Supporting Information

Pd/ sensory component-catalyzed homocoupling reactions of aryl halides

Fengyu Bao,*a Zhikai Liu,b Haixin Bai,a Haiyan Zhang,a Pengfei Liu,*b Qidong Zhang,c Guobi Chai*c

aCollege of Science, Henan Agricultural University, Zhengzhou 450002, China
bCollege of Tobacco, Henan Agricultural University, Zhengzhou 450002, China
cZhengzhou Tobacco Research Institute, Zhengzhou 450001, China

Table of contents
General information………………………………………………………………………………..S2
General procedure for the preparation of sensory components from tobacco leaves………………………………………………………………………………………..S2
General procedure for the coupling reactions of aryl halides …………………..S2
Characterization data of compounds 2…………………………………………………………..S3
References……………………………………………………………………………………………………..S7
Copies of NMR results………………………………………………………………………………..S8
General information
All chemicals are commercial available and used without purification. All reactions were conducted in air and monitored by thin layer chromatography (TLC). TLC analysis was carried out on silica gel GF254 plates and performed under UV light (254 nm). GC analysis was carried out on GC7890N using decane as an internal standard. Column chromatography was conducted using silica gel (200-300 mesh). Tobacco leaves were collected from Xuchang, Henan province, China, and flue-cured before use. Separation of tobacco leaves extract by gel permeation chromatography was performed on a Bio-rad Quest 10 Plus NGC Chromatography system equipped with glass column (20 mm × 1000 mm) and Sephadex LH-20 from GE healthcare (particle size range from 18 μm-111 μm when dry) was used as stationary phase. $^1$H and $^{13}$C NMR were measured on a Bruker AVANCE III 400 using tetramethylsilane as an internal standard. HRMS were measured on an Agilent 1290-6540 Ultra High Performance Liquid Chromatography-Q-Time of Flight/ High Resolution Mass Spectrometer. GC-MS were measured on an Agilent 7890A-5975C Gas Chromatography/Mass Spectrometry.

General procedure for the preparation of sensory components from tobacco leaves
Tobacco leaves (100 g) were shattered and extracted by 75% ethanol (500 mL) under refluxing condition for 2 hours using a three-necked flask equipped with condenser. After removing of solvent under vacuum, 35 g of the extract was afforded. The afforded extract (6 g) was separated by gel permeation chromatography using water as eluent and monitored by UV detector. Each fraction was tasted and the sensory components were eluted in the order of sweet (150-180 mL), sour (190-240 mL), peppery (250-270 mL) and bitter (280-370 mL). Fractions with same taste were collected and dried by a freeze dryer. Sweet taste component (1.0 g, light yellow viscous solid), sour taste component (0.5 g, light yellow viscous solid), peppery component (0.7 g, light brown viscous solid), and bitter taste component (0.1 g, white flocculent solid) were afforded. It should be noted that although the UV signals could give some useful information, the sensory evaluation of each fraction by tasting was still necessary in the first separation to locate and collected fractions. In the meanwhile, parallel experiments showed that in the following separations the eluent volumes are quite stable and could be used along with UV signals as indicators for collection. The obtained sensory components were stored in a refrigerator. After GC-MS analysis, the main ingredient of peppery component was found to be nicotine (71.8 mg/g).

General procedure for the coupling reactions of aryl halides
Aryl halide (0.5 mmol) was added to a mixture of Pd(OAc)$_2$ (0.05 mmol, 10 mol%), sensory component (8 mg), base (1.0 mmol, 2 equiv) in DMF (10 mL). The mixture was stirred and heated in oil bath at 100 °C for 24 hours. The mixture was extracted by ethyl acetate (20 mL × 3). The combined organic phases were dried over anhydrous MgSO$_4$, filtered, concentrated under reduced pressure and purified by a silica gel column chromatography.
Characterization data of compounds 2

1,1'-binaphthalene (2a)\(^1\)

2a was obtained according to the general procedure using 1-iodonaphthlene and purified by column chromatography (petroleum ether). Yield: 55 mg (87%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.93-7.96 (m, 4H), 7.57-7.60 (m, 2H), 7.44-7.50 (m, 4H), 7.39 (d, \(J = 8.36\) Hz, 2H), 7.26-7.30 (m, 2H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 138.5, 133.5, 132.9, 128.2, 127.9, 127.8, 126.6, 126.0, 125.8, 125.4.

1,1'-biphenyl (2b)\(^2\)

2b was obtained according to the general procedure using iodobenzene and purified by column chromatography (petroleum ether). Yield: 31 mg (81%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.59 (d, \(J = 7.32\) Hz, 4H), 7.44 (t, \(J = 7.32\) Hz, 4H), 7.34 (t, \(J = 7.32\) Hz, 2H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 141.3, 128.8, 127.3, 127.2.

4,4'-dimethyl-1,1'-biphenyl (2c)\(^3\)

2c was obtained according to the general procedure using 1-iodo-4-methylbenzene and purified by column chromatography (petroleum ether). Yield: 22 mg (49%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.47 (d, \(J = 7.96\) Hz, 4H), 7.23 (d, \(J = 7.96\) Hz, 4H), 2.39 (s, 6H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 138.3, 136.7, 129.4, 126.8, 21.1.

3,3'-dimethyl-1,1'-biphenyl (2d)\(^3\)

2d was obtained according to the general procedure using 1-iodo-3-methylbenzene and purified by column chromatography (petroleum ether). Yield: 22 mg (48%); colorless liquid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.38 (d, \(J = 8.84\) Hz, 4H), 7.32 (t, \(J = 7.52\) Hz, 2H), 7.15 (d, \(J = 7.52\) Hz, 2H), 2.42 (s, 6H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 141.4, 138.2, 128.6, 128.0, 127.9, 124.3, 21.5.

4,4'-di-(tert)-butyl-1,1'-biphenyl (2e)\(^4\)

2e was obtained according to the general procedure using 1-(tert-butyl)-4-iodobenzene and purified by column chromatography (petroleum ether). Yield: 36 mg (55%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.52 (d, \(J = 8.52\) Hz, 4H), 7.45 (d, \(J = 8.52\) Hz, 4H), 1.36 (s, 18H). \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 149.9, 138.2, 126.7, 125.6, 34.5, 31.4

4,4'-dimethoxy-1,1'-biphenyl (2f)\(^5\)

2f was obtained according to the general procedure using 1-iodo-4-methoxybenzene and purified by column chromatography (ethyl acetate: petroleum ether = 1: 5). Yield:
40 mg (76%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.47 (d, \(J = 8.84\) Hz, 4H), 6.95 (d, \(J = 8.84\) Hz, 4H), 3.84 (s, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 158.7, 133.5, 127.7, 114.2, 55.4.

3,3′,4,4′,5,5′-hexamethoxy-1,1′-biphenyl (2g)

2g was obtained according to the general procedure using 5-iodo-1,2,3-trimethoxybenzene and purified by column chromatography (ethyl acetate: petroleum ether = 1: 3). Yield: 48 mg (58%); light yellow solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 6.72 (s, 4H), 3.93 (s, 12H), 3.89 (s, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 153.4, 137.7, 137.6, 104.6, 61.0, 56.3. HRMS: calculated for C\(_{18}\)H\(_{23}\)O\(_6\) [M+H]^+: 335.1494, found, 335.1491.

4,4′-biphenol (2h)

2h was obtained according to the general procedure using 4-iodophenol under refluxing condition for 48 hours and purified by column chromatography (ethyl acetate: petroleum ether = 1: 5). Yield: 25 mg (53%); yellow solid. \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): δ 9.36 (s, 2H), 7.36 (d, \(J = 8.64\) Hz, 4H), 6.79 (d, \(J = 8.64\) Hz, 4H). \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): δ 156.2, 131.1, 126.9, 115.5.

di-tert-butyl [1, 1′-biphenyl]-4, 4′-diyldicarbamate (2j)

2j was obtained according to the general procedure using tert-butyl (4-iodophenyl)carbamate for 7 days and purified by column chromatography (ethyl acetate: petroleum ether = 1: 3). Yield: 18 mg (19%); white solid. \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): δ 9.40 (s, 2H), 7.51 (s, 8H), 1.49 (s, 18H). \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): δ 153.7, 139.4, 134.4, 127.2, 119.3, 80.0, 29.1.

2,2′-difluoro-1,1′-biphenyl (2k)

2k was obtained according to the general procedure using 1-fluoro-2-iodobenzene and purified by column chromatography (petroleum ether). Yield: 26 mg (54%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.34-7.41 (m, 4H), 7.19-7.25 (m, 2H), 7.14-7.19 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 161.1, 158.6, 131.6, 129.8, 129.8, 129.7, 124.1, 123.6, 123.6, 123.5, 123.5, 115.9, 115.8, 115.7, 115.7. GC-MS (%): 190.1 (M^+, 100), 170.1 (12.2), 94.0 (5.7), 75.0 (3.7). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): δ -114.8 (s).

4,4′-difluoro-1,1′-biphenyl (2l)

2l was obtained according to the general procedure using 1-fluoro-4-iodobenzene and purified by column chromatography (petroleum ether). Yield: 32 mg (67%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.48 (dd, \(J = 8.68\) Hz, 4H), 7.11 (t, \(J = 8.68\) Hz, 4H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 163.7, 161.2, 136.4, 136.4, 128.6,
128.5, 115.8, 115.6. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta -115.7\) (s).

**2,2'-dichloro-1,1'-biphenyl (2m)**

2m was obtained according to the general procedure using 1-chloro-2-iodobenzene and purified by column chromatography (petroleum ether). Yield: 20 mg (36%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.46-7.50\) (m, 2H), 7.29-7.35 (m, 4H), 7.25-7.28 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 138.4, 133.5, 131.2, 129.5, 129.3, 126.5\).

**2,2'-bis(trifluoromethyl)-1,1'-biphenyl (2n)**

2n was obtained according to the general procedure using 1-iodo-2-(trifluoromethyl)benzene and purified by column chromatography (petroleum ether). Yield: 17 mg (23%); colorless liquid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.74-7.76\) (m, 2H), 7.49-7.57 (m, 4H), 7.28-7.30 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 137.5, 131.5, 130.7, 128.9, 128.6, 128.1, 126.0, 125.2, 122.5, 119.8\). GC-MS (%): 290.1 (M\(^+\), 100), 271.1 (26.6), 201.0 (25.3), 152.0 (16.9). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta -58.1\) (s).

**3,3'-bis(trifluoromethyl)-1,1'-biphenyl (2o)**

2o was obtained according to the general procedure using 1-iodo-3-(trifluoromethyl)benzene and purified by column chromatography (petroleum ether). Yield: 42 mg (58%); colorless liquid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.83\) (s, 2H), 7.77 (d, \(J = 7.72\) Hz, 2H), 7.66 (d, \(J = 7.72\) Hz, 2H), 7.60 (t, \(J = 7.72\) Hz, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 140.6, 132.0, 131.7, 131.3, 131.0, 130.5, 129.6, 128.1, 125.4, 124.8, 124.8, 124.7, 124.7, 124.1, 124.0, 124.0, 124.0, 122.7, 120.0\). GC-MS (%): 290.0 (M\(^+\), 100), 271.0 (20.5), 201.0 (27.5), 152.0 (14.8). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta -62.7\) (s).

**4,4'-bis(trifluoromethyl)-1,1'-biphenyl (2p)**

2p was obtained according to the general procedure using 1-iodo-4-(trifluoromethyl)benzene and purified by column chromatography (petroleum ether). Yield: 48 mg (66%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.73\) (d, \(J = 8.48\) Hz, 4H), 7.69 (d, \(J = 8.48\) Hz, 4H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 143.3, 130.8, 130.5, 130.1, 129.8, 128.2, 127.6, 126.0, 125.9, 125.9, 125.5, 122.8, 120.1\). GC-MS (%): 290.1 (M\(^+\), 100), 271.1 (21.8), 201.0 (12.3), 152.1 (13.6). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta -62.6\) (s).

**1,1'-(11,1'-biphenyl)-4,4'-diyl)bis(ethan-1-one) (2q)**

2q was obtained according to the general procedure using 1-(4-iodophenyl)ethan-1-one and purified by column chromatography (ethyl acetate: petroleum ether, 2:1). Yield: 59 mg (60%); white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.62-7.66\) (m, 6H), 7.49-7.54 (m, 4H), 7.31-7.35 (m, 4H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 151.1, 143.3, 131.7, 130.5, 130.1, 129.8, 128.2, 127.6, 126.0, 125.9, 125.5, 122.8, 120.1\). GC-MS (%): 290.1 (M\(^+\), 100), 271.1 (21.8), 201.0 (12.3), 152.1 (13.6). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \(\delta -62.6\) (s).
petroleum ether = 1: 6). Yield: 11 mg (19%); white solid. $^1$H NMR (400 MHz, CDCl$_3$): δ 8.06 (d, $J = 8.48$ Hz, 4H), 7.72 (d, $J = 8.48$ Hz, 4H), 2.65 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 197.6, 144.3, 136.6, 129.0, 127.5, 26.7.

[1,1'-biphenyl]- 4,4'-dicarbonitrile (2r)$^8$

2r was obtained according to the general procedure using 4-iodobenzonitrile and purified by column chromatography (ethyl acetate: petroleum ether = 1: 5). Yield: 31 mg (61%); white solid. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.79 (d, $J = 8.52$ Hz, 4H), 7.70 (d, $J = 8.52$ Hz, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 143.5, 132.9, 128.0, 118.4, 112.5.

[1,1'-biphenyl]- 4,4'-dicarbaldehyde (2s)$^9$

2s was obtained according to the general procedure using 4-iodobenzaldehyde and purified by column chromatography (ethyl acetate: petroleum ether = 1: 5). Yield: 47 mg (89%); white solid. 2s was also obtained according to the general procedure using 4-bromobenzaldehyde for 4 days. Yield: 24 mg (45%). $^1$H NMR (400 MHz, CDCl$_3$): δ 10.09 (s, 2H), 8.00 (d, $J = 8.24$ Hz, 4H), 7.81 (d, $J = 8.24$ Hz, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 191.7, 145.6, 136.0, 130.4, 112.5.

[1,1'-biphenyl]- 2,2'-dicarbaldehyde (2t)$^{10}$

2t was obtained according to the general procedure using 2-iodobenzaldehyde and purified by column chromatography (ethyl acetate: petroleum ether = 1: 5). Yield: 33 mg (64%); yellow liquid. $^1$H NMR (400 MHz, CDCl$_3$): δ 9.84 (s, 2H), 8.07-8.70 (m, 2H), 8.39-8.41 (m, 2H), 7.80-7.84 (m, 2H), 7.30-7.33 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 191.0, 141.2, 134.6, 133.4, 131.7, 128.8, 128.6.

2,2'-bipyridine (2u)$^{11}$

2u was obtained according to the general procedure using 2-iodopyridine and purified by column chromatography (ethyl acetate: petroleum ether = 1: 1). Yield: 30 mg (77%); white solid. $^1$H NMR (400 MHz, CDCl$_3$): δ 8.68-8.70 (m, 2H), 8.39-8.41 (m, 2H), 7.80-7.84 (m, 2H), 7.30-7.33 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 156.2, 149.2, 136.9, 123.7, 121.1.

2, 2'-bithiophene (2v)$^{12}$

2v was obtained according to the general procedure using 2-iodothiophene and purified by column chromatography (petroleum ether). Yield: 15 mg (35%); colorless liquid. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.21 (dd, $J = 5.08$, 1.04 Hz, 2H), 7.18 (dd, $J = 3.6$, 1.04 Hz, 2H), 7.02 (dd, $J = 5.08$, 3.6 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ


137.4, 127.8, 124.4, 123.8.

4,4'-dinitro-1,1'-biphenyl (2w)\(^4\)

\(2w\) was obtained according to the general procedure using 1-iodo-4-nitrobenzene and purified by column chromatography (ethyl acetate: petroleum ether = 1: 3). Yield: 42 mg (68%); light yellow solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.37 (d, \(J = 8.80 \text{ Hz}, 4\)H), 7.79 (d, \(J = 8.80 \text{ Hz}, 4\)H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 148.1, 145.0, 128.3, 124.4.

Dimethyl [1,1'-biphenyl]-4,4'-dicarboxylate (2x)\(^{13}\)

\(2x\) was obtained according to the general procedure using methyl-4-iodobenzoate and purified by column chromatography (ethyl acetate: petroleum ether = 1: 3). Yield: 51 mg (76%); white solid. \(2x\) was also obtained according to the general procedure using methyl-4-bromobenzoate. Yield: 22 mg (32%). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.13 (d, \(J = 8.48 \text{ Hz}, 4\)H), 7.69 (d, \(J = 8.48 \text{ Hz}, 4\)H), 3.95 (s, 6H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 166.8, 144.4, 130.2, 129.7, 127.2, 52.2.

References