Electronic Supplementary Information

**Nickel-catalyzed C-O bond reduction of aryl and benzyl 2-pyridyl ethers**

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I. Experimental procedures and spectral data

General
All reactions were performed under nitrogen atmosphere using standard Schlenk and vacuum line techniques. Toluene, THF and Et₂O were purified by JC Meyer Phoenix Solvent Systems. 1,4-Dioxane and xylene were distilled over sodium under nitrogen. DMF was dried over 4 Å molecular sieve, fractionally distilled under reduced pressure and stored under nitrogen. Ni(COD)₂ was purchased from Strem Chemicals Inc and used as received. 3-(Biphenyl-4-yloxy)pyridine and 4-(biphenyl-4-yloxy)pyridine were purchased from Energy Chemical and used as received. NHC ligands,² aryl and benzyl 2-pyridyl ethers³,⁴ and related starting materials⁵ were prepared according to reported procedures. All other chemicals were obtained from commercial vendors and used as received. Gas chromatography (GC) analysis was conducted on a Agilent 7820A instrument. NMR spectra were recorded on a Bruker Avance III 400 spectrometer at ambient temperature. The chemical shifts of the ¹H NMR spectra were referenced to TMS or internal solvent resonance and the chemical shifts of the ¹³C NMR spectra were referenced to internal solvent resonance.

1. Preparation of sodium isopropoxide¹
Sodium (0.23 g, 10 mmol) and xylene (20 cm³) were placed in a N₂-filled three-neck flask and heated until the sodium melted. The flask was closed with a rubber stopper, and the sodium was finely powdered by vigorous shaking. Then the xylene was removed by filtration and the powdered sodium was washed with two 10 cm³ portions of diethyl ether. 30 cm³ of diethyl ether was added, and the flask was placed on a 50 °C oil bath with a condenser. Anhydrous isopropanol (0.77 cm³, 10 mmol) was added dropwise with stirring. The reaction mixture was refluxed with stirring for 8 h. The solvent was removed by filtration. The residual solid was washed twice with diethyl ether and dried under vacuum.

2. Typical procedure for the nickel-catalyzed hydrogenation of aryl 2-pyridyl ethers
A Schlenk tube was charged with Ni(COD)₂ (1.7 mg, 0.006 mmol), IPr·HCl (2.6 mg, 0.006 mmol), i-PrONa (25 mg, 0.30 mmol), 2-([1,1'-biphenyl]-4-yloxy)pyridine (49.4 mg, 0.2
mmol) and THF (1 cm³). The mixture was stirred at 60 °C for 2 h. Volatiles were removed by rotary evaporation. The residue was purified by column chromatography on silica gel or preparative thin layer chromatography (petroleum ether/EtOAc 60:1 v/v) to give 1,1'-biphenyl as a white solid, yield 30.5 mg (99%).

3. Nickel-catalyzed hydrogenation of 2-(biphenyl-4-yloxy)pyridine (4 mmol scale)
A Schlenk tube was charged with Ni(COD)₂ (33 mg, 0.12 mmol), IPr·HCl (51 mg, 0.12 mmol), i-PrONa (0.492 g, 6 mmol), 2-([1,1'-biphenyl]-4-yloxy)pyridine (0.988 g, 4 mmol) and THF (8 cm³). The mixture was stirred at 60 °C for 2 h. Volatiles were removed by rotary evaporation. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc 60:1 v/v) to give 1,1'-biphenyl as a white solid, yield 0.527 g (86%).

4. Spectral data for the cross-coupling products
(1) 1,1'-biphenyl (2a)

![1,1'-biphenyl](image)

Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 30.8 mg (99%). ¹H NMR (400 MHz, CDCl₃): δ 7.67 (d, J = 8.0 Hz, 4H), 7.51 (t, J = 7.5 Hz, 4H), 7.41 (t, J = 7.2 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 141.34, 128.88, 127.38, 127.29.

(2) oxydibenzene (2c)

![Oxydibenzene](image)

Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 31.1 mg (90%). ¹H NMR (400 MHz, CDCl₃): δ 7.42–7.30 (m, 4H), 7.13 (t, J = 7.4 Hz, 2H), 7.08–6.99 (m, 4H). ¹³C NMR (101 MHz, CDCl₃): δ 157.38, 129.87, 123.34, 119.02.

(3) (benzyloxy)benzene (2d)

![Benzyloxybenzene](image)

Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 36.0 mg (98%). ¹H NMR (400 MHz, CDCl₃): δ 7.36 (d, J = 7.2 Hz, 2H), 7.30 (t, J = 7.3 Hz, 2H), 7.27–7.16 (m,
3H), 6.95–6.83 (m, 3H), 4.98 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 158.89, 137.18, 129.62, 128.71, 128.07, 127.62, 121.06, 114.95, 70.01

(4) 4-fluoro-1,1'-biphenyl (2f)$^7$

\[\begin{array}{c}
\text{F} \\
\text{H} \\
\text{H} \\
\text{C} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{H}
\end{array}\]

Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 29.5 mg (86%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.59–7.50 (m, 4H), 7.44 (t, $J$ = 7.6 Hz, 2H), 7.39–7.32 (m, 1H), 7.13 (t, $J$ = 8.7 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 162.59 (d, $J$ = 246.2 Hz), 140.39, 137.47 (d, $J$ = 3.2 Hz), 128.96, 128.83 (d, $J$ = 8.0 Hz), 127.40, 127.16, 115.75 (d, $J$ = 21.4 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ –115.85.

(5) (E)-1,2-diphenylethene (2g)$^6$

\[\begin{array}{c}
\text{Ph} \\
\text{C} \\
\text{H} \\
\text{H}
\end{array}\]

Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 35.5 mg (99%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.57–7.46 (m, 4H), 7.35 (t, $J$ = 7.6 Hz, 4H), 7.29–7.21 (m, 2H), 7.11 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 137.43, 128.81, 127.75, 126.64.

(6) N-phenylacetamide (2h)$^6$

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

Eluent: petroleum ether/ethyl acetate = 1:1 (v/v). White solid, yield 24.2 mg (90%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.99–7.62 (br, 1H), 7.50 (d, $J$ = 8.0 Hz, 2H), 7.29 (t, $J$ = 7.6 Hz, 2H), 7.09 (t, $J$ = 7.2 Hz, 1H), 2.15 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 168.87, 138.06, 129.03, 124.39, 120.13, 24.60.

(7) tert-butyl methyl(phenyl)carbamate (2i)$^6$

\[\begin{array}{c}
\text{Boc} \\
\text{N} \\
\text{Me} \\
\text{Ph}
\end{array}\]

Eluent: petroleum ether/ethyl acetate = 5:1 (v/v). Colorless oil, yield 28.9 mg (70%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.25 (t, $J$ = 7.8 Hz, 2H), 7.16 (d, $J$ = 7.6 Hz, 2H), 7.09 (t, $J$ = 7.2 Hz, 2H), 7.04 (t, $J$ = 7.2 Hz, 2H), 7.02 (t, $J$ = 7.2 Hz, 2H), 7.00 (t, $J$ = 7.2 Hz, 2H), 6.98 (t, $J$ = 7.2 Hz, 2H), 6.96 (t, $J$ = 7.2 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 158.32, 137.16, 129.62, 128.71, 128.07, 127.62, 121.06, 114.95, 70.01.
Hz, 1H), 3.19 (s, 3H), 1.38 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 154.92, 143.93, 128.67, 125.65, 125.50, 80.34, 37.44, 28.44.

(8) benzophenone (2k)$^8$

![Image](image1.png)

Eluent: petroleum ether/ethyl acetate = 20:1 (v/v). White solid, yield 35.7 mg (98%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.86–7.76 (m, 4H), 7.59 (t, $J = 7.4$ Hz, 2H), 7.48 (t, $J = 7.6$ Hz, 4H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 196.91, 137.69, 132.55, 130.19, 128.40.

(9) $N,N$-diethylbenzamide (2l)$^9$

![Image](image2.png)

Eluent: petroleum ether/ethyl acetate = 2:1 (v/v). Colorless oil, yield 29.0 mg (82%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.45–7.28 (m, 5H), 3.54 (br, 2H), 3.24 (br, 2H), 1.24 (br, 3H), 1.09 (br, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 171.39, 137.36, 129.17, 128.49, 126.34, 43.36, 39.30, 14.31, 13.00.

(10) 4-methyl-1,1'-biphenyl (4a)$^{10}$

![Image](image3.png)

Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 27.7 mg (83%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.65–7.58 (m, 2H), 7.53 (d, $J = 8.1$ Hz, 2H), 7.45 (t, $J = 7.6$ Hz, 2H), 7.35 (t, $J = 7.4$ Hz, 1H), 7.28 (d, $J = 7.9$ Hz, 2H), 2.43 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 141.29, 138.48, 137.16, 129.62, 128.85, 127.13, 127.11, 21.25.

(11) 2-methylnaphthalene (4d)$^{11}$

![Image](image4.png)

Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 23.4 mg (83%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.84 (d, $J = 7.8$ Hz, 1H), 7.82–7.75 (m, 2H), 7.65 (s, 1H), 7.53–7.41 (m, 2H), 7.36 (dd, $J = 8.4$, 1.4 Hz, 1H), 2.56 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 135.56, 133.79, 131.82, 128.24, 127.82, 127.73, 127.36, 126.96, 125.99, 125.08, 21.85.
(12) 6-methylquinoline (4e)\textsuperscript{12}

Eluent: petroleum ether/ethyl acetate = 5:1 (v/v). Colorless oil, yield 24.1 mg (84%). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 8.84 (dd, J = 4.2, 1.5 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.61 – 7.49 (2 H, m), 7.34 (dd, J = 8.3, 4.2 Hz, 1H), 2.53 (s, 3H). \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}): δ 149.63, 146.98, 136.51, 135.51, 131.87, 129.18, 128.43, 126.70, 121.18, 21.69.

(13) diphenylmethane (4f)\textsuperscript{13}

Performed on 0.4 mmol scale. Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 25.1 mg (31%). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.33–7.24 (m, 4H), 7.22–7.14 (m, 6H), 3.98 (s, 2H). \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}): δ 141.25, 129.07, 128.59, 126.20, 42.08.

II. Reaction mechanism

(1) Deuterium labeling experiment

A Schlenk tube was charged with Ni(COD)\textsubscript{2} (1.7 mg, 0.006 mmol), IPr·HCl (2.6 mg, 0.006 mmol), (CD\textsubscript{3})\textsubscript{2}CDONa (27 mg, 0.30 mmol), 2-[(1,1'-biphenyl]-4-yloxy)pyridine (49.4 mg, 0.2 mmol) and THF (1 cm\textsuperscript{3}). The mixture was stirred at 60 °C for 2 h. Volatiles were removed by rotary evaporation. The residue was purified by preparative thin-layer chromatography (developing solvent: petroleum ether/EtOAc = 60:1 v/v) to give the reductive product as a white solid, yield 28.4 mg (92%). The deuterium content at the initial position of C-O bond was approximately 93% determined by \textsuperscript{1}H NMR spectroscopy (Figure S1).
Figure S1 $^1$H and $^{13}$C NMR spectra of 1,1'-biphenyl-4-d.
(2) Kinetic isotope effect experiment

\[
\text{Ph} \text{O} \text{N} + \text{i-PrONa} \quad 0.4 \text{ mmol} \\
\text{Ph} \text{O} \text{N} + \text{i-PrONa-D7} \quad 0.4 \text{ mmol}
\]

A Schlenk tube was charged with Ni(COD)$_2$ (3.3 mg, 0.012 mmol), IPr-HCl (5.2 mg, 0.012 mmol), i-PrONa (49.2 mg, 0.60 mmol), 2-([1,1'-biphenyl]-4-yloxy)pyridine (98.8 mg, 0.4 mmol), THF (2 cm$^3$) and dodecane (30 μl). The mixture was stirred at 60 °C. A 0.1 cm$^3$ aliquot was taken from the reaction mixture at 3, 6, 9, and 12 min., which were separately quenched with H$_2$O (1 cm$^3$) and diluted with EtOAc (3 cm$^3$). The GC yields were determined using dodecane as an internal standard. The reaction with i-PrONa-D$_7$ was carried out and monitored under exact same conditions. The experimental results are showed in Figure S2. The calculated KIE value is 1.41.

Figure S2 Intermolecular parallel KIE experiment with i-PrONa and i-PrONa-D$_7$. For group with i-PrONa, $y = 1.117x - 2.0345$, $R^2 = 0.990$; For group with i-PrONa-D$_7$, $y = 0.7915x - 1.1399$, $R^2 = 0.9858$. Thus KIE value is 1.41.
References
III. Copies of NMR spectra

(1) 1,1'-biphenyl (2a)
(2) oxydibenzene (2c)
(3) (benzyloxy)benzene (2d)
(4) 4-fluoro-1,1'-biphenyl (2f)
$^{19}$F NMR (376 MHz, CDCl$_3$)
(5) (E)-1,2-diphenylethane (2g)
(6) \( N \)-phenylacetamide (2h)

\[ \text{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3})} \]

\[ \text{\textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3})} \]
(7) *tert*-butyl methyl(phenyl)carbamate (2i)
(8) benzophenone (2k)
(9) N,N-diethylbenzamide (21)
(10) 4-methyl-1,1’-biphenyl (4a)
(11) 2-methylnaphthalene (4d)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
(12) 6-methylquinoline (4e)

\[ \text{H NMR (400 MHz, CDCl}_3) \]

\[ \text{13C NMR (101 MHz, CDCl}_3) \]
(13) diphenylmethane (4f)