# Unlocking the Potential of High-Throughput Experimentation for Electrochemistry with a Standardized Microscale Reactor

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## General Practices, Materials, and Instrumentation

All reactions were conducted under a nitrogen atmosphere unless otherwise noted. Flash chromatography was performed using silica gel P60 from SiliCycle. Commercial reagents and anhydrous solvents were purchased from Sigma Aldrich, Alfa Aesar, Acros, TCI, AK Scientific, Combi-Blocks and Oakwood and used as received with the following exceptions: acetonitrile was dried with molecular sieves and THF was dried via the sodium metal and benzophenone method for experiments conducted in sections 11–13. Heating of reaction mixtures was performed using a temperature-controlled hotplate equipped with stirring and an active thermocouple. Stirring of reaction mixtures was performed using magnetic stirring, unless noted otherwise. Evaporation of solvent (concentration) were done in vacuo using variable vacuum using a rotary evaporator attached to a vacuum controller (ca. 400–40 mmHg).

All proton NMR spectra in Section 11–13 were recorded on either a Varian-Mercury 300 (300 MHz), Varian Mercury 400 (400 MHz), or Inova 500 (500 MHz) spectrometers at 20 °C. All proton nuclear magnetic resonance ($^{1}$H NMR) spectra, proton decoupled carbon nuclear magnetic resonance ($^{13}$C{$^{1}$H} NMR) spectra, proton coupled fluorine nuclear magnetic resonance ($^{19}$F NMR), and proton decoupled fluorine nuclear magnetic resonance ($^{19}$F{1H} NMR) in section 14 were recorded at 25 °C (unless stated otherwise) on a 500 MHz Bruker spectrometer. Chemical shifts for proton are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent: δ($CDCl_3$) = 7.26 ppm or δ($d_6$-DMSO) = 2.50 ppm. Carbon ($^{13}$C{$^{1}$H} NMR) was referenced to the carbon resonances of the solvent: δ($CDCl_3$) = 77.16 or δ($d_6$-DMSO) = 39.52 ppm. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet), coupling constants (*J*) in Hertz (Hz). Quantitative $^{1}$H NMR analysis ($^{1}$H qNMR) refers to standard $^{1}$H NMR using the following parameters: d1 = 60 seconds, number of scans = 4.

The HT*e*$^{-}$Chem was assembled from commercially available components. Some pieces required assembly prior to use, namely the PCB, sealing plate, and power controllers. A detailed description of the assembly is contained herein (Section 5─8, page S14─S24). The G10 plates and the components of the PCB were custom made relying on the technical drawings contained in SI2, “Technical Drawings and CAD files”. A complete bill of materials as well as the vendors used to manufacture the components used in this work can be found in SI3, “Bill of Materials”. For additional detail on using the HT*e*$^{-}$Chem, see Video SI4, “Video Setup”. Efforts are currently underway to commercialize the HT*e*$^{-}$Chem.

The experiments for Section 11─13, pages S31─S50 were carried out at Cornell University, while the library synthesis in Section 14, pages S51─S69 was performed at Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

**Abbreviations:** Ac = acetyl group, CC = constant current, CV = constant voltage, DC = direct current, DCM = dichloromethane, DIPEA = diisopropyl ethyl amine, DMA = dimethylacetamide, DMF = dimethylformamide, DMSO = dimethyl sulfoxide, ePTFE = expanded polytetrafluoroethylene, $Et_2O$ = diethyl ether, EtOAc = ethyl acetate, EtOH = ethanol, F = faraday, GC = gas chromatography, GVL = gamma-valerolactone, HCl = hydrochloric acid, HFIP = hexafluoro isopropanol, HPLC = high pressure liquid chromatography, HTE = high throughput experimentation, LED

= light-emitting diode, MeCN = acetonitrile, $MeNO_2$ = nitromethane, MeOH = methanol, MS = mass spectrometry, nBu = *n*-butyl group, $NEt_3$ = triethylamine, NMP = N-methyl-2-pyrrolidone, NMR = nuclear magnetic resonance, PCB = printed circuit board, Ph = phenyl group, PyHCl = pyridinium chloride, RMA = Rosin-mildly activated, r.t. = room temperature, TAC = trisaminocyclopropenium, TBA = tetrabutylammonium tBu = *tert*-butyl group, TEMPO = 2,2,6,6-tetramethylpiperidine-1-oxy radical, TFA = trifluoroacetic acid, TFE = 2,2,2-trifluoro ethanol, THF = tetrahydrofuran, TMS = trimethylsilyl, UPLC = ultra-high pressure liquid chromatography,

## General Plate Setup A- HT*e*-Chem

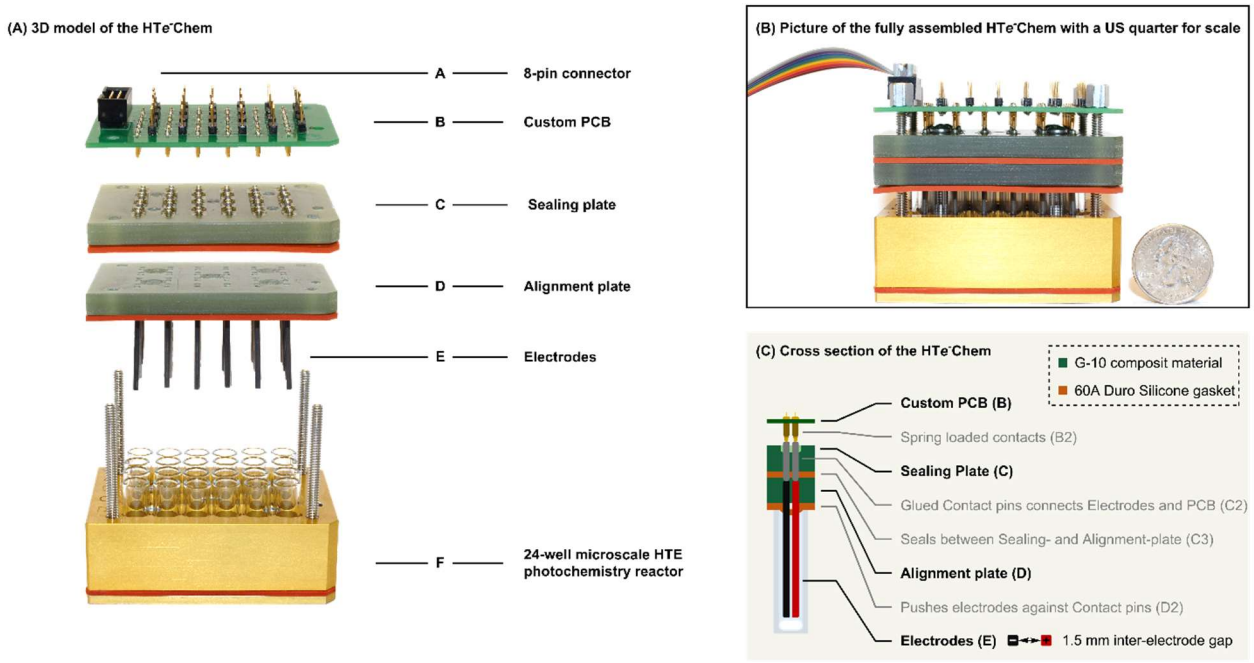



**Figure S1.** (A) 3D model of the HT*e*-Chem. (B) Picture of the fully assembled HT*e*-Chem with a US quarter for scale. (C). Cross section of a single HT*e*-Chem vial.

1. Gather the 24-well microscale HTE photochemistry reactor (F), alignment plate (D), silicone rubber gasket (D2), 48 reactor vials (24 for step 2 and 24 for step 4), and 48 31.3 mm long electrodes.

2. Fill the reactor plate (F) with vials, push down the silicone gasket (D2) so that it is flush with the vials and add the alignment plate.

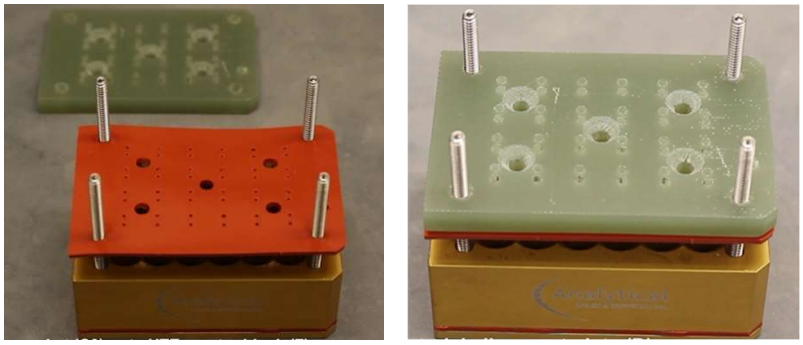


**Figure S2.** Pictures of the process of adding the silicone gasket (D2) and the alignment plate (D).

*Tip: make sure the hole for the temperature probe in the reactor plate (F) gasket (D2) and alignment plate (D) are all aligned. It can be useful to mark the A1 corner with a permanent marker to avoid assembly errors.*

3. Push the electrodes through the alignment plate (D) and gasket (D2) so that 5-10 mm of electrodes remains above the alignment plate.

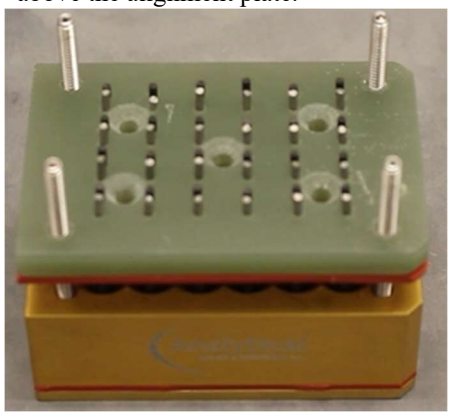


**Figure S3.** The alignment plate (D) charged with graphite anodes and nickel chrome cathodes.

*Tip: graphite electrodes can be prone to breaking if you push down from the top. Hold the electrode close to the alignment plate (D) and push them in gently at first. It can be helpful to mark the alignment plate with a plus or minus to denote which row is the anode and which is the cathode. If you set up the reactor as we have described, when A1 is in the upper left corner the top row of electrodes is the anode and the bottom row of electrodes is the cathode. If your electrodes are old, or homemade, they can cause failure if they do not slide cleanly through the alignment plate, it can help to check that the electrodes cleanly slide through the alignment plate.*

4. Set the alignment plate (D) aside, replace the vials in the reactor (F) and charge the vials with magnetic stir bars.

   *Tip: for air- and water- free applications the reactor can be assembled inside a glovebox under inert atmosphere. To transfer the apparatus into the glovebox it can be helpful to dry assembled reactor (F) in a 150 °C oven.*

5. Gather the sealing plate (C) and another silicone rubber gasket (C3). Add the gasket (C3) to the bottom of the sealing plate (C).

   *Tip: be sure to use a flat tool like a spatula to make sure the sealing gasket (C3) is firmly and totally pressed flush with the sealing plate (C).*

6. Prepare your stock solutions.

   *Tip: many electrochemical reactions can be affected by dissolved gasses, consider degassing your solutions and/or setting the reaction up under an inert atmosphere.*

7. Add the stock solutions to the vials in the reactor plate using micropipettors.

   *Tip: suspensions can be added by micropipettor if the suspension is stirred to uniformity while pipetting. Cutting the tip of the pipettes might be necessary to accommodate larger particle sizes. It can be helpful to practice uniformly pipetting organic solvents before attempting to set up a reaction.*

8. Place the alignment plate (D) charged with electrodes onto the baseplate and insert the short flat headed screw into the center hole. Tighten the center screw to 5 lbf-in (0.6 Nm) of torque. Then press the electrodes flush with the alignment plate (D).

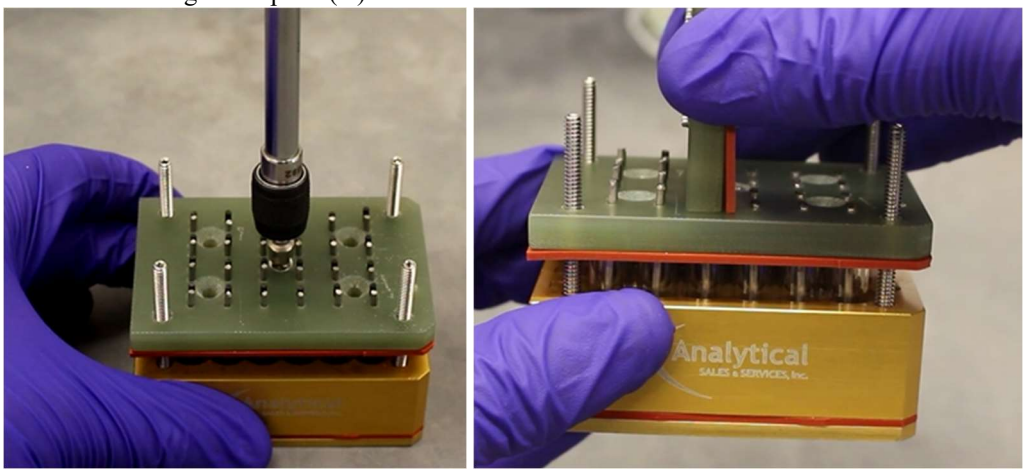



**Figure S4.** Tightening the alignment plate (D) onto the reactor (F) and pressing the electrodes flush with the top of the alignment plate.

*Tip: use a manual torque screwdriver or an electronic screwdriver that has been appropriately calibrated to deliver 5 lbf-in (0.6 Nm) of torque. For a Milwaukee M4 Volt Lithium-Ion Cordless 1/4 in. Hex Screwdriver this can be achieved by using the tool on speed 1 with torque setting 3. Over tightening can lead to connectivity issues and under tightening can lead to leaking.*

9. Gently place the sealing plate (C) onto the reactor. Insert the longer pan headed screws into the remaining four holes. Tighten the four screws in a star pattern so that no corner of the sealing plate is pushed down further than the others until all screws are tightened to 5 lbf-in (0.6 Nm) of torque.

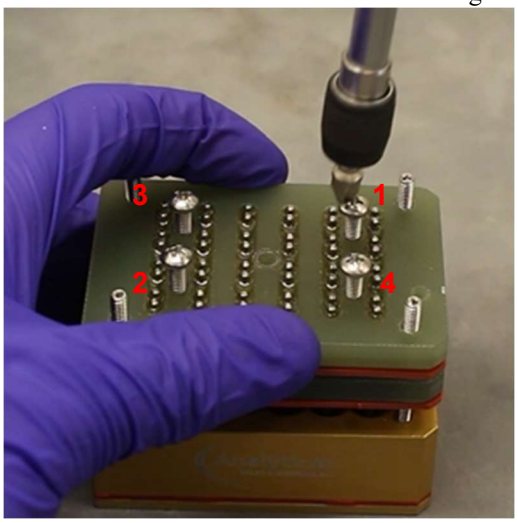



**Figure S5.** The star pattern for tightening the sealing plate (C) onto the reactor block (F).

*Tip: use a marker to mark the A1 corner of the sealing plate so that the holes for the temperature probe in the reactor plate (F), alignment plate (D), and sealing plate (C) are aligned. Use a manual torque screwdriver or an electronic screwdriver that has been appropriately calibrated to deliver 5 lbf-in (0.6 Nm) of torque. For a Milwaukee M4 Volt Lithium-Ion Cordless 1/4 in. Hex Screwdriver this can be achieved by using the tool on speed 1 with torque setting 3. Over tightening can lead to connectivity issues and under tightening can lead to leaking. After sealing, the reaction vials are airtight and can be removed from the glovebox without compromising the reactions.*

10. Add the constant current custom PCB (B) and use nuts to tighten the PCB against the sealing plate (C) using the corner threaded rods. Make sure the chamfered corners of the PCB are aligned with the chamfered corners of the reactor.

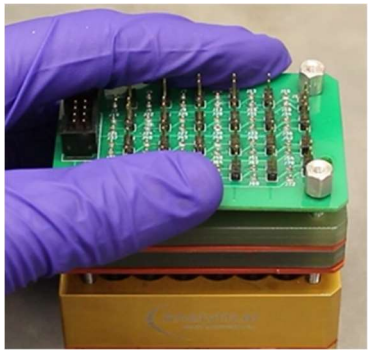


**Figure S6.** Placing the PCB onto the sealing plate.

*Tip: this connection doesn't need to be overly tight, gentle contact with the sealing plate (C) is all that is required. This step is recommended even when constant potential electrolysis is being assessed.*

**For constant current electrolysis:**

11a. Set the power controllers to the desired current. Attach the LED indicator array to an external DC power supply as indicated in Figure S15, page S15, "Assembly of the Power controller setup for the HTe-Chem". Set the external DC power supply to maximum voltage.

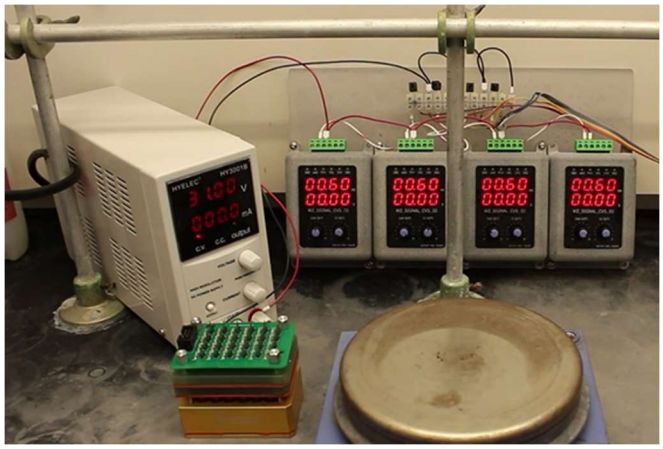


**Figure S7.** The fully assembled constant current power assembly.

*Tip: for longer electrolysis, be sure the power suppliers are plugged in and charging.*

12a. If no electrolysis conditions are being investigated, add skipper pins to the PCB to short circuit the desired wells.

12a. Attach the 8-wire ribbon to the 8-pin connector (A) on the constant current custom PCB (B).

13a. Check the LED indicators to verify that all rows are conducting efficiently.

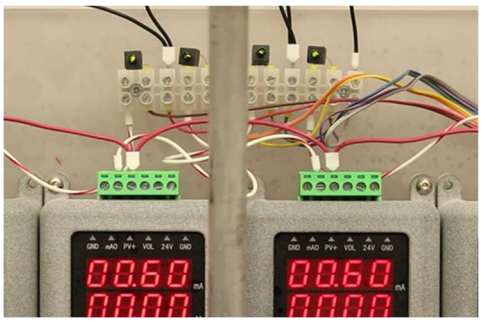


**Figure S8.** The lit indicator lights which indicate successful electrolysis under constant current conditions.

*Tip: many factors can lead to a failure to conduct electricity and if even one reaction fails to conduct electricity all connected reactions will also fail to electrolyze. Skipper pins can be used to identify which reactions are failing to electrolyze and restore current to the remaining row. For some common causes of failed electrolysis, and solutions to prevent them from happening or correct them without skipping the well* *see page S28, "There is no current when I start the electrolysis".*

14a. Bring to the desired temperature and electrolyze, with stirring, for the desired amount of electron equivalents. Skip wells to prevent electrolysis as desired.

*Tip: the desired electron equivalents can be converted to time using the following equation*

$$reaction\ time\ (min) = \frac{mmol\ substrate \times desired\ electron\ equivalents \times 96485\ C{\cdot}mol^{-1}}{current\ (mA) \times 60\ min{\cdot}h^{-1}}$$

**For constant voltage electrolysis:**

11b. Set the power controllers to apply minimal current, Attach the 8-wire ribbon to the 8-pin connector (A) on the constant current custom PCB (B).

12b. Check the LED indicators to verify that all rows are conducting efficiently.

*Tip: many factors can lead to a failure to conduct electricity and if even one reaction fails to conduct electricity all connected reactions will also fail to electrolyze. Skipper pins can be used to identify which reactions are failing to electrolyze and restore current to the remaining row. For some common causes of failed electrolysis, and solutions to prevent them from happening or correct them without skipping the well* *see page S28, "There is no current when I start the electrolysis".*

13b. Remove the constant current PCB, if no electrolysis conditions are being investigated and block the contact pins on the sealing plate (C) with tape.

14b. Add the constant voltage custom PCB (B) and use nuts to tighten the PCB against the sealing plate (C) using the corner threaded rods.

*Tip: this connection doesn't need to be overly tight, gentle contact with the sealing plate (C) is all that is required.*

15b. Set the power controllers to the desired voltage, bring the reactor to the desired temperature, attach the ribbon cable to the PCB (B) and electrolyze, with stirring, for the desired amount of time.

*Tip: for longer electrolysis, be sure the power controllers are plugged in and charging.*

**Reactor disassembly and reaction analysis:**

16. After the reactions are complete disconnect the ribbon wire from the 8-pin connector (A), turn off the power supplies and power controllers.

17. Remove the PCB (B).

18. As quickly as possible, but with minimal agitation, remove the sealing plate (C) and release the pressure in the alignment plate (D) by loosening the center screw.

    *Tip: under oxidative protocols in which hydrogen evolution or other gas evolution is present, the reactor can build up significant positive pressure within the reaction vials. Once the sealing plate is removed, reaction mixture can be pushed out of the wells by a combination of positive pressure and capillary action. This process is typically slow to start and if the pressure can be released immediately after the sealing plate is loosened nearly all solvent loss can be prevented. Some small solvent loss can still be observed in extreme cases, but this minimal solvent loss appears to have a negligible effect on reaction yields.*

19. Gently remove the alignment plate, with slight agitation to dislodge any drops of reaction mixture into the reaction vial.

20. Add internal standard solution, or workup your reactions as needed. Analysis can be conducted by UPLC, HPLC, GC, NMR or isolation depending on the particular use case.

**Heating of the HT*e*-Chem:**

The HT*e*-Chem can be heated using a temperature-controlled hotplate equipped with stirring and an active thermocouple. The reactor has an insert for a conventional temperature probe. If a careful control of temperature and heating rate is desired some aluminum rack adapter (catalog number 24245 from Analytical Sales and Services, Inc.) may be employed. The rack adapter can be preheated prior to insertion of the HT*e*-Chem, which significantly shortens the time needed to reach the desired temperature.

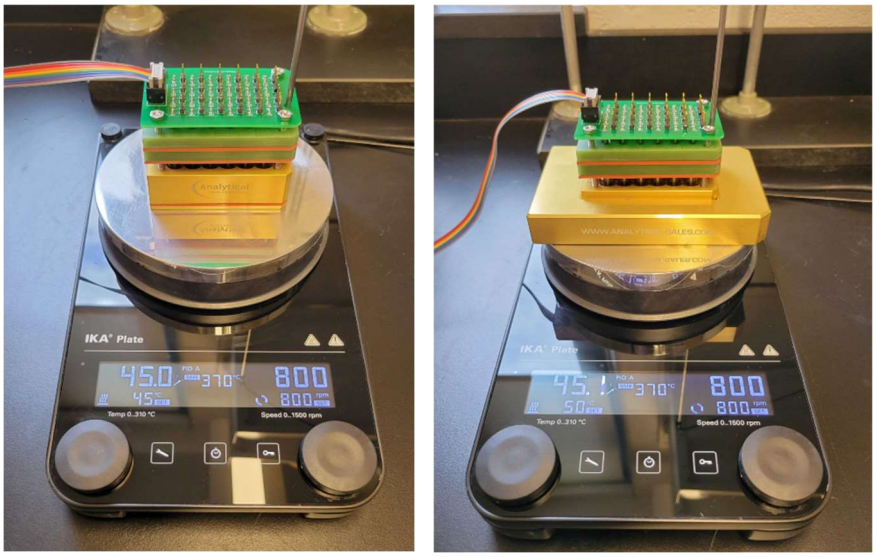



**Figure S9.** Left: HT*e*-Chem with a temperature probe without the "rack adapter". Right: HT*e*-Chem with a temperature probe with a rack adapter.

## General Plate Setup B- HT*e*-Chem-Prototype

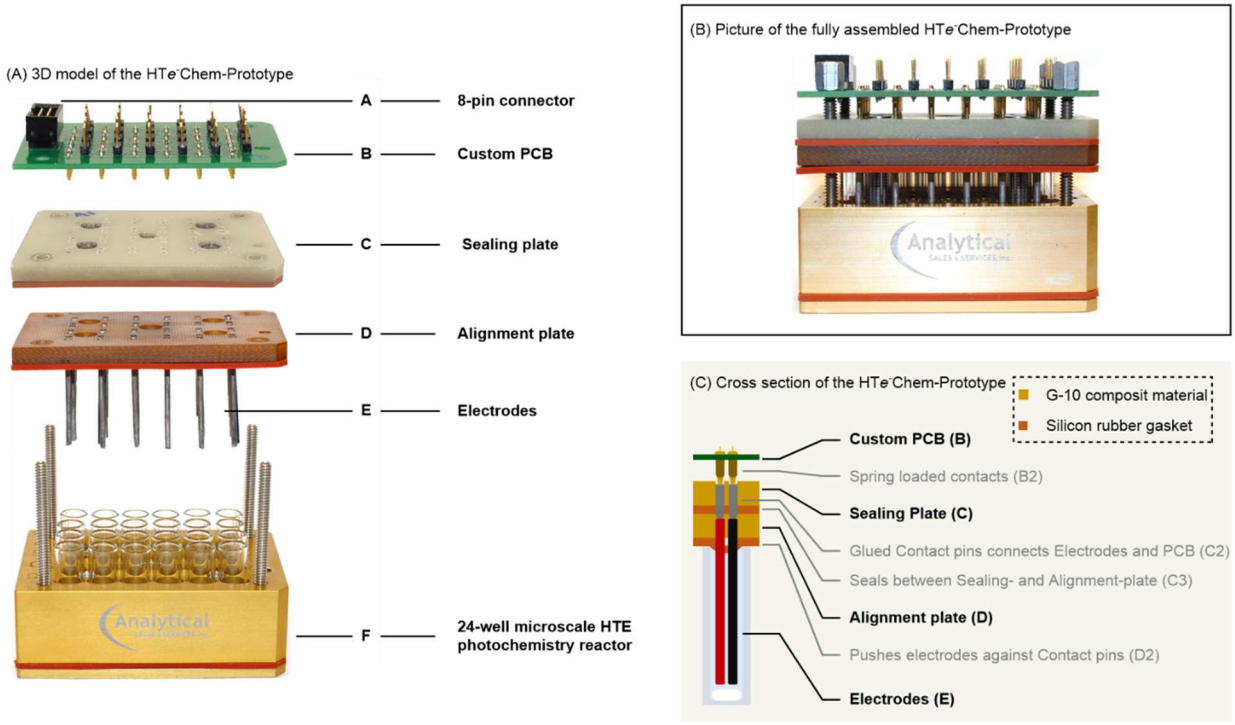



**Figure S10.** (A) 3D model of the HT*e*-Chem. (B) Picture of the fully assembled HT*e*-Chem with a US quarter for scale. (C). Cross section of a single HT*e*-Chem vial.

Set up exactly as General Procedure A except using 30.8 mm long electrodes and with G-10 sealing and alignment plates that are 3/16 in thick rather than 1/4 in thick.

## General Plate Setup C- HT*e*-Chem-noSeal

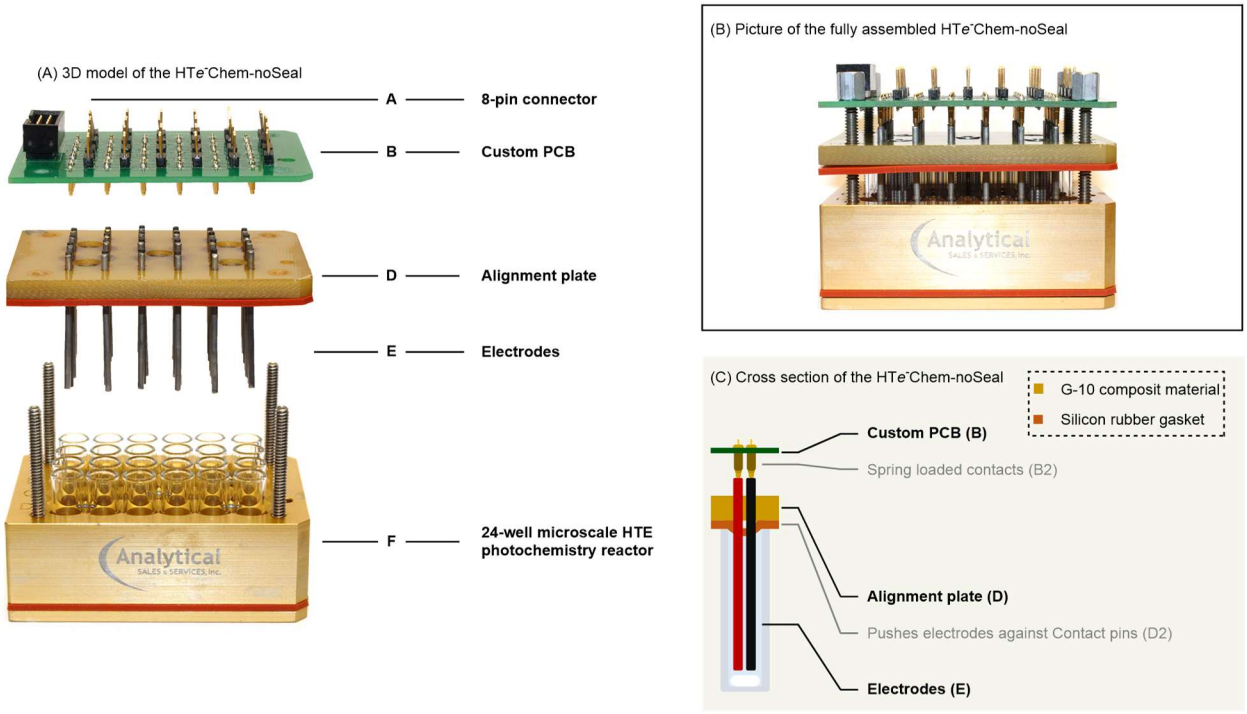



**Figure S11.** (A) 3D model of the HTe-Chem. (B) Picture of the fully assembled HTe-Chem with a US quarter for scale. (C). Cross section of a single HTe-Chem vial.

*Note: this variant of the HTe-Chem does not include a sealing plate and so will not hold positive pressure in the vials. Under many oxidative conditions hydrogen evolution reaction will cause positive pressure which, along with capillary action, can overcome the elastic seal of the silicone gasket (D2) against the electrodes. This can cause considerable leaking of reaction solvent. It is not recommended to use this variant under oxidative conditions. Additionally, the G-10 composite alignment plate (D) used is 3/16 in rather than 1/4 in.*

1. Gather the 24-well microscale HTE photochemistry reactor (F), alignment plate (D), 2 blank 1/16 in thick silicone rubber gasket, standard waterjet cut silicone rubber gasket, 48 reactor vials (24 for step 3 and 24 for step 5), and 48 35 mm long electrodes.

2. Stack 2 blank 1/16 in silicone rubber gaskets, place a precut gasket on top to use as a guide. Using a 1.0 mm leather hole punch and a hammer, punch out the 48 electrode holes in the blank gaskets. Use a 2.5 mm leather hole punch and hammer to punch out the 9 screw holes and the hole for the temperature probe.

   *Tip: Use a little bit of water to get the gaskets to stick together. Punch out the corners of the electrode array first so that if the gaskets become misaligned with the guide they can be realigned. Punch the holes as vertically as possible with one hammer stroke. Punching two gaskets at once provides a unique hole size and shape that provides a superior seal to punching one gasket alone.*

3. Fill the reactor plate (F) with vials, push down the silicone gasket (D2) so that it is flush with the vials and add the alignment plate.

   *Tip: make sure the hole for the temperature probe in the reactor plate (F) gasket (D2) and alignment plate (D) are all aligned. It can be useful to mark the A1 corner with a permanent marker to avoid assembly errors.*

4. Push the electrodes through the alignment plate (D) and gasket (D2) so that 1/4 in of electrodes remains above the alignment plate.

   *Tip: graphite electrodes can be prone to breaking if you push down from the top. Hold the electrode close to the alignment plate (D) and push them in gently at first. It can be helpful to mark the alignment plate with a plus or minus to denote which row is the anode and which is the cathode. If you set up the reactor as we have described, when A1 is in the upper left corner the top row of electrodes is the anode and the bottom row of electrodes is the cathode.*

5. Set the alignment plate (D) aside, replace the vials in the reactor (F) and charge the vials with magnetic stir bars.

   *Tip: for air- and water- free applications the reactor can be assembled inside a glovebox under inert atmosphere.*

6. Prepare your stock solutions.

   *Tip: many electrochemical reactions can be affected by dissolved gasses, consider degassing your solutions and/or setting the reaction up under an inert atmosphere.*

7. Add the stock solutions to the vials in the reactor plate using micropipettors.

   *Tip: suspensions can be added by micropipettor if the suspension is stirred to uniformity while pipetting. Cutting the tip of the pipettes might be necessary to accommodate larger particle sizes. It can be helpful to practice uniformly pipetting organic solvents before attempting to set up a reaction.*

8. Place the alignment plate (D) charged with electrodes onto the baseplate and insert five flat headed screws into the screw holes. Tighten the center screw and then the four corner screws in a star pattern so that no corner of the sealing plate is pushed down further than the others until all screws are tightened to 10 lbf-in of torque.

   *Tip: use a manual torque screwdriver or an electronic screwdriver that has been appropriately calibrated to deliver 10 lbf-in of torque. Over tightening can lead to broken graphite electrodes and under tightening can lead to leaking. Make sure the holes for the temperature probe in the reactor plate (F) and alignment plate (D) are aligned. After sealing, the reaction vials are airtight and can be removed from the glovebox without compromising the reactions.*

9. Uniformly set the height of all electrodes to 3/16 in above the alignment plate

   *Tip: this can be done with the assistance of corner nuts or by 3-D printing a tool to size all electrodes in a row or column. Gentle application of force is necessary if soft metal electrodes or graphite are used to prevent electrodes from bending or breaking.*

10. Add the constant current custom PCB (B) or constant voltage PCB and use nuts to tighten the PCB against the alignment plate (D) using the corner threaded rods.

    *Tip: this connection doesn't need to be overly tight, gentle contact with the sealing plate (C) is all that is required.*

11. Set the power controllers to the desired current or voltage. For constant current electrolysis, attach the LED indicator array to an external DC power supply as indicated in Figure S15, page S16, "Assembly of the Power controller setup for the HT*e*-Chem". Set the external DC power supply to maximum voltage.

    *Tip: for longer electrolysis, be sure the power suppliers are plugged in and charging.*

12. If no electrolysis conditions are being investigated, add skipper pins to the PCB to short circuit the desired wells.

13. Attach the 8-wire ribbon to the 8-pin connector (A) on the PCB (B).

14. For constant current electrolysis, check the LED indicators to verify that all rows are conducting efficiently.

    *Tip: many factors can lead to a failure to conduct electricity and if even one reaction fails to conduct electricity all connected reactions will also fail to electrolyze. Skipper pins can be used to identify which reactions are failing to electrolyze and restore current to the remaining row. For some common causes of failed electrolysis, and solutions to prevent them from happening or correct them without skipping the well see page S28, "There is no current when I start the electrolysis". Under constant voltage electrolysis the LEDs will be lit even if no electrolysis is occurring.*

15. Bring to the desired temperature and electrolyze, with stirring, for the desired amount of electron equivalents. Skip wells to prevent electrolysis as desired.

    *Tip: the desired electron equivalents can be converted to time using the following equation*

$$reaction\ time\ (min) = \frac{mmol\ substrate \times desired\ electron\ equivalents \times 96485\ C{\cdot}mol^{-1}}{current\ (mA) \times 60\ min{\cdot}h^{-1}}$$

16. After the reactions are complete disconnect the ribbon wire from the 8-pin connector (A), turn off the power supplies and power controllers.

17. Remove the PCB (B).

18. Gently remove the alignment plate (D), with slight agitation to dislodge any drops of reaction mixture into the reaction vial.

19. Add internal standard solution, or workup your reactions as needed. Analysis can be conducted by UPLC, HPLC, GC, NMR or isolation depending on the particular use case.

## Assembly of the Power controller setup for the HT$e^-$Chem

### Constant Current Electrolysis:

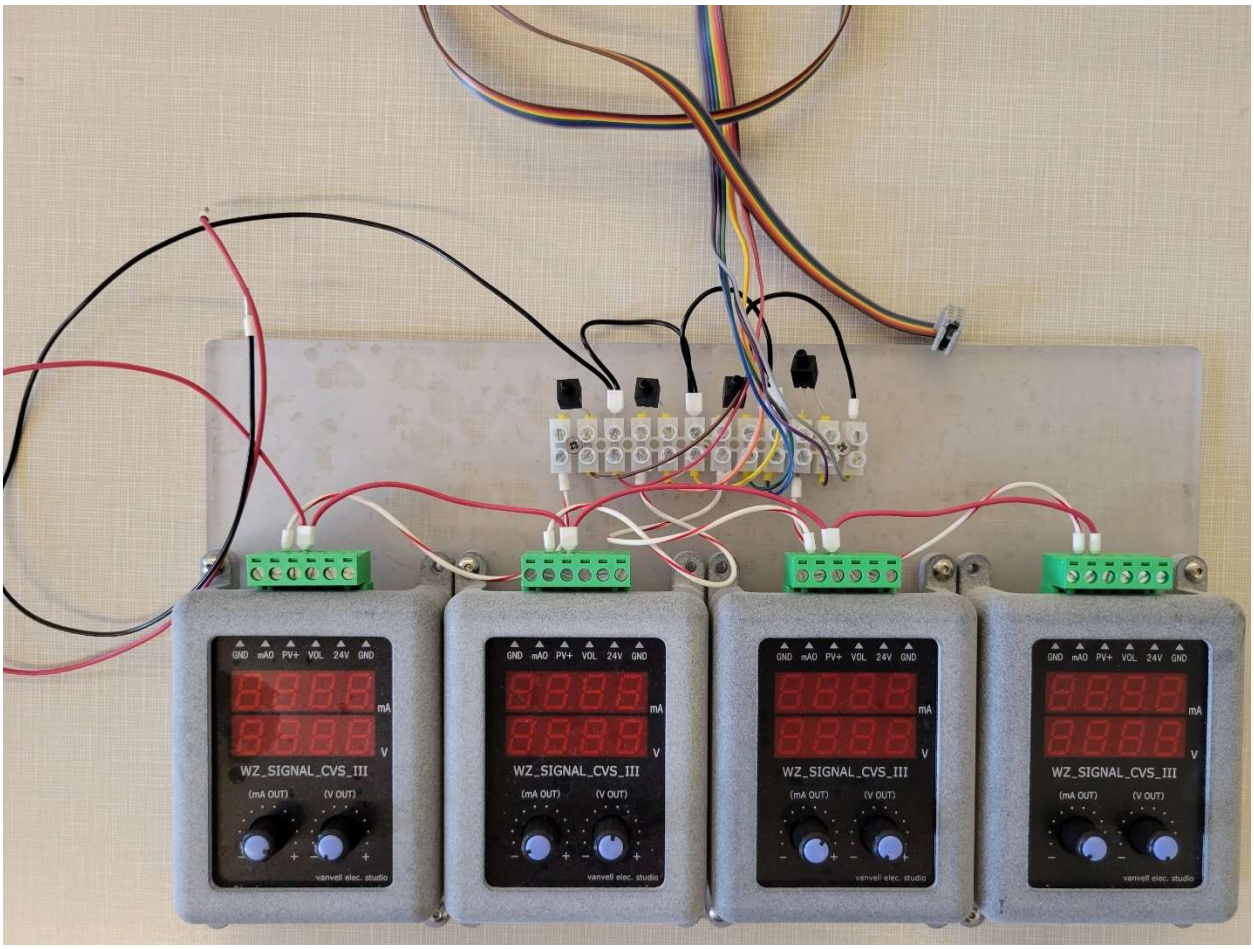



**Figure S12.** The fully assembled constant current power supply assembly.

1) Connect the cathode connecting cable (black), the four LEDs and the 8-pin ribbon cable to the terminal connector as shown in the picture below.

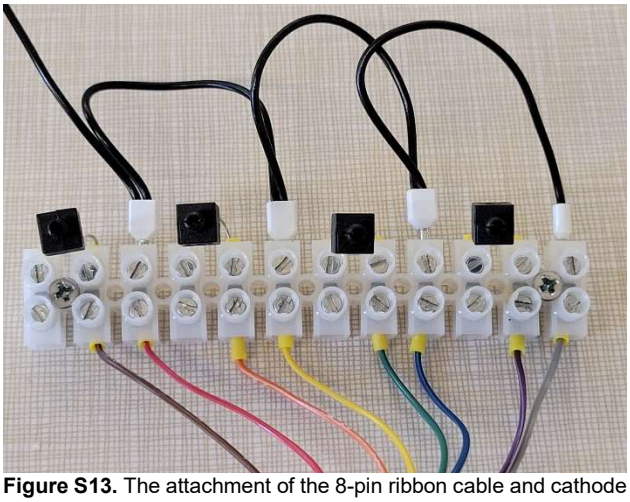


**Figure S13.** The attachment of the 8-pin ribbon cable and cathode connecting cable to the LED array.

2) Connect the anode connecting cable (red) and the four short cables (red/white) to the four power controllers that are mounted on the polycarbonate support plate.

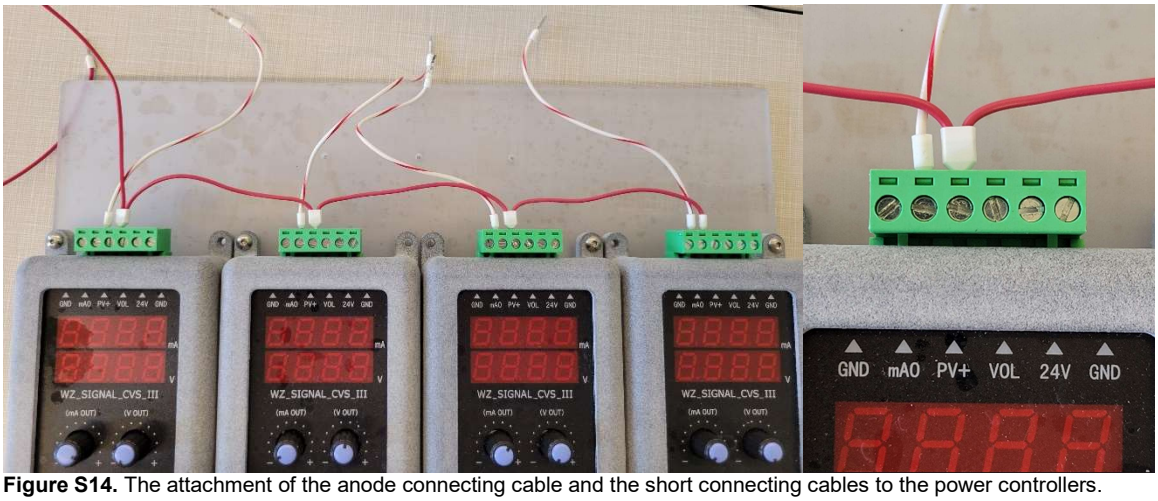



**Figure S14.** The attachment of the anode connecting cable and the short connecting cables to the power controllers.

3) Connect the four short cables (red/white) to the terminal connector.

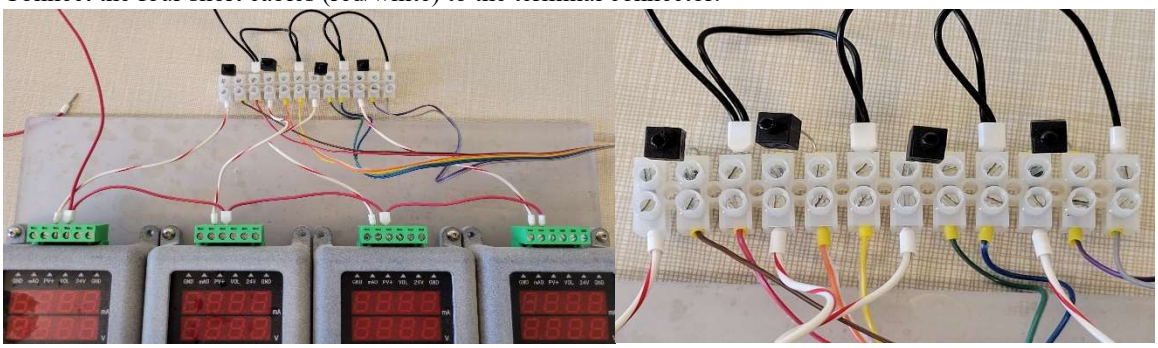


**Figure S15.** The connection of the short connecting cables to the LED indicator array.

4) Then connect the anode (red) and the cathode (black) cable to a DC power supply set to a current limit higher than the total current of all four power controllers and set the voltage limit to 31 V. Turn on each of the four power controllers, by shifting the on and off switch. The power controller may be charged by connecting them to a commonplace 5V micro USB charger. They can either operate on their internal battery or be used while connected to the charger. The current is dialed in by turning the "mA out" to the desired applied current. The electrolysis is started by connecting the ribbon cable to the 8-pin the HT*e*-Chem equipped with a constant voltage PCB. The four LEDs will light up if the setup is connected properly during the electrolysis.

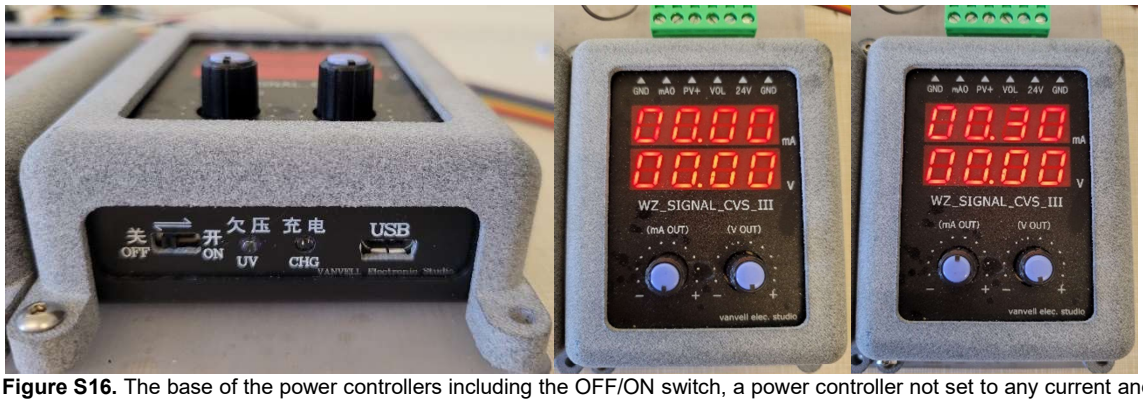



**Figure S16.** The base of the power controllers including the OFF/ON switch, a power controller not set to any current and one set to 0.30 mA.

*Tip: To check if the connector assembly is connected properly a multimeter set to measure currents (mA) is used. The ribbon cable is connected to the 8-pin connector of a constant current PCB charged with 5 skipper pins in row A (A1-A5). The power controllers are set to a current (here: 0.5 mA). When the probes of the multimeter are connected to the empty connector for the skipper pin in cell A6, there should be a positive current with the magnitude of the set current. The positive terminal of the multimeter should be connected to the anodic connector (top) and the negative terminal of the multimeter is connected to the cathodic connector (bottom). If there is a negative current the wiring needs to be corrected in step 1) by switching brown and red, orange, and yellow, blue and green, and purple and grey.*

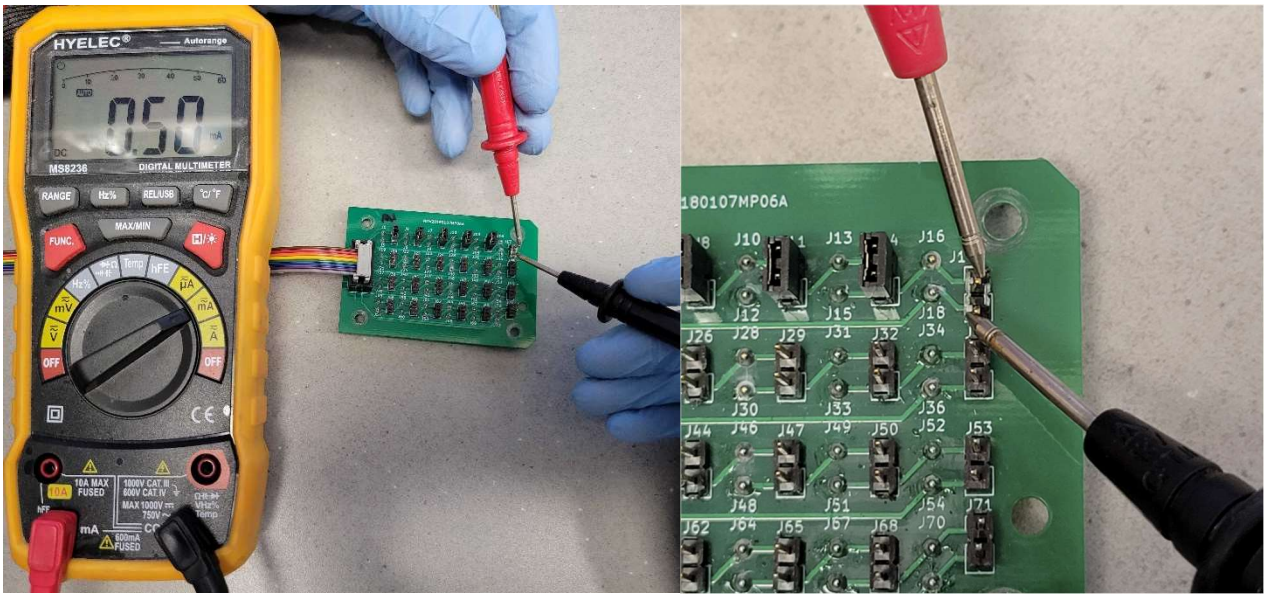



**Figure S17.** Connecting the empty connectors for the skipper pins to a multimeter in order to read the exact current supplied to the PCB.

**Constant Voltage Electrolysis:**

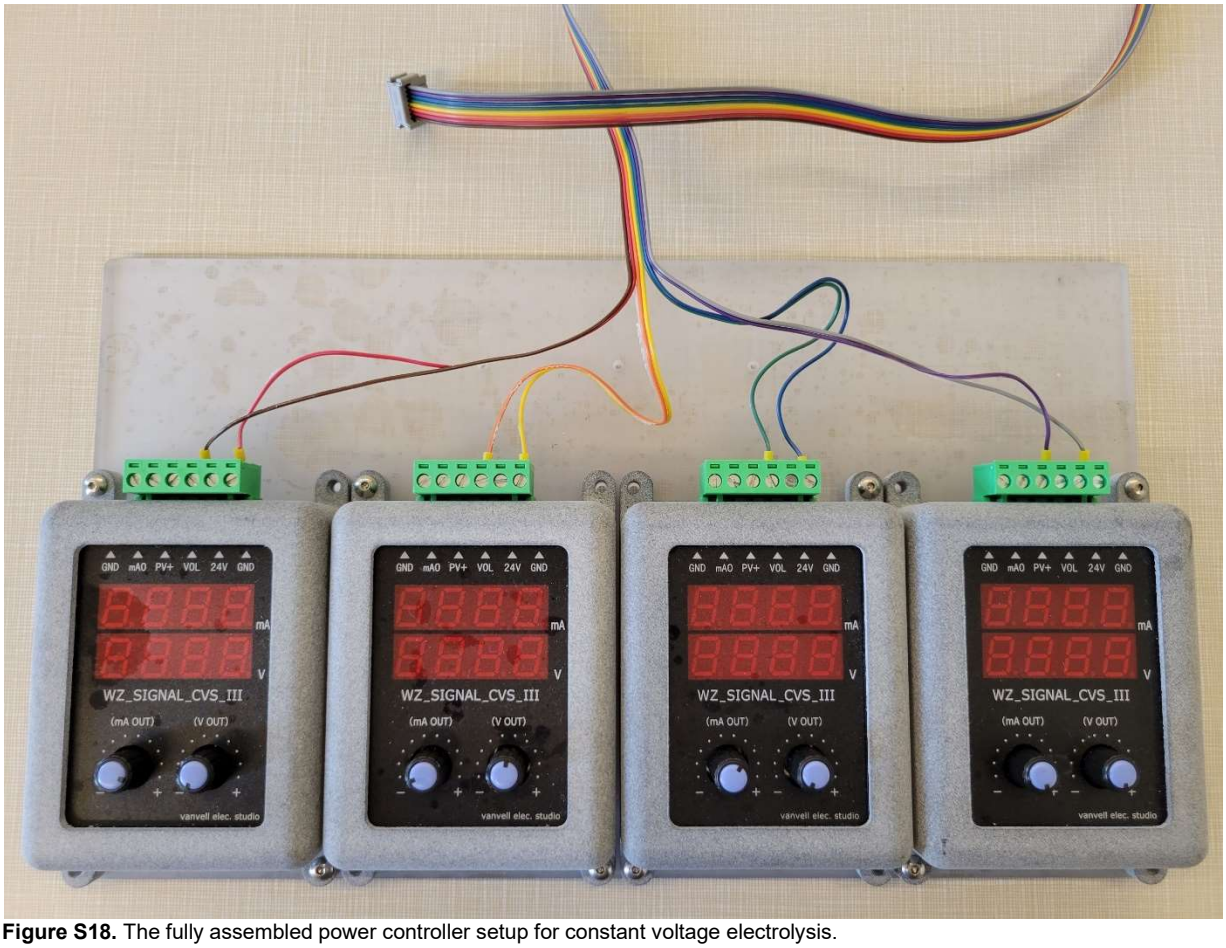



**Figure S18.** The fully assembled power controller setup for constant voltage electrolysis.

1) Connect the ribbon cable to the four power controllers that are mounted on the polycarbonate support plate.

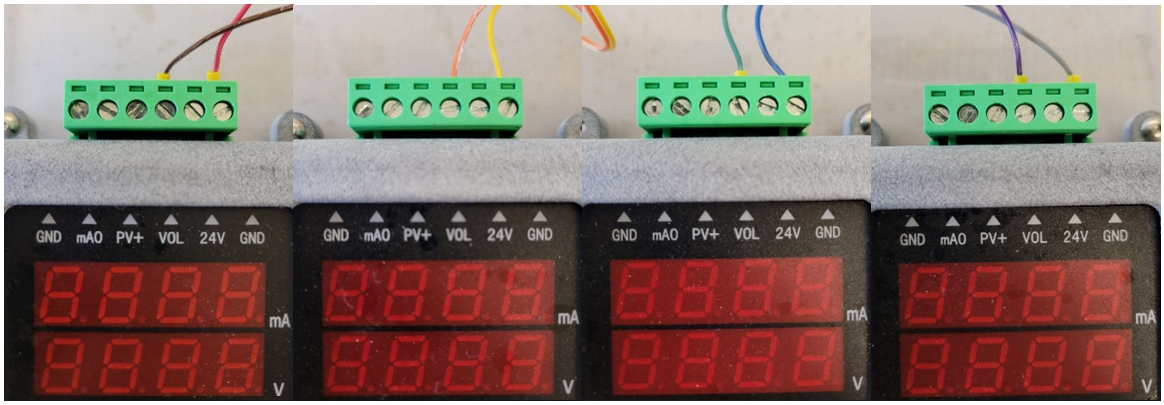



**Figure S19.** The connection of the ribbon cables to the power controllers.

2) Turn on each of the four power controllers, by shifting the on and off switch. The power controller may be charged by connecting them to a commonplace 5V micro USB charger. They can either operate on their internal battery or be used while connected to the charger. The voltage is dialed in by turning the “V out” to the desired cell voltage. The electrolysis is started by connecting the ribbon cable to the 8-pin connector on the HT*e*-Chem equipped with a constant voltage PCB.

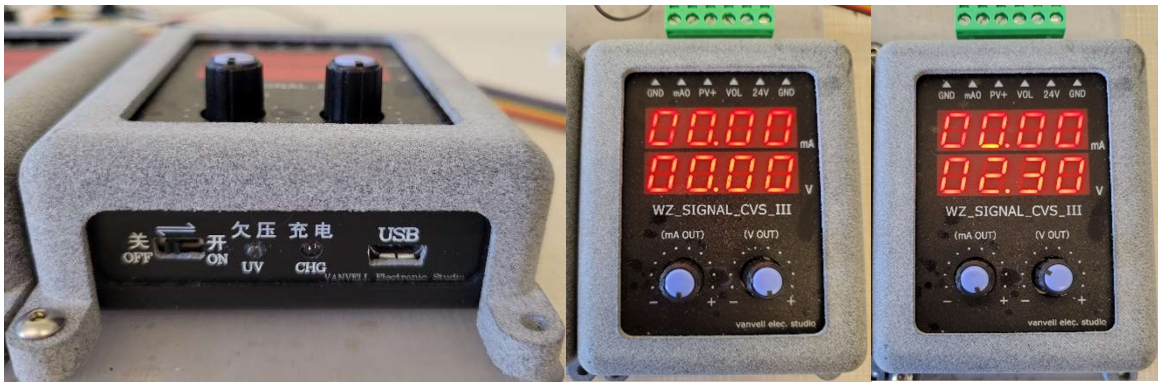



**Figure S20.** The base of the power controllers including the OFF/ON switch, a power controller not set to any voltage and one set to 2.30 V.

*Tip: To check if the connector assembly is connected properly a multimeter set to measure voltage (V) is used. The ribbon cable is connected to the 8-pin connector of constant voltage PCB. The power controllers are set to a voltage (here: 2 V). The probes of the multimeter are connected to the soldering on the PCB corresponding to the spring loaded connectors of the anodes and cathodes. The positive terminal of the multimeter is connected to a anodic pin (top) and the negative terminal of the multimeter is connected to a cathodic pin (bottom). The voltage should be the positive voltage set by the power controller. If there is a negative voltage the wiring in has to be corrected step 1) by switching brown and red, orange and yellow, blue and green, and purple and grey.*


**Figure S21.** Connecting the top of the PCB to a multimeter in order to read the exact voltage supplied.

## CC or CV PCB Assembly Procedure- HT*e*Chem

1. Gather the materials indicated in the "CC PCB" or "CV PCB" section of the Bill of Materials Excel workbook.

2. Place the Mill-Max gold spring pins in one of the G10 electrode holder pieces. This will keep the pins straight while they are being assembled to the PCB

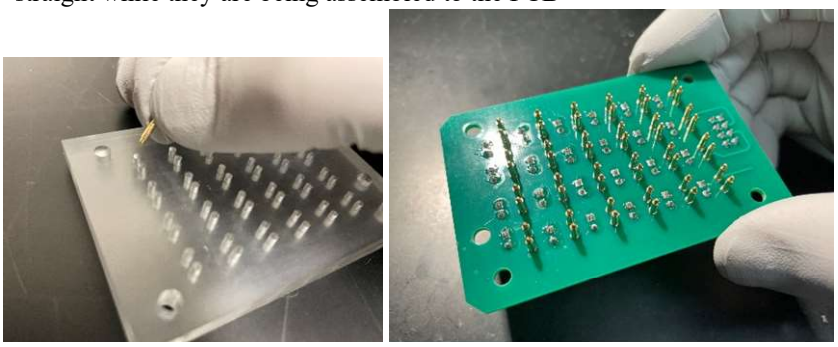


**Figure S22.** Placing the Mill-Max gold spring pins into a G10 electrode holder.

3. Place the bare PCB on top of the pins protruding from the G10 electrode holder piece. Solder the pins into place using RMA no-clean solder. Then remove the PCB from the G10 piece.

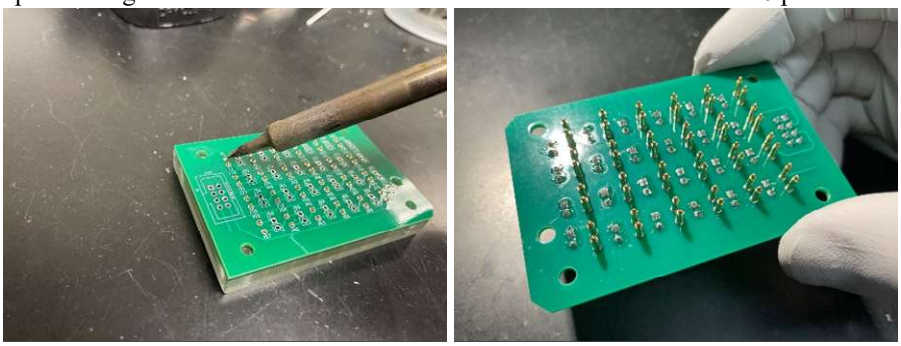


**Figure S23.** Soldering the pins to the PCB.

4. (CC board only) Using a pair of wire cutters, cut the strip of header pins into two pin segments.

**Figure S24.** Cutting the header pins from the strip.

5. (CC board only) Place a second bare PCB on top of two G10 electrode holder pieces, or other pieces of material approximately 0.250” in thickness. Place the two pin segments in the holes in the second PCB, so that the shorter pins protrude from the top.

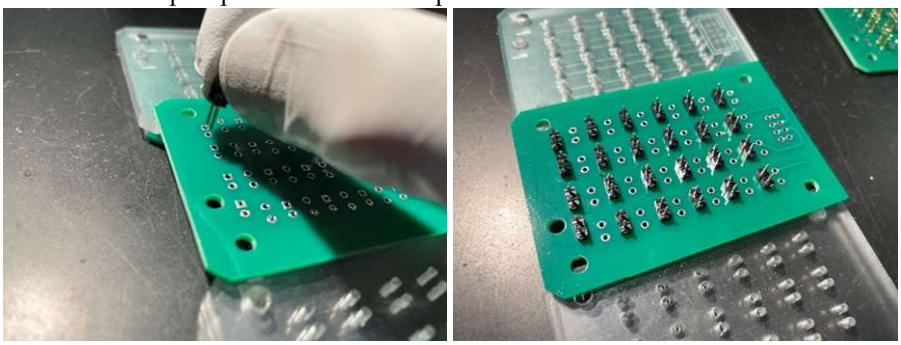


**Figure S25.** Placing pins into a second PCB.

6. (CC board only) Place the first PCB onto the pins protruding from the second PCB. Solder the pins into place. Remove the first circuit board from on top of the second circuit board.

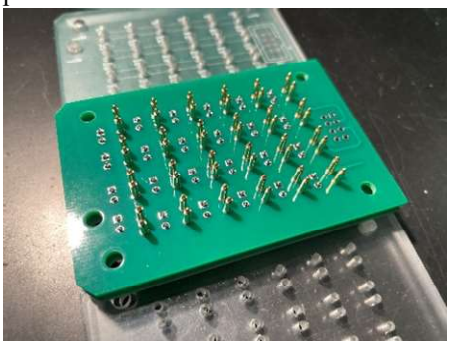


**Figure S26.** The skipper pins soldered into the circuit board.

7. Place three 8 pin connectors face down on the bench, so that the pins are facing up. Place one of these connectors through the holes in the PCB. Make sure that the keying slot in the connector lines up with the white keying slot outline on the circuit board. Place the other two connectors so that they support the sides of the board. Solder the 8 pin connector into place.

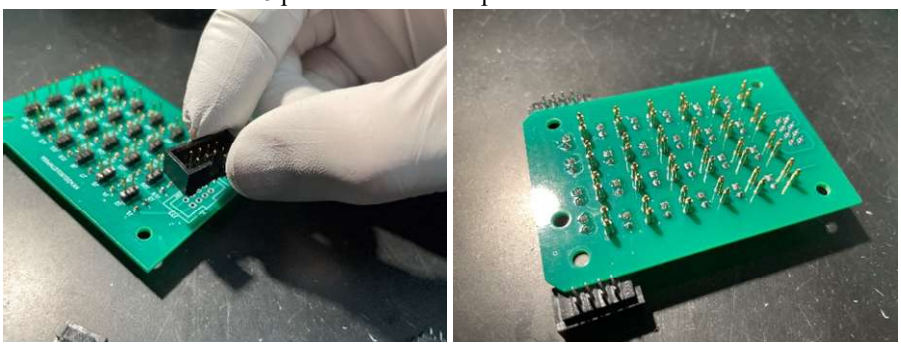


**Figure S27.** Soldering the 8-pin connector into the PCB.

8. Inspect the completed board to ensure that all solder joints have a smooth, shiny appearance, and that all connections are mechanically secure. If desired, flux residue can be removed from the board with isopropyl alcohol.

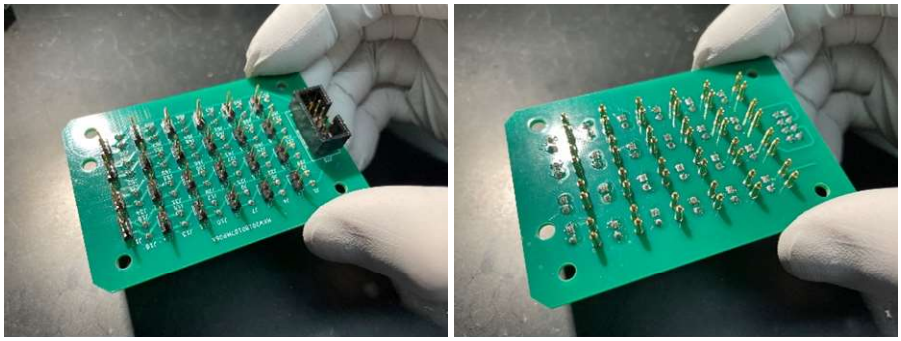


**Figure S28.** The top and bottom of a freshly prepared CC PCB.

## Sealing Plate Assembly Procedure- HT*e*-Chem

1. Gather the materials indicated in the "Sealing Plate" section of the Bill of Materials Excel workbook.

2. Use a Scotch-Brite fine grit (maroon) pad or equivalent abrasive to scuff sand the exterior of the 1/16" stainless steel pins. This helps the epoxy to adhere better to the surface of the pins.

**Figure S29.** Scotch-Brite pad with scuffed stainless steel pins.

3. Clean the G10 plate, the stainless pins, and the silicone gaskets with compressed air and isopropyl alcohol.
4. Place two silicone gaskets underneath the side of the G10 plate without pockets. Insert the stainless pins from the side opposite the gaskets, and allow them to protrude slightly from the surface of the lower silicone gasket. Note that the gaskets pictured are white ePTFE. The silicone gaskets will be red in color.

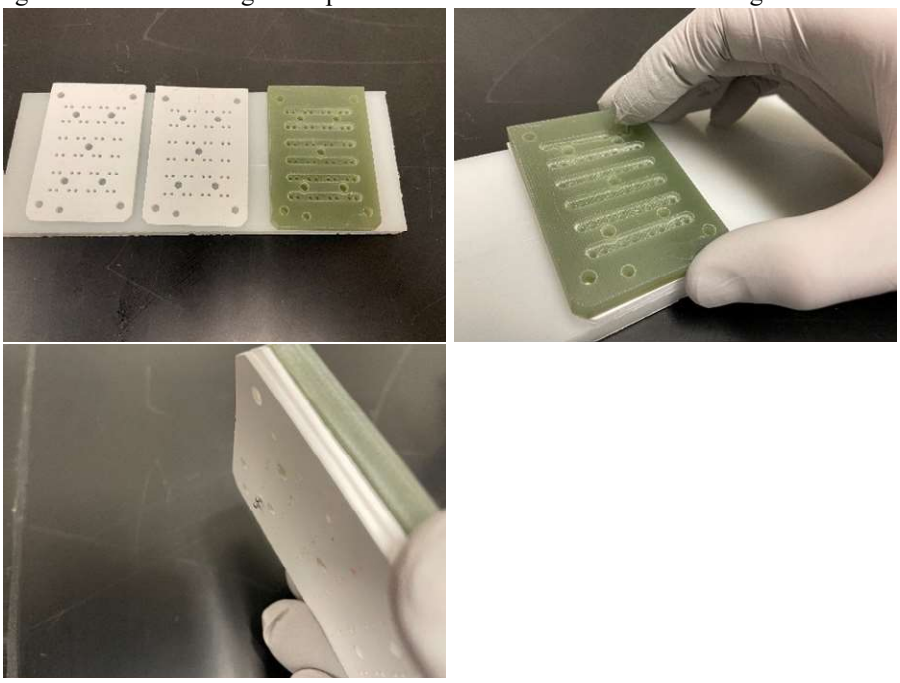


**Figure S30.** The required ePTFE gaskets and the assembly for measuring the correct depth for gluing pins.

5. Once all of the pins have been inserted, place the plate onto a backing board and press down on the G10 plate, so that the ends of the pins are flush with the bottom of the lower gasket. This ensures that the pins protrude below the bottom of the G10 plate by 1/8", and above the top of the G10 plate by 1/16". Use two small clamps with light pressure to secure the G10 plate assembly to the backing board. Press down on the tops of the pins to ensure they rest against the surface of the backing board.

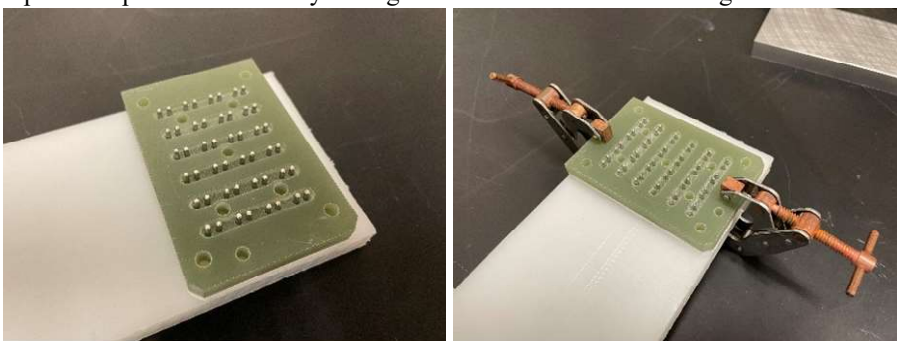


**Figure S31.** The inserted pins and the fully clamped G10 plate assembly.

6. Place the epoxy dispensing cartridge into the dispensing gun, install the mixing nozzle onto the cartridge, and install the 18 gauge luer tip onto the end of the nozzle. Pull the trigger to dispense epoxy onto a waste paper towel until the nozzle is completely filled and any large air bubbles have been removed from the mixing nozzle.

**Figure S32.** 18-gauge luer tipped epoxy dispensing gun.

7. Dispense epoxy into the pockets on the top surface of the G10 plate. The level of the epoxy should be slightly below the top surface of the G10 plate, so that it does not interfere with the sealing screws that will be used with the plate. It works well to fill each pocket in two passes. One pass down the left side, and then a second pass down the right side. The first picture below shows partially filled pockets after one pass. When filling the second pass, you can push the luer tip into the epoxy laid down in the first pass and work it back and forth a bit as you're dispensing to fill the pocket. It is not necessary to work quickly when dispensing the epoxy. The working time for the epoxy is 80 minutes. The long curing time and the low viscosity allow the epoxy to settle into any voids and create a better seal between the pins and the plate.

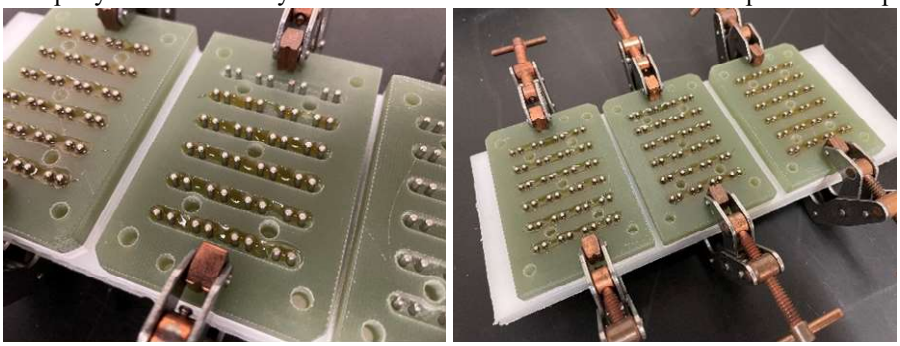


**Figure S33.** Fully glued sealing plates set out to cure.

8. After at least 24 hours of curing time, remove the clamps. Remove the gaskets from the bottom of the plate. Place a sheet of fine grit sandpaper on a flat surface and use it to polish the tops of the pins on both sides. This removes any epoxy residue that may have been deposited on the tops of the pins. Full cure is achieved after 14 days, so you may want to wait a few days before using the plates. Heat can be used during the curing process to accelerate the curing time. Refer to 3M DP190 technical data sheet for additional information on surface preparation and curing.

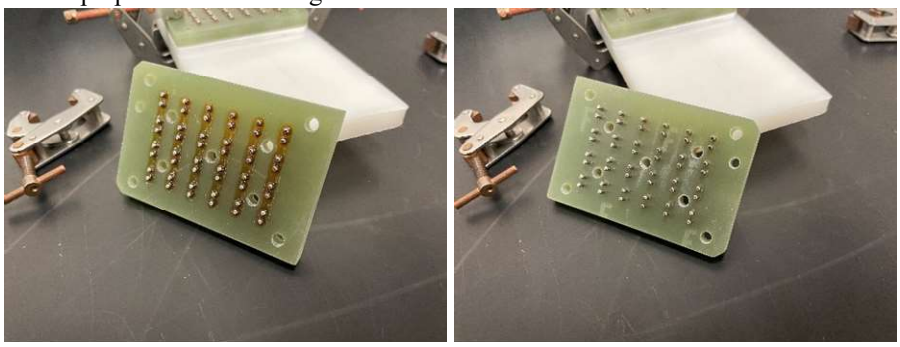


**Figure S34.** Top and bottom of a freshly prepared sealing plate.

## Guide for Design of Experiment

Generally, the HT*e*-Chem can be used to investigate virtually any parameter in detail. Further the parallel electrosynthesis enables the exploration of the interaction of experimental conditions. Initially it can be helpful to broadly investigate the intersection of different parameters to identify which features are most relevant to improving a given reaction.

**Plate map design:**

The number of parameters screened times the variations in each should multiply to give 24 to investigate the full experimental space (Figure S34). This is also beneficial for the reaction setup, as it allows for the use of stock solutions for each the conditions. When designing experiments, it is imperative to consider that the applied current or the cell voltage is constant in each row of the HT*e*-Chem; thus, these two parameters can only be varied by rows.

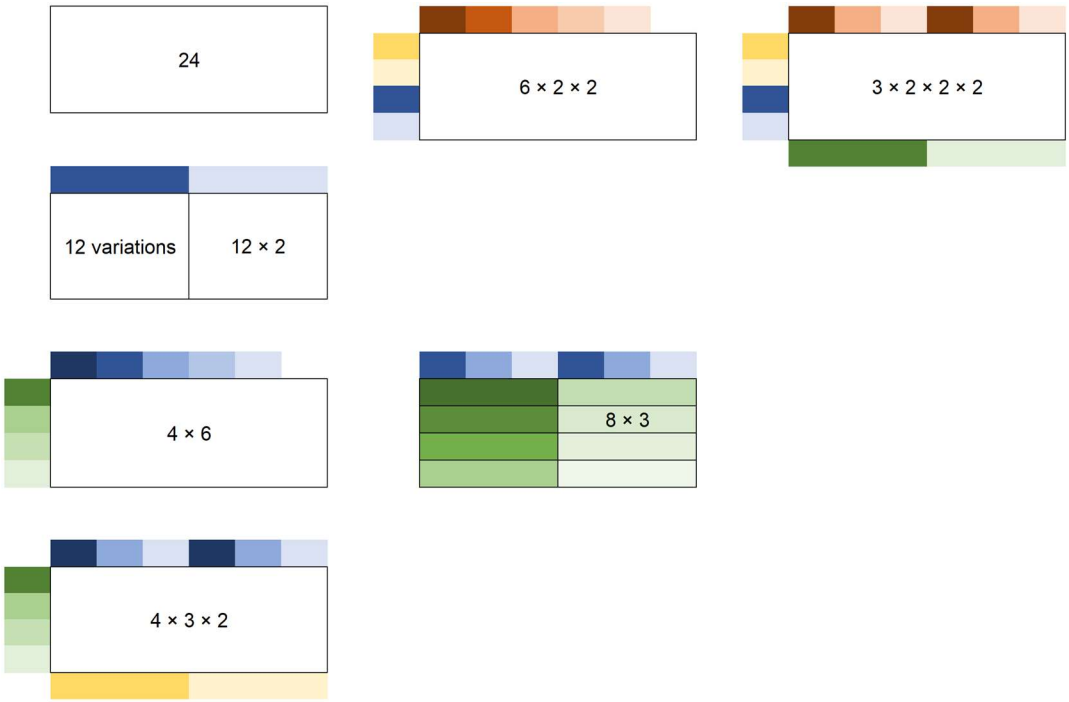



**Figure S35.** Visual representation of possible plate maps, that investigate the experimental space. Each Color gradient represents an experimental parameter that is varied.

To limit reagent consumption the experimental design should consider minimizing the number of required stock solutions. It is often beneficial to consider the entire screening campaign. This can be illustrated with a hypothetical reaction optimization aiming to cover the entire experimental space with 72 combinations of 3 catalysts, 3 solvents, and 8 electrolytes. This involves 3 HT*e*-Chem plates and can be done in several ways:

*Inefficient procedure* (3 × 27 solutions)

If each of the plates is done with one catalyst, and screens 8 electrolytes and 3 solvents (8 × 3) the setup requires 8 electrolyte solutions for each of the three solvents (24 stock solutions) and a catalyst solution (with substrate) for each solvent (3 solutions).

*Efficient procedure* (3 × 12 solutions)

If each of the plates is done with one solvent, and screens eight 8 electrolytes and 3 catalyst (8 × 3) the setup requires 8 electrolyte solutions, 3 catalyst solutions, and 1 substrate solution (12 solutions).

## Troubleshooting Guide and Frequently Asked Questions:

**Is the sealing plate required for all transformations?**

The sealing plate is recommended for all transformations. However, if you produce your own silicone rubber gasket, as described in General Procedure C (page S11) the system can maintain a good seal unless gas evolution is present.

**How should I add my reagents to the HT*e*-Chem?**

Reagents should be added as stock solution whenever possible. The stock solutions are dispensed using pipettors or multichannel pipettors to achieve an accurate transfer of chemicals.

**How should I add reagents that are insoluble in my desired solvent?**

Reagents that are insoluble in the reaction medium can be added via slurry addition, by suspending and agitating the solids in the solvent while pipetting. Slurry is significantly less accurate than the addition as solution or solid transfer and thus should be limited to reagents used in excess or where the exact amount of material does not significantly affect the reaction outcome.

A more accurate alternative to slurry addition is the addition as a solution in a different solvent, followed by the evaporation of excess solvent. The evaporation can be performed under a continuous nitrogen flow using commercial evaporators for HTE well plates or by vacuumed centrifugation systems.

**What materials are incompatible with the HT*e*-Chem?**

To test the chemical resistance of the silicon rubber seal, three tests were conducted to test its durability.

**Test 1** (Solvent vapor test): A sheet of silicon rubber mat was placed on top of a 1 ml solution of the solvent and pressed on top by a weight (250 g) at room temperature for 3 hours. The results were evaluated by visual inspection. Passed = no visual change, swelling = visible swelling, dissolved = material was dissolved in solution.

| **Solvent** | **result** | **Solvent** | **result** | **Solvent** | **result** |
|---|---|---|---|---|---|
| 5% HCl | Passed | DMF | Passed | $Et_3N$ | Passed |
| 10% HCl | Passed | Ether | Passed | THF | Passed |
| 20% HCl | Passed | AcOH | Passed | MeOH | Passed |
| Pyridine | Passed | TFA | dissolved | TFA/MeCN 1:4 | Passed |
| DIPEA | Passed | $MeNO_2$ | Passed | TBAF/MeCN | Passed |
| DMSO | Passed | Sulfolane | Passed | 5% $Br_2$/MeCN | Passed |
| Benzene | Passed | NMP | Passed | DCM | Passed |
| GVL | Passed | EtOH | Passed | | |

**Test 2** (Short duration immersion): A (0.3 x 1.0) cm piece of silicon rubber mat was placed in a 1 ml solution of the solvent and left to soak for 5 minutes at room temperature. The results were evaluated by visual inspection. Passed = no visual change, swelling = visible swelling, dissolved = material was dissolved in solution.

| **Solvent** | **result** | **Solvent** | **result** | **Solvent** | **result** |
|---|---|---|---|---|---|
| 5% HCl | Passed | DMF | Passed | $Et_3N$ | Passed |
| 10% HCl | Passed | Ether | Passed | THF | Passed |
| 20% HCl | Passed | AcOH | Passed | MeOH | Passed |
| Pyridine | Passed | TFA | dissolved | TFA/MeCN 1:4 | Passed |
| DIPEA | Passed | $MeNO_2$ | Passed | TBAF/MeCN | passed |
| DMSO | Passed | Sulfolane | Passed | 5% $Br_2$/MeCN | passed |
| Benzene | Passed | NMP | Passed | DCM | Passed |
| GVL | Passed | EtOH | passed | | |

**Test 3** (Long duration immersion): A (0.3 x 1.0) cm piece of silicon rubber mat was placed in a 1 ml solution of the solvent and left to soak for 12 hours at room temperature. The results were evaluated by visual inspection. Passed = no visual change, swelling = visible swelling, dissolved = material was dissolved in solution.

| **Solvent** | **result** | **Solvent** | **result** | **Solvent** | **result** |
|---|---|---|---|---|---|
| 5% HCl | Passed | DMF | Passed | $Et_3N$ | Swelling |
| 10% HCl | Passed | Ether | Swelling | THF | Swelling |
| 20% HCl | Passed | AcOH | Passed | MeOH | Passed |
| Pyridine | Passed | TFA | dissolved | TFA/MeCN 1:4 | Passed |
| DIPEA | Passed | $MeNO_2$ | Passed | TBAF/MeCN | Passed |
| DMSO | Passed | Sulfolane | Passed | 5% $Br_2$/MeCN | Passed |
| Benzene | Swelling | NMP | Passed | DCM | Swelling |
| GVL | Passed | EtOH | Passed | | |

**Can the HT*e*-Chem be used in the Glovebox?**

The reactor can be brought into the glovebox. The reactor baseplate, vials, stirbars, silicone mats, and electrodes can be dried in a 150 °C oven. If your glovebox is set up for electrochemical reactions the reactor can be set up and run in the glovebox. If your glovebox is not set up for electrochemical reactions, it can be assembled in the glovebox and then removed without harming the reactions.

**Graphite electrodes keep breaking when inserting them in alignment plate:**

Try pushing the electrodes in from the bottom with your fingers at the alignment plate. If you are breaking electrodes it is often because you are pushing them in at an angle.

**Trouble with reproducibility/confusing trends in data:**

If you are questioning the reproducibility of the plate set up it can be helpful to run identical conditions in all 24 wells. This can highlight systemic problems like pipetting inconsistencies, poor stirring, or uneven heating, cooling, or illumination that manifest themselves as edge effects. In designing HTE experiments try including a positive control condition to compare between plates and help identify day to day variances in your reaction. Things like fluctuating room temperatures, high humidity, and aging reagents can affect experiments differently over time.

**There is no current when I start the electrolysis:**

Under constant current electrolysis all reactions within the same row are connected in series. If one or multiple cells in a row are not conducting electricity the LED indicator light will also not light up. Additionally, if the LED light is unusually dim, or if it is blinking on and off, it is a sign that there is a conductivity problem in the corresponding row. To avoid losing the data from the rest of the row, one or multiple "skipper pin" can be used to exclude the failing cells from electrolysis. The following are the most common reasons for a low conductivity:

(1) The reaction solution is not conductive, which can in most cases be attributed to one of the following:
   I. A solvent with a low dialectical constant is being used. For efficient electrolysis at reasonable cell potentials a polar solvent should be utilized, common solvents used in organic electrosynthesis include MeCN, DMF, DMA, MeOH, EtOH, TFE, HFIP, THF, DCM, $H_2O$, NMP, GVL and many more. Solvents that generally result in poor conductivity are EtOAc, toluene, $Et_2O$, hexanes.
   II. Insufficient amounts or an insoluble electrolyte is being used. A good starting point for the discovery of new reactions is to use an electrolyte concentration between 0.05-0.5 M. Further, it is very important that the electrolyte is soluble in a desired solvent and stays soluble during electrolysis.
   III. The anodic or cathodic reaction is slow and requires a very large potential. When designing an electrochemical experiment is important to consider both the anodic and cathodic reactions. Many electrochemical oxidations employ protons as a sacrificial oxidant, and a (weak) acid is added to the reaction mixture to facilitate hydrogen evolution. For electrochemical reductions sacrificial zinc or magnesium anodes or easily oxidized compounds such as tertiary amines can be added.
   IV. If the reaction fails to conduct during electrolysis, this might be caused electrode passivation or by accumulation of heterogeneous by-products. This can be observed in some reductions using sacrificial electrodes if the zinc or magnesium cations generated crash out of solutions as insoluble salts. Potential solutions are lowering the reaction concentration or switching to a more polar solvent.

(2) The electrode is broken. Graphite electrodes are fragile, and they can break during reaction set up. If this occurs and you do not notice it until beginning electrolysis you can either skip the well with a "skipper pin" or you can disassemble the reactor to expose the alignment plate and push the broken electrode into the reaction with a new electrode. In many cases efficient conversion is observed even when the reaction is conducted in the presence of a broken electrode.

(3) There is poor contact between the electrode and the sealing plate. This can occur when the electrodes have a rough or pinched end that does not slide effortlessly through the alignment plate. This can also occur when the alignment plate or the sealing plate are over tightened or unevenly tightened. Often adjusting the tightness of the sealing plate can return full connectivity. Additionally, skipping the poorly connecting reactions with "skipper pins" can restore connectivity to the rest of the row.

**Can the electrodes be reused?**

Generally, all non-sacrificial electrodes can be reused after cleaning:

*Graphite electrodes:*

The graphite electrodes are rinsed with acetone and then sonicated in 0.5 N HCl, water for 1-2 min each. After that the electrodes are sonicated for 5 min in acetone. To make sure that the electrode surface is as reproducible as possible the graphite electrode is polished with a paper towel until the surface of the area exposed to the solvent is visually undifferentiable form the rest of the electrode or until it has a metallic shine.

*Chromel, stainless steel, Cu, etc.*

The metal electrodes are rinsed with acetone and then sonicated in 0.5 N HCl, water for 1-2 min each. After that the electrodes are sonicated for 5 min in acetone. After this procedure, the electrodes should have a metallic shine and not be discolored.

*Platinum:*

The platinum electrodes are rinsed with acetone and then sonicated in 0.5 N HCl, water for 1-2 min each. After that the electrodes are sonicated for 5 min in acetone. If the electrodes are not clean, they can be sonicated for 1-2 min in aqua regia and water for 1-2 min each. After that the electrodes are sonicated for 5 min in acetone.

**How much time does the HT*e*$^-$Chem save in screening vs traditional benchtop scale experimentation?**

It is difficult to provide an accurate quantification of timesaving, as every reaction has unique requirements. Most electrochemical reactions developed in our labs take about 5-15 min to setup for a single reaction performed at a large scale (approximately 0.3 to 2 mmol) using an Electrasyn 2.0 or a vial in a homemade setup, while the HT*e*$^-$Chem requires between 30-90 min to setup 24 reactions. Increasing the throughput by at least 4-fold. The slowest part of setting up the HT*e*$^-$Chem in our experience is making stock solutions and pipetting into the vials, which is a process common to any plate based HTE. A detailed breakdown of time required for the setup and work-up of the azidooxygenation of alkenes with the HT*e*$^-$Chem and on benchtop scale is outlined below (the Setup closely follows the video SI):

**HT*e*$^-$Chem's total time = 28 min**

*Preparation of the HTe$^-$Chem (5 min):*

1) Assembly of the sealing plate
2) Charging the reactor base with 24 vials and 24 stir bars
3) Placing alignment plate and silicon gasket onto the HT*e*$^-$Chem
4) Inserting of electrodes into the alignment plate

*Preparation of stock solutions (5 min):*

1) Weighing 4-methoxy styrene and TEMPO and addition of acetonitrile (sparge with nitrogen)
2) Weighing in sodium azide and addition of deionized water (sparge with nitrogen)

*Plating out the reaction mixture into each well with a micropipette (3 min with pipettor or 30 s with a multichannel pipettor)*

*Sealing of the HTe$^-$Chem (2 min):*

1) Tighten alignment plate with electrodes with a torque screwdriver or electric screwdriver
2) Sealing the HT*e*$^-$Chem with the sealing plate

*Starting the electrolysis (3 min)*

1) Securing CCE PCB onto the reactor
2) Dialing in the desired current with the current controller
3) Connecting the 8-pin connector to the PCB

*Work-up (10 min):*

1) Preparation of internal standard stock solution
2) Opening HT*e*$^-$Chem by unscrewing the sealing and alignment plates
3) Addition of internal standard with a pipettor or a multichannel pipettor

4) Stirring for 2 min
5) Addition of 1 mL of acetonitrile to HPLC vial with pipettor
6) Addition of 50 μL reaction mixture to each HPLC sample

**Electrasyn 2.0's total time = 10–17 min**
*Charging the cap Electrasyn 2.0 with electrodes and the vial with a stir bar (1 min)*
*Weighing 4-methoxy styrene, TEMPO, and sodium azide and addition of acetonitrile and water via syringe (sparge with nitrogen) (4 min)*
*Attaching electrolysis cap onto the vial and connecting it to the Electrasyn 2.0; setting up electrolysis parameters (2 min)*
*Work-up (3 min for HPLC yield or 10 min for NMR yield)*
1) Weighing internal standard and addition to the reaction mixture
2) Stirring for 2 min
3) Transfer of an aliquot to a HPLC vial and diluting with acetonitrile
or

3) Concentrate reaction mixture and filter through a silica plug column with diethyl ether
4) Concentrate crude product and addition of $CDCl_3$ for the preparation of a NMR sample

**Timesaving:** The HT*e*-Chem is 12–20-fold faster per reaction for the setup of the azidooxygenation of alkenes.

There are several key factors that allow us to save time when setting up an HTe-Chem experiment. (1) Compatibility with existing equipment for reagent addition: Using standard 24 well plate, one can easily employ a multichannel pipettor or even a reagent-handling robot for reagent addition, which substantially reduces the time and manual labor needed for 24 independent electrolysis setups. Additionally, the HT*e*-Chem can take advantage of existing HTE infrastructure such as pre-plated reagent libraries to further accelerate screening campaigns. (2) Facile work-up and analysis: The HT*e*-Chem significantly accelerates the work-up/analysis as addition of internal standard and sample preparation for analysis, typically via HPLC, is easily parallelizable with multichannel pipettors. Work-up of a plate and sample preparation generally requires less than 15 min. (3) The time savings of HT*e*-Chem are compounded if the electrolysis requires inert conditions such as exclusion of air and water, as only one transfer into a glovebox is required while a traditional setup would require time intensive sparging or mutliple transfers into a glovebox to achieve the same number of reactions. Alternatively, the HT*e*-Chem can be run and maintained in a glovebox.

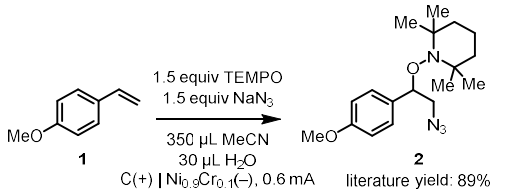
We also note that the microscale of HT*e*-Chem can enable screening campaigns with limited amounts of starting materials which not only saves cost, but also saves time in the synthesis of valuable starting materials.

**Where can I get an HT*e*-Chem?**

The complete bill of materials as well as the technical drawings needed for manufacturing the G-10 plates and PCB are included as Supporting Information SI2 and SI3. Detailed explanations for assembling the electrochemical apparatus are included in Section 5─8, pages S14─S30.

## Experimental Procedures- HT*e*-Chem

(A)




(B)

| | | | | | |
|---|---|---|---|---|---|
| 88 | 87 | 90 | 89 | 86 | 86 |
| 88 | 92 | 88 | 90 | 88 | 92 |
| 93 | 87 | 85 | 90 | 89 | 91 |
| 90 | 91 | 90 | 89 | 90 | 88 |

Average yield- 89.1%

Standard deviation- 2.0

Relative standard deviation- 2.2%

(C)

| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| A | MeCN | 10 mL | 350 µL | 4-MeOStyrene | 17.5 | 1 | 67.1 mg |
| | | | | TEMPO | 26.25 | 1.5 | 117.2 mg |
| B | water | 1 mL | 30 µL | sodium azide | 26.25 | 1.5 | 56.9 mg |

**Figure S36.** (A) Reaction conditions for HT*e*-Chem with literature yields. (B) Plate map and yields as determined by HPLC, dimethylterephthalate as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HT*e*-Chem was assembled with graphite rod anodes and nickel chrome cathodes according to plate assembly procedure B. Solution A (350 µL) and solution B (30 µL) was added to each well. The alignment plate, sealing plate and constant potential PCB were added and the HT*e*-Chem was stirred at 800 rpm while being electrolyzed at 0.6 mA for 2.0 F (94 min).

**Plate Analysis:** A solution of dimethyl terephthalate (42.5 mg in 10 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Agilent 1290 Infinity II  UPLCMS

Column: InfinityLab Poroshell 120 EC-C18, 2.1 x 50 mm, 2.7-Micron

Method: Flowrate 1 ml/min. Increase from 30 to 42% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 2 min. Hold at 42% MeCN (+0.1% formic acid) in water (+0.1% formic acid) for 0.1 min. Increase from 42 to 100% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 0.5 min. Hold at 100% MeCN (+0.1% formic acid) for 0.4 min.

Retention Times: Dimethyl terephthalate – 1.229 min, Azidooxygenated product **2** – 2.860 min

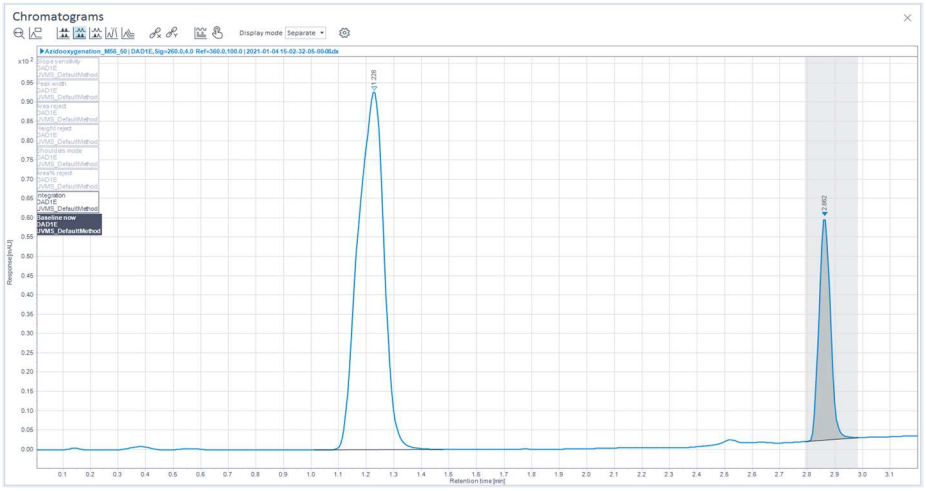



**Figure S37.** UPLC chromatograph of purified product standard **2** and internal standard.

Standard Curve:

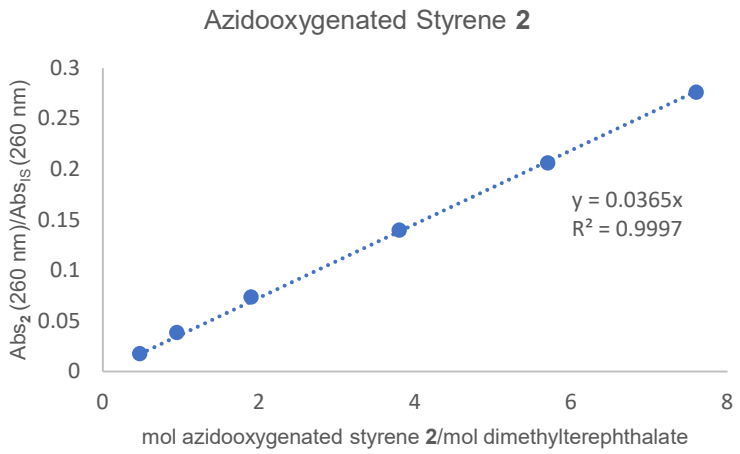
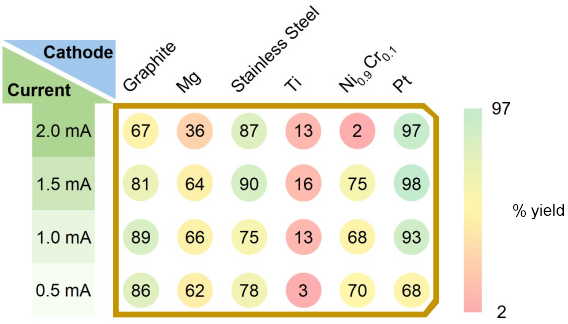



**Figure S38.** Standard curve for determination of yield of **2**.

(A)


(B)




(C)

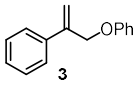
| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| A | THF | 2.6 mL | 100 µL |  3 | 17.5 | 1 | 95.7 mg |
| B | THF | 2.0 mL | 100 µL | $TBACIO_4$ | 60 | [0.2 M] | 410.3 mg |
| C | THF | 3.0 mL | 100 µL | TMSCl | 52.5 | 3 | 199.9 µL |

**Figure S39.** (A) Reaction conditions for HT*e*-Chem with literature yields. The parameters that are varied are shown in bold. (B) Plate map and yields as determined by HPLC, trimethoxybenzene as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HT*e*-Chem was assembled with magnesium rod sacrificial anodes and graphite rod, magnesium rod, stainless steel rod, nickel chrome rod, titanium rod, and platinum rod cathodes as indicated above, according to plate assembly procedure C. Solutions A, B and C were prepared in a glovebox using rigorously dry and degassed solvents. In a glovebox, solutions A (100 µL), B (100 µL), and C (100 µL) were added to each well. The alignment plate, sealing plate and constant current PCB were added and the reactor was removed from the glovebox. The HT*e*-Chem was stirred at 800 rpm while being electrolyzed at 0.5 mA, 1.0 mA, 1.5 mA, and 2.0 mA, as indicated above, for 2.5 F (94 min).

**Plate Analysis:** A solution of trimethoxy benzene (36.8 mg in 10 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Shimadzu LC-20

Column: Chiralpak IA, 4.6 x 250 mm, 5 µm

Method: Flowrate 1 ml/min. Increase from 0.1 to 3% iPrOH in hexane over 10 min. Increase from 3 to 10% iPrOH in hexane for 1 min. Hold at 10% iPrOH in hexane for 4 min.

Retention Times: 1,3,5-Trimethoxybenzene- 7.549 min, Silylated product **4**- 3.333 min

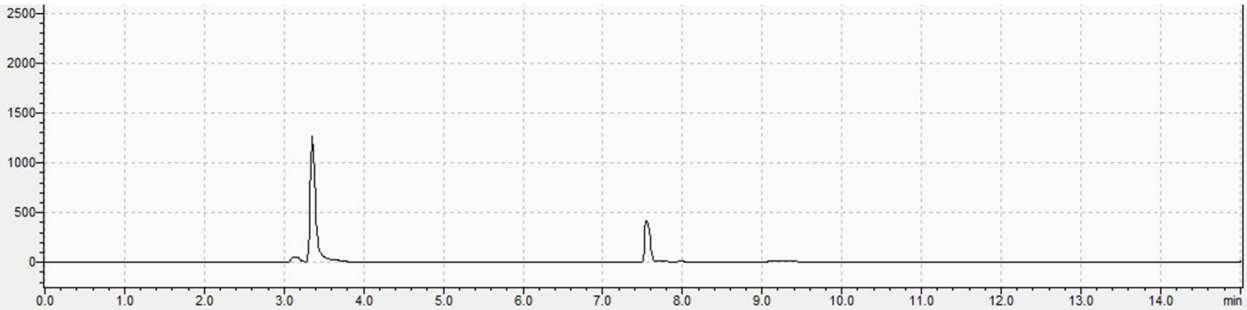



**Figure S40.** HPLC chromatograph of purified product standard **4** and internal standard.

Standard Curve:

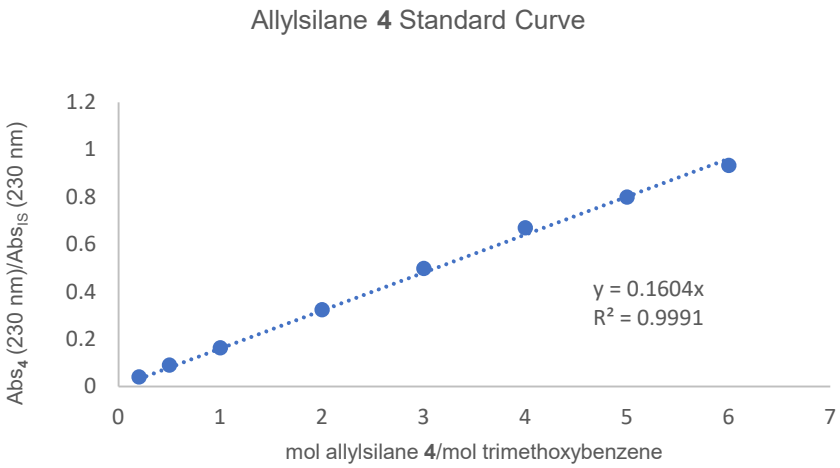
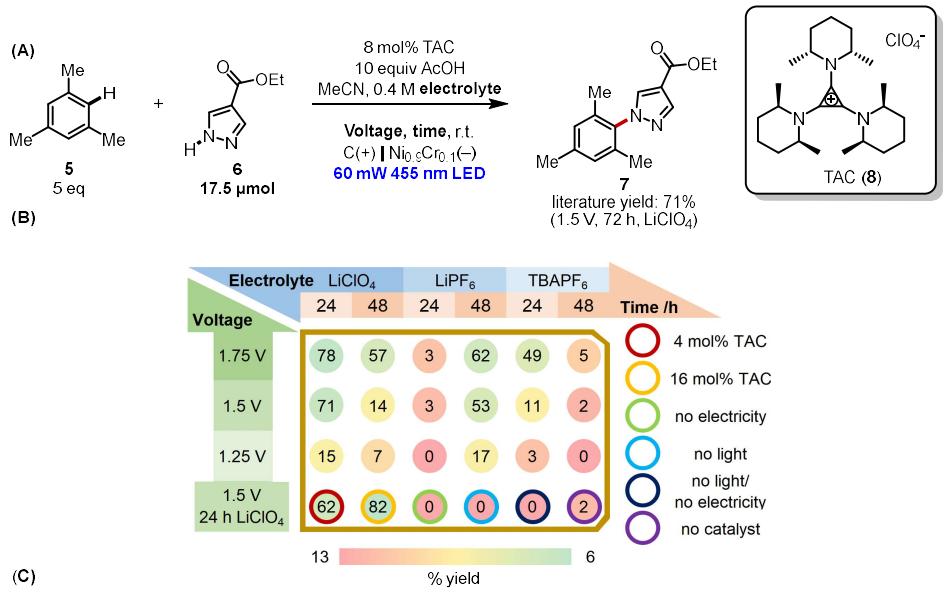



**Figure S41.** Standard curve for determination of yield of **4**.




| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| | | | | Ethyl pyrazole-4-carboxylate **(6)** | 17.5 | 1 | 122.6 mg |
| A | MeCN | 5.0 mL | 100 µL | Mesitylene **(5)** | 61.25 | 3.5 | 386.1 mg |
| | | | | AcOH | 175 | 10 | 525.5 mg |
| B | MeCN | 1.3 mL | 50 µL | TAC **(8)** | 1.4 | 0.08 | 17.2 mg |
| C | MeCN | 3.0 mL | 100 µL | $LiPF_6$ | 105 | [0.4 M] | 475.7 mg |
| D | MeCN | 3.0 mL | 100 µL | $TBAPF_6$ | 105 | [0.4 M] | 1.22 g |
| E | MeCN | 3.0 mL | 100 µL | $LiClO_4$ | 105 | [0.4 M] | 333.9 mg |

**Figure S42.** (A) Reaction conditions for HT*e*-Chem with literature yields. The parameters that are varied are shown in bold. (B) Plate map and yields as determined by HPLC, dimethylterephthalate as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HT*e*-Chem was assembled with graphite rod anodes and nickel chrome rod cathodes according to plate assembly procedure B being sure to use a photochemistry base plate. All solutions were prepared in a glovebox using rigorously dry and degassed solvents. In a glovebox, solution A (100 µL) was added to all wells. Electrolyte solutions C, D, and E (100 µL) were added as indicated above. Lastly solution B (50 µL) and MeCN (50 µL) were added to all wells except D1, D2, and D6. 25 µL of solution B was added to D1 along with 75 µL of MeCN. 75 µL of solution B was added to D2 along with 25 µL of MeCN. No solution B was added to D6, instead 100 µL of MeCN was added. The alignment plate and sealing plate were added and the reactor was removed from the glovebox. Black marker was used to obscure the bottom of wells under no light conditions in D4 and D5. The connectivity of all wells was verified by applying a constant current PCB. The constant current PCB was removed. Duct tape was applied to no electricity wells D3 and D4 to prevent connectivity with the PCB. A constant potential PCB was added, and the reactor was placed upon a 24 well blue LED array in which the LEDs corresponding to no light controls, D4 and D5, had been covered with aluminum foil. The HT*e*-Chem was stirred at 800 rpm while being irradiated with 455 nm light at 60 mW, and electrolyzed at 1.25 V, 1.5 V, and 1.75 V for 24 hours. At which point, the constant potential PCB was removed, and duct tape was applied to prevent connectivity to row D and columns 1, 3 and 5 as indicated above. Additionally, black marker was used to obscure the bottom of wells in row D as well as columns 1, 3 and 5. Aluminum foil was added to the 24 well blue LED array to the positions corresponding to row D as well as columns 1, 3, and 5. The constant potential PCB was reattached, and the HT*e*-Chem was allowed to continue as before for an additional 24 h.

**Plate Analysis:** A solution of dimethyl terephthalate (42.5 mg in 10 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Agilent 1290 Infinity II  UPLCMS

Column: InfinityLab Poroshell 120 EC-C18, 2.1 x 50 mm, 2.7-Micron

Method: Flowrate 0.4 ml/min. Hold at 30% MeCN (+0.1% formic acid) in water (+0.1% formic acid) for 1 min. Increase from 30 to 100% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 5 min. Hold at 100% MeCN (+0.1% formic acid) for 2 min.

Retention Times: Dimethylterepthalate- 2.669 min, Mesitylated pyrazole **7**- 4.002 min.

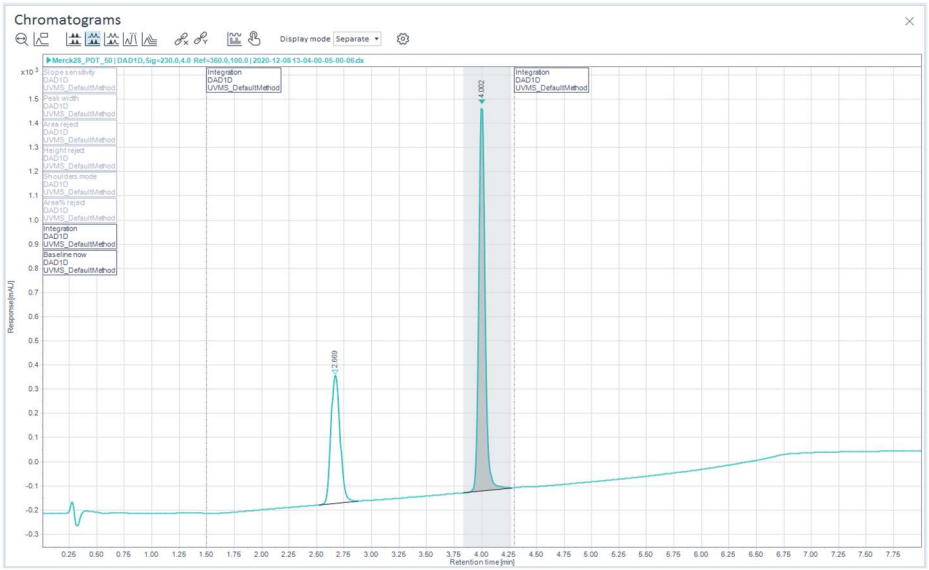



**Figure S43.** UPLC chromatograph of purified product standard **7** and internal standard.

Standard Curve:

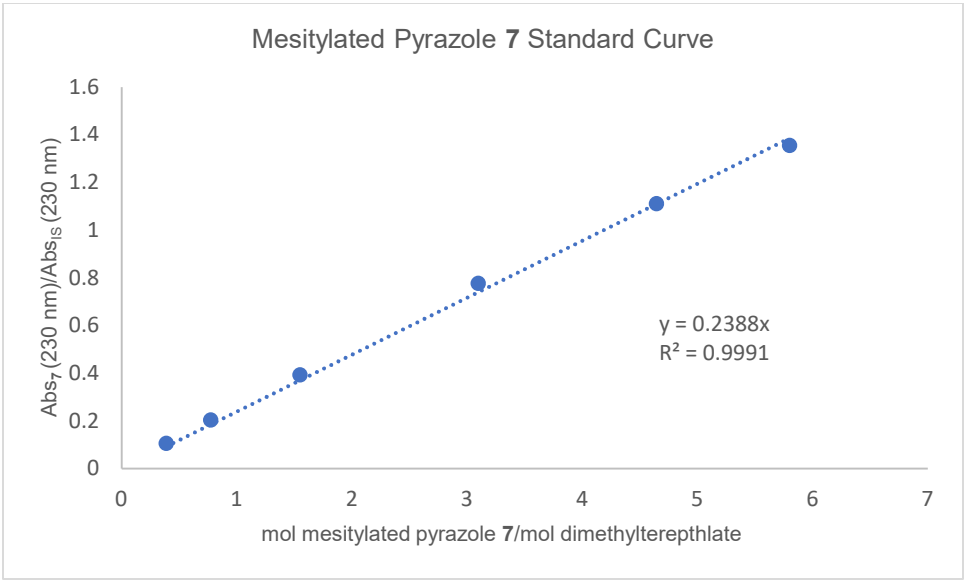
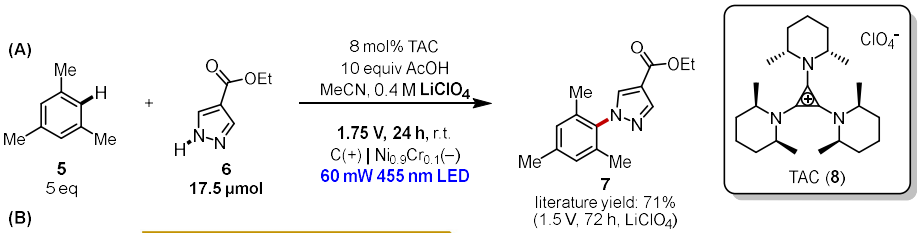



**Figure S44.** Standard curve for determination of yield of **7**.




(B)

| | | | | | |
|---|---|---|---|---|---|
| 75 | 81 | 76 | 73 | 71 | 77 |
| 79 | 77 | 74 | 70 | 75 | 70 |
| 75 | 72 | 75 | 73 | 71 | 73 |
| 23 | 78 | 79 | 85 | 70 | 72 |

Average yield*- 75.0%

Standard deviation*- 3.9%

Relative standard deviation*- 5.2%

*well D1 excluded from analysis

(C)

| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| | | | | ethyl pyrazole-4-carboxylate (**6**) | 17.5 | 1 | 81.7 mg |
| | | | | Mesitylene (**5**) | 61.25 | 3.5 | 245.4 mg |
| A | MeCN | 10.0 mL | 300 µL | AcOH | 175 | 10 | 350.3 mg |
| | | | | TAC (**8**) | 1.4 | 0.08 | 22.0 mg |
| | | | | $LiClO_4$ | 105 | [0.4 M] | 309.2 mg |

**Figure S45.** (A) Reaction conditions for HT*e*-Chem with literature yields. (B) Plate map and yields as determined by HPLC, dimethylterephthalate as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HT*e*-Chem was assembled with graphite rod anodes and nickel chrome rod cathodes according to plate assembly procedure A being sure to use a photochemistry base plate. All solutions were prepared in a glovebox using rigorously dry and degassed solvents. In a glovebox, solution A (300 µL) was added to all wells. The alignment plate and sealing plate were added and the reactor was removed from the glovebox. The connectivity of all wells was verified by applying a constant current PCB. The constant current PCB was removed and a constant potential PCB was added. The HT*e*-Chem was placed upon a 24 well blue LED array. Unfortunately, the LED corresponding to well D1 was damaged and thus well D1 was removed from analysis. The HT*e*-Chem was stirred at 800 rpm while being irradiated with 455 nm light at 60 mW, and electrolyzed at 1.75 V for 24 hours.

**Plate Analysis:** A solution of dimethyl terephthalate (42.5 mg in 10 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Agilent 1290 Infinity II UPLCMS

Column: InfinityLab Poroshell 120 EC-C18, 2.1 x 50 mm, 2.7-Micron

Method: Flowrate 0.4 ml/min. Hold at 30% MeCN (+0.1% formic acid) in water (+0.1% formic acid) for 1 min. Increase from 30 to 100% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 5 min. Hold at 100% MeCN (+0.1% formic acid) for 2 min.

Retention Times: Dimethylterepthalate- 2.669 min, Mesitylated pyrazole **7**- 4.002 min.

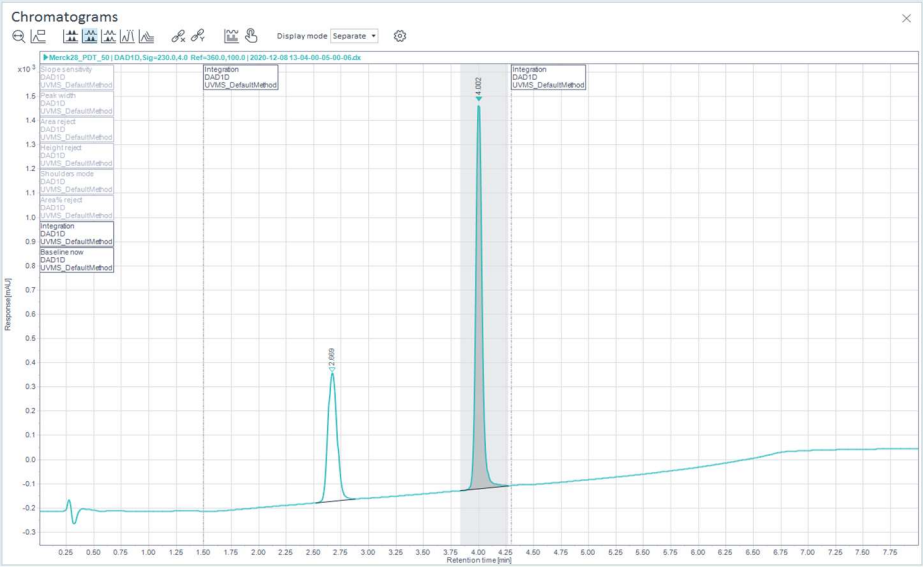



**Figure S46.** UPLC chromatograph of purified product standard **7** and internal standard.

Standard Curve:

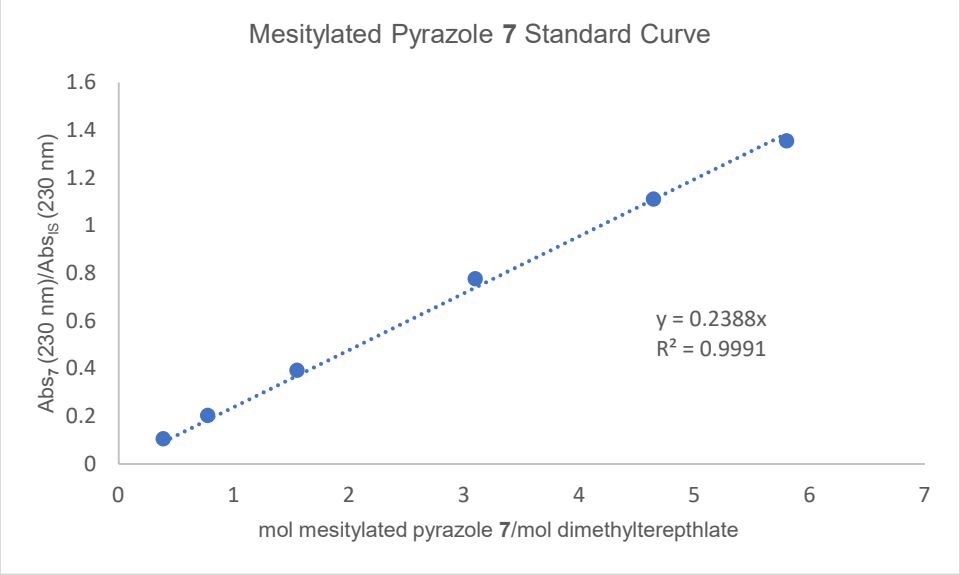
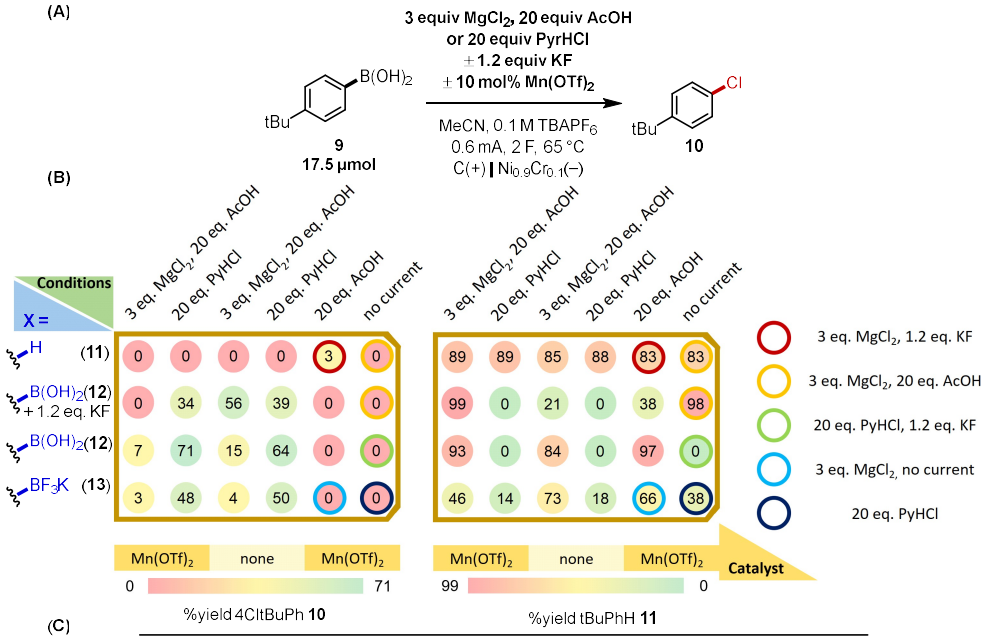



**Figure S47.** Standard curve for determination of yield of **7**.




| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| A | DCM | 3.0 mL | 150 µL | 4-tButylphenyl boronic acid | 17.5 | 1 | 62.3 mg |
| B | MeCN | 1.0 mL | 70 µL | tButylbenzene | 17.5 | 1 | 33.6 mg |
| C | MeCN | 3.0 mL | 70 µL | KF | 21 | 1.2 | 52.3 mg |
| D | MeCN | 2.0 mL | 150 µL | pyridinium chloride | 350 | 20 | 539.3 mg |
| E | MeCN | 3.0 mL | 100 µL | $MgCl_2$ | 52.5 | 3 | 150.0 mg |
| F | MeCN | 2.0 mL | 70 µL | $Mn(OTf)_2$ | 1.75 | 0.1 | 17.7 mg |
| G | MeCN | 2.0 mL | 50 µL | AcOH | 350 | 20 | 840 mg |
| H | MeCN | 3.0 mL | 70 µL | $TBAPF_6$ | 35 | [0.1 M] | 581.1 mg |

**Figure S48.** (A) Reaction conditions for HT*e*-Chem with literature yields. The parameters that are varied are shown in bold. (B) Plate map and yields as determined by HPLC, dimethylterephthalate as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HT*e*-Chem was assembled with graphite rod anodes and nickel chrome rod cathodes according to plate assembly procedure B. Solution A (150 µL) was prepared and added to 12 vials charged with stirbars. Solution A was allowed to evaporate over 4 h, with stirring, under $N_2$ leaving a white amorphous solid. The remaining solutions were prepared in a glovebox using rigorously dry degassed solvents. Solution B (70 µL) was added to row A, the vials containing 4tbutylphenyl boronic acid were added to rows B and C. Potassium 4tbutylphenyl trifluoroboronate (3.7 mg, 17.5 µmol, 1 eq) was added to all vials in row D. Solutions C, D, E, F, G, and H were added to vials as indicated above. It should be noted that solution E required slurry addition as $MgCl_2$ is poorly soluble in MeCN. Enough MeCN was added to each well to bring the total volume to 360 µL. The alignment plate, sealing plate and constant current PCB were added and the reactor was removed from the glovebox. Skippers were added to the constant current PCB to prevent electrolysis in column 6 and D5. The HT*e*-Chem was then heated to 65 °C and stirred at 800 rpm. Once the temperature of 65 °C was reached 0.6 mA of current was applied for 2 F (94 min).

**Plate Analysis:** A solution of dimethyl terephthalate (42.5 mg in 10 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Agilent 1290 Infinity II UPLCMS

Column: InfinityLab Poroshell 120 EC-C18, 2.1 x 50 mm, 2.7-Micron

Method: Flowrate 0.4 ml/min. Hold at 30% MeCN (+0.1% formic acid) in water (+0.1% formic acid) for 1 min. Increase from 30 to 100% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 5 min. Hold at 100% MeCN (+0.1% formic acid) for 2 min.

Retention Times: Dimethyl terephthalate- 2.669 min, 4-chlorotbutylbenzene **10**- 5.170 min, tButylbenzene **11**- 4.700 min.

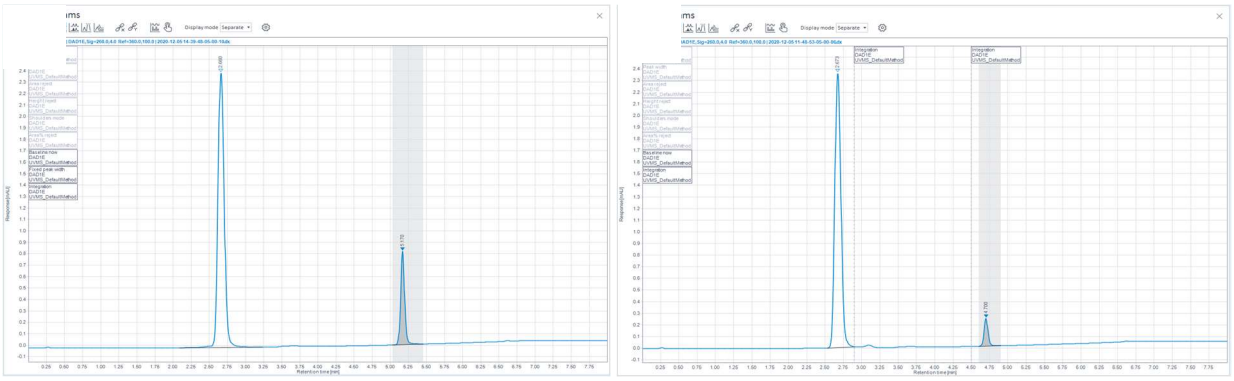


**Figure S49.** UPLC chromatograph of product standards **10** (A) and **11** (B) with internal standard.

Standard Curve:

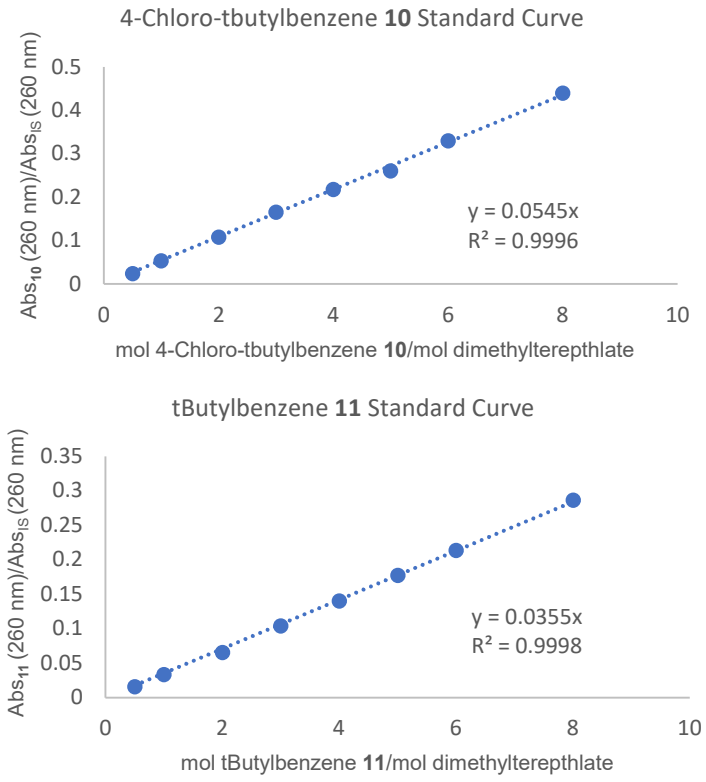
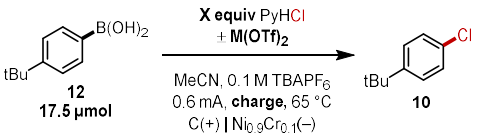
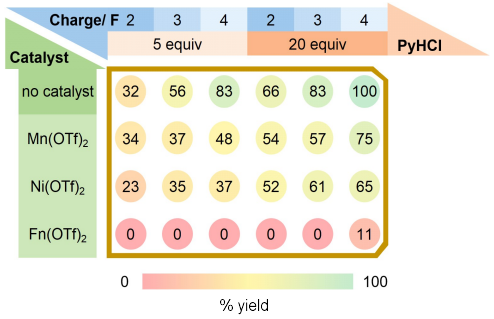



**Figure S50.** Standard curve for determination of yield of **10** and **11**.

(A)




(B)




(C)

| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| A | DCM | 10.0 mL | 150 µL | 4-tButylphenyl boronic acid | 17.5 | 1 | 207.7 mg |
| B | MeCN | 1.0 mL | 100 µL | $Mn(OTf)_2$ | 350 | 0.1 | 6.2 mg |
| C | MeCN | 1.0 mL | 100 µL | $Ni(OTf)_2$ | 52.5 | 0.1 | 6.2 mg |
| D | MeCN | 1.0 mL | 100 µL | $Fe(OTf)_2$ | 1.75 | 0.1 | 6.2 mg |
| E | MeCN | 3.0 mL | 50 µL | $TBAPF_6$ | 35 | [0.1 M] | 406.8 mg |
| F | MeCN | 4.0 mL | 50 µL | Pyridinium chloride | 35 | 5 eq | 808.9 mg |

**Figure S51.** (A) Reaction conditions for HT*e*-Chem with literature yields. The parameters that are varied are shown in bold. (B) Plate map and yields as determined by HPLC, dimethylterephthalate as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HT*e*-Chem was assembled with graphite rod anodes and nickel chrome rod cathodes according to plate assembly procedure A. Solution A (150 µL) was prepared and added to 24 vials charged with stirbars. Solution A was allowed to evaporate over 4 h, with stirring, under $N_2$ leaving a white amorphous solid. The remaining solutions were prepared in a glovebox using rigorously dry degassed solvents. Solution B (100 µL) was added to row B, solutions C and D (100 µL) were added to rows C and D as indicated above. MeCN (100 µL) was added to row A. Solution E (50 µL) was added to all wells. Solution F (50 µL) was added to columns 1, 2, and 3 along with 150 µL of MeCN. Solution F (200 µL) was added to columns 4, 5, and 6. The alignment plate, sealing plate and constant current PCB were added and the reactor was removed from the glovebox. The HT*e*-Chem was then heated to 65 °C and stirred at 800 rpm. A current of 0.6 mA was applied once the HT*e*-Chem reached 65 °C. After 2 F (94 min), skippers were added to columns 1 and 4. After 3 F (140 min) skippers were added to columns 2 and 5 and the remaining wells were electrolyzed for 4 F (188 min).

**Plate Analysis:** A solution of dimethyl terephthalate (42.5 mg in 10 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Agilent 1290 Infinity II  UPLCMS

Column: InfinityLab Poroshell 120 EC-C18, 2.1 x 50 mm, 2.7-Micron

Method: Flowrate 0.4 ml/min. Hold at 30% MeCN (+0.1% formic acid) in water (+0.1% formic acid) for 1 min. Increase from 30 to 100% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 5 min. Hold at 100% MeCN (+0.1% formic acid) for 2 min.

Retention Times: Dimethyl terephthalate- 2.669 min, 4-chlorotbutylbenzene **10**- 5.170 min, tButylbenzene **11**- 4.700 min.

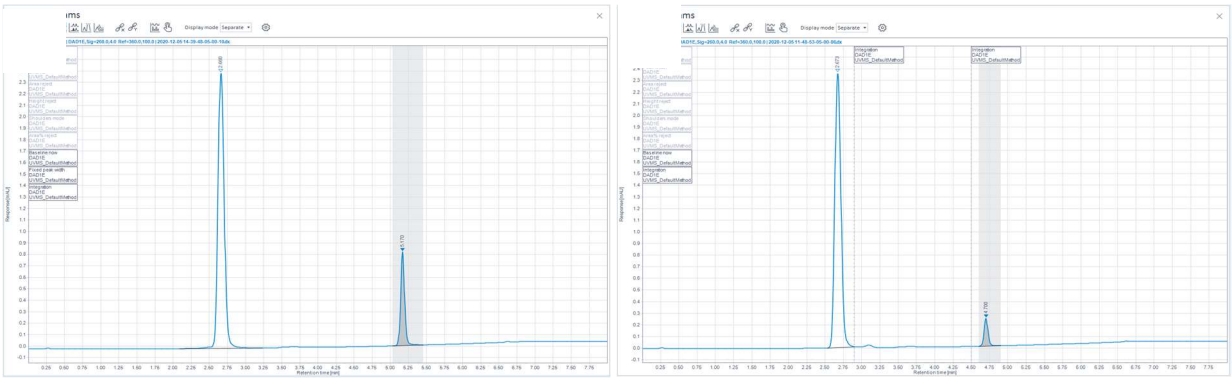


**Figure S52.** UPLC chromatograph of product standards **10** (A) and **11** (B) with internal standard.

Standard Curve:

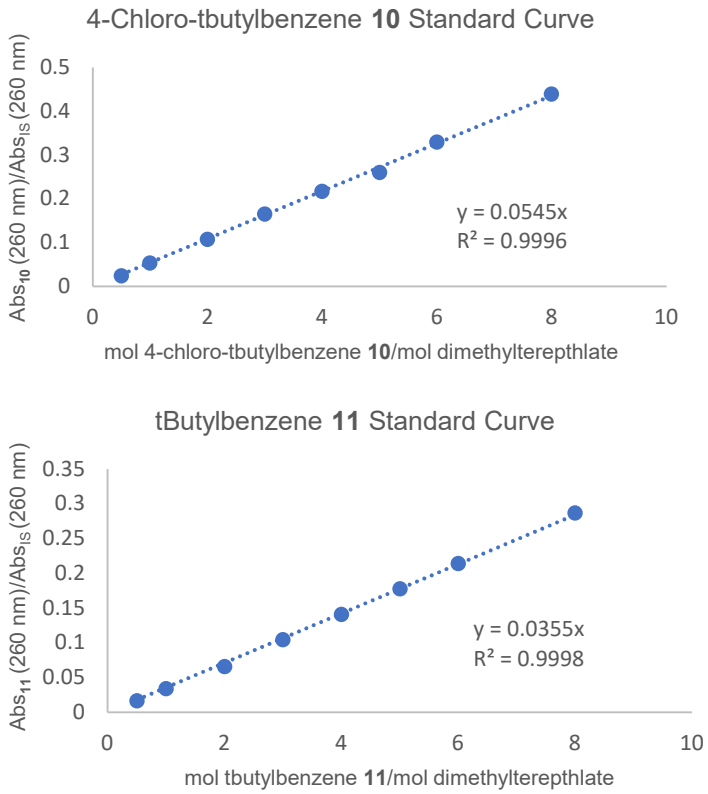
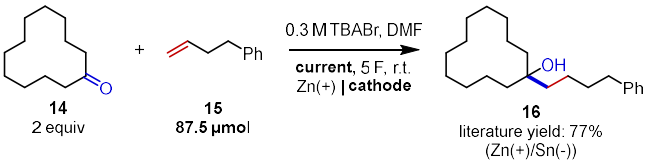



**Figure S53.** Standard curve for determination of yield of **10** and **11**.

(A)

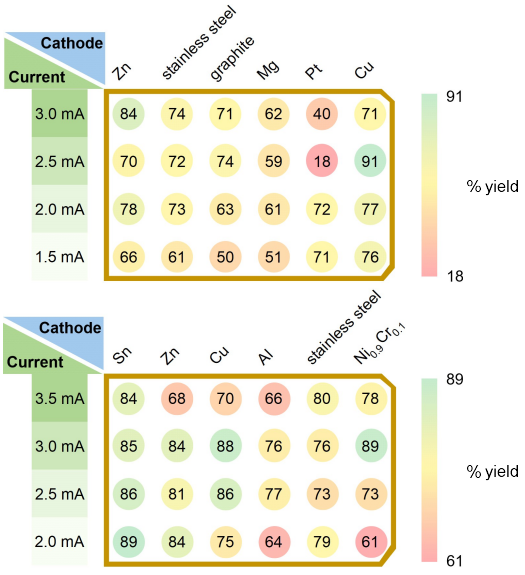



**14**
2 equiv

**15**
**87.5 µmol**

**16**
literature yield: 77%
(Zn(+)/Sn(-))

(B)




(C)

| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| | | | | 4-Phenylbutene | 87.5 | 1 | 462 mg |
| A | DMF | 10.0 mL | 250 µL | Cyclododecanone | 175 | 2 | 1276 mg |
| | | | | TBABr | 75 | [0.3 M] | 967 mg |

**Figure S54.** (A) Reaction conditions for HTe-Chem with literature yields. The parameters that are varied are shown in bold. (B) Plate map and yields as determined by HPLC, trimethoxybenzene as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HTe-Chem was assembled with zinc rod anodes and zinc rod, stainless steel rod, graphite rod, magnesium rod, platinum rod, and copper rod cathodes according to plate assembly procedure B, as indicated above. Solution A (250 µL) was added to each well. The alignment plate, sealing plate and constant current PCB were added and the reactor was stirred at 800 rpm while being electrolyzed at 1.5 mA, 2.0 mA, 2.5 mA, and 3.0 mA as indicated above.

**Plate Analysis:** A solution of trimethoxybenzene (36.8 mg in 10 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Agilent 1290 Infinity II UPLCMS

Column: InfinityLab Poroshell 120 EC-C18, 2.1 x 50 mm, 2.7-Micron

Method: Flow rate 1 ml/min. Increase from 30 to 100% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 2 min. Hold at 100% MeCN (+0.1% MeCN) for 0.5 min.

Retention Time- 1,3,5-Trimethoxybenzene– 6.686 min, Tertiary alcohol **16-** 2.781 min.

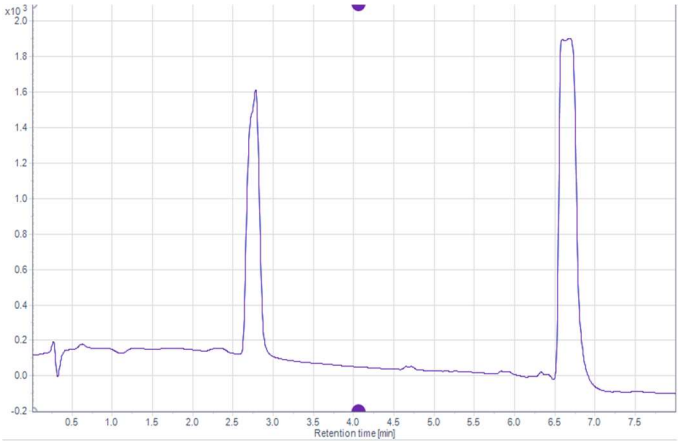



**Figure S55.** UPLC chromatograph of purified product standard **16** and internal standard.

Standard Curve:

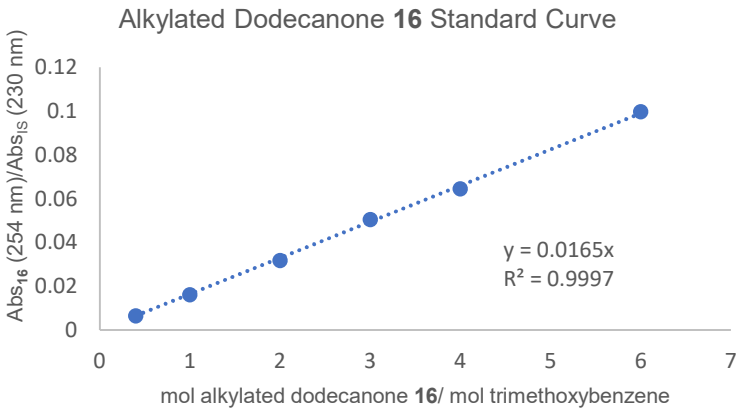
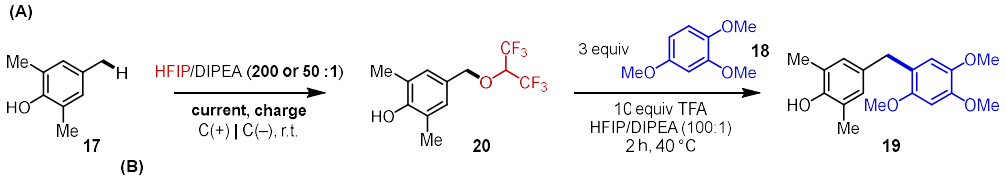



**Figure S56.** Standard curve for determination of yield of **16**.




(B)

| Charge/ F | 2 | 2.2 | 2.5 | 2 | 2.2 | 2.5 |
|---|---|---|---|---|---|---|
| Current | 200:1 | | | 50:1 | | (HFIP:DIPEA) |
| 0.3 mA | 67 | 82 | 81 | 85 | 88 | 86 |
| 0.6 mA | 85 | 90 | 90 | 88 | 92 | 93 |
| 0.9 mA | 87 | 84 | 90 | 88 | 94 | 88 |
| 1.2 mA | 85 | 91 | 101 | 89 | 97 | 95 |

67 — 101 % yield

(C)

| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| A | HFIP | 4.0 mL | 150 µL | Trimethylphenol | 17.5 | 1 | 207.7 mg |
| B | HFIP | 1.7 mL | 25 µL | DIPEA | 10 | 0.57 | 119 µL |
| C | HFIP | 2.0 mL | 50 µL | 1,2,4-Trimethoxybenzene | 52.5 | 3 | 353 mg |
| D | HFIP | 2.0 mL | 50 µL | TFA | 175 | 10 | 536 µL |

**Figure S57.** (A) Reaction conditions for HT*e*-Chem with literature yields. The parameters that are varied are shown in bold. (B) Plate map and yields as determined by HPLC, 4,4'-ditbutylbiphenyl as internal standard. (C) Table of reaction solutions and equivalencies for plate setup.

**Plate Setup:** The HT*e*-Chem was assembled with graphite rod anodes and cathodes according to plate assembly procedure B. HFIP was distilled and DIPEA was distilled and then purified over basic alumina prior to use. Solution A (150 µL) was added to each well. Solution B (25 µL) was added to columns 1, 2, and 3 along with 175 µL of HFIP. Solution B (100 µL) was added to columns 4, 5, and 6 along with 100 µL of HFIP. The alignment plate, sealing plate and constant current PCB were added and the HT*e*-Chem was stirred at 800 rpm while being electrolyzed at 0.3 mA, 0.6 mA, 0.9 mA, and 1.2 mA as indicated above. Skippers were employed to stop electrolysis at 2 F, 2.2 F, and 2.5 F as indicated above. Upon completion, the constant current PCB, sealing plate, and alignment plate were removed revealing clear yellow solutions post-electrolysis. Solution C (50 µL) was added to every well, followed by solution D (50 µL) at which point the reactions turned dark red. A solid silica rubber mat and aluminum top plate were used to reseal the reactor and the plate was heated to 40 °C, with stirring at 800 rpm, for 2 h.

**Plate Analysis:** A solution of 4,4'-ditbutyl-biphenyl (145.7 mg in 25 mL of MeCN, 21.9 µmol/mL) was prepared as an internal standard. Upon completion, internal standard solution (200 µL, 4.375 µmol) was added to each well. The reactions were diluted 20-fold, filtered and analyzed by HPLC.

**HPLC Analysis:** Agilent 1290 Infinity II  UPLCMS

Column: InfinityLab Poroshell 120 EC-C18, 2.1 x 50 mm, 2.7-Micron

Method: Flow rate 1 ml/min. Increase from 30 to 100% MeCN (+0.1% formic acid) in water (+0.1% formic acid) over 2 min. Hold at 100% MeCN (+0.1% MeCN) for 0.5 min.

Retention Times: Arylated phenol **19**- 1.030 min, 4-4'ditbutylbiphenyl- 2.229 min.

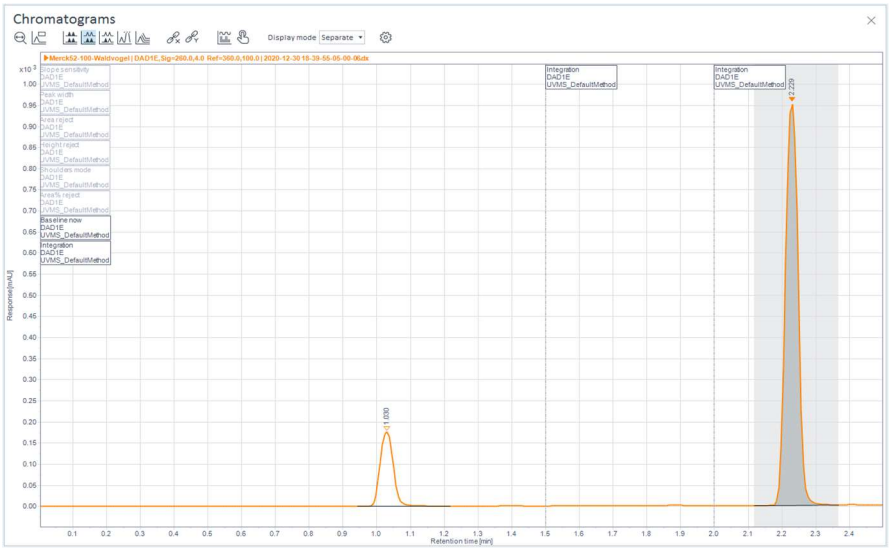



**Figure S58.** UPLC chromatograph of purified product standard **19** and internal standard.

Standard Curve:

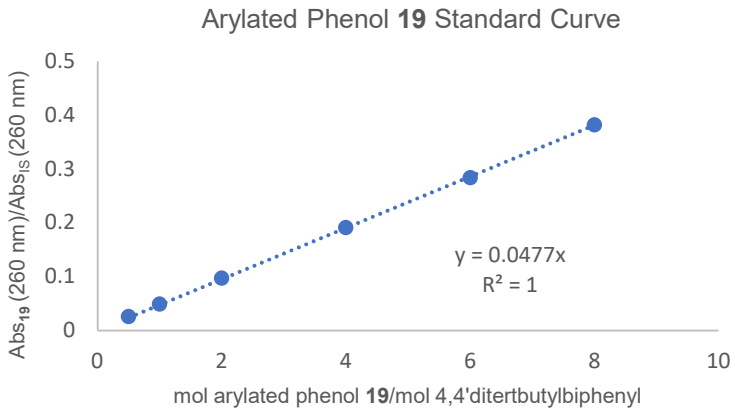
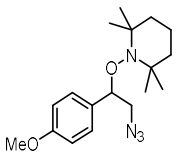



**Figure S59.** Standard curve for determination of yield of **19**.

## Experimental Procedures- Substrate and Product Standard Synthesis

Unless noted here all product standards and substrates were purchased from commercial sources and used without further purification.

1-(2-azido-1-(4-methoxyphenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (**2**)

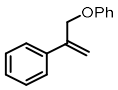



**2**

Azido-oxygenated styrene **2** was synthesized according to literature procedures and product NMRs matched those previously reported.[1]

**$^1$H NMR** (400 MHz, $CDCl_3$) δ = 7.26 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.77 (dd, *J* = 7.1, 4.8 Hz, 1H), 3.81 (s, 3H), 3.77 – 3.54 (m, 2H), 1.58 – 1.26 (m, 9H), 1.18 (s, 3H), 1.02 (s, 3H), 0.69 (s, 3H).

(3-phenoxyprop-1-en-2-yl)benzene (**3**)

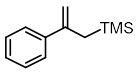



**3**

Allylic ether **3** was synthesized according to literature procedures and product NMRs matched those previously reported.[2]

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 7.56 (dt, *J* = 6.1, 1.4 Hz, 2H), 7.47 – 7.33 (m, 5H), 7.08 – 7.02 (m, 3H), 5.69 (s, 1H), 5.55 (s, 1H), 4.97 (s, 2H).

trimethyl(2-phenylallyl)silane (**4**)

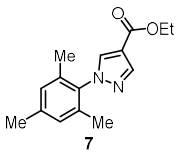



**4**

Allylic silane **4** was synthesized according to literature procedures and product NMRs matched those previously reported.[2]

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 7.45 – 7.40 (m, 2H), 7.35 – 7.30 (m, 2H), 7.27 (d, *J* = 7.1 Hz, 1H), 5.15 (d, *J* = 1.7 Hz, 1H), 4.91 – 4.87 (s, 1H), 2.05 (s, 2H), -0.07 (s, 9H).

ethyl 1-mesityl-1H-pyrazole-4-carboxylate (**7**)

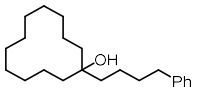


**7**

Functionalized mesitylene **7** was isolated from the HT*e*-Chem. Wells A1, A2, B1, D1, and D2 were combined (Figure S42), the volume was increased with diethyl ether (10 mL) and the organic layer was washed with brine (10 mL). The organic layer was dried with magnesium sulfate and concentrated. Purification by preparatory TLC in 15% ethyl acetate in hexane yielded **7** as a waxy solid (12.1 mg, 54% yield). NMR data of functionalized mesitylene **7** matched those previously reported.[3]

**$^1$H NMR** (400 MHz, $CDCl_3$) δ = 8.10 (s, 1H), 7.91 (s, 1H), 6.93 (s, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.32 (s, 3H), 1.96 (s, 6H), 1.36 (t, *J* = 7.1 Hz, 3H).

1-(4-phenylbutyl)cyclododecan-1-ol (**16**)

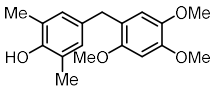


**16**

Tertiary alcohol **16** was synthesized according to literature procedures and product NMRs matched those previously reported.[4]

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 7.30 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.23 – 7.18 (m, 3H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.65 (ddd, *J* = 9.4, 5.5, 2.0 Hz, 2H), 1.58 – 1.27 (m, 26H, overlapped with $H_2O$ peak).

2,6-dimethyl-4-(2,4,5-trimethoxybenzyl)phenol (**19**)



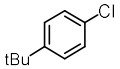
**19**

The arylated phenol **19** was isolated form the HT*e*-Chem plate (Figure S57). After the after removing an aliquot for HPLC analysis all vials were combined and concentrated *in vacuo*. The product was purified *via* flash chromatography with a silica gel stationary phase and eluting with a hexane/ethyl acetate mobile phase (gradient from 10% to 20% ethyl acetate in hexanes). The product NMRs matched those previously reported.[5]

**$^1$H NMR** (400 MHz, $CDCl_3$) δ = 6.79 (s, 2H), 6.64 (s, 1H), 6.54 (s, 1H), 4.48 (s, 1H), 3.88 (s, 3H), 3.81 – 3.75 (m, 8H), 2.19 (s, 6H).

## Experimental Procedures- Scaling Up from HT*e*-Chem

1-(*tert*-butyl)-4-chlorobenzene (**10**)



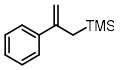
**10**

4-*tert*-Butylphenyl boronic acid (178 mg, 1.0 mmol, 1 equiv), pyridinium chloride (578 mg, 5 mmol, 5 equiv), and tetrabutyl ammonium hexafluorophosphate (775 mg, 2 mmol) were added to a 20 mL Electrasyn 2.0 vial charged with a stir bar. The Electrasyn 2.0 cap equipped with a graphite anode and a chromel cathode (made by bending a chromel wire to fit in the electrode holder of the cap) was screwed onto the vial. Dry, degassed acetonitrile was added (15 mL) and the reaction mixture was sparged for 2 min with nitrogen. The reaction vessel was heated with stirring to 65 °C in an oil bath and then subjected to 6.8 mA of current for 4 F (189 min) applied via an DC powersupply (alternatively a Electrasyn 2.0 with a IKA ElectraSyn GOGO Module can be used). The electrolysis was stopped, and the reaction was allowed to come to room temperature before being separated between diethyl ether (100 mL) and saturated ammonium chloride. The aqueous layer was washed twice with diethy ether (100 mL) and the combined organic layers were washed with brine (100 mL), dried over magnesium sulfate, and concentrated. The crude product was purified by gradient silica gel chromatography in 1-5% ethyl acetate in hexanes. Chlorinated product **10** isolated as a colorless oil (155 mg, 92% yield) and NMR data of **10** matched those previously reported.[6]

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 7.37 – 7.33 (m, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 1.34 (s, 9H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 149.62, 131.15, 128.09, 126.77, 34.48, 31.30.

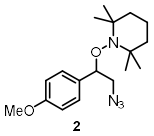
trimethyl(2-phenylallyl)silane (**4**)



**4**

Allylic silane **4** was synthesized according to literature procedures previously reported with modifications to the catode material and the applied current.[2] To investigate the effect of cathode material and current a platinum electrode was used a current of 12.5 mA (3.7 mA/cm$^2$) was applied until 2.5 F of charge was passed. The reaction mixture was diluted with 20 mL of diethyl ether and passed through a silica gel plug column. The solution was concentrated and 1,3,5-trimethoxybenzene as the internal standard. The reaction mixture was analyzed by quantitative $^1$H NMR with furnished an NMR yield of 74%.

1-(2-azido-1-(4-methoxyphenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (**2**)



**2**

4-*tert*-Butylphenyl boronic acid (134 mg, 1.0 mmol, 1 equiv), TEMPO (243 mg, 1.5 mmol, 1.5 equiv), and sodium azide (97.5 mg, 1.5 mmol, 1.5 equiv) were added to a 20 mL Electrasyn 2.0 vial charged with a stir bar. The Electrasyn 2.0 cap equipped with a graphite anode and a chromel cathode (made by bending a chromel wire to fit in the electrode holder of the cap) was screwed onto the vial. Acetonitrile (13.5 mL) and deionized water (1.5 mL) were added to the reaction mixture. The Electasyn 2.0 vial was connected and a current of 15 mA was applied until 2.2 F of charge was passed. The reaction mixture was concentrated and passed through a silica plug column with diethyl ether. The crude

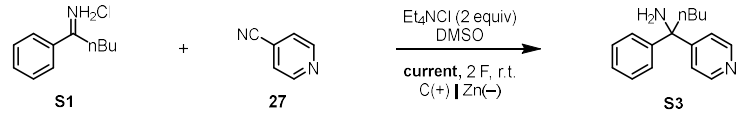
product was purified by gradient silica gel chromatography in 1-5% ethyl acetate in hexanes. The functionalized styrene **2** was isolated as a colorless oil (283 mg, 85% yield) and NMR data matched those previously reported.[1]

**$^1$H NMR** (400 MHz, $CDCl_3$) δ = 7.26 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.77 (dd, *J* = 7.1, 4.8 Hz, 1H), 3.81 (s, 3H), 3.77 – 3.54 (m, 2H), 1.58 – 1.26 (m, 9H), 1.18 (s, 3H), 1.02 (s, 3H), 0.69 (s, 3H).

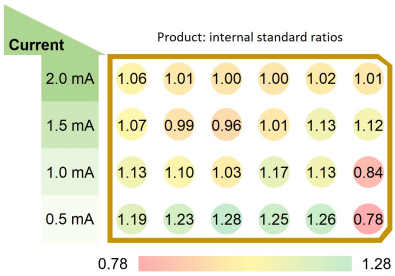
## Library Synthesis of Primary Amines – Procedures and Product Identification

### 1. Optimization of current density

(A)




(B)




(C)

| Solution | Solvent | $Vol_{Total}$ | Vol/well | Reagent | µmol/well | equiv | Reagent Added |
|---|---|---|---|---|---|---|---|
| B | DMSO | 25.0 mL | – | biphenyl | 19.49 | 0.5 | 241.0 mg |
| | | | | Solution A | | 10.92 mL | |
| | | | | 4-cyanopyridine (**27**) | 38.98 | 1 | 142.1 mg |
| A | – | – | 350 µL | tetraethylammonium chloride | 79.96 | 2 | 452.4 mg |
| | | | | 1-phenylpentan-1-imine hydrochloride (**S1**) | 85.36 | 2.2 | 593.1 mg |

**Figure S60.** (A) Reaction conditions for HT*e*-Chem. The parameters that are varied are shown in bold. (B) Plate map and product to internal standard ratios as determined by HPLC. (C) Table of reaction solutions and equivalencies for plate setup.

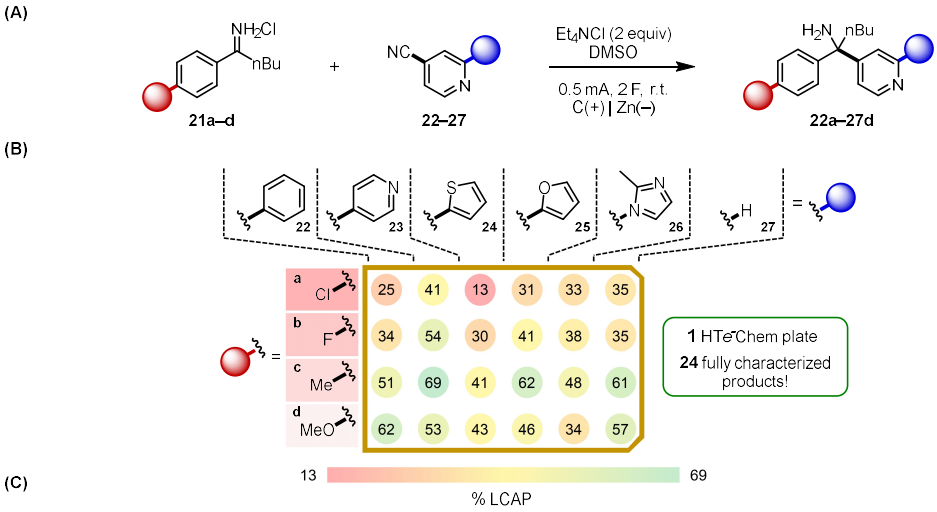
**General considerations:** The reaction involves a reductive coupling mechanism and can therefore be sensitive to atmospheric oxygen, therefore reagent transfers, additions, and the HT*e*-Chem plate assembly were accomplished inside a nitrogen-purged glovebox. However, the sealed plate was taken outside of the glovebox and electrolysis was conducted inside a fume hood under ambient conditions. Zinc electrodes were treated briefly (ca. 3–5 min) with 0.1 M HCl solution until shiny, rinsed with deionized water and then acetone, and used immediately. Cyanopyridine derivatives were commercially available and imine hydrochloride derivatives were synthesized following representative procedures described in the literature.[7,8]

**Plate Setup:** Into a 25 mL volumetric flask was added biphenyl (241.0 mg, 1.56 mmol) as an internal standard, and DMSO was added up to the 25 mL mark on the flask. A 20 mL scintillation vial containing a stir bar was charged with 4-cyanopyridine (142.1 mg, 1.37 mmol, limiting reagent), $Et_4NCl$ (electrochemical grade, 452.4 mg, 2.73 mmol) and 1-phenylpentan-1-imine hydrochloride (593.1 mg, 3.00 mmol). The biphenyl DMSO stock solution (10.92 mL) was transferred into the scintillation vial, which was then capped and stirred until homogenous (ca. 5 min). To each of the 24 reaction wells was added 350 µL of the above reaction mixture (38.98 µmol limiting reagent per well). The HT*e*-Chem reactor was equipped with graphite anodes and zinc cathodes and the plate was sealed according to General Procedure A. The plate was then taken out of the glovebox, and electrolysis was conducted at 0.5 mA (4 h 10 min), 1.0 mA (2 h 5 min), 1.5 mA (1 h 23 min), 2.0 mA (1 h 2 min) for rows A, B, C, and D, respectively, keeping the total charge applied at 2 F/mol. Upon completion of the electrolysis, the plate was disassembled and an aliquot (4 µL) of the crude reaction mixture was diluted with 200 µL of DMSO and analyzed by UPLC-MS.

**General UPLC-MS method:** Samples were dissolved in DMSO and 1 µL injection volumes were used. A Waters Acquity UPLC was equipped with an ACQUITY UPLC™ BEH C18 VanGuard Pre-column (130 Å pore size, 1.7 µm particle size, 2.1 mm × 5 mm length; part number for 3/pkg: 186003975) flowing into an ACQUITY UPLC™ HSS T3 Column (100 Å pore size, 1.8 µm particle size, 2.1 mm internal diameter × 50 mm length; part number 186003538) operating at 55 °C with a 0.8 mL/min flow rate of a binary eluent mixture (eluent A and B, prepared as described below). The 4 min method used the following eluent gradient: gradient from 95%A, 5%B at $t = 0$ min to 80%A, 20%B at $t = 1.50$ min, followed by a gradient to reach 0.1%A, 99.9%B at $t = 3.90$ min, and a subsequent change to 95%A, 5%B at $t = 3.91$ min until $t = 4.00$ min. Two different eluent systems were used: (system 1) eluent A = aqueous mobile

phase (3960 mL $H_2O$, 40 mL pH 3.5 buffer, details below), eluent B = organic mobile phase (3600 mL MeCN, 360 mL $H_2O$, 40 mL pH 3.5 buffer. The pH 3.5 buffer was prepared by dissolving ammonium formate (12.6 g, 0.200 mol) and formic acid (7.9 mL, 9.6 g, 0.21 mol) in 1000 mL $H_2O$.

## 2. 24-Membered Library Synthesis




(C)

| Solution | Reagent | Concentration (M) | Amount (mg) | Total Vol (µL) | Vol/well (µL) |
|---|---|---|---|---|---|
| A | 1-(4-fluorophenyl)pentan-1-imine hydrochloride (**21b**) | 0.75 | 299.46 | 1551 | 114.3 |
| B | 1-(4-chlorophenyl)pentan-1-imine hydrochloride (**21a**) | 0.75 | 322.30 | 1529 | 114.3 |
| C | 1-(*p*-tolyl)pentan-1-imine hydrochloride (**21c**) | 0.75 | 293.95 | 1557 | 114.3 |
| D | 1-(4-methoxyphenyl)pentan-1-imine hydrochloride(**21d**) | 0.75 | 316.17 | 1535 | 114.3 |
| E | biphenyl | 0.5 | 187.74 | 2245 | 39.0 |
| F | tetraethylammonium chloride | 0.5 | 724.93 | 8078 | 155.9 |
| G | 2-phenylisonicotinonitrile (**22**) | 0.75 | 107.82 | 690 | 52.0 |
| H | [2,4'-bipyridine]-4-carbonitrile (**23**) | 0.75 | 108.41 | 689 | 52.0 |
| I | 2-(thiophen-2-yl)isonicotinonitrile (**24**) | 0.75 | 111.43 | 686 | 52.0 |
| J | 2-(furan-2-yl)isonicotinonitrile (**25**) | 0.75 | 101.81 | 696 | 52.0 |
| K | 2-(2-methyl-1*H*-imidazol-1-yl)-isonicotinonitrile (**26**) | 0.75 | 110.21 | 688 | 52.0 |
| L | 4-cyanopyridine (**27**) | 0.75 | 62.29 | 742 | 52.0 |

**Figure S61.** (A) Reaction conditions for HTe-Chem with literature yields. (B) Plate map and liquid chromatography area percentages (LCAP) for the products. (C) Table of reaction solutions and equivalencies for plate setup.

**General procedure for library synthesis:** Stock solutions of all reagents and biphenyl internal standard were prepared as follows in anhydrous DMSO. The volumes of these reagents dosed per well are shown in the last column of Table 1. The reagents that were not fully soluble were dosed as a slurry while stirring vigorously.

After all stock solutions were prepared inside the glovebox, solutions E (39.0 µL) and F (155.9 µL) were added into all 24 vials containing stir bars using a multi-channel pipettor. Solution B (114.3 µL) was added to vial A1–A6. Solution A (114.3 µL) was added to vial B1–B6. Solution C (114.3 µL) was added to vial C1–C6. Solution D (114.3 µL) was added to vial D1–D6. Next, solution G (52.0 µL) was added to vial A1, B1, C1, and D1. Solution H (52.0 µL) was added to vial A2, B2, C2, and D2. Solution I (52.0 µL) was added to vial A3, B3, C3 and D3. Solution J (52.0 µL) was added to vial A4, B4, C4, and D4. Solution K (52.0 µL) was added to vial A5, B5, C5, and D5. Solution L (52.0 µL) was to vial A6, B6, C6 and D6. After all stock solutions were dosed, the HT*e*-Chem reactor (equipped with graphite anodes and zinc cathodes) was sealed using the assembly procedure A and then taken outside of the glovebox. Electrolysis was conducted at 0.5 mA for 2 F/mol (total time = 4 h 10 min) for all wells. Upon reaction completion, the plate was disassembled and an aliquot (4 µL) of the crude reaction mixture was diluted with 200 µL of DMSO and analyzed by UPLC-MS. Purification of the crude samples was accomplished using preparative reverse-phase HPLC, using either TFA or $NH_4OH$ as modifier on a X-Bridge Prep-C-18 OBD column (19 × 100 mm, SN# 212133033113 09).

After purification, for some reactions, the isolated product contained residual DMSO (due to minor co-elution of DMSO with the desired product) and diamine byproduct from dimerization of the iminium chlorides. In these cases, the actual weight of the desired product could be calculated from $^1$H NMR experiments by taking into account impurity signals and their corresponding number of protons. In addition, the amine•*n*TFA salt could form during the purification process if TFA was used as the modifier. The number of TFA molecules per product molecule ("*n*") could be obtained by comparing the $^1$H NMR spectra and $^{19}$F NMR spectra using 4-(trifluoromethyl)anisole as the internal standard. After these corrections, the yields are referred to as "corrected yields".

To liberate the free amine from the TFA salt, the purified product was re-dissolved in 50 mL EtOAc, and transferred into a 125 mL separatory funnel. The solution was washed with 5% NaOH solution (1 × 35 mL) and then satd. aq. NaCl solution. The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain the free amine products and their "isolated yields". In addition, these products were used to obtain calibration curves (against biphenyl as the internal standard on UPLC-MS) to obtain the "assay yields" based on the product : biphenyl ratios.

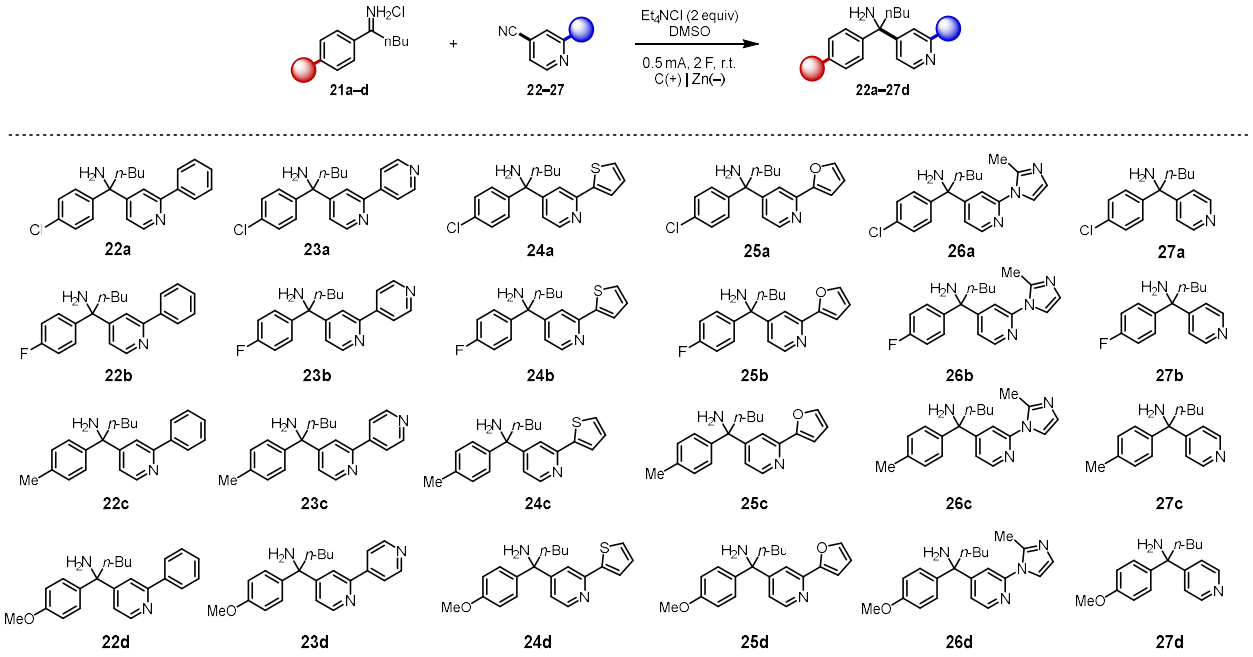



**Figure S62.** Chemical structures of all compounds synthesized in the library synthesis of the hindered amines.

**Procedure for quantifying TFA in products that were obtained as TFA salts:** in the example below, the $^{1}H$ NMR spectrum shows that product : standard ratio is 1 : 1.6, while the $^{19}F$ NMR spectrum shows that TFA : standard ratio is 2.4 : 1. Taking both ratios into account, the calculated product : TFA ratio is 1 : 4. The extra TFA molecules could be attributed to the mobile phase from the purification process that was difficult to remove completely. Note: the terminal $CH_3$ protons in products (shown in red) and the methoxy $CH_3$ protons (shown in blue) were consistently used for all cases to determine TFA quantities.

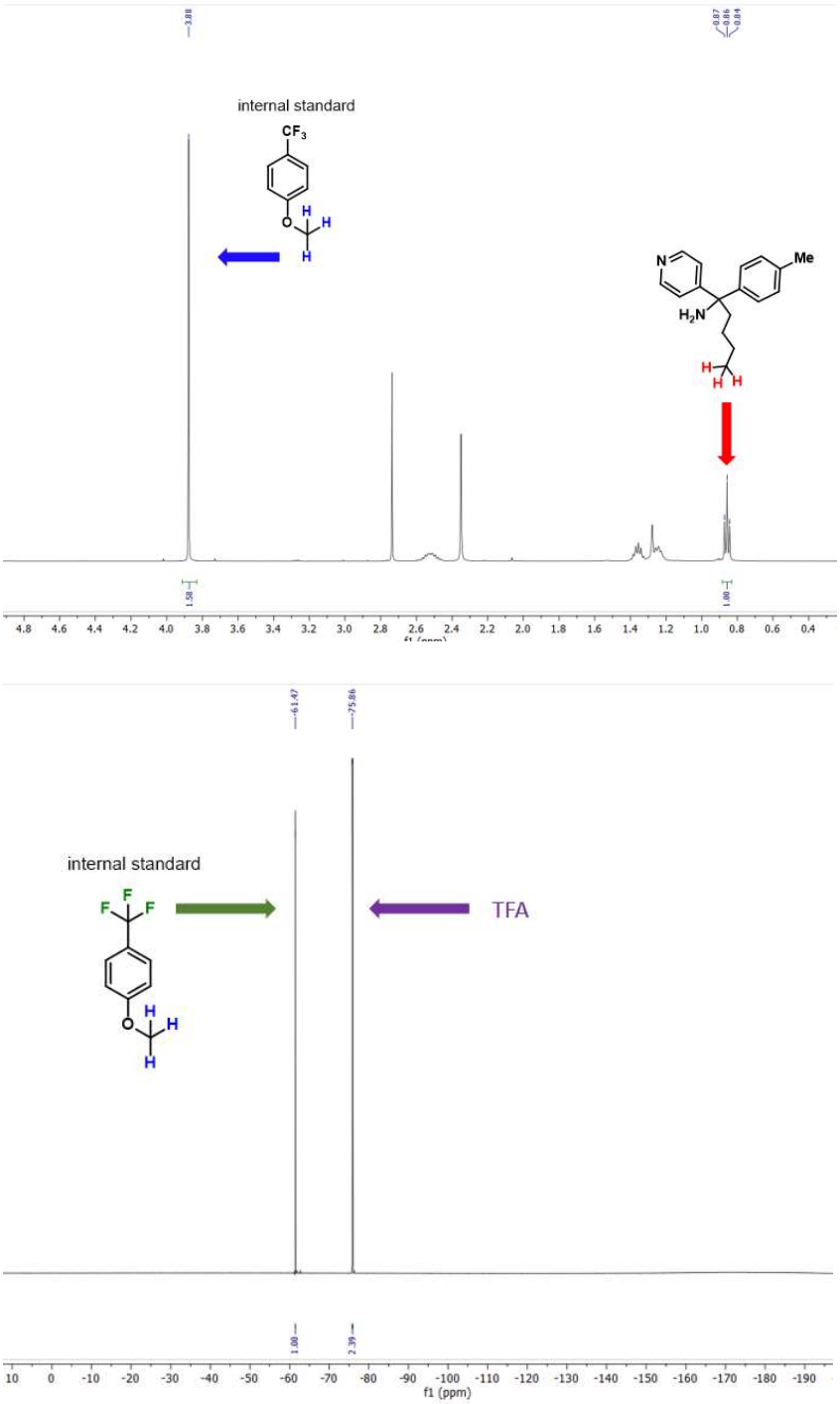



**Figure S63.** $^{1}H$ (top) and $^{19}F$ NMR (bottom) spectra showing the ratios between the internal standard and product or TFA.

**Procedure for obtaining calibration curves from free amines:**

Five 20 mL scintillation vials were labeled as vial A, B, C, D, and E, respectively. Next, stock solutions of biphenyl (0.1 M) and the isolated free amine product (0.1 M) were individually prepared in DMSO. Biphenyl stock solution (50 µL) was added into each vial. Next, 10 µL of the free amine stock solution was added into vial A and diluted with more DMSO (9940 µL) to 10 mL (corresponding to 20% yield); 20 µL of the free amine stock solution was added into vial B and diluted with more DMSO (9930 µL) to 10 mL (corresponding to 40% yield); 30 µL of the free amine stock solution was added into vial C and diluted with more DMSO (9920 µL) to 10 mL (corresponding to 60% yield); 40 µL of the free amine stock solution was added into vial D and diluted with more DMSO (9910 µL) to 10 mL (corresponding to 80% yield); and 50 µL of the free amine stock solution was added into vial E and diluted with more DMSO (9900 µL) to 10 mL (corresponding to 100% yield).

UPLC-MS analysis (using the General UPLC-MS method, detection at 210 nm) was conducted on these five solutions to obtain five product : biphenyl ratios, and a calibration curve was constructed by plotting yields (0.2, 0.4, 0.6, 0.8 and 1.0, y-axis) against the product : biphenyl ratios (x-axis) in Microsoft Excel. An equation and $R^2$ value for the calibration curve were obtained, and the equation was used to calculate the assay yields using experimentally observed product : biphenyl ratios.

In the example below (for compound **24b**), the experimentally observed product : biphenyl ratio was 1.25 : 1. Plugging this number into the equation and taking into account biphenyl equivalence in the reaction setup (50 mol%) give an assay yield of 78%.

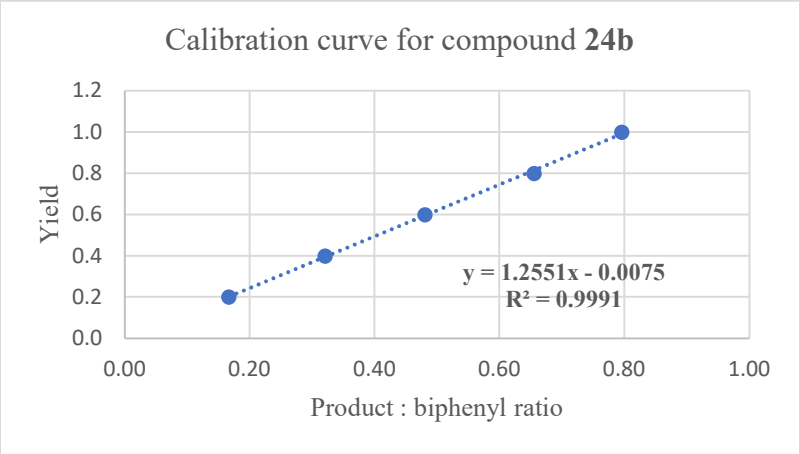
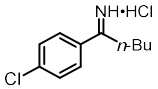



**Figure S46.** Standard curve for determination of yield of **24b**.

1-(4-chlorophenyl)pentan-1-iminium chloride (**21a**)



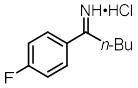

**21a**

**Synthesis of 21a**. A 250 mL round bottom flask containing a PTFE coated stir bar under $N_2$ atmosphere was charged with 4-chlorobenzonitrile (7.80 g, 56.7 mmol) and 2-methyltetrahydrofuran (100 mL) and rendered homogenous at room temperature using rotary magnetic stirring, followed by cooling to –78 ºC for 30 min. To the mixture was added *n*-butyllithium (2.5 M in hexanes, 25.0 mL, 62.5 mmol) followed by aging the mixture for 15 min prior to addition of MeOH (3.45 mL, 2.73 g, 85 mmol). The mixture was allowed to warm to RT and age for 1 h accompanied with magnetic rotary stirring. The mixture was filtered through a pad of Celite® using MTBE as the solvent and the filtrate was concentrated *in vacuo*. The residue was dissolved in MTBE (ca. 20 mL), filtered one more time through a pad of Celite® using MTBE as the eluent solvent. The filtrate was collected in a round bottom flask, the flask was sealed with a rubber septum and deoxygenated by sparging with $N_2$ for 5 min followed by addition of HCl (2 M in $Et_2O$, 28.4 mL, 56.8 mmol). The resulting solid was collected via vacuum filtration and the solid was washed with MTBE (3 × 5 mL). The solid was triturated using MeCN (ca. 20 mL) at RT and collected via vacuum filtration followed by washing with MeCN (3 × 5 mL) to afford **21a** as a white solid (8.11 g, 62%).

**$^1$H NMR** (500 MHz, $d_6$-DMSO) δ 13.17 (br s, 2H), 8.19 (d, $J$ = 8.7 Hz, 2H), 7.72 (d, $J$ = 8.7 Hz, 2H), 3.27 (t, $J$ = 7.6 Hz, 2H), 1.53 (p, $J$ = 7.6 Hz, 2H), 1.31 (hept, $J$ = 7.3 Hz, 2H), 0.84 (t, $J$ = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $d_6$-DMSO) δ 187.37, 140.48, 131.64, 129.43, 128.38, 33.75, 29.32, 21.61, 13.40.

1-(4-fluorophenyl)pentan-1-iminium chloride (**21b**)




**21b**

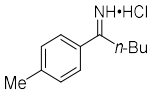
**Synthesis of 21b**. A 250 mL round bottom flask containing a PTFE coated stir bar under $N_2$ atmosphere was charged with 4-fluorobenzonitrile (6.88 g, 56.8 mmol) and 2-methyltetrahydrofuran (100 mL) and rendered homogenous at room temperature using rotary magnetic stirring, followed by cooling to –78 ºC for 30 min. To the mixture was added *n*-butyllithium (2.5 M in hexanes, 25.0 mL, 62.5 mmol) followed by aging the mixture for 15 min prior to addition of MeOH (3.45 mL, 2.73 g, 85 mmol). The mixture was allowed to warm to RT and age for 1 h accompanied with magnetic rotary stirring. The mixture was filtered through a pad of Celite® using MTBE as the solvent and the filtrate was concentrated *in vacuo*. The residue was dissolved in MTBE (ca. 20 mL), filtered one more time through a pad of Celite® using MTBE as the eluent solvent. The filtrate was collected in a round bottom flask, the flask was sealed with a rubber septum and deoxygenated by sparging with $N_2$ for 5 min followed by addition of HCl (2 M in $Et_2O$, 28.4 mL, 56.8 mmol). The resulting solid was collected via vacuum filtration and the solid was washed with MTBE (3 × 5 mL). The solid was triturated using MeCN (ca. 20 mL) at RT and collected via vacuum filtration followed by washing with MeCN (3 × 5 mL) to afford **21b** as a white solid (10.29 g, 84%).

**$^1$H NMR** (500 MHz, $d_6$-DMSO) δ 13.07 (br s, 2H), 8.31 (dd, $J$ = 8.9, 5.2 Hz, 2H), 7.51 (t, $J$ = 8.8 Hz, 2H), 3.27 (t, $J$ = 7.6 Hz, 2H), 1.54 (p, $J$ = 7.6 Hz, 2H), 1.32 (hept, $J$ = 7.3 Hz, 2H), 0.84 (t, $J$ = 7.4 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $d_6$-DMSO) δ 186.91, 166.25 (d, $J$ = 256.2 Hz), 133.19 (d, $J$ = 10.0 Hz), 126.10 (d, $J$ = 2.8 Hz), 116.64 (d, $J$ = 22.3 Hz), 33.72, 29.52, 21.62, 13.40.
**$^{19}$F{$^1$H} NMR** (471 MHz, $d_6$-DMSO) δ –101.81 (s, 1F).

**$^{19}$F NMR** (471 MHz, $d_6$-DMSO) δ –101.81 (tt, $J$ = 8.9, 5.3 Hz, 1F).

1-(p-tolyl)pentan-1-iminium chloride (**21c**)

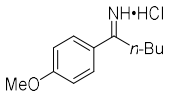



**Synthesis of 21c**. A 250 mL round bottom flask containing a PTFE coated stir bar under $N_2$ atmosphere was charged with 4-methylbenzonitrile (6.78 mL, 6.66 g, 56.8 mmol) and 2-methyltetrahydrofuran (100 mL) and rendered homogenous at room temperature using rotary magnetic stirring, followed by cooling to –78 ºC for 30 min. To the mixture was added *n*-butyllithium (2.5 M in hexanes, 25.0 mL, 62.5 mmol) followed by aging the mixture for 15 min prior to addition of MeOH (3.45 mL, 2.73 g, 85 mmol). The mixture was allowed to warm to RT and age for 1 h accompanied with magnetic rotary stirring. The mixture was filtered through a pad of Celite® using MTBE as the solvent and the filtrate was concentrated *in vacuo*. The residue was dissolved in MTBE (ca. 20 mL), filtered one more time through a pad of Celite® using MTBE as the eluent solvent. The filtrate was collected in a round bottom flask, the flask was sealed with a rubber septum and deoxygenated by sparging with $N_2$ for 5 min followed by addition of HCl (2 M in $Et_2O$, 28.4 mL, 56.8 mmol). The resulting solid was collected via vacuum filtration and the solid was washed with MTBE (3 × 5 mL). The solid was triturated using MeCN (ca. 20 mL) at RT and collected via vacuum filtration followed by washing with MeCN (3 × 5 mL) to afford **21c** as a white solid (7.84 g, 65%).

**$^1$H NMR** (500 MHz, $d_6$-DMSO) δ 12.86 (br s, 2H), 8.08 (d, $J$ = 8.3 Hz, 2H), 7.46 (d, $J$ = 8.1 Hz, 2H), 3.23 (t, $J$ = 7.6 Hz, 2H), 2.42 (s, 3H), 1.55 (p, $J$ = 7.6 Hz, 2H), 1.33 (hept, $J$ = 7.3 Hz, 2H), 0.85 (t, $J$ = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $d_6$-DMSO) δ 187.52, 146.89, 129.98, 129.84, 126.60, 33.40, 29.77, 21.63, 21.30, 13.41.

1-(4-methoxyphenyl)pentan-1-iminium chloride **(21d)**

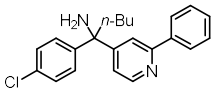



**Synthesis of 21d**. A 250 mL round bottom flask containing a PTFE coated stir bar under $N_2$ atmosphere was charged with 4-methoxybenzonitrile (7.56 g, 56.8 mmol) and 2-methyltetrahydrofuran (100 mL) and rendered homogenous at room temperature using rotary magnetic stirring, followed by cooling to –78 ºC for 30 min. To the mixture was added *n*-butyllithium (2.5 M in hexanes, 25.0 mL, 62.5 mmol) followed by aging the mixture for 15 min prior to addition of MeOH (3.45 mL, 2.73 g, 85 mmol). The mixture was allowed to warm to RT and age for 1 h accompanied with magnetic rotary stirring. The mixture was filtered through a pad of Celite® using MTBE as the solvent and the filtrate was concentrated *in vacuo*. The residue was dissolved in MTBE (ca. 20 mL), filtered one more time through a pad of Celite® using MTBE as the eluent solvent. The filtrate was collected in a round bottom flask, the flask was sealed with a rubber septum and deoxygenated by sparging with $N_2$ for 5 min followed by addition of HCl (2 M in $Et_2O$, 28.4 mL, 56.8 mmol). The resulting solid was collected via vacuum filtration and the solid was washed with MTBE (3 × 5 mL). The solid was triturated using MeCN (ca. 20 mL) at RT and collected via vacuum filtration followed by washing with MeCN (3 × 5 mL) to afford **21d** as a white solid (4.02 g, 31%).

**$^1$H NMR** (500 MHz, $d_6$-DMSO) δ 11.66 (br s, 2H), 8.28 (d, $J$ = 9.0 Hz, 2H), 7.13 (d, $J$ = 9.0 Hz, 2H), 3.86 (s, 3H), 3.22 (t, $J$ = 7.6 Hz, 2H), 1.52 (p, $J$ = 7.7 Hz, 2H), 1.29 (hept, $J$ = 7.3 Hz, 2H), 0.79 (t, $J$ = 7.4 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $d_6$-DMSO) δ 185.49, 165.35, 132.81, 120.96, 114.89, 56.11, 33.03, 30.38, 21.67, 13.42.

1-(4-chlorophenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22a**)



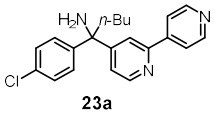
**22a**

Compound **22a•3TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 25%, corrected yield = 26%). The desired product was obtained as a clear oil and observed at $t_r$ = 3.312 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.66 (d, *J* = 6.3 Hz, 1H), 8.09 (d, *J* = 1.5 Hz, 1H), 7.82 – 7.79 (m, 1H), 7.77 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 2.64 – 2.55 (m, 1H), 2.54 – 2.43 (m, 1H), 1.43 – 1.14 (m, 4H), 0.85 (t, *J* = 7.2 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**ESI LRMS** *m/z* calcd. for $C_{22}H_{24}ClN_2$ ($[M + H]^+$) 351.2, found 351.5.

1-([2,4'-bipyridin]-4-yl)-1-(4-chlorophenyl)pentan-1-amine (**23a**)



**23a**

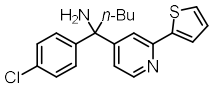
Compound **23a** was prepared following the General Procedure for Library Synthesis (LCAP = 41%, corrected yield = 46%, assay yield = 53%, isolated yield = 38%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.761 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.75 – 8.67 (m, 2H), 8.63 (d, *J* = 5.2 Hz, 1H), 7.89 – 7.79 (m, 3H), 7.36 – 7.27 (m, 5H), 2.21 (dd, *J* = 9.3, 7.2 Hz, 2H), 1.85 (s, 2H), 1.35 (hept, *J* = 7.2 Hz, 2H), 1.24 – 1.06 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 158.60, 154.87, 150.41, 150.09, 146.54, 145.66, 132.88, 128.62, 127.89, 121.83, 121.20, 118.78, 60.56, 41.79, 26.07, 23.08, 14.01.

**ESI LRMS** *m/z* calcd. for $C_{21}H_{23}ClN_3$ ($[M + H]^+$) 352.2, found 352.7.

1-(4-chlorophenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24a**)



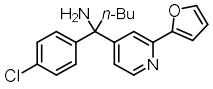

**24a**

Compound **24a•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 13%, corrected yield = 22%). The desired product was obtained as a clear oil and observed at $t_r$ = 3.297 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.56 (d, *J* = 6.1 Hz, 1H), 7.95 (d, *J* = 3.2 Hz, 1H), 7.87 (s, 1H), 7.62 (d, *J* = 5.0 Hz, 1H), 7.51 (d, *J* = 5.0 Hz, 1H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.21 – 7.13 (m, 1H), 2.59 – 2.39 (m, 2H), 1.43 – 1.31 (m, 2H), 1.25 – 1.06 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**ESI LRMS** *m/z* calcd. for $C_{20}H_{22}ClN_2S$ ($[M + H]^+$) 357.1, found 357.3.

1-(4-chlorophenyl)-1-(2-(furan-2-yl)pyridin-4-yl)pentan-1-amine (**25a**)



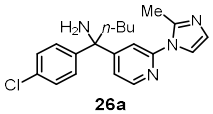

**25a**

Compound **25a•3TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 31%, corrected yield = 44%). The desired product was obtained as a brown oil and observed at $t_r$ = 3.025 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.59 (d, *J* = 6.3 Hz, 1H), 8.02 (d, *J* = 1.5 Hz, 1H), 7.67 (d, *J* = 1.4 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.41 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 6.65 (dd, *J* = 3.7, 1.7 Hz, 1H), 2.63 – 2.40 (m, 2H), 1.43 – 1.13 (m, 4H), 0.86 (t, *J* = 7.3 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**ESI LRMS** *m/z* calcd. for $C_{20}H_{22}ClN_2O$ ($[M + H]^+$) 341.1, found 341.7.

1-(4-chlorophenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26a**)



**26a**

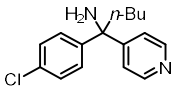
Compound **26a** was prepared following the General Procedure for Library Synthesis (LCAP = 33%, corrected yield = 30%, assay yield = 55%, isolated yield = 30%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.417 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.56 (d, *J* = 5.3 Hz, 1H), 8.14 (s, 1H), 7.73 (d, *J* = 2.0 Hz, 1H), 7.42 – 7.29 (m, 5H), 7.06 (dd, *J* = 5.3, 1.4 Hz, 1H), 4.77 (br s, 2H), 2.88 (s, 3H), 2.62 – 2.51 (m, 1H), 2.49 – 2.36 (m, 1H), 1.36 (m, 3H), 1.10 (m, 1H), 0.85 (t, *J* = 7.0 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 160.74, 150.98, 149.04, 145.29, 144.88, 133.06, 128.72, 127.85, 127.76, 120.37, 119.02, 115.21, 60.51, 41.72, 26.04, 23.05, 15.32, 14.00.

**ESI LRMS** *m/z* calcd. for $C_{20}H_{24}ClN_4$ ($[M + H]^+$) 355.2, found 355.7.

1-(4-chlorophenyl)-1-(pyridin-4-yl)pentan-1-amine (**27a**)



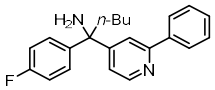
**27a**

Compound **27a•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 35%, corrected yield = 41%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.412 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 6.6 Hz, 2H), 7.96 (d, *J* = 6.7 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.28 (s, 2H), 2.61 – 2.42 (m, 2H), 1.35 (dt, *J* = 14.7, 7.3 Hz, 2H), 1.24 – 1.16 (m, 2H), 0.86 (t, *J* = 7.3, 6.7 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**ESI LRMS** *m/z* calcd. for $C_{16}H_{20}ClN_2$ ($[M + H]^+$) 275.1, found 275.4.

1-(4-fluorophenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22b**)



**22b**

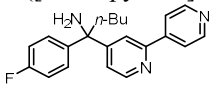
Compound **22b•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 34%, corrected yield = 36%). The desired product was obtained as a clear oil and observed at $t_r$ = 3.341 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 6.3 Hz, 1H), 8.11 (d, *J* = 1.4 Hz, 1H), 7.83 – 7.74 (m, 3H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.35 (dd, *J* = 8.8, 4.8 Hz, 2H), 7.12 (t, *J* = 8.4 Hz, 2H), 2.65 – 2.44 (m, 2H), 1.44 – 1.14 (m, 4H), 0.86 (t, *J* = 7.2 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**$^{19}$F{H} NMR** (471 MHz, $CDCl_3$) δ = -110.72 (s, 1F).

**ESI LRMS** *m/z* calcd. for $C_{22}H_{24}FN_2$ ($[M + H]^+$) 335.2, found 335.7.

1-([2,4'-bipyridin]-4-yl)-1-(4-fluorophenyl)pentan-1-amine (**23b**)



23b

Compound **23b** was prepared following the General Procedure for Library Synthesis (LCAP = 54%, corrected yield = 58%, assay yield = 78%, isolated yield = 47%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.455 min (detection at 210 nm) using the general UPLC-MS method.

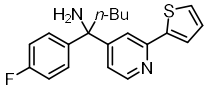
**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.85 – 8.71 (m, 5H), 8.68 (s, 1H), 7.38 (dd, *J* = 8.8, 4.9 Hz, 2H), 7.12 – 7.00 (m, 3H), 2.65 – 2.55 (m, 1H), 2.52 – 2.42 (m, 1H), 1.42 – 1.28 (m, 3H), 1.19 – 1.07 (m, 1H), 0.84 (t, *J* = 7.0 Hz, 3H). Signal corresponding the $NH_2$ was not observed.

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 161.63 (d, *J* = 246.4 Hz), 158.86, 154.81, 150.38, 150.05, 146.60, 142.92 (d, *J* = 3.2 Hz), 128.12 (d, *J* = 7.9 Hz), 121.87, 121.19, 118.80, 115.27 (d, *J* = 21.2 Hz), 60.49, 41.98, 26.10, 23.08, 14.01.

**$^{19}$F{$^1$H} NMR** (471 MHz, $CDCl_3$) δ = -115.68 (s, 1F).

**ESI LRMS** *m/z* calcd. for $C_{21}H_{23}FN_3$ ($[M + H]^+$) 336.2, found 336.7.

1-(4-fluorophenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24b**)



24b

Compound **24b** was prepared following the General Procedure for Library Synthesis (LCAP = 30%, corrected yield = 39%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.955 min (detection at 210 nm) using the general UPLC-MS method.

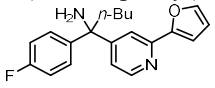
**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.46 (d, *J* = 5.3 Hz, 1H), 7.74 – 7.67 (m, 1H), 7.55 (dd, *J* = 3.7, 0.9 Hz, 1H), 7.43 – 7.30 (m, 3H), 7.14 – 7.04 (m, 2H), 7.00 (t, *J* = 8.7 Hz, 2H), 2.27 – 2.13 (m, 2H), 1.72 (s, 2H), 1.35 (hept, *J* = 7.1 Hz, 2H), 1.28 – 1.08 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 161.59 (d, *J* = 246.1 Hz), 158.26, 152.69, 149.52, 145.03, 143.11 (d, *J* = 3.2 Hz ), 128.16 (d, *J* = 7.9 Hz), 127.98, 127.60, 124.57, 120.19, 116.50, 115.15 (d, *J* = 21.2 Hz), 60.41, 41.91, 26.12, 23.11, 14.03.

**$^{19}$F{$^1$H} NMR** (471 MHz, $CDCl_3$) δ = -115.95 (s, 1F).

**ESI LRMS** *m/z* calcd. for $C_{20}H_{22}FN_2S$ ($[M + H]^+$) 341.1, found 341.7.

1-(4-fluorophenyl)-1-(2-(furan-2-yl)pyridin-4-yl)pentan-1-amine (**25b**)




**25b**

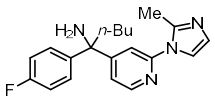
Compound **25b•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 41%, corrected yield = 60%). The desired product was obtained as a brown oil and observed at $t_r$ = 2.699 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.62 (d, *J* = 6.3 Hz, 1H), 7.99 (d, *J* = 1.5 Hz, 1H), 7.66 (d, *J* = 1.4 Hz, 1H), 7.60 (t, *J* = 3.9 Hz, 2H), 7.33 (dd, *J* = 8.9, 4.8 Hz, 2H), 7.13 (t, *J* = 8.5 Hz, 2H), 6.65 (dd, *J* = 3.7, 1.7 Hz, 1H), 2.62 – 2.42 (m, 2H), 1.36 (m, 2H), 1.25 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**$^{19}$F {$^1$H} NMR** (471 MHz, $CDCl_3$) δ = -110.40 (s, 1F).

**ESI LRMS** *m/z* calcd. for $C_{20}H_{22}FN_2O$ ($[M + H]^+$) 325.2, found 325.7.

1-(4-fluorophenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26b**)




**26b**

Compound **26b** was prepared following the General Procedure for Library Synthesis (LCAP = 38%, corrected yield = 39%, assay yield = 60%, isolated yield = 35%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.095 min (detection at 210 nm) using the general UPLC-MS method.

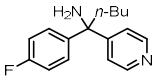
**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.43 (d, *J* = 5.3 Hz, 1H), 7.40 – 7.32 (m, 3H), 7.26 – 7.23 (m, 2H), 7.06 – 6.96 (m, 3H), 2.51 (s, 3H), 2.25 – 2.13 (m, 2H), 1.91 (s, 2H), 1.35 (hept, *J* = 6.6 Hz, 2H), 1.29 – 1.05 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 161.69 (d, *J* = 246.8 Hz), 161.03, 150.94, 149.00, 144.85, 142.59 (d, *J* = 3.3 Hz), 128.02 (d, *J* = 7.9 Hz), 127.84, 120.38, 119.02, 115.37 (d, *J* = 21.3 Hz), 115.28, 60.44, 41.91, 26.07, 23.05, 15.29, 14.00.

**$^{19}$F{$^1$H} NMR** (471 MHz, $CDCl_3$) δ -115.38 (s, 1F).

**ESI LRMS** *m/z* calcd. for $C_{20}H_{24}FN_4$ ($[M + H]^+$) 339.2, found 339.7.

1-(4-fluorophenyl)-1-(pyridin-4-yl)pentan-1-amine (**27b**)




**27b**

Compound **27b** was prepared following the General Procedure for Library Synthesis (LCAP = 35%, corrected yield = 46%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.146 min (detection at 210 nm) using the general UPLC-MS method.

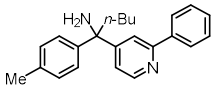
**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.55 – 8.48 (m, 2H), 7.34 – 7.29 (m, 2H), 7.28 – 7.26 (m, 2H), 6.98 (t, *J* = 8.7 Hz, 2H), 2.22 – 2.09 (m, 2H), 1.82 (s, 2H), 1.33 (hept, *J* = 7.2 Hz, 2H), 1.23 – 1.04 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 161.55 (d, *J* = 246.0 Hz), 157.54, 149.78, 143.07 (d, *J* = 3.2 Hz), 128.15 (d, *J* = 7.9 Hz), 121.60, 115.08 (d, *J* = 21.2 Hz), 60.29, 41.90, 26.07, 23.08, 14.00.

**$^{19}$F{$^1$H} NMR** (471 MHz, $CDCl_3$) δ = -116.07 (s, 1F).

**ESI LRMS** *m/z* calcd. for $C_{16}H_{20}FN_2$ ($[M + H]^+$) 259.2, found 259.7.

1-(2-phenylpyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**22c**)




**22c**

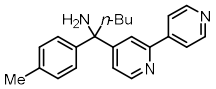
Compound **22c** was prepared following the General Procedure for Library Synthesis (LCAP = 51%, corrected yield = 60%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.946 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.58 (d, *J* = 5.2 Hz, 1H), 8.00 – 7.90 (m, 2H), 7.81 – 7.75 (m, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 7.5 Hz, 2H), 7.21 (dd, *J* = 5.2, 1.7 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 2H), 2.33 (s, 3H), 2.22 (p, *J* = 7.0 Hz, 2H), 1.69 (br s, 2H, coincidental with $H_2O$ signal), 1.35 (hept, *J* = 7.1 Hz, 2H), 1.30 – 1.20 (m, 1H), 1.20 – 1.08 (m, 1H), 0.88 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 158.64, 157.47, 149.53, 144.61, 139.75, 136.42, 129.09, 128.84, 128.68, 127.07, 126.31, 120.42, 118.60, 60.63, 41.91, 26.20, 23.18, 20.95, 14.05.

**ESI LRMS** *m/z* calcd. for $C_{23}H_{27}N_2$ ($[M + H]^+$) 331.2, found 331.8.

1-([2,4'-bipyridin]-4-yl)-1-(p-tolyl)pentan-1-amine (**23c**)




**23c**

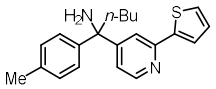
Compound **23c** was prepared following the General Procedure for Library Synthesis (LCAP = 69%, corrected yield = 74%, assay yield = 68%, isolated yield = 63%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.485 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.75 (q, *J* = 7.0 Hz, 5H), 8.65 (s, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.20 – 7.13 (m, 3H), 2.64 – 2.43 (m, 2H), 2.31 (s, 3H), 1.42 – 1.28 (m, 3H), 1.22 – 1.11 (m, 1H), 0.85 (t, *J* = 7.1 Hz, 3H). Signal corresponding the $NH_2$ was not observed.

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 159.21, 154.62, 150.34, 149.91, 146.74, 144.29, 136.62, 129.20, 126.23, 122.06, 121.23, 118.96, 60.63, 41.88, 26.16, 23.14, 20.95, 14.03.

**ESI LRMS** *m/z* calcd. for $C_{22}H_{26}N_3$ ($[M + H]^+$) 332.2, found 332.7.

1-(2-(thiophen-2-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**24c)**




**24c**

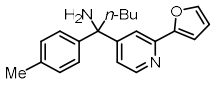
Compound **24c** was prepared following the General Procedure for Library Synthesis (LCAP = 41%, corrected yield = 7%). The desired product was obtained as a clear oil and observed at $t_r$ = 3.129 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.44 (d, *J* = 5.3 Hz, 1H), 7.74 (s, 1H), 7.56 (d, *J* = 2.9 Hz, 1H), 7.37 (d, *J* = 5.0 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.17 – 7.05 (m, 4H), 2.33 (s, 3H), 2.20 (p, *J* = 7.0 Hz, 2H), 1.60 (br s, 2H, coincidental with $H_2O$ signal), 1.35 (hept, *J* = 7.3 Hz, 2H), 1.25 (m, 1H), 1.20 – 1.08 (m, 1H), 0.88 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 158.58, 152.53, 149.37, 145.21, 144.51, 136.49, 129.11, 127.94, 127.45, 126.28, 124.49, 120.42, 116.64, 60.55, 41.81, 26.18, 23.17, 20.95, 14.04.

**ESI LRMS** *m/z* calcd. for $C_{21}H_{25}N_2S$ ($[M + H]^+$) 337.2, found 337.8.

1-(2-(furan-2-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**25c**)



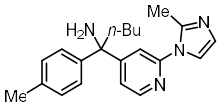

**25c**

Compound **25c•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 62%, corrected yield = 61%). The desired product was obtained as a brown oil and observed at $t_r$ = 2.698 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.52 (d, *J* = 6.2 Hz, 1H), 8.07 (d, *J* = 1.5 Hz, 1H), 7.61 (d, *J* = 1.4 Hz, 1H), 7.55 (d, *J* = 3.6 Hz, 1H), 7.52 (dd, *J* = 6.2, 1.7 Hz, 1H), 7.20 (s, 4H), 6.60 (dd, *J* = 3.7, 1.7 Hz, 1H), 2.58 – 2.43 (m, 2H), 2.32 (s, 3H), 1.43 – 1.29 (m, 2H), 1.27 – 1.16 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**ESI LRMS** *m/z* calcd. for $C_{21}H_{25}N_2O$ ($[M + H]^+$) 321.2, found 321.8.

1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**26c**)




**26c**

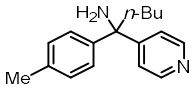
Compound **26c** was prepared following the General Procedure for Library Synthesis (LCAP = 48%, corrected yield = 48%, assay yield = 78%, isolated yield = 44%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.157 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.52 (d, *J* = 5.3 Hz, 1H), 8.17 (s, 1H), 7.73 (d, *J* = 2.1 Hz, 1H), 7.30 (d, *J* = 2.1 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 7.08 (dd, *J* = 5.3, 1.4 Hz, 1H), 4.21 (br s, 2H) 2.88 (s, 3H), 2.60 – 2.51 (m, 1H), 2.50 – 2.40 (m, 1H), 2.33 (s, 3H), 1.41 – 1.29 (m, 3H), 1.19 – 1.08 (m, 1H), 0.85 (t, *J* = 7.1 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 161.46, 150.80, 148.85, 144.84, 143.92, 136.81, 129.28, 127.75, 126.12, 120.56, 119.08, 115.50, 60.59, 41.82, 26.13, 23.11, 20.94, 15.25, 14.02.

**ESI LRMS** *m/z* calcd. for $C_{21}H_{27}N_4$ ($[M + H]^+$) 335.2, found 335.7.

1-(pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**27c**)



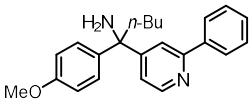

**27c**

Compound **27c•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 61%, corrected yield = 70%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.239 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.68 (d, *J* = 6.5 Hz, 2H), 8.54 (br s, 2H), 7.94 (d, *J* = 6.6 Hz, 2H), 7.20 (dd, *J* = 8.4 Hz, 4H), 2.59 – 2.43 (m, 2H), 2.33 (s, 3H), 1.34 (hept, *J* = 7.2 Hz, 2H), 1.26 – 1.15 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H).

**ESI LRMS** *m/z* calcd. for $C_{17}H_{23}N_2$ ($[M + H]^+$) 255.2, found 255.7.

1-(4-methoxyphenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22d**)




**22d**

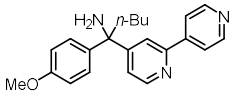
Compound **22d** was prepared following the General Procedure for Library Synthesis (LCAP = 62%, corrected yield = 63%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.744 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.58 (d, *J* = 5.2 Hz, 1H), 7.99 – 7.90 (m, 2H), 7.78 – 7.73 (m, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.40 (dd, *J* = 8.3, 6.2 Hz, 1H), 7.33 – 7.27 (m, 2H), 7.21 (dd, *J* = 5.2, 1.7 Hz, 1H), 6.88 – 6.82 (m, 2H), 3.79 (s, 3H), 2.21 (dd, *J* = 9.0, 7.4 Hz, 2H), 1.91 (s, 2H), 1.34 (p, *J* = 7.2 Hz, 2H), 1.30 – 1.20 (m, 1H), 1.20 – 1.08 (m, 1H), 0.88 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 158.64, 158.31, 157.48, 149.52, 139.68, 139.51, 128.87, 128.69, 127.61, 127.06, 120.35, 118.60, 113.67, 60.50, 55.26, 41.96, 26.21, 23.15, 14.04.

**ESI LRMS** *m/z* calcd. for $C_{23}H_{27}N_2O$ ($[M + H]^+$) 347.2, found 347.7.

1-([2,4'-bipyridin]-4-yl)-1-(4-methoxyphenyl)pentan-1-amine (**23d**)




**23d**

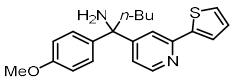
Compound **23d** was prepared following the General Procedure for Library Synthesis (LCAP = 53%, corrected yield = 67%, assay yield = 83%, isolated yield = 59%). The desired product was obtained as a brown oil and observed at $t_r$ = 2.324 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.70 – 8.66 (m, 2H), 8.61 (d, *J* = 5.2 Hz, 1H), 7.90 – 7.79 (m, 3H), 7.34 – 7.24 (m, 3H), 6.89 – 6.78 (m, 2H), 3.78 (s, 3H), 2.28 – 2.14 (m, 2H), 2.03 (s, 2H), 1.35 (hept, *J* = 7.2 Hz, 2H), 1.29 – 1.18 (m, 1H), 1.17 – 1.06 (m, 1H), 0.87 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 159.30, 158.38, 154.62, 150.33, 149.92, 146.73, 139.31, 127.52, 122.00, 121.22, 118.93, 113.76, 60.42, 55.25, 42.00, 26.17, 23.12, 14.03.

**ESI LRMS** *m/z* calcd. for $C_{22}H_{26}N_3O$ ($[M + H]^+$) 348.2, found 348.8.

1-(4-methoxyphenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24d**)



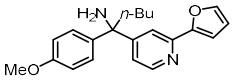

**24d**

Compound **24d•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 43%, corrected yield = 37%). The desired product was obtained as a yellow oil and observed at $t_r$ = 2.721 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 6.2 Hz, 1H), 8.01 – 7.96 (m, 1H), 7.92 (d, *J* = 1.4 Hz, 1H), 7.62 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.57 (dd, *J* = 6.2, 1.6 Hz, 1H), 7.25 (d, *J* = 9.0 Hz, 2H), 7.17 (dd, *J* = 4.9, 4.0 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 2.50 (m, 2H), 1.42 – 1.31 (m, 2H), 1.25 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**ESI LRMS** *m/z* calcd. for $C_{21}H_{25}N_2OS$ ($[M + H]^+$) 353.2, found 353.8.

1-(2-(furan-2-yl)pyridin-4-yl)-1-(4-methoxyphenyl)pentan-1-amine (**25d**)



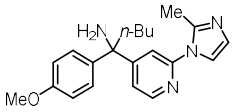

**25d**

Compound **25d•4TFA** was prepared following the General Procedure for Library Synthesis (LCAP = 46%, corrected yield = 51%). The desired product was obtained as a yellow oil and observed at $t_r$ = 2.531 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 6.1 Hz, 1H), 8.00 (s, 1H), 7.60 (d, *J* = 1.4 Hz, 1H), 7.53 (d, *J* = 3.7 Hz, 2H), 7.25 (d, *J* = 9.1 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 6.59 (dd, *J* = 3.6, 1.7 Hz, 1H), 3.78 (s, 3H), 2.57 – 2.40 (m, 2H), 1.40 – 1.30 (m, 2H), 1.28 – 1.13 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H). The protonated $NH_2$ signal cannot be accurately integrated.

**ESI LRMS** *m/z* calcd. for $C_{21}H_{25}N_2O_2$ ($[M + H]^+$) 337.2, found 337.8.

1-(4-methoxyphenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26d**)




**26d**

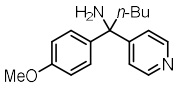
Compound **26d** was prepared following the General Procedure for Library Synthesis (LCAP = 34%, corrected yield = 33%, assay yield = 58%, isolated yield = 39%). The desired product was obtained as a clear oil and observed at $t_r$ = 1.961 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 5.3 Hz, 1H), 8.13 (s, 1H), 7.73 (d, *J* = 2.1 Hz, 1H), 7.32 (d, *J* = 2.1 Hz, 1H), 7.28 (d, *J* = 8.9 Hz, 2H), 7.08 (dd, *J* = 5.3, 1.4 Hz, 1H), 6.89 (d, *J* = 8.9 Hz, 2H), 5.37 (br s, 2H), 3.79 (s, 3H), 2.87 (s, 3H), 2.59 – 2.49 (m, 1H), 2.48 – 2.36 (m, 1H), 1.41 – 1.28 (m, 3H), 1.20 – 1.06 (m, 1H), 0.85 (t, *J* = 7.1 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 161.57, 158.49, 150.79, 148.86, 144.83, 138.94, 127.70, 127.42, 120.52, 119.07, 115.46, 113.85, 60.37, 55.28, 41.94, 26.14, 23.10, 15.23, 14.03.

**ESI LRMS** *m/z* calcd. for $C_{21}H_{27}N_4O$ ($[M + H]^+$) 351.2, found 351.8.

1-(4-methoxyphenyl)-1-(pyridin-4-yl)pentan-1-amine (**27d**)




**27d**

Compound **27d** was prepared following the General Procedure for Library Synthesis (LCAP = 57%, corrected yield = 71%). The desired product was obtained as a clear oil and observed at $t_r$ = 2.096 min (detection at 210 nm) using the general UPLC-MS method.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ = 8.49 (d, *J* = 6.2 Hz, 2H), 7.33 – 7.19 (m, 4H), 6.83 (d, *J* = 8.9 Hz, 2H), 3.78 (s, 3H), 2.22 – 2.10 (m, 2H), 2.01 (s, 2H, coincidental with EtOAc signal), 1.32 (hept, *J* = 7.2 Hz, 2H), 1.23 – 1.15 (m, 1H), 1.14 – 1.04 (m, 1H), 0.86 (t, *J* = 7.3 Hz, 3H).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ = 158.28, 157.99, 149.61, 139.51, 127.56, 121.71, 113.61, 60.22, 55.24, 41.92, 26.14, 23.12, 14.02.

**ESI LRMS** *m/z* calcd. for $C_{17}H_{23}N_2O$ ($[M + H]^+$) 271.2, found 271.7.

## Reaction Mechanisms

### Oxidative azidooxygenation of alkenes:

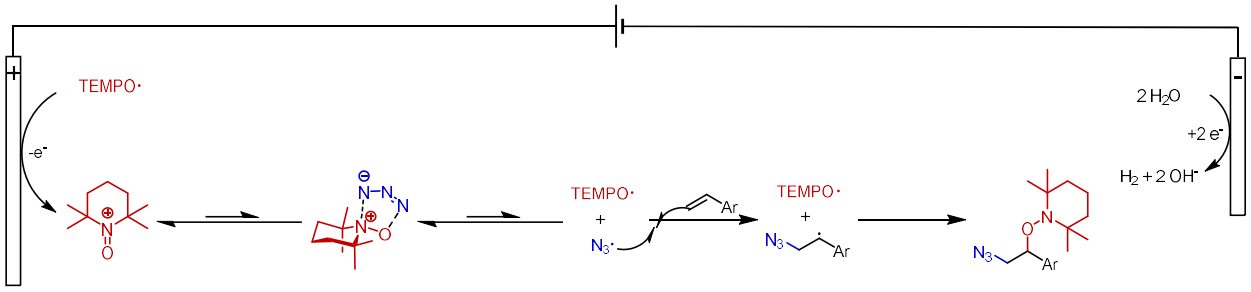



**Figure S65.** Reaction mechanism for the electrochemical azidooxygenation of alkenes.[1] The transformation is an inner-sphere mediated oxidation (ECC) of the styrene via a charge-transfer complex formed between the azide and an oxoammonium cation generated by oxidation of TEMPO.

### Reductive silylation:

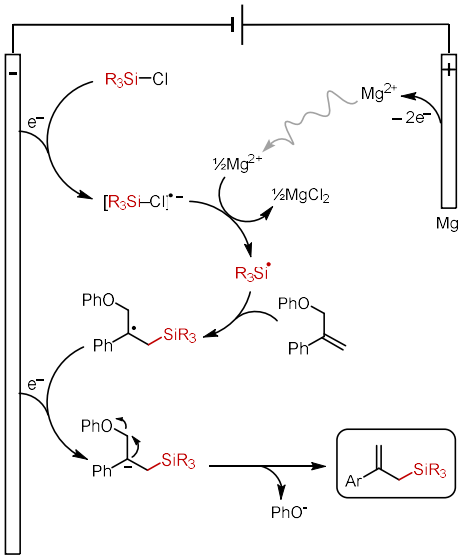



**Figure S66.** Reaction mechanism for the reductive allyl silane synthesis from allyl ethers.[2] This reaction is proposed to undergo an ECEC mechanism wherein trimethylsilyl chloride is first directly reduced to a trimethylsilyl radical, which adds to an allylether to generate a carbon-centered radical. This radical is further reduced to a carbanion and subsequently eliminates phenolate to deliver the allyl silane.

**Electrophotocatalytic oxidative C–H amination of arenes:**

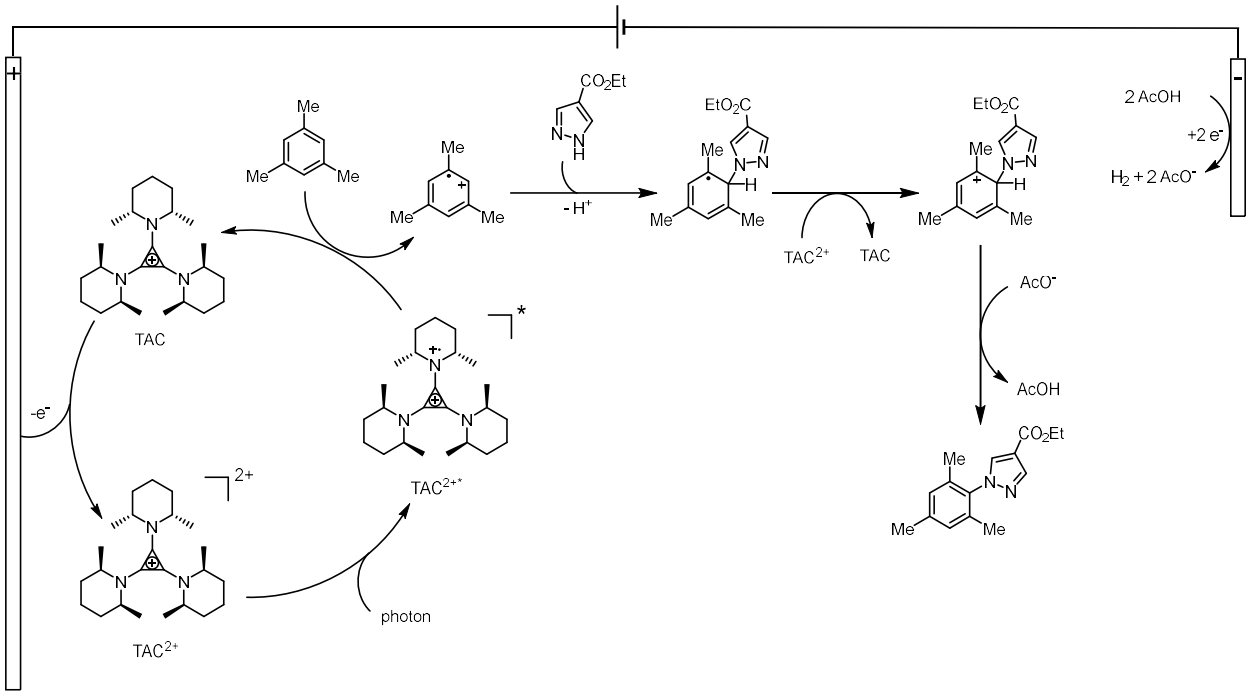



**Figure S67.** Reaction mechanism for the electrophotocatalytic oxidative C–H amination of arenes.[3] In this mediated electrochemical reaction, the catalyst (TAC) is oxidized at the anode to generate the corresponding radical dication ($TAC^{2+}$), which is then photoexcited and reductively quenched by an arene. The resultant highly reactive arene radical cation is trapped by pyrazole to construct the desired C–N bond prior to rearomatization.

**Reductive olefin-ketone coupling:**

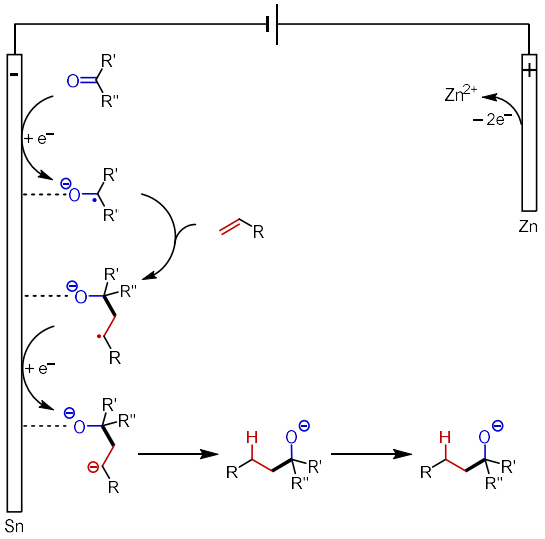



**Figure S68.** Reaction mechanism for the reductive olefine-ketone coupling is a direct cathodic electrolysis adopts an ECEC mechanism wherein a ketyl radical is generated by cathodic reduction of a ketone (14).[4] This ketyl radical adds to the alkene (15) to form the C–C bond, and the resultant C-centered radical undergoes further reduction and protonation to yield the C–C coupled product.

**Oxidative C–H/C–H coupling to form diarylmethanes:**

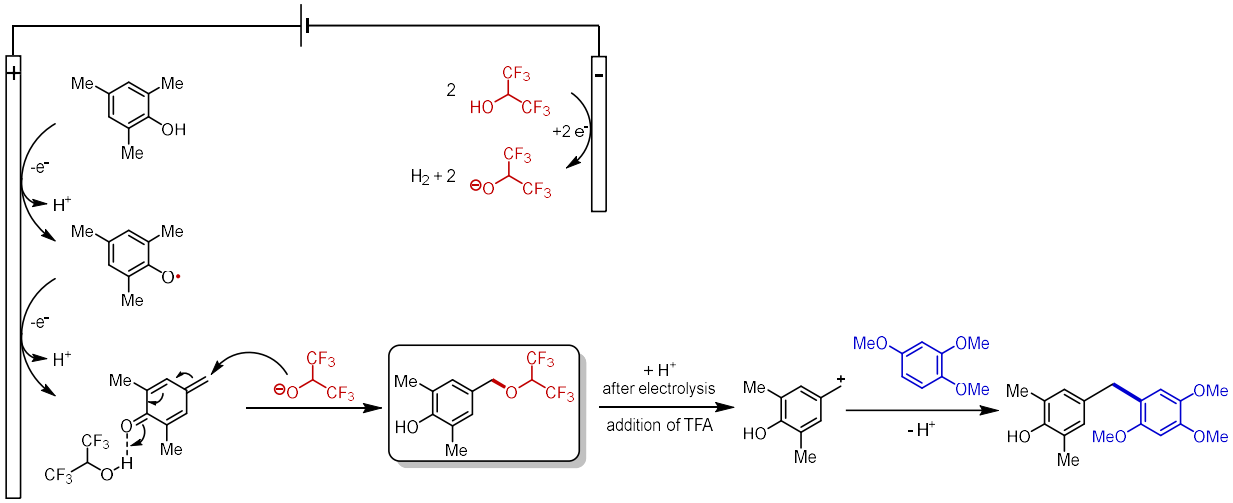



**Figure S69.** Reaction mechanism of the oxidative C–H/C–H coupling to form diarylmethanes in a one-pot sequence.[5] In this transformation, a convergent paired electrolysis generates a pair of p-quinone methide electrophile (via ECE oxidation of a 4-methylphenol) and hexafluoroisopropoxide nucleophile. These intermediates react with one another to yield benzyl hexafluoroisopropyl ether. In a subsequent operation in the same pot, the ether undergoes substitution with an electron-rich arene 18 in the presence of trifluoroacetic acid.

**Reductive synthesis of hindered amines**:

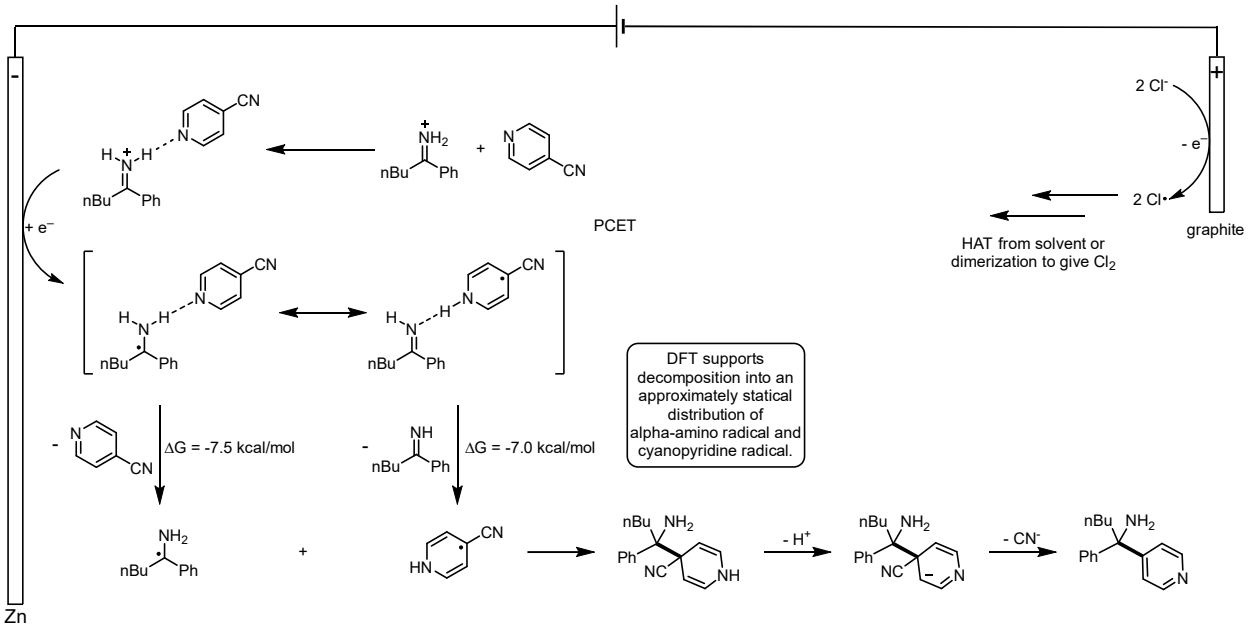
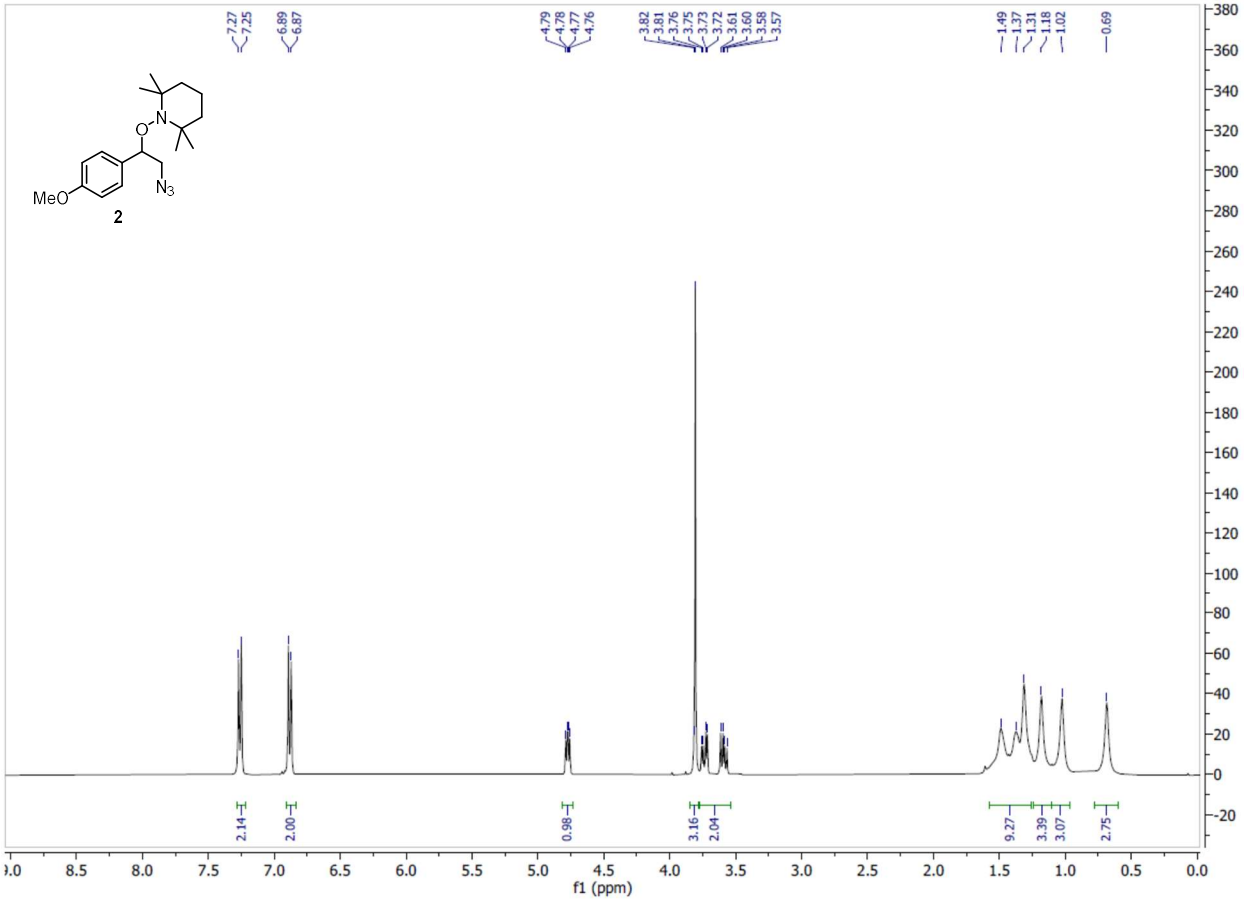


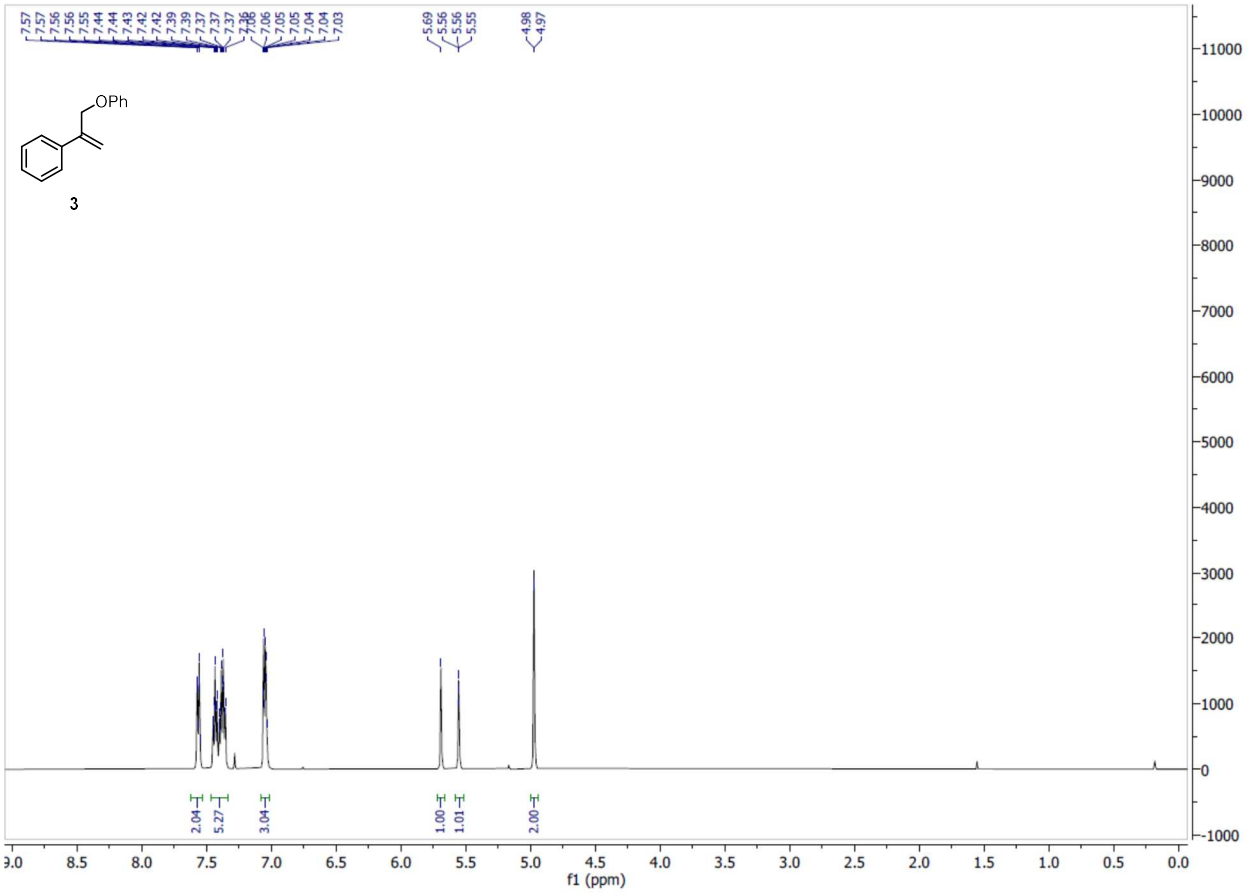

**Figure S70.** Reaction mechanism of the reductive electrosynthesis of hindered primary amines via the coupling of iminium chlorides with cyanopyridines.[8] The key step of the cathodic coupled electrolysis is the radical coupling between an alpha-amino radical and a cyanopyridine radical formed via a common intermediate generated through proton-coupled electron transfer. Subsequent loss of a proton and cyanide delivers the hindered amine.

## NMR Data

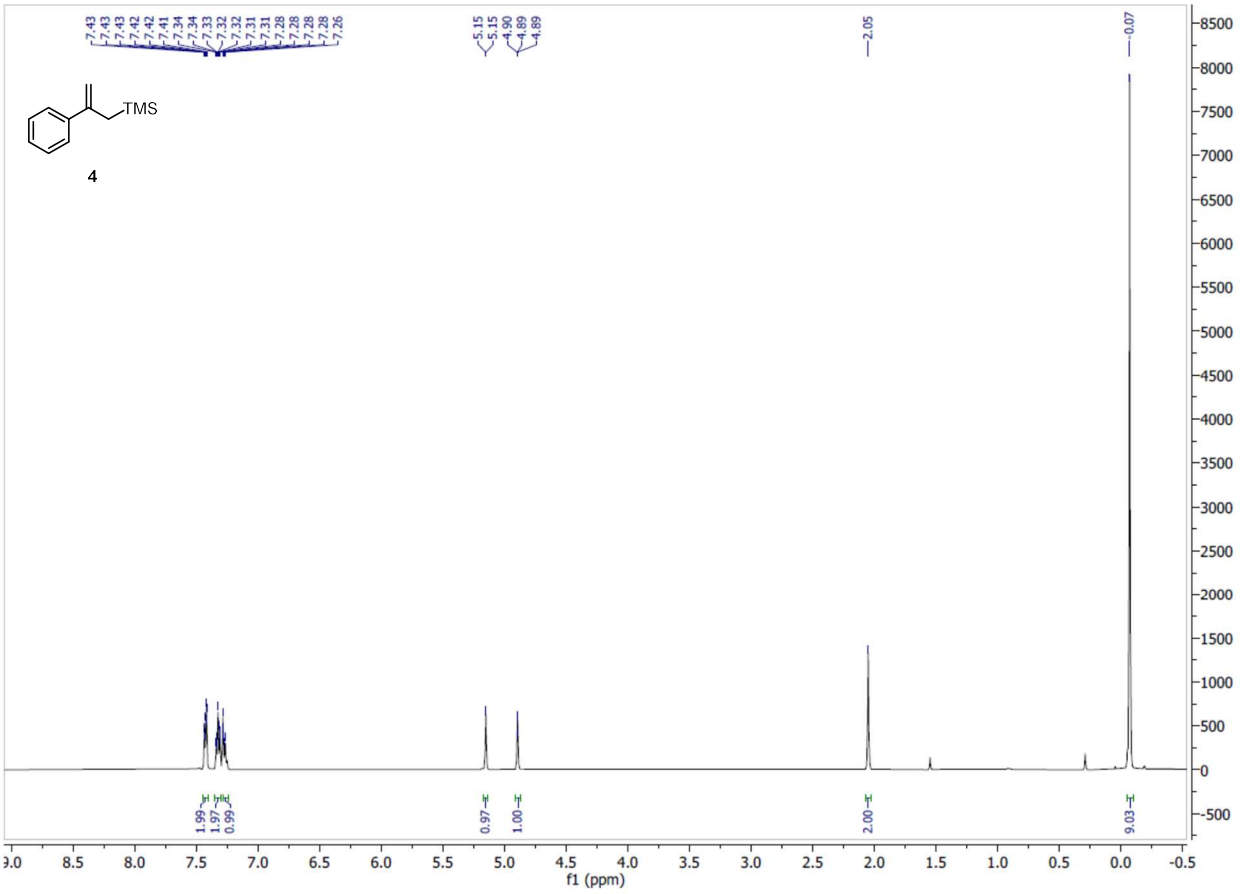
1-(2-azido-1-(4-methoxyphenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (**2**) $^{1}$H NMR (400 MHz, $CDCl_3$, $^{1}$HNMR)



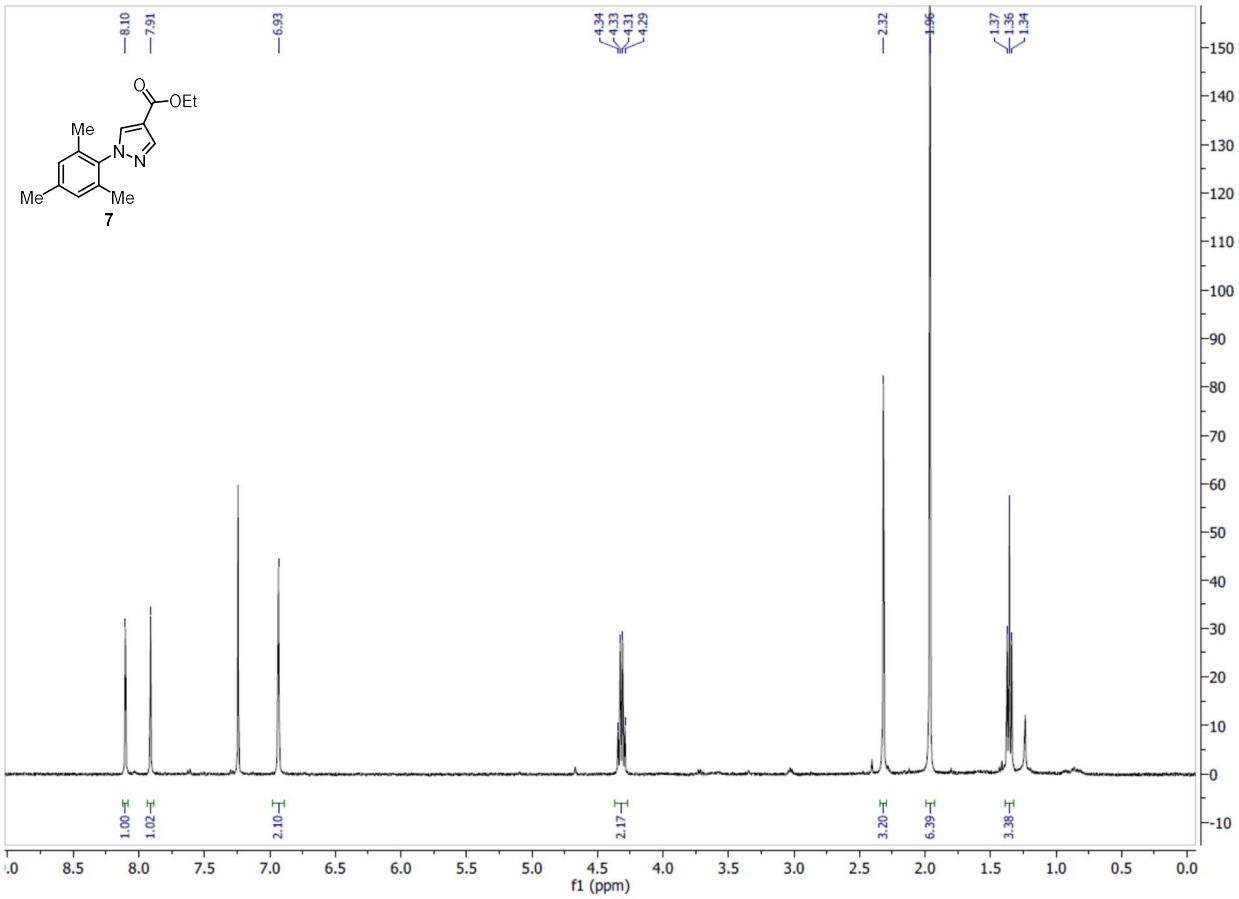
(3-phenoxyprop-1-en-2-yl)benzene (**3**) $^{1}$H NMR (500 MHz, $CDCl_3$, $^{1}$HNMR)



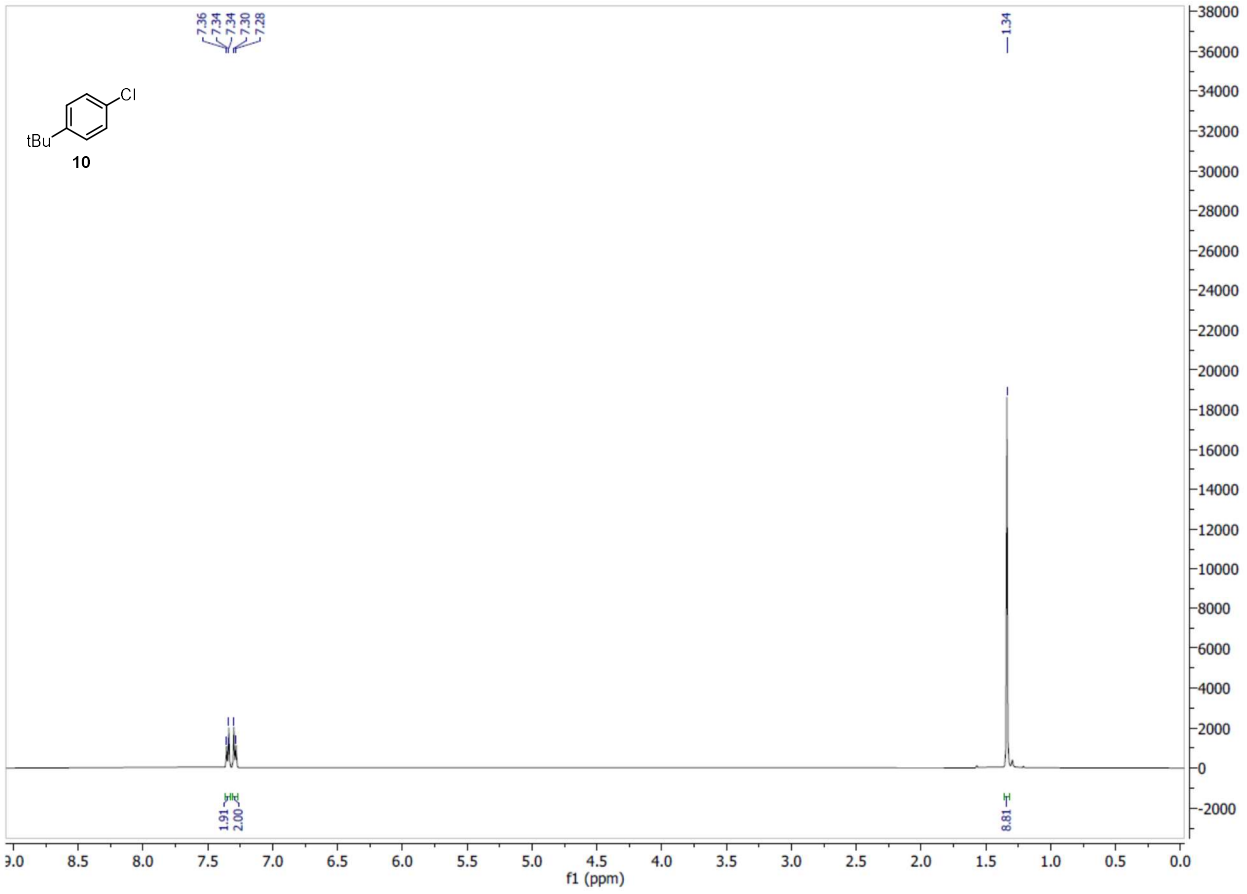
trimethyl(2-phenylallyl)silane (**4**) (500 MHz, $CDCl_3$, $^1$HNMR)



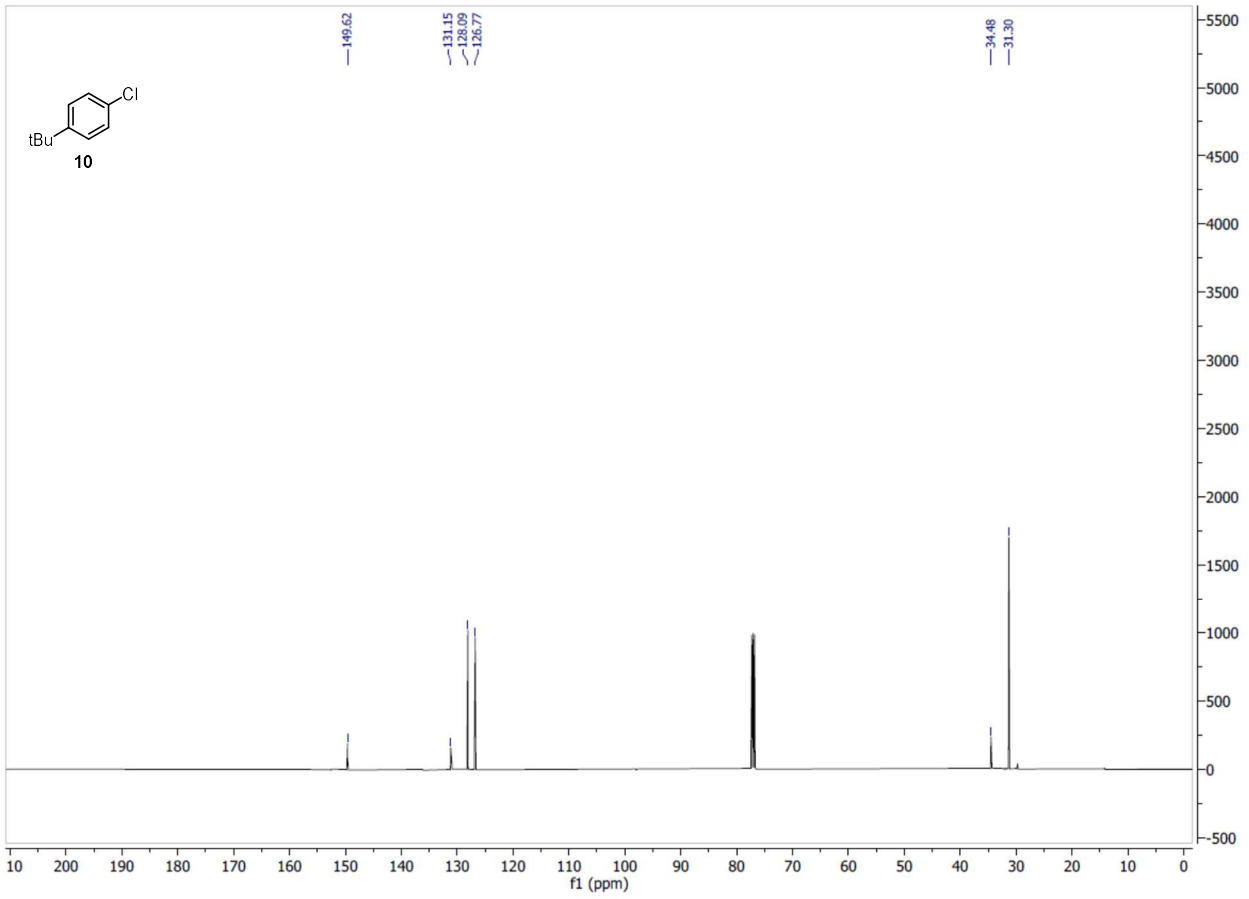
ethyl 1-mesityl-1H-pyrazole-4-carboxylate (**7**) (400 MHz, $CDCl_3$, $^1$HNMR)



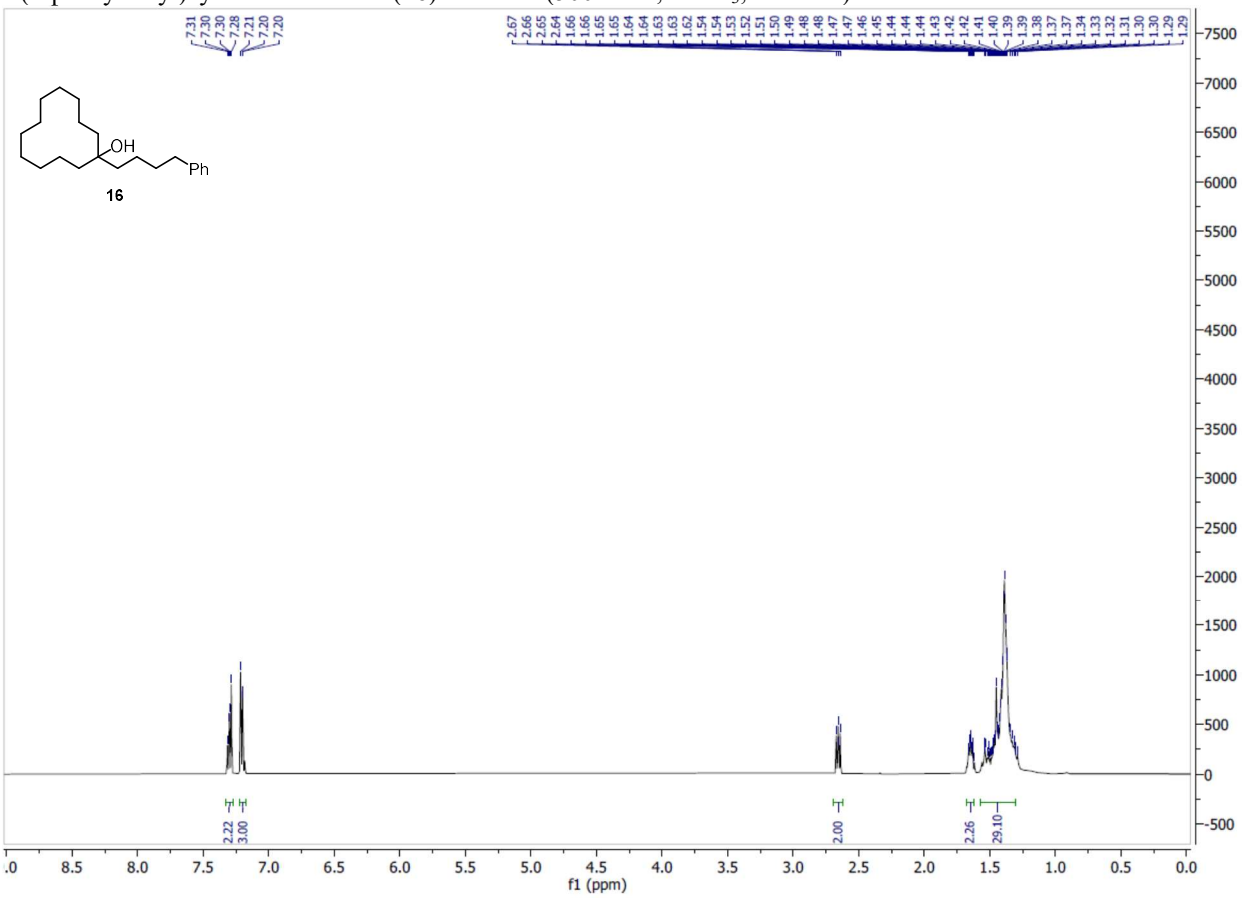
1-(*tert*-butyl)-4-chlorobenzene (**10**) (500 MHz, $CDCl_3$, $^1$HNMR)



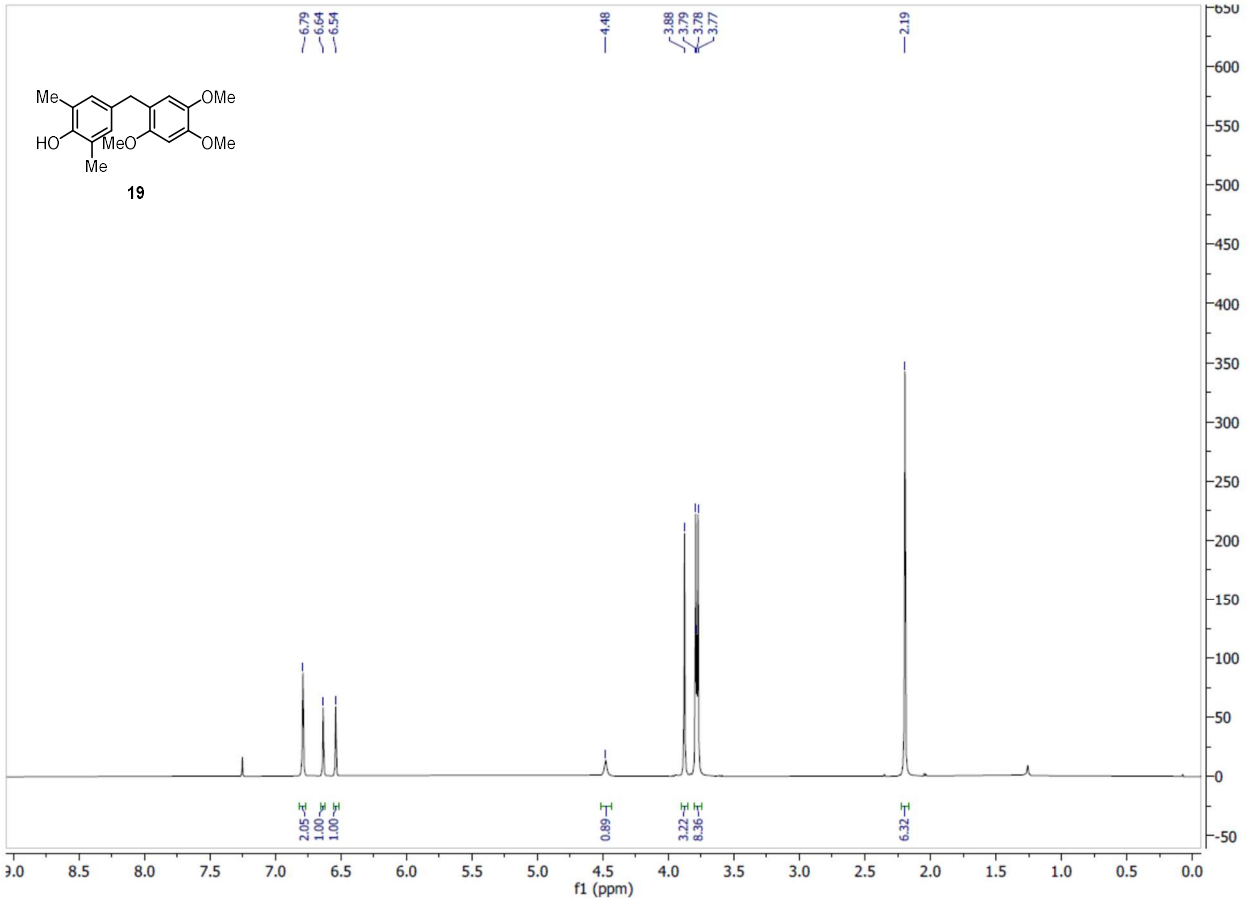
1-(*tert*-butyl)-4-chlorobenzene (**10**) (500 MHz, $CDCl_3$, $^{13}CNMR$)



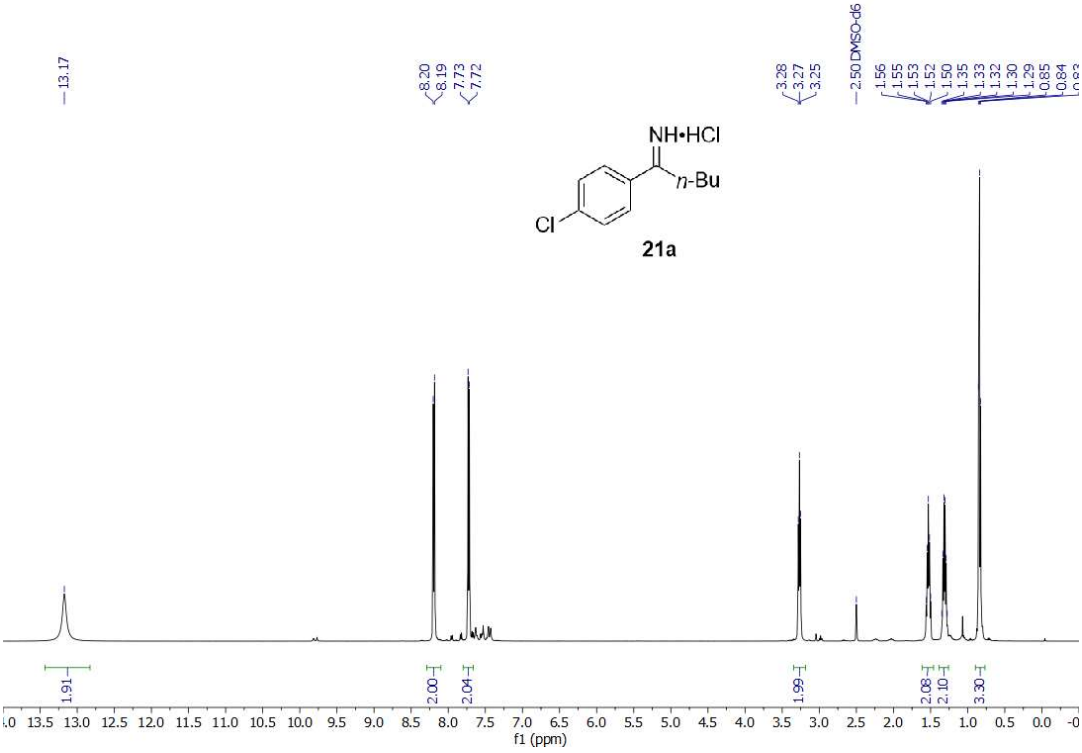
1-(4-phenylbutyl)cyclododecan-1-ol (**16**) $^{1}$H NMR (500 MHz, $CDCl_3$, $^{1}$HNMR)



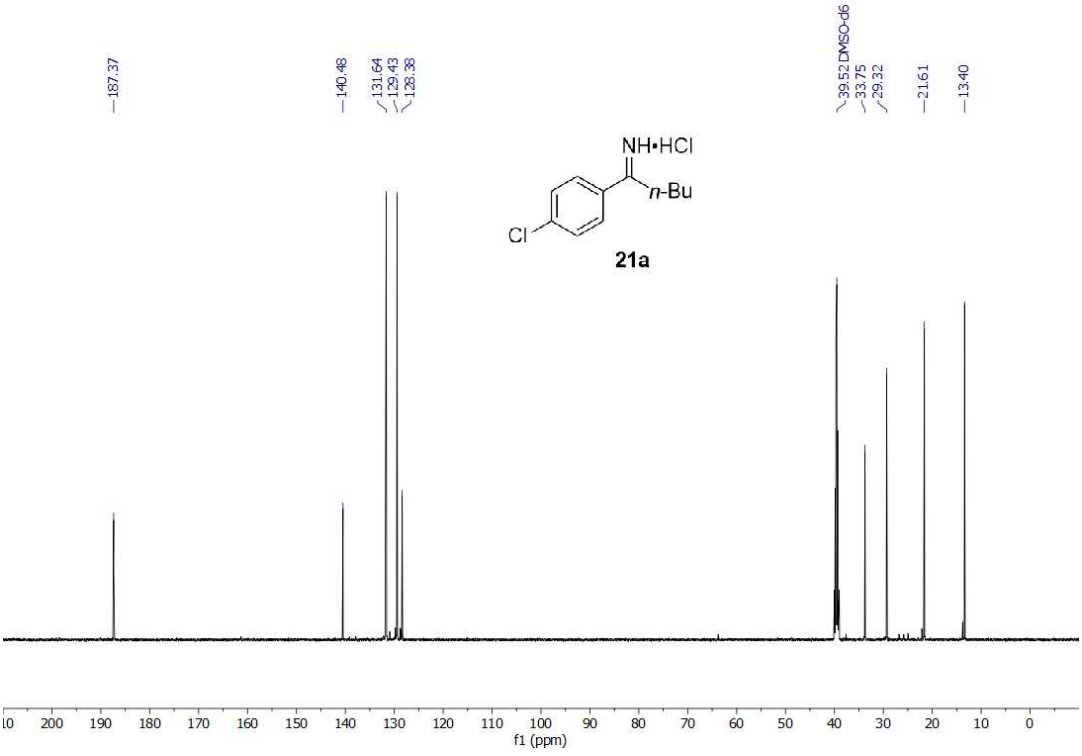
2,6-dimethyl-4-(2,4,5-trimethoxybenzyl)phenol (**19**) (400 MHz, $CDCl_3$, $^1$HNMR)



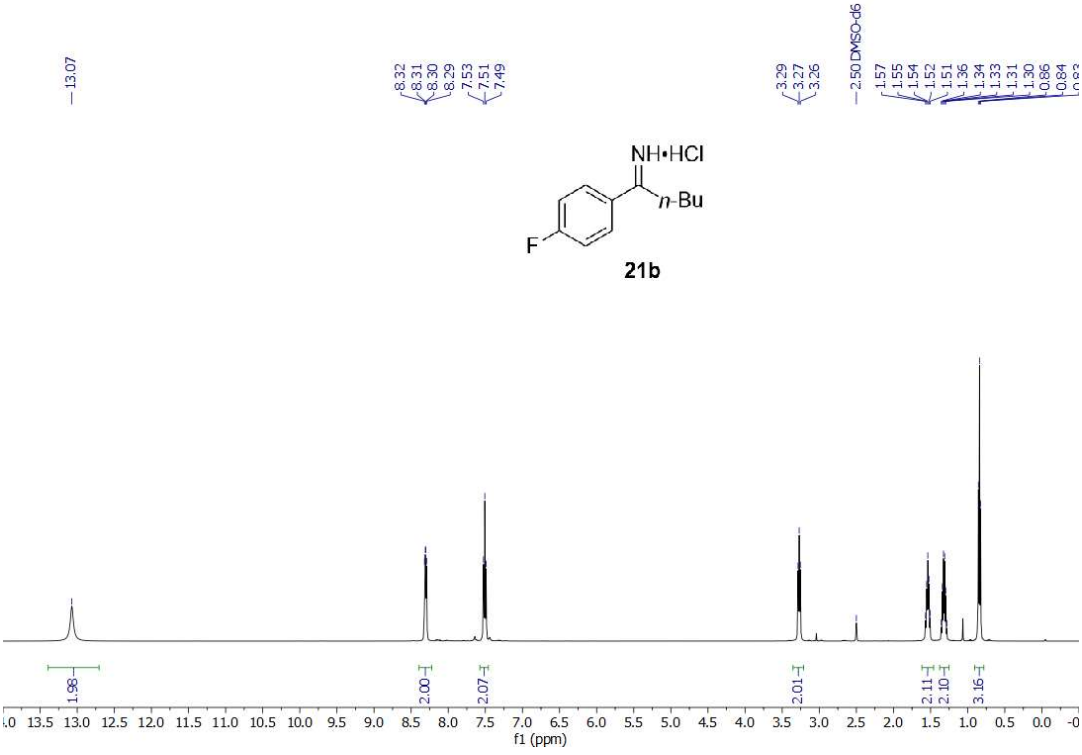
1-(4-chlorophenyl)pentan-1-iminium chloride (**21a**) (500 MHz, $d_6$-DMSO, $^1$HNMR)



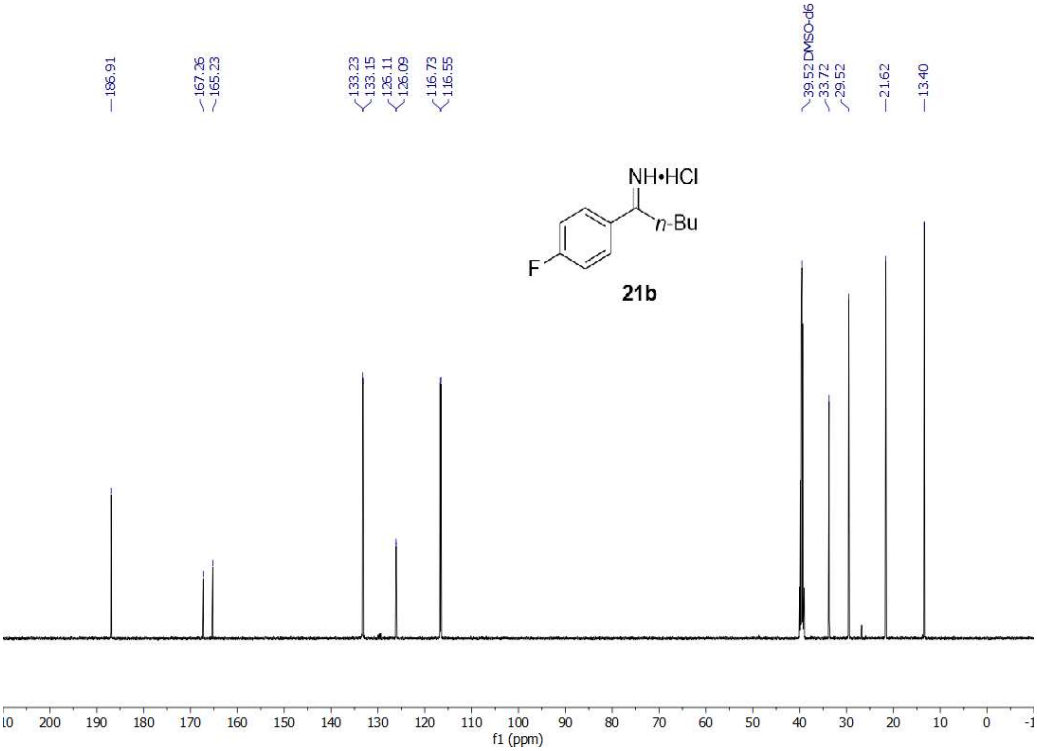
1-(4-chlorophenyl)pentan-1-iminium chloride (**21a**) (126 MHz, $d_6$-DMSO, $^{13}$C NMR)



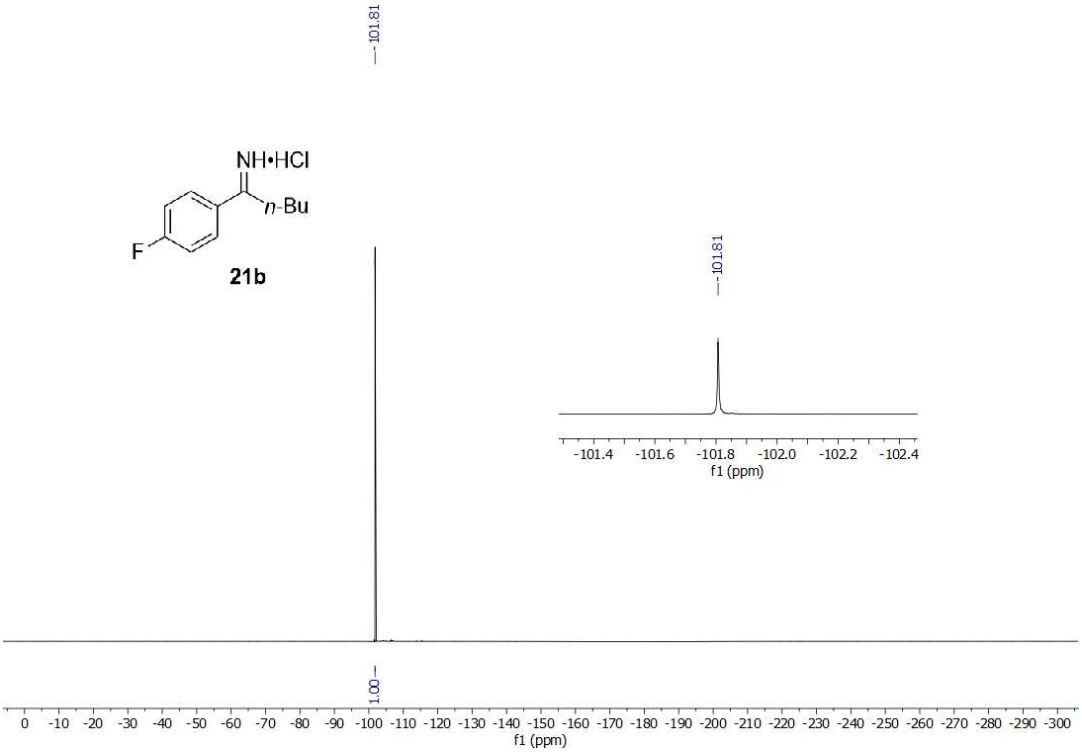
1-(4-flurophenyl)pentan-1-iminium chloride (**21b**) (500 MHz, $d_6$-DMSO, $^1$HNMR)



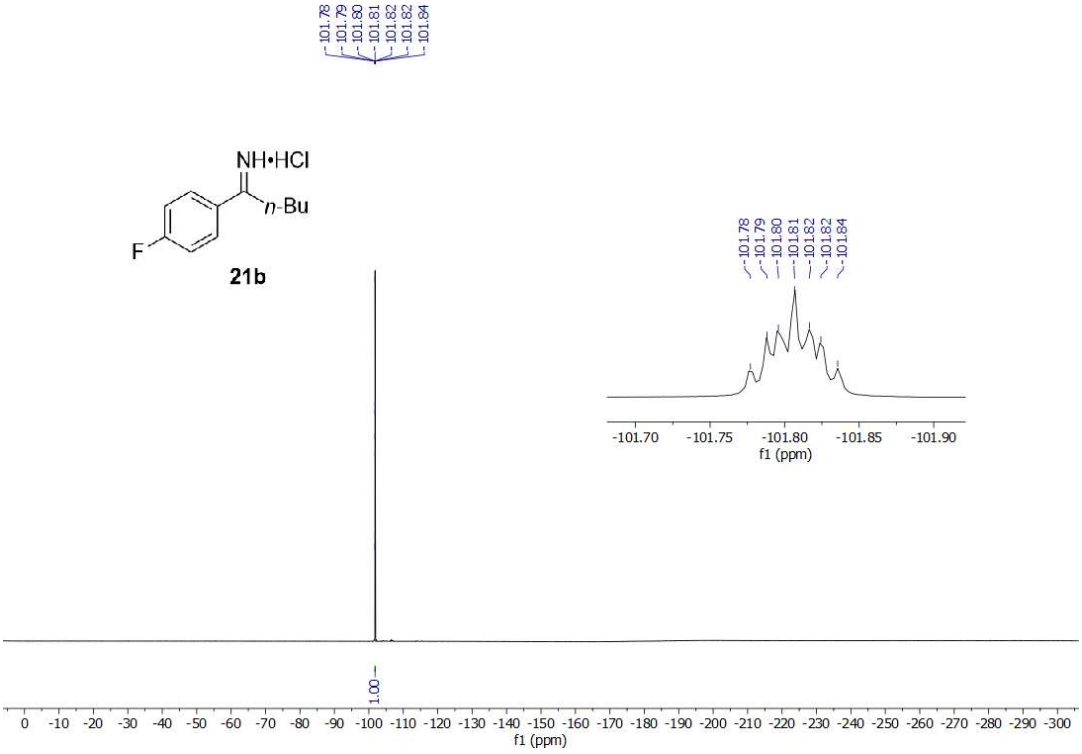
1-(4-flurophenyl)pentan-1-iminium chloride (**21b**) (126 MHz, $d_6$-DMSO, $^{13}$C NMR)



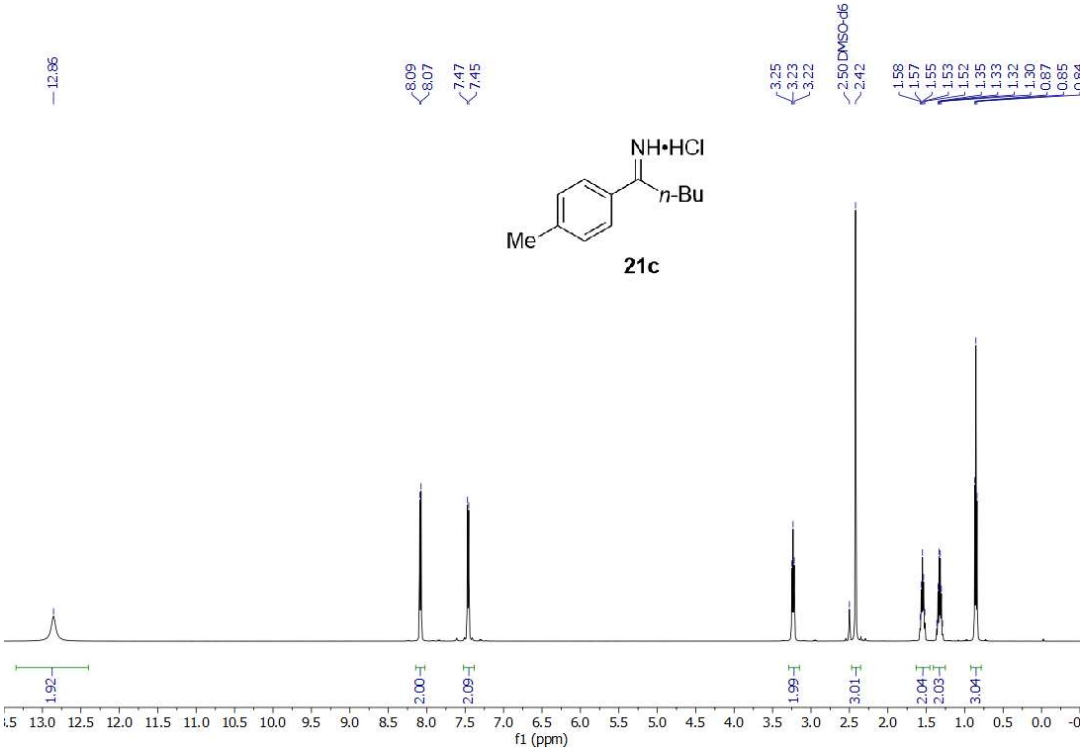
1-(4-flurophenyl)pentan-1-iminium chloride (**21b**) (471 MHz, $d_6$-DMSO, $^{19}F\{^1H\}$ NMR)



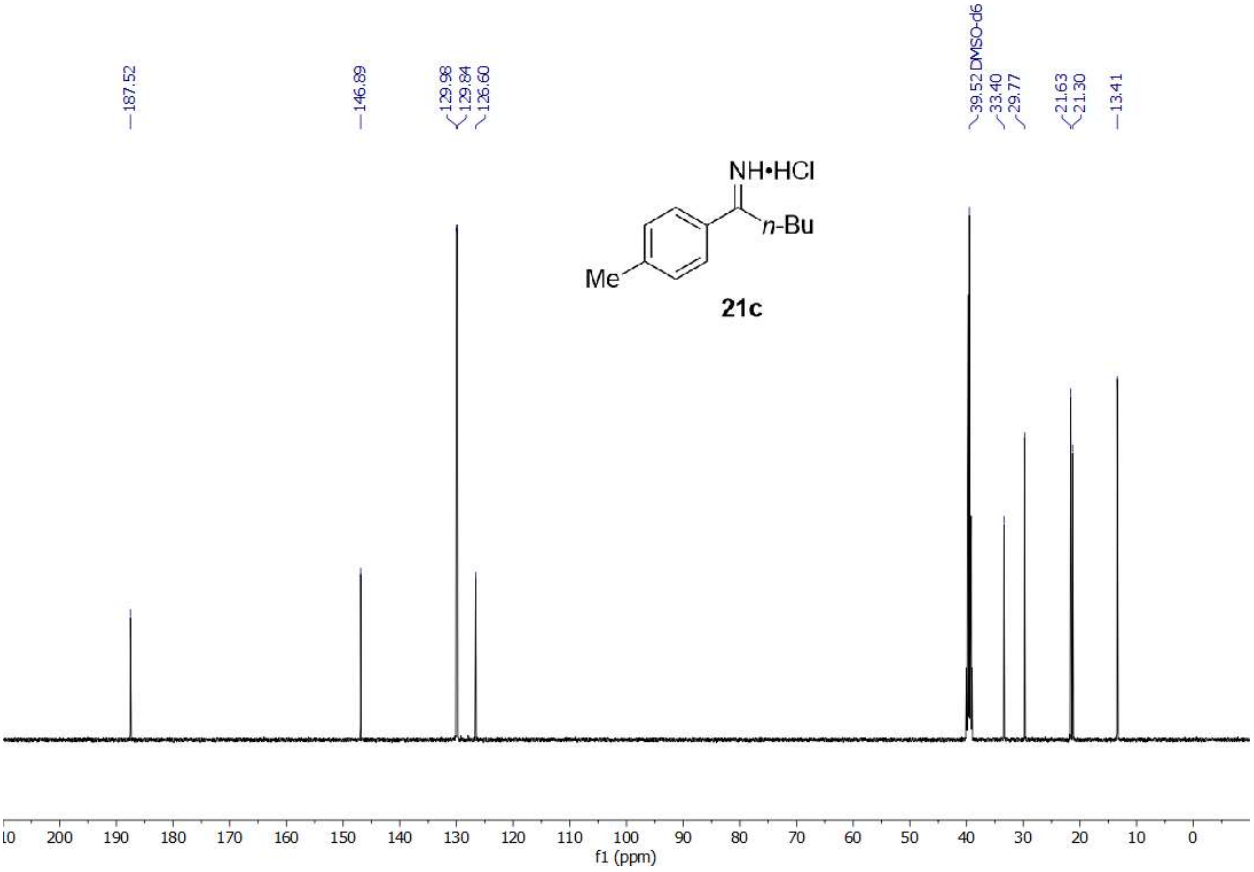
1-(4-flurophenyl)pentan-1-iminium chloride (**21b**) (471 MHz, $d_6$-DMSO, $^{19}$F NMR)



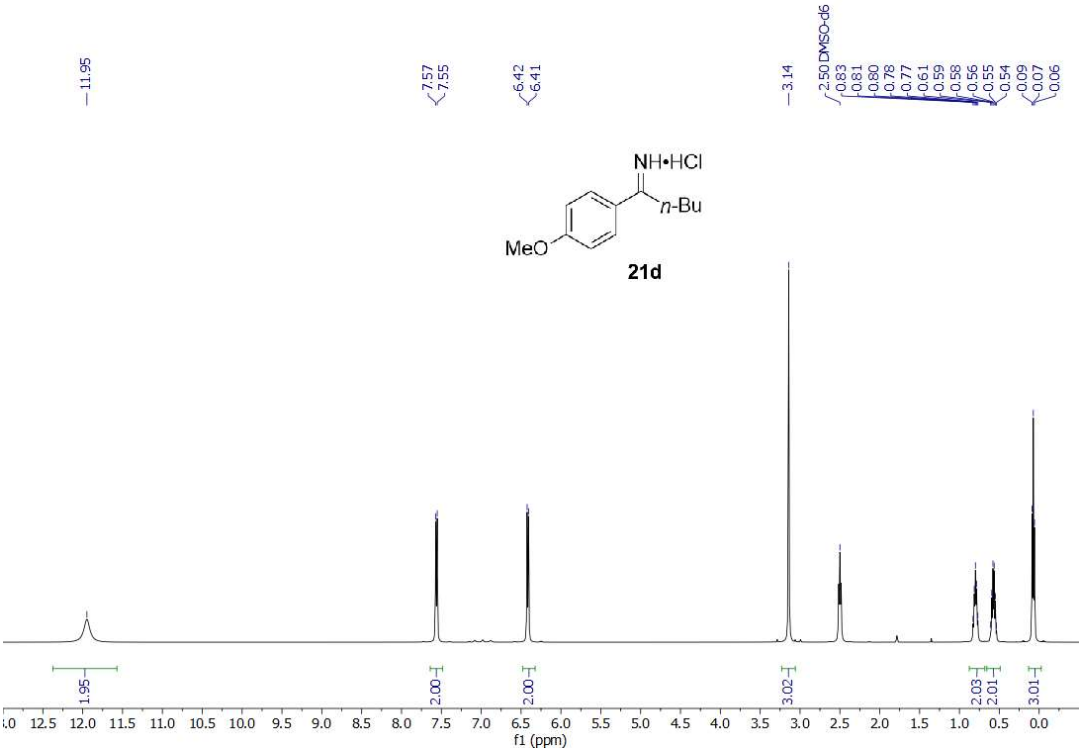
1-(p-tolyl)pentan-1-iminium chloride (**21c**) (500 MHz, $d_6$-DMSO, $^1$HNMR)



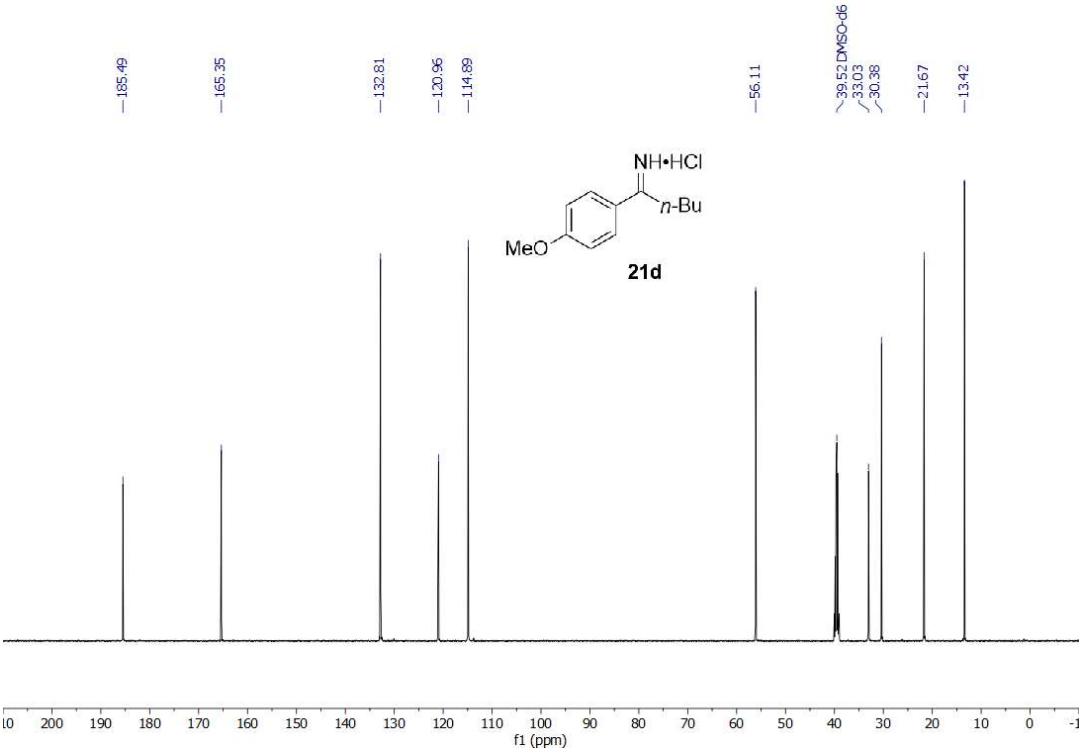
1-(p-tolyl)pentan-1-iminium chloride (**21c**) (126 MHz, $d_6$-DMSO, $^{13}$C NMR)



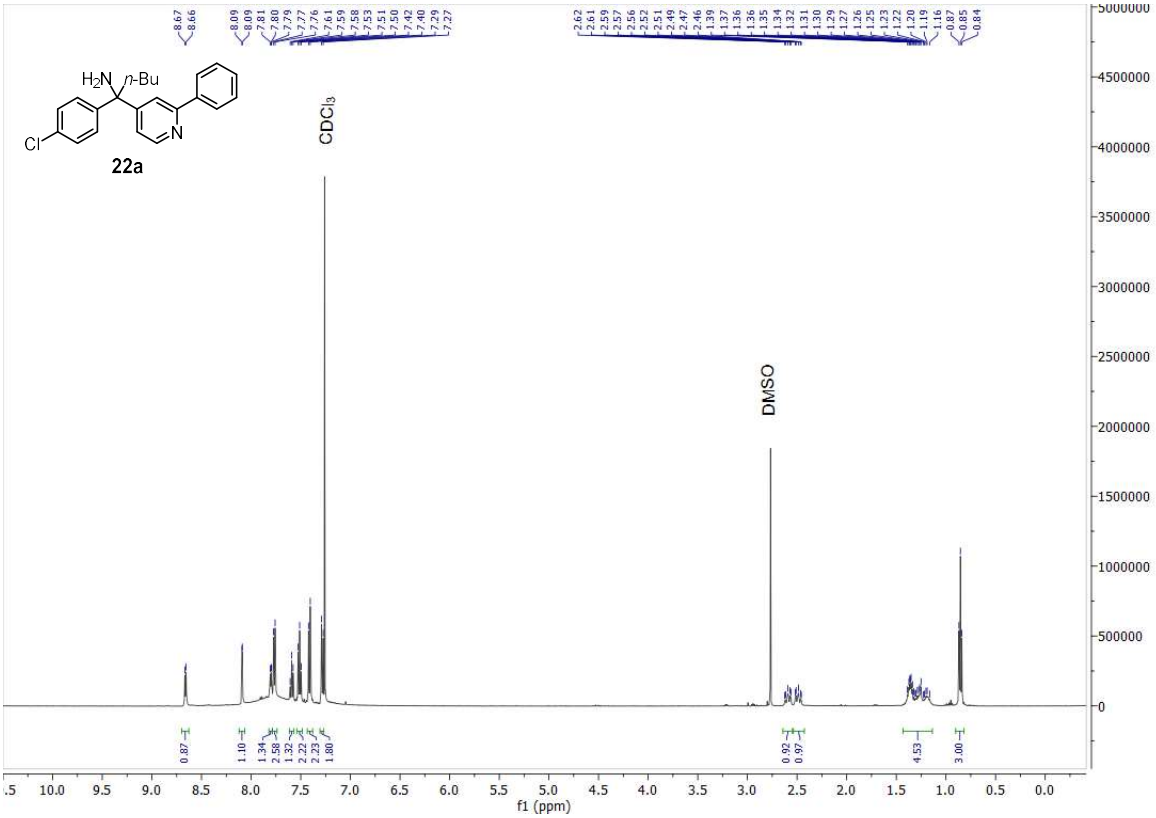
1-(4-methoxyphenyl)pentan-1-iminium chloride **(21d)** (500 MHz, $d_6$-DMSO, $^1$HNMR)



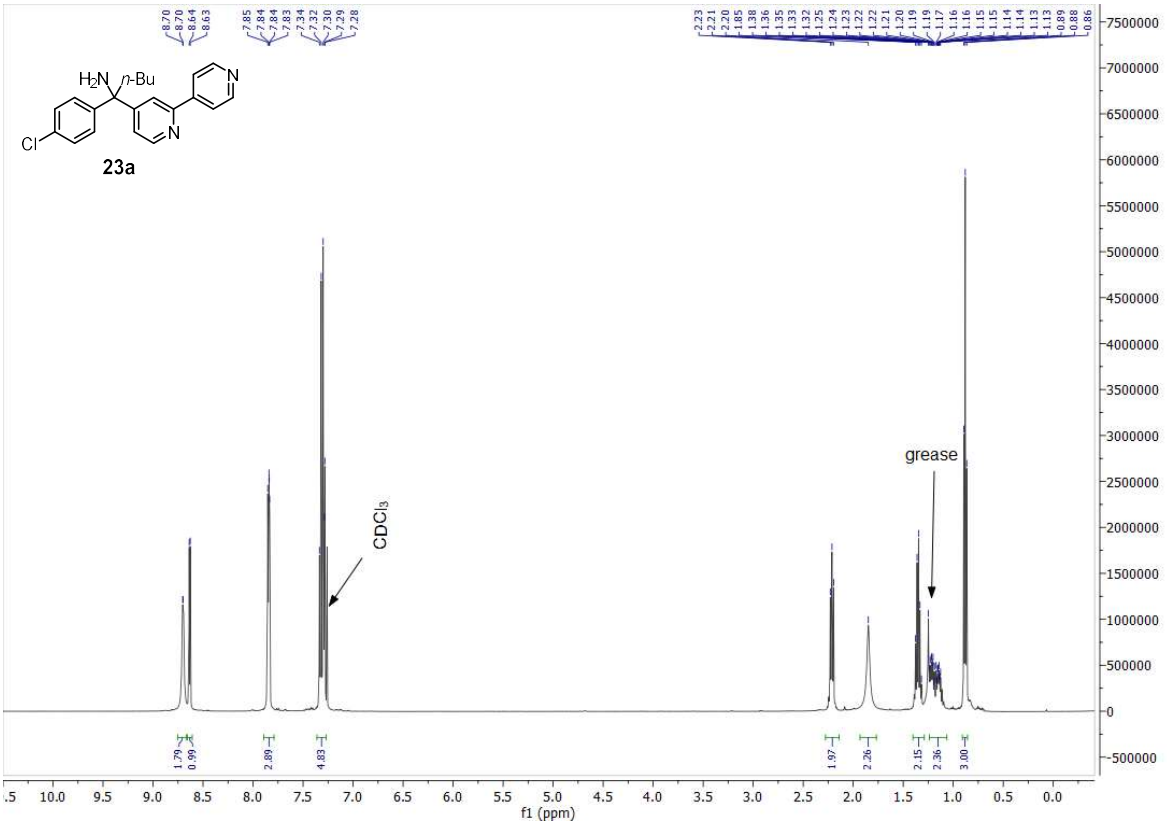
1-(4-methoxyphenyl)pentan-1-iminium chloride **(21d)** (126 MHz, $d_6$-DMSO, $^{13}$C NMR)



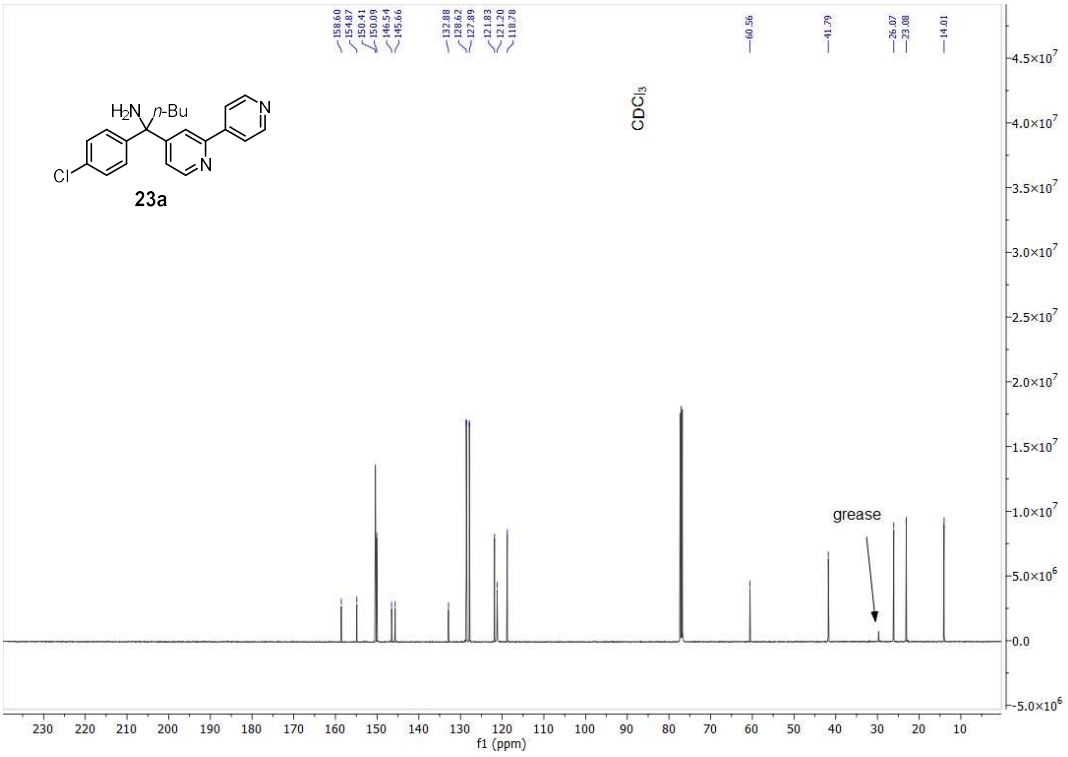
1-(4-chlorophenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22a•3TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



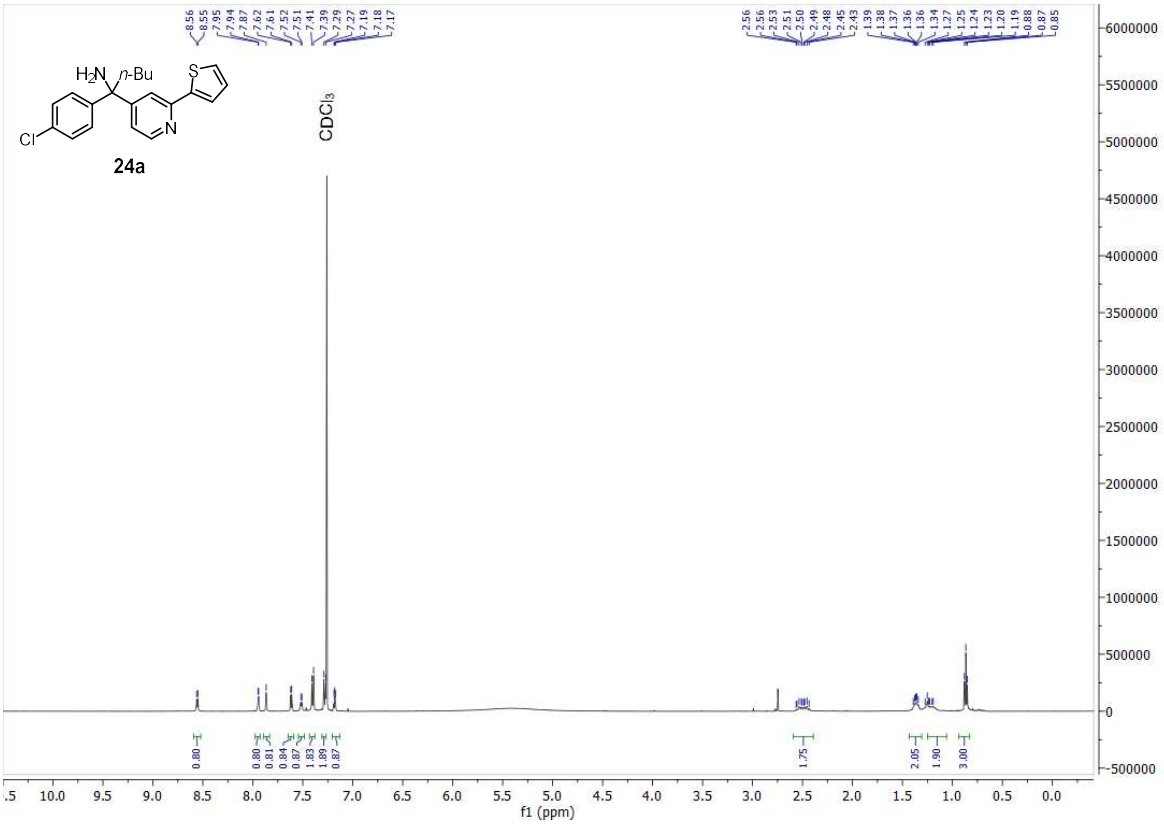
1-([2,4'-bipyridin]-4-yl)-1-(4-chlorophenyl)pentan-1-amine (**23a**) (500 MHz, $CDCl_3$, $^1$HNMR)



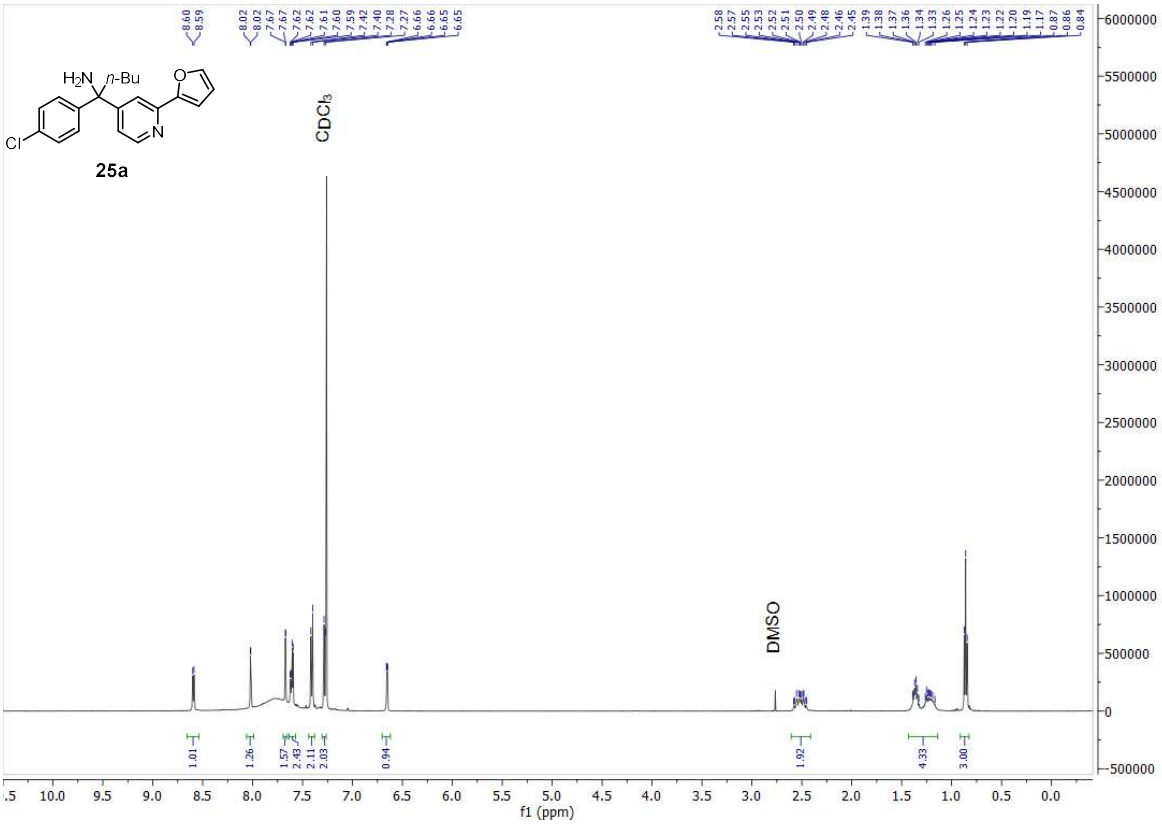
1-([2,4'-bipyridin]-4-yl)-1-(4-chlorophenyl)pentan-1-amine (**23a**) (126 MHz, $CDCl_3$, $^{13}CNMR$)



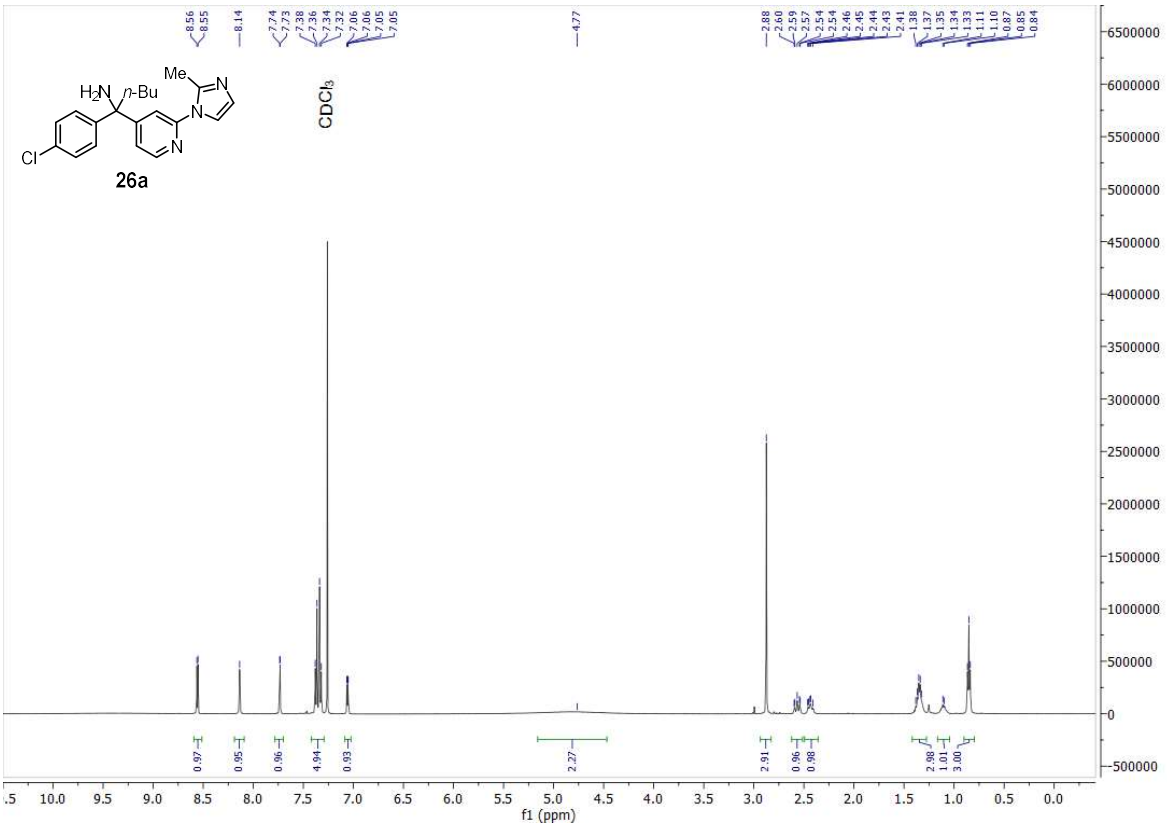
1-(4-chlorophenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24a•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



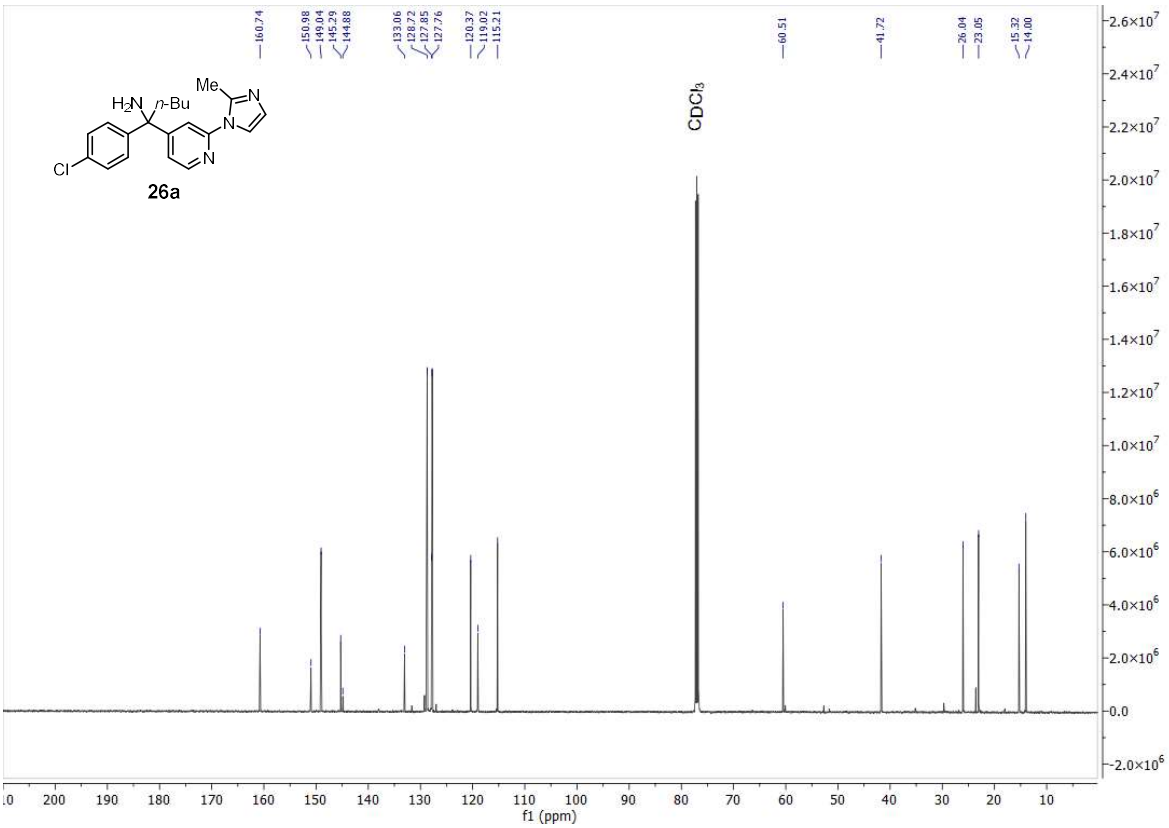
1-(4-chlorophenyl)-1-(2-(furan-2-yl)pyridin-4-yl)pentan-1-amine (**25a•3TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



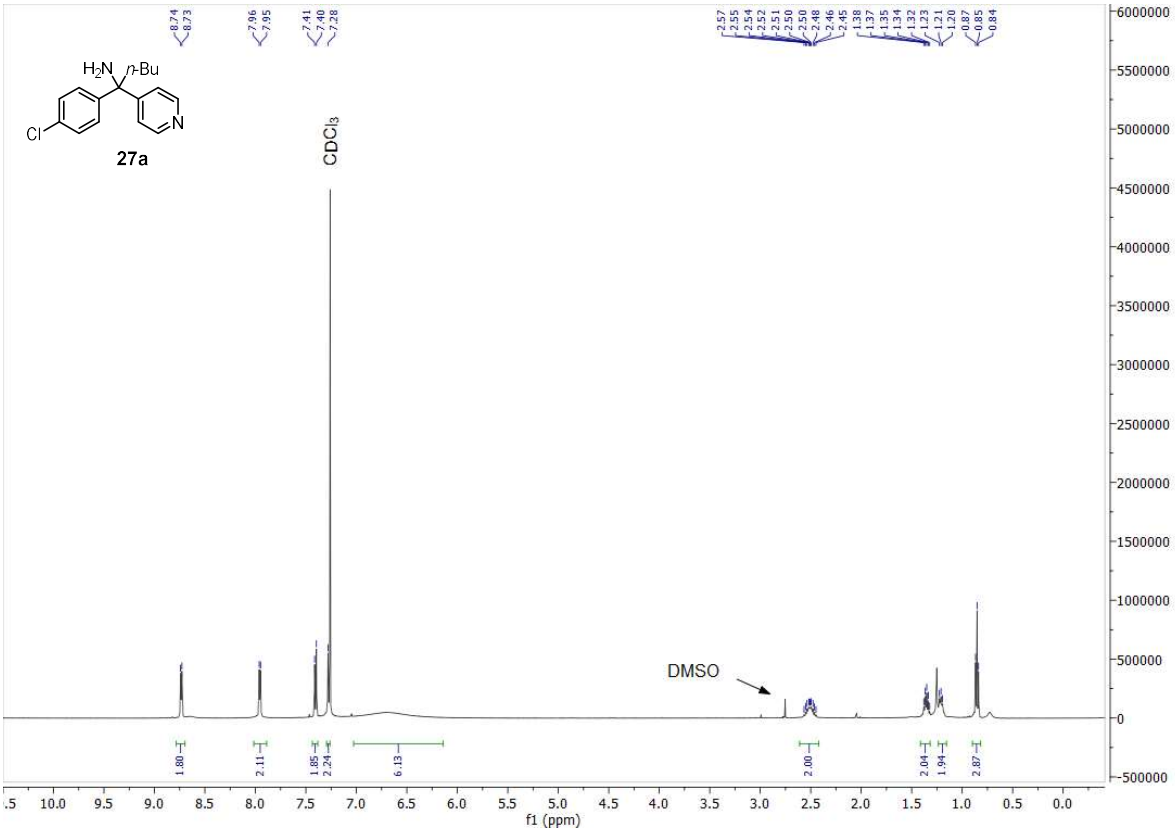
1-(4-chlorophenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26a**) (500 MHz, $CDCl_3$, $^1$HNMR)



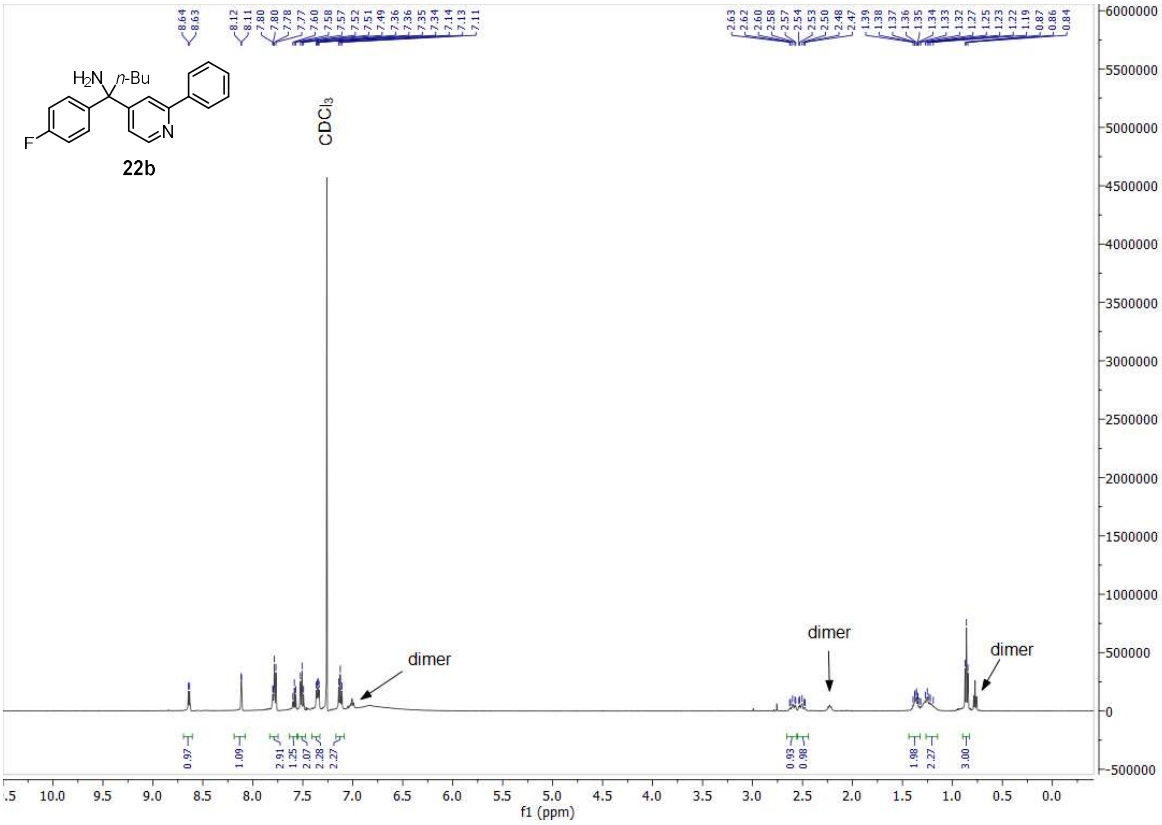
1-(4-chlorophenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26a**) (126 MHz, $CDCl_3$, $^{13}CNMR$)



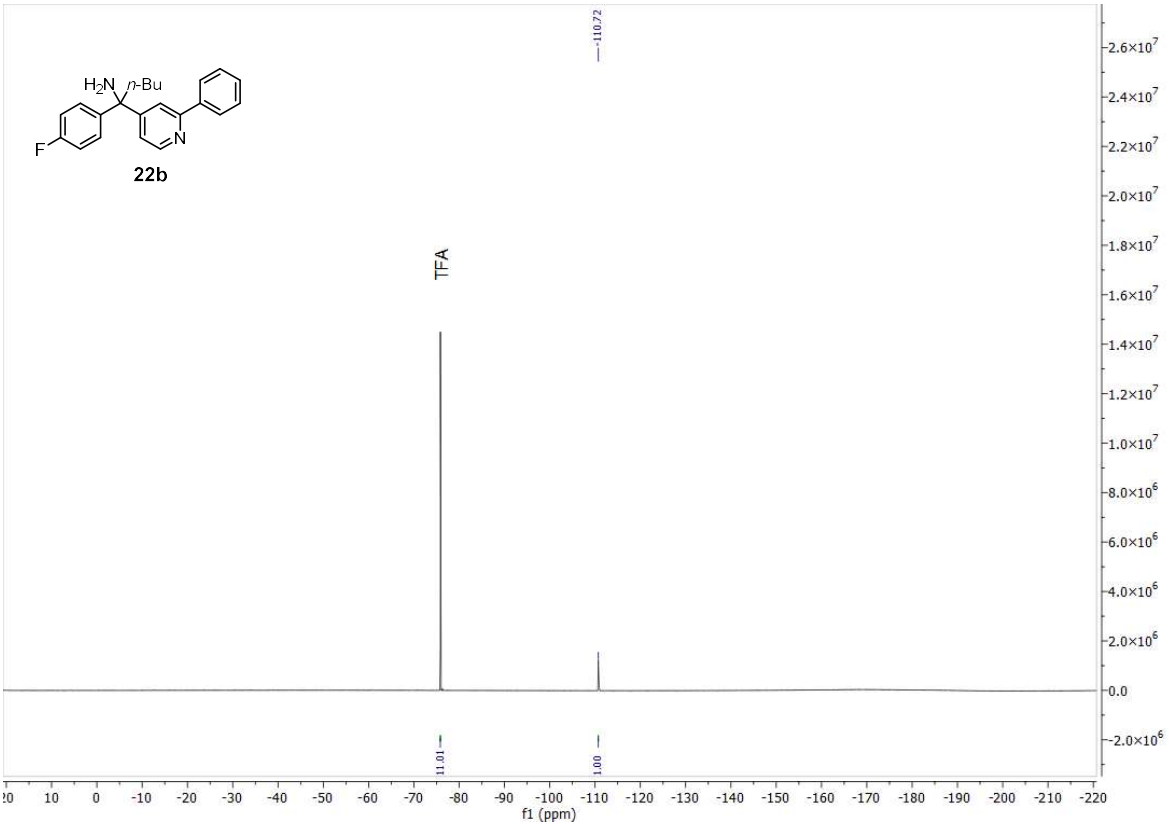
1-(4-chlorophenyl)-1-(pyridin-4-yl)pentan-1-amine (**27a•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



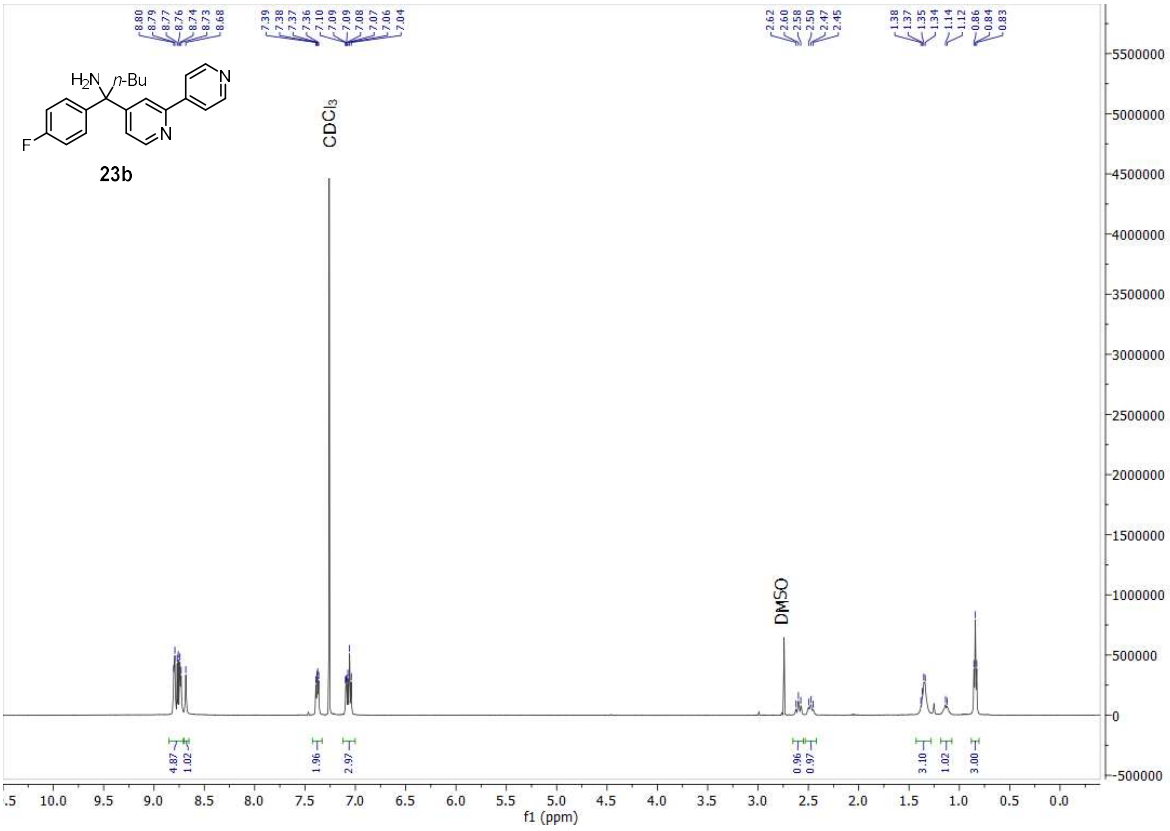
1-(4-fluorophenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22b•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



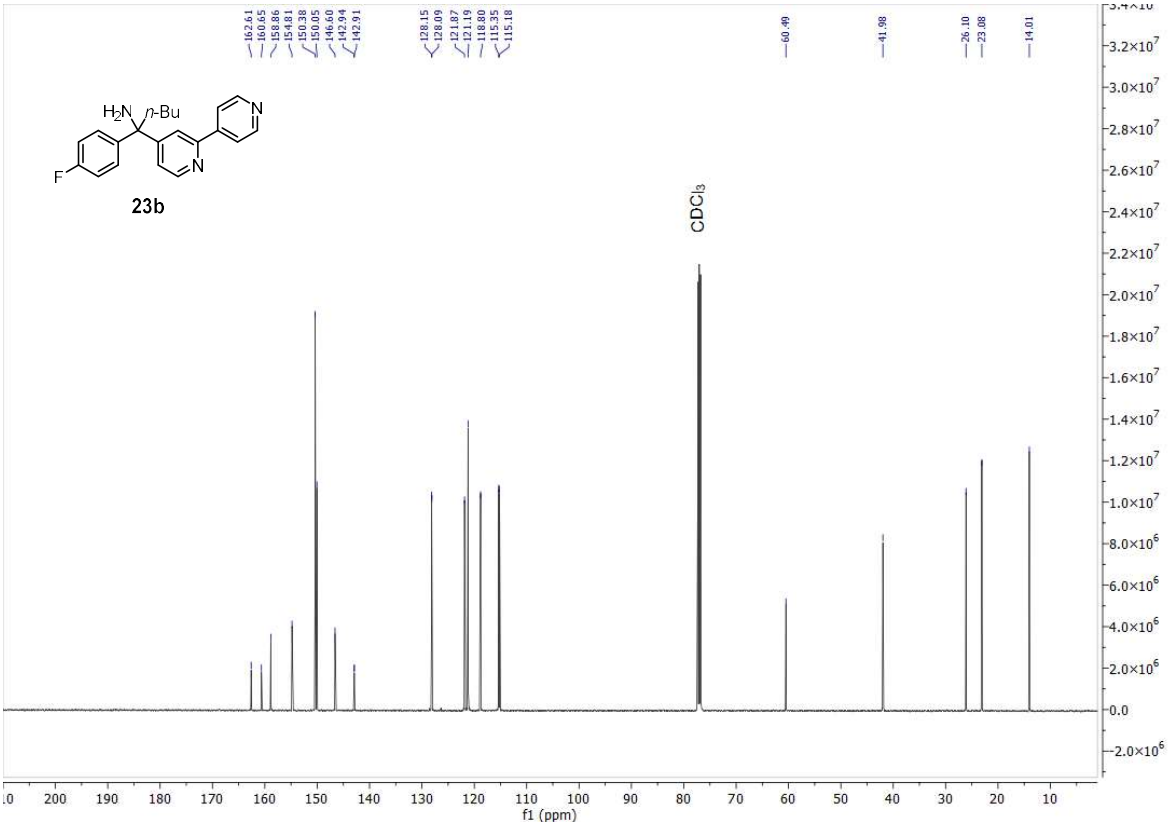
1-(4-fluorophenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22b•4TFA**) (471 MHz, $CDCl_3$, $^{19}F\{H\}$ NMR)



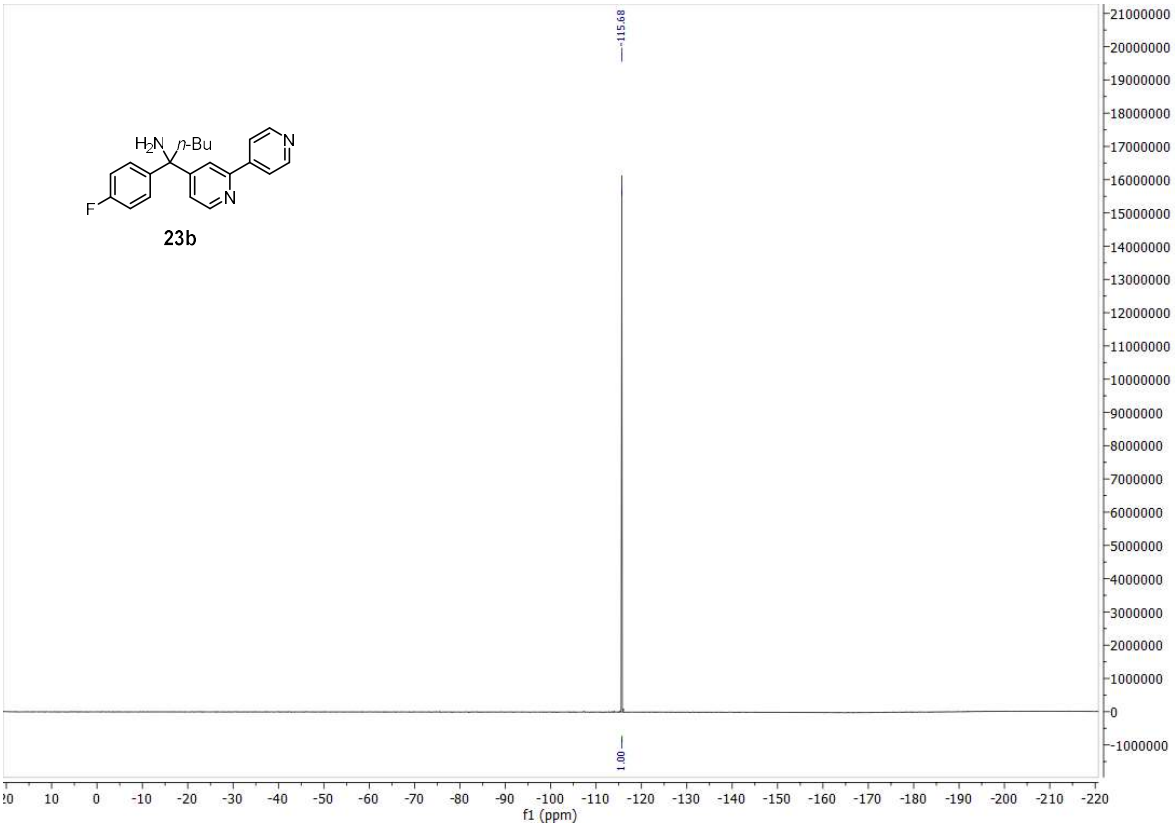
1-([2,4'-bipyridin]-4-yl)-1-(4-fluorophenyl)pentan-1-amine (**23b**) (500 MHz, $CDCl_3$, $^1$HNMR)



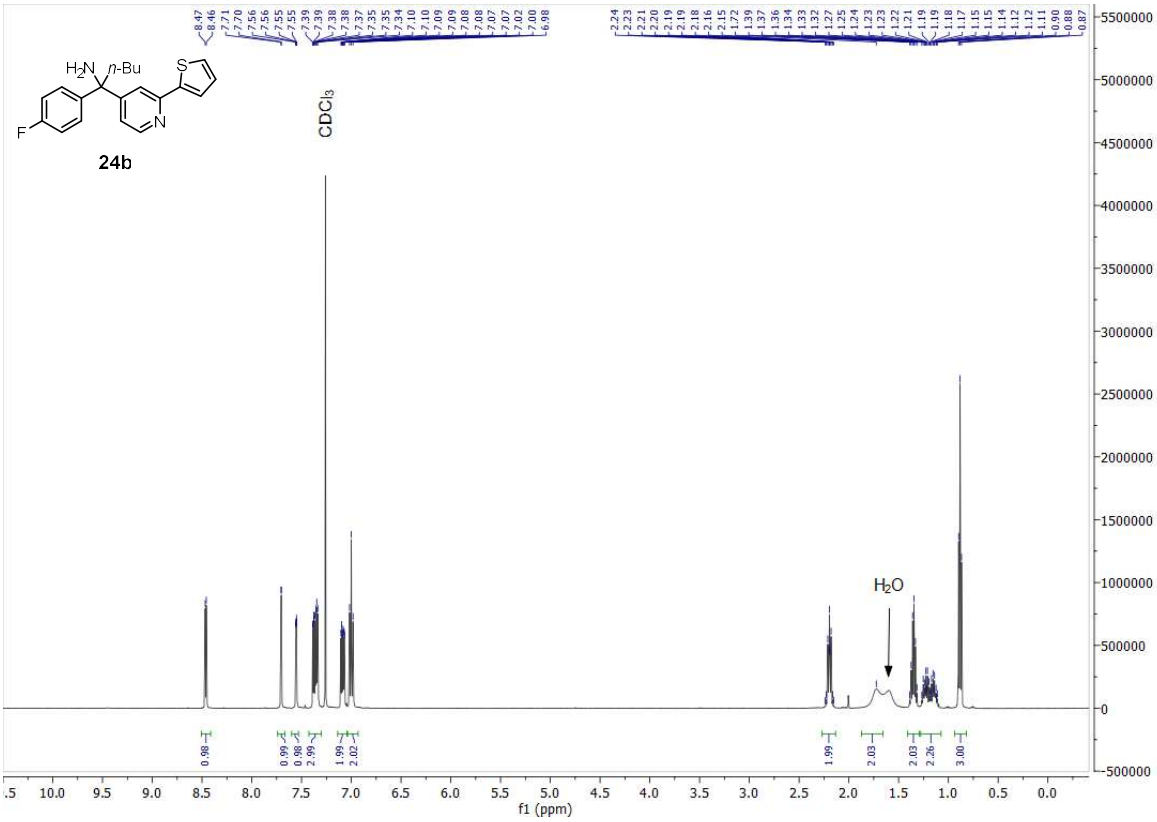
1-([2,4'-bipyridin]-4-yl)-1-(4-fluorophenyl)pentan-1-amine (**23b**) (126 MHz, $CDCl_3$, $^{13}CNMR$)



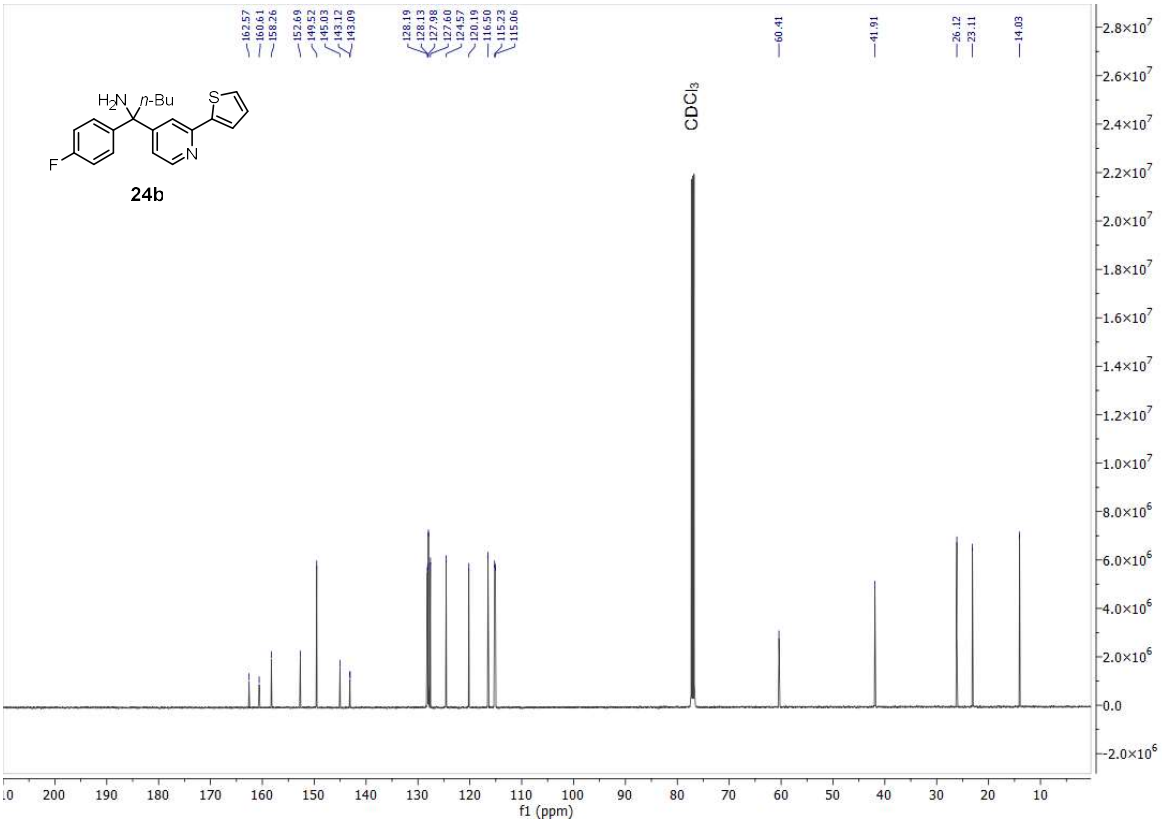
1-([2,4'-bipyridin]-4-yl)-1-(4-fluorophenyl)pentan-1-amine (**23b**) (471 MHz, $CDCl_3$, $^{19}F\{H\}$ NMR)



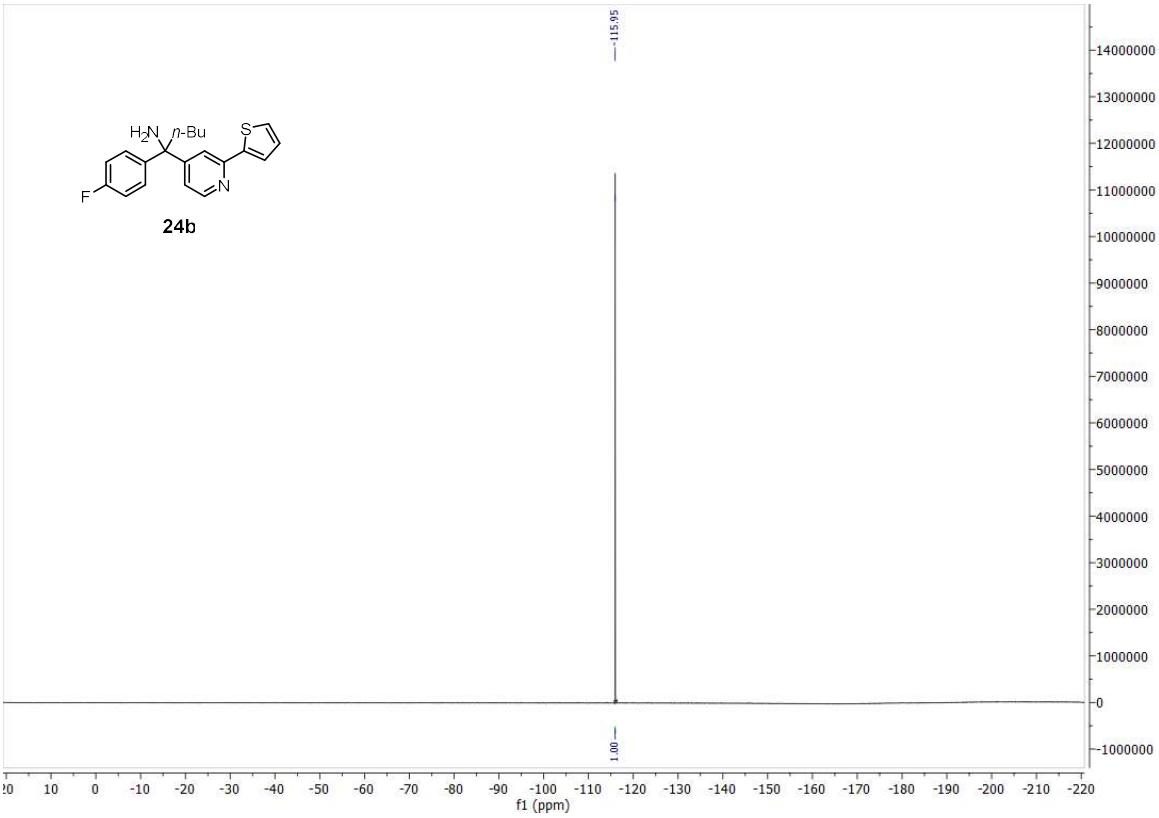
1-(4-fluorophenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24b**) (500 MHz, $CDCl_3$, $^1$HNMR)



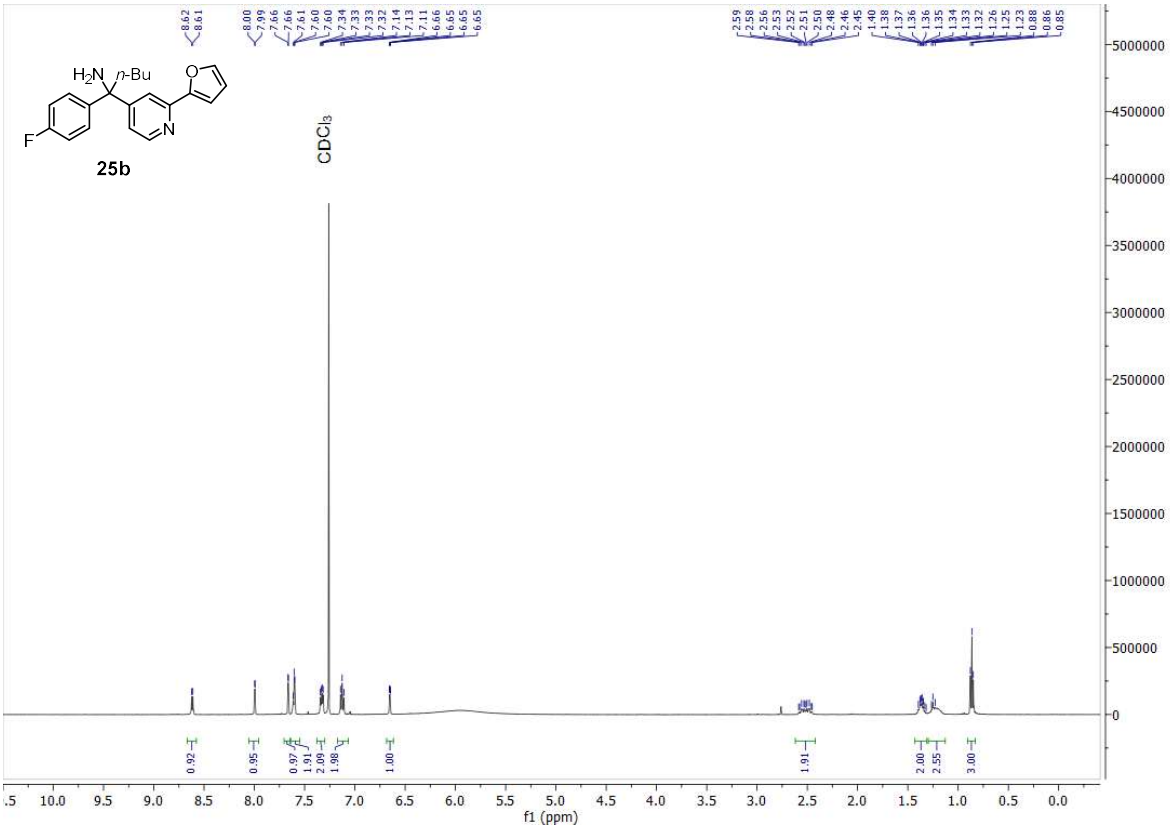
1-(4-fluorophenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24b**) (126 MHz, $CDCl_3$, $^{13}CNMR$)



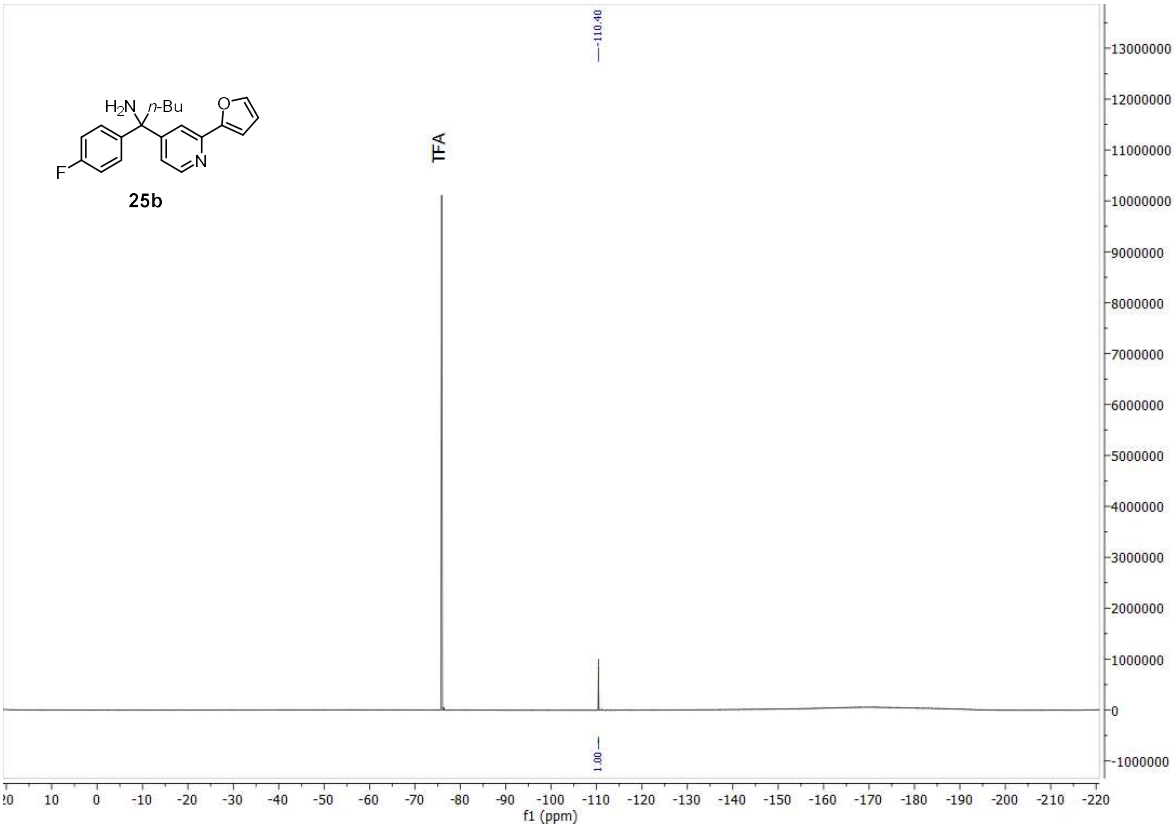
1-(4-fluorophenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24b**) (471 MHz, $CDCl_3$, $^{19}F\{H\}$ NMR)



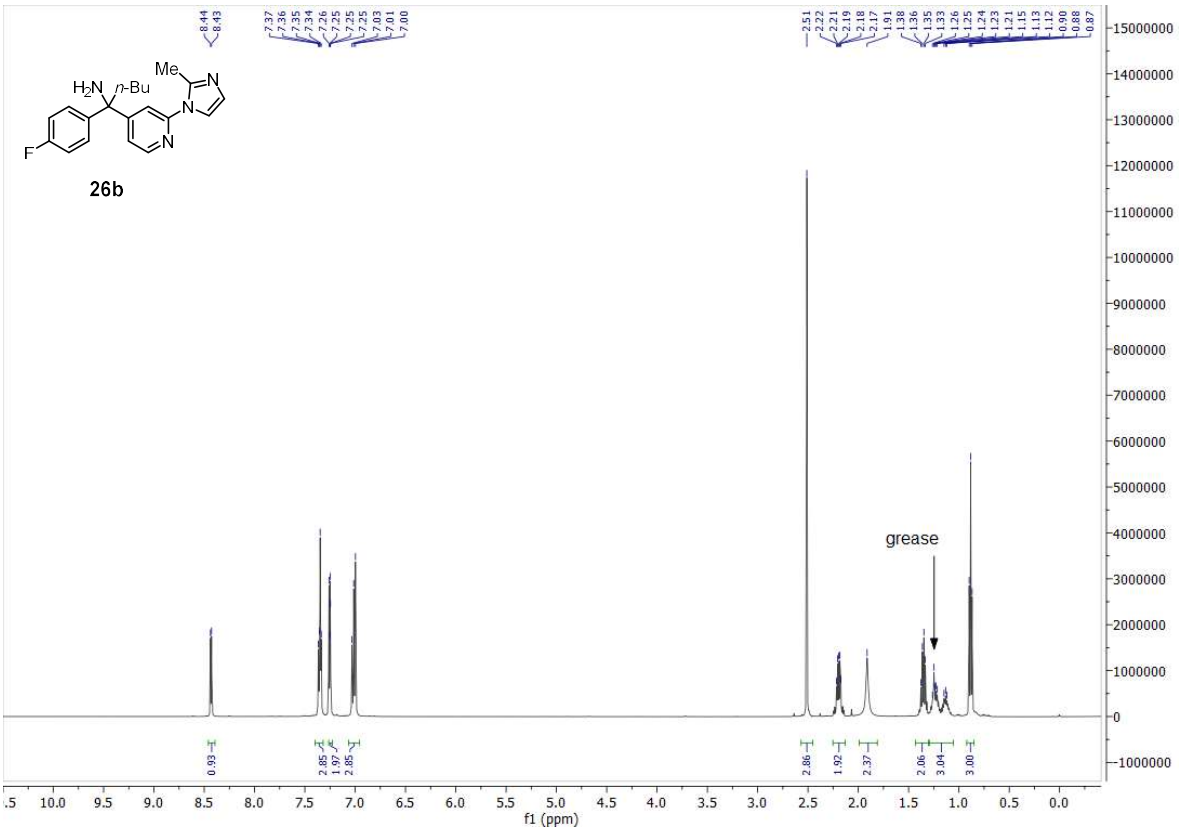
1-(4-fluorophenyl)-1-(2-(furan-2-yl)pyridin-4-yl)pentan-1-amine (**25b•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



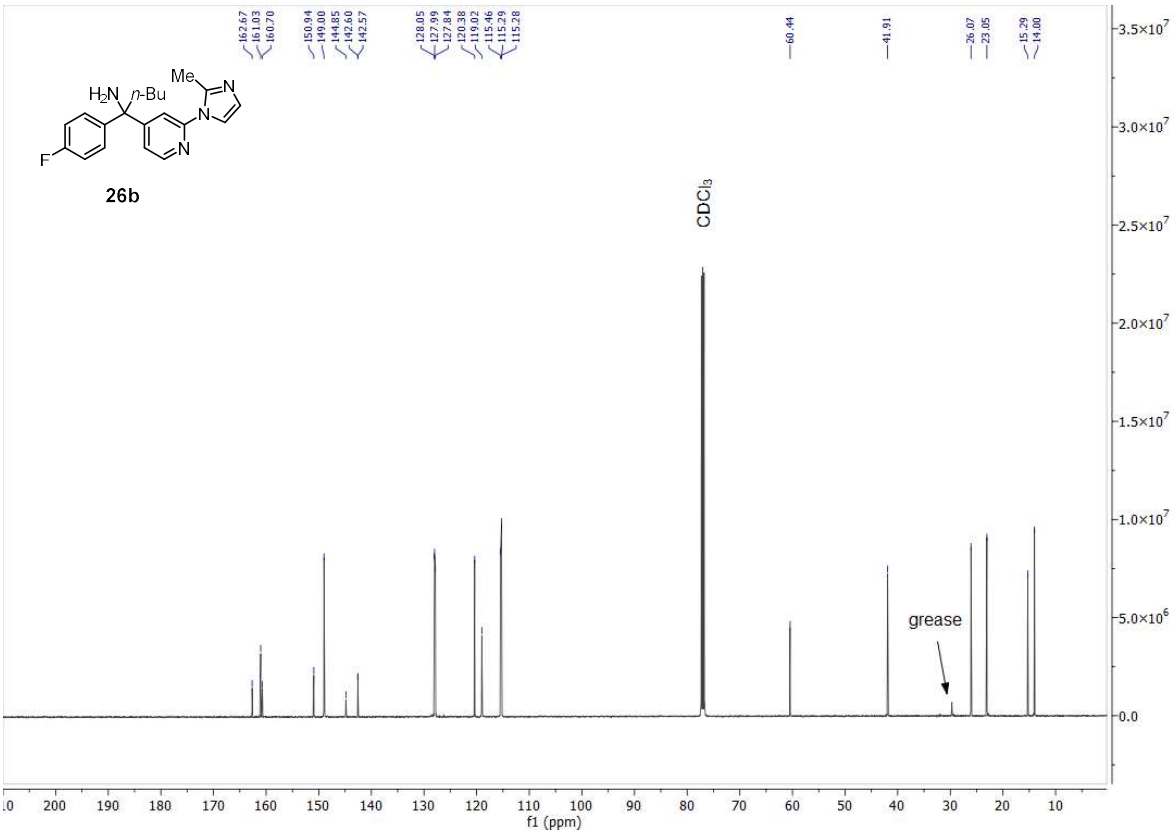
1-(4-fluorophenyl)-1-(2-(furan-2-yl)pyridin-4-yl)pentan-1-amine (**25b•4TFA**) (471 MHz, $CDCl_3$, $^{19}F\{H\}$ NMR)



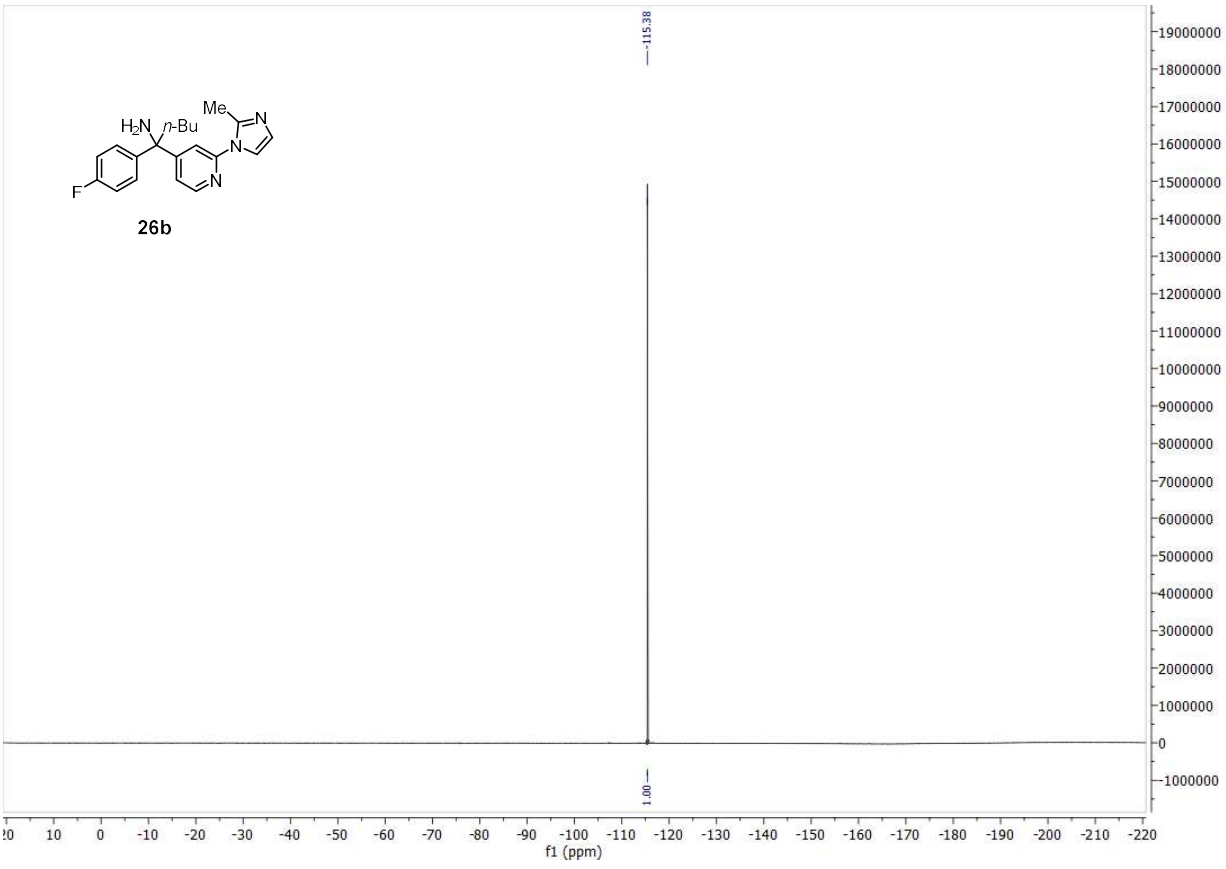
1-(4-fluorophenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26b**) (500 MHz, $CDCl_3$, $^1$HNMR)



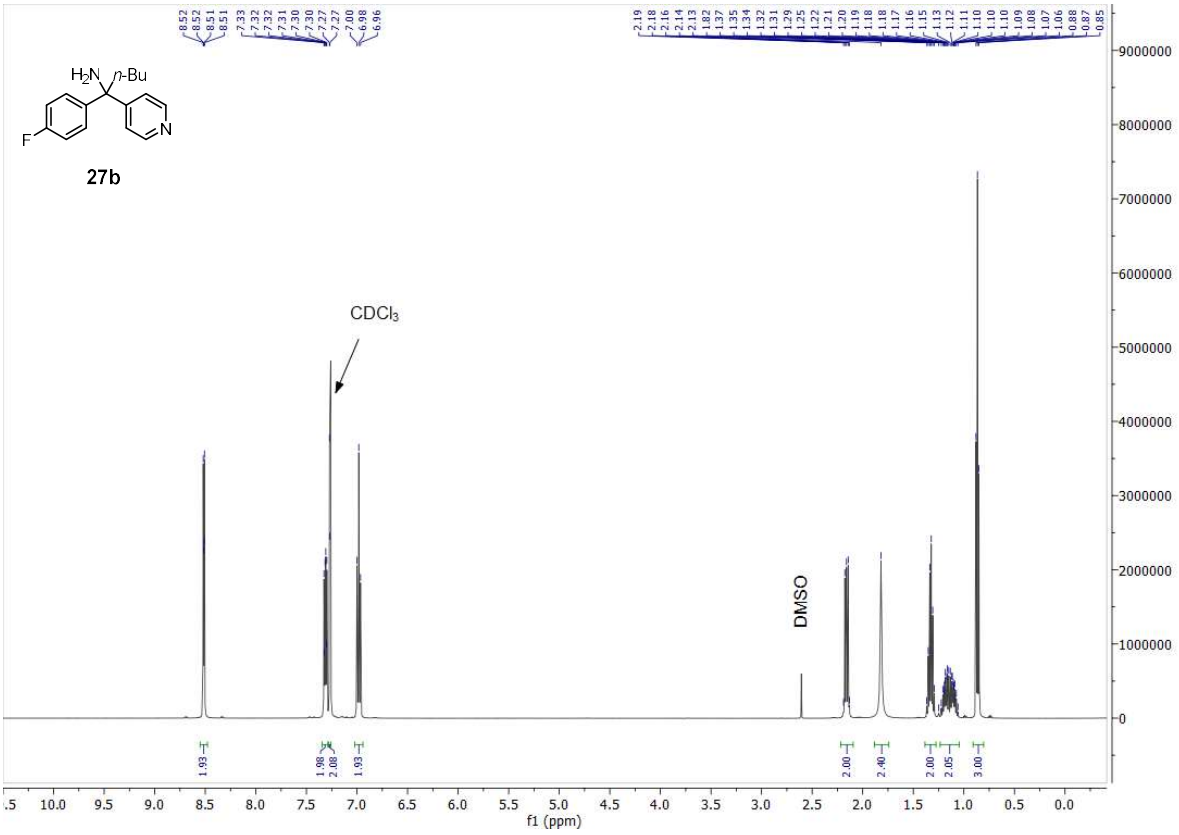
1-(4-fluorophenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26b**) (126 MHz, $CDCl_3$, $^{13}$CNMR)



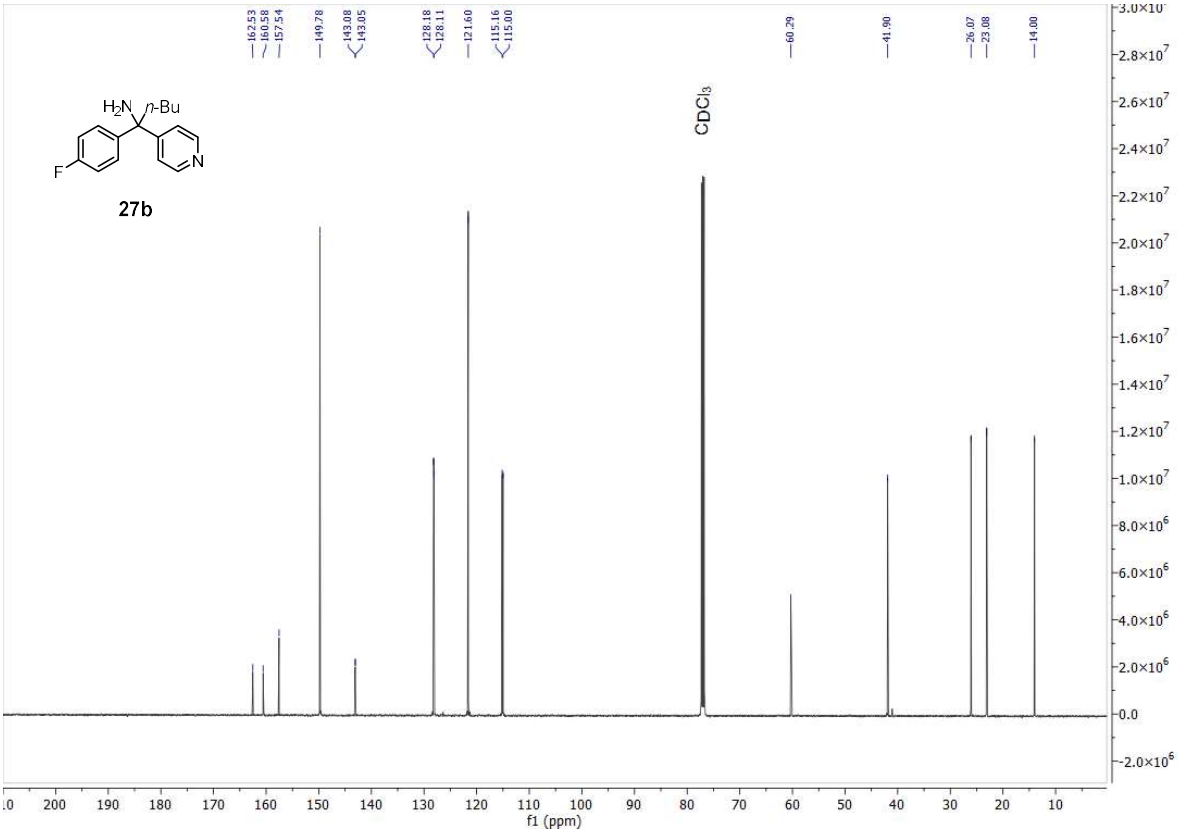
1-(4-fluorophenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26b**) (471 MHz, $CDCl_3$, $^{19}F\{H\}$ NMR)



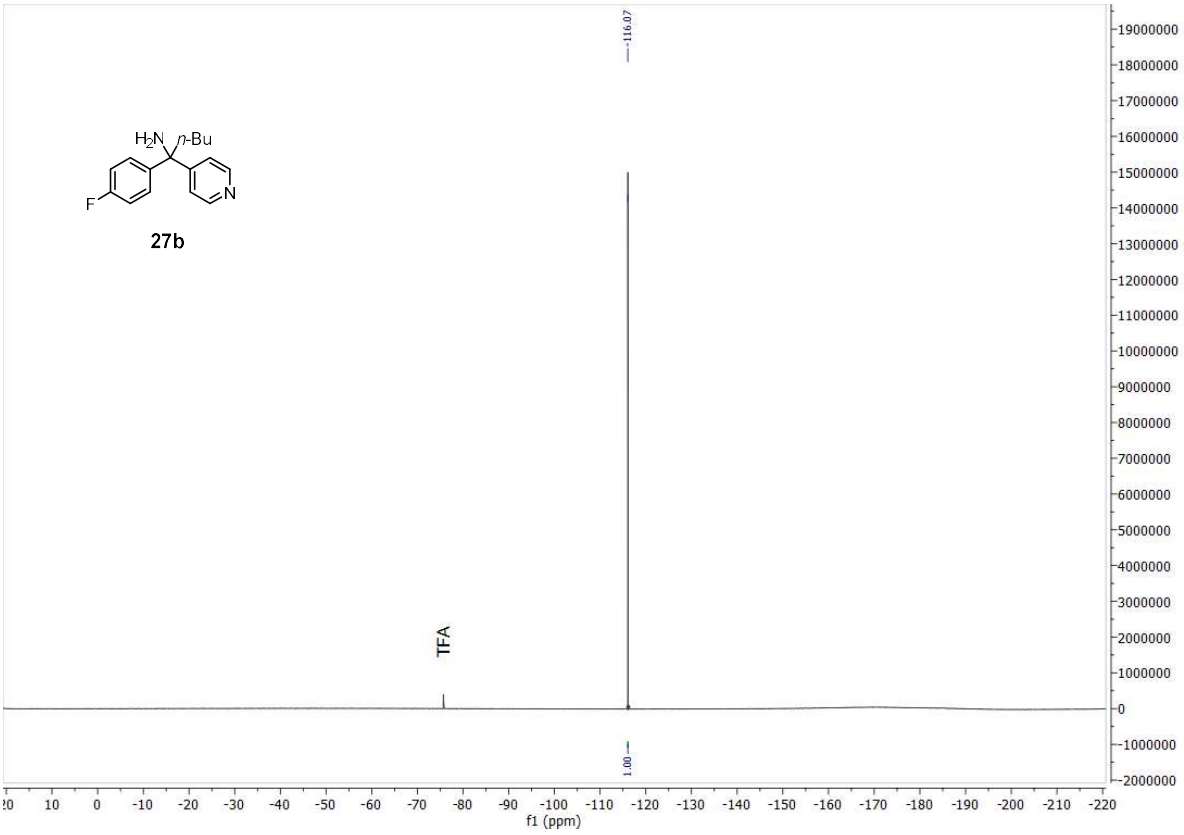
1-(4-fluorophenyl)-1-(pyridin-4-yl)pentan-1-amine (**27b**) (500 MHz, $CDCl_3$, $^1$HNMR)



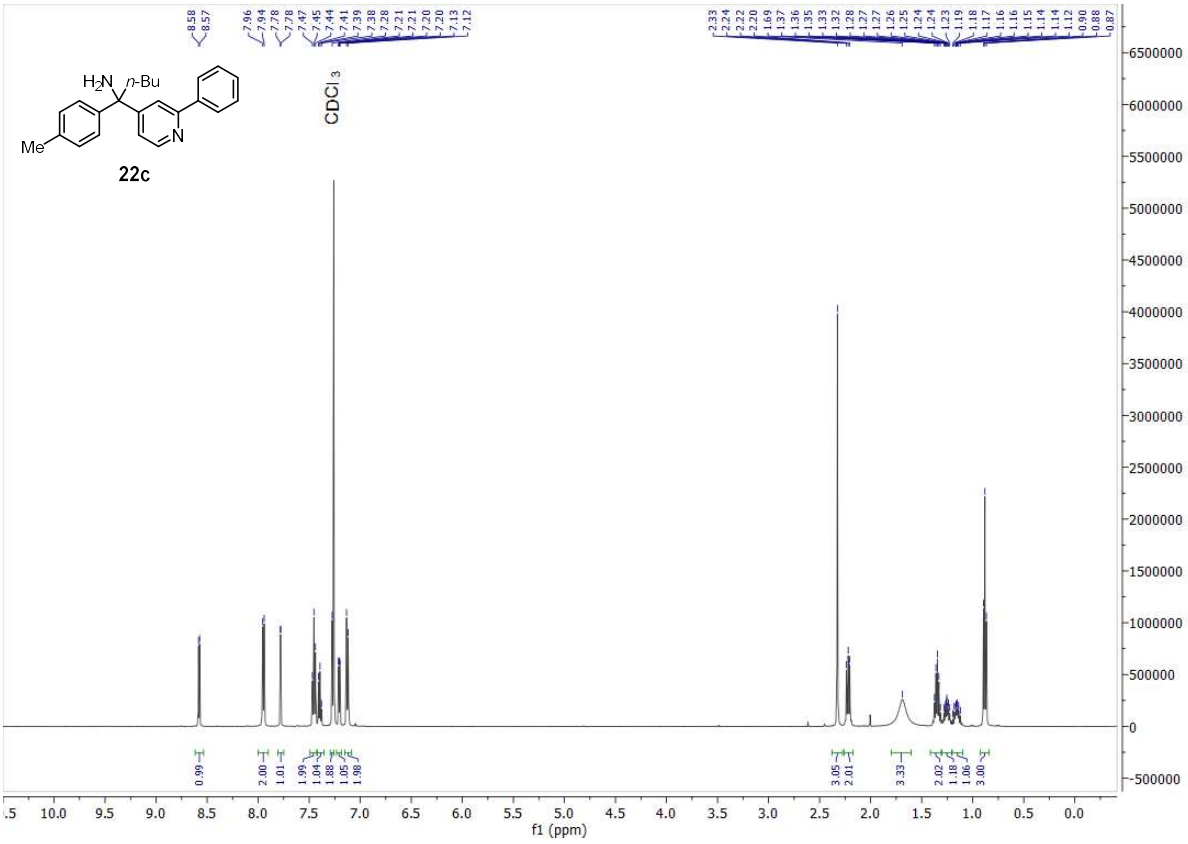
1-(4-fluorophenyl)-1-(pyridin-4-yl)pentan-1-amine (**27b**) (126 MHz, $CDCl_3$, $^{13}$CNMR)



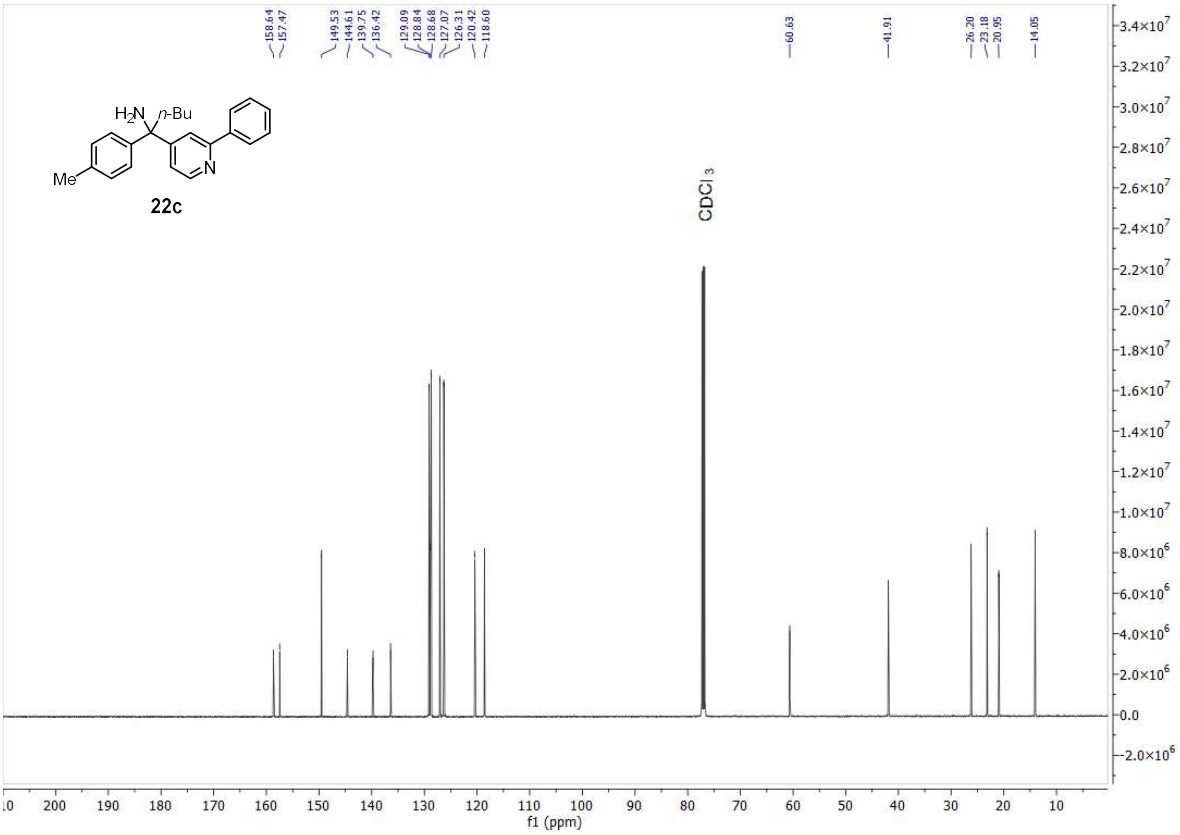
1-(4-fluorophenyl)-1-(pyridin-4-yl)pentan-1-amine (**27b**) (471 MHz, $CDCl_3$, $^{19}F\{H\}$ NMR)



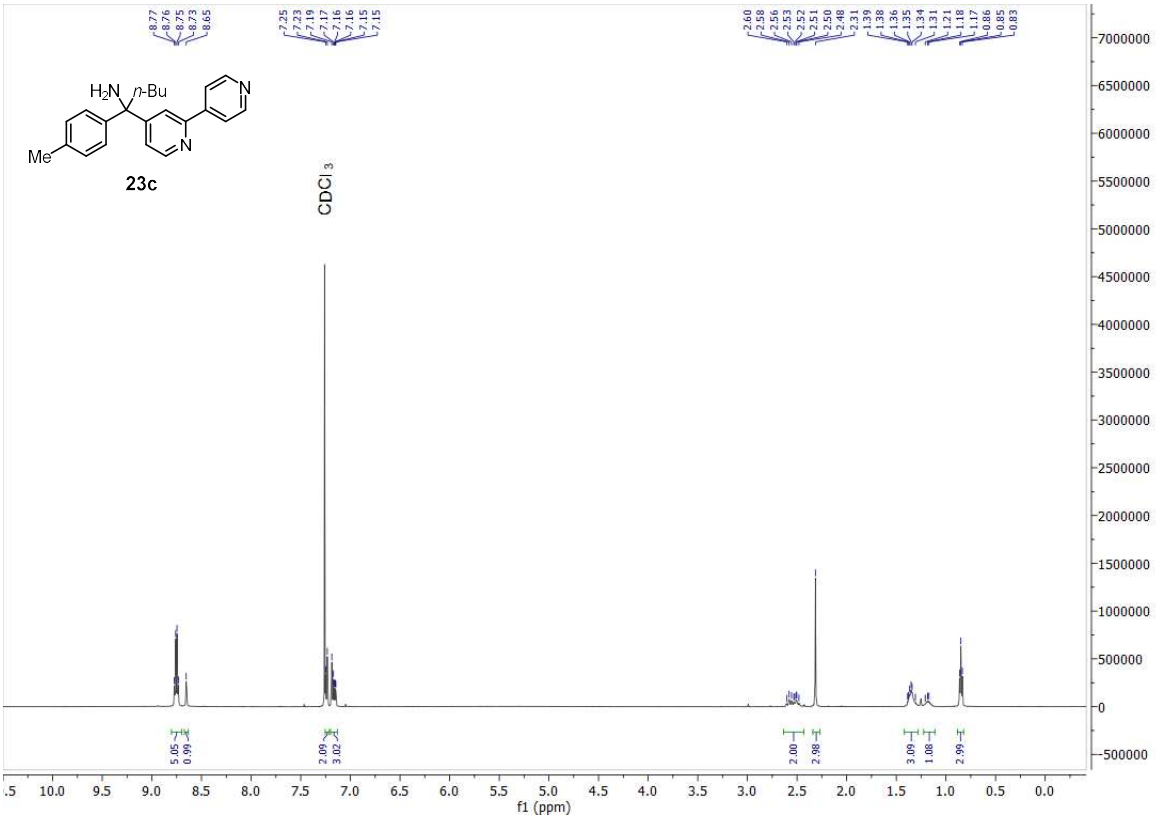
1-(2-phenylpyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**22c**) (500 MHz, $CDCl_3$, $^1$HNMR)



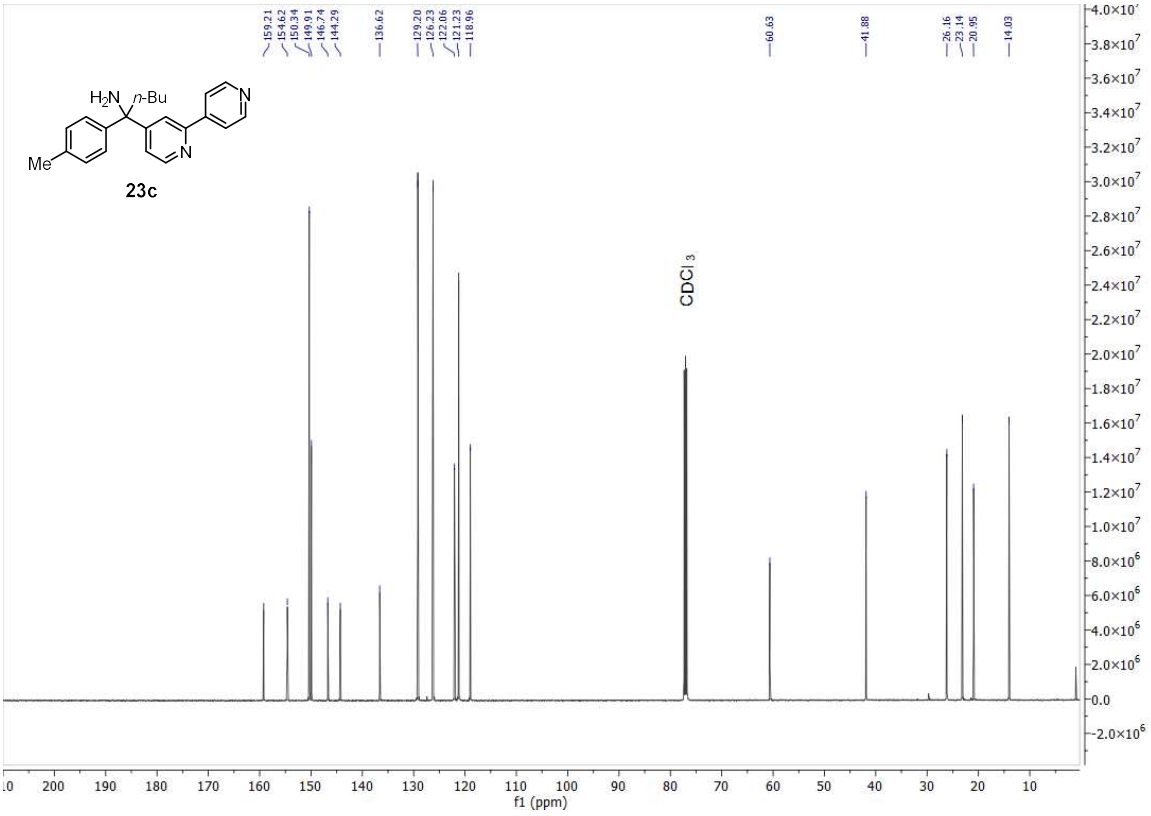
1-(2-phenylpyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**22c**) (126 MHz, $CDCl_3$, $^{13}CNMR$)



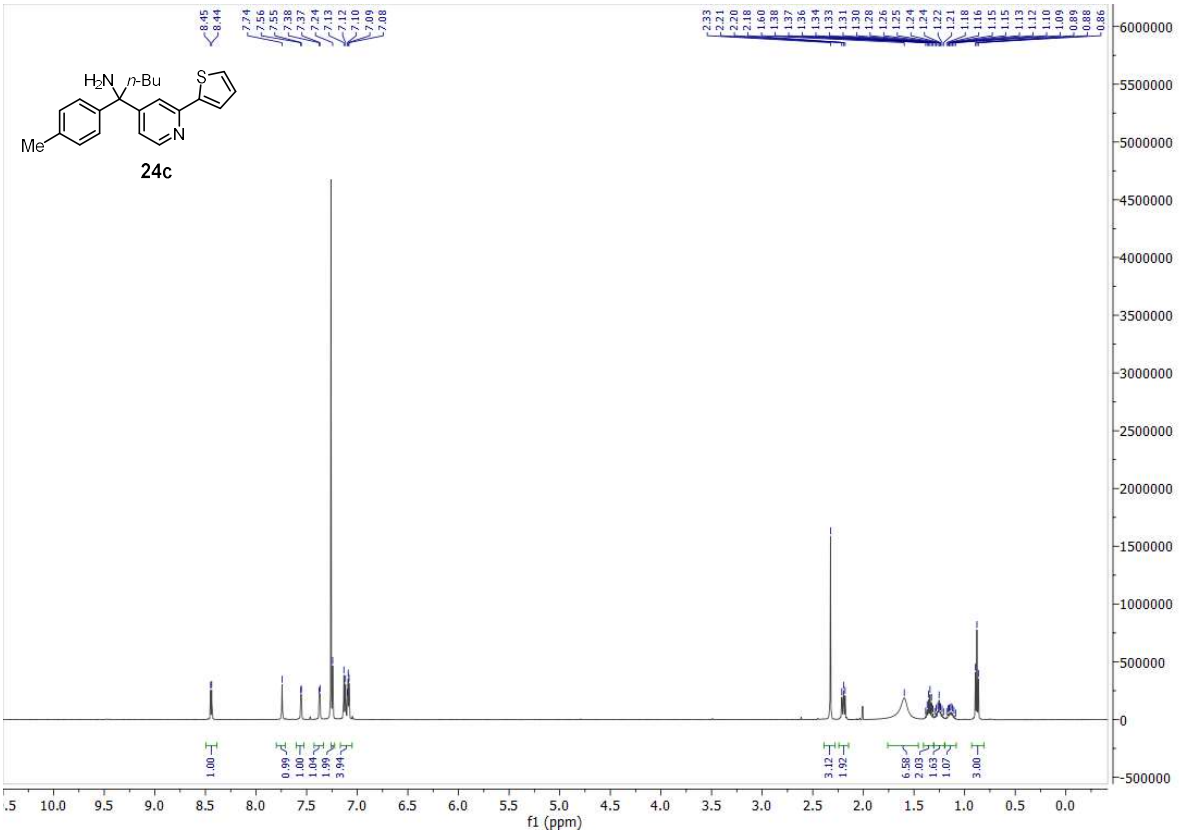
1-([2,4'-bipyridin]-4-yl)-1-(p-tolyl)pentan-1-amine (**23c**) (500 MHz, $CDCl_3$, $^1$HNMR)



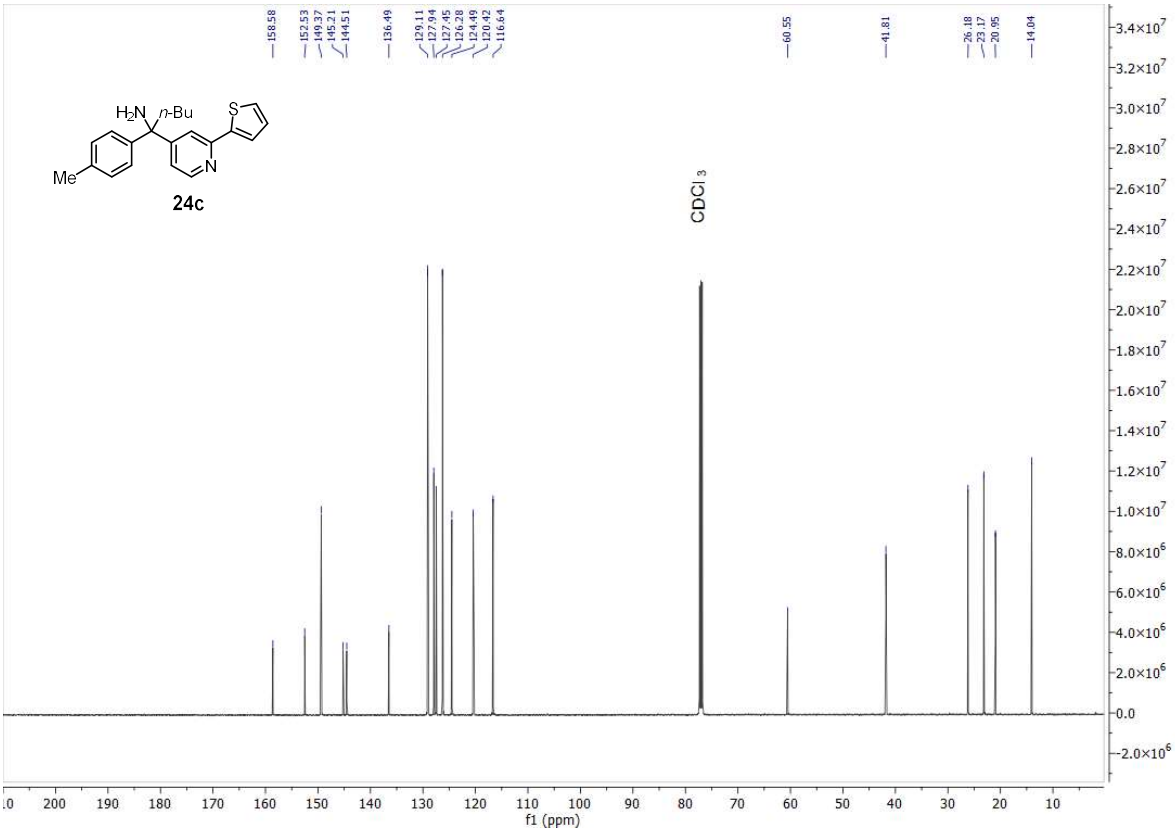
1-([2,4'-bipyridin]-4-yl)-1-(p-tolyl)pentan-1-amine (**23c**) (126 MHz, $CDCl_3$, $^{13}$CNMR)



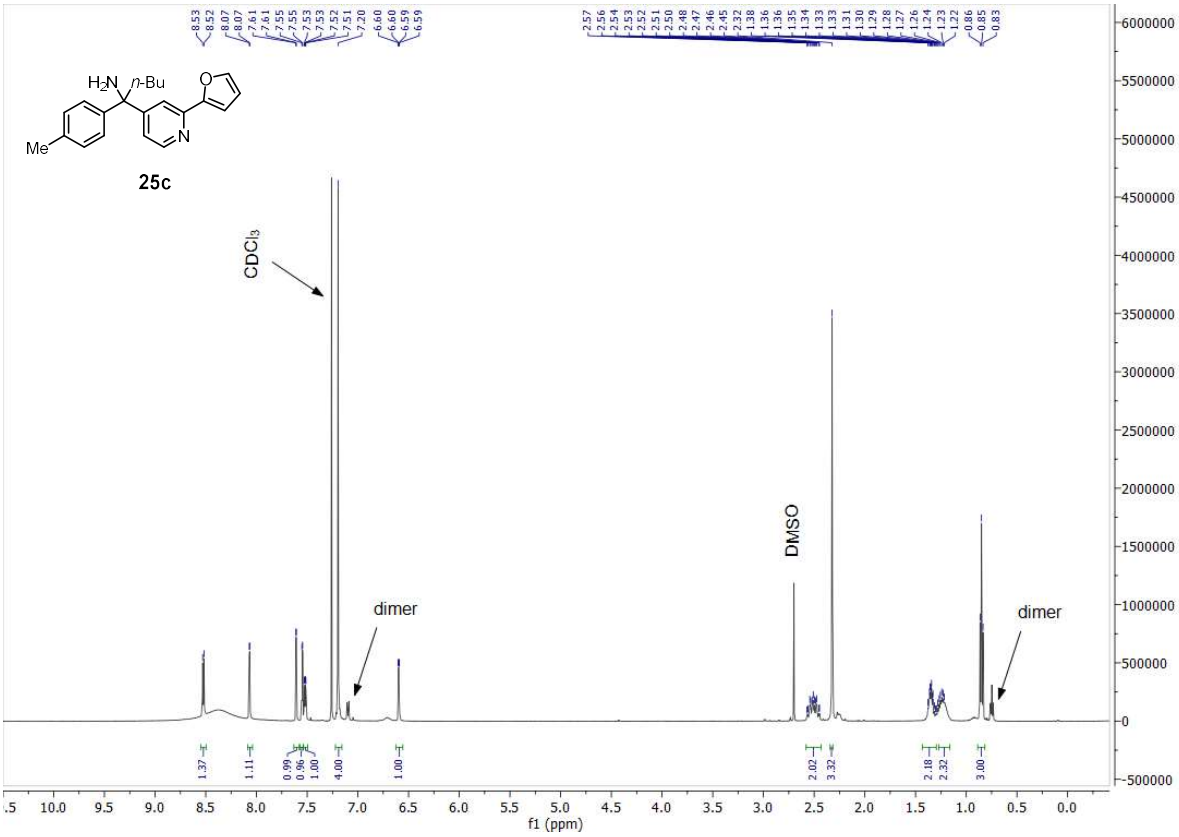
1-(2-(thiophen-2-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**24c**) (500 MHz, $CDCl_3$, $^1$HNMR)



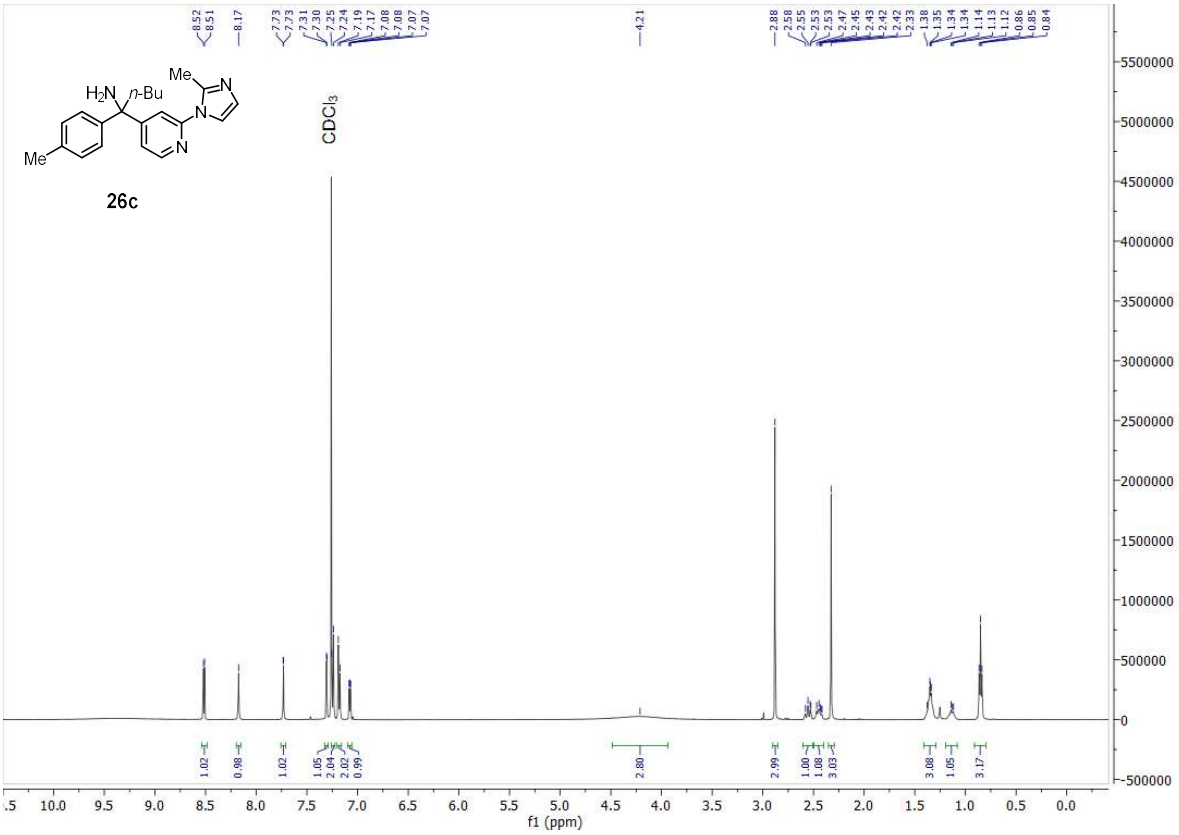
1-(2-(thiophen-2-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**24c**) (126 MHz, $CDCl_3$, $^{13}CNMR$)



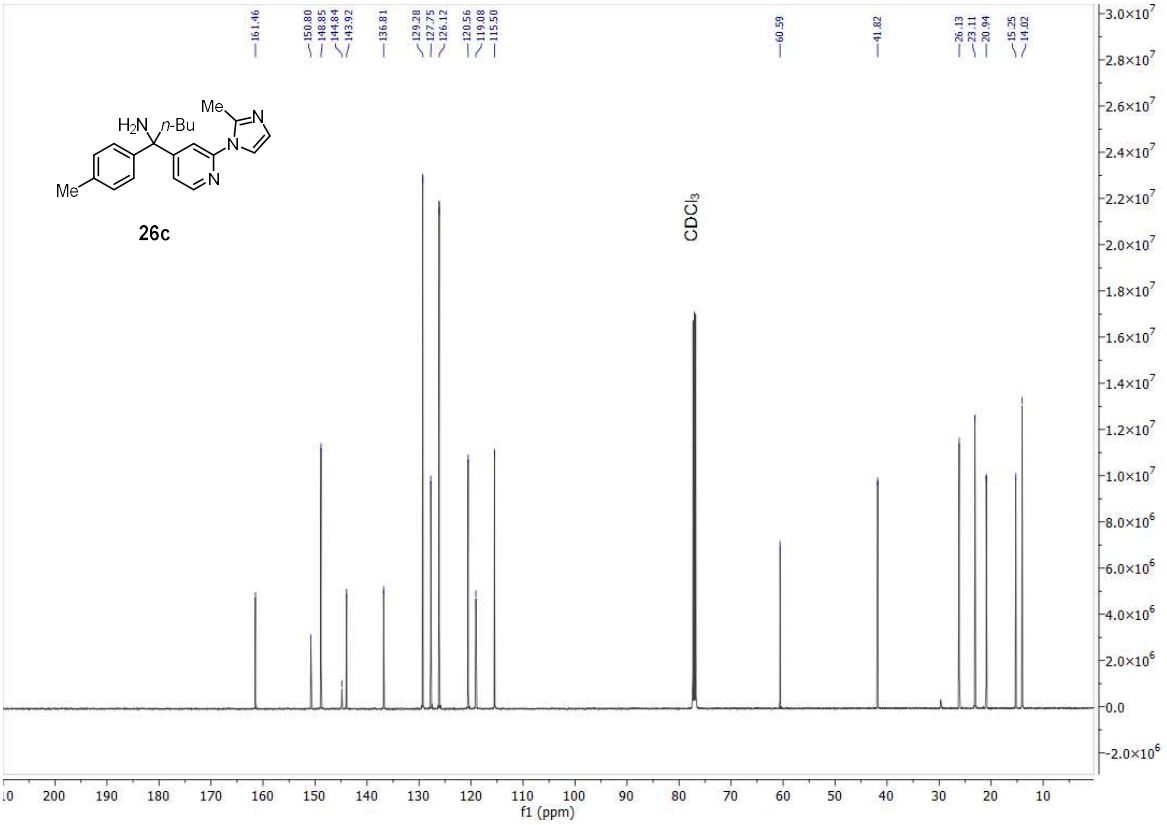
1-(2-(furan-2-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**25c•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



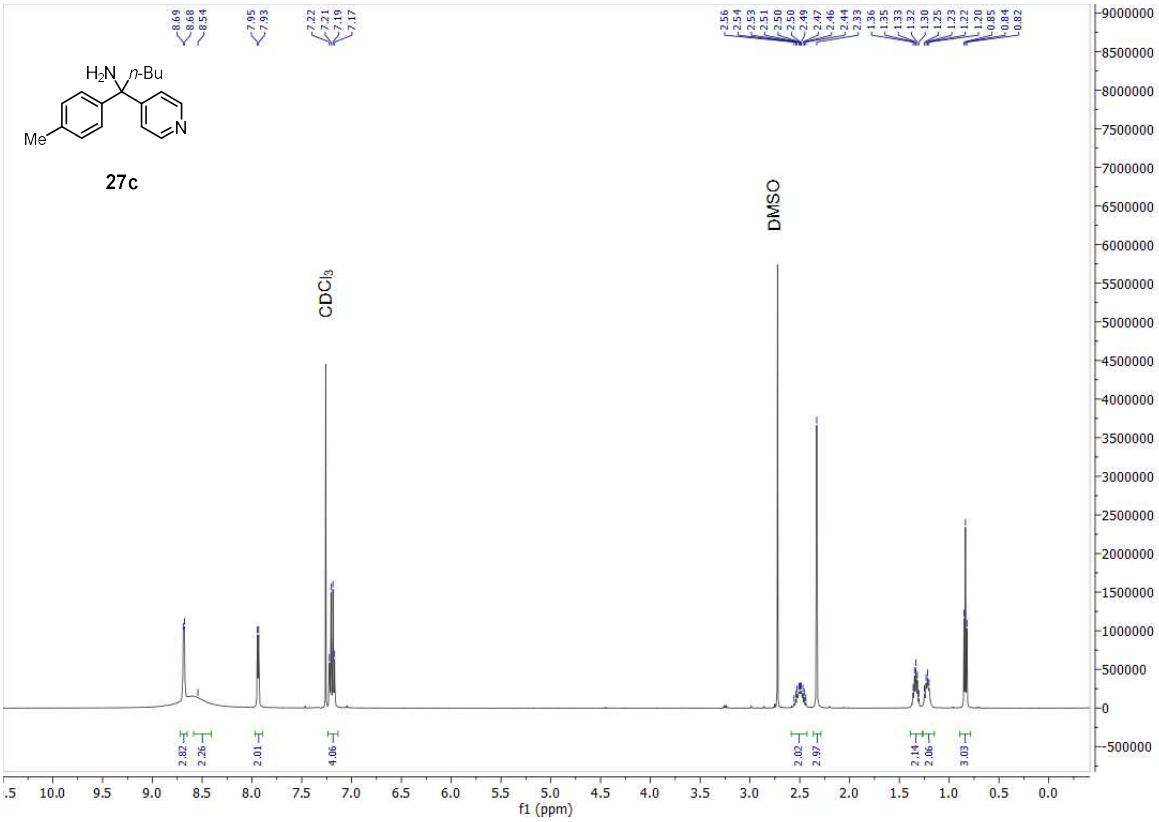
1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**26c**) (500 MHz, $CDCl_3$, $^1$HNMR)



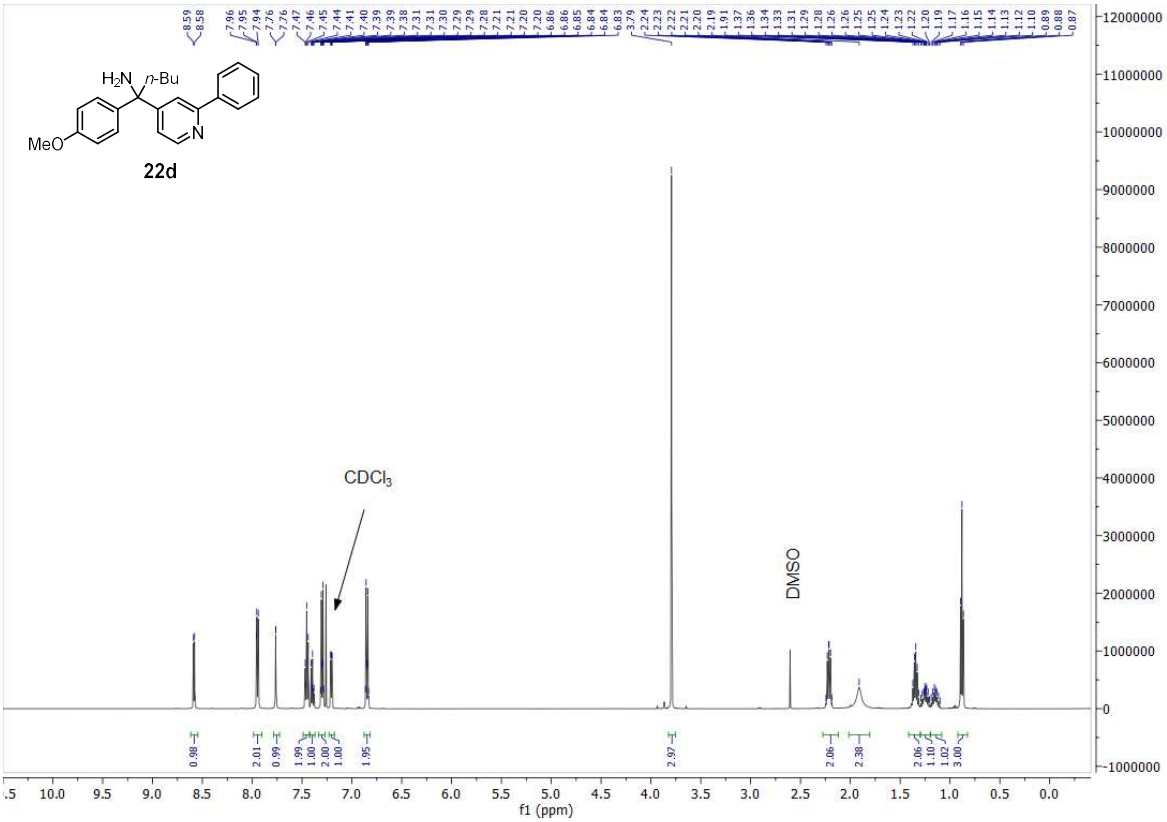
1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**26c**) (126 MHz, $CDCl_3$, $^{13}$CNMR)



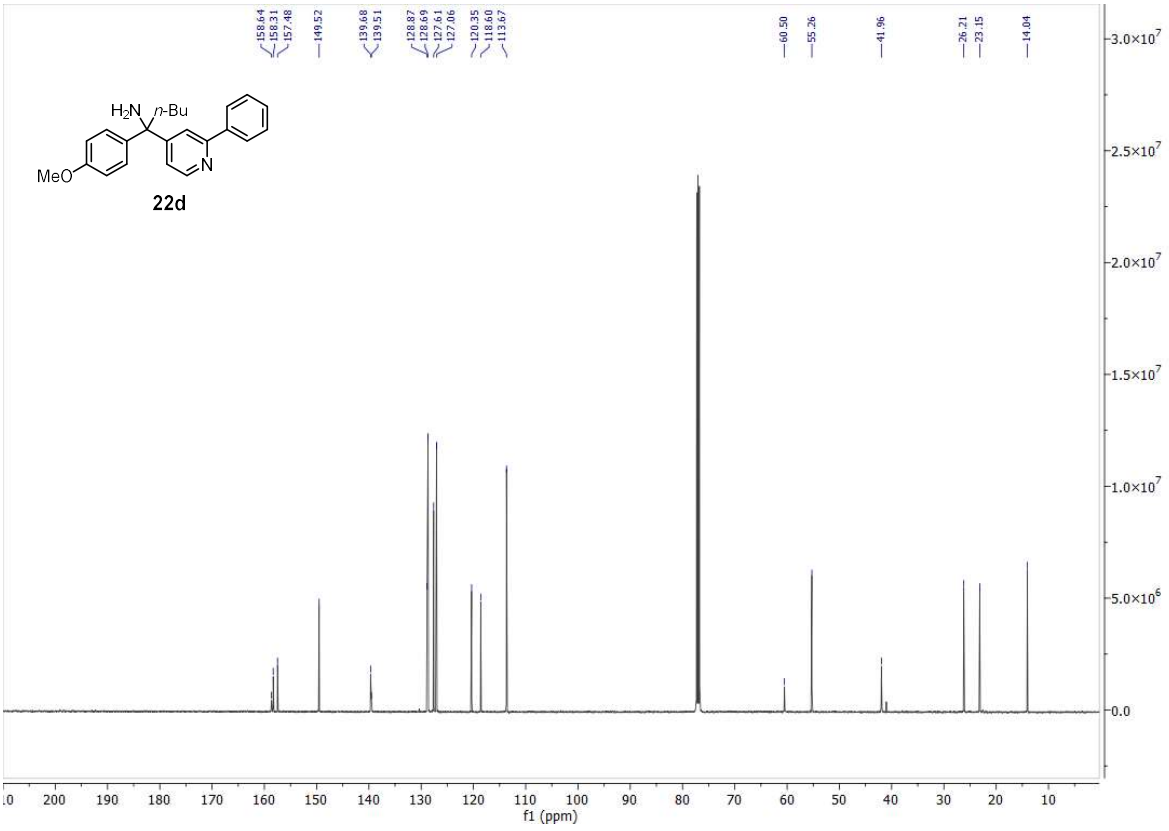
1-(pyridin-4-yl)-1-(p-tolyl)pentan-1-amine (**27c•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



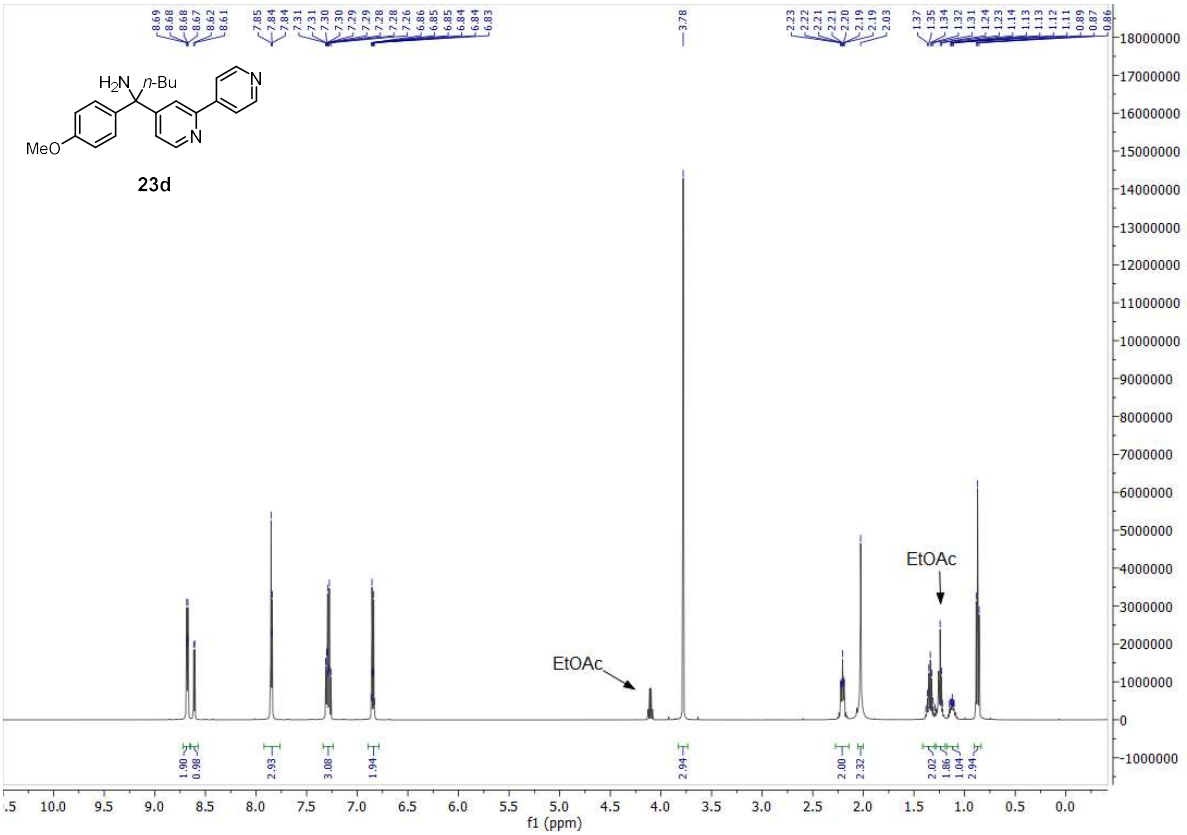
1-(4-methoxyphenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22d**) (500 MHz, $CDCl_3$, $^1$HNMR)



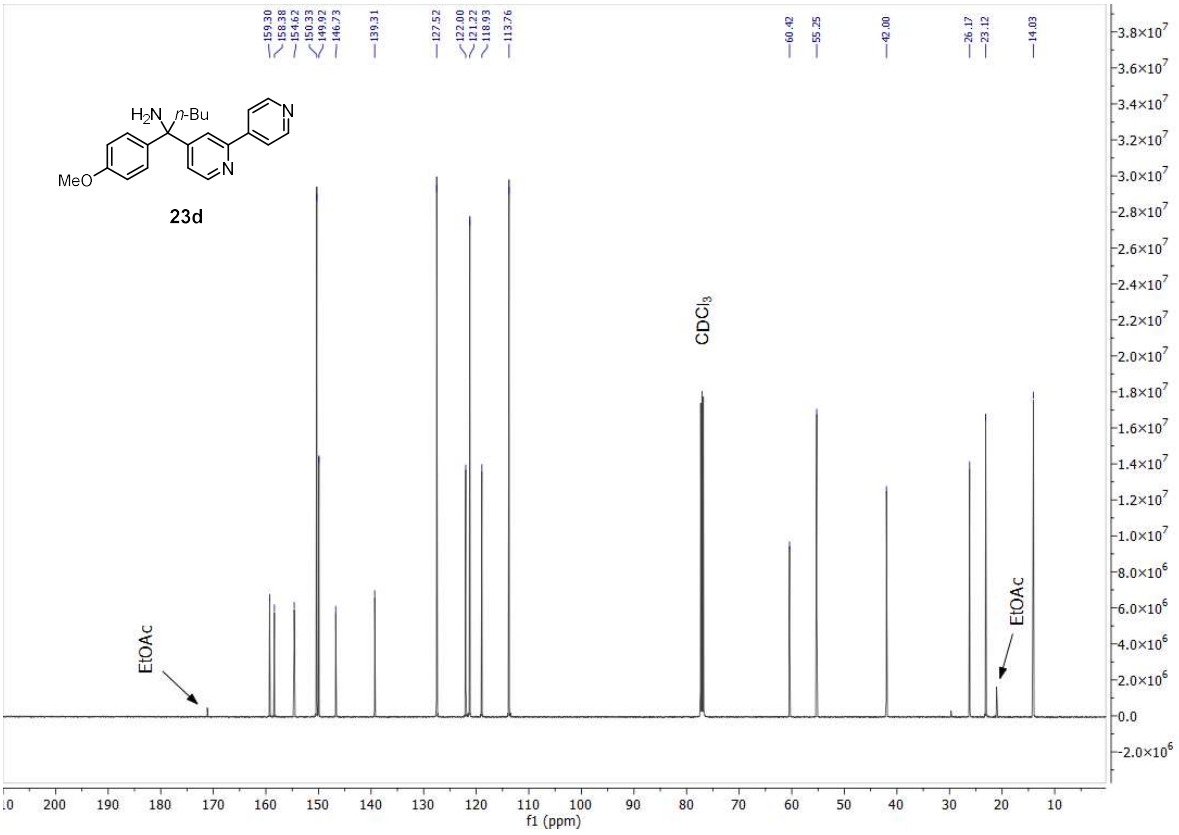
1-(4-methoxyphenyl)-1-(2-phenylpyridin-4-yl)pentan-1-amine (**22d**) (126 MHz, $CDCl_3$, $^{13}$CNMR)



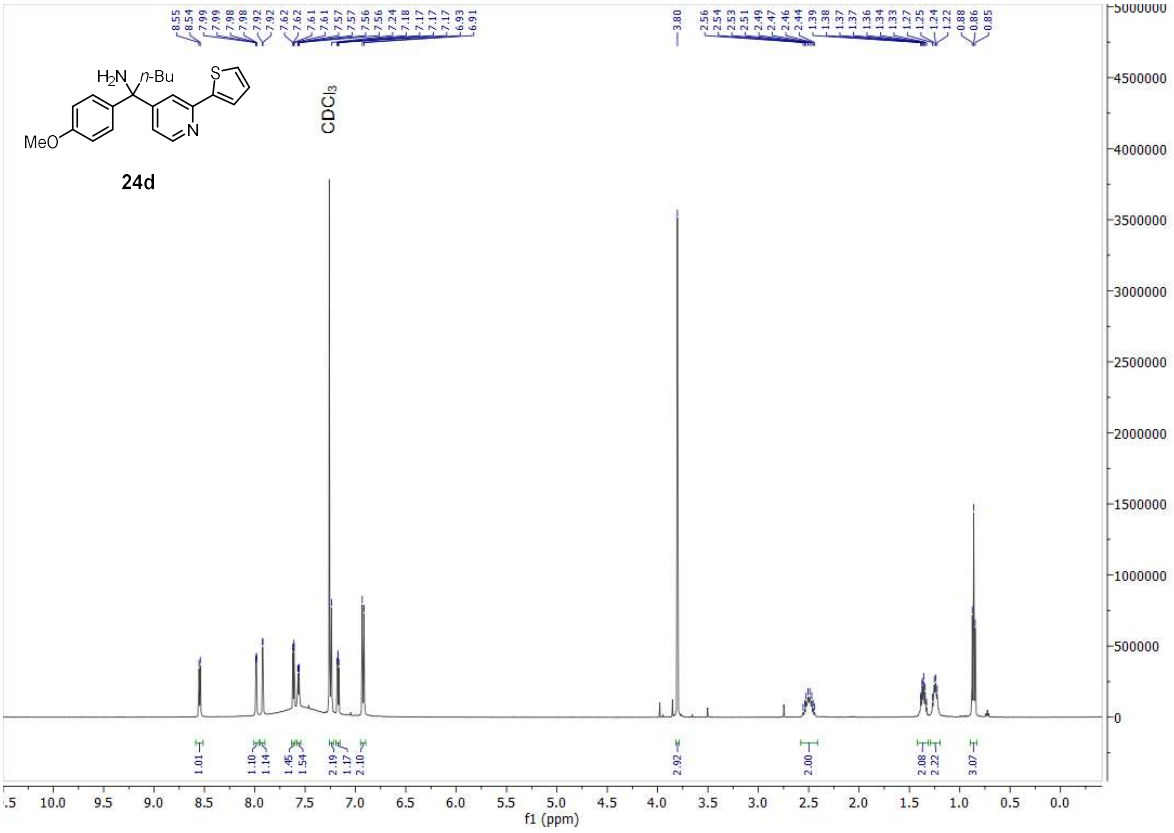
1-([2,4'-bipyridin]-4-yl)-1-(4-methoxyphenyl)pentan-1-amine (**23d**) (500 MHz, $CDCl_3$, $^1$HNMR)



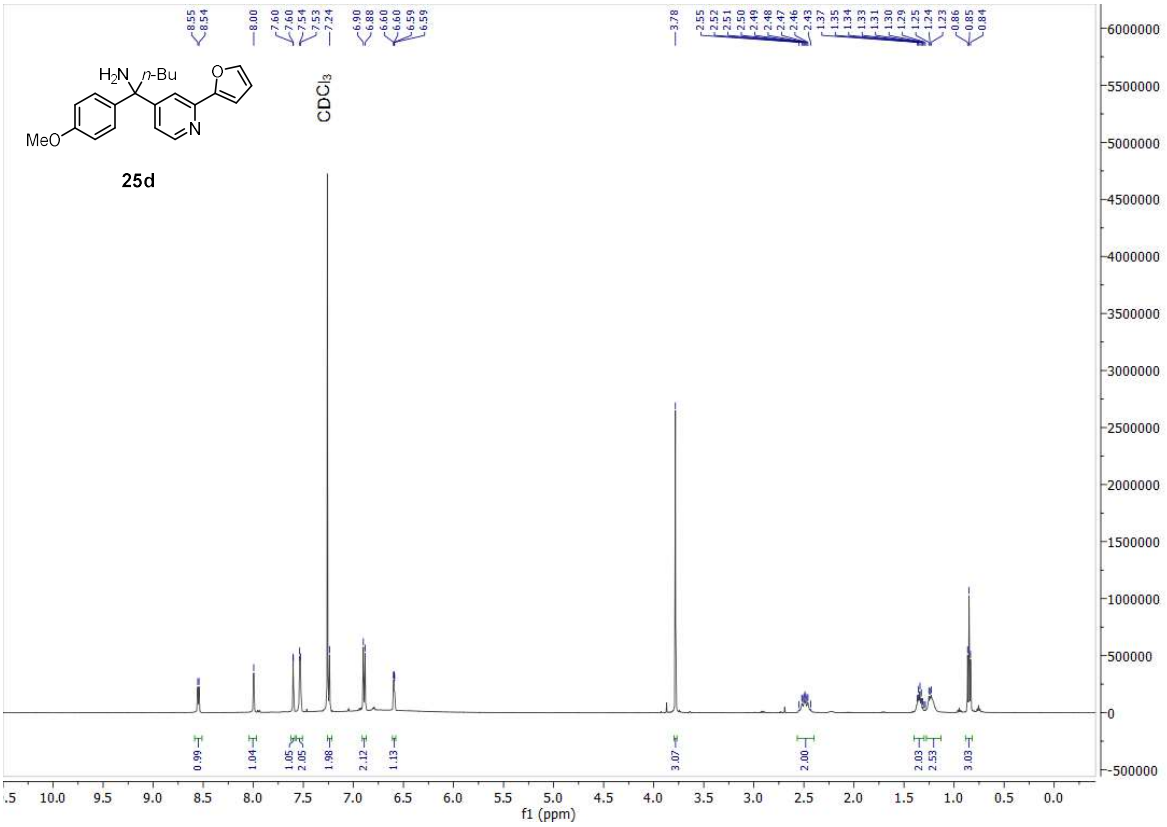
1-([2,4'-bipyridin]-4-yl)-1-(4-methoxyphenyl)pentan-1-amine (**23d**) (126 MHz, $CDCl_3$, $^{13}CNMR$)



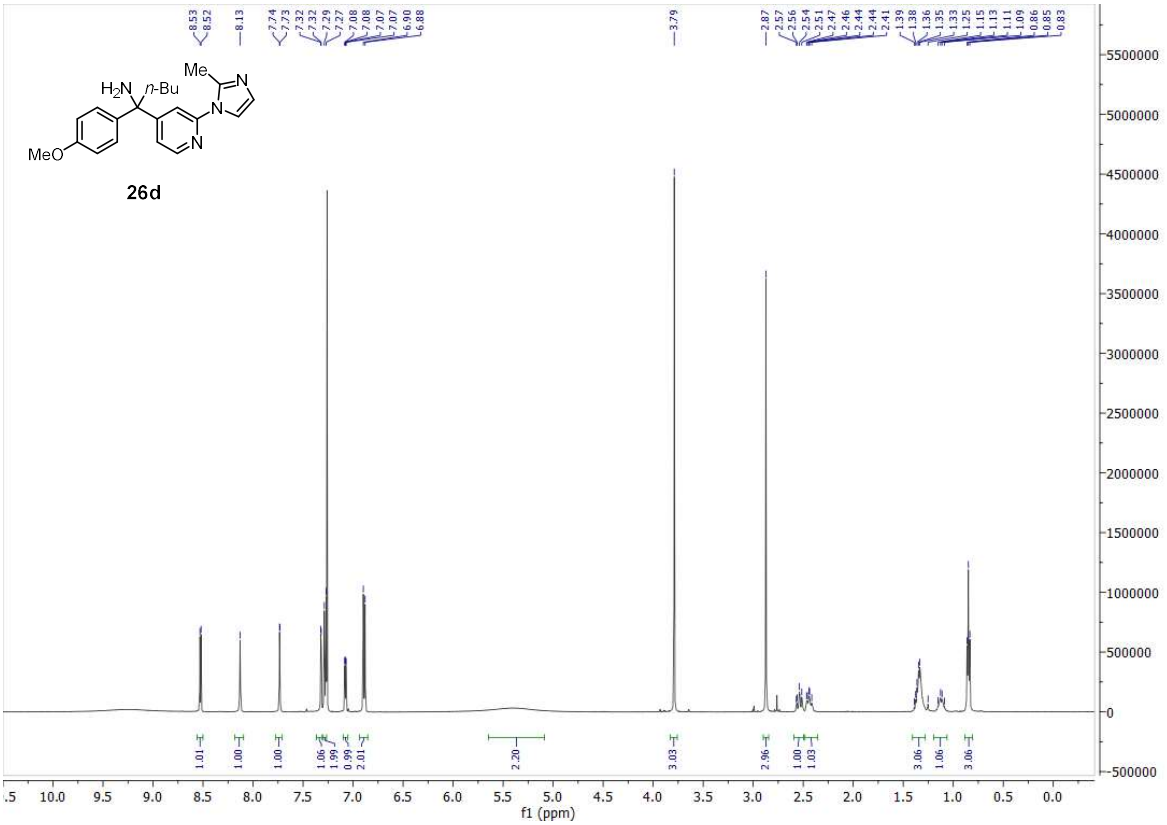
1-(4-methoxyphenyl)-1-(2-(thiophen-2-yl)pyridin-4-yl)pentan-1-amine (**24d•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



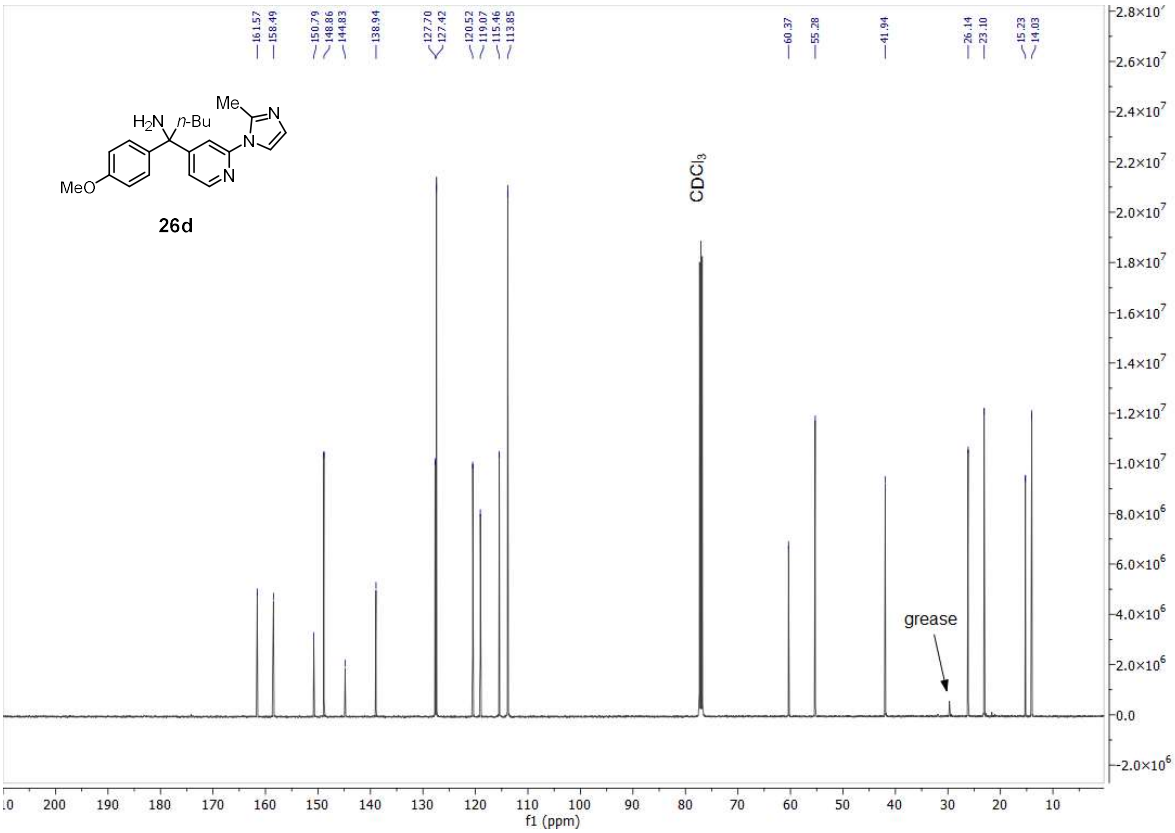
1-(2-(furan-2-yl)pyridin-4-yl)-1-(4-methoxyphenyl)pentan-1-amine (**25d•4TFA**) (500 MHz, $CDCl_3$, $^1$HNMR)



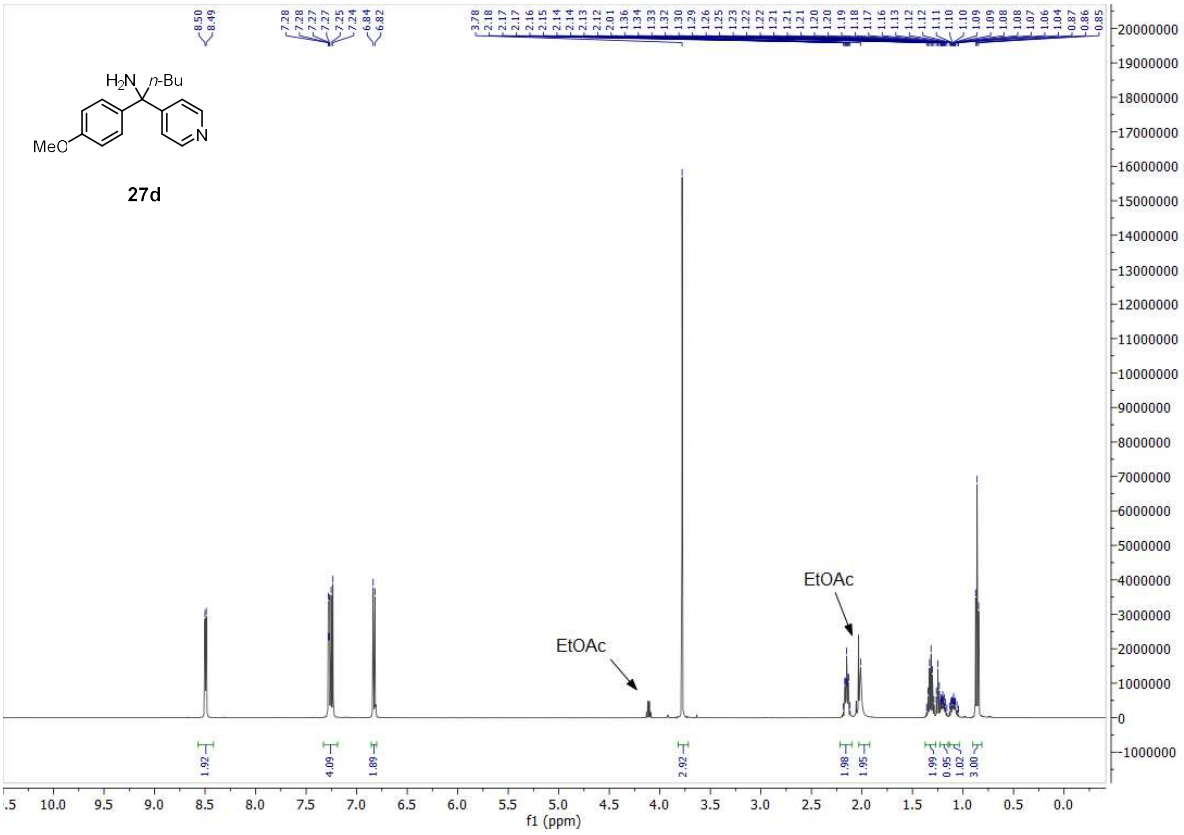
1-(4-methoxyphenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26d**) (500 MHz, $CDCl_3$, $^1$HNMR)



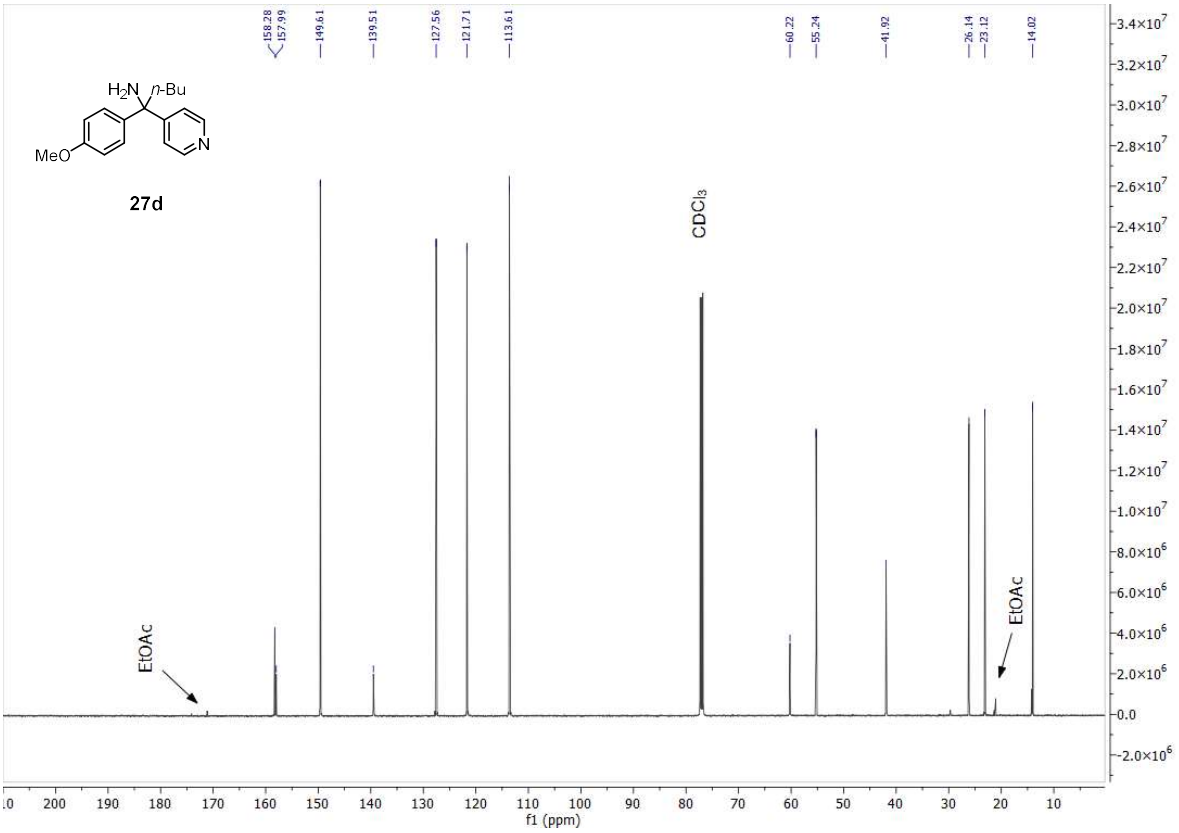
1-(4-methoxyphenyl)-1-(2-(2-methyl-1H-imidazol-1-yl)pyridin-4-yl)pentan-1-amine (**26d**) (126 MHz, $CDCl_3$, $^{13}$CNMR)



1-(4-methoxyphenyl)-1-(pyridin-4-yl)pentan-1-amine (**27d**) (500 MHz, $CDCl_3$, $^1$HNMR)



1-(4-methoxyphenyl)-1-(pyridin-4-yl)pentan-1-amine (**27d**) (126 MHz, $CDCl_3$, $^{13}$CNMR)



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1. Siu, J. C.; Sauer, G. S.; Saha, A.; MacEy, R. L.; Fu, N.; Chauviré, T.; Lancaster, K. M.; Lin, S. Electrochemical Azidooxygenation of Alkenes Mediated by a TEMPO-N3 Charge-Transfer Complex. *J. Am. Chem. Soc.* **2018**, *140* (39), 12511–12520.
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