Cross-Nucleophile coupling: synthesis of a new C-C bond between alkylboranes and boronates

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Abstract

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Many general methods are now available for the cross-coupling of carbon nucleophiles with carbon electrophiles, and even the couplings between two electrophiles have been gradually developed in the last decade. There remain problems with the synthesis of these electrophiles and their toxicity is not negligible. Reactions that directly couple two carbon nucleophiles, "cross-nucleophiles coupling reactions," avoid this challenge, but these reactions have not been extensively developed. Herein we reported a new method for cross-nucleophile coupling utilizing copper catalyst with NHC ligands to synthesize a new C-C bond between alkylboranes and boronates. This new reaction

tolerates a variety of functional groups, which can be accomplished in the presence of esters, nitriles, aryl bromides, ethers, alkyl chlorides, anilines, and a wide range of nitrogen-containing heteroaromatic compounds. We propose that the reaction is realized through the transmetallation competition of the borates over boranes. Hydrogen gas was observed during the reaction, and it is hypothesized to be formed through the presence of a copper hydride.

Table of Contents

1. Introduction 6

1.1 Traditional cross-coupling reactions 6

1.2 Cross-electrophile coupling reactions 8

1.3 Cross-nucleophile coupling reactions 10

2. Optimization of the reaction 12

2.1 Base screens 13

2.2 Alcohol screens 15

2.3 Temperature screens 17

2.4 Solvent screens 18

2.5 Boronate screens 20

2.6 Reaction time screens 23

2.7 Stoichiometry Screens 24

2.8 Catalyst screens 25

3. Scope of the reaction 26

4. The hypothesis of the mechanism 28

5. Supporting materials 29

Bibliography 32

1. Introduction

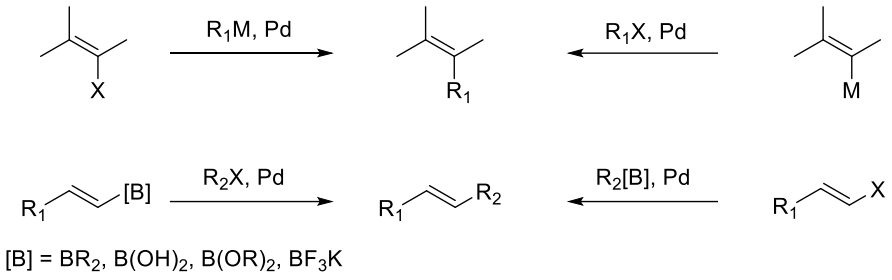
1.1 Traditional cross-coupling reactions

The metal-catalyzed cross-coupling reaction is an important method to form new C-C bonds, especially in the synthesis of complex organic molecules.[1] This reaction involves the coupling of two different molecules, nucleophile and electrophile. The nucleophile is an electron-rich chemical reactant that potentially donates both bonding electrons to the electrophile while forming a chemical bond. Organometallic reagents, such as a Grignard reagent or alkylborane, are typical nucleophiles.[2] While an electrophile is a chemical species that forms bonds with nucleophiles by accepting an electron pair.[3]

There is a wide variety of metal-catalyzed reactions to prepare functionalized alkenes which are obtained either through reactions of alkenylmetals with alkyl halides and related electrophiles[4-6], or by reactions of alkylmetals with alkenyl electrophiles.[7, 8] (Scheme 1) The protocols often employ transition metal-catalyzed transformations involving palladium[9-11], nickel[12, 13], copper[6, 14], iron[8], or cobalt[15], and proceed through a series of oxidative addition, transmetalation, and reductive elimination steps, to complete the synthesis of alkenes. Different metal-catalyzed systems are able to offer selective transformation with high efficiency.

Among the high-efficiency palladium-catalyzed reactions to form new alkenes, the Mizoroki–Heck coupling reaction[16] of alkenes with aryl and vinyl electrophiles and the Suzuki–Miyaura coupling[17] between organoboron compounds and electrophiles have a significant influence. Electron-rich and bulky ligands like phosphines[18], NHCs[19, 20], and palladacycles[21, 22] are a significant advancement in high-turnover palladium catalysts. These catalytic systems offer coordinatively unsaturated electron-rich palladium (0)

complexes that can easily perform oxidative addition reactions even with inert substrates.[23] Each catalytic reaction requires the optimization of various factors to find out the best set of conditions, such as the metal counteraction, the base, the leaving group, the palladium catalyst, the additive, the solvent, and the temperature.

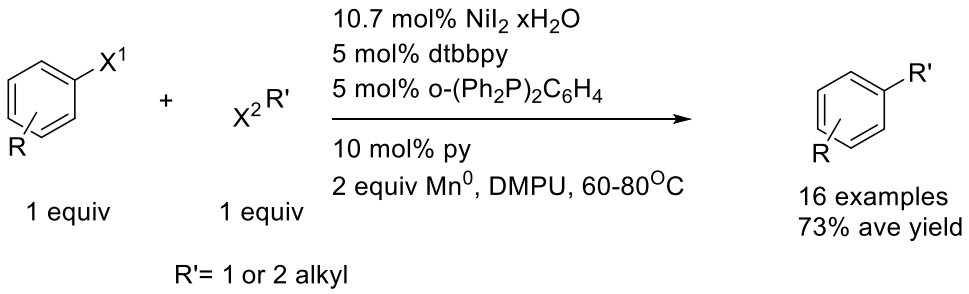


Scheme 1 Synthesis of Alkenes by Palladium-Catalyzed Cross-Coupling Reactions

In conventional cross-coupling reactions[24], the selectivity is mainly determined by the different reactivity of nucleophiles and electrophiles: nucleophiles undergo transmetalation with the catalyst, and electrophiles undergo oxidative addition. However, some organometallic compounds are unstable and commercial-unavailable. Additionally, most of the organometallic reagents or their precursors have strict reaction conditions excluding water and oxygen. [25] Likewise, the intrinsic reactivity of the reagents (RMgX and RZnX) or additives needed to enable transmetalation ($RB(OR')_2$ and $RSiR'_3$) restricts the use of substrates that have electrophilic functional groups or have acidic protons. And thus, a new trend of developing cross-electrophile coupling methods arises to avoid the challenges of preformed carbon nucleophiles.

1.2 Cross-electrophile coupling reactions

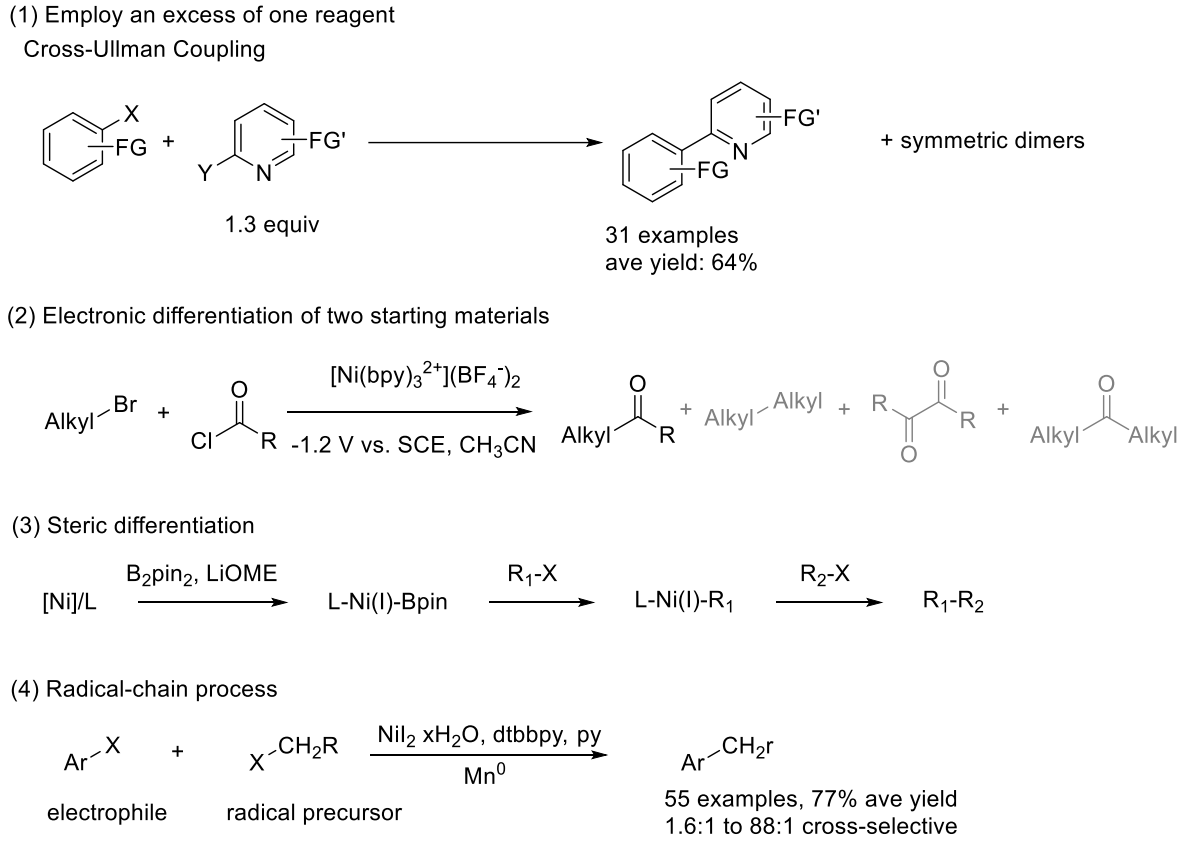
The first well-known example of cross electrophile coupling reaction is the dimerization of electrophiles reported over 100 years ago[26], followed by the Wurtz–Fittig reaction[27] that couples alkyl halides with aryl halides through sodium metal and is cross-selective in some cases. Not until recent decades have scientists found methods using familiar chemical-reducing agents to realize cross-electrophile coupling. In 2010, the Weix group[28] first made progress in applying the reductive cross-coupling reactions in two different organohalides instead of being constrained by the few organometallic reagents that exist. (Scheme 2) It was realized with aryl halides and alkyl halides in the presence of a low loading of nickel catalyst and generally afforded high yields. Moreover, this efficient reaction required a synergistic effect of the phosphine and pyridine-type ligands to avoid the formation of intermediate organomanganese species.



Scheme 2 The first transition-catalyzed cross-electrophile coupling by the Weix group

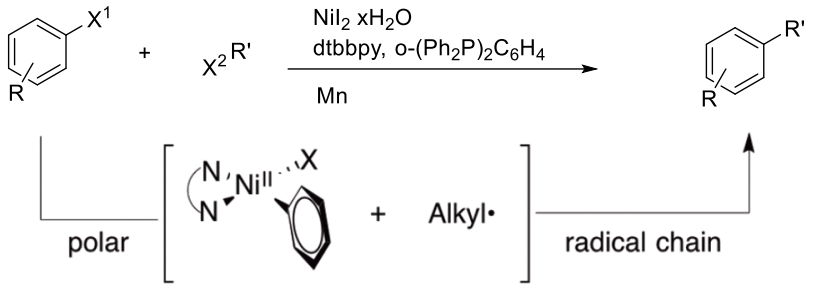
However, there remains a challenge of selectivity with two chemically similar electrophilic starting materials. It is caused by the competition of the electrophiles in a reaction with the same transition-metal catalyst through oxidative addition. As a result, the key question is how a catalyst system can tell apart two substrates that react in a

similar way and then join them selectively to make the cross-product rather than homocoupling products. To achieve useful yields of cross-coupled products, there are four methods (Scheme 3): (1) Employ an excess of one reagent[29, 30]; (2) Electronic differentiation of two starting materials[31]; (3) Steric differentiation[32]; (4) Radical-chain process. [28, 33]



Scheme 3 Transition-metal-catalyzed cross coupling strategies that alleviate limitations imposed by nucleophilic coupling partners.

It took the Weix group three years to elucidate the mechanism of their first cross-electrophile coupling reactions and establish that the selectivity arises from an unusual catalytic cycle that combines both polar and radical steps to form the new C-C bond. [33]



Scheme 4 Mechanism of the Weix's cross electrophile coupling

The Weix group continued to research in this undeveloped field and developed a variety of cross-electrophile coupling reactions and recently, and they found a new, decarbonylative reaction to form a Csp2–Csp3 bond from the reaction of activated carboxylic acids via O-pyridyl esters with activated alkyl groups derived from amines via N-alkyl pyridinium salts and alcohols via alkyl halides.[34] The Weix group also reported the use of 1° and 2° alcohols with aryl and vinyl halides to form C(sp3)–C(sp2) bonds in a one-pot strategy utilizing a very fast bromination.

Although cross-electrophile coupling has been an innovative and inspiring method in drug design, the remaining electrophiles in the final steps require more attention to be eliminated due to their toxicity. Meanwhile, the human body is a nucleophilic environment because it contains a variety of amino acids, nucleic acids, and proteins. [35] And thus, residuals of electrophiles could be destructive. It's worthwhile to discover alternative pathways avoiding using electrophiles but merely nucleophiles.

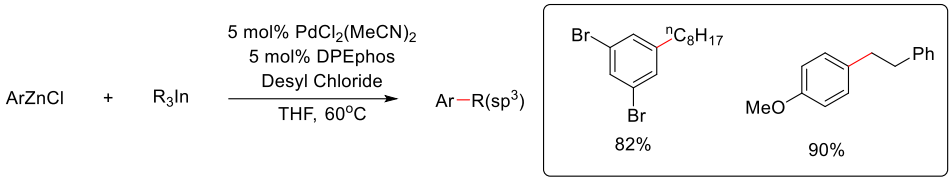
1.3 Cross-nucleophile coupling reactions

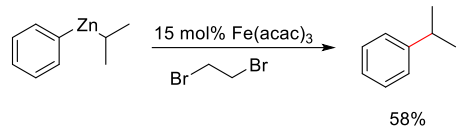
With the help of some high-valent transition metals, oxidative steps in organic synthesis have allowed the reaction between two nucleophiles to be realized. C-M group (RMgX,

RZnCl, $RB(OH)_2$, etc.) is a typical class of nucleophiles in organic synthesis, which is compatible with different kinds of functional groups in transition metal catalyzed reactions.

Selectivity is also one of the main challenges of cross-coupling between organometallic compounds, which is caused by homocoupling and the possibility of the self-oxidation of the organometallic compounds. It is important to control two organometallic compounds separately reacting in trans-metalation.

To form a new Csp2-Csp3 bond through cross nucleophile coupling, (Figure 4) the Lei group[37] identified arylzinc reagents and alkylindium reagents as two ideal nucleophiles. The reaction was catalyzed by palladium in the presence of desyl chloride as an oxidant. (Scheme 5) Later, Cahiez et al.[38] reported another example of cross-nucleophile coupling in the presence of a Fe (III) catalyst. Unsymmetric alkyl-aryl zinc reagents were found to undergo formal reductive elimination reactions to form the alkylarenes by employing catalytic amounts of Fe(acac)3 in the presence of 1,2-dibromoethane as the oxidant. (Scheme 5) Besides, there are limited research results in the field of cross nucleophile coupling reactions. This area is underexplored and underdeveloped compared with traditional cross-coupling reactions.

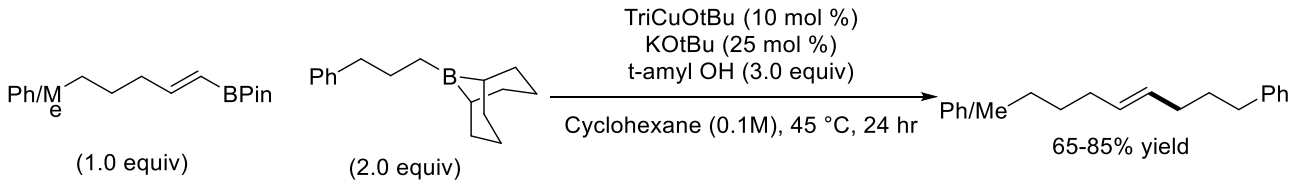




Scheme 5 Research of forming a new Csp2-Csp3 bond through cross nucleophile coupling.

Here, we explored a new cross-nucleophile coupling reaction between alkylboranes (R-9BBN) and boronates (alkenyl pinacol boronate), in the presence of a copper catalyst (TriCuOtBu), and t-amyl alcohol to synthesize a new Csp2-Csp3 bond, stereo-specifically forming the alkene.

2. Optimization of the reaction



Scheme 5. Optimization of Reaction Conditions

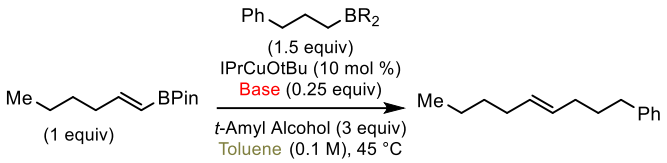
During the development of the reaction, several observations were made about the reaction parameters.

2.1 Base screens

The first screen (Table 1) was performed in toluene with hexenyl boronate to test different bases and thus at the end of the reaction most of the starting material remained intact. Of all the metal alkoxides, potassium salts worked the best leaving the least amount of the remaining starting materialat the end of the reaction. However, the mass balance was low. If the reaction was implemented without base, the vinyl boronic ester would still be consumed and a small amount of product was formed. (Table 1, entry 14)

With phenyl pentenyl boronate as a substrate, more bulky potassium bases were screened using cyclohexane as a solvent (Table 2). The yields improved and there were no remaining vinyl boronic esters. The results also confirmed that the sterically bulky potassium bases are best for this reaction.

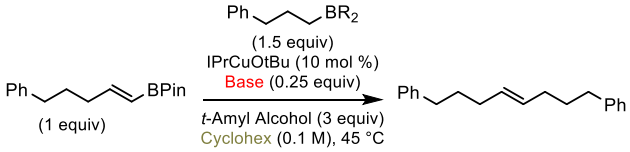
Decreasing or increasing the amount of base between 0.1 and 1 equivalent did not seem to influence the reaction and the yields were fluctuating within a narrow range. (Table 3)



entry	Base	R.M. (BPin) / %	Product %
1	NaOPh	38	5
2	LiOtBu	81	8
3	NaOtBu	66	19
4	KOtBu	13	39
5	LiOTMS	46	5
6	NaOTMS	47	10
7	KOTMS	19	13
8	LiOiPr	74	4
9	KOMe	11	8
10	LiOEt	60	5
11	NaOEt	43	14
12	KOEt	33	9
13	$Mg(OtBu)_2$	48	5
14	none	46	5

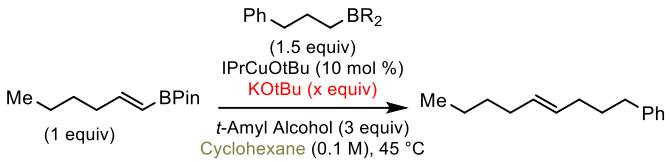
Table 1 Base screens

*Each data is calculated based on the corresponding starting materials.



entry	Base	Ph	from boran / %	R.M. (BPin) / %	Product / %
1	$KOMe_3$		69	0	70
2	$KOMe_2Et$		73	0	67
3	KOtBu		70	0	73

Table 2 Base screens (bulkier potassium base)



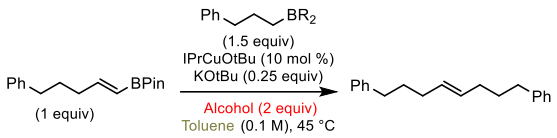
entry	KOtBu (x equiv)	R.M. (BPin) / %	Product / %
1	0.1	0	50
2	0.25	0	54
3	0.5	0	51
4	0.75	0	54
5	1.0	0	49
6	2.0	0	40

Table 3 Base stoichiometry screens

2.2 Alcohol screens

A variety of alcohols were screened in a standard reaction with phenyl pentenyl boronate as the limiting reagent. With toluene as a solvent, the entire system was massy as it was observed before. Smaller alcohols led to more protodeboronation reactions in both boronates and boranes, while sterically bulkier alcohols resulted in more sluggish reaction but far less protodeboronation. (Table 4)

Within all the screening results, the bulky t-amyl alcohols worked well, and a good mass balance was observed. (Table 5) Meanwhile, its stoichiometry was tested within the range of 2.0 to 4.0 equivalent. A lower loading gave worse results. (Table 6)



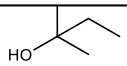
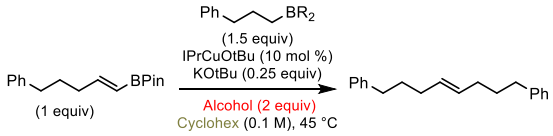
entry	Alcohol	Ph	Ph	R.M. (BPin) / %	Product / %
1		23	0	14	42
2		93	40	17	9
3		99	43	23	0
4		81	27	37	3

Table 4 Alcohol screens



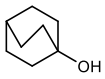
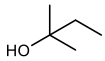
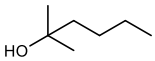
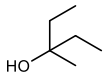
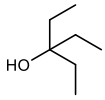
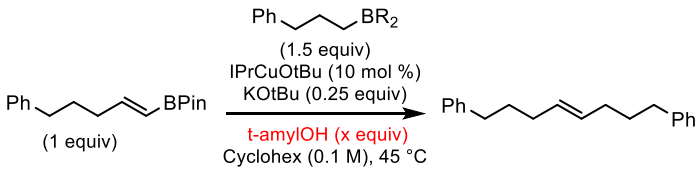
entry	Alcohol	Ph	Ph	R.M. (BPin) / %	Product / %
1		86	0	0	21
2		84	0	0	38
3		57	0	10	45
4		61	0	0	51
5		15	0	30	35
6		10	0	18	33

Table 5 Alcohol screens (Bulkier alcohols)

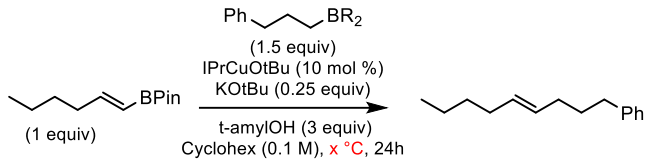


entry	t-amylOH (x equiv)	Ph	Ph	R.M. (BPin) / %	Product / %
1	1.0	49	0	0	21
2	1.5	47	0	0	35
3	2.0	57	0	8	45
4	2.5	45	0	0	48
5	3.0	30	0	5	50
6	4.0	17	0	0	49

Table 6 Alcohol stoichiometry screens

2.3 Temperature screen

Reaction with hexenyl boronate was carried out at room temperature, 45, and 60 degrees. (Table 7) After a day, half of the hexenyl boronate remained in the reaction at room temperature and a low yield of the desired alkene was obtained. 45 Degrees centigrade was proved to be an appropriate temperature as the higher one decreased the yield of the product, and no starting materials were left as well.



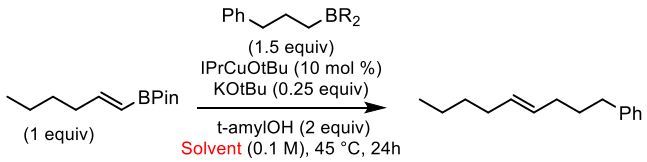
entry	x °C	R.M. (BPin) / %	Product / %
1	20	50	21
2	45	0	67
3	60	0	53

Table 7 Temperature screen

2.4 Solvent screen

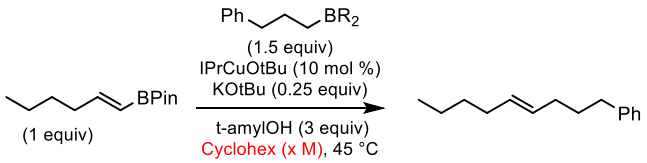
A variety of hydrocarbon solvents as well as some regular ether type solvents were chosen to modify the reaction and the results showed that hydrocarbon solvents were preferred. If a longer reacting time was provided for the choice of toluene, all the vinyl boronic ester was consumed and the yield was raised by five percent. The best yield was achieved using cyclohexane with the greatly increased protodeboronation. (Table 8)

Concentration did not affect the yield much between 0.2M and 0.025M while 0.1 M cyclohexane was able to offer a cleaner reaction mixture with relatively less protodeboronation. (Table 9) Although a more diluted reaction mixture could decrease the protodeboronation, the yield of the desired product also dropped. And a higher concentration did not improve the reaction.



entry	Solvent	R.M. (BPin) / %	Product / %
1	Toluene	19	40
2	Benzene	20	32
3	Xylenes	15	45
4	Mesitylene	10	41
5	Chlorobenzene	7	44
6	Dodecane	8	44
7	Isoocatane	0	44
8	Pentane	8	41
9	Cyclohexan	0	52
10	Dioxane	64	15
11	CPME	39	29
12	DME	63	7

Table 8 Solvent screen



entry	Cyclohex (x M)	Ph	Ph	R.M. (BPin) / %	Product / %
1	0.01	35	0	87	17
2	0.025	55	3	43	36
3	0.05	74	3	26	51
4	0.1	109	0	4	75
5	0.25	147	3	0	75
6	0.5	148	5	2	69
7	1	154	3	3	65
8	2	151	4	0	50

Table 9 Concentration screens

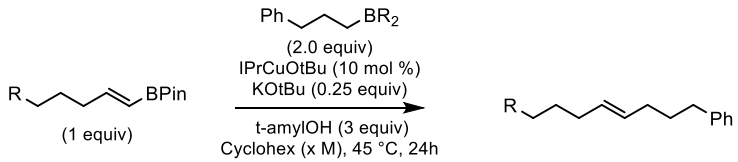
2.5 Boronate screen

Within several accessible boronates, several provided a relatively good result (Table 10, entries 1, 4, and 5), while dioxaborinane and the boronic acid provided worse results (Table 10, entry 2 and 3). The screen of other allyl boronates sources also did a good work. (Table 10, entry 4 & 5)

Different types of pinacol boronates were tested to get a broad version of the substrate scope. When it comes to trans alkenyl boronate (Table 11, entry 1, 2, 3), the results all showed that the stereochemistry was retained after the reaction and the starting material was consumed.

The stereochemistry did not change even with the attempt of using cis-phenyl pentenyl boronate as well as the cis-styrene boronate. (Table 12, entry 1, 2) However, with trans styrenyl boronate, (Scheme 6) which was the only exception in this reaction, a mix product of cis- and trans-1,5-diphenyl-1-pentene with the ratio of approximately 1:2 was defined through the NMR.

Moreover, this reaction could be realized through 1,1-disubstituted alkenyl boronate (Table 11, entry 4) but encountered several failures with cyclohexenyl boronate (Table 11, entry 5) and 1,1,2-trisubstituted alkenyl boronate. (Table 11, entry 6)



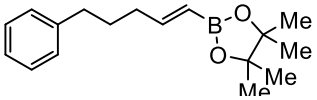
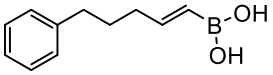
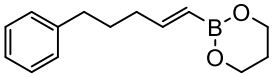
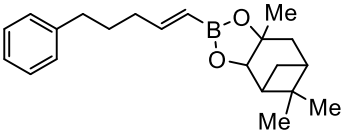
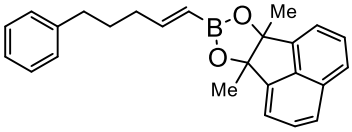
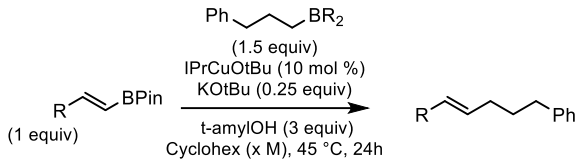
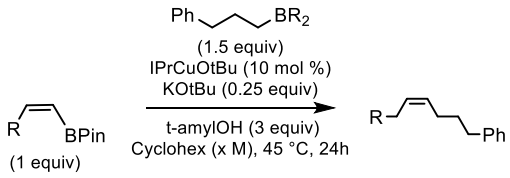
entry	vinyl boronic ester	Ph	R.M. (BPin) / %	Product / %
1		42	4	68
2		88	87	0
3		60	41	39
4		49	3	63
5		38	0	69

Table 10 Boronates screen



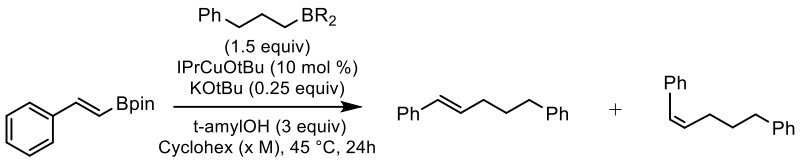
entry	R BPin	R.M. (BPin) / %	Product / %
1	BPin	0	74
2	Ph BPin	0	69
3	BPin	0	35
4	Bpin	0	60
5	Bpin	0	0
6	Bpin	0	0

Table 11 Trans-pinacolboronate screens



entry	R BPin	R.M. (BPin) / %	Product / %
1	Ph BPin	35	30
2	Bpin	0	50

Table 12 Cis-pinacol boronate screens

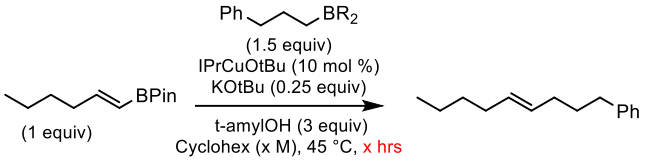


Overall yield 30%
trans:cis = 2:1
No starting materials left

Scheme 6 Stereochemistry in the reaction of trans-styrenyl boronate

2.6 Reaction time screen

This cross coupling was proved to require a long reaction time. (Table 13) The remaining amount of starting material and the yield of product were determined at several time points. Seven identical reactions were set up in seven reaction flasks. Each flask was carried out of the glovebox at the specific time point and then worked up for analysis by GC. After 24 hours, the boronate was consumed. Additionally, extending the time to 48 hours did not offer much improvement.



entry	x hrs	Ph	R.M. (BPin) / %	Product / %
1	0.75	7	98	4
2	1.5	12	87	12
3	3	17	78	18
4	6	27	61	29
5	16	35	5	54
6	24	41	0	65
7	48	77	0	67

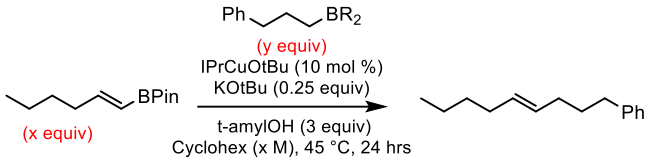
Table 13 Reaction time screen

2.7 Stoichiometry Screen

The boronate was set up to be the limiting reagent and the stoichiometry of the alkylboranes was tested. Although a lower amount of the boranes was expected, 2.0 equivalent was a required number as some part of it might undergo protodeboronation. (Table 14, entry 1-5)

Additionally, if the sequence of the addition was changed, although there was not a long pause between the additions the boronate and the borane, there would be a drop in the yield. (Table 14, entry 6)

While changing the limiting reagent to alkylboranes, the presence of more boronate did not improve the yield of the desired alkene. (Table 14, entry 7)

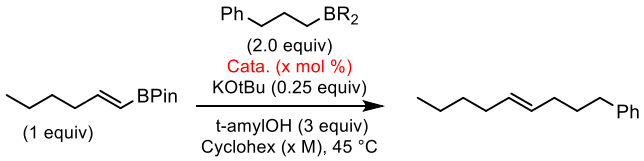


entry	(x equiv)	(y equiv)	R.M. (BPin) / %	Product / %
1	1.0	1.0	15	39
2	1.0	1.2	7	46
3	1.0	1.5	0	66
4	1.0	2.0	0	72
5	1.0	4.0	0	70
6	1.0	2.0 added first	0	41
7	2.0	1.0	40	27

Table 14 Reacting reagents stoichiometry Screen

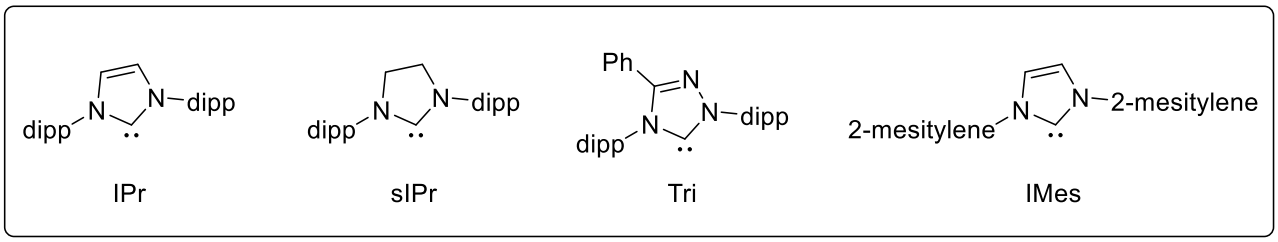
2.8 Catalyst screen

As in most other copper-catalyzed functionalization reactions[36] of alkynes, catalysts supported by IPr and the closely related SIPr ligands worked well in this reaction. (Table 15, entry 5-8) And the silver catalyst did not perform well in this reaction (Table 15, entry 9). Although the prepared IPrCuOtBu already offered decent results around 60%, the introductory of TriCuOtBu is able to raise another 5-10% of yield. At the same time, even with a lower catalyst loading of TriCuOtBu (5 mol%), the yield remained good (Table 15, entry 2).



entry	Catalyst	Loading / mol%	R.M. (BPin) / %	Product / %
1	TriCuOtBu	10	3	66
2	TriCuOtBu	5	27	65
3	TriCuOtBu	2	45	42
4	TriCuCl	10	0	59
5	IPrCuOtBu	10	0	58
6	IPrCuCl	10	0	60
7	IMesCuCl	10	0	31
8	sIPrCuCl	10	25	38
9	IPrAgCl	10	40	21

Table 15 Catalyst screen



Scheme 7 NHC ligands

3. Scope of the reaction

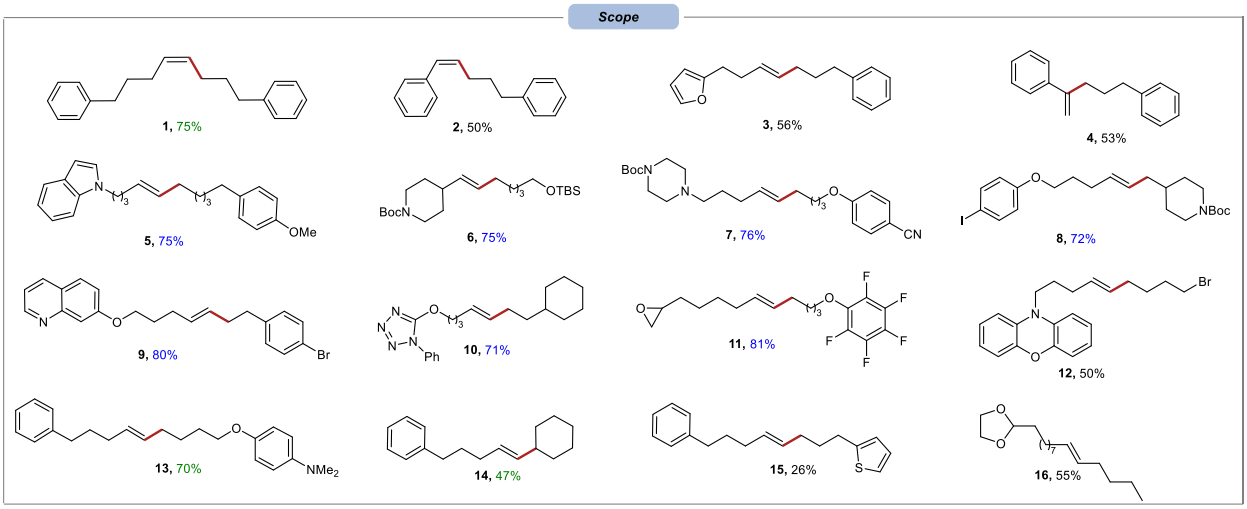


Table 16 Scope of the reaction

[a] Conditions: TriCuOtBu(10 mol %), alkyl borane (1.5 equiv), KOt-Bu (0.25 equiv), t-amylOH (3.0 equiv), cyclohexane (0.5 M), 45 °C, 24 h.

[b] Yield determined by ^{1}H NMR.

[c] Reactions were performed on a 0.5 mmol scale. Alkylboranes were prepared in situ by stirring the corresponding alkene (1 equiv) and 9-borabicyclo [3.3.1] nonane dimer (0.42 equiv) in toluene (1 M) at 60 °C.

The new transformation developed for the stereospecific synthesis of alkenes as exclusive products proved general for a range of substrates (Table 16). Functionalized vinyl boronic ester generated from alkyl alkynes could be successfully used in the reaction together with alkyl boranes, which originated in situ from both electron-rich and electron-poor aryl or alkyl terminal alkenes.

The alkene products maintain the same stereochemistry as the boronates. Phenyl pentenyl or styrene Z-type boronic ester provided the same Z-alkenes (1, 2) in good yield. 1,1-disubstituted vinyl borates also react in the same conditions (4).

Furthermore, a wide range of functional groups was tolerated. Alkene products were formed in the presence of Boc-protected secondary amines (6), aryl iodides (8), epoxides (11), and acetals (16), which are realized through the boronates part.

Alkene formed through this new transformation could also tolerate functional groups originated from the alkylboranes. Aryl (1), silyl ether (6), cyanobenzene ether (7), bromides (9), aryl fluorides (11), alkyl bromides (12), tertiary amines (13) are tolerated. Secondary boranes (14) derived from cyclohexene gives a decent result as well.

Heterocycles such as indole (5), quinoline (9), protected piperazine (7), tetrazole (10), and phenoxazine (12) were also compatible with the reaction conditions.

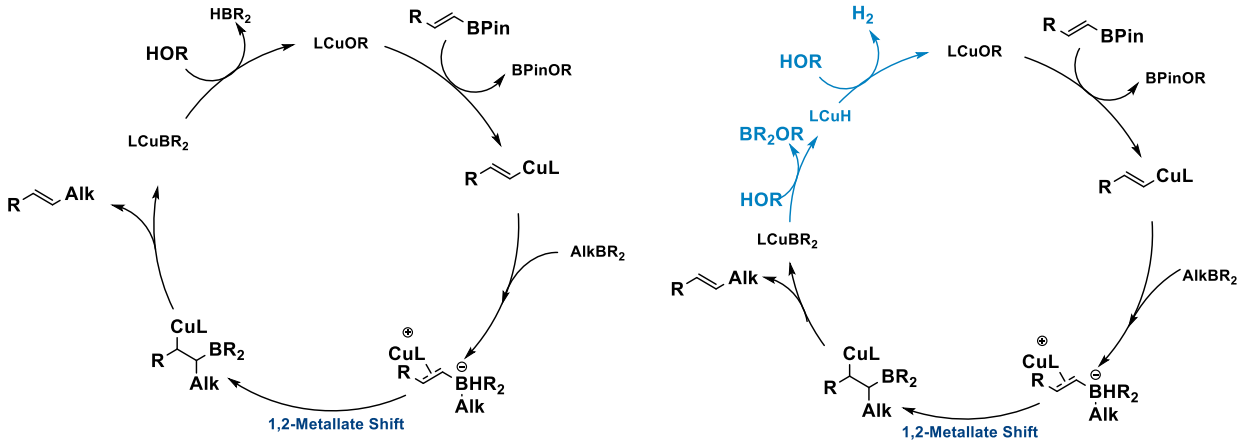
Additionally, we tried a mix-and-match scope. This new transformation could be established with the presence of two different function groups, halides with epoxides and heterocycles, and electron-drawing groups with electron-withdrawing groups.

4. The mechanistic hypothesis

At this point we do not understand the mechanism of the new reaction. However, our initial hypothesis is presented in Scheme 8. We propose that the initial transmetalation of the copper catalyst with boronates was followed by the activation of alkylboranes. The intermediate undergoes a 1,2-metallate shift and then product is acquired through elimination. (Scheme 8a)

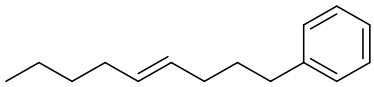
The catalyst can be regenerated through the alcohol as the turnover reagent. However, bubbles appeared in the NMR tube and the spectrum provided evidence of the presence of hydrogen. Presumably, hydrogen might have originated from copper hydride which could be generated from alcohol, and another equivalent of alcohol helped the copper hydride to regenerate the catalyst and finish the catalytic cycle. (Scheme 8b) Further research aimed at understanding the reaction mechanism is underway.

a) b)

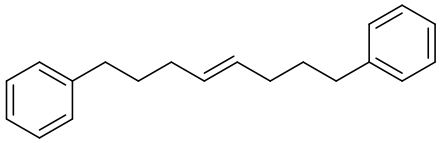


Scheme 8 Hypothesis of the catalytic cycle

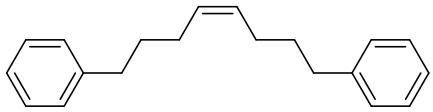
5. Supporting materials



(Z)-4-noneyl-benzene compound was isolated as a colorless liquid (69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (s, 2H), 7.20 (d, *J* = 7.1 Hz, 3H), 5.44 (d, *J* = 4.2 Hz, 2H), 2.66 (dt, *J* = 28.8, 8.0 Hz, 3H), 2.03 (d, *J* = 16.9 Hz, 4H), 1.70 (p, *J* = 7.6 Hz, 4H), 1.40 – 1.31 (m, 2H), 0.99-0.88 (m, 2H). ^{13}C NMR (126 MHz, CDCl3) δ 142.6, 130.0, 129.9, 128.6, 128.4, 125.8, 35.6, 34.0, 32.9, 31.6, 29.0, 28.0, 27.2, 27.0. GCMS (EI) calculated for [M]+ 202.34, found 202.40. FTIR (neat, cm^{-1}): 3060(m), 3002(m), 2930(m), 2855(m), 1602(s), 1495(s), 1452(s), 970(s).

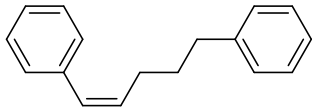


(E)-1,8-diphenyloct-4-ene compound was isolated as a colorless liquid (74% yield). ^{1}H NMR (500 MHz, CDCl3) δ 7.34 – 7.26 (m, 4H), 7.23 – 7.19 (m, 6H), 5.49 – 5.44 (m, 2H), 2.86 – 2.44 (m, 4H), 2.11 – 2.05 (m, 4H), 1.78 – 1.68 (m, 4H).^{13}C NMR (126 MHz, CDCl3) δ 142.7, 130.5, 128.6, 128.4, 125.8, 35.5, 32.3, 31.5. GCMS (EI) calculated for [M]+ 264.19, found 264.10. FTIR (neat, cm^{-1}): 3058(m), 3005(m), 2931(m), 2856(m), 1602(m), 1600(m), 1494(s), 1454(s), 1227(s), 1010(s), 906(w).

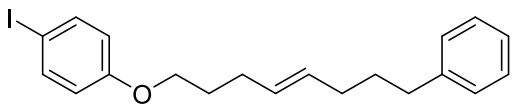


(Z)-1,8-diphenyloct-4-ene compound was isolated as a colorless liquid (75% yield). ^{1}H NMR (500 MHz, CDCl3) δ 7.33 – 7.26 (m, 4H), 7.21 – 7.14 (m, 6H), 5.54 – 5.30 (m, 2H), 2.68 – 2.54 (m, 4H), 2.12 – 2.00 (m, 4H), 1.76 – 1.60 (m, 4H).^{13}C NMR (126 MHz,

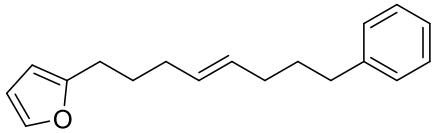
CDCl3) δ 142.6, 130.0, 128.6, 128.4, 125.8, 35.6, 31.6, 27.0. GCMS (EI) calculated for [M]+ 264.19, found 264.2. FTIR (neat, cm-1): 3061(m), 3005(m), 2931(m), 2856(m), 1602(m) 1495(s), 1452(s), 1217(s), 1030(s), 906(w).



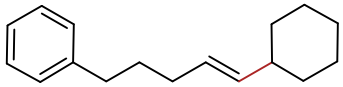
(Z)-1,5-Diphenyl-2-pentene compound was isolated as a colorless liquid (50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 8.0 Hz, 2H), 7.25 – 7.14 (m, 3H), 6.47 (d, *J* = 11.6 Hz, 1H), 5.72 (d, *J* = 0.0 Hz, 1H), 2.67 (t, *J* = 7.8 Hz, 2H), 2.43 – 2.37 (m, 2H), 1.82 (q, *J* = 7.9 Hz, 2H).^{13}C NMR (126 MHz, CDCl3) δ 142.1, 141.3, 134.8, 129.0, 128.6 (q, J = 27.6 Hz), 128.6, 128.2, 126.0, 125.2, 124.5, 35.5, 31.6, 28.1. GCMS (EI) calculated for $[M]^+$ 222.14, found 222.20. FTIR (neat, cm^{-1}): 3062(m), 3025(m), 2931(m), 2858(m), 1614(s), 1496(s), 1453(s), 1420(m), 1326(s), 1164(s), 1124(s), 1067(s), 1016(s), 837(s).



1-iodo-4-{[(4E)-8-phenyloct-4-en-1-yl]oxy}benzene compound was isolated as a colorless liquid (93% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.42 (m, 2H), 7.29 (d, *J* = 1.9 Hz, 2H), 7.21 – 7.11 (m, 3H), 6.70 – 6.61 (m, 2H), 5.52 – 5.38 (m, 2H), 3.91 (t, *J* = 6.5 Hz, 2H), 2.63 – 2.56 (m, 2H), 2.03 (td, *J* = 7.3, 4.7 Hz, 2H), 1.90 – 1.77 (m, 2H). ^{13}C NMR (126 MHz, CDCl3) δ 159.1, 142.5, 138.3, 130.8, 128.9, 128.5, 128.4, 125.8, 117.0, 82.6, 67.2, 35.6, 31.5, 29.1, 27.0, 23.7. GCMS (EI) calculated for $[M]^+$ 406.08, found 406.1. FTIR (neat, cm^{-1}): 3060(m), 3024(m), 3001(m), 2933(m), 2855(m), 1586(s), 1485(s), 1467(s), 1282(s), 1243(s), 1174(s), 819(s), 698(s).



(E)-2-[8-phenyl-4-octenyl]-furan compound was isolated as a colorless liquid (56% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.9 Hz, 4H), 7.21 – 7.15 (m, 6H), 5.42 (t, *J* = 4.8 Hz, 2H), 2.61 (t, *J* = 7.7 Hz, 4H), 2.10 – 2.02 (m, 4H), 1.68 (p, *J* = 7.6 Hz, 4H). ^{13}C NMR (126 MHz, CDCl3) δ 156.7, 142.6, 140.8, 136.7, 130.0, 128.6, 128.2, 127.7, 110.2, 104.7, 40.8, 33.5, 32.6, 29.5, 28.8, 28.1. GCMS (EI) calculated for $[M]^+$ 254.37, found 254.40. FTIR (neat, cm^{-1}): 3012 (w), 2923 (s), 2851 (s), 1710 (m), 1604 (w), 1596 (m), 1508 (m), 1448 (s), 1349 (w), 1147 (s), 1006 (s), 967 (s), 745 (s).



(E)-(5-cyclohexylpent-4-en-1-yl)benzene compound was isolated as a colorless liquid (47% yield). ^{1}H NMR (500 MHz, CDCl3) δ 7.37 – 7.32 (m, 2H), 7.26 – 7.22 (m, 3H), 5.51 – 5.38 (m, 2H), 2.70 – 2.65 (m, 2H), 2.12 – 1.93 (m, 3H), 1.80 – 1.70 (m, 7H), 1.41 – 1.06 (m, 5H). ^{13}C NMR (75 MHz, CDCl3) δ 142.9, 137.2, 128.6, 128.4, 127.3, 125.7, 40.9, 35.5, 33.5, 32.3. 31.5, 26.4, 26.3. GCMS (EI) calculated for $[M]^+$ 228.19, found 228.20. FTIR (neat, cm^{-1}): 3024 9 (m), 2922 (s), 2850 (s), 1604 (w), 1495 (m), 1448 9m), 1029 (w), 967 (s), 891 (w), 744 (m), 697 (s).

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