Supporting information

Metal-Ligand Cooperation and Synergistic Palladium Catalysis for the Dual Ligand System [2,2′-bipyridin]-6(1*H*)-one/PCy_3: Milder conditions for the Undirected C–H Arylation of Arenes

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Table of contents

1. Experimental details

1.1- General considerations.

^{1}H, $^{13}C\{^{1}H\}$, $^{31}P\{^{1}H\}$ and ^{19}F NMR spectra were recorded on Agilent MR-500, Agilent MR-400 or Bruker AV-400 spectrometers at the Laboratorio de Técnicas Instrumentales (LTI) of the UVa. Chemical shifts (in δ units, ppm) were referenced to $SiMe_4$ (^{1}H and ^{13}C), $CFCl_3$ (^{19}F) and H_3PO_4 (85%, ^{31}P). The spectral data were recorded at 298 K unless otherwise noted. The GC-MS analyses were performed in a Thermo-Scientific Focus DSQ II GC/MS apparatus. HRMS analyses were carried out on a Bruker Maxis Impact mass spectrometer at the Laboratorio de Técnicas Instrumentales (LTI) of the UVa. Elemental analyses were carried out in a Thermo Scientific FLASH 2000 microanalyzer (at the Parque Científico Tecnológico of the UBU, Burgos, Spain).

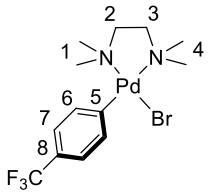
Solvents were distilled from appropriate drying agents under nitrogen and stored over 3 Å or 4 Å molecular sieves (toluene) or used directly from the storage with the drying agent (anisole, ethyl benzoate, α,α,α-trifluorotoluene, fluorobenzene and *N*,*N*-dimethylaniline). DMA, pinacolone, toluene-d_8 and pyridine were purchased as anhydrous and stored under nitrogen over 3 Å or 4 Å molecular sieves. In the case of DMA, used as co-solvent in the catalytic reactions, the drying procedure was the following: it was stored over molecular sieves for a week and then transferred to a flask with freshly activated molecular sieves and kept for another week prior to use.

The haloaryl derivatives, caesium carbonate, palladium acetate, tricyclohexylphosphine, tricyclohexylphosphonium tetrafluoroborate, triphenylphosphine, tri-*tert*-butylphosphine, 2,2'-bipyridine, *N*-acetylglycine, 2-pyridone and X-Phos are commercially available and were purchased from Sigma-Aldrich, Acros Organics, Alfa Aesar, BLD Pharm or Fluorochem. Commercial reagents were used as received unless otherwise noted.

[2,2'-bipyridin]-6(1*H*)-one (bipy-6-OH),[1] [2,2′-bipyridin]-4(1H)-one (bipy-4-OH),[1] [Pd(bipy-6-OH)Br(C_6F_5)] (**4**),[1] (NBu_4)[Pd(bipy-6-O)Br(C_6F_5)] (**6**),[1] [Pd(C_6H_4-*p*-CF_3)I(TMEDA)], [2] [Pd_2dba_3].$CHCl_3$,[3] and [PdBr(C_6F_5)($NCMe)_2$],[4] were prepared according to the procedures in the literature.

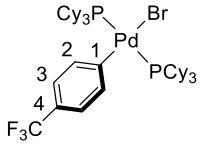
1.2- Synthesis of Palladium complexes.

[PdBr(C_6H_4-*p*-CF_3)(TMEDA)].[2] [Pd(C_6H_4-*p*-CF_3)I(TMEDA)] (120.7 mg, 0.244 mmol) and acetone (2 mL) were introduced in a flask and cooled to -5 °C. In a beaker, KBr (34.8 mg, 0.29 mmol) was dissolved in the minimum amount of distilled water and $AgNO_3$ (49.7 mg, 0.29 mmol) was added to the solution. A yellow solid (AgBr) appeared and the liquid phase was removed. The solid was washed twice with distilled water and added to the solution of the palladium complex. The flask was stirred at -5 °C for 20 h. A white solid appeared and the mixture was filtered. The solvent was evaporated and cold Et_2O was added to the residue with vigorous stirring. A yellow solid precipitated, which was filtered, washed with cold Et_2O and air-dried. Yield: 57 mg, (52 %).



^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.44 (d, J = 7.9 Hz, 2H, H^7), 7.18 (d, J = 7.9 Hz, 2H, H^6), 2.77 (m, 2H, H^2), 2.67 (s, 6H, H^4), 2.61 (m, 2H, H^3), 2.43 (s, 6H, H^1). $^{13}C\{^1H\}$ NMR (125.78 MHz, δ, $CDCl_3$): 154.5 (C^5), 135.3 (C^6), 125.5 (q, J = 32 Hz, C^8), 124.9 (C^{CF3}),* 122.7 (q, J = 3.8 Hz, C^7), 62.7 (C^2), 58.3 (C^3), 50.7 (C^1), 48.7 (C^4). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -61.86 (s, CF_3). *The chemical shift was determined by ^{13}C-^{19}F HSQC. HRMS (ESI-TOF): Calcd. for $C_{13}H_{20}BrF_3N_2NaPd$ $(M+Na)^+$ 468.9689, found 468.9703.

[PdBr(C_6H_4-*p*-CF_3)(PCy_3)$_2$] (1). [PdBr(C_6H_4-*p*-CF_3)(TMEDA)] (76.1 mg, 0.17 mmol) and dry dichloromethane (2 mL) were introduced into a N_2 flushed flask. PCy_3 (95.3 mg, 0.34 mmol) was added and the reaction mixture was stirred at room temperature for 3 h. The solvent was removed and cold Et_2O was added to the residue. A yellow solid appeared. The solid was filtered, washed with cold Et_2O and air-dried. Yield: 115.7 mg (76 %).



^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.55 (d, J = 8.3 Hz, 2H, H^3), 7.16 (d, J = 8.3 Hz, 2H, H^2), 2.10-0.96 (m, 66H, H^{PCy3}). $^{13}C\{^1H\}$ NMR (125.78 MHz, δ, $CDCl_3$): 161.9 (C^1), 138.2 (C^3), 124.9 (C^{CF3})*, 124.5 (C^4), 122.5 (C^2), 34.2 (*pseudo*-t, $^1J_{P-C}$ = 9.6 Hz, CH PCy_3), 30.1 (s, CH_2 PCy_3), 27.6 (*pseudo*-t, $^2J_{P-C}$ = 5.2 Hz, CH_2 PCy_3), 26.5 (s, CH_2 PCy_3).^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.06 (s, CF_3). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, $CDCl_3$): 19.8. *The chemical shift was determined by ^{13}C-^{19}F HSQC. HRMS (ESI-TOF): Calcd. for $C_{43}H_{70}F_3P_2Pd$ $(M\text{-}Br)^+$ 811.395, found 811.3946.

[$PdCl_2(PCy_3)_2$].[5] $PdCl_2$ (400 mg, 2.3 mmol) was introduced into a round bottom flask. Concentrated HCl(aq) (1.25 mL) and water (3 mL) were added and the mixture was stirred at room temperature. In a two necked flask PCy_3 (1.28 g, 4.6 mmol) was introduced under N_2 and dry acetone (25 mL) was added. The palladium solution was added dropwise to the phosphine solution. The mixture was stirred for 4 h at room temperature. A yellow solid appeared in an orange solution. The mixture was filtered, and the solid was washed with acetone and air-dried. Yield: 1.43 g (84 %). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, $CDCl_3$): 24.98. HRMS (ESI-TOF): Calcd. for $C_{36}H_{66}ClP_2Pd$ $(M\text{-}Cl)^+$ 701.3368, found 701.3353.

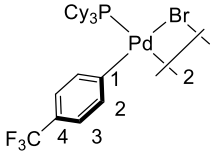
[Pd(C_6H_4-*p*-CF_3)(μ-OH)(PCy_3)]$_2$. Following a similar synthesis described in the literature,[6] [$PdCl_2(PCy_3)_2$] (410 mg, 0.56 mmol), *p*-$CF_3C_6H_4Cl$ (6 mL), KOH (2.1 g, 37 mmol) and water (6 mL) were introduced into a round bottom flask. The mixture was refluxed for 6 h with vigorous stirring. After cooling down the solution, the organic phase was collected and the solvent evaporated. Toluene was added and the mixture was filtered. The resulting solution was evaporated to dryness and upon addition of *n*-hexane to the residue a white solid appeared. The suspension was filtered and the solid was washed with *n*-hexane and air-dried. A mixture of two isomers was obtained (ratio = 1:0.4) (65 %) impurified with the aryl halide (15 %) and its homocoupling product (20 %). The mixture was used without further purification. Yield: 100.1 mg (16 %). The isomers were not fully characterized.

Major isomer: ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -61.89 (s, CF_3). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, $CDCl_3$): 37.13. Minor isomer: ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.04 (s, CF_3). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, $CDCl_3$): 35.65.

[Pd(C$_6$H$_4$-*p*-CF$_3$)(μ-OAc)(PCy$_3$)]$_2$. Following a similar synthesis described in the literature,[7] [Pd(C$_6$H$_4$-*p*-CF$_3$)(μ-OH)(PCy$_3$)]$_2$ (97.5 mg, 0.09 mmol) was dissolved in toluene (5 mL) and acetic acid (20 μL, 0.35 mmol) was added dropwise to the solution. It was stirred at room temperature for 20 min. The solvent was evaporated and *n*-hexane was added to the residue. A white solid appeared, which was filtered, washed with *n*-hexane and air-dried. Yield: 102 mg (96 %). A mixture of two isomers was obtained (ratio = 1:0.3) and they were not fully characterized.

Major isomer: ^{19}F NMR (470.168 MHz, δ, CDCl$_3$): -62.17 (s, CF$_3$). ^{31}P{^{1}H} NMR (202.31 MHz, δ, CDCl$_3$): 43.04. Minor isomer: ^{19}F NMR (470.168 MHz, δ, CDCl$_3$): -61.98 (s, CF$_3$). ^{31}P{^{1}H} NMR (202.31 MHz, δ, CDCl$_3$): 38.63.

[Pd(μ-Br)(C$_6$H$_4$-*p*-CF$_3$)(PCy$_3$)]$_2$ (2). Following a similar synthesis described in the literature,[8] [Pd(C$_6$H$_4$-*p*-CF$_3$)(μ-OAc)(PCy$_3$)]$_2$ (100 mg, 0.08 mmol) was dissolved in CH$_2$Cl$_2$ (1 mL), and NBu$_4$Br (69 mg, 0.21 mmol) was added to the mixture while stirring. Acetone (10 mL) and water (0.2 mL) were added to the solution. A white solid appeared. The mixture was stirred at room temperature for 3 h. The suspension was filtered and the solid was washed with water and acetone and air-dried. Yield: 70 mg (67 %).



^{1}H NMR (500.13 MHz, δ, CDCl$_3$): 7.55 (d, J = 7.6 Hz, 2H, H^2), 7.18 (d, J = 7.6 Hz, 2H, H^3), 2.0-0.93 (m, 33H, H^{PCy3}). ^{13}C{^{1}H} NMR (125.78 MHz, δ, CDCl$_3$): 157.4 (C^1), 136.3 (C^2), 125.2 (C^4),* 124.8 (C^{CF3})*, 122.9 (C^3), 35.1 (d, J$_{P-C}$ = 22 Hz, C^{ipso}, PCy$_3$), 30 (s, C^{meta}, PCy$_3$), 27.4 (d, J$_{P-C}$ = 11 Hz, C^{ortho}, PCy$_3$), 26.3 (s, C^{para}, PCy$_3$). ^{19}F NMR (470.168 MHz, δ, CDCl$_3$): -61.95 (s, CF$_3$). ^{31}P{^{1}H} NMR (202.31 MHz, δ, CDCl$_3$): 37.74. *The chemical shift was determined by ^{13}C-^{19}F HSQC and HMBC. Anal. Calc. for C$_{50}$H$_{74}$Br$_2$F$_6$P$_2$Pd$_2$: C, 49.08 %; H, 6.10 %; found: C, 49.07 %; H, 6.11 %.

1.3- Catalytic Reactions.

General procedure for the direct arylation of arenes.

$Pd(OAc)_2$ (3.8 mg, 0.017 mmol), bipy-6-OH (1.5 mg, 0.0085 mmol) and cesium carbonate (222 mg, 0.68 mmol) were introduced in a Schlenk flask under a nitrogen atmosphere. The corresponding aryl halide (0.34 mmol), PCy_3 (4.7 mg, 0.017 mmol) dissolved in the corresponding arene (1.5 mL) and DMA (1.5 mL) were added to the flask. The mixture was stirred at 100 °C and checked by ^{19}F NMR at the indicated time. When total conversion was observed, the solvent was evaporated in vacuo and the organic product was extracted with a mixture of *n*-hexane (8 mL) and ethyl acetate (2 mL). The extract was filtered through kieselgur and evaporated to dryness. The product was checked by NMR and GC-MS.

The yields and characterization data for the products obtained are collected below. For known compounds the spectral data conforms to those in the literature (references are given). Isomer ratios were determined by ^{19}F NMR of the crude mixture or ^{1}H NMR for samples without fluorine.

Toluene as arene.

ArX = ***p*-$CF_3C_6H_4Br$** (**3aa**). Mixture of three isomers in a ratio o:m:p = 1.5:1.1:1. The product was obtained as a colorless oil. Yield: 0.065 g (80%). ArX = ***p*-$CF_3C_6H_4Cl$**. Ratio of isomers o:m:p = 1.8:1.1:1. Yield: 0.061 g (76%). The characterization of 2-methyl-4'-(trifluoromethyl)-1,1'-biphenyl, 3-methyl-4'-(trifluoromethyl)-1,1'-biphenyl and 4-methyl-4'-(trifluoromethyl)-1,1'-biphenyl has been reported before.[1,9,10]

2-Methyl-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.68-7.66 (m, 2H), 7.44 (d, J = 8 Hz, 2H), 7.30-7.26 (m, 3H), 7.21 (d, J = 8 Hz, 1H), 2.27 (s, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.41 (s, CF_3).

3-Methyl-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.68-7.66 (m, 4H, Ar_{CF3}), 7.4 (m, 2H), 7.37 (t, J = 7.8, 1H), 7.24 (d, J = 7.8 Hz, 1H), 2.46 (s, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.40 (s, CF_3).

4-Methyl-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.68-7.66 (m, 4H, Ar_{CF3}), 7.52 (m, 2H), 7.31 (m, 2H), 2.44 (s, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.37 (s, CF_3).

ArX = ***p*-MeOC$_6$H$_4$Br** (**3ab**). Mixture of three isomers in a ratio o:m:p = 1:2.5:1.7. The product was obtained as a white solid. Yield: 0.049 g (73%). ArX = ***p*-MeOC$_6$H$_4$Cl**. Ratio of isomers o:m:p = 1.2:1.9:1. Yield: 0.048 g (71%). The characterization of 2-methyl-4'-(methoxy)-1,1'-biphenyl, 3-methyl-4'-(methoxy)-1,1'-biphenyl and 4-methyl-4'-(methoxy)-1,1'-biphenyl has been reported before.[1,9,11]

2-Methyl-4'-(methoxy)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.26–7.22 (m, 6H), 6.94 (m, 2H), 3.84 (s, 3H, OMe), 2.27 (s, 3H, CH_3).

3-Methyl-4'-(methoxy)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.51 (m, 2H), 7.36 (s, 1H), 7.35 (m, 1H), 7.30 (t, J = 7 Hz, 1H), 7.12 (d, J = 7.0 Hz, 1H), 6.96 (m, 2H), 3.84 (s, 3H, OMe), 2.41 (s, 3H, CH_3).

4-Methyl-4'-(methoxy)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.51 (m, 2H), 7.44 (m, 2H), 7.22 (m, 2H), 6.97 (m, 2H, Ar_{CF3}), 3.84 (s, 3H, OMe), 2.38 (s, 3H, CH_3).

ArX = ***p*-*t*BuC$_6$H$_4$Br** (**3ac**). Mixture of three isomers in a ratio o:m:p = 1:1.5:1.3. The product was obtained as a white solid. Yield: 0.064 g (84%). The characterization of 2-methyl-4'-(*t*-butyl)-1,1'-biphenyl, 3-methyl-4'-(*t*-butyl)-1,1'-biphenyl and 4-methyl-4'-(*t*-butyl)-1,1'-biphenyl has been reported before.[12]

2-Methyl-4'-(*t*-butyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.53-7.4 (m, 2H), 7.3-7.24 (m, 6H), 2.32 (s, 3H, CH_3), 1.40 (s, 9H, ^{t}Bu).

3-Methyl-4'-(*t*-butyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.55 (m, 2H), 7.48 (m, 2H), 7.42 (m, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.17 (m, 1H), 2.44 (s, 3H, CH_3), 1.39 (s, 9H, ^{t}Bu).

4-Methyl-4'-(*t*-butyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.53-7.4 (m, 6H), 7.3-7.24 (m, 2H), 2.42 (s, 3H, CH_3), 1.39 (s, 9H, ^{t}Bu).

ArX = ***p*-FC$_6$H$_4$Br** (**3ad**). Mixture of three isomers in a ratio o:m:p = 1:2.9:2.2. The product was obtained as a yellow oil. Yield: 0.047 g (74%). ArX = ***p*-FC$_6$H$_4$Cl**. Ratio of isomers o:m:p = 1:2:1.6. Yield: 0.045 g (71%). The characterization of 2-methyl-4'-(fluoro)-1,1'-biphenyl, 3-methyl-4'-(fluoro)-1,1'-biphenyl, 4-methyl-4'-(fluoro)-1,1'-biphenyl has been reported before.[13]

2-Methyl-4'-(fluoro)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.29-7.20 (m, 6H), 7.14-7.10 (m, 2H), 2.27 (s, 3H, CH_3).^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -116.18 (m).

3-Methyl-4'-(fluoro)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.56-7.52 (m, 2H), 7.42-7.33 (m, 3H), 7.14-7.24 (m, 3H), 2.44 (s, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -116.04 (m).

4-Methyl-4'-(fluoro)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.56-7.52 (m, 2H), 7.45 (m, 2H), 7.29-7.24 (m, 2H), 7.15-7.10 (m, 2H), 2.41 (s, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -116.35 (m).

ArX = ***p*-CHOC$_6$H$_4$Br** (**3ae**). Mixture of three isomers in a ratio o:m:p = 1.6:1:1. The product was obtained as a yellow oil. Yield: 0.046 g (69%). The characterization of 2'-methyl-[1,1'-biphenyl]-2-carbaldehyde, 3'-methyl-[1,1'-biphenyl]-2-carbaldehyde and 4'-methyl-[1,1'-biphenyl]-2-carbaldehyde has been reported before.[14]

2'-Methyl-[1,1'-biphenyl]-2-carbaldehyde. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 10.09 (s, 1H, CHO), 7.95 (d, J = 8 Hz, 2H), 7.5 (d, J = 8 Hz, 2H), 7.33-7.2 (4H), 2.29 (s, 3H, CH_3).

3'-Methyl-[1,1'-biphenyl]-2-carbaldehyde. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 10.06 (s, 1 H, CHO), 7.95 (d, 2H), 7.75 (d, J = 8 Hz, 2H), 7.38 (t, J = 8.0 Hz, 1H), 7.31 (s, 1H), 7.3-7.2 (m, 2H), 2.43 (s, 3 H, CH_3).

4'-Methyl-[1,1'-biphenyl]-2-carbaldehyde. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 10.07 (s, 1H, CHO), 7.96 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8 Hz, 2H), 7.56 (m, 2H), 7.45 (m, 2H), 2.46 (s, 3H, CH_3).

Benzene as arene. ArX = ***p*-CF$_3$C$_6$H$_4$Br** (**3ba**). The product was obtained as a white solid. Yield: 0.067 g (89 %). The characterization of 4-(trifluoromethyl)biphenyl has been reported before.[15]

^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.68 (s, 4 H, Ar_{CF3}), 7.61 (m, 2H,), 7.50 (m, 2H), 7.42 (m, 1H). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.42 (CF_3).

Ethyl benzoate as arene. ArX = ***p*-CF$_3$C$_6$H$_4$Br** (**3ca**). The product was obtained as a yellow oil, mixture of three isomers in a ratio o:m:p = 1:10:3. Yield: 0.061 g (61%). The characterization of ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate, ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-3-carboxylate and ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate has been reported before.[1,9,16]

Ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.9 (dd, J = 8.2, 1.7 Hz, 1H), 7.65 (m, 2H, Ar_{CF3}), 7.56 (td, J = 7.5 Hz, 1.7 Hz, 1H), 7.47 (td, J = 8 Hz, 1.7 Hz, 1H), 7.42 (m, 2H, Ar_{CF3}), 7.33 (dd, J = 8, 1.7 Hz, 1H), 4.11 (q, J = 7.2 Hz, 2H, CH_2), 1.02 (t, J = 7.2 Hz, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.41 (s, CF_3).

Ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-3-carboxylate. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 8.28 (t, J = 1.8 Hz, 1H), 8.08 (ddd, J = 7.5, 1.8, 1.8 Hz, 1H), 7.78 (ddd, J = 7.5, 1.8, 1.0 Hz, 1H), 7.73 (s, 4H, Ar_{CF3}), 7.55 (t, J = 7.5 Hz, 1H), 4.43 (q, J = 7 Hz, 2H, CH_2), 1.43 (t, J = 7 Hz, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.50 (s, CF_3).

Ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 8.14 (m, 2H), 7.72 (s, 4H, Ar_{CF3}), 7.66 (m, 2H), 4.42 (q, J = 7 Hz, 2H, CH_2), 1.43 (t, J = 7 Hz, 3H, CH_3). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.55 (s, CF_3).

Fluorobenzene as arene. ArX = ***p*-$CF_3C_6H_4Br$** (**3da**). The product was obtained as a colourless oil, mixture of three isomers in a ratio o:m:p = 14:1:1. Yield: 0.061 g (75%). The characterization of 2-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl, 3-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl and 4-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl has been reported before.[1,9,10]

2-Fluoro-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.70 (m, 2H, Ar_{CF3}), 7.67 (m, 2H, Ar_{CF3}), 7.44 (td, J = 7.7, 1.9 Hz, 1H), 7.38 (m, 1H), 7.25 (td, J = 7.7, 1.2 Hz, 1H), 7.19 (m, 1H). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.60 (s, 3F, CF_3), -117.87 (m, 1F, F).

3-Fluoro-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.73-7-63 (4H, Ar_{CF3}), 7.44 (m, 1H), 7.38 (m, 1H), 7.30 (m, 1H), 7.1 (m, 1H). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.53 (s, 3F, CF_3), -112.5 (m, 1F, F).

4-Fluoro-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.73-7-63 (4H, Ar_{CF3}), 7.56 (m, 2H), 7.17 (m, 2H). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.46 (s, 3F, CF_3), -114.18 (m, 1F, F).

Trifluoromethylbenzene as arene. ArX = ***p*-MeC_6H_4Br** (**3ef**). Mixture of two isomers in a ratio o:m:p = 0:5:1. The product was obtained as a white solid. Yield: 0.060 g (75%). The characterization of 4-methyl-3'-(trifluoromethyl)biphenyl and 4-methyl-4'-(trifluoromethyl)biphenyl has been reported before.[17]

4-Methyl-3'-(trifluoromethyl)biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.81 (s, 1H), 7.75 (m, 1H), 7.60-7.49 (m, 4H), 7.29 (m, 2H), 2.42 (s, 3H). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.64 (s, CF_3).

4-Methyl-4'-(trifluoromethyl)biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.69 (s, 4H), 7.51 (m, 2H), 7.29 (m, 2H), 2.42 (s, 3H).^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.40 (s, CF_3).

Anisole as arene. ArX = ***p*-$CF_3C_6H_4Br$** (**3ga**). Mixture of three isomers in a ratio o:m:p = 6:1:2. The product was obtained as a yellow oil. Yield: 0.070 g (81%). The characterization of 2-methyl-4'-(trifluoromethyl)-1,1'-biphenyl, 3-methyl-4'-(trifluoromethyl)-1,1'-biphenyl and 4-methyl-4'-(trifluoromethyl)-1,1'-biphenyl has been reported before.[1,9]

2-methyl-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.65 (m, 4H, Ar_{CF3}), 7.37 (m, 1H), 7.32 (dd, J = 7.5, 1.9 Hz, 1H), 7.06 (td, J = 7.5, 1.9, 1H), 7.01 (m, 1H), 3.83 (s, 3H, OMe). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.42 (s, CF3).

3-methyl-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.69 (s, 4H, Ar_{CF3}), 7.39 (m, 1H,), 7.18 (m, 1H), 7.13 (dd, J = 2.6, 1.6 Hz, 1H), 6.95 (m, 1H), 3.88 (s, 3H, OMe). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.43 (s, CF_3).

4-methyl-4'-(trifluoromethyl)-1,1'-biphenyl. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.65 (m, 4H, Ar_{CF3}), 7.55 (m, 2H), 7.00 (m, 2H), 3.87 (s, 3H, OMe). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.34 (s, CF_3).

***N, N*-dimethylaniline** as arene. ArX = ***p*-$CF_3C_6H_4Br$** (**3ha**). The product was obtained as a yellow oil, mixture of two isomers in a ratio o:m:p = 0:1.4:1. Yield: 0.053 g (59%). The characterization of *N, N*-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-3-amine and *N, N*-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-4-amine has been reported before.[18]

N, N-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-3-amine. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.68 (m, 4H, Ar_{CF3}), 7.33 (t, J = 7.9 Hz, 1H), 6.97-6.89 (br, 2H), 6.80 (br, 1H), 3.02 (s, 6H, Me). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.36 (s, CF_3)

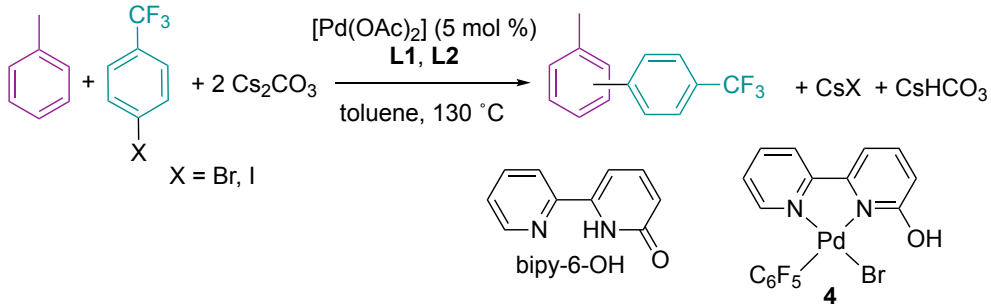
N, N-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-4-amine. ^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 7.63 (m, 4H, Ar_{CF3}), 7.52 (m, 2H), 6.8 (br, 2H), 3.02 (s, 6H, Me). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.22 (s, CF_3).

Pyridine as arene. ArX = ***p*-$CF_3C_6H_4Br$**. The product was obtained as a yellow oil and only the *metha* isomer. Yield: 0.047 g (63%). The characterization of 3-(3-(trifluoromethyl)phenyl)pyridine has been reported before.[1]

^{1}H NMR (500.13 MHz, δ, $CDCl_3$): 8.86 (d, J = 2 Hz, 1H), 8.66 (dd, J = 5.0, 1.6 Hz, 1H), 7.9 (dt, J = 8, 1.6 Hz, 1H), 7.74, 7.69 (AB system, 4H, Ar_{CF3}), 7.42 (dd, J = 8, 5 Hz, 1H). ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -62.61 (s, CF_3).

Additional experiments

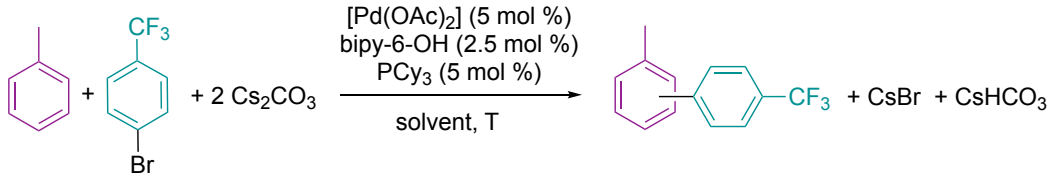
Table S1. Arylation of toluene with *p*-$CF_3C_6H_4X$ using different catalysts.[a]



Entry	[Pd] (mol %)	X	L1 (mol %)	L2 (mol %)	Crude yield, %, (Conv, %), 6 h[b]	Crude yield, %, (Conv, %), 24 h[b]
1[c]	$Pd(OAc)_2$ (5)	I	bipy-6-OH (5)	-	20 (22)	91 (100)
2	$Pd(OAc)_2$ (5)	I	bipy-6-OH (2.5)	PCy_3 (5)	90 (100)	
3	$Pd(OAc)_2$ (5)	Br	bipy-6-OH (5)	-	16 (16)	75 (75)
4	$Pd(OAc)_2$ (5)	Br	bipy-6-OH (2.5)	PCy_3 (5)	59 (65)	90 (100)
5	$Pd(OAc)_2$ (5)	Br	bipy-6-OH (2.5)	PPh_3 (5)	5 (10)	35 (63)
6	$Pd(OAc)_2$ (5)	Br	bipy-6-OH (2.5)	P^tBu_3 (5)	14 (17)	31 (38)
7	$Pd(OAc)_2$ (5)	Br	-	PCy_3 (10)	3 (6)	3 (7)
8	$[Pd_2dba_3]$ (5)	Br	bipy-6-OH (2.5)	PCy_3 (5)	34 (88)	52 (100)
9	$[PdCl_2(NCMe)_2]$ (5)	Br	bipy-6-OH (2.5)	PCy_3 (5)	13 (19)	36 (48)
10	$Pd(OAc)_2$ (2.5) **4** (2.5)	Br	-	PCy_3 (5)	71 (87)	86 (100)
11	$Pd(OAc)_2$ (5)	Br	bipy-6-OH (2.5)	PCy_3 (7.5)	59 (72)	83 (100)
12	$Pd(OAc)_2$ (5)	Br	bipy-6-OH (2.5)	PCy_3 (2.5)	19 (22)	57 (68)
13[d]	$Pd(OAc)_2$ (5)	Br	bipy-6-OH (2.5)	PCy_3 (5)	25 (28)	48 (55)

[a]Reaction conditions: *p*-$CF_3C_6H_4Br$ (0.34 mmol), Cs_2CO_3 (0.68 mmol), toluene (3 mL). [b]Crude yields determined by ^{19}F NMR of the reaction mixture. The reduction or the arylbromide (ArH) and the homocoupling (Ar-Ar) are the observed byproducts. [c]Data from the literature. [d] At 100 ºC.

Table S2. Co-solvent and temperature screening in the direct arylation of toluene.[a]



Entry	Co-solvent[b]	Toluene:ArBr mol ratio	T (°C)	Crude yield, %, (Conv, %), 6 h[c]	Crude yield, %, (Conv, %), 24 h[c]
1	DMA	41:1	130	88 (100)[d]	
2	DMA	41:1	100	90 (94)[e]	
3	DMA	41:1	90	42 (44)	96 (100)
4	DMA	41:1	80	15 (15)	33 (35)
5	DMA	10:1	100	0 (0)	29 (40)
6	Pinacolone	41:1	100	7 (56)	19 (88)
7	Pinacolone	10:1	100	13 (62)	23 (94)

[a] Reaction conditions: *p*-$CF_3C_6H_4Br$ (0.34 mmol), $Pd(OAc)_2$ (5 mol %), bipy-6-OH (2.5 mol %), PCy_3 (5 mol %), Cs_2CO_3 (0.68 mmol). [b] Toluene (1.5 mL), co-colvent (1.5 mL): entries 1-4 and 6. Co-solvent (3 mL): entries 5 and 7. [c] Crude yields determined by ^{19}F NMR of the reaction mixture. The reduction or the arylbromide (ArH) and the homocoupling (Ar-Ar) are the observed byproducts. [d]After 90 min. [e]After 3 h.

Table S3. Catalyst screening at 100 ºC and using DMA as co-solvent.[a]

Entry	[Pd] (mol %)	L1 (mol %)	L2 (mol %)	Crude yield, %, (Conv, %), 6h[b]	Crude yield, %, (Conv, %), 24h[b]
1	$Pd(OAc)_2$ (5)	Bipy-6-OH (2.5)	PCy_3 (5)	90 (94)[c]	
2	$Pd(OAc)_2$ (5)	Bipy-6-OH (5)	-	0 (100)	
3	$Pd(OAc)_2$ (5)	-	PCy_3 (10)	0 (100)	
4	$Pd(OAc)_2$ (5)	Bipy (2.5)	PCy_3 (5)	0 (22)	0 (100)
5	$Pd(OAc)_2$ (5)	Bipy-4-OH (2.5)	PCy_3 (5)	0 (0)	0 (100)
6	$Pd(OAc)_2$ (5)	BipyCH_2-6-OH (2.5)	PCy_3 (5)	3 (10)	8 (16)
7	$Pd(OAc)_2$ (5)	*N*-Ac-Gly (2.5)	PCy_3 (5)	0 (5)	0 (10)
8	$Pd(OAc)_2$ (5)	2-PyOH (2.5)	PCy_3 (5)	3 (12)	5 (21)
9	$Pd(OAc)_2$ (5)	Bipy-6-OH (2.5)	PPh_3 (5)	38 (45)	41 (49)
10	$Pd(OAc)_2$ (5)	Bipy-6-OH (2.5)	P^tBu_3 (5)	4 (9)	14 (19)
11	$Pd(OAc)_2$ (5)	Bipy-6-OH (2.5)	XPhos (5)	80 (85)	88 (92)
12	$Pd(OAc)_2$ (5)	Bipy-6-OH (2.5)	$(HPCy_3)BF_4$ (5)	93 (97)[c]	
13	$Pd(OAc)_2$ (5)	Bipy-6-OH (5)	PCy_3 (5)	78 (84)[c]	
14	$Pd(OAc)_2$ (5)	Bipy-6-OH (5)	PCy_3 (10)	31 (40)	85 (91)
15	$Pd(OAc)_2$ (5)	Bipy-6-OH (2.5)	PCy_3 (7.5)	46 (54)	78 (89)
16	$Pd(OAc)_2$ (5)	Bipy-6-OH (2.5)	PCy_3 (2.5)	35 (38)	79 (87)
17	$Pd(OAc)_2$ (2.5) $[Pd(PCy_3)_2]$ (2.5)	Bipy-6-OH (2.5)	-	92 (95)	
18	$Pd(OAc)_2$ (2.5) **1** (2.5)	Bipy-6-OH (2.5)	-	72 (75)	
19	$Pd(OAc)_2$ (2.5) **2** (1.25)	Bipy-6-OH (2.5)	-	27 (35)	87 (98)
20	$Pd(OAc)_2$ (2.5) **2** (1.25)/ $(HPCy_3)BF_4$ (1.25)	Bipy-6-OH (2.5)	-	98 (98)	

[a]Reaction conditions: *p*-$CF_3C_6H_4Br$ (0.34 mmol), Cs_2CO_3 (0.68 mmol), toluene (1.5 mL), DMA (1.5 mL). [b]Crude yields determined by ^{19}F NMR of the reaction mixture. The reduction or the arylbromide (ArH) and the homocoupling (Ar-Ar) are the observed byproducts. [c]After 3h.

1.4- Mechanistic experiments.

1.4.1. Active catalyst formation

PCy_3 (5.6 mg, 0.02 mmol) was mixed with 0.6 mL of toluene-d_8 and introduced into an NMR tube. Then, $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) was added to the solution. The species formed at room temperature were examined by $^{31}P\{^1H\}$ NMR (Figure S1).

The spectroscopic data of the identified species are given below.

$[Pd(PCy_3)_2(OAc)_2]$: $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, toluene-d_8): 20.81.

$[Pd(PCy_3)_2]$: $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, toluene-d_8): 44.7.

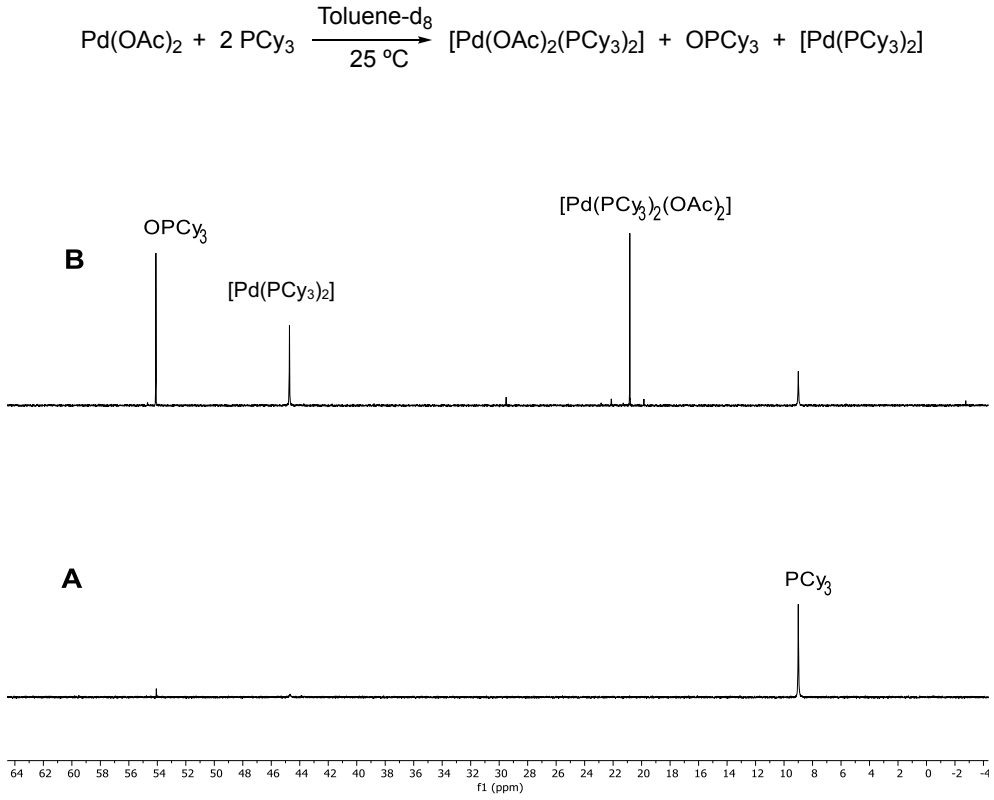


Figure S1. $^{31}P\{^1H\}$ NMR spectra (202.31 MHz). A) PCy_3 in toluene-d_8. B) Sample A after adding $Pd(OAc)_2$.

1.4.2. Thermal stability of complex 1

Complex **1** (8.9 mg, 0.01 mmol) was dissolved in 0.3 mL of dry toluene and 0.3 mL of dry DMA into an NMR tube along with a sealed glass capillary filled with DMSO-d_6 as NMR lock

signal. The mixture was heated for 1 h at 100 ºC. The species formed in solution were examined by ^{19}F (Figure S2).

1: ^{19}F NMR (470.168 MHz, δ, toluene/DMA (1:1)/DMSO-d_6 capillary): -61.0 (CF_3). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, toluene/DMA (1:1)/DMSO-d_6 capillary): 20.8.

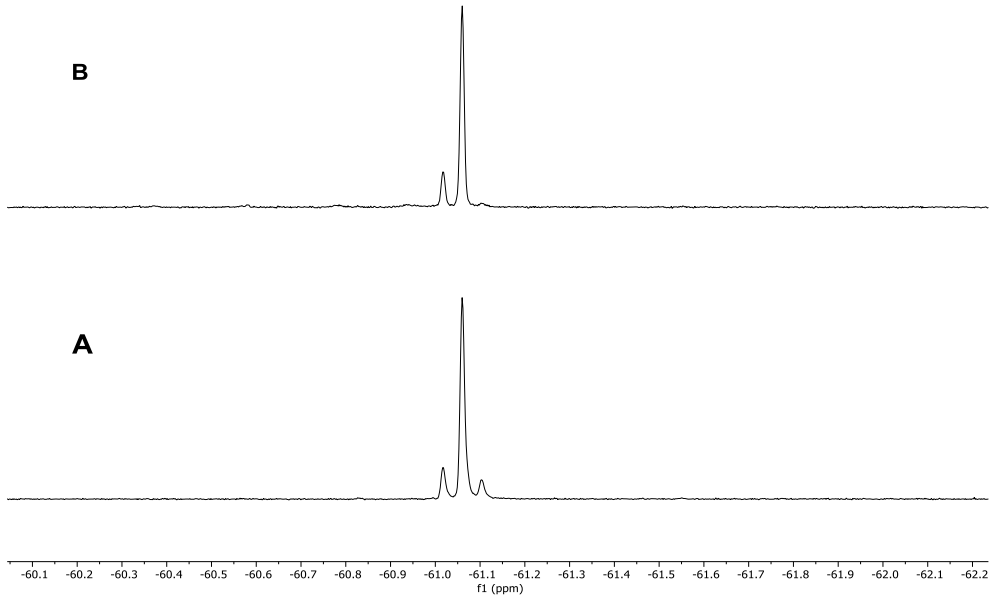


Figure S2. ^{19}F NMR spectra (470.168 MHz). A) Complex **1** in toluene:DMA (1:1). B) Sample A after heating 1h at 100°C.

1.4.3. Ligand exchange experiments

Complex **4** (6.2 mg, 0.013 mmol) was dissolved in dry $CDCl_3$ (0.6 mL) in an NMR tube. One equivalent of PCy_3 (3.1 mg, 0.013 mmol) was added to the mixture. The species formed in solution at room temperature were examined by NMR. Then, a second equivalent of PCy_3 was added (3.1 mg, 0.013 mmol). The species formed in solution at room temperature were examined again by NMR (Figures S3 and S4).

4: ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -119.2 (m, 2F, F_{ortho}), -158.8 (t, J = 20.1 Hz, 1F, F_{para}), -161.9 (m, 2F, F_{meta}).

5: ^{19}F NMR (470.168 MHz, δ, $CDCl_3$): -108.2 (m, 2F, F_{ortho}), -161.4 (t, J = 22.0 Hz, 1F, F_{para}), -163.0 (m, 2F, F_{meta}). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, $CDCl_3$): 28.1.

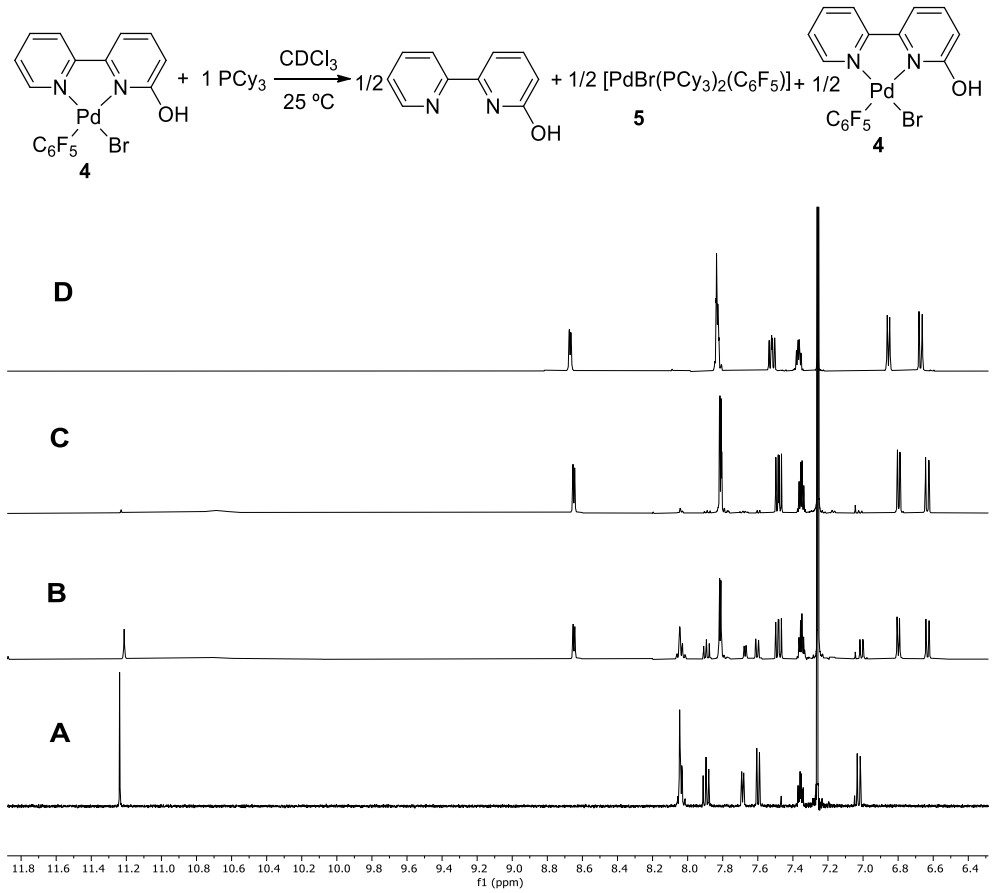


Figure S3. ^{1}H NMR spectra (500.13 MHz). A) Complex **4** in $CDCl_3$. B) Sample A after adding 1 equivalent of PCy_3. C) Sample B after adding 1 more equivalent of PCy_3. D) Free bipy-6-OH in $CDCl_3$.

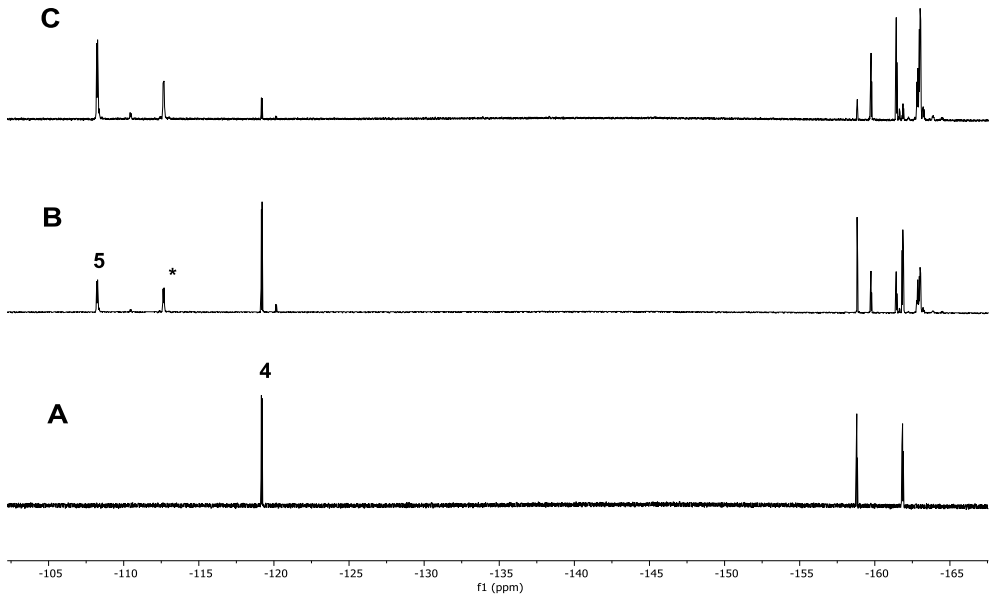


Figure S4. ^{19}F NMR spectra (470.168 MHz). A) Complex **4** in $CDCl_3$. B) Sample A after adding 1 equivalent of PCy_3. C) Sample B after adding 1 more equivalent of PCy_3. Only the F_{ortho} region is labeled for simplicity. * Unidentified species.

The identity of **5** was confirmed by addition of a two fold molar amount of PCy_3 to $[PdBr(C_6F_5)(NCMe)_2]$.

Complex **4** (6.2 mg, 0.013 mmol) was dissolved in 0.3 mL of dry DMA and 0.3 mL of dry toluene and the solution was placed in an NMR tube along with a sealed glass capillary filled with DMSO-d_6 as NMR lock signal. PCy_3 (7.2 mg, 0.026 mmol) was added to the solution. The species formed in solution at room temperature were examined by NMR (Figures S5-S7).

The spectroscopic data of the identified species are given below.

4 (mixture of isomers A and B): Isomer A: ^{19}F NMR (470.168 MHz, δ, toluene:DMA (1:1)/DMSO-d_6 capillary): -119.2 (m, 2F, F_{ortho}), -166.5 (m, 1F, F_{para}), -168.3 (m, 2F, F_{meta}). Isomer B: ^{19}F NMR (470.168 MHz, δ, Tol/DMA (1:1)/$DMSO_6$ capillary): -119.2 (m, 2F, F_{ortho}), -161.6 (m, 1F, F_{para}), -164.2 (m, 2F, F_{meta}).

5: ^{19}F NMR (470.168 MHz, δ, toluene:DMA (1:1)/DMSO-d_6 capillary): -108.0 (m, 2F, F_{ortho}), -162.9 (t, J = 21.4 Hz, 1F, F_{para}), -163.8 (m, 2F, F_{meta}). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, toluene:DMA (1:1)/DMSO-d_6 capillary): 28.1.

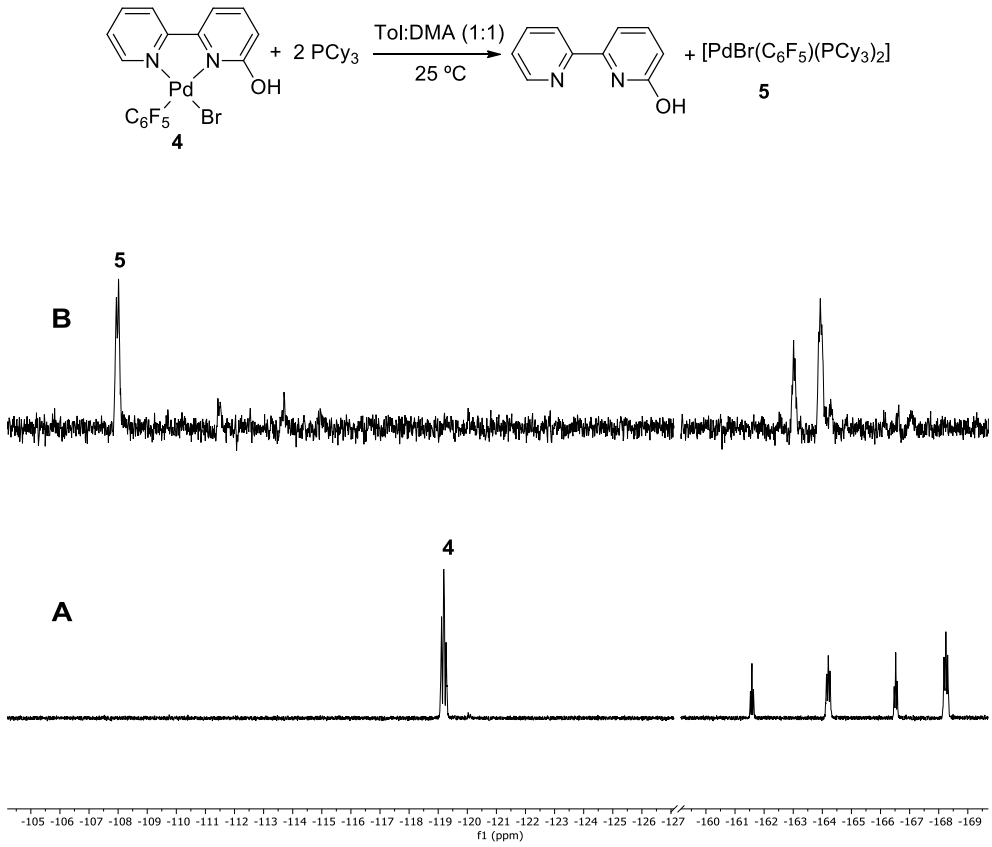


Figure S5. ^{19}F NMR spectra (470.168 MHz). A) Complex **4** in toluene:DMA (1:1) as a mixture of isomers. B) Sample A after adding 2 equivalents of PCy_3. Only the F_{ortho} region is labeled for simplicity.

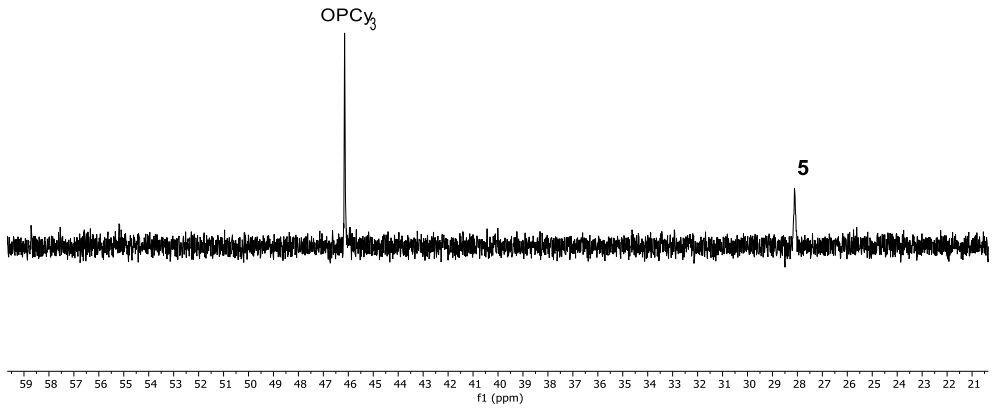


Figure S6. $^{31}P\{^{1}H\}$ NMR spectra (202.31 MHz). Mixture of complex **4** and 2 equivalents of PCy_3 in toluene:DMA (1:1).

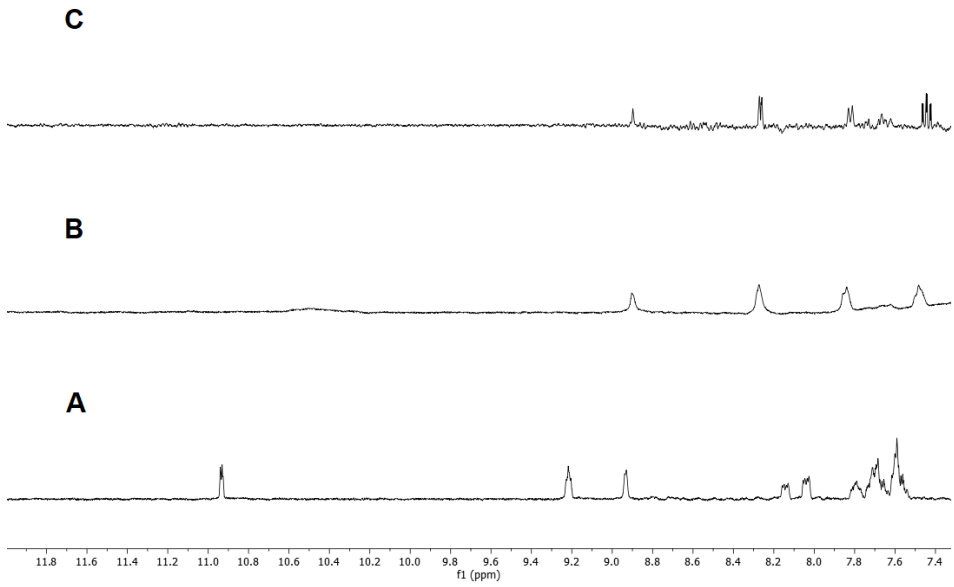


Figure S7. ^{1}H NMR spectra (500.13 MHz). A) Complex **4** in toluene:DMA (1:1). B) Sample A after adding 2 equivalents of PCy_3. C) Free bipy-6-OH in toluene:DMA (1:1).

Complex **6** (7.2 mg, 0.01 mmol) was dissolved in 0.3 mL of dry DMA and 0.3 mL of dry toluene and the solution was placed in an NMR tube along with a sealed glass capillary filled with DMSO-d6 as NMR lock signal. Then, PCy_3 (5.6 mg, 0.02 mmol) was added to the mixture. The species formed in solution at room temperature and after heating for 30 min at 100 ºC were examined by ^{1}H, ^{19}F and $^{31}P\{^{1}H\}$ NMR (Figures S8-S10).

In addition to the species mentioned in former experiments, complexes **6** and **7** were identified.

6: ^{19}F NMR (470.168 MHz, δ, toluene:DMA (1:1)/DMSO-d6 capillary): -118.5 (m, 2F, F_{ortho}), -169.9 (m, 1F, F_{para}), -170.1 (m, 2F, F_{meta}).

7: ^{19}F NMR (470.168 MHz, δ, toluene:DMA (1:1)/DMSO-d6 capillary): -110.9 (br, 2F, F_{ortho}), -163.3 (t, J = 18.4 Hz, 1F, F_{para}), -164.3 (br, 2F, F_{meta}). $^{31}P\{^{1}H\}$ NMR (202.31 MHz, δ, toluene/DMA (1:1)/DMSO-d6 capillary): 21.9.

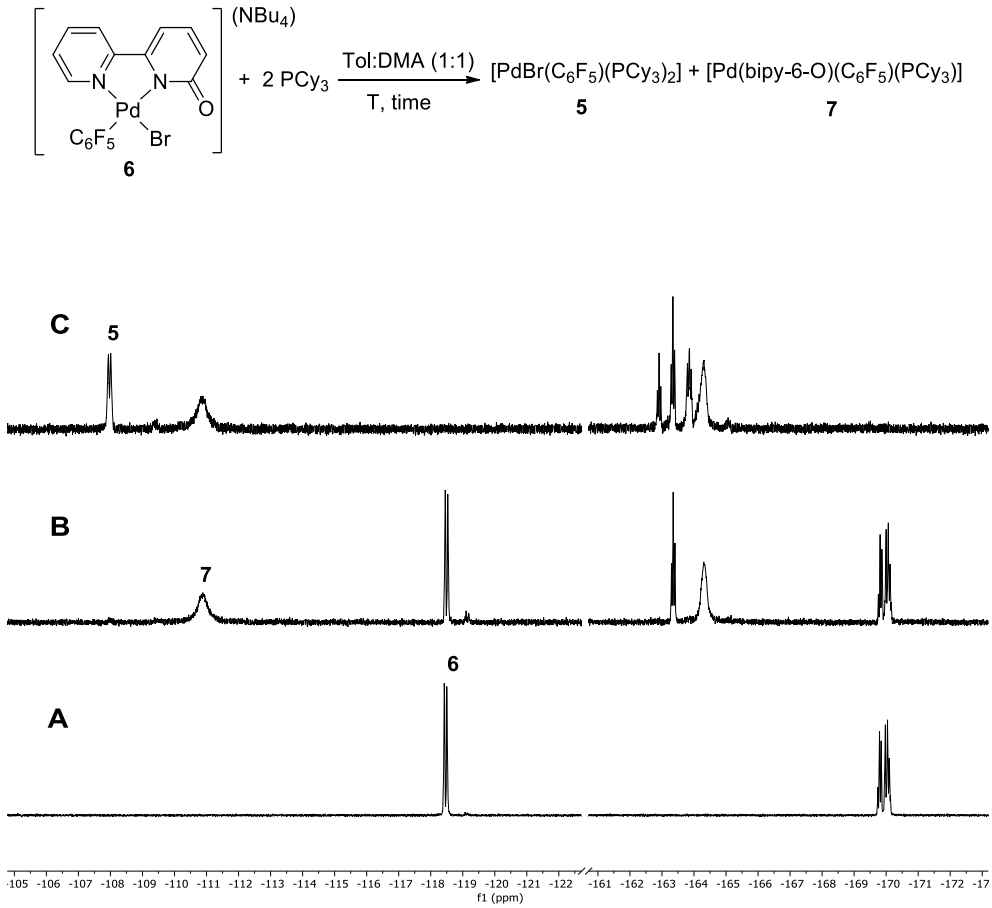


Figure S8. ^{19}F NMR spectra (470.168 MHz). A) Complex **6** in toluene:DMA (1:1). B) Sample A after adding 2 equivalents of PCy_3, standing for 1 hour at room temperature. C) Sample B after heating for 30 min at 100 ºC. Only the F_{ortho} region is labeled for simplicity.

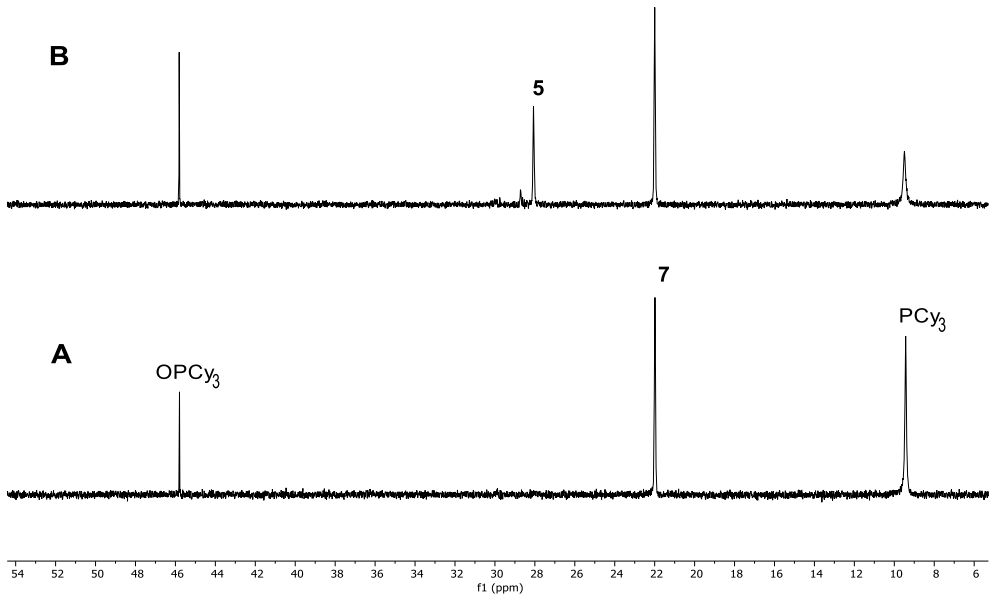


Figure S9. ^{31}P NMR spectra (202.31 MHz). A) Complex **6** and 2 equivalents of PCy_3 in toluene:DMA (1:1), 1 hour at room temperature after the addition. B) Sample A after heating for 30 min at 100 ºC.

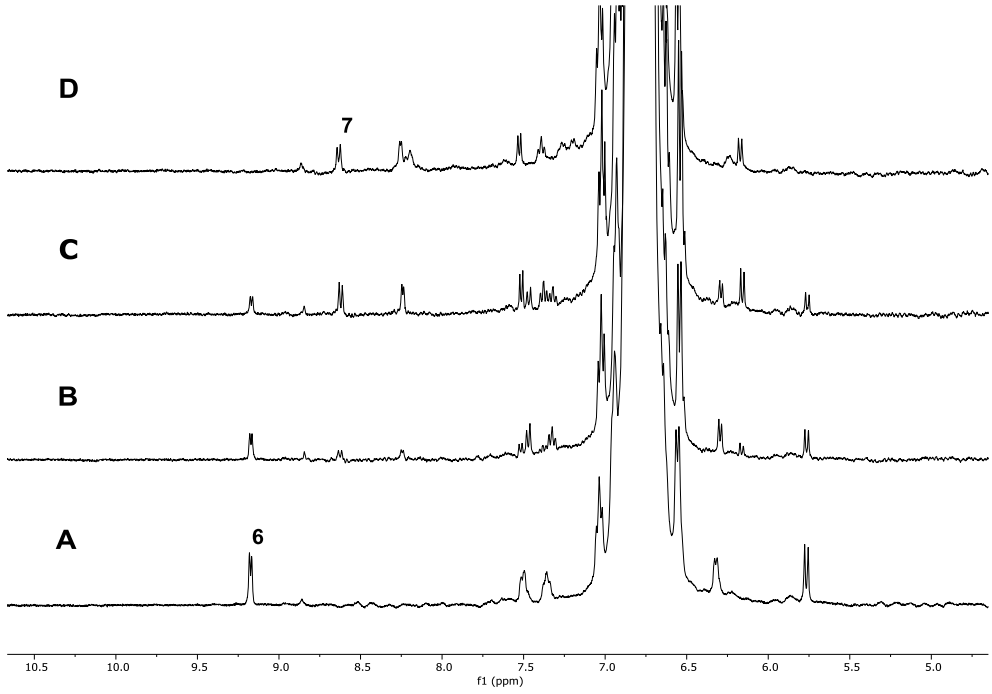


Figure S10. ^{1}H NMR spectra (500.13 MHz); only the aromatic region is showed for clarity. A) Complex **6** in toluene:DMA (1:1). B) Sample A after adding 2 equivalents of PCy_3. C) Sample B after 1 h at room temperature. D) Sample C after heating for 30 min at 100 ºC.

Complex **1** (4.2 mg, 4.7x10^{-3} mmol) was mixed with 0.3 mL of dry DMA and 0.3 mL of dry toluene and the solution was placed in an NMR tube along with a sealed glass capillary filled with DMSO-d6 as NMR lock signal. Bipy-6-OH (0.8 mg, 4.7x10^{-3} mmol) was added to the mixture. After checking the species by NMR, Cs_2CO_3 (3.0 mg, 9.4x10^{-3} mmol) was introduced and the tube was shaken vigorously. The species formed in solution at room temperature were examined again by ^{19}F NMR (Figure S11).

The spectroscopic data of the identified species are given above.

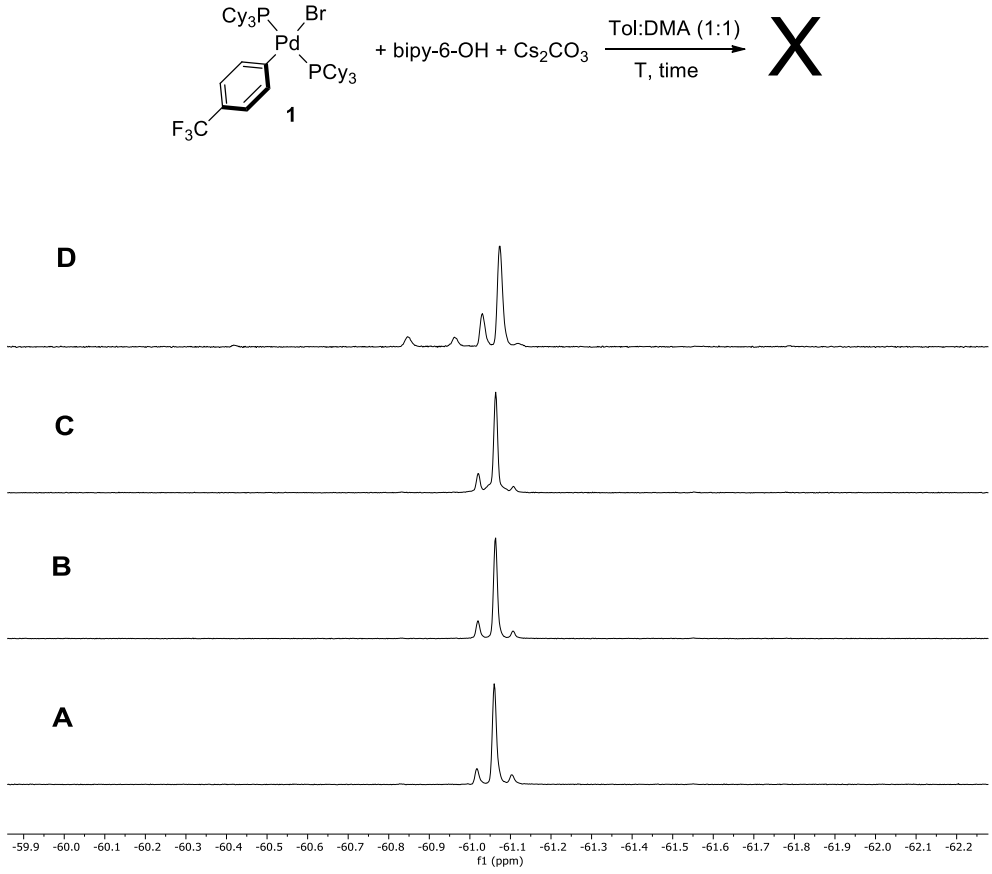


Figure S11. ^{19}F NMR spectra (470.168 MHz). A) Complex **1** in toluene:DMA (1:1). B) Sample A after adding 1 equivalent of bipy-6-OH. C) Sample B after adding 2 equivalents of Cs_2CO_3. D) Sample C after heating for 30 min at 100 ºC.

1.4.4. Transmetalation experiments

*Reaction of [Pd(bipy-6-O)(C_6F_5)DMA] (**8**) with [PdBr(p-CF_3-C_6H_4)(PCy_3)$_2$] (**1**).*

[Pd(bipy-6-OH)Br(C_6F_5)] (**4,** 5.2 mg, 0.01 mmol) was mixed with 0.6 mL of dry DMA and Ag_2CO_3 (5.5 mg, 0.02 mmol). The mixture was stirred for 5 min and then it was filtered. The solution, containing complex **8**, was checked by ^{19}F NMR using a sealed glass capillary filled with DMSO-d6 as NMR lock signal. Complex **1** (8.9 mg, 0.01 mmol) was then introduced into the tube. The mixture was heated at 100 ºC for the specified time. The species formed in solution at room temperature were examined by ^{19}F NMR (Figure S12).

The spectroscopic data of the identified species are given below.

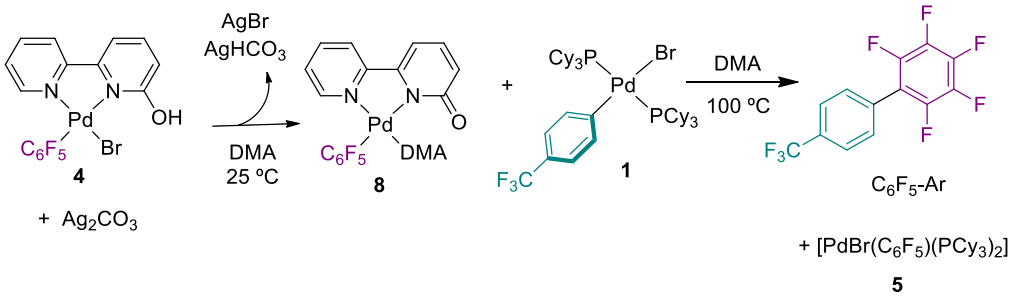
4: (mixture of isomers A and B):[19] Isomer A: ^{19}F NMR (470.168 MHz, δ, DMA/DMSO-d6 capillary): -119.3 (m, 2F, F_{ortho}), -164.4 (m, 1F, F_{para}), -168.4 (m, 2F, F_{meta}). Isomer B: ^{19}F NMR (470.168 MHz, δ, DMA/DMSO-d6 capillary): -119.5 (m, 2F, F_{ortho}), -161.7 (m, 1F, F_{para}), -166.6 (m, 2F, F_{meta}).

8:[19] ^{19}F NMR (470.168 MHz, δ, DMA/DMSO-d6 capillary): -118.8 (m, 2F, F_{ortho}), -162.3 (t, J = 19.6 Hz, 1F, F_{para}), 164.7 (m, 2F, F_{meta}).

1: ^{19}F NMR (470.168 MHz, δ, DMA/DMSO-d6 capillary): -61.87 (CF_3). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, DMA/DMSO-d6 capillary): 19.93.

5: ^{19}F NMR (470.168 MHz, δ, DMA/DMSO-d6 capillary): -108.0 (m, 2F, F_{ortho}), -162.9 (t, J = 21.4 Hz, 1F, F_{para}), -163.8 (m, 2F, F_{meta}). $^{31}P\{^1H\}$ NMR (202.31 MHz, δ, DMA/DMSO-d6 capillary): 28.1.

C_6F_5-*p*-(CF_3)C_6H_4 (C_6F_5-Ar): ^{19}F NMR (470.168 MHz, δ, DMA/DMSO-d6 capillary): -62.75 (s, 3F, F_{CF3}), -144.38 (m, 2F, F_{ortho}), -156.78 (t, J = 21.6 Hz, 1F, F_{para}), -164.11 (m, 2F, F_{meta}).



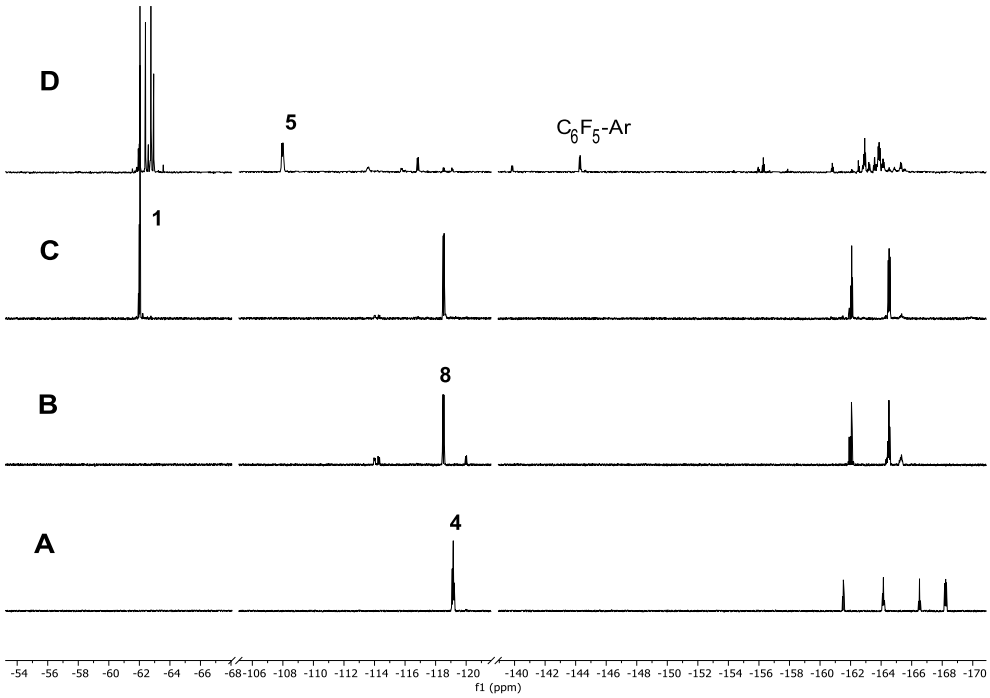


Figure S12. ^{19}F NMR spectra (470.168 MHz). A) Complex **4** in DMA (mixture of isomers). B) Sample A + Ag_2CO_3 in DMA. C) Sample B after adding complex **1**. D) Sample C after heating for 30 min at 100 °C. (C_6F_5-Ar 14 %). No changes were observed after heating at 100 ˚C for 3 h.

*Reactions of [Pd(bipy-6-O)(C_6F_5)DMA] (**8**) with [Pd(μ-Br)(p-CF_3-C_6H_4)(PCy_3)]$_2$ (**2**).*

Complex **4** (5.2 mg, 0.01 mmol) was mixed with 0.6 mL of dry DMA and Ag_2CO_3 (5.5 mg, 0.02 mmol). The mixture was stirred 5 min and then it was filtered. The solution, containing complex **8**, was checked by ^{19}F NMR using a sealed glass capillary filled with DMSO-d_6 as NMR lock signal. Complex **2** (6.1 mg, 0.005 mmol) was introduced into the tube. The mixture was heated at 100 ºC for the specified time. The species formed in solution at room temperature were examined by ^{19}F NMR (Figure S13).

The same experiment was carried out in the presence of Cs_2CO_3 (0.02 mmol, added along complex **2**) (Figure S14).

The spectroscopic data of the identified species are given below.

2: Slightly soluble.^{19}F NMR (470.168 MHz, δ, DMA/DMSO-d6 capillary): -61.95 (CF_3). ^{31}P NMR (202.31 MHz, δ, DMA/DMSO-d6 capillary): 37.74.

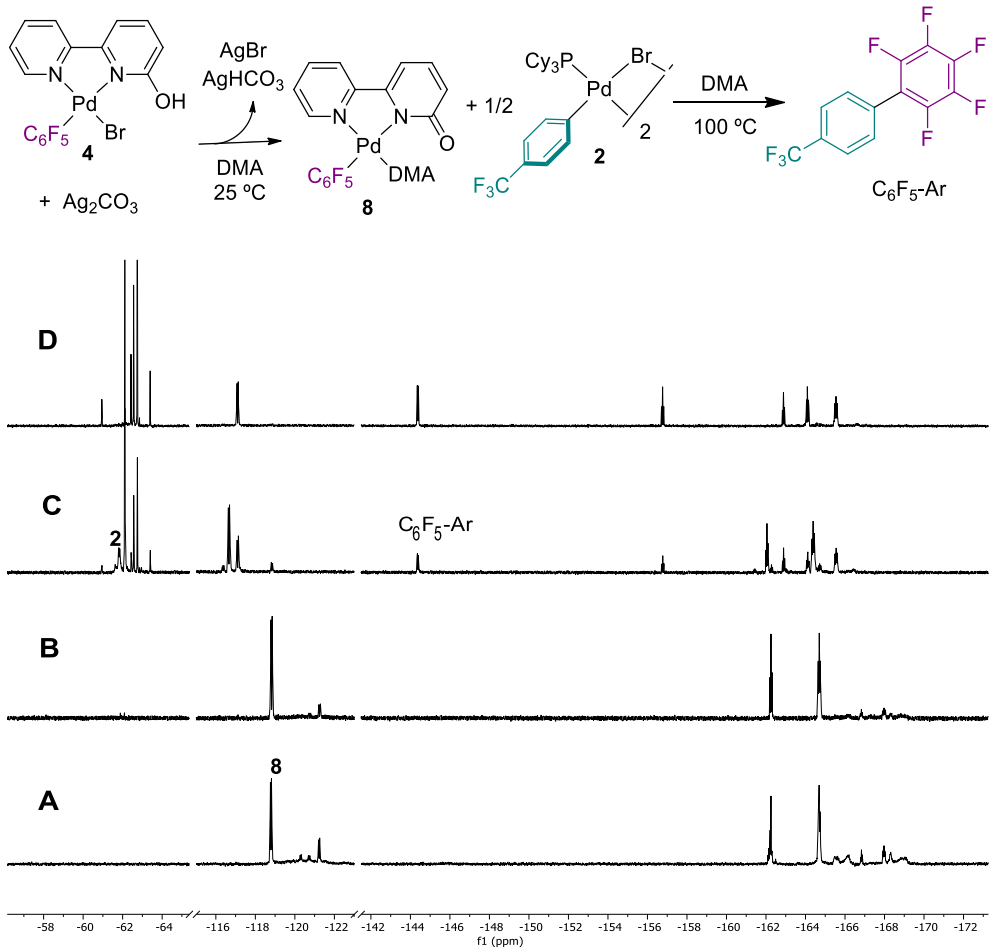


Figure S13. ^{19}F NMR spectra (470.168 MHz). A) Complex **8** in DMA. B) Sample A after adding complex **2** (not soluble). C) Sample B after heating for 30 min at 100 °C. (C_6F_5-Ar 12 %). D) Sample C after heating for 3 h at 100 ºC (C_6F_5-Ar 48 %).

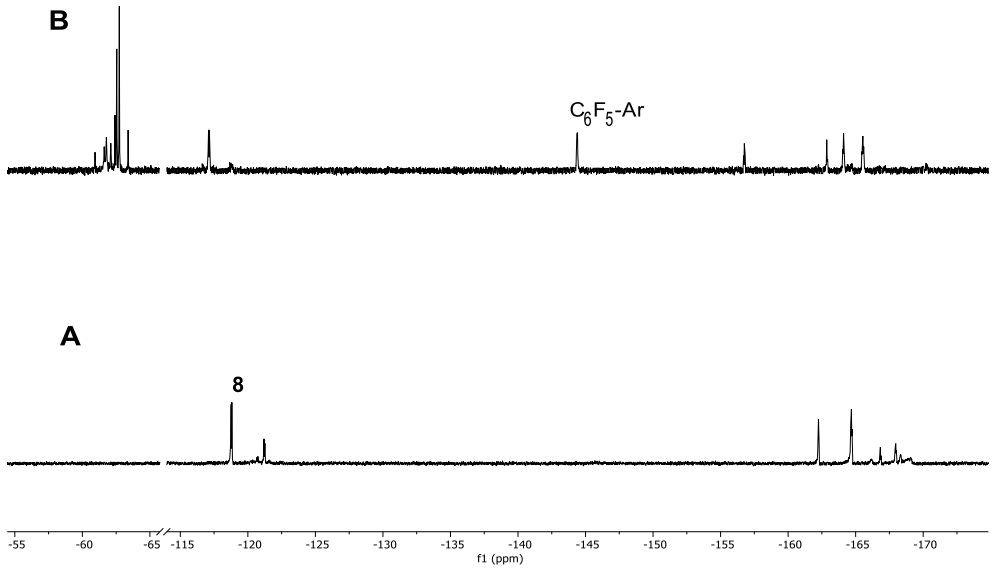


Figure S14. ^{19}F NMR spectra (470.168 MHz). A) Complex **8** in DMA. B) Sample A after adding **2** and Cs_2CO_3 and heating for 30 min a 100 ºC (C_6F_5-Ar 45%).

1.5- Kinetic data.

1.5.1. Determination of the KIE

Two Schlenk flasks equipped with a septum cap and a Teflon stirring bar were charged with $Pd(OAc)_2$ (3.8 mg, 0.017 mmol), bipy-6-OH (1.5 mg, 0.0085 mmol), PCy_3 (4.7 mg, 0.017 mmol) and cesium carbonate (222 mg, 0.68 mmol) in a nitrogen atmosphere. 4-bromobenzotrifluoride (47 μL, 0.34 mmol) was added to each flask. Then, toluene (1.5 mL) was added to one flask and toluene-d_8 (1.5 mL) to the other. Finally, DMA (1.5 mL) was added to each flasks ($[ArBr]_0$ = 0.12 M). The mixtures were heated at 100 °C with constant stirring. At the indicated time, an aliquot was taken and analyzed by ^{19}F NMR adding 0.5 mL of $CDCl_3$. The concentration of the product was determined by integration of the distinct trifluoromethyl signals of reagents and products. The ratio of initial rate constants for both experiments (k_H/k_D) gave the reported KIE value (see below, Table S4 and Figure S15).

The same procedure was followed for the KIE determining experiments for the analogous aryl chloride 4-chlorobenzotrifluoride (Table S5 and Figure S16).

Table S4. Time and product concentration data for the KIE determining experiments for ArBr = 4-bromobenzotrifluoride.[a]

	Toluene		**Toluene-d_8**
Time (min)	**[Product] (M)**	**Time (min)**	**[Product] (M)**
0	0	0	0
30	0.0057	30	0.0015
60	0.0147	60	0.0036
90	0.0249	90	0.0060
120	0.0363	120	0.0090
150	0.0487	150	0.0124

[a]Initial concentration $[ArBr]_0$ = 0.113 M.

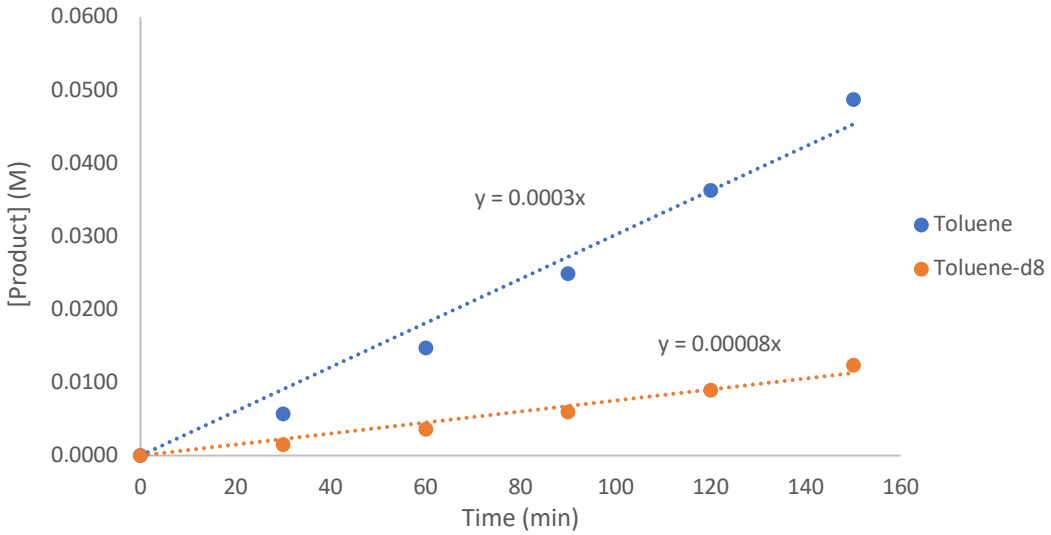


Figure S15. Concentration-time plots of the direct arylation of toluene and toluene-d_8 (ArBr = 4-bromobenzotrifluoride).

The ratio of initial reaction rate constants gives the KIE value:

$k_H = 3.29 \pm 0.19 \times 10^{-4}$; $k_D = 8.2 \pm 0.6 \times 10^{-5}$; KIE = $k_H/k_D = 4.0 \pm 0.5$

Table S5. Time and product concentration data for the KIE determining experiments for ArCl = 4-chlorobenzotrifluoride.[a]

	Toluene		**Toluene-d_8**
Time (min)	**[Product] (M)**	**Time (min)**	**[Product] (M)**
0	0	0	0.0000
10	0.0034	20	0.0011
20	0.0091	40	0.0034
30	0.0136	60	0.0068
40	0.0193	80	0.0091
50	0.0238	100	0.0125
60	0.0306	120	0.0159
		140	0.0181
		160	0.0227

[a]Initial concentration $[ArCl]_0 = 0.113$ M.

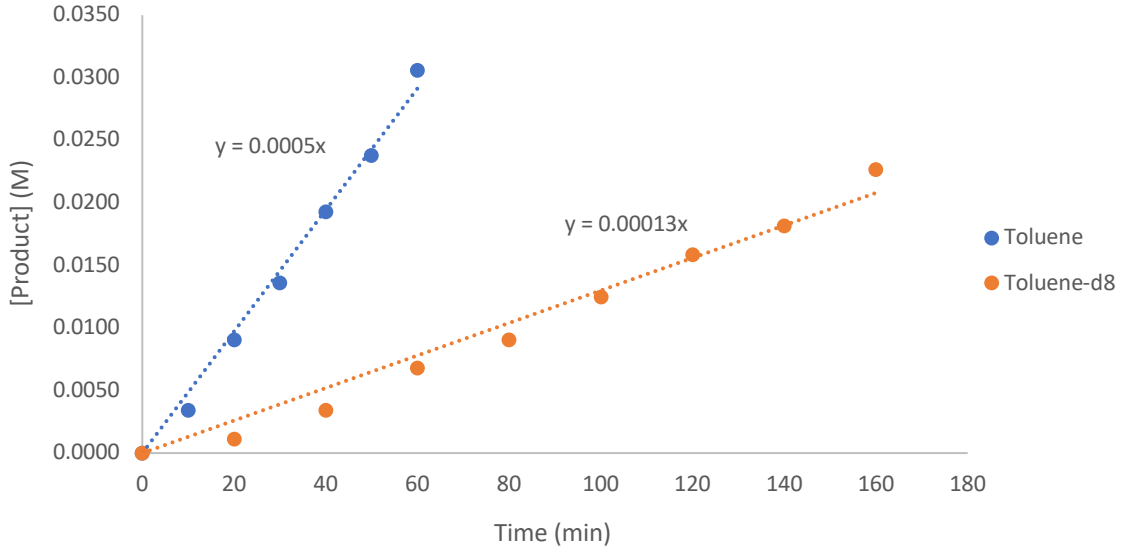


Figure S16. Concentration-time plots of the direct arylation of toluene and toluene-d_8 (ArCl = 4-chlorobenzotrifluoride).

The ratio of initial reaction rate constants gives the KIE value:

$k_H = 5.10 \pm 0.16 \times 10^{-4}$; $k_D = 1.43 \pm 0.06 \times 10^{-4}$; KIE = $k_H/k_D = 3.5 \pm 0.3$

1.5.2. Rate dependence on the reactant concentration.

<u>Order in catalyst and aryl bromide</u>

A Schlenk flask equipped with a septum cap and a Teflon stirring bar was charged, in a nitrogen atmosphere, with $Pd(OAc)_2$ (3.8 mg, 0.017 mmol), bipy-6-OH (1.5 mg, 0.0085 mmol), PCy_3 (4.7 mg, 0.017 mmol) and cesium carbonate (222 mg, 0.68 mmol). Then, 4-bromobenzotrifluoride (47 µL, 0.34 mmol), toluene (1.5 mL) and DMA (1.5 mL) were added. The Schlenk flask was heated at 100 °C with constant stirring. At the indicated time, an aliquot was taken and analyzed by ^{19}F NMR adding 0.5 mL of $CDCl_3$. The concentration of the product was determined by integration of the distinct trifluoromethyl signals of reagents and products.

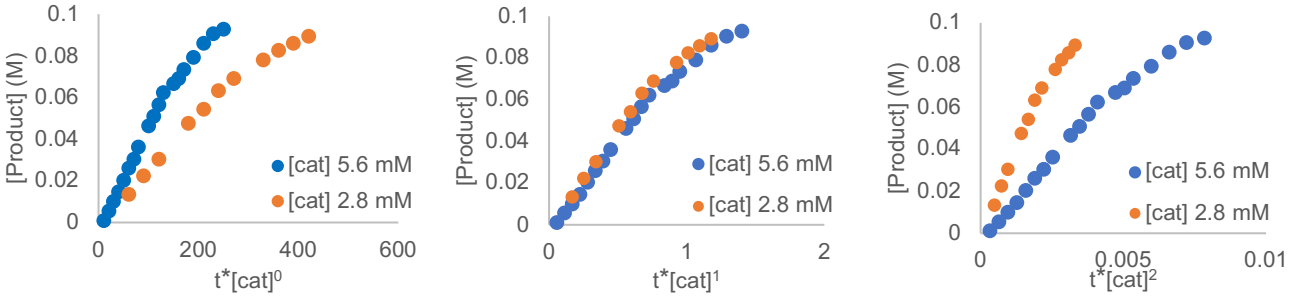
The variable time normalization analysis (VTNA) reported by Burés,[20] was used to determine the order on the reactants for the catalytic reaction (catalyst and aryl bromide). In addition to the experiment above (Experiment 1) two other experiments were performed each time varying one of the reagent's initial concentrations (Table S6). The resulting plots are represented in Figure S17.

Table S6. Initial concentration values for the kinetic experiments.

Experiment	[Cat][a] (M)	[ArBr] (M)
1	0.0056	0.113
2	0.0028	0.113
3	0.0056	0.227

[a] [Cat] = $Pd(OAc)_2$/ 0.5 bipy-6-OH/ PCy_3; the concentration of each of the three components was halved in experiment 2. The given concentration corresponds to the Pd precursor.

Order in catalyst



Order in aryl halide

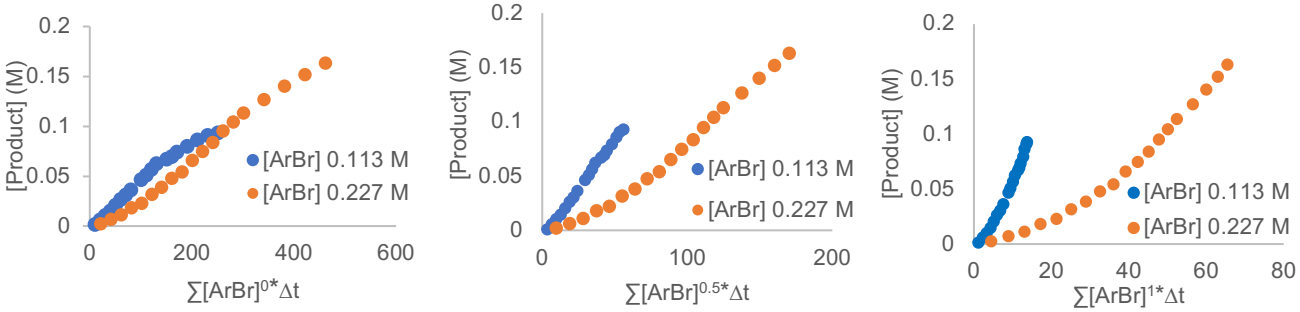


Figure S17. Plots derived from the variable time normalization analysis (VTNA). Overlay of plots from two different experiments gives the order in the reagent whose initial concentration is changed (power value in abscissa axis).

The lower reaction rate observed upon addition of a higher excess of ArBr (Figure S17, left) could be due to competition of ArBr with toluene for coordination to the metal. This has been observed before.[9]

Table S7. Kinetic data (product concentration at different times) for experiments 1-3 (Table S6).

Experiment	Time (min)	[Product] (M)
[Cat] = 0.0056 M [ArBr] = 0.113 M	10	0.0011
	20	0.0057
	30	0.0102
	40	0.0147
	50	0.0204
	60	0.0261
	70	0.0306
	80	0.0363
	100	0.0465
	110	0.0510
	120	0.0567
	130	0.0623
	150	0.0669
	160	0.0691
	170	0.0737
	190	0.0793
	210	0.0861
	230	0.0907
	250	0.0929
[Cat] = 0.0028 M [ArBr] = 0.113 M	60	0.0136
	90	0.0227
	120	0.0306
	180	0.0476
	210	0.0544
	240	0.0635
	270	0.0691
	330	0.0782
	360	0.0827
	390	0.0861
	420	0.0895
	450	0.0941

	20	0.0023
	40	0.0068
	60	0.0113
	80	0.0181
	100	0.0227
	120	0.0317
	140	0.0385
	160	0.0476
	180	0.0544
	200	0.0657
	220	0.0748
[Cat] = 0.0056 M	240	0.0839
[ArBr] = 0.227 M	260	0.0952
	280	0.1042
	300	0.1133
	340	0.1269
	380	0.1405
	420	0.1519
	460	0.1632

Order in aryl chloride

A Schlenk flask equipped with a septum cap and a Teflon stirring bar was charged, in a nitrogen atmosphere, with $Pd(OAc)_2$ (3.8 mg, 0.017 mmol), bipy-6-OH (1.5 mg, 0.0085 mmol), PCy_3 (4.7 mg, 0.017 mmol) and cesium carbonate (222 mg, 0.68 mmol). Then, 4-chlorobenzotrifluoride, toluene (1.5 mL) and DMA (1.5 mL) were added. The Schlenk flask was heated at 100 °C with constant stirring. At the indicated time, an aliquot was taken and analyzed by ^{19}F NMR adding 0.5 mL of $CDCl_3$. The concentration of the product was determined by integration of the distinct trifluoromethyl signals of reagents and products.

As above, the variable time normalization analysis (VTNA) reported by Burés, was used to determine the order on the aryl chloride. Two experiments were carried out in the way just described using the same catalyst concentration ($[Pd]_0$ = 0.0056 M) and different initial concentrations of ArCl:

Experiment 1: $[ArCl]_0$ = 0.113 M); Experiment 2: $[ArCl]_0$ = 0.227 M). The resulting plots are represented in Figure S18.

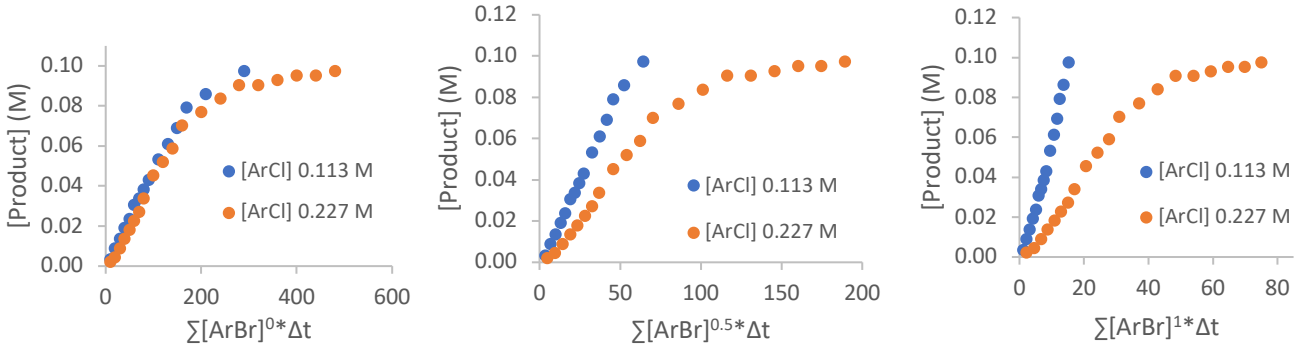


Figure S18. Plots derived from the variable time normalization analysis (VTNA). Overlay of plots from two different experiments gives the order in the reagent whose initial concentration is changed (power value in abscissa axis).

Table S8. Kinetic data (product concentration at different times) for experiments with different initial ArCl concentrations.

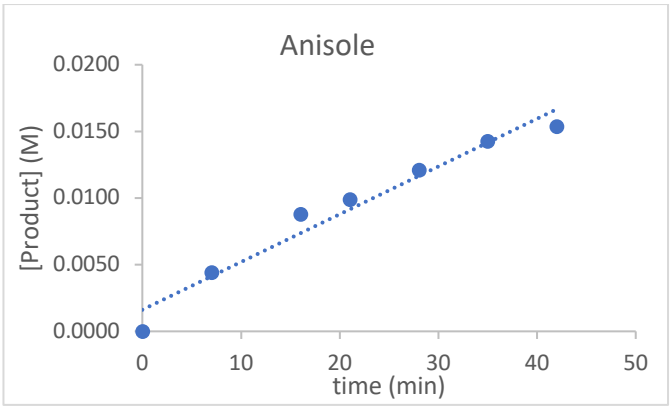
Experiment	Time (min)	[Product] (M)
[Cat] = 0.0056 M [ArCl] = 0.113 M	0	0.0000
	10	0.0034
	20	0.0091
	30	0.0136
	40	0.0193
	50	0.0238
	60	0.0306
	70	0.0340
	80	0.0385
	90	0.0431
	110	0.0533
	130	0.0612
	150	0.0691
	170	0.0793
	210	0.0861
	290	0.0975

	0	0.0000
	10	0.0023
	20	0.0045
	30	0.0091
	40	0.0136
	50	0.0181
	60	0.0227
	70	0.0272
	80	0.0340
	100	0.0453
	120	0.0521
[Cat] = 0.0056 M	140	0.0589
[ArCl] = 0.227 M	160	0.0703
	200	0.0771
	240	0.0839
	280	0.0907
	320	0.0907
	360	0.0929
	400	0.0952
	440	0.0952
	480	0.0975

1.5.3. Effect of the electronic properties of the arene.

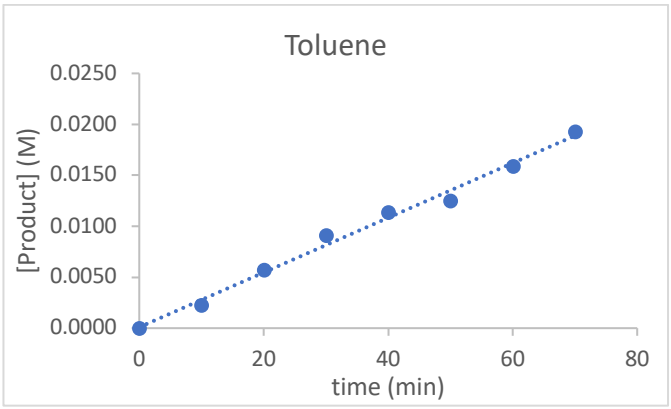
Three Schlenk flasks equipped with septum caps and Teflon stirring bars were charged, in a nitrogen atmosphere, with $Pd(OAc)_2$ (3.8 mg, 0.017 mmol), bipy-6-OH (1.5 mg, 0.0085 mmol), PCy_3 (4.7 mg, 0.017 mmol) and cesium carbonate (222 mg, 0.68 mmol). Then, 4-bromobenzotrifluoride (47 µL, 0.34 mmol), the corresponding arene (1.5 mL) and DMA (1.5 mL) were added. The Schlenk flask was heated at 100 °C with constant stirring. At the indicated time, an aliquot was taken and analyzed by ^{19}F NMR adding 0.5 mL of $CDCl_3$. The concentration of the product was determined by integration of the distinct trifluoromethyl signals of reagents and products.

The initial rates method was used to determine the kinetic constant for each experiment.



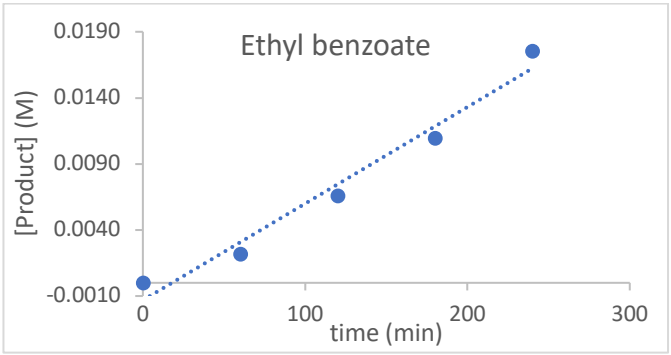
$y = mx + y_0$

$m = 3.6 \pm 0.3 \times 10^{-4}$



$y = mx + y_0$

$m = 2.7 \pm 0.1 \times 10^{-4}$



$y = mx + y_0$

$m = 7.3 \pm 0.7 \times 10^{-5}$

Figure S19. Concentration-time plots for different arenes.

Table S9. Product concentration at different times for experiments in Figure S19.[a]

Arene	Time (min)	[Product] (M)	v_0 (min^{-1})
	0	0	
	7	0.0044	
	16	0.0088	
Anisole	21	0.0099	3.6×10^{-4}
	28	0.0121	
	35	0.0143	
	42	0.0154	

Toluene	0	0	2.7×10^{-4}
	10	0.0023	
	20	0.0057	
	30	0.0091	
	40	0.01113	
	50	0.0125	
	60	0.0159	
	70	0.0193	
Ethyl benzoate	0	0	7.3×10^{-5}
	60	0.0022	
	120	0.0066	
	180	0.0110	
	240	0.0175	

[a]Initial concentration $[ArBr]_0 = 0.113$ M.

2. Computational details

2.1- Computational methods.

The DFT studies have been performed with the M06 functional,[21] as implemented in the Gaussian09 program package.[22] The 6-31+G(d) basis set was used for C, O, N, F and H,[23] and LANL2TZ(f) for Pd, Cs and Br[24] (BS I). Solvent effects have been considered trough the continuum model SMD for the experimental solvent, DMA, which was introduced in all the optimizations, frequency calculations and potential energy refinement. All structure optimizations were carried out in solvent phase with no symmetry restrictions. Gibbs energy corrections were calculated at 373.15 K (the experimental temperature) and 10^5 Pa pressure, including zero-point energy corrections (ZPE), and the energies were converted to 1M standard state in solution (adding/subtracting 2.89 kcal mol^{-1} for non-unimolecular processes). Vibrational frequency calculations were performed in order to confirm that the stationary points were minima (without imaginary frequencies) or transition states (with one imaginary frequency). Connectivity of the transition state structures was confirmed by relaxing the transition state geometry towards both the reactant and the product. Final potential energies were refined by performing additional single-point energy calculations (also in solution); Pd, Cs and Br were still described with LANL2TZ(f) basis set, and the remaining atoms were treated with 6-311++G(d,p) basis set (BS II). All energies presented below correspond to Gibbs energies in solution, obtained from potential energies (including solvation) with basis set II plus Gibbs energy corrections with basis set I. Cartesian Coordinates can be found in a separate .xyz formatted document.

2.2- Energy values for the calculated species (atomic units).

c1
SCF Energy = -958.1608857
Thermal Correction to Gibbs Free Energy = 0.131816

c2
SCF Energy = -1196.42962028
Thermal Correction to Gibbs Free Energy = 0.26153

TS c2-c3
SCF Energy = -1196.41155963
Thermal Correction to Gibbs Free Energy = 0.254663

c3
SCF Energy = -1196.43474532
Thermal Correction to Gibbs Free Energy = 0.260134

c4
SCF Energy = -1298.26539282
Thermal Correction to Gibbs Free Energy = 0.163538

c5
SCF Energy = -1536.53782506
Thermal Correction to Gibbs Free Energy = 0.291016

TS c5-c6
SCF Energy = -1536.51547091
Thermal Correction to Gibbs Free Energy = 0.288262

c6
SCF Energy = -1536.54233197
Thermal Correction to Gibbs Free Energy = 0.29068

c7
SCF Energy = -1756.03896347
Thermal Correction to Gibbs Free Energy = 0.546309

c8
SCF Energy = -2242.51517205
Thermal Correction to Gibbs Free Energy = 0.0.710657

TS c8-c9
SCF Energy = -2242.51466635
Thermal Correction to Gibbs Free Energy = 0.705519

c9
SCF Energy = -2242.54408335
Thermal Correction to Gibbs Free Energy = 0.71371

CsBr
SCF Energy = -33.1206435953
Thermal Correction to Gibbs Free Energy = -0.034855

Toluene
SCF Energy = -271.415146858
Thermal Correction to Gibbs Free Energy = 0.089006

CsOAc
SCF Energy = -248.36435675
Thermal Correction to Gibbs Free Energy = 0.007157

3. *Selected NMR spectra*

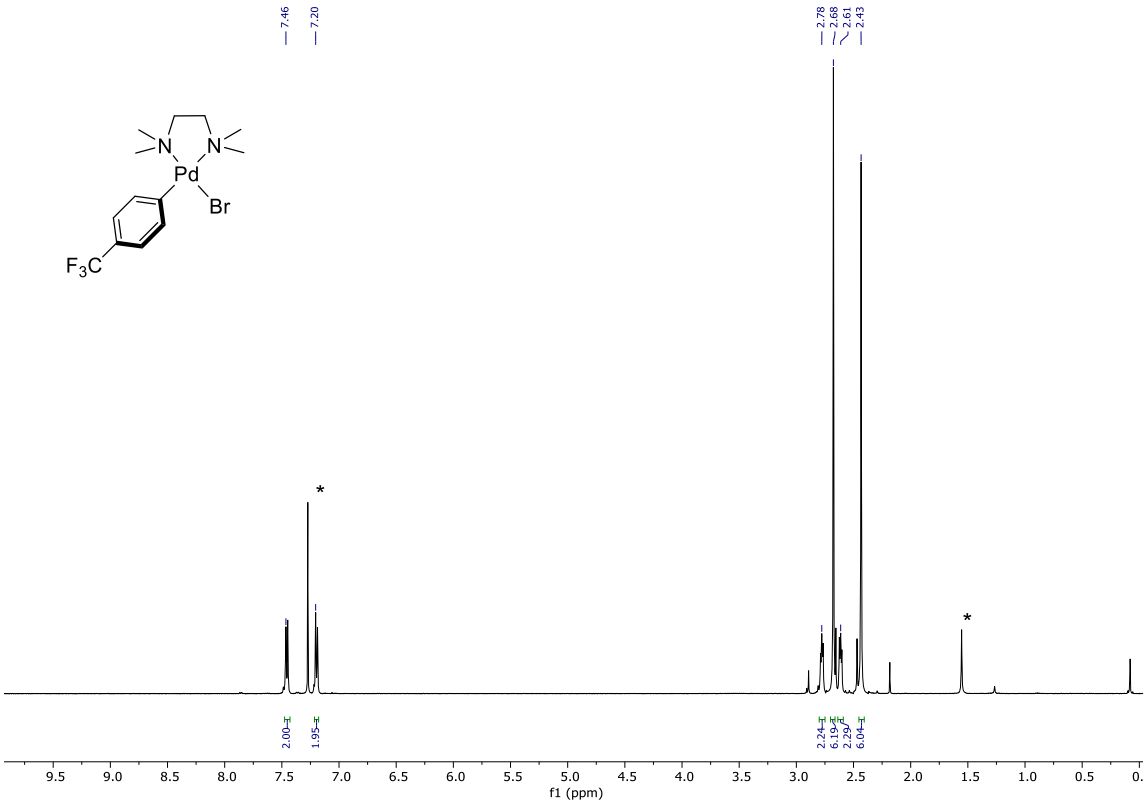


Figure S20. ^{1}H NMR (500.13 MHz, CD_3Cl) of [PdBr(C_6H_4-*p*-CF_3)(TMEDA)]. (*) Signals corresponding to solvent impurities ($CHCl_3$ and H_2O).

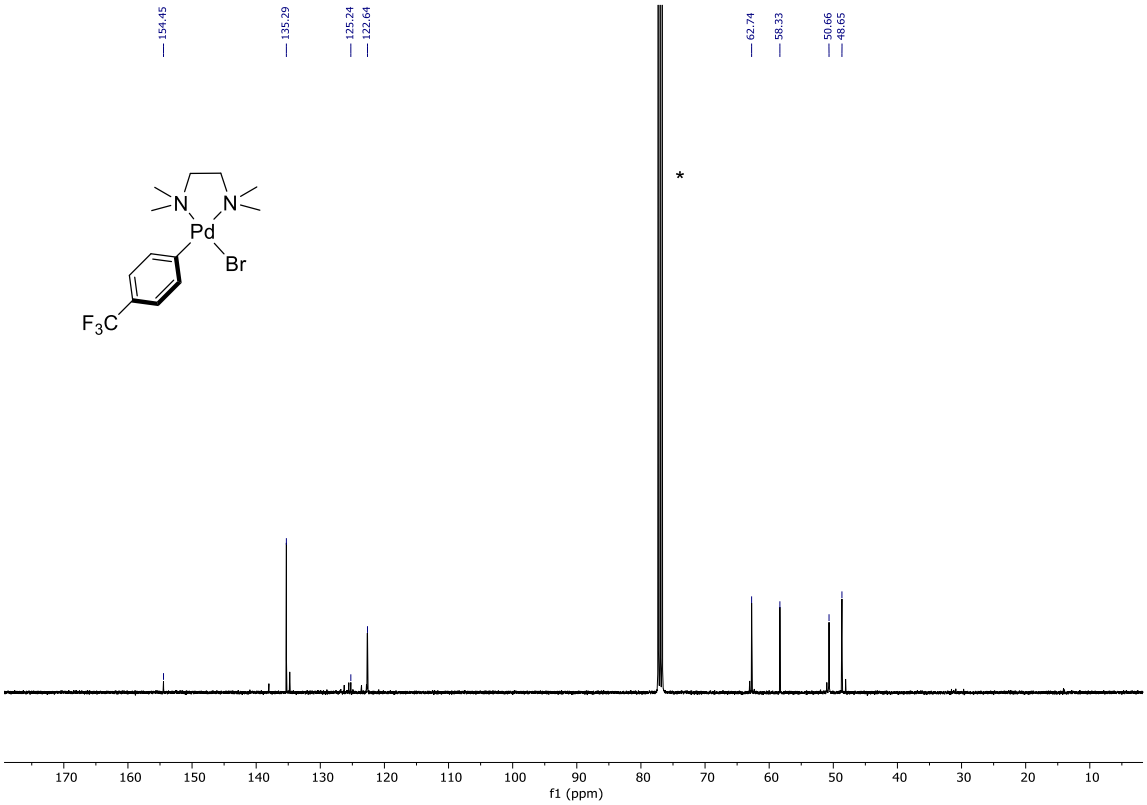


Figure S21. $^{13}C\{^{1}H\}$ NMR (125.78 MHz, CD_3Cl) of [PdBr(TMEDA)(C_6H_4-*p*-CF_3)]. (*) Signals corresponding to solvent (chloroform).

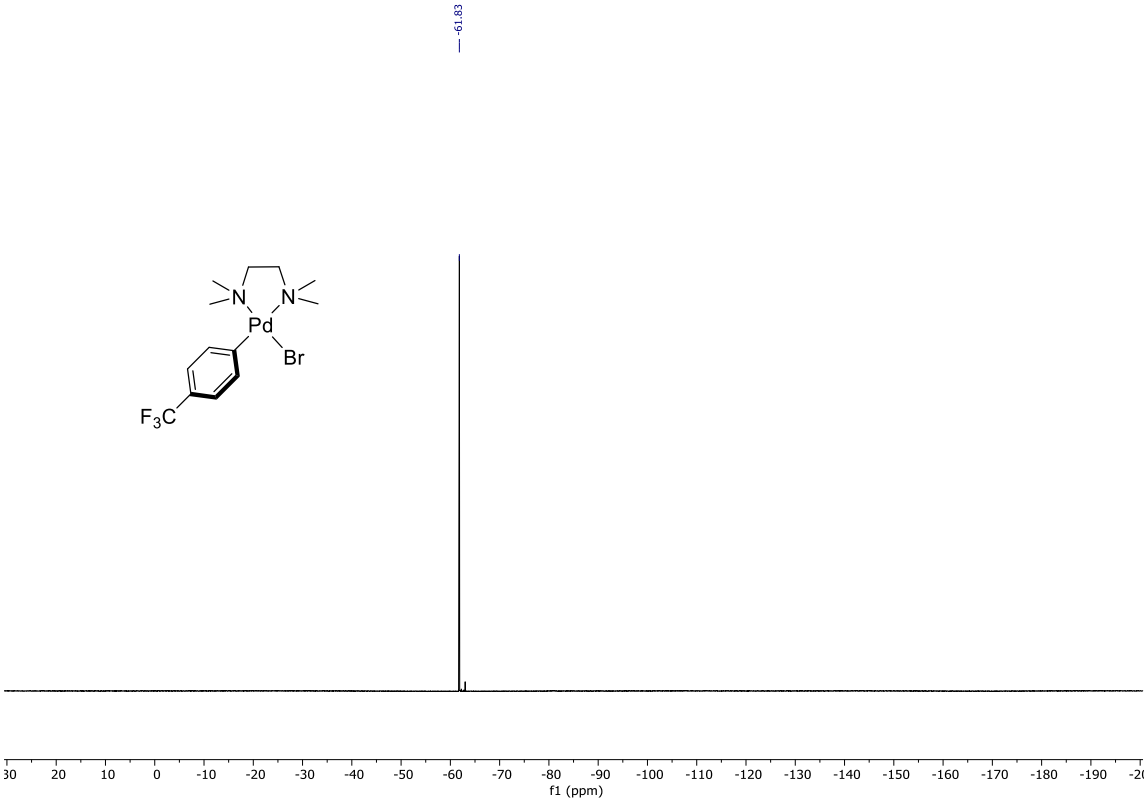


Figure S22. ^{19}F NMR (470.168 MHz, CD_3Cl) of [PdBr(TMEDA)(C_6H_4-*p*-CF_3)].

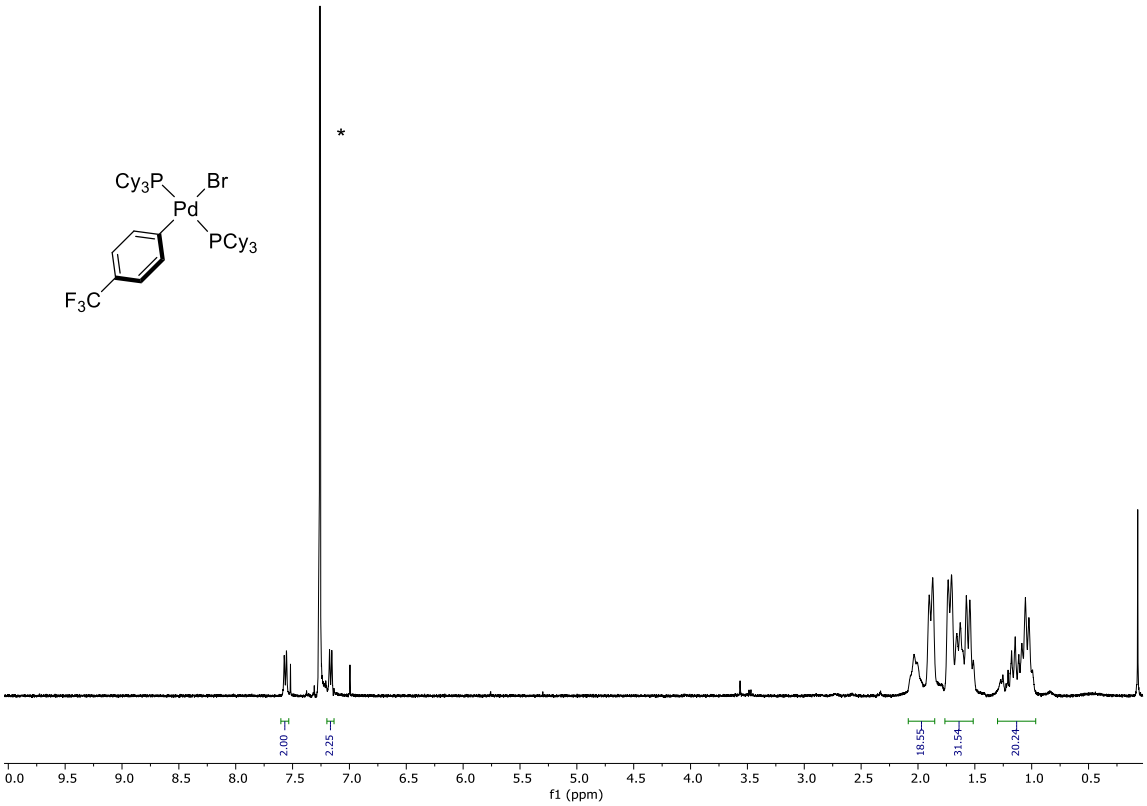


Figure S23. ^{1}H NMR (500.13 MHz, CD_3Cl) of **1.** (*) Signals corresponding to solvent (chloroform).

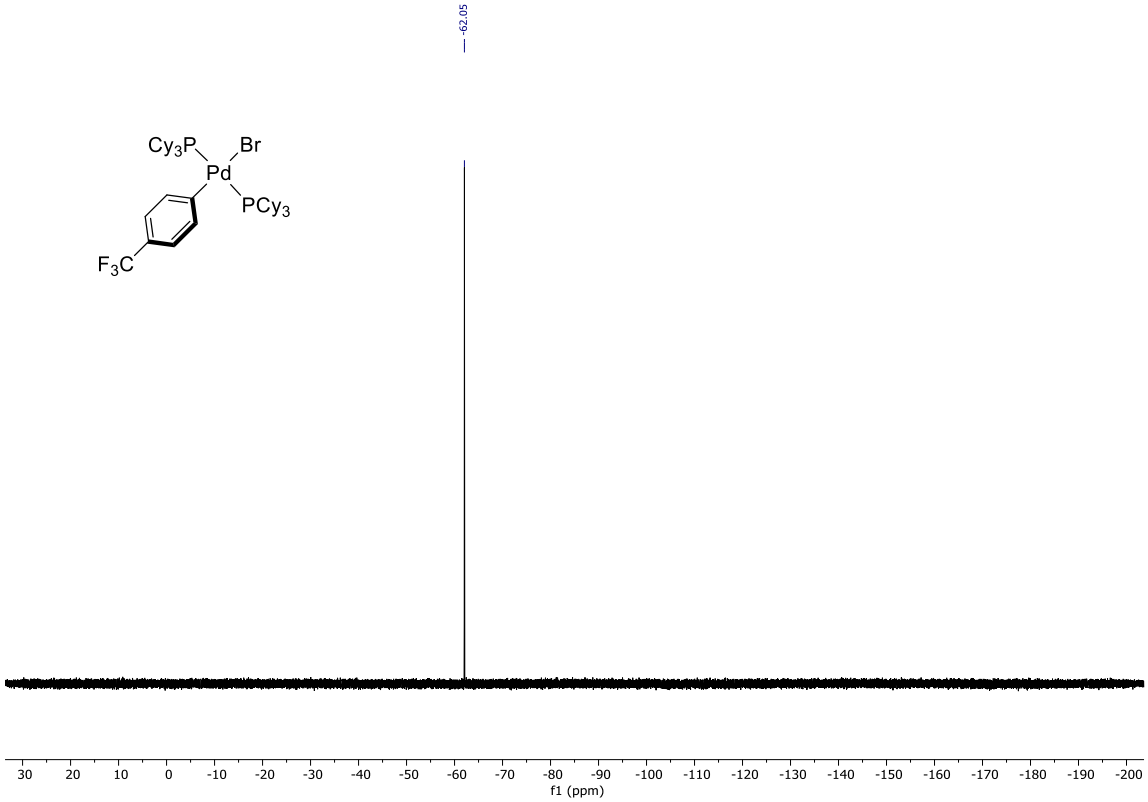


Figure S24. ^{19}F NMR (470.168 MHz, CD_3Cl) of **1**.

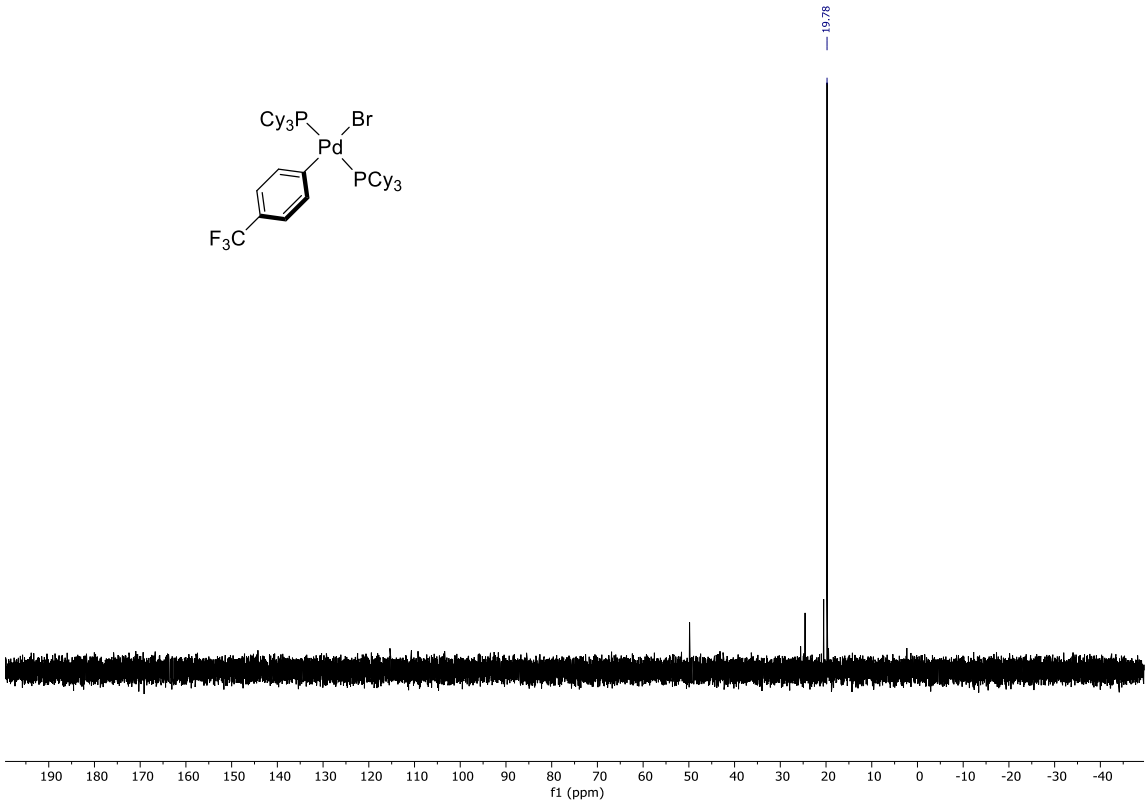


Figure S25.^{31}P NMR (202.31 MHz, $CDCl_3$) of **1**.

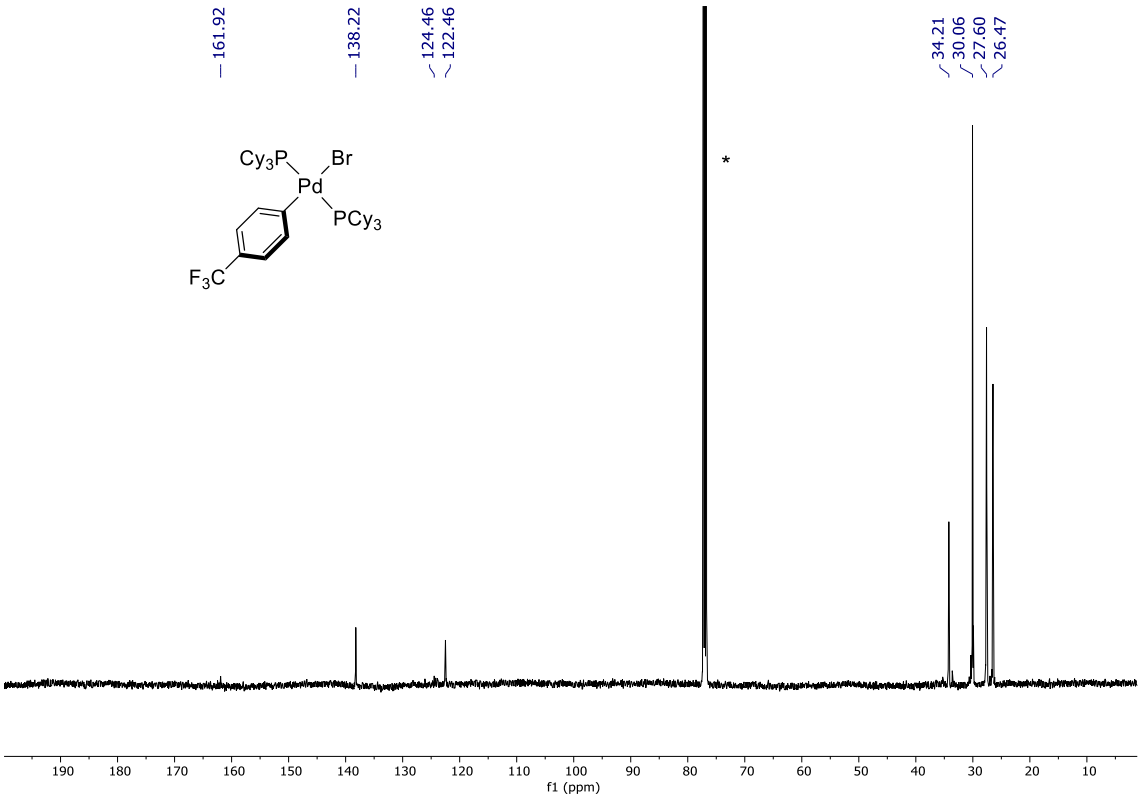


Figure S26. $^{13}C\{^{1}H\}$ NMR (125.78 MHz, CD_3Cl) of **1.** (*) Signals corresponding to solvent (chloroform).

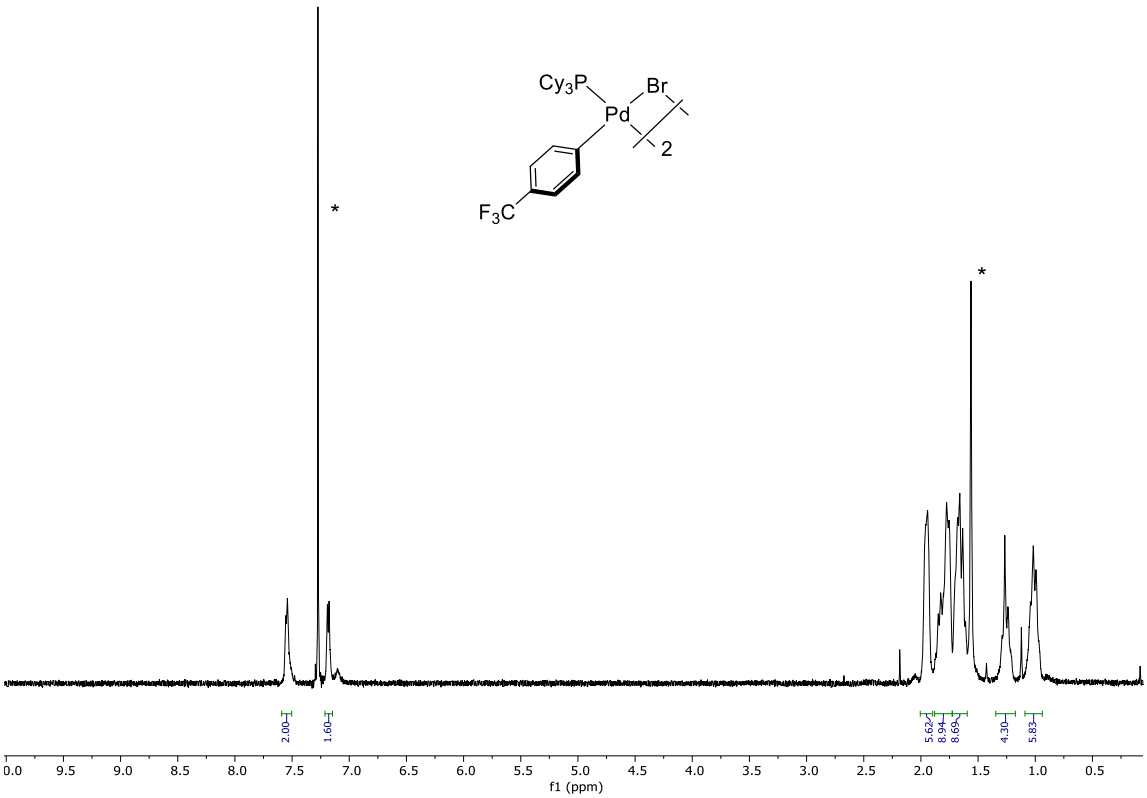


Figure S27. ^{1}H NMR (500.13 MHz, CD_3Cl) of **2.** (*) Signals corresponding to solvent impurities ($CHCl_3$ and H_2O).

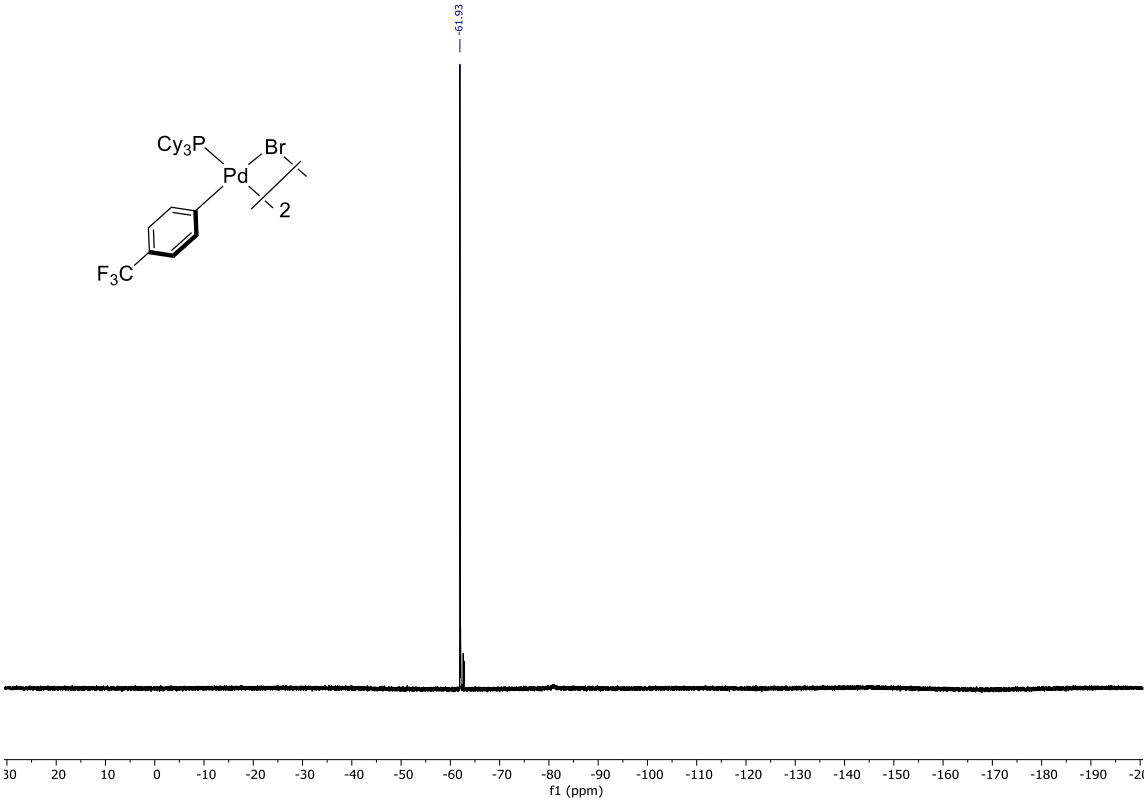


Figure S28. ^{19}F NMR (470.168 MHz, CD_3Cl) of **2.**

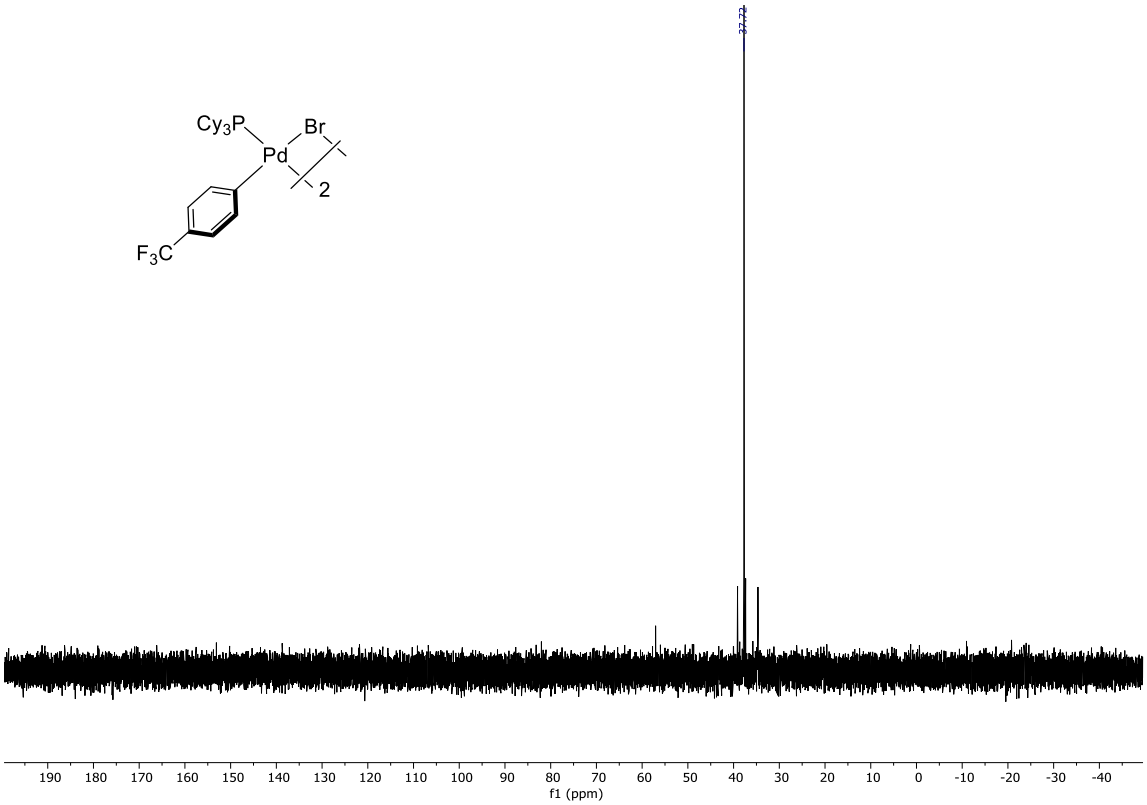


Figure S29. $^{31}P\{^1H\}$ NMR (202.31 MHz, $CDCl_3$) of **2.**

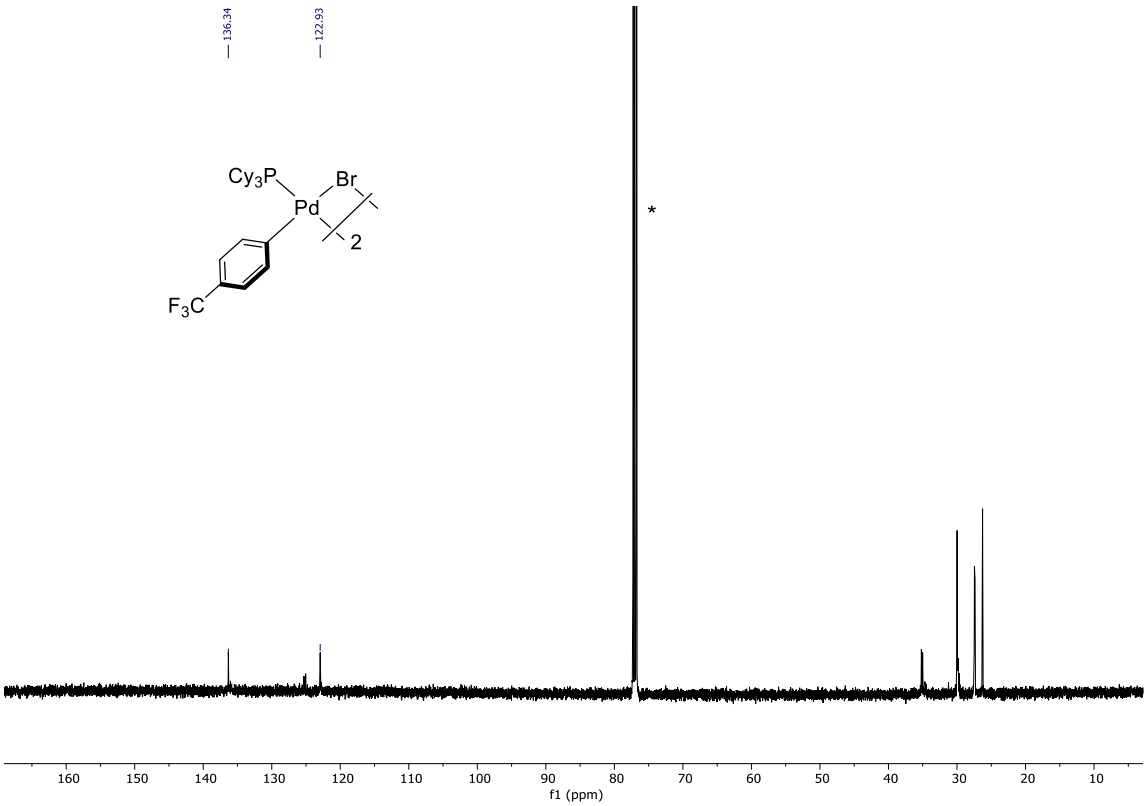


Figure S30. $^{13}C\{^{1}H\}$ NMR (125.78 MHz, CD_3Cl) of **2.** (*) Signals corresponding to solvent (chloroform).

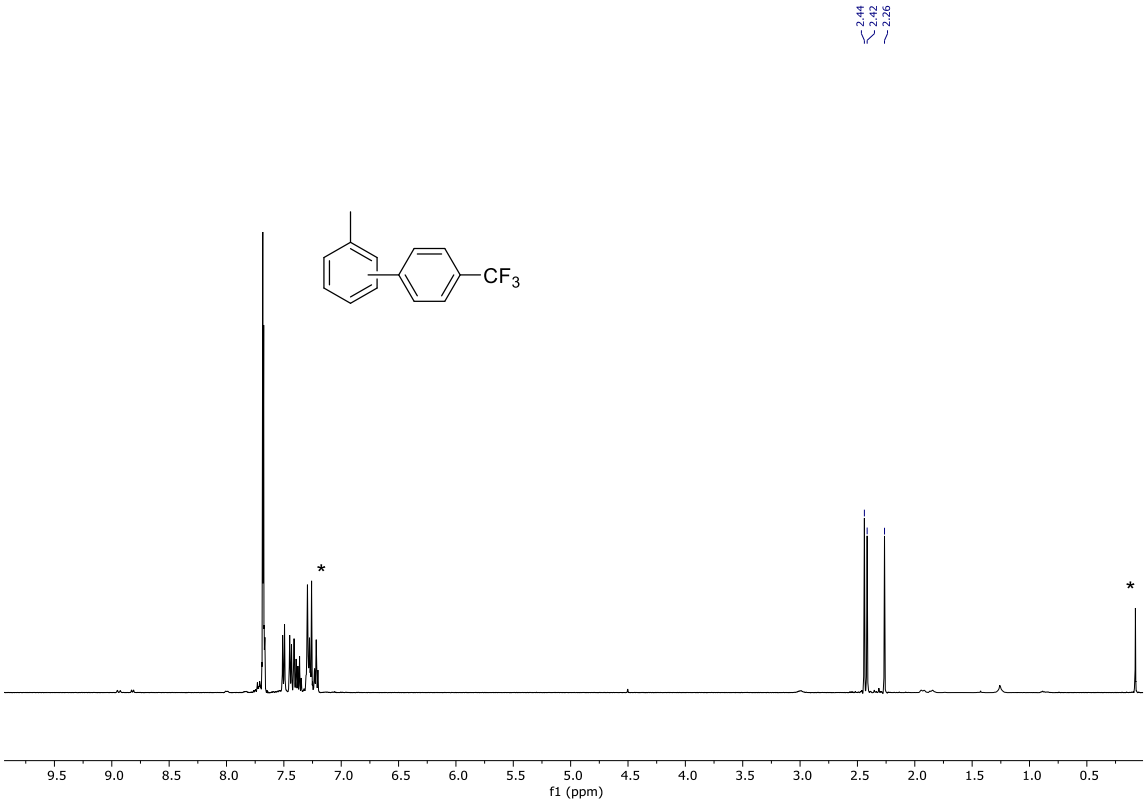


Figure S31. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3aa**, mixture of isomers 2-methyl-4'-(trifluoromethyl)-1,1'-biphenyl, 3-methyl-4'-(trifluoromethyl)-1,1'-biphenyl and 4-methyl-4'-(trifluoromethyl)-1,1'-biphenyl. (*) Signals corresponding to solvent (chloroform) and silicone grease.

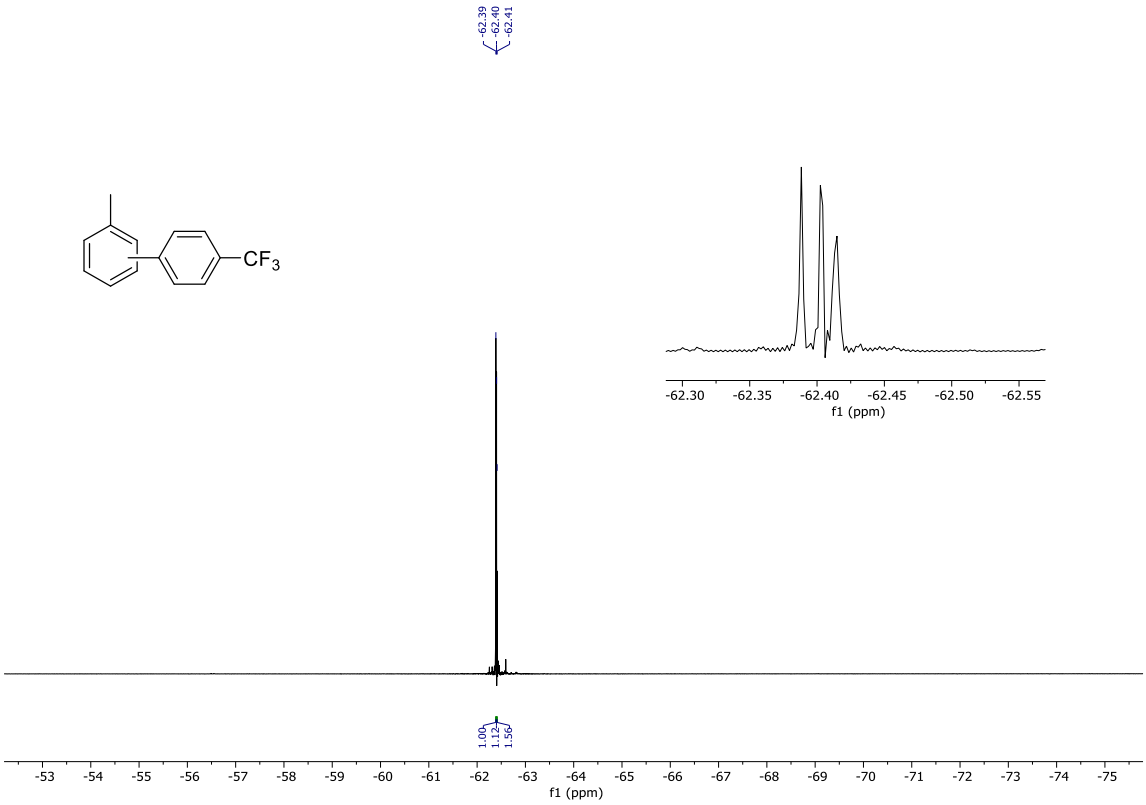


Figure S32. ^{19}F NMR spectra (470.168 MHz, $CDCl_3$) of **3aa**, mixture of 2-methyl-4'-(trifluoromethyl)-1,1'-biphenyl, 3-methyl-4'-(trifluoromethyl)-1,1'-biphenyl and 4-methyl-4'-(trifluoromethyl)-1,1'-biphenyl in an isomer ratio o:m:p = 1.5:1.1:1.

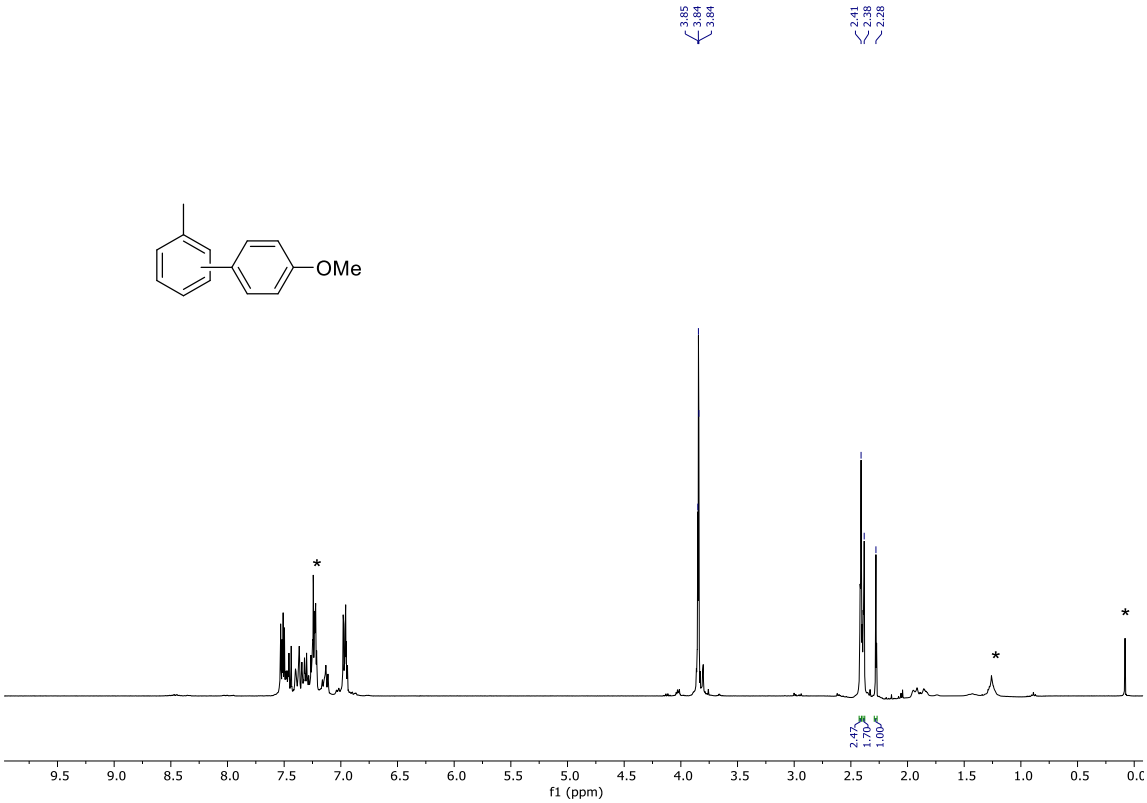


Figure S33. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3ab**, mixture of 2-methyl-4'-(methoxy)-1,1'-biphenyl, 3-methyl-4'-(methoxy)-1,1'-biphenyl, 4-methyl-4'-(methoxy)-1,1'-biphenyl in a ratio o:m:p = 1:2.5:1.7. (*) Signals corresponding to solvent (chloroform) hexane and silicon grease.

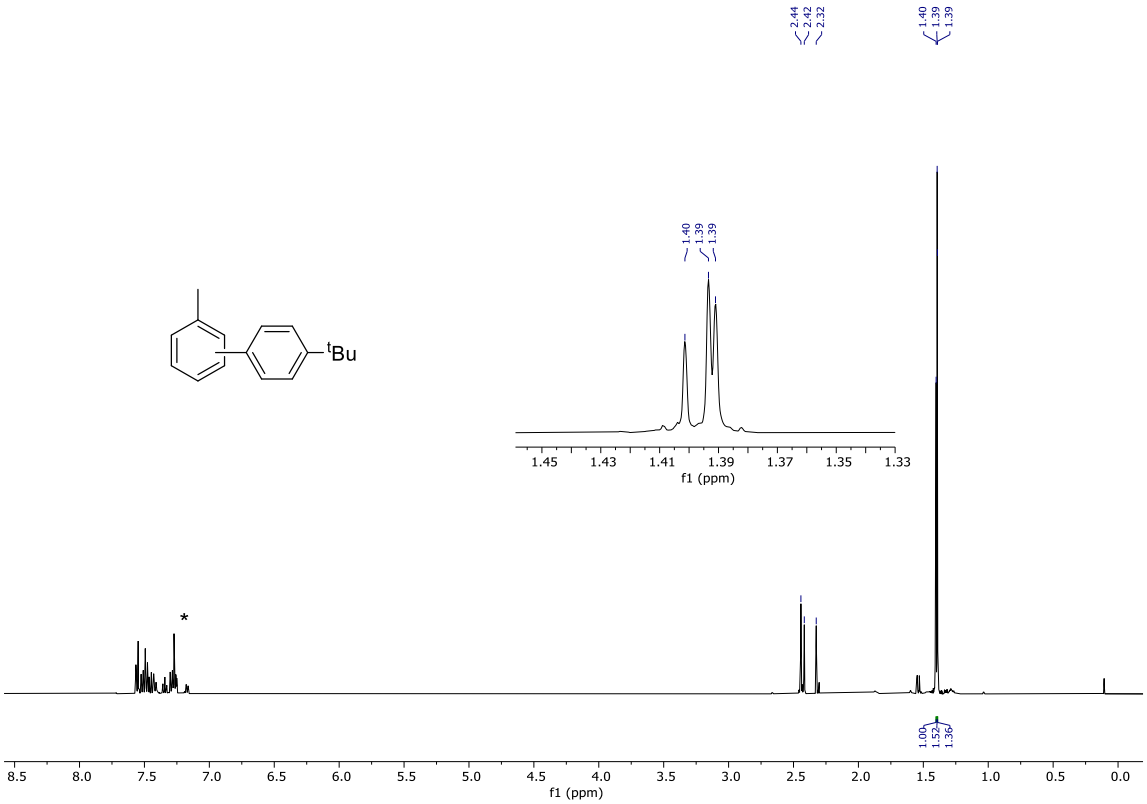


Figure S34. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3ac**, mixture of 2-methyl-4'-(*t*-butyl)-1,1'-biphenyl, 3-methyl-4'-(*t*-butyl)-1,1'-biphenyl, 4-methyl-4'-(*t*-butyl)-1,1'-biphenyl in an isomer ratio o:m:p = 1:1.5:1.3. (*) Signals corresponding to solvent (chloroform).

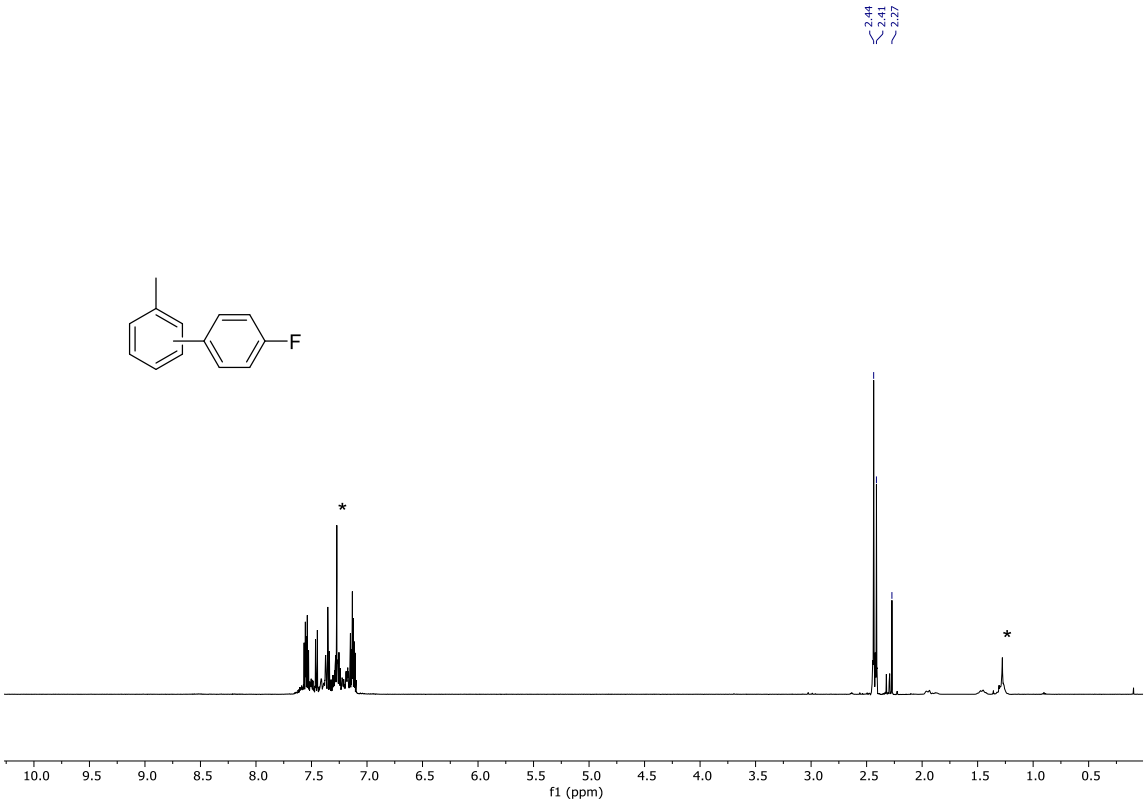


Figure S35. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3ad**, mixture of isomers 2-methyl-4'-(fluoro)-1,1'-biphenyl, 3-methyl-4'-(fluoro)-1,1'-biphenyl, 4-methyl-4'-(fluoro)-1,1'-biphenyl. (*) Signals corresponding to solvent (chloroform) and grease.

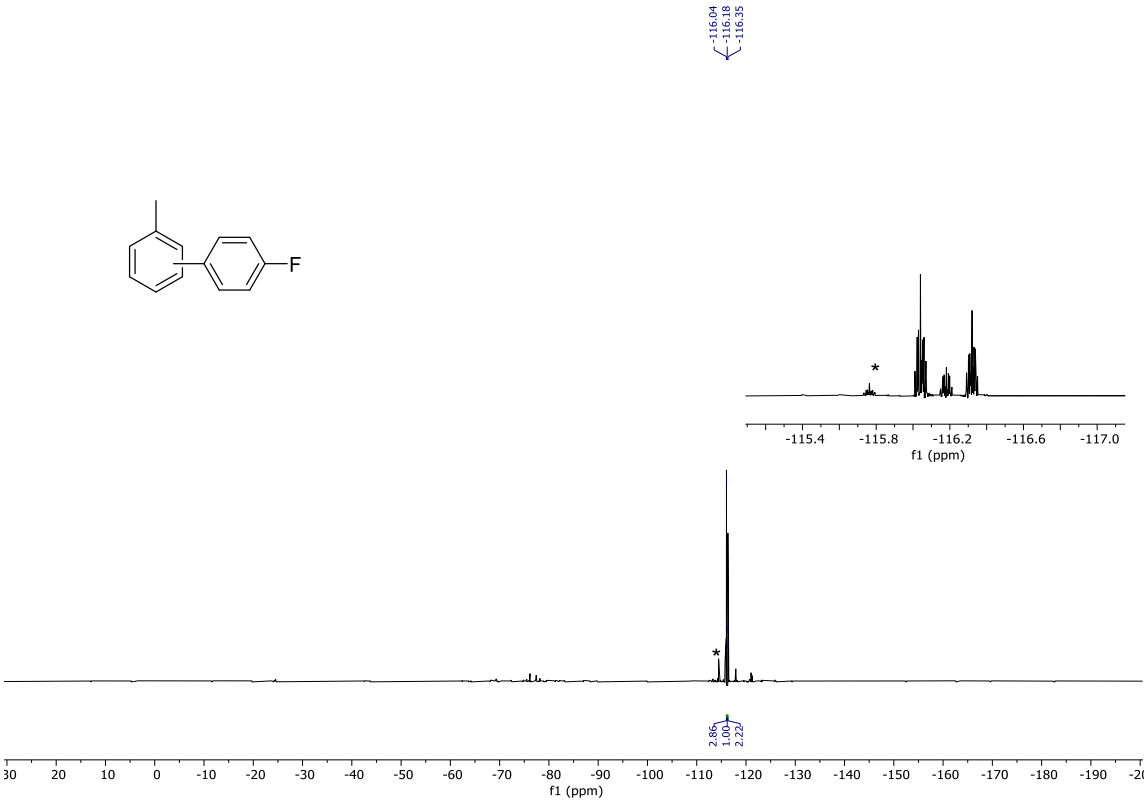


Figure S36. ^{19}F NMR spectra (470.168 MHz, $CDCl_3$) of **3ad**, mixture of 2-methyl-4'-(fluoro)-1,1'-biphenyl, 3-methyl-4'-(fluoro)-1,1'-biphenyl, 4-methyl-4'-(fluoro)-1,1'-biphenyl in isomer ratio o:m:p =1:2.9:2.2. (*) Signal corresponding to a minor unidentified compound.

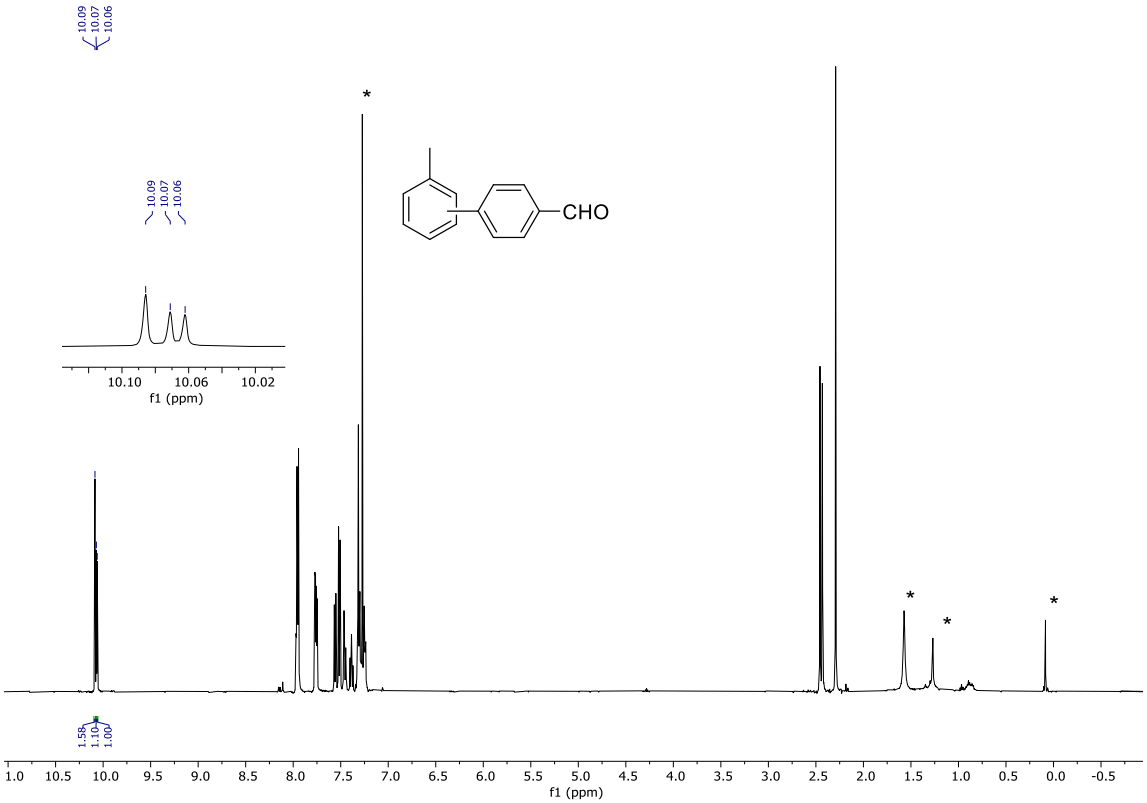


Figure S37. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3ae**, mixture of 2'-methyl-[1,1'-biphenyl]-2-carbaldehyde, 3'-methyl-[1,1'-biphenyl]-2-carbaldehyde and 4'-methyl-[1,1'-biphenyl]-2-carbaldehyde in an isomer ratio o:m:p = 1.6:1:1. (*) Signals corresponding to solvent (chloroform and H_2O) and grease.

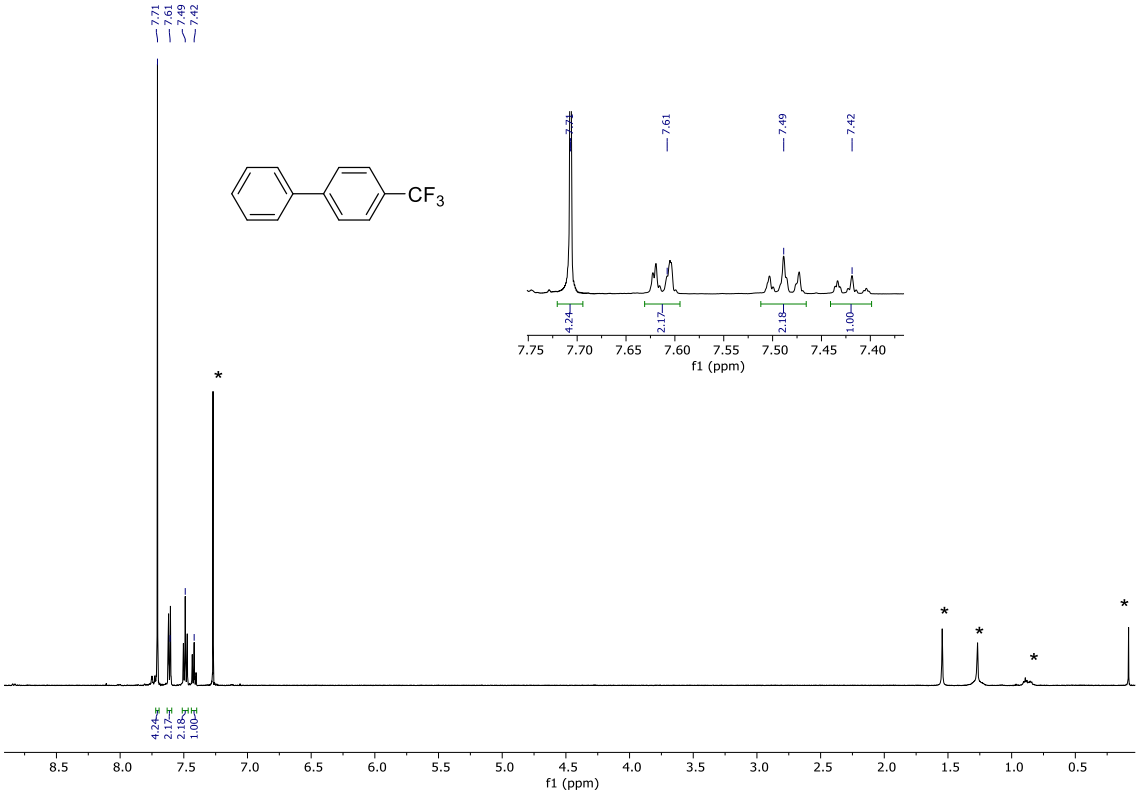


Figure S38. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of 4-(trifluoromethyl)biphenyl (**3ba**). (*) Signals corresponding to solvent (chloroform and H_2O) and grease.

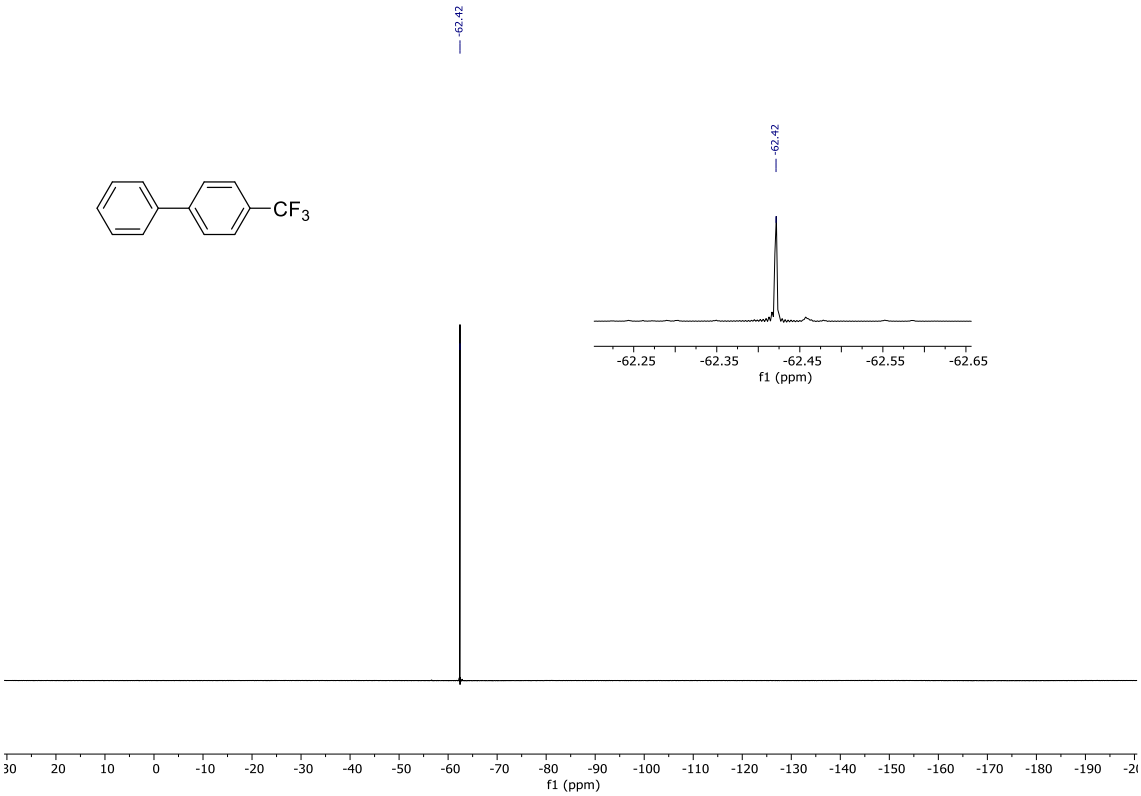


Figure S39. ^{19}F NMR spectra (470.168 MHz, $CDCl_3$) of 4-(trifluoromethyl)biphenyl (**3ba**).

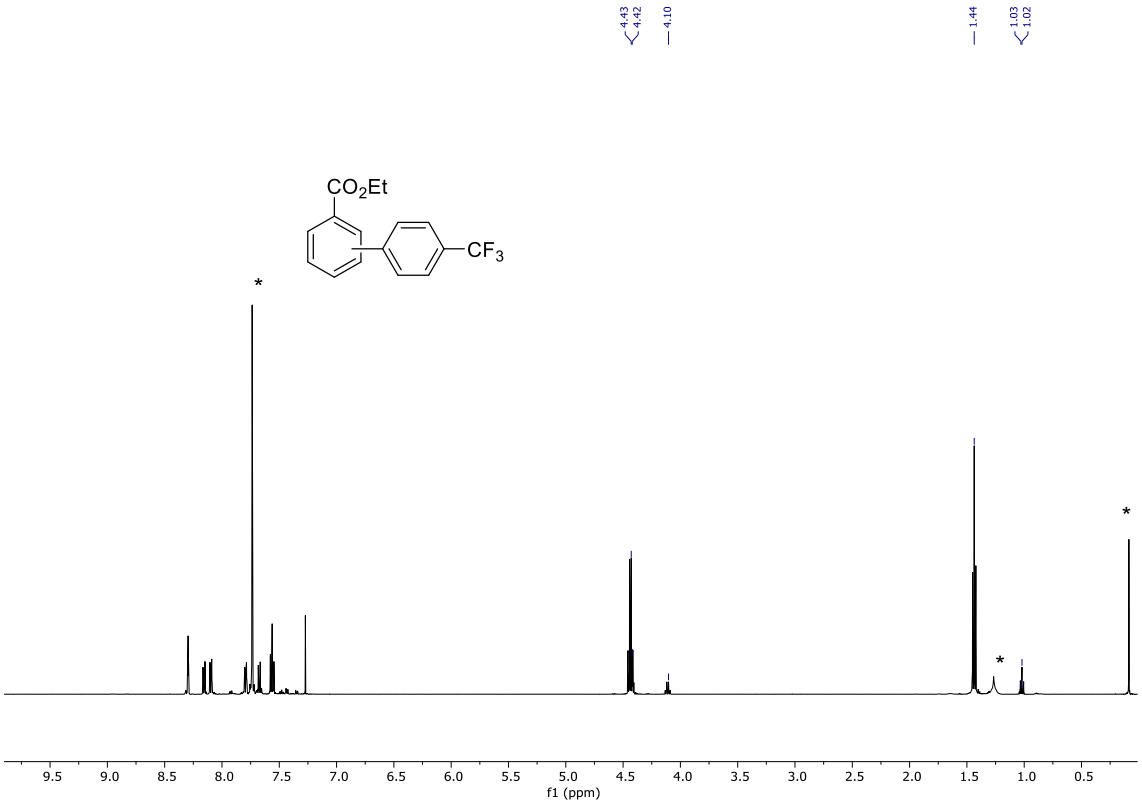


Figure S40. [1]H NMR spectra (500.13 MHz, $CDCl_3$) of **3ca**, mixture of isomers ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate, ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-3-carboxylate and ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate. (*) Signals corresponding to solvent (chloroform and water) and grease.

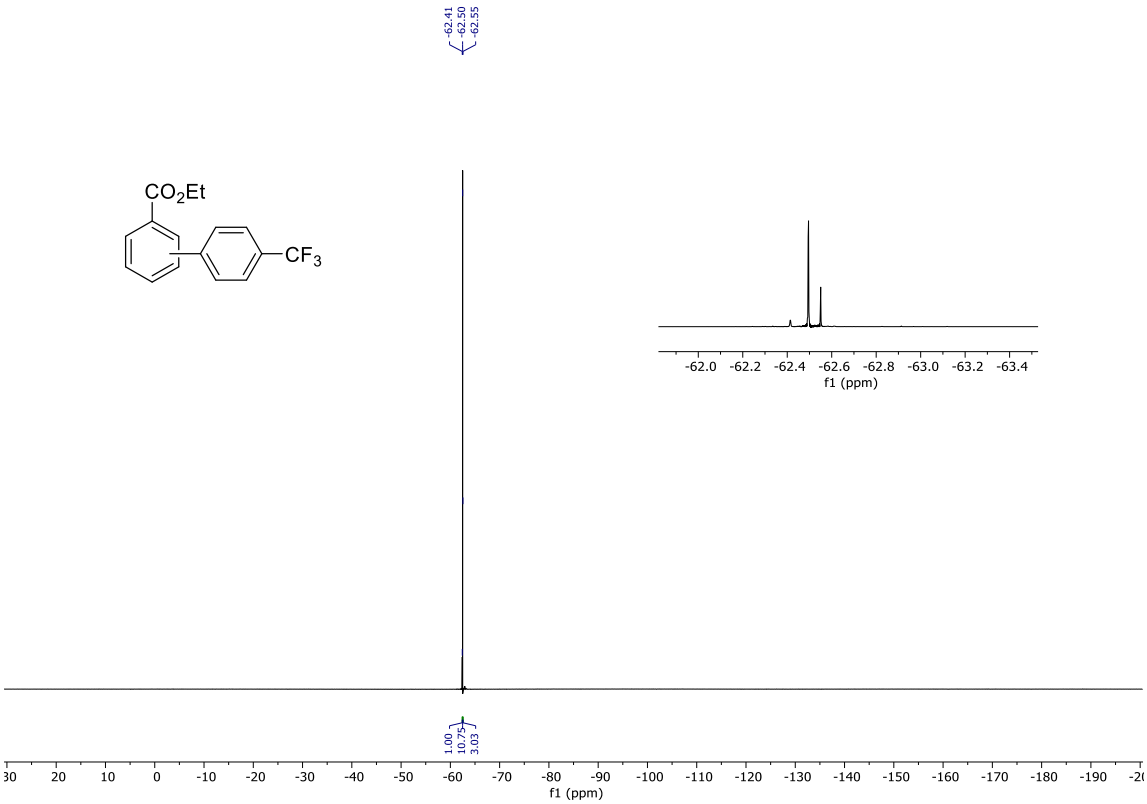


Figure S41. [19]F NMR spectra (470.168 MHz, $CDCl_3$) of **3ca**, mixture of ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate, ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-3-carboxylate and ethyl 4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate in an isomer ratio o:m:p = 1:10:3.

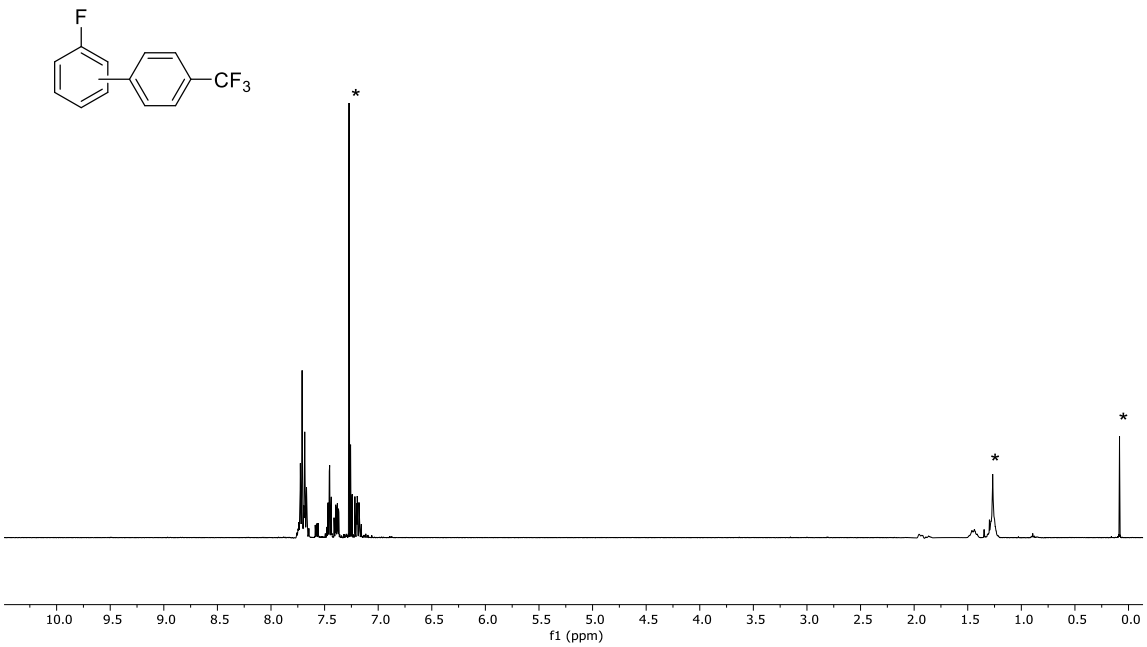


Figure S42. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3da**, mixture of isomers 2-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl, 3-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl and 4-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl. (*) Signals corresponding to solvent (chloroform and H_2O) and grease.

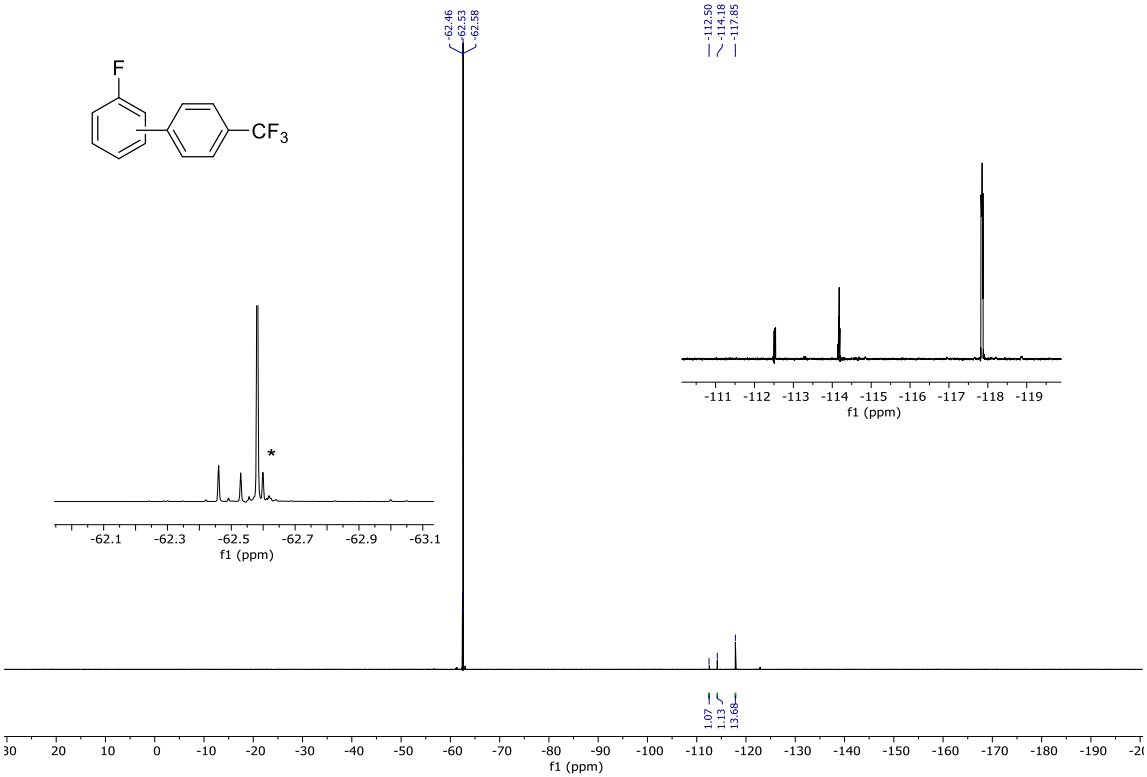


Figure S43. ^{19}F NMR spectra (470.168 MHz, $CDCl_3$) of **3da**, mixture of 2-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl, 3-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl and 4-fluoro-4'-(trifluoromethyl)-1,1'-biphenyl in an isomer ratio o:m:p = 14:1.1:1. (*) Signal corresponding to the Ar-Ar homocoupling product (Ar = *p*-$CF_3C_6H_4$).

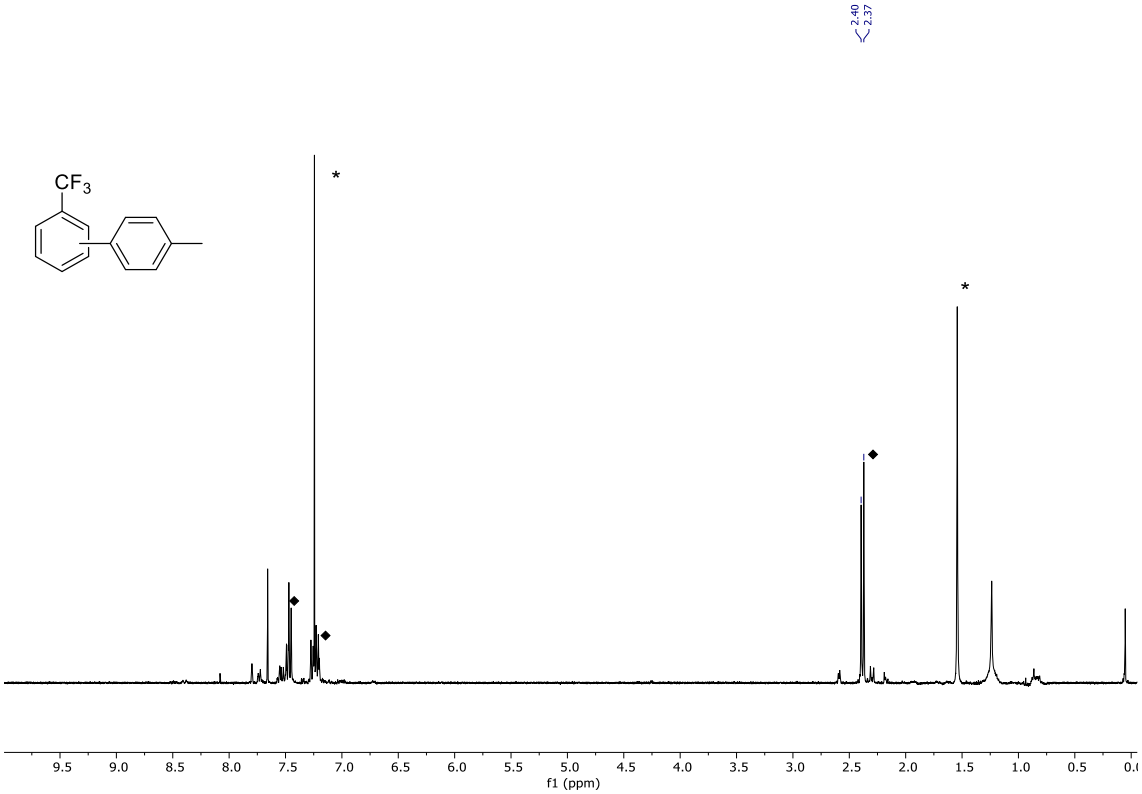


Figure S44. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3ef**, mixture of 4-methyl-3'-(trifluoromethyl)-biphenyl and 4-methyl-4'-(trifluoromethyl)biphenyl in isomer ratio o:m:p = 0:5:1. Some homocoupling derivative, 4,4'dimethyl biphenyl (◆) is also observed. (*) Signals corresponding to solvent (chloroform and H_2O).

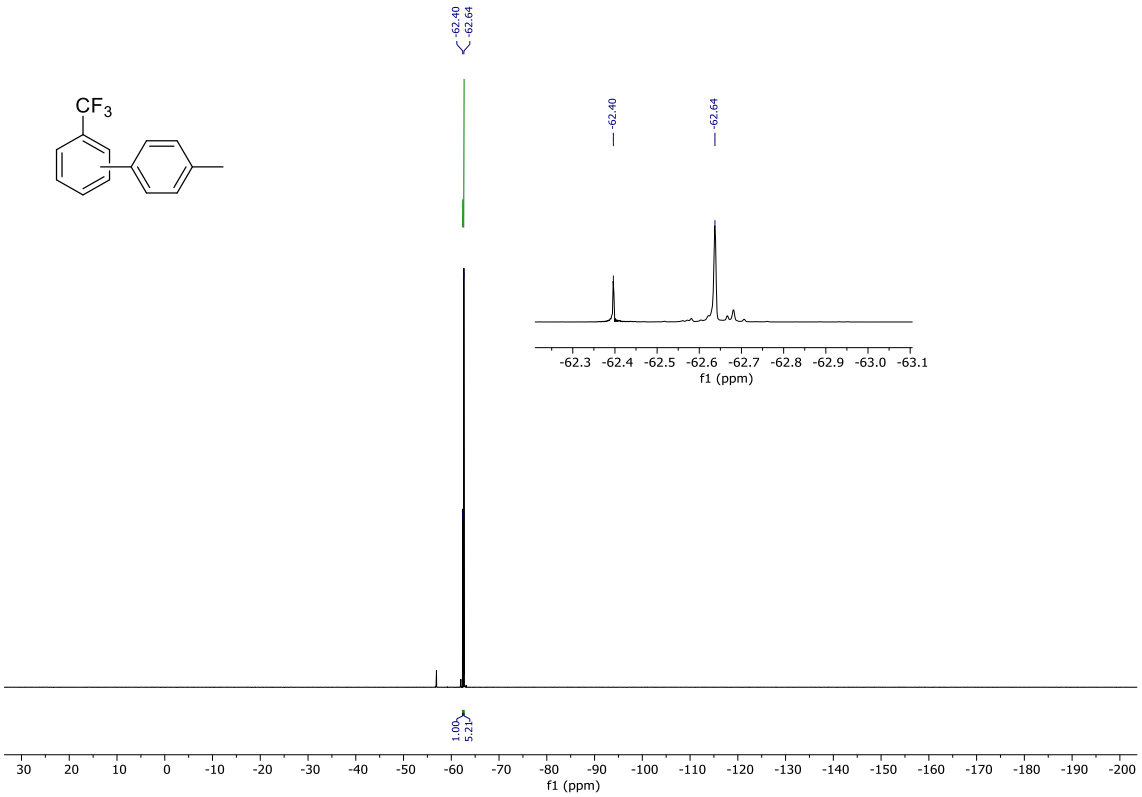


Figure S45. ^{19}F NMR spectra (470.168 MHz, $CDCl_3$) of **3ef**, mixture of 4-methyl-3'-(trifluoromethyl)biphenyl and 4-methyl-4'-(trifluoromethyl)biphenyl in an isomer ratio o:m:p =0:5:1.

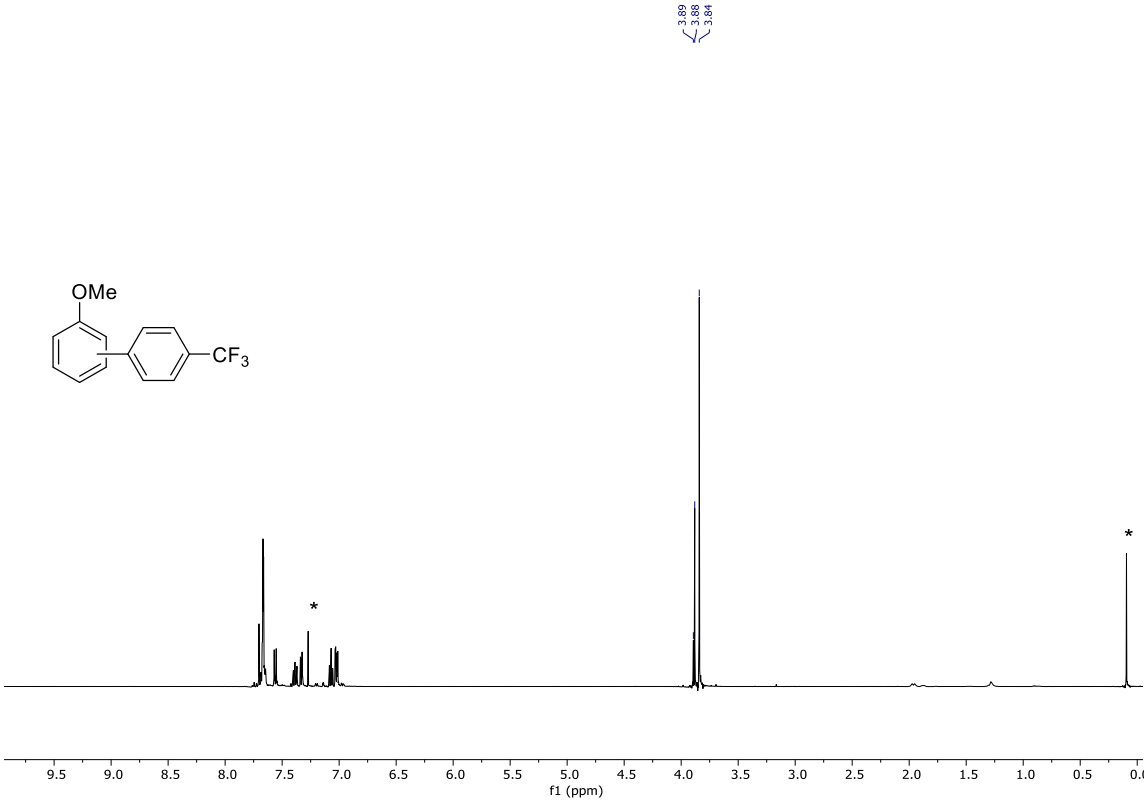


Figure S46. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3ga**, mixture of isomers 2-methyl-4'-(trifluoromethyl)-1,1'-biphenyl, 3-methyl-4'-(trifluoromethyl)-1,1'-biphenyl and 4-methyl-4'-(trifluoromethyl)-1,1'-biphenyl. (*) Signals corresponding to solvent (chloroform) and silicone grease.

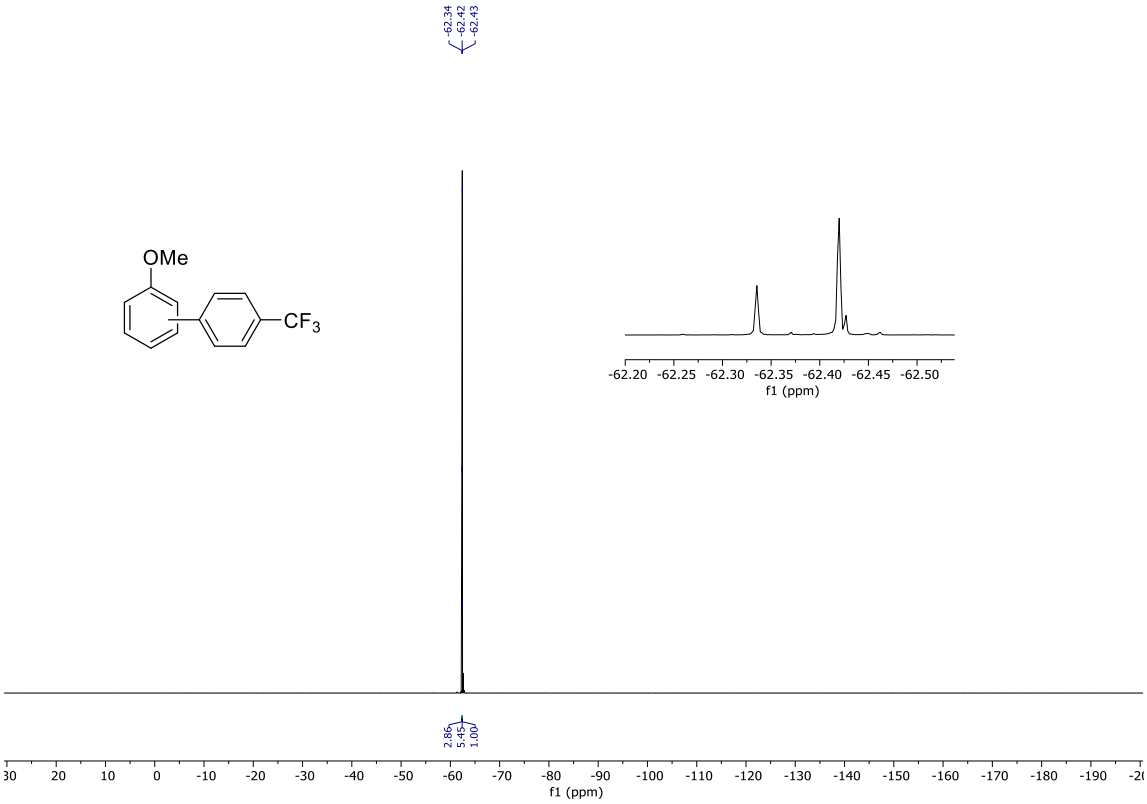


Figure S47. ^{19}F NMR spectra (470.168 MHz, $CDCl_3$) of **3ga**, mixture of 2-methyl-4'-(trifluoromethyl)-1,1'-biphenyl, 3-methyl-4'-(trifluoromethyl)-1,1'-biphenyl and 4-methyl-4'-(trifluoromethyl)-1,1'-biphenyl in isomer ratio o:m:p = 5.5:1:2.9.

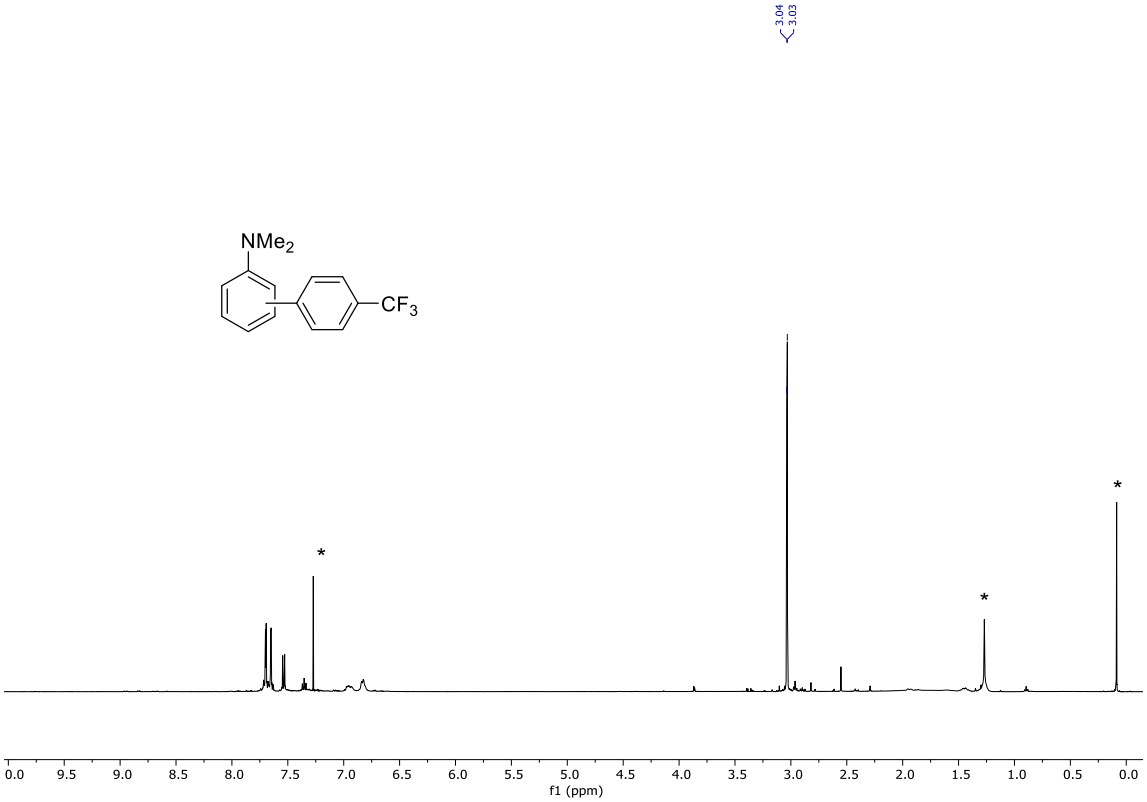


Figure S48. ^{1}H NMR spectra (500.13 MHz, $CDCl_3$) of **3ha**, mixture of isomers *N, N*-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-3-amine and *N, N*-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-4-amine. (*) Signals corresponding to solvent (chloroform and H_2O) and grease.

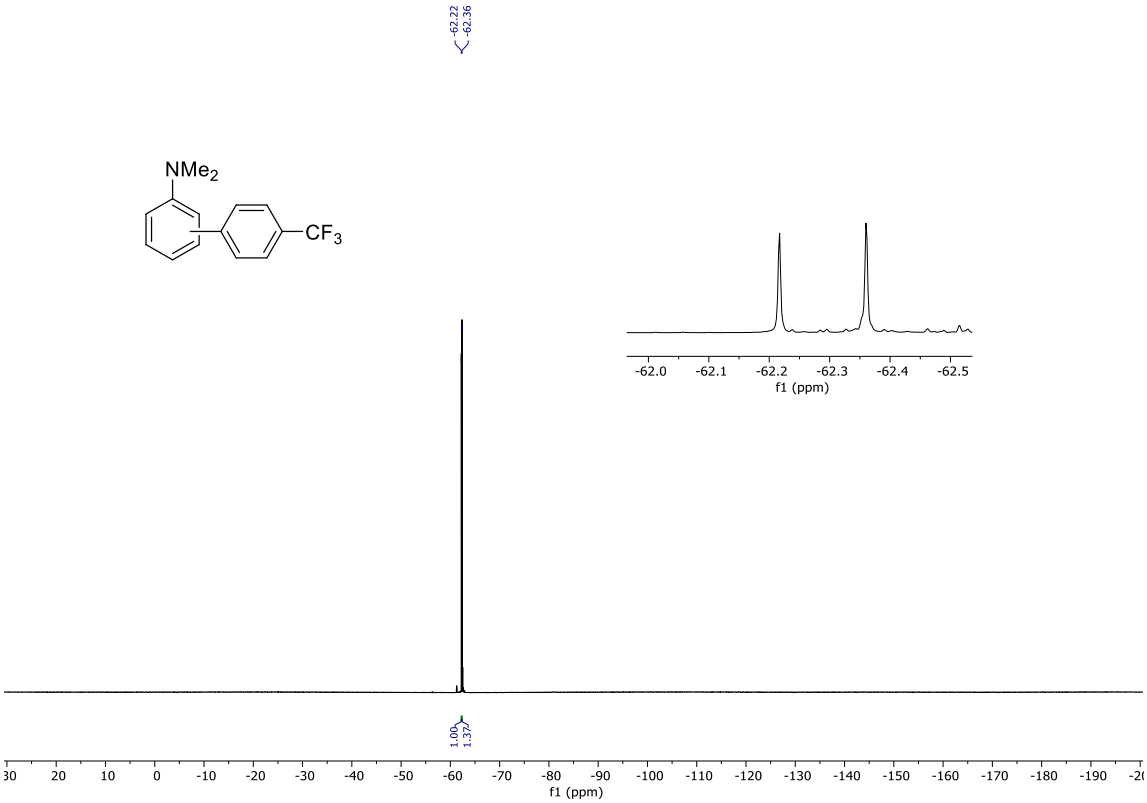


Figure S49. ^{19}F NMR spectra (470.168 MHz, $CDCl_3$) of **3ha**, mixture of *N, N*-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-3-amine and *N, N*-dimethyl-4'-(trifluoromethyl)[1,1'-biphenyl]-4-amine in isomer ratio o:m:p = 0:1.4:1.

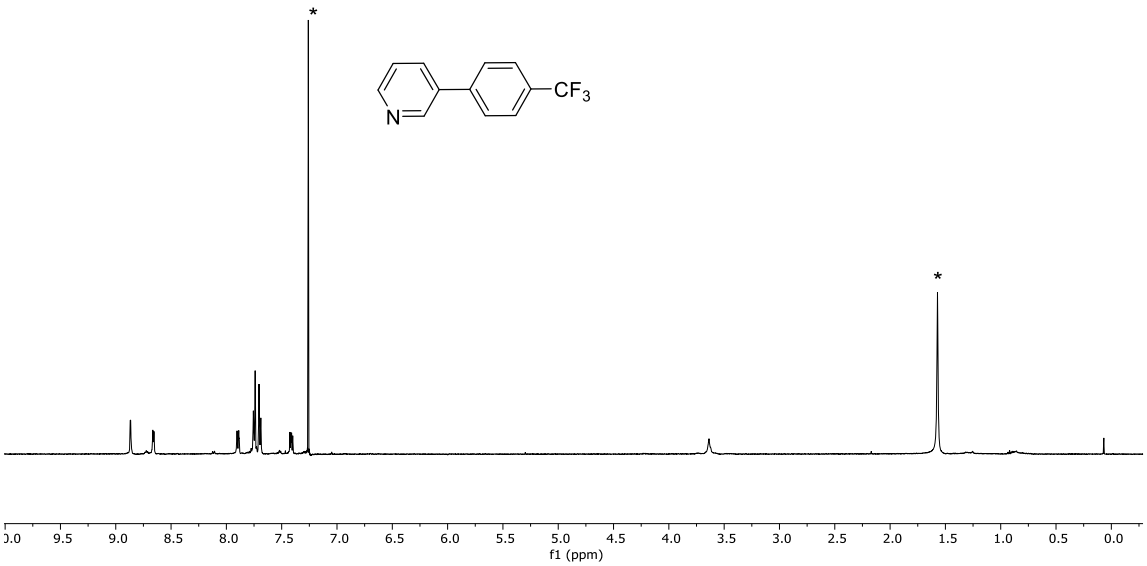


Figure S50. [1]H NMR spectra (500.13 MHz, $CDCl_3$) of 3-(3-(trifluoromethyl)phenyl)pyridine (**3ka**). (*) Signals corresponding to solvent (chloroform and H_2O).

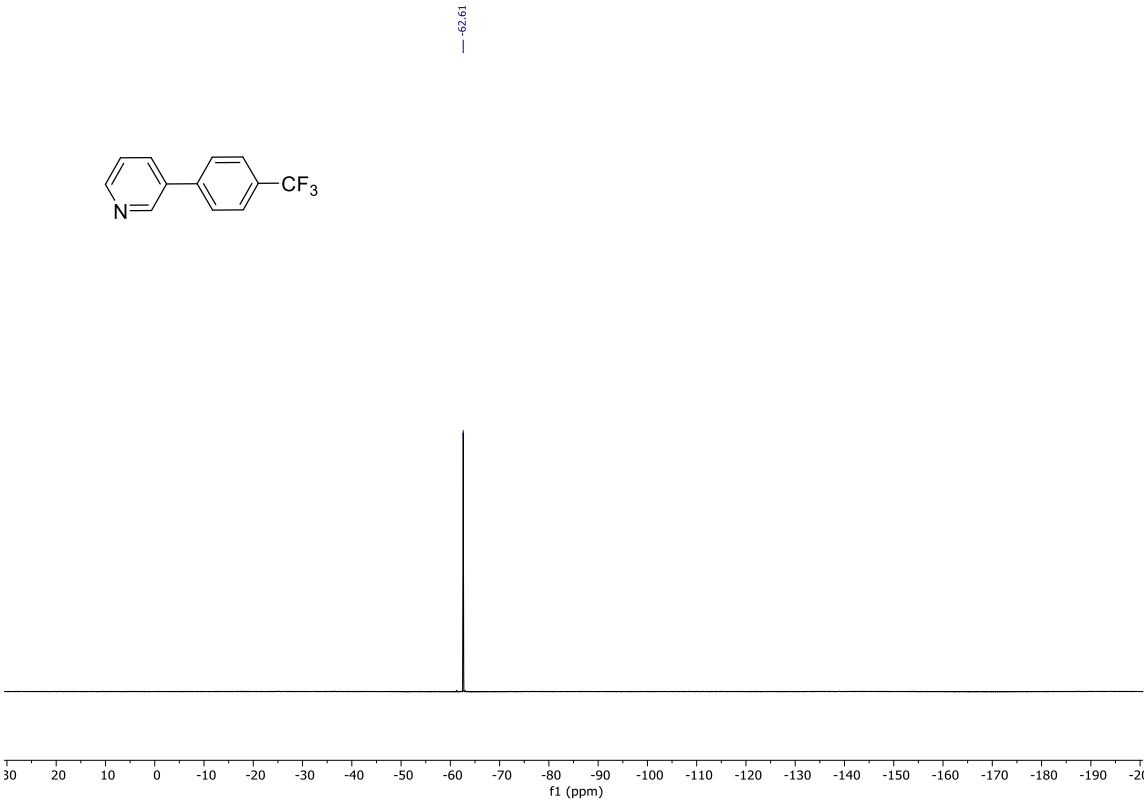


Figure S51. [19]F NMR spectra (470.168 MHz, $CDCl_3$) of 3-(3-(trifluoromethyl)phenyl)pyridine (**3ka**).

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