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REVIEW

Advancements in the synthesis of oxazolines

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Abstract

Heterocyclic compounds have always gained much recognition in synthetic organic chemistry. Oxazoline is one of the most important five-membered heterocyclic species having one nitrogen and one oxygen in its backbone. Many oxazoline-based ring structures presently available are noticeable for their biological activities. Oxazoline moiety displays a large number of applications mainly in the field of pharmaceuticals, industrial, natural product chemistry, polymers and so on. As a result, plentiful investigations ensued on oxazoline synthesis and is also still continuing. In this context, we have compiled a review giving an overview of the synthesis of oxazolines covering literature up to 2021. Here we have classified various synthetic protocols of oxazolines based on the substrates involved—as amino alcohols, carboxylic acids, carbonyl compounds, alkenes, etc.

Graphical abstract

Keywords Amino alcohols · Carbonyl compounds · Green chemistry · One-pot synthesis · Oxazolines

Introduction

Heterocyclic compounds play vital roles in many fields including medicinal chemistry, catalysis, material science, polymers, etc. Heterocycles are mainly classified based on

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the number of atoms in their ring [1, 2]. Three-, four-, five-, six-, and seven-membered are some of the common heterocycles. Among these, the ones having more than one heteroatom are also present such as morpholine [3], thiadiazole [4], etc. Fused heterocycles such as quinolone [5] and indole [6] are another important kind of heterocycles. These kinds of heterocyclic framework are predominant in majority of drugs, dyes, and catalysts [7, For reviews on heterocyclic chemistry see: 8, 9; For books on heterocyclic chemistry see: 10–14; 15].

Among the various heterocycles, the five-membered ones owe great importance due to the possession of various biological properties [16]. Pyrroles [17], furans [18], and thiophenes [19] are some of the familiar five-membered heterocycles having one heteroatom. But there are certain other heterocycles bearing two heteroatoms in their ring skeleton like imidazoles [20], oxazoles [21], thiazoles [22], oxazolines [23], oxazolidines [24], etc.

Oxazoline is a five-membered heterocycle having one nitrogen and one oxygen in its structure [23]. It was first synthesized in 1884 [25] and after 5 years, the structure of oxazoline was properly assigned (Fig. 1) [26]. The saturated form of oxazoline is termed oxazolidine [27]. Oxazoline exists in three structural isomeric forms depending on the position of the double bond as 2-oxazoline, 3-oxazoline, and 4-oxazoline. Among these, only 2-oxazolines are common. Isoxazoline is another kind of isomer in which the oxygen and nitrogen atoms are at the 1,2 positions (Fig. 2) [28].

Oxazolines hold a wide range of applications in diverse fields. Oxazolines having different biological activities have been synthesized and many of these are observed to showcase anti-microbial [29], anti-malarial [30], anti-viral [31], anti-bacterial [32], anti-pyretic [33], anti-inflammatory [34], etc. effects. Oxazolines having anti-tumour property is also discovered, which provides a good expectation in the therapeutic field [35]. Some of the biologically active compounds having oxazoline backbone are portrayed in Fig. 3.

Oxazolines are widely employed in surface area coatings and they can act as surface-active agents or emulsifiers in aqueous medium [36]. Oxazoline derivatives obtained from long-chain fatty acids and amino alcohols are efficient plasticizers and have facilitated access towards various tough, strong, and

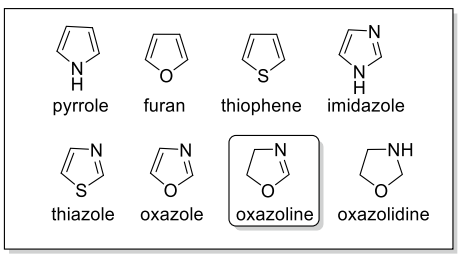


Fig. 1 Structures of important five membered heterocycles

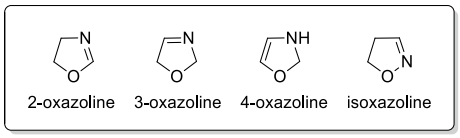


Fig. 2 Isomeric structures of oxazolines

flexible films [37]. The surface tension of oxazoline is higher than that of amides, by virtue of which they can function as good surface-active agents [38]. Oxazoline monomer can be converted to linear polymer structures having high molecular mass. The mixing of gasoline with some substituted oxazolines decreases surface ignition and provides carburetor cleanliness [39]. Mercapto-oxazolines are realized as corrosion inhibitors in lubricating oils [40]. Oxazoline based organic acid salts are employed as corrosion protective films on metals [41]. The derivatives of oxazolines are employed as anti-foam agents and help to regulate foaming in the fermentation process [42]. Some mixtures of oxazolines with mineral oils and acids serve as textile chemicals [43]. Various derivatives of 2-oxazolines form the backbone of many pharmaceutically significant compounds. Substituted arylamino-2-oxazolines are applicable for enhancing blood sugar levels and also can act as a blood pressure depressant [44]. Oxazolines can also wield as stabilizers for chlorinated hydrocarbons and aqueous formaldehyde solutions [45]. The addition of oxazolines in detergents helps to promote foam stability [46]. The practical applications of oxazolines can also be seen in the areas of photography [47] and agriculture [48]. Oxazolines have also marked their importance in the field of catalysis. Several ligands in various metal-catalyzed enantioselective reactions have oxazoline moiety in their structures [49]. They are also used as ligands in

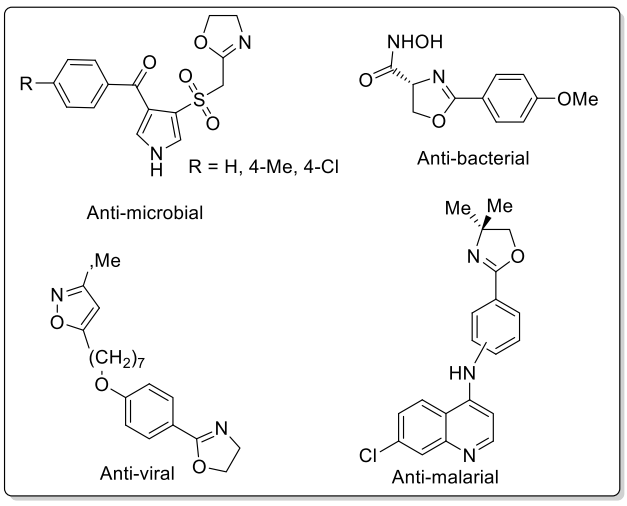


Fig. 3 Some biologically important compounds containing oxazoline backbone

asymmetric catalysis and as protecting groups for carboxylic acids [50]. There are various classes of ligands with oxazoline motifs, based on their chirality, denticity and donor atoms. The ligand structures have been designed with one or more oxazoline ring skeletons.

Moreover, many of their derivatives are also promising in the catalytic realm. 2-Oxazoline-1,10-phenanthrolinyl metal dichlorides were used as catalysts for the oligomerization of ethylene [51]. Nickel(II) complexes bearing phosphinooxazoline ligand were also employed for the ethylene oligomerization [52]. Nickel(II) complexes having oxazole ring system displayed enhanced catalytic activity for the polymerization of norbornene [53]. 2-(Oxazol-2-yl)-pyridines were efficient ligands in Suzuki–Miyaura cross-coupling [54]. Besides this, there are several benzoxazole derivatives showcasing various applications in organic synthesis [55–59].

Because of the wide applications of oxazolines, there is great relevance in the synthetic strategies of this particular compound and its derivatives [60]. A number of approaches for the synthesis of this skeleton, and the applications of these compounds are reported so far. A recent review on the synthetic strategies of oxazoline was reported by Hargaden et al. in 2019 [61], which discusses the construction of oxazoline using nitriles, aldehydes, carboxylic acids, and amide derivatives. Herein, we have compiled a review summarizing the various strategies on the synthesis of oxazolines from amino alcohols, nitriles, carboxylic acids, carbonyl compounds, alkenes, α-oxo-ketene *N*,*N*-acetals, benzoxazines, sulfoxides, alkyl trichloroimidates, ketoaziridines, aryl bromides, benzylidene acetal, and epoxides covering literature up to 2021. For brevity and better clarity, the topic is classified based on the starting materials employed for the synthesis of oxazolines.

From amino alcohols

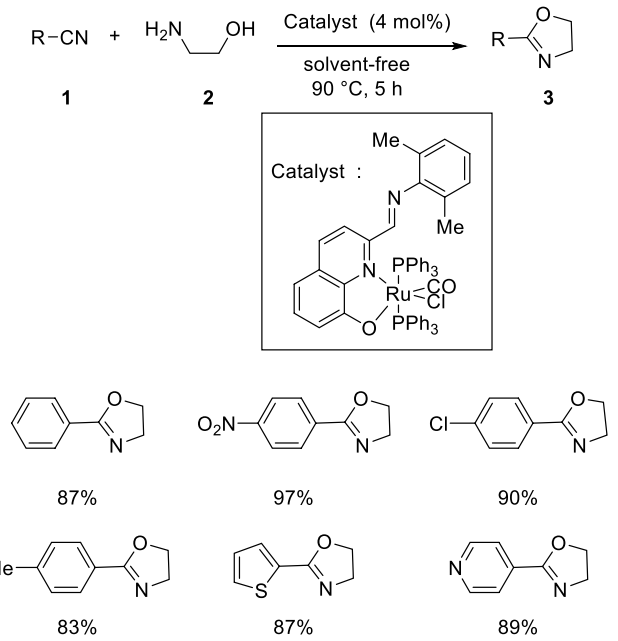
Amino alcohols are important class of organic compounds that contain a hydroxyl group and an amino group (primary, secondary, or tertiary) on the alkane chain. Among the various classifications of amino alcohols, 2-amino alcohols have gained more significance in synthetic organic chemistry, especially in the synthesis of oxazolines.

This classification deals with synthetic protocols of oxazoline by the reaction of amino alcohols with nitriles, carboxylic acid, and aldehydes.

Reactions of amino alcohols and nitriles

Organic compounds having C≡N are termed as nitriles. The reaction of nitriles with amino alcohols generally proceeds through a nucleophilic addition of nitriles to amino alcohols followed by an intramolecular cyclization.

Scheme 1



A novel protocol for ruthenium(II) catalyzed synthesis of 2-oxazolines **3** was designed by the reaction of ethanolamine **2** and aryl nitriles **1** using 4 mol% [RuCl(CO)(PPh_3)2(L)] as the most effective catalyst under neat conditions (Scheme 1) [62]. It was also observed that, the maximum conversion was attained with quinolinolate ligands which acted as bidentate NO donors. Good to high yields were obtained by various substituted nitriles. The presence of electron-deficient groups on aryl nitriles provided excellent yields.

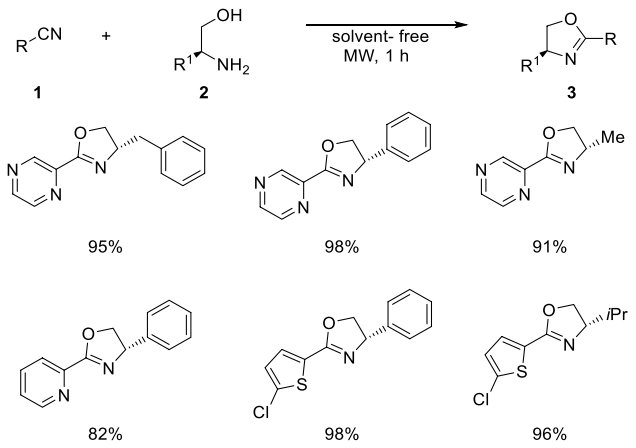
Another solvent-free method towards the synthesis of 2-oxazolines **3** was established by the reaction of nitriles **1** with amino alcohols **2** under microwave irradiation affording good to high yields (Scheme 2) [63]. The maximum yield was obtained when the reaction was performed at 150 °C.

Yan and co-workers reported a method to construct D-oxazoline **3** ligands under moisture-free conditions [64]. Various nitriles **1** and amino alcohols **2** were reacted in presence of $ZnCl_2$ as a Lewis acid catalyst in chlorobenzene (Scheme 3). Several substrates were analysed and provided good yields of product.

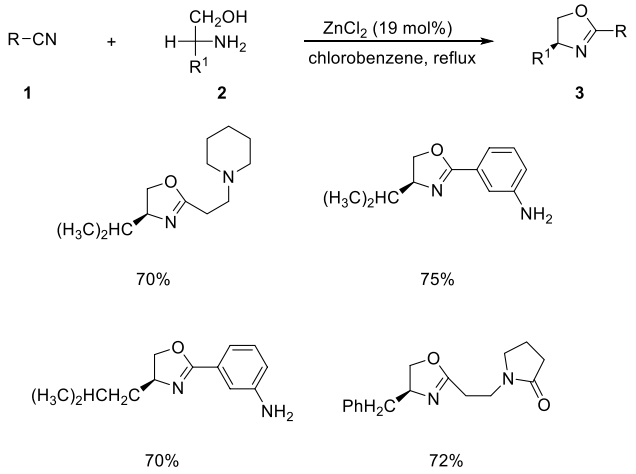
A solvent-free protocol to synthesize 2-oxazolines **3** was established by the reaction of aromatic nitriles **1** and 2-amino alcohols **2** in presence of a biopolymer-based catalyst-cellulose sulfuric acid (CSA) [65]. A range of substrates was investigated and obtained good to excellent yields (Scheme 4).

Bis-oxazolines **5** and their derivatives were synthesized by the modular reaction between dicyanobenzenes **4** and amino alcohols **2** [66]. The reaction underwent smoothly in presence of $ZnCl_2$ as Lewis acid catalyst under anaerobic conditions (Scheme 5). Different dicyanobenzenes

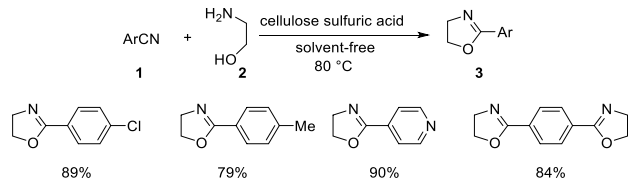
Scheme 2



Scheme 3



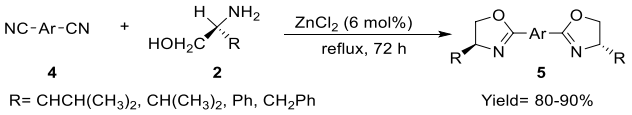
Scheme 4



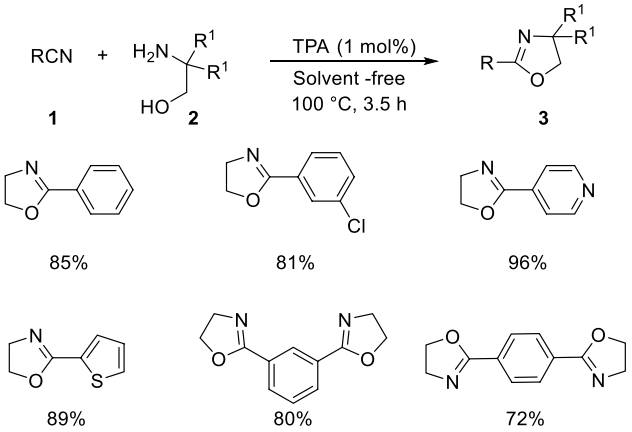
were analysed, which afforded good yields. The product yield depended on the amount of amino alcohol taken and maximum yield was obtained when the ratio of nitrile to amino alcohol was 1:3.

A green protocol for the construction of oxazolines **3** using 1 mol% of catalyst tungstophosphoric acid (TPA) was designed (Scheme 6) [67]. In this method, aromatic nitriles **1** reacted with amino alcohols **2** under neat conditions. Mono- and bis-oxazolines were selectively formed from dicyanobenzenes. A range of substrates were analysed and obtained high to excellent yields. Through the

Scheme 5



Scheme 6



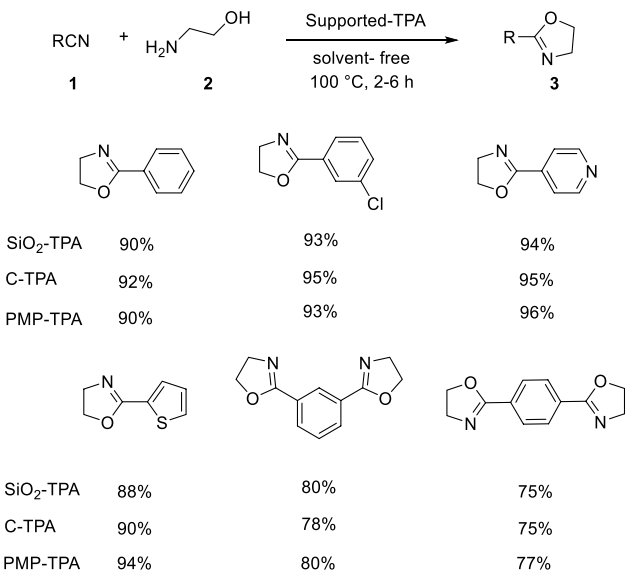
same procedure imidazolines were also formed from nitriles and ethylene diamine.

An effective conversion of amino alcohols **2** and nitriles **1** towards oxazolines **3** was performed in the presence of 12-tungstophosphoric acid catalyst under neat conditions (Scheme 7) [68]. The catalyst was supported on silica, activated carbon or poly(4-styrylmethyl)pyridinium chloride (PMP) for enhancing the catalytic activity. Mono- and bis-oxazolines were obtained from the corresponding cyanobenzenes. Several substituted aromatic nitriles provided good to excellent yields. Heteroaromatic nitriles also gave better yields.

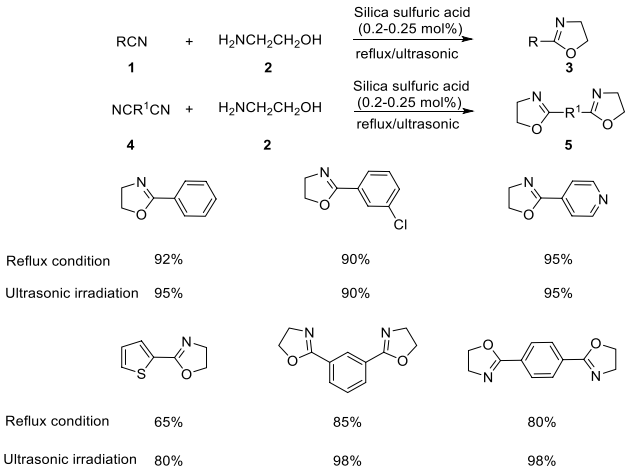
Silica sulfuric acid (SSA) was established as an efficient and reusable catalyst for the formation of oxazolines **3** under neat condition (Scheme 8) [69]. Different nitriles **1** and amino alcohols **2** were reacted towards the formation of product under reflux conditions as well as ultrasonic irradiations. Maximum yields and short reaction times were achieved under ultrasonic irradiations. Different substituted mono- **3** and bis-oxazolines **5** were attained from the corresponding nitriles **1**, **4** in good to excellent yields.

A novel protocol to construct 2-oxazolines **3** under microwave irradiation was established by the reaction of nitriles **1** and *β*-amino alcohols **2** along with a mild Lewis acid catalyst under MW irradiations [70]. Here, the amino alcohol performed the role of reactant as well as solvent. Both alkyl and aryl nitriles were analysed and achieved good to high yields (Scheme 9). Aromatic nitriles having both electron-releasing and electron-withdrawing groups provided better yields. In the case of 2-substituted benzonitrile, only

Scheme 7



Scheme 8



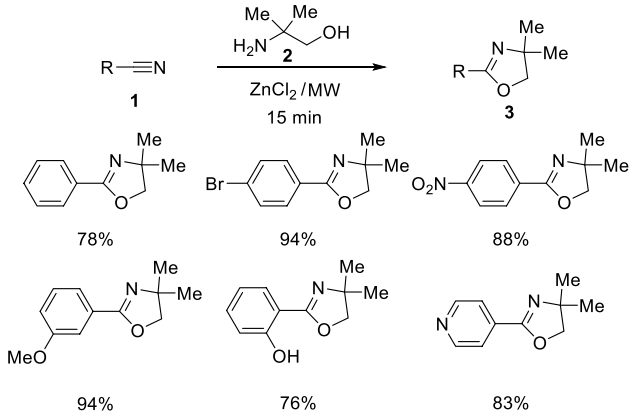
electron-withdrawing groups gave high yields. Aliphatic nitriles took longer time to complete the reaction.

Reactions of amino alcohols and carboxylic acid

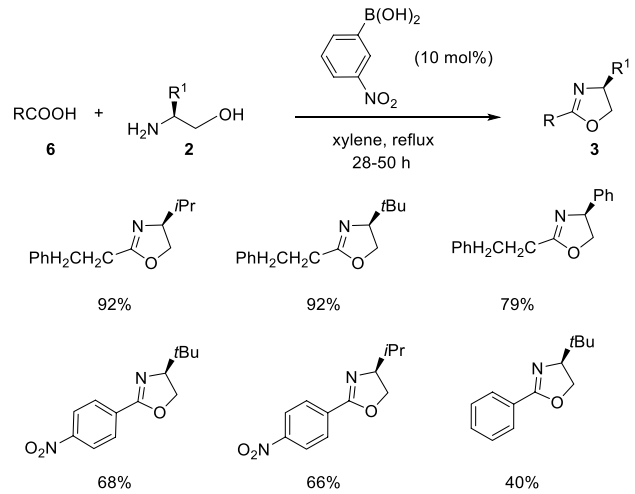
Carboxylic acid is composed of a carbonyl carbon bonded to a hydroxyl group. Usually, the synthesis of oxazolines from amino alcohols and carboxylic acid involves a nucleophilic attack and an intramolecular cyclization.

A new strategy for oxazoline **3** synthesis from carboxylic acids **6** and amino alcohols **2** was established in presence of boronic acid catalyst (Scheme 10) [71]. The condensation of acids with amino alcohols in refluxing xylene led to the oxazoline product. Maximum yield was observed

Scheme 9



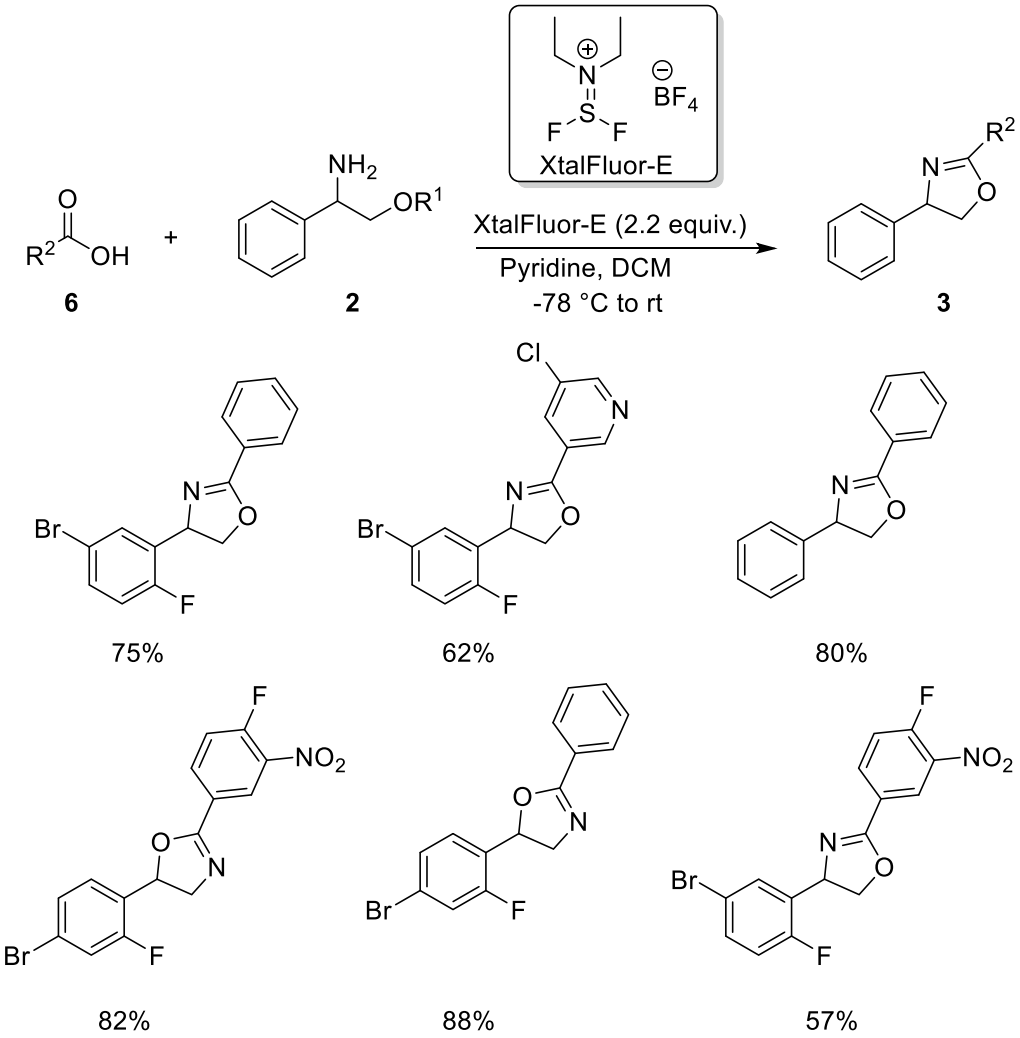
Scheme 10



when 3-nitrophenylboronic acid was used as a catalyst for dehydration. Several carboxylic acids and amino alcohols bearing different moieties reacted through a combinatorial way and afforded moderate to excellent yields.

XtalFluor-E was established as a worthy reagent for oxazoline **3** synthesis from *o*-silylated amino alcohols **2a** and carboxylic acids **6** in DCM solvent and pyridine at − 78 °C to rt (Scheme 11) [72]. Isopropyldimethylsilyl (IPDMS) protected alcohols exhibited a better yield of 85% among other silyl protected ones. The reaction begins with the formation of an intermediate **7** by the nucleophilic attack on XtalFluor-E by the oxygen of the aromatic acid (Scheme 12). A further attack on the carbonyl carbon of the resultant intermediate by the nitrogen of amine leads to the generation of intermediate **8**. Elimination of fluoride ion produces intermediate **9**, which on deprotection of the silyl group, renders intermediate **10**. Formation of the desired oxazoline occurs by the reaction of intermediate **10** with XtalFluor-E and subsequent cyclization.

Scheme 11



Reactions of amino alcohols and aldehydes

A nucleophilic attack at the electrophilic centre of aldehydes by amino alcohols leads to the generation of an intermediate, which then undergoes a cyclization within the molecule and provides oxazoline in the reaction between amino alcohols and aldehydes.

A novel route towards 2-oxazolines **3** by the condensation of 2-amino alcohol **2** and aldehydes **11** was disclosed [73]. In the optimised conditions, the product was obtained by adding molecular iodine (3 equiv.) along with 3 equiv. of K_2CO_3 in *t*BuOH under ultrasound irradiation at 35–40 °C (Scheme 13). Moderate to good yields were attained with substrates having different substituents. The rate of conversion of aromatic aldehydes having electron-withdrawing moieties was faster than those containing electron-donating groups, presumably due to enhanced imine formation from aldehydes with electron-withdrawing group. Due to the conjugation of carbonyl group, *para*-substituted aldehydes provided better yield compared to the *meta*-substituted one.

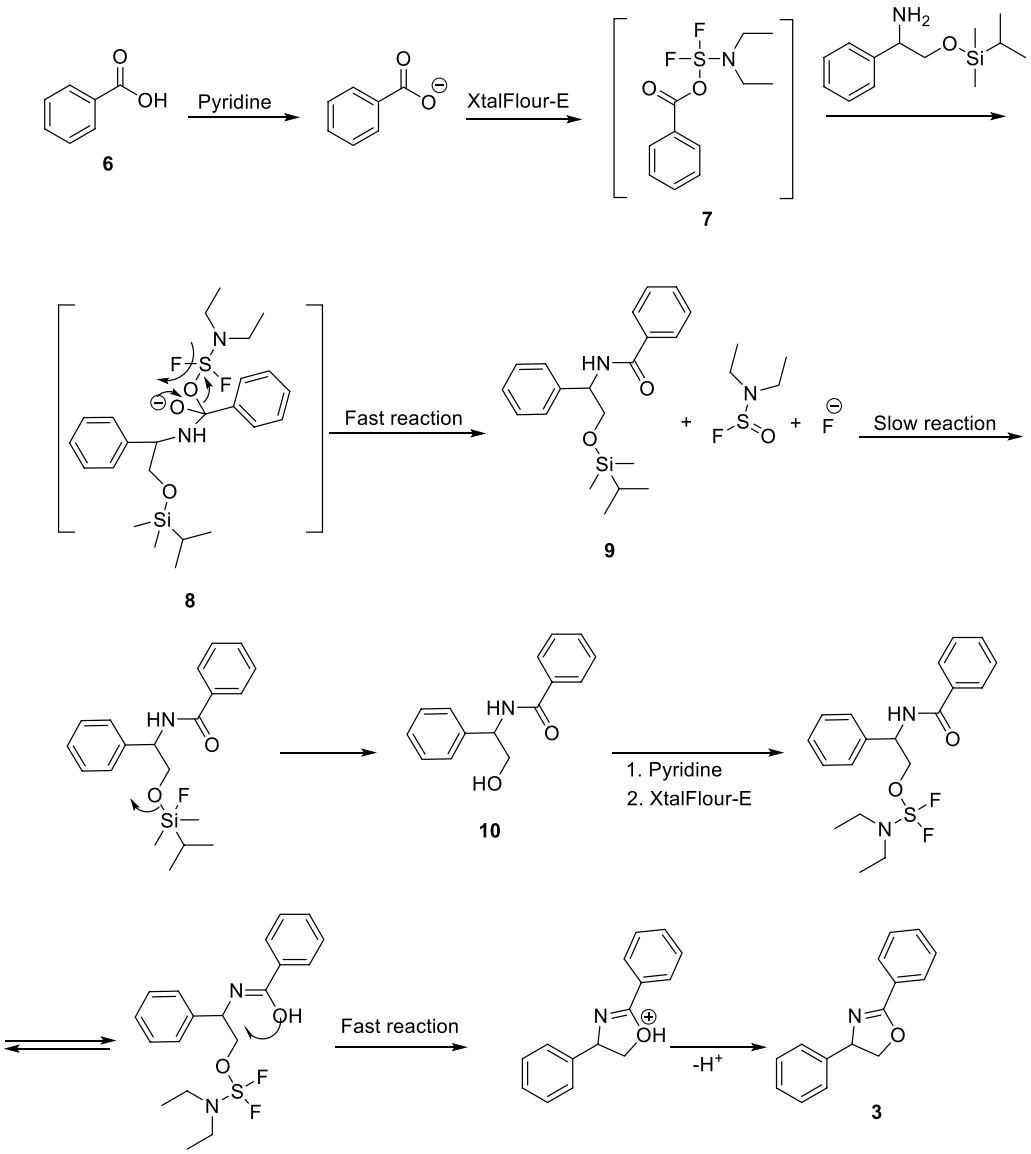
Construction of 2-oxazolines **3** from aromatic aldehydes **11** and amino alcohols **2** was designed by Sayama and co-workers using pyridinium hydrobromide perbromide (PHPB) in water at rt (Scheme 14) [74]. A range of aromatic aldehydes were analysed, which afforded good to excellent yields of the product. Imidazolines could also be obtained through the same strategy.

Other amino alcohol reactions

Herein, we have summarized the investigations of oxazoline formation from the reaction of amino alcohols with various substrates other than nitriles, carboxylic acids and aldehydes.

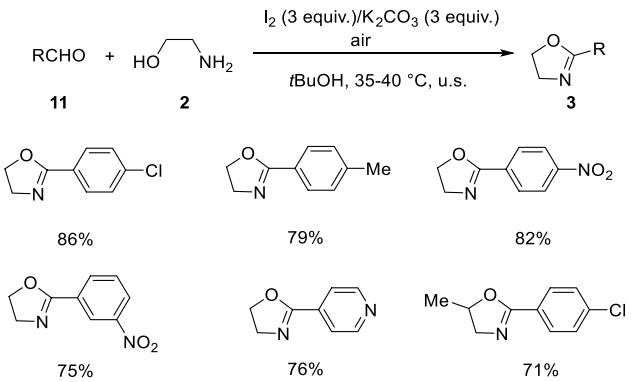
Synthesis of 2-oxazolines **3** from thioamides **12** and 2-aminoethanol **2** was reported by Pathak and co-workers

Scheme 12

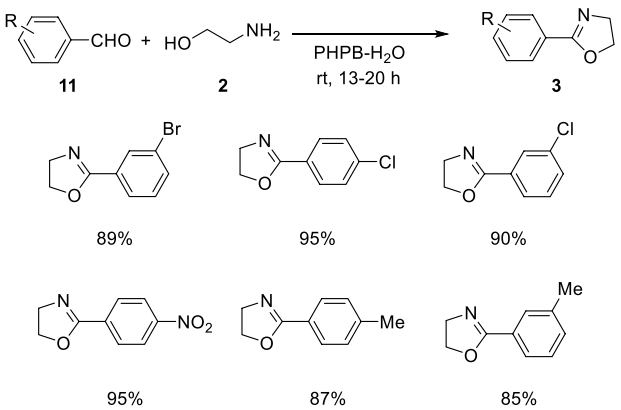


Reproduced with permission from ref. [72]

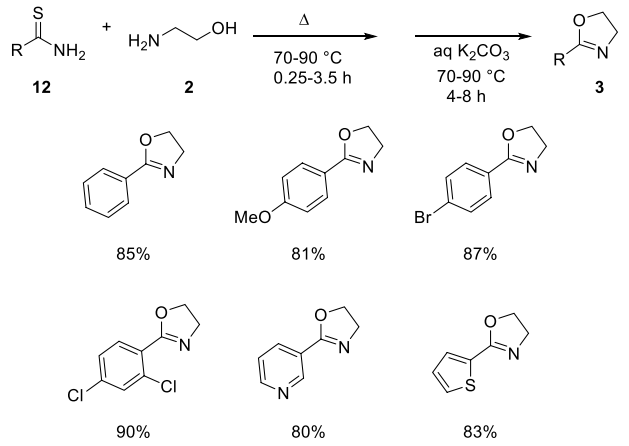
Scheme 13



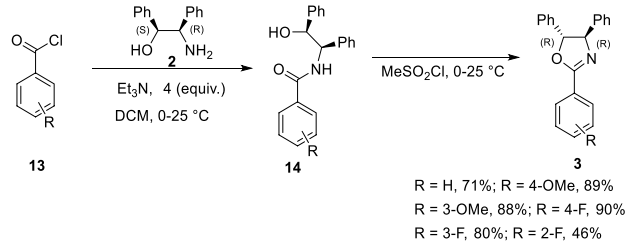
Scheme 14



Scheme 15



Scheme 16



[75]. The substrates underwent transamidation, followed by cyclodehydrosulfurization to form the desired product at 80 °C under solvent-free condition (Scheme 15). After the disappearance of thiobenzamide, the addition of aqueous potassium carbonate led to the desired product. A range of substrates were explored, which afforded the products in good to high yields. No remarkable electronic effect could be observed. However, due to steric effects, the *ortho*-substituted substrates provided comparatively lower yields.

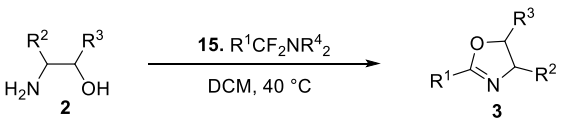
An efficient one-pot strategy towards oxazolines **3** was described by Clayden et al. by the coupling reaction between benzoyl chlorides **13** and amino alcohol **2** along with equiv. of triethylamine (Scheme 16) [76]. A β-hydroxyamide **14** was generated as an intermediate, which upon treatment with methanesulfonyl chloride led to the product formation in high yields. Here only the anti-diphenyl oxazolines are formed due to the inversion at C-5 position of oxazoline. Various substrates having different groups tolerate the reaction conditions well affording good to excellent yields. Lower yields were attained when electron-deficient moieties were present at the *ortho* position of benzoyl chlorides.

A new strategy for the synthesis of optically active oxazolines **3** from *β*-amino alcohols **2** and various *α*,*α*-difluoroalkylamines **15** was reported in DCM affording good to excellent yields (Scheme 17) [77].

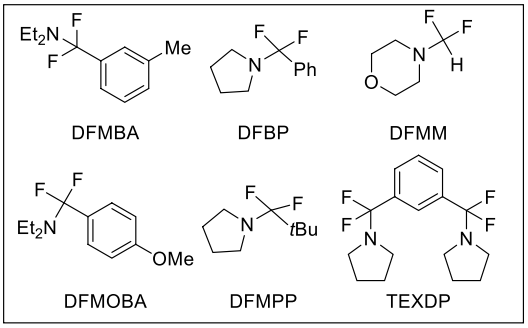
Enantioselective conversion of aminotriols **16** to oxazolines **3** through Cu-catalyzed pathway was proposed by Onomura and co-workers [78]. Here, *N*-benzoyl aminotriols **16** were used as the reactants to get the desired product in good yield upon treatment with 2.5 equiv. of *p*-TsCl, 10 mol% copper triflate, and 10 mol% (*R*,*R*)-PhBOX in presence of 4 equiv. Na_2CO_3 in acetonitrile at rt for 15 h (Scheme 18). The aminotriols underwent mono-sulfonylation followed by intramolecular ring formation to yield oxazoline diols, and finally a desymmetrization of the oxazoline diols led to the expected products.

Better yield and enantiomeric excess were observed when an electron-donating group was present at the *ortho* position of the benzoyl moiety than those at the *meta* and *para* positions. Similar trend in the yield was observed in the case of an electron-withdrawing group containing benzoyl moiety, but the yield obtained was not as high as the previous example.

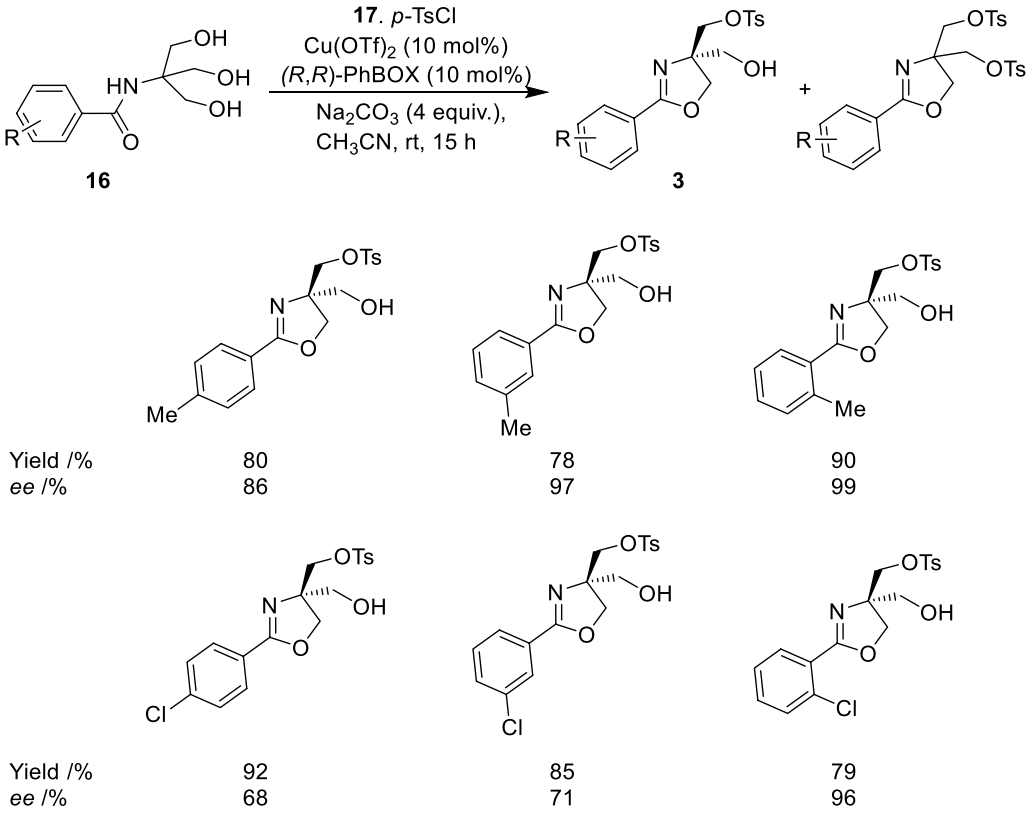
Scheme 17



R^2	R^3	$R^1CF_2NR^4_2$	Yield /%	*ee* /%
Bn	H	DFMBA	85	95
Ph	H	DFMBA	82	99
Ph	H	TFXDP	79	99
COOMe	H	DFBP	86	98
COOEt	Me	DFMBA	84	99
COOMe	Me	DFMOBA	89	99



Scheme 18



From carbonyl compounds

The structures with C=O functional group comes under the class of carbonyl compounds, which is one of the most important electrophilic groups in organic chemistry. Several explorations have been carried out on the construction of many biologically significant structures by using carbonyl compounds. Aldehydes, ketones, carboxylic acids, amides, esters, and acid chlorides are the familiar classification of carbonyl compounds based on the groups attached at the carbonyl carbon. In the underlying section we have provided the various strategies for the synthesis of oxazoline using different carbonyl compounds.

Reactions of aldehydes

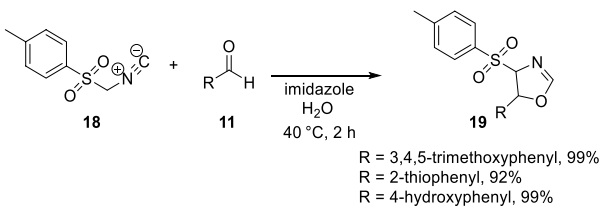
Aldehydes are important class of carbonyl compounds in which the electrophilic carbon is linked to a hydrogen atom and also to an alkyl group. Oxazolines were effectively synthesized from the reaction of aldehydes with nitriles and this proceeded through a nucleophilic addition at the carbonyl carbon to generate an intermediate and finally an intramolecular cyclization fostered the desired oxazoline.

Prakash and team disclosed a strategy which utilized aldehydes **11** and tosylmethyl isocyanide (TosMIC) [79]. **18** as the substrates in water, which also performed as an oxidant, in presence of imidazole at 40 °C to realize oxazoline **19** (Scheme 19) [80]. Different moieties on the aldehydes resulted in good to excellent yields. This strategy also discusses the application of oxazoline as an antibiofilm agent.

Diastereoselective synthesis of oxazolines **3** from methyl isocyanoacetate **20** and aldehydes **11** was established when 5 mol% of CuCl was used as a catalyst with 10 mol% of PPh_3 affording good yields of product with *trans* selectivity (Scheme 20) [81]. Substrate scope investigation revealed that both electron-rich and electron-poor aromatic rings preferentially gave the *trans* products with above 85% diastereomeric ratio.

Trifluoromethyl-substituted oxazolines **22** were synthesized efficiently through [3 + 2]-cycloaddition of α-trifluoromethylated methyl isocyanide **21** and a polar double bond in presence of 5 mol% of Ag_2CO_3 and 10 mol% DBU (Scheme 21) [82]. The in situ generation of a stable carbanion was the key step in the process. Among a range of substrates, aryl aldehydes **11** and aryl isocyanides **21** bearing electron-withdrawing and electron-neutral moieties were observed to proceed at a faster rate. Various alkyl,

Scheme 19



aryl, and heterocyclic substrates afforded excellent yields and diastereoselectivity.

An efficient catalytic strategy towards oxazolines **3** from isocyanide **23** and aldehydes **11** was developed in the presence of water along with proazaphosphatrane *(i*Bu-PAP) to activate benzylic isocyanide (Scheme 22) [83]. The basic nature of *i*Bu-PAP enables the deprotonation of isocyanide in the initial step. Various aldehydes bearing different substituents underwent the reaction realizing good to excellent yields and diastereoselectivities of product. The best selectivities were observed with sterically demanding aldehydes.

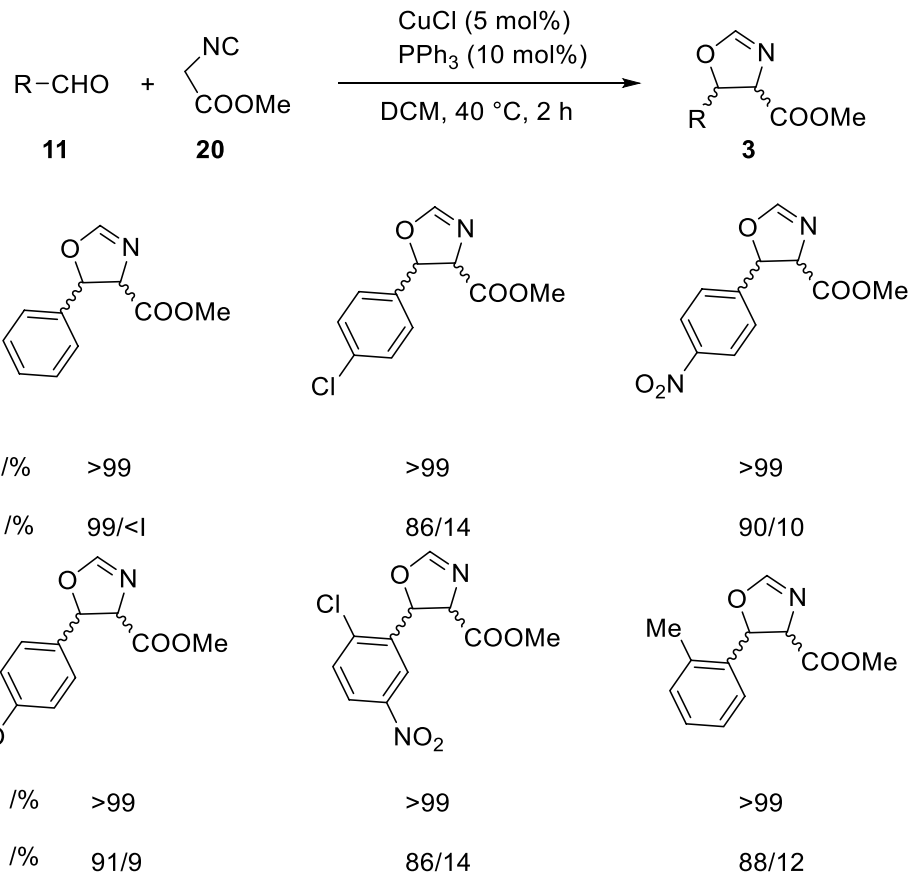
Perez and co-workers reported a methodology to generate a triazolidine gold(I) complex and studied its application in oxazoline **3** synthesis using KPF_6 as additive and N*i*Pr_2Et as base affording moderate yield and stereoselectivity of the product (Scheme 23) [84]. When the reaction was extended to the corresponding silver catalyzed oxazolines formation, the results were disappointing [85].

Verkade and co-workers developed a diastereoselective synthetic pathway towards 2-oxazolines **3** from ethyl isocyanoacetate **20** and different aldehydes **11** in the presence of 5–30 mol% of $P(RNCH_2CH_2)_3$ N-catalyst affording good yields (Scheme 24) [86]. The maximum diastereoselectivity of 95:5 was achieved when the reaction was carried out in isobutyronitrile.

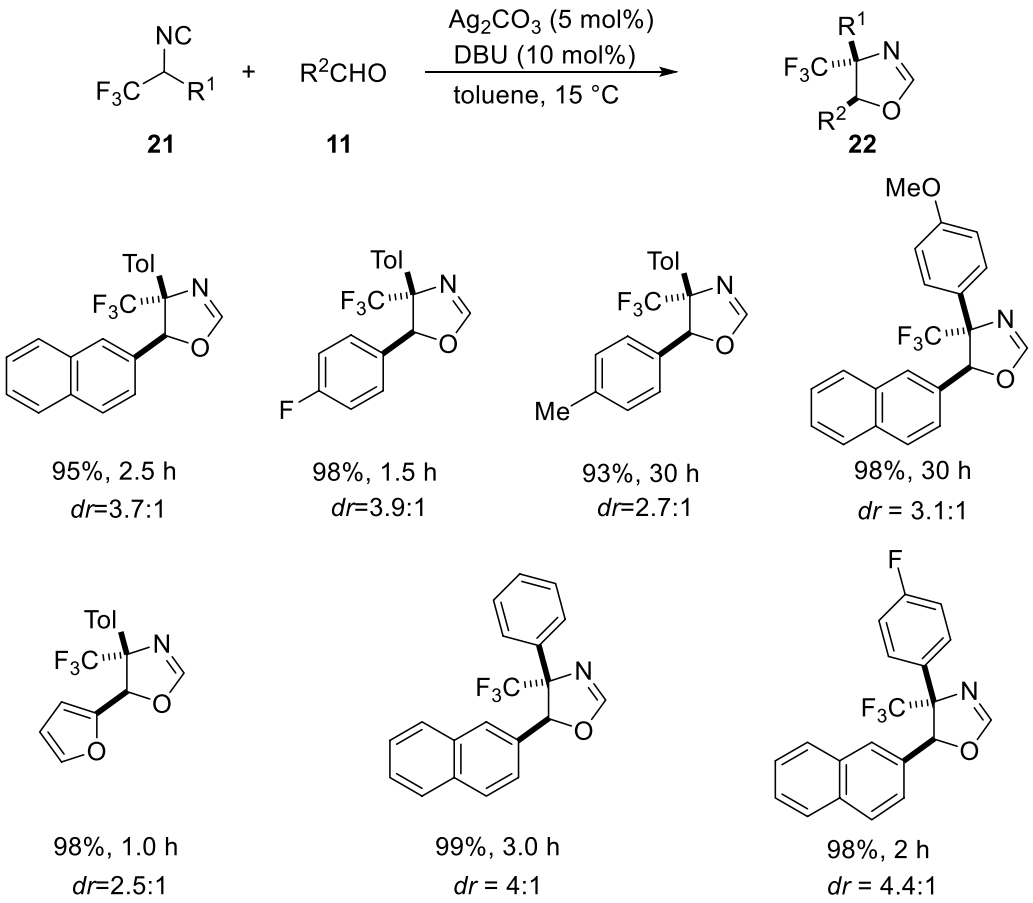
A solvent-free protocol to prepare 2-oxazolines **3** was described by Bazureau et al. by reacting imidates **24** through a cycloaddition with different aldehydes **11** at 70 °C (Scheme 25) [87]. The reaction pathway followed a cycloadduct **25** formation and the final product was attained by the removal of ethanol from it. Various oxazolines were obtained in moderate to good yields from different aldehydes. Trisubstituted oxazolines were also produced, but from ketones.

Asymmetric synthesis of oxazolines **3** was carried out effectively with chiral ferrocenylamine ligand on aldehydes **11** and nitriles **20** (Scheme 26) [88]. The stereochemistry of

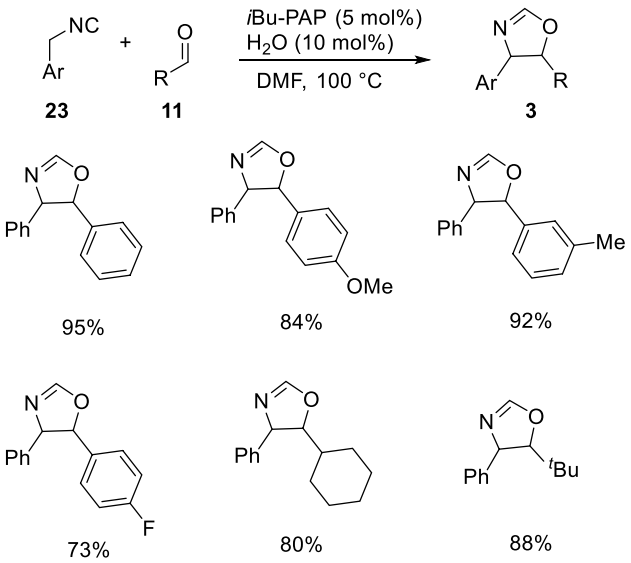
Scheme 20



Scheme 21



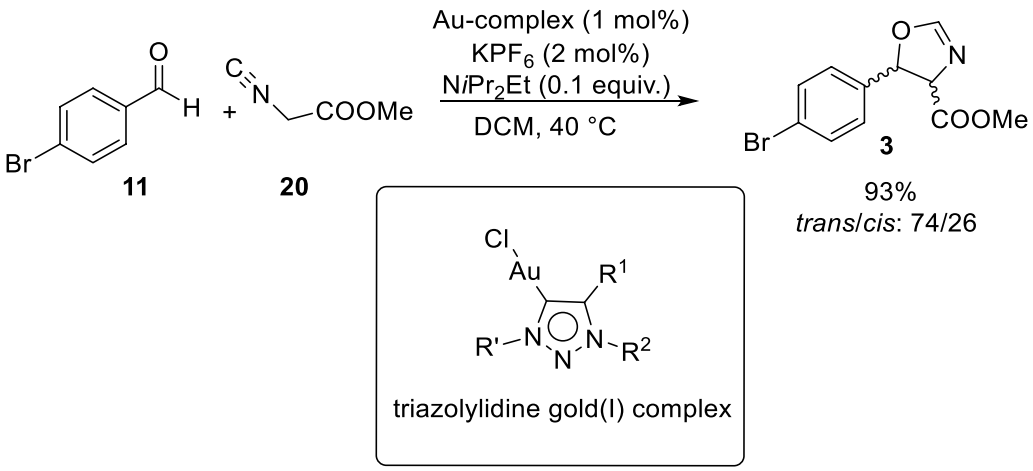
Scheme 22



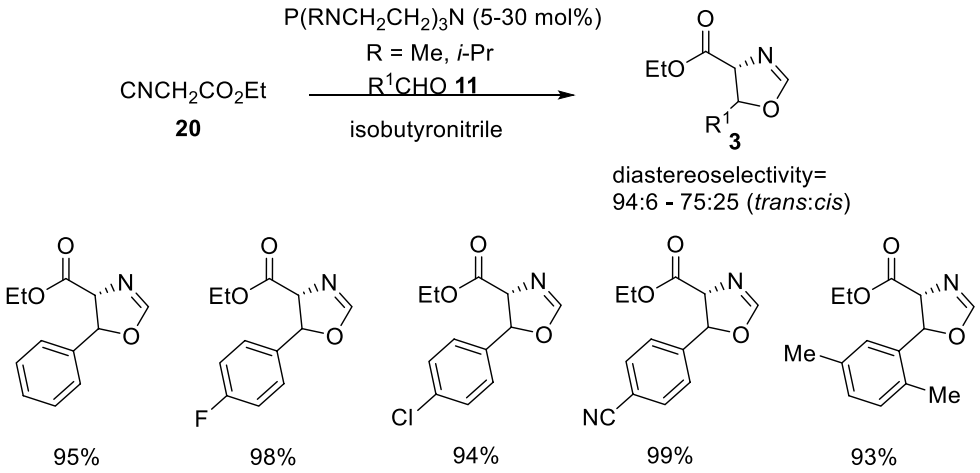
the desired oxazolines was strongly influenced by the chirality on the stereogenic carbon, which was present on the side chain of the ferrocene. Multiple trials were performed by changing the stereochemistry of ferrocenylamine ligand. In this strategy *trans*-oxazolines were selectively formed as the major product.

An efficient idea was put forward by Vchislo et al. to synthesize oxazolines **27** from tosyl methyl isocyanide **18** and propynals **26** using Et_3N as the base and $CHCl_3$ as solvent in 24 h (Scheme 27) [89]. K_2CO_3 in acetonitrile at 55 °C reduced the reaction time to 2 h and obtained comparatively good yield than the former one performed at rt. Through the same strategy oxazole was also synthesized selectively, but by using K_2CO_3 in methanol as the solvent.

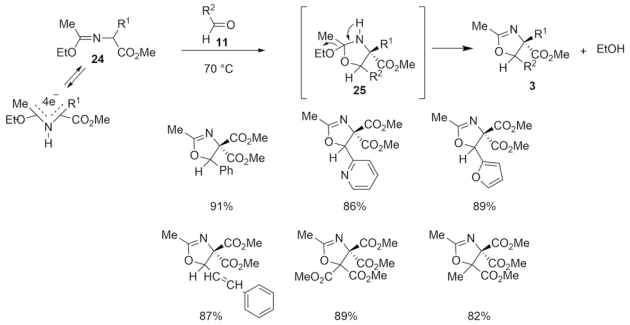
Scheme 23



Scheme 24



Scheme 25

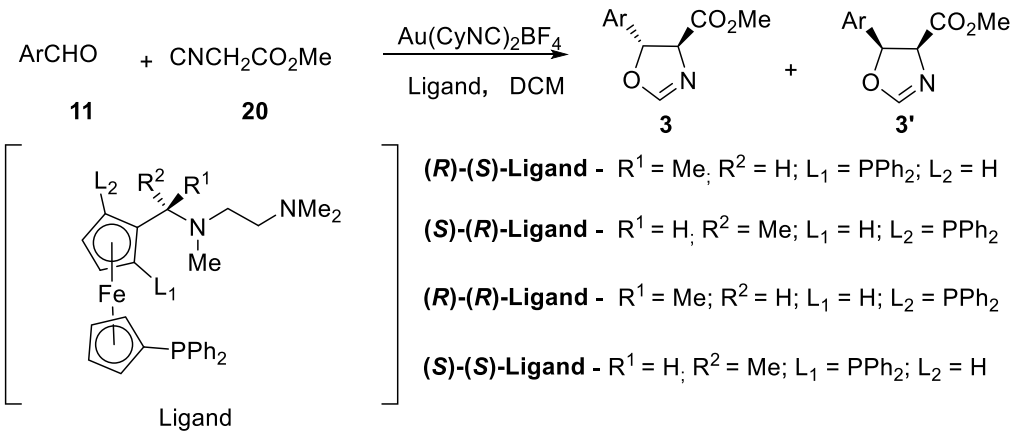


Reactions of ketones

The carbonyl carbon of ketone is bonded to two alkyl groups. The reaction mechanism for oxazoline synthesis from ketones involved a nucleophilic addition at the electrophilic centre of the ketones followed by intramolecular cyclization.

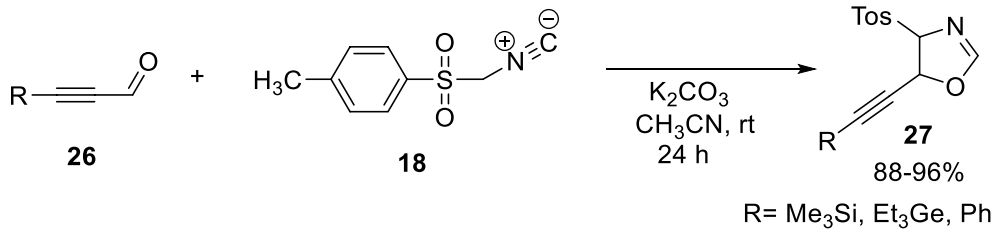
An efficient I_2-catalyzed conversion of β-acylamino ketones **28** to oxazolines **3** was reported by Wei et al. using 2 equiv. of TBHP as an oxidant and 3 equiv. of K_2CO_3 as a base (Scheme 28) [90]. New bond formation occurred between carbon and oxygen in the acylamino ketone, which was followed by dehydrogenation to form the desired product. Good to excellent yields of 2-oxazolines were achieved from various substituted acylamino ketones. Oxazoles could also be formed through this pathway.

Scheme 26



Ligand	% of *trans*	*ee* %
(*R*)-(*S*)-Ligand	90	91 (4*S*,5*R*)
(*S*)-(*S*)-Ligand	84	41 (4*S*,5*S*)
(*S*)-(*R*)-Ligand	90	90 (4*R*, 5*R*)

Scheme 27



From acid chlorides

Acid chlorides are one of the classes of carbonyl compounds where the electrophilic carbon is fastened to a chlorine atom and also to an alkyl chain. The electrophilicity of the carbonyl carbon is enhanced by the chlorine due to its electron-withdrawing effect. Here also a nucleophilic attack on acid chloride and a final cyclization led to the oxazoline formation.

A palladium-catalyzed cyclization en route to 2-oxazoline **30** from acid chlorides **13** and propargylamines **29** in presence of 5 mol% $Pd(OAc)_2$ with triethylamine as base in toluene at 100 °C was achieved by Telvekar et al., which proceeded through in situ subsequential nucleophilic addition/elimination followed by *5-exo dig* cyclization (Scheme 29) [91]. Several acid chlorides having different groups gave moderate to high yields except the heterocyclic one.

From amides

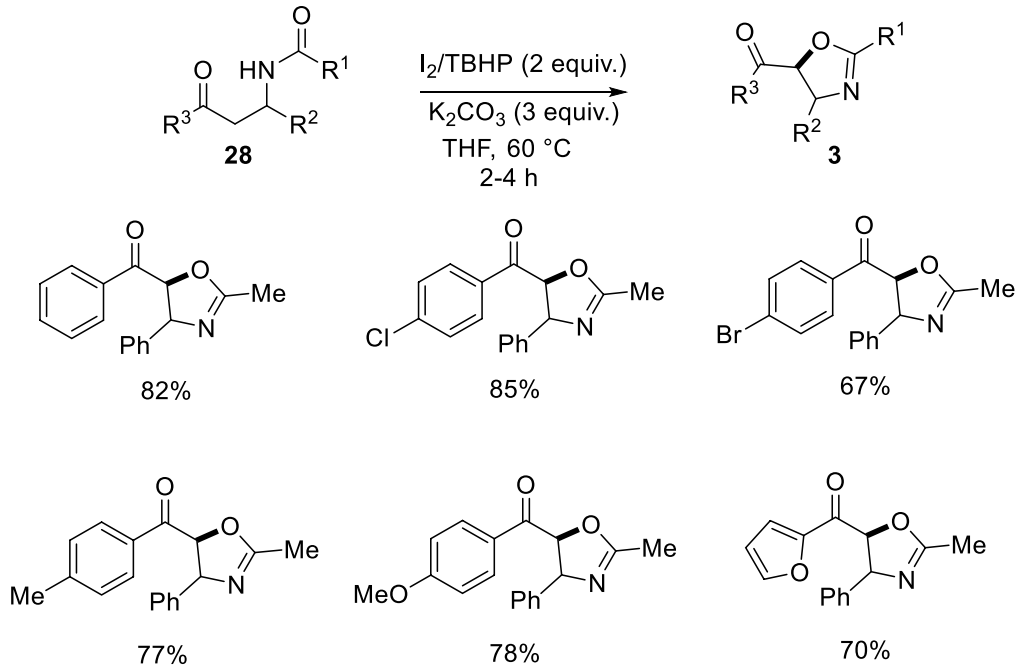
Amides are another class of carbonyl compounds in which the carbonyl carbon is bonded to amino moiety and to an alkyl group. Among the various amides analysed, allylamides were highly employed for oxazoline generation in most of the studies. On this account, we have compiled various strategies of oxazoline synthesis from allylamides and this section also deals with the reactions of some other amides.

Reactions of allylamides

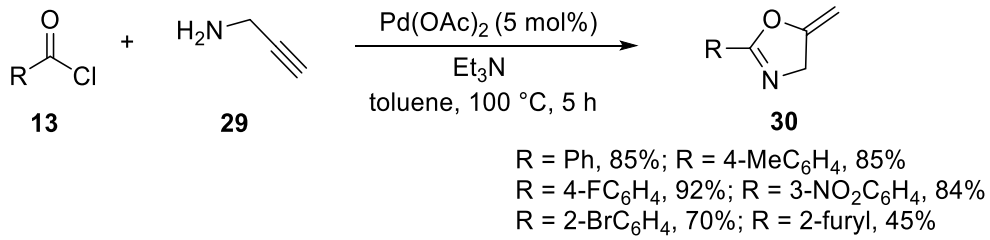
Allylamides contains a double bond at allyl position of nitrogen in the amide group. Mostly, the conversion of allylamides towards oxazolines progressed through an intramolecular cyclization and a suitable elimination.

The electrophilic cyclization of allylic amides **31** was reported as a new preparative method for 5-[(phenyl thio) methyl] derivatives of oxazoline **33** (Scheme 30) [92]. This reaction was enhanced by Brønsted acid and tetrabutyl-ammonium chloride (TBAC). The notable advantage of this protocol is that it can be done under mild conditions. Here, the allylic amide reacted with PhS-succinimide **32** under optimal condition of 20 mol% TBAC and 20 mol% camphor sulfonic acid (CSA) in DMF at 40 °C. There were no remarkable electronic effects of the substituents on aryl group of benzamide.

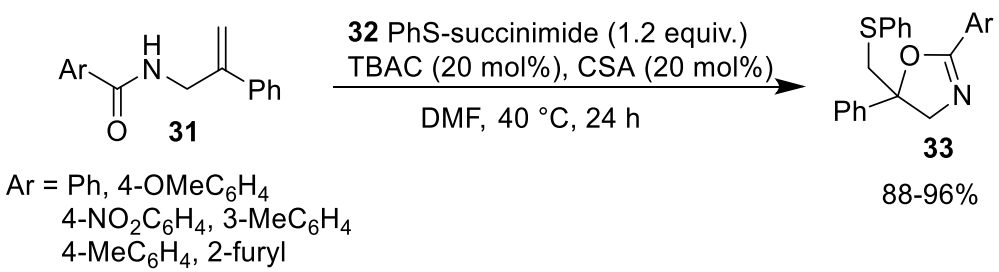
Scheme 28



Scheme 29



Scheme 30



A different approach towards oxazoline **33** was carried out by the reaction of *N*-allylamides **31** with $ArS(ArSSAr)^+$ **35** which was generated electrochemically at − 78 °C in moderate yields (Scheme 31) [93]. The present reaction involves two steps, the formation of $ArS(ArSSAr)^+$ followed by the reaction of allylamide and $ArS(ArSSAr)^+$. The substrate scope studies revealed that good yield was gained when Ar of ArSSAr **34** was *p*-FC_6H_4. The above reactants could also be directed to render the product through in situ electrochemical oxidation (Scheme 32). A possible mechanism for the reaction is also proposed (Scheme 33).

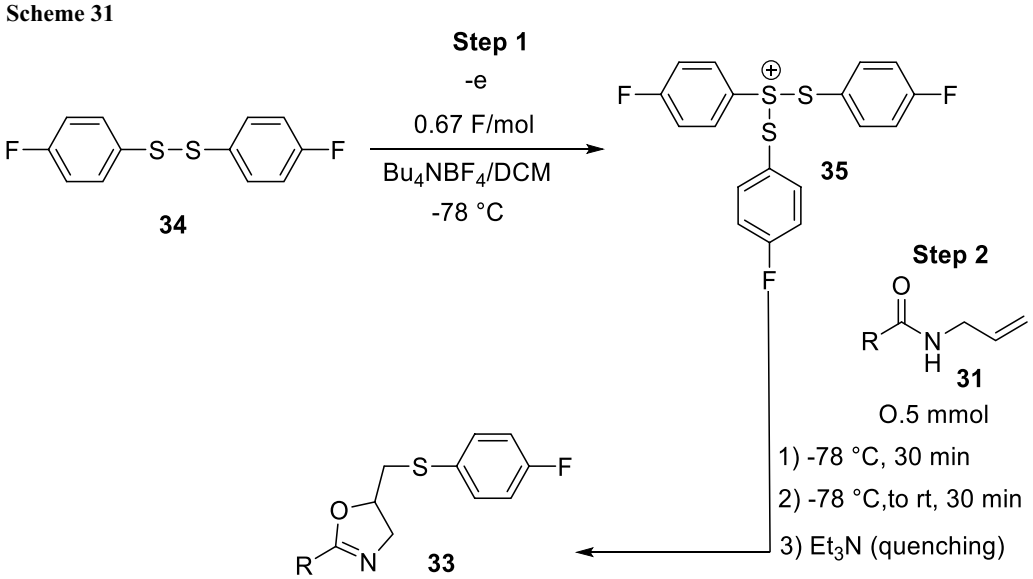
An efficient method towards oxazolines **3** using an organocatalyst was developed by Kokotos and co-workers in presence of H_2O_2 and aq. buffer [94]. Here the allylamides **31** were converted to the product through an epoxide intermediate **36** (Scheme 34). The epoxide formation occurred effectively with 20 mol% $PhCOCF_3$, which is used as an organocatalyst. This resulted in an intermediate formation at rt. In the second step, maximum yield of product was achieved with *t*BuOK in DCM at 50 °C. Both aromatic and aliphatic allylamides afforded high yields of the product. Dihydrooxazines could also be formed under this protocol.

Bisallylic amide **37** was converted enantioselectively to oxazoline **3** via desymmetrization of the amide through catalytic bromocyclization with BINAP monoxide by Hamashima et al. (Scheme 35) [95]. Here, 10 mol% of this catalyst along with 1.2 equiv. of N-bromosuccinimide (NBS) **38** at − 78 °C provided the product in good yield and enantioselectivity with preferential formation of the *cis* isomer of product over the *trans*.

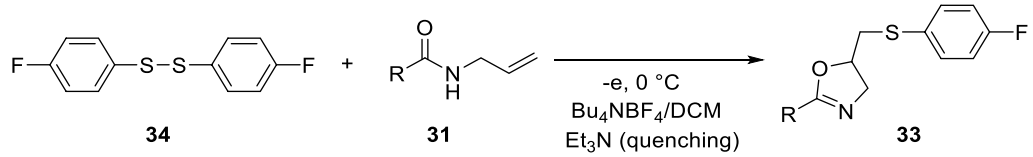
The aromatic substrates having different groups at *ortho*, *meta*, and *para* offered excellent yields and stereoselectivity except for the *ortho*-methyl one, which showed lesser selectivity. Furyl ring also delivered good enantioselectivity.

A transition metal-free approach towards oxazoline **3** from *N*-allylamides **39** was developed by Krishna and co-workers through an intramolecular cyclization strategy using 2.5 equiv. of $PhI(OAc)_2$ together with 10 equiv. of hydrogen fluoride-pyridine system (HF·Py) (Scheme 36) [96]. A variety of substrates carrying electron-rich and electron-deficient substituents were analysed, which offered good yields

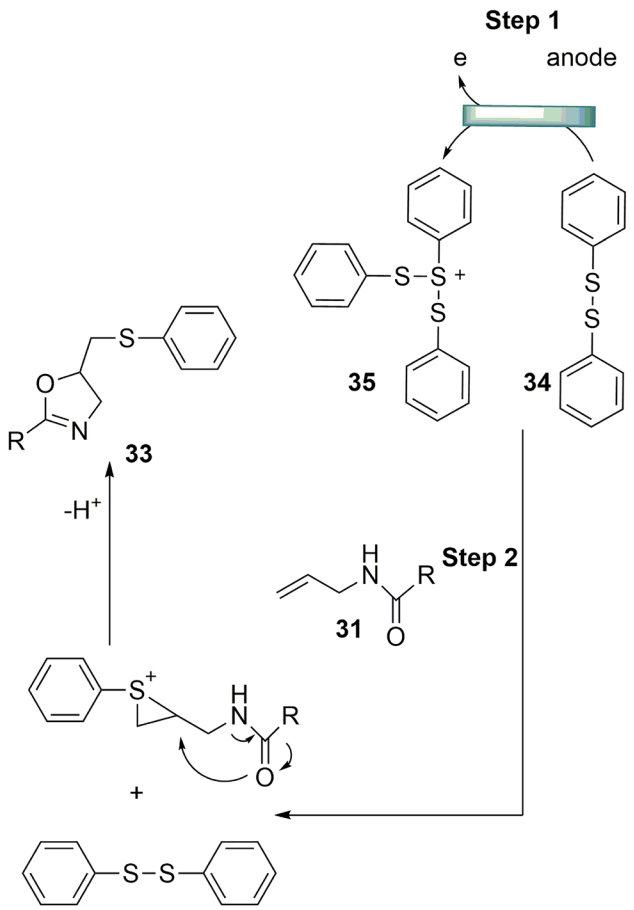
Scheme 31



Scheme 32



Scheme 33



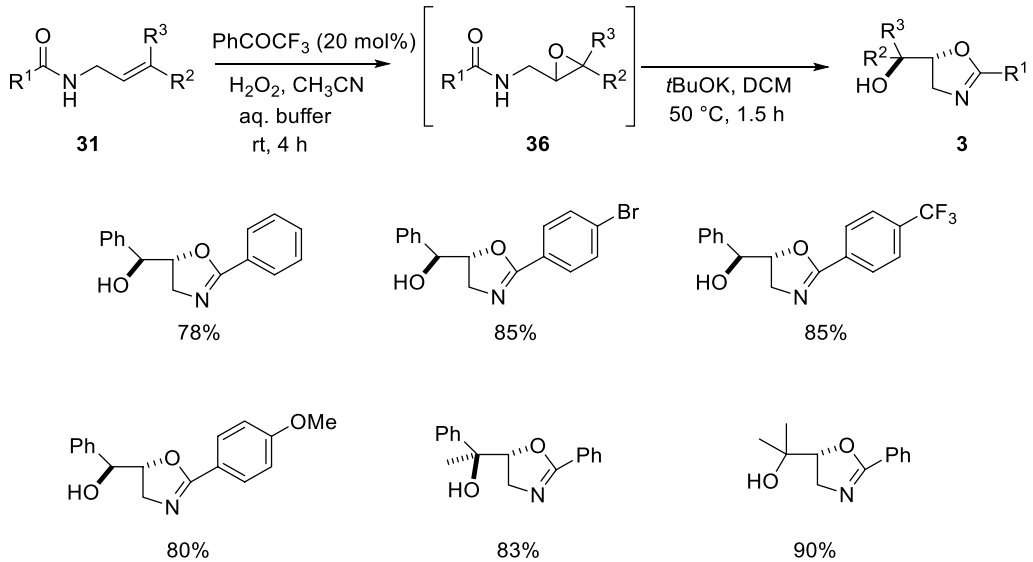
of the product. A feasible mechanism was also described by the authors (Scheme 37).

Wan and co-workers have proposed a NIS-mediated synthetic pathway for oxazoline **3** formation from allylamides **40** in DCM at rt (Scheme 38) [97]. The substrate underwent a ring-closing followed by ring opening en route to the aliphatic compound having iodine group **41**, and this was the starting molecule for oxazoline formation. The efficient formation of oxazolines was carried out by NaN_3 and PPh_3. In this study H_2O was used as a nucleophile in the generation of iodinated chain product.

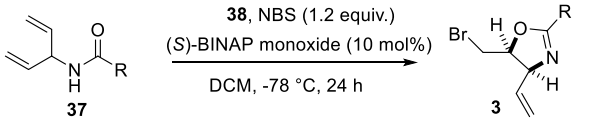
A novel protocol to synthesize oxazolines **3** from allylic amides **31** was established by Nicewicz et al. (Scheme 39) [98]. A dual catalytic method was involved in the reaction and this was performed under mild conditions. The combined effect of 9-mesityl-*N*-methylacridinium tetrafluoroborate and phenyl disulfide provided better yield and anti-Markovnikov selectivity for the desired product. A variety of allylic amides were analysed and rendered moderate to good yields**.**

Iodine(III)-assisted conversion of *N*-allylamides **31** towards oxazolines **3** was reported involving 1.2 equiv. of $PhI(OAc)_2$ **43** as catalyst along with 1.2 equiv. of $BF_3.OEt_2$ as additive at rt in presence of 10 equiv. AcOH in DCM solvent (Scheme 40) [99]. Different substrates were analysed to get moderate to good yields and branched substrates provided good diastereoselectivity also (Scheme 41). The suggested mechanism was also portrayed (Scheme 42).

Scheme 34



Scheme 35



R	Yield /%	*ee* /%	*cis/trans*
3-BrC_6H_4	87	90	12:1
4-BrC_6H_4	87	92	14:1
3-$OMeC_6H_4$	92	91	16:1
4-$OMeC_6H_4$	88	95	15:1
2-MeC_6H_4	85	56	11:1
2-furyl	89	86	11:1

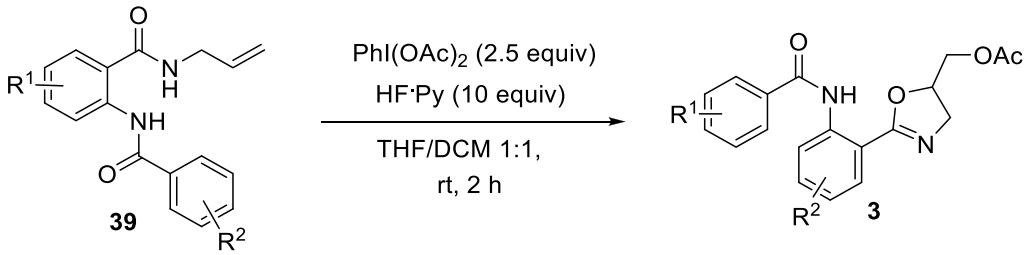
Reactions of other amides

Hither we have gathered various synthetic strategies for the formation of oxazolines by using different types of amides other than allylamide.

Palladium-catalyzed synthesis of oxazolines **3** from amides **44** was reported by Shi et al. [100]. Here, the metal catalyst has functionalized the methyl C–H bond. The optimal conditions involve 5 mol% of $Pd(OAc)_2$ along with 2 equiv. of $CuCl_2$ and 5 equiv. of acetic acid at 120 °C (Scheme 43). The generation of a chlorinated intermediate and it's in situ capture was observed through the preliminary studies. As a further extension, *β*-amino alcohols could also be synthesized from the obtained oxazolines.

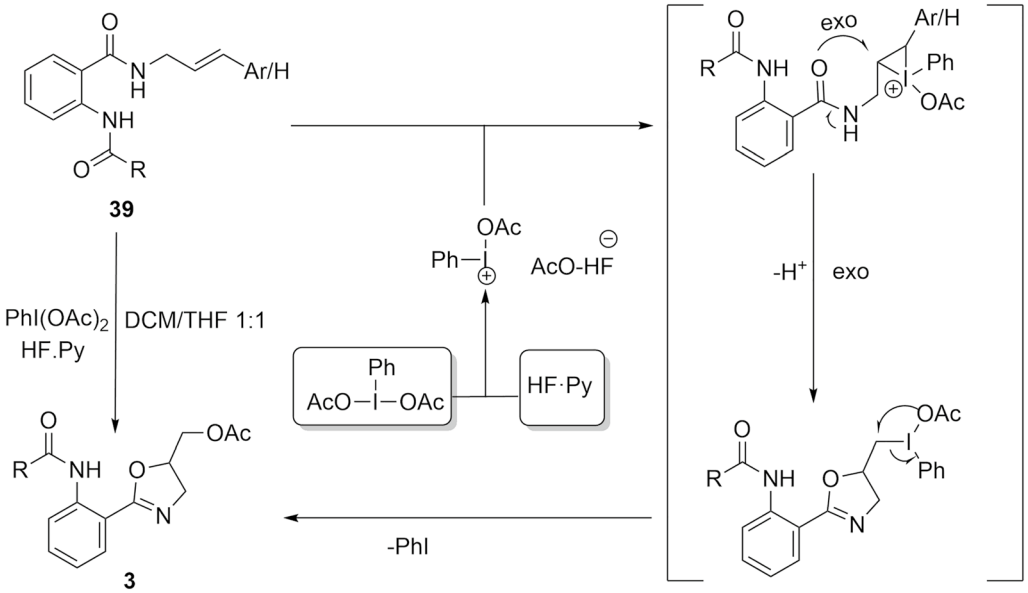
A novel protocol to synthesize oxazolines **3** from amides **46** and alkenes **45** was proposed by Minataka et al. (Scheme 44) [101]. The reaction was effectively carried out

Scheme 36

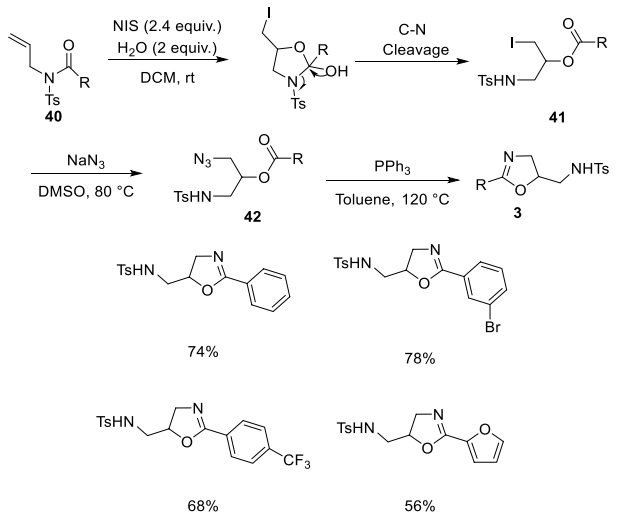


R^1 = 4-MeO-Ph, R^2 = Ph, 80% R^1 = 4-CF_3-Ph, R^2 = Ph, 90%
R^1 = 4-F-Ph, R^2 = Ph, 85% R^1 = 4-CF_3-Ph, R^2 = 3-F-Ph, 87%
R^1 = Ph, R^2 = 4-Cl-Ph,73% R^1 = Ph, R^2 = 3-F-Ph, 75%

Scheme 37



Scheme 38



with 1.5 mmol of *tert*-butyl hypoiodite (*t*BuOI), which was generated in situ from 1.5 mmol of *t*BuOCl and 1.5 mmol of NaI. Maximum yields of product were obtained when acetonitrile was used as the solvent at rt. *p*-Nitrobenzamide exhibited better conversion among other amides. Various aliphatic and aromatic olefins were analysed, which achieved moderate to good yields. The authors also proposed a possible mechanism for the reaction (Scheme 45).

Another catalytic protocol to synthesize 2-oxazolines **3** was developed by Sun and co-workers [102]. The intramolecular cyclization of oxetane **47** to oxazoline proceeded in presence of 10 mol% of $In(OTf)_3$ in the presence of DCM at 40 °C (Scheme 46). Both aliphatic and aromatic amide bearing oxetane ring resulted in remarkable yields.

A transition-metal-free strategy of [3 + 2] cycloaddition between 1,2-benzisoxazole **48** and azaoxyallyl cation **49** was reported in presence of 2 equiv. of Na_2CO_3 as the base in hexafluoroisopropanol (HFIP) (Scheme 47) [103]. It was observed that electron deficient group on 1,2-benzisoxazole offered good to excellent yields of oxazoline **50**. The authors also suggested a possible mechanism of this cycloaddition (Scheme 48).

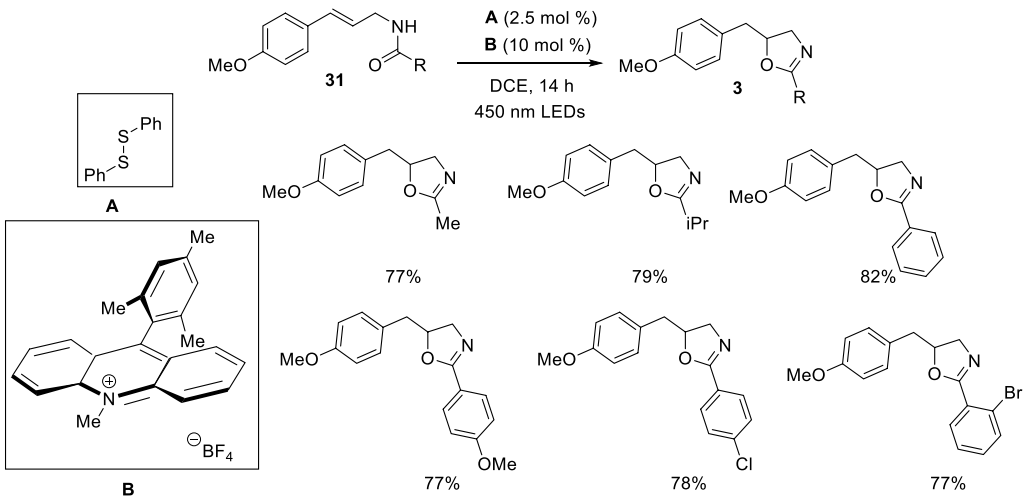
A similar protocol towards oxazoline **50** was also reported by Xuanzi et al., which involved the use of NaOH as base in hexafluoroisopropanol under a mild and transition-metal-free condition (Scheme 49) [104]. Both electron-donating and electron-withdrawing species on 1,2-benzisoxazole **48** underwent the reaction smoothly affording good amount of the products.

Copper-catalyzed synthesis of derivatives of oxazolines **30** from 3-aryl propargylamides **51** and diaryliodonium salts **52** was established (Scheme 50) [105]. An exo double bond having complete substitutions was generated on the heterocyclic ring. Maximum yield was achieved under the condition of 10 mol% of CuCl in EtOAc at 50 °C. Various substituted 3-aryl propargylamides and iodonium salts were examined. Which afforded moderate to good yields. A plausible mechanism was described by the authors (Scheme 51).

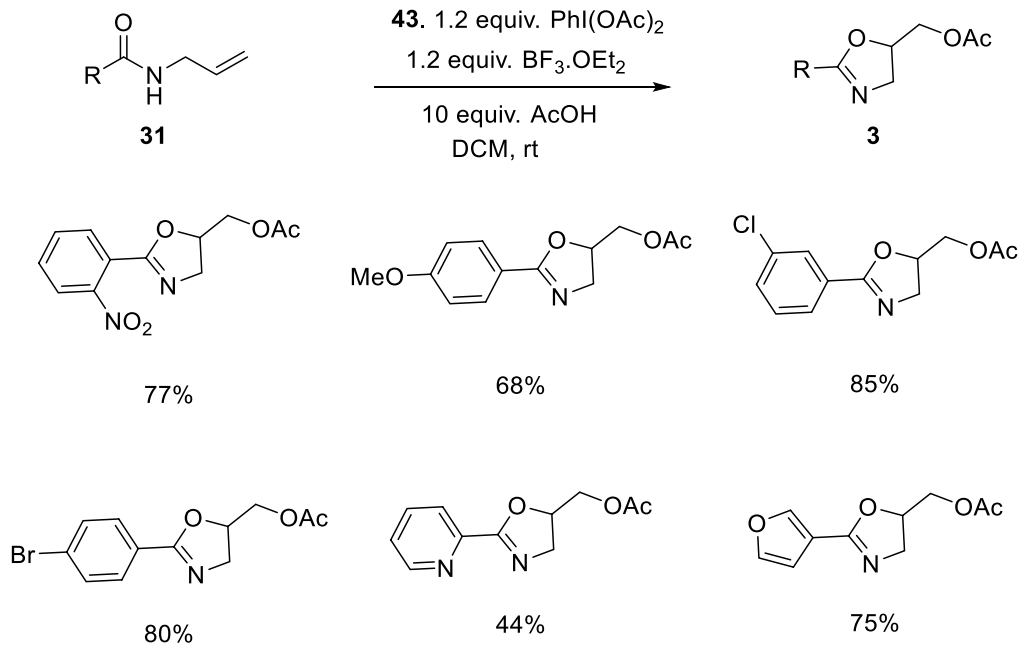
An efficient conversion of β-hydroxy amides **53** with Deoxo-Fluor towards oxazolines **3** was proposed by Ley and co-workers using $NaHCO_3$ in anhydrous DCM affording excellent yields and diastereoselectivities (Scheme 52) [106]. Further oxidation of the oxazolines towards oxazoles was also studied.

Molybdenum oxides were found to be effective catalysts in the preparation of oxazolines from *N*-acylserines as well as *N*-acylthreonines **53** [107]. Here, the maximum yields

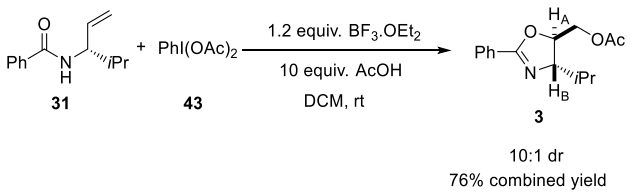
Scheme 39



Scheme 40



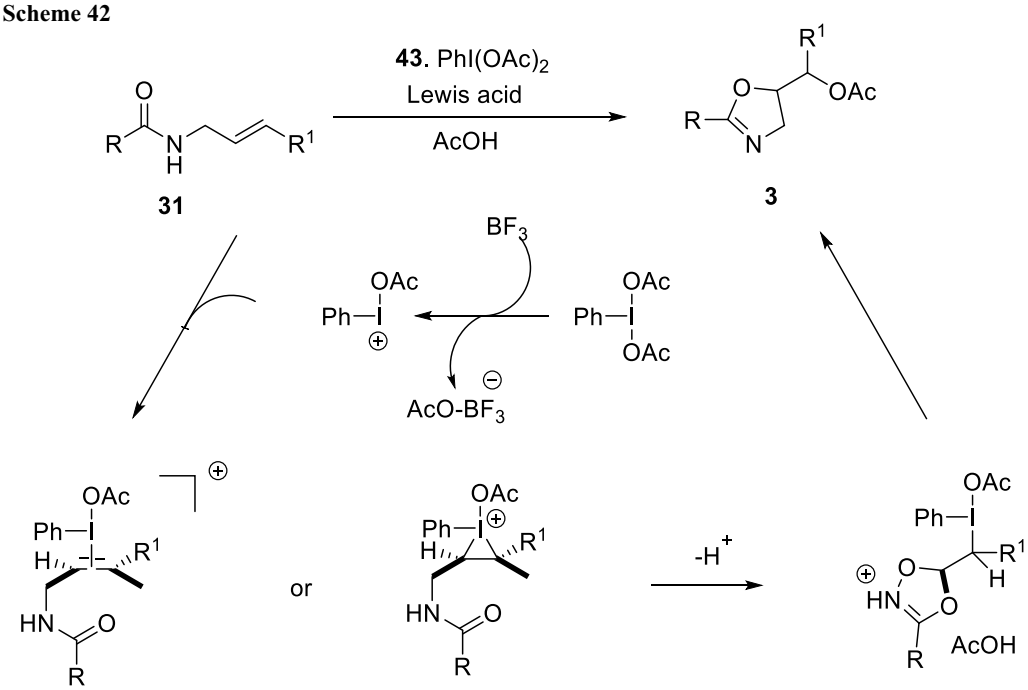
Scheme 41



of product were observed when 10 mol% of catalyst was used in toluene (Scheme 53). Bis-oxazolines **5** were also synthesized from *bis*-amides **54** together with 20 mol% of $(NH_4)_2MoO_4$ (Scheme 54).

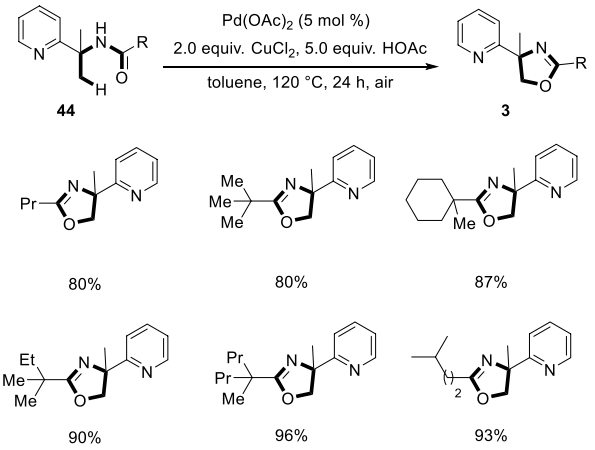
Synthesis of oxazolines **3** was also achieved by Wuts and co-workers by using Vilsmeier reagent **55** [108]. Here

Scheme 42

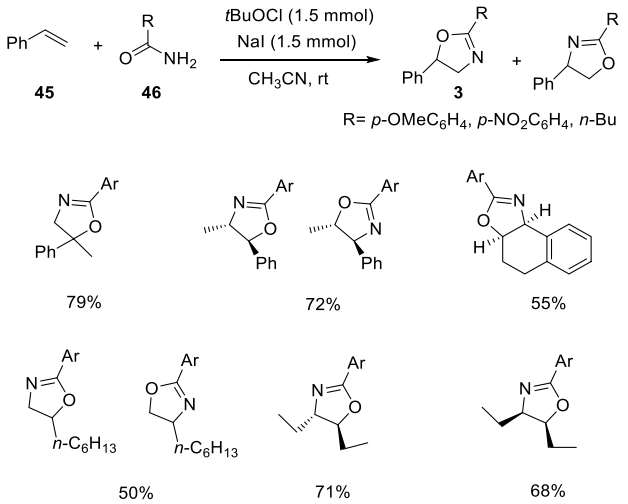


Reproduced with permission from ref. [99]

Scheme 43



Scheme 44



anti amido alcohols **53** were successfully converted into the desired oxazolines having inverted configuration at the alcohol (Scheme 55). A variety of substrates were examined, which afforded good to high yields. In some cases, a chloride product **56** was also obtained along with the expected oxazoline. This chloride was further converted to oxazoline upon reaction with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (Scheme 56).

Ingress to a range of oxazolines from 2-amido allylic alcohols was achieved by Yang and group [109]. Here, various 2-amido allylic alcohols reacted with cyclohexyl-fused SPINOL-derived phosphoric acids (Cy-SPA) in toluene at 10 °C to afford the desired oxazolines in moderate yields (Scheme 57). The oxazolines were realized with exceptional enantioselectivities. Excellent substrate scope was a major highlight of this protocol.

Solid-phase synthesis of 2-oxazolines **3** from peptides **57** was described by Meldal and co-workers [110]. The procedure included iodination of peptides having serine, followed by a nucleophilic attack of the carbonyl oxygen from the nearest amino acid (Scheme 58). A range of substrates were investigated with different peptides and afforded moderate to good yields. Phosphine 2-oxazoline ligands **58**, **59** were also synthesized in this study (Scheme 59).

An efficient route to the diastereoselective synthesis of derivatives of oxazoline **3** using precursors of acyl imine **43** and sulfur ylides **60** was developed as an extension of Corey-Chaykovsky reaction [111]. Maximum selectivity of 1:2 mixture of aziridine oxazoline was obtained when 3 equiv. of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was used as the base in DCM (Scheme 60). Further conversion of aziridine **61** to oxazoline was realized with good yield when BF_3OEt_2 was used as the Lewis acid. Here, the thermodynamically stable *trans* product dominated as the major diastereomer.

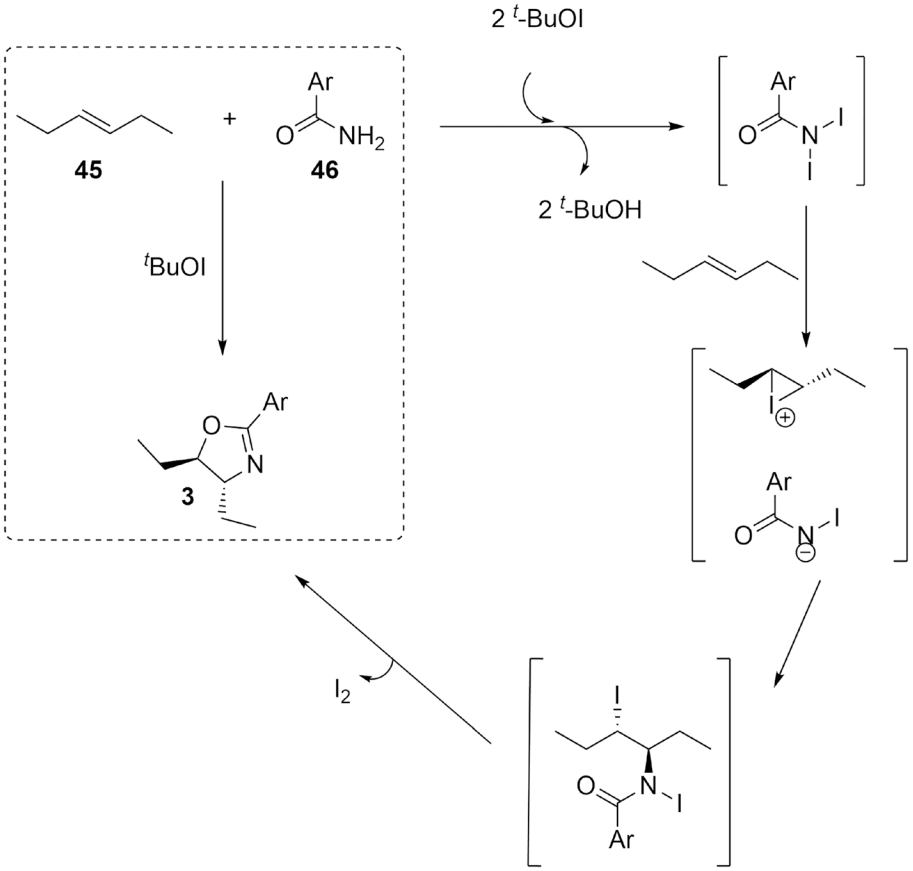
Analysis of the scope of substrate of sulfonium ylides was performed with several substituents having electron-donating and electron-withdrawing groups, and resulted in 30–70% yield. The nitro substituted aromatic ring showed exceptionally low yield due to Stevens rearrangement [112, 113] of sulfonium salt and it was surpassed by using tetrahydro thiophene as the substrate (Scheme 61). A proposed mechanism of ring opening of aziridine to oxazoline was also discussed (Scheme 62). Here, the cationic intermediate **62** was generated through the ring expansion process and their isomerisation led to the *trans*-oxazoline as major product.

The Lewis acid assisted cyclization of acetylenic amides **50** to construct oxazolines **30** was designed by Wang et al. using 1 equiv. of ZnI_2 as the Lewis acid at rt (Scheme 63) [114]. The starting amides were generated from the corresponding amines **63** and acid chlorides **13** by using 2 equiv. of Et_3N. Varieties of amides tolerated the reaction conditions and achieved good to excellent yields. Substrates having electron-rich species at *ortho*, *meta*, and *para* positions provided better yields. Oxazoles could also be formed from the same amides with $FeCl_3$.

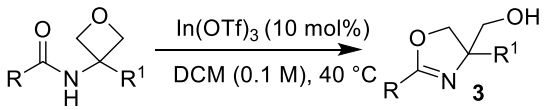
From alkenes

Alkenes are the hydrocarbons having C=C functional group in their alkyl chain. Alkenes possess high synthetic importance as they serve as substrates for several organic compounds. Oxazolines can be constructed by using alkenes, and this generally occurred through an addition reaction on alkene by suitable substrate, later an intramolecular cyclization provided the desired product.

Scheme 45



Scheme 46



R = Ph, R^1 = H, 93%
R = 4-ClC_6H_4, R^1= H, 92%
R = 4-$NO_2C_6H_4$, R^1= H, 90%
R = 4-CNC_6H_4, R^1 = H, 89%
R = 2-MeC_6H_4, R^1 = H, 90%
R = 2-naphthyl, R^1 = H, 90%

Efficient conversion of the alkenes towards oxazolines in a single step was accomplished using nitriles and 0.05 equiv. of $Cu(OTf)_3$ or $Zn(OTf)_3$ together with 1.2 equiv. of $NaHCO_3$ and same equiv. of water (Scheme 64) [115]. Several benzonitriles and acetonitriles were tried against different alkenes and obtained high yields and good stereoselectivities.

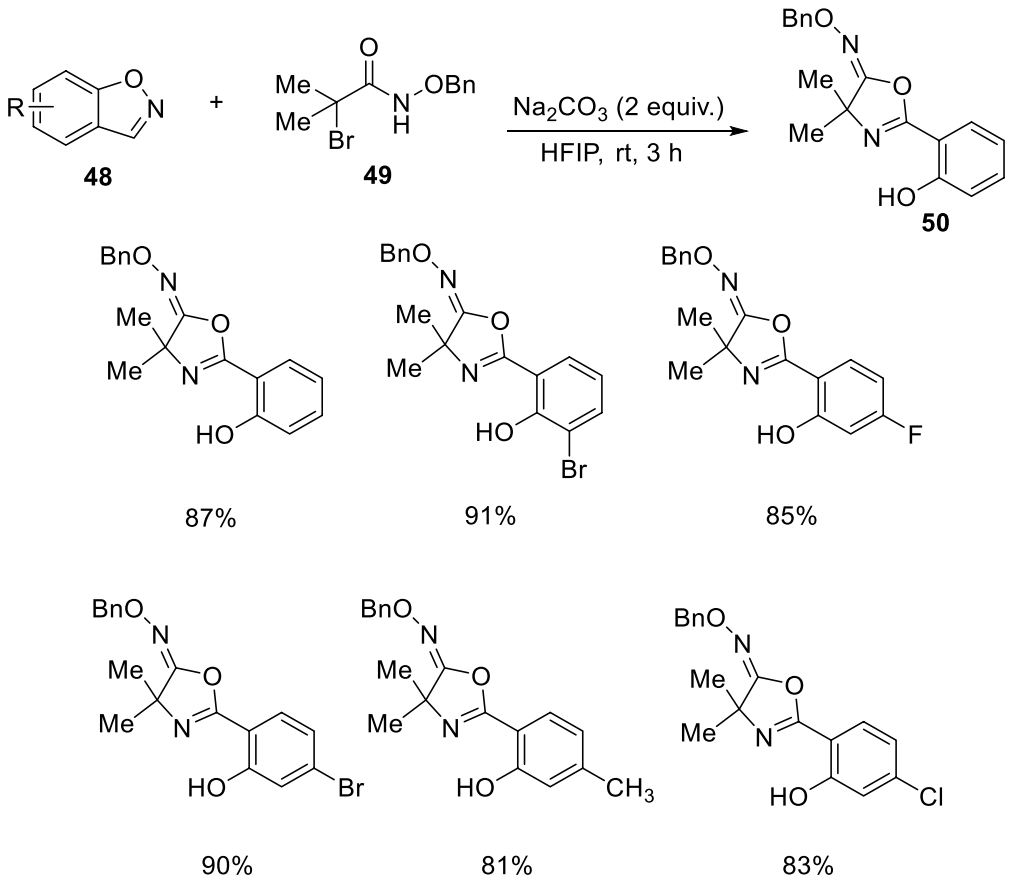
A novel protocol to prepare chiral oxazolines **3** from olefins **45** was achieved by reacting olefins with chiral nitridomanganese complex **64** in the presence of acid chlorides **13** (Scheme 65) [116]. Various styrene derivatives and acid chlorides were analysed and obtained good to excellent yields. *Trans*-styrene derivatives were converted to the desired product with excellent yields than the *cis*-styrenes. The reaction protocol was performed with high enantioselectivity of the *trans* product.

Tellurium-based methodology to synthesise 2-oxazoline **3** was described involving reaction of an alkene **45** with benzene tellurinyl trifluoroacetate at 75 °C in the presence of boron trifluoride etherate and nitriles **1** (Scheme 66) [117]. The desired product was obtained through the amidotrellurinylation pathway.

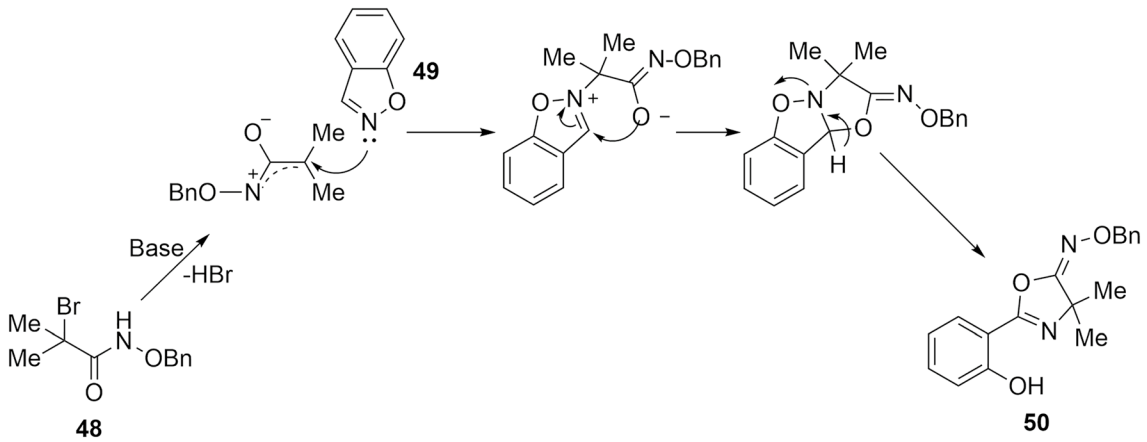
A novel strategy towards oxazoline **3** through regioselective cycloaddition activated by visible light was disclosed by reacting benzoyl azide **65** and alkene **45** using 2.5 mol% of $Ru(bPy)_3Cl_2.6H_2O$ as the photocatalyst and 2 equiv. of H_3PO_4 as an additive affording moderate yields (Scheme 67) [118]. This work was extended to synthesize a bioactive compound having oxazoline moiety (Scheme 68). The group has also given a plausible mechanism for the reaction (Scheme 69).

Tong and co-workers proposed a 1,3-dipolar cycloaddition of nitrile oxide **66** with alkene **45** or alkyne **67**

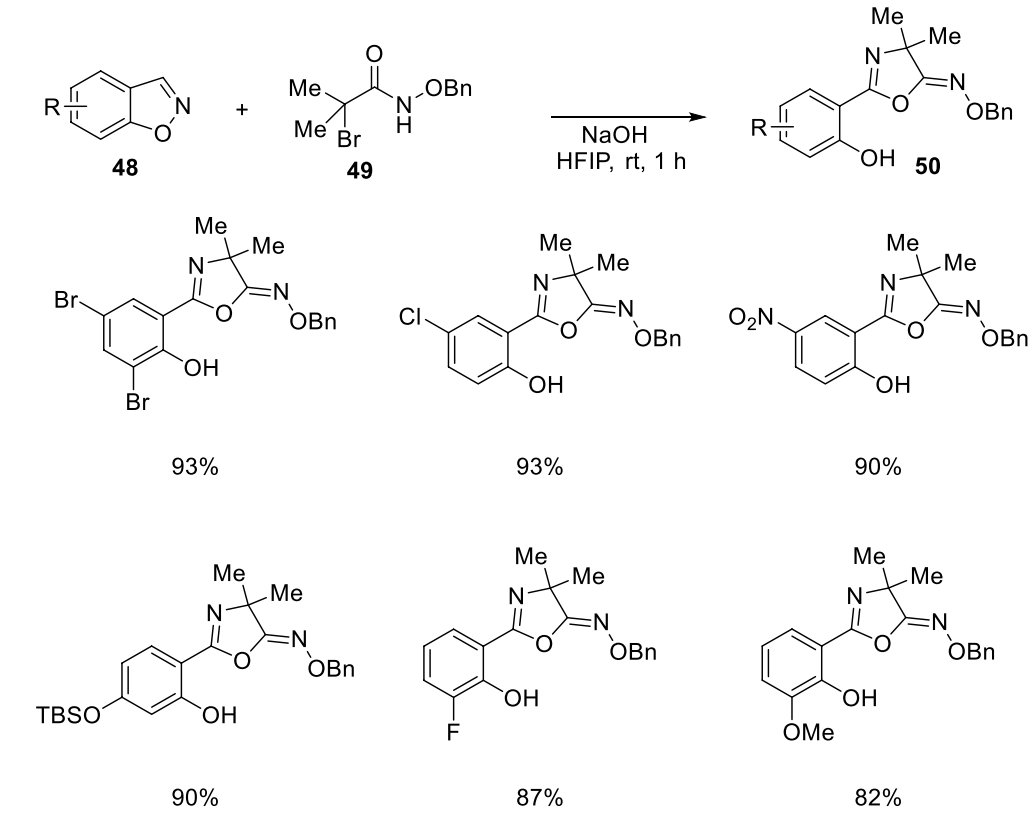
Scheme 47



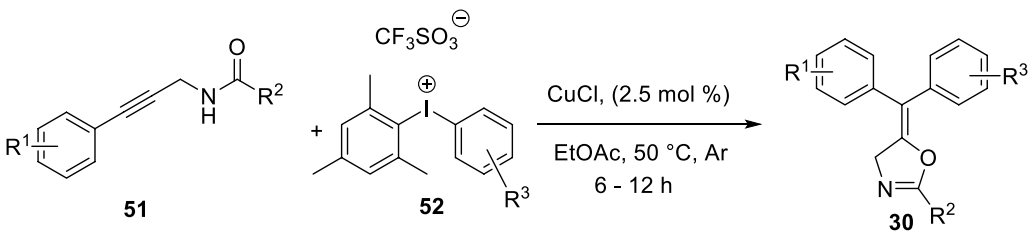
Scheme 48



Scheme 49



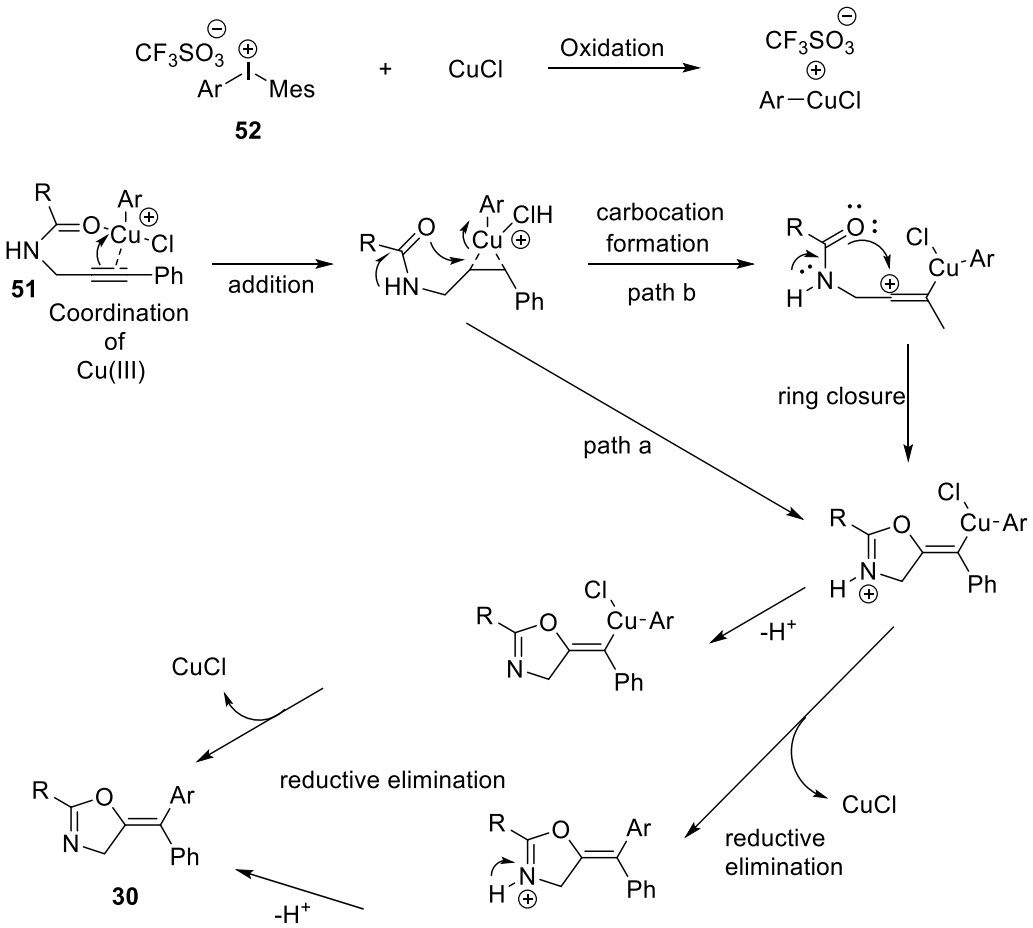
Scheme 50



R^1	R^2	R^3	Yield /%
H	H	H	60
4-COOMe	H	H	86
4-Cl	H	H	69
H	4-OMeC_6H_4	H	70
4-COOEt	H	H	65
H	*t*-Bu	4-COOEt	64

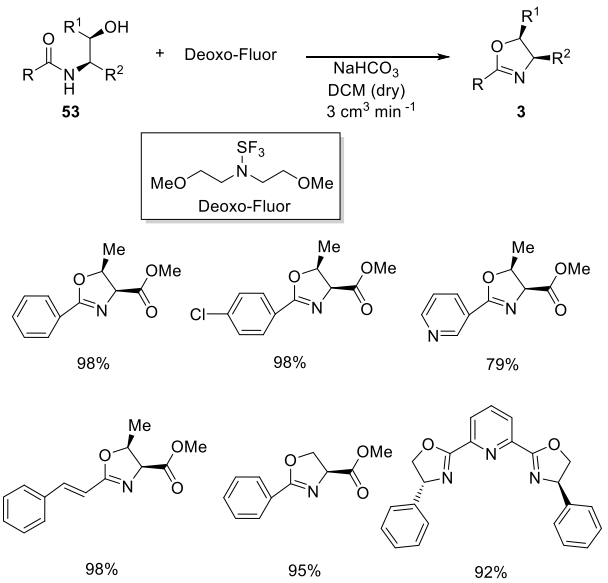
for the synthesis of oxazoline **3** (Scheme 70) [119]. The in situ formation of nitrile oxide from various aldoxime through NaCl-oxone oxidation was found as the key step in this reaction. Better yield was afforded by 0.7 equiv. of NaCl, 1.1 equiv. of oxone and 1.5 equiv. of Na_2CO_3 in acetonitrile–water mixture (20:1). Except for the alkynyl aldoxime, the product was obtained in good yield with various substituted aldoximes. Conjugated aldoximes were also attempted with *tert*-butyl acrylate and ended up in

Scheme 51

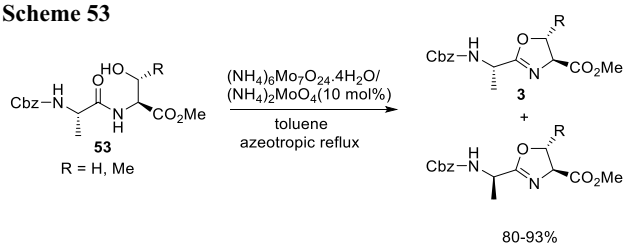


Reproduced with permission from ref. [105]

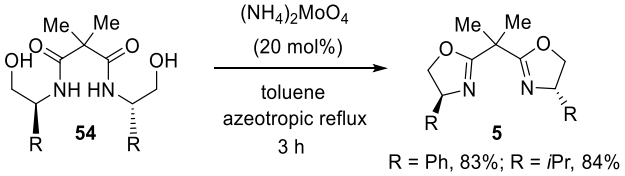
Scheme 52



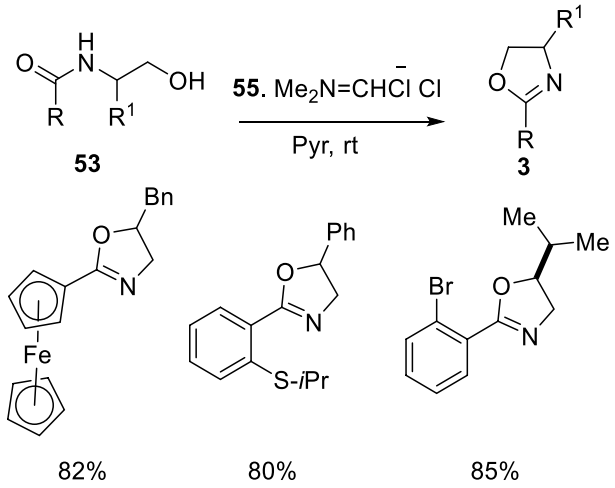
Scheme 53



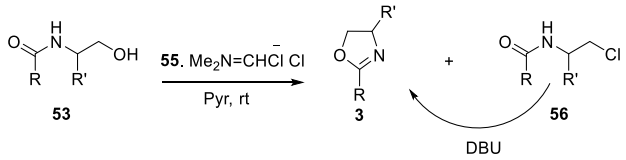
Scheme 54



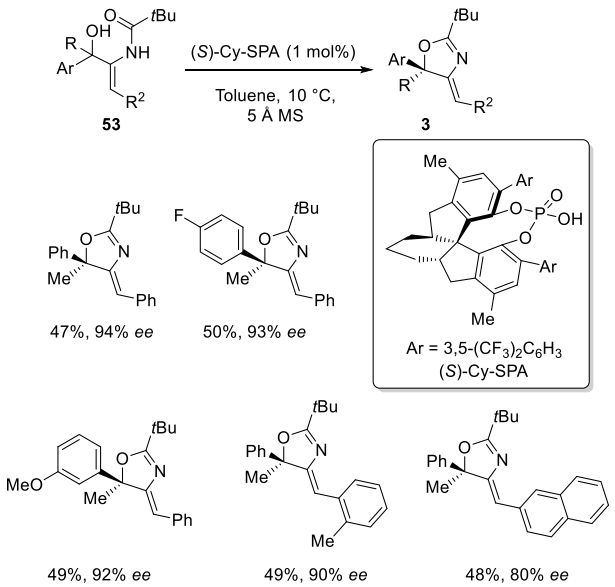
Scheme 55



Scheme 56



Scheme 57



decent results**.** They also proposed a reaction pathway for this transformation (Scheme 71).

From α-oxo-ketene *N,N*-acetals

Here, the oxazoline moiety was realized by the breaking of a C=C bond present in α-oxo-ketene *N,N*-acetals followed by a cyclization.

A transition metal-free protocol towards substituted oxazolines **69** by cleavage of C=C in α-oxo-ketene *N,N*-acetals **68** was established mediated by $PhI(OAc)_2$ (PIDA), which functioned as an oxidant, along with K_2CO_3 in DCM at 80 °C affording good yields (Scheme 72) [120].

From benzoxazines

Oxazolines could be synthesized from benzoxazine via an epoxide intermediate formation by nucleophilic attack at the electrophilic centre of benzoxazine followed by an intramolecular cyclization.

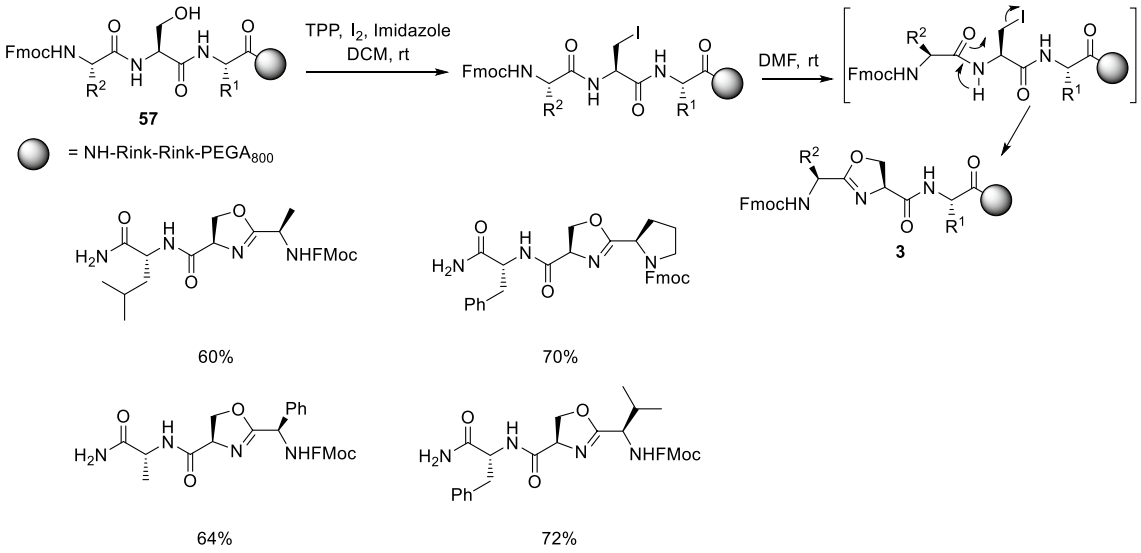
A metal-free conversion of benzoxazine **70** towards 2,5-disubstituted oxazolines **3** was disclosed, wherein 2.5 equiv. of *m*-CPBA and 2 equiv. of allylamine and benzoxazine in DCM at rt were used to afford good to high yields (Scheme 73) [121]. Here the *ortho* amide groups played a significant role in *m*-CPBA oxidation. The suggested mechanism for the reaction is showcased (Scheme 74).

From sulfoxides

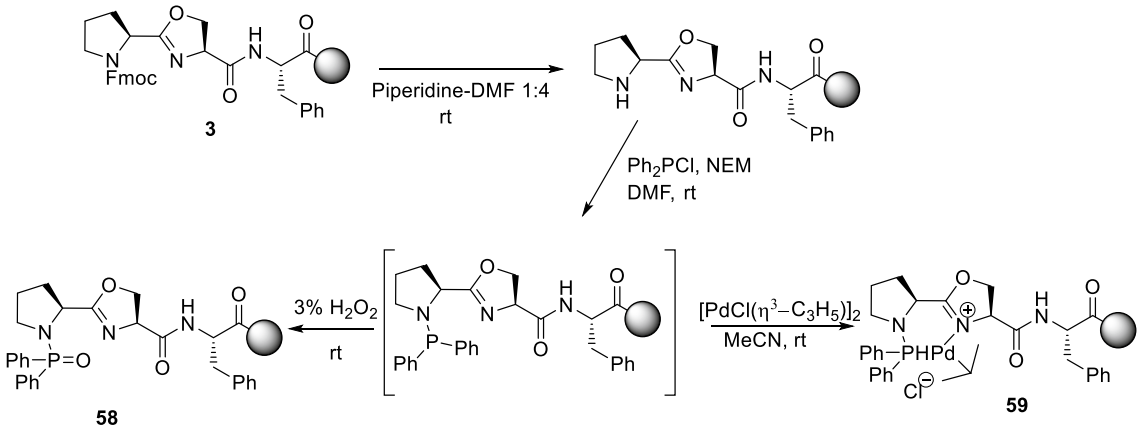
Sulfoxides are derivatives of sulfides in which sulfinyl group is bonded to two alkyl groups. Here, a nucleophilic addition at the electron-deficient carbon next to sulfinyl group followed by intramolecular cyclization rendered oxazolines.

5-Thiooxazoline **74** synthesis from sulfoxides **71** was established by the use of 0.6 equiv. of oxalyl chloride **72** followed by 5 equiv. of $NH_3.H_2O$ **73** (Scheme 75) [122]. This method has evolved as an extension of Pummerer reaction [123, 124]. There were no striking electronic effects on the corresponding sulfides.

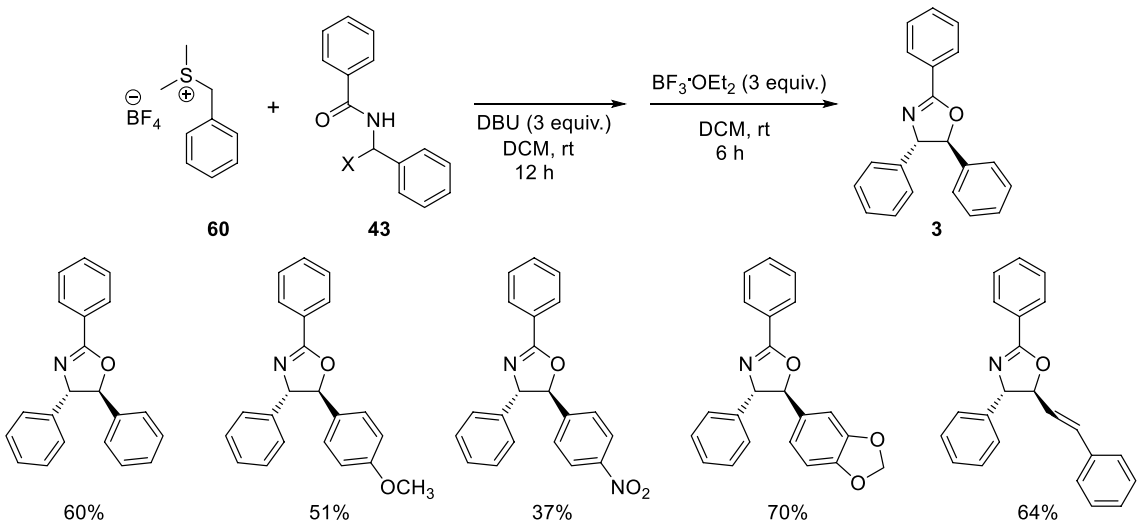
Scheme 58



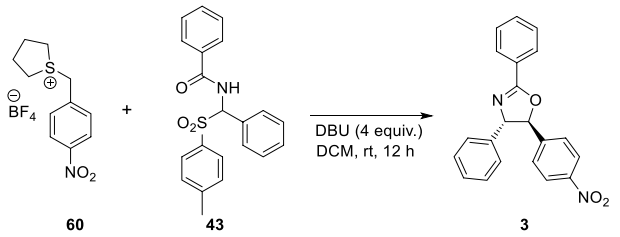
Scheme 59



Scheme 60



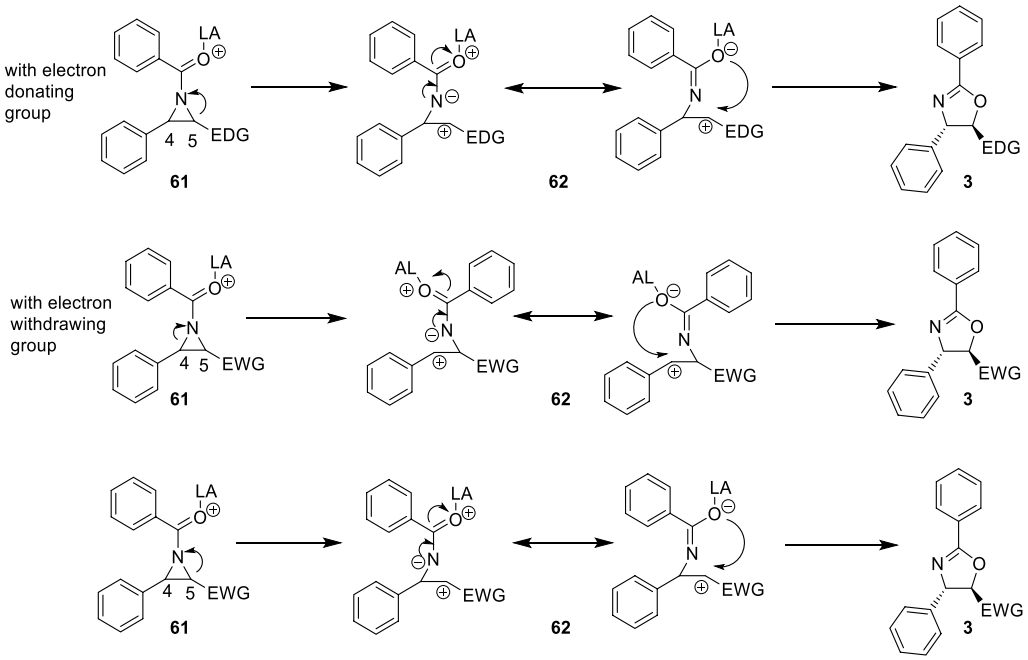
Scheme 61



From alkyl trichloroimidates

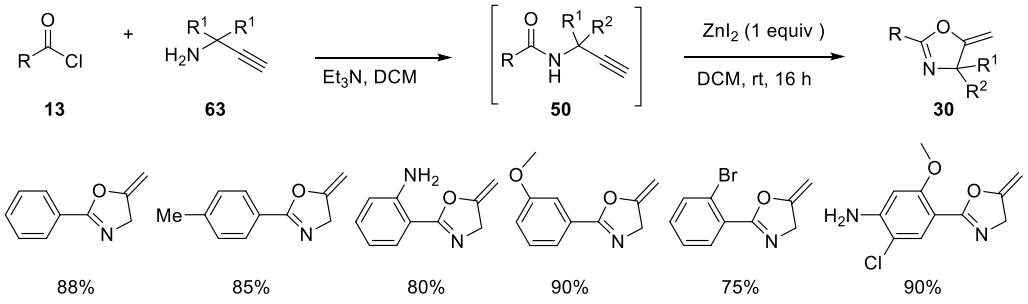
An intramolecular cyclization of trimethylsilyl-substituted trichloroimidates offered the desired oxazolines. Oxazolines **76** were synthesized from alkyl trichloroimidates **75** through an intramolecular cyclization using bispyridylsilver(I) complex [125]. *E*-and *Z*-selectivity in the formation of 4-bromooxazolines was effectively controlled by silver catalyzed pathway (Scheme 76). Trimethyl silyl-substituted starting

Scheme 62

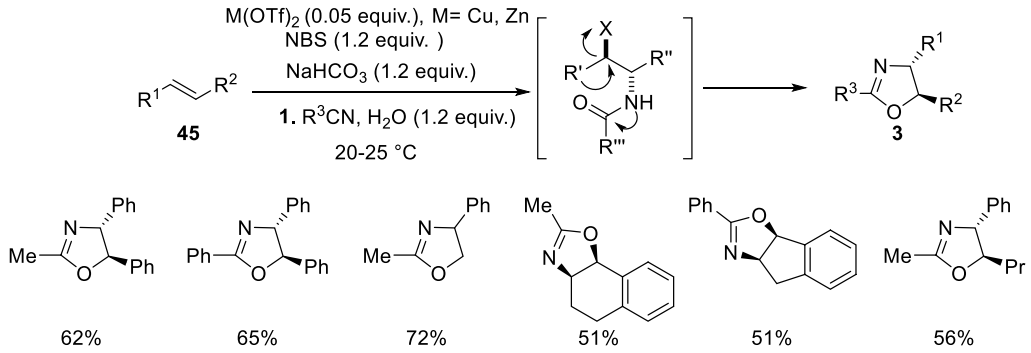


Reproduced with permission from ref. [111]

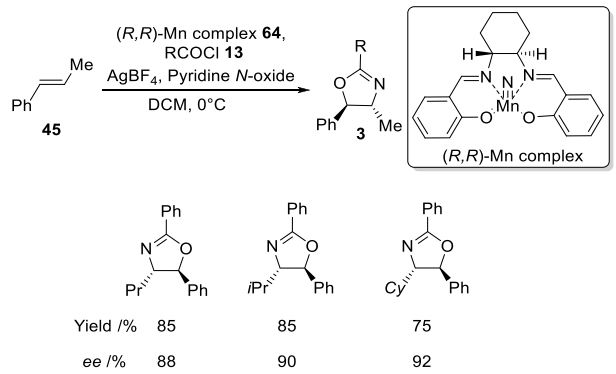
Scheme 63



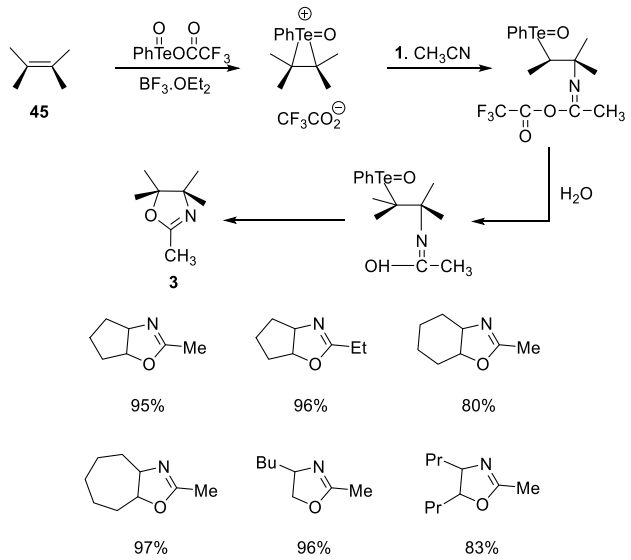
Scheme 64



Scheme 65



Scheme 66



compounds could also be converted to the corresponding product (Scheme 77).

From ketoaziridines

Aziridines are three-membered heterocycles which contain a nitrogen as the heteroatom. One of the carbons in the aziridine skeleton is attached to a carbonyl group to form ketoaziridine. Their ring opening reaction and further construction of a five-membered cycle afforded oxazolines.

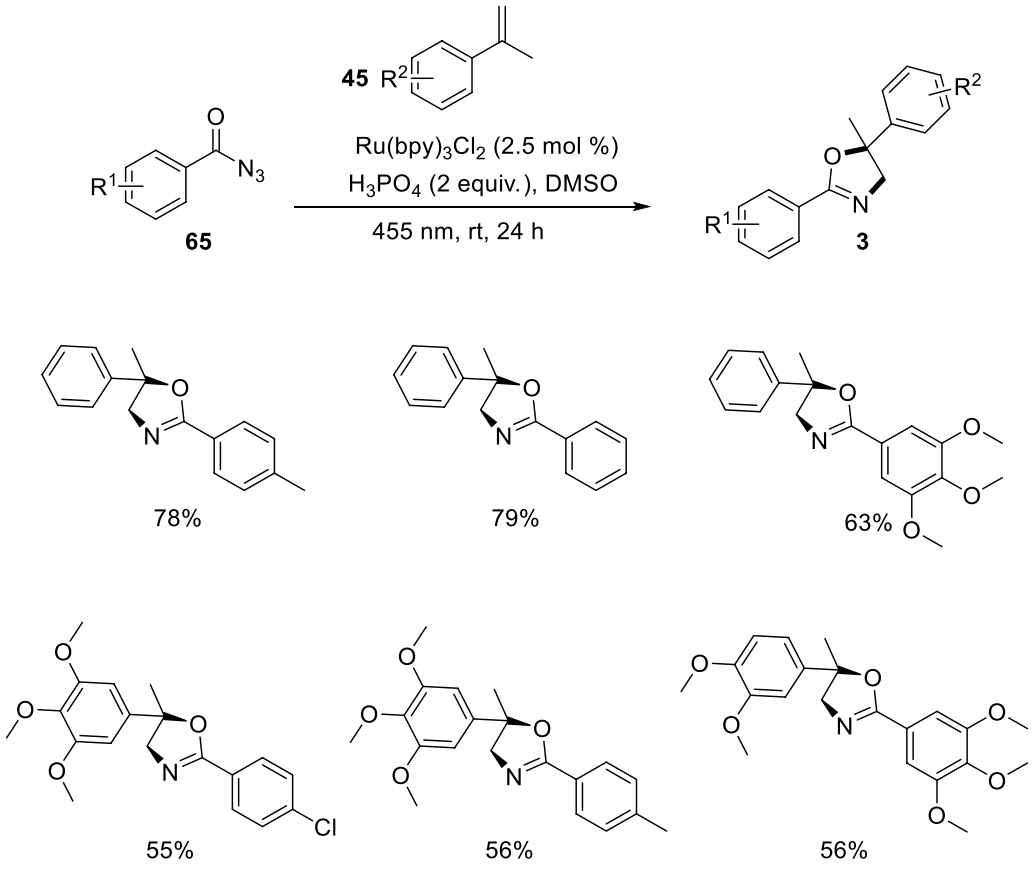
A one-pot conversion of ketoaziridines **77** to the corresponding oxazolines **3** under $K_5[PW_{11}ZnO_{39}]\cdot 23H_2O$-catalyzed conditions along with benzoic acid **78** and DCC was accomplished in acetonitrile (Scheme 78) [126]. The ring expansion of aziridines under the above conditions provided good stereo- and regioselective products. Moderate to high yields of oxazolines were achieved from substrates having electron-deficient moieties.

From aryl bromides

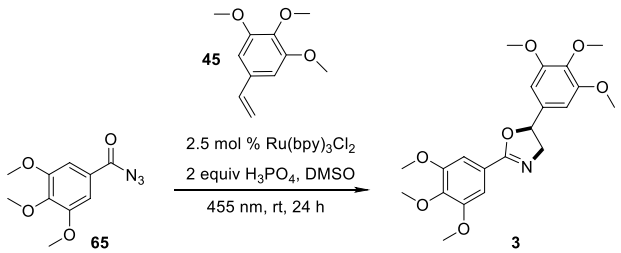
Aryl halides are a class of organic compounds that are composed of an aromatic moiety with substitution by halide functionality. Herein, oxazolines were constructed from the reaction of aryl bromide through a catalytic protocol.

Palladium-catalyzed formation of 2-aryloxazolines **3** from aryl bromides **79**, CO (**80**), and chloroethylamine (**81**) was established using $Pd(OAc)_2$ along with $BuPAd_2$ as ligand in presence of 1 mmol of $MgSO_4$ as additive and NEt_3 as a base (Scheme 79) [127]. The reaction proceeded

Scheme 67



Scheme 68

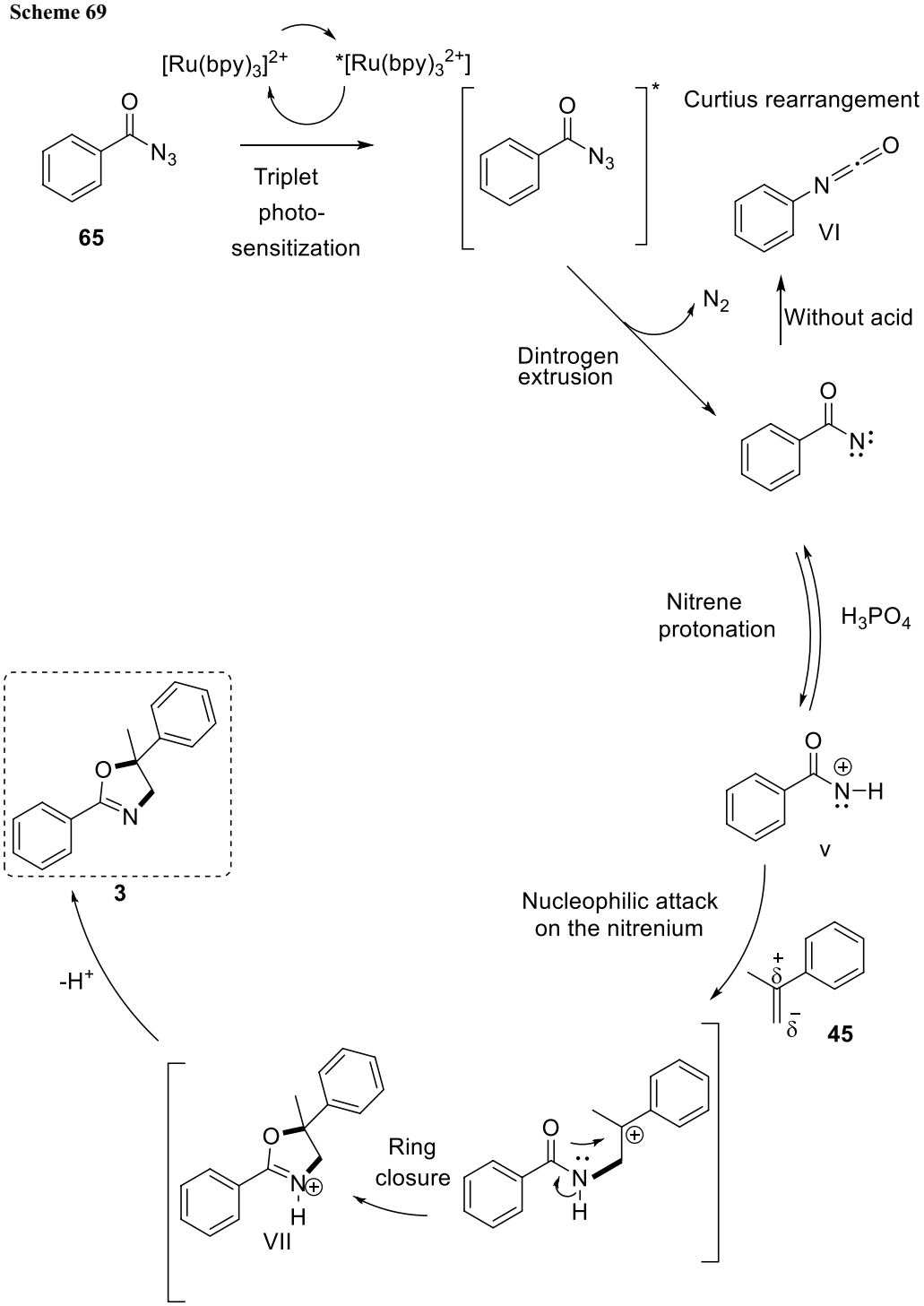


through an acylpalladium intermediate, which was formed by the oxidative addition of bromobenzene to Pd(0) and followed by a carbon monoxide insertion. Further attack of chloroethylamine followed by reductive elimination led to the generation of an arylamide intermediate **83** and the action of NEt_3 on **83** directed to the desired oxazoline. Both electron-donating and electron-accepting species performed well under the optimized condition. A possible mechanism was also showcased (Scheme 80).

From benzylidene acetal

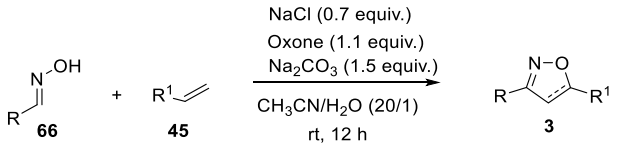
Benzylidene acetal with an azide moiety could be effectively converted to oxazoline. The reaction proceeded through the formation of an amino-diazonium ion intermediate by azide attack at the benzylic carbon. Later, a 1,2-hydride shift followed by an elimination of nitrogen and a proton led to the oxazoline generation.

Scheme 69



Reproduced with permission from ref. [118]

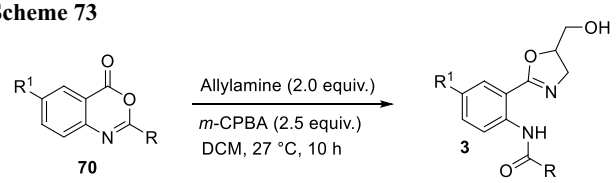
Scheme 70



R = *i*Pr, R^1 = CH_2Br, 86.5%
R = *i*Pr, R^1= C_2H_4OTIPS, 91%
R = Ph, R^1 = CO_2tBu, 96%
R = 4-$OMeC_6H_4$, R^1 = CO_2tBu, 97%
R = 4-$NO_2C_6H_4$, R^1 = CO_2tBu, 95%
R = 3-$NO_2C_6H_4$, R^1 = CO_2tBu, 91%
R = 4-ClC_6H_4, R^1 = CO_2tBu, 92%

A novel protocol to synthesize 2-phenyloxazolines **3** in a stereoselective manner was reported from benzylidene acetal **84** having an azide group via an intramolecular cyclization initiated by the Lewis acid BF_3OEt_2 under mild conditions (Scheme 81) [128].

Scheme 73

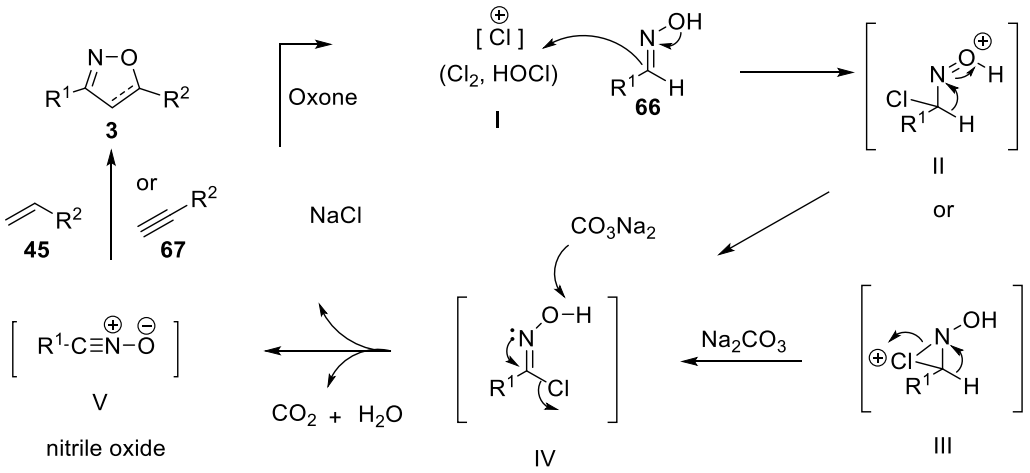


R = H, R^1 = 4-$OMeC_6H_4$, 87%
R = H, R^1 = 4-FC_6H_4, 84%
R = H, R^1 = 4-$CF_3C_6H_4$, 78%
R = Cl, R^1 = Ph, 78%
R = I, R^1 = Ph, 74%
R = H, R^1 = Me, 85%

From epoxide

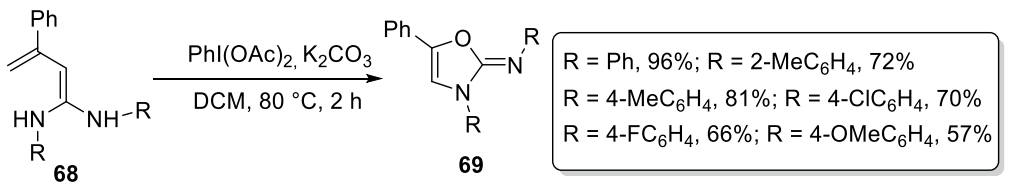
An epoxide is a three-membered heterocycle incorporated with an oxygen and is also a cyclic ether. Here, oxazolines were afforded through a nucleophilic ring opening of epoxide and a latter intramolecular cyclization.

Scheme 71

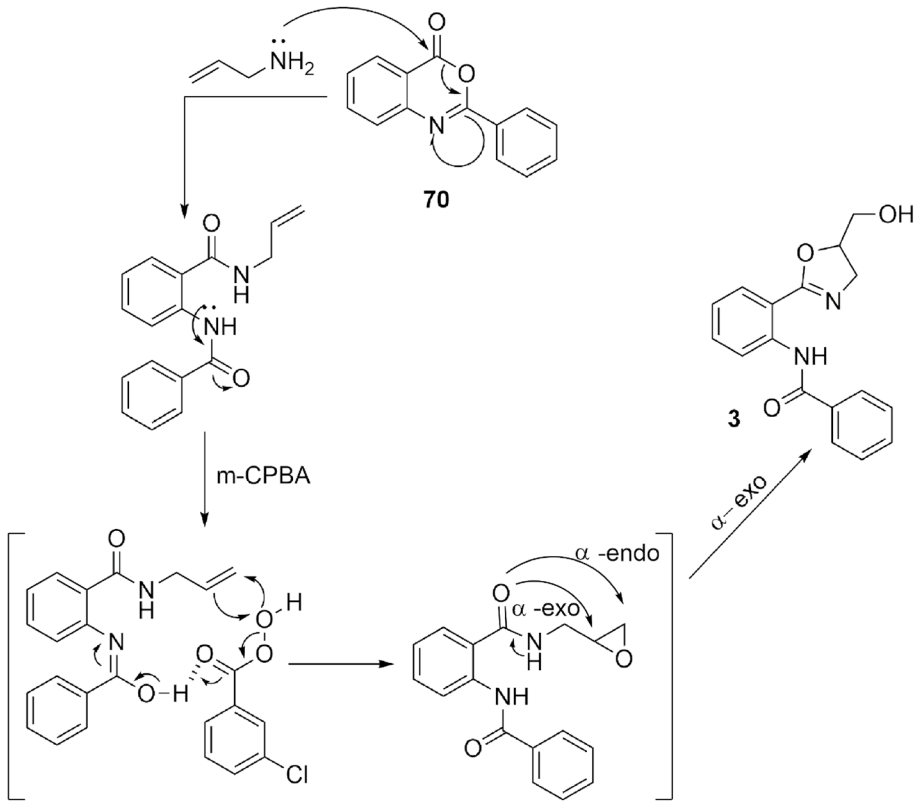


Reproduced with permission from ref. [119]

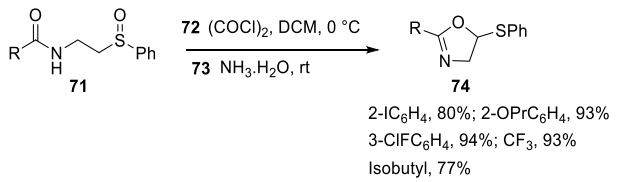
Scheme 72



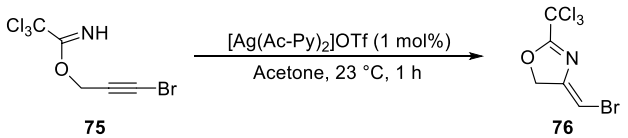
Scheme 74



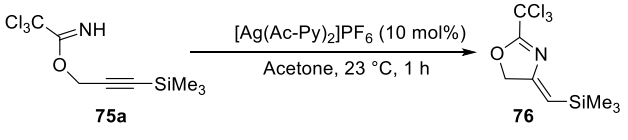
Scheme 75



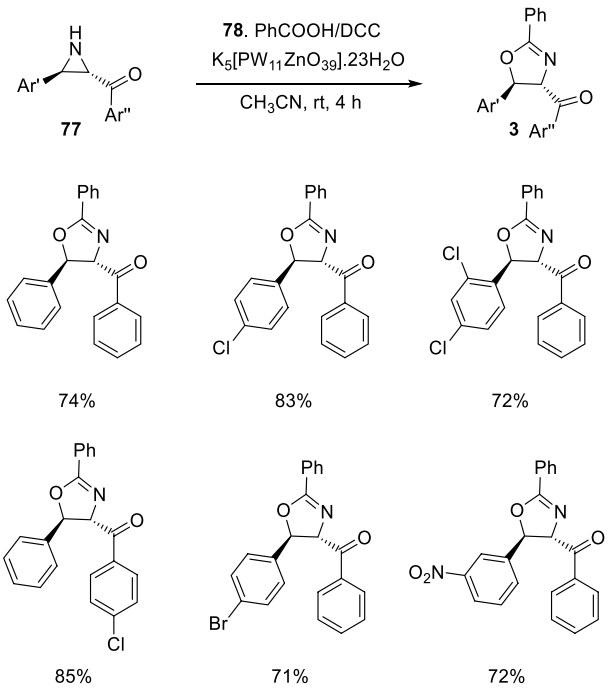
Scheme 76



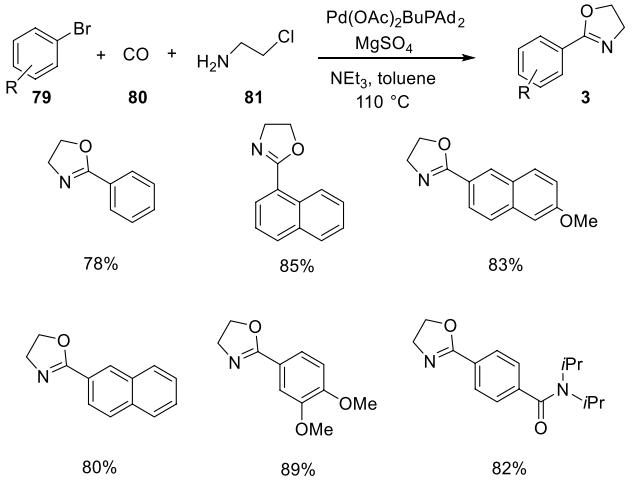
Scheme 77



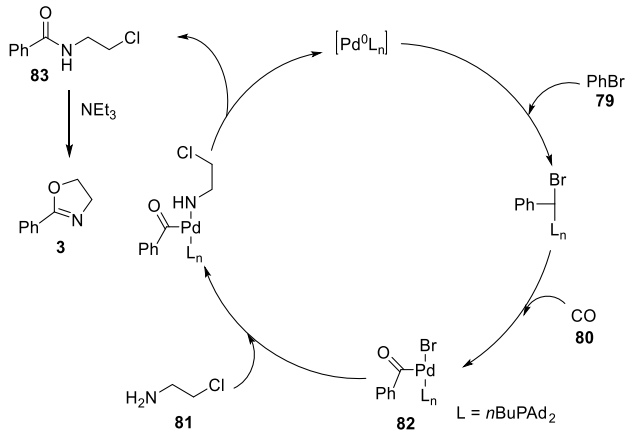
Scheme 78



Scheme 79

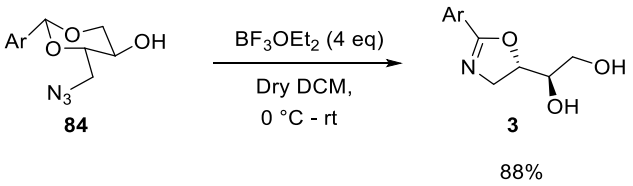


Scheme 80



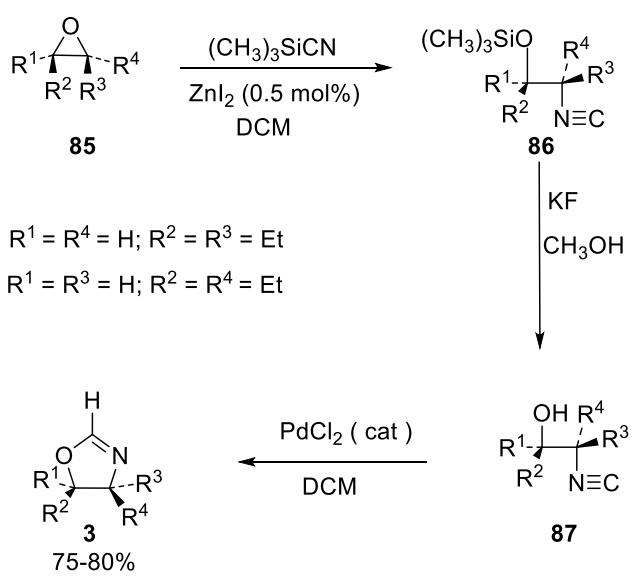
Reproduced with permission from ref. [127]

Scheme 81



Oxazolines **3** were efficiently synthesized from epoxides by reacting substituted epoxides **85** with 2 equiv. of trimethylsilyl cyanide in the presence of 0.5 mol% of zinc iodide as catalyst (Scheme 82) [129]. The initial step leads to the formation of trimethylsilyl ether **86** of β-hydroxy isonitriles followed by treatment of 3 equiv. of KF in methanol for the deprotection of silyl group. The compound **87** undergoes

Scheme 82



cyclization under palladium catalyzed condition towards the oxazoline.

Conclusion

Oxazoline is a heterocyclic compound having both oxygen and nitrogen as hetero atoms in its ring skeleton. Since the first synthesis in 1884, oxazolines witnessed a lot of advancements in its synthesis. This is majorly owing to the tremendous biological activity of this particular compound and its medicinal properties. This review gives an overview of the various methodologies accomplished for the synthesis and applications of oxazolines. A wide spectrum of substrates such as amino alcohols, aldehydes, ketones, acid chlorides, amides, olefins, benzoxazines, sulfoxides, etc. were converted to oxazolines. Among these, amino alcohols and allylamides were observed as the most investigated ones. The biological importance of oxazoline derivatives and its facile synthetic preparations have inspired researchers across the globe to produce more interesting outputs, which still continues.

Acknowledgements MN thanks the University Grants Commission (UGC), New Delhi for a research fellowship.

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