Palladium-Mediated Fluorination of Arylboronic Acids

Fluorination

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Transition-Metal-Mediated Carbon–Fluorine Bond Formation**

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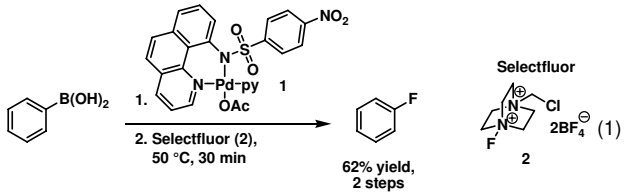
Fluorinated organic molecules have become increasingly important as pharmaceuticals[1] and tracers for positron-emission tomography (PET), a powerful technology for non-invasive molecular imaging.[2] The nucleus of choice for PET is fluorine-18 (^{18}F), which is typically introduced into PET tracers through the formation of carbon–fluorine bonds using nucleophilic fluoride ($^{18}F^-$) under harsh reaction conditions.[3] The short half-life of ^{18}F of 109 minutes requires that carbon–fluorine bond formation occur at a late stage of the PET tracer synthesis, ideally as the last step. Many promising PET tracers for imaging are currently inaccessible due to the lack of suitable chemistry for the general, late-stage introduction of fluorine into complex, functionalized molecules.[3, 4] Here, we present a new strategy for carbon–fluorine bond formation that relies on the fluorination of arylboronic acids via palladium complexes (eq 1). The reaction permits a general, regiospecific late-stage formation of carbon–fluorine bonds in the presence of a large variety of functional groups found in medicinally active molecules. Ultimately, we anticipate our new fluorination reaction will provide a chemical solution for the synthesis of currently inaccessible PET tracers to increase both knowledge and understanding of basic, biomedical, and pharmaceutical research through molecular imaging.[5-8]



Carbon–fluorine bond formation is a challenging chemical transformation, and no general, functional-group-tolerant fluorination reaction of arenes is currently available for the synthesis of complex molecules. Simple fluoroarenes are typically synthesized by pyrolysis of diazonium tetrafluoroborates,[9] direct fluorination using highly reactive elemental fluorine,[10] or nucleophilic aromatic substitution reactions of electron-poor aromatic molecules.[11,12] Common aromatic organometallics, such as aryllithiums and aryl Grignard reagents can afford arylfluorides when using electrophilic fluorine sources; however, neither aryllithiums nor aryl Grignard reagents can be used for the late-stage fluorination of arenes bearing electrophiles such as aldehydes or protic functionalities such as alcohols, limiting their general utility.[13] Organometallics with lower basicity such as arylzinc halides, arylsilanes, arylstannanes, and arylboronic acids afford the formation of fluorobenzene in less than 10% yield (see Supporting Information). The electrophilic fluorination of specific carbon–hydrogen bonds of phenylpyridine derivatives and related structures was reported in 2006 by Sanford, and uses catalytic palladium (II) acetate and N-fluoropyridinium salts.[14] The reaction takes advantage of a covalently attached pyridine directing group and affords fluorinated arylpyridine derivatives using microwave irradiation (100–150 °C, 1–4 h, 33–75% yield). A different approach, the reductive elimination of arylfluorides from palladium (II) fluoride complexes, would obviate the use of directing groups and has been investigated over the past decade by Grushin and Yandulov.[15,16] Carbon–fluorine bond formation to form aryl fluorides by reductive elimination from a Pd (II) fluoride complex has not yet been substantiated.[16,17] In general, all methods mentioned above cannot be employed for late-stage fluorination of structurally complex molecules due to either harsh reaction conditions or limited substrate scope.

We have sought a new regiospecific, late-stage fluorination reaction of arenes that encompasses a larger substrate scope than currently accessible, tolerates the presence of a variety of functional groups, is not limited to a particular class of arenes, and is not dependent on a directing group. Our strategy is illustrated in equation 1, and consists of the synthesis of new aryl palladium complexes that react with the electrophilic fluorination reagent Selectfluor™[18] to afford fluoroarenes. Our initial investigations for the design of transition-metal complexes that afford efficient fluorination was guided by the observation that palladium has been successfully employed in several carbon-heteroatom bond formations,[19,20] including carbon–fluorine bonds for specific substrates.[14, 21] Additionally, the development of our methodology was directed by the necessity to predict and control the exact location of fluorination and the need to introduce fluorine at any desired aromatic position. Therefore, the target molecules for fluorination are pre-functionalized with boronic acids at the position where fluorine is desired. Boronic acids are readily accessible, compatible with a variety of functional groups present in PET tracers, competent nucleophiles for transmetallation to palladium, and can be introduced into complex molecules.[22]

Several aryl palladium complexes based on ligands that are commonly used for palladium chemistry did not yield carbon–fluorine bond formation when evaluated for fluorination. We therefore designed new aryl palladium complexes that are derived from a bidentate nitrogenous ligand that contains a neutral and an anionic nitrogen donor atom for coordination to palladium. Our design was based on the assumptions that nitrogenous ligands resist oxidation by electrophilic fluorination reagents, can support high-valent aryl palladium fluorides for subsequent carbon–fluorine reductive elimination, and do not induce competing nitrogen–fluorine reductive elimination. We prepared the new palladium acetate complex **1** by known sulfonamide insertion[23] into the

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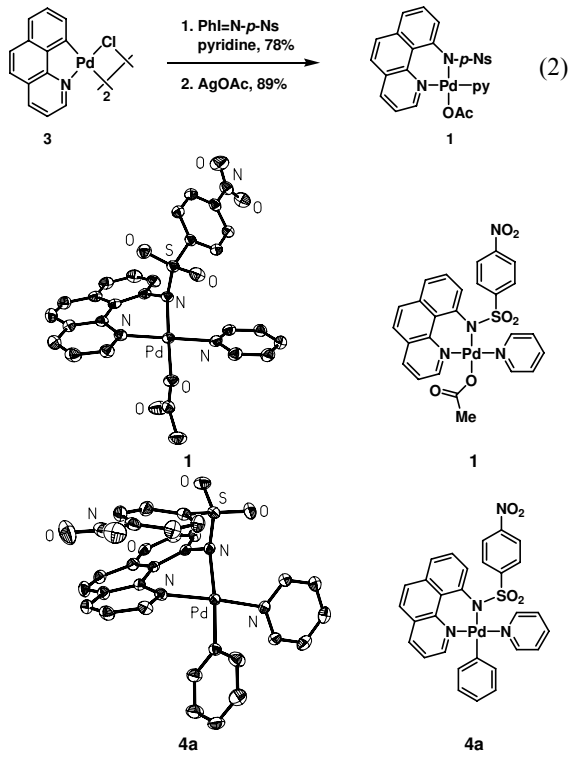
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

palladium–carbon bond of benzoquinoline-derived palladacycle **3**,[24] followed by chloride-acetate ligand exchange (eq 2). The aryl palladium complexes **4a–m** were prepared by transmetallation using 12 different arylboronic acids (Table 1). Transmetallation proceeded at 23 °C in a basic methanol/benzene solution and afforded the palladium complexes as moisture and air stable yellow solids in 65–91% yield on a 400 mg scale after purification by chromatography on silica gel. The aryl palladium complexes derived from **1** are tolerant toward the presence of a variety of functional groups found in medicinally active compounds, including alcohols, an indole, and a primary amide. The phenyl palladium sulfonamide **4a** (R = H) crystallized in a square planar geometry with the aryl group trans to the κ^1-sulfonamide ligand (Figure 1). The trans relationship may be crucial to prevent undesired carbon–nitrogen bond formation through reductive elimination of the aryl and sulfonamide substituents.[25]

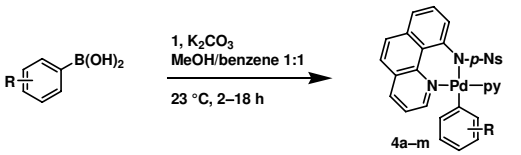


(2)

Figure 1. ORTEP diagrams of **1** and **4a** with thermal ellipsoids at 50% probability showing the trans relationship of the sulfonamide nitrogen atom to the acetate and aryl ligand, respectively.

Fluorination of the aryl palladium complexes **4a–m** using the electrophilic reagent Selectfluor™ (**2**) afforded the arylfluorides **5a–m** regiospecifically in 31–82% isolated yield (Table 2). Our fluorination reaction tolerates the presence of a variety of functional-groups, most notably protic functionalities that are not typically compatible with nucleophilic aromatic substitution methods due to the high basicity of fluoride ion in anhydrous solvents suitable for nucleophilic displacement.[10] Additionally, electron-rich fluoroarenes (**5b**, **5g**, **5h**), which cannot be synthesized through late-stage fluorination using nucleophilic displacement, are accessible regiospecifically. The scope of the reaction was further extended to electron-poor (**5e**, **5l**), hetero (**5m**), and ortho-substituted arenes (**5k**). Fluorination proceeds in 30 minutes when performed in acetonitrile or acetone at 50 °C. While fluorination

Table 1. Transmetallation to form arylpalladium (II) complexes.



(3)

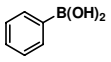
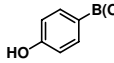
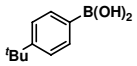
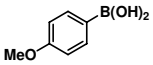
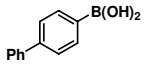
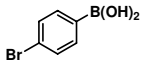
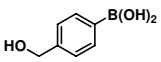
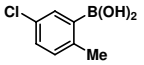
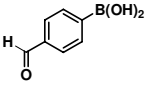
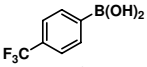
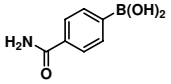
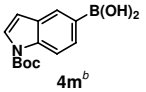
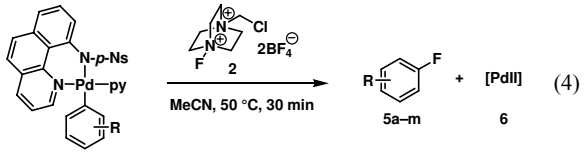
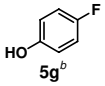
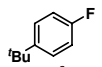
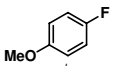
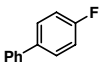
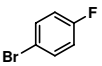
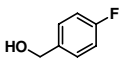
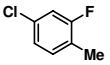
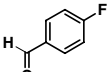
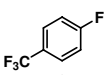
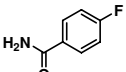
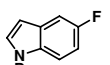
boronic acid	yield	boronic acid	yield
 **4a**	76%	 **4g**	70%
 **4b**	85%	 **4h**	79%
 **4c**	91%	 **4i**	65%
 **4d**	80%	 **4k**	90%
 **4e**	71%	 **4l**[a]	88%
 **4f**	73%	 **4m**[b]	76%

Table 2. Electrophilic fluorination of arylpalladium complexes.



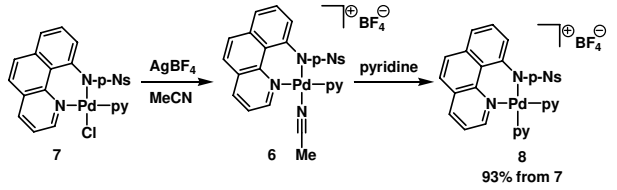
(4)

4	product	yield	4	product	yield
4a	 **5a**[a]	81%	**4g**	 **5g**[b]	31%
4b	 **5b**[a]	79%	**4h**	 **5h**[b]	46%
4c	 **5c**	72%	**4i**	 **5i**	73%
4d	 **5d**	70%	**4k**	 **5k**	82%
4e	 **5e**	61%	**4l**	 **5l**[a]	54%
4f	 **5f**	74%	**4m**	 **5m**[b]	60%

[a] Yield for this entry determined by ^{19}F NMR analysis due to low boiling point of product. [b] Acetone used as solvent.

was observed at 23 °C, the highest yields were obtained at a reaction temperature of 50 °C. Yields of isolated products were identical when the fluorination reactions were performed under rigorous exclusion of air and moisture or open to the atmosphere.

The fate of the palladium after fluorination was determined to be cationic palladium complex **6**, which was independently synthesized by treatment of palladium chloride **7** with silver tetrafluoroborate in acetonitrile (Scheme 1). Subsequent reaction of **6** with one equivalent of pyridine afforded the stable palladium tetrafluoroborate salt **8**, which was isolated and characterized. Addition of pyridine after termination of the reaction displayed in equation 4, table 2 also afforded **8**, which suggests that the pyridine-sulfonamide ligand remained coordinated to palladium throughout the reaction. The stability of the ligand-metal complex is advantageous for a prospective catalytic version of the presented fluorination reaction.



Scheme 1. Independent synthesis of palladium byproduct **6**.

Transition-metal catalysis for carbon–fluorine bond formations is a valuable goal in itself. However, for the synthesis of PET tracers, a fluorination reaction using stoichiometric amounts of transition-metal is superior to a catalytic version. Reactions stoichiometric in transition-metal are faster than the corresponding catalyzed reactions, and time is the most important factor for the efficient preparation of PET tracers due to the short half-life of ^{18}F. Moreover, price and toxicity of palladium are of lesser importance for applications in molecular imaging because PET tracers are used in picomolar quantities and are purified by HPLC before injection in vivo.

Two possible mechanisms for the presented fluorination reaction are electrophilic palladium–carbon bond cleavage and carbon–fluorine reductive elimination from a discrete, high-valent palladium fluoride.[21] The redox activity of palladium (II) may play a crucial role for fluorination, which suggests a high-valent, discrete palladium fluoride complex as an intermediate before carbon–fluorine reductive elimination. Neither of the two mechanisms can be ruled out based on our experimental observations.

In conclusion, we report a fluorination reaction of arylboronic acids mediated by palladium, in which carbon–fluorine bond formation is the final synthetic step. The functional group tolerance, broad substrate scope, and regiospecificity of the reaction provide a general method for the late-stage fluorination of functionalized arenes. This new chemistry could be the basis for the development of a general solution for the synthesis of PET tracers for biomedical applications. Electrophilic ^{18}F sources are available, but from a biomedical perspective nucleophilic $^{18}F^-$ is the preferred source of fluorine for PET imaging because it can be prepared in high specific activity.[3] A subsequent goal is therefore the development of an electrophilic fluorine source originating from nucleophilic fluoride ($^{18}F^-$). Further development of the transformation presented herein, in combination with known or new electrophilic fluorine sources, may deliver promising PET tracers to impact biomedical research in the fields of cancer, neurodegenerative diseases, gene therapy, and drug development.

Experimental Section

A representative transmetallation/fluorination sequence is described below:

Aryl palladium complex **4c**: To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12 mL) and benzene (12 mL) at 23 ºC is added 4-biphenyl boronic acid (140 mg, 0.706 mmol, 1.10 equiv) and K2CO3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 11 h, and the solvent is removed in vacuo. To the solid residue is added CHCl3 (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with CHCl3 (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na2SO4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 1:1 (v/v) to afford 418 mg of the title compound as a yellow solid (91% yield).

4-Fluorobiphenyl **5c**: To 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo-[2.2.2]octane bis(tetrafluoroborate) (**2**) (85.0 mg, 0.240 mmol, 1.20 equiv) in acetonitrile (6.0 mL) at 50 ºC is added aryl palladium complex **4c** as a solid (143 mg, 0.200 mmol, 1.00 equiv) in 10 portions over 10 min. The reaction mixture is subsequently stirred at 50 ºC for 20 min. After cooling to 23 ºC, pyridine is added to the reaction mixture (8.1 µL, 0.10 mmol, 1.0 equiv), and the reaction mixture is filtered through a plug of celite. The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 99:1 (v/v) to afford 24.8 mg of the title compound as a white solid (72% yield).

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Keywords: fluorination · PET · palladium · boron · pyridine-sulfonamide

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[23] A. R. Dick, M. S. Remy, J. W. Kampf, M. S. Sanford *Organometallics* **2007**, *26*, 1365–1370.
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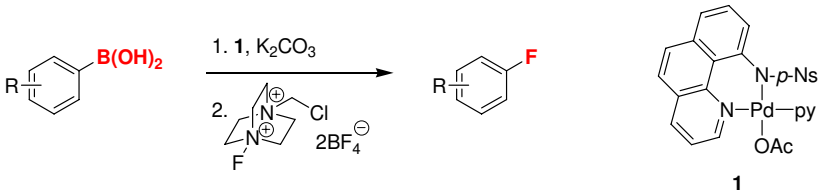
Entry for the Table of Contents

Fluorination

Takeru Furuya, Hanns Martin Kaiser, and Tobias Ritter* _____ **Page – Page**

Transition-Metal-Mediated Carbon-Fluorine Bond Formation



1

We report a mild, regiospecific, and functional-group-tolerant two-step fluorination reaction of arylboronic acids via novel arylpalladium complexes. The functional-group tolerance, broad substrate scope, and regiospecificity of the fluorination reaction presented herein expand the scope of other fluorination methods previously reported.

Supporting Information

Transition-Metal Mediated Carbon-Fluorine Bond Formation

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Cambridge, Massachusetts 02138

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Materials and Methods

All reactions were carried out under an ambient atmosphere unless otherwise mentioned. Except as indicated otherwise, reactions were magnetically stirred and monitored by thin layer chromatography (TLC) using EMD TLC plates pre-coated with 250 μm thickness silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained using ceric ammonium molybdate or potassium permanganate stain. Flash chromatography was performed on Dynamic Adsorbents Silica Gel 40–63 μm particle size using a forced flow of eluant at 0.3–0.5 bar pressure.[1] Concentration under reduced pressure was performed by rotary evaporation at 25–30 ºC at appropriate pressure. Purified compounds were further dried under high vacuum (0.01–0.05 Torr). Yields refer to purified and spectroscopically pure compounds. Melting points were measured on a Büchi 510 apparatus. All melting points were measured in open capillaries and are uncorrected. NMR spectra were recorded on a Varian Unity/Inova 500 spectrometer operating at 500MHz and 125MHz for ^{1}H and ^{13}C acquisitions, respectively, or on a Varian Mercury 400 spectrometer operating at 375 MHz for ^{19}F acquisition. Chemical shifts (δ) of ^{1}H-NMR and ^{13}C-NMR spectra are reported in ppm with the solvent resonance as the internal standard. Chemical shifts (δ) of ^{19}F-NMR measurements are reported relatively to $CFCl_3$ as the external standard. Data is reported as follows: s = singlet, br = broad, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants in Hz; integration. High-resolution mass spectra were obtained on Jeol AX-505 or SX-102 spectrometers at the Harvard University Mass Spectrometry Facilities. THF was distilled from sodium/ benzophenone prior to use. Benzo[*h*]quinoline was purchased from TCI America. Iodobenzene diacetate, 4-nitrobenzenesulfonyl amide, phenyllithium (1.6 M in dibutylether), phenylmagnesium bromide (1.0 M in THF), 4-chlorophenylmagnesium bromide (1.0 M in Et2O), tributylphenyltin, and N-fluorobenzene-sulfonimide were purchased from Aldrich. Palladium acetate and boronic acids were purchased from Frontier Scientific or Boron Molecular. Phenyltrimethylsilane and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) were purchased from VWR and used as received. Phenylzinc chloride[2] and potassium phenyltrifluoroborate[3] were synthesized according to the literature procedures.

---

[1] Still, W. C., Kahn, M. & Mitra, A. Rapid chromatographic technique for preparative separations with moderate resolution. *J. Org. Chem.* **43**, 2923-2925 (1978).

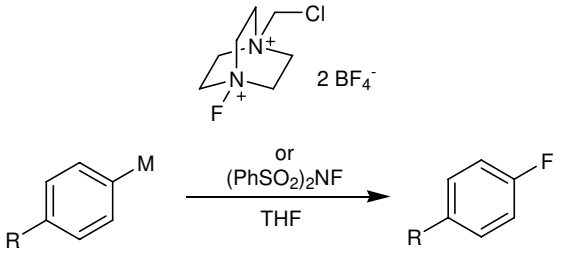
[2] Jansen, A. & Krause, N. Transition metal-promoted synthesis of functionalized and unfunctionalized pyridylallenes. *Synthesis* **14**, 1987-1993 (2002).

[3] Vedejs, E., Chapman, R. W., Fields, S.C., Lin, S & Schrimpf, M. R. Conversion of arylboronic acids into potassium aryltrifluoroborates: convenient precursors of arylboron difluoride lewis acids. *J. Org. Chem.* **60**, 3020–3027 (1995).

Experimental Data

Experimental Procedures and Compound Characterization

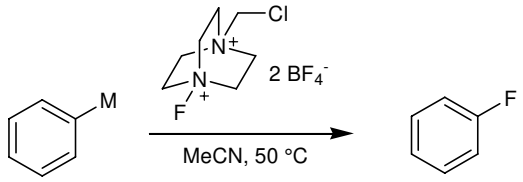
General procedure A for the fluorination of aryllithium, arylmagnesium, and arylzinc substrates:



R = H, Cl; M = Li, MgBr, ZnCl

Under nitrogen atmosphere, the main-group organometallic (0.0400 mmol, 1.00 equiv) is added to 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoro-borate) (14.2 mg, 0.0400 mmol, 1.00 equiv) or N-fluorobenzenesulfoneimide (12.6 mg, 0.0400 mmol, 1.00 equiv) in THF (0.4 mL) at 23 ºC. The reaction mixture is stirred at 23 ºC for 12 hr and to the reaction mixture is added 3-nitrofluorobenzene (4.00 μL, 0.0376 mmol). The yields are determined by comparing integration of the ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC) resonance of fluorobenzene (–115.3 ppm) or 1-chloro-4-fluorobenzene (–116.5 ppm) and that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S1.

General procedure B for the fluorination of arysilane, arylstannate, and arylboronic acid derivatives:



M = $SiMe_3$, $SnBu_3$, $B(OH)_2$, BF_3K

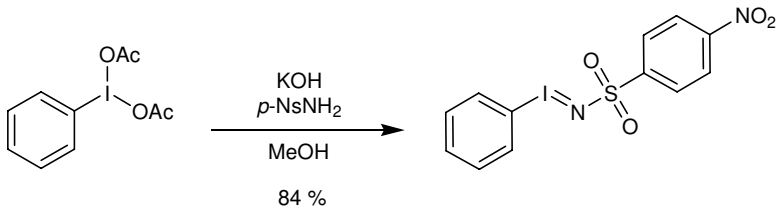
To 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (14.2 mg, 0.0400 mmol, 1.00 equiv) in acetonitrile (0.4 mL) at 23 ºC is added the main-group organometallic (0.0400 mmol, 1.00 equiv). The reaction mixture is stirred at 50 ºC for 12 hr and to the reaction mixture is added 3-nitrofluorobenzene (4.00 μL, 0.0376 mmol). The yields are determined by comparing integration of the ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC) resonance of fluorobenzene (–115.3 ppm) and that of 3-nitrofluorobenzene (–112.0 ppm). Yields are reported in Table S1.

Table S1.: Direct synthesis of fluorobenzene derivatives employing electrophilic fluorine sources:

Organometallic	Reagent	Product	Yield [%] (19F-NMR)
PhLi	$(PhSO_2)_2NF$	PhF[a]	39
PhMgBr	$(PhSO_2)_2NF$	PhF[a]	50
4-Cl-C_6H_4MgBr	$(PhSO_2)_2NF$	4-Cl-C_6H_4F[a]	38
PhZnCl	Selectfluor	PhF[a]	6
$PhB(OH)_2$	Selectfluor	PhF[b]	4
$PhSiMe_3$	Selectfluor	–[b]	0
$PhSnBu_3$	Selectfluor	–[b]	0

[a] following general procedure A
[b] following general procedure B

[{(4-Nitrophenyl)sulfonyl}imino]phenyliodinane[4,5]



To 4-nitrobenzenesulfonyl amide (5.00 g, 24.8 mmol, 1.00 equiv) in methanol (100 mL) at 23 ºC is added potassium hydroxide (3.48 g, 62.0 mmol, 2.50 equiv). The reaction mixture is stirred at 23 ºC for 10 min and cooled to 0 ºC. To the reaction mixture at 0 ºC is added iodobenzene diacetate (7.98 g, 24.8 mmol, 1.00 equiv). The reaction mixture is stirred at 0 ºC for 10 min and further stirred at 23 ºC for 2.0 h. The reaction mixture is poured onto cold water (700 mL) and kept at 0 ºC for 4 h. The suspension is filtered off and the filter cake is washed with water (2 × 200 mL) and methanol (2 × 200 mL) to afford 8.39 g of the title compound as a white solid (84% yield).

^{1}H-NMR (500 MHz, DMSO-*d*-6, 23 ºC): δ 8.02 (d, J = 9.0 Hz, 2H), 7.73 (d, J = 9.0 Hz, 2H), 7.71 (d, J = 6.5 Hz, 2H), 7.41 (t, J = 7.0 Hz, 1H), 7.26 (dd, J = 8.0 Hz, J = 7.5 Hz, 2H); ^{13}C-NMR (125 MHz, DMSO-*d*-6, 23 ºC): δ 151.7, 148.6, 134.4, 131.4, 130.9, 128.2, 124.3, 117.9. These spectroscopic data correspond to the

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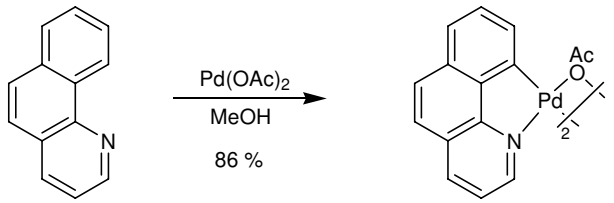
reported data in reference 5.

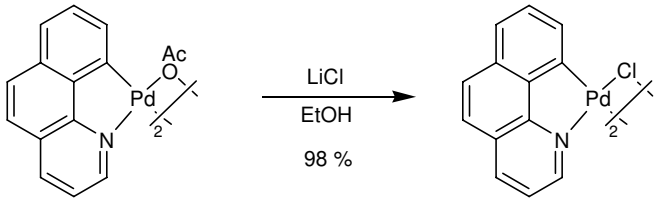
Benzo[*h*]quinolinyl palladium acetate dimer[6]



To benzo[*h*]quinoline (2.60 g, 14.5 mmol, 1.00 equiv) in MeOH (230 mL) at 23 ºC is added palladium acetate (3.26 g, 14.5 mmol, 1.00 equiv). After stirring for 3.0 h, the suspension is filtered off and the filter cake is washed with MeOH (100 mL) and Et_2O (100 mL) to afford 4.27 g of the title compound as a yellow solid (86% yield).

^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 7.80 (dd, J = 5.5 Hz, 1.5 Hz, 1H), 7.43 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H), 7.24–7.18 (m, 3H), 7.08 (dd, J = 7.0 Hz, J = 1.5 Hz, 1H), 6.97 (d, J = 9.0 Hz, 1H), 6.46 (dd, J = 7.5 Hz, 5.0 Hz, 1H), 2.38 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 182.5, 153.2, 148.9, 148.8, 140.0, 135.3, 132.4, 129.0, 127.9, 127.7, 125.0, 122.9, 122.1, 119.8, 25.2. These spectroscopic data correspond to the reported data in reference 6.

Benzo[*h*]quinolinyl palladium chloro dimer[7]



To benzo[*h*]quinolinyl palladium acetate dimer (4.27 g, 12.4 mmol, 1.00 equiv) in EtOH (100mL) at 0 ºC is added lithium chloride (10.5 g, 24.8 mmol, 20.0 equiv). The reaction mixture is warmed to 23 ºC and stirred for 1.0 h. The reaction mixture is filtered off and the filter cake is washed with water (3 × 100 mL), MeOH (2 × 100 mL), and Et_2O (100 mL) to afford 3.89 g of the title compound as a pale yellow solid (98% yield).

^{1}H-NMR (500 MHz, DMSO-*d*-6, 23 ºC): δ 9.44 (d, J = 4.5 Hz, 1.0 Hz, 1H), 8.72 (br), 8.67 (d, J = 7.5 Hz, 1H), 8.61 (br), 8.22 (d, J = 7.0 Hz, 1H), 7.91 (d, J = 9.0 Hz, 1H), 7.86–7.74 (m, 3H), 7.73 (br), 7.60 (br), 7.53

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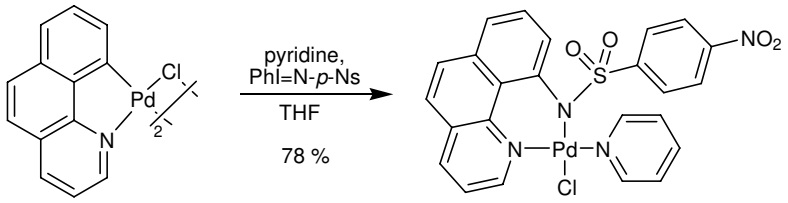
[6] Dick, A. R., Hull , K. L. & Sanford, M. S. A Highly selective catalytic method for the oxidative functionalization of C-H bonds. *J. Am. Chem. Soc.* **126**, 2300–2301(2004).

[7] Hartwell, G. E., Lawrence, R. W. & Smas, M. J. The formation of palladium(II)– and platinum(II)–carbon bonds by proton abstraction from benzo[*h*]quinoline and 8-methylquinoline**.** *J. Chem. Soc. D.: Chem. Commun.* 912 (1970).

(dd, J = 7.5 Hz, J = 7.0 Hz 1H), 7.38 (br); ^{13}C-NMR (125 MHz, DMSO-*d*-6, 23 ºC): δ 153.9, 152.2, 150.7, 150.6, 148.0, 141.7, 139.9, 134.4, 130.8, 129.6, 129.4, .127.5, 125.1, 124.4, 123.0, 122.9. Note: The complicated ^{1}H and ^{13}C-NMR spectra are probably due to the mixture of the title compound and solvent adduct in DMSO-*d*-6. The title compound is not soluble in non-coordinating solvents.

Chloro palladium complex 7[8]

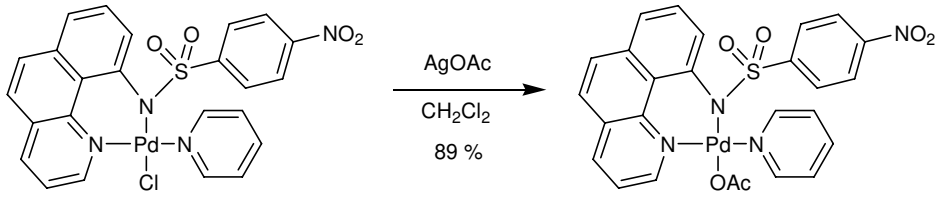


3 **7**

To chloropalladium dimer **3** (1.60 g, 5.00 mmol, 1.00 equiv) in THF (75.0 mL) at 23 ºC is added pyridine (3.20 mL, 40.0 mmol, 8.00 equiv) and PhI=N-*p*-Ns (3.00 g, 7.50 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 17 h. The reaction mixture is filtered off and the filter cake is washed with Et_2O (2 × 10 mL) to afford 2.40 g of the title compound as a light brown solid (78% yield).

^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 9.20 (dd, J = 4.5 Hz, 1.0 Hz, 1H), 8.97 (d, J = 4.5 Hz, 2H), 8.07 (dd, J = 6.5 Hz, 1.0 Hz, 1H), 7.92–7.82 (m, 5H), 7.53–7.45 (m, 5H), 7.39 (dd, J = 6.5 Hz, 4.5 Hz, 1H), 7.32 (d, J = 6.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 154.1, 152.5, 148.3, 147.3, 141.6, 138.9, 137.8, 137.7, 136.1, 130.7, 130.1, 128.3, 127.1, 126.9, 126.8, 126.2, 125.3, 124.5, 122.5, 122.3. These spectroscopic data correspond to the reported data in reference 6.

Acetato palladium complex 1



7 **1**

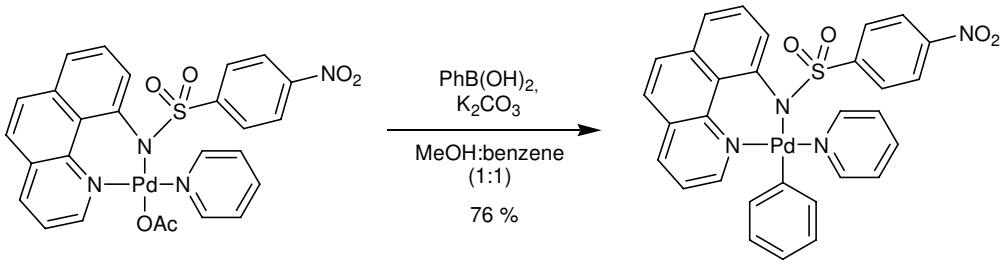
To chloro palladium complex **7** (2.22 g, 3.70 mmol, 1.00 equiv) in CH_2Cl_2 (74.0 mL) at 23 ºC is added AgOAc (3.09 g, 18.5 mmol, 5.00 equiv). The suspension is stirred at 40 ºC for 2.0 h. After cooling to 23 ºC, the suspension is filtered through a plug of celite. The filtrate is concentrated in vacuo and the residue is

[6] Dick, A. R., Remy, M. S., Kampf, J. W. & Sanford, M. S. Carbon-nitrogen bond-forming reactions of palladacycles with hypervalent iodine reagents. *Organometallics* **26**, 1365–1370 (2007).

triturated with Et_2O (50 mL). The solids are filtered off and washed with Et_2O (2 × 50 mL) to afford 2.04 g of the title compound as an orange yellow solid (89% yield).

m.p.: 211 °C (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.93 (d, J = 4.5 Hz, 2H), 8.71 (dd, J = 4.5 Hz, 1.5 Hz, 1H), 8.06 (d, J = 6.5 Hz, 1H), 7.90–7.76 (m, 5H), 7.52 (d, J = 7.0 Hz, 2H) 7.48–7.41 (m, 5H), 7.34 (dd, J = 6.5 Hz, 4.5 Hz, 1H), 1.79 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 177.8, 152.0, 151.4, 148.4, 147.9, 141.8, 139.0, 138.8, 138.1, 136.2, 130.8, 130.5, 129.1, 127.5, 127.0, 126.8, 126.3, 125.3, 124.5, 122.6, 122.2, 24.0; HRMS-FIA (*m/z*): [M – OAc + MeCN]$^+$ calcd for $C_{26}H_{20}N_4O_6PdS$, 604.0265; found, 604.0308. Anal: calcd for $C_{26}H_{20}N_4O_6PdS$: C, 50.13; H, 3.24; N, 9.00; found: C, 49.93; H, 3.44; N, 8.79. Crystal structure is shown in the X-ray Crystallographic Analysis section.

Aryl palladium complex 4a

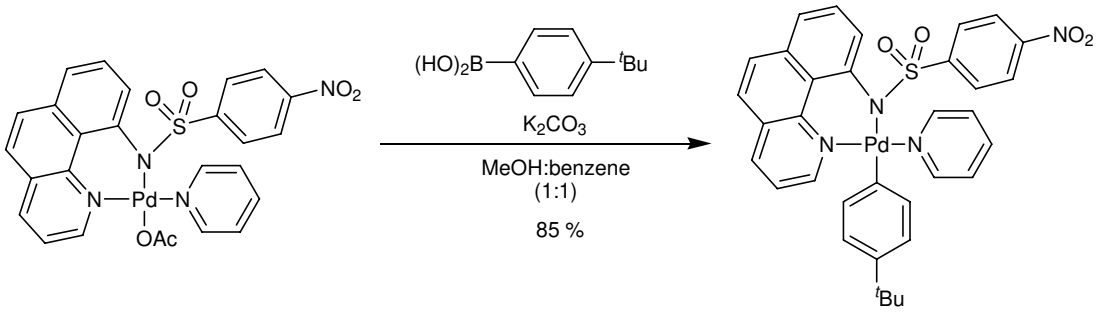


1 **4a**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added phenylboronic acid (86.0 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 2.5 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 1:1 (v/v) to afford 314 mg of the title compound as a pale yellow solid (76% yield).

TLC (hexane/EtOAc 1:1, v/v): R_F = 0.23; m.p.: 205 °C (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 9.00 (d, J = 6.5 Hz, 2H), 8.27 (dd, J = 5.5 Hz, 1.5 Hz, 1H), 7.93 (dd, J = 8.0 Hz, 1.5Hz, 1H), 7.79–7.69 (m, 5H), 7.48 (d, J = 9.0 Hz, 2H), 7.38 (d, J = 9.0 Hz, 2H), 7.35–7.28 (m, 4H), 7.03 (dd, J = 8.0 Hz, 6.5 Hz, 1H), 6.84–6.76 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 155.3, 153.9, 153.3, 149.4, 147.8, 144.6, 144.3, 138.0, 137.9, 136.5, 134.8, 130.5, 130.2, 128.5, 127.6, 127.2, 127.0, 126.8, 125.2, 124.7, 124.4, 123.8, 122.4, 121.5; HRMS-FIA (*m/z*): [M + H]$^+$ calcd for $C_{30}H_{22}N_4O_4PdS$, 641.0475; found, 641.0475. Anal: calcd for $C_{30}H_{22}N_4O_4PdS$: C, 56.21; H, 3.46; N, 8.74; found: C, 55.94; H, 3.48; N, 8.40. Crystal structure is shown in the X-ray Crystallographic Analysis section.

Aryl palladium complex 4b

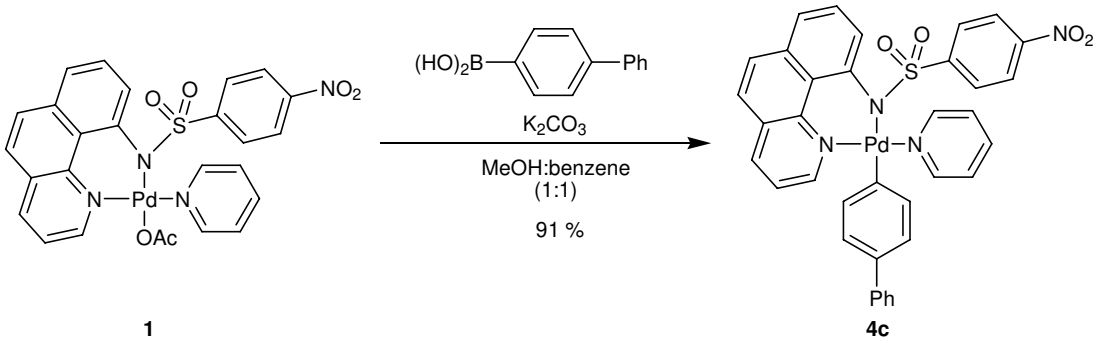


1 **4b**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-tert-butylphenylboronic acid (126 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 13 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 3:2 (v/v) to afford 381 mg of the title compound as a yellow solid (85% yield).

TLC (hexane/EtOAc 1:1, v/v): R_F = 0.49; m.p.: 171 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 9.00 (d, J = 5.0 Hz, 2H), 8.27 (dd, J = 5.5 Hz 1.5 Hz, 1H), 7.92 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.80–7.70 (m, 5H), 7.48 (d, J = 9.0 Hz, 2H), 7.38 (d, J = 8.5 Hz, 1H), 7.36–7.30 (m, 4H), 7.03 (dd, J = 8.0 Hz, 5.0 Hz, 1H), 6.81 (d, J = 9.0 Hz, 2H), 6.70 (d, J = 8.5 Hz, 2H), 1.19 (s, 9H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 154.0, 153.4, 150.5, 149.5, 147.8, 146.4, 144.6, 142.3, 137.9, 137.8, 136.4, 134.0, 130.4, 130.1, 128.5, 127.4, 126.9, 126.8, 125.1, 124.6, 124.4, 124.2, 122.4, 121.4, 34.1, 31.7; HRMS-FIA (*m*/*z*): $[M + H]^+$ calcd for $C_{34}H_{30}N_4O_4PdS$, 697.1095; found, 697.1082. Anal: calcd for $C_{34}H_{30}N_4O_4PdS$: C, 58.58; H, 4.34; N, 8.04; found: C, 58.27; H, 4.37; N, 7.84.

Aryl palladium complex 4c



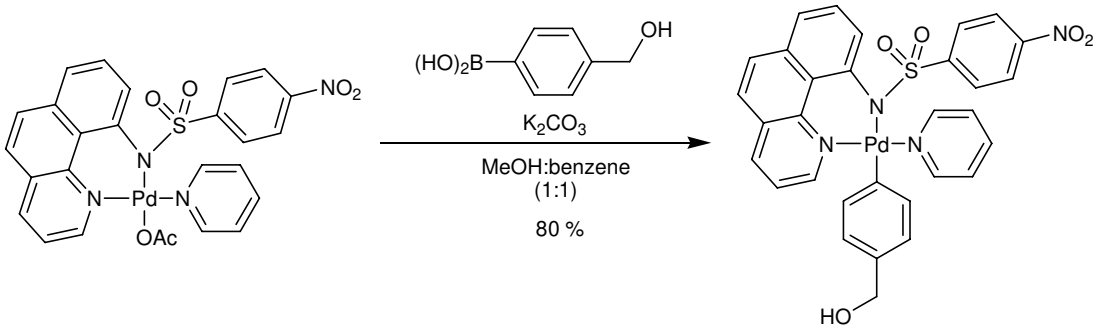
1 **4c**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-biphenyl boronic acid (140 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963

mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 11 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 1:1 (v/v) to afford 418 mg of the title compound as a yellow solid (91% yield).

TLC (hexane/EtOAc 3:7, v/v): R_F = 0.79; m.p.: 180 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 9.04 (d, J = 6.5 Hz, 2H), 8.32 (dd, J = 5.0 Hz, 2.0 Hz, 1H), 7.95 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.81–7.71 (m, 5H), 7.50–7.45 (m, 4H), 7.40 (d, J = 9.0 Hz, 1H), 7.38–7.29 (m, 6H), 7.24 (t, J = 7.5 Hz, 1H), 7.09–7.05 (m, 3H), 6.88 (d, J = 8.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 154.6, 154.1, 153.4, 149.3, 147.8, 144.6, 142.2, 141.4, 138.1, 138.0, 136.5, 135.1, 130.5, 130.2, 128.9, 128.6, 127.6, 127.1, 127.0, 126.9, 126.8, 126.7, 125.6, 125.2, 124.7, 124.4, 122.4, 121.6; HRMS-FIA (m/z): $[M + H]^+$ calcd for $C_{36}H_{26}N_4O_4PdS$, 717.0782; found, 717.0786. Anal: calcd for $C_{36}H_{26}N_4O_4PdS$: C, 60.30; H, 3.65; N, 7.82; found: C, 60.27; H, 3.65; N, 7.60.

Aryl palladium complex 4d



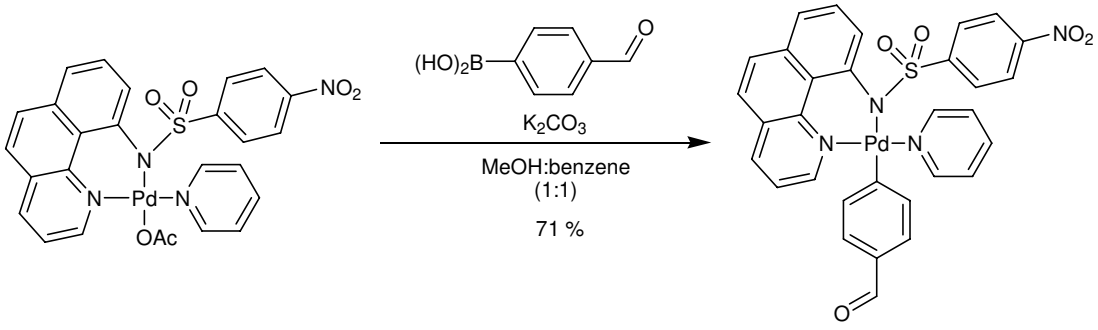
1 **4d**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-(hydroxymethyl)phenylboronic acid (133 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 11 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 1:4 (v/v) to afford 344 mg of the title compound as a yellow solid (80% yield).

TLC (hexane/EtOAc 3:7, v/v): R_F = 0.37; m.p.: 158 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.99 (d, J = 6.5 Hz, 2H), 8.25 (dd, J = 5.5 Hz, 1.5 Hz, 1H), 7.94 (dd, J = 8.5Hz, 2.0 Hz, 1H), 7.80–7.69 (m, 5H), 7.47 (d, J = 9.0 Hz, 2H), 7,39 (d, J = 9.0 Hz, 1H), 7.36–7.27 (m, 4H), 7.04 (dd, J = 8.5 Hz, 6.5 Hz, 1H), 6.81 (m, 4H), 4.50 (d, J = 4.0 Hz, 2H), 1.49 (t, J = 4.0 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 154.6, 153.9, 153.3, 149.3, 147.8, 144.5, 142.2, 138.0, 137.9, 136.5, 136.2, 134.8, 130.5, 130.2, 128.5, 127.5, 126.9, 126.8, 126.2, 125.2, 124.7, 124.4, 121.5, 122.4, 65.5; HRMS-FIA (m/z): $[M + H]^+$ calcd for $C_{31}H_{24}N_4O_5PdS$,

671.0575; found, 617.0598. Anal: calcd for $C_{31}H_{24}N_4O_5PdS$: C, 55.49; H, 3.61; N, 8.35; found: C, 55.10; H, 3.51; N, 7.99.

Aryl palladium complex 4e

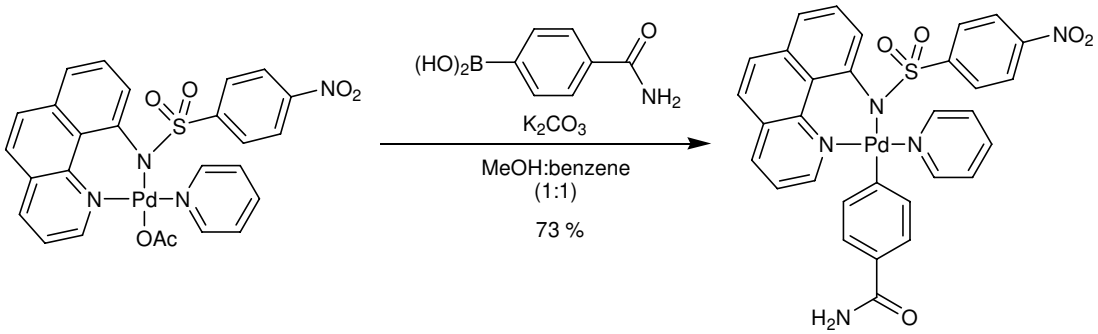


1 **4e**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-formylphenylboronic acid (133 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 18 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 1:1 (v/v) to afford 304 mg of the title compound as a yellow solid (71% yield).

TLC (hexane/EtOAc 3:7, v/v): R_F = 0.40; m.p.: 166 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 9.77 (s, 1H), 8.97 (d, J = 6.0 Hz, 2H), 8.17 (dd, J = 6.5 Hz, 1.5 Hz, 1H), 7.98 (dd, J = 7.5 Hz, 1.5Hz, 1H), 7.84–7.79 (m, 2H), 7.76–7.71 (m, 3H), 7.48 (d, J = 8.0 Hz, 2H), 7.44–7.36 (m, 3H), 7.31–7.25 (m, 4H), 7.12 (d, J = 7.5 Hz, 2H), 7.07 (dd, J = 8.0 Hz, 5.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 192.9, 169.1, 153.7, 153.2, 149.0, 147.9, 144.4, 141.9, 138.4, 138.3, 136.5, 135.5, 133.2, 130.7, 130.4, 128.5, 127.7, 127.6, 126.9, 126.8, 125.4, 124.8, 124.4, 122.4, 121.7; HRMS-FIA (m/z): $[M + H]^+$ calcd for $C_{31}H_{22}N_4O_5PdS$, 669.0419; found, 669.0426. Anal: calcd for $C_{31}H_{22}N_4O_5PdS$: C, 55.65; H, 3.31; N, 8.38; found: C, 55.43; H, 3.58; N, 8.09.

Aryl palladium complex 4f

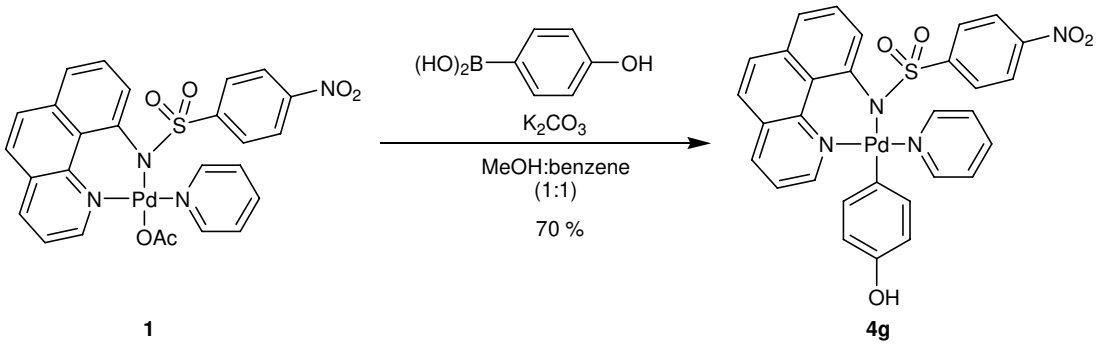


1 **4f**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-aminocarbonylphenylboronic acid (116 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 11 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with EtOAc to afford 319 mg of the title compound as a yellow solid (73% yield).

TLC (EtOAc): R_F = 0.21; m.p.: 175 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.97 (d, J = 5.5 Hz, 2H), 8.19 (dd, J = 6.5 Hz, 1.5 Hz, 1H), 7.97 (dd, J = 7.5 Hz, 1.5Hz, 1H), 7.83–7.70 (m, 5H), 7.47 (d, J = 7.0 Hz, 2H), 7.43–7.30 (m, 3H), 7.28 (dd, J = 9.0 Hz, 1.5 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 7.06 (dd, J = 8.5 Hz, 5.5Hz, 1H), 6.89 (d, J = 7.5 Hz, 2H), 5.88 (br, 1H), 5.40 (br, 1H); ^{13}CNMR (125 MHz, $CDCl_3$, 23 ºC): δ 163.3, 153.8, 153.3, 149.0, 144.4, 143.1, 142.0, 138.3, 138.2, 136.5, 135.1, 130.6, 130.3, 129.0, 128.5, 127.6, 126.9, 126.8, 126.0, 125.5, 125.4, 124.8, 124.4, 122.4, 121.6; HRMS-FIA (m/z): $[M + H]^+$ calcd for $C_{31}H_{23}N_5O_5PdS$, 684.0528; found, 684.0537. Anal: calcd for $C_{31}H_{23}N_5O_5PdS$: C, 54.43; H, 3.39; N, 10.24; found: C, 54.43; H, 3.67; N, 9.95.

Aryl palladium complex 4g

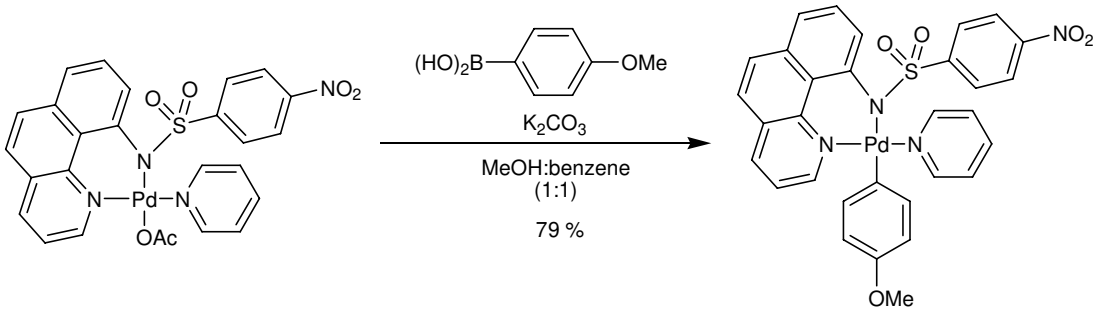


1 **4g**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-hydroxyphenylboronic acid (97 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 15 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 2:3 (v/v) to afford 295 mg of the title compound as a yellow solid (70%yield).

TLC (hexane/EtOAc, 1:1 v/v): R_F = 0.17; m.p.: 174 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.99 (d, J = 6.5 Hz, 2H), 8.27 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 7.94 (dd, J = 7.5 Hz, 1.5Hz, 1H), 7.79–7.68 (m, 5H), 7.47 (d, J = 9.0 Hz, 2H), 7.40–7.27 (m, 5H), 7.04 (dd, J = 7.5 Hz, 5.5 Hz, 1H), 6.60 (d, J = 8.0 Hz, 2H), 6.38 (d, J = 8.0 Hz, 2H), 4.40 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 154.1, 153.4, 152.7, 149.2, 147.8, 147.4, 144.6, 143.4, 142.2, 137.9, 136.4, 134.8, 130.5, 130.1, 128.5, 127.5, 127.0, 126.8, 125.1, 124.7, 124.3, 122.4, 121.4, 114.5; HRMS-FIA (m/z): $[M + H]^+$ calcd for $C_{30}H_{22}N_4O_5PdS$, 657.0419; found, 657.0433. Anal: calcd for $C_{30}H_{22}N_4O_5PdS$: C, 54.84; H, 3.38; N, 8.53; found: C, 54.56; H, 3.53; N, 8.26.

Aryl palladium complex 4h



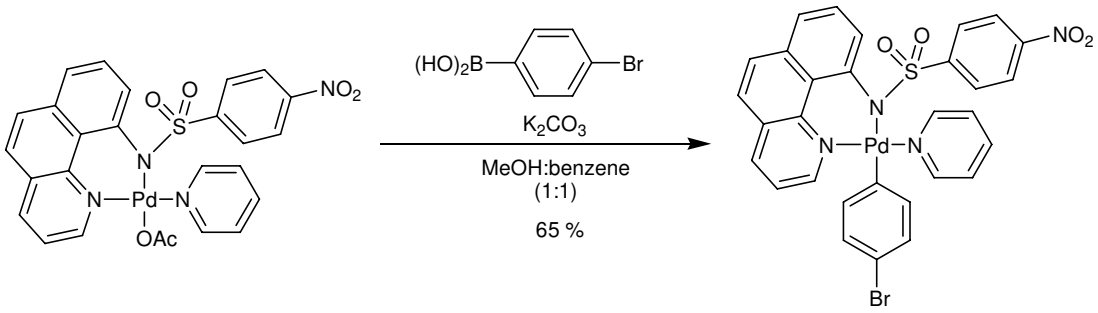
1 **4h**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-methoxyphenylboronic acid (107 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 3.0 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 1:1 (v/v) to afford 340 mg of the title compound as a yellow solid (79% yield).

TLC (hexane/EtOAc 1:1, v/v): R_F = 0.29; m.p.: 154 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.99 (d, J = 5.5 Hz, 2H), 8.27 (d, J = 5.5 Hz, 1H), 7.94 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.80–7.68 (m, 5H), 7.47 (d, J = 6.0 Hz, 2H), 7.38 (d, J = 8.5 Hz, 1H), 7.35–7.28 (m, 4H), 7.04 (dd, J = 8.0 Hz, 5.5 Hz, 1H), 6.64 (d, J = 8.0 Hz, 2H), 6.44 (d, J = 8.0 Hz, 2H), 3.65 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 156.9, 154.1, 153.5,

149.3, 147.8, 144.6, 143.5, 142.3, 137.9, 137.9, 136.5, 134.7, 130.5, 130.1, 128.6, 127.5, 127.0, 126.8, 125.1, 124.7, 124.3, 122.4, 121.5, 113.1, 55.1; HRMS-FIA (*m*/*z*): $[M + H]^+$ calcd for $C_{31}H_{24}N_4O_5PdS$, 671.0575; found, 671.0598. Anal: calcd for $C_{31}H_{24}N_4O_5PdS$: C, 55.49; H, 3.61; N, 8.35; found: C, 55.71; H, 3.37; N, 8.12.

Aryl palladium complex 4i

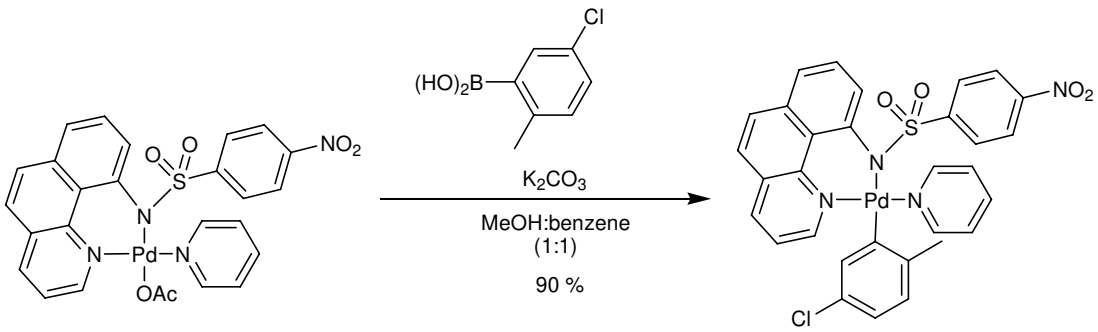


1 **4i**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-bromophenylboronic acid (142 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 3.5 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 3:2 (v/v) to afford 300 mg of the title compound as a yellow solid (65% yield).

TLC (hexane/EtOAc, 1:1 v/v): R_F = 0.79; m.p.: 201 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.96 (d, *J* = 5.0 Hz, 2H), 8.22 (d, *J* = 5.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.82–7.68 (m, 5H), 7.47 (d, *J* = 9.0 Hz, 2H) 7.42–7.26 (m, 5H), 7.09 (dd, *J* = 7.5 Hz, 5.0 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 154.0, 153.5, 153.3, 149.1, 147.9, 142.0, 138.2, 138.1, 136.5, 136.3, 130.6, 130.3, 129.9, 128.5, 127.6, 126.9, 126.8, 125.3, 124.8, 124.4, 122.8, 122.4, 121.7, 118.3; HRMS-FIA (*m*/*z*): $[M + H]^+$ calcd for $C_{30}H_{21}BrN_4O_4PdS$, 718.9575; found, 718.9578. Anal: calcd for $C_{30}H_{21}BrN_4O_4PdS$: C, 50.05; H, 2.94; N, 7.78; found: C, 50.03; H, 2.91; N, 7.51.

Aryl palladium complex 4k

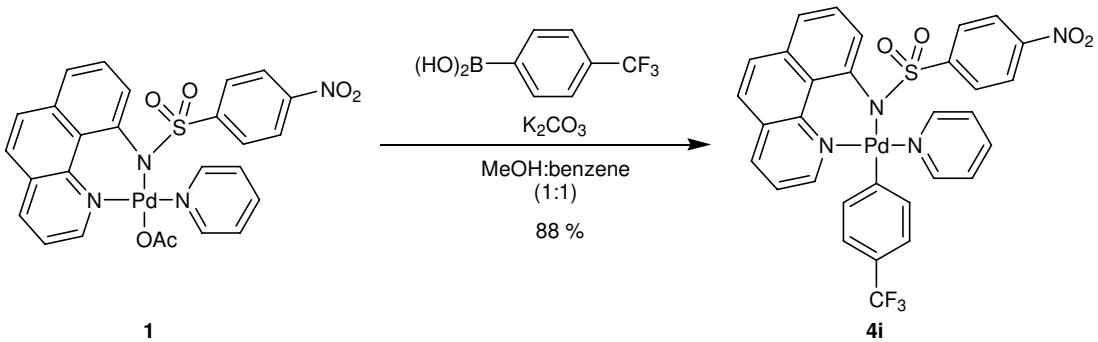


1 **4k**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 5-chloro-2-methylphenylboronic acid (120 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 10 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 3:2 (v/v) to afford 398 mg of the title compound as a yellow solid (90% yield, 1:1.3 atropisomeric mixture with respect to the palladium–carbon bond).

TLC (hexane/EtOAc, 1:1 v/v): R_F = 0.37; m.p.: 178 ºC (decomp.); ^{1}H-NMR, both rotamers (500 MHz, $CDCl_3$, 23 ºC): δ 8.98 (d, J = 5.5 Hz), 8.91 (d, J = 5.5 Hz), 8.28 (d, J = 5.0 Hz), 7.96–7.90 (m), 7.81–7.66 (m), 7.55–7.46 (m), 7.40–7.28 (m), 7.08–6.98 (m), 6.81 (d, J = 8.0 Hz), 6.74 (dd, J = 8.0 Hz, 2.0 Hz), 6.62 (d, J = 2.0 Hz), 6.44 (d, J = 8.0 Hz), 2.99 (s), 1.69 (s); ^{13}C-NMR, both rotamers (125 MHz, $CDCl_3$, 23 ºC): δ 159.6, 159.1, 153.6, 153.4, 152.9, 152.8, 149.4, 147.9, 144.7, 144.6, 142.0, 141.8, 140.1, 139.1, 138.2, 138.1, 138.0, 136.5, 133.4, 132.8, 130.7, 130.6, 130.4, 130.3, 130.2, 129.9, 129.2, 129.0, 128.5, 128.4, 127.8, 127.3, 127.0, 126.8, 126.7, 125.4, 125.2, 125.0, 124.8, 124.5, 124.3, 123.9, 123.8, 122.5, 122.4, 121.6, 24.5, 24.2; HRMS-FIA (m/z): $[M + H]^+$ calcd for $C_{31}H_{23}ClN_4O_4PdS$, 689.0236; found, 689.0251. Anal: calcd for $C_{31}H_{23}ClN_4O_4PdS$: C, 54.00; H, 3.36; N, 8.13; found: C, 53.72; H, 3.10; N, 8.03.

Aryl palladium complex 4l

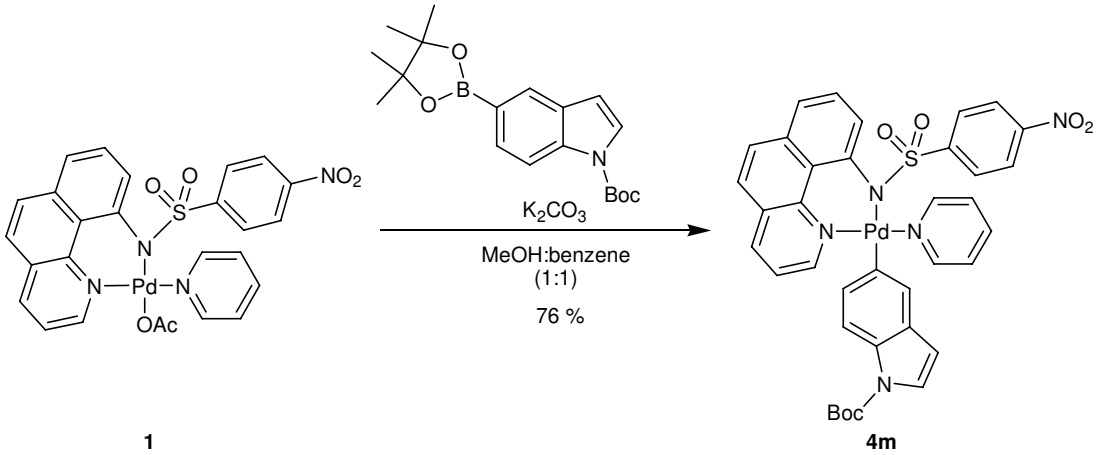


1 **4i**

To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 4-(trifluoromethyl)phenylboronic acid (134 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 10 h, and the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 3:2 (v/v) to afford 400 mg of the title compound as a yellow solid (88% yield).

TLC (hexane/EtOAc, 1:1 v/v): R_F = 0.43; m.p.: 171 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.97 (d, J = 5.5 Hz, 2H), 8.18 (dd, J = 4.5 Hz, 1.5 Hz, 1H), 7.97 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.82–7.70 (m, 5H), 7.48 (d, J = 7.0 Hz, 2H), 7.42–7.26 (m, 5H), 7.09 (dd, J = 8.0 Hz, 5.0 Hz, 1H), 7.02 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 161.3, 153.9, 153.3, 149.0, 147.9, 144.4, 141.9, 138.3, 138.2, 136.5, 135.0, 130.6, 129.5 (q, J = 238 Hz), 127.6, 126.9, 126.8, 126.2 (q, J = 23 Hz), 125.4, 124.8, 124.4, 123.9, 123.2, 122.4, 121.7; ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –62.5; HRMS-FIA (*m*/*z*): [M + H]$^+$ calcd for $C_{31}H_{21}F_3N_4O_4PdS$, 709.0343; found, 709.0321. Anal: calcd for $C_{31}H_{21}F_3N_4O_4PdS$: C, 52.51; H, 2.99; N, 7.90; found: C, 52.29; H, 2.98; N, 7.78.

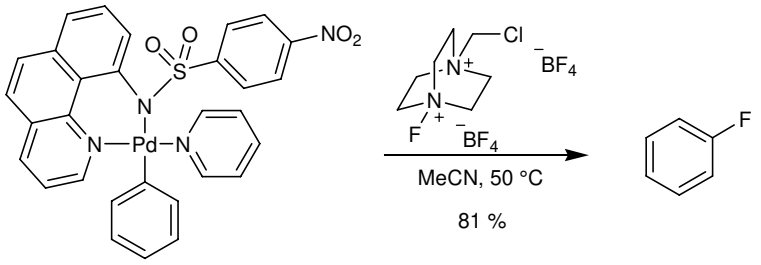
Aryl palladium complex 4m



To acetato palladium complex **1** (400 mg, 0.642 mmol, 1.00 equiv) in MeOH (12.8 mL) and benzene (12.8 mL) at 23 ºC is added 1-Boc-indole-5-boronic acid pinacol ester (242 mg, 0.706 mmol, 1.10 equiv) and K_2CO_3 (133 mg, 0.963 mmol, 1.50 equiv). The reaction mixture is stirred at 23 ºC for 6.0 h. After filtered through a plug of celite, the solvent is removed in vacuo. To the solid residue is added $CHCl_3$ (5 mL) and water (5 mL). The phases are separated and the aqueous phase is extracted with $CHCl_3$ (3 × 5 mL). The combined organic phases are washed with brine (5 mL) and dried (Na_2SO_4). The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 1:1 (v/v) to afford 380 mg of the title compound as a yellow solid (76% yield).

TLC (hexane/EtOAc, 3:7 v/v): R_F = 0.26; m.p.: 175 ºC (decomp.); ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 9.01 (d, J = 5.0 Hz, 2H), 8.28 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 7.91 (dd, J = 8.5 Hz, 1.5Hz, 1H), 7.80–7.70 (m, 5H), 7.61 (br, 1H) 7.47 (d, J = 9.0 Hz, 2H), 7.38 (d, J = 9.0 Hz, 2H), 7.33–7.28 (m, 4H), 7.00–6.95 (m, 2H), 6.81 (d, J = 8.0 Hz, 1H), 6.25 (d, J = 2.0 Hz, 1H), 1.60 (s, 9H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 153.9, 153.4, 150.1, 149.3, 147.8,147.7, 144.6, 142.3, 137.9, 136.5, 130.5, 130.1, 130.0, 128.6, 127.5, 127.0, 126.8, 126.0, 125.1, 125.0, 124.7, 124.6, 124.4, 122.4, 121.5, 119.9, 113.8, 106.8, 83.4, 28.4; HRMS-FIA (m/z): [M + Na]$^+$ calcd for $C_{37}H_{31}N_5O_6PdS$, 802.0922; found, 802.0895. Anal: calcd for $C_{37}H_{31}N_5O_6PdS$: C, 56.96; H, 4.01; N, 8.98; found: C, 56.84; H, 3.94; N, 8.65.

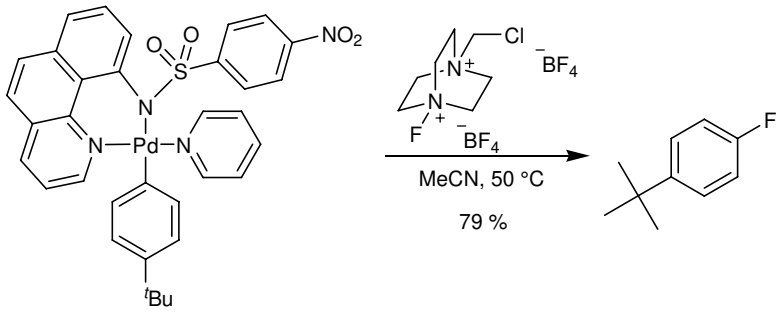
Fluorobenzene 5a



4a **5a**

To 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**), (4.3 mg, 0.012 mmol, 1.2 equiv) in acetonitrile-*d*-3 (0.3 mL) at 50 ºC is added aryl palladium complex **4a** (6.4 mg, 0.010 mmol, 1.0 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20min. The reaction mixture is cooled to 23 ºC, and the yield is determined by comparing integration of the ^{19}F-NMR (375 MHz, acetonitrile-*d*-3, 23 ºC) resonance of fluorobenzene (–115.3 ppm) and that of 3-nitrofluorobenzene (–112.0 ppm, 2.00 μL, 0.0188 mmol). (81% yield). The ^{19}F-NMR chemical shift of the product corresponds to that of authentic sample purchased from Aldrich.

1-*tert*-Butyl-4-fluorobenzene 5b

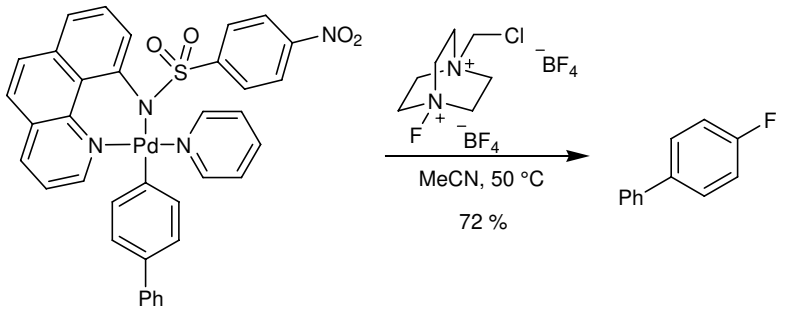


4b **5b**

To 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (4.3 mg, 0.012 mmol, 1.2 equiv) in acetonitrile-*d*-3 (0.3 mL) at 50 ºC is added aryl palladium complex **4b** (7.0 mg, 0.010 mmol, 1.0

equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. The reaction mixture is cooled to 23 ºC, and the yield is determined by comparing integration of the ^{19}F-NMR (375 MHz, acetonitrile-*d*-3, 23 ºC) resonance of 1-*tert*-butyl-4-fluorobenzene (–120.7 ppm) and that of 3-nitrofluorobenzene (–112.0 ppm, 2.00 μL, 0.0188 mmol). (79% yield). The ^{19}F-NMR chemical shift of the product corresponds to that of reported data.[9]

4-Fluorobiphenyl 5c

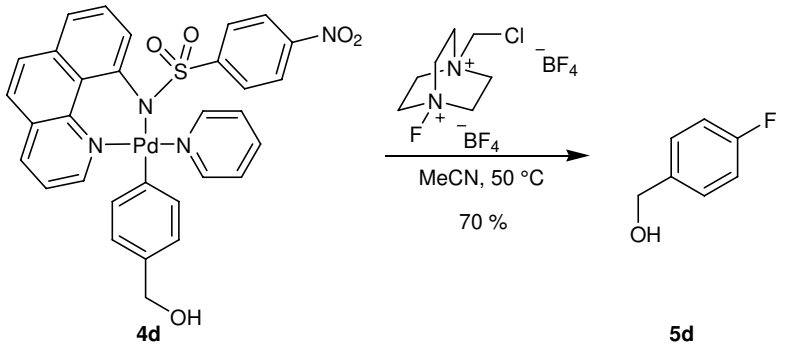


4c **5c**

To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (85.0 mg, 0.240 mmol, 1.20 equiv) in acetonitrile (6.0 mL) at 50 ºC is added aryl palladium complex **4c** (143 mg, 0.200 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv), and filtered through a plug of celite. The filtrate is concentrated in vacuo and the residue is purified by chromatography on silica gel eluting with hexane/EtOAc 99:1 (v/v) to afford 24.8 mg of the title compound as a white solid (72% yield). TLC (hexane/EtOAc, 19:1 v/v): R_F = 0.60; ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 7.60–7.54 (m, 4H), 7.47 (dd, J = 7.5 Hz, 7.0 Hz, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.14 (dd, J = 8.0 Hz, 7.5 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 162.7 (d, J = 244 Hz), 140.5, 137.6, 129.0, 128.9 (d, J = 8.5 Hz), 127.5, 127.3, 115.8 (d, J = 21 Hz); ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –116.2. These spectroscopic data correspond to those of authentic sample purchased from Alfa Aesar.

[9] Laali, K. K., Okazaki, T. Bunge, S. D. *N*-(Trifluoromethylsulfonyl)aryloxytrifluoromethylsulfoximines [ArO-SO(CF_3)=NTf] and *N*-aryltriflimides Ar-N($Tf)_2$ by thermal and photolytic dediazoniation of [ArN_2][BF_4] in [BMIM][Tf_2N] ionic liquid: exploiting the ambident nucleophilic character of a "nonnucleophilic" anion. *J. Org. Chem.* **72**, 6758-6762 (2007).

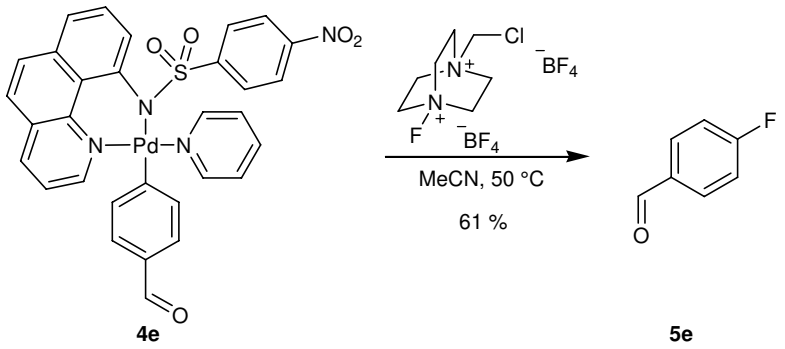
4-Fluorobenzylalcohol 5d



To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (42.5 mg, 0.120 mmol, 1.20 equiv) in acetonitrile (3.0 mL) at 50 ºC is added aryl palladium complex **4d** (67.1 mg, 0.100 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with pentane/Et_2O 7:3 (v/v) to afford 8.8 mg of the title compound as colorless oil (70% yield).

TLC (hexane/EtOAc 7:3 v/v): R_F = 0.61; ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 7.29–7.25 (m, 2H), 7.05–7.00 (dd, J = 8.0 Hz, 7.5 Hz, 2H), 4.55 (s, 2H), 3.10 (br, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 162.5 (d, J = 243 Hz), 136.8, 129.0 (d, J = 8.3 Hz), 115.6 (d, J = 21 Hz), 64.5; ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –115.4. These spectroscopic data correspond to those of authentic sample purchased from Alfa Aesar.

4-Fluorobenzaldehyde 5e

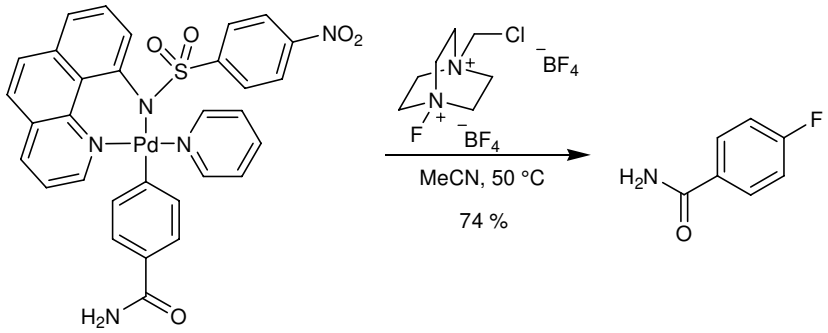


To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (42.5 mg, 0.120 mmol, 1.20 equiv) in acetonitrile (3.0 mL) at 50 ºC is added aryl palladium complex **4e** (66.9 mg, 0.100 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with pentane/Et_2O 7:3 (v/v) to afford 8.8 mg of the title compound as colorless oil (61% yield).

TLC (hexane/EtOAc, 7:3 v/v): R_F = 0.77; ^{1}H-NMR (500 MHz, $CDCl_3$ 23 ºC): δ 9.95 (s, 1H), 7.92–7.88 (m,

2H), 7.22–7.18 (dd, J = 8.0 Hz, 7.5 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 190.7, 166.7 (d, J = 255 Hz), 133.2, 132.5 (d, J = 9.9 Hz), 116.6 (d, J = 22 Hz); ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –102.9. These spectroscopic data correspond to those of authentic sample purchased from Aldrich.

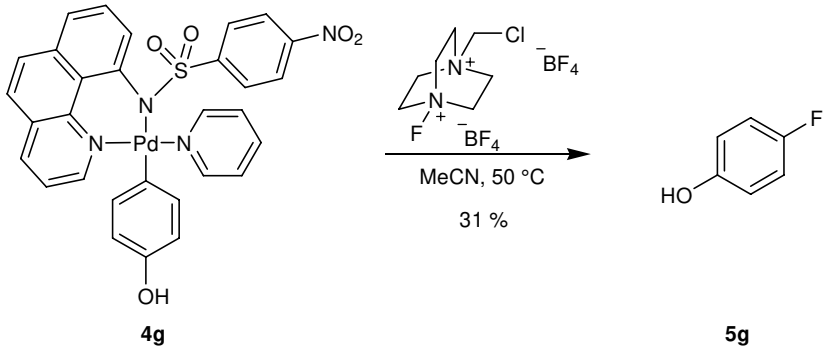
4-Fluorobenzmide 5f



To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (42.5 mg, 0.120 mmol, 1.20 equiv) in acetonitrile (3.0 mL) at 50 ºC is added aryl palladium complex **4f** (68.4 mg, 0.100 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with EtOAc to afford 10.3 mg of the title compound as colorless oil (74% yield).

TLC (EtOAc): R_F = 0.40; ^{1}H-NMR (500 MHz, DMSO-*d*-6, 23 ºC): δ 8.02 (br, 1H), 7.95 (dd, J = 9.0 Hz, 6.0Hz, 2H), 7.42 (br, 1H), 7.26 (dd, J = 7.5 Hz, 7.0 Hz, 2H); ^{13}C-NMR (125 MHz, DMSO-*d*-6, 23 ºC): δ 167.6, 164.6 (d, J = 247 Hz), 131.4, 130.8 (d, J = 14 Hz), 115.8 (d, J = 21 Hz); ^{19}F-NMR (375 MHz, DMSO-*d*-6, 23 ºC): δ –110.0. These spectroscopic data correspond to those of authentic sample purchased from Alfa Aesar.

4-Fluorophenol 5g

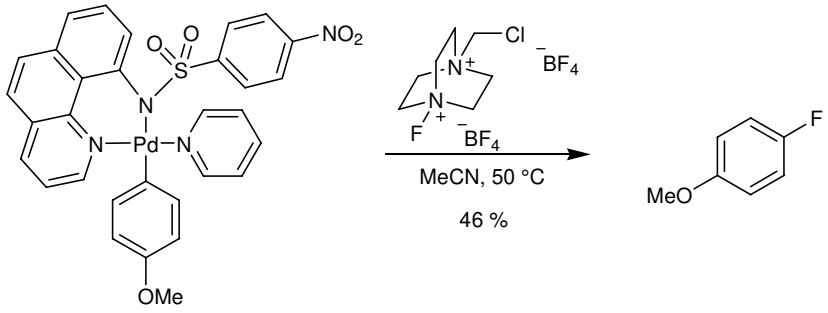


To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (85.0 mg, 0.240 mmol, 1.20 equiv) in acetone (6.0 mL) at 50 ºC is added aryl palladium complex **4g** (131 mg, 0.200 mmol,

1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (16 μL, 0.20 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with Hexane/EtOAc 7:3 (v/v) to afford 6.9 mg of the title compound as a white solid (31% yield).

TLC (hexane/EtOAc, 7:3 v/v): R_F = 0.58; ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 6.95–6.95 (dd, J = 8.0 Hz, 7.5 Hz, 2H), 6.80–6.76 (m, 2H), 5.41 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 157.6 (d, J = 237 Hz), 151.5, 116.5 (d, J = 8.0 Hz), 116.3 (d, J = 21 Hz); ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –124.3. These spectroscopic data correspond to those of authentic sample purchased from Aldrich.

4-Fluoroanisole 5h

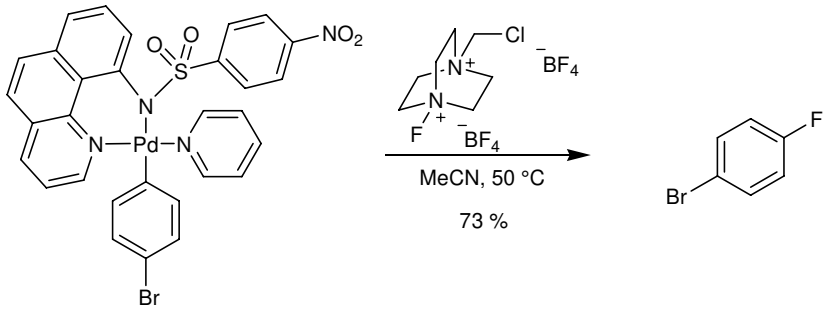


4h **5h**

To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (85.0 mg, 0.240 mmol, 1.20 equiv) in acetone (6.0 mL) at 50 ºC is added aryl palladium complex **4h** (134 mg, 0.200 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (16 μL, 0.20 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with pentane/Et_2O 9:1 (v/v) to afford 11.6 mg of the title compound as colorless oil (46% yield).

TLC (hexane/EtOAc, 9:1 v/v): R_F = 0.55; ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 7.01–6.95 (m, 2H), 6.87–6.81 (m, 2H), 3.79 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 157.4 (d, J = 247 Hz), 155.9, 116.0 (d, J = 23 Hz), 115.0 (d, J = 7.7 Hz), 56.0; ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –124.8. These spectroscopic data correspond to those of authentic sample purchased from Alfa Aesar.

1-Bromo-4-fluorobenzene 5i

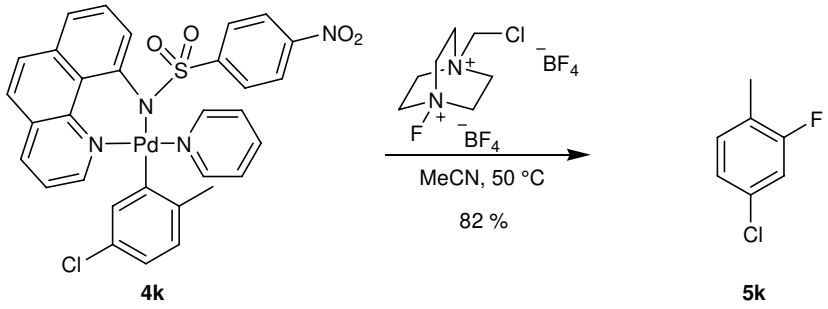


4i **5i**

To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (42.5 mg, 0.120 mmol, 1.20 equiv) in acetonitrile (3.0 mL) at 50 ºC is added aryl palladium complex **4i** (72.0 mg, 0.100 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with pentane/Et_2O 19:1 (v/v) to afford 12.8 mg of the title compound as colorless oil (73% yield).

TLC (hexane/EtOAc, 19:1 v/v): R_F = 0.70; ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 7.47–7.42 (m, 2H), 6.98–6.92 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 162.1 (d, J = 245 Hz), 133.2, (d, J = 8.5 Hz), 117.5 (d, J = 23 Hz), 116.8; ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –115.7. These spectroscopic data correspond to those of authentic sample purchased from Alfa Aesar.

4-Chloro-2-fluorotoluene 5k



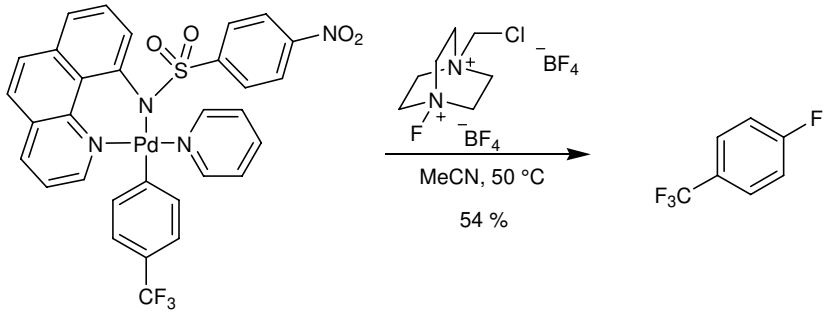
4k **5k**

To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (42.5 mg, 0.120 mmol, 1.20 equiv) in acetonitrile (3.0 mL) at 50 ºC is added aryl palladium complex **4k** (68.9 mg, 0.100 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with pentane/Et_2O 9:1 (v/v) to afford 11.9 mg of the title compound as colorless oil (82% yield).

TLC (hexane/EtOAc, 9:1 v/v): R_F = 0.72; ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 7.13–7.08 (dd, J = 7.5 Hz, 7.0 Hz, 2H), 7.05–7.01 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 161.3 (d, J = 246 Hz), 132.3, 132.2 (d,

J = 5.9 Hz), 124.3, 123.6 (d, *J* = 17 Hz), 116.0 (d, *J* = 26 Hz), 14.4; ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –115.1; These spectroscopic data correspond to those of authentic sample purchased from Alfa Aesar.

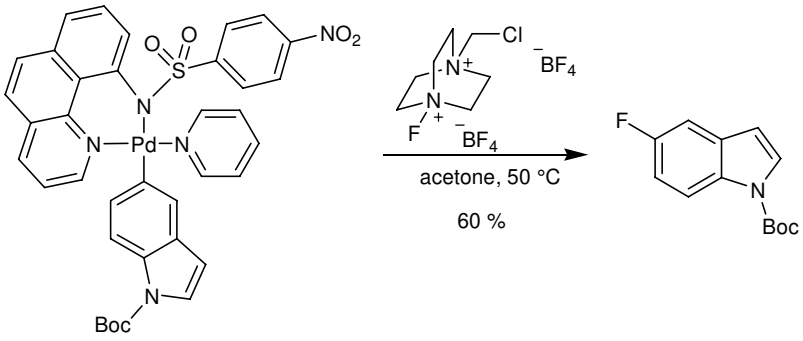
4-Fluorobenzotrifluoride 5l



4l **5l**

To 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (4.3 mg, 0.012 mmol, 1.2 equiv) in acetonitrile-*d*-3 (0.3 mL) at 50 ºC is added aryl palladium complex **4l** (6.4 mg, 0.010 mmol, 1.0 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. The reaction mixture is cooled to 23 ºC, and the yield is determined by comparing integration of the ^{19}F-NMR (375 MHz, acetonitrile-*d*-3, 23 ºC) resonance of 4-fluorobenzotrifluoride (–109.4 ppm) and that of 3-nitrofluorobenzene (–112.0 ppm, 2.00 μL, 0.0188mmol). (54% yield). The ^{19}F-NMR chemical shift of the product corresponds to that of authentic sample purchased from Alfa Aesar.

N-Boc-5-fluoroindole 5m



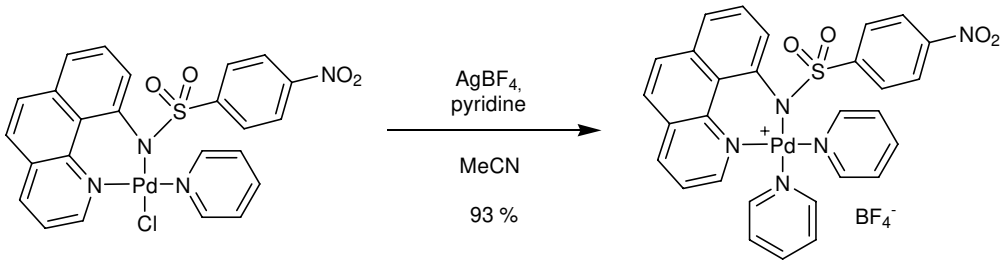
4m **5m**

To 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**2**) (42.5 mg, 0.120 mmol, 1.20 equiv) in acetone (3.0 mL) at 50 ºC is added aryl palladium complex **4m** (78.0 mg, 0.100 mmol, 1.00 equiv) as a solid in 10 portions over 10 min. The reaction mixture is stirred at 50 ºC for 20 min. After cooled to 23 ºC, to the reaction mixture is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv). After concentrated in vacuo, the residue is purified by preparative TLC eluting with hexane/EtOAc 7:3 (v/v) to afford 14.1 mg of the title compound as colorless oil (60% yield).

TLC (hexane/EtOAc 7:3 v/v): R_F = 0.753; ^{1}H-NMR (500 MHz, $CDCl_3$, 23 ºC): δ 8.08 (br, 1H), 7.62 (d, *J* =

4.0 Hz, 1H), 7.20 (dd, *J* = 6.5 Hz, *J* = 2.0 Hz, 1H), 7.03 (ddd, *J* = 7.0 Hz, 6.5 Hz, 2.0 Hz, 1H), 6.52 (d, *J* = 4.0 Hz, 1H), 1.68 (s, 9H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 159.5 (d, *J* = 238 Hz), 149.7, 131.8, 131.6 (d, *J* = 10 Hz), 127.7, 116.3 (d, *J* = 9.1 Hz), 112.2 (d, *J* = 24 Hz), 107.2, 106.5 (d, *J* = 24 Hz), 84.1, 28.4; ^{19}F-NMR (375 MHz, $CDCl_3$, 23 ºC): δ –121.7. These spectroscopic data correspond to those of authentic sample independently synthesized from 5-fluoroinodole and Boc_2O.

Bispyridine palladium tetrafluoroborate salt 8



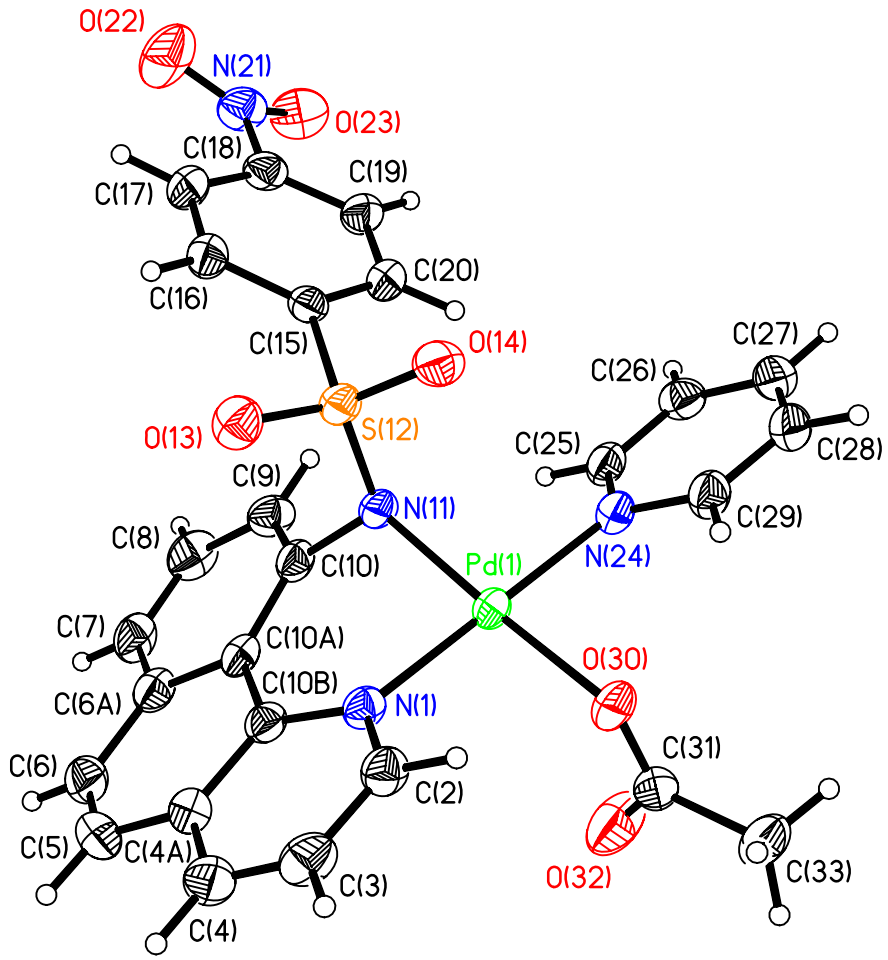
7 **8**

To chloro palladium complex **7** (59.9 mg, 0.100 mmol, 1.00 equiv) in acetonitrile (1.0mL) at 23 ºC is added $AgBF_4$ (38.8 mg, 0.200 mmol, 2.00 equiv). The suspension is stirred at 23 ºC for 1.0 hour and to the suspension is added pyridine (8.1 μL, 0.10 mmol, 1.0 equiv). The suspension is filtered through a plug of celite and the filtrate is concentrated in vacuo to afford 67.9 mg of the title compound as an orange solid (67.9 mg, 93% yield).

^{1}H-NMR (500 MHz, acetone-*d*-6, 23 ºC): δ 9.29 (d, *J* = 5.5 Hz, 2H), 8.99 (d, *J* = 5.5 Hz, 2H), 8.51 (dd, *J* = 5.5 Hz, 1.5 Hz, 1H), 8.44 (dd, *J* = 7.5 Hz, 1.0 Hz, 1H), 8.15–8.08 (m, 3H), 8.01 (dd, *J* = 8.0 Hz, 7.5 Hz, 1H), 7.89 (t, *J* = 7.5 Hz, 1H), 7.80–7.70 (m, 4H), 7.66 (d, *J* = 9.0 Hz, 2H), 7.59–7.52 (m, 4H), 7.48 (dd, *J* = 8.0 Hz, 5.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$, 23 ºC): δ 152.6, 152.4, 152.3, 152.2, 152.9, 152.8, 148.7, 147.2, 141.4, 140.8, 140.7, 140.6, 140.5, 140.3, 140.2, 137.7, 136.5, 130.8, 130.6, 130.3, 129.2, 128.8, 127.9, 127.8, 127.4, 127.2, 126.9, 126.8, 126.7, 126.5, 125.2, 124.9, 123.9, 123.8, 123.1, 122.9, 118.4. The complex ^{13}C spectrum is presumably due to pyridine exchange with the NMR solvent acetone. ^{19}F-NMR (375 MHz, acetone-*d*-6, 23 ºC): δ –151.5; HRMS-FIA (*m*/*z*): $[M - C_5H_5N + C_2H_3N - BF_4]^+$ calcd for $C_{31}H_{24}N_4O_5PdS$, 604.0265; found, 604.0228.

X-ray Crystallographic Analysis

Firgure S1.: acetato palladium complex 1 (CCDC 67599)

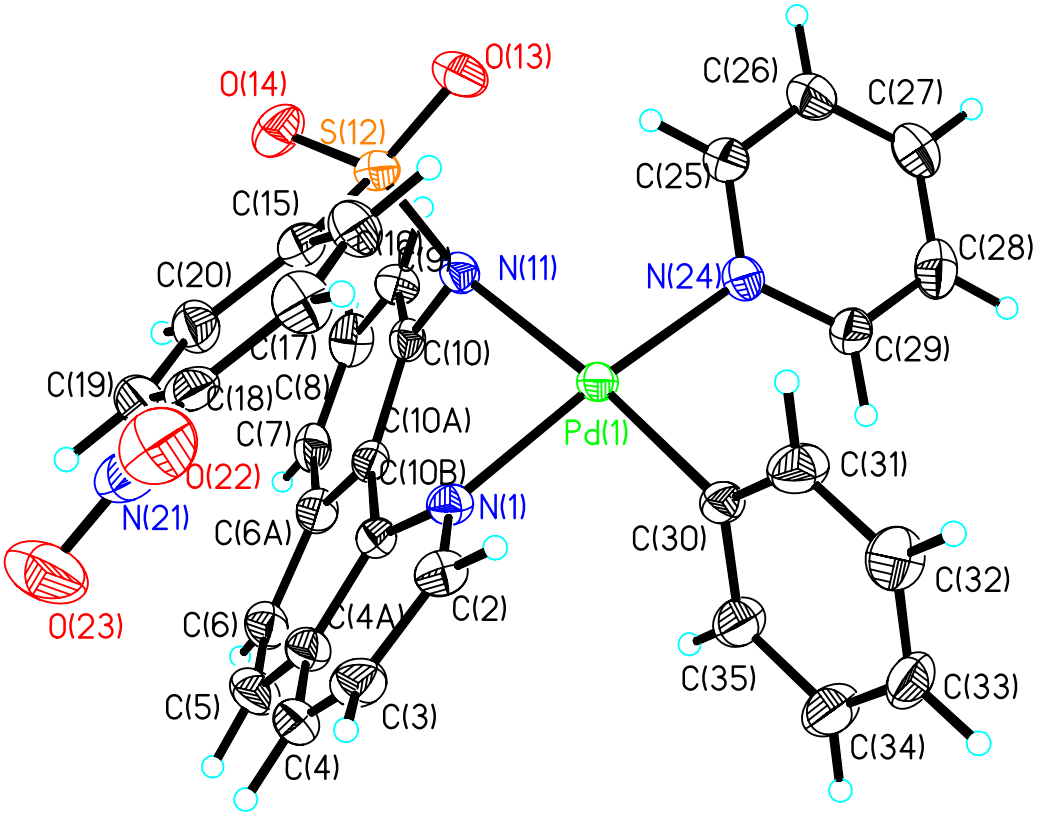


The x-ray structure of acetato palladium complex **1** with hydrogens and with the atom labeling scheme employed. The nonhydrogen atoms are depicted with 50% probability ellipsoids.

Table S2.: Crystal data and structure refinement for acetato palladium complex 1.

Identification code	CCDC 675999 = $[Pd(C_5H_5N)(C_2H_3O_2)(C_{19}H_{12}N_3O_4S)]$	
Formula	C26 H20 N4 O6 Pd S	
Formula weight	622.92	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P$\bar{1}$ (No. 2)	
Unit cell dimensions	a = 9.1803(2) Å	α= 67.735(1)°
	b = 11.3199(2) Å	β= 87.215(1)°
	c = 12.8456(2) Å	γ = 75.798(1)°
Volume	1196.16(4) $Å^3$	
Z	2	
Density (calculated)	1.730 Mg/m^3	
Absorption coefficient	0.916 mm^{-1}	
F(000)	628	
Crystal size	0.175 x 0.150 x 0.025 mm^3	
Theta range for data collection	1.72 to 27.50°	
Index ranges	-11<=h<=11, -14<=k<=14, -16<=l<=16	
Reflections collected	17370	
Independent reflections	5486 [R(int) = 0.0586]	
Completeness to theta = 27.50°	100.0 %	
Absorption correction	Numerical	
Max. and min. transmission	0.9775 and 0.8562	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5486 / 0 / 344	
Goodness-of-fit on F^2	1.030	
Final R indices [I>2sigma(I)]	R1 = 0.0376, wR2 = 0.0859	
R indices (all data)	R1 = 0.0518, wR2 = 0.0935	
Largest diff. peak and hole	0.525 and -0.543 e.$Å^{-3}$	

Figure S2.: aryl palladium complex 4a (CCDC 676000)

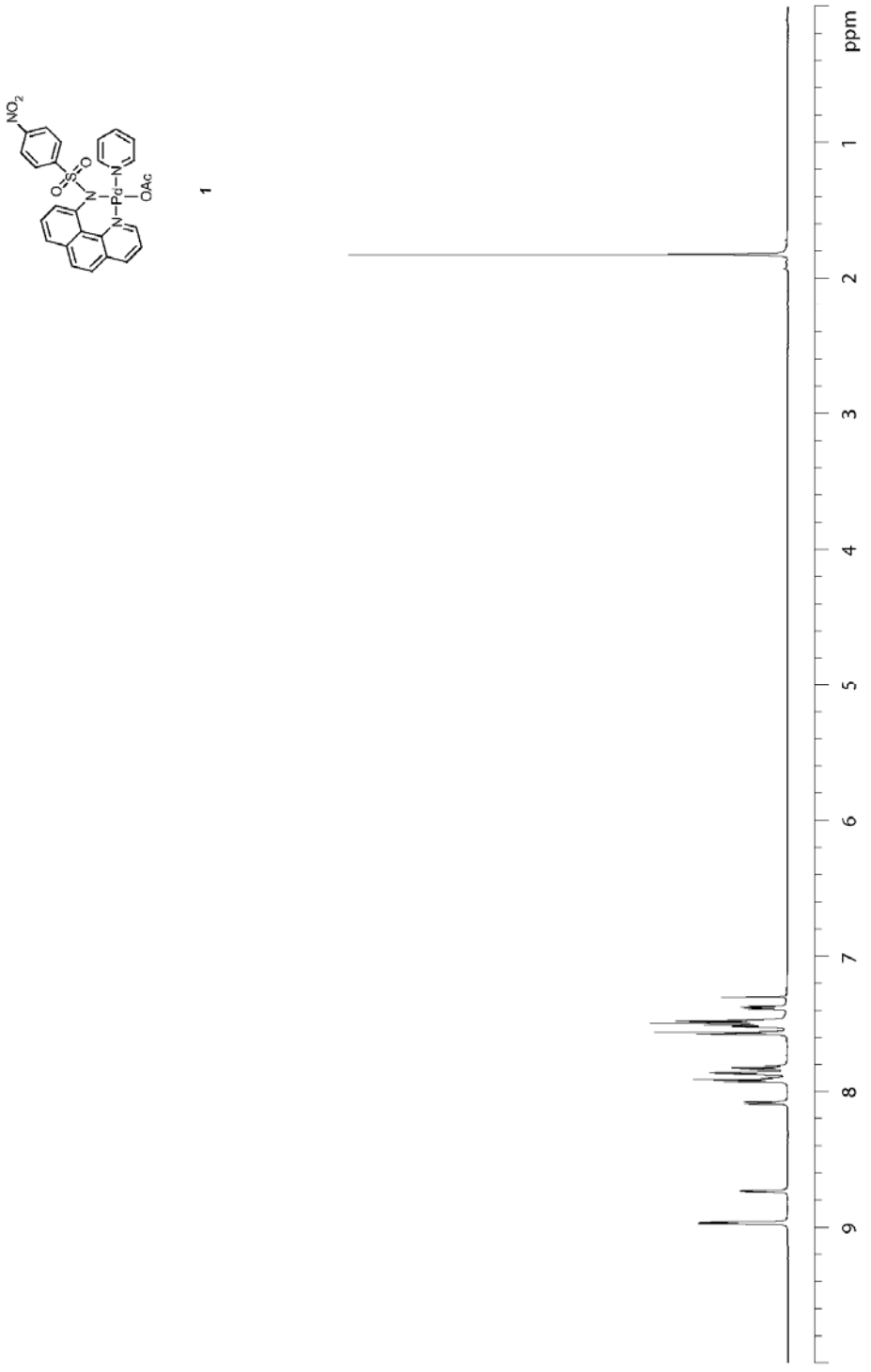


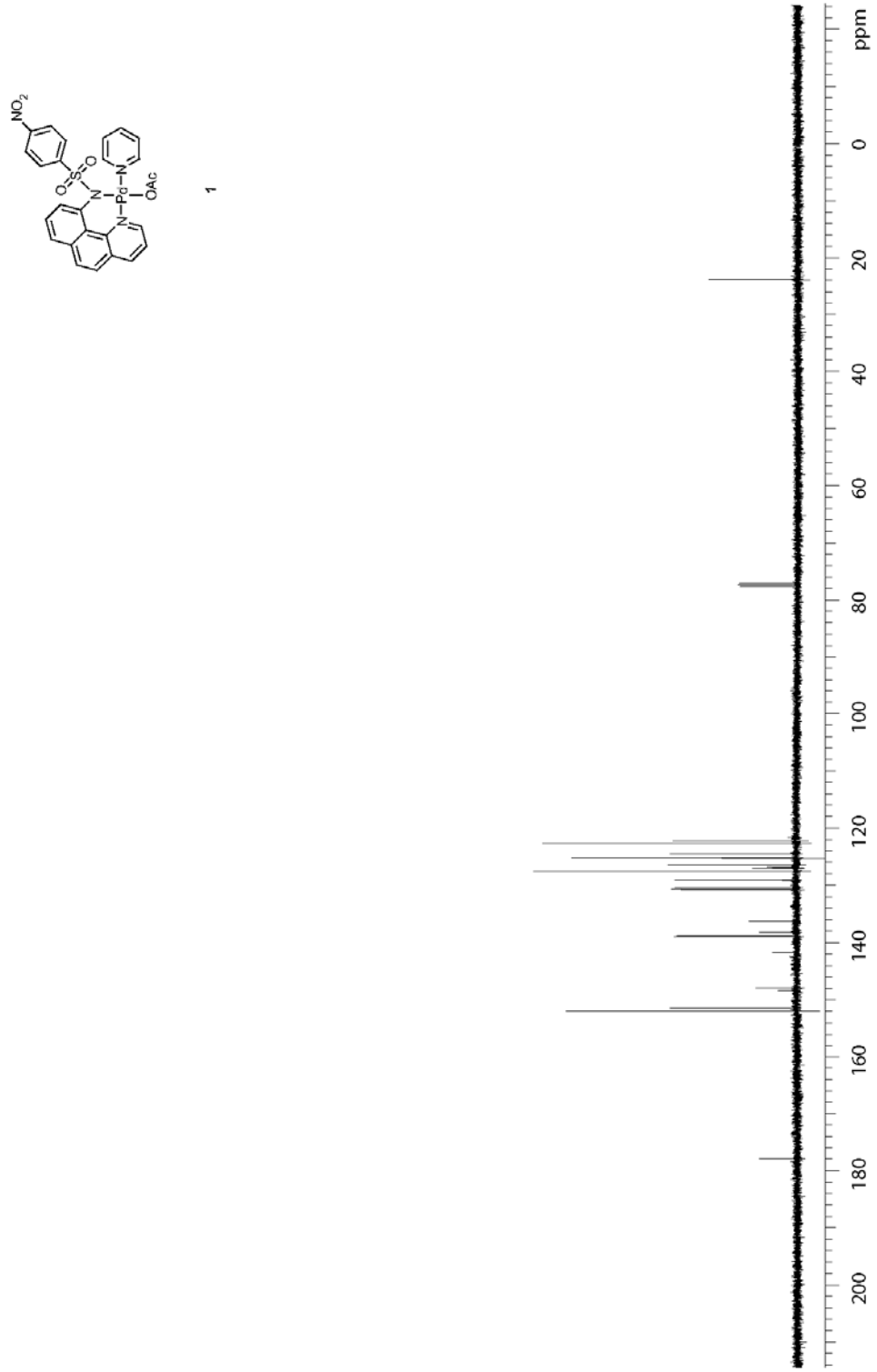
The x-ray structure of aryl palladium complex **4a** with hydrogens and with the atom labeling scheme employed. The nonhydrogen atoms are depicted with 50% probability ellipsoids.

Table S3.: Crystal data and structure refinement for aryl palladium complex 4a.

Identification code	CCDC 676000 = [Pd(C_5H_5N)(C_6H_5)($C_{19}H_{12}N_3O_4S$)]	
Empirical formula	C30 H22 N4 O4 Pd S	
Formula weight	640.98	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$ (No. 19)	
Unit cell dimensions	a = 9.5439(2) Å	α= 90°
	b = 13.8697(2) Å	β= 90°
	c = 19.5047(3) Å	γ = 90°
Volume	2581.86(8) $Å^3$	
Z	4	
Density (calculated)	1.649 Mg/m^3	
Absorption coefficient	0.846 mm^{-1}	
F(000)	1296	
Crystal size	0.125 x 0.075 x 0.050 mm^3	
Theta range for data collection	1.80 to 27.50°	
Index ranges	-12<=h<=12, -18<=k<=18, -25<=l<=25	
Reflections collected	67549	
Independent reflections	5932 [R(int) = 0.1052]	
Completeness to theta = 27.50°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9589 and 0.9016	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5932 / 0 / 361	
Goodness-of-fit on F^2	1.050	
Final R indices [I>2sigma(I)]	R1 = 0.0329, wR2 = 0.0657	
R indices (all data)	R1 = 0.0427, wR2 = 0.0698	
Absolute structure parameter	-0.03(2)	
Largest diff. peak and hole	0.488 and -0.576 e.$Å^{-3}$	

Spectroscopic Data

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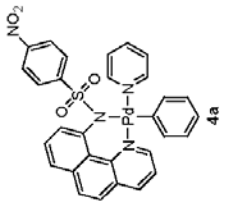
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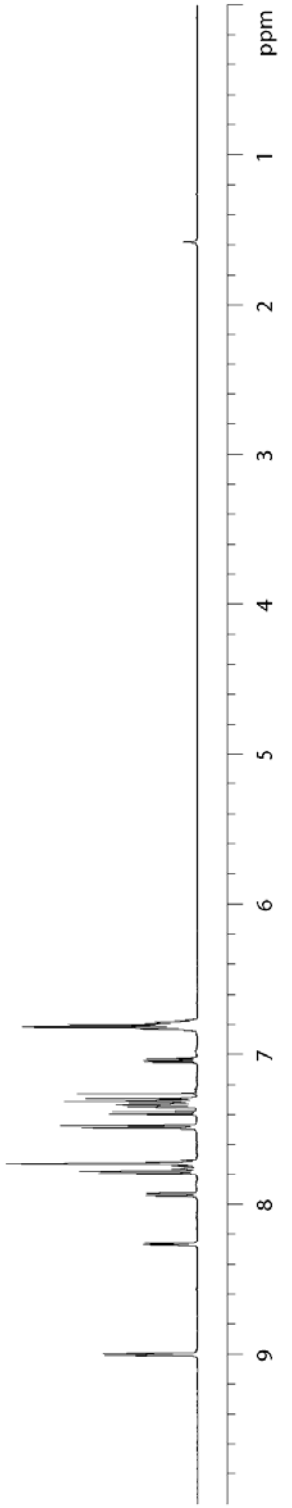
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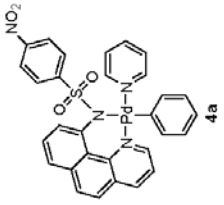
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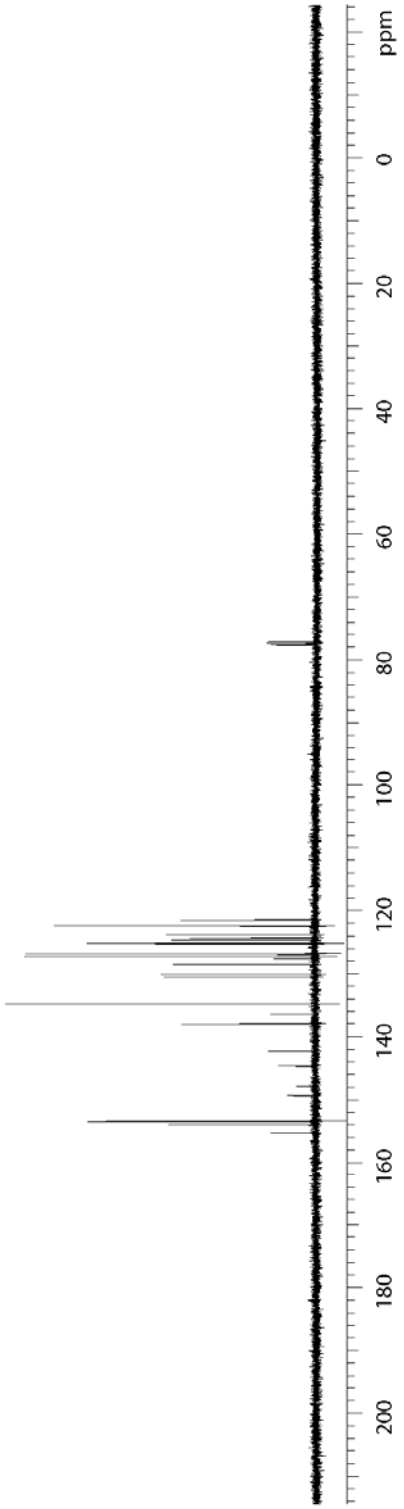
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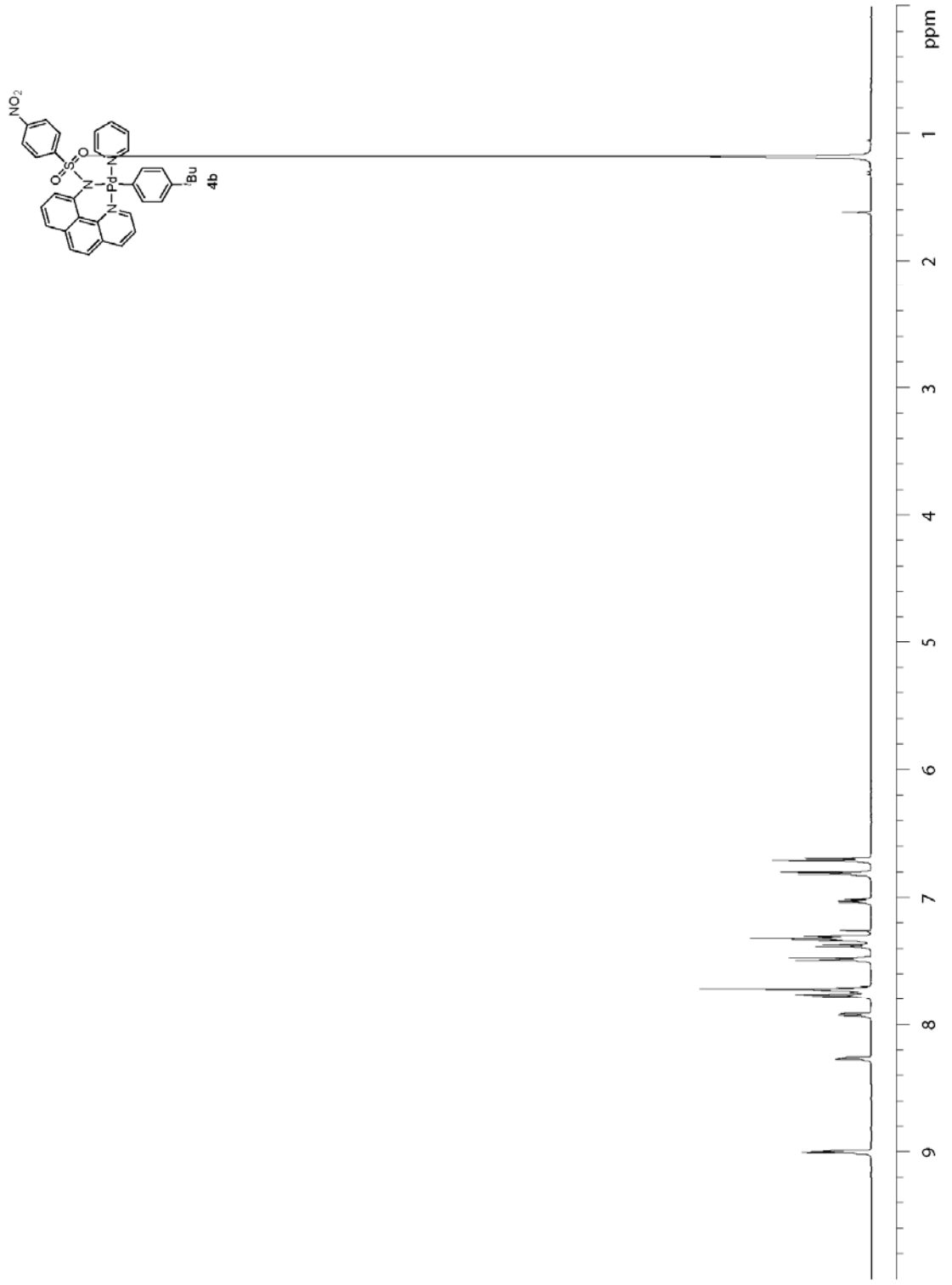
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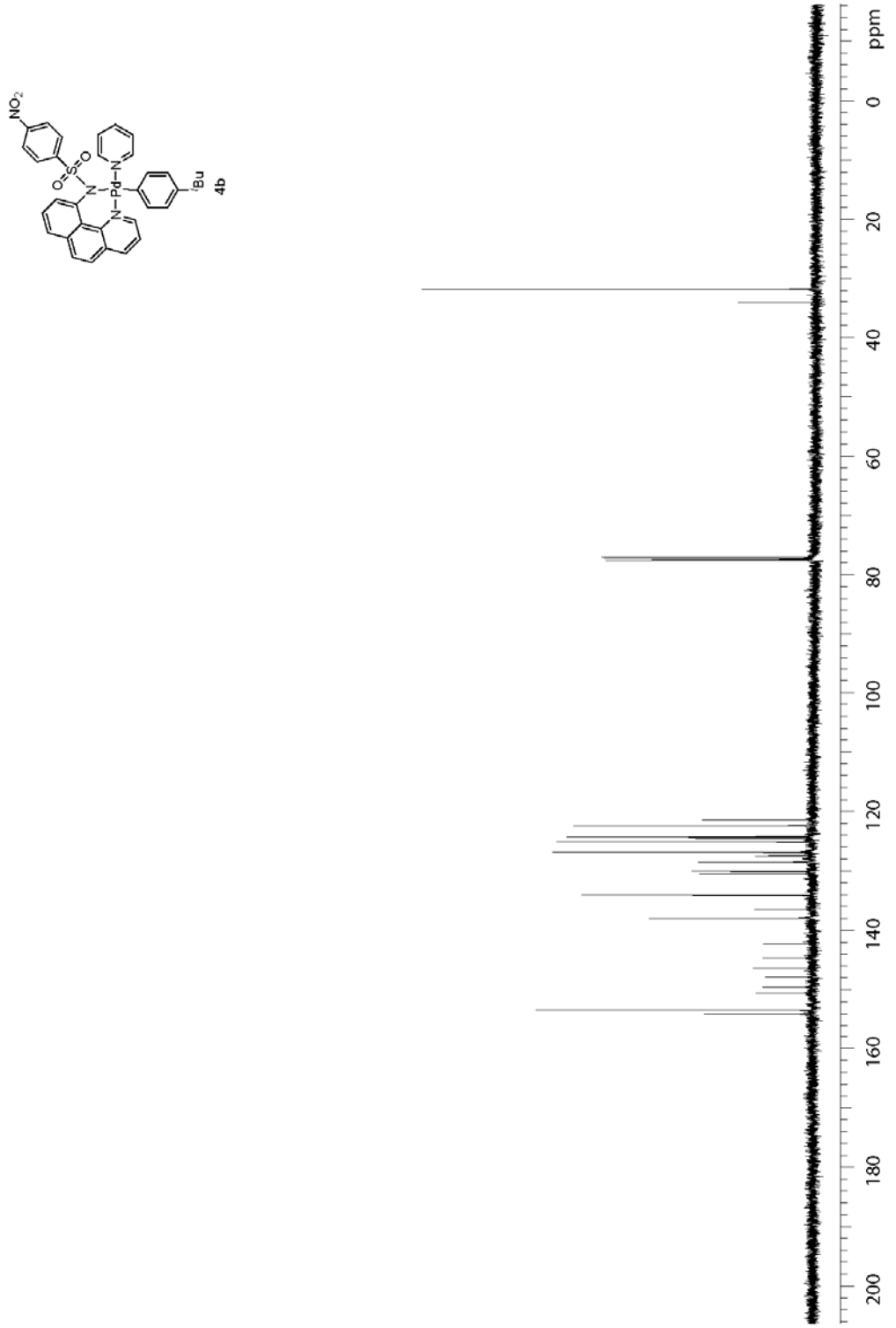
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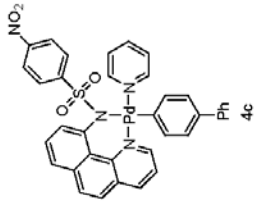
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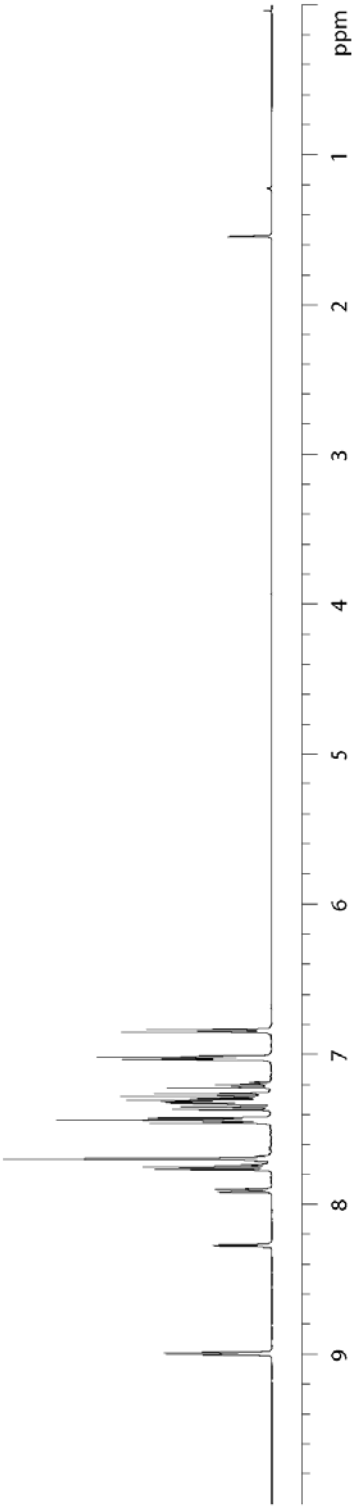
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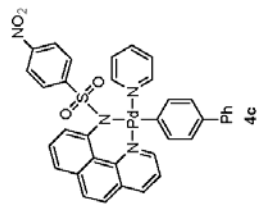
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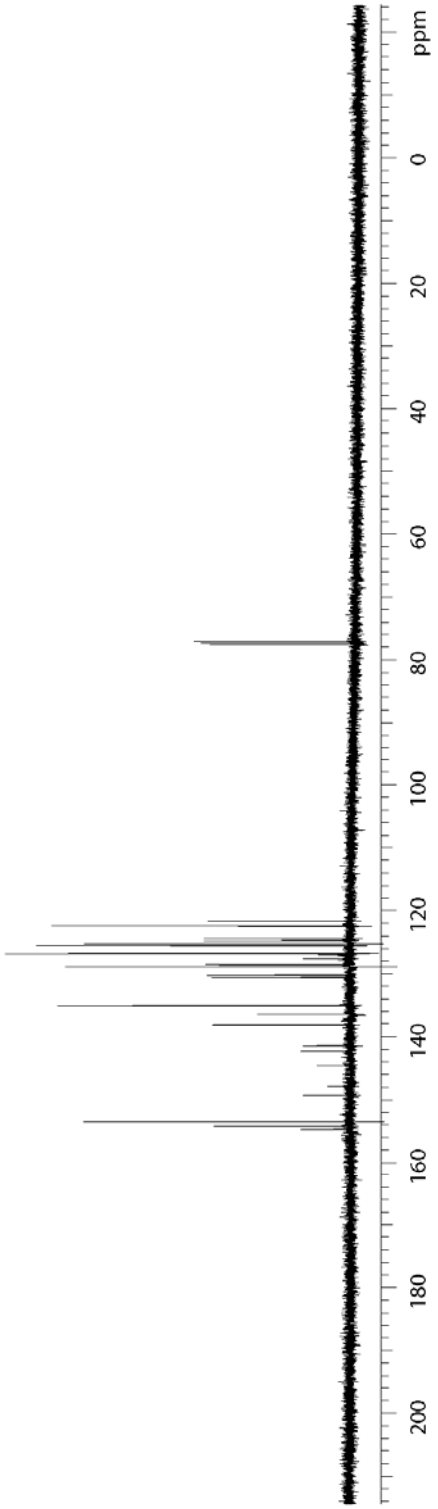
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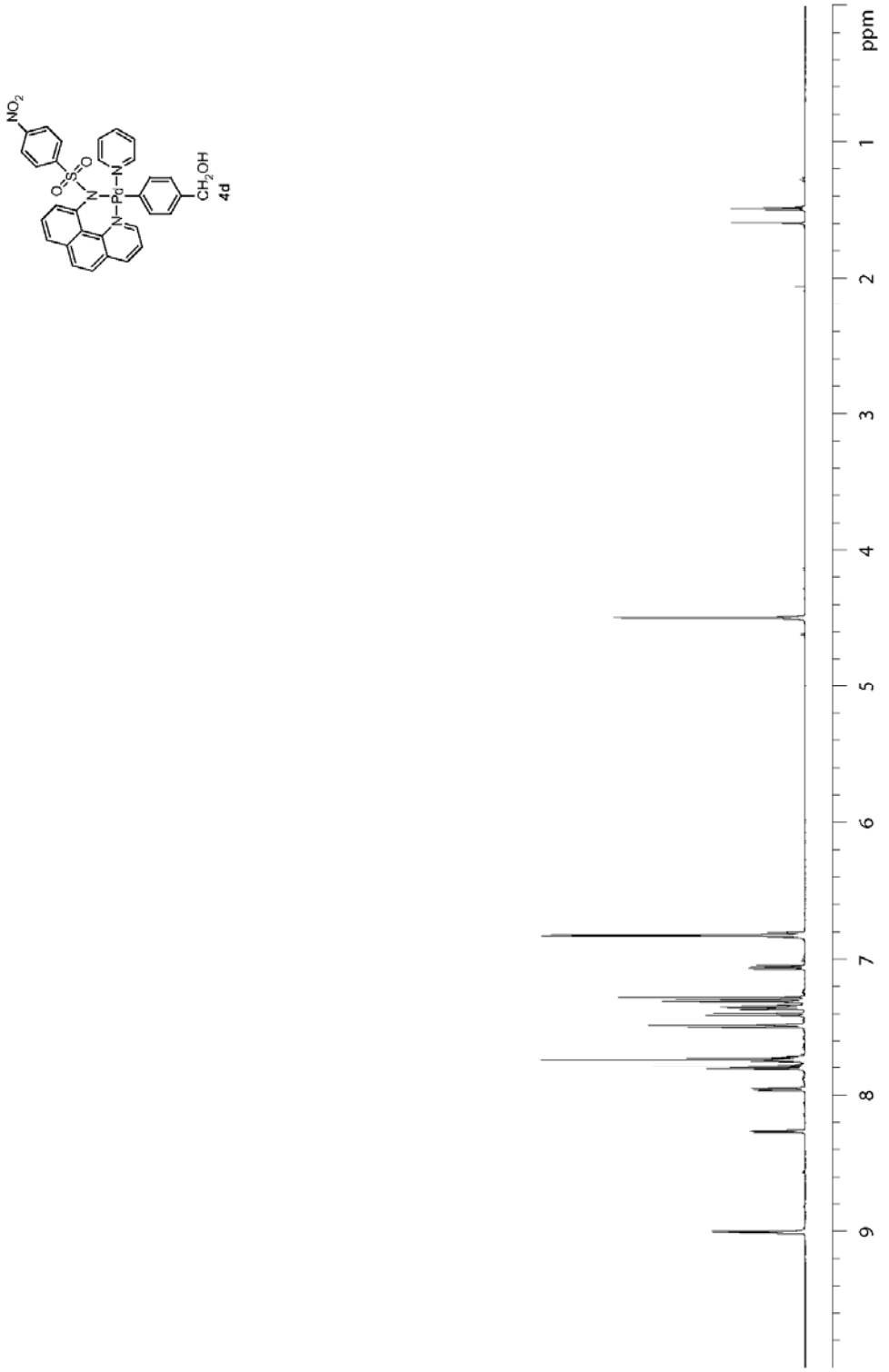
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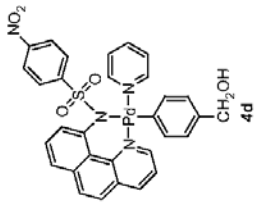
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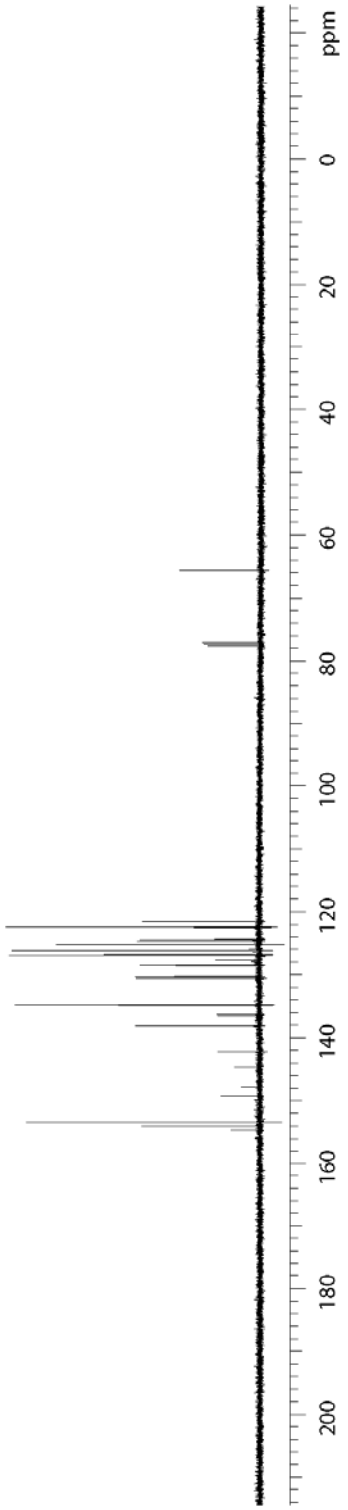
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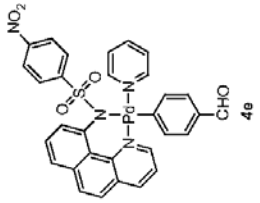
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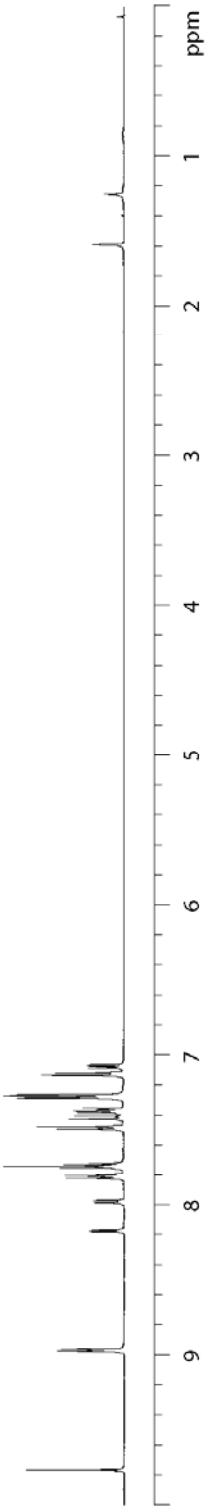
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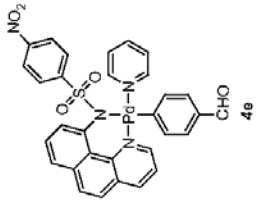
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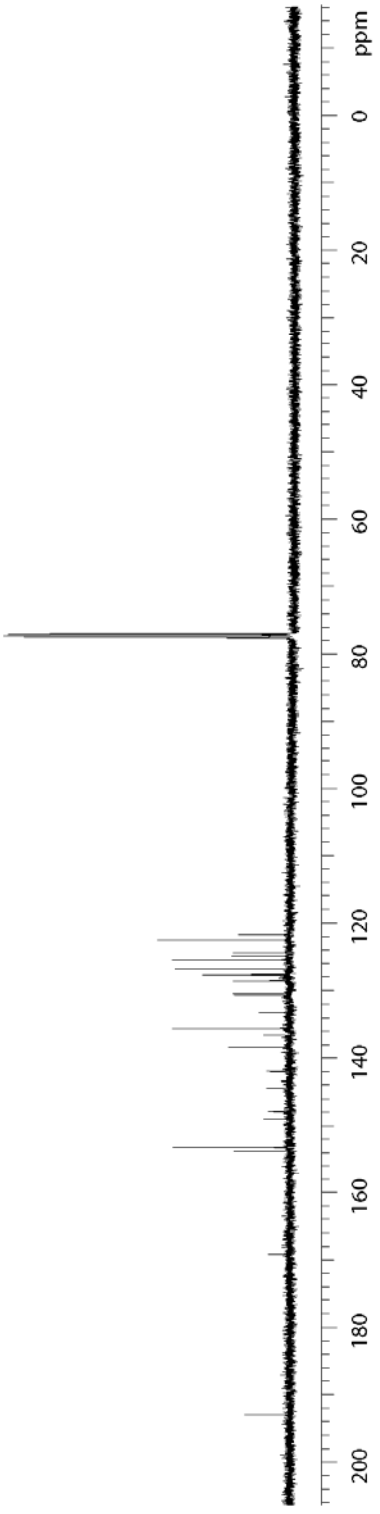
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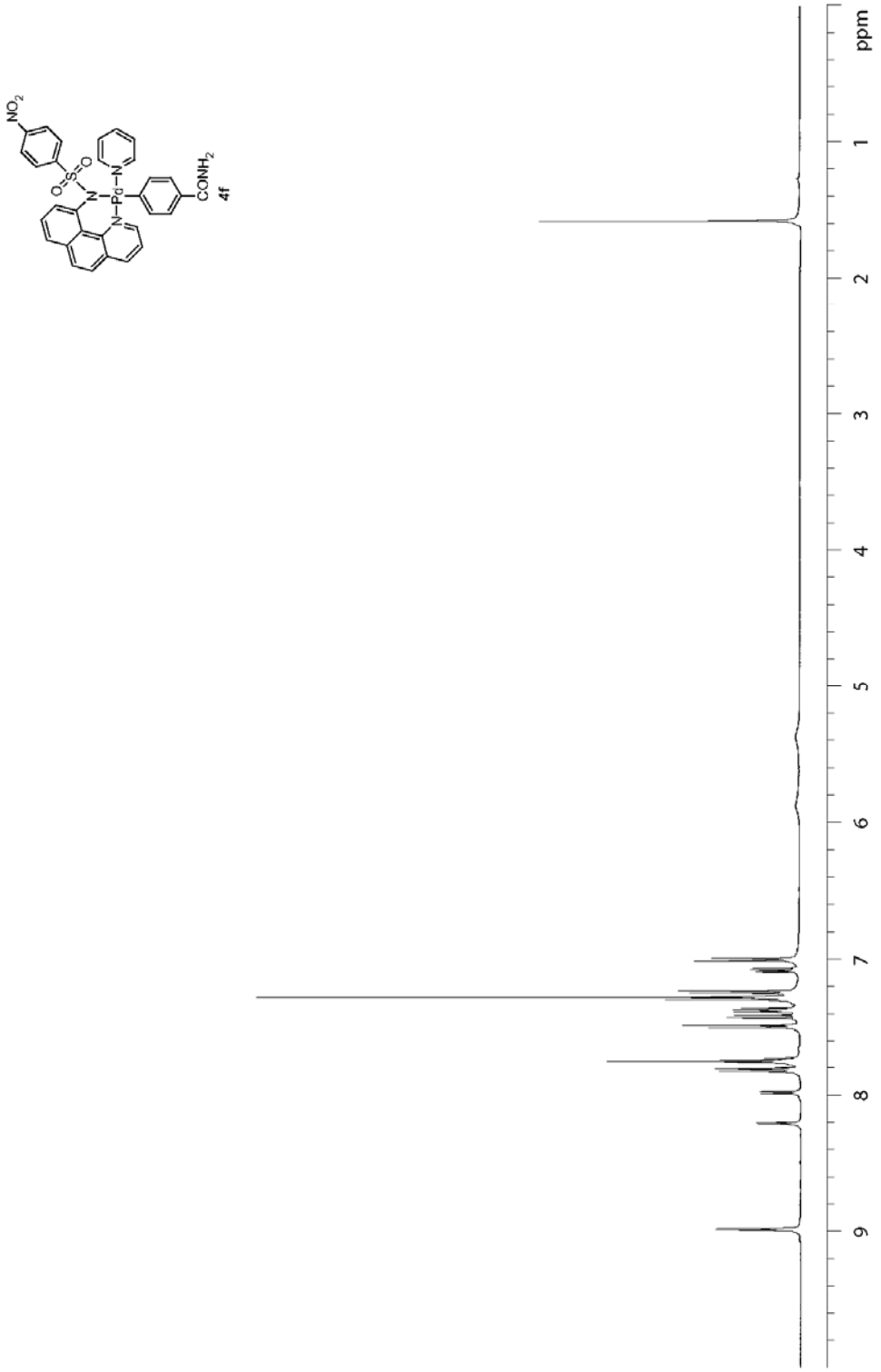
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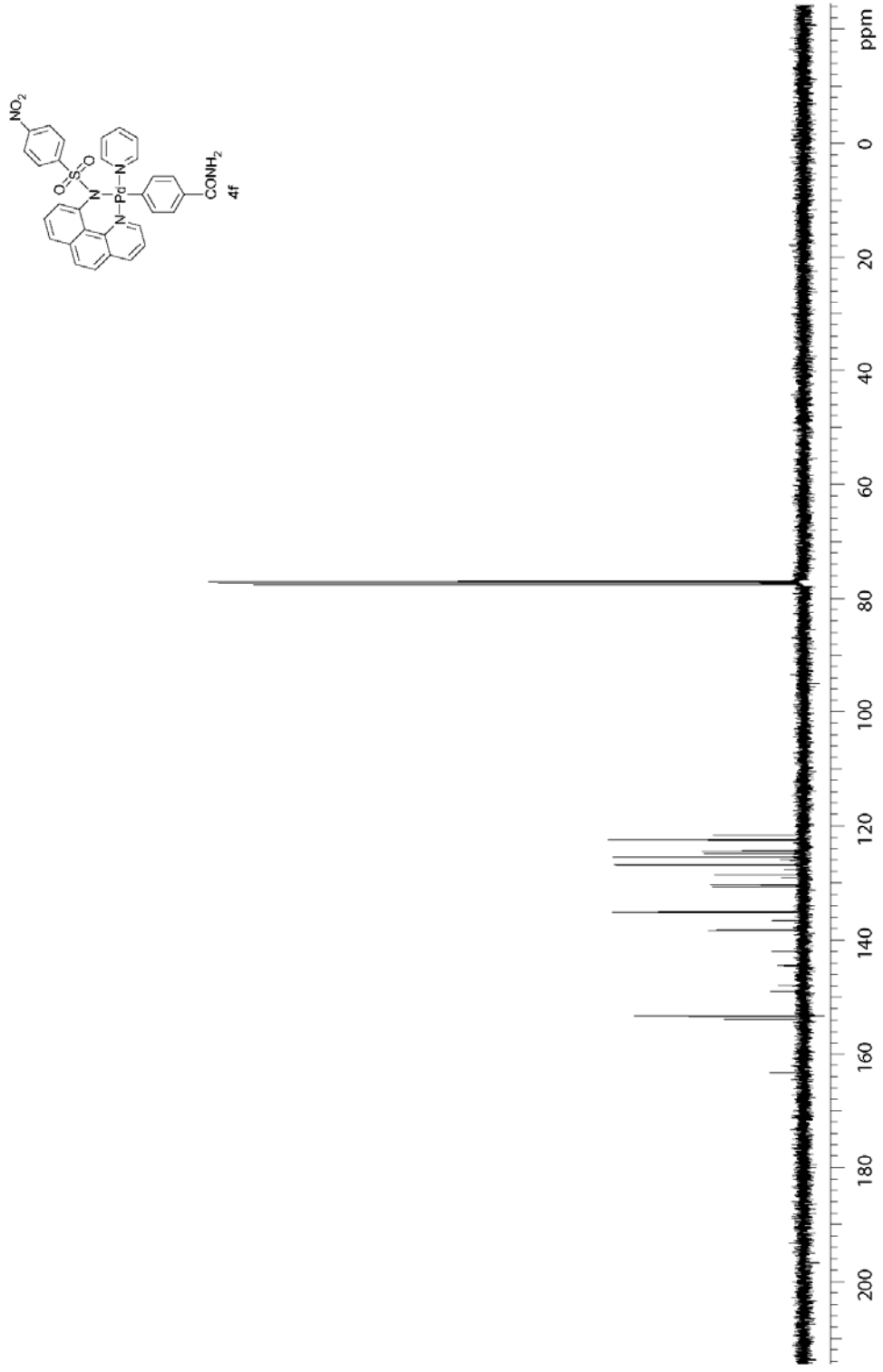
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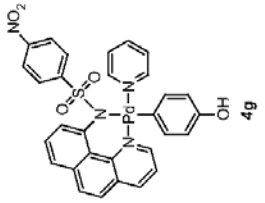

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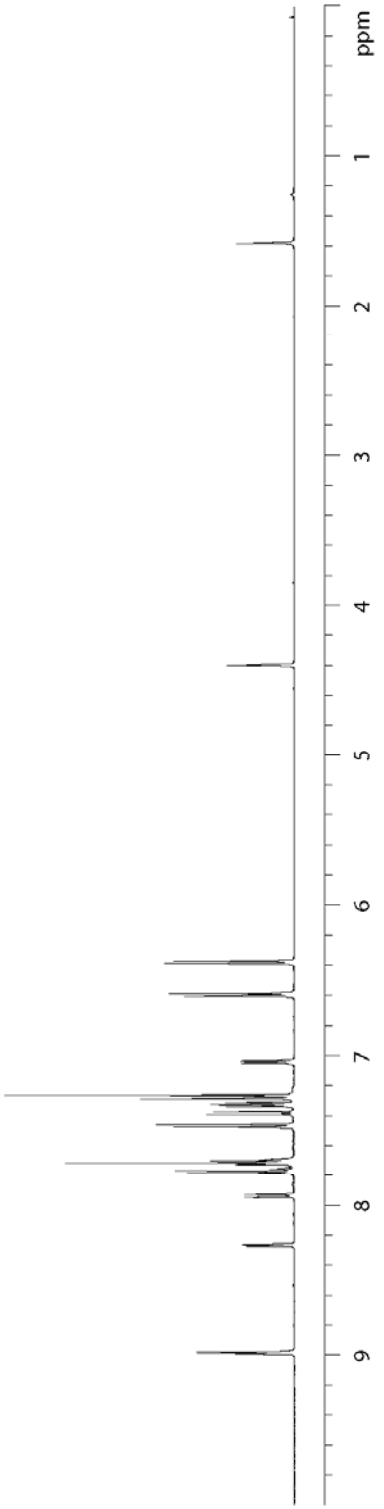

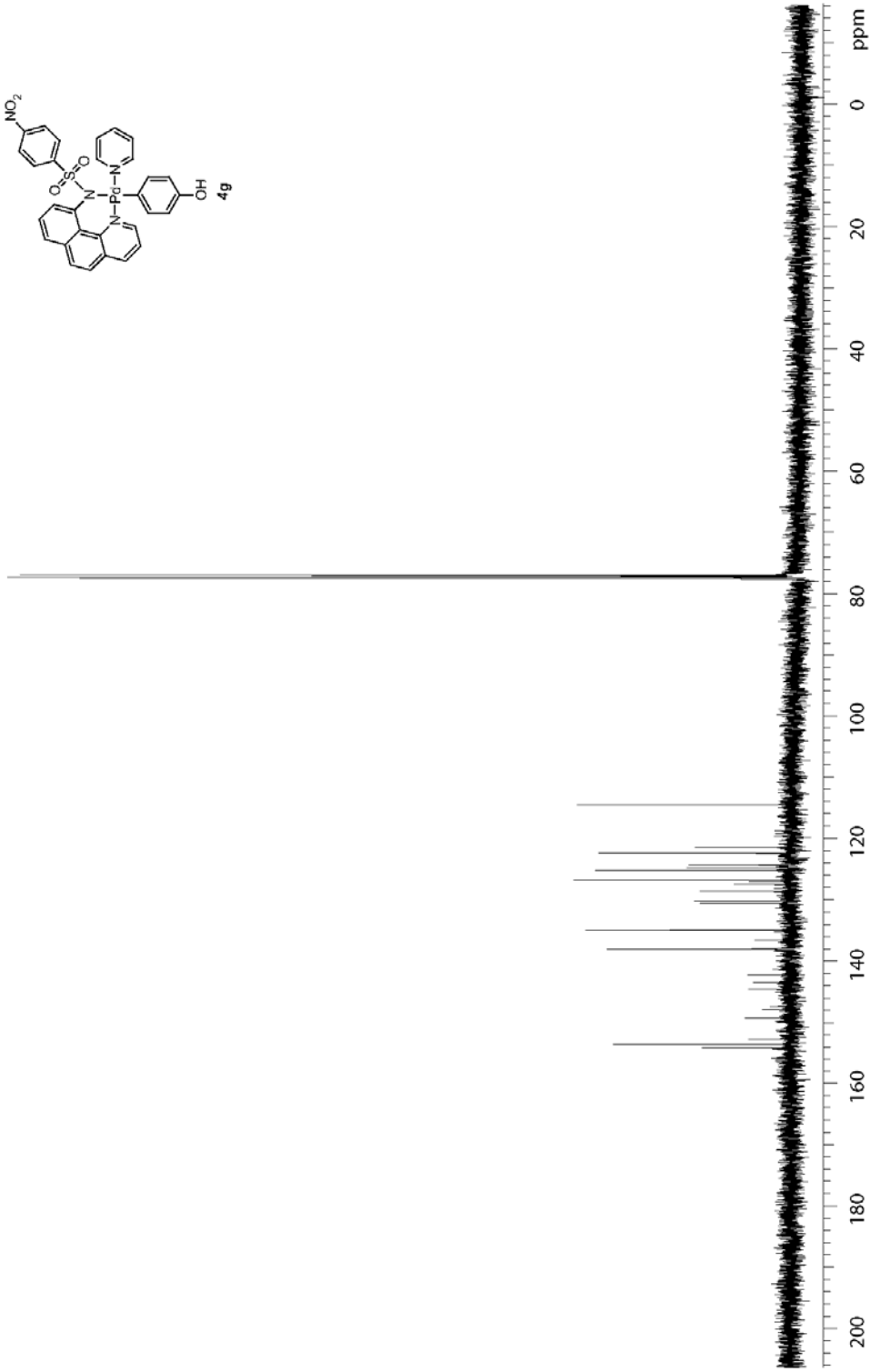
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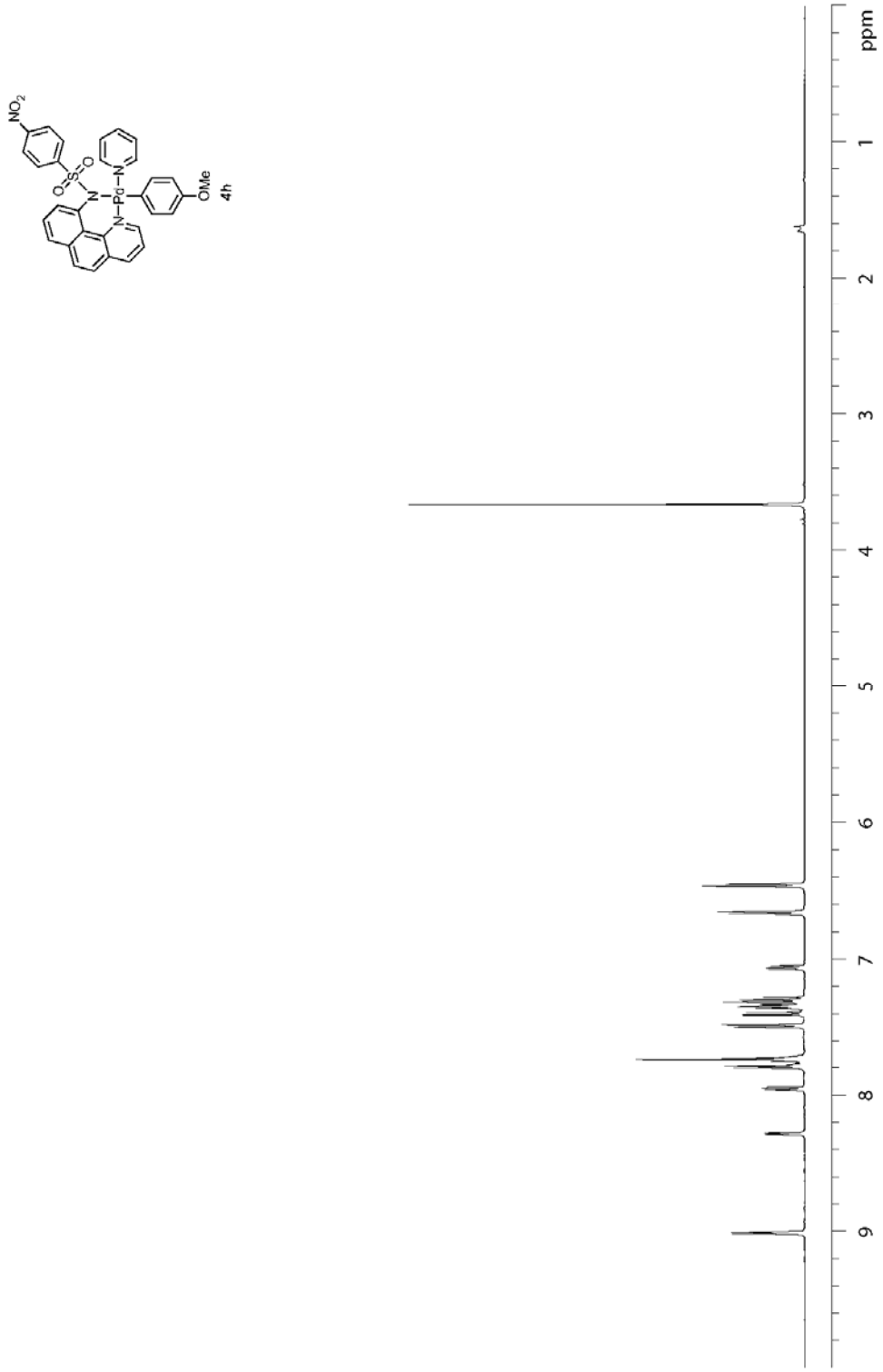
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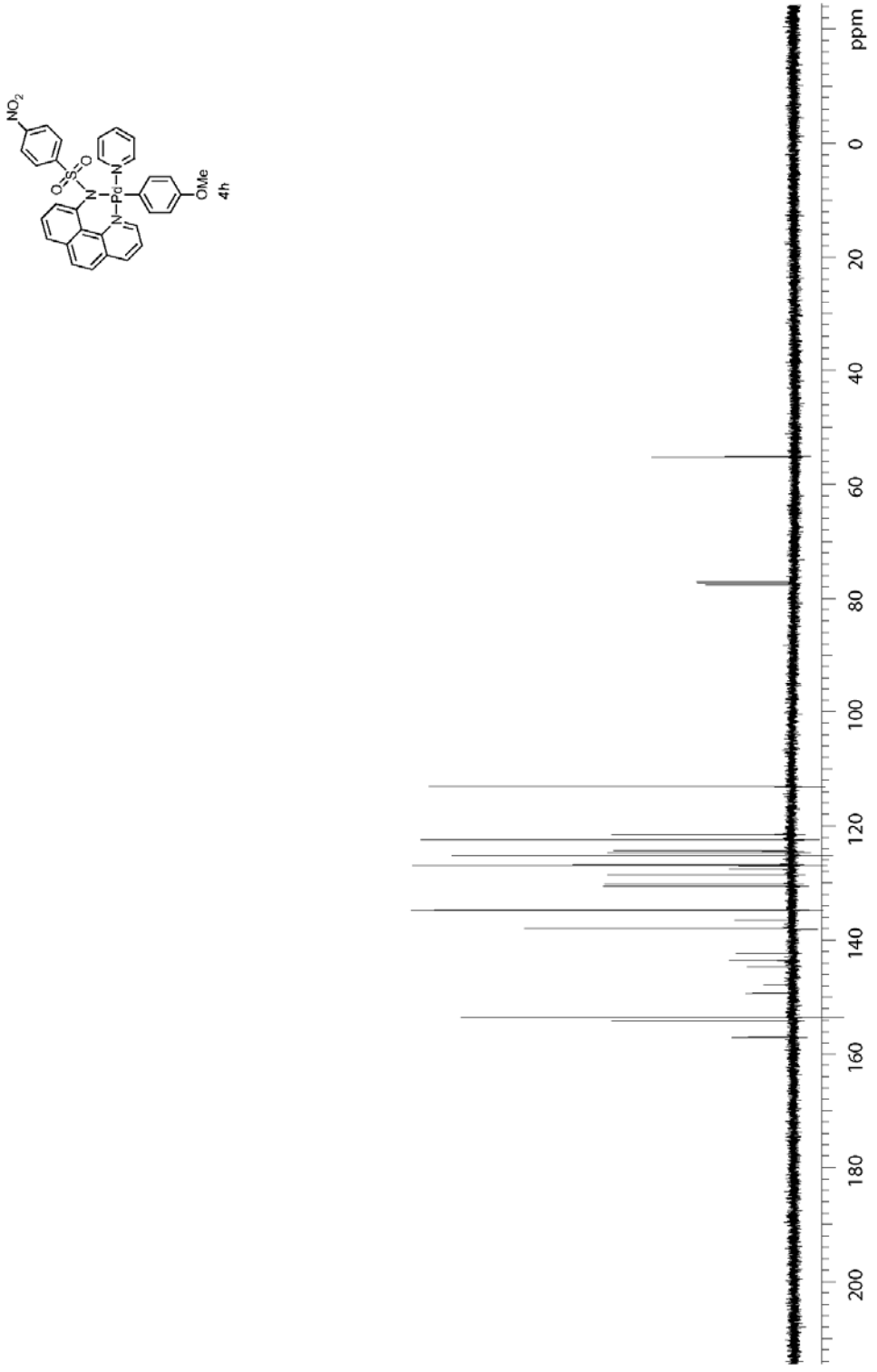
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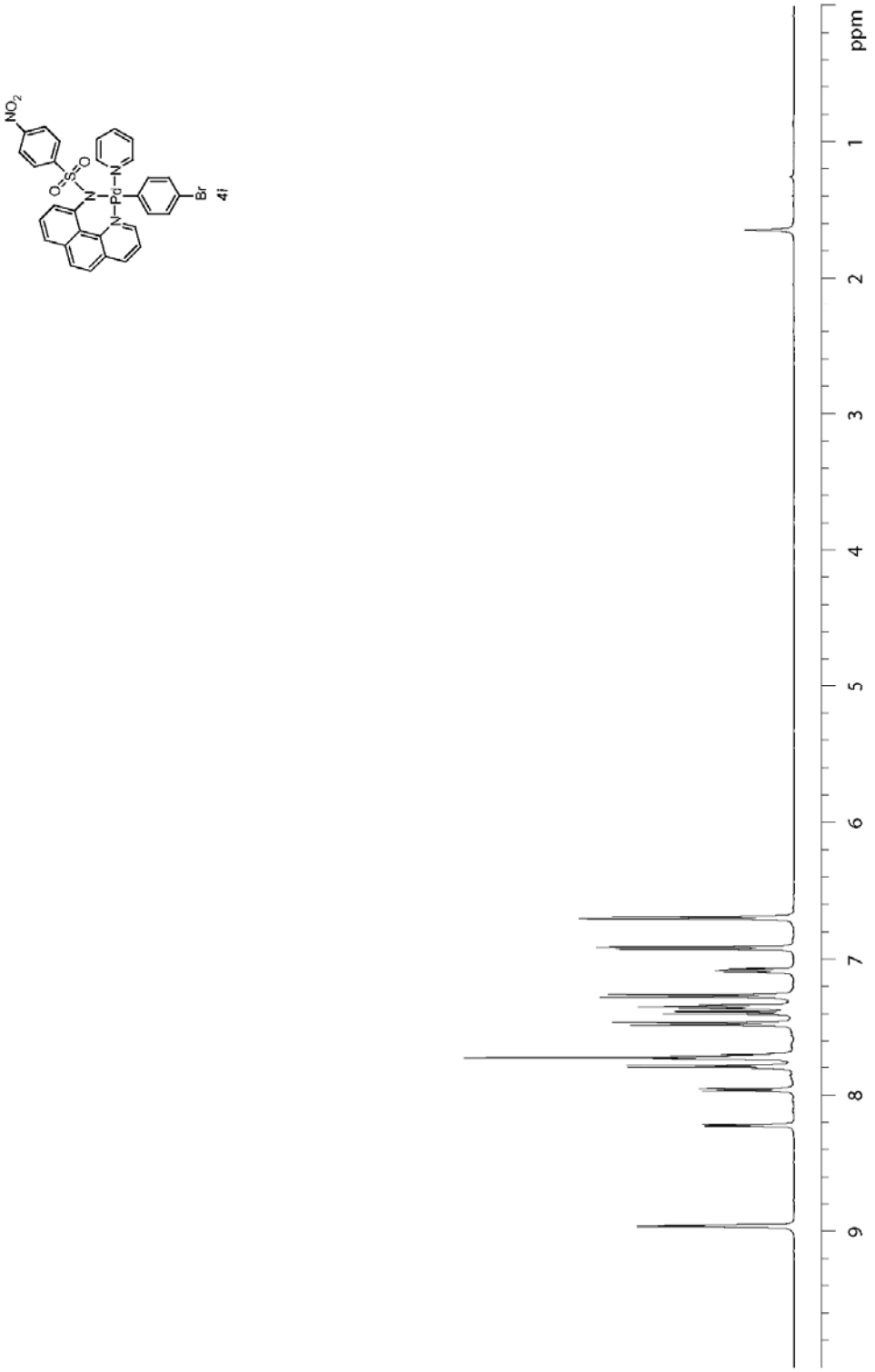
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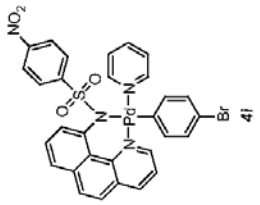
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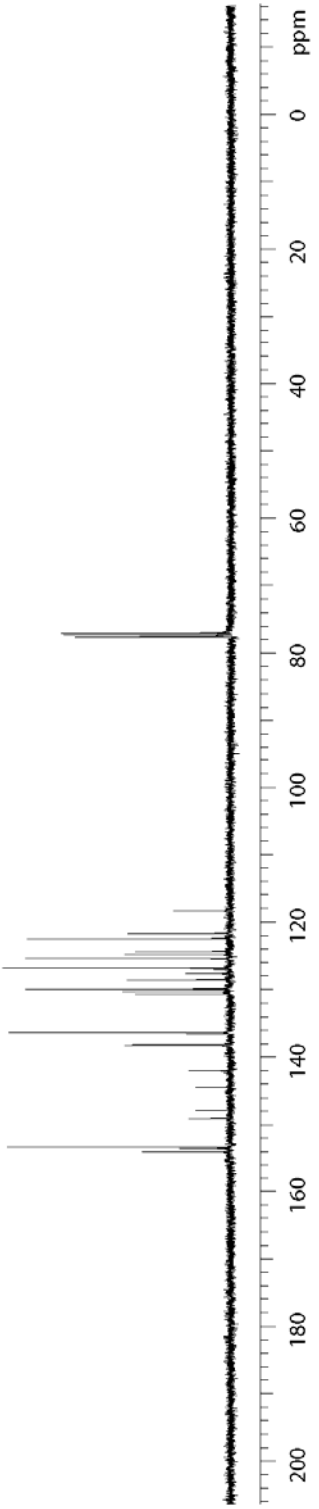
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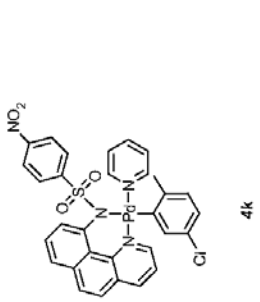

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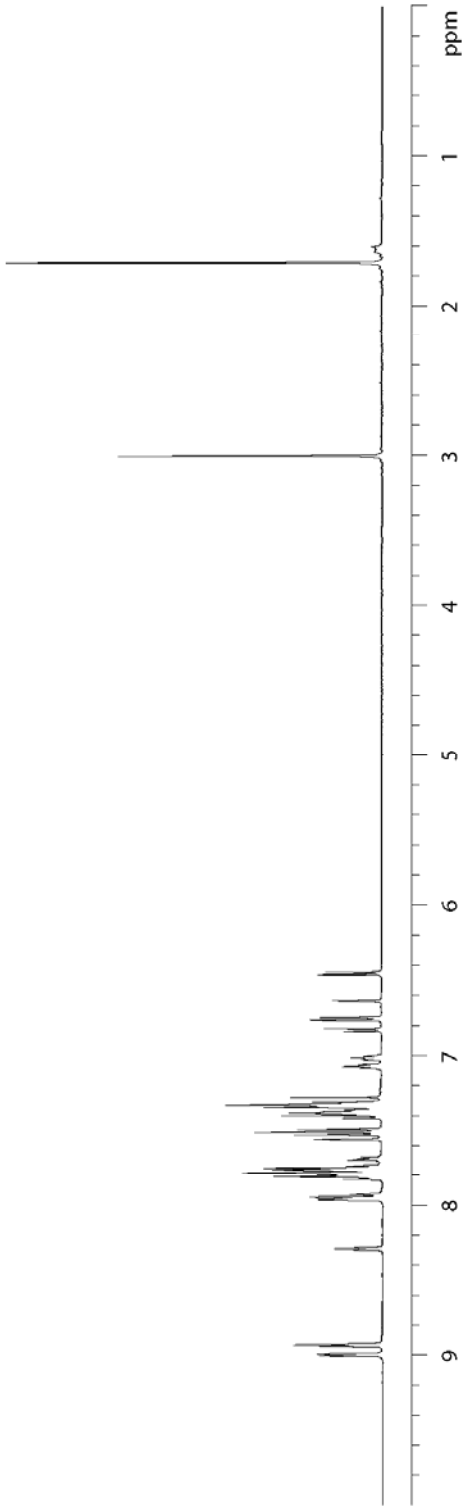

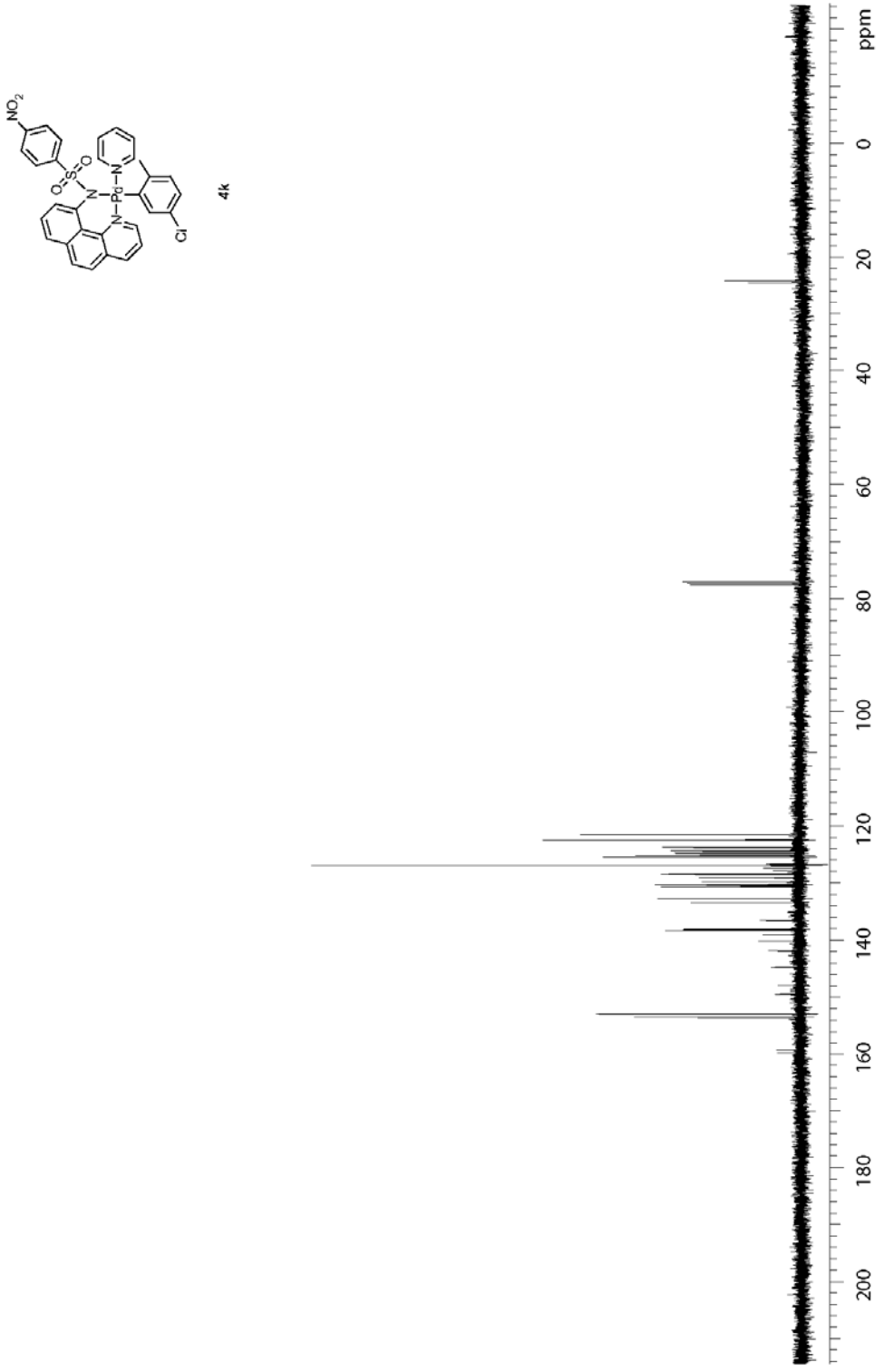
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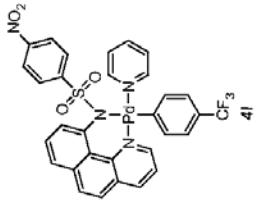

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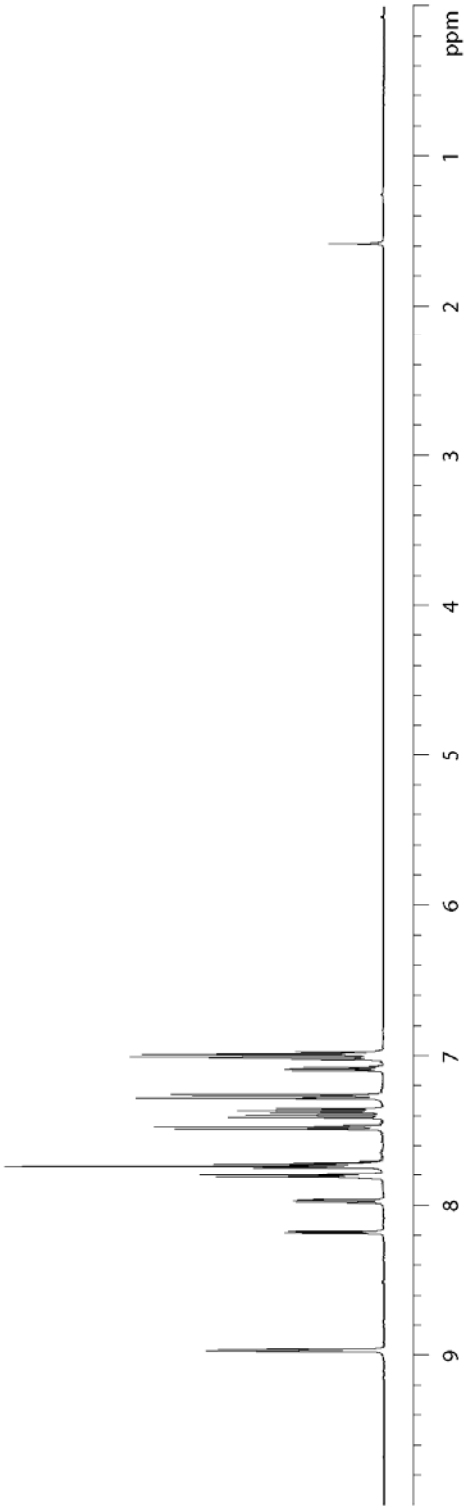

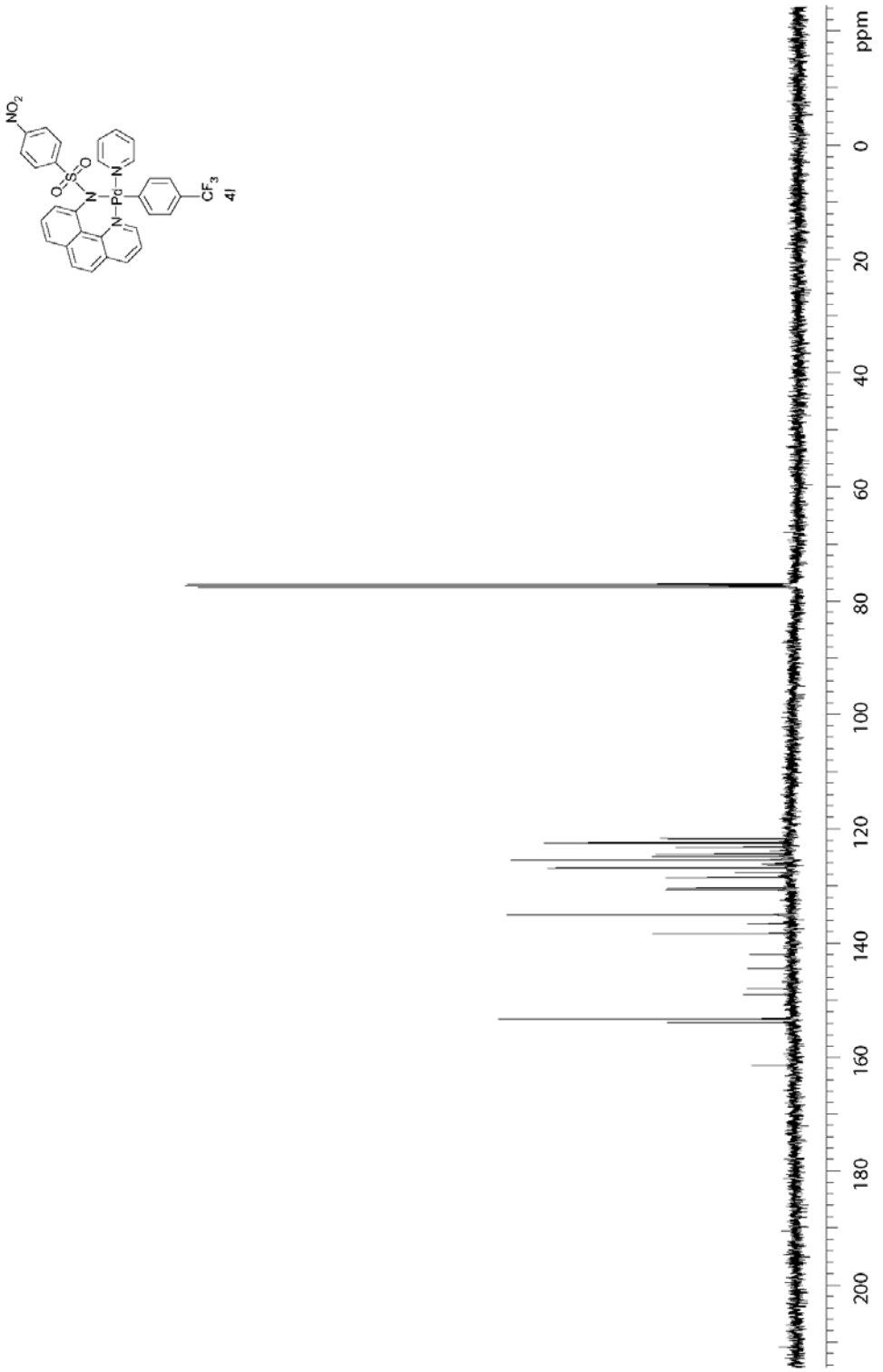
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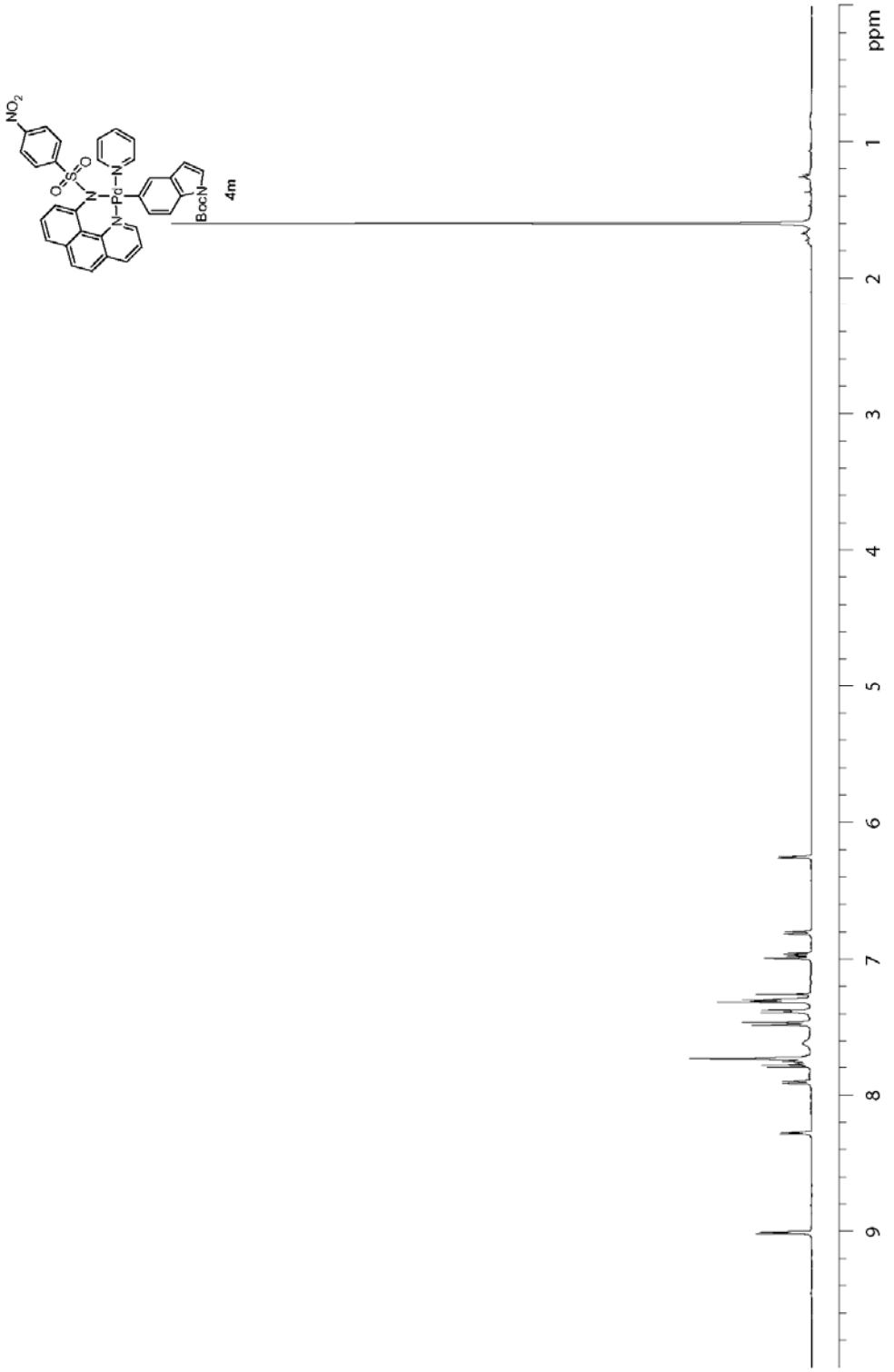
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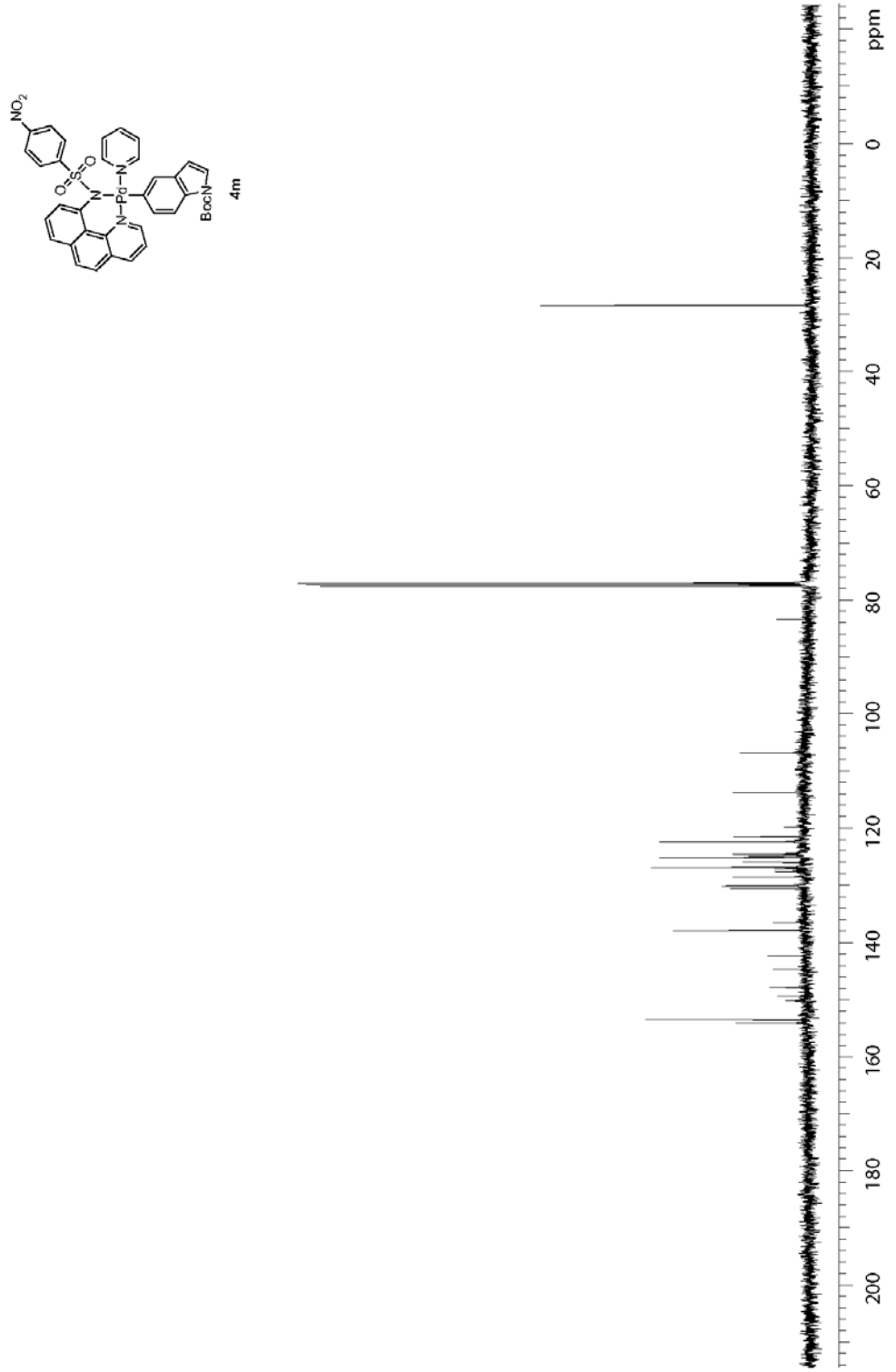
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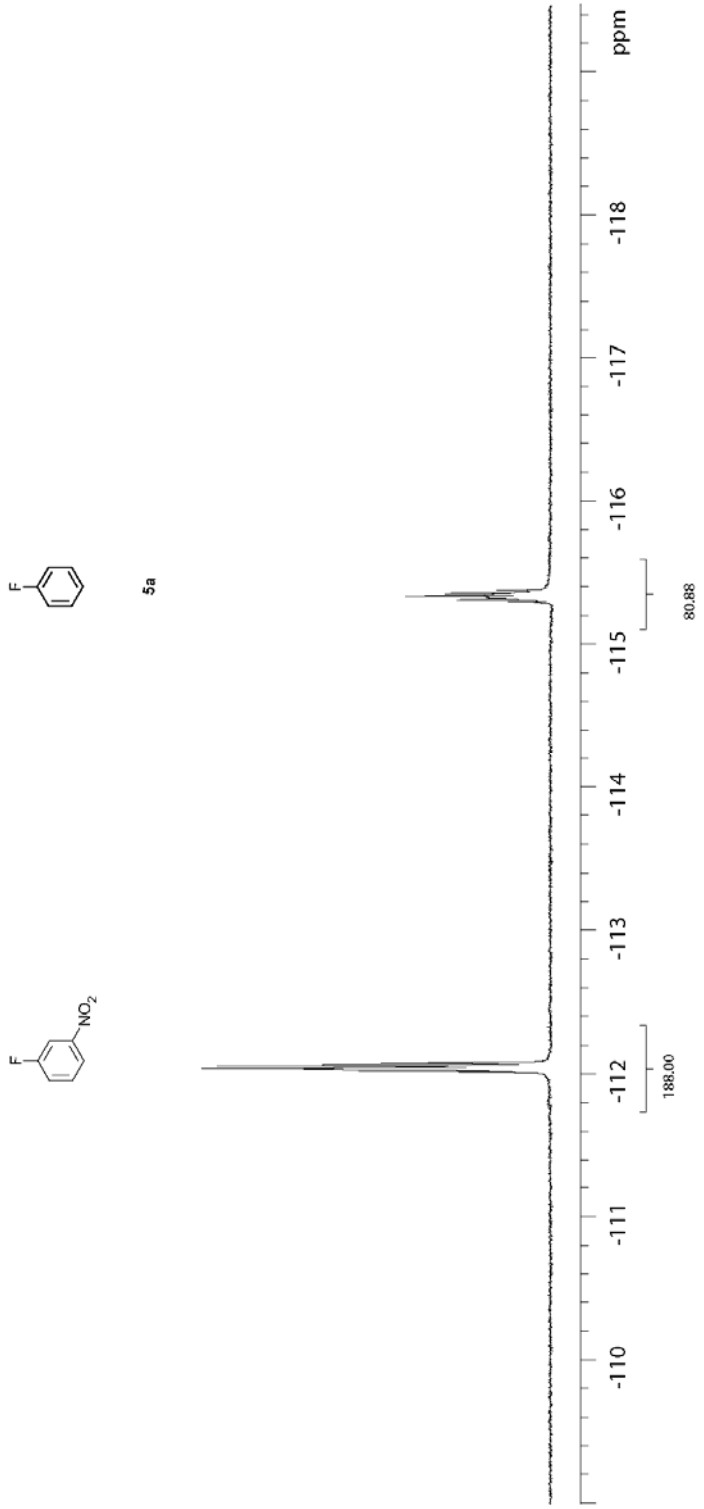
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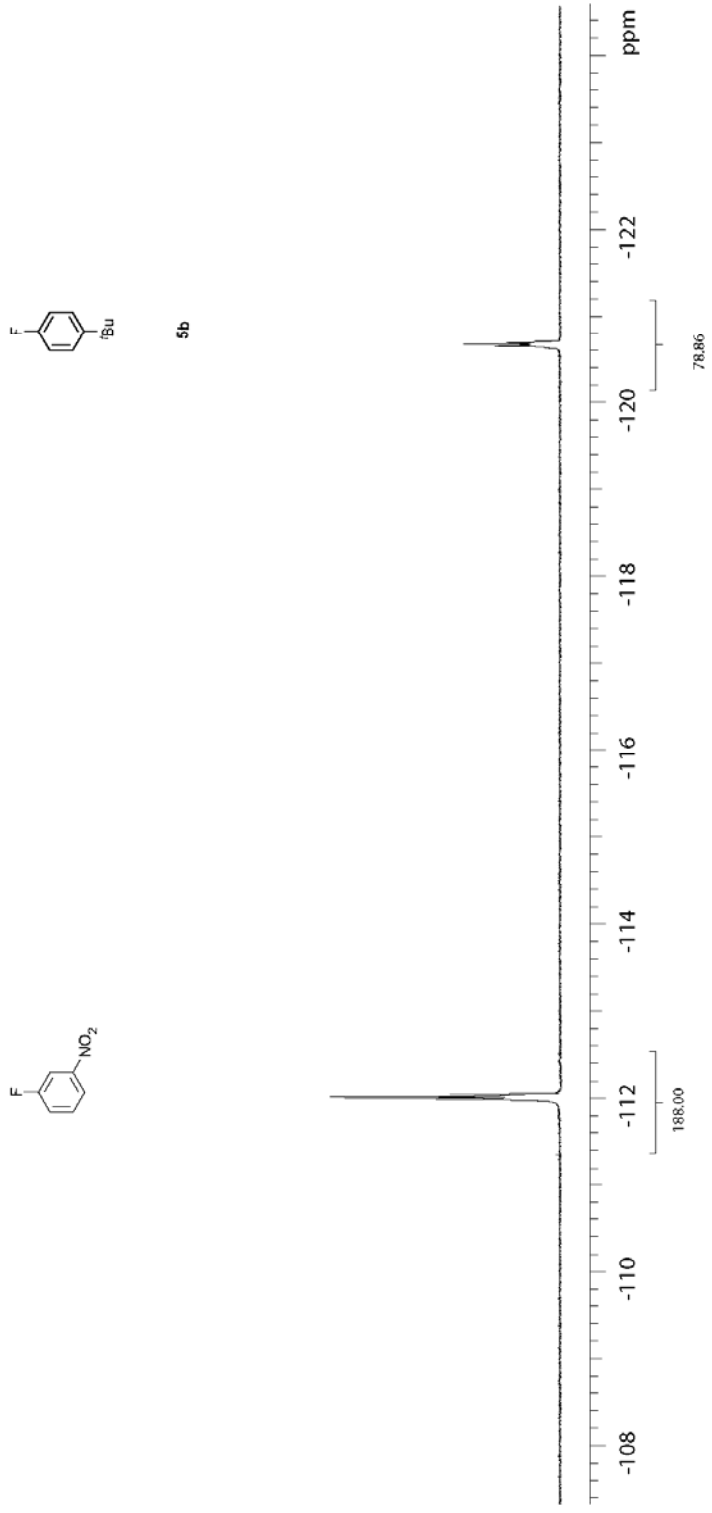
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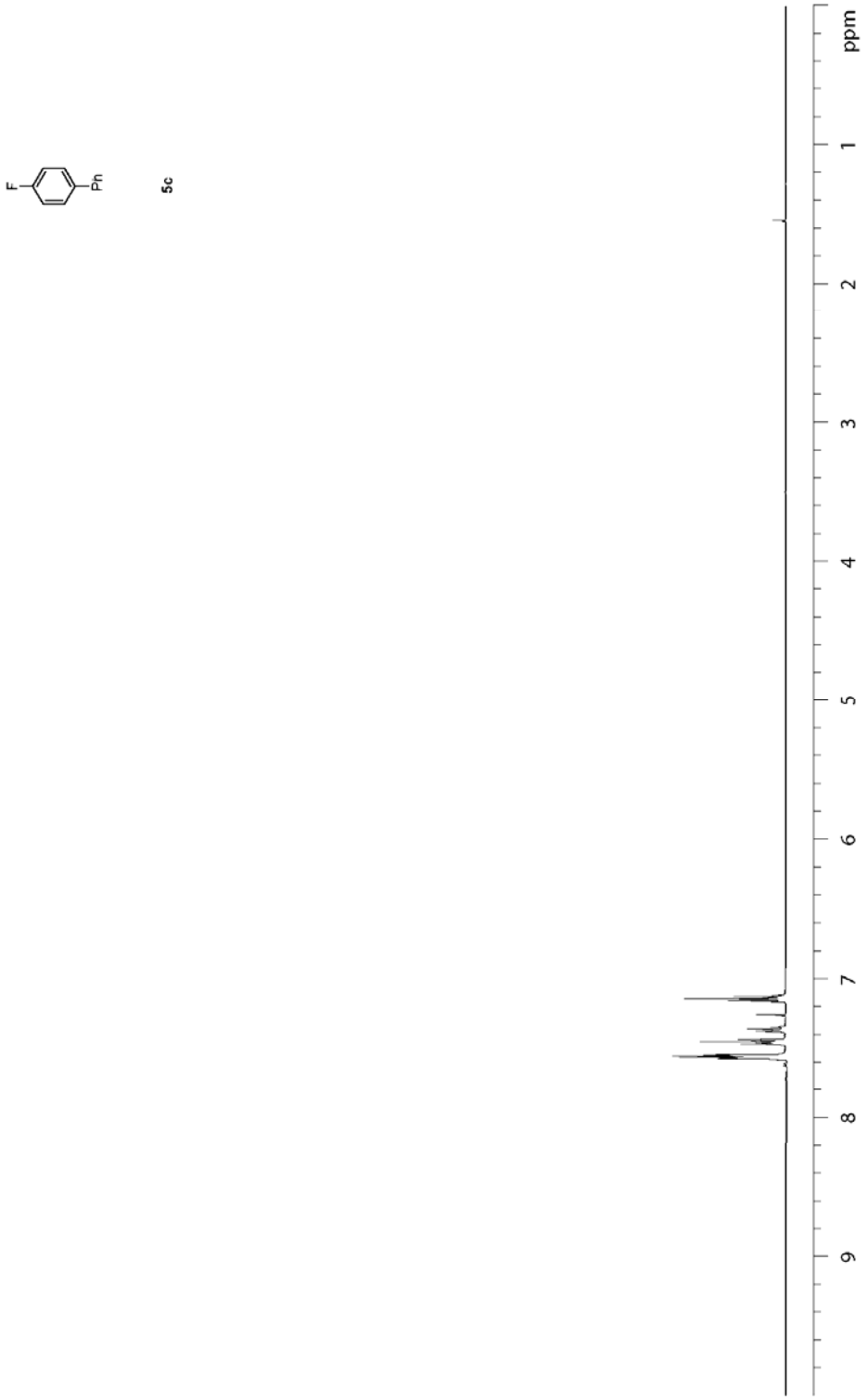
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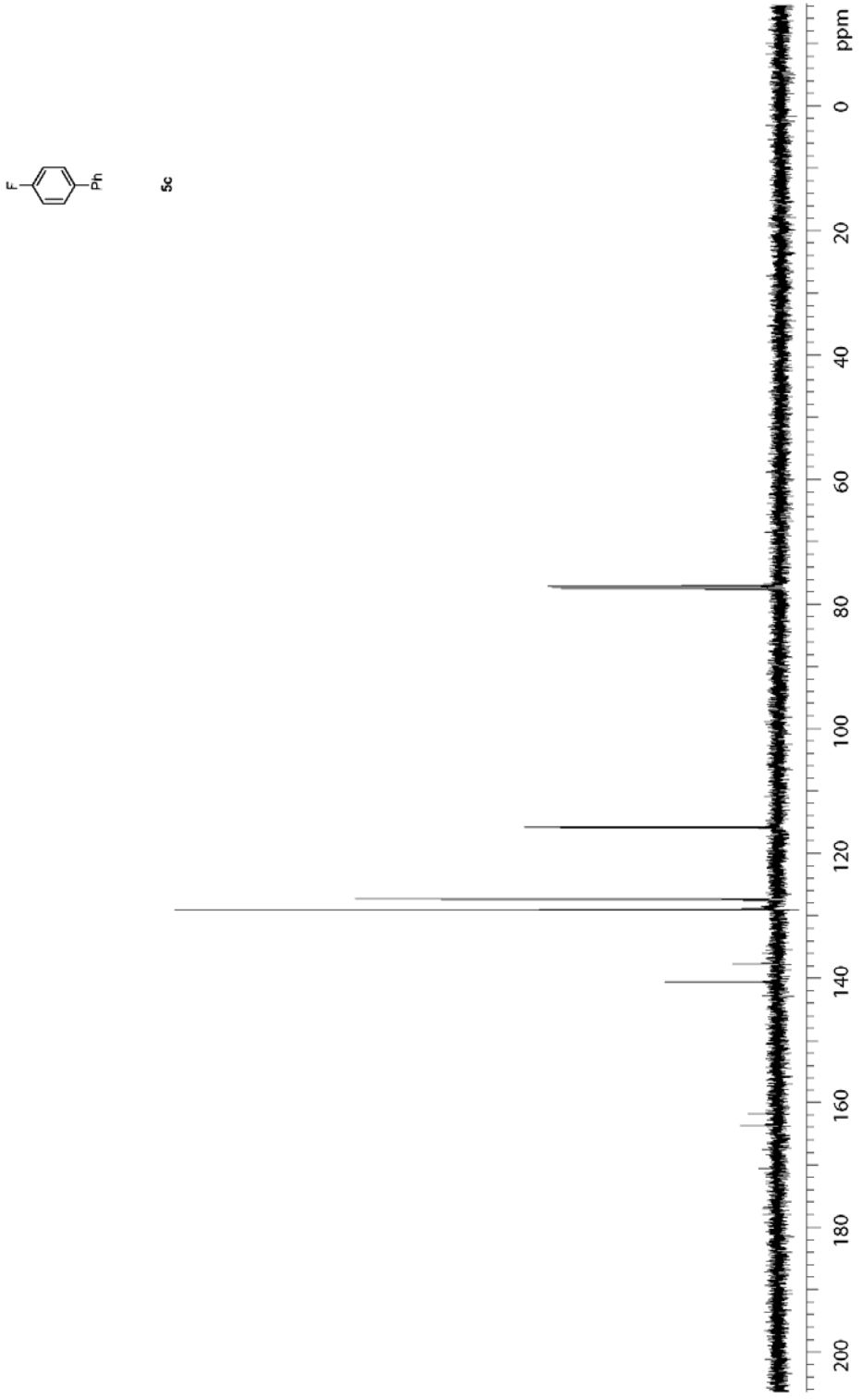
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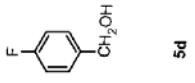

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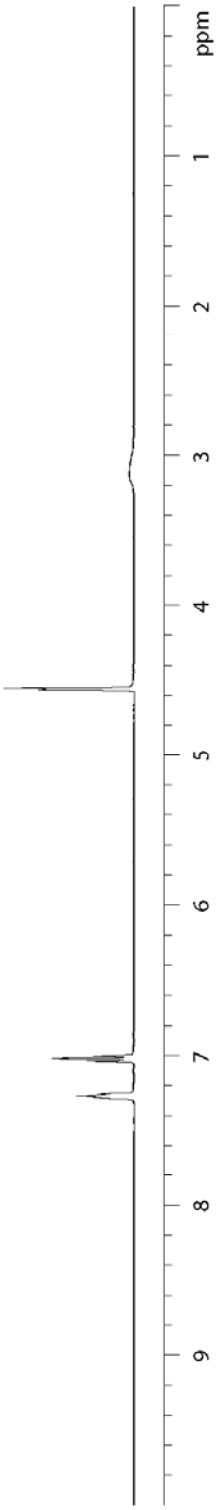

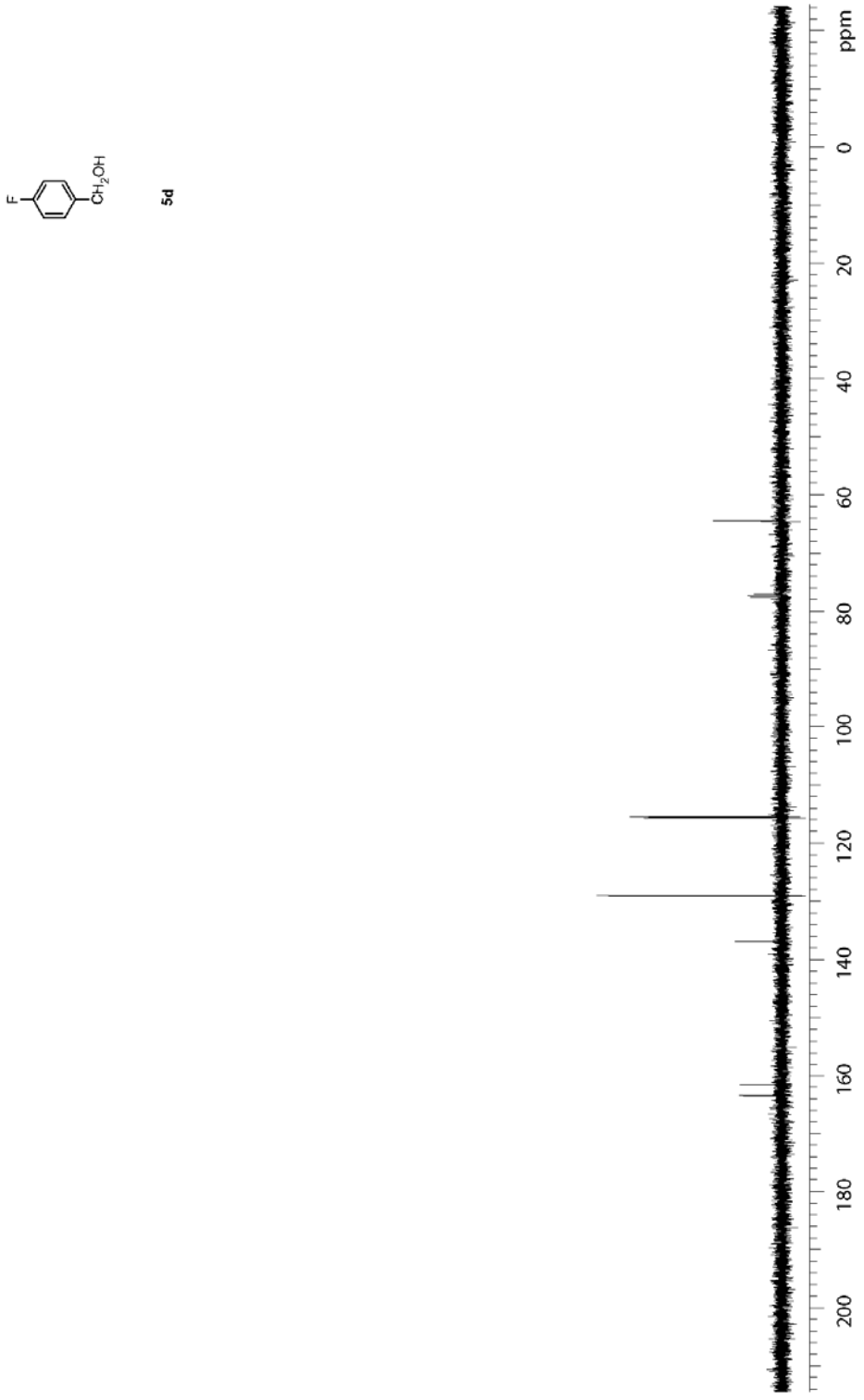
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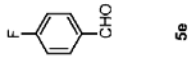

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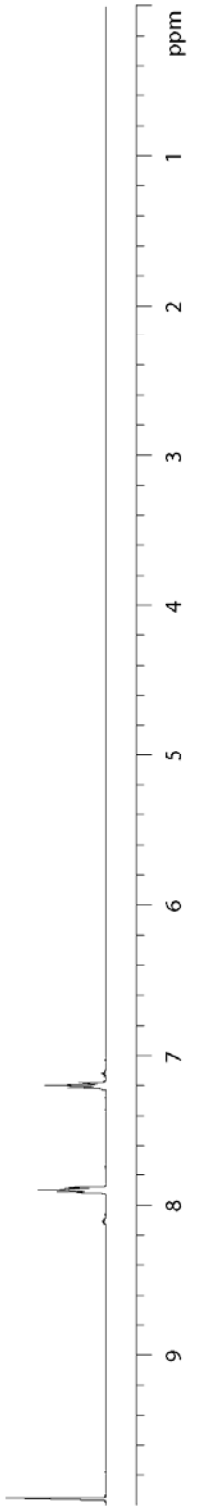

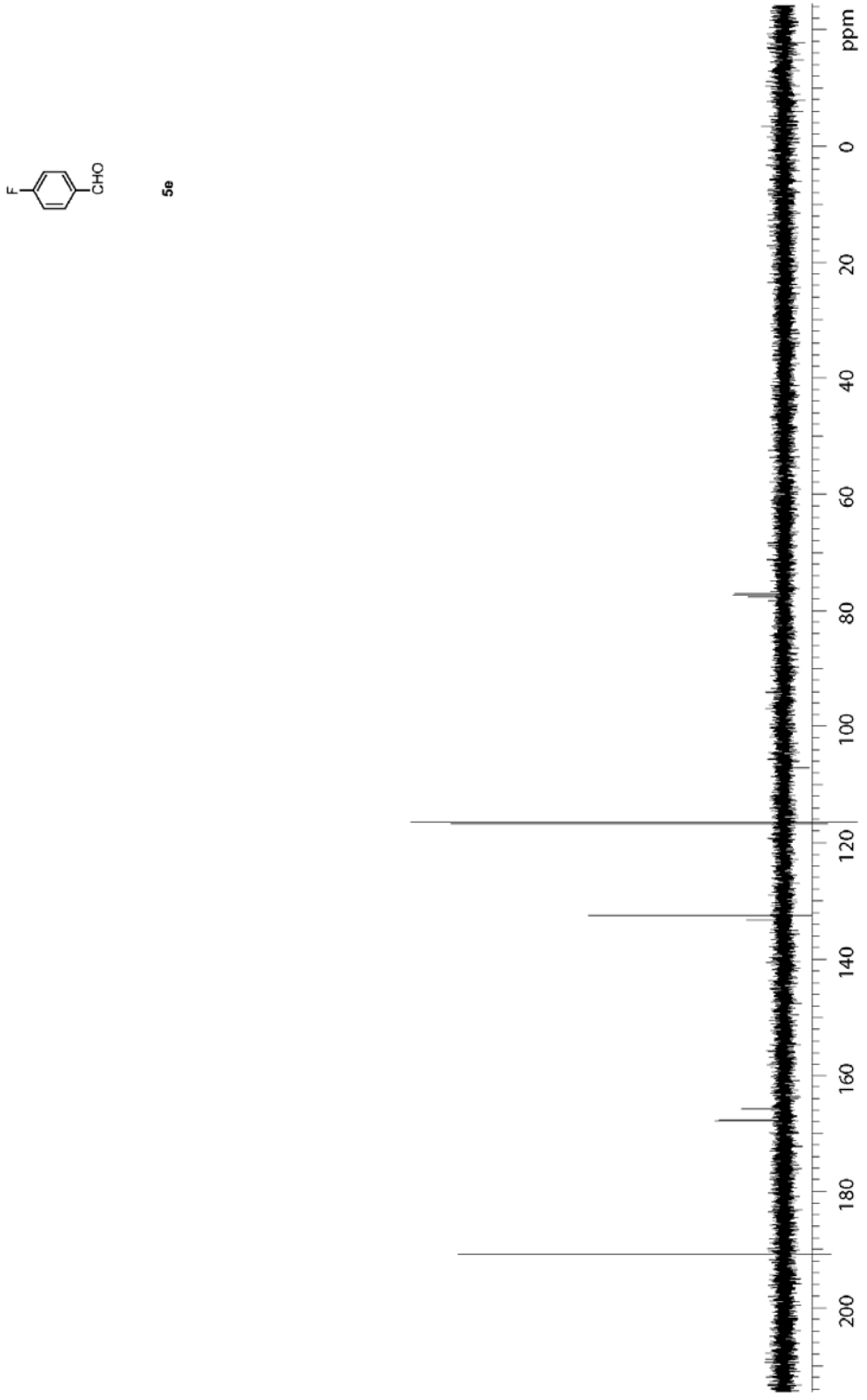
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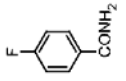

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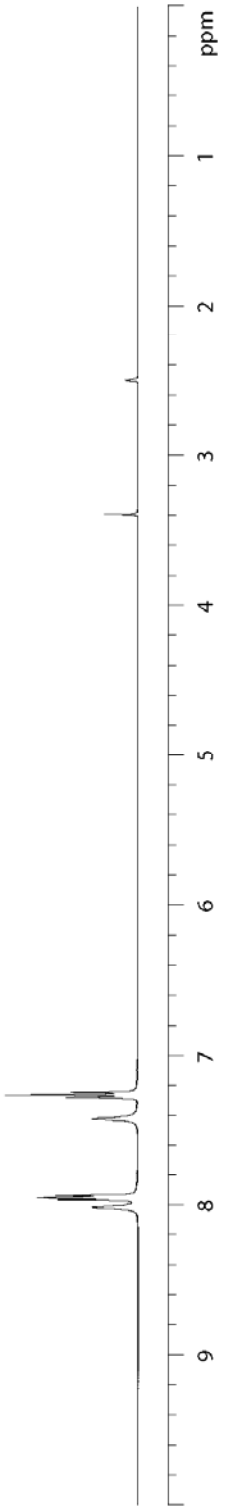

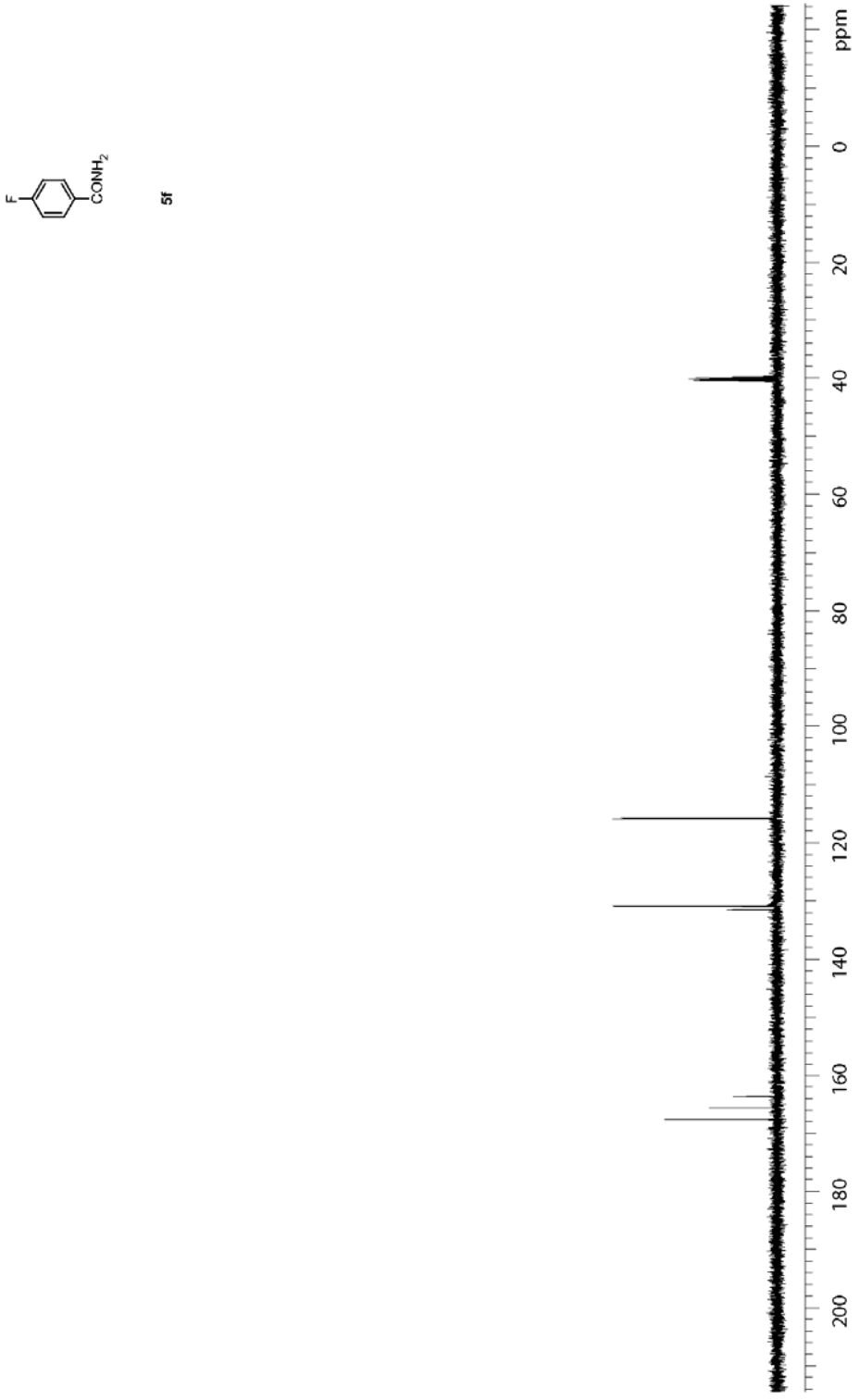
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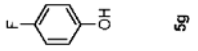

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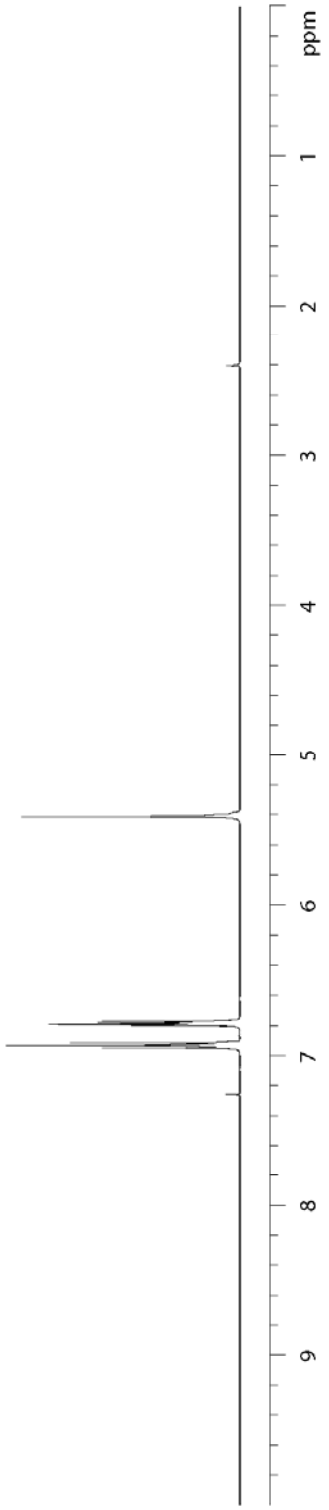

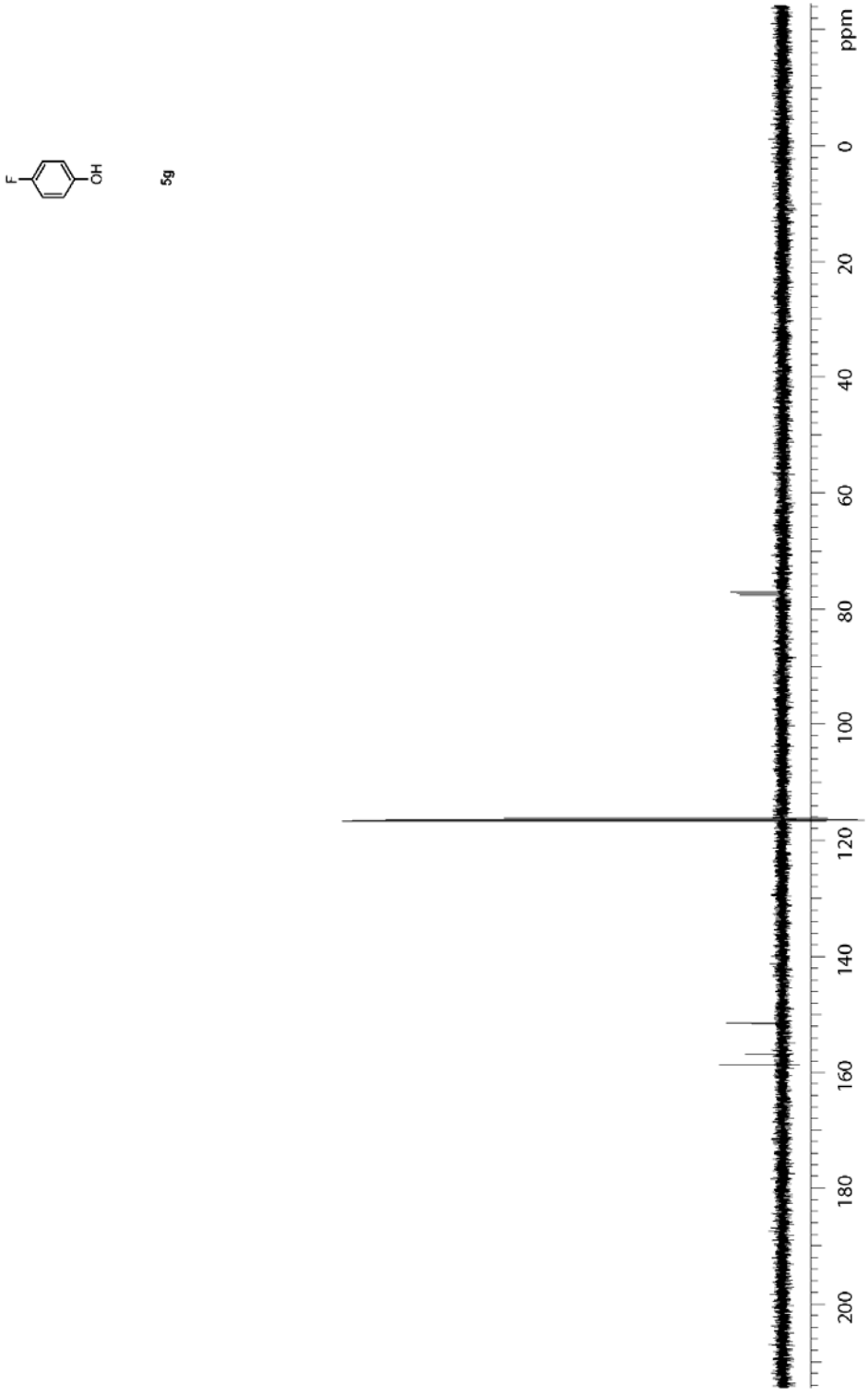
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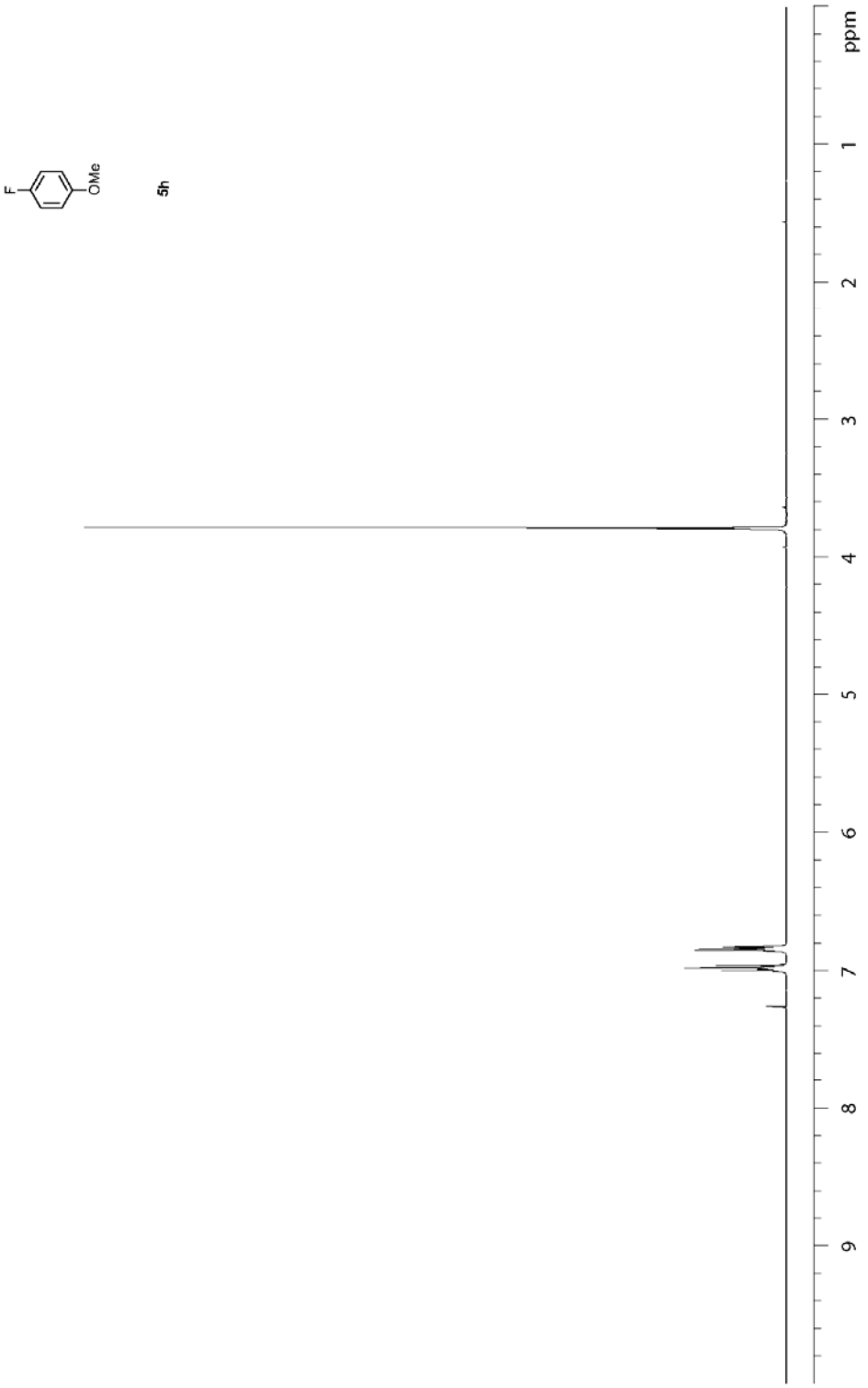
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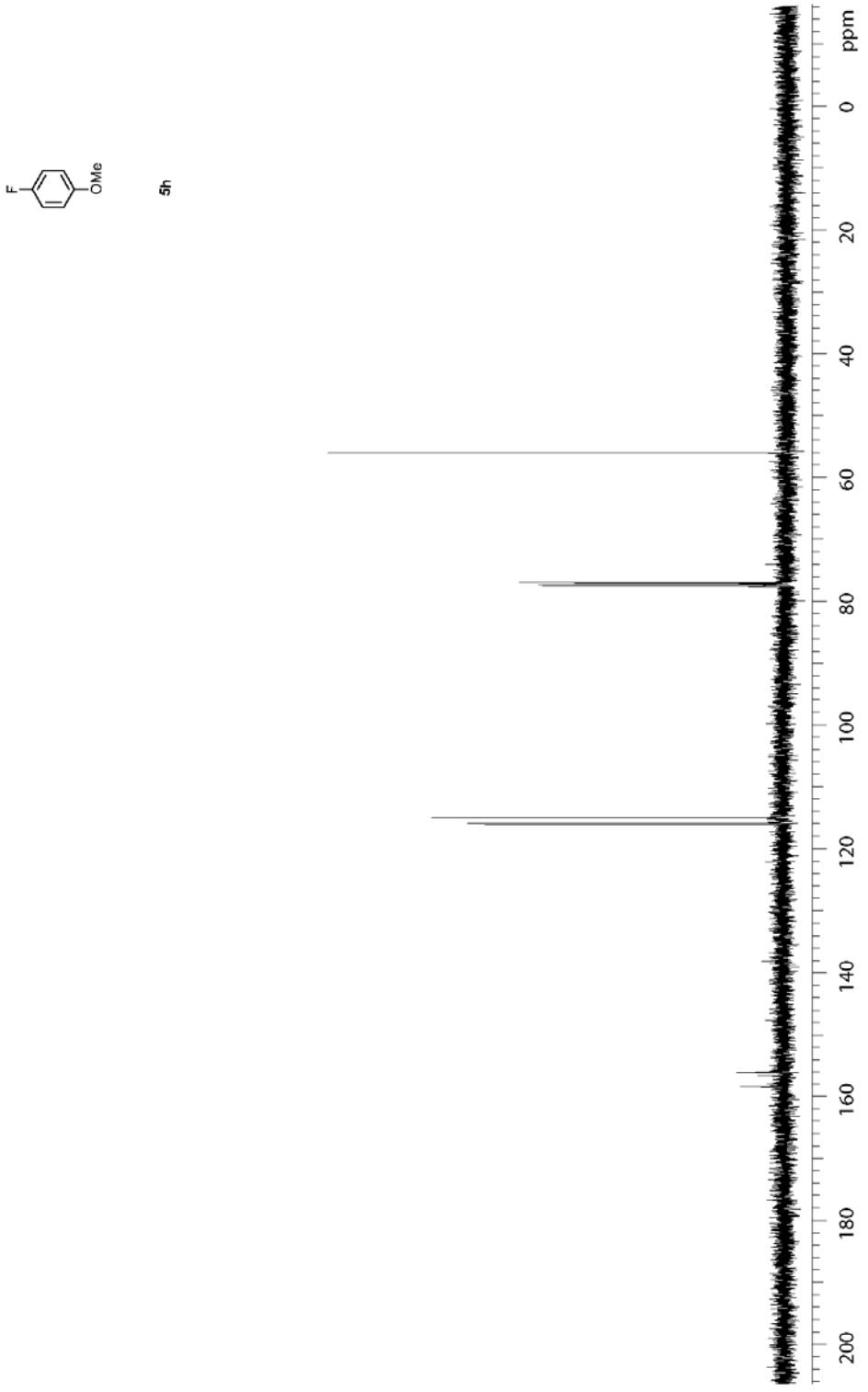
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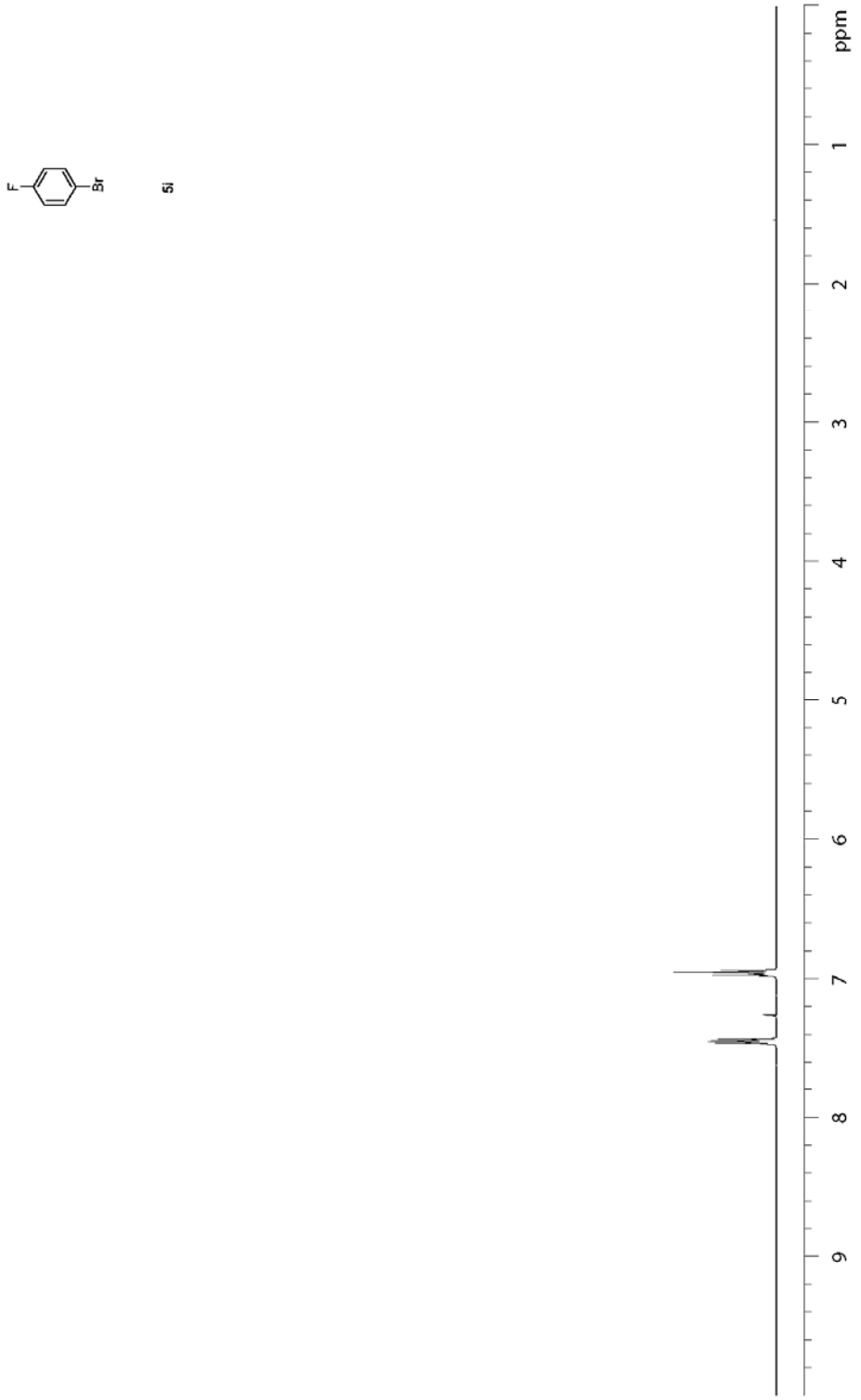
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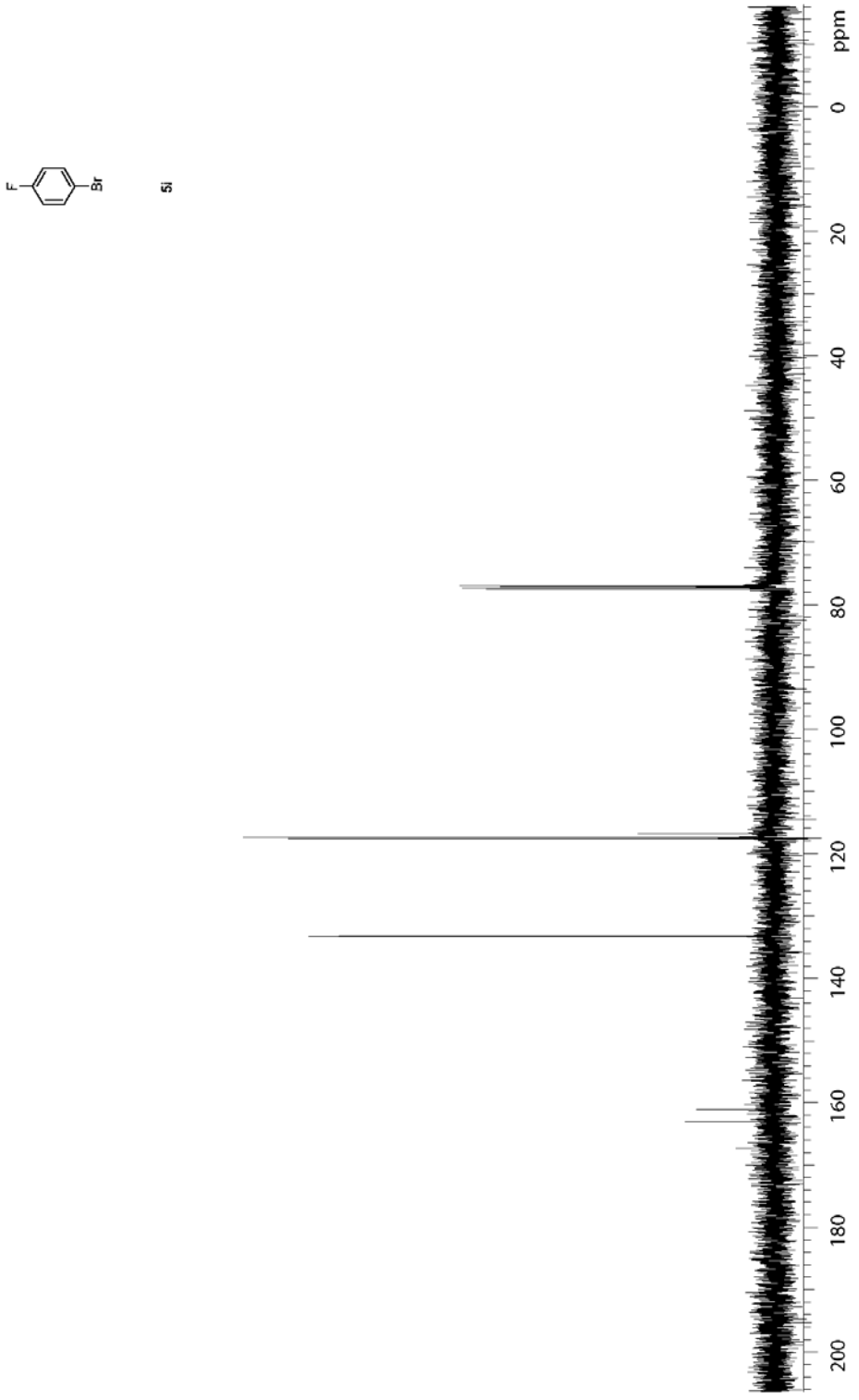
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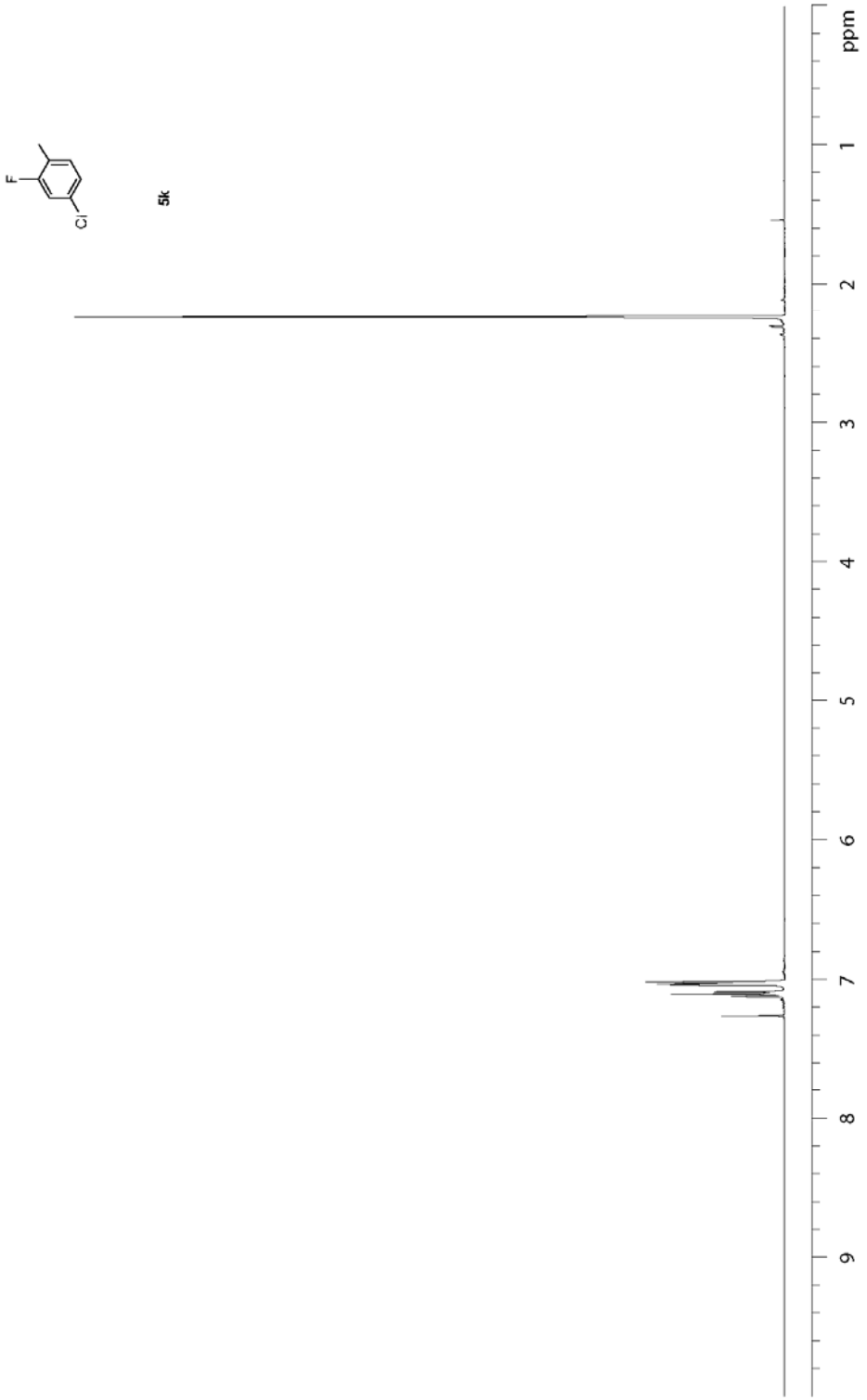
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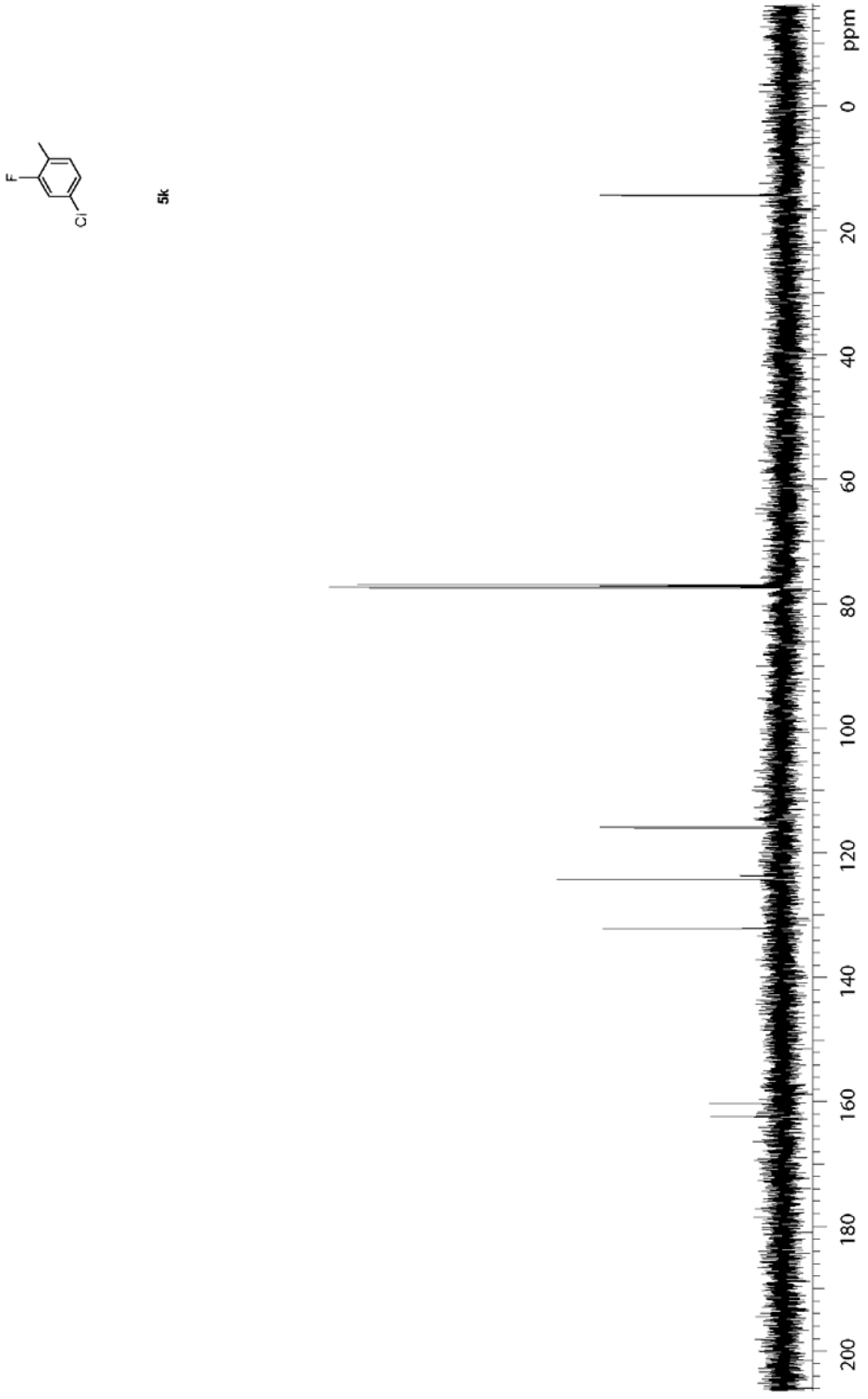
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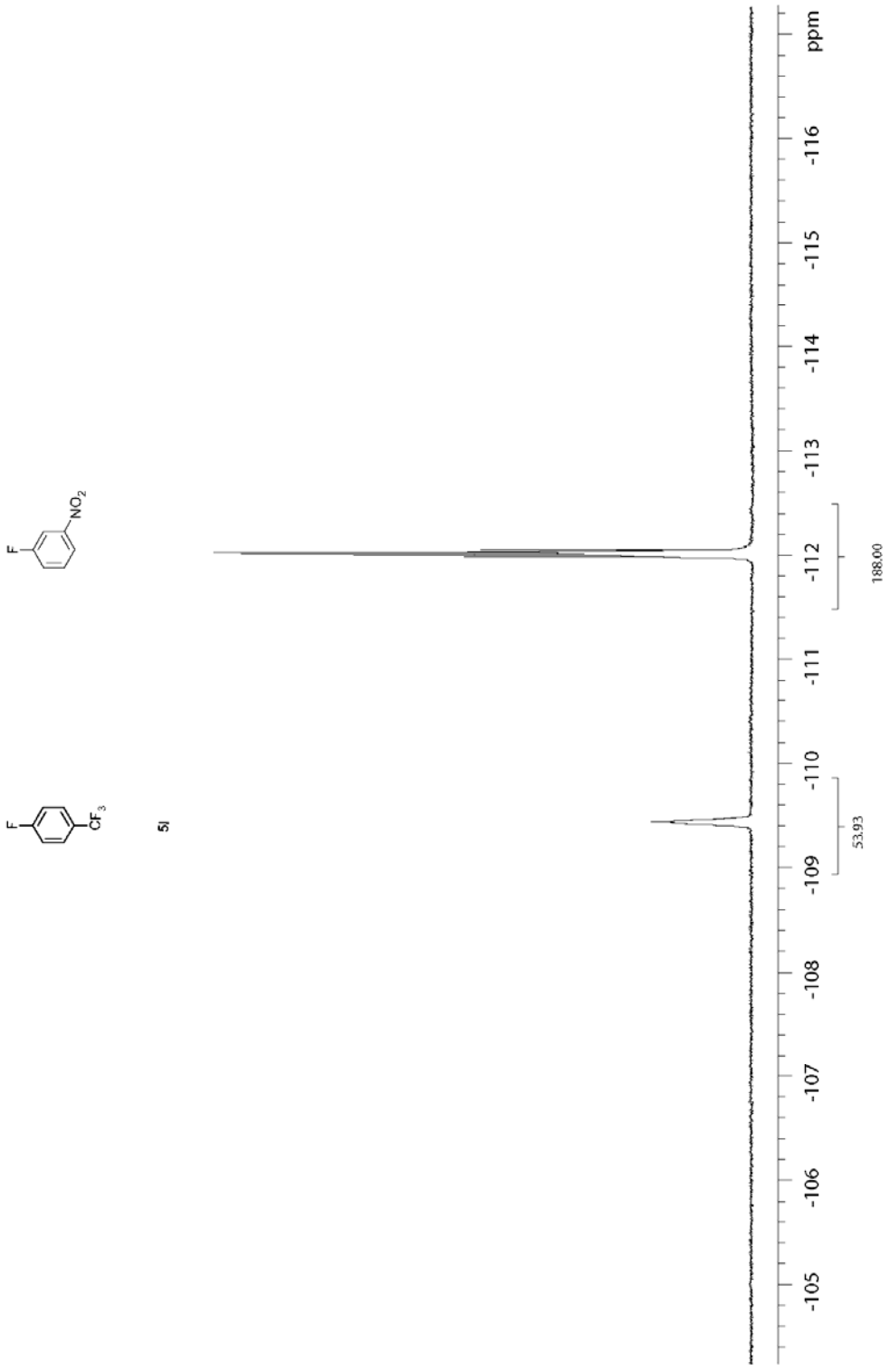
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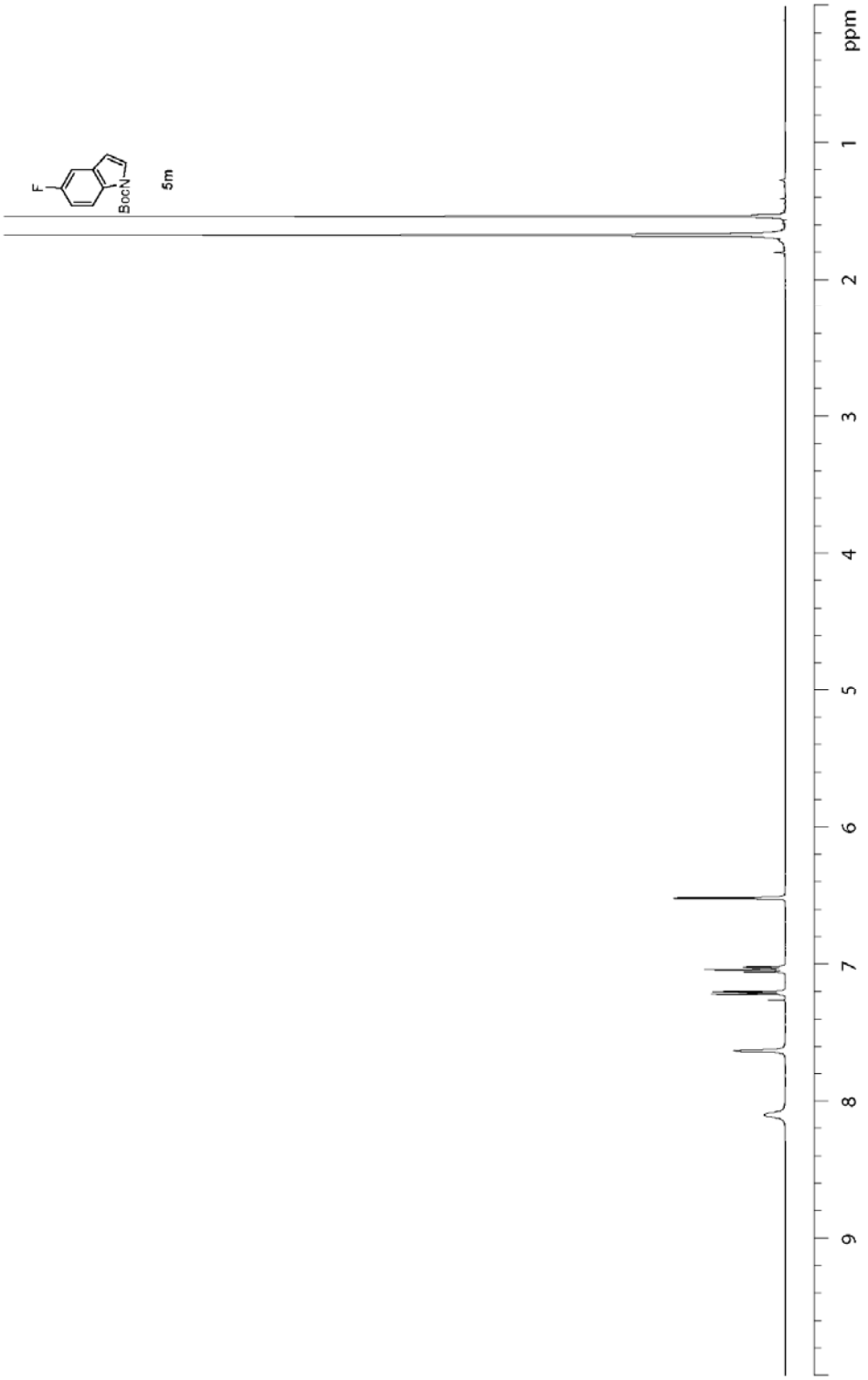
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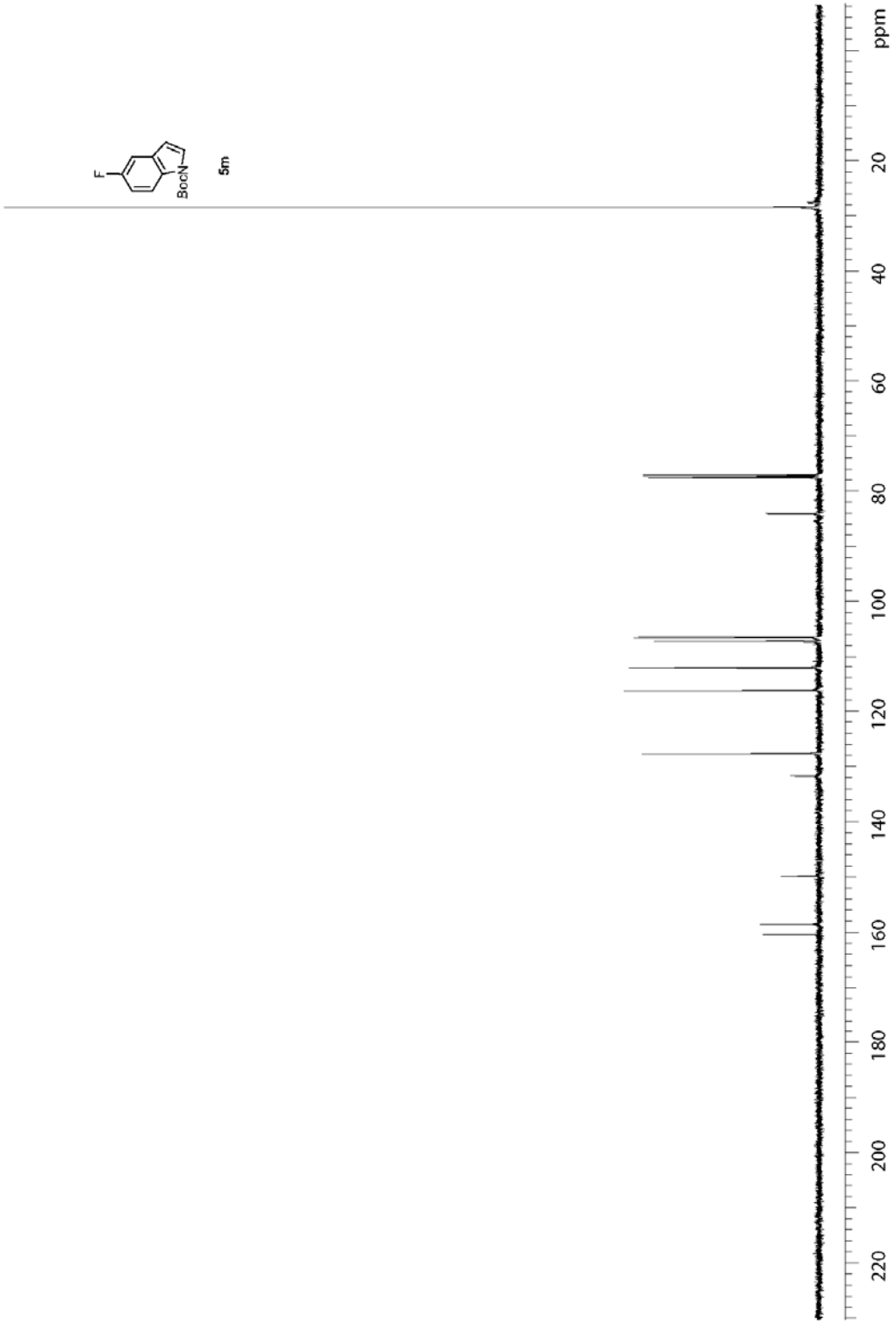
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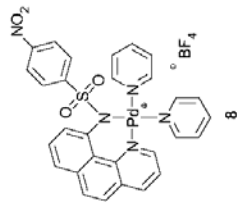
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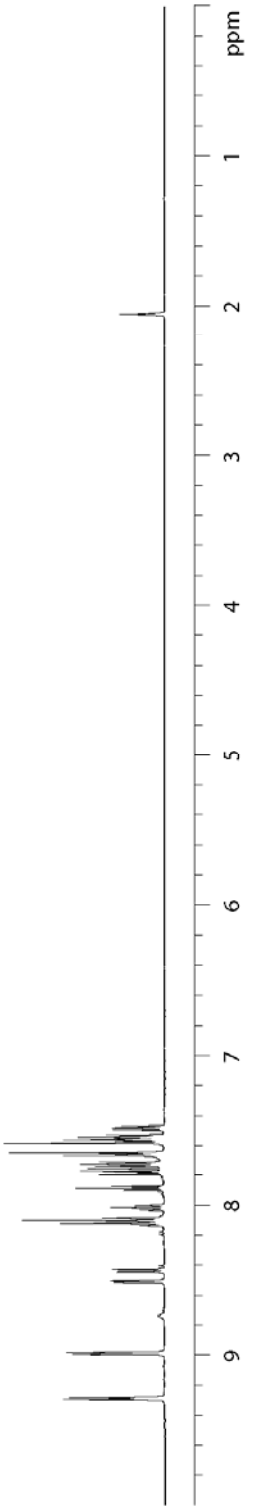
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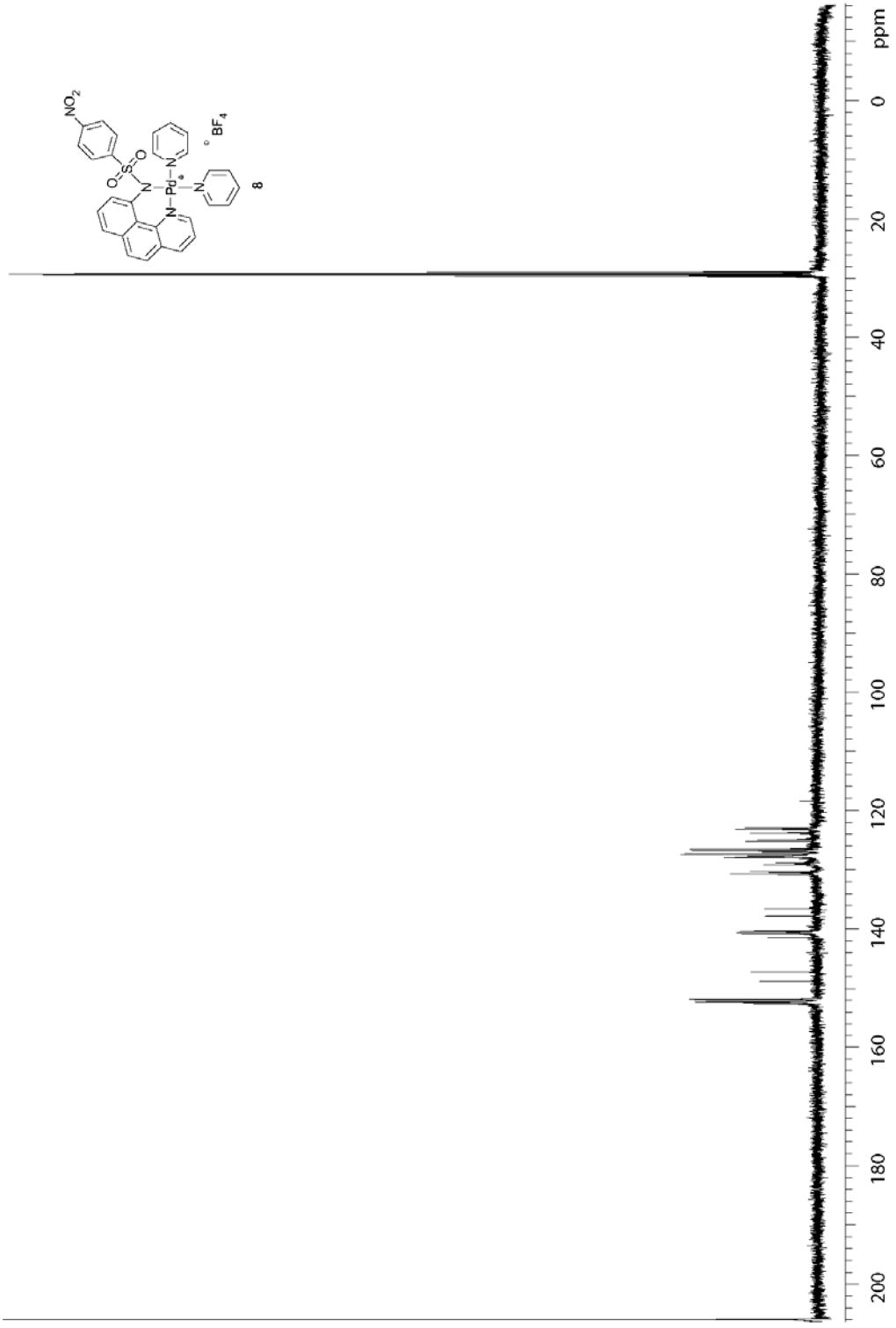
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