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Manganese catalyzed C-alkylation of methyl N-heteroarenes

with primary alcohols

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1. General information.

All the catalytic and stoichiometric reactions have been carried out under argon or nitrogen atmosphere using a standard Schlenk line and glove box technique in oven dried glassware. Reaction temperatures are disclosed as the temperature of the bath surrounding the vessel unless otherwise mentioned.

Chemicals. Commercially available chemicals were purchased from Avra Synthesis, TCI, Sigma Aldrich, and Alfa Aesar chemicals without further purifications. Dry and deoxygenated solvents were prepared according to standard procedures.

Analytical: ¹H, ¹³C{1H}, ¹⁹F NMR spectra were collected using Bruker (¹H: 500 MHz, ¹³C{1H}: 126 MHz) and JEOL (¹H: 400 MHz, ¹³C{1H}: 100 MHz) and were referenced to the resonances of the solvent used. Coupling constants (J) are reported in Hertz (Hz). Coupling patterns are indicated as: br (broad), s (singlet), d (doublet), t (triplet), dd (doublet of doublet), or m (multiplet). FT-IR spectra were recorded by Perkin–Elmer FT–IR Spectrometer. The elemental analyses were carried out with a Perkin-Elmer 240C elemental analyzer. Mass spectral analyses were done in Bruker micrOTOF-Q II Spectrometer.

Chromatography. Gas chromatography were recorded in the Thermofisher GC-MS spectrometer with an appropriate internal standard. For thin layer chromatography (TLC) analysis Merck pre-coated TLC plates (silica gel 60 F254 0.25 mm) were used. Visualization was accomplished by UV light (254 nm), KMnO₄, and ceric ammonium molybdate strain.

2. Synthesis of manganese complexes.

2.1 Synthesis of manganese complex [Mn(CO)₂(Br)C₁₂H₁₂N₄] (Mn-1)].

To a solution of (E)-2-(2-(1-(pyridin-2-yl)ethylidene)hydrazineyl)pyridine (21 mg, 0.1 mmol, 1.0 equiv.) in Toluene (2 mL) was added $Mn(CO)_5Br$ (27.4 mg, 1.0 equiv.) and the mixture was heated at 80 °C for 2h. Orange color precipitate formed. Solvent was removed from the reaction mixture and solid compound was washed with hexane (3 × 2 mL). Orange color solid compound was found as a mixture of cationic and neutral complex. The analytical data are consistent with those previously reported literature.¹ Selected **IR** (KBr, cm⁻¹): 2022 (C=O), 1913 (C=O), 1857 (C=O), 1611, 1463, 1278, 1246, 1109, 775.

2.2 Synthesis of manganese complex [(4-Ph)Triaz(NHPⁱPr₂)₂Mn(CO)₂Br] (Mn-2).



In a 15mL Schlenk tube, $(4-Ph)Triaz(NHP'Pr_2)_2$ (42 mg, 0.1 mmol, 1 equiv.) and manganese pentacarbonyl bromide (0.1 mmol, 27.4 mg, 1 equiv.) were suspended in toluene (2 mL) and heated to reflux for 16 h. After cooling to room temperature, the supernatant solution was filtered off and the precipitate was washed three times with haxene and dried in vacuo to afford [(4-Ph)Triaz(NHP'Pr_2)_2Mn(CO)_2Br] (**Mn-2**) as a

bright yellow powder (91%). The analytical data are consistent with those previously reported literature.² Selected **IR** (KBr, cm⁻¹): 1937 (C=O), 1867 (C=O).

2.3 Synthesis of manganese complex [Mn(CO)₂(Br)NH(C₂H₄PⁱPr₂)₂] (Mn-3).



In a 15 mL schlenk tube under an urgon atmosphere, $Mn(CO)_5Br$ (85.3 mg, 0.31 mmol) was suspended in toluene (4 mL). Then $[NH(C_2H_4P^iPr_2)_2]$ (100 mg, 0.33 mmol) was added dropwise via syringe at room temperature. After 10 min of stirring the mixture was heated at 100 °C for 24 h. After removing solvent under reduced pressure yellow solid compound

Mn-3 was observed. Washing this solid with hexane $(3 \times 2 \text{ mL})$ and drying under high vacuum provided [Mn(CO)₂(Br)NH(C₂H₄P^{*i*}Pr₂)₂] (Mn-3) as a yellow solid (98%, 0.30 mmol, 150 mg) as complex. The analytical data are consistent with those previously reported literature.³ Selected IR (ATR, cm⁻¹): 1903 (C=O), 1815(C=O), 1464.8, 1406.8, 1384.5, 1366.2, 1248.4, 1091.6, 828.5.

2.4 Synthesis of manganese complex [Mn(CO)₂(Br)NH(C₂H₄PPh₂)₂] (Mn-4).



In a 15 mL schlenk tube, Bis[2-(diphenylphosphino)ethyl]amine hydrochloride (47.8 mg, 0.1 mmol), toluene (0.8 mL), water (0.2 mL) and NaOH (12 mg, 0.3 mmol, 3 equiv.) were taken. The reaction mixture was stirred at 45 °C for 30 min. Two phases were separated and the organic layer was concentrated under reduced pressure. Subsequently

Mn-4 toluene (1.2 mL) and $MnBr(CO)_5$ (0.1 mmol, 27.4 mg, 1 equiv.) were added to the schlenk tube. The reaction mixture was stirred for 20 h at reflux temperature. After removing solvent under reduced pressure yellow solid compound was observed. Washing this solid with hexane (3*2 mL) and drying under high vacuum provided [Mn(CO)₂(Br)NH(C₂H₄PPh₂)₂] (**Mn-4**) as a yellow solid (91%, 58 mg,

0.091 mmol) as a complex. The analytical data are matched with the previously reported literature.⁴ Selected **IR** (ATR, cm⁻¹): 1910 (C=O), 1826 (C=O).

2.5 Synthesis of manganese complex [Mn(CO)₃(Br)C₁₁H₁₁N₃S] (Mn-5).



In a schlenk tube, the hydrazone ligand (21.7 mg, 0.1 mmol) prepared from corresponding ketone and hydrazine and $Mn(CO)_5Br$ were taken. After adding THF (2 mL) to the reaction mixture, schlenk tube was sealed and heated at 90 °C for 4 h. Yellow color crystals started to coming out upon cooling. Hexane was added and the yellow crystals are collected upon decanting the solvent from the Schlenk tube,

washed with hexane and dried. 40.1 mg, 92% yield of $[Mn(CO)_3(Br)C_{11}H_{11}N_3S]$ (**Mn-5**) was obtained. The analytical data are matches with our previously reported literature.⁵ Selected **IR** (KBr, cm⁻¹): 2026 (C=O), 1934.8 (C=O), 1908.7 (C=O), 1617.4, 1574, 1487, 1104.3.

2.6 Synthesis of manganese complex $[Mn(CO)_3(Br)C_{11}H_{12}N_2S]$ (Mn-6) and $[Mn(CO)_3(Br)C_{14}H_{16}N_2S]$ (Mn-7).



Manganese complexes **Mn-6** and **Mn-7** were prepared according to our previously published literature.⁶ In a schlenk tube, amine ligand (0.1 mmol) prepared from the corresponding aldehyde and 2 aminomethyl pyridine, $Mn(CO)_5Br$ (28 mg, 1.02 equiv.) and THF (2 mL) were taken and the schlenk tube was sealed and heated at 90 °C for 4 h. The color of the solution turns into red during that time. After evaporation of solvent under Ar atmosphere it turns amorphous yellow color solids which were washed with hexane (3 × 2 mL) and dried. Brown color solid compounds were obtained in 70% and 96% yields, respectively. For **Mn-6**, Selected **IR** (ATR, cm⁻¹): 3182.3 (N-H), 2019.7 (C=O), 1938.1 (C=O), 1865.3 (C=O), 1619.9, 1462.9, 1271.1, 1120.2, 1026.4, 965.2, 791.8, 706.1 and for Mn-7, Selected **IR** (ATR, cm⁻¹): 3045, 2928, 2860, 2025 (C=O), 1962 (C=O), 1913(C=O), 1605, 1478, 1429, 1088, 751, 697.

3. Detailed optimization of the reaction conditions.

General procedure: In a 15 mL reaction tube [**Mn**] (2 mol%) and base (0.2 mmol) were taken. After that ^{*t*}AmOH (0.1 mL), **1a** (0.2 mmol) and **2a** (0.3 mmol) were added and the tube was closed before the mixture was placed in a preheated oil bath at 140 °C for 24 h. Upon completion the reaction mixture was quenched with water (2 mL) and extracted with ethyl acetate (3×5 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100–200 mesh) with hexane/ethyl acetate mixture as eluent.

Table S1. Catalyst optimization.^a

| | + Ph OH (2 mol%) 'BuOK, 'AmOH | | + Ph N Ph |
|-----------------|--|---------------------|----------------------|
| 1a | 140 °C, 24 h 2a | 3aa | 4aa |
| Entry | [Mn] (2 mol%) | Yield%(3aa) | Yield% (4aa) |
| 1. ^b | Mn-1 (2.5 mol%) in ^t BuOH) | - | 89 |
| 2. ^c | Mn-2 (0.5 mol%), KOH in ^t BuOH/PhM | Me) - | 94 |
| 3. | Mn-3 | 98 (95) | trace |
| 4. | Mn-4 | 96 (92) | trace |
| 5. | Mn-5 | trace | trace |
| 6. | Mn-6 | trace | trace |
| 7. | Mn-7 | 55 | 19 |

^a2-methylquinoline **1a** (0.2 mmol), benzyl alcohol **2a** (0.3 mmol), [**Mn**] (2 mol%), ^{*i*}BuOK (0.2 mmol), ^{*i*}AmOH (0.1 mL) at 140 °C, 24 h. Yields were measured by gas chromatography using mesitylene as an internal standard. ^{*b*}ref – 1. ^{*c*}ref – 2b

Table S2. Solvent optimization.^a

| l 1a | + N | Ph OH Mn-3 (2 mc [/] BuOK, Solv 140 °C, 24 | vent ^I h 3aa | Ph |
|---------|--------|---|-------------------------------|----|
| | Entry | solvent | Yield (%) | |
| - | 1. | ^t AmOH | 98 | |
| | 2. | Toluene | 63 | |
| | 3. | Dioxane | 91 | |

^a2-methylquinoline **1a** (0.2 mmol), benzylalcohol **2a** (0.3 mmol), **Mn-3** (2 mol%), ^bBuOK (0.2 mmol), **Solvent** (0.1 mL) at 140 °C, 24 h. Yields were measured by GC-MS taking mesitylene as an internal standard.

Table S3. Base optimization.^a

| 1: | + N + | Ph OH Mn-3 (2 mol%) Base, ^t AmOH 140 °C, 24 h | - Contraction of the second se | ۶h |
|----|----------|--|--|----|
| | Entry | Base (1 equiv.) | Yield (%) | |
| | 1. | ^t BuOK | 98 | |
| | 2. | ^t BuONa | 24 | |
| | 3. | ^t BuOLi | trace | |
| | 4. | Cs_2CO_3 | trace | |
| | 5. | КОН | 96 | |

^{*a*}2-methylquinoline **1a** (0.2 mmol), benzylalcohol **2a** (0.3 mmol), **Mn-3** (2 mol%), **Base** (0.2 mmol), ^{*t*}AmOH (0.1 mL) at 140 °C, 24 h. Yields were measured by GC-MS taking mesitylene as an internal standard.

Table S4. Alcohol optimization.^a



^{*a*}2-methylquinoline **1a** (0.2 mmol), benzylalcohol **2a** (1-2 equiv.), **Mn-3** (2 mol%), ^{*t*}BuOK (0.2 mmol), ^{*t*}AmOH (0.1 mL) at 140 °C, 24 h. Yields were measured by GC-MS taking mesitylene as an internal standard.

Table S5. Optimization of base equivalency.^a

| ĺ | 1a 2a | Mn-3 (2 mol%) ^t BuOK (x equiv.) ^t AmOH (0.1 mL), 140 °C, 24 h | 3aa | + Ph 4aa |
|---|-------|---|-------------------------|-------------------------|
| | Entry | ^f BuOK (equiv.) | Yield of 3aa (%) | Yield of 4aa (%) |
| _ | 1. | 1 | 98 | - |
| | 2. | 0.5 | 15 | 18 |
| | 3. | 0.1 | - | - |

^{*a*}2-methylquinoline **1a** (0.2 mmol), benzylalcohol **2a** (0.3 mmol), **Mn-3** (2 mol%), ^{*t*}BuOK (0.1-1 equiv.), ^{*t*}AmOH (0.1 mL) at 140 °C, 24 h. Yields were measured by GC-MS taking mesitylene as an internal standard.

4. Manganese catalysed C-alkylations of methyl N-heteroarenes with primary alcohols.

General procedure:

In a 15 mL reaction tube **Mn-3** (0.004 mmol) and ^{*t*}BuOK (0.2 mmol) were taken. After that ^{*t*}AmOH (0.1 mL), **1a** (0.2 mmol) and **2a** (0.3 mmol) were added and the tube was closed before the mixture was placed in a preheated oil bath at 140 °C for 24 h. Upon completion the reaction mixture was quenched with water (2 mL) and extracted with ethyl acetate (3×5 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100–200 mesh) with hexane/ethyl acetate mixture as eluent.

2-phenethylquinoline (3aa):⁷ Yield: 95% (44 mg, 0.190 mmol). The title compound was isolated as a light

brown oil eluting with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, J = 8.5 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.71 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.50 (dd, J = 11.3, 4.2 Hz, 1H), 7.34 – 7.17 (m, 6H), 3.35 – 3.28 (m, 2H), 3.18 (dd, J = 9.8, 6.2 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 161.9, 148.1, 141.7, 136.3, 129.5, 129.0, 128.6, 128.5, 127.6, 126.9, 126.1, 125.9, 121.7, 41.1, 36.0.

2-(4-methylphenethyl)quinolone (3ab):⁸ Yield: 91% (45 mg, 0.186 mmol). The title compound was



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isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (dd, J = 19.8, 8.2 Hz, 2H), 7.78 (dd, J = 8.0, 0.9 Hz, 1H), 7.70 (ddd, J = 8.2, 6.8, 1.3 Hz, 1H), 7.55 – 7.45 (m, 1H), 7.24 (d, J = 8.5 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 7.9 Hz,

2H), 3.33 – 3.25 (m, 2H), 3.13 (dd, *J* = 9.8, 6.4 Hz, 2H), 2.33 (s, 3H). ¹³**C NMR** (101 MHz, CDCl₃) δ 162.1, 148.1, 138.5, 136.4, 135.6, 129.5, 129.2, 129, 128.5, 127.6, 126.9, 126, 121.7, 41.2, 35.7, 21.1.

2-(4-methoxyphenethyl)quinoline (**3ac**):⁷ Yield: 91% (48 mg, 0.182 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.09 (d, J = 8.5 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.70 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.50 (dd,

J = 11.1, 4.1 Hz, 1H), 7.22 (d, J = 8.5 Hz, 1H), 7.16 (d, J = 8.6 Hz, 2H),

6.83 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.27 (dd, *J* = 9.7, 6.4 Hz, 2H), 3.11 (dd, *J* = 9.6, 6.5 Hz, 2H). ¹³C **NMR** (101 MHz, CDCl₃) δ 162.0, 158, 148.1, 136.3, 133.7, 129.5, 129, 127.6, 126.9, 125.9, 121.7, 113.9, 55.3, 41.4, 35.2.

2-(2-([1,1'-biphenyl]-4-yl)ethyl)quinoline (3ad): Yield: 74% (46 mg, 0.148 mmol). The title compound was isolated as a white solid with 2% ethyl acetate in hexane. Selected IR (DCM, cm⁻¹): 2950.6, 2926.8, 2852.0, 1603.2, 1561.1, 1501.0, 1487.3, 1451.2, 1425.5, 1405.7, 1116.4, 977.3, 762.1, 689.4, 489.0. ¹H NMR

(500 MHz, CDCl₃) δ 8.11 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.72 (t, *J*

= 7.6 Hz, 1H), 7.60 (d, J = 7.8 Hz, 2H), 7.52 (dd, J = 16.8, 7.8 Hz, 3H), 7.44 (t, J = 7.6 Hz, 2H), 7.34 (d, J = 7.9 Hz, 3H), 7.27 (d, J = 8.3 Hz, 1H), 3.35 (dd, J = 9.6, 6.5 Hz, 2H), 3.26 - 3.19 (m, 2H); **13C NMR** (126 MHz, CDCl₃) δ 161.9, 148.2, 141.2, 140.8, 139.1, 136.4, 129.5, 129.1, 129.0, 128.8, 127.7, 127.3, 127.2, 127.1, 127.0, 125.9, 121.7, 41.0, 35.6; **HRMS** (ESI) m/z: [M+H]⁺ Calcd for C₂₃H₁₉N: 310.1590; Found 310.1580.

2-(4-chlorophenethyl)quinoline (3ae):⁹ Yield: 72% (38 mg, 0.144 mmol). The title compound was



isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.06 (t, J = 8.7 Hz, 2H), 7.81 – 7.75 (m, 1H), 7.70 (ddd, J = 8.4, 7.0, 1.4 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.26 (s, 1H), 7.24 – 7.15 (m, 3H), 7.13 - 7.08 (m, 1H), 3.30 - 3.24 (m, 2H), 3.14 (dd, J = 9.6,

6.2 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 161.3, 148.1, 143.7, 136.5, 134.2, 129.8, 129.6, 129, 128.8, 127.7, 127, 126.9, 126.3, 126.0, 121.6, 40.7, 35.5.

2-(3-methoxyphenethyl)quinolone (3af):⁸ Yield: 95% (50 mg, 0.190 mmol). The title compound was



isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.06 (dd, J = 19.3, 8.5 Hz, 2H), 7.77 (d, J = 8.0Hz, 1H), 7.70 (ddd, J = 8.5, 7.0, 1.4 Hz, 1H), 7.49 (ddd, J = 7.9, 6.8, 0.9

Hz, 1H), 7.22 (dd, J = 16.6, 8.2 Hz, 2H), 6.89 – 6.80 (m, 2H), 6.76 (dd, J = 8.2, 2.7 Hz, 1H), 3.76 (s, 3H), 3.33 - 3.25 (m, 2H), 3.15 (dd, J = 9.8, 6.3 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 161.9, 159.7, 148.1, 143.2, 136.3, 129.5, 129.4, 128.9, 127.6, 126.9, 125.9, 121.7, 121, 114.2, 111.6, 55.2, 41, 36.1.

2-(2-methylphenethyl)quinoline (3ag):⁸ Yield: 92% (45 mg, 0.184 mmol). The title compound was



isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.71 (ddd, J = 8.4, 7.1, 1.5 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.21 (dd, *J* = 8.3, 4.6 Hz, 2H), 7.15 (dt, *J* = 8.9, 4.6 Hz, 3H), 3.32 – 3.23 (m, 2H), 3.21

- 3.12 (m, 2H), 2.36 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 162.1, 148.1, 139.8, 136.3, 136.1, 130.3, 129.5, 129.0, 128.9, 127.6, 126.9, 126.3, 126.2, 125.9, 121.6, 39.8, 33.4, 19.5.

2-(3,5-dimethoxyphenethyl)quinoline (3ah):¹⁰ Yield: 82% (48 mg, 0.164 mmol). The title compound was



isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR $(500 \text{ MHz}, \text{CDCl}_3) \delta 8.07 \text{ (dd}, J = 19.4, 8.4 \text{ Hz}, 2\text{H}), 7.78 \text{ (d, J = 8.1)}$ Hz, 1H), 7.71 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.26 (t, J = 5.7 Hz, 1H), 6.44 (d, J = 2.1 Hz, 2H), 6.34 (t, J = 2.2 Hz, 1H),3.76 (s, 6H), 3.30 (dd, J = 9.5, 6.7 Hz, 2H), 3.12 (dd, J = 9.6, 6.7 Hz,

2H). ¹³C NMR (126 MHz, CDCl₃) δ 161.7, 160.8, 148.0, 143.9, 136.2, 129.4, 128.8, 127.5, 126.8, 125.8, 121.5, 106.5, 98.2, 55.2, 55.1, 40.7, 36.2.

2-(3,4-dimethoxyphenethyl)quinoline (3ai):¹¹ Yield: 92% (54 mg, 0.184 mmol). The title compound was



isolated as a light brown oil with 10% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ 8.09 (dd, J = 18.5, 8.4 Hz, 2H), 7.80 (d, J = 8.1Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.25 (d, J = 100

8.4 Hz, 1H), 6.79 (d, *J* = 15.5 Hz, 3H), 3.87 (s, 3H), 3.82 (s, 3H), 3.30 (dd, *J* = 9.3, 6.8 Hz, 2H), 3.13 (dd, *J* = 9.4, 6.7 Hz, 2H); ¹³**C NMR** (126 MHz, CDCl₃) δ 161.8, 148.8, 147.9, 147.3, 136.3, 134.1, 129.5, 128.8, 127.5, 126.8, 125.8, 121.6, 120.3, 112, 111.3, 55.9, 55.7, 41.2, 35.6.

2-(2-(naphthalen-2-yl)ethyl)quinoline (3aj):⁸ Yield: 62% (35 mg, 0.124 mmol). The title compound was isolated as a white solid with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, J = 8.2



Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.83 – 7.75 (m, 4H), 7.74 – 7.68 (m, 2H), 7.51 (ddd, J = 7.8, 6.8, 1.0 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.28 – 7.22 (m, 1H), 3.40 (ddd, J = 9.1, 5.9, 2.0 Hz, 2H), 3.37 – 3.30 (m, 2H); ¹³C

NMR (126 MHz, CDCl₃) δ 161.9, 148.2, 139.2, 136.4, 133.8, 132.2, 129.6, 129.0, 128.1, 127.8, 127.7, 127.6, 127.5, 127.0, 126.7, 126.1, 126.0, 125.4, 121.7, 41.0, 36.2.

2-(2-(furan-2-yl)ethyl)quinoline (3ak):¹² Yield: 77% (34 mg, 0.154 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹**H NMR** (400 MHz, CDCl₃) δ 8.05 (dd, *J* =



8.4, 4.3 Hz, 2H), 7.79 – 7.75 (m, 1H), 7.69 (ddd, J = 8.3, 6.8, 1.3 Hz, 1H), 7.50 (dd, J = 11.1, 4.2 Hz, 1H), 7.32 (d, J = 1.6 Hz, 1H), 7.23 (d, J = 8.4 Hz, 1H), 6.26 (dd, J = 3.0, 2.0 Hz, 1H), 6.00 (d, J = 2.9 Hz, 1H), 3.36 – 3.30 (m, 2H),

3.22 – 3.16 (m, 2H); ¹³**C NMR** (126 MHz, CDCl₃) δ 161.4, 155.2, 148.1, 141.1, 136.4, 129.5, 129, 127.6, 127, 126, 121.5, 110.3, 105.5, 37.5, 28.0.

2-(2-(pyridin-3-yl)ethyl)quinolone (3al):8 Yield: 98% (46 mg, 0.196 mmol). The title compound was



isolated as a light brown oil with 30% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ 8.49 (s, 2H), 8.05 (dd, J = 8.1, 4.9 Hz, 2H), 7.83 – 7.63 (m, 2H), 7.59 – 7.41 (m, 2H), 7.20 (d, J = 8.3 Hz, 2H), 3.34 – 3.25 (m, 2H), 3.22 – 3.13 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 160.9, 148.1, 136.5, 129.7,

129, 127.7, 126.9, 126.1, 121.6, 40.3, 33.

2-pentylquinoline (3am):¹² Yield: 73% (29 mg, 0.146 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.05 (dd, *J* = 8.4, 2.5 Hz, 2H),

7.76 (d, J = 8.0 Hz, 1H), 7.67 (ddd, J = 8.3, 6.9, 1.4 Hz, 1H), 7.50 – 7.43 (m, 1H), 7.29 (d, J = 8.4 Hz, 1H), 2.96 (dd, J = 8.6, 7.2 Hz, 2H), 1.87 – 1.73 (m, 2H), 1.38 (pd, J = 9.4, 3.0 Hz, 4H), 0.90 (t, J = 7.0 Hz, 3H); ¹³**C NMR** (126 MHz, CDCl₃) δ 163.3, 148.1, 136.3, 129.4, 129, 127.6, 126.8, 125.7, 121.5, 39.5, 31.9, 29.9, 22.7, 14.1. **2-octylquinoline (3an):**⁸ Yield: 75% (36 mg, 0.15 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ 8.05 (dd, *J* = 8.4, 2.7 Hz, 2H), 7.76 (d,

J = 8.1 Hz, 1H), 7.70 - 7.64 (m, 1H), 7.47 (dd, J = 7.9, 7.0 Hz, 1H),7.29 (d, J = 8.4 Hz, 1H), 3.02 - 2.92 (m, 2H), 1.87 - 1.75 (m, 2H),

1.48 – 1.24 (m, 12H), 0.87 (t, *J* = 6.8 Hz, 3H). ¹³**C NMR** (126 MHz, CDCl₃) δ 163.27, 148.06, 136.2, 129.4, 129, 127.6, 126.8, 125.7, 121.5, 39.6, 32.0, 30.2, 29.8, 29.7, 29.6, 29.4, 22.8, 14.2.

2-undecylquinoline (**3ao**):¹² Yield: 70% (40 mg, 0.140 mmol). The title compound was isolated as a light brown oil with 1% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.05 (dd, *J* = 8.4, 5.8 Hz, 2H),



7.80 – 7.75 (m, 1H), 7.68 (ddd, J = 8.3, 6.8, 1.3 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.30 (d, J = 8.5 Hz, 1H), 3.01 – 2.92 (m, 2H), 1.86 – 1.78 (m, 2H), 1.45 – 1.25 (m, 16H), 0.88 (t, J = 6.9 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 163.3, 148.1,

136.3, 129.4, 129.0, 127.6, 126.9, 125.8, 121.5, 39.6, 32.1, 31.0, 30.2, 29.8, 29.75, 29.72, 29.70, 29.67, 29.5, 22.8, 14.3.

2-heptadecylquinoline (3ap): Yield: 68% (50 mg, 0.136 mmol). The title compound was isolated as a amorphous brown solid with 1% ethyl acetate in hexane. Selected **IR** (DCM, cm⁻¹): 2920.1, 2850.7, 1738.5,



1601.2, 1563.2, 1504.8, 1471.5, 1426.7, 1374.4, 1264.3, 740.3; ¹H NMR (500 MHz, CDCl₃) δ 7.95 (t, *J* = 8.1 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.62 – 7.52 (m, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 2.91 – 2.80 (m, 2H), 1.71

(dt, J = 15.6, 7.7 Hz, 2H), 1.35 - 1.14 (m, 28H), 0.78 (t, J = 6.9 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 163.1, 147.9, 136.1, 129.2, 128.8, 127.4, 126.7, 125.6, 121.3, 39.4, 31.9, 30.0, 29.56 (overlapped), 29.3, 22.6, 14.1; **HRMS (ESI)** m/z: [M+H]⁺ Calcd for C₂₆H₄₁N: 368.3312; Found 368.3306.

2-nonadecylquinoline (**3aq**): Yield: 53% (42 mg, 0.106 mmol). The title compound was isolated as a amorphous white solid with 1% ethyl acetate in hexane. Selected **IR** (DCM, cm⁻¹): 2019.0, 2849.5, 1618.7,

1601.0, 1562.8, 1504.1, 1472.0, 1427.1, 826.6, 717.4, 619.3; ¹H NMR (500 MHz, CDCl₃) δ 8.05 (t, J = 8.0 Hz, 2H), 7.77 (d, J = 7.9 Hz, 1H), 7.71 – 7.64 (m, 1H), 7.48 (t, J = 7.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 2.99 – 2.95 (m, 2H), 1.86 – 1.75 (m, 2H), 1.47 – 1.13 (m, 32H), 0.88 (t, J = 6.9 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 163.3, 148.1, 136.3, 129.4, 129.0, 127.6, 126.9, 125.8, 121.5, 39.6, 32.1, 30.2, 30.08 – 29.68 (overlapped), 22.8, 14.3. HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₈H₄₅N: 396.3625; Found 396.3624.

2-(2-cyclohexylethyl)quinoline (3ar):¹² Yield: 79% (38 mg, 0.158 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, J =



8.3 Hz, 2H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.70 – 7.63 (m, 1H), 7.47 (dd, *J* = 11.1, 4.1 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 3.03 – 2.92 (m, 2H), 1.88 – 1.76 (m, 2H), 1.76 – 1.64 (m, 5H), 1.39 – 1.15 (m, 4H), 0.97 (qd, *J* = 12.2, 3.0 Hz,

2H); ¹³C NMR (126 MHz, CDCl₃) δ 163.6, 148.1, 136.3, 129.4, 128.9, 127.6, 126.8, 125.7, 121.5, 37.9, 37.8, 37.0, 33.4, 26.8, 26.5.

2-(2-cyclopropylethyl)quinoline (3as):¹² Yield: 82% (32 mg, 0.164 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, *J* =

8.4 Hz, 2H), 7.78 – 7.73 (m, 1H), 7.70 – 7.64 (m, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 3.07 (dd, J = 8.7, 7.0 Hz, 2H), 1.77 – 1.68 (m, 2H), 0.84 – 0.72 (m, 1H), 0.47 – 0.39 (m, 2H), 0.07 (q, J = 5.0 Hz, 2H); ¹³C NMR (126

MHz, CDCl₃) δ 163, 148.1, 136.2, 129.4, 129, 127.6, 126.8, 125.7, 121.7, 39.5, 35.2, 11.0, 4.7.

(**R**)-2-(4,8-dimethylnon-7-en-1-yl)quinoline (3at):¹² Yield: 93% (52 mg, 0.186 mmol). The title compound was isolated as a colorless oil with 2% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ

8.05 (dd, *J* = 8.4, 4.3 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.67 (t, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 5.09 (t, *J* = 6.7 Hz, 1H), 3.01 – 2.89 (m, 2H), 1.96 (qd, *J* = 14.5, 7.3 Hz, 2H), 1.89 – 1.78 (m, 2H), 1.67 (s, 3H), 1.58 (s, 3H), 1.51 – 1.40 (m, 2H), 1.34 (dt, *J* = 15.1, 5.8 Hz, 1H), 1.25

(dt, *J* = 10.9, 5.5 Hz, 1H), 1.15 (dt, *J* = 22.3, 7.0 Hz, 1H), 0.89 (d, *J* = 6.3 Hz, 3H); ¹³**C NMR** (126 MHz, CDCl₃) δ 163.2, 148.1, 136.3, 131.2, 129.4, 129.0, 127.6, 126.9, 125.8, 125.1, 121.5, 39.8, 37.2, 37, 32.5, 27.7, 25.8, 25.7, 19.7, 17.8.

6-methyl-2-phenethylquinoline (**3ba**):⁷ Yield: 82% (41 mg, 0.164 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.00 – 7.93



(m, 2H), 7.57 - 7.51 (m, 2H), 7.27 (dt, J = 11.0, 7.0 Hz, 4H), 7.23 - 7.16 (m, 2H), 3.31 - 3.24 (m, 2H), 3.15 (dd, J = 9.8, 5.9 Hz, 2H), 2.53 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 161, 146.7, 141.7, 135.7, 131.8, 128.7,

128.5, 126.9, 126.6, 126.1, 121.7, 41.1, 36.2, 21.6.

6-methoxy-2-phenethylquinoline (**3ca**):⁸ Yield: 75% (40 mg, 0.150 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane.



¹**H NMR** (400 MHz, CDCl₃) δ 7.94 (dd, J = 14.5, 8.8 Hz, 2H), 7.35 (dd, J = 9.2, 2.8 Hz, 1H), 7.25 (dd, J = 12.0, 6.8 Hz, 4H), 7.18 (t, J = 8.4 Hz, 2H), 7.04 (d, J = 2.8 Hz, 1H), 3.91 (s, 3H), 3.24 (dd, J = 9.7, 6.0 Hz, 2H), 3.13 (dd, J = 9.8, 6.1 Hz, 2H). ¹³**C NMR** (126 MHz, CDCl₃) δ

 $159.3,\,157.4,\,141.7,\,135.2,\,130.4,\,128.6,\,128.5,\,127.8,\,126.1,\,122.0,\,121.9,\,105.3,\,55.6,\,40.8,\,36.2.$

7-chloro-2-phenethylquinoline (3da):¹³ Yield: 71% (38 mg, 0.142 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ 8.09 (d, J = 1.7 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 8.7 Hz, 1H), 7.44 (dd, J = 8.6, 2.0 Hz, 1H), 7.32 – 7.27 (m,

2H), 7.25 (t, *J* = 5.7 Hz, 2H), 7.23 – 7.18 (m, 2H), 3.29 (dd, *J* = 9.6, 6.4 Hz, 2H), 3.16 (dd, *J* = 9.5, 6.5 Hz, 2H); ¹³**C** NMR (126 MHz, CDCl₃) δ 163.1, 148.5, 141.6, 136.0, 135.3, 128.8, 128.6, 128.5, 128.1, 126.9, 126.2, 125.2, 121.9, 41, 35.8.

5,7-dichloro-2-phenethylquinoline (3ea): Yield: 60% (36 mg, 0.119 mmol). The title compound was isolated as a light brown solid with 2% ethyl acetate in hexane. Selected **IR** (DCM, cm⁻¹): 3062.8, 3027.3,



2925.2, 2854.6, 1605.8, 1553.2, 1453.6, 1391.0, 1331.9, 1136.8, 1061.0, 967.0, 859.6, 747.3; ¹H NMR (400 MHz, CDCl₃) δ 8.38 (d, *J* = 8.6 Hz, 1H), 8.00 (d, *J* = 1.6 Hz, 1H), 7.56 (d, *J* = 1.9 Hz, 1H), 7.32 – 7.25 (m, 3H), 7.22 (dd, *J* = 8.8, 4.3 Hz, 3H), 3.34 – 3.26 (m, 2H), 3.16 (dd, *J* = 9.4, 6.4 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 164.0, 148.8, 141.3, 134.7,

133.0, 132.2, 128.6, 127.5, 126.8, 126.3, 123.6, 122.7, 40.8, 35.6. **HRMS (ESI)** m/z: [M+H]⁺ Calcd for C₁₇H₁₃Cl₂N: 302.0498, Found 302.0510.

4-phenethylquinoline (3fa):¹² Yield: 92% (43 mg, 0.184 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹**H NMR** (400 MHz, CDCl₃) δ 8.79 (d, *J* = 4.4 Hz, 1H), 8.14 (d,



J = 8.4 Hz, 1H), 8.08 (d, J = 8.3 Hz, 1H), 7.72 (ddd, J = 8.3, 6.9, 1.1 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.3 Hz, 2H), 7.22 (ddd, J = 17.4, 10.3, 3.6 Hz, 4H), 3.39 (dd, J = 9.3, 6.9 Hz, 2H), 3.08 (dd, J = 9.4, 6.7 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 150.3, 148.5, 147.5, 141.1, 130.4, 129.2, 128.7, 128.5, 127.6, 126.6, 126.5, 123.5, 121.0, 36.28, 34.2.

2-phenethylquinoxaline (3ga):⁸ Yield: 69% (32 mg, 0.138 mmol). The title compound was isolated as a pale yellow oil with 2% ethyl acetate in hexane.



¹**H NMR** (400 MHz, CDCl₃) δ 8.61 (s, 1H), 8.06 (dd, J = 7.9, 1.7 Hz, 2H), 7.78 – 7.67 (m, 2H), 7.30 – 7.16 (m, 5H), 3.32 (dd, J = 9.3, 6.4 Hz, 2H), 3.18 (dd, J = 9.4, 6.4 Hz, 2H); ¹³**C NMR** (126 MHz, CDCl₃) δ 156.6, 145.9, 142.4, 141.4, 140.9, 130.1, 129.3, 129.2, 129.0, 128.7, 128.6, 126.4, 38.2, 35.4.

1-benzyl-2-phenethyl-1H-benzo[d]imidazole (3ha):⁷ Yield: 97% (61 mg, 0.194 mmol). The title compound was isolated as a light brown solid with 15% ethyl acetate in hexane. ¹H NMR (400 MHz,



CDCl₃) δ 7.84 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 5.8 Hz, 6H), 7.22 (d, J = 4.3 Hz, 3H), 7.17 (d, J = 7.2 Hz, 2H), 7.02 – 6.95 (m, 2H), 5.18 (s, 2H), 3.16 (d, J = 10.0 Hz, 4H); ¹³C NMR (101 MHz, CDCl₃) δ 154.6, 142.6, 140.9, 136, 135.4, 129.1, 128.6, 128.5, 128, 126.4, 126.2, 122.5, 122.2, 119.4, 109.6, 46.7, 34.1, 29.7.

1-benzyl-5,6-dichloro-2-phenethyl-1H-benzo[d]imidazole (3ia): Yield: 87% (66 mg, 0.174 mmol). The



title compound was isolated as a light brown solid with 10% ethyl acetate in hexane. Selected **IR** (DCM, cm⁻¹): 3027.2, 2855.0, 1605.2, 1511.2, 1496.6, 1453.6, 1403.0, 1308.5, 1095.8, 1076.9, 947.2, 841.0, 697.64. ¹H NMR (400 MHz, CDCl₃) δ 7.84 (s, 1H), 7.32 – 7.17 (m, 7H), 7.12 (dd, *J* = 5.0, 3.2 Hz,

2H), 6.92 (dd, *J* = 6.5, 2.9 Hz, 2H), 5.08 (s, 2H), 3.19 – 3.04 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ 156.9, 142.2, 140.6, 135.2, 134.8, 129.3, 128.8, 128.5, 128.4, 126.7, 126.6, 126.4, 126.1, 120.7, 111.1, 47.1, 34.0, 29.8; HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₂H₂₈Cl₂N₂: 381.0920; Found 381.0930.

2-phenethylbenzo[d]oxazole (3ja):⁸ Yield: 78% (35 mg, 0.157 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 7.70 – 7.65 (m, 1H),



7.50 – 7.45 (m, 1H), 7.33 – 7.17 (m, 7H), 3.23 (d, J = 3.1 Hz, 4H); ¹³C NMR (101 MHz, CDCl₃) δ 156.8, 144.8, 144.2, 142.4, 140.9, 128.6, 128.5, 126.3, 37.3, 35.5.

4-phenethylpyrimidine (3ka):¹⁴ Yield: 77% (28 mg, 0.154 mmol). The title compound was isolated as a

light brown oil with 5% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ 9.18 (s, 1H), 8.59 (d, *J* = 3.0 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.21 (dd, *J* = 15.8, 7.5 Hz, 3H), 7.10 (d, *J* = 4.2 Hz, 1H), 3.10 (s, 4H); ¹³C NMR (126 MHz, CDCl₃)

 $\delta \ 169.7, \ 158.9, \ 156.8, \ 140.7, \ 128.6, \ 128.5, \ 126.4, \ 120.8, \ 39.6, \ 34.8$

N,N-dibenzyl-4-phenethylpyrimidin-2-amine (3la): Yield: 82% (62 mg, 0.164 mmol). The title compound was isolated as a light brown oil with 2% ethyl acetate in hexane. Selected IR (DCM, cm⁻¹): 3085.4, 3061.4, 3028.2, 1575.4, 1556.9, 1503.6, 1452.6, 1421.8, 1348.9, 696.6; ¹H NMR (500 MHz, CDCl₃) δ 8.23 (d, J =

4.9 Hz, 1H), 7.37 - 7.31 (m, 4H), 7.31 - 7.24 (m, 8H), 7.19 (dd, J = 12.6, 7.1 Hz, 3H), 6.39 (d, J = 4.9 Hz, 1H), 4.92 (s, 4H), 3.04 (t, J = 7.7 Hz, 2H), 2.93 (t, J = 7.8 Hz, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 170.3, 162.3, 157.8, 141.7, 138.9, 128.6, 126.5, 128.4, 127.9, 127.1, 126.0, 109.3, 49.14, 39.50, 34.29. HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₆H₂₄N₃: 380.2121; Found 380.2133.

2-phenethylpyrazine (**3ma**):¹⁴ Yield: 99% (36 mg, 0.198 mmol). The title compound was isolated as a light brown oil with 5% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.52 – 8.48 (m, 1H), 8.41



- 8.32 (m, 2H), 7.26 (t, J = 7.3 Hz, 2H), 7.21 – 7.12 (m, 3H), 3.14 – 3.08 (m, 2H), 3.08 – 3.02 (m, 2H); ¹³**C NMR** (126 MHz, CDCl₃) δ 156.9, 144.8, 144.2, 142.5, 140.9, 128.6, 128.5, 126.3, 37.3, 35.5.

3-phenethylpyridazine:¹⁵ (**3na**) Yield: 60% (22 mg, 0.120 mmol). The title compound was isolated as a light brown oil with 40% ethyl acetate in hexane. ¹**H NMR** (500 MHz, CDCl₃) δ 9.08 (d, *J* = 3.9 Hz, 1H),



7.35 (dd, J = 8.1, 4.6 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.21 (q, J = 7.5 Hz, 4H), 3.35 – 3.29 (m, 2H), 3.19 – 3.13 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 170.2, 163, 149.7, 140.7, 128.5, 126.5, 126.3, 126.2, 38.2, 35.6.

2-(2-([1,1'-biphenyl]-4-yl)ethyl)pyridine (3od):¹⁶ Yield: 62% (32 mg, 0.124 mmol). The title compound was isolated as a white solid with 10% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, *J* =



4.7 Hz, 1H), 7.62 – 7.55 (m, 3H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.25 (m, 3H), 7.16 – 7.09 (m, 2H), 3.18 – 3.07 (m, 4H); **13C NMR** (126 MHz, CDCl₃) δ 161.3, 149.5, 141.2, 140.9, 139.0, 136.5, 129.0, 128.9,

127.3, 127.2, 127.1, 123.2, 121.3, 40.3, 35.8.

2-(2-(naphthalen-2-yl)ethyl)pyridine (3oj):¹⁷ Yield: 54% (25 mg, 0.108mmol). The title compound was isolated as a white solid with 10% ethyl acetate in hexane. ¹H NMR (400 MHz, CDCl₃) δ 8.58 (dd, *J* = 4.8,



1.3 Hz, 1H), 7.77 (ddd, J = 9.1, 8.1, 5.2 Hz, 3H), 7.63 (s, 1H), 7.55 (td, J = 7.7, 1.9 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.36 (dd, J = 8.4, 1.7 Hz, 1H), 7.11 (ddd, J = 15.4, 7.6, 4.3 Hz, 2H), 3.26 – 3.16 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ

161.3, 149.5, 139.2, 136.5, 133.8, 132.2, 128.0, 127.7, 127.6, 127.5, 126.7, 126.0, 125.3, 123.2, 121.3, 40.2, 36.3.

4-(2-([1,1'-biphenyl]-4-yl)ethyl)pyridine (3pd):¹⁴ Yield: 77% (40 mg, 0.154 mmol). The title compound was isolated as a white solid with 10% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ 8.52 (d, *J* =

 N
 5.2 Hz, 2H), 7.60 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 7.6 Hz, 2H), 7.13 (d, J = 7.6 Hz, 2H), 7.14 (d, J = 7.

5.4 Hz, 2H), 2.99 (s, 4H); ¹³**C NMR** (126 MHz, CDCl₃) δ 150.4, 149.7, 140.8, 139.7, 139.2, 128.8, 128.7, 127.2, 127.1, 126.9, 123.9, 37.0, 36.1.

4-(2-(naphthalen-2-yl)ethyl)pyridine (3pj):¹⁴ Yield: 81% (38 mg, 0.162 mmol). The title compound was isolated as a white solid with 10% ethyl acetate in hexane. ¹**H NMR** (500 MHz, CDCl₃) δ 8.49 (d, J = 4.7



Hz, 2H), 7.85 – 7.71 (m, 3H), 7.58 (s, 1H), 7.50 – 7.39 (m, 2H), 7.30 (d, J = 8.3 Hz, 1H), 7.10 (d, J = 5.0 Hz, 2H), 3.14 – 3.06 (m, 2H), 3.05 – 2.98 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 150.6, 149.9, 138.3, 133.7, 132.3, 128.2,

127.8, 127.6, 127.2, 126.7, 126.2, 125.5, 124.1, 37.1, 36.9.

4-(2-cyclopropylethyl)pyridine (3ps): Yield: 65% (19 mg, 0.130 mmol). The title compound was isolated as a light brown oil with 5% ethyl acetate in hexane. Selected **IR** (DCM, cm⁻¹): 3076.2, 2998.1, 2923.4,

2855.5, 1557.8, 1602.7, 1415.7, 1016.0, 799.8, 521.9; ¹**H NMR** (500 MHz, CDCl₃) δ 8.47 (s, 2H), 7.11 (d, *J* = 3.2 Hz, 2H), 2.70 (t, *J* = 7.6 Hz, 2H), 1.52 (dd, *J* = 15.0, 7.2 Hz, 2H), 0.68 (dd, *J* = 9.7, 4.7 Hz, 1H), 0.43 (q, *J* = 5.0 Hz, 2H), 0.08 – 0.02 (m, 2H);

¹³C NMR (126 MHz, CDCl₃) δ 151.7, 149.7, 124.2, 35.6, 35.5, 10.7, 4.7; HRMS (ESI) m/z: [M+H]⁺ Calcd for C₁₀H₁₃N: 148.1121; Found 148.1118.

(R)-4-(4,8-dimethylnon-7-en-1-yl)pyridine (3pt): Yield: 63% (29 mg, 0.126 mmol). The title compound

was isolated as a light brown oil with 5% ethyl acetate in hexane Selected **IR** (DCM, cm⁻¹): 2926.1, 2856.1, 1603.4, 1558.7, 1456.0, 1415.5, 1376.9, 1219.4, 1069.1, 993.0, 797.4; ¹H NMR (500 MHz, CDCl₃) δ 8.47 (d, *J* = 4.9 Hz, 2H), 7.09 (d, *J* = 5.0 Hz, 2H), 5.08 (t, *J* = 6.9 Hz, 1H), 2.57 (td, *J* = 8.1, 3.3 Hz, 2H), 2.02 – 1.87 (m,

2H), 1.67 (s, 3H), 1.66 – 1.59 (m, 2H), 1.58 (s, 3H), 1.42 (dt, J = 13.0, 6.6 Hz, 1H), 1.37 – 1.27 (m, 2H), 1.15 (tdd, J = 12.9, 8.2, 4.5 Hz, 2H), 0.86 (d, J = 6.6 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 151.9, 149.7, 131.3, 125, 124.0, 37.1, 36.6, 35.7, 32.4, 27.9, 25.8, 25.6, 19.6, 17.8; HRMS (ESI) m/z: [M+H]⁺ Calcd for C₁₆H₂₅N: 232.2060; Found 232.2072.

2,5-diphenethylpyrazine (3qaa):¹⁴ Yield: 52% (30 mg, 0.104mmol). The title compound was isolated as



a light yellow solid with 2% ethyl acetate in hexane. ¹H NMR (500 MHz, CDCl₃) δ 8.25 (s, 2H), 7.28 – 7.22 (m, 4H), 7.16 (dd, J = 16.9, 7.7 Hz, 6H), 3.09 – 2.99 (m, 8H); ¹³C NMR (126 MHz, CDCl₃) δ 154, 143.8, 141.1, 128.6,

128.5, 126.3, 37, 35.7.

2,4,6-triphenethyl-1,3,5-triazine (3raaa): Yield: 50% (39 mg, 0.099mmol). The title compound was isolated as a light brown solid with 5% ethyl acetate in hexane. Selected **IR** (CDCl₃, cm⁻¹): 3085.8, 3063.0,



3027.0, 2929.5, 2860.9, 1541.5, 1496.2, 1453.5, 1383.4, 1076.5, 1029.0, 909.8, 696.8, 747.7, 544.8, 488.6; ¹H NMR (500 MHz, CDCl₃) δ 7.27 (dq, *J* = 16.7, 7.4 Hz, 15H), 3.23 – 3.11 (m, 12H); ¹³C NMR (126 MHz, CDCl₃) δ 178.2, 141, 128.5, 128.4, 126.1, 40.4, 33.6; HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₇H₂₇N₃: 394.2278; Found 394.2285.

5. Synthesis of drug molecules (\pm) -cuspareine $(5ai)^{18}$ and (\pm) -angustureine $(5am)^{19}$.





2-(3,4-dimethoxyphenethyl)quinoline **3ai** (77 mg, 0.26 mmol) and NiCl₂.6H₂O (0.052 mmol) were taken in a 50 mL round bottom flask and dissolved in 3 mL of methanol. After that, NaBH₄ (1.105 mmol) was added in portion at 0 °C and stirred for 30 min at RT. After completion of reaction, methanol was evaporated and dissolve in 10% HCl, the acidic solution was then basified by adding concentrated ammonium hydroxide solution and extracted with ether. The extract was dried over Na₂SO₄, evaporated and purified by column chromatography. The desired product, 2-(3,4-dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline was obtained in 93% (72 mg, 0.24 mmol) isolated yield. 2-(3,4-dimethoxyphenethyl)-1,2,3,4tetrahydroquinoline was obtained in 93% (72 mg, 0.24 mmol) K₂CO₃ (33 mg, 0.24 mmol) and MeI (1.44 mmol) in THF (3 mL) were charged in a 15 mL sealed tube and reflux for 20h. After completion of reaction, the reaction mixture was cooled to room temperature and quenched by adding H₂O. The reaction mixture was extracted with EtOAC, dried over Na₂SO₄ then concentrated in vacuo. Purification was done by column chromatography to yield of the desired product **5ai** in 80% (60 mg, 0.192 mmol).

2-(3,4-dimethoxyphenethyl)-1-methyl-1,2,3,4-tetrahydroquinoline (5ai):¹⁸ ¹H NMR (500 MHz, CDCl₃) δ 7.12 (t, J = 7.7 Hz, 1H), 7.02 (d, J = 7.3 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.78 – 6.73 (m, 2H), 6.63 (t, J = 7.3 Hz, 1H), 6.57 (d, J = 8.2 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.32 (td, J = 8.4, 4.2 Hz, 1H), 2.95 (s, 3H), 2.93 – 2.84 (m, 1H), 2.76 – 2.67 (m, 2H), 2.57 (ddd, J = 14.0, 10.1, 6.5 Hz, 1H), 2.03 – 1.90 (m, 3H), 1.82 – 1.72 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 149.0, 147.3, 145.4, 134.8, 128.8, 127.2, 121.8, 120.2, 115.5, 111.8, 111.5, 110.7, 58.5, 56.00, 55.9, 38.2, 33.2, 32.0, 24.5, 23.7.

5.2 (\pm) -Angustureine $(5am)^{19}$.



2-pentylquinoline (**3am**) (0.16 mmol) and NiCl₂.6H₂O (0.028 mmol) were taken in a 50 mL RB and dissolve in 2 mL of methanol. After that, NaBH₄ (0.64 mmol) was added in portion at 0 °C and stirred for 30 min at RT. After completion of reaction, methanol was evaporated and dissolve in 10% HCl, the acidic solution was then basified by adding concentrated ammonium hydroxide solution and extracted with ether. The extract was dried over Na₂SO₄, evaporated and purified by column chromatography. The desired product 2-pentyl-1,2,3,4-tetrahydroquinoline was obtained in 89% (29 mg, 0.142 mmol) isolated yield. 2-pentyl-1,2,3,4-tetrahydroquinoline (29 mg, 0.142 mmol), K₂CO₃ (20 mg, 0.142 mmol) and MeI (0.62 mmol) in THF (2 mL) were charged in a 15 mL sealed tube and reflux for 20h. After completion of reaction, the reaction mixture was cooled to room temperature and quenched by adding H₂O. The reaction mixture was done by column chromatography to yield of the desired product **5am** in 82% (25 mg, 0.115 mmol).

1-methyl-2-pentyl-1,2,3,4-tetrahydroquinoline (**5am**):¹² ¹**H NMR** (400 MHz, CDCl₃) δ 7.09 (t, *J* = 7.7 Hz, 1H), 6.98 (d, *J* = 7.2 Hz, 1H), 6.59 (t, *J* = 7.3 Hz, 1H), 6.53 (d, *J* = 8.2 Hz, 1H), 3.24 (td, *J* = 8.5, 4.1 Hz, 1H), 2.94 (s, 3H), 2.87 – 2.76 (m, 1H), 2.66 (dt, *J* = 16.2, 4.2 Hz, 1H), 1.90 (dt, *J* = 12.3, 4.5 Hz, 2H), 1.66 – 1.57 (m, 1H), 1.45 – 1.26 (m, 7H), 0.91 (t, *J* = 6.8 Hz, 3H); ¹³**C NMR** (126 MHz, CDCl₃) δ 145.6, 128.8, 127.2, 122.0, 115.3, 110.6, 59.1, 38.1, 32.2, 31.4, 25.9, 24.6, 23.7, 22.8, 14.2.

6. Mechanistic studies.





In a 15 mL reaction tube, **1a** (0.1 mmol), α,α -D₂-**2d** (0.15 mmol), **Mn-3** (2 mol%) and ^{*t*}BuOK (1 equiv.) were taken. Then ^{*t*}AmOH (0.05 mL) was added and the tube was closed before the reaction mixture was placed in a preheated oil bath at 140 °C for 24 h. After completion, reaction mixture was quenched with water (0.05 mL) and extracted with ethylacetate (3 × 2). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100–200 mesh) with hexane/ethyl acetate mixture as eluent. 28 mg, 0.091 mmol (91%) yield of the desired product (**3ad-D**) was obtained.

88.14 88.12 88.12 88.12 88.12 88.12 83.33 83.33 83.33 83.33 83.33 83.33 83.33 83.33 84.44 84.47 84.47 84.45



Figure S1. ¹H NMR of 3ad-D for the estimation of deuterium incorporation.

6.2.1 Reaction with isotope labeled alcohol in dioxane solvent.



In a 15 mL reaction tube, **1a** (0.1 mmol), α,α -D₂-**2d** (0.15 mmol), **Mn-3** (2 mol%) and 'BuOK (1 equiv.) were taken. Then dioxane (0.05 mL) was added and the tube was closed before the reaction mixture was placed in a preheated oil bath at 140 °C for 24 h. After completion, reaction mixture was quenched with water (0.05 mL) and extracted with ethylacetate (3 × 2). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated. The residue was purified by column chromatography over silica gel (100–200 mesh) with hexane/ethyl acetate mixture as eluent. 29 mg, 0.093 mmol (93%) yield of the desired product (**3ad**-D) was obtained.



Figure S2. ¹H NMR of 3ad-D for the estimation of deuterium incorporation.

6.2.2 Determination of kinetic isotope effect.



Two parallel reactions were carried out by **1a** (0.1 mmol) with **2d** (0.15 mmol) and α,α -D₂-**2d** (0.15 mmol) under the standard reaction condition in dioxane solvent for 1 h. GC analysis revealed 39% and 21% yields of the desired product respectively. This corresponds to $k_{\rm H}/k_{\rm D} = 1.85$.

6.3. Olefination of 2-methyl quinoline (1a) with benzaldehyde without catalyst.



2-methyl quinoline **1a** (0.1 mmol), benzaldehyde **2'a** (0.1 mmol) and ^{*t*}BuOK (1 equiv.) in ^{*t*}AmOH were taken in a 15 mL sealed tube under argon atmosphere. After that, the reaction mixture was placed in a preheated oil bath at 140 °C. After 2h, the crude reaction mixture was analyzed by GC and 20% yield of **4aa** was obtained using mesitylene as an internal standard.

6.4. Olefination of 2-methyl quinoline (1a) with benzaldehyde with catalyst.



2-methyl quinoline **1a** (0.1 mmol), benzaldehyde **2'a** (0.1 mmol), **Mn-3** (2 mol%) and ^{*t*}BuOK (1 equiv.) in ^{*t*}AmOH were taken in a 15 mL sealed tube under argon atmosphere. After that, the reaction mixture was placed in a preheated oil bath at 140 °C. After 2h, the crude reaction mixture was analyzed by GC and 25% yield of **4aa** was obtained using mesitylene as an internal standard.

6.5. Manganese catalyzed hydrogenation of (*E*)-2-(2-([1,1'-biphenyl]-4-yl)vinyl)quinoline (4ad) with 2d.



In a 15 mL sealed tube, **Mn-3** (2 mol%), **4ad** (0.1 mmol), biphenyl methanol **2d** (0.1 mmol), 'BuOK (1 equiv.) and dioxane (0.05 mL) were taken and tube was sealed. After that, the reaction mixture was placed in a preheated oil bath at 140 °C for 12h under argon atmosphere. Upon completion of reaction, the reaction mixture was quenched with water and extracted with ethyl acetate. 83% of the isolated yield of the hydrogenation product **3ad** was obtained. The formation of corresponding ester **5d** in 62% yield was observed. We could also notice the aldehyde **2'd** in trace amount, which were confirmed by ¹H NMR spectroscopy.



Figure S3. ¹H NMR of a mixture of ester (5d) and aldehyde (2'd).

6.6. Manganese catalyzed hydrogenation of (E)-2-(2-([1,1'-biphenyl]-4-yl)vinyl)quinoline (4ad) with α, α -D₂-2d.



In a 15 mL sealed tube, **Mn-3** (2 mol%), **4ad** (0.1 mmol), α,α -D₂-**2d** (0.1 mmol), ^{*t*}BuOK (1 equiv.) in dioxane (0.05 mL) were taken and tube was sealed. After that, the reaction mixture was placed in a preheated oil bath at 140 °C for 12h under argon atmosphere. Upon completion of reaction, the reaction mixture was quenched with water and extracted with ethyl acetate. 97% of the isolated yield of the desired product was obtained (**3ad**-D) with 35% deuterium incorporation at the β position and 22% deuterium incorporation at α -position of the desired product.

8.10 8.06 8.08 8.08 8.08 8.08 8.09 8.09 8.00 8.01 8.02 8.03 8.04 8.05 8.06 8.06 8.07 8.08 8.09 8.09 8.06 8.06 8.06 8.06 8.06 8.06 8.06 8.06 8.06 8.07 8.06 8.07 8.06 8.06 8.06 8.06 8.06 8.07 8.06 8.07 8.06 8.07 8.07 8.06 8.07 8.07 8.07 8.07 8.07 8.07 8.07 8.07 <t



Figure S4. ¹H NMR of **3ad**-D for the estimation of deuterium incorporation.

6.7 Kinetic monitoring of the reaction.

In a 15 mL sealed tube, 2-methylquinoline **1a** (0.1 mmol), benzyl alcohol **2a** (0.15 mmol), **Mn-3** (2 mol%) and 'BuOK (0.1 mmol) were taken under argon atmosphere. After that the tube was closed before the reaction mixture was placed in preheated oil bath at 140 °C. The reaction mixture was analyzed by GC using mesitylene as an internal standard at specified time interval.

| Time (h) | [1a] mmol | [2a] mmol | [3a] mmol | [4aa] mmol | [2'a] mmol |
|----------|--------------------|--------------------|--------------------|---------------------|---------------------|
| 0 | 0.1 | 0.15 | 0 | 0 | 0 |
| 0.5 | 0.07 | 0.107 | 0.01 | 0.019 | 0.001 |
| 1 | 0.051 | 0.073 | 0.032 | 0.014 | 0.003 |
| 2 | 0.025 | 0.028 | 0.06 | 0.013 | 0.002 |
| 4 | 0.02 | 0.012 | 0.077 | 0.004 | 0.0015 |
| 6 | 0.015 | 0.011 | 0.081 | 0.003 | 0.0015 |
| 8 | 0.011 | 0.001 | 0.085 | 0.002 | 0.001 |
| 12 | 0.001 | 0 | 0.095 | 0 | 0 |

 Table S5. Kinetic monitoring of the reaction of 1a with 2a.



Figure S5: Graphical representation for the kinetic profile.

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8. Copies of ¹H and ¹³C NMR spectra.































250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 fl (ppm)



110 100 f1 (ppm) 130 120



110 100 f1 (ppm) 130 120 -10



$\begin{array}{c} 2.99\\ 2.95\\ 2.95\\ 2.95\\ 1.83\\ 1.79\\ 1.79\\ 1.79\\ 1.77\\ 1.79\\$



















7.93 7.95 </tr





110 100 f1 (ppm) . 50 130 120 -10



110 100 f1 (ppm) -10 130 120

















¹H NMR in CDCl₃ (400 MHz)



























- 2.99











 $\left\langle \begin{array}{c} 2.71 \\ 2.70 \\ 2.68 \end{array} \right\rangle$

 $\begin{pmatrix} 1.54 \\ 1.53 \\ 1.51 \\ 1.51 \\ 1.50 \end{pmatrix}$

~ 0.68 0.44 0.41 0.41 0.04 0.03 0.03

-8.47

 ${}^{7.12}_{7.11}$











