## Supporting Information

## for

# Catalytic Chan-Lam coupling using a 'tube-in-tube' reactor to deliver molecular oxygen as an oxidant 

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## Experimental procedures and characterization data for all new compounds

Unless specified, reagents were obtained from commercial sources and used without further purification. Solvents were obtained from Fisher scientific, and $\mathrm{H}_{2} \mathrm{O}$ was deionised before use.
NMR spectra were recorded on either Bruker Avance-400, Varian VNMRS-600 or Varian VNMRS-700 instrument and was calibrated to the residual solvent according to the literature [1]. Assignments are based on DEPT-135, COSY, NOESY, HSQC and HMBC spectra.
Liquid chromatography-mass spectrometry (LCMS) was performed on an Agilent HP 1100 series chromatograph (Mercury Luna $3 \mu \mathrm{C} 18$ (2) column) attached to a Waters ZQ2000 mass spectrometer with ESCi ionisation source in ESI mode. Elution was carried out at a flow rate of $0.6 \mathrm{~mL} / \mathrm{min}$ using a reverse phase gradient of MeCN -water containing $0.1 \%$ formic acid. Gradient $=0-1 \mathrm{~min}$ : hold $\mathrm{MeCN} 5 \%, 1-4 \mathrm{~min}$ : ramp MeCN 5-95\%, 4-5 min: hold MeCN 95\%, 5-7 min: ramp MeCN 95-5\%, 7-8 min: hold MeCN 5\%. Retention times are reported as Rt.
High resolution mass spectra (HRMS) were recorded on a Waters Micromass LCT Premier spectrometer using time of flight with positive electrospray ionisation (ESI+), an ABI/MDS Sciex Q-STAR Pulsar with ESI+ and an ASAP (atmospheric pressure solids analysis probe ionisation), or a Bruker BioApex II 4.7e FTICR utilising either ESI+ or a positive electron ionisation (EI+) source equipped with a direct insertion probe. The mass reported is that containing the most abundant isotopes ( ${ }^{35} \mathrm{Cl}$ and $\left.{ }^{79} \mathrm{Br}\right)$. Limit: $\pm 5 \mathrm{ppm}$.
IR spectra were recorded neat on a Perkin-Elmer Spectrum Two FTIR spectrometer using Universal ATR sampling accessories. Letters in parentheses refer to the relative absorbency of the peak: w - weak ( $<40 \%$ of the most intense peak), m - medium ( $40-75 \%$ of the most intense peak), s - strong ( $>75 \%$ of the most intense peak) and br - broad.
Melting points were recorded on an Optimelt automated melting point system with a heating rate of $1^{\circ} \mathrm{C} / \mathrm{min}$ ( $70 \%$ onset point and $10^{\circ}$ clear point) and are uncorrected.

X-ray diffraction experiment for $\mathbf{3 3}$ was carried out on a D8 Venture 3-circle diffractometer (Bruker AXS) with a PHOTON 100 CMOS area detector, using Mo $\mathrm{K} \alpha$ radiation ( $\bar{\lambda}=0.71073 \AA$ ) from an $I \mu \mathrm{~S}$ microsource with focusing mirrors. The crystal was maintained at $T=120 \mathrm{~K}$ using a Cryostream (Oxford Cryosystems) open-flow $\mathrm{N}_{2}$ cryostat. The structure was solved by direct methods and refined by full-matrix least squares against $F^{2}$ of all reflections, using OLEX2 [2], SHELXS 2013/1 [3] and SHELXL 2014/7 [4] software. Crystallographic data for structure 33 have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC-1479349.

## A) Catalytic Chan-Lam in flow:

A solution was prepared from the amine $(0.781 \mathrm{mmol})$ in DCM $(5.5 \mathrm{~mL})$ and the boronic acid $(1.25 \mathrm{mmol})$ and $\mathrm{NEt}_{3}(0.039 \mathrm{~g}, 54 \mu \mathrm{~L}, 0.391 \mathrm{mmol})$ were added. A second solution was prepared with $\mathrm{Cu}(\mathrm{OAc})_{2} \cdot \mathrm{H}_{2} \mathrm{O}(0.195 \mathrm{mmol}, 0.25$ equiv $), \mathrm{NEt}_{3}(0.039 \mathrm{~g}, 54 \mu \mathrm{~L}, 0.391 \mathrm{mmol})$ and pyridine ( $0.062 \mathrm{~g}, 63 \mu \mathrm{~L}, 0.781 \mathrm{mmol}$ ) in DCM ( 5.5 mL ). The two solutions were introduced to independent 5 mL sample loop as shown in (Scheme 1). The dispensing HPLC pumps were each set at $0.125 \mathrm{~mL} / \mathrm{min}$ to achieve a residence time of 2 h . Two reverse "tube-in-tube" reactors were used in series to achieve a combined reactor volume of 30 mL which were heated at $40^{\circ} \mathrm{C}$. The reaction mixture was then passed through an Omnifit column ( $\mathrm{r}=$ $0.33 \mathrm{~cm}, \mathrm{~h}=10.00 \mathrm{~cm}$ ) filled with QP-DMA followed by a back pressure regulator ( 175 psi ). The crude reaction mixture was passed through a plug of silica to remove base line residue and the solvent evaporated under reduced pressure. The resultant crude material was then purified using flash chromatography.


Scheme 1: General flow scheme for catalytical Chan Lam reaction.

## Spectroscopic and experimental data:

## 1-(4-Methoxyphenyl)-3-phenyl-1H-pyrazole, 19:



Consistent with published data [5].
Prepared using general procedure A: Isolated yield; 0.139 g ( $79 \%, 0.70 \mathrm{mmol}$ scale);
Colourless crystals; Rf: 0.36 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR $\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.94-7.90(\mathrm{~m}, 2 \mathrm{H}), 7.85(\mathrm{~d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.69-7.65(\mathrm{~m}$, 2H), $7.46-7.41$ (m, 2H), 7.34 (ddt, $J=7.4,5.6,1.3 \mathrm{~Hz}, 1 \mathrm{H}), 7.01-6.97$ (m, 2H), 6.75 (d, J $=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 3.85(\mathrm{~s}, 3 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $176 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 158.3$ (C), 152.7 (C), 134.2 (C), 133.4 (C), 128.8 (CH), $128.2(\mathrm{CH}), 128.0(\mathrm{CH}), 125.9(\mathrm{CH}), 120.9(\mathrm{CH}), 114.7(\mathrm{CH}), 104.7(\mathrm{CH}), 55.7\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=3003$ (w), 1529 (m), 1516 (s), 1458 (m), 1363 (m), 1257 (s), 1234 (m), 1045 (m), 1025 (m), 956 (m) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.63 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=251.1[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{16} \mathrm{H}_{15} \mathrm{~N}_{2} \mathrm{O} 251.1184$, found $251.1192(\Delta=3.2 \mathrm{ppm})$;
M.p. $107-108{ }^{\circ} \mathrm{C}(i \mathrm{PrOH})\left(\right.$ Literature: $106-107^{\circ} \mathrm{C}$, aq. EtOH) [6].

Ethyl 2-(4-methoxyphenyl)-6-methyl-3-oxo-2,3-dihydropyridazine-4-carboxylate, 20:


Prepared using general procedure A: Isolated yield; 0.162 g ( $81 \%, 0.697 \mathrm{mmol}$ scale);
Yellow crystals; Rf: 0.24 (1/1, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 7.65(\mathrm{~s}, 1 \mathrm{H}), 7.52-7.45(\mathrm{~m}, 2 \mathrm{H}), 6.99-6.92(\mathrm{~m}, 2 \mathrm{H})$, $4.40(\mathrm{q}, J=7.1 \mathrm{~Hz}, 2 \mathrm{H}), 3.83(\mathrm{~s}, 3 \mathrm{H}), 2.42(\mathrm{~s}, 3 \mathrm{H}), 1.38(\mathrm{t}, J=7.1 \mathrm{~Hz}, 3 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $8 / \mathrm{ppm} 163.9$ (C), 159.5 (C), 156.5 (C), 143.9 (C), 134.74 (CH), $134.66(\mathrm{C}), 131.4(\mathrm{C}), 126.9(\mathrm{CH}), 114.1(\mathrm{CH}), 62.3\left(\mathrm{CH}_{2}\right), 55.7\left(\mathrm{CH}_{3}\right), 21.0\left(\mathrm{CH}_{3}\right), 14.3$ $\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=3022(\mathrm{w}), 2971(\mathrm{w}), 1739(\mathrm{~s}, \mathrm{C}=\mathrm{O}), 1658(\mathrm{~m}, \mathrm{C}=\mathrm{O}$ of lactam), 1604 (m), 1510 (m), 1314 (m), 1250 (m), 1229 (s), 1150 (m), 1025 (m), 841 (s) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $2.64 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=289.4[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{~N}_{2} \mathrm{O}_{4} 289.1188$, found $289.1198(\Delta=3.5 \mathrm{ppm})$;

Elemental analysis: calculated for $\mathrm{C}_{15} \mathrm{H}_{16} \mathrm{~N}_{2} \mathrm{O}_{4} \mathrm{C}: 62.49 \%, \mathrm{H}: 5.59 \%, \mathrm{~N}: 9.72 \%$; measured C: $62.63 \%(\Delta=0.14), \mathrm{H}: 5.59 \%(\Delta=0.00), \mathrm{N}: 9.73 \%(\Delta=0.01)$;
M.p. $80-81^{\circ} \mathrm{C}(i \mathrm{PrOH})$.

## 4-Methoxy- $N$-phenylaniline, 21:



Consistent with published data [7].
Prepared using general procedure A: Isolated yield; 0.125 g ( $90 \%, 0.69 \mathrm{mmol}$ scale);
Colourless crystals; Rf: 0.36 (8/2, EtOAc/hexanes);
${ }^{1}{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 7.28-7.22(\mathrm{~m}, 2 \mathrm{H}), 7.14-7.08(\mathrm{~m}, 2 \mathrm{H}), 6.98-6.83(\mathrm{~m}$, 5 H ), 5.54 (s, br, 1H), 3.83 (s, 3H);
${ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 155.4$ (C), 145.3 (C), 135.9 (C), 129.4 (CH), 122.4 $(\mathrm{CH}), 119.7(\mathrm{CH}), 115.8(\mathrm{CH}), 114.8(\mathrm{CH}), 55.7\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=3387$ (m), 3010 (w), 2958 (w), 2839 (w), 1595 (m), 1507 (s), 1499 (s), 1462 (w), 1443 (m), 1316 (m), 1298 (m), 1248 (s), 1236 (s), 1182 (m), 1169 (m), 1033 (w), 812 (m), 750 (s), 694 (s) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.15 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=200.6[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{13} \mathrm{H}_{14} \mathrm{NO} 200.1075$, found $200.1072(\Delta=1.5 \mathrm{ppm})$;
M.p. $102-104{ }^{\circ} \mathrm{C}(\mathrm{MeCN})$ (Literature: $101-103{ }^{\circ} \mathrm{C}$, no solvent reported) [7].

## Diphenylamine, 22:



Consistent with published data [8].
Prepared using general procedure A: Isolated yield; 0.108 g ( $92 \%, 0.69 \mathrm{mmol}$ scale);
Colourless crystals; Rf: 0.47 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta / \mathrm{ppm} 7.33-7.26(\mathrm{~m}, 4 \mathrm{H}), 7.13-7.07(\mathrm{~m}, 4 \mathrm{H}), 6.96(\mathrm{tt}, J=$ $7.3,1.1 \mathrm{~Hz}, 2 \mathrm{H}), 5.82(\mathrm{~s}, \mathrm{br}, 1 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 143.2(\mathrm{C}), 129.5(\mathrm{CH}), 121.2(\mathrm{CH}), 118.0(\mathrm{CH})$;
IR (neat) $v=3408$ (w), 3384 (m), 3042 (w), 1739 (w, br), 1596 (s), 1519 s), 1496 (s), 1459 (m), 1419 (m), 1319 (m), 1173 (m), 749 ( s$), 744$ ( s$), 690$ ( s$) \mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.22 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=170.1[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{12} \mathrm{H}_{12} \mathrm{~N} 170.0970$, found $170.0966(\Delta=2.4 \mathrm{ppm})$;
M.p. $53-54{ }^{\circ} \mathrm{C}(95 \% \mathrm{EtOH})$ (Literature: $54-55^{\circ} \mathrm{C}$, no solvent reported) [8].

## 5-Bromo- $N$-phenylpyridin-3-amine, 23:



Prepared using general procedure A: Isolated yield; 0.085 g ( $50 \%, 0.69 \mathrm{mmol}$ scale);
Colourless crystals; Rf: 0.20 ( $8 / 2$, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 8.24(\mathrm{~d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H}), 8.16(\mathrm{~d}, J=2.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.52(\mathrm{t}$, $J=2.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.38-7.30(\mathrm{~m}, 2 \mathrm{H}), 7.15-7.03(\mathrm{~m}, 3 \mathrm{H}), 6.02(\mathrm{~s}, \mathrm{br}, 1 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 141.9(\mathrm{CH}), 141.5$ (C), 140.7 (C), 137.5 (CH), 130.0 $(\mathrm{CH}), 124.6(\mathrm{CH}), 123.4(\mathrm{CH}), 121.0(\mathrm{C}), 119.7(\mathrm{CH})$;

IR (neat) $v=3257$ (w), 3083 (w), 3047 (w), 2992 (w), 2365 (w), 1739 (w, br), 1614 (w), 1578 (s), 1570 (s), 1497 (s), 1444 (s), 1343 (m), 1331 (m), 1219 (m), 1096 (m), 1005 (m), 854 (s), 750 (s), 693 (s) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.09 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=249.0[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{11} \mathrm{H}_{10} \mathrm{~N}_{2} \mathrm{Br} 249.0027$, found $249.0023(\Delta=1.6 \mathrm{ppm})$;
M.p. $160^{\circ} \mathrm{C}(\mathrm{DCM})$.

## 4-Chloro- $N$-phenylaniline, 24:



Consistent with published data [7].
Prepared using general procedure A: Isolated yield; 0.201 g ( $71 \%, 1.39 \mathrm{mmol}$ scale);
Yellow oil; Rf: 0.44 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 7.32-7.25(\mathrm{~m}, 3 \mathrm{H}), 7.24-7.19(\mathrm{~m}, 2 \mathrm{H}), 7.08-7.03(\mathrm{~m}$, 2H), 7.02 - 6.93 (m, 3H), 5.79 (s, br, 1H);
${ }^{13}{ }^{13}$ NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 142.7$ (C), 141.9 (C), 129.6 (CH), 129.4 (CH), 125.7 (C), $121.7(\mathrm{CH}), 119.0(\mathrm{CH}), 118.3(\mathrm{CH})$.

IR (neat) $v=3400$ (w, br), 3062 (w), 3029 (w), 1588 (s), 1501 (s), 1499 (s), 1496 (s), 1486 (s), 1310 (s), 1173 (m), 1091 (m), 816 (m), 748 (s), 693 (s) cm ${ }^{-1}$;

LC-MS (MeCN), Rt. $3.29 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=204.11[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{12} \mathrm{H}_{11} \mathrm{NCl} 204.0580$, found $204.0579(\Delta=0.5 \mathrm{ppm})$.
(Rac)-methyl 3-(4-hydroxyphenyl)-2-(phenylamino)propanoate, 25:


Prepared using general procedure A: Isolated yield; 0.049 g ( $26 \%, 0.69 \mathrm{mmol}$ scale);
Colourless crystals; Rf: 0.12 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta / \mathrm{ppm} 7.18(\mathrm{dd}, J=7.3, \mathrm{~Hz}, 2 \mathrm{H}), 7.02(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}), 6.76$ $(\mathrm{t}, J=7.3 \mathrm{~Hz}, 1 \mathrm{H}), 6.74(\mathrm{~d}, J=8,4 \mathrm{~Hz}, 2 \mathrm{H}), 6.63(\mathrm{~d}, J=7.7 \mathrm{~Hz}, 2 \mathrm{H}), 5.08(\mathrm{~s}, 1 \mathrm{H}), 4.33(\mathrm{t}, J$ $=6.1 \mathrm{~Hz}, 1 \mathrm{H}), 4.15(\mathrm{~s}, \mathrm{br}, 1 \mathrm{H}), 3.68(\mathrm{~s}, 3 \mathrm{H}), 3.14-3.00(\mathrm{~m}, 2 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 174.0(\mathrm{C}), 154.8(\mathrm{C}), 146.4(\mathrm{C}), 130.6(\mathrm{CH}), 129.5$ $(\mathrm{CH}), 128.3(\mathrm{C}), 118.7(\mathrm{CH}), 115.6(\mathrm{CH}), 113.8(\mathrm{CH}), 58.0(\mathrm{CH}), 52.3\left(\mathrm{CH}_{3}\right), 37.9\left(\mathrm{CH}_{2}\right)$;

IR (neat) $v=3391$ (m, br), 3028 (w). 2954 (w), 1727 (m, C=O), 1603 (s), 1515 (s), 1437 (w), 1221 ( $\mathrm{m}, \mathrm{br}$ ) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $2.61 \mathrm{~min} \mathrm{~m} / \mathrm{z}=272.4[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{16} \mathrm{H}_{18} \mathrm{NO}_{3} 272.1287$, found $272.1281(\Delta=2.2 \mathrm{ppm})$.

## (Rac)-methyl 3-(4-phenoxyphenyl)-2-(phenylamino)propanoate, 26:



The results from the 2D NMR spectra (2D-NOESY) are consistent with the second alkylation on the phenol rather than the secondary amine. The fact that correlation is present with the ortho-protons on the phenol attached to the amine and the methyl and methylene protons but no other correlation to other aromatic protons with the same methane and methylene protons, indicates that the other phenyl ring is not in the same environment. Unfortunately no correlation with the ortho-protons of the phenyl rings separated by the ether bond is present, but this could be due to the conformation of the molecule with the phenyl rings perpendicular to each other.

Prepared using general procedure A: Isolated yield; $8 \mathrm{mg}(3 \%, 0.69 \mathrm{mmol}$ scale);
Colourless crystals; Rf: 0.40 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR $\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta / \mathrm{ppm} 7.35-7.31(\mathrm{~m}, 2 \mathrm{H}), 7.20-7.16(\mathrm{~m}, 2 \mathrm{H}), 7.14-7.08(\mathrm{~m}$, $3 \mathrm{H}), 7.00-6.97(\mathrm{~m}, 2 \mathrm{H}), 6.95-6.92(\mathrm{~m}, 2 \mathrm{H}), 6.76(\mathrm{tt}, J=7.3,1.1 \mathrm{~Hz}, 1 \mathrm{H}), 6.64-6.60(\mathrm{~m}$, 2 H ), $4.35(\mathrm{t}, J=6.2 \mathrm{~Hz}, 1 \mathrm{H}), 3.69(\mathrm{~s}, 3 \mathrm{H}), 3.18-3.06(\mathrm{~m}, 2 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $176 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 173.6$ (C), 157.3 (C), 156.5 (C), 146.3 (C), 131.2 (C), $130.7(\mathrm{CH}), 129.9(\mathrm{CH}), 129.5(\mathrm{CH}), 123.4(\mathrm{CH}), 119.04(\mathrm{CH}), 119.01(\mathrm{CH}), 118.8(\mathrm{CH})$, $113.9(\mathrm{CH}), 58.1(\mathrm{CH}), 52.3\left(\mathrm{CH}_{3}\right), 38.1\left(\mathrm{CH}_{2}\right)$;

IR (neat) $v=3404$ (w), 3030 (w), 2954 (w), 1739 (m, C=O), 1603 (m), 1591 (m), 1506 (s), 1489 (s), 1239 (s) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.67 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=348.2[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{22} \mathrm{H}_{22} \mathrm{NO}_{3} 348.1600$, found $348.1609(\Delta=2.6 \mathrm{ppm})$.

## Methyl 4-methyl-2-(phenylamino)pentanoate, 27:



Prepared using general procedure A: Isolated yield; 0.153 g ( $60 \%, 0.69 \mathrm{mmol}$ scale);
Amorphous solid; Rf: 0.52 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 7.22-7.14(\mathrm{~m}, 2 \mathrm{H}), 6.75(\mathrm{tt}, J=7.4,1.1 \mathrm{~Hz}, 1 \mathrm{H}), 6.65-$ $6.60(\mathrm{~m}, 2 \mathrm{H}), 4.11(\mathrm{dd}, J=7.8,6.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.00(\mathrm{~s}, \mathrm{br}, 1 \mathrm{H}), 3.71(\mathrm{~s}, 3 \mathrm{H}), 1.81(\mathrm{dh}, J=13.3$, $6.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.72-1.59(\mathrm{~m}, 2 \mathrm{H}), 1.00(\mathrm{~d}, J=6.6 \mathrm{~Hz}, 3 \mathrm{H}), 0.95(\mathrm{~d}, J=6.6 \mathrm{~Hz}, 3 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 175.3$ (C), 147.1 (C), 129.5 (CH), 118.5 (CH), 113.5 $(\mathrm{CH}), 55.2(\mathrm{CH}), 52.2\left(\mathrm{CH}_{3}\right), 42.5\left(\mathrm{CH}_{2}\right), 25.0(\mathrm{CH}), 22.9\left(\mathrm{CH}_{3}\right), 22.32\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=3384(\mathrm{w}, \mathrm{br}), 3028$ (w), 2955 (m), 2870 (w), 1734 (s), 1602 (s), 1507 (m), 1433 (w), 1198 (m), 1155 (s), 748 (s), 691 (s) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.39 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=222.2[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{13} \mathrm{H}_{20} \mathrm{NO}_{2} 222.1494$, found $222.1496(\Delta=0.9 \mathrm{ppm})$.

## 1-(3,4-Dimethoxyphenyl)-3,4-dimethyl-1H-1,2,4-triazol-5(4H)-one, 28:



Prepared using general procedure A: Isolated yield; 0.045 g ( $26 \%, 0.702 \mathrm{mmol}$ scale);
Off-white crystals (recrystallised using $i \mathrm{PrOH}$ ); Rf: 0.12 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $600 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 7.56(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.45(\mathrm{dd}, J=8.8,2.4 \mathrm{~Hz}, 1 \mathrm{H})$, $6.89(\mathrm{~d}, J=8.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.93(\mathrm{~s}, 3 \mathrm{H}), 3.89(\mathrm{~s}, 3 \mathrm{H}), 3.29(\mathrm{~s}, 3 \mathrm{H}), 2.30(\mathrm{~s}, 3 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 152.3$ (C), 149.0 (C), 146.5 (C), 143.8 (C), 131.6 (C), $111.2(\mathrm{CH}), 110.7(\mathrm{CH}), 103.2(\mathrm{CH}), 56.1\left(\mathrm{CH}_{3}\right), 55.9\left(\mathrm{CH}_{3}\right), 27.4\left(\mathrm{CH}_{3}\right), 11.8\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=2943$ (w), 2842 (w), 1701 (s), 1604 (w). 1590 (w), 1515 (s), 1466 (m), 1250 (s), 1220 (m), 1027 (m) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $2.48 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=250.1[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{12} \mathrm{H}_{16} \mathrm{~N}_{3} \mathrm{O}_{3} 250.1192$, found 250.1196 ( $\Delta=1.6 \mathrm{ppm}$ );

Elemental analysis: calculated for $\mathrm{C}_{12} \mathrm{H}_{15} \mathrm{~N}_{3} \mathrm{O}_{3} \mathrm{C}: 57.82 \%, \mathrm{H}: 6.07 \%, \mathrm{~N}: 16.86 \%$; measured C: $57.60 \%(\Delta=0.22), \mathrm{H}: 6.08 \%(\Delta=0.01), \mathrm{N}: 16.51 \%(\Delta=0.35)$;
M.p. $145-146{ }^{\circ} \mathrm{C}(i \mathrm{PrOH})$.

## 1,3-Diphenyl-1H-pyrazole, 29:



Consistent with published data [5,9].
Prepared using general procedure A: Isolated yield; 0.249 g ( $81 \%, 0.70 \mathrm{mmol}$ scale);
Colourless crystals (recrystallised using $i \mathrm{PrOH}$ ); Rf: 0.40 ( $8 / 2$, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR $\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.99-7.95(\mathrm{~m}, 1 \mathrm{H}), 7.93(\mathrm{dd}, J=7.8,1.5 \mathrm{~Hz}, 2 \mathrm{H}), 7.80-7.76$ $(\mathrm{m}, 2 \mathrm{H}), 7.50-7.46(\mathrm{~m}, 2 \mathrm{H}), 7.44(\mathrm{t}, J=7.6 \mathrm{~Hz}, 2 \mathrm{H}), 7.37-7.33(\mathrm{~m}, 1 \mathrm{H}), 7.32-7.28(\mathrm{~m}$, 1H), $6.80-6.77$ (m, 1H);
${ }^{13} \mathrm{C}$ NMR ( $176 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 153.1$ (C), 140.4 (C), 133.2 (C), $129.6(\mathrm{CH}), 128.8$ (CH), $128.2(\mathrm{CH}), 128.1(\mathrm{CH}), 126.5(\mathrm{CH}), 126.0(\mathrm{CH}), 119.2(\mathrm{CH}), 105.2(\mathrm{CH})$;

IR (neat) $v=3137$ (w), 3065 (w), 1599 (m), 1526 (m), 1506 (m), 1457 (m), 1360 (m), 1303 (w), 1265 (m), 1045 (m), 954 (m), 940 (m) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.53 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=221.2[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{15} \mathrm{H}_{13} \mathrm{~N}_{2} 221.1079$, found $221.1090(\Delta=5.0 \mathrm{ppm})$;
M.p. $84-85^{\circ} \mathrm{C}(i \mathrm{PrOH})\left(\right.$ Literature: $83-84^{\circ} \mathrm{C}$, no solvent reported) [9].

## 1-(3-(Methylthio)phenyl)-3-phenyl-1H-pyrazole, 30:



Prepared using general procedure A: Isolated yield; 0.286 g ( $77 \%, 1.4 \mathrm{mmol}$ scale );
Colourless oil; Rf: 0.50 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $600 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 7.95(\mathrm{~d}, J=1.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.94-7.92(\mathrm{~m}, 2 \mathrm{H}), 7.73(\mathrm{t}, J=$ $2.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.49(\mathrm{ddd}, J=8.2,2.2,0.9 \mathrm{~Hz}, 1 \mathrm{H}), 7.45(\mathrm{dd}, J=8.2,7.1 \mathrm{~Hz}, 2 \mathrm{H}), 7.36(\mathrm{t}, J=$ $7.7 \mathrm{~Hz}, 2 \mathrm{H}), 7.19-7.15(\mathrm{~m}, 1 \mathrm{H}), 6.78(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.56(\mathrm{~s}, 3 \mathrm{H}) ;$
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 153.1$ (C), 140.7 (C), 140.5 (C), 133.1 (C), 129.7 (CH), $128.8(\mathrm{CH}), 128.2(\mathrm{CH}), 128.2(\mathrm{CH}), 126.0(\mathrm{CH}), 124.2(\mathrm{CH}), 117.0(\mathrm{CH}), 115.5(\mathrm{CH})$, $105.3(\mathrm{CH}), 15.8\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=3062$ (w), 2920 (w), 1591 (s), 1583 (s), 1530 (w), 1502 (s), 1479 (m), 1454 (s), 1360 (s), 1045 (s), 963 (m), 945 (m) cm ${ }^{-1}$;

LC-MS (MeCN), Rt. $4.409 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=267.1[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $267.0956 \mathrm{C}_{16} \mathrm{H}_{15} \mathrm{~N}_{2} \mathrm{~S}$, found $267.0966(\Delta=3.7 \mathrm{ppm})$.

## 1-(2-Methoxyphenyl)-3-phenyl-1H-pyrazole, 31:



Consistent with published data ${ }^{5}$
Prepared using general procedure A: Isolated yield; 0.227 g ( $65 \%, 1.4 \mathrm{mmol}$ scale );
Colourless oil; Rf: 0.43 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 8.09(\mathrm{~d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.94-7.90(\mathrm{~m}, 2 \mathrm{H}), 7.87$ (dd, $J$ $=7.9,1.7 \mathrm{~Hz}, 1 \mathrm{H}), 7.44-7.40(\mathrm{~m}, 2 \mathrm{H}), 7.35-7.29(\mathrm{~m}, 2 \mathrm{H}), 7.09(\mathrm{td}, J=7.7,1.3 \mathrm{~Hz}, 1 \mathrm{H})$, $7.06(\mathrm{dd}, J=8.3,1.3 \mathrm{~Hz}, 1 \mathrm{H}), 6.74(\mathrm{~d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H}), 3.91(\mathrm{~s}, 3 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 151.8$ (C), 151.2 (C), 133.3 (C), 133.0 (CH), 129.8 (C), $128.5(\mathrm{CH}), 127.8(\mathrm{CH}), 127.8(\mathrm{CH}), 125.9(\mathrm{CH}), 125.2(\mathrm{CH}), 121.3(\mathrm{CH}), 112.3(\mathrm{CH})$, $103.7(\mathrm{CH}), 56.0\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=3060(\mathrm{w}), 2940(\mathrm{w}), 2839$ (w), 1597 (m), 1530 (m), 1508 (s), 1455 (s), 1286 (m), 1259 (m), 1242 (s), 1127 (m), 1022 ( s$), 954$ (m), $942(\mathrm{~m}) \mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.53 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=251.2[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $251.14182 \mathrm{C}_{16} \mathrm{H}_{15} \mathrm{~N}_{2} \mathrm{O}$, found $251.1182(\Delta=0.0 \mathrm{ppm})$.

## 1-(3-Methoxyphenyl)-3-phenyl-1H-pyrazole, 32:



Consistent with published data [5].
Prepared using general procedure A: Isolated yield; 0.287 g ( $82 \%, 1.4 \mathrm{mmol}$ scale);
Colourless oil; Rf: 0.36 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 8.01-7.97(\mathrm{~m}, 2 \mathrm{H}), 7.96(\mathrm{~d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.52-7.44$ $(\mathrm{m}, 3 \mathrm{H}), 7.43-7.32(\mathrm{~m}, 3 \mathrm{H}), 6.88(\mathrm{ddd}, J=8.0,2.5,1.2 \mathrm{~Hz}, 1 \mathrm{H}), 6.80(\mathrm{~d}, J=2.5 \mathrm{~Hz}, 1 \mathrm{H})$, 3.92 (s, 3H);
${ }^{13}{ }^{13}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 160.6(\mathrm{C}), 152.9(\mathrm{C}), 141.4(\mathrm{C}), 133.2(\mathrm{C}), 130.2(\mathrm{CH})$, $128.7(\mathrm{CH}), 128.2(\mathrm{CH}), 128.1(\mathrm{CH}), 125.9(\mathrm{CH}), 112.1(\mathrm{CH}), 111.1(\mathrm{CH}), 105.2(\mathrm{CH})$, $105.1(\mathrm{CH}), 55.6\left(\mathrm{CH}_{3}\right)$;

IR (neat) $v=3065$ (w), 2961 (w), 1606 (s), 1593 (s), 1530 (m), 1504 (s), 1362 (m), 1246 (m), 1217 (s), 1170 (m), 1045 (s), 966 (m) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $3.35 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=251.1[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{16} \mathrm{H}_{15} \mathrm{~N}_{2} \mathrm{O} 251.1184$, found $251.1194(\Delta=4.0 \mathrm{ppm})$.

## 4-(3-Phenyl-1H-pyrazol-1-yl)benzonitrile, 33:



Prepared using general procedure A: Isolated yield; 0.264 g ( $76 \%, 1.4 \mathrm{mmol}$ scale $)$;
Colourless crystals (recrystallised using $i \mathrm{PrOH}$ ); Rf: 0.26 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $600 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $8.02(\mathrm{~d}, J=2.6 \mathrm{~Hz}, 1 \mathrm{H}), 7.94-7.88(\mathrm{~m}, 4 \mathrm{H}), 7.78-7.73(\mathrm{~m}$, $2 \mathrm{H}), 7.45$ (dd, $J=8.3,7.0 \mathrm{~Hz}, 2 \mathrm{H}), 7.41-7.36(\mathrm{~m}, 1 \mathrm{H}), 6.84(\mathrm{~d}, J=2.6 \mathrm{~Hz}, 1 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 154.2$ (C), 142.9 (C), 133.6 (CH), 132.3 (C), 128.8 $(\mathrm{CH}), 128.6(\mathrm{CH}), 128.0(\mathrm{CH}), 126.0(\mathrm{CH}), 118.7(\mathrm{CH}), 118.5(\mathrm{CN}), 109.3(\mathrm{C}), 106.5(\mathrm{CH})$;

IR (neat) $v=3138(\mathrm{w}), 3123(\mathrm{w}), 2228(\mathrm{~m}, \mathrm{CN}), 1604(\mathrm{~m}), 1533(\mathrm{~m}), 1520(\mathrm{~m}), 1517(\mathrm{~m})$, 1457 (m), 1394 (w), 1363 (m), 1183 (m), 953 (m), 939 (m) cm ${ }^{-1}$;

LC-MS (MeCN), Rt. $3.36 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=246.1[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{16} \mathrm{H}_{12} \mathrm{~N}_{3} 246.1031$, found $246.1032(\Delta=0.4 \mathrm{ppm})$;
M.p. $126-131{ }^{\circ} \mathrm{C}(i \mathrm{PrOH})$.

Crystal Data: 33, $\mathrm{C}_{16} \mathrm{H}_{11} \mathrm{~N}_{3}(M=245.28 \mathrm{~g} / \mathrm{mol})$ : monoclinic, space group $\mathrm{P} 2{ }_{1} / \mathrm{c}$ (no. 14), $a=$ 10.9809(6) $\AA, b=\quad 11.0294(6) \AA, c=\quad 11.0655(6) \AA, \beta=\quad 113.0712(17)^{\circ}, V=$ 1232.98(12) $\AA^{3}, Z=4, T=120 \mathrm{~K}, \mu(\mathrm{MoK} \alpha)=0.081 \mathrm{~mm}^{-1}$, Dcalc $=1.321 \mathrm{~g} / \mathrm{cm}^{3}, 26247$ reflections measured $\left(5.446^{\circ} \leq 2 \Theta \leq 60.176^{\circ}\right), 3621$ unique ( $R_{\text {int }}=0.0290, \mathrm{R}_{\text {sigma }}=0.0186$ ) which were used in all calculations. The final $R_{1}$ was 0.0457 ( $\mathrm{I}>2 \sigma(\mathrm{I})$ ) and $w R_{2}$ was 0.1236 (all data).

## 3-(3-Phenyl-1H-pyrazol-1-yl)benzonitrile, 34:



Chemical Formula: $\mathrm{C}_{16} \mathrm{H}_{11} \mathrm{~N}_{3}$
Exact Mass: 245.0953

Consistent with published data [5].
Prepared using general procedure A but using 2 equiv. of $\mathrm{NEt}_{3}$ to aid solubility: Isolated yield; $0.067 \mathrm{~g}(40 \%, 0.69 \mathrm{mmol}$ scale $)$;

Colourless oil; Rf: 0.30 (8/2, EtOAc/hexanes);
${ }^{1}{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 8.16-8.11(\mathrm{~m}, 1 \mathrm{H}), 8.04-7.97(\mathrm{~m}, 2 \mathrm{H}), 7.96-7.91(\mathrm{~m}$, $2 \mathrm{H}), 7.63-7.55(\mathrm{~m}, 2 \mathrm{H}), 7.52-7.45(\mathrm{~m}, 2 \mathrm{H}), 7.43-7.37(\mathrm{~m}, 1 \mathrm{H}), 6.85(\mathrm{~d}, J=2.6 \mathrm{~Hz}, 1 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 153.9$ (C), 140.7 (C), 132.5 (C), 130.5 (CH), 129.5 $(\mathrm{CH}), 128.9(\mathrm{CH}), 128.6(\mathrm{CH}), 127.9(\mathrm{CH}), 126.0(\mathrm{CH}), 122.6(\mathrm{CH}), 122.1(\mathrm{CH}), 118.3(\mathrm{C})$, 113.7 (C), 106.3 (CH);

IR (neat) $v=3148$ (w), 3064 (w), 2232 (m, CN), 1604 (s), 1587 (s), 1533 (m), 1506 (s), 1455 (s), 1437 (m), 1398 (m), 1368 (s), 1388 (w), 1051 (m), 967 (m) cm ${ }^{-1}$;

LC-MS (MeCN) Rt. $3.18 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=246.4[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{16} \mathrm{H}_{15} \mathrm{~N}_{2} \mathrm{O} 246.1031$, found $246.1040(\Delta=3.7 \mathrm{ppm})$.

## 2-(3-Phenyl-1H-pyrazol-1-yl)benzonitrile: 35;



Consistent with published data [10].
Prepared using general procedure A but using 2 equiv. of $\mathrm{NEt}_{3}$ to aid solubility: Isolated yield; 0.064 g ( $38 \%, 0.69 \mathrm{mmol}$ scale);

Colourless oil; Rf: 0.22 (8/2, EtOAc/hexanes);
${ }^{1} \mathrm{H}$ NMR ( $700 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta / \mathrm{ppm} 8.19(\mathrm{~d}, J=2.6 \mathrm{~Hz}, 1 \mathrm{H}), 7.96-7.91(\mathrm{~m}, 2 \mathrm{H}), 7.88(\mathrm{dd}, J$ $=8.3,1.1 \mathrm{~Hz}, 1 \mathrm{H}), 7.79(\mathrm{dd}, J=7.8,1.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.71(\mathrm{ddd}, J=8.3,7.5,1.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.47-$ $7.43(\mathrm{~m}, 2 \mathrm{H}), 7.41(\mathrm{td}, J=7.6,1.1 \mathrm{~Hz}, 1 \mathrm{H}), 7.37(\mathrm{ddt}, J=8.0,6.8,1.3 \mathrm{~Hz}, 1 \mathrm{H}), 6.86(\mathrm{~d}, J=$ $2.6 \mathrm{~Hz}, 1 \mathrm{H})$;
${ }^{13} \mathrm{C}$ NMR ( $176 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 154.2 (C), $142.0(\mathrm{C}), 134.8(\mathrm{CH}), 134.1(\mathrm{CH}), 132.6(\mathrm{C}), 130.7$ $(\mathrm{CH}), 128.9(\mathrm{CH}), 128.6(\mathrm{CH}), 127.0(\mathrm{CH}), 126.2(\mathrm{CH}), 123.8(\mathrm{CH}), 117.4(\mathrm{C}), 106.2(\mathrm{CH})$, 104.9 (C);

IR (neat) $v=3143$ (w), 3065 (w), 2226 (w, CN), 1601 (m), 1580 (m), 1532 (m), 1505 (s), 1455 (s), 1392 (w), 1364 (m), 1310 (w), 1259 (w), 1046 (m), 955 (m), 941 (m) cm ${ }^{-1}$;

LC-MS (MeCN) Rt. $3.11 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=246.4[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{16} \mathrm{H}_{12} \mathrm{~N}_{3} 246.1031$, found $246.1036(\Delta=2.0 \mathrm{ppm})$.
(E/Z)-ethyl 2-(1-ethoxyethylidene)hydrazinecarboxylate, 38:


Literature procedure [11].
Ethyl acetimidate hydrochloride ( $4.96 \mathrm{~g}, 10 \mathrm{mmol}$ ) was dissolved in absolute EtOH ( 200 mL ) and cooled using an ice bath. Ethyl hydrazine carboxylate ( $4.16 \mathrm{~g}, 10 \mathrm{mmol}$ ) was dissolved in absolute $\mathrm{EtOH}\left(80 \mathrm{~mL}\right.$ ) and added dropwise and reaction left to stir for 6 h at $0^{\circ} \mathrm{C}$. The solvent was evaporated under reduced pressure and the residue was purified using flash chromatography (9:1, DCM/MeOH) to give the pure product as white crystals ( $5.27 \mathrm{~g}, 76 \%$ yield) as a mixture of two $E / Z$ isomers (45:55).

Isolated yield: $5.27 \mathrm{~g}(76 \%, 10 \mathrm{mmol}$ scale $)$;
White crystals; Rf: 0.72 (1/9, DCM/MeOH);
Isomer 1: ${ }^{1} \mathrm{NMR}\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta / \mathrm{ppm} 8.06(\mathrm{~s}, \mathrm{br}, 1 \mathrm{H}), 4.08(\mathrm{q}, J=7.0 \mathrm{~Hz}, 4 \mathrm{H}), 2.09(\mathrm{~s}$, $3 \mathrm{H}), 1.33(\mathrm{t}, J=7.0 \mathrm{~Hz}, 6 \mathrm{H})$.

Isomer 2: ${ }^{1} \mathrm{NMR}\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta / \mathrm{ppm} 6.79(\mathrm{~s}, \mathrm{br}, 1 \mathrm{H}), 4.14(\mathrm{q}, J=7.0 \mathrm{~Hz}, 4 \mathrm{H}), 1.94(\mathrm{~s}$, $3 \mathrm{H}), 1.27$ (t, $J=7.0 \mathrm{~Hz}, 6 \mathrm{H})$.

IR (neat) $v=3408$ (w), 3274 (w, br), 2986 (w), 2938 (w), 1713 (s), 1657 (s), 1500 (br), 1447 (m), 1379 (m), 1338 (w), 1243 (br), 1047 (s), 1017 (w) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $2.63 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=174.8[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS $\left({ }^{+}\right.$ESI-TOF) calculated for $\mathrm{C}_{7} \mathrm{H}_{14} \mathrm{~N}_{2} \mathrm{O}_{3} 175.1083$, found $175.1078(\Delta=4.6 \mathrm{ppm})$.
M.p. $60-65^{\circ} \mathrm{C}(\mathrm{MeOH})$ (Literature: $68^{\circ} \mathrm{C}$, Pet. Ether) [12].

## 3,4-Dimethyl-1H-1,2,4-triazol-5(4H)-one, 39:



Literature procedure. ${ }^{13}$

Methylamine hydrochloride ( $2.70 \mathrm{~g}, 40 \mathrm{mmol}$ ) was dissolved in absolute EtOH ( 200 mL ) to which a suspension of sodium ethoxide ( $2.72 \mathrm{~g}, 40 \mathrm{mmol}$ ) in absolute EtOH ( 70 mL ) was added and reaction was stirred for 5 min at room temperature. A solution of ( $E$ )-ethyl 2-(1ethoxyethylidene)hydrazine carboxylate ( $\mathbf{3 8}, 3.48 \mathrm{~g}, 20 \mathrm{mmol}$ ) in absolute $\mathrm{EtOH}(50 \mathrm{~mL})$ was added dropwise and reaction refluxed for 4 h . The reaction was then cooled to room temperature and filtered over a celite pad. The eluant was dried under reduced pressure and the resultant residue was recrystallised (through a hot filtration) from EtOAc to give the pure product.

Isolated yield: 0.904 g ( $40 \%, 20 \mathrm{mmol}$ scale);
White crystals (recrystallised from EtOAc); Rf: 0.31 (1/9, DCM/MeOH);
${ }^{1} \mathrm{H}$ NMR ( 600 MHz, DMSO- $d_{6}$ ) $\delta / \mathrm{ppm} 11.28$ (s, br, 1H), 3.06 (s, 3H), 2.12 (s, 3H);
${ }^{13} \mathrm{C}$ NMR ( 151 MHz, DMSO- $d_{6}$ ) $\delta / \mathrm{ppm} 155.1(\mathrm{C}), 144.8(\mathrm{C}), 26.3\left(\mathrm{CH}_{3}\right), 11.4\left(\mathrm{CH}_{3}\right)$;
IR (neat) $v=3139(\mathrm{w}, \mathrm{br}), 3057(\mathrm{w}, \mathrm{br}), 3001(\mathrm{w}, \mathrm{br}), 2815(\mathrm{w}, \mathrm{br}), 1701(\mathrm{~s}), 1663(\mathrm{~s}), 1590$ (m), 1477 (m), 1474 (m), 1437 (m), 1400 (m), 1376 (m), 976 (m), 797 (m). 736 (s), 609 (s) $\mathrm{cm}^{-1}$;

LC-MS (MeCN), Rt. $0.77 \mathrm{~min}, \mathrm{~m} / \mathrm{z}=114.4[\mathrm{M}+\mathrm{H}]^{+}$. HR-MS (ESI-TOF) calculated for $\mathrm{C}_{4} \mathrm{H}_{7} \mathrm{~N}_{3} \mathrm{O} 114.0667$, found $114.0647(\Delta=17.5 \mathrm{ppm}$ or $-2.0 \mathrm{mDa})$.
M.p. $146-149{ }^{\circ} \mathrm{C}$ (EtOAc) (Literature: $147^{\circ} \mathrm{C}$, no solvent reported) [13].
${ }^{1} H$ NMR $\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{1 9 )}$

${ }^{13}$ C NMR ( $176 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (19)

${ }^{1} H$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{2 0})$

${ }^{13} C N M R\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{2 0})$

${ }^{1} H$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (21)

${ }^{13} C N M R\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{2 1})$

${ }^{1} H$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (22)

${ }^{13} C \operatorname{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{2 2})$

${ }^{1} H$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (23)

${ }^{1} H$ NMR (400 MHz, $\left.\mathrm{CDCl}_{3}\right)(\mathbf{2 4})$

${ }^{1} H$ NMR (700 MHz, $\left.\mathrm{CDCl}_{3}\right)(\mathbf{2 5})$

${ }^{13} C N M R\left(176 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{2 5})$
(
${ }^{1} H$ NMR (700 MHz, $\left.\mathrm{CDCl}_{3}\right)(\mathbf{2 6})$

${ }^{13} C N M R\left(176 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{2 6})$

${ }^{1} H$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (27)

${ }^{13}$ C NMR (101 MHz, $\mathrm{CDCl}_{3}$ ) (27)

${ }^{1} H$ NMR ( $600 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (28)

${ }^{13} C N M R\left(151 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{2 8})$

${ }^{1} H$ NMR (700 MHz, $\left.\mathrm{CDCl}_{3}\right)(\mathbf{2 9 )}$

${ }^{13}$ C NMR ( $176 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (29)

${ }^{1} H$ NMR ( $600 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (30)

${ }^{1} H$ NMR ( $600 \mathrm{MHz}, \mathrm{CDCl}_{3}$ )(31)

${ }^{13}$ C NMR ( $151 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (31)

${ }^{1} H$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ )(32)
(s)
${ }^{13} C N M R\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{3 2})$

${ }^{1} H N M R\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(33)$

${ }^{13} C \operatorname{NMR}\left(176 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(33)$

${ }^{1} H$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (34)

${ }^{13} C N M R\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{3 4})$

${ }^{1} H$ NMR $\left(700 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{3 5})$

${ }^{1} H$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (38)

${ }^{13} C \operatorname{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)(\mathbf{3 8})$

${ }^{1} H$ NMR ( $600 \mathrm{MHz}, \mathrm{CDCl}_{3}$ )(39)


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