RSC Advances

REVIEW

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2026, **16**, 2475

Advancing total synthesis through the Stille cross-coupling: recent innovations and case studies

Elaheh Hashemi * and Mohammad Teimoury

Received 1st September 2025
Accepted 18th November 2025

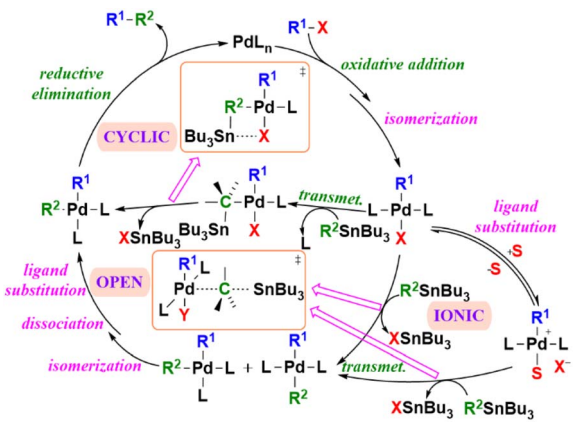
DOI: 10.1039/d5ra06557g

rsc.li/rsc-advances

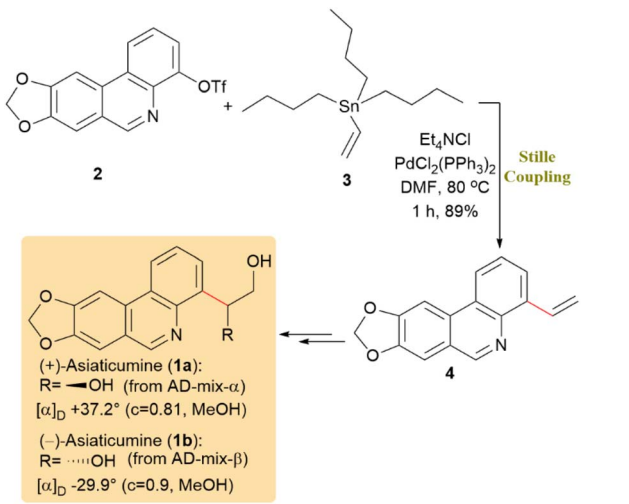
The Stille reaction, a pivotal palladium-catalyzed cross-coupling, continues to drive advancements in the total synthesis of highly complex natural products, pharmaceuticals, and functional materials. Originating from *John K. Stille*'s foundational work, this method has evolved through innovations in catalysis, ligand design, and eco-friendly protocols to address challenges like tin toxicity. This review highlights its application in constructing complex molecules and emphasizes advancements in bond-forming strategies. The reaction's versatility in both intermolecular and intramolecular contexts, coupled with its functional group tolerance, underscores its enduring relevance in modern organic synthesis of naural products.

1. Introduction

Cross-coupling reactions are among the most fundamental tools in modern synthetic chemistry, enabling the precise construction of key molecular frameworks found in natural products, polymers, and bioactive compounds.[1] The ability to form carbon–carbon (C–C) bonds is a cornerstone of organic synthesis and lies at the heart of strategies used to build natural product scaffolds and complex molecular architectures.[2,3] These reactions have drawn increasing attention due to their mild and versatile conditions, made possible by the use of active ligands and transition-metal complexes. Such catalytic systems allow the efficient creation of intricate structures relevant to materials science, pharmaceuticals, and agrochemicals.[4,5] Among transition-metal-mediated transformations, palladium-catalyzed C–C couplings are especially important for their profound impact on molecular architecture and for enabling the efficient assembly of complex carbon frameworks.[6–8] Their global significance was recognized in the 2010 Nobel Prize in Chemistry, awarded to Heck, Negishi, and Suzuki for pioneering palladium-catalyzed cross-coupling reactions.[5] The first iron-catalyzed cross-coupling reaction was reported by Tamura and Kochi,[9] leading to the key strategies such as Suzuki,[10,11] Heck,[12,13] Sonogashira,[14,15] Negishi,[16,17] Stille,[18–20] Cadiot–Chodkiewicz,[21] Castro–Stephens,[22] Hiyama,[23] Liebeskind–Srogl,[24] and Kumada reactions,[25] expanding the role of cross-coupling in

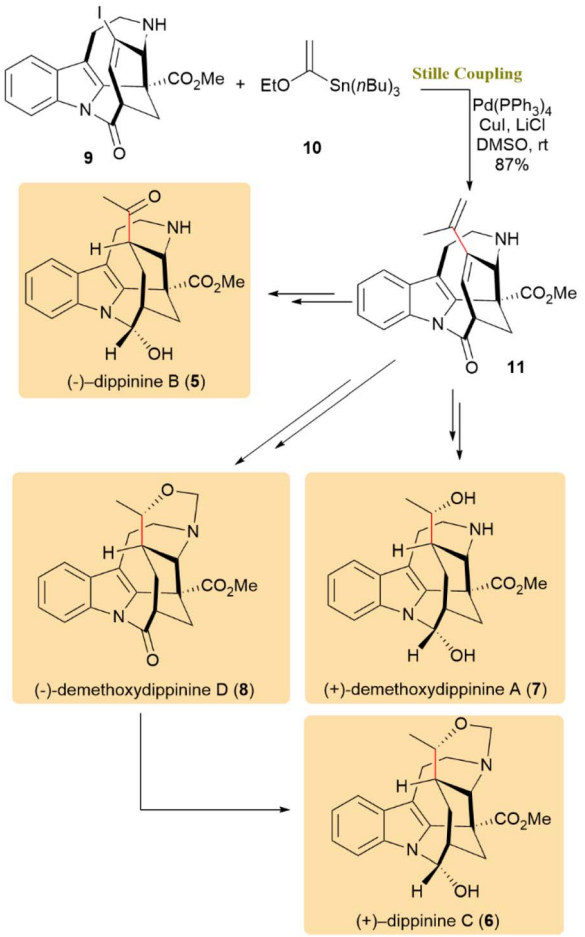


Scheme 1 Pd-catalyzed Stille coupling mechanism.

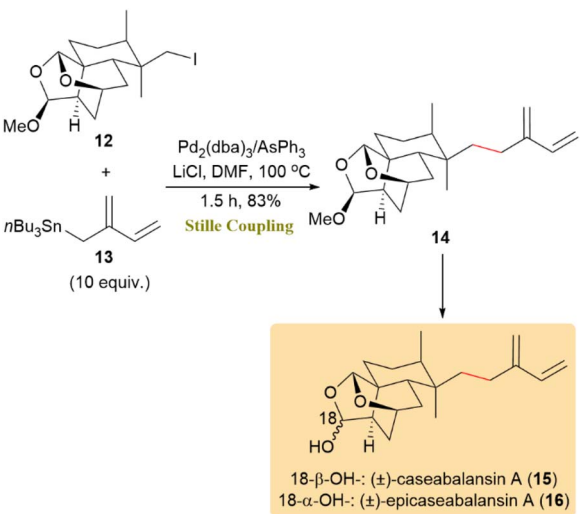


Scheme 2 Coupling of triflate **2** with vinyltributyltin **3** formed 4-vinylphenanthridine (**4**), the key precursor to (+)-asiaticumine (**1a**) and (−)-asiaticumine (**1b**).

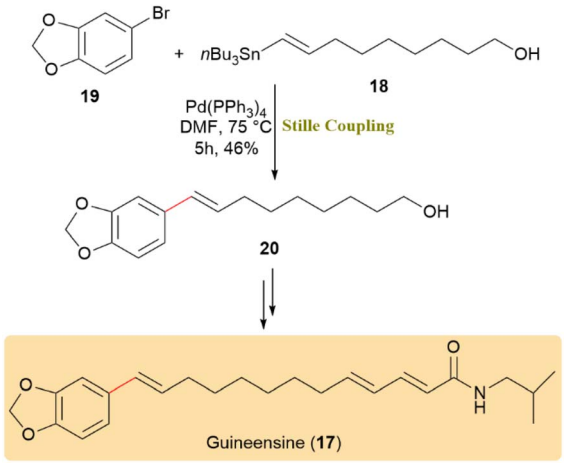
Department of Chemistry, Faculty of Sciences, Shahid Rajaee Teacher Training University, P.O. Box: 1678815811, Tehran, Iran. E-mail: e.hashemi@sru.ac.ir



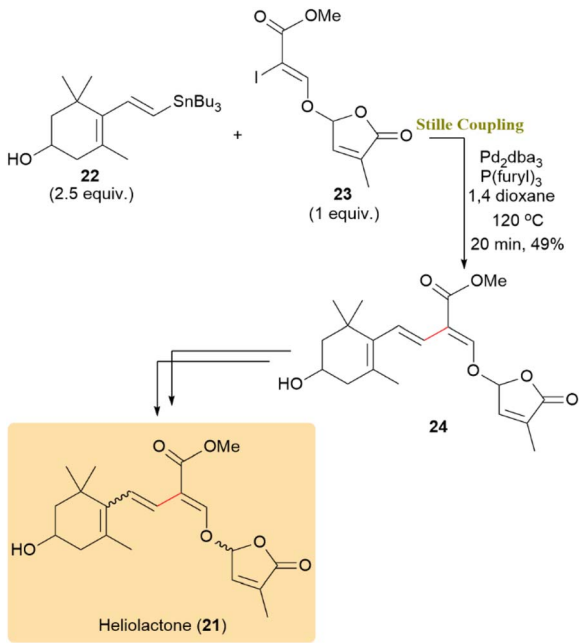
Scheme 3 Stille coupling between 9 and ethoxyvinylstannane 10 to afford diene 11, which was elaborated into dippinine B (5), dippinine C (6), 11-demethoxydippinine A (7), and D (8).



Scheme 4 Coupling of alkyl iodide 12 with organostannane 13 gave compound 14, the intermediate which led to (±)-caseabalansin A (15) and (±)-18-epicaseabalansin A (16).



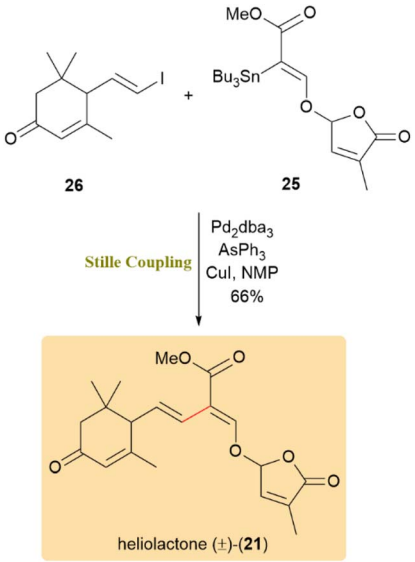
Scheme 5 Stille reaction between stannane 18 and bromide 19 provided alcohol 20, a key intermediate en route to guineensine (17).



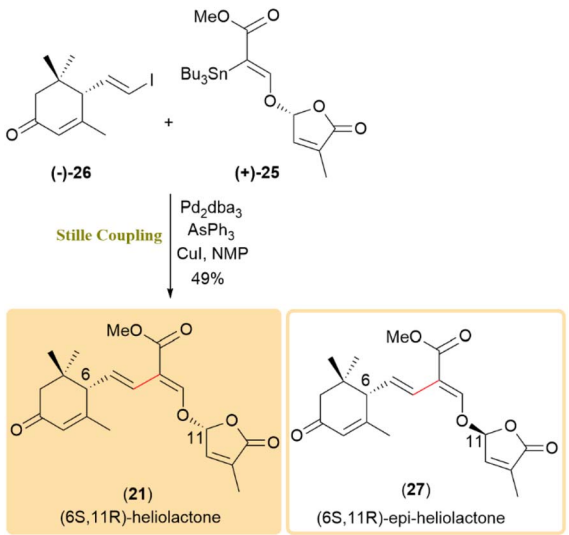
Scheme 6 Coupling of dienyl stannane 22 with vinyl iodide 23 to afford compound 24, precursor to heliolactone (21).

organic synthesis. Given their broad applicability, numerous reviews have highlighted recent advances in these methodologies.[26–28] Due to their unique properties, natural products often serve as core structures in drug development.[29]

Among these reactions, the Stille coupling—a palladium-catalyzed cross-coupling between organostannanes and organic electrophiles—stands out for its robustness, tolerance of diverse functional groups, and efficiency in forming C–C bonds under mild conditions. Originally introduced by Kosugi[30] and later refined by John K. Stille,[18,20] this reaction has evolved over nearly four decades into a highly reliable and versatile method for bond construction.[31] The general reaction involves coupling an organic halide or pseudohalide (R_1–X) with an



Scheme 7 Reversed coupling of partners **25** and **26** delivered racemic heliolactone (±-**21**).



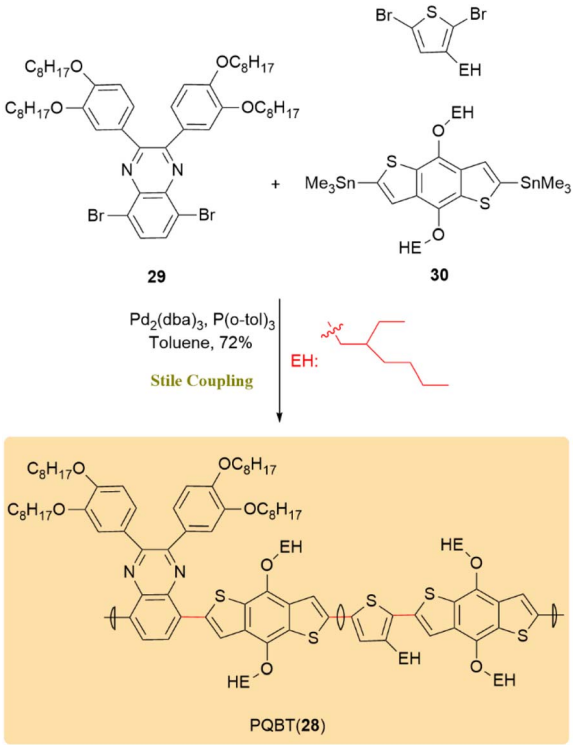
Scheme 8 Enantioselective couplings of (−)-**25**/(+)-**26** and (−)-**25**/(−)-**26** produced heliolactone (**21**) and 11-*epi*-heliolactone (**27**).

organostannane (R_2–SnR_3) in the presence of a palladium catalyst to afford the coupled product (R_1–R_2), as shown in eqn (1).

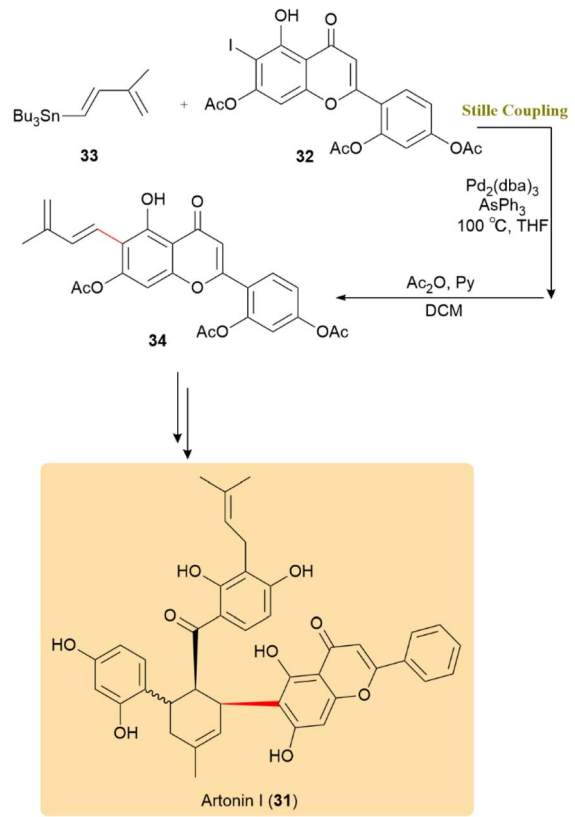
$$R^1 - X + R^2 - SnR_3 \xrightarrow{[Pd]} R^1 - R^2 + SnR_3 - X \quad (1)$$

Its mild conditions, air and moisture stability, and high selectivity make it ideal for synthesizing complex molecules, including natural products and pharmaceuticals such as kinase inhibitors.[32,33] Despite concerns over tin toxicity,[34] innovations like bulky phosphines,[35] bimetallic catalysis,[36–38] and greener systems[39] have sustained its relevance in modern organic synthesis.

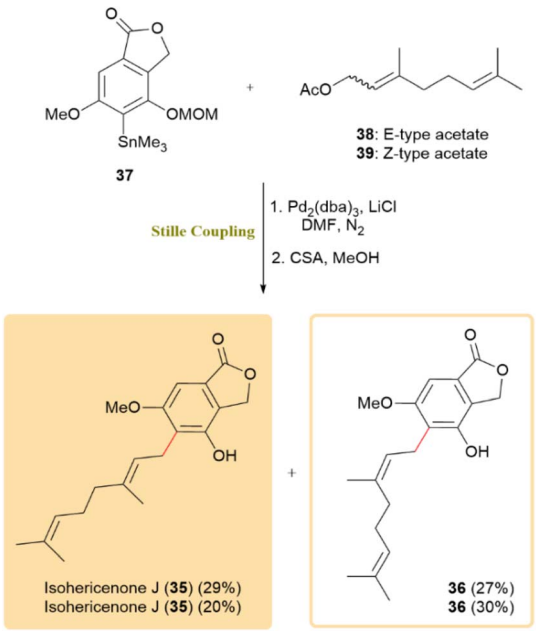
Mechanistically, the Stille coupling involves a catalytic cycle consisting of oxidative addition, transmetalation, and reductive



Scheme 9 Coupling of quinoxaline **29** with benzodithiophene **30** to afford polymer **28** (PQBT).

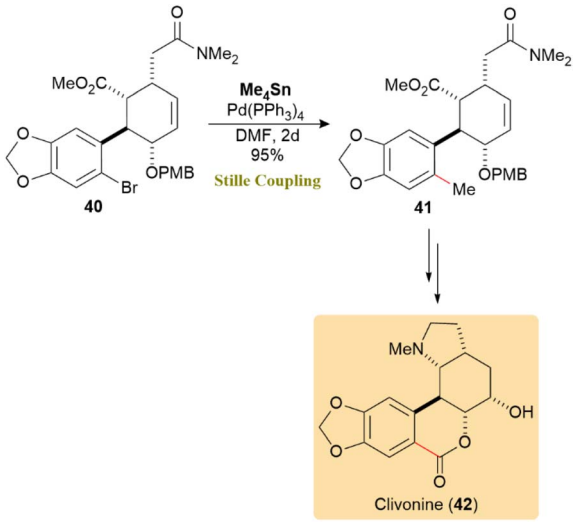


Scheme 10 Iodide **32** couples with diene stannane **33** to form intermediate **34**, enabling total synthesis of artonin I (**31**).



Scheme 11 Affording isohericenone J (**35**) and its isomer (**36**) using Sille coupling.

elimination, with possible participation of both cyclic and ionic pathways. *Espinet* and *Echavarren* provided detailed mechanistic studies highlighting the transmetalation step as the rate-determining and stereochemically sensitive process.[40] This mechanistic complexity reflects the delicate interplay of ligands, solvents, and additives that govern product distribution and efficiency. The refined mechanistic model (Scheme 1) illustrates not only the canonical three-step pathway but also its dynamic, reversible intermediates that influence overall selectivity and yield.[41]



Scheme 12 A $Pd(PPh_3)_4$-catalyzed Stille reaction of aryl bromide **40** gave product **41** and completed the synthesis of (±)-clivonine (**42**).

The Stille reaction remains a cornerstone of total synthesis, particularly in assembling complex natural products and functional materials. Building on foundational reviews,[42,43] this work provides an updated overview of post-2018 developments and representative examples, highlighting both intermolecular and intramolecular variants that demonstrate the reaction's versatility, mechanistic diversity, and enduring significance in modern synthetic chemistry.

2. The intermolecular Stille coupling

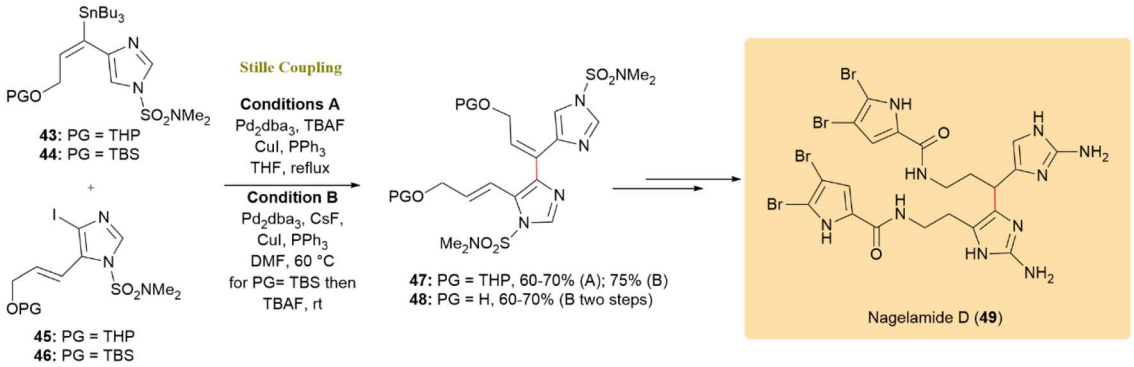
(+)-Asiaticumine A (**1a**) is a phenanthridine alkaloid with structural similarity to known bioactive natural products and is currently under evaluation for its biological activity. The initial synthesis of **1a** and its enantiomer **1b** was accomplished through the Stille reaction between triflate **2** and vinyltributyltin **3**, employing $PdCl_2(PPh_3)_2$ as the catalyst, resulting in the formation of 4-vinylphenanthridine (**4**) with an 89% yield. Compound **4** was subsequently transformed into **1a** and its enantiomer **1b** through Sharpless asymmetric dihydroxylation (Scheme 2).[44]

The enantioselective total synthesis of the natural post-iboga indole alkaloids dippinine B (**5**) and C (**6**), along with analogues 11-demethoxydippinine A (**7**) and D (**8**), was initially reported by Han and colleagues.[45] The synthesis involved the Stille cross-coupling of compound **9** with ethoxyvinylstannane **10**, resulting in diene **11** with an 87% yield. This diene was then further processed to obtain the target alkaloids **5**, **6**, **7**, and **8**, which are of particular interest due to their unique structures and potential anticancer activity, notably against vincristine-resistant cells (Scheme 3).[45]

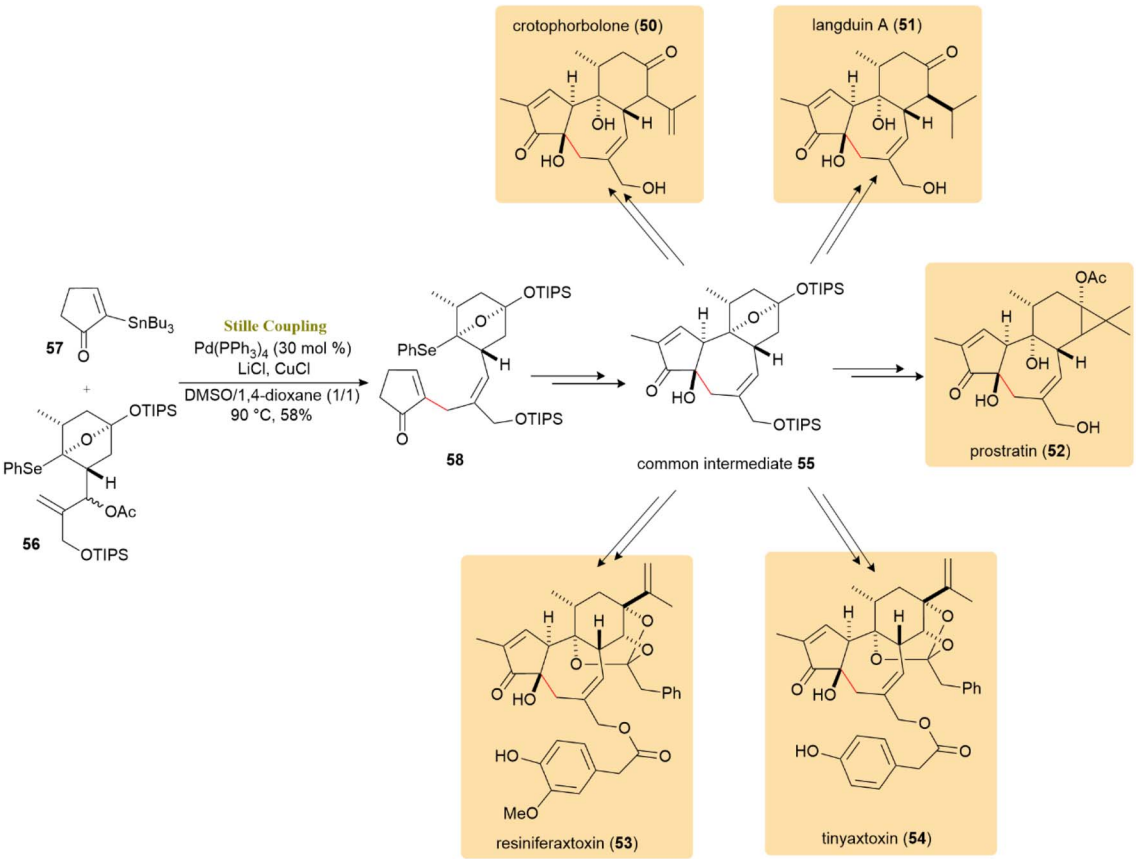
As illustrated in Scheme 4, a side chain added through the $C(sp^3)$–$C(sp^3)$ Stille coupling of alkyl iodide **12** and organostannane **13**, yielding the formation of key compound **14** under $Pd_2(dba)_3/AsPh_3$ catalysis, which minimized the formation of undesired by-products. Compound **14** was then transfomed into (±)-caseabalansin A (**15**) and (±)-18-epicaseabalansin A (**16**), which are promising clerodane diterpenoids with selective cytotoxic activity against PC3 cancer cells.[46]

Guineensine (**17**), a plant-derived natural product, has gained attention for its powerful and selective inhibition of endocannabinoid uptake. It shows significant potential as a pharmacological tool and lead compound for the treating anxiety, pain, and inflammation. To obtain this bioactive molecule, a synthetic strategy based on cross-coupling was used. The synthesis involved the early introduction of the benzodioxole moiety through a Stille coupling between stannane **18** and bromide **19**. This reaction yielded alcohol **20** in a 46% yield using $Pd(PPh_3)_4$ at 75 °C (Scheme 5).[47]

Heliolactone (**21**), a non-canonical strigolactone, exhibits promising biological activity by enhancing seed germination and inducing leaf senescence in both crops and parasitic weeds, making it a potential candidate for sustainable agricultural applications. Two independent total syntheses of heliolactone (**21**) have been reported, both of which involve a key Stille cross-coupling serving as the central bond-forming step.



Scheme 13 Vinylstannanes **43** and **44** coupled with iodoimidazoles **45** and **46** to form the bis-imidazolyl framework **47** leading to nagelamide D (**49**).

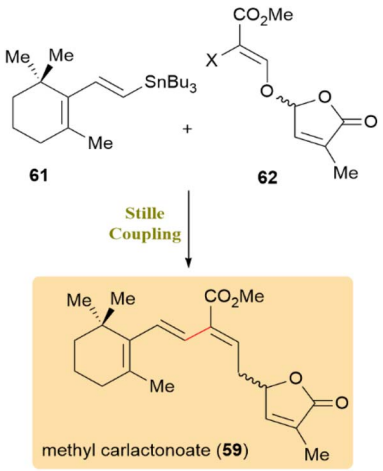


Scheme 14 A π-allyl Stille coupling between **56** and **57** generated *E*-olefin **58**, the key intermediate for crotophorbolone (**50**) and related diterpenoids.

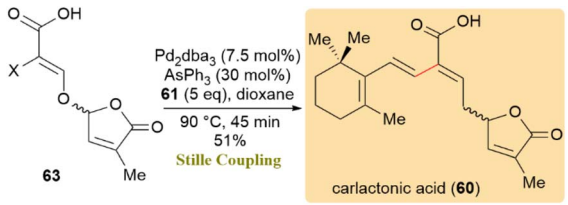
In one strategy, a palladium-mediated cross-coupling was employed to couple dienyl stannane **22** and racemic vinyl iodide **23**. Utilizing Pd_2dba_3 in combination with $AsPh_3$, the transformation furnished the targeted coupling product in moderate yield. Screening of different catalytic systems demonstrated that the use of Pd_2dba_3 along with tris(2-furyl)phosphine, in the absence of any additive, delivered the most favorable result, affording compound **24** in a 49% isolated yield (Scheme 6).[48]

As shown in Scheme 7, The complete synthesis of heliolactone (**21**) was accomplished separately through a crucial Stille cross-coupling with reversed nucleophile–electrophile coupling partners. The optimization process involved preparing coupling partners **25** and **26**, resulting in the racemic Heliolactone (±)-(**21**) being obtained at a yield of 66% under room temperature conditions.

Furthermore, enantioselective synthesis of heliolactone (**21**) was successful using (–)-**25** and (+)-**26**, resulting in the



Scheme 15 Vinyl stannane **61** and vinyl iodide **62** coupled to produce methyl carlactonoate (**59**).



Scheme 16 Carboxylic acid **63** and stannane **61** underwent Stille coupling to yield carlactonic acid (**60**).

formation of heliolactone. Additionally, coupling (−)-**25** with (−)-**26** produced 11-*epi*-heliolactone (**27**) similarly (Scheme 8).[49]

The Stille coupling served as a critical step in assembling PQBT (**28**), a multifunctional polymer that exhibits ambipolar electrochromic behavior. This reaction facilitated the formation of the polymer backbone by linking quinoxaline **29** and benzodithiophene **30** units. $Pd_2(dba)_3$ in combination with P(*o*-tol)$_3$ was employed as the catalytic system in toluene, resulting in a yield of 72% (Scheme 9). The mild reaction conditions, broad functional group compatibility, and efficiency of the Stille coupling were key factors in synthesizing a complex polymer with multifunctional properties.[50]

The reaction conditions for the Stille coupling, which was instrumental in the chemoenzymatic total synthesis of artonin I (**31**), were optimized to significantly increase yields from 5% to 75% by replacing $Pd(OAc)_2$ with $Pd_2(dba)_3$ in the presence of $AsPh_3$. In this reaction, iodide **32** and diene stannane **33** underwent coupling to afford diene precursor **34** (Scheme 10). This underscores the importance of catalyst choice and reaction conditions in organic synthesis and highlights the efficiency of the Stille reaction, particularly when integrated with enzymatic methods for natural product synthesis and drug discovery.[51]

Isohericenone J (**35**), a cytotoxic metabolite isolated from *Hericium erinaceum*, along with its isomer (**36**), were synthesized through an optimized two-step sequence involving a Stille coupling followed by deprotection using D-camphorsulfonic acid, affording a combined yield of 29%. The critical Stille cross-coupling step was performed between a stannane intermediate bearing a lactone moiety (**37**) and (*E*)-3,7-dimethylocta-2,6-dien-1-yl acetate (**38**), enabling the formation of the C5–C1′ carbon–carbon linkage. Furthermore, employing (*Z*)-3,7-dimethylocta-2,6-dien-1-yl acetate (*Z*) under identical conditions generated a mixture of geometric isomers, yielding both *E*- and *Z*-products in a 2 : 3 ratio (Scheme 11).[52]

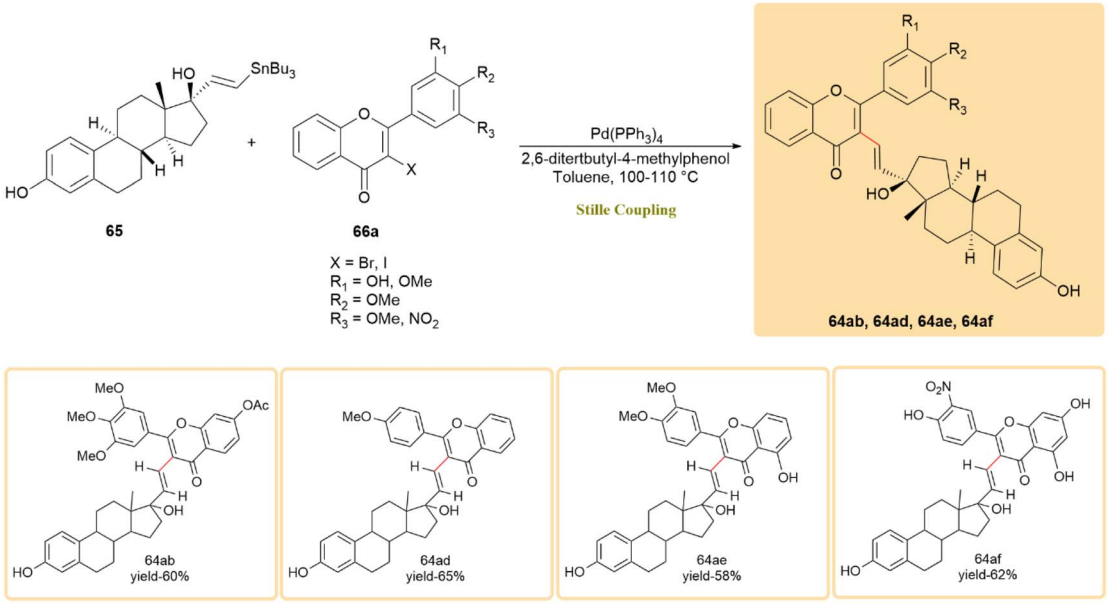
(±)-Clivonine, a lycorenine-type Amaryllidaceae alkaloid with significant anticancer, antimicrobial, and neuroprotective properties, serves as a valuable scaffold in medicinal chemistry. As shown in Scheme 12, the Stille reaction, facilitated by a $Pd(PPh_3)_4$ catalyst, exhibited high efficacy in coupling aryl bromide **40**, resulting in product **41** with an impressive 95% yield over a 2-day period. This successful application highlights the versatility of the Stille reaction in forming aryl–aryl bonds, domenstrating its key involvement in assembling natural products like (±)-clivonine (**42**).[53]

The nagelamides, a class of dimeric alkaloids from marine sponges, were synthesized through a Stille cross-coupling between vinylstannanes (**43**, **44**) with iodoimidazoles (**45**, **46**) using *Baldwin*'s modified conditions. This method, which CuI in combination with fluoride additives as co-catalytic agents, proved effective for sterically and electronically demanding substrates. Efficient cross-coupling was achieved under optimized conditions employing either CuI/TBAF in THF or CuI/CsF in DMF to produce the bis imidazolyl framework (**47**). Subsequent transformations resulted in the key intermediate **48** and ultimately led to the total synthesis of nagelamide D (**49**). CsF-mediated protocols consistently provided a 75% yield on scale-up, while TB AF-mediated yields were lower (Scheme 13).[54]

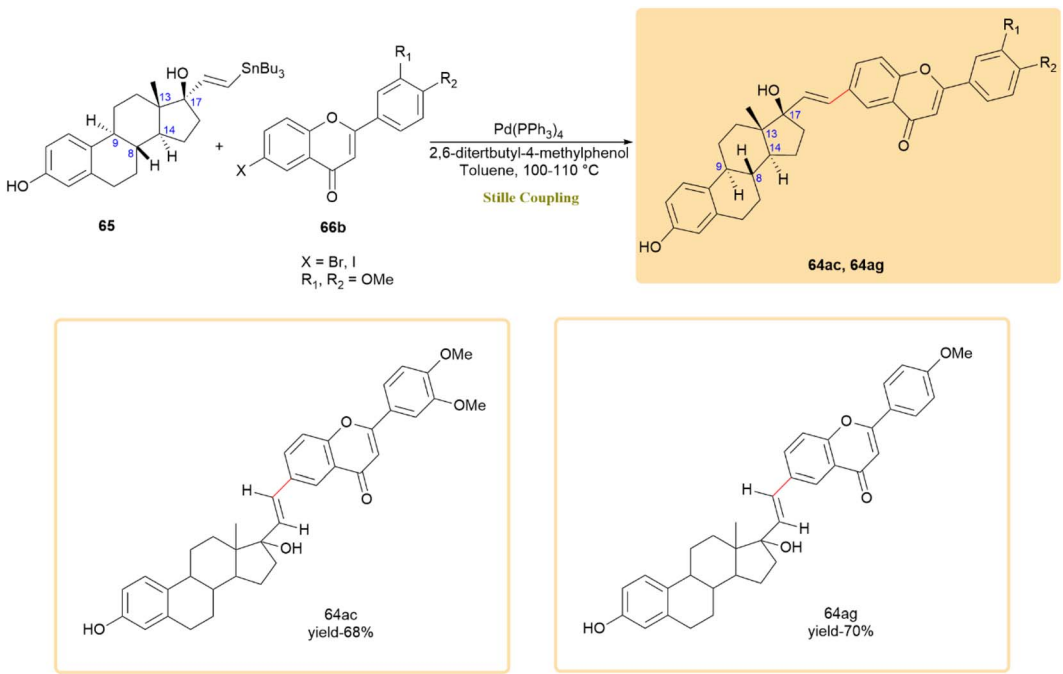
A novel, unified strategy was devised for the efficient total synthesis of five prominent compounds across the

Table 1 Optimization of palladium catalysts and reaction conditions for the Stille coupling of vinyl stannane **61** and vinyl iodide **62** in the synthesis of methyl carlactonoate (**59**)

No.	Catalyst (mol%)/halide	Additive/ solvent	Temp (°C), time (min)	Conv. (%)	Yield (%)
1	$Pd(PPh_3)_4$ (20)/I	—/Toluene	100, 60	∼5%	Trace
2	$PdCl_2(PPh_3)_2$ (20)/I	CuI/DMF	100, 60	100%	10
3	$Pd_2(dba)_3$ (10) + $AsPh_3$ (40)/I	—/Dioxane	100, 60	100%	30
4	$Pd_2(dba)_3$ (7.5) + $AsPh_3$ (30)/I	—/Dioxane	90, 45	100%	75
5	$Pd_2(dba)_3$ (10) + $AsPh_3$ (40)/Br	—/Dioxane	100, 60	30%	Trace



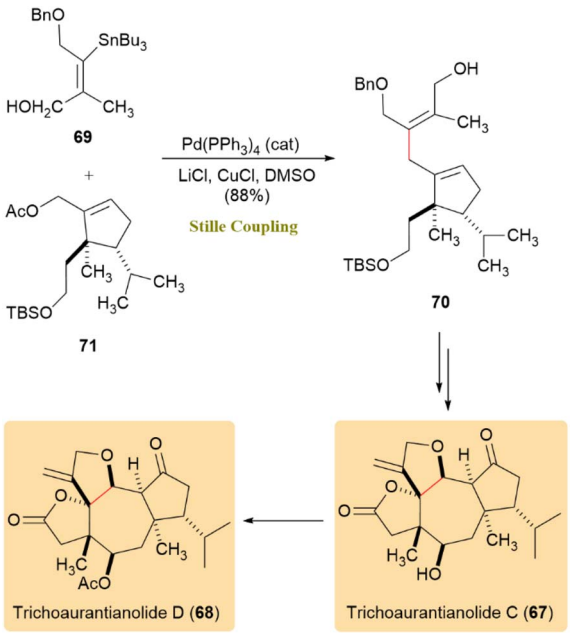
Scheme 17 Tin estradiol derivative **65** and flavone **66a** were coupled to form flavone-estradiol adducts **64ab–64af**.



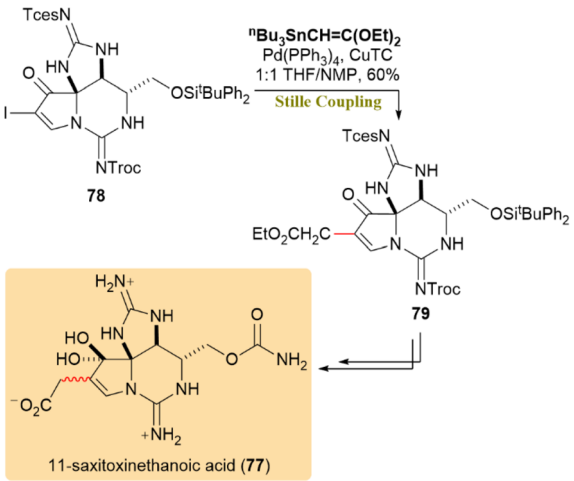
Scheme 18 Tin estradiol **65** and flavone **66b** underwent Stille reaction to produce flavone-estradiol adducts **64ab–64af**.

rhamnofolane, tigliane, and daphnane diterpenoids families: crotophorbolone (**50**), langduin A (**51**), prostratin (**52**), resiniferatoxin (**53**), and tinyatoxin (**54**). Intermediate **55**, with six stereocenters, was synthesized *via* a π-allyl variant of the Stille cross-coupling and then diversified into compounds 1–5 by selectively installing various functional groups. Treatment of compound **56** with vinyl tributylstannane **57**, along with CuCl, LiCl and catalytic $Pd(PPh_3)_4$ in DMSO/1,4-dioxane at 90 °C, provided the target trisubstituted *E*-olefin, furnishing compound **58** as a stereochemically pure product in 58% yield (Scheme 14).[55]

A concise and effective route to enantiopure noncanonical strigolactones was established through a Stille coupling approach, which was achieved by synthesizing of methyl carlactonoate (**59**) and carlactonic acid (**60**). As shown in Scheme 15, this method involved the coupling of vinyl stannane **61** and



Scheme 19 π-allyl Stille coupling to yield trichoaurantianolides C (**67**) and D (**68**).



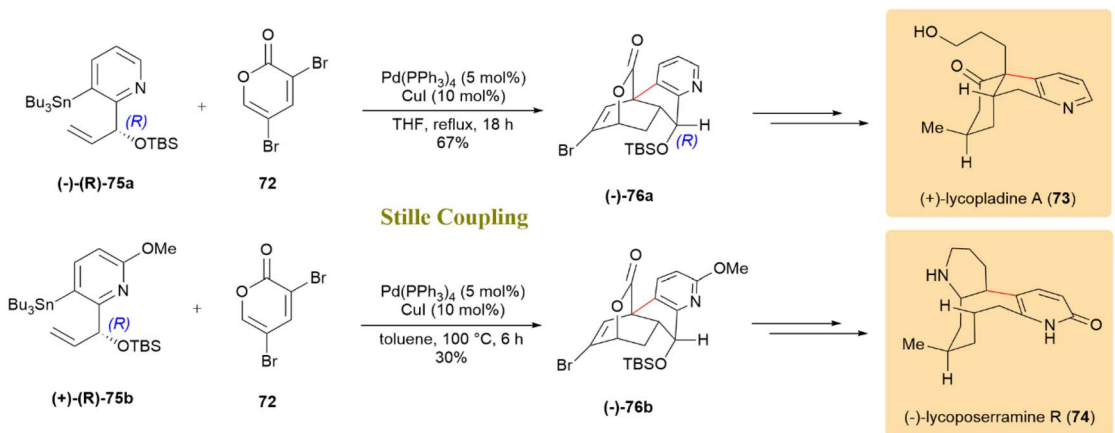
Scheme 21 Vinyl iodide **78** and (2,2-diethoxyvinyl)tin coupled to form **79**, a key precursor of 11-saxitoxinethanoic acid (**77**).

vinyl iodide **62** *via* the Stille reaction to synthesize methyl carlactonoate (**59**). Optimization of catalytic systems revealed $Pd_2dba_3/AsPh_3$ as the most effective, yielding 75% of the desired product (Table 1).

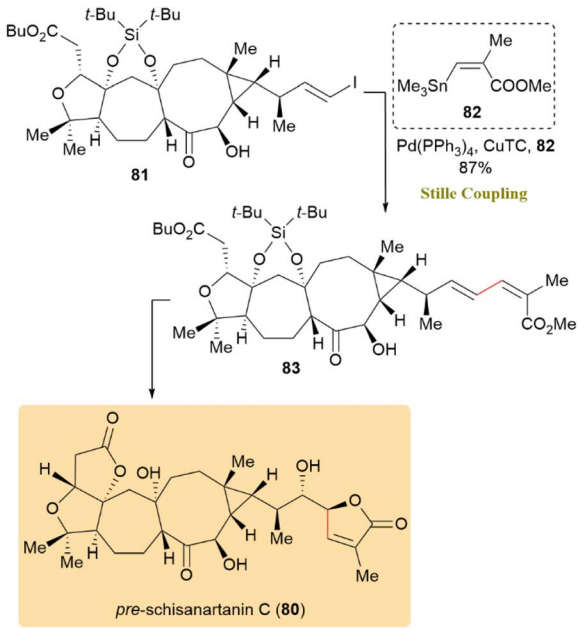
Furthermore, the synthesis of carlactonic acid (**60**) was explored, resulting in a 51% yield *via* Stille cross-coupling between carboxylic acid **63** and a surplus of stannane **61** (Scheme 16). Notably, carlactonic acid (**60**) exhibited enhanced stability compared to methyl carlactonoate (**59**), remaining unchanged when maintained at −80 °C under inert argon for 30 days.[56]

Flavone–estradiol adducts (**64ab–64af**), which combine the estrogenic activity of estradiol with the anticancer properties of flavones, were synthesized *via* Still coupling.[57] Tin estradiol derivatives **65** and flavone derivatives **66a** (Scheme 17) and **66b** (Scheme 18) reacted using a palladium catalyst and 3 crystals of 2,6-di-*tert*-butyl-4-methyl phenol in toluene at 100–110 °C, yielding products **64ab–64af** in up to 70% yield within 2 days. These adducts were synthesized from natural 17β-estradiol and therefore retain its native stereochemistry (8*R*, 9*S*, 13*S*, 14*S*, 17*S*; 17β-OH), with no new chiral center formed at the coupling site.[58]

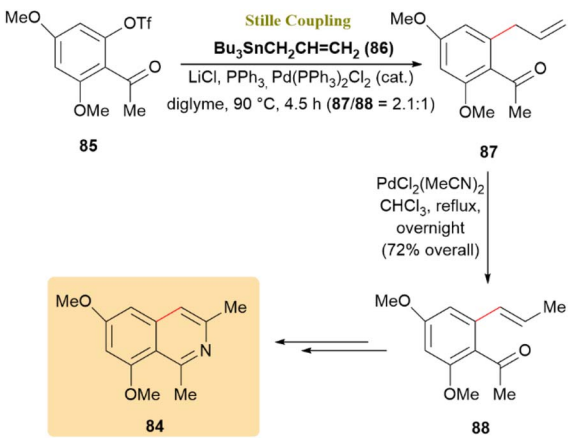
A complete synthetic route to trichoaurantianolides C (**67**) and D (**68**), diterpenoid natural products isolated from tricholoma aurantium and tricholoma fracticum, was investigated. Demonstrating excellent stereocontrol, the π-allyl variant of Stille coupling was applied to generate nonconjugated 1,4-skipped dienes from tri- and tetrasubstituted alkenes. The stannane **69** substrate showed high reactivity, producing tetrasubstituted alkene **70** with an 88% yield and retention of olefin geometry when combined with allylic acetate **71** (Scheme 19). These results indicated that the Stille cross-coupling is



Scheme 20 A tandem Stille/IMDA sequence from pyridine stannanes **75a**, **75b** to complete lycopladine A (**73**) and lycoposerramine R (**74**) synthesis.



Scheme 22 Produced **83** using Stille coupling, which was converted to pre-schisanartanin C (**80**).

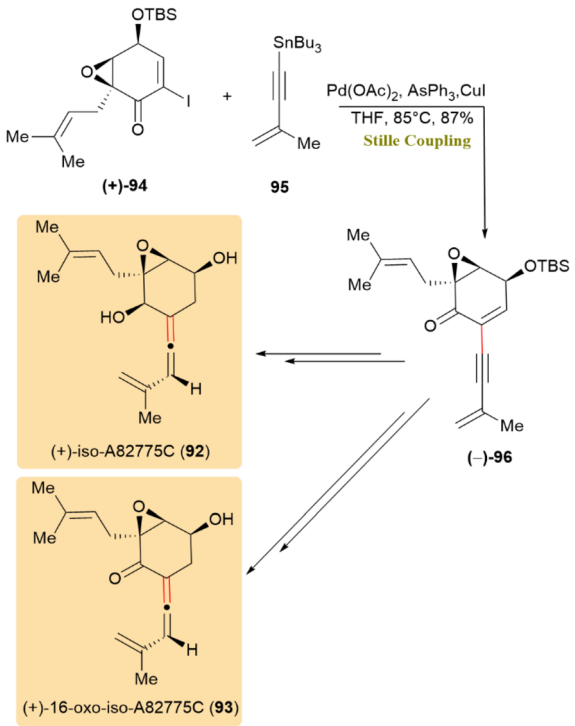


Scheme 23 Completing the synthesis of 6,8-dimethoxy-1,3-dimethylisoquinoline (**84**).

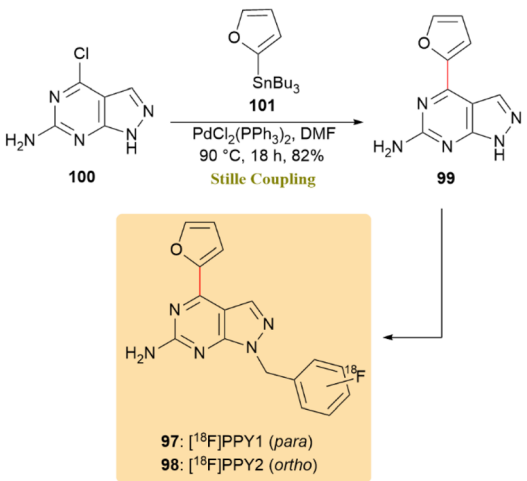
Scheme 24 Chalaniline B (**89**) was formed from **90** through a palladium-catalyzed Stille coupling.

a preferred approach for synthesizing highly substituted, stereodefined 1,4-dienes.[59]

As shown in Scheme 20, 2-pyrone derivative (**72**), bearing a chiral branched allylic silyl ether moiety, participated in an

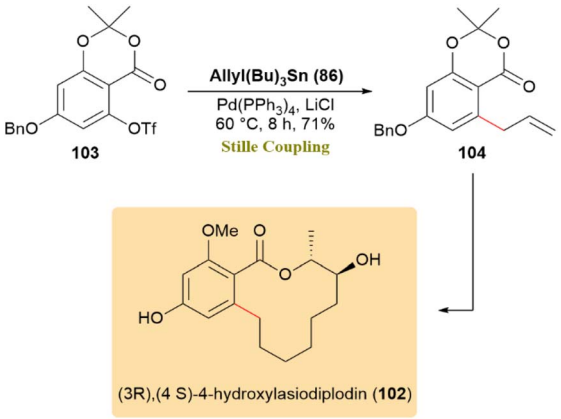


Scheme 25 Iodide **94** and stannane **95** coupled to give alkyne **96**, precursor of (+)-iso-A82775C (**92**) and (+)-16-oxo-iso-A82775C (**93**).



Scheme 26 Stille coupling afforded **99**, an intermediate for radiotracers [^{18}F]PPY1 (**97**) and [^{18}F]PPY2 (**98**).

intramolecular Diels–Alder (IMDA) reaction, exhibiting excellent selectivity. This process yielded pure cycloadducts that were then transformed into (+)-lycopladine A (**73**) and (−)-lycoposerramine R (**74**). The tandem coupling/IMDA reaction involving pyridine stannane (−)-(*R*)-**75a** afforded tetracyclic lactone (−)-**76a** in a 67% yield, under reflux conditions with $Pd(PPh_3)_4$, successfully completing the total synthesis of **73**. Subsequently, the synthesis of **74** was accomplished by employing pyridine stannane (+)-(*R*)-**75b**, leading to the



Scheme 27 Triflate **103** and allylstannane **86** underwent Stille coupling to form **104**, an intermediate toward (3*R*,4*S*)-4-hydroxylasiodiplodin (**102**).

formation of the IMDA adduct (−)-**76b** in a 30% yield with $Pd(PPh_3)_4$ serving as the catalyst at 100 °C.[60]

The Stille coupling was utilized to synthesize 11-saxitoxinethanoic acid (SEA) (77), a model compound for zetekitoxin AB, which is known for its potent inhibition of voltage-gated sodium channels (NaVs). Vinyl iodide **78** reacted with (2,2-diethoxyvinyl)tin employing $Pd(PPh_3)_4$ and CuTC, resulting in the formation of compound **79** with a 60% yield and consistent results (Scheme 21).[61]

The enantioselective total synthesis of pre-schisanartanin C (**80**), a Schisandra nortriterpenoid with significant antihepatitis, anti-tumor, and anti-HIV properties, has been reported. Vinyl iodide **81** underwent a Pd-catalyzed Stille reaction with trimethylstannylacrylate **82** and CuTC, yielding product **83** in an 87% yield. Further treatment of product **83** led to the isolation of pre-schisanartanin C (**80**) as the sole product (Scheme 22).[62]

The total synthesis of 6,8-dimethoxy-1,3-dimethylisoquinoline (**84**), a natural product from *Ancistrocladus tectorius*, along with evaluation of its cytotoxic activity, was investigated. A $Pd(PPh_3)_2Cl_2$-mediated allylation of triflate **85** with allyltributyltin (**86**) in DMF at 100 °C afforded allyl **87** and propenyl **88** in a 2.1 : 1 ratio over 20 hours. This result was not unexpected, as the conversion of allyl benzenoids to 1-propenyl derivatives is common in Pd-catalyzed cross-couplings, particularly with electron-withdrawing substituents. Further treatment yielded 72% of **88**, thereby achieving the synthesis of **84** (Scheme 23).[63]

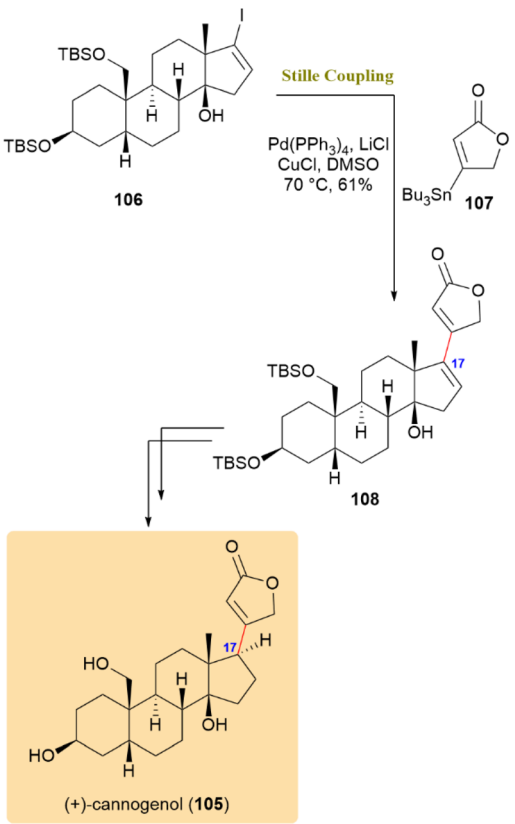
Chalaniline B (**90**), an antibiotic aminoxanthone, was synthesized from *Chalara* sp. treated with vorinostat. As shown in Scheme 24, compound **90** was converted directly into **89** through a palladium -catalyzed cross-coupling reaction using the unprotected variant of Migita's reagent (**91**), yielding 22%.[64]

Epoxyquinoid natural products, which are a family of secondary metabolites with a complex cyclohexane core, exhibit antibiotic, antifungal, and antitumoral activities. The synthesis of (+)-iso-A82775C (**92**) and (+)-16-oxo-iso-A82775C (**93**) was achieved through Stille coupling. Iodide (+)-**94** and organostannane **95** were coupled with an 87% yield using $Pd(OAc)_2$, triphenylarsine, and copper(I) iodide, resulting in alkyne (−)-**96**, which was then further processed to obtain **92** and **93** (Scheme 25).[65]

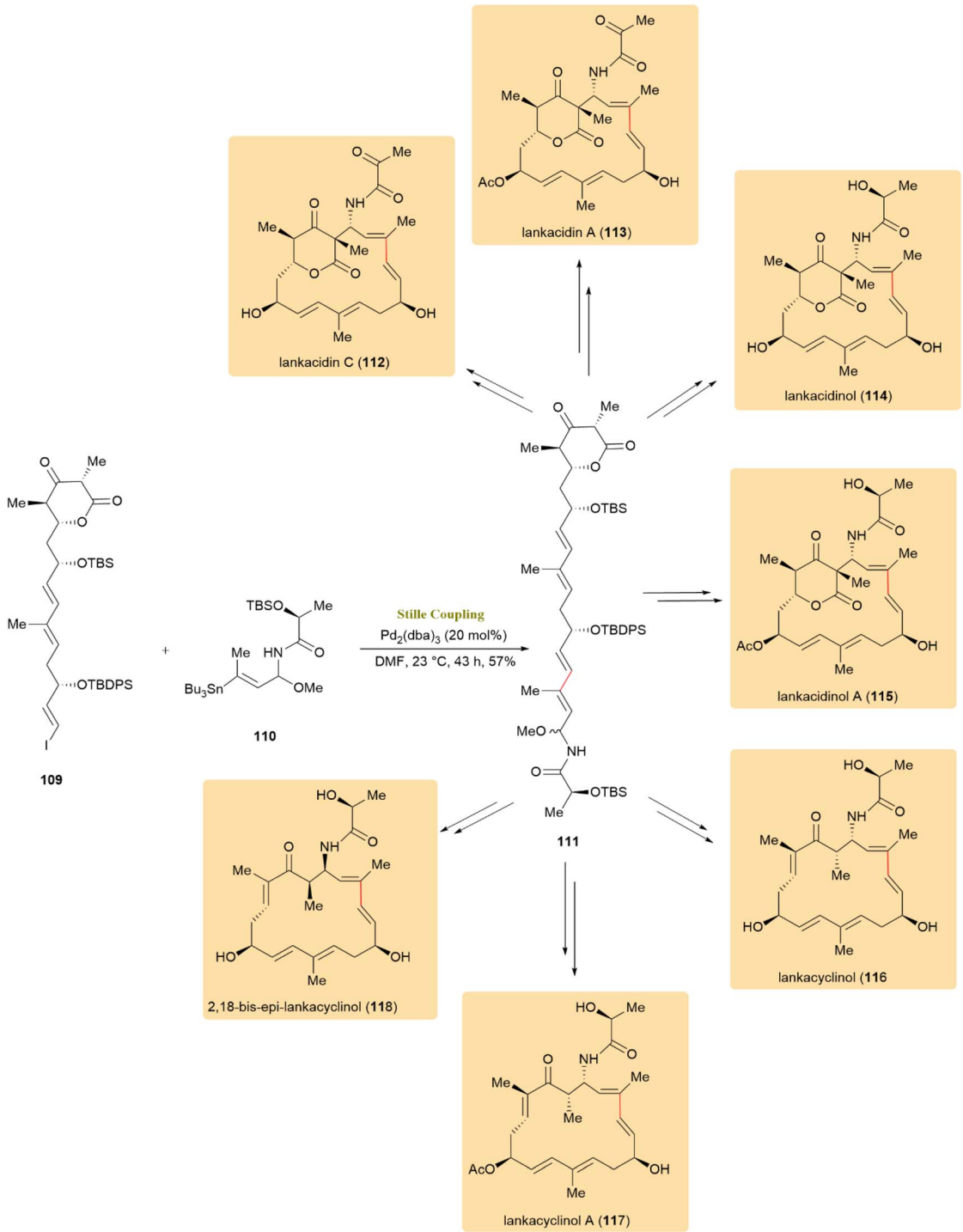
A set of novel fluorinated pyrazolo[2,3-*d*]pyrimidine analogues (PPY1–PPY22) was prepared with the objective of developing an ^{18}F-labeled PET radiotracer targeting the A_2A adenosine receptor ($A_{2A}R$) for brain imaging. This was accomplished by structural modification of a recently reported lead compound (PPY). The radiosynthesis of [^{18}F]PPY1 (**97**) and [^{18}F]PPY2 (**98**) was successfully performed using a newly developed alcohol-assisted, copper-mediated one-step ^{18}F-labeling protocol. As shown in Scheme 26, compound **99** synthesized *via* stille coupling, served as a crucial intermediate for the development of subsequent derivatives. The optimization of the stille coupling process was achieved through the direct application of unprotected compound **100**, resulting in a yield of 82% for compound **99** at 90 °C in the presence of tributyl(furan-2-yl)stannane **101**.[66]

The total synthesis of (3*R*,4*S*)-4-hydroxylasiodiplodin (**102**), a bioactive resorcylic acid macrolactone with cytotoxic, antimicrobial, and prostaglandin biosynthesis inhibitory properties, was achieved using a Stille coupling as a pivotal step.

The triflate compound **103** was utilized to form a C–C bond through palladium-catalyzed Stille coupling, employing allylstannane **86**, LiCl, and $Pd(PPh_3)_4$, to afford compound **104** in



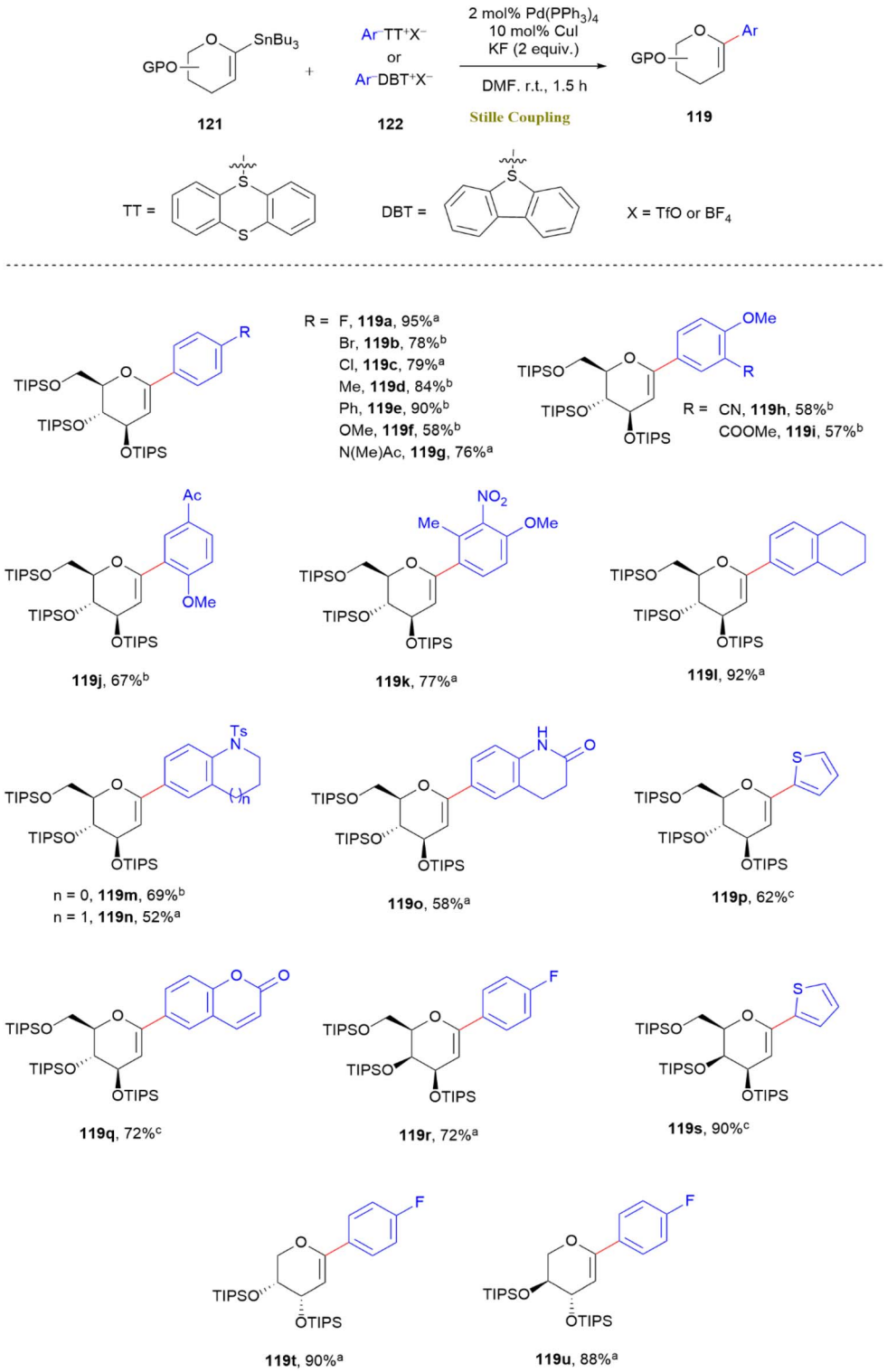
Scheme 28 Stille coupling of compound **106** with tributylstannyl butenolide **107** serves as a key step in the synthesis of (+)-cannogenol (**105**).



Scheme 29 Compounds **109** and **110** coupled to give **111**, converted into lankacidin derivatives **112–118**.

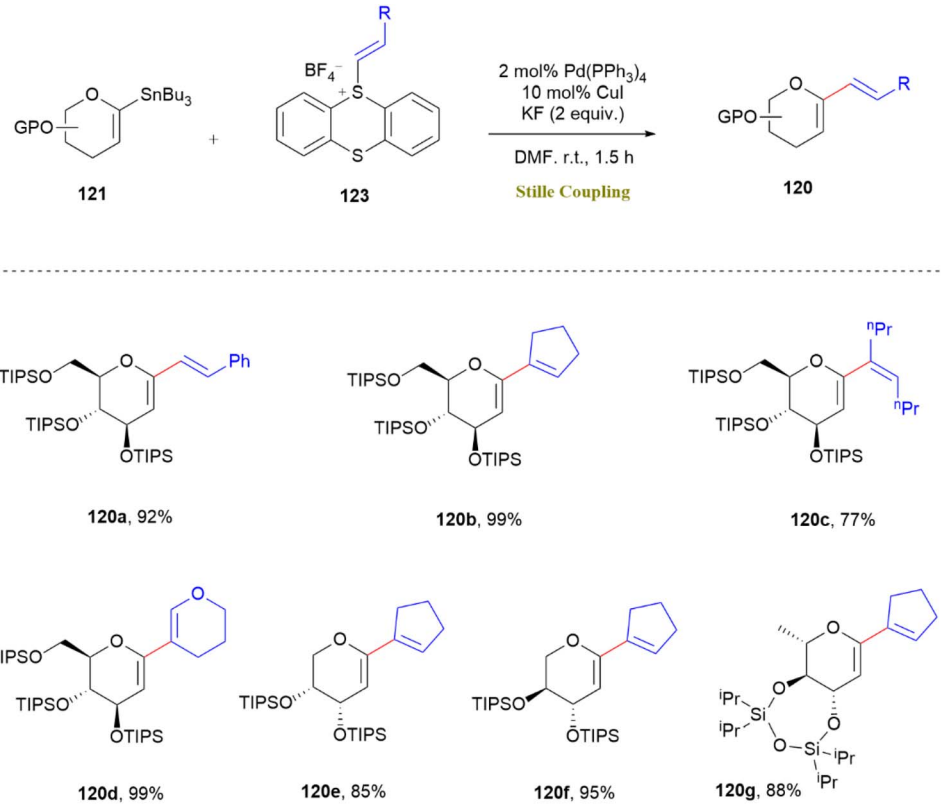
71% yield (Scheme 27). This intermediate facilitated the synthesis of compound **102**.[67]

(+)-Cannogenol (**105**), an aglycone common to several biologically important cardiotonic glycosides, was synthesized through a key Stille coupling step. As shown in Scheme 28, the coupling of compound 106 with tributylstannyl butenolide **107** using $Pd(PPh_3)_4$, LiCl, and CuCl at 70 °C afforded compound 108 in 61% yield. This transformation efficiently installed the characteristic butenolide moiety at C17 of the steroid framework, a transformation that is challenging by other mSethods due to steric congestion and the sensitivity of the polyoxygenated D-ring. The LiCl/CuCl additives accelerated the transmetalation process and ensured clean coupling, highlighting the Stille reaction's superior tolerance toward complex functionalized steroid systems.[68]



Scheme 30 Synthesis of *C*-aryl glycals *via* Pd/Cu co-catalyzed coupling of glycosyl stannane **121** (0.1 mmol) and sulfonium salt **122** (0.12 mmol). Conditions: $Pd(PPh_3)_4$ (2 mol%), CuI (10 mol%), KF (0.2 mmol), DMF (1 mL), under N_2. Yields are isolated. a = TT, TfO^-; b = TT, BF_4^-; c = DBT, TfO^-.

Lankacidin antibiotics, known for their unique architectures and biological significance, have been extensively studied. The successful method involved the Stille reaction between compounds **109** and **110** under optimized conditions (20 mol% $[Pd_2(dba)_3]$, DMF, 23 °C), yielding the hypersensitive *N*,*O*-acetal **111** with an isolated yield of 57%. Alternative methods proved unsuccessful, highlighting the crucial role of this reaction. Compound **111** was subsequently converted into various

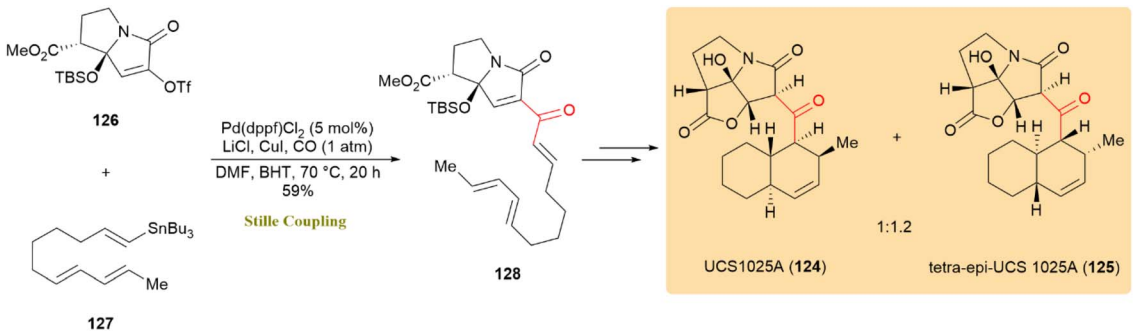


Scheme 31 *C*-Alkenyl glycal synthesis *via* Pd/Cu-catalyzed coupling of stannane 121 (0.1 mmol) and sulfonium salt 123 (0.12 mmol) conditions: $Pd(PPh_3)_4$ (2 mol%), CuI (10 mol%), DMF (1 mL), KF (0.2 mmol), under N_2. Yields are isolated.

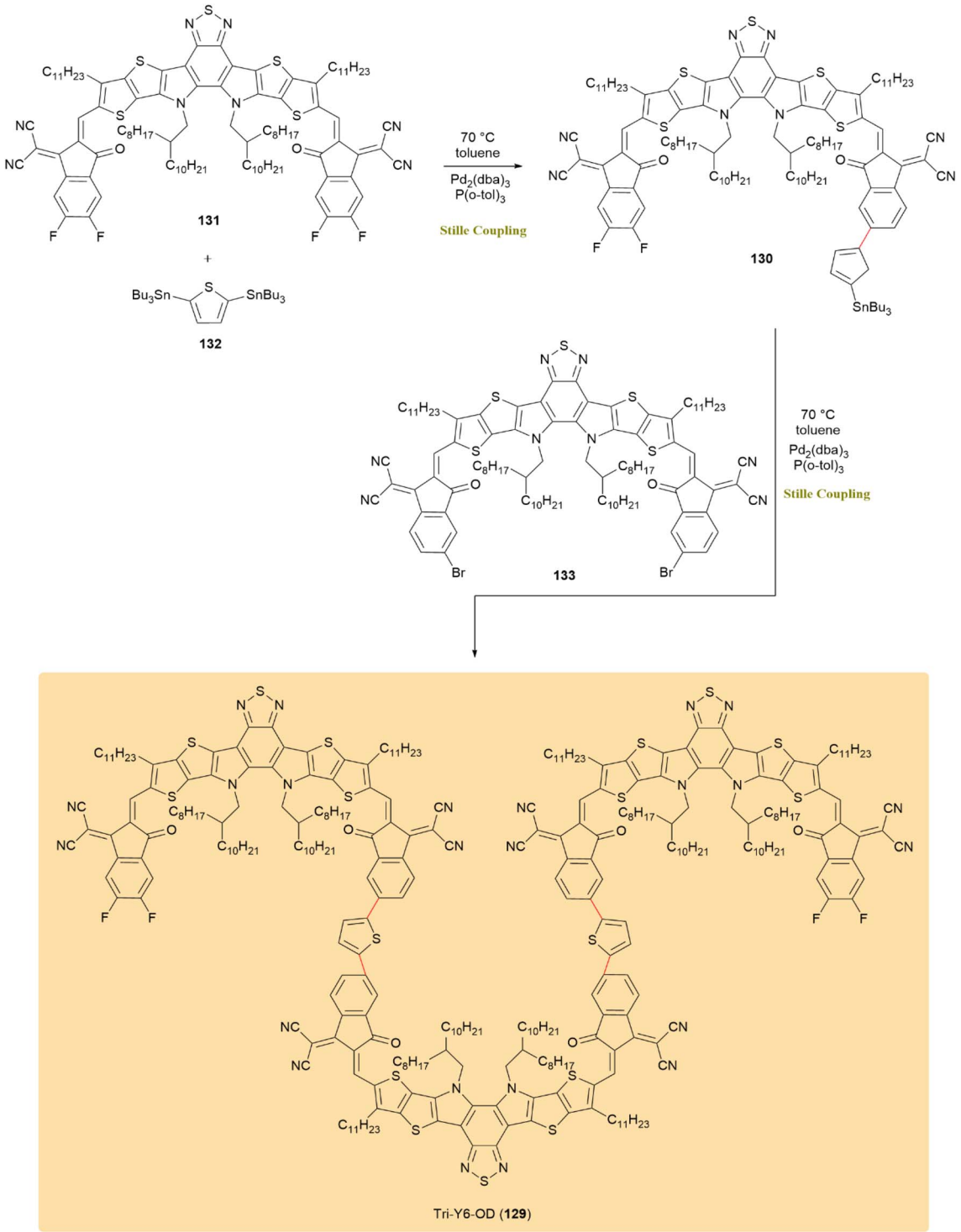
lankacidin derivatives, spincluding Lankacidin C (**112**), Lankacidin A (**113**), Lankacidinol (**114**), Lankacidinol A (**115**), Lankacyclinol (**116**), and Lankacyclinol A (**117**). Additionally, it was transformed into 2,18-bis-*epi*-lankacyclinol (**118**), a newly identified natural product, contributing to the understanding of lankacidin structural diversity (Scheme 29).[69]

A highly efficient Pd/Cu-catalyzed Stille cross-coupling method has been devised for the preparation of *C*-ary (**119**-series) and *C*-alkenyl glycals (**120**-series) through the reaction of glycosyl stannanes (**121**) with aryl (**122**-series) and alkenyl (**123**-series) sulfonium salts. This methodology takes advantage of the synergistic roles of palladium and copper. Pd(0) undergoes oxidative addition with sulfonium salts, followed by CuI-facilitated transmetallation and reductive elimination. The reaction occurs under mild, scalable conditions without the need for prefunctionalized aryl halides. It demonstrates broad functional group tolerance, including cyano, ester, nitro, ketone, methoxy, and alkyl substituents (Scheme 30).

Additionally, the strategy enabled one-pot formal C–H glycosylation, streamlining the incorporation of glycosylmoieties onto arenes. Notably, alkenyl sulfonium salts (**123**-series) exhibited higher reactivity than their aryl counterparts, resulting in alkenylated products (**120a–120g**) without *E*/*Z* isomerization (Scheme 31). This approach expanded the utility of the Stille reaction in carbohydrate chemistry, making it easier to



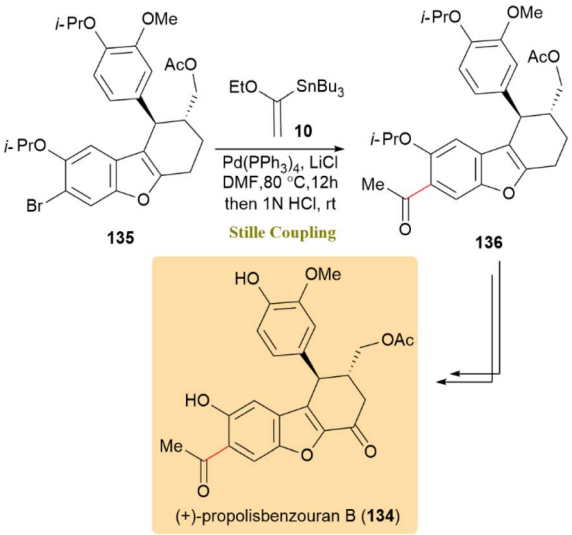
Scheme 32 Vinyl triflate **126** and vinylstannane **127** underwent carbonylative Stille coupling to afford enone **128**, a precursor of UCS1025A (**124**).



Scheme 33 Monomer **131** and bis(stannyl)thiophene **132** coupled to form intermediate **130** for trimer acceptor tri-Y6-OD (**129**).

synthesize of bioactive glycals relevant to drug discovery and natural product synthesis.[70]

A convergent synthetic approach was established for the total synthesis of UCS1025A (**124**) and its diastereomer, tetra-*epi*-UCS1025A (**125**). This method employed a tandem carbonylative Stille coupling followed by a Diels–Alder cycloaddition to establish a critical carbon–carbon bond and assemble the *trans*-decalin core structure. UCS1025A (**124**) belongs to a class of natural compounds with antibacterial, antifungal, and anticancer activities. The carbonylative Stille cross coupling was applied to vinyl triflate **126** and vinylstannane **127**, resulting in the smooth production of carbonylation enone **128** with $Pd(dppf)Cl_2$ as a catalyst, achieving a 59% yield under specific conditions (Scheme 32).[71]

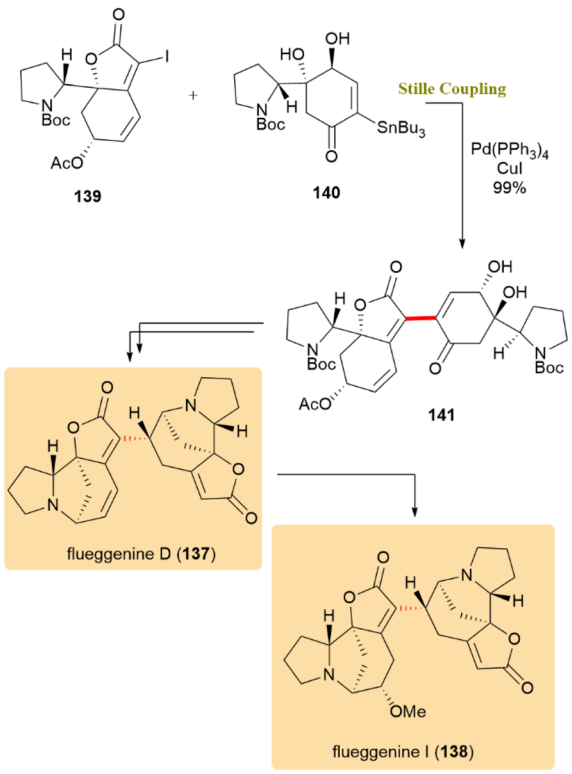


Scheme 34 Stille coupling of tricyclic core **135** and (α-ethoxyvinyl) tributyltin 10 led to (+)-propolisbenzofuran B (**134**).

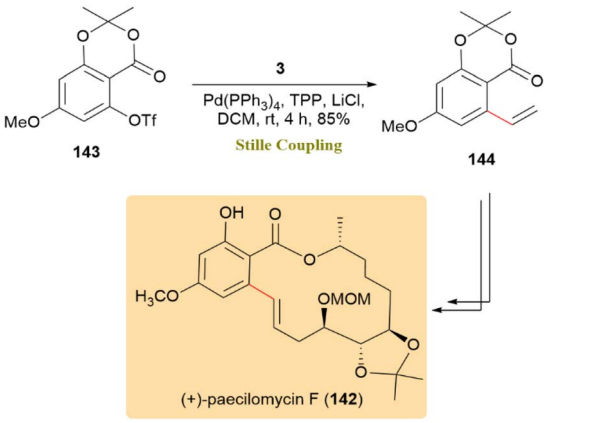
A stepwise method utilizing the Stille coupling was developed for synthesizing oligomer acceptors in organic-based solar cells. The successful synthesis of a trimer acceptor, Tri-Y6-OD (**129**), demonstrated the effectiveness of this approach, with oligomerization shown to improve both device performance and stability. The crucial intermediate **130** was obtained through a Stille coupling between a monobrominated monomer **131** with an excess 2,5-bis(tributylstannanyl)thiophene **132** mediated by $Pd_2(dba)_3$ in combination with P(*o*-tol)$_3$. After purification by methanol precipitation and ethanol rinsing, the final product, Tri-Y6-OD 5, was obtained through a subsequent Stille coupling with dibrominated monomer **133** (Scheme 33).[72]

The first enantioselective synthesis of the cytotoxic natural compound (+)-propolisbenzofuran B (**134**) was completed in 11 synthetic steps. The key step involved a $Pd(PPh_3)_4$-catalyzed Stille coupling of the advanced tricyclic core **135** with (α-ethoxyvinyl)tributyltin **10**, serving as a masked acetylating agent, in DMF at 80 °C. Acidic treatment afforded the intended C6-acetyl compound **136** with a yield of 84%. Subsequent treatment of this compound successfully produced **134** (Scheme 34).[73]

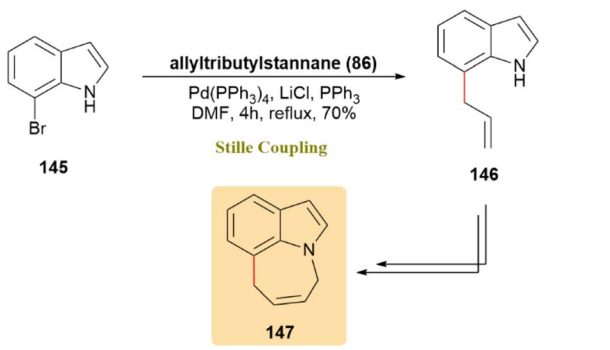
The total synthesis of flueggenines D (**137**) and I (**138**), representative dimeric Securinega alkaloids, was achieved through a key Stille coupling. This crucial step, which involved α-iodobutenolide **139** and stannane **140**, employing $Pd(PPh_3)_4$ with CuI, yielded intermediate **141** in 99% yield (Scheme 35). These alkaloids are valuable models for exploring biosynthetic oligomerization pathways and for studying stereocontrolled conjugate reductions in natural product synthesis.[74]



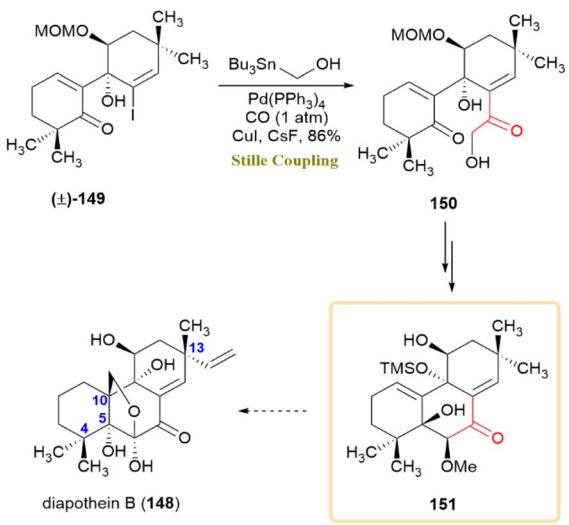
Scheme 35 α-Iodobutenolide **139** and stannane **140** coupled to produce intermediate **141** toward flueggenines D (**137**) and I (**138**).



Scheme 36 Triflate **143** and tributyl(vinyl)tin 3 coupled to afford vinylated ester **144**, precursor of (+)-paecilomycin F (**142**).



Scheme 37 Synthesis of azepino[3,2,1-hi]indole (**147**) through Stille coupling.

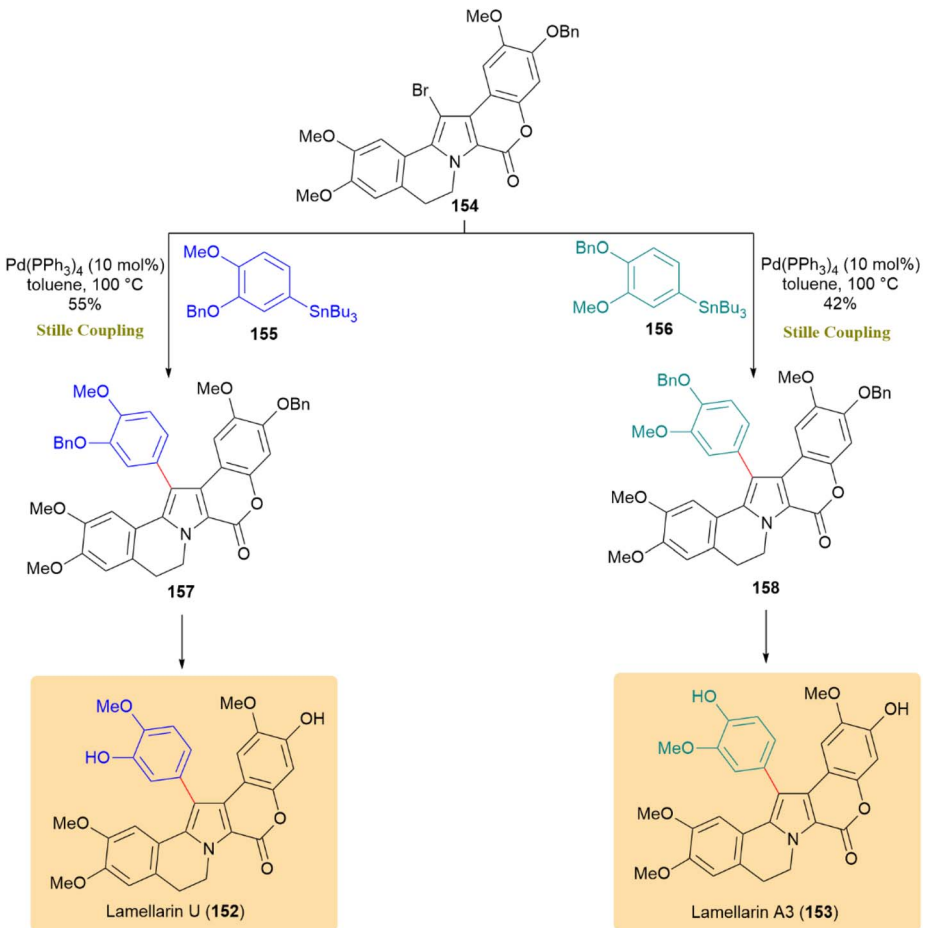


Scheme 38 Carbonylative Stille coupling of vinyl iodide **149** furnished α-hydroxyketone **150**, an advanced intermediate toward diaporthein B (**148**).

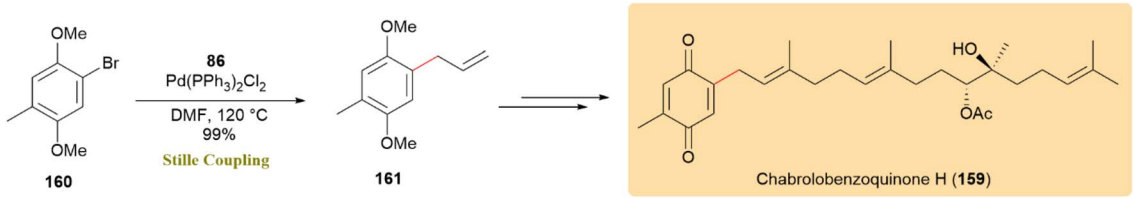
The synthesis of protected (+)-paecilomycin F (**142**), a β-resorcylic acid lactone with significant antiplasmodial, antifungal, and antiviral activity, has been successful accomplished. A crucial step in the process included a Stille coupling of triflate **143** with tributyl(vinyl)tin (**3**) under $Pd(PPh_3)_4$, TPP, LiCl and DCM reaction conditions, leading to the creation of the vinylated aromatic ester **144** intermediate with an 85% yield (Scheme 36).[75]

Azepino[3,2,1-hi]indoles, which contain seven-membered ring tricyclic structures, have been recognized for their significance in medicinal chemistry. In an effort to develop new synthetic strategies for these compounds, commercially available 7-bromo-1*H*-indole (**145**) was treated with allyltributylstannane **86** employing a Pd(0) catalyst for cross-coupling, yielding the allyl derivative (**146**) with a 70% yield. Subsequent treatments of compound **146** resulted in the formation of azepino[3,2,1-hi]indole derivatives, including [3,2,1-hi]indole (**147**) (Scheme 37).[76]

A synthetic strategy for the extensively oxidized carbon scaffold of diaporthein B (**148**) was developed through a 10-step sequence, employing convergent and diastereoselective fragment coupling techniques. This methodology successfully established the C4 and C13 quaternary centers, yet challenges emerged in forming the C10 quaternary center and achieving



Scheme 39 Compound **154** and aryl stannanes **155**/**156** coupled to give **157** and **158**, completing lamellarins U (**152**) and A3 (**153**).



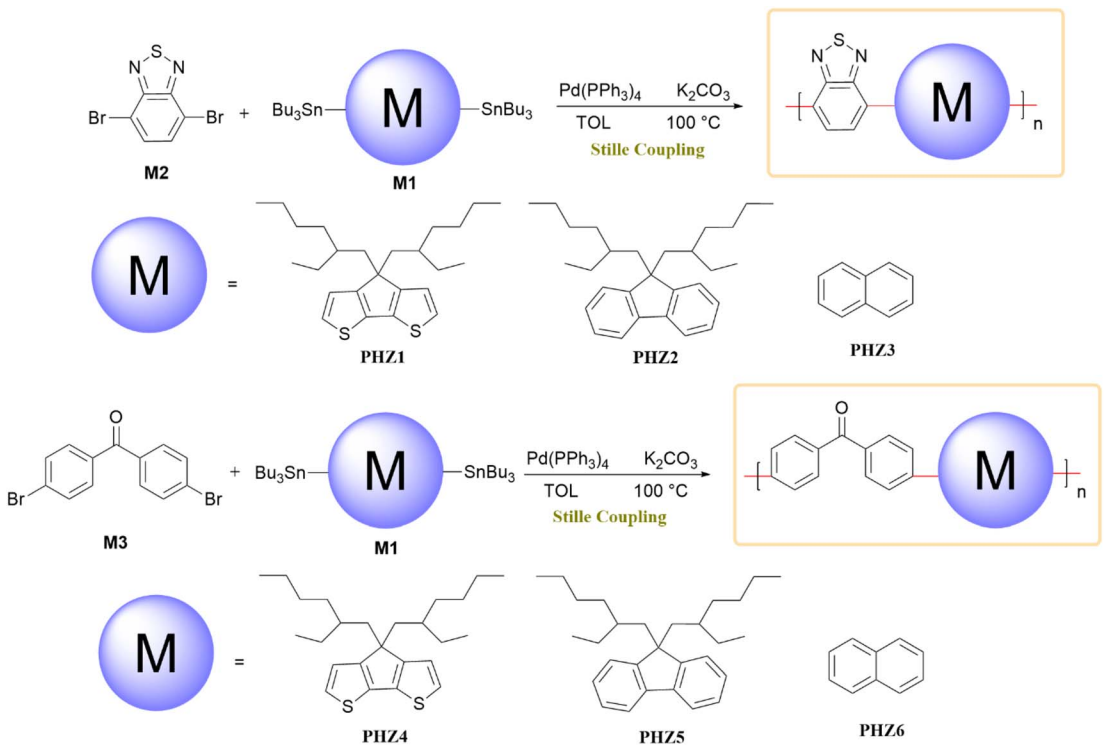
Scheme 40 Bromide **160** and allyltributyltin **86** coupling led to formation chabrolobenzoquinone H (**159**).

the desired stereochemistry at C5. A key transformation involved a carbonylative Stille coupling of vinyl iodide **149**, yielding α-hydroxyketone **150** in a single step with an 86% yield (Scheme 38). The most advanced intermediate, compound **151**, exhibited a highly oxidized tricyclic core resembling the carbon framework of **148**. Although the total synthesis remained incomplete, the strategy provided a foundation for future synthetic efforts targeting **148** and related pimarane diterpenes.[77]

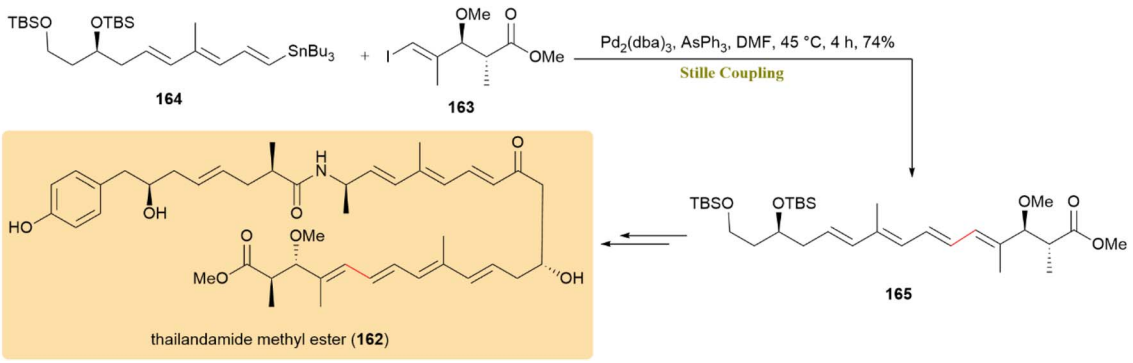
The total synthesis of lamellarins U (**152**) and A3 (**153**), marine-derived pyrrole alkaloids with potent cytotoxic and multidrug resistance reversal activities, was achieved *via* a late-stage Kosugi–Migita–Stille coupling. Compound **154** underwent Stille coupling with arylstannanes **155** or **156** using $Pd(PPh_3)_4$ (10 mol%) as the catalyst under standard conditions. The reaction process is illustrated in Scheme 39. This reaction produced compounds **157** and **158** in modest yields, accompanied by partial reductive debromination.[78]

Chabrolobenzoquinone H (**159**), a cytotoxic meroditerpene metabolite, was synthesized through a concise sequence in which a key Stille coupling joined bromide 160 with allylBu_3Sn 86 using $Pd(PPh_3)_2Cl_2$ and LiCl to afford the allyl derivative 161 in 99% yield. This transformation was strategically chosen because the Stille reaction tolerates the quinone and polyunsaturated functionalities of the meroditerpene framework, which are typically incompatible with other organometallic couplings. The use of LiCl enhanced transmetalation efficiency and minimized side reactions. Subsequent oxidative steps converted intermediate **161** into the target compound **159** (Scheme 40).[79]

Six conjugated oligomers, designated **PHZ1–PHZ6**, were synthesized using the Stille coupling. They demonstrated excellent solubility in common solvents and exhibited distinct electrochromic color variations. The synthesis procedures, as outlined in Scheme 41, involved the reaction of monomer **M1** with dibromides (**M2** and **M3**) using K_2CO_3 and $Pd(PPh_3)_4$ in toluene under a nitrogen atmosphere for three days. After purification, the oligomers yielded **PHZ1** (63%), **PHZ2** (61%), **PHZ3** (52%), **PHZ4** (62%), **PHZ5** (63%), and **PHZ6** (58%). In this design, the Stille coupling played a crucial role in constructing



Scheme 41 Monomer **M1** and dibromides **M2** and **M3** coupled to yield oligomers **PHZ1–PHZ6**.



Scheme 42 Stille coupling of vinyl iodide **163** and stannane **164** serves as a pivotal step in the synthesis of thailandamide A methyl ester (**162**).

well-defined donor–acceptor π-conjugated frameworks, enabling precise control over electronic communication between the benzothiadiazole or benzophenone acceptors and the thiophene-based donors. The reaction's mild conditions minimized side reactions and preserved functional integrity, offering advantages over other cross-coupling strategies which are less tolerant of heteroaromatic systems. This efficiency directly influenced the optical and electrochromic behaviors of the resulting oligomers.[80]

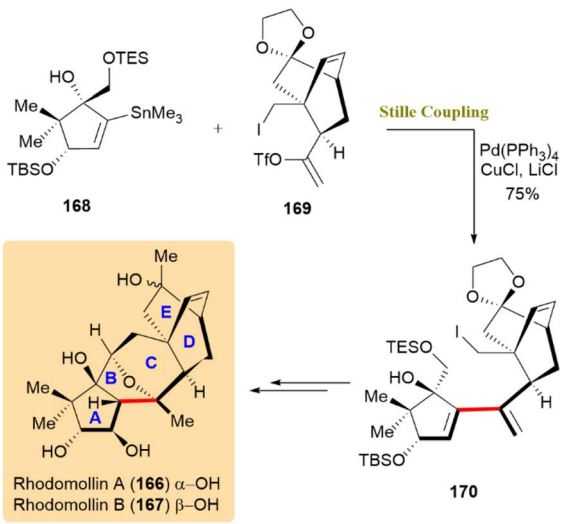
A well-optimized Stille cross-coupling was reported as an essential step in the stereoselective synthesis of thailandamide A methyl ester (**162**), a complex polyene polyketide. Initial attempts were unsuccessful until the Stille coupling was employed. The vinyl iodide methyl ester **163** was efficiently coupled with organostannane **164** using $Pd_2(dba)_3$/$AsPh_3$ in DMF, leading to the formation of compound **165**, which was subsequently converted to product **162** (Scheme 42).[81]

The Stille coupling is essential a crucial role in the total synthesis of rhodomollins A (**166**) and B (**167**), as it is critical to constructing the tetracyclic carbon skeleton of these complex grayanoids. By coupling the A-ring fragment (compound **168**), a stannylated intermediate, with the D/E-ring fragment (compound **169**), a triflated intermediate, the reaction efficiently forms the conjugated diene intermediate (compound **170**) in a 75% yield, setting the stage for subsequent transformations (Scheme 43).[82]

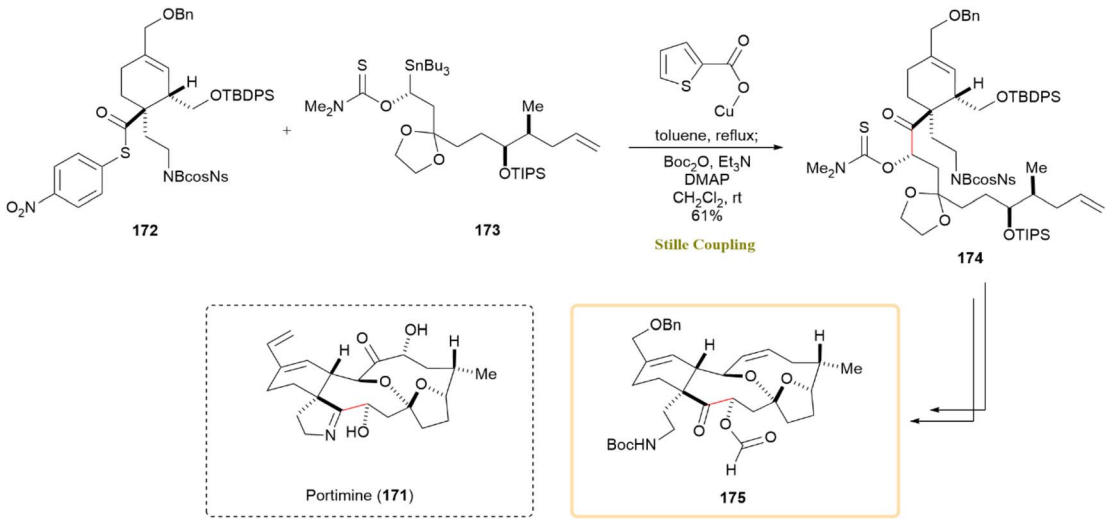
A synthetic approach toward the marine natural product portimine (**171**) was investigated, with a focus on a copper-mediated, stereoretentive $C(sp^3)$–$C(sp^2)$ Stille-like coupling for assembling functionalized fragments. Unlike the traditional Pd-catalyzed Stille reaction, which primarily facilitates $C(sp^2)$–$C(sp^2)$ couplings, the use of copper(I) thiophene-2-carboxylate (CuTC) as a catalyst enabled a stereospecific $C(sp^3)$–$C(sp^2)$ coupling. This strategy follows the Falck/Liebeskind approach, which employs copper catalysis to achieve high stereochemical fidelity in couplings involving α-heteroatom-substituted alkylstannanes.[83,84] The key reaction between thioester **172** and thiocarbamate **173** produced compound **174** with a 61% yield, retaining the chirality of α-alkoxyalkylstannane **173**. The synthesis successfully produced alcohol **175**, which retained the core skeleton of portimine. The reaction pathway is shown in Scheme 44. Further investigations are being pursued to finalize the total synthesis of portimine (**171**).[85]

In 2008, Fürstner developed a modified Stille–Migita cross-coupling utilizing $[Pd(PPh_3)_4]$, CuTC, and $[Ph_2PO_2][NBu_4]$ as the catalytic system. This fluoride-free approach significantly improved reaction yields while preserving sensitive functional groups, like *O*-silyl and *C*-silyl groups, which are usually prone to degradation. The modification increased functional group tolerance and prevented undesired side reactions, making it particularly effective in complex natural product syntheses. Several challenging cross-coupling reactions were demonstrated, confirming the method's usefulness in palladium-catalyzed bond formation.[86]

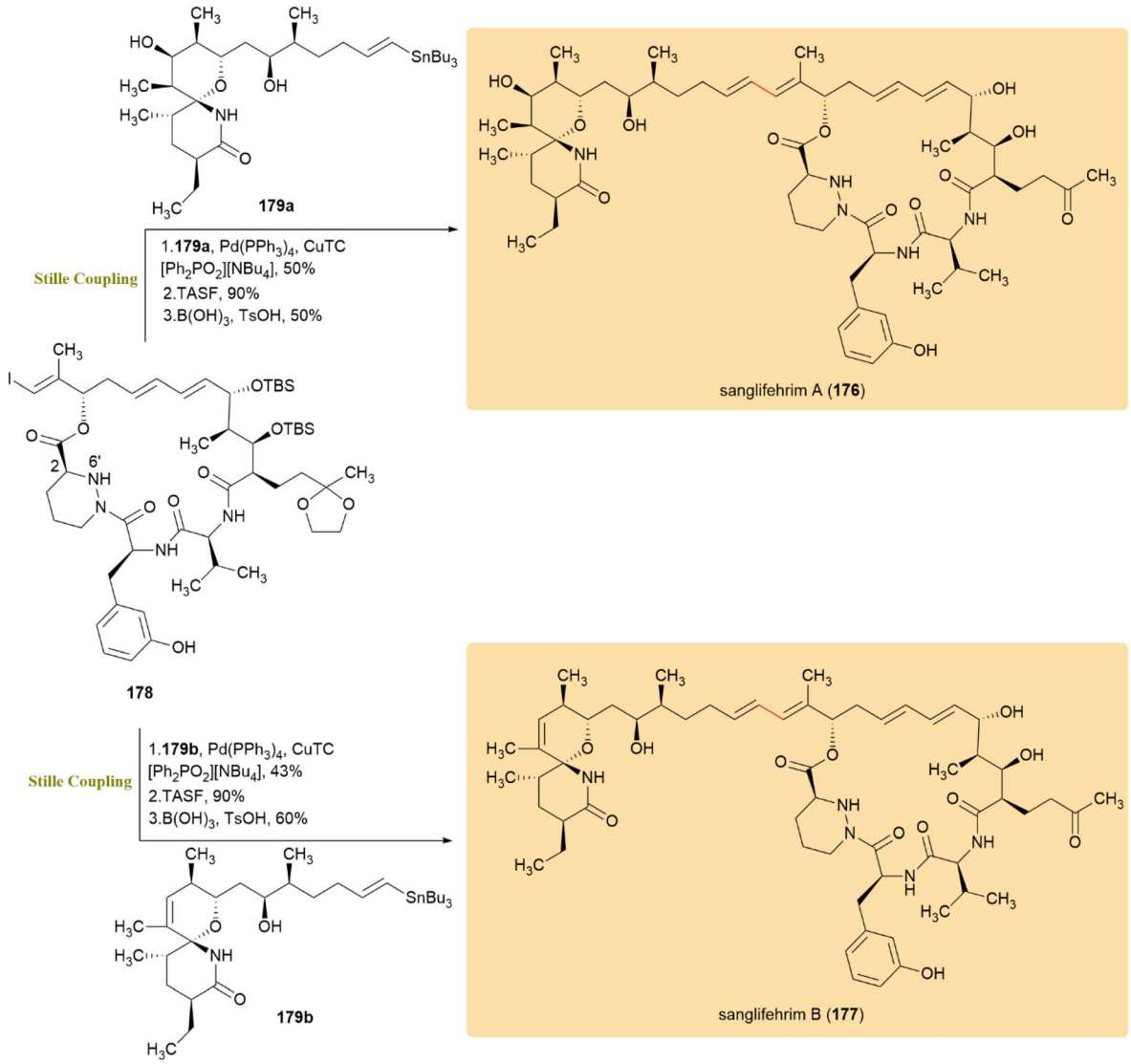
A convergent enantioselective strategy enabled access to sanglifehrin A (**176**) and the first complete synthesis of sanglifehrin B (**177**), two immunosuppressive macrocyclic natural products featuring a distinctive spirocyclic lactam. Vinyl iodide **178** was coupled with stannane **179a** *via* the Stille–Migita protocol reported by Fürstner *et al.* to yield **176** in 50%, while **179b** afforded **177** in 43% (Scheme 45). This cross-coupling represented a pivotal union step between the macrocyclic and



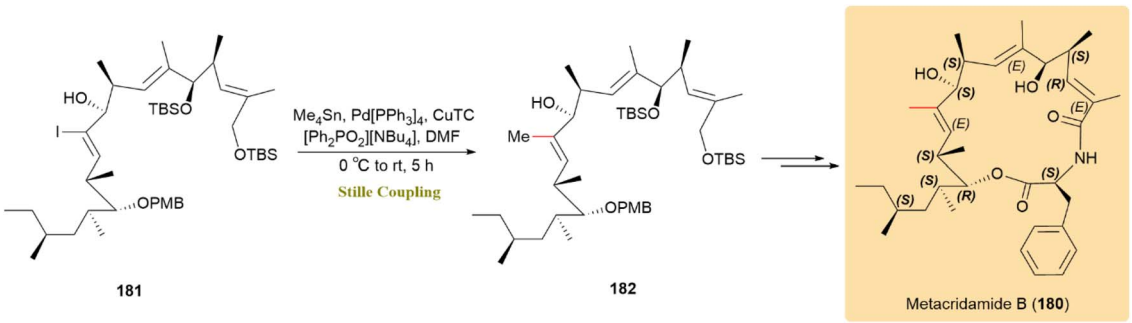
Scheme 43 Fragments **168** and **169** coupled to form diene **170**, key to rhodomollins A (**166**) and B (**167**).



Scheme 44 Thioester **172** and hiocarbamate **173** underwent CuTC-mediated Stille-like coupling to yield **174**, precursor to portimine (**171**).



Scheme 45 Vinyl iodide **178** and stannanes **179a**/**179b** coupled to produce sanglifehrin A (**176**) and sanglifehrin B (**177**).



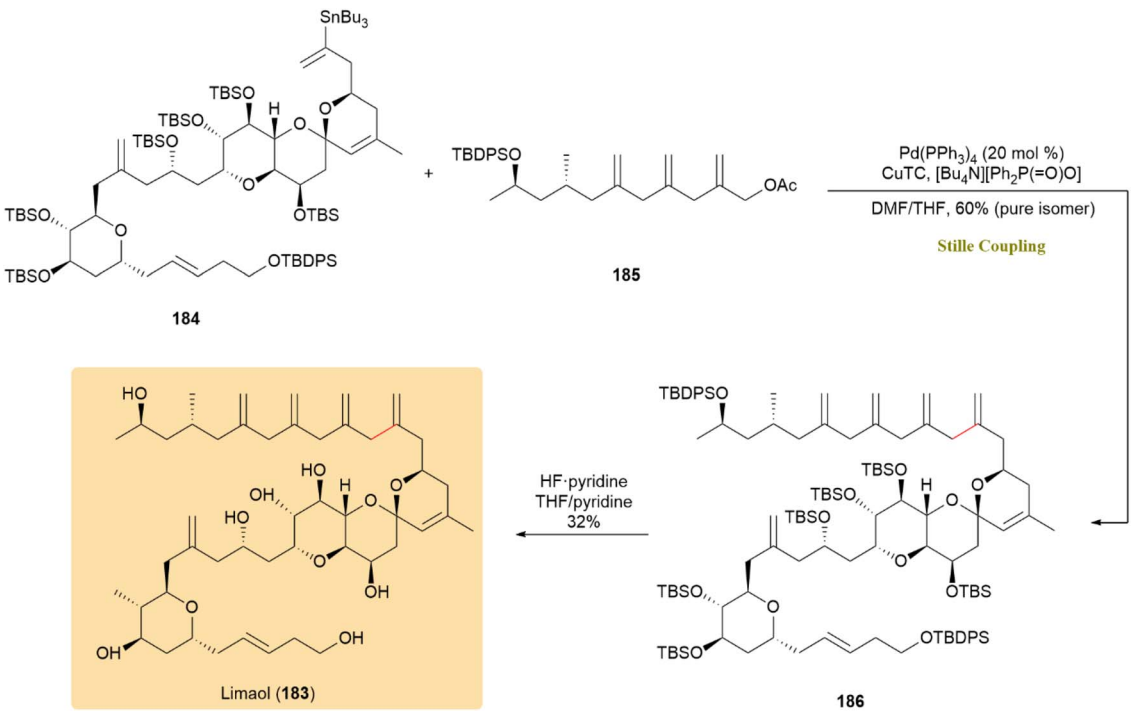
Scheme 46 Iodide **181** and Me_4Sn coupled to form **182**, leading to metacridamide B (**180**).

spirolactam fragments, achieving chemoselective C–C bond formation under conditions mild enough to preserve the densely functionalized, stereochemically rich framework—an advantage over alternative coupling methods that are less compatible with nitrogen-rich macrocycles. The efficiency of this step facilitated late-stage diversification and enabled biological evaluation. Both **176** and **177** selectively bind cyclophilin A, with sanglifehrin B exhibiting greater antiproliferative potency in Jurkat T cells, highlighting their utility in studying protein–protein interactions and immunosuppres sion.[87]

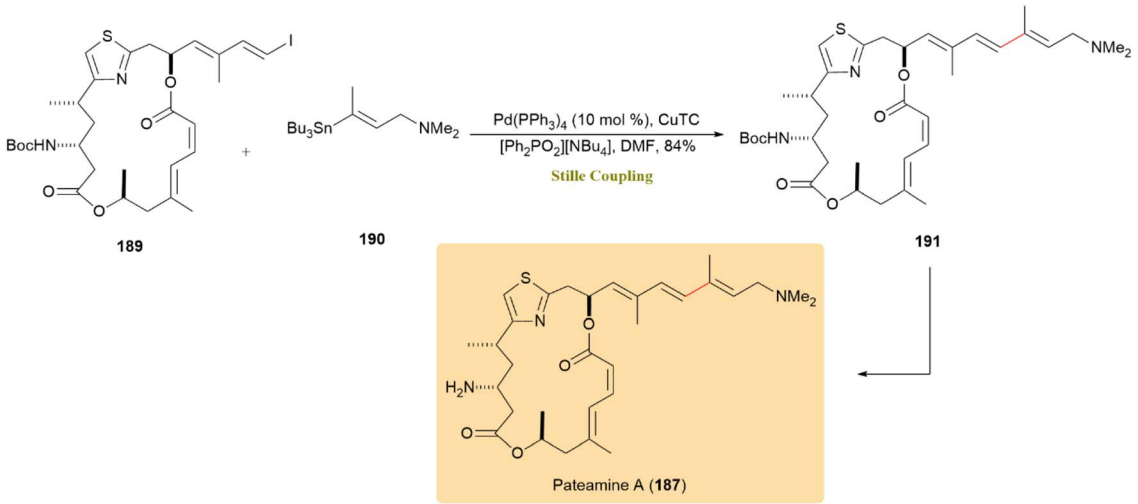
The Stille reaction was used to synthesize metacridamide B (**180**), a cytotoxic 17-membered macrocyclic amide from *Metarhizium acridum*. This reaction forms carbon–carbon bonds between specific compounds. Its compatibility with various functional groups ensured successful bond formation, as demonstrated by an 84% yield in the coupling of iodide **181** and Me_4Sn using the Fürstner method, resulting in the formation of compound **182** (Scheme 46). Metacridamide B (**180**) has shown activity against HepG2/C3A liver cancer cells, highlighting its potential in anticancer drug development.[88]

The comprehensive synthesis of limaol (**183**), a marine-derived C40-polyketide, was described, with a focus on its distinctive feature of four skipped methylene groups in the hydrophobic tail. As shown in Scheme 47, the tail region, which contains these "exo"-methylene groups, was successfully incorporated through palladium-catalyzed fragment coupling of compounds **184** and **185** using Fürstner conditions. This approach yielded compound **186** with a 60% pure isomer yield, resulting in the successful synthesis of **183**.[89]

Efficient management of protecting groups a modern Stille coupling protocol enabled the synthesis of pateamine A (**187**) and its analogue DMDA-Pat A (**188**). These compounds exhibit significant anticancer activity, with DMDA-Pat A also showing potential for reducing tumor growth and preventing of cancer-



Scheme 47 Fragments **184** and **185** coupled under Fürstner conditions to yield **186**, completing limaol (**183**).

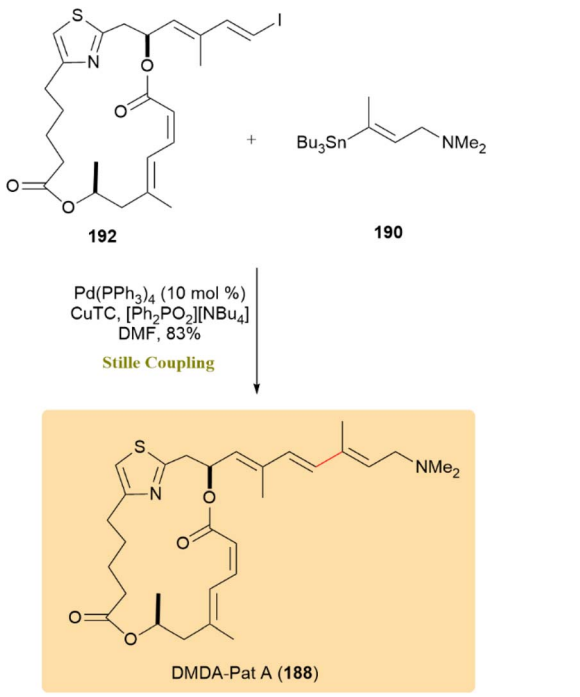


Scheme 48 Alkenyl iodide **189** and stannane **190** coupled to form intermediate **191**, converted to pateamine A (**187**).

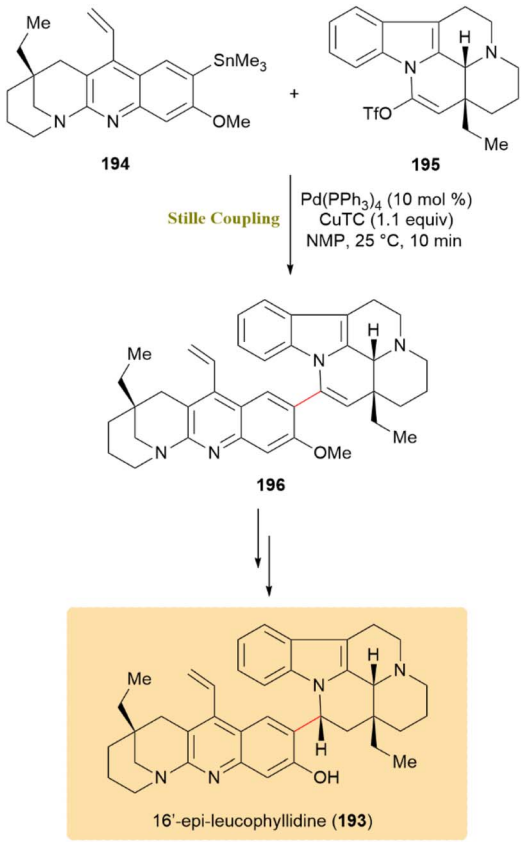
related muscle loss. The reaction of alkenyl iodide **189** with stannane **190**, using the Fürstner method, yielded compound **39** with 84% efficiency, which was then converted to Pateamine A (**187**) (Scheme 48).

Similarly, coupling compound **192** with stannane **190** produced DMDA-Pat A (**188**) with 83% yield (Scheme 49).[90]

As shown in Scheme 50, the total synthesis of 16′-*epi*-leucophyllidine (**193**), a synthetic analogue of the cytotoxic alkaloid leucophyllidine, was facilitated by the efficient cross-coupling of trimethylstannane **194** with triflate **195**, employing $Pd(PPh_3)_4$ and copper(I) thiophene-2-carboxylate (CuTC), inspired by Fürstner modification, resulting in dimer **196** with a 69% yield after 10 minutes. This transformation served as the key bond-forming step, efficiently uniting two highly functionalized indole fragments under exceptionally mild conditions. The use of CuTC accelerated the transmetalation step, allowing rapid coupling while preserving the sensitive indole and amide



Scheme 49 Compound **192** and stannane **190** coupled to give **193**, precursor to DMDA-Pat A (**188**).



Scheme 50 Stille coupling of trimethylstannane **194** and triflate **195** serves a pivotal step in the synthesis of 16′-*epi*-leucophyllidine (**193**).

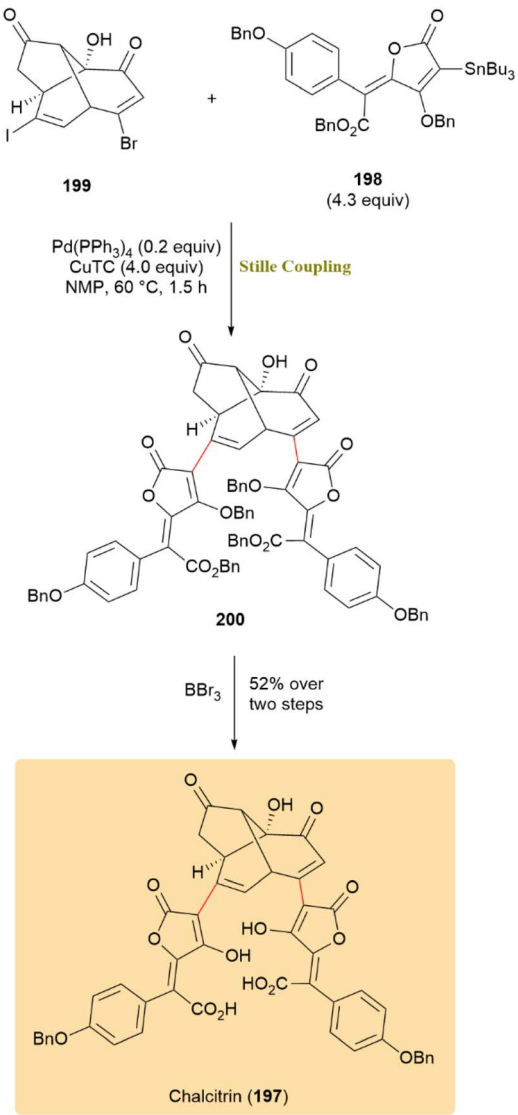
functionalities—a hallmark advantage of the Stille–Fürstner protocol in complex alkaloid synthesis. The resulting 16′-*epi*-leucophyllidine (**193**) retained the biological activities of leucophyllidine, including cytotoxic and nitric-xide-synthase-inhibitory properties.[91]

With similar condition, the first accomplished total synthesis of chalcitrin (**197**), a rare fungal pigment and pulvinic acid dimer with potential metal-ion binding properties, was achieved through a double Stille coupling at the late stage. Stannyl **198** was successfully coupled with double vinyl halide **198** at both reactive sites using catalytic $Pd(PPh_3)_4$ and CuTC, forming compound **200**. Subsequent deprotection of all six benzyl groups with excess BBr_3 produced **197** in 52% yield for the last two steps (Scheme 51).[92]

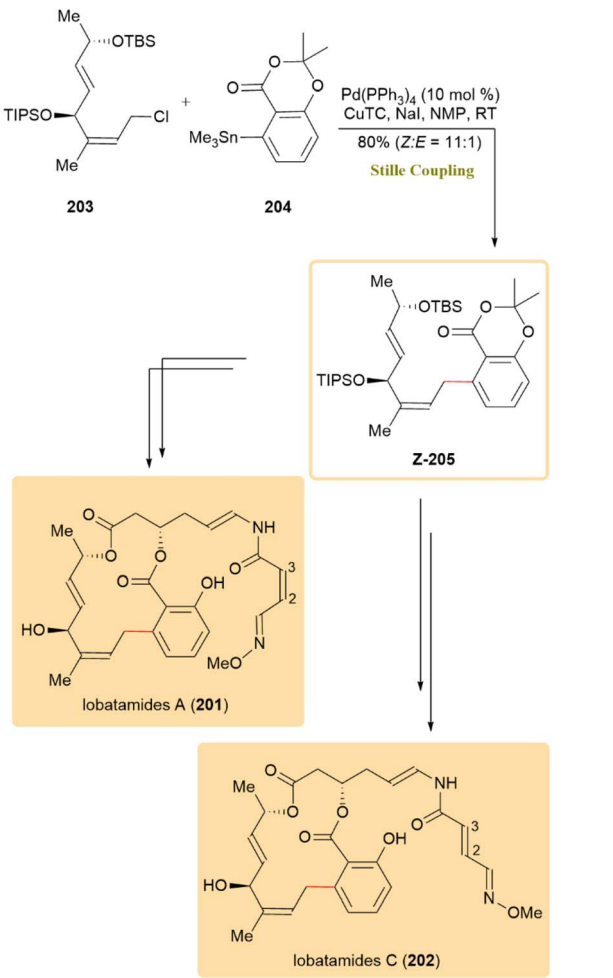
The complete synthetic route for lobatamides A (**201**) and C (**202**) was reported, with particular focus on the formation of their macro-benzolactone and enamide side chains, both known for V-ATPase inhibition and antitumor activity. The two compounds differ only in the geometry of the C2–C3 double bond in the enamide: **201** has a (*Z*,*E*)-configuration, while lobatamide **202** has an (*E*,*E*)-configuration. A key allylic aryl structure was constructed using a Migita–Kosugi–Stille coupling. In this step, allylic chloride **203** was coupled with aryl stannane **204** under conditions similar to those reported by Fürstner, employing 10 mol% $Pd(PPh_3)_4$, CuTC, and NaI in NMP. This reaction produced the allylic aryl intermediate ***Z*-205** in 80% yield with a $Z:E$ ratio of 11 : 1 (Scheme 52).[93]

3. The intramolecular Stille coupling

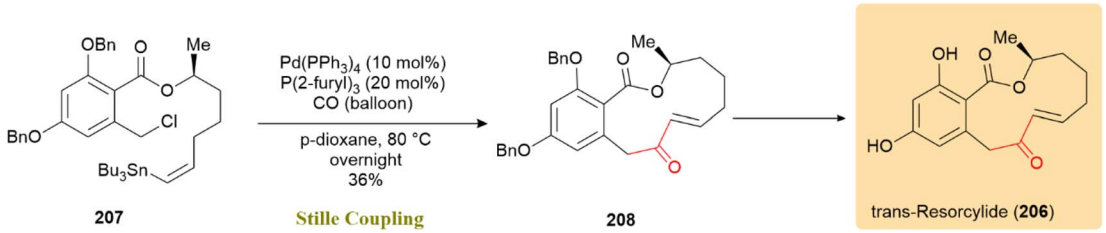
The total synthesis of *trans*-resorcylide (**206**), a bioactive member of the resorcylic macrolide family with plant growth inhibitory, antifungal, and cytotoxic properties, was achieved *via* a palladium-catalyzed Stille carbonylation. This key step constructed the 12-membered macrocycle by converting *cis*-vinylstannane intermediate **207** into *trans*-enone **208** using 10 mol% $Pd(PPh_3)_4$ and 20 mol% P(2-furyl)$_3$, affording the product in 36% yield (Scheme 53). This reaction not only



Scheme 51 Double Stille coupling of stannyl **198** with vinyl halide **199** formed **200**, leading to chalcitrin (**197**).



Scheme 52 Allylic chloride **203** and aryl stannane **204** coupled to give *Z*-**205**, precursor to lobatamides A (**201**) and C (**202**).

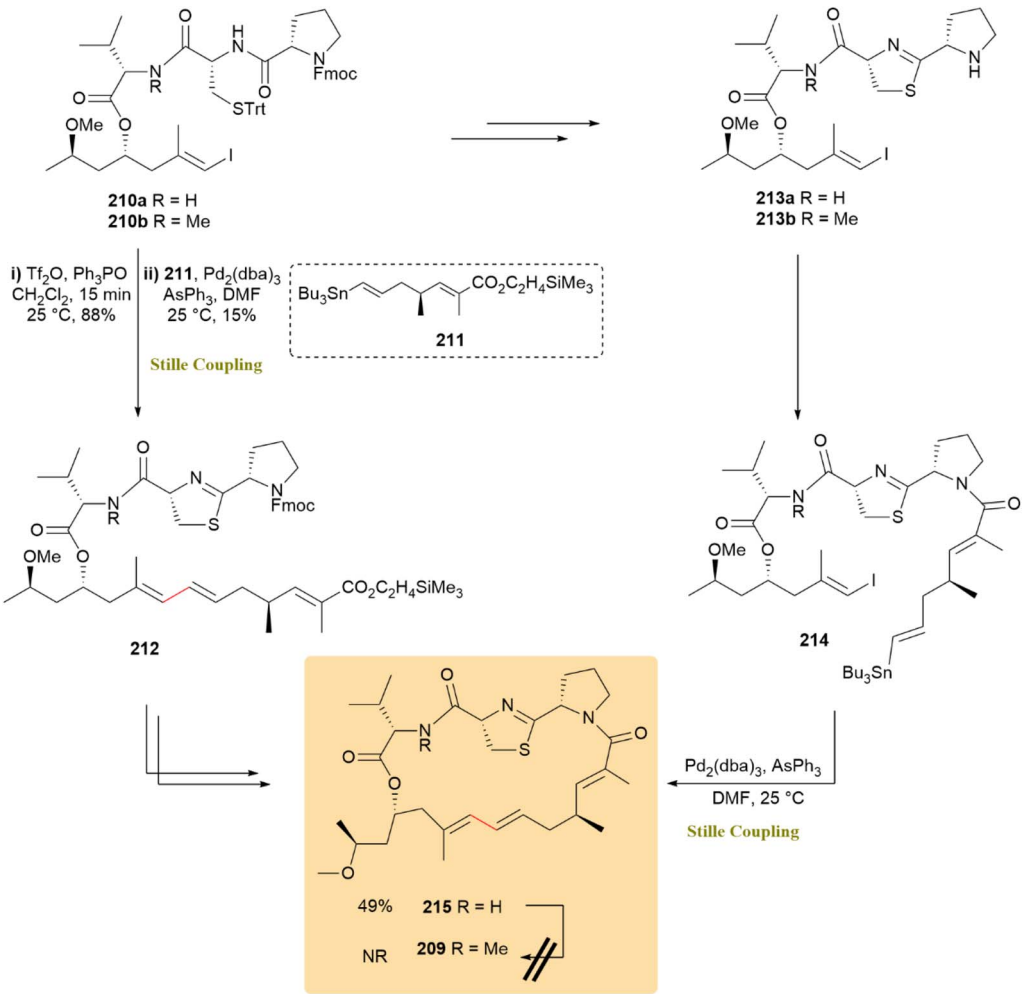


Scheme 53 Vinylstannane **207** underwent carbonylative Stille coupling to form *trans*-enone **208**, completing *trans*-resorcylide (**206**).

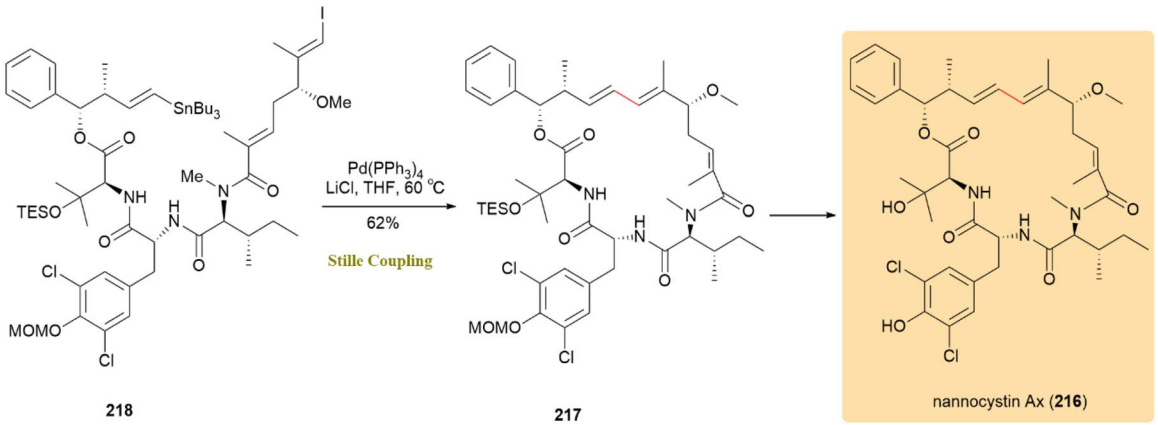
represents the first example of a macrocyclic Stille carbonylation applied to a benzyl chloride substrate but also provided an efficient alternative to traditional macrolactonization or ring-closing metathesis strategies, which often fail under such sterically constrained and functionalized conditions. The transformation proceeds through an intramolecular carbonylative coupling that constructs the macrocyclic enone with complete chemoselectivity, underscoring the power of the Stille carbonylation in complex macrocycle formation.[94]

The synthesis of the neurotoxin alotamide A (**209**) was investigated by employing an intramolecular Stille reaction (C sp^2–C sp^2) along with a macrolactam-forming step. An advanced intermediate was prepared, leading to the development of an efficient stereoselective synthesis protocol for the polyketide fragment, although complete synthesis was not achieved. Iodide **210a** was coupled with stannane **211**, yielding product **212** at 15% using $Pd_2(dba)_3$ and $AsPh_3$. Another route involved treating iodide **210a** to produce **213a** and then intermediate **214**, followed by intramolecular Stille cross-coupling, which isolated compound **215** with a 49% yield (Scheme 54).[95]

A complete synthesis of nannocystin Ax (**216**) was reported, highlighting the construction of a distinctive 21-membered



Scheme 54 Stille coupooling of iodide **210a**, yielded compound **215**, an advanced intermediate toward alotamide A (**209**).

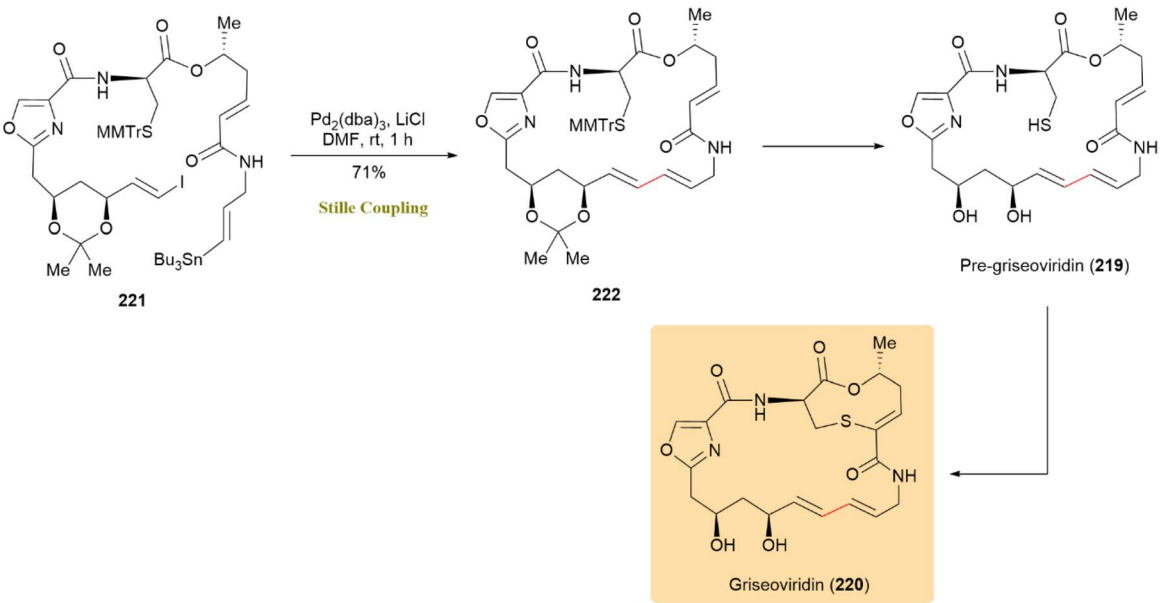


Scheme 55 Affording nannocystin Ax (**216**) *via* intramolecular Stille coupling.

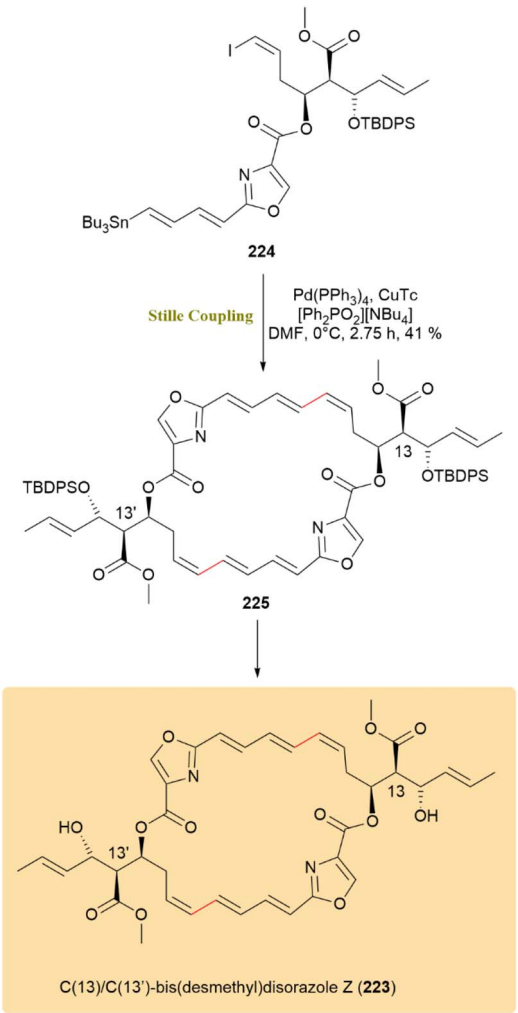
macrocyclic core with over seven stereocenters, incorporating tripeptide and polyketide elements. Biological studies exhibited potent cytotoxic activity against a range of tumor cell lines and a strong antifungal effect by nannocystin A. Compound **217** was synthesized from compound **218** in a 62% yield *via* intramolecular Stille cross-coupling in dilute THF with $Pd(PPh_3)_4$ and LiCl at 60 °C, enabling the completion of product **216** synthesis (Scheme 55).[96]

The first total synthesis of pre-griseoviridin (**219**), which was later converted to griseoviridin (**220**), a broad-spectrum antibacterial group A streptogramin from Streptomyces, was achieved through an intramolecular Stille reaction. Compound **221** participated in this reaction with $Pd_2(dba)_3$ and LiCl, yielding macrocycle **222** with a 64% yield. Initial deprotection efforts were hindered by the stability of the trityl group; however, replacing it with a 4-monomethoxytrityl (MMTr) group and adding LiCl improved the yield to 71% (Scheme 56).[97]

The synthesis of the bioactive disorazole Z analogue, C(13)/C(13′)-bis(desmethyl)disorazole Z (**223**), known for its microtubule-disrupting and anticancer effects, was completed *via* total synthesis. A key transformation in the synthetic route was the application of the Fürstner method in an intramolecular Stille coupling, highlighting its utility in complex macrocycle formation. The use of double inter- and intramolecular Stille cross-coupling in the cyclodimerization of a bifunctional vinyl stannane/iodide precursor represented a significant advancement in macrodiolide synthesis. Under Fürstner's condition at 0 °C, stannyl vinyl iodide **224** underwent a double inter-/intramolecular Stille reaction to obtain macrodiolide **225** in 41% yield, with preservation of the triene configuration and no observable isomerization (Scheme 57).[98]



Scheme 56 Compound **221** underwent intramolecular Stille coupling to form macrocycle **222**, precursor to griseoviridin (**220**).



Scheme 57 Double inter-/intramolecular Stille coupling of precursor 224 to afford disorazole Z analogue 223.

4. Conclusions

Over the past decade, the Stille coupling has continued to evolve as a crucial and versatile method in the synthesis of natural products. Its exceptional tolerance for diverse functional groups, compatibility with a wide range of substrates, and mild operating conditions have allowed for the efficient creation of intricate molecular structures with high stereo- and regioselectivity. Recent advancements such as bimetallic and heterogeneous catalysis, copper co-catalyzed systems, and new ligand designs have significantly broadened the reaction's capabilities, enhancing yields, selectivity, and suitability for more challenging substrates. Despite these developments, the field is increasingly focused on addressing environmental and safety concerns. The dependence on organotin reagents and difficulties in catalyst recovery and metal leaching remain significant limitations, encouraging the development of greener, tin-free, and recyclable catalytic systems. Although organotin toxicity presents challenges, organostannanes still offer valuable reliability in complex coupling processes. Continued progress in enantioselective protocols and environmentally considerate methods underscores the ongoing evolution of the Stille reaction. Demonstrated through numerous successful syntheses of marine alkaloids, diterpenoids, macrolides and complex polyenes, the Stille coupling remains a fundamental aspect of modern synthetic strategies, ready to meet future challenges in the construction of complex molecules and sustainable chemistry.

Conflicts of interest

There are no conflicts to declare.

Data availability

No new experimental data were generated in this study. This review is based entirely on previously published literature, and all cited sources are properly referenced in the manuscript.

Acknowledgements

The authors gratefully acknowledge the support of this work by the Shahid Rajaee Teacher Training University under contact number 1404/395128.

Notes and references

1 S. Majhi and S. K. Jash, Recent developments of nanocatalysts for Stille coupling reaction, *Synth. Commun.*, 2023, **53**, 2061–2087, DOI: 10.1080/00397911.2023.2269585.
2 S. E. Denmark and J. H. C. Liu, Silicon-based cross-coupling reactions in the total synthesis of natural products, *Angew. Chem., Int. Ed.*, 2010, **49**, 2978–2986, DOI: 10.1002/anie.200905657.
3 V. F. Slagt, A. H. M. De Vries, J. G. De Vries and R. M. Kellogg, Practical aspects of carbon-carbon cross-coupling reactions using heteroarenes, *Org. Process Res. Dev.*, 2010, **14**, 30–47, DOI: 10.1021/op900221v.
4 A. R. Kapdi and D. Prajapati, Regioselective palladium-catalysed cross-coupling reactions: A powerful synthetic tool, *RSC Adv.*, 2014, **40**, 41245–41259, DOI: 10.1039/c4ra07895k.
5 H. Li, C. C. C. Johansson Seechurn and T. J. Colacot, Development of preformed Pd catalysts for cross-coupling reactions, beyond the 2010 nobel prize, *ACS Catal.*, 2012, **2**, 1147–1164, DOI: 10.1021/cs300082f.
6 K. C. Nicolaou, P. G. Bulger and D. Sarlah, Palladium-catalyzed cross-coupling reactions in total synthesis, *Angew. Chem., Int. Ed.*, 2005, **44**, 4442–4489, DOI: 10.1002/anie.200500368.
7 A. R. Siamaki, A. E. R. S. Khder, V. Abdelsayed, M. S. El-Shall and B. F. Gupton, Microwave-assisted synthesis of palladium nanoparticles supported on graphene: A highly active and recyclable catalyst for carbon-carbon cross-coupling reactions, *J. Catal.*, 2011, **279**, 1–11, DOI: 10.1016/j.jcat.2010.12.003.

8 X. Chen, K. M. Engle, D. H. Wang and Y. Jin-Quan, Palladium(II)-cataIyzed C-H aetivation/C-C cross-coupling reactions: Versatility and practicality, *Angew. Chem., Int. Ed.*, 2009, **48**, 5094–5115, DOI: 10.1002/anie.200806273.

9 M. Tamura and J. Kochi, Vinylation of Grignard Reagents. Catalysis by Iron, *J. Am. Chem. Soc.*, 1971, **93**, 1487–1489, DOI: 10.1021/ja00735a030.

10 N. Miyaura, K. Yamada and A. Suzuki, A new stereospecific cross-coupling by the palladium-catalyzed reaction of 1-alkenylboranes with 1-alkenyl or 1-alkynyl halides, *Tetrahedron Lett.*, 1979, **20**, 3437–3440, DOI: 10.1016/S0040-4039(01)95429-2.

11 T. Kubo, G. M. Scheutz, T. S. Latty and B. S. Sumerlin, Synthesis of functional and boronic acid-containing aliphatic polyesters: Via Suzuki coupling, *Chem. Commun.*, 2019, **55**, 5655–5658, DOI: 10.1039/c9cc01975h.

12 K. F. Heck and J. P. Nolley, Palladium-Catalyzed Vinylic Hydrogen Substitution Reactions with Aryl, Benzyl, and Styryl Halides, *J. Org. Chem.*, 1972, **37**, 2320–2322, DOI: 10.1021/jo00979a024.

13 J. A. Gurak and K. M. Engle, Practical Intermolecular Hydroarylation of Diverse Alkenes via Reductive Heck Coupling, *ACS Catal.*, 2018, **8**, 8987–8992, DOI: 10.1021/acscatal.8b02717.

14 K. Sonogashira, Y. Tohda and N. Hagihara, A convenient synthesis of acetylenes: catalytic substitutions of acetylenic hydrogen with bromoalkenes, iodoarenes and bromopyridines, *Tetrahedron Lett.*, 1975, **16**, 4467–4470, DOI: 10.1016/S0040-4039(00)91094-3.

15 N. Touj, S. Yaşar, N. Özdemir, N. Hamdi and İ. Özdemir, Sonogashira cross-coupling reaction catalysed by mixed NHC-Pd-PPh3 complexes under copper free conditions, *J. Organomet. Chem.*, 2018, **860**, 59–71, DOI: 10.1016/j.jorganchem.2018.01.017.

16 E. ichi Negishi, A. O. King and N. Okukado, Selective Carbon-Carbon Bond Formation via Transition Metal Catalysis. 3. A Highly Selective Synthesis of Unsymmetrical Biaryls and Diarylmethanes by the Nickel- or Palladium-Catalyzed Reaction of Aryl- and Benzylzinc Derivatives with Aryl Halides, *J. Org. Chem.*, 1977, **42**, 1821–1823, DOI: 10.1021/jo00430a041.

17 G. A. Price, A. Hassan, N. Chandrasoma, A. R. Bogdan, S. W. Djuric and M. G. Organ, Pd-PEPPSI-IPent-SiO 2 : A Supported Catalyst for Challenging Negishi Coupling Reactions in Flow, *Angew. Chem.*, 2017, **129**, 13532–13535, DOI: 10.1002/ange.201708598.

18 D. Milstein and J. K. Stiile, A General, Selective, and Facile Method for Ketone Synthesis from Acid Chlorides and Organotin Compounds Catalyzed by Palladium, *J. Am. Chem. Soc.*, 1978, **100**, 3636–3638, DOI: 10.1021/ja00479a077.

19 J. Holz, C. Pfeffer, H. Zuo, D. Beierlein, G. Richter, E. Klemm and R. Peters, In Situ Generated Gold Nanoparticles on Active Carbon as Reusable Highly Efficient Catalysts for a Csp3 −Csp3 Stille Coupling, *Angew. Chem., Int. Ed.*, 2019, **58**, 10330–10334, DOI: 10.1002/anie.201902352.

20 D. Milstein and J. K. Stille, Palladium-Catalyzed Coupling of Tetraorganotin Compounds with Aryl and Benzyl Halides. Synthetic Utility and Mechanism, *J. Am. Chem. Soc.*, 1979, **101**, 4992–4998, DOI: 10.1021/ja00511a032.

21 P. C. Knutson, H. E. Fredericks and E. M. Ferreira, Synthesis of 1,3-Diynes via Cadiot-Chodkiewicz Coupling of Volatile, in Situ Generated Bromoalkynes, *Org. Lett.*, 2018, **20**, 6845–6849, DOI: 10.1021/acs.orglett.8b02975.

22 T. Besset, T. Poisson and X. Pannecoucke, Access to difluoromethylated alkynes through the castro-stephens reaction, *Eur. J. Org. Chem.*, 2014, **2014**, 7220–7225, DOI: 10.1002/ejoc.201402937.

23 L. Zhang, J. Qing, P. Yang and J. Wu, Palladium-catalyzed hiyama cross-coupling reactions of aryl mesylates, *Org. Lett.*, 2008, **10**, 4971–4974, DOI: 10.1021/ol802049t.

24 Q. Sun, F. Suzenet and G. Guillaumet, Optimized Liebeskind-Srogl coupling reaction between dihydropyrimidines and tributyltin compounds, *Tetrahedron Lett.*, 2012, **53**, 2694–2698, DOI: 10.1016/j.tetlet.2012.03.067.

25 J. Breitenfeld, J. Ruiz, M. D. Wodrich and X. Hu, Bimetallic oxidative addition involving radical intermediates in nickel-catalyzed alkyl-alkyl Kumada coupling reactions, *J. Am. Chem. Soc.*, 2013, **135**, 12004–12012, DOI: 10.1021/ja4051923.

26 R. Akhtar, A. F. Zahoor, B. Parveen and M. Suleman, Development of environmental friendly synthetic strategies for Sonogashira cross coupling reaction: An update, *Synth. Commun.*, 2019, **49**, 167–192, DOI: 10.1080/00397911.2018.1514636.

27 M. Yousaf, A. F. Zahoor, R. Akhtar, M. Ahmad and S. Naheed, Development of green methodologies for Heck, Chan–Lam, Stille and Suzuki cross-coupling reactions, *Mol. Divers.*, 2020, **24**, 821–839, DOI: 10.1007/s11030-019-09988-7.

28 I. Munir, A. F. Zahoor, N. Rasool, S. A. R. Naqvi, K. M. Zia and R. Ahmad, Synthetic applications and methodology development of Chan–Lam coupling: a review, *Mol. Divers.*, 2019, **23**, 215–259, DOI: 10.1007/s11030-018-9870-z.

29 S. Sarker and P. Nahar, S. D. Sarker and L. Nahar, *"Natural Products Isolation"*, ed. J. Walker, Humana Press/Springer Verlag, USA, 3rd edn, 2012, ISBN: 978-1-617-79623-4.

30 M. Kosugi, K. Sasazawa, Y. Shimizu and T. Migita, Reactions of Allyltin Compounds Iii. Allylation of Aromatic Halides With Allyltributyltin in the Presence of Tetrakis(Triphenylphosphine)Palladium(O), *Chem. Lett.*, 1977, **6**, 301–302, DOI: 10.1246/cl.1977.301.

31 C. Cordovilla, C. Bartolomé, J. M. Martínez-Ilarduya and P. Espinet, The stille reaction, 38 years later, *ACS Catal.*, 2015, **5**, 3040–3053, DOI: 10.1021/acscatal.5b00448.

32 K. C. Nicolaou, C. N. C. Boddy, S. Bräse and N. Winssinger, Chemistry, biology, and medicine of the glycopeptide antibiotics, *Angew. Chem., Int. Ed.*, 1999, **38**, 2096–2152, DOI: 10.1002/(sici)1521-3773(19990802)38:15<2096::aid-anie2096>3.0.co;2-f.

33 J. A. Ragan, J. W. Raggon, P. D. Hill, B. P. Jones, R. E. McDermott, M. J. Munchhof, M. A. Marx, J. M. Casavant, B. A. Cooper, J. L. Doty and Y. Lu, Cross-

coupling methods for the large-scale preparation of an imidazole - Thienopyridine: Synthesis of [2-(3-methyl-3H-imidazole-4-yl)-thieno[3,2-b]pyridin-7-yl] -(2-methyl-1H-indol-5-yl)-amine, *Org. Process Res. Dev.*, 2003, **7**, 676–683, DOI: 10.1021/op0340457.

34 A. G. Davies, M. Gielen, K. H. Pannell and E. R. T. Tiekink, Tin Chemistry: Fundamentals, Frontiers, and Applications, *Tin Chemistry: Fundamentals, Frontiers, and Applications*, 2008, pp. 1–729, DOI: 10.1002/9780470758090.

35 A. F. Littke, L. Schwarz and G. C. Fu, Pd/P(t-Bu)3: A mild and general catalyst for stille reactions of aryl chlorides and aryl bromides, *J. Am. Chem. Soc.*, 2002, **124**, 6343–6348, DOI: 10.1021/ja020012f.

36 M. H. Pérez-Temprano, J. A. Casares and P. Espinet, Bimetallic catalysis using transition and group 11 metals: An emerging tool for C-C coupling and other reactions, *Chem.–Eur. J.*, 2012, **18**, 1864–1884, DOI: 10.1002/chem.201102888.

37 M. H. Pérez-Temprano, J. A. Casares, Á. R. De Lera, R. Álvarez and P. Espinet, Strong metallophilic interactions in the palladium arylation by gold aryls, *Angew. Chem., Int. Ed.*, 2012, **51**, 4917–4920, DOI: 10.1002/anie.201108043.

38 J. delPozo, D. Carrasco, M. H. Pérez-Temprano, M. García-Melchor, R. Álvarez, J. A. Casares and P. Espinet, Stille Coupling Involving Bulky Groups Feasible with Gold Cocatalyst, *Angew. Chem.*, 2013, **125**, 2245–2249, DOI: 10.1002/ange.201209262.

39 N. Louaisil, P. D. Pham, F. Boeda, D. Faye, A. S. Castanet and S. Legoupy, Ionic liquid supported organotin reagents: Green tools for stille cross-coupling reactions with brominated substrates, *Eur. J. Org. Chem.*, 2011, 143–149, DOI: 10.1002/ejoc.201001195.

40 P. Espinet and A. M. Echavarren, The mechanisms of the Stille reaction, *Angew. Chem., Int. Ed.*, 2004, **43**, 4704–4734, DOI: 10.1002/anie.200300638.

41 J. K. Stille, The Palladium-Catalyzed Cross-Coupling Reactions of Organotin Reagents with Organic Electrophiles[New Synthetic Methods(58)], *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508–524, DOI: 10.1002/ANIE.198605081.

42 M. M. Heravi, E. Hashemi and F. Azimian, Recent developments of the Stille reaction as a revolutionized method in total synthesis, *Tetrahedron*, 2014, **70**, 7–21, DOI: 10.1016/j.tet.2013.07.108.

43 M. M. Heravi and L. Mohammadkhani, Recent applications of Stille reaction in total synthesis of natural products: An update, *J. Organomet. Chem.*, 2018, **869**, 106–200, DOI: 10.1016/j.jorganchem.2018.05.018.

44 T. Nishiyama, S. Takaiwa, R. Kotouge, S. Tani, R. Yoshinaga, E. Hamada, M. Endo, Y. Sugino, N. Hatae, S. Hibino and T. Choshi, First asymmetric enantioselective total synthesis of phenanthridine alkaloid, (S)-(+)-asiaticumine and its enantiomer, *Tetrahedron Lett.*, 2019, **60**, 151278, DOI: 10.1016/j.tetlet.2019.151278.

45 J. Zhou, D. X. Tan and F. S. Han, A Divergent Enantioselective Total Synthesis of Post-Iboga Indole Alkaloids, *Angew. Chem., Int. Ed.*, 2020, **59**, 18731–18740, DOI: 10.1002/anie.202008242.

46 N. Okutomi, A. Matsuzawa and K. Sugita, Diastereoselective Total Syntheses of (±)-Caseabalansin A and (±)-18-Epicaseabalansin A via Intramolecular Robinson-type Annulation, *Chem. Asian J.*, 2019, **14**, 2077–2081, DOI: 10.1002/asia.201900368.

47 R. Bartholomäus, S. Nicolussi, A. Baumann, M. Rau, A. C. Simão, J. Gertsch and K. H. Altmann, Total Synthesis of the Endocannabinoid Uptake Inhibitor Guineensine and SAR Studies, *ChemMedChem*, 2019, **14**, 1590–1596, DOI: 10.1002/cmdc.201900390.

48 M. Yoshimura, R. Fonné-Pfister, C. Screpanti, K. Hermann, S. Rendine, M. Dieckmann, P. Quinodoz and A. De Mesmaeker, Total Synthesis and Biological Evaluation of Heliolactone, *Helv. Chim. Acta*, 2019, **102**(11), DOI: 10.1002/hlca.201900211.

49 S. Woo and C. S. P. McErlean, Total Synthesis and Stereochemical Confirmation of Heliolactone, *Org. Lett.*, 2019, **21**, 4215–4218, DOI: 10.1021/acs.orglett.9b01402.

50 M. Yasa, S. Surmeli, T. Depci, L. Toppare and S. O. Hacioglu, Synthesis of a Multifunctional Quinoxaline and Benzodithiophene Bearing Polymer and Its Electrochromic Device Applications, *Macromol. Chem. Phys.*, 2020, **221**, 1–10, DOI: 10.1002/macp.201900470.

51 X. Liu, J. Yang, L. Gao, L. Zhang and X. Lei, Chemoenzymatic Total Syntheses of Artonin I with an Intermolecular Diels–Alderase, *Biotechnol. J.*, 2020, **15**(11), DOI: 10.1002/biot.202000119.

52 W. Cao, P. Chen and Y. Tang, Total Synthesis of Isohericenone J via a Stille Coupling Reaction, *J. Nat. Prod.*, 2020, **83**, 1701–1705, DOI: 10.1021/acs.jnatprod.9b01251.

53 C. D. Wang, Q. Chen, S. Shin and C. G. Cho, Total Synthesis of (±)-Clivonine via Diels-Alder Reactions of 3,5-Dibromo-2-pyrone, *J. Org. Chem.*, 2020, **85**, 10035–10049, DOI: 10.1021/acs.joc.0c01283.

54 M. R. Bhandari, A. K. Herath, S. Rasapalli, M. Yousufuddin and C. J. Lovely, Total Synthesis of the Nagelamides - Synthetic Studies toward the Reported Structure of Nagelamide D and Nagelamide e Framework, *J. Org. Chem.*, 2020, **85**, 12971–12987, DOI: 10.1021/acs.joc.0c01617.

55 A. Hirose, A. Watanabe, K. Ogino, M. Nagatomo and M. Inoue, Unified Total Syntheses of Rhamnofolane, Tigliane, and Daphnane Diterpenoids, *J. Am. Chem. Soc.*, 2021, **143**, 12387–12396, DOI: 10.1021/jacs.1c06450.

56 M. C. Dieckmann, P. Y. Dakas and A. De Mesmaeker, Synthetic Access to Noncanonical Strigolactones: Syntheses of Carlactonic Acid and Methyl Carlactonoate, *J. Org. Chem.*, 2018, **83**, 125–135, DOI: 10.1021/acs.joc.7b02465.

57 I. T. L. Ramos, R. J. M. Silva, T. M. S. Silva and C. A. Camara, Palladium-catalyzed coupling reactions in flavonoids: A retrospective of recent synthetic approaches, *Synth. Commun.*, 2021, **51**, 3520–3545, DOI: 10.1080/00397911.2021.1988643.

58 G. K. Pathe, N. K. Konduru, I. Parveen and N. Ahmed, Anti-proliferative activities of flavone-estradiol Stille-coupling

adducts and of indanone-based compounds obtained by SnCl4/Zn-catalysed McMurry cross-coupling reactions, *RSC Adv.*, 2015, **5**, 83512–83521, DOI: 10.1039/c5ra15685h.

59 D. R. Williams, Strategies and discoveries leading to the synthesis of trichoaurantianolide natural products, Strategies and discoveries leading to the synthesis of trichoaurantianolide natural products, *Elsevier*, 2022, **15**, 335–364, DOI: 10.1016/B978-0-12-822212-6.00002-3.

60 K. H. Sim, T. ul Ansari, Y. G. Park, Y. Jeong, S. H. Oh, H. W. Min, D. Y. Jeon, H. Kim and C. G. Cho, A Regio- and Diastereoselective Stille Coupling/Intramolecular Diels–Alder Cascade for the Generation of Fused Pyridines and Application in the Synthesis of (+)-Lycopladine A and (−)-Lycoposerramine R, *Angew. Chem., Int. Ed.*, 2022, **61**, 3–7, DOI: 10.1002/anie.202212016.

61 J. R. Walker, J. E. Merit, R. Thomas-Tran, D. T. Y. Tang and J. Du Bois, Divergent Synthesis of Natural Derivatives of (+)-Saxitoxin Including 11-Saxitoxinethanoic Acid, *Angew. Chem., Int. Ed.*, 2019, **58**, 1689–1693, DOI: 10.1002/anie.201811717.

62 Y. L. Jiang, H. X. Yu, Y. Li, P. Qu, Y. X. Han, J. H. Chen and Z. Yang, Asymmetric Total Synthesis of Pre-schisanartanin C, *J. Am. Chem. Soc.*, 2020, **142**, 573–580, DOI: 10.1021/jacs.9b11872.

63 I. Cortés, C. M. Borini Etichetti, J. E. Girardini, T. S. Kaufman and A. B. J. Bracca, Total Synthesis and Cytotoxic Activity of 6,8-Dimethoxy-1,3-dimethylisoquinoline Isolated from Ancistrocladus tectorius: A 6π-Azaelectrocyclization Approach, *Synthesis*, 2019, **51**, 433–440, DOI: 10.1055/s-0037-1610276.

64 M. Khoshbakht, B. Thanaussavadate, C. Zhu, Y. Cao, L. N. Zakharov, S. Loesgen and P. R. Blakemore, Total Synthesis of Chalaniline B: An Antibiotic Aminoxanthone from Vorinostat-Treated Fungus Chalara sp. 6661, *J. Org. Chem.*, 2021, **86**, 7773–7780, DOI: 10.1021/acs.joc.1c00528.

65 G. Kim, T. Kim and S. Han, Total Synthesis of (+)-Pestalofone A and (+)-Iso-A82775C, *J. Org. Chem.*, 2020, **85**, 6815–6821, DOI: 10.1021/acs.joc.0c00770.

66 T. H. Lai, S. Schröder, M. Toussaint, S. Dukić-Stefanović, M. Kranz, F. A. Ludwig, S. Fischer, J. Steinbach, W. Deuther-Conrad, P. Brust and R. P. Moldovan, Development of18f-labeled radiotracers for pet imaging of the adenosine a2a receptor: Synthesis, radiolabeling and preliminary biological evaluation, *Int. J. Mol. Sci.*, 2021, **22**, 1–26, DOI: 10.3390/ijms22052285.

67 J. S. Reddy, P. Manimala, M. Gangababu, A. Rammohan and J. S. Yadav, Total Synthesis of (3R, 4 S)-4-Hydroxylasiodiplodin via Ring Closing Metathesis Protocol, *ChemistrySelect*, 2019, **4**, 5345–5347, DOI: 10.1002/slct.201900189.

68 S. Watanabe, T. Nishikawa and A. Nakazaki, Total Synthesis of the Cardiotonic Steroid (+)-Cannogenol, *J. Org. Chem.*, 2021, **86**, 3605–3614, DOI: 10.1021/acs.joc.0c02966.

69 K. Zheng and R. Hong, The Fruit of Gold: Biomimicry in the Syntheses of Lankacidins, *Acc. Chem. Res.*, 2021, **54**, 3438–3451, DOI: 10.1021/acs.accounts.1c00340.

70 W. Yan, M. Zheng, P. Chuang, H. Sun, S. Wang, C. Xu and F. E. Chen, Synergistic Pd/Cu catalysis enabled cross-coupling of glycosyl stannanes with sulfonium salts to access C-aryl/alkenyl glycals, *Chin. Chem. Lett.*, 2023, **34**(7), DOI: 10.1016/j.cclet.2022.108021.

71 C. Cui and M. Dai, Total Synthesis of UCS1025A via Tandem Carbonylative Stille Cross Coupling and Diels-Alder Reaction, *Chin. J. Chem.*, 2023, **41**, 3019–3024, DOI: 10.1002/cjoc.202300331.

72 C. Zhang, J. Song, J. Xue, S. Wang, Z. Ge, Y. Man, W. Ma and Y. Sun, Facile, Versatile and Stepwise Synthesis of High-Performance Oligomer Acceptors for Stable Organic Solar Cells, *Angew. Chem., Int. Ed.*, 2023, **62**(40), DOI: 10.1002/anie.202308595.

73 B. Sen, M. Bera, M. S. Singh and S. Hajra, Asymmetric total synthesis of (+)-propolisbenzofuran B, *Chem. Commun.*, 2023, **59**, 8254–8257, DOI: 10.1039/d3cc02054a.

74 G. Kang, S. Park and S. Han, Synthesis of High-Order and High-Oxidation State Securinega Alkaloids, *Acc. Chem. Res.*, 2023, **56**, 140–156, DOI: 10.1021/acs.accounts.2c00719.

75 R. Gurram and S. Pabbaraja, A Convergent Approach for Protected (+)-Paecilomycin F, *Lett. Org. Chem.*, 2022, **20**, 185–192, DOI: 10.2174/1570178619666220523094936.

76 S. Kotha and P. Meher, Expanding the Diversity of Azepino [3,2,1-hi] Indoles via Transition Metal-based Strategies such as Cross-coupling Reaction and Ring Closing Metathesis, *Asian J. Org. Chem.*, 2023, **12**, 1–9, DOI: 10.1002/ajoc.202300287.

77 I. T. Hsu and S. B. Herzon, Fragment Coupling Approach to Diaporthein B, *J. Org. Chem.*, 2023, **88**, 2221–2244, DOI: 10.1021/acs.joc.2c02655.

78 Y. Okui, Y. Yasuda, A. Mori and K. Okano, Total Synthesis of Lamellarins U and A3 by Interrupting Halogen Dance, *Synthesis*, 2022, **54**, 2647–2660, DOI: 10.1055/a-1736-7337.

79 S. R. Rizos, K. A. Ouzounthanasis and A. E. Koumbis, Enantiospecific Total Synthesis and Absolute Configuration Assignment of Chabrolobenzoquinone H, *J. Org. Chem.*, 2022, **87**, 1313–1324, DOI: 10.1021/acs.joc.1c02634.

80 Z. He, B. Mei, H. Chu, Y. Hou and H. Niu, D–A Structural Oligomers Containing Benzothiadiazole or Benzophenone as Novel Multifunctional Materials for Electrochromic and Photodetector Devices, *Polymers*, 2023, **15**(10), DOI: 10.3390/polym15102274.

81 H. Sharma, S. Ganguly, M. H. Sahana and R. K. Goswami, Stereoselective synthesis of thailandamide A methyl ester, *Org. Biomol. Chem.*, 2024, **22**, 1409–1419, DOI: 10.1039/d3ob02107f.

82 W. Zhao, D. Zhang, Y. Wang and M. Yang, Total Syntheses of Rhodomollins A and B, *J. Am. Chem. Soc.*, 2023, **145**, 27160–27166, DOI: 10.1021/jacs.3c12249.

83 J. R. Falck, R. K. Bhatt and J. Ye, Tin—Copper Transmetalation: Cross-Coupling of α-Heteroatom-Substituted Alkyltributylstannanes with Organohalides, *J. Am. Chem. Soc.*, 1995, **117**, 5973–5982, DOI: 10.1021/ja00127a010.

84 H. Li, A. He, J. R. Falck and L. S. Liebeskind, Stereocontrolled synthesis of α-amino-α′-alkoxy ketones by a copper-catalyzed

cross-coupling of peptidic thiol esters and α-alkoxyalkylstannanes, *Org. Lett.*, 2011, **13**, 3682–3685, DOI: 10.1021/ol201330j.

85 D. Sato, M. Sasaki and A. Umehara, Stereocontrolled Synthesis of the Portimine Skeleton via Organocatalyst-Mediated Asymmetric Stannylation and Stereoretentive C(sp3)-C(sp2) Stille Coupling, *Org. Lett.*, 2025, 12–17, DOI: 10.1021/acs.orglett.4c04245.

86 A. Fürstner, J. A. Funel, M. Tremblay, L. C. Bouchez, C. Nevado, M. Waser, J. Ackerstaff and C. C. Stimson, A versatile protocol for Stille-Migita cross coupling reactions, *Chem. Commun.*, 2008, 2873–2875, DOI: 10.1039/b805299a.

87 C. F. Chang, H. A. Flaxman and C. M. Woo, Enantioselective Synthesis and Biological Evaluation of Sanglifehrin A and B and Analogs, *Angew. Chem., Int. Ed.*, 2021, **60**, 17045–17052, DOI: 10.1002/anie.202103022.

88 A. Sharma, S. Athe, R. P. I, K. Vishali and S. Ghosh, Total synthesis of the proposed structure of metacridamide B, *Tetrahedron Lett.*, 2021, **82**, 153374, DOI: 10.1016/j.tetlet.2021.153374.

89 S. N. Hess, X. Mo, C. Wirtz and A. Fürstner, Total Synthesis of Limaol, *J. Am. Chem. Soc.*, 2021, **143**, 2464–2469, DOI: 10.1021/jacs.0c12948.

90 C. X. Zhuo and A. Fürstner, Catalysis-Based Total Syntheses of Pateamine A and DMDA-Pat A, *J. Am. Chem. Soc.*, 2018, **140**, 10514–10523, DOI: 10.1021/jacs.8b05094.

91 C. E. Reimann, A. Ngamnithiporn, K. Hayashida, D. Saito, K. M. Korch and B. M. Stoltz, The Enantioselective Synthesis of Eburnamonine, Eucophylline, and 16′-epi-Leucophyllidine, *Angew. Chem., Int. Ed.*, 2021, **60**, 17957–17962, DOI: 10.1002/anie.202106184.

92 M. Yang, F. Yin, H. Fujino and S. A. Snyder, The Total Synthesis of Chalcitrin, *J. Am. Chem. Soc.*, 2019, **141**, 4515–4520, DOI: 10.1021/jacs.8b12612.

93 S. Yasui, S. Banjo, Y. Nagashima, Y. Okada, K. Yoshikawa, K. Nakata, N. Chida, T. Okamura and T. Sato, Total Synthesis of Lobatamides A and C, *Angew. Chem., Int. Ed.*, 2024, **63**, 1–5, DOI: 10.1002/anie.202402335.

94 Y. Luo, X. Yin and M. Dai, Total Synthesis of trans-Resorcylide via Macrocyclic Stille Carbonylation, *J. Antibiot.*, 2019, **72**, 482–485, DOI: 10.1038/s41429-019-0145-4.

95 J. A. Souto, D. Román, M. Domínguez and Á. R. de Lera, Synthetic Studies on Alotamide A: Construction of N-Demethylalotamide A, *Eur. J. Org. Chem.*, 2021, **2021**, 6057–6070, DOI: 10.1002/ejoc.202101104.

96 R. Liu, M. Xia, Y. Zhang, S. Fu and B. Liu, The journey of total synthesis toward nannocystin Ax, *Tetrahedron*, 2019, **75**, 1781–1794, DOI: 10.1016/j.tet.2018.12.021.

97 C. N. Stout and H. Renata, Total Synthesis Facilitates In Vitro Reconstitution of the C-S Bond-Forming P450 in Griseoviridin Biosynthesis, *J. Am. Chem. Soc.*, 2024, **146**, 21815–21823, DOI: 10.1021/jacs.4c06080.

98 C. P. Bold, D. Lucena-Agell, M. Á. Oliva, J. F. Díaz and K. H. Altmann, Synthesis and Biological Evaluation of C(13)/C(13′)-Bis(desmethyl)disorazole Z, *Angew. Chem., Int. Ed.*, 2023, **62**(5), DOI: 10.1002/anie.202212190.