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General Copper-Catalyzed Coupling of Alkyl-, Aryl-, and Alkynylaluminum Reagents with Organohalides

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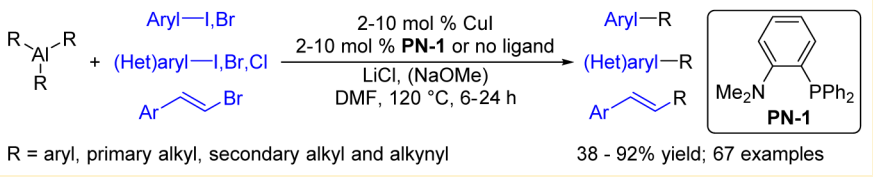
Supporting Information



ABSTRACT: We report the first example of a very general Cu-catalyzed cross-coupling of organoaluminum reagents with organohalides. The reactions proceed for the couplings of alkyl-, aryl-, and alkynylaluminum reagents with aryl and heteroaryl halides and vinyl bromides, affording the cross-coupled products in good to excellent yields. Both primary and secondary alkylaluminum reagents can be utilized as organometallic coupling partners. These reactions are not complicated by β-hydride elimination, and as a result rearranged products are not observed with secondary alkylaluminum reagents even for couplings with heteroaryl halides under "ligand-free" conditions. Radical clock experiment with a radical probe and relative reactivity study of Ph_3Al with two haloarenes, 1-bromonaphthalene and 4-chlorobenzonitrile, having two different redox potentials indicates that the reaction does not involve free aryl radicals and radical anions as intermediates. These results combined with the result of the Hammett plot obtained by reacting Ph_3Al with iodoarenes containing *p*-H, *p*-Me, *p*-F, and *p*-CF_3 substituents, which shows a linear curve (R^2 = 0.99) with a ρ value of +1.06, suggest that the current transformation follows an oxidative addition−reductive elimination pathway.

INTRODUCTION

Cross-couplings remain one of the most versatile transformations for carbon−carbon (C−C) bond formation in organic synthesis.[1] The versatility of these reactions, generally catalyzed by Pd and Ni, stems from their excellent ability to exploit a wide range of organometallic reagents, including those of Mg, Zr, Zn, Sn, Al, B, Si, and In as sources of nucleophiles. These organometallic reagents undergo facile transmetalation with transition metals such as Pd and Ni, the catalysts of choice for cross-coupling reactions. Interestingly, a majority of these organometallic reagents are also known to transmetalation with Cu-salts with ease under remarkably mild conditions.[2] However, despite their ability to undergo facile transmetalation with Cu-salts to generate organocopper complexes and extensive application of Cu catalysts in C−C bond forming reactions[3] since the discovery of the dimerization of alkynylcopper(I) complexes by Glaser in 1869,[4] the application of Cu-based catalysts for coupling reactions has proven to be formidably challenging. As such, the scope of the Cu-catalyzed cross-coupling reactions remained limited to the highly reactive and less functional group tolerant Grignard reagents[5] in most cases and toxic organotin reagents[6] in some instances. A limited application of benign, stable, and functional group tolerant organometallic reagents was also known but was primarily limited to the couplings of zirconacyclopentadienyl compounds[2e,7] using stoichiometric amounts of Cu-salts and reactive arylboronic acids[8] with catalytic quantities of Cu-salts. Recently, our group reported an efficient cross-coupling of different organoboron reagents using a catalyst derived from the combination of CuI and a PN ligand, 2-(di-*tert*-butylphosphino)-*N*,*N*-dimethylaniline (PN-2).[9] Our PN/CuI catalyst system remained versatile and enabled the cross-couplings of a variety of other organometallic reagents, such as organosilicon,[10] organoindium,[11] organozirconium,[12] and organozinc[13] reagents. Brown and co-workers[14] also showed that similar arylboronate esters could be coupled with aryl iodides using CuCl/Xantphos as a catalyst to generate biaryl products. Alkyl- and arylboron reagents have also been shown to couple with primary alkyl halides and pseudohalides, which proceed via a traditional S_N2 process.[15] Recently, Riant[16] and Takeda[2f,17] also disclosed Cu-catalyzed reactions of aryl and vinylsilicon reagents with alkyl, benzyl, and alkynyl halides.[10c] Despite these tremendous efforts in recent times in showcasing the effectiveness of Cu catalysts for cross-coupling various organometallic reagents with organohalides, a general reaction that encompasses a wide substrate scope is still far from reality. The reported reactions generally proceed efficiently with aryl iodides. In limited cases, electron-deficient aryl bromides and chlorides have separately been shown to react when Grignard,[5e] aryltin,[18] arylindium,[11] and arylboron[8b,19] reagents are utilized as coupling partners.

As our long-term interests in developing Cu-based catalytic systems for cross-coupling, we are constantly exploring the feasibility of using various organometallic reagents as nucleophile

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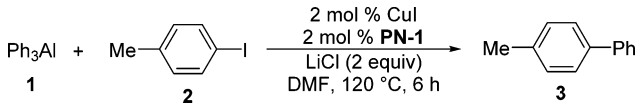
sources that can undergo transmetalation to Cu-salts. Among different metals whose organometallic complexes are known to participate in transmetalation with Cu-salts, Al tenders a distinctive feature owing to its high chemoselectivity and Lewis acidity.[20] In addition, Al also has low toxicity and remains one of the most inexpensive and earth-abundant metals. A recent seminal work by Knochel and co-workers[21] that revealed a convenient reaction protocol for the synthesis of various functionalized organoalanes directly from metallic aluminum further highlights the potential scope of organoaluminum reagents in organic synthesis. However, despite widespread applications of organometallic reagents derived from Si, B, Mg, Zn, and Sn in cross-coupling with Pd and Ni, utility of similar organometallic complexes of Al is limited. Successful reactions are largely restricted to the couplings of arylalanes[21a,b,22] and alkenylalanes,[23] while those of alkylalanes are still limited.[24] In many cases, direct transmetalation of organoalanes to Pd has been found to be slow and shown to require the addition of $ZnCl_2$ or $CdCl_2$ as intermediaries to facilitate reactions through sequential transmetalations.[23c] In some circumstances, intramolecular coordination to Al has been shown to enable cross-coupling of alkylalanes with organohalides.[24a,25] Surprisingly, Knochel,[21c,26] Hoveyda,[27] and others[2i] have shown that organoaluminum reagents undergo a facile transmetalation with Cu-salts as demonstrated by their participation in the allylic and conjugate addition reactions. Encouraged by these literature reports and our recent studies, we anticipated that organoaluminum reagents could potentially be excellent coupling partners for Cu-catalyzed cross-coupling reactions. In this article, we disclose for the first time that organoaluminum reagents are versatile coupling partners for Cu catalysts that enable cross-couplings to proceed with a variety of organohalides such as aryl iodides and electron-deficient aryl and heteroaryl bromides, heteroaryl chlorides, and vinyl bromides in good to excellent product yields. In these reactions, organoaluminum reagents such as aryl-, alkyl-, and alkynylalanes can be utilized as coupling partners.

RESULTS AND DISCUSSION

Our initial investigation began with an attempt to cross-couple commercially available triphenylaluminum reagent with *p*-iodotoluene under our previsously reported conditions using 2 mol % of 2-(diphenylphosphino)-*N*,*N*-dimethylaniline (PN-1)/CuI in DMF at 120 °C. However, the reaction produced the coupled product, 4-phenyltoluene (**3**), only in 45% yield (Table 1, entry 1). Further screening of the reaction conditions using various bases and additives revealed that LiCl had a dramatic effect which enabled the coupling to proceed with the formation of the product **3** in 88% GC yield in 6 h (entry 2). While addition of 3 equiv of LiCl also afforded the product **3** in a comparable yield (entry 3), 2 equiv of LiCl remained optimal for the standard reaction with the commercially available Ph_3Al. Increasing or decreasing the amounts of LiCl to 1 or 4 equiv resulted in lower product yields (entries 4 and 5). The reaction did not proceed at all in the absence of CuI and formed the product **3** only in 26% yield in the absence of PN-1 (entries 6 and 7). The reaction furnished the product **3** in only 17% yield in the absence of both PN-1 and LiCl (entry 8). Decreasing the reaction time to 3 h also diminished the product yield to 73% (entry 9). The reaction can also be performed with [CuO*t*Bu) purified by sublimation, affording the coupled product **3** in 73% yield (entry 10). Replacing CuI with Pd or Ni catalysts, well-established catalysts for cross-coupling, produced the product **3** only in low yields

Table 1. Optimization of Reaction Conditions[a]



entry	modified conditions	yield (%)[b]
1	without LiCl	45
2	none	88 (82)
3	3 equiv LiCl	82
4	1 equiv LiCl	60
5	4 equiv LiCl	39
6	without CuI	0
7	without PN-1	26
8	without LiCl and PN-1	17
9	3 h	73
10	[CuO*t*Bu] (sublimed) instead of CuI	73
11	1 mol % $Pd(OAc)_2$ instead of CuI	33
12	1 mol % $Pd(dba)_2$ instead of CuI	9
13	1 mol % $NiBr_2$ instead of CuI	24
14	1 mol % $(Ph_3P)_4Ni$ instead of CuI	18
15	1 mol % $(Ph_3P)_3CoCl$ instead of CuI	11
16	1 mol % $Fe(OAc)_2$ instead of CuI	0

[a]Reactions were run 0.1 mmol scale in 0.5 mL DMF. One equiv of **1** was used with respect to **2**. [b]Calibrated GC yields (average of at least two parallel runs). Value in parentheses is the isolated yield (1.0 mmol).

(entries 11−14), suggesting that the current reaction is unlikely to be catalyzed by low levels of Pd and Ni contaminants. Use of Co- and Fe catalysts instead of CuI furnished the product **3** in 11% and 0% yields, respectively (entries 15 and 16).

Next, we examined the effects of various types of ligands that are either analogous to PN-1 or are well-known for Cu-based catalytic reactions. Various types of ligands used in the reaction are shown in Scheme 1 and the corresponding yields of the product **3** are presented in the bar diagram in Figure 1. Replacing Ph_2P group in PN-1 with $(t\text{Bu})_2P$ group (PN-2) decreased the product yield significantly (56%). Use of PN-3 and PN-4 in which the dimethylamino goup of PN-1 was replaced by piperidinyl (PN-3) and morpholinyl (PN-4) groups afforded significantly low product yields (54% and 72%, respectively). Changing the dimethylamino group of PN-1 to pyridinyl (PN-5 and PN-6) and carbazolyl (PN-7) groups also furnished the product **3** only in 30%, 36% and 21% yields, respectively. Use of rotationally flexible ligand PN-8 also afforded the product **3** in 35% yield. Diphenylphosphorus amide ligand PN-9 provided the product **3** in a reasonable yield (65%). Bidentate phosphine-based ligands such as bis(diphenylphosphino)benzene (PP-1) afforded the product **3** in lower yield (29%) than the reaction without a ligand (45%). Phenanthroline (NN-1) and bidentate amine-based ligands (NN-2, NN-3, and NN-4) that are known to generate excellent Cu catalysts for arylation of amines and phenols[28] also affected the reaction adversely and decreased the product yields to 32%, 23%, 35%, and 28%, respectively. Similarly, anionic ligands such as 8-hydroxyquinoline (NO-1) and 2,2,6,6-tetramethyl-3,5-heptanedione (OO-1), which are also excellent ligands for C−N and C−O bond formation,[28] afforded lower product yields (27% and 26%, respectively) than without a ligand. N-heterocyclic carbene (NHC) ligands, such as 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (SIMes·HCl), also decreased the product yield (25%).

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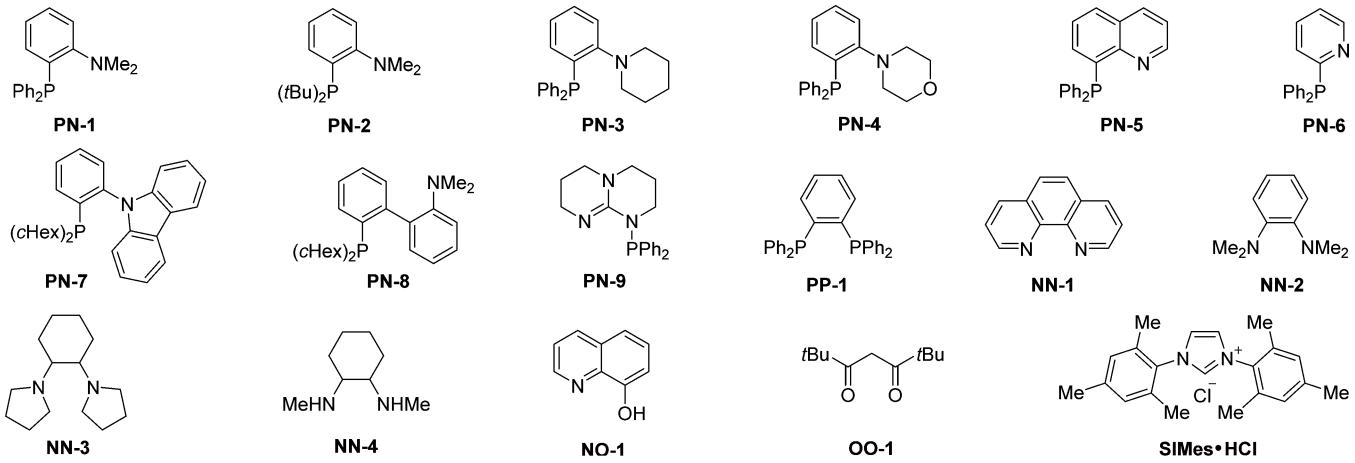
Scheme 1. Ligands Used for Reaction Optimization



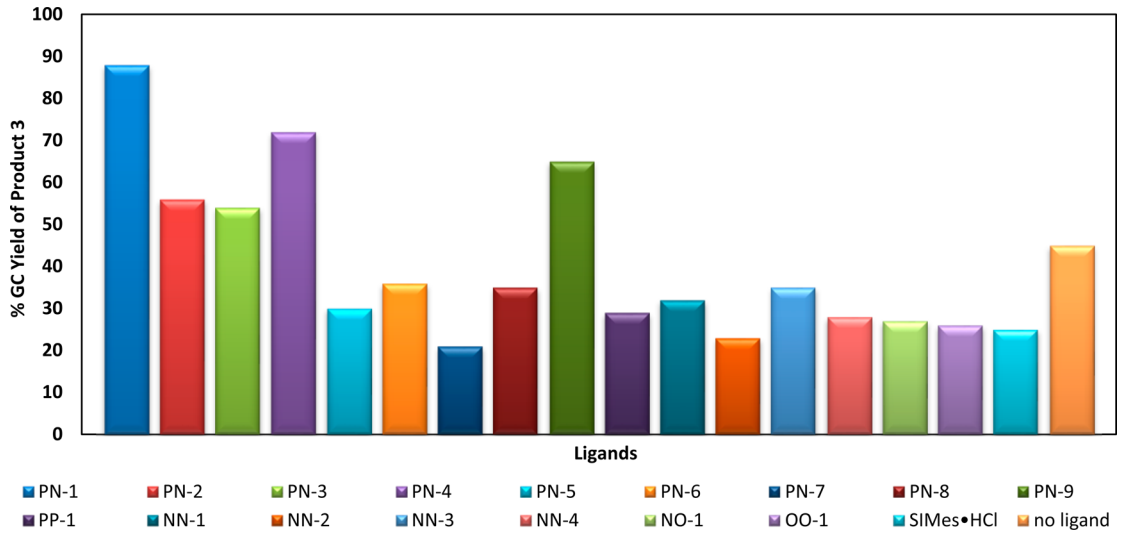


Figure 1. Bar diagram showing the percentage yields of 4-phenyltoluene (**3**) from the reaction of triphenylaluminum reagent with 4-iodotoluene in the presence of various types of ligands instead of PN-1 under the standard reaction conditions from Table 1, entry 2. Yields are GC yields (average of at least two parallel runs) of the product **3** calibrated against 2-nitrobiphenyl as an external standard.

After establishing the combination of PN-1 and CuI as the best catalyst, we began to explore the substrate scope of the reaction. The reaction proceeds with electron-neutral and electron-rich triarylaluminum reagents (Table 2). The reactions of these triarylaluminum reagents proceed with both electron-poor and electron-rich aryl iodides and afford corresponding biaryl products in good yields. The reaction tolerates sensitive functional groups such as nitrile, thiomethoxy, and TBS-protected alcohol (entries 4−6) and sterically hindered substituents like the isopropyl group at the ortho-position of iodoarenes (entry 7).

Biaryl molecules containing heteroarenes widely occur in natural products, pharmaceuticals, drug candidates, and bioactive molecules.[29] These heteroarenes are previliged structures, which play vital roles in biological functions.[30] We are pleased to report that our current reaction conditions can be applied to the arylation of heteroaryl iodides for the synthesis of a variety of heterobiaryl compounds (Table 3). These reactions afford heterobiaryl molecules in best yields without the addition of the PN-1 ligand. Reactions with heteroaryl iodides under the standard conditions that contain PN-1 ligand afford the cross-coupled products in lower yields. Reactions can be performed with nitrogen-containing heteroaryl iodides such as 2-iodopyridine, 2-chloro-4-iodopyridine, 6-iodoquinoline, 7-chloro-4-iodiquinoline, 1-iodoisoquinoline, and 2-iodopyrazine, and the corresponding heterobiaryl compounds are obtained in good to excellent yields. This reactivity pattern of Cu^{I} catalysts is in constrast to the reactivity of established metals Pd and Ni for cross-coupling with heteroaryl halides. Generally, the known Pd- and Ni-catalyzed cross-coupling reactions are less tolerant of heteroarenes because the heteroaryl substrates compete with ligands to bind with these transition metals. Consequently, the Pd and Ni catalysts are deactivated eventually leading to the termination of the cross-coupling reactions.[31] Therefore, Pd- and Ni-based catalytic systems for coupling with heteroaryl halides generally require sterically hindered, bulky phosphine- or carbene-based ligands[32] in order to suppress multiple ligations of heteroaryl substrates to prevent the untoward deactivation pathway. In this respect, Cu^{I}-based catalysts, which are d^{10} congeners of Pd^{0} and Ni^{0}, display a unique property in the current cross-coupling reactions with heteroaryl substrates. This unique reactivity pattern is very general and was observed previously by our group in the cross-couplings of arylboron,[9] arylsilicon,[10a,b] organoindium,[11] arylzirconium,[12] and organozinc

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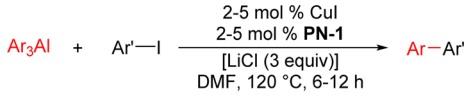
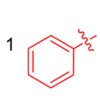
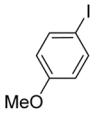
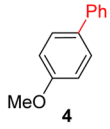
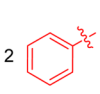
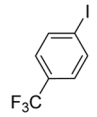
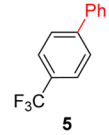
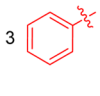
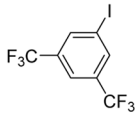
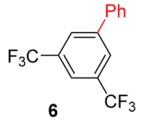
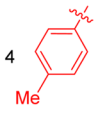
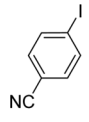
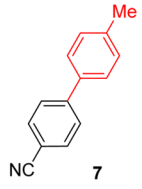
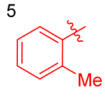
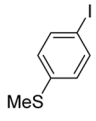
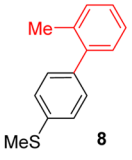
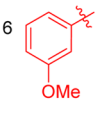
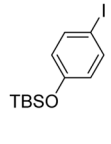
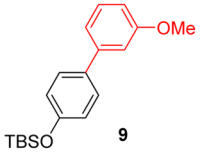
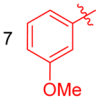
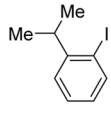
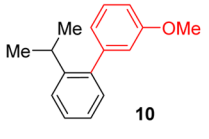
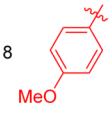
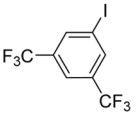
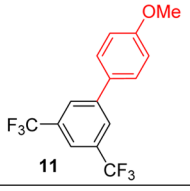
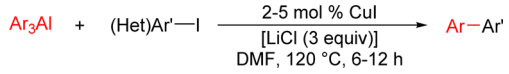
Table 2. Coupling of Triarylaluminum Reagents with Aryl Iodides[a]

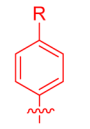
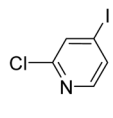
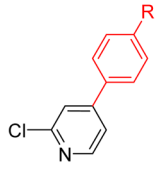
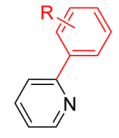
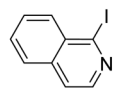
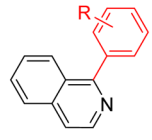
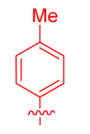
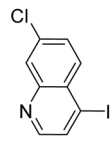
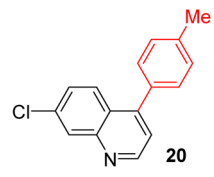


entry	Ar in Ar_3Al	Ar'—I	Ar—Ar'	yield (%)[b]
1			 **4**	87[c]
2			 **5**	83[d]
3			 **6**	54[d]
4			 **7**	70[d]
5			 **8**	62[c]
6			 **9**	40[d]
7			 **10**	38[c]
8			 **11**	49[c]

[a]Reactions were run in 1.0 mmol scale in 5 mL DMF. One equiv of Ar_3Al was used with respect to ArI. Reactions for entries 1, 4, 6, and 8 were run for 12 h. Reactions for entries 2, 3, 5, and 7 were run for 6 h. Each reaction contains 3 equiv of LiCl, written in parentheses below the reaction arrow, which is generated during the preparation of triarylaluminum reagents. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction. [c]5 mol % CuI/PN-1 was used. [d]2 mol % CuI/PN-1 was used.

Table 3. Coupling of Triarylaluminum Reagents with Heteroaryl Iodides[a]



entry	Ar in Ar_3Al	(Het)Ar'—I	Ar—Ar'	yield (%)[b]
1 2			 **12**, R = H **13**, R = Me	46[c] 55[d]
3 4 5			 **14**, R = H **15**, R = *m*-Me **16**, R = *p*-Me	73[c] 65[d] 71[d]
6 7 8			 **17**, R = H **18**, R = *m*-Me **19**, R = *m*-OMe	91[c] 82[d] 71[d]
9			 **20**	92[c]
10			**21**	41[c]
11			**22**	68[d]

[a]Reactions were run in 1.0 mmol scale in 5 mL DMF. One equiv of Ar_3Al was used with respect to ArI. Reactions for entries 1, 3, 6, 9, and 10 were run for 6 h. Reactions for entries 2, 4, 5, 7, 8, and 11 were run for 12 h. Each reaction contains 3 equiv of LiCl, written in parentheses below the reaction arrow, which is generated during the preparation of triarylaluminum reagents. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction. [c]2 mol % CuI was used. [d]5 mol % CuI was used.

reagents[13a] with heteroaryl halides. In addition, Hintermann and co-workers[5e] have previously demonstrated that Grignard reagents could be coupled with heteroaryl chlorides under "ligand-free" conditions using CuI as a catalyst. Nitrogen-based molecules are known to be excellent ligands in many Cu-catalyzed arylation of amines, amides, and phenols.[28] Catalytically competent discrete Cu^I complexes that contain nitrogen-based ligands have also been synthesized and fully characterized structurally.[33] Therefore, we believe that the N-based heteroaryl substrates and products function as ligands in our current reaction.

We also found that our current reaction conditions enable the cross-coupling of electron-deficient aryl and heteroaryl bromides and afford products in good to excellent yields when 10 mol %

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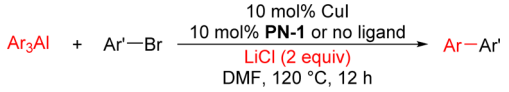
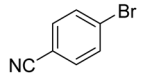
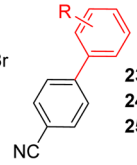
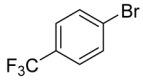
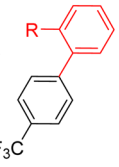
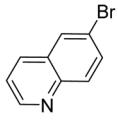
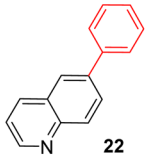
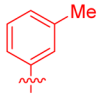
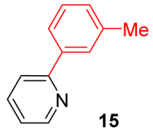
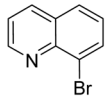
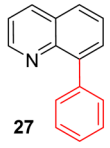
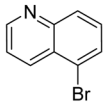
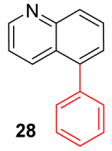
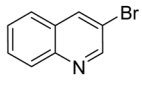
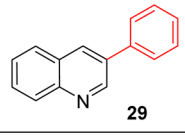
CuI or CuI/PN-1 was used as a catalyst (Table 4). However, in situ generated triarylaluminum reagents usually gave lower product yields than purified triarylalumimun reagents. As such, pure triarylaluminum reagents were used for all the reactions with aryl bromides, which gave the best product yields. The triarylaluminum reagents were prepared and purified according to the literature procedure.[34] Consistent with the reactivity with aryl iodides, the reaction of aryl bromides requires PN-1 ligand. The reaction proceeds well with electron-deficient aryl bromides such as 4-bromobenzonitrile and 4-bromobenzotrifluoride, affording the cross-coupled products in 62−90% yields (entries 1−5). The reaction also proceeds with a variety of nitrogen-based heteroaryl bromides and affords the heterobiaryl products in good yields in the absence of the PN-1 ligand (entries 6−10). Heteroaryl bromides such as 2-bromopyridine, 3-bromoquinoline, 5-bromoquinoline, 6-bromoquinoline and 8-bromoquinoline are good substrates for the current reaction.

Cu-catalyzed cross-coupling that involves aryl chlorides as coupling partners is formidably challenging and therefore is rare. Hintermann and co-workers have previously utilized CuI as a catalyst to couple Grignard reagents with various nitrogen-based heterocyclic chlorides.[5e] It has also been reported that Cu-nanoparticles can catalyze the coupling of arylboronic acids with aryl chlorides.[8b] However, the reaction requires the addition of molecular iodine, which is proposed to convert aryl chlorides to aryl iodides in situ as reactive species via an iodide-chloride (I/Cl) exchange (aromatic Finkelstein reaction).[35] Therefore, this reaction only represents a "formal" reaction with aryl chorides. Pleasingly, our current reaction condition can also be applied for cross-couplings with heteroaryl chlorides (Table 5). The reaction provides products in good to excellent yields for the cross-couplings of arylaluminum reagents with nitrogen-based heteroaryl chlorides such as 2-chlorobenzothiazole, 2-chloroquinoxaline, and 4-chloro-2-phenylquinazoline.

Cu-catalyzed cross-couplings of alkylorganometallic reagents with organohalides are also rare. Alkylmagnesium halides,[5] α-heteroatom-substituted alkyltributylstannanes,[6c,d] and β-alkyl-9-

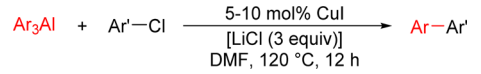
Table 4. Coupling of Triarylaluminum Reagents with Electron-Deficient Aryl and Heteroaryl Bromides[a]

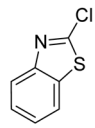
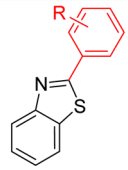
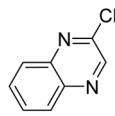
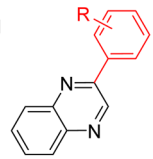
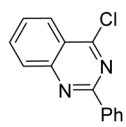
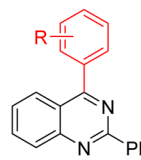


entry	Ar in Ar_3Al	Ar'—Br	Ar—Ar'	yield (%)[b]
1				**23**, R = H 90
2				**24**, R = *o*-Me 66
3				**25**, R = *m*-Me 69
4				**5**, R = H 75
5				**26**, R = Me 62
6			 **22**	59
7			 **15**	65
8			 **27**	79
9			 **28**	61
10			 **29**	73

[a]Reactions were run 1.0 mmol scale in 5 mL DMF. One equiv of Ar_3Al was used with respect to ArBr. Reactions for entries 1−5 require 10 mol % PN-1 ligand. No ligand was added to the reactions for entries 6−10. Since pure triarylaluminum reagents were used, 2 equiv of LiCl was added to the reactions. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction.

Table 5. Coupling of Triarylaluminum Reagents with Heteroaryl Chlorides[a]



entry	Ar in Ar_3Al	Ar'—Cl	Ar—Ar'	yield (%)[b]
1				**30**, R = *o*-Me 65[c]
2				**31**, R = *m*-Me 89[d]
3				**32**, R = *p*-Me 63[d]
4				**33**, R = H 75[c]
5				**34**, R = *p*-Me 66[d]
6				**35**, R = H 91[c]
7				**36**, R = *o*-Me 59[c]
8				**37**, R = *p*-Me 80[d]
9				**38**, R = *m*-Me 73[d]

[a]Reactions were run in 1.0 mmol scale in 5 mL DMF. One equiv of Ar_3Al was used with respect to ArCl. Each reaction contains 3 equiv of LiCl, written in parentheses below the reaction arrow, which is generated during the preparation of triarylaluminum reagents. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction. [c]5 mol % CuI was used. [d]10 mol % CuI was used.

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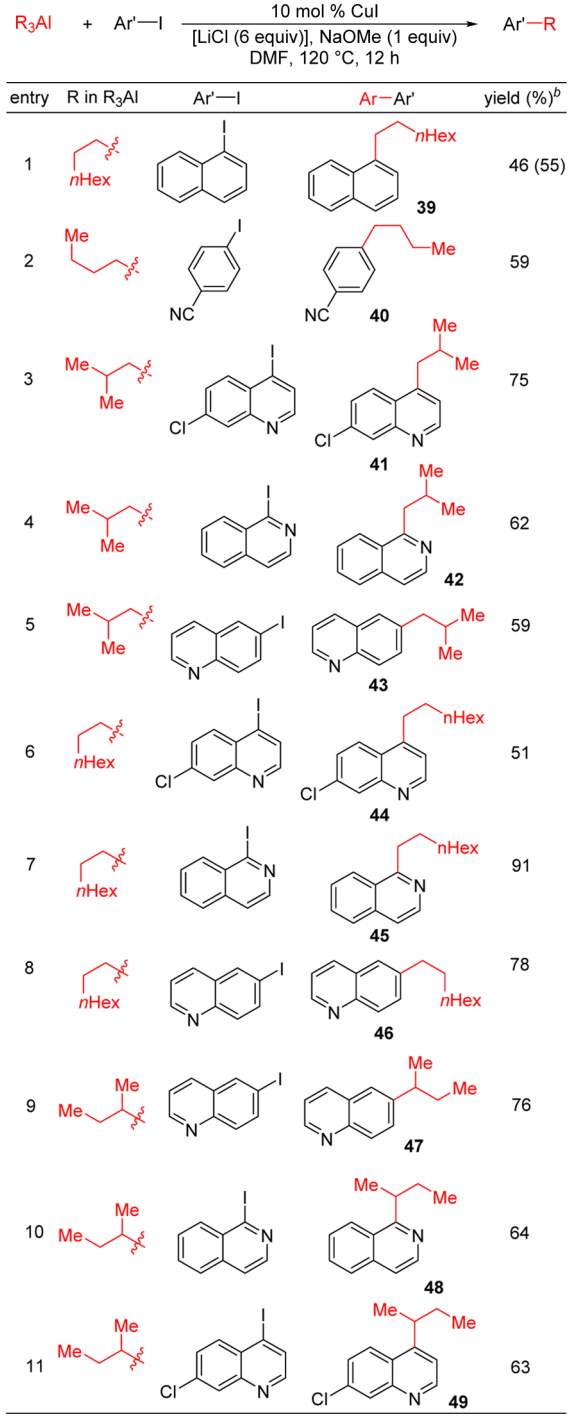
borabicyclo[3.3.1]nonane (β-alkyl-9-BBN)[15] have previously been shown to react with alkyl halides and aryl halides in limited cases. We have recently shown that Cu catalysts can also cross-couple alkylindium[11] and alkylzinc[13a] reagents with aryl halides. We are now pleased to find that our current reaction conditions are also amenable for the coupling of trialkylaluminum reagents with aryl and heteroaryl halides when 10 mol % CuI or CuI/PN-1 was used a catalyst (Table 6). Under the reaction conditions optimized for the coupling of triarylaluminum reagents, commercially available trioctylaluminum reacted with 1-iodonaphthalene to afford the alkylated product **39** in 30% GC yield (entry 1). Further optimization of the reaction conditions in the presence of various bases (see the Supporting Information for details) indicated that the alkylated product was formed in the best yield (55% GC yield; 46% isolated) when NaOMe was used as a base in combination with 6 equiv of LiCl. Under this newly optimized conditions, reactions of trialkylaluminum reagents proceed with electron-neutral and electron-deficient aryl iodides such as 1-iodonaphthalene and 4-iodobenzonitrile, affording the products in good yields (entries 1 and 2). The reactions also proceed in good yields with heteroaryl iodides such as 6-iodoquinoline, 7-chloro-4-iodoquinoline and 1-iodoisoquinoline (entries 3–11). Both primary and secondary alkylaluminum reagents are good substrates for the current reactions. The new conditions can also be used for the couplings of primary alkylaluminum reagents with heteroaryl chlorides such as 2-chlorobenzothiazole, 1-chloroisoquinoline, and 4-chloro-2-phenylquinazoline, which afford the coupled products in good yields (Table 7). Consistent with the reactivity pattern observed with triarylaluminum reagents, reactions of trialkylaluminum reagents also require PN-1 ligands for coupling with nonheteroaryl iodides and no ligands for coupling with heteroaryl iodides. Despite the absence of exogenous ligands, it is surprising to observe that the coupling reactions of both primary and secondary alkylaluminum reagents are not complicated by β-hydride elimination and that no rearranged product is formed with secondary alkylaluminum reagents. It is noteworthy that coupling of alkylorganometallic reagents with established metals such as Pd and Ni is generally complicated by β-hydride elimination, and rearranged products are usually observed when coupling is performed with secondary alkylorganometallic reagents.[36] Coupling of alkylorganometallic reagents with heteroaryl halides is further challenging due to complications from both β-hydride elimination of alkyl substrates and catalyst deactivation by heteroarenes.[31] As a result, these reactions usually require custom-designed, sterically hindered phosphine- or carbene-based ligands to prevent both β-hydride elimination and catalyst deactivation.[32] Therefore, the current Cu-catalyzed reaction protocols offer a convenient and practical method for the coupling of alkylorganometallic reagents with aryl halides.

Pd-[37] or Cu-catalyzed[38] Sonogashira coupling of alkynes with aryl halides is one of the straightforward methods to synthesize arylalkynes. Alternatively, Cahiez and co-workers have shown that alkynyl halides can also be used as a coupling partner in Cu-catalyzed cross-coupling with aryl halides to afford arylalkynes.[5c] Riant and co-workers recently disclosed a similar reaction for coupling vinyltriethoxysilanes with alkynyl bromides.[16a] CuI, ligated by 8-hydroxyquinoline, has also been used as an active catalyst to facilitate the coupling of arylboronic acids with alkynyl bromides.[8e] Pd-catalyzed cross-couplings of alkynylsilane,[39] alkynylboron,[40] alkynylzinc,[41] and alkynyltin[42] reagents with aryl halides are also powerful methods to synthesize arylalkynes. Similarly, in situ generated alkynylcopper(I) intermediates are

Table 6. Coupling of Trialkylaluminum Reagents with Electron-Deficient Aryl and Heteroaryl Iodides[a]



[a]Reactions were run in 1.0 mmol scale in 5 mL DMF. One equiv of R_3Al was used with respect to ArI. Reactions for entries 1 and 2 require 10 mol % PN-1 ligand. No ligand was added to the reactions for entries 3–11. Six equiv of LiCl was added to the reactions of commercially available tri-*n*-octylbutyl- and tri-isobutylaluminum reagents. Reactions of tri-*n*-butyl- and tri-*sec*-butylaluminum reagents also contain 6 equiv of LiCl, 3 equiv generated during the preparation of trialkylaluminum reagents plus extra 3 equiv added separately. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction. Value in parentheses is the calibrated GC yield.

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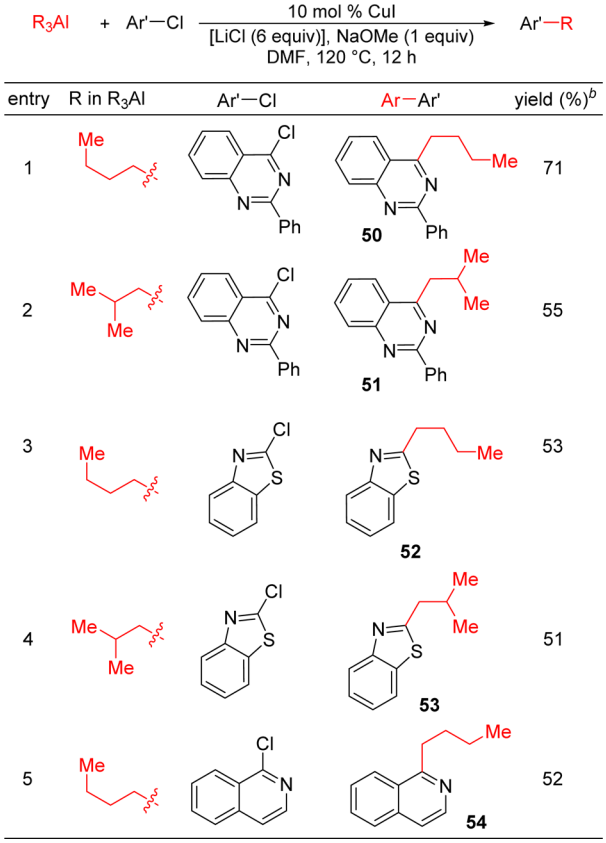
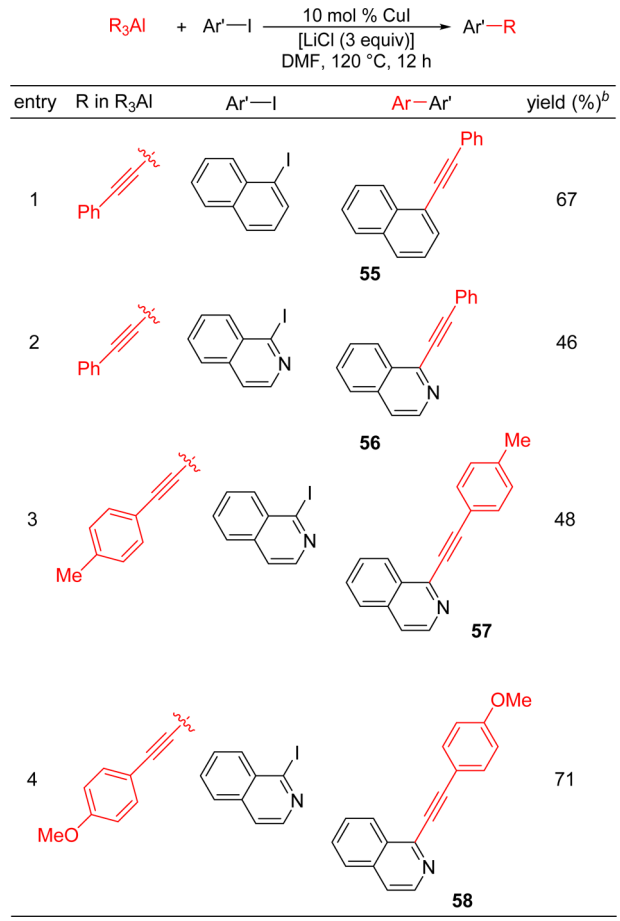
Table 7. Coupling of Trialkylaluminum Reagents with Heteroaryl Chlorides[a]



[a]Reactions were run in 1.0 mmol scale in 5 mL DMF. One equiv of R_3Al was used with respect to ArCl. Six equiv of LiCl was added to the reactions of commercially available tri-isobutylaluminum reagent. Reaction of tri-*n*-butylaluminum reagent also contain 6 equiv of LiCl, 3 equiv generated during the preparation of tri-*n*-butylaluminum reagent plus extra 3 equiv added separately. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction.

Table 8. Coupling of Trialkynylaluminum Reagents with Aryl and Heteroaryl Iodides[a]



[a]Reactions were run in 1.0 mmol scale in 5 mL DMF. One equiv of R_3Al was used with respect to ArI. Reaction for entry 1 requires 10 mol % PN-1 ligand. No ligand was added to the reactions for entries 2–4. Each reaction contains 3 equiv of LiCl, written in parentheses below the reaction arrow, which is generated during the preparation of trialkynylaluminum reagents. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction.

also used as coupling partners in Pd-catalyzed Sonogashira couplings co-catalyzed by Cu-salts.[37] A few examples of Ni-catalyzed cross-couplings of alkynylalanes with benzylic and aryl halides have also been reported.[43] Nishihara demonstrated that alkynylboron[44] and alkynylsilane[45] reagents could be coupled with aryl iodides using a CuI/Ph_3P catalyst. We have recently shown that alkynylcopper(I) species could also be generated in situ from the transmetalation of alkynylzinc halides with CuI that directly react with aryl iodides to form cross-coupled products.[13a] We now demonstrate here that trialkynylaluminum reagents are also viable nucleophiles that undergo transmetalation with CuI and subsequently react with aryl iodides to offer arylalkynes as cross-coupled products (Table 8). In these reactions, neutral and electron-rich triarylaluminum reagents, such as triphenylaluminum, tri-*p*-tolylaluminum and tri-*p*-anisolylaluminum, can be utilized as coupling partners to react with aryl iodides such as iodonaphthalene and 1-iodoisoquinoline, which afford cross-coupled products in good yields.

While a number of reports on Cu-catalyzed cross-couplings have focused on the couplings of aryl halides, application of vinyl halides as electrophiles is limited. A few examples of couplings of organotin reagents with vinyl halides are known in the literature that are performed with stoichiometric or catalytic amounts of Cu-salts.[6a−c] Li and co-workers utilized a combination of CuI and 1,4-diazabicyclo[2.2.2]-octane as a catalyst for coupling arylboronic acids with vinyl iodides and bromides.[8c] Despite these devopments, Cu-catalyzed cross-coupling of simple alkylorganometallic reagents with vinyl halides is not known. We are pleased to report that our current reaction conditions also allow the coupling of both aryl- and alkylaluminum reagents with vinyl halides and afford the products in good yields (Table 9).[46] The reactions proceed well for the couplings of triphenylaluminum, tri-*o*-tolylaluminum, tri-*m*-tolylaluminum and tri-*p*-tolylaluminum reagents with *trans*-β-bromostyrene and *trans*-4-methyl-β-bromostyrene (entries 1−5). Similarly, the reactions also work well for the couplings of tri-*n*-butylaluminum and tri-isobutylaluminum reagents with *trans*-β-bromostyrene and *trans*-4-methyl-β-bromostyrene (entries 6−8).

We also propose a catalytic cycle for the current reaction (Scheme 2) based on literature reports and our recent work on Cu-catalyzed cross-couplings.[9−11] Optimization of reaction conditions showed that both PN-1 and LiCl are critical for the Cu-catalyzed cross-coupling of organoaluminum reagents with organohalides (Table 1, entries 2 and 8). As such, we reason that

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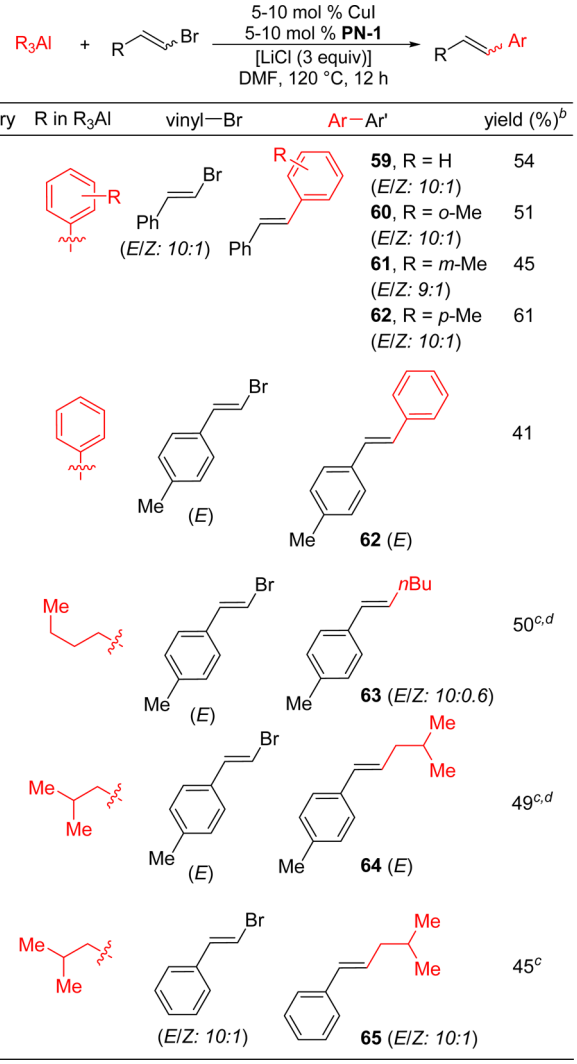
Table 9. Coupling of Triaryl- and Trialkylaluminum Reagents with Vinyl Bromides[a]

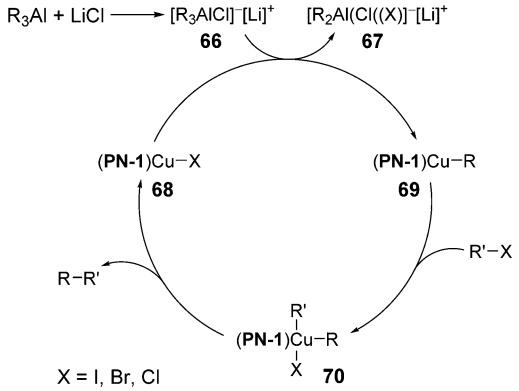


entry	R in R_3Al	vinyl—Br	Ar—Ar'	yield (%)[b]
1			**59**, R = H (*E/Z: 10:1*)	54
2		(*E/Z: 10:1*)	**60**, R = *o*-Me (*E/Z: 10:1*)	51
3			**61**, R = *m*-Me (*E/Z: 9:1*)	45
4			**62**, R = *p*-Me (*E/Z: 10:1*)	61
5		(*E*)	**62** (*E*)	41
6		(*E*)	**63** (*E/Z: 10:0.6*)	50[c,d]
7		(*E*)	**64** (*E*)	49[c,d]
8		(*E/Z: 10:1*)	**65** (*E/Z: 10:1*)	45[c]

[a]Reactions were run in 1.0 mmol scale in 5 mL DMF. One equiv of R_3Al was used with respect to vinyl bromides. Five mol % CuI/PN-1 was used for the reactions of arylaluminum reagents (entries 1–5). Ten mol % CuI/PN-1 was used for the reactions of alkylaluminum reagents (entries 6–8). Three equiv of LiCl was added to the reactions of commercially available tri-isobutylaluminum reagent. Reaction of tri-*n*-butyl- and triarylaluminum reagents contain 3 equiv of LiCl, which is generated during the preparation of tri-*n*-butyl- and triarylaluminum reagents. *E*/*Z* ratios of the products were determined by ^{1}H NMR. [b]Yields are for analytically pure products isolated by column chromatography from a 1.0 mmol scale reaction. [c]Reactions require 1 equiv of NaOMe. [d]Reactions were run for 24 h.

organoaluminate complexes such as **66**, generated from the complexation of LiCl with three-coordinate organoaluminum reagents, could be the active species in solution that transmetalate with the PN-bound CuX (X = I, Br or Cl) to generate (PN)CuR complexes as the orgnaocopper(I) intermediates. Triorganoaluminum complexes have previously been shown to form triorganoaluminate species in the presence of anions in solution due to their Lewis acidity, and a few of such complexes have been previously synthesized and fully characterized.[34,47] In addition, organoaluminum reagents have been shown to participate in allylic and conjugate addition reactions,[2i,21c,26,27] suggesting that they are capable of transmetalating to Cu-salts.

Scheme 2. Proposed Catalytic Cycle



The (PN)CuR intermediates then react with organohalides to afford the cross-coupled products. We have recently synthesized and fully characterized (PN)CuPh as a three-coordinate complex, which readily reacts with ArI at 120 °C in DMF to afford biaryl products.[9] A number of other "ligandless"[48] and ligated [CuAr] species[33e] have also been shown to react with aryl halides to afford biaryl products. Reactions of Cu^I species, either generated in situ during reactions or as discrete isolated complexes, with aryl halides have been a subject of debate for years. These reactions are generally considered to proceed via either radical or nonradical processes.[49] We have recently demonstrated in our previous work that Cu-catalyzed cross-couplings do not involve aryl free radicals based on reactions of aryl halides with organometallic reagents in the presence of radical scavengers under catalytic reaction conditions as well as with discrete, fully characterized organocopper(I) complexes, and radical clock experiments.[10,12] We believe that a similar mechanism could be operating in the current Cu-catalyzed cross-coupling of organoaluminum reagents with organohalides.

We have conducted further experiments to understand the mechanism of the current reaction. In order to probe the possibility of the presence of free aryl radicals in the reaction generated via a single electron transfer (SET) to aryl halides, we have utilized a radical clock experiment. The radical probe **71** is known to undergo cyclization in DMF at 50 °C with a rate constant of 5.0×10^8 s^{-1} when the corresponding aryl radical **73** is generated to form the cyclic product **75** after proton abstraction by the primary alkyl radical **74**.[50] Similar radical probes have also been shown previously to undergo tandem radical cyclization coupling in Cu-catalyzed coupling reactions under conditions that are amenable to the formation of aryl radicals via SET.[51] Cu-catalyzed coupling reactions that do not involve aryl radicals have been shown to afford direct coupling products without cyclization when similar radical probes are utilized as substrates for radical clock experiments.[33b,c] Under our current reaction conditions, cross-coupling of Ph_3Al with the radical probe **71** afforded the direct cross-coupling product **72** in 50% GC yield (Scheme 3). The cyclized product **75** and the tandem cylization-coupling product **76** were not formed, suggesting that the current reaction is unlikely to proceed via the generation of free aryl radicals.

In order to provide further evidence for or against SET in the current Cu-catalyzed cross-coupling reaction, we studied the relative rates of reactions of 1-bromonaphthalene and 4-chlorobenzonitrile with Ph_3Al in a competition experiment. 4-Chlorobenzonitrile has a lower reduction potential (−2.03 V vs SCE in DMF) than 1-bromonaphthalene (−2.17 V vs SCE in

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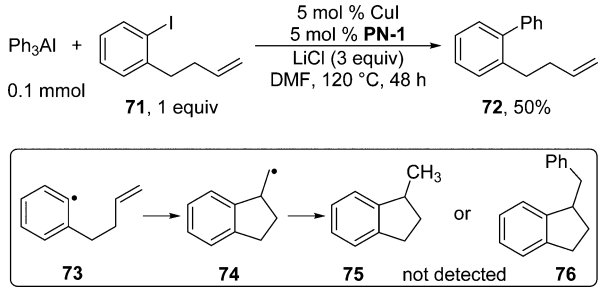
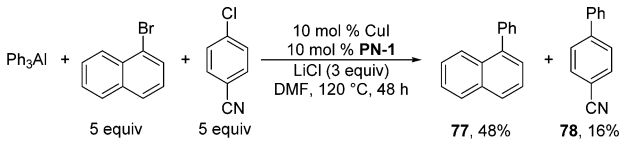
Scheme 3. Radical Clock Experiment



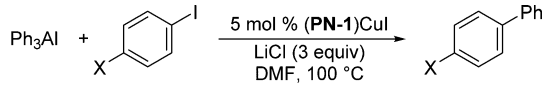
DMF)[52] and, therefore, should be easier to reduce by SET to generate a radical anion that eventually leads to the formation of an aryl radical after the dissociation of the halide anion. Despite having a more favorable environment for the reduction of 4-chlorobenzonitrile by SET, 1-bromonapthalene reacted much faster with Ph_3Al, affording the respective cross-coupling products **77** and **78** in 48% and 16% GC yields (3:1 ratio) (Scheme 4). This experimental result is consistent with a previous Cu-catalyzed coupling in which the reaction was shown to proceed via an oxidative addition−reductive elimination pathway,[33b,c] and in sharp constrast to another similar coupling reaction which was demonstrated to proceed by a SET mechanism.[51] Therefore, we believe that the current Cu-catalyzed cross-coupling of organoaluminum reagents with organohalides does not involve aryl radicals and radical anions as intermediates and likely proceeds via a nonradical mechanism such as oxidative addition−reductive elimination pathway.[53]

Scheme 4. Competition for the Reaction of Ph_3Al with 1-Bromonaphthalene and 4-Chlorobenzonitrile



Finally, we obtained a Hammett relationship for the quantitative assessment of the effect of the electronic properties of substituted iodoarenes on the rate of the reaction with triarylaluminum reagents to form biaryl products. The initial rates of reaction of Ph_3Al with iodobenzene, *p*-iodotoluene, *p*-iodofluorobenzene, and *p*-iodobenzotrifluoride were determined by GC for <30% product formation that showed a linear curve at different time points by quantifying the products using 2-nitrobiphenyl as a calibration standard (Table 10). A plot of log values of the ratio of initial rates of substituted iodoarenes to unsubstituted iodoarene (iodobenzene) versus σ was linear (R^2 = 0.99) with a ρ value of +1.06 (Figure 2).[54] This result is consistent with oxidative addition of aryl halides to electron-rich metal centers in which electron-deficient aryl halides oxidize low-valent to high-valent metals faster than electron-rich aryl halides.[55] Therefore, we believe, based on the result of the linear free-energy relationship and the evidence for the lack of aryl radicals and aryl radical anions, that the Cu-catalyzed cross-coupling reaction of organoaluminum reagents with organohalides proceeds via oxidative addition−reductive elimination pathway as proposed in the catalytic cycle in Scheme 2.

Table 10. Iodoarenes Used for the Hammett Plot and the Values for the Initial Rates of Reactions



iodoarenes	$k_{X(initial)}$ ($M\ s^{-1}$)	$\log[k_{X(initial)}/k_{H(initial)}]$	σ
X = H	1.9×10^{-5}	0.0000	0.00
X = Me	1.3×10^{-5}	−0.1576	−0.17
X = F	2.2×10^{-5}	0.05541	0.06
X = CF_3	7.5×10^{-5}	0.5894	0.54

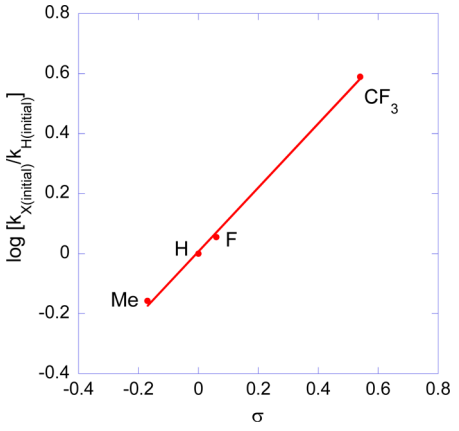


Figure 2. Hammett plot for the reaction of Ph_3Al with 5.0 equiv of iodobenzene, *p*-iodotoluene, *p*-iodofluorobenzene, and *p*-iodobenzotrifluoride. The curve depicts the result of an unweighted least-squares fit to $y = a^*x + b$ (a = +1.06, $b = 7.27 \times 10^{-3}$, R^2 = 0.99).

CONCLUSION

In summary, we have developed the first Cu-catalyzed cross-coupling of organoaluminum reagents with organohalides. Unlike previously reported Cu-catalyzed cross-coupling with other organometallic reagents, couplings with organoaluminum reagents are more general and show a wide substrate scope for both the organoaluminum reagents and organohalides. The reactions can be performed using various organoaluminum reagents, such as alkyl-, aryl-, and alkynylaluminum, and a variety of organohalides like aryl and heteroaryl iodides, aryl and heteroaryl bromides, heteroaryl chlorides, and vinyl bromides. Reactions proceed with both the primary and secondary alkylaluminum reagents in good yields. The reactions for alkyl−aryl, aryl−aryl, and aryl−vinyl coupling require the addition of PN-1 ligand to obtain the best yields of the products. However, the couplings with heteroaryl halides do not require a PN-1 ligand even for reactions that cross-couple primary and secondary alkylaluminum reagents with heteroaryl halides. These "ligand-free" cross-couplings are not complicated by the formation of rearranged products that are known to arise usually by rapid β-hydride elimination and olefin reinsertion process with established transition metals such as Pd and Ni. Preliminary mechanistic studies with a radical probe and relative reactivity studies for the reaction of of Ph_3Al with 1-bromonaphthalene and 4-chlorobenzonitrile indicate that the transformation does not involve aryl radicals or aryl radical anions as intermediates. These results combined with the result of the linear free-energy relationship (the Hammett plot) study suggest that the reaction is likely to proceed via an oxidative addition−reductive elimination pathway.

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EXPERIMENTAL SECTION

General Information. Unless stated otherwise, all the reactions and chemicals were handled inside a nitrogen-filled glovebox. Glassware was dried in an oven immediate before their use. All commercial reagents were used as received without further purification. Triphenylaluminum, tri-isobutylaluminum and tri-*n*-octylaluminum were purchased from a commerical source. Triorganoaluminum reagents were prepared from the reaction of 3 equiv of RLi reagents with $AlCl_3$ (99.99% purity) in THF at room temperature and were used without further purification. Pure triarylaluminum reagents other than Ph_3Al were synthesized following the reported procedure.[34] Ligands PN-2, PN-6, PN-7, PN-8, PP-1, NN-1, NN-4, NO-1, OO-1, and SIMes·HCl were purchased from commercial sources. Ligands PN-1, PN-3, PN-4, PN-5, PN-9,[56] NN-2,[57] and NN-3[58] were synthesized following the reported procedures.[59] ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a 300, 75, and 282 MHz, respectively, and internally referenced to the residual solvent signals of $CDCl_3$ for ^1H and ^{13}C NMR at 7.26 and at 77.16 ppm, respectively, and C_6F_6 for ^{19}F NMR at −164.9 ppm.

General Procedure for Cross-Coupling with Triarylaluminum Reagents. To a suspension of $AlCl_3$ (133.3 mg, 1.0 mmol) in THF (2 mL) was added dropwise a solution of aryllithium (3.0 mmol) (generated from the lithiation of aryl iodides with *n*-BuLi in THF) at room temperature. After 45 min, the solvent was removed to obtain a triarylaluminum reagent containing 3 equiv of LiCl, which was then dissolved in DMF (5 mL). Aryl halide (1.0 mmol) and CuI (3.8−19.0 mg, 0.020−0.10 mmol) were then added to the solution of the triarylaluminum reagent. For reactions containing nonheteroaryl halides, PN-1 (6.1−30.5 mg, 0.020−0.10 mmol) was added to the reaction mixture. For reactions containing heteroaryl halides, no ligand was added. The reaction mixture was then tightly capped, taken out of the glovebox, placed in an oil bath preheated to 120 °C, and vigorously stirred. After 6−24 h, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (15 mL) and washed with H_2O (5 mL × 3). The aqueous fraction was extracted back with ethyl acetate (5 mL × 3) and combined with the first ethyl acetate fraction. The combined ethyl acetate fraction was dried over Na_2SO_4, and the solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography using hexanes as an eluting solvent for nonheterocyclic products and 10−20% ethyl acetate/hexanes for heterocyclic products.

General Procedure for Cross-Coupling with Trialkylaluminum Reagents. To a suspension of $AlCl_3$ (133.3 mg, 1.0 mmol) in THF (2 mL) was added dropwise a solution of alkyllithium (3.0 mmol) at room temperature. After 45 min, the solvent was removed to obtain a trialkylaluminum reagent containing 3 equiv of LiCl, which was then dissolved in DMF (5 mL). Aryl halide (1.0 mmol), NaOMe (54.0 mg, 1.0 mmol), CuI (19.0 mg, 0.10 mmol), and LiCl (127.2 mg, 3.0 mmol, except for reactions with vinyl bromides, which do not need additional LiCl) were then added to the solution of the trialkylaluminum reagent. For reactions containing nonheteroaryl halides, PN-1 (30.5 mg, 0.10 mmol) was added to the reaction mixture. For reactions containing heteroaryl halides, no ligand was added. The reaction mixture was then tightly capped, taken out of the glovebox, placed in an oil bath preheated to 120 °C, and vigorously stirred. After 12−24 h, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (15 mL), and washed with H_2O (5 mL × 3). The aqueous fraction was extracted back with ethyl acetate (5 mL × 3) and combined with the first ethyl acetate fraction. The combined ethyl acetate fraction was dried over Na_2SO_4, and the solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography using hexanes as an eluting solvent for nonheterocyclic products and 10−20% ethyl acetate/hexanes for heterocyclic products.

General Procedure for Cross-Coupling with Trialkynylaluminum Reagents. To a suspension of $AlCl_3$ (133.3 mg, 1.0 mmol) in THF (2 mL) was added dropwise a solution of alkynyllithium (3.0 mmol) (generated from the lithiation of arylacetylene with *n*-BuLi in THF) at room temperature. After 45 min, the solvent was removed to obtain a trialkynylaluminum reagent containing 3 equiv of LiCl, which was then dissolved in DMF (5 mL). Aryl halide (1.0 mmol) and CuI (19.0 mg, 0.10 mmol) were then added to the solution of the trialkynylaluminum reagent. For reactions containing nonheteroaryl halides, PN-1 (30.5 mg, 0.10 mmol) was added to the reaction mixture. For reactions containing heteroaryl halides, no ligand was added. The reaction mixture was then tightly capped, taken out of the glovebox, placed in an oil bath preheated to 120 °C, and vigorously stirred. After 12 h, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (15 mL), and washed with H_2O (5 mL × 3). The aqueous fraction was extracted back with ethyl acetate (5 mL × 3) and combined with the first ethyl acetate fraction. The combined ethyl acetate fraction was dried over Na_2SO_4, and the solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography using 5−20% ethyl acetate/hexanes for heterocyclic products.

*4-Phenylanisole (**4**).*[60] The title compound **4** was obtained as a white solid (160 mg, 87% yield) after purification by silica gel column chromatography. Mp 83 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, 3H), 7.04−7.09 (m, 2H), 7.36−7.42 (m, 1H), 7.47−7.54 (m, 2H), 7.60−7.67 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.4, 114.3, 126.8, 126.8, 128.2, 128.8, 133.8, 140.9, 159.3; HRMS (APPI$^+$/TOF) calcd for $C_{13}H_{12}O$ $(M)^+$ 184.0888, found 184.0892.

*4-Trifluoromethyl-1,1′-biphenyl (**5**).*[61] The title compound **5** was obtained as a white solid (184 mg, 83% yield from the reaction of 1-iodo-4-(trifluoromethyl)benzene with triphenylaluminum reagent and 167 mg, 75% yield from the reaction of 1-bromo-4-(trifluoromethyl)-benzene with triphenylaluminum reagent) after purification by silica gel column chromatography. Mp 64 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−3.52 (m, 3H), 7.58−7.63 (m, 2H), 7.70 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 125.6 (q, J_{CF} = 3.8 Hz), 125.9, 127.4, 127.6, 127.8, 128.3, 129.1, 139.9, 144.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ −65.0; HRMS (APPI$^+$/TOF) calcd for $C_{13}H_{19}F_3$ $(M)^+$ 222.0656, found 222.0660.

*3,5-Bis(trifluoromethyl)-1,1′-biphenyl (**6**).*[62] The title compound **6** was obtained as colorless oil (157 mg, 54% yield) after purification by silica gel column chromatography. ^1H NMR (300 MHz, $CDCl_3$) 7.46−7.55 (m, 2H), 7.60−7.64 (m, 2H), 7.87 (s, 1H), 8.01−8.04 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 121.1, 121.8, 125.4, 127.4, 129.0, 129.4, 132.3 (q, J_{CF} = 33.0 Hz), 138.4, 143.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.9; GC-MS (m/z) 290.1.

*4-Tolylbenzonitrile (**7**).*[63] The title compound **7** was obtained as a white solid (135 mg, 70% yield) after purification by silica gel column chromatography. ^1H NMR (300 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.29 (d, J = 8.1 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.65−7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 110.7, 119.2, 127.2, 127.6, 130.0, 132.7, 136.4, 138.9, 145.7; HRMS (APPI$^+$/TOF) calcd for $C_{14}H_{11}N$ $(M)^+$ 193.0891, found 193.0895.

*4-(2-Methylphenyl)thioanisole (**8**).*[64] The title compound **8** was obtained as colorless oil (133 mg, 62% yield) after purification by silica gel column chromatography. ^1H NMR (300 MHz, $CDCl_3$) δ 2.28 (s, 3H), 2.53 (s, 3H), 7.21−7.33 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 20.6, 125.9, 126.4, 127.4, 129.8, 129.9, 130.5, 135.5, 137.0, 138.9, 141.4; HRMS (APPI$^+$/TOF) calcd for $C_{14}H_{14}S$ $(M)^+$ 214.0816, found 214.0818.

*4′-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-methoxy-1,1′-biphenyl (**9**).*[65] The title compound **9** was obtained as yellow oil (126 mg, 40% yield) after purification by silica gel column chromatography. ^1H NMR (300 MHz, $CDCl_3$) δ 0.24 (s, 6H), 1.02 (s, 9H), 3.87 (s, 3H), 6.84−6.93 (m, 3H), 7.09−7.10 (m, 1H), 7.13−7.16 (m, 1H), 7.31−7.36 (m, 1H), 7.44−7.49 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ − 4.2, 18.4, 25.9, 55.4, 112.2, 112.7, 119.5, 120.4, 128.3, 129.8, 134.3, 142.6, 155.6, 160.1; HRMS (APPI$^+$/TOF) calcd for $C_{19}H_{26}O_2Si$ $(M)^+$ 314.1702, found 314.1712.

*2-Isopropyl-3′-methoxy-1,1′-biphenyl (**10**).* The title compound **10** was obtained as colorless oil (86 mg, 38% yield) after purification by silica gel column chromatography. ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (d, J = 6.0 Hz, 6H), 3.04−3.17 (m, 1H), 3.85 (s, 3H), 6.87−6.95 (m, 3H), 7.31−7.43 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.5, 29.5, 55.3, 112.4, 115.1, 121.9, 125.4, 125.7, 127.8, 129.1, 129.9, 141.1, 143.6, 146.5, 159.3; HRMS (APPI$^+$/TOF) calcd for $C_{16}H_{18}O$ $(M)^+$ 226.1358, found 226.1362.

*4′-Methoxy-3,5-bis(trifluoromethyl)-1,1′-biphenyl (**11**).*[66] The title compound **11** was obtained as colorless oil (157 mg, 49% yield) after

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purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (s, 3H), 7.03−7.07 (m, 2H), 7.56−7.60 (m, 2H), 7.82 (s, 1H), 7.99 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.6, 114.8, 120.3 (q, J_{CF} = 3.8 Hz), 125.4, 126.8, 128.5, 130.8, 132.2 (q, J_{CF} = 33.0 Hz), 143.0, 160.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.9; HRMS (APPI$^+$/TOF) calcd for $C_{15}H_{10}F_6O$ $(M)^+$ 320.0636, found 320.0638.

*2-Chloro-4-phenylpyridine (**12**).*[67] The title compound **12** was obtained as a white solid (87 mg, 46% yield) after purification by silica gel column chromatography. Mp 58 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, J = 3.0, 6.0 Hz, 1H), 7.46−7.55 (m, 4H), 7.60−7.63 (m, 2H), 8.43 (dd, J = 3.0, 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 120.6, 122.2, 127.2, 129.4, 129.8, 137.0, 150.1, 151.7, 152.4; HRMS (ESI$^+$/TOF) calcd for $C_{11}H_9ClN$ $(MH)^+$ 190.0424, found 190.0427.

*2-Chloro-4-(4-methylphenyl)pyridine (**13**).*[68] The title compound **13** was obtained as a white solid (112 mg, 55% yield) after purification by silica gel column chromatography. Mp 50 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.29 (d, J = 6.0 Hz, 2H), 7.40 (dd, J = 6.0, 3.0 Hz, 1H), 7.49−7.53 (m, 3H), 8.39 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 120.3, 121.8, 126.9, 130.1, 133.9, 140.1, 150.0, 151.6, 152.3; HRMS (ESI$^+$/TOF) calcd for $C_{12}H_{11}ClN$ $(MH)^+$ 204.0580, found 204.0578.

*2-Phenylpyridine (**14**).*[60] The title compound **14** was obtained as a white solid (114 mg, 73% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−7.24 (m, 1H), 7.39−7.51 (m, 3H), 7.72−7.74 (m, 2H), 7.01 (d, J = 9.0 Hz, 2H), 8.71 (d, J = 4.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 120.6, 122.2, 126.9, 128.8, 129.0, 136.8, 139.5, 149.6, 157.6; HRMS (ESI$^+$/TOF) calcd for $C_{11}H_{10}N$ $(MH)^+$ 156.0813, found 156.0816.

*2-(3-Methylphenyl)-pyridine (**15**).*[69] The title compound **15** was obtained as colorless oil (111 mg, 65% yield from the reaction of 2-iodo pyridine with tris(3-tolyl)aluminum reagent and 111 mg, 65% yield from the reaction of of 2-bromo pyridine with tris(3-tolyl)aluminum reagent) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.20−7.26 (m, 2H), 7.37 (t, J = 6.0 Hz, 1H), 7.71−7.78 (m, 3H), 7.84 (s, 1H), 8.68−8.71 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 120.7, 122.1, 124.1, 127.8, 128.8, 129.8, 136.8, 138.5, 139.5, 149.8, 157.8; HRMS (ESI$^+$/TOF) calcd for $C_{12}H_{12}N$ $(MH)^+$ 170.0970, found 170.0972.

*2-(4-Methylphenyl)pyridine (**16**).*[63] The title compound **16** was obtained as yellow oil (121 mg, 71% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.13−7.21 (m, 1H), 7.26−7.31 (m, 2H), 7.68−7.70 (m, 2H), 7.89−7.94 (m, 2H), 8.67−8.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 120.2, 121.8, 126.8, 129.5, 136.6, 138.9, 138.9, 149.6, 157.4; HRMS (ESI$^+$/TOF) calcd for $C_{12}H_{12}N$ $(MH)^+$ 170.0970, found 170.0971.

*1-Phenylisoquinoline (**17**).*[70] The title compound **17** was obtained as a white solid (188 mg, 91% yield) after purification by silica gel column chromatography. Mp 150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49−7.56 (m, 4H), 7.63−7.73 (m, 4H), 7.87 (d, J = 6.0 Hz, 1H), 8.12 (d, J = 9.0 Hz, 1H), 8.63 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 119.9, 126.8, 127.0, 127.2, 127.6, 128.4, 128.3, 130.0, 130.0, 136.9, 139.7, 142.3, 160.8; HRMS (ESI$^+$/TOF) calcd for $C_{15}H_{12}N$ $(MH)^+$ 206.0970, found 206.0970.

*1-(3-Methylphenyl)isoquinoline (**18**).*[71] The title compound **18** was obtained as colorless oil (180 mg, 82% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 7.31 (d, J = 6.0 Hz, 1H), 7.39−7.55 (m, 4H), 7.62−7.70 (m, 2H), 7.87 (d, J = 9.0 Hz, 1H), 8.13 (d, J = 9.0 Hz, 1H), 8.62 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 119.9, 126.8, 127.0, 127.2, 127.7, 128.2, 129.4, 130.0, 130.6, 136.9, 138.2, 139.6, 142.3, 161.0; HRMS (ESI$^+$/TOF) calcd for $C_{16}H_{14}N$ $(MH)^+$ 220.1126, found 220.1132.

*1-(3-Methoxyphenyl)isoquinoline (**19**).*[71] The title compound **19** was obtained as colorless oil (168 mg, 71% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.04 (dd, J = 9.0, 6.0 Hz, 1H), 7.26−7.28 (m, 2H), 7.40−7.52 (m, 2H), 7.60−7.67 (m, 2H), 7.84 (d, J = 9.0 Hz, 1H), 8.13 (d, J = 9.0 Hz, 1H), 8.60 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.3, 114.6, 115.1, 119.9, 122.4, 126.6, 126.9, 127.1, 127.5, 129.3, 129.9, 136.8, 140.9, 142.1, 159.6, 160.5; HRMS (ESI$^+$/TOF) calcd for $C_{16}H_{14}NO$ $(MH)^+$ 236.1075, found 236.1079.

*7-Chloro-4-(4-methylphenyl)quinoline (**20**).*[10b] The title compound **20** was obtained as a white solid (234 mg, 92% yield) after purification by silica gel column chromatography. Mp 92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.47(s, 3H), 7.30−7.39 (m, 5H), 7.43 (dd, J = 9.0, 3.0 Hz, 1H), 7.89 (d, J = 9.0 Hz, 1H), 8.16 (d, J = 3.0 Hz, 1H), 8.92 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 121.6, 125.5, 127.6, 127.6, 128.8, 12.5, 129.5, 134.7, 135.3, 138.8, 148.8, 149.3, 151.1; HRMS (ESI$^+$/TOF) calcd for $C_{16}H_{13}ClN$ $(MH)^+$ 254.0737, found 254.0740.

*2-Phenylpyrazine (**21**).*[70] The title compound **21** was obtained as a white solid (64 mg, 41% yield) after purification by silica gel column chromatography. Mp 66 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47−7.55 (m, 3H), 8.00−8.04 (m, 2H), 8.52 (d, J = 3.0 Hz, 1H), 8.64 (dd, J = 2.4, 1.8 Hz, 1H), 9.03 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 127.1, 129.2, 130.1, 136.5, 142.4, 143.1, 144.3, 153.0; HRMS (ESI$^+$/TOF) calcd for $C_{10}H_9N_2$ $(MH)^+$ 157.0766, found 157.0769.

*6-Phenylquinoline (**22**).*[72] The title compound **22** was obtained as a yellowish white solid (140 mg, 68% yield from the reaction of 6-iodoquinoline with triphenylaluminum reagent and 122 mg, 59% yield from the reaction of of 6-bromoquinoline with triphenylaluminum reagent) after purification by silica gel column chromatography. Mp 106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.52 (m, 4H), 7.69.7.72 (m, 2H), 7.96.7.99 (m, 2H), 8.15−8.20 (m, 2H), 8.92 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.5, 125.5, 127.5, 127.8, 128.5, 129.0, 129.3, 130.0, 136.3, 139.4, 140.4, 147.8, 150.5; HRMS (ESI$^+$/TOF) calcd for $C_{15}H_{12}N$ $(MH)^+$ 206.0970, found 206.0969.

*4-Phenylbenzonitrile (**23**).*[61] The title compound **23** was obtained as a white solid (161 mg, 90% yield) after purification by silica gel column chromatography. Mp 78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.54 (m, 3H), 7.60−7.64 (m, 2H), 7.69−7.77 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 111.1, 119.0, 127.3, 127.8, 128.8, 129.2, 132.7, 139.3, 145.8; HRMS (APPI$^+$/TOF) calcd for $C_{13}H_9N$ $(M)^+$ 179.0735, found 179.0743.

*4-(2-Methylphenyl)benzonitrile (**24**).*[73] The title compound **24** was obtained as a pale yellow solid (128 mg, 66% yield) after purification by silica gel column chromatography. Mp 62 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26 (s, 3H), 7.18−7.32 (m, 4H), 7.43−7.46 (m, 2H), 7.69−7.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 110.9, 119.1, 126.2, 128.4, 129.5, 130.1, 130.8, 132.1, 135.2, 140.1, 146.9; HRMS (ESI$^+$/TOF) calcd for $C_{14}H_{12}N$ $(MH)^+$ 194.0976, found 194.0976.

*4-(3-Methylphenyl)benzonitrile (**25**).*[74] The title compound **25** was obtained as yellow oil (134 mg, 69% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.22−7.26 (m, 1H), 7.34−7.41 (m, 3H), 7.65−7.73 (m, 4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 110.9, 119.1, 124.5, 127.9, 128.1, 129.1, 129.5, 132.7, 138.9, 139.3, 145.9; HRMS (APPI$^+$/TOF) calcd for $C_{14}H_{11}N$ $(M)^+$ 193.0891, found 193.0900.

*4-(2-Methylphenyl)trifluoromethylbenzene (**26**).*[75] The title compound **26** was obtained as yellow oil (146 mg, 62% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.27 (s, 3H), 7.19−7.32 (m, 4H), 7.44 (d, J = 6.0 Hz, 2H), 7.66−7.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 125.2 (q, J_{CF} = 3.8 Hz), 126.1, 127.8, 128.0, 129.6, 130.6, 135.3, 140.6, 145.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ −60.9; GC-MS (m/z) 236.1.

*8-Phenylquinoline (**27**).*[76] The title compound **27** was obtained as colorless oil (163 mg, 79% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.64 (m, 5H), 7.72−7.77 (m, 3H), 7.84 (dd, J = 6.0, 2.1 Hz, 1H), 8.21 (dd, J = 9.0, 3.0 Hz, 1H), 8.98 (dd, J = 6.0, 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.1, 126.4, 127.5, 127.6, 128.1, 128.8, 130.4, 130.7, 136.3, 139.7, 141.1, 146.2, 150.4; HRMS (ESI$^+$/TOF) calcd for $C_{15}H_{12}N$ $(MH)^+$ 206.0970, found 206.0975.

*5-Phenylquinoline (**28**).*[77] The title compound **28** was obtained as yellow oil (126 mg, 61% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (dd, J = 9.0, 3.0 Hz, 1H), 7.44−7.53 (m, 6H), 7.76 (dd, J = 8.4, 6.9 Hz, 1H), 8.12−8.16 (m, 1H), 8.22−8.26 (m, 1H), 8.93 (dd, J = 4.2, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.2, 126.8, 127.4, 127.8, 128.6, 129.0, 129.1,

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130.1, 134.5, 139.5, 140.6, 148.6, 150.4; HRMS (ESI$^+$/TOF) calcd for $C_{15}H_{12}N$ $(MH)^+$ 206.0970, found 206.0970.

*3-Phenylquinoline (**29**).*[67] The title compound **29** was obtained as yellow oil (150 mg, 73% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.60 (m, 4H), 7.69−7.75 (m, 3H), 7.78 (dd, J = 9.0, 3.0 Hz, 1H), 8.15 (d, J = 9.0 Hz, 1H), 8.29 (d, J = 2.1 Hz, 1H), 9.2 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 127.1, 127.5, 127.8, 128.1, 128.2, 128.5, 129.3, 129.4, 129.5, 133.3, 138.0, 147.5, 150.0; HRMS (ESI$^+$/TOF) calcd for $C_{15}H_{12}N$ $(MH)^+$ 206.0970, found 206.0970.

*2-(2-Methylphenyl)benzothiazole (**30**).*[78] The title compound **30** was obtained as a white solid (147 mg, 65% yield) after purification by silica gel column chromatography. Mp 52 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.68 (s, 3H), 7.30−7.55 (m, 5H), 7.78 (d, J = 9.0 Hz, 1H), 7.94 (d, J = 9.0 Hz, 1H), 8.12 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 121.5, 123.5, 125.2, 126.2, 130.1, 130.6, 131.6, 133.2, 135.7, 137.4, 153.9, 168.1; HRMS (ESI$^+$/TOF) calcd for $C_{14}H_{12}NS$ $(MH)^+$ 226.0690, found 226.0696.

*2-(3-Methylphenyl)benzothiazole (**31**).*[78] The title compound **31** was obtained as a yellow solid (201 mg, 89% yield) after purification by silica gel column chromatography. Mp 68 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.30 (d, J = 6.0 Hz, 1H), 7.35−7.40 (m, 2H), 7.47−7.52 (m, 1H), 7.86−7.91 (m, 2H), 7.95−7.97 (m, 1H), 8.08−8.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 121.7, 123.2, 124.4, 125.2, 126.3, 128.1, 128.9, 131.9, 133.6, 135.1, 138.9, 154.2, 168.4; HRMS (ESI$^+$/TOF) calcd for $C_{14}H_{12}NS$ $(MH)^+$ 226.0690, found 226.0689.

*2-(4-Methylphenyl)benzothiazole (**32**).*[78] The title compound **32** was obtained as a white solid (142 mg, 63% yield) after purification by silica gel column chromatography. Mp 78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.30−7.34 (m, 2H), 7.36−7.42 (m, 1H), 7.48−7.54 (m, 1H), 7.89−7.93 (m, 1H), 8.00−8.03 (m, 2H), 8.07−8.11 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 121.7, 123.2, 125.1, 126.4, 127.6, 129.8, 131.1, 135.1, 141.5, 154.3, 168.3; HRMS (ESI$^+$/TOF) calcd for $C_{14}H_{12}NS$ $(MH)^+$ 226.0690, found 226.0692.

*2-Phenylquinoxaline (**33**).*[79] The title compound **33** was obtained as a yellow solid (155 mg, 75% yield) after purification by silica gel column chromatography. Mp 120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.61 (m, 3H), 7.72−7.82 (m, 2H), 8.11−8.23 (m, 4H), 9.34 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 127.7, 128.5, 129.3, 129.6, 130.3, 130.4, 136.9, 136.9, 141.7 142.4, 143.5, 151.9; HRMS (ESI$^+$/TOF) calcd for $C_{14}H_{11}N_2$ $(MH)^+$ 207.0922, found 207.0929.

*2-(4-Methylphenyl)quinoxaline (**34**).*[80] The title compound **34** was obtained as a pale brown solid (146 mg, 66% yield) after purification by silica gel column chromatography. Mp 88 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.35−7.38 (m, 2H), 7.69−7.80 (m, 2H), 8.08−8.16 (m, 4H), 9.31 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 127.5, 129.2, 129.4, 129.7, 130.0, 130.3, 134.1, 140.6, 141.6, 142.5, 143.4, 151.9; HRMS (ESI$^+$/TOF) calcd for $C_{15}H_{13}N_2$ $(MH)^+$ 221.1079, found 221.1079.

*2, 4-Biphenylquinazoline (**35**).*[81] The title compound **35** was obtained as a white solid (258 mg, 91% yield) after purification by silica gel column chromatography. Mp 110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.63 (m, 7H), 7.86−7.93 (m, 3H), 8.11−8.19 (m, 2H), 8.73−8.76 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.8, 127.1, 128.6, 128.8, 129.3, 130.0, 130.3, 130.6, 133.6, 137.8, 138.3, 152.1, 160.3, 166.9, 163.7, 168.4; HRMS (ESI$^+$/TOF) calcd for $C_{20}H_{15}N_2$ $(MH)^+$ 283.1235, found 283.1234.

*4-(2-Methylphenyl)-2-phenylquinazoline (**36**).*[82] The title compound **36** was obtained as a white solid (175 mg, 59% yield) after purification by silica gel column chromatography. Mp 139 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26 (s, 3H), 7.26−7.57 (m, 8H), 7.71 (d, J = 9.0 Hz, 1H), 7.89 (t, J = 6.0 Hz, 1H), 8.19 (d, J = 9.0 Hz, 1H), 8.69−8.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1, 122.8, 125.7, 127.1, 127.2, 128.6, 128.9, 129.2, 129.3, 129.8, 130.6, 130.8, 133.8, 136.6, 137.1, 138.4, 151.6, 160.4, 169.8; HRMS (ESI$^+$/TOF) calcd for $C_{21}H_{17}N_2$ $(MH)^+$ 297.1392, found 297.1398.

*4-(4-Methylphenyl)-2-phenylquinazoline (**37**).*[81] The title compound **37** was obtained as a white solid (238 mg, 80% yield) after purification by silica gel column chromatography. Mp 98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 3H), 7.42 (d, J = 9.0 Hz, 2H), 7.50−7.58 (m, 4H), 7.80−7.91 (m, 3H), 8.14−8.17 (m, 2H), 8.70−8.74 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 121.8, 126.9, 127.2, 128.6, 128.8, 129.3, 129.6, 130.3, 130.6, 133.5, 135.0, 138.4, 140.3, 152.1, 160.3, 168.4; HRMS (ESI$^+$/TOF) calcd for $C_{21}H_{17}N_2$ $(MH)^+$ 297.1392, found 297.1396.

*4-(3-Methylphenyl)-2-phenylquinazoline (**38**).* The title compound **38** was obtained as a yellowish white solid (217 mg, 73% yield) after purification by silica gel column chromatography. Mp 84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.53 (s, 3H), 7.42 (d, J = 9.0 Hz, 1H), 7.47−7.60 (m, 5H), 7.66−7.73 (m, 2H), 7.86−7.91 (m, 1H), 8.12−8.19 (m, 2H), 8.73−8.76 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 121.8, 127.0, 127.2, 127.4, 128.4, 128.6, 128.8, 129.2, 130.6, 130.7, 130.8, 133.6, 137.7, 138.4, 138.4, 152.0, 160.3, 168.7; HRMS (ESI$^+$/TOF) calcd for $C_{21}H_{17}N_2$ $(M)^+$ 297.1392, found 297.1390.

*1-n-Octylnapthalene (**39**).*[64] The title compound **39** was obtained as yellow oil (110 mg, 46% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 6.0 Hz, 3H), 1.19−1.47 (m, 10H), 1.72−1.82 (m, 2H), 3.08 (t, J = 9.0 Hz, 2H), 7.32−7.55 (m, 4H), 7.70−7.73 (m, 1H), 7.85−7.88 (m, 1H), 8.05−8.08 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 22.8, 29.5, 29.7, 29.9, 30.0, 32.1, 33.3, 124.1, 125.5, 125.7, 125.7, 126.0, 126.5, 128.9, 132.1, 134.0, 139.2; HRMS (APPI$^+$/TOF) calcd for $C_{18}H_{24}$ $(M)^+$ 240.1878, found 240.1887.

*4-n-Butylbenzonitrile (**40**).*[83] The title compound **40** was obtained as colorless oil (94 mg, 59% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 6.0 Hz, 3H), 1.31−1.41 (m, 2H), 1.55−1.65 (m, 2H), 2.66 (t, J = 7.5 Hz, 2H), 7.27 (d, J = 7.5 Hz, 2H), 7.55 (d, J = 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 22.2, 33.1, 35.8, 109.5, 119.2, 129.2, 132.1, 148.6; HRMS (APPI$^+$/TOF) calcd for $C_{11}H_{14}N$ $(MH)^+$ 160.1126, found 160.1133.

*7-Chloro-4-isobutylquinoline (**41**).* The title compound **41** was obtained as yellow oil (165 mg, 75% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (d, J = 6.0 Hz, 6H), 1.99−2.08 (m, 1H), 2.88 (d, J = 6.0 Hz, 2H), 7.17 (d, J = 4.5 Hz, 1H), 7.47 (dd, J = 9.0, 3 Hz, 1H), 7.94 (d, J = 9.0 Hz, 1H), 8.09 (d, J = 3.0 Hz, 1H), 8.78 (d, J = 6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 29.6, 41.6, 122.2, 125.4, 126.5, 127.2, 129.2, 134.9, 147.9, 149.1, 151.1; HRMS (ESI$^+$/TOF) calcd for $C_{13}H_{15}ClN$ $(MH)^+$ 220.0893, found 220.0892.

*1-Isobutylisoquinoline (**42**).*[84] The title compound **42** was obtained as colorless oil (115 mg, 62% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (d, J = 6.0 Hz, 6H), 2.22−2.36 (m, 1H), 3.16 (d, J = 6.0 Hz, 2H), 7.49 (d, J = 6.0 Hz, 1H), 7.54−7.67 (m, 2H), 7.80 (d, J = 9.0 Hz, 1H), 8.15 (d, J = 9.0 Hz, 1H), 8.45 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 29.1, 44.3, 119.2, 125.7, 126.9, 127.4, 127.5, 129.8, 136.4, 141.9, 161.7; HRMS (ESI$^+$/TOF) calcd for $C_{13}H_{16}N$ $(MH)^+$ 186.1283, found 186.1287.

*6-Isobutylisoquinoline (**43**).* The title compound **43** was obtained as colorless oil (110 mg, 59% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (d, J = 6.0 Hz, 6H), 1.89−2.09 (m, 1H), 2.65 (d, J = 6.0 Hz, 2H), 7.35 (q, J = 6.0 Hz, 1H), 7.52−7.55 (m, 2H), 8.10−8.00 (m, 2H), 8.85 (dd, J = 4.5, 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5, 30.3, 45.5, 121.1, 127.0, 128.3, 129.2, 131.7, 135.7, 140.3, 147.3, 149.7; HRMS (ESI$^+$/TOF) calcd for $C_{13}H_{16}N$ $(MH)^+$ 186.1283, found 186.1289.

*7-Chloro-4-n-octylquinoline (**44**).*[11] The title compound **44** was obtained as yellow oil (141 mg, 51% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J = 6.3 Hz, 3H), 1.23−1.44 (m, 10H), 1.68−1.78 (m, 2H), 3.02 (t, J = 9.0 Hz, 2H), 7.21 (d, J = 3.0 Hz, 1H), 7.49 (dd, J = 9.0, 2.1 Hz, 1H), 7.96 (d, J = 9.0 Hz, 1H), 8.09 (d, J = 2.4 Hz, 1H), 8.78 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.7, 29.3, 29.5, 29.7, 30.2, 31.9, 32.2, 121.0, 125.2, 126.2, 127.3, 129.2, 134.9, 149.0, 149.1, 151.3; HRMS (ESI$^+$/TOF) calcd for $C_{17}H_{23}ClN$ $(MH)^+$ 276.1519, found 276.1526.

*1-n-Octylisoquinoline (**45**).* The title compound **45** was obtained as yellow oil (220 mg, 91% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J = 6.6 Hz, 3H), 1.25−1.32 (m, 10H), 1.81−1.91 (m, 2H), 3.28 (t, J = 9.0 Hz, 2H), 7.48 (d, J = 6.0 Hz, 1H), 7.61 (m, 2H), 7.78−7.82 (m, 1H), 8.14−8.17 (m, 1H), 8.43 (d, J = 6.0 Hz,1H); ^{13}CNMR(75 MHz,$CDCl_3$) δ 14.2,

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22.8, 29.4, 29.6, 29.9, 30.0, 32.0, 35.7, 119.2, 125.5, 127.0, 127.1, 127.5, 129.8, 136.4, 142.1, 162.6; HRMS (ESI$^+$/TOF) calcd for $C_{17}H_{24}N$ $(MH)^+$ 242.1909, found 242.1915.

*6-n-Octylquinoline (**46**).*[85] The title compound **46** was obtained as yellow oil (189 mg, 78% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J = 6 Hz, 3H), 1.27−1.38 (m, 10H), 1.66−1.75 (m, 2H), 2.79 (t, J = 6.0 Hz, 2H), 7.35 (q, J = 6.0 Hz, 1H), 7.54−7.58 (m, 2H), 8.00−8.09 (m, 2H), 8.85 (dd, J = 6.0, 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.8, 29.4, 29.4, 29.6, 31.4, 32.0, 36.1, 121.1, 126.1, 128.5, 129.3, 131.2, 135.6, 141.5, 147.3, 149.7; HRMS (ESI$^+$/TOF) calcd for $C_{17}H_{24}N$ $(MH)^+$ 242.1909, found 242.1915.

*6-sec-Butylquinoline (**47**).*[86] The title compound **47** was obtained as yellow oil (141 mg, 76% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, J = 7.5 Hz, 3H), 1.32 (d, J = 6.0 Hz, 3H), 1.64−1.72 (m, 2H), 2.76−2.83 (m, 1H), 7.35 (q, J = 4.2 Hz, 1H), 7.56 (s, 1H), 7.60 (d, J = 2.1 Hz, 1H), 8.03−8.11 (m, 2H), 8.85 (dd, J = 6.0, 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.3, 21.9, 31.1, 41.8, 121.1, 125.0, 128.4, 129.5, 129.6, 135.8, 146.1, 147.5, 149.7; HRMS (ESI$^+$/TOF) calcd for $C_{13}H_{16}N$ $(MH)^+$ 186.1283, found 186.1286.

*1-sec-Butylisoquinoline (**48**).*[13a] The title compound **48** was obtained as yellow oil (119 mg, 64% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 7.5 Hz, 3H), 1.41 (d, J = 6.0 Hz, 3H), 1.72−1.81 (m, 1H), 2.08−1.99 (m, 1H), 3.68−3.75 (m, 1H), 7.48 (d, J = 6.0 Hz, 1H), 7.55−7.67 (m, 2H), 7.81 (d, J = 6.0 Hz, 1H), 8.22 (d, J = 6.0 Hz, 1H), 8.50 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5, 20.3, 29.7, 37.9, 118.9, 124.9, 126.9, 127.0, 127.6, 129.6, 136.5, 142.1, 166.0; HRMS (ESI$^+$/TOF) calcd for $C_{13}H_{16}N$ $(MH)^+$ 186.1283, found 186.1286.

*7-Chloro-4-s-butylquinoline (**49**).*[11] The title compound **49** was obtained as colorless oil (167 mg, 63% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J = 6.0 Hz, 3H), 1.35 (d, J = 6.0 Hz, 3H), 1.64−1.86 (m, 2H), 3.39−3.51 (m, 1H), 7.25−7.27 (m, 1H), 7.49 (dd, J = 9.0, 3.0 Hz, 1H), 8.03 (d, J = 9.0 Hz, 1H), 8.11 (d, J = 3.0 Hz, 1H), 8.84 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.2, 20.8, 30.2, 35.3, 118.0, 124.7, 126.0, 127.3, 129.4, 134.8, 149.1, 151.5, 153.9; HRMS (ESI$^+$/TOF) calcd for $C_{13}H_{15}ClN$ $(MH)^+$ 220.0893, found 220.0898.

*4-n-Butyl-2-phenylquinazoline (**50**).*[81] The title compound **50** was obtained as yellow oil (187 mg, 71% yield) after purification by silica gel column chromatography.^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (t, J = 9.0 Hz, 3H), 1.51−1.60 (m, 2H), 1.95−2.05 (m, 2H), 3.34 (t, J = 9.0 Hz, 2H), 7.48−7.60 (m, 4H), 7.82−7.88 (m, 1H), 8.07−8.14 (m, 2H), 8.65 (dd, J = 9.0, 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.9, 30.8, 34.4, 122.6, 124.7, 126.8, 128.6, 129.2, 129.5, 130.4, 133.3, 138.6, 150.8, 160.2, 171.6; HRMS (ESI$^+$/TOF) calcd for $C_{18}H_{19}N_2$ $(MH)^+$ 263.1548, found 263.1550.

*4-(2-Methylpropyl)-2-phenylquinazoline (**51**).* The title compound **51** was obtained as yellow oil (145 mg, 55% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (d, J = 6.0 Hz, 6H), 2.45−2.59 (m, 1H), 3.21 (d, J = 6.0 Hz, 2H), 7.52−7.60 (m, 4H), 7.81−7.86 (m, 1H), 8.11 (d, J = 9.0 Hz, 2H), 8.69−8.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 28.7, 43.3, 123.1, 124.8, 126.7, 128.6, 128.7, 129.5, 130.4, 133.3, 138.6, 150.9, 160.1, 170.8; HRMS (ESI$^+$/TOF) calcd for $C_{18}H_{19}N_2$ $(MH)^+$ 263.1548, found 263.1541.

*2-n-Butylbenzothiazole (**52**).*[87] The title compound **52** was obtained as yellow oil (102 mg, 53% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (t, J = 7.5 Hz, 3H), 1.41−1.53 (m, 2H), 1.81−1.92 (m, 2H), 3.11 (t, 7.5 Hz, 2H), 7.26−7.36 (m, 1H), 7.41−7.47 (m, 1H), 7.81−7.85 (m, 1H), 7.96 (d, J = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.4, 31.9, 34.2, 121.6, 122.6, 124.7, 125.9, 135.3, 153.4, 172.5; HRMS (ESI$^+$/TOF) calcd for $C_{11}H_{14}NS$ $(MH)^+$ 192.0847, found 192.0852.

*2-(2-Methylpropyl)benzothiazole (**53**).*[88] The title compound **53** was obtained as yellow oil (98 mg, 51% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (d, J = 6.0 Hz, 6H), 2.15−2.29 (m, 1H), 2.98 (d, J = 9.0 Hz, 2H), 7.30−7.35 (m, 1H), 7.41−7.46 (m, 1H), 7.80−7.84 (m, 1H), 7.96−7.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5, 29.8, 43.3, 121.5, 122.6, 124.7, 125.9, 135.3, 153.4, 171.3; HRMS (ESI$^+$/TOF) calcd for $C_{11}H_{14}NS$ $(MH)^+$ 192.0847, found 192.0849.

*1-n-Butylisoquinoline (**54**).*[89] The title compound **54** was obtained as yellow oil (97 mg, 52% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, J = 6.0 Hz, 3H), 1.44−1.56 (m, 2H), 1.80−1.90 (m, 2H), 3.29 (t, J = 9.0 Hz, 2H), 7.48 (d, J = 6.0 Hz, 1H), 7.54−7.67 (m, 2H), 7.89 (d, J = 9.0 Hz, 1H), 8.15 (d, J = 9.0 Hz, 1H), 8.43 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 23.1, 32.0, 35.4, 119.2, 125.5, 127.0, 127.1, 127.5, 129.8, 136.4, 142.1, 162.6; HRMS (ESI$^+$/TOF) calcd for $C_{13}H_{16}N$ $(MH)^+$ 186.1283, found 186.1281.

*1-(2-Phenylethynyl)napthalene (**55**).*[90] The title compound **55** was obtained as yellow oil (153 mg, 67% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.69 (m, 8H), 7.77−7.90 (m, 3H), 8.47 (d, J = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 87.7, 94.5, 121.1, 123.6, 125.4, 126.4, 126.6, 126.9, 128.5, 128.6, 128.6, 128.9, 130.5, 131.8, 133.4, 133.4; HRMS (APPI$^+$/TOF) calcd for $C_{18}H_{12}$ $(M)^+$ 228.0939, found 228.0946.

*1-(2-Phenylethynyl)isoquinoline (**56**).*[91] The title compound **56** was obtained as yellow oil (106 mg, 46% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.44 (m, 3H), 7.62−7.75 (m, 5H), 7.82−7.86 (m, 1H), 8.49−8.53 (m, 1H), 8.56 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.9, 94.0, 120.6, 122.3, 126.9, 127.0, 128.0, 128.5, 129.3, 129.4, 130.6, 132.2, 135.8, 143.0, 144.4; HRMS (ESI$^+$/TOF) calcd for $C_{17}H_{12}N$ $(MH)^+$ 230.0970, found 230.0973.

*1-[2-(4-Methylphenyl)ethynyl]isoquinoline (**57**).*[91] The title compound **57** was obtained as a pale brown solid (117 mg, 48% yield) after purification by silica gel column chromatography. Mp 92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3H), 7.20 (d, J = 9.0 Hz, 2H), 7.57−7.70 (m, 5H), 7.77−7.80 (m, 1H), 8.47−8.50 (m, 1H), 8.53 (d, J = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 86.4, 94.4, 119.2, 120.4, 126.9, 127.0, 127.9, 129.3, 130.6, 132.2, 135.8, 139.6, 142.9, 144.6; HRMS (ESI$^+$/TOF) calcd for $C_{18}H_{14}N$ $(MH)^+$ 244.1126, found 244.1120.

*1-[2-(4-Methoxyphenyl)ethynyl]isoquinoline (**58**).*[91] The title compound **58** was obtained as yellow oil (185 mg, 71% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.92−96.95 (m, 2H), 7.59−7.74 (m, 5H), 7.81−7.84 (m, 1H), 8.48−8.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.5, 86.0, 94.5, 114.3, 120.4, 127.0, 127.2, 127.9, 129.4, 130.7, 133.4, 135.9, 143.1, 144.8, 160.6; HRMS (ESI$^+$/TOF) calcd for $C_{18}H_{14}NO$ $(MH)^+$ 260.1075, found 260.1082.

*1,1′-(1E)-1,2-Ethenediylbisbenzene (**59**).*[92] The title compound **59** was obtained as a white solid (97 mg, 54% yield) after purification by silica gel column chromatography. Mp 116 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (s, 2H), 7.26−7.32 (m, 2H), 7.36−7.42 (m, 4H), 7.53−7.57 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 126.7, 127.8, 128.8, 137.5; HRMS (APPI$^+$/TOF) calcd for $C_{14}H_{12}$ $(M)^+$ 180.0939, found 180.0942.

*1-Methyl-2[(1E)-2-phenylethenyl]benzene (**60**).*[93] The title compound **60** was obtained as colorless oil (99 mg, 51% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) 2.45 (s, 3H), 7.00 (d, J = 9.0 Hz, 1H), 7.18−7.41 (m, 7H), 7.54 (d, J = 7.5 Hz, 2H), 7.61 (d, J = 6.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 20.1, 125.5, 126.3, 126.7, 127.7, 127.7, 126.8, 130.2, 130.5, 135.9, 136.6, 137.8; HRMS (APPI$^+$/TOF) calcd for $C_{15}H_{14}$ $(M)^+$ 194.1096, found 194.1101.

*1-Methyl-3[(1E)-2-phenylethenyl]benzene (**61**).*[93] The title compound **61** was obtained as a white solid (87 mg, 45% yield) after purification by silica gel column chromatography. Mp 54 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.15 (s, 3H), 7.28−7.44 (m, 6H), 7.55−5.58 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 123.8, 126.6, 127.3, 127.6, 128.6, 128.6, 128.7, 128.7, 128.9, 137.4, 137.5, 138.3; HRMS (APPI$^+$/TOF) calcd for $C_{15}H_{14}$ $(M)^+$ 194.1096, found 194.1099.

*1-Methyl-4[(1E)-2-phenylethenyl]benzene (**62**).*[92] The title compound **62** was obtained as a white solid (118 mg, 61% yield from the reaction of β-bromostyrene with tris(4-tolyl)aluminum reagent and 80 mg, 41% yield from the reaction of 1-[(1*E*)-2-bromoethenyl]-4-

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methylbenzene with triphenyl aluminum reagent) after purification by silica gel column chromatography. Mp 116 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.38 (s, 3H), 7.10 (d, J = 3.0 Hz, 2H), 7.19 (d, J = 9.0 Hz, 2H), 7.23−7.29 (m, 1H), 7.34−7.45 (m, 4H), 7.51−7.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 126.5, 126.6, 127.5, 127.8, 128.8, 129.5, 134.7, 137.7; HRMS (APPI$^+$/TOF) calcd for $C_{15}H_{14}$ $(M)^+$ 194.1096, found 194.1101.

*1-(1E)-1-Hexen-1-yl-4-methylbenzene (**63**).*[94] The title compound **63** was obtained as colorless oil (87 mg, 50% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 6.0 Hz, 3H), 1.32−1.52 (m, 4H), 2.17−2.25 (m, 2H), 2.34 (s, 3H), 6.13−6.23 (m, 1H), 6.36 (d, J = 18.0 Hz, 1H), 7.10−7.26 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 21.2, 22.4, 31.7, 32.8, 125.9, 129.3, 129.7, 130.3, 135.3, 136.5; GC-MS (m/z) 174.1.

*1-Methyl-4-[(1E)-4-methyl-1-penten-1-yl]benzene (**64**).*[95] The title compound **64** was obtained as colorless oil (87 mg, 49% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (d, J = 9.0 Hz, 6H), 1.65−1.78 (m, 1H), 2.06−2.11 (m, 2H), 2.32 (s, 3H), 6.11−6.21 (m, 1H), 6.34 (d, J = 18.0 Hz, 1H), 7.10 (d, J = 6.0 Hz, 2H), 7.25 (d, J = 9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 22.5, 28.8, 42.6, 125.9, 128.9, 129.3, 130.8, 135.3, 136.6; GC-MS (m/z) 174.1.

*[(1E)-4-Methyl-1-penten-1-yl]benzene (**65**).*[95] The title compound **65** was obtained as colorless oil (72 mg, 45% yield) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (d, J = 9.0 Hz, 6H), 1.69−1.83 (m, 1H), 2.10−2.15 (m, 2H), 6.19−6.29 (m, 1H), 6.40 (d, J = 15.9 Hz, 1H), 7.19−7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5, 28.7, 42.5, 126.1, 126.9, 128.6, 130.0, 130.9, 138.1; GC-MS (m/z) 160.1.

Radical Clock Experiment. In a glovebox, Ph_3Al (25.8 mg, 0.10 mmol), LiCl (12.6 mg, 0.30 mmol), *o*-(3-butenyl)iodobenzene (25.8 mg, 0.10 mmol), CuI (0.9 mg, 0.005 mmol), and PN-1 (1.5 mg, 0.005 mmol) were weighed in a 1 dram borosilicate vial. The reaction mixture was then dissolved in 0.5 mL DMF and tightly capped. The reaction solution was taken out of the glovebox, placed an aluminum hot plate preheated to 120 °C, and vigorously stirred. After 48 h, the reaction mixture was cooled to room temperature, and 50 μL of 2-nitrobiphenyl from a 0.20 M stock solution was added as a calibration standard. The reaction mixture was then diluted with ethyl acetate (15 mL), filtered through a short pad of silica gel, and analyzed by both GC and GC-MS. The direct cross-coupling product **72** was formed in 50% GC yield. The cyclized product **75** and the tandem cyclization-coupling product **76** were not formed in detectable amounts.

Competition Reaction of Ph_3Al with 1-Bromonaphthalene and 4-Chlorobenzonitrile. In a glovebox, Ph_3Al (25.8 mg, 0.10 mmol), LiCl (12.6 mg, 0.30 mmol), 1-bromonaphthalene (103.5 mg, 0.50 mmol), 4-chlorobenzonitrile (69.0 mg, 0.50 mmol), CuI (1.9 mg, 0.01 mmol), and PN-1 (3.0 mg, 0.01 mmol) were weighed in a 1 dram borosilicate vial. The reaction mixture was then dissolved in 0.5 mL DMF and tightly capped. The reaction solution was taken out of the glovebox, placed an aluminum hot plate preheated to 120 °C, and vigorously stirred. After 48 h, the reaction mixture was cooled to room temperature, and 50 μL of 2-nitrobiphenyl from a 0.20 M stock solution was added as a calibration standard. The reaction mixture was then diluted with ethyl acetate (15 mL), filtered through a short pad of silica gel, and analyzed by both GC. The cross-coupling products **77** and **78** were formed in 48% and 16% yields, respectively.

Measurement of Initial Rates for the Hammett Plot. In a glovebox, Ph_3Al (206.4 mg, 0.80 mmol), LiCl (100.8 mg, 2.40 mmol), aryl iodide (4.0 mmol), and (PN-1)CuI[9] (19.8 mg, 0.040 mmol) were weighed in a 2 mL volumetric flask. The mixture was then dissolved in DMF and diluted to make the volume to 2.0 mL. The solution was further diluted with additional 2.0 mL DMF to make a total volume of 4.0 mL. Seven reactions were then set up with each reaction containing 0.50 mL of the reaction solution in a 1 dram borosilicate vial. The reactions were run by placing the vials in an aluminum hot plate preheated to 100 °C and vigorously stirred. These reactions were stopped at 2, 4, 8, 12, 16, 20, and 24 min for 4-iodobenzotrifluoride by immediately immersing the reaction vial in liquid nitrogen. Reactions were similarly stopped at 5, 10, 15, 20, 25, 30, and 35 min for other aryl iodides. The reactions were run in duplicates. 50 μL of 2-nitrobiphenyl from a 0.20 M stock solution was then added to each of the reaction, diluted with ethyl acetate, filtered through a short pad of silica gel, and analyzed by GC to determine the product yield. Product yield was plotted against the reaction time, and the slope of the linear portion of the curve (for less than 30% yield) was used to determine the initial rates of the reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02077.

Experimental procedures, and the ^{1}H and ^{13}C NMR spectra of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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