JOC*Article*

The Palladium-Catalyzed Addition of Aryl- and Heteroarylboronic Acids to Aldehydes

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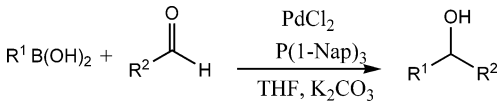

R^1 = Ar , Het-Ar

R^2 = Ar or $PhCH_2CH_2$-

Reaction of aryl- or heteroarylboronic acids with aldehydes, in the presence of $PdCl_2$ and $P(1\text{-Nap})_3$, afforded carbinol derivatives in good to excellent yields. The efficiency of this reaction was demonstrated by the compatibility with nitro, cyano, acetamido, acetoxy, acetyl, carboxyl, trifluoromethyl, fluoro, and chloro groups and the possibility of involving aliphatic aldehyde or hindered substrates. Moreover, the rigorous exclusion of air/moisture is not required in these transformations.

Introduction

In the past few years, great strides have been made in the development of catalytic methods for addition of organometallics reagents to unsaturated C—C,[1] C═O,[2] C≡N,[3] N═N[4] and C═N bonds.[5] Recent publications describing the rhodium-catalyzed addition of organoboron reagents to aldehydes deserve particular mention.[6] Such transformations have drawn considerable interest not only because organoboron reagents enjoy high prestige in the metal-catalyzed C—C bond formation thanks to their advantages of low toxicity, stability to air or moisture, and good functional group tolerance,[7] but also due to the versatility of the addition products, which are important precursors for the synthesis of a number of pharmacologically active compounds. For example, the 1,1-diarylalkyl structural element is found in compounds with reported activity as antimuscarinics,[8] antidepressants,[9] and endothelin antagonists.[10] As such, there is a need for practical synthetic methodologies for the preparation of a wide variety of carbinol derivatives.

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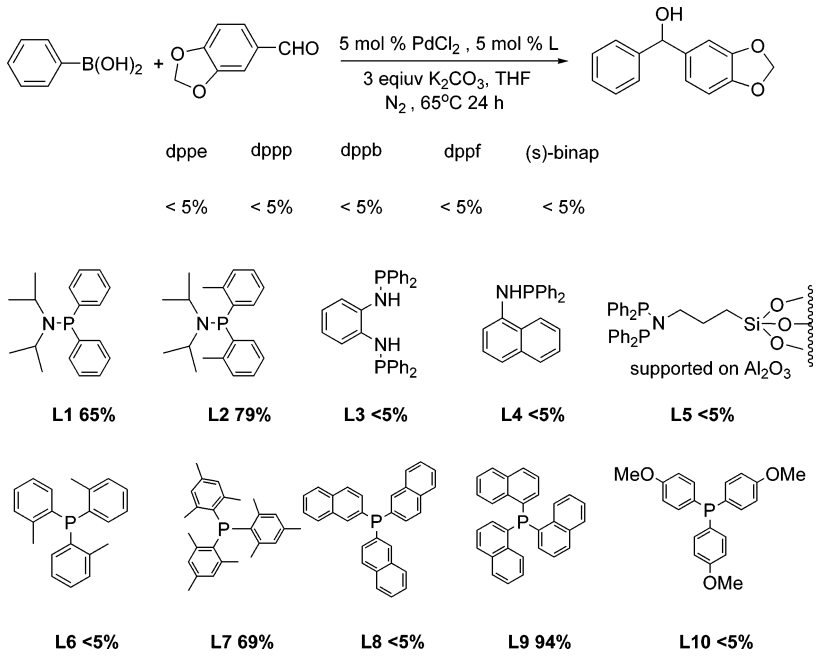
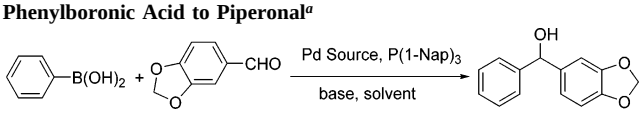
CHART 1. Ligand Screening



However, less attention has been paid to the corresponding palladium-catalyzed transformation. The phosphapalladacyclic complex described by Cole-Hamilton and co-workers catalyzes the 1,2-addition of phenylboronic acid to 4-chlorobenzaldehyde.[11] The palladium complex with chloroform described by Ohta and co-workers catalyzes the 1,2-addition of arylboronic acids to aldehydes.[12] Aoyama, Kondo, and co-workers reported the chloroform-free version of $Pd(OAc)_2$-(±)-tol-binap catalyzes the arylation reaction of aromatic aldehydes with arylboronic acids in the presence of strong base NaO^tBu.[13] Very recently, Hu and co-workers reported anionic four-electron donor-based palladacycles as catalysts for addition reactions of arylboronic acids with α,β-unsaturated ketones, aldehydes, and α-ketoesters.[14]

However, among the conditions described above, examples of using hindered substrates or involving heteroarylboronic acid and aliphatic aldehydes under an air atmosphere for general palladium-catalyzed addition to aldehydes are scarce. Our interest in the development of palladium-catalyzed chemistry led us to explore the possibility of using a simple catalytic system for such transformations. Herein, we report an efficient Pd-catalyzed addition of aryl- or heteroarylboronic acids to

TABLE 1. Effects of Pd Sources, Bases, Solvents, and the Amounts of Ligand on the Palladium-Catalyzed Addition of Phenylboronic Acid to Piperonal[a]



entry	Pd source	base	solvent	L/Pd ratio	yield (%)[b]	yield (%)[c]
1	$PdCl_2$	K_2CO_3	THF	1	94	95
2	$Pd(OAc)_2$	K_2CO_3	THF	1	38	28
3	$PdCl_2(PPh_3)_2$	K_2CO_3	THF	1	16	35
4	$PdCl_2(PhCN)_2$	K_2CO_3	THF	1	50	77
5	$Pd(PPh_3)_4$	K_2CO_3	THF	1	56	74
6	$Pd_2(dba)_3$	K_2CO_3	THF	1	70	80
7	Pd/C	K_2CO_3	THF	1	<5	<5
8	$PdCl_2$	Na_2CO_3	THF	1	70	69
9	$PdCl_2$	$KF{\cdot}2H_2O$	THF	1	79	70
10	$PdCl_2$	DMAP	THF	1	<5	<5
11	$PdCl_2$	DABCO	THF	1	<5	<5
12	$PdCl_2$	$^i Pr_2NEt$	THF	1	<5	<5
13	$PdCl_2$	DBN	THF	1	<5	<5
14	$PdCl_2$	K_2CO_3	THF	2	89	90
15	$PdCl_2$	K_2CO_3	THF	3	88	89
16	$PdCl_2$	K_2CO_3	DMF	1	<5	<5
17	$PdCl_2$	K_2CO_3	CH_3CN	1	<5	<5
18	$PdCl_2$	K_2CO_3	toluene	1	35	69

[a] All reactions were run with piperonal (1.0 mmol), phenylboronic acid (2.0 mmol), base (3.0 mmol), Pd source (5 mol %), and indicated P(1-Nap)$_3$/Pd ratio in 5 mL of solvent at 65 °C for 24 h. [b] Isolated yield and reaction was conducted under N_2 atmosphere and dry solvent. [c] Isolated yield and reaction was conducted under air and undried solvents.

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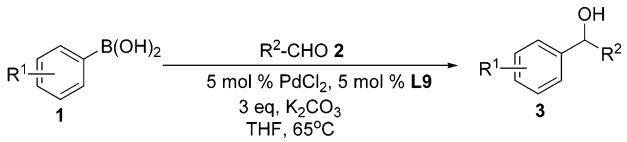
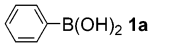
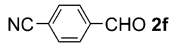
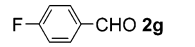
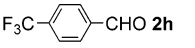
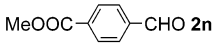
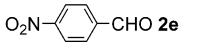
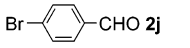
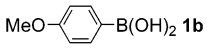
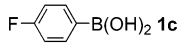
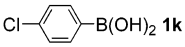
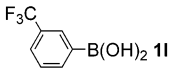
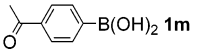
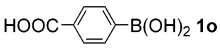
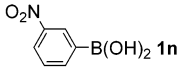
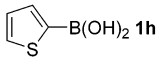
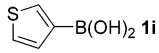
TABLE 2. Addition Aryl- and Heteroarylboronic Acids to Electron-Deficient Aldehydes



entry	boronic acids	R^2-CHO	addition product	time (h)	% isolated yield[a]
1	 **1a**	 **2f**	**3af**	8	96(98)
2	**1a**	 **2g**	**3ag**	10	96(99)
3	**1a**	 **2h**	**3ah**	0.5	98(99)
4	**1a**	 **2n**	**3an**	12	95(96)
5	**1a**	 **2e**	**3ae**	0.5	98(99)
6	**1a**	 **2j**	**3aj**	10	59(65)[b]
7	 **1b**	**2e**	**3be**	1	96(97)
8	 **1c**	**2e**	**3ce**	0.5	94(91)
9	 **1k**	**2e**	**3ke**	0.5	98(99)
10	 **1l**	**2e**	**3le**	1.5	93(91)
11	 **1m**	**2e**	**3me**	20	51(71)
12	 **1o**	**2e**	**3oe**	24	56(35)
13	 **1n**	**2e**	**3ne**	16	55(80)
14	 **1h**	**2e**	**3he**	24	39(66)
15	 **1i**	**2e**	**3ie**	24	83(93)

[a] N_2 atmosphere and dry solvent (in the parentheses); air atmosphere and undried solvents (out of the parentheses). [b] Biphenyl-4-yl(phenyl)methanol was obtained.

aldehydes, using inorganic base and easily prepared P(1-Nap)$_3$ in common organic solvent, providing carbinol derivatives in one pot with yields ranging from moderate to excellent.

Results and Discussions

Initial studies of the reaction conditions were conducted by using the common PPh_3 as ligand and the addition of phenylboronic acid to piperonal as a model reaction. However, despite extensive investigation with a variety of parameters, such as Pd sources, bases, solvents, and PPh_3/Pd ratios, no synthetically useful results were obtained with use of this approach (see the Supporting Information). Since ligands always play important roles in metal-catalyzed chemistry,[15] we then turned our attention to the screening of ligands (Chart 1).

Through the screening progress, it was observed that the electronic effect and steric hindrance played important roles in this system. In the rhodium-catalyzed reaction,[6f] such a transformation was induced by phosphane complexes having a large P−Rh−P angle, which may affect the rate of carbonyl insertion into the Rh−C bond. Thus, monodentate phosphanes and dppe were ineffective to some degree; nevertheless, dppp[6f] and dppb[6b] exhibited high catalytic activity in such a rhodium-catalyzed transformation. In our system, however, ligands such as dppe, dppp, dppb, **L6**, **L8**, and **L10** have no catalytic activity. Bidentate phosphines with large bite angles with rhodium such

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(11) Gibson, S.; Foster, D. F.; Eastham, G. R.; Tooze, R. P.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 779.
(12) Yamamoto, T.; Ohta, T.; Ito, Y. *Org. Lett.* **2005**, *7*, 4153.
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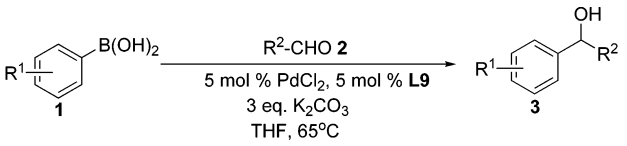
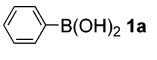
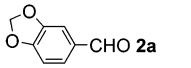
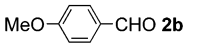
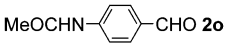
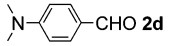
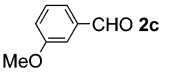
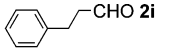
TABLE 3. Addition Arylboronic Acids to 3-Phenylpropanal or Electron-Rich Aldehydes



entry	aryl boronic acids	R^2-CHO	addition product	time (h)	% isolated yield[a]
1	 **1a**	 **2a**	**3aa**	24	94(95)
2	**1a**	 **2b**	**3ab**	24	67(64)
3	**1a**	 **2o**	**3ao**	24	41(49)
4	**1a**	 **2d**	**3ad**	24	40(41)
5	**1a**	 **2c**	**3ac**	20	90(91)
6	**1a**	 **2i**	**3ai**	24	91(95)
7	**1b**	**2a**	**3ba**	18	89(90)

[a] N_2 atmosphere and dry solvents (in the parentheses); air atmosphere and undried solvents (out of the parentheses).

as dppf[6b,h] were excellent ligands in such transformations of rhodium-catalyzed addition reactions; nevertheless, ligands such as dppf and (s)-binap were much less effective ligands in our reaction. To our delight, aminophisphine ligands **L1** and **L2** gave the desired product with isolated yield in 65% and 79%, respectively, but aminophisphine ligands **L3**, **L4**, and **L5** were unexpectedly totally ineffective. It should be noted that monodentate phosphanes **L7** with a mean C−P−C angle of 109.7°,[15a] a large value reported for a free phosphine, could furnish the desired 3-dihydroisobenzofuran-5-yl(phenyl)methanol in 69% isolated yield. Interestingly, only when the phosphine was changed to the bulky, electron-rich P(1-Nap)$_3$ **L9** did the yield dramatically increased to 94%.

Further investigations into the optimization of the reaction conditions, such as palladium catalysts, the ratio of Pd/**L9**, bases, and solvents for phenylation of piperonal are listed in Table 1.

Among the palladium sources used, $PdCl_2$, $Pd(OAc)_2$, $PdCl_2(PPh_3)_2$, $PdCl_2(PhCN)_2$, $Pd_2(dba)_3$, Pd/C, and $Pd(PPh_3)_4$, $PdCl_2$ exhibited the highest catalytic activity. Increasing the amount of **L9** in the system had little influence on the yield (Table 1, entries 14 and 15). K_2CO_3 was superior to some other bases such as Na_2CO_3, KF·2H$_2$O, DMAP, ^{i}Pr$_2$NEt, DBN, and DABCO. The choice of solvent was also crucial to the success of the catalytic reaction. THF appeared to be the best among the common solvents such as DMF, CH_3CN, and toluene employed.

For the next stage, we explored the scope of the addition reaction in the presence of a variety of functional groups. As shown in Tables 2 and 3, the addition reaction proceeded smoothly in the presence of a large variety of functional groups including nitro, cyano, acetamido, acetoxy, acetyl, carboxyl, trifluoromethyl, fluoro, and chloro groups.

Furthermore, electron-withdrawing aldehydes reacted with organoboronic acids easily and gave biarylmethanols in high yield. Interestingly, 4-chlorophenylboronic acid could proceed smoothly with **2e** to afford **3ke** in 99% isolated yield and keep the chloro group untouched. On the other hand, electron-rich aldehydes gave the corresponding secondary alcohol in relatively low yields. However, as for the **2a** and **2c**, high yields were still obtained in 95% and 91%, respectively (Table 3, entries 1 and 5). Even if the amount of $PdCl_2$ was decreased to 2.5 mol %, **3aa** was still isolated with the yield of 80%. Of particular note was the addition of phenylboronic acid to 3-phenylpropanal, which proceeded at the standard condition to give a 95% yield of isolated product **3ai** (Table 3, entry 6). Arylboronic acids with an electron-withdrawing substituted group, which are less nucleophilic and, hence, transmetalate more slowly than electron-neutral analogues, are prone to homocoupling and protodeboronation side reactions.[16] In our system, however, **1c**, **1*l***, and **1n** could proceed smoothly with **2e**, and the products **3ce**, **3*l*e**, and **3ne** were isolated in 91%, 91%, and 80% yield, respectively (Table 2, entries 8, 10, and 13). Although the heteroatoms in the heteroarylboronic acid may coordinate to transition metal,[17] heteroarylboronic acids such as **1h** and **1i** were still good patterns in this procedure, and once again, the coupling products were isolated in 66% and 93% yield, respectively (Table 2, entries 14 and 15).

Having demonstrated the utility of the addition reaction conditions on a number of functional groups, mostly at the para position, we chose to test the generality of the functional group tolerance at the ortho position. As shown in Table 4.

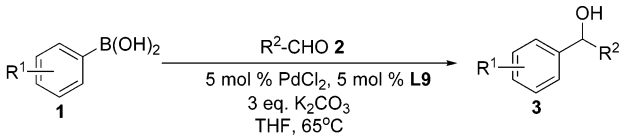
A monosubstitution in the ortho position of one or both of the coupling partners did not alter their reactivity. For

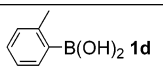
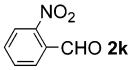
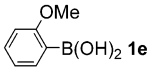
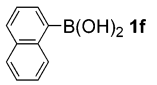
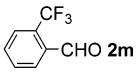
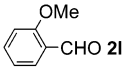
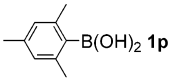
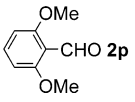
(15) (a) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313. (b) Braga, A. A. C.; Morgon, N. H.; Ujaque, G.; Liedós, A.; Maseras, F. *J. Organomet. Chem.* **2006**, *691*, 4459. (c) Braga, A. A. C.; Morgon, N. H.; Ujaque, G.; Maseras, F. *J. Am. Chem. Soc.* **2005**, *127*, 9298. (d) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685. (e) Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **1995**, *14*, 3081. (f) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176.

(16) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685 and references therein.

(17) (a) Yang, Y. *Synth. Commun.* **1989**, *19*, 1001. (b) Menard, F.; Chapman, T. M.; Dockendorff, C.; Lautens, M. *Org. Lett.* **2006**, *8*, 4569.

TABLE 4. Addition Crowded Arylboronic Acids to Crowded Aldehydes



entry	aryl boronic acids	R^2-CHO	addition product	time (h)	% isolated yield[a]
1	 **1d**	**2e**	**3de**	12	94(94)
2	**1d**	 **2k**	**3dk**	12	97(98)
3	 **1e**	**2k**	**3ek**	12	98(98)
4	 **1f**	**2k**	**3fk**	3	98(98)
5	**1e**	 **2m**	**3em**	12	85(89)
6	**1e**	 **2l**	**3el**	12	98(98)
7	 **1p**	**2e**	**3pe**	24	<5
8	**1a**	 **2p**	**3ap**	24	<5

[a] N_2 atmosphere and dry solvent (in the parentheses), 24 h; air atmosphere and undried solvents (out of the parentheses), indicated time.

example, **1d**, **1e**, and **1f** could react with **2k** to furnish **3dk**, **3ek**, and **3fk** in 97%, 98%, and 98% isolated yield, respectively (Table 4, entries 2, 3, and 4). Moreover, **1e** could react with **2m** and **2*l*** to afford **3em** and **3e*l*** in 89% and 98% isolated yield, respectively (Table 4, entries 5 and 6). Disappointingly, the feasibility of access to highly hindered diarylmethols by use of di-ortho-substituted and electron-rich 2,6-dimethoxylbenzaldehyde or mesitylboronic acid failed. To the best of our knowledge, examples of such transformation using heteroarylboronic acid or involving such hindered substrates as well as compatibility with so many functional groups such as nitro, cyano, acetamido, acetoxy, acetyl, carboxyl, trifluoromethyl, fluoro, and chloro groups are scarce or have not been reported before.

We continued our investigation by exploring the reaction time for each substrate, and the rate of reaction of the electron-deficient aldehydes is higher than those of electron-rich aldehydes, which may partly be due to the electron-rich substituted groups weakened C═O bond activity. Moreover, the rigorous exclusion of air/moisture is not required in these transformations, and comparable results are obtained in the presence of air and undried solvents as well as in the absence of air and freshly distilled solvent. As such, this represents an exceedingly practical method for the synthesis of carbinol derivatives and offers an attractive alternative to traditional strong organometallic addition procedures.

Conclusions

The addition reaction of aryl- and heteroarylboronic acids with aldehydes catalyzed by the combination of a simple palladium precursor and easy-handling P(1-Nap)$_3$ has proved to be efficient and versatile and may provide potential opportunities in the synthesis of multifunctional carbinol derivatives. Mechanistic investigations[18] and the application to asymmetric synthesis is currently in progress in our laboratory.

Experimental Section

General Procedure. A Schlenk reaction tube was charged with $PdCl_2$ (8.8 mg, 0.05 mmol), **L9** (20.6 mg, 0.05 mmol), organoboronic acid (2.0 mmol), aldehyde (1.0 mmol), K_2CO_3 (414 mg, 3 mmol), and THF (5 mL). The reaction tube was purged with N_2 under −40 °C. The mixture was stirred for 0.5 h at room temperature. Then, the mixture was heated at 65 °C for 24 h, then cooled to room temperature. The reaction mixture was extracted with diethyl ether (3 × 10 mL). The combined ether extracts were concentrated in vacuo and the residue was purified by flash column chromatography on silica gel to give the desired product.

2-Nitrophenyl(*o*-tolyl)methanol (3dk): mp 93−94 °C; IR (KBr, cm^{-1}) 3295 (−OH), 3015, 1608, 1524, 1490, 1462, 1344, 1301, 1016, 849, 790, 759, 733, 688, 676; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.25 (s, 3H), 2.81 (d, J = 4.7 Hz, 1H), 6.55 (d, J = 4.6 Hz, 1H), 7.18−7.24 (m, 4H), 7.45−7.59 (m, 3H), 7.96 (d, J = 9.1 Hz, 1H); ^{13}C NMR (75 MHz) δ 18.9, 68.5, 124.6, 126.0, 126.1, 128.0, 128.4, 129.2, 130.6, 133.2, 135.8, 138.0, 139.3, 148.5; MS (EI) *m*/*z* 225 $(M - H_2O)^+$. Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.18; H, 5.26; N, 5.65. Found: C, 69.12; H, 5.39; N, 5.66.

(18) Reaction of $PdCl_2$ (1 equiv) with P(1-Nap)$_3$ (1 equiv) in THF obtained a yellow precipitate that was insoluble in common organic solvents. MALDI-TOF showed a peak at 516.0269 ascribed to the formula of $C_{30}H_{19}$-PPd. A yield of 5 mol % of this precipitate exhibited high activity and **3ae** was still produced in 92 % yield within 1 h.

2-Methoxyphenyl(2-nitrophenyl)methanol (3ek): mp 81−82 °C; IR (KBr, cm^{-1}) 3502(−OH), 3009, 2939, 2834, 1597, 1490, 1461, 1286, 1242, 1161, 1286, 1242, 1164, 1108, 1021, 934, 863, 789, 754, 646, 608, 574; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.21 (m, 1H), 3.74 (s, 3H), 6.64 (d, J = 4.4 Hz, 1H), 6.85−7.24 (m, 2H), 7.25−7.61 (m, 3H), 7.87−7.89 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz) δ 55.3, 66.6, 110.5, 120.6, 124.1, 126.7, 128.0, 129.1, 129.3, 130.2, 132.9, 137.8, 148.7, 156.3; MS (EI) m/z 279 (M^+). Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.91; H, 4.87; N, 5.66.

Naphthalen-1-yl(2-nitrophenyl)methanol (3fk): mp 68−70 °C; IR (KBr, cm^{-1}) 3290 (−OH), 3010, 1486, 1344, 801, 783, 724; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.46 (d, J = 4.2 Hz, 1H, −O*H*), 7.04 (d, J = 3.9 Hz, 1H), 7.37−7.48 (m, 7H), 7.78−7.89 (m, 3H), 7.98 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz) δ 68.4, 123.4, 124.4, 124.9, 125.3, 125.9, 126.6, 128.7, 128.9, 120.0, 129.6, 130.8, 133.5, 133.9, 136.9, 138.1, 148.5; MS (EI) m/z 279 (M^+). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.04; H, 5.06; N, 4.65. Found: C, 73.11; H, 4.69; N, 5.02.

4-Nitrophenyl(thiophen-3-yl)methanol (3ie): mp 88−90 °C; IR (KBr, cm^{-1}) 3413 (−OH), 3012, 1604, 1515, 1345, 1149, 1109, 1033, 1013, 858, 835, 783, 761, 720, 699; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.97 (s, 1H), 5.95 (s, 1H), 6.94−6.96 (m, 1H), 7.18−7.19 (m, 1H), 7.29−7.30 (m, 1H), 7.54 (d, J = 8.7 Hz, 2H), 8.14 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz) δ 71.5, 122.4, 123.6, 125.9, 126.9, 143.8, 147.1, 150.3; MS (EI) m/z 235 (M^+). Anal. Calcd for $C_{11}H_9NSO_3$: C, 56.13; H, 3.92; N, 5.88. Found: C, 56.16; H, 3.86; N, 5.95.

4-Chlorophenyl(4-nitrophenyl)methanol (3ke): mp 133−134 °C; IR (KBr, cm^{-1}) 3420 (−OH), 3019, 1605, 1518, 1489, 1374, 1345, 1185, 1109, 1089, 1041, 1027, 1013, 867, 827, 198, 722, 711, 685, 682; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.37 (d, J = 4.3 Hz), 5.91 (d, J = 3.3 Hz), 7.27−7.36 (m, 4H), 7.56 (d, J = 8.7 Hz, 2H), 8.21 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz) δ 74.8, 123.8, 127.1, 128.0, 129.1, 134.3, 141.1, 147.4, 150.2; MS (EI) m/z 263 (M^+). Anal. Calcd for $C_{13}H_{10}ClNO_3$: C, 59.22; H, 3.93; N, 5.22. Found: C, 59.22; H, 3.82; N, 5.31.

2-Methoxyphenyl(2-(trifluoromethyl)phenyl)methanol (3em): oil; IR (KBr, cm^{-1}) 3483 (−OH), 3024, 1601, 1521, 1490, 1423, 1313, 1163, 1128, 1037, 929, 849, 627; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.17 (d, J = 2.5 Hz, 1H), 3.83 (s, 3H), 6.54 (s, 1H), 6.89−6.94 (m, 2H), 6.99 (d, J = 7.5 Hz, 1H), 7.27−7.32 (t, 1H), 7.42−7.44 (t, 1H), 7.54−7.59 (t, 1H), 7.69 (d, J = 7.0 Hz, 1H); ^{13}C NMR (75 MHz) δ 55.2, 67.1, 76.5, 76.9, 77.4, 110.3, 110.6, 114.4, 120.0, 120.3, 121.3, 122.5, 125.4, 125.5, 125.6, 125.7, 126.1, 127.2, 127.4, 127.5, 127.6, 128.0, 128.8, 129.2, 131.2, 131.9, 140.9, 156.5; MS (EI) m/z 282 (M^+). Anal. Calcd for $C_{15}H_{13}F_3O_2$: C, 63.83; H, 4.64. Found: C, 64.07; H, 4.66.

4-Nitrophenyl(3-(trifluoromethyl)phenyl)methanol (3le): oil; IR (KBr, cm^{-1}) 3438 (−OH), 3076, 2927, 1602, 1522, 1448, 1179, 1328, 1249, 1166, 1126, 1070, 1045, 908, 855, 796, 766, 704; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.13 (d, J = 2.8 Hz, 1H), 5.95 (d, J = 2.3 Hz, 1H), 7.44−7.66 (m, 6H), 8.12−8.17 (d, J = 13.3 Hz, 2H); ^{13}C NMR (75 MHz) δ 74.7, 123.09, 123.14, 123.19, 123.24, 123.8, 124.89, 124.94, 124.99, 125.04, 127.1, 129.3, 129.9, 143.5, 147.2, 150.0; MS (EI) m/z 297 (M^+). Anal. Calcd for $C_{14}H_{10}F_3NO_3$: C, 56.57; H, 3.39; N, 4.71. Found: C, 56.87; H, 3.62; N, 4.56.

1-(4-(Hydroxy(4-nitrophenyl)methyl)phenyl)ethanone (3me): oil; IR (KBr, cm^{-1}) 3482 (−OH), 3075, 2924, 1675, 1602, 1518, 1412, 1346, 1270, 1181, 1115, 1050, 960, 832, 799, 711, 598, 506; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.54 (s, 3H), 3.37 (d, J = 3.6 Hz, 1H), 5.96 (d, J = 2.7 Hz, 1H), 7.44 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 8.14 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz) δ 26.5, 74.8, 123.7, 126.6, 127.1, 128.8, 136.5, 147.1, 147.7, 150.1, 198.0; MS (EI) m/z 271 (M^+). Anal. Calcd for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.40; H, 4.82; N, 5.17.

3-Nitrophenyl(4-nitrophenyl)methanol (3ne): mp 118−119 °C; IR (KBr, cm^{-1}) 3468 (−OH), 3009, 2924, 1602, 1516, 1346, 1182, 1083, 1046, 860, 802, 735, 706; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.72 (d, J = 3.2 Hz, 1H), 6.03 (d, J = 2.1 Hz, 1H), 7.52−7.60 (m, 3H), 7.69 (d, J = 7.6 Hz, 1H), 8.15−8.28 (m, 4H); ^{13}C NMR (75 MHz) δ 74.4, 121.3, 123.1, 124.0, 127.1, 129.8, 132.4, 144.5, 147.5, 148.4, 149.3; MS (EI) m/z 274 (M^+). Anal. Calcd for $C_{13}H_{10}N_2O_5$: C, 56.94; H, 3.68; N, 10.22. Found: C, 57.16; H, 3.94; N, 9.84.

4-(Hydroxy(4-nitrophenyl)methyl)benzoic acid (3oe): mp 153−156 °C; IR (KBr, cm^{-1}) 3430 (−OH), 3114, 2927, 2854, 1726, 1603, 1520, 1447, 1349, 1275, 1114, 1007, 849, 788, 717, 505; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.50 (s, 2H), 7.62 (d, J = 8.6 Hz, 2H), 8.23−8.33 (m, 6H); ^{13}C NMR (75 MHz) δ 66.1, 123.7, 124.0, 128.7, 130.9, 134.8, 142.3, 147.9, 150.8, 164.3; MS (EI) m/z 273 (M^+). Anal. Calcd for $C_{14}H_{11}NO_5$: C, 61.54; H, 4.06; N, 5.13. Found: C, 61.86; H, 4.48; N, 5.44.

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Supporting Information Available: Experimental procedures along with copies of spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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