Supporting Information
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Electronic supporting information

Ru-catalyzed, microwave-mediated [2+2+2] cycloaddition: a useful combination for the synthesis of 2-aminopyridines

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I. General information

$^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker AV400 instruments. All signals are expressed as ppm ($\delta$) and are referenced to the non-deuterated solvent peak CHCl$_3$ (7.26 ppm for $^1$H and 77.16 ppm for $^{13}$C). Coupling constants ($J$) are given in Hz and refer to apparent peak multiplicities. The following abbreviations are used: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad.

Mass spectrometry analyses (direct introduction by electronic impact) were performed at the Ecole Nationale Supérieure de Chimie de Paris (ENSCP).

Sigma-Aldrich Silica gel (high-purity grade, pore size 60 Å, 230-400 mesh particle size, 40-63 μm particle size) was employed for flash column chromatography. Analytical thin layer chromatography (TLC) was carried out using commercial silica-gel plates (Merck 60 F254), spots were detected with UV light (254 nm) and revealed with a KMnO$_4$ stain solution.
II. Ru-catalyzed [2+2+2] cycloaddition of α,ω-diynes under microwave conditions

4-(4-Bromo-7-methyl-2-tosyl-2,3-dihydro-1H-pyrrolo[3,4-c]pyridin-6-yl)morpholine (3a)

Starting from diyne 1a (70 mg, 0.2 mmol), morpholine-4-carbonitrile (2a) (28 mg, 0.3 mmol) and Cp*Ru(CH3CN)3PF6 (2 mg, 0.004 mmol). Purification by filtration through a silica pad and bulb to bulb distillation afforded pyridine 3a as a brown solid (95 mg, quant.).

1H NMR (400 MHz, CDCl3) δ 7.76 (d, J = 8.3 Hz, 2H), 7.36 – 7.30 (m, 2H), 4.55 (t, J = 2.0 Hz, 2H), 4.49 (t, J = 1.9 Hz, 2H), 3.83 – 3.73 (m, 4H), 3.11 – 3.02 (m, 4H), 2.41 (s, 3H), 2.05 (s, 3H).

13C NMR (100 MHz, CDCl3) δ 161.2, 148.8, 144.2, 133.5, 130.5, 130.1, 127.6, 127.5, 118.2, 66.9, 54.0, 53.6, 50.3, 21.6, 14.6.

The analytical data were identical to those reported in the literature.1

4-Chloro-N,N,7-trimethyl-2-tosyl-2,3-dihydro-1H-pyrrolo[3,4-c]-pyridin-6-amine (3b)

Starting from diyne 1b (90 mg, 4.0 mmol), dimethylcyanamide (2b) (26 mg, 0.4 mmol) and Cp*Ru(CH3CN)3PF6 (3 mg, 0.006 mmol). Purification by filtration through a silica pad afforded pyridine 3b as a white solid (113 mg, quant.).

Gram-scale preparation: Starting from diyne 1b (1 g, 3.0 mmol), dimethylcyanamide (2b) (317 mg, 4.5 mmol) and Cp*Ru(CH3CN)3PF6 (34 mg, 0.07 mmol). Purification by filtration on silica pad afforded 3b as a white solid (1.24 g, quant.).

\[ \text{H NMR (400 MHz, CDCl}_3\text{) }\delta 7.80 - 7.73 (m, 2H), 7.39 - 7.30 (m, 2H), 4.52 (s, 4H), 2.79 (s, 6H), 2.41 (s, 3H), 2.07 (s, 3H). \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{) }\delta 162.3, 149.2, 144.1, 139.5, 133.6, 130.1, 127.6, 122.9, 116.4, 53.9, 52.4, 41.9, 21.6, 15.2. \]

The analytical data were identical to those reported in the literature.\(^1\)

3-Morpholino-5,7-dihydro-6H-cyclopenta[c]pyridine-6,6-dicarbonitrile (3c)

\[
\begin{align*}
&\text{Chemical Formula: C}_{14}\text{H}_{14}\text{N}_4\text{O} \\
&\text{Exact Mass: 254.1168}
\end{align*}
\]

Starting from diyne 1c (70 mg, 0.5 mmol), morpholine-4-carbonitrile (2a) (72 mg, 0.6 mmol) and Cp*Ru(CH\(_3\)CN\(_3\))PF\(_6\) (5 mg, 0.01 mmol). Purification by filtration through a silica pad and bulb to bulb distillation afforded pyridine 3c as a brown oil (112 mg, 90%).

\[ \text{H NMR (400 MHz, CDCl}_3\text{) }\delta 8.08 (d, J = 1.1 \text{ Hz}, 1H), 6.53 (d, J = 1.1 \text{ Hz}, 1H), 3.83 - 3.71 (m, 4H), 3.60 (d, J = 1.0 \text{ Hz}, 2H), 3.58 (d, J = 1.0 \text{ Hz}, 2H), 3.53 - 3.44 (m, 4H). \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{) }\delta 159.8, 147.6, 143.8, 121.7, 115.9, 102.5, 66.6, 45.7, 44.3, 41.8, 33.9. \]

The analytical data were identical to those reported in the literature.\(^1\)

4-Bromo-7-methyl-6-(pyrrolidin-1-yl)-1,3-dihydrofuro[3,4-c]-pyridine (3d)

\[
\begin{align*}
&\text{Chemical Formula: C}_{12}\text{H}_{15}\text{BrN}_2\text{O} \\
&\text{Exact Mass: 282.0368}
\end{align*}
\]

Starting from diyne 1d (70 mg, 0.4 mmol), pyrrolidine-1-carbonitrile (2c) (43 mg, 0.5 mmol) and Cp*Ru(CH\(_3\)CN\(_3\))PF\(_6\) (4 mg, 0.008 mmol). Purification by filtration through a silica pad and bulb to bulb distillation afforded pyridine 3d as a brown oil (71 mg, 66%).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.04 (d, $J = 1.9$ Hz, 2H), 4.97 (d, $J = 1.9$ Hz, 2H), 3.57 – 3.40 (m, 4H),
2.11 (s, 3H), 1.96 – 1.82 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.3, 152.0, 128.5, 125.6, 111.5, 74.0, 73.7, 50.4, 25.7, 16.1.

The analytical data were identical to those reported in the literature.$^1$

4-Bromo-N,N,7-trimethyl-1,3-dihydrofuro[3,4-c]pyridin-6-amine (3e).

![Chemical structure of 4-Bromo-N,N,7-trimethyl-1,3-dihydrofuro[3,4-c]pyridin-6-amine (3e).]

Chemical Formula: C$_{16}$H$_{13}$BrN$_2$O
Exact Mass: 256.0211

Starting from diyne 1d (70 mg, 0.4 mmol), dimethylcyanamide (2b) (32 mg, 0.5 mmol) and
Cp*Ru(CH$_3$CN)$_3$PF$_6$ (4 mg, 0.008 mmol). Purification by filtration through a silica pad afforded
pyridine 3e as a brown oil (84 mg, 86%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.09 – 5.01 (m, 2H), 4.98 (t, $J = 1.9$ Hz, 2H), 2.83 (s, 6H), 2.09 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.4, 152.2, 128.8, 128.4, 115.7, 73.9, 73.6, 42.1, 15.3.

The analytical data were identical to those reported in the literature.$^1$

Dimethyl 1-iodo-4-methyl-3-morpholino-5H-cyclopenta[c]pyridine-6,6(7H)-dicarboxylate (3f)

![Chemical structure of Dimethyl 1-iodo-4-methyl-3-morpholino-5H-cyclopenta[c]pyridine-6,6(7H)-dicarboxylate (3f).]

Chemical Formula: C$_{17}$H$_{21}$IN$_2$O$_5$
Exact Mass: 460.0495
Starting from diyne 1e (70 mg, 0.2 mmol), morpholine-4-carbonitrile (2a) (29 mg, 0.3 mmol) and Cp*Ru(CH₃CN)₃PF₆ (2 mg, 0.004 mmol). Purification by filtration through a silica pad and bulb to bulb distillation afforded pyridine 3f as a brown oil (92 mg, quant.).

¹H NMR (400 MHz, CDCl₃) δ 3.84 – 3.78 (m, 4H), 3.77 (s, 6H), 3.57 (s, 2H), 3.49 (s, 2H), 3.09 – 3.05 (m, 4H), 2.11 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 171.6, 160.9, 150.6, 136.4, 120.1, 109.8, 67.0, 58.3, 53.4, 50.5, 43.3, 41.0, 14.5.

The analytical data were identical to those reported in the literature.²

Dimethyl 3-(dimethylamino)-1-iodo-4-methyl-5H-cyclopenta[c]pyridine-6,6(7H)-dicarboxylate (3g)

Starting from diyne 1e (70 mg, 0.2 mmol), dimethylcyanamide (2b) (29 mg, 0.3 mmol) and Cp*Ru(CH₃CN)₃PF₆ (2 mg, 0.004 mmol). Purification by filtration through a silica pad afforded pyridine 3g as a brown oil (84 mg, quant.).

Gram-scale preparation: Starting from diyne 1e (1 g, 3.0 mmol), dimethylcyanamide (2b) (242 mg, 3.5 mmol) and Cp*Ru(CH₃CN)₃PF₆ (29 mg, 0.06 mmol). Purification by filtration through a silica pad afforded pyridine 3g as a brown oil (1.21 g, quant.).

Rₓ = 0.29 (Cyclohexane/Ethyl acetate: 80/20, KMnO₄, UV).

¹H NMR (400 MHz, CDCl₃) δ 3.76 (s, 6H), 3.55 (s, 2H), 3.47 (d, J = 1.9 Hz, 2H), 2.76 (s, 6H), 2.11 (d, J = 1.9 Hz, 3H).

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\[ ^{13}\text{C NMR} \text{ (100 MHz, CDCl}_3\text{)} \delta 171.6, 162.1, 150.4, 134.9, 118.9, 109.3, 58.3, 53.3, 43.2, 42.2, 41.0, 15.0. \]

**MS (EI):** \( m/z = 419 \ [M + H]^+ \).

1,4-Dimethyl-3-(pyrrolidin-1-yl)-5,7-dihydrospiro[cyclopenta[c]pyridine-6,2'-indene]-1',3'-dione (3h)

\[ \text{Chemical Formula: } C_{22}H_{22}N_2O_2 \]

**Exact Mass: 346.1681**

Starting from diyne 1f (90 mg, 0.3 mmol), pyrrolidine-1-carbonitrile (2c) (41 mg, 0.4 mmol) and Cp*Ru(CH_3CN)_3PF_6 (4 mg, 0.007 mmol). Purification on silica gel (Cyclohexane/Ethyl acetate gradient from 90/10 to 40/60) and bulb to bulb distillation afforded pyridine 3h as a yellow oil (112 mg, 90%).

\[ R_f = 0.32 \text{ (Cyclohexane/Ethyl acetate: 70/30, KMnO}_4\text{, UV).} \]

\[ ^1\text{H NMR} \text{ (400 MHz, CDCl}_3\text{)} \delta 8.02 \text{ (dd, } J = 5.7, 3.1 \text{ Hz, 2H), 7.88 \text{ (dd, } J = 5.7, 3.1 \text{ Hz, 2H), 3.50 – 3.41 (m, 4H), 3.21 \text{ (d, } J = 4.8 \text{ Hz, 4H), 2.31 – 2.22 (m, 3H), 2.14 (s, 3H), 1.95 – 1.84 (m, 4H).} \]

\[ ^{13}\text{C NMR} \text{ (100 MHz, CDCl}_3\text{)} \delta 203.1, 159.4, 151.0, 147.3, 141.7, 136.0, 125.2, 123.8, 113.5, 58.6, 50.3, 39.6, 25.6, 21.9, 15.9. \]

**MS (EI):** \( m/z = 347 \ [M + H]^+ \).

3-(Dimethylamino)-1,4-dimethyl-5,7-dihydrospiro[cyclopenta[c]pyridine-6,2'-indene]-1',3'-dione (3i)

\[ \text{Chemical Formula: } C_{20}H_{20}N_2O_2 \]

**Exact Mass: 320.1525**
Starting from diyne 1f (90 mg, 0.3 mmol), dimethylcyanamide (2b) (30 mg, 0.4 mmol) and Cp*Ru(CH\(_3\)CN)\(_3\)PF\(_6\) (4 mg, 0.008 mmol). Purification by filtration through a silica pad afforded pyridine 3i as a yellow solid (115 mg, quant.).

\( R_f \) = 0.17 (Cyclohexane/Ethyl acetate: 80/20, KMnO\(_4\), UV).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.01 (dd, \( J = 5.7, 3.1 \) Hz, 2H), 7.87 (dd, \( J = 5.7, 3.1 \) Hz, 2H), 3.21 (d, \( J = 4.1 \) Hz, 4H), 2.79 (s, 6H), 2.30 (d, \( J = 0.9 \) Hz, 3H), 2.13 (d, \( J = 0.9 \) Hz, 3H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 203.0, 161.8, 151.1, 147.7, 141.6, 136.1, 127.8, 123.8, 117.3, 58.5, 42.5, 39.6, 39.5, 21.8, 14.9.

MS (EI): m/z = 321 [M + H]\(^+\).

(3-(Dimethylamino)-1,4-dimethyl-6,7-dihydro-5H-cyclopenta[c]pyridine-6,6-diyl)dimethanol (3j)

Starting from diyne 1g (55 mg, 0.3 mmol), dimethylcyanamide (2b) (26 mg, 0.4 mmol) and Cp*Ru(CH\(_3\)CN)\(_3\)PF\(_6\) (5 mg, 0.009 mmol). Purification on silica gel (Ethyl acetate/Methanol gradient from 95/5 to 80/20) afforded pyridine 3j as a bright-yellow oil (62 mg, 83%).

\( R_f \) = 0.13 (Cyclohexane/Ethyl acetate: 40/60, KMnO\(_4\), UV).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 3.75 \text{–} 3.64 (m, 4H), 3.29 (br s, 2H), 2.76 (s, 6H), 2.70 (s, 2H), 2.66 (s, 2H), 2.28 (s, 3H), 2.11 (s, 3H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 161.0, 152.5, 148.4, 129.2, 118.2, 69.4, 48.6, 42.5, 37.9, 36.5, 21.5, 14.8.

MS (EI): m/z = 251 [M + H]\(^+\).
Starting from diyne 1h (25 mg, 0.2 mmol), N-benzyl-N-methylcyanamide (2d) (60 mg, 0.3 mmol) and Cp*Ru(CH\textsubscript{3}CN)\textsubscript{3}PF\textsubscript{6} (5 mg, 0.01 mmol). Purification through a silica gel (Cyclohexane/Ethyl acetate gradient from 90/10 to 80/20) afforded pyridine 3k as a white solid (20 mg, 37%).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.34 – 7.26 (m, 2H), 7.26 – 7.21 (m, 3H), 6.11 (s, 1H), 4.81 (s, 2H), 4.65 (s, 2H), 3.89 (t, J = 5.7 Hz, 2H), 3.00 (s, 3H), 2.73 (t, J = 5.7 Hz, 2H), 2.23 (s, 3H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 157.2, 151.7, 143.9, 139.4, 128.5, 127.4, 126.9, 116.7, 102.3, 65.9, 64.7, 53.1, 36.0, 29.0, 21.2

The analytical data were identical to those reported in the literature.\textsuperscript{1}
III. NMR Spectra of new compounds