Dimerization of aromatic compounds using palladium-carbon catalyzed Suzuki-Miyaura cross-coupling by One-Pot

Fangyu Du, Qifan Zhou, Dongdong Liu, Ting Fang, Yajie Shi, Yang Du, Guoliang Chen*

Key Laboratory of Structure-Based Drug Design & Discovery of Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, China

Experimental Section:

Solvents and all commercially available reagents were used directly without further purification. Palladium-carbon contains 10% of palladium. Reactions were monitored by thin-layer chromatography (TLC) on glass plates coated with silica gel with a fluorescent indicator (GF254). Column chromatography was performed on silica gel (160-200 mesh). All the $^1$H-NMR spectra were recorded on a Bruker 400 MHz or 600 MHz spectrometer in DMSO-$d_6$ or CDCl$_3$. All the $^{13}$C-NMR spectra were recorded on a Bruker 600 MHZ AVIII HD in DMSO-$d_6$ or CDCl$_3$. Chemical shifts (δ) were expressed in parts per million using tetramethylsilane as an internal reference. ESI-MS data were obtained using an Agilent 1100 instrument. GC-MS data were obtained using an Agilent Technologies 6890N-5975 GC/MS. Melting points were measured on X-4 digital melting point instrument.

General procedure:

To a solution of brominated aromatic compounds (1 equiv), bis(pinacolate)diboron (1.5 equiv) and anhydrous ethanol (15 mL) were added 10%palladium-carbon (0.01 equiv), followed by potassium acetate (3 equiv) under
argon. The mixture was heated in a 60 °C with stirring for the indicated time. The reactor was cooled to room temperature, and the reaction mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was extracted with dichloromethane (20 mL×3), and organic layer was washed with water (20 mL×2) and once with brine (25 mL), dried over magnesium sulfate and concentrated in vacuo. The product was purified by silica gel flash chromatography on silica gel using petroleum as eluent.

**Biphenyl (3a):**

According to general procedure: bromobenzene (2.00 g, 12.74 mmol), bis(pinacolat) diboron (4.85 g, 19.10 mmol), potassium acetate (3.75 g, 38.22 mmol), palladium-carbon (0.14 g, 0.13 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 6 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford biphenyl 3a (0.97 g, 98.7%) as a pale solid. m.p.69-71 °C, Rf=0.23 (PE). $^1$H-NMR (400 MHz, CDCl$_3$) δ: 7.60 (t, J=1.24 Hz, 2H), 7.44 (t, J=7.20 Hz, 2H), 7.34 (t, J=7.36 Hz, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$) δ: 141.2, 128.7, 127.2, 127.1. GC-MS: m/z=154.2.

**4, 4'-dimethyl-1, 1'-biphenyl (3b):**

According to general procedure: 4-methylbromobenzene (1.00 g, 5.85 mmol), bis(pinacolat) diboron (2.23 g, 8.77 mmol), potassium acetate (1.72 g, 17.54 mmol), palladium-carbon (0.06 g, 0.06 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 12 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 4, 4'-dimethyl-1, 1'-biphenyl 3b (0.52 g, 98.1%) as a white solid. m.p.125 °C, Rf=0.50 (PE). $^1$H-NMR (600 MHz, CDCl$_3$) δ: 7.45 (d, J=7.68 Hz, 2H), 7.24 (d, J=8.22 Hz, 2H), 2.38 (s, 6H). $^{13}$C-NMR (150 MHz, CDCl$_3$) δ: 138.3, 136.7, 129.4, 126.8, 21.1. GC-MS: m/z=182.2.

**Benzerythrene (3c):**

According to general procedure: 4-biphenyl bromide (1.00 g, 4.29 mmol),
bis(pinacolate)diboron (1.63 g, 6.43 mmol), potassium acetate (1.26 g, 12.87 mmol), palladium-carbon (0.05 g, 0.04 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 5 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford benzerythrene 3c (0.20 g, 30.3%) as a white solid. m.p.>300 ℃, Rf =0.57 (EtOAc:PE=1:10). 1H-NMR (400 MHz, CDCl3) δ: 7.77-7.37 (m, 18H).

13C-NMR (150 MHz, CDCl3) δ: 140.7, 140.3, 139.6, 128.8, 127.6, 127.5, 127.1.

GC-MS: m/z=306.2.

5,5',5',8,8,8',8'-octamethyl-5,5',6,6',7,7',8,8'-octahydro-2,2'-binaphthalene (3d):
According to general procedure:
6-bromo-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene (1.00 g, 3.74 mmol), bis(pinacolate)diboron (1.43 g, 5.61 mmol), potassium acetate (1.10 g, 11.23 mmol), palladium-carbon (0.04 g, 0.04 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 8 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 5,5',5',8,8,8',8'-octamethyl-5,5',6,6',7,7',8,8'-octahydro-2,2'-binaphthalene 3d (0.35 g, 50.0%) as a colorless oily liquid. Rf=0.41 (PE). 1H-NMR (400 MHz, CDCl3) δ: 7.49 (s, 2H), 7.48-7.32 (m, 4H), 1.73 (s, 8H), 1.35 (d, J=5.08 Hz, 24H). 13C-NMR (150 MHz, CDCl3) δ: 144.9, 143.5, 138.9, 126.7, 125.3, 124.5, 35.2, 35.1, 34.3, 34.1, 31.9, 31.8. GC-MS: m/z=374.3.

3, 3'-dimethoxy-1, 1'-biphenyl (3e):
According to general procedure: 3-methoxy-1-bromobenzene (1.00 g, 5.35 mmol), bis(pinacolate)diboron (2.04 g, 8.02 mmol), potassium acetate (1.57 g, 16.04 mmol), palladium-carbon (0.06 g, 0.05 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 3 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 3, 3'-dimethoxy-1, 1'-biphenyl 3e (0.38 g, 66.7%) as a colorless oily liquid. Rf=0.57 (EtOAc:PE=1:5). 1H-NMR (600 MHz, CDCl3) δ: 7.32 (t, J=7.86
Hz, 2H), 7.17~7.15 (m, 2H), 7.11 (t, J=2.22 Hz, 2H), 6.88~6.86 (m, 2H), 3.81 (s, 6H).

$^{13}$C-NMR (150 MHz, CDCl₃) δ: 159.9, 142.6, 129.7, 119.7, 112.9, 112.8, 55.2.

GC-MS: m/z=214.2.

2, 2'-dimethoxy-1, 1'-biphenyl (3f):

According to general procedure: 2-methoxy-1-bromobenzene (1.00 g, 5.35 mmol), bis(pinacolate)diboron (2.04 g, 8.02 mmol), potassium acetate (1.57 g, 16.04 mmol), palladium-carbon (0.06 g, 0.05 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 3 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 2, 2'-dimethoxy-1, 1'-biphenyl 3f (0.50 g, 87.7%) as a white solid. m.p.154~155 ℃, R_f=0.60 (EtOAc:PE=1:3). $^1$H-NMR (400 MHz, CDCl₃) δ: 7.35~7.31 (m, 2H), 7.26~7.02 (m, 2H), 7.00 (q, $J_1=7.44$ Hz, $J_2=6.60$ Hz, 4H), 3.77 (s, 6H).

$^{13}$C-NMR (150 MHz, CDCl₃) δ: 157.0, 131.4, 128.6, 127.8, 120.3, 111.1, 55.7.


2,2'-Biphenol (3g):

According to general procedure: 2-bromophenol (2.00 g, 13.0 mmol), bis(pinacolate)diboron (4.95 g, 19.5 mmol), potassium acetate (3.82 g, 39.0 mmol), palladium-carbon (0.12 g, 0.12 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 12 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 2,2'-biphenol 3g (0.41 g, 75.5%) as a colorless oily liquid. R_f=0.35 (EtOAc:PE=1:3). $^1$H-NMR (400 MHz, CDCl₃) δ: 7.38-7.33 (m, 2H), 7.30 (d, $J=1.36$ Hz, 1H), 7.10-7.05 (q, $J_1=1.00$ Hz, $J_2=8.64$ Hz, 4H), 5.40 (br, 2H). $^{13}$C-NMR (150 MHz, CDCl₃) δ: 152.0, 130.6, 129.2, 122.9, 120.9, 115.9. ESI-MS: [M+H]$^+$=184.9.

4,4'-Biphenol (3h):

According to general procedure: 3-bromophenol (2.00 g, 11.56 mmol), bis(pinacolate)diboron (4.40 g, 17.34 mmol), potassium acetate (3.40 g, 34.68 mmol), palladium-carbon (0.12 g, 0.12 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 12 h. The reaction mixture was worked up
according to the general procedure and purified by flash column chromatography on silica gel to afford 4,4'-biphenol 3h (0.86 g, 90.0%) as a white solid. m.p.283°C, Rf=0.50 (EtOAc:PE=1:2). ¹H-NMR (400 MHz, DMSO-d₆) δ: 9.38 (s, 2H), 7.37 (d, J=8.52 Hz, 4H), 6.79 (d, J=8.52 Hz, 4H). ¹³C-NMR (150 MHz, DMSO-d₆) δ: 155.7, 130.5, 126.3, 115.0. ESI-MS: [M+H]⁺=184.9.

4,4'-Bianiline (3i):
According to general procedure: 4-bromobenzenamine (1.00 g, 5.81 mmol), bis(pinacolate) diboron (2.21 g, 8.72 mmol), potassium acetate (1.71 g, 17.44 mmol), palladium-carbon (0.06 g, 0.06 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 8 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 4,4'-bianiline 3i (0.50 g, 94.3%) as a brown solid. m.p.117~119 °C, Rf=0.15(EA:PE=1:3). ¹H-NMR (400 MHz, CDCl₃) δ: 7.35 (d, J=7.8 Hz, 4H), 6.74 (d, J=7.8 Hz, 4H), 3.67 (s, 4H).

3,3'-Diaminobiphenyl (3j):
According to general procedure: 3-bromobenzenamine (1.00 g, 5.81 mmol), bis(pinacolate) diboron (2.21 g, 8.72 mmol), potassium acetate (1.71 g, 17.44 mmol), palladium-carbon (0.06 g, 0.06 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 8 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 3,3'-diaminobiphenyl 3j (40 mg, 7.4%) as a brown solid. m.p.89~90°C, Rf=0.26 (EtOAc:PE=1:5). ¹H-NMR (400 MHz, CDCl₃) δ: 7.22-7.16 (q, J₁=8.32 Hz, J₂=16.08 Hz, 2H), 6.95 (d, J=7.64 Hz, 2H), 6.84 (s, 2H), 6.64-6.62 (q, J₁=1.44Hz, J₂=7.88 Hz, 2H). ¹³C-NMR (150 MHz, DMSO-d₆) δ: 146.2, 128.0, 125.4, 113.7. ESI-MS: [M+H]⁺=185.1.

5,5'-difluoro-2,2'-bipyridine (3k):
According to general procedure: 2-bromo-5-fluoropyridine (1.00 g, 5.68 mmol), bis(pinacolate) diboron (2.16 g, 8.52 mmol), potassium acetate (1.67 g, 17.05 mmol),
palladium-carbon (0.06 g, 0.06 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 18 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 5, 5'-difluoro-2, 2'-bipyridine 3k (0.54 g, 98.2%) as an off-white solid. m.p.153-154 °C, Rf=0.87 (EtOAc:PE=1:5). 1H-NMR (600 MHz, CDCl3) δ: 8.50 (d, J=2.34 Hz, 2H), 8.39 (dd, J1=4.38 Hz, J2=8.76 Hz, 2H), 7.54~7.51 (m, 2H). 13C-NMR (150 MHz, CDCl3) δ: 160.7, 159.0, 151.4, 151.42, 137.3, 137.1, 123.9, 123.8, 122.3, 122.2. GC-MS: m/z=192.2.

2, 2'-bipyridine (3l):
According to general procedure: 2-bromopyridin (2.00 g, 12.66 mmol), bis(pinacolate)diboron (4.82 g, 18.99 mmol), potassium acetate (3.73 g, 37.97 mmol), palladium-carbon (0.13 g, 0.13 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 12 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 2, 2'-bipyridine 3l (0.41 g, 41.8%) as a white solid. m.p.72 °C, Rf=0.27 (EtOAc:PE=1:5). 1H-NMR (600 MHz, CDCl3) δ: 8.71 (d, J=4.26 Hz, 2H), 8.44 (d, J=7.86 Hz, 2H), 7.85 (t, J=7.62 Hz, 2H), 7.34 (t, J=5.4 Hz, 2H). 13C-NMR (150 MHz, CDCl3) δ: 156.0, 149.1, 137.1, 123.8, 121.2. ESI-MS: [M+H]+=157.1.

4,4'-bis(methoxycarbonyl)biphenyl (3m):
According to general procedure: 4-bromobenzoic acid methyl ester (1.00 g, 4.65 mmol), bis(pinacolate)diboron (1.77 g, 6.98 mmol), potassium acetate (1.37 g, 13.95 mmol), palladium-carbon (0.05 g, 0.05 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 8 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 4,4'-bis(methoxycarbonyl)biphenyl 3m (0.30 g, 48.4%) as a white solid. m.p.224 °C, Rf=0.56 (EtOAc:PE=1:5). 1H-NMR (400 MHz, CDCl3) δ: 8.15 (d, J=8.36 Hz, 4H), 7.72 (q, J1=8.40 Hz, J2=1.60 Hz, 4H), 3.97 (s, 6H). 13C-NMR (150 MHz, DMSO-d6) δ: 167.4, 143.7, 130.4, 129.1, 127.8, 52.7. GC-MS: m/z=270.2.
1, 2-diphenylethane (3n):
According to general procedure: benzyl bromide (2.00 g, 11.70 mmol), bis(pinacolate)diboron (4.46 g, 17.54 mmol), potassium acetate (3.44 g, 35.09 mmol), palladium-carbon (0.12 g, 0.12 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 3 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 1,2-diphenylethane 3n (0.83 g, 78.0%) as a white solid. m.p.48~50 ℃, Rf=0.37 (EtOAc:PE=1:5). 1H-NMR (400 MHz, CDCl₃) δ: 7.28 (m, 5H), 7.20 (m, 5H), 2.92 (s, 4H).

13C-NMR (150 MHz, CDCl₃) δ: 141.8, 128.4, 128.3, 125.9, 37.9.

GC-MS: m/z=182.2.

2-naphthoic acid (3o):
According to general procedure: 6-bromo-2-naphthylacetic acid (1.00 g, 3.98 mmol), bis(pinacolate)diboron (1.52 g, 5.98 mmol), potassium acetate (1.17 g, 11.95 mmol), palladium-carbon (0.04 g, 0.04 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 6 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford 2-naphthoic acid 3o (0.68 g, 98.8%) as a white solid. m.p.174~180 ℃, Rf=0.57 (EtOAc:PE:AcOH=1:3:0.2). 1H-NMR (600 MHz, CDCl₃) δ: 8.74 (s, 1H), 8.15 (d, J=8.52 Hz, 1H), 8.02 (d, J=8.16 Hz, 1H), 7.93 (t, J=9.18 Hz, 2H), 7.66~7.58 (m, 2H). 13C-NMR (150 MHz, CDCl₃) δ: 171.9, 136.0, 132.4, 132.2, 129.6, 128.7, 128.4, 127.8, 126.8, 126.4, 125.4. ESI-MS: [M-H]=[170.9.

Benzoic acid (3p):
According to general procedure: 4-bromobenzoic acid (0.50 g, 4.10 mmol), bis(pinacolate)diboron (1.56 g, 6.15 mmol), potassium acetate (1.21 g, 12.30 mmol), palladium-carbon (0.04 g, 0.04 mmol), anhydrous ethanol (15 mL) were mixed under Ar and heated at 60 °C with stirring for 7 h. The reaction mixture was worked up according to the general procedure and purified by flash column chromatography on silica gel to afford benzoic acid 3p (0.47 g, 93.3%) as a white solid. m.p.120~121 ℃, Rf=0.60 (EtOAc:PE=1:5). 1H-NMR (600 MHz, CDCl₃) δ: 8.13 (dd, J=1.02 Hz, 2H).
$J_2=8.10$ Hz, 2H), 7.63-7.61 (m, 1H), 7.49 (t, $J=7.68$ Hz, 2H). $^{13}$C-NMR (150 MHz, CDCl$_3$) $\delta$: 172.4, 133.8, 130.2, 129.3, 128.5. ESI-MS: [M-H]$^-$=120.9.

$^1$H, $^{13}$C NMR and MS

Biphenyl (3a):

$^1$H NMR spectra of 3a (in CDCl$_3$)

$^{13}$C NMR spectra of 3a (in CDCl$_3$)
MS spectra of 3a
4, 4'-dimethyl-1, 1'-biphenyl (3b):

$^1$H NMR spectra of 3b (in CDCl$_3$)

$^{13}$C NMR spectra of 3b (in CDCl$_3$)
MS spectra of 3b
Benzerythrene (3c):

$^1$H NMR spectra of 3c (in CDCl$_3$)

$^{13}$C NMR spectra of 3c (in CDCl$_3$)
MS spectra of 3c
$5,5',5',8,8,8',8'$-octamethyl-$5,5',6,6',7,7',8,8'$-octahydro-$2,2'$-binaphthalene (3d):

$^1$H NMR spectra of 3d (in CDCl$_3$)

$^{13}$C NMR spectra of 3d (in CDCl$_3$)
MS spectra of 3d
3, 3’-dimethoxy-1, 1’-biphenyl (3e):

$^1$H NMR spectra of 3e

$^{13}$C NMR spectra of 3e
MS spectra of 3e
2, 2'-dimethoxy-1, 1 '-biphenyl (3f):

$^1$H NMR spectra of 3f (in CDCl$_3$)

$^{13}$C NMR spectra of 3f (in CDCl$_3$)
MS spectra of 3f

2,2'-Biphenol (3g):

\(^1\)H NMR spectra of 3g (in CDCl₃)
MS spectra of 3g

4,4'-Biphenol (3h):

$^1$H NMR spectra of 3h (in DMSO-$d_6$)
$^{13}$C NMR spectra of 3h (in DMSO-$d_6$)
MS spectra of 3h

4,4’-Bianiline (3i):
$^1$H NMR spectra of 3i (in CDCl$_3$)

$^{13}$C NMR spectra of 3i (in DMSO-$d_6$)
3,3'-Diaminobiphenyl (3j):
$^1$H NMR spectra of 3j (in CDCl$_3$)

$^{13}$C NMR spectra of 3j (in DMSO-$d_6$)
5, 5'-difluoro-2, 2'-bipyridine (3k):

$^1$H NMR spectra of 3k (in CDCl$_3$)
$^{13}$C NMR spectra of 3k (in CDCl$_3$)
MS spectra of 3k
2, 2'-bipyridine (3l):

$^1$H NMR spectra of 3l (in CDCl$_3$)

$^{13}$C NMR spectra of 3l (in CDCl$_3$)
MS spectra of 3l
4,4'-bis(methoxycarbonyl)biphenyl (3m):

$^1$H NMR spectra of 3m (in CDCl$_3$)
$^{13}$C NMR spectra of 3m (in DMSO-$d_6$)
MS spectra of 3m
1, 2-diphenylethane (3n):

$^1$H NMR spectra of 3n (in CDCl$_3$)

$^{13}$C NMR spectra of 3n (in CDCl$_3$)
MS spectra of 3n
2-naphthoic acid (3o):

$^1$H NMR spectra of 3o (in CDCl$_3$)

$^{13}$C NMR spectra of 3o (in CDCl$_3$)
MS spectra of 3o

Benzoic acid (3p):
$^1$H NMR spectra of 3p (in CDCl$_3$)

$^{13}$C NMR spectra of 3p (in CDCl$_3$)
MS spectra of 3p

\(^1\)H NMR spectra of 3q (in CDCl\(_3\))
MS spectra of 3q

Molecular Weight 218.10