Supplementary Material (ESI) for Chemical Communications

Palladium-Catalyzed Decarboxylative Coupling of Aromatic Acids with Aryl Halides or Unactivated Arenes Using Microwave Heating

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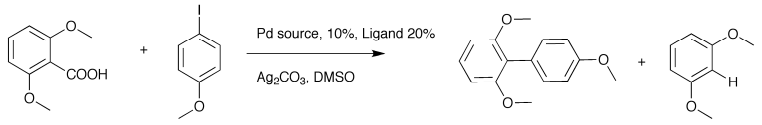
CONTENTS:

General

Dimethylsulfoxide and dimethylformamide were dried and degassed over activated 4 Å molecular sieves. Anhydrous deuterated dimethylsulfoxide (d_6-DMSO) was obtained from Cambridge Isotopes in 1-mL ampules and used immediately after opening. All reactions and manipulations involving organometallic compounds were carried out under dry nitrogen and in oven-dried glassware. Reagents were obtained from commercial sources and were used without further purification: ^{t}BuXPhos[12] was obtained from Sigma-Aldrich; $Pd(OAc)_2$ was obtained from Strem Chemicals. N,N'-dimethylimidazolium carboxylate was prepared as previously reported.[13] ^{1}H- and ^{13}C-NMR spectra were recorded on Bruker 300, 400 or 500 MHz spectrometers. Coupling constants *J* are quoted in Hz. A Biotage Initiator microwave unit was used for all microwave heating. Microwave reactor tubes were obtained from Biotage. Compounds **1**[1], **2**[2], **3**[3], **4**[4], **6**[5], **7**[6], **8**[7], **9**[8], **10**[9], **11**[10], **12**[11] were previously described.

Screening of catalytic conditions for catalytic coupling of benzoic acids with aryl iodides



1 **2**

Table 1. Screening of reaction conditions for the reaction shown:

Entry	*Ligand*	*% yield **1***	*% yield **2***	*Ratio **1/2***
1	Silver oxide	62	29	2.13
2	Silver carbonate	60	23	2.52
3	Silver oxide 0.5 equiv	56	44	1.28
4	Copper(I) iodide + K_2CO_3	29	59	0.49

5	Copper(II) carbonate + KF	25	42	0.62
6	Silver benzoate	16	37	0.42
7	Copper(I) oxide	15	75	0.2
8	Silver trifluroacetate	0	0	n/a
9	Silver formate	0	31	0
10	K_2CO_3 – control	0	23	n/a

Conditions: 270 µmol 2,6-dimethoxybenzoic acid, 280 µmol iodoanisole, 10% $Pd(OAc)_2$ 20% ligand, 270 µmol silver carbonate, 1 mL d_6-DMSO, 200˚C microwave heating, 5 min. Reported yields are based on NMR quantization using 10 µL cyclooctane as internal standard.

Table 2. Screening of additives for the reaction shown above (Scheme 2).

Entry	*Ligand*	*% yield **1***	*% yield **2***	*Ratio **1/2***
1	$AsPh_3$	59	23	2.54
2	^{t}BuXPhos	52	46	1.13
3	dppf	43	40	1.06
4	$AsPh_3$, NaOAc	39	52	0.75
5	PPh_3	38	53	0.72
6	$OPPh_3$	38	33	1.16
7	DPEPhos	36	30	1.2
8	PCy_3	32	23	1.4
9	XantPhos	23	12	2
10	$SbPh_3$	21	28	0.76
11	bipyridine	20	66	0.3
12	NHC-CO_2[a]	9	86	0.1

13	pyridine	4	60	0.06

[a]NHC-CO_2: N,N'-dimethylimidazolium carboxylate[13]; Conditions: 270 µmol 2,6-dimethoxybenzoic acid, 280 µmol iodoanisole, 10% $Pd(OAc)_2$ 20% $AsPh_3$, 270 µmol additive, 1 mL d_6-DMSO, 200°C microwave heating, 5 min. Reported yields are based on NMR using 10 µL cyclooctane as internal standard and average of two trials.

General catalytic protocol for coupling of benzoic acids with aryl iodides

A microwave reactor tube was loaded with 2,6-dimethoxybenzoic acid (0.0500 g, 270 µmol), iodoanisole (0.0655 g, 270 µmol), $Pd(OAc)_2$ (0.0061 g, 27 µmol), ^{t}BuXPhos (0.0264 g, 54 µmol), Ag_2CO_3 (0.0833 g, 30 µmol, 1.1 equiv), 0.100 g 4Å activated molecular sieves and a stir bar. d_6-DMSO was added and the suspension was stirred for 5 min at room temperature. The tube was then sealed with a septum, and heated to 200 ^{o}C in a Biotage microwave unit at 100 W maximum power for 5 min. After completion, the mixture was allowed to cool to 50 ^{o}C then diluted with 30 mL ethyl acetate and filtered through Celite. The organic fraction was washed with saturated NaCl solution (2 x 20 mL), dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography using hexanes/ethyl acetate (80:20) to give pure 2,4',6-trimethoxybiphenyl after drying (**1**, 0.0501 g, 75%).

General catalytic protocol for coupling of benzoic acids with unsubstituted arenes

A microwave reactor tube was loaded with 2,6-dimethoxybenzoic acid (0.0500 g, 270 µmol), $Pd(OAc)_2$ (0.0061 g, 27 µmol), ^{t}BuXPhos (0.0264 g, 54 µmol), Ag_2CO_3 (0.0833 g, 30 µmol, 1.1 equiv), 0.100 g 4Å activated molecular sieves and a stir bar. d_6-DMSO and 2-phenylpyridine (50 µL, 270 µmol),was added and the suspension was stirred for 5 min at room temperature. The tube was then sealed with a septum, and heated to 200 ^{o}C in a Biotage microwave unit at 100 W maximum power for 5 min, with initial power set to 50 W. After completion, the mixture was allowed to cool to 50 ^{o}C then diluted with 30 mL ethyl acetate and filtered through Celite. The organic fraction was washed with

saturated NaCl solution (2 x 20 mL), dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by column chromatography using hexanes/ether (80:20) to give pure 2,4',6-trimethoxybiphenyl after drying (**11**, 0.0459 g, 69%).

Characterization of organic products

2,4',6-Trimethoxybiphenyl (1): ^{1}H NMR (500 MHz, CDCl3) δ: 3.67 (s, 6H), 3.76 (s, 3H), 6.75 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.19 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ:5̃2̲5̃9̃1̃4̲2̲1̲1̃3̲3̲1̲1̃9̲1̲1̲2̃6̲1̲1̲2̃8̃4̲1̲3̲2̲1̃5̃7̃8̲1̃5̃8̃4̃

ı̣̃3Dimethoxybenzene (2): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.72 (s, 6H), 6.42 (m, 3H), 7.11 (t, *J* = 8.2 Hz, 1H). ^{13}C NMR (125 MHz; $CDCl_3$) δ: 54.2, 99.5, 105.2, 128.8, 159.9.

4-Fluoro-4'-methoxybiphenyl (**3**): ^{1}H NMR (400 MHz, $CDCl_3$): 3.92 (s, 3H), 7.02 (d, *J* = 6.78 Hz, 2H), 7.21 (d, *J* = 8.63 Hz, 2H), 7.52-7.61 (m, 3H). ^{13}C NMR (125 MHz; $CDCl_3$) δ: 55.45, 104.78, 114.76, 125.52, 128.85, 129.25, 131.25, 158.23, 160.23.

1-(4-Methoxyphenyl)naphthalene (4): ^{1}H NMR (400 MHz; $CDCl_3$) δ: 3.93 (s, 3H), 7.08 (d, *J* = 8.6 Hz, 2H), 7.45-7.49 (m, 4H), 7.52-7.56 (m, 2H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz; CDCl3) δ: 56.1, 114.2, 125.5, 125.9, 127.1, 126.5, 127.7, 128.3, 129.6, 132.2, 132.9, 134.3, 134.9, 141.1, 160.

2,4,6-Triisopropyl-4'-methoxybiphenyl (5) ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.15 (d, *J* = 6.9 Hz, 12H), 1.38 (d, J = 6.9 Hz, 6H), 2.73 (sept, J = 6.9 Hz, 2H), 3.01 (sept, *J* = 6.9 Hz, 1H), 3.92 (s, 3H), 7.01 (d, J = 8.7 Hz, 2H), 7.13 (s, 2H), 7.17 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, CDCl3) δ: 24.2, 30.1, 34.2, 55.0, 113.2, 120.4, 129.2, 130.5, 132.5, 136.3, 147.0, 147.6, 158.1.

4'-Methoxy-4-methylbiphenyl (6): ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.24 (s, 3H), 3.79 (s, 3H), 6.85 (d, J = 8.5 Hz, 2H), 7.17 (d, J = 8.5 Hz, 2H), 7.48-7.41 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ:2̃3̲5̃3̲5̲1̲1̃2̲6̲1̲2̃5̲2̲1̲2̃6̲6̲1̃3̲5̲1̃3̲2̃6̲1̃3̲5̲1̲1̲2̃7̃3̲1̃5̃9̃5̃

2,3,4,5,6-Pentafluoro-4'-methoxybiphenyl (7): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.85 (s, 3H), 7.02 (d, *J* = 8.8 Hz, 2H), 7.33 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, CDCl3 (except for C6F5)) δ 55.8, 114.1, 118.7, 131.3, 160.2; ^{19}F NMR (282 MHz, CDCl3) δ:163.7 (m, 2F),157.7 (t, *J* = 21.0 Hz, 1F), 144.9 (dd, *J* = 7.1, 23.1 Hz, 2F).

TABLE 2

2,6-Dimethoxy-4'-methylbiphenyl (1b): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.40 (s, 3H), 3.75 (s, 6H), 6.69 (d, *J* = 8.3 Hz, 2H), 7.30 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): d 21.2, 55.7, 104.3, 120.0, 127.2, 127.4, 127.5, 128.2, 131.3, 133.9, 137.0, 157.6.

2,6-Dimethoxy-4'-acetylbiphenyl (1c): ^{1}H NMR (400 MHz, CDCl3) δ (ppm): 2.54 (s, 3H), 3.65 (s, 6H), 6.60 (d, *J* = 8.3 Hz, 2H), 7.28 (t, *J* = 8.3 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 2H), 8.04 (d, *J* = 8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$) 26.2, 56.4, 95.9, 105.5, 120.2, 132.1, 133.4, 162.5, 193.8; MS (*m*/*z*) 256.

9-(2',6'-Dimethoxyphenyl)-anthracene (1d): ^{1}H NMR (400 MHz, CDCl3) δ 8.34 (s, 1 H), 7.62 (d, *J* = 8.5 Hz, 2 H), 7.49 (dd, *J* = 8.5, 1.0 Hz, 2 H), 7.38 (t, *J* = 8.3 Hz, 1 H), 7.35-7.42 (m, 2 H), 7.23-7.35 (m, 2 H), 6.68 (d, *J* = 8.3 Hz, 2 H), 3.39 (s, 6 H); ^{13}C NMR (100 MHz, CDCl3) δ 159.1, 131.7, 130.7, 130.4, 129.8, 128.7, 126.7, 126.6, 125.2, 125.1, 115.6, 104.4, 56.1;

3-(2,6-Dimethoxyphenyl)-pyridine (1f): ^{1}H NMR (500 MHz, CDCl3) δ:3.74 (s, 6H), 6.67 (d, *J* = 8 Hz, 2H), 7.30-7.33 (m, 2H), 7.69 (d, *J* = 8 Hz, 1H), 8.52 (d, *J* = 5 Hz, 1H), 8.60 (d, *J* = 2 Hz, 1H). ^{13}C NMR (125 MHz, CDCl3) δ: 55.8, 115.6, 120.2, 122.6, 129.5, 129.9, 138.4. 147.6 151.8, 157.6.

TABLE 3

2-(2',6'-dimethoxybiphenyl-2-yl)pyridine (10): ^{1}H NMR (400 MHz, CD_2Cl2) δ:3̃75̲s, 6H), 6.82 (d, *J* = 7.6 Hz, 2H), 6.98 (t, *J* = 8.3, 1H), 7.16 (d, J = 8.3 Hz, 1H), 7.32-29 (m,

3H), 7.43 (m, 3H), 7.72 (m, 1H), 7.90 (m, 1H), 8.12 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, CD_2Cl_2) δ: 55.72, 102.91, 122.36, 122.89, 125.32, 128.55, 128.89, 129.53, 130.25, 131.23, 132.04, 136.23, 140.05, 147.54, 156.98, 157.55.

***N*-(2',6'-dimethoxybiphenyl-2-yl)acetamide (11):** ^{1}H NMR (300 MHz, CD_2Cl_2) δ:2µs3H37s6H5.92 (s, 1H), 6.87 (d, *J* = 8.3 Hz), 7.25 (t, *J* = 8.5 Hz, 1H), 7.38 (t, *J* = 8.5 Hz, 1H), 7.47 (t, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 8.6 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, CD_2Cl_2) δ: 23.56, 56.23, 105.36, 120.38, 121.54, 122.67, 123.82, 128.43, 129.67, 131.35, 140.68, 154.58, 168.74. Mol. wt. calculated for Chemical Formula: $C_{16}H_{17}NO_3$: 271.3111 m/z, found: 271.3178.

1-(2',6'-dimethoxybiphenyl-3-yl)ethanone (12): ^{1}H NMR (300 MHz, CD_2Cl_2) δ:24s, 3H), 3.72 (s, 6H), 6.85 (d, *J* = 8.3 Hz, 2H), 7.21 (t, *J* = 8.5 Hz, 1H), 7.45 (t, *J* = 8.5 Hz, 1H) 7.59 (t, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, CD_2Cl_2) δ: 27.31, 56.33, 104.12, 104.76, 122.65, 128.54, 128.98, 129.65, 130.44, 131.16, 140.30, 140.05, 157.92. Mol. wt. calculated for Chemical Formula: $C_{16}H_{16}O_3$: 256.2964 m/z, found: 256.2934.

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