Supporting Information

A Novel Three-Component One-Pot Synthesis of 1*H*-imidazol-4-yl-pyridines

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¹H and ¹³C NMR spectra were obtained in the mentioned solvents and detected with a Varian Mercury VX 400 spectrometer. Chemical shifts are expressed in ppm (δ) with respect to TMS as an internal standard. Electron spray ionisation mass spectra (ESI) were obtained using a MSD (Hewlett-Packard HPLC 1100 driven electro spray MS instrument). The purity was determined utilizing a Hewlett-Packard LC 1100 system [YMC column, 2mm x 50mm, 2µm ODSA, 220nm and 254nm; 0.6mL/min, 6min gradient from 90% H₂O to 10% H₂O (0.5% CH₃COOH) vs. CH₃CN]

All starting material are commercial available. Some isocyanides are available at www.priaton.de

General Procedure: 1 mmol of *ortho*-picolylamine and 1 mmol aldehyde is dissolved in 3ml methanol at room temperature. 50mol-% InCl₃ and 1 mmol isocyanide is added after 5 minutes. The reaction mixture is allowed to stir for 16 h at room temperature. After evaporation of the solvent the residue is filtrated through a silica gel pad using MeOH/CHCl₃ as solvent to remove the polar impurities. The resulting semi pure product is purified via prep. HPLC after evaporation of the solvent.

2-[1-Benzyl-2-(4-chloro-phenyl)-1*H*-imidazol-4-yl]-pyridine 4a

Yield: 34%

¹H NMR (400MHz, CDCl₃): δ = 4.44 (s, 2H, CH₂Ph), 6.88-6.91 (m, 2H, Ar), 7.04-7.07 (m, 3H, Ar), 7.47, 7.63 (AB, 4H, ³J=8.8 Hz, Ar), 8.10-8.26 (m, 3H, 3CH_{pyridine}), 8.99 (s, 1H, CH_{imidazole}), 10.84 (d, 1H, ³J=6.0 Hz, CH=N_{pyridine}).

^{13}C NMR (100MHz, CDCl_3): δ = 49.8 (CH_2Ph), 126.5, 127.8, 127.9, 128.7, 129.2, 130.6, 131.8, 133.0, 135.1, 136.3, 136.4, 137.4, 137.9, 138.4, 138.5.
 $\text{C}_{21}\text{H}_{16}\text{ClN}_3$ (345.83) MS (ESI) m/z : 346.1 $[\text{M}+\text{H}]^+$

2-(1-Furan-2-ylmethyl-2-phenethyl-1*H*-imidazol-4-yl)-pyridine 4b

Yield: 27%

^1H NMR (400MHz, $\text{DMSO}-d_6$): δ = 2.92 (t, 2H, $^3J=8.0$ Hz, CH_2), 3.26 (t, 2H, $^3J=8.0$ Hz, CH_2), 4.88 (s, 2H, $\text{CH}_{2\text{furyl}}$), 6.26-6.29 (m, 1H, CH_{furyl}), 6.36-6.39 (m, 1H, CH_{furyl}), 7.08-7.54 (m, 10H, Ar), 8.86 (d, 1H, $^3J=7.6$ Hz, $\text{CH}=\text{N}_{\text{pyridine}}$).

^{13}C NMR (100MHz, $\text{DMSO}-d_6$): δ = 21.1 ($\text{CH}_2\text{CH}_2\text{Ph}$), 34.0 ($\text{CH}_2\text{CH}_2\text{Ph}$), 48.5 ($\text{CH}_{2\text{furyl}}$), 105.8 (CH_{furyl}), 110.3 (CH_{furyl}), 123.4, 125.4, 125.8, 128.0, 128.2, 128.3, 133.3, 133.4, 137.5, 141.3, 141.6, 145.6, 155.4, 172.0.

$\text{C}_{21}\text{H}_{19}\text{N}_3\text{O}$ (329.41) MS (ESI) m/z : 330.1 $[\text{M}+\text{H}]^+$

2-{2-Cyclohexyl-1-[2-(3,4-dimethoxy-phenyl-ethyl)-1*H*-imidazol-4-yl]}-pyridine 4c

Yield: 55%

^1H NMR (400MHz, CD_3OD): δ = 1.29-1.58 (m, 3H, cyclohexyl), 1.73-1.92 (m, 7H, cyclohexyl), 2.94 (t, 2H, $^3J=6.0$ Hz, CH_2), 3.16-3.24 (m, 1H, cyclohexyl), 3.60 (t, 2H, $^3J=6.0$ Hz, CH_2), 3.72 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 6.60-6.74 (m, 3H, Ar), 8.04 (t, 1H, $^3J=7.2$ Hz, $\text{CH}_{\text{pyridine}}$), 8.32 (t, 1H, $^3J=8.0$ Hz, $\text{CH}_{\text{pyridine}}$), 8.50 (d, 1H, $^3J=8.4$ Hz, $\text{CH}_{\text{pyridine}}$), 9.02 (d, 1H, $^3J=6.8$ Hz, $\text{CH}=\text{N}_{\text{pyridine}}$), 9.31 (s, 1H, $\text{CH}_{\text{imidazole}}$).

$\text{C}_{24}\text{H}_{29}\text{N}_3\text{O}_2$ (391.52) MS (ESI) m/z : 392.1 $[\text{M}+\text{H}]^+$

2-[2-Phenyl-1-(tetrahydro-furan-2-ylmethyl)-1*H*-imidazol-4-yl]-pyridine 4d

Yield: 17%

^1H NMR (400MHz, DMSO- d_6): δ = 1.36-1.45 (m, 1H), 1.67 (quin, 2H, $^3J=6.8$ Hz, CH_2), 1.78-1.85 (m, 1H), 2.66 (dd, 1H, $^2J=14.4$ Hz, $^3J=6.0$ Hz), 2.79 (dd, 1H, $^2J=14.4$ Hz, $^3J=5.2$ Hz), 3.47 (dd, 2H, $^2J=14.8$ Hz, $^3J=6.8$ Hz), 3.56 (dd, 2H, $^2J=14.8$ Hz, $^3J=6.8$ Hz), 3.83 (quin, 1H, $^3J=6.8$ Hz, CH), 6.97 (t, 1H, $^3J=6.0$ Hz, Ar), 7.24-7.45 (m, 8H, Ar), 8.79 (d, 1H, $^3J=6.8$ Hz, $\text{CH}=\text{N}_{\text{pyridine}}$).

^{13}C NMR (100MHz, DMSO- d_6): δ = 25.8 (CH_2), 29.7 (CH_2), 56.7 ($\text{CH}_2\text{-N}$), 67.9, 80.2, 116.2, 122.9, 127.8, 128.1, 128.2, 128.5, 128.6, 131.2, 131.3, 134.0, 140.9, 141.0.

$\text{C}_{19}\text{H}_{19}\text{N}_3\text{O}$ (305.38) MS (ESI) m/z : 306.1 $[\text{M}+\text{H}]^+$

2-(1-Butyl-2-isobutyl-1*H*-imidazol-4-yl)-pyridine 4e

Yield: 49%

^1H NMR (400MHz, DMSO- d_6): δ = 0.84 (t, 3H, $^3J=6.8$ Hz, CH_3), 0.92 (d, 6H, $^3J=6.8$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.26 (sxt, 2H, $^3J=6.8$ Hz, CH_2), 1.65 (quin, 2H, $^3J=6.8$ Hz, CH_2), 2.24 (quin, 1H, $^3J=6.8$ Hz, $\text{CH}(\text{CH}_3)_2$), 2.99 (d, 2H, $^3J=6.8$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 3.18 (t, 2H, $^3J=6.8$ Hz, CH_2), 8.22 (t, 1H, $^3J=7.2$ Hz, Ar), 8.40 (t, 1H, $^3J=7.2$ Hz, Ar), 8.73 (d, 1H, $^3J=8.0$ Hz, Ar), 9.35 (d, 1H, $^3J=7.2$ Hz, $\text{CH}=\text{N}_{\text{pyridine}}$), 9.51 (s, 1H, $\text{CH}_{\text{imidazole}}$).

^{13}C NMR (100MHz, DMSO- d_6): δ = 14.4, 20.3, 22.9, 28.2, 32.7, 42.0, 47.2, 126.8, 128.1, 131.1, 134.9, 136.9, 139.9, 142.8, 145.2.

$\text{C}_{16}\text{H}_{23}\text{N}_3$ (257.38) MS (ESI) m/z : 258.1 $[\text{M}+\text{H}]^+$

2-[1-(3-tert.-Butyl-benzyl)-2-isobutyl-1*H*-imidazol-4-yl]-3-methyl-pyridine 4g

Yield: 39%

^1H NMR (400MHz, CDCl_3): δ = 0.91 (t, 3H, $^3J=7.6$ Hz, CH_3), 1.66 (sxt, 2H, $^3J=7.6$ Hz, CH_2CH_3), 2.33 (s, 3H, CH_3), 2.94 (t, 2H, $^3J=7.6$ Hz, CH_2), 4.96 (s, 2H, CH_2), 6.77 (t, 1H, Ar), 6.98 (d, 1H, Ar), 7.41 (m, 2H, Ar), 7.51 (m, 1H, Ar), 7.62 (m, 2H, Ar), 9.07 (d, 1H, Ar).

^{13}C NMR (100MHz, CDCl_3): δ = 14.0, 18.5, 22.5, 39.6, 52.4, 123.6, 124.2, 127.0, 129.0, 130.9, 133.6, 141.8, 142.5.

$\text{C}_{20}\text{H}_{20}\text{F}_3\text{N}_3$ (359.40) MS (ESI) m/z : 360.1 $[\text{M}+\text{H}]^+$

2-(1-Benzyl-2-cyclopropyl-1*H*-imidazol-4-yl)-3-methyl-pyridine 4h

Yield: 43%

^1H NMR (400MHz, CDCl_3): δ = 1.14 (m, 2H, CH_2), 1.23 (m, 2H, CH_2), 2.45 (m, 1H, CH), 2.67 (s, 3H, CH_3), 5.06 (s, 2H, CH_2), 7.05 (m, 1H, Ar), 7.22 (m, 2H, Ar), 7.37 (d, 2H, Ar), 7.65 (m, 2H, Ar), 8.63 (s, 1H, $\text{CH}_{\text{imidazole}}$), 9.89 (d, 1H, $\text{CH}=\text{N}_{\text{pyridine}}$).

^{13}C NMR (100MHz, CDCl_3): δ = 11.4, 15.8, 18.9, 22.2, 51.6, 122.9, 128.8, 128.9, 132.1, 133.4, 134.0, 139.5, 140.6.

$\text{C}_{19}\text{H}_{19}\text{N}_3$ (289.38) MS (ESI) m/z : 290.1 $[\text{M}+\text{H}]^+$

cf_62_
STANDARD 1H OBSERVE

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory: auto_15Mar2002

Pulse Sequence: gDQCOSY

Solvent: cdcl3
Ambient temperature
Sample #18
File: cf_62_06
Mercury-400BB "mercury400"

Relax. delay 1.000 sec
Acq. time 0.204 sec
Width 5012.5 Hz
2D Width 5012.5 Hz
8 repetitions
2 x 128 increments
OBSERVE H1, 400.4502800 MHz
DATA PROCESSING
Sq. sine bell 0.153 sec
Shifted by -0.102 sec
F1 DATA PROCESSING
Sq. sine bell 0.038 sec
Shifted by -0.026 sec
FT size 2048 x 2048
Total time 45 min, 28 sec

cf_62
STANDARD 1H OBSERVE

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory: auto_15Mar2002

Pulse Sequence: gDQCOSY

Solvent: cdcl3
Ambient temperature
Sample #5
File: cf_62_06
Mercury-400BB "mercury400"

Relax. delay 1.000 sec
Acq. time 0.204 sec
Width 5012.5 Hz
2D Width 5012.5 Hz
8 repetitions
2 x 128 increments
OBSERVE H1, 400.4502800 MHz
DATA PROCESSING
Sq. sine bell 0.153 sec
Shifted by -0.102 sec
F1 DATA PROCESSING
Sq. sine bell 0.038 sec
Shifted by -0.026 sec
FT size 2048 x 2048
Total time 45 min, 28 sec

cf_62_
STANDARD 1H OBSERVE

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory: auto_15Mar2002

Pulse Sequence: NOESY

Solvent: cdcl3
Ambient temperature
Sample #5
File: cf_62_07
Mercury-400BB "mercury400"

Relax. delay 1.000 sec
Mixing 0.200 sec
Acq. time 0.204 sec
Width 5012.5 Hz
2D Width 5012.5 Hz
64 repetitions
2 x 128 increments
OBSERVE H1, 400.4502800 MHz
DATA PROCESSING
Gauss apodization 0.095 sec
F1 DATA PROCESSING
Gauss apodization 0.024 sec
FT size 2048 x 2048
Total time 6 hr, 43 min, 47 sec

cf_62_
STANDARD 1H OBSERVE

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory: auto_15Mar2002

Pulse Sequence: ROESY

Solvent: cdc13
Ambient temperature

Sample #5

File: cf_62_08

Mercury-400BB "mercury400"

Relax. delay 1.000 sec
Mixing 0.200 sec
Acq. time 0.204 sec
Width 5012.5 Hz
2D Width 5012.5 Hz
64 repetitions
2 x 256 increments
OBSERVE H1, 400.4502800 MHz
DATA PROCESSING
Gauss apodization 0.095 sec
F1 DATA PROCESSING
Gauss apodization 0.047 sec
FT size 2048 x 2048
Total time 13 hr, 35 min, 10 sec