SYNLETT
Spotlight 452

# Oxaziridines

Compiled by Laura Buglioni

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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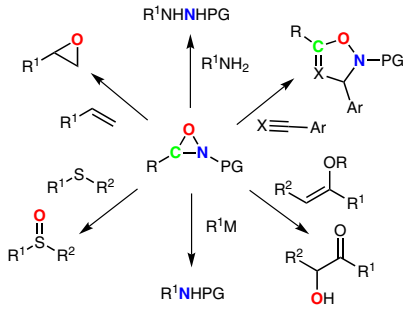
## Introduction

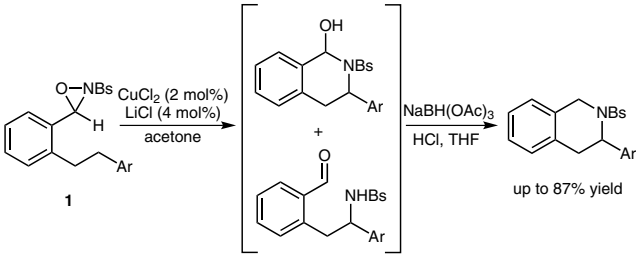
An oxaziridine is a strained, three-membered ring, consisting of weakly bound carbon, nitrogen, and oxygen atoms. This heterocycle is synthesized by oxidation of the corresponding imine, most commonly with *m*-chloroperbenzoic acid. Also, reagents such as *t*-butyl hydroperoxide and urea hydrogen peroxide complex can be used.[1] Oxaziridines are very reactive due to the presence of three different atoms with different electronegativities. They can transfer the nitrogen or the oxygen atom and can undergo [3+2] cycloadditions. The high reactivity has been applied in many transformations with a wide range of reactants, such as sulfides, organometallic reagents, amines, and silyl enol ethers (Scheme 1).[2] In this article, some examples have been selected in order to provide an overview of the recent synthetic achievements.



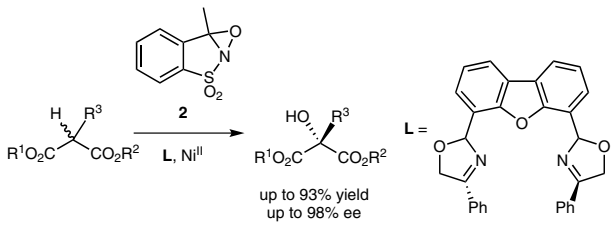

**Scheme 1** Reactivity of oxaziridines

## Abstracts

(A) *Intramolecular Amination:*
*N*-Sulfonyl oxaziridines **1** have recently been used in the activation of C($sp^3$)–H bonds in an intramolecular aminohydroxylation reaction catalyzed by copper(II) salts. Surprisingly, rather than donation an oxygen atom, a new C–N bond is formed in a highly regioselective manner. The proposed mechanism involves the abstraction of the proton in the δ-position leading to the formation of a six-membered transition state.[3]




(B) *Dynamic Kinetic Asymmetric Hydroxylation:*
In the presence of a chiral nickel(II) complex, oxaziridine **2** could perform the α-hydroxylation of racemic malonates. The attack of **2** occurs preferentially on the *si* face of the malonate, affording the products in excellent enantioselectivities and yields. This methodology was extended to the synthesis of *(R)*-bicalutamide, an important anti-androgen drug used in the treatment of prostate cancer.[4]

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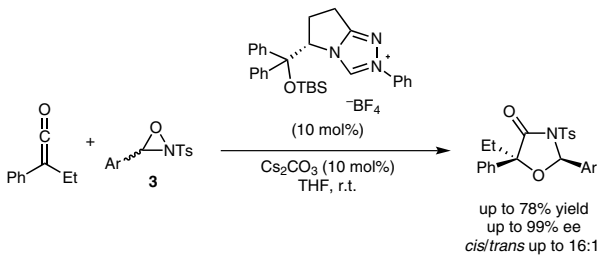
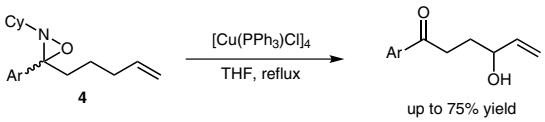
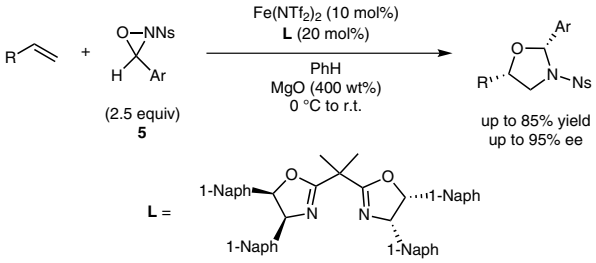
(C) *[3+2] Cycloaddition:*
Oxaziridines easily undergo [3+2] cycloaddition with imines, nitriles, alkenes, and alkynes.[5] Recently, this transformation catalyzed by chiral N-heterocyclic carbenes was developed with ketenes and oxaziridine **3**, affording oxazolin-4-ones in moderate to good yields and excellent enantioselectivities.[6]



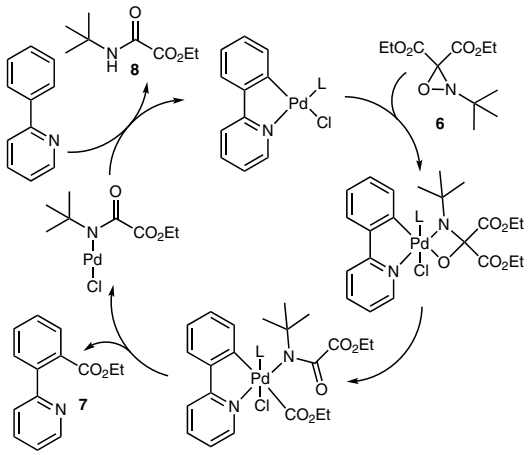

(D) *Oxidation of C–H Bonds:*
A copper(I)-catalyzed intramolecular oxidation of C–H bonds was developed starting from the oxaziridine **4** to selectively give the corresponding allylic alcohol in moderate to good yields. The proposed mechanism involves the formation of a copper-bound radical anion arising from a single electron transfer, followed by hydrogen atom abstraction.[7]




(E) *Asymmetric Oxyamination:*
Chiral iron(II) complexes have been showed to catalyze reactions between alkenes and *N*-nosyl oxaziridines **5**, affording the corresponding substituted oxazolidines with moderate to good yields and high enantiomeric excesses. The *cis* selectivity of this transformation is explained by a kinetic resolution in which only one of the enantiomers of **5** participates in the oxyamination. As a consequence, 2.5 equivalents of **5** are necessary for high yields.[8]




(F) *C–H Ethoxycarbonylation:*
Oxaziridine **6** showed unprecedented reactivity and has been used to transfer an ethoxycarbonyl group to substituted 2-phenylpyridines in moderate yields. The proposed mechanism of this reaction, catalyzed by a palladium(II) complex, involves activation of the *ortho* C–H bond of the phenyl moiety, followed by oxidative insertion of the metal into the N–O bond of **6**, forming an intermediate palladium(IV) species. C–C bond cleavage of **6** followed by reductive elimination leads to the formation of the ethoxycarbonylated product **7** and amide **8** as the by-product. This transformation has been subsequently applied to aryl urea derivatives with moderate yields.[9]

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