Electronic Supplementary Information

Continuous Slurry Plug Flow Fe/ppm Pd Nanoparticle-Catalyzed Suzuki-Maiyaura Couplings in Water Utilizing Novel Solids Handling Equipment

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1. General Information

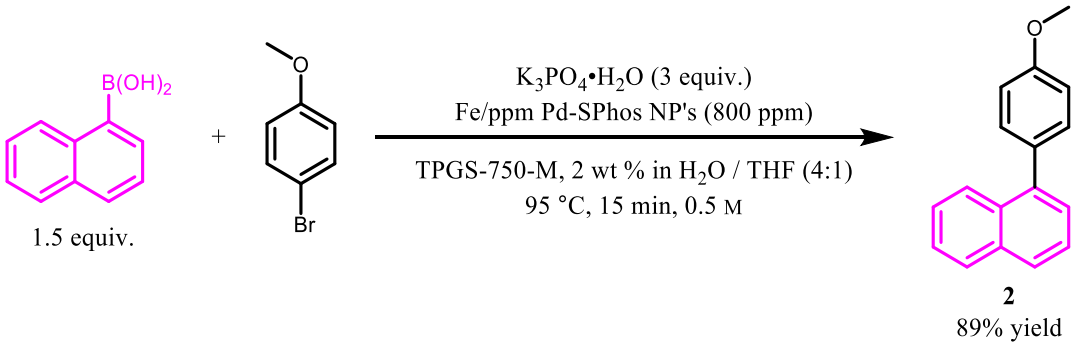
All commercial reagents were used without further purification. Organic solvents such as THF, tetrahydrofurfural alcohol (THFA), EtOAc, heptanes, and DCM were used as is from commercial sources and were not dried or degassed. Fe/ppm Pd (SPhos) NP catalyst was prepared as noted previously in the literature and stored at room temperature under N_2 atmosphere for short periods of time.[1] The surfactant, TPGS-750-M, was prepared via a standard literature procedure,[2] or can be purchased from Millipore-Sigma (catalog #733857 for a 2 wt % solution of the wax dissolved in water). A standard aqueous solution of TPGS-750-M was prepared by dissolving the wax into thoroughly degassed (steady stream of argon, minimum of 1 hour bubbling time with stirring) HPLC grade water over the course of 12 hour under N_2 gas pressure (**NOTE:** Do not attempt to degas the water with surfactant wax submerged; vigorous foaming to the point of overflow will occur). ^{1}H and ^{13}C NMR were recorded at 25 °C on a Varian Unity Inova 400 MHz, a Varian Unity Inova 500 MHz, or on a Varian Unity Inova 600 MHz spectrometer in $CDCl_3$ with residual $CHCl_3$ (^{1}H = 7.26 ppm, ^{13}C = 77.16 ppm) as internal standard. Chemical shifts are reported in parts per million (ppm). NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, t = triplet, td = triplet of doublets, q = quartet, quin = quintet, m = multiplet), coupling constant (if applicable), and integration.

[1] S. Handa, Y. Wang, F. Gallou, B. H. Lipshutz, *Science*, 2015, **349**, 1087–1091.

[2] B. H. Lipshutz, S. Ghorai, A. R. Abela, R. Moser, T. Nishikata, C. Duplais, A. Krasovskiy, *J. Org. Chem.*, **2011**, *76*, 4379–4391.

2. Experimental Section

Synthesis of 2 in Batch Mode



To a 2.0-5.0 mL conical microwave vial equipped with a magnetic stir vane was added 4-bromoanisole (95.1 mg, 0.508 mmol, 1.00 equiv), naphthalene-1-ylboronic acid (133 mg, 0.773 mmol, 1.52 equiv), potassium phosphate tribasic monohydrate (351 mg, 1.525 mmol, 3.00 equiv), and Fe/ppm Pd (SPhos) nanoparticles (20 mg). TPGS-750-M, 2 wt % in water (0.8 mL) and tetrahydrofuran (0.2 mL) was then added and the vial was sealed using an aluminum crimp-cap fitted with a septum. The contents of the vial were then allowed to stir at rt until a homogeneous mixture had formed. The vial was then placed in a microwave reactor and allowed to react for 15 min at 95 °C. The resulting reaction mixture was then extracted with EtOAc (3 x 0.5 mL) and passed through a plug of silica gel resulting in **2** as an off-white solid (106 mg, 89% yield).

Note: Screening of subsequent examples of NP-catalyzed coupling reactions in plug flow were tested using microwave conditions in a similar manner as a guide towards optimization. For example, this reaction was found to undergo 100% conversion via UPLC UV/Vis analysis within 2 min of reaction time. All other reactions were tested within a 2-10 min reaction window at 95 °C using either $K_3PO_4•H_2O$ or triethylamine as base, and reagent flow rates were adjusted accordingly.

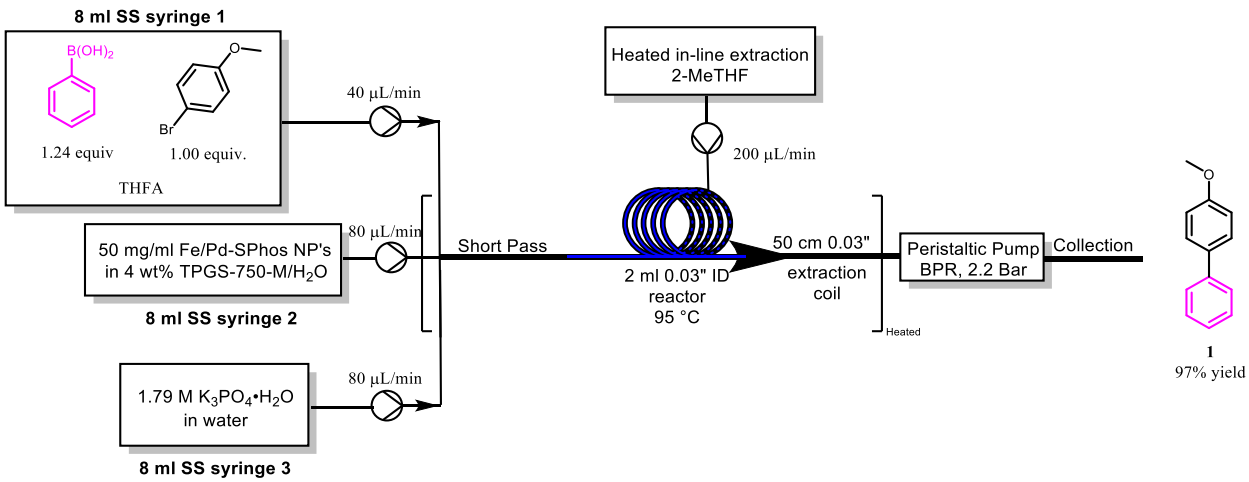
Batch-to-Flow Synthesis of 2

A flow reactor was prepared by pumping a 4:1 ratio solution of TPGS-750-M, 2 wt % in water and tetrahydrofuran using a VapourTec E-Series peristaltic pump into a 10 mL reactor coil (PFA tubing, 0.3" ID) pre-heated to 95 °C. A VapourTec E-Series pump configured to act as a back-pressure regulator set to 3 bar was used on the downstream end of the reactor prior to collection.

To a 2-dram vial equipped with a stir bar was added 4-bromoanisole (179.0 mg, 0.948 mmol, 1 equiv), naphthalene-1-ylboronic acid (283.0 mg, 1.645 mmol, 1.74 equiv), potassium phosphate tribasic monohydrate (685 mg, 2.97 mmol, 3.14 equiv), and Fe/ppm Pd (SPhos) NPs (41 mg). TPGS-750-M, 2 wt % in water (1.6 mL) and tetrahydrofuran (0.4 mL) were then added to the vial and the contents were then allowed to stir at rt until a homogeneous mixture had formed. The resulting suspension was then stirred continuously at rt and pumped using the TPGS/THF pre-conditioned peristaltic pump into the 10 mL reactor coil at a 0.667 mL/min flow rate. After the entirety of the suspension was injected into the reactor coil, a timer was started for 15 min (the residence time of the reaction) and the reaction slug was chased with a mixture of aqueous TPGS/THF immediately afterwards.

After 15 min, the peristaltic pump and reaction coil were washed with EtOAc at a flow rate of 2 mL/min for 10 min, and the aqueous inside of the reaction coil along with the organics were collected and pooled together. The resulting bi-phase was then separated and the aqueous phase was extracted with EtOAc (2 x 10 mL). The crude organics were then passed through a plug of silica gel, evaporated under reduced vacuum, and dried until constant mass using a vacuum oven resulting in **2** as an off-white solid (154 mg, 69% yield).

Synthesis of 1 in Flow



Syringe 1: To a 5 mL volumetric flask was added 4-bromoanisole (1,150 mg, 6.14 mmol, 1.00 equiv) and phenylboronic acid (930 mg, 7.62 mmol, 1.24 equiv). The flask was then mostly filled with tetrahydrofurfuryl alcohol (THFA) and the starting reagents were dissolved using gentle heating. Upon dissolution, the flask was cooled to rt and filled to the volumetric line using THFA. The resulting solution was then transferred to an 8 mL stainless steel syringe prior to the reaction and set to deliver 40 µL/min.

Syringe 2: A 50 mg/mL catalyst stock solution was prepared by suspending 1 g of freshly prepared Fe/ppm Pd (SPhos) NP catalyst in 20 mL of TPGS-750-M, 4 wt % in water. After the addition of the aqueous surfactant solution to the NPs the mixture was sonicated for 20 min in a rt water bath and stirred continuously prior to use. The catalyst suspension was transferred to an 8 mL stainless steel syringe immediately prior to a coupling reaction in flow and set to deliver at 80 µL/min.

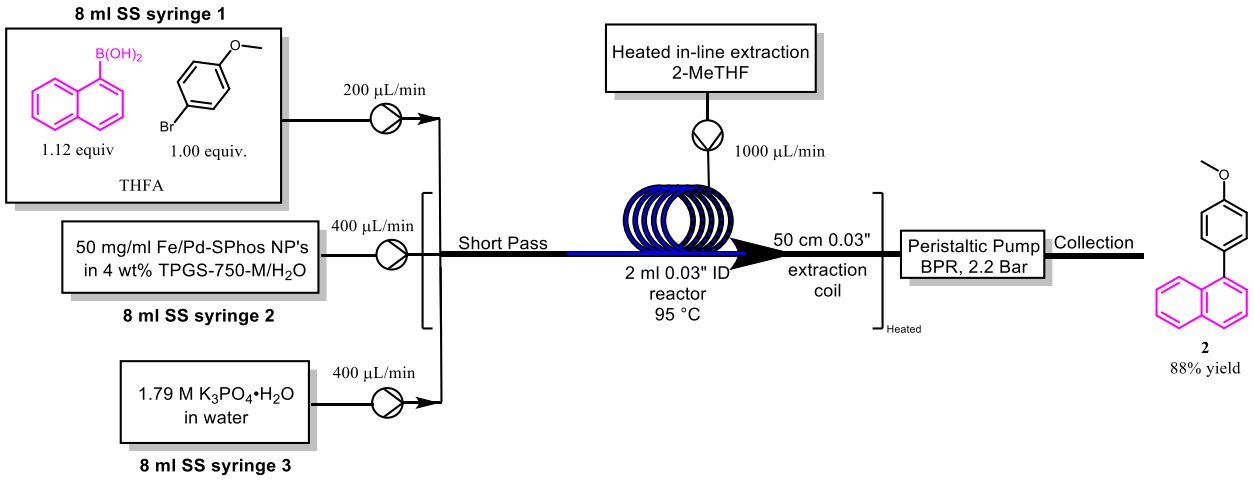
Syringe 3: A 1.78 M stock solution of $K_3PO_4 \bullet H_2O$ was transferred into an 8 mL stainless steel syringe prior to the reaction. The syringe was then set to deliver at 80 µL/min.

Reactor Design: The three prepared syringes were plumbed into a cross mixer (Tefzel, 0.03" ID) such that **Syringe 2**, containing the NPs, was delivered at 180° through the mixer and that **Syringes 1 and 3** were

delivered perpendicular and through check-valves. The cross mixer was then plumbed directly into a 2 mL reactor coil (PFA, 0.03" ID). The reactor coil was then plumbed into a T-mixer (Tefzel, 0.03" ID) wherein 2-methyltetrahydrofuran is delivered perpendicularly through a check valve into that stream as an in-line extractor. The cross mixer, reaction coil, and in-line extraction units are all heated to 95 °C and held at this temperature during the run. The extraction mixture prior to the run is then delivered through a VapourTec E-Series peristaltic pump configured to act as a back-pressure regulator holding at 2.2 bar.

The 2 mL reactor / back-pressure system described above was then pre-filled with TPGS-750-M, 2 wt % in water prior to fitting the syringes containing the starting reagents to the cross mixer. All three syringes were then simultaneously turned on, and the reaction was allowed to run for a combined flow rate of 200 µL/min for four residence times (40 min) prior to steady state. The reaction was then collected for a total of five residence times (50 min) with simultaneous in-line extraction using 2-MeTHF at 200 µL/min. The combined aqueous and organics were then separated, and the solvent was evaporated under reduced pressure. The residual organics were then treated with 200 mL of water resulting in the precipitation of a solid. This solid was then recovered via filtration, dissolved in DCM, and passed through a plug of silica gel resulting in the product as an off-white solid (431 mg, 97% yield).

Synthesis of 2 in Flow



Syringe 1: To a 5 mL volumetric flask was added 4-bromoanisole (1,150 mg, 6.14 mmol, 1.00 equiv) and naphthalene-1-ylboronic acid (1,185 mg, 6.89 mmol, 1.12 equiv). The flask was then mostly filled with tetrahydrofurfuryl alcohol (THFA) and the starting reagents were dissolved using gentle heating. Upon dissolution, the flask was cooled to rt and filled to the volumetric line using THFA. The resulting solution was then transferred to an 8 mL stainless steel syringe prior to the reaction and set to deliver 200 µL/min.

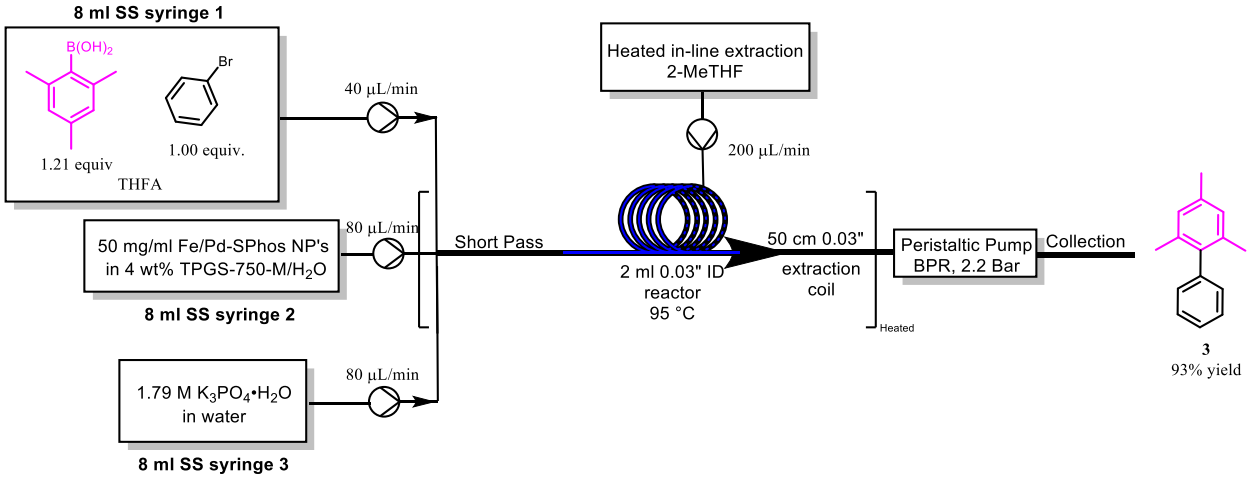
Syringe 2: A 50 mg/mL catalyst stock solution was prepared in a similar manner as the synthesis of **1**. The catalyst suspension was transferred to an 8 mL stainless steel syringe immediately prior to a coupling reaction in flow and set to deliver 400 µL/min.

Syringe 3: A 1.78 M stock solution of $K_3PO_4•H_2O$ was transferred into an 8 mL stainless steel syringe prior to the reaction. The syringe was then set to deliver at 400 µL/min.

Reactor Design: This synthesis was performed using the same apparatus prepared for the flow synthesis of **1** and run in a similar fashion using the flow rates listed above. The combined flow rate of 1 mL/min was allowed to run for two residence times on the 2 mL reactor to reach steady state. Seven residence times were then collected using a 1 mL/min heated in-line extraction using 2-MeTHF.

The crude product stream was then worked up as in example **1**, resulting in the product as an off-white solid (685 mg, 88% yield).

Synthesis of 3 in Flow



Syringe 1: To a 5 mL volumetric flask was added phenyl bromide (925 mg, 5.89 mmol, 1.00 equiv) and mesitylboronic acid (1,175 mg, 7.16 mmol, 1.21 equiv). The flask was then mostly filled with tetrahydrofurfuryl alcohol (THFA) and the starting reagents were dissolved using gentle heating. Upon dissolution, the flask was cooled to rt and filled to the volumetric line using THFA. The resulting solution was then transferred to an 8 mL stainless steel syringe prior to the reaction and set to deliver 40 µL/min.

Syringe 2: A 50 mg/ml catalyst stock solution was prepared in a similar manner as the synthesis of **1**. The catalyst suspension was transferred to an 8 mL stainless steel syringe immediately prior to a coupling reaction in flow and set to deliver 80 µL/min.

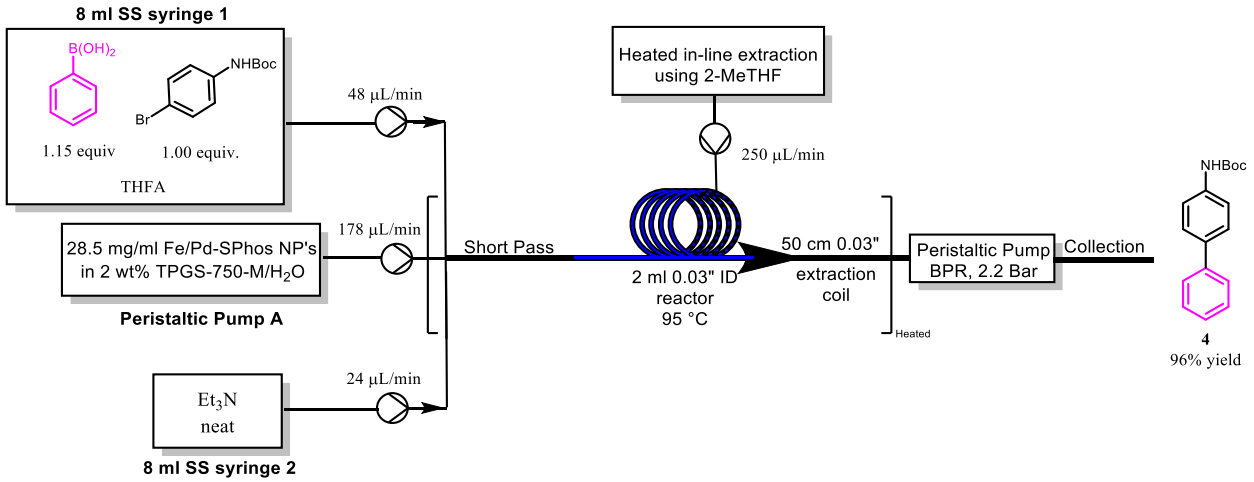
Syringe 3: A 1.78 M stock solution of $K_3PO_4•H_2O$ was transferred into an 8 mL stainless steel syringe prior to the reaction. The syringe was then set to deliver at 80 µL/min.

Reactor Design: This synthesis was performed using the same apparatus prepared for the flow synthesis of **1** and run in a similar fashion using the flow rates listed above. The combined flow rate of 200 µl/min

was allowed to run for two residence times on the 2 mL reactor to reach steady state. A product mixture sample of 4.9 residence times was then collected using a 200 µL/min heated in-line extraction using 2-MeTHF.

The resulting bi-phase was then separated and the organics were concentrated down to an oil under reduced pressure. The residual organics were then treated with water (200 mL) and extracted with heptane (3 x 50 mL). The organics were then dried over sodium sulfate, filtered, evaporated under reduced pressure, and passed through a plug of silica gel using EtOAc. The organics were then dried under hi-vacuum until constant mass resulting in product as a tan oil (431 mg, 93% yield).

Synthesis of 4 in Flow



Syringe 1: To a 5 mL volumetric flask was added *tert*-butyl (4-bromophenyl)carbamate (1,650 mg, 6.06 mmol, 1.00 equiv) and phenylboronic acid (850 mg, 6.97 mmol, 1.15 equiv). The flask was then mostly filled with tetrahydrofurfuryl alcohol (THFA) and the starting reagents were dissolved using gentle heating. Upon dissolution, the flask was cooled to rt and filled to the volumetric line using THFA. The resulting solution was then transferred to an 8 mL stainless steel syringe prior to the reaction and set to deliver 48 µL/min.

Peristaltic Pump A: A 28.5 mg/mL catalyst stock solution was prepared by suspending 570 mg of freshly prepared Fe/ppm Pd (SPhos) NP catalyst in 20 mL of TPGS-750-M, 2 wt % in water. Upon addition of the aqueous surfactant solution to the NPs, the mixture was sonicated for 20 min in a rt water bath and stirred continuously prior to use. The catalyst suspension was then stirred continuously on a stir plate and was used to prime a VapourTec E-Series peristaltic pump immediately prior to a flow coupling reaction. The peristaltic pump was then set to deliver 178 µL/min.

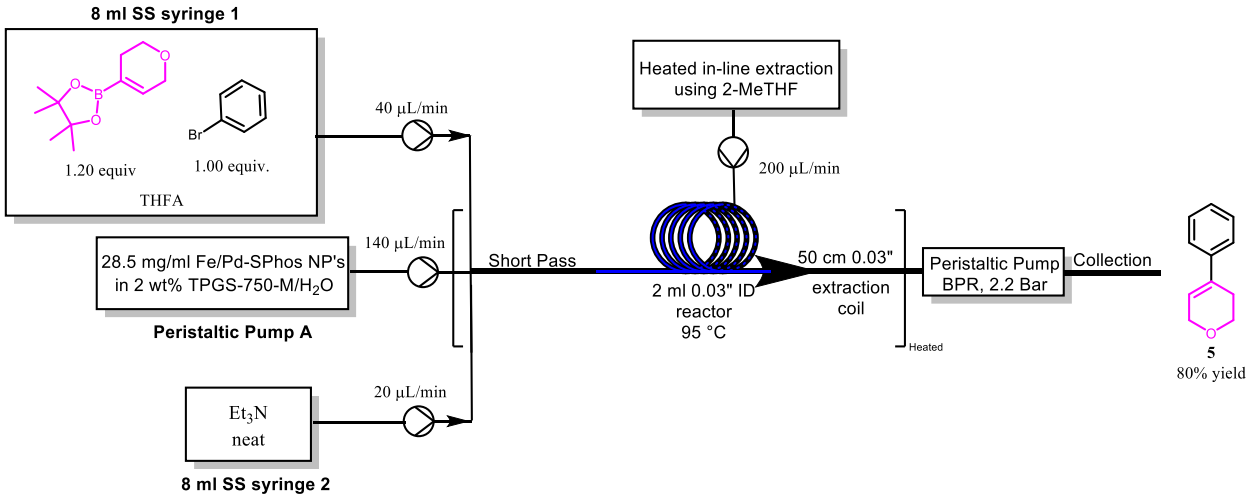
Syringe 2: An 8 mL stainless steel syringe was charged with neat trimethylamine and set to deliver 24 µL/min.

Reactor Design: The two syringes and peristaltic pump were plumbed into a cross mixer (Tefzel, 0.03" ID) such that **Peristaltic Pump A**, containing the nanoparticles, was delivered at 180° through the mixer and that **Syringes 1 and 2** were delivered perpendicular and through check-valves (DATA). The cross mixer was then plumbed directly into a 2 mL reactor coil (PFA, 0.03" ID). The reactor coil was then plumbed into a T-mixer (Tefzel, 0.03" ID) wherein which 2-methyltetrahydrofuran is delivered perpendicularly through a check valve into that stream as an in-line extractor. The cross mixer, reaction coil, and in-line extraction units are all heated to 95 °C and held at temperature during the run. The extraction mixture prior to the run is then delivered through a VapourTec E-Series peristaltic pump configured to act as a back-pressure regulator holding at 2.2 bar.

The 2 mL reactor / back-pressure system described above was then pre-filled with TPGS-750-M, 2 wt % in water prior to fitting the syringes and peristaltic pump to the cross mixer. The two syringes and pump were then started simultaneously, and the flow system was allowed to reach steady state for four residence times of a combined flow rate of 250 µL/min (8 min retention time). The reaction was then collected for a total of five residence times with simultaneous heated in-line extraction using 250 µL/min 2-MeTHF after the 2 mL reactor coil.

The collected bi-phase was then separated and the organics were evaporated under reduced pressure. The residual oil was then treated with cold water (200 mL) and allowed to rest in an ice bath. The resulting precipitate was then filtered, collected, and dissolved in EtOAc. The organics were then passed through a plug of sodium sulfate followed by silica gel, evaporated under reduced pressure, and dried under hi-vacuum until constant mass was achieved resulting in a yellow crystalline solid (480 mg, 96% yield).

Synthesis of 5 in Flow



Syringe 1: To a 5 mL volumetric flask was added bromobenzene (927.5 mg, 5.91 mmol, 1.00 equiv) and 2-(3,6-dihydro-2*H*-pyran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1,484 mg, 7.07 mmol, 1.20 equiv). The flask was then mostly filled with tetrahydrofurfuryl alcohol (THFA) and the starting reagents were dissolved using gentle heating. Upon dissolution, the flask was cooled to rt and filled to the volumetric line using THFA. The resulting solution was then transferred to an 8 mL stainless steel syringe prior to the reaction and set to deliver 40 µL/min.

Peristaltic Pump A: A 28.5 mg/mL catalyst stock solution was prepared in a similar manner as the synthesis of **4**. The catalyst suspension was stirred continuously on a stir plate and used to prime a VapourTec E-Series peristaltic pump prior to a flow coupling reaction. The peristaltic pump was then set to deliver 140 µL/min.

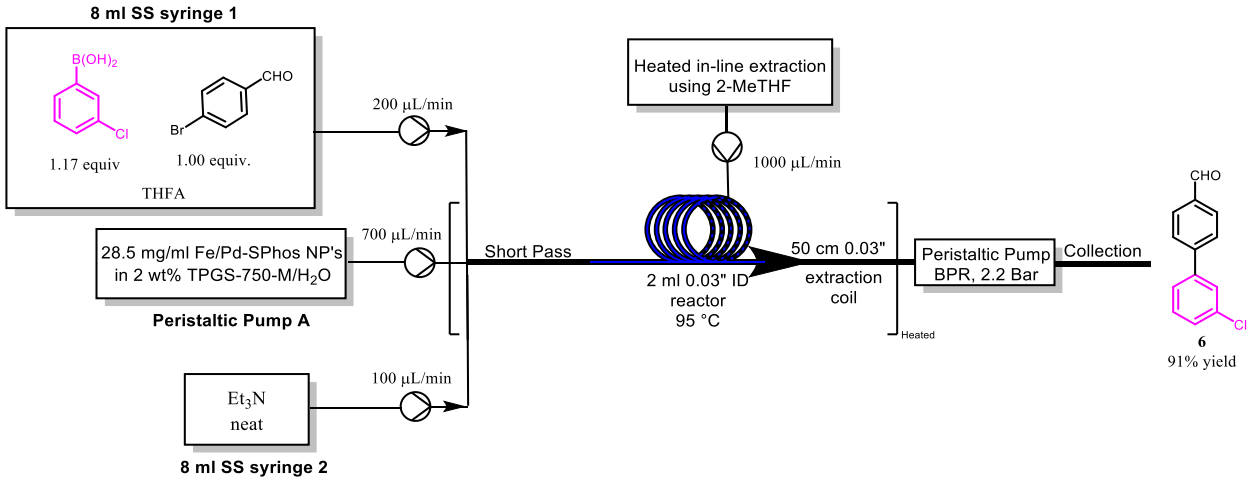
Syringe 2: An 8 mL stainless steel syringe was charged with neat trimethylamine and set to deliver 20 µL/min.

Reactor Design: This synthesis was performed using the same apparatus prepared for the flow synthesis of **4** and run in a similar fashion using the flow rates listed above. The combined flow rate of 200 µl/min

was allowed to run for four residence times (40 min) to reach steady state. The steady state product mixture was then collected for five residence times (50 min) with a simultaneous heated in-line extraction using 200 µL/min 2-MeTHF.

The collected bi-phase was then separated and the organic solvent was evaporated under reduced pressure. The residual oil was then treated with 200 mL of cold water and allowed to sit an ice bath. The resulting solid was then filtered and washed with cold water. The retained material was then dissolved in EtOAc and passed through a plug of sodium sulfate followed by silica gel. The solvent was then removed, and the product was dried under hi-vacuum until constant mass was achieved resulting in product as a yellow solid (300 mg, 80% yield).

Synthesis of 6 in Flow



Syringe 1: To a 5 mL volumetric flask was added 4-bromobenzaldehyde (1,14.7 mg, 6.02 mmol, 1.00 equiv) and (3-chlorophenyl)boronic acid (1098.9 mg, 7.03 mmol, 1.17 equiv). The flask was then mostly filled with tetrahydrofurfuryl alcohol (THFA) and allowed to dissolve at rt.

NOTE: This mixture should not be heated; heating will result in acetal formation between THFA and 4-bromobenzaldehyde which will not couple under the reaction conditions.

Once homogeneous, the flask was then filled to the volumetric line using THFA. The resulting solution was then transferred to an 8 mL stainless steel syringe prior to the reaction and set to deliver 200 µL/min.

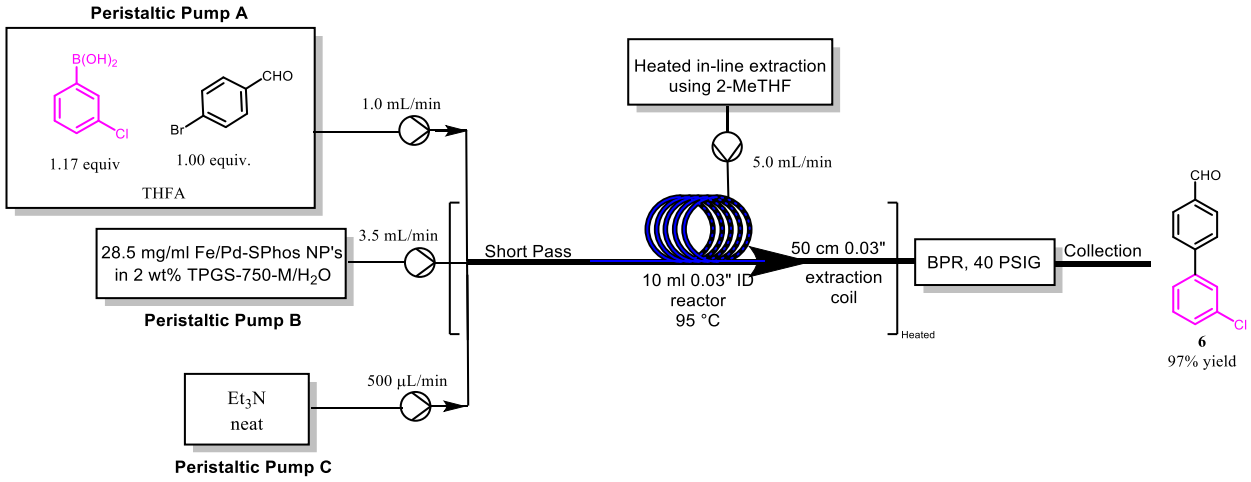
Peristaltic Pump A: A 28.5 mg/mL catalyst stock solution was prepared in a similar manner as the synthesis of **4**. The catalyst suspension was stirred continuously on a stir plate and used to prime a VapourTec E-Series peristaltic pump prior to a flow coupling reaction. The peristaltic pump was then set to deliver 700 µL/min.

Syringe 2: An 8 mL stainless steel syringe was charged with neat trimethylamine and set to deliver 100 µL/min.

Reactor Design: This synthesis was performed using the same apparatus prepared for the flow synthesis of **4** and run in a similar fashion using the flow rates listed above. The combined flow rate of 1000 µL/min was allowed to run for four residence times (8 min) to reach steady state. The steady state product mixture was then collected for five residence times (10 min) with a simultaneous heated in-line extraction using 1000 µL/min 2-MeTHF.

The collected bi-phase was then separated and the organic solvent was evaporated under reduced pressure. The residual oil was then dissolved in 3 mL of DCM and stirred vigorously with 3 mL of 1 N HCl to remove any acetal formation of the product. The organics were then removed and the aqueous was then extracted with DCM (2 x 1 mL). The product solution was then dried over sodium sulfate and purified via SiO_2 column (3:7 EtOAc/heptanes). The collected fractions were then combined and the solvent evaporated until constant mass was achieved resulting in product as a yellow solid (475.5 mg, 91% yield).

Scale-Up Synthesis of 6 in Flow



Peristaltic Pump A: To a 250 mL volumetric flask was added 4-bromobenzaldehyde (55.75 g, 301.32 mmol, 1.00 equiv) and (3-chlorophenylboronic acid (54.95 g, 351.37 mmol, 1.17 equiv). The flask was then mostly filled with tetrahydrofurfuryl alcohol (THFA) and allowed to dissolve at rt

NOTE: This mixture should not be heated; heating will result in acetal formation between THFA and 4-bromobenzaldehyde which will not couple under the reaction conditions.

Once homogeneous, the flask was then filled to the volumetric line using THFA. This solution was then used to prime a VapourTec E-Series pump prior to a flow coupling run. The peristaltic pump was then set to deliver 1 mL/min.

Peristaltic Pump B: A 28.5 mg/mL catalyst stock solution was prepared by suspending 28.5 g of freshly prepared Fe/ppm Pd (SPhos) NPs in 1 L of TPGS-750-M, 2 wt % in water. Upon addition of the aqueous surfactant solution to the NPs, the mixture was sonicated for 1 h in a rt water bath and stirred continuously prior to use. The catalyst suspension was then stirred continuously on a stir plate and was used to prime a VapourTec E-Series peristaltic pump immediately prior to a flow coupling reaction. The peristaltic pump was then set to deliver 3.5 mL/min.

Peristaltic Pump C: A VapourTec E-Series pump was primed using neat triethylamine and set to deliver 0.5 mL/min.

Reactor Design: The three peristaltic pumps were plumbed into a cross mixer (Tefzel, 0.03" ID) such that **Peristaltic Pump B**, containing the NPs, was delivered at 180 °C through the mixer and that **Peristaltic Pumps A and C** were delivered perpendicular and through check-valves (DATA). The cross mixer was then plumbed directly into a 10 mL reactor coil (PFA, 0.03" ID). The reactor coil was then plumbed into a T-mixer (Tefzel, 0.03" ID) wherein which 2-methyltetrahydrofuran is delivered perpendicularly through a check valve into that stream as an in-line extractor. The cross mixer, reaction coil, and in-line extraction units are all heated to 95 °C and held at that temperature during the run. The extraction mixture prior to the run is then delivered into a self-draining pressurized back-pressure regulator held at 40 PSIG.

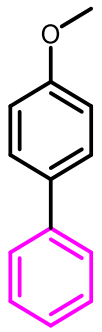
The 10 mL reactor / back-pressure system described above was then pre-filled with TPGS-750-M, 2 wt % in water prior to fitting peristaltic pumps to the cross mixer. The three peristaltic pumps were then turned on simultaneously and the system was allowed to reach steady state at a combined flow rate of 5 mL/min over three residence times (6 min). The product mixture was then collected, along with a 5 mL/min heated in-line extraction using 2-MeTHF, over the course of 90 min.

After the flow reaction was complete, the collected bi-phase was then separated and the organics were evaporated under reduced pressure. The resulting residual oil was then treated with water (500 mL) in a separatory funnel and the crude oil was collected from the bottom. The aqueous was then extracted with DCM (2 x 100 mL), which was then combined with the collected oil. The DCM layer was then treated with 1 N HCl (100 mL) to remove any acetal formation from the product. The DCM layer was then removed, and the aqueous layer was extracted with DCM (1 x 50 mL). The combined organics were then dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude organics were then purified via SiO_2 column (3:7 EtOAc/heptanes). The recovered fractions were then

evaporated under reduced pressure and dried under hi-vacuum until constant mass was achieved resulting in a yellow solid (22.8 g, 97% yield).

3. Analytical Data

4-Methoxy-1,1'-biphenyl (1)

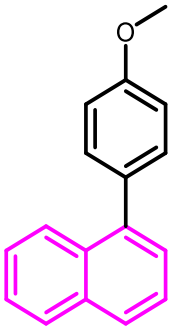


1

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 – 7.52 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.34 – 7.30 (m, 1H), 7.04 – 6.95 (m, 2H), 3.87 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.3, 141.0, 133.9, 128.9, 128.3, 126.9, 127.0, 114.3, 55.5.[3]

1-(4-Methoxyphenyl)naphthalene (2)

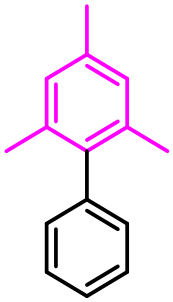


2

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.50 – 7.42 (m, 4H), 7.11 – 7.04 (m, 2H), 3.92 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.1, 140.0, 134.0, 133.2, 132.0, 131.2, 128.4, 127.5, 127.0, 126.2, 126.0, 125.8, 125.5, 113.8, 55.5.[4]

2,4,6-Trimethyl-1,1'-biphenyl (3)

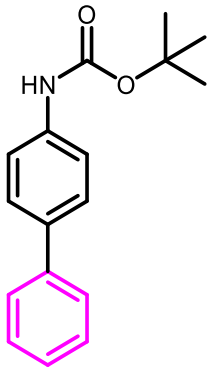


3

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (tt, *J* = 8.0, 1.5 Hz, 2H), 7.40 – 7.34 (m, 1H), 7.22 – 7.16 (m, 2H), 7.00 (s, 2H), 2.39 (s, 3H), 2.07 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 141.2, 139.2, 136.8, 136.1, 129.4, 128.5, 128.2, 126.6, 21.2, 20.9.[5]

***Tert*-butyl [1,1'-biphenyl]-4-ylcarbamate (4)**

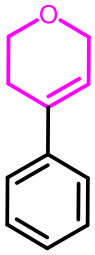


4

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (ddd, *J* = 15.6, 7.5, 1.8 Hz, 4H), 7.50 – 7.38 (m, 4H), 7.37 – 7.28 (m, 1H), 6.61 (s, 1H), 1.55 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 152.9, 140.8, 137.8, 136.0, 128.9, 127.7, 127.0, 126.9, 119.0, 80.8, 28.5.[6]

4-Phenyl-3,6-dihydro-2H-pyran (5)

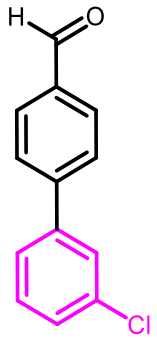


5

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 – 7.40 (m, 2H), 7.37 (td, *J* = 6.9, 1.9 Hz, 2H), 7.32 – 7.26 (m, 1H), 6.15 (dp, *J* = 3.0, 1.6 Hz, 1H), 4.36 (q, *J* = 2.8 Hz, 2H), 3.97 (t, *J* = 5.4 Hz, 2H), 2.56 (dddq, *J* = 5.6, 3.9, 2.9, 1.4 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 140.4, 134.2, 128.5, 127.4, 124.8, 122.5, 66.0, 64.6, 27.3.[7]

3'-Chloro-[1,1'-biphenyl]-4-carbaldehyde (6)



6

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.06 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.60 (t, *J* = 2.0 Hz, 1H), 7.50 (dt, *J* = 7.1, 1.8 Hz, 1H), 7.43 – 7.36 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 191.9, 145.7, 141.6, 135.7, 135.1, 130.4, 130.4, 128.6, 127.8, 127.6, 125.6.[8]

4. References

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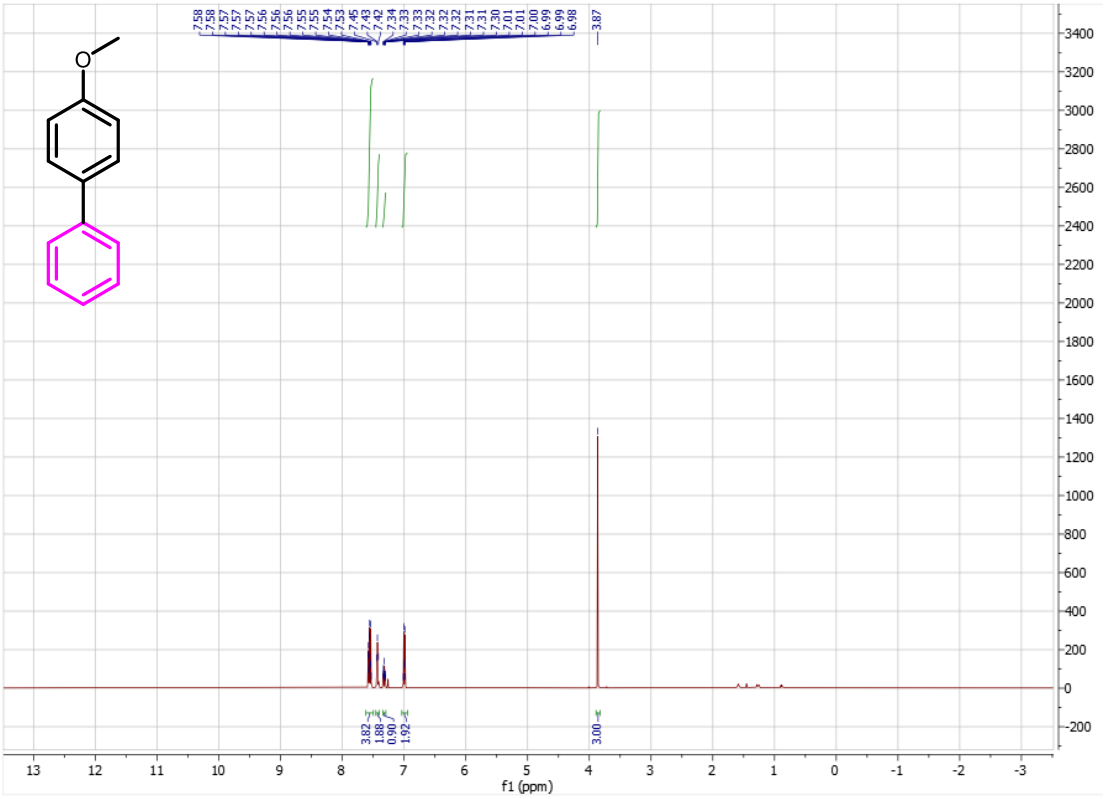
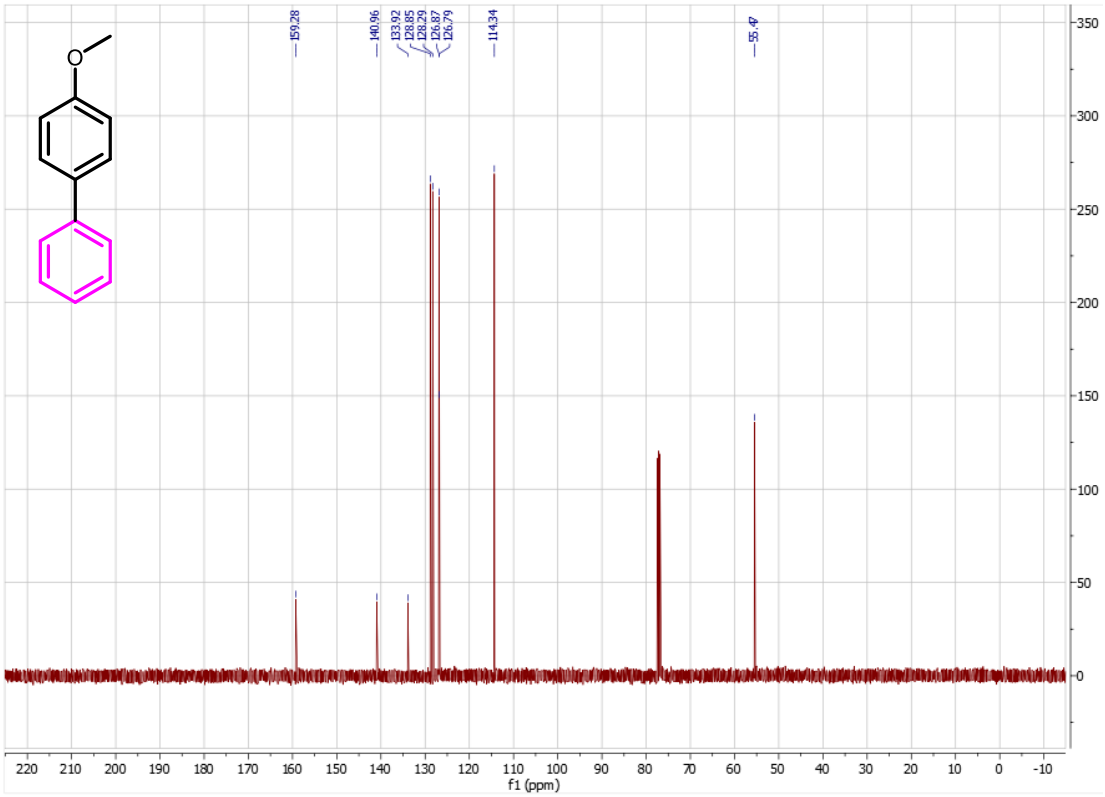
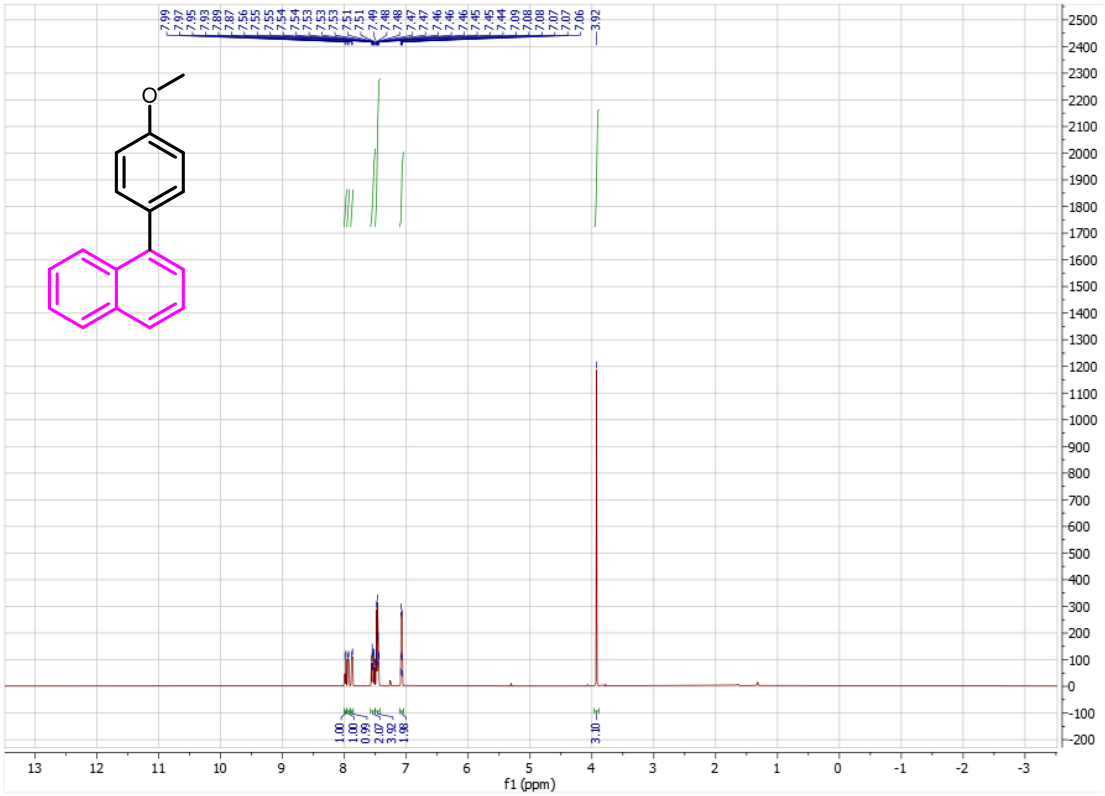
5. NMR Spectral Data



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7.54
7.54
7.53
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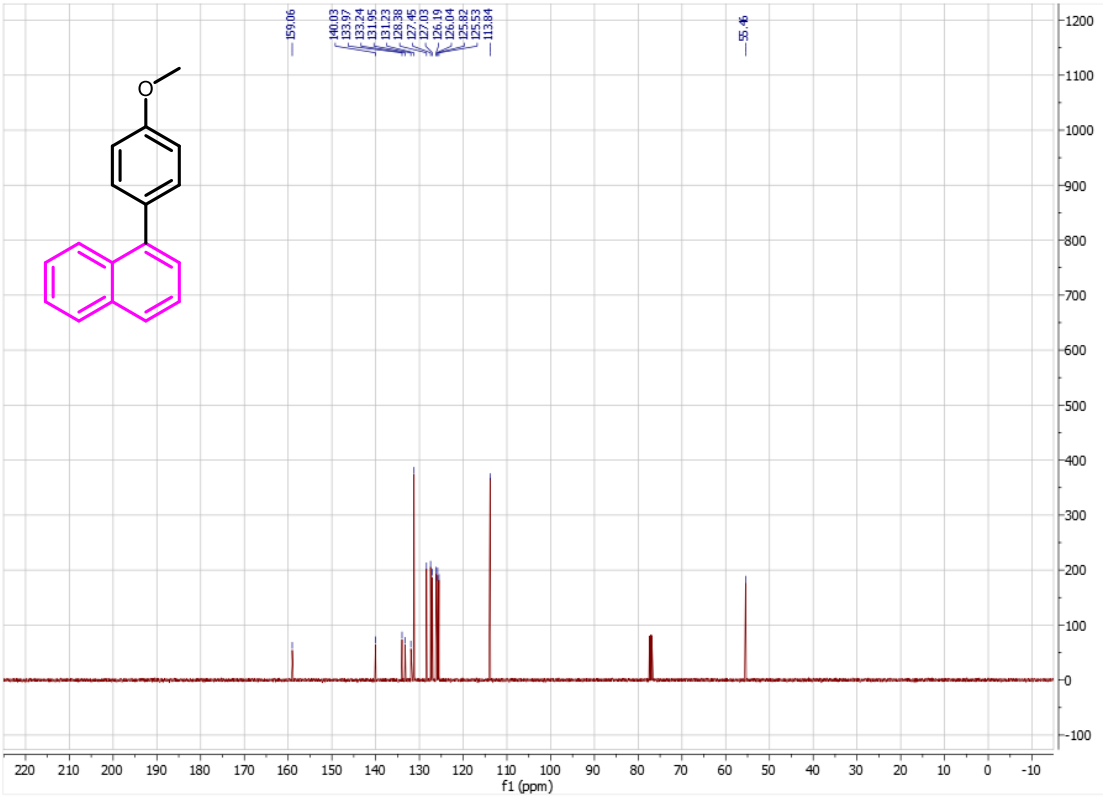
7.53
7.51
7.51
7.49
7.48
7.48
7.47
7.47
7.46
7.46
7.46
7.45
7.45
7.44
7.09
7.08
7.08
7.07
7.07
7.06
3.92
1.00
1.00
1.09
0.97
3.92
1.08
3.10
f1 (ppm)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133.24
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131.23
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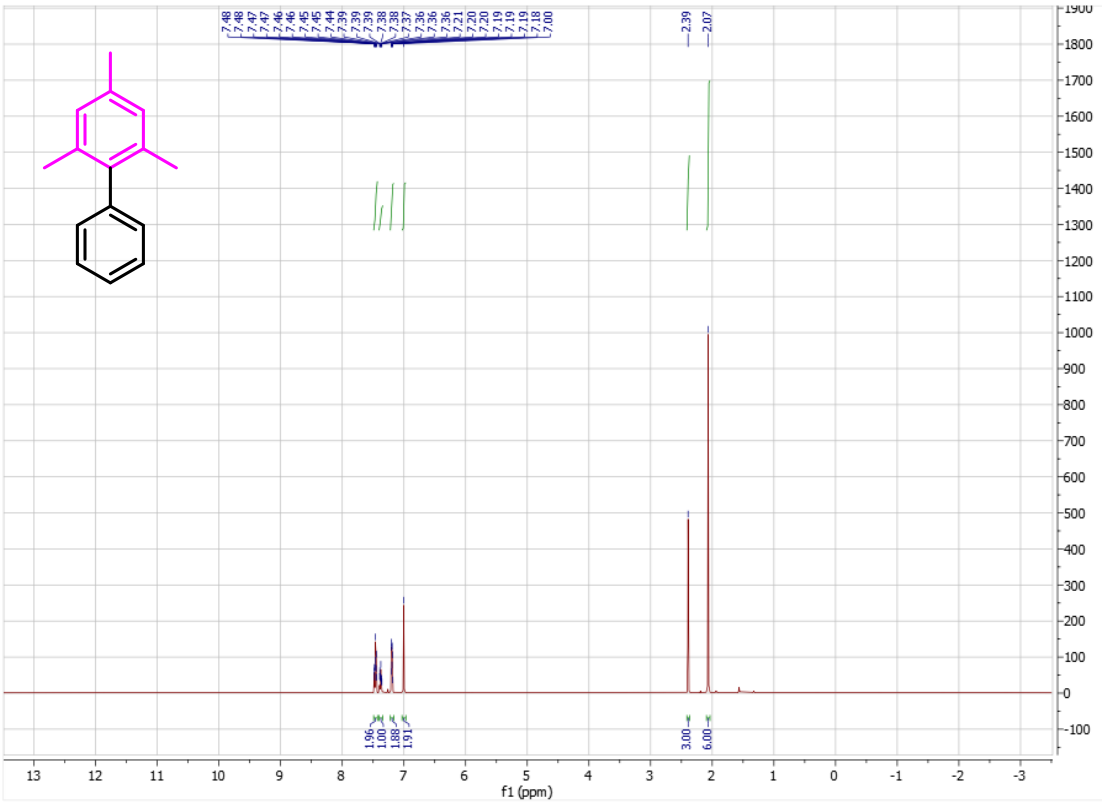
127.45
127.03
126.19
125.64
125.62
125.53
113.84
55.46
f1 (ppm)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7.46
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7.45
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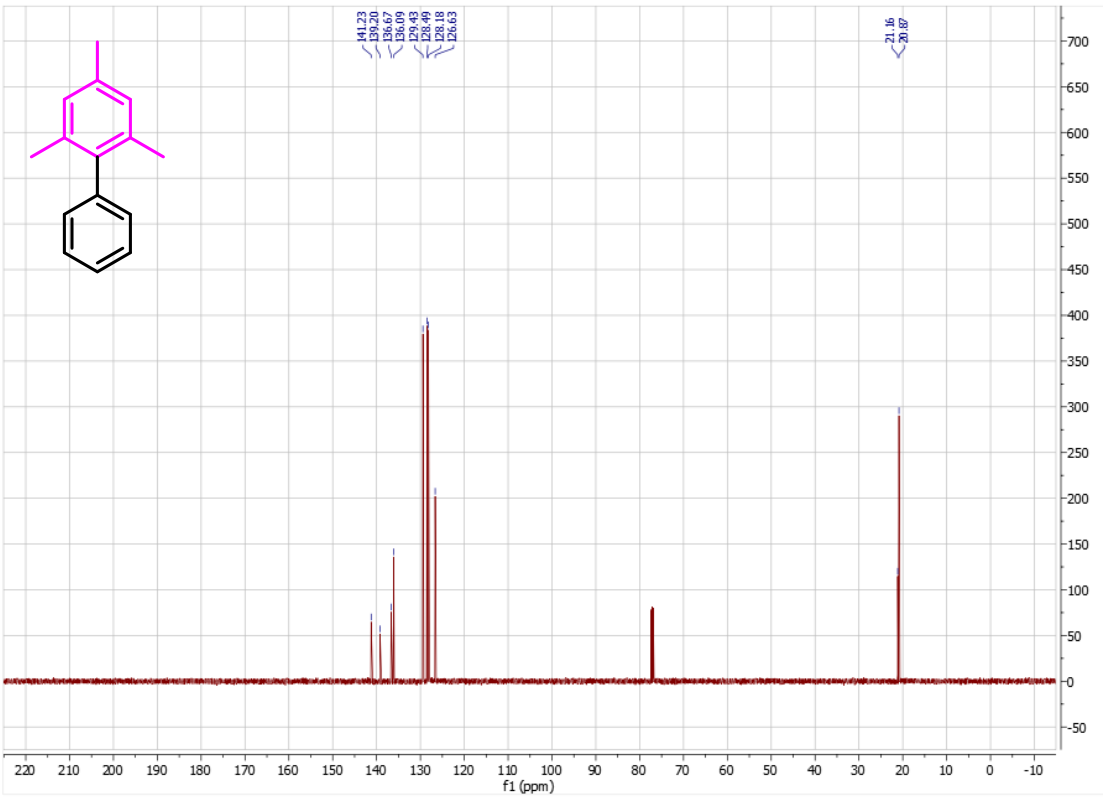
7.39
7.39
7.39
7.38
7.38
7.37
7.36
7.36
7.21
7.20
7.20
7.19
7.19
7.19
7.18
7.00
2.39
2.07
1.96
1.00
1.88
1.91
3.00
6.00
f1 (ppm)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136.67
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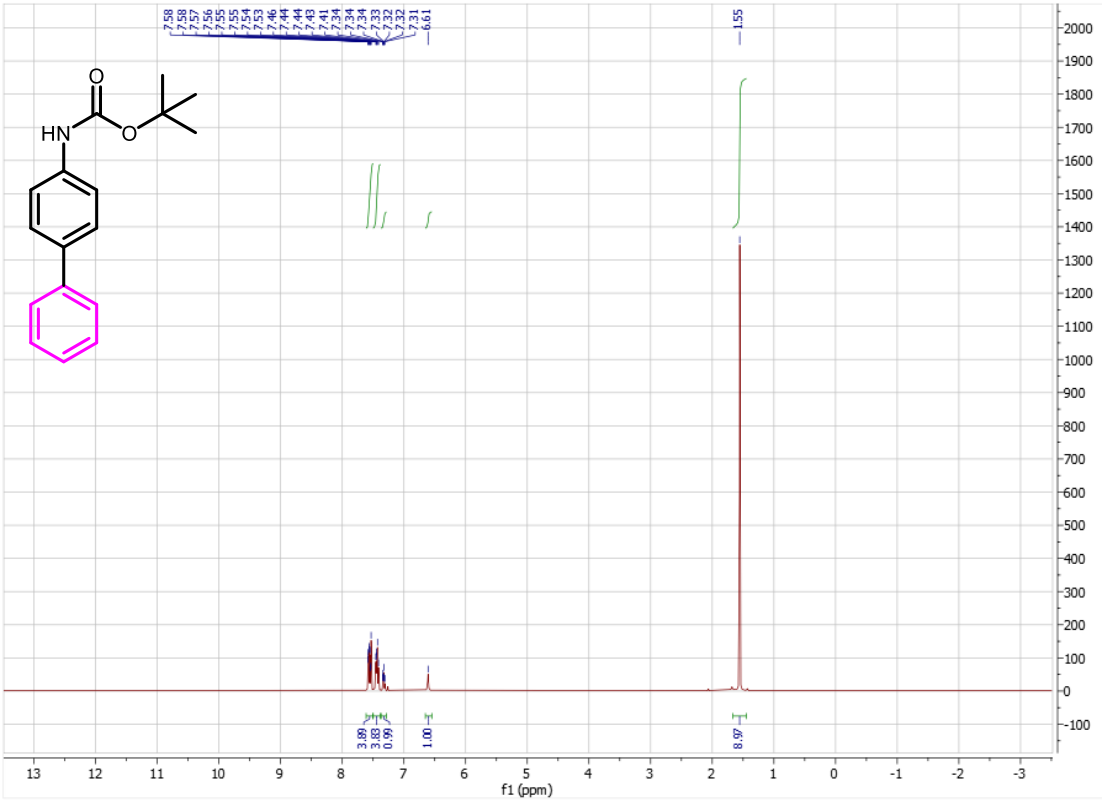
129.43
128.49
128.18
126.63
21.16
20.87
f1 (ppm)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O
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7.58
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7.56
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7.55
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7.53
7.46
7.44
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7.43
7.41
7.34
7.34
7.33
7.32
7.32
7.31
6.61
1.55
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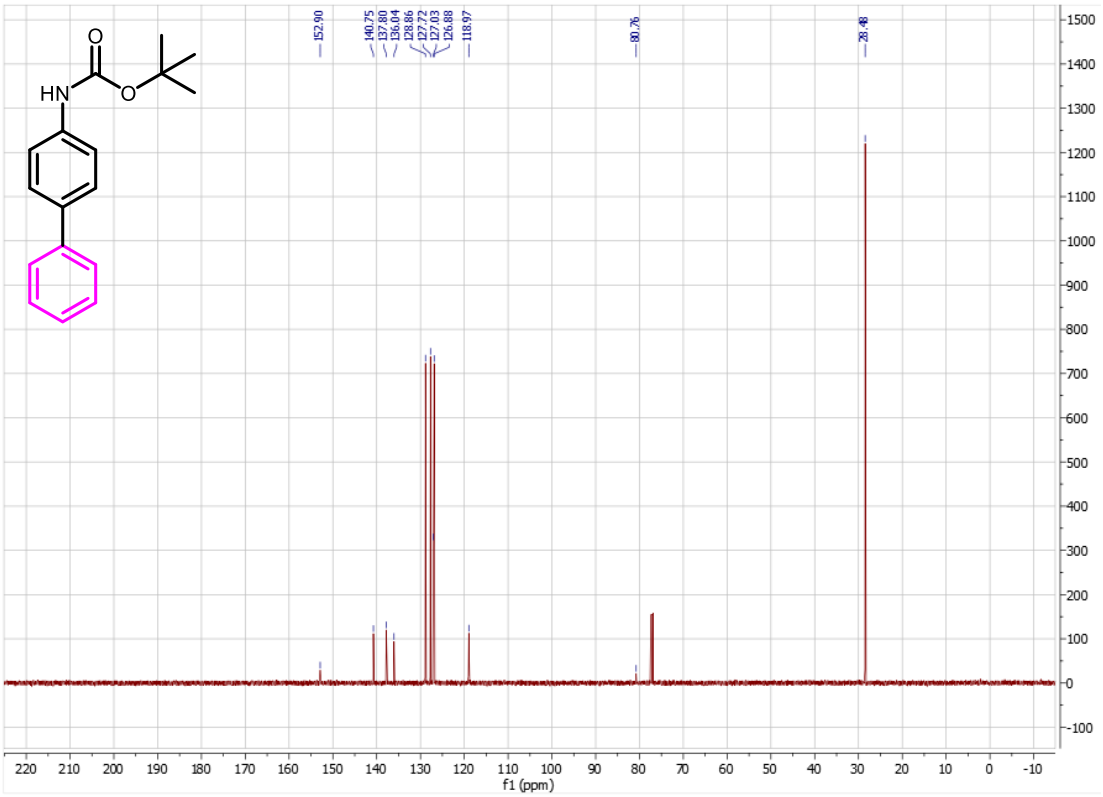
8.97
f1 (ppm)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80.76
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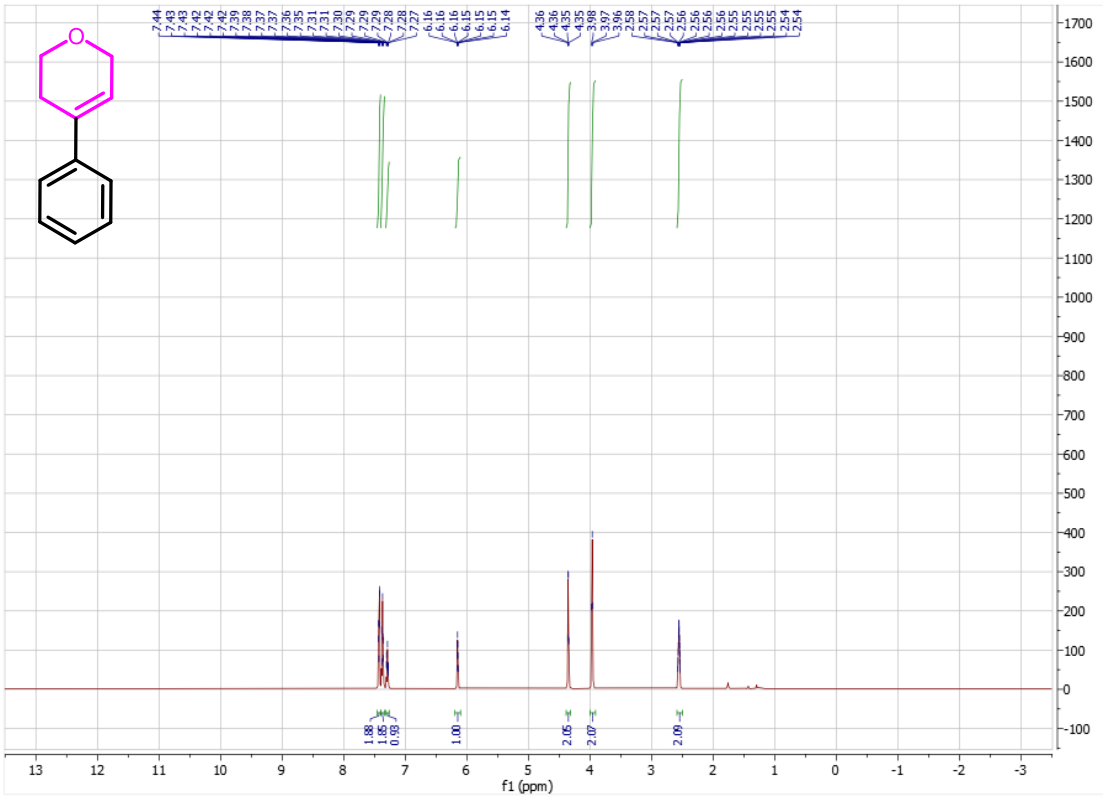
f1 (ppm)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2.56
2.56
2.56
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1.85
0.93
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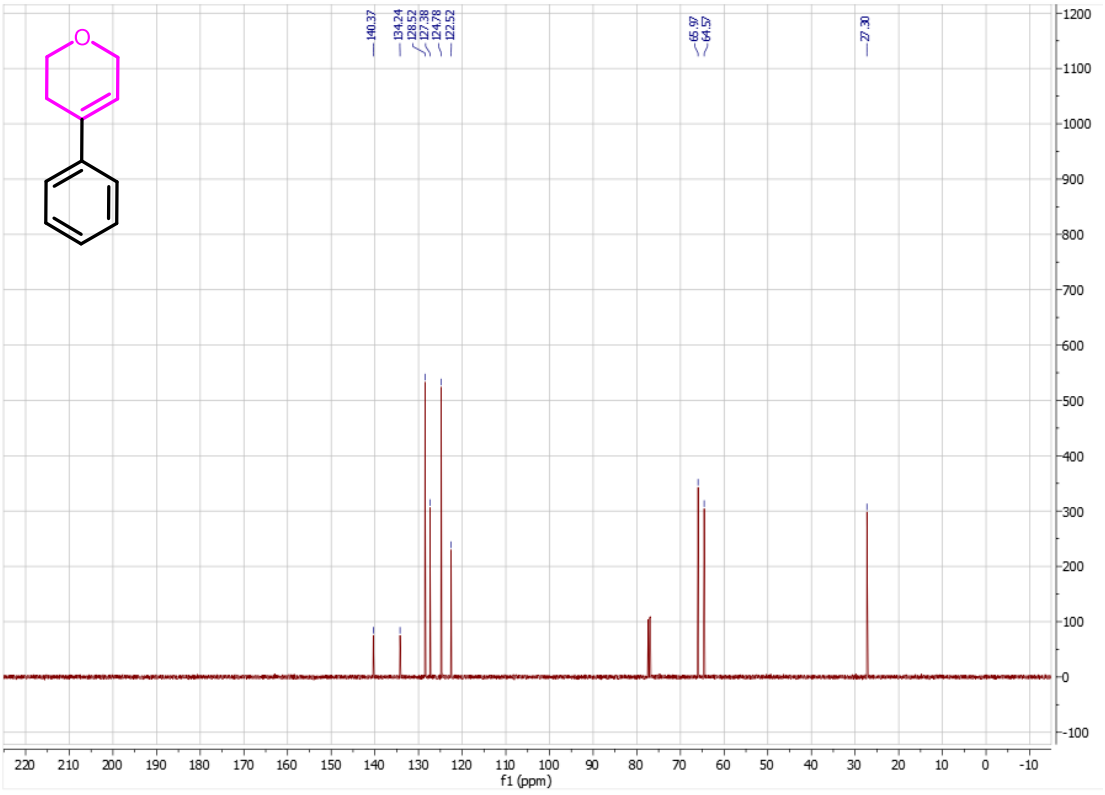
2.07
2.09
f1 (ppm)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124.78
122.52
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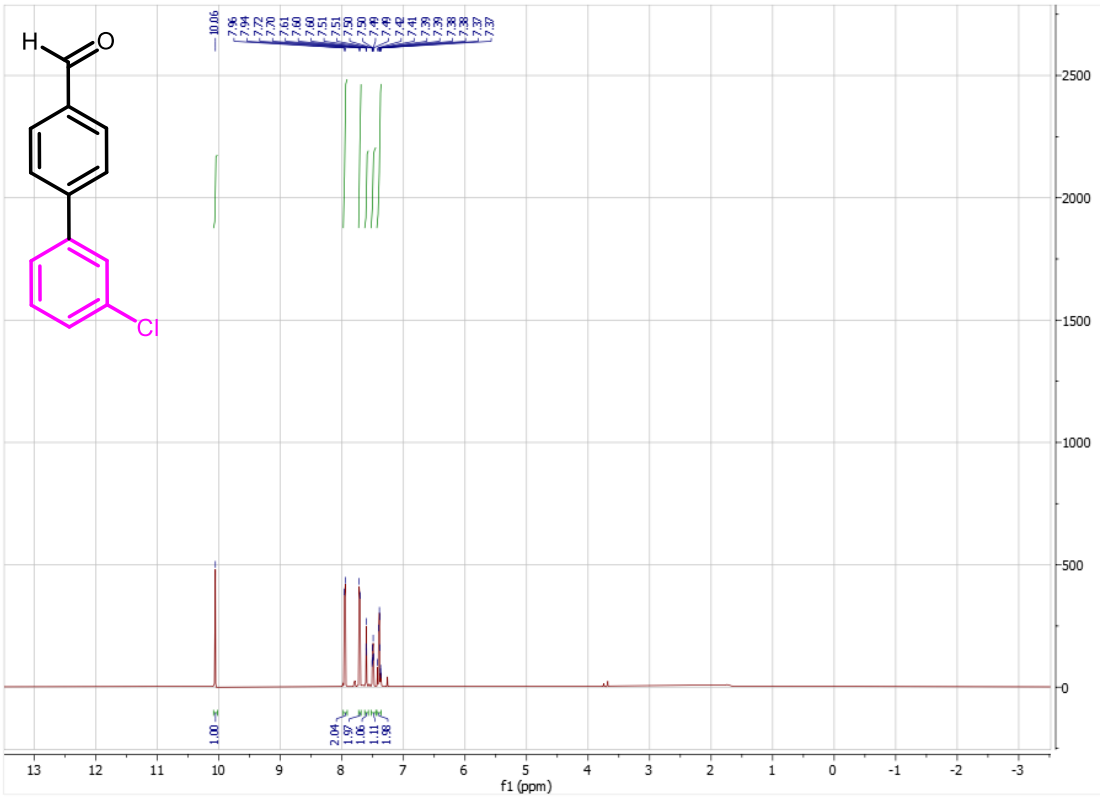
64.57
27.30
f1 (ppm)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7.61
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7.60
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7.51
7.50
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7.49
7.49
7.42
7.41
7.39
7.39
7.38
7.38
7.37
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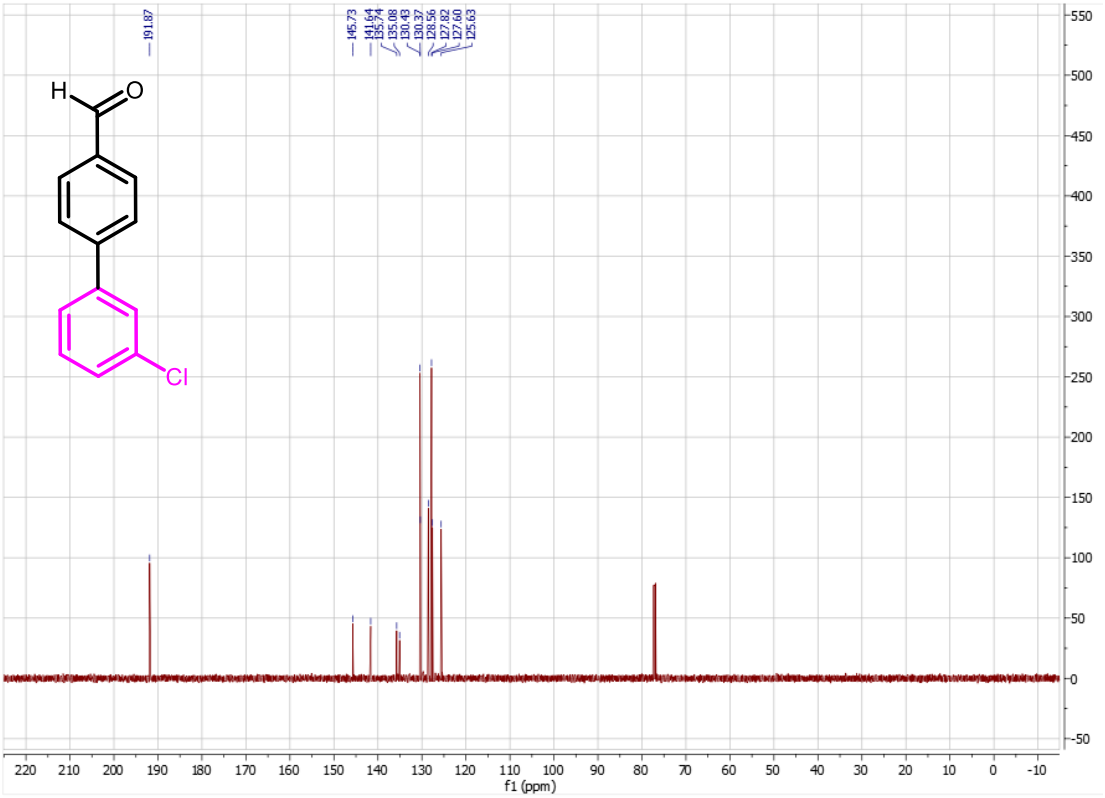
1.00
2.04
1.97
1.06
1.11
1.98
f1 (ppm)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127.60
125.63
f1 (ppm)