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Palladium-Catalyzed Hiyama Cross-Couplings of Arylsilanes with 3-Iodoazetidine: Synthesis of 3-Arylazetidines

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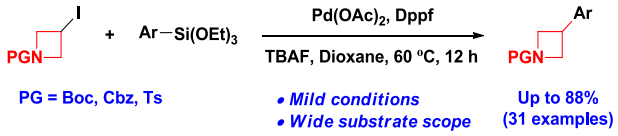
Supporting Information Placeholder



ABSTRACT: The first palladium-catalyzed Hiyama cross-coupling reactions of arylsilanes with 3-iodoazetidine were described. The protocol provides a convenient access to a variety of useful 3-arylazetidines which are of great interest in pharmaceutical labs in moderate to good yields (30%-88%). In addition, this strategy has the advantage of easy operation and mild reaction conditions.

■ INTRODUCTION

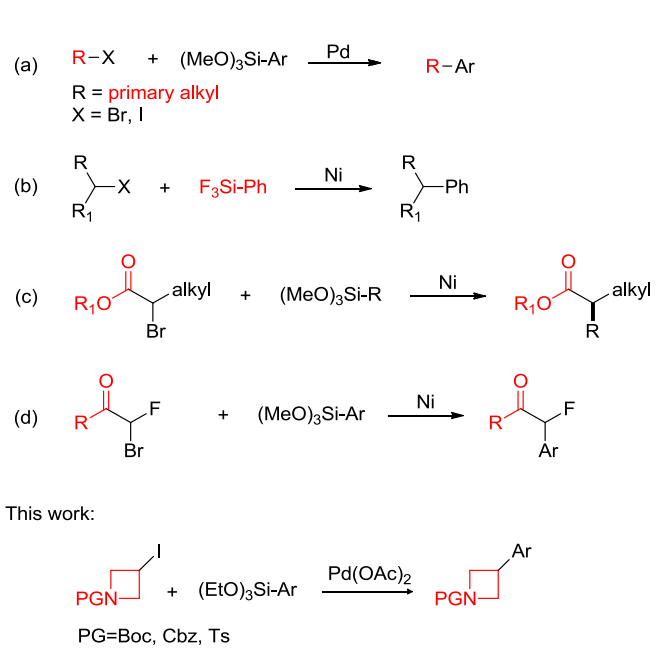
The palladium-catalyzed cross-coupling reaction between organometallic reagents and organic halides or pseudohalides is one of the most useful methods to construct C-C bonds in organic synthesis.[1] Among them, the efficient formation of Csp^3-Csp^2 bonds from cross-coupling reactions of alkyl electrophiles and organometallic nucleophiles, compatible with an extensive variety of functional groups, represent one of the issues remaining to be solved. This issue is commonly attributed to the following reasons: the oxidative addition step of alkyl electrophiles is relatively slow, moreover, the generated alkyl metal complex may undergo a fast β-hydride elimination to prevent the coupling process[2a] or stepwise migrate reinsertion followed by reductive elimination results the formation of undesired isomeric products.[2b] For these reasons, strict choice of Pd source, the ligand, and even the base is necessary for the reactions in order to obtain the desired products.

Azetidines are particularly interesting motifs of four-membered azaheterocycles because of their reasonable chemical properties, as well as their ring strain.[3] Arylazetidines are important building modules which have been found to show biological activities.[4-5] The synthetic methods for arylazetidines reported in recent years focus on direct arylation of azetidine derivatives at the 3-position as well as the functionalization of 2-position since Billotte showed the Negishi coupling reactions of azetidine-zinc complex and aryl electrophiles.[6-7] Duncton group reported the preparation of arylazetidine derivatives by use of nickel-mediated Csp^3-Csp^2 Suzuki coupling and Minisci reaction;[6b-c] In 2014, O'Neill and Ley groups descriped reductive cross-coupling reactions of (hetero)aryl bromides and saturated heterocyclic bromides, and the metal-free couplings of boronic acids with hydrazones respectively;[6d-e] Moreover, cross-coupling reactions of Grignard reagents with alkyl halides catalyzed by iron(II) and iron(III) was developed by Cossy and Rueping;[6f-g] In 2016, MacMillan group reported the cross-coupling reactions of tris(trimethylsilyl)silane with alkyl or (hetero)aryl bromides using metallaphotoredox catalysis; Baran group dicovered Csp^3-Csp^2 cross-coupling reactions of secondary redox-active esters under nickel-catalysis, and Buchwald group investigated Lipshutz-Negishi cross-coupling reactions of aryl electrophiles and alkyl halides.[7e-g] Although these progress greatly facilitated the synthesis of arylazetidines and afforded structurally diverse arylazetidines for pharmaceutical industry. It is still necessary to develop new systems for easy access to 3-arylazetidines.

The Hiyama cross-coupling reaction, especially the coupling of arylsilanes and various alkyl electrophiles, has been used as a powerful method to construct Csp^3-Csp^2 bond.[8-9] In addition, significant benefits of the Hiyama coupling involving tractability, and high tolerance to functional groups associated with organosilicon compounds.[10] Fu and co-workers accomplished the palladium-catalyzed Hiyama couplings of unactivated alkyl iodides or bromides, which was mainly effective for primary alkyl halides (Scheme 1a).[8a] After

that, Ni-catalyzed Hiyama couplings of unactivated secondary alkyl halides were reported by Fu and Wang groups which needed the high toxic trifluoro(phenyl)silane or electron-withdrawing groups at α-C of secondary alkyl halides (Scheme 1b-d).[8b-f] Therefore, palladium-catalyzed Hiyama coupling of iodoazetidine would be a suitable starting point for achieving the aforementioned goals. Herein, as a part of our ongoing efforts in development of the palladium catalysis[11] and the new conditions for the synthesis of various azetidine derivatives,[12] we reported the Pd-catalyzed Hiyama cross-coupling reactions of 3-iodoazetidine and arylsilanes under mild reaction conditions.

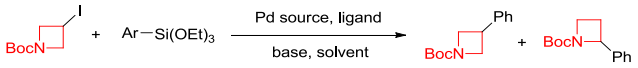
Scheme 1. The Csp^3-Csp^2 Couplings of Hiyama reactions.



■ RESULTS AND DISCUSSION

Initially, 1-Boc-3-iodoazetidine (**1a**) and triethoxy(phenyl)silane (**2a**) were chosen as model substrates to optimize the reaction conditions, and the results were summarized in Table 1. When the cross-coupling of **1a** (1.0 equiv) and **2a** (2.0 equiv) was carried out in THF using $Pd(PPh_3)_4$ as a catalyst and in the presence of TBAF[10b,13] at 60 ℃ under argon for 12 h, 70% yield of **3a** was obtained together with the formation of **4a** (**3a**:**4a**, 94:6) in the crude products (Table 1, entry 1). The minor 2-arylazetidines (**4**) were generated via ß-hydride elimination either after oxidative addition or after the next transmetallation and migratory insertion followed by reductive elimination, which were in compliance with our previous works.[12a,12b] To improve the yield of the reaction, a variety of Pd sources were investigated with PPh_3 as ligand and $Pd(OAc)_2$ provided the best reactivity (Table 1, entries 2-5). The commonly used mono- and bidentate phosphine ligands were also screened extensively (Scheme 2). Dppf was found to be a highly effective reagent in promoting the yield of cross-coupling product **3a** while suppressing the yield of **4a** (Table 1, entries 6-10) (for details, see the Supporting Information (SI)). The yield of **3a** was improved to 81% with good regioselectivity when dioxane was used as solvent (Table 1, entry 11). Increasing the amount of base to 2.5 equiv and the volume of solvent to 3.0 mL, the product **3a** was obtained in 89% yield with excellent regioselectivity (Table 1, entry 12). The optimum reaction conditions were then determined as follows: 1-Boc-3-iodoazetidine (**1a**, 1.0 equiv), triethoxy(phenyl)silane (**2a**, 2.0 equiv), 5 mol% $Pd(OAc)_2$, 10 mol% Dppf and 2.5 equiv TBAF (1.0 M in THF) in 3.0 mL dioxane at 60 ℃ under an argon atmosphere for 12 hours.

Table 1. Optimization of the reaction conditions.[a]

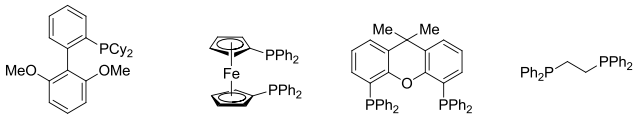


1a 2a 3a 4a

Entry	Pd source	Ligand	Solvent	Yield of **3a** (%)[b] (**3a**:**4a**)
1	$Pd(PPh_3)_4$	-	THF	70 (94:6)
2	$PdCl_2$	PPh_3	THF	42 (96:4)
3	$Pd(OAc)_2$	PPh_3	THF	42 (97:3)
4	$Pd(acac)_2$	PPh_3	THF	24 (96:4)
5	$Pd(dba)_2$	PPh_3	THF	6 (93:7)
6	$Pd(OAc)_2$	PCy_3	THF	trace
7	$Pd(OAc)_2$	S-Phos	THF	70 (84:16)
8	$Pd(OAc)_2$	Dppf	THF	70 (97:3)
9	$Pd(OAc)_2$	Dppe	THF	16 (85:15)
10	$Pd(OAc)_2$	Xantphos	THF	trace
11	$Pd(OAc)_2$	Dppf	Dioxane	81 (93:7)
12[c]	$Pd(OAc)_2$	Dppf	Dioxane	89 (>99:1)

[a]Reaction conditions: **1a** (0.5 mmol, 1.0 eq), **2a** (1.0 mmol, 2.0 eq), Pd source (5 mol%), ligand (10 mol%), TBAF (1.0 M in THF, 1.5 eq), solvent (2.0 mL), 60 ℃, under Ar, 12 h; [b]The yields of **3a** are detected by GC analysis using dipentyl phthalate as an internal standard; The ratio of product **3a** and **4a** are given within parentheses; [c]Run with 2.5 equiv TBAF (1.0 M in THF) and 3.0 mL dioxane.

Scheme 2. The structures of phosphine ligands.



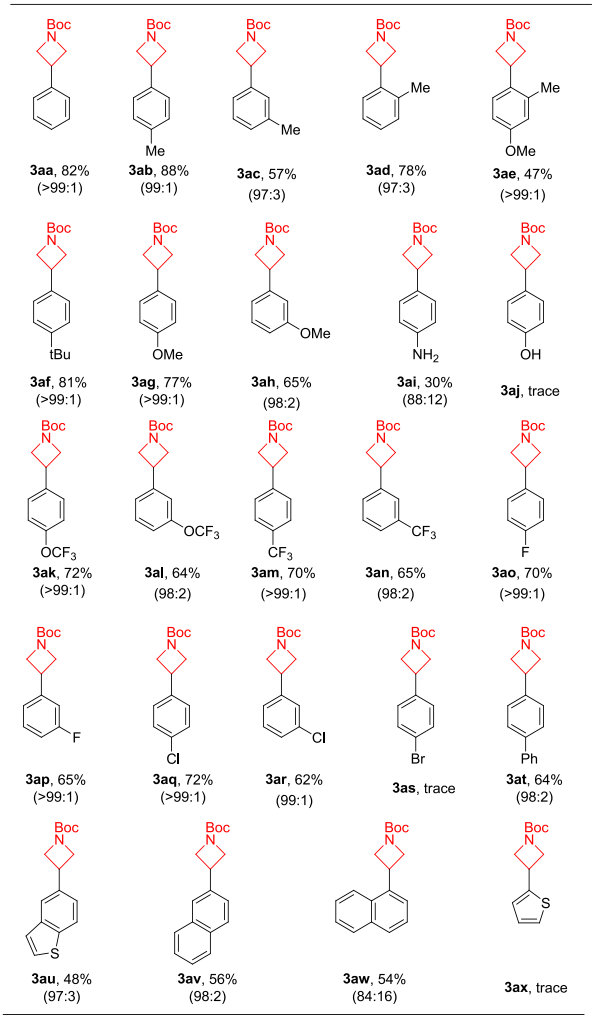
S-Phos Dppf Xantphos Dppe

Under the optimized reaction conditions, 1-Boc-3-iodoazetidine (**1a**) was reacted with diverse aryl siloxanes to give the desired products in moderate to good yields with a decent regioselectivity (Table 2). It was found that alkyl, alkoxy, halide, amino and aryl substitute aryl siloxanes could be used as effective substrates for this cross-coupling. The results indicated that triethoxy(phenyl)silane with the methyl group substituted at *ortho*-, *meta*- and *para*- position proceeded smoothly to give the desired products in 78%, 57% and 88% yields respectively (Table 2, **3ab**-**3ad**). Triethoxy(phenyl)silane possessing electron-donating groups, such as *t*-Bu-, and CH_3O- gave the desired products in 47%-81% yields (**3ae**-**3ah**). It should be noted that 4-(triethoxysilyl)aniline was also compatible to this catalytic system, and gave **3i** in 30% yield. However, no desired product was observed when 4-(triethoxysilyl)phenol (**2j**) was employed as substrate. Triethoxy(phenyl)silane containing

electron-withdrawing group such as OCF_3- and CF_3- gave the desired products in 64%-72% yields (**3ak-3an**). The halogen-containing triethoxy(phenyl)silane were also compatible and delivered the corresponding products in good yields except for (4-bromophenyl)triethoxysilane (**3ao-3as**). When (4-bromophenyl)triethoxysilane (**2s**) was used as substrate, the conversion of the reaction was very low, and a significant amount of tert-butyl 3-iodoazetidine-1-carboxylate (**1a**) was detected in GC-MS. The main by-product of the reaction was the homocoupling product of (**2s**). Aryl siloxanes with substituents in the *para*- position worked comparatively well than the ones with substituents in the *meta*- position (**3ab *vs* 3ac**, **etc**). Moreover, the reaction seemed to be sensitive to steric effects (**3ab** vs **3ad**, **3ag** vs **3ae**). [1,1'-biphenyl]-4-yltriethoxysilane proceeded smoothly in the reaction conditions to give **3at** in 64% yield. In addition, benzo[b]thiophen-5-yltriethoxysilane, triethoxy(naphthalen-2-yl)silane, and triethoxy(naphthalen-1-yl)silane were tolerated as well in the reaction to form the desired products in moderate yields 48%, 56%, and 54% respectively (**3au-3aw**). When triethoxy(thiophen-2-yl)silane was used under the optimal reaction conditions, no desired product was obtained (**3ax**).

Table 2. **Substrate scope of various aryl siloxanes.**[a,b,c]

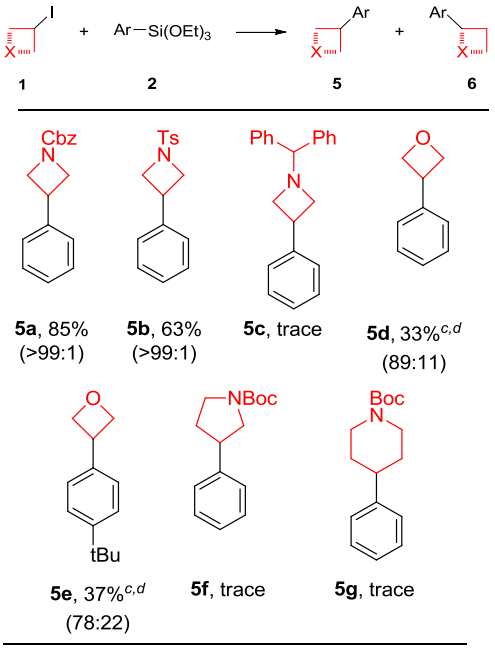
1a **2a-2x** **3aa-3ax** **4aa-4ax**



[a]Standard reaction conditions: **1a** (0.5 mmol, 1.0 eq), **2** (1.0 mmol, 2.0 eq), $Pd(OAc)_2$ (5 mol%), Dppf (10 mol%), TBAF (1.0 M in THF, 2.5 eq), dioxane (3.0 mL), at 60 ℃, under Ar, 12 h; [b]Isolated yield; [c]The **3**/**4** ratio was determined by GC-MS analysis of the crude mixture.

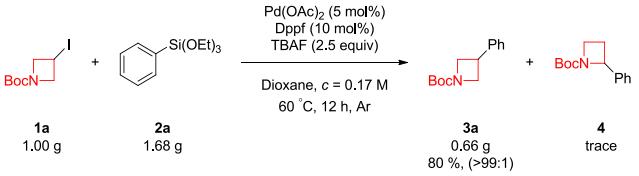
To establish the scope of this palladium-catalyzed Hiyama cross-coupling reaction, some heterocycloalkyl iodides were investigated under optimized conditions (Table 3). Cbz-protected iodoazetidine gave the corresponding product in 85% yield (**5a**). Comparatively, Ts-protected iodoazetidine resulted in slightly lower yield (**5b**). When 1-benzhydryl-3-iodoazetidine was used as substrate, the desired product **5c** could only be detected in trace amount, indicated that the electron-withdrawing protecting group of iodoazetidine possibly had a positive effect on this reaction. When triethoxy(phenyl)silane and (4-(tert-butyl)phenyl)triethoxysilane reacted with 3-iodooxetane resulted the desired products in slightly low yields (**5d-5e)**. When $Pd(PhCN)_2Cl_2$ instead of $Pd(OAc)_2$ was used, the yields of **5d** and **5e** were slightly higher. The results demonstrated that the property of the ring in the substrates might influence the reaction. Tert-butyl 2, 3-dihydro-1*H*-pyrrole-1-carboxylate and tert-butyl 5, 6-dihydropyridine-1(2*H*)-carboxylate instead of target products were obtained when 1-Boc-3-iodopyrrolidine and 1-Boc-4-iodopiperidine were used as substrates (**5f-5g**).

Table 3. **Substrate scope of heterocycloalkyl iodides.**[a,b]



[a]Standard reaction conditions: **1** (0.5 mmol, 1.0 eq), **2** (1.0 mmol, 2.0 eq), $Pd(OAc)_2$ (5 mol%), Dppf (10 mol%), TBAF (1.0 M in THF, 2.5 eq), dioxane (3.0 mL), 60 ℃, under Ar, 12 h; [b]Isolated yield; [c]**1** (0.5 mmol, 1.0 eq), **2** (1.0 mmol, 2.0 eq), $Pd(PhCN)_2Cl_2$ (10 mol%), Dppf (20 mol%), TBAF (1.0 M in THF, 2.5 eq), dioxane (3.0 mL), 60 ℃, under Ar, 1 h; [d]The **5**/**6** ratio determined by ^{1}H NMR analysis of the crude product.

Scheme 3. Scalability of the Palladium-Catalyzed Hiyama Cross-Couplings of 1a to 3a.



To investigate the further synthetic utility of this method, a gram-scale reaction of 1-Boc-3-iodoazetidine (**1a**, 1.00 g, 3.5 mmol) and triethoxy(phenyl)silane (**2a**, 1.68 g, 7.0 mmol) was performed under the optimal reaction conditions (Scheme 3). As a result, the cross-coupling reaction proceeded smoothly to afford tert-butyl 3-phenylazetidine-1-carboxylate **3a** in 80% yield.

■ CONCLUSION

In summary, the palladium-catalyzed Hiyama cross-coupling between 3-iodoazetidine and triethoxy(phenyl)silane has been described. This method exhibits broad substrate scope and mild reaction conditions. A variety of arylazetidines were obtained in moderate to good yields. The present work provides an operationally simple and efficient methodology to synthesize arylazetidines. We believe this method will be practical in synthetic applications.

■ EXPERIMENTAL SECTION

All reactions were carried out in dried glass reaction tube equipped with a magnetic stir bar under an argon atmosphere. Unless otherwise specified, solvents and reagents were purchased from commercial sources and used as received. Flash column chromatography was performed using 100−200 mesh silica gel with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography was performed using glass plates precoated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Melting points were recorded by an XT4A micro melting-point measurement instrument, and the thermometer was unrevised. GC yields were determined on GC (Shimadzu GC-2010 Plus). The 3-arylazetidines/2-arylazetidines ratio were detected by GC-MS (Thermo Fisher Scientific ISQ). Mass spectra were measured on LC/MSD Trap XCT instrument. The high-resolution mass spectra (HRMS) were obtained via an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS, with ESI as the ion source. NMR spectra were acquired on Bruker AVANCE III systems using tetramethylsilane (TMS) as the internal standard substance, using $CDCl_3$ or DMSO-d_6 as the solvent, at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, and 376 MHz for ^{19}F NMR.

General procedure for the synthesis of substrates (1a-1f, 2b-2x).

All 3-Iodoazetidines, 1-Boc-3-iodopyrrolidine, 1-Boc-4-iodopiperidine and arylsilanes were prepared according to the reported procedure.[6,14,15]

tert-butyl 3-iodoazetidine-1-carboxylate ***(1a)***.[6f] The crude product was purified by flash chromatography on silica gel (Petroleum ether/Ethyl acetate = 30:1) to provide the product **1a** as a colorless oil (7.4 g, 90%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 4.66-4.61 (m, 2 H), 4.49-4.43 (m, 1 H), 4.30-4.26 (m, 2 H), 1.43 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm): δ = 155.6, 80.2, 61.6, 28.3, 2.6.

benzyl 3-iodoazetidine-1-carboxylate ***(1b)***.[15c] The crude product was purified by flash chromatography on silica gel (Petroleum ether/Ethyl acetate = 10:1) to provide the product **1b** as a brown oil (4.6 g, 50%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.38-7.32 (m, 5 H), 5.10 (s, 2 H), 4.75-4.70 (m, 2 H), 4.53-4.43 (m, 1 H), 4.38-4.34 (m, 2 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm): δ = 155.9, 136.4, 128.7, 128.3, 128.2, 67.1, 61.8, 2.4.

3-iodo-1-tosylazetidine ***(1c)***.[15e] The crude product was purified by flash chromatography on silica gel (Petroleum ether/Ethyl acetate = 10:1) to provide the product **1c** as a white solid (4.9 g, 50%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.75-7.73 (m, 2 H), 7.41-7.39 (m, 2 H), 4.48-4.44 (m, 2 H), 4.36-4.29 (m, 1 H), 4.10-4.06 (m, 2 H), 2.48 (s, 3 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm): δ = 144.8, 131.3, 130.0, 128.5, 62.0, 21.8, 0.5.

1-benzhydryl-3-iodoazetidine ***(1d)***.[6g] The crude product was purified by flash chromatography on silica gel (Petroleum ether/Ethyl acetate = 10:1) to provide the product **1d** as a white solid (4.9 g, 50%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.40-7.39 (m, 4 H), 7.29-7.25 (m, 4 H), 7.21-7.17 (m, 2 H), 4.52 (s, 1 H), 4.47-4.40 (m, 1 H), 3.88-3.84 (m, 2 H), 3.53-3.49 (m, 2 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm): δ = 141.7, 128.7, 127.5, 78.1, 65.5, 4.9. GC−MS (EI, *m/z*): $[M]^+$ 349.00

tert-butyl 3-iodopyrrolidine-1-carboxylate ***(1e)***.[6f] The crude product was purified by flash chromatography on silica gel (Petroleum ether/Ethyl acetate = 10:1) to provide the product **1e** as a mixture of two rotamers as a colourless oil (5.2 g, 81%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 4.36-4.33 (m, 1 H), 3.83-3.65 (m, 2 H), 3.62-3.52 (m, 1 H), 3.46-3.38 (m, 1 H), 2.26-2.20 (m, 2 H), 1.46 (s, 9 H). ^{13}C{1H} NMR (100 MHz,

$CDCl_3$, ppm): δ = 154.1, 79.8, 57.4 (57.1), 45.1 (44.8), 38.4 (37.6), 28.5, 19.9.

tert-butyl 4-iodopiperidine-1-carboxylate (***1f***).[6f] The crude product was purified by flash chromatography on silica gel (Petroleum ether/Ethyl acetate = 10:1) to provide the product **1f** as a white solid (2.6 g, 43%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 4.37-4.31 (m, 1 H), 3.51-3.45 (m, 2 H), 3.20-3.14 (m, 2 H), 1.93-1.89 (m, 4 H), 1.35 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm): δ = 154.7, 79.8, 43.9, 37.3, 28.4, 27.7.

triethoxy(p-tolyl)silane (***2b***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (7.8 g, yield 51%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.58 (d, J = 7.9 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 3.86 (q, J = 7.0 Hz, 6H), 2.36 (s, 3H), 1.24 (t, J = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 140.3, 134.9, 128.7, 127.3, 58.7, 21.6, 18.2.

triethoxy(m-tolyl)silane (***2c***).[14a,14b] The product was prepared by following the literature procedure and was obtained as a colorless liquid (6.4 g, yield 42%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.51-7.49 (m, 2H), 7.32-7.26 (m, 2H), 3.90 (q, J = 7.0 Hz, 6H), 2.39 (s, 3H), 1.28 (t, J = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 137.1, 135.4, 131.8, 131.2, 130.7, 127.8, 58.7, 21.5, 18.2.

triethoxy(o-tolyl)silane (***2d***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (7.9 g, yield 52%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.74-7.72 (m, 1H), 7.34-7.30 (m, 1H), 7.19-7.15 (m, 2H), 3.87 (q, J = 7.0 Hz, 6H), 2.51 (s, 3H), 1.25 (t, J = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 144.5, 136.5, 130.5, 129.9, 129.7, 124.7, 58.5, 22.4, 18.2.

triethoxy(4-methoxy-2-methylphenyl)silane (***2e***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (11.1 g, yield 65%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.66-7.64 (m, 1H), 6.73-6.70 (m, 2H), 3.84 (q, *J* = 7.0 Hz, 6H), 3.80 (s, 3H), 2.48 (s, 3H), 1.24 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 161.5, 146.6, 138.2, 121.1, 115.7, 110.0, 58.4, 54.9, 22.6, 18.2. GC−MS (EI, *m/z*): $[M]^+$ 284.23.

(4-(tert-butyl)phenyl)triethoxysilane (***2f***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (6.2 g, yield 35%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.61-7.59 (m, 2H), 7.41-7.39 (m, 2H), 3.87 (q, *J* = 7.0 Hz, 6H), 1.32 (s, 9H), 1.25 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 153.3, 134.7, 127.3, 124.8, 58.7, 34.7, 31.2, 18.2. GC−MS (EI, *m/z*): $[M]^+$ 296.15.

triethoxy(4-methoxyphenyl)silane (***2g***).[14a,14b] The product was prepared by following the literature procedure and was obtained as a colorless liquid (8.6 g, yield 53%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.62-7.60 (m, 2H), 6.93-6.91 (m, 2H), 3.86 (q, *J* = 7.0 Hz, 6H), 3.81 (s, 3H), 1.24 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 161.3, 136.4, 121.9, 113.6, 58.6, 54.9, 18.2.

triethoxy(3-methoxyphenyl)silane (***2h***).[14a,14b] The product was prepared by following the literature procedure and was obtained as a colorless liquid (5.7 g, yield 35%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.24-7.22 (m, 1H), 7.19-7.17 (m, 1H), 7.14-7.13 (m, 1H), 6.91-6.88 (m, 1H), 3.80 (q, *J* = 7.0 Hz, 6H), 3.74 (s, 3H), 1.17 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 159.0, 132.4, 129.1, 127.1, 119.8, 116.0, 58.8, 55.1, 18.2.

4-(triethoxysilyl)aniline (***2i***).[14b] The product was prepared by following the literature procedure and was obtained as a colorless liquid (1.2 g, yield 50%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.48-7.45 (m, 2H), 6.70-6.67 (m, 2H), 3.84 (q, *J* = 7.0 Hz, 6H), 3.78 (s, 2H), 1.23 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 148.4, 136.3, 118.7, 114.4, 58.6, 18.2.

4-(triethoxysilyl)phenol (***2j***).[14b] The product was prepared by following the literature procedure and was obtained as a colorless liquid (0.6 g, yield 23%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.58-7.54 (m, 2H), 6.86-6.83 (m, 2H), 3.85 (q, *J* = 7.0 Hz, 6H), 1.24 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ =157.7, 136.7, 121.8, 115.1, 58.7, 18.2.

triethoxy(4-(trifluoromethoxy)phenyl)silane (***2k***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (9.7 g, yield 50%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.71-7.69 (m, 2H), 7.23-7.21 (m, 2H), 3.87 (q, *J* = 7.0 Hz, 6H), 1.25 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 151.0 (d, *J* = 1.4 Hz), 136.5, 130.0, 120.4 (q, *J* = 255.8 Hz), 120.0, 58.8, 18.1. MS (ESI, m/z): $[M+H]^+$ 325.6.

triethoxy(3-(trifluoromethoxy)phenyl)silane (***2l***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (8.2 g, yield 42%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.59-7.58 (m, 1H), 7.50 (m, 1H), 7.43-7.39 (m, 1H), 7.28-7.27 (m, 1H), 3.88 (q, *J* = 7.0 Hz, 6H), 1.25 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 149.0, 134.1, 133.0, 129.5, 126.9, 122.8, 121.8 (d, *J* = 255.7 Hz), 58.9, 18.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_{20}F_3O_4Si$ 325.1077; found 325.1075.

triethoxy(4-(trifluoromethyl)phenyl)silane (***2m***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (9.4 g, yield 51%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.81-7.79 (m, 2H), 7.63-7.61 (m, 2H), 3.88 (q, *J* = 7.0 Hz, 6H), 1.25 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 136.0, 135.1, 132.1 (q, *J* = 32.1 Hz), 124.4 (d, *J* = 3.7 Hz), 124.1 (q, *J* = 270.6 Hz), 58.9, 18.2. *triethoxy(3-(trifluoromethyl)phenyl)silane* (***2n***).[14a,13] The product was prepared by following the literature procedure and was obtained as a colorless liquid (8.5 g, yield 46%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.92-7.91 (m, 1H), 7.86-7.84 (m, 1H), 7.68-7.66 (m, 1H), 7.52-7.48 (m, 1H), 3.88 (q, *J* = 7.0 Hz, 6H), 1.26 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 138.0 (d, *J* = 1.1 Hz), 132.7, 131.8 (q, *J* = 3.6 Hz), 130.1 (q, *J* = 31.8 Hz), 128.1, 126.9 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 270.7 Hz), 58.9, 18.1.

triethoxy(4-fluorophenyl)silane (***2o***).[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (7.1 g, yield 46%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.68-7.64 (m, 2H), 7.10-7.05 (m, 2H), 3.86 (q, *J* = 7.0 Hz, 6H), 1.24 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 165.7 (d, *J* = 248.1 Hz), 136.9 (d, *J* = 7.5 Hz), 126.7 (d, *J* = 3.6 Hz), 115.2 (d, *J* = 19.7 Hz), 58.8, 18.2.

triethoxy(3-fluorophenyl)silane (***2p***).[14a,16b] The product was prepared by following the literature procedure and was obtained as a colorless liquid (5.1 g, yield 33%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.44-7.42 (m, 1H), 7.38-7.33 (m, 2H), 7.13-7.08 (m, 1H), 3.88 (q, *J* = 7.0 Hz, 6H), 1.25 (t, *J* =

7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 163.8 (d, *J* = 246.4 Hz), 134.1 (d, *J* = 4.7 Hz), 130.3 (d, *J* = 3.0 Hz), 129.7 (d, *J* = 6.8 Hz), 121.2 (d, *J* = 19.1 Hz), 117.4 (d, *J* = 21.0 Hz), 58.8, 18.2.

*(4-chlorophenyl)triethoxysilane (**2q**).*[14a,16a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (9.9 g, yield 60%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.61-7.59 (m, 2H), 7.37-7.35 (m, 2H), 3.86 (q, *J* = 7.0 Hz, 6H), 1.24 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 136.7, 136.1, 129.4, 128.1, 58.7, 18.1.

*(3-chlorophenyl)triethoxysilane (**2r**).*[14a,16a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (9.2 g, yield 56%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.63-7.62 (m, 1H), 7.54-7.52 (m, 1H), 7.41-7.38 (m, 1H), 7.33-7.29 (m, 1H), 3.87 (q, *J* = 7.0 Hz, 6H), 1.25 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 134.5, 134.3, 133.8, 132.7, 130.4, 129.3, 58.9, 18.2.

*(4-bromophenyl)triethoxysilane (**2s**).*[14b] The product was prepared by following the literature procedure and was obtained as a colorless liquid (4.0 g, yield 31%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.55-7.50 (m, 4H), 3.86 (q, *J* = 7.0 Hz, 6H), 1.24 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 136.5, 131.2, 130.1, 125.5, 58.9, 18.3. GC−MS (EI, *m/z*): $[M]^+$ 319.1.

*[1,1'-biphenyl]-4-yltriethoxysilane (**2t**).*[14a,16a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (8.0 g, yield 42%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.80-7.78 (m, 1H), 7.65-7.63 (m, 4H), 7.49-7.45 (m, 2H), 7.40-7.37 (m, 1H), 3.94 (q, *J* = 7.0 Hz, 6H), 1.30 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 143.0, 141.0, 135.3, 129.6, 128.8, 127.6, 127.2, 126.6, 58.8, 18.3.

*benzo[b]thiophen-5-yltriethoxysilane (**2u**).*[14a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (5.3 g, yield 30%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.22-8.17 (m, 1H), 7.93-7.91 (m, 1H), 7.63-7.61 (m, 1H), 7.44-7.43 (m, 1H), 7.38-7.36 (m, 1H), 3.90 (q, *J* = 7.0 Hz, 6H), 1.27 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 141.9, 139.2, 130.8, 129.7, 126.1, 126.0, 124.0, 122.1, 58.8, 18.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{20}O_3SSiNa$ 319.0795; found 319.0793.

*triethoxy(naphthalen-2-yl)silane (**2v**).*[14a,16a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (10.1 g, yield 58%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.36-8.23 (m, 1H), 7.90-7.83 (m, 3H), 7.74-7.71 (m, 1H), 7.53-7.49 (m, 2H), 3.93 (q, *J* = 7.0 Hz, 6H), 1.29 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 136.4, 134.5, 132.9, 130.4, 128.5, 127.8, 127.2, 126.9, 126.0, 58.9, 18.3.

*triethoxy(naphthalen-1-yl)silane (**2w**).*[14a,16a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (7.0 g, yield 40%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 8.37-8.35 (m, 1H), 8.02-8.00 (m, 1H), 7.93-7.91 (m, 1H), 7.86-7.84 (m, 1H), 7.55-7.46 (m, 3H), 3.90 (q, *J* = 7.0 Hz, 6H), 1.25 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 137.1, 136.3, 133.3, 131.2, 129.1, 128.7, 128.6, 126.3, 125.6, 125.0, 58.8, 18.3.

*triethoxy(thiophen-2-yl)silane (**2x**).*[14b,16a] The product was prepared by following the literature procedure and was obtained as a colorless liquid (4.1 g, yield 41%). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.66-7.65 (m, 1H), 7.49-7.48 (m, 1H), 7.23-7.21 (m, 1H), 3.89 (q, *J* = 7.0 Hz, 6H), 1.26 (t, *J* = 7.0 Hz, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 136.9, 132.0, 129.3, 128.2, 59.1, 18.2.

General procedure for the synthesis of arylazetidines.

A dried glass reaction tube equipped with a magnetic stir bar was charged with 1 (0.5 mmol, 1.0 equiv), 2 (1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.025 mmol, 5 mol %, 5.6 mg), Dppf (0.05 mmol, 10 mol %, 27.7 mg), TBAF (1.25 mmol, 2.5 equiv, 1.0 M in THF, 1.25 mL,), and dioxane (3.0 mL). The resulting mixture was then stirred at 60 ℃ parallel reactor under Ar for 12 h (unless otherwise noted). After cooling to room temperature, the yield of standard reaction were obtained by GC (dipentyl phthalate as an internal standard). The crude production was diluted with ethyl acetate and filtered through a pad of celite, then the resulting mixture was concentrated in vacuo, and purified by flash column chromatograph to give the pure products. The products were characterized by ^{1}H NMR, ^{13}C NMR, MS or HRMS.

*tert-butyl 3-phenylazetidine-1-carboxylate (**3aa**).*[6b] Colorless oil (96 mg, yield 82%), purified by flash chromatography (PE:EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.37 - 7.30 (m, 4 H), 7.28 - 7.24 (m, 1 H), 4.33 (t, *J* = 8.7 Hz, 2 H), 4.00 - 3.97 (m, 2 H), 3.77 - 3.70 (m, 1 H), 1.47 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.4, 142.3, 128.7, 127.0, 126.8, 79.5, 56.6, 33.5, 28.4. MS (ESI, m/z): $[M+H]^+$ 256.1.

*tert-butyl 3-(p-tolyl)azetidine-1-carboxylate (**3ab**).*[6b] Colorless oil (108 mg, yield 88%), purified by flash chromatography (PE:EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.21 - 7.15 (m, 4 H), 4.31 (t, *J* = 8.7 Hz, 2 H), 3.97 - 3.94 (m, 2 H), 3.73 - 3.66 (m, 1 H), 2.34 (s, 3 H), 1.47 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.4, 139.2, 136.6, 129.4, 126.7, 79.5, 56.8, 33.2, 28.4, 21.0. MS (ESI, m/z): $[M+H]^+$ 248.6.

*tert-butyl 3-(m-tolyl)azetidine-1-carboxylate (**3ac**).* Colorless oil (70 mg, yield 57%), purified by flash chromatography (PE:EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.17 - 7.13 (m, 1 H), 7.04 - 6.97 (m, 3 H), 4.22 (t, *J* = 8.7 Hz, 2 H), 3.90 - 3.86 (m, 2 H), 3.64 - 3.56 (m, 1 H), 2.27 (s, 3 H), 1.39 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.4, 142.2, 138.4, 128.6, 127.7, 127.5, 123.8, 79.5, 56.6, 33.4, 28.4, 21.4. MS (ESI, m/z): $[M+Na]^+$ 270.1.

*tert-butyl 3-(o-tolyl)azetidine-1-carboxylate (**3ad**).*[6f] Colorless oil (96 mg, yield 78%), purified by flash chromatography (PE:EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.36 - 7.34 (m, 1 H), 7.25 - 7.22 (m, 1 H), 7.17 - 7.15 (m, 2 H), 4.31 (t, *J* = 8.4 Hz, 2 H), 4.05 - 4.00 (m, 2 H), 3.98 - 3.92 (m, 1 H), 2.22 (s, 3 H), 1.46 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.5, 139.4, 135.9, 130.3, 126.8, 126.3, 125.3, 79.5, 54.9, 30.8, 28.4, 19.5. MS (ESI, m/z): $[M+H]^+$ 248.1.

*tert-butyl 3-(4-methoxy-2-methylphenyl)azetidine-1-carboxylate (**3ae**).* Colorless oil (65 mg, yield 47%), purified by flash chromatography (PE:EA = 10:1). ^{1}H NMR (400 MHz, CDCl3, ppm): δ = 7.18 - 7.16 (m, 1 H), 6.69 - 6.63 (m, 2 H), 4.20 (t, *J* = 8.2 Hz, 2 H), 3.92-3.88 (m, 2 H), 3.85 - 3.79 (m, 1 H), 3.70 (s, 3 H), 2.11 (s, 3 H), 1.38 (s, 9 H). ^{13}C{1H} NMR

(100 MHz, $CDCl_3$, ppm) δ = 158.3, 156.5, 137.2, 131.7, 126.4, 116.1, 111.1, 79.4, 55.2, 30.1, 28.4, 28.4, 19.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{23}NO_3Na$ 300.1570; found 300.1575.

*tert-butyl 3-(4-(tert-butyl)phenyl)azetidine-1-carboxylate (**3af**).* Colorless oil (117 mg, yield 81%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.41 - 7.39 (m, 2 H), 7.28 - 7.26 (m, 2 H), 4.33 (t, *J* = 8.6 Hz, 2 H), 4.02 - 3.94 (m, 2 H), 3.78 - 3.70 (m, 1 H), 1.49 (s, 9 H), 1.35 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 156.5, 149.9, 139.2, 126.5, 125.6, 79.4, 56.8, 34.5, 33.1, 31.3, 28.4. MS (ESI, m/z): $[M+Na]^+$ 312.1.

*tert-butyl 3-(4-methoxyphenyl)azetidine-1-carboxylate (**3ag**).*[7g] Colorless oil (101 mg, yield 77%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.23 - 7.20 (m, 2 H), 6.89 - 6.85 (m, 2 H), 4.29 (t, *J* = 8.7 Hz, 2 H), 3.94-3.90 (m, 2 H), 3.78 (s, 3 H), 3.74 - 3.60 (m, 1 H), 1.46 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 158.6, 156.4, 134.3, 127.8, 114.1, 79.4, 56.8, 55.3, 32.9, 28.4. MS (ESI, m/z): $[M+Na]^+$ 286.1.

*tert-butyl 3-(3-methoxyphenyl)azetidine-1-carboxylate (**3ah**).*[6f] Colorless oil (85 mg, yield 65%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.27 - 7.23 (m, 1 H), 6.89 - 6.77 (m, 3 H), 4.30 (t, *J* = 8.7 Hz, 2 H), 3.98-3.95 (m, 2 H), 3.80 (s, 3 H), 3.73 - 3.66 (m, 1 H), 1.46 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 159.9, 156.4, 143.9, 129.7, 119.0, 112.6, 112.2, 79.5, 56.5, 55.2 (d, J = 2.2 Hz), 33.5, 28.4. MS (ESI, m/z): $[M+Na]^+$ 286.1.

*tert-butyl 3-(4-aminophenyl)azetidine-1-carboxylate (**3ai**).* Colorless oil (37 mg, yield 30%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.11 - 7.09 (m, 2 H), 6.68 - 6.66 (m, 2 H), 4.27 (t, *J* = 8.6 Hz, 2 H), 3.93-3.89 (m, 2 H), 3.66-3.59 (m, 3 H), 1.46 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 156.5, 145.3, 132.2, 127.7, 115.3, 79.4, 56.8, 32.9, 28.4. MS (ESI, m/z): $[M+Na]^+$ 271.9.

*tert-butyl 3-(4-(trifluoromethoxy)phenyl)azetidine-1-carboxylate (**3ak**).*[17] Colorless oil (114 mg, yield 72%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.35 - 7.31 (m, 2 H), 7.20 - 7.18 (m, 2 H), 4.33 (t, *J* = 8.7 Hz, 2 H), 3.96 - 3.91 (m, 2 H), 3.76 - 3.69 (m, 1 H), 1.46 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 156.4, 148.1 (d, *J* = 1.6 Hz), 141.0, 128.1, 121.3, 120.5 (q, *J* = 255.4 Hz), 79.7, 56.5, 32.9, 28.4. ^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ = - 57.9. MS (ESI, m/z): $[M+Na]^+$ 340.2.

*tert-butyl 3-(3-(trifluoromethoxy)phenyl)azetidine-1-carboxylate (**3al**).*[17] Colorless oil (101 mg, yield 64%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32 - 7.28 (m, 1 H), 7.19 - 7.17 (m, 1 H), 7.07 - 7.03 (m, 2 H), 4.27 (t, *J* = 8.8 Hz, 2 H), 3.90 - 3.86 (m, 2 H), 3.70 - 3.63 (m, 1 H), 1.39 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$): δ = 156.3, 149.6 (d, *J* = 1.6 Hz), 144.6, 130.1, 125.1, 120.4 (q, *J* = 255.6 Hz), 119.5, 119.4, 79.6, 56.2, 33.2, 28.4. ^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ = - 57.8. MS (ESI, m/z): $[M+Na]^+$ 340.1.

*tert-butyl 3-(4-(trifluoromethyl)phenyl)azetidine-1-carboxylate (**3am**).*[17] Colorless oil (105 mg, yield 70%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.2 Hz, 2 H), 7.43 (d, *J* = 8.2 Hz, 2 H), 4.35 (t, *J* = 8.7 Hz, 2 H), 3.98 - 3.92 (m, 2 H), 3.81 - 3.73 (m, 1 H), 1.46 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$): δ = 156.3, 146.3, 129.3 (q, *J* = 32.3 Hz), 127.1, 125.7 (q, *J* = 3.7 Hz), 124.1 (q, *J* = 270.3 Hz), 79.8, 56.3, 33.3, 28.4. ^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ = - 62.5. MS (ESI, m/z): $[M+Na]^+$ 324.2.

*tert-butyl 3-(3-(trifluoromethyl)phenyl)azetidine-1-carboxylate (**3an**).*[17] Colorless oil (98 mg, yield 65%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.53 - 7.45 (m, 4 H), 4.36 (t, *J* = 8.7 Hz, 2 H), 3.98 - 3.95 (m, 2 H), 3.82 - 3.74 (m, 1 H), 1.47 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 156.4, 143.2, 131.1 (q, *J* = 40.0 Hz), 130.1, 129.3, 124.0 (q, *J* = 270.7 Hz), 123.9 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 3.7 Hz), 79.8, 56.3, 33.3, 28.4. ^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ = - 62.6. MS (ESI, m/z): $[M+K]^+$ 340.0.

*tert-butyl 3-(4-fluorophenyl)azetidine-1-carboxylate (**3ao**).*[6b] Colorless oil (88 mg, yield 70%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.21 - 7.17 (m, 2 H), 6.98 - 6.92 (m, 2 H), 4.24 (t, *J* = 8.8 Hz, 2 H), 3.87-3.83 (m, 2 H), 3.66 - 3.59 (m, 1 H), 1.39 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 163.0 (d, *J* = 243.9 Hz), 156.4, 138.0 (d, *J* = 3.3 Hz), 128.3 (d, *J* = 8.0 Hz), 115.6 (d, *J* = 21.3 Hz), 79.6, 56.7, 32.9, 28.4. ^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ = - 115.7. MS (ESI, m/z): $[M+Na]^+$ 274.1

*tert-butyl 3-(3-fluorophenyl)azetidine-1-carboxylate (**3ap**).*[17] Colorless oil (82 mg, yield 65%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.25 - 7.19 (m, 1 H), 7.00 - 6.99 (m, 1 H), 6.96 - 6.92 (m, 1 H), 6.89 - 6.84 (m, 1 H), 4.25 (t, *J* = 8.8 Hz, 2 H), 3.88 - 3.83 (m, 2 H), 3.67 - 3.60 (m, 1 H), 1.39 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 163.3 (d, *J* = 244.8 Hz), 155.3, 143.9 (d, *J* = 7.0 Hz), 129.3 (d, *J* = 8.2 Hz), 121.4 (d, *J* = 2.8 Hz), 113.0 (d, *J* = 15.1 Hz), 112.8 (d, *J* = 15.8 Hz), 78.6, 55.4, 32.3, 27.4. ^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ = - 112.7. MS (ESI, m/z): $[M+Na]^+$ 274.3.

*tert-butyl 3-(4-chlorophenyl)azetidine-1-carboxylate (**3aq**).*[6f] Colorless oil (96 mg, yield 72%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.31 - 7.28 (m, 2 H), 7.24 - 7.22 (m, 2 H), 4.33-4.29 (m, 2 H), 3.94-3.89 (m, 2 H), 3.71 - 3.64 (m, 1 H), 1.45 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 156.3, 140.8, 132.7, 128.8, 128.1, 79.6, 56.6, 33.0, 28.4. MS (ESI, m/z): $[M+Na]^+$ 290.1.

*tert-butyl 3-(3-chlorophenyl)azetidine-1-carboxylate (**3ar**).*[17] Colorless oil (83 mg, yield 62%), purified by flash chromatography (PE:EA = 10:1). ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.23 - 7.11 (m, 4 H), 4.25 (t, *J* = 8.7 Hz, 2 H), 3.89-3.84 (m, 2 H), 3.66 - 3.58 (m, 1 H), 1.39 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 156.3, 144.3, 134.6, 130.0, 127.2, 127.0, 124.9, 79.7, 56.4, 33.2, 28.4. MS (ESI, m/z): $[M+Na]^+$ 290.0.

*tert-butyl 3-([1,1'-biphenyl]-4-yl)azetidine-1-carboxylate (**3at**).* White solid (99 mg, yield 64%), purified by flash chromatography (PE:EA = 10:1). m.p. 89-91 ℃. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.61 - 7.59 (m, 4 H), 7.47 - 7.43 (m, 2 H), 7.41 - 7.34 (m, 3 H), 4.37 (t, *J* = 8.7 Hz, 2 H), 4.05 - 4.01 (m, 2 H), 3.82 - 3.75 (m, 1 H), 1.50 (s, 9 H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ = 155.4, 140.3, 139.7, 138.9, 127.8, 126.4, 126.3, 126.2, 126.0, 78.5, 55.5, 32.2, 27.4. MS (ESI, m/z): $[M+K]^+$ 348.1.

*tert-butyl 3-(benzo[b]thiophen-5-yl)azetidine-1-carboxylate (**3au**).* White solid (69 mg, yield 48 %), purified by flash chromatography (PE:EA = 10:1). m.p. 96-98 ℃. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.85 - 7.83 (m, 1 H), 7.74 - 7.73 (m, 1 H), 7.45 - 7.44 (m, 1 H), 7.31 - 7.29 (m, 2 H), 4.38 (t, *J*

= 8.6 Hz, 2 H), 4.05 - 4.01 (m, 2 H), 3.87 - 3.79 (m, 1 H), 1.49 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.5, 140.0, 138.5, 138.4, 127.2, 123.7, 123.2, 122.8, 121.6, 79.6, 56.9, 33.6, 28.5. MS (ESI, m/z): $[M+Na]^+$ 312.1.

*tert-butyl 3-(naphthalen-2-yl)azetidine-1-carboxylate (**3av**).*[6g] White solid (79 mg, yield 56%), purified by flash chromatography (PE:EA = 10:1). m.p. 69-71 ℃. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.75 - 7.60 (m, 4 H), 7.40 - 7.33 (m, 3 H), 4.29 (t, *J* = 8.7 Hz, 2 H), 4.00-3.96 (m, 2 H), 3.86 - 3.74 (m, 1 H), 1.40 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.5, 139.5, 133.4, 132.5, 128.7, 127.7, 127.6, 126.4, 125.8, 125.4, 124.8, 79.6, 56.4, 33.7, 28.5. MS (ESI, m/z): $[M+H]^+$ 284.0

*tert-butyl 3-(naphthalen-1-yl)azetidine-1-carboxylate (**3aw**).* Colorless oil (76 mg, yield 54 %), purified by flash chromatography (PE:EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.90 - 7.88 (m, 1 H), 7.79 - 7.71 (m, 2 H), 7.54 - 7.45 (m, 4 H), 4.52 - 4.22 (m, 5 H), 1.49 (s, 9 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.5, 137.0, 133.9, 131.3, 129.1, 127.5, 126.3, 125.9, 125.4, 123.2, 123.0, 79.6, 54.5, 30.8, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{21}NO_2Na$ 306.1465; found 306.1467.

*benzyl 3-phenylazetidine-1-carboxylate (**5a**).*[6g] Colorless oil (113 mg, yield 85%), purified by flash chromatography (PE:EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.31 - 7.16 (m, 10 H), 5.06 (s, 2 H), 4.33 (t, *J* = 8.8 Hz, 2 H), 4.01 - 3.93 (m, 2 H), 3.74 - 3.67 (m, 1 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 156.5, 141.9, 136.7, 128.8, 128.5, 128.1, 128.0, 127.1, 126.7, 66.7, 56.7, 33.9. MS (ESI, m/z): $[M+H]^+$ 268.1.

*3-phenyl-1-tosylazetidine (**5b**).*[18] White solid (90 mg, yield 63%), purified by flash chromatography (PE:EA = 10:1). m.p. 120-122 ℃. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.80 - 7.78 (m, 2 H), 7.43 - 7.41 (m, 2 H), 7.25 - 7.20 (m, 3 H), 6.98 - 6.95 (m, 2 H), 4.15 (t, *J* = 8.4 Hz, 2 H), 3.82 - 3.78 (m, 2 H), 3.64 - 3.57 (m, 1 H), 2.49 (s, 3 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 144.3, 140.6, 131.4, 129.9, 128.7, 128.6, 127.3, 126.9, 57.9, 33.2, 21.7. MS (ESI, m/z): $[M+H]^+$ 288.1.

*3-phenyloxetane (**5d**).*[5] Colorless oil (22 mg, yield 33%), purified by flash chromatography (PE:EA = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.42 - 7.35 (m, 4 H), 7.30 - 7.25 (m, 1 H), 5.09 - 5.06 (m, 2 H), 4.80 - 4.77 (m, 2 H), 4.27 - 4.20 (m, 1 H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 141.6, 128.8, 127.0, 126.8, 78.9, 40.3. MS (ESI, m/z): $[M+K]^+$ 173.3.

*3-(4-(tert-butyl)phenyl)oxetane (**5e**).* Colorless oil (35 mg, yield 37%), purified by flash chromatography (PE:EA = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.43 - 7.37 (m, 2 H), 7.36 - 7.35 (m, 2 H), 5.09 - 5.05 (m, 2 H), 4.82 - 4.79 (m, 2 H), 4.27 - 4.19 (m, 1 H), 1.33 (s, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$, ppm) δ = 150.0, 138.5, 126.5, 125.6, 79.0, 40.0, 34.5, 31.4. MS (ESI, m/z): $[M+Na]^+$ 213.0.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Optimization of the partial reaction conditions, plausible mechanism of Hiyama cross-coupling of 1-Boc-3-iodoazetidine with arylsilanes, references, characterization data of the substrates and the products (PDF).

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Notes

The authors declare no competing financial interest.

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