

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

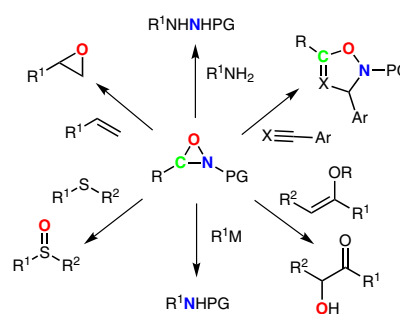
Laura Buglioni was born in Camerino (Italy) and studied Chemistry and Advanced Chemical Methodologies at the University of Camerino. She received her M.Sc. degree in 2011. Currently she is working as a doctoral student under the supervision of Professor Carsten Bolm at RWTH Aachen University (Germany). Her research interest is focused on the synthesis and reactivity of sulfoximines and sulfilimines.

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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 ex-

amples have been selected in order to provide an overview of the recent synthetic achievements.

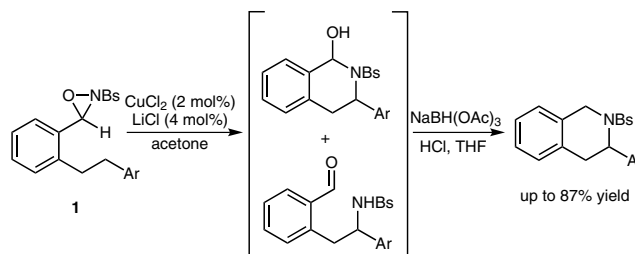


Scheme 1 Reactivity of oxaziridines

Abstracts

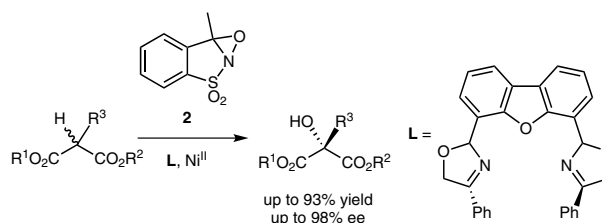
(A) Intramolecular Amination:

N-Sulfonyl oxaziridines **1** have recently been used in the activation of C(sp³)-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



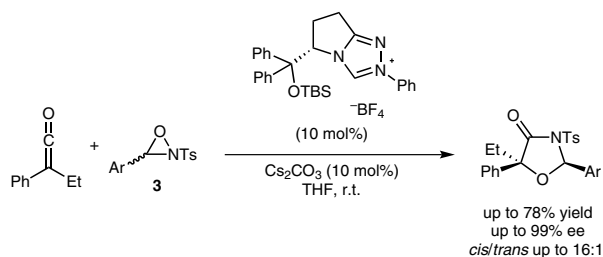
(B) Dynamic Kinetic Asymmetric Hydroxylation:

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



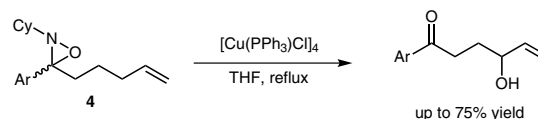
(C) [3+2] Cycloaddition:

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



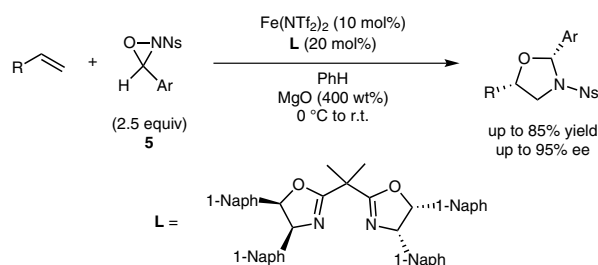
(D) Oxidation of C–H Bonds:

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



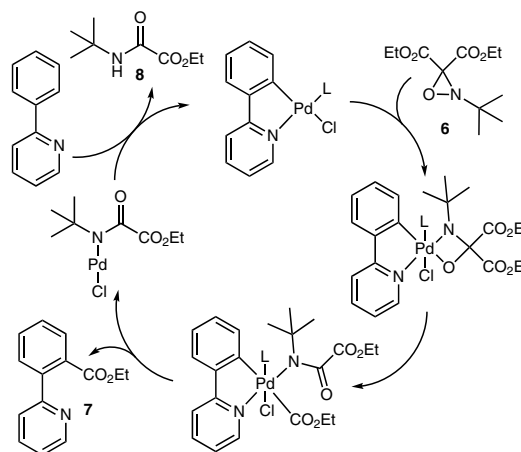
(E) Asymmetric Oxyamination:

Chiral iron(II) complexes have been shown 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



References

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