

Recent Developments in Radical Mediated Synthesis of Organostannanes.

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Abstract: The present review aims to provide an overview of the recent developments in the preparation of aryl- or alkenyl stannanes via carbon- and tin-centered radicals enabling chemists to synthesize organostannyl derivatives with high efficiency and under mild conditions.

Keywords: Carbon centered radicals; Stannyl radicals; Photocatalysis; Organotin derivatives; Radical chemistry

1. Introduction

Since Colin Eaborn, Masanori Kosugi, Toshihiko Migita and John Kenneth Stille pioneered the use of organostannanes^[1] in the seventies, such derivatives have become key-intermediates in transition metal-catalyzed cross-coupling reactions,^[2] for the formation of C–C,^[3] and C-heteroatom bonds,^[4] as well as in the multistep preparation of bioactive compounds.^[5] Despite the toxicity of organotin derivatives, the Stille reaction (also known as the Migita-Kosugi-Stille coupling) operates without the need of an alkaline environment (in contrast to the Suzuki-Miyaura process) and under homogeneous conditions with a large functional group tolerance.^[6] In this context, the adoption of efficient and user-friendly protocols for the formation of C–Sn bonds (e.g. in aryl stannanes and alkenyl stannanes) is a pivotal focus within the contemporary organic synthetic strategies.

The conventional approach to aryl stannanes makes use of R₃Sn–X and aryl containing organometallic reagents (Ar–Met) as suitable partners (Scheme 1, path

a). An alternative strategy that exhibits a more favourable functional group tolerance involves the conversion of aryl halides^[7] or aryl esters (mainly triflates, path b)^[8] into the target compounds under transition metal-catalyzed conditions. Other approaches exploit a transition metal catalyzed Ar–H activation (path c),^[9] the decarboxylative conversion of aryl derivatives (path d),^[10] the generation of an aryl anion as the key-intermediate,^[11] as well as the acid catalyzed stannylation of aryl triazenes.^[12]

Analogously, vinyl stannanes hold significant applications in organic synthesis including, among the others, the already mentioned Stille reactions.^[11] In this context, the transition metal (mainly Pd) catalyzed hydrostannylation of alkynes is the ultimate choice, despite mechanistic issues are still under discussion.^[13]

The impressive advancements recently documented in photocatalysis^[14] and electrochemistry^[15] in radical generation, led to the development of different strategies for the synthesis of organostannanes. In most cases, as described in Scheme 2, such procedures are based either on an atom transfer reaction involving a



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Adrián Luguera Ruiz holds a MSc in Organic Chemistry from the Complutense University of Madrid. He has developed his career in organic and medicinal chemistry through roles as an organic chemist at Janssen, Eurofins-Villapharma, and the Medicinal Chemistry Institute (IQM-CSIC). He pursued his PhD in “Chemical and Pharmaceutical Sciences, and

Related Industrial Innovation” at the University of Pavia (Italy). During this period, he also collaborated with the University of Amsterdam and J&J Innovative Medicines (Toledo, Spain). Currently, Adrián works as an R&D Scientist at Galchimia, (GSK R&D site, Tres Cantos, Spain), where he focuses on implementing automated high-throughput chemical synthesis and advanced chemical technologies to accelerate medicinal chemistry programs at GSK.



Maurizio Fagnoni is currently a Full Professor in Organic Chemistry at the University of Pavia (PhotoGreen Lab, Italy). His research interests are mainly focused on the photo-induced or photocatalytic generation of reactive intermediates such as (bi)radicals, (phenyl) cations and radical ions and their application in eco-sustainable synthesis or in photolithography as well as biological application. He is currently a member of the committees of the Interdivisional group of Green Chemistry and Photochemistry of the Italian Society of Chemistry. In 2022 he was recipient of the Theresian Medal from the University of Pavia.



Stefano Protti completed his PhD in Pavia (2007). Since 2018 is Associate Professor at the University of Pavia, Italy. He is currently editor of the Specialist Periodical Reports in Photochemistry of the Royal Society of Chemistry, member of the International Advisory Board of the European Journal of Organic Chemistry. Stefano Protti is co-author of about 180 research articles and reviews, besides 26 contributed chapters in multi-authored books. His work is mainly focused on the development of visible light mediated synthetic strategies.

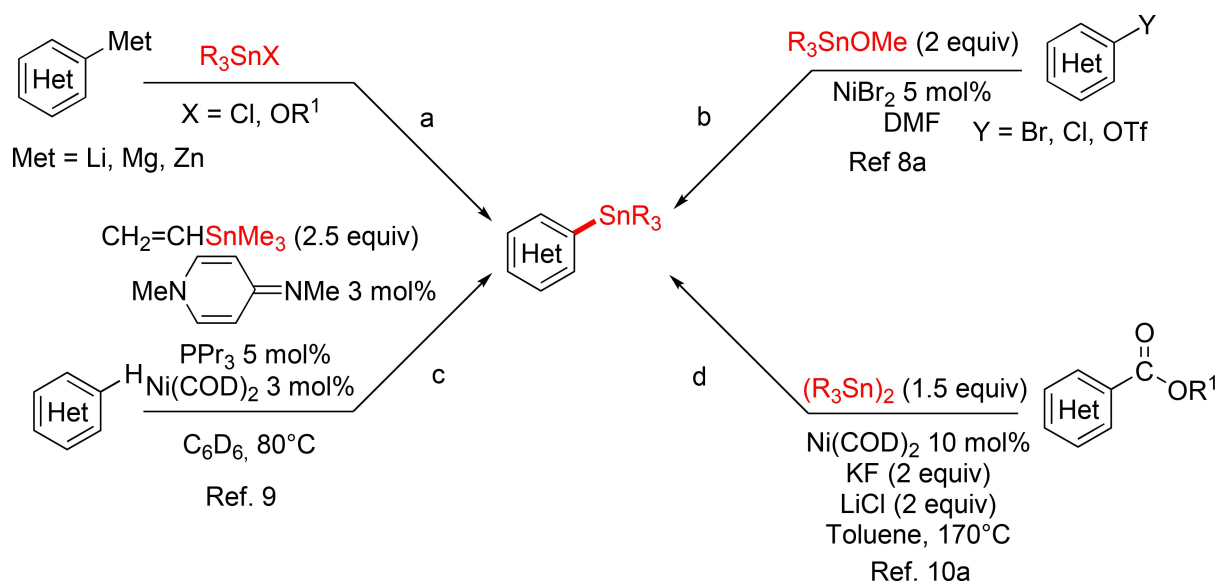


Di Qiu was born in Tianjin, China, in 1987. He received his B.S. degree from Peking University in 2010 obtained his Ph.D. degree from Peking University in 2015 (Supervisor: Prof. Jianbo Wang's). In 2015, he joined in Tianjin Normal University as an assistant professor. He is currently an associate professor at college of chemistry, Tianjin Normal University. His research interests lie in C-Sn and C-P bond formation and functional group transformations in aromatic compounds.

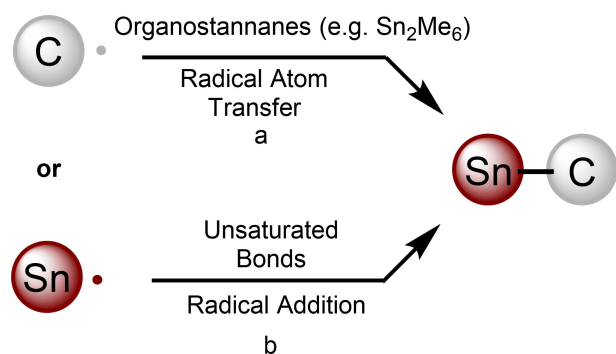
carbon centered radical and tin derivatives (in most cases $(R_3Sn)_2$, path a) or the addition of an organotin radical onto a C–C unsaturated bond (path b).

A comprehensive review in this field, however, is lacking and this pushed us to provide readers with an

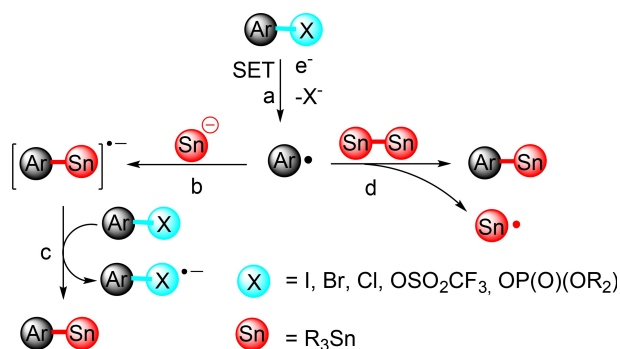
overview of the various radical-mediated stannylation. The synthetic strategies have been classified and described on the basis of the targeted compounds.



Scheme 1. Non radical based approaches to Aryl Stannanes.

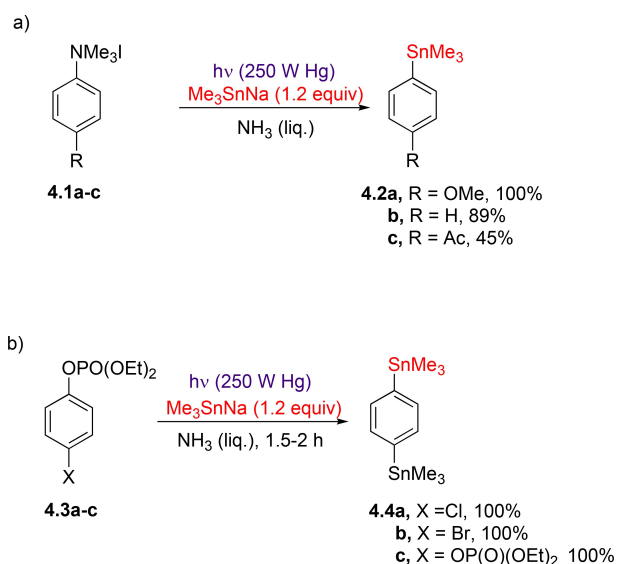


Scheme 2. Stannylation proceeding via carbon- or tin-based radical intermediates.



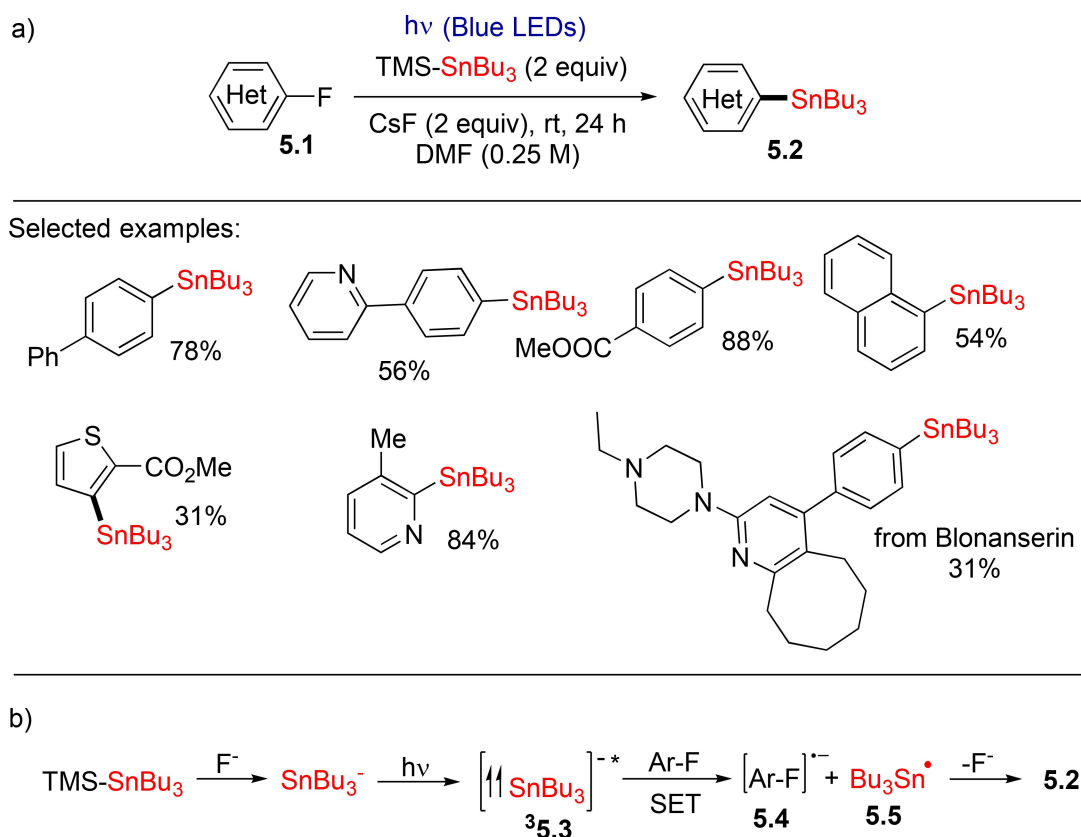
Scheme 3. Reaction pathways for the preparation of aryl stannanes via an $\text{ArS}_{\text{RN}}1$ (left) or a radical substitution reaction (right). SET = Single Electron Transfer

2. Synthesis of Aryl Stannanes

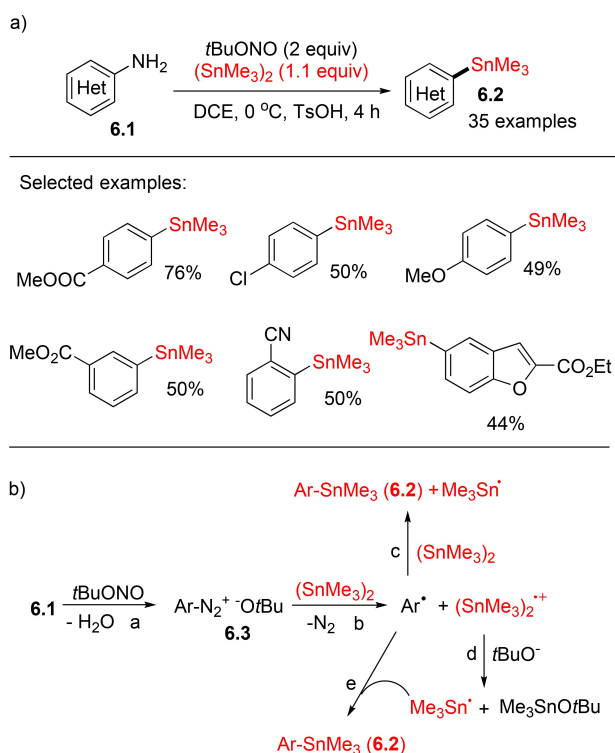


Scheme 4. UV-light mediated preparation of a) aryl stannanes and b) aryl distannanes in liquid ammonia under $\text{S}_{\text{RN}}1$ conditions.

Aryl radicals are elective intermediates for the preparation of aryl stannanes. These compounds may be obtained following two main pathways, namely an aromatic $\text{S}_{\text{RN}}1$ reaction^[16] and a free radical substitution mechanism, as summarized in Scheme 3. In the first case, a Single Electron Transfer (SET) occurs on an aryl halide, ester or an ammonium salt (Ar-X). The loss of a stable anion (or a stable molecule, e.g. an amine) results in the release of the aryl radical intermediate (path a), that couples with the trialkyltin anion to form $\text{ArSnR}_3^{\bullet-}$ (path b), which subsequently forms the desired ArSnMe_3 through a new thermal



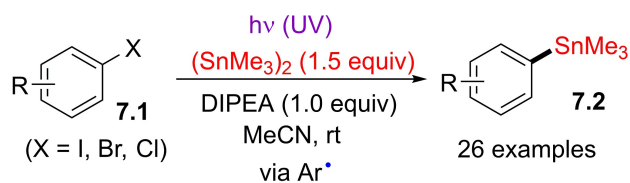
Scheme 5. a) Blue Light mediated stannylation of aryl fluorides and b) suggested mechanism.



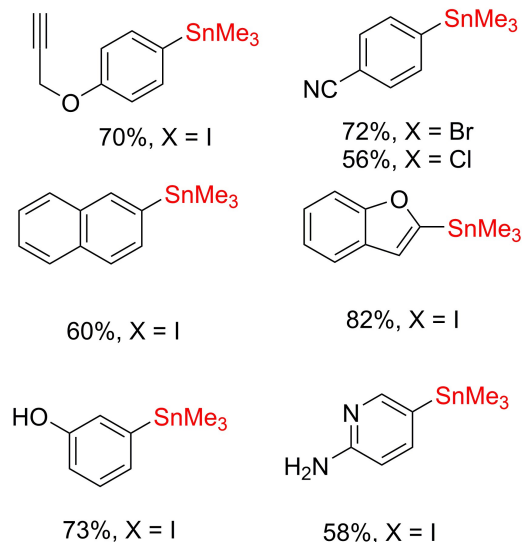
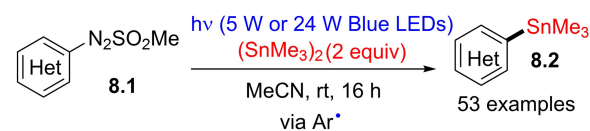
Scheme 6. a) Sandmeyer-type stannylation of aromatic amines **6.1** and b) suggested mechanism.

SET with Ar–X thus restoring the cycle (path c). In alternative, the product is formed by a substitution reaction of Ar• intercepted by a distannane (path d). In some cases, as described in the next paragraphs, Ar• can be also obtained via direct photolysis of properly designed substrates (e.g. arylazo sulfones)^[17] or via a halogen atom transfer (XAT) reaction.^[18]

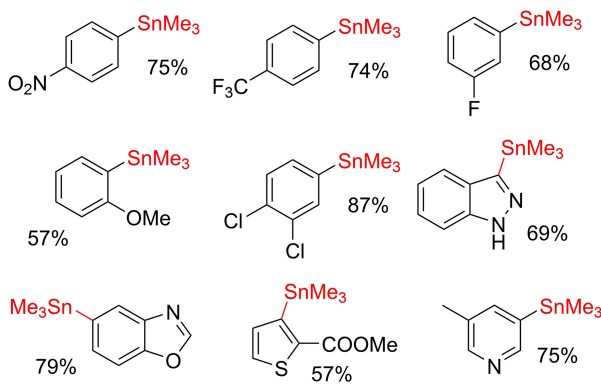
A seminal photochemical approach to aryl stannanes has been proposed by the research group of Chopa in 2001,^[19] that employed aryltrimethylammonium salts **4.1 a-c**, (prepared *in situ* from anilines), sodium trimethylstannate as the coupling partner and liquid ammonia as the reaction medium. (Scheme 4). The reaction occurs in a rather short reaction time and with high efficiency but exhibits limited functional groups tolerance. Indeed, halogens may undergo a competitive halogen/tin exchange upon irradiation (while dehalogenative hydrogenation could take place in the dark) and other groups may be affected by the alkaline conditions used. Furthermore, the use of liquid ammonia as the solvent and a 250 W Hg lamp as the (UV) light source significantly limit the scale up of the process. Analogous conditions have been employed for the preparation of aryl distannanes from haloarylphosphates **4.3 a-c** (Scheme 4b),^[19a] such



Selected Examples:

Scheme 7. Photochemical stannylation of aryl halides **7.1**.

Selected examples

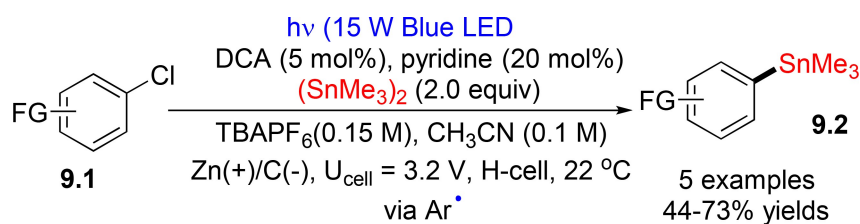
Scheme 8. Visible light-driven stannylation of arylazo sulfones **8.1**.

strategy was applied to the three-steps preparation of aryl boranes from phenols.^[19b]

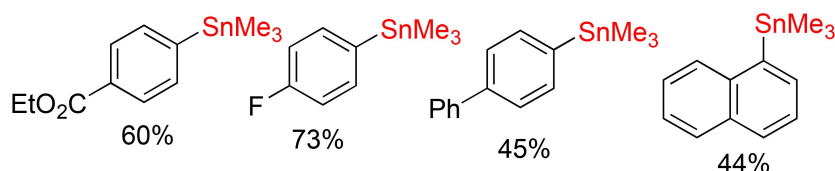
Trialkylstannane anions can be converted photochemically to their triplet (T_1) stannyl diradicals upon Blue light excitation. Starting from these preliminary observations, Uchiyama and coworkers harnessed the potent single-electron reduction capability of the methylstannane anion to achieve defluorostannylation of aryl fluorides **5.1** (and iodides) in the presence of tri-*n*-butylstannyl trimethylsilane as the tin source under Blue light irradiation to form (among others) an antipsychotic Blonanserin derivative^[20] (Scheme 5a). The reaction occurred in moderate to satisfactory yields and with a large applicability to substrates bearing electron-withdrawing substituents like cyano and esters, which often exhibit a limited tolerance toward trialkylstannane ions. The protocol was applied to the one pot synthesis of biphenyls in a Stille-type coupling, via the *in situ* prepared aryl stannanes. As hinted above, the reaction mechanism is akin to a $S_{RN}1$ mechanism. Thus, the photogenerated diradical methylstannane **5.3** underwent SET with aryl fluoride **5.1** yielding the radical anion **5.4** which loss fluoride anion and the resulting aryl radical coupled with tri-*n*-butylstannyl radicals **5.5** to afford the desired product **5.2**. The same strategy was also exploited for the synthesis of vinyl stannanes from the corresponding alkynes.^[20]

Aryl radicals can also directly cleave the Sn–Sn bond in bis-stannanes via a radical chain mechanism. In 2013 Wang et al pioneered a method to synthesize arylstannanes **6.2** (Scheme 6) from aromatic amines **6.1** under Sandmeyer-type conditions.^[21] The method stands out for its efficiency, mild conditions and excellent functional group tolerance. In the suggested mechanism, aryl diazonium salt **6.3** (in turn prepared *in situ* by treating aniline **6.1** with tert-butyl nitrite, path a) reacted with the distannane $(Me_3Sn)_2$ (path b) via a single electron transfer (SET), thus releasing, upon nitrogen loss, an aryl radical Ar^\bullet and radical cation (path b). The aryl radical react with $(Me_3Sn)_2$, leading to the formation of the corresponding stannylation product and Me_3Sn^\bullet (path c).^[21] An alternative (despite the rather short lifetime of the involved intermediates^[22]) proposed by the authors involves the interaction of tert-butoxy anion with $Me_6Sn_2^{2+}$ to produce trimethylstannyl radicals Me_3Sn^\bullet which coupled with Ar^\bullet (path e). An analogous approach was applied to prepare trimethylstannyl arylboronates that have been then used in orthogonal cross-coupling Suzuki and Stille reactions.^[21b] Notably, the obtained products underwent subsequent tandem one-pot Suzuki reactions and Stille cross-coupling reactions, enabling the divergent selective C-arylation of the starting substrates.

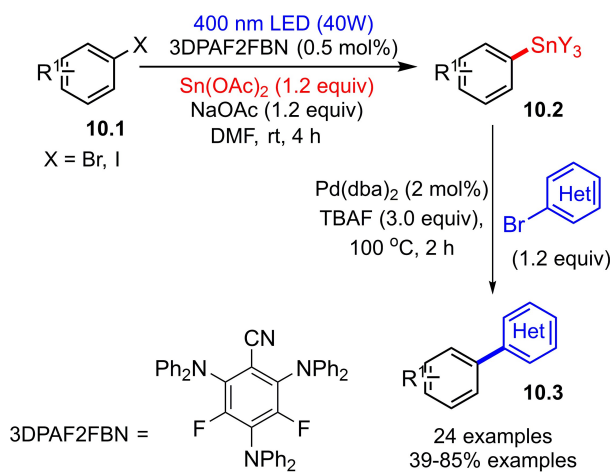
Irradiation of haloarenes **7.1** (including bromides and chlorides) with UV light in polar solvents (e.g. MeCN) generates aryl radicals via homolytic cleavage of the Ar-halogen bond that react with $(Me_3Sn)_2$ to



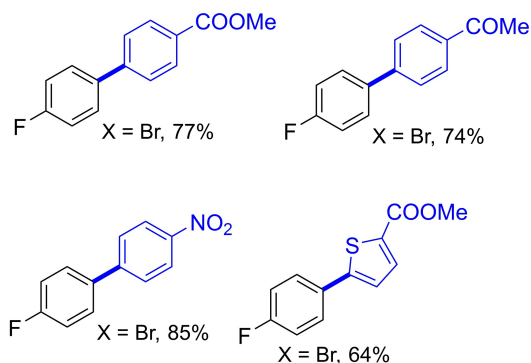
Selected Examples



Scheme 9. Photoelectrochemical stannylation of aryl chlorides **9.1**.



Selected Examples



Scheme 10. Visible light-driven stannylation reaction of aryl halides **10.1** by tin(II) acetate.

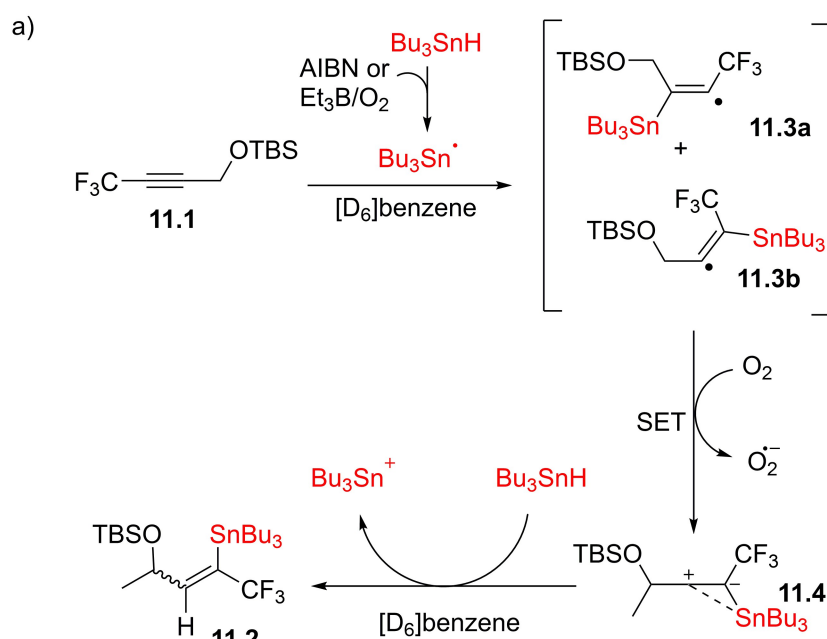
yield the corresponding aryltrimethylstannanes **7.2** (Scheme 7).^[23] In the optimized conditions, *N,N*-diisopropylethylamine (DIPEA) was added to inhibit the formation of hydrodehalogenation byproducts. The

method can be successfully applied also for the synthesis of stannylated heterocycles such as benzofurans, benzothiophenes, pyridines, and pyrimidines.^[23]

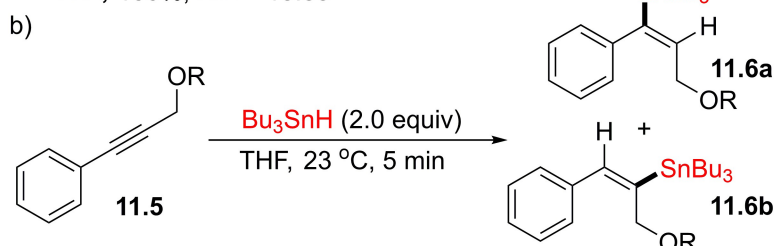
Our research groups successfully proposed a versatile visible light driven stannylation of arylazo sulfones **8.1**^[24] in the presence of hexamethylditin as the stannylating agent. As described in Scheme 8, blue light irradiation of **8.1** caused the homolytic cleavage of the N–S bond, generating, after nitrogen release from the aryldiazanyl radical, the corresponding aryl radical Ar[•] (along with methanesulfonyl radical CH₃SO₂[•]) that is responsible (analogously to what described in Scheme 6b) for the Ar–Sn bond formation. The protocol showed an excellent functional group tolerance and minimal electronic effects yielding both aromatic and heterocyclic derivatives in good to quantitative yields.^[24]

The stannylation (and borylation) of poorly reducible aryl chlorides **9.1** (Scheme 9) was achieved under photoelectrochemical conditions,^[25] by exploiting the potentialities of 9,10-dicyanoanthracene (DCA) as redox mediator. In the proposed mechanism, DCA was initially electrochemically reduced to the corresponding radical anion DCA^{•-} that was in turn photoexcited. The resulting DCA^{•-} was thus able to generate aryl radicals via mono-electronic reduction of aryl chlorides. By bypassing the need for harsh reaction conditions and expensive catalysts and ligands, this method marked a significant breakthrough in the selective cleavage of carbon-chlorine bonds in aryl chlorides.^[25]

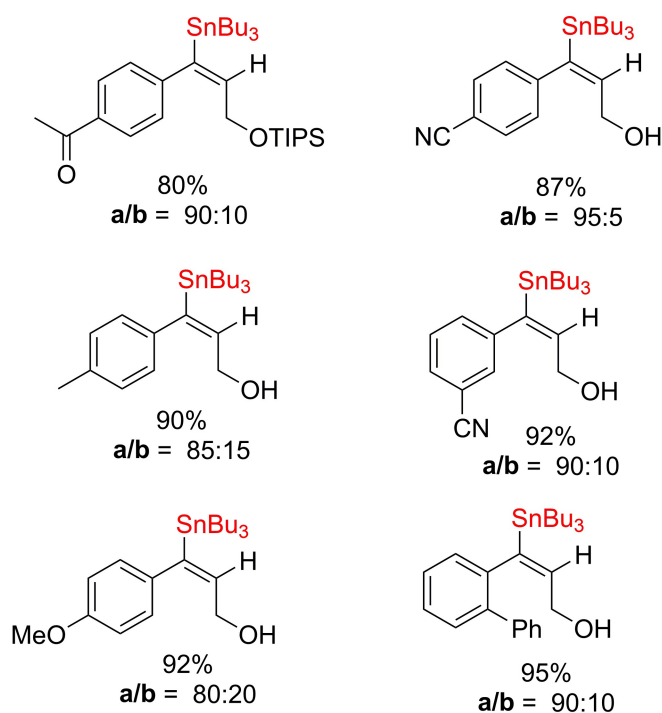
The research group of Dilman proposed a strategy to activate aryl halides **10.1** (mainly bromides and iodides, as indicated in Scheme 10) via a visible light mediated photocatalyzed XAT strategy,^[18] by employing Sn(OAc)₂ as the tin source and cyanoarene 3DPA2FBN as the photoredox catalyst.^[26] The reaction proceeded via the stannyl radical intermediate Y₃Sn[•]



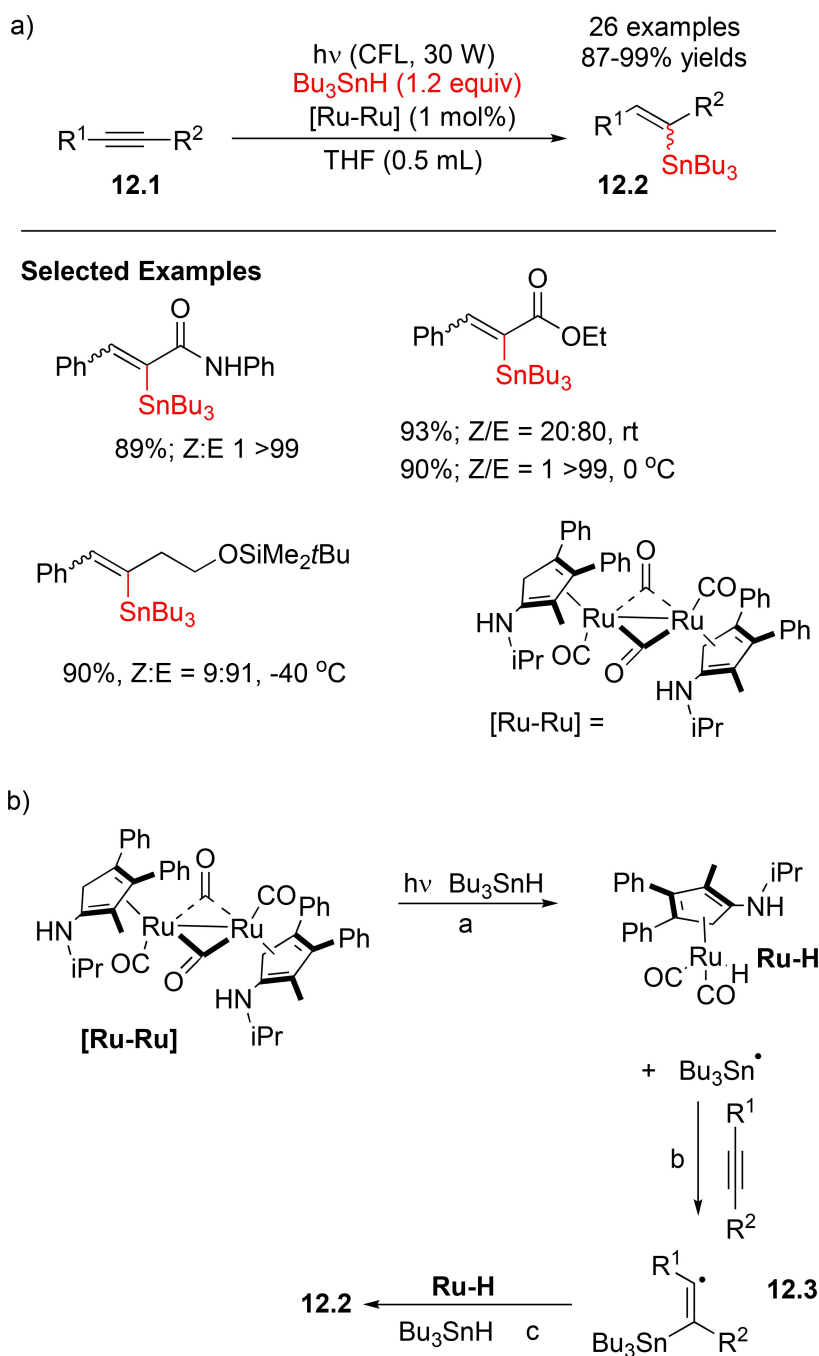
11.2, 100%, *E/Z* = 15:85



Selected examples



Scheme 11. a) Mechanism suggested for the free radical catalyzed hydrostannylation reaction; b) synthesis of 3-stannyl allyl alcohols **11.6a,b**

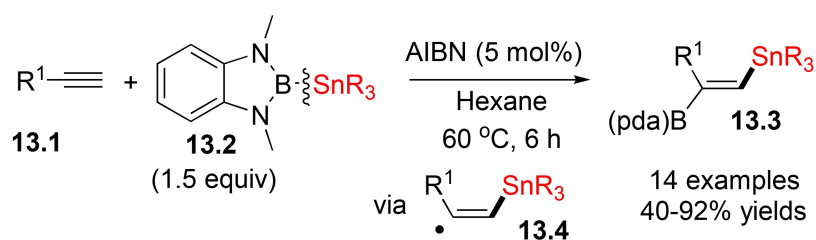


Scheme 12. a) Ruthenium-catalyzed hydrostannylation of alkynes and b) suggested mechanism.

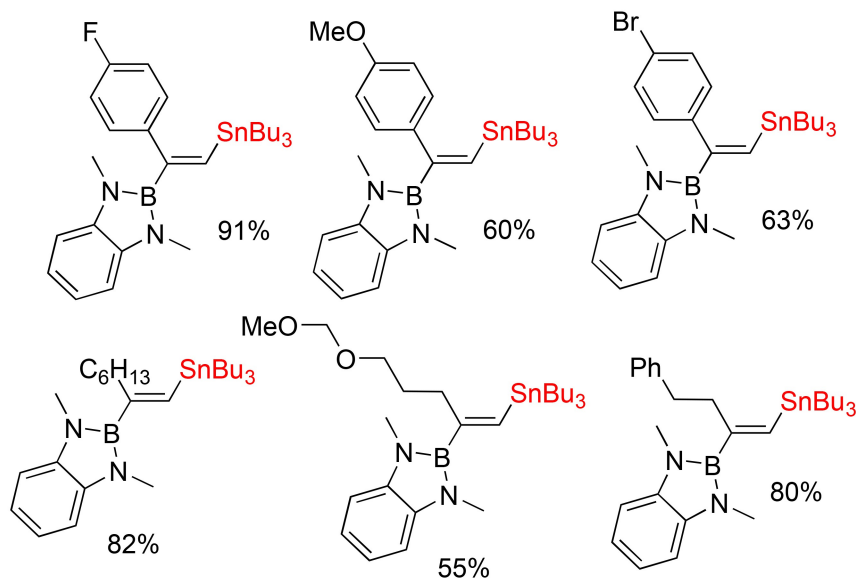
(Y = OAc, I, Br) that was responsible for the XAT step and the subsequent formation of the aryl radical Ar^\bullet . The resulting products **10.2** have been then employed in situ in a Stille-like coupling for the preparation of biaryls **10.3**.^[26] Aryl halides have been recently stannylated also via a visible light driven procedure (developed and optimized by the research group of D. Qiu) that merged a photoredox catalytic cycle with an XAT step.^[27]

3. Synthesis of Alkenyl Stannanes

The preparation of alkenyl stannanes has been described by following different strategies including, among the others, the addition of tin hydrides onto carbon-carbon triple bonds in alkynes, also known as hydrostannylation reaction.^[13] Free-radical variants of such an approach have been extensively investigated in the past, in view of the satisfactory *E/Z* stereo-selectivity. Since seminal works of Leusink in the 60's,



Selected examples



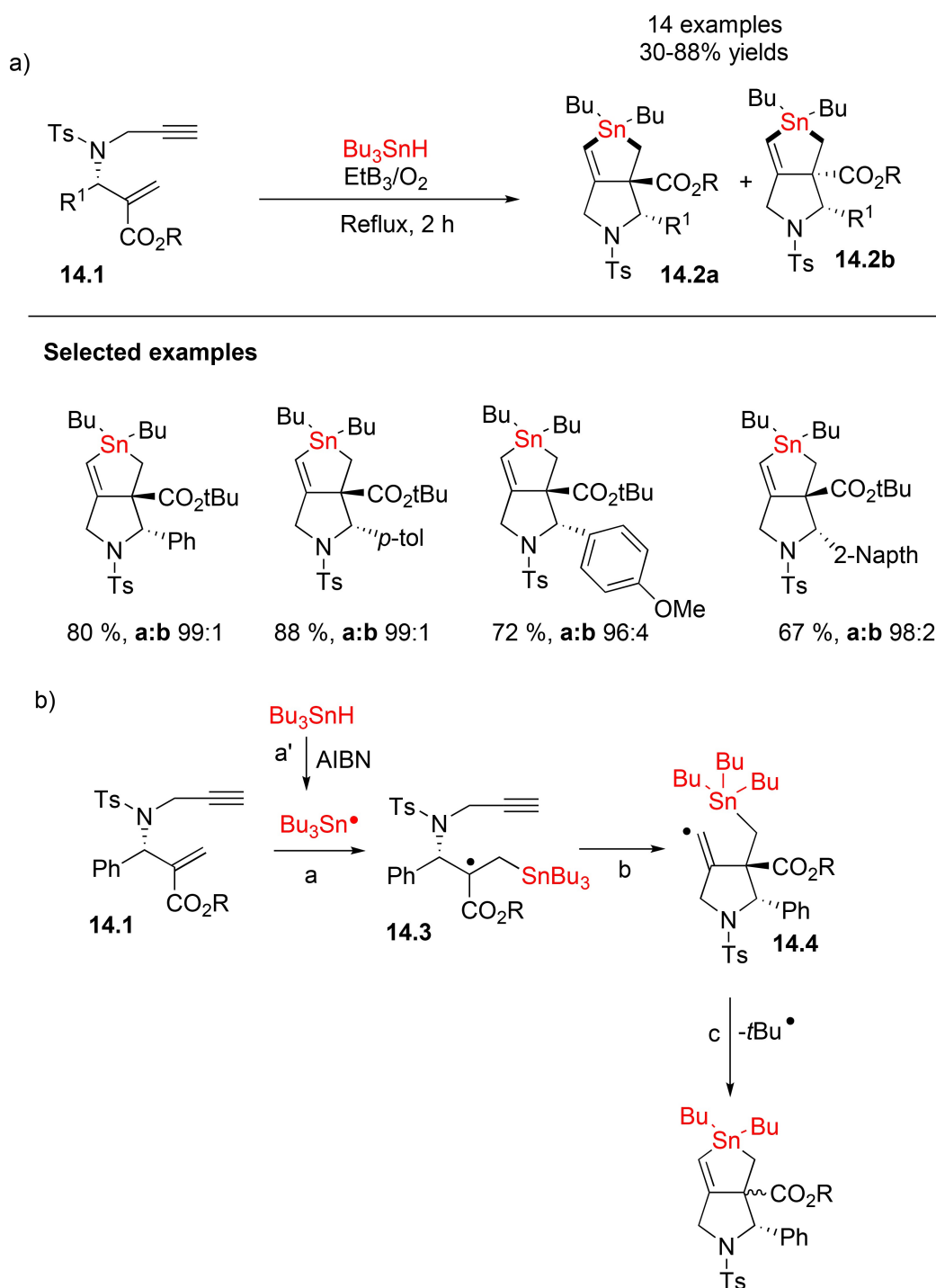
Scheme 13. Transition-metal-free catalyzed (o-phenylenediamine-based) borostannane-alkylation of terminal alkynes **13.1**.

it has been widely accepted that the reaction mechanism involved free radical intermediates, typically generated by means of free radical initiators such as AIBN or Et_3B .^[28]

The generation and the nature of the intermediates was later revised^[29] by focusing on the use of Et_3B and AIBN as free radical initiators under air atmosphere. Thus, an autoxidative interaction between molecular oxygen and Et_3B (and to a lesser extent between molecular oxygen and AIBN) was required to facilitate the tin radical formation and to improve the reaction efficiency. It was thus proposed that the addition of stannyl radicals to alkynes lacks regioselectivity, initially resulting in a mixture of vinyl radicals **11.3 a,b** (Scheme 11a). Such mixture underwent a Single Electron Transfer (SET) with molecular oxygen, to form three-center vinyl cation intermediate **11.4** along with oxygen superoxide anions. Intermediate **11.4** then reacted with tributylstannane, yielding the kinetic product **11.2** and the tributylstannyl cation Bu_3Sn^+ , which was rapidly reduced back to the tributylstannyl radical $\text{Bu}_3\text{Sn}^\bullet$ by $\text{O}_2^{\bullet-}$ thus restoring the catalytic cycle.^[29] The same research group applied these skills to the stereoselective preparation of various 3-stannyl

allyl alcohols and ethers **11.6 a,b** from the corresponding propargyl derivatives **11.5** with almost complete regioselectivity (Scheme 11b).^[30] The mechanism of hydrostannylation of alkynes and the role of radical initiators and the oxygen has been the subject of further and detailed investigation in recent years.^[31–33]

The research group of Park described the regio- and stereoselective ruthenium catalyzed hydrostannylation of alkynes **12.1** at room temperature, catalyzed by a diruthenium complexes (Ru-Ru in Scheme 12a).^[34] The mechanism, based on experimental observation led to the formation of ruthenium hydride complex **Ru-H** upon irradiation (Scheme 12b, path a), along with stannyl radical $\text{Bu}_3\text{Sn}^\bullet$, which was in turn trapped by the alkyne (path b). The so generated vinyl radical abstracted a hydrogen atom from Ru-H ; the Ruthenium centered radical was in turn restored by Bu_3SnH . The same reaction applied to 1,6-enynes followed by an acidic destannylation affords methylenecyclopentanes via a 5-exo cyclization or methylenecyclohexanes via a 6-endo cyclization, respectively with high selectivity towards the former compounds as the kinetic product.^[35]

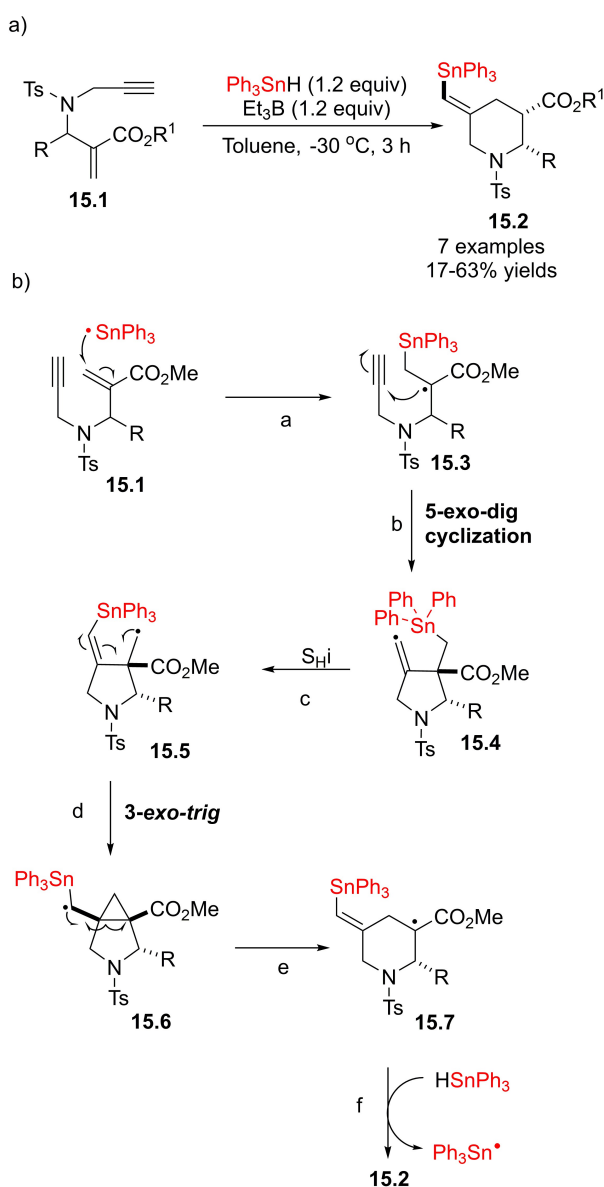


Scheme 14. Preparation of tin complexes of triangular bipyramidal derivatives **14.2** via a radical pathway.

Konno et al. described the regio- and stereoselective conversion of α -CF₃ diynyl derivatives into the corresponding cis-vinylstannane, in the presence of Et₃B as the radical initiator.^[36] Analogous targets have been achieved via direct UV-light induced Sn–H homolysis in trialkyltin hydrides^[37] and the resulting β -trifluoromethyl substituted organotin derivatives have

been then used in a Stille coupling in a two-step one-pot fashion.

The transition-metal-free anti 1,2-borostannane alkylation of terminal alkynes **13.1** (Scheme 13) by using (o-phenylenediamine-based) borostannanes as the defunctionalizing agent was recently described (Scheme 13).^[38] In the proposed mechanism, arising from both experimental and computational investiga-



Scheme 15. a) stereoselective synthesis of *exo*-methylene piperidines **15.2** by tin radical addition onto aza-1,6-enynes **15.1** and b) suggested mechanism.

tions, thermal decomposition of AIBN (that acted as the radical initiator) causes the generation of trialkylstannyl radicals $\text{R}_3\text{Sn}^\bullet$ from **13.2**. The tin-based radical was then trapped by the alkyne and the generated vinyl radicals **13.4** coupled with **13.2** to form the desired 1,2-difunctionalized alkenes **13.3** via subsequent C–Sn and C–B bond formation.^[38]

3.1. Aryl and Alkenyl Stannanes via Radical Cyclization

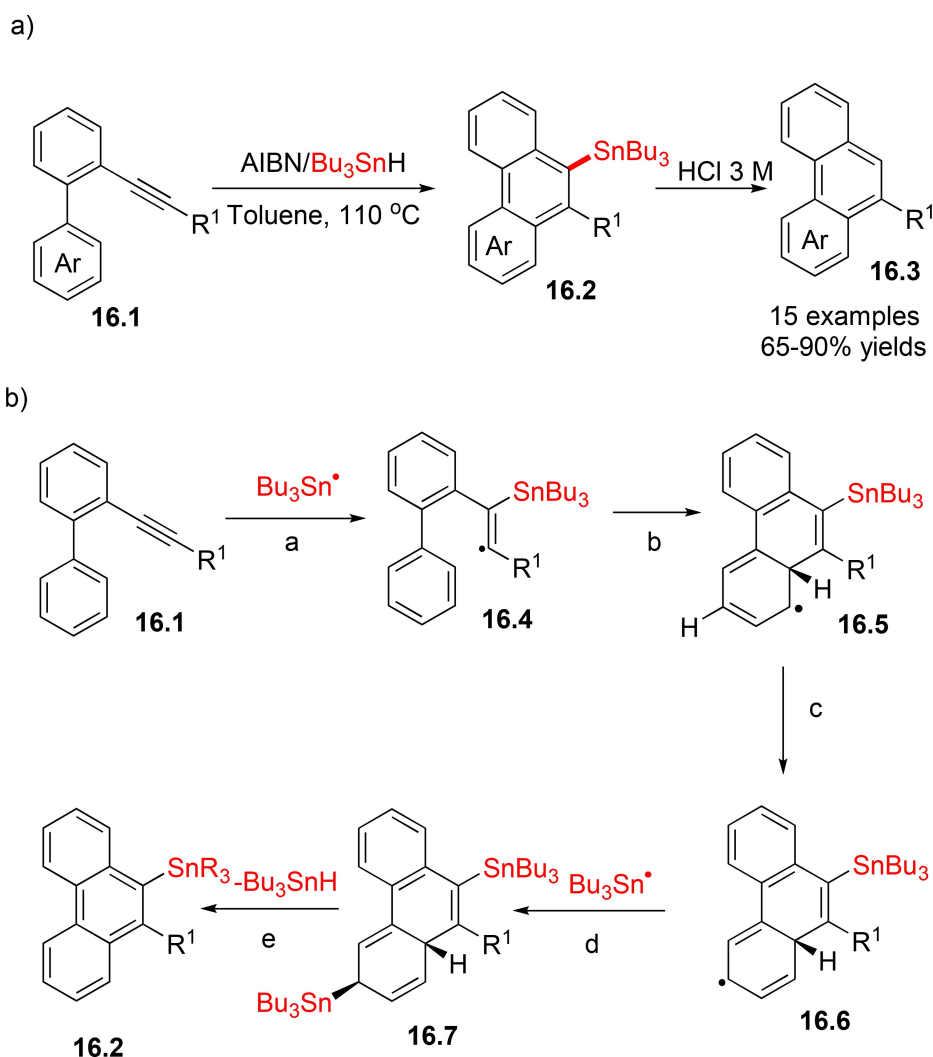
Free radical cyclization is one of the elective strategies to prepare macrocyclic molecules, as well as in the

production of polyaromatic structural units.^[39] A representative example is the synthesis of bicyclic stannolanes **14.2 a,b** from enynes **14.1** (Scheme 14).^[40] On the basis of a detailed computational and experimental investigation,^[40] the reaction was supposed to proceed through the addition of a nucleophilic trialkyltin radical $\text{R}_3\text{Sn}^\bullet$ (Scheme 14a, path a) onto the electron poor alkene moiety in **14.1**. The resulting carbon centered radical **14.3** (path b) added intramolecularly (in a 5-*exo* fashion) to the triple bond to give intermediate **14.4**. A radical substitution (path c) then released a *t*-butyl radical and the final dihydro-1*H*-stannole from it as a mixture of diastereoisomers **14.2 a,b**.

The same group later reported a method for synthesizing stereoselective *exo*-methylene piperidines **15.2** starting from the same aza-1,6-enynes **15.1** (Scheme 15a).^[41] Despite the detection of pyrrolidine and stannylpyrrolidine intermediates in the reaction system, high yields of piperidine were achieved by lowering the concentration of Ph_3SnH . The authors proposed a radical process for this reaction different from that reported in Scheme 14. After the radical addition and the 5-*exo* cyclization to give **15.4** (Scheme 15b, paths a,b), a 1,4-tin migration took place to release radical **15.5** that upon 3-*exo* cyclization followed by carbon-carbon bond cleavage (paths c,d) and subsequent ring expansion (path e) released the end piperidine **15.2** (Scheme 15b). Expanding on their earlier research, the Kamimura team recently employed amide-type 1,6-enynes for the preparation of bicyclic 2,3-dihydrostannole lactams.^[42]

In the same year, the Alabugin research group introduced a method making use of AIBN in the double role of a free radical initiator and an oxidant, allowing for the selective synthesis of stannylated phenanthrenes **16.2** via a free radicals cascade (Scheme 16a).^[43] The method relies on AIBN to initiate the generation of trialkylstannyl radicals and simultaneously terminates the cyclization reaction. Through potential energy calculations, the Authors proposed a mechanism for this reaction (Scheme 16b). The attack of a tin radical on biphenyl aryl acetylenes **16.1** formed vinyl radical **16.4** (path a) that upon 6-*endo*-dig cyclization (attacking the π -system of the adjacent benzene ring, path b) led to the cyclic radical intermediate **16.5**. This intermediate may combine with a trialkylstannyl radical (path d) and upon destannylation of the distannane **16.7** yielded the desired product (path e). An alternative mechanism involved the α -cyano radical produced by the decomposition of AIBN that acted as a HAT agent. The R_3Sn group in **16.2** could be then smoothly removed by treatment with HCl 3 M (Scheme 16a).^[43]

After successfully achieving the selective radical cascade reaction of alkynes to prepare phenanthrene and its derivatives, the research group shifted its focus



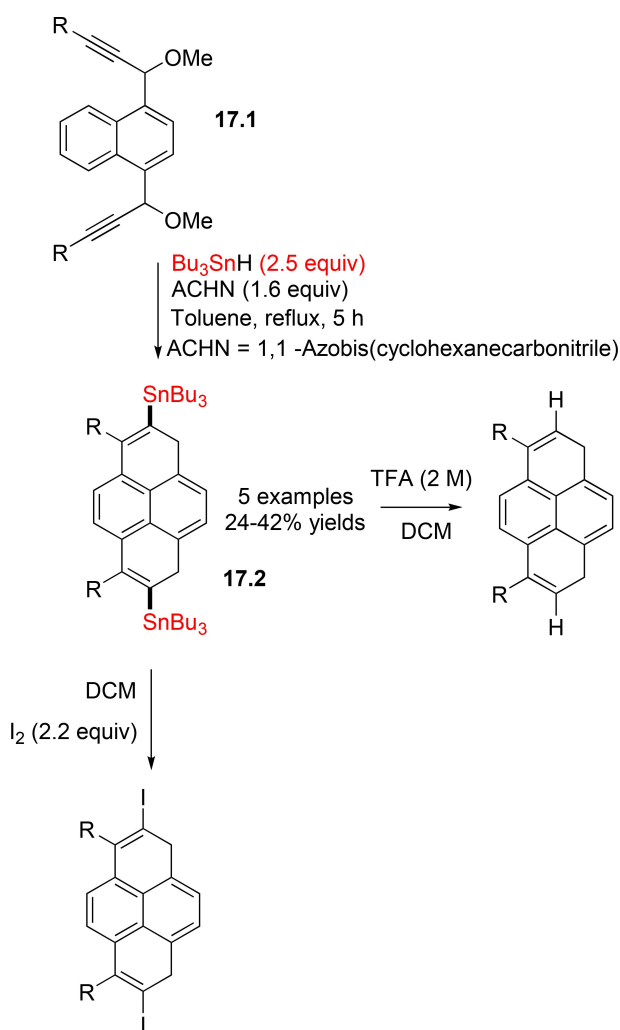
Scheme 16. a) AIBN-catalyzed preparation of phenanthrenes **16.2** via selective radical cascade reaction and b) suggested mechanism.

in utilizing olefins as synthetic equivalents of alkynes for synthesizing α -Sn-substituted naphthalenes again via a radical enyne cascade.^[44] In such a way, 6-endo-dig products were accessed by coupling cyclization/rearrangement cascade.^[44]

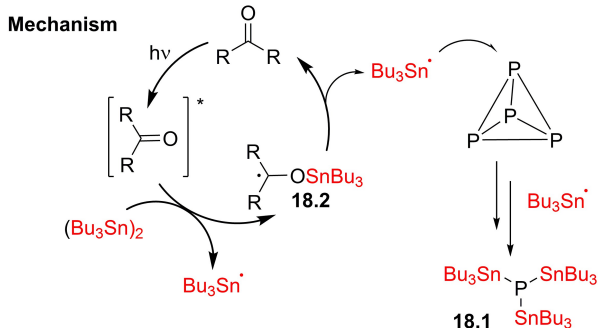
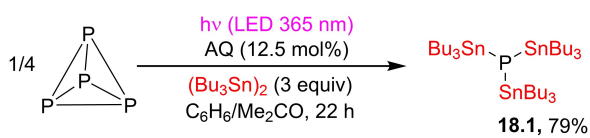
In 2020, the Alabugin research group further reported a method for preparing (although in moderate yields) bis(tributylstannyl)pyrenes **17.2** via double radical *peri*-annulations (Scheme 17).^[45] The strategy relies on the use of propargylic OMe traceless directing groups (TDGs) in substrates **17.1** to induce a regioselective Sn-radical addition to the triple bonds. The Bu_3Sn groups incorporated in the aromatics serve as chemical handles thus allowing further derivatization via direct cross-coupling, iodination, or protodestannylation (see some examples in Scheme 17). Noteworthy, the removal of the tin-based groups caused an up to 10-fold fluorescence increase of the pyrene derivatives.^[45]

3.2. Miscellaneous

A peculiar case is the synthesis of tristannyl phosphines from commercially available distannane, $(\text{Bu}_3\text{Sn})_2$ and white phosphorus (P_4 , Scheme 18).^[46] The reaction was photocatalyzed by anthraquinone (AQ) that upon UV absorption released both a $\text{Bu}_3\text{Sn}^\bullet$ radical and the stannylated ketyl radical **18.2**. The tin-based radicals generated attack P_4 and formed the stannylated monophosphine **18.1** via P–P bond cleavage. The obtained **18.1** can be then smoothly converted into acylated phosphines and tetraalkylphosphonium salts. Analogously, the photoinitiated hydrostannylation of *red phosphorous* occurred under inert atmosphere by using Bu_3SnH as the tin source. The stannylphosphines can be converted in a wide range of valuable products including the flame retardant tetrakis(hydroxymethyl)phosphonium chloride.^[47]



Scheme 17. Synthesis of bis(tributylstannyl)pyrenes **17.2** via radical cascade and ensuing derivatization.



Scheme 18. Anthraquinone photocatalyzed synthesis of stannylated monoposphine $(\text{Bu}_3\text{Sn})_3\text{P}$.

4. Summary and Perspectives

The present review summarizes recent representative synthetic methods to prepare organotin compounds based on radical intermediates. In most cases, the approaches presented herein represent a versatile and mild alternative to the transition metal catalyzed synthesis of organostannanes, and are promising for both applications in medicinal chemistry and classical functional group transformations. However, there are still unexplored fields in the radical based forging of C–Sn bonds. Accordingly, the synthesis of organostannanes via radical intermediates has a broad development prospect, and future research should focus on i) exploring different generation modes of stannyl radicals ii) testing different radical traps for these radicals other than alkynes (or olefins) iii) transition metal free and photocatalyst free generation of aryl radicals for the synthesis of aryl stannanes. iv) achieving the synthesis of highly enantioselective organotin derivatives v) synthesizing organotin reagents via carbon radical intermediates via alkyl (but not only aryl) radical precursors. After facing the above issues, it is believed that the synthesis of organostannanes (key compounds in organic synthesis despite their toxicity) via radical intermediates will have a long-lasting impact and progress on the current research and production.

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