New Friedel-Crafts strategy of preparing 3-acylindoles

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General information

Column chromatography was carried out on silica gel. $^1$H NMR spectra were recorded on 400 MHz in CDCl$_3$ and DMSO-$d_6$. $^{13}$C NMR spectra were recorded on 100 MHz in CDCl$_3$ and DMSO-$d_6$. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) and DMSO-$d_6$ as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), q (quartet), or m (multiplet). Their $^1$H NMR and $^{13}$C NMR spectra are provided in the Supporting Information. The HRMS was obtained using a Q-TOF instrument equipped with ESI source. Data collections for crystal structure were performed at room temperature (293 K) using Mo Kα radiation on a Bruker APEXII diffractometer. Melting points were measured with micro melting point apparatus.

The substituted amides were prepared according to the literature. $^1$ Trifluoromethanesulfonic anhydride (Tf$_2$O) was commercially available. Solvents were dried using standard methods. All commercially available reagents were used with further purification. The toluene was distilled over CaH$_2$. 
Optimization of the reaction conditions

Table S1 Additional optimization of the reaction a,b

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a Reaction conditions: To a mixture of indole 1a (X equiv.), amide 2a (Y equiv.) and base (Z equiv.) in solvent (3.0 mL) was added T3O (2.0 equiv.) at -78 °C under an Ar atmosphere. After 20 min, the reaction mixture was stirred at the reported temperature.

b All reactions were carried out on 0.2 mmol scale. c The additive (0.5 equiv.) was added. d Isolated yields. DCM = dichloromethane, DCE = 1, 2-dichloroethane, Tf = trifluoromethanesulfonyl, TMS = trimethylsilyl.

S3
General procedure for the synthesis of desired 3-acylindoles

\[
\text{Indole} \quad + \quad \text{Amide} \quad \xrightarrow{\text{Cs}_2\text{CO}_3, \text{CsF, Tf}_2\text{O}} \quad \text{3-acylindole}
\]

The amide (0.32 mmol, 1.6 equiv), Cs$_2$CO$_3$ (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The indole (0.2 mmol, 1.0 equiv), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf$_2$O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated NaHCO$_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na$_2$SO$_4$, concentrated in vacuum and subjected to column chromatography.
Further application

The amide 2a (0.32 mmol, 1.6 equiv.), Cs$_2$CO$_3$ (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The N,N-dimethyl aniline 4a (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf$_2$O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated NaHCO$_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na$_2$SO$_4$, concentrated in vacuum and subjected to column chromatography, afforded acylated aniline 5aa 7.59 mg in 15% isolated yield.

The amide 2a (0.32 mmol, 1.6 equiv.), Cs$_2$CO$_3$ (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The pyrrole 6a (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf$_2$O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated NaHCO$_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na$_2$SO$_4$, concentrated in vacuum and subjected to column chromatography, afforded product 7aa 22 mg in 55% isolated yield.
The amide 2a (0.32 mmol, 1.6 equiv.), Cs₂CO₃ (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The 1,2,3-trimethoxybenzene 8a (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf₂O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated NaHCO₃ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na₂SO₄, concentrated in vacuum and subjected to column chromatography, afforded product 9aa 16.2 mg in 27% isolated yield.

The amide 2a (0.32 mmol, 1.6 equiv.), Cs₂CO₃ (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The veratrole 10a (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf₂O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated NaHCO₃ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na₂SO₄, concentrated in vacuum and subjected to column chromatography, afforded product 11aa 6.48 mg in 12% isolated yield.
Mechanistic studies

a) Deuterated labelling experiment

The amide 2k (0.32 mmol, 1.6 equiv.), Cs$_2$CO$_3$ (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The indole 1a (0.2 mmol, 1 equiv.) or 1a-3d (0.2 mmol, 1 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf$_2$O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 30 minutes, the mixture was quenched by the saturated NaHCO$_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na$_2$SO$_4$, concentrated in vacuum and added p-bromotoluene (0.2 mmol) as internal standard, subjected to NMR tube. KIE value ($k_{H}/k_{D} = 1.11$) was determined by $^1$H NMR analysis (400 MHz, CDCl$_3$).
b) Monitoring experiment and NMR spectra

The first $^{13}$C NMR (100 MHz, CDCl$_3$) was standard spectrum of substrate 2k.

Four sets of the amide 2k (0.32 mmol, 1.6 equiv.), Cs$_2$CO$_3$ (0.52 mmol), CsF (0.1 mmol) were added to four dried round bottom flasks and put under an Ar atmosphere, respectively. The indole 1a (0.2 mmol, 1 equiv.), toluene (2.0 mL) were each added to four flasks and the solutions were cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf$_2$O (0.4 mmol) via syringe, respectively. All of four reactions kept under -78 °C for 20 minutes. Then, the first reaction was stopped without heating and concentrated in vacuum. The mixture was added to NMR tube and the second $^{13}$C NMR was acquired. The second reaction was heated at 70 °C for 15 minutes and stopped and concentrated in vacuum. The mixture was added to NMR tube and the third $^{13}$C NMR was acquired. The third reaction was heated for 1 hour and stopped and concentrated in vacuum. The mixture was added to NMR tube and the fourth $^{13}$C NMR was acquired. The fourth reaction was heated for 14 hours and stopped and concentrated in vacuum. The mixture was added to NMR tube and the fifth $^{13}$C NMR was acquired.

The sixth $^{13}$C NMR was standard spectrum of product 3ak.
c) Survey of intermediate I and analysis

The amide 2k (0.32 mmol, 1.6 equiv) and Cs$_2$CO$_3$ (0.52 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The toluene (2.0 mL) was added to the flask and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf$_2$O (0.4 mmol) via syringe. The reaction kept under -78 °C for 20 minutes. Then, the reaction was warmed to the room temperature and concentrated in vacuum. The mixture was added to NMR tube and the $^{13}$C NMR and $^{19}$F NMR were acquired as 2k+Tf$_2$O+Cs$_2$CO$_3$.

Analysis: Comparing the $^{13}$C NMR spectra of 2k+Tf$_2$O+Cs$_2$CO$_3$+indole 1a and 2k+Tf$_2$O+Cs$_2$CO$_3$ at low temperature labeling as 0 min, it was noticed that when the amide was treated with Tf$_2$O and Cs$_2$CO$_3$ without indole, the system was detected out only B signal, and that could be assigned to intermediate I, and when the system was added indole, the intermediate I could be transferred into intermediate II by the attack of indole in short time. Therefore, the signals B and C are relevant $^{13}$C NMR signal.
Analysis: Comparing the $^{19}$F NMR spectra of $2k +$Tf$_2$O+$Cs_2$CO$_3$ at low temperature and Tf$_2$O, it was confirmed that $2k$ could transfer into intermediate I.
$Zn + Cs_2CO_3 + TlF, 78^\circ C$

$TlF$
d) Recycling experiment of starting material 2k

The amide 2k (0.32 mmol, 1.6 equiv.), Cs₂CO₃ (0.52 mmol), CsF (0.1 mmol) were added to dried round bottom flask and put under an Ar atmosphere. The indole 1a (0.2 mmol, 1 equiv.), toluene (2.0 mL) were added to the flask and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf₂O (0.4 mmol) via syringe. The reaction kept under -78 °C for 20 minutes, and then heated to 70 °C. After 14 h, the reaction was quenched by the saturated NaHCO₃ solution and mixture was transferred to separation funnels, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na₂SO₄, concentrated in vacuum and subjected to column chromatography, afforded product 3ak 79% and recycled 47% of proportion of starting material 2k.
X-ray structures of Tetrazoles 3aa, 3al, 3ga, 3ua

The crystal structure of product 3aa

Crystallorgraphic data for compound 3aa (CCDC-1857322) has been deposited with Crystallorgraphic Data Centre. Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)

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The ellipsoid contour percent probability level is 30% in the caption of the thermal ellipsoid plot.
The crystal structure of product 3al

Crystallorgraphic data for compound 3al (CCDC-1857189) has been deposited with Crystallorgraphic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)

The ellipsoid contour percent probability level is 30% in the caption of the thermal ellipsoid plot.

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The crystal structure of product 3ga

Crystalllographic data for compound 3ga (CCDC-1857188) has been deposited with Crystalllographic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)

Bond precision: C-C = 0.0046 Å
Wavelength=1.54184 Å

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The crystal structure of product 3ua

Crystallographic data for compound 3ua (CCDC-1857187) has been deposited with Crystallographic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)

The ellipsoid contour percent probability level is 30% in the caption of the thermal ellipsoid plot.

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Characterization of compounds

(3aa) 1-(1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

brownish red crystal, 44.7 mg, 85%, m.p. 57-59 °C

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.43 – 8.38 (m, 1H), 7.64 (s, 1H), 7.34 – 7.25 (m, 7H), 7.23 – 7.16 (m, 1H), 3.79 (s, 3H), 3.19 – 3.14 (m, 2H), 3.14 – 3.07 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 194.4, 141.7, 137.3, 135.2, 128.4, 126.2, 125.9, 123.2, 122.5, 116.3, 109.5, 41.6, 33.4, 30.7.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{18}$H$_{17}$NO) requires m/z 264.1383, found m/z 264.1383.

(3ab) 1-(1-methyl-1H-indol-3-yl)propan-1-one

transparent crystal, 21.3 mg, 57%, m.p. 74-76 °C

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.50 – 8.28 (m, 1H), 7.69 (s, 1H), 7.44 – 7.27 (m, 3H), 3.81 (s, 3H), 2.86 (q, $J$ = 7.4 Hz, 2H), 1.25 (t, $J$ = 7.4 Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 196.3, 137.3, 134.9, 126.2, 123.1, 122.3, 116.1, 109.5, 33.4, 32.8, 8.9.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{12}$H$_{13}$NO) requires m/z 188.1070, found m/z 188.1069.

(3ac) 1-(1-methyl-1H-indol-3-yl)butan-1-one

crimson oily liquid, 26.1 mg, 65%

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.42 – 8.37 (m, 1H), 7.68 (s, 1H), 7.33 – 7.27 (m, 3H), 3.80 (s, 3H), 2.79 (t, $J$ = 7.2 Hz, 2H), 1.85 – 1.75 (m, 2H), 1.01 (t, $J$ = 7.2 Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 195.7, 137.3, 135.1, 126.2, 123.1, 122.5, 122.3, 116.5, 109.5, 41.8, 33.3, 18.6, 14.0.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{13}$H$_{15}$NO) requires m/z 202.1226, found m/z 202.1225.

(3ad) 1-(1-methyl-1H-indol-3-yl)pentan-1-one
bright red liquid, 25.0 mg, 58%

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 8.42 - 8.36 \ (m, 1H), 7.69 \ (s, 1H), 7.33 - 7.27 \ (m, 3H), 3.82 \ (s, 3H), 2.82 \ (t, J = 8.0 \text{ Hz, 2H}), 1.80 - 1.71 \ (m, 2H), 1.48 - 1.37 \ (m, 2H), 0.95 \ (t, J = 7.2 \text{ Hz, 3H}). \]

\[ ^{13}\text{C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 195.9, 137.4, 135.1, 126.3, 123.2, 122.6, 122.4, 116.5, 109.5, 39.6, 33.4, 27.3, 22.6, 13.9. \]

HRMS (ESI+): exact mass calculated for [M+H]+ (C14H17NO) requires m/z 216.1383, found m/z 216.1382.

(3ae) 1-(1-methyl-1H-indol-3-yl)hexan-1-one


crimson liquid, 24.3 mg, 53%

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 8.43 - 8.37 \ (m, 1H), 7.70 \ (s, 1H), 7.30 \ (dt, J = 7.6, 2.4 \text{ Hz, 3H}), 3.83 \ (s, 3H), 2.82 \ (t, J = 7.8 \text{ Hz, 2H}), 1.82 - 1.73 \ (m, 2H), 1.42 - 1.32 \ (m, 4H), 0.95 - 0.87 \ (m, 3H). \]

\[ ^{13}\text{C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 195.9, 137.4, 135.1, 126.3, 123.2, 122.6, 122.4, 116.5, 109.5, 39.9, 33.4, 27.3, 24.9, 22.5, 13.9. \]

HRMS (ESI+): exact mass calculated for [M+H]+ (C15H19NO) requires m/z 230.1539, found m/z 230.1539.

(3af) 1-(1-methyl-1H-indol-3-yl)heptan-1-one


aubergine liquid, 27.7 mg, 57%

\[ ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 8.41 - 8.37 \ (m, 1H), 7.69 \ (s, 1H), 7.33 - 7.27 \ (m, 3H), 3.81 \ (s, 3H), 2.84 - 2.79 \ (m, 2H), 1.82 - 1.72 \ (m, 2H), 1.42 - 1.35 \ (m, 2H), 1.35 - 1.29 \ (m, 4H), 0.91 - 0.86 \ (m, 3H). \]

\[ ^{13}\text{C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 195.9, 137.4, 135.1, 126.3, 123.1, 122.5, 122.4, 116.5, 109.5, 39.9, 33.4, 31.7, 29.2, 25.2, 22.5, 14.0. \]

HRMS (ESI+): exact mass calculated for [M+H]+ (C16H21NO) requires m/z 244.1696, found m/z 244.1696.

(3ag) 4-methyl-1-(1-methyl-1H-indol-3-yl)pentan-1-one
rufous liquid, 31.1 mg, 68%

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.41 – 8.37 (m, 1H), 7.68 (s, 1H), 7.32 – 7.27 (m, 3H), 3.81 (s, 3H), 2.85 – 2.79 (m, 2H), 1.70 – 1.63 (m, 3H), 0.95 (d, $J = 6.0$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.1, 137.4, 135.1, 126.3, 123.2, 122.5, 122.4, 116.4, 109.5, 37.9, 34.1, 33.4, 27.9, 22.4.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{15}$H$_{19}$NO) requires $m/z$ 230.1539, found $m/z$ 230.1539.

(3ah) 3-cyclopentyl-1-(1-methyl-1H-indol-3-yl)propan-1-one

red liquid, 31.1 mg, 61%

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.42 – 8.37 (m, 1H), 7.69 (s, 1H), 7.33 – 7.27 (m, 3H), 3.82 (s, 3H), 2.86 – 2.80 (m, 2H), 1.87 – 1.74 (m, 5H), 1.68 – 1.46 (m, 4H), 1.20 – 1.10 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.0, 137.4, 135.1, 135.0, 126.3, 123.1, 122.6, 122.4, 116.4, 109.4, 39.9, 39.2, 33.4, 32.5, 31.5, 25.1.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{17}$H$_{21}$NO) requires $m/z$ 256.1696, found $m/z$ 256.1696.

(3ai) 3,5,5-trimethyl-1-(1-methyl-1H-indol-3-yl)hexan-1-one

aubergine liquid, 35.2 mg, 65%

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.44 – 8.39 (m, 1H), 7.66 (s, 1H), 7.32 – 7.27 (m, 3H), 3.81 (s, 3H), 2.76 (dd, $J = 14.8$, 6.0 Hz, 1H), 2.66 (dd, $J = 14.8$, 8.0 Hz, 1H), 2.36 – 2.26 (m, 1H), 1.36 (dd, $J = 14.0$, 4.0 Hz, 1H), 1.17 (dd, $J = 14.0$, 6.4 Hz, 1H), 1.01 (d, $J = 6.4$ Hz, 3H), 0.92 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 195.5, 137.4, 135.2, 126.3, 123.2, 122.6, 122.4, 117.3, 109.4, 51.1, 49.5, 33.4, 31.1, 30.0, 27.0, 23.0.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{18}$H$_{25}$NO) requires $m/z$ 272.2009, found $m/z$ 272.2009.

(3aj) 2-methyl-1-(1-methyl-1H-indol-3-yl)propan-1-one
crimson liquid, 18.1 mg, 45%

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.51 – 8.31 (m, 1H), 7.73 (s, 1H), 7.40 – 7.27 (m, 3H), 3.84 (s, 3H), 3.31 (p, $J = 6.8$ Hz, 1H), 1.25 (d, $J = 6.8$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 200.8, 137.4, 135.0, 126.5, 123.2, 123.2, 122.7, 122.4, 115.1, 109.4, 37.0, 33.4, 19.7.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{13}$H$_{15}$NO) requires $m/z$ 202.1226, found $m/z$ 202.1226.

(3ak) 1-(1-methyl-1H-indol-3-yl)-2-phenylethan-1-one

white crystal, 39.34 mg, 79%, m.p. 112-113 ºC

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.50 – 8.33 (m, 1H), 7.69 (s, 1H), 7.34 – 7.26 (m, 7H), 7.24 – 7.19 (m, 1H), 4.09 (s, 2H), 3.75 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 192.5, 137.3, 135.8, 135.7, 129.2, 128.5, 126.5, 126.5, 123.4, 122.6, 122.6, 116.0, 109.5, 46.8, 33.4.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{17}$H$_{19}$NO) requires $m/z$ 250.1226, found $m/z$ 250.1225.

(3al) 1-(1-methyl-1H-indol-3-yl)-2-phenylbutan-1-one

pink crystal, 35.0 mg, 63%, m.p. 166-168 ºC

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.49 – 8.44 (m, 1H), 7.69 (s, 1H), 7.39 (d, $J = 8.0$ Hz, 2H), 7.30 – 7.23 (m, 5H), 7.18 (t, $J = 7.2$ Hz, 1H), 4.17 (t, $J = 7.3$ Hz, 1H), 3.73 (s, 3H), 2.34 – 2.22 (m, 1H), 1.94 – 1.82 (m, 1H), 0.93 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 195.2, 141.1, 137.3, 135.5, 135.3, 128.5, 127.9, 123.3, 122.8, 122.5, 116.4, 109.3, 57.0, 33.4, 26.9, 12.5.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{19}$H$_{19}$NO) requires $m/z$ 278.1539, found $m/z$ 278.1540.

(3am) 2,2-dimethyl-1-(1-methyl-1H-indol-3-yl)propan-1-one
brown crystal, 11 mg, 25%, m.p. 115-116 °C

\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.57 – 8.45 (m, 1H), 7.79 (s, 1H), 7.34 – 7.28 (m, 3H), 3.85 (s, 3H), 1.42 (s, 9H).

\(^13\)C NMR (100 MHz, Chloroform-\(d\)) \(\delta\) 201.98, 136.42, 128.22, 123.37, 123.19, 122.45, 112.70, 109.17, 44.05, 33.46, 28.94.

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) (C\(_{14}\)H\(_{17}\)NO) requires \(m/z\) 216.1383, found \(m/z\) 216.1382.

(3an) cyclobutyl(1-methyl-1H-indol-3-yl)methanone

light red crystal, 28.5 mg, 67%, m.p. 89-90 °C

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.44 – 8.38 (m, 1H), 7.59 (s, 1H), 7.33 – 7.27 (m, 3H), 3.80 (s, 4H), 2.53 – 2.42 (m, 2H), 2.29 – 2.19 (m, 2H), 2.12 – 1.99 (m, 1H), 1.97 – 1.87 (m, 1H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 196.6, 137.3, 134.9, 126.4, 123.1, 122.5, 114.7, 109.4, 43.0, 33.4, 25.2, 18.3.

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) (C\(_{14}\)H\(_{15}\)NO) requires \(m/z\) 214.1226, found \(m/z\) 214.1227.

(3ao) cyclopentyl(1-methyl-1H-indol-3-yl)methanone

dark brown liquid, 24.5 mg, 54%

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.45 – 8.40 (m, 1H), 7.70 (s, 1H), 7.34 – 7.26 (m, 3H), 3.82 (s, 3H), 3.54 – 3.46 (m, 1H), 2.03 – 1.85 (m, 4H), 1.83 – 1.73 (m, 2H), 1.69 – 1.60 (m, 2H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 198.5, 137.4, 135.1, 126.5, 123.1, 122.6, 122.4, 116.2, 109.4, 47.8, 33.4, 30.5, 26.3.

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) (C\(_{15}\)H\(_{17}\)NO) requires \(m/z\) 228.1383, found \(m/z\) 228.1379.

(3ap) cyclohexyl(1-methyl-1H-indol-3-yl)methanone
aubergine crystal, 24.1 mg, 50%, m.p. 133-135 °C

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.44 – 8.36 (m, 1H), 7.73 (s, 1H), 7.35 – 7.27 (m, 3H), 3.83 (s, 3H), 3.06 – 2.97 (m, 1H), 1.94 – 1.82 (m, 4H), 1.77 – 1.70 (m, 1H), 1.68 – 1.56 (m, 2H), 1.45 – 1.25 (m, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 199.4, 137.5, 134.9, 126.5, 123.2, 122.69, 122.44, 115.39, 109.49, 47.78, 33.46, 33.40, 29.8, 26.0, 25.9.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{16}$H$_{19}$NO) requires m/z 242.1539, found m/z 242.1539.

(3aq) (1-methyl-1H-indol-3-yl)(phenyl)methanone

light red crystal, 18.3 mg, 39%, m.p. 108-109 °C

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.55 – 8.39 (m, 1H), 7.82 (s, 1H), 7.80 (s, 1H), 7.57 – 7.44 (m, 4H), 7.39 – 7.32 (m, 3H), 3.83 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 190.8, 140.8, 137.9, 137.9, 137.4, 131.0, 128.6, 128.2, 127.1, 123.6, 122.6, 115.4, 109.5, 33.5.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{16}$H$_{13}$NO) requires m/z 236.1070, found m/z 236.1069.

(3ar) 4-(1-methyl-1H-indole-3-carbonyl)benzonitrile

brownish crystal, 14.6 mg, 28%, m.p. 204-206 °C

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.41 – 8.36 (m, 1H), 7.89 – 7.84 (m, 2H), 7.79 – 7.74 (m, 2H), 7.47 (s, 1H), 7.42 – 7.35 (m, 3H), 3.87 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 188.6, 144.6, 137.9, 137.6, 132.8, 129.0, 126.8, 124.1, 123.2, 122.6, 118.3, 115.1, 114.4, 109.8, 33.7.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{17}$H$_{12}$N$_2$O) requires m/z 261.1022, found m/z 261.1025.

(3as)1-methyl-1H-indole-3-carbaldehyde

brownish crystal, 25 mg, 79%, m.p. 71-73 °C

$^1$H NMR (400 MHz, Chloroform-d) δ 9.95 (s, 1H), 8.32 – 8.27 (m, 1H), 7.62 (s, 1H), 7.36 – 7.29 (m, 3H), 3.83 (s, 3H).

$^{13}$C NMR (100 MHz, Chloroform-d) δ 184.3, 139.2, 137.8, 125.2, 123.9, 122.8, 121.9, 117.9, 109.8,
33.6.

**HRMS (ESI+):** exact mass calculated for [M+H]+ (C_{10}H_{9}NO) requires m/z 160.0757, found m/z 160.0759.

(3ba) 1-(4-fluoro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

![Chemical structure of 1-(4-fluoro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one]

brownish red crystal, 25.9 mg, 46%, m.p. 80-82 °C

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \delta 7.69 \text{ (s, 1H), 7.31 – 7.26 (m, 4H), 7.25 – 7.15 (m, 2H), 7.11 (d, J = 8.0 Hz, 1H), 6.99 – 6.93 (m, 1H), 3.80 (s, 3H), 3.31 – 3.25 (m, 2H), 3.12 – 3.07 (m, 2H).} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3 \delta 193.6, 157.6, 155.1, 141.8, 140.3 (d, J = 11.0 Hz), 135.8, 128.4 (d, J = 8.0 Hz), 125.8, 123.8 (d, J = 8.0 Hz), 116.3 (d, J = 5.0 Hz), 113.8 (d, J = 20.0 Hz), 108.1 (d, J = 22.0 Hz), 105.9 (d, J = 4.0 Hz), 42.5 (d, J = 7.0 Hz), 33.8, 30.7.} \]

**HRMS (ESI+):** exact mass calculated for [M+H]+ (C_{18}H_{16}FNNO) requires m/z 282.1289, found m/z 282.1288.

(3ca) 1-(4-chloro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

![Chemical structure of 1-(4-chloro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one]

light yellow crystal, 42.1 mg, 71%, m.p. 82-84 °C

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \delta 7.49 \text{ (s, 1H), 7.29 – 7.22 (m, 5H), 7.20 – 7.14 (m, 3H), 3.72 (s, 3H), 3.20 – 3.13 (m, 2H), 3.12 – 3.04 (m, 2H).} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3 \delta 193.7, 141.6, 139.1, 135.7, 128.4, 128.8, 127.2, 125.9, 123.7, 123.6, 123.3, 117.4, 108.3, 43.5, 33.5, 30.9.} \]

**HRMS (ESI+):** exact mass calculated for [M+H]+ (C_{18}H_{16}ClNO) requires m/z 298.0993, found m/z 298.0993.

(3da) 1-(1,4-dimethyl-1H-indol-3-yl)-3-phenylpropan-1-one

![Chemical structure of 1-(1,4-dimethyl-1H-indol-3-yl)-3-phenylpropan-1-one]
light yellow crystal, 31.1 mg, 56%, m.p. 95-96 °C

\[ ^1\text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.58 (s, 1H), 7.31 – 7.28 (m, 1H), 7.27 – 7.23 (m, 3H), 7.22 – 7.16 (m, 2H), 7.10 (d, \( J = 8.0 \) Hz, 1H), 7.04 (d, \( J = 7.2 \) Hz, 1H), 3.72 (s, 3H), 3.18 – 3.12 (m, 2H), 3.11 – 3.05 (m, 2H), 2.85 (s, 3H).

\[ ^{13}\text{C NMR (100 MHz, CDCl}_3 \] \( \delta \) 193.5, 141.7, 138.2, 136.1, 133.6, 128.4, 125.9, 125.0, 124.3, 123.5, 118.2, 107.0, 42.3, 33.4, 31.2, 23.0.

HRMS (ESI+): exact mass calculated for [M+H]+ (C\(_{18}\)H\(_{17}\)NO) requires \( m/z \) 278.1539, found \( m/z \) 278.1539.

\( ^1\text{H NMR (400 MHz, CDCl}_3 \) \( \delta \) 7.61 (s, 1H), 7.30 – 7.22 (m, 5H), 7.20 – 7.15 (m, 1H), 6.95 – 6.91 (m, 1H), 6.68 (d, \( J = 7.6 \) Hz, 1H), 3.91 (s, 3H), 3.74 (s, 3H), 3.42 – 3.37 (m, 2H), 3.10 – 3.04 (m, 2H).

\[ ^{13}\text{C NMR (100 MHz, CDCl}_3 \] \( \delta \) 196.2, 153.9, 142.1, 139.3, 134.4, 128.3, 128.3, 125.7, 123.8, 118.0, 115.1, 103.0, 102.5, 55.3, 43.6, 33.5, 31.1.

HRMS (ESI+): exact mass calculated for [M+H]+ (C\(_{19}\)H\(_{19}\)NO\(_2\)) requires \( m/z \) 294.1489, found \( m/z \) 294.1485.

gray white crystal, 26.4 mg, 45%, m.p. 81-82 °C

\[ ^1\text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 8.38 – 8.36 (m, 1H), 7.55 (d, \( J = 2.8 \) Hz, 1H), 7.31 – 7.28 (m, 1H), 7.27 – 7.23 (m, 3H), 7.21 – 7.16 (m, 2H), 7.16 – 7.12 (m, 1H), 3.73 (s, 3H), 3.11 – 3.05 (m, 4H).

\[ ^{13}\text{C NMR (100 MHz, CDCl}_3 \] \( \delta \) 194.0, 141.5, 135.9, 135.6, 128.4, 128.4, 127.1, 126.0, 123.5, 121.9, 115.7, 110.5, 41.3, 33.5, 30.5.

HRMS (ESI+): exact mass calculated for [M+H]+ (C\(_{18}\)H\(_{16}\)ClNO) requires \( m/z \) 298.0991, found \( m/z \) 298.0991.

rufous crystal, 33.3 mg, 56%, m.p. 130-132 °C

\[ ^1\text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 8.38 – 8.36 (m, 1H), 7.55 (d, \( J = 2.8 \) Hz, 1H), 7.31 – 7.28 (m, 1H), 7.27 – 7.23 (m, 3H), 7.21 – 7.16 (m, 2H), 7.16 – 7.12 (m, 1H), 3.73 (s, 3H), 3.11 – 3.05 (m, 4H).

\[ ^{13}\text{C NMR (100 MHz, CDCl}_3 \] \( \delta \) 194.0, 141.5, 135.9, 135.6, 128.4, 128.4, 127.1, 126.0, 123.5, 121.9, 115.7, 110.5, 41.3, 33.5, 30.5.

HRMS (ESI+): exact mass calculated for [M+H]+ (C\(_{18}\)H\(_{16}\)ClNO) requires \( m/z \) 298.0991, found \( m/z \) 298.0991.

(3ea) 1-(4-methoxy-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

(3fa) 1-(5-chloro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

(3ga) 1-(5-bromo-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one
light pink crystal, 46.4 mg, 68%, m.p. 142-144 °C

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.53 - 8.50 (m, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.33 - 7.27 (m, 2H), 7.27 - 7.23 (m, 3H), 7.21 - 7.16 (m, 1H), 7.09 - 7.04 (m, 1H), 3.71 (s, 3H), 3.09 - 3.05 (m, 4H).

\[ \text{13C NMR (100 MHz, CDCl}_3\text{)} \delta 193.9, 141.5, 135.7, 128.4, 127.6, 125.0, 124.9, 116.1, 115.66, 110.98, 41.31, 33.5, 30.5.

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) \(\text{C}_{18}\text{H}_{16}\text{BrNO}\) requires \(m/z\) 342.0488, found \(m/z\) 342.0486.

(3ha) 1-(5-methoxy-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

dark red crystal, 32.3 mg, 55%, m.p. 72-74 °C

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.93 (d, J = 2.8 Hz, 1H), 7.56 (s, 1H), 7.30 - 7.25 (m, 4H), 7.21 - 7.16 (m, 2H), 6.93 (dd, J = 8.8, 2.8 Hz, 1H), 3.89 (s, 3H), 3.74 (s, 3H), 3.15 - 3.07 (m, 4H).

\[ \text{13C NMR (100 MHz, CDCl}_3\text{)} \delta 194.4, 156.4, 141.7, 135.3, 132.3, 128.4, 127.1, 125.8, 115.9, 113.9, 113.8, 110.4, 110.3, 103.6, 55.6, 41.3, 33.7, 30.7.

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) \(\text{C}_{19}\text{H}_{19}\text{NO}_2\) requires \(m/z\) 294.1482, found \(m/z\) 294.1490.

(3ia) 1-(6-fluoro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

dark red crystal, 37.1 mg, 66%, m.p. 82-84 °C

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.32 (dd, J = 8.8, 5.6 Hz, 1H), 7.56 (s, 1H), 7.31 - 7.22 (m, 4H), 7.21 - 7.16 (m, 1H), 7.06 - 7.00 (m, 1H), 6.94 (dd, J = 9.2, 2.0 Hz, 1H), 3.70 (s, 3H), 3.14 - 3.04 (m, 4H).
\textbf{13C NMR (100 MHz, CDCl\textsubscript{3})} \ \delta 194.2, 161.5, 159.1, 141.61, 137.5 (d, J = 12.0 Hz), 135.44, 128.4 (d, J = 4.0 Hz), 125.9, 123.6 (d, J = 10.0 Hz), 122.6, 116.4, 110.9 (d, J = 24.0 Hz), 96.2 (d, J = 26.0 Hz), 41.3, 33.4, 30.6.

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]\textsuperscript{+} \ ((C\textsubscript{18}H\textsubscript{16}FN\textsubscript{5}O) requires \(m/z\) 282.1289, found \(m/z\) 282.1290.

\textbf{(3ja) 1-(6-bromo-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one}

\begin{figure}
\centering
\includegraphics[width=0.2\textwidth]{image.png}
\end{figure}

pink crystal, 52.5 mg, 77%, m.p. 127-128 \degree C

\textbf{1H NMR (400 MHz, CDCl\textsubscript{3})} \ \delta 8.24 (d, J = 8.4 Hz, 1H), 7.55 (s, 1H), 7.43 (d, J = 1.6 Hz, 1H), 7.37 (dd, J = 8.4, 1.6 Hz, 1H), 7.31 – 7.23 (m, 4H), 7.21 – 7.16 (m, 1H), 3.72 (s, 3H), 3.15 – 3.05 (m, 2H), 3.10 – 3.05 (m, 2H).

\textbf{13C NMR (100 MHz, CDCl\textsubscript{3})} \ \delta 194.2, 141.5, 138.1, 135.4, 128.4, 126.0, 125.7, 125.0, 123.8, 116.9, 116.4, 112.7, 41.5, 33.5, 30.6.

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]\textsuperscript{+} \ ((C\textsubscript{18}H\textsubscript{16}BrNO) requires \(m/z\) 342.0488, found \(m/z\) 342.0486.

\textbf{(3ka) 1-(6-methoxy-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one}

\begin{figure}
\centering
\includegraphics[width=0.2\textwidth]{image.png}
\end{figure}

crimson liquid, 20.0 mg, 34%

\textbf{1H NMR (400 MHz, CDCl\textsubscript{3})} \ \delta 8.26 (dd, J = 8.8, 0.4 Hz, 1H), 7.52 (d, J = 1.2 Hz, 1H), 7.31 – 7.28 (m, 1H), 7.27 – 7.24 (m, 3H), 7.21 – 7.16 (m, 1H), 6.94 (dd, J = 8.8, 2.0 Hz, 1H), 6.74 (d, J = 2.0 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 3H), 3.15 – 3.05 (m, 4H).

\textbf{13C NMR (100 MHz, CDCl\textsubscript{3})} \ \delta 194.5, 157.3, 141.9, 138.4, 134.5, 128.5, 126.0, 123.4, 120.5, 116.5, 111.9, 93.4, 55.8, 41.5, 33.5, 31.0.

HRMS (ESI\textsuperscript{+}): exact mass calculated for [M+H]\textsuperscript{+} \ ((C\textsubscript{19}H\textsubscript{15}NO\textsubscript{2}) requires \(m/z\) 294.1489, found \(m/z\) 294.1485.

\textbf{(3la) 1-(1-benzyl-5-bromo-1H-indol-3-yl)-3-phenylpropan-1-one}
nacarat oil, 27.5 mg, 33%

\[ ^1H \text{NMR} \ (400 \text{ MHz, CDCl}_3) \delta 8.60 \ (d, J = 1.6 \text{ Hz, 1H}), 7.63 \ (s, 1H), 7.34 - 7.26 \ (m, 5H), 7.26 - 7.22 \ (m, 3H), 7.20 - 7.15 \ (m, 1H), 7.12 - 7.07 \ (m, 3H), 5.26 \ (s, 2H), 3.15 - 3.10 \ (m, 2H), 3.10 - 3.05 \ (m, 2H). \]

\[ ^13C \text{NMR} \ (100 \text{ MHz, CDCl}_3) \delta 194.2, 141.5, 135.6, 135.2, 135.1, 129.1, 128.4, 128.3, 128.0, 126.9, 126.5, 126.0, 125.3, 116.4, 111.5, 50.9, 41.5, 30.6. \]

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) \( (C_{24}H_{20}BrNO) \) requires \( m/z \) 418.0801, found \( m/z \) 418.0802.

(3ma) 1-(1H-indol-3-yl)-3-phenylpropan-1-one

rufous powder, 21.4 mg, 43%, m.p. 157-159 °C

\[ ^1H \text{NMR} \ (400 \text{ MHz, DMSO-d}_6) \delta 11.90 \ (s, 1H), 8.35 \ (d, J = 3.2 \text{ Hz, 1H}), 8.22 - 8.19 \ (m, 1H), 7.47 - 7.44 \ (m, 1H), 7.32 - 7.24 \ (m, 4H), 7.23 - 7.14 \ (m, 3H), 3.22 - 3.16 \ (m, 2H), 3.00 - 2.95 \ (m, 2H). \]

\[ ^13C \text{NMR} \ (100 \text{ MHz, DMSO-d}_6) \delta 194.3, 141.7, 136.7, 133.9, 128.4, 128.3, 125.8, 125.4, 122.7, 121.7, 121.4, 116.3, 112.1, 30.4. \]

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) \( (C_{17}H_{15}NO) \) requires \( m/z \) 250.1226, found \( m/z \) 250.1225.

(3na) 1-(4-chloro-1H-indol-3-yl)-3-phenylpropan-1-one

dark red liquid, 27.7 mg, 49%

\[ ^1H \text{NMR} \ (400 \text{ MHz, DMSO-d}_6) \delta 12.16 \ (s, 1H), 8.37 \ (d, J = 3.1 \text{ Hz, 1H}), 7.46 - 7.41 \ (m, 1H), 7.31 - 7.24 \ (m, 4H), 7.20 - 7.14 \ (m, 3H), 3.26 - 3.20 \ (m, 2H), 2.99 - 2.92 \ (m, 2H). \]
$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 192.9, 141.6, 138.8, 134.7, 128.5, 128.3, 125.8, 125.7, 123.6, 122.9, 122.5, 117.3, 111.2, 42.0, 30.4.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{17}$H$_{14}$ClN$_{2}$O) requires $m/z$ 284.0837, found $m/z$ 284.0844.

(3oa) 1-(4-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

brown powder, 27.3 mg, 52%, m.p. 110-112 °C

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.87 (s, 1H), 7.30 – 7.22 (m, 5H), 7.21 – 7.13 (m, 3H), 7.03 – 7.00 (m, 1H), 3.18 – 3.13 (m, 2H), 3.11 – 3.05 (m, 2H), 2.82 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 194.9, 141.5, 137.3, 133.2, 132.0, 128.5, 128.4, 126.0, 124.4, 124.1, 123.9, 119.7, 109.0, 42.4, 31.2, 23.0.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{18}$H$_{17}$NO) requires $m/z$ 264.1383, found $m/z$ 264.1381.

(3pa) 1-(5-chloro-1H-indol-3-yl)-3-phenylpropan-1-one

brown yellow powder, 26.6 mg, 47%, m.p. 188-189 °C

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 12.10 (s, 1H), 8.43 (d, $J$ = 2.8 Hz, 1H), 8.19 (d, $J$ = 2.0 Hz, 1H), 7.48 (d, $J$ = 8.8 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.24 – 7.20 (m, 1H), 7.19 – 7.13 (m, 1H), 3.22 – 3.17 (m, 2H), 3.00 – 2.94 (m, 2H).

$^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 194.4, 141.6, 135.3, 135.2, 128.4, 128.3, 126.6, 126.5, 125.8, 122.8, 120.5, 115.9, 113.8, 39.0, 30.2.

HRMS (ESI+): exact mass calculated for [M+H]$^+$ (C$_{18}$H$_{15}$ClNO) requires $m/z$ 284.0837, found $m/z$ 284.0835.

(3qa) 1-(5-bromo-1H-indol-3-yl)-3-phenylpropan-1-one

s32
brownish powder, 35.9 mg, 55%, m.p. 182-183 °C

\[ ^1H\text{ NMR (400 MHz, DMSO-}d_6\text{)} \delta 12.11 (s, 1H), 8.41 (d, J = 2.8 Hz, 1H), 8.36 (d, J = 2.0 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.34 (dd, J = 8.4, 2.0 Hz, 1H), 7.31-7.24 (m, 4H), 7.19-7.13 (m, 1H), 3.19 (t, J = 7.6 Hz, 2H), 2.96 (t, J = 7.6 Hz, 2H). \]

\[ ^{13}C\text{ NMR (100 MHz, DMSO-}d_6\text{)} \delta 194.4, 141.6, 135.4, 135.1, 128.4, 128.2, 127.2, 125.8, 125.3, 123.5, 115.79, 114.5, 114.2, 38.9, 30.2. \]

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) \((C_{17}H_{14}BrNO)\) requires \(m/z\) 328.0332, found \(m/z\) 328.0344.

(3ra) 1-(5-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

white powder, 20.0 mg, 38%, m.p. 208-210 °C

\[ ^1H\text{ NMR (400 MHz, DMSO-}d_6\text{)} \delta 11.79 (s, 1H), 8.28 (d, J = 3.1 Hz, 1H), 8.02 (s, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.31-7.24 (m, 4H), 7.19-7.14 (m, 1H), 7.02 (dd, J = 8.4, 2.0 Hz, 1H), 3.20-3.14 (m, 2H), 2.99-2.94 (m, 2H), 2.40 (s, 3H). \]

\[ ^{13}C\text{ NMR (100 MHz, DMSO-}d_6\text{)} \delta 194.2, 141.7, 135.0, 133.9, 130.4, 128.4, 128.2, 125.8, 125.7, 124.2, 121.2, 115.9, 111.7, 30.4, 21.4. \]

HRMS (ESI+): exact mass calculated for [M+H]\(^+\) \((C_{18}H_{17}NO)\) requires \(m/z\) 264.1383, found \(m/z\) 264.1386.

(3sa) 1-(6-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

dark red oily liquid, 36.8 mg, 70%
\[^{1}\text{H NMR (400 MHz, DMSO-\text{d}_6)} \delta 11.77 (s, 1H), 8.27 (d, J = 3.2 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.32 – 7.23 (m, 5H), 7.19 – 7.13 (m, 1H), 7.02 – 6.99 (m, 1H), 3.20 – 3.14 (m, 2H), 3.00 – 2.93 (m, 2H), 2.40 (s, 3H). \]

\[^{13}\text{C NMR (100 MHz, DMSO-\text{d}_6)} \delta 194.1, 141.8, 137.1, 132.0, 128.4, 128.3, 125.8, 123.3, 121.1, 116.3, 111.8, 38.0, 30.4, 21.3. \]

HRMS (ESI\(^{+}\)): exact mass calculated for [M+H]\(^{+}\) \((\text{C}_{18}\text{H}_{17}\text{NO})\) requires \(m/z\) 264.1383, found \(m/z\) 264.1383.

(3ta) 3-phenyl-1-(2-phenyl-1H-indol-3-yl)propan-1-one

\[ \text{celadon crystal, 29.9 mg, 46%, m.p. 187-188 } ^\circ\text{C} \]

\[^{1}\text{H NMR (400 MHz, DMSO-\text{d}_6)} \delta 12.09 (s, 1H), 8.22 – 8.18 (m, 1H), 7.62 – 7.58 (m, 2H), 7.56 – 7.51 (m, 3H), 7.45 – 7.42 (m, 1H), 7.26 – 7.15 (m, 4H), 7.13 – 7.08 (m, 1H), 6.99 – 6.94 (m, 2H), 2.84 – 2.78 (m, 2H), 2.76 – 2.71 (m, 2H). \]

\[^{13}\text{C NMR (100 MHz, DMSO-\text{d}_6)} \delta 195.7, 144.5, 141.4, 135.5, 132.8, 129.9, 129.3, 128.5, 128.2, 128.1, 127.1, 125.7, 122.9, 121.8, 121.6, 113.9, 111.7, 42.7, 30.4. \]

HRMS (ESI\(^{+}\)): exact mass calculated for [M+H]\(^{+}\) \((\text{C}_{23}\text{H}_{19}\text{NO})\) requires \(m/z\) 326.1539, found \(m/z\) 326.1540.

(3ua) 1-(2-methyl-1H-indol-3-yl)-3-phenylpropan-1-one

\[ \text{pink crystal, 41.0 mg, 78%, m.p. 141-142 } ^\circ\text{C} \]

\[^{1}\text{H NMR (400 MHz, DMSO-\text{d}_6)} \delta 11.83 (s, 1H), 8.02 – 7.96 (m, 1H), 7.39 – 7.34 (m, 1H), 7.20 – 7.10 (m, 3H), 3.21 (t, J = 7.2 Hz, 2H), 2.98 (t, J = 7.2 Hz, 2H), 2.68 (s, 3H). \]

\[^{13}\text{C NMR (100 MHz, DMSO-\text{d}_6)} \delta 194.5, 144.1, 142.0, 134.8, 128.4, 126.7, 125.7, 121.7, 121.3, 120.6, 113.1, 111.2, 43.4, 29.7, 15.3. \]

HRMS (ESI\(^{+}\)): exact mass calculated for [M+H]\(^{+}\) \((\text{C}_{18}\text{H}_{17}\text{NO})\) requires \(m/z\) 264.1383, found \(m/z\) 264.1387.

(5aa) 1-(4-(dimethylamino)phenyl)-3-phenylpropan-1-one
transparent crystal, 7.59 mg, 15%, m.p. 76-78 °C

\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.91 – 7.85 (m, 2H), 7.32 – 7.23 (m, 4H), 7.22 – 7.16 (m, 1H), 6.66 – 6.61 (m, 2H), 3.22 – 3.17 (m, 2H), 3.04 (s, 8H).

\(^{13}\)C NMR (100 MHz, Chloroform-\(d\)) \(\delta\) 197.3, 153.3, 141.8, 130.2, 128.4, 125.9, 124.9, 110.6, 39.9, 39.7, 30.7.

HRMS (ESI\(^+\)): exact mass calculated for \([M+H]^+\) \((C_{17}H_{19}NO)\) requires \(m/z\) 254.1539, found \(m/z\) 254.1538.

(7aa) 3-phenyl-1-(1H-pyrrol-2-yl)propan-1-one

light yellow solid, 22 mg, 55%, m.p 54-56 °C

\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 9.77 (s, 1H), 7.32 – 7.22 (m, 4H), 7.22 – 7.17 (m, 1H), 6.92 – 6.89 (m, 1H), 6.28 – 6.23 (m, 1H), 3.15 – 3.01 (m, 4H).

\(^{13}\)C NMR (100 MHz, Chloroform-\(d\)) \(\delta\) 189.7, 141.2, 131.7, 128.4, 126.1, 124.7, 116.2, 110.5, 39.57, 30.7.

HRMS (ESI\(^+\)): exact mass calculated for \([M+H]^+\) \((C_{13}H_{13}NO)\) requires \(m/z\) 200.1070, found \(m/z\) 200.1070.

(9aa) 3-phenyl-1-(3,4,5-trimethoxyphenyl)propan-1-one

clear liquid, 16.2 mg, 27%

\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.48 (d, \(J = 8.8\) Hz, 1H), 7.32 – 7.22 (m, 4H), 7.22 – 7.16 (m, 1H), 6.71 (d, \(J = 8.9\) Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.86 (s, 3H), 3.32 – 3.25 (m, 2H), 3.06 – 2.99 (m, 2H).

\(^{13}\)C NMR (100 MHz, Chloroform-\(d\)) \(\delta\) 199.9, 157.2, 153.9, 142.0, 141.6, 128.4, 125.9, 125.5, 107.1, 61.4, 60.8, 56.1, 44.6, 30.5.

HRMS (ESI\(^+\)): exact mass calculated for \([M+H]^+\) \((C_{18}H_{20}O)\) requires \(m/z\) 301.1434, found \(m/z\) 301.1433.

(11aa) 1-(3,4-dimethoxyphenyl)-3-phenylpropan-1-one
light yellow liquid, 6.48 mg, 12%

**H NMR (400 MHz, Chloroform-d)** δ 7.58 (dd, J = 8.4, 2.0 Hz, 1H), 7.53 (d, J = 1.9 Hz, 1H), 7.33 – 7.24 (m, 5H), 7.24 – 7.18 (m, 1H), 6.87 (d, J = 8.4 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.29 – 3.24 (m, 2H), 3.09 – 3.04 (m, 2H).

**13C NMR (100 MHz, Chloroform-d)** δ 197.8, 153.2, 149.0, 141.4, 130.1, 128.5, 126.1, 122.6, 110.1, 109.9, 56.0, 40.0, 30.4.

**HRMS (ESI+):** exact mass calculated for [M+H]+ (C17H18O3) requires m/z 271.1329, found m/z 271.1331.
Separate characterization of 3aa of table 4

2A → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.42 – 8.37 (m, 1H), 7.55 (s, 1H), 7.30 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.71 (s, 3H), 3.15 – 3.05 (m, 4H).

2B → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 – 8.37 (m, 1H), 7.56 (s, 1H), 7.31 – 7.23 (m, 7H), 7.21 – 7.15 (m, 1H), 3.72 (s, 3H), 3.15 – 3.05 (m, 4H).

2C → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 – 8.36 (m, 1H), 7.55 (s, 1H), 7.31 – 7.23 (m, 7H), 7.22 – 7.15 (m, 1H), 3.71 (s, 3H), 3.15 – 3.04 (m, 4H).

2D → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 – 8.36 (m, 1H), 7.56 (s, 1H), 7.31 – 7.22 (m, 7H), 7.20 – 7.15 (m, 1H), 3.72 (s, 3H), 3.15 – 3.05 (m, 4H).

2E → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 – 8.36 (m, 1H), 7.55 (s, 1H), 7.30 – 7.23 (m, 7H), 7.21 – 7.16 (m, 1H), 3.70 (s, 3H), 3.15 – 3.05 (m, 4H).

2F → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.42 – 8.37 (m, 1H), 7.65 (s, 1H), 7.34 – 7.25 (m, 7H), 7.22 – 7.16 (m, 1H), 3.80 (s, 3H), 3.23 – 3.08 (m, 4H).

2G → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 – 8.36 (m, 1H), 7.54 (s, 1H), 7.30 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.70 (s, 3H), 3.15 – 3.05 (m, 4H).

2H → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.42 – 8.37 (m, 1H), 7.64 (s, 1H), 7.33 – 7.25 (m, 7H), 7.22 – 7.16 (m, 1H), 3.79 (s, 3H), 3.19 – 3.07 (m, 4H).

2I → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.42 – 8.37 (m, 1H), 7.64 (s, 1H), 7.34 – 7.25 (m, 7H), 7.22 – 7.17 (m, 1H), 3.80 (s, 3H), 3.19 – 3.07 (m, 4H).

2J → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.42 – 8.37 (m, 1H), 7.62 (s, 1H), 7.33 – 7.25 (m, 7H), 7.22 – 7.16 (m, 1H), 3.78 (s, 3H), 3.18 – 3.07 (m, 4H).

2K → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 – 8.37 (m, 1H), 7.61 (s, 1H), 7.32 – 7.24 (m, 7H), 7.21 – 7.16 (m, 1H), 3.77 (s, 3H), 3.18 – 3.07 (m, 4H).

2L → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.42 – 8.37 (m, 1H), 7.57 (s, 1H), 7.31 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.73 (s, 3H), 3.16 – 3.05 (m, 4H).

2M → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.41 – 8.37 (m, 1H), 7.57 (s, 1H), 7.31 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.74 (s, 3H), 3.16 – 3.05 (m, 4H).

2N → 3aa

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.42 – 8.37 (m, 1H), 7.63 (s, 1H), 7.34 – 7.26 (m, 7H), 7.22 – 7.17 (m, 1H), 3.79 (s, 3H), 3.20 – 3.08 (m, 4H).
Recycling experiment characterization

2k-recycled

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.34 – 7.26 (m, 4H), 7.25 – 7.21 (m, 1H), 3.65 (s, 2H), 3.49 (t, $J$ = 6.8 Hz, 2H), 3.41 (t, $J$ = 6.8 Hz, 2H), 1.95 – 1.87 (m, 2H), 1.87 – 1.79 (m, 2H).
Copies of NMR Spectra

3aa

3aa
Separate copies of $^1$H NMR spectra of 3aa of table 4
References