Ligand-free Iron/Copper Cocatalyzed N-Arylations of Aryl Halides with Amines under Microwave Irradiation

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**General Information**

The reagents (chemicals) were purchased from commercial chemical reagent company, and used without further purification unless otherwise stated. All of the microwave-assistant reactions were performed in an Initiator™ EXP microwave system (Biotage, Inc.) at the specified temperature using the standard mode of operation. Analytical thin-layer chromatography (TLC) was HSGF 254. All products were characterized by their NMR and LRMS and HRMS spectra. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and broad (br).

**General procedure for the Coupling reaction:** A mixture of Fe₂O₃ (32 mg, 0.2 mmol), Cu(acac)₂ (26 mg, 0.1 mmol), and Cs₂CO₃ (650 mg, 2.0 mmol) was dissolved in DMSO(3 mL). Subsequently, iodobenzene (160 μL, 1.5 mmol), morpholine (88 μL, 1.0 mmol) and H₂O (3 mL) were added to this mixture. The vial was sealed and the mixture was then irradiated for 30 min at 150 °C. The mixture was then cooled to room temperature, and diluted with dichloromethane, washed with brine, dried over using anhydrous Na₂SO₄, and concentrated in vacuum. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 10 : 1) to yield the expected product 1g (135 mg, 83% yield). The identity and purity of the product was confirmed by ¹H and ¹³C NMR spectroscopic analysis.
Spectroscopic and Analytical Data

N-butylbenzenamine (1a)

\[
\begin{align*}
\text{\textit{1}H NMR (300 MHz, CDCl}_3\text{): } & \delta 7.19-7.14 (m, 2H), 6.70-6.66 (m, 1H), 6.61-6.58 (m, 2H), 3.12-3.07 (m, 2H), 1.61-1.54 (m, 2H), 1.46-1.38 (m, 2H), 0.98-0.93 (m, 3H). \\
\text{\textit{13}C NMR (100 MHz, CDCl}_3\text{): } & \delta 148.4, 129.1, 117.0, 112.6, 43.6, 31.6, 20.2, 13.8. \\
\text{MS (EI, m/z): } & 149 [M]^+; \text{ HRMS (EI): Calcd. for C}_{10}H_{15}N [M]^+: 149.1204; \text{ Found: 149.1208.}
\end{align*}
\]

N-(2-methoxyethyl)benzenamine (1b)

\[
\begin{align*}
\text{\textit{1}H NMR (300 MHz, CDCl}_3\text{): } & \delta 7.20-7.15 (m, 2H), 6.74-6.69 (m, 1H), 6.64-6.61 (m, 2H), 3.58 (t, J=5.1 Hz, 2H), 3.37 (s, 3H), 3.27 (t, J=5.1 Hz, 2H). \\
\text{\textit{13}C NMR (100 MHz, CDCl}_3\text{): } & \delta 148.1, 129.1, 117.5, 113.0, 70.9, 58.6, 43.3. \\
\text{MS (EI, m/z): } & 151 [M]^+; \text{ HRMS (EI): Calcd. for C}_{9}H_{13}NO [M]^+: 151.0997; \text{ Found: 151.0990.}
\end{align*}
\]

N-(3-methoxypropyl)benzenamine (1c)

\[
\begin{align*}
\text{\textit{1}H NMR (300 MHz, CDCl}_3\text{): } & \delta 7.19-7.14 (m, 2H), 6.71-6.66 (m, 1H), 6.62-6.59 (m, 2H), 3.50 (t, J=6.0 Hz, 2H), 3.35 (s, 3H), 3.21 (t, J=6.0 Hz, 2H), 1.91-1.83 (m, 2H). \\
\text{\textit{13}C NMR (100 MHz, CDCl}_3\text{): } & \delta 148.4, 129.1, 117.0, 112.6, 71.1, 58.6, 41.6, 29.2.
\end{align*}
\]
MS (EI, m/z): 165 [M]+; HRMS (EI): Calcd. for C_{10}H_{15}NO [M]+: 165.1154; Found: 165.1149.

N-(cyclopropylmethyl)benzenamine (1d)

![Structure of N-(cyclopropylmethyl)benzenamine (1d)]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.19-7.14 (m, 2H), 6.71-6.66 (m, 1H), 6.61-6.58 (m,2H), 2.94 (d, $J$=6.3Hz, 2H), 1.11-1,06 (m, 1H), 0.57-0.51 (m,2H), 0.25-0.20 (m,2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 148.4, 129.2, 117.2, 112.7, 49.0, 10.8, 3.4.

MS (EI, m/z): 147 [M]+; HRMS (EI): Calcd. for C$_{10}$H$_{13}$N [M]+: 147.1048; Found: 147.1044.

N-cyclohexylbenzenamine (1e)

![Structure of N-cyclohexylbenzenamine (1e)]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.18-7.12 (m, 2H), 6.68-6.63 (m, 1H), 6.59-6.56 (m, 2H), 3.29-3.21 (m, 1H), 2.08-2.03 (m, 2H), 1.79-1.72 (m, 2H), 1.68-1.62 (m, 1H), 1.44-1.08 (m, 5H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 147.3, 129.2, 116.8, 113.1, 51.6, 33.4, 25.9, 25.0.

MS (EI, m/z): 175 [M]+; HRMS (EI): Calcd. for C$_{12}$H$_{17}$N [M]+: 175.1361; Found: 175.1362.

N-phenylpiperidine (1f)

![Structure of N-phenylpiperidine (1f)]
$^1$H NMR (300 MHz, CDCl$_3$): δ 7.26-7.21 (m, 2H), 6.94-6.92 (m, 2H), 6.83-6.78 (m, 1H), 3.14 (t, J=5.7 Hz, 4H), 1.74-1.66 (m, 4H), 1.59-1.54 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 152.2, 128.9, 119.2, 116.5, 50.6, 25.8, 24.2.

MS (EI, m/z): 161 [M$^+$]; HRMS (EI): Calcd. for C$_{11}$H$_{15}$N [M$^+$]: 161.1204; Found: 161.1201.

4-phenylmorpholine (1g)

$^1$H NMR (300 MHz, CDCl$_3$): δ 7.30-7.25 (m, 2H), 6.92-6.85 (m, 3H), 3.85 (t, J=4.8 Hz, 4H), 3.14 (t, J=4.8 Hz, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 151.2, 129.1, 120.0, 115.6, 66.9, 49.3.

MS (EI, m/z): 163 [M$^+$]; HRMS (EI): Calcd. for C$_{10}$H$_{13}$NO [M$^+$]: 163.0997; Found: 163.0995.

N-benzylbenzenamine (1h)

$^1$H NMR (300 MHz, CDCl$_3$): δ 7.34-7.24 (m, 5H), 7.18-7.12 (m, 2H), 6.73-6.68 (m, 1H), 6.61-6.58 (m, 2H), 4.27 (s, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 148.0, 139.3, 129.2, 128.6, 127.4, 127.1, 117.5, 112.8, 48.2.

MS (EI, m/z): 183 [M$^+$]; HRMS (EI): Calcd. for C$_{13}$H$_{13}$N [M$^+$]: 183.1048; Found: 183.1090.
N-phenethylbenzenamine (1i)

\[ \text{\chem{H\-N\-C\(\cdot\cdot\cdot\)C}} \]

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.35-7.30 (m, 2H), 7.26-7.15 (m, 5H), 6.75-6.69 (m, 1H), 6.61-6.59 (m, 2H), 3.40 (t, \(J=6.9\) Hz, 2H), 2.91 (t, \(J=6.9\) Hz, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 147.9, 139.2, 129.2, 128.7, 128.5, 126.4, 117.4, 112.9, 45.0, 35.4.

MS (EI, m/z): 197 \([\text{M}]^+\); HRMS (EI): Calcd. for C\(_{14}\)H\(_{15}\)N \([\text{M}]^+\): 197.1204; Found: 197.1218.

1-phenyl-1H-pyrazole (1j)

\[ \text{\chem{\text{\(\cdot\cdot\cdot\)N\-C}}}} \]

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.92-7.91 (m, 1H), 7.74-7.69 (m, 3H), 7.48-7.42 (m, 2H), 7.31-7.26 (m, 1H), 6.47-6.45 (m, 1H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 141.0, 140.0, 129.3, 126.6, 126.3, 119.0, 107.4.

MS (EI, m/z): 144 \([\text{M}]^+\); HRMS (EI): Calcd. for C\(_9\)H\(_8\)N\(_2\) \([\text{M}]^+\): 144.0687; Found: 144.0691.

1-phenyl-1H-indole (1k)

\[ \text{\chem{\text{\(\cdot\cdot\cdot\)N}}\-\text{\chem{\text{\(\cdot\cdot\cdot\)C}}}} \]

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.70-7.67 (m, 1H), 7.57-7.54 (m, 1H), 7.49-7.46 (m, 4H), 7.34-7.30 (m, 2H), 7.24-7.14 (m, 2H), 6.67-6.66 (m, 1H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 139.8, 135.8, 129.5, 129.3, 127.9, 126.4, 124.3, 122.3,
121.1, 120.3, 110.4, 103.5.


4-methoxy-N-phenylaniline (1l)

\[
\text{O} \quad \text{H} \\
\text{N}
\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.23-7.19 (m, 2H), 7.08-7.06 (m, 2H), 6.91-6.81 (m, 5H), 5.49 (s, br, 1H), 3.70 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 155.2, 145.1, 135.7, 129.3, 122.1, 119.5, 115.6, 114.6, 55.5.


Diphenylamine (1m)

\[
\text{H} \quad \text{N}
\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.29-7.25 (m, 4H), 7.08-7.06 (m, 4H), 6.96-6.91 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 143.0, 129.3, 121.0, 117.8.


4-(4-methoxyphenyl)morpholine (2a)

\[
\text{MeO} \quad \text{N} \quad \text{O}
\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 6.91-6.83 (m, 4H), 3.87-3.84 (m, 4H), 3.77 (s, 3H),
3.07-3.04 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 153.9, 145.5, 117.8, 114.5, 67.0, 55.5, 50.8.


4-(3-methoxyphenyl)morpholine (2b)

\[
\text{MeO} \quad \text{N} \quad \text{O}
\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.23-7.17 (m, 1H), 6.56-6.52 (m, 1H), 6.47-6.44 (m, 2H), 3.85 (t, $J$=4.8 Hz, 4H), 3.80 (s, 3H), 3.15 (t, $J$=4.8 Hz, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 160.5, 152.6, 129.8, 108.3, 104.6, 102.1, 66.7, 55.0, 49.1.


4-(2-methoxyphenyl)morpholine (2c)

\[
\text{O} \quad \text{Me} \quad \text{N} \quad \text{O}
\]

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.03-6.99 (m, 1H), 6.94-6.92 (m, 2H), 6.89-6.86 (m, 1H), 3.89 (t, $J$=4.8 Hz, 4H), 3.86 (s, 3H), 3.07 (t, $J$=4.8 Hz, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 152.1, 141.0, 123.1, 120.9, 117.9, 111.1, 67.1, 55.2, 51.1.


4-p-tolylmorpholine (2d)
$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.21-7.19 (m, 2H), 7.05-7.02 (m, 2H), 3.87 (t, $J=4.5$ Hz, 4H), 2.93 (t, $J=4.5$ Hz, 4H), 2.33 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 153.4, 148.8, 130.0, 129.6, 116.3, 115.1, 66.8, 50.1, 20.4.

MS (EI, m/z): 177 [M]$^+$; HRMS (EI): Calcd. for C$_{11}$H$_{15}$NO [M]$^+$: 177.1154; Found: 177.1158.

4-m-tolylmorpholine (2e)

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.20-7.17 (m, 1H), 6.77-6.73 (m, 3H), 3.89-3.86 (m, 4H), 3.19-3.16 (m, 4H), 2.35 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 151.2, 138.8, 128.9, 120.9, 116.5, 112.8, 66.8, 49.4, 21.7.

MS (EI, m/z): 177 [M]$^+$; HRMS (EI): Calcd. for C$_{11}$H$_{15}$NO [M]$^+$: 177.1154; Found: 177.1151.

4-(4-(trifluoromethyl)phenyl)morpholine (2g)

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.50 (d, $J=6.6$ Hz, 2H), 6.92 (d, $J=6.6$ Hz, 2H), 3.87 (t, $J=3.6$ Hz, 4H), 3.24 (t, $J=3.6$ Hz, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 153.3, 126.5, 126.4, 114.3, 66.6, 48.1.

MS (EI, m/z): 231 [M]$^+$; HRMS (EI): Calcd. for C$_{11}$H$_{12}$F$_3$NO [M]$^+$: 231.0871; Found: 231.0871.
4-(3-(trifluoromethyl)phenyl)morpholine (2h)

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{N} \\
\text{O} & \\
\end{align*}
\]

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\ 7.39\text{-}7.33\) (m, 1H), 7.17\text{-}7.11 (m, 2H), 7.08\text{-}7.05 (m, 1H), 3.91\text{-}3.88 (m, 4H), 3.22\text{-}3.20 (m, 4H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\ 151.4, 129.6, 118.4, 116.3, 116.2, 111.9, 111.8, 66.7, 48.8\).


4-(4-nitrophenyl)morpholine (2j)

\[
\begin{align*}
\text{O}_2\text{N} & \quad \text{N} \\
\text{O} & \\
\end{align*}
\]

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\ 8.16\text{-}8.12\) (m, 2H), 6.93\text{-}6.90 (m, 1H), 6.84\text{-}6.81 (m, 1H), 3.87 (t, \(J=5.1\) Hz, 4H), 2.93 (t, \(J=5.1\) Hz, 4H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\ 155.0, 138.9, 126.2, 125.9, 115.6, 112.6, 66.3, 47.1\).


4-(4-chlorophenyl)morpholine (2k)

\[
\begin{align*}
\text{Cl} & \quad \text{N} \\
\text{O} & \\
\end{align*}
\]

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\ 7.23\text{-}7.20\) (m, 2H), 6.84\text{-}6.81 (m, 2H), 3.86\text{-}3.83 (m, 4H), 3.13\text{-}3.09 (m, 4H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\ 149.8, 129.0, 124.8, 116.8, 66.7, 49.3\).

**Indoline (3a)**

\[
\begin{array}{c}
\text{N} \\
\text{H}
\end{array}
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\text{)}: \delta 7.13-7.10 \text{ (m, 1H)}, 7.04-6.98 \text{ (m, 1H)}, 6.73-6.70 \text{ (m 1H)}, 6.68-6.62 \text{ (m, 1H)}, 3.64 \text{ (s, br, 1H)}, 3.52 \text{ (t, } J=8.1 \text{ Hz, 2H)}, 3.01 \text{ (t, } J=8.1 \text{ Hz, 2H}).
\]

\(^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}: \delta 151.4, 129.3, 127.1, 124.5, 118.6, 109.4, 47.2, 29.7.


**2-(cyclohexylamino)benzoic acid (3b)**

\[
\begin{array}{c}
\text{COOH} \\
\text{N} \\
\text{H}
\end{array}
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\text{)}: \delta 7.99-7.96 \text{ (m, 1H)}, 7.38-7.33 \text{ (m, 1H)}, 6.73-6.70 \text{ (m 1H)}, 6.58-6.53 \text{ (m, 1H)}, 3.43-3.42 \text{ (d, br, 1H)}, 2.07-2.02 \text{ (m, 3H)}, 1.80-1.77 \text{ (m, 2H)}, 1.43 \text{ (s, 1H)}, 1.40-1.28 \text{ (m, 5H}).
\]

\(^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}: \delta 174.8, 151.0, 135.4, 132.8, 114.0, 111.8, 108.3, 50.6, 32.8, 25.8, 24.7.


**2-methylquinazolin-4(3H)-one (3c)**
$^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 12.2 (s, br, 1H), 8.07 (d, 1H, $J = 7.8$ Hz), 7.76 (t, 1H, $J = 7.2$ Hz), 7.56 (d, 1H, $J = 7.8$ Hz), 7.44 (t, 1H, $J = 7.2$ Hz), 2.35 (s, 3H).

$^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 161.7, 154.3, 149.0, 134.2, 126.6, 125.8, 125.7, 120.6, 21.4.

MS (EI, m/z): 160 [M$^+$]; HRMS (EI): Calcd. for C$_9$H$_8$N$_2$O [M$^+$]: 160.0637; Found: 160.0641.
Copies of $^1$H NMR and $^{13}$C NMR of Compounds

N-butylbenzenamine (1a)
N-(2-methoxyethyl)benzenamine (1b)
N-(3-methoxypropyl)benzenamine (1c)
N-(cyclopropylmethyl)benzenamine (1d)
N-cyclohexylbenzenamine (1e)
N-phenylpiperidine (1f)
4-phenylmorpholine (1g)
N-benzylbenzenamine (1h)
N-phenethylbenzenamine (1i)
1-phenyl-1H-pyrazole (1j)
1-phenyl-1H-indole (1k)
4-methoxy-N-phenylaniline (II)
Diphenylamine (1m)
4-(4-methoxyphenyl)morpholine (2a)
4-(3-methoxyphenyl)morpholine (2b)
4-(2-methoxyphenyl)morpholine (2c)
4-p-tolylmorpholine (2d)
4-m-tolylmorphone (2e)
4-(4-(trifluoromethyl)phenyl)morpholine (2g)
4-(3-(trifluoromethyl)phenyl)morpholine (2h)
4-(4-nitrophenyl)morpholine (2j)
4-(4-chlorophenyl)morpholine (2k)
Indoline (3a)
2-(cyclohexylamino)benzoic acid (3b)
2-methylquinazolin-4(3H)-one (3c)