Oxidizing agents in metal-catalyzed and
metal-free C-H functionalization of heteroarenes

**Irina A. Utepova,*[a,b] Oleg N. Chupakhin,[a,b] Maria A. Trestsova,[a]
Alexandra A. Musikhina,[a,b] Alexandr V. Shchepochkin,[b] and Olga N. Zabelina[a,b]**

[a]Ural Federal University, 620002 Ekaterinburg, Russia
*[b]Institute of Organic Synthesis of the Ural Branch of the Russian Academy of Sciences,
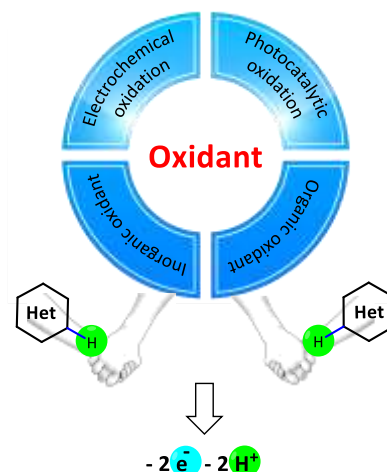620108 Ekaterinburg, Russia*
Email: i.a.utepova@urfu.ru

Abstract

Oxidative C-H functionalization represents a crucial method to make new C-C, C-X (X = heteroatom) bonds. An optimal selection of the oxidizing agent goes hand in hand with the insight into the reaction mechanism. This review covers recent advances in methods of direct oxidative C-H functionalization of azines and their derivatives with heteroaromatic nucleophiles. Also we review the data on application of inorganic and organic oxidants for implementation of these reactions. C-H functionalizations under electrochemical and photocatalytic oxidation conditions are included as well.

**Keywords:** Direct C-H functionalization, heteroarene, oxidizing agents

Table of Contents

1. Introduction

Functionalization of the $C(sp^2)$-H bond in arenes and heteroarenes has been extensively applied as an ideal approach for the construction of new chemical bonds.[1,2,3] These direct approaches for construction of complex molecules as well provide an atom- and step-economy efficient access to new C-C and C-X bonds according to the principles of green chemistry opposed to metal-catalyzed cross-coupling reactions of halogen derivatives with organometallic compounds (Sonogashira reactions, Negishi, Suzuki, Miyaura, Heck, Buchwald-Hartwig, etc.). Moreover C-H functionalization does not require preliminary modification of parent compounds and activation of labile and hard in preparation substrates.[4,5]

      Oxidative C-H functionalization reactions are realized in catalytic and non-catalytic ways. Despite the widespread using, the first method still does not meet the requirements of modern technological processes. The toxicity and high cost of transition metals (Pd is the most prominent agent) hamper the ability of catalytic way to be attractive (Figure 1).[6] In some processes catalysts have no the possibility of reuse, other problems deal with the elaborated separation of target compounds from metal containing by-products.

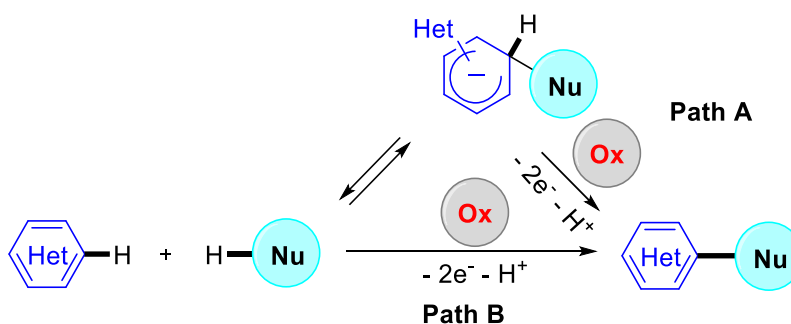   Metal-catalyzed C-H functionalization proceeds with a cleavage of the C-H bond in a substrate and via the formation of an organometallic intermediate with a nucleophile followed by the coordination of substrate to complex. Further combination of reagents leads to the induction of C-C, C-X bonds. The oxidant in its turn promotes the regeneration of an active form of catalyst, closing the catalytic cycle (Figure 1).
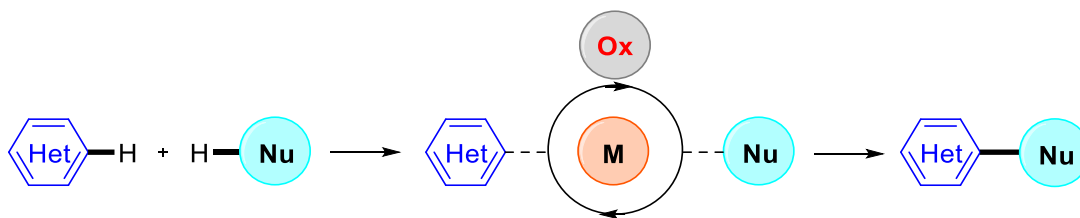
Figure 1. Metal-catalyzed reactions of C-H functionalization.

However, over the last few decades, metal-free catalytic oxidative C-H functionalization has become a promising trend in the heterocyclic chemistry and organic synthesis in general. Such type of reactions is currently united under the general name OCDC processes (Oxidative Cross-Dehydrogenative Coupling).

Among the large scope of metal-free C-H functionalization transformations, nucleophilic substitution of hydrogen (S_N^H) is known to be an efficient tool for the synthesis of substituted heterocycles.[7] The generally accepted mechanism for S_N^HAr reactions in the oxidative version represents the addition – oxidation scheme S_N^H(AO) (Figure 2). At the first stage, the electron-donating reagent (nucleophile, Nu) attaches to azine with a formation of intermediate σ^H-adduct. Further, since the spontaneous elimination of H$^-$ from the σ^H-adduct is unlikely, the involvement of an oxidant **Ox** in the reaction is unequivocally required. Such transformations can be carried out both via isolation of intermediate compounds (σ^H-adducts) (Figure 2, path A), and as a direct three-component synthesis, when the oxidant is introduced into the reaction mixture simultaneously with the reaction partners (Figure 3, path B).

Figure 2. Metal-free oxidative C-H functionalization (S_N^H reaction).

In contrast to metal-catalyzed C-H functionalization and cross-couplings of halogen derivatives with organometallic compounds, S_N^H reactions have a number of significant advantages:
- transformations occur under mild conditions;
- pre-functionalization of the starting materials is unnecessary;
- one-pot strategy;
- minimization of the number of stages;
- time-consuming purification of final products is unnecessary.

For oxidative S_N^H processes, the use of stoichiometric amounts of an oxidizing agent is as important as the presence of two reaction agents. These processes need the right choice of an oxidizing agent since both intermediate and electron-donating reagent (**Nu**) are sensitive to oxidation.

S_N^H processes as well as oxidation methods comprise the modern trends in organic synthesis. The reactions occur with previously selected both organic and inorganic (one- and two-electron) oxidants. It is worth

highlighting that electrochemical methods, photocatalysts, and air oxygen represent the oxidizing ways, enabling contemporary effective and low-waste technology.

Related metal-free processes comprise oxidative C-H functionalizations with the compounds of hypervalent iodine, which are given special attention in the chemical literature.[8] According to the generally accepted mechanism, a hypervalent iodine reagent **B** acts as an oxidative mediator converting one of the reaction partners into a reactive particle **C** (Figure 3).[9] Next stage proceeds as the formation of a three-component transition state **E**. The latter is transformed into the combination product **F** with elimination of H^+ and iodine compound.
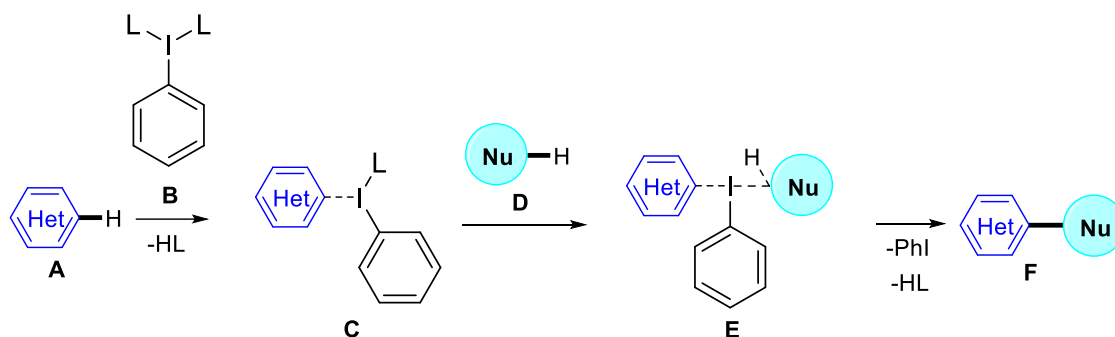
Figure 3. Oxidative C-H functionalization using hypervalent iodine compounds.

Recently, C-H functionalizations, in particular metal-catalyzed, have gained a remarkable attention in terms of issued reviews.[6,10-19] This includes a selection of catalytic reagents, the types of transformations. As for oxidants impact, in particular, in functionalization of $C(sp^2)$-H in heteroarenes, no attempt to capture data in a systematic way has been made until this review despite a fundamental role of an oxidizing agent. The manuscript covers specific and reasonably general approaches of metal-catalyzed and metal-free C-H functionalizations in heteroarenes, enabling application of inorganic, organic oxidizing agents. Moreover, the novel promising ways such as electrosynthetic methods and photocatalysis are also considered.

Generalization and systematization of data regarding the mechanisms of C-H functionalization reactions and the oxidizing systems used in these processes are of great practical utility for the modification of natural compounds, synthesis of biologically active substances, new ligand systems and materials bearing a heterocyclic fragment in the structure.

Thus, we have focused our forces on summarizing the chemistry of oxidizing reagents in the direct oxidative C-H functionalizations with heteroarenes emphasizing application of the products in medicinal chemistry and chemistry of materials. The review provides an assessment of both metal-catalyzed and metal-free transformations. The literature coverage is over the past twenty years.

2. Inorganic Oxidizing Agents

2.1. Silver or copper salts and oxides
2.1.1. Metal-catalyzed reactions. Despite a large number of works on the C-H functionalization of azines with fragments of five-membered heterocycles, in some cases problems arise with its implementation, since very often π-excessive heterocycles undergo destruction under oxidative conditions. However, some azines enter into reactions of C-H bond functionalization only after additional activation. The most common activation

method of azines is the introduction of N-oxide function. So, the energy value of pyridine LUMO is higher (-0.732 eV) than value for its oxidative form (-1.160 eV) (The calculations were carried out with Orca 4.0.1 software using DFT B3LYP, 6-311G* methodology[20-23]). Such lower value of the LUMO energy corresponds to the more electrophilicity, and, as a consequence, the higher reactivity in CDC (Cross-Dehydrogenative Coupling) processes. In 2011 Gond *et al.* proposed the technique of Pd-catalyzed oxidizing cross-coupling of azines *N*-oxides **1** with *N*-substituted indoles **2** (Scheme 1).[24] The reaction proceeds selectively at the C3- and C2-position of indole and *N*-oxide respectively. To enhance efficiency, the oxidizing agent Ag_2CO_3 was steadied by an addition of four equivalents of pyridine and 20 mol% of tetrabutyl ammonium bromide (TBAB). The reaction affords the products **3a-j** in 45 - 81% yields. The authors report, that pyridine was applied as an additive in palladium-catalyzed oxidation reactions to stabilize the palladium (II) catalyst. Almost all target products were achieved in the presence of pyridine as an additive. For pyridine N-oxides bearing Ph and electron-withdrawing groups (Br, CN) this coupling proceeded smoothly in the presence of 30 mol% pivalic acid (PivOH). Probably oxygen atom undergoes transfer to pyridine and *in situ* generated simple pyridine N-oxide.
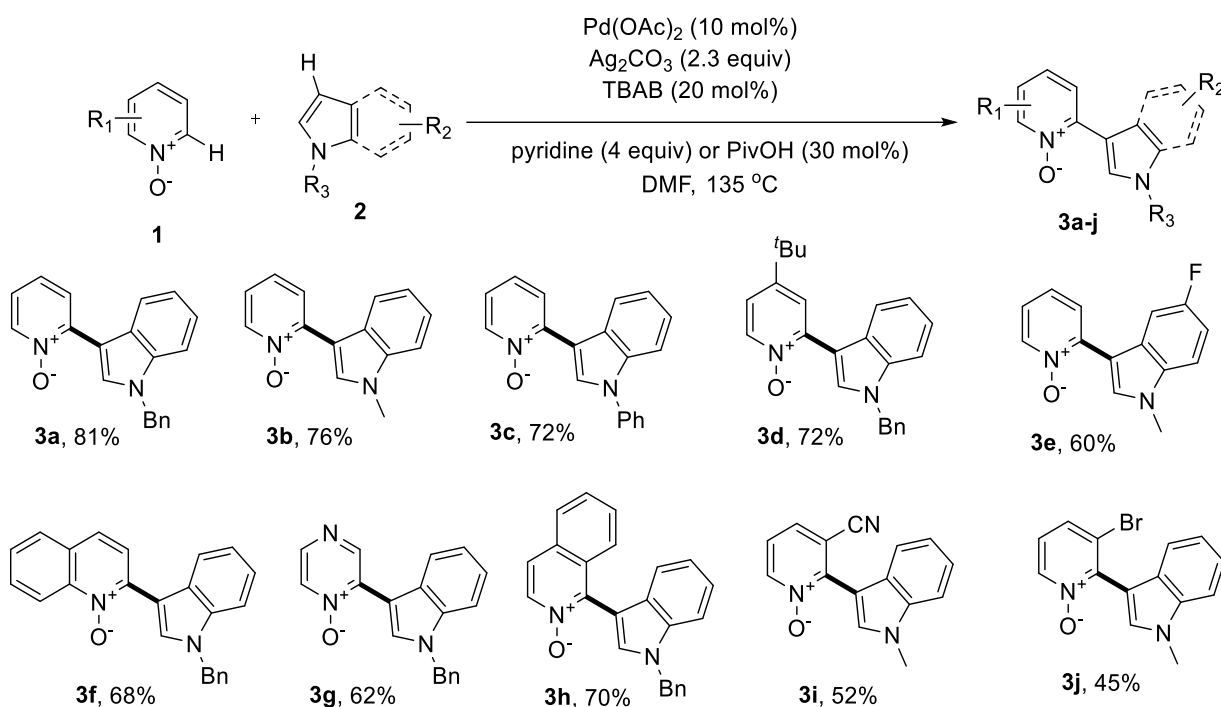
Scheme 1. Pd(II)-catalyzed oxidative coupling between pyridine *N*-oxides and *N*-substituted indoles using Ag_2CO_3 as an oxidant.

One more example of oxidizing C-H/C-H coupling of indoles **2** or pyrroles **4** with azines *N*-oxides **1** is shown on the Scheme 2.[25] Optimization of the reaction conditions showed that an increase in the yields of compounds **5a-c,g-k** occurs when AgOAc is used as an oxidizing agent. In addition, the best results were obtained with indoles and pyrroles bearing protective groups in their structure, such as MOM - methoxymethyl or Ts - toluenesulfonyl. 2,6-Lutidine was used as a ligand. It was shown that the C2 / C3 regioselectivity of pyrroles could be controlled by introducing a protective group to the nitrogen atom. The C-H/C-H coupling proceeds at the C3 position when using Ts-protected pyrroles.
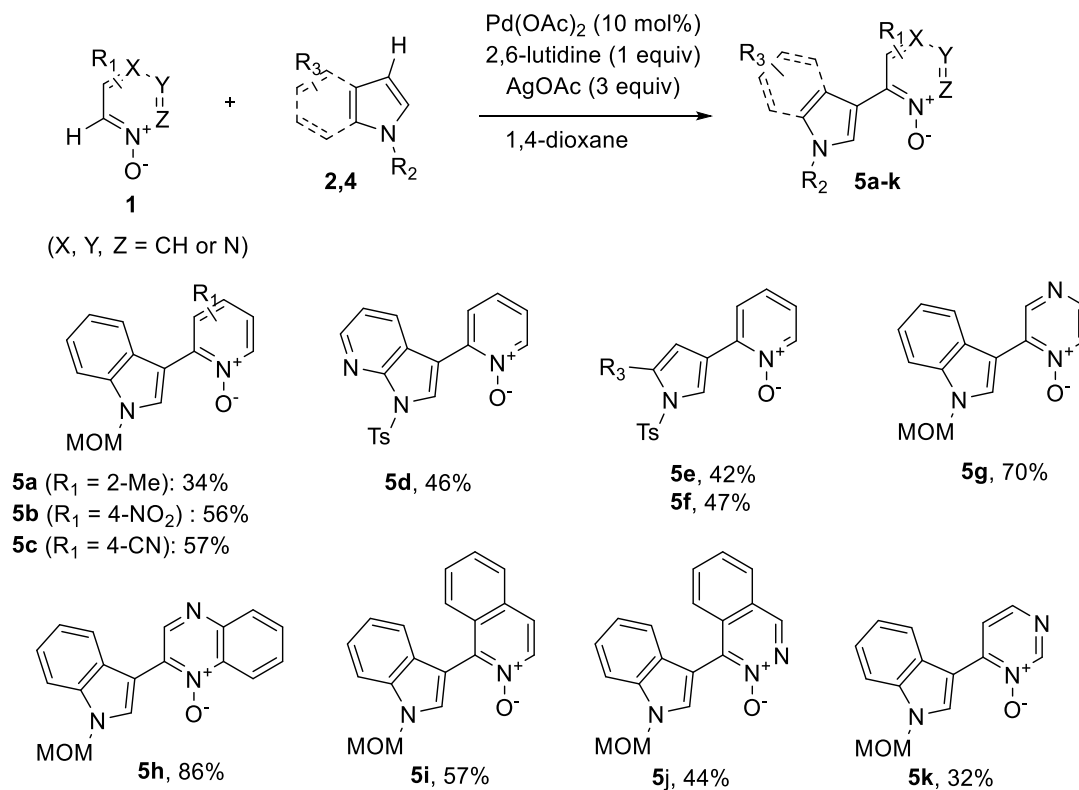
Scheme 2. Pd-catalyzed C-H/C-H coupling of indoles/pyrroles with *N*-heteroarene *N*-oxides using AgOAc as an oxidant.
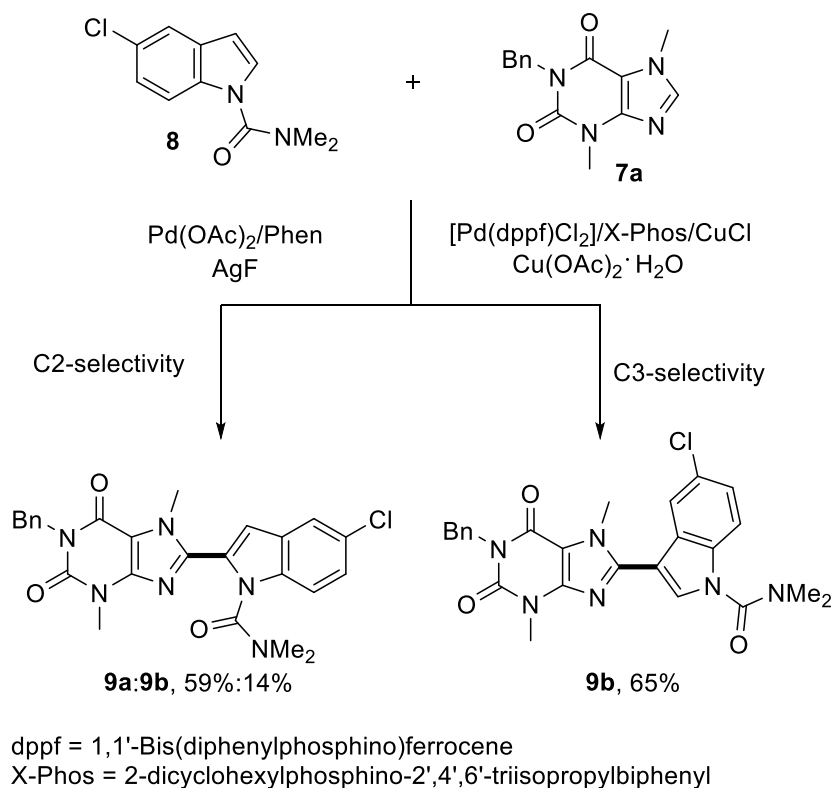
Thus, by means of tosyl protection, the reactions with pyrroles and azaindole gave **5d-f**. The process goes selectively at the C3- and C2-position of indoles/pyrroles and azines *N*-oxides respectively. Applying this approach, the researchers synthesized alkaloid eudistomin U. The latter was utilized in DNA binding and demonstrated an antimicrobial activity.

Wang and co-workers used Cu(OAc)$_2$•H$_2$O as an oxidant and showed that azines N-oxides **1** coupled with indoles **2** and pyrroles **4** yielding **6a-f** (Scheme 3).[26] It was found that the introduction of a directing functional group at the nitrogen atom of indoles and pyrroles leads to the activation of the C2 position, suppressing the preferred C3 selectivity.

Moreover, biologically active alkaloids – xanthines undergo this transformation. The C2/C3 selectivity of heteroarylation of indoles/pyrroles with xanthines could be regulated through the use of different directing groups, oxidants, and ligands. For instance, the reaction of benzylic theobromine **7a** with *N,N*-dimethylcarbamoylindole **8** in the presence of the catalytic system Pd(OAc)$_2$ and 1,10-phenanthroline (Phen) conjuncted with the oxidizing agent AgF (Scheme 4) afforded **9a** and **9b** in 59 and 14% yield, respectively. In turn the system [Pd(dppf)Cl$_2$], CuCl and X-Phos with Cu(OAc)$_2$•H$_2$O as an oxidant mainly gave the C3-heteroarylated product **9b** in 65% yield (Scheme 4). The authors assumed that presence of the F$^-$ anion might facilitate the formation of monomeric Pd species rather than trinuclear Pd carboxylate clusters, which favored the C2 site selectivity.
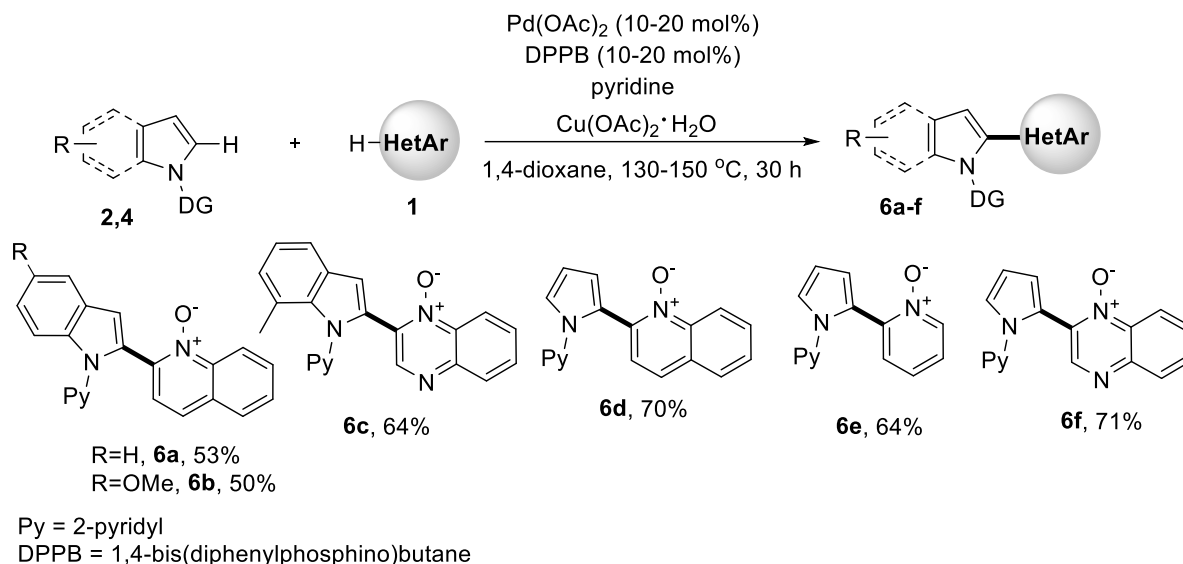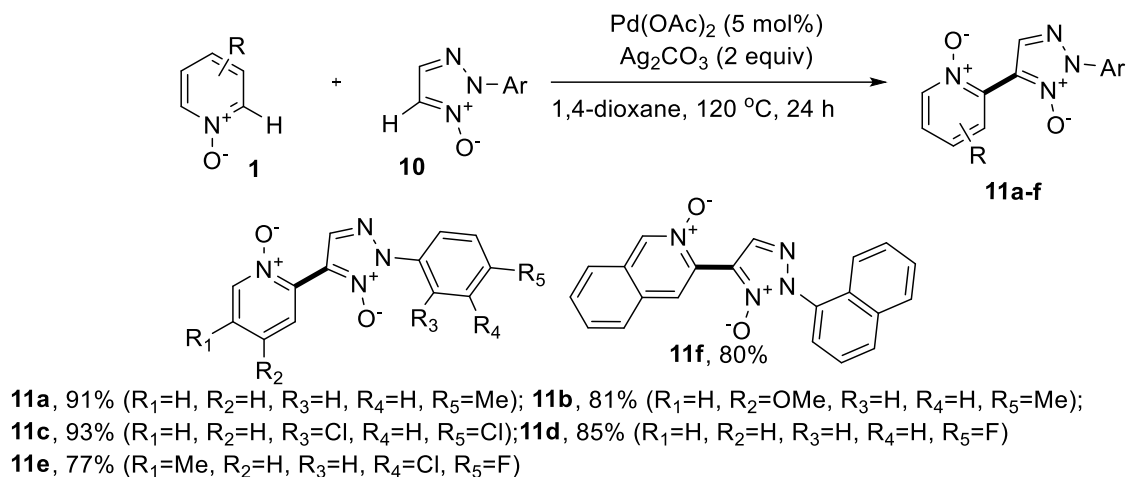
Scheme 3. Oxidative cross-coupling of indoles/pyrroles with *N*-heteroarene N-oxides using Cu(OAc)2•H2O as an oxidant.

dppf = 1,1'-Bis(diphenylphosphino)ferrocene
X-Phos = 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

Scheme 4. Catalytic system-based switching of the regioselectivity of C-H heteroarylation of indole with benzylic theobromine.

Several examples of oxidative cross-coupling of azides *N*-oxides and electron-deficient heteroarenes have been reported so far. These reactions are known to be very complicated to perform. An effective method of oxidative cross-coupling of azines *N*-oxides **1** with 2-aryl-1,2,3-triazole **10** (Scheme5) was reported by Liu and

co-workers in 2013.[27] The novel approach enables ones to give symmetrical and non-symmetrical biheterocyclic *N,N*-dioxides **11a-f**. Ag_2CO_3 proved to be more effective oxidizing agent than $Cu(OAc)_2 \bullet 3H_2O$, AgOAc, Ag_2O, Ag_2SO_4 и $AgNO_3$.

11a, 91% (R$_1$=H, R$_2$=H, R$_3$=H, R$_4$=H, R$_5$=Me); **11b**, 81% (R$_1$=H, R$_2$=OMe, R$_3$=H, R$_4$=H, R$_5$=Me);
11c, 93% (R$_1$=H, R$_2$=H, R$_3$=Cl, R$_4$=H, R$_5$=Cl);**11d**, 85% (R$_1$=H, R$_2$=H, R$_3$=H, R$_4$=H, R$_5$=F)
**11e**, 77% (R$_1$=Me, R$_2$=H, R$_3$=H, R$_4$=Cl, R$_5$=F)

Scheme 5. Pd-catalyzed oxidative C-H/C-H direct coupling of heterocyclic *N*-oxides with 2-aryl-1,2,3-triazole N-oxides using Ag_2CO_3 as an oxidant.

The plausible mechanism of C-H bond functionalization reaction includes the easily abstraction of hydrogen from the 2-substituted 1,2,3-triazole *N*-oxides to the palladium(II) intermediate (**A**) and the formation of bisheteroarylpalladium species (**B**) by C-H substitution of **A** with pyridine *N*-oxide. In this case, limita (I) converted to Ag (0) to regenerate palladium (II) acetate (Figure 4).[28]
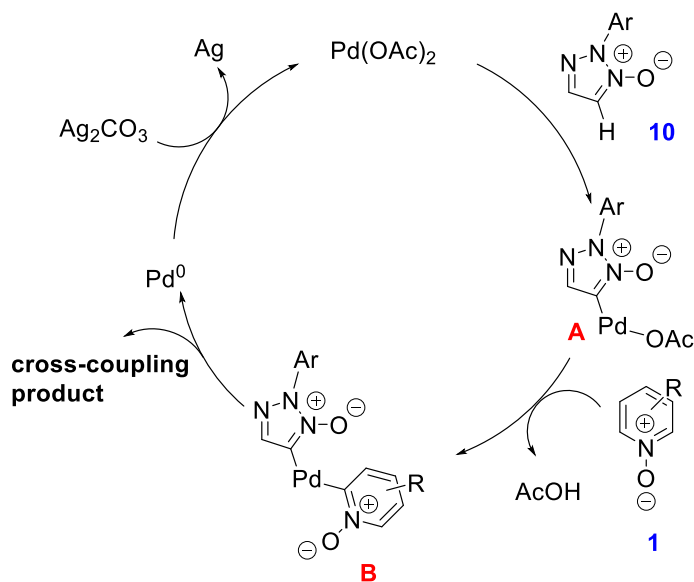

Figure 4. Plausible catalytic cycle.

Later the same group of scientists expanded a substrate scope with 1-benzyl-1,2,3-triazoles **12**. The latter react with *N*-oxides **1** to give **13a-l** (Scheme 6).[29]
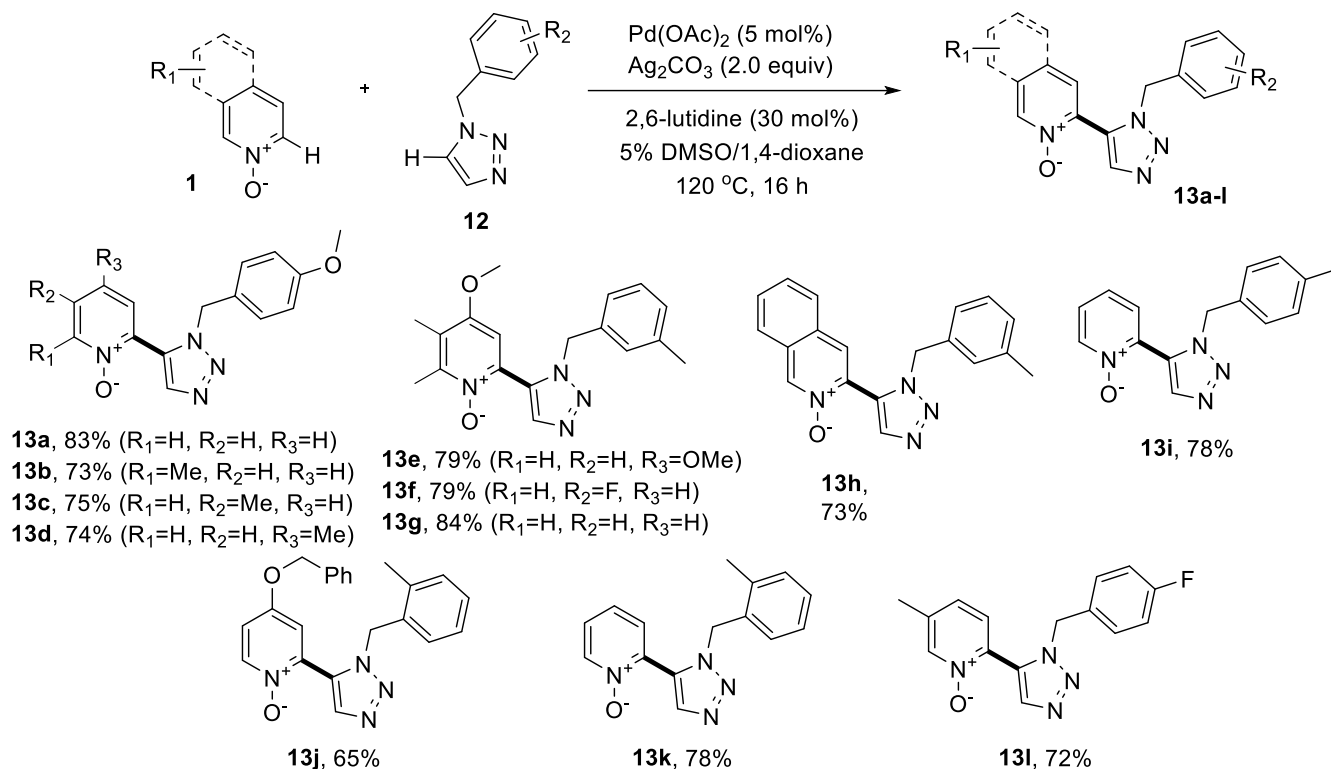
Scheme 6. Pd-catalyzed oxidative C-H/C-H cross-coupling of pyridine *N*-oxides with 1-benzyl-1,2,3-triazoles using Ag_2CO_3 as an oxidant.

Fu, Xuan, Liu and co-workers developed an efficient protocol for Pd-catalyzed cross-coupling of azine N-oxides **1** with electron-deficient thiazoles **14** and benzothiazoles **15** (Scheme7).[30]
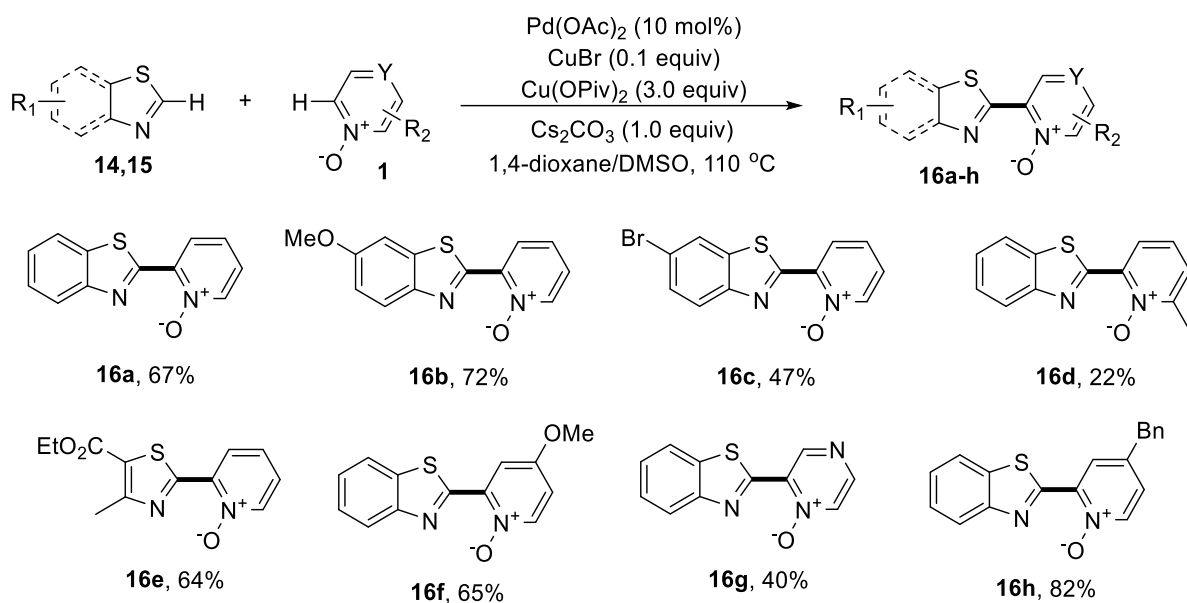
Scheme 7. Pd-catalyzed cross-dehydrogenative-coupling (CDC) of thiazoles with azine N-oxides.

Copper(II) pivalate was used as an oxidizing agent and activator of the C-H bond. Interestingly, an addition of Cu(OPiv)$_2$ promoted inhibition of homocoupling providing 2-thiazolylpyridines **16a-h** in yields ranging

from 22 to 82%. The addition of either a catalytic or stoichiometric amount of cesium pivalate showed no effect. Whereas in the presence of Cu(OPiv)$_2$, the desired product **16a** was obtained in 67% yield as well as the yield of homocoupling byproduct decreased to 11%. At the same time kinetic isotope effect (KIE) of the cleavage of the pyridine *N*-oxide C-H bond was about $k_H/k_D = 3.0$, thus indicating it as the limitation stage. Based on these observations a plausible reaction mechanism of this transformation was proposed (Figure 5).
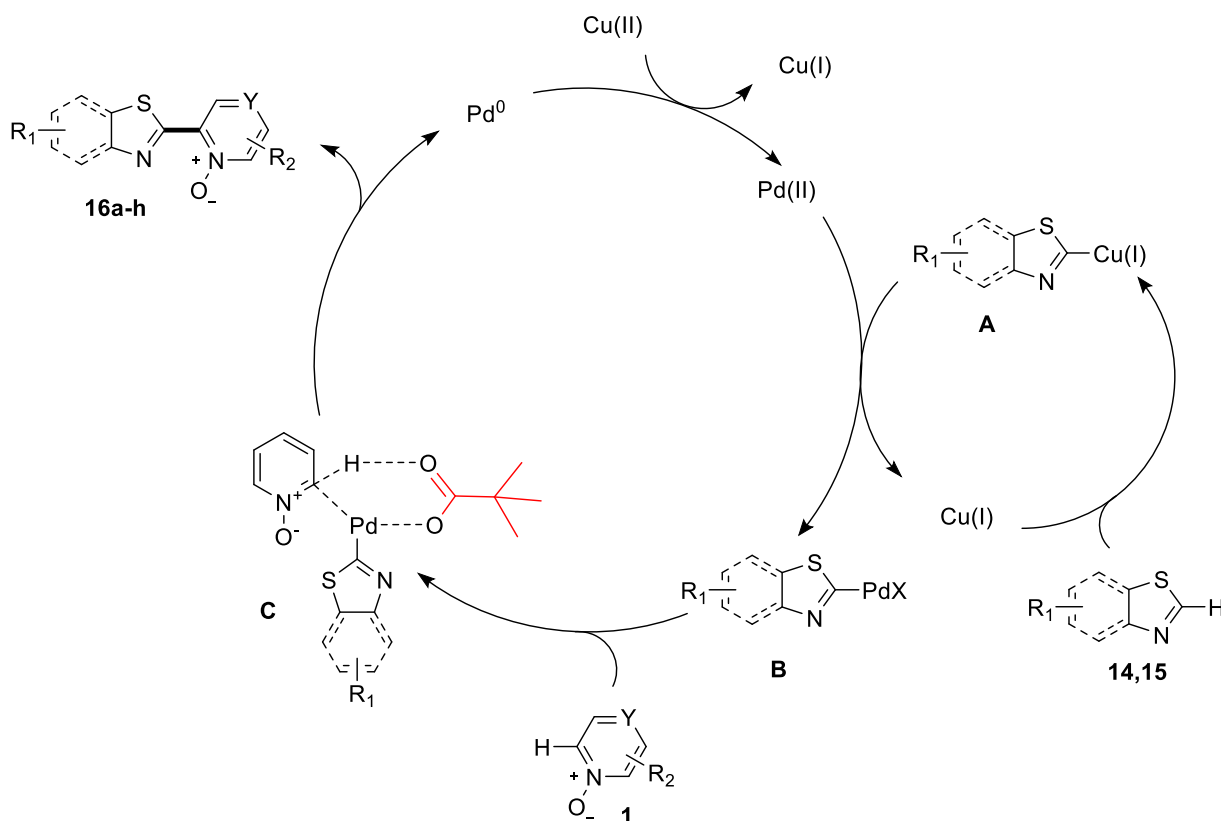

Figure 5. Plausible reaction pathways for oxidative cross coupling between benzothiazole and pyridine N-oxide.

Willis and co-workers described the first palladium-catalyzed cross-dehydrogenative coupling reaction of pyridine N-oxides and thiazoles in water (Scheme 8).[31] This protocol was regioselective with respect to the N-oxide and operationally simple and did not require an inert atmosphere. Optimization of the reaction conditions showed that an increase in the yields of compounds **17** occured when Ag$_2$CO$_3$ and X-Phos were used as an oxidizing agent and an addition to stabilise the catalyst respectively.

In 2014 Kianmehr *et al.* accomplished regioselective dehydrogenational C-H/C-H-coupling of pyridine-*N*-oxides **1** with 1,3-dialkyluracils **18** in the presence of oxidant Ag$_2$CO$_3$ (Scheme 9).[32] Uracil substituted *N*-oxides **19** readily transformed into the corresponding pyridines **20** making the approach significant to furnish 5-pyridine substituted uracils.
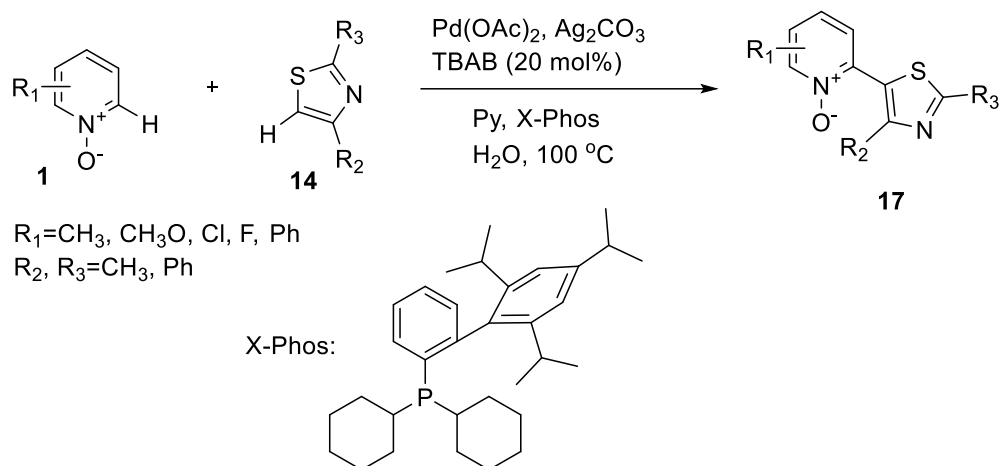
Scheme 8. Pd-catalyzed cross-dehydrogenative-coupling (CDC) of thiazoles with azine N-oxides.
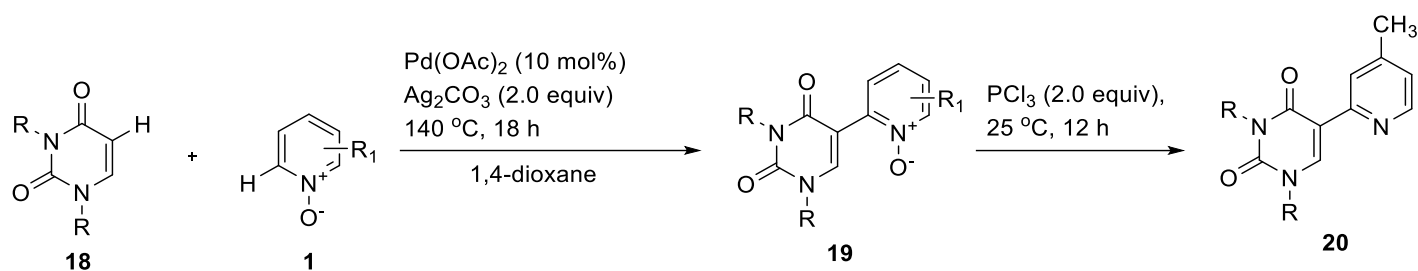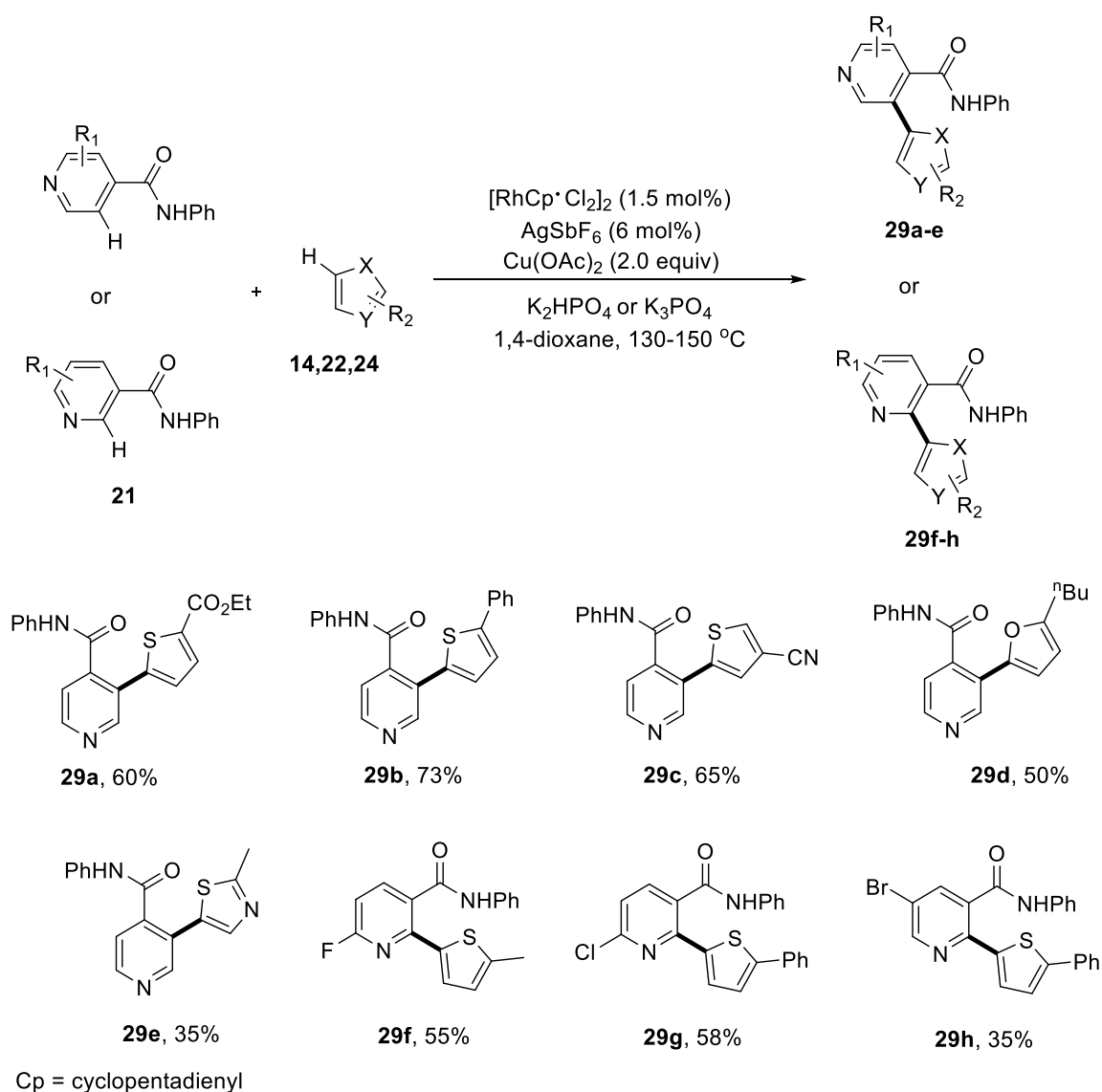

Scheme 9. Pd-catalyzed dehydrogenative cross-coupling of pyridine-*N*-oxides with uracils.
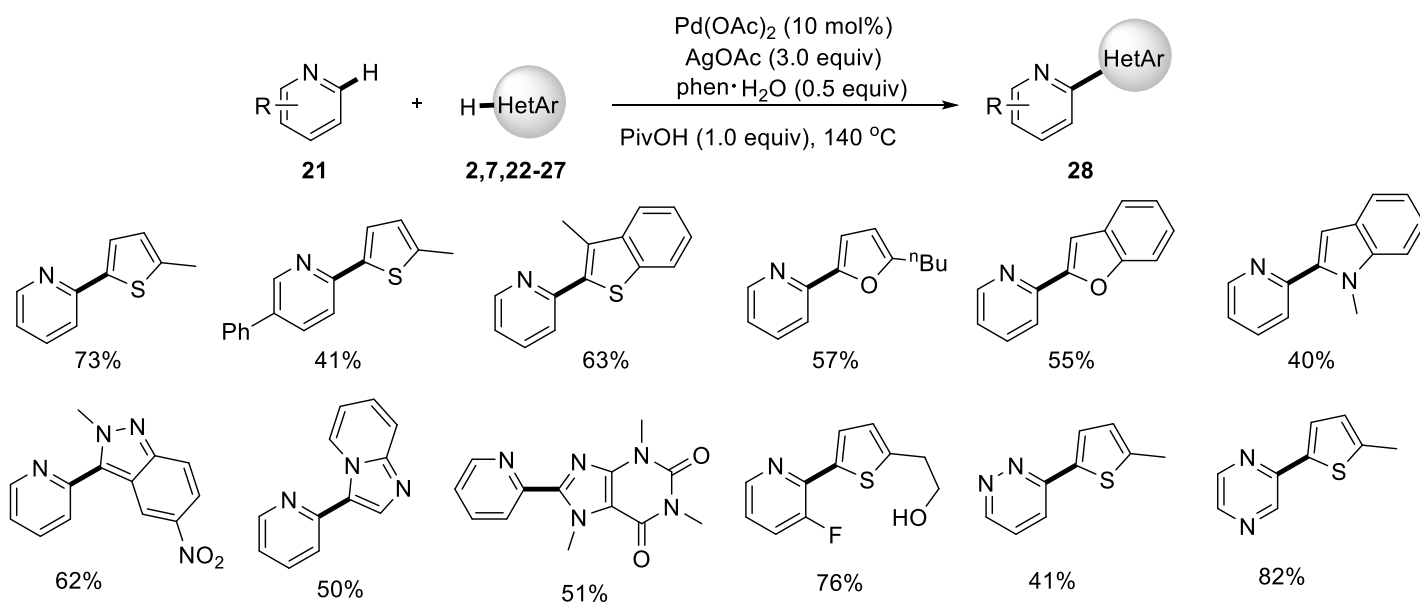
Scheme 10. Pd-catalyzed oxidative C–H/C–H coupling of pyridines with heteroarenes using AgOAc as an oxidant.

Dehydrogenative heteroarylation of pyridines is very complicated due to the low electronic density of the ring. Liu, Huang and colleagues developed a regioselective oxidizing C-H/C-H cross-coupling of pyridines **21** with heteroarenes, using the catalytic system Pd(OAc)$_2$/phen/AgOAc/PivOH (Scheme 10).[33] A wide scope of heteroarenes, including indoles **2**, furanes **22**, benzofurans **23**, thiophenes **24**, benzothiophenes **25**, indazoles **26**, imidazopyridines **27** and xanthines **7** selectively couple with pyridines at the C2-position. C3-substituted pyridines used as the substrates make it possible to conduct the C6-heteroarylation. The yields of the compounds **28** are ranging from 41 to 82%.

In 2014 Shang *et al.* proposed one more example of heteroarylation of pyridines. The approach is based on Rh(III)-catalyzed cross-coupling with heterocyclic compounds. The reaction proceeds selectively at the *ortho*-position relatively the amide group in pyridine (Scheme 11).[34] Such heteroarenes as thiazoles **14**, furanes **22** and thiophenes **24** regioselectively react with pyridines **21** in the presence of [RhCp•Cl$_2$]$_2$ (1.5 mol%), AgSbF$_6$ (6 mol%), K$_3$PO$_4$ (1.5 equiv.) and an oxidizing agent Cu(OAc)$_2$ giving **29a-h**. Last year three manuscripts were focused on the *ortho*-heteroarylation of phenols in the presence of catalytic system [RhCp•Cl$_2$]$_2$/AgSbF$_6$ or [IrCp•Cl$_2$]$_2$/AgSbF$_6$ and Ag$_2$O.[35-37]

**Scheme 11.** Rh(III)-Catalyzed amide-directed cross-dehydrogenative heteroarylation of pyridines.

Earlier the same Rh-catalyzed system in the presence of Ag_2CO_3 oxidizing agent was employed by Qin and co-workers to conduct C2-selective oxidative cross-coupling of indoles **2** and pyrroles **4** with electron efficient furanes **22**, thiophenes **24** and indolizines **30** and electron deficient thiazoles **14**, benzothiazoles **15**, oxazoles **31** and azides *N*-oxides **1** (Scheme 12).[38] Strikingly, the reactions proceed regioselectively at the C2-position of indoles and pyrroles instead of the preferred C3-position to produce **32**.
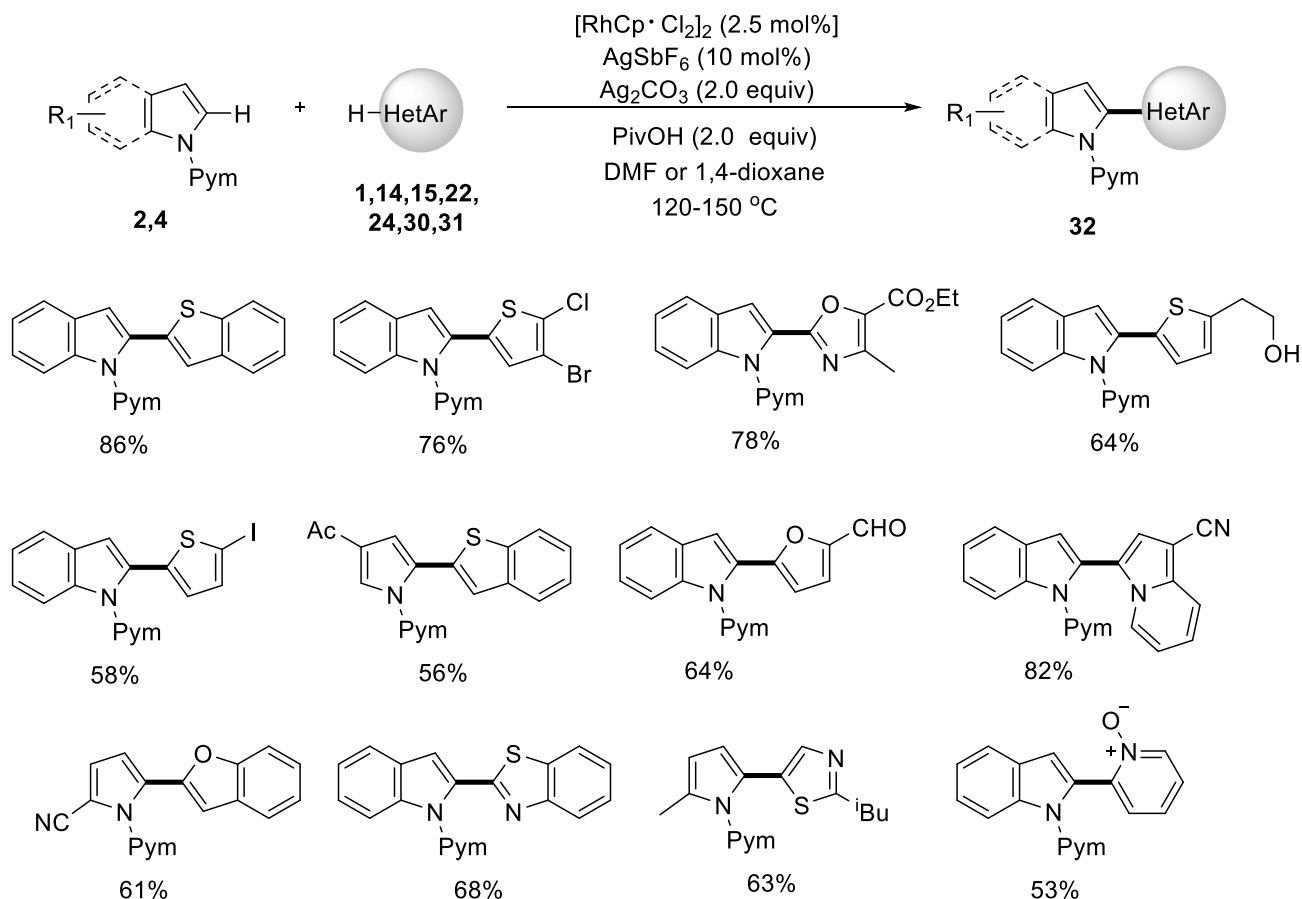
Scheme 12. Chelation-assisted Rh(III)-catalyzed C2-selective oxidative C–H/C–H coupling of indoles/pyrroles with heteroarenes.

Benzothiazole-containing biheteroarenes often combine the biological activity with unique optical properties. As a result, the benzothiazole moiety is found in numerous pharmaceutical and biochemical compounds.[39-41] Pd-catalyzed heteroarylation of benzothiazoles **15** with *S*-containing five-membered heterocycles **14**, **24** at the C2-position was reported by Yang`s group (Scheme 13).[42] $AgNO_3$ proved to be more effective oxidizing agent than AgOAc and Ag_2CO_3.
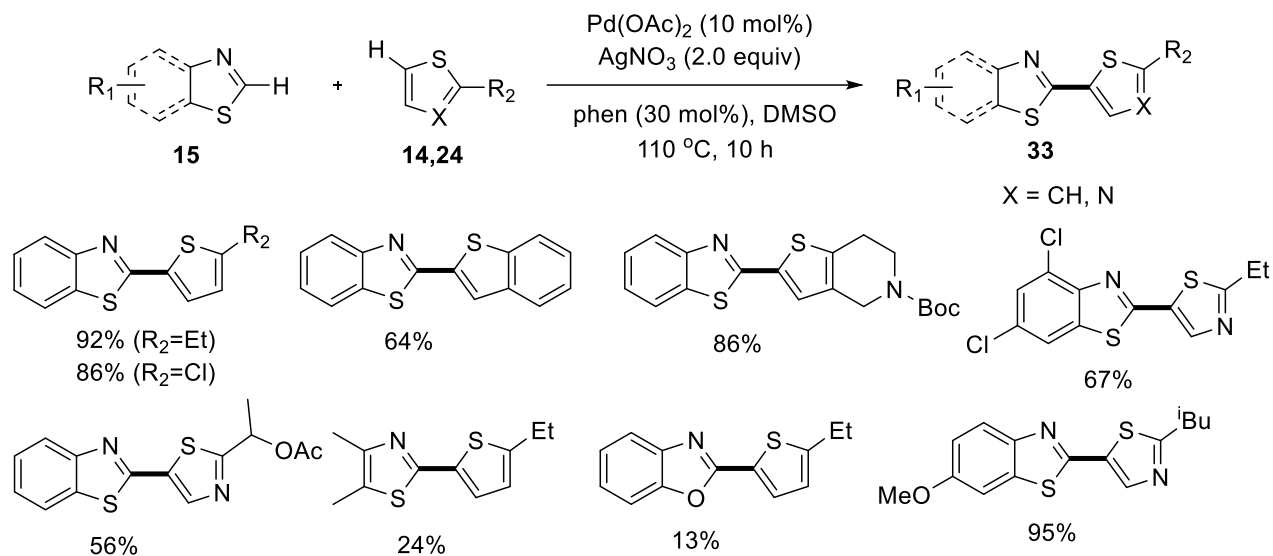
Scheme 13. Pd-catalyzed oxidative C–H/C–H cross-coupling of benzothiazoles with thiophenes and thiazoles using AgNO₃ as an oxidant.

The reaction was carried out in DMSO (3,0 ml) within 10 h at 110 °C catalyzed by Pd(OAc)₂ (10 mol%), AgNO₃ (2,0 equiv.) and 30 mol% phenanthroline monohydrate to furnish **33** in best yields. The protocol provides the products of coupling not only between electron efficient and electron deficient heteroarenes but also between two electron deficient heterocycles.
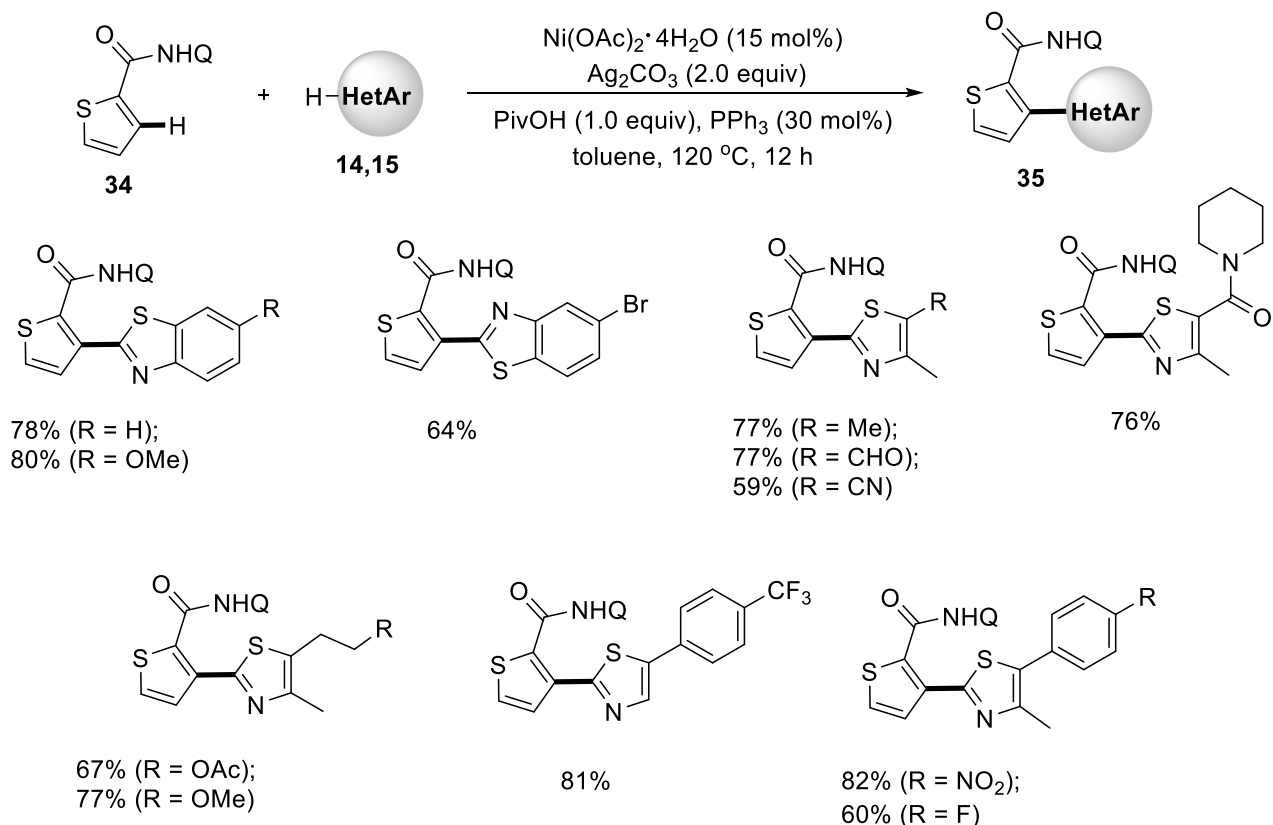
Scheme 14. Ni-catalyzed oxidative C–H/C–H coupling reactions between two *S*-containing heteroarenes.

Another protocol of C-H/C-H cross-coupling of heteroarenes with *S*-containing heterocycles was developed by You`s group (Scheme 14).[43] They used 8-aminoquinoline group as an efficient *N,N*-bidentate coordinating group in the C-H functionalization catalyzed by transition metals. Ni-catalyzed coupling of *N*-(quinoline-8-yl)thiophene-2-carbonic acid **34** and heteroarenes such as thiazoles **14** and benzothiazoles **15** with an oxidant Ag_2CO_3 afforded **35** in good yields. The oxidizing agents ($Mn(OAc)_2 \bullet 4H_2O$), $NaClO_3$, $K_2S_2O_8$, organic oxidants benzoquinone and DDQ turned out to be ineffective.

Fan with colleagues performed cross-coupling between benzothiazoles **15** and thiazoles with the aid of CuI catalyst, *t*-BuOLi base in toluene (Scheme 15).[44] According to the proposed mechanism, a copper compound is formed with one of the initial heteroarenes. Ag_2CO_3 plays the role of an oxidizing agent in this transformation. In the absence of CuI or Ag_2CO_3, the formation of target products was not observed in the reaction mixture. This approach makes it possible to obtain unsymmetrical 2,2'-bisthiazoles **36** in good yields and with high regioselectivity. Interestingly, that AgOAc, $AgNO_3$, air and O_2 showed a low oxidizing activity or did not reveal it at all.
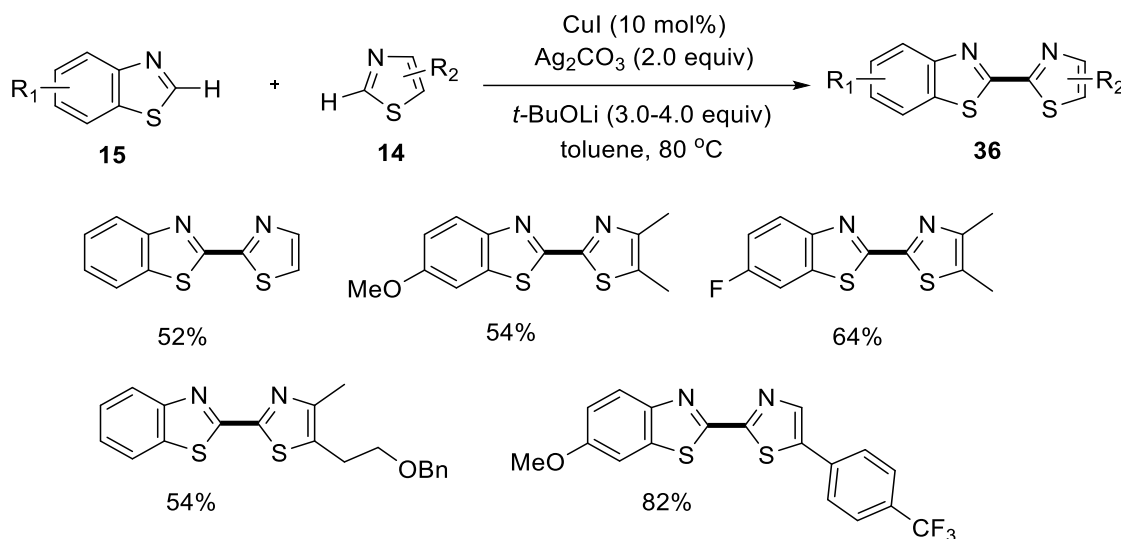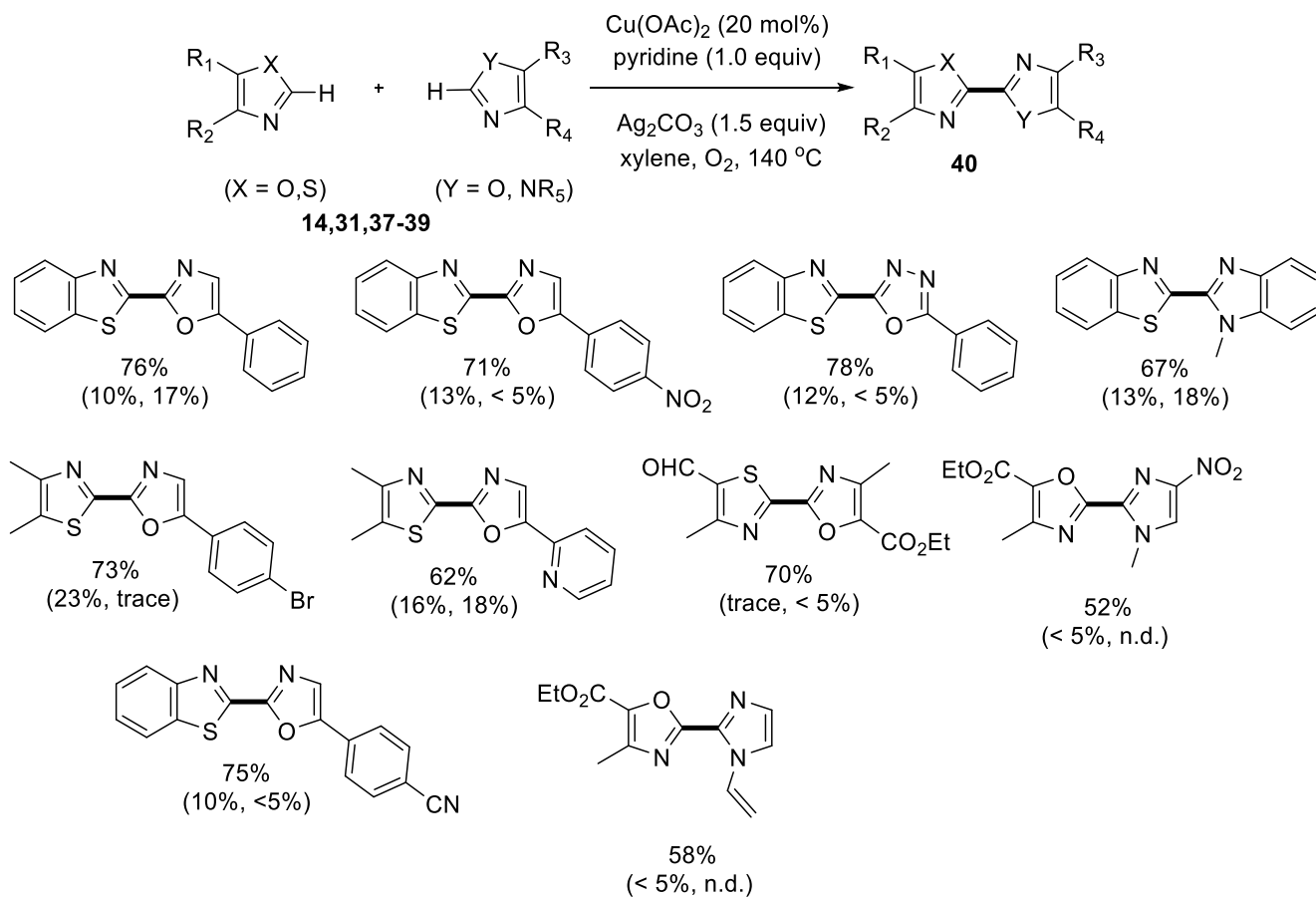

Scheme 15. Cu-catalyzed dehydrogenative cross-coupling of benzothiazoles with thiazoles.

In 2012 Qin with the group reported that two azoles underwent oxidizing cross-coupling chemoselectively to produce nonsymmetric biazoles **40** (Scheme 16).[45] $Cu(OAc)_2$ and Ag_2CO_3 with pyridine in xylene generated the desired products in synthetically useful yields. A range of azoles (thiazoles **14**, oxazoles **31**, imidazoles **37**, benzimidazoles **38** and oxadiazoles **39**) was prepared under the optimal conditions. The proposed approach tolerated a large variety of functional groups (e.g. halogens, nitro, cyano, ether, aldehyde and vinyl groups).

The C-H/C-H coupling reactions between two electron-rich heteroarenes described above proceed with the formation of homo-coupling products.

Ofial and co-workers successfully performed the oxidative cross-coupling between two identical heteroarenes without the formation of homo-coupling products (Scheme 17).[46] The authors discovered that benzothiazoles **15** and benzimidazoles **38** selectively reacted with c *N*-, *O*- and *S*-containing azoles. For instance, thiazoles **14** oxazoles **31** and imidazoles **37** in the presence of $KF/AgNO_3$ or AgF provided 2,2'-biheteroaryles **41** in good yields.

(The number in parentheses is the homocoupling yield of azoles)

Scheme 16. Cu(II)-catalyzed dehydrogenative cross-couplings between benzothiazole with azoles and two nonbenzo-fused azoles.

method A: Pd(OAc)$_2$ (5 mol%), KF (3.0 equiv), AgNO$_3$ (1.5 equiv), 24 h
method B: Pd(OAc)$_2$ (5-10 mol%), AgF (2.0 equiv), 24-48 h
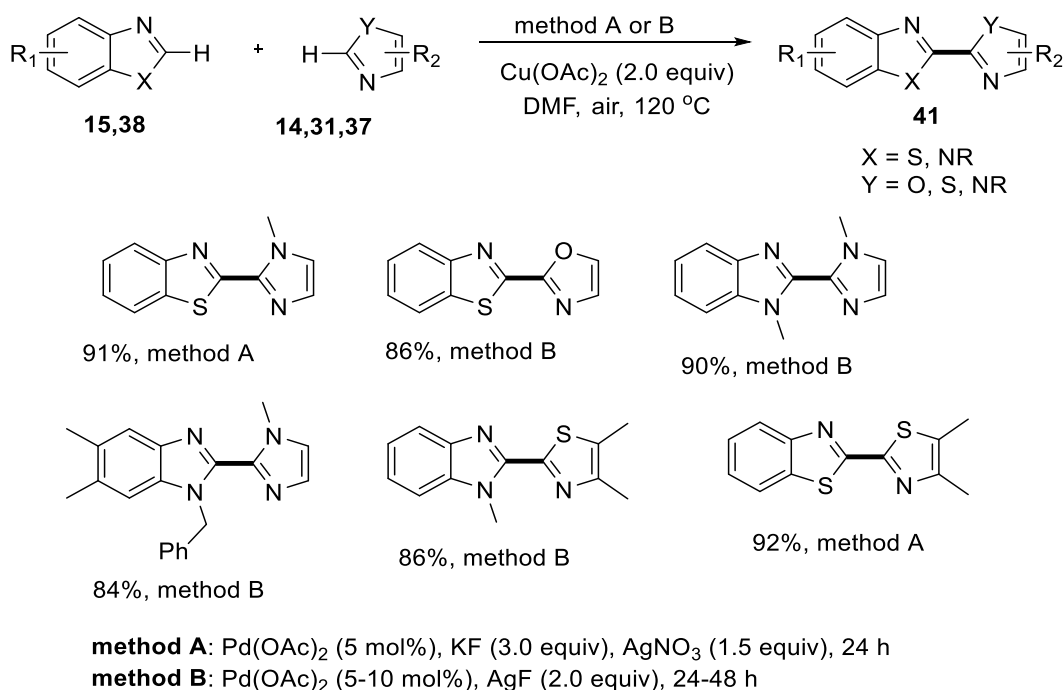
Scheme 17. Pd-catalyzed oxidative dehydrogenative cross-couplings of benzazoles with azoles.

Salvanna, Reddy and Das firstly designed a protocol for oxidative cross-coupling of 1,3,4-oxadiazoles **39** with benzothiazoles **15** using a catalytic system Pd(OAc)$_2$/Cu(OAc)$_2$/AgNO$_3$/KF (Scheme 18).[47] The reaction furnished **42** in high yields.
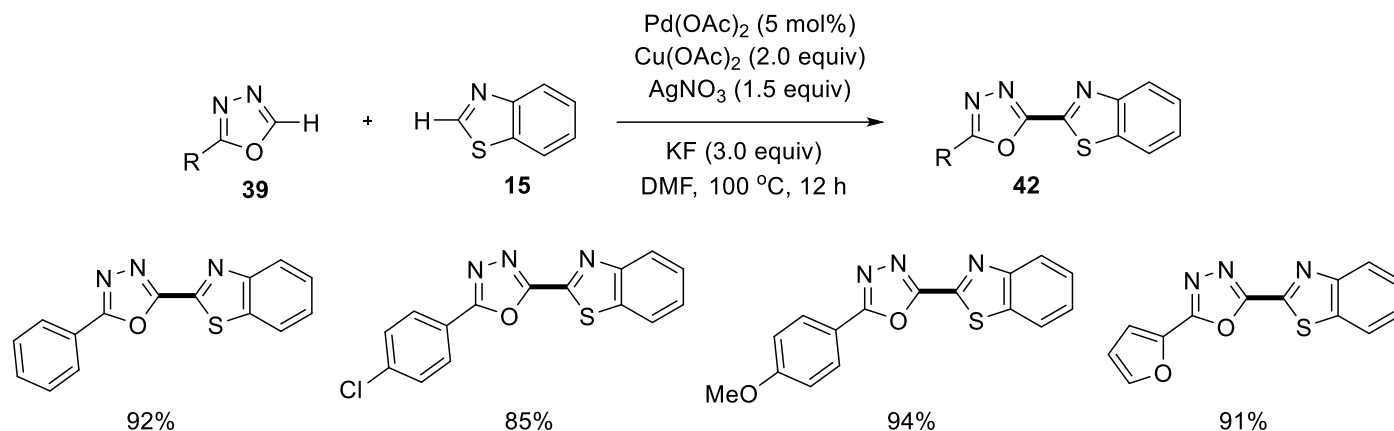
Scheme 18. Pd-catalyzed cross-couplings of 1,3,4-oxadiazoles with benzothiazoles using Cu(OAc)$_2$ as an oxidant.
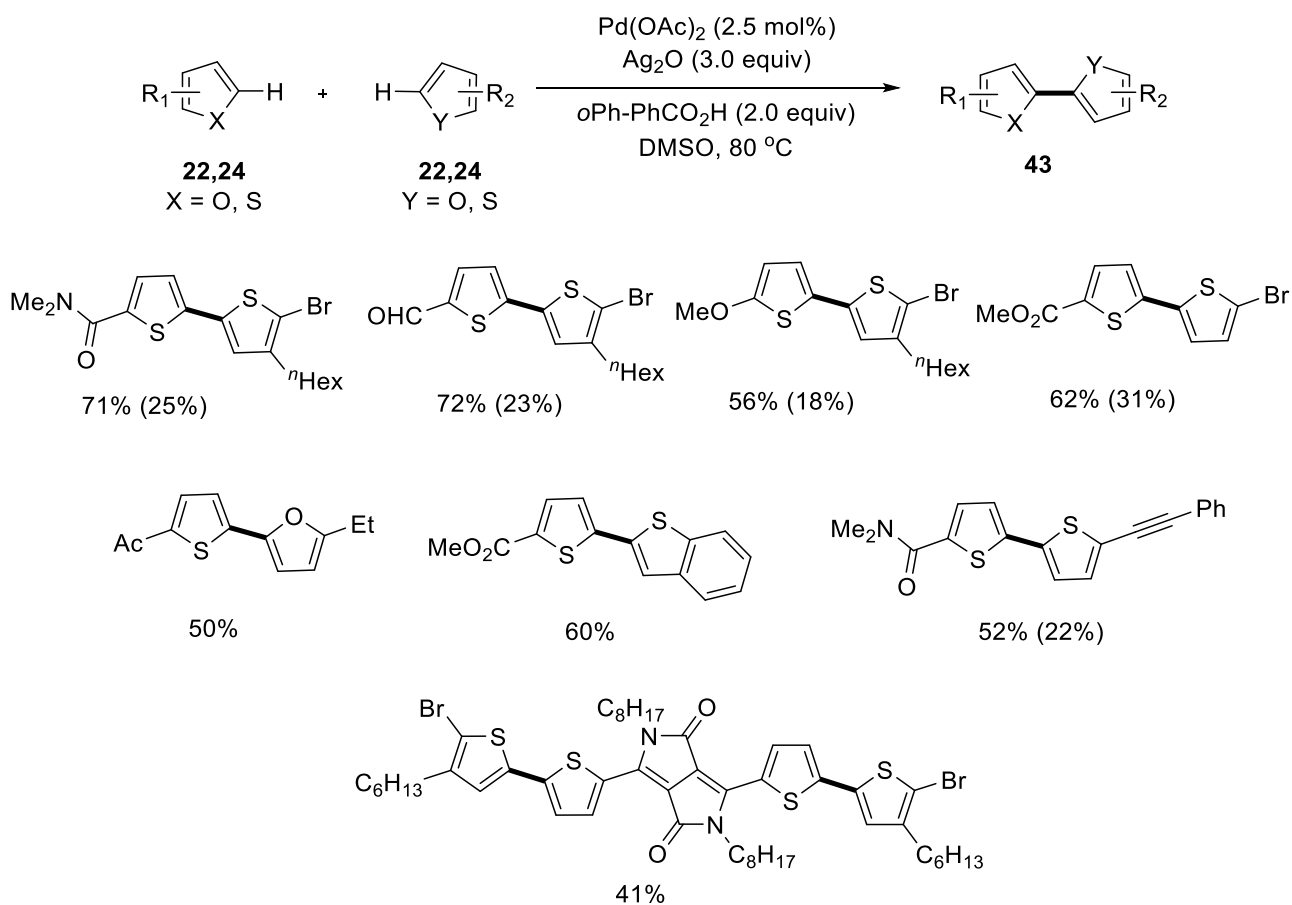
(The number in parentheses is the homocoupling yield of compound **22** or **24**)

Scheme 19. Pd-catalyzed oxidative cross-coupling between two electron-rich heteroarenes using Ag$_2$O as an oxidant.

The homo-coupling between two S-containing heteroarenes does not occur smoothly. This might be one of the reasons why cross-couplings of these compounds have not been widely studied so far. To attend high chemoselectivity a lower reactive substrate is taken in excess. Zhang`s group accomplished oxidative cross-coupling of two electron efficient heterocycles (furans **22** and thiophenes **24**), having similar structures and electronic properties (Scheme 19).[48] Pd(OAc)$_2$ and AgO were utilized as a catalyst and an oxidant respectively. *o*-Phenylbenzoic acid has been shown to play a critical role to increase the reaction efficiency. The process afforded **43** in good yields, but undesirable side-products of homo-coupling were obtained in efficient amounts in the most of reactions.

In 2012 Glorius and co-workers effectively employed [RhCp•Cl$_2$]$_2$ as a catalyst in oxidative cross-coupling between furans **22** and thiophenes **24** as well as between *N*-substituted indoles **2** and pyrrols **4** with benzofuran **23** and benzothiophene **25** (Scheme 20).[49] The authors found that Cu^{II}(2-ethylhexanoate)$_2$ was sufficient for high yields and chemoselectivity of **44**. Cu(OAc)$_2$, Cu$_2$O and Cu(OH)$_2$ turned out to enhance the yields and selectivity not significantly.
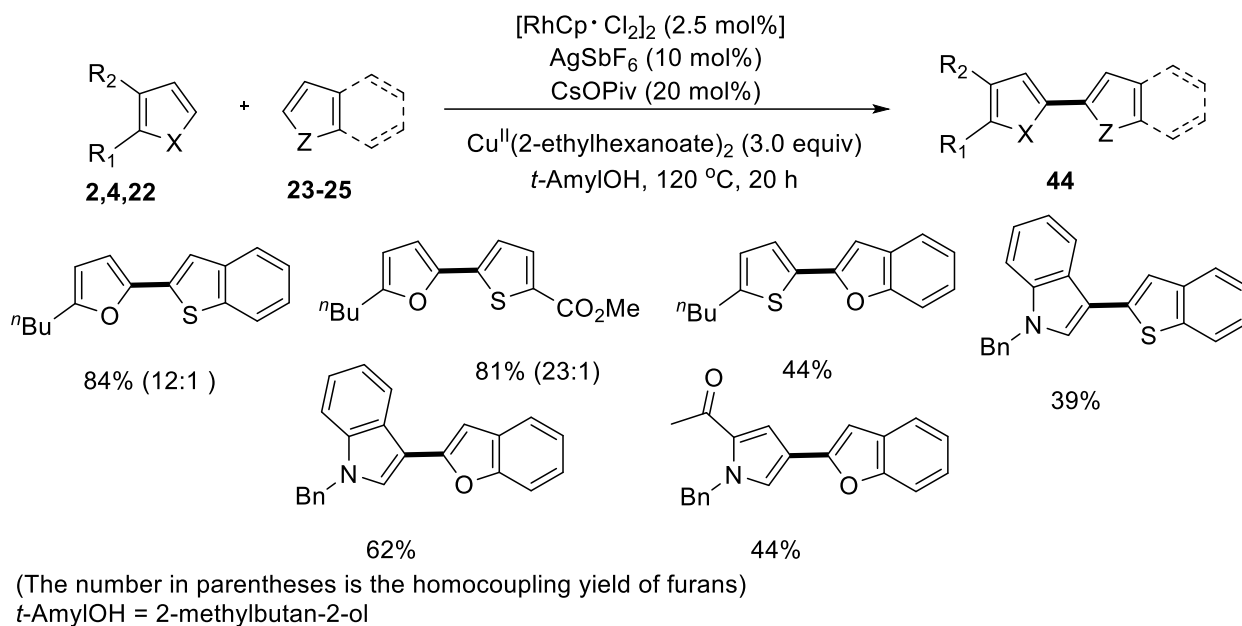
Scheme 20. Rh(III)-Catalyzed cross-dehydrogenative coupling of furan and thiophene derivatives using Cu^{II}(2-ethylhexanoate)$_2$ as an oxidant.

Hetero(bi)arenes are known to be a substantial structure fragment for fluorophores construction. In this regard Cheng and co-workers developed Pd-catalyzed oxidative C-H/C-H cross-coupling between electron-poor 2*H*-indazoles **26** and electron rich heteroarenes such as indoles **2**, pyrroles **4**, furans **22**, benzofurans **23**, thiophenes **24** and benzothiophenes **25** resulting in a wide array of biheteroaryl fluorophores **45** (Scheme 21).[50]
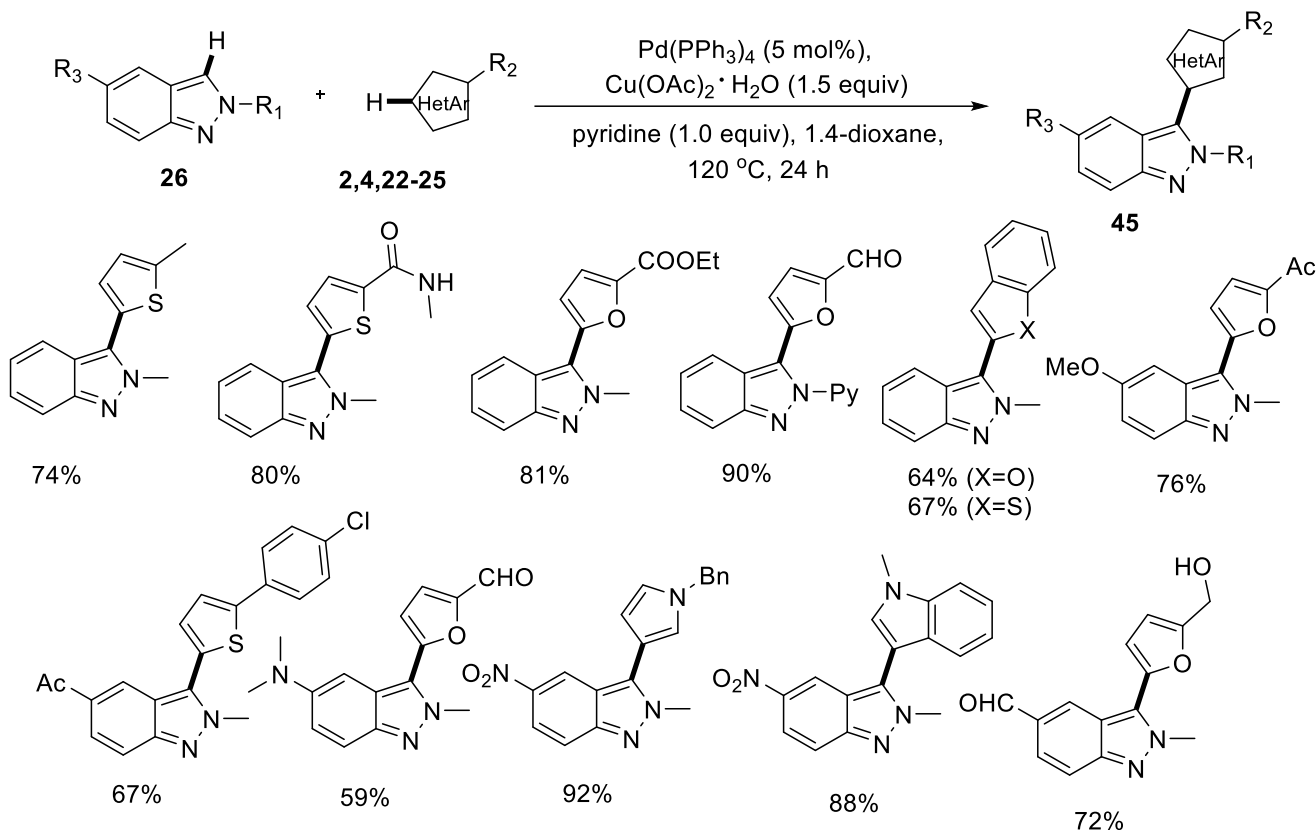
Scheme 21. Direct oxidative C−H/C−H cross-coupling of 2*H*-indazoles with various electron-rich heteroarenes.

2-Arylsubstituted thiazolo[5,4-*d*]pyrimidines are prominent building blocks of biologically active compounds. In 2014 Yang, Su and Sun designed a protocol for the synthesis of such compounds via oxidative C-H/C-H cross-coupling between thiazolo[5,4-*d*]pyrimidine **46** and pyrroles **4**, thiazoles **14** and pyrazoles **47** using Pd(PPh₃)₂Cl₂ as a catalyst and Ag₂CO₃ as an oxidant (Scheme 22).[51] The reaction led to C-2 hetarylsubstituted thiazolopyrimidines **48**.
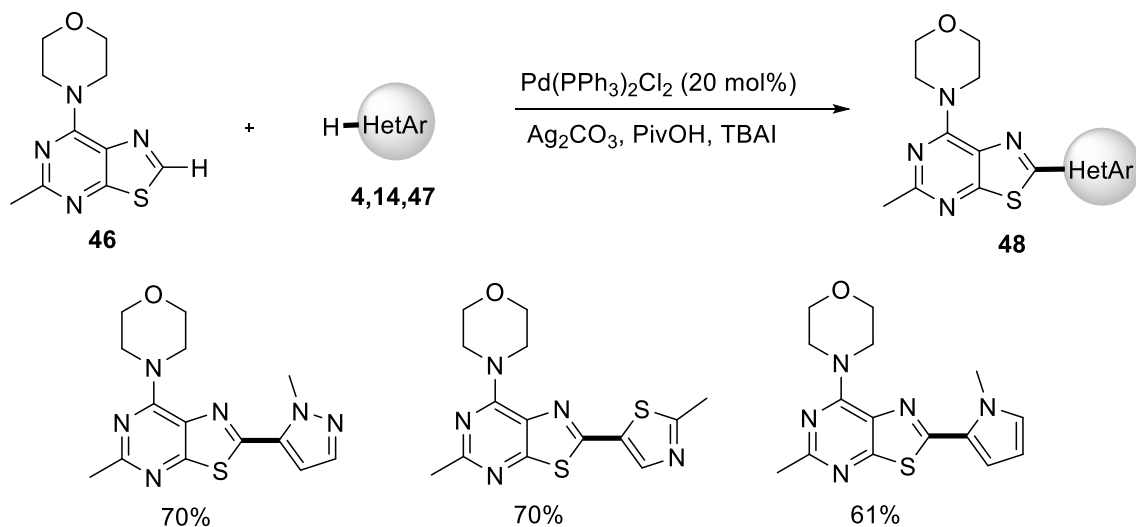
TBAI = tetra-*n*-butylammonium iodide

Scheme 22. Pd-catalyzed oxidative C-H functionalization of thiazolo[5,4-*d*]pyrimidine with aromatic (hetero)cycles.

**2.1.2. Copper- and silver-mediated C-H functionalizations.** As mentioned above, the design of non-catalyzed C-H functionalizations has grown to an extensively evolving field. These processes are highly desirable for gaining organic compounds, for example, drugs or solar cells, in which the presence of any metal-containing impurities is excluded.

Wand *et al.* carried out an oxidative cross-coupling between benzoazoles and azoles (S, N, O-containing, including benzannelated analogues **14**, **15**, **31**, **37-39**, **49**) (Scheme 23) in the presence of $Cu(OAc)_2$ resulting in **50** in good yields.[52] Any other employed copper salts turned out to be ineffective. 2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO) did not change the reactivity thus excluding a radical process.
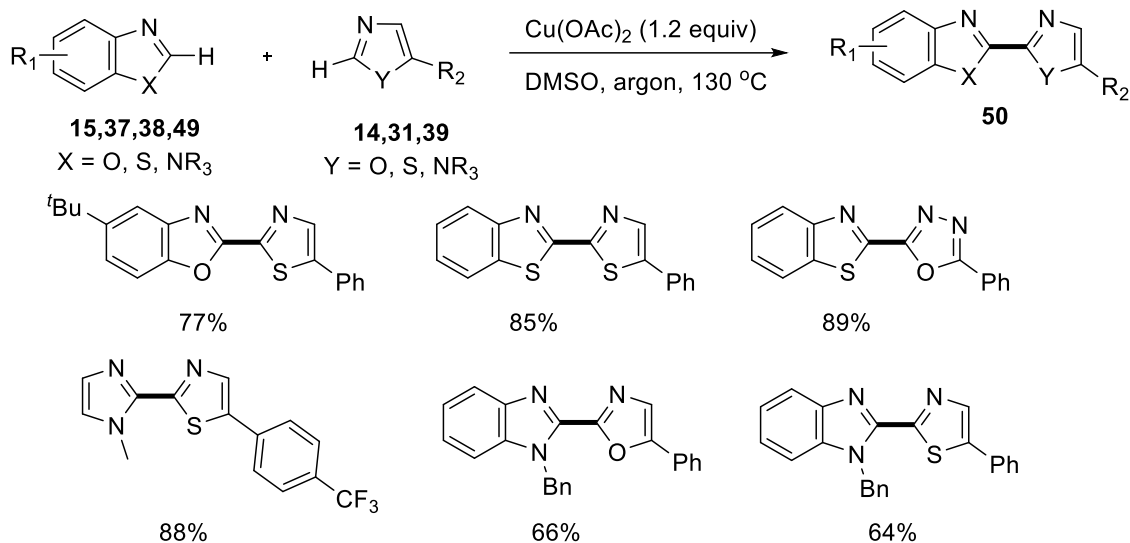
Scheme 23. $Cu(OAc)_2$-mediated dehydrogenative cross-coupling between two heteroarenes.

Jiang, Yang and Wu reported that aza-BODIPY **51** (BODIPY - 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene) underwent oxidative C-H/C-H-coupling with indoles to produce compounds **52-60** donor-acceptor (D-A) and donor-acceptor-donor (D-A-D) type revealing double-band absorption (Scheme 24).[53] Inexpensive and effective $Cu(OAc)_2$ represents an alternative to the salts of noble-metals as an oxidative agent/mediator. Owing to the proposed rapid approach, electron poor aza-BODIPY is expected to be included in D-A system to generate promising molecules. The compounds could be used in design of optoelectronic materials.
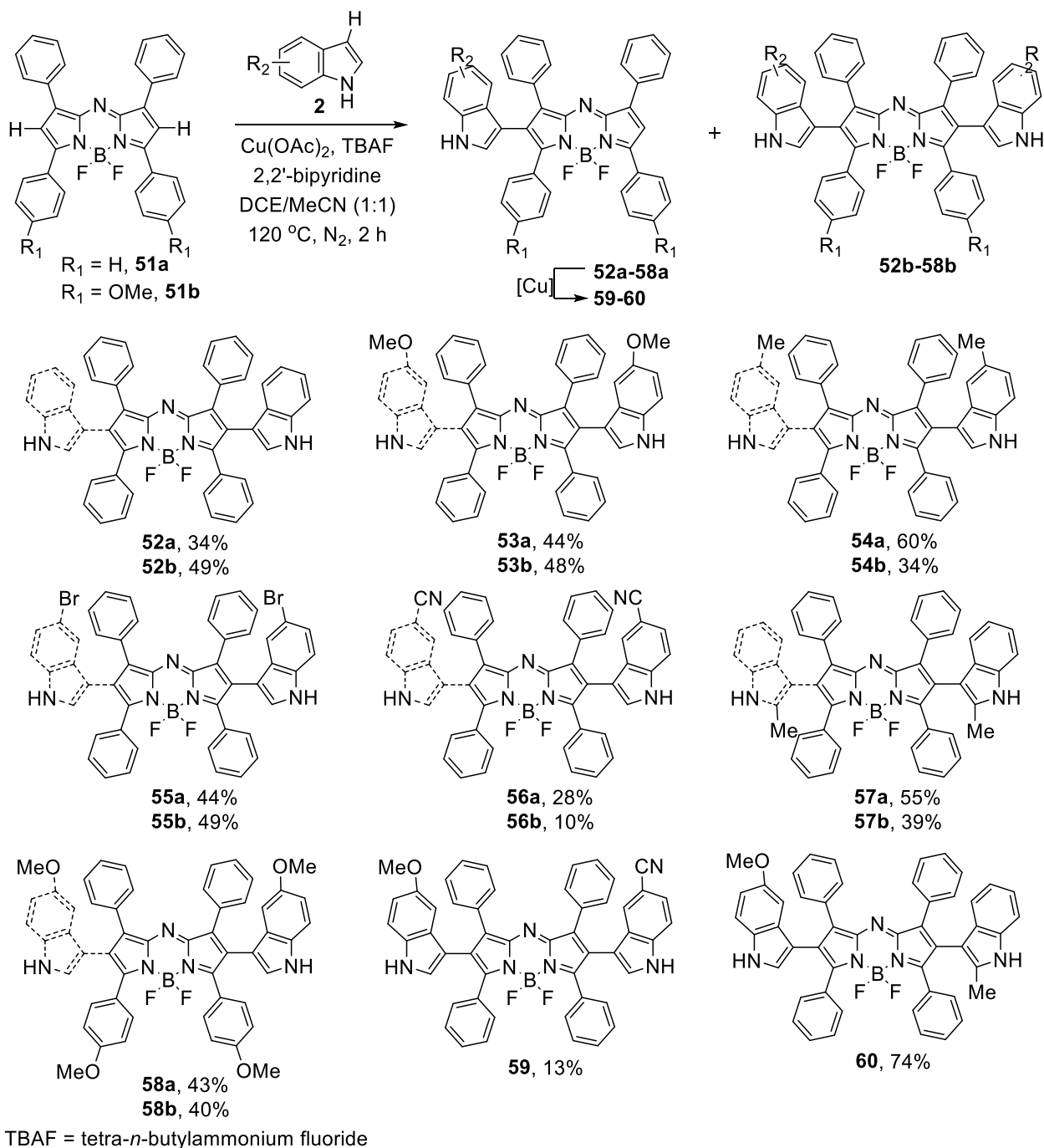
Scheme 24. Oxidative C–H/C–H cross-coupling reaction of aza-BODIPY.

One of the interesting and unusual examples of the use of C-H functionalization reactions is described in the work (Scheme 25).[54] Oxidative hetero-coupling between unprotected indoles **2** and an equivalent of chiral glycine complex of nickel (II) **61** was employed to generate 3-indolyl glycine derivatives **63**. Cu(acac)$_2$ turned to be the most effective oxidative agent in comparison with copper (II) acetate, Fe(acac)$_3$, iodine and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). The desired adducts **62** were obtained with high diastereoselectivity. Decomposition of the adducts enabled the derivatives of 3-indolyl glycine **63** in high enantiomeric excess (97-98% *ee*) and yields (85-93%). Optically active non-proteinogenic amino acid 3-indolylglycine and its derivatives

are widely used in organic synthesis in the development of medicinal compounds.[55,56] The chiral ligand (*S*)-BPB could be readily isolated from the reaction mass to be reused.

R_1 = H, Me, COOEt, Ph
R_2 = H, 5-OMe, 5-F, 5-Cl, 5-Br, 4-Me, 5-Me, 6-Me, 7-Me
LDA = lithium diisopropylamide

Yield 33-74%
de = 96->99%

(*S*, 2*S*)-**62a**, R = H
(*S*, 2*S*)-**62b**, R = Ph

(*S*)-**63a**, R = H
(*S*)-**63b**, R = Ph

Yield 85-93%
ee = 97-98%

(*S*)-BPB
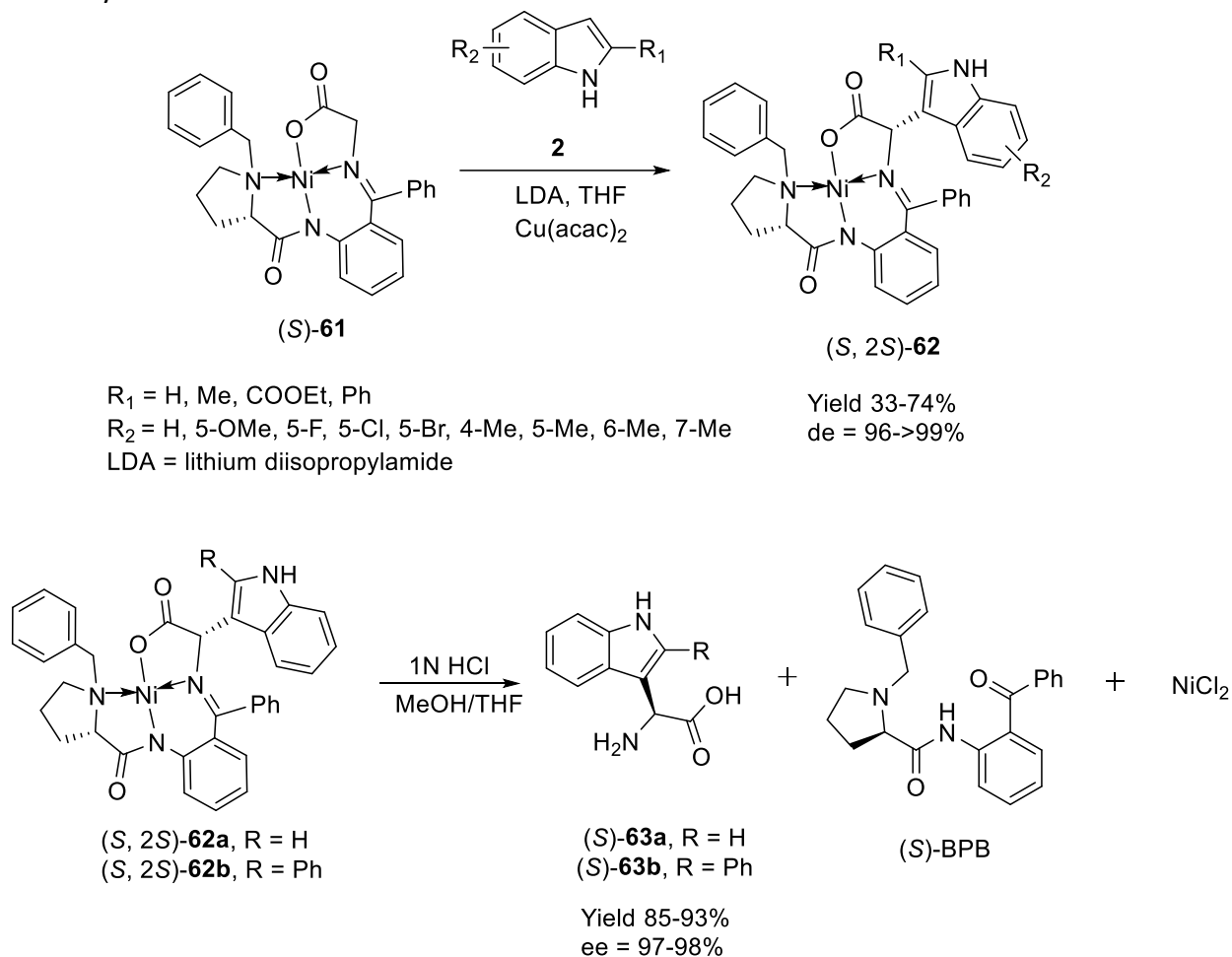
Scheme 25. Oxidative heterocoupling reaction of unprotected indoles and chiral equivalent of nucleophilic glycine. Decomposition of nickel (II) complex to release 3-indolylglycine derivatives.

Metal-metal oxidative C-H functionalization and metal catalyzed cross-coupling could be the complementary processes. The Suzuki reaction could be used to modify the C5-position in lower active for nucleophile`s attack pyrimidine ring, while C-H functionalization, namely nucleophilic substitution of hydrogen in heteroaromatic compounds ($S_N^H$ reactions) is effective for nucleophile`s attack at the C4-position. Combination of two types of C-C coupling, addition-oxidation (AO) or addition-elimination (AE) afforded 4-(hetero)aryl- **66**, 5-bromine-4-(hetero)aryl- **67**, 5-(hetero)aryl- **68** or 4,5-bi(hetero)arylsubstituted pyrimidines **69** from 5-bromine pyrimidine **64** and heteroaryls **2,4,22,24,65** with addition of an oxidative system $K_3Fe(CN)_6$-KOH/H_2O (Scheme 26).[57-65]

Lewis acid = CF$_3$COOH; BF$_3$·Et$_2$O/MeOH
Oxidant = K$_3$Fe(CN)$_6$-KOH/H$_2$O

AE = addition-elimination
AO = addition-oxidation
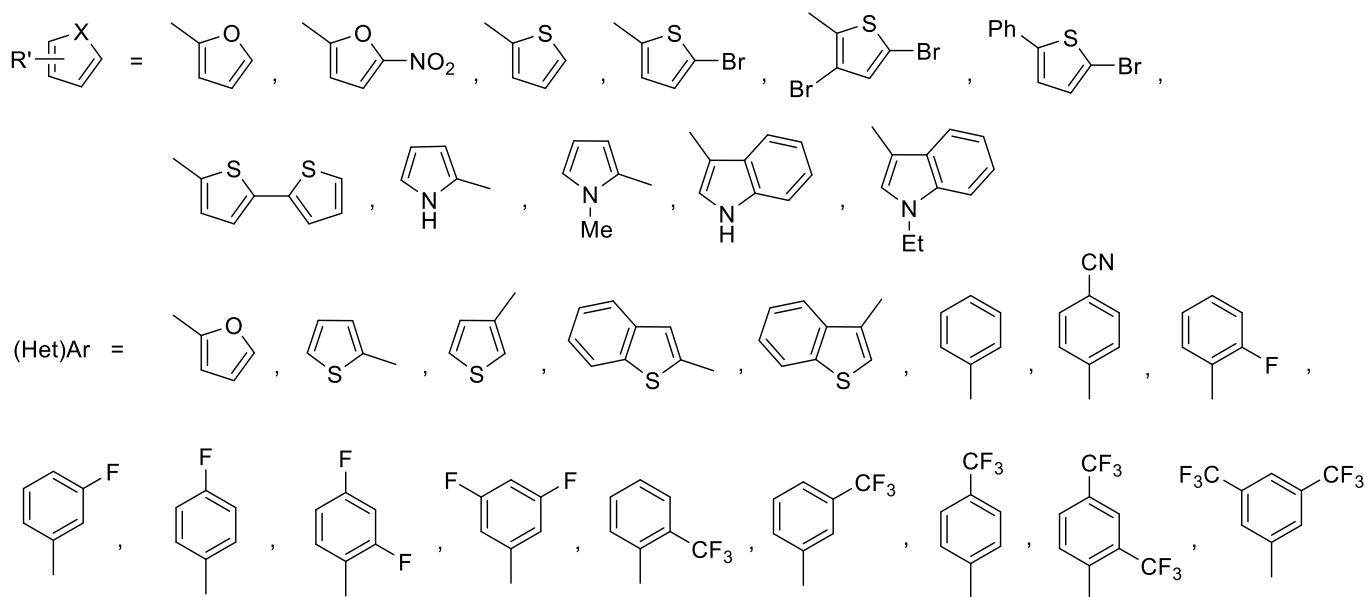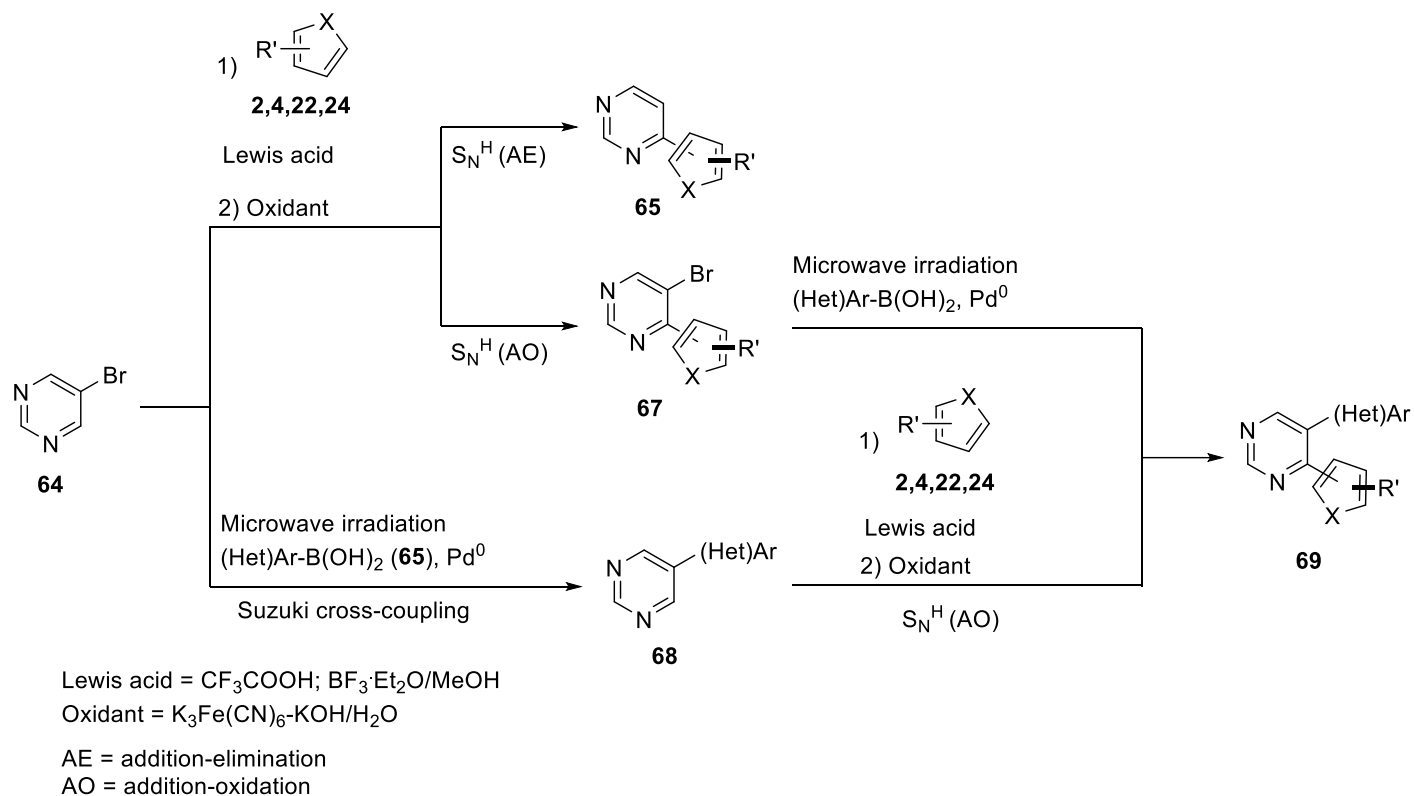
Scheme 26. Combination of the Suzuki-Miyaura cross-coupling and nucleophilic aromatic substitution of hydrogen (S$_N$^{H}) reactions.

The novel approach of mutual reinforcement of metal-free and metal-catalyzed couplings was developed by Mandal and colleagues.[66] They synthesized Dragmacidin D is a biologically active natural compound, potential inhibitor of protein serine-threonine phosphatase. The combination of Pd-catalyzed regioselective C-H/C-I coupling of thiophene-indole (**2+24**), Pd-catalyzed regioselective coupling of indole with *N*-oxide pyrazine (**71+1**) and acid-catalyzed C-H/C-H coupling of indole with pyrazinone (**2+73**) generates the desired product (Scheme 27). The proposed approach represents a good example of a rapid increasing in molecular complexity by constructing simple molecules.
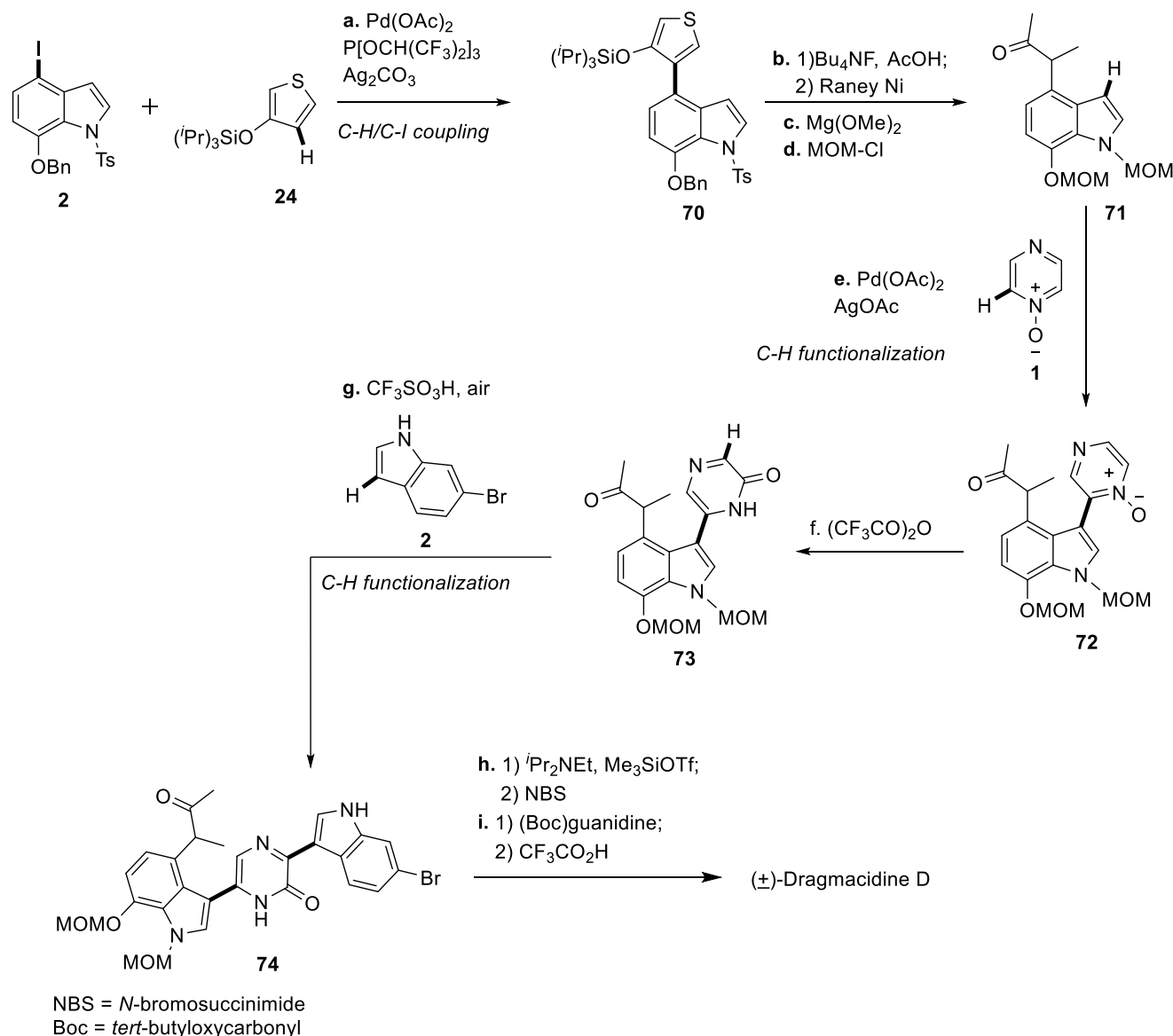
Scheme 27. Synthesis of Dragmacidin D.

2.2. Oxygen

Using of air oxygen or molecular oxygen as an oxidizing agent makes an oxidative C-H functionalization efficient, ecologically friendly and cost-effective process. In the last decade a considerable attention has been payed to the couplings in the presence of oxygen. At the same time an implementation of oxygen in oxidative C-H/C-H cross-couplings between two heteroarenes still remains scantily explored.

2.2.1. Molecular oxygen. In 2011 Prabhu and co-workers developed an aerobic oxidative C-H functionalization of 1,2,3,4-tetrahydroizoquinoline **75** using a vanadium catalyst (10 mol%) in aqueous medium. Molecular oxygen was used as an oxidant.[67] Doyle *et al.* in 2013 reported a different approach to this transformation and employed $FeCl_3 \cdot 6(H_2O)$ as a catalyst.[68] The method allows ones to run the reactions with indoles **2** and pyrrole **4** resulting in **76** in good yields with high conversions (Scheme 28).
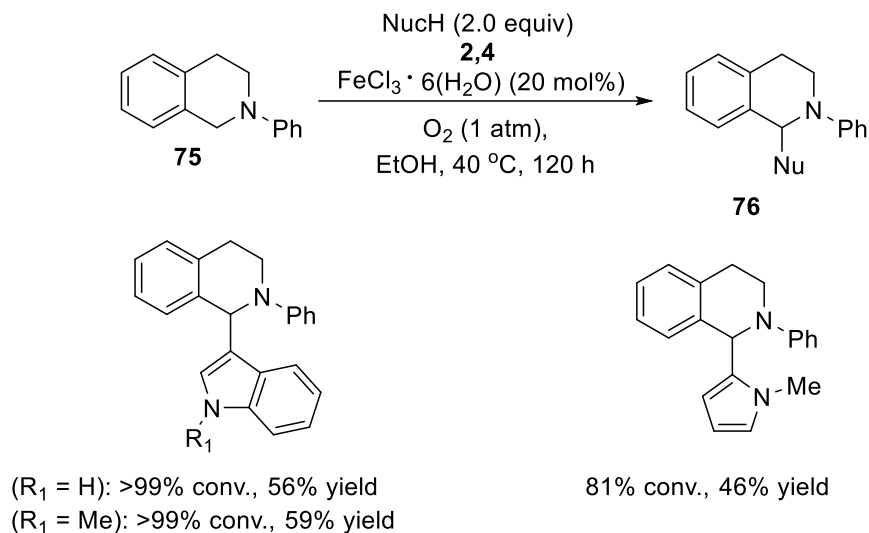
Scheme 28. Iron-catalyzed aerobic C-H functionalization of *N*-phenyltetrahydroisoquinoline.

The use of molecular oxygen as an oxidant in C-H/C-H cross-couplings between π-excessive heterocycles and *N*-containing heteroarenes was reported in 2015 by You *et al.* (Scheme 29).[69] Biheteroarenes **78** were obtained in good yields. A wide scope of π-excessive heterocycles (indoles **2**, pyrroles **4**, furanes **22** and thiophenes **24**) can react with azaheterocycles such as *N*-oxides azines **1**, indolizines **30** and purines **77**.
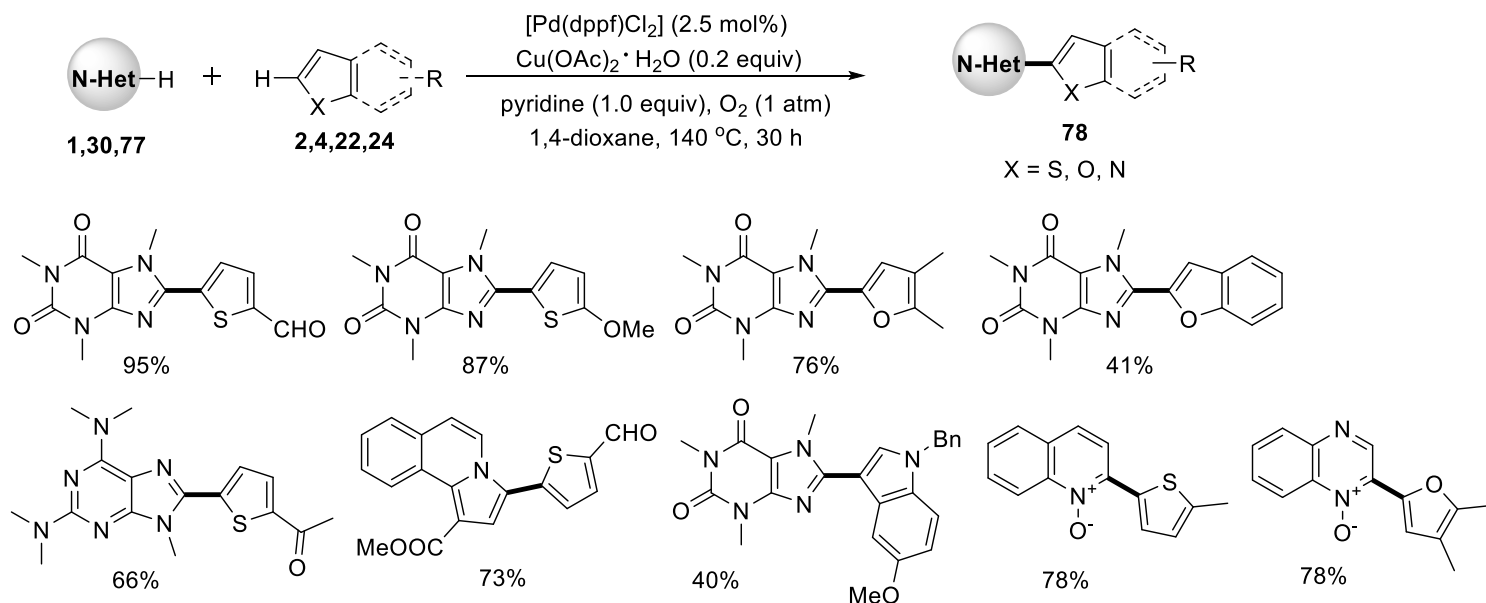
Scheme 29. Palladium/copper-cocatalyzed oxidative cross-dehydrogenative coupling between two heteroarenes by using molecular oxygen as an oxidant.

2.2.2. Air oxygen. Air oxygen as an oxidizing agent in homo- and cross-coupling between two azoles in the presence of Cu(OAc)₂ was used by Li and co-workers (Scheme 30).[70] The reaction products **79** were obtained in good yields. The protocol could be applied for oxidative coupling of azoles (thiazoles **14**, imidazoles **37**, benzimidazoles **38**, oxodiazoles **39** and benzoxazoles **49**).
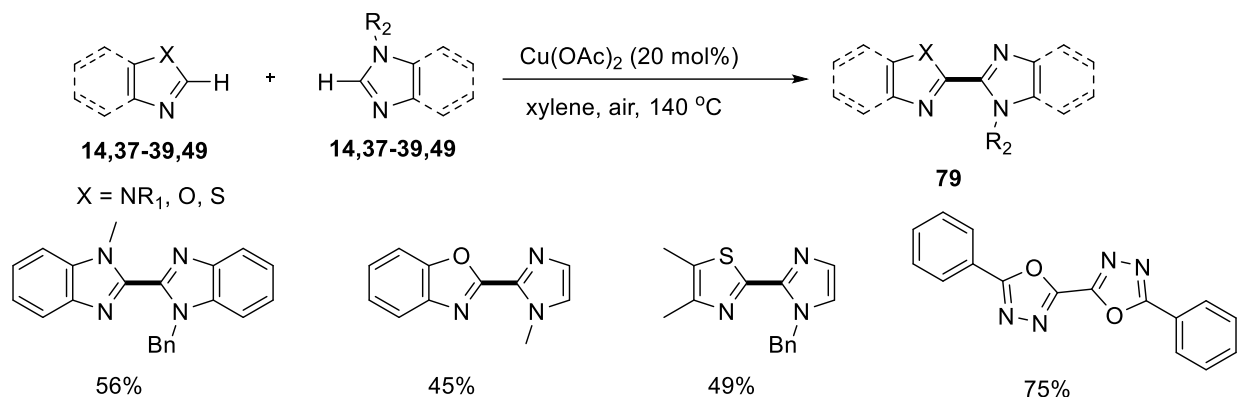
Scheme 30. Cu(OAc)$_2$/air mediated oxidative coupling of azoles.

The same system Cu(OAc)$_2$/O$_2$ was employed by Miura`s group in cross-coupling between indoles **2** and 1,3-azoles (oxazoles **31** and benzoxazoles **49**) (Scheme 31).[71] Biheteroaryls **80a-k** were obtained in good yields. Pyrimidine substitute in substrate provided a regioselectivity of the reaction. It should be noted that the developed method is used to obtain 3- and 5-chloroindole derivatives **80e-f**. The formation of such compounds under other conditions is difficult to carry out with high regioselectivity due to the occurrence of a side dechlorination reaction.
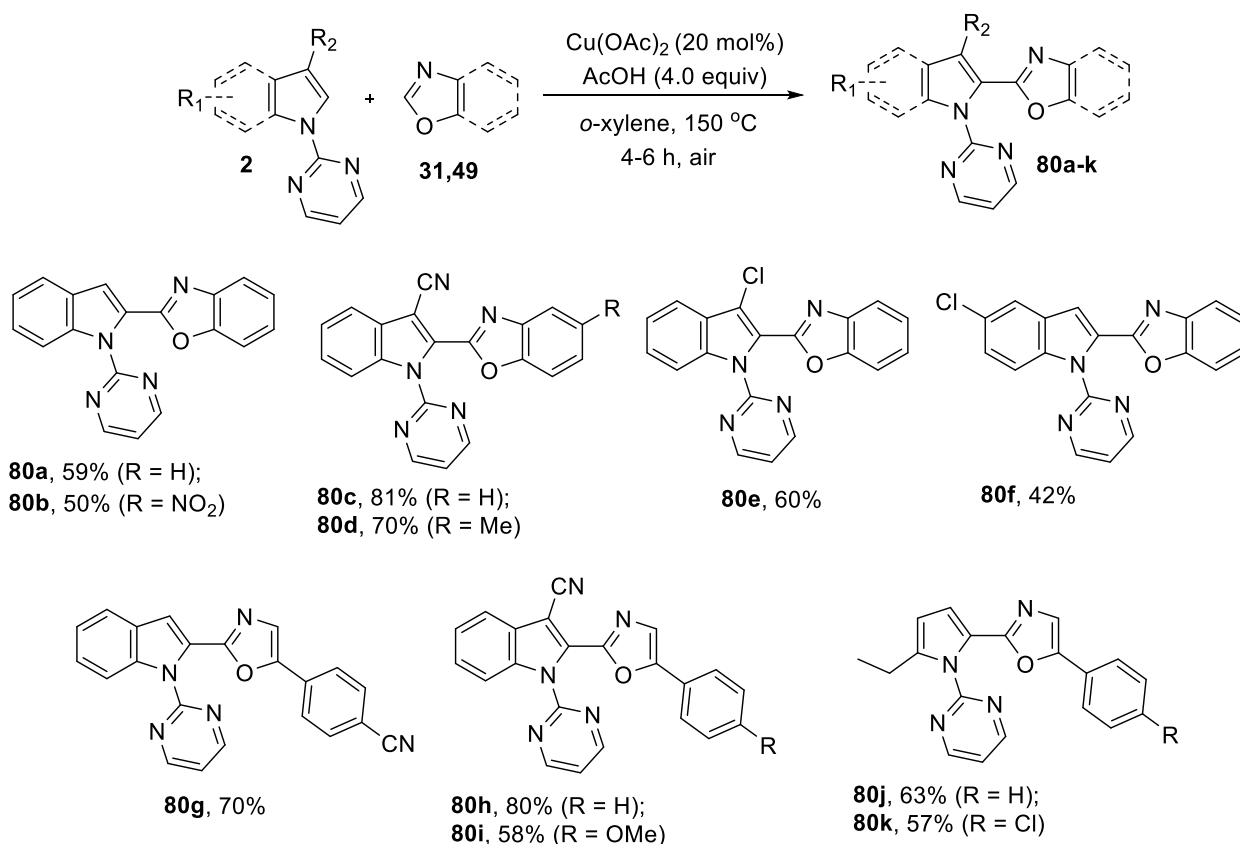
Scheme 31. Copper-catalyzed cross-coupling of indoles and 1,3-azoles.

Later Miura with colleagues continued their research and developed a method of direct C6-selective heteroarylation of pyridones in the presence of Cu(OAc)$_2$ and air oxygen (Scheme 32).[72] 2-Pyridones represent

the widespread heterocyclic systems occurring in biologically active compounds and natural products. The products **82** are formed as the result of coupling between 2-pyridones **81** and 1,3-azoles, such as thiazoles **14**, benzothiazoles **15**, oxazoles **31**, benzoxazoles **49**, benzimidazoles **38** and 1,3,4-oxadiazoles **39**.
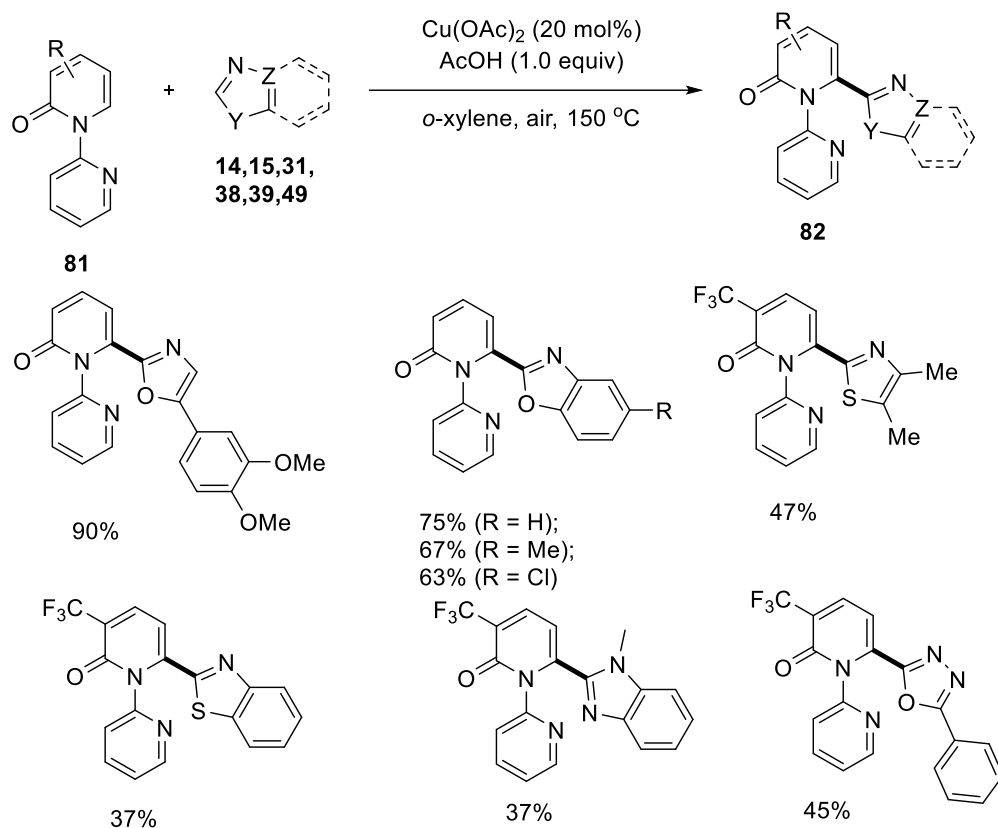
Scheme 32. Copper-mediated C6-selective dehydrogenative heteroarylation of 2-pyridones with 1,3-azoles.

In 2018 Chandrasekharam *et al.* reported a copper-catalyzed direct oxidative C-H functionalization of tetrahydroquinoline **83** with various indoles **2** in aqueous and open-air medium with the formation of products **84** in 42-74% yields (Scheme 33).[73] The use of inexpensive copper catalyst, water as a solvent, and open-air conditions made the CDC reaction a green process.
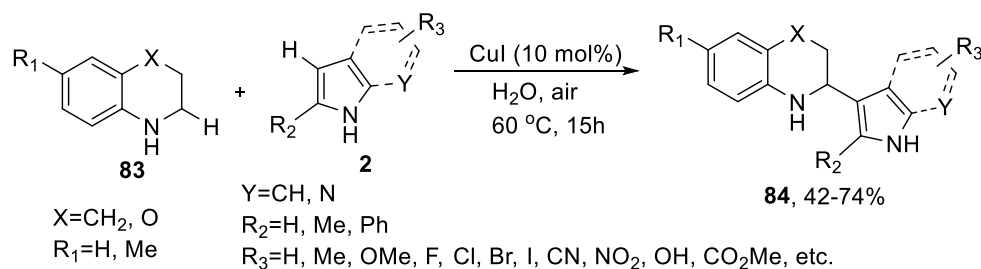
Scheme 33. Copper-catalyzed direct oxidative C-H functionalization of tetrahydroquinoline in water.

Catalyst $CuCl_2$ and air oxygen as an oxidizing agent were employed in coupling between the quinazoline N-oxides **1** and various indoles **2** (Scheme 34).[74] Method provides the target compounds **85** in good yields and with high selectivity (52-93%).
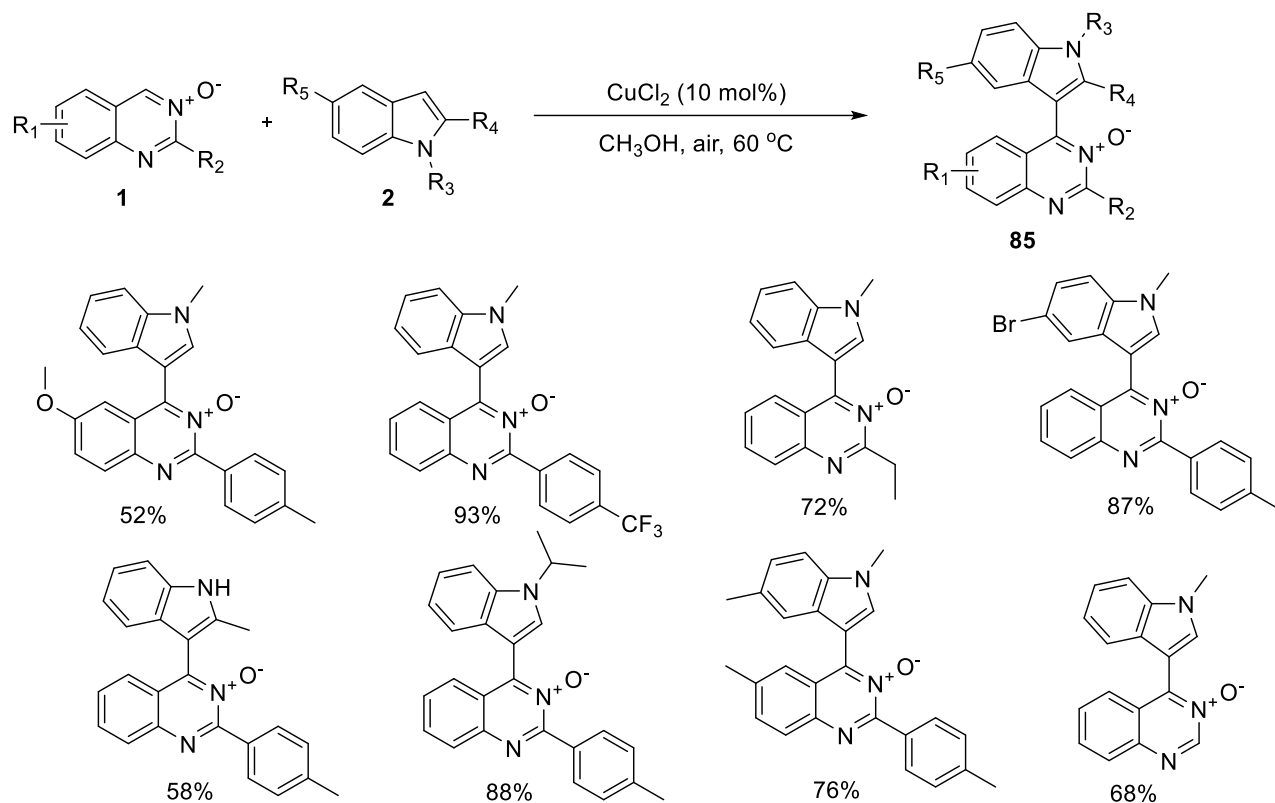
Scheme 34. Copper-catalyzed cross-dehydrogenative coupling between quinazoline-3-oxides and indoles.
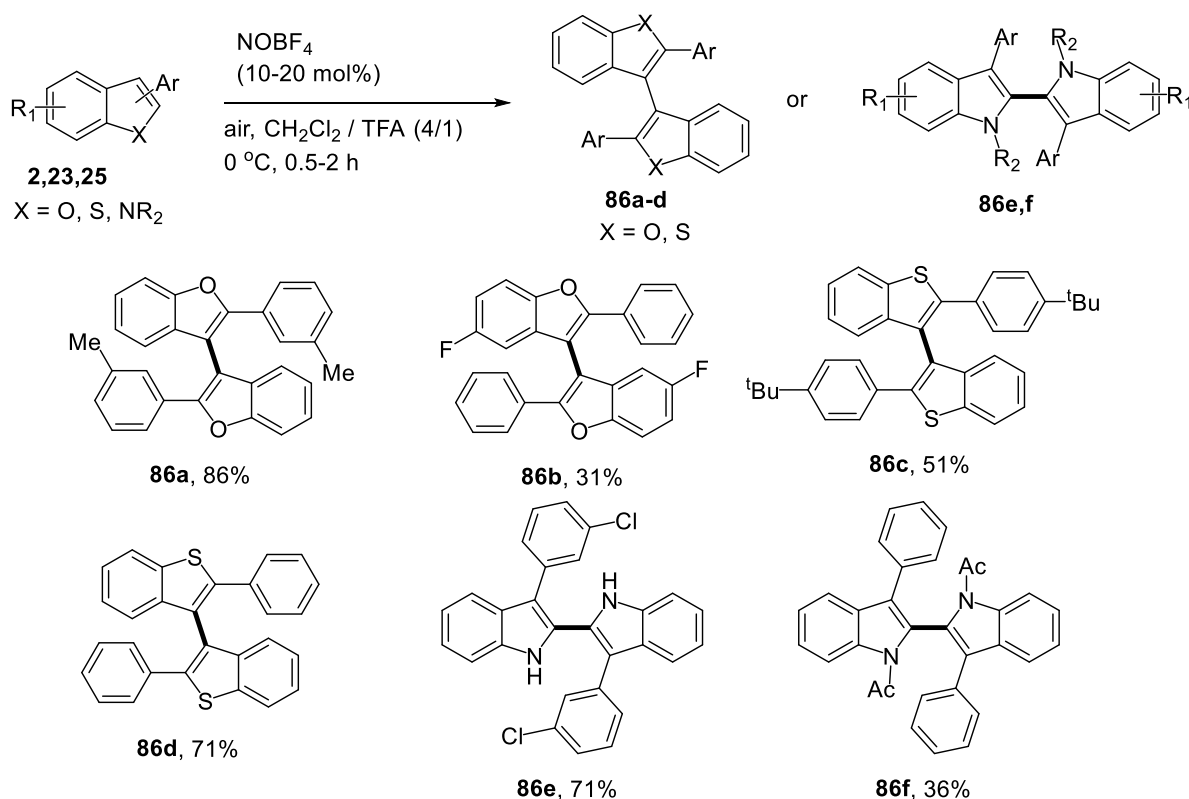
Scheme 35. Nitrosonium ion-catalyzed dehydrogenative coupling of arylated heteroarenes.

Bering with colleagues employed tetrafluoroborate nitrosonium as a catalyst in coupling between indoles **2**, benzofuranes **23** and benzothiophens **25** under mild conditions to obtain dimeric products **86a-e** (Scheme 35).[75]

Recently, the whole series of works dedicated to nucleophilic substitution of hydrogen have enabled the pioneering installation of benzoannelated crown-ethers **87** into triazine cycle **88**. One of the advantages of these transformations is the successful use of air oxygen as an oxidizing agent. The reaction proceeded in acidic medium at ambient temperature. Aromatiztion of adducts **89** to compounds **90** occurred in DMFA in the presence of air oxygen (Scheme 36).[76]

R^1 = Ph(a), *p*-Tol(b), 4-Cl-Ph(c), SC_2H_5(d)
R^2 = CH_3, CF_3
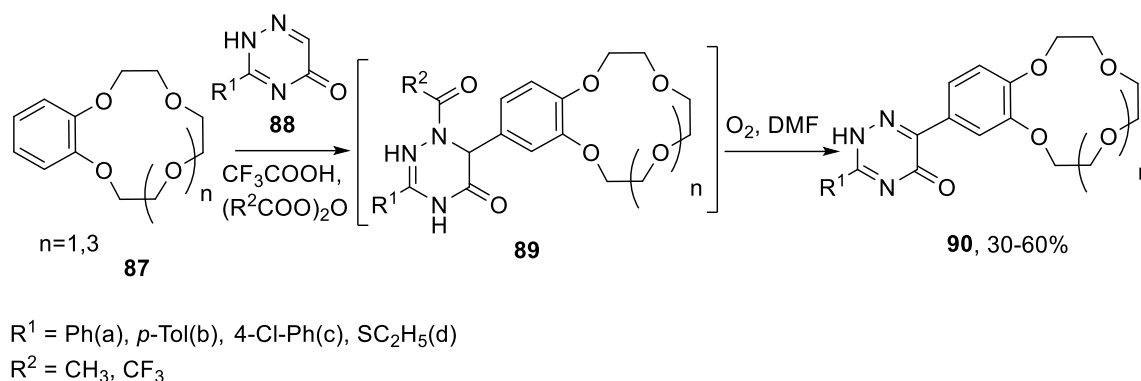
Scheme 36. Direct modification of benzoannelated crown ethers with 1,2,4-triazin-5(2*H*)-one moieties.

In 2004 Chupakhin with his group reported that diazines **91** as electrophiles underwent the same transformation (Scheme 37).[77] Pyrimidine and quinazoline afforded **92** in 58-60% yields.
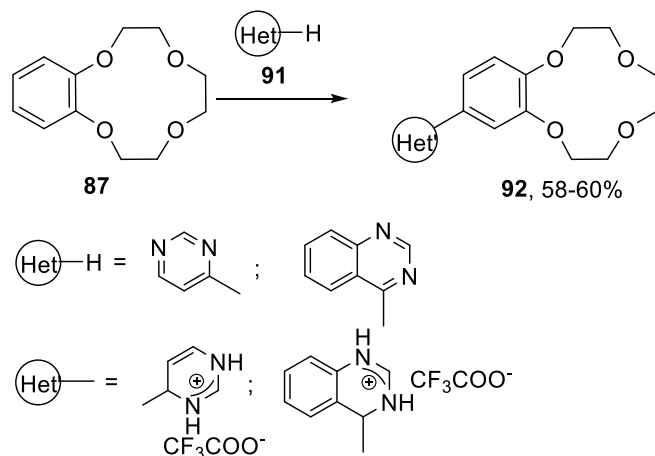
Scheme 37. Direct C-H functionalization of 1,3-diazines and 1,2,4-triazines aryl-containing macrocyclic compounds.

The methodology of nucleophilic substitution of hydrogen could be applied in the synthesis of heterocyclic free radicals – 4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazol-1-oxyls, revealing the kinetic stability and intramolecular delocalization of unpaired electron density on paramagnetic fragment. These products are prone to act as the bridge elements in self-assembling of heterospin coordination systems serving to play the role of high effective channels for the transfer of exchange interaction between paramagnetic centers.

This class of compounds has a tighter range of synthetic approaches. To produce heterocyclic nitroxiles derivatives of 2-imidazolines **94a-h**, **97**, **100a,b** and **101a,b** Chupakhin`s group developed an efficient protocol for the direct coupling of lithium nitroxyl **93-Li** and π-deficient heteroarenes *via* S_N^H-reactions (Scheme 38).[78-80]

R = Ph (**a**), 4-EtC$_6$H$_4$ (**b**)
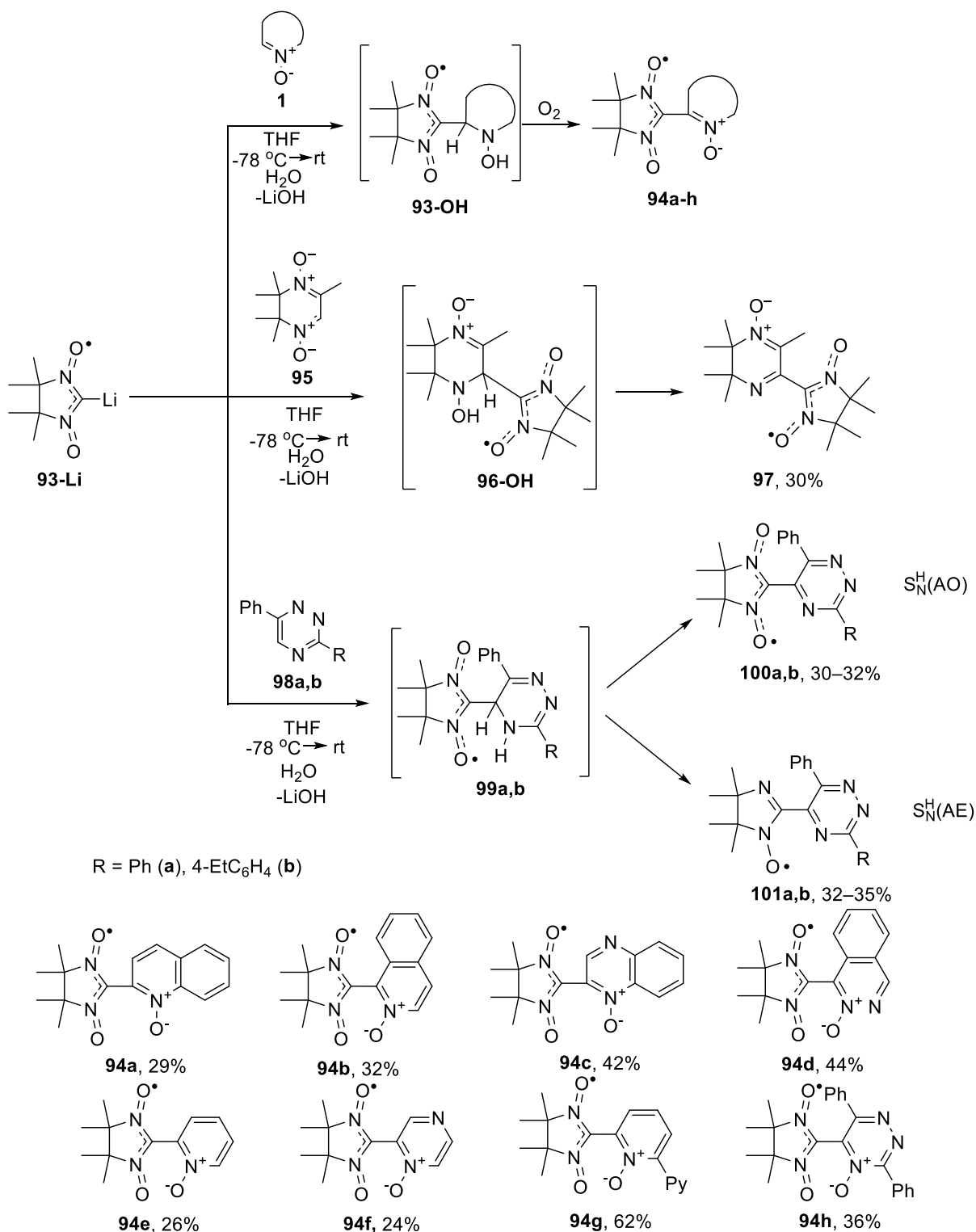
Scheme 38. S_N^H reaction of the lithium salt of nitronyl nitroxide with azine-*N*-oxides and 1,2,4-triazines.

The aromatization of intermediate unstable compounds **93-OH**, **96-OH**, **99a,b** occurs with the help of an oxidizing agent - air oxygen. A relative arrangement of the active centers (N- and O-atoms) provides a tendency of the synthesized structures to complexation. The reaction proceeds with *N*-oxides **1** and their analogue **95**, which does not have a cyclic conjugated system of π-bonds. In the case of non-activated azines, reactions proceed only with highly electrophilic 1,2,4-triazines **98a,b**. Any efforts to generate mono- and diazinyl containing products have failed.

In 2015 Kumar and co-workers showed that *β*-arylation of unprotected indoles **2** with nitroarenes **102** could be realized chemo- and regioselectively with the aim of *t*-BuOK at ambient air with the formation of aryl-indole systems **103** (Scheme 39).[81]
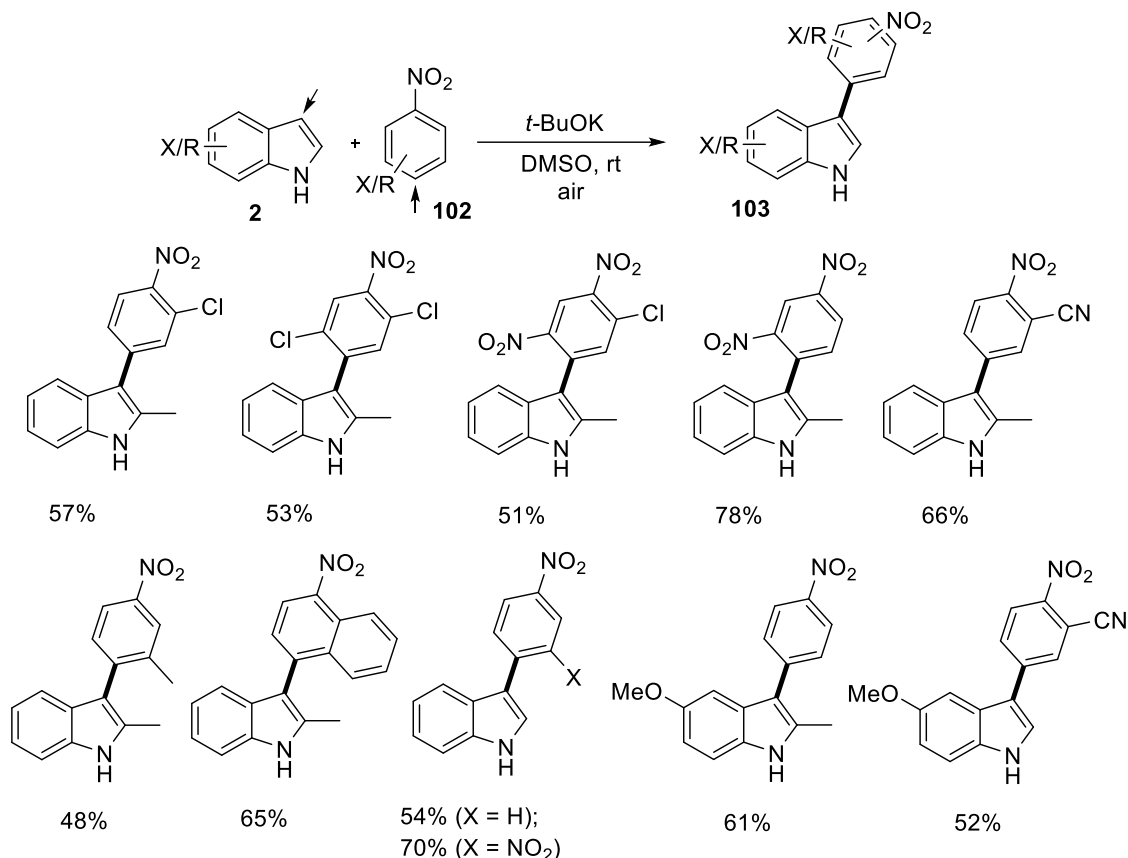
Scheme 39. *t*-BuOK-Mediated aerobic transition-metal-free regioselective *β*-arylation of indoles.

Yuan *et al.* reported an effective protocol for the synthesis of 3-(indol-3-yl)quinoxaline-ones **105** from quinoxalin-2-ones **104** and indoles **2** in the presence of catalyst TfOH (trifluoromethanesulfonic acid) and air oxygen as an oxidant (Scheme 40).[82]
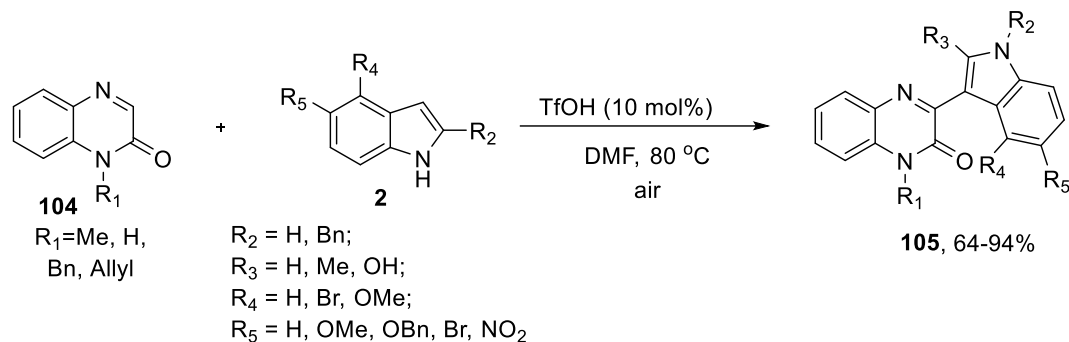
Scheme 40. TfOH-catalyzed coupling reaction between quinoxalin-2-ones and indoles using air as an oxidant.

3. Organic Oxidants

3.1. Hypervalent derivatives of iodine (III)

Over the past 30 years, a substantial progress has been made in the utilization of the methodology for the formation of C-C bonds mediated by hypervalent iodine compounds.[83-86] Here we highlight the examples of hypervalent iodine (III) derivatives implementation in the couplings of two heteroarenes.

2,2`-Dithiophenes have been successfully applied for the synthesis of conductive polymers. To date the non-catalyzed by transition metals synthesis of dithiophenes has not been the feasible challenge. It deals with an oxidative potential and with the control of a regioselectivity. In 2003 Tohma *et al*. in their first trials to produce dithiophenes determined that system $PhI(CO_2CF_3)_2$-$BF_3 \cdot Et_2O$ resulted in the mixture of regioisomers "head to head" and "head to tail" without definite selectivity.[87] Later the selective dimer "head-tail" **106** was obtained with employment of the system HTIB [hydroxy(tosyloxy)]iodobenzene, PhI(OH)OTs] − TMSBr (trimethylsilylbromide) (Scheme 41).[88-90] According to the plausible mechanism the C-3 monosubstituted

HFIP = hexafluoroisopropanol
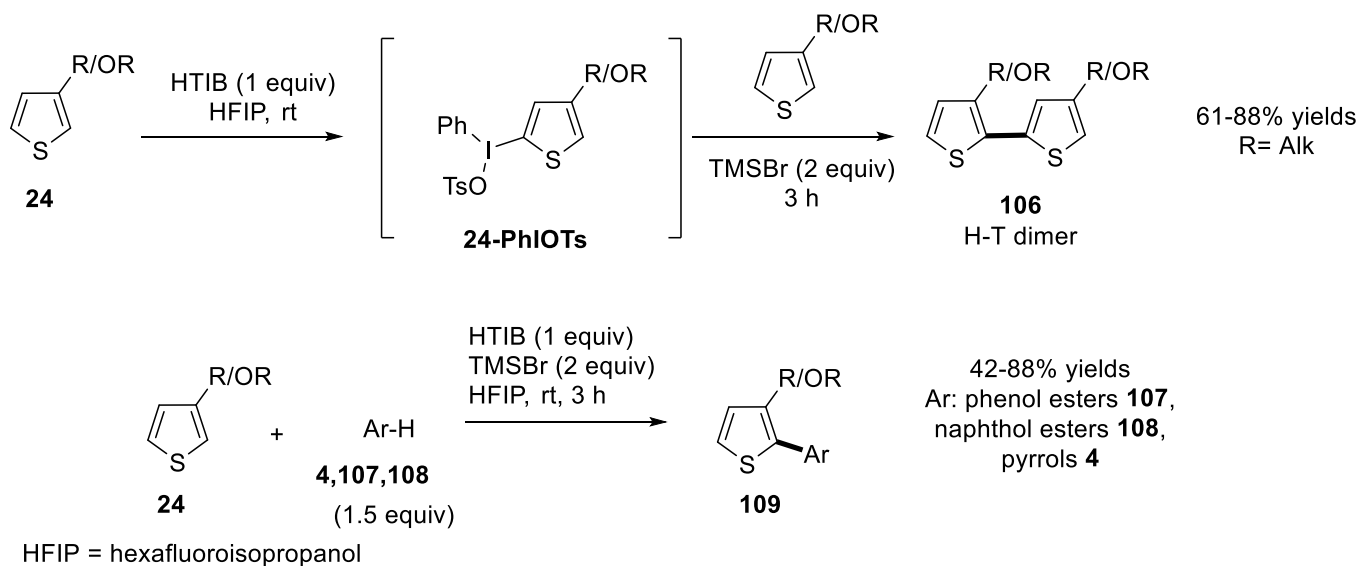
Scheme 41. Metal-free oxidative coupling reactions via iodonium intermediates.

thiophene **24** is more active for reactions at the C2 position and it reacts with HTIB on this position to form the phenyliodoniumthiophene intermediate **24-PhIOTs**. In the second step, phenyliodoniumthiophene reacts with one more equivalent of thiophene at the C5-position. The proposed sequence of reactions enables selective formation of the product. Later the reaction was generalized including heterodimerization of thiophenes with a broad array of aromatic compounds, such as pyrrols **4**, phenol ethers **107** and naphthols **108**.[91]

         Gu and Wang developed an approach of the direct oxidative cross-coupling between *N*-acetylindoles **2** and anizoles **110** using PIFA [phenyliodine bis(trifluoroacetate), PhI(OCOCF$_3$)$_2$] as an oxidizing agent (Scheme 42).[92] C3-arylindoles **111** were selectively obtained.

R$_1$ = H, NO$_2$, CO$_2$CH$_3$, OCH$_3$, Br
R$_2$ = H, 2-Me, 3-Me, 3-*t*-Bu, 2-OMe, 3-OMe, 2-Br, 2-I
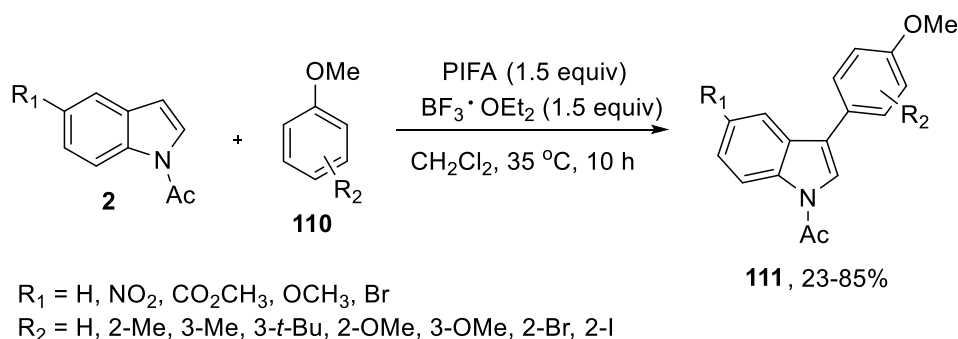
Scheme 42. Direct C-3 arylation of *N*-acetylindoles with anizoles using phenyliodine bis(trifluoroacetate) (PIFA).

         The reaction of indoles **2** with diphenyliodonium-triflate (and/or tetrafluoroborate) with a catalytic amount of Cu(OTf)$_2$ gave the corresponding C3-substituted indoles **112** in good yields (Scheme 43).[93] It is worth noting that 2,6-di-tert-butylpyridine (dtbpy) is essential to suppress the indole`s dimerization.

72% (C3/C2 14/1)

74% (C3/C2 >20/1)

71% (C3/C2 10/1)

57% (C3/C2 8/1)

38% (C3/C2 >20/1)
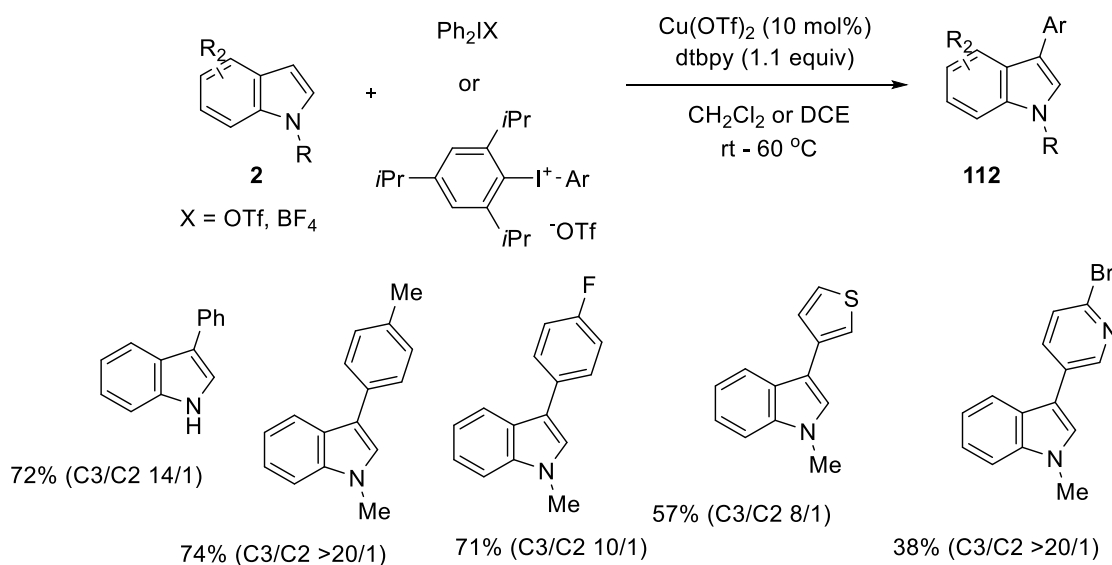
Scheme 43. Cu(II)-Catalyzed direct arylation of indoles.

         In 2014 Kita *et al*. reported oxidative C-N coupling of azoles **10** with pyrroles **4** and indoles **2** using the combination of a hypervalent iodine(III) reagent [phenyliodine diacetate, PIDA] with bromotrimethylsilane

(TMSBr) as an activator of *in situ*-generated stable pyrrole iodonium intermediates (Scheme 44).[94] Method provides the target compounds **113** in good yields, with N^1-selectivity under mild reaction conditions.
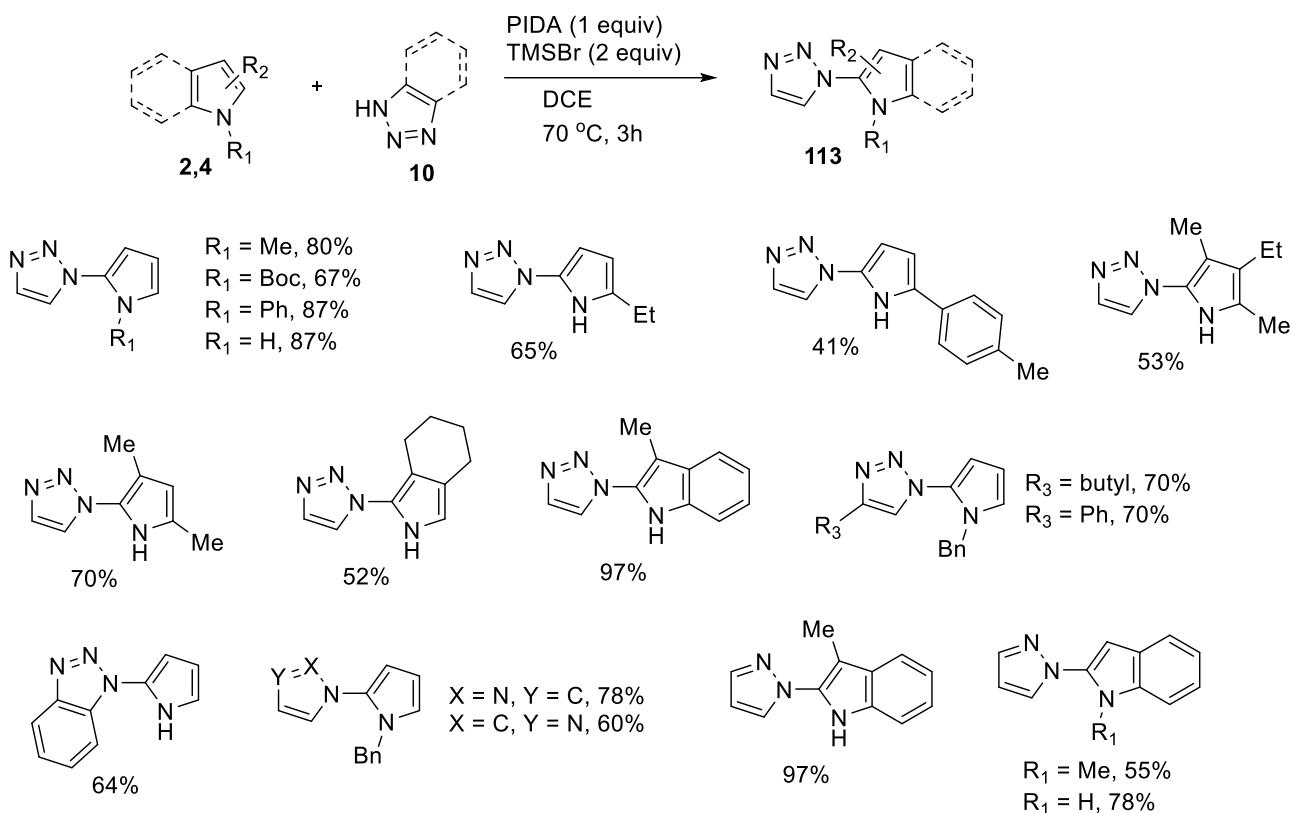
Scheme 44. N^1-Selective oxidative C-N coupling of azoles with pyrroles and indoles using a hypervalent iodine reagent.

3.2. Arylbromides

Itami`s group discovered that organic halogenides can participate in oxidative CDC processes. The novel class of "functional" oxidants makes it possible to conduct the cross-couplings between pyridines and benzoxazoles in the presence of Pd catalyst.[95] A regioselectivity of the reaction turned out to depend on organic halogen compounds. The reaction of pyridines **21** with benzoxazoles **49** in the presence of mesityl bromide (MesBr) or 2-bromo-1,3,5-triisopropylbenzene (TIPBr) mostly afforded the C3-functionalized products **114** (Scheme 45), whereas oxidant benzylbromide gave the C2-substituted pyridines **115** (Scheme 46). However, the detailed mechanism of regiodivergent CDC reactions has not yet been investigated. Nevertheless, authors performed several control experiments to confirm whether the labile benzyl bromide remained intact under the basic reaction conditions and worked as the oxidant. Benzyl bromide could react *in situ* with pyridine or ces

ium pivalate to form the pyridinium salt or benzyl pivalate, respectively, which play the roles of a substrate or an oxidant. In order to test this possibility, the CDC reaction was conducted in the presence of benzylpyridinium bromide or benzyl pivalate. No coupling product was observed when pyridinium bromide was used. Although benzyl pivalate worked as an oxidant, the yield was not as good as in the reaction with benzyl bromide. The reaction did not proceed in the absence of an oxidant.
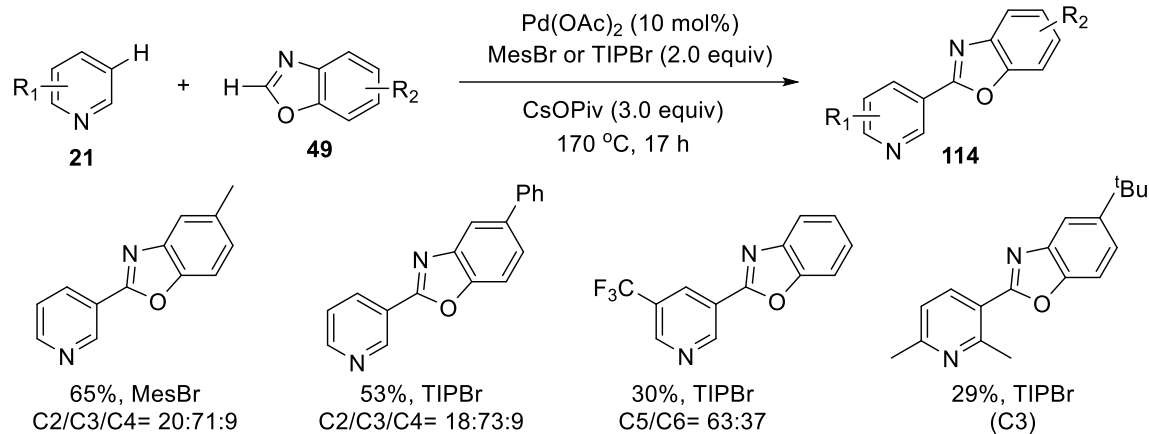
Scheme 45. C3-selective cross-dehydrogenative coupling of pyridines with benzoxazoles.
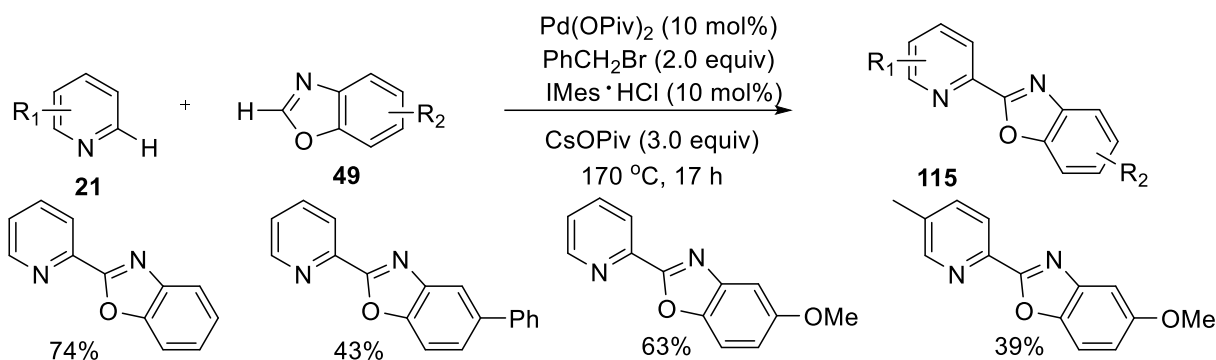
Scheme 46. C2-selective cross-dehydrogenative coupling of pyridines with benzoxazoles.

3.3. Peroxides

Cu-catalyzed coupling between benzothiazoles and thiazoles in the presence of Ag_2CO_3 oxidant is demonstrated in Scheme 15. Zhang`s group failed in attempts to employ the same conditions in couplings of benzothiazoles **15** with pentafluorobenzene **116**. The efficiency of the method was greatly improved after exploring of the reaction parameters. CuCl was employed as a catalyst, 4,4`-dimethoxy-2,2`-bipyridine and di-tert-butylperoxide (DTBP) were used as a ligand and an oxidant respectively (Scheme 47).[44] The reaction resulted in 2-polyfluoroarylthiazoles **117**.

        Oxidative cross-coupling of isochroman **118** with indole`s derivatives **2** with addition of DTBP as an oxidant is shown on the Scheme 48.[96] Manifold α-functionalized cyclic ethers **119** were obtained in 39-79% yields.
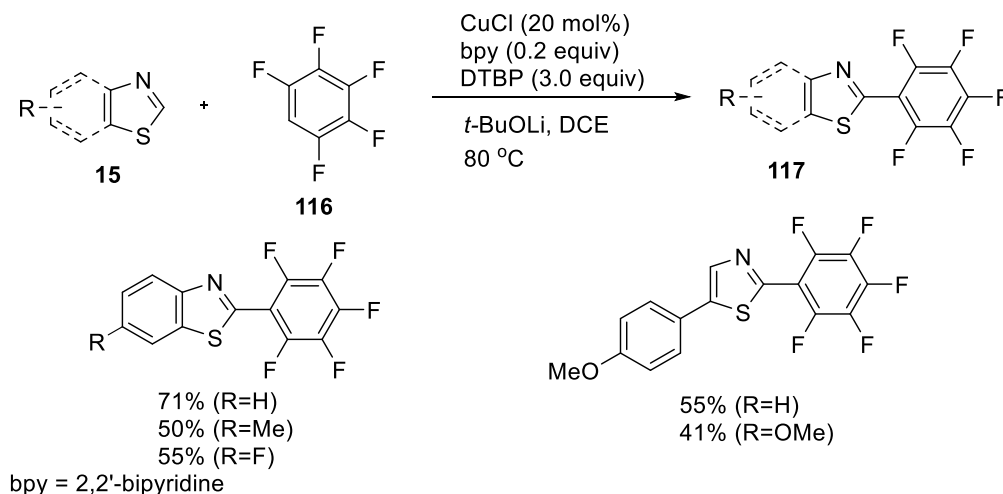
Scheme 47. Cu-Catalyzed dehydrogenative cross-coupling of benzothiazoles with pentafluorobenzene.
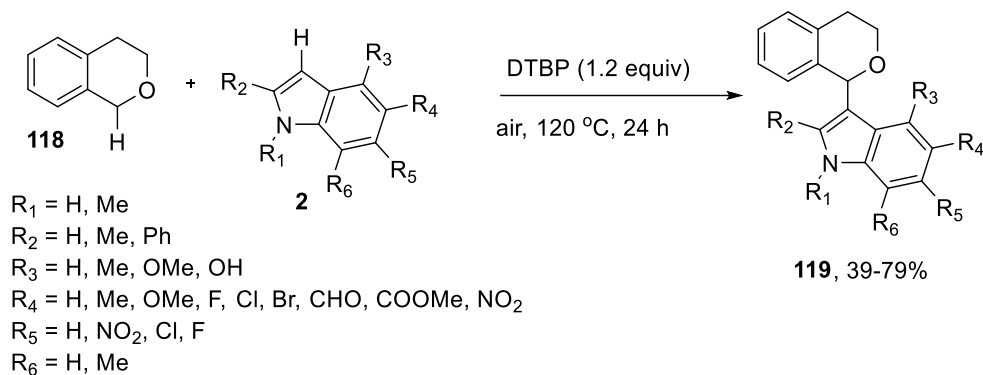
Scheme 48. Di-*tert*-butyl peroxide (DTBP)-mediated oxidative cross-coupling of isochroman and indole derivatives.

3.4. 2,2,6,6-Tetramethylpyperidine-1-oxyl (TEMPO)

A contemporary approach for 2-(pyridine-4-yl)-1*H*-indole **120** from available reagents was proposed by Liu and co-workers.[97] They reported that C4 selective coupling of pyridines **21** with indoles **2** occurred in one stage in the presence of (di-*tert*-butyl dicarbonate) (Boc)$_2$O (Scheme 49). The comparative tests in examined couplings revealed TEMPO as the most effective oxidizing agent in comparison with tert-butyl hydroperoxide (TBHP), H$_2$O$_2$ and DDQ.
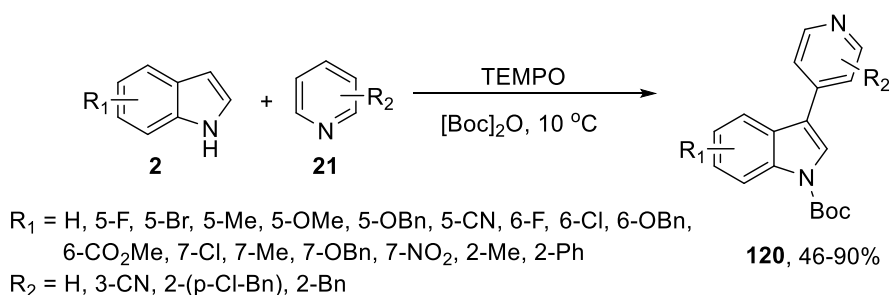
Scheme 49. Metal-free (Boc)$_2$O-mediated C4-selective direct indolation of pyridines using TEMPO.

3.5. Quinones

Quinones, especially those containing ring acceptor substituents, are widely used strong oxidizing agents in organic synthesis. Tetrachloro-1,4-benzoquinone[98,99] and DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone)[100-105] are employed in the development of new reaction methods, including the study of dehydrogenation C-H/C-H cross-couplings.

Garcia *et al*. developed a method of C(6)-H functionalization of *N*-methyl-5,6-dihydrobenzo[*c*]phenanthridine **121** via Cu-catalyzed cross-coupling with indoles **2** and pyrrole **4** using DDQ as an oxidant (Scheme 50).[106] Iminium cation, forming as a result of one-electron transfer **121** with DDQ, reacts with indoles **2** and pyrrole **4** to form compounds **122**.
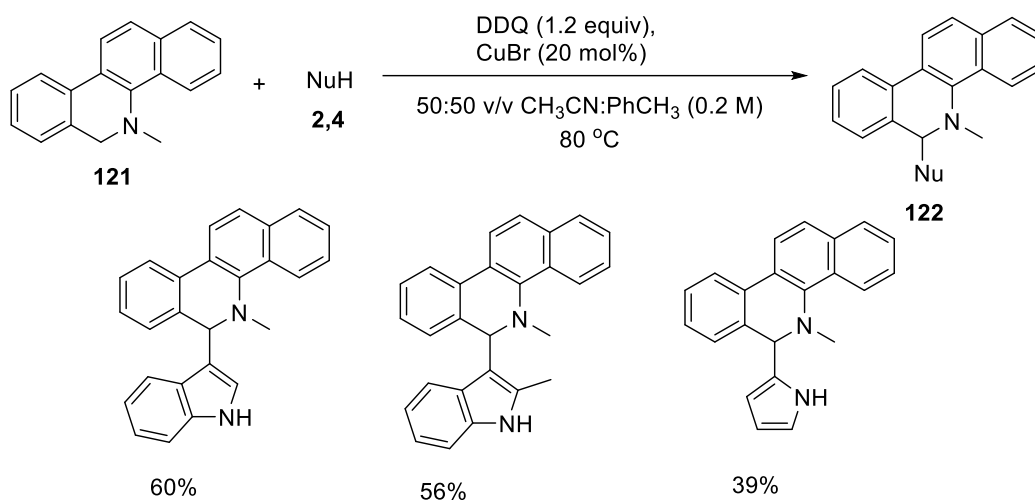
Scheme 50. DDQ-mediated cross-dehydrogenative coupling reactions between *N*-methyl-5,6-dihydrobenzo[*c*]phenanthridine and nucleophiles.

4. Electrochemical Oxidation

Not so long ago, the electrochemistry of organic compounds has experienced a renewed interest as an extremely popular methodology for the synthesis and functionalization of complex molecules[107,108]. Over the past few years, more than a dozen review articles have been published on cation pool methods[109], arylation[110], the application of microreactors and flow-through electrochemical cells[111,112], the use of new electrode materials and electron transfer mediators[113,114], the formation of C-N bond[115], the synthesis of heterocyclic structures[116,117] and other various aspects of organic electrosynthesis[118,119]. The selection of a suitable oxidizing agent is known to be a crucial key for successful implementation of C-H functionalizations (S_N^H transformations). Organic electrochemistry is a practical tool enabling realization in one stage a one-pot, atom-economic method of oxidative coupling, which corresponds to the principle of PASE (Pot-Atom-Step-Economic)[120,121]. Despite the relatively recent application of electrochemistry in C-H functionalizations, the potential of this technique can hardly be overestimated. It offers insights into the reaction Ag, and most importantly, ensures a sustainable choice of a chemical oxidant. No wonder, the methods of direct preparative electrochemical C-H functionalization of heterocycles have been intensively developed.

The C-H amination was successfully realized using the strategy of electrochemical cross-coupling. Ackermann and co-workers described a novel protocol to couple morpholine **123** and thiophene **24**,

benzothiophene **25** and benzofuran **49** with the aim of Co-catalyzed C-H activation to generate compounds **124** (Scheme 51).[122] The reactions proceed under mild conditions at 40 °C in γ-valerolactone (GVL). γ-Valerolactone refers to the "green" solvents obtained from renewable organic raw materials.
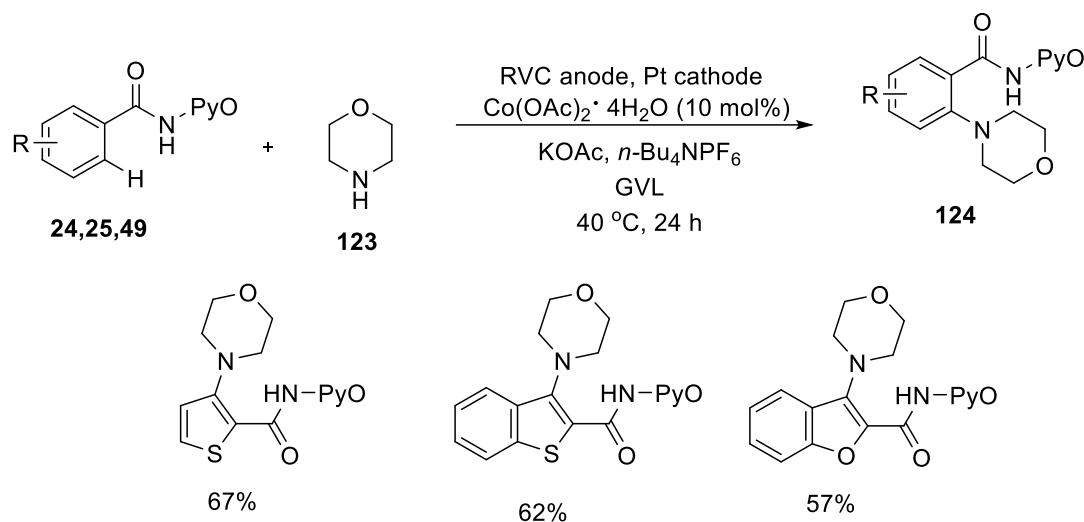
Scheme 51. Electrochemical C-H amination by cobalt catalysis in a renewable solvent.

In 2018 Lei`s group employed Co-catalyzed electrochemical C-H amination of thiophene carboxamides **24**, furan **22** and benzothiophene **25** with the formation of products **125** in 32-74% yields (Scheme 52).[123]
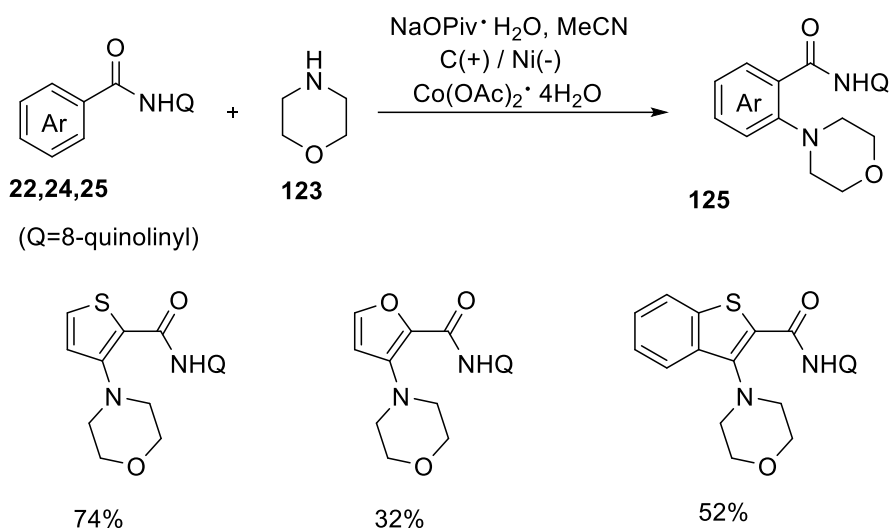
Scheme 52. Cobalt(II)-catalyzed electrooxidative C-H amination of arenes with alkylamines.

Later they extended their protocol to conduct an electrochemical thioarylation of electron-rich arenes (indoles, pyrroles and thiophenes) with thiophenols **126** (Scheme 53) despite a possible oxidation of thiols/thiophenols in electrocatalytic dehydrogenative C-H/S-H cross-coupling.[124] Thiophenol is prone to be oxidized under reaction conditions to corresponding disulfide. Aryl radical cation is supposed to interact with disulfide or intermediate sulfur-centered radical resulting in thioarylation products **127** in 35-96% yields.
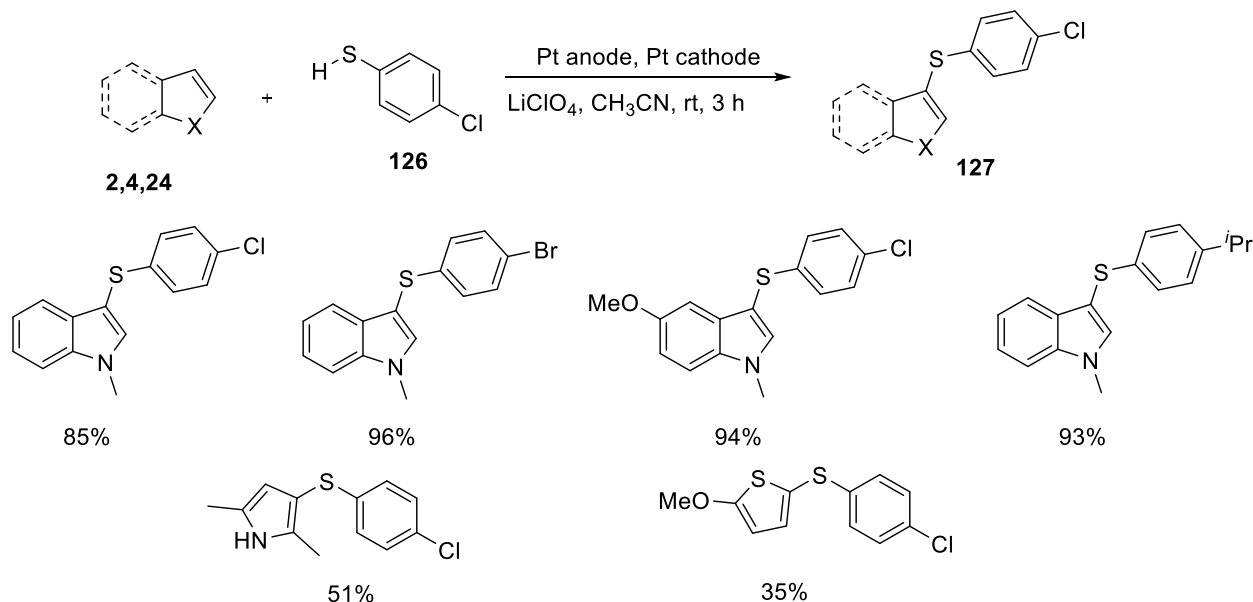
Scheme 53. Electrocatalytic oxidant-free dehydrogenative C-H/S-H cross-coupling.

To select the optimal conditions for aromatization of intermediates of S_N^H reactions Chupakhin *et al*. demonstrated a method of electrochemical oxidation of dihydroacridines **128**, obtained as a result of direct C-H functionalization of N-methylacridinium cations with C-nucleophiles.[125] The 9-(hetero)aryl-*N*-methylacridinium salts **129** were obtained from the corresponding compounds **128** bearing electron-donating and electron-withdrawing aryl and heteroaryl substitutes (Scheme 54).[126]
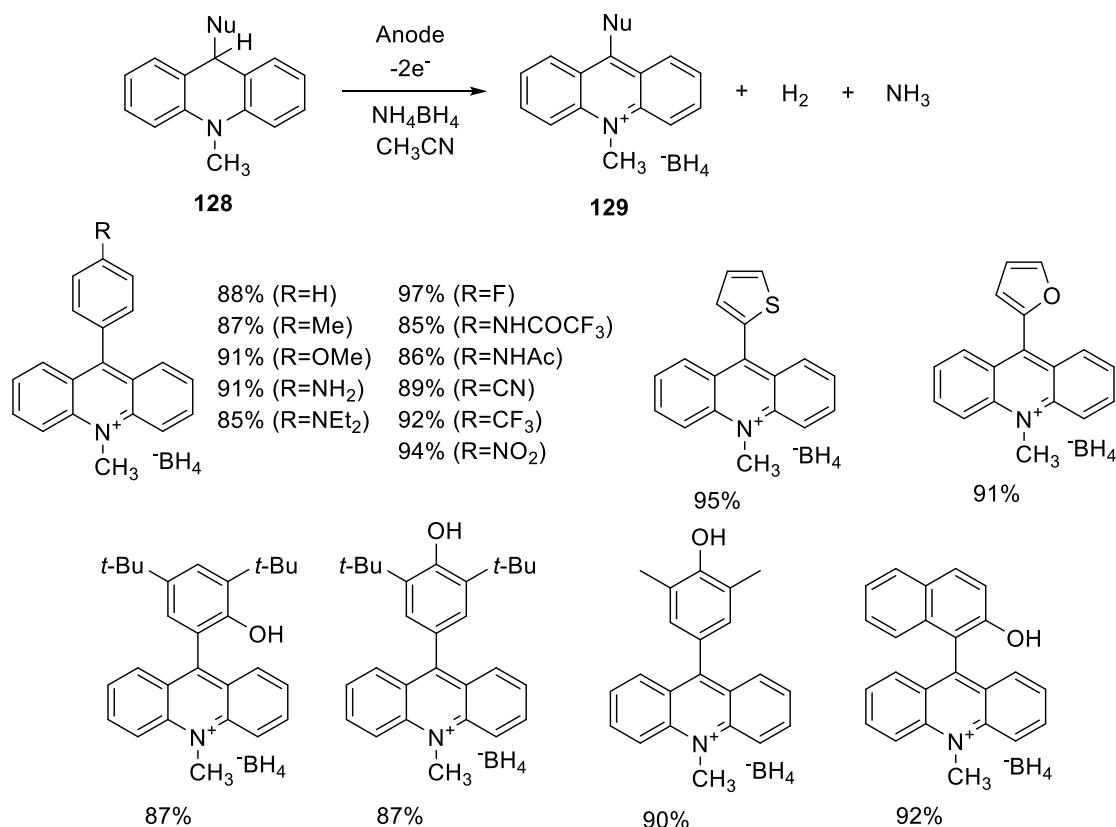
Scheme 54. Anodic dehydroaromatization of 9-(hetero)aryl-9,10-dihydroacridines.

The reaction proceeds selectively without a formation of any side-products providing high yields (85-95%) of the desired products.

The method is applicable to direct oxidative C-H/C-H coupling of azaaromatic compounds (diazines **91**, 5-phenyloxadiazolpyrazines **130**, 6-phenyltriazinone **131**) with aromatic and heteroaromatic nucleophiles (indole **2**, anyzole **110** and phenol **132**) (Scheme 55).[127] The yields of the products **133** were in the range from 82% to 90%.
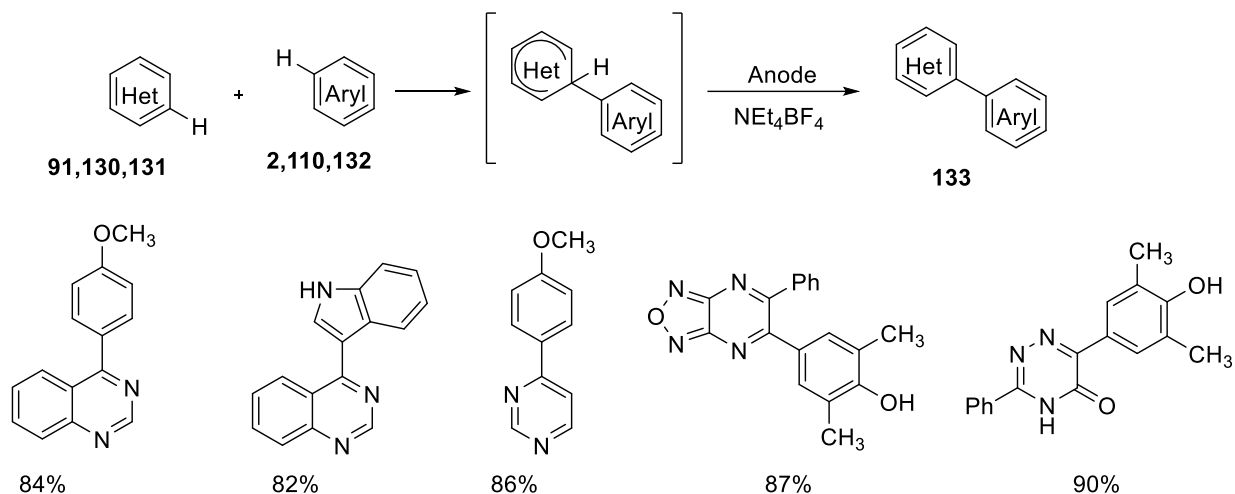
Scheme 55. Nucleophilic arylation of azaaromatics via electrochemical oxidative cross C–C coupling reactions.

Waldvogel`s group demonstrated an effective protocol of dehydrogenative C-C cross-coupling between thiophenes **24** and phenols **132** in combination with boron doped diamond electrodes (BDD) and hexafluoroisopropanol (HFIP) (Scheme 56).[128] The approach affords biheteroaryls **134** in high selectivity.
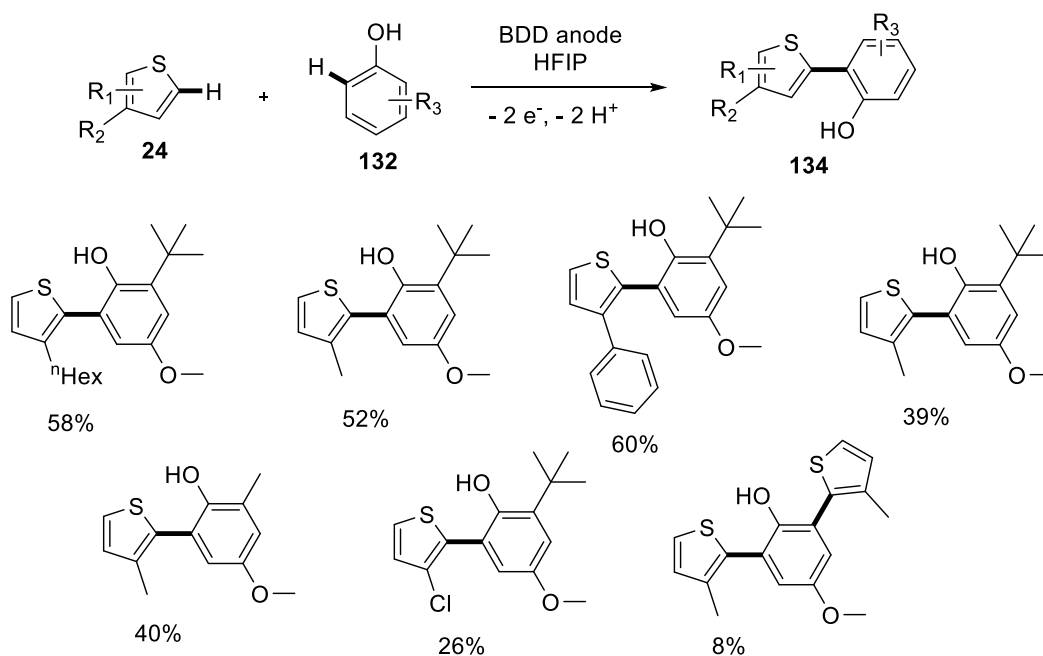
Scheme 56. Metal- and reagent-free anodic OCD coupling of phenols with thiophenes.

Later the same group of scientists reported an electrochemical cross-coupling of benzofurans **23** with phenols **132** (Scheme 57).[129] The reaction afforded a scope of compounds **135** in yields up to 61%. Interestingly, 3-(2-hydroxyphenyl)benzofurans were generated regardless the C2- or C3-position of substituent. Non-catalyzed C-H azolation of phenols and anylated by-products was implemented via electrochemical cross-coupling.[130]

61% (R_1=Me, R_2=Me, R_3=Me, R_4=H, R_5=H, R_6=tBu)
53% (R_1=F, R_2=H, R_3=Me, R_4=H, R_5=H, R_6=tBu)
53% (R_1=H, R_2=H, R_3=Me, R_4=Me, R_5=Me, R_6=Me)
39% (R_1=H, R_2=H, R_3=Ph, R_4=H, R_5=H, R_6=tBu)
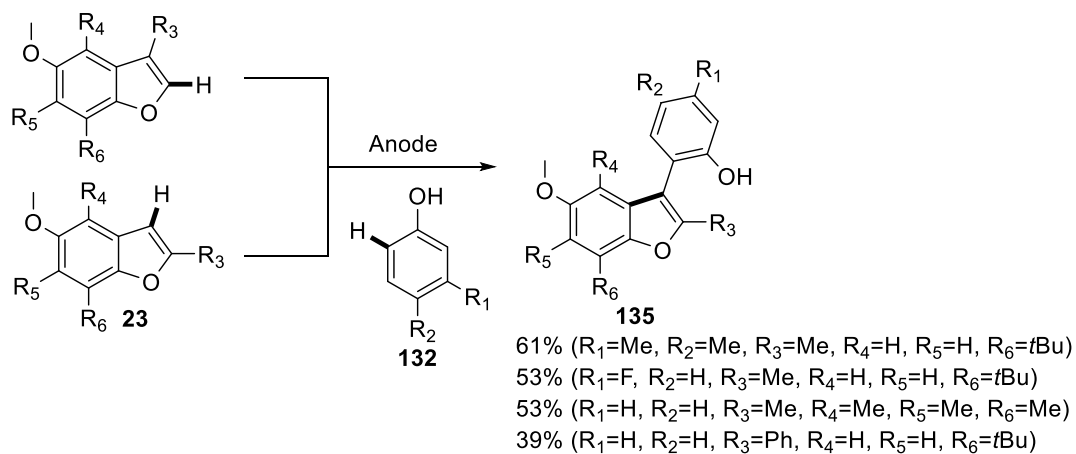
Scheme 57. Anodic C-C cross-coupling of phenols with benzofurans leading to a furan metathesis.

According to the mechanism proposed by the authors (Figure 6), the coupling between the C2 carbon of phenol and the C3 of benzofuran leads to a formation of neutral radical (**II**), which is easily oxidized to cationic particles (**III**). Intramolecular nucleophilic attack of the hydroxyl group at the C2 position of benzofuran gives protonated dihydrobenzofuro[2,3-*b*]benzofuran (**IV**). Next, the most stable cation (**V**) is generated and then it undergoes the ring opening and proton elimination, leading to product **135**.
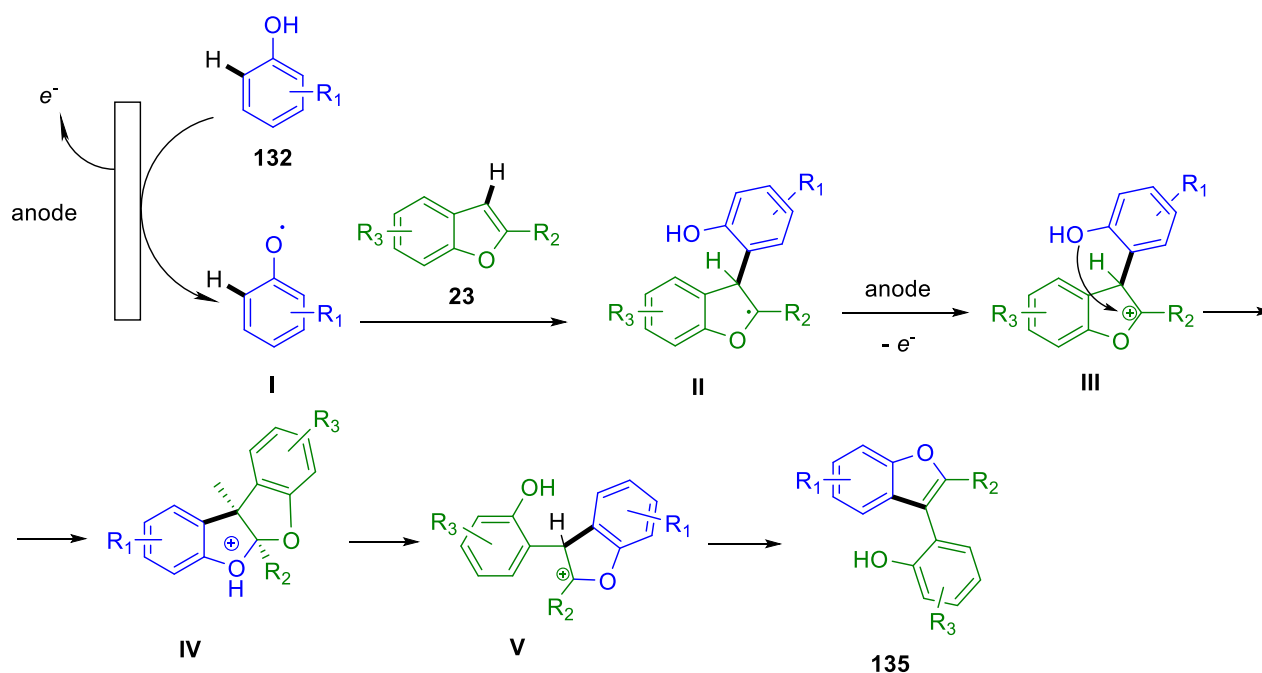
Figure 6. Postulated mechanistic concourse for 2-substituted benzofurans as starting materials.

In the case of another initial isomer, an intermediate cation (**III'**) is also formed and undergoes an intramolecular attack at the C3 position of benzofuran (Figure 7). The generation of dihydrobenzofuro[3,2-*b*]benzofuran system (**IV'**) occurs through a different scheme of substitution in benzofuran. Further ring opening results in the benzofuran derivative (**V'**) followed by intramolecular rearrangement and rearomatization to give product **VII**.
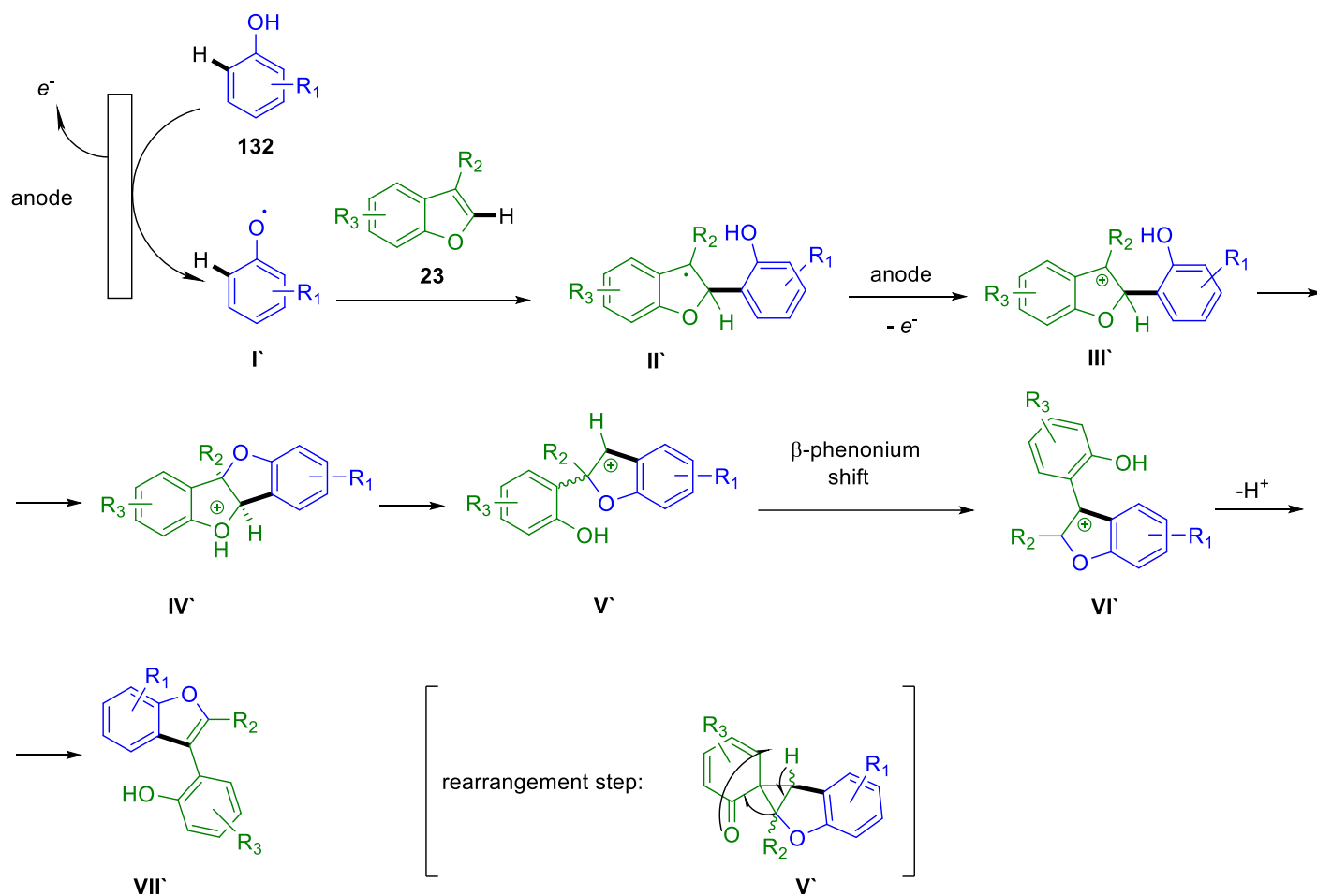
Figure 7. Postulated mechanistic concourse for 3-substituted benzofurans as starting materials.

5. Photocatalytic Oxidation

In the recent decade, a special attention is paid to the photocatalytic processes in heterogeneous systems based on TiO_2. Photooxidation catalysts based on nanosized TiO_2 demonstrate indisputable advantages, such as high oxidizing ability, photo- and chemical stability, reusability, and low toxicity.

Palmisano with colleagues described the reactions of heterocyclic bases with ethers in the presence of TiO_2 and induced by sunlight.[131,132] The reactions of trioxane **136** with quinolines **137a-c**, quinoxaline **138**, isoquinoline **139** and pyridine **21** are shown on Scheme 58. The same transformations have been carried out in the absence of TiO_2 giving no resulting products **140a-g** or giving lower yields.
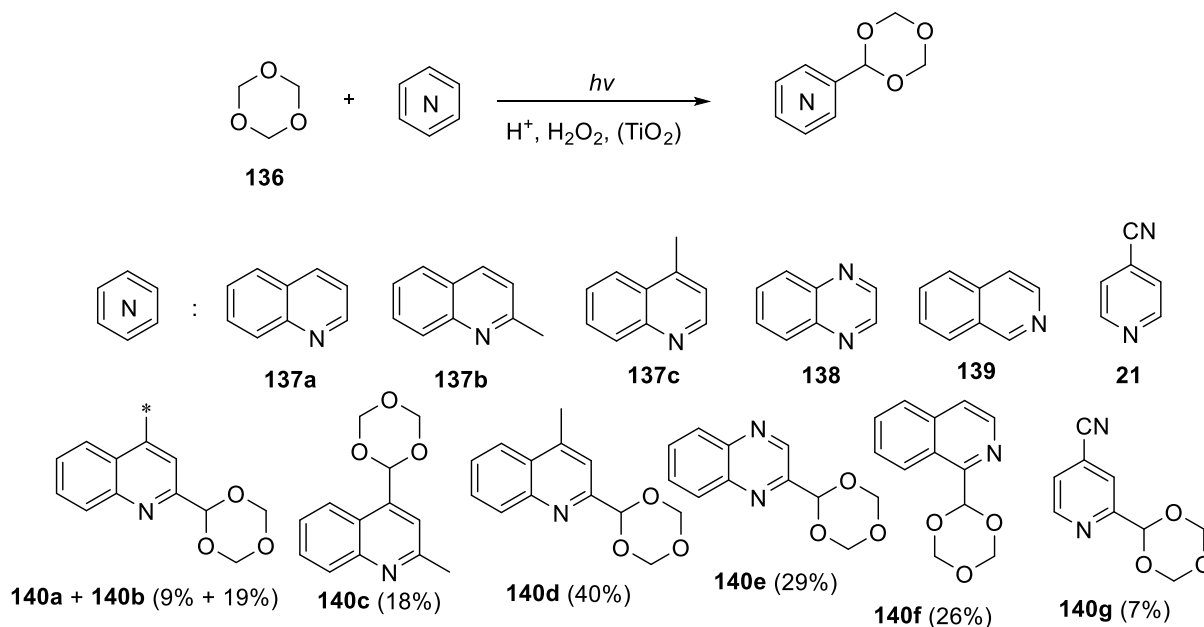
Scheme 58. Sunlight-induced reactions of heterocyclic bases with trioxane in the presence of TiO_2.

It was found that activation of oxidative processes with the participation of TiO_2 is associated with the formation of an electron-hole pair on its surface under irradiation (e^-/h^+). The interaction of an electron with oxygen molecule leads to the formation of a superoxide radical $O_2^{\cdot-}$ as an oxidizing agent.[133-136] Heterophase photocatalytic system air O_2/nanosized TiO_2 (Hombifine, 100% anatase)/visible light was employed to carry out the reactions of oxidative C-H functionalization of azines (mono-, di-, triazines benzoannelated and non-annelated, including azines bearing substituents in the ring) **141** with (hetero)aromatic nucleophiles **142** (Scheme 59).[137]
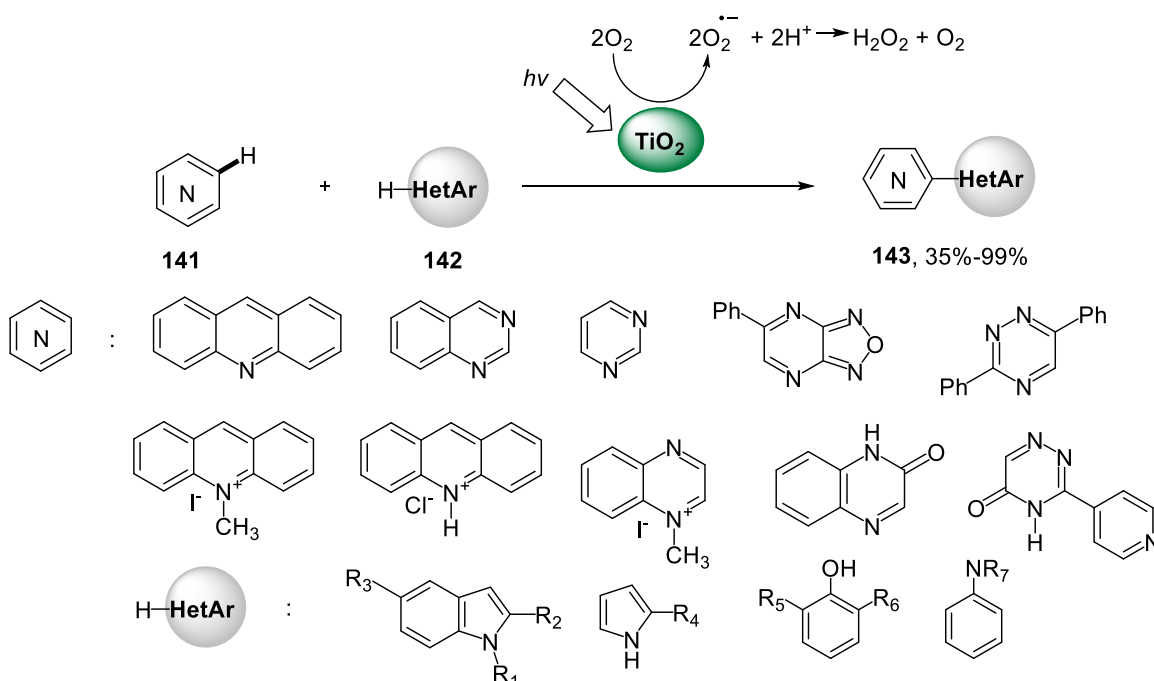
Scheme 59. Aerobic oxidative C–H functionalization of azines with heterocyclic nucleophiles in the presence of TiO_2 nanoparticles as a photocatalyst.

This approach resulted in regioselective formation of biheteroaryls **143** under mild conditions in 35-99% yields. It should be noted that the presented reactions could also be carried out under irradiation with light in the visible range, using the composite material CdS/TiO$_2$ as a photocatalyst.[138] These methods possess the features of "green" nature-like process: oxidant - air oxygen, high yields, side product - water, easily separable heterophase catalyst, the absence of reagent homocouplings.

In 2013, Wu's group reported a highly efficient and selective visible-light-induced CDC reaction of *N*-phenyl-1,2,3,4-tetrahydroisoquinoline **75** with indole **2** by using a catalytic amount (0.25 mol%) of a platinum(II) terpyridyl complex (Scheme 60).[139] Addition of FeSO$_4$ (2.0 equiv) improved the reaction selectivity remarkably and desired cross-coupling products **144** were obtained in 78-95% yields. Another methodology was developed by the Han's group.[140] Cu$_2$O nanoparticles (NPs) on a nitrogen-doped porous carbon yolk–shell cuboctahedral (CNPC) framework have been employed as an efficient photocatalyst for the direct cross-dehydrogenative coupling reaction between N-aryltetrahydroisoquinolines and indoles.

R$_1$ = H, Me, OMe, F, Br, CN   R$_2$ = H, Me; R$_3$ = H, Me; R$_4$ = H, Me, OMe, Cl, COOMe, NO$_2$ **144**, 78-95%

Oxidation potential E_{ox} (0.82 V), reduction potential E_{red} (-1.18 V)
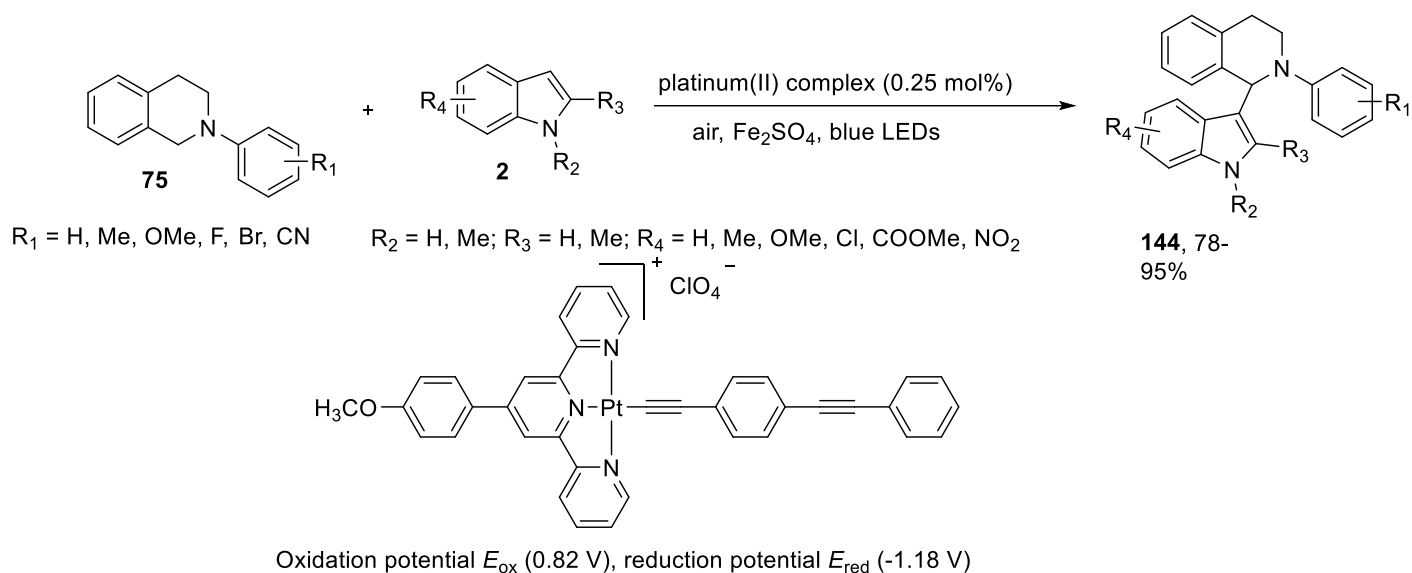
Scheme 60. Visible-light catalysis of indolation with tetrahydroisoquinolines by a platinum(II) complex.

One more example of photocatalyzed CDC reaction between *N*-phenyl-1,2,3,4-tetrahydroisoquinoline **75** and indole **2** in water is shown in Scheme 61. Using mixed-phase chemically exfoliated graphene-supported RuO$_2$ nanocomposite (G-RuO$_2$)[141], Co(dmgH)$_2$Cl$_2$ (dmgH = dimethylglyoxime) complex[142] or 2D-MoS$_2$[143] as catalyst and Eosin Y as photosensitizer, the transformation resulted in good to excellent yields of the corresponding products **145** under visible light irradiation at room temperature.
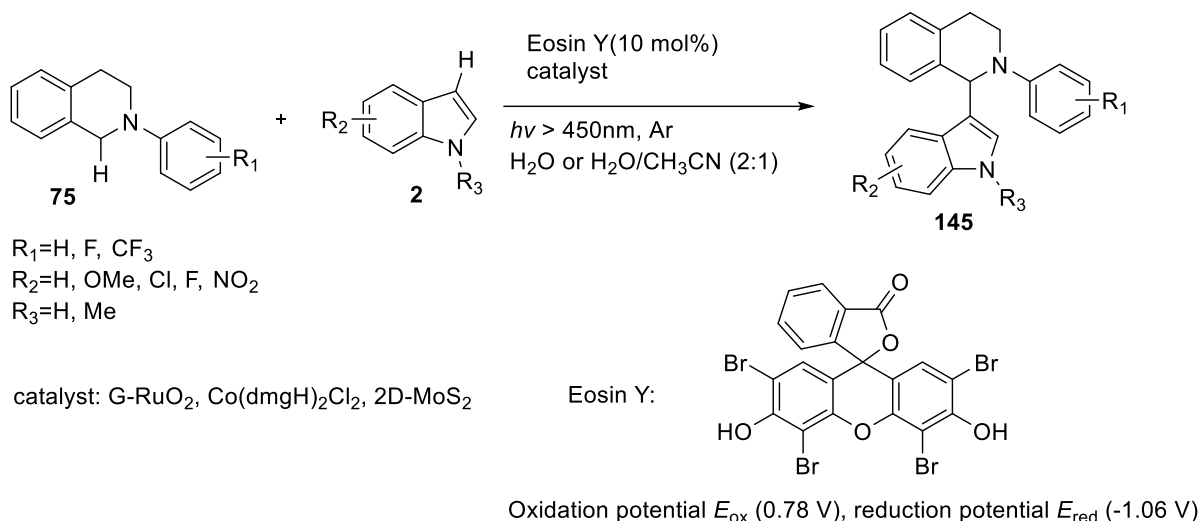
Scheme 61. Cross-dehydrogenative coupling reaction between N-aryl tetrahydroisoquinolines and indoles employing the combination of eosin Y and catalyst (G-RuO$_2$, Co(dmgH)$_2$Cl$_2$ or 2D-MoS$_2$).

In 2015, Wu *et al.* reported a new strategy in the cross-coupling of *N*-phenyl-1,2,3,4-tetrahydroisoquinolines **75** with indoles **2** under the irradiation of blue LEDs (λmax = 450 nm) at room temperature (Scheme 62).[144]
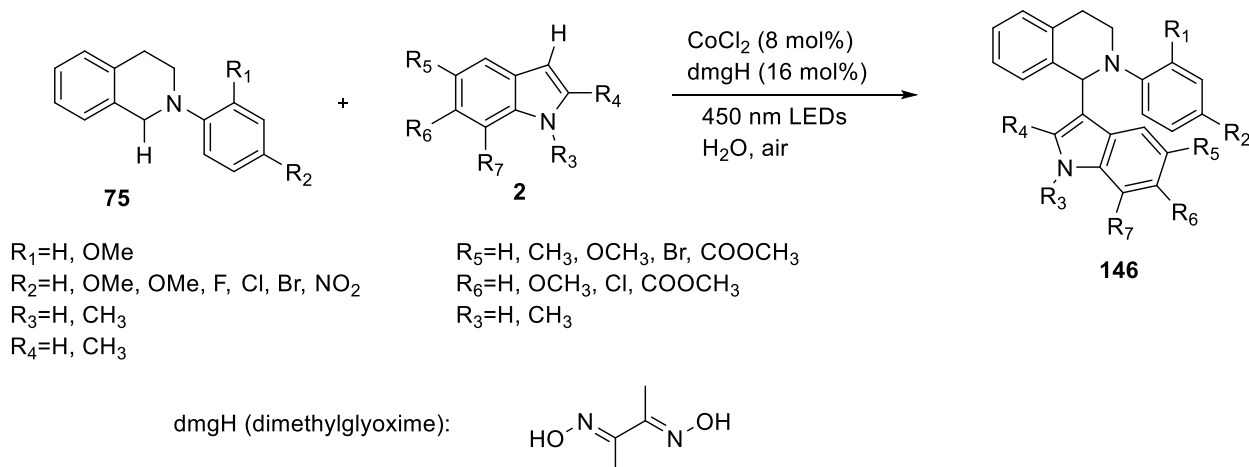
Scheme 62. Cobalt-catalyzed cross-dehydrogenative coupling reaction of *N*-phenyl-1,2,3,4-tetrahydroisoquinolines and indoles in water by visible light.

According to the mechanism proposed by the authors (Figure 8), CoCl$_2$ together with dmgH under air conditions resulted in the formation of CoIII(dmgH)$_2$Cl$_2$. Upon irradiation by the visible light, CoIII(dmgH)$_2$Cl$_2$ reached its excited state and then abstracted one electron from **75** to generate **75$^{+\cdot}$** and a Co(II) intermediate. Subsequently, the Co(II) intermediate reacted with O$_2$ to produce the superoxide radical anion and to regenerate CoIII(dmgH)$_2$Cl$_2$. Superoxide radical anion abstracted one proton from **75$^{+\cdot}$** to create the HOO$^\cdot$ radical, which continued to capture a hydrogen atom to form H$_2$O$_2$. The generated **75$^\cdot$** further lost one electron to afford iminium ion **75$^+$**, followed by nucleophile addition to give rise to the desired product **146**.
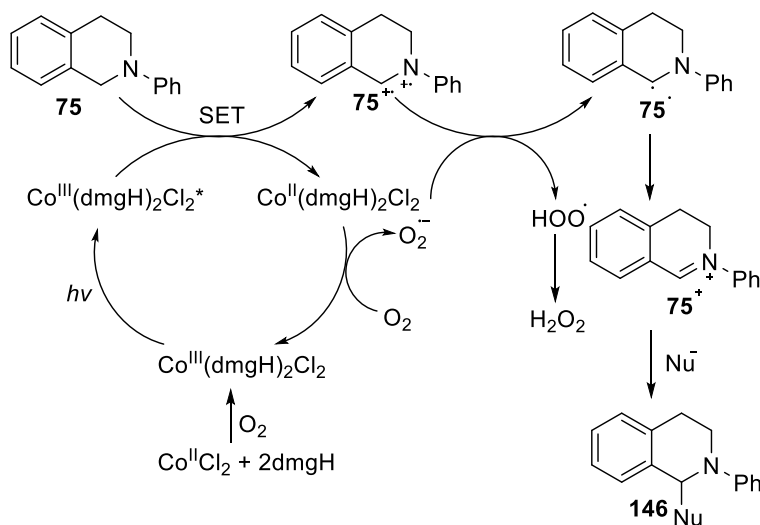
Figure 8. Proposed mechanism of the visible light-mediated cobalt-catalyzed CDC reaction in water.

Visible-light-promoted metal-free cross-dehydrogenative coupling between imidazo[1,2-*a*]pyridine **27** and *N*-phenyltetrahydroisoquinoline **75** using rose bengal as photosensitizer under aerobic conditions was reported by Hajra and co-workers (Scheme 63).[145]
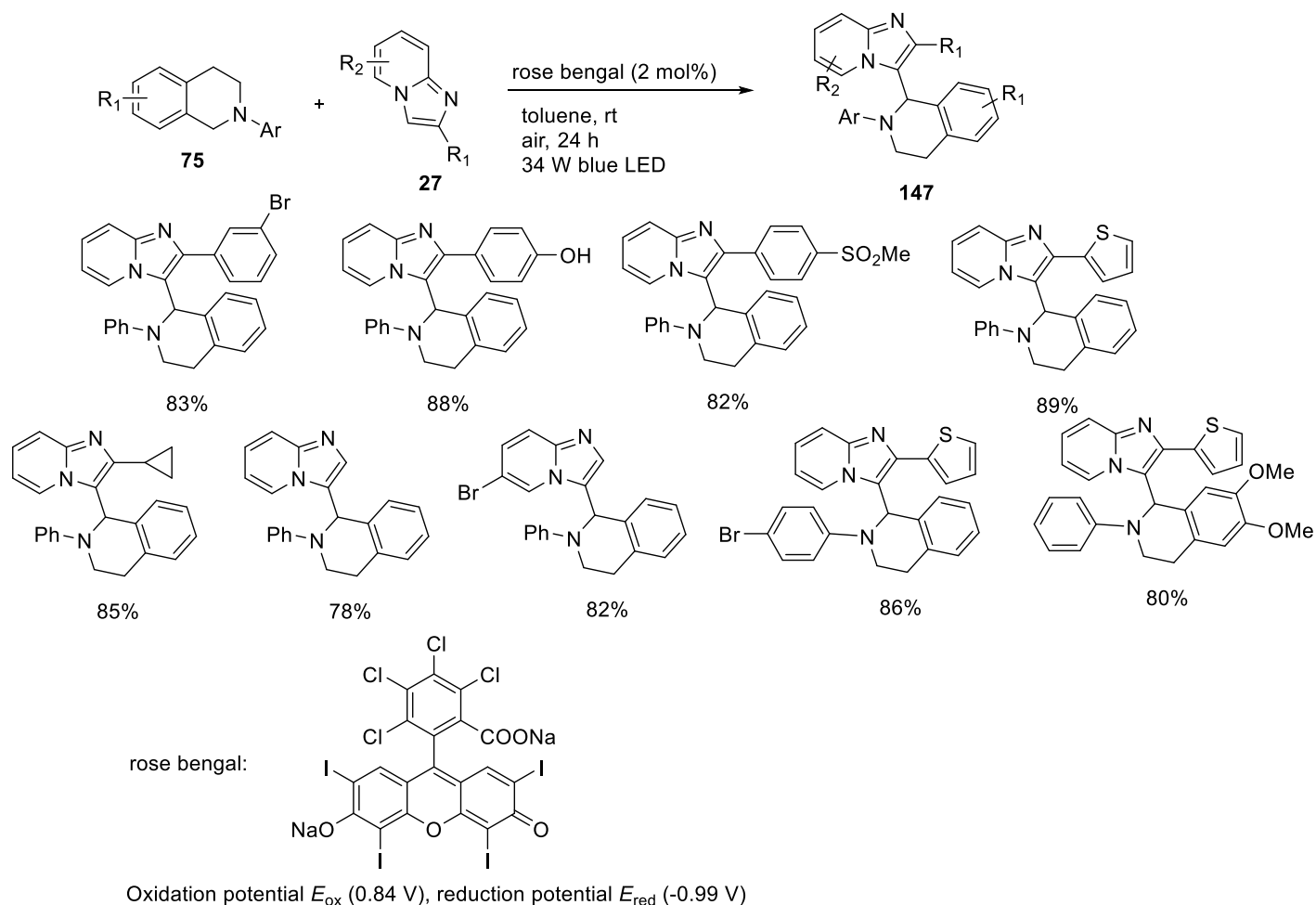
Scheme 63. Visible-light-promoted cross-dehydrogenative coupling of N-phenyltetrahydroisoquinoline with imidazopyridine.

In addition, this method is also applicable to other heterocycles like imidazo[1,2-*a*]pyrimidine **148**, indolizines **30**, indole **2** and pyrrole **4** (Scheme 64).
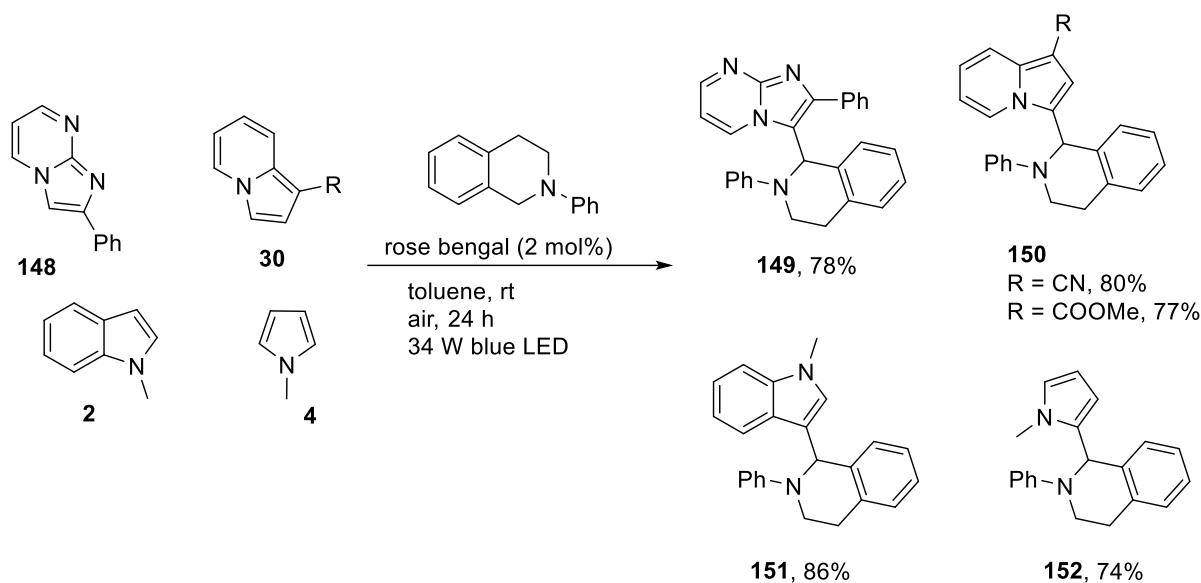
Scheme 64. Cross-dehydrogenative coupling of N-phenyl tetrahydroisoquinoline with N-heterocycles.

He et al. developed CDC reaction of 3,4-dihydro-1,4-benzoxazin-2-ones **153** with indoles **2** through visible-light photoredox catalysis and oxygen from air as an oxidant. (Scheme 65).[146] Various 3-arylated 3,4-dihydro-1,4-benzoxazin-2-one derivatives **154** were prepared with yields of up to 80% employing the photocatalyst Ru(bpy)$_3$Cl$_2$.

R_1 = H, 6-Me
R_1 = Ph, 2-OCH$_3$C$_6$H$_4$, 4-OCH$_3$C$_6$H$_4$, 3-CH$_3$C$_6$H$_4$, 4-ClC$_6$H$_4$, propyl, benzyl
R_1 = H, 1-CH$_3$, 2-CH$_3$, 4-CH$_3$, 5-CH$_3$, 6-CH$_3$, 7-CH$_3$, 5-OCH$_3$, 5-Br, 5-I
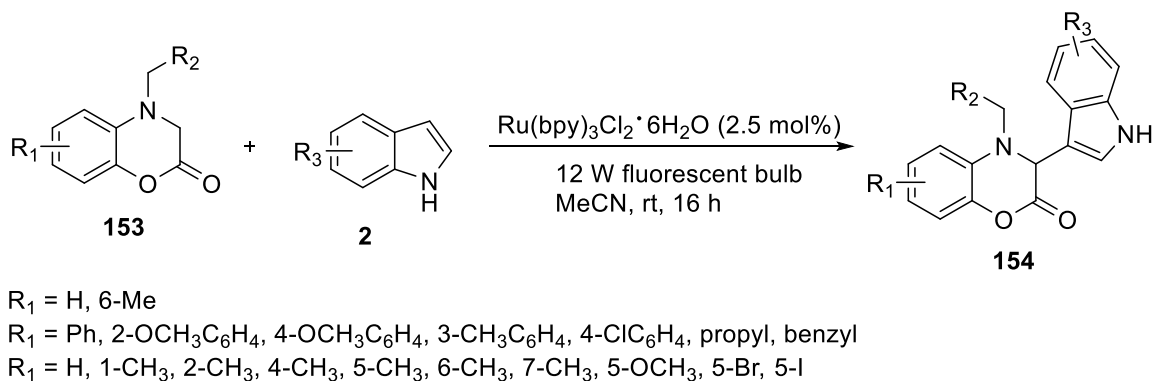
Scheme 65. Oxidative cross-dehydrogenative-coupling reaction of 3,4-dihydro-1,4-benzoxazin-2-ones through visible-light photoredox catalysis.

Itoh and co-workers reported a visible light catalyzed C-N coupling of indoles **2** with phthalimide **155** using 2-tert-butylanthraquinone (2-^{t}Bu-AQN) as a photocatalyst, and aerobic oxygen as the sole oxidant under mild condition (Scheme 66).[147] The desired products **156** were obtained in yields ranging from 29% to 93%.

R$_1$ = H, Ac, Ph, Bn, MOM, CH$_2$CO$_2$Me, Me
R$_2$ = H, Ac, Ph, Bn, MOM, CH$_2$CO$_2$Me, Me, CO$_2$Me, 4-Me-C$_6$H$_4$, 4-*t*-Bu-C$_6$H$_4$, 4-OMe-C$_6$H$_4$, 4-CHO-C$_6$H$_4$, 4-CO$_2$-C$_6$H$_4$, 4-Br-C$_6$H$_4$, 4-CF$_3$-C$_6$H$_4$, 4-CH$_2$OTBS-C$_6$H$_4$, 4-OMe-C$_6$H$_4$, 2-Me-C$_6$H$_4$, 2-thienyl, 4-pyridinyl
R$_3$ = H, Cl, OMe, Me
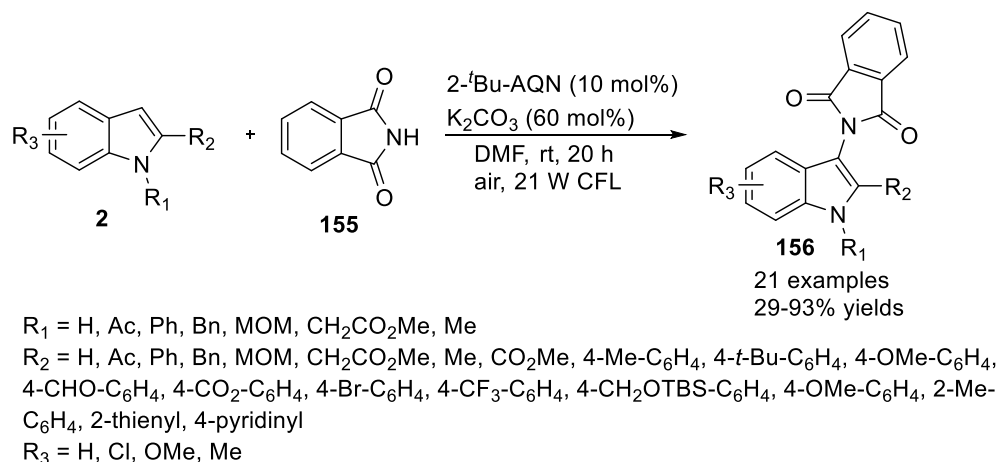
Scheme 66. Cross-dehydrogenative C–H amination of indoles under aerobic photo-oxidative conditions.

Lei with group proposed a dual catalytic system containing acridinium photosensitizer and cobaloxime catalyst and demonstrated a regioselective functionalization of imidazoheterocycles **27** with azoles **47** through oxidative photo-induced C-H/N-H cross-coupling strategy with H$_2$ evolution (Scheme 67).[148]

R$_1$ = H, CO$_2$Me, Me, F
R$_2$ = H, Me, Br, I
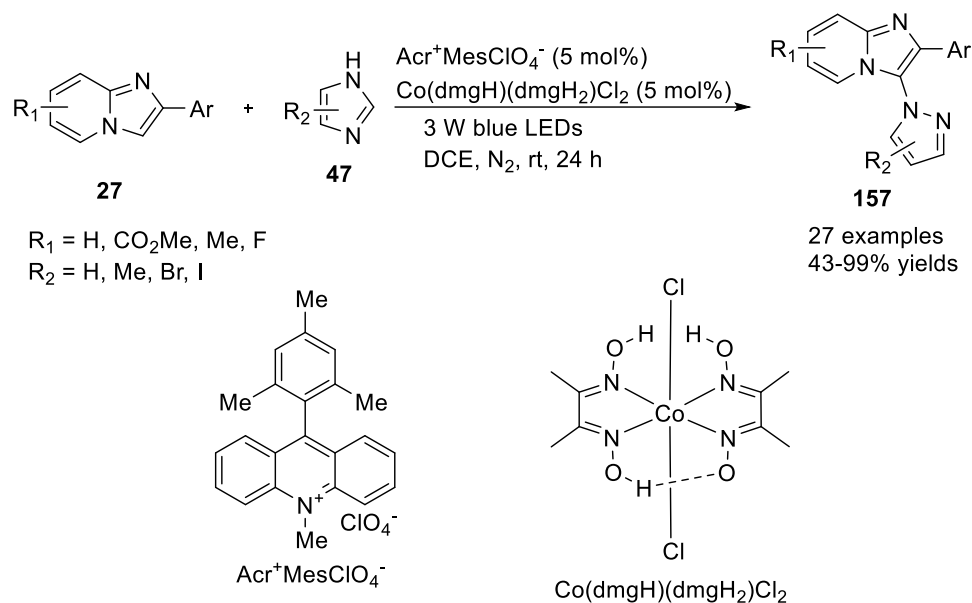
Scheme 67. Site-selective amination of 2-arylimidazoheterocycles on the C3-position using photo-induced external oxidant-free strategy.

Very recently, Varaksin *et al.* reported an original Selectfluor®-mediated method for the C(sp^2)–H azolation of cyclic aldonitrones **158** with NH-azoles **10** by visible light irradiation (Scheme 68).[149] The novel cyclic ketonitrone derivatives **159** bearing azolyl substituents were obtained in good to excellent yields.
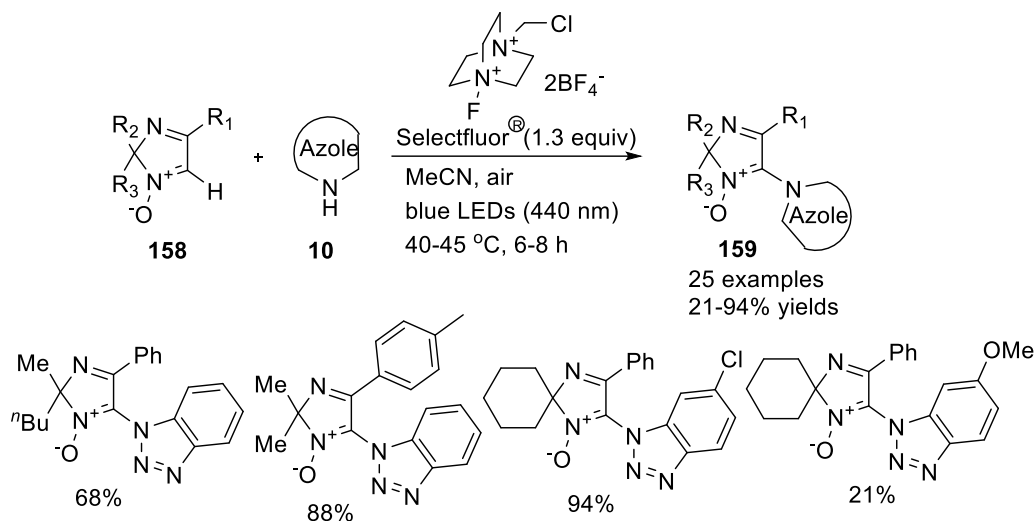
Scheme 68. Blue-light-promoted radical C–H azolation of cyclic nitrones enabled by Selectfluor®

Conclusions

In this review we have summarized recent advances in the application of oxidizing agents for oxidative nucleophilic C-H functionalizations, including metal-metal catalyzed transformations (S_N^H reactions). Analysis of literature data unambiguously shows that metal-free C-H functionalization of heteroarenes is a widespread and increasingly popular tool for the synthesis of organic compounds.[8,150-152] Moreover, this method enhances the atomic efficiency of reactions due to the rejection of functional groups in substrates and auxiliary reagents, and in some cases from metal catalysis. Various oxidants (inorganic and organic, one- and two-electron) could be applied in the reactions of C-H functionalization. But for some time, the main trend in the development of these reactions is associated with the application of oxygen, oxidation photocatalysts or electrochemical oxidation methods. Determination of the quantitative redox potentials of reactants and intermediates makes it possible to obtain the new data concerning the reactions mechanisms followed by deliberate choice of oxidizing reagents. The ability to control electrochemical processes creates the basis for the regio-specific functionalization of the C-H bond in heteroarenes, despite the presence of various substituents in their structure. Luckily, the utilization of photooxidation catalysts lets us to create the close to nature technological processes. In this case, the application of air oxygen as an oxidizer, release of water as a by-product, and reusing of catalysts meet the requirements of environmental acceptability and enabling the compliance with the "green" vector of modern technologies. There really is some basis for thinking that the development of oxidative C-H functionalization methods leads to atom-economic and environmentally favorable processes of modern organic synthesis.

      Finally, a survey of literature unequivocally indicates that C-H functionalization could be effectively applied to synthesize bi(hetero)aryls that constitute the desirable building blocks for pharmaceutical chemistry, macro-, supramolecular and coordination chemistry.

Acknowledgements

References

1. Valdés, H.; García-Eleno, M. A.; Canseco-Gonzalez, D.; Morales-Morales, D. *ChemCatChem* **2018**, *10*, 3136.
   https://doi.org/10.1002/cctc.201702019.
2. Valdés, H.; Rufino-Felipe, E.; Morales-Morales D. *J. Organomet. Chem.* **2019**, *898*, 120864.
   https://doi.org/10.1016/j.jorganchem.2019.07.015.
3. Rufino-Felipe, E.; Osorio-Yáñez, R. N.; Vera, M.; Valdés, H.; González-Sebastián, L.; Reyes-Sanchez, A.; Morales-Morales, D. *Polyhedron* **2021**, *204*, 115220.
   https://doi.org/10.1016/j.poly.2021.115220.
4. Murakami, K.; Yamada, S.; Kaneda, T.; Itami, K. *Chem. Rev.* **2017**, *117*, 9302.
   http://dx.doi.org/10.1021/acs.chemrev.7b00021.
5. *Metal-catalyzed Cross-coupling Reactions*, 2th Edn.; de Meijere, A.; Diederich, F. Eds.; Wiley-VCN, Weinheim, 2004.
   http://dx.doi.org/10.1002/9783527619535.
6. Yang, Y.; Lan, J.; You, J. *Chem. Rev.* **2017**, *117*, 13, 8787.
   https://doi.org/10.1021/acs.chemrev.6b00567.
7. Chupakhin, O. N.; Charushin, V. N.; van der Plas. H. C. *Nucleophilic Aromatic Substitution of Hydrogen*; San Diego, Academic Press, 1994; 368 pp.
8. V. N. Charushin, O. N. Chupakhin (Eds.). *Metal-Free C–H Functionalization of Aromatics: Nucleophilic Displacement of Hydrogen*. In: *Topics Heterocyclic Chemistry*; Vol. 37. Series Editors: B.U.W. Maes, J. Cossy, S. Polanc. Springer: Heidelberg, New York, Dordrecht, London, 2014; 283 pp.
   https://doi.org/10.1007/7081_2013_119.
9. Samanta, R.; Matcha, K.; Antonchick, A. P. *Eur. J. Org. Chem.* **2013**, 5769.
   https://doi.org/10.1002/ejoc.201300286.
10. Lv, F.; Yao, Z.-J. *Sci. China Chem.* **2017**, *60*, 701.
    https://doi.org/10.1007/s11426-016-0435-5.
11. Zhang, H.; Lei, A. *Asian J. Org. Chem.* **2018**, *7*, 1164.
    https://doi.org/10.1002/ajoc.201800214.
12. Zhang, H.; Lei, A. *Synthesis* **2019**, *51*, 83.
    https://doi.org/10.1055/s-0037-1610380.
13. Morimoto, K. *Chem. Pharm. Bull.* **2019**, *67*, 1259.
    https://doi.org/10.1248/cpb.c19-00286.
14. Wang, H.; Gao, X.; Lv, Z.; Abdelilah, T.; Lei, A. *Chem. Rev.* **2019**, *119*, 6769.
    https://doi.org/10.1021/acs.chemrev.9b00045.
15. Budhwan, R.; Yadav, S.; Murarka, S. *Org. Biomol. Chem.* **2019**, *17*, 6326.
    https://doi.org/10.1039/C9OB00694J.
16. Grzybowski, M.; Sadowski, B.; Butenschön, H.; Gryko, D. T. *Angew. Chem. Int. Ed.* **2020**, *59*, 2998.
    https://doi.org/10.1002/anie.201904934.

17. Phillips, A. M. F.; Guedes da Silva, M. F. C.; Pombeiro, A. J. L. *Catalysts* **2020**, *10*, 529.
https://doi.org/10.3390/catal10050529.

18. Fricke, Ch.; Reid, W. B.; Schoenebeck, F. *Eur. J. Org. Chem.* **2020**, 7119.
https://doi.org/10.1002/ejoc.202000856.

19. Chan, Ch.-M.; Chow, Y.-Ch.; Yu, W.-Y. *Synthesis* **2020**, *52*, 2899.
https://doi.org/10.1055/s-0040-1707136.

20. Krishnan, R.; Binkley, J. S.; Seeger R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.
https://doi.org/10.1063/1.438955

21. McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639.
https://doi.org/10.1063/1.438980

22. Clark, T.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Comp. Chem.* **1983**, *4,* 294.
https://doi.org/10.1002/jcc.540040303

23. Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265.
https://doi.org/10.1063/1.447079

24. Gong, X.; Song, G.; Zhang, H.; Li, X. *Org. Lett.* **2011**, *13*, 1766.
https://doi.org/10.1021/ol200306y.

25. Yamaguchi, A. D.; Mandal, D.; Yamaguchi, J.; Itami, K. *Chem. Lett.* **2011**, *40*, 555.
https://doi.org/10.1246/cl.2011.555.

26. Wang, Z.; Song, F.; Zhao, Y.; Huang, Y.; Yang, L.; Zhao, D.; Lan, . J.; You, J. *Chem. Eur. J.* **2012**, 18, 16616.
https://doi.org/10.1002/chem.201203004.

27. Liu, W.; Li, Y.; Wang, Y.; Kuang, C. *Org. Lett.* **2013**, *15*, 4682.
https://doi.org/10.1021/ol4019776.

28. Masui, K.; Ikegami, H.; Mori, A. *J. Am. Chem. Soc.* **2004**, *126*, 5074.
https://doi.org/10.1021/ja031855p

29. Liu, W.; Li, Y.; Wang, Y.; Kuang, C. *Chem. Commun*. **2014**, *50,* 9291.
https://doi.org/10.1039/C4CC04129A.

30. Fu, X.-P.; Xuan, Q.-Q.; Liu, L.; Wang, D.; Chen, Y.-J.; Li, C.-J. *Tetrahedron* **2013**, *69*, 4436.
https://doi.org/10.1016/j.tet.2012.10.048.

31. Willis, N. J.; Smith, J. M. *RSC Adv.* **2014**, *4*, 11059.
https://doi.org/10.1039/C3RA44411B.

32. Kianmehr, E.; Rezaeefard, M.; Khalkhali, M. R.; Khan, K. M. *RSC Adv.* **2014**, *4*, 13764.
https://doi.org/10.1039/C4RA01034E.

33. Liu, B.; Huang, Y.; Lan, J.; Song, F.; You, J. *Chem. Sci.* **2013**, *4*, 2163.
https://doi.org/10.1039/C3SC50348H.

34. Shang, Y.; Jie, X.; Zhao, H.; Hu, P.; Su, W. *Org. Lett.* **2014**, *16*, 416.
https://doi.org/10.1021/ol403311b.

35. Wu, Y.; Li, W.; Jiang, L.; Zhang, L.; Lan, J.; You, J. *Chem. Sci.* **2018**, 9, 6878.
https://doi.org/10.1039/C8SC02529K.

36. He, Sh.; Tan, G.; Luo, A.; You, J. *Chem. Commun.* **2018**, *54*, 7794.
https://doi.org/10.1039/C8CC04027C.

37. Tan, G.; You, Q.; You, J. *ACS Catal.* **2018**, *89*, 8709.
https://doi.org/10.1021/acscatal.8b02639.

38. Qin, X.; Liu, H.; Qin, D.; Wu, Q.; You, J.; Zhao, D.; Guo, Q.; Huang, X.; Lan, J. *Chem. Sci.* **2013**, *4*, 1964.
https://doi.org/10.1039/C3SC22241A.

39. Andrade, C.; Yanez, C. O.; Ahn, H.-Y.; Urakami, T.; Bondar, M. V.; Komatsu M.; Belfield, K. D. *Bioconjugate Chem.* **2011**, *22*, 2060.
https://doi.org/10.1021/bc200299z.

40. Rai, G.; Vyjayanti, V. N.; Dorjsuren, D.; Simeonov, A.; Jadhav, A.; Wilson D. M.; Maloney, D. J. *J. Med. Chem.* **2012**, *55*, 3101.
https://doi.org/10.1021/jm201537d.

41. Rodrigues, J. R.; Charris, J.; Camacho, J.; Barazarte, A.; Gamboa, N.; Nitzsche, B.; Hoepfner, M.; Lein, M.; Jung K.; Abramjuk, C. *J. Pharm. Pharmacol.* **2013**, *65*, 411.
https://doi.org/10.1111/j.2042-7158.2012.01607.x.

42. Chen, X.; Huang, X.; He, Q.; Xie, Y.; Yang, C. *Chem. Commun.* **2014**, *50*, 3996.
https://doi.org/10.1039/C4CC00362D.

43. Cheng, Y.; Wu, Y.; Tan, G.; You, J. *Angew. Chem. Int. Ed.* **2016**, *55*, 12275.
https://doi.org/10.1002/anie.201606529.

44. Fan, S.; Chen, Z.; Zhang, X. *Org. Lett.* **2012**, *14*, 4950.
https://doi.org/10.1021/ol3023165.

45. Qin, X.; Feng, B.; Dong, J.; Li, X.; Xue, Y.; Lan, J.; You, J. *J. Org. Chem.* **2012**, *77*, 7677.
https://doi.org/10.1021/jo301128y.

46. Han, W.; Mayer, P.; Ofial, R. *Angew. Chem. Int. Ed.* **2011**, *50*, 2178.
https://doi.org/10.1002/anie.201006208.

47. Salvanna, N.; Reddy, G. C.; Das, B. *Tetrahedron* **2013**, *69*, 2220.
https://doi.org/10.1016/j.tet.2012.12.080.

48. He, C.-Y.; Wang, Z.; Wu, C.-Z.; Qing, F.-L.; Zhang, X. *Chem. Sci.* **2013**, *4*, 3508.
https://doi.org/10.1039/C3SC51278A.

49. Kuhl, N.; Hopkinson, M. N.; Glorius, F. *Angew. Chem. Int. Ed.* **2012**, *51*, 8230.
https://doi.org/10.1002/anie.201203792.

50. Cheng, Y.; Li, G.; Liu, Y.; Shi, Y.; Gao, G.; Wu, D.; Lan, J.; You, J. *J. Am. Chem. Soc.* **2016**, *138*, 4730.
https://doi.org/10.1021/jacs.5b09241.

51. Yang, S.-W.; Su, Y.-X.; Sun, L.-P. *Tetrahedron* **2014**, *70*, 3730.
https://doi.org/10.1016/j.tet.2014.03.103.

52. Mao, Z.; Wang, Z.; Xu, Z.; Huang, F.; Yu, Z.; Wang, R. *Org. Lett.* **2012**, *14*, 3854.
https://doi.org/10.1021/ol301517y.

53. Jiang, R.; Yang, X.; Wu, D. *Org. Biomol. Chem*. **2017**, *15*, 6888.
https://doi.org/10.1039/C7OB01344B.

54. Lin, D.; Wang, J.; Zhang, X.; Zhou, Sh.; Lian, J.; Jiang, H.; Liu, H. *Chem. Commun.* **2013**, *49*, 2575.
https://doi.org/10.1039/c3cc38908a.

55. Rudd, M. T.; McCauley, J. A.; Butcher, J. W.; Romano, J. J.; McIntyre, C. J.; Nguyen, K. T.; Gilbert, K. F.; Bush, K. J.; Holloway, M. K.; Swestock, J.; Wan, B. L.; Carroll, S. S.; DiMuzio, J. M.; Graham, D. J.; Ludmerer, S. W.; Stahlhut, M. W.; Fandozzi, C. M.; Trainor, N.; Olsen, D. B.; Vacca, J. P.; Liverton, N. J. *ACS Med. Chem. Lett.* **2011**, *2*, 207.
https://doi.org/10.1021/ml1002426.

56. Yan, F.; Cao, X. X.; Jiang, H. X.; Zhao, X. L.; Wang, J. Y.; Lin, Y. H.; Liu, Q. L.; Zhang, C.; Jiang B. A.; Guo, F. *J. Med. Chem.* **2010**, *53*, 5502.
https://doi.org/10.1021/jm1001698.

57. Verbitskiy, E. V.; Cheprakova, E. M.; Slepukhin, P. A.; Kodess, M. I.; Ezhikova, M. A.; Pervova, M. G.; Rusinov, G. L.; Chupakhin, O. N.; Charushin, V. N. *Tetrahedron* **2012**, *68*, 5445.
https://doi.org/10.1016/j.tet.2012.04.095.

58. Verbitskiy, E. V.; Rusinov, G. L.; Charushin, V. N.; Chupakhin, O. N.; Cheprakova, E. M.; Slepukhin, P. A.; Pervova, M. G.; Ezhikova, M. A.; Kodess, M. I. *Eur. J. Org. Chem.* **2012**, 6612.
https://doi.org/10.1002/ejoc.201201035.

59. Verbitskiy, E. V.; Cheprakova, E. M.; Zhilina, E. F.; Kodess, M. I.; Ezhikova, M. A.; Pervova, M. G.; Slepukhin, P. A.; Subbotina, J. O.; Schepochkin, A. V.; Rusinov, G. L.; Chupakhin, O. N. Charushin, V. N. *Tetrahedron* **2013**, *69*, 5164.
https://doi.org/10.1016/j.tet.2013.04.062.

60. Kravchenko, M. A.; Verbitskiy, E. V.; Medvinskiy, I. D.; Rusinov, G. L.; Charushin, V. N. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 3118.
https://doi.org/10.1016/j.bmcl.2014.05.006.

61. Cheprakova, E. M.; Verbitskiy, E. V.; Ezhikova, M. A.; Kodess, M. I.; Pervova, M. G.; Slepukhin, P. A.; Toporova, M. S.; Kravchenko, M. A.; Medvinskiy, I. D.; Rusinov, G. L.; Charushin, V. N. *Russ. Chem. Bull.* **2014**, *63*, 1350.
https://doi.org/10.1007/s11172-014-0602-y.

62. Verbitskiy, E. V.; Cheprakova, E. M.; Slepukhin, P. A.; Kravchenko, M. A.; Skornyakov, S. N.; Rusinov, G. L.; Chupakhin, O. N.; Charushin, V. N. *Eur. J. Med. Chem.* **2015**, *97*, 225.
https://doi.org/10.1016/j.ejmech.2015.05.007.

63. Verbitskiy, E. V.; Baskakova, S. A.; Kravchenko, M. A.; Skornyakov, S. N.; Rusinov, G. L.; Chupakhin, O. N.; Charushin, V. N. *Bioorg. Med. Chem.* **2016**, *24*, 3771.
https://doi.org/10.1016/j.bmc.2016.06.020.

64. Verbitskiy, E. V.; Rusinov, G. L.; Chupakhin, O. N.; Charushin, V. N. *ARKIVOC* **2016**, *4*. 204.
http://dx.doi.org/10.3998/ark.5550190.p009.623.

65. Verbitskiy, E. V.; Baskakova, S. A.; Gerasimova, N. A.; Evstigneeva, N. P.; Zil'berberg, N. V.; Kungurov, N. V.; Kravchenko, M. A.; Skornyakov, S. N.; Pervova, M. G.; Rusinov, G. L.; Chupakhin, O. N.; Charushin, V. N. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 3003.
https://doi.org/10.1016/j.bmcl.2017.05.013.

66. Mandal, D.; Yamaguchi, A. D.; Yamaguchi, J.; Itami, K. *J. Am. Chem. Soc.* **2011**, *133*, 19660.
https://doi.org/10.1021/ja209945x.

67. Alagiri, K.; Kumara, G. S. R.; Prabhu, K. R. *Chem. Commun.* **2011**, *47*, 11787.
https://doi.org/10.1039/C1CC15050B.

68. Ratnikov, M. O.; Xu, X.; Doyle, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 9475.
https://doi.org/10.1021/ja402479r.

69. Shi, Y.; Wang, Z.; Cheng, Y.; Lan, J.; She, Z.; You, J. *Sci. China: Chem.* **2015**, *58*, 1292.
https://doi.org/10.1007/s11426-015-5386-x.

70. Li, Y.; Jin, J.; Qian, W.; Bao, W. *Org. Biomol. Chem.* **2010**, *8*, 326.
https://doi.org/10.1039/B919396K.

71. Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 6993.
https://doi.org/10.1002/anie.201201491.

72. Odani, R.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 10784.
https://doi.org/10.1002/anie.201406228.

73. Ramana, D. V.; Chandrasekharam, M. *Adv. Synth. Catal.* **2018**, *360*, 4080.

https://doi.org/10.1002/adsc.201800684.

74. Yang, Q.; Yin, Zh.; Zheng, L.; Yuan, J.; Wei, S.; Ding, Q.; Peng, Y. *RSC Adv.* **2019**, *9*, 5870.
https://doi.org/10.1039/C8RA09864F.

75. Bering, L.; Paulussen, F. M.; Antonchick, A. P. *Org. Lett.* **2018**, *20*. 1978.
https://doi.org/10.1021/acs.orglett.8b00521.

76. Rusinov, G. L.; Beresnev, D. G.; Itsikson, N. A.; Chupakhin, O. N. *Heterocycles* (Japan) **2001**, *55*, 2349.
https://doi.org/10.3987/COM-01-9349.

77. Itsikson, N. A.; Beresnev, D. G.; Rusinov, G. L.; Chupakhin, O. N. *ARKIVOC* **2004**, *xii*, 6.
https://doi.org/10.3998/ark.5550190.0005.c02.

78. Chupakhin, O. N.; Utepova, I. A.; Varaksin, M. V.; Tretyakov, E. V.; Romanenko, G. V.; Stass, D. V.; Ovcharenko, V. I. *J. Org. Chem.* **2009**, *74*, 2870.
https://doi.org/10.1021/jo900085s.

79. Tretyakov, E. V.; Utepova, I. A.; Varaksin, M. V.; Tolstikov, S. E.; Romanenko, G. V.; Bogomyakov, A. S.; Stass, D. V.; Ovcharenko, V. I.; Chupakhin, O. N. *ARKIVOC* **2011**, *8*, 76.
https://doi.org/10.3998/ark.5550190.0012.806.

80. Varaksin, M. V.; Utepova, I. A.; Chupakhin, O. N. *Chem. Heterocycl. Comp.* **2012**, *48*, 1213.
https://doi.org/10.1007/s10593-012-1124-x.

81. Kumar, Sh.; Rathore, V.; Verma, A.; Prasad, Ch. D.; Kumar, A.; Yadav, A.; Jana, S.; Sattar, Moh.; Meenakshi; Kumar, S. *Org. Lett.* **2015**, *17*, 82.
https://doi.org/10.1021/ol503274z.

82. Han, Y.-Y.; Wub, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *Tetrahedron Lett.* **2010**, *51*, 2023.
https://doi.org/10.1016/j.tetlet.2010.02.031.

83. Moriarty, R. M.; Vaid, R. K. *Synthesis (Stuttg)* **1990**, 431.
https://doi.org/10.1055/s-1990-26898.

84. Ochiai, M.; Zhdankin, V. V.; Koser, G. F.; Tohma, H.; Kita, Y. *Hypervalent Iodine Chemistry - Modern Developments in Organic Synthesis*; Wirth, T. Ed.; Topics in Current Chemistry, Springer-Verlag, Berlin Heidelberg, 2003, 224.
https://doi.org/10.1007/3-540-46114-0.

85. Dohi, T.; Kita, Y. *Oxidative C-C Bond Formation (Couplings, Cyclizations, Cyclopropanation, Etc.)*. In: *PATAI'S Chemistry of Functional Groups*; Wiley, 2018.
https://doi.org/10.1002/9780470682531.pat0952.

86. Hyatt, I. F. D.; Dave, L.; David, N.; Kaur, K.; Medard, M.; Mowdawalla, C. *Org. Biomol. Chem.* **2019**, *17*, 7822.
https://doi.org/10.1039/C9OB01267B.

87. Tohma, H.; Iwata, M.; Maegawa, T.; Kiyono, Y.; Maruyama, A.; Kita, Y. *Org. Biomol. Chem.* **2003**, *1*, 1647.
https://doi.org/10.1039/B302462H.

88. Dohi, T.; Morimoto, K.; Kiyono, Y.; Maruyama, A.; Tohma, H.; Kita, Y. *Chem. Commun.* **2005**, 2930.
https://doi.org/10.1039/B503058G.

89. Morimoto, K.; Yamaoka, N.; Ogawa, C.; Nakae, T.; Fujioka, H.; Dohi, T.; Kita, Y. *Org. Lett.* **2010**, *12*, 3804.
https://doi.org/10.1021/ol101498r.

90. Morimoto, K.; Morimoto, K.; Nakae, T.; Yamaoka, N.; Dohi, T.; Kita, Y. *Eur. J. Org. Chem.* **2011**, 6326.
https://doi.org/10.1002/ejoc.201100969.

91. Kita, Y.; Morimoto, K.; Ito, M.; Ogawa, C.; Goto, A.; Dohi, T. *J. Am. Chem. Soc.* **2009**, *131*, 1668.
https://doi.org/10.1021/ja808940n.

92. Gu, Y.; Wang, D. *Tetrahedron Lett*. **2010**, *51*, 2004.

https://doi.org/10.1016/j.tetlet.2010.02.022.

93. Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172.
https://doi.org/10.1021/ja801767s.

94. Morimoto, K.; Ohnishi, Y.; Nakamura, A.; Sakamoto, K.; Dohi, T.; Kita, Y. *Asian J. Org. Chem.* **2014**, *3*, 382.
https://doi.org/10.1002/ajoc.201400027.

95. Yamada, S.; Murakami, K.; Itami, K. *Org. Lett*. **2016**, *18*, 2415.
https://doi.org/10.1021/acs.orglett.6b00932.

96. Jin, L.; Feng, J.; Lu, G.; Caia, Ch. *Adv. Synth. Catal.* **2015**, *357*, 2105.
https://doi.org/10.1002/adsc.201500048.

97. Qin, W.-B.; Zhu, J.-Y.; Kong, Y.-B.; Bao, Y.-H.; Chen, Zh.-W.; Liu, L.-X. *Org. Biomol. Chem.* **2014**, *12*, 4252.
https://doi.org/10.1039/C4OB00356J.

98. Cheng, Q.; Wang, Zh.; Li, H.-W.; Shan, Ch.-Y.; Zheng, P.-F.; Shuai, L.; Li, Y.-L.; Chen, Y.-Ch.; Ouyang, Q. *Org. Lett.* **2020**, *22*, 300.
https://doi.org/10.1021/acs.orglett.9b04330.

99. Trofimov, B. A.; Volkov, P. A.; Telezhkin, A. A.; Khrapova, K. O.; Ivanova, N. I.; Albanov, A. I.; Gusarova, N. K. *J. Org. Chem.* **2020**, *85*, 4927.
https://doi.org/10.1021/acs.joc.0c00084.

100. Cheng, D.; Bao, W. *Adv. Synth. Catal.* **2008**, *350*, 1263.
https://doi.org/10.1002/adsc.200800085.

101. Muramatsu, W.; Nakano, K.; Li Ch.-J. *Org. Lett.* **2014**, *16*, 644.
https://doi.org/10.1021/ol403686g.

102. Wang, H.; Zhao, Y.-L.; Li, L.; Li, Sh.-Sh.; Liu, Q. *Adv. Synth. Catal.* **2014**, *356*, 3157.
https://doi.org/10.1002/adsc.201400357.

103. Alagiri, K.; Devadig, P.; Prabhu, K. R. *Chem. Eur. J.* **2012**, *18*, 5160.
https://doi.org/10.1002/chem.201200100.

104. Guo, Sh.; Li, Y.; Wang, Y., Guo, X.; Meng, X.; Chena, B. *Adv. Synth. Catal.* **2015**, *357*, 950.
https://doi.org/10.1002/adsc.201400938.

105. Yang, F.; Li, Y.; Floreancig, P. E.; Li, X.; Liu, L. *Org. Biomol. Chem.* **2018**, *16*, 5144.
https://doi.org/10.1039/C8OB00949J.

106. Romo-Pérez, A.; Miranda, L. D.; Garcia, A. *Tetrahedron Lett.* **2015**, *56*, 6669.
https://doi.org/10.1016/j.tetlet.2015.10.018.

107. Yan, M.; Kawamata, Y.; Baran, P. S. *Chem. Rev*. **2017**, *117*, 13230.
https://doi.org/10.1021/acs.chemrev.7b00397.

108. Wiebe, A.; Gieshoff, T.; Mçhle, S.; Rodrigo, E.; Zirbes, M.; Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2018**, *57*, 5594.
https://doi.org/10.1002/anie.201711060.

109. Yoshida, J.; Shimizu, A.; Hayashi, R. *Chem. Rev*. **2018**, *118*, 4702.
https://doi.org/10.1021/acs.chemrev.7b00475.

110. Waldvogel, S. R.; Lips, S.; Selt, M.; Riehl, B.; Kampf, C. J. *Chem. Rev*. **2018**, *118*, 6706.
https://doi.org/10.1021/acs.chemrev.8b00233.

111. Atobe, M.; Tateno, H.; Matsumura, Y. *Chem. Rev*. **2018**, *118*, 4541.
https://doi.org/10.1021/acs.chemrev.7b00353.

112. Pletcher, D.; Green, R. A.; Brown, R. C. D. *Chem. Rev*. **2018**, *118*, 4573.
https://doi.org/10.1021/acs.chemrev.7b00360.

113. Nutting, J. E.; Rafiee, M.; Stahl, S. S. *Chem. Rev.* **2018**, *118*, 4834.
https://doi.org/10.1021/acs.chemrev.7b00763.
114. Lips, S.; Waldvogel, S. R. *ChemElectroChem.* **2019**, *6*, 1649.
https://doi.org/10.1002/celc.201801620.
115. Kärkäs, M. D. *Chem. Soc. Rev.* **2018**, *47*, 5786.
https://doi.org/10.1039/C7CS00619E.
116. Elinson, M. N.; Vereshchagin, A. N.; Ryzkov, F. V. *Curr. Org. Chem.* **2017**, *21*, 1427.
https://doi.org/10.2174/1385272820666161017170200.
117. Jiang, Y.; Xu, K.; Zeng, C. *Chem. Rev.* **2018**, *118*, 4485.
https://doi.org/10.1021/acs.chemrev.7b00271.
118. Möhle, S.; Zirbes, M.; Rodrigo, E.; Gieshoff, T.; Wiebe, A.; Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2018**, *57*, 6018.
https://doi.org/10.1002/anie.201712732.
119. Schulz, L.; Waldvogel, S. R. *Synlett* **2019**, *30*, 275.
https://doi.org/10.1055/s-0037-1610303.
120. Shchepochkin, A. V.; Chupakhin, O. N.; Charushin, V. N.; Petrosyan, V. A. *Russ. Chem. Rev.* **2013**, *82*, 747.
https://doi.org/10.1070/RC2013v082n08ABEH004386.
121. Chupakhin, O. N.; Shchepochkin, A. V.; Charushin. *Adv. Heterocycl. Chem.* **2020**, *131*, 1.
https://doi.org/10.1016/bs.aihch.2019.11.002.
122. Sauermann, N.; Mei, R.; Ackermann, L. *Angew. Chem. Int. Ed.* **2018**, *57*, 5090.
https://doi.org/10.1002/anie.201802206.
123. Gao, X.; Wang, P.; Zeng, L.; Tang, S.; Lei, A. *J. Am. Chem. Soc.* **2018**, *140*, 4195.
https://doi.org/10.1021/jacs.7b13049.
124. Wang, P.; Tang, S.; Huang, P.; Lei, A. *Angew. Chem. Int. Ed.* **2017**, *56*, 3009.
https://doi.org/10.1002/anie.201700012.
125. Chupakhin, O. N.; Shchepochkin, A. V.; Charushin, V. N.; Maiorova, A. V.; Kulikova, T. V.; Shunyaev, K. Yu.; Enyashin, A. N.; Slepukhin, P. A.; Suvorova, A. I. *Chem. Heterocycl. Compd.* **2019**, *55*, 956.
https://doi.org/10.1007/s10593-019-02562-x.
126. Shchepochkin, A. V.; Chupakhin, O. N.; Charushin, V. N.; Steglenko, D. V.; Minkin, V. I.; Rusinov, G. L.; Matern, A. I. *RSC Adv.* **2016**, *6*, 77834.
https://doi.org/10.1039/C6RA17783B.
127. Chupakhin, O. N.; Shchepochkin, A. V.; Charushin, V. N. *Green Chem.* **2017**, *19*, 2931.
https://doi.org/10.1039/C7GC00789B.
128. Wiebe, A.; Lips, S.; Schollmeyer, D.; Franke, R.; Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2017**, *56*, 14727.
https://doi.org/10.1002/anie.201708946.
129. Lips, S.; Frontana-Uribe, B. A.; Dçrr, M.; Schollmeyer, D.; Franke, R.; Waldvogel, S. R. *Chem. Eur. J.* **2018**, *24*, 6057.
https://doi.org/10.1002/chem.201800919.
130. Feng, P.; Ma, G.; Chen, X.; Wu, X.; Lin, L.; Liu, P.; Chen, T. *Angew. Chem. Int. Ed.* **2019**, *58*, 8400.
https://doi.org/10.1002/anie.201901762.
131. Caronna, T.; Gambarotti, C.; Palmisano, L.; Punta, C.; Recupero, F. *J. Photochem. Photobiol. A Chem.* **2005**, *171*, 237.
https://doi.org/10.1016/j.jphotochem.2004.10.017.
132. Gambarotti, C.; Punta, C.; Recupero, F.; Caronna, T.; Palmisano, L. *Curr. Org. Chem.* **2010**, *14*, 1153.

https://doi.org/10.2174/138527210791317111.

133. Kisch, H. *Angew. Chem. Int. Ed.* **2013**, *52*, 812.
https://doi.org/10.1002/anie.201201200.

134. Koohgard, M.; Hosseini-Sarvari, M. *Catal. Commun.* **2018**, *111*, 10.
https://doi.org/10.1016/j.catcom.2018.03.026.

135. Wang, Z.; Lang, X. *Appl. Catal. B Environ.* **2018**, *224*, 404.
https://doi.org/10.1016/j.apcatb.2017.10.002.

136. Feizpour, F.; Jafarpour, M.; Rezaeifard, A. *New J. Chem.* **2018**, *42*, 807-811.
https://doi.org/10.1039/C7NJ03651E.

137. Utepova, I. A.; Trestsova, M. A.; Chupakhin, O. N.; Charushin, V. N.; Rempel, A. A. *Green Chem.* **2015**, *17*, 4401.
https://doi.org/10.1039/C5GC00753D.

138. Utepova, I. A.; Chupakhin, O. N.; Trestsova, M. A.; Musikhina, A. A.; Kucheryavaya, D. A.; Charushin, V. N.; Rempel, A. A.; Kozhevnikova, N. S.; Valeeva, A. A.; Mikhaleva, A. I.; Trofimov, B. A. *Russ. Chem. Bull.* **2016**, *65*, 445.
https://doi.org/10.1007/s11172-016-1319-x.

139. Zhong, J.-J.; Meng, Q.-Y.; Wang, G.-X.; Liu, Q.; Chen, B.; Feng, K.; Tung, C.-H.; Wu, L.-Z. *Chem. Eur. J.* **2013**, *19*, 6443.
https://doi.org/10.1002/chem.201204572.

140. Han, X.; He, X.; Sun, L.; Han, X.; Zhan, W.; Xu, J.; Wang, X.; Chen, J. *ACS Catal.* **2018**, *8*, 3348.
https://doi.org/10.1021/acscatal.7b04219.

141. Meng, Q.-Y.; Zhong, J.-J.; Liu, Q.; Gao, X.-W.; Zhang, H.-H.; Lei, T.; Li, Z.-J.; Wang, G.-X.; Feng, K.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *J. Am. Chem. Soc.* **2013**, *135*, 19052.
https://doi.org/10.1021/ja408486v.

142. Zhong, J.-J.; Meng, Q.-Y.; Liu, B.; Li, X.-B.; Gao, X.-W.; Lei, T.; Wu, C.-J.; Li, Z.-J.; Tung, C.-H.; Wu, L.-Z. *Org. Lett.* **2014**, *16*, 1988.
https://doi.org/10.1021/ol500534w.

143. Girish, Y. R.; Jaiswal, K.; Prakash, P.; De, M. *Catal. Sci. Technol.* **2019**, *9*, 1201.
https://doi.org/10.1039/C8CY02532K.

144. Wu, C.-J.; Zhong, J.-J.; Meng, Q.-Y.; Lei, T.; Gao, X.-W.; Tung, C.-H.; Wu, L.-Z. *Org. Lett.* **2015**, *17*, 884.
https://doi.org/10.1021/ol503744a.

145. Kibriya, G.; Bagdi, A. K.; Hajra, A. *J. Org. Chem.* **2018**, *83*, 10619.
https://doi.org/10.1021/acs.joc.8b01433.

146. Zhang, G.-Y.; Yu, K.-X.; Zhang, C.; Guan, Z.; He, Y.-H. *Eur. J. Org. Chem.* **2018**, 525.
https://doi.org/10.1002/ejoc.201701683.

147. Yamaguchi, T.; Yamaguchi, E.; Itoh, A. *Org. Lett.* **2017**, *19*, 1282.
https://doi.org/10.1021/acs.orglett.7b00026.

148. Chen, H.; Yi, H.; Tang, Z.; Bian, C.; Zhang, H.; Lei, A. *Adv. Synth. Catal.* **2018**, *360*, 3220.
https://doi.org/10.1002/adsc.201800531.

149. Akulov, A. A.; Varaksin, M. V.; Tsmokalyuk, A. N.; Charushin, V. N.; Chupakhin, O. N. *Green Chem.* **2021**, *23*, 2049.
https://doi.org/10.1039/D1GC00175B.

150. Liu, Ch.; Yuan, J.; Gao, M.; Tang, Sh.; Li, W.; Shi, R.; Lei, A. *Chem. Rev.* **2015**, *115*, 12138.
https://doi.org/10.1021/cr500431s.

151. Sun, Ch.-L.; Shi, Zh.-J. *Chem. Rev.* **2014**, *114*, 9219.
https://doi.org/10.1021/cr400274j.
152. Chupakhin, O. N.; Charushin, V. N. *Pure Appl. Chem.* **2017**, *89*, 1195.
https://doi.org/10.1515/pac-2017-0108.

Authors' Biographies

Irina A. Utepova gratuated from the Ural State Technical University in 2002. In 2008, she earned her PhD in Organic Chemistry and Doctor of Science degree in 2017. Her research interests include asymmetric synthesis; organocatalysis; photocatalysis; metal and metal-free C–H functionalization; the development of novel approaches to new (hetero)aromatic compounds exhibiting biological activity and/or luminescence properties; green chemistry; coordination chemistry.

Oleg N. Chupakhin is a full member of the Russian Academy of Sciences, Professor and ex-Head of the Department of Organic & Biomolecular Chemistry at Ural Federal University, and Chief Researcher at Postovsky Institute of Organic Synthesis of Ural Branch of RAS. Prof. Chupakhin graduated with honors from Ural Polytechnic Institute in 1957. He earned his PhD in Organic Chemistry in 1962 and Doctor of Science degree in 1976. Current research interests: new methodologies in organic synthesis, structural analysis of organic compounds, mechanisms of organic reactions, heterocyclic chemistry, green chemistry, industrial chemistry, environmental chemistry, medicinal chemistry, chemosensors, molecular recognition and supramolecular chemistry.

Maria A. Trestsova gratuated from the Ural State Technical University in 2012. In 2019, she earned her PhD in Organic Chemistry. Her current research interest includes the employment of visible light photocatalysis in the synthesis and functionalization of nitrogen-containing heterocycles.

Alexandra A. Musikhina received her master's in Chemistry (2010) from Ural State Technical University. In 2013, she earned her PhD in Organic Chemistry. Her research interest includes asymmetric synthesis, the development of novel pot, atom, and step economical approaches based on the methodology of C-H bond functionalization in both (hetero)aromatic substrates.

Alexander V. Shchepochkin graduated from Institute of Chemistry and Technology of Ural Federal University in 2010, and has Master's degree in Chemical Technology. He defended his PhD thesis devoted to functionalization

of azines using electrochemical methods in 2018. Now he is a senior researcher at Institute of Organic Synthesis RAS. His research interests include green chemistry, electrochemical synthesis and direct C-H functionalization.

Olga N. Zabelina graduated from the Ural State University in 2002. She earned her PhD in Organic Chemistry in 2007. Her main research interests focus on application of high-perfomance liquid chromatography and mass-spectrometry in analysis of organic compounds.