Supporting Information

Synthesis of multiply substituted 1,6-dihydropyridines through Cu(I)-catalyzed 6-endo cyclization

Haruki Mizoguchi¹, Ryo Watanabe,¹ Shintaro Minami¹, Hideaki Oikawa¹ and Hiroki Oguri¹,²*

¹Division of Chemistry, Graduate School of Science, Hokkaido University, North 10, West 8, Kita-ku, Sapporo 060-0810, Japan
²JST, PRESTO, 4-1-8 Honcho, Kawaguchi, Saitama, 332-0012, Japan

*Corresponding Author: oguri@sci.hokudai.ac.jp

Table of contents

S2: General Methods & Materials.

S3-S9: Synthesis of N-propargylenamines.

S11-S17: Cu(I)-catalyzed Cyclization of N-propargylenamine

S18-S19: Cu(I)-catalyzed cyclization of a deuterium labeled N-propargylenamine

S19: References

S20-S66: The ¹H, ¹³C-NMR spectra of synthetic compounds.
General Methods

All reactions were performed under a nitrogen atmosphere unless otherwise specified. Microwave reactions were performed using a Biotage Initiator. NMR spectra were recorded on JEOL JNM-ECP 300 (\(^1\text{H}/300\text{ MHz}, \ ^{13}\text{C}/75\text{ MHz}\)) spectrometer, JEOL JNM-ECX 400 (\(^1\text{H}/400\text{ MHz}, \ ^{13}\text{C}/100\text{ MHz}\)) spectrometer, JEOL JNM-ECX 600 (\(^1\text{H}/600\text{ MHz}, \ ^{13}\text{C}/150\text{ MHz}\)) spectrometer and Bruker VSP 500 (\(^1\text{H}/500\text{ MHz}, \ ^{13}\text{C}/125\text{ MHz}\)) spectrometer. Chemical Shifts are reported in δ (ppm) using chloroform, acetonitrile as an internal standard of δ 7.26, 1.94, and 77.16, 118.26 for \(^1\text{H}\) and \(^{13}\text{C}\)-NMR, respectively. Data for \(^1\text{H}\)-NMR are reported as follows: chemical shift (number of hydrogens, multiplicity, coupling constant). Multiplicity is abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet), br (broad). ESI-Mass spectra were recorded on JEOL AccuTOF LC-Plus JMS-T100. The medium pressure liquid chromatography (MPLC) purifications were performed on a YAMAZEN YFLC-AI-580. Where necessary, solvents were distilled from appropriate drying agents prior to use. Reactions were monitored by thin layer chromatography using Merck Millipore TLC Silica gel F\(_{254}\) plates (0.25 mm) which were visualized using UV light, \(p\)-anisaldehyde stain and PMS stain. Flash column chromatography was performed using Kanto Silica Gel 60N.

Materials

Commercial solvents and reagents were used as received with the following exceptions. The cationic Cu(I) complex, [Cu(BINAP)(MeCN)]PF\(_6\), [Cu(dppf)(MeCN)]PF\(_6\), were prepared with modified protocol reported by Kim and co-workers\(^1\) and purified by precipitation from CH\(_2\)Cl\(_2\)/Et\(_2\)O=1/1 solution. [Cu(Xantphos)(MeCN)]PF\(_6\)^2, and (S)-4-benzyl-3-propioloyloxazolidin-2-one\(^3\) were prepared by applying reported protocols.
Synthesis of \(N\)-propargylenamines

**Methyl 3-(benzyl(prop-2-yn-1-yl)amino)propanoate (4)**

A solution of benzyl amine \(\text{3} (1.83 \text{ ml, 16.8 mmol})\) and methyl acrylate \((1.66 \text{ ml, 18.5 mmol})\) in MeOH \((5.0 \text{ ml})\) was stirred at \(65 \degree \text{C}\) for \(10\) min under microwave irradiation. After concentration of the mixture \textit{in vacuo}, the residue was purified by silica-gel chromatography to afford methyl 3-(benzylamino)propanoate \(\text{S1} (2.68 \text{ g, 13.9 mmol, 83%})\).

A solution of secondary amine \(\text{S1} (6.43 \text{ g, 33.3 mmol})\), propargyl bromide \((3.16 \text{ ml, 36.6 mmol})\), \(\text{K}_2\text{CO}_3 (9.20 \text{ g, 66.6 mmol})\), and \(\text{Et}_3\text{N (4.64 ml, 33.3 mmol)}\) in acetonitrile \((133 \text{ ml})\) was stirred at \(70 \degree \text{C}\) for \(16\) h. The resulting mixture was then treated with another portion of propargyl bromide \((1.44 \text{ ml, 16.7 mmol})\). After being stirred at \(85 \degree \text{C}\) for \(6\) h, the mixture was concentrated \textit{in vacuo} and then added with EtOAc and \(\text{H}_2\text{O}\). Organic phase was washed with water, brine and the dried over \(\text{Na}_2\text{SO}_4\). After concentration, the residue was purified by silica-gel chromatography to afford tertiary amine \(\text{4} (5.78 \text{ g, 25.0 mmol, 75%})\).

\(\text{4} : ^1\text{H-NMR (500 MHz, CDCl}_3\): } \delta 7.37-7.20 \text{ (5H, m), 3.68 (3H, s), 3.65 (2H, s), 3.32 (2H, d, } J = 2.2 \text{ Hz), 2.91 (2H, t, } J = 6.9 \text{ Hz), 2.53 (2H, t, } J = 6.9 \text{ Hz), 2.24 (1H, t, } J = 2.2 \text{ Hz); } ^{13}\text{C-NMR (125 MHz, CDCl}_3\): } \delta 172.92, 138.55, 129.14, 128.43, 127.35, 78.32, 73.47, 57.79, 51.74, 49.15, 41.44, 33.27; \text{HRMS (ESI, m/z): } [\text{M+H}^+] \text{ calcd. for C}_{14}\text{H}_{18}\text{NO}_2 232.1332; \text{found 232.1330.}

The \(^1\text{H-NMR and }^{13}\text{C-NMR spectra of 4 are shown in Figure S1 and S2.}\)

**(E)-Methyl 3-(benzyl(prop-2-yn-1-yl)amino)acrylate (1a)**

\(\text{4} \xrightarrow{\text{E}-\text{CO}_2\text{Me}} \text{1a}\)

\(\text{CF}_3\text{CH}_2\text{OH, 1,2-dichloroethane}\)
A solution of amine 4 (1.08 g, 4.67 mmol) and methyl propiolate (0.91 ml, 10.2 mmol) in 1,2-dichloroethane/2,2,2-trifluoroethanol = 1/1 (24 ml) was stirred at r.t. for 14 h. The mixture was treated with saturated aqueous solution of NaHCO₃ and extracted with EtOAc. The combined organic extracts were washed with brine and dried over Na₂SO₄. The residue was concentrated in vacuo and purified by silica-gel chromatography to afford 1a (962 mg, 4.20 mmol, 90%).

1a: TLC Rf = 0.35 (Hex:AcOEt = 4:1); ¹H NMR (500 MHz, CDCl₃): δ 7.60 (1H, d, J = 13.1 Hz), 7.38-7.27 (3H, m), 7.24 (2H, d, J = 6.9 Hz), 4.83 (1H, d, J = 13.1 Hz), 4.41 (2H, s), 3.81 (2H, d, J = 2.2 Hz), 3.68 (3H, s), 2.30 (1H, t, J = 2.2 Hz); ¹³C-NMR (125 MHz, CDCl₃): 169.83, 151.42, 135.70, 128.98, 128.16, 127.81, 87.43, 73.67, 50.87; HR-MS (ESI, m/z): [M+H]+ calcd. For C₁₄H₁₆NO₂ 230.1176; found 230.1216.

The ¹H-NMR and ¹³C-NMR spectra of 1a are shown in Figure S3 and S4.

(E)-4-Benzyl-3-(3-((4-methoxybenzyl)(prop-2-yn-1-yl)amino)acryloyl)oxazolidin-2-one (1b)

A solution of N-(4-methoxybenzyl)prop-2-yn-1-amine S2 (858 mg, 4.90 mmol) and (S)-4-benzyl-3-propioloxyoxazolidin-2-one (1.12 g, 4.90 mmol) in CH₂Cl₂ (16 ml) was stirred at r.t. for 1.5 h. The residue was concentrated in vacuo and purified by silica-gel chromatography to afford 1b (1.91 g, 4.72 mmol, 96%).

1b: ¹H-NMR (500 MHz, CDCl₃): δ 7.89 (1H, d, J = 12.6 Hz), 7.33 (2H, t, J = 7.3 Hz), 7.29-7.18 (5H, m), 6.89 (2H, m), 6.40 (1H, br-d, J = 12.6 Hz), 4.75 (1H, m), 4.45 (2H, s), 4.14 (1H, dd, J = 16.4, 8.8 Hz), 4.11 (1H, dd, J = 8.8, 3.2 Hz), 3.89 (2H, br-s), 3.81 (3H, s), 3.37 (1H, dd, J = 13.2, 3.2 Hz), 2.78 (1H, dd, J = 13.2, 9.8 Hz), 2.35 (1H, br-s); ¹³C-NMR (125 MHz, CDCl₃): δ 166.61, 159.74, 154.17, 153.13, 136.20, 129.68, 129.62, 128.98, 127.22, 114.43, 87.62, 65.86, 55.58, 55.45, 38.61; HRMS (ESI, m/z): [M+Na]+ calcd. for C₂₄H₂₄N₂O₄Na, 427.1628; found, 427.1641.

The ¹H-NMR and ¹³C-NMR spectra of 1b are shown in Figure S5 and S6.
(E)-N-Benzyl-N-(2-tosylvinyl)prop-2-yn-1-amine (1c)

A solution of amine 4 (62.4 mg, 0.270 mmol) and ethynyl p-tolylsulfone (58.6 mg, 0.330 mmol) in 1,2-dichloroethane/2,2,2-trifluoroethanol = 1/1 (540 μl) was stirred at r.t. for 12 h. The mixture was treated with saturated aqueous solution of NaHCO₃ at 0 °C and extracted with EtOAc. The combined organic extracts were washed with saturated aqueous solution of NaHCO₃, brine and dried over Na₂SO₄. The residue was concentrated and purified by silica-gel chromatography to afford 1c (70.1 mg, 0.215 mmol, 80%).

1c: TLC Rf = 0.61 (Hex:AcOEt = 1:1); ¹H NMR (500 MHz, CDCl₃): δ 7.74 (2H, d, J = 8.2 Hz), 7.50 (1H, d, J = 12.9 Hz), 7.37-7.29 (3H, m), 7.27 (2H, d, J = 8.2 Hz), 7.23-7.19 (2H, m), 5.20 (1H, d, J = 12.9 Hz), 4.39 (2H, s), 3.77 (2H, s), 2.41 (2H, s), 2.30 (1H, s); ¹³C NMR (125 MHz, CDCl₃): 149.19, 142.64, 141.68, 135.00, 129.61, 129.07, 128.37, 127.84, 126.51, 96.64, 76.72, 74.32, 21.61; HRMS (ESI, m/z): [M+Na]+ calcd. for C₁₉H₁₉NO₂SNa 348.1028, found 348.1044.

The ¹H-NMR and ¹³C-NMR spectra of 1c are shown in Figure S7 and S8.

(E)-3-(benzyl(prop-2-yn-1-yl)amino)-1-phenylprop-2-en-1-one (1d)

A mixture of amine 4 (1.77 g, 7.65 mmol) and 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-one (5) (2.32 g, 11.5 mmol) in 1,2-dichloroethane/2,2,2-trifluoroethanol=1/1 (26 ml) was stirred at 45 °C for 10 h 40 min. After concentrated in vacuo, the residue was purified by silica-gel chromatography to afford 1d (1.93 g, 7.01 mmol, 92%).
1d: $^1$H-NMR (500 MHz, CDCl$_3$): δ 7.95 (1H, d, $J = 12.6$ Hz), 7.89 (2H, d, $J = 7.3$ Hz), 7.49-7.45 (1H, m), 7.44-7.34 (4H, m), 7.35-7.31 (1H, m), 7.30-7.26 (2H, m), 6.02 (1H, d, $J = 12.6$ Hz), 4.54 (2H, s), 3.93 (2H, br-s), 2.36 (1H, s); $^{13}$C-NMR (125 MHz, CDCl$_3$): δ 189.28, 152.59, 140.13, 135.24, 131.34, 129.01, 128.27, 127.83, 127.71, 94.55, 76.99, 74.08; HRMS (ESI, m/z): [M+H]$^+$ calcd. for C$_{19}$H$_{18}$NO, 276.1383; found, 276.1385.

The $^1$H-NMR and $^{13}$C-NMR spectra of 1d are shown in Figure S9 and S10.

Methyl (E)-3-(benzyl(prop-2-yn-1-yl)amino)but-2-enoate (1e)

To a solution of N-benzylprop-2-yn-1-amine 6 (475 mg, 3.27 mmol) and methyl acetoacetate (0.705 ml, 6.54 mmol) in benzene (8.8 ml) was added p-toluenesulfonic acid monohydrate (37.3 mg, 0.196 mmol) and stirred at 95 °C for 12 h using a Dean - Stark apparatus. After cooled to room temperature, the mixture was washed with aqueous solution of 1N NaOH, water and brine, dried over Na$_2$SO$_4$. After filtration, the residue was concentrated in vacuo and purified by silica-gel chromatography to afford 1e (318 mg, 1.31 mmol, 40%).

1e: TLC $R_f$ = 0.60 (Hex:AcOEt = 1:1); $^1$H-NMR (500 MHz, CDCl$_3$): δ 7.34 (2H, t, $J = 7.3$ Hz), 7.28 (1H, t, $J = 7.3$ Hz), 7.18 (2H, d, $J = 7.3$ Hz), 4.92 (1H, s), 4.53 (2H, s), 3.93 (2H, d, $J = 2.2$ Hz), 3.63 (3H, s), 2.56 (3H, s), 2.28(1H, t, $J = 2.2$ Hz); $^{13}$C-NMR (125 MHz, CDCl$_3$): 169.41, 160.38, 136.70, 128.93, 127.67, 126.82, 87.46, 78.24, 73.04, 53.05, 50.38, 39.35, 15.60; HR-MS (ESI, m/z): [M+H]$^+$ calcd. for C$_{15}$H$_{18}$NO$_2$ 244.1332, found 244.1357.

The $^1$H-NMR and $^{13}$C-NMR spectra of 1e are shown in Figure S11 and S12.
3-(benzyl(prop-2-yn-1-yl)amino)cyclohex-2-en-1-one (1f)

To a solution of benzyl amine (4.26 ml, 39.0 mmol) in toluene (6.3 ml) was added propargyl bromide (0.560 ml, 6.50 mmol) and stirred at r.t. for 14 h. After concentrated in vacuo, the residue was purified by silica-gel chromatography to afford 6 (839 mg, 5.78 mmol, 89%).

To a solution of amine 6 (145 mg, 1.00 mmol) in benzene (10 ml) was added 1,3-cyclohexanedione (178 mg, 1.60 mmol) and p-toluenesulfonic acid monohydrate (11.4 mg, 0.06 mmol) and heated under reflux for 12 h using a Dean - Stark apparatus. After cooled to room temperature, the mixture was washed with aqueous solution of 1M NaOH and brine, dried over Na2SO4. The residue was concentrated in vacuo and purified by silica-gel chromatography to afford 1f (109 mg, 0.455 mmol, 46%).

1f: TLC Rf = 0.20 (Hex:AcOEt = 1:5); 1H-NMR (500 MHz, CDCl3): δ 7.38-7.33 (2H, m), 7.32-7.27 (1H, m), 7.18 (2H, d, J = 7.9 Hz), 5.41 (1H, s), 4.56 (2H, s), 3.97 (2H, d, J = 2.2 Hz), 2.55 (2H, m, J = 6.3 Hz), 2.39-2.30 (2H, m), 2.31 (1H, s), 2.05-1.99 (2H, m); 13C NMR (125 MHz, CDCl3): 197.62, 164.56, 136.15, 129.10, 127.95, 126.77, 101.21, 77.78, 73.60, 53.31, 39.53, 35.88, 27.10, 22.37; HRMS (ESI, m/z): calcd. for C16H18NO [M+H]+ 240.1383, found 240.1388.

The 1H-NMR and 13C-NMR spectra of 1f are shown in Figure S13 and S14.

Methyl (E)-3-(benzyl(3-phenylprop-2-yn-1-yl)amino)acrylate (1g)

To a solution of benzyl amine (4.26 ml, 39.0 mmol) in toluene (6.3 ml) was added propargyl bromide (0.560 ml, 6.50 mmol) and stirred at r.t. for 14 h. After concentrated in vacuo, the residue was purified by silica-gel chromatography to afford 6 (839 mg, 5.78 mmol, 89%).

To a solution of amine 6 (145 mg, 1.00 mmol) in benzene (10 ml) was added 1,3-cyclohexanedione (178 mg, 1.60 mmol) and p-toluenesulfonic acid monohydrate (11.4 mg, 0.06 mmol) and heated under reflux for 12 h using a Dean - Stark apparatus. After cooled to room temperature, the mixture was washed with aqueous solution of 1M NaOH and brine, dried over Na2SO4. The residue was concentrated in vacuo and purified by silica-gel chromatography to afford 1f (109 mg, 0.455 mmol, 46%).

1f: TLC Rf = 0.20 (Hex:AcOEt = 1:5); 1H-NMR (500 MHz, CDCl3): δ 7.38-7.33 (2H, m), 7.32-7.27 (1H, m), 7.18 (2H, d, J = 7.9 Hz), 5.41 (1H, s), 4.56 (2H, s), 3.97 (2H, d, J = 2.2 Hz), 2.55 (2H, m, J = 6.3 Hz), 2.39-2.30 (2H, m), 2.31 (1H, s), 2.05-1.99 (2H, m); 13C NMR (125 MHz, CDCl3): 197.62, 164.56, 136.15, 129.10, 127.95, 126.77, 101.21, 77.78, 73.60, 53.31, 39.53, 35.88, 27.10, 22.37; HRMS (ESI, m/z): calcd. for C16H18NO [M+H]+ 240.1383, found 240.1388.

The 1H-NMR and 13C-NMR spectra of 1f are shown in Figure S13 and S14.
A mixture of amine 4 (762 mg, 3.29 mmol), Pd(PPh₃)₄ (87.7 mg, 0.076 mmol), CuI (43.4 mg, 0.228 mmol), Et₃N (0.530 ml, 3.80 mmol) and PhI (0.282 ml, 2.53 mmol) in MeCN (16.5 ml) was heated at 60 °C for 3 h. After concentrated in vacuo, the residue was purified by silica-gel chromatography to afford methyl 3-(benzyl(3-phenylprop-2-yn-1-yl)amino)propanoate S3 (867 mg).

To a solution of S3 (867 mg) in 1,2-dichloroethane/2,2,2-trifluoroethanol = 1/1 (14.7 ml) was added methyl propiolate (0.277 ml, 3.10 mmol) and stirred at r.t. for 12 h. The mixture was quenched with saturated aqueous solution of NaHCO₃ and extracted with EtOAc. The combined organic extracts were washed with brine and dried over Na₂SO₄. After concentration in vacuo, the residue was purified by silica-gel chromatography to afford 1g (775 mg, 2.54 mmol, quant. for 2 steps).

1g: TLC Rf = 0.35 (Hex:AcOEt = 4:1); ¹H-NMR (500 MHz, CDCl₃): δ 7.68 (1H, d, J = 13.2 Hz), 7.43-7.26 (10H, m), 4.88 (1H, d, J = 13.2 Hz), 4.47 (2H, s), 4.05 (2H, br-s), 3.69 (3H, s); ¹³C-NMR (75 MHz, CDCl₃): 169.85, 151.49, 135.85, 131.79, 128.85, 128.36, 127.97, 127.69, 122.33, 86.99, 85.45, 82.72, 55.68, 50.73, 40.81; HRMS (ESI, m/z): calcd. for C₂₀H₂₀NO₂ [M+H]⁺ 306.1489, found 306.1489.

The ¹H-NMR and ¹³C-NMR spectra of 1g are shown in Figure S15 and S16.

Dimethyl 3,3’-(hexa-2,4-diyne-1,6-diylbis(benzylazanediyl))(2E,2’E)-diacrylate (1h)

To a solution of amine 4 (565 mg, 2.44 mmol) in acetone (2.0 ml) was added a solution of preliminary mixed CuCl (21.4 mg, 0.216 mmol) and N,N,N’,N’-tetramethylethylenediamine (11 μl, 0.072 mmol) in acetone (2.0 ml) and stirred at r.t. for 12 h under O₂ atmosphere. After concentrated in vacuo, the residue was purified by silica-gel column chromatography to afford S4 (553 mg, 1.20 mmol, 98%).

To a solution of amine S4 (530 mg, 1.15 mmol) in 1,2-dichloroethane/2,2,2-trifluoroethanol=1/1 (9.0 ml) was added methyl propiolate (383 μl, 4.60 mmol) and stirred at r.t. for 19 h. After concentrated in vacuo, the residue was purified by silica-gel chromatography to afford 1h (423 mg, 0.927 mmol, 81%).
**1h**: $^1$H-NMR (500 MHz, CDCl$_3$): $\delta$ 7.56 (2H, d, $J = 12.9$ Hz), 7.38-7.28 (6H, m), 7.22 (4H, d, $J = 6.9$ Hz), 4.83 (2H, d, $J = 12.9$ Hz), 4.39 (4H, s), 3.85 (4H, s), 3.68 (6H, s); $^{13}$C-NMR (125 MHz, CDCl$_3$): $\delta$ 169.66, 151.28, 135.45, 129.04, 128.29, 127.87, 87.94, 72.81, 69.18, 56.25, 50.90, 40.08; HRMS (ESI, m/z): [M+H]$^+$ calcd. for C$_{28}$H$_{29}$N$_2$O$_4$, 457.2122; found, 457.2117.

The $^1$H-NMR and $^{13}$C-NMR spectra of 1h are shown in Figure S17 and S18.

**Methyl (E)-3-(benzyl(2-methylbut-3-yn-2-yl)amino)acrylate (1i)**

![Reaction scheme](image)

To a solution of amine S5$^5$ (182 mg, 1.25 mmol) in 1,2-dichloroethane/2,2,2-trifluoroethanol=1/1 (6 ml) was added methyl propiolate (209 $\mu$l, 2.51 mmol) and stirred at 45 °C for 19 h. After concentrated in vacuo, the residue was purified by silica-gel column chromatography to afford 1i (263 mg, 0.970 mmol, 78%).

**1i**: $^1$H-NMR (500 MHz, CDCl$_3$): $\delta$ 8.06 (1H, d, $J = 12.9$ Hz), 7.30 (2H, t, $J = 7.6$ Hz), 7.23 (1H, t, $J = 7.6$ Hz), 7.20 (2H, d, $J = 7.6$ Hz), 4.54 (1H, d, $J = 12.9$ Hz), 4.52 (2H, s), 3.61 (3H, s), 2.47 (1H, s), 1.64 (6H, s); $^{13}$C-NMR (125 MHz, CDCl$_3$): $\delta$ 169.97, 147.59, 137.01, 128.7, 127.1, 126.24, 88.45, 85.86, 72.94, 56.95, 50.69, 50.42, 29.57; HRMS (ESI, m/z): [M+H]$^+$ calcd. for C$_{16}$H$_{20}$NO$_2$, 258.1489; found, 258.1482.

The $^1$H-NMR and $^{13}$C-NMR spectra of 1i are shown in Figure S19 and S20.

**Methyl (E)-3-(benzyl(but-2-yn-1-yl)amino)-3-phenylacrylate (1j)**

![Reaction scheme](image)

To a solution of N-benzylbut-2-yn-1-amine S6 (195 mg, 1.23 mmol) in methanol (1.2 ml) was added methyl 3-phenylpropiolate (0.19 ml, 1.29 mmol) at room temperature and then stirred at
70 °C for 16 h. After concentrated in vacuo, the residue was purified by silica-gel chromatography to afford **1j** (176 mg, 0.551 mmol, 45%).

**1j**: TLC Rf = 0.38 (Hex:AcOEt = 2:1); $^1$H-NMR (500 MHz, CDCl$_3$): δ 7.43-7.40 (3H, m), 7.33-7.31 (4H, m), 7.29-7.25 (1H, m), 7.23 (1H, br-d, $J$ = 7.4 Hz), 5.13 (1H, s), 4.33 (2H, br-s), 3.74 (2H, br-s), 3.48 (3H, s), 1.84 (3H, t, $J$ = 2.2 Hz); $^{13}$C-NMR (75 MHz, CDCl$_3$): 167.97, 162.56, 136.75, 136.08, 128.73, 128.58, 128.48, 128.23, 127.40, 89.75, 80.78, 73.36, 52.63, 50.20, 39.34, 3.52

$^1$H-NMR and $^{13}$C-NMR spectra of **1j** are shown in Figure S21 and S22.
**Cu(I)-catalyzed Cyclization of N-propargylenamine**

**General procedure**
A solution of N-propargylenamine (0.200 mmol) and [Cu(Xantphos)(MeCN)]PF$_6$ (0.020 mmol) in CH$_2$Cl$_2$ (2.0 ml) was stirred at r.t. for several hours. The reaction mixture was then treated with 1,10-phenanthroline (0.020 mmol) to deactivate the copper catalyst. After concentration *in vacuo*, 4-nitrobenzonitrile (0.200 mmol) was added as internal standard for $^1$H-NMR. Yield of desired product was calculated based on the value of integral for a signal of 4-nitrobenzonitrile and that of desired product. The $^1$H-NMR and $^{13}$C-NMR of the internal standard are shown in Figure S45 and S46.

**Methyl 1-benzyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (2a)**

![Reaction scheme](image)

A solution of N-propargylenamine 1a (251 mg, 1.09 mmol) and [Cu(Xantphos)(MeCN)]PF$_6$ (90.6 mg, 0.109 mmol) in CH$_2$Cl$_2$ (11 ml) was stirred at r.t. for 40 min. The reaction mixture was then treated with 1,10-phenanthroline (25.2 mg, 0.140 mmol) to deactivate the copper catalyst. After concentrated *in vacuo*, 4-nitrobenzonitrile (162 mg, 1.09 mmol) was added. Due to instability of 2a to silica-gel chromatography, the yield of 2a (98%) was calculated based on $^1$H-NMR.

2a: TLC $R_f$ = 0.45 (Hex:Acetone = 4:1); $^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ 7.43-7.28 (6H, m), 6.30 (1H, m), 4.96 (1H, dt, $J$ = 10.1, 3.1 Hz), 4.20 (2H, s), 4.01 (2H, dd, $J$ = 3.1, 1.9 Hz), 3.68 (3H, s); $^{13}$C-NMR (75 MHz, CDCl$_3$): 167.00, 147.94, 134.95, 128.92, 128.20, 127.89, 122.20, 109.85, 96.04, 60.08, 50.63, 47.98; HR-MS (ESI): calcd. for the corresponding pyridinium salt C$_{14}$H$_{14}$NO$_2$[M]$^+$ 228.1019, found 228.1019.

$^1$H-NMR and $^{13}$C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S23 and S24.
4-Benzyl-3-(1-(4-methoxybenzyl)-1,6-dihydropyridine-3-carbonyl)oxazolidin-2-one (2b)

A solution of \( N \)-propargylenamine \( 1b \) (63.7 mg, 0.170 mmol) and \([Cu(Xantphos)(MeCN)]PF_6\) (14.1 mg, 0.0170 mmol) in \( CH_2Cl_2 \) (1.7 ml) was stirred at r.t. for 180 min. The reaction mixture was then treated with 1,10-phenanthroline (3.1 mg, 0.017 mmol) to deactivate the copper catalyst. After concentration in vacuo, 4-nitrobenzonitrile (26.8 mg, 0.181 mmol) was added. Due to instability of \( 2b \) to silica-gel chromatography, the yield of \( 2b \) (84%) was calculated based on \(^1\)H-NMR.

\( 2b \): TLC \( R_f = 0.38 \) (Hex:AcOEt = 1:1); \(^1\)H-NMR (500 MHz, CDCl3): \( \delta \) 7.45 (1H, s), 7.32-7.17 (7H, m), 6.92 (2H, d, \( J = 8.5 \) Hz), 6.33 (1H, d, \( J = 10.4 \) Hz), 5.05 (1H, dt, \( J = 10.1, 3.2 \) Hz), 4.90 (1H, ddd, \( J = 17.0, 8.5, 3.5 \) Hz), 4.30-4.24 (2H, m), 4.18 (1H, d, \( J = 14.5 \) Hz), 4.12-4.06 (3H, m), 3.18 (3H, s), 3.26 (1H, dd, \( J = 13.6, 3.5 \) Hz), 2.83 (1H, dd, \( J = 13.6, 8.8 \) Hz); \(^{13}\)C NMR (125 MHz, CDCl3): 164.98, 159.78, 155.33, 152.49, 135.63, 129.59, 129.55, 128.73, 127.09, 125.84, 122.31, 114.42, 109.88, 98.58, 66.57, 60.38, 55.54, 55.37, 48.36, 37.89; HR-MS (ESI): calcd. for \( C_{24}H_{24}N_2O_4Na \) [M+Na]+ 427.1628, found 427.1565.

\(^1\)H-NMR and \(^{13}\)C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S25 and S26.

1-Benzyl-5-tosyl-1,2-dihydropyridine (2c)

A solution of \( N \)-propargylenamine \( 1c \) (50.2 mg, 0.154 mmol) and \([Cu(Xantphos)(MeCN)]PF_6\) (13.0 mg, 0.0157 mmol) in \( CH_2Cl_2 \) (1.6 ml) was stirred at r.t. for 4 h. The reaction mixture was treated with 1,10-phenanthroline (3.8 mg, 0.0211 mmol) to deactivate the copper catalyst. After concentration in vacuo, 4-nitrobenzonitrile (22.8 mg, 0.181 mmol) was added. The yield of \( 2c \)
(99%) was calculated based on $^1$H-NMR.

2c: TLC $R_f = 0.48$ (Hex:Acetone = 2:1); $^1$H-NMR (500 MHz, CDCl$_3$): $\delta$ 7.67 (2H, m), 7.32-7.18 (8H, m), 5.90 (1H, m), 4.90 (1H, dt, $J = 10.2, 3.2$ Hz), 4.13 (2H, s), 3.89 (2H, dd, $J = 3.2, 1.9$ Hz), 2.34 (3H, s); $^{13}$C-NMR (75 MHz, CDCl$_3$): 145.57, 142.48, 140.76, 134.35, 129.57, 128.93, 128.30, 127.92, 126.39, 119.35, 111.59, 104.29, 59.91, 47.77, 21.44; HR-MS (ESI): calcd. for the corresponding pyridinium salt C$_{19}$H$_{18}$NO$_2$S [M]$^+$ 324.1053, found 324.1091. $^1$H-NMR and $^{13}$C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S27 and S28.

(1-Benzyl-1,6-dihydropyridin-3-yl)(phenyl)methanone (2d)

![Diagram](image)

A solution of N-propargylenamine 1d (100 mg, 0.364 mmol) and [Cu(Xantphos)(MeCN)]PF$_6$ (30.2 mg, 0.0365 mmol) in 1,2-dichloroethane (3.6 ml) was stirred at 65 °C for 3 h. The reaction mixture was then treated with 1,10-phenanthroline (11.2 mg, 0.0621 mmol) to deactivate the copper catalyst. After concentration in vacuo, 4-nitrobenzonitrile (53.9 mg, 0.364 mmol) was added. The yield of 2d (93%) was calculated based on $^1$H-NMR.

2d: TLC $R_f = 0.33$ (Hex:AcOEt = 2:1); $^1$H-NMR (500 MHz, CDCl$_3$): $\delta$ 7.52-7.50 (2H, m), 7.40-7.33 (6H, m), 6.63 (1H, m), 5.14 (1H, dt, $J = 10.2, 3.3$ Hz), 4.19 (2H, s), 4.11 (2H, dd, $J = 3.3, 1.9$ Hz); $^{13}$C-NMR (125 MHz, CDCl$_3$): 190.18, 152.71, 140.40, 134.41, 129.88, 129.12, 128.49, 128.34, 128.12, 127.90, 122.25, 111.70, 107.35, 60.46, 48.79; HRMS (ESI): calcd. for C$_{19}$H$_{17}$NONa [M+Na]$^+$ 298.1202, found 298.1201. $^1$H-NMR and $^{13}$C-NMR spectra of the crude reaction mixture for 2d including the internal standard are shown in Figure S29 and S30.
Methyl 1-benzyl-2-methyl-1,6-dihydropyridine-3-carboxylate (2e)

A solution of N-propargylenamine 1e (48.0 mg, 0.197 mmol) and [Cu(Xantphos)(MeCN)]PF$_6$ (16.7 mg, 0.0202 mmol) in CH$_2$Cl$_2$ (2.0 ml) was stirred at r.t. for 2 h. The reaction mixture was then treated with 1,10-phenanthroline (4.7 mg, 0.0261 mmol) to deactivate the copper catalyst. After concentration in vacuo, 4-nitrobenzonitrile (29.2 mg, 0.197 mmol) was added. Yield of 2e (80%) was calculated based on $^1$H-NMR due to instability of 2e to silica-gel chromatography.

2e: TLC $R_f = 0.38$ (Hex:Acetone = 5:1); $^1$H-NMR (500 MHz, CDCl$_3$): $\delta$ 7.40-7.37 (2H, m), 7.32-7.24 (3H, m), 6.54 (1H, m), 5.00 (1H, dt, $J = 9.8, 3.7$ Hz), 4.50 (2H, s), 4.01 (2H, m), 3.70 (3H, s), 2.52 (3H, s); $^{13}$C-NMR (75 MHz, CDCl$_3$): 167.85, 157.65, 136.19, 128.96, 127.59, 126.46, 125.45, 107.19, 97.54, 54.44, 50.63, 50.57, 16.16; HR-MS (ESI): calcd. for C$_{15}$H$_{17}$NO$_2$Na [M+Na]$^+$ 266.1151, found 266.1120.

$^1$H-NMR and $^{13}$C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S31 and S32.

1-Benzyl-2,6,7,8-tetrahydroquinolin-5(1H)-one (2f)

A solution of N-propargylenamine 1f (138 mg, 0.578 mmol) and [Cu(Xantphos)(MeCN)]PF$_6$ (48.5 mg, 0.0586 mmol) in 1,2-dichloroethane (6.0 ml) was stirred at 65 °C for 2 h. The reaction mixture was treated with 1,10-phenanthroline (13.8 mg, 0.0767 mmol) to deactivate the copper catalyst.
After concentration in vacuo, 4-nitrobenzonitrile (85.6 mg, 0.578 mmol) was added. The yield of 2f (94%) was calculated based on 1H-NMR.

2f: TLC Rf = 0.36 (Hex:Acetone = 1:2); 1H-NMR (500 MHz, CDCl3): δ 7.37-7.21 (5H, m), 6.60 (1H, m), 5.08 (1H, dt, J = 10.1, 3.3 Hz), 4.41 (2H, s), 4.13 (2H, dd, J = 3.3, 1.7 Hz), 2.47 (2H, t, J = 6.3 Hz), 2.28 (2H, t, J = 6.3 Hz), 1.90 (2H, quin, J = 6.3 Hz); 13C-NMR (75 MHz, CDCl3): 191.24, 161.45, 135.25, 129.08, 127.81, 126.33, 121.06, 110.71, 106.32, 53.97, 51.41, 35.42, 26.28, 21.23; HR-MS (ESI): calcd. for C16H18NO [M+H]+ 240.1383, found 240.1382.

1H-NMR and 13C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S33 and S34.

Methyl 1-benzyl-4-phenyl-1,6-dihydropyridine-3-carboxylate (2g)

A solution of N-propargylenamine 1g (70.4 mg, 0.231 mmol) and [Cu(Xantphos)(MeCN)]PF6 (20.0 mg, 0.0241 mmol) in CH2Cl2 (2.3 ml) was stirred at r.t. for 110 min. The reaction mixture was then treated with 1,10-phenanthroline (4.14 mg, 0.0230 mmol) to deactivate the copper catalyst. After concentration in vacuo, 4-nitrobenzonitrile (28.7 mg, 0.194 mmol) was added. Yield of 2g (82%) was calculated based on 1H-NMR.

2g: TLC Rf = 0.45 (Hex:AcOEt = 4:1); 1H-NMR (500 MHz, CDCl3): δ 7.70 (1H, s), 7.42-7.37 (2H, m), 7.37-7.30 (3H, m), 7.30-7.21 (3H, m), 7.20-7.16 (2H, m), 4.91 (1H, t, J = 4.1 Hz), 4.32 (2H, s), 4.04 (2H, d, J = 4.1 Hz), 3.51 (3H, s); 13C-NMR (125 MHz, CDCl3): 166.67, 150.11, 141.49, 137.28, 135.06, 129.02, 128.30, 128.00, 127.45, 127.29, 126.67, 110.60, 98.13, 59.88, 50.41, 48.07; HR-MS (ESI): calcd. for C20H19NO2Na [M+Na]+ 328.1308, found 328.1311.

1H-NMR and 13C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S35 and S36.
Dimethyl 1,1'-dibenzyl-1,1',6,6'-tetrahydro-[4,4'-bipyridine]-3,3'-dicarboxylate (2h)

A solution of \(N\)-propargylenamine \(1h\) (53.1 mg, 0.116 mmol) and \([Cu(Xantphos)(MeCN)]PF_6\) (19.2 mg, 0.0232 mmol) in \(CH_2Cl_2\) (1.2 ml) was stirred at r.t. for 3 h. The reaction mixture was then treated with 1,10-phenanthroline (4.18 mg, 0.0232 mmol) to deactivate the copper catalyst. After concentration \textit{in vacuo}, 4-nitrobenzonitrile (17.9 mg, 0.121 mmol) was added. The yield of 2h (75%) was calculated based on \(^1\)H-NMR.

2h: TLC Rf = 0.28 (Hex:AcOEt = 1:1); \(^1\)H-NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.50 (2H, s), 7.39-7.27 (10H, m), 4.78 (2H, t, \(J = 3.5\) Hz), 4.28 (2H, br-d, \(J = 14.8\) Hz), 4.16 (2H, br-d, \(J = 14.8\) Hz), 4.02 (2H, br-d, \(J = 14.2\) Hz), 3.95 (2H, br-d, \(J = 14.2\) Hz), 3.59 (6H, s); \(^13\)C-NMR (125 MHz, CDCl\(_3\)): 166.48, 147.83, 137.24, 135.39, 128.91, 128.08, 127.97, 108.67, 98.98, 59.96, 50.38, 48.17; HR-MS (ESI): calcd. for C\(_{28}\)H\(_{28}\)N\(_2\)O\(_4\)Na [M+Na]\(^+\) 479.1898, found 479.1871.

\(^1\)H-NMR and \(^13\)C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S37 and S38.

Methyl 1-benzyl-6,6-dimethyl-1,6-dihydropyridine-3-carboxylate (2i)

A solution of \(N\)-propargylenamine \(1i\) (47.0 mg, 0.183 mmol) and \([Cu(Xantphos)(MeCN)]PF_6\) (15.7 mg, 0.0190 mmol) in 1,2-dichloroethane (1.8 ml) was stirred at 65 °C for 20 h. The reaction mixture was then treated with 1,10-phenanthroline (5.6 mg, 0.0311 mmol) to deactivate the copper catalyst. After concentration \textit{in vacuo}, 4-nitrobenzonitrile (27.7 mg, 0.187 mmol) was added. The yield of 2i (99%) was calculated based on \(^1\)H-NMR spectra. The crude mixture was purified by silica-gel chromatography to afford 2i (40.5 mg, 0.157 mmol, 86%).
2i: TLC 
Rf = 0.29 (Hex:AcOEt = 4:1); 1H-NMR (500 MHz, CDCl3): \( \delta 7.38-7.35 (2H, m), 7.31-7.25 (3H, m), 6.35 (1H, dd, J = 9.8, 1.3 Hz), 4.85 (1H, d, J = 9.8 Hz), 4.45 (2H, s), 3.68 (3H, s), 1.28 (6H, s); ^{13}C NMR (125 MHz, CDCl3): 167.11, 147.60, 138.74, 128.93, 127.69, 126.94, 120.46, 120.13, 97.70, 58.01, 53.35, 50.77, 28.59; HRMS (ESI, m/z): calcd. for C16H20NO2 [M+H]^+ 258.1489, found 258.1485.

1H-NMR and 13C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S39 and S40.

Methyl 1-benzyl-4-methyl-2-phenyl-1,6-dihydropyridine-3-carboxylate (2j)

To a solution of N-propargylenamine 1j (70.4 mg, 0.221 mmol) and [Cu(Xantphos)(MeCN)]PF6 (18.3 mg, 0.022 mmol) in 1,2-dichloroethane (2.2 ml) was stirred at r.t. for 3 h. The reaction mixture was then treated with 1,10-phenanthroline (4.9 mg, 0.0272 mmol) to deactivate the copper catalyst. After concentration in vacuo, 4-nitrobenzonitrile (32.7 mg, 0.221 mmol) was added. Yield of 2j (89%) was calculated based on 1H-NMR.

2j: TLC 
Rf = 0.50 (Hex:AcOEt = 2:1); 1H-NMR (500 MHz, CDCl3): \( \delta 7.36-7.16 (10H, m), 4.81-4.77 (1H, m), 4.11 (2H, s), 3.93-3.91 (2H, m), 3.22 (3H, s), 2.06-2.03 (3H, m); ^{13}C NMR (75 MHz, CDCl3): 168.82, 156.49, 137.81, 136.83, 133.66, 128.85, 128.69, 128.58, 128.26, 127.38, 127.05, 106.83, 105.17, 55.21, 50.20, 48.85, 21.01.

1H-NMR and 13C-NMR spectra of the crude reaction mixture including the internal standard are shown in Figure S41 and S42.
Cu-catalyzed cyclization of a deuterium labeled \( N \)-propargylenamine

\( N \)-Benzyprop-2-yn-1-amine-d1 (S9)

![Chemical Structure](image)

To a solution of benzyl amine (2.34 ml, 21.4 mmol) in toluene (4.2 ml) was added 1-bromo-2-butyne (0.380 ml, 4.34 mmol) and stirred at r.t. for 14 h. After concentrated \textit{in vacuo}, the residue was purified by silica-gel chromatography to afford S6 (636 mg, 3.99 mmol, 92%). The amine S6 (301 mg, 1.89 mmol) was then dissolved in CH\textsubscript{3}OD (3.5 ml) and stirred at r.t. for 1 h, and after concentrated \textit{in vacuo}, treated again with CH\textsubscript{3}OD (3.0 ml) at r.t. for further 1 h. Removal of the solvent \textit{in vacuo} afforded S6-D (240 mg, 1.50 mmol, 79%).

Methyl 1-benzyl-4-methyl-2-phenyl-1,6-dihydropyridine-3-carboxylate-5-d1 (2j-D)

![Chemical Structure](image)

To a solution of benzyl amine S6-D (274 mg, 1.71 mmol) in CD\textsubscript{3}OD (1.6 ml) was added methyl 3-phenylpropiolate (0.260 ml, 1.76 mmol) and stirred at 70 °C for 10 h. After concentrated \textit{in vacuo}, the residue was purified by silica-gel chromatography to afford 1j-D (482 mg, 1.51 mmol, 88%). Deuterium incorporation (80%) at C3 proton was determined based on \textsuperscript{1}H-NMR analysis.

A solution of \( N \)-propargylenamine 1j-D (70.1 mg, 0.219 mmol) and [Cu(Xantphos)(MeCN)]PF\textsubscript{6} (18.3 mg, 0.0219 mmol) in dichloromethane (2.2 ml) was stirred at r.t. for 3 h. The reaction mixture was then treated with 1,10-phenanthroline (5.0 mg, 0.0277 mmol) to deactivate the copper catalyst.
After concentration in vacuo, 4-nitrobenzonitrile (32.4 mg, 0.219 mmol) was added as an internal standard. Yield of 2j-D (83%) as well as percentage of deuteration of C5 proton (66%) were calculated based on 1H-NMR.

1H-NMR spectra of 1j-D and the crude reaction mixture of 2j-D including the internal standard are shown in Figure S43 and S44.

References


The $^1$H, $^{13}$C-NMR spectra of synthetic compounds.
Figure S1. A $^1$H-NMR spectrum of 4 in CDCl$_3$. 
Figure S2. A $^{13}$C-NMR spectrum of 4 in CDCl$_3$. 
Figure S3. A $^1$H-NMR spectrum of 1a in CDCl$_3$. 
Figure S4. A $^{13}$C-NMR spectrum of 1a in CDCl$_3$. 
Figure S5. A $^1$H-NMR spectrum of 1b in CDCl$_3$. 
Figure S6. A $^{13}$C-NMR spectrum of 1b in CDCl$_3$. 
Figure S7. A $^1$H-NMR spectrum of 1c in CDCl$_3$. 
Figure S8. A $^{13}$C-NMR spectrum of 1c in CDCl$_3$. 
Figure S9. A $^1$H-NMR spectrum of 1d in CDCl$_3$. 
Figure S10. A $^{13}$C-NMR spectrum of 1d in CDCl$_3$. 

Figure S11. A $^1$H-NMR spectrum of 1e in CDCl$_3$. 
Figure S12. A $^{13}$C-NMR spectrum of 1e in CDCl$_3$. 
Figure S13. A $^1$H-NMR spectrum of 1f in CDCl$_3$. 
Figure S14. A $^{13}$C-NMR spectrum of 1f in CDCl$_3$. 
Figure S15. A $^1$H-NMR spectrum of 1g in CDCl$_3$. 
Figure S16. A $^{13}$C-NMR spectrum of 1g in CDCl$_3$. 
Figure S17. A $^1$H-NMR spectrum of 1h in CDCl$_3$. 
Figure S18. A $^{13}$C-NMR spectrum of 1h in CDCl$_3$. 
Figure S19. A $^1$H-NMR spectrum of 1i in CDCl$_3$. 
Figure S20. A $^{13}\text{C}$-NMR spectrum of 1i in CDCl$_3$. 
Figure S21. A $^1$H-NMR spectrum of 1j in CDCl$_3$. 
Figure S22. A $^{13}$C-NMR spectrum of 1j in CDCl$_3$. 
Figure S23. A $^1$H-NMR spectrum for the crude mixture of 2a in CDCl$_3$. 
Figure S24. A $^{13}$C-NMR spectrum for the crude mixture of 2a in CDCl$_3$. 
Figure S25. A $^1$H-NMR spectrum for the crude mixture of 2b in CDCl$_3$. 
Figure S26. A $^{13}$C-NMR spectrum for the crude mixture of 2b in CDCl$_3$. 
Figure S27. A $^1$H-NMR spectrum for the crude mixture of 2c in CDCl$_3$. 
Figure S28. A $^{13}$C-NMR spectrum for the crude mixture of 2c in CDCl$_3$. 
Figure S29. A $^1$H-NMR spectrum for the crude mixture of 2d in CDCl$_3$. 
Figure S30. A $^{13}$C-NMR spectrum for the crude mixture of 2d in CDCl$_3$. 

S50
Figure S31. A $^1$H-NMR spectrum for the crude mixture of 2e in CDCl$_3$. 

S51
Figure S32. A $^{13}$C-NMR spectrum for the crude mixture of 2e in CDCl$_3$. 
Figure S33. A $^1$H-NMR spectrum for the crude mixture of 2f in CDCl$_3$. 
Figure S34. A $^{13}$C-NMR spectrum for the crude mixture of 2f in CDCl$_3$. 
Figure S35. A $^1$H-NMR spectrum for the crude mixture of 2g in CDCl$_3$. 
Figure S36. A $^{13}$C-NMR spectrum for the crude mixture of 2g in CDCl$_3$. 
Figure S37. A $^1$H-NMR spectrum for the crude mixture of 2h in CDCl$_3$. 
Figure S38. A $^{13}$C-NMR spectrum for the crude mixture of 2h in CDCl$_3$. 
Figure S39. A $^1$H-NMR spectrum of 2i in CDCl$_3$. 
Figure S40. A $^{13}$C-NMR spectrum of 2i in CDCl$_3$. 
Figure S41. A $^1$H-NMR spectrum for the crude mixture of 2j in CDCl$_3$. 

S61
Figure S42. A $^{13}$C-NMR spectrum for the crude mixture of 2j in CDCl$_3$. 
Figure S43. A $^1$H-NMR spectrum of 1j-D in CDCl$_3$. 
Figure S44. A $^1$H-NMR spectrum for the crude mixture of 2j-D in CDCl$_3$. 
Figure S45. A $^1$H-NMR spectrum of 4-nitrobenzonitrile in CDCl$_3$. 
Figure S46. A $^{13}$C-NMR spectrum of 4-nitrobenzonitrile in CDCl$_3$. 