was also performed.



Stereospecific Iron-Catalyzed Carbon (sp²)—Carbon (sp²) Cross-Coupling of Aryllithium with Vinyl Halides

Peng Chen, Zhi-Yong Wang, Xiao-Shui Peng,* and Henry N.C. Wong*



ransition-metal-catalyzed cross-coupling reactions target- \bot ing to selective C–C bond formation enable the facile preparation of structurally diversified molecules and facilitate the development of modern drugs and organic materials.¹⁻⁴ Traditionally, catalysis by palladium, ruthenium, and nickel has been commonly used in the cross-coupling reactions involving many organometallic reagents.^{1,5–10} However, because of their intrinsic limitations such as high reactivities and low selectivities, the direct application of organolithium reagents in cross-coupling reactions has not been fully explored and still remains an enormous challenge, despite that organolithium reagents are either commercially available or easily accessible through direct metalation or halogen-lithium exchange processes. Early studies by Murahashi and co-workers pioneered the palladium-catalyzed cross-coupling procedure involving alkyllithium/aryllithium reagents and alkenyl halides in 1970s.¹¹ Feringa and co-workers developed some elegant palladium-based catalytic systems to directly generate C-C bonds by using organolithium compounds as cross-coupling partners.¹² Moreover, they also disclosed for the first time palladium catalytic systems for alkenyllithium or lithium acetylides as cross-coupling partners.^{12g-j} However, iron has attracted a great deal of interest toward the catalysis of crosscoupling reactions because of its low cost, low toxicity, earthabundance, as well as its novel reactivity as compared with those analogous reactions with precious metals (i.e., palladium). Accordingly, the development of iron-catalyzed crosscoupling reactions is expectedly undergoing an explosive growth.¹³ In 1971, Kochi demonstrated that simple iron salts were able to catalyze the stereoselective generation of C-C bonds.¹⁴ Subsequently, the research groups of Fürstner, Nakamura, Bedford, and Cahiez have all contributed significantly to iron-catalyzed cross-coupling reactions.¹¹ In 2016, our group exploited an efficient iron-catalyzed crosscoupling reaction under mild conditions, involving organolithium compounds and a variety of organic bromides. Our examples included the formation of $C(sp^2)-C(sp^3)$ bonds and

 $C(sp^3)-C(sp^3)$ bonds, consequently providing valuable alternatives to existing methodologies by demonstrating for the first time that organolithium reagents could be employed as cross-coupling partners in iron-catalyzed cross-coupling procedures.^{19a} Soon after, iron-catalyzed $C(sp^2)-C(sp^2)$ bonds and other C–C bond cross-coupling reactions were also realized in good yields.^{19b,c} Furthermore, highly practical and efficient iron-catalyzed $C(sp^2)-C(sp^2)$ oxidative homocoupling reactions of alkenyllithium and aryllithium reagents were also achieved, leading to the formation of symmetric 1,3butadienes and biaryls in moderate to good yields, respectively.^{19d,e}

Vinyl arenes are privileged scaffolds frequently found in bioactive natural products, pharmaceuticals, and polymers.²⁰ Metal-catalyzed cross-coupling methods are also among the most deployed synthetic methodologies for the realization of substituted styrenes. As shown in Scheme 1, while such reactions are usually dominated by palladium,²¹ nickel,²² and cobalt²³ catalysts, an iron-catalyzed Kumada process was also reported in 2011.²⁴ Herein, we report the stereoselective construction of vinyl arenes under a mild iron-catalyzed cross-coupling process between aryllithium compounds and vinyl halides.

As shown in Table 1, we commenced the preliminary screening on this cross-coupling reaction by reacting p-anisyllithium 2, freshly prepared by treatment of 4-bromoanisole with *t*-BuLi, with (*E*)-2-iodovinylbenzene 1a in the presence of various commonly used iron catalysts in toluene. Without any iron catalyst or ligand, no reaction

 Received:
 April 16, 2021

 Published:
 May 19, 2021





pubs.acs.org/OrgLett

Scheme 1. Transition-Metal-Catalyzed Cross-Coupling Reactions to Form a C-C Bond

a) Cobalt-catalyzed vinylation of aromatic halides using β -halostyrene

$$\mathsf{R}^{1} \xrightarrow[\mathbb{N}]{\mathsf{H}}^{\mathsf{H}} \xrightarrow{\mathsf{CoBr}_{2} (10 \text{ mol}\%)}_{\mathsf{CH}_{3} (10 \text{ mol}\%)} \xrightarrow{\mathsf{Ph}_{3} (10 \text{ mol}\%)}_{\mathsf{CH}_{3} \mathsf{CN}, 50 \ ^{\mathsf{C}}} \xrightarrow{\mathsf{Ph}_{4} \xrightarrow{\mathsf{Ph}_{3}} X}_{\mathsf{X} = \mathsf{Cl or Br}} \mathsf{R}^{1} \xrightarrow{\mathsf{H}_{4} \xrightarrow{\mathsf{Ph}_{4}} \mathsf{Ph}_{4}}_{\mathsf{H}_{3} \mathsf{Cl}} \mathsf{R}^{1} \xrightarrow{\mathsf{H}_{4} \xrightarrow{\mathsf{Ph}_{4}} \mathsf{Ph}_{4}}_{\mathsf{H}_{4} \mathsf{Cl}} \mathsf{R}^{1} \xrightarrow{\mathsf{Ph}_{4} \xrightarrow{\mathsf{Ph}_{4}} \mathsf{Ph}_{4}}_{\mathsf{Ph}_{4} \mathsf{Cl}} \mathsf{R}^{1} \xrightarrow{\mathsf{Ph}_{4} \xrightarrow{\mathsf{Ph}_{4}} \mathsf{Ph}_{4}}_{\mathsf{Ph}_{4} \mathsf{Cl}} \mathsf{R}^{1} \xrightarrow{\mathsf{Ph}_{4} \xrightarrow{\mathsf{Ph}_{4}} \mathsf{Ph}_{4}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}} \mathsf{R}^{1} \xrightarrow{\mathsf{Ph}_{4} \xrightarrow{\mathsf{Ph}_{4}} \mathsf{Ph}_{4}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}} \mathsf{R}^{1} \xrightarrow{\mathsf{Ph}_{4} \xrightarrow{\mathsf{Ph}_{4}} \mathsf{Ph}_{4}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_{\mathsf{Ph}_{4} \mathsf{Cl}}_{\mathsf{Ph}_{4} \mathsf{Cl}}}_$$

b) Nickel-catalyzed reductive coupling of aryl halides with vinyl bromides.

$$\begin{array}{c} \mathsf{N}^{1} \stackrel{(I)}{\amalg}_{\mathsf{Het}} \mathsf{Het} & \mathsf{K} \\ \mathsf{K} - \mathsf{R}^{\mathsf{r}} \mathsf{L} & \mathsf{R} \\ \mathsf{K} - \mathsf{R}^{\mathsf{r}} \mathsf{L} & \mathsf{R} - \mathsf{and} \mathsf{alkel} \end{array}$$

c) Iron-catalyzed reductive aryl-alkenyl cross-coupling reactions

d) Iron-catalyzed organolithium compounds cross-coupling reactions - our previous work



Table 1. Optimization of Reaction Conditions a,b

\bigcirc	+ Li	OMe [Fe] (1 Ligand (Solvent, 0	0 mol%) (10 mol%)) °C –23 °C		OMe
1a	2 addition ov	er 2 h			3a
entry	Fe	ligand	Li ^c	solvent	yield (%)
1	-	-	2	toluene	0
2	FeCl ₂	-	2	toluene	17
3	FeCl ₃	-	2	toluene	48
4	FeBr ₂	-	2	toluene	38
5	FeBr ₃	-	2	toluene	48
6	$Fe(acac)_2$	-	2	toluene	50
7	$Fe(acac)_3$	-	2	toluene	45
8	$Fe(acac)_2$	-	3	toluene	60
9	$Fe(acac)_2$	XPhos	3	THF	trace
10	$Fe(acac)_2$	XPhos	3	Et_2O	52
11	$Fe(acac)_2$	BrettPhos	3	toluene	64
12	$Fe(acac)_2$	MePhos	3	toluene	67
13	$Fe(acac)_2$	$SIPr-HBF_4$	3	toluene	55
14	Fe(acac) ₂	XPhos	3	toluene	74
15	$Fe(acac)_2$	XPhos	3	toluene	57 ^d

^{*a*}Reaction conditions: To a solution of compound 1a (0.2 mmol), iron catalyst (10 mol %) and ligand (10 mol %) in toluene (2.0 mL) was added a solution of 2 (c = 0.2 mmol/mL) in Et₂O over 2 h by a syringe pump at 0 °C. ^{*b*}Isolated yield. ^{*c*}The equiv of 2. ^{*d*}5 mol % Fe(acac)₂ and 5 mol % Xphos were used.

occurred (entry 1). With iron catalysts, cross-coupling product **3a**, together with some homocoupling products, were observed. Subsequently, several iron catalysts were screened (entries 2-7), and the highest yield among these entries was 50% when Fe(acac)₂ was used. It is noteworthy that with 3.0 equiv of **2**, all starting materials were consumed, and the yield was improved to 60% (entry 8). However, a further increase of the amount of **2** to 4.0 equiv led to a decrease of the yield of **3a** to 48%. Although different solvents were respectively

attempted (entries 9, 10, and 14), no significant improvement was realized. We then examined several NHC ligands (entry 13), Buchwald ligands, and other commonly used phosphinecontaining, amine-containing monodentate as well as bidentate ligands (entries 11, 12; see Table S3 in the Supporting Information). Relevant results showed that Xphos was a better ligand for this reaction. Moreover, lower loading of iron catalyst (5 mol %) was found to reduce slightly the overall transformation efficiency (entry 15). Eventually, the best condition was found to be Fe(acac)₂ and Xphos, in which 74% of **3a** was obtained (entry 14; other details can be found in the Supporting Information).

With the optimized reaction condition in hand, the substrate scope of the iron-catalyzed cross-coupling reaction of 2 with (*E*)-vinyl iodides 1 was further examined. The results are shown in Scheme 2. Gratifyingly, vinyl iodides with both

Scheme 2. Scope of (E)-Vinyl Iodides^{*a*,*b*}



"Reaction conditions: $Fe(acac)_2$ (0.02 mmol), Xphos (0.02 mmol), 1 (0.2 mmol), in 2.0 mL of toluene under Ar, added a solution of 2 in Et₂O over 2 h by a syringe pump at 0 °C, then at 23 °C for 6 h. ^bIsolated yield.

electron-donating groups, such as *t*-butyl (viz. 1b) and *n*-butyl (viz. 1c), and electron-deficient aromatic ring, for example, the pharmaceutically useful trifluoromethylvinyl iodide 1d, smoothly underwent this coupling reaction to generate the desired stilbenes in moderate to good yields (3b, 3c, and 3d). Moreover, *ortho-, meta-,* and *para-*methylphenylvinyl iodides (1e, 1f, and 1g) were also studied, generating 3e, 3f, and 3g, respectively, with 3g notably being isolated in excellent yield (82%). Meanwhile, stilbene 3k was also afforded with good yield. The steric hindrance exerted by one *ortho-*methyl group was found to be less obvious than that shown by two *ortho*-methyl groups (3e vs 3j). Fluorine-substituted phenylvinyl iodides 1h and 1i successfully underwent the cross-coupling with excellent chemoselectivity and moderate to good yields, affording the corresponding fluorinated stilbenes 3h and 3i.

Table 2. Substrate Scope^{*a,b*}

	\mathbb{R}^{2} \mathbb{R}^{3} \mathbb{R}^{3}	X + Li-Aryl	Fe(acac Xphos Toluene,	$(10 \text{ mol}\%) \xrightarrow{(10 \text{ mol}\%)} R^1$ $(10 \text{ mol}\%) \xrightarrow{(10 \text{ mol}\%)} R^2 \xrightarrow{(10 \text{ mol}\%)} R^3$ R^3		
	4	5		6		
\mathbb{R}^1	R ²	R ³	Х	Ar	product	yield (%)
Н	3-MeOC ₆ H ₄	Н	Ι	Ph	6a	72
Н	3-MeOC ₆ H ₄	Н	Ι	$4-MeC_6H_4$	6b	81
Н	3-MeOC ₆ H ₄	Н	Ι	$4-\text{EtC}_6\text{H}_4$	6c	62
Н	3-MeOC ₆ H ₄	Н	Ι	4 - $^{t}BuC_{6}H_{4}$	6d	60
Н	3-MeOC ₆ H ₄	Н	Ι	4 - ^{<i>i</i>} PrC_6H_4	6e	62
Н	BnOCH ₂	Н	Ι	$4-MeC_6H_4$	6f	55
Н	$BnO(CH_2)_4$	Н	Ι	$4-MeC_6H_4$	6g	72
Н	3, 5-(MeO) ₂ C ₆ H ₃	Н	Ι	$4-MeC_6H_4$	6h	56
Н	Ph	Н	Ι	4-MeO-3,5-(Me) ₂ C ₆ H ₂	6 i	57
Н	$3,5-(MeO)_2 C_6H_3$	Н	Ι	Ph	6j	46
Н	Ph	Н	Ι	3,4-(OCH ₂ O)C ₆ H ₃	6k	42
Me	Me	Me	Br	4-MeOC ₆ H ₄	61	32
Ph	Н	Н	Ι	4-MeOC ₆ H ₄	6m	54
2-naphthyl	Н	Н	Br	4-MeOC ₆ H ₄	6n	62 ^c

^{*a*}Reaction conditions: $Fe(acac)_2$ (0.02 mmol), Xphos (0.02 mmol), 4 (0.2 mmol), in 2.0 mL toluene under Ar, added a solution of 5 in Et₂O over 2 h by a syringe pump at 0 °C, then at 23 °C for 6 h. ^{*b*}Isolated yield. ^{*c*}The Z/E ratio was determined by ¹H NMR, Z/E > 10:1.

Nevertheless, 4-chlorine-, 4-bromine-, and 4-iodo-phenylvinyl iodides were chemoselectively incompatible with this protocol. Furthermore, alkylvinyl iodides 11, 1m, and 1n were successfully employed, as exemplified by the generation of products 3l, 3m, and 3n in 55%-76% yields, respectively. The application of conjugated olefin 10 as substrate was also feasible and furnished the desired product 30 in 68% yield. It was also uncovered that the sterically hindered (1-iodovinyl)cyclopentane 1p formed the corresponding coupling product 3p in 52% yield. In addition, compounds 3r and 3s were formed with high yields, when the reactions were carried out by allowing iodomethylenecyclohexane (1r) or iodomethylenecycloheptane (1s) to react with 2. A benzyloxymethylvinyl iodide 1q was also examined, and as a result, 3q was obtained in 40% yield. To our delight, freshly prepared (E)- β -3thienylvinyl iodide (1t) also successfully furnished the corresponding product 3t. In addition, the application of this protocol to couple the stanolone derivative 1u with 2 successfully led to the desired product 3u, albeit in only 45% yield.

On the basis of the scope of various vinyl iodides 1 in Scheme 2, we further explored the scope of this protocol by coupling vinyl halides 4 with aryllithiums 5 (Table 2). Under the standard condition, aryllithiums 5 bearing electrondonating alkyl groups such as Me, Et, t-Bu, and i-Pr underwent the cross-coupling reaction smoothly with (E)-1-(2-iodovinyl)-3-methoxybenzene (4a) to afford stilbenes 6a-6e in good to excellent yields. In addition, 4 containing electron-donating groups coupled with different aryllithiums, resulting in the formation of products 6f-6k in good yields as well. To our delight, the sterically hindered tetrasubstituted 2-bromo-3methylbut-2-ene (41), also furnished successfully the corresponding product 61 in 32% yield. In order to explore the reaction diversity, two examples with Z-alkenyl halides were investigated. Experimental results showed that both compounds reacted under our optimized condition to give 6m and 6n, respectively. Moreover, regardless of yields, it is interesting to note that a very small percentage of isomerization was found

in the latter two cases, which lends support to our hypothesis that this reaction might likely go through a nonradical pathway. To demonstrate the synthetic utility of our work, we

attempted to carry out the reaction at a larger scale of 1 g, as can be seen in Scheme 3. Two typical scale-up reactions in approximately 1 g scale provided the corresponding stilbenes in satisfactory yields.

Scheme 3. Gram-Scale Reactions



In order to gain a better mechanistic understanding of the reaction, additional studies were performed on the basis of our previous work (Scheme 4).^{19c} Thus, the reaction of **4m** was carried out and monitored very carefully, but only a small amount of isomerization product **3a** was observed (Z/E > 7:1). Moreover, good cross-coupling result was also obtained for (Z)-2-(2-bromovinyl)naphthalene (**4n**), leading to the formation of high Z/E ratio product **6n** in 62% yield (Z/E > 10:1). Additionally, a radical clock experiment of **1n** was also performed. The results indicated that no ring-opening products were observed, therefore hinting at the absence of transient radical intermediates. These observations suggested that radical pathways were not likely to be involved in this reaction (for other details, please see Supporting Information).

In summary, we have demonstrated an efficient highly stereospecific Fe(II)-catalyzed cross-coupling process by using organolithium reagents and vinyl halides. More than 30 examples were obtained with moderate to good yields. The reaction could be scaled up to gram scale. This method pubs.acs.org/OrgLett

Scheme 4. Control Experiments



displays broad substrate scope and excellent functional group tolerance. Retention of the double bond configuration to a very great extent was observed under these conditions. Preliminary mechanistic investigations showed evidence that this reaction likely does not involve radical intermediates.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c01318.

Experimental procedures and compound characterization (PDF)

AUTHOR INFORMATION

Corresponding Authors

- Xiao-Shui Peng Department of Chemistry, and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Hong Kong SAR, China; School of Science and Engineering, The Chinese University of Hong Kong (Shenzhen), Shenzhen 518172, China; orcid.org/0000-0001-9528-8470; Email: xspeng@cuhk.edu.cn
- Henry N.C. Wong Department of Chemistry, and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Hong Kong SAR, China; School of Science and Engineering, The Chinese University of Hong Kong (Shenzhen), Shenzhen 518172, China; orcid.org/0000-0002-3763-3085; Email: hncwong@cuhk.edu.hk

Authors

- Peng Chen Department of Chemistry, and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Hong Kong SAR, China
- Zhi-Yong Wang Department of Chemistry, and State Key Laboratory of Synthetic Chemistry, The Chinese University of Hong Kong, Hong Kong SAR, China

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c01318

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by grants from National Natural Science Foundation of China (NSFC) (21971219, 21672181),

Research Grants Council (Hong Kong) (RGC) in the form of GRF (CUHK14304819, CUHK14309216, CUHK14303815, and 403012), and the Innovation and Technology Commission (Hong Kong) in the form of subsidy to the State Key Laboratory of Synthetic Chemistry, the open grant to CUHK-Shenzhen from the State Key Laboratory of Synthetic Chemistry, Direct Grant from CUHK, and the University Development Fund Grants from The Chinese University of Hong Kong, Shenzhen.

DEDICATION

This work is dedicated to the memory of Professor Klaus Hafner.

REFERENCES

(1) Negishi, E. Magical Power of Transition Metals: Past, Present, and Future (Nobel Lecture). *Angew. Chem., Int. Ed.* **2011**, *50*, 6738–6764.

(2) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. Synthetic Methods Palladium-Catalyzed Cross-Coupling Reactions in Total Synthesis. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442–4489.

(3) (a) Corbet, J.; Mignani, G. Selected Patented Cross-Coupling Reaction Technologies. *Chem. Rev.* 2006, 106, 2651-2710.
(b) Guérinot, A.; Cossy, J. Cobalt-Catalyzed Cross-Couplings between Alkyl Halides and Grignard Reagents. *Acc. Chem. Res.* 2020, 53, 1351-1363.

(4) Magano, J.; Dunetz, J. R. Large-Scale Applications of Transition Metal-Catalyzed Couplings for the Synthesis of Pharmaceuticals. *Chem. Rev.* 2011, 111, 2177–2250.

(5) Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize. *Angew. Chem., Int. Ed.* **2012**, *51*, 5062–5085.

(6) (a) Stille, J. K. 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. (b) Espinet, P.; Echavarren, A. M. The Mechanisms of the Stille Reaction. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704–4734.

(7) Suzuki, A. Cross-Coupling Reactions Of Organoboranes: An Easy Way To Construct C-C Bonds (Nobel Lecture). *Angew. Chem., Int. Ed.* **2011**, *50*, 6722–6737.

(8) (a) Phapale, V. B.; Cárdenas, D. J. Nickel-catalysed Negishi cross-coupling reactions: scope and mechanisms. *Chem. Soc. Rev.* **2009**, *38*, 1598–1607. (b) Negishi, E.-i. Magical Power of Transition Metals: Past, Present, and Future (Nobel Lecture). *Angew. Chem., Int. Ed.* **2011**, *50*, 6738–6764. (c) Haas, D.; Hammann, J. M.; Greiner, R.; Knochel, P. Recent Developments in Negishi Cross-Coupling Reactions. ACS Catal. **2016**, *6*, 1540–1552.

(9) (a) Tamao, K.; Sumitani, K.; Kumada, M. Selective carboncarbon bond formation by cross-coupling of Grignard reagents with organic halides. Catalysis by nickel-phosphine complexes. *J. Am. Chem. Soc.* **1972**, *94*, 4374–4376. (b) Knappke, C. E. I.; von Wangelin, A. J. 35 years of palladium-catalyzed cross-coupling with Grignard reagents: how far have we come? *Chem. Soc. Rev.* **2011**, *40*, 4948–4962.

(10) (a) Hiyama, T.; Nakao, Y. Silicon-based cross-coupling reaction: an environmentally benign version. *Chem. Soc. Rev.* 2011, 40, 4893–4901. (b) Denmark, S. E.; Regens, C. S. Palladium-Catalyzed Cross-Coupling Reactions of Organosilanols and Their Salts: Practical Alternatives to Boron- and Tin-Based Methods. *Acc. Chem. Res.* 2008, 41, 1486–1499.

(11) (a) Yamamura, M.; Moritani, I.; Murahashi, S.-I. The reaction of σ -vinylpalladium complexes with alkyllithiums. Stereospecific syntheses of olefins from vinyl halides and alkyllithiums. *J. Organomet. Chem.* **1975**, *91*, C39–C42. (b) Murahashi, S.-I.; Yamamura, M.; Yanagisawa, K.-I.; Mita, N.; Kondo, K. Stereoselective synthesis of

alkenes and alkenyl sulfides from alkenyl halides using palladium and ruthenium catalysts. J. Org. Chem. 1979, 44, 2408–2417.

(12) (a) Giannerini, M.; Fañanas-Mastral, M.; Feringa, B. L. Direct catalytic cross-coupling of organolithium compounds. Nat. Chem. 2013, 5, 667-672. (b) Giannerini, M.; Hornillos, V.; Vila, C.; Fañanas-Mastral, M.; Feringa, B. L. Hindered Aryllithium Reagents as Partners in Palladium-Catalyzed Cross-Coupling: Synthesis of Triand Tetra-ortho-Substituted Biaryls under Ambient Conditions. Angew. Chem., Int. Ed. 2013, 52, 13329-13333. (c) Hornillos, V.; Giannerini, M.; Vila, C.; Fañanaś- Mastral, M.; Feringa, B. L. Catalytic Direct Cross-Coupling of Organolithium Compounds with Aryl Chlorides. Org. Lett. 2013, 15, 5114-5117. (d) Vila, C.; Giannerini, M.; Hornillos, V.; Fañanas-Mastral, M.; Feringa, B. L. Palladiumcatalysed direct cross-coupling of secondary alkyllithium reagents. Chem. Sci. 2014, 5, 1361-1367. (e) Vila, C.; Hornillos, V.; Giannerini, M.; Fañanas-Mastral, M.; Feringa, B. L. Palladium-Catalysed Direct Cross-Coupling of Organolithium Reagents with Aryl and Vinyl Triflates. Chem. - Eur. J. 2014, 20, 13078-13083. (f) Heijnen, D.; Hornillos, V.; Corbet, B. P.; Giannerini, M.; Feringae, B. L. Palladium-Catalyzed C(sp3)-C(sp²) Cross-Coupling of (Trimethylsilyl)methyllithium with (Hetero)Aryl Halides. Org. Lett. 2015, 17, 2262-2265. (g) Hornillos, V.; Giannerini, M.; Vila, C.; Fañanas-Mastral, M.; Feringa, B. L. Direct catalytic cross-coupling of alkenyllithium compounds. Chem. Sci. 2015, 6, 1394-1398. (h) Pinxterhuis, E. B.; Giannerini, M.; Hornillos, V.; Feringa, B. L. Fast, greener and scalable direct coupling of organolithium compounds with no additional solvents. Nat. Commun. 2016, 7, 11698. (i) Heijnen, D.; Tosi, F.; Vila, C.; Stuart, M. C. A.; Elsinga, P. H.; Szymanski, W.; Feringa, B. L. Oxygen Activated, Palladium Nanoparticle Catalyzed, Ultrafast Cross-Coupling of Organolithium Reagents. Angew. Chem., Int. Ed. 2017, 56, 3354-3359. (j) Hornillos, V.; Guduguntla, S.; Fañanás-Mastral, M.; Pérez, M.; Bos, P. H.; Rudolph, A.; Harutyunyan, S. R.; Feringa, B. L. Cu-catalyzed enantioselective allylic alkylation with organolithium reagents. Nat. Protoc. 2017, 12, 493-505. (k) Helbert, H.; Visser, P.; Hermens, J. G. H.; Buter, J.; Feringa, B. L. Palladium-catalysed cross-coupling of lithium acetylides. Nat. Catal. 2020, 3, 664-671. (1) Mateos-Gil, j.; Mondal, A.; Castiñeira Reis, M.; Feringa, B. L. Synthesis and Functionalization of Allenes by Direct Pd-Catalyzed Organolithium Cross-Coupling. Angew. Chem., Int. Ed. 2020, 59, 7823-7829.

(13) (a) Bauer, I.; Knölker, H.-J. Iron Catalysis in Organic Synthesis. Chem. Rev. 2015, 115, 3170-3387. (b) Bedford, R. B.; Brenner, P. B. Topics in Organometallic Chemistry; Springer: Heidelberg, 2015. (c) Bedford, R. B. How Low Does Iron Go? Chasing the Active Species in Fe-Catalyzed Cross-Coupling Reactions. Acc. Chem. Res. 2015, 48, 1485-1493. (d) Fürstner, A. Iron Catalysis in Organic Synthesis: A Critical Assessment of What It Takes To Make This Base Metal a Multitasking Champion. ACS Cent. Sci. 2016, 2, 778-789. (e) Shang, R.; Ilies, L.; Nakamura, E. Iron-Catalyzed C-H Bond Activation. Chem. Rev. 2017, 117, 9086-9139. (f) Wei, D.; Darcel, C. Iron Catalysis in Reduction and Hydrometalation Reactions. Chem. Rev. 2019, 119, 2550-2610. (g) Anugu, R. R.; Munnuri, S.; Falck, J. R. Picolinate-Directed Arene meta-C-H Amination via FeCl₃ Catalysis. J. Am. Chem. Soc. 2020, 142, 5266-5271. (h) Ilies, L.; Nakamura, E. Iron-Catalyzed Cross-Coupling Reactions. In The Chemistry of Organoiron Compounds; Marek, I., Rappoport, Z., Eds.; John Wiley & Sons, Ltd.: Chichester, U.K., 2014. (i) Nakamura, E.; Hatakeyama, T.; Ito, S.; Ishizuka, K.; Ilies, L.; Nakamura, M. Iron-Catalyzed Cross-Coupling Reactions. In Organic Reactions; Denmark, S. E., Ed.; Vol. 83; John Wiley & Sons: 2014.

(14) (a) Tamura, M.; Kochi, J. K. Vinylation of Grignard reagents. Catalysis by iron. J. Am. Chem. Soc. 1971, 93, 1487–1489.
(b) Tamura, M.; Kochi, J. K. Coupling of Grignard Reagents with Organic Halides. Synthesis 1971, 1971, 303–305.

(15) (a) Echeverria, P.-G.; Fürstner, A. An Iron-Catalyzed Bond-Making/Bond-Breaking Cascade Merges Cycloisomerization and Cross-Coupling Chemistry. *Angew. Chem., Int. Ed.* **2016**, *55*, 11188–11192. (b) Tindall, D. J.; Krause, H.; Fürstner, A. Iron-Catalyzed Cross-Coupling of 1-Alkynylcyclopropyl Tosylates and

Related Substrates. *Adv. Synth. Catal.* **2016**, 358, 2398–2403. (c) Casitas, A.; Krause, H.; Goddard, R.; Fürstner, A. Elementary Steps of Iron Catalysis: Exploring the Links between Iron Alkyl and Iron Olefin Complexes for their Relevance in C-H Activation and C-C Bond Formation. *Angew. Chem., Int. Ed.* **2015**, 54, 1521–1526. (d) Sun, C.-L.; Krause, H.; Fürstner, A. A Practical Procedure for Iron-Catalyzed Cross-Coupling Reactions of Sterically Hindered Aryl-Grignard Reagents with Primary Alkyl Halides. *Adv. Synth. Catal.* **2014**, 356, 1281–1291.

(16) (a) Sekine, M.; Ilies, L.; Nakamura, E. Iron-Catalyzed Allylic Arylation of Olefins via C(sp³)-H Activation under Mild Conditions. *Org. Lett.* **2013**, *15*, 714–717. (b) Jin, M.; Adak, L.; Nakamura, M. Iron-Catalyzed Enantioselective Cross-Coupling Reactions of α -Chloroesters with Aryl Grignard Reagents. *J. Am. Chem. Soc.* **2015**, *137*, 7128–7134. (c) Nakagawa, N.; Hatakeyama, T.; Nakamura. Iron-Catalyzed Diboration and Carboboration of Alkynes. *Chem.* -*Eur. J.* **2015**, *21*, 4257–4261. (d) Zhou, B.; Sato, H.; Ilies, L.; Nakamura, E. Iron-Catalyzed Remote Arylation of Aliphatic C-H Bond via 1,5-Hydrogen Shift. *ACS Catal.* **2018**, *8*, 8–11.

(17) (a) Bedford, R. B.; Brenner, P. B.; Elorriaga, D.; Harvey, J. N.; Nunn, J. The influence of the ligand chelate effect on iron-aminecatalysed Kumada cross-coupling. *Dalton Trans* 2016, 45, 15811– 15817. (b) Bedford, R. B.; Gallagher, T.; Pye, D. R.; Savage, W. Towards Iron-Catalysed Suzuki Biaryl Cross-Coupling: Unusual Reactivity of 2-Halobenzyl Halides. *Synthesis* 2015, 47, 1761–1765.
(c) Bedford, R. B.; Brenner, P. B.; Carter, E.; Cogswell, P. M.; Haddow, M. F.; Harvey, J. N.; Murphy, D. M.; Nunn, J.; Woodall, C. H. TMEDA in Iron-Catalyzed Kumada Coupling: Amine Adduct versus Homoleptic "ate" Complex Formation. *Angew. Chem., Int. Ed.* 2014, 53, 1804–1808. (d) O'Brien, H. M.; Manzotti, M.; Abrams, R. D.; Elorriaga, D.; Sparkes, H. A.; Davis, S. A.; Bedford, R. B. Ironcatalysed substrate-directed Suzuki biaryl cross-coupling. *Nat. Catal.* 2018, 1, 429–437.

(18) (a) Benischke, A. D.; Breuillac, A. J. A.; Moyeux, A.; Cahiez, G.; Knochel, P. Iron-Catalyzed Cross-Coupling of Benzylic Manganese Chlorides with Aryl and Heteroaryl Halides. *Synlett* **2016**, *27*, 471– 476. (b) Cahiez, G.; Gager, O.; Buendia, J.; Patinote, C. Iron Thiolate Complexes: Efficient Catalysts for Coupling Alkenyl Halides with Alkyl Grignard Reagents. *Chem. - Eur. J.* **2012**, *18*, 5860–5863. (c) Cahiez, G.; Foulgoc, L.; Moyeux, A. Iron-Catalyzed Oxidative Heterocoupling Between Aliphatic and Aromatic Organozinc Reagents: A Novel Pathway for Functionalized Aryl-Alkyl Cross-Coupling Reactions. *Angew. Chem., Int. Ed.* **2009**, *48*, 2969–2972.

(19) (a) Jia, Z.; Liu, Q.; Peng, X.-S.; Wong, H. N. C. Iron-catalysed cross-coupling of organolithium compounds with organic halides. *Nat. Commun.* **2016**, *7*, 10614. (b) Liu, Q.; Wang, Z.-Y.; Peng, X.-S.; Wong, H. N. C. Ligand-Free Iron-Catalyzed Carbon(sp²)-Carbon-(sp²) Cross-Coupling of Alkenyllithium with Vinyl Halides. *J. Org. Chem.* **2018**, *83*, 6325–6333. (c) Lu, X.-L.; Shannon, M.; Peng, X.-S.; Wong, H. N. C. Stereospecific Iron-Catalyzed Carbon(sp²)-Carbon-(sp³) Cross-Coupling with Alkyllithium and Alkenyl Iodides. *Org. Lett.* **2019**, *21*, 2546–2549. (d) Zhong, Z.; Wang, Z.-Y.; Ni, S.-F.; Dang, L.; Lee, H. K.; Peng, X.-S.; Wong, H. N. C. Ligand-Free Iron-Catalyzed Carbon(sp²)-Carbon(sp²) Oxidative Homo-Coupling of Alkenyllithiums. *Org. Lett.* **2019**, *21*, 700–704. (e) Wang, Z.-Y.; Peng, X.-S.; Wong, H. N. C. Ligand-Free Iron-Catalyzed Homo-Coupling of Aryllithium Reagents. *Asian J. Org. Chem.* **2020**, *9*, 1834–1840.

(20) (a) Zhang, Z.; Qin, Y. Structurally Diverse Poly(thienylene vinylene)s (PTVs) with Systematically Tunable Properties through Acyclic Diene Metathesis (ADMET) and Postpolymerization Modification. *Macromolecules* **2016**, *49*, 3318–3327. (b) Rivière, C.; Pawlus, A. D.; Mérillon, J.-M. Natural stilbenoids: distribution in the plant kingdom and chemotaxonomic interest in Vitaceae. *Nat. Prod. Rep.* **2012**, *29*, 1317–1333. (c) Niesen, D. B.; Hessler, C.; Seeram, N. P. Beyond resveratrol: A review of natural stilbenoids identified from 2009–2013. J. Berry Res. **2013**, *3*, 181–196.

(21) (a) Mizoroki, T.; Mori, K.; Ozaki, A. Arylation of Olefin with Aryl Iodide Catalyzed by Palladium. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581–581. (b) Heck, R. F.; Nolley, J. P. Palladium-catalyzed vinylic

hydrogen substitution reactions with aryl, benzyl, and styryl halides. J. Org. Chem. 1972, 37, 2320–2322. (c) Beletskaya, I. P.; Cheprakov, A. V. The Heck Reaction as a Sharpening Stone of Palladium Catalysis. Chem. Rev. 2000, 100, 3009–3066.

(22) Liu, J.; Ren, Q.; Zhang, X.; Gong, H. Preparation of Vinyl Arenes by Nickel-Catalyzed Reductive Coupling of Aryl Halides with Vinyl Bromides. *Angew. Chem., Int. Ed.* **2016**, *55*, 15544–15548.

(23) (a) Gosmini, C.; Moncomble, A. Cobalt-Catalyzed Cross-Coupling Reactions of Aryl Halides. *Isr. J. Chem.* **2010**, *50*, 568–576. (b) Moncomble, A.; Floch, P. L.; Lledos, A.; Gosmini, C. Cobalt-Catalyzed Vinylation of Aromatic Halides Using β -Halostyrene: Experimental and DFT Studies. *J. Org. Chem.* **2012**, *77*, 5056–5062.

(24) Czaplik, W. M.; Mayer, M.; Jacobi von Wangelin, A. Iron-Catalyzed Reductive Aryl-Alkenyl Cross-Coupling Reactions. *Chem-CatChem* **2011**, *3*, 135–138.