Epoxide Oxidations: A Valuable Tool in Organic Synthesis

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Abstract: This article focuses on stoichiometric and catalytic epoxide oxidations and their scope in organic synthesis. The work on Bi/O 2 -catalysed oxidation, developed in our group over the last ten years, is presented with various reactions leading to several oxidised compounds.

1 Introduction

2 Epoxide Oxidations Involving C–C Bond Cleavage

2.1 Stoichiometric Oxidations

2.2 Catalytic Oxidations

3 Epoxide Oxidations Without C–C Bond Cleavage

3.1 Stoichiometric Oxidations

3.2 Catalytic Oxidations

4 Conclusion

Key words: epoxides, oxidations, catalysis, bismuth, oxygen

1 Introduction

Easily prepared from olefins or carbonyl compounds, epoxides are known to be precious intermediates in organic synthesis, having the ability to be converted into a large number of functional groups, by various ring-opening addition and isomerisation reactions.

The synthesis of chiral epoxides followed by ring-opening reactions allows access to a variety of chiral compounds. The asymmetric ring-opening reactions of prochiral epoxides constitute also synthetically useful methods.

In spite of the high number of papers dealing with epoxide transformations, oxidation reactions have only received a limited amount of interest.

The oxirane ring oxidation can lead to various products; after the oxidative cleavage of the carbon-carbon bond, carbonyl compounds or carboxylic acids are generally obtained. α-Functionalised ketones are formed when the C–C bond of the epoxide remains uncleaved (Scheme 1).

Selective reagents have been developed for most of the reactions, and interestingly, catalytic processes have been reported in recent years.

2 Epoxide Oxidations Involving C–C Bond Cleavage

Various oxidation systems, both stoichiometric and catalytic, have been described for epoxide transformations involving the oxidative cleavage of the carbon-carbon bond.

2.1 Stoichiometric Oxidations

Periodic acid, HIO 4, a well-known oxidising agent, has shown particular efficiency in the oxidative cleavage of glycols and related compounds. It has also been used in the oxidative cleavage of 1,2-disubstituted epoxides to dialdehydes in aqueous medium. Thus, the treatment of cyclic epoxides such as 5,6-epoxycyclooctene and epoxycyclohexane in aqueous HIO 4 at pH 7.2 led to the formation of (cis)-4-octenedial and 1,6-hexanedial, in 76% and 82% yields, respectively (Scheme 2).

Using the same system, styrene oxide has been converted to benzaldehyde in 70% yield.

A proposed mechanism of the periodate cleavage reaction involves a first step of epoxide hydrolysis to the corresponding 1,2-glycol followed by oxidation to the dialdehyde by periodic acid.
Using a similar procedure, the selective oxidation of a trisubstituted double bond in the presence of two disubstituted ones in (6R,9Z,13Z)-2,6-dimethylnonadeca-2,9,13-triene, followed by HIO₄ cleavage, afforded (4R,7Z,11Z)-(−)-4-methyltetradec-7,11-dienal (Scheme 3). ¹²

The HIO₄-mediated reaction is also efficient with terminal epoxides of a C(n) chain, which may be converted into the corresponding C(n−1) aldehydes in organic solvents. Thus, 1,2-epoxy-13-methyltetradecane afforded 12-methyltridecanal in 66% yield in THF–Et₂O. ¹³ In a biphasic system (CH₂Cl₂–H₂O), a chiral functionalised cyclohexene oxide derivative was converted into the corresponding hexanediol derivative in 78% yield,¹⁴ at room temperature, without modification of the chiral moieties (Scheme 4).

Similarly, sodium periodate has been efficiently used instead of periodic acid in H₂O–THF for the oxidation of terminal conjugated epoxides to afford cis,cis-unsaturated aldehydes with one less carbon atom.¹⁵ Thus, (E,Z)-deca-2,4-dienal, a flavour component of peanuts and carrot root,¹⁶ has been prepared in 90% isomeric purity.

The HIO₄ methodology has been efficiently applied to the oxidation of hindered substrates, particularly in the case of strained cyclic epoxides (Scheme 5). Thus, the selective oxidation of epoxide 1 led to the cyclic diketone 2 in 90% yield.¹⁷

Tetrasubstituted strained epoxide 3 has been oxidised by HIO₄ to [4]perystilane-2,6-dione 4 in 76% yield, in an efficient and short route (Scheme 5).¹⁸ The mechanism of oxidation of these strained epoxides is assumed to proceed via the unusual formation of the cis-diol followed by the oxidative cleavage by HIO₄.¹⁹

The oxidative cleavage of the oxirane ring by periodic acid has found also some applications in the field of analytical chemistry.²⁰,²¹ These studies involve the determination of the oxirane position at the nanogram-scale by gas chromatography, by using a periodic acid pre-column that will oxidise the epoxide function into carbonyl groups.

Biographical Sketches

Sylvain Antoniotti was born in Nice, France in 1975. He studied Life Sciences and Chemistry at the University of Nice-Sophia Antipolis, France, and he received his Ph.D. in chemistry on the catalytic oxidation of epoxides by bismuth compounds under the scientific advisory of E. Duñach at the same university. He is currently a post-doctoral researcher at the Rensselaer Polytechnic Institute, Troy (NY), USA, in the group of Prof. J. S. Dordick.

Elisabet Duñach was born in Barcelona, Spain. She got her Ph.D. in Organic Chemistry at the University of Barcelona in 1981 under the supervision of Prof. J. Castells. A post-doctoral stay at the University California, Berkeley with Prof. K. P. C. Vollhardt (1981–1983) was followed by a second post-doctoral period at the University Paris XIII, Orsay with Prof. H. Kagan (1983–1985). In 1985 she became a CNRS researcher at LEC- SO, Thiais (France) in the group of Prof. J. Périchon, she then joined the Laboratoire de Chimie Moléculaire at the University of Nice (Prof. J. Riess) in 1991. She is now Director of Research at the CNRS at the University of Nice. She develops novel methodology in organic synthesis, including catalysis, electrochemistry and ‘green’ chemistry; activation of small molecules such as CO₂, O₂, S₈, and synthetic applications in the field of fine chemistry, and particularly in the field of flavours and perfumes.
Epoxide oxidations by lead tetraacetate have been reported also. The use of lead tetraacetate is usually compared with that of periodic acid, due to their close reactivity.³ Both reagents are complementary: whereas periodic is preferentially used in aqueous media, Pb(OAc)₄ reactions occur in organic solvents.

The oxidative cleavage of α,β-epoxy alcohols by lead tetraacetate has been reported to afford α-acetoxy ketones in yields of 43–91% (Scheme 6).²² The reaction was efficient in the case of linear α,β-epoxy alcohols but did not proceed well in the case of cyclic substrates. Although the mechanism of this transformation has not been studied, the authors suggested a nucleophilic ring opening of the epoxide mediated by lead tetraacetate leading to an α-acetoxy glycol. This intermediate would undergo an oxidative cleavage under the reaction conditions.

Scheme 6

CAN has also been used as a stoichiometric reagent for the direct oxidative cleavage of epoxides to carbonyl compounds.²³ This reaction, carried out in aqueous acetonitrile at room temperature, has been applied to the oxidation of various epoxides, leading to the corresponding aldehydes or ketones in yields of 70–82% (Scheme 7). Thus, benzaldehyde was obtained in the oxidation of styrene oxide, and the treatment of indene oxide by CAN afforded the expected dialdehyde (individual yields were not reported).

Sodium dichromate has been reported for the oxidation of isophorone oxide ⁵ to δ-keto-3,3-dimethylhexanoic acid ⁶ in 82% yield, according to Scheme 8.²⁴ The reaction was carried out in aqueous sulfuric acid with two equivalents of sodium dichromate.

A diperoxo chromium complex, PyCrO(O₂)₂, has been reported to oxidise 5,6-dihydro-2,3-diphenyl-1,4-dioxine ⁷ to ethane-1,2-dibenzoate and benzil (Scheme 9).²⁵ A proposed intermediate of this oxidation was the corresponding epoxide, 2,3-epoxy-2,3-diphenyl-1,4-dioxolan-8, which resulted from the first step, oxidation of the olefin function. The epoxide ⁸ was independently synthesised and oxidised by the chromium diperoxide. As expected, the treatment of ⁸ by stoichiometric amounts of Py-CrO(O₂)₂ (epoxide/chromium diperoxide 1:0.5) afforded also the dibenzoate ester produced from the C–C bond oxidative cleavage, together with benzil resulting from the dioxolane C–O bond cleavage.

Scheme 7

Scheme 8

The oxidation of ⁷ with the analogous Mo(VI) diperoxo complex, PyMoO(O₂)₂ gave the dibenzoate in 40% yield and the benzil in 60% yield.²³ A Mo(VI) complex has also been used for the oxidation of epoxides to carbonyl compounds with cleavage of the oxirane C–C bond.²⁶ The active metallic species was the diperoxo molybdenum complex MoO(O₂)₂L (L = hexamethylphosphoric triamide, HMPT, or tridodecylphosphoric triamide, TDPT) used in homogeneous, stoichiometric conditions (Scheme 10). Epoxides could be mono-, di- or trisubstituted, particularly by methyl or phenyl groups. The yields, determined after the peroxo-Mo concentration and measured by iodometric titration, were in the range of 25–86%.

Scheme 9
In the cases of 2-butene oxide and stilbene oxide, significant differences were revealed between the reactivity of cis- and trans-isomers; the cis-derivatives were remarkably more reactive than the trans-epoxides.\(^{24}\)

The oxidation of mono- and disubstituted aryl epoxides such as styrene oxide, α-methylstyrene oxide and 1,1-diphenylethene oxide by alkaline hydrogen peroxide has been described to afford the corresponding C(n–1) carboxylic acids or ketones in the range of 71–88% (Scheme 11).\(^{27,28}\) The conversion of an aliphatic terminal disubstituted epoxide such as 1-methyl-1-propylethene oxide afforded 2-pentanone in 45% yield. No cleavage reaction was observed with internal epoxides. The reaction was proposed to proceed via the formation of β-hydroxyperoxides, fragmented in situ.\(^{29}\)

Electrochemical processes have been reported for the oxidation of epoxides involving the formation of transient radical cations, which were rapidly decomposed in aqueous acetonitrile, leading to the corresponding carbonyl compounds after C–C bond cleavage (Scheme 12).\(^{30}\)

The electrochemical C–C cleavage of epoxides in methanol solutions led to mixtures of acetals.\(^{31}\) Thus, the oxidation of epoxide 9 to the corresponding diacetal 10 has been reported to occur in 87% yield. The reaction, carried out in MeOH–H\(_2\)SO\(_4\), was proposed to proceed through initial hydrolysis to the gem-diol, followed by anodic methoxylation (Scheme 13).\(^{32}\)

The electrochemical oxidative cleavage of epoxy ketones has been extended to the terpenoid series. Thus, the oxidation of pulegone oxide 11 occurred in a MeOH–EtOAc–LiClO\(_4\) system, affording the corresponding diester 12 in 83% yield (Scheme 14).\(^{33}\)

The nature of the supporting electrolyte was shown to strongly influence the yield of the reaction.

### 2.2 Catalytic Oxidations

The use of oxidants such as organic peroxides, H\(_2\)O\(_2\) or molecular oxygen, constitutes an interesting alternative to the use of stoichiometric metal-based oxidants that produce embarrassing amounts of wastes, and rarely allow scale-up of the procedures.

A catalytic oxidation of epoxides has been described using molecular oxygen and DMSO with bismuth(III)-mandelate as the catalyst.\(^{34}\) The C–C bond cleavage occurred mainly with terminal epoxides, which led to the corresponding carboxylic acids and CO\(_2\). The yields of carboxylic acids were in the range of 10–60% (Scheme 15).

The catalysts were bismuth(III) carboxylates, such as Bi(III)-mandelate, an O-bridged dimer of type [Bi(mand)\(_2\)]\(_2\)O. Several other bismuth(III) carboxylates with ligands such as pyridine carboxylates or dicarboxylates have been described to be efficient catalysts in the oxidative cleavage of aryl epoxides.\(^{36}\) The oxidation was shown to proceed through an α-hydroxyacetophenone-type intermediate.

The study of the substituent effects on the kinetics of the oxidation of styrene oxide derivatives afforded a Hammet-type linear correlation, and indicated that the rate of epoxide consumption was linearly related to the Hammet σ constants, with a slope \(p = -1.08\).\(^{37}\) The negative \(p\) value indicated that some positive charge was developed at the α- or β-aryl carbon atom at the transition state. The reaction was accelerated by electron-donating substituents able to stabilise this positive charge, and was slowed down by electron-withdrawing groups.
An oxidation mechanism involving both DMSO and \( \text{O}_2 \) as the oxidants has been proposed, as depicted in Scheme 16. A first Bi(III) coordination to the epoxide was followed by the oxirane ring-opening by DMSO. Evolution of dimethylsulfide led to a proposed enediolate intermediate, which was cleaved to the carboxylic acid by \( \text{O}_2 \)/DMSO. The oxidative cleavage of cyclohexene oxide to adipic acid has been reported to occur in moderate yields (32-40%) using various Bi(III) carboxylates in DMSO under molecular oxygen (Scheme 17).

In a novel catalytic system, Bi(0)/\( \text{O}_2 \) in DMSO has also been reported for terminal aryl epoxide oxidation. Bi(III) derivatives could be generated in situ, using metallic bismuth powder and carboxylic acids in DMSO. Several carboxylic acids were used in the oxidation of styrene oxide to benzoic acid, obtained in 32–50% yields (Scheme 18). It constituted the first example of the use of Bi(0)/\( \text{O}_2 \) as a catalytic system in organic synthesis. This system was also efficient for the oxidation of \( \beta \)-ketols and \( \beta \)-hydroxy acids. The oxidation involving a Bi(III)/Bi(0) redox couple was proposed for the first time in catalytic reactions involving dioxygen.

When the oxidation of styrene oxide was carried out under the same conditions, but under a nitrogen atmosphere instead of \( \text{O}_2 \), the yield of benzoic acid dropped to 8%, and a grey precipitate was formed and identified as metallic bismuth. These results indicated that in the absence of oxygen, only a stoichiometric reaction occurred. Comparing the results depicted in Schemes 15 and 18, Bi(0)/mandelic acid and Bi(III)-mandelate shows similar behaviour in the oxidation of styrene oxide in DMSO under molecular oxygen. A Bi(III) species, produced during the oxidative dissolution of metallic bismuth under \( \text{O}_2 /\text{H}^+ \), was proposed as being the active intermediate for the epoxide oxidation.

A Mo(VI)-based catalytic oxidation of epoxides to carbonyl compounds by \( \text{H}_2 \text{O}_2 \) has been described in a biphasic medium (Scheme 19). Sodium molybdate/\( \text{H}_2 \text{O}_2 \), with added HMPT or TDPT could oxidise styrene and \( \beta \)-methyl styrene oxides into benzaldehyde in 51% and 63% yields, respectively.

### 3 Epoxide Oxidations without C–C Bond Cleavage

#### 3.1 Stoichiometric Oxidations

Peroxides such as \( \text{H}_2 \text{O}_2 \) or tert-butyl hydroperoxide and cumyl hydroperoxide were described as epoxide oxidants leading to the formation of \( \beta \)-hydroxyalkylperoxides. Thus, the conversion of ethene, propene and isobutene oxides to the corresponding adducts under basic conditions was reported to occur in yields of 2–53%. Under basic conditions, the fragmentation reaction of the \( \beta \)-hydroxyalkylperoxides to the corresponding \( \alpha \)-ketols increased with increasing substitution on the starting epoxide. The oxidative ring opening of epoxides with ammonium molybdate–\( \text{H}_2 \text{O}_2 \) system has been reported. Terminal epoxides could be chemoselectively converted into the corresponding \( \alpha \)-ketols rather than to the \( \alpha \)-hydroxy aldehyde isomers (Scheme 20). The reaction takes place via the formation of the glycol derivative, formed from epoxide ring-opening, which was followed by selective oxidation of the secondary alcohol. The reaction did not proceed in the absence of ammonium molybdate. Products were obtained in high yields with one equivalent of ammonium molybdate and an excess of \( \text{H}_2 \text{O}_2 \) in THF at room temperature.
Swern et al. worked successfully on the use of DMSO associated with an activating agent for organic oxidations.\textsuperscript{44} DMSO-based oxidative systems have been widely studied and are particularly efficient for secondary alcohols,\textsuperscript{45} nevertheless, epoxide oxidations with DMSO systems are of limited scope. Reactions of various mono-, di- or trisubstituted epoxides with DMSO–(COCl)\textsubscript{2} in basic medium afforded the corresponding α-chlorocarbonyl compounds in 74–93% yields (Scheme 21).\textsuperscript{46,47}

The mechanism was proposed to proceed through initial formation of a chlorodimethylsulfonium cation from DMSO–(COCl)\textsubscript{2}. This active intermediate presumably activated the oxirane ring to allow for nucleophilic attack of chloride anion via a $\text{S}_{\text{N}}$\textsubscript{2} mechanism. The α-chloroalkoxysulfonium adduct could then react with a base, e.g. triethylamine, to give, after elimination, an α-chloroketone and dimethylsulfide. Steric hindrance determines the regioselectivity of the nucleophilic attack on non-symmetrical epoxides.

The in situ generated halodimethylsulfonium cation, which appears to be the active species in the process, has also been reported to result from the reaction of dimethylsulfide with molecular chlorine or bromine. DMSO–Cl\textsubscript{2} or DMSO–Br\textsubscript{2} systems converted linear and cyclic epoxides to the corresponding α-haloketones, after basic treatment, in yields of 68–87%.\textsuperscript{48} Some functionalised epoxides, such as α-nitroepoxides, have been converted into the corresponding 1,2-diketones. Oxidations with DMSO–BF\textsubscript{3}·Et\textsubscript{2}O\textsuperscript{49} (yields 61–77%) or DMSO–ClSiMe\textsubscript{3}\textsuperscript{50} (yields 57–87%) have been described to occur via the nucleophilic ring opening of the oxirane ring by DMSO with the concomitant loss of the nitro group, followed by the deprotonation of the intermediate to afford α-diketones and dimethylsulfide. In the presence of nucleophiles such as halide ions or primary amines, the corresponding α-haloketones or α-amino ketones could be obtained in yields of 57–88%.\textsuperscript{50}

The synthesis of antifungal Sch 42427/SM 9164 using TMSiOTf as the Lewis acid has been achieved in several steps, starting with the oxidation of chiral aryl epoxides to the corresponding α-ketols by DMSO (Scheme 22).\textsuperscript{51} Thus, chiral trans-β-methyl styrene oxides (αS,βS or αR,βR) were converted into the corresponding chiral α-ketols in yields of 80% and 83%, respectively, with complete retention of the configuration at the carbon bearing the alcohol centre. An interesting feature of this approach was the use of TMSiOTf as a Lewis acid. This reagent offered efficient activation of the oxirane ring and was also a protecting group for the alcohol function, allowing the enantioselective synthesis of protected α-ketol 13.

### 3.2 Catalytic Oxidations

In relation to the stoichiometric conversion of α-nitroepoxides to α-diketones previously described, a similar Pd(0)-catalysed reaction has been reported (yields 40–75%) (Scheme 23).\textsuperscript{52}

The ring opening-oxidation of terminal epoxides has been reported to afford α-hydroxy acids in good yields by a nitric acid oxidation catalysed by metallic copper.\textsuperscript{53} Interestingly, this reaction presented a different reactivity when applied to either alkyl or perfluoroalkyl terminal epoxides. Thus, trifluoromethyloxirane and pentafluorophenyleoxirane were selectively converted to the corresponding α-hydroxy acids in yields of 84% and 93%, respectively (Scheme 24), whereas the homologous alkyl epoxides led to mixtures of oxidation products such as α-hydroxy acids, α-keto acids and carboxylic acids, the latter formed after an oxidative decarboxylation.

This oxidation procedure was applied to optically active 1,2-epoxy-3,3,3-trifluoropropane affording α-hydroxy-3,3,3-trifluoropropanoic acid with complete retention of configuration. This fluorinated hydroxyacid constitutes a key intermediate for the further synthesis of fluorinated organic compounds.\textsuperscript{53} Internal epoxides have been reported to be precursors of α-hydroxyketones, when treated with DMSO under mild conditions, in a BF\textsubscript{3}-catalysed reaction.\textsuperscript{54} The oxidation was applied to cyclic epoxides such as cyclohexene oxide, 2β,3β-epoxy-5α-cholestan and 2α,3α-epoxy-5α-chole-
tane, leading to the corresponding α-ketols in yields of 76%, 55% and 45%, respectively (Scheme 25). Styrene oxide was also described to afford phenacyl alcohol in 57% yield.

Various linear and cyclic epoxides were converted into their corresponding α-hydroxycarbonyl derivatives in the presence of DMSO–CF$_3$COOH or DMSO–HBF$_4$·OMe$_2$ and 4 Å molecular sieves in yields of 20–88%. The acid additives were used in a ratio of 4–10 mol% relative to the starting epoxide and molecular sieves were shown to accelerate the oxidation.$^{55}$

The mechanism of this acid-catalysed oxidation of epoxides by DMSO has been studied.$^{56}$ The proposed intermediate was an α-hydroxyalkoxysulfonium salt such as 14 (Scheme 26). Various strong Brønsted acids, with anions of low nucleophilicity such as methanesulfonic acid, were used for the oxidation of styrene oxide, and the corresponding hydroxyalkoxysulfonium salt could be isolated in yields of 47–86%. This intermediate 14 was converted into the α-ketol derivative in moderate yields by treatment with base, or by heating (Scheme 26).

The acid-catalysed oxidative ring opening of epoxides by DMSO has been successfully applied to the synthesis of taxane derivatives in terpenoid chemistry.$^{57}$

An interesting alternative within the DMSO-based strategy for epoxide oxidation to α-ketols has been proposed using KSF-clay as the activating agent, combined with microwave irradiation instead of thermal or basic treatment (Scheme 27).$^{58}$

The use of 2,6-dimethylpyridine N-oxide as an oxygen transfer agent to epoxides has been reported for the oxidation of styrene oxide and cyclohexene oxide in the presence of trifluoroacetic or perchloric acids.$^{59}$ The base-induced or thermal decomposition of the alkoxyammonium intermediate salts led to the formation of phenacyl alcohol and 2-hydroxycyclohexanone in moderate yields.$^{60}$

The conversion of 2,3-epoxy-3-(2-nitrophenyl)-propiophenone 15 to 6-chloro-1,3-dihydroxy-2-phenylquinolin-4(1H)-one 16 by ethereal hydrogen chloride has been reported to occur via an intramolecular redox reaction involving the epoxide oxidation with the first nucleophilic ring opening by the nitro function (Scheme 28).$^{61}$

The catalytic oxidation of epoxides involving the activation by molecular oxygen has also been reported in oxidative oxirane ring-opening reactions. Thus, a catalytic system using bismuth derivatives such as BiBr$_3$ has been described to afford cyclic carbonates from terminal epoxides and DMF, under an oxygen atmosphere.$^{52}$ A series of monosubstituted oxiranes were converted into the corresponding cyclic carbonates in yields of 32–76%, using 10 mol% of BiBr$_3$ (Scheme 29).
The proposed mechanism involved the ring opening of epoxide, activated by BiBr₃ as a Lewis acid, followed by the insertion of DMF and oxidation by Bi(III). After dioxygen transfer to the substrate, final cyclisation afforded cyclic carbonates with regeneration of the Bi(III) species. Carbon dioxide incorporation into epoxides by an electrochemical nickel-catalysed method has also been developed, affording cyclic carbonates or benzo-lactones under mild conditions, depending on the structure of the starting epoxide.

A bismuth(0)-catalysed oxidation in DMSO combined with molecular oxygen for the conversion of internal epoxides to α-diketones has been reported. α-Diketones were selectively obtained in yields of 31–77% in a one-pot procedure. The reactions were carried out in DMSO at 100 °C under molecular oxygen (pressure of 1 atm) in the presence of 5-10 mol% of Bi(0) powder and 2.5–8 mol% of Cu(OTf)₂ or 9–20 mol% of TfOH as the additives (Scheme 30).

The reaction has been studied using cyclohexene oxide as a model substrate, and it was shown that the oxidation to α-diketone was similarly achieved by both Bi(0)–additive and Bi(III)-based systems, showing only quantitative differences. A Bi(III) species intermediate has been proposed as the featuring oxidant of the process, generated in situ in the presence of O₂/H⁺ in DMSO. The comparison of Bi(0)/Cu(OTf)₂, Bi(0)/TfOH, Bi(OTf)₃ and Cu(OTf)₂ systems is presented in Figure 1, providing the α-diketone yields obtained after total conversion of the starting epoxide, with 5–10 mol% of catalyst and 2.5–20 mol% of additives. Reactions were carried out in DMSO at 100 °C, under an oxygen atmosphere.

This strategy has been applied to the synthesis of 2,3-pentanedione, an industrial key-flavour compound having a buttery note, and formed in 38% from 2-pentene oxide. This system was extended to the synthesis of quinoxaline derivatives by the direct oxidative coupling of various epoxides with ene-1,2-diamines, such as phenylene diamine, diaminomaleonitrile or 2,3-diaminopyridine. Mono- and disubstituted quinoxalines were obtained from mono- and disubstituted epoxides in yields of 53–70% (Scheme 31). Interestingly, although styrene oxide was unselectively cleaved to benzoic acid and benzaldehyde during Bi/O₂ oxidation instead of being converted into the expected phenylglyoxal, this unstable phenylglyoxal intermediate was efficiently trapped, before undergoing oxidative cleavage, as the corresponding 2-phenylquinoxaline ring.

Scheme 30

The oxidative coupling of cyclohexene oxide and 2,3-diaminopyridine led also to the expected nitrogen-containing heterocycle. This novel synthesis of aromatic heterocycles showed the compatibility of the oxidation method regarding various functional groups such as olefin, nitrile or halogen functions. Quinoxaline rings being the skeleton of several interesting anti-tumoral compounds, the presence of these functional groups allow the further elaboration of the quinoxaline derivatives for the synthesis of potentially bioactive compounds.

Scheme 31

Tetrahydroquinoxaline derivatives were similarly formed from cyclohexene oxides and 1,2-diaminomaleonitrile in yields of 53–71% (Scheme 32).

Scheme 32

The oxidative coupling of cyclohexene oxide and 2,3-diaminopyridine led also to the expected nitrogen-containing heterocycle. This novel synthesis of aromatic heterocycles showed the compatibility of the oxidation method regarding various functional groups such as olefin, nitrile or halogen functions. Quinoxaline rings being the skeleton of several interesting anti-tumoral compounds, the presence of these functional groups allow the further elaboration of the quinoxaline derivatives for the synthesis of potentially bioactive compounds.

4 Conclusion

This review illustrates the possibilities of selective epoxide oxidations leading to different and valuable products (flavouring agent, bioactive molecules), as well as to interesting synthetic intermediates. High selectivities can be attained with several oxidation systems, either involving epoxide ring-opening or ring-cleavage reactions. The oxirane oxidative cleavage has an interesting synthetic potential in reducing a carbon chain of terminal epoxides by one carbon atom or in the cleavage of an unsaturated chain. In particular, the oxidation of terminal...
aryl epoxides to (n−1) carboxylic acids has been well developed. The selective cleavage of terminal aliphatic epoxides still remains a synthetic challenge.

The direct and catalytic oxidation of epoxides to \( \alpha \)-diketones has been recently described. This new transformation provides easy access to useful synthetic intermediates. Ozone has been recently described. This new transformation provides easy access to useful synthetic intermediates.

The development of new methodologies involving environmentally benign reagents has become an essential issue. Catalytic systems applied to epoxide oxidations using molecular oxygen as well as hydrogen peroxide or organic peroxides constitute interesting promising processes in green chemistry.

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