Sustainable Multicomponent Indole Synthesis with Broad Scope

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1. Experimental materials and methods

All the reagents and solvents were purchased from Sigma-Aldrich, AK Scientific, Fluorochem, Abcr GmbH, Acros and were used without further purification. All microwave irradiation reactions were carried out in a Biotage Initiator™ Microwave Synthesizer. Thin layer chromatography was performed on Millipore precoated silica gel plates (0.20 mm thick, particle size 25 μm). Nuclear magnetic resonance spectra were recorded on Bruker Avance 500 spectrometers (1H NMR (500 MHz), 13C NMR (126 MHz)). Chemical shifts for 1H NMR were reported as δ values and coupling constants were in hertz (Hz). The following abbreviations were used for spin multiplicity: s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, dd = double of doublets, ddd = double doublet of doublets, m = multiplet. Chemical shifts for 13C NMR were reported in ppm relative to the solvent peak. High resolution mass spectra were recorded using a Q-Exactive Plus Orbitrap MS (Thermo) via direct infusion in 50 μL/min.
2. Synthetic procedures and analytical data

**General procedure for the Ugi 4-component reaction (U-4CR)**

\[
\begin{align*}
R^1\text{NH}_2 & + R^2\text{NC} \xrightarrow{\text{CHO, rt, 1-2h}} \text{MeOH, rt} \\
\text{HCOOH} & \rightarrow 1a-t
\end{align*}
\]

To a stirred solution of the corresponding aniline (1.0 mmol) in MeOH (1.0 mL), 2,2-dimethoxyacetaldehyde (1.0 mmol), the corresponding isocyanide (1.0 mmol) and formic acid (1.0 mmol) were added at room temperature. The reaction mixture was stirred vigorously for 1-2 h. The solvent was removed under reduced pressure and the reaction mixture was purified with column chromatography (PE-EA 4:1-1:1) to give compounds 1a-t.

**General procedure for the cyclization**

\[
\begin{align*}
1a-t & \xrightarrow{\text{MSA, 0-70 °C, 0.5-1 h}} \\
& \rightarrow 2a-t
\end{align*}
\]

The corresponding indole-2-carboxamides (1.0 mmol) are dissolved into methanesulfonic acid (MSA) (1.0 mL) at 0 °C and then heated up to 70 °C for 0.5 - 1.0 h. Then, the reaction mixture was cooled to room temperature and neutralized with an aqueous solution of NaHCO₃, followed by extractions with ethyl acetate. The organic layer was dried with Na₂SO₄, the solvent is removed under reduced pressure. If solid appears, the resulting solid was filtered and washed with Et₂O or hexane. Alternatively, the solvent is removed under reduced pressure and the residue is purified by column chromatography (PE-EA, 8:1-1:1) to give the compounds 2a-t.
**Reaction mechanism**

The first step which is an Ugi four-component reaction has been multiple time reported and it is considered to be well established, therefore we propose the following pathway for the acidic closure step.
The gram-scale synthesis of 1a and 2a

To a stirred solution of 2,2-dimethoxyacetaldehyde (10.0 mmol, 1.04 g) in MeOH (10.0 mL), the 3,4,5-trimethoxyaniline (10.0 mmol, 1.83 g), benzyl isocyanide (10.0 mmol, 1.17 g) and formic acid (10.0 mmol, 0.46 g) were added in a 50 mL flask. The reaction mixture was stirred vigorously for 2 h. Then, the solvent was removed under reduced pressure and the reaction mixture was purified with column chromatography (PE-EA 4:1-1:1) to give compound 1a (4.06 g, 94%) as yellow solid. Afterwards, the N-benzyl-3,3-dimethoxy-2-(N-(3,4,5-trimethoxyphenyl)formamido)propanamide (1a, 5.0 mmol, 2.16 g) was dissolved into methanesulfonic acid (5.0 mL) at 0 °C and then heated up to 70 °C for 0.5 h. Then, the reaction mixture was cooled to room temperature neutralized with an aqueous solution of NaHCO₃ to pH 7, followed by extractions with ethyl acetate (3 x 30 mL). The organic layer was dried with Na₂SO₄ and the solvent was removed under reduced pressure. the reaction mixture was purified with column chromatography (PE-EA 4:1-1:1) to give compound 2a (1.55 g, 91%) as yellow solid.

One-pot two-step approach towards 2a, 2d and 2q-t

To a stirred solution of 2,2-dimethoxyacetaldehyde (1.0 mmol) in MeOH (1.0 mL), the corresponding aniline (1.0 mmol), the corresponding isocyanide (1.0 mmol) and formic acid (1.0 mmol) were added in a 5.0 mL vial. The reaction mixture was stirred vigorously for 2 h. Then, the solvent was removed under reduced pressure and the
intermediate products were obtained, directly used in the next step without further purification. Afterwards, the methanesulfonic acid (1.0 mL) was added at 0°C and heated up to 70°C for 0.5 h. The reaction mixture was neutralized with an aqueous solution of NaHCO$_3$, followed by extractions with ethyl acetate. The organic layer was dried with MgSO$_4$ and the solvent was removed under reduced pressure. The resulting solid was purified by column chromatography (PE-EA, 4:1-1:1) to give compounds 2a, 2d and 2q-t in 2-steps.

$N$-benzyl-3,3-dimethoxy-2-(N-(3,4,5-trimethoxyphenyl)formamido)propenamide (1a)

![Chemical structure of 1a]

397 mg, 92% yield, yellow solid, mp 86-90°C. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.33 (s, 1H), 7.36 - 7.33 (m, 2H), 7.32 - 7.29 (m, 3H), 7.18 - 7.16 (m, 1H), 6.63 (s, 2H), 4.98 (d, $J$ = 8.3 Hz, 1H), 4.82 (d, $J$ = 8.3 Hz, 1H), 4.51 (d, $J$ = 5.9 Hz, 2H), 3.87 (s, 3H), 3.83 (s, 6H), 3.44 (s, 3H), 3.31 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 167.4, 163.6, 153.4, 138.0, 137.7, 135.4, 128.7, 127.6, 127.4, 104.9, 104.6, 103.5, 100.9, 60.9, 60.7, 56.38, 56.2, 55.7, 54.1, 43.5, 43.3. HRMS (ESI) m/z calcd for C$_{22}$H$_{29}$N$_2$O$_7$ [M + H]$^+$ 433.1969, found 433.1963.

$N$-(4-cyanobenzyl)-3,3-dimethoxy-2-(N-(3,4,5-trimethoxyphenyl)formamido)propenamide (1b)

![Chemical structure of 1b]

425 mg, 93% yield, yellow solid, mp 111-114°C. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.34 (s, 1H), 7.64 (d, $J$ = 8.2 Hz, 2H), 7.41 (d, $J$ = 8.2 Hz, 2H), 7.36 (t, $J$ = 5.8 Hz, 1H), 6.64 (s, 2H), 5.02 (d, $J$ = 8.1 Hz, 1H), 4.76 (d, $J$ = 8.1 Hz, 1H), 4.62 (dd, $J$ = 15.9, 6.0 Hz, 1H), 4.52 (dd, $J$ = 15.9, 6.0 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 6H), 3.44 (s, 3H), 3.33 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 167.8, 163.6, 153.5, 143.6, 137.8, 135.4, 132.5, 127.8,
118.7, 111.2, 104.5, 101.0, 61.3, 60.9, 56.3, 55.5, 54.6, 43.1. HRMS (ESI) m/z calcd for C$_{23}$H$_{27}$NaN$_3$O$_7$ [M + Na]$^+$ 480.1741, found 480.1735.

*N*-cyclohexyl-3,3-dimethoxy-2-(*N*-({3,4,5-trimethoxyphenyl})formamido)propenamide (1c)

![Chemical structure of 1c](image)

407 mg, 96% yield, white solid, mp 131-134 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.31 (s, 1H), 6.66 - 6.65 (m, 3H), 4.92 (d, $J$ = 8.4 Hz, 1H), 4.72 (d, $J$ = 8.4 Hz, 1H), 3.85 - 3.84 (m, 9H), 3.45 (s, 3H), 3.27 (s, 3H), 1.92 - 1.89 (m, 2H), 1.70 - 1.67 (m, 2H), 1.61 - 1.57 (m, 1H), 1.41 - 1.34 (m, 2H), 1.26 - 1.18 (m, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 166.5, 163.6, 153.4, 137.7, 135.5, 104.6, 101.1, 61.0, 60.7, 56.3, 55.9, 54.0, 48.3, 32.8, 32.7, 25.6, 24.6. HRMS (ESI) m/z calcd for C$_{21}$H$_{32}$NaN$_2$O$_7$ [M + Na]$^+$ 447.2102, found 447.2097.

3,3-dimethoxy-*N*-phenyl-2-(*N*-({3,4,5-trimethoxyphenyl})formamido)propenamide (1e)

![Chemical structure of 1e](image)

376 mg, 90% yield, yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.76 (s, 1H), 8.38 (s, 1H), 7.57 (d, $J$ = 7.9 Hz, 2H), 7.36 (t, $J$ = 7.9 Hz, 2H), 7.16 - 7.15 (m, 1H), 6.67 (s, 2H), 5.10 (d, $J$ = 8.2 Hz, 1H), 4.89 (d, $J$ = 8.2 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 6H), 3.53 (s, 3H), 3.37 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 165.4, 163.8, 153.5, 137.8, 137.6, 135.4, 129.0, 124.6, 120.0, 104.6, 101.0, 62.0, 61.0, 56.3, 56.0, 54.3. HRMS (ESI) m/z calcd for C$_{21}$H$_{26}$NaN$_2$O$_7$ [M + Na]$^+$ 441.1632, found 441.1624.
methyl (2-(N-(3,5-dimethylphenyl)formamido)-3,3-dimethoxypropanoyl) glycinate (1f)

306 mg, 87% yield, brown oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.33 (s, 1H), 7.52 (s, 1H), 6.96 (s, 3H), 5.13 (d, $J = 8.3$ Hz, 1H), 4.70 (d, $J = 8.3$ Hz, 1H), 4.16 (dd, $J = 18.3, 5.3$ Hz, 1H), 4.08 (dd, $J = 18.3, 5.3$ Hz, 1H), 3.78 (s, 3H), 3.50 (s, 3H), 3.33 (s, 3H), 2.34 (s, 6H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 170.1, 167.5, 163.6, 140.3, 139.2, 129.4, 123.8, 100.6, 61.6, 55.3, 54.1, 52.3, 41.4, 21.3. HRMS (ESI) m/z calcd for C$_{17}$H$_{24}$NaN$_2$O$_6$ [M + Na]$^+$ 375.1527, found 375.1522.

N-(4-chlorophenyl)-2-(N-(3,5-dimethylphenyl)formamido)-3,3-dimethoxypropanamide (1g)

347 mg, 89% yield, yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.99 (s, 1H), 8.36 (d, $J = 1.8$ Hz, 1H), 7.54 (d, $J = 8.5$ Hz, 2H), 7.31 - 7.29 (m, 1H), 7.00 - 6.98 (m, 3H), 5.14 (d, $J = 8.2$ Hz, 1H), 4.83 (d, $J = 8.2$ Hz, 1H), 3.51 (s, 3H), 3.34 (s, 3H), 2.35 (s, 6H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 165.5, 164.1, 139.8, 139.3, 136.3, 129.7, 129.4, 129.0, 124.0, 121.3, 101.0, 62.5, 55.7, 54.2, 21.3. HRMS (ESI) m/z calcd for C$_{20}$H$_{23}$ClNaN$_2$O$_4$ [M + Na]$^+$ 413.1239, found 413.1234.
2-(N-(3,5-dimethylphenyl)formamido)-3,3-dimethoxy-N-(2-methoxybenzyl) propenamide (1h)

360 mg, 90% yield, yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.28 (s, 1H), 7.31 - 7.26 (m, 3H), 6.95 - 6.92 (m, 2H), 6.90 - 6.88 (m, 1H), 6.85 (s, 2H), 4.99 (d, $J = 8.4$ Hz, 1H), 4.78 (d, $J = 8.4$ Hz, 1H), 4.55, 4.45 (ABq, $J = 14.6$, 6.0 Hz, 2H), 3.88 (s, 3H), 3.42 (s, 3H), 3.28 (s, 3H), 2.30 (s, 6H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 167.1, 163.5, 157.5, 139.7, 139.1, 129.6, 129.5, 128.8, 126.1, 124.3, 120.6, 110.2, 100.7, 60.5, 55.6, 55.3, 53.4, 39.6, 21.2. HRMS (ESI) m/z calcd for C$_{22}$H$_{26}$N$_2$O$_5$ [M + H]$^+$ 401.2071, found 401.2069.

2-(N-(3,5-dimethylphenyl)formamido)-3,3-dimethoxy-N-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) propanamide (1i)

334 mg, 86% yield, yellow oil, dr~1:4. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.33 (s, 0.2H), 8.32 (s, 0.8H), 7.10 - 6.97 (m, 4H), 5.09 - 5.04 (m, 1H), 4.67 - 4.62 (m, 1H), 4.30 - 4.25 (m, 1H), 3.96 - 3.91 (m, 1H), 3.47 - 3.44 (m, 3H), 3.30 - 3.27 (m, 3H), 2.34 - 2.33 (m, 6H), 1.91 - 1.69 (m, 3H), 1.65 - 1.40 (m, 2H), 1.34 - 1.15 (m, 2H), 0.96 (d, $J = 3.1$ Hz, 3H), 0.89 (d, $J = 4.9$ Hz, 2H), 0.86 - 0.82 (m, 4H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.6, 166.3, 163.8, 163.7, 163.6, 140.3, 139.1, 129.4, 129.3, 129.3, 129.2, 123.9, 123.8, 123.6, 100.8, 100.7, 56.8, 56.7, 55.2, 55.1, 54.0, 53.9, 48.7, 48.5, 47.1, 44.9, 39.1, 39.0, 37.6, 37.5, 36.0, 35.9, 28.3, 28.1, 27.1, 21.3, 20.3, 20.1, 19.8, 18.7, 13.8, 13.6, 11.9, 11.8. HRMS (ESI) m/z calcd for C$_{24}$H$_{36}$NaN$_2$O$_4$ [M + Na]$^+$ 439.2567, found 439.2547.
2-(N-(3,4-dimethylphenyl)formamido)-N-(2-isopropylphenyl)-3,3-dimethoxypropanamide (1j)

294 mg, 74% yield, yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.72 (s, 1H), 8.39 (s, 1H), 7.90 (d, $J = 7.9$ Hz, 1H), 7.32 (d, $J = 7.6$ Hz, 1H), 7.25 - 7.14 (m, 5H), 5.13 (d, $J = 8.2$ Hz, 1H), 4.98 (d, $J = 8.2$ Hz, 1H), 3.52 (s, 3H), 3.36 (s, 3H), 3.12 - 3.07 (m, 1H), 2.30 (s, 3H), 2.29 (s, 3H), 1.31 - 1.28 (m, 6H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 165.9, 163.9, 139.7, 137.9, 137.6, 136.6, 134.2, 130.4, 127.6, 126.3, 125.7, 125.4, 124.0, 123.9, 100.9, 61.6, 55.7, 53.9, 27.8, 23.1, 23.0, 19.9, 19.4. HRMS (ESI) m/z calcd for C$_{23}$H$_{31}$N$_2$O$_4$ [M + H]$^+$ 399.2278, found 399.2272.

N-(4-chlorobenzyl)-3,3-dimethoxy-2-(N-(3-methoxyphenyl)formamido)propenamide (1k)

361 mg, 89% yield, yellow solid, mp 88-91 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.35 (s, 1H), 7.32 - 7.29 (m, 3H), 7.25 - 7.17 (m, 3H), 6.94 - 6.89 (m, 3H), 5.02 (d, $J = 8.3$ Hz, 1H), 4.81 (d, $J = 8.3$ Hz, 1H), 4.52 - 4.44 (m, 2H), 3.81 (s, 3H), 3.42 (s, 3H), 3.28 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 167.4, 163.6, 160.3, 141.0, 136.6, 130.4, 128.9, 128.8, 118.6, 113.5, 112.2, 100.8, 60.7, 55.5, 55.4, 53.9, 42.9. HRMS (ESI) m/z calcd for C$_{20}$H$_{23}$ClNaN$_2$O$_5$ [M + H]$^+$ 429.1188, found 429.1184.
**N-benzyl-3,3-dimethoxy-2-(N-(3-methoxyphenyl)formamido)propanamide (1l)**

![Chemical structure](image)

334 mg, 90% yield, white solid, mp 87-92 °C. ^1^H NMR (500 MHz, CDCl₃) δ 8.36 (s, 1H), 7.37 - 7.34 (M, 1H), 7.32 - 7.28 (m, 4H), 7.16 (s, 1H), 6.96 (t, J = 2.1 Hz, 1H), 6.94 (d, J = 7.7 Hz, 1H), 6.91 - 6.89 (m, 1H), 5.03 (d, J = 8.3 Hz, 1H), 4.84 (d, J = 8.3 Hz, 1H), 4.52 (d, J = 5.8 Hz, 2H), 3.81 (s, 3H), 3.43 (s, 3H), 3.28 (s, 3H). ^13^C NMR (126 MHz, CDCl₃) δ 167.4, 163.6, 160.3, 141.1, 138.0, 130.1, 128.7, 127.5, 127.4, 118.7, 113.6, 112.2, 100.8, 60.7, 55.6, 55.4, 53.8, 43.6. HRMS (ESI) m/z calcd for C₂₀H₂₄NaN₂O₅ [M + Na]^+ 395.1577, found 395.1574.

**N-benzyl-2-(N-(3-bromophenyl)formamido)-3,3-dimethoxypropanamide (1m)**

![Chemical structure](image)

409 mg, 85% yield, yellow solid, mp 83-86 °C. ^1^H NMR (500 MHz, CDCl₃) δ 8.30 (s, 1H), 7.57 (t, J = 1.8 Hz, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.38 - 7.33 (m, 3H), 7.31 - 7.26 (m, 4H), 7.17 - 7.15 (m, 1H), 4.98 (d, J = 8.2 Hz, 1H), 4.81 (d, J = 8.2 Hz, 1H), 4.56 - 4.47 (m, 2H), 3.42 (s, 3H), 3.29 (s, 3H). ^13^C NMR (126 MHz, CDCl₃) δ 166.9, 163.2, 141.2, 137.9, 131.1, 130.6, 129.9, 128.7, 128.5, 127.50, 127.48, 125.5, 122.7, 100.8, 60.6, 55.5, 54.0, 43.7. HRMS (ESI) m/z calcd for C₁₉H₂₁BrNaN₂O₄ [M + Na]^+ 443.0577, found 443.0573.
**N-(2-(1H-indol-3-yl)ethyl)-3,3-dimethoxy-2-(N-o-tolylformamido)propenamide (1n)**

368 mg, 90% yield, yellow oil. \( ^1H \) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 8.13 (s, 1H), 8.05 (s, 1H), 7.66 (d, \( J = 8.0 \) Hz, 1H), 7.48 (d, \( J = 6.3 \) Hz, 1H), 7.38 (d, \( J = 8.0 \) Hz, 1H), 7.29 - 7.27 (m, 2H), 7.25 - 7.20 (m, 2H), 7.15 - 7.11 (m, 2H), 7.02 (s, 1H), 5.05 - 4.78 (m, 1H), 4.88 (s, 1H), 4.57 (s, 1H), 3.68 (d, \( J = 6.2 \) Hz, 2H), 3.29 (s, 3H), 3.22 (s, 3H), 3.04 (t, \( J = 6.9 \) Hz, 2H), 2.28 (s, 3H). \( ^{13}C \) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 164.3, 136.4, 136.0, 131.3, 128.6, 128.4, 127.3, 126.9, 122.2, 122.1, 119.4, 118.8, 112.9, 111.2, 39.9, 25.2, 17.9. HRMS (ESI) m/z calcd for C\(_{23}\)H\(_{27}\)NaN\(_3\)O\(_4\) [M + Na\(^+\)] 432.1894, found 432.1890.

**N-benzyl-3,3-dimethoxy-2-(N-phenylformamido)propenamide (1o)**

280 mg, 82% yield, colorless oil. \( ^1H \) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 8.32 (d, \( J = 0.9 \) Hz, 1H), 7.42 - 7.39 (m, 2H), 7.37 - 7.33 (m, 5H), 7.31 - 7.26 (m, 3H), 7.21 (s, 1H), 4.97 (d, \( J = 8.3 \) Hz, 1H), 4.88 (d, \( J = 8.3 \) Hz, 1H), 4.52 (d, \( J = 5.7 \) Hz, 2H), 3.41 (d, \( J = 0.9 \) Hz, 3H), 3.25 (d, \( J = 0.9 \) Hz, 3H). \( ^{13}C \) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 167.4, 163.7, 139.8, 138.0, 129.4, 128.7, 127.9, 127.5, 127.4, 126.8, 100.8, 60.4, 55.7, 53.7, 43.6. HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{22}\)NaN\(_2\)O\(_4\) [M + Na\(^+\)] 365.1472, found 365.1469.
3,3-dimethoxy-N-phenyl-2-(N-phenylformamido)propenamide (1p)

![Chemical structure of 1p]

249 mg, 76% yield, red oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.81 (s, 1H), 8.40 (s, 1H), 7.59 (d, $J$ = 8.2 Hz, 2H), 7.46 - 7.39 (m, 4H), 7.37 - 7.34 (m, 3H), 7.15 (t, $J$ = 7.4 Hz, 1H), 5.06 (d, $J$ = 8.3 Hz, 1H), 4.97 (d, $J$ = 8.3 Hz, 1H), 3.51 (s, 3H), 3.31 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 165.5, 164.0, 139.7, 137.7, 129.5, 129.0, 128.0, 126.7, 124.5, 120.1, 100.9, 61.5, 56.0, 53.9. HRMS (ESI) m/z calcd for C$_{18}$H$_{20}$NaN$_2$O$_4$ [M + Na]$^+$ 351.1315, found 351.1310.

$N$-benzyl-4,5,6-trimethoxy-1H-indole-2-carboxamide (2a)

![Chemical structure of 2a]

303 mg, 89% yield, yellow solid, mp 182-184 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.48 (s, 1H), 7.39 (d, $J$ = 4.3 Hz, 4H), 7.36 - 7.32 (m, 1H), 6.92 (d, $J$ = 2.2 Hz, 1H), 6.66 (s, 1H), 6.44 (t, $J$ = 5.6 Hz, 1H), 4.71 (d, $J$ = 5.6 Hz, 2H), 4.10 (s, 3H), 3.88 (s, 6H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 161.4, 153.4, 138.0, 133., 128.9, 127.8, 127.7, 115.5, 100.3, 89.3, 61.5, 60.9, 56.1, 43.6. HRMS (ESI) m/z calcd for C$_{19}$H$_{21}$N$_2$O $[M + H]^+$ 341.1496, found 341.1493.

$N$-(4-cyanobenzyl)-4,5,6-trimethoxy-1H-indole-2-carboxamide (2b)

![Chemical structure of 2b]

336 mg, 92% yield, colorless solid, mp 184-186 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.15 (s, 1H), 7.66 (d, $J$ = 8.2 Hz, 2H), 7.48 (d, $J$ = 8.2 Hz, 2H), 6.97 (d, $J$ = 2.1 Hz, 1H), 6.64 (s, 1H), 6.57 (t, $J$ = 5.8 Hz, 1H), 4.74 (d, $J$ = 6.2 Hz, 2H), 4.11 (s, 3H), 3.92 (s, 3H), 3.84 (s, 3H), 3.74 (s, 3H).
3.89 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 161.5, 153.7, 146.3, 143.7, 136.4, 133.6, 132.6, 128.1, 118.7, 115.6, 111.5, 100.7, 89.2, 61.5, 60.9, 56.2, 43.1. HRMS (ESI) m/z calcd for C$_{20}$H$_{20}$N$_3$O$_4$ [M + H]$^+$ 366.1448, found 366.1446.

$N$-cyclohexyl-4,5,6-trimethoxy-1$H$-indole-2-carboxamide (1c)

302 mg, 91% yield, brown solid, mp 230-233 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.42 (s, 1H), 6.87 (d, $J$ = 2.1 Hz, 1H), 6.66 (s, 1H), 5.99 (d, $J$ = 8.0 Hz, 1H), 4.13 (s, 3H), 4.03 - 4.00 (m, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 2.09 - 2.06 (m, 2H), 1.82 - 1.78 (m, 2H), 1.72 - 1.70 (m, 1H), 1.49 - 1.41 (m, 2H), 1.33 - 1.24 (m, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 160.6, 153.2, 146.2, 136.2, 133.4, 129.3, 115.5, 99.6, 89.4, 61.5, 60.9, 56.1, 48.5, 33.3, 25.5, 25.0. HRMS (ESI) m/z calcd for C$_{18}$H$_{25}$N$_2$O$_4$ [M + H]$^+$ 333.1809, found 333.1805.

$N$-((1$R$,3$S$,5$r$,7$r$)-adamantan-2-yl)-4,5,6-trimethoxy-1$H$-indole-2-carboxamide (2d)

323 mg, 84% yield, white solid, mp 209-212 °C. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 11.33 (s, 1H), 7.69 (d, $J$ = 6.9 Hz, 1H), 7.40 (s, 1H), 6.67 (s, 1H), 4.09 - 4.08 (m, 1H), 4.02 (s, 3H), 3.80 (s, 3H), 3.70 (s, 3H), 2.15 (d, $J$ = 12.5 Hz, 2H), 1.99 - 1.98 (m, 2H), 1.86 - 1.84 (m, 6H), 1.74 (s, 2H), 1.55 (d, $J$ = 12.5 Hz, 2H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) $\delta$ 161.0, 152.5, 146.2, 135.4, 134.1, 130.4, 114.9, 102.0, 90.2, 61.3, 60.8, 56.2, 54.1, 37.7, 37.4, 31.9, 31.6, 27.3. HRMS (ESI) m/z calcd for C$_{22}$H$_{28}$NaN$_2$O$_4$ [M + Na]$^+$ 407.1941, found 407.1937.
4,5,6-trimethoxy-N-phenyl-1H-indole-2-carboxamide (2e)

301 mg, 92% yield, brown solid, mp 229-232 °C. 1H NMR (500 MHz, CDCl₃) δ 9.49 (s, 1H), 7.81 (s, 1H), 7.69 (d, J = 8.2 Hz, 2H), 7.42 (t, J = 7.9 Hz, 2H), 7.19 (t, J = 7.4 Hz, 1H), 7.08 (d, J = 1.2 Hz, 1H), 6.66 (s, 1H), 4.16 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H). 13C NMR (126 MHz, CDCl₃) δ 159.4, 153.8, 146.3, 137.6, 129.2, 128.8, 124.5, 120.0, 100.8, 89.3, 61.5, 61.0, 56.1. HRMS (ESI) m/z calcd for C₁₈H₁₉N₂O₄ [M + H]+ 327.1339, found 327.1336.

methyl (4,6-dimethyl-1H-indole-2-carbonyl)glycinate (2f)

198 mg, 76% yield, pink solid, mp 189-191 °C. 1H NMR (500 MHz, DMSO-d₆) δ 11.45 (s, 1H), 8.88 (t, J = 5.9 Hz, 1H), 7.16 (s, 1H), 7.04 (s, 1H), 6.69 (s, 1H), 4.05 (d, J = 5.9 Hz, 2H), 3.67 (s, 3H), 2.45 (s, 3H), 2.35 (s, 3H). 13C NMR (126 MHz, DMSO-d₆) δ 171.0, 162.1, 137.3, 133.4, 130.5, 130.3, 125.7, 122.3, 110.0, 102.3, 100.0, 52.2, 22.0, 18.9. HRMS (ESI) m/z calcd for C₁₄H₁₇N₂O₃ [M + H]+ 261.1234, found 261.1231.

N-(4-chlorophenyl)-4,6-dimethyl-1H-indole-2-carboxamide (2g)

221 mg, 74% yield, yellow solid, mp 258-261 °C. 1H NMR (500 MHz, Acetone-d₆) δ 10.80 (s, 1H), 9.69 (s, 1H), 7.92 - 7.90 (m, 2H), 7.40 - 7.39 (m, 2H), 7.35 (s, 1H), 7.21 (s, 1H), 6.77 (s, 1H), 2.50 (s, 3H), 2.41 (s, 3H). 13C NMR (126 MHz, Acetone-d₆) δ 159.9, 138.2, 137.6, 134.3, 130.7, 128.6, 127.7, 125.9, 122.4, 121.2, 121.2, 109.5, 109.5,
102.1, 21.1, 17.8. HRMS (ESI) m/z calcd for C_{17}H_{16}ClN_{2}O [M + H]^+ 299.0946, found 299.0948.

**N-(2-methoxybenzyl)-4,6-dimethyl-1H-indole-2-carboxamide (2h)**

![Chemical Structure](image)

192 mg, 62% yield, white solid, mp 199-202 °C. ¹H NMR (500 MHz, CDCl₃) δ 9.16 (s, 1H), 7.39 (dd, J = 7.4, 1.6 Hz, 1H), 7.32 (td, J = 8.0, 1.7 Hz, 1H), 7.07 (s, 1H), 6.98 (td, J = 7.5, 0.9 Hz, 1H), 6.95 (d, J = 8.2 Hz, 1H), 6.80 - 6.79 (dd, J = 2.7, 1.8 Hz, 2H), 6.64 (s, 1H), 3.94 (s, 5H), 2.52 (s, 3H), 2.44 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 161.5, 157.7, 136.5, 134.7, 131.0, 129.9, 129.7, 129.1, 126.1, 125.7, 122.8, 120.8, 110.5, 109.1, 100.3, 55.5, 39.5, 21.8, 18.6. HRHRMS (ESI) m/z calcd for C₁₉H₂₁N₂O₂ [M + H]^+ 309.1598, found 309.1599.

**4,6-dimethyl-N-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)-1H-indole-2-carboxamide (2i)**

![Chemical Structure](image)

213 mg, 72% yield, white solid, mp 126-128 °C, dr~1:5:15. ¹H NMR (500 MHz, CDCl₃) δ 9.68 (s, 0.2H), 9.63 (s, 0.6H), 9.53 (s, 0.05H), 7.13 (s, 0.2H), 7.12 (s, 0.6H), 6.85 (d, J = 1.4 Hz, 0.2H), 6.81 (d, J = 3.7 Hz, 0.8H), 6.71 (d, J = 1.4 Hz, 0.6H), 6.29 (d, J = 6.8 Hz, 0.03H), 6.22 (d, J = 9.0 Hz, 0.2H), 6.13 (d, J = 8.9 Hz, 0.6H), 4.59 - 4.54 (m, 0.12H), 4.40 - 4.34 (m, 0.02H), 4.24 - 4.19 (m, 0.6H), 2.56 - 2.55 (m, 3H), 2.46 - 2.45 (m, 3H), 2.03 - 1.99 (m, 1H), 1.87 - 1.68 (m, 4H), 1.53 - 1.41 (m, 1H), 1.36 - 1.24 (m, 0.1H), 1.09 - 1.07 (m, 3H), 0.97 - 0.92 (m, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 162.00, 161.2, 136.7, 134.5, 130.9, 130.8, 129.9, 125.7, 125.7, 122.8, 109.4, 109.3, 99.9, 99.5, 56.9, 54.0, 49.8, 49.1, 48.3, 47.2, 45.02, 44.99, 39.2, 37.9, 36.0, 28.5, 28.2, 27.1, 21.9, 20.0, 19.9, 18.73, 18.66, 13.8, 11.9. HRMS (ESI) m/z calcd for C₂₁H₂₉N₂O [M + H]^+ 325.2274, found 325.2276.
**S-17**

**N-(2-isopropylphenyl)-5,6-dimethyl-1H-indole-2-carboxamide (2j)**

\[
\begin{align*}
\text{H} & \quad \text{N} \\
\text{H} & \quad \text{O} \\
\text{H} & \quad \text{N}
\end{align*}
\]

190 mg, 62% yield, Colorless solid, mp 159-162 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.32 (s, 1H), 7.31 - 7.28 (m, 2H), 7.24 (dd, \(J = 7.5, 1.2\) Hz, 1H), 7.20 - 7.16 (m, 2H), 7.09 - 7.05 (m, 2H), 6.99 (s, 1H), 3.27 (dt, \(J = 13.6, 6.8\) Hz, 1H), 2.32 (s, 3H), 2.29 (s, 3H), 1.40 (d, \(J = 6.8\) Hz, 6H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 159.0, 138.3, 137.8, 133.4, 132.4, 131.3, 130.5, 128.7, 123.8, 123.0, 122.1, 122.1, 122.0, 117.9, 108.2, 27.1, 22.8, 20.0, 19.1. HRMS (ESI) m/z calcd for C\(_{20}\)H\(_{23}\)N\(_2\)O \([M + H]^+\) 307.1805, found 307.1806.

**N-(4-chlorobenzyl)-6-methoxy-1H-indole-2-carboxamide (2k)**

\[
\begin{align*}
\text{O} & \quad \text{H} \\
\text{O} & \quad \text{H} \\
\text{N}
\end{align*}
\]

301 mg, 96%(ratio=15:1) yield, White solid, mp 208-211 °C. \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) \(\delta\) 11.44 (s, 1H), 8.95 (t, \(J = 6.0\) Hz, 1H), 7.49 (d, \(J = 8.7\) Hz, 1H), 7.41 (d, \(J = 8.5\) Hz, 2H), 7.36 (d, \(J = 8.5\) Hz, 2H), 7.11 (s, 1H), 6.89 (d, \(J = 2.0\) Hz, 1H), 6.70 (dd, \(J = 8.7, 2.2\) Hz, 1H), 4.49 (d, \(J = 6.0\) Hz, 2H), 3.77 (s, 3H). \(^{13}\)C NMR (126 MHz, DMSO-\(d_6\)) \(\delta\) 161.7, 157.5, 139.3, 137.9, 131.8, 130.8, 129.5, 128.7, 122.8, 122.7, 121.8, 111.5, 111.4, 103.5, 94.5, 55.6, 41.9. HRMS (ESI) m/z calcd for C\(_{17}\)H\(_{16}\)ClN\(_2\)O\(_2\) \([M + H]^+\) 315.0895, found 315.0896.

**N-benzyl-6-methoxy-1H-indole-2-carboxamide (2l)**

\[
\begin{align*}
\text{O} & \quad \text{H} \\
\text{O} & \quad \text{H} \\
\text{N}
\end{align*}
\]

260 mg, 93%(ratio=16:1) yield, White solid, mp 206-208 °C. \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) \(\delta\) 11.39 (s, 1H), 8.89 (t, \(J = 6.0\) Hz, 1H), 7.49 (d, \(J = 8.7\) Hz, 1H), 7.34 (d, \(J = 4.2\) Hz, 4H), 7.27-7.24 (m, 1H), 7.11 (d, \(J = 1.4\) Hz, 1H), 6.89 (d, \(J = 1.6\) Hz, 1H), 6.70 (dd, \(J = 8.7, 2.1\) Hz, 1H), 4.51 (d, \(J = 6.0\) Hz, 2H), 3.77 (s, 3H). \(^{13}\)C NMR (126 MHz, DMSO-\(d_6\)) \(\delta\) 161.6, 157.5, 140.2, 137.9, 131.0, 128.8, 127.7, 127.2, 122.7, 121.9, 111.4, 103.4, 94.6, 55.6, 42.6. HRMS (ESI) m/z calcd for C\(_{17}\)H\(_{17}\)N\(_2\)O\(_2\) \([M + H]^+\)
281.1285, found 281.1288.

**N-benzyl-6-bromo-1H-indole-2-carboxamide (2m)**

128 mg, 39% (2m:2m'(3:2)) yield, ice cream solid. $^1$H NMR (500 MHz, Acetone-$d_6$) $\delta$ 11.21 (s, 0.2H), 11.02 (s, 0.3H), 8.52 (s, 0.4H), 8.39 (s, 0.6H), 7.78 (s, 0.6H), 7.61 - 7.58 (m, 1H), 7.43 - 7.39 (m, 2H), 7.37 - 7.32 (m, 5H), 7.30 (s, 0.3H), 7.27 - 7.16 (m, 3H), 4.67 (d, $J = 6.1$ Hz, 0.8H), 4.64 (d, $J = 6.1$ Hz, 1.6H). $^{13}$C NMR (126 MHz, Acetone-$d_6$) $\delta$ 160.9, 160.8, 139.5, 137.5, 137.0, 128.345766, 128.345763, 127.5087, 127.5086, 126.9330, 126.9329, 124.6172, 124.6169, 123.3135, 123.3121, 123.1896, 123.1895, 122.7897, 122.7896, 116.69513, 116.69508, 114.8611, 114.8610, 102.2391, 102.2388, 101.9828, 101.9826, 42.7. HRMS (ESI) m/z calcd for C$_{16}$H$_{14}$BrN$_2$O [M + H]$^+$ 329.0284, found 329.0284.

**N-(2-(1H-indol-2-yl)ethyl)-7-methyl-1H-indole-2-carboxamide (2n)**

168 mg, 53% yield, yellow oil. *Mixture of rotamers observed.* $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.44 (s, 0.4H), 8.33 (s, 0.4H), 7.45 - 7.44 (m, 0.5H), 7.39 (s, 0.5H), 7.31 - 7.23 (m, 6H), 7.09 (d, $J = 7.2$ Hz, 1H), 7.01 - 6.95 (m, 2H), 6.79 (dd, $J = 7.9$, 4.2 Hz, 1H), 5.60 (dd, $J = 8.1$, 5.3 Hz, 1H), 4.16 - 4.07 (m, 1H), 4.00 - 3.93 (m, 1H), 3.45 - 3.36 (m, 1H), 2.53 - 2.46 (m, 1H), 2.43 (s, 1.5H), 2.38 (s, 1.5H), 1.90 - 1.83 (m, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 163.1, 162.9, 159.5, 158.3, 142.8, 142.6, 139.5, 136.0, 135.5, 133.6, 133.0, 132.3, 131.5, 131.2, 129.0, 128.8, 128.7, 128.2, 128.1, 127.6, 127.1, 126.9, 125.5, 125.3, 122.8, 122.4, 115.8, 109.5, 109.4, 46.1, 45.1, 18.4. HRMS (ESI) m/z calcd for C$_{20}$H$_{20}$N$_3$O [M + H]$^+$ 318.1601, found 318.1602.
N-benzyl-1H-indole-2-carboxamide (2o)

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

56 mg, 22% yield, ice cream solid, mp 204-207 °C. \(^1\)H NMR (500 MHz, Acetone-\(d_6\)) \(\delta\)
10.83 (s, 1H), 8.32 (s, 1H), 7.63 (d, \(J = 8.0\) Hz, 1H), 7.57 (d, \(J = 8.3\) Hz, 1H), 7.41 -
7.33 (m, 4H), 7.28 - 7.22 (m, 2H), 7.18 (s, 1H), 7.08 (t, \(J = 7.5\) Hz, 1H), 4.64 (d, \(J = 6.2\)
Hz, 2H). \(^{13}\)C NMR (126 MHz, Acetone-\(d_6\)) \(\delta\) 139.7, 128.3, 127.5, 126.9, 123.6, 121.6,
120.0, 112.2, 102.1, 42.6. HRMS (ESI) m/z calcd for C\(_{16}\)H\(_{15}\)N\(_2\)O [M + H]\(^+\) 251.1179,
found 251.1183.

N-phenyl-1H-indole-2-carboxamide (2p)

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

101 mg, 43% yield, ice cream solid, mp 217-219 °C. \(^1\)H NMR (500 MHz, Acetone-\(d_6\)) \(\delta\)
11.14 (s, 1H), 7.57 - 7.51 (m, 3H), 7.46 - 7.38 (m, 5H), 7.30 (t, \(J = 7.5\) Hz, 1H), 7.17
(t, \(J = 7.5\) Hz, 1H), 7.05 (t, \(J = 7.2\) Hz, 1H). \(^{13}\)C NMR (126 MHz, Acetone-\(d_6\)) \(\delta\) 141.2,
133.3, 132.8, 129.3, 125.7, 125.6, 122.4, 122.0, 121.5, 119.5, 119.4, 114.7, 107.3.
HRMS (ESI) m/z calcd for C\(_{15}\)H\(_{13}\)N\(_2\)O [M + H]\(^+\) 237.1022, found 237.1027.

N-(4-fluorobenzyl)-5,7-dimethyl-1H-indole-2-carboxamide (2q)

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

189 mg, 64% yield, yellow oil. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.25 (s, 1H), 7.35 (dd, \(J =
8.5, 5.4\) Hz, 2H), 7.26 (s, 1H), 7.08 - 7.04 (m, 2H), 6.95 (s, 1H), 6.80 (d, \(J = 2.1\) Hz,
1H), 6.53 (s, 1H), 4.66 - 4.14 (m, 1H), 2.48 (s, 3H), 2.43 (s, 3H), 2.36 - 2.28 (m, 1H).
\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 162.3(d, \(^1\)J\(_{C,F}\) = 245.7 Hz), 161.8, 134.6, 133.9(d, \(^4\)J\(_{C,F}\)
= 2.5 Hz), 130.4, 130.1, 129.5 (d, \(^3\)J\(_{C,F}\) = 8.8 Hz), 127.5, 127.1, 121.0, 118.8, 115.7(d,
\(^2\)J\(_{C,F}\) = 21.4 Hz), 102.2, 43.0, 21.4, 16.6. \(^{19}\)F NMR (471 MHz, CDCl\(_3\)) \(\delta\) -114.72. HRMS
(ESI) m/z calcd for C\(_{16}\)H\(_{18}\)FN\(_2\)O [M + H]\(^+\) 297.1398, found 297.1400.
7-methyl-N-phenyl-1H-indole-2-carboxamide (2r)

\[
\text{ \includegraphics[width=0.2\textwidth]{image}}
\]
143 mg, 57% yield, yellow solid, mp 129-134 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.53 (s, 1H), 7.46 - 7.44 (m, 1H), 7.41 - 7.39 (m, 1H), 7.35 - 7.29 (m, 2H), 7.28 - 7.26 (m, 3H), 7.21 - 7.18 (m, 1H), 7.12 (td, \(J = 7.5, 1.1\) Hz, 1H), 7.03 (s, 1H), 2.36 (s, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 159.1, 138.5, 134.0, 131.5, 131.4, 131.3, 126.9, 125.8, 125.6, 124.2, 123.3, 122.1, 122.0, 115.2, 108.1, 17.9. HRMS (ESI) m/z calcd for C\(_{16}\)H\(_{15}\)N\(_2\)O [M + H] \(^+\) 251.1179, found 251.1174.

N-cyclooctyl-4,6-dimethyl-1H-indole-2-carboxamide (2s)

\[
\text{ \includegraphics[width=0.2\textwidth]{image}}
\]
244 mg, 82% yield, colorless oil. Spectral data are in accordance to reported data.\(^{[1]}\) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.47 (s, 1H), 7.10 (s, 1H), 6.80 (d, \(J = 1.1\) Hz, 2H), 6.13 (d, \(J = 8.0\) Hz, 1H), 4.31 - 4.26 (m, 1H), 2.54 (s, 3H), 2.45 (s, 3H), 2.03 - 1.98 (m, 2H), 1.77 - 1.60 (m, 12H). HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{27}\)N\(_2\)O [M + H] \(^+\) 299.2118, found 299.2121.

N-cyclohexyl-4,6-dimethyl-1H-indole-2-carboxamide (2t)

\[
\text{ \includegraphics[width=0.2\textwidth]{image}}
\]
248 mg, 86% yield, white solid, mp 217-220 °C. Spectral data are in accordance to reported data.\(^{[1]}\) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.18 (s, 1H), 7.08 (s, 1H), 6.80 (dd, \(J = 2.2, 0.8\) Hz, 2H), 6.01 (d, \(J = 7.8\) Hz, 1H), 4.09 - 3.95 (m, 1H), 2.54 (s, 3H), 2.45 (s, 3H), 2.11 - 2.05 (m, 2H), 1.84 - 1.78 (m, 2H), 1.74 - 1.68 (m, 1H), 1.48 (ddt, \(J = 11.9, 9.9, 6.1\) Hz, 2H), 1.34 - 1.24 (m, 3H). HRMS (ESI) m/z calcd for C\(_{17}\)H\(_{25}\)N\(_2\)O [M + H] \(^+\) 271.1805, found 271.1809.
3. Exemplary copies of NMR spectra of novel compounds

\(N\)-benzyl-3,3-dimethoxy-2-\(N\)-(3,4,5-trimethoxyphenyl)formamido)propenamide (1a)
N-(4-cyanobenzyl)-3,3-dimethoxy-2-(N-(3,4,5-trimethoxyphenyl)formamido) propenamide (1b)
**N-cyclohexyl-3,3-dimethoxy-2-(N-(3,4,5-trimethoxyphenyl)formamido) propenamide (1c)**
3,3-dimethoxy-N-phenyl-2-(N-(3,4,5-trimethoxyphenyl)formamido)propenamide (1e)
methyl (2-[(3,5-dimethylphenyl)formamido]-3,3-dimethoxypropanoyl) glycinate (1f)
\[N-(4\text{-chlorophenyl})-2-(N-(3,5\text{-dimethylphenyl})\text{formamido})-3,3\text{-dimethoxypropanamide} \ (1g)\]
2-(N-(3,5-dimethylphenyl)formamido)-3,3-dimethoxy-N-(2-methoxybenzyl)propenamide (1h)
2-(N-(3,5-dimethylphenyl)formamido)-3,3-dimethoxy-N-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)propanamide (1i)
2-(N-(3,4-dimethylphenyl)formamido)-N-(2-isopropylphenyl)-3,3-dimethoxypropanamide (1j)
$N$-(4-chlorobenzyl)-3,3-dimethoxy-2-($N$-(3-methoxyphenyl)formamido) propenamide (1k)
$N$-benzyl-$3,3$-dimethoxy-$2$-($N$-($3$-methoxyphenyl)formamido)propenamide (11)
N-benzyl-2-(N-(3-bromophenyl)formamido)-3,3-dimethoxypropanamide (1m)
N-(2-(1H-indol-3-yl)ethyl)-3,3-dimethoxy-2-(N-o-tolyformamido)propenamide (1n)
N-benzyl-3,3-dimethoxy-2-(N-phenylformamido)propenamide (1o)
3,3-dimethoxy-N-phenyl-2-(N-phenylformamido)propenamide (1p)
$N$-benzyl-4,5,6-trimethoxy-1$H$-indole-2-carboxamide (2a)
$N$-(4-cyanobenzyl)-4,5,6-trimethoxy-$1H$-indole-2-carboxamide (2b)
$N$-cyclohexyl-4,5,6-trimethoxy-1$H$-indole-2-carboxamide (1c)
$N\-((1R,3S,5r,7r\-adamantan\-2\-yl)\-4,5,6\-trimethoxy\-1H\-indole\-2\-carboxamide\ (2d)$
4,5,6-trimethoxy-N-phenyl-1H-indole-2-carboxamide (2e)
methyl (4,6-dimethyl-1H-indole-2-carbonyl)glycinate (2f)
N-(4-chlorophenyl)-4,6-dimethyl-1H-indole-2-carboxamide (2g)
$N$-(2-methoxybenzyl)-4,6-dimethyl-1$H$-indole-2-carboxamide (2h)
4,6-dimethyl-\textit{N}-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)-1\textit{H}-indole-2-carboxamide (2i)
N-(2-isopropylphenyl)-5,6-dimethyl-1H-indole-2-carboxamide (2j)
$N$-(4-chlorobenzyl)-6-methoxy-$1H$-indole-2-carboxamide (2k)
N-benzyl-6-methoxy-1H-indole-2-carboxamide (2l)
$N$-benzyl-6-bromo-$1H$-indole-2-carboxamide (2m)
$N$-(2-$\text{H-indol-2-yl}$)ethyl)-7-methyl-$\text{H-indole-2-carboxamide}$ (2n)
N-benzyl-1H-indole-2-carboxamide (2o)
N-phenyl-1H-indole-2-carboxamide (2p)
N-(4-fluorobenzyl)-5,7-dimethyl-1H-indole-2-carboxamide (2q)
7-methyl-N-phenyl-1H-indole-2-carboxamide (2r)
$N$-cyclooctyl-4,6-dimethyl-$1H$-indole-2-carboxamide (2s)

$N$-cyclohexyl-4,6-dimethyl-$1H$-indole-2-carboxamide (2t)
4. Environmental factor (E-factor), Process Mass Intensity (PMI) and Atom Economy (AE) calculations

The reaction conditions of \(N\)-cyclohexyl-4,6-dimethyl-1H-indole-2-carboxamide (2t) synthesis were taken from literature.\(^2\) While calculating the E-factors, we didn’t consider the amount of silica gel used for flash column chromatography as it is generally not reported.

In our case, for a 1 mmol scale reaction we used 15 g of 100 - 200 mesh size silica for the purification in only one step (one-pot synthesis of 2t). However, the amount of silica gel that is employed on the other three methods is considerably higher due to the purification of at least two steps and the increased scale of the reactions described. Therefore, the inclusion of silica gel waste would considerably increase the difference in E-factor between our reported synthesis and the previous ones.

Calculations of the E-factor, PMI and AE (atom economy) values for the \(N\)-cyclohexyl-4,6-dimethyl-1H-indole-2-carboxamide syntheses:

\[
\text{E-factor} = \frac{\text{Mass (waste)}}{\text{Mass (product)}}
\]

\[
\text{PMI} = \frac{\text{Mass (total)}}{\text{Mass (product)}} = \text{E-factor} + 1
\]

\[
\text{AE} = \left( \frac{\text{Molecular mass of desired product}}{\text{Sum of molecular masses of all reactants}} \right) \times 100\%
\]
For the AE calculation any material that is incorporated into an intermediate or product during the synthesis is taken into account. This includes protecting groups, catalysts used in stoichiometric quantities and acids or bases used for hydrolysis. Solvents, reagents or materials used in catalytic quantities are omitted from the analysis, as they do not contribute atoms to an intermediate and/or product.\[8\]

<table>
<thead>
<tr>
<th>Reagents</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,5-dimethylphenylhydrazine hydrochloride</td>
<td>0.5 g</td>
</tr>
<tr>
<td>ethyl pyruvate</td>
<td>0.5 g</td>
</tr>
<tr>
<td>p-Toluenesulfonic acid monohydrate</td>
<td>1.1 g</td>
</tr>
<tr>
<td>Benzen (assuming 90% recovery)</td>
<td>9.9 ml x (0.876 g/ml) x 10% = 0.9 g</td>
</tr>
<tr>
<td>Sat. NaHCO₃ sol. (calculated by weight)</td>
<td>7.2 ml x 1.1 g/ml = 7.9 g</td>
</tr>
<tr>
<td>Sat. NaCl sol. (calculated by weight)</td>
<td>15.0 ml x 1.2 g/ml = 18 g</td>
</tr>
<tr>
<td>Water</td>
<td>5 g + 2.3 g + 2.18 g = 9.5 g</td>
</tr>
<tr>
<td>LiOH</td>
<td>0.2 g</td>
</tr>
<tr>
<td>HCl(aq) (6N)</td>
<td>1.85 ml x 1.1 g/ml = 2.0 g</td>
</tr>
<tr>
<td>HOBt</td>
<td>0.2 g</td>
</tr>
<tr>
<td>TEA</td>
<td>0.2 g</td>
</tr>
<tr>
<td>EDC HCl</td>
<td>0.2 g</td>
</tr>
<tr>
<td>cyclohexanamine</td>
<td>0.1 g</td>
</tr>
<tr>
<td>DMF</td>
<td>4.4 ml x 0.944 g/ml = 4.1 g</td>
</tr>
<tr>
<td>Na₂SO₄ used for drying (assuming 1g/mmol)</td>
<td>2.87 g + 1.09 g = 4.0 g</td>
</tr>
<tr>
<td>EtOH (assuming as 90% recovery)</td>
<td>2.3 ml x (0.789 g/ml) x 10% = 0.2 g</td>
</tr>
<tr>
<td>Hexane (assuming as 90% recovery)</td>
<td>335ml x (0.661 g/ml) x 10% = 26.4 g</td>
</tr>
<tr>
<td>EtOAc (assuming as 90% recovery)</td>
<td>124 ml x (0.902 g/ml) x 10% = 11.2 g</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>87.2 g</strong></td>
</tr>
</tbody>
</table>

**Amount of product = 0.27 g**

E-Factor = Amount of waste/Amount of product = (87.2-0.27) g/0.27 g = 322.0

**E-factor = 322.0**

\[
AE = \frac{270}{(172+1.5x116+2x190+18+5x24+99+135+1.5x101+192)} \times 100\% = \frac{270}{1441.5} \times 100\% = 18.7\%
\]

Reagents | Amount
---|---
3,5-dimethylphenylhydrazine hydrochloride | 2.0 g
ethyl pyruvate | 2.0 g
p-Toluenesulfonic acid monohydrate | 4.4 g
EtOH (assuming as 90% recovery) | 47.44 mL x (0.789 g/mL) x 10% = 3.7 g
Sat. NaHCO₃ sol. | 50 mL x 1.1 g/mL = 55 g
Sat. NaCl sol. | 20 mL x 1.2 g/mL = 24.0 g
Water | 27.4 mL x 1.0 g/mL = 27.4 g
NaOH | 0.7 g
HCl(aq) (6N) | 3.2 mL x 1.1 g/mL = 3.5 g
DCC | 0.5 g
DMAP | 0.1 g
cyclohexanamine | 0.2 g
DCM (assuming as 90% recovery) | 31.7 mL x (1.33 g/mL) x 10% = 4.2 g
Na₂SO₄ used for drying (assuming 1g/mmol) | 11.6 g
Hexane (assuming as 90% recovery) | 1254 mL x (0.661 g/mL) x 10% = 82.9 g
EtOAc (assuming as 90% recovery) | 343 mL x (0.902 g/mL) x 10% = 30.9 g
Total | 253.1 g

Amount of product = 0.27 g

E-Factor = Amount of waste/Amount of product = (253.1-0.27) g/0.27 g = 936.4

E-factor = 936.4

AE = (270/(172+1.5x116+2x190+18+5x40+99+1.2x206)) x 100%=(270/1249) x 100% = 21.6%

Reagents | Amount
--- | ---
3,5-dimethylphenylhydrazine hydrochloride | 0.3 g
ethyl pyruvate | 0.3 g
p-Toluenesulfonic acid monohydrate | 0.6 g
Toluene (assuming 90% recovery) | 5.6 ml x (0.876 g/ml) x 10% = 0.5 g
Sat. NaHCO₃ sol. (calculated by weight) | 4.1 ml x 1.1 g/ml = 4.5 g
Sat. NaCl sol. (calculated by weight) | 13.0 ml x 1.2 g/ml = 15.6 g
Water | 3 g + 1.5 g + 2.18 g = 6.7 g
LiOH | 0.2 g
HCl(aq) (6N) | 1.24 ml x 1.1 g/ml = 1.4 g
N-methyl morpholine | 0.2 g
HOBt | 0.2 g
EDC.HCl | 0.2 g
cyclohexanamine | 0.1 g
DMF | 4.4 ml x 0.944 g/ml = 4.1 g
Na₂SO₄ used for drying (assuming 1g/mmol) | 1.7 g + 1.09 g = 2.8 g
EtOH (assuming as 90% recovery) | 1.5 ml x (0.789 g/ml) x 10% = 0.1 g
Hexane (assuming as 90% recovery) | 193.8 ml x (0.661 g/ml) x 10% = 12.8 g
EtOAc (assuming as 90% recovery) | 63.9 ml x (0.902 g/ml) x 10% = 5.6 g
Total | 62.0 g

Amount of product = 0.27 g

E-Factor = Amount of waste/Amount of product = (62.0-0.27) g/0.27 g = 228.6

E-factor = 228.6

AE = (270/(172+1.5x116+2x190+18+5x24+99+135+1.5x101+192)) x 100% = (270/1441.5) x 100% = 18.7%
4. Our current work

\[
\begin{align*}
\text{NH}_2 & \quad \text{NC} \\
\text{CHO} & \quad \text{HCOOH}
\end{align*}
\]

\[
\begin{align*}
140 \text{ mg} & + \quad 136 \text{ mg} \\
201 \text{ mg} & \quad 53 \text{ mg}
\end{align*}
\]

\[
\begin{align*}
\text{MeOH} (1.2 \text{ ml}) \\
\text{MSA (1.5 g)} \text{ sat. NaHCO}_3 \text{ sol. (calculated by weight)}
\end{align*}
\]

\[
\begin{align*}
\text{Na}_2\text{SO}_4 \text{ used for drying (assuming 1g/mmol)} & = 1.2 \text{ g} \\
\text{MeOH (assuming as 90% recovery)} & = 1.2 \text{ ml} \times (0.792 \text{ g/ml}) \times 10\% = 0.1 \text{ g} \\
\text{Petroleum ether (assuming as 90% recovery)} & = 93 \text{ ml} \times (0.653 \text{ g/ml}) \times 10\% = 6.1 \text{ g} \\
\text{EtOAc (assuming as 90% recovery)} & = 29 \text{ ml} \times (0.902 \text{ g/ml}) \times 10\% = 2.6 \text{ g}
\end{align*}
\]

\[
\begin{array}{|c|c|}
\hline
\text{Reagents} & \text{Amount} \\
\hline
3,5-dimethylaniline & 0.1 \text{ g} \\
2,2-dimethoxyacetalddehyde & 0.2 \text{ g} \\
isocyanocyclohexane & 0.1 \text{ g} \\
formic acid & 0.1 \text{ g} \\
MSA & 1.5 \text{ g} \\
\text{Sat. NaHCO}_3 \text{ sol. (calculated by weight)} & 10 \text{ ml} \times 1.1 \text{ g/ml} = 11 \text{ g} \\
\text{Na}_2\text{SO}_4 \text{ used for drying (assuming 1g/mmol)} & 1.2 \text{ g} \\
\text{MeOH (assuming as 90% recovery)} & 1.2 \text{ ml} \times (0.792 \text{ g/ml}) \times 10\% = 0.1 \text{ g} \\
\text{Petroleum ether (assuming as 90% recovery)} & 93 \text{ ml} \times (0.653 \text{ g/ml}) \times 10\% = 6.1 \text{ g} \\
\text{EtOAc (assuming as 90% recovery)} & 29 \text{ ml} \times (0.902 \text{ g/ml}) \times 10\% = 2.6 \text{ g} \\
\hline
\text{Total} & 23 \text{ g}
\end{array}
\]

Amount of product = 0.27 g

\[
\text{E-Factor} = \frac{\text{Amount of waste}}{\text{Amount of product}} = \frac{(23-0.27) \text{ g}}{0.27 \text{ g}} = 84.2
\]

\[
\text{E-factor} = 84.2
\]

\[
\begin{align*}
\text{Mt:} & \quad 270 \\
\text{Mt:} & \quad 121 \\
\text{Mt:} & \quad 109 \\
\text{Mt:} & \quad 104 \\
\text{Mt:} & \quad 46
\end{align*}
\]

\[
\begin{align*}
\text{AE} & = \frac{270}{(121+104+109+46)} \times 100\% = \frac{270}{380} \times 100\% = 71.1\%
\end{align*}
\]

**Note:** The experimental procedures of 1-3 follow the Fischer indole synthesis; the differences are based on the solvents, timeframes and various additives. The amounts were calculated based on the experimental procedures reported on each paper or the references mentioned there. Importantly, inclusion of the phenylhydrazine syntheses (many of which are not commercially available or quite expensive) would considerably worsen the PMI and E-factors of the competing procedures.

Thus, herein we summarized the E-factor, PMI and AE calculations of the various literature process of N-cyclohexyl-4,6-dimethyl-1H-indole-2-carboxamide synthesis.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reference</th>
<th>E-factor</th>
<th>PMI</th>
<th>AE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kondreddi et al. 2013</td>
<td>322.0</td>
<td>323.0</td>
<td>18.7</td>
</tr>
<tr>
<td>2</td>
<td>Franz et al. 2017</td>
<td>936.4</td>
<td>937.4</td>
<td>21.6</td>
</tr>
<tr>
<td>3</td>
<td>Bishai et al. 2015</td>
<td>228.6</td>
<td>229.6</td>
<td>18.7</td>
</tr>
<tr>
<td>4</td>
<td>Present work</td>
<td>84.2</td>
<td>85.2</td>
<td>71.1</td>
</tr>
</tbody>
</table>
Isocyanide E-factor calculation

\[
\text{NH}_2 + \text{EtOCHO} (135 \text{ mg}) \rightarrow \text{H}_2\text{N} - \text{N} = \text{O} \rightarrow \text{NC}
\]

1.22 mmol, 121 mg  \[\rightarrow\]  1.2 mmol, 99%

POCl₃ (0.153 g), TEA (0.51 g)
DCM (0.5 ml)
Purification by flash silica column using ether/DCM:ether 2.2ml, DCM 0.35 ml

1.16 mmol 126 mg, 96 %

<table>
<thead>
<tr>
<th>Reagents</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclohexanamine</td>
<td>0.1 g</td>
</tr>
<tr>
<td>EtOCHO</td>
<td>0.1 g</td>
</tr>
<tr>
<td>TEA</td>
<td>0.5 g</td>
</tr>
<tr>
<td>POCl₃</td>
<td>0.2 g</td>
</tr>
<tr>
<td>diethyl ether (assuming as 90% recovery)</td>
<td>2.2 ml x (0.706 g/ml) x 10% = 0.2 g</td>
</tr>
<tr>
<td>DCM (assuming as 90% recovery)</td>
<td>0.85 ml x (1.33 gm/ml) x 10% = 0.1 g</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1.2 g</strong></td>
</tr>
</tbody>
</table>

Amount of product = 0.27 g

E-Factor = Amount of waste/Amount of product = 1.2 g/0.27 g = 4.4

**E-factor = 4.4**
5. Single crystal x-ray structure determination

Data for compound 2f

Single crystals of C_{14}H_{16}N_{2}O_{3} (2f) were carefully collected under a microscope. A suitable crystal was selected and measured with a Bruker APEX-II CCD diffractometer. The crystal was kept at 210.00 K during data collection. Using Olex2, the structure was solved with the SHELXT structure solution program using Intrinsic Phasing and refined with the SHELXL refinement package using Least Squares minimization. All non-H atoms were refined with anisotropic thermal parameters. H-atoms were introduced at calculated positions and allowed to ride on their carrier atoms. Crystal data and structure refinement parameters for 2f are given in table 1 (CCDC No: 2174979).

Crystal structure determination of 2f

Crystal Data for C_{14}H_{16}N_{2}O_{3} (M =260.29 g/mol): monoclinic, space group P2\(_1\)/c (no. 14), a = 15.1633(10) Å, b = 5.1388(3) Å, c = 17.4106(11) Å, β = 101.494(3)°, V = 1329.45(14) Å\(^3\), Z = 4, T = 209.99 K, μ(CuKα) = 0.760 mm\(^{-1}\), D\(_\text{calc}\) = 1.300 g/cm\(^3\), 11578 reflections measured (5.948° ≤ 2Θ ≤ 118.014°), 1910 unique (R\(_\text{int}\) = 0.0360, R\(_\text{sigma}\) = 0.0268) which were used in all calculations. The final R\(_1\) was 0.0384 (I > 2σ(I)) and wR\(_2\) was 0.1248 (all data)

Table 1. Crystal data and structure refinement for 2f.

<table>
<thead>
<tr>
<th>Identification code</th>
<th>cu_lxf_118nl_2_0m_a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{14}H_{16}N_{2}O_{3}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>260.29</td>
</tr>
<tr>
<td>Temperature/K</td>
<td>209.99</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P2(_1)/c</td>
</tr>
<tr>
<td>a/Å</td>
<td>15.1633(10)</td>
</tr>
<tr>
<td>b/Å</td>
<td>5.1388(3)</td>
</tr>
<tr>
<td>c/Å</td>
<td>17.4106(11)</td>
</tr>
<tr>
<td>α/°</td>
<td>90</td>
</tr>
<tr>
<td>β/°</td>
<td>101.494(3)</td>
</tr>
<tr>
<td>γ/°</td>
<td>90</td>
</tr>
<tr>
<td>Volume/Å(^3)</td>
<td>1329.45(14)</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>(\rho) calc/g/cm(^3)</td>
<td>1.300</td>
</tr>
<tr>
<td>μ/mm(^{-1})</td>
<td>0.760</td>
</tr>
<tr>
<td>F(000)</td>
<td>552.0</td>
</tr>
</tbody>
</table>
Crystal size/mm$^3$ 0.06 $\times$ 0.04 $\times$ 0.02

Radiation CuK$\alpha$ ($\lambda$ = 1.54178)

2$\Theta$ range for data collection/$^\circ$ 5.948 to 118.014

Index ranges \[-16 \leq h \leq 16, -5 \leq k \leq 5, -19 \leq l \leq 19\]

Reflections collected 11578

Independent reflections 1910 [$R_{int} = 0.0360, R_{\sigma} = 0.0268$]

Data/restraints/parameters 1910/0/176

Goodness-of-fit on $F^2$ 1.142

Final R indexes [$I>2\sigma (I)$] $R_1 = 0.0384, wR_2 = 0.1097$

Final R indexes [all data] $R_1 = 0.0426, wR_2 = 0.1248$

Largest diff. peak/hole / e Å$^{-3}$ 0.18/-0.19
Data for compound 2g

Single crystals of C\textsubscript{17}H\textsubscript{15}ClN\textsubscript{2}O (2g) were carefully collected under a microscope. A suitable crystal was selected and measured with a Bruker APEX-II CCD diffractometer. The crystal was kept at 200.00 K during data collection. Using Olex2,\textsuperscript{4} the structure was solved with the SHELXT\textsuperscript{5} structure solution program using Intrinsic Phasing and refined with the SHELXL\textsuperscript{6} refinement package using Least Squares minimization. All non-H atoms were refined with anisotropic thermal parameters. H-atoms were introduced at calculated positions and allowed to ride on their carrier atoms. Crystal data and structure refinement parameters for 2g are given in table 2 (CCDC No: 2174980).

Crystal structure determination of 2g

Crystal Data for C\textsubscript{17}H\textsubscript{15}ClN\textsubscript{2}O (M = 298.76 g/mol): triclinic, space group P-1 (no. 2), a = 9.4666(3) Å, b = 9.9691(3) Å, c = 16.3110(4) Å, α = 100.1530(10)°, β = 104.0720(10)°, γ = 92.7510(10)°, V = 1463.08(7) Å\textsuperscript{3}, Z = 4, T = 199.98 K, μ(CuKα) = 2.304 mm\textsuperscript{-1}, D\textsubscript{calc} = 1.356 g/cm\textsuperscript{3}, 36534 reflections measured (5.694° ≤ 2Θ ≤ 149.102°), 5942 unique (R\textsubscript{int} = 0.0245, R\textsubscript{sigma} = 0.0157) which were used in all calculations. The final R\textsubscript{1} was 0.0375 (I > 2σ(I)) and wR\textsubscript{2} was 0.1122 (all data).

Table 2. Crystal data and structure refinement for 2g.

<table>
<thead>
<tr>
<th>Identification code</th>
<th>cu_LXF125_nl_0m_a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C\textsubscript{17}H\textsubscript{15}ClN\textsubscript{2}O</td>
</tr>
<tr>
<td>Formula weight</td>
<td>298.76</td>
</tr>
<tr>
<td>Temperature/K</td>
<td>199.98</td>
</tr>
<tr>
<td>Crystal system</td>
<td>triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P-1</td>
</tr>
<tr>
<td>a/Å</td>
<td>9.4666(3)</td>
</tr>
<tr>
<td>b/Å</td>
<td>9.9691(3)</td>
</tr>
<tr>
<td>c/Å</td>
<td>16.3110(4)</td>
</tr>
<tr>
<td>α/°</td>
<td>100.1530(10)</td>
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<tr>
<td>β/°</td>
<td>104.0720(10)</td>
</tr>
<tr>
<td>γ/°</td>
<td>92.7510(10)</td>
</tr>
<tr>
<td>Volume/Å\textsuperscript{3}</td>
<td>1463.08(7)</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>ρ\textsubscript{calc}/g/cm\textsuperscript{3}</td>
<td>1.356</td>
</tr>
<tr>
<td>μ/mm\textsuperscript{-1}</td>
<td>2.304</td>
</tr>
<tr>
<td>F(000)</td>
<td>624.0</td>
</tr>
<tr>
<td>Crystal size/mm\textsuperscript{3}</td>
<td>0.06 × 0.04 × 0.02</td>
</tr>
<tr>
<td>Radiation</td>
<td>CuKα (λ = 1.54178)</td>
</tr>
</tbody>
</table>
2θ range for data collection/° 5.694 to 149.102

Index ranges

-11 ≤ h ≤ 11, -12 ≤ k ≤ 12, -20 ≤ l ≤ 20

Reflections collected 36534

Independent reflections 5942 [Rint = 0.0245, Rsigma = 0.0157]

Data/restraints/parameters 5942/0/384

Goodness-of-fit on F^2 1.065

Final R indexes [I>2σ (I)] R_1 = 0.0375, wR_2 = 0.1080

Final R indexes [all data] R_1 = 0.0413, wR_2 = 0.1122

Largest diff. peak/hole / e Å^3 0.23/-0.30
References