Electronic Supplementary Information

Catalytic meta-selective C-H functionalization to construct quaternary carbon centres.

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# Contents

General Considerations: .......................................................................................................................... 3  
Reaction Optimisation ................................................................................................................................. 5  
Synthesis of 2-Substituted Pyridine Derivatives ...................................................................................... 10  
Synthesis of *meta*-Substituted 2-Phenylpyridine Derivatives .................................................................. 15  
Mechanistic Studies .................................................................................................................................. 29  
  Synthesis of Complex A ............................................................................................................................. 29  
  Catalytic Reaction using Complex A ......................................................................................................... 29  
  Reactions with Substrates 1j-1l ............................................................................................................. 30  
  Reactions with TEMPO ............................................................................................................................ 32  
References ................................................................................................................................................... 33  
NMR Spectra ............................................................................................................................................... 34
General Considerations:

$^1$H, $^{13}$C and $^{19}$F nuclear magnetic resonance (NMR) spectra were recorded on an Agilent Technologies spectrometer ($^1$H NMR at 500 MHz, $^{13}$C NMR at 126 MHz, and $^{19}$F NMR at 470 MHz). Chemical shifts for protons are reported downfield from tetramethylsilane and are referenced to residual protium in the solvent ($^1$H NMR: CHCl$_3$ at 7.26 ppm). Chemical shifts for carbons are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent peak ($^{13}$C NMR: CDCl$_3$ at 77.0 ppm). Chemical shifts for fluorine resonances are reported in parts per million referenced to CFCl$_3$.

NMR data are represented as follows: chemical shift (integration, multiplicity [s = singlet, bs = broad singlet, d = double, dd = doublet of doublet, t = triplet, q = quartet, hept = heptet, m = multiplet], coupling constants (Hz)). IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrophotometer, with absorbencies quoted as $\nu$ in cm$^{-1}$.

High resolution mass spectrometry was performed on a Bruker Daltonik µTOF electrospray time-of-flight (ESI-TOF) mass spectrometer. HPLC analysis was conducted on an Agilent 1260 infinity quaternary LC instrument equipped with a Zorbax Eclipse XDB-C18 4.6 x 250 mm 5 $\mu$m analytical column. Analytical thin layer chromatography (TLC) were performed using aluminium-backed plates coated with Alugram$^\text{®}$ SIL G/UV$_{254}$ purchased from Macherey-Nagel and visualised by UV light (254 nm) and/or KMnO$_4$, staining. Silica gel column chromatography was carried out using 60 Å, 200-400 mesh particle size silica gel purchased from Sigma-Aldrich.

Materials:

All reactions were carried out under an atmosphere of argon, in oven-dried glassware unless otherwise stated. Anhydrous solvents were used in all experiments and stored under an atmosphere of argon prior to use. [RuCl$_2$ ($p$-cymene)$_2$] was purchased from Strem chemicals. Boronic acids were purchased from Fronteer Scientific. 2-chloro-2-methylpropane, 2-bromo-2-methylpropane, 2-bromo-2methylbutane, 1-bromo adamantine and 3-chloro-3-ethyl pentane were purchased from sigma Aldrich. All other chemicals were bought from Alfa Aesar. All commercially bought chemicals were used without further purification.

Reaction Conversions

Reaction conversions were calculated using $^1$H NMR and confirmed using $^{19}$F NMR where possible. With the exception of those carried out using ethyl 2-bromoisobutrate (2c) all reactions formed one product exclusively and thus conversions represent conversion of the starting material to the desired product. Suitably resolved signals in the crude reaction mixture were used for these calculations. Orthogonal analysis using TLC and HPLC-MS revealed negligible by-products. This is exemplified below.

![Reaction Scheme](image-url)
Conversion by $^1$H NMR of Crude Reaction Mixture: Signal at 8.05 ppm (dd, $J = 1.8$ Hz, 1H) from product 3a and signal at 8.00 – 7.98 (m, $J = 5.3, 3.4$ Hz, 2H) from starting material 1a used for conversion calculation.

HPLC analysis of the crude reaction mixture showing the major components: starting material 1a (retention time 5.93 min) and product 3a (retention time 11.28 min).

Sample prepared to approximate 10 μmol / mL in acetonitrile
Column: Zorbax Eclipse XDB-C18 4.6 x 250 mm 5 μm analytical column
Mobile Phase: Isocratic 70/30 acetonitrile/H$_2$O with 0.1% formic acid
Flow Rate: 0.5 mL / min
UV detection: 254 nm
Reaction Optimisation

General Procedure

To an oven dried, argon purged ampule equipped with magnetic stirrer was added 2-phenylpyridine (1 mmol, 0.14 mL), a solvent (4 mL), 2-Bromo-2-methylpropane, [RuCl₂(p-cymene)]₂ and a base in the amounts specified. The ampule was then sealed and refluxed on a carousel at 120 °C for the amount of time specified. After cooling to room temperature, aqueous NaHCO₃ (saturated) and EtOAc were added. A sample of the organic phase was taken, evaporated to dryness and then conversions analysed by ¹H NMR and HPLC-MS.

Base Screen

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Solvent Screen

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<td>Cyclopentyl methyl ether</td>
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<td>2-Butanone</td>
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Catalyst Loading

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<td>7.5</td>
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KOAc Stoichiometry

\[
\begin{align*}
&\text{Conversions (\%)} \\
&\text{No Base} & 0 \\
&0.5 & 24 \\
&1.5 & 58 \\
&1.75 & 65 \\
&2 & 74 \\
&2.5 & 72 \\
&3 & 56 \\
&4 & 59 \\
\end{align*}
\]

Alkyl Halide Stoichiometry

\[
\begin{align*}
&\text{Conversion (\%)} \\
&1 & 0 \\
&1.5 & 38 \\
&2 & 58 \\
&3 & 74 \\
&\text{As solvent} & 72 \\
\end{align*}
\]

Temperature

\[
\begin{align*}
&\text{Conversion (\%)} \\
&25 & 0 \\
&80 & 18 \\
&100 & 50 \\
&120 & 74 \\
&135 & 65 \\
\end{align*}
\]
Reaction Time

Multiple reactions were set up in series and after the designated reaction time were immediately cooled in an ice bath, worked up and analysed as per the general procedure.

\[
\begin{align*}
\text{Reaction:} & \quad \text{N} \quad \text{Br} \\
\text{Conditions:} & \quad 1,4\text{-Dioxane, } 120^\circ\text{C, x h} \\
\text{Catalyst:} & \quad [\text{Ru}(\text{p-cymene})\text{Cl}_2]_2 (5 \text{ mol%}) \\
\text{Base:} & \quad \text{KOA} \text{c} (2 \text{ eq}) \\
\end{align*}
\]

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<td>1200</td>
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Reaction Atmosphere

![Reaction Diagram]

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<tr>
<td>Oxygen</td>
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*No formation of 3a, starting material 1a completely destroyed.

Optimisation for 2-Chloro-2-methylpropane

![Optimisation Diagram]

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<th>KOAc Equivalents</th>
<th>K$_2$CO$_3$ Equivalents</th>
<th>Conversion (%)</th>
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<tbody>
<tr>
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<td>2</td>
<td>27</td>
</tr>
<tr>
<td>0.5</td>
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<td>63</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>38</td>
</tr>
<tr>
<td>1.5</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>
Synthesis of 2-Substituted Pyridine Derivatives

General Procedure

[Diagram]

To an oven dried, argon purged flask equipped with magnetic stirrer and condenser was added Pd(PPh₃)₄ (1 mol%), K₂CO₃ (2 eq) and ethanol (1 M). A solution of the boronic acid (1.5 eq) in EtOH (1 M) was then added via a dropping funnel to the reaction vessel followed by the addition of 2-bromopyridine (1 eq). The reaction mixture was then heated to 100 °C and refluxed for 15 hours. After cooling to room temperature, aqueous NaOH (1 M) was added and extracted three times with EtOAc. The organic extracts were then combined, washed with brine, dried with MgSO₄ and then concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography (Hexane / EtOAc).

2-(4-methoxyphenyl)pyridine (1c)

2-bromopyridine (25 mmol, 2.4 mL), 4-methoxyphenyl boronic acid (33 mmol, 5.0 g), Pd(PPh₃)₄ (0.25 mmol, 289 mg), K₂CO₃ (50 mmol, 6.90 g) were reacted together in EtOH (25 mL) according to the general procedure to afford the title compound as a white solid (4.4 g, 95%).

¹H NMR (500 MHz, CDCl₃) δ 8.65 (ddd, J = 4.8, 1.7, 1.0 Hz, 1H), 7.96 (d, J = 8.9 Hz, 2H), 7.76 – 7.64 (m, 2H), 7.17 (ddd, J = 7.2, 4.8, 1.3 Hz, 1H), 7.00 (d, J = 8.9 Hz, 2H), 3.87 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 160.43, 157.08, 149.47, 136.67, 131.92, 128.15, 121.38, 119.79, 114.11, 55.34.

Data conforms to literature.¹
2-(4-fluorophenyl)pyridine (1d)

2-bromopyridine (20 mmol, 1.9 mL), 4-fluorophenyl boronic acid (30 mmol, 4.20 g), Pd(PPh₃)₄ (0.2 mmol, 231 mg), and K₂CO₃ (40 mmol, 5.52 g) were reacted together in EtOH (20 mL) according to the general procedure to afford the title compound as a yellow / white crystalline solid (3.20 g, 92%).

1H NMR (500 MHz, CDCl₃) δ 8.68 (ddd, J = 4.8, 1.6, 0.9 Hz, 1H), 7.98 (dd, J = 8.9, 5.4 Hz, 2H), 7.77 – 7.72 (m, 1H), 7.68 (dt, J = 8.0, 1.0 Hz, 1H), 7.22 (ddd, J = 7.4, 4.8, 1.1 Hz, 1H), 7.16 (t, J = 8.7 Hz, 2H).

13C NMR (126 MHz, CDCl₃) δ 163.51 (d, 1J_C-F = 248.4 Hz), 135.51 (d, 4J_C-F = 3.1 Hz), 128.68 (d, 3J_C-F = 8.4 Hz), 115.63 (d, 2J_C-F = 21.6 Hz).

19F NMR (470 MHz, CDCl₃) δ -113.14 – -113.24 (m).

Data conforms to literature.¹

2-(4-chlorophenyl)pyridine (1e)

2-bromopyridine (13 mmol, 1.2 mL), 4-chlorophenyl boronic acid (20 mmol, 3.04 g), Pd(PPh₃)₄ (0.13 mmol, 150 mg), and K₂CO₃ (26 mmol, 3.58 g) were reacted together in EtOH (13 mL) according to the general procedure to afford the title compound as a pale yellow crystalline solid (1.20 g, 89%).

1H NMR (500 MHz, CDCl₃) δ 8.69 (dd, J = 4.8, 0.8 Hz, 1H), 7.95 (d, J = 8.4 Hz, 2H), 7.81 – 7.74 (m, 1H), 7.71 (dd, J = 7.9, 0.9 Hz, 1H), 7.45 (d, J = 8.5 Hz, 2H), 7.29 – 7.24 (m, 1H).

13C NMR (126 MHz, CDCl₃) δ 155.97, 149.35, 149.35, 137.31, 137.26, 135.30, 128.97, 128.23, 122.45, 120.49.

Data conforms to literature.¹
2-(4-(ethoxycarbonyl)phenyl)pyridine (1f)

2-bromopyridine (13 mmol, 1.2 mL), 4-(methoxycarbonyl)phenyl boronic acid (20 mmol, 3.04 g), Pd(PPh₃)₄ (0.13 mmol, 150 mg), and K₂CO₃ (26 mmol, 3.58 g) were reacted together in EtOH (13 mL) according to the general procedure to afford the title compound as a white solid (2.42 g, 82%).

¹H NMR (500 MHz, CDCl₃) δ 8.73 (d, J = 4.6 Hz, 1H), 8.15 (d, J = 8.2 Hz, 2H), 8.07 (d, J = 8.3 Hz, 2H), 7.87 – 7.71 (m, 2H), 7.29 (dd, J = 8.3, 4.8 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 166.56, 156.38, 149.93, 143.42, 137.15, 130.90, 130.16, 126.95, 123.00, 121.19, 77.16, 61.22, 14.50.

Data conforms to literature.¹

2-(4-(trifluoromethyl)phenyl)pyridine (1g)

2-bromopyridine (10 mmol, 0.92 mL), 4-(trifluoromethyl)phenyl boronic acid (15 mmol, 2.85 g), Pd(PPh₃)₄ (0.10 mmol, 115 mg), and K₂CO₃ (20 mmol, 2.76 g) were reacted together in EtOH (10 mL) according to the general procedure to afford the title compound as an off white solid (1.38 g, 62%).

¹H NMR (500 MHz, CDCl₃) δ 8.73 (d, J = 4.7 Hz, 1H), 8.11 (d, J = 8.2 Hz, 2H), 7.84 – 7.69 (m, 4H), 7.33 – 7.27 (m, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 155.98 (s), 150.03 (s), 142.77 (s), 137.13 (s), 130.91 (q, ²J_C-F = 32.5 Hz), 127.31 (s), 125.81 (q, ³J_C-F = 3.8 Hz), 124.32 (q, ¹J_C-F = 272.0 Hz), 123.09 (s), 121.00 (s).

¹⁹F NMR (470 MHz, CDCl₃) δ -62.61 (s).

Data conforms to literature.²
2-(4-(trifluoromethyl)phenyl)pyridine (1h)

2-bromopyridine (4.5 mmol, 0.43 mL), 4-nitrophenyl boronic acid (6 mmol, 1.0 g), Pd(PPh₃)₄ (0.045 mmol, 52 mg), and K₂CO₃ (9 mmol, 1.24 g) were reacted together in EtOH (5 mL) according to the general procedure to afford the title compound as a yellow solid (609 mg, 68%).

¹H NMR (500 MHz, CDCl₃) δ 8.76 (d, J = 4.7 Hz, 1H), 8.34 (d, J = 8.6 Hz, 2H), 8.19 (d, J = 8.6 Hz, 2H), 7.89 – 7.74 (m, 2H), 7.35 (t, J = 5.6 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 155.03, 150.30, 148.22, 145.41, 137.26, 127.83, 124.16, 123.66, 121.36

Data conforms to literature.¹

2-(2,6-dimethylphenyl)pyridine (1i)

2-bromopyridine (13 mmol, 1.2 mL), 2,6-dimethylphenylboronic acid (20 mmol, 3.0 g), Pd(PPh₃)₄ (0.13 mmol, 150 mg), and K₂CO₃ (26 mmol, 3.59 g) were reacted together in EtOH (15 mL) according to the general procedure to afford the title compound as a red oil (1.96 g, 82%).

¹H NMR (500 MHz, CDCl₃) δ 8.74 (d, J = 4.5 Hz, 1H), 7.82 (dd, J = 7.6 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.28 (d, J = 8.2 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.12 (d, J = 7.6 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 159.56, 149.17, 139.76, 137.09, 135.93, 128.25, 127.72, 124.93, 122.02, 77.16, 20.33.

Data conforms to literature.³
2-(3-dimethylphenyl)pyridine (1j)

2-bromopyridine (5 mmol, 0.46 mL), 3-methylphenylboronic acid (7 mmol, 1.0 g), Pd(PPh₃)₄ (0.05 mmol, 58 mg), and K₂CO₃ (10 mmol, 1.38 g) were reacted together in EtOH (7.5 mL) according to the general procedure to afford the title compound as a yellow oil (772 mg, 91%).

¹H NMR (500 MHz, CDCl₃) δ 8.73 (d, J = 4.7 Hz, 1H), 7.87 (s, 1H), 7.84 – 7.73 (m, 3H), 7.39 (dd, J = 7.6 Hz, 1H), 7.29 – 7.24 (m, 2H), 2.46 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 157.40, 149.18, 138.81, 138.50, 137.16, 129.94, 128.69, 127.72, 124.09, 122.11, 120.86, 21.51.

Data conforms to literature.

2-(2-methylphenyl)pyridine (1i)

2-bromopyridine (20 mmol, 1.84 mL), 2-methylphenylboronic acid (30 mmol, 4.08 g), Pd(PPh₃)₄ (0.2 mmol, 231 mg), and K₂CO₃ (40 mmol, 5.52 g) were reacted together in EtOH (30 mL) according to the general procedure to afford the title compound as a yellow oil (2.96 g, 88%).

¹H NMR (500 MHz, CDCl₃) δ 8.71 (d, J = 3.9 Hz, 1H), 7.85 – 7.69 (m, 1H), 7.42 (dd, J = 13.6, 4.5 Hz, 2H), 7.33 – 7.25 (m, 4H), 2.29 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 159.67, 149.18, 138.81, 138.50, 137.16, 129.94, 128.69, 127.72, 124.09, 124.30, 121.76, 20.27.

Data conforms to literature.
Synthesis of meta-Substituted 2-Phenylpyridine Derivatives.

General Procedure A

To an oven dried, argon purged ampule equipped with magnetic stirrer was added the 2-phenylpyridine derivative (1 mmol), the alkyl halide (3mmol), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), KOAc (2 mmol, 196 mg) and 1,4-Dioxane (4 mL). The ampule was then sealed and refluxed on a carousel at 120 °C for the amount of time specified. After cooling to room temperature, aqueous NaHCO₃ (saturated) was added and then was extracted three times with EtOAc. The organic extracts were then combined, washed with brine, dried with MgSO₄ and then concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography (Hexane / EtOAc).

General Procedure B

To an oven dried, argon purged ampule equipped with magnetic stirrer was added the 2-phenylpyridine derivative (1 mmol), the alkyl halide (3mmol), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg), K₂CO₃ (1.5 mmol, 207 mg) and 1,4-Dioxane (4 mL). The ampule was then sealed and refluxed on a carousel at 120 °C for the amount of time specified. After cooling to room temperature, aqueous NaHCO₃ (saturated) was added and then was extracted three times with EtOAc. The organic extracts were then combined, washed with brine, dried with MgSO₄ and then concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography (Hexane / EtOAc).
2-(3-tert-butylphenyl)pyridine (3a)

2-phenylpyridine (1 mmol, 0.14 mL), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a yellow oil (15 mg, 7%).

¹H NMR (500 MHz, CDCl₃) δ 8.71 (d, J = 4.8 Hz, 1H), 8.05 (dd, J = 1.8 Hz, 1H), 7.86 – 7.65 (m, 3H), 7.47 (d, J = 7.9 Hz, 1H), 7.42 (t, J = 7.7 Hz, 1H), 7.22 (ddd, J = 6.7, 4.9, 1.9 Hz, 1H), 1.40 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 158.19, 151.74, 149.75, 139.32, 136.78, 128.57, 126.20, 124.30, 124.10, 122.04, 120.90, 77.16, 35.01, 31.54.

HR-MS (ESI) m/z: calculated for C₁₅H₂₁N [M+H]⁺ 212.1439, found: 212.1395

νmax (neat) / cm⁻¹: 2960, 1584, 1564, 1461

2-(3-tert-butyl-4-methylphenyl)pyridine (3b)

2-(4-methylphenyl)pyridine (1 mmol, 0.17 mL), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (12 mg, 5%).

¹H NMR (500 MHz, CDCl₃) δ 8.70 (d, J = 4.0 Hz, 1H), 8.05 (s, 1H), 7.77 (dd, J = 7.4 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.24 (d, J = 7.6 Hz, 2H), 2.60 (s, 3H), 1.49 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 157.83, 151.32, 149.12, 148.63, 137.41, 133.47, 125.07, 124.54, 122.86, 121.93, 120.90, 36.18, 30.98, 23.27.

HR-MS (ESI) m/z: calculated for C₁₆H₂₂N [M+H]⁺ 226.1596, found: 226.1594

νmax (neat) / cm⁻¹: 2958, 1586, 1464, 1433
2-(3-tert-butyl-4-methoxyphenyl)pyridine (3c)

2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (100 mg, 42%).

\[
{^1}H \text{ NMR (500 MHz, CDCl}_3) \delta 8.67 (d, J = 4.7 Hz, 1H), 7.96 (d, J = 1.3 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.19 (br s, 1H), 6.98 (d, J = 8.5 Hz, 1H), 3.90 (s, 3H), 1.44 (s, 9H).
\]

\[
{^{13}}C \text{ NMR (126 MHz, CDCl}_3) \delta 159.84, 157.66, 149.06, 138.70, 137.25, 126.05, 125.71, 121.40, 120.38, 111.84, 77.16, 55.29, 35.19, 29.84.
\]

\[
HR-MS (ESI) m/z: \text{calculated for C}_{16}H_{19}NO [M+H]^+ 242.1545, \text{found: 242.1549}
\]

\[
\nu_{max} (\text{neat}) / \text{cm}^{-1}: 2954, 1586, 1462, 1430
\]

2-(3-tert-butyl-4-fluorophenyl)pyridine (3d)

2-(4-fluorophenyl)pyridine (1 mmol, 173 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K₂CO₃ (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (140 mg, 61%).

\[
{^1}H \text{ NMR (500 MHz, CDCl}_3) \delta 8.68 (d, J = 4.6 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.79 – 7.74 (m, 1H), 7.70 (dd, J = 7.1 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.22 – 7.16 (m, 1H), 7.08 (dd, J = 12.0, 8.6 Hz, 1H), 1.46 (s, 9H).
\]

\[
{^{13}}C \text{ NMR (126 MHz, CDCl}_3) \delta 162.83 (d, {^1}J_{CF} = 250.7 Hz), 157.14 (s), 149.60 (s), 137.41 (d, {^2}J_{CF} = 12.1 Hz), 136.82 (s), 135.13 (d, {^3}J_{CF} = 3.0 Hz), 126.29 (d, {^4}J_{CF} = 6.4 Hz), 126.25 (d, {^5}J_{CF} = 9.3 Hz), 121.89 (s), 120.43 (s), 116.64 (d, {^3}J_{CF} = 25.0 Hz), 34.53 (d, {^4}J_{CF} = 2.7 Hz), 29.97 (d, {^4}J_{CF} = 3.4 Hz).
\]

\[
{^{19}}F \text{ NMR (470 MHz, CDCl}_3) \delta -109.38 (s).
\]

\[
HR-MS (ESI) m/z: \text{calculated for C}_{16}H_{16}NF [M+H]^+ 230.1345, \text{found: 230.1342}
\]

\[
\nu_{max} (\text{neat}) / \text{cm}^{-1}: 2959, 1589, 1461, 1433
\]
2-(3-tert-butyl-4-chlorophenyl)pyridine (3e)

![Chemical Structure](image)

2-4-(chlorophenyl)pyridine (1 mmol, 190 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (70 mg, 25%).

**¹H NMR** (500 MHz, CDCl₃) δ 8.72 (d, J = 4.1 Hz, 1H), 8.10 (d, J = 2.2 Hz, 1H), 7.81 (td, J = 7.8, 1.8 Hz, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.72 (d, J = 8.3 Hz, 1H), 7.45 (d, J = 8.2 Hz, 1H), 7.29 (ddd, J = 7.3, 4.9, 0.8 Hz, 1H), 1.55 (s, 9H).

**¹³C NMR** (126 MHz, CDCl₃) δ 156.47, 148.97, 146.95, 137.60, 136.82, 135.08, 132.37, 126.67, 125.65, 122.36, 120.91, 36.31, 29.58.

**HR-MS** (ESI) m/z: calculated for C₁₅H₁₆NCl [M+H]⁺ 246.1050, found: 246.1030

νₘₐₓ (neat) / cm⁻¹: 2960, 1586, 1459, 1431

**ethyl 2-tert-butyl-4-(pyridin-2-yl)benzoate (3f)**

![Chemical Structure](image)

2-(4-(ethoxycarbonyl)phenyl)pyridine (1 mmol, 190 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (23 mg, 8%).

**¹H NMR** (500 MHz, CDCl₃) δ 8.74 (d, J = 3.7 Hz, 1H), 8.17 (s, 1H), 7.85 – 7.78 (m, J = 13.6, 7.5 Hz, 2H), 7.75 (d, J = 7.8 Hz, 1H), 7.42 (d, J = 7.9 Hz, 1H), 7.33 – 7.28 (m, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.48 (s, 9H), 1.40 (t, J = 7.1 Hz, 3H).

**¹³C NMR** (126 MHz, CDCl₃) δ 171.75, 156.49, 149.00, 148.31, 139.50, 137.64, 133.94, 129.34, 125.93, 124.05, 122.62, 121.26, 61.48, 36.20, 31.36, 14.08.

**HR-MS** (ESI) m/z: calculated for C₁₈H₂₁NO₂ [M+H]⁺ 284.1651, found: 284.1645

νₘₐₓ (neat) / cm⁻¹: 2965, 1722, 1586, 1464, 1434
2-(3-(adamantan-1-yl)phenyl)pyridine (4a)

2-Phenylpyridine (1 mmol, 140 µL), 1-adamantyl bromide (3.00 mmol, 645 mg), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K₂CO₃ (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a white solid (15 mg, 5%).

¹H NMR: (500 MHz, CDCl₃) δ 8.75 (d, J = 4.6 Hz, 1H), 8.14 – 7.96 (m, 1H), 7.85 – 7.74 (m, 3H), 7.50 – 7.42 (m, 2H), 7.31 – 7.24 (m, 1H), 2.14 (s, 3H), 2.02 (s, 6H), 1.85 – 1.76 (m, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 158.29, 152.00, 149.76, 149.76, 136.74, 136.74, 128.60, 125.79, 124.36, 123.80, 122.00, 120.87, 43.34, 36.95, 36.54, 29.13.

HR-MS (ESI) m/z: calculated for C₂₁H₂₃NO [M+H]⁺ 290.1909, found: 290.1883

νₘₐₓ (neat) / cm⁻¹: 3252, 2898, 2856, 1622, 1584, 1564, 1461
2-(3-(adamantan-1-yl)-4-methoxyphenyl)pyridine (4c)

2-(4-Methoxyphenyl)pyridine (1 mmol, 185 mg), 1-adamantyl bromide (3.00 mmol, 645 mg), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K₂CO₃ (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a white solid (114 mg, 36%). Crystals large enough for single crystal X-ray analysis were generated using CHCl₃ / Hexane.

¹H NMR (500 MHz, CDCl₃) δ 8.66 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H), 7.92 (d, J = 2.3 Hz, 1H), 7.81 (dd, J = 8.5, 2.3 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.68 (ddd, J = 8.0, 1.2 Hz, 1H), 7.17 (ddd, J = 7.0, 4.9, 1.4 Hz, 1H), 6.97 (d, J = 8.5 Hz, 1H), 3.89 (s, 3H), 2.20 – 2.15 (m, J = 2.9 Hz, 6H), 2.09 (s, 3H), 1.79 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 159.99, 157.81, 149.31, 138.83, 136.95, 131.29, 125.67, 125.64, 121.32, 120.22, 111.90, 55.24, 40.64, 37.29, 37.25, 29.22

HR-MS (ESI) m/z: calculated for C₂₂H₂₅NO [M+H]⁺ 320.2014, found: 320.2008

Crystal Data 4c, C₂₂H₂₅NO (M = 319.43 g/mol): monoclinic, space group P2₁/c (no. 14), a = 12.82457(18), b = 6.61539(9), c = 20.0798(3) Å, β = 93.3829(13)°, U = 1700.59(4) Å³, Z = 4, T = 150(2) K, μ(CuKα) = 0.581 mm⁻¹, Dcalc = 1.248 g/cm³, 17596 reflections measured (8.82° ≤ 2θ ≤ 143.96°), 3328 unique (Rint = 0.0403, Rsigma = 0.0297) which were used in all calculations. The final R1 was 0.0384 (I>2σ(I)) and wR2 was 0.0964 (all data).

Crystallographic data have been deposited with Cambridge Crystallographic Data Centre; CCDC-1064109. Copies of these data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; email: deposit@ccdc.cam.ac.uk).
2-[4-methoxy-3-(2-methylbutan-2-yl)phenyl]pyridine (5c)

2-(4-Methoxyphenyl)pyridine (1 mmol, 185 mg), 2-chloro-2-methylbutane (367 µL, 3 mmol), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K₂CO₃ (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (139 mg, 54%).

¹H NMR (500 MHz, CDCl₃) δ 8.67 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H), 7.90 (d, J = 2.3 Hz, 1H), 7.83 (dd, J = 8.5, 2.3 Hz, 1H), 7.73 – 7.69 (m, 1H), 7.68 (dd, J = 8.0, 1.2 Hz, 1H), 7.21 – 7.05 (m, 1H), 6.96 (d, J = 8.5 Hz, 1H), 3.87 (s, 3H), 1.89 (q, J = 7.5 Hz, 2H), 1.41 (s, 6H), 0.66 (t, J = 7.5 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 159.68, 157.79, 149.33, 136.91, 136.87, 131.11, 126.92, 125.89, 121.30, 120.20, 111.62, 55.28, 38.79, 33.22, 28.01, 9.78.

HR-MS (ESI) m/z: calculated for C₁₇H₂₁NO [M+H]⁺ 256.1701, found: 256.1725

ν_max (neat) / cm⁻¹: 2979, 1602, 1585, 1562, 1460

2-[3-(2-methylnonan-2-yl)phenyl]pyridine (6a)

2-Phenylpyridine (1 mmol, 140 µL), 2-chloro-2-methylnonane (3 mmol, 530 mg), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K₂CO₃ (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (146 mg, 43%).

¹H NMR: (500 MHz, CDCl₃) δ 8.72 (d, J = 4.7 Hz, 1H), 8.00 – 7.96 (m, 1H), 7.83 – 7.71 (m, 3H), 7.46 – 7.39 (m, 2H), 7.28 – 7.22 (m, 1H), 1.70 – 1.62 (m, 2H), 1.37 (s, 6H), 1.30 – 1.04 (m, 10H), 0.84 (t, J = 7.1 Hz, 3H).

¹³C NMR: (126 MHz, CDCl₃) δ 157.85, 150.47, 149.20, 138.55, 137.09, 128.43, 126.85, 124.58, 124.14, 121.98, 120.95, 44.63, 37.90, 31.87, 30.31, 29.23, 29.01, 24.76, 22.65, 14.09.

HR-MS (ESI) m/z: calculated for C₂₁H₂₉NO [M+H]⁺ 296.2378, found: 296.2401

ν_max (neat) / cm⁻¹: 2957, 2926, 2855, 1584, 1564, 1461
2-[4-methoxy-3-(2-methylnonan-2-yl)phenyl]pyridine (6c)

2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), 2-chloro-2-methylnonane (3 mmol, 530 mg), \([\text{RuCl}_2(p\text{-cymene})]_2\) (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K$_2$CO$_3$ (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (139 mg, 54%).

$^1$H NMR: (500 MHz, CDCl$_3$) $\delta$ 8.67 (d, $J = 4.6$ Hz, 1H), 7.91 (d, $J = 1.9$ Hz, 1H), 7.84 (dd, $J = 8.5$, 2.3 Hz, 1H), 7.74 – 7.65 (m, 2H), 7.20 – 7.12 (m, 1H), 6.95 (d, $J = 8.5$ Hz, 1H), 3.87 (s, 3H), 1.93 – 1.78 (m, 2H), 1.44 (d, $J = 6.7$ Hz, 6H), 1.31 – 1.15 (m, 8H), 1.06 – 0.97 (m, 2H), 0.85 (t, $J = 7.1$ Hz, 3H).

$^{13}$C NMR: (126 MHz, CDCl$_3$) $\delta$ 159.59, 157.64, 149.17, 137.12, 136.84, 130.93, 126.64, 125.77, 121.20, 120.09, 111.51, 55.13, 40.80, 38.42, 31.89, 30.39, 29.21, 28.48, 25.26, 22.69, 14.12.

HR-MS (ESI) $m/z$: calculated for C$_{22}$H$_{31}$NO $[\text{M+H}]^+$ 326.2484, found: 326.2521

$\nu_{\text{max}}$ (neat) / cm$^{-1}$: 2951, 2921, 2854, 1602, 1588, 1498, 1462

2-(3-(3-ethylpentan-3-yl)-4-methoxyphenyl)pyridine (7c)

2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), 3-chloro-3-ethylpentane (1.70 mmol, 229 mg), \([\text{RuCl}_2(p\text{-cymene})]_2\) (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K$_2$CO$_3$ (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (139 mg, 54%).

$^1$H NMR: (500 MHz, CDCl$_3$) $\delta$ 8.69 (s, 1H), 7.95 – 7.68 (m, 4H), 7.22 (s, 1H), 6.97 (d, $J = 6.2$ Hz, 1H), 3.86 (s, 3H), 1.88 (q, $J = 7.2$ Hz, 6H), 0.66 (t, $J = 7.3$ Hz, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 160.11, 157.43, 148.85, 137.83, 135.10, 129.89, 128.57, 126.10, 121.57, 120.67, 111.80, 77.16, 55.44, 44.78, 26.21, 8.65.

HR-MS (ESI) $m/z$: calculated for C$_{19}$H$_{25}$NO $[\text{M+H}]^+$ 284.1936, found: 284.1949

$\nu_{\text{max}}$ (neat) / cm$^{-1}$: 2979, 2888, 1603, 1587, 1494, 1460
2-phenylpyridine (1 mmol, 0.14 mL), ethyl 2-bromoisobutyrate (3 mmol, 0.44 mL), [RuCl\(_2\)(p-cymene)]\(_2\) (5 mol\%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield products 8a (125 mg, 46\%) as a colourless oil and product 9a (25 mg, 9\%) as a colourless oil.

**ethyl 2-methyl-2-[3-(pyridin-2-yl)phenyl]propanoate (8a)**

![Chemical structure of ethyl 2-methyl-2-[3-(pyridin-2-yl)phenyl]propanoate (8a)](image)

**\(^1\)H NMR** (500 MHz, CDCl\(_3\)) \(\delta\) 8.69 (ddd, \(J = 4.9, 1.7, 1.0\) Hz, 1H), 7.99 (dd, \(J = 1.9\) Hz, 1H), 7.86 – 7.83 (m, 1H), 7.77 – 7.74 (m, 1H), 7.71 (ddd, \(J = 8.0, 1.1\) Hz, 1H), 7.43 (dd, \(J = 7.7\) Hz, 1H), 7.40 – 7.37 (m, 1H), 7.23 (ddd, \(J = 7.3, 4.9, 1.3\) Hz, 1H), 4.13 (q, \(J = 7.1\) Hz, 2H), 1.64 (s, 6H), 1.18 (t, \(J = 7.1\) Hz, 3H).

**\(^{13}\)C NMR** (126 MHz, CDCl\(_3\)) \(\delta\) 176.80, 157.50, 149.54, 145.50, 139.34, 137.05, 128.87, 126.72, 125.45, 124.36, 122.27, 120.92, 60.96, 46.73, 26.70, 14.18.

**HR-MS** (ESI) \(m/z\): calculated for C\(_{17}\)H\(_{19}\)NO\(_2\) [M+H]\(^+\) 270.1494, found: 270.1533

\(\nu_{\text{max}}\) (neat) / cm\(^{-1}\): 2978, 1722, 1584, 1461, 1433
diethyl 2,2,3-trimethyl-3-[3-(pyridin-2-yl)benzyl]butanedioate (9a)

\[
\begin{align*}
\text{H NMR} &\quad (500 \text{ MHz, CDCl}_3) \quad \delta 8.70 (d, J = 4.8 \text{ Hz}, 1H), 8.02 (s, 1H), 7.86 (d, J = 7.3 \text{ Hz}, 1H), 7.77 (dd, J = 7.6 \text{ Hz}, 1H), 7.72 (d, J = 7.9 \text{ Hz}, 1H), 7.47 – 7.39 (m, 2H), 7.26 – 7.23 (m, 1H), 4.24 – 3.98 (m, 4H), 2.64 (d, J = 14.5 \text{ Hz}, 1H), 2.56 (d, J = 14.5 \text{ Hz}, 1H), 1.57 (s, 3H), 1.25 (t, J = 7.1 \text{ Hz}, 3H), 1.20 (t, J = 7.1 \text{ Hz}, 3H), 1.20 (s, 3H), 1.13 (s, 3H). \\
\text{C NMR} &\quad (126 \text{ MHz, CDCl}_3) \quad \delta 178.44, 176.08, 157.25, 149.16, 145.42, 137.59, 136.00, 128.97, 127.11, 125.76, 124.90, 122.43, 121.20, 61.19, 60.69, 49.64, 48.05, 41.92, 29.35, 23.99, 21.04, 14.20, 14.09. \\
\text{HR-MS (ESI) } m/z &\quad \text{calculated for C}_{23}H_{29}NO_4 \text{Na [M+Na]}^+ 406.1994, \text{ found: 406.1971} \\
\nu_{\text{max}} \text{ (neat) / cm}^{-1} &\quad 2979, 1721, 1584, 1461
\end{align*}
\]
2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield products 8c (170 mg, 57%) as a white amorphous solid and product 9c (45 mg, 12%) as a colourless oil.

**ethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8c)**

\[ \text{MeO} \quad \text{N} \quad \text{I} \xrightarrow{\text{Br}} \quad \text{MeO} \quad \text{N} \quad \text{CO}_2\text{Et} \]

\[ \text{[Ru(p-cymene)]Cl}_2 \text{ (5 mol%) KOAc (2 eq)} \]

\[ \text{1,4-Dioxane} \quad 120^\circ\text{C}, 15 \text{ h} \]

\[ \text{MeO} \quad \text{N} \quad \text{I} \xrightarrow{\text{Br}} \quad \text{MeO} \quad \text{N} \quad \text{CO}_2\text{Et} \]

**¹H NMR** (500 MHz, CDCl₃) δ 8.66 (d, J = 4.4 Hz, 1H), 7.99 (d, J = 2.1 Hz, 1H), 7.86 (dd, J = 8.4, 1.9 Hz, 1H), 7.73 (dd, J = 7.5 Hz, 1H), 7.69 (d, J = 7.9 Hz, 1H), 7.21 – 7.14 (m, 1H), 6.94 (d, J = 8.5 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.59 (s, 6H), 1.15 (t, J = 7.1 Hz, 3H).

**¹³C NMR** (126 MHz, CDCl₃) δ 177.87, 157.87, 157.36, 149.31, 137.08, 134.68, 131.52, 126.70, 124.68, 121.55, 120.28, 110.96, 60.44, 55.37, 44.55, 25.74, 14.32.

**HR-MS (ESI) m/z:** calculated for C₁₈H₂₂NO₃ [M+H]⁺ 300.1600, found: 300.1613

ν_{max} (neat) / cm⁻¹: 2979, 1727, 1587, 1465
diethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9c)

\[\text{\includegraphics[width=0.3\textwidth]{diagram}}\]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.66 (ddd, $J = 4.8$, 1.7, 1.0 Hz, 1H), 7.91 (d, $J = 2.2$ Hz, 1H), 7.89 (dd, $J = 8.4$, 2.2 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.69 (ddd, $J = 8.0$, 1.3 Hz, 1H), 7.17 (ddd, $J = 6.9$, 4.8, 1.5 Hz, 1H), 6.90 (d, $J = 8.4$ Hz, 1H), 4.11 – 4.02 (m, 2H), 3.87 – 3.82 (m, $J = 7.2$, 1.5 Hz, 2H), 3.81 (s, 3H), 2.67 (d, $J = 14.8$ Hz, 1H), 2.50 (d, $J = 14.8$ Hz, 1H), 1.64 (s, 3H), 1.18 (s, 3H), 1.12 (t, $J = 7.1$ Hz, 3H), 1.11 (t, $J = 7.1$ Hz, 3H), 0.88 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 177.98, 177.32, 159.13, 156.04, 135.99, 132.74, 130.08, 128.28, 128.06, 127.10, 122.09, 121.53, 111.27, 60.67, 60.43, 55.50, 48.06, 44.59, 41.47, 28.10, 27.38, 23.16, 14.21, 14.11.

HR-MS (ESI) $m/z$: calculated for C$_{24}$H$_{31}$NO$_5$Na [M+Na]$^+$ 436.2100, found: 436.2096

$\nu_{\text{max}}$ (neat) / cm$^{-1}$: 2979, 1727, 1587, 1465
2-(4-fluorophenyl)pyridine (1 mmol, 173 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield products 8c (135 mg, 47%) as a colourless oil, product 9e (50 mg, 13%) as a colourless oil and product 9d (15 mg, 3%).

**ethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8d)**

\[ \text{ethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8d)} \]

\[
{\text{F}}_{\text{EtO}_{\text{2}}{\text{C}}}^{\text{N}}\text{I}  
\]

**\( ^1H\) NMR** (500 MHz, CDCl₃) δ 8.68 (d, \( J = 4.1 \) Hz, 1H), 8.03 (dd, \( J = 7.7, 2.2 \) Hz, 1H), 7.82 (ddd, \( J = 8.3, 4.8, 2.2 \) Hz, 1H), 7.77 (dd, \( J = 7.6 \) Hz, 1H), 7.70 (d, \( J = 7.9 \) Hz, 1H), 4.15 (q, \( J = 7.1 \) Hz, 2H), 1.63 (s, 6H), 1.17 (t, \( J = 7.1 \) Hz, 3H).

**\( ^13C\) NMR** (126 MHz, CDCl₃) δ 176.65 (s), 161.64 (d, \( ^1J_{C-F} = 249.7 \) Hz), 156.59 (s), 149.40 (s), 137.32 (s), 135.14 (s), 133.31 (d, \( ^2J_{C-F} = 14.0 \) Hz), 127.19 (d, \( ^3J_{C-F} = 9.2 \) Hz), 125.76 (d, \( ^3J_{C-F} = 5.2 \) Hz), 122.24 (s), 120.70 (s), 116.00 (d, \( ^2J_{C-F} = 23.2 \) Hz), 61.03 (s), 44.37 (s), 25.84 (d, \( ^4J_{C-F} = 0.7 \) Hz), 14.14 (s).

**\( ^19F\) NMR** (470 MHz, CDCl₃) δ -112.82.

**HR-MS (ESI) m/z:** calculated for C₁₇H₁₄FNO₂Na [M+H]⁺ 288.1400, found: 288.1402

\( \nu_{\text{max}} \) (neat) / cm⁻¹: 2980, 1723, 1589, 1464
diethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9d)

\[
\begin{align*}
&\text{1H NMR (500 MHz, CDCl}_3) \ \delta \ 8.69 \ (d, \ J = 4.1 \ Hz, \ 1H), \ 7.96 \ (dd, \ J = 7.7, 2.2 \ Hz, \ 1H), \ 7.89 \ (ddd, \ J = 8.2, 4.7, 2.2 \ Hz, \ 1H), \ 7.79 \ (dd, \ J = 7.1 \ Hz, \ 1H), \ 7.71 \ (d, \ J = 7.9 \ Hz, \ 1H), \ 7.31 – 7.23 \ (m, \ 1H), \ 7.09 \ (dd, \ J = 11.3, 8.5 \ Hz, \ 1H), \ 4.19 – 4.07 \ (m, \ 2H), \ 3.98 – 3.80 \ (m, \ 2H), \ 2.61 \ (d, \ J = 14.9 \ Hz, \ 1H), \ 2.58 \ (d, \ J = 14.9 \ Hz, \ 1H), \ 1.65 \ (s, \ 3H), \\
&\quad 1.20 \ (s, \ 3H), \ 1.18 \ (t, \ J = 7.2 \ Hz, \ 3H), \ 1.16 \ (t, \ J = 7.2 \ Hz, \ 3H), \ 0.96 \ (s, \ 3H).
\end{align*}
\]

\[
\begin{align*}
&\text{13C NMR (126 MHz, CDCl}_3) \ \delta \ 177.83 \ (s), \ 176.17 \ (s), \ 161.89 \ (d, \ ^1J_{C,F} = 249.9 \ Hz), \ 156.36 \ (s), \ 149.19 \ (s), \ 137.60 \ (s), \ 131.69 \ (d, \ ^2J_{C,F} = 12.9 \ Hz), \ 127.63 \ (d, \ ^2J_{C,F} = 9.4 \ Hz), \ 127.40 \ (d, \ ^3J_{C,F} = 5.0 \ Hz), \ 122.32 \ (s), \ 120.85 \ (s), \ 116.12 \ (d, \ ^2J_{C,F} = 23.9 \ Hz), \ 61.22 \ (s), \ 60.53 \ (s), \ 47.98 \ (s), \ 45.44 \ (d, \ ^3J_{C,F} = 2.8 \ Hz), \ 41.49 \ (s), \ 27.63 \ (s), \\
&\quad 27.13 \ (s), \ 22.48 \ (s), \ 14.04 \ (s), \ 14.03 \ (s).
\end{align*}
\]

\[
\begin{align*}
&\text{19F NMR (470 MHz, CDCl}_3) \ \delta \ -110.60.
\end{align*}
\]

\[
\begin{align*}
&\text{HR-MS (ESI) m/z: calculated for C}_{23}\text{H}_{30}\text{FNO}_{4}\text{Na [M+Na}]^+ 424.1900, found: 424.1905}
\end{align*}
\]

\[
\begin{align*}
&\nu_{\text{max}} \ (\text{neat}) / \text{cm}^{-1}; \ 2980, 1723, 1589, 1463
\end{align*}
\]

triethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-3,5-dimethylhexane-2,3,5-tricarboxylate (9e)

\[
\begin{align*}
&\text{1H NMR (500 MHz, CDCl}_3) \ \delta \ 8.72 \ (s, \ 1H), \ 8.03 – 7.89 \ (m, \ J = 21.0, 11.2, 4.3 \ Hz, \ 2H), \ 7.86 \ (s, \ 1H), \ 7.77 \ (s, \ 1H), \ 7.36 – 7.28 \ (m, \ J = 10.0, 5.7 \ Hz, \ 1H), \ 7.16 – 7.04 \ (m, \ 1H), \ 4.21 – 3.95 \ (m, \ 4H), \ 3.73 – 3.56 \ (m, \ J = 46.8, \ 10.8, 7.2 \ Hz, \ 2H), \ 2.83 – 2.65 \ (m, \ 1H), \ 2.42 – 2.29 \ (m, \ J = 25.8, 13.9 \ Hz, \ 1H), \ 2.21 – 2.09 \ (m, \ 1H), \ 2.09 – 1.95 \ (m, \ 1H), \ 1.71 – 1.59 \ (m, \ 3H), \ 1.31 – 1.05 \ (m, \ 15H), \ 1.03 – 0.95 \ (m, \ 3H).
\end{align*}
\]

\[
\begin{align*}
&\text{19F NMR (470 MHz, CDCl}_3) \ \delta \ -109.10.
\end{align*}
\]

\[
\begin{align*}
&\text{HR-MS (ESI) m/z: calculated for C}_{29}\text{H}_{38}\text{FNO}_{6}\text{Na [M+Na}]^+ 538.2580, found: 538.2611}
\end{align*}
\]

\[
\begin{align*}
&\nu_{\text{max}} \ (\text{neat}) / \text{cm}^{-1}; \ 2980, 1723, 1589, 1464
\end{align*}
\]
Mechanistic Studies

Synthesis of Complex A

Complex A was synthesised according to literature procedure.\(^5\) To an oven dried, argon purged round bottom flask was added \([\text{RuCl}_2(\text{p-cymene})]_2\) (1.5 mmol, 918 mg), KOAc (6 mmol, 588 mg) followed by 2-phenylpyridine (3 mmol, 0.42 mL) and dry MeOH (30 mL). The reaction was stirred at room temperature for 48 h. The reaction was then concentrated to dryness, dissolved in a minimal amount of EtOAc and then purified through neutral alumina with EtOAc as the solvent to yield the title compound as a yellow solid (1.1 g, 86%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.23 (d, \(J = 5.5\) Hz, 1H), 8.15 (d, \(J = 7.5\) Hz, 1H), 7.70 (d, \(J = 7.9\) Hz, 1H), 7.65 (dd, \(J = 7.6\) Hz, 1H), 7.60 (d, \(J = 7.6\) Hz, 1H), 7.17 (dd, \(J = 7.3\) Hz, 1H), 7.06 – 6.99 (m, 2H), 5.58 (d, \(J = 5.8\) Hz, 1H), 5.55 (d, \(J = 5.9\) Hz, 1H), 5.17 (d, \(J = 5.9\) Hz, 1H), 4.98 (d, \(J = 5.8\) Hz, 1H), 2.43 (hept, \(J = 6.8\) Hz, 1H), 2.04 (s, 3H), 0.98 (d, \(J = 6.9\) Hz, 3H), 0.88 (d, \(J = 6.9\) Hz, 3H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 181.50, 165.44, 154.70, 143.41, 139.67, 136.70, 129.53, 123.96, 122.57, 121.48, 118.87, 100.73, 100.59, 90.83, 89.72, 84.24, 82.27, 30.89, 22.61, 21.81, 18.85.

Data conforms to literature.\(^5\)

Catalytic Reaction using Complex A

2-phenylpyridine (1 mmol, 0.14 mL), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), Complex A (10 mol%, 41 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield product 8a as a colourless oil (115 mg, 43%). Data in accordance with previous synthesis.
Reactions with Substrates 1j-11

2-(2,6-dimethylphenyl)pyridine (1 mmol, 183 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. No conversion of the starting material was observed.

2-(3-methylphenyl)pyridine (1 mmol, 169 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford product 10 as a yellow solid (60 mg 35%).

2,2'-(4,4'-dimethylbiphenyl-2,2'-diyl)dipyridine (10)

\[ \begin{align*}
\text{1H NMR (500 MHz, CDCl}_3) & \delta 8.34 \text{ (d, } J = 2.7 \text{ Hz, 2H), 7.43 - 7.33 \text{ (m, 4H), 7.29 \text{ (d, } J = 7.7 \text{ Hz, 2H), 7.25 \text{ (t, } J = 6.7 \text{ Hz, 2H), 7.06 \text{ (bs, 1H), 6.80 \text{ (d, } J = 7.7 \text{ Hz, 2H), 2.40 \text{ (s, 6H).}}}
\end{align*} \]

\[ \begin{align*}
\text{13C NMR (126 MHz, CDCl}_3) & \delta 157.80, 148.48, 138.98, 137.69, 136.81, 136.07, 131.42, 130.80, 129.78, 124.80, 121.52, 21.17. 
\end{align*} \]

\[ \begin{align*}
\text{HR-MS (ESI) } m/z: \text{ culated for C}_{24}\text{H}_{20}\text{N}_2 [M+Na]^+ 359.1524, \text{ found: 359.1533} 
\end{align*} \]

Data conforms to literature.\(^6\)
Benzoquinoline (1 mmol, 179 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield product 11 as a colourless oil (63 mg, 22%)

**ethyl 2-(benzo[h]quinolin-7-yl)-2-methylpropanoate (11)**

$$\text{EtO}_2C\text{-}\begin{array}{c}
\text{N} \\
\text{C} \\
\text{Br}
\end{array}\text{-}\begin{array}{c}
\text{N} \\
\text{C} \\
\text{C} \\
\text{Br}
\end{array}\text{-}\begin{array}{c}
\text{C} \\
\text{C} \\
\text{C} \\
\text{C}
\end{array}\text{-}\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H}
\end{array}\text{-}\begin{array}{c}
\text{O} \\
\text{O}
\end{array}\text{-}\text{C}_2\text{H}_5$$

**¹H NMR** (500 MHz, CDCl₃) δ 9.38 (d, J = 8.0 Hz, 1H), 9.00 (dd, J = 4.4, 1.8 Hz, 1H), 8.15 (dd, J = 8.0, 1.7 Hz, 1H), 7.90 (d, J = 9.3 Hz, 1H), 7.77 (dd, J = 7.5, 1.4 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.66 (d, J = 9.3 Hz, 1H), 7.50 (dd, J = 8.0, 4.4 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 1.80 (s, 7H), 1.02 (t, J = 7.1 Hz, 3H).

**¹³C NMR** (126 MHz, CDCl₃) δ 178.85, 148.81, 146.83, 141.08, 135.81, 132.46, 131.42, 126.65, 125.53, 125.22, 125.07, 124.07, 123.96, 121.96, 61.15, 46.58, 27.88, 14.05.

**HR-MS (ESI) m/z**: calculated for C₁₉H₁₉NO₂ [M+H]⁺ 294.1494, found: 294.1517

ν<sub>max</sub> (neat) / cm⁻¹: 2979, 1718, 1592, 1428

2-(2-methylphenyl)pyridine (1 mmol, 169 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), [RuCl₂(p-cymene)]₂ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford product 12 as a white solid (50 mg 29%).
2,2’-(3,3’-dimethylbiphenyl-2,2’-diyl)dipyridine (12)

![Chemical structure](image)

**¹H NMR** (500 MHz, CDCl₃) δ 8.57 (d, J = 4.2 Hz, 2H), 7.55 (t, J = 7.1 Hz, 2H), 7.36 – 7.30 (m, J = 6.2 Hz, 2H), 7.10 – 7.06 (m, 2H), 7.04 (d, J = 7.5 Hz, 2H), 6.93 (t, J = 7.6 Hz, 2H), 6.77 (d, J = 7.6 Hz, 2H), 2.10 (s, 6H).

**¹³C NMR** (126 MHz, CDCl₃) δ 159.38, 148.63, 140.35, 139.62, 136.03, 135.83, 128.89, 128.75, 126.83, 125.87, 121.40, 20.64.

**HR-MS** (ESI) *m/z*: calculated for C₂₄H₂₀N₂ [M+Na]+ 359.1524, found: 359.1517

Data conforms to literature.⁵

**Reactions with TEMPO**
Reactions were carried out as per general procedure A.

![Reaction scheme](image)

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Reaction with ethyl 2-bromoisobutrate carried out as per general procedure A. No trapped TEMPO adducts could be observed or isolated.

![Reaction scheme](image)
References


NMR Spectra

2-(3-tert-butylphenyl)pyridine (3a)
2-(3-tert-butyl-4-methylphenyl)pyridine (3b)
2-(3-tert-butyl-4-methoxyphenyl)pyridine (3c)

Parameter | Value
---|---
1 Spectrometer | vnmr
2 Author | 
3 Solvent | cdcl3
4 Temperature | 25.0
5 Pulse Sequence | 629ul
6 Number of Scans | 128
7 Receiver Gain | 30
8 Relaxation Delay | 3.0000
9 Pulse Width | 0.0000
10 Acquisition Time | 2.0497
11 Acquisition Date | 2015-02-27T02:12:49
12 Modification Date | 2015-02-27T02:17:34
13 Spectrometer Frequency | 500.06
14 Spectral Width | 8013.8
15 Lowest Frequency | -666.5
16 Nucleus | 1H
17 Acquired Size | 16384
18 Spectral Size | 32768

Parameter | Value
---|---
1 Spectrometer | vnmr
2 Author | 
3 Solvent | cdcl3
4 Temperature | 25.0
5 Pulse Sequence | 629ul
6 Number of Scans | 128
7 Receiver Gain | 30
8 Relaxation Delay | 3.0000
9 Pulse Width | 0.0000
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11 Acquisition Date | 2015-02-27T02:14:41
12 Modification Date | 2015-02-27T02:17:31
13 Spectrometer Frequency | 505.75
14 Spectral Width | 32760.0
15 Lowest Frequency | -1760.3
16 Nucleus | 13C
17 Acquired Size | 16384
18 Spectral Size | 65536
2-(3-tert-butyl-4-fluorophenyl)pyridine (3d)
2-(3-tert-butyl-4-chlorophenyl)pyridine (3e)
ethyl 2-tert-butyl-4-(pyridin-2-yl)benzoate (3f)
2-(3-(adamantan-1-yl)phenyl)pyridine (4a)

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![NMR Spectrum Image]

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![NMR Spectrum Image]
2-(3-(adamantan-1-yl)-4-methoxyphenyl)pyridine (4c)

Parameter | Value
--- | ---
1 Spectrometer | vnmr
2 Author | 
3 Solvent | dcl3
4 Temperature | 25.6
5 Pulse Sequence | 429
6 Number of Scans | 128
7 Receiver Gain | 20
8 Relaxation Delay | 1.0000
9 Pulse Width | 0.0000
10 Acquisition Time | 2.0445
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12 Modification Date | 2015-03-09T20:19:13
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15 Lowest Frequency | -1500.0
16 Nucleus | H
17 Acquired Size | 16384
18 Spectral Size | 32768

Parameter | Value
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1 Spectrometer | vnmr
2 Author | 
3 Solvent | dcl3
4 Temperature | 25.6
5 Pulse Sequence | 429
6 Number of Scans | 128
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13 Spectrometer Frequency | 600.16
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15 Lowest Frequency | -1500.0
16 Nucleus | H
17 Acquired Size | 16384
18 Spectral Size | 32768
2-[4-methoxy-3-(2-methylbutan-2-yl)phenyl]pyridine (5c)
2-[3-(2-methylnonan-2-yl)phenyl]pyridine (6a)

Parameter | Value
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1 Spectrometer | VnmrA
2 Author | 
3 Solvent | cdcl3
4 Temperature | 25.0
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16 Nucleus | 1H
17 Acquired Size | 16384
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Parameter | Value
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5 Pulse Sequence | 629ul
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13 Spectrometer Frequency | 125.75
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16 Nucleus | 13C
17 Acquired Size | 524288
18 Spectral Size | 65536
2-[4-methoxy-3-(2-methylnonan-2-yl)phenyl]pyridine (6c)

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![NMR Spectrum of 2-[4-methoxy-3-(2-methylnonan-2-yl)phenyl]pyridine (6c)](image-url)
2-(3-(3-ethylpentan-3-yl)-4-methoxyphenyl)pyridine (7c)

Parameter | Value
--- | ---
1. Spectrometer | varims
2. Author |
3. Solvent | cdcl3
4. Temperature | 25.0
5. Pulse Sequence | 62µs
6. Number of Scans | 32
7. Receiver Gain | 32
8. Relaxation Delay | 3.0000
9. Pulse Width | 0.0000
10. Acquisition Time | 2.0447
11. Acquisition Date | 2015-03-09T12:00:43
12. Modification Date | 2015-04-10T14:05:18
13. Spectrometer Frequency | 500.06
14. Spectral Width | 8012.8
15. Lowest Frequency | 300.6
16. Nucleus | 1H
17. Acquired Size | 16384
18. Spectral Size | 32768

![NMR Spectrum](image)

Parameter | Value
--- | ---
1. Spectrometer | varims
2. Author |
3. Solvent | cdcl3
4. Temperature | 25.0
5. Pulse Sequence | 62µs
6. Number of Scans | 32
7. Receiver Gain | 32
8. Relaxation Delay | 3.0000
9. Pulse Width | 0.0000
10. Acquisition Time | 2.0447
11. Acquisition Date | 2015-03-09T12:00:43
12. Modification Date | 2015-04-10T14:05:18
13. Spectrometer Frequency | 500.06
14. Spectral Width | 8012.8
15. Lowest Frequency | 300.6
16. Nucleus | 1H
17. Acquired Size | 16384
18. Spectral Size | 32768

![NMR Spectrum](image)
ethyl 2-methyl-2-[3-(pyridin-2-yl)phenyl]propanoate (8a)
diethyl 2,2,3-trimethyl-3-[3-(pyridin-2-yl)benzyl]butanedioate (9a)
ethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8c)
diethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9c)
ethyl 2-(2-fluoro-5-(pyridin-2-yl)phenyl)-2-methylpropanoate (8d)
diethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9d)
triethyl 2-{2-fluoro-5-(pyridin-2-yl)phenyl}-3,5-dimethylhexane-2,3,5-tricarboxylate (9e)
2,2'-(4,4'-dimethylbiphenyl-2,2'-diyl)dipyridine (10)
ethyl 2-(benzo[h]quinolin-7-yl)-2-methylpropanoate (11)
$2,2'-(3,3'\text{-dimethylbiphenyl}-2,2'\text{-diyl})\text{dipyridine (12)}$

Parameter | Value
--- | ---
1 Spectrometer | Varian
2 Author |
3 Solvent | d6DMSO
4 Temperature | 25.0
5 Pulse Sequence | 62pul
6 Number of Scans | 8
7 Receiver Gain | 26
8 Relaxation Delay | 1.0000
9 Pulse Width | 0.0000
10 Acquisition Time | 0.0000
11 Acquisition Date | 2015-05-07T12:42:36
12 Modification Date | 2015-05-07T12:32:39
13 Spectrometer Frequency | 500.00
14 Spectral Width | 8002.8
15 Lowest Frequency | 1000.5
16 Nucleus | 1H
17 Acquired Size | 16384
18 Spectral Size | 32768

Chemical structure of $2,2'-(3,3'\text{-dimethylbiphenyl}-2,2'\text{-diyl})\text{dipyridine (12)}$