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Oxazinoazaarenes as Versatile Intermediates for Regioselective Late-Stage C–H-Functionalization and Skeletal Editing of Pyridines, Isoquinolines and Quinolines

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Abstract: Azaarenes, particularly pyridines, represent some of the most important structural and functional motifs across various fields. Consequently, late-stage C–H bond functionalization and skeletal editing of azaarenes hold significant value, particularly for accelerating structure–activity relationship studies. Dearomatized intermediates derived from such azaarenes offer an innovative strategy for selectively modifying these valuable cores. Among them, oxazinoazaarenes are a practical and scalable platform for regioselective *meta*- and *para*-C–H functionalization and skeletal editing of the azaarene moiety. This short review highlights the advancements in oxazinoazaarene-based pyridine modification methods achieved by our group and others.

Keywords: Azaarene · Late-stage C–H-functionalization · Pyridine · Skeletal editing · Temporary dearomatization

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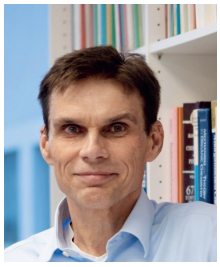

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1. Introduction

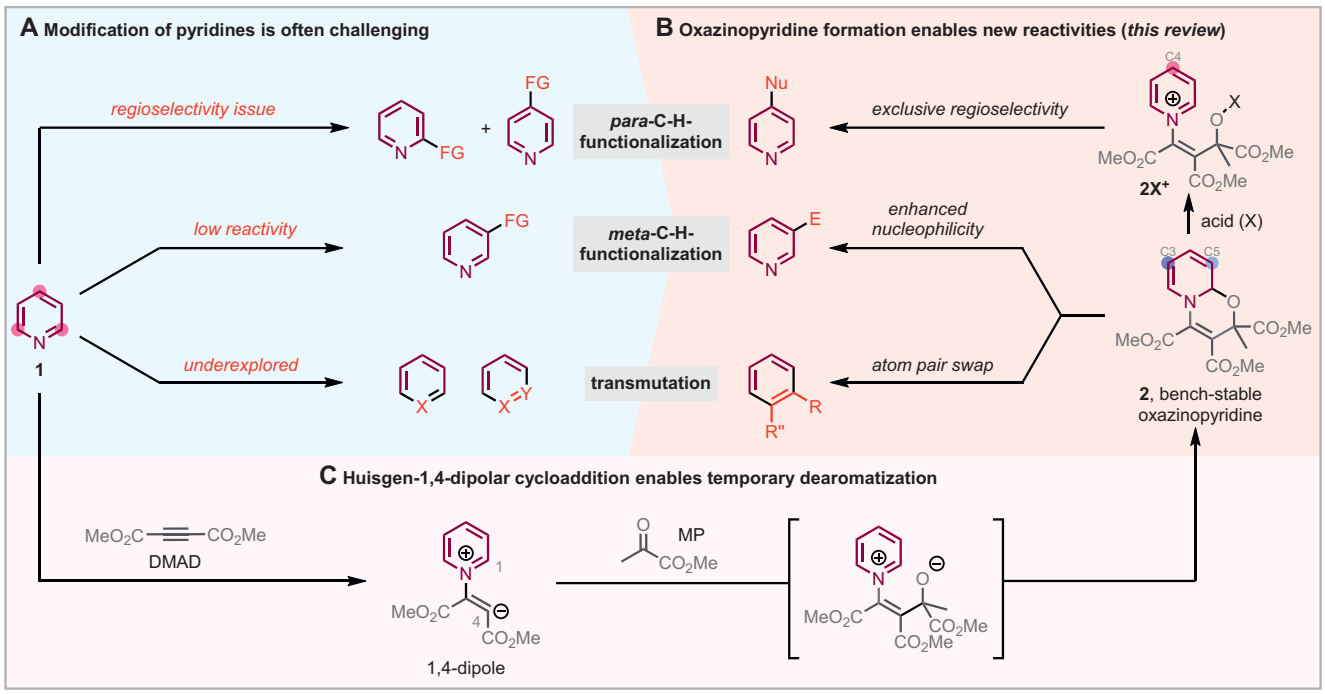
Azaarene cores serve as a structural framework in biologically active compounds, drugs, agrochemicals, ligands, and functional materials.[1,2] Pyridine is the most frequently featured heteroarene core and the second most common heterocycle found in FDA-approved drugs.[3] Different substituents and the 'necessary N effect' of the azine core influence physical, chemical, and pharmacological properties. Late-stage C–H functionalization is a step-economic approach to modify these properties and is consequently therefore highly relevant, especially in drug discovery campaigns.[4] However, achieving regioselective C–H-functionalization of unbiased pyridines and other azaarenes is challenging (Scheme 1A). The strong directing nature of the N-center renders C2-selective C–H-functionalization relatively easy, while achieving regioselective C4-chemical modification suppressing C2-functionalization is less straightforward.[5,6]

Meta-C–H-functionalization[7] is even more challenging and often requires harsh reaction conditions as there is no electronic bias towards this position.[8]

Skeletal editing of azaarenes involves atom(s) deletion, addition, and transmutation providing an attractive alternative for late-stage modification altering the physicochemical properties of biologically active compounds.[9–11] While significant progress has been made in this area recently, skeletal editing of pyridines still remains underexplored due to the energy compensation required for the loss of aromaticity during the course of these reactions.[12]

Recently, temporary dearomatization became a popular approach to access the *meta*-position of azaarenes in a highly regioselective way. In such a strategy, the electron deficient azaarene core is usually converted into an electron rich (di-)enamine intermediate, which is nucleophilic at the C3 and C5-positions (nomenclature relative to the parent pyridine). These nucleophilic centers engage in reactions with a wide range of electrophilic reagents and can then be finally rearomatized to the corresponding *meta*-functionalized azaarenes.[8]

Initial strategies for temporary dearomatization suffered from low stability of the generated (di-)enamine intermediates and/or



Scheme 1. Challenges in selective C–H-functionalization and skeletal editing of pyridines and our temporary dearomatization approach as one way to achieve these difficult transformations. DMAD = dimethyl acetylenedicarboxylate, MP = methyl pyruvate.

harsh reaction conditions limiting their compatibility with electrophilic reagents and their application in late-stage functionalization.[8] In 2022, Wang and coworkers developed an efficient one-pot reaction sequence to functionalize the *meta*-position promoted through frustrated Lewis pair catalyzed hydroboration of pyridine to 1,4-dihydropyridine, which is nucleophilic at the C3-position.[13] Moreover, the McNally group explored acyclic Zincke-imine intermediates,[14] while our group identified cyclic oxazinoazaarenes (Scheme 1B, **2**)[15] to be suitable for enabling various formal *meta*-C–H functionalizations, which were subsequently followed by further modifications. Both of these dearomatized intermediates are isolable and bench-stable, but are still easily rearomatized.

This short review focusses on our and other group's contributions to the field of oxazinoazaarene-based (late-stage) modification of pyridines and other azaarenes (Scheme 1B). First, the discovery and synthesis of oxazinoazaarenes is discussed followed by the exploitation of their nucleophilic C3- and C5-reactivity for formal *meta*-C–H functionalization and skeletal editing. Finally, the electrophilic C4-position of protonated oxazinoazaarenes is discussed to achieve selective *para*-C–H functionalization.

2. Synthesis of Oxazinopyridines Using a Huisgen 1,4-Dipolar Cycloaddition

A 1,4-dipolar cycloaddition is a stepwise reaction between a polarized multiple bond and a 1,4-dipole, which is often generated *in situ* with a suitable donor-acceptor combination.[16] The origin of 1,4-dipoles of azaarenes can be traced back to 1932, where Diels and Alder isolated a red colored compound formed by the reaction of pyridine and dimethyl acetylenedicarboxylate (DMAD).[17] The structure of this zwitterionic species was correctly assigned by Acheson, describing it as a 1,3-dipole.[18–21] In 1967, Huisgen and coworkers rephrased it as a 1,4-dipole during the development of their 1,4-dipolar cycloaddition of azaarenes.[22] The 1,4-dipolar cycloaddition starts with the azaarene attacking the electrophilic DMAD generating a 1,4-dipole *in situ*, which then reacts with an electrophilic partner to form the dearomatized cycloaddition product. These products were later utilized by Nair *et al*. for the functionalization of aldehydes, imines and electron-deficient alkenes, but besides that their synthetic utility remained largely underexplored.[16]

Inspired by Huisgen's pioneering work, our group developed an efficient and scalable 1,4-cycloaddition sequence using methyl pyruvate (MP) as the electrophilic partner (Scheme 1C).[15] The two inseparable oxazinoazaarene-diastereomers formed are bench stable compounds consisting of an electron-rich cyclic dienamine core. After the desired C–H functionalization they are readily rearomatized by treatment with aqueous HCl upon heating, with all diastereomers converging to the same functionalized azaarene. Notably, *meta*-substituted pyridines can form two regioisomeric oxazinoazaarenes, with either the C3- or C5-position being blocked. These regioisomers can exhibit different reactivity in the subsequent C–H functionalization (*vide infra*).

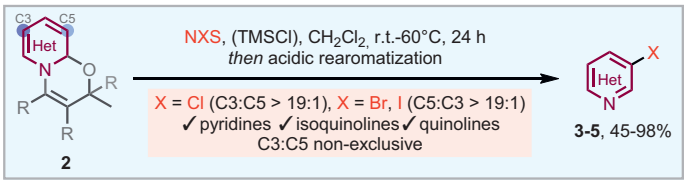
Since our initial work in 2022,[15] our group has been intensively working on the area of oxazinoazaarene-based selective formal C–H functionalization and skeletal editing of azaarenes. To date, we have dearomatized more than 50 azaarenes, including pyridines, isoquinolines, quinolines and thiazoles, with yields typically exceeding 80%, showcasing the scalability and accessibility of these oxazinoazaarenes in a 25 mmol large-scale reaction.[23] For this dearomatization, a wide range of substituents is tolerated at the *meta*- and *para*-position of the pyridine, while substituents at the *ortho*-position are mostly limited to phenyl and alkynyl-groups.[15] If multiple azaarene cores are present in a molecule, selectivity for oxazinoazaarene formation is governed by steric hindrance and nucleophilicity of the nitrogen atom, which can be exploited for selective mono- or difunctionalization of such compounds.[15]

3. Reactivity of Oxazinopyridines

3.1 *Reactions at the Nucleophilic C3- and C5-Positions*

We first employed oxazinoazaarenes for formal *meta*-C–H-functionalization of azaarenes. Our initial work covered radical *meta*-trifluoromethylation and other radical (per-)fluoroalkylations as well as ionic *meta*-halogenation of oxazinopyridines, -isoquinolines and -quinolines.[15]

Meta-halogenation of oxazinoazaarenes (Scheme 2) was achieved by nucleophilic attack of the oxazinoazaarene to the corresponding *N*-halo-succinimide (NXS).[15]



Scheme 2. Ionic *meta*-halogenation of oxazinoazaarenes, R = CO_2Me.

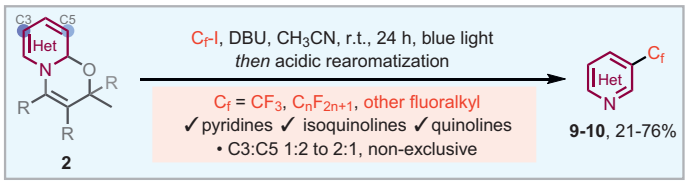
We proposed that a cationic intermediate (**INT1**-type, Scheme 3A) is generated followed by deprotonation, yielding the *meta*-functionalized oxazinoazaarene (**INT2a**-type). Acidic rearomatization eventually yields *meta*-chlorinated (**3**), -brominated (**4**) or -iodinated (**5**) pyridines, isoquinolines, and quinolines in moderate to high yields (45–98%).[15]

Only the monofunctionalized products were formed, except for *para*-substituted pyridines (*e.g.* 5:1 mono:di for *para*-phenylpyridine). Notably, positional selectivity in the dienamine structural core of the oxazinoazaarene intermediate was also pronounced. Chlorination occurred preferably at the kinetic C3 position, while bromination and iodination afforded the thermodynamic C5-halogenated products. We proposed that this effect is caused by the reversible formation of the bromonium and iodonium intermediates while the chloronium formation is irreversible.[15]

If the preferred *meta*-position was already substituted, the other ('free') *meta*-position gets functionalized, which we call non-exclusive regioselectivity in contrast to some of the following *meta*-functionalizations, which are exclusively C3-selective. Along with the *meta*-halogenations we also demonstrated that -SePh (**6**), -SPh (**7**) and -NO_2 (**8**) moieties can be introduced at the *meta*-position.[15]

The radical trifluoromethylation is initiated through blue light-induced generation of an electrophilic trifluoromethyl radical from CF_3I (Scheme 4).[15]

The polarity of the electrophilic CF_3-radical matches with the nucleophilicity of the oxazinoazaarene's *meta*-positions enabling radical addition to either the C3 or C5-position. From the generated carbon-centered adduct radical (**INT3**-type, Scheme 3B)

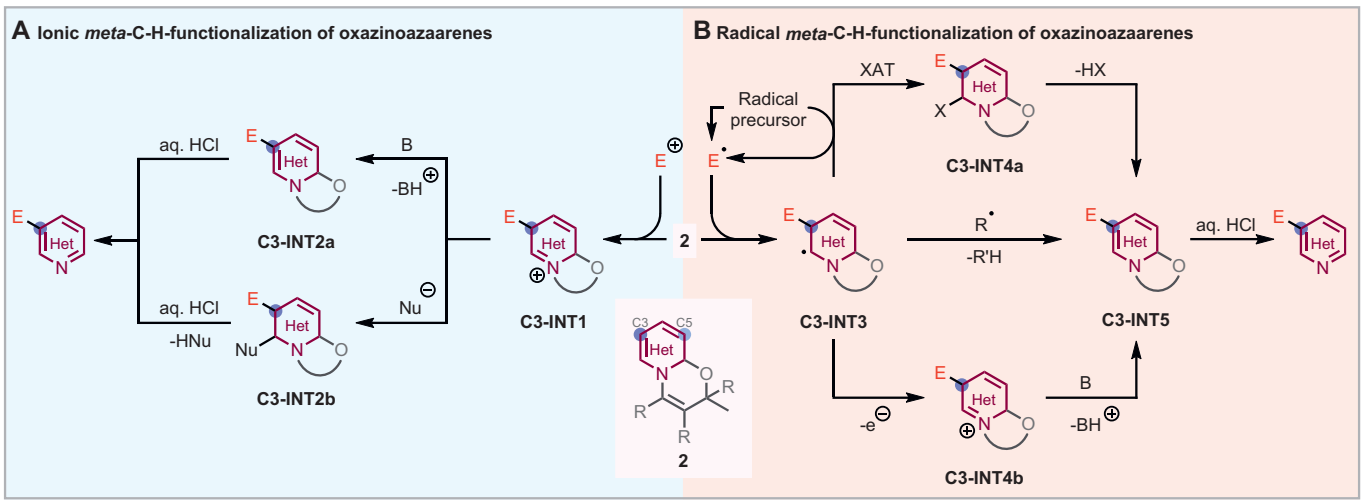


Scheme 4. Radical (per-)fluoroalkylation of oxazinoazaarenes. DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene; R = CO_2Me.

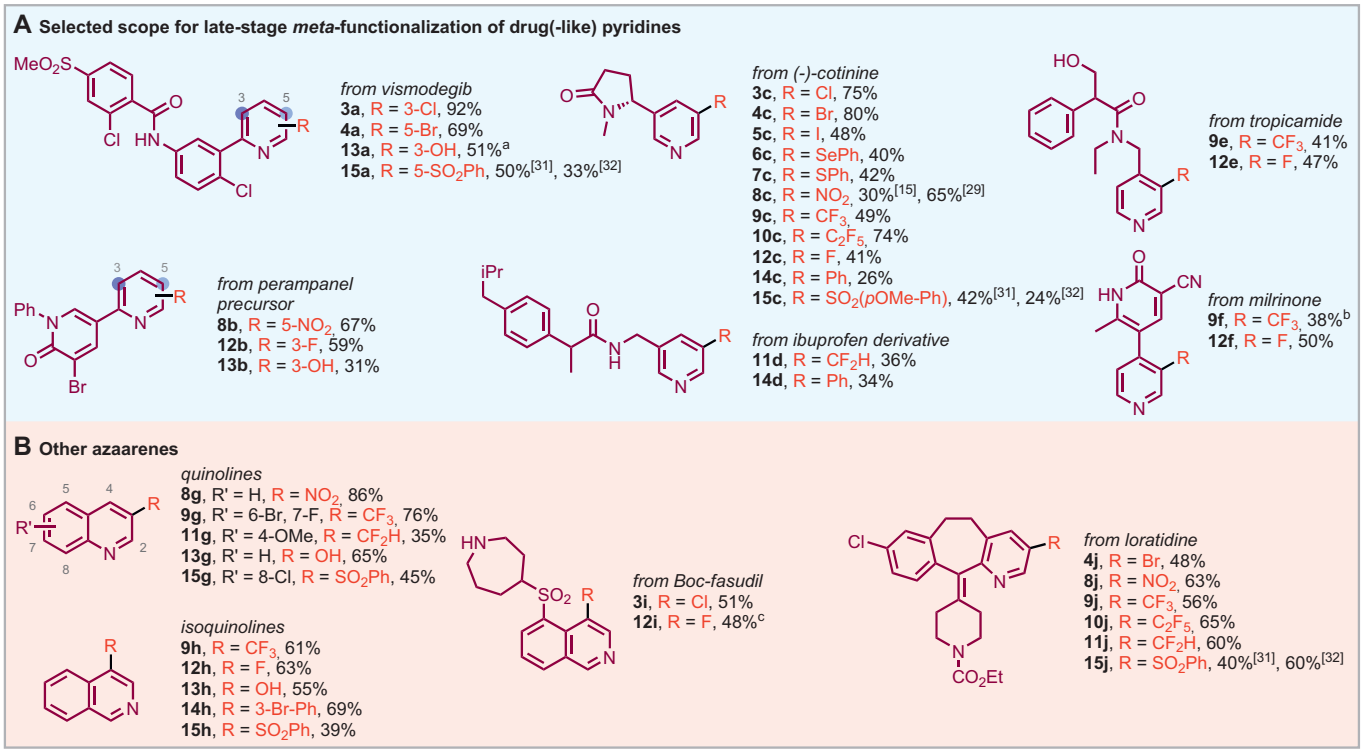
different paths can lead to the *meta*-functionalized azaarene. For the trifluoromethylation we proposed that halogen-atom-transfer (XAT) from the CF_3I radical precursor followed by DBU mediated elimination of HI from the iodine atom transfer adduct (**INT4a**-type) gives the *meta*-functionalized oxazinoazaarene (**INT5**-type), which is finally rearomatized under our standard acidic conditions. The XAT step generates a new trifluoromethyl radical thereby sustaining the radical chain.[15]

This method enabled formal *meta*-C–H-trifluoromethylation (**9**) as well as the introduction of other (per-)fluoroalkyl groups (**10**) in moderate to good yields (21–76%). Selectivity for mono-functionalization was generally high, likely due to the deactivating effect of the introduced electron-withdrawing (per-)fluoroalkyl group. The trifluoromethylation of milrinone was an exception, resulting in a 1:1 mixture of the mono- and difunctionalized products. Unfortunately, C3:C5 regioselectivity was low in these radical perfluoroalkylations ranging from 2:1 to 1:2 depending on the substrates.[15]

Before discussing the follow-up studies, we outline some common features shared by these works, based on the findings of the initial study: 1) The synthetic utility of the presented methods was demonstrated in late-stage functionalization of drug(-like) molecules, a selected scope of which is presented in Scheme 5. 2) For azaarenes, that are easily dearomatized (no *ortho*-substituent, no strongly electron withdrawing substituents), the *meta*-functionalization protocol can often be performed in a one-pot sequence starting from the azaarene, delivering yields comparable to those of the two-pot process. If a solvent that is not miscible with water is used for the *meta*-functionalization step, solvent removal is required before the rearomatization step. For *ortho*-substituted or electron-poor azaarenes, isolation of the oxazinoazaarenes usually results in significantly higher yields of the *meta*-functionalized products. 3) Selectivity for mono-functionalization over difunctionalization is usually high, except for pyridines bearing electron donating *para*-substituents. 4) For C2-substituted ox-



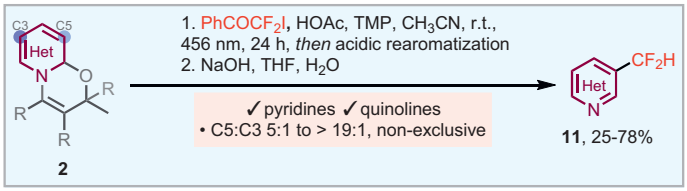
Scheme 3. Proposed mechanistic pathways for ionic and radical *meta*-C–H-functionalization of oxazinoazaarenes. For clarity the corresponding pathways for C5-functionalization are omitted. B = Base; E = Electrophile; R = CO_2Me; XAT = Halogen-atom transfer.



Scheme 5. Selected scope of *meta*-functionalized pyridine drug (precursor) derivatives, isoquinolines and quinolines synthesized by our oxazino-azaarene-based approach. Yields are based on the corresponding oxazinoazaarenes. Compound numbers correspond to the introduced functional groups, letters to the starting materials. [a]From dearomatized Boc-vismodegib; [b]Isolated as a 1:1 mixture of the mono- and difunctionalized product; [c]Isolated as 1:1 adduct with 18-crown-6.

azinopyridines, the regioselectivity likely depends on the size of the electrophile and the reversibility of the C–E-bond formation, which is dictated by the C–E bond strength. Stabilization of the generated cationic (**INT1**-type) or radical (**INT3**-type) intermediates can also influence the regioselectivity (*vide infra*).

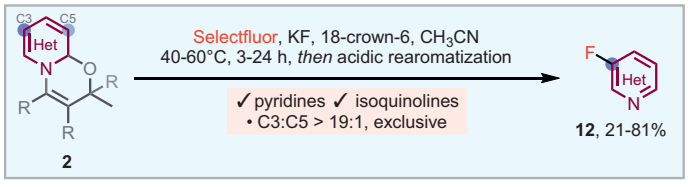
While several (per-)fluoroalkyl groups were successfully conjugated to the azaarene core in our initial work, introduction of the medicinally relevant CF_2H-group required further attention.[24] A $^{\bullet}CF_2H$-radical is considered to be nucleophilic in reactions with heterocycles resulting in a polarity mismatch in the reaction with an oxazinoazaarene.[24,25] However, replacing the H-substituent in HCF_2I with an electron-withdrawing benzoyl group leads to $PhCOCF_2I$, which upon irradiation generates the [$^{\bullet}CF_2$(COPh)] radical. This electrophilic radical can readily add to the nucleophilic oxazinoazaarene in analogy to the trifluoromethyl radical (Scheme 6).[24]



Scheme 6. Radical *meta*-difluoromethylation of oxazinoazaarenes. R = CO_2Me; TMP = 2,2,6,6-tetramethylpiperidine.

After acidic rearomatization, the benzoyl group can be hydrodeacylated with NaOH yielding *meta*-difluoromethylated pyridines and quinolines (**11**) in moderate to high yields (25–78%). Selectivity for monofunctionalization was found to be good to excellent for both C2 and C4 substituted oxazinopyridines (3:1 to >19:1). The reaction proceeds in a non-exclusive C5-selective manner (C5:C3 5:1 to >19:1) with higher C5 selectivity as compared to the trifluoromethylation likely due to the larger size of the [$^{\bullet}CF_2$(COPh)] radical.[24]

Monofluorinated pyridines are highly relevant for pharmaceuticals, agrochemicals, materials, and as ligands, due to the change in the physicochemical properties introduced by a fluorine substituent. However, treatment of oxazinoazaarenes with Selectfluor led to their decomposition, affording only trace amounts of the desired *meta*-fluorinated azaarenes upon rearomatization. We solved this problem by using KF and 18-crown-6 as additives (Scheme 7).[26]

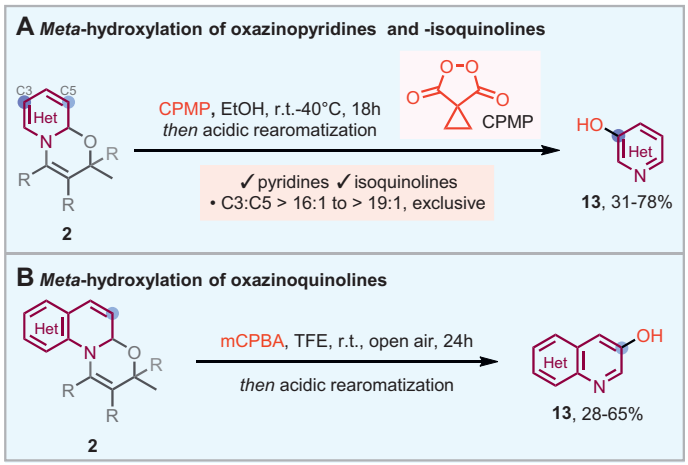


Scheme 7. *Meta*-fluorination of oxazinoazaarenes, R = CO_2Me.

Mechanistic investigations ran on 4-phenyl oxazinopyridine revealed that the cationic oxazinopyridinium intermediate formed after electrophilic fluorination (Scheme 3A, **C3-INT1**-type) is not directly deprotonated, but instead trapped by fluoride forming a stable C2, C3-difluorinated intermediate (**C3-INT2b**-type). Under our standard acidic rearomatization conditions, elimination of HF then yields the desired *meta*-fluorinated pyridines or isoquinolines (**12**). Furthermore, the presence of KF leads to decomposition of Selectfluor, which could reduce the amount of undesired side reactions.[26]

This protocol allowed for formal *meta*-C–H-fluorination of pyridines and isoquinolines in moderate to high yields (21–81%).

Notably, the reaction proceeds in a highly selective manner for monofunctionalization and with exclusive C3 selectivity, likely due to the high strength of the C–F-bond (kinetic product).[26]

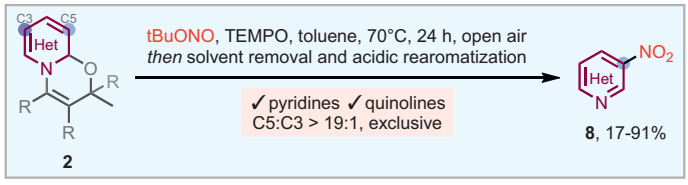


Scheme 8. *Meta*-hydroxylation of oxazinoazaarenes. CPMP = cyclopropyl malonyl peroxide, *m*CPBA = *meta*-chloroperoxybenzoic acid, R = CO_2Me.

While fluorinated moieties can act as bioisosteres of pharmaceutically highly relevant hydroxy groups,[27] methods for *meta*-C–H-hydroxylation of azaarenes are still highly desirable.[28] Recently, we disclosed an oxazinoazaarene-based protocol for such a formal *meta*-hydroxylation of azaarenes (Scheme 8).[28]

Utilizing cyclopropyl malonyl peroxide (CPMP) *meta*-hydroxylation of oxazinopyridines and isoquinolines was achieved in moderate to good yields (**13**, 31–78%) with high selectivity for mono-hydroxylation. The reaction occurred with high C3-selectivity (>16:1), but its exclusivity prevented the use of C3-substituted oxazinopyridines or oxazinoquinolines. However, oxazinoquinolines were C5-hydroxylated in moderate to good yields (28–65%) by using *meta*-chloroperoxybenzoic acid (*m*CPBA) instead of malonyl peroxide. The *meta*-hydroxy group was also exploited as a synthetic handle for several follow-up reactions, further underlining the synthetic value of this method.[28]

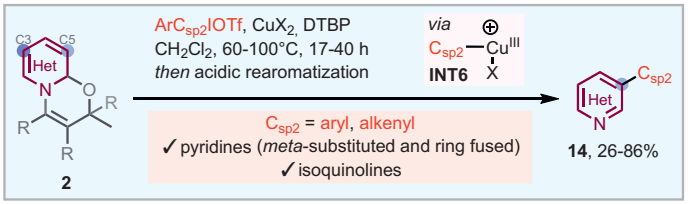
Additional pharmaceutically and synthetically relevant functional groups have also been recently introduced at the *meta*-position of oxazinopyridines. For example, we recently developed a method for formal *meta*-nitration of oxazinoazaarenes utilizing *tert*-butyl-nitrite as an NO-radical precursor in combination with TEMPO and air (Scheme 9).[29]



Scheme 9. Radical *meta*-nitration of oxazinoazaarenes. R = CO_2Me, TEMPO = (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl.

In this transformation, the NO-radical generated upon thermal homolyis of the nitrite is oxidized by TEMPO and O_2 (from air) to an electrophilic NO_2 radical, which can react with the nucleophilic *meta*-positions of the oxazinoazaarene. The generated carbon centered adduct radical (Scheme 3B, **INT3**-type) is stabilized by reversible trapping with TEMPO. Hydrogen atom abstraction (HAT) by TEMPO or O_2 from the carbon centered radical followed by acidic rearomatization yields *meta*-nitro pyridines and quinolines in moderate to excellent yields (**8**, 17–91%). Selectivity for mono-nitration is high (13:1) and the reaction displays exclusive C5-selectivity, which is likely caused by the steric demand of TEMPO and the reversible C–N-bond formation. In follow-up reactions, the *meta*-nitro-azaarenes were easily reduced to the corresponding *meta*-amino azaarenes, demonstrating their synthetic value.[29]

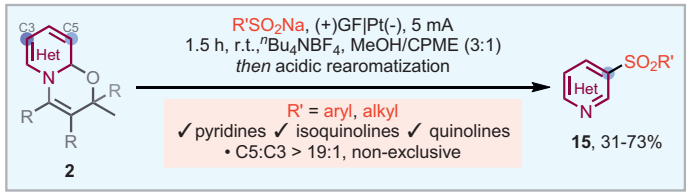
We further expanded the scope of formal *meta*-functionalization by employing transition metal catalysis and reported a copper-catalyzed formal *meta*-arylation of oxazinopyridines and isoquinolines (Scheme 10).[30]



Scheme 10. Copper-catalyzed *meta*-arylation and -alkenylation of oxazinoazaarenes. DTBP = 2,6-di-tert-butylpyridine, R = CO_2Me.

Oxidative addition of a diaryl-iodine(III) reagent to the Cu(I) salt generates a highly electrophilic Cu(III)-aryl species (**INT6**) that forms a C–Cu bond at one of the *meta*-positions of the oxazinoazaarene. Reductive elimination followed by deprotonation and acidic rearomatization yields the desired *meta*-arylated pyridines and isoquinolines (**14**). Different aryl groups were introduced in moderate to good yields (26–86%). Additionally, the protocol was extended to *meta*-alkenylation by employing the corresponding alkenyl-I(III) reagents (38–73%). Notably, due to steric hindrance, the scope of oxazinopyridine substrates is limited to *meta*-substituted oxazinopyridines and fused pyridine systems.[30]

Recently, other research groups have also begun exploring the potential of oxazinoazaarenes for formal *meta*-functionalization. Qin *et al*. disclosed an electrochemical *meta*-sulfonylation of oxazinopyridines, -isoquinolines and -quinolines (Scheme 11). Electrochemical generation of an electrophilic sulfonyl radical from the corresponding sodium sulfinate and addition to the oxazinoazaarene leads a resonance stabilized radical intermediate (Scheme 3B, **INT3**-type).[31]

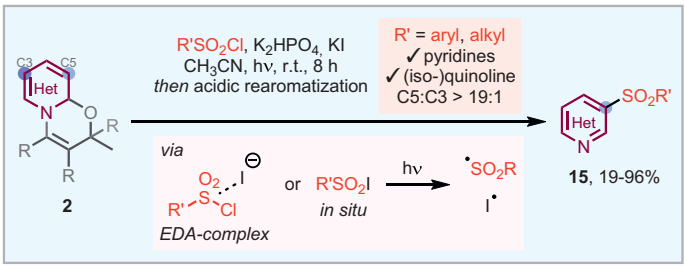


Scheme 11. Electrochemical *meta*-sulfonylation of oxazinoazaarenes. CPME = cyclopentyl methyl ether, R = CO_2Me.

Anodic oxidation followed by deprotonation and acidic rearomatization of the cationic **INT4b**-type intermediate finally provides the corresponding *meta*-sulfonylated azaarenes (**15**). The reaction works with aryl- and alkyl-sulfinates, and the substituted azaarenes were obtained in moderate to good yields (31–73%).

This transformation showed complete selectivity for mono-sulfonylation and high, but non-exclusive C5-selectivity.[31] In a follow-up work, the same group used *cis*-[Ru(II)(bpy)$_2$]Cl$_2$•H$_2$O as a photoredox catalyst and sulfonyl chlorides as the S-radical precursors to get the same products.[32]

Very recently Yang and coworkers disclosed a photochemical oxazinoazaarene-based C5-selective formal *meta*-sulfonylation of pyridines, isquinoline, and quinoline that does not require a photocatalyst (Scheme 12).[33] Instead, the authors utilize a combination of aryl or alkyl sulfonyl chlorides and KI. They propose that the corresponding sulfonyl radical is either generated from an EDA-complex between the sulfonyl chloride and iodide or that the sulfonyl iodide is formed *in situ* through ionic substitution and the sulfonyl radical is then generated through homolytic S–I cleavage. Yields are comparable to the previously described methods (**15**, 19–96%). The reaction is highly C5-selective, showing high selectivity towards mono-functionalization.[33] Moreover, Roy *et al.* presented an iridium-catalyzed enantioselective *meta*-allenylation of oxazinopyridines.[34]



Scheme 12. Photocatalyst-free *meta*-sulfonylation of oxazinoazaarenes, R = CO$_2$Me.

In addition to the *meta*-functionalization, we also leveraged the nucleophilicity of the C5-position of oxazinopyridines for skeletal editing (Scheme 13).[12] In these sequences, the oxazinopyridine (**2**) functions as an electron-rich diene that undergoes a Diels-Alder reaction with electron-deficient alkynes or arynes acting as dienophiles. The generated cycloaddition products (**INT7**) subsequently undergo a retro-Diels-Alder reaction furnishing the respective disubstituted benzenes or naphthalenes in moderate to high yields (**16**, 24–88%) with the aromaticity of these products as the main driving force for the cycloreversion process.[12]

Different electron-deficient alkynes and arynes as well as differently substituted pyridines were employed, including examples for late-stage functionalization, and coupling of two drug fragments. Notably, most reactions were conducted as a one-pot process from the corresponding pyridine (**1**). The use of *meta*-substituted pyridines as well as unsymmetric alkynes or arynes can result in the formation of two regioisomers, with regioselectivities strongly depending on sterics and electronics of the substrates. Notably, oxazinoquinolines and isoquinolines do not engage in Diels–Alder reactions under these conditions, as this would lead to the loss of aromaticity in the fused ring system.[12]

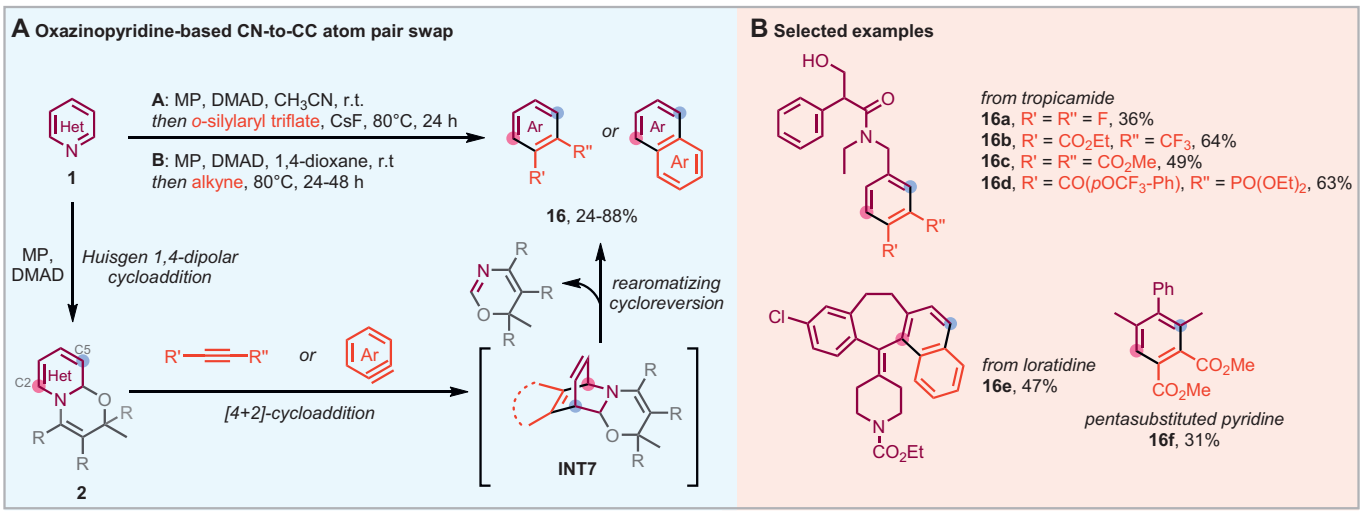
3.2 *Reactions at the Electrophilic C4-Position of Protonated Oxazinoazaarenes*

While a large excess of acid in combination with water and heating results in rearomatization of the oxazinoazaarenes, addition of only a slight excess of acid under non-aqueous conditions gives a protonated oxazinoazaarene species (2X$^+$, Scheme 14).[35] Due to steric crowding around the N-atom, the protonated oxazinoazaarene acts as an electrophilic anchor to intercept a nucleophilic partner with high selectivity at the C4-position.

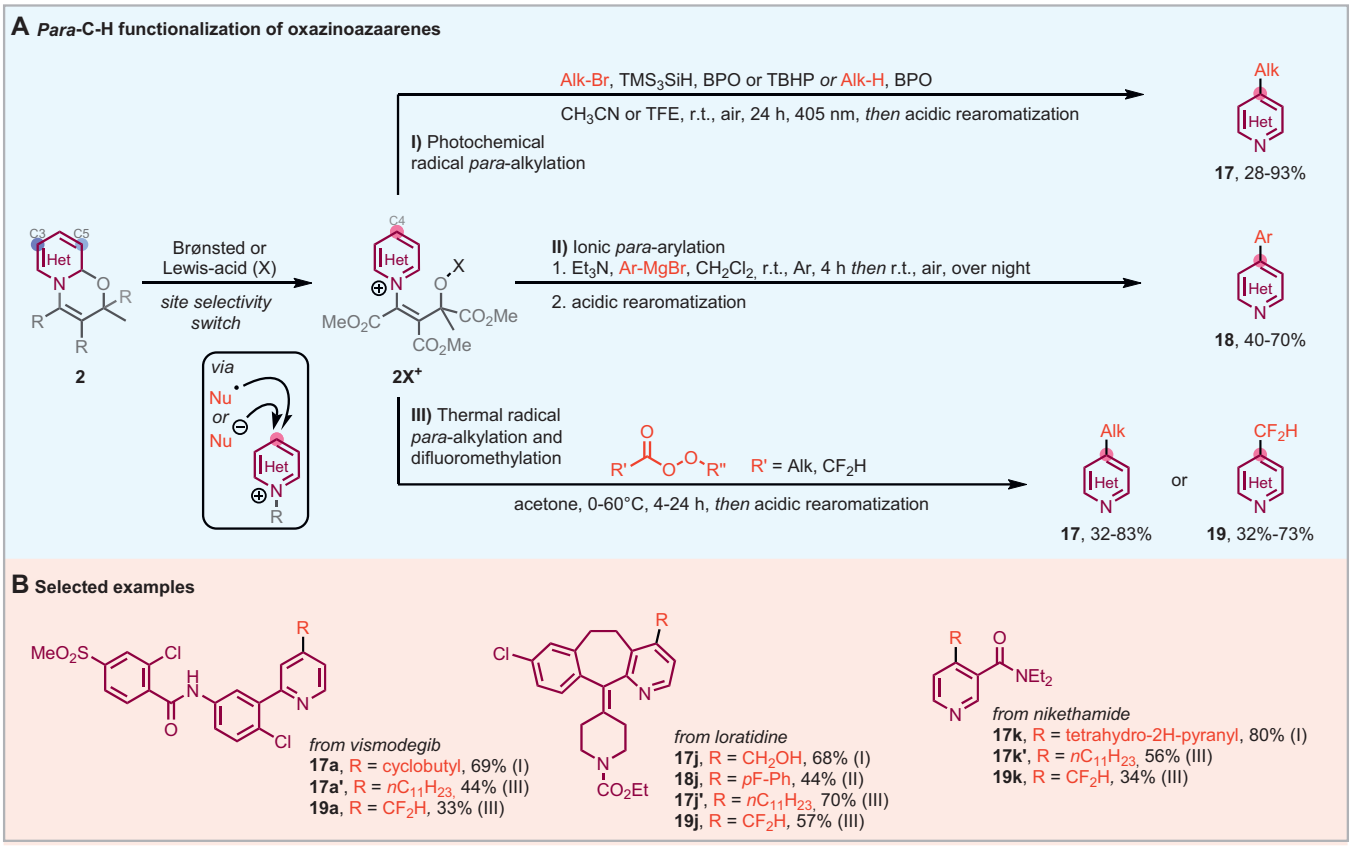
In our first report along these lines, alkyl bromides and alkanes were used as precursors for nucleophilic alkyl radicals, which regioselectively add to the C4 position of the oxazinopyridinium salt in a Minisci-type reaction (Scheme 14A, I).[35]

After deprotonation and oxidation by O$_2$ or BPO, the *para*-functionalized oxazinopyridinium was rearomatized under our standard acidic conditions to afford *para*-alkylated pyridines in moderate to excellent yields (**17**, 28–93%). Of note, ionic *para*-arylation using aryl Grignard compounds on oxazinopyridinium salts is also feasible (Scheme 14A, II). For compatibility with the strongly basic Grignard reagent instead of Brønsted acids, TMSOTf as a Lewis acid was used to generate the oxazinopyridinium salt from the corresponding oxazinoazaarene. After oxidation under air followed by acidic rearomatization, the *para*-arylated pyridines were isolated in moderate to good yields (**18**, 40–70%).[35]

Later, the *para*-alkylation was simplified by using alkyl carboxylic acid-derived diacyl peroxides or peresters as nucleophilic alkyl radical precursors and internal oxidants under thermal conditions yielding *para*-alkylated pyridines and quinolines in comparable yields (Scheme 14A, III, **17**).[36] Furthermore, *para*-difluoromethylation of protonated oxazinoazaarenes was achieved by generating nucleophilic •CF$_2$H radicals from bis(difluoroacetyl) peroxide in moderate to good yields (32–73%, Scheme 14A, III, **19**).[24]



Scheme 13. Oxazinopyridine-based CN-to-CC-atom swap. DMAD = dimethyl acetylenedicarboxylate, MP = methyl pyruvate, R = CO$_2$Me.



Scheme 14. Formal *para*-C–H-functionalization of azaarenes *via* protonated oxazinoazaarenes. BPO = benzoyl peroxide, R = CO_2Me, TBHP = *tert*-Butyl hydroperoxide.

4. Conclusion

In conclusion, our oxazinoazaarene based temporary dearomatization approach was used by our group and others to introduce several synthetically and pharmacologically valuable functional groups to the *meta*- or *para*-positions of pyridines, isoquinolines, and quinolines. Additionally, this dearomatization strategy enabled skeletal editing of pyridines *via* a transmutation from CN to CC generating disubstituted benzenes and naphthalenes. Our group aims to further expand the scope of oxazinoazaarene-based formal C–H-functionalizations to other synthetically valuable functional groups and to find new ways of oxazinopyridine based skeletal editing.

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