RECENT SYNTHETIC APPROACHES TOWARDS SELENOPHENE SCAFFOLDS

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Abstract. *Selenophenes are a special family of heterocyclic compounds present in several bioactive molecules and organic functional materials. In the past decade, several synthetic methodologies using harsh conditions were applied to their synthesis. In recent years, methods based on cheap reagents, mild and safer conditions, minimized steps, and high efficiency have been reported to produce diversely functionalized five-membered selenium rings. The present chapter is intended to review the most recent synthetic advances to furnish selenophene derivatives, their reactivity toward Pd-catalyzed C-H bond functionalization, and the preparation of selenoacenes.*

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1. Introduction

The selenophene core is found in a wide variety of compounds, many of which are pharmacologically important, due to their biological activities. These include antioxidant,[1] anti-inflammatory,[2] anticancer,[3-5] as well as antibacterial,[6] antinociceptive,[7] antihypertensive,[8] and anticonvulsant,[9] among others. This core has been embedded into certain natural products, and selenophene-containing drug analogues have also been prepared.[10]

Additionally, selenophenes have attracted growing interest as building blocks in organic synthesis and materials science, in view of their potential technological applications in organic light emitting diodes (OLEDs),[11] organic field effect transistors (OFETs),[12] organic solar cells,[13-14] and other electronic components.[15] Some of these privileged structures are demonstrated in the Figure 1.

The development of efficient and new methodologies for accessing the diversity of scaffolds containing a selenophene core is of great importance to different areas of chemistry. In the last decade, several synthetic methods for the preparation of this nucleus and its derivatives have been described, and consequently reviewed.[16-21] The formation of non-substituted selenophene from elemental selenium and acetylene gas using aluminum oxide, sand or glass beads as support materials for 450 °C hot columns was the suitable method for large scale preparations in the past.[22-23] On the other hand, most recent explored protocols aimed at preparing highly substituted selenophene rings are based on the addition of either nucleophilic or electrophilic selenium species to acyclic π-systems under mild conditions.[24-27]

The selenophene ring is a multifaceted synthon regarding its reactivity, being able to react through electrophilic aromatic substitution, oxidation of the selenium atom, transition metal-catalyzed cross coupling reactions, and so on.[28-29] Conveniently, the reactivity of halo-selenophenes through metal-halogen exchange

conditions is an alternative approach to generate nucleophilic carbon species able to react with electrophilic carbon and heteroatom sources.[30-31] Still, approaches to prepare π-conjugated selenophenes through transition metal-catalyzed alkenylation, alkynylation and arylation reactions have been widely reported.[32-24] These combined protocols gave access to selenophene-based new materials including hetero(poly)acenes, copolymers and dipolar dyes for optoelectronic devices, and organic solar cells.[11-15]

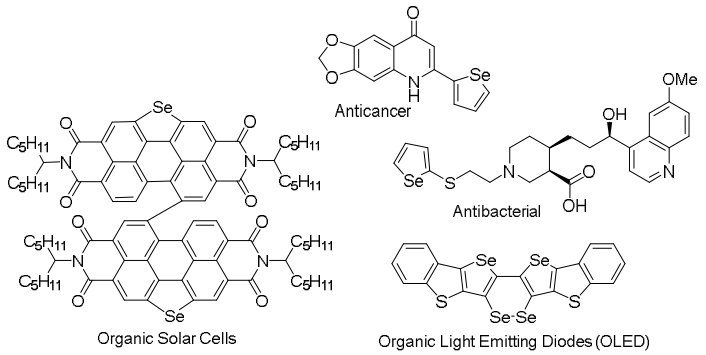


Figure 1. Examples of bioactive and technologically interesting selenophene derivatives.

Therefore, due to the synthetic, pharmacological and industrial importance of selenophene-containing compounds, we present in this chapter some of the most recent advances in the preparation and synthetic applications of selenophenes, covering the period from 2017 until the first quarter of 2020.

2. New approaches to the synthesis of selenophenes

In this section, the most recent methodologies to access diverse selenophene rings, as independent unities and fused cores, are presented. The analysis of these methods revealed the success of employing alkynes, vinyl bromides, and heteroarenes containing active C-H bonds as the prominent substrates used in recent years.

2.1. Starting from alkynes bearing an organoselenium substituent

Alkynes bearing a nucleophilic heteroatom have been largely used as substrates to prepare a wide variety of heterocyclic systems, specially, throughout electrophilic cyclization conditions. In this context, the intramolecular cyclization reaction mediated by iodine, bromine, copper(II) halides and $BuTeBr_3$ have been a convenient and mild protocol applied for the preparation of selenophene derivatives.[26,30,34-36]

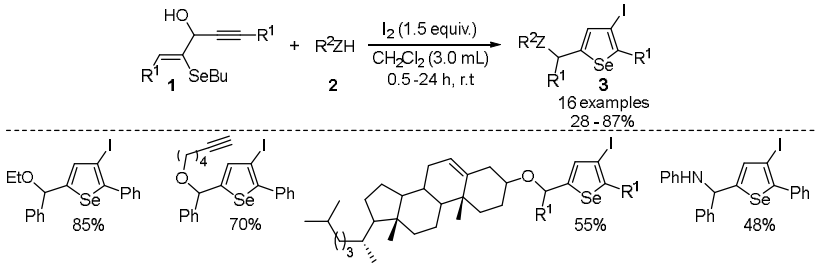
In this context, Zeni and coworkers reported in 2017 the 5-*endo-dig* electrophilic cyclization of propargyl alcohols containing selanylalkenes as substituents **1** using molecular iodine in dichloromethane at room temperature.[37] The authors employed a variety of selenoenynes **1** and appropriate nucleophiles, such as differently substituted alcohols and amines **2**, to give the respective 3-iodo-selenophenes **3**. This method allowed the preparation of 16 new compounds in up to 87% yield (Scheme 1).

According to the authors, this reaction involves the initial formation of an iodonium intermediate **4**, which undergoes a regioselective *5-endo-dig* intramolecular nucleophilic attack by the neighboring selenium atom and generates **5**. Then, an intermolecular reaction occurs, followed by a water elimination step, to give the target molecule **3**, as shown in Scheme 2.

In continuation to their studies, Zeni and coworkers also described the cyclization of butylselanyl homopropargyl alcohols **6** to prepare 4,5,6,7-tetrahydrobenzo[*b*]selenophenes and 2,3,4-trisubstituted-selenophenes **7** (Scheme 3).[38] In this context, three different reaction conditions were employed: (i) I_2/CH_2Cl_2/40 °C, (ii) $CuBr_2$/THF/r.t., and (iii) PhSeSePh/CuI/DMSO/110 °C. By these approaches, it was possible to prepare 37 different examples of 3-iodo-selenophenes, 3-bromo-selenophenes and 3-(phenylselanyl)-selenophenes, respectively.

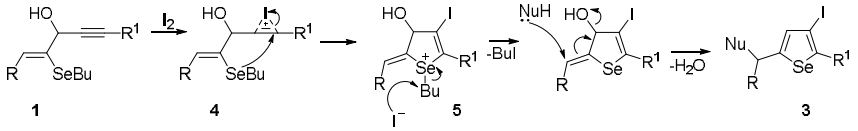
In an approach to prepare 2-organylchalcogenyl-benzo[*b*]selenophenes **9**, Perin, Roehrs and coworkers performed the iodocyclization of sulfanyl- and selanylalkynes **8**.[39] The reaction was carried out with I_2 (1.1

equiv.) in dichloromethane to give ten 3-iodoselenophenes **9** in good to excellent yields. The reaction did not show to be sensible to electronic effects of the substituents directly bonded to the benzene ring, and the products were obtained in short reaction times (12-30 min). On the other hand, an aliphatic sulfanylalkyne (R^2=C_3H_7) was less reactive under the iodocyclization conditions and the desired product **9f** was obtained in lower yield. Similarly, when an electron-withdrawing group attached to aryl ring in **8** was used (R^1=5-Cl), the expected product **9g** was obtained in 68% yield after 30 minutes of reaction. Differently substituted selanylalkynes were successfully used in this electrophilic cyclization reaction, giving the desired products in very good yields (Scheme 4).

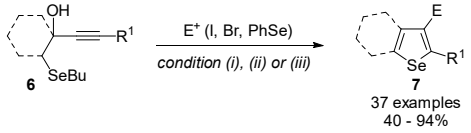


R^1= C_6H_5, 4-MeC_6H_4, 4-ClC_6H_4; When Z= O; R^2= Me, Et, Bu, *i*-Pr, *t*-Bu, Bn, hexynyl, propargyl, allyl, cholesterol.
For Z= N; R^2= C_6H_5, 4-MeC_6H_4, 4-ClC_6H_4

Scheme 1. Synthesis of 3-iodo-selenophenes **3** from propargyl alcohols bearing selenoalkenes **1**.

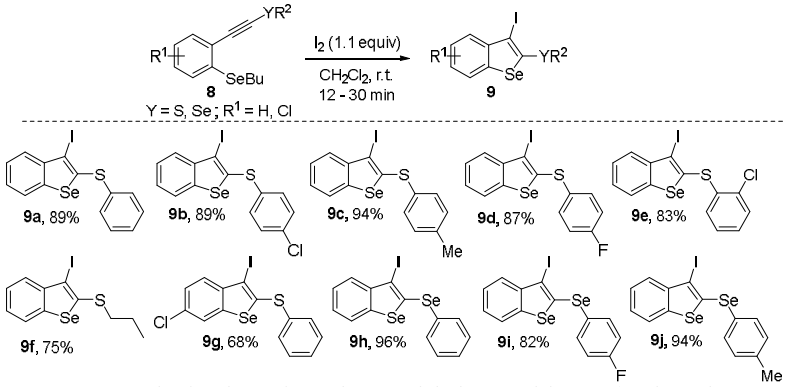


Scheme 2. Proposed mechanism to synthesize 3-iodo-selenophenes **3**.



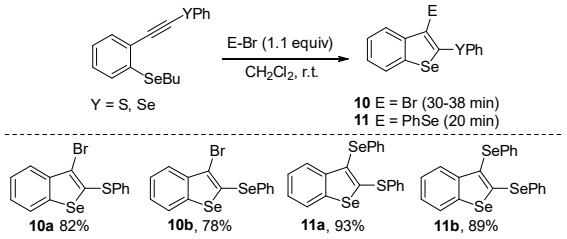
R^1= C_6H_5, 4-MeC_6H_4, 3-MeC_6H_4, 4-MeOC_6H_4, 2-MeOC_6H_4, 4-ClC_6H_4, 2-ClC_6H_4, 4-BrC_6H_4, 3-$CF_3C_6H_4$, 2-naphtyl, 1-naphtyl, cyclohexenyl.

Scheme 3. Cyclization of butylselanyl homopropargyl alcohols to obtain 3-substituted selenophenes **7**.



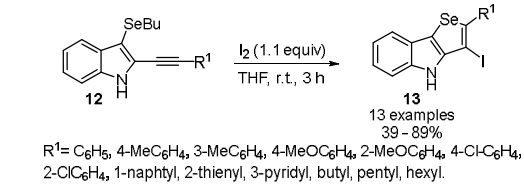
Scheme 4. Synthesis of a variety of organylchalcogenyl-benzo[*b*]selenophenes **9**.

The application of alternative electrophilic sources, such as Br_2 and PhSeBr, was also evaluated. Thus, it was possible to observe that electrophilic selenium species reacted slightly better and faster than bromine, as shown in Scheme 5.



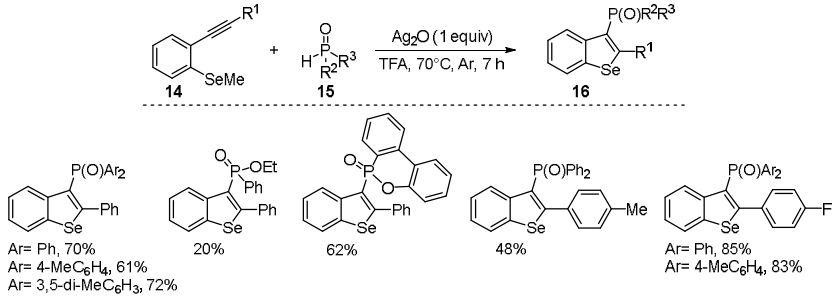
Scheme 5. Synthesis of benzo[*b*]selenophenes **10** and **11**.

Zeni and coworkers also performed the iodocyclization of 3-organoselanyl-2-alkynylindoles **12** to give selenophene-fused indoles **13**.[40] In this case, the authors employed molecular iodine (1.1 equiv.) and THF as solvent at room temperature for 3 h (Scheme 6). Alternatively, a condition using $FeCl_3$ and dialkyl diselenides was also employed as a tool to obtain 3-alkylselanyl-selenophene-fused indoles in good yields.



Scheme 6. Synthesis of 3-iodo-selenophene-fused indoles **13**.

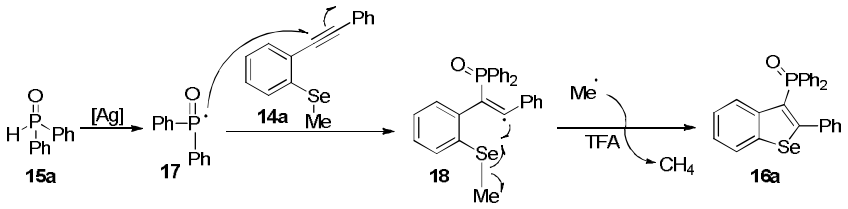
In 2019, Gao and coworkers described their results on the Ag-mediated radical cyclization of 2-alkynyl-selenoanisoles **14** with secondary phosphine oxides **15** to obtain 3-phosphinoylbenzo[*b*]selenophenes **16** in good yields (Scheme 7).[41] In this work, the authors used Ag_2O (1 equiv.) in trifluoracetic acid at 70 °C for 7 h. These reaction conditions allowed the preparation of eight compounds in yields ranging from 20% to 85%.



Scheme 7. Scope of the silver-mediated formation of 3-phosphinoylbenzoselenophenes **16**.

After performed several control experiments employing 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and butylated hydroxytoluene (BHT) as radical scavengers, the authors proposed a radical mechanism. In this mechanism, the phosphine oxide **15a** reacts with Ag_2O to generate the phosphoryl radical **17**. The radical species **17** attacks the triple bond of **14a** to furnish the vinyl radical **18**. Then, a 5-*endo-trig*

cyclization occurs to generate the product **16a**, along with the release of a methyl radical, which forms methane *via* a H abstraction from TFA (Scheme 8).



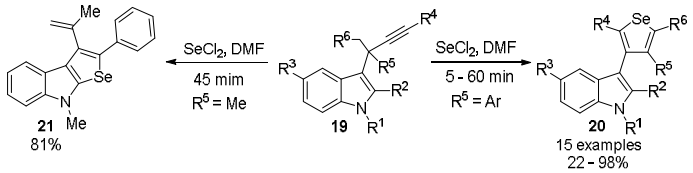
Scheme 8. Proposed mechanism described by Gao and coworkers.

2.2. Starting from alkynes and an external selenium source

The selenophene core has also been prepared by intermolecular cyclization reactions applying a wide variety of alkynes and external selenium sources such as selenium powder, $SeCl_2$, diorganyl diselenides, and $SePPh_3$. This kind of reaction is particularly interesting for the preparation of multi-functionalized target molecules, in few steps and without the pre-functionalization of the starting materials.

Thus, considering the preparation of polysubstituted compounds, in 2018 Silveira, Kaufman and coworkers, reported a new and efficient $SeCl_2$-mediated synthesis of indole-containing selenophenes **20** and **21**.[42] The standard reaction system consists of 1 equiv. amount of $SeCl_2$, which is generated *in situ* by reacting elemental selenium with sulfuryl chloride (SO_2Cl_2) (1.0:2.0 equiv.), and dimethylformamide, as solvent. The reactions were carried out at room temperature under argon atmosphere.

In order to evaluate the scope and limitations of the new selenophene-forming reaction, the authors explored a range of starting materials **19**. These included the substituents attached to the indole ring (R^3), to the terminal position of the alkyne (R^4) and to the propargylic position (R^5). Although the reaction proceeded smoothly to afford the desired compounds **20** in good yields, when a starting material with an aliphatic group bonded to the terminal position of the alkyne was employed, only 22% yield was obtained for the 2-alkylsubstituted-selenophene. On the other hand, the nature of the substituent of the indole nitrogen was crucial to the success of the reaction. *N*-methyl- and *N*-benzyl-substituted indoles were suitable substrates, but no product was formed when the *N*-Boc derivative was used. Additionally, an interesting result was obtained when a methyl group at the propargylic position was used. In this case, the vinyl-substituted indole[2,3-*b*]selenophene derivative **21** was obtained in 81% yield (Scheme 9).



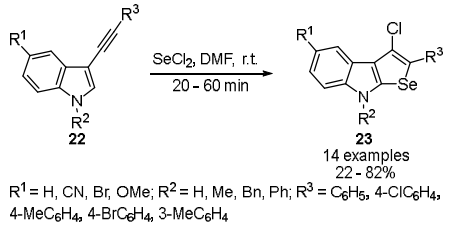
R^1 = H, Me, Bn, Boc; R^2 = H, Me; R^3 = H, CN, OMe, Br; R^4 = C_6H_5, 4-ClC_6H_4, 4-MeC_6H_4, 4-BrC_6H_4, *n*-Bu; R^5 = Me, C_6H_5, 4-ClC_6H_4, 4-$MeOC_6H_4$; R^6 = H, Me

Scheme 9. Synthesis of indole-containing selenophenes **20** and **21**.

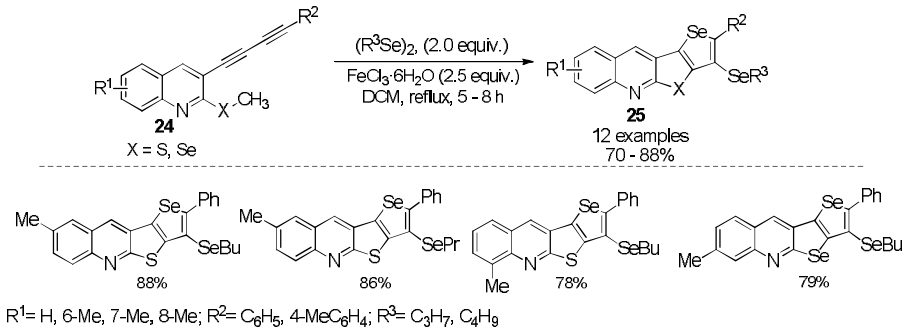
One year later, the same group published their results on the synthesis and antifungal activity of 2-aryl-3-chloroselenophene[2,3-*b*]indoles **23** using $SeCl_2$ as the selenium source.[43] The reaction of 3-alkynylindoles **22** with $SeCl_2$ in DMF at room temperature allowed the preparation of 14 derivatives with yields ranging from 22% to 82% (Scheme 10). The reaction was unsuccessful using *N*-Boc-substituted indole (R^2=Boc) and alkyl-substituted alkynes (R^3=alkyl).

In the same year, Koketsu and coworkers developed a new methodology for the construction of selenophene-fused quinoline-based heteroacene scaffolds applying Fe(III)-promoted linear intramolecular cascade cyclization of 1,3-diynes **24** and **26** and dialkyl diselenides.[44] Initially, the authors carried out several reactions with different catalysts and solvents and in reaction times between 4 and 12 h, to determine

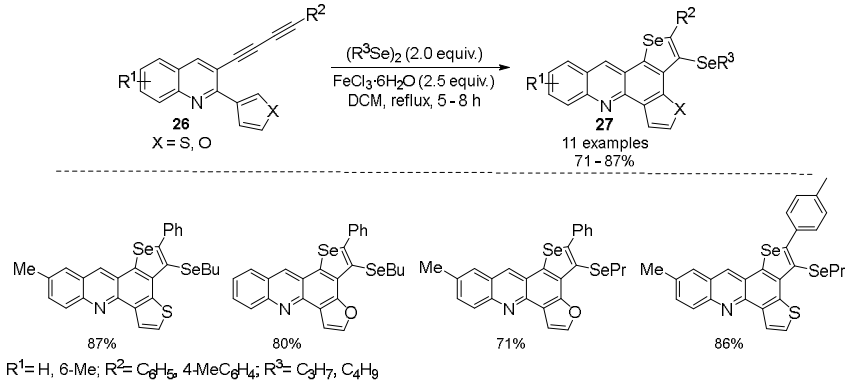
the best condition for the reaction. $FeCl_3 \cdot 6H_2O$ was selected as an ideal catalyst and DCM as the best solvent. By using this cascade protocol, the authors prepared a range of thieno[2,3-*b*]quinolines and selenopheno[2,3-*b*]quinolines **25** in 70% to 88% yield (Scheme 11). Still, selenophene-fused to thieno[2,3-*c*]acridines and furo[2,3-*c*]acridines **27** could be obtained in up to 87% yield (Scheme 12).



Scheme 10. $SeCl_2$-mediated synthesis of 2-aryl-3-chloroselenophene[2,3-*b*]indoles **23**.



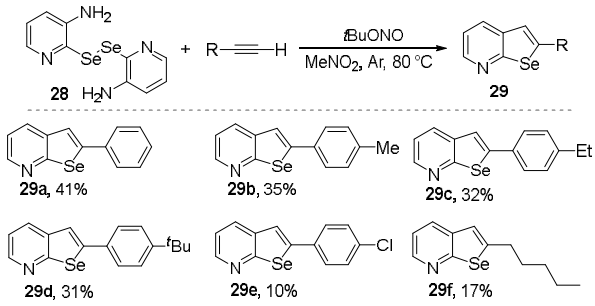
Scheme 11. Synthesis of thieno[2,3-*b*]quinolines and selenopheno[2,3-*b*]quinolines **25**.



Scheme 12. Synthesis of thieno[2,3-*c*]acridines and furo[2,3-*c*]acridines **27**.

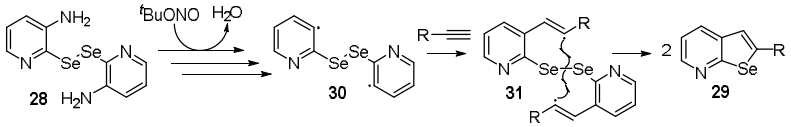
Considering the diversity of selenium species that can be used to prepare a selenophene ring *via* intermolecular reactions, Perin, Schumacher and coworkers stand out the synthetic application of bis(3-amino-2-pyridyl)diselenide **28** in this regard.[45] In their work published in 2019, they described an alternative method to prepare 2-organylselenopheno[2,3-*b*]pyridines **29** starting from the diselenide **28** and terminal alkynes in the presence of *tert*-butyl nitrite and in $MeNO_2$ as the solvent. This new synthetic strategy provided six selenophene-fused pyridines in yields ranging from 10% to 41%. Scheme 13 shows that, when the reaction was performed with arylalkynes bearing electron-donating groups pending at the

aromatic ring, the obtained results were similar to the neutral phenylacetylene. However, in the presence of the electron-withdrawing Cl-substituent, or using heptyne, lower yields were obtained.



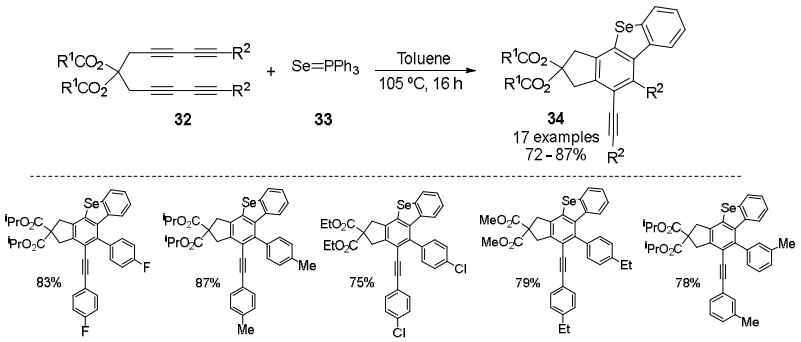
Scheme 13. Synthesis of 2-organylselenopheno[2,3-*b*]pyridines **29**.

Aiming at collecting evidences about the reaction pathway, the authors carried out several control experiments and a plausible mechanism to obtain 2-organylselenopheno[2,3-*b*]pyridines **29** was proposed. Firstly, the reaction between pyridylamine and *tert*-butyl nitrite results in the radical species **30**, which reacts with the alkyne to afford the vinyl radical **31**. Then, an intramolecular homolytic substitution at the selenium atom leads to 2 equiv. of the final product, as shown in Scheme 14.



Scheme 14. Proposed radical mechanism to obtain 2-organylselenopheno[2,3-*b*]pyridines **29**.

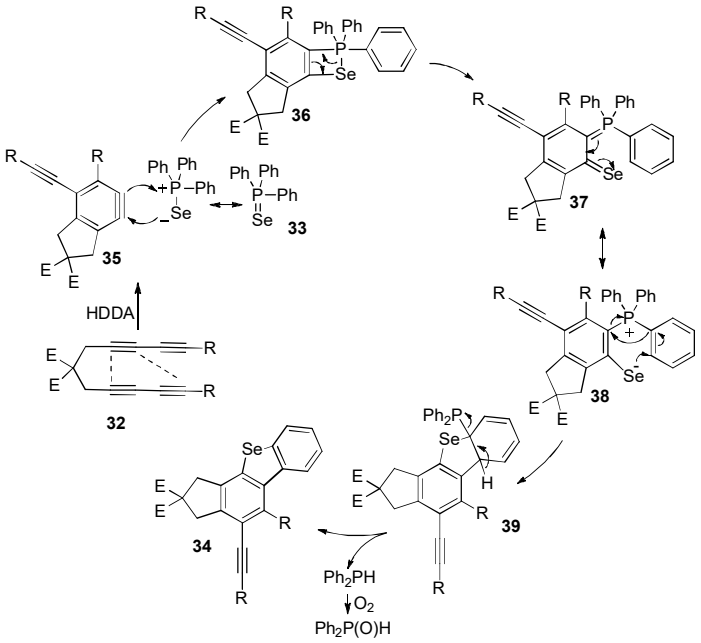
In 2019, Hu and coworkers described a strategy to prepare multifunctional seleno-containing compounds based on reactions between tetraynes **32** and triphenylphosphine selenide **33**.[46] This new methodology was capable to produce various 2,3-dihydro-1*H*-benzoindenoselenophenes **34** *via* a one-pot cascade cycloaddition reaction. According to the authors, the benefits of this protocol are the preparation of fused cycles without the necessity of catalysts, oxidants, bases or metals, besides the good regioselectivity to generate the expected products in very good yields. Scheme 15 shows that electron-withdrawing and electron-donating groups attached to the aryl ring of the tetraynes are compatible with the reaction conditions and gave the products in similar results.



R^1= Me, Et, *i*Pr; R^2= C_6H_5, 4-FC_6H_4, 4-MeC_6H_4, 4-ClC_6H_4, 4-EtC_6H_4, 4-PrC_6H_4, 3-MeC_6H_4;

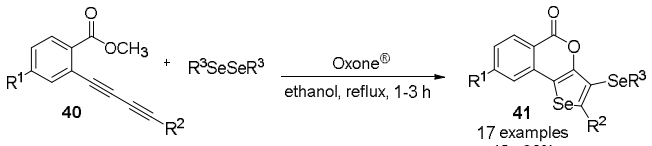
Scheme 15. Synthesis one-pot of fused benzoselenophenes **34**.

A plausible mechanism for the formation of dibenzoselenophenes **34** is shown in Scheme 16.[47-49] Firstly, the aryne intermediate **35**, that was generated *via* the hexadehydro-Diels-Alder (HDDA) reaction of tetrayne **32**, reacts with the negatively charged selenium of the phosphorus ylide at the least hindered carbon atom. This reaction produces the four-membered ring intermediate **36**, which is converted to the intermediate **37** *via* a 4π-electrocyclic ring-opening reaction involving the breaking of the P-Se bond. The active intermediate **37** (in resonance with **38**) then undergoes an intramolecular nucleophilic addition reaction to form **39**. Finally, the aromatic system is restored and generates the desired compound **34** by releasing $HP(Ph)_2$, which is oxidized to $(Ph)_2P(O)H$.



Scheme 16. Proposed mechanism to prepare fused dibenzoselenophenes **34.**

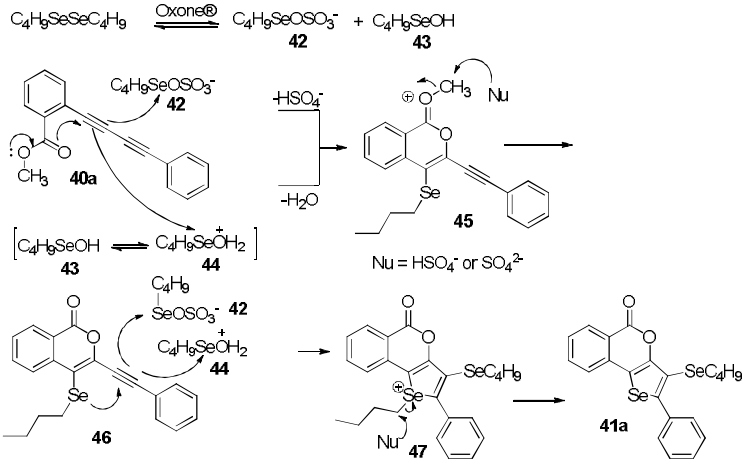
In 2019, Perin and coworkers described for the first time the synthesis of isochromenone-fused selenophenes.[50] The compounds 5*H*-selenopheno[3,2-*c*]isochromen-5-ones **41** were prepered through a double intramolecular cyclization reaction of diynes **40** with electrophilic selenium species, generated *in situ* from the reaction of dialkyl diselenides with Oxone®. These reactions were conducted in ethanol as solvent at reflux temperature and gave the heterocycles after 1 to 3 h. A range of 1,3-diynes and dialkyl diselenides were used as substrates, and seventeen compounds **41** were selectively obtained in moderate to good yields (40-86%) (Scheme 17).



R^1= H, F; R^2= C_6H_5, 4-$MeOC_6H_5$, 2-$MeOC_6H_5$, 4-MeC_6H_5, 2-MeC_6H_5, 4-ClC_6H_5, 2-$MeCO_2C_6H_5$, *n*-C_4H_9, 1-naphthyl; R^3= *n*-C_4H_9, C_2H_5, C_8H_{17}

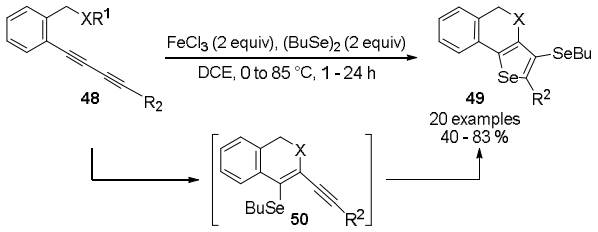
Scheme 17. Synthesis of 5*H*-selenopheno[3,2-*c*]isochromen-5-ones **41**.

To propose a plausible mechanism, the authors performed several control experiments. Firstly, the reaction was conducted in the presence of radical inhibitors, and the results suggest that a radical pathway is not involved in the reaction. Also, several reactions were performed and analyzed by ^{77}Se NMR, which was useful to determine some intermediate species. First of all, the diselenide reacts with Oxone® to form two intermediates: **42** and **43**.[51] The species **43** can react with H^+ from the reaction medium, leading to $C_4H_9SeOH_2^+$ **44**. The intermediates **42** and **44**, the most probably active electrophiles in the reaction medium,[52] interact with substrate **40a** leading to the cyclic intermediate **45**, releasing HSO_4^- and H_2O. The displacement of the methyl group from **45** by a nucleophile, affords the intermediate **46**. Following, this specie reacts in the same way with **42** and **44** to give the fused-selenophene cation intermediate **47**. The displacement of the butyl group from the selenonium cation **47** affords the desired product **41a** (Scheme 18).



Scheme 18. Proposed mechanism to prepare the compounds **41**.

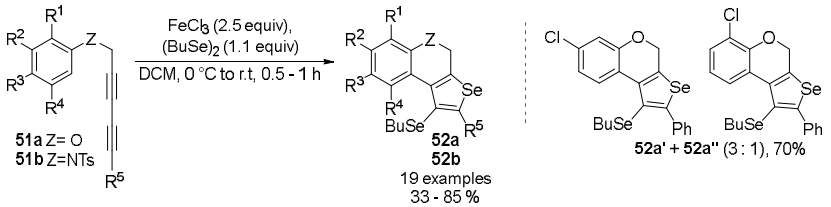
Zeni and coworkers also studied cascade cyclization reactions using the iron(III) chloride/dialkyl diselenide system. In a first report, *ortho*-diynyl benzyl chalcogenides **48** were used as starting materials to obtain isochromene-fused selenophenes **49**.[53] This work shows a double cyclization followed by the functionalization at the 3-position of the selenophene ring, in a one-pot procedure. In the first step, the intramolecular cyclization generates the intermediate 3-ethynyl-4-(butylselanyl)-isochalcogenochromene **50**, which undergoes a second cyclization to produce the three fused ring **49** (Scheme 19). According to the authors, the capability of iron(III) chloride to generate both electrophilic and nucleophilic selenium species from dialkyl diselenide is crucial for the success of the reaction. Additionally, they also highlighted the syntheses of new selenoisochromene-fused tellurophenes bearing a butyl telluride as substituent by replacing dibutyl diselenide by dibutyl ditelluride as reagent.



R^1= Me, Bu; R^2= C_6H_5, 2-MeC_6H_4, 3-MeC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 2-ClC_6H_4, 4-ClC_6H_4, 4-FC_6H_4, 3-$MeOC_6H_4$, 2-naphthyl, 2-thienyl; X= Se, O

Scheme 19. Synthesis of selenophene-fused isochalcogenechromenes mediated by $FeCl_3$.

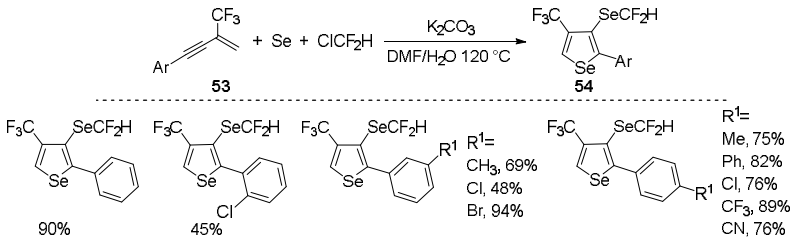
In 2020, Zeni and coworkers explored the cascade synthesis of selenophene-fused chromenes **52a** (Z=O) using 1,3-diynyl propargyl aryl ethers **51a**, iron(III) chloride and dibutyl diselenide in DCM as the solvent, at room temperature.[54] The same reaction conditions were applied to propargyl *N*-tosyl-anilines **51b**, leading to the formation of selenophene-fused dihydroquinolines **52b** (Z=NTs) (Scheme 20). The dropwise addition of the reagents **51** solubilized in CH_2Cl_2 to a previously prepared solution containing $FeCl_3$ and BuSeSeBu at 0 °C under argon atmosphere, proved to have a crucial influence in the product formation in good yields. It was described that the regioselectivity of the nucleophilic attack of the aromatic ring on the alkyne can be orientated by steric factors, once a 3:1 mixture of products **52a'** and **52a''** is obtained when a *meta*-substituted (R^1=H and R^4=Cl) aryl group directly bonded to the oxygen atom is used.



R^1= H, Me, *t*-Bu, I, Br; R^2= H, Cl; R^3= H, C_6H_5, OMe, I, Me, F; R^4= H, Cl; R^5= C_6H_5, 4-MeC_6H_4, 4-$MeOC_6H_4$, 2-$MeOC_6H_4$, 4-ClC_6H_4, 2-BrC_6H_4, 3-MeC_6H_4, 2-naphthyl

Scheme 20. Cascade synthesis of selenophene-fused chromenes and quinolines.

A radical strategy to construct highly functionalized selenophenes and thiophenes was described by Song and coworkers in 2020.[55] Specifically for selenophenes **54**, this work describes a multicomponent reaction of [(3-trifluoromethyl)but-3-en-1-yn-1-yl]arenes **53** with 4 equiv. of elemental selenium in an atmosphere of chlorodifluoromethane (freon gas). The reaction is conducted in the presence of K_2CO_3 as base and in a mixture of DMF:H_2O (20:1) as solvent and proton source, at 120 °C. The 2-aryl-3-$SeCF_2H$-4-CF_3-selenophenes **54** were obtained in yields ranging from 45% to 94% (Scheme 21).



Scheme 21. Synthesis of $SeCF_2H$-substituted selenophenes **54**.

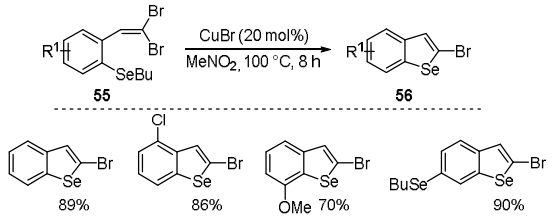
2.3. Starting from vinyl bromides bearing an organoselenium substituent

In addition to alkynes, *gem*-dihaloalkenyl arenes have also demonstrated to be suitable starting materials to prepare a diversity of heterocycles, including thiopehenes, furans and indoles, *via* transition metal-catalyzed intramolecular cyclization reactions.[56]

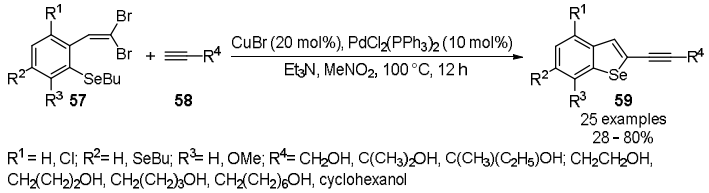
In this regard, Zeni and coworkers reported their results on the copper-catalyzed reaction of *gem*-dibromovinyl selenides **55** to prepare 2-bromo-benzo[*b*]selenophenes **56**.[57] During the optimization of the reaction conditions, CuBr (20 mol%) proved to be the ideal catalyst in nitromethane as the solvent at 100 °C, under inert atmosphere for 8 h. By using these reaction conditions, the authors prepared four benzoselenophenes **56** in good to excellent yields (Scheme 22).

Thereafter, the challenge to promote a sequential cyclization/Sonogashira-type cross coupling reaction was faced by the authors. Typically, Sonogashira-type cross-couplings are conducted using a cooperative palladium/copper-catalyst system under basic conditions.[33-35] In this case, the authors found $PdCl_2(PPh_3)_2$ (10 mol%), CuBr (20 mol%) in the presence of Et_3N as base, and $MeNO_2$ as solvent at 100 °C, to be the best

conditions to synthesize 2-alkynylbenzo[*b*]selenophenes **59** from *gem*-dibromovinyl selenides **55** (Scheme 23). Under these conditions, 25 products were obtained in moderate to good yields. The lability of the Csp^2-Se bond for cross-coupling reactions in the presence of palladium and copper salts did not affect the intramolecular ring closure, and undesired coupling products were not detected. It should be noted that only alkynes **58** bearing an alcoholic group were suitable substrates for this reaction. Phenylacetylene and 1-pentyne were not good substrates in this protocol, giving the expected products together with an inseparable mixture of homocoupling byproducts.

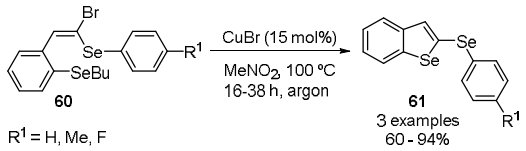


Scheme 22. Copper-catalyzed synthesis of 2-bromoselenophenes **56**.



Scheme 23. Pd/Cu-catalyzed cooperative synthesis of 2-alkynylbenzo[*b*]selenophenes **59**.

In 2018, Perin, Lenardão and coworkers developed an efficient protocol to prepare 2-arylselanylbenzo[*b*]selenophene **61** derivatives through the Cu(I)-catalyzed annulation of vinyl selenides **60**.[58] The key starting vinyl selenides **60** were easily prepared from properly functionalized 1,1-dibromostyrenes. When these starting materials were placed in a reaction system containing 15 mol% of CuBr as catalyst and nitromethane as solvent at 100 ºC under argon atmosphere, benzo[*b*]selenophenes **61** were obtained in 60% to 94% yield (Scheme 24). The authors also focused on the preparation of 2-chalcogenylfurans and thiophenes, demonstrating the versatility of the developed methodology.

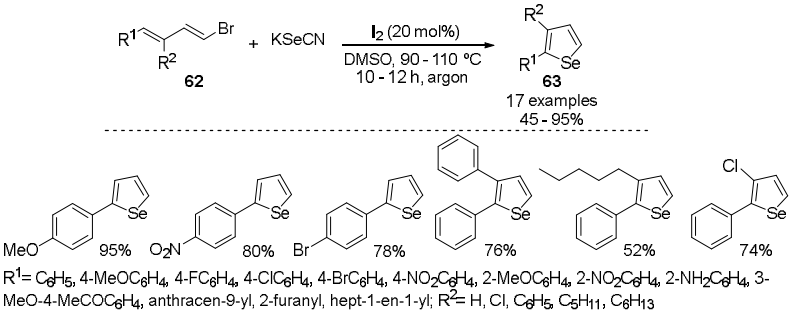


Scheme 24. Cu(I)-catalyzed synthesis of 2-arylselanylbenzo[*b*]selenophenes **61**.

2.4. Starting from vinyl bromides and an external selenium source

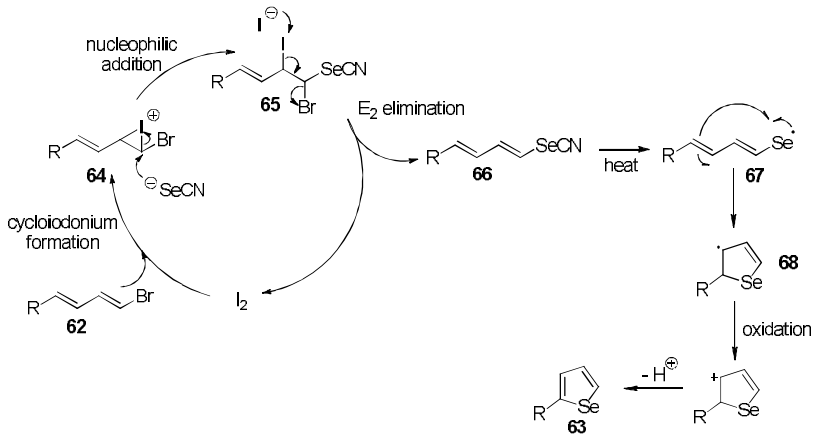
Notably, vinyl bromides have shown to be versatile substrates to construct selenophene-containing compounds in the presence of an external selenium source. In this context, in 2017 Maitya and Ranu described a transition metal-free iodine-catalyzed reaction between 1,3-dienyl bromides **62** and KSeCN to synthesize 2-aryl-selenophenes **63**.[59] The standard condition uses 20 mol% of iodine as catalyst and DMSO as solvent, with temperatures ranging between 90 and 110 ºC for up to 12 h, as presented in Scheme 25. A variety of differently substituted 1,3-dienyl bromides **62** underwent selenylation followed by cyclization reaction to produce the corresponding target products **63**. For example, starting materials with electron-donating (OMe) or electron-withdrawing (NO_2) groups afforded the corresponding 2-arylselenophenes in good yields. Halogen-substituted (R^1=C_6H_4F, C_6H_4Cl and C_6H_4Br)

[(1*E*,3*E*)-4-bromobuta-1,3-dien-1-yl]benzenes **62** also provided the corresponding selenophenes in excellent yields. Furthermore, reactions with 1,3-dienyl bromides having aryl, alkyl and halogen substituents on the internal vinyl carbon (R^2) were successfully employed to produce the corresponding 2-phenyl-3-substituted-selenophenes **63**.



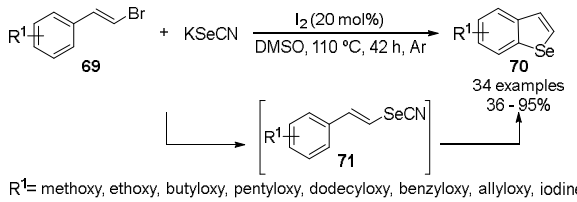
Scheme 25. Synthesis of selenophenes **63** employing 1,3-dienyl bromides **62** and KSeCN.

Based on several experiments, the authors proposed a probable reaction pathway to the selenophene formation, as depicted in Scheme 26. Initially, the starting material 1,3-dienyl bromide **62** reacts with iodine to form an iodonium ion **64**, which undergoes a nucleophilic attack by $NCSe^-$ to furnish the intermediate **65**. This intermediate produces the corresponding *trans*-1,3-dienyl selenocyanate **66** *via* a E_2 elimination and I_2 is regenerated to the system. In the next step, selenocyanate **66** is homolytically cleaved to afford the 1,3-dienyl selenium radical **67**, which is trapped by the styrene double bond to provide the five-membered cyclic intermediate **68**, that leads to selenophene **63** through an oxidation and H^+ elimination steps.



Scheme 26. Mechanism of the preparation of 2-aryl-selenophenes **63**.

The preparation of benzo[*b*]selenophenes also received the attention of Ranu and coworkers, who developed the reaction of electron-rich styryl bromides **69** with KSeCN in the presence of catalytic I_2 (20 mol%) for 42 h.[60] Electron-rich styryl bromides bearing alkoxy groups in the aryl ring were used to synthesize 34 highly substituted benzoselenophenes **70**, *via* intermediacy of styryl selenocyanates **71** (Scheme 27). The presence of iodine at the *meta*-position of the benzene ring was also tolerated, whithout be affected by the reactiom media. However, when *ortho*-iodo-substituted styryl bromides were used, a mixture of regioisomeric selenophenes was obtained.

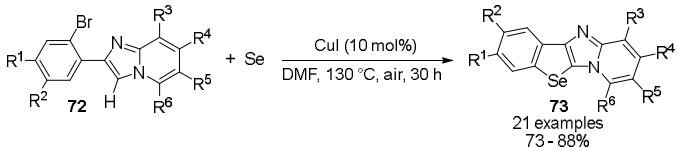


Scheme 27. Synthesis of benzoselenophene **70** from styryl bromides **69** and KSeCN.

2.5. C-H bond functionalization of (hetero)arenes by an external selenium source

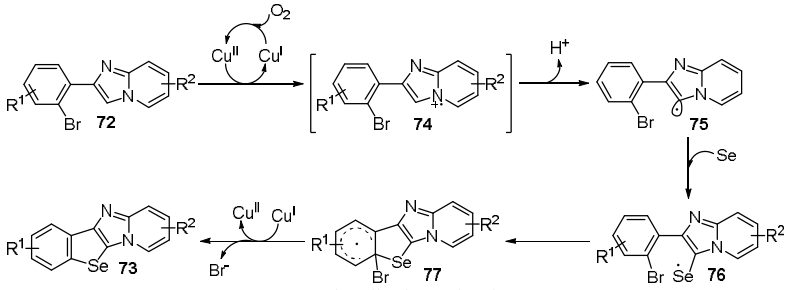
The transition metal-catalyzed inter- and intramolecular cyclization reactions are a powerful tool widely used in organic synthesis for the construction of a variety of carbocyclic and heterocyclic compounds.[61,62] More specifically, copper salts have been used as catalysts in a large number of cases including mostly intramolecular C-C, C-N and C-S bond formations.[63,64]

In 2017, Yang, Wang and coworkers reported the copper(I)-catalyzed direct selenylation reaction of 2-(2-bromoaryl)imidazo[1,2-*a*]pyridines **72** with selenium powder to produce imidazo[1,2-*a*]pyridine-fused benzo[*b*]selenophene derivatives **73**.[65] The reaction is conducted in DMF as solvent at 130 °C for 30 h (Scheme 28). The products were obtained in moderate to good yields, and no clear evidences of electronic or steric effects affecting the product formation were observed. Additionaly, 6-(2-bromophenyl)imidazo[2,1-*b*]benzo[*d*]thiazole also showed to be a suitable substrate for this transformation.



Scheme 28. Copper-catalyzed synthesis of imidazo[1,2-*a*]pyridine-fused benzo[*b*]selenophene **73**.

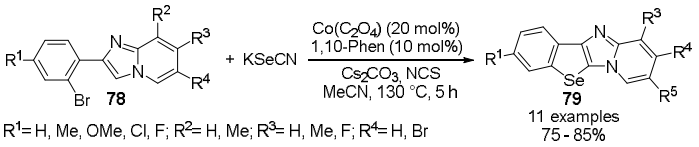
In this reaction, the regioselective cleavage of Csp^2-Br and Csp^2-H bonds *via* a radical pathway is responsible for the formation of two new C-Se bonds to generate the selenophene core. According to the authors, insights to the mechanism proposal came from electron spin resonance (ESR) spectra and six control experiments: (i) the reaction conducted in the presence of TEMPO suppressed the formation of the selenophene; (ii) molecular oxygen is necessary once the expected product is not observed when the reaction is conducted under nitrogen atmosphere; (iii) in the absence of CuI, no product is formed; (iv) a diorganyl disselenide is obtained when 2-phenyl-imidazo[1,2-*a*]pyridine and elemental selenium react under the optimal conditions; (v) the formation of a trapping product was detected by GC-MS analysis when 2 equiv. of TEMPO was used, suggesting that **75** (Scheme 29) is possibly the key intermediary and (vi) when 3-bromo-2-(2-bromophenyl)-imidazo[1,2-*a*]pyridine was used as reactant, no product was formed.



Scheme 29. Proposed radical mechanism to prepare **73**.

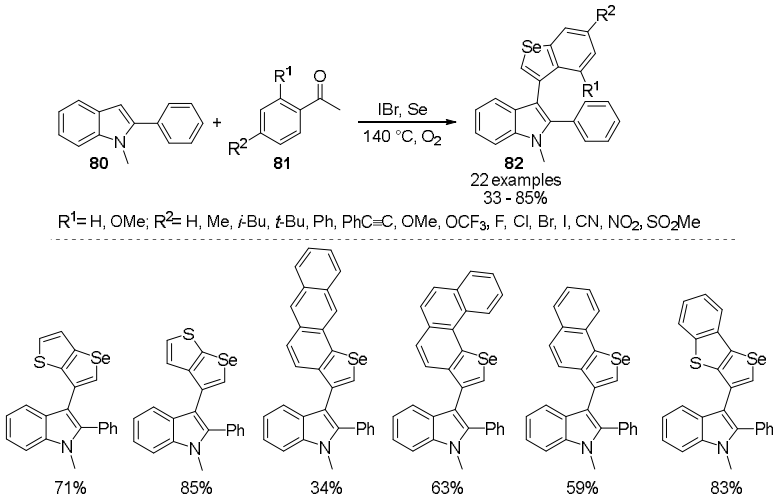
The proposed mechanism involves firstly the oxidation of the Cu(I) species to Cu(II) by molecular oxygen. Then, a single electron transfer (SET) takes place between **72** and Cu(II) to furnish the radical cation **74** which loses a proton to give the radical intermediate **75**. This intermediate reacts with elemental selenium to give **76** and subsequently **77**. Then, bromide abstraction mediated by Cu(II) occurs to produce the expected product **73** and release a Cu(II) species (Scheme 29).

Alternativelly to the use of copper catalysis, the preparation of benzo[*b*]selenophene-fused imidazo[1,2-*a*]pyridines **79** using cobalt(II) oxalate (20 mol%) as an inexpensive and commercial available catalyst was reported by Jiang, Xu and coworkers.[66] Potassium selenocyanate was employed as selenium source, 1,10-phenantroline (10 mol%) as ligand, *N*-chlorosuccinimide (NCS) as an additive and Cs_2CO_3 as base in acetonitrile at 130 °C. In this case, eleven differently substituted 2-(2-bromoaryl)-imidazo[1,2-*a*]pyridines **78** were reacted with KSeCN to give the expected products in up to 85% yield. Both electron-donating and electron-withdrawing groups were tolerated under the standard reaction conditions, giving the new selenophene ring in good yields. The synthesis of benzo[*b*]selenophene-fused imidazo[2,1-*b*]thiazole was also achieved in 74% yield (Scheme 30).



Scheme 30. Cobalt-catalyzed synthesis of benzo[*b*]selenophene-fused imidazo[1,2-*a*]pyridines **79**.

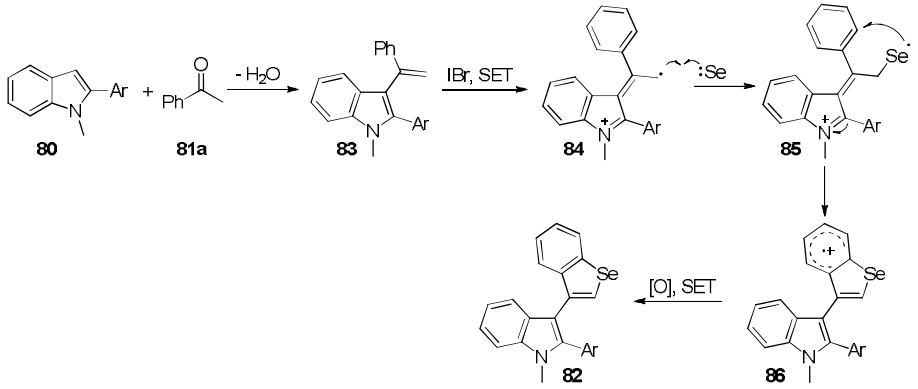
A metal-free process to the construction of 3-indole-benzo[*b*]selenophenes **82** was presented by Xiao, Deng and coworkers in 2019.[67] Their strategy was based on a multicomponent [4+1]-cycloaddition reaction using indoles **80**, acetophenones **81** and selenium powder as reagents. For this purpose, several iodine containing compounds were investigated and IBr (1.2 equiv.) proved to be the most suitable oxidant agent. The reactions were conducted in *N*-methyl-2-pyrrolidone (NMP) as solvent at 140 °C under O_2 atmosphere. Acetophenones **81**, bearing different strong electron-donating or electron-withdrawing groups at the *para*-position were well tolarated, giving 22 examples of benzo[*b*]selenophenes **82** in 33% to 85% yields, as shown in Scheme 31.



Scheme 31. Synthesis of 3-indole-benzo[*b*]selenopehens **82** under metal-free conditions.

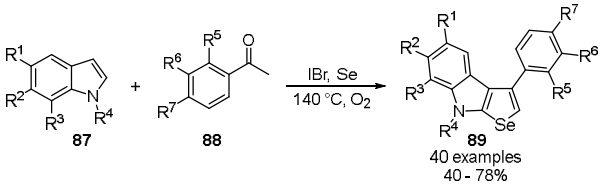
The authors also highlighted that halogen substituents on the phenyl ring are suitable for this transformation. Still, according to the authors, *meta*-substituted acetophenones gave a near 1:1 mixture of regioisomers. To complete the investigation, differently substituted indoles were explored in the presence of acetophenone under the optimal reacion conditions, and additionally 18 new 3-indole-benzo[*b*]selenophenes **82** were obtained in moderate to good yields. Limitations in the methodology were observed for indoles C-2 substituted by alkyl, silyl, ester and alkynyl groups, and largerly sterically hindered aromatic fused rings. Also, propiophenone and aliphatic ketones did not give the desired products (Scheme 31).

According to the authors, the reaction mechanism has the vinyl substrate **83** as the key intermediate, which is generated by dehydrative condensation between **80** and **81a**. Then, a dual C-H oxidative selenylation proceding through a free radical pathway is belived to occur. First, the vinyl radical intermediate **84** is generated *via* a single electron transfer (SET). Following, the intermediate **84** reacts with selenium to give the selenium-centered free radical **85**, which through an intramolecular cyclization is converted to **86**. The oxidation of **86** furnishes the final product **82** (Scheme 32).



Scheme 32. Possible reaction mechanism for the formation of **82**.

In 2019, Huang, Deng and coworkers explored the same strategy to synthesize fused selenophene[2,3-*b*]indoles **89**.[68] To achieve this goal, indoles **87**, acetophenones **88** and elemental selenium were used as substrates in a tandem alkenylation/C-H oxidative selenylation process. Acetophenones and indoles containing EDG and EWG substituents were explored and well tolerated by the reaction conditions, giving the selenophenes **89** in 40% to 78% yield (Scheme 33). According to the authors, an unexpected result was obtained when a methyl group at the C-4 position of indole was present, which almost prevents the product formation, and only trace amounts were detected.

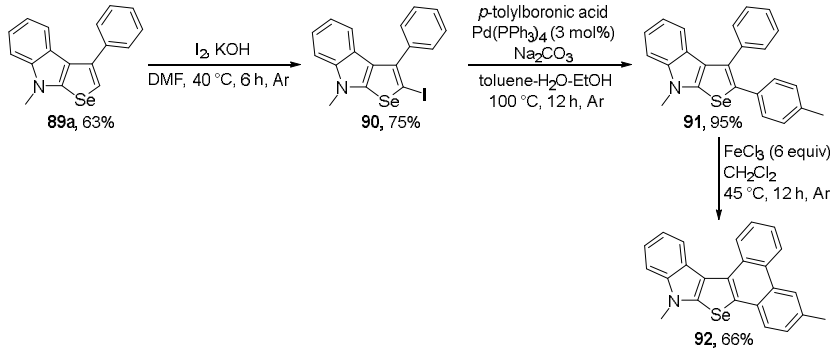


R^1= H, Me, OMe, Br; R^2= H, Me, Cl; R^3= H, Me; R^4= H, Me, Et, Bn; R^5= H, OMe, F, Cl; R^6= H, OMe, F, Cl, Br, CF_3, NO_2; R^7= H, Me, Ph, CO_2Me, OMe, OCF_3, F, Cl, Br, I, CN, NO_2, SO_2Me

Scheme 33. Reaction conditions to obtain selenophene[2,3-*b*]indoles **89**.

The authors also depicted a synthetic application of these selenophene[2,3-*b*]indoles **89** in the preparation of 6,10-dimethyl-10*H*-phenanthro[9',10':4,5]selenopheno[2,3-*b*]indole **92** (Scheme 34).[68] The compound **92** was obtained in three reaction steps: in the first one, the selenophene[2,3-*b*]indole **89a** reacts

with molecular iodine in DMF under argon atmosphere to give the iodinated product **90** in 72% yield. In the second step, compound **90** reacts with *p*-tolylboronic acid using $Pd(PPh_3)_4$ (3 mol%) as catalyst in a Suzuki-Miyaura cross-coupling reaction to afford **91** in 95% yield. Finally, product **92** is obtained in 66% yield by a dehydrogenative annulation of **91** using $FeCl_3$.



Scheme 34. Synthesis of the phenanthro-selenophene-indole **92**.

3. Reactivity and application of selenophenes

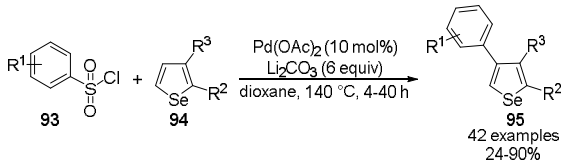
This section will deliver the recent applications of selenophenes in the synthesis of highly functionalized π-conjugated systems, through the transition metal-catalyzed olefination, intra- or intermolecular arylations and in the heteroacenes preparation.

3.1. Pd-catalyzed C-H bond functionalization

Classical transition metal-catalyzed cross-coupling reactions such as Suzuki-Myaura, Negishi, Stille and Kumada, for example, represent the most reliable methods to access highly functionalized heteroarenes. These methodologies, however, require preactivated starting materials, and an organoboron or organometallic reagent as partner, which is frequently difficult to produce. In this sense, methods that avoid tedious multistep processes and large waste generation have received attention in the last years, and in this scenario, the direct C-H bond functionalization appeared as a promising field of research in the chemistry of heterocycles.[32,69]

In the regards of selenophenes, Mori, Koumura and coworkers reported the first Pd-catalyzed direct C5-arylation of 2-formylselenophenes,[70] while Schneider and coworkers reported their results on the C2-arylation of selenophenes in a reaction catalyzed by palladium(II) acetate.[71]

Direct C-3 or C-4 arylation of selenophenes **94** through a desulfitative coupling reaction was reported by Doucet and coworkers, using arylsulfonyl chlorides **93** as aryl source.[72] Using $Pd(OAc)_2$ (10 mol%) as catalyst in the presence of Li_2CO_3 (6 equiv.) as base in dioxane at 140 °C, 42 derivatives were synthesized in 24% to 90% yield. This regiospecific β-arylation of selenophenes tolerates a wide variety of substituents, both on the arylsulfonyl chloride **93** and on the selenophene **94**, as depicted in Scheme 35.

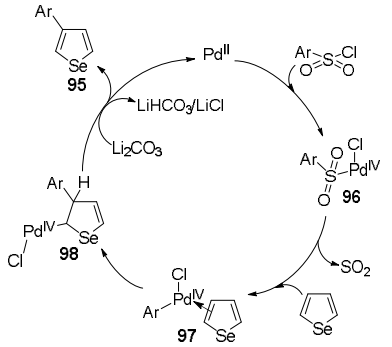


R^1 = H, 4-NO_2, 4-CN, 4-CF_3, 4-Cl, 4-F, 4-Me, 4-C(Me)$_3$, 4-OMe, 3-CF_3, 3-Cl, 3-F, 2-NO_2, 2-CN, 2-Cl, 3,4-di-F, 3,4-di-OMe, 3,5-di-CF_3, 3,5-di-Cl, 2-Cl-4-F, 2,4-di-F, 2,3,4-tri-F, 3,4-di-F, 2-Cl-4-F, 3,4-di-Br, 4-I, 4-Br, 2-Br, 2-Et-4-Br, 2-Br-5-CF_3, 2-Br-4-F, 2-Br-4,6-di-F, 3,4-di-Br, 2,5-di-Br, 4-I;
R^2= H, 4-ClC_6H_4, 4-MeCOC_6H_4, 4-MeC_6H_4, 4-PhC_6H_4, Br; R^3= H, 4-MeOC_6H_4

Scheme 35. Palladium-catalyzed *β*-arylation of selenophenes.

The behavior of several (poly)halobenzenesulfonyl chlorides containing F, Cl, Br, and I was investigated in the coupling with selenophenes. Although C-halogen bonds are very sensitive to cleavage in the presence of palladium catalysts, the authors emphasized that the expected coupling products **95** were selectively obtained. The regioselectivity of the arylation was also investigated conducting reactions using 2- or 3-substituted selenophenes. In all cases, the only product detected corresponds to the arylation at the C4-position of the selenophene (Scheme 35).

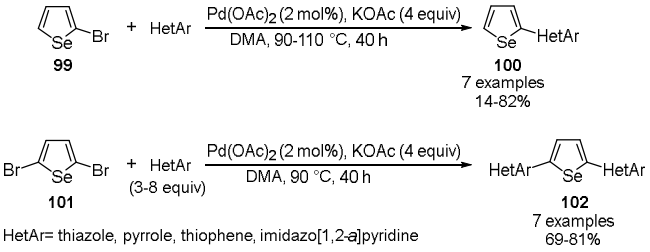
A catalytic cycle was proposed which begins with the oxidative addition of the $ArSO_2Cl$ to the Pd(II) species to afford the Pd(IV) intermediate **96**. Afterward, the elimination of SO_2 occurs, which allows the coordination of selenophene to Pd(IV) atom to produce the intermediate **97**. Then, a selenophene C2-Pd(IV) bond formation, with subsequent migration of the aryl group to the C-3 atom, generates **98**. Finally, a base-assisted proton abstraction gives the 3-aryl-selenophene **95** with the regeneration of Pd(II) species (Scheme 36). The authors also commented that a Heck-type Pd(0)/Pd(II) mechanism, or a base-assisted E_2 elimination are possible pathways.



Scheme 36. Proposed mechanism for the Pd-catalyzed *β*-arylation of selenophenes.

In 2014, Wipf and coworkers demonstrated an effective Pd-catalyzed heteroarylation reaction of 2,5-dibromoselenophene with ethyl-oxazole-4-carboxylate, providing the linked 5-membered heterocycle in 45% yield.[73] The electron-withdrawing nature of the ester group proved to be essential for the reactivity of the oxazole and, especially for the activation of the C-2 carbon-hydrogen bond, when compared to the ethyl 5-oxazole carboxylate, that gave the bis-coupled product in only 5% yield.

More recently, Doucet and coworkers described their results on the preparation of heteroarylated selenophenes **100** and **102** using 2-bromo-selenophene **99** and 2,5-dibromoselenophene **101** in palladium-catalyzed coupling reactions with electron-rich thiazoles, thiophenes, *N*-protected pyrrole and imidazo[1,2-*a*]pyridine.[74] The reactions were catalyzed by 2 mol% of $Pd(OAc)_2$ in the presence of an excess of KOAc in DMA at 90-110 °C (Scheme 37).

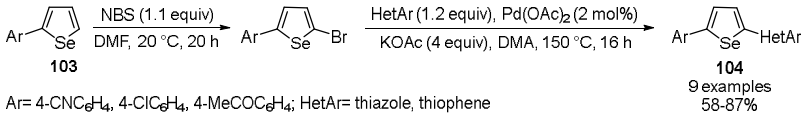


Scheme 37. Heteroarylation of 2-bromo- and 2,5-dibromoselenophenes.

Although good yields were obtained for the reactions using 2-bromoselenophene and thiazole or imidazo[1,2-*a*]pyridine, the cross-coupling reaction was less effective when thiophenes and

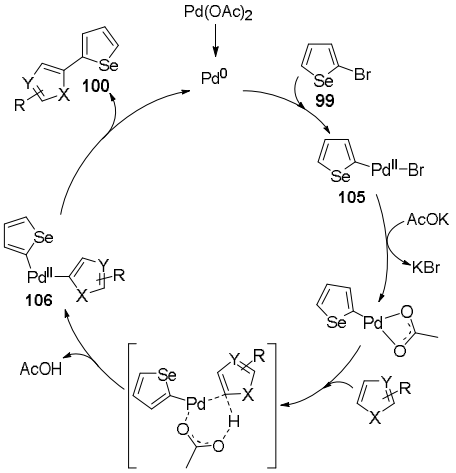
N-phenyl-pyrrole were used. The authors assumed that the higher Gibbs free energies of activation for the cleavage of C-H bonds in thiophene or pyrrole systems may be responsible for the lower reactivity in reactions which proceed *via* a concerted metalation-deprotonation process. On the other hand, the reaction of 2,5-dibromo-selenophene with 3 equiv. of thiazoles and thiophenes gave good yields of the expected symmetrical products. When the reaction was conducted using 1-methyl-pyrrole, a larger excess of this reagent was required, and the 2,5-diarylated selenophene was obtained in 81% yield. The reaction of 2,5-dibromo-selenophene with imidazo[1,2-*a*]pyridine was not presented (Scheme 37).

In the same work,[74] a sequential transformation leading to 2-aryl-5-(heteroaryl)selenophenes **104** was reported. In this case, starting from 2-aryl-selenophenes **103**, previously prepared, a bromination reaction at the C-5 position was described. This was the basis for the sequential heteroarylation reaction catalyzed by palladium to access non-symmetrical thiophene- and thiazole-containing selenophenes **104** in yields ranging from 58% to 87% (Scheme 38).



Scheme 38. Preparation of 2-aryl-5-heteroarylselenophenes **104**.

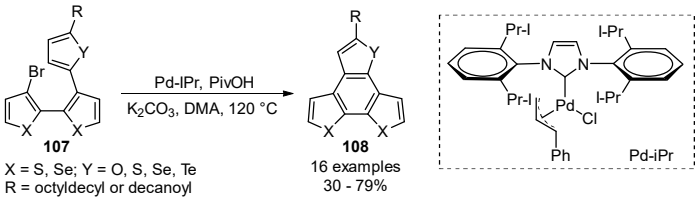
Although the mechanism of this reaction was not well elucidated, the authors made the proposal for a catalytic cycle, as depicted in Scheme 39. The first step suggests the oxidative addition of 2-bromo-selenophene **99** to Pd(0) to afford the Pd(II) intermediate **105**. Then, through a concerted metalation-deprotonation transition state, the intermediate **106** is formed. Afterward, a reductive elimination furnishes the 2-heteroarylated selenophene **100**, while the Pd(0) species is regenerated.



Scheme 39. Catalytic cycle of the palladium-catalyzed heteroarylation of selenophenes.

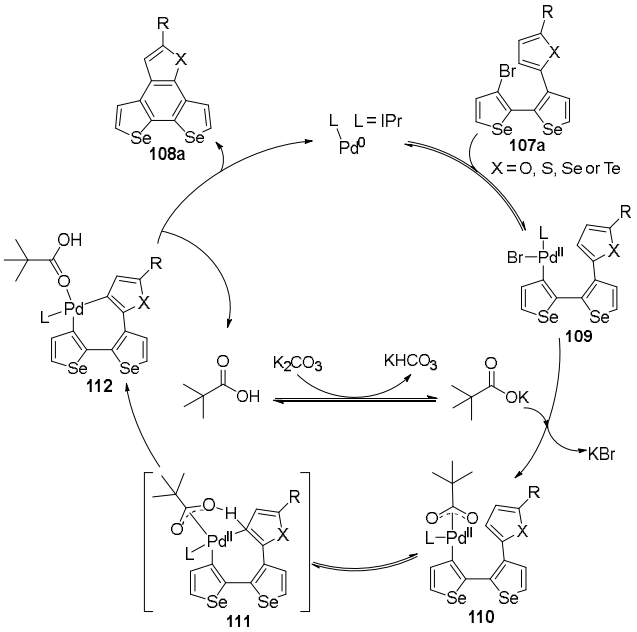
Unsymmetrical benzotrichalcogenophenes **108** were synthesized by Cheng and coworkers through a *N*-heterocyclic carbene-palladium-catalyzed intramolecular direct C-3 arylation.[75] In this case, several 3-bromo-2,2'-bisthiophenes and 3-bromo-2,2'-bisselenophenes **107** containing furan, thiophene, selenophene and tellurophene subunits, were selected as starting materials. The use of conventional palladium catalysts, such as $Pd(OAc)_2$, $Pd(PPh_3)_4$ and $Pd_2(dba)_3$ were not effective in this intramolecular direct C-3 arylation. A previous report had already documented that the C3-arylation of thiophenes was much less effective than C2/C5-arylations.[76] In this work, the *N*-heterocyclic carbene-based palladium catalyst [1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene]chloro[3-phenylallyl]palladium(II) was employed to

carry out a successful intramolecular C-3 arylation of selenophene and thiophene motifs. The reactions were conducted in the presence of pivalic acid as additive, K_2CO_3 as base in DMA at 120 °C for 17 h, affording sixteen new unsymmetrical benzotrichalcogenophenes **108** in yields ranging from 30-79% (Scheme 40).



Scheme 40. Synthesis of unsymmetrical benzotrichalcogenophenes **108**.

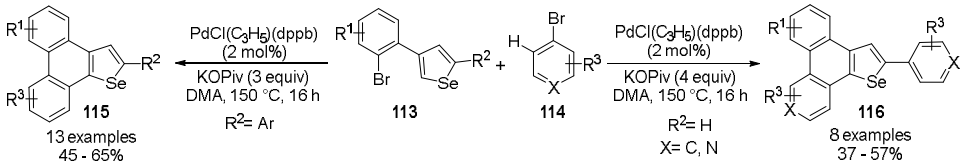
The proposed mechanism involves at first the generation of a Pd(0) species. Next, the oxidative addition of C-Br bond of compound **107a** to Pd(0) occurs to afford the intermediate **109**. A pivalate ion then coordinates to **109** to generate the intermediate **110**, which is converted to **112** *via* the intramolecular concerted metalation-deprotonation transition state **111**. The pivalic acid dissociation, followed by a reductive elimination, regenerates the active Pd(0) species and affords the product **108a** (Scheme 41).



Scheme 41. Proposed mechanism of the Pd-catalyzed intramolecular C-3 arylation.

In 2019, Soulé, Doucet and coworkers focused on the preparation of a phenanthroselenophene series, using palladium(II) as catalyst.[77] The β-(2-bromoaryl)selenophenes **113** used as starting materials were obtained using the procedure previously reported by the same group, by reacting selenophenes with 2-bromoarylsulfonyl chlorides under palladium(II) acetate as a catalyst (see Scheme 35).[72] With these compounds in hand, the authors investigated the one-pot Pd-catalyzed tandem C-5 arylation with aryl bromides **114**, followed by an annulation reaction, to generate the phenanthro[*b*]selenophenes. The best reaction conditions to obtain the phenanthroselenophenes **115** and **116** involved the use of the diphosphine-palladium catalyst [PdCl(C_3H_5)(dppb)] in the presence of KOPiv in DMA at 150 °C for 16 h

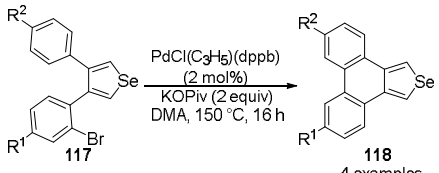
(Scheme 42). The reaction was conducted using aryl bromides **114** substituted with electron-withdrawing groups at *ortho*, *meta* and *para* positions, which furnished the expected products in good yields. The authors suggested that electron-poor aryl bromides are ideal substrates to this reaction, because the oxidative addition of the C-Br bond to Pd(0) is faster when compared to C-Br bond present at the C-4-phenyl unit of selenophene **113**. When electron-rich aryl bromides were used as starting materials, a complex mixture, without the formation of the desired product, was observed. When a larger amount of KOPiv was used in the presence of the same Pd(II) catalyst (2 mol%), 3-(2-bromophenyl)selenophene (**113a**, R^1=R^2=H) was diarylated at the C-2 and C-5 positions giving the phenanthroselenophenes **116** *via* a threefold C-H bond arylation.



R^1= H, 4-CF_3, 3-F; R^2= 4-ClC_6H_4, 4-MeC_6H_4, 2-naphtyl, 4-pyridine; R^3= 4-CN, 4-CF_3, 4-COC_2H_5, 4-F, 4-Cl, 3-CF_3, 2-CN, 2-CF_3

Scheme 42. Synthesis of phenanthroselenophenes **115** and **116**.

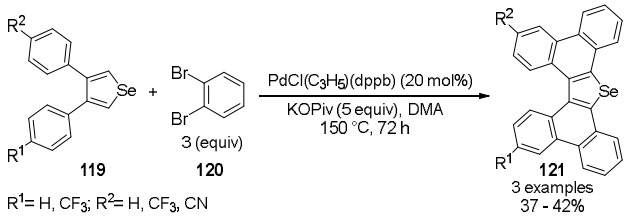
Starting from the 3,4-diarylselenophenes **117** as starting materials, in which one of the aryl group is a 2-bromoaryl, the Pd(II) catalyzed formation of phenanthro[*c*]selenophenes **118** was evaluated.[77] The annulative conditions for the reaction are using $PdCl(C_3H_5)(dppb)$ (2 mol%), KOPiv (2 equiv.), in DMA as solvent at 150 °C for 16 h. Under the optimal conditions, 4 examples bearing different functional groups on the aryl unit, such as CN, NO_2, CH_3O, and CF_3 were obtained (Scheme 43).



R^1= H, CF_3; R^2= H, CN, NO_2, OMe, CF_3

Scheme 43. General route to obtain phenanthro[*c*]selenophenes **118**.

The same strategy was used by the authors to prepare diphenanthro[*b*:*d*]selenophenes **121**, in a one-pot reaction, starting from 3,4-diarylselenophenes **119** and 3 equiv. of 1,2-dibromobenzene **120**. In this case, 20 mol% of the Pd(II) catalyst and 5 equiv. of KOPiv were required, in DMA at 150 °C for 72 h. It is interesting to observe that symmetrical and unsymmetrical diphenanthroselenophenes **121** are possible to be obtained in moderate yields (Scheme 44).

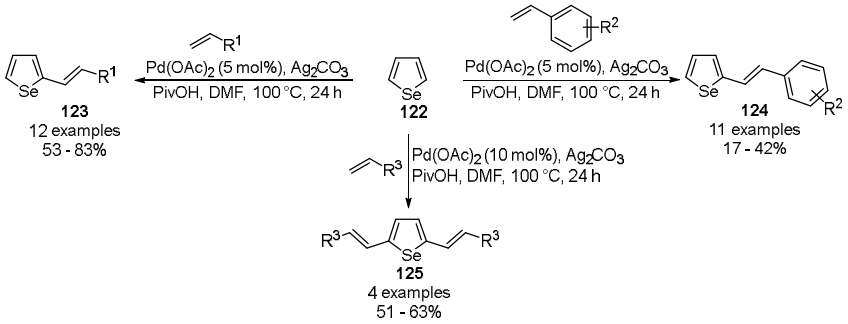


R^1= H, CF_3; R^2= H, CF_3, CN

Scheme 44. Synthesis of diphenanthro[*b*:*d*]selenophenes **121.**

Recently, Cheng and coworkers described their results on the direct dehydrogenative mono- and diolefination of selenophenes catalyzed by palladium(II) acetate.[78] The reactions were conducted using silver

carbonate as oxidant (crucial for the reaction to proceed) and pivalic acid as an additive in DMF as solvent at 100 °C for 24-30 h. This work demonstrates the direct mono-olefination of non-substituted selenophene **122** with carbonyl- and phenyl-substituted olefins, which showed that the reaction yield is dependent on the electron density of the olefins. For instance, electron-deficient olefins containing ester, keto, aldehyde, sulfone, and amide substituents, gave better yields when compared to electron-rich phenyl-substituted ones. Still, the same electronic effect was noticed comparing differently substituted styrenes having electron-donating substituents, such as methyl and methoxy groups, or electron-withdrawing substituents, such as fluoro and nitro groups. The protocol was successfully extended to selenophenes substituted at C-2 and C-3 positions in a direct monoolefination process to prepare highly functionalized products. This reaction allowed the synthesis of fifteen new products and tolerates the presence of bromo, aldehyde, nitrile and alkene as substituents on the selenophene counterpart (Scheme 45).



R^1 = ester, ketone, aldehyde, sulfone, amide; R^2 = H*, 4-Me, 4-OMe*, 3,4-di-OMe*, 4-NO_2, 4-F, 4-Cl, 4-Br, 4-$N(C_6H_5)_2$, 4-C_6H_5*; R^3 = CO_2Me, $CO_2(CH_2)_3CH_3$, C_6H_5, 4-F-C_6H_4

* $Pd_2(dba)_3$ (5 mol%) was used insted of $Pd(OAc)_2$.

Scheme 45. Direct dehydrogenative mono- and diolefination of selenophene.

The proposed mechanism involves the reaction of selenophene **122** with $Pd(OAc)_2$ *via* a concerted metalation-deprotonation process to afford the intermediate **126**. The subsequent elimination of acetic acid furnishes the palladium-selenophene species **127**, which is then coordinated with an olefin to generate **128**. The intermediate **128** undergoes a 1,2-migratory insertion to afford **129** that, after a β-hydride elimination, generates Pd(0) and produces the coupling products **123**, **124** and **125**. Afterward, Ag_2CO_3 in the presence of pivalic acid acts to reoxidize Pd(0) to Pd(II), allowing a new catalytic cycle to occur. The presence of a silver mirror was observed by the authors, highlighting the importance of the silver salt as an oxidizing agent in the reaction (Scheme 46).

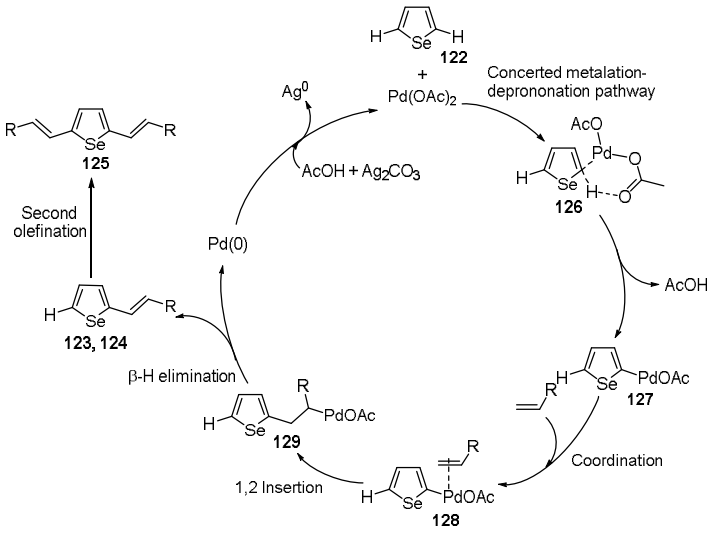
3.2. Preparation of selenophene-based heteroacenes

In recent years, thiophene-based heteroacences have been studied in the field of organic functional materials because of their potential for applications in electronic devices. However, the synthesis, chemical stability and electronic properties of π-conjugated polycyclic molecules containing selenophene rings remain much less explored.[78,79]

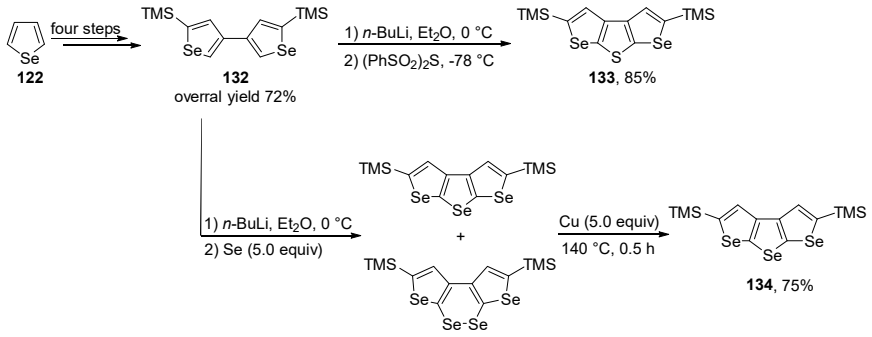
Two selenohelicenes **130** and **131** were synthesized by Wang and coworkers in 2017.[79] The synthetic route includes the preparation of 2,5-dibromoselenophene from selenophene **122** as the first step. Then, through a Br/Li exchange, followed by trimethylsilanyl protection, bromine dance and oxidative coupling using $CuCl_2$, the 5,5'-di(trimethylsilanyl)-3,3'-diselenophene **132** was obtained in around 72% overall yield (Scheme 47). The synthesis of compound **132** was crucial to obtain the triacenes **133** and **134**, after deprotonation using *n*-BuLi, followed by chalcogen capture/cyclization using bis(phenylsulfonyl)sulfide and elemental selenium, respectively.

Substrates **133** and **134** were then allowed to react through a three-step process: monobromination, formylation and McMurry intermolecular reductive coupling, to furnish the alkenes **135** and **136**, respectively. The synthesis of the desired products *rac*-**130** and *rac*-**131** was accomplished through oxidative

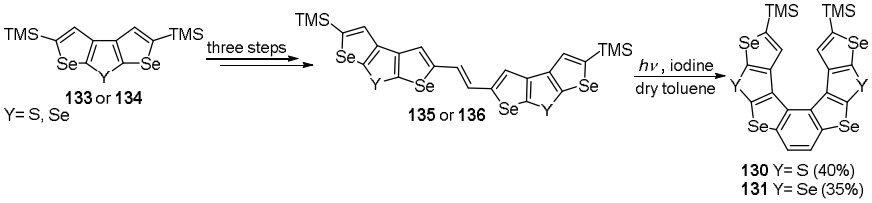
photocyclization reactions in the presence of iodine and benzene as solvent, *via* irradiation with a 450 W Hg medium pressure lamp (Scheme 48). Starting from selenophene **122**, the authors obtained 6.1% and 6.5% total yield for the production of 5,5′-di(trimethylsilanyl)benzo[1,2-*b*:3,4-*b*′]bis-(diseleno[2,3-*b*:3′,2′-*d*]thiophene) **130** and 5,5′-di(trimethylsilanyl)benzo[1,2-*b*:3,4-*b*′]bis-(diseleno[2,3-*b*:3′,2′-*d*]selenophene) **131**, respectively. Crystallographic analysis of the compounds **130** and **131** shows intermolecular interactions type C-Se, C-S and Se-Se in solid state among six and five adjacent molecules, respectively. Still, the helical structures of **130** and **131** demonstrate an interplanar angle of 51.8° and 49.0°, respectively, as result of a repulsion of the facing terminal selenophene rings.



Scheme 46. Catalytic cycle for the direct olefination of selenophene **122**.

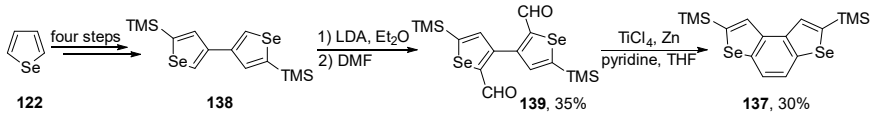


Scheme 47. Synthetic route to produce heteroacenes **133** and **134**.



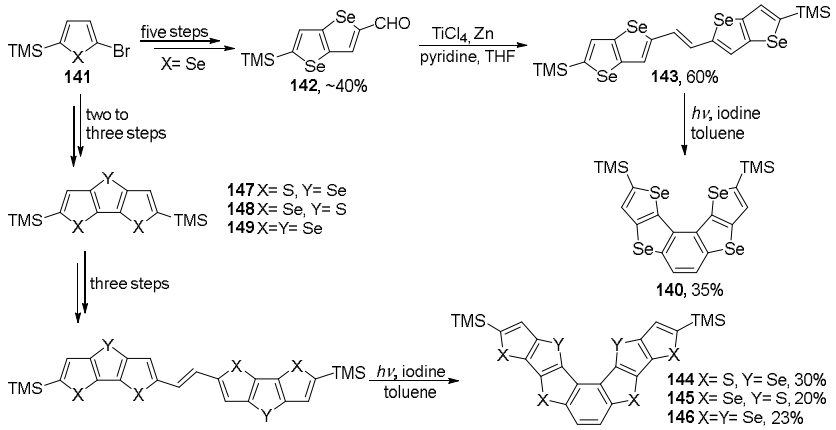
Scheme 48. Synthetic route to prepare [7]helicenes **130** and **131**.

In 2018, Wang and coworkers reported the synthesis of selenophene-based heteroacenes with up to seven fused rings by intramolecular cyclization of dicarbanions and oxidative photocyclization reactions.[80] Scheme 49 demonstrates a multistep synthesis of the three fused-ring selenotriacene **137** that was obtained starting from selenophene unit **122**. After four steps, the compound **138** could be obtained according the method described in Scheme 47.[79] Compound **138** was submitted to a α,α'-deprotonation at the selenophene rings using LDA as base, which was followed by DMF addition to produce the 3,3'-biselenophene-2,2'-dicarbaldehyde **139** in 35% yield. In the last step, a McMurry reaction was conducted using $TiCl_4$, Zn and pyridine to produce the desired product **137** in 30% yield. According to the authors, the total yield was 7.5% after six steps.



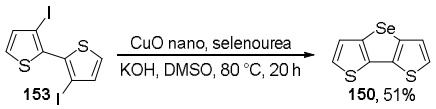
Scheme 49. Multistep synthesis of selenotriacene **137**.

After that, the authors focused on the preparation of the five fused-ring selenoacene **140**. Starting from compound **141** (X=Se), compound **142** was obtained after five steps. These steps included the preparation of a dihalogenated derivative, a Sonogashira cross-coupling reaction and an intramolecular cyclization in the presence of selenium powder to generate the selenopheno[3,2-*b*]selenophene core, which is fundamental to achieve compound **142**. Then, an intermolecular McMurry reaction was conducted to produce the alkene **143** in 60% yield. Finally, the product **140** was isolated in 35% yield through an oxidative photocyclization reaction using a 450 W Hg medium pressure lamp in the presence of iodine in dry toluene for 40 min. The overall yield of **140** was approximately 4% after seven steps (Scheme 50). For the construction of three chalcogenoacenes containing seven fused rings **144-146**, the authors made use of 2-bromo-5-trimethylsilanechalcogenophene **141** (X=S or Se) as starting material. The following reactions, such as deprotonation and treatment with selenium powder or $(PhSO_2)_2S$ as chalcogen sources, gave the valuable building blocks triacenes **147-149**. Next, a sequence of four reactions was conducted, including bromination, formylation, McMurry reaction and photocyclization, to produce the products **144-146** (Scheme 50). The overall yield of compounds **144-146** was described as 0.6%, 3% and 4%, respectively. According to the authors, in the last step, the use of a photoirradiation system was crucial to achieve the synthesis of the fused rings. Also, the authors highlighted that single-crystal X-ray diffraction of compounds **137**, **140** and **146** shown Se···H and Se···C short interactions, which may be a desired property in organic field-effect transistors (OFET).

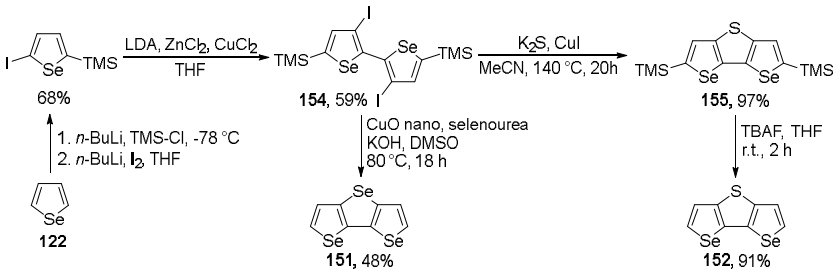


Scheme 50. Synthetic route to prepare chalcogenoacenes containing five and seven fused rings.

The synthesis of heterotriacenes containing selenophene, their structures and packing motifs in the solid state, optoelectronic properties, and electrooxidative polymerization were recently investigated by Bäuerle and coworkers.[81] A multistep synthetic route to produce three heteroacenes **150**-**152** with increasing number of selenium atoms was developed. The selenopheno[3,2-*b*:4,5-*b'*]dithiophene **150** (Scheme 51) and diselenopheno[3,2-*b*:2',3'-*d*]selenophene **151** (Scheme 52) were obtained from diiodinated bischalcogenophenes **153** and **154** through a C-Se cross-coupling/cyclization reaction with selenourea as selenium source and CuO nanoparticles as catalyst. This protocol was firstly reported by Rao and coworkers in the synthesis of symmetrical diaryl selenides.[82] The diselenopheno[3,2-*b*:2',3'-*d*]thiophene **152**, in turn, was synthesized in two steps starting from compound **154**. Firstly, a copper-catalyzed cross-coupling/ring closure reaction using K_2S as sulfur source and CuI as catalyst in acetonitrile was performed, giving product **155** in 97% yield. In the second step, a deprotection reaction was performed using tetrabutylammonium fluoride trihydrate in THF as solvent to give the expected heterotriacene **152** in 91% yield (Scheme 52). It should be noted that the selenium analog **151** was directly obtained from the TMS-protected iodinated biselenophene **154**, without the necessity of a deprotection step. However, parallel dehalogenation reaction was observed as a competitive pathway, decreasing the product yield.



Scheme 51. CuO-catalyzed preparation of selenopheno-fused dithiophene **150**.



Scheme 52. Synthetic route to the synthesis of triacenes **151** and **152**.

4. Conclusions

This chapter provides an up-to-date review of the diverse synthetic methodologies to prepare selenophene rings. These methods include reactions of alkynes and alkenes directly attached to organoseleniun units, and reactions of alkynes, alkenes and activated C-H bonds in aromatic systems with external selenium especies. Among the different selenium sources are seleniun powder, $SeCl_2$, KSeCN and diorganyl diselenides. Reactions involving copper and iron salts, molecular iodine and Oxone® represent the inovative and efficient new findings. These protocols include from direct intramolecular cyclization to intermolecular cascade processes. Additionally, through the use of a selected chemical literature, the most recent approaches regarding the reactivity and synthetic application of selenophenes have been presented. These are mainly focused on the C-H bond functionalization catalyzed by palladium and in the preparation of selenophene-based heteroacenes as precursors of organic functional materials.

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References

1. Tavadyan, L. A.; Manukyan, Z. H.; Harutyunyan, L. H.; Musayelyan, M. V.; Sahakyan, A. D.; Tonikyan, H. G. *Antioxidants* **2017**, *6*, 22.
2. Abdel-Hafez, S. H. *Eur. J. Med. Chem.* **2008**, *43*, 1971-1977.
3. Juang, S.-H.; Lung, C.-C.; Hsu, P.-C.; Hsu, K.-S.; Li, Y.-C.; Hong, P.-C.; Shiah, H.-S.; Kuo, C.-C.; Huang, C.-W.; Wang, Y.-C.; Huang, L.; Chen, T. S.; Chen, S.-F.; Fu, K.-C.; Hsu, C.-L.; Lin, M.-J.; Chang, C.-J.; Ashendel, C.L.; Chan, T.C.K.; Chou, K.-M.; Chang, J.-Y. *Mol. Cancer Ther.* **2007**, *6*, 193-202.
4. Domracheva, I.; Kanepe-Lapsa, I.; Jackevica, L.; Vasiljeva, J.; Arsenyan, P. *Life Sci.* **2017**, *186*, 92-101.
5. Chen, C.-T.; Hsu, M.-H.; Cheng, Y.-Y.; Liu, C.-Y.; Chou, L.-C.; Huang, L.-J.; Wu, T.-S.; Yang, X.; Lee, K.-H.; Kuo, S.-C. *Eur. J. Med. Chem*. **2011**, *46*, 6046-6056.
6. Wiles, J. A.; Phadke, A. S.; Bradbury, B. J.; Pucci, M. J.; Thanassi, J. A.; Deshpande, M. *J. Med. Chem*. **2011**, *54*, 3418-3425.
7. Wilhelm, E. A.; Jesse, C. R.; Bortolatto, C. F.; Nogueira, C. W.; Savegnago, L. *Pharmacol., Biochem. Behav*. **2009**, *93*, 419-425.
8. Grange, R. L.; Ziogas, J.; North, A. J.; Angus, J. A.; Schiesser, C. H. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1241-1244.
9. Wilhelm, E. A.; Jessea, C. R.; Cristiani F. Bortolatto, C. F.; Nogueira, C. W.; Savegnago, L. *Brain Res. Bull.* **2009**, *79*, 281-287.
10. Heller, L.; Sommerwerk, S.; Tzschöckell, F.; Wiemann, J.; Schwarz, S.; Siewert, B.; Al-Harrasi, A.; Csuk, R. *Arch. Pharm*. **2015**, *348*, 889-896.
11. Yamaguchi, S.; Xu, C. H.; Okamoto, T. *Pure Appl. Chem*. **2006**, *78*, 721-730.
12. Yamamoto, T.; Takimiya, K. J. *Am. Chem. Soc*. **2007**, *129*, 2224-2225.
13. Heeney, M.; Zhang, W.; Crouch, D. J.; Chabinyc, M. L.; Gordeyev, S.; Hamilton, R.; Higgins, S. J.; McCulloch, I.; Skabara, P. J.; Sparrowe, D.; Tierney, S. *Chem. Commun*. **2007**, 5061-5063.
14. Meng, D.; Sun, D.; Zhong, C.; Liu, T.; Fan, B.; Huo, L.; Li, Y.; Jiang, W.; Choi, H.; Kim, T.; Kim, Y. J.; Sun, Y.; Wang, Z.; Heeger, A. J. *J. Am. Chem. Soc.* **2016**, *138*, 375-380.
15. Hollinger, J.; Gao, D.; Seferos, D. S. *Isr. J. Chem*. **2014**, *54*, 440-453.
16. Sommen, G. L. *Mini-Rev. Org. Chem*. **2005**, *2*, 375-388.
17. Pelkey, E. T. Selenophenes. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier: New York, **2008**, 975-1006.
18. Logan, M. E.; Lang, M. A.; Detty, M. R. In *The Chemistry Organic Selenium and Tellurium Compounds*; Rappoport, Z. Liebman, J. F.; Marek, I.; Patai, S., Eds.; Wiley: New York, **2014**, Vol. 4, 1279-1360.
19. Vasiljeva, E.; Arsenyan, P. *Chem. Heterocycl. Compd*. **2012**, *48*, 981-992.
20. Schatz, J.; Sessler, M. Selenophenes. In *Science of Synthesis*; Thieme: Stuttgart, Germany, **2010**; vol. 9, 81-97.
21. Diakov, M. Y.; Prodanov, M. F.; Vashchenko, V. V. *Curr. Org. Synth*. **2017**, *14*, 683-690.
22. Mohmand, S.; Bargon, J.; Waltman, R. J. *J. Org. Chem.* **1983**, *48*, 3545-3548.
23. Gronowitz, S.; Frejd, T.; Moberg-Ogard, A.; Trege, L. *J. Heterocycl. Chem.* **1976**, *13*, 1319-1320.
24. Okamoto, T.; Kudoh, K.; Wakamiya, A.; Yamaguchi, S. *Org. Lett.* **2005**, *7*, 5301-5304.
25. Stein, A. L.; Alves, D.; Rocha, J. B. T.; Nogueira, C. W.; Zeni G. *Org. Lett.* **2008**, *10*, 4983-4986.
26. Kesharwani, T.; Worlikar, S. A.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 2307-2312.
27. Elsherbini, M.; Hamama, W.; Zoorob, H. H. *Coord. Chem. Rev.* **2016**, *312*, 149-177.
28. Masuda, T.; Inagaki, Y.; Momma, H.; Kwon, E.; Setaka, W. *New J. Chem.* **2016**, *40*, 8593-8599.
29. Rhoden, C. R. B.; Zeni, G. *Org. Biomol. Chem.* **2011**, *9*, 1301-1313.
30. Alves, D.; Luchese, C.; Nogueira, C. W.; Zeni, G. *J. Org. Chem.* **2007**, *72*, 6726-6734.
31. Shi, S.; Tang, L.; Guo, H.; Uddin, M. A.; Wang, H.; Yang, K.; Liu, B.; Wang, Y.; Sun, H.; Woo, H. Y.; Guo, X. *Macromolecules* **2019**, *52*, 7301-7312.
32. Skhiri, A.; Salem, R. B.; Soulé, J.-F.; Doucet, H. *ChemCatChem* **2017**, *9*, 2895-2913.
33. Ehlers, P.; Dang, T. T.; Patonay, T.; Villinger, A.; Langer, P. *Eur. J. Org. Chem.* **2013**, *2013*, 2000-2007.

34. Schumacher, R. F.; Rosário, A. R.; Souza, A. C. G.; Menezes, P. H.; Zeni, G. *Org. Lett.* **2010**, *12*, 1952-1955.
35. Schumacher, R. F.; Rosário, A. R.; Leite, M. R.; Zeni, G. *Chem. Eur. J.* **2013**, *19*, 13059-13064.
36. Alves, D.; Prigol, M.; Nogueira, C. W.; Zeni, G. *Synlett* **2008**, *2008*, 914-918.
37. Pistoia, R. P.; Roehrs, J. A.; Davi F. Back, D. F.; Zeni, G. *Org. Chem. Front*. **2017**, *4*, 277-282.
38. Casola, K. K.; Gomes, M. R.; Back, D. F.; Zeni, G. *J. Org. Chem.* **2018**, *83*, 6706-6718.
39. Perin, G.; Roehrs, J. A.; Hellwig, P. S.; Stach, G.; Barcellos, T.; Lenardão, E. J.; Jacob, R. G.; Q. Luz, E. Q. *ChemistrySelect* **2017**, *2*, 4561-4566.
40. Leonel, G.; Back, D. F.; Zeni, G. *Adv. Synth. Catal.* **2020**, *362*, 585-593.
41. Cai, T.; Liu, J.; Zhang, H.; Wang, X.; Feng, J.; Shen, R.; Gao, Y. *Org. Lett.* **2019**, *21*, 4605-4608.
42. Martins, G. M.; Back, D. F.; Kaufman, T. D.; Silveira, C. C. *J. Org. Chem*. **2018**, *83*, 3252-3264.
43. Martins, G. M.; Carmo, G.; Morel, A. F.; Kaufman, T. S.; Silveira, C. C. *Asian J. Org. Chem.* **2019**, *8*, 369-371.
44. Sonawane, A.; Kubota, Y. D.; Koketsu, M. *J. Org. Chem.* **2019**, *84*, 8602-8614.
45. Perin, G.; Peglow, T. J.; Bartz, R. H.; Cargnelutti, R.; Lenardão, E. J.; Schumacher, R. F. *Arkivoc* **2019**, *ii*, 50-64.
46. Liu, B.; Hu, Q.; Wen, Y.; Fang, B.; Xu, X.; Hu, Y. *Front. Chem.* **2019**, *7*, article No. 374.
47. Wang, T.; Hoye, T. R. *J. Am. Chem. Soc*. **2016**, *138*, 13870-13873.
48. Gupta, S.; Xie, P. P.; Xia, Y. Z.; Lee, D. S *Org. Chem. Front.* **2018**, *5*, 2208-2213.
49. Yoshioka, E.; Kohtani, S.; Miyabe, H. *Angew. Chem. Int. Ed.* **2011**, *50*, 6638-6642.
50. Goulart, H. A.; Neto, J. S. S.; Barcellos, A. M.; Barcellos, T.; Silva, M. S.; Alves, D.; Jacob, R. G.; Lenardão, E. J.; Perin, G. *Adv. Synth. Catal*. **2019**, *361*, 3403-3411.
51. Perin, G.; Nobre, P, G.; Mailahn, D. H.; Silva, M. S.; Barcellos, T.; Jacob, R. G.; Lenardão, E. J.; Santi, C.; Roehrs, J. A. *Synthesis* **2019**, *51*, 2293-2304.
52. Tiecco, M.; Testaferri, L.; Tingoli, T.; Chianelli, D.; Bartoli, D. *Tetrahedron Lett.* **1989**, *30*, 1417-1420.
53. Pinheiro, R. C.; Back, D. F.; Zeni, G. *Adv. Synth. Catal.* **2019**, *361*, 1866-1873.
54. Lutz, G.; Back, D. F.; Zeni, G. *Adv. Synth. Catal.* **2020**, *362*, 1096-1105.
55. Jin, S.; Kuang, Z.; Song, Q. *Org. Lett.* **2020**, *22*, 615-619.
56. Chelucci, G. *Chem. Rev.* **2012**, *112*, 1344-1462.
57. Bilheri, F. N.; Pistoia, R. P.; Back, D. F.; Zeni, G. *Adv. Synth. Catal.* **2017**, *359*, 4208-4216.
58. Stach, G.; Peglow, T. J.; Roehrs, J. A.; Penteado, F.; Barcellos, T.; Jacob, R. G.; Lenardão, E. J.; Perin, G. *Synthesis* **2019**, *51*, 578-586.
59. Maitya, P.; Ranu, B. C. *Adv. Synth. Catal*. **2017**, *359*, 4369-4378.
60. Maity, P.; Paroi, B.; Ranu, B. C. *Org. Lett.* **2017**, *19*, 5748-5751.
61. Tanaka, K.; Tajima, Y. *Eur. J. Org. Chem.* **2012**, *2012*, 3715-3725.
62. Nájera, C.; Beletskaya, I. P.; Yus, M. *Chem. Soc. Rev.* **2019**, *48*, 4515-4618.
63. Guo, X.-X.; Gu, D.-W.; Wu, Z.; Zhang, W. *Chem. Rev.* **2015**, *115*, 1622-1651.
64. Mancuso, R.; Gabriele, B. *Molecules* **2014**, 15687-15719.
65. Sun, P.; Jiang, M.; Wei, W.; Min, Y.; Zhang, W.; Li, W.; Yang, D.; Wang, H. *J. Org. Chem.* **2017**, *82*, 2906-2913.
66. Wang, T.; Chen, J.; Wang, J.; Xu, S.; Lin, A.; Yao, H.; Jiang, S.; Xu, J. *Org. Biomol. Chem.* **2018**, *16*, 3721-3725.
67. Ni, P.; Tan, J.; Zhao, W.; Huang, H.; Xiao, F.; Deng, G.-J. *Org. Lett.* **2019**, *21*, 3518-3522.
68. Ni, P.; Tan, J.; Zhao, W.; Huang, H.; Deng, G.-J. *Adv. Synth. Catal.* **2019**, *361*, 5351-5356.
69. Yang, Y.; Lan, J.; You, J. *Chem. Rev.* **2017**, *117*, 8787-8863.
70. Tamba, S.; Fujii, R.; Mori, A.; Hara, K.; Koumura, N. *Chem. Lett.* **2011**, *40*, 922-924.
71. Rampon, D. S.; Wessjohann, L. A.; Schneider, P. H. *J. Org. Chem.* **2014**, *79*, 5987-5992.
72. Skhiri, A.; Salem, R. B.; Soulé, J.-F.; Doucet, H. *Chem. Eur. J.* **2017**, *23*, 2788-2791.
73. Salamoun, J.; Anderson, S.; Burnett, J. C.; Gussio, R.; Wipf, P. *Org. Lett.* **2014**, *16*, 2034-2037.
74. Skhiri, A.; Salem, R. B.; Soulé, J.-F.; Doucet, H. *Beilstein J. Org. Chem.* **2017**, *13*, 2862-2868.
75. Chen, S.-Y.; Pao, Y.-C.; Sahoo, S. K.; Huang, W.-C.; Lai, Y.-Y.; Cheng, Y.-J. *Chem. Commun.* **2018**, *54*, 1517-1520.

76. Daniels, M. H.; Armand, J. R.; Tan, K. L. *Org. Lett.* **2016**, *18*, 3310-3313.
77. Shi, X.; Mao, S.; Roisnel, T.; Doucet, H.; Soulé, J.-F. *Org. Chem. Front.* **2019**, *6*, 2398-2403.
78. Chen, S.-Y.; Sahoo, S. K.; Huang, C.-L.; Chan, C. T.-H.; Cheng, Y.-J. *Org. Lett.* **2020**, *22*, 2318-2322.
79. Xu, W.; Wu, L.; Fang, M.; Ma, Z.; Shan, Z.; Li, C.; Wang, H. *J. Org. Chem.* **2017**, *82*, 11192-11197.
80. Xu, W.; Wang, M.; Ma, Z.; Shan, Z.; Li, C.; Wang, H. *J. Org. Chem.* **2018**, *83*, 12154-12163.
81. Schwartz, P.-O.; Förtsch, S.; Vogt, A.; Mena-Osteritz, E.; Bäuerle, P. *Beilstein J. Org. Chem.* **2019**, *15*, 1379-1393.
82. Reddy, V. P.; Kumar, A. V.; Rao, K. R. *J. Org. Chem.* **2010**, *75*, 8720-8723.