which allow the survival of acid-sensitive functions or protecting groups, notwithstanding the highest charged amounts of catalyst and anhydride.[227] Finally, the most recent one describes the best conditions in terms of charged reagents and reaction times and yield, but it does not report any peracetylatable substrate.[229] However it is the only one that describes the acylation with other acylating agents in order to generalize the catalytic efficiency, and the geminal dicarboxylates are obtained in 88−93% yields with the following reactivity order: propionic > butyric > isobutyric anhydride.

6.2.3. 1,3-Dicarbonyls (Enol Ethers and Enaminones)

β-Keto enol ethers, β-enamino esters, and β-enamino ketones represent important classes of useful functionalized building blocks in several organic transformations. They are generally prepared by acidic catalysis from 1,3-dicarbonyl compounds.

$HClO_4/SiO_2$ is found to be an efficient heterogeneous catalyst for the rapid and high-yielding (71−95%) synthesis of β-keto enol ethers from cyclic 1,3-diketones under very mild reaction conditions.[232] The reaction takes place within only a few minutes at room temperature and under solvent-free conditions.

The same catalyst converts both β-diketones (linear and cyclic) and β-ketoesters into enaminones (90−99% yield) under very similar reaction conditions.[233] The merit of the catalyst is to avoid the use of a dehydrating agent, which is necessary with other catalysts. Water is, in fact, the byproduct of the reaction, and its removal is often a critical point.

Hydrated zinc perchlorate (5 mol %), for example, can act as the catalyst for the synthesis of β-enaminones, but the catalytic activity must be enhanced by the presence of anhydrous $MgSO_4$ (30 mol %). Under these conditions, $Zn(ClO_4)_2 \cdot 6H_2O$ shows a strong catalytic activity in promoting the condensation of amines with 1,3-dicarbonyl substrates (71−99% yield).[234]

The contemporary use of a hydrated and an anhydrous salt seems contradictory, but often only hydrated cations are able to act as Lewis acids. Carbonyl compounds can be activated by fast water exchange with the metal hydrated cation, whereas dry cations cannot be dissociated from the counterion, and catalysis does not occur. Therefore, a very subtle equilibrium between these two opposite needs must occur: there must be water to hydrate the cation and exploit catalysis but not so much to reverse the equilibrium back toward the reagents.[235]

6.2.4. Imines, Hydrazones, and Oximes

The same considerations can be extended to the synthesis of imines where the presence of water more drastically influences the position of the equilibrium.

The condensation of amines and hydrazines with carbonyl compounds is a venerable and useful organic transformation, because the resultant imines (hydrazones) are used as versatile components in various reactions. Often they are prepared without the requirement of any additional reagent/catalyst, but the presence of electron-donating groups on aromatic aldehydes reduces the electrophilicity of the carbonyl carbon through resonance, and strong electron-withdrawing substituents decrease the nucleophilicity of the amine group in aniline derivatives.

The use of $Mg(ClO_4)_2$ (5 mol %) results in quantitative formation of the corresponding imine in DCE at room temperature within 8 h. The reaction conditions are extended to structurally diverse carbonyl compounds and various amines to afford excellent results (80−95% yield).[236]

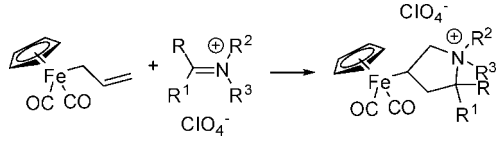
The same reaction conditions [$Mg(ClO_4)_2$ (5 mol %) in DCE at room temperature] afford quantitative formation of the phenylhydrazones in 2−30 min. Particularly 3,4-dimethoxybenzaldehyde, 3,4,5-trimethoxybenzaldehyde, and acetophenone afford 98%, 90%, and 95% yields of the corresponding phenylhydrazones, whereas no significant reaction is observed when these substrates are treated with phenylhydrazine in the absence of catalyst.

Regeneration of aldehydes and ketones from their oximes has been performed by employing a mixture of KBr (20 mol %), $(NH_4)_6Mo_7O_{24} \cdot 4H_2O$ (20 mol %), 30% H_2O_2 (1 mL), and $HClO_4$ (0.1 mL) at ambient temperature.[237] The catalytic oxidative mixture is very similar to that reported above for the oxathiane protection removal.[221] Aldehydes are yielded in 78−98% in reasonable times unaccompanied by any byproduct arising out of its further oxidation.

Ferric perchlorate catalyzes the reactions of oximes with arylhydrazines in DCE to give directly arylhydrazones. A variety of benzaldoximes and ketoximes are converted into the corresponding parent arylhydrazones in 72−98% yields. The catalyst has the ability to tolerate a variety of substituents.[238]

Finally, an interesting application of lithium perchlorate (300 mol %) is performed in the *in situ* generation of iminium salts from an aldehyde and a secondary amine in CH_2Cl_2,

Scheme 79



which are then used in the [3 + 2] cycloaddition reaction with allyl(cyclopentadienyl)iron(II) dicarbonyl to prepare new series of five-membered rings of ammonium salts substituted with an iron complex in 80−95% overall yields (Scheme 79).[239]

6.3. Amines

The development of mild and selective methods for the protection of the amine group is important for organic synthesis, especially for the preparation of peptides, amino acids, and other natural products. Due to its stability toward catalytic hydrogenolysis and extreme resistance toward basic and nucleophilic reactions, the Boc group is one of the most useful functions for the protection of amines. Although alkylamines are well-known to give the monoprotected derivatives without the assistance of any catalyst, the analogous reactions of some poorly reactive primary and secondary arylamines proceed sluggishly, since various side reactions often occur. Basic catalysis has generally been employed, but a few methods using a Lewis acid are available, and interestingly, they employ perchlorate derivatives.

The first easily available Lewis acid exploited in such a transformation was $Zn(ClO_4)_2 \cdot 6H_2O$ (5 mol %).[240] The reaction works with primary and secondary aromatic amines under mild conditions (6−168 h, rt), and the protecting agent is used only in a small excess (Scheme 80). Reaction rates and yields are governed by the nucleophilicities of the amines. In particular, activated anilines give the *N*-Boc derivatives in very good yields (83−99%), while on the other hand, deactivated substrates give the protected derivatives with acceptable results (50−68%) in view of their low reactivity. The protection reaction is chemoselective: the amine is exclusively protected in the presence of amide, acid, indole, and thiol groups.

Subsequently, a similar procedure involving the use of $LiClO_4$ (20 mol %) appeared in the literature. Various functionalized aromatic amines, hydroxylamines, hydrazines, and sulfonamides could be protected as their *N*-Boc derivatives in high yields (74−90%) and relatively shorter times (5 h, rt).[241]

Then silica-supported $HClO_4$ (1 mol %) was also found to be a very efficient catalyst (90−100% yield) for the introduction of Boc protection.[242] Various aromatic, heteroaromatic, aliphatic, and heterocyclic amines were treated with equimolar amounts of $(Boc)_2O$ under solvent-free conditions at 30−35 °C during 1 min to 3 h. The catalyst was compatible with various functionalities, and excellent chemoselectivity was observed for substrates with an OH/SH group, as well $Zn(ClO_4)_2 \cdot 6H_2O$.

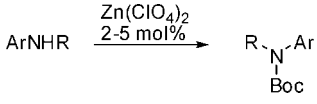
Actually, acetylation of structurally diverse amines, particularly sterically hindered and electron-deficient ones, was performed with 1 equiv of Ac_2O at room temperature in 5−30 min under solvent-free conditions and reported in the first paper describing the merits of $HClO_4-SiO_2$.[8]

A new method for the synthesis of 1,3,5-trisubstituted aminotetrazolium salts based on alkylation of 1- and 5-aminotetrazoles with the *t*-BuOH−$HClO_4$ (70% in water) system recently appeared in the literature.[243] Even if it is not properly an amino-protection reaction, we included it here bacause of the similarity to the other reactions presented in this section. Depending on the structure of the tetrazole substrate and reaction conditions, alkylation proceeds at the endocyclic nitrogen atoms, as well as at the amino groups, leading to tetrazolium perchlorates, which are interesting in the chemistry of energetic materials and convenient precursors for mesoionic 5-aminotetrazole derivatives.

A particular case of amino protection is the simple and efficient synthesis of *N*-acylsulfonamides by the reaction of sulfonamides with anhydrides under solvent-free conditions in the presence of $HClO_4-SiO_2$, which very recently appeared in the literature.[244]

Regarding deprotection reactions, $Mg(ClO_4)_2$ in organic solvents was found to act as an extremely mild reagent for repetitive 2-(biphenyl-4-yl)propan-2-yloxycarbonyl or 2-(3,5-dimethoxyphenyl)propan-2-yloxycarbonyl deprotection during solid phase peptide synthesis even in the presence of the acid labile moieties with excellent yields.[245]

Scheme 80



7. Three-Membered Ring Reactions

7.1. Epoxides

Epoxides are one of the more useful classes of substrates available to the synthetic organic chemist. In fact, the inherent polarity and strain of the three-membered oxirane ring make them susceptible to reaction with a wide number of reagents including nucleophiles, acids, bases, and reducing and oxidizing agents.

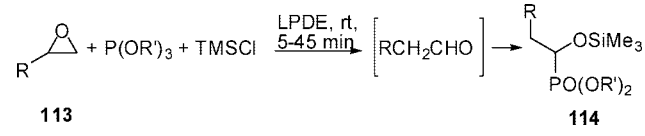
The acid-catalyzed rearrangement of epoxides to carbonyl compounds is a well-known synthetic transformation and a number of reagents have been elaborated for this purpose. Among them $BiOClO_4 \cdot xH_2O$ allowed the high-yielding (68−98%), selective rearrangement of aromatic and aliphatic epoxides containing a tertiary epoxide carbon to carbonyl compounds. However, simple cyclohexene oxide does not undergo rearrangement even when refluxed for 12 h.[246]

LPDE was found to be a more desirable mild reagent for effecting chemo- and regioselectively this rearrangement, and it has been reviewed.[11,12]

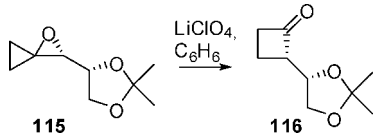
In addition, some interesting synthetic applications appeared recently in the literature. Saidi exploits the direct conversion of epoxides (**113**) into α-hydroxyphosphonates (**114**, 74−92% yield) by treatment with a trialkylphosphite in LPDE (Scheme 81).[247]

Moreover Bernard and Piras succeed in the ring expansion of an oxaspiropentane into a cyclobutanone, using $LiClO_4$ as the acid reagent. Interestingly the expansion preferentially occurred with retention of configuration (*S*,*R*)-**115** → (*S*,*S*)-**116** (Scheme 82).[248]

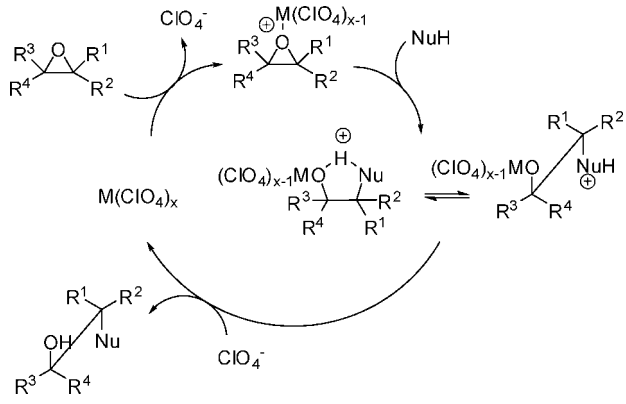
Scheme 81



Scheme 82



Scheme 83



However the epoxide ring-opening reactions by nucleophiles are certainly the most useful reaction of epoxides. The catalytic activity of various metal perchlorates is found to follow the order $Zn(ClO_4)_2 \cdot 6H_2O$ > $Cu(ClO_4)_2 \cdot xH_2O$ > $Co(ClO_4)_2 \cdot xH_2O$ > $Fe(ClO_4)_3 \cdot xH_2O \approx Fe(ClO_4)_2 \cdot xH_2O$ > $ZrO(ClO_4)_2 \cdot xH_2O \gg BiOClO_4 \cdot xH_2O$ > $Mg(ClO_4)_2 \cdot 6H_2O$ > $Ba(ClO_4)_2 \cdot 6H_2O \gg LiClO_4$.[249,250]

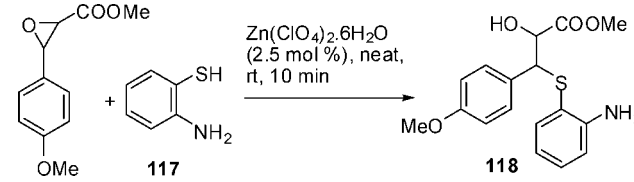
This order reflects the stronger oxophilicity of Zn^{2+} because of the higher charge-to-size ratio and the increasing tendency of the other metal ions to hydrolyze compared with Zn^{2+}; that is, the water molecules in other metal perchlorate hydrates decrease the oxophilicity of the central metal cation (Scheme 83).

Perchlorates are also compared with other salts and the relative catalytic efficiency may be explained by taking into consideration that the Lewis acidic property of the central metal cation is influenced by the counteranion and a salt of a stronger protic acid should be a better Lewis acid. These results are in complete accordance with those found in the reaction of pyrocarbonates described above.[211]

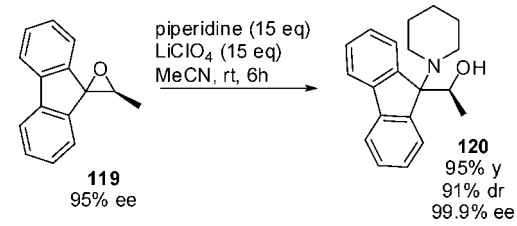
Excellent regioselectivity is generally observed for unsymmetrical epoxides. Preferential nucleophilic attack takes place at the sterically less hindered position of the epoxide ring of unsymmetrical nonstyrenoid alkene oxides. In the case of styrene oxide instead, the nucleophilic attack at both carbons of the epoxide generally takes place, and regioselectivity varies depending on catalyst, reaction conditions, and nucleophile. Reaction with cycloalkene oxides leads to stereoselective formation of the *trans*-isomer. These general features of the reaction found many applications. For example, the ring-opening reaction of different classes of epoxides with alcohols and water in the presence of ferric perchlorate, alone or silica-supported, has already been reviewed.[10]

Zinc perchlorate hexahydrate is found to be a highly effective catalyst for opening of epoxide rings by thiols (2.5 mol %, 80−99% yield)[249] or amines (2 mol %, 57−100%)[250] under solvent-free conditions at room temperature, except for secondary amines, for which 80 °C is required. On the other hand in dichloromethane solution, catalysis does not occur, but with alumina-supported $Zn(ClO_4)_2$ as the catalyst, yields range between 85% and 95%.[251]

Scheme 84



Scheme 85



An interesting application of the regioselective (only product from attack at the benzylic epoxide carbon is observed) and chemoselective (only sulfur acts as the nucleophile) epoxide ring-opening by thiol is the synthesis of the key intermediate **118** of the antihypertensive drug diltiazem (Scheme 84).

Ring-opening of 1,10-phenanthroline-5,6-epoxide with a variety of nitrogen nucleophiles is accomplished using magnesium perchlorate (150 mol %) as the Lewis acid in acetonitrile at 80 °C in 73−97% yield.[252]

After the pioneering work of Crotti in 1991 on the ring-opening of epoxides with nucleophiles such as lithium enolates[253] and amines,[254] in recent years, the Azizi and Saidi group has improved and developed the applications of $LiClO_4$ as a promoter in this reaction with various nucleophiles such as amines (20 mol %, 80−97% yield),[255] thiols (12.5 mol %, 90−98%),[256] chlorides (10 mol %, 82−97%),[257] azides (33 mol %, 45−78%),[257] and cyanides (10 mol %, 84−97%)[258] under solvent-free conditions at room temperature. It should be noted that the reaction of cyclohexene oxide with TMSCN is carried out in the presence of other perchlorates (Mg(II), Ni(II), Fe(III), and $LiClO_4-SiO_2$) under solvent-free conditions, but they show lower activity.[258]

Acyl chlorides and acetic anhydride are added to epoxides leading to acyl-protected chlorohydrins (64−94% yield) and 1,2-diacetates (65−94%) by catalysis of $LiClO_4$ (20 mol % at room temperature and 50 mol % at 60 °C, respectively).[257]

LPDE catalyzes the ring-opening of epoxides with poor nucleophiles such as O-silylated hydroxylamine and $BH_3 \cdot Et_3N$ complex to give, at ambient temperature in time ranging from 0.5 to 1.5 h and in 77−98% yields, the corresponding ring-opening products (β-hydroxyhydroxylamines and alcohol derivatives, respectively). Indoles reacted more poorly, and yield ranged 52−67%.[259]

Finally lithium perchlorate induces ring-opening of (15*S*)-15-methylspiro[fluorene-9,3′-oxirane] (**119**, Scheme 85) with piperidine in MeCN to afford a mixture of regioisomeric amino alcohols **120**, ratio of which can be modulated by the $LiClO_4$ concentration and the reaction temperature and varies from 44:56 (20% yield at 50 °C with 10 mol % of catalyst after 24 h) to 91:9 (95% yield at 25 °C with 1500 mol % of catalyst after 6 h). Very interestingly, after separation, the enantiomeric composition of the major isomer is also enriched (up to >99.9% ee when starting from epoxide of 95% ee).[260]

7.2. Aziridines

Aziridines are the nitrogen equivalents of epoxides and show very similar features; that is, they are well-known carbon electrophiles capable of reacting with various nucleophiles undergoing regioselective ring-opening reactions. Moreover, they are useful intermediates for the synthesis of many biologically interesting molecules. Regio- and stereoselectivity of unsymmetrical aziridines largely parallel that observed for unsymmetrical epoxides. However, conversely from epoxides, a systematic study on the best perchlorate salt has never been reported.

Most of the work on lithium perchlorate catalysis applied to this interesting heterocycle has been developed by Yadav and co-workers. First, they found that 10 mol % $LiClO_4$ in acetonitrile provided an easy three-component synthesis of aziridine carboxylates, from aldimines (generated *in situ* from aldehydes and amines) and ethyl diazoacetate in high yields (75−91%), with diastereoselectivity ranging from 82/18 to exclusive (Scheme 86). It is noteworthy that aziridine formation from enolizable aldehydes has also been achieved without enamine formation to any extent.[261]

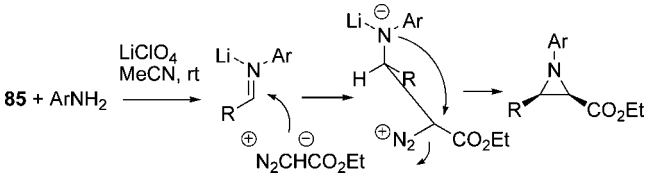
The same catalytic system (10 mol % $LiClO_4$ in acetonitrile) is then used for ring-opening of aziridines with many nucleophiles. In this manner, β-amino-sulfides from thiols, β-azido-amines from sodium azide or β-cyano-amines from sodium cyanide are obtained in 82−93%,[262] 85−92%,[263] and 80−87%[263] yields, respectively, at reflux temperature. 1,2-Diamines from aromatic amines and β-amino-thiocyanates from potassium thiocyanate are obtained in 83−95%[264] and 75−86% yield,[265] respectively, at room temperature as well.

The coupling of aziridine carboxylate (**122**) with a variety of substituted indoles, poor nucleophiles, is accomplished with $Sc(ClO_4)_3$, a stronger Lewis acid than $LiClO_4$, with a ratio of indole/aziridine/perchlorate of 2:1:1 in dichloromethane at 0 °C. The reactions proceed in moderate yields (36−70%) with high regioselectivity (88/12 to 95/5) and *N*-alkylindoles give better yields (61−75%).[266] This reaction finds an interesting application in the synthesis of α-*C*-mannosyltryptophan; in fact, the protected intermediate **123** is regioselectively obtained in 66% yield (Scheme 87).[267]

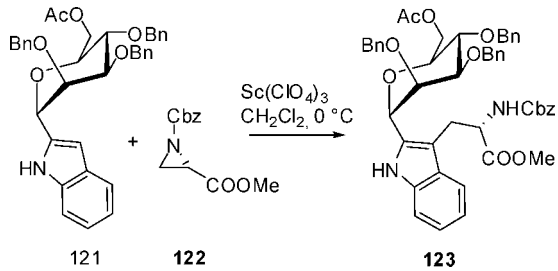
7.3. Seleniranium Ion

Treatment of 1,2-hydroxyselenides with a strong proton source such as perchloric acid leads to a seleniranium ion, a particular three-membered ring that can undergo nucleophilic ring-opening as well as epoxides or aziridines.[268,269] In particular, the presence of other OH moieties capable of undergoing cyclization affords both tetrahydrofurans and tetrahydropyrans. The former are kinetic products and can be isolated after 1 min, while the latter are thermodynamic products and are obtained later. Actually under these experimental conditions, the reaction is always under thermodynamic control, as demonstrated by the lack of selectivity also in the furan formation.

Scheme 86



Scheme 87



8. Ring Synthesis

In the realm of natural and synthetic organic chemistry, cyclic units are interesting because of their occurrence in biologically active compounds, natural products, and therapeutic and medicinally important drugs. This section will review the synthesis of various cyclic and heterocyclic systems, all performed by the use of perchlorate or perchloric acid as the Lewis catalyst. In contrast to the previous chapters that are based on a main reaction, here the target molecule is the driving idea. Therefore both polar and pericyclic reactions will be collected here. Many polar reactions are Lewis acid catalyzed syntheses that resemble what was reported in the previous sections.

Pericyclic reactions are pathways that occur by a concerted process through a cyclic transition state and include cycloadditions, sigmatropic rearrangements, and electrocyclizations. In particular, the Diels−Alder reaction, a [4 + 2] cycloaddition, has become one of the most important reactions in organic synthesis and has been utilized for the synthesis of six-membered carbocycles and heterocycles by the combination of various 1,3-dienes and dienophiles. Analogously, [3 + 2] cycloaddition of 1,3 dipoles is one of the most utilized reactions for the synthesis of five-membered heterocycles. The importance of these reactions in organic chemistry is witnessed by over 300 items in the last 5 years, when "cycloaddition reaction" and "review" keywords are put in the search field of the ISI database.

Some reactions, however, are unsuccessful because of the low reactivity of the reaction system, and the use of Lewis acid catalysts can sometimes accelerate the reaction. The effect of $LiClO_4$ on the rates of Diels−Alder reaction has been known since 1986.[270] In the cited *Tetrahedron* report,[12] Heydari dedicated the whole section 2 to pericyclic reactions in LPDE. In our previous minireview on perchlorate, other examples are reported.[13] Therefore in this review, we focus our attention only on the most recent developments in this field referring to previous literature for older papers.

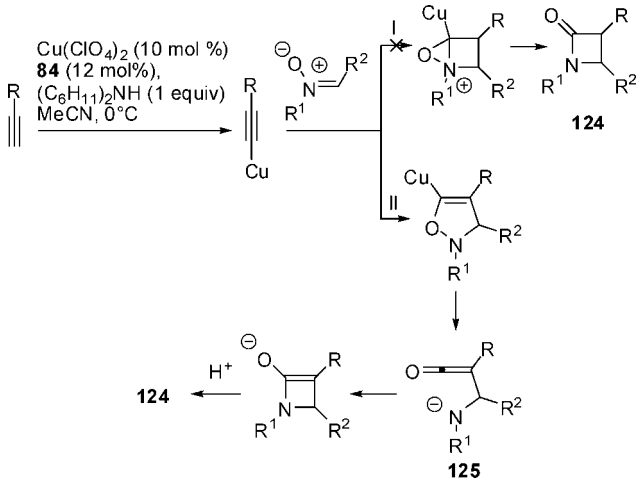
Finally, pyridinium perchlorate undergoes a unique photocyclization reaction to produce bicyclic-aziridines with high synthetic potential for applications in natural and non-natural products of biomedical interest. The reactivity of this system was recently reviewed by Mariano in a perspective article.[271]

8.1. Four-Membered Rings

β-Lactam is a core structure of many natural and synthetic antibiotics, as well as a useful synthetic intermediate in organic synthesis.

Bifunctional catalysis was attempted for the synthesis of these compounds via a [2 + 2] cycloaddition reaction of ketene and imine with little results. For example, when $Cu(MeCN)_4ClO_4$ is used coupled with benzoylquinine, the

Scheme 88



metal binds to the quinuclidine nitrogen, thereby reducing the catalyst efficacy.[272]

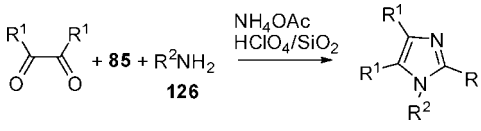
The binding ability of copper is, in turn, applied to asymmetric Kinugasa reaction,[273] an easy access to optically pure β-lactams with different structures. In the literature, the Kinugasa reaction is proposed to proceed via a [3 + 2] cycloaddition reaction, followed by a rearrangement to give the β-lactams **124** (path I in Scheme 88). However the catalytic system trisoxazoline **84**/$Cu(ClO_4)_2 \cdot 6H_2O$ complex as the chiral Lewis acid (see Scheme 55, section 5.2) is demonstrated to occur via ketene **125**, followed by an intramolecular cyclization, finally enolate is protonated to afford the desired **124** (path II, Scheme 88).[274] Under the optimal reaction conditions, the reaction is general (25−98% yields, 2/1 to 31/1 *cis/trans* ratio, 46−85 ee%), but both yields and enantioselectivities are affected by the electronic character on carbons of nitrones of aromatic groups. Product **123** is not obtained when either R^1 or R^2 are alkyl groups, whereas both aryl and alkyl alkynes work well. Noticeably, ethyl propiolate (R = COOEt) gives reversed *cis/trans* ratios.

Finally, irradiation of 2-(trimethylsilylmethyl)phenyl ketones with a high-pressure mercury lamp in the presence of equimolecular amount of magnesium perchlorate in acetonitrile gives the less hindered of the two possible benzocyclobutenols, that is, the isomer with OH and trimethylsilyl groups *cis*. Since irradiation of the substrate in the absence of $Mg(ClO_4)_2$ initially gives the *trans* isomer, it should convert via photoinduced disrotatory cyclization of a dimethylenecyclohexadiene intermediate faster than the reversion to the starting ketone.[275]

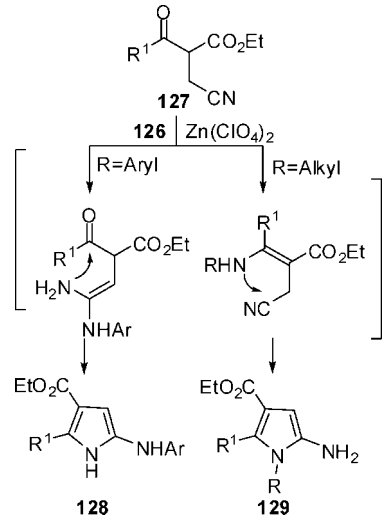
8.2. Five-Membered Rings

The imidazole ring is the core molecule in many biological systems such as histidine, histamine, and biotin. Among the numerous synthetic routes toward imidazoles, an interesting synthesis involves a multicomponent reaction catalyzed by supported perchloric acid (1 mol %) (Scheme 89).[276] The aqueous perchloric acid also accomplishes the reaction to form imidazoles after longer reaction time. The obtained

Scheme 89



Scheme 90



yields range between 56% and 98% without formation of any side products, which are normally observed under the influence of strong acids.

Pyrroles are used widely in both synthetic organic chemistry and material science as building blocks in naturally occurring and biologically active compounds. In particular, aminopyrroles have been found to show interesting biological properties and are not readily available through general pyrrole ring-formation methods. Moreover, 3-phosphonylated pyrroles have much biological potential as conformationally restricted bioisosteres of amino acids. Both compounds are synthesized starting from 3-substituted 4-oxocianides by using 5 mol % of commercial $Zn(ClO_4)_2$. Typically, when α-cyanomethyl-β-ketoesters (**127**) is allowed to react with amine in the presence of $Zn(ClO_4)_2$, 2-aminopyrrole is formed (Scheme 90).[277] The reaction can be applied to the synthesis of various multifunctionalized aminopyrroles (70−94% yields), and surprisingly water can be used as the solvent but with longer reaction times.

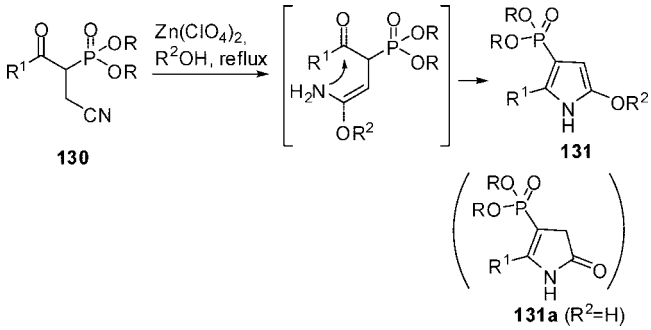
Interestingly, the regiochemistry is influenced by the nature of the amine. Zinc ion can coordinate both the C═O and CN bond. Coordination of nitrile to the Zn followed by the addition of the amine into the CN bonds would prevail with aromatic amines to afford 2-(arylamino)pyrroles (**128**). On the other hand, coordination of Zn to C═O, followed by a dehydrative coupling giving the enamino-ester (see section 6.2.3),[234] would prevail with alkyl amines. Annulation by the CN affords *N*-alkyl-2-aminopyrroles (**129**).

Discovered the preferential coordination of Zn to the nitrile framework, the reaction is naturally extended to α-cyanomethyl-β-ketophosphonates (**130**). Since restricted bioisosteres of amino acids are 2-oxygenated derivatives, the nucleophile is an external alcohol under anhydrous conditions.

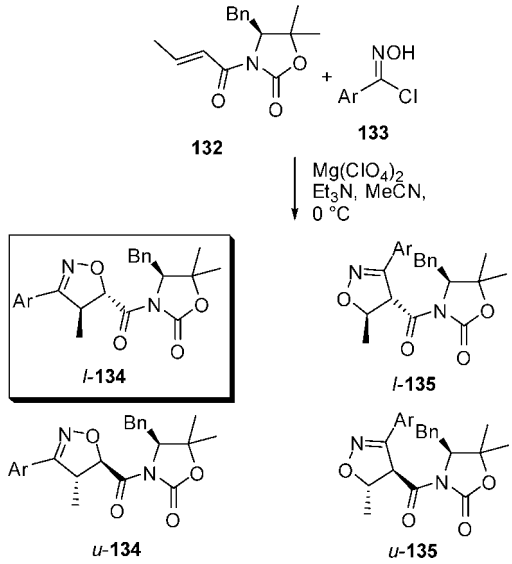
Under water-free conditions, the 5-alkoxypyrrole-3-phosphonates (**131**, Scheme 91) are obtained in 72−89% yields. The same reaction carried out in water−alcohol or in water furnished the corresponding pyrrolinones (**131a**) in 82−85% yields.[278]

However, 1,3-dipolar cycloaddition is often the reaction of choice, yielding five-membered heterocyclic compounds. Nitrile oxides, nitrones, and azomethyne ylides are used as the dipole and alkenes, alkynes, aldehydes, ketones, and nitriles as the dipolarophiles. The diastereoselectivity of the

Scheme 91



Scheme 92



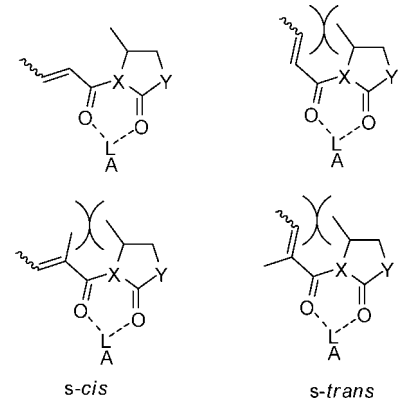
cycloaddition reaction is significantly improved as a result of the coordination of the dipolarophile to the added Lewis acids.

For example, an effective Lewis acid for nitrile oxide cycloaddition reactions is magnesium perchlorate. In fact, an equimolecular amount improves the yields (71−87%) of the reaction of substituted benzonitrile oxides (**133**) with 4-benzyl-3-crotonoyl-5,5-dimethyl-1,3-oxazolidin-2-one (**132**), as well as both the regioselectivity and diastereoselectivity, the like-isomer (*l*-**134**) being the most abundant among the four possible stereoisomers with respect to the corresponding reaction in the absence of a catalyst (Scheme 92).[279]

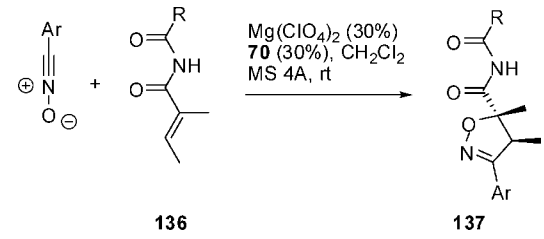
Modifications of these reactions in order to avoid the introduction of equimolecular amounts of the optically active auxiliary oxazolidinone before and afterward its removal are also reported. Generally, in enantiocatalysis, rotamer control is a central requirement for reactions involving unsaturated carbonyl compounds. Traditional templates such as **60** or **132** are well-suited for crotonates because they provide organized chelation, reacting exclusively via the *s-cis* rotamer. On the other hand, substitution at the α-carbon results in problematic steric interactions for both the *s-cis* and the *s-trans* rotamers (Scheme 93). However, the steric requirement of nitrile oxide cycloaddition is not satisfied by these templates, and very low enantiomeric excess is obtained from the reaction with chiral Lewis acids, such as 2,6-bis(2-isoxazolidinyl)pyridines.[280]

The use of pyrazolone (like **56**, Scheme 33) or N−H imide (**136**) templates relieve strain, reduce twisting, and restore selectivity. Actually, Ni(ClO$_4$)$_2$−**70** complex catalyzes highly

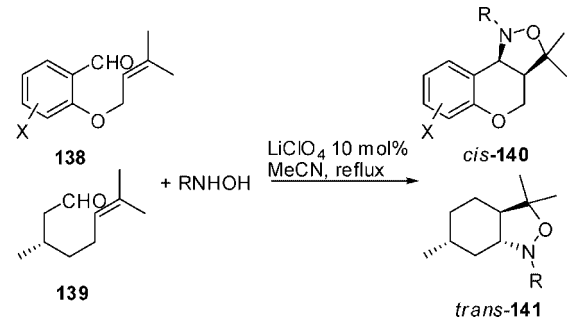
Scheme 93



Scheme 94



Scheme 95



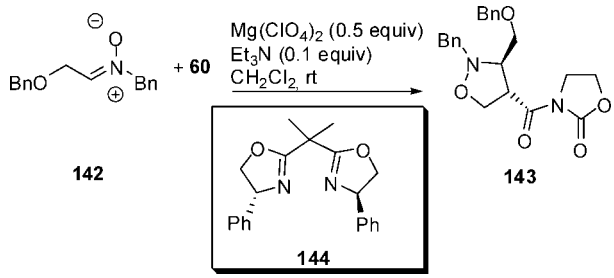
enantioselective and regioselective nitrile oxide additions to crotonoylpyrazolidinones,[281] while Mg(ClO$_4$)$_2$ provides good catalysis for acrylimides.[282] In the latter reaction, Mg(ClO$_4$)$_2$ gives slightly higher ee's than Ni(ClO$_4$)$_2$ (81% vs 77%) and the regioselectivity for the C-adduct **137**, in which the carbon terminus of the dipole adds to α-carbon of the acceptor, is complete (Scheme 94).

Regarding nitrone cycloadditions, many reactions are performed in the presence of perchlorates. For example, the intramolecular nitrone cycloaddition reaction is catalyzed by 10 mol % lithium perchlorate in acetonitrile, and it is one of the most powerful synthetic methods for the construction of fused bicyclic isoxazolidine derivatives under essentially neutral conditions.

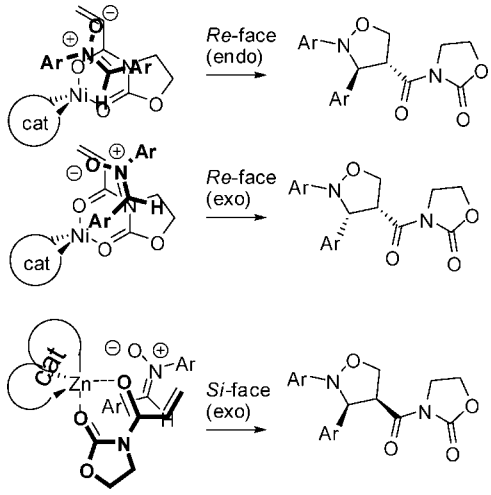
Treatment of the *O*-prenyl derivative of substituted salicylaldehydes (**138**) or citronellal (**139**) with hydroxylamines affords the corresponding polycyclic compound in 75−92% yield in a few hours at reflux (Scheme 95).[283] The authors also reported that in the absence of any catalyst, mixtures of isomers and lower yields are obtained and that LPDE effects the reaction at room temperature, but without reporting data.

Catalyzed enantioselective 1,3-dipolar cycloadditions of nitrones provide direct synthetic access to enantiomers of isoxazolidines whose high synthetic potential is based on

Scheme 96



Scheme 97



their transformations to γ-amino alcohols through reductive cleavage of the nitrogen−oxygen bond.

Crotonoyloxazolidinones are generally the template of choice and many C_2-axially chiral catalysts are employed with metal perchlorates as Lewis acid donor. In fact, in the reaction of *N*-benzyl-2-benzyloxyethylideneamine *N*-oxide (**142**) with 3-acryloyl-1,3-oxazolidin-2-one (**60**, R = H) in dichloromethane at room temperature in the presence of 0.5 equiv of $Mg(ClO_4)_2$ together with 0.1 equiv of NEt_3, the maximum regioselectivity is obtained when the major isomer (**143**) has the same regiochemistry as **135** (Scheme 96).[284]

A detailed study of this reaction was performed on diphenylnitrone and **60** (R = H) in the presence of many perchlorate salts and chiral catalysts. The main features derived from this study are that the presence of molecular sieves shifts the stereoselectivity in favor of the *exo* adducts (the **143**-like adduct with *cis* relationship) and influences the enantioselectivity, as well as the use of chiral catalyst with *trans*-geometry (**142**, Scheme 84).

Regarding the counterion behavior, both $Mg(ClO_4)_2$- and $Ni(ClO_4)_2$-based catalysts favor the nitrone approach to the *Re* face of the coordinated dipolarophile, whereas the Zn(II)-based catalyst prefers a *Si* face approach, and the Co(II)-based catalyst gives intermediate results (Scheme 97).[285] In the presence of the complex DPFOX-Ph (**59**)/$Ni(ClO_4)_2 \cdot 3H_2O$ (10 mol %), 1,3-dipolar cycloadditions between nitrones and crotonate oxazolidinones **60** occur with high diastero- and enantioselectivities to give *trans*-3,4-isoxazolidines in high yields.[286]

Moreover, the DBFOX-Ph complex catalyzed enantioselective nitrone reactions can be extended to every α,β-unsaturated aldehyde. The sterically controlled isoxazolidine-5-carbaldehydes are produced in the reactions of 2-alkyl- and 2-arylacroleins in the presence of either nickel(II) or magnesium complexes, while the electronically controlled isoxazolidine-4-carbaldehydes are given in the zinc(II) complex catalyzed reactions with 2-bromoacrolein. Enantioselectivities up to 99.5% ee are observed in the reactions performed at room temperature (Table 4).[287,288]

Other C_2-symmetric chiral ligands that are used in these syntheses are 2,6-bis[(4*R*)-4-substituted-oxazolinyl)pyridines (**145**). At room temperature, in both apolar and protic solvents and in the presence of MS 4 Å, crotonate **60** reacts with nitrone leading almost exclusively to the *endo* adducts in 80−99% yield and 90−99% ee with 20 mol % of the complex **145**/$Ni(ClO_4)_2 \cdot H_2O$ (Scheme 98).[289–291]

Xanthene analogues (**148**, Scheme 99) gives the highest enantioselectivities with various nitrones and **60** when coordinated with Mn(II) and Mg(II) perchlorate hydrates. The cycloadducts are obtained with excellent stereoselectivities for all of the nitrones (78−96% yields, diastereoselectivity ranging from 96/4 to >99/1 with 85−95% ee for the major diastereomer).[292]

The combination of $Ni(ClO_4)_2 \cdot 6H_2O$ and chiral binaphthyldiimine ligand introduced by Suga (**66**, Scheme 37) is employed also in 1,3-dipolar cycloaddition of nitrones with 3-(2-alkenoyl)-2-thiazolidinethiones (up to 85% yield and 95% ee)[293] and **60** (up to 81% ee of the corresponding *endo*-cycloadduct with *endo*-selectivity up to 96:4) in the presence of MS 4 Å.[294]

Also trimethylsilyldiazomethane is used as dipolarophile in the reaction with **60**, in the presence of **59**−metal perchlorate complexes. In particular **59**/$Zn(ClO_4)_2 \cdot 3H_2O$ at −40 °C produces (4*S*,5*R*)-1-acetyl-5-(2-oxo-3-oxazolidinylcarbonyl)-2-pyrazoline in 99% ee, while an almost complete switch of the enantioselectivity is performed simply by adding two methyl substituents at the 4-position the achiral chelating auxiliary (**143**) and using $Mg(ClO_4)_2$ (97% ee of the 4*R*,5*S* diastereomer).[295]

In section 5, we encountered *ortho*-quinone methides (**86**, Scheme 56) as valuable intermediates for the formal Friedel−Crafts alkylation of indoles. The same key intermediate can undergo [4 + 1] cycloaddition with isonitriles in a three-component aminobenzofuran (**149**) formation from phenols (Scheme 100). Yields are not very high (47−76%).[164]

The 1,3-dipolar cycloaddition of azomethyne ylides to electron-deficient alkenes is one of the most powerful methods for the construction of highly substituted pyrrolidine and proline rings (**151**, Scheme 101) with four asymmetric centers. Many laboratories have reported catalytic asymmetric [3 + 2] cycloadditions with azomethyne ylides (most from glycine imines, **150**) by means of a variety of ligand−metal combinations following the steps above-described for nitrones.

For example, $Cu(CH_3CN)_4ClO_4$ and the planar chiral P,S-ligand 1-(diphenylphosphino)-2-(*t*-butylthio)ferrocene (0.5−3 mol %), afforded the *endo* adducts with up to 97% yield and 99% ee.[296]

Scheme 98

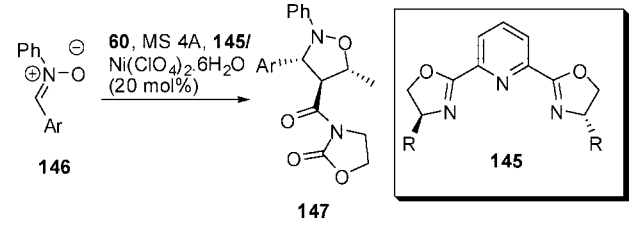
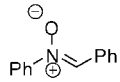
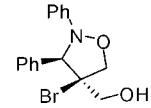
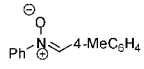
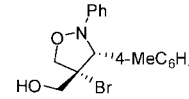
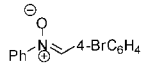
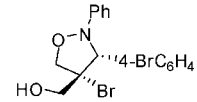
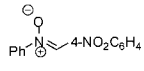
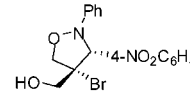
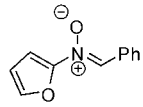
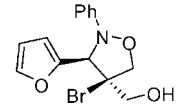
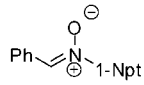
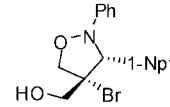
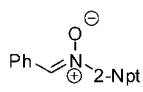
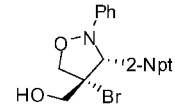
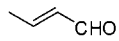
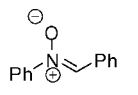
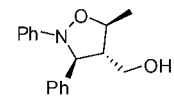
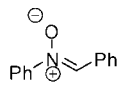
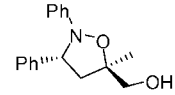
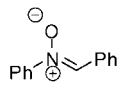
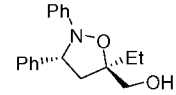
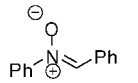
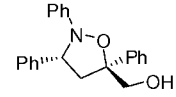
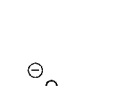
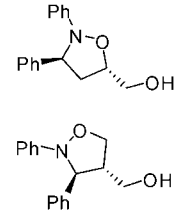
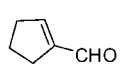
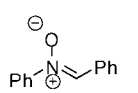
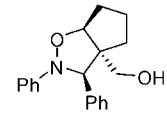
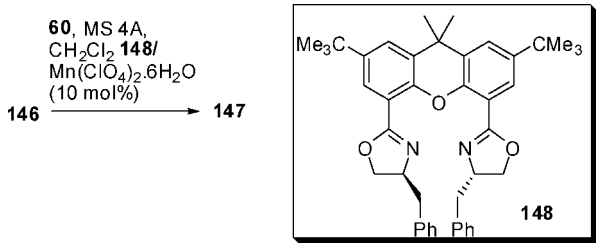


Table 4. Enantioselective Nitrone Cycloaddition to α,β-Unsaturated Aldehydes in the Presence of 59 (10 mol %) and MS 4 Å at rt in CH_2Cl_2, Followed by Reduction with $NaBH_4$[a]

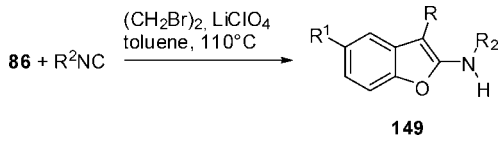
Aldehyde	Nitrone	Conditions	Results	Product
		$ZnI_2/AgClO_4$ (10 mol% each), 0.5 h	y: 94%; ds:98/2; ee: 97%	
		$ZnI_2/AgClO_4$ (10% mol% each), 1 h	y: 96%; ds:98/2; ee: 97%	
		$ZnI_2/AgClO_4$ (10% mol% each), 0.5 h	y: 95%; ds:91/9; ee: 97%	
		$ZnI_2/AgClO_4$ (10% mol% each), 2 h	y: 97%; ds:99/1; ee: 99%	
		$ZnI_2/AgClO_4$ (10% mol% each), 18 h	y: 76%; ds:91/9; ee: 90%	
		$ZnI_2/AgClO_4$ (10% mol% each), 1 h	y: 98%; ds:98/2; ee: 88%	
		$ZnI_2/AgClO_4$ (10% mol% each), 1 h	y: 97%; ds:90/10; ee: 99.5%	
		$ZnI_2/AgClO_4$ (10% mol% each), 69 h	y: 78%; ds:80/20; ee: 84%	
		$Ni(ClO_4)_2·6H_2O$ (10 mol%), 22 h	y: 98%; ee: 99%	
		$Ni(ClO_4)_2·6H_2O$ (10 mol%), 29 h	y: quant; ee: 92%	
		$Ni(ClO_4)_2·6H_2O$ (10 mol%), 24 h	y: 67%; ee: 84%	
		$Ni(ClO_4)_2·6H_2O$ (10 mol%), 24 h, -10 °C	y: 75%; rs: 95/5, ds: single, 95/5; ee: 98, 91%	
		$Co(ClO_4)_2·6H_2O$ (10 mol%), 24 h, rt	y: 46%; ee: 92%	

[a] Npt = naphthyl; y = yield; ds = diastereomeric ratio; rs = regioisomeric ratio; ee = enantiomeric excess.

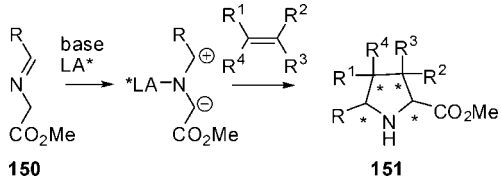
Scheme 99



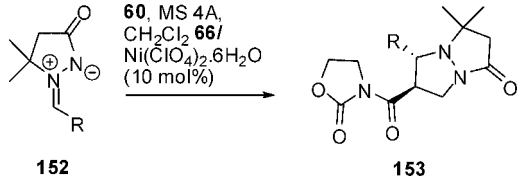
Scheme 100



Scheme 101



Scheme 102



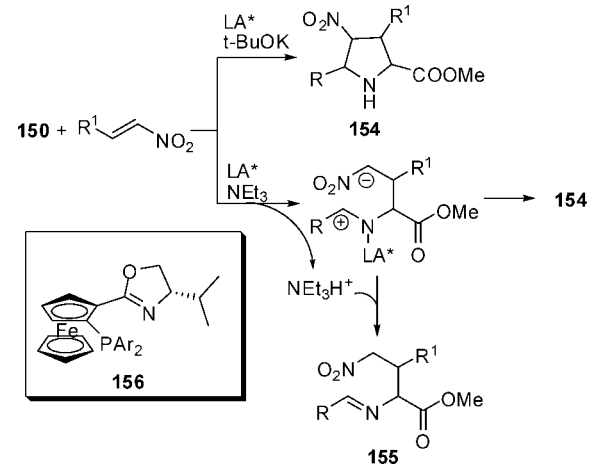
Moreover the combination of $Ni(ClO_4)_2 \cdot 6H_2O$ and chiral binaphthyldiimine ligand (**66**) with cyclic azomethyne imines (**152**) and **60** leads to fused **153** with up to 93% yield and 97% ee,[297] while simple azomethyne ylides and *N*-arylmaleimides provide up to 92% yield and 91% ee (Scheme 102).[298]

The Cu(I)-catalyzed asymmetric 1,3-dipolar cycloaddition of azomethyne ylides to nitroalkenes shows an interesting behavior. First the use of a weak base such as NEt_3 leads to a stepwise mechanism where the pyrrolidine derivatives (**154**) are obtained with high ee, but in moderate yields owing to Michael addition to **155**, which occurs as a side reaction (Scheme 103).

A high yield (64−98%) of **154** can be achieved with a stronger base such as *t*-BuOK, and either *exo* (up to exclusive diastereoselectivity) or *endo* (up to 94% diastereoselectivity) adducts are obtained, with excellent enantioselectivity (83−99% ee), by using electron-rich or electron-deficient aryl groups on the P atom of chiral P,N-ferrocene ligands (**156**), respectively.[299]

Finally, the reaction of fullerenes C_{60}, $Fe(ClO_4)_3 \cdot 6H_2O$, and various nitriles (C_{60}/$Fe(ClO_4)_3 \cdot 6H_2O$/nitrile = 1:1:100) to afford fullerooxazoles in 51−81% yields should be mentioned in this section. The direct melting of the mixture of reactants and catalyst is crucial for the successful realization of the reaction. A plausible reaction mechanism involves Lewis acid catalyzed addition of water to the nitrile followed by homolytical addition to fullerene and ring closure with release of Fe(II).[300]

Scheme 103



8.3. Six-Membered Rings

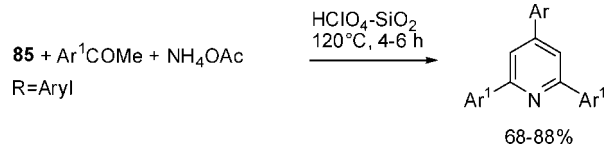
Saturated and partially saturated pyridine derivatives have attracted considerable attention in recent years in biologically active compounds, natural products, drugs and agrochemicals.

Among methods for pyridine synthesis, the three-component reaction of aldehydes, ammonium acetate, and acetophenones is of interest for this review (Scheme 104). In fact, $HClO_4$ supported on silica gel is an efficient catalyst to bring about the preparation of symmetrical 2,4,6-triarylpyridines. The reaction is carried out at 120 °C for 4−6 h under solvent-free conditions in 68−88% yields and without significant effect of substituents on the aromatic ring.[301]

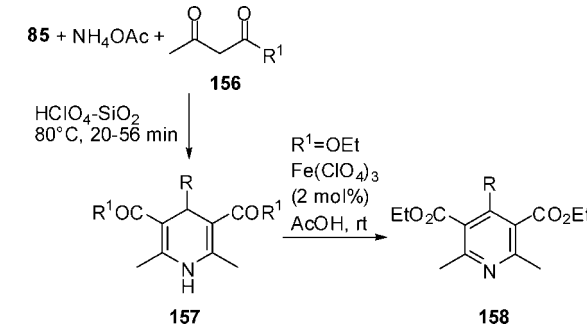
Regarding partially saturated pyridines, current literature continues to report new protocols for the preparation of 1,4-dihydropyridines, owing to the important pharmacological and biological activities of these compounds. A slight modification of the previous protocol, for example, with the substitution of acetophenone with a β-dicarbonyl compound, allows the synthesis of functionalized dihydropyridines (**157**) in 82−95% yields (Scheme 105). The experimental procedure has the ability to tolerate a large variety of functional groups.[302]

Moreover, a catalytic amount of ferric perchlorate in acetic acid allows the oxidation of 1,4-dihydropyridines (**157**, R^1 = OEt) to pyridines (**158**) in 78−97% yields. The concentra-

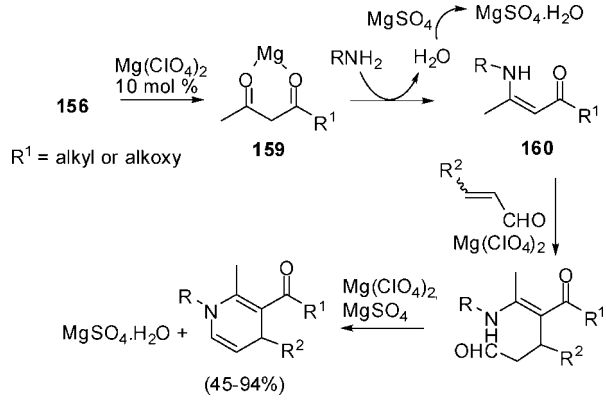
Scheme 104



Scheme 105



Scheme 106



tion of oxygen in the air is good enough to facilitate ferric ⇌ ferrous turn over. The reaction proceeds via radical cation intermediates, so secondary alkyl and benzyl groups (e.g., **158**, R = *i*-Pr, $PhCH_2$), owing to the electron-releasing ability of the corresponding radicals, are expelled with the formation of dealkylated products.[303]

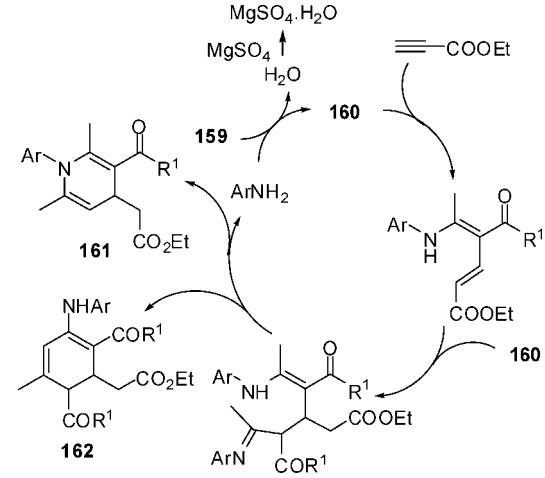
The reaction of β-enamino ester or ketone with aldehydes provides a valuable protocol for this synthesis. $Mg(ClO_4)_2$ proves to be the best choice among perchlorates; the addition of a double amount of $MgSO_4$ with respect to perchlorate as dehydrating agent is necessary. β-Enamino esters are generally more reactive than and β-enamino ketones, and reactivity is independent of the nature of the ester group in the former compounds and of the *N*-substituent in both cases, whereas the nature of the aldehyde affects the rate of the reaction, that is, the presence of an electron-withdrawing group requires longer reaction times. Yields range from 32% to 75% with 10 mol % of catalyst. Sometimes small amounts of pyridinium salt are also recovered.[304]

Considering the ability of perchlorates to catalyze the formation of the enamino derivatives from carbonyl derivatives and amines,[234] a more convenient three-component procedure to obtain dihydropyridine is also possible (Scheme 106).

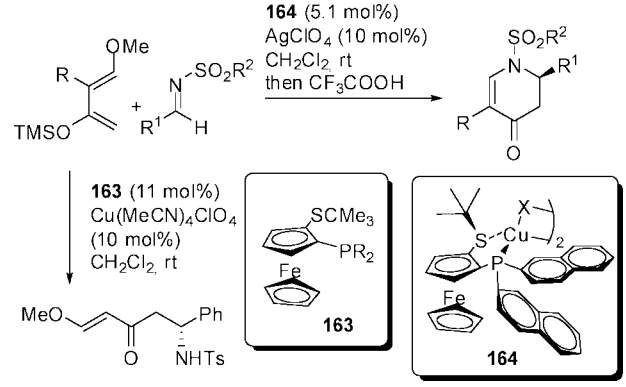
When the reaction is studied with α,β-acetylenic systems and aromatic amines, a surprising result is obtained. In fact, the reaction of enamino esters with ethyl propiolate does not give the expected pyridone, but a dihydropyridine **161** derived from a double conjugate addition of enamino derivative **160** to propiolate, followed by an intramolecular condensation with elimination of amine (Scheme 107).[305] The reaction was tested with differently substituted anilines (39−95% yield), and electron-donating substituents had no effect on the yields whereas a decrease with weak deactivating group was observed. Hindered amines lead to increasing amounts of side product **162**, and in particular, 2-*tert*-butylaniline gives exclusively **162**.

The tosylimine of aldehydes reacts with Danishefsky's diene, in the presence of 10 mol % enantiopure planar chiral 1-phophino-2-sulfenylferrocenes ligands (**163**) and $Cu(MeCN)_4ClO_4$ or $AgClO_4$, affording mainly the acyclic Mannich-type addition product rather than the Diels−Alder adduct in good yields and moderate ee. Then acid cyclization with trifluoroacetic acid gives the formal aza-Diels−Alder adduct.[306] However dimeric complexes (**164**) of ferrocene derivatives with cuprous halides and $AgClO_4$, as halide scavenger, followed by acid cyclization, provide dihydropyridones in 39−90% yields and 73−94% ee (Scheme 108). The presence of an additional substituent at the diene or a

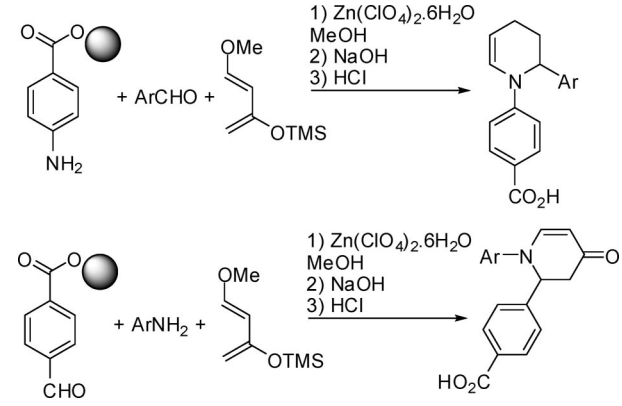
Scheme 107



Scheme 108



Scheme 109

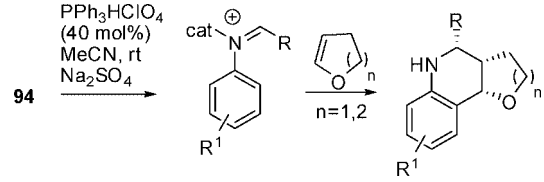


change in the arylsulfonyl group of the formal heterodienophile does not substantially modify chemical yield and enantioselectivity.

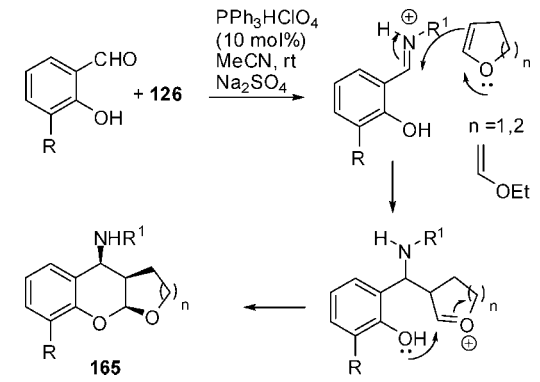
A true aza-Diels−Alder reaction has been developed for the construction of structurally diverse 2,3-dihydro-4-pyridones on a soluble polymer support, starting from aryl imines. In fact, a one-pot three-component reaction of PEG-supported amine (aldehyde), aromatic aldehydes (amines), and Danishefsky's diene, in the presence of 0.1 equiv of $Zn(ClO_4)_2 \cdot 6H_2O$ in MeOH at room temperature for 12 h affords a library of pyridones in 61−99% yields and 48−98% purity (Scheme 109).[307]

Quinoline is a well-known structural unit in alkaloids, therapeutics, and synthetic analogues with interesting biological activities. In addition, polysubstituted quinolines have

Scheme 110



Scheme 111



been found to undergo hierarchical self-assembly into a variety of nano- and mesostructures with enhanced electronic and photonic functions.

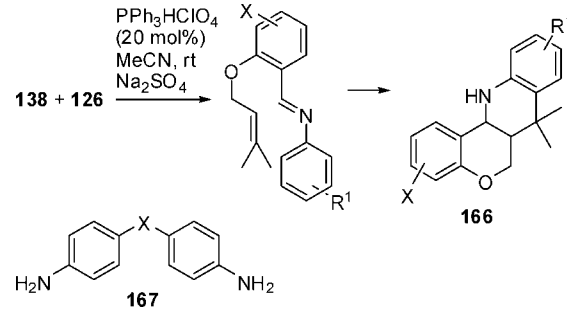
The imino-Diels−Alder reaction provides a rapid means for the construction of functionalized quinolines with control of regio-, diastero-, and enantioselectivity; however, it is necessary to activate the imine double bond. This is due to the low electrophilicity of the imines compared with the corresponding carbonyl compounds. The activation of the imine can be achieved by coordination at the imine nitrogen of triphenylphosphonium perchlorate ($PPh_3 \cdot HClO_4$). In the presence of 40 mol % of this catalyst in acetonitrile at ambient temperature, *N*-aryl imines (**94**, R = Ar) react with dihydropyran or cyclopentadiene in 65−95% yield with slight or exclusive predominance of the *cis* adduct. The reaction can be carried out in comparable yields in multicomponent fashion, mixing aldehyde, imine, and dienophile in the presence of Na_2SO_4 as dehydrating agent (Scheme 110).

It should be noted that perchloric acid alone promotes the polymerization of the aldimine and no cycloadduct can be separated.[308] Moreover, it must be outlined how little structural changes sharply modify the reaction mechanism. In fact, cycloaddition occurs on the heterodiene C=C−N=C (Scheme 110), but not on the C=C−C=N, where polar addition occurs under very similar reaction and catalytic conditions (Scheme 111). In fact, salicylaldimines react with enol ethers in the presence of 10 mol % $PPh_3 \cdot HClO_4$ in acetonitrile at room temperature, affording chromanes (**165**) in 83−98% or 72−85% yields with cyclic enol ethers or ethyl vinyl ether, respectively. As reported above, addition of Na_2SO_4 as water scavenger allows the reaction to be carried out in one pot in comparable yields (83−93%).[309]

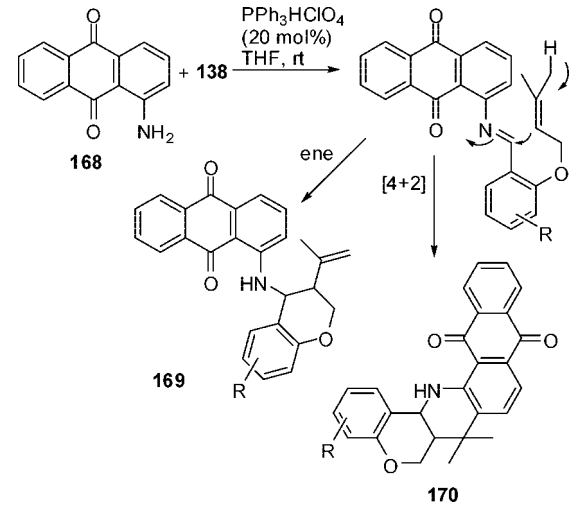
LPDE, indeed, is found to catalyze imino-Diels−Alder reactions of *N*-aryl aldimines with 3,4-dihydro-2*H*-pyran and indene to afford the corresponding quinoline derivatives in 75−95% yields. It should be noted that also normal (cyclohexenone) demanding dienophiles are involved in this reaction, albeit in longer reaction times.[310]

More recently, the use of magnesium perchlorate (5 mol %) as the Lewis catalyst allows the opposite stereochemistry to be reached. In fact, pyrano- and furanoquinolines are obtained

Scheme 112



Scheme 113



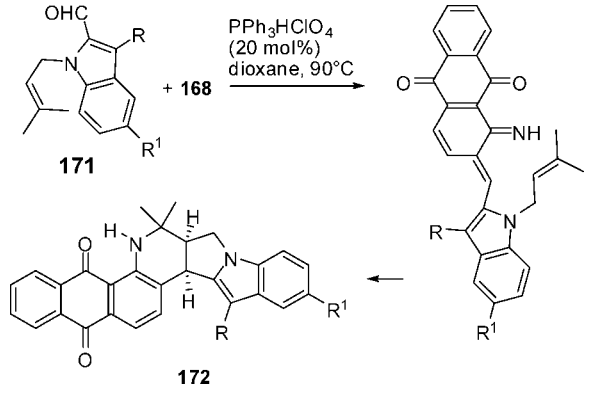
in 81−92% yields with predominantly *trans* geometry. Other perchlorates give worse results in reaction rates and selectivity.[311]

Another remarkable catalytic activity of $PPh_3 \cdot HClO_4$ (20 mol %) is the synthesis of tetrahydrochromano[4,3-*b*]quinolines (**166**) in 82−94% yields and about 1:1 diastereomeric ratio from aromatic amines and *O*-allyl derivatives of salicylaldehydes (**138**) via an intramolecular version of the previous reaction (Scheme 112). Similarly, the reaction of imines derived from 4,4′-methylenedianiline (**167**, X = CH_2) or 4,4′-oxadianiline (**167** X = O) in the presence of 40 mol % of the catalyst undergo intramolecular bis-cyclization to give the corresponding bis-**166** as a mixture of three isomers in nearly a 1:1:1 ratio.[312]

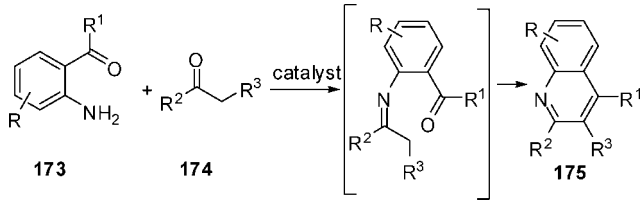
As well as for the intermolecular reaction, LPDE is found to catalyze this intramolecular cyclization of aldimines derived from **138** to afford **166** in 75−90% yields, once more in almost 1:1 diastereomeric ratio.[313]

Anthraquinone−quinoline heterocycles and also their bis-analogues are biologically interesting products, pharmaceutical and DNA intercalating agents. Their synthesis can be achieved by a modification of these protocols, that is, a $PPh_3 \cdot HClO_4$-catalyzed imino-Diels−Alder reaction of 1-aminoanthraquinone and 1,5-diaminoanthraquinone with either **138** or **139**.[314] The reactions are carried out in a one-pot procedure without isolating the imine and are complete in 5−15 min in good yields. Surprisingly the reaction with salicylaldehydes **138** is influenced by the nature of substituents, and the reaction pathway changes from normal, leading to **170**, to ene-type cyclization giving **169** (Scheme 113). The donation of electrons by the tautomeric keto−enol form of the anthraquinone ring and contemporary electron-

Scheme 114



Scheme 115



withdrawing effect on salicylaldehydes alters the energy levels of LUMO−HOMO, and hence ene-type cyclization is obtained.

On the other hand, in the reaction with *N*-prenylated indole carboxyaldehydes (**171**), **168** undergoes a quite different pathway to lead to pyrrolizinoquinolines (**172**).[315] The different reaction conditions (higher temperature and dioxane as the solvent), in fact, sharply modify the reaction course and Friedel−Crafts reaction instead of imine formation is the step preceding the cycloaddition (Scheme 114). The reactions are highly stereoselective, leading to the exclusive formation of *cis* isomer in 66−85% yields.

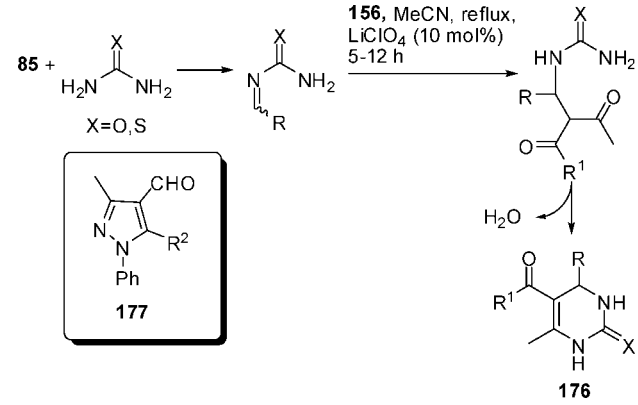
Another ene-type reaction is promoted by lithium perchlorate dispersed on silica gel, which is found to be a mild, effective, and recyclable catalyst for intramolecular ene reactions of activated 1,6- and 1,7-dienes. In contrast, the reactions are very sluggish in LPDE or in lithium perchlorate suspended in dichloromethane.[316]

The Friedlander annulation is the condensation followed by a cyclodehydration between 2-aminoaryl ketones and α-methylene ketones. The reaction is catalyzed by both acids and bases, so it is a candidate for the use of perchlorate and perchloric acid as the catalyst (Scheme 115). Actually among the various metal salts studied for this transformation, $Mg(ClO_4)_2$ (10 mol %) is found to be effective (42−97% yield) for the reaction at 60 °C in EtOH.[317]

The same reaction is also carried out in acetonitrile at reflux temperature in the presence of silica-supported perchloric acid. Both ketones and β-keto esters afford 90−96% yields of products in a short reaction time.[318]

Dihydropyrimidinones and functionalized dihydropyrimidines have been found to be an important class of compounds due to their therapeutic and pharmacological activities including antiviral, antitumor, antibacterial, and anti-inflammatory activities. In addition, 4-aryldihydropyrimidines have emerged as potent calcium channel blockers, and the dihydropyrimidinone-5-carboxylate core unit is found in many marine natural products. The synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones by a very simple one-pot condensation reaction of an aldehyde, β-ketoester, and urea in the presence

Scheme 116



of a strongly acidic catalyst is known as the Biginelli reaction, first reported by the Italian chemist Pietro Biginelli in 1893.[319] In recent years, several improved procedures have been reported with the use of a number of Lewis acid catalysts, as well as protic acids. Some of them are of interest for this review.

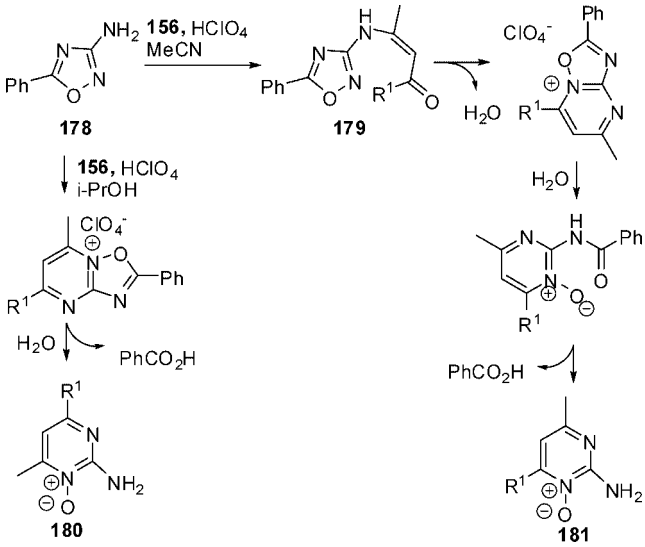
For example, the reaction of several aromatic, aliphatic, and heterocyclic aldehydes, β-keto esters, or acetylacetone and urea in the presence of 20 mol % lithium perchlorate in refluxing acetonitrile result in the formation of dihydropyrimidinone **176** in 75−90% yield (Scheme 116).[320] The neutral and simple reaction conditions render this method effective for aromatic, aliphatic, α,β-unsaturated, and heterocyclic aldehydes. As well as many other reactions, 3,4-dihydropyrimidinones or thiones are also obtained in 85−99% yield, using silica-supported perchloric acid as a heterogeneous catalyst under solvent-free conditions.[321]

An interesting and particular supplement to this procedure involves the use of 5-chloro/phenoxyl-3-methyl-1-phenyl-4-formylpyrazole (**177**) instead of conventional aldehydes and $Mg(ClO_4)_2$ (10 mol %) in ultrasound irradiation for the synthesis of a series of novel 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1*H*)-(thio)ones in 57−92% yields.[322]

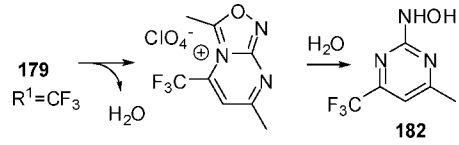
3-Amino-1,2,4-oxadiazoles (like **178**) react with β-diketones in the presence of perchloric acid to give azolopyrimidinium perchlorates. Ring-opening reactions of the azole moiety allowed the synthesis of 2-amino-pyrimidine *N*-oxides.[323,324] A plausible reaction path involves the enamino ketone intermediate species **178**, which will undergo a four-atom side-chain rearrangement where the N(2) of the oxadiazole ring acts as a nucleophilic center and the carbonyl of the enamino ketone as an electrophilic center (Scheme 117). The regiochemistry of the reaction depends on the employed solvent: isomers **180** and **181** are predominantly obtained in isopropanol and acetonitrile, respectively. More recently this procedure has been extended to trifluoromethylated β-diketones. Actually, the corresponding trifluoromethylated 2-amino-pyrimidine *N*-oxides have been synthesized.[325] However, besides the expected 2-aminopyrimidine *N*-oxides **177**, significant amounts of 2-(hydroxylamino)pyrimidines **178** are isolated (Scheme 118). This pathway is absent in the case of unfluorinated diketones; therefore it is explained by authors as an effect of trifluoromethyl substituent on the conformational stability of the enamino ketone side chain or on the protonation of oxadiazole nitrogens.

The 1,2-dihydroisoquinoline ring is found in many natural products and pharmaceuticals with remarkable biological activities. Because of their importance, significant effort

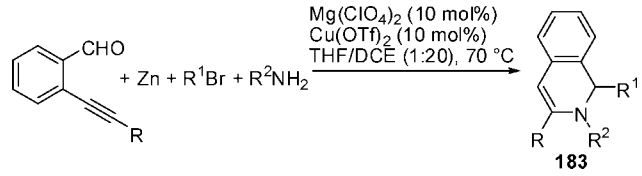
Scheme 117



Scheme 118



Scheme 119



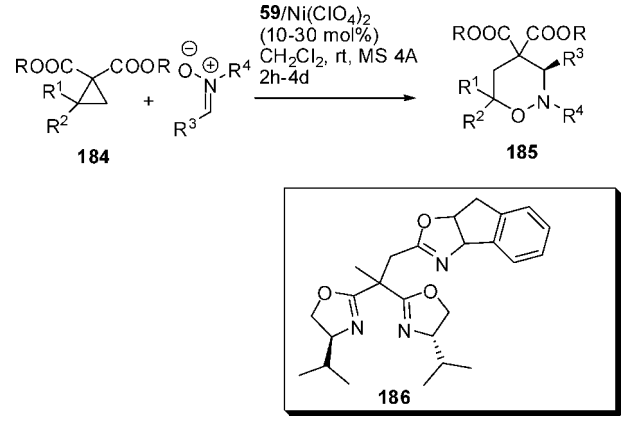
continues to be given to the development of new 1,2-dihydroisoquinoline-based structures.

Recently a multicomponent reaction of 2-alkynylbenzaldehydes, anilines, zinc dust, and allyl or benzyl bromide catalyzed by the combination of $Mg(ClO_4)_2$ (10 mol %) and $Cu(OTf)_2$ (10 mol %) in THF/DCE (1:20) at 70 °C appears in the literature (Scheme 119). The 1,2-dihydroisoquinolines (**183**) are obtained in 68−90% yields.[326] Inferior results are obtained when aliphatic amines are employed in this reaction (i.e., 35% and 20% yield with benzylamine and *iso*-butylamine, respectively).

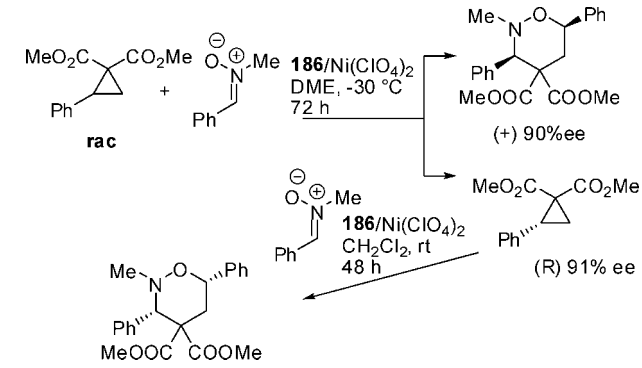
Diactivated cyclopropanes undergo cycloaddition reaction with nitrones, which results in ring-opened products, the synthesis of tetrahydro-1,2-oxazines. They have potential as substructures of drugs and as chiral building blocks, especially if prepared in an enantioselective manner. The use of the **59**/$Ni(ClO_4)_2$ complex provides a valuable entry to this topic. Very high yields (often almost quantitative) and high enantioselectivity are reached (89−96% ee) with 10−30 mol % catalyst. Only for the products from nitrones derived from cinnamyl aldehyde and furfural, the enantioselectivity is low, while spiro[5.2]octane give low yields (Scheme 120).[327]

Moreover, the switch of the chiral catalyst from **59** to **186** and of the reaction conditions to −30 °C in DME does not influence substantially the yields (62−99%) and the ee (80−97%), but interestingly, when an excess of the cyclopropane derivative is used, the remaining cyclopropane can be recovered with a good ee value, providing a valuable

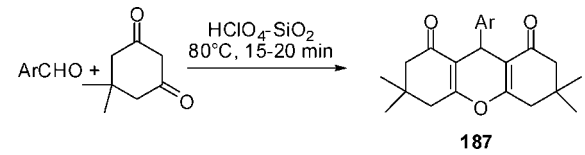
Scheme 120



Scheme 121



Scheme 122



method for the kinetic resolution of 2-substituted cyclopropane-1,1-dicarboxylates.

Furthermore, a combination of the asymmetric cycloaddition and the kinetic resolution/cycloaddition provides straightforward access to both enantiomers of tetrahydro-1,2-oxazines (Scheme 121).[328]

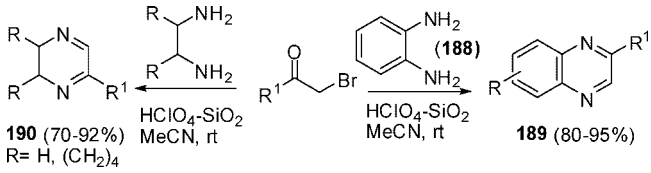
Silica-supported perchloric acid allows the synthesis of 1,8-dioxo-octahydroxanthenes (**187**) with 96−82% yields in solvent-free conditions (Scheme 122) with a synthesis very similar to that reported in Scheme 105, in the absence of ammonium acetate.[329] It should be noted that other authors reported that in solvent but also at 140 °C the cyclization does not completely occur, leading to a mixture of **187** and open compound after 3 h.[330]

The Pechmann condensation to coumarins has already been mentioned in section 5.2 as a Friedel−Crafts modification.[158]

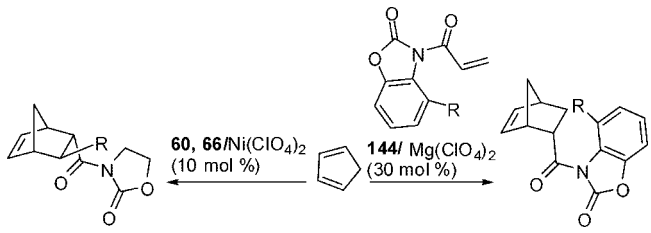
The synthesis of quinoxalines (**189**) and dihydropyrazines (**190**) can be accomplished by the condensation of a 1,2-diamine with an α-bromoketone in the presence of acids (Scheme 123).

Therefore the use of $HClO_4$−SiO_2 as the reaction promoter is a simple and logical choice for the catalyst. Actually a series of α-bromoketones were treated with both aromatic and aliphatic 1,2-diamines at room temperature to afford the products in 70−95% yields. Steric factors affect the rate of the reaction increasing reaction time.[331]

Scheme 123



Scheme 124



Finally, the synthesis of six-membered carbocycles by Diels−Alder reaction cannot be skipped. Also some of them, in fact, are catalyzed by perchlorates. For example, thianthrenium perchlorate is found to be an easy source of benzynes, when treated with LDA in THF at reflux. Thus-formed benzynes react regiospecifically with various β-amino carbonyl compounds and 2-aminophenylbenzenesulfonate to give diverse heterocyclic compounds (47−87% yield).[332]

Suga and co-workers experimented with their chiral catalyst (**66**) in the reaction of alkenes with 3-(2-alkenoyl)-2-oxazolidinones (**60**) (Scheme 124, left), indicating high levels of asymmetric induction in Diels−Alder reactions (up to 94% yield and 94% ee).[333]

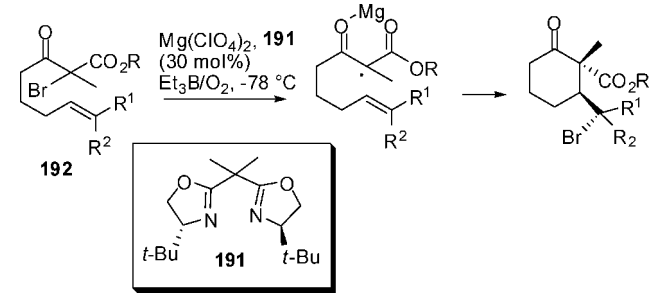
The Diels−Alder reaction between cyclopentadiene and oxazolones, similar to **60**, is carried out with the chiral catalyst **144** and $Mg(ClO_4)_2$ (Scheme 124 right). The system is sensitive to water content: when magnesium perchlorate is used without extra drying, ee is moderate (46%), but the reaction is fast, whereas with dry salt, ee increases up to 70%, but the reaction rate significantly slows.[334]

The Diels−Alder reaction with dienes of 1,2-thiazinylium perchlorate is also reported, and it will be described in section 9.4.

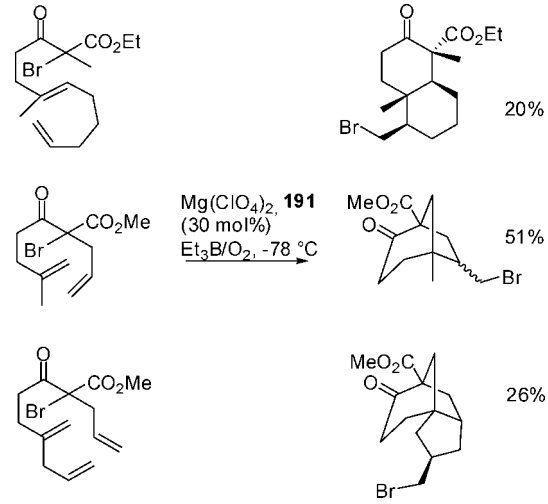
The atom-transfer radical cyclization reaction is another powerful method for the synthesis of a wide range of highly functionalized cyclic compounds under mild conditions. This reaction involves the transfer of a halogen atom from one carbon center to another with concomitant ring formation. Lewis acid catalyzed tandem reactions are more interesting since polycyclic compounds are obtained with multiple stereocenters constructed in one step under excellent stereocontrol. Yang's work on this reaction uses magnesium perchlorate as an effective Lewis acid catalyst, often compared with ytterbium triflate, but he never makes a definitive choice among the two catalysts, since their efficiency hardly depends on the substrates. It should be noted that 2-bromo-3-alkenylacetoacetates (**192**) are cyclized with the $Mg(ClO_4)_2/CH_2Cl_2$ and $Mg(ClO_4)_2$/toluene systems with *trans* geometry, in contrast to *cis* geometry observed in the atom transfer radical cyclization induced by light-irradiated $(Me_3Sn)_2$. Addition of a chiral ligand (**191**) similar to **143** and molecular sieves allows yields up to 82% and ee up to 95% (Scheme 125).[335]

The tandem version sets up four stereocenters in one step and can be applied to substrates either with the second double bond in the R^1 group or with an allyl substituent on the intercarbonyl carbon (Scheme 126).[336] Yields are moderate

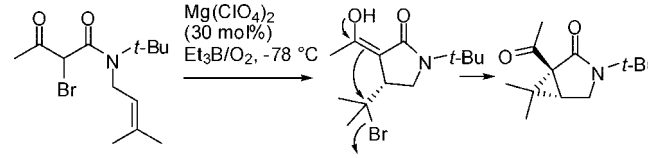
Scheme 125



Scheme 126



Scheme 127



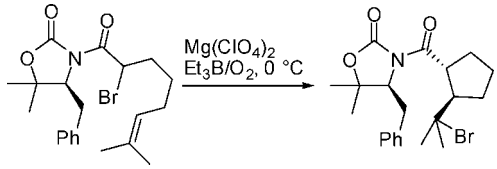
and the major side products are the corresponding reductive debromination and monocyclization products. The enantioselective tandem cyclization gives poor ee values in the absence of MS 4 Å or at low temperature, whereas their presence or higher temperatures improve ee values but drastically decrease yields.

Cyclization of olefinic β-keto amides instead of esters resulted, as well as esters, in exclusive formation of the *trans* cyclization products (the 2-amide group *trans* to the 3-alkyl group) in 57−74% yield. This reaction can follow either a radical or polar mechanism, but the cyclization product is formed via a radical process rather than an ionic pathway, since substrates are stable toward $Mg(ClO_4)_2$ without the radical initiator.[337] Interestingly in one case (Scheme 127), subsequent intramolecular cyclopropanation via 1,3-elimination of HBr from product is observed, while this reaction is more frequent with ytterbium triflate.

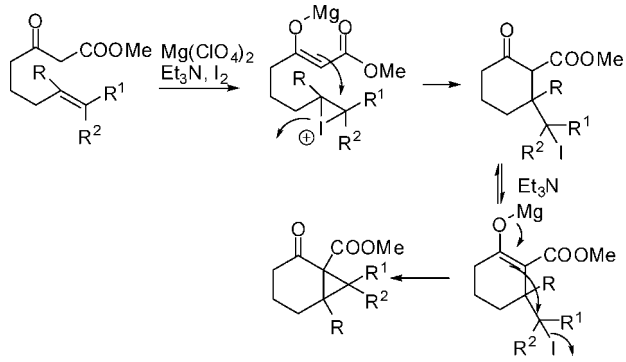
On amides the chiral catalysis is not set up, but enantioselective reactions are carried out on unsaturated α-bromo-oxazolidinone imides, where the oxazolidinone moiety acts as the chiral auxiliary. The only diastereomer depicted in Scheme 128 is in fact separated in 78% yield. The same reaction is then extended to achiral oxazolidinones with high yield (up to 87%) of the *trans* cyclic products.[338]

The Lewis acid promoted phenylseleno group transfer radical cyclization was also attempted, and it was found to

Scheme 128



Scheme 129



represent an efficient (56−80% yield), regioselective, and stereoselective tool for the formation of monocyclic and bicyclic compounds. This reaction applies better to amides than esters; irradiation with UV light is necessary to avoid unselective ionic cyclization.[339]

Finally, an interesting double cyclization reaction via a polar pathway but with many characteristics analogous to atom transfer radical cyclization should be mentioned, that is, a modified Taguchi's iodine-mediated carbocyclization reaction of unsaturated β-ketoesters.[340] Among various Lewis acids tested, dry $Mg(ClO_4)_2$ and $Yb(OTf)_3$ give good yields (47−92%), whereas no reaction is observed with hydrated $Zn(ClO_4)_2$. The best reaction conditions are I_2 (4 equiv)/$Mg(ClO_4)_2$ (2 equiv)/Et_3N (2.5 equiv)/CH_2Cl_2 (Scheme 129).

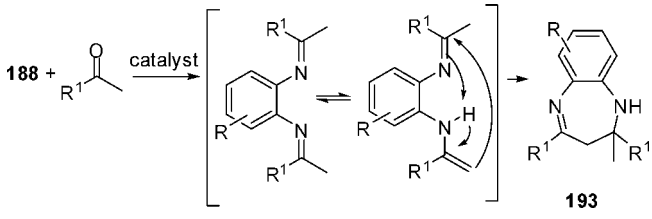
8.4. Seven-Membered Rings

Benzodiazepines and benzothiazepines possess a broad spectrum of biological activities and applications in medicinal chemistry. Moreover, they are useful synthons for the synthesis of various fused rings, making them privileged structures in combinatorial drug discovery libraries. These features have stimulated interest to develop new methodologies for their synthesis.

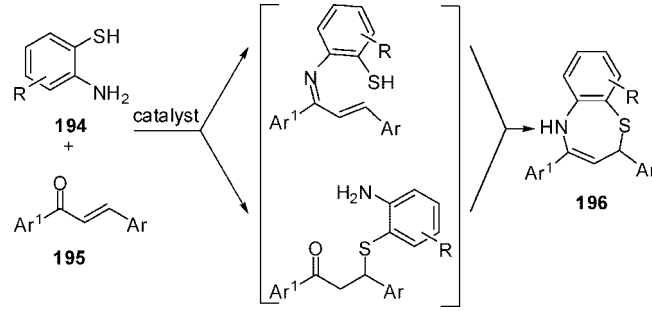
The acid-catalyzed condensation of diamines and carbonyl derivatives is generally the strategy of choice for the synthesis of benzodiazepines. In particular benzodiazepine preparation involves the condensation of *o*-phenylenediamine (**188**) with 2 mol of a ketone. The cyclization needs also an aldol step, so the ketones should contain at least one α-hydrogen (Scheme 130).

Among catalysts, 2 mol % $Fe(ClO_4)_3$ works at room temperature for 15−35 min in solvent-free conditions to give

Scheme 130



Scheme 131



the desired products in 82−93% yields. It is noteworthy that by starting from an unsymmetrical ketone, the ring closure occurs selectively only from the methyl side of the carbonyl group yielding a single product. No electronic effect of substituents on the aromatic rings of the diamines was observed.[341]

A series of 2,3-dihydro-1*H*-1,5-benzodiazepines were also prepared using different *o*-phenylenediamines and ketones with $HClO_4-SiO_2$ as the catalyst. The reaction shows the same features with respect ferric perchlorate, both in electronic effect of substituents on the aromatic ring and in regioselectivity on the ketone sides. The yields of 1,5-benzodiazepines are found to range from 79% to 98% in relatively short reaction times (2−3 h).[342,343] Interestingly, higher catalyst loading shortens reaction times, but with comparable yields; for example, the reaction of phenylenediamine and acetone is reported to occur in 2 h and in 91% yield or in 1 h and in 92% yield, as well as acetophenone reacted with 4,5-dimethylphenylenediamine in 3 h and in 81% yield or in 2 h and in 79% yield with 25[342] or 50 mg/mmol of catalyst,[343] respectively.

The common strategy for the construction of the 1,5-benzothiazepine moiety (**196**) is very similar, employing the reaction of 2-aminothiophenol (**194**) with 1,3-diarylprop-2-enones (**195**, Scheme 131).

During his long-term work on perchlorates, Chakraborti has studied this reaction with many salts and found that dry $Mg(ClO_4)_2$ is superior to $Mn(ClO_4)_2$, $BiOClO_4 \cdot xH_2O$, $Zn(ClO_4)_2 \cdot 6H_2O$, $ZrO(ClO_4)_2 \cdot 8H_2O$, $Cu(ClO_4)_2 \cdot 6H_2O$, $LiClO_4$, and $Ba(ClO_4)_2$. The use of $Mg(ClO_4)_2 \cdot 6H_2O$ lowers the yield. Noteworthy $Zn(ClO_4)_2 \cdot 6H_2O$ is inferior to dry $Mg(ClO_4)_2$, although the former is a better electrophilic activation agent for thia-Michael addition (section 4.2).[116] These lead to the interesting conclusions that $Zn(ClO_4)_2 \cdot 6H_2O$ favors the thia-Michael adduct but not the imine formation, while $Mg(ClO_4)_2$ is a unique electrophilic activator and has the dual catalytic property for thia-Michael and imine formation (section 6.2.4).[236]

Moreover, Chakraborti himself utilizes the chemoselective thia-Michael addition over aza-Michael addition during intramolecular competitive reactions with 2-aminothiophenol (section 4.2) for an efficient one-pot synthesis of benzothiazepines.[113] After these considerations, the reaction is carried out in 1,2-dichloroethane under reflux with 5 mol % of the catalyst and the desired 1,5-benzothiazepines are obtained in 80−90% yields after 0.5−2 h.[344]

8.5. Nazarov Reaction

The Nazarov cyclization converts a divinyl ketone through a pentadienyl cation under the influence of a Brønsted acid or a Lewis acid into a cyclopentenone. In its aliphatic form,

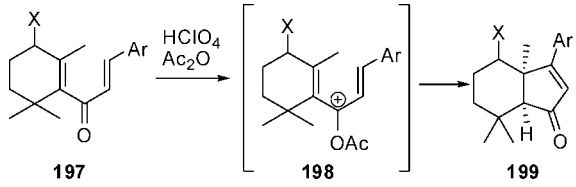
it can be seen as it is a thermally allowed electrocyclic ring closure, while in the aromatic form, it can be termed intramolecular vinylogous Friedel−Crafts acylation. To avoid two different sections on this reaction, we decided to review it here.

Diluted solutions of perchloric acid and acetic anhydride in ethyl acetate (10^{-2} M $HClO_4$/1 M Ac_2O/ethyl acetate) are introduced as the catalyst for cationic Nazarov cyclizations (Scheme 132). Acetic anhydride is needed to obtain the pentadienyl cation intermediate **198**. However, yields are not very satisfactory with nucleophilic aromatic substrates (**197**, Ar = furan, where a competitive Friedel−Crafts acylation take place) or with molecules carrying other enolizable carbonyls (**197**, C−X = C=O, where competitive formation of unreactive enol acetate can occur). Better results are obtained with hydroxyl substituents (**197**, X = OH) and excellent ones with alkenes or saturated substrates where no competitive acylation can occur.[345]

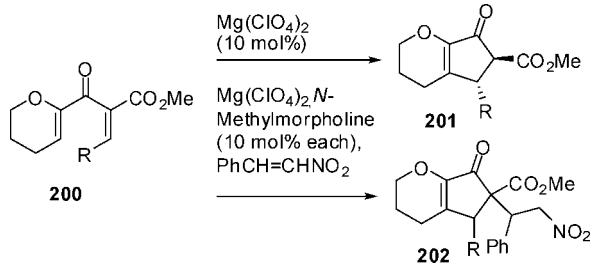
Also magnesium perchlorate was found to accomplish Nazarov product (**201**) from alkylidene β-ketoesters, but as expected, **201** is unable to give **202** by Michael addition to nitrostyrene under these experimental conditions (Scheme 133). As described in section 4.1, double catalysis is needed to perform this reaction, and actually, addition of a base leads in one pot to **202**. Interestingly, the diastereomeric ratio increases from 3:1 to 5:1 with prolonged stirring, very likely owing to the reversibility of the Michael addition.[346]

$Sc(ClO_4)_3$ is found to catalyze Nazarov cyclizations of heteroaromatic ketones (Scheme 134), but indeed the mixture of $LiClO_4$ (100 mol %) and $Sc(OTf)_3$ (5 mol %) is a superior catalyst, giving the best results (36−97%) and the most convenient and cost-efficient procedure. Actually, $LiClO_4$ has been already described in this review as an important additive in Friedel−Crafts acylations (see Table 1, section 5.1).[347]

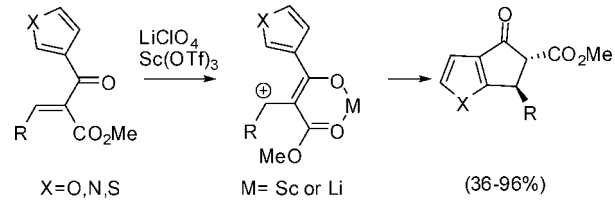
Scheme 132



Scheme 133



Scheme 134



9. Miscellaneous

Many other reactions are catalyzed by perchlorate salts or perchloric acid, but they cannot be classified on wide categories or they are marginal contributions to their reaction category. Therefore these reactions will be collected in this section.

9.1. Multicomponent Reactions (MCRs)

Multicomponent reactions are widely used in organic synthesis not only because more than one bond is formed in one pot but also because the methodology is useful for making a broad variety of compound libraries in short times. Some examples have been already mentioned in this review, as in sections 4.3 and 7.2 and mainly in the previous section on ring closure reactions. However there are many other examples involving perchlorate catalysis not included there, and they will be collected here. Most of the three-component reactions involve aldehydes and amino derivatives, which *in situ* form an imine or an iminium ion, followed by addition of a nucleophile to prepare the final product (Scheme 135).

These reactions are collected in Table 5, and some considerations should be made for some of them. For example, the LPDE-catalyzed three-component reaction of hydrazines to form α-alkylhydrazinephosphonates,[348] as well as of *O*-trimethylsilyl hydroxylamine to form 3-hydroxyamino esters,[349] cannot be applied to aryl aldehydes and cinnamyl aldehyde, whose hydrazones and oxime ethers are inert to nucleophilic addition. It is worth noting that allyl stannane addition to oxime ethers only succeeds with aromatic aldehydes, contrary to the reaction of ketene acetals.[349]

Moreover, it should be noted that the use of hexamethyldisilazane as a source of amine under solvent-free conditions and $LiClO_4$ (2 equiv), followed by hydrolysis, allows the synthesis of primary α-amino phosphonates in 80−92% yield. The reaction proceeds via imine formation, as the first intermediate. In the presence of trialkyl phosphite, imine is converted into the imino derivative of the α-aminophosphonates, which after hydrolysis under acidic conditions gives the target product.[350]

In his synthesis of α-aminophosphonates, Chakraborti reports a detailed study on various metal perchlorates and triflates, as well as magnesium salts, concluding that magnesium perchlorate is superior to the other salts.[365]

Only one three-component reaction does not involve an amino derivative, the condensation of carbonyl compounds with silyl ethers and allenyl silanes, where homopropargylic ethers are obtained. The reaction occurs through the formation of an acetal intermediate, which undergoes nucleophilic displacement by the allenylsilane.[361] It should be noted that when temperature is lowered to −78 °C, allenyl instead of homopropargylic ethers are obtained in 80−93% yield with benzaldehyde and 1-trimethylsilyl-2-butyne. This reaction is also applied to polycondensation, by reacting isophthalaldehyde, 1,10-bis(trimethylsilyloxy)decane, and 1-trimethylsilyl-2-butyne with 10 mol % of $TrClO_4$ in CH_2Cl_2 at −50 °C for 24 h to yield a polyether having allenyl side chains with the number-averaged molecular weight of 6600.[370]

Scheme 135

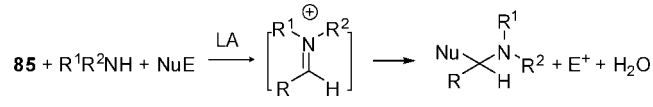


Table 5. Three-Component Reactions Involving Aldehydes, Amino Derivatives, and Nucleophiles

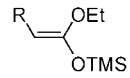
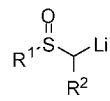
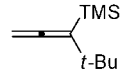
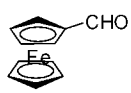
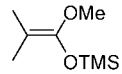
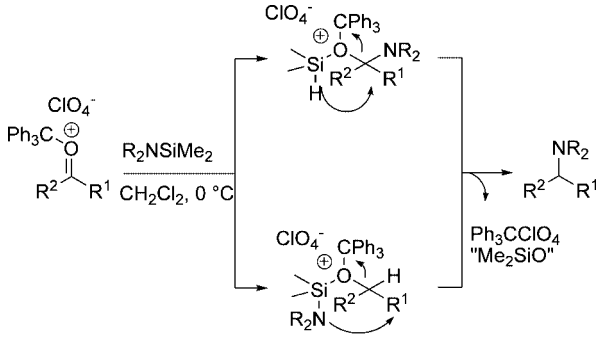
Comp. 1	Comp. 2	Comp. 3	LA	Yield (%)	Ref
		RLi, RMgX		77-95	
PhCHO, *i*-PrCHO	R^1_2NTMS		LPDE 5 M, rt	83-87[a]	351
RCHO, ArCHO	R^1_2NH	TMSCN	LPDE 5 M, rt	88-95	352
RCHO, ArCHO	R^1_2NH	$(MeO)_2POH$	LPDE 5 M, rt	87-97	353
RCHO, ArCHO	R^1NHOH	TMSCN	LPDE 5 M, rt	85-99	354
PhCHO	Pyrrolydine, Me_2NH		LPDE 5 M, rt	58-91[a]	355
	Pyrrolydine, Me_2NH, Et_2NH	$MeSO_2CH_2Li$		30-90	
RCHO	Me_2NNH_2	$(MeO)_2POTMS$	LPDE 5 M, rt	85-97	348
RCHO, ArCHO	R^1NHTMS	RLi, $BrZnCH_2CO_2R^2$	LPDE 5 M, rt	44-86	356
RCHO, ArCHO	PhNHOH	$(MeO)_2POTMS$	LPDE 5 M, rt	87-99[d]	357
ArCHO		RZnBr	LPDE 5 M, rt	60-94[b,c]	358
RCHO, ArCHO, cyclohexanone	R^1NH_2	$P(OR^2)_3$	LPDE 5 M, rt	85-98[b]	359
RCHO, ArCHO	$ArNH_2$	$AllylSnBu_3$	$LiClO_4$ (10 mol %), rt	75-90	360
RCHO, ArCHO, cyclohexanone	R^2OTMS		$TrClO_4$ (5 mol %) -20 °C	12-93	361
RCHO, ArCHO	R^1_2NH, R^1_2NTMS	$P(OR^2)_3$	LPDE 5 M, rt	84-98	362
RCHO, ArCHO, cyclohexanone	R^1_2NH	$P(OR^2)_3$	$LiClO_4$ dry(200 mol %), rt	65-92	363
RCHO, ArCHO	$ArNH_2$	$AllylSnBu_3$	$HClO_4$-SiO_2 (0.5 mol %), rt	81-90	364
RCHO, ArCHO Ketones	R^1_2NH	$P(OR^2)_3$	$Mg(ClO_4)_2$ dry (5 mol %), rt	75-98 80-92	365
	R^1_2NH	TMSCN	$LiClO_4$ (100 mol %), rt	93-100	366
ArCHO	Ar^1NH_2	Ketones	$HClO_4$-SiO_2 (2 mol %), rt	75-98[e]	367

Table 5. Continued

Comp. 1	Comp. 2	Comp. 3	LA	Yield (%)	Ref
RCHO, ArCHO	R^1NH_2	$NaBH_4$, $LiAlH_4$	LPDE 4M, 60 °C	45-100	368
RCHO	NH_2OTMS		LPDE 5 M, rt	71-84[b]	349
ArCHO		$AllylSnBu_3$		45-67	
RCHO, ArCHO, Ketone	$R^1{}_2NH$, Me_2NNH_2,[b] NH_2OTMS[b]	$(Ppyz)Zr(BH_4)_2Cl_2$	$LiClO_4$ (5 mol %), 40 °C	75-95	369

[a] Very low diastereoselectivity. [b] Me_3SiCl added as promoter. [c] de 60−95%. [d] Recovered as NH_2OTMS. [e] High *anti* selectivity when cyclohexanone is used as the ketone.

Scheme 136



In the Mannich reaction catalyzed by supported $HClO_4$, the *anti*-isomer predominates because the transition state producing it provides more space for the aryl groups of the aldimine and less steric repulsion between the aryl groups and the catalyst except for 4-bromoaniline. Moreover electron-withdrawing substituents both on the aniline and on the benzaldehyde inhibit the reaction.[367] Also solid $LiClO_4$ is used as catalyst for direct Mannich-type reaction of aryl aldehydes, aryl amines, and diethyl malonic ester under solvent-free conditions, affording the corresponding β-amino esters in good yields.[371]

Reductive amination of aldehydes and ketones, that is, reduction of *in situ* generated imines and iminium salts, provides a useful and important tool for the synthesis of amines. In Table 5, an example is reported,[368] but another one is difficult to classify, because it provides the amine and the reducing agent in the same molecule. This is the case of the reductive amination of benzaldehyde, acetophenone, 3-phenylpropanal, and 4-phenyl-2-butanone using methyl *N*-(dimethylsilyl)carbamate in the presence of $TrClO_4$ (5 mol %). In fact, silane provides both the amino moiety and the hydride responsible for the reduction. Yields are 94%, 53%, 88%, and 86% (Scheme 136).[372]

Finally, supported $HClO_4$ efficiently catalyzes the three-component condensation of benzaldehydes, enolizable ketones, acetyl chloride, and acetonitrile or benzonitrile for the synthesis of β-amido carbonyl compounds in good yields.[373]

9.2. Polymerizations

The effect of perchloric acid on polymerization of many monomers under cationic conditions is well documented over the past century, and its discussion is beyond the scope of this review. However, some interesting papers recently have appeared in the literature, and they will be quickly reported here. Polyaniline nanofibers, for example, are readily formed using interfacial polymerization, and the average diameter of the nanofibers can be tuned from 30 nm, using hydrochloric acid, to 120 nm, using perchloric acid.[374]

On the other hand, weight distribution in the anionic polymerization of methyl methacrylate, using 1,1-diphenylhexyllithium as the initiator, is greatly influenced by the addition of $LiClO_4$, indicating the formation of a unique salt-coordinated active species responsible for the propagation instead of many active centers having different reactivity, when perchlorate is absent.[375]

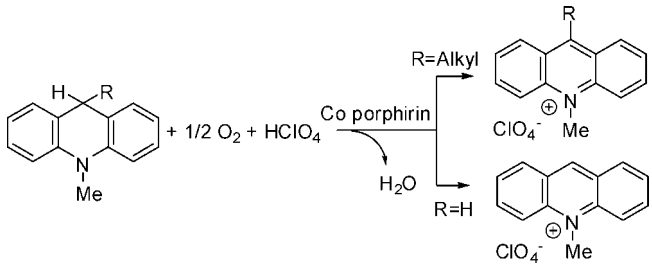
9.3. Oxidations

Although perchlorate possesses a highly oxidized chlorine atom, oxidations of organic compounds generally do not involve reduction of perchlorate ion, confirming Long's statement reported at the start of section 2.[14]

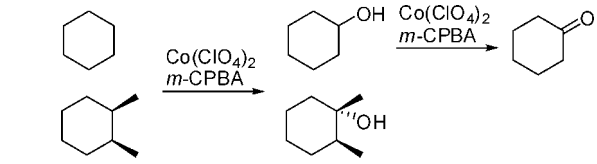
Most organic compounds that have singlet ground states are unreactive toward oxygen, which has a triplet ground state, because the reactions are spin-forbidden. In contrast, electron transfer from organic donors to O_2 to produce the radical cations of organic donors and the oxygen radical anion is spin-allowed. In the presence of acids, the thermal electron-transfer reduction of O_2 becomes energetically much more favorable than that in the absence of acids. So the dehydrogenation of 10-methyl-9,10-dihydroacridine (a template for natural NADH) by O_2 proceeds efficiently in the presence of $HClO_4$ accompanied by the two-electron and four-electron reductions to produce H_2O_2 and H_2O, which are effectively catalyzed by cobalt porphyrins (Scheme 137).[376,377] Moreover, in 9-alkyl-10-methyl-9,10-dihydroacridines with sterically hindered alkyl groups, under the same experimental conditions, the catalytic two-electron and four-electron reductions of O_2 result in oxygenation of the alkyl group leading to the corresponding hydroperoxides (ROOH) and the alcohol (ROH), respectively.

Oxidation of organic compounds was also carried out, and once more, perchlorate ion was only the counterion of the oxidant or of the Lewis or Brønsted acid catalyst and not the oxidizing agent. For example, the kinetics of the oxidation of ketones to acids was studied with a catalytic mixture

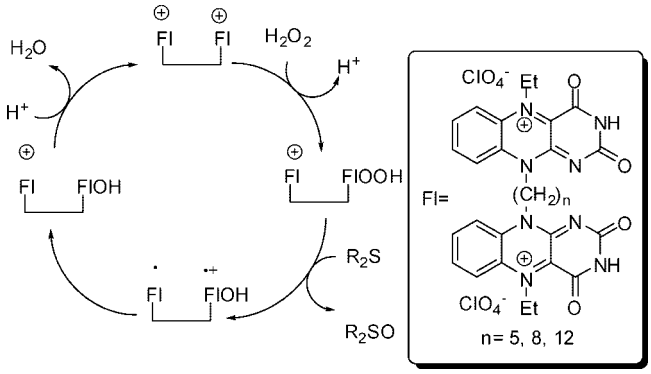
Scheme 137



Scheme 138



Scheme 139



formed by $IrCl_3$ and $Ce(ClO_4)_4$ in aqueous perchloric acid, where the oxidizing agent was Ce(IV). This catalytic mixture was found to surpass the classical osmium and ruthenium salts both in efficiency and cost.[378]

Metal perchlorates associated with *m*-chloroperbenzoic acid, as the true oxidant, are able to conduct stereoselective alkane hydroxylations via a mechanism involving metal-based oxidants. The catalytic activity of the metal salts is in the order of $Co(ClO_4)_2 > Mn(ClO_4)_2 > Fe(ClO_4)_2$, whereas other metal perchlorates such as $Cr(ClO_4)_3$, $Ni(ClO_4)_2$, $Cu(ClO_4)_2$, and $Zn(ClO_4)_2$ are ineffective. All the oxidation occurs with retention of the configuration, that is, *cis*-1,2-dimethylcyclohexane gives exclusively *cis*-1,2-dimethylcyclohexanol (Scheme 138).[379]

Organocatalytic oxidations with hydrogen peroxide attract much attention as important tools for environmentally benign oxidative transformations. Among organocatalytic oxidants for sulfide oxidation to sulfoxides, flavinium ion (Fl^+) shows interesting results. Bis-flavinium perchlorates (0.5 mol %) linked with a methylene spacer at the N10-position exhibit high catalytic activities, and kinetic studies reveal that the reaction rates are dependent on the spacer length of the catalysts due to their specific intramolecular electrochemical behaviors. The mechanism involves the reaction of flavinium cation with hydrogen peroxide to give an active flavinium hydroperoxy species, which undergoes oxygen transfer to substrates and subsequent rate-determining dehydration of hydroxyflavin to regenerate cation (Scheme 139).[380] Moreover, amphiphilic flavinium perchlorate (1−2 mol %) solubilized in micelles catalyzes the oxidation of thioanisole to its corresponding sulfoxide. Reaction rates are strongly dependent on the type of micellar matrix and on the pH value but often exceed those of the reactions catalyzed by hydrophilic flavinium perchlorates.[381]

Finally the synthesis of pyrylium ions by oxygen insertion in cyclopentadienes via silver reduction is another example, but it will be discussed in section 9.6, among organic perchlorate salt preparations.

9.4. Carbonyl Activation

The Lewis acid power of perchlorates can be easily exploited in reactions involving carbonyl derivatives. Examples are the Michael additions reported in section 4, protection and deprotection reactions described in section 6.2, and most of the polar ring closures described in section 8. However some simple activations of carbonyl compounds remain excluded from these categories, and they will be collected here. Two main reaction families can be recognized: addition to the carbonyl double bond and activation of the α-position.

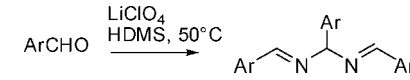
Among the former reactions, a variation of the three-component synthesis of primary α-amino phosphonates reported in section 9.1 should be mentioned.[350] In fact, in the absence of the third component (trialkylphosphite), at 50 °C, solid $LiClO_4$ promoted diimine formation from aldehydes and excess HMDS in 85−94% yields (Scheme 140).[350]

A stereoselective metal-catalyzed intramolecular Canizzaro reaction can be properly mentioned as another example of addition to the carbonyl double bond.[382] This transformation results in the production of synthetically useful α-hydroxy esters from readily available glyoxals under neutral conditions. Of the 20 metal complexes examined by the authors, $Cu(ClO_4)_2 \cdot 6H_2O$, $Cu(OTf)_2$, and $Cr(ClO_4)_3 \cdot 6H_2O$ give the highest levels of reactivity, whereas perchlorates of Fe, Mg, Al, Li, and Y provide no product. In particular, $Cr(ClO_4)_3 \cdot 6H_2O$ exploits the reaction with isolated yields ranging from 40% to 84% (Scheme 141). The enantioselective reaction was attempted with $Cu(OTf)_2$ and **144**.

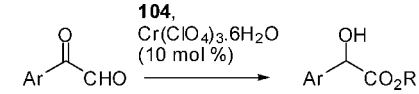
The cyanation reaction of carbonyl compounds is one of the most powerful procedures for the synthesis of polyfunctional molecules, and the synthesis of cyanohydrins is another typical acid-catalyzed carbonyl addition reaction. Both $HClO_4-SiO_2$ (0.6 mol %)[383] and stoichiometric solid $LiClO_4$[384] act as highly effective catalysts (88−98% and 90−100% yields, respectively) for cyanation of various aldehydes to the corresponding *O*-trimethylsilyl cyanohydrins with trimethylsilylcyanide. Actually, only $LiClO_4$ catalysis can be efficiently extended to ketones (85−98%) (Scheme 142).[384]

Allylation reactions of carbonyl compounds, which afford homoallylic alcohols, are a subject of extensive investigation in organic chemistry. The development of easily handled allylation reactions has attracted great attention, and allyltributyltin is often used for this reason. However this reagent requires activation of the carbonyl, and cadmium perchlorate

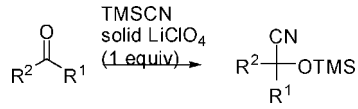
Scheme 140



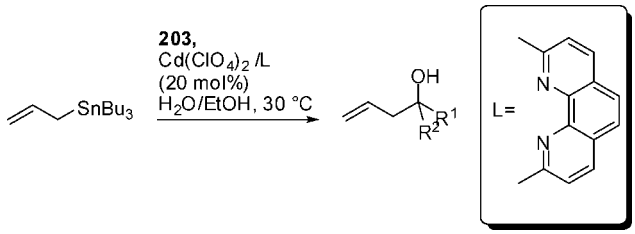
Scheme 141



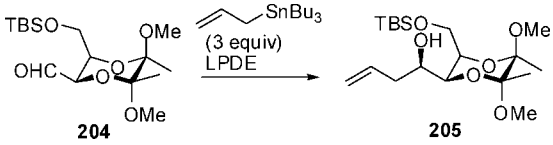
Scheme 142



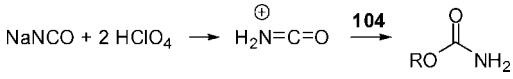
Scheme 143



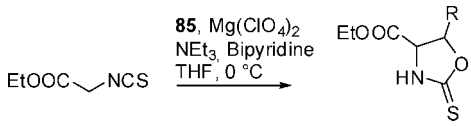
Scheme 144



Scheme 145



Scheme 146



is found to very efficiently catalyze allylation reactions in aqueous media especially in the presence of nitrogen ligands. This accelerated catalytic system gives allylation products of various aldehydes and ketones in 86−98% yields (Scheme 143).[385]

Moreover, in a step of the synthesis of the polyhydroxylated macrolactone (+)-aspicilin, allyltributyltin is added to equatorially disposed carboxaldehyde **204** in the presence of LPDE to lead to the two diastereomers in a ratio of 9:1, and the major diastereomer **205** is isolated in 70% yield after workup (Scheme 144).[386]

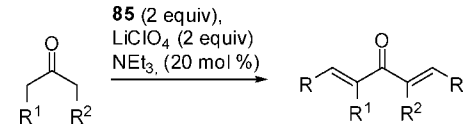
A particular example of addition to a carbonyl double bond is the synthesis of carbamates, widely used nowadays in many chemical fields. In the presence of $HClO_4-SiO_2$, various alcohols and phenols add to sodium cyanate with high efficiency (58−83% yields). The reaction mechanism involves double protonation of sodium cyanate with $HClO_4$, followed by nucleophilic attack of the alcohol (**104**) carbon on the protonated isocyanic acid intermediate (Scheme 145).[387]

Examples of activation of the α-position of the C=O double bond are also very frequent, that is, reaction where the perchlorate Lewis acid favors the keto−enol tautomerism.

Among them, the combination of NEt_3 (20 mol %), $Mg(ClO_4)_2$ (10 mol %), and bipyridine (10 mol %) generates a catalyst system for the efficient addition of a range of aromatic aldehydes to ethyl isothiocyanatoacetate, to form protected β-hydroxy α-amino acids in 67−89% yield with *syn*/*anti* selectivity ranging from 3:2 to 3:1 (Scheme 146).[388]

The cross-aldol condensation is another typical example of activation of carbonyl α-position. In particular, the double

Scheme 147



cross-aldol condensation to prepare α,β-unsaturated carbonyl compounds is very important, since these compounds are useful intermediates for the preparation of many technological products and drugs. It is found that perchlorate in addition to an amine for aldehyde activation can be used as catalysts in these reactions. Stoichiometric amounts of solid $LiClO_4$ and triethylamine (10 mol %) allow double condensations of many aldehydes with acyclic and cyclic ketones except for oxygen-substituted derivatives. On the other hand, this method works even in the presence of enolizable aldehydes. Yields range from 45% to quantitative (Scheme 147).[389]

A particular example of this reaction is the double condensation of a variety of aromatic aldehydes with tetrahydrothiopyran-4-one in the presence of *N*-(trimethylsilyl)diethylamine as the aldehyde activator and LPDE at room temperature. 3,5-Bis(arylmethylidene)thiopyranones are achieved in a one-pot procedure with 92−97% yields.[390]

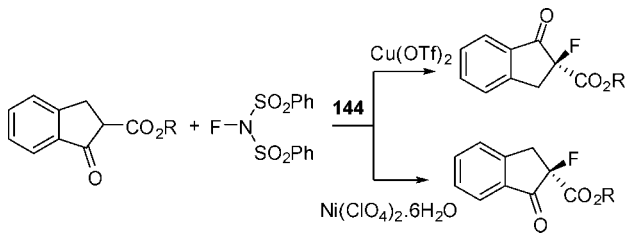
The classical Knoevenagel condensation can be considered an extension to a methylene active compound of the cross-aldol condensation and has been recently carried out in the presence of acid catalysis, in particular, $Mg(ClO_4)_2$[391] and $HClO_4-SiO_2$.[330]

The latter reaction has been already mentioned in section 8.3, Scheme 122 being part of the multistep synthesis of 1,8-dioxo-octahydroxanthenes. The former is a natural extension of our work already described in the same section (Schemes 106[304] and 107[305]). The use of $Mg(ClO_4)_2$ (10 mol %) and of $MgSO_4$ (20 mol %) as water scavenger allows the Knoevenagel condensation of aliphatic and aromatic aldehydes with β-diketones and β-ketoesters without any traces of byproduct in 55−88% yields. $Zn(ClO_4)_2 \cdot 6H_2O$ proved to be less effective and α,β-unsaturated compound gave not very satisfactory results (30%).

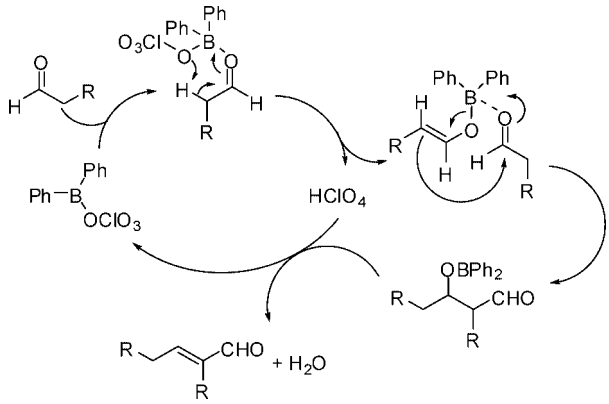
Another classical application of keto−enol tautomerism is the α-halogenations of carbonyl compounds. In this field, supported perchloric acid was found to be a highly efficient catalyst for the selective α-bromination of carbonyl compounds using NBS under mild and heterogeneous conditions.[392] Moreover, a catalytic enantioselective fluorination reaction using bis(oxazoline) **144** was also reported. The most significant outcome of this reaction is that the **144**/$Cu(OTf)_2$ complex provides the fluorination product with opposite configuration to the one obtained by the use of **144**/$Ni(ClO_4)_2$. Thus, the two enantiomers can be obtained by a simple change of the metal salt, although with relatively not very high enantioselectivity [up to 84% ee by Cu(II), and up to 93% ee by Ni(II)] (Scheme 148).[393]

Diphenylboron perchlorate (Ph_2BOClO_3) prepared from Ph_2BCl and $AgClO_4$, has a covalent character in the B−O bond, in contrast to the ionic character with trityl perchlorate. Therefore it is expected to possess peculiar catalytic activity. For example, Ph_2BOClO_3 catalyzed self- and cross-condensation reactions of aldehydes at room temperature in nitroethane (Scheme 149). Self-condensation yields range from 54% to 97%, while those of cross-condensation reactions of excess of aryl aldehydes and enolizable aldehydes range from 57% to 90%. Interestingly, butyraldehyde with benzaldehyde

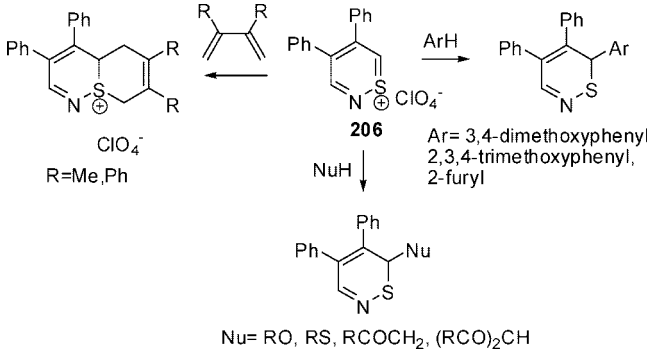
Scheme 148



Scheme 149



Scheme 150



affords 3-benzyloxy-2,2-dimethyl-3-phenylpropanoic acid in 69% yield. Its formation can be accounted for by intramolecular oxidation of the terminal aldehyde, that is, another example of intramolecular Cannizzaro reaction, as described at the start of this section.[394]

1,2-Thiazinylium perchlorate (**206**) can be considered as a thioketone from the point of view of its reactivity, and therefore its reactivity is described here. However, this compound can be seen as a dienophile in Diels−Alder reaction with dienes and as an electrophile in Friedel−Crafts alkylation, and references to this section are made in the proper sections of this review. The strong polar double bond allows the addition of various nucleophiles such as alcoholates, trimethylsilylenol ethers, sodium malonate and acetoacetate, and thiolates in 42−100% yield (Scheme 150). Addition is regioselective at the 6-position.[395]

Electron-rich aromatic compounds (di- and trimethoxybenzene and furan) are a particular class of nucleophiles that add to thiazinylium perchlorate (31−46% yield), and the reaction can be considered a Friedel−Crafts alkylation from the aromatic compound point of view.[395]

Moreover,[396] 2,3-dimethyl-, and 2,3-diphenylbutadiene and isoprene undergo [4 + 2^+] cycloaddition in 99%, 99%, and 84% yield, respectively. Isoprene gives a 98:2 mixture of regioisomers with prevalence of the 6-methyl isomer. According to frontier orbital calculations, experiments showed no cycloadduct across the N=S^+ bond.

9.5. Substitution Reactions

Some particular leaving groups can be substituted through perchlorate catalysis, often via transient alkylperchlorates. For example, treatment of benzyl halides with $AgClO_4$ and TMSCN in CH_2Cl_2 followed by cleavage of the carbon−silicon bond with aqueous $NaHCO_3$ or TBAF directly affords the corresponding isocyanides in 52−90% yields via the generation of the corresponding benzyl perchlorate. It should be noted that secondary benzyl isocyanides were converted to cyanide in the reaction medium as the reaction time became longer, owing to rearrangement of the isocyanic group due to the stability of the *sec*-benzyl cation.[397] Isonitriles are then intermediate for the synthesis of aminobenzofurans (see Scheme 100, section 8.2) through another perchlorate-catalyzed reaction.[164]

1-Aryl-3,3-(pentanediyl)triazenes (a stable synthetic equivalent of aryl diazonium salts) react with equimolecular amounts of $Zn(ClO_4)_2$ and $Zn(CN)_2$ in acetonitrile at reflux for 3 h to produce arylnitriles in 45−98% yields (Scheme 151). The reaction very likely involves aryl radicals rather than aryl cations.[398]

Finally, the hydroxy group of allylic alcohols can be replaced by enolates (introduced as silyl enol ethers) in the presence of a catalytic amount of $[Ir(cod)(PPh_3)_2]X$ activated by hydrogen. The anion part plays an important role to enhance the rate and product yields, the efficacy increasing in the order of $PF_6^- < ClO_4^- < TfO^-$.[399]

9.6. Synthesis of Salts

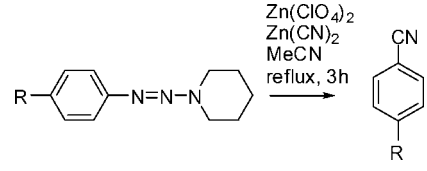
The stability of perchlorate anion allows the synthesis and the isolation of some organic cations. An example is compound **206**, whose multistep preparation is reported.[395,396]

Pyrylium cations by insertion of an oxygen atom into the cyclopentadiene ring can be obtained from phenyl-substituted cyclopentadienes in the presence of $AgClO_4$. A reasonable mechanistic explanation for this reaction involves a sequential process, starting from the action of the silver ion with the double bond of cyclopentadiene to the addition of a water molecule, ring-opening, rearrangement, cyclization, and oxidation to generate the final six-membered pyrylium ring and silver(0) (Scheme 152).[400]

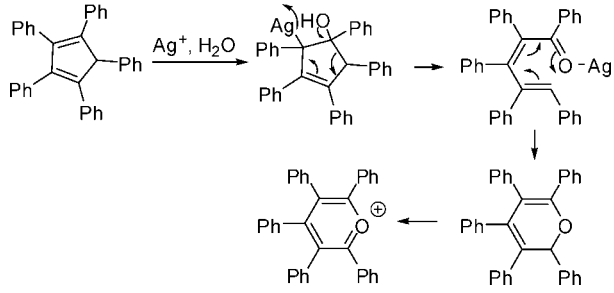
N,*N*-Disubstituted 2-aminothiophenes have been used for preparing different types of organic dyes, in particular, the deeply colored their methinium compounds. Nucleophilic addition of the 5-lithio derivative with many esters such as alkyl thiophene-2-carboxylates, oxalates, benzene di- and tricarboxylates, naphthalene 2,6-dicarboxylate, and biphenyl 4,4′-dicarboxylate, followed by reaction with perchloric acid, yields salts **207** in 23−88% (Scheme 153).[401]

An interesting explosive compound is "vinamidinium" bisperchlorate (**208**), whose differential scanning calorimetric analysis shows it to be quite shock sensitive, exploding at

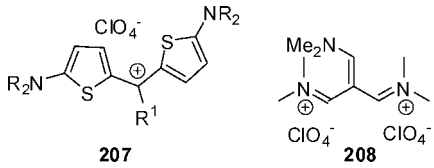
Scheme 151



Scheme 152



Scheme 153



an impact energy of 7 J, making it a higher energy material than trinitrotoluene.[402]

Many chiral pyridinium salts have been prepared by reaction of pyridine and chloromethyl-(−)-menthyl ether followed by anion exchange. Among them, the perchlorate derivative was characterized, and its antimicrobial activity was tested.[403]

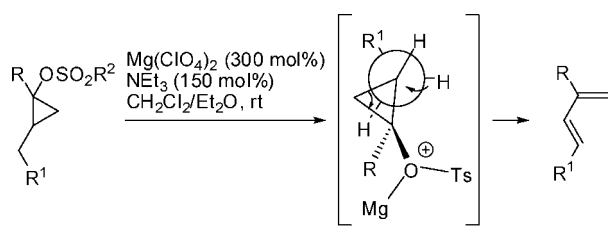
We already encountered thianthrenium perchlorate as benzyne precursor in section 8.3,[332] Moreover, calix[4]arenes having an electron-donating group at the lower rim react with thianthrenium radical perchlorate in CH_3CN at room temperature to give the corresponding thianthrenium perchlorates in 80−89% yields.[404]

9.7. Ring-Opening Reactions

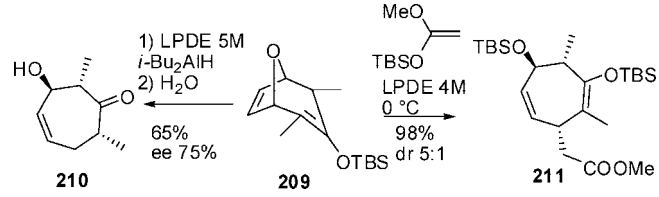
Sulfonates of *cis*-1,2-disubstituted cyclopropanols are converted into 2-substituted 1,3-alkadienes in 35−80% yields under the action of $Mg(ClO_4)_2$ and NEt_3. The stereochemical outcome in the reaction (that is, a high *trans*-stereoselectivity) is consistent with a concerted reaction mechanism involving cationic cyclopropyl−allyl isomerization accompanied by a deprotonation (Scheme 154).[405]

Oxabicyclo[3.2.1]octenes such as **209** can be opened at the bridgehead employing silyl ketene acetals[406] or hydrides[407] in 4.0−5.0 M LPDE to give rise to highly functionalized cycloheptadienes (**211**, Scheme 155) that can be further manipulated for use in natural product synthesis, for example, in the construction of the C(19)−C(27) fragment of rifamycin S or C(19)−C(26) and C(27)−C(32) fragments of scytophycin C, respectively. Moreover the reaction can be extended to other bicyclooctenes and silyl ketenes in 60−95% yield.[406]

Scheme 154



Scheme 155



10. Conclusion

This review provides a survey of the chemical literature on perchlorates and perchloric acid as reagents or catalysts for various organic reactions mainly in this century. Perchloric acid is potentially an explosive compound when it is heated and contacted with combustible materials. Therefore, it must be handled very cautiously, but absorption on silica gel produces great improvement in terms of handling, being inexpensive, nontoxic, available, and safe. The metal ions of perchlorates act as Lewis acids, and the Lewis acidity is dependent on the solvent basicity, since perchlorate ion has very low basicity. Perchlorate salts promote several synthetic transformations that are otherwise difficult to perform. Apart from the acceleration of the rate of the reaction, high chemo-, regio-, and stereoselectivities have been observed, as demonstrated by the many examples cited in the text. The reactions are generally carried out under very mild conditions, often at room temperature and under essentially neutral reaction and workup conditions.

11. Abbreviations

Bn	benzyl ($PhCH_2$)
Boc	*t*-butoxycarbonyl
Bz	benzoyl (PhC═O)
Cbz	benzyloxycarbonyl ($PhCH_2OC$═O)
Cp	cyclopentadienyl
DEAD	diethylazadicarboxylate
DCE	dichloroethane
R,*R*-DBFOX-Ph	(*R*,*R*)-4,6-dibenzofurandiyl-2,2′-bis(4-phenyloxazoline)
DMF	dimethylformamide
HMDS	hexamethyldisilazane [$(Me_3Si)_2NH$]
IDCP	iodonium dicollidinium perchlorate
IX	ion exchange
Le^A	Lewis A saccharide antigen
Le^x	Lewis X saccharide antigen
LPDE	5 M lithium perchlorate in diethyl ether
m-CPBA	3-chloroperbenzoic acid
MS	molecular sieves
MW	microwaves
NADH	reduced nicotinamide adenine dinucleotide
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
Npt	naphthyl
Ppyz	piperazine
RfD	reference dose
TBS	*tert*-butyldimethylsilyl (t-$C_4H_9Me_2Si$)
TBDPS	*tert*-butyldiphenylsilyl (t-$C_4H_9Ph_2Si$)
THP	tetrahydropyranyl
TMS	trimethylsilyl (Me_3Si)
TMP	2,2,6,6-tetramethylpiperidine
Tol	*p*-toluensolfonyl (4-$MeC_6H_4SO_2$)
Tr	trityl (Ph_3C)
Troc	2,2,2-trichloroethoxycarbonyl (CCl_3CH_2OC═O)
US EPA	United States Environmental Protection Agency

12. References

(1) von Stadion, F. *Gilbert's Ann. Phys.* **1816**, *52*, 197.
(2) Serullas, G. S. *Ann. Chim. Phys.* **1830**, *45*, 270.

(3) Serullas, G. S. *Ann. Chim. Phys.* **1830**, *45*, 297.
(4) Serullas, G. S. *Ann. Chim. Phys.* **1830**, *45*, 323.
(5) Roscoe, H. C. *Proc. R. Soc.* **1862**, *11*, 493.
(6) US EPA *External Review Draft*; National Center for Environmental Assessment, Office of Research and Development: Washington, DC 2002.
(7) Schilt, A. A. *Perchloric Acid and Perchlorates*; GFS Chemical Inc.: Powell, OH, 2003.
(8) Chakraborti, A. K.; Gulhane, R. *Chem. Commun.* **2003**, 1896.
(9) *Perchlorate Environmental Occurrence, Interactions and Treatment*; Springer: New York, 2006.
(10) Heravi, M. M.; Behbahani, F. K. *J. Iran. Chem. Soc.* **2007**, *4*, 375.
(11) Sankararaman, S.; Nesakumar, J. E. *Eur. J. Org. Chem.* **2000**, 2003.
(12) Heydari, A. *Tetrahedron* **2002**, *58*, 6777.
(13) Bartoli, G.; Locatelli, M.; Melchiorre, P.; Sambri, L. *Eur. J. Org. Chem.* **2007**, 2037.
(14) Long, J. R. *Chem. Health Saf.* **2002**, *9*, 12.
(15) Department of Toxic Substance Control CA. *Perchlorate*; State of California, 2007.
(16) Department of Toxic Substance Control CA. *Final Regulations Perchlorate Best Management Practices*; State of California, 2007.
(17) US EPA. Integrated Risk Information System:Washington, DC, 2005.
(18) Boldyrev, V. V. *Thermochim. Acta* **2006**, *443*, 1.
(19) Kelly, R. J. *Chem. Health Saf.* **2000**, *7*, 5.
(20) El-Awad, A. M.; Gabr, R. M.; Girgis, M. M. *Thermochim. Acta* **1991**, *184*, 205.
(21) www.sciencelab.com/xMSDS-Magnesium_perchlorate-9924555.
(22) Wikipedia the free encyclopedia, www.wikipedia.org, 2008.
(23) http://www.mallbaker.com/.
(24) http://www.sigmaaldrich.com.
(25) Ramamurthy, S.; Shrotri, P. G. *J. Energ. Mater.* **1996**, *14*, 97.
(26) Keenan, A. G.; Siegmund, R. F. *Quart. Rev.* **1969**, *23*, 430.
(27) Parker, D. R. *Environ. Chem.* **2009**, *6*, 10.
(28) Cai, Y. Q.; Shi, Y. L.; Zhang, P.; Mou, S. F.; Jiang, G. B. *Progr. Chem.* **2006**, *18*, 1554.
(29) Dasgupta, P. K.; Martinelango, P. K.; Jackson, W. A.; Anderson, T. A.; Tian, K.; Tock, R. W.; Rajagopalan, S. *Environ. Sci. Technol.* **2005**, *39*, 1569.
(30) Charnley, G. *Food Chem. Toxicol.* **2008**, *46*, 2307.
(31) NAS/NRC. *Health Implications of Perchlorate Ingestion*; The National Academies Press: Washington, DC, 2005.
(32) Logan, B. E. *Environ. Sci. Technol.* **2001**, *35*, 482A–487A.
(33) http://www.clu-in.org/contaminantfocus/default.focus/sec/perchlorate/cat/Overview.
(34) Urbansky, E. T. *Perchlorate in the Environment*; Plenum: New York, 2000.
(35) Stroo, H. F.; Ward, C. H., Eds. *In Situ Bioremediation of Perchlorate in Groundwater*; Springer: Berlin, 2009.
(36) Bansal, R.; Deobald, L.; Crawford, R.; Paszczynski, A. *Biodegradation* **2009**, *20*, 603.
(37) Böhm, G.; Waldmann, H. *Liebigs Ann.* **1996**, 613.
(38) Paulsen, H. *Angew. Chem., Int. Ed.* **1982**, *21*, 155.
(39) Mukaiyama, T.; Kobayashi, S.; Shoda, S.-i *Chem. Lett.* **1984**, *13*, 907.
(40) Mukaiyama, T.; Shimpuku, T.; Takashima, T.; Kobayashi, S. *Chem. Lett.* **1989**, *18*, 145.
(41) Shimomura, N.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2532.
(42) Matsumoto, T.; Maeta, H.; Suzuki, K.; Gen-ichi Tsuchihashi, l. *Tetrahedron Lett.* **1988**, *29*, 3575.
(43) Matsumoto, T.; Maeta, H.; Suzuki, K.; Tsuchihashi, l. G.-i. *Tetrahedron Lett.* **1988**, *29*, 3567.
(44) Suzuki, K.; Maeta, H.; Matsumoto, T.; Tsuchihashi, l. G.-i. *Tetrahedron Lett.* **1988**, *29*, 3571.
(45) Matsumoto, T.; Hosoya, T.; Suzuki, K. *Tetrahedron Lett.* **1990**, *31*, 4629.
(46) Mukaiyama, T.; Katsurada, M.; Takashima, T. *Chem. Lett.* **1991**, *20*, 985.
(47) Iimori, T.; Azumaya, I.; Shibazaki, T.; Ikegami, S. *Heterocycles* **1997**, *46*, 221.
(48) Uchiro, H.; Mukaiyama, T. *Chem. Lett.* **1996**, *25*, 79.
(49) Hachiya, I.; Kobayashi, S. *Tetrahedron Lett.* **1994**, *35*, 3319.
(50) Suzuki, K. *Pure Appl. Chem.* **1994**, *66*, 1557.
(51) Colinas, P. A.; Nunez, N. A.; Bravo, R. D. *J. Carbohydr. Chem.* **2008**, *27*, 141.
(52) Toshima, K. *Carbohydr. Res.* **2000**, *327*, 15.
(53) Mukaiyama, T.; Murai, Y.; Shoda, S.-i *Chem. Lett.* **1981**, *10*, 431.
(54) Mukaiyama, T.; Hashimoto, Y.; Shoda, S.-i *Chem. Lett.* **1983**, *12*, 935.
(55) Suzuki, K.; Maeta, H.; Matsumoto, T. *Tetrahedron Lett.* **1989**, *30*, 4853.
(56) Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1989**, *30*, 833.
(57) Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1988**, *29*, 6935.
(58) Maeta, H.; Matsumoto, T.; Suzuki, K. *Carbohydr. Res.* **1993**, *249*, 49.
(59) Kim, W.-S.; Hosono, S.; Sasai, H.; Shibasaki, M. *Tetrahedron Lett.* **1995**, *36*, 4443.
(60) Kim, W.-S.; Hosono, S.; Sasai, H.; Shibasaki, M. *Heterocycles* **1996**, *42*, 795.
(61) Kim, W.-S.; Sasai, H.; Shibasaki, M. *Tetrahedron Lett.* **1996**, *37*, 7797.
(62) Böhm, G.; Waldmann, H. *Liebigs Ann.* **1996**, 621.
(63) Schmid, U.; Waldmann, H. *Liebigs Ann.* **1997**, 2573.
(64) Grieco, P. A. *Aldrichimica Acta* **1991**, *24*, 59.
(65) Schmidt, R. R.; Behrendt, M.; Toepfer, A. *Synlett* **1990**, 694.
(66) Böhm, G.; Waldmann, H. *Tetrahedron Lett.* **1995**, *36*, 3843.
(67) Schmid, U.; Waldmann, H. *Chem.—Eur. J.* **1998**, *4*, 494.
(68) Waldmann, H.; Böhm, G.; Schmid, U.; Röttele, H. *Angew. Chem., Int. Ed.* **1994**, *33*, 1944.
(69) Mukhopadhyay, B.; Maurer, S. V.; Rudolph, N.; van Well, R. M.; Russell, D. A.; Field, R. A. *J. Org. Chem.* **2005**, *70*, 9059.
(70) Du, Y.; Wei, G.; Cheng, S.; Hua, Y.; Linhardt, R. J. *Tetrahedron Lett.* **2006**, *47*, 307.
(71) Veeneman, G. H.; van Leeuwen, S. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 1331.
(72) Mukhopadhyay, B.; Collet, B.; Field, R. A. *Tetrahedron Lett.* **2005**, *46*, 5923.
(73) Mukherjee, C.; Misra, A. K. *Synthesis* **2007**, 683.
(74) Misra, A. K.; Tiwari, P.; Madhusudan, S. K. *Carbohydr. Res.* **2005**, *340*, 325.
(75) Schene, H.; Waldmann, H. *Eur. J. Org. Chem.* **1998**, 1227.
(76) Bielawska, H.; Michalska, M. *Tetrahedron Lett.* **1998**, *39*, 9761.
(77) Yamanoi, T.; Fujioka, A.; Inazu, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1488.
(78) Yamanoi, T.; Inazu, T. *Chem. Lett.* **1990**, *19*, 849.
(79) Yamanoi, T.; Nakamura, K.; Sada, S.; Goto, M.; Furusawa, Y.; Takano, M.; Fujioka, A.; Yanagihara, K.; Satoh, Y.; Hosokawa, H.; Inazu, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2617.
(80) Yamanoi, T.; Nakamura, K.; Takeyama, H.; Yanagihara, K.; Inazu, T. *Chem. Lett.* **1993**, *22*, 343.
(81) Yamanoi, T.; Nakamura, K.; Takeyama, H.; Yanagihara, K.; Inazu, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1359.
(82) Yamanoi, T.; Oda, Y.; Matsuda, S.; Yamazaki, I.; Matsumura, K.; Katsuraya, K.; Watanabe, M.; Inazu, T. *Tetrahedron* **2006**, *62*, 10383.
(83) Inazu, T.; Hosokawa, H.; Satoh, Y. *Chem. Lett.* **1985**, *14*, 297.
(84) Inazu, T.; Yamanoi, T. *Chem. Lett.* **1989**, *18*, 69.
(85) Hayakawa, Y.; Kawai, R.; Hirata, A.; Sugimoto, J.-i.; Kataoka, M.; Sakakura, A.; Hirose, M.; Noyori, R. *J. Am. Chem. Soc.* **2001**, *123*, 8165.
(86) Schmid, U.; Waldmann, H. *Tetrahedron Lett.* **1996**, *37*, 3837.
(87) Petersen, L.; Jensen, K. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2175.
(88) Petersen, L.; Laursen, J. B.; Larsen, K.; Motawia, M. S.; Jensen, K. J. *Org. Lett.* **2003**, *5*, 1309.
(89) Laursen, J. B.; Petersen, L.; Jensen, K. J.; Nielsen, J. *Org. Biomol. Chem.* **2003**, *1*, 3147.
(90) Larsen, K.; Worm-Leonhard, K.; Olsen, P.; Hoel, A.; Jensen, K. J. *Org. Biomol. Chem.* **2005**, *3*, 3966.
(91) Grathe, S.; Thygesen, M. B.; Larsen, K.; Petersen, L.; Jensen, K. J. *Tetrahedron: Asymmetry* **2005**, *16*, 1439.
(92) Worm-Leonhard, K.; Larsen, K.; Jensen, K. J. *J. Carbohydr. Chem.* **2007**, *26*, 349.
(93) López, J. C.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1992**, 94.
(94) Byerley, A. L. J.; Kenwright, A. M.; Lehmann, C. W.; MacBride, J. A. H.; Steel, P. G. *J. Org. Chem.* **1998**, *63*, 193.
(95) Boga, S. B.; Balasubramanian, K. K. *ARKIVOC* **2004**, *viii*, 87.
(96) Tiwari, P.; Agnihotri, G.; Misra, A. K. *Carbohydr. Res.* **2005**, *340*, 749.
(97) Agarwal, A.; Rani, S.; Vankar, Y. D. *J. Org. Chem.* **2004**, *69*, 6137.
(98) Misra, A. K.; Tiwari, P.; Agnihotri, G. *Synthesis* **2005**, 260.
(99) Colinas, P. A.; Bravo, R. D. *Carbohydr. Res.* **2007**, *342*, 2297.
(100) Kamble, V. T.; Bandgar, B. P.; Khobragade, C. N.; Gacche, R. N.; Kamble, V. A. *Lett. Org. Chem.* **2006**, *3*, 658.
(101) Pelzer, S.; Kauf, T.; van Wüllen, C.; Christoffers, J. *J. Organomet. Chem.* **2003**, *684*, 308.
(102) Saidi, M. R.; Azizi, N.; Akbari, E.; Ebrahimi, F. *J. Mol. Catal. A: Chem.* **2008**, *292*, 44.
(103) Itoh, K.; Hasegawa, M.; Tanaka, J.; Kanemasa, S. *Org. Lett.* **2005**, *7*, 979.
(104) Itoh, K.; Kanemasa, S. *Tetrahedron Lett.* **2003**, *44*, 1799.
(105) Itoh, K.; Oderaotoshi, Y.; Kanemasa, S. *Tetrahedron: Asymmetry* **2003**, *14*, 635.
(106) Yanagita, H.; Kodama, K.; Kanemasa, S. *Tetrahedron Lett.* **2006**, *47*, 9353.

(107) Itoh, K.; Kanemasa, S. *J. Am. Chem. Soc.* **2002**, *124*, 13394.
(108) Shi, M.; Zhang, W. *Adv. Synth. Catal.* **2005**, *347*, 535.
(109) Saidi, M. R.; Brown, R. S.; Rajabi, F. *J. Iran. Chem. Soc.* **2005**, *2*, 300.
(110) Suga, H.; Kitamura, T.; Kakehi, A.; Baba, T. *Chem. Commun.* **2004**, 1414.
(111) Das, B.; Majhi, A.; Banerjee, J. *Tetrahedron Lett.* **2006**, *47*, 7619.
(112) Khan, A. T.; Ghosh, S.; Choudhury, L. H. *Eur. J. Org. Chem.* **2006**, 2226.
(113) Khatik, G. L.; Sharma, G.; Kumar, R.; Chakraborti, A. K. *Tetrahedron* **2007**, *63*, 1200.
(114) Rajabi, F.; Saidi, M. R. *J. Sulfur Chem.* **2005**, *26*, 251.
(115) Ziyaei-Halimjani, A.; Saidi, M. R. *J. Sulfur Chem.* **2005**, *26*, 149.
(116) Garg, S. K.; Kumar, R.; Chakraborti, A. K. *Synlett* **2005**, 1370.
(117) Kanemasa, S.; Oderaotoshi, Y.; Wada, E. *J. Am. Chem. Soc.* **1999**, *121*, 8675.
(118) Mukherjee, C.; Misra, A. K. *Lett. Org. Chem.* **2007**, *4*, 54.
(119) Singh, S. P.; Kumar, T. V.; Chandrasekharam, M.; Giribabu, L.; Reddy, P. Y. *Synth. Commun.* **2009**, *39*, 3982.
(120) Azizi, N.; Saidi, M. R. *Tetrahedron* **2004**, *60*, 383.
(121) Kobayashi, S.; Kakumoto, K.; Sugiura, M. *Org. Lett.* **2002**, *4*, 1319.
(122) Saidia, M. R.; Browna, R. S.; Rajabi, F. *J. Iran. Chem. Soc.* **2005**, *2*, 300.
(123) Nakama, K.; Seki, S.; Kanemasa, S. *Tetrahedron Lett.* **2002**, *43*, 829.
(124) Sibi, M. P.; Liu, M. *Org. Lett.* **2001**, *3*, 4181.
(125) Sibi, M. P.; Soeta, T. *J. Am. Chem. Soc.* **2007**, *129*, 4522.
(126) Azizi, N.; Saidi, M. R. *Tetrahedron Lett.* **2002**, *43*, 4305.
(127) Iserloh, U.; Curran, D. P.; Kanemasa, S. *Tetrahedron: Asymmetry* **1999**, *10*, 2417.
(128) Sibi, M. P.; Asano, Y.; Sausker, J. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 1293.
(129) He, L.; Srikanth, G. S. C.; Castle, S. L. *J. Org. Chem.* **2005**, *70*, 8140.
(130) Sibi, M. P.; Petrovic, G.; Zimmerman, J. *J. Am. Chem. Soc.* **2005**, *127*, 2390.
(131) Mukaiyama, T.; Ohno, T.; Nishimura, T.; Suda, S.; Kobayashi, S. *Chem. Lett.* **1991**, *20*, 1059.
(132) Mukaiyama, T.; Suzuki, K. *Chem. Lett.* **1992**, *21*, 1751.
(133) Suzuki, K.; Kitagawa, H.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3729.
(134) Arai, S.; Sudo, Y.; Nishida, A. *Tetrahedron* **2005**, *61*, 4639.
(135) Kawada, A.; Mitamura, S.; Matsuo, J.-i.; Tsuchiya, T.; Kobayashi, S. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2325.
(136) Mukaiyama, T.; Suzuki, K.; Han, J. S.; Kobayashi, S. *Chem. Lett.* **1992**, *21*, 435.
(137) Hachiya, I.; Moriwaki, M.; Kobayashi, S. *Tetrahedron Lett.* **1995**, *36*, 409.
(138) Hachiya, I.; Moriwaki, M.; Kobayashi, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2053.
(139) Kawada, A.; Mitamura, S.; Kobayashi, S. *Chem. Commun.* **1996**, 183.
(140) Kobayashi, S.; Komoto, I. *Tetrahedron* **2000**, *56*, 6463.
(141) Poupaert, J. H.; Depreux, P.; McCurdy, C. R. *Monatsh. Chem.* **2003**, *134*, 823.
(142) Kobayashi, S.; Komoto, I.; Matsuo, J.-i *Adv. Synth. Catal.* **2001**, *343*, 71.
(143) Chapman, C. J.; Frost, C. G.; Hartley, J. P.; Whittle, A. J. *Tetrahedron Lett.* **2001**, *42*, 773.
(144) Bartoli, G.; De Nino, A.; Dalpozzo, R.; Maiuolo, L.; Nardi, M.; Procopio, A.; Tagarelli, A. *Lett. Org. Chem.* **2001**, *2*, 51.
(145) Bartoli, G.; Bosco, M.; Marcantoni, E.; Massaccesi, M.; Rinaldi, S.; Sambri, L. *Tetrahedron Lett.* **2002**, *43*, 6331.
(146) Kim, J. K.; Kim, Y. H.; Nam, H. T.; Kim, B. T.; Heo, J. N. *Org. Lett.* **2008**, *10*, 3543.
(147) Berkes, D.; Jakubec, P.; Winklerova, D.; Povazanec, F.; Daich, A. *Org. Biomol. Chem.* **2007**, *5*, 121.
(148) Bandgar, B. P.; Kamble, V. T.; Sadavarte, V. S.; Uppalla, L. S. *Synlett* **2002**, 735.
(149) Bandgar, B. P.; Kamble, V. T.; Bavikar, S. N. *J. Chem. Res. S* **2003**, 287.
(150) Bandgar, B. P.; Kamble, V. T.; Fulse, D. B.; Deshmukh, M. V. *New J. Chem.* **2002**, *26*, 1105.
(151) Zaltsgendler, I.; Leblanc, Y.; Bernstein, M. A. *Tetrahedron Lett.* **1993**, *34*, 2441.
(152) Kinart, W. J.; Kinart, C. M.; Tran, Q. T.; Oszczeda, R.; Nazarski, R. B. *Appl. Organomet. Chem.* **2004**, *18*, 398.
(153) Kinart, W. J.; Kinart, C. M. *J. Organomet. Chem.* **2003**, *665*, 233.
(154) Kinart, W. J.; Kinart, C. M.; Tran, Q. T.; Oszczeda, R. *Appl. Organomet. Chem.* **2005**, *19*, 147.
(155) Kinart, W. J.; Kinart, C. M. *J. Organomet. Chem.* **2006**, *691*, 1441.
(156) Cativiela, C.; Fraile, J. M.; García, J. I.; Lafuente, G.; Mayoral, J. A.; Tahir, R.; Pallarés, A. *J. Catal.* **2004**, *226*, 192.
(157) De Castro, K. A.; Rhee, H. *Synthesis* **2008**, 1841.
(158) Maheswara, M.; Siddaiah, V.; Damu, G. L. V.; Rao, Y. K.; Rao, C. V. *J. Mol. Catal. A: Chem.* **2006**, *255*, 49.
(159) Nagarajan, R.; Perumal, P. T. *Synth. Commun.* **2002**, *32*, 105.
(160) Kamble, V. T.; Kadam, K. R.; Joshi, N. S.; Muley, D. B. *Catal. Commun.* **2007**, *8*, 498.
(161) Yadav, J. S.; Subba Reddy, B. V.; Murthy, C. V. S. R.; Mahesh Kumar, G.; Madan, C. *Synthesis* **2001**, 783.
(162) Li, D. P.; Guo, Y. C.; Ding, Y.; Xiao, W. J. *Chem. Commun.* **2006**, 799.
(163) Zhou, J.; Tang, Y. *J. Am. Chem. Soc.* **2002**, *124*, 9030.
(164) Kaïm, L. E.; Grimaud, L.; Oble, J. *Org. Biomol. Chem.* **2006**, *4*, 3410.
(165) Kim, S.; Kitano, Y.; Tada, M.; Chiba, K. *Tetrahedron Lett.* **2000**, *41*, 7079.
(166) Kumar, A.; Sharma, S.; Maurya, R. A. *Tetrahedron Lett.* **2009**, *50*, 5937.
(167) Mahdavinia, G. H.; Bigdeli, M. A.; Heravi, M. M. *Chin. Chem. Lett.* **2008**, *19*, 1171.
(168) Khodaei, M. M.; Khosropour, A. R.; Moghanian, H. *Synlett* **2006**, 916.
(169) Das, B.; Kumar, D. N.; Laxminarayana, K.; Ravikanth, B. *Helv. Chim. Acta* **2007**, *90*, 1330.
(170) Bigdeli, M. A.; Heravi, M. M.; Mahdavinia, G. H. *J. Mol. Catal. A: Chem.* **2007**, *275*, 25.
(171) Shaterian, H. R.; Yarahmadi, H.; Ghashang, M. *Tetrahedron* **2008**, *64*, 1263.
(172) Saidi, M. R.; Azizi, N. *Tetrahedron: Asymmetry* **2003**, *14*, 389.
(173) Saidi, M. R.; Azizi, N.; Naimi-Jamal, M. R. *Tetrahedron Lett.* **2001**, *42*, 8111.
(174) Goldberg, Y.; Alper, H. *J. Org. Chem.* **1993**, *58*, 3072.
(175) Bagheri, M.; Azizi, N.; Saidi, M. R. *Can. J. Chem.* **2005**, *83*, 146.
(176) Pearson, W. H.; Hutta, D. A.; Fang, W.-k. *J. Org. Chem.* **2000**, *65*, 8326.
(177) Chakraborti, A. K.; Sharma, L.; Gulhane, R. *Tetrahedron* **2003**, *59*, 7661.
(178) Rajesh, G.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2007**, *264*, 208.
(179) Bartoli, G.; Bosco, M.; Dalpozzo, R.; Marcantoni, E.; Massaccesi, M.; Sambri, L. *Eur. J. Org. Chem.* **2003**, 4611.
(180) Bartoli, G.; Bosco, M.; Dalpozzo, R.; Marcantoni, E.; Massaccesi, M.; Rinaldi, S.; Sambri, L. *Synlett* **2003**, 39.
(181) Chakraborti, A. K.; Gulhane, R. *Synlett* **2003**, 1805.
(182) Nakae, Y.; Kusaki, I.; Sato, T. *Synlett* **2001**, 1584.
(183) Jeyakumar, K.; Chand, D. K. *J. Mol. Catal. A: Chem.* **2006**, *255*, 275.
(184) Heravi, M. M.; Behbahani, F. K.; Hekmat Shoar, R.; Oskooie, H. A. *Catal. Commun.* **2006**, *7*, 136.
(185) Misra, A. K.; Tiwari, P.; Madhusudan, S. K. *Carbohydr. Res.* **2005**, *340*, 325.
(186) Lu, K.-C.; Hsieh, S.-Y.; Patkar, L. N.; Chen, C.-T.; Lin, C.-C. *Tetrahedron* **2004**, *60*, 8967.
(187) Binch, H.; Stangier, K.; Thiem, J. *Carbohydr. Res.* **1998**, *306*, 409.
(188) Tiwari, P.; Misra, A. K. *Tetrahedron Lett.* **2006**, *47*, 3573.
(189) Clapham, B.; Lee, S.-H.; Koch, G.; Zimmermann, J.; Janda, K. D. *Tetrahedron Lett.* **2002**, *43*, 5407.
(190) Goossen, L.; Döhring, A. *Adv. Synth. Catal.* **2003**, *345*, 943.
(191) Bartoli, G.; Bosco, M.; Carlone, A.; Dalpozzo, R.; Marcantoni, E.; Melchiorre, P.; Sambri, L. *Synthesis* **2007**, 3489.
(192) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Marcantoni, E.; Melchiorre, P.; Palazzi, P.; Sambri, L. *Eur. J. Org. Chem.* **2006**, 4429.
(193) Mukaiyama, T.; Shiina, I.; Miyashita, M. *Chem. Lett.* **1992**, *21*, 625.
(194) Mukaiyama, T.; Izumi, J.; Miyashita, M.; Shiina, I. *Chem. Lett.* **1993**, *22*, 907.
(195) Shiina, I.; Miyoshi, S.; Miyashita, M.; Mukaiyama, T. *Chem. Lett.* **1994**, *23*, 515.
(196) Shiina, I.; Mukaiyama, T. *Chem. Lett.* **1994**, *23*, 677.
(197) Shiina, I. *Tetrahedron* **2004**, *60*, 1587.
(198) Bartoli, G.; Boeglin, J.; Bosco, M.; Locatelli, M.; Massaccesi, M.; Melchiorre, P.; Sambri, L. *Adv. Synth. Catal.* **2005**, *347*, 33.
(199) Chakraborti, A. K.; Singh, B.; Chankeshwara, S. V.; Patel, A. R. *J. Org. Chem.* **2009**, *74*, 5967.
(200) Yoo, W.-J.; Li, C.-J. *Tetrahedron Lett.* **2007**, *48*, 1033.
(201) Bandgar, B. P.; Sadavarte, V. S.; Uppalla, L. S. *Synlett* **2001**, 1338.
(202) Heravi, M. M.; Behbahani, F. K.; Shoar, R. H.; Oskooie, H. A. *J. Mol. Catal. A: Chem.* **2006**, *244*, 8.
(203) Heravi, M. M.; Behbahani, F. K.; Oskooie, H. A.; Hekmat Shoar, R. *Tetrahedron Lett.* **2005**, *46*, 2543.
(204) Babu, B. S.; Balasubramanian, K. K. *Tetrahedron Lett.* **1998**, *39*, 9287.
(205) Khan, A. T.; Parvin, T.; Choudhury, L. H. *Synthesis* **2006**, 2497.
(206) Yamanaka, D.; Matsunaga, S.; Kawamura, Y.; Hosokawa, T. *Tetrahedron Lett.* **2008**, *49*, 53.

(207) Salehi, P.; Iranpoor, N.; Kargar Behbahani, F. *Tetrahedron* **1998**, *54*, 943.
(208) Behbahani, F.; Heravi, M.; Oskooie, H. *Monatsh. Chem.* **2009**, *140*, 181.
(209) Takaç, S.; San, F. G. B.; Kavdır, E. *React. Kinet. Catal. Lett.* **2005**, *85*, 291.
(210) Bartoli, G.; Bosco, M.; Locatelli, M.; Marcantoni, E.; Melchiorre, P.; Sambri, L. *Org. Lett.* **2005**, *7*, 427.
(211) Bartoli, G.; Bosco, M.; Carlone, A.; Dalpozzo, R.; Locatelli, M.; Melchiorre, P.; Sambri, L. *J. Org. Chem.* **2006**, *71*, 9580.
(212) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Marcantoni, E.; Melchiorre, P.; Sambri, L. *Adv. Synth. Catal.* **2006**, *348*, 905.
(213) Azizi, N.; Saidi, M. R. *Organometallics* **2004**, *23*, 1457.
(214) Azizi, N.; Yousefi, R.; Saidi, M. R. *J. Organomet. Chem.* **2006**, *691*, 817.
(215) Shaterian, H. R.; Shahrekipoor, F.; Ghashang, M. *J. Mol. Catal. A: Chem.* **2007**, *272*, 142.
(216) Shaterian, H. R.; Khorami, F.; Amirzadeh, A.; Ghashang, M. *Phosphorus, Sulfur Silicon Relat. Elem.* **2008**, *183*, 2865.
(217) Agarwal, A.; Vankar, Y. D. *Carbohydr. Res.* **2005**, *340*, 1661.
(218) Kumar, R.; Kumar, D.; Chakraborti, A. K. *Synthesis* **2007**, 299.
(219) Mukhopadhyay, B.; Russell, D. A.; Field, R. A. *Carbohydr. Res.* **2005**, *340*, 1075.
(220) Agnihotri, G.; Misra, A. K. *Tetrahedron Lett.* **2006**, *47*, 3653.
(221) Mondal, E.; Sahu, P. R.; Khan, A. T. *Synlett* **2002**, 463.
(222) Rudrawar, S.; Besra, R. C.; Chakraborti, A. K. *Synthesis* **2006**, 2767.
(223) Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Procopio, A.; Russo, B.; Tagarelli, A. *ARKIVOC* **2006**, *vi*, 181.
(224) Kensler, J. D. L.; Kohn, G. K.; Walgenbach, D. D. Br. Patent 1,382,010, 1975.
(225) Marshall, J. A.; Wuts, P. G. M. *J. Org. Chem.* **1977**, *42*, 1794.
(226) Ziyaei, A.; Azizi, N.; Saidi, M. R. *J. Mol. Catal. A: Chem.* **2005**, *238*, 138.
(227) Khan, A. T.; Choudhury, L. H.; Ghosh, S. *J. Mol. Catal. A: Chem.* **2006**, *255*, 230.
(228) Kumar, R.; Tiwari, P.; Maulik, P. R.; Misra, A. K. *J. Mol. Catal. A: Chem.* **2006**, *247*, 27.
(229) Kamble, V. T.; Jamode, V. S.; Joshi, N. S.; Biradar, A. V.; Deshmukh, R. Y. *Tetrahedron Lett.* **2006**, *47*, 5573.
(230) Kumar, R.; Thilagavathi, R.; Gulhane, R.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2006**, *250*, 226.
(231) Yang, S. T. *J. Chem. Res. S* **2006**, 199.
(232) Das, B.; Laxminarayana, K.; Ravikanth, B. *J. Mol. Catal. A: Chem.* **2007**, *271*, 131.
(233) Das, B.; Venkateswarlu, K.; Majhi, A.; Reddy, M. R.; Reddy, K. N.; Rao, Y. K.; Ravikumar, K.; Sridhar, B. *J. Mol. Catal. A: Chem.* **2006**, *246*, 276.
(234) Bartoli, G.; Bosco, M.; Locatelli, M.; Marcantoni, E.; Melchiorre, P.; Sambri, L. *Synlett* **2004**, 239.
(235) Dalpozzo, R.; De Nino, A.; Nardi, M.; Russo, B.; Procopio, A. *Synthesis* **2006**, 1127.
(236) Chakraborti, A. K.; Bhagat, S.; Rudrawar, S. *Tetrahedron Lett.* **2004**, *45*, 7641.
(237) Ganguly, N. C.; Barik, S. K. *Synthesis* **2008**, 425.
(238) Oskooie, H. A.; Heravi, M. M.; Sadnia, A.; Safarzadegan, M.; Behbahani, F. K. *Mendeleev Commun.* **2007**, *17*, 190.
(239) Ipaktschi, J.; Halimehjani, A. Z.; Saidi, M. R. *Organometallics* **2007**, *26*, 201.
(240) Bartoli, G.; Bosco, M.; Locatelli, M.; Marcantoni, E.; Massaccesi, M.; Melchiorre, P.; Sambri, L. *Synlett* **2004**, 1794.
(241) Heydari, A.; Hosseini; Seyed, E. *Adv. Synth. Catal.* **2005**, *347*, 1929.
(242) Chakraborti, A. K.; Chankeshwara, S. V. *Org. Biomol. Chem.* **2006**, *4*, 2769.
(243) Voitekhovich, S. V.; Gaponik, P. N.; Lyakhov, A. S.; Ivashkevich, O. A. *Tetrahedron* **2008**, *64*, 8721.
(244) Wu, L. Q.; Yang, C. G.; Zhang, C.; Yang, L. M. *Lett. Org. Chem.* **2009**, *6*, 234.
(245) Wildemann, D.; Drewello, M.; Fischer, G.; Schutkowski, M. *Chem. Commun.* **1999**, 1809.
(246) Anderson, A. M.; Blazek, J. M.; Garg, P.; Payne, B. J.; Mohan, R. S. *Tetrahedron Lett.* **2000**, *41*, 1527.
(247) Azizi, N.; Saidi, M. R. *Tetrahedron Lett.* **2003**, *44*, 7933.
(248) Bernard, A. M.; Frongia, A.; Piras, P. P.; Secci, F. *Org. Lett.* **2003**, *5*, 2923.
(249) Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2007**, *263*, 137.
(250) Pujala, B.; Chakraborti, A. K. *J. Org. Chem.* **2007**, *72*, 3713.
(251) Maheswara, M.; Rao, K. S. V. K.; Do, J. Y. *Tetrahedron Lett.* **2008**, *49*, 1795.
(252) Schoffers, E.; Tran, S. D.; Mace, K. *Heterocycles* **2003**, *60*, 769.
(253) Chini, M.; Crotti, P.; Favero, L.; Pineschi, M. *Tetrahedron Lett.* **1991**, *32*, 7583.
(254) Chini, M.; Crotti, P.; Macchia, F. *J. Org. Chem.* **1991**, *56*, 5939.
(255) Azizi, N.; Saidi, M. R. *Can. J. Chem.* **2005**, *83*, 505.
(256) Azizi, N.; Saidi, M. R. *Catal. Commun.* **2006**, *7*, 224.
(257) Azizi, N.; Mirmashhori, B.; Saidi, M. R. *Catal. Commun.* **2007**, *8*, 2198.
(258) Mirmashhori, B.; Azizi, N.; Saidi, M. R. *J. Mol. Catal. A: Chem.* **2006**, *247*, 159.
(259) Heydari, A.; Mehrdad, M.; Maleki, A.; Ahmadi, N. *Synthesis* **2004**, 1563.
(260) Reddy, K. S.; Solà, L.; Moyano, A.; Pericàs, M. A.; Riera, A. *Synthesis* **2000**, 165.
(261) Yadav, J. S.; Reddy, B. V. S.; Shesha Rao, M.; Reddy, P. N. *Tetrahedron Lett.* **2003**, *44*, 5275.
(262) Yadav, J. S.; Reddy, B. V. S.; Baishya, G.; Venkatram Reddy, P.; Narsaiah, A. V. *Catal. Commun.* **2006**, *7*, 807.
(263) Yadav, J. S.; Subba Reddy, B. V.; Parimala, G.; Venkatram Reddy, P. *Synthesis* **2002**, 2383.
(264) Yadav, J. S.; Reddy, B. V. S.; Jyothirmai, B.; Murty, M. S. R. *Synlett* **2002**, 53.
(265) Yadav, J. S.; Reddy, B. V. S.; Jyothirmai, B.; Murty, M. S. R. *Tetrahedron Lett.* **2005**, *46*, 6385.
(266) Nishikawa, T.; Kajii, S.; Wada, K.; Ishikawa, M.; Isobe, M. *Synthesis* **2002**, 1658.
(267) Nishikawa, T.; Ishikawa, M.; Wada, K.; Isobe, M. *Synlett* **2001**, 945.
(268) Gruttadauria, M.; Aprile, C.; D'Anna, F.; Lo Meo, P.; Riela, S.; Noto, R. *Tetrahedron* **2001**, *57*, 6815.
(269) Gruttadauria, M.; Lo Meo, P.; Noto, R. *Tetrahedron* **2001**, *57*, 1819.
(270) Braun, R.; Sauer, J. *Chem. Ber.* **1986**, *119*, 1269.
(271) Zou, J.; Mariano, P. S. *Photochem. Photobiol. Sci.* **2008**, *7*, 393.
(272) France, S.; Wack, H.; Hafez, A. M.; Taggi, A. E.; Witsil, D. R.; Lectka, T. *Org. Lett.* **2002**, *4*, 1603.
(273) Kinugasa, M.; Hashimoto, S. *J. Chem. Soc., Chem. Commun.* **1972**, 466.
(274) Ye, M.-C.; Zhou, J.; Tang, Y. *J. Org. Chem.* **2006**, *71*, 3576.
(275) Saito, M.; Saito, A.; Ishikawa, Y.; Yoshioka, M. *Org. Lett.* **2005**, *7*, 3139.
(276) Kantevari, S.; Vuppalapati, S. V. N.; Biradar, D. O.; Nagarapu, L. *J. Mol. Catal. A: Chem.* **2007**, *266*, 109.
(277) Demir, A. S.; Emrullahoglu, M. *Tetrahedron* **2006**, *62*, 1452.
(278) Demir, A. S.; Tural, S. *Tetrahedron* **2007**, *63*, 4156.
(279) Hayashi, S.; Mori, A.; Nishina, M.; Sumimoto, M.; Hori, K.; Yamamoto, H. *J. Chem. Res. S* **2007**, 394.
(280) Yamamoto, H.; Hayashi, S.; Kubo, M.; Harada, M.; Hasegawa, M.; Noguchi, M.; Sumimoto, M.; Hori, K. *Eur. J. Org. Chem.* **2007**, 2859.
(281) Sibi, M. P.; Itoh, K.; Jasperse, C. P. *J. Am. Chem. Soc.* **2004**, *126*, 5366.
(282) Sibi, M. P.; Ma, Z.; Itoh, K.; Prabagaran, N.; Jasperse, C. P. *Org. Lett.* **2005**, *7*, 2349.
(283) Yadav, J. S.; Reddy, B. V. S.; Narsimhaswamy, D.; Narsimulu, K.; Kunwar, A. C. *Tetrahedron Lett.* **2003**, *44*, 3697.
(284) Dugovic, B.; Fisera, L.; Hametner, C. *Synlett* **2004**, 1569.
(285) Desimoni, G.; Faita, G.; Mella, M.; Boiocchi, M. *Eur. J. Org. Chem.* **2005**, 1020.
(286) Kanemasa, S.; Oderaotoshi, Y.; Tanaka, J.; Wada, E. *J. Am. Chem. Soc.* **1998**, *120*, 12355.
(287) Shirahase, M.; Kanemasa, S.; Hasegawa, M. *Tetrahedron Lett.* **2004**, *45*, 4061.
(288) Shirahase, M.; Kanemasa, S.; Oderaotoshi, Y. *Org. Lett.* **2004**, *6*, 675.
(289) Iwasa, S.; Tsushima, S.; Shimada, T.; Nishiyama, H. *Tetrahedron Lett.* **2001**, *42*, 6715.
(290) Iwasa, S.; Tsushima, S.; Shimada, T.; Nishiyama, H. *Tetrahedron* **2002**, *58*, 227.
(291) Iwasa, S.; Maeda, H.; Nishiyama, K.; Tsushima, S.; Tsukamoto, Y.; Nishiyama, H. *Tetrahedron* **2002**, *58*, 8281.
(292) Iwasa, S.; Ishima, Y.; Widagdo, H. S.; Aoki, K.; Nishiyama, H. *Tetrahedron Lett.* **2004**, *45*, 2121.
(293) Suga, H.; Nakajima, T.; Itoh, K.; Kakehi, A. *Org. Lett.* **2005**, *7*, 1431.
(294) Suga, H.; Kakehi, A.; Ito, S.; Sugimoto, H. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 327.
(295) Kanemasa, S.; Kanai, T. *J. Am. Chem. Soc.* **2000**, *122*, 10710.
(296) Cabrera, S.; Arrayas, R. G.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 16394.
(297) Suga, H.; Funyu, A.; Kakehi, A. *Org. Lett.* **2006**, *9*, 97.
(298) Shi, J.-W.; Zhao, M.-X.; Lei, Z.-Y.; Shi, M. *J. Org. Chem.* **2008**, *73*, 305.
(299) Yan, X.-X.; Peng, Q.; Zhang, Y.; Zhang, K.; Hong, W.; Hou, X.-L.; Wu, Y.-D. *Angew. Chem., Int. Ed.* **2006**, *45*, 1979.
(300) Li, F.-B.; Liu, T.-X.; Wang, G.-W. *J. Org. Chem.* **2008**, *73*, 6417.
(301) Nagarapu, L.; Peddiraju, A. R.; Apuri, S. *Catal. Commun.* **2007**, *8*, 1973.
(302) Maheswara, M.; Siddaiah, V.; Rao, Y. K.; Tzeng, Y.-M.; Sridhar, C. *J. Mol. Catal. A: Chem.* **2006**, *260*, 179.
(303) Heravi, M. M.; Behbahani, F. K.; Oskooie, H. A.; Hekamt Shoar, R. *Tetrahedron Lett.* **2005**, *46*, 2775.

(304) Bartoli, G.; Babiuch, K.; Bosco, M.; Carlone, A.; Galzerano, P.; Melchiorre, P.; Sambri, L. *Synlett* **2007**, 2897.
(305) Bartoli, G.; Bosco, M.; Galzerano, P.; Giri, R.; Mazzanti, A.; Melchiorre, P.; Sambri, L. *Eur. J. Org. Chem.* **2008**, 3970.
(306) Mancheno, O. G.; Arrayas, R. G.; Carretero, J. C. *J. Am. Chem. Soc.* **2004**, *126*, 456.
(307) Guo, H.; Wang, Z.; Ding, K. *Synthesis* **2005**, 1061.
(308) Nagarajan, R.; Chitra, S.; Perumal, P. T. *Tetrahedron* **2001**, *57*, 3419.
(309) Anniyappan, M.; Muralidharan, D.; Perumal, P. T. *Tetrahedron* **2002**, *58*, 10301.
(310) Yadav, J. S.; Subba Reddy, B. V.; Srinivas, R.; Madhuri, C.; Ramalingam, T. *Synlett* **2001**, 240.
(311) Kamble, V. T.; Ekhe, V. R.; Joshi, N. S.; Biradar, A. V. *Synlett* **2007**, 1379.
(312) Anniyappan, M.; Muralidharan, D.; Perumal, P. T. *Tetrahedron Lett.* **2003**, *44*, 3653.
(313) Yadav, J. S.; Reddy, B. V. S.; Rao, C. V.; Srinivas, R. *Synlett* **2002**, 993.
(314) Gaddam, V.; Meesala, R.; Nagarajan, R. *Synthesis* **2007**, 2503.
(315) Gaddam, V.; Nagarajan, R. *J. Org. Chem.* **2007**, *72*, 3573.
(316) Sarkar, T. K.; Nandy, S. K.; Ghorai, B. K.; Mukherjee, B. *Synlett* **1996**, 97.
(317) Wu, J.; Zhang, L.; Diao, T.-N. *Synlett* **2005**, 2653.
(318) Narasimhulu, M.; Reddy, T. S.; Mahesh, K. C.; Prabhakar, P.; Rao, C. B.; Venkateswarlu, Y. *J. Mol. Catal. A: Chem.* **2007**, *266*, 114.
(319) Biginelli, P. *Gazz. Chim. Ital.* **1893**, *23*, 360.
(320) Yadav, J. S.; Subba Reddy, B. V.; Srinivas, R.; Venugopal, C.; Ramalingam, T. *Synthesis* **2001**, 1341.
(321) Maheswara, M.; Oh, S. H.; Kim, K.; Do, J. Y. *Bull. Korean Chem. Soc.* **2008**, *29*, 1752.
(322) Zhang, X.; Li, Y.; Liu, C.; Wang, J. *J. Mol. Catal. A: Chem.* **2006**, *253*, 207.
(323) Buscemi, S.; Macaluso, G.; Frenna, V.; Vivona, N. *J. Heterocycl. Chem.* **1986**, *23*, 1175.
(324) Vivona, N.; Buscemi, S.; Frenna, V.; Ruccia, M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 17.
(325) Buscemi, S.; Pace, A.; Palumbo Piccionello, A.; Vivona, N.; Pani, M. *Tetrahedron* **2006**, *62*, 1158.
(326) Gao, K.; Wu, J. *J. Org. Chem.* **2007**, *72*, 8611.
(327) Sibi, M. P.; Ma, Z.; Jasperse, C. P. *J. Am. Chem. Soc.* **2005**, *127*, 5764.
(328) Yan-Biao, K.; Xiu-Li, S.; Yong, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 3918.
(329) Mahdavinia, G. H.; Bigdeli, M. A.; Hayeniaz, Y. S.; Nemati, F. *Heterocycles* **2008**, *75*, 3077.
(330) Kantevari, S.; Bantu, R.; Nagarapu, L. *J. Mol. Catal. A: Chem.* **2007**, *269*, 53.
(331) Das, B.; Venkateswarlu, K.; Suneel, K.; Majhi, A. *Tetrahedron Lett.* **2007**, *48*, 5371.
(332) Yoon, K.; Ha, S. M.; Kim, K. *J. Org. Chem.* **2005**, *70*, 5741.
(333) Suga, H.; Kakehi, A.; Mitsuda, M. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 561.
(334) Quaranta, L.; Corminboeuf, O.; Renaud, P. *Org. Lett.* **2002**, *4*, 39.
(335) Yang, D.; Gu, S.; Yan, Y.-L.; Zhu, N.-Y.; Cheung, K.-K. *J. Am. Chem. Soc.* **2001**, *123*, 8612.
(336) Yang, D.; Gu, S.; Yan, Y.-L.; Zhao, H.-W.; Zhu, N.-Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 3014.
(337) Yang, D.; Yan, Y.-L.; Law, K.-L.; Zhu, N.-Y. *Tetrahedron* **2003**, *59*, 10465.
(338) Yang, D.; Zheng, B.-F.; Gu, S.; Chan, P. W. H.; Zhu, N.-Y. *Tetrahedron: Asymmetry* **2003**, *14*, 2927.
(339) Yang, D.; Gao, Q.; Lee, O.-Y. *Org. Lett.* **2002**, *4*, 1239.
(340) Yang, D.; Gao, Q.; Lee, C.-S.; Cheung, K.-K. *Org. Lett.* **2002**, *4*, 3271.
(341) Heravi, M. M.; Zadsirjan, V.; Behbahani, F. K.; Oskooie, H. A. *J. Mol. Catal. A: Chem.* **2006**, *259*, 201.
(342) Das, B.; Majjigapu Ravinder, R.; Ramu, R.; Kongara Ravinder, R.; Geethangili, M. *J. Chem. Res. S* **2005**, *2005*, 598.
(343) Meshram, H. M.; Reddy, P. N.; Murthy, P. V.; Yadav, J. S. *Synth. Commun.* **2007**, *37*, 4117.
(344) Khatik, G. L.; Kumar, R.; Chakraborti, A. K. *Synthesis* **2007**, 541.
(345) Fernández Mateos, A.; Martín de la Nava, E. M.; Rubio González, R. *Tetrahedron* **2001**, *57*, 1049.
(346) Janka, M.; He, W.; Haedicke, I. E.; Fronczek, F. R.; Frontier, A. J.; Eisenberg, R. *J. Am. Chem. Soc.* **2006**, *128*, 5312.
(347) Malona, J. A.; Colbourne, J. M.; Frontier, A. J. *Org. Lett.* **2006**, *8*, 5661.
(348) Heydari, A.; Javidan, A.; Schaffie, M. *Tetrahedron Lett.* **2001**, *42*, 8071.
(349) Tavakol, H.; Zakery, S.; Heydari, A. *J. Organomet. Chem.* **2007**, *692*, 1924.
(350) Azizi, N.; Rajabi, F.; Saidi, M. R. *Tetrahedron Lett.* **2004**, *45*, 9233.
(351) Saidi, M. R.; Heydari, A.; Ipaktschi, J. *Chem. Ber.* **1994**, *127*, 1761.
(352) Heydari, A.; Fatemi, P.; Alizadeh, A.-A. *Tetrahedron Lett.* **1998**, *39*, 3049.
(353) Heydari, A.; Karimian, A.; Ipaktschi, J. *Tetrahedron Lett.* **1998**, *39*, 6729.
(354) Heydari, A.; Larijani, H.; Emami, J.; Karami, B. *Tetrahedron Lett.* **2000**, *41*, 2471.
(355) Naimi-Jamal, M. R.; Ipaktschi, J.; Saidi, M. R. *Eur. J. Org. Chem.* **2000**, 1735.
(356) Saidi, M. R.; Azizi, N.; Zali-Boinee, H. *Tetrahedron* **2001**, *57*, 6829.
(357) Heydari, A.; Zarei, M.; Alijanianzadeh, R.; Tavakol, H. *Tetrahedron Lett.* **2001**, *42*, 3629.
(358) Saidi, M. R.; Azizi, N. *Tetrahedron: Asymmetry* **2002**, *13*, 2523.
(359) Saidi, M. R.; Azizi, N. *Synlett* **2002**, 1347.
(360) Yadav, J. S.; Reddy, B. V. S.; Reddy, P. S. R.; Shesha Rao, M. *Tetrahedron Lett.* **2002**, *43*, 6245.
(361) Niimi, L.; Hiraoka, S.; Yokozawa, T. *Tetrahedron* **2002**, *58*, 245.
(362) Azizi, N.; Saidi, M. R. *Tetrahedron* **2003**, *59*, 5329.
(363) Azizi, N.; Saidi, M. R. *Eur. J. Org. Chem.* **2003**, 4630.
(364) Nagarapu, L.; Paparaju, V.; Pathuri, G.; Kantevari, S.; Pakkiru, R. R.; Kamalla, R. *J. Mol. Catal. A: Chem.* **2007**, *267*, 53.
(365) Bhagat, S.; Chakraborti, A. K. *J. Org. Chem.* **2007**, *72*, 1263.
(366) Yousefi, R.; Azizi, N.; Saidi, M. R. *J. Organomet. Chem.* **2005**, *690*, 76.
(367) Bigdeli, M. A.; Nemati, F.; Mahdavinia, G. H. *Tetrahedron Lett.* **2007**, *48*, 6801.
(368) Saidi, M. R.; Brown, R. S.; Ziyaei-Halimjania, A. *J. Iran. Chem. Soc.* **2007**, *4*, 194.
(369) Heydari, A.; Khaksar, S.; Esfandyari, M.; Tajbakhsh, M. *Tetrahedron* **2007**, *63*, 3363.
(370) Niimi, L.; Shiino, K.; Hiraoka, S.; Yokozawa, T. *Tetrahedron Lett.* **2001**, *42*, 1721.
(371) Aryanasab, F.; Saidi, M. R. *Synth. Commun.* **2008**, *38*, 4036.
(372) Miura, K.; Ootsuka, K.; Suda, S.; Nishikori, H.; Hosomi, A. *Synlett* **2001**, 1617.
(373) Shaterian, H. R.; Hosseinian, A.; Ghashang, M. *Synth. Commun.* **2008**, *38*, 3766.
(374) Huang, J.; Kaner, R. B. *J. Am. Chem. Soc.* **2003**, *126*, 851.
(375) Mahua, G. D.; Durairaj, B.; Swaminathan, S. *Macromol. Chem. Phys.* **2003**, *204*, 1567.
(376) Fukuzumi, S.; Okamoto, K.; Gros, C. P.; Guilard, R. *J. Am. Chem. Soc.* **2004**, *126*, 10441.
(377) Fukuzumi, S.; Okamoto, K.; Tokuda, Y.; Gros, C. P.; Guilard, R. *J. Am. Chem. Soc.* **2004**, *126*, 17059.
(378) Tandon, P. K.; Sahgal, S.; Singh, A. K.; Gayatri; Purwar, M. *J. Mol. Catal. A: Chem.* **2005**, *232*, 83.
(379) Nam, W.; Ryu, J. Y.; Kim, I.; Kim, C. *Tetrahedron Lett.* **2002**, *43*, 5487.
(380) Imada, Y.; Ohno, T.; Naota, T. *Tetrahedron Lett.* **2007**, *48*, 937.
(381) Baxová, L.; Cibulka, R.; Hampl, F. *J. Mol. Catal. A: Chem.* **2007**, *277*, 53.
(382) Russell, A. E.; Miller, S. P.; Morken, J. P. *J. Org. Chem.* **2000**, *65*, 8381.
(383) Heydari, A.; MáMani, L. *Appl. Organomet. Chem.* **2008**, *22*, 12.
(384) Azizi, N.; Saidi, M. R. *J. Organomet. Chem.* **2003**, *688*, 283.
(385) Kobayashi, S.; Aoyama, N.; Manabe, K. *Synlett* **2002**, 483.
(386) Dixon, D. J.; Foster, A. C.; Ley, S. V. *Org. Lett.* **2000**, *2*, 123.
(387) Modarresi-Alam, A. R.; Khamooshi, F.; Nasrollahzadeh, M.; Amirazizi, H. A. *Tetrahedron* **2007**, *63*, 8723.
(388) Willis, M. C.; Piccio, V. J. D. *Synlett* **2002**, 1625.
(389) Arnold, A.; Markert, M.; Mahrwald, R. *Synthesis* **2006**, 1099.
(390) Abaee, M. S.; Mojtahedi, M. M.; Zahedi, M. M. *Synlett* **2005**, 2317.
(391) Bartoli, G.; Bosco, M.; Carlone, A.; Dalpozzo, R.; Galzerano, P.; Melchiorre, P.; Sambri, L. *Tetrahedron Lett.* **2008**, *49*, 2555.
(392) Gupta, R.; Gupta, M.; Paul, S.; Loupy, A. *Lett. Org. Chem.* **2008**, *5*, 153.
(393) Shibata, N.; Ishimaru, T.; Nagai, T.; Kohno, J.; Toru, T. *Synlett* **2004**, 1703.
(394) Kiyooka, S.-i.; Fujimoto, H.; Mishima, M.; Kobayashi, S.; Uddin, K. M.; Fujio, M. *Tetrahedron Lett.* **2003**, *44*, 927.
(395) Shimizu, H.; Okada, N.; Yoshimatsu, M. *Tetrahedron* **2001**, *57*, 8965.
(396) Shimizu, H.; Hatano, T.; Matsuda, T.; Iwamura, T. *Tetrahedron Lett.* **1999**, *40*, 1505.
(397) Kitano, Y.; Manoda, T.; Miura, T.; Chiba, K.; Tada, M. *Synthesis* **2006**, 405.
(398) Patrick, T. B.; Juehne, T.; Reeb, E.; Hennessy, D. *Tetrahedron Lett.* **2001**, *42*, 3553.
(399) Matsuda, I.; Wakamatsu, S.; Komori, K.-i.; Makino, T.; Itoh, K. *Tetrahedron Lett.* **2002**, *43*, 1043.
(400) Ning, G. L.; Li, X. C.; Munakata, M.; Gong, W. T.; Maekawa, M.; Kamikawa, T. *J. Org. Chem.* **2004**, *69*, 1432.

(401) Noack, A.; Schroder, A.; Hartmann, H.; Rohde, D.; Dunsch, L. *Org. Lett.* **2003**, *5*, 2393.
(402) Ragan, J. A.; McDermott, R. E.; Jones, B. P.; am Ende, D. J.; Clifford, P. J.; McHardy, S. J.; Heck, S. D.; Liras, S.; Segelstein, B. E. *Synlett* **2000**, 1172.
(403) Pernak, J.; Feder-Kubis, J. *Tetrahedron: Asymmetry* **2006**, *17*, 1728.
(404) Yoon, K.; Kim, K. *J. Org. Chem.* **2005**, *70*, 427.
(405) Kozyrkov, Y. Y.; Kulinkovich, O. G. *Synlett* **2004**, 344.
(406) Hunt, K. W.; Grieco, P. A. *Org. Lett.* **2001**, *3*, 481.
(407) Hunt, K. W.; Grieco, P. A. *Org. Lett.* **2002**, *4*, 245.

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