Current Chemistry Letters 15 (2026) 665–674

Contents lists available at GrowingScience

Current Chemistry Letters

homepage: www.GrowingScience.com

(3+2) Cycloaddition reactions with the participation of hetarene *N*-oxides: a review

Roman Nahatskyi[a] and Agnieszka Łapczuk[b*]

[a]*Cracow University of Technology, CUT Doctoral School, Faculty of Chemical Engineering and Technology, Warszawska 24, 31-155 Cracow, Poland*
[b]*Cracow University of Technology, Faculty of Chemical Engineering and Technology, Warszawska 24, 31-155 Cracow, Poland*

C H R O N I C L E

Article history:
Received January 2, 2026
Received in revised form
January 24, 2026
Accepted March 18, 2026
Available online
March 18, 2026

Keywords:
Isoxazolidine
Cycloaddition
Hetarene N-oxides
Stereoselectivity
Regioselective functionalization

A B S T R A C T

This review presents the current state of knowledge on the (3+2) cycloaddition (32CA) reactions involving heteroarene *N*-oxides. While aromatic amine oxides behave similarly to nitrones, their participation in cycloaddition processes is chemically distinct due to the thermodynamic stability of the aromatic ring system. The manuscript critically examines these reactions, focusing on the competition between the formation of stable fused isoxazolidines and the tendency toward rearomatization. The latter often leads to spontaneous ring opening, elimination, or complex rearrangements rather than the isolation of the primary cycloadduct.

© 2026 by the authors; licensee Growing Science, Canada.

1. Introduction

The isoxazolidine ring, also known as tetrahydro-1,2-oxazole, represents a fundamental class of saturated five-membered heterocyclic compounds containing nitrogen and oxygen atoms in adjacent positions (1 and 2)[1]. It serves as the saturated analogue of isoxazole and is isomeric with 1,3-oxazolidine, where the heteroatoms are separated by one carbon atom. In the realm of medicinal chemistry, the isoxazolidine scaffold is recognised as a 'privileged structure' due to its remarkable ability to mimic essential biological motifs, including nucleosides, carbohydrates, peptide nucleic acids (PNA), amino acids, and steroids[2-3]. Consequently, isoxazolidine-containing derivatives have attracted considerable attention in pharmaceutical research.

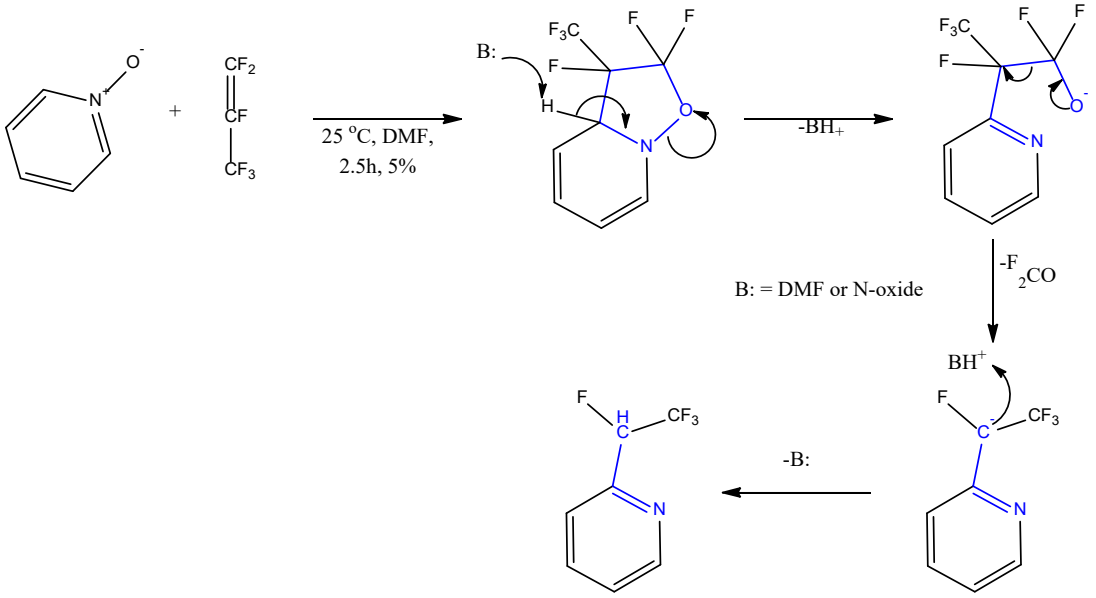
Extensive studies have demonstrated the broad spectrum of biological activities exhibited by these compounds. Isoxazolidine-based drugs have shown potent antiviral properties, acting as inhibitors of HIV-1 replication, as well as significant antibacterial, anti-inflammatory, and antifungal activities[4-7]. Furthermore, these molecular frameworks have been identified as effective DNA intercalators, transcriptional activators, and inhibitors of advanced glycation end (AGE) product formation. The most universal method for the synthesis of isoxazolidines is via (3+2) cycloaddition (32CA)[8-10] reactions involving nitrones[11-12]. Much work has been devoted to these reactions, from preparative[2,13-17], kinetic[18-20], and mechanistic [21-24] perspectives. Although oxides of aromatic amines are not formally classified as nitrones, they possess a structural motif that allows them, in practice, to react as three-atom components (TACs) within the 32CA scheme[24]. However, the reactivity of heteroarene *N*-oxides is fundamentally distinct from that of classic nitrones. The participation of an aromatic *N*-oxide in a cycloaddition requires the disruption of its aromatic ring system. Consequently, the primary fused isoxazolidine adducts are often thermodynamically unstable due to the loss of resonance energy. Experimental evidence has shown that these initial intermediates frequently undergo spontaneous transformations—such as ring opening,

* Corresponding author
E-mail address agnieszka.lapczuk@pk.edu.pl (A. Łapczuk)
© 2026 by the authors; licensee Growing Science, Canada
doi: 10.5267/j.ccl.2026.3.004

elimination, or rearrangement, driven by the strong thermodynamic tendency of the system to rearomatize[20-23]. This work is an attempt to illustrate the scientific efforts in this specific area, analyzing the current state of knowledge regarding the (3+2) cycloaddition reactions involving heteroarene *N*-oxides.

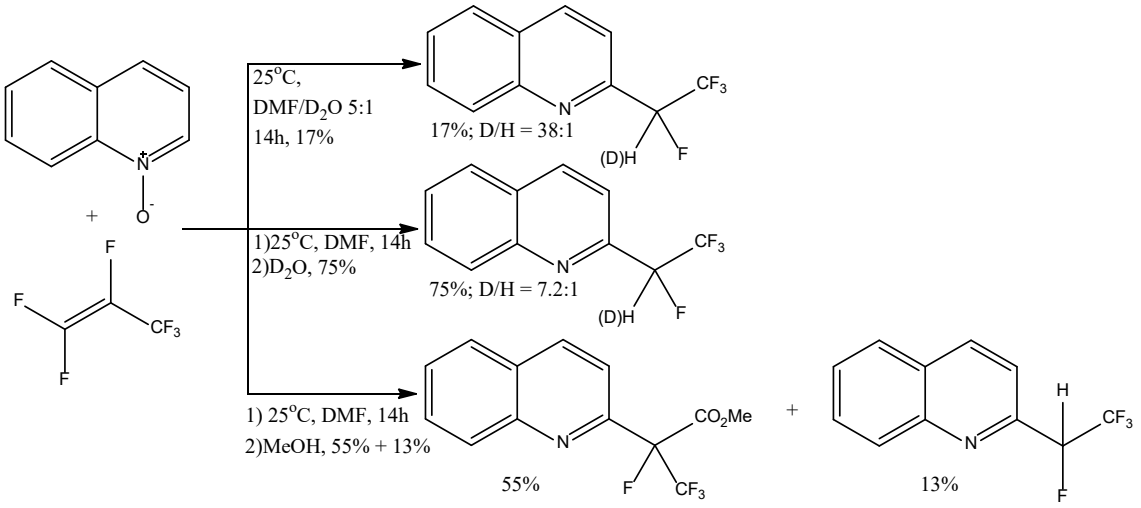
2. Analysis of the state of knowledge (3+2) cycloaddition of heteroarene *N*-oxides

An example of the aforementioned processes can be found in the reaction of the parent hetarene N-oxide (pyridine *N*-oxide) with perfluoropropylene (**Scheme 1**)[1]. Indeed, it was reported earlier that pyridine *N*-oxide reacted with HFP (hexafluoropropylene**)** at elevated temperatures and pressures (autoclave) to give 2-(1,2,2,2-tetrafluoroethyl)pyridine[25]. This result was later confirmed by Banks et al.[26] who expanded the scope of the reaction and attempted to elucidate its mechanism. It was suggested that the reaction proceeded via initial cycloaddition (probably, stepwise) of HFP to *N*-oxide with the formation of 2,2,3-trifluoro-3-(trifluoromethyl)-3,3a-dihydro-2H-isoxazolo[2,3-a]pyridine. Subsequent elimination and rearomatization gives an anion, which undergoes a retro-aldol-type fragmentation to provide the final product. This supposition was supported by the formation of difluorophosgene, but isoxazolidine intermediate was never observed, perhaps because under harsh conditions it rapidly reacted further. Under much milder conditions, it was possible to isolate and characterise intermediate isoxazolidine although in a low yield of 5%[27].



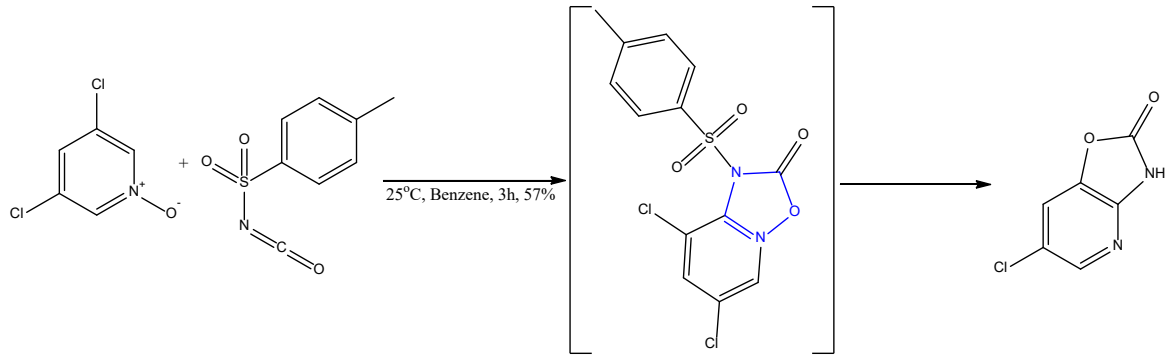
Scheme 1. Reaction of pyridine *N*-oxide with perfluoropropylene.

Investigation into the cycloaddition of HFP and quinoline *N*-oxide under different conditions revealed that tetrafluoroethyl-substituted azines are not the sole products. This finding prompted a reassessment of the reaction (**Scheme 2**)[28]. Notably, conducting the reaction in a DMF/D_2O mixture.



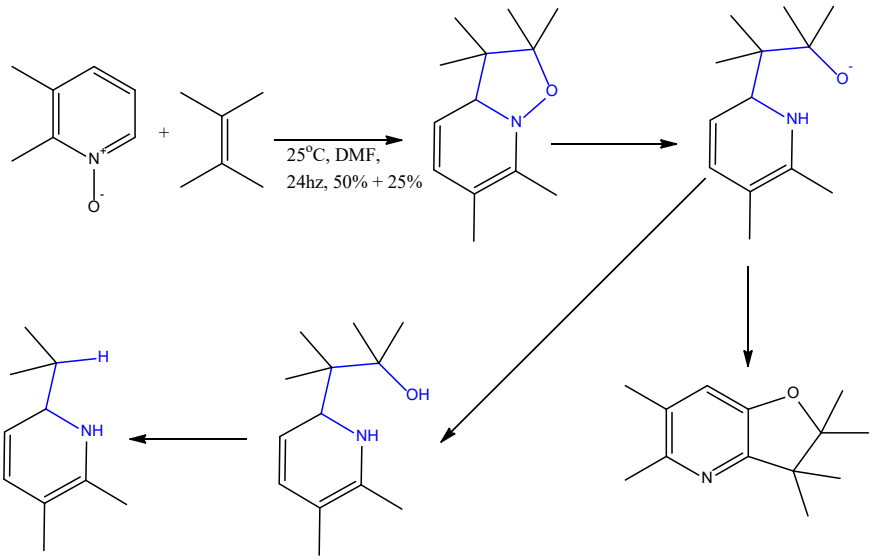
Scheme 2. Influence of D_2O and MeOH on reactions of quinoline *N*-oxide with HFP.

As another example, in the 32CA of 3,5-dichloropyridine *N*-oxide and tosyl isocyanate an unstable oxa-2,4-diazoline system is formed[29]. The cycloaddition proceeds at room temperature in a benzene solution with full regioselectivity. This adduct, under the reaction conditions, converts spontaneously into the corresponding benzazo-1,3-oxazole system (**Scheme 3**).

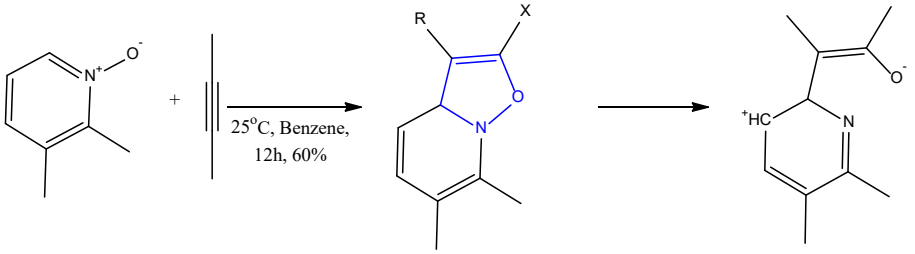


Scheme 3. 32CA of 3,5-dichloropyridine *N*-oxide and tosyl isocyanate.

The formation of a stable cycloadduct has been observed in only a few cases upon the reaction of *N*-oxides with alkenes. The driving force for such reactions is apparently a reduction in the strain in these molecules (**Scheme 4, 5).** This example faces same elimination as in the example above (**Scheme 2)**, therefore it reinforces the theory proposed by Loska R. and Makosza[28].

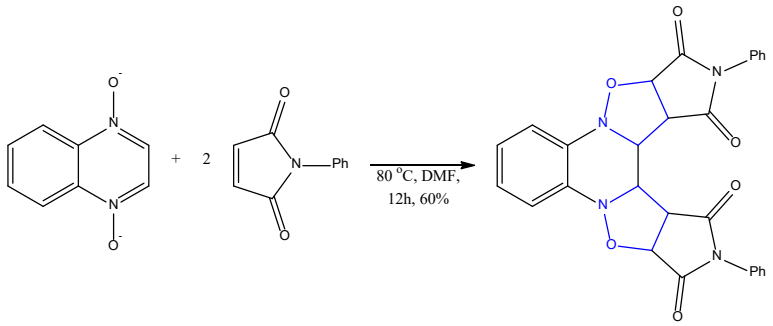


Scheme 4. Postulated mechanism for the reaction of 2,3-dimethylpyridine C-oxide with alkenes



Scheme 5. Postulated mechanism for the reaction of 2,3-dimethylpyridine *N*-oxide with but-2-yne.

Quinoxaline *N,N'*-dioxide has a greater tendency than other *N*-oxides to give stable cycloadducts. An example of this can be found in the reaction of this dioxide with *N*-phenylmaleimide, which proceeds at 80 °C in DMF for 12 h at both the *N*-oxide groups (**Scheme 6)**:



Scheme 6. Reaction of quinoxaline *N,N'*-dioxide with *N*-phenylmaleimide.

The successful isolation of compound 2,2,3-trifluoro-3-(trifluoromethyl)-3,3a-dihydro-2H-isoxazolo[2,3-a]quinoline (**Fig. 1**) may be attributed to a lower resonance energy, and hence lower driving force for aromatization in the quinoline ring system than in the pyridine series. Interestingly, it is stable at room temperature, and it does not undergo spontaneous transformation into the elimination product, although the reaction of quinoline *N*-oxide with alkene proceeds readily at room temperature. Apparently, the presence of a basic solvent (DMF) is necessary to initiate the elimination process. Note that HFP reacts similarly with nitrones to give stable isoxazolidines. Azine *N*-oxides are analogues of nitrones. However, due to loss of aromaticity in the adduct, they are unstable and convert to substituted azines[27].

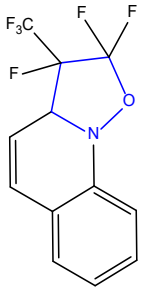
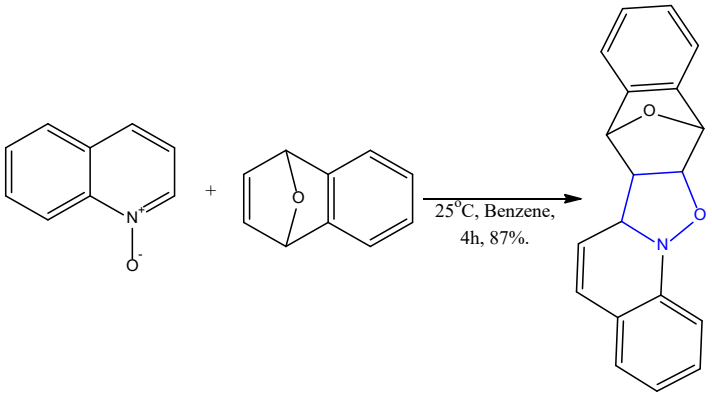


Fig. 1. 2,2,3-trifluoro-3-(trifluoromethyl)-3,3a-dihydro-2H-isoxazolo[2,3-a]quinoline.

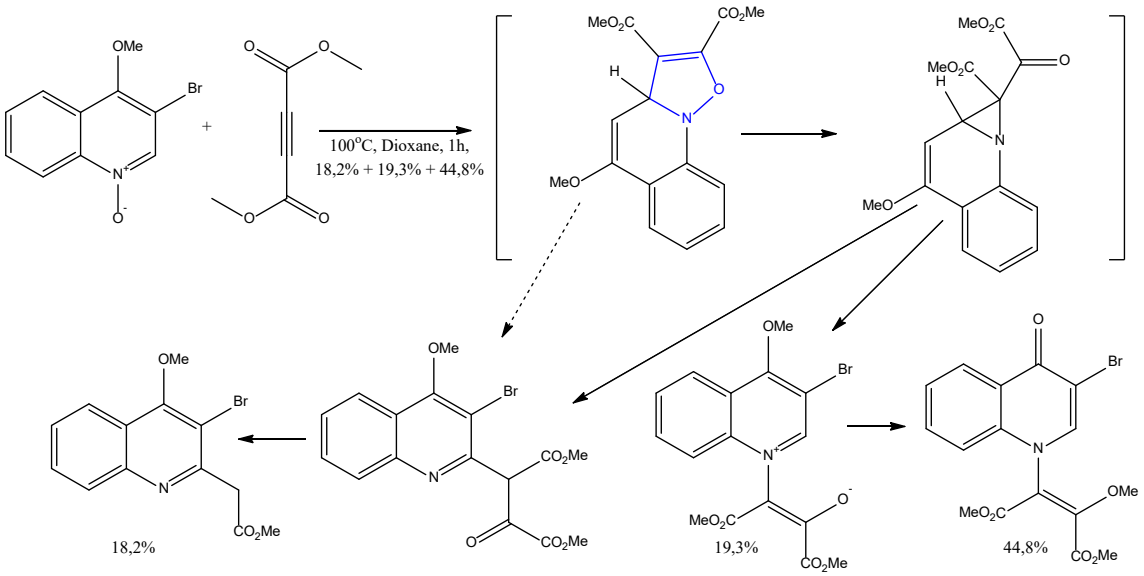
The primary requirement for a successful cycloaddition is the complementary electronic nature of the reagents. However, in most reported reactions, the electron density in the *N*-oxide is greater than in 2-pi-components. Thus, the reagents are matched: the most reactive alkenes bear the largest number of electron-withdrawing substituents, while the most reactive *N*-oxides possess the largest number of electron-donating substituents. Furthermore, the activity of *N*-oxides increases in going from monocyclic to polycyclic compounds. The question of the possibility of carrying out reactions with inversed electronic nature of the reagents remains open. In this regard, considerable interest is found in the work of Wittig and Steinhoff, who described the reaction of quinoline *N*-oxide or pyridine *N*-oxides containing electron-withdrawing substituents with 1,4-epoxy- 1,4-dihydronaphthalene **(Scheme 7).** In this case, the reaction occurs between the HOMO of the 1,4-epoxy-1,4-dihydronaphthalene and the LUMO of the *N*-oxide. We should note that a stable (3+2)-cycloadduct is isolated as the reaction product.



Scheme 7. Reaction of quinoline *N*-oxide with 1,4-epoxy- 1,4-dihydronaphthalene.

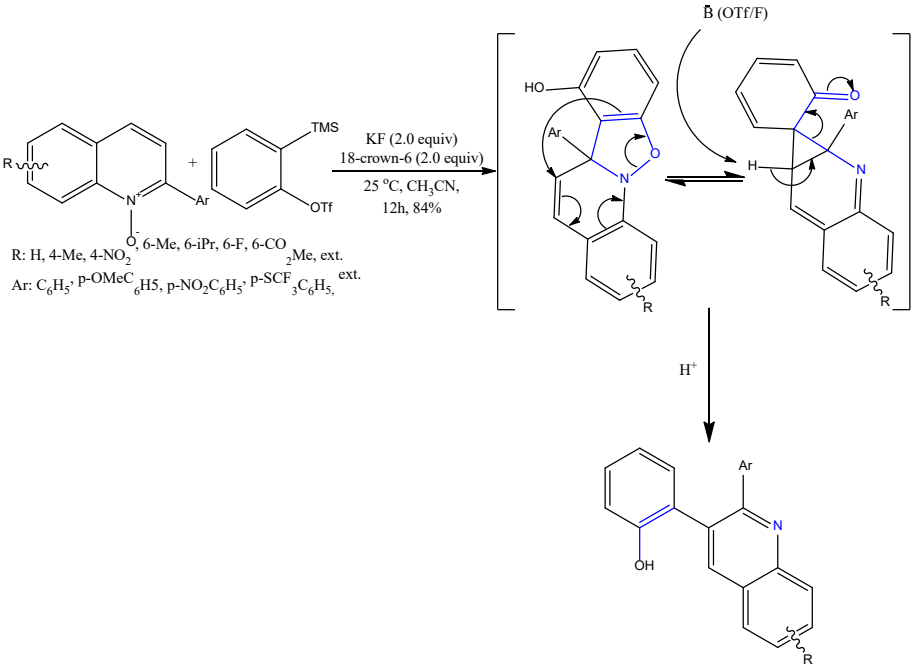
Dimethyl acetylenedicarboxylate (DMAD) was one of the first chemicals used to bond with aromatic *N*-oxides. Hamana and others showed how unordinary these reactions could be when they studied how quinoline *N*-oxide reacted with DMAD.

Their work showed that these reactions could go in many different ways[30]. The reaction of 3-bromo-4-methoxyquinoline *N*-oxide with DMAD under dioxane conditions (room temperature or reflux) resulted in a complex product mixture. Analysis suggests that these compounds likely arise from an initial isoxazoline intermediate (**Scheme 8**). While one product was consistent with a simple N-O bond cleavage pathway, the formation of the other two, a methyl 2-(3-bromo-4-methoxyquinolin-2-yl)acetate, and a dimethyl 2-(3-bromo-4-oxoquinolin-1(4H)-yl)-3-methoxymaleate, implied a more intricate mechanism. By postulating an aziridine intermediate, the subsequent C–C bond fragmentation can account for the ylide and vinylquinoline products. In contrast, C–N bond cleavage provides a plausible route to (Z)-3-(3-bromo-4-methoxyquinolin-1-ium-1-yl)-1,4-dimethoxy-1,4-dioxobut-2-en-2-olate. A similar reaction course has been observed for the cycloaddition of DMAD to 1,2-dimethylbenzimidazole 3-oxide [31-32].



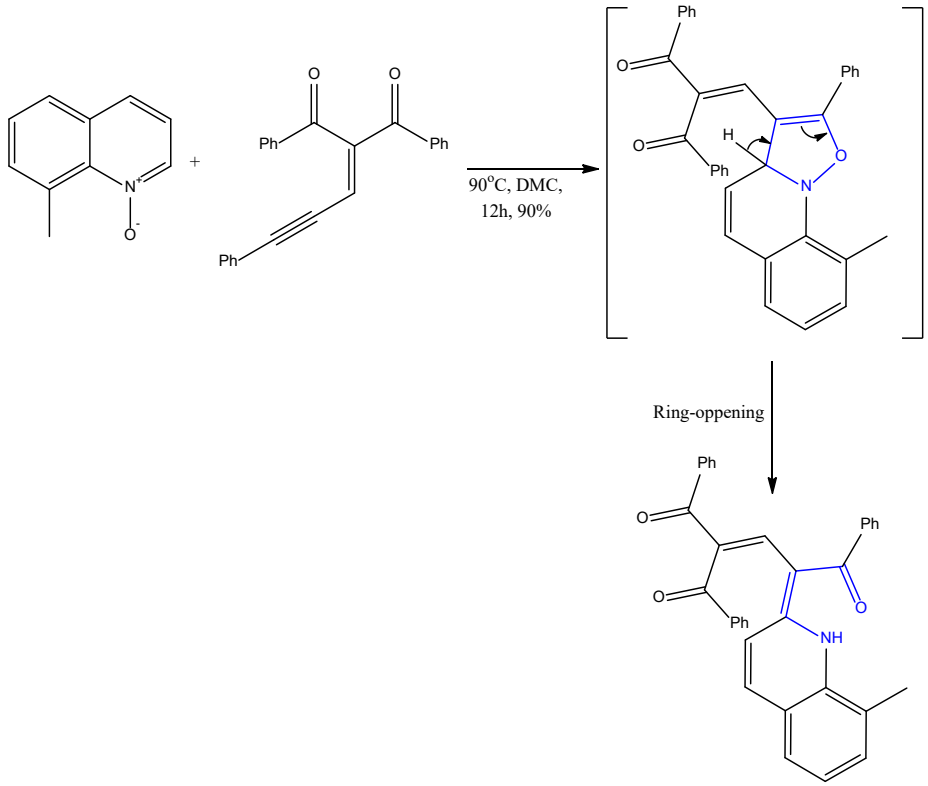
Scheme 8. Cycloaddition of DMAD and 3-bromo-4-methoxyquinoline *N*-oxide.

Building upon their previous findings, Sharma et al. investigated the scope of this reaction using substituted quinoline *N*-oxides. Initially, a series of 2-arylquinoline *N*-oxides bearing diverse aryl substituents were reacted with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate under optimized conditions. Applying 18-crown-6 with KF as the fluorine ion source to substituted(R – H, Ar – C_6H_5) 2-arylquinoline in acetonitrile resulted in exclusively the desired product and 84% yield (**Scheme 9)**. Sufficient yields of the desired products were obtained when employing quinoline *N*-oxides equipped with either electron-donating (e.g., -OMe) or electron-withdrawing (-NO_2) para-substituents on the aryl group[33].



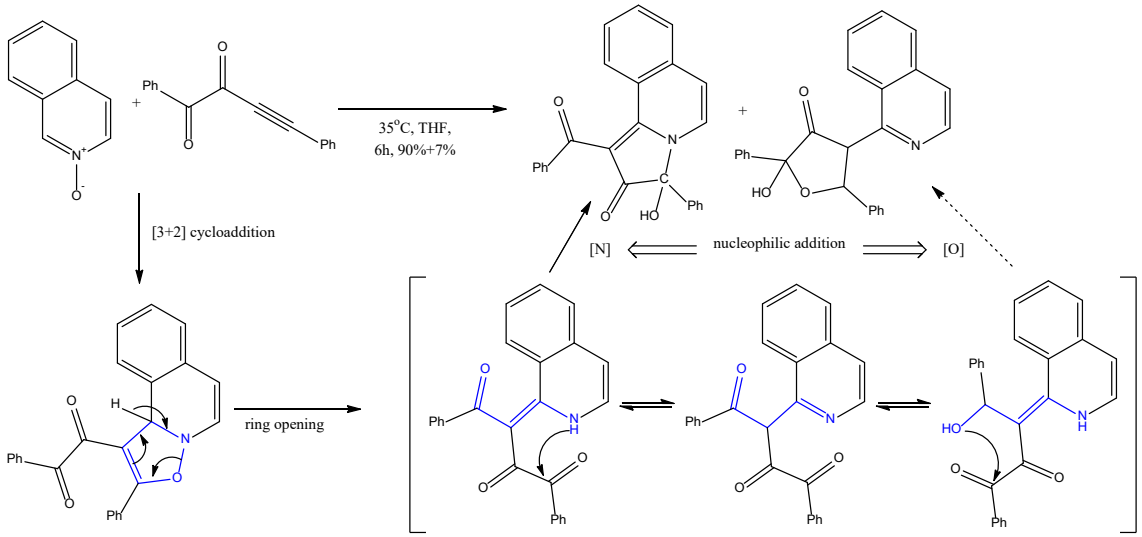
Scheme 9. Reaction and mechanism of substituted 2-arylquinolines with 2-(trimethylsilyl)phenyl trifluoromethanesulfonatesekwencja.

A novel synthetic strategy was conceived for the efficient preparation of pyrrolo[2,1-a]isoquinolines and pyrrolo[1,2-α]quinolines. The proposed mechanism involves a tandem (3+2) cycloaddition/ring-opening/N-nucleophilic addition sequence, conducted under catalyst- and additive-free conditions. Initial research focused on generating an isoxazolo[3,2-α]quinoline intermediate, such as 1,3-diphenyl-2-((2-phenyl-3aH-isoxazolo[2,3-α]quinolin-3-yl)methylene)propane-1,3-dione, through a (3+2) cycloaddition reaction (**Scheme 10**)[34]. Only the stage involving cycloadduct formation is illustrated, as the subsequent transformations are beyond the scope of this review.



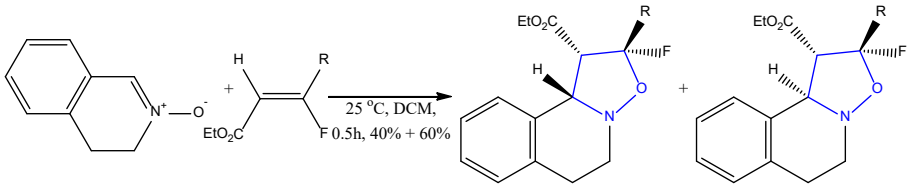
Scheme 10. Generation of 1,3-diphenyl-2-((2-phenyl-3aH-isoxazolo[2,3-a]quinolin-3-yl)methylene)propane-1,3-dione.

1,4-diphenylbut-3-yne-1,2-dione and isoquinoline *N*-oxide were employed as the model substrates to screen reaction conditions (**Scheme 11**). To the delight of the research group, dione smoothly reacted with *N*-oxide in CH_3CN at 35 °C, affording the desired cycloaddition that is followed by ring opening and nucleophilic addition, the final reaction products were obtained in high yields, and their structures were confirmed by X-ray product. Other solvents were applied in course of studies, with THF resulting in the best yield of 90%. Side product 2-hydroxy-4-(isoquinolin-1-yl)-2,5-diphenyldihydrofuran-3(2H)-one, formed via O-nucleophilic addition, was identified as the major byproduct and was obtained in no more than 7% yield.



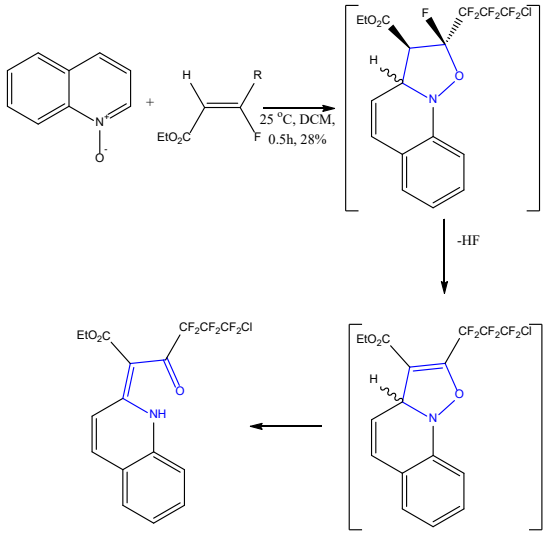
Scheme 11. Synthesis of 1-benzoyl-3-hydroxy-3-phenylpyrrolo[2,1-a]isoquinolin-2(3H)-one

In a study focused on synthesizing fluorine-containing heterocycles, researchers developed several versatile building blocks. One such building block, ethyl-2-hydropolyfluoroalk-2-enoates (where R is a polyfluoroalkyl or perfluoroalkyl group), has been extensively investigated. These compounds were found to react efficiently with certain *N*-oxides, yielding the corresponding 32CA product in high yields. The cycloaddition reaction was conducted in methylene chloride at room temperature. Ethyl-2-hydropolyfluoroalk-2-enoates readily reacted with 3,4-dihydroisoquinoline *N*-oxide to produce stereoisomeric 5-fluoroalkylisoxazolidines (**Scheme 12**).



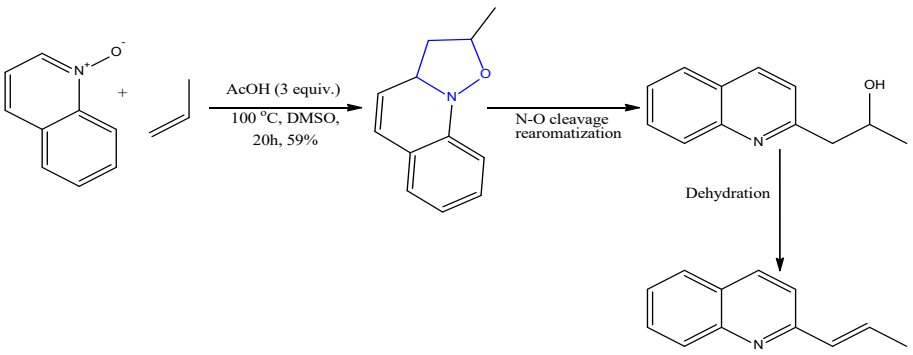
Scheme 12. 32CA of 3,4-dihydroisoquinoline 2-oxide with 2-hydropolyfluoroalk-2-enoates.

When quinoline *N*-oxide was reacted with ethyl-2-hydropolyfluoroalk-2-enoates, the anticipated cycloadduct was not observed in the postreaction mixture (**Scheme 13**). Instead, a product of ring-opening was isolated. In summary, the regiospecific (3+2) cycloaddition reaction between ethyl-2-hydropolyfluoroalk-2-enoates and nitrones was successfully achieved under mild conditions[35].



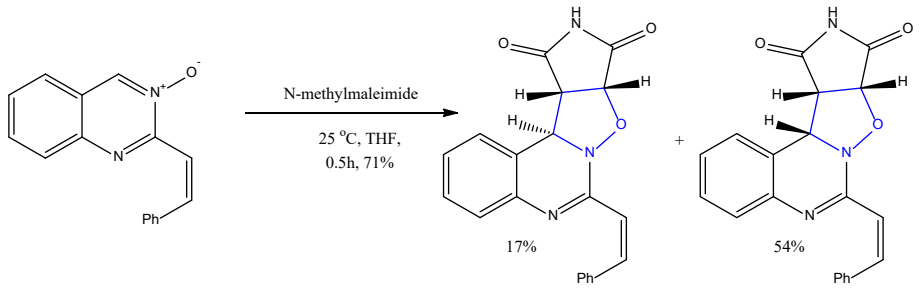
Scheme 13. Reaction of quinoline *N*-oxide with 2-hydropolyfluoroalk-2-enoate.

A method for C-2 alkenylation of quinoline *N*-oxides was reported, using a simple Brønsted acid as the catalyst. It was found that the very common and inexpensive acetic acid (AcOH) was the best additive to drive this reaction. The process was carried out in DMSO solvent at 140 °C for 40 hours. Under these conditions, quinoline *N*-oxides successfully coupled with both acrylates and styrenes.



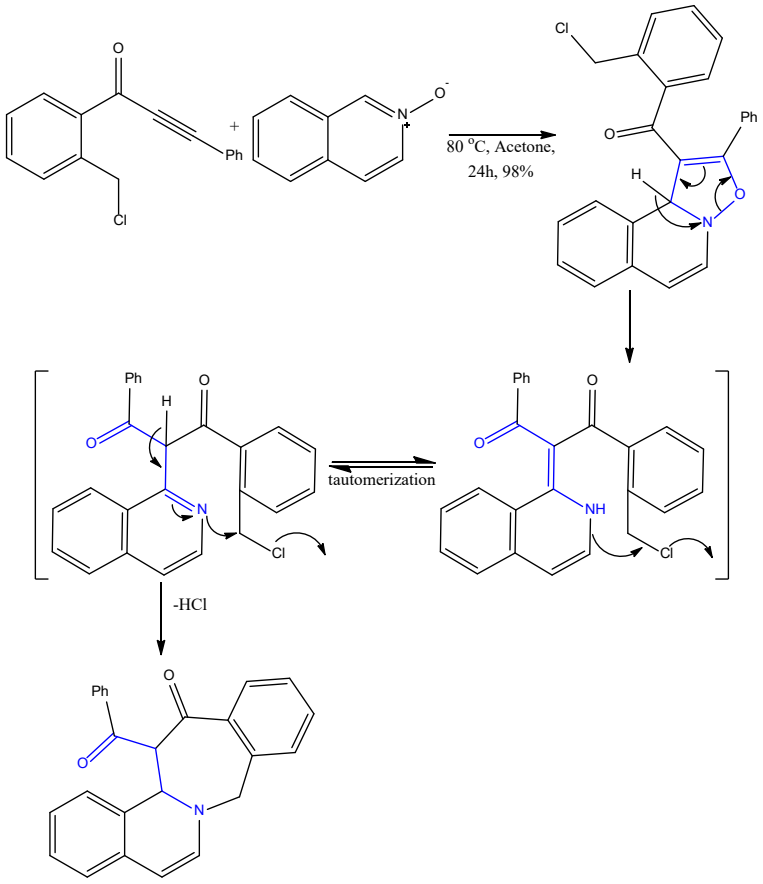
Scheme 14. C-2 alkenylation of quinoline *N*-oxide, using a simple Brønsted acid as the catalyst.

This reaction was noted for being very easy to perform and readily scalable to make large, gram-scale quantities of the product. The general mechanism for these Brønsted acid-catalysed reactions follows the same sequence: It begins with a cycloaddition where the quinoline *N*-oxide reacts with alkene to form a five-membered ring intermediate called an isoxazolidine. This intermediate then undergoes cleavage of the N–O bond and a process called rearomatization to restore the stability of the quinoline ring, resulting in an alcohol molecule. Finally, the AcOH catalyst promotes an elimination reaction (removing water, a process known as dehydration) to yield the final alkenylated product (**Scheme 14**)[3]. Heteroaromatic *N*-oxides have the ability to take part in (3+2)-cycloaddition reactions when treated with electron-deficient alkenes. A number of examples of this reactivity have been documented (**Scheme 15**). As a representative instance, the cycloaddition between N-methyl maleimide and (Z)-2-styrylquinazoline 3-oxide proceeded smoothly at ambient temperature. This reaction successfully yielded the cycloadduct as a mixture of two diastereomeric isoxazolidines in high combined yield[36].



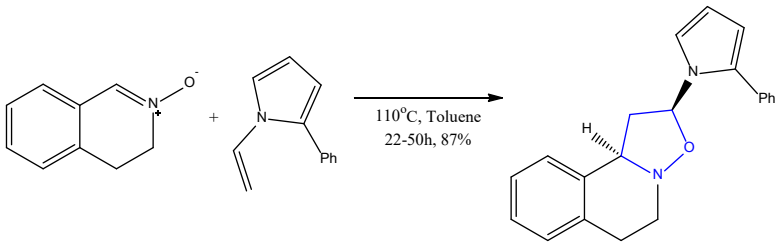
Scheme 15. The cycloaddition between N-methyl maleimide and quinoline (Z)-2-styrylquinazoline 3-oxide.

In a different study involving a (3+2) cycloaddition between an alkynone and isoquinoline *N*-oxide, the initial product formed is an isoxazolo[3,2-a]isoquinoline. Subsequent ring opening of the isoxazolo moiety generates an intermediate that rapidly equilibrates with its tautomeric form via imine–enamine tautomerism. The reaction is completed by an intramolecular nucleophilic substitution involving one of the stable tautomeric forms of the intermediate. This final step yields the complex fused ring system, 14-benzoylbenzo[5,6]azepino[2,1-a]isoquinolin-13(8H)-one, as the final product (**Scheme 16**)[37].



Scheme 16. Proposed reaction mechanism of (3+2) cycloaddition between an alkynone and isoquinoline *N*-oxide, with the initial product formed as isoxazolo[3,2-a]isoquinoline.

An experimental study was conducted on the (3+2) cycloaddition (32CA) reaction using 3,4-dihydroisoquinoline-*N*-oxides and N-vinylpyrrole. This reaction was designed to create a new type of polyheterocyclic compound, specifically, pyrrolyl-substituted isoxazolo[3,2-a]isoquinolines (**Scheme 17**). The authors observed that this transformation proceeded without the use of any catalyst. It exclusively yielded the ortho pyrrolyl-substituted tetrahydro-1H-isoxazolo[3,2-a] isoquinoline[38].



Scheme 17. An experimental study was conducted on the (3+2) cycloaddition (32CA) reaction using 3,4-dihydroisoquinoline 2-oxide with 2-phenyl-1-vinyl-1H-pyrrole.

3. Conclusion

A comprehensive analysis of the literature demonstrates that the (3+2) cycloaddition of heteroarene *N*-oxides constitutes a unique and chemically complex subset of cycloaddition reactions. While these heteroaromatic substrates can formally react as cyclic nitrones to form fused isoxazolidine rings, their chemical behavior is overwhelmingly dictated by the thermodynamic driving force to restore aromaticity. As highlighted by numerous studies, the isolation of the primary (3+2) cycloadduct is generally the exception rather than the rule. In most instances, the loss of resonance energy upon cycloaddition renders the isoxazolidine intermediate highly unstable, promoting rapid N–O bond cleavage. This inherent instability leads the reaction along various pathways, typically yielding products of rearomatization, such as alkenylated heterocycles, or complex rearranged scaffolds instead of the simple cycloadducts obtained from standard nitrones. Stable fused isoxazolidine systems are typically achieved only when the resonance energy of the starting heterocycle is comparatively low, or when highly reactive 2-π-electron components are employed under carefully controlled, mild conditions. Consequently, the (3+2) cycloaddition of heteroarene *N*-oxides should be regarded not simply as a preparative route to isoxazolidines, but rather as a highly versatile strategy for the regio- and stereoselective functionalization of heteroaromatic cores via transient isoxazolidine intermediates.

References

1 Takeuchi Y., and Furusaki F. (**1977**) The chemistry of isoxazolidines. *Adv. Heterocycl. Chem.*, 21, 207-251.
2 Fryźlewicz A., Łapczuk-Krygier A., Kula K., Demchuk O. M., Dresler E., and Jasiński R. (**2020**) Regio-and stereoselective synthesis of nitrofunctionalized 1, 2-oxazolidine analogs of nicotine. *Chem. Heterocycl. Compd.*, 56 (1) 120-122.
3 Kouznetsov V. V., Vargas Méndez L. Y., Puerto Galvis C. E., and Ortiz Villamizar M. C. (**2019**) The direct C–H alkenylation of quinoline N-oxides as a suitable strategy for the synthesis of promising antiparasitic drugs. *New J. Chem.*, 44 (1) 12-19.
4 Loh B., et al. (**2010**) Inhibition of HIV-1 replication by isoxazolidine and isoxazole sulfonamides. *Chem. Biol. Drug Des.*, 75 (5) 461.
5 Ghannay S., et al. (**2024**) Identification of dual-target isoxazolidine-isatin hybrids with antidiabetic potential: Design, synthesis, in vitro and multiscale molecular modeling approaches. *Heliyon*, 10 (4) e25911.
6 Al-Adhreai A., et al. (**2023**) Enhanced synthesis of novel multisubstituted isoxazolidines as potential antimicrobial and antioxidant agents using zinc (II) catalyst, and in silico studies. *J. Mol. Struct.*, 1292 (15) 136146.
7 Mosbah H., et al. (**2019**) Biological activities evaluation of enantiopure isoxazolidine derivatives: In vitro, in vivo and in silico studies. *Appl. Biochem. Biotechnol.*, 187 (3) 1113-1130.
8 Doroszko C., and Jarzyński S. (**2025**) Recent progress in cycloaddition reactions of maleimides (microreview). *Chem. Heterocycl. Compd.*, 61 (7) 311-313.
9 Kącka-Zych A. (**2025**) Synthesis of heterocycles via cycloaddition reactions with the participation of cyano-substituted nitroalkenes (microreview). *Chem. Heterocycl. Compd.*, 61 (7) 317-319.
10 Rama Krishna Veni P., Vijaya Saradhi C., and Usha Rani G. (**2024**) Zn(OAc)2•2H2O-catalyzed synthesis of chromeno[2,3-d] pyrimidinones under solvent-free conditions. *Curr. Chem. Lett.*, 13, 677-682.
11 Murahashi S. I., and Imada Y. (**2019**) Synthesis and transformations of nitrones for organic synthesis. *Chem. Rev.*, 119 (7) 4684-4716.
12 Hamer J., and Macaluso A. (**1964**) Nitrones. *Chem. Rev.*, 64 (4) 473-495.
13 Jasiński R., Mróz K., and Kącka A. (**2016**) Experimental and theoretical DFT study on synthesis of sterically crowded 2, 3, 3,(4) 5-tetrasubstituted-4-nitroisoxazolidines via 1, 3-dipolar cycloaddition. *J. Heterocycl. Chem.*, 53 (5) 1424-1429.
14 Jasiński R., Żmigrodzka M., Dresler E., and Kula K. (**2017**) A full regioselective and stereoselective synthesis of 4-nitroisoxazolidines via stepwise cycloaddition reactions between (Z)-C-(9-anthryl)-N-arylnitrones. *J. Heterocycl. Chem.*, 54 (6) 3314-3320.

15 Jasiński R. (**2009**) Cycloaddition reaction of triphenylnitrone to nitroethene. *Chem. Heterocycl. Compd.*, 45 (6).
16 Jasiński R. (**2009**) Regio- and stereoselectivity of cycloaddition of nitroethene to (Z)-N-aryl-C-phenylnitrones. *Collect. Czech. Chem. Commun.*, 74 (9) 1341-1349.
17 Zawadzińska K., Gadocha Z., Pabian K., Wróblewska A., Wielgus E., and Jasiński R. (**2022**) Cycloadditions with the participation of (E)-3,3,3-tribromo-1-nitroprop-1-ene. *Materials*, 15 (21) 7584.
18 Jasiński R. (**2015**) Kinetic aspects of cycloaddition reactions between (E)-3, 3, 3-trichloro-1-nitroprop-1-ene and ketonitrones. *React. Kinet. Mech. Catal.*, 116 (1) 35-41.
19 Jasiński R. (**2015**) In the searching for zwitterionic intermediates on reaction paths of cycloaddition reactions between 2, 2, 4, 4-tetramethyl-3-thiocyclobutanone S-methylide. *RSC Adv.*, 5.
20 Fałowska A., Ząbkowska M., Sambora K., Kula K., Łapczuk A., and Jasiński R. (**2026**) Application of DFT models for the prediction of geometries and energies of the transition states in [4+2]-π-electron cycloadditions. *Curr. Chem. Lett.*, 15 (1) 169-174.
21 Dresler E., Kącka-Zych A., Kwiatkowska M., and Jasiński R. (**2018**) Regioselectivity, stereoselectivity, and molecular mechanism of [3+2] cycloaddition reactions between 2-methyl-1-nitroprop-1-ene and (Z)-C-aryl-N-phenylnitrones: A DFT computational study. *J. Mol. Model.*, 24 (11) 329.
22 Alnajjar R. A., and Jasiński R. (**2019**) Competition between [2+1]- and [4+1]-cycloaddition mechanisms in reactions of conjugated nitroalkenes with dichlorocarbene in the light of a DFT computational study. *J. Mol. Model.*, 25 (6) 157.
23 Sadowski M., Kula K., and Jasiński R. (**2026**) On the question of the transformation of amino acids into aldimine N-oxides (nitrones): Molecular electron density theory (MEDT) considerations. *Monatsh. Chem.*, 157 (1) 73-84.
24 Jasiński R. (**2023**) Heterocycles in focus: Recent progress in the synthesis of nitroisoxazoles and their hydrogenated analogs via [3+2] cycloaddition reactions (microreview). *Chem. Heterocycl. Compd.*, 59 (11-12) 730-732.
25 Mailey E. A., and Ocone L. R. (**1968**) Fluoroalkylpyridines. A novel rearrangement. *J. Org. Chem.*, 33 (8) 3343-3344.
26 Banks R. E., Haszeldine R. N., and Robinson J. M. (**1976**) Heterocyclic polyfluoro-compounds. Part XXIII. Reaction of some 2-, 3-, and 4-substituted pyridine 1-oxides, 5-methylpyrimidine 1-oxide, and quinoline 1-oxide with perfluoropropene, and of pyridine 1-oxide with perfluoro-(2-methylpent-2-ene): Synthesis of 2-(1,2,2,2-tetrafluoroethyl)-pyridines or -pyrimidines and their N-oxides and of 2,2,3-trifluoro-2,3-dihydro-3-trifluoromethylfuro[3,2-b]pyridine. *J. Chem. Soc. Perkin* 1, (11) 1226.
27 Loska R., and Mąkosza M. (**2006**) Simple method for the introduction of tetrafluoroethyl substituents into nitrogen heterocycles. *Mendeleev Commun.*, 16 (3) 161-163.
28 Loska R., and Mąkosza M. (**2008**) New synthesis of 2-heteroarylperfluoropropionic acids derivatives by reaction of azine N-oxides with hexafluoropropene. *Chem. Eur. J.*, 14 (8) 2577-2589.
29 Hisano T., Harano K., Fukuoka R., Matsuoka T., Muraoka K., and Shinohara I. (**1986**) Reaction of aromatic N-oxides with dipolarophiles. XI 1,3-dipolar cycloaddition reaction of pyridine N-oxides with tosyl isocyanate and one-pot synthesis of 2-oxooxazolo(4,5-b)pyridine derivatives. *Chem. Pharm. Bull.*, 34 (4) 1485-1492.
30 Hamana M., et al. (**1983**) The reaction of 3-bromo-4-methoxyquinoline 1-oxide with dimethyl acetylenedicarboxylate. *Heterocycles*, 20 (2) 193.
31 Takahashi S., and Kanō H. (**1965**) Benzimidazole N-oxides. V. Reactions of 1,2-dimethylbenzimidazole 3-oxide with acetylenecarboxylates. *J. Org. Chem.*, 30 (4) 1118-1122.
32 Hamanal M., Ueda I., and Kawano S. (**1983**) The reaction of 3-bromo-4-methoxyquinoline 1-oxide with dimethyl acetylenedicarboxylate. *Heterocycles*, 20 (2).
33 Dhiman A. K., Kumar R., Kumar R., and Sharma U. (**2017**) Metal-free synthesis of 2-substituted 3-(2-hydroxyaryl)quinolines and 4-(2-hydroxyaryl)acridines via benzyne chemistry. *J. Org. Chem.*, 82 (23) 12307-12317.
34 Sreenivasulu G., Raju C. E., Palaci M. S., Sridhar B., and Karunakar G. V. (**2023**) Synthesis of isoquinoline-derived diene esters and quinolin-2(1H)-ylidene-substituted 1,5-diones from enynones and (iso) quinoline N-oxides. *Org. Lett.*, 25 (1) 115-119.
35 Liu J., Jin Q., Lü H., and Huang W. (**2004**) Synthesis of 5-fluoroalkyl isoxazolidines via 1,3-dipolar cycloaddition of ethyl 2-hydropolyfluoroalk-2-enoates with nitrones. *Chin. J. Chem.*, 22 (9) 945-949.
36 Heaney F., Lawless E., Mahon M., McArdle P., and Cunningham D. (**2006**) 1,3-Dipolar character of 2-vinyl quinazoline 3-oxides; first and second generation cycloaddition products. *Org. Biomol. Chem.*, 4 (12) 2408-2416.
37 Li X., Zhou G., Du X., Wang T., and Zhang Z. (**2019**) Catalyst- and additive-free cascade reaction of isoquinoline N-oxides with alkynones: An approach to benzoazepino[2,1-a]isoquinoline derivatives. *Org. Lett.*, 21 (14) 5630-5633.
38 Afanaseva K. K., Efremova M. M., Kuznetsova S. V., Ivanov A. V., Starova G. L., and Molchanov A. P. (**2018**) The (3+2)- and formal (3+3)-cycloadditions of N-vinylpyrroles with cyclic nitrones and C,N-cyclic azomethine imines. *Tetrahedron*, 74 (39) 5665-5673.

© 2026 by the authors; licensee Growing Science, Canada. This is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license (http://creativecommons.org/licenses/by/4.0/).