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Synthesis of Diarylmethanes via Metal-Free Reductive Cross-Coupling of Diarylborinic Acids with Tosyl Hydrazones

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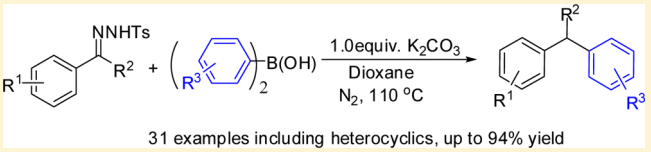
Supporting Information

ABSTRACT: This paper describes a practical and efficient procedure that takes advantage of diarylborinic acids as a cost-effective alternative to arylboronic acids for synthesis of diarylmethanes through metal-free reductive cross-coupling with *N*-tosylhydrazones of aromatic aldehydes and ketones. The procedure tolerates hydroxyl, halide, amine, and allyl functionality, complementary to the transition-metal catalyzed cross-coupling techniques.



Diarylmethanes have attracted intensive attention because of the presence of their structural motif in supramolecular architectures,[1] pharmaceuticals, and biologically active compounds,[2] such as piritrexim, papaverine, beclobrate, and dimetindene (Figure 1).

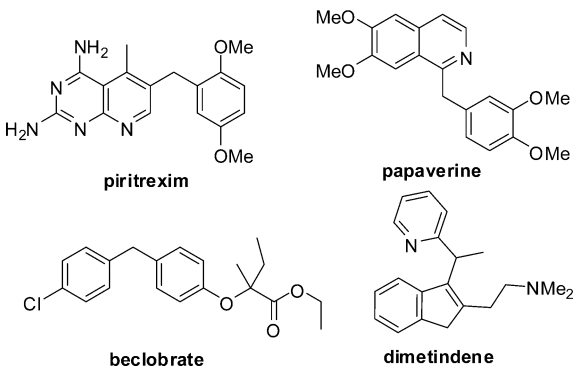


Figure 1. Selected biologically active diarylmethanes.

The direct method for synthesis of diarylmethanes is Friedel–Crafts benzylation. Although there have been many modifications to the traditional Friedel–Crafts benzylation using new catalysts and benzyl sources,[2a,3] the intrinsic problems of regioselectivity and oversubstitution, except for the presence of strong directing effects, often decrease the effectiveness of Friedel–Crafts benzylation in the synthesis of diarylmethanes. To overcome the drawbacks of Friedel–Crafts benzylation, transition-metal-catalyzed cross-coupling reactions have been extensively explored for synthesis of diarylmethanes[4] using organoboronic acids (Suzuki coupling),[4b−d] organomagnesium reagents (Kumada coupling), and zinc reagents (Negishi coupling),[4e−j] among which Suzuki coupling is particularly attractive due to the friendly properties of organoboronic acids, e.g., nontoxicity, air/moisture stability, and tolerance of a variety of functional groups. Although the transition-metal-catalyzed cross-coupling approaches have proven highly effective in the synthesis of symmetrical and unsymmetrical diarylmethanes, metal-free cross-coupling procedures are still advantageous considering the possible toxicity, cost, and metal residual in final products of transition-metal catalysts. Generally, only highly reactive substrates, such as aryl iodides[5] and allyl bromides,[6] could be used in metal-free Suzuki coupling unless unconventional conditions were applied.[7] However, Barluenga and Valdés reported a novel metal-free reductive carbon−carbon cross-coupling between *N*-tosylhydrazones and organoboronic acids under mild conditions in 2009,[8] inspiring great interest in exploring *N*-tosylhydrazones in metal-free cross-coupling reactions.[9]

Compared with arylboronic acids, high-order arylborons, e.g., diarylborinic acids ($Ar_2B(OH)$), triarylboranes (Ar_3B), and tetraarylborates ($[Ar_4B]^-$), have higher atom economy as aryl reagents and could be more economically prepared from aryl halides, boronates, and magnesium under noncryogenic conditions.[10] However, high-order arylborons have been rarely applied as aryl sources in cross-coupling.[11] We have recently found that diarylborinic acids, which have properties closest to arylboronic acids among the high-order arylborons, could take part in Suzuki coupling as efficient as arylboronic acids under proper conditions.[10c] As part of our ongoing efforts to use diarylborinic acids as a cost-effective alternative to arylboronic acids, we report herein a general and practical synthesis of symmetrical and unsymmetrical diarylmethanes through a metal-free reductive cross-coupling of tosylhydrazones with diarylborinic acids or anhydrides.

It has been well established from the elegant work by Aggarwal et al. that the key to using *N*-tosylhydrazones as a safe and effective source of active diazo compounds lies in their controllable decomposition.[12] Therefore, reaction of *N*-tosylhydrazone (**1a**) of acetophenone with bis(4-methoxyphenyl)borinic acid (**2a**) was chosen as model reaction to screen conditions for the metal-free reductive cross-coupling

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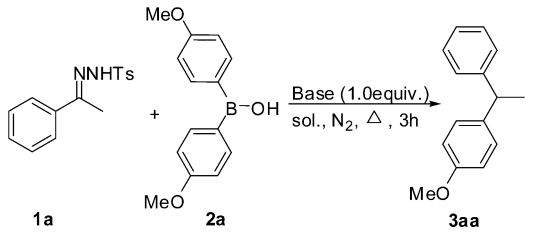
considering both of the substrates could be readily monitored by TLC (Table 1).

Table 1. Reductive Coupling of *N*-Tosylhydrazone 1a with Diarylborinic Acid 2a[a]



1a 2a 3aa

entry	base	solvent	*T* (°C)	time (h)	yield (%)[b]
1	$K_3PO_4·3H_2O$	dioxane	reflux	3	65
2	K_2CO_3	dioxane	reflux	3	92
3	Na_2CO_3	dioxane	reflux	3	26
4	NaOAc	dioxane	reflux	12	trace
5	$Ba(OH)_2·8H_2O$	dioxane	reflux	3	trace
6	KOH	dioxane	reflux	3	trace
7[c]	K_2CO_3	dioxane	reflux	6	53
8	K_2CO_3	dioxane	80	12	38[d]
9[e]	K_2CO_3	dioxane	reflux	3	92
10[f]	K_2CO_3	dioxane	reflux	6	81
11[g]	K_2CO_3	dioxane	reflux	3	94
12	K_2CO_3	pyridine	reflux	12	50[h]
13	K_2CO_3	DMF	110	6	24
14	K_2CO_3	*n*-BuOH	reflux	6	59
15	K_2CO_3	PEG-400	110	6	43
16	K_2CO_3	CH_3CN	reflux	12	15
17	K_2CO_3	THF	reflux	12	20

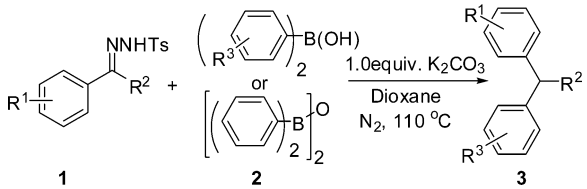
[a]Reaction conditions: **1a**, 1.0 mmol; **2a**, 0.6 mmol (1.2 equiv); solvent, 5 mL. [b]Isolated yield. [c]In air. [d]32% of **1a** was recovered. [e]2.0 equiv of K_2CO_3 was used. [f]1.0 equiv of **2a** was used. [g]1.5 equiv of **2a** (0.75 mmol) was used. [h]1,2-Bis(1-phenylethylidene)hydrazine was isolated as the major byproduct.

The model reaction proceeded smoothly to offer the desired product **3aa** in 65%, 92%, and 26% yields with a slight excess of borinic acid **2a** (1.2 equiv) after refluxing for 3 h under nitrogen in dioxane in the presence of 1.0 equiv of K_3PO_4, K_2CO_3, and Na_2CO_3, respectively, while either weaker or stronger bases, e.g., NaOAc, $Ba(OH)_2$, and KOH, failed (Table 1, entries 1–6). When the reaction was run in air, the yield of **3aa** decreased to 53% (Table 1, entry 7). Increasing the stoichiometry of bis(4-methoxyphenyl)borinic acid (**2a**) or K_2CO_3 showed no remarkable influence on the reaction while a significant decrease of **3aa** yields from 92% to 81% was observed with a loading of 1.0 equiv of **2a**, possibly due to the common side reaction of organoborons, proton deboronation (Table 1, entries 9–11).

The reaction appeared to strongly depend on solvents (Table 1, entries 12–17). Product **3aa** was isolated in low yields, and byproducts acetophenone from hydrolysis of *N*-tosylhydrazone (**1a**) and 1,2-bis(1-phenylethylidene)hydrazine from trapping the corresponding carbene by phenyldiazoethane were also isolated when the model reaction was conducted in DMF and pyridine, respectively. When the reaction was run in *n*-butanol **3aa** was isolated in 59% yield due to the formation of some 1-methylbenzyl butyl ether.[13] A metal-free cross-coupling of aryl iodides with arylboronic acids was reported to occur to afford biaryls in PEG preferably over conventional organic solvents.[5a] Therefore, we tested the model reaction in PEG-400 under otherwise identical conditions, but the coupling product **3aa** was isolated in only 43% yield. The poor performance of THF and CH_3CN in the model reaction could, at least partly, be attributed to their low boiling points considering a slow reaction observed at low temperature (80 °C) in dioxane (Table 1, entries 8, 16, and 17).

Generality of the synthesis of diarylmethanes via the metal-free reductive cross-coupling of *N*-tosylhydrazones with diarylborinic acids was investigated (Table 2). Because of the

Table 2. Scope of Cross-Coupling of *N*-Tosylhydrazones with Diarylborinic Acids[a]



1 2 3

entry	R^1/R^2 (**1**)	R^3 (**2**)	**3**	time (h)	yield[b] (%)
1	H/Me (**1a**)	H (**2b**)	**3ab**	2	78
2	H/Et (**1b**)	H (**2b**)	**3bb**	2.5	82
3	4-Br/Me (**1c**)	H (**2b**)	**3cb**	2	93
4	4-OH/Me (**1d**)	H (**2b**)	**3db**	2.5	85
5	4-NO_2/Me (**1e**)	H (**2b**)	**3eb**	2.5	35
6	4-NH_2/Me (**1f**)	H (**2b**)	**3fb**	2.5	72
7	4-MeO/H (**1g**)	H (**2b**)	**3gb**	1	92
8	4-CN/H (**1h**)	H (**2b**)	**3hb**	1	94
9	4-OH/H (**1i**)	H (**2b**)	**3ib**	1	93
10	2-OH/H (**1j**)	H (**2b**)	**3jb**	1	79
11	2-OAllyl/H (**1k**)	H (**2b**)	**3kb**	1.5	75
12	2,4-$(Cl)_2$/H (**1l**)	H (**2b**)	**3lb**	1	86
13	4-Br/Me (**1c**)	4-OMe (**2a**)	**3ca**	3	89
14	4-NO_2/Me (**1e**)	4-OMe (**2a**)	**3ea**	2	14
15	4-CN/H (**1h**)	4-OMe (**2a**)	**3ha**	1	83
16	4-OH/H (**1i**)	4-OMe (**2a**)	**3ia**	1.5	92
17	H/Me (**1a**)	4-F (**2c**)	**3ac**	2	75
18	H/Et (**1b**)	4-F(**2c**)	**3bc**	3	93
19	4-Br/Me (**1c**)	4-F (**2c**)	**3cc**	2.5	88
20	4-NO_2/Me (**1e**)	4-F (**2c**)	**3ec**	3	37
21	4-MeO/H (**1g**)	4-F(**2c**)	**3gc**	1	91
22	4-CN/H (**1h**)	4-F (**2c**)	**3hc**	1	84
23	2,4-$(Cl)_2$/H (**1l**)	4-F (**2c**)	**3lc**	1	80
24	2-OH/H (**1j**)	4-F (**2c**)	**3jc**	1.5	80
25	H/Me (**1a**)	2-Me (**2e**)	**3ae**	2.5	79
26	H/Et (**1b**)	2-Me (**2e**)	**3be**	2.5	70
27	4-Br/Me (**1c**)	4-Me (**2d**)	**3cd**	2.5	90
28	4-Br/Me (**1c**)	2-Me (**2e**)	**3ce**	2.5	71

[a]Reaction run on 1.0 mmol scale of **1** with 0.6 mmol of **2a**, **2c**–**e** or 0.3 mmol of **2b** in anhydride form in 5 mL of dioxane. [b]Isolated yield.

ready dehydration, diphenylborinic acid was used in anhydride form for convenient stoichiometry. A variety of symmetrical and unsymmetrical diarylmethanes with a wide range of functional groups, such as CN, OH, NH_2, halide, and allyl groups, could be readily obtained in good to excellent yields, while the presence of a NO_2 group in *N*-tosylhydrazones appeared to be deleterious, leading to complicated reactions and low yields (14–37%) of the desired coupling products (Table 2, entries 5, 14, and 20). The tolerance of halide and allyl groups make the metal-free method complementary to

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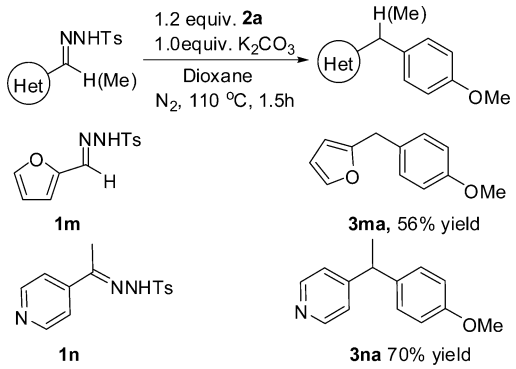
transition-metal-catalyzed techniques, which generally destroy C−X (X ≠ F) and allyl groups. Generally, *N*-tosylhydrazones of aryl alkyl ketones required longer reaction time to give comparable results than aryl aldehydes. No reaction was observed for *N*-tosylhydrazone of diphenylketone. A small steric effect was observed in the reaction with respect to both *N*-tosylhydrazones and diarylborinic acids. For example, although *N*-tosylhydrazones of propiophenone and acetophenone reacted similarly to provide the desired diarylmethanes **3ab** and **3bb** in comparable yields (78% and 82%), reaction of *N*-tosylhydrazones of 2-hydroxybenzaldehyde and 2-allyloxybenzaldehyde with diphenylborinic anhydride **2b** gave products **3jb** and **3kb** in lower yields (75 and 79%) than that of 4-hydroxybenzaldehyde (93%) (Table 2, entries 9−11). Similarly, yields of diarylmethanes from ortho-substituted diarylborinic acids, such as di(2-methylphenyl)borinic acid, were lower than those from para- or nonsubstituted ones (Table 2, entries 1, 2, and 25−28).

Electronic effects of substituents at aryl moieties of both *N*-tosylhydrazones and diarylborinic acids appeared to be negligible except for NO_2-containing *N*-tosylhydrazones that seemed to competitively decompose under the reaction conditions. For example, reaction of diphenylborinic anhydride (**2b**) with *N*-tosylhydrazones bearing both electron-donating (OH, OMe and NH_2) and -withdrawing (CN and Cl) groups at the para-position of the benzene ring proceeded similarly with respect to rate and yields (Table 2, entries 4, 6, 7, 8, and 12). *p*-Methoxy- (**2a**) and *p*-fluoro-substituted (**2c**) diarylborinic acids also showed little difference from diphenylborinic anhydride (**2b**) in the reaction. It is worth pointing out that, in all of the cases investigated, hydroxyl and amino groups on aromatic rings of *N*-tosylhydrazones survived, and no aryl ether or amine product was detected in our experiments although that oxygen and sulfur ethers could be synthesized from reaction of *N*-tosylhydrazones with phenols and arylthiols, respectively, under similar conditions.[13] Reaction of *N*-tosylhydrazones of heterocyclic carbonyls, such as 2-fufural (**1m**) and 4-acetylpyridine (**1n**), with **2a** also afforded the desired products **3ma** and **3na** in 56% and 70% yields, respectively (Scheme 1).

Scheme 1. Synthesis of Pyridyl/Furylarylmethanes



In conclusion, metal-free reductive cross-coupling of *N*-tosylhydrazones of aromatic aldehydes and aryl alkyl ketones with diarylborinic acids or anhydrides was shown to be a practical and efficient protocol for synthesis of diarylmethanes under mild conditions in good yields. The higher process and atom economies of diarylborinic acids over arylboronic acids promise a more cost-effective synthesis of diarylmethanes. The other features of this procedure include elimination of possible toxicity, cost, and metal residual of transition-metal catalysts, and tolerance of hydroxyl, halide, amine, and allyl functionality, thus complementary to the transition-metal catalyzed cross-coupling techniques.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a nitrogen atmosphere unless otherwise stated. Commercially available chemicals were used as received. *N*-Tosylhydrazones[14] and diarylborinic acids[10c] were prepared according to previously reported procedures. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at ambient temperature. Chemical shifts in NMR were reported in ppm (δ), relative to the internal standard of tetramethylsilane (TMS). The signals observed were described as s (singlet), d (doublet), t (triplet), dd(double doublet), m (multiplets), br (board). The number of protons (n) for a given resonance was indicated as nH. Coupling constants were reported as *J* in hertz. The high-resolution mass spectra (HRMS) were performed on an electron ionization mass spectrometer with a quadrupole analyzer.

General Procedure for Reductive Coupling Reaction. Under a N_2 atmosphere, to a 10 mL flask were added *N*-tosylhydrazone (1.0 mmol), diarylborinic acid (0.6 mmol) or anhydride (0.3 mmol), K_2CO_3 (1.0 mmol), and dioxane (5 mL). The mixture was stirred at 110 °C and monitored by TLC until *N*-tosylhydrazone was completely consumed. The reaction mixture was diluted with CH_2Cl_2 (20 mL), followed by washing twice with H_2O (2 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated under reduced pressure to give crude product diarylmethane, which was purified by column chromatography on silica gel with EtOAc/petroleum ether.

1-Methoxy-4-(1-phenylethyl)benzene (**3aa**):[15] colorless liquid (0.195 g, 92%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27−7.12 (m, 7H), 6.82 (d, *J* = 8.4 Hz, 2H), 4.10 (q, *J* = 7.2 Hz, 1H), 3.76 (s, 3H), 1.61 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.8, 145.7, 137.5, 127.4, 127.3, 126.5, 124.9, 112.7, 54.1, 42.9, 21.0.

Ethane-1,1-diyldibenzene (**3ab**):[3a] colorless liquid (0.142 g, 78%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29−7.15 (m, 10H), 4.14 (q, *J* = 7.2 Hz, 1H), 1.63 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.5, 128.5, 127.7, 126.1, 44.9, 22.0.

Propane-1,1-diyldibenzene (**3bb**):[16] colorless liquid (0.161 g, 82%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27−7.21 (m, 8H), 7.16−7.12 (m, 2H), 3.77 (t, *J* = 8.0 Hz, 1H), 2.10−2.02 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.3, 128.5, 128.1, 126.2, 53.4, 28.7, 12.9.

1-Bromo-4-(1-phenylethyl)benzene (**3cb**):[3a] light yellow liquid (0.243 g, 93%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, *J* = 8.4 Hz, 2H), 7.30−7.26 (m, 2H), 7.20−7.17 (m, 3H), 7.08 (d, *J* = 8.4 Hz, 2H), 4.10 (q, *J* = 7.2 Hz, 1H), 1.61 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.8, 145.5, 131.5, 129.5, 128.6, 127.6, 126.4, 119.9, 44.3, 21.9.

4-(1-Phenylethyl)phenol (**3db**):[17] light yellow liquid (0.168 g, 85%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26 (t, *J* = 7.2 Hz, 2H), 7.19−7.14 (m, 3H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 7.6 Hz, 2H), 5.37 (br. s, 1H), 4.06 (q, *J* = 7.2 Hz, 1H), 1.58 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.7, 147.0, 138.9, 128.9, 128.6, 127.7, 126.2, 115.5, 44.1, 22.2.

1-Nitro-4-(1-phenylethyl)benzene (**3eb**):[18] yellow liquid (0.079 g, 35%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (dd, *J* = 2.0, 6.8 Hz, 2H), 7.30−7.21 (m, 4H), 7.17−7.10 (m, 3H), 4.17 (q, *J* = 7.2 Hz, 1H), 1.59 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.1, 146.4, 144.6, 128.7, 128.5, 127.6, 126.7, 123.7, 44.8, 21.5.

4-(1-Phenylethyl)aniline (**3fb**):[19] yellow liquid (0.142 g, 72%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26−7.15 (m, 5H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.59 (d, *J* = 8.4 Hz, 2H), 4.04 (q, *J* = 7.2 Hz, 1H), 3.51 (br. s, 2H), 1.58 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.3, 144.6, 136.6, 128.5, 128.4, 127.7, 126.0, 115.3, 44.0, 22.2.

1-Benzyl-4-methoxybenzene (**3gb**):[20] light yellow liquid (0.182 g, 92%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29−7.25 (m, 2H), 7.22−7.15 (m, 3H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 3.92 (s,

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2H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.9, 140.5, 132.2, 128.8, 127.7, 127.4, 124.9, 112.8, 54.1, 40.0.

4-Benzylbenzonitrile (**3hb**):[15] colorless liquid (0.182 g, 94%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55 (d, J = 8.0 Hz, 2H), 7.36−7.21 (m, 5H), 7.15 (d, J = 7.2 Hz, 2H), 4.02 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.8, 139.4, 132.3, 129.7, 129.0, 128.8, 126.7, 119.1, 110.0, 42.0.

4-Benzylphenol (**3ib**):[15] white solid (0.171 g, 93%); mp 83−84 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.18−7.15 (m, 2H), 7.10−7.05 (m, 3H), 6.93−6.91 (m, 2H), 6.64−6.61 (m, 2H), 5.35 (br. s, 1H), 3.79 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.7, 141.6, 133.6, 130.2, 128.9, 128.6, 126.1, 115.5, 41.1.

2-Benzylphenol (**3jb**):[21] yellow liquid (0.145 g, 79%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.27 (m, 2H), 7.23−7.18 (m, 3H), 7.14−7.10 (m, 2H), 6.88 (t, J = 7.2 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 4.78 (br. s, 1H), 3.99 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.8, 140.1, 131.1, 128.8, 128.7, 127.9, 127.2, 126.4, 121.0, 115.8, 36.4.

1-(Allyloxy)-2-benzylbenzene (**3kb**):[22] colorless liquid (0.168 g, 75%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27−7.07 (m, 7H), 6.89−6.82 (m, 2H), 6.05−5.95 (m, 1H), 5.36 (dd, J = 1.6, 17.2 Hz, 1H), 5.23 (dd, J = 1.6, 10.4 Hz, 1H), 4.51 (d, J = 4.8 Hz, 2H), 4.00 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.4, 141.2, 133.6, 130.6, 130.2, 129.1, 128.3, 127.5, 125.9, 120.8, 117.1, 111.8, 68.8, 36.2.

1-Benzyl-2,4-dichlorobenzene (**3lb**):[23] light yellow liquid (0.204 g, 86%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, J = 2.4 Hz, 1H), 7.31−7.14 (m, 6H), 7.05 (d, J = 8.4 Hz, 1H), 4.06 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.0, 137.4, 134.9, 132.7, 131.8, 129.4, 129.0, 128.7, 127.2, 126.6, 38.7.

1-Bromo-4-(1-(4-methoxyphenyl)ethyl)benzene (**3ca**):[17] colorless liquid (0.259 g, 89%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30 (d, J = 8.4 Hz, 2H), 7.03−6.98 (m, 4H), 6.75 (d, J = 8.8 Hz, 2H), 3.98 (q, J = 7.2 Hz, 1H), 3.70 (s, 3H), 1.50 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.9, 144.7, 136.7, 130.3, 128.3, 127.4, 118.6, 112.8, 54.1, 42.3, 20.9.

1-Methoxy-4-(1-(4-nitrophenyl)ethyl)benzene (**3ea**):[18] yellow liquid (0.036 g, 14%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 4.12 (q, J = 7.2 Hz, 1H), 3.70 (s, 3H), 1.56 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.3, 154.5, 146.3, 136.7, 128.5, 128.4, 123.7, 114.1, 55.3, 44.0, 21.7.

4-(4-Methoxybenzyl)benzonitrile (**3ha**):[8] white solid (0.185 g, 83%); mp 48−49 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 3.96 (s, 2H), 3.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.4, 147.3, 132.3, 131.5, 130.0, 129.6, 119.1, 114.2, 109.9, 55.3, 41.1.

4-(4-Methoxybenzyl)phenol (**3ia**):[15] light yellow solid (0.197 g, 92%); mp 81−82 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.06 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 5.75 (br. s, 1H), 3.82 (s, 2H), 3.75 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.8, 153.9, 134.0, 133.8, 130.0, 129.9, 115.4, 114.0, 55.4, 40.2.

1-Fluoro-4-(1-phenylethyl)benzene (**3ac**):[3a] light yellow liquid (0.150 g, 75%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.26 (m, 2H), 7.20−7.14 (m, 5H), 6.98−6.93 (m, 2H), 4.13 (q, J = 7.2 Hz, 1H), 1.61 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.4 (d, J = 242.4 Hz), 146.3, 142.1 (d, J = 3.1 Hz), 129.1 (d, J = 7.7 Hz), 128.5, 127.6, 126.3, 115.2 (d, J = 20.9 Hz), 44.1, 22.1.

1-Fluoro-4-(1-phenylpropyl)benzene (**3bc**): light yellow liquid (0.199 g, 93%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29−7.16 (m, 7H), 6.95 (t, J = 8.8 Hz, 2H), 3.77 (t, J = 8.0 Hz, 1H), 2.08−2.00 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.3 (d, J = 242.3 Hz), 145.0, 140.9 (d, J = 3.0 Hz), 129.3 (d, J = 7.7 Hz), 128.5, 127.9, 126.2, 115.1 (d, J = 21.0 Hz), 52.5, 28.8, 12.8; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{15}F$ 214.1158, found 214.1163.

1-Bromo-4-(1-(4-fluorophenyl)ethyl)benzene (**3cc**):[3a] light yellow liquid (0.245 g, 88%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, J = 8.4 Hz, 2H), 7.15−7.11 (m, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.98−6.94 (m, 2H), 4.08 (q, J = 7.2 Hz, 1H), 1.59 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.4 (d, J = 242.9 Hz), 145.3, 141.5 (d, J = 3.1 Hz), 131.6, 129.4, 129.0 (d, J = 7.6 Hz), 120.0, 115.3 (d, J = 21.1 Hz), 43.6, 22.0.

1-Fluoro-4-(1-(4-nitrophenyl)ethyl)benzene (**3ec**): yellow liquid (0.091 g, 37%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.8 Hz, 2H), 7.08−7.05 (m, 2H), 6.92−6.88 (m, 2H), 4.15 (q, J = 7.2 Hz, 1H), 1.57 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.5 (d, J = 243.7 Hz), 152.8, 145.4, 139.2 (d, J = 3.1 Hz), 128.0 (d, J = 7.8 Hz), 127.3, 122.7, 114.4 (d, J = 21.1 Hz), 43.0, 20.6; HRMS (EI) m/z (M^+) calcd for $C_{14}H_{12}FNO_2$ 245.0852, found 245.0855.

1-Fluoro-4-(4-methoxybenzyl)benzene (**3gc**):[24] colorless liquid (0.197 g, 91%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.05−6.98 (m, 4H), 6.89−6.84 (m, 2H), 6.75 (d, J = 8.8 Hz, 2H), 3.80 (s, 2H), 3.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.3 (d, J = 242.2 Hz), 157.0, 136.2 (d, J = 3.1 Hz), 132.0, 129.1 (d, J = 7.7 Hz), 128.7, 114.1 (d, J = 21.1 Hz), 112.9, 54.1, 39.1.

4-(4-Fluorobenzyl)benzonitrile (**3hc**):[25] light yellow liquid (0.177 g, 84%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.01 (dd, J = 5.6, 12.4 Hz, 2H), 7.00−6.86 (m, 2H), 4.00 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.6 (d, J = 243.5 Hz), 145.5, 134.1 (d, J = 3.3 Hz), 131.3, 129.4 (d, J = 7.9 Hz), 128.5, 117.9, 114.5 (d, J = 21.1 Hz), 109.1, 40.0.

2,4-Dichloro-1-(4-fluorobenzyl)benzene (**3lc**): light yellow liquid (0.204 g, 80%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (s, 1H), 7.18−6.95 (m, 6H), 4.02 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.6 (d, J = 243.3 Hz), 137.2, 134.8, 134.6 (d, J = 3.2 Hz), 132.9, 131.7, 130.3 (d, J = 7.9 Hz), 129.4, 127.2, 115.4 (d, J = 21.2 Hz), 37.9. HRMS (EI) m/z (M^+) calcd for $C_{13}H_9Cl_2F$ 254.0065, found 254.0061.

2-(4-Fluorobenzyl)phenol (**3jc**):[2d] Light yellow liquid (0.162 g, 80%), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.21−7.06 (m, 4H), 6.96−6.86 (m, 3H), 6.73 (d, J = 7.6 Hz, 1H), 4.93 (br. s, 1H), 3.93 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.5 (d, J = 242.3 Hz), 153.6, 135.8, 130.9, 130.2 (d, J = 7.8 Hz), 127.9, 127.1, 121.1, 115.7, 115.3 (d, J = 21.1 Hz), 35.4.

1-Methyl-2-(1-phenylethyl)benzene (**3ae**):[3c] colorless liquid (0.155 g, 79%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28−7.11 (m, 9H), 4.31 (q, J = 7.2 Hz, 1H), 2.22 (s, 3H), 1.60 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.4, 144.0, 136.2, 130.5, 128.4, 127.8, 126.8, 126.2, 126.1, 125.9, 41.1, 22.3, 19.9.

1-Methyl-2-(1-phenylpropyl)benzene (**3be**):[26] colorless liquid (0.147 g, 70%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33−7.09 (m, 9H), 3.97 (t, J = 7.6 Hz, 1H), 2.25 (s, 3H), 2.05 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.9, 143.0, 136.5, 130.6, 128.4, 128.3, 126.7, 126.1, 126.0, 125.9, 48.9, 29.2, 20.1, 13.0.

1-Bromo-4-(1-p-tolylethyl)benzene (**3cd**): light yellow liquid (0.248 g, 90%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.36 (m, 2H), 7.10−7.06 (m, 6H), 4.06 (q, J = 7.2 Hz, 1H), 2.30 (s, 3H), 1.59 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.8, 142.9, 135.9, 131.5, 129.5, 129.3, 127.5, 119.9, 44.0, 22.0, 21.2; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{15}Br$ 274.0357, found 274.0359.

1-(1-(4-Bromophenyl)ethyl)-2-methylbenzene (**3ce**): light yellow liquid (0.195 g, 71%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36 (d, J = 8.4 Hz, 2H), 7.24−7.11 (m, 4H), 7.01 (d, J = 8.4 Hz, 2H), 4.26 (q, J = 7.2 Hz, 1H), 2.20 (s, 3H), 1.57 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.4, 143.3, 136.1, 131.5, 130.6, 129.6, 126.7, 126.5, 126.3, 119.7, 40.6, 22.1, 19.8; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{15}Br$ 274.0357, found 274.0359.

2-(4-Methoxybenzyl)furan (**3ma**):[27] colorless liquid (0.105 g, 56%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22 (d, J = 1.2 Hz, 1H), 7.06 (d, J = 8.8 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 6.19 (dd, J = 2.8, 1.6 Hz, 1H), 5.88 (d, J = 2.8 Hz, 1H), 3.81 (s, 2H), 3.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.3, 155.1, 141.4, 130.2, 129.7, 113.9, 110.3, 106.0, 55.3, 33.6.

4-(1-(4-Methoxyphenyl)ethyl)pyridine (**3na**):[8] light yellow liquid (0.149 g, 70%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.50 (br s, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 4.07 (q, J = 7.8 Hz, 1H), 3.78 (s, 3H), 1.61 (d, J = 8.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.3, 156.3, 136.3, 128.6, 123.2, 114.0, 55.3, 43.5, 21.2.

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■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all compounds and HRMS for new compounds reported. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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