Sulfur-DMSO Promoted Oxidative Coupling of Active Methylhetarenes with Amines: Access to Amides

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General information

Reagents were obtained from commercial supplier and used without further purification. Analytical thin layer chromatography (TLC) was purchased from Merck KGaA (silica gel 60 F254). Visualization of the chromatogram was performed by UV light (254 nm) or phosphomolybdic acid or vanilline stains. Flash column chromatography was carried out using kieselgel 35-70 µm particle sized silica gel (230-400 mesh). NMR Chemical shifts are reported in (δ) ppm relative to tetramethylsilane (TMS) with the residual solvent as internal reference (CDCl3, δ 7.26 ppm, DMSO, δ 2.50 ppm for 1H). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration.

General procedure for the synthesis of amides 3

A mixture of methylhetarene 1 (1 mmol), amine 2 (1 mmol), sulfur (1.25 mmol, 40 mg) in DMSO (0.3 mL) in a 7 mL test tube closed with a rubber septum equipped with a deflated rubber balloon was heated at 120-150 ºC (see Schemes 1-3) for 16 h. Unless otherwise noted, the crude mixture was purified by column chromatography on silica gel (EtOAc:hexane or CH2Cl2:EtOAc) to provide the expected amide. The reactions catalyzed by FeCl2•4H2O, CoCl2•6H2O or NiCl2•6H2O was performed in the same manner with metallic salt added to the reaction mixture at the beginning. Similar procedure was applied for the synthesis of amides 7 and 9.

Characterizations of amide products 3, 7 and 9

N-Phenylquinoline-2-carboxamide (3aa)1

Purification of the crude mixture by column chromatography (eluent: dichloromethane) afforded the product (186 mg, 75%).

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$^1$H NMR (500 MHz, CDCl$_3$) δ 8.97 (broad s, 1H), 7.14 (d, $J = 8.4$ Hz, 1H), 7.08 (d, $J = 8.5$ Hz, 1H), 6.92 (d, $J = 8.5$ Hz, 1H), 6.66 – 6.59 (m, 3H), 6.56 – 6.52 (m, 1H), 6.40 – 6.36 (m, 1H), 6.21 – 6.14 (m, 2H), 5.93 (t, $J = 7.4$ Hz, 1H).

$^{13}$C {$^1$H} NMR (126 MHz, CDCl$_3$) δ 162.22, 149.75, 146.37, 137.89 (2C), 130.38, 129.75, 129.49, 129.19 (2C), 128.22, 127.89, 124.42, 119.85 (2C), 118.81.

$N$-Phenylpicolinamide (3ca)$^2$

![Structure of 3ca](image)

Purification of the crude mixture by column chromatography (eluent: heptane:EtOAc 7:3) afforded the product (93 mg, 47%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 10.04 (s, 1H), 8.62 (d, $J = 4.6$ Hz, 1H), 8.31 (d, $J = 7.6$ Hz, 1H), 7.92 (t, $J = 7.8$ Hz, 1H), 7.79 (d, $J = 8.1$ Hz, 2H), 7.52 – 7.47 (m, 1H), 7.39 (t, $J = 7.8$ Hz, 2H), 7.15 (t, $J = 7.2$ Hz, 1H).

$^{13}$C {$^1$H} NMR (100 MHz, CDCl$_3$) δ 162.06, 149.86, 148.03, 137.83, 137.75, 129.16 (2C), 126.53, 124.38, 122.46, 119.75 (2C).

$N$-Phenylisonicotinamide (3ba)$^3$

![Structure of 3ba](image)

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 1:1) afforded the product (169 mg, 85%).

$^1$H NMR (500 MHz, DMSO-d$_6$) δ 10.49 (s, 1H), 8.81 – 8.77 (m, 2H), 7.89 – 7.85 (m, 2H), 7.79 (d, $J = 7.9$ Hz, 2H), 7.38 (t, $J = 7.8$ Hz, 2H), 7.14 (t, $J = 7.4$ Hz, 1H).

$^{13}$C {$^1$H} NMR (126 MHz, DMSO-d$_6$) δ 163.96, 150.22 (2C), 141.95, 138.58, 128.67 (2C), 124.16, 121.55 (2C), 120.49 (2C).

$N$-(m-Tolyl)isonicotinamide (3bb)$^4$


Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 3:1) afforded the product (138 mg, 65%)

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.71 (broad s, 1H), 8.65 – 8.60 (m, 2H), 7.67 – 7.62 (m, 2H), 7.45 (s, 1H), 7.38 (d, $J = 8.1$ Hz, 1H), 7.20 (t, $J = 7.8$ Hz, 1H), 6.97 (d, $J = 7.5$ Hz, 1H), 2.29 (s, 3H).

$^{13}$C $^1$H NMR (126 MHz, CDCl$_3$) δ 164.19, 150.48 (2C), 142.35, 139.16, 137.35, 129.00, 126.16, 121.49, 121.21 (2C), 117.93, 21.51.

$N$-(4-Methoxyphenyl)isonicotinamide (3bd)$^5$

Purification of the crude mixture by column chromatography (eluent: heptane : ethyl acetate 4:1 to EtOAc) afforded the product (189 mg, 83%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.69 (d, $J = 3.1$ Hz, 2H), 8.34 (s, 1H), 7.67 (d, $J = 2.8$ Hz, 2H), 7.51 (d, $J = 7.7$ Hz, 2H), 6.87 (d, $J = 8.5$ Hz, 2H), 3.79 (s, 3H).

$^{13}$C $^1$H NMR (100 MHz, CDCl$_3$) δ 163.93, 157.19, 150.67 (2C), 142.29, 130.40, 122.58 (2C), 121.12 (2C), 114.41 (2C), 55.61.

$N$-(2-Chlorophenyl)isonicotinamide (3bf)$^6$

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 1:1) afforded the product (151 mg, 65%)

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.80 (d, $J = 5.7$ Hz, 2H), 8.49 (s, 1H), 8.46 (d, $J = 8.2$ Hz, 1H), 7.72 (d, $J = 5.8$ Hz, 2H), 7.41 (d, $J = 8.0$ Hz, 1H), 7.32 (m, $J = 7.8$ Hz, 1H), 7.11 (m, $J = 7.7$ Hz, 1H).

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$^{13}$C{$^1$H} NMR (126 MHz, CDCl$_3$) $\delta$ 163.39, 151.00 (2C), 141.65, 134.10, 129.27, 128.06, 125.66 (2C), 121.98, 120.88 (2C).

$N$-(3-Chlorophenyl)isonicotinamide (3bg)$^6$

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 1:1 to dichloromethane:ethyl acetate 1:2) afforded the product (158 mg, 68%).

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 10.66 (s, 1H), 8.80 (d, $J$ = 3.4 Hz, 2H), 7.96 (s, 1H), 7.85 (d, $J$ = 3.7 Hz, 2H), 7.70 (d, $J$ = 8.2 Hz, 1H), 7.41 (t, $J$ = 8.0 Hz, 1H), 7.20 (d, $J$ = 7.9 Hz, 1H).

$^{13}$C{$^1$H} NMR (100 MHz, DMSO-d$_6$) $\delta$ 164.31, 150.36 (2C), 141.59, 140.10, 133.05, 130.48, 123.94, 121.60 (2C), 119.89, 118.81.

$N$-(4-Chlorophenyl)isonicotinamide (3bh)$^7$

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 1:1 to dichloromethane : ethyl acetate 1:2) afforded the product (165 mg, 71%).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.10 (broad s, 1H), 8.64 – 8.59 (m, 2H), 7.67 – 7.62 (m, 2H), 7.56 (d, $J$ = 8.4 Hz, 2H), 7.28 (d, $J$ = 2.0 Hz, 2H).

$^{13}$C{$^1$H} (126 MHz, CDCl$_3$) $\delta$ 164.32, 150.38 (2C), 142.09, 136.05, 130.43, 129.19 (2C), 122.13 (2C), 121.30 (2C).

$N$-(4-Bromophenyl)isonicotinamide (3bi)$^7$

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 1:1) afforded the product (197 mg, 71%).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.75 (d, $J = 5.0$ Hz, 2H), 8.19 (broad s, 1H), 7.67 (d, $J = 5.0$ Hz, 2H), 7.53 (d, $J = 8.5$ Hz, 2H), 7.48 (d, $J = 8.5$ Hz, 2H).

$^{13}$C ($^1$H) NMR (126 MHz, CDCl$_3$) $\delta$ 163.96, 150.86 (2C), 141.93, 136.47, 132.36 (2C), 122.14 (2C), 121.02 (2C), 118.17.

**Methyl 3-(isonicotinamido)benzoate (3bj)$^8$**

![Methyl 3-(isonicotinamido)benzoate (3bj)](image)

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 1:1 to 2:1) afforded the product (174 mg, 67%).

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 10.71 (s, 1H), 8.81 (s, 2H), 8.46 (s, 1H), 8.07 (d, $J = 7.6$ Hz, 1H), 7.89 (s, 2H), 7.72 (d, $J = 7.3$ Hz, 1H), 7.52 (t, $J = 7.7$ Hz, 1H), 3.86 (s, 3H).

$^{13}$C ($^1$H) (126 MHz, DMSO-d$_6$) $\delta$ 166.06, 164.21, 150.33 (2C), 141.58, 139.06, 130.14, 129.24, 124.86, 124.78, 121.66, 120.97 (2C), 52.26.

**N-Phenethylisonicotinamide (3as)$^9$**

![N-Phenethylisonicotinamide (3as)](image)

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 1:1 to ethyl acetate) afforded the product (170 mg, 75%).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.61 (d, $J = 5.9$ Hz, 2H), 7.55 – 7.47 (m, 2H), 7.30 (t, $J = 7.4$ Hz, 2H), 7.25 – 7.17 (m, 3H), 6.73 (s, 1H), 3.69 (q, $J = 6.8$ Hz, 2H), 2.91 (t, $J = 6.9$ Hz, 2H).

$^{13}$C ($^1$H) (126 MHz, CDCl$_3$) $\delta$ 165.68, 150.49 (2C), 141.87, 138.64, 128.83 (2C), 126.81 (2C), 120.95 (2C), 41.36, 35.53, 1C missing due to overlap.

**N-Cyclohexylisonicotinamide (3bt)$^{10}$**

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Purification of the crude mixture by column chromatography (eluent: dichloromethane) afforded the product (133 mg, 65%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.64 (s, 2H), 7.57 (s, 2H), 6.34 (s, 1H), 3.93 (d, $J = 4.3$ Hz, 1H), 1.99 (d, $J = 11.6$ Hz, 2H), 1.73 (d, $J = 11.9$ Hz, 2H), 1.64 (d, $J = 11.8$ Hz, 1H), 1.45 – 1.31 (m, 2H), 1.30 – 1.09 (m, 3H).

$^{13}$C{$_^1$H} (100 MHz, CDCl$_3$) δ 164.79, 150.49 (2C), 142.27, 121.05 (2C), 49.18, 33.11 (2C), 25.53, 24.98 (2C).

**Morpholino(pyridin-4-yl)methanone (3bu)**

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.65 (d, $J = 5.2$ Hz, 2H), 7.26 – 7.21 (m, 2H), 3.73 (s, 4H), 3.57 (s, 2H), 3.32 (s, 2H).

$^{13}$C{$_^1$H} NMR (126 MHz, CDCl$_3$) δ 167.76, 150.38 (2C), 142.97, 121.23 (2C), 66.73 (2C), 47.88, 45.14.

**Morpholino(quinolin-2-yl)methanone (3au)**

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.21 (d, $J = 8.4$ Hz, 1H), 8.04 (d, $J = 8.5$ Hz, 1H), 7.79 (d, $J = 8.1$ Hz, 1H), 7.70 (t, $J = 7.2$ Hz, 2H), 7.54 (t, $J = 7.5$ Hz, 1H), 3.81 (m, 4H), 3.68 (d, $J = 7.1$ Hz, 4H).

$^{13}$C{$_^1$H} NMR (100 MHz, CDCl$_3$) δ 167.50, 153.19, 146.45, 137.26, 130.11, 129.65, 128.04, 127.68, 127.65, 120.87, 67.01, 66.78, 42.79, 42.76.

**Piperidin-1-yl(quinolin-2-yl)methanone (3av)**

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Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 5:1 to dichloromethane : ethyl acetate 2:1) afforded the product (169 mg, 70%).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.20 (d, $J = 8.4$ Hz, 1H), 8.07 (d, $J = 8.5$ Hz, 1H), 7.80 – 7.78 (m, 1H), 7.72 – 7.68 (m, 1H), 7.61 (d, $J = 8.4$ Hz, 1H), 7.55 – 7.52 (m, 1H), 3.77 (t, $J = 5.2$ Hz, 2H), 3.47 (t, $J = 5.5$ Hz, 2H), 1.72 – 1.64 (m, 4H), 1.53 – 1.58 (m, 2H).

$^{13}$C{$^1$H} NMR (126 MHz, CDCl$_3$) $\delta$ 167.73, 154.50, 146.80, 137.09, 129.98, 129.72, 127.93, 127.65, 127.37, 120.39, 48.33, 43.35, 26.52, 25.61, 24.59.

(6-Methylpyridin-2-yl)(morpholino)methanone (3du)$^{13}$

Purification of the crude mixture by column chromatography (eluent: ethyl acetate) afforded the product (134 mg, 65%).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.62 (t, $J = 7.7$ Hz, 1H), 7.40 – 7.33 (m, 1H), 7.14 (m, 1H), 3.74 (s, 4H), 3.58 (m, 4H), 2.50 (s, 3H).

$^{13}$C{$^1$H} NMR (75 MHz, CDCl$_3$) $\delta$ 167.65, 157.47, 153.01, 137.31, 124.16, 120.73, 66.94, 66.76, 47.75, 42.67, 24.35.

$N$-Phenyl-1H-benzo[d]imidazole-2-carboxamide (3ea)$^{14}$

Purification of the crude mixture by column chromatography (eluent: dichloromethane : ethyl acetate 99:1) afforded the product (90 mg, 38%).

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 13.47 (s, 1H), 10.91 (s, 1H), 7.95 (d, $J = 5.1$ Hz, 2H), 7.80 (s, 1H), 7.59 (s, 1H), 7.37 (s, 4H), 7.13 (s, 1H).


S8
\[^{13}C\{^1H\}\] NMR (100 MHz, DMSO-d\(_6\)) \(\delta\) 157.39, 145.62, 142.54, 138.31, 134.77, 128.71, 124.48, 124.14, 122.80, 120.51, 120.08 (2C), 112.70 (2C).

**N-(2-Methoxyphenyl)quinoline-2-carboxamide (3ac)**\(^{15}\)

![Chemical Structure]

Purification of the crude mixture by column chromatography (eluent: heptane : dichloromethane 1:3) afforded the product (200 mg, 72%).

\(^1H\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.78 (broad s, 1H), 8.70 – 8.69 (m, 1H), 8.36 (d, \(J = 8.4\) Hz, 1H), 8.25 (d, \(J = 8.5\) Hz, 1H), 8.15 (d, \(J = 8.4\) Hz, 1H), 7.81 – 7.79 (m, 1H), 7.74 – 7.71 (m, 1H), 7.57 – 7.53 (m, 1H), 7.11 – 7.04 (m, 2H), 6.93 – 6.91 (m, 1H), 3.97 (s, 3H).

\[^{13}C\{^1H\}\] NMR (126 MHz, CDCl\(_3\)) \(\delta\) 162.06, 150.02, 148.82, 146.28, 137.54, 130.03, 129.87, 129.21, 127.94, 127.65, 127.60, 123.96, 121.03, 119.66, 118.60, 110.14, 55.85.

**N-(4-Methoxyphenyl)quinoline-2-carboxamide (3ad)**\(^{12}\)

![Chemical Structure]

Purification of the crude mixture by column chromatography (eluent: heptane : dichloromethane 1:5) afforded the product (153 mg, 55%).

\(^1H\) NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.12 (broad s, 1H), 8.39 (d, \(J = 8.5\) Hz, 1H), 8.34 (d, \(J = 8.5\) Hz, 1H), 8.19 – 8.14 (m, 1H), 7.90 – 7.88 (m, 1H), 7.83 – 7.74 (m, 3H), 7.65 – 7.62 (m, 1H), 6.99 – 6.92 (m, 2H), 3.83 (s, 3H).

\[^{13}C\{^1H\}\] NMR (126 MHz, CDCl\(_3\)) \(\delta\) 162.01, 156.56, 149.98, 146.44, 137.89, 131.23, 130.38, 129.76, 129.49, 128.16, 127.93, 121.46 (2C), 118.86, 114.40 (2C), 55.62.

**N-(2-Fluorophenyl)quinoline-2-carboxamide (3ae)**\(^{16}\)

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Purification of the crude mixture by column chromatography (eluent: heptane : ethyl acetate 4:1) afforded the product (194 mg, 73%).

\[ \delta \begin{align*}
1^1H \text{ NMR} & \begin{align*}
(400 \text{ MHz, CDCl}_3) & \delta 10.55 (s, 1H), 8.62 (t, J = 7.8 \text{ Hz}, 1H), 8.36 (s, 2H), 8.20 (d, J = 8.2 \text{ Hz}, 1H), 7.89 (d, J = 8.0 \text{ Hz}, 1H), 7.80 (t, J = 7.4 \text{ Hz}, 1H), 7.64 (t, J = 7.2 \text{ Hz}, 1H), 7.17 (m, 3H).
\end{align*} \\
13^1C \{^1H \} \text{ NMR} & \begin{align*}
(100 \text{ MHz, CDCl}_3) & \delta 162.4, 153.0 (d, J = 244.6 \text{ Hz}), 149.4, 146.4, 137.98, 130.47, 130.04, 129.57, 128.41, 127.85, 126.58 (d, J = 10.1 \text{ Hz}), 124.8 (d, J = 3.7 \text{ Hz}), 124.5 (d, J = 7.6 \text{ Hz}), 121.37, 118.73, 115.1 (d, J = 19.0 \text{ Hz}).
\end{align*} \\
\end{align*} \]

\[ \text{N-(3-Chlorophenyl)quinoline-2-carboxamide (3ag)}^{12} \]

Purification of the crude mixture by column chromatography (eluent: heptane : dichloromethane 1:2) afforded the product (201 mg, 71%).

\[ \begin{align*}
1^1H \text{ NMR} & \begin{align*}
(500 \text{ MHz, CDCl}_3) & \delta 10.23 (\text{broad s, } 1H), 8.39 – 8.31 (m, 2H), 8.16 (d, J = 8.5 \text{ Hz}, 1H), 7.96 (t, J = 2.0 \text{ Hz}, 1H), 7.90 – 7.88 (m, 1H), 7.80 – 7.78 (m, 1H), 7.72 – 7.61 (m, 2H), 7.31 (t, J = 8.0 \text{ Hz}, 1H), 7.14 – 7.12 (m, 1H).
\end{align*} \\
13^1C \{^1H \} \text{ NMR} & \begin{align*}
(126 \text{ MHz, CDCl}_3) & \delta 162.33, 149.33, 146.37, 139.06, 138.06, 134.90, 130.54, 130.19, 129.76, 129.61, 128.42, 127.95, 124.46, 119.90, 118.79, 117.85.
\end{align*} \\
\end{align*} \]

\[ \text{Methyl 3-(quinoline-2-carboxamido)benzoate (3aj)}^{17} \]

Purification of the crude mixture by column chromatography (eluent: heptane : ethyl acetate 10:1 to heptane : ethyl acetate 6:1) afforded the product (205 mg, 67%).

\[ \begin{align*}
\text{17} & \begin{align*}
\text{B. Nijampatnam, P. Ahirwar, P. Pukkanasut, H. Womack, L. Casals, H. Zhang, X. Cai, S. M. Michalek, H. Wu, S. E. Velu, } & \begin{align*}
\text{ACS Med. Chem. Lett. 2021, 12, 48.}
\end{align*} \\
\end{align*} \]
\[^1\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 10.26 (s, 1H), 8.30 (m, 3H), 8.18 (m, 1H), 8.12 (d, \textit{J} = 8.5 \text{ Hz}, 1H), 7.83 (d, \textit{J} = 8.1 \text{ Hz}, 1H), 7.80 (d, \textit{J} = 7.7 \text{ Hz}, 1H), 7.75 (m, 1H), 7.59 (t, \textit{J} = 7.5 \text{ Hz}, 1H), 7.44 (t, \textit{J} = 7.9 \text{ Hz}, 1H), 3.92 (s, 3H).\]

\[^{13}\text{C\{}^1\text{H}\text{ NMR (126 MHz, CDCl}_3\text{)} \delta 166.8, 162.3, 149.3, 146.3, 138.1, 137.9, 131.0, 130.4, 129.7, 129.47, 129.3, 128.3, 127.8, 125.3, 124.1, 120.6, 118.7, 52.3.\]

*Methyl 4-(quinoline-2-carboxamido)benzoate (3ak)*

\[
\begin{array}{c}
\text{N} \\
\text{H} \\
\text{O} \\
\text{H} \\
\text{COOCH}_3
\end{array}
\]

Purification of the crude mixture by column chromatography (eluent: toluene : ethyl acetate 1:1) afforded the product (202 mg, 66%).

\[^1\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 10.39 (\text{broad s, 1H}), 8.40 – 8.32 (m, 2H), 8.17 (d, \textit{J} = 8.5 \text{ Hz}, 1H), 8.09 (d, \textit{J} = 8.4 \text{ Hz}, 2H), 7.95 – 7.87 (m, 3H), 7.79 – 7.82 (m, 1H), 7.65 (t, \textit{J} = 7.5 \text{ Hz}, 1H), 3.91 (s, 3H).\]

\[^{13}\text{C\{}^1\text{H}\text{ NMR (126 MHz, CDCl}_3\text{)} \delta 166.75, 162.48, 149.27, 146.38, 142.01, 138.13, 131.05 (2C), 130.60, 129.79, 129.66, 128.51, 127.97, 125.80, 119.06 (2C), 118.81, 52.12.\]

*N-(4-Cyanophenyl)quinoline-2-carboxamide (3al)*

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

Purification of the crude mixture by column chromatography (eluent: toluene : ethyl acetate 20:1) afforded the product (172 mg, 63%).

\[^1\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 10.42 (\text{broad s, 1H}), 8.39 – 8.31 (m, 2H), 8.16 (d, \textit{J} = 8.5 \text{ Hz}, 1H), 7.99 – 7.93 (m, 2H), 7.92 – 7.90 (m, 1H), 7.83 – 7.78 (m, 1H), 7.68 – 7.65 (m, 3H).\]

\[^{13}\text{C\{}^1\text{H}\text{ NMR (126 MHz, CDCl}_3\text{)} \delta 162.58, 148.83, 146.31, 141.81, 138.23, 133.43 (2C), 130.71, 129.71, 128.67, 127.99, 119.73 (2C), 119.00, 118.72, 107.26 (1C missing due to overlap).\]

*N-(3-Nitrophenyl)quinoline-2-carboxamide (3an)*

\[
\begin{array}{c}
\text{N} \\
\text{H} \\
\text{O} \\
\text{H} \\
\text{NO}_2
\end{array}
\]
Purification of the crude mixture by column chromatography (eluent: heptane : dichloromethane 1:2) afforded the product (191 mg, 65%).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 10.45 (broad s, 1H), 8.69 (t, $J = 2.1$ Hz, 1H), 8.38 (s, 2H), 8.26 – 8.22 (m, 1H), 8.19 (d, $J = 8.5$ Hz, 1H), 8.01 – 7.99 (m, 1H), 7.93 – 7.92 (m, 1H), 7.85 – 7.81 (m, 1H), 7.69 – 7.66 (m, 1H), 7.56 (t, $J = 8.2$ Hz, 1H).

$^{13}$C{$^1$H} NMR (126 MHz, CDCl$_3$) $\delta$ 162.67, 148.89, 146.40, 139.07, 138.27, 130.74, 130.07, 129.79 (2C), 128.66, 128.01, 125.41, 118.97, 118.79, 114.58. (1C missing due to overlap)

$N$-(4-nitrophenyl)quinoline-2-carboxamide (3ao)$^{15}$

Purification of the crude mixture by column chromatography (eluent: heptane : dichloromethane 1:2), followed by washing the obtained solid with methanol afforded the product (132 mg, 45%).

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.31 (s, 1H), 8.65 (d, $J = 8.5$ Hz, 1H), 8.28 (q, $J = 9.6$ Hz, 6H), 8.13 (d, $J = 8.0$ Hz, 1H), 7.94 (t, $J = 7.6$ Hz, 1H), 7.78 (t, $J = 7.4$ Hz, 1H).

$^{13}$C{$^1$H} NMR (100 MHz, DMSO-d$_6$) $\delta$ 162.73, 148.81, 146.41, 143.68, 138.39, 130.84, 129.79, 128.81, 128.07, 126.48, 125.37, 119.39 (2C), 118.84 (2C), 113.52.

2-(Quinoline-2-carboxamido)benzoic acid (3ap)$^{18}$

Purification of the crude mixture by trituration with methanol afforded the product as a pale-yellow solid (149 mg, 51%).

$^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 13.82 (s, 1H), 13.43 (s, 1H), 8.91 (d, $J = 8.1$ Hz, 1H), 8.63 (d, $J = 8.5$ Hz, 1H), 8.28 (d, $J = 8.5$ Hz, 1H), 8.14 – 8.06 (m, 3H), 7.94 – 7.88 (m, 1H), 7.78 – 7.65 (m, 2H), 7.26 – 7.19 (m, 1H).

$^{13}$C{$^1$H} NMR (75 MHz, DMSO-d$_6$) $\delta$ 169.05, 162.74, 149.55, 145.78, 140.29, 138.32, 134.13, 131.41, 130.75, 129.16, 129.02, 128.47, 128.12, 123.01, 119.64, 118.54, 117.02.

**N-(Pyridin-2-yl)quinoline-2-carboxamide (3aq)**\(^{12}\)

![Structural formula of N-(Pyridin-2-yl)quinoline-2-carboxamide (3aq)](image)

Purification of the crude mixture by column chromatography (eluent: dichloromethane) afforded the product (154 mg, 62%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.70 (s, 1H), 8.46 (d, \(J = 8.3\) Hz, 1H), 8.37 (d, \(J = 4.1\) Hz, 1H), 8.31 (t, \(J = 7.5\) Hz, 2H), 8.12 (d, \(J = 8.4\) Hz, 1H), 7.82 (d, \(J = 8.1\) Hz, 1H), 7.74 (t, \(J = 6.7\) Hz, 2H), 7.57 (t, \(J = 7.4\) Hz, 1H), 7.12 – 7.01 (m, 1H).

\(^{13}\)C\(^{1}\)H NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.7, 151.24, 148.96, 148.25, 146.40, 138.40, 137.78, 130.40, 129.91, 129.48, 128.36, 127.70, 119.91, 118.58, 113.96.

**N-(Pyridin-3-yl)quinoline-2-carboxamide (3ar)**

![Structural formula of N-(Pyridin-3-yl)quinoline-2-carboxamide (3ar)](image)

Purification of the crude mixture by column chromatography (eluent: toluene : ethyl acetate 3:1 to toluene : ethyl acetate 1:1) afforded the product (167 mg, 67%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.25 (broad s, 1H), 8.89 (d, \(J = 2.7\) Hz, 1H), 8.42 – 8.38 (m, 2H), 8.32 (d, \(J = 1.4\) Hz, 2H), 8.14 (d, \(J = 8.5\) Hz, 1H), 7.87 – 7.85 (m, 1H), 7.79 – 7.75 (m, 1H), 7.64 – 7.57 (m, 1H), 7.33 – 7.30 (3, 1H).

\(^{13}\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \(\delta\) 162.76, 149.04, 146.33, 145.40, 141.46, 138.05, 134.68, 130.55, 129.71, 129.57, 128.46, 127.89, 126.76, 123.79, 118.67.

HRMS (ESI+) calcd for C\(_{15}\)H\(_{12}\)N\(_3\)O [M + H]\(^+\) 250.0980. Found 250.0968.

**N-Phenylbenzamide (7)**\(^{19}\)

![Structural formula of N-Phenylbenzamide (7)](image)

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.88-7.85 (m, 2H), 7.67-7.62 (m, 2H), 7.58-7.45 (m, 3H), 7.40-7.34 (m, 2H), 7.18-7.13 (m, 1H).

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\[ ^{13}\text{C} \text{NMR (126 MHz, CDCl} _3\text{)} \delta 165.8, 137.9, 135.0, 131.8, 129.1, 128.8, 127.0, 124.6, 120.2. \]

*N-Benzy1benzamide (9)*

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

\[ ^{1}\text{H} \text{NMR (500 MHz, CDCl} _3\text{)} \delta 7.80-7.78 (m, 2\text{H}), 7.52-7.48 (m, 1\text{H}), 7.44-7.41 (m, 2\text{H}), 7.36-7.35 (m, 4\text{H}), 7.32-7.28 (m, 1\text{H}), 6.45 (\text{broad s, 1H}), 4.65-4.64 (m, 2\text{H}). \]

\[ ^{13}\text{C} \text{NMR (126 MHz, CDCl} _3\text{)} \delta 167.4, 138.2, 134.4, 131.6, 128.8, 128.6, 127.9, 127.6, 127.0, 44.2. \]
Copies of $^1$H and $^{13}$C NMR spectra of amide products 3

$N$-Phenylquinoline-2-carboxamide (3aa)
N-Phenylpicolinamide (3ca)

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

$^{13}$C $^1$H NMR (100 MHz, CDCl$_3$)
$N$-Phenylisonicotinamide (3ba)

$^1$H NMR (500 MHz, DMSO-$d_6$)

$^{13}$C NMR (126 MHz, DMSO-$d_6$)
N-(m-Tolyl)isonicotinamide (3bb)

$^{1}H$ NMR (500 MHz, CDCl$_3$)

$^{13}C \{^1H\}$ NMR (126 MHz, CDCl$_3$)
$N$-(4-Methoxyphenyl)isonicotinamide (3bd)
$N$-(2-Chlorophenyl)isonicotinamide (3bf)

$N$-(3-Chlorophenyl)isonicotinamide (3bg)
$^{1}H$ NMR (400 MHz, DMSO-d$_6$)

$^{13}C$($^1H$) NMR (100 MHz, DMSO-d$_6$)
N-(4-Chlorophenyl)isonicotinamide (3bh)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C ($^1$H) NMR (126 MHz, CDCl$_3$)
$N$-(4-Bromophenyl)isonicotinamide (3bi)
Methyl 3-(isonicotinamido)benzoate (3bj)
$N$-Phenethylisonicotinamide (3as)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C ($^1$H) NMR (126 MHz, CDCl$_3$)
N-Cyclohexylisonicotinamide (3bt)
Morpholino(pyridin-4-yl)methanone (3bu)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (126 MHz, CDCl$_3$)
Morpholino(quinolin-2-yl)methanone (3au)

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

$^{13}$C $^1$H NMR (100 MHz, CDCl$_3$)
Piperidin-1-yl(quinolin-2-yl)methanone (3av)
(6-Methylpyridin-2-yl)(morpholino)methanone (3du)
$N$-Phenyl-1H-benzo[d]imidazole-2-carboxamide (3ea)

$^1$H NMR (400 MHz, DMSO-$d_6$)

$^{13}$C($^1$H) NMR (100 MHz, DMSO-$d_6$)
$N$-(2-Methoxyphenyl)quinoline-2-carboxamide (3ac)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C ($^1$H) NMR (126 MHz, CDCl$_3$)
$N$(4-Methoxyphenyl)quinoline-2-carboxamide (3ad)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C ($^1$H) NMR (126 MHz, CDCl$_3$)
$N$-(2-fluorophenyl)quinoline-2-carboxamide (3ae)

\[ \text{\( }^{1}\text{H NMR (400 MHz, CDCl}_3\text{)} \]

\[ \text{\( }^{13}\text{C (\( ^{1}\text{H}) \text{ NMR (100 MHz, CDCl}_3\text{)} \]

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$N$-(3-Chlorophenyl)quinoline-2-carboxamide (3ag)
Methyl 3-(quinoline-2-carboxamido)benzoate (3aj)
Methyl 4-(quinoline-2-carboxamido)benzoate (3ak)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (126 MHz, CDCl$_3$)
$N$-(4-Cyanophenyl)quinoline-2-carboxamide (3al)

$^1$H NMR (500 MHz, CDCl₃)

$^{13}$C $^1$H NMR (126 MHz, CDCl₃)
$N$-(3-Nitrophenyl)quinoline-2-carboxamide (3aj)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (126 MHz, CDCl$_3$)
N-(4-nitrophenyl)quinoline-2-carboxamide (3ao)
2-(Quinoline-2-carboxamido)benzoic acid (3ap)

$\text{H NMR (500 MHz, DMSO-d}_6\text{)}$

$\text{C NMR (126 MHz, DMSO-d}_6\text{)}$
N-(Pyridin-2-yl)quinoline-2-carboxamide (3aq)
$N$-(Pyridin-3-yl)quinoline-2-carboxamide (3ar)

$\text{H NMR (500 MHz, CDCl}_3\text{)}$

$\text{C$^1$H NMR (126 MHz, CDCl}_3\text{)}$
$N$-Phenylbenzamide (7)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C{$^1$H} NMR (75 MHz, CDCl$_3$)
$N$-Benzylbenzamide (9)

$^1$H NMR (500 MHz, CDCl$_3$)

$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (126 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (126 MHz, CDCl$_3$)