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Note

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Palladium-Catalyzed Hiyama Coupling of Benzylic Ammonium Salts via C−N Bond Cleavage

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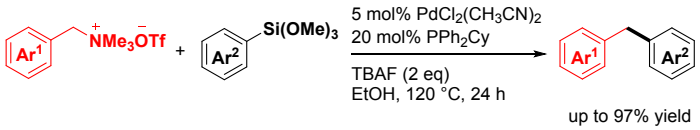
Supporting Information

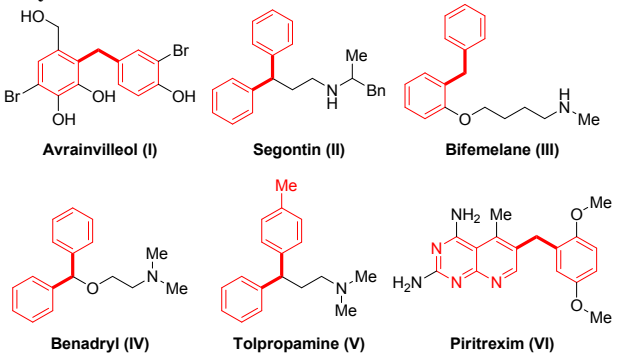
ABSTRACT: The first palladium-catalyzed Hiyama cross-coupling of arylsilanes with benzyltrimethyl-ammonium salts is reported. The reaction proceeds smoothly to facilitate C(sp^2)−C(sp^3) bond formation via cleavage of the C−N bond, and provides a useful approach to various diarylmethanes with a broad substrate scope and excellent functional group tolerance in good to excellent yields.



Diarylmethane is an important scaffold in a large number of bioactive natural products and pharmaceuticals (Figure 1).[1] For example, the marine natural product Avrainvilleol (**I**) which contains the diarylmethane unit, has been reported to exhibit both antibacterial[2] and antioxidant activities.[3] Moreover, a number of commercially available drugs such as Segontin (**II**) (for the treatment of coronary heart disease),[4] the antidepressant Bifemelane (**III**),[5] the antiallergic medicines Benadryl (**IV**)[6] and Tolpropamine (**V**)[7], and the anticancer agent Piritrexim (**VI**),[8] contain the diarylmethane sub-structure. The development of efficient methods for the synthesis of this skeleton has therefore attracted considerable attention over the past few decades.[9] More specifically, classic strategies including the Friedel−Crafts reaction[10] and the reduction of diarylmethane derivatives[11] have been established to construct the diarylmethane skeleton. Although efficient, these methods often suffer from disadvantages, such as harsh reaction conditions, poor regioselectivities and difficult available substrates. Recently, transition metal-catalyzed cross-coupling reactions have emerged as powerful methods for the direct construction of diarylmethane derivatives,[12] with palladium being undoubtedly one of the most effective catalysts due to its widespread application and versatility.[13] In these palladium-catalyzed reactions, a variety of nucleophiles have been employed for the syntheses of diarylmethane derivatives, with examples including organoboranes,[14] organoindium reagents[15] and organostannanes.[16] Compared with these organometallic reagents, organosilicon nucleophiles are an attractive alternative coupling partner in the palladium-catalyzed Hiyama coupling reaction due to their facile synthesis and low toxicity.[17] However, to date, nearly all studies of the palladium-catalyzed Hiyama coupling reaction have focused on C(sp^2)−C(sp^2) bond formation.[18] In contrast, very few examples of the construction of C(sp^2)−C(sp^3) bonds have been reported based on this strategy.[19] As such, a novel and efficient palladium-catalyzed Hiyama cross-coupling reaction for the preparation of diarylmethanes via C(sp^2)−C(sp^3) bond formation is highly desirable.

Recently, ammonium salts emerged as electrophiles which have been widely used in transition metal-catalyzed cross-coupling reactions *via* C−N cleavage.[20] Since the pioneering work by Sarandeses,[21] many efforts have been made in this field by the groups of Wang,[22] MacMillan,[23] Watson,[24] and Tortosa,[25] among others.[26] In this context, our group is interested in the palladium-catalyzed cross-coupling reaction via the cleavage of C−N bond,[27] and we have reported the palladium-catalyzed Suzuki cross-coupling of benzyltrimethylammonium salts for the synthesis of diarylmethane[28] and triarylmethane derivatives.[29] Based on our previous successes, we envisioned that arylsilanes could also be used as coupling partners to react with benzylic ammonium salts for the C(sp^2)-C(sp^3) bond formation in the presence of palladium catalyst. In such context, we herein report the first palladium-catalyzed Hiyama cross-coupling of benzyltrimethyl-ammonium salts for the construction of diarylmethane derivatives.

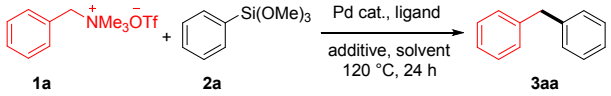
Figure 1. Bioactive Compounds Containing the Diarylmethane Motif



Initial exploratory experiments to optimize the reaction conditions for the coupling reaction were performed with benzyltrimethylammonium salt **1a** and trimethoxy(phenyl)-silane **2a** as the model substrates (Table 1). To our delight, the desired coupling product **3aa** was indeed obtained, albeit in 20% yield when the reaction was performed at 120 °C for 24 h in the presence of 5 mol% $Pd(OAc)_2$, 20 mol% PPh_3, and 2.0 equiv of tetrabutylammonium fluoride (TBAF) in EtOH under a nitrogen atmosphere (Table 1, entry 1). A brief screening of palladium catalysts revealed that $PdCl_2(CH_3CN)_2$ gave a relatively good performance (Table 1, entries 2−4). Rapid screening with other solvents led to a complex reaction or lower yields (Table 1, entries 5−9). When PPh_2Cy was used as the ligand instead of PPh_3, the coupling product was obtained with

a dramatically increased yield (85%) (Table 1, entries 10−11). For the bidentate ligand BINAP, trace amounts of the product was obtained (Table 1, entry 12). Considering the beneficial effect of the fluoride ion for activation of the C−Si bond,[17b] other fluoride salts such as AgF, CsF, and KF were examined in this coupling reaction, but a dramatic decrease in reactivity was observed (Table 1, entries 13−15). In addition, only trace amount of product was observed when the reaction was performed in the absence of an additive (Table 1, entry 16). Furthermore, reducing of the amount of **2a** from 2.0 equiv to 1.5 equiv did not result in any remarkable decrease in the reaction efficiency (Table 1, entry 18).

Table 1. Optimization of the Reaction Conditions[a]



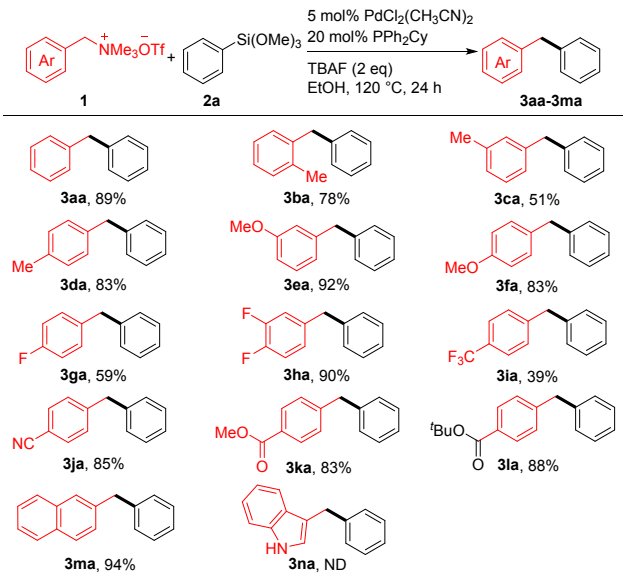
1a 2a 3aa

entry	catalyst	ligand	additive	solvent	yield (%)[b]
1	$Pd(OAc)_2$	PPh_3	TBAF	EtOH	20
2	$PdCl_2$	PPh_3	TBAF	EtOH	26
3	$Pd_2(dba)_3$	PPh_3	TBAF	EtOH	11
4	$PdCl_2(CH_3CN)_2$	PPh_3	TBAF	EtOH	55
5	$PdCl_2(CH_3CN)_2$	PPh_3	TBAF	PhMe	7
6	$PdCl_2(CH_3CN)_2$	PPh_3	TBAF	DMSO	10
7	$PdCl_2(CH_3CN)_2$	PPh_3	TBAF	DMF	8
8	$PdCl_2(CH_3CN)_2$	PPh_3	TBAF	CH_3CN	50
9	$PdCl_2(CH_3CN)_2$	PPh_3	TBAF	THF	trace
10	**$PdCl_2(CH_3CN)_2$**	**PPh_2Cy**	**TBAF**	**EtOH**	**85 (89)**
11	$PdCl_2(CH_3CN)_2$	X-Phos	TBAF	EtOH	63
12	$PdCl_2(CH_3CN)_2$	BINAP	TBAF	EtOH	trace
13	$PdCl_2(CH_3CN)_2$	PPh_2Cy	AgF	EtOH	trace
14	$PdCl_2(CH_3CN)_2$	PPh_2Cy	CsF	EtOH	9
15	$PdCl_2(CH_3CN)_2$	PPh_2Cy	KF	EtOH	trace
16	$PdCl_2(CH_3CN)_2$	PPh_2Cy	--	EtOH	trace
17[c]	$PdCl_2(CH_3CN)_2$	PPh_2Cy	TBAF	EtOH	58
18[d]	$PdCl_2(CH_3CN)_2$	PPh_2Cy	TBAF	EtOH	79

[a]Reaction conditions: **1a** (0.10 mmol), **2a** (0.20 mmol), palladium catalyst (5 mol%), ligand (20 mol%) and additive (2.0 eq) in solvent (2.0 mL) at 120 °C under a nitrogen atmosphere. [b]GC yields with naphthalene as an internal standard. Isolated yield is in parentheses. [c]3 mol% $PdCl_2(CH_3CN)_2$ was uesd. [d]0.15 mmol **2a** was used.

With the optimized reaction conditions in hand, we then evaluated the substrate scope of this palladium-catalyzed cross-coupling of trimethoxy(phenyl)silane (**2a**) with various benzylammonium salts (**1**). As shown in Scheme 1, electron-donating groups such as 2-Me-, 3-Me-, 4-Me-, 3-OMe-, and 4-OMe- on the phenyl ring were compatible and the corresponding coupling products (**3ba**−**fa**) were obtained in moderate to excellent yields. In addition, benzylammonium salts bearing electron-withdrawing groups (i.e., 4-F and 3,4-difluoro groups) afford the desired coupling products **3ga** and **3ha** in yields of 59% and 90%, respectively. In the case of the 4-trifluoromethyl benzylammonium salt, the coupling reaction also proceeded smoothly to afford the expected product (**3ia**) in an acceptable yield. Moreover, sensitive or strong electron-withdrawing groups, such as CN (**3ja**) and ester functionalities (**3ka** and **3la**), were well-tolerated giving 83−88% yields under the standard reaction conditions. However, although

Scheme 1. Scope of the Benzylammonium Salts[a]

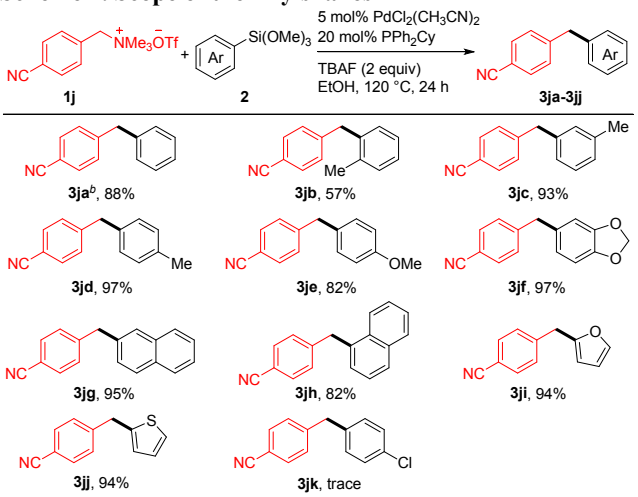


[a]Reaction conditions: **1** (0.20 mmol), **2a** (0.40 mmol), $PdCl_2(CH_3CN)_2$ (5 mol%), PPh_2Cy (20 mol%) and TBAF (0.40 mmol) in ethanol (2.0 mL) at 120 °C for 24 h under nitrogen atmosphere.

the naphthyl substrate exhibited an excellent reactivity (**3ma**), the indolyl substrate failed to afford the desired product (**3na**).

Having demonstrated the broad scope of benzylammonium salts that can be used in the palladium-catalyzed Hiyama cross-coupling reaction, we next sought to explore a variety of arylsilane substrates (Scheme 2). Interestingly, substrate $PhSi(OEt)_3$ also reacted with benzylammonium salts (**1j**) under the standard conditions to afford the coupling product **3ja** in 88% yield, thereby demonstrating a comparable reactivity to $PhSi(OMe)_3$. With respect to the trimethoxy arylsilanes, the substrates bearing electron-donating groups (i.e., 2-Me-, 3-Me-, 4-Me-, and 4-OMe-) on the phenyl ring effectively provided the desired coupling products (**3jb**−**je**) in

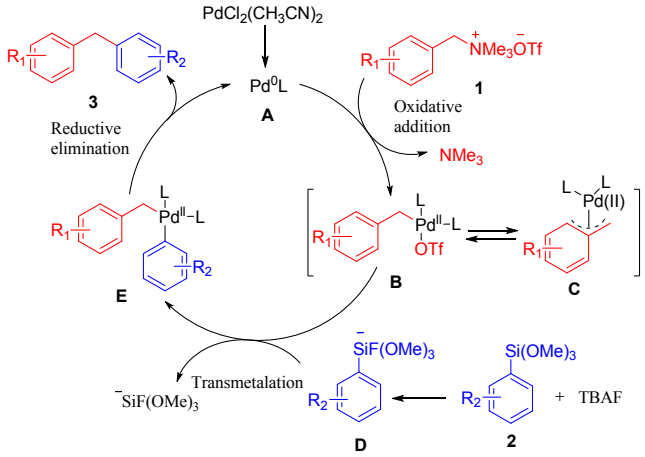
Scheme 2. Scope of the Arylsilanes[a]



[a]Reaction conditions: **1j** (0.20 mmol), **2** (0.40 mmol), $PdCl_2(CH_3CN)_2$ (5 mol %), PPh_2Cy (20 mol%) and TBAF (0.40 mmol) in ethanol (2.0 mL) at 120 °C for 24 h under nitrogen atmosphere. [b]$PhSi(OEt)_3$ was used as the substrate.

moderate to excellent yields. The reaction also showed a good tolerance toward a special substrate, namely benzo[*d*]-[1,3]dioxol-5-yltrimethoxysilane, to give (**3jf**) in a 97% yield. In addition, trimethoxy(naphthalen-2-yl)silane and trimethoxy (naphthaalen-1-yl)silane reacted to afford the corresponding products (**3jg** and **3jh**) in yields of 95% and 82%, respectively. Furthermore, substrates bearing heterocycles, such as the furan (**3ji**) and thiophene (**3jj**) moieties, were well-tolerated in this reaction. However, the *p*-chloro-substituted phenylsilane derivative only provided a trace amount of the expected coupling product (**3jk**).

Scheme 3. Proposed Reaction Mechanism



A plausible mechanistic pathway for the palladium-catalyzed Hiyama cross-coupling reaction is described in Scheme 3. Firstly, Pd(0) species **A** is formed in situ from $PdCl_2(CH_3CN)_2$ under the optimized reaction conditions. Subsequently, **A** underoges an oxidative addition with benzyltrimethyl-ammonium salt **1** to produce C(sp^3)−Pd complex **B** through C−N bond cleavage, releasing trimethylamine as a by product. Palladium complex **E** is then produced via transmetalation of C(sp^3)−Pd complex **B** with arylsilane **D**, the latter of which is formed via the activation of substrate **2** by TBAF.[17b, 18a] Finally, the coupling product **3** is released upon the reductive elimination of palladium complex **E**, and Pd(0) is regenerated to complete the catalytic cycle.

■ CONCLUSIONS

In summary, we have successfully developed an un-precedented palladium-catalyzed Hiyama cross-coupling reaction of benzyltrimethylammonium salts for the synthesis of diarylmethane derivatives. The relatively mild and simple reaction conditions employed, the use of readily available substrates, and the moderate to excellent yields obtained render this method synthetically attractive for organic synthesis.

■ EXPERIMENTAL SECTION

All reactions were performed in oven-dried glassware under a N_2-atmosphere unless otherwise noted. Materials were obtained from commercial suppliers and were used without further purification. All of the reactions were monitored by thin-layer chromatography (TLC); products purification was carried out using silica gel column chromatography.

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 400 MHz and Bruker AMX 400 MHz spectrometer at 400 and 100 MHz, respectively. ^{1}H NMR spectra were recorded in $CDCl_3$ and referenced to residual $CHCl_3$ at 7.26 ppm, while the ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.0 ppm. GC yields were obtained using naphthalene as an internal standard. Flash column chromatography purification was carried out by a gradient elution method using ethyl acetate (EA) in light petroleum ether (PE). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

General Procedure and Characterization Data of 3. The benzylic ammonium salts (0.20 mmol), $PdCl_2(CH_3CN)_2$ (0.01 mmol), PPh_2Cy (0.04 mmol), and TBAF (0.40 mmol) were added sequentially to an oven-dried Schlenk tube equipped with a stirrer bar. After the addition of all solid reagents, a balloon filled with N_2 was connected to the Schlenk tube via the side tube and the reaction vessel was purged three times. EtOH (2.0 mL) containing the arylsilanes (0.40 mmol) was then added to the tube via a syringe. After stirring the reaction mixture at 120 °C for 24 h, it was cooled to room temperature. The reaction was then quenched using water and extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified by silica gel preparative thin layer chromatography to give the desired product.

Diphenylmethane ***(3aa)***.[13d] Purified by column chromatography on silica gel (pure PE) to give the desired product: 29.9 mg, 89% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.23 (m, 4H), 7.23−7.16 (m, 6H), 3.98 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 141.1, 129.0, 128.5, 126.1, 42.0.

1-Benzyl-2-methylbenzene ***(3ba)***.[30] Purified by column chromatography on silica gel (pure PE) to give the desired product: 28.4 mg, 78% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.23 (m, 2H), 7.22−7.06 (m, 7H), 3.98 (s, 2H), 2.24 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.4, 139.0, 136.7, 130.3, 130.0, 128.8, 128.4, 126.5, 126.0, 125.9, 39.5, 19.7.

1-Benzyl-3-methylbenzene ***(3ca)***.[30] Purified by column chromatography on silica gel (pure PE) to give the desired product: 18.6 mg, 51% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.24 (m, 2H), 7.22−7.14 (m, 4H), 7.00 (t, J = 7.2 Hz, 3H), 3.94 (s, 2H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 141.3, 141.1, 138.1, 129.8, 129.0, 128.5, 128.4, 126.9, 126.03, 126.00, 41.9, 21.4.

1-Benzyl-4-methylbenzene ***(3da)***.[13d] Purified by column chromatography on silica gel (pure PE) to give the desired product: 30.2 mg, 83% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.23 (m, 2H), 7.21−7.15 (m, 3H), 7.12−7.04 (m, 4H), 3.94 (s, 2H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 141.5, 138.1, 135.6, 129.2, 128.9, 128.8, 128.5, 126.0, 41.6, 21.0.

1-Benzyl-3-methoxybenzene ***(3ea)***.[30] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 36.5 mg, 92% yield; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.24 (m, 2H), 7.20 (t, J = 8.2 Hz, 4H), 6.76 (dd, J = 17.3, 7.0 Hz, 3H), 3.95 (s, 2H), 3.76 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.8, 142.7, 140.9, 129.4, 128.9, 128.5, 126.1, 121.4, 114.8, 111.4, 55.2, 42.0.

1-Benzyl-4-methoxybenzene ***(3fa)***.[13d] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 30.9 mg, 83% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.24 (m, 2H), 7.22−7.14 (m, 3H), 7.12−7.06 (m, 2H), 6.86−6.77 (m, 2H), 3.91 (s, 2H), 3.76 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.0, 141.6, 133.2, 129.8, 128.8, 128.4, 125.9, 113.9, 55.2, 41.0.

1-Benzyl-4-fluorobenzene ***(3ga)***.[30] Purified by column chromatography on silica gel (pure PE) to give the desired product: 22.0 mg, 59% yield; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.25 (m, 2H), 7.23−7.09 (m, 5H), 7.00−6.91 (m, 2H), 3.95 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (d, $^1J_{C\text{-}F}$ = 243.9 Hz), 141.0, 136.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 130.3 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 128.8, 128.6, 126.2, 115.2 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 41.1.

4-Benzyl-1,2-difluorobenzene ***(3ha)***.[31] Purified by column chromatography on silica gel (pure PE) to give the desired product: 36.8 mg, 90% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.27 (m, 2H), 7.26−7.19 (m, 1H), 7.15 (dd, J = 7.8, 0.9 Hz, 2H), 7.05 (dt, J = 10.3, 8.3 Hz, 1H), 6.95 (ddd, J = 11.2, 7.6, 2.1 Hz, 1H), 6.92−6.86 (m, 1H), 3.92 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.8 (dd, $J_{C\text{-}F}$ = 132.4, 12.7 Hz), 148.4 (dd, $J_{C\text{-}F}$ = 130.8, 12.7 Hz), 140.1, 138.1 (dd, $J_{C\text{-}F}$ = 5.4, 3.9 Hz), 128.9, 128.7, 126.5, 124.6 (dd, $J_{C\text{-}F}$ = 6.1, 3.5 Hz), 117.6 (d, $J_{C\text{-}F}$ = 17.0 Hz), 117.1 (d, $J_{C\text{-}F}$ = 16.9 Hz), 41.1 (d, $J_{C\text{-}F}$ = 1.1 Hz).

1-Benzyl-4-(trifluoromethyl)benzene ***(3ia)***.[13d] Purified by column chromatography on silica gel (pure PE) to give the desired product: 18.4 mg, 39% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.1 Hz, 2H), 7.35−7.26 (m, 4H), 7.26−7.21 (m, 1H), 7.17 (d, J = 7.2 Hz, 2H), 4.03 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 145.2, 140.0, 129.2, 129.0, 128.7, 128.6 (q, $^2J_{C\text{-}F}$ = 33.0 Hz), 126.5, 125.4 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.3 (q, $^1J_{C\text{-}F}$ = 271.4 Hz), 41.7.

4-Benzylbenzonitrile ***(3ja)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 32.9 mg, 85% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59−7.51 (m, 2H), 7.35−7.19 (m, 5H), 7.15 (dd, J = 7.7, 0.9 Hz, 2H), 4.02 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.8, 139.4, 132.3, 129.7, 129.0, 128.8, 126.7, 119.0, 110.1, 42.0.

Methyl 4-benzylbenzoate ***(3ka)***.[13e] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 37.6 mg, 83% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.1 Hz, 2H), 7.34−7.21 (m, 5H), 7.17 (d, J = 7.5 Hz, 2H), 4.03 (s, 2H), 3.89 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.1, 146.5, 140.1, 129.8, 129.0, 128.6, 128.1, 126.4, 52.0, 41.9.

Tert-Butyl 4-benzylbenzoate ***(3la)***.[13d] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 47.2 mg, 88% yield; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.86 (m, 2H), 7.33−7.19 (m, 5H), 7.16 (dd, J = 7.8, 0.9 Hz, 2H), 4.02 (s, 2H), 1.58 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.8, 145.9, 140.3, 130.0, 129.7, 128.9, 128.8, 128.6, 126.3, 80.8, 41.9, 28.2.

2-Benzylnaphthalene ***(3ma)***.[32] Purified by column chromatography on silica gel (pure PE) to give the desired product: 41.0 mg, 94% yield; white solid; mp 56−58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.72 (m, 3H), 7.63 (s, 1H), 7.43 (m, 2H), 7.29 (dd, J = 11.6, 8.1 Hz, 3H), 7.21 (dd, J = 12.6, 7.1 Hz, 3H), 4.14 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.0, 138.6, 133.7, 132.1, 129.1, 128.5, 128.1, 127.67, 127.66, 127.6, 127.1, 126.2, 126.0, 125.4, 42.1.

4-(2-Methylbenzyl)benzonitrile ***(3jb)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 23.6 mg, 57% yield; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59−7.51 (m, 2H), 7.24−7.14 (m, 5H), 7.12−7.05 (m, 1H), 4.03 (s, 2H), 2.19 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.2, 137.2, 136.6, 132.3, 130.6, 130.1, 129.4, 127.1, 126.3, 119.0, 109.9, 39.6, 19.6.

4-(3-Methylbenzyl)benzonitrile ***(3jc)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 37.7 mg, 93% yield; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.32−7.23 (m, 2H), 7.22−7.15 (m, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.95 (d, J = 8.6 Hz, 2H), 3.97 (s, 2H), 2.31 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.9, 139.3, 138.5, 132.3, 129.8, 129.7, 128.7, 127.5, 126.0, 119.1, 110.0, 42.0, 21.4.

4-(4-Methylbenzyl)benzonitrile ***(3jd)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 40.2 mg, 97% yield; yellow solid; mp 60−61 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 7.2 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H), 6.96 (d, J = 7.9 Hz, 2H), 3.89 (s, 2H), 2.23 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 147.1, 136.3, 136.3, 132.3, 129.6, 129.5, 128.9, 119.1, 110.0, 41.6, 21.1.

4-(4-Methoxybenzyl)benzonitrile ***(3je)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 36.6 mg, 82% yield; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.50 (m, 2H), 7.30−7.23 (m, 2H), 7.11−7.03 (m, 2H), 6.88−6.80 (m, 2H), 3.96 (s, 2H), 3.78 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.4, 147.3, 132.3, 131.4, 130.0, 129.5, 119.0, 114.2, 110.0, 55.3, 41.1.

4-(Benzo[d][1,3]dioxol-5-ylmethyl)benzonitrile ***(3jf)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 46.0 mg, 97% yield; white solid; mp 108−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.6 Hz, 2H), 7.26 (d, J = 7.6 Hz, 2H), 6.74 (d, J = 7.7 Hz, 1H), 6.62 (d, J = 10.6 Hz, 2H), 5.92 (s, 2H), 3.93 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.0, 146.9, 146.4, 133.1, 132.3, 129.5, 122.0, 119.0, 110.1, 109.4, 108.4, 101.1, 41.7.

4-(Naphthalen-1-ylmethyl)benzonitrile ***(3jg)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 39.9 mg, 82% yield; white solid; mp 88−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.76 (m, 3H), 7.57−7.38 (m, 5H), 7.33−7.21 (m, 3H), 4.47 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.4, 134.9, 134.1, 132.3, 131.9, 129.4, 128.9, 127.9, 127.7, 126.3, 125.9, 125.6, 123.9, 119.0, 110.1, 39.2.

4-(Naphthalen-2-ylmethyl)benzonitrile ***(3jh)***.[28] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 46.2 mg, 95% yield; white solid; mp 114−116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.72 (m, 3H), 7.64−7.53 (m, 3H), 7.50−7.41 (m, 2H), 7.32 (d, J = 10.4 Hz, 2H), 7.28–7.21 (m, 1H), 4.18 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.6, 136.8, 133.6, 132.4, 132.3, 129.8, 128.5, 127.7, 127.6, 127.4, 127.3, 126.3, 125.8, 119.0, 110.2, 42.1.

4-(Furan-2-ylmethyl)benzonitrile ***(3ji)***.[33] Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 34.4 mg, 94% yield; colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.5 Hz, 3H), 6.31 (dd, J = 3.0, 1.9 Hz, 1H), 6.06 (dd, J = 3.1, 0.6 Hz, 1H), 4.02 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.6, 143.7, 142.0, 132.3, 129.4, 118.8, 110.6, 110.4, 107.0, 34.5.

4-(Thiophen-2-ylmethyl)benzonitrile ***(3jj)***. Purified by column chromatography on silica gel (PE/EtOAc = 100/1) to give the desired product: 37.5 mg, 94% yield; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.22−7.13 (m, 1H), 6.95 (dd, J = 5.0, 3.5 Hz, 1H), 6.82 (d, J = 2.5 Hz, 1H), 4.21 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.9, 141.7, 132.4, 129.4, 127.1, 125.9, 124.7, 119.0, 110.4, 36.0. HRMS (ESI, m/z) calcd for $C_{12}H_{10}NS$ $[M + H]^+$: 200.0528, found: 200.0527.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org.

Copies of ^{1}H and ^{13}C NMR spectra for all compounds

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Notes
The authors declare no competing financial interests.

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