Silver versus gold-catalyzed sequential oxidative cyclizations of unprotected 2-alkynylanilines with oxone

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1. General Informations

$^1$H-NMR spectra were recorded at 400 MHz on Bruker instrument. Chemical shifts (in ppm) were referenced to tetramethylsilane ($\delta = 0$ ppm) in CDCl$_3$ or in acetone-d$_6$ as an internal standard. $^{13}$C-NMR spectra were recorded at 100.6 MHz and were calibrated with CDCl$_3$ ($\delta = 77.00$ ppm) or acetone-d$_6$ ($\delta = 30.50$ ppm). HRMS-ESI data were performed at the University P. et M. Curie and Università dell'Aquila on a TOF mass spectrometer. Unless otherwise stated, all starting materials, catalysts, and solvents were commercially available and were used as purchased. Reaction products were purified by flash chromatography on silica gel by elution with $n$-hexane/EtOAc mixtures. The products $1a$, $1b$, $1c$, $1d$, $1e$, $1f$, $1g$, $1h$, $1j$, $1k$, $1l$, $1m$, $1n$, and $4a-c$ are known products and were identified by comparison of their physical and spectral data reported in the cited references.

2. Experimental procedures and characterization of products.

Synthesis of 2-[(2-aminophenyl)ethynyl]-5-methylphenyl acetate (1i):

![Structure of 2-[(2-aminophenyl)ethynyl]-5-methylphenyl acetate (1i)]

To a solution of 2-iodo-4-methylphenyl acetate (1.120 g, 4.06 mmol) in DMF (2.0 mL) was added Pd(PPh$_3$)$_2$Cl$_2$ (0.065 g, 0.094 mmol), Et$_3$N (1.8 mL) and 2-ethynylaniline (0.365 g, 3.12 mmol). After 4 h of stirring at 90 °C under N$_2$, 200 mL of HCl 1 M and 200 mL of EtOAc were added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 95:5) afforded 1i (0.573 g, 75% yield): $^1$H-NMR (CDCl$_3$, 400 MHz): $\delta = 2.32$ (s, 6H, OCCH$_3$ and CH$_3$), 4.29 (bs, 2H, NH$_2$), 6.67-6.71 (m, 2H), 6.97-7.00 (m, 1H), 7.11-7.15 (m, 2H), 7.30 (dd, 1H, $J=7.9$ Hz, $J=1.5$ Hz), 7.36-7.37 (m, 1H); $^{13}$C-NMR (CDCl$_3$, 100.6 MHz): $\delta = 20.7$ (CH$_3$), 21.0 (CH$_3$), 89.7 (C), 90.5 (C), 102.4 (C), 110.9 (C), 114.3 (CH), 117.8 (CH), 121.9 (CH), 130.0 (CH), 130.2 (CH), 132.0 (CH), 133.2 (CH), 135.7 (C), 148.1 (C), 149.1 (C), 169.3 (C=O); HRMS m/z (ESI) positive ion, calculated for C$_{17}$H$_{16}$NO$_2$: [M+1]$^+$ 266.1176; Found: 266.1149.
Synthesis of 4-[(2-amino-4-(trifluoromethyl)phenyl)ethynyl]benzonitrile (1o):

![Chemical structure](image)

To a solution of 4-iodobenzonitrile (0.790 g, 3.45 mmol) in THF (10 mL) and Et₃N (1.5 mL) were added PdCl₂ (0.012 g, 0.069 mmol), dppf (0.037 g, 0.069 mmol) and 2-ethynyl-5-(trifluoromethyl)aniline (0.425 g, 2.30 mmol). After 6 h of stirring at room temperature under N₂, 150 mL of HCl 1 M and 150 mL of EtOAc were added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 90:10) afforded 1o (0.526 g, 80% yield):

**1H-NMR** (CDCl₃, 400 MHz): δ = 4.48 (bs, 2H, NH₂), 6.95-6.97 (m, 2H), 7.45 (dt, 1H, J = 7.7 Hz, J = 0.9 Hz), 7.60-7.67 (m, 4H);

**13C-NMR** (CDCl₃, 100.6 MHz): δ = 89.0 (C), 94.6 (C), 109.9 (q, J = 1.5 Hz, C), 111.0 (q, J = 4.0 Hz, CH), 112.0 (C), 114.4 (q, J = 3.8 Hz, CH), 118.4 (CN), 123.8 (q, J = 272.5 Hz, CF₃), 127.6 (C), 132.0 (2CH), 132.20 (2CH), 132.23 (q, J = 32.2 Hz, C), 132.9 (CH), 148.1 (C);

**HRMS** m/z (ESI) positive ion, calculated for C₁₆H₁₀F₃N₂: [M+1]+ 287.0791; Found: 287.0766.

Typical procedure for the domino gold-catalyzed hydroamination/oxidation reaction of 2-alkynylanilines 1: NaAuCl₄·2H₂O (0.010 g, 0.025 mmol) and oxone (0.314 g, 0.51 mmol) were added to a solution of 2-(p-tolylethynyl)aniline 1c (0.106 g, 0.51 mmol) in CH₃CN (7 mL). The mixture was stirred at 80 °C and the reaction was monitored by TLC and GC-MS. Then, the mixture after stirring for 6 h was cooled and filtered through a pad of fluorisil. The filtrate was evaporated and subjected to column chromatography on silica gel (eluent: hexane/EtOAc = 90:10) to give 2-(p-tolyl)-4H-benzo[d][1,3]oxazin-4-one (4c) (0.085 g, 72% yield).

Procedure for a two-step one-pot gold-catalyzed hydroamination/oxidation 2-alkynylaniline 1a: NaAuCl₄·2H₂O (0.010 g, 0.026 mmol) was added to a solution of 2-(phenylethynyl)aniline 1a (0.103 g, 0.53 mmol) in CH₃CN (7 mL). The mixture was stirred at 80 °C for 1 h until the complete conversion of the starting 1a into the corresponding 2-phenyl-1H-indole 5a as monitored by GC-MS. Then, oxone (0.652 g, 1.06 mmol) was added and the mixture after stirring under reflux for 1 h was cooled and filtered through a pad of fluorisil. The filtrate was evaporated and subjected to column chromatography on silica gel (eluent: hexane/EtOAc = 99:1) to give 2-phenyl-4H-benzo[d][1,3]oxazin-4-one (4a) (0.074 g, 63% yield).
Typical procedure for silver-catalyzed oxidative cyclization of 2-alkynylanilines 1 with oxone.

Synthesis of 2,1-benzisoxazol-3-yl(phenyl)methanone (6a):

![Chemical structure of 6a]

AgNO₃ (0.010 g, 0.059 mmol) and oxone (0.726 g, 1.18 mmol) were added to a solution of 2-(phenylethynyl)aniline 1a (0.114 g, 0.59 mmol) in CH₃CN/H₂O (3.5 mL/3.5 mL). The mixture was stirred at 60 °C and the reaction was monitored by TLC and GC-MS. Then, the mixture after stirring for 1 h was cooled and 150 mL of H₂O and 150 mL of CH₂Cl₂ were added. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. The filtrate was evaporated and subjected to column chromatography on silica gel (eluent: hexane/EtOAc = 98:2) to give the benzo[c]isoxazol-3-yl(phenyl)methanone (6a) (0.115 g, 88% yield). ¹H-NMR (CDCl₃, 400 MHz): δ = 7.24 (t, 1H, J=7.6 Hz), 7.38 (t, 1H, J=7.7 Hz), 7.54 (t, 2H, J=7.5 Hz), 7.64 (t, 1H, J=7.3 Hz), 7.71 (d, 1H, J=9.0 Hz), 8.09 (d, 1H, J=8.8 Hz), 8.27 (d, 2H, J=8.0 Hz); ¹³C-NMR (CDCl₃, 100.6 MHz): δ = 115.8 (C), 121.5 (C), 121.6 (CH), 128.4 (CH), 128.7 (2CH), 130.1 (2CH), 131.3 (CH), 133.8 (CH), 135.9 (C), 157.2 (C), 160.3 (C), 181.3 (C=O). HRMS m/z (ESI) positive ion, calculated for C₁₄H₁₀NO₂: [M+H]⁺ 224.0706; Found: 224.0701.

2,1-benzisoxazol-3-yl(4-methoxyphenyl)methanone (6b):

![Chemical structure of 6b]

¹H-NMR (CDCl₃, 400 MHz): δ = 3.93 (s, 3H, OMe), 7.04-7.08 (m, 2H), 7.27 (ddd, 1H, J=8.8 Hz, J=6.4 Hz, J=0.7 Hz), 7.42 (ddd, 1H, J=9.1 Hz, J=6.4 Hz, J=1.0 Hz), 7.74 (ddd, 1H, J=9.1 Hz, J=1.2 Hz, J=0.8 Hz), 8.14 (dt, 1H, J=8.8 Hz, J=1.0 Hz), 8.34-8.37 (m, 2H); ¹³C-NMR (CDCl₃, 100.6 MHz): δ = 55.6 (OMe), 114.2 (2CH), 115.8 (CH), 121.5 (C), 121.9 (CH), 128.1 (CH), 128.9 (C), 131.4 (CH), 132.7 (2CH), 157.3 (C), 161.0 (C), 164.3 (C), 179.8 (C=O); HRMS m/z (ESI) positive ion, calculated for C₁₅H₁₂NO₃: [M+H]⁺ 254.0814; Found: 254.0811.
2,1-benzisoxazol-3-yl(4-methylphenyl)methanone (6c):

\[ \text{6c} \]

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \( \delta = 2.45 \) (s, 3H, Me), 7.25 (ddd, 1H, \( J=8.8 \) Hz, \( J=6.4 \) Hz, \( J=0.8 \) Hz), 7.34-7.37 (m, 2H), 7.39 (ddd, 1H, \( J=9.1 \) Hz, \( J=6.4 \) Hz, \( J=1.0 \) Hz), 7.73 (ddd, 1H, \( J=9.1 \) Hz, \( J=1.2 \) Hz, \( J=0.8 \) Hz), 8.11 (dt, 1H, \( J=8.8 \) Hz, \( J=1.1 \) Hz), 8.19 - 8.22 (m, 2H); \(^{13}\)C-NMR (CDCl\(_3\), 100.6 MHz): \( \delta = 21.8 \) (Me), 115.8 (CH), 121.5 (C), 121.8 (CH), 128.3 (CH), 129.5 (2CH), 130.3 (2CH), 131.3 (CH), 133.4 (C), 144.9 (C), 157.2 (C), 160.6 (C), 180.9 (C=O); HRMS \( m/z \) (ESI) positive ion, calculated for C\(_{15}\)H\(_{12}\)NO\(_2\): [M+H]\(^+\) 238.0862; Found: 238.0862.

2,1-benzisoxazol-3-yl[4-(trifluoromethyl)phenyl]methanone (6d):

\[ \text{6d} \]

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \( \delta = 7.32 \) (ddd, 1H, \( J=8.8 \) Hz, \( J=6.5 \) Hz, \( J=0.8 \) Hz), 7.44 (ddd, 1H, \( J=9.1 \) Hz, \( J=6.5 \) Hz, \( J=1.0 \) Hz), 7.77 (ddd, 1H, \( J=9.1 \) Hz, \( J=1.2 \) Hz, \( J=0.8 \) Hz), 7.82-7.86 (m, 2H), 8.12 (dt, 1H, \( J=8.8 \) Hz, \( J=1.1 \) Hz), 8.38 - 8.41 (m, 2H); \(^{13}\)C-NMR (CDCl\(_3\), 100.6 MHz): \( \delta = 116.1 \) (CH), 121.5 (CH), 122.0 (C), 123.6 (q, \( J=272.8 \) Hz, CF\(_3\)), 125.8 (q, \( J=3.7 \) Hz, 2CH), 129.2 (CH), 130.4 (2CH), 131.6 (CH), 134.9 (q, \( J=32.8 \) Hz, C), 138.7 (C), 157.4 (C), 159.7 (C), 180.3 (C=O); HRMS \( m/z \) (ESI) positive ion, calculated for C\(_{15}\)H\(_{9}\)F\(_3\)NO\(_2\): [M+H]\(^+\) 292.0579; Found: 292.0580.

2,1-benzisoxazol-3-yl(3-methylphenyl)methanone (6e):

\[ \text{6e} \]

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \( \delta = 2.46 \) (s, 3H, Me), 7.27 (ddd, 1H, \( J=8.8 \) Hz, \( J=6.4 \) Hz, \( J=0.8 \) Hz), 7.40 (ddd, 1H, \( J=9.1 \) Hz, \( J=6.5 \) Hz, \( J=1.0 \) Hz), 7.74-7.47 (m, 2H), 7.74 (ddd, 1H, \( J=9.1 \) Hz, \( J=1.2 \) Hz, \( J=0.8 \) Hz), 8.11 (dt, 1H, \( J=8.8 \) Hz, \( J=1.1 \) Hz), 8.19 - 8.22 (m, 2H); HRMS \( m/z \) (ESI) positive ion, calculated for C\(_{15}\)H\(_{12}\)NO\(_2\): [M+H]\(^+\) 292.0579; Found: 292.0580.
Hz, $J=0.8$ Hz), 8.05 - 8.09 (m, 2H), 8.11 (dt, 1H, $J=8.8$ Hz, $J=1.1$ Hz); $^{13}$C-NMR (CDCl$_3$, 100.6 MHz): $\delta = 21.4$ (Me), 115.8 (CH), 121.5 (C), 121.7 (CH), 127.4 (CH), 128.4 (CH), 128.6 (CH), 130.5 (CH), 131.3 (CH), 134.6 (CH), 136.0 (C), 138.6 (C), 157.2 (C), 181.6 (C=O); HRMS $m/z$ (ESI) positive ion, calculated for C$_{13}$H$_{12}$NO$_2$: [M+H]$^+$ 238.0862; Found: 238.0862.

2,1-benzisoxazol-3-yl(4-chlorophenyl)methanone (6f):

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta = 7.30$ (ddd, 1H, $J=8.8$ Hz, $J=6.4$ Hz, $J=0.8$ Hz), 7.43 (ddd, 1H, $J=9.1$ Hz, $J=6.4$ Hz, $J=1.0$ Hz), 7.52-7.56 (m, 2H), 7.75 (dt, 1H, $J=9.1$ Hz, $J=1.0$ Hz), 8.12 (dt, 1H, $J=8.8$ Hz, $J=1.1$ Hz), 8.25-8.28 (m, 2H); $^{13}$C-NMR (CDCl$_3$, 100.6 MHz): $\delta = 115.9$ (CH), 121.6 (CH), 121.8 (C), 128.8 (CH), 129.1 (2CH), 131.46 (CH), 131.52 (2CH), 134.2 (C), 140.5 (C), 157.2 (C), 160.0 (C), 179.9 (C=O); HRMS $m/z$ (ESI) positive ion, calculated for C$_{14}$H$_{9}$ClNO$_2$: [M+H]$^+$ 258.0316; Found: 258.0319.

2,1-benzisoxazol-3-yl(3-bromophenyl)methanone (6g):

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta = 7.32$ (ddd, 1H, $J=8.8$ Hz, $J=6.5$ Hz, $J=0.8$ Hz), 7.44 (ddd, 1H, $J=9.0$ Hz, $J=6.5$ Hz, $J=1.0$ Hz), 7.46 (td, 1H, $J=7.9$ Hz, $J=0.6$ Hz), 7.76-7.81 (m, 2H), 8.13 (dt, 1H, $J=8.8$ Hz, $J=1.1$ Hz), 8.26 (ddd, 1H, $J=7.8$ Hz, $J=1.7$ Hz, $J=1.0$ Hz), 8.40 (ddd, 1H, $J=2.1$ Hz, $J=1.6$ Hz, $J=0.5$ Hz); $^{13}$C-NMR (CDCl$_3$, 100.6 MHz): $\delta = 116.0$ (CH), 121.6 (CH), 121.9 (C), 123.0 (C), 128.7 (CH), 128.9 (CH), 130.3 (CH), 131.5 (CH), 132.9 (CH), 136.6 (CH), 137.6 (C), 157.3 (C), 159.8 (C), 179.8 (C=O); HRMS $m/z$ (ESI) positive ion, calculated for C$_{14}$H$_{9}$BrNO$_2$: [M+H]$^+$ 301.9811; Found: 301.9813.
1-[4-(2,1-benzisoxazol-3-ylcarbonyl)phenyl]ethanone (6h):

\[
\begin{align*}
\text{H-NMR (CDCl}_3, 400 MHz): \delta &= 2.70 (s, 3H, Me), 7.33 (ddd, 1H, J=8.8 Hz, J=6.5 Hz, J=0.8 Hz), \\
&7.45 (ddd, 1H, J=9.1 Hz, J=6.5 Hz, J=1.0 Hz), 7.78 (td, 1H, J=9.1 Hz, J=1.0 Hz), 8.12-8.15 (m, 3H), 8.35-8.39 (m, 2H); \\
\text{C-NMR (CDCl}_3, 100.6 MHz): \delta &= 27.0 (CH3), 116.0 (CH), 121.5 (CH), 121.9 (C), 128.5 (2CH), 129.0 (CH), 130.3 (2CH), 131.5 (CH), 139.2 (C), 140.5 (C), 157.3 (C), 159.9 (C), 180.7 (C=O), 197.4 (C=O); \\
\text{HRMS m/z (ESI) positive ion, calculated for C}_{16}H_{12}NO_3: [M+H]^+ 266.0811; Found: 266.0814.}
\end{align*}
\]

2-(2,1-benzisoxazol-3-ylcarbonyl)-5-methylphenyl acetate (6i):

\[
\begin{align*}
\text{H-NMR (CDCl}_3, 400 MHz): \delta &= 2.12 (s, 3H, OCMc), 2.43 (s, 3H, Me), 7.16 (dt, 1H, J=8.3 Hz, J=0.4 Hz), 7.28 (ddd, 1H, J=8.8 Hz, J=6.5 Hz, J=0.8 Hz), 7.42 (ddd, 1H, J=9.1 Hz, J=6.5 Hz, J=1.0 Hz), 7.44 (ddd, 1H, J=8.3 Hz, J=2.2 Hz, J=0.7 Hz), 7.66 (ddd, 1H, J=2.2 Hz, J=0.7 Hz, J=0.4 Hz), 7.75 (ddd, 1H, J=9.1 Hz, J=1.2 Hz, J=0.8 Hz), 7.98 (dt, 1H, J=8.8 Hz, J=1.1 Hz); \\
\text{C-NMR (CDCl}_3, 100.6 MHz): \delta &= 20.8 (Me), 20.9 (Me), 116.0 (CH), 120.9 (C), 121.3 (CH), 123.4 (CH), 128.6 (CH), 129.3 (C), 131.1 (CH), 131.4 (CH), 134.3 (CH), 135.9 (C), 147.0 (C), 157.5 (C), 159.8 (C), 169.3 (C=O), 180.9 (C=O); \\
\text{HRMS m/z (ESI) positive ion, calculated for C}_{17}H_{14}NO_4: [M+1]^+ 296.0923; Found: 296.0919.}
\end{align*}
\]

2,1-benzisoxazol-3-yl(pyridin-2-yl)methanone (6j):

\[
\begin{align*}
\text{H-NMR (CDCl}_3, 400 MHz): \delta &= 2.12 (s, 3H, OCMc), 2.43 (s, 3H, Me), 7.16 (dt, 1H, J=8.3 Hz, J=0.4 Hz), 7.28 (ddd, 1H, J=8.8 Hz, J=6.5 Hz, J=0.8 Hz), 7.42 (ddd, 1H, J=9.1 Hz, J=6.5 Hz, J=1.0 Hz), 7.44 (ddd, 1H, J=8.3 Hz, J=2.2 Hz, J=0.7 Hz), 7.66 (ddd, 1H, J=2.2 Hz, J=0.7 Hz, J=0.4 Hz), 7.75 (ddd, 1H, J=9.1 Hz, J=1.2 Hz, J=0.8 Hz), 7.98 (dt, 1H, J=8.8 Hz, J=1.1 Hz); \\
\text{C-NMR (CDCl}_3, 100.6 MHz): \delta &= 20.8 (Me), 20.9 (Me), 116.0 (CH), 120.9 (C), 121.3 (CH), 123.4 (CH), 128.6 (CH), 129.3 (C), 131.1 (CH), 131.4 (CH), 134.3 (CH), 135.9 (C), 147.0 (C), 157.5 (C), 159.8 (C), 169.3 (C=O), 180.9 (C=O); \\
\text{HRMS m/z (ESI) positive ion, calculated for C}_{17}H_{14}NO_4: [M+1]^+ 296.0923; Found: 296.0919.}
\end{align*}
\]
H-NMR (CDCl₃, 400 MHz): δ = 7.29 (ddd, 1H, J=8.8 Hz, J=6.5 Hz, J=0.8 Hz), 7.41 (ddd, 1H, J=9.1 Hz, J=6.5 Hz, J=1.0 Hz), 7.60 (ddd, 1H, J=7.6 Hz, J=4.7 Hz, J=1.2 Hz), 7.78 (dt, 1H, J=9.1 Hz, J=1.0 Hz), 7.78 (td, 1H, J=7.8 Hz, J=1.7 Hz), 8.08 (dt, 1H, J=8.8 Hz, J=1.1 Hz), 8.21 (dt, 1H, J=7.9 Hz, J=1.1 Hz), 8.88 (ddd, 1H, J=4.7 Hz, J=1.7 Hz, J=0.9 Hz); ¹³C {¹H} NMR (CDCl₃, 100.6 MHz): δ = 116.1 (CH), 121.6 (C), 121.8 (CH), 124.7 (CH), 127.4 (CH), 128.6 (CH), 131.1 (CH), 137.2 (CH), 149.5 (CH), 153.2 (C), 157.3 (C), 159.9 (C), 180.7 (C=O); HRMS m/z (ESI) positive ion, calculated for C₁₃H₉N₂O₂: [M+H]^+ 225.0658; Found: 225.0659.

2,1-benzisoxazol-3-yl(1H-pyrazol-4-yl)methanone (6k):

![6k]

H-NMR (DMSO, 400 MHz): δ = 7.41 (ddd, 1H, J=8.8 Hz, J=6.4 Hz, J=0.6 Hz), 7.57 (ddd, 1H, J=9.1 Hz, J=6.4 Hz, J=1.0 Hz), 7.88 (dt, 1H, J=9.1 Hz, J=0.8 Hz), 8.08 (dt, 1H, J=8.8 Hz, J=1.0 Hz), 8.60 (bs, 2H) 13.81 (bs, 1H, NH) and ¹³C {¹H} NMR (DMSO, 100.6 MHz): δ = 115.5 (CH), 119.6 (C), 120.2 (C), 120.9 (CH), 128.7 (CH), 132.0 (CH), 134.3 (bs, CH), 140.1 (bs, CH), 156.8 (C), 160.1 (C), 173.7 (C=O); HRMS m/z (ESI) positive ion, calculated for C₁₁H₈N₃O₂: [M+H]^+ 214.0611; Found: 214.0612.

1-(2,1-benzisoxazol-3-yl)heptan-1-one (6l):

![6l]

H-NMR (CDCl₃, 400 MHz): δ = 0.90 (t, 3H, J=7.1 Hz), 1.32-1.46 (m, 6H), 1.82 (qt, 2H, J=7.5 Hz), 3.17 (t, 2H, J=7.4 Hz), 7.26 (ddd, 1H, J=8.8 Hz, J=6.4 Hz, J=0.8 Hz), 7.40 (ddd, 1H, J=9.1 Hz, J=6.5 Hz, J=1.0 Hz), 7.72 (ddd, 1H, J=9.1 Hz, J=1.1 Hz, J=0.8 Hz), 8.05 (dt, 1H, J=8.8 Hz, J=1.1 Hz); ¹³C {¹H} NMR (CDCl₃, 100.6 MHz): δ 14.0 (CH₃), 22.5 (CH₂), 23.6 (CH₂), 28.9 (CH₂), 31.6 (CH₂), 40.2 (CH₂), 115.9 (CH), 119.1 (C), 121.3 (CH), 128.4 (CH), 131.3 (CH), 157.6 (C), 159.8 (C), 190.5 (C=O); HRMS m/z (ESI) positive ion, calculated for C₁₄H₁₈NO₂: [M+H]^+ 232.1332; Found: 232.1332.
(5-methyl-2,1-benzisoxazol-3-yl)(phenyl)methanone (6m):

\[\text{H}_3\text{C}-\text{C} = \text{O}-\text{N} = \text{C}-\text{H} \]

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta = 2.43\) (s, 3H), 7.24 (dd, 1H, \(J=9.2\) Hz, \(J=1.5\) Hz), 7.55-7.58 (m, 2H), 7.64-7.68 (m, 2H), 7.88 (td, 1H, \(J=2.5\) Hz, \(J=1.2\) Hz), 8.27-8.30 (m, 2H); \(^{13}\)C-NMR (CDCl\(_3\), 100.6 MHz): \(\delta = 22.1\) (Me), 115.5 (CH), 119.0 (CH), 122.3 (C), 128.7 (2CH), 130.1 (2CH), 133.6 (CH), 134.8 (CH), 136.2 (C), 139.1 (C), 156.7 (C), 159.2 (C), 181.5 (C=O); HRMS \(m/z\) (ESI) positive ion, calculated for C\(_{15}\)H\(_{12}\)NO\(_2\): \([\text{M+H}]^+\) 238.0862; Found: 238.0862.

Phenyl[6-(trifluoromethyl)-2,1-benzisoxazol-3-yl]methanone (6n):

\[\text{F}_3\text{C}-\text{C} = \text{O}-\text{N} = \text{C}-\text{H} \]

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.44\) (ddd, 1H, \(J=9.2\) Hz, \(J=1.4\) Hz, \(J=0.3\) Hz), 7.59-7.63 (m, 2H), 7.69-7.73 (m, 1H), 8.14 (td, 1H, \(J=2.4\) Hz, \(J=1.2\) Hz), 8.30-8.32 (m, 3H); \(^{13}\)C-NMR (CDCl\(_3\), 100.6 MHz): \(\delta = 114.9\) (q, \(J=5.3\) Hz, CH), 122.7 (C), 123.1 (q, \(J=273.2\) Hz, CF\(_3\)), 123.9 (CH), 124.0 (q, \(J=2.7\) Hz, CH), 129.0 (2CH), 130.2 (2CH), 133.7 (q, \(J=32.8\) Hz, C), 134.3 (CH), 135.6 (C), 156.2 (C), 161.6 (C), 181.1 (C=O); HRMS \(m/z\) (ESI) positive ion, calculated for C\(_{15}\)H\(_9\)F\(_3\)NO\(_2\): \([\text{M+H}]^+\) 292.0580; Found: 292.0588.

4-[(6-(trifluoromethyl)-2,1-benzisoxazol-3-yl)carbonyl]benzonitrile (6o):

\[\text{F}_3\text{C}-\text{C} = \text{O}-\text{N} = \text{C}-\text{CN} \]

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.50\) (dd, 1H, \(J=9.2\) Hz, \(J=1.4\) Hz), 7.90-7.93 (m, 2H), 8.18 (td, 1H, \(J=2.4\) Hz, \(J=1.2\) Hz), 8.34 (dt, 1H, \(J=9.1\) Hz, \(J=0.9\) Hz), 8.41-8.44 93 (m, 2H); \(^{13}\)C-NMR (CDCl\(_3\), 100.6 MHz): \(\delta = 115.1\) (q, \(J=5.2\) Hz, CH), 117.5 (C), 117.7 (C), 123.0 (q, \(J=273.1\) Hz,
CF₃), 123.5 (CH), 124.9 (q, 11=2.7 Hz, CH), 128.8 (C), 130.5 (2CH), 132.7 (2CH), 134.0 (q, 11=33.0 Hz, C), 138.6 (C), 156.3 (C), 160.6 (C) 179.6 (C=O); HRMS m/z (ESI) positive ion, calculated for C₁₆H₈F₃N₂O₂: [M+1]⁺ 317.0532; Found: 317.0532.

4-[(2-nitro-4-(trifluoromethyl)phenyl)ethynyl]benzonitrile (8o):

![Structure](image)

H-NMR (CDCl₃, 400 MHz): δ = 7.70 (s, 4H), 7.88-7.89 (m, 2H), 8.40 (ddd, 1H, 11=2.2 Hz, 11=1.5 Hz, 11=0.7 Hz); 13C-NMR (CDCl₃, 100.6 MHz): δ = 87.3 (C), 97.6 (C), 113.2 (C), 118.2 (CN), 121.4 (q, 11=1.0 Hz, C), 122.4 (q, 11=3.9 Hz, CH), 122.5 (q, 11=273.0 Hz, CF₃), 127.9 (C), 129.5 (q, 11=3.5 Hz, CH), 131.6 (q, 11=34.6 Hz, C), 132.3 (2CH), 132.7 (2CH), 135.5 (CH), 149.6 (C); HRMS m/z (ESI) positive ion, [M+1] 317.0532; Found: 317.0529.

**Synthesis of 1-nitroso-2-(phenylethynyl)benzene 9a**

2-Iodoaniline (1.63 g, 7.45 mmol,) was dissolved in 22 ml of DCM. To this solution Oxone (8.95 g, 14.90 mmol) dissolved in 900 ml of water was added. The solution was stirred at room temperature until TLC monitoring indicated complete consumption of the starting material (2.5 h). After separation of the layers, the aqueous layer was extracted with DCM twice. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 99/1) afforded the 1-iodo-2-nitrosobenzene (0.500 g, 29%). To a solution of 1-iodo-2-nitrosobenzene (0.350 g, 1.50 mmol) in DMF (2.0 mL) was added Et₃N (2.0 mL), phenyacetylene (0.183 g, 1.80 mmol), Pd(PPh₃)₂Cl₂ (0.021 g, 0.03 mmol) and CuI (0.006 g, 0.03 mmol). After 1 h of stirring at 80 °C under N₂, 200 mL of HCl 1 M and 200 mL of CH₂Cl₂ were added. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with water, dried over sodium sulfate, filtered and concentrated. Purification of the residue by flash chromatography (eluent: hexane/EtOAc = 95:5) afforded 9a (0.124 g, 40% yield):

**1-iodo-2-nitrosobenzene**

H-NMR (Acetone-d₆, 400 MHz): δ = 6.23 (dd, 1H, 11=8.0 Hz, 11=1.7 Hz), 7.48 (td, 1H, 11=7.5 Hz, 11=1.4 Hz), 7.57 (td, 1H, 11=7.5 Hz, 11=1.5 Hz), 8.43 (dd, 1H, 11=7.8 Hz, 11=1.2 Hz); 13C-NMR
(Acetone-d6, 100.6 MHz): $\delta = 109.4$ (CH), 109.7 (C), 129.6 (CH), 138.4 (CH), 142.6 (CH), 163.7 (C); HRMS m/z (ESI) positive ion, calculated for C$_6$H$_4$INO: [M+1]$^+$ 233.9416; Found: 233.9490

9a

$^1$H-NMR (Acetone-d6, 400 MHz): $\delta = 6.59$-6.73 (m, 1H), 7.11-7.15 (m, 1H), 7.26-7.28 (m, 1H), 7.33-7.38 (m, 4H), 7.51-7.53 (m, 2H); $^{13}$C-NMR (CDCl$_3$, 100.6 MHz): $\delta = 85.9$ (C), 94.7 (C), 114.4 (CH), 118.0 (CH), 128.2 (CH), 128.4 (2CH), 129.7 (CH), 131.5 (2CH), 132.1 (CH), 133.0 (C), 133.8 (C), 147.8 (C); HRMS m/z (ESI) positive ion, calculated for C$_{14}$H$_{10}$NO: [M+1]$^+$ 208.0762; Found: 208.0802.

3. References


6e
1-iodo-2-nitrosobenzene
1-iodo-2-nitrosobenzene