
Supplementary information

Lewis acid-mediated Suzuki–Miyaura cross-coupling reaction

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Supplementary Information for

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Supplementary Note: Instrumentation and chemicals

All reactions were performed under argon atmosphere unless otherwise indicated. All manipulations of air- and/or moisture-sensitive compounds were performed either using standard Schlenk techniques or in a MIWA DBO-1KH-NYWS glovebox under an atmosphere of argon. Unless otherwise noted, zinc-mediated Suzuki–Miyaura cross-coupling (SMC) reactions were conducted in a 4 mL (15 × 45 mm) screw-thread clear vial (Thermo Scientific, Cat. No. C4015-1) with a cap assembled with a septum (Thermo Scientific, Cat. No. C4015-75A).

Analytical thin-layer chromatography (TLC) was performed on precoated (0.25 mm) silica-gel plates (Merck, Merck Silica Gel 60 F₂₅₄). Column chromatography was conducted by hand using silica-gel (SiliCycle Inc., SiliaFlash) or on a YAMAZEN Automated Flash Chromatography System that consists of AI-580 and Parallel Frac FR-360 with silica-gel-packed column (Biotage Zip cartridge). Recycling preparative high-performance liquid chromatography (HPLC) was performed by LC-Forte/R (YMC Co., Ltd.) with high-resolution gel permeation chromatography (GPC) column (YMC Co., Ltd., YMC-GPC T-2000).

Melting points (mp) were measured with an OptiMelt automated melting point apparatus (Stanford Research Systems, Inc.) and were uncorrected.

¹H NMR (400 MHz), ¹³C{¹H} NMR (100 MHz), ¹⁹F NMR (373 MHz), ¹¹B NMR (127 MHz), and ³¹P NMR (160 MHz) spectra were obtained from measurements at ambient temperature on a JEOL 400SS spectrometer unless otherwise noted. Chloroform-*d*₁ (CDCl₃) containing 0.05% tetramethylsilane (TMS) (99.8%D, Cambridge Isotope Laboratories, Inc.), acetone-*d*₆ (99.9%D, Merck KGaA), dimethyl sulfoxide-*d*₆ (DMSO-*d*₆, 99.9%D, Cambridge Isotope Laboratories, Inc.), methanol-*d*₄ (MeOH-*d*₄, 99.8%D, Merck KGaA), or tetrahydrofuran-*d*₈ (THF-*d*₈, 99.5%D, Eurisotop) was used as a solvent for NMR measurements. Chemical shifts (δ) for are given in parts per million (ppm) downfield from signal of TMS (δ 0.00 ppm for ¹H NMR), CDCl₃ (δ 77.20 ppm for ¹³C{¹H} NMR), residual acetone (δ 2.05 ppm for ¹H NMR), acetone-*d*₆ (δ 29.84 ppm for ¹³C{¹H} NMR), residual DMSO (δ 2.50 ppm for ¹H NMR), DMSO-*d*₆ (δ 39.52 ppm for ¹³C{¹H} NMR), residual MeOH (δ 3.31 ppm for ¹H NMR), MeOH-*d*₄ (δ 49.00 ppm for ¹³C{¹H} NMR), residual THF (δ 1.72 ppm for ¹H NMR), and THF-*d*₈ (δ 25.31 ppm for ¹³C{¹H} NMR) as an internal standard with coupling constants (*J*) in hertz (Hz). For chemical shifts of ¹⁹F, ¹¹B, and ³¹P NMR, (trifluoromethyl)benzene (δ –63.0 ppm in CDCl₃ for ¹⁹F NMR), BF₃·OEt₂ (δ 0.00 ppm in CDCl₃ for ¹¹B NMR), or 85% H₃PO₄ (δ 0.00 ppm in D₂O for ³¹P NMR) was used as an external standard, respectively. The abbreviations s, d, t, q, m, and br signify singlet, doublet, triplet, quartet, multiplet, and broad, respectively.

Infrared (IR) spectra were measured by attenuated total reflection (ATR) method on a Shimadzu IRPrestige-21 spectrometer equipped with a PIKE Technologies MIRacle™ single reflection ATR optical attachment and a ZnSe crystal plate at room temperature unless otherwise noted. The absorption bands are given in wavenumber (cm⁻¹).

High-resolution mass spectra (HRMS) were measured on a Thermo Fisher Scientific Exactive™ Plus Orbitrap mass spectrometer under positive or negative electrospray ionization (ESI⁺ or ESI⁻) conditions. Theoretical values of molecular weights were calculated on Qual Browser built in Thermo Xcalibur 4.0.27.19.

Single crystal X-ray diffraction data were measured at 90 K with a RIGAKU AFC-8 diffractometer equipped a Saturn70 CCD detector. The structures were solved by a dual space method with the SHELXT-2018/2 program,²⁹ and were refined by a full-matrix least-squares method with the SHELXL-2018/3 program.³⁰

Powder X-ray diffraction data were collected on a Rigaku SmartLab by $\theta/2\theta$ scans in a reflection geometry using Cu-K α radiation ($\lambda = 1.54187$ Å) (40 kV, 30 mA) at room temperature.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. (*N,N,N',N'*-Tetramethylethylenediamine)zinc(II) dibromide ((tmeda)ZnBr₂),¹ (1,5-cyclooctadiene)bis(trimethylsilylmethyl)palladium(II) ((cod)Pd(CH₂TMS)₂),² 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene](chloro)silver(I),³ indomethacin methyl ester,⁴ and ethyl 2-acetylamino-6-bromo-7-[2-(*N,N*-diethylamino)ethyloxy]benzo[*b*]thiophene-3-carboxylate⁵ were prepared according to the reported procedure.

4-Fluorobromobenzene (**1**), zinc(II) triflate (Zn(OTf)₂), *N,N,N',N'*-tetramethylethylenediamine (TMEDA), copper(II) triflate (Cu(OTf)₂), potassium hydrogen difluoride (KHF₂), phenylboronic acid (**2b**), triphenylboroxine (**2c**), phenylboronic acid pinacol ester (**2d**), phenylboronic acid neopentyl glycol ester (**2e**), MIDA boronate (**2f**), phenyl(naphthalene-1,8-diamino)boron (**2g**), 4-bromobiphenyl, triphenyl phosphine, tri(4-methylphenyl)phosphine, tri(4-fluorophenyl)phosphine, tri(2-furyl)phosphine, triphenylarsine, tricyclopentylphosphine, 1,1'-bis(diphenylphosphino)ferrocene, 2-methyltetrahydrofuran (2-MeTHF), 4-trifluoromethoxybromobenzene, *N*-butoxycarbonylpyrrol-2-ylboronic acid, 1,1,2,2-tetrachloroethane, 1-bromo-*N,N*-dimethylaniline, 4-chloroanisole, 2-(3-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 1-bromo-3,5-diformylbenzene, 2-amino-4'-bromobenzophenone, 2-bromopyridine, 5-bromo-1-methylindole, 4-bromoisoquinoline, penfluridol, indomethacin, nicergoline, 4-fluorophenyl(trifluoro)borate, potassium 4-

methoxy(trifluoro)phenyl borate, 4-hydroxyphenylboronic acid, and cloperastine were purchased from Tokyo Chemical Industry Co., Ltd.

Potassium phenyl(trifluoro)borate (**2a**), 1-fluoro-4-trifluoromethylbenzene, $\text{Pd}_2(\text{dba})_3$, potassium acetate (KOAc), silver(I) triflate (AgOTf), silver(I) tetrafluoroborate (AgBF_4), indium triflate ($\text{In}(\text{OTf})_3$), lanthanum(III) triflate ($\text{Ln}(\text{OTf})_3$), bismuth(III) triflate ($\text{Bi}(\text{OTf})_3$), samarium(III) triflate ($\text{Sm}(\text{OTf})_3$), iron (II) triflate ($\text{Fe}(\text{OTf})_2$), lithium triflate (LiOTf), dicyclohexyl(4-dimethylaminophenyl)phosphine (Cy-Amphos), di(*tert*-butyl)phenylphosphine, dicyclohexyl(phenyl)phosphine, tri(*tert*-butyl)phosphine, di(*tert*-butyl)methylphosphine, biphenyl-2-yl(di-*tert*-butyl)phosphine (JohnPhos), biphenyl-2-yl(dicyclohexyl)phosphine (CyJohnPhos), 2-di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl ($\text{Me}_4'\text{BuXPhos}$), 2-di-*tert*-butylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl ($'\text{BuXPhos}$), 2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl (XPhos), 2-dicyclohexylphosphino-2',6'-triisopropoxy-1,1'-biphenyl (RuPhos), 2-dicyclohexylphosphino-2'-dimethylamino-1,1'-biphenyl (DavePhos), 1,3-bis(diphenylphosphino)propane, 1,2-bis(dicyclohexyl)phosphinoethane, 4,4'-di(*tert*-butyl)-2,2-bipyridyl, pentafluorophenylboronic acid, (1,1'-bis(diphenylphosphino)ferrocene)dichloropalladium(II) dichloromethane adduct ($\text{PdCl}_2(\text{dppf})\cdot\text{CH}_2\text{Cl}_2$) potassium 4-carboxyphenyl(trifluoro)borate, potassium (2-fluoropyrimidin-5-yl)(trifluoro)borate, 7-bromo-4-hydroxy-2*H*-chromen-2-one, potassium 3-furanyl(trifluoro)borate, 2-thienyl(trifluoro)borate, potassium 4-chlorophenyl(trifluoro)borate, potassium 2,6-dimethylphenyl(trifluoro)borate, potassium 2,6-difluorophenyl(trifluoro)borate, potassium dibenzothiophene-2-yl(trifluoro)borate, potassium 1-propen-2-yl(trifluoro)borate, and potassium (2-chloropyridin-3-yl)(trifluoro)borate were purchased from Sigma–Aldrich Japan Inc.

Bis(di-*tert*-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II) ($\text{PdCl}_2(\text{amphos})_2$), di-*tert*-butyl(4-dimethylaminophenyl)phosphine (Amphos), potassium 4-nitrophenyl(trifluoro)borate, potassium 4-hydroxyphenyl(trifluoro)borate, potassium 4-cyanophenyl(trifluoro)borate, and potassium trifluoro(4-trifluorophenyl)borate were purchased from BLD Pharmtech Ltd.

Tetrahydrofuran (THF, deoxidized), *n*-hexane (deoxidized), benzene (super dehydrated), 1,4-dioxane (super dehydrated), cyclopentyl methyl ether (CPME, super dehydrated), *N,N*-dimethylformamide (DMF, deoxygenated), acetonitrile (MeCN, super dehydrated), methanol (MeOH, deoxidized), zinc oxide (ZnO), tetra(*n*-butyl)ammonium trifluoromethanesulfonate (TBAOTf), bis(pinacolato)diboron (B_2pin_2), and pyridine-*d*₅ were purchased from FUJIFILM Wako Pure Chemical Corporation.

Acetonitrile (MeCN), diethyl ether (Et_2O), THF, nickel(II) triflate ($\text{Ni}(\text{OTf})_2$), trimethylsilyl trifluoromethanesulfonate (TMSOTf), trifluoromethanesulfonic acid (TfOH), boron trifluoride

diethyl ether complex ($\text{BF}_3 \cdot \text{OEt}_2$), (trifluoromethyl)benzene, tetra(*n*-butyl)ammonium bromide (TBAB), sodium sulfate (Na_2SO_4), ammonium chloride (NH_4Cl), Celite[®], sodium hydrogen carbonate, chlorobenzene, trifluoroacetic acid (TFA), dipotassium hydrogenphosphate (KH_2PO_4), tri(*n*-butyl)phosphine, magnesium sulfate, potassium hydrogen difluoride (KHF_2), 4-chlorobenzaldehyde, 1-bromomesitylene, zinc(II) bromide (ZnBr_2), ethyl acetate (EtOAc), chloroform (CHCl_3), palladium(II) acetate ($\text{Pd}(\text{OAc})_2$), potassium carbonate (K_2CO_3), sodium carbonate (Na_2CO_3), ethanol (EtOH), and acetone were purchased from Nacalai Tesque, Inc.

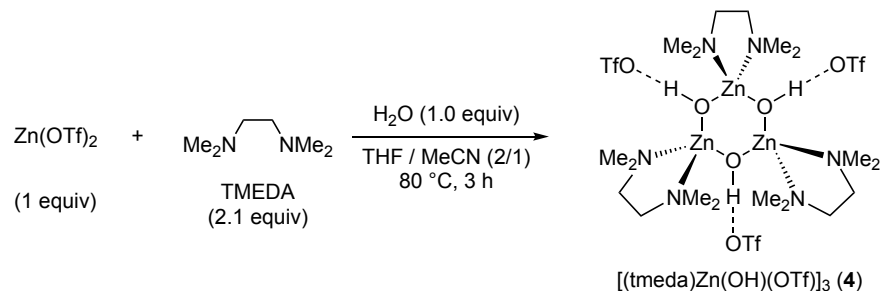
n-Pentane was purchased from Kanto Chemical Co., Ltd. Tri(adamantly)phosphine was purchased from Strem Chemicals, Inc. Tricyclohexylphosphine was purchased from Frontier Scientific Inc. Potassium 2-phenylethynyl(trifluoro)borate was purchased from Apollo Scientific Ltd. 2,3,5,6-Tetrafluorophenylboronic acid was purchased from Alfa Aesar. Boron nitride was purchased from Kojundo Chemical Laboratory Co., Ltd.

Supplementary Method 1: Optimization study for zinc-mediated SMC reaction

General procedure for optimization study

To a 4 mL capped vial equipped with a magnetic stir bar were added a palladium source, a zinc source, a ligand, potassium aryl(trifluoro)borate (1.1 equiv), and a solvent (1.0 mL) in a glovebox filled with argon gas. After stirring for 1 min at room temperature, to this was added aryl halide (0.200 mmol, 1 equiv) in a solvent (0.5 mL). The reaction vial was taken out from the glovebox and stirred for 3 h at 80 °C with an aluminium heat block. After cooling to room temperature, to the reaction mixture was added saturated aqueous NaHCO₃ (ca. 1 mL), Et₂O (ca. 1 mL), and PhCF₃ (12.3 μL, 0.100 mmol). After vigorous stirring, a portion of the organic phase (ca. 0.4 mL) was transferred into an NMR tube, followed by dilution with CDCl₃ (ca. 0.4 mL). ¹⁹F NMR measurement was performed to determine the yield of 4-fluorobiphenyl (**3**) by comparison of an integrated value of the signal that corresponds to the fluorine atom of **3** (δ –115.1 ppm) or **1** (δ –114.2 ppm) with that corresponds to the trifluoromethyl group of PhCF₃ (δ –62.5 ppm). The data are summarized in Supplementary Tables 2–4 and Supplementary Fig. 2.

Preparation of [(tmeda)Zn(OH)(OTf)]₃ (**4**)

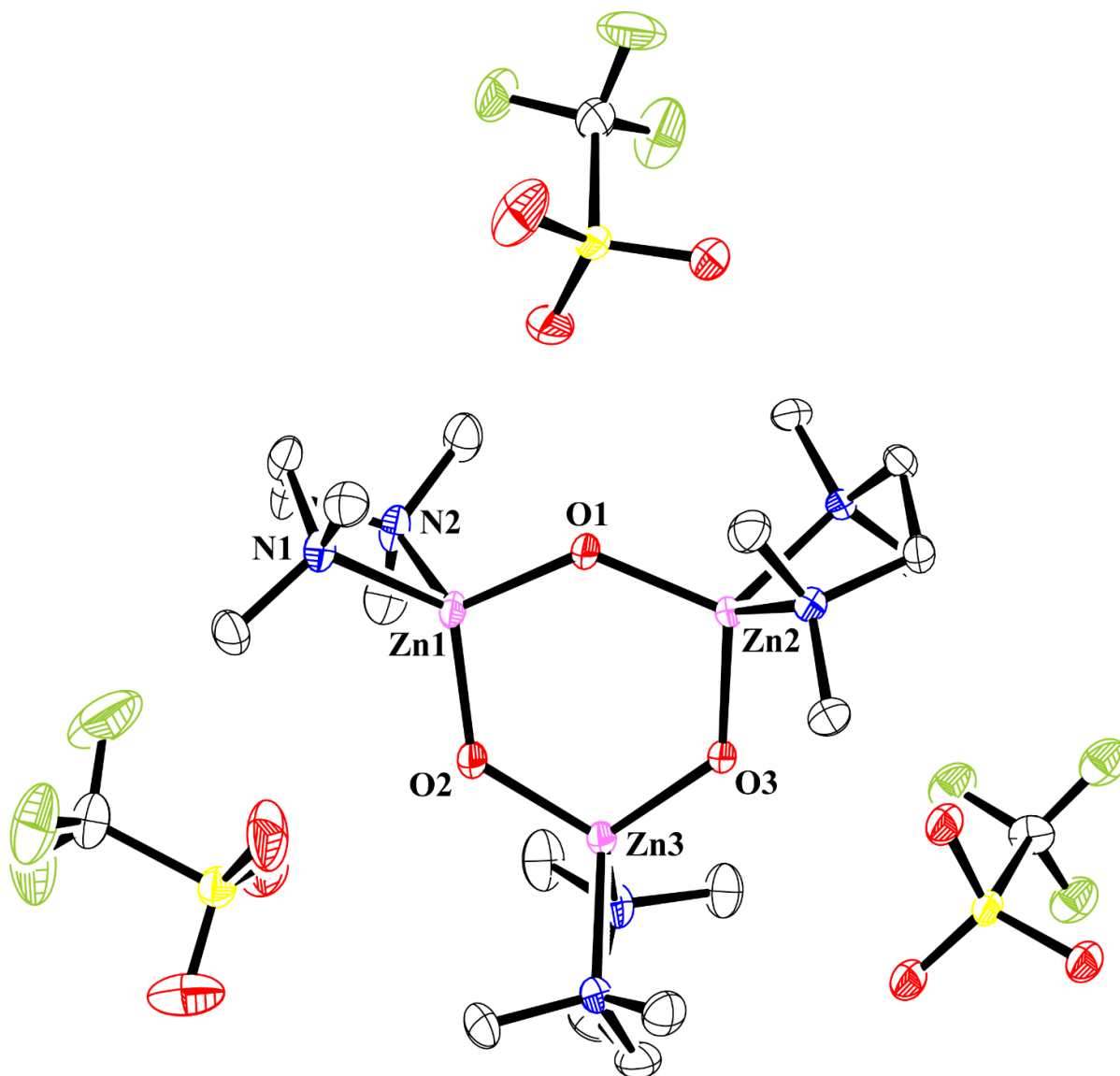


To a round-bottom 500 mL flask equipped with a magnetic stir bar were added Zn(OTf)₂ (10.9 g, 30.0 mmol, 1 equiv), THF (120 mL), and MeCN (24 mL). To this mixture were added water (541 μL, 30.0 mmol, 1.0 equiv) and TMEDA (9.39 mL, 63.0 mmol, 2.1 equiv), and the mixture was stirred for 2 h at 80 °C. After cooling to room temperature, the solvents were removed under reduced pressure, and the residue was dried under vacuum. To this was added THF (ca. 200 mL), the insoluble solid was collected by filtration, washed with Et₂O, and dried under vacuum to give **4** (9.95 g, 9.54 mmol, 95.4%) as a white solid;

Mp: 203–205 °C; ¹H NMR (MeCN-*d*₃) δ 2.85 (s, 6H), 2.80 (s, 6H), 2.60 (s, 18H), 2.53 (s, 18H) (the signal for the proton that corresponds to the hydroxy group was not observed); ¹³C{¹H} NMR (MeCN-*d*₃) δ 57.3 (3C), 54.5 (3C), 47.2 (6C), 44.5 (6C) (the signal for the carbon that corresponds to the triflate group was not observed); ¹⁹F NMR (MeCN-*d*₃) δ –79.3; ¹H NMR (DMSO-*d*₆) δ 3.49 (br, 3H), 2.37 (s, 12H), 2.19 (s, 36H); ¹³C{¹H} NMR (DMSO-*d*₆) δ 120.7 (q, *J*_{C–F} = 322.3 Hz, 3C),

56.2 (6C), 46.1 (12C); ^{19}F NMR ($\text{DMSO-}d_3$) δ -77.7 ; IR (ZnSe , cm^{-1}) 1470, 1246, 1223, 1153, 1128, 1026, 1009, 951, 802, 637.

Single crystals suitable for X-ray diffraction measurement were prepared by vapor-diffusion crystallization from a saturated solution of the product in MeCN with a THF vapor at room temperature to afford a trimer with 1.5 equivalents of MeCN. The crystallographic data are shown in Supplementary Table 1.



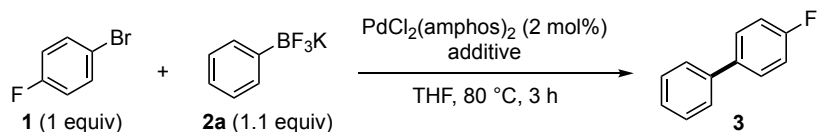
Supplementary Fig. 1. ORTEP drawing of 4 with thermal ellipsoids at the 50% probability level. CCDC reference number is 2073815. All hydrogen atoms and solvent molecules (MeCN) are omitted for clarity. Selected bond length ($\text{\AA}$) and angle (deg): Zn1–O1 1.9086(13), Zn1–O2 1.9057(14), Zn1–N1 2.0809(15), Zn1–N2 2.0809(17), Zn1–O1–Zn2 129.68(8), O1–Zn1–O2 108.76(6), and N1–Zn1–N2 88.47(6).

Supplementary Table 1. Crystallographic data of 4.

Complex	4
empirical formula	C ₂₄ H _{55.50} F ₉ N _{7.5} O ₁₂ S ₃ Zn ₃
formula weight	1104.55
color, description	Colorless, block
temperature, K	90
cryst. System	monoclinic
space group	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> , Å	15.75023(13)
<i>b</i> , Å	12.09484(10)
<i>c</i> , Å	24.5087(2)
α , °	90
β , °	90.4156(7)
γ , °	90
<i>V</i> , Å ³	4668.70(7)
<i>Z</i>	4
calculated density, Mg·m ⁻³	1.571
$2\theta_{max}$, °	32.671
limiting indices	$-23 \leq h \leq 22, -18 \leq k \leq 18, -35 \leq l \leq 35$
absorption coefficient, mm ⁻¹	1.755
<i>F</i> (000)	2268.00
crystal size, mm	0.153 × 0.131 × 0.125
goodness-of-fit on <i>F</i> ²	1.081
reflections collected / unique	127096 / 16078 [R(int) = 0.0271]
no. of variables	575
<i>R</i> ₁ , <i>wR</i> ₂ [<i>I</i> > 2σ(<i>I</i>)] ^a	0.0386, 0.1004
<i>R</i> ₁ , <i>wR</i> ₂ (all data) ^a	0.0417, 0.1023
residual electron density, e·Å ⁻³	1.308 (max), -0.951 (min)

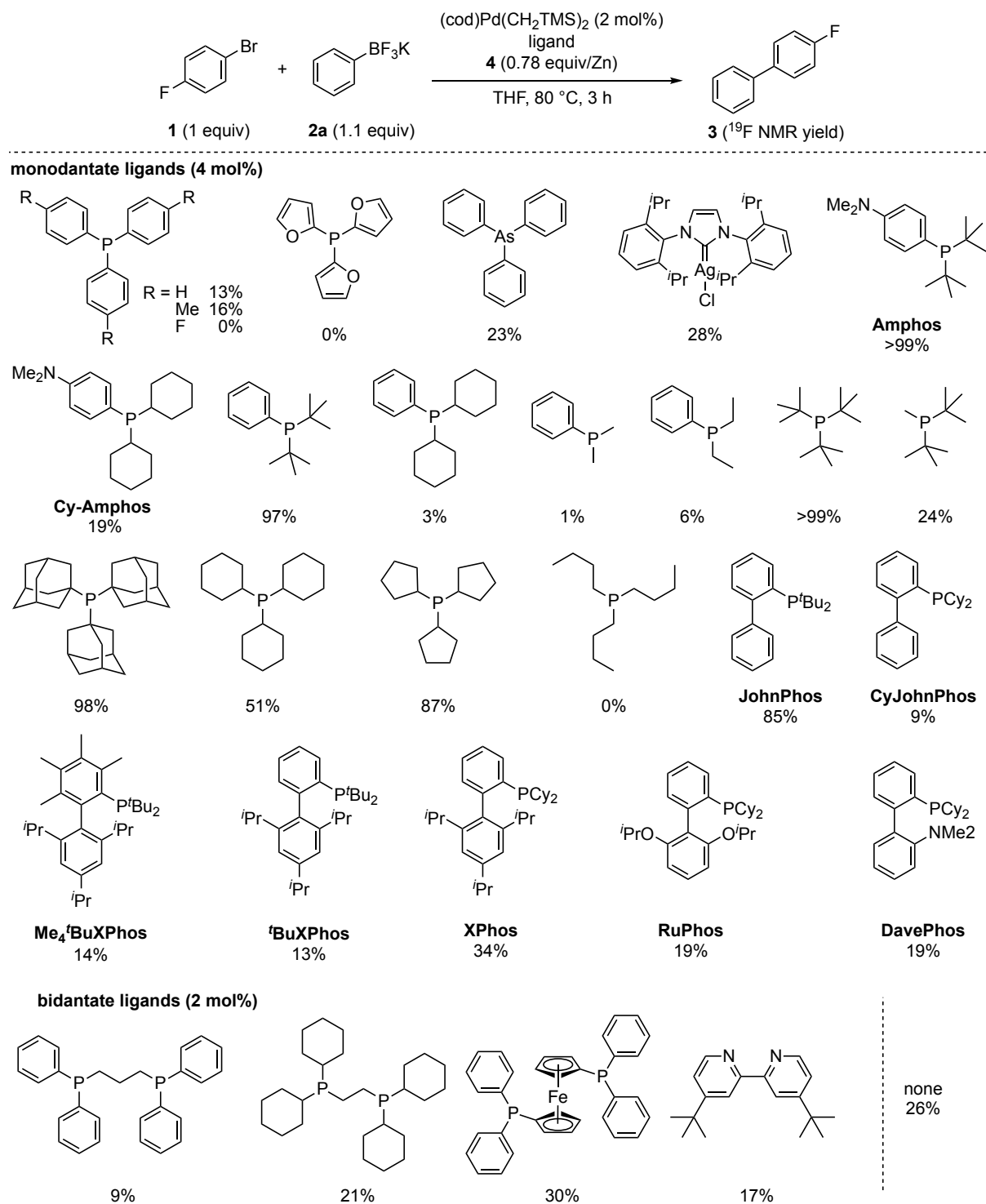
^a*R*₁ = (Σ||*F*_o| - |*F*_c||) / Σ|*F*_o|. *wR*₂ = [Σ*w*(*F*_o² - *F*_c²)² / Σ(*wF*_o⁴)]^{1/2}; The function minimized: *w*(*F*_o² - *F*_c²)².

Supplementary Table 2. Optimization of Lewis acid.



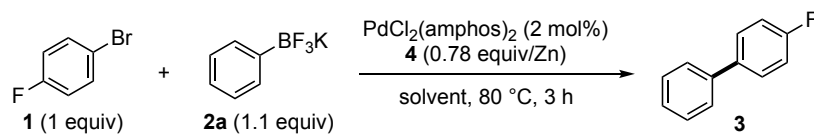
entry	additive	Yield of 3 (%) ^a
1	4 (0.78 equiv/Zn)	>99
2	Zn(OTf) ₂ (0.72 equiv)	50
3	Zn(OTf) ₂ (0.6 equiv), TMEDA (0.72 equiv)	53
4	In(OTf) ₃ (0.72 equiv)	18
5	In(OTf) ₃ (0.6 equiv), TMEDA (0.72 equiv)	71
6	Cu(OTf) ₂ (0.6 equiv), TMEDA (0.72 equiv)	27
7	Ni(OTf) ₂ (0.6 equiv), TMEDA (0.72 equiv)	10
8	Fe(OTf) ₂ (0.6 equiv), TMEDA (0.72 equiv)	6
9	Ln(OTf) ₃ (0.6 equiv), TMEDA (0.72 equiv)	1
10	Bi(OTf) ₃ (0.6 equiv), TMEDA (0.72 equiv)	11
11	Sm(OTf) ₃ (0.6 equiv), TMEDA (0.72 equiv)	5
12	LiOTf (0.6 equiv), TMEDA (0.72 equiv)	0
13	(tmeda)ZnBr ₂ (1.1 equiv)	0
14	AgOTf (1.2 equiv)	8
15	AgBF ₄ (1.2 equiv)	9
16	TMSOTf (2 equiv)	0
17	TfOH (1.2 equiv)	0
18	TMEDA (2 equiv)	0
19	KHF ₂ (2 equiv)	0

^aDetermined by ¹⁹F NMR analysis.



Supplementary Fig. 2. Optimization of ligand of palladium catalyst.

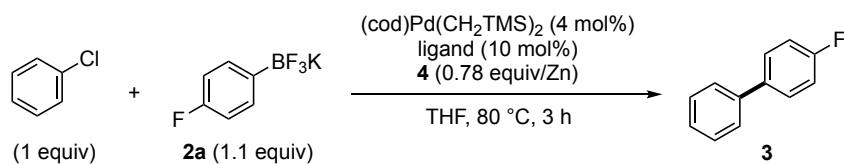
Supplementary Table 3. Optimization of solvent.



entry	solvent	yield of 3a (%) ^a
1	<i>n</i> -hexane	42
2	benzene	>99
3	1,4-dioxane	>99
4	CPME	>99
5	2-MeTHF	>99
6	THF	>99
7	DMF	68
8	MeCN	32
9	THF/MeCN (4:1)	50
10	MeOH	32

^aDetermined by ^{19}F NMR analysis.

Supplementary Table 4. Optimization of ligand of palladium catalyst for aryl chloride coupling.

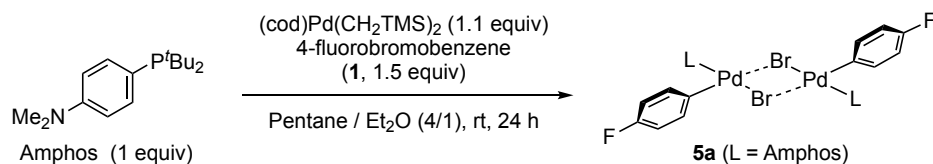


entry	ligand	yield of 3a (%) ^a
1	PCy ₃	12
2	XPhos	49
3	RuPhos	21
4	DavePhos	16
5	^t BuXPhos	11
6	Me ₄ ^t BuXPhos	2
7 ^b	XPhos	58

^aDetermined by ^{19}F NMR analysis. ^bReaction performed in CPME at 120 °C.

Supplementary Method 2: Stoichiometric reactions

Synthesis of **5a**



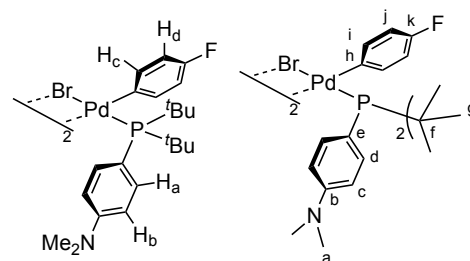
5a was prepared according to the reported procedure with a minor modification.⁶

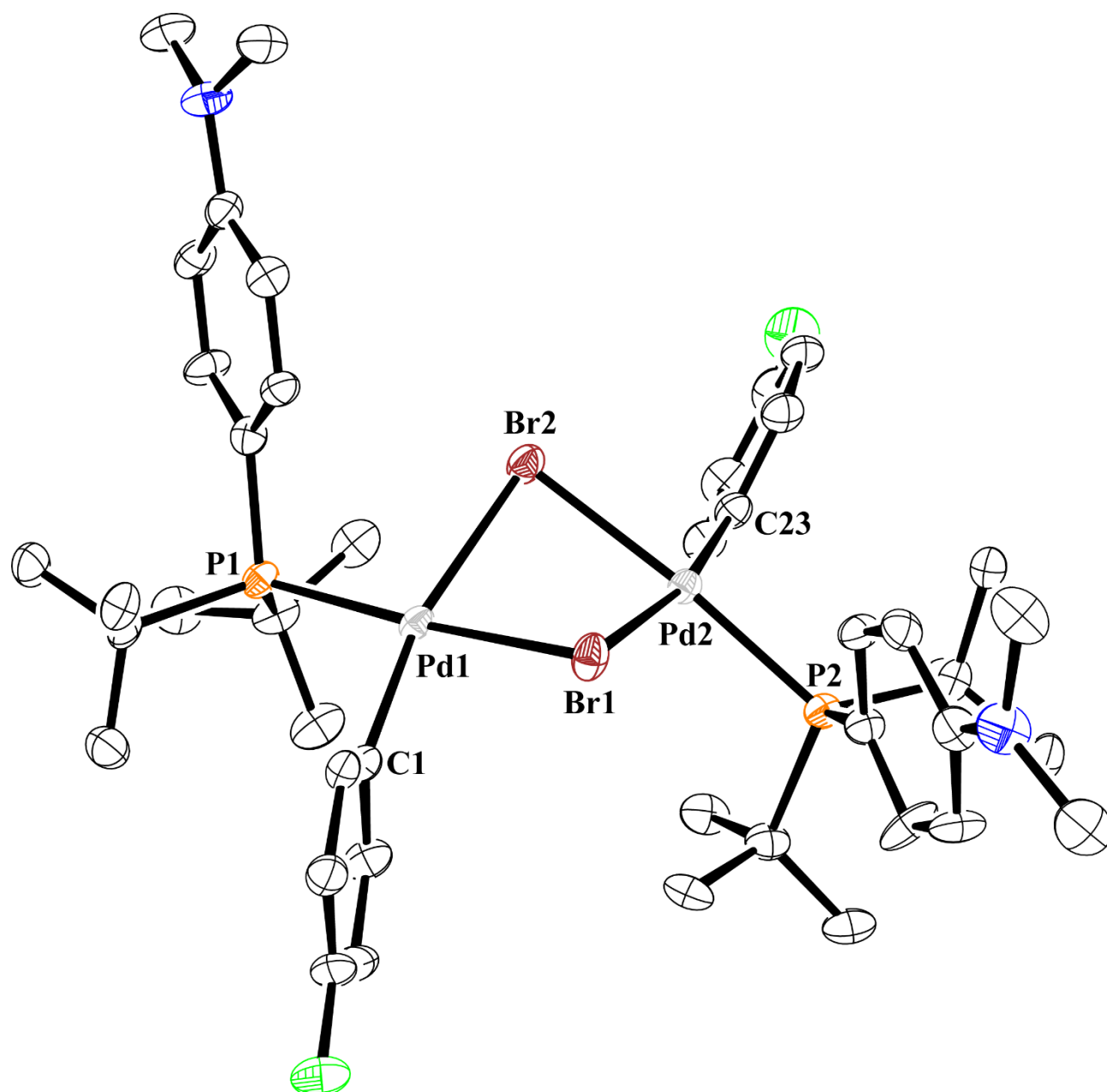
To a 50 mL capped vial were added Amphos (421 mg, 1.59 mmol, 1 equiv), 4-fluorobromobenzene (**1**, 0.261 mL, 2.38 mmol, 1.5 equiv), Et₂O (12 mL), and *n*-pentane (48 mL). To this solution was added (cod)Pd(CH₂TMS)₂ (680 mg, 1.75 mmol, 1.1 equiv) as a solid, and the suspension was stirred for 24 h at room temperature in a glovebox filled with argon gas. After stirring, the reaction vial was taken out from the glovebox. The insoluble powder was collected by filtration, washed with *n*-pentane, and dried under vacuum to give **5a** (726 mg, 1.33 mmol, 83.6%) as a pale brown solid. Single crystals suitable for X-ray diffraction measurement were prepared by recrystallization from a saturated solution of **5a** in THF at −30 °C.

Mp: 145 °C (decomp.); ¹H NMR (THF-*d*₈) δ 7.84–7.79 (H_a, m, 4H), 7.32–7.30 (H_c, m, 4H), 6.62–6.55 (H_b + H_d, m, 8H), 2.98 (NMe₂, s, 12H), 1.32 (^{*t*}Bu, s, 18H), 1.29 (^{*i*}Bu, s, 18H);

¹³C{¹H} NMR (THF-*d*₈) δ 161.3 (C_k, d, *J*_{C-F} = 239.2 Hz, 2C), 151.9 (C_b, 2C), 139.1 (C_h, 2C), 139.0 (C_i, d, *J*_{C-F} = 10.5 Hz, 4C), 138.8 (C_d, d, *J*_{C-P} = 21.9 Hz, 4C), 115.8 (C_e, d, *J*_{C-P} =

41.9 Hz, 2C), 113.5 (C_j, d, *J*_{C-F} = 18.1 Hz, 4C), 110.5 (C_c, d, *J*_{C-P} = 10.6 Hz, 4C), 39.9 (C_a, s, 4C), 38.4 (C_f, d, *J*_{C-P} = 16.2 Hz, 4C), 31.2 (C_g, 6C), 31.1 (C_g, 6C); ¹⁹F NMR (THF-*d*₈) δ −124.7; ³¹P NMR (THF-*d*₈) δ 61.1; IR (ZnSe, cm^{−1}) 1599, 1514, 1474, 1362, 1206, 1153, 1098, 1009, 806, 604; HRMS (ESI⁺) *m/z* 1013.1760 (1013.1764 calcd for C₄₄H₆₄⁸¹BrF₂N₂P₂Pd₂⁺, [M-Br]⁺); Signals in the ¹H and ¹³C NMR spectra were assigned by combination use of 2D NMR technique. All NMR spectra obtained for characterization, including ¹H, ¹³C{¹H}, ¹⁹F, ³¹P, ¹H-¹H COSY, HMQC, and HMBC measurements, are shown in the NMR spectra section. The crystallographic data are shown in Supplementary Table 5. The checkCIF service pointed out possibility of twinning of the specimen of **5a** with ‘alert B’ level as follows: ‘_vrf_PLAT930_ArPdBr PROBLEM: FCF-based Twin Law (10-3-2)[1 0 0] Est.d BASF 0.15 Check’. Based on the report, we introduced the twinning law into the structure refinement processes. The treatment was mentioned in the CIF of **5a** as follows: ‘RESPONSE: The refinements were performed applying the (10 -3 -2)[1 0 0] twin law with a matrix, (1 0 0/-0.586 -1 0/-0.419 0 -1)’.





Supplementary Fig. 3. ORTEP drawing of 5a with thermal ellipsoids at the 50% probability level. CCDC reference number is 2073816. All hydrogen atoms and the solvent molecule (THF) are omitted for clarity. Selected bond length (Å) and angle (°): Pd1–Br1 2.5057(9), Pd1–Br2 2.5841(9), Pd1–C1 2.007(7), Pd1–P1 2.3008(19), Pd2–Br1 2.5560(9), Pd2–Br2 2.5117(9), Pd2–C23 2.001(7), Pd2–P2 2.3189(19), Br1–Pd1–Br2 82.55(3), Br1–Pd1–P1 174.92(6), Br2–Pd1–P1 95.63(5), C1–Pd1–P1 97.3(2), Br1–Pd2–Br2 83.00(3), Br1–Pd2–P2 93.60(5), Br2–Pd2–P2 175.28(6), and C23–Pd2–P2 97.9(2).

Supplementary Table 5. Crystallographic data of 5a.

complex	5a
empirical formula	C ₄₈ H ₇₂ Br ₂ F ₂ N ₂ OP ₂ Pd ₂
formula weight	1165.63
color, description	Colorless, plate
temperature, K	90
cryst. System	triclinic
space group	<i>P</i> -1
<i>a</i> , Å	11.0942(2)
<i>b</i> , Å	12.7797(2)
<i>c</i> , Å	18.5983(4)
α , °	94.0858(16)
β , °	97.1816(17)
γ , °	104.7448(18)
<i>V</i> , Å ³	2515.40(8)
<i>Z</i>	2
calculated density, Mg·m ⁻³	1.539
$2\theta_{max}$, °	27.500
limiting indices	$-14 \leq h \leq 14, -16 \leq k \leq 16, -24 \leq l \leq 24$
absorption coefficient, mm ⁻¹	2.410
<i>F</i> (000)	1184.00
crystal size, mm	0.140 × 0.051 × 0.030
goodness-of-fit on <i>F</i> ²	1.174
reflections collected / unique	100718 / 11556 [R(int) = 0.0542]
no. of variables	549
<i>R</i> ₁ , <i>wR</i> ₂ [<i>I</i> > 2σ(<i>I</i>)] ^a	0.0599, 0.1670
<i>R</i> ₁ , <i>wR</i> ₂ (all data) ^a	0.0674, 0.1712
residual electron density, e·Å ⁻³	2.969 (max), -0.891 (min)

^a*R*₁ = (Σ||*F*_o| - |*F*_c||) / Σ|*F*_o|. *wR*₂ = [Σ*w*(*F*_o² - *F*_c²)² / Σ(*wF*_o⁴)]^{1/2}; The function minimized: *w*(*F*_o² - *F*_c²)².

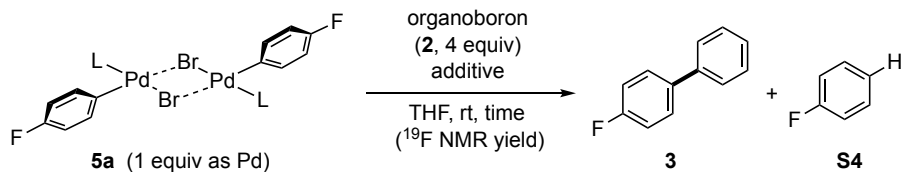
Stoichiometric reactions of **5a** with organoborons

To confirm the necessity of the additives and the involvement of **5a** as the intermediate of the transformation, we performed stoichiometric reactions of **5a** with organoborons **2** in the presence of additives (Supplementary Table 6).

To a 4 mL capped vial equipped with a magnetic stir bar were added **5a** (10.9 mg, 20.0 μ mol, 1 equiv), organoboron (80 μ mol, 4.0 equiv), and THF (1 mL). To the solution was added an additive, and the mixture was stirred for the indicated time at room temperature. To this mixture were added saturated aqueous NaHCO₃ (ca. 1 mL) and Et₂O (ca. 1 mL) followed by PhCF₃ (12.3 μ L, 0.100 mmol) as an internal standard. After stirring the mixture vigorously, a portion of the resulting organic phase (approx. 0.3 mL) was transferred into an NMR tube. To this was added CDCl₃ (approx. 0.5 mL), and then ¹⁹F NMR measurement was conducted. The yields were determined by comparison of integrated values of the signal that corresponds to **3** (δ -116.3 ppm) or fluorobenzene (**S4**, δ -113.5 ppm) with that of PhCF₃ (δ -63.0 ppm).

The reactions of **5a** with organoborons **2a–c** occurred in the presence of **4** to afford **3** in moderate to high yields (entries 1–3). Phenylboronic acid pinacol ester (**2d**) did not participate in this reaction same as a result obtained in the catalytic conditions (entry 4, Fig. 2B). The main byproduct was fluorobenzene (**S4**), probably caused by the reduction of **5a** with palladium(0) species formed after the reaction. Indeed, the addition of the ligand for stabilization of the resultant palladium complex(0) (entry 5) or an aryl bromide (entry 6) for consuming the palladium(0) complex by oxidative addition improved the yields of **3**. In the stoichiometric conditions, the use of silver salts is also effective to obtain **3** in excellent yields (entries 7–10), while **2d** was not applicable even under the conditions (entry 11). We confirmed that zinc complex is necessary for this reaction (entry 12), whereas **2b** can react with **5a** without any additive to afford **3** in moderate yield (entry 13).

Supplementary Table 6. Stoichiometric reactions of 5a with organoborons with additives.^a

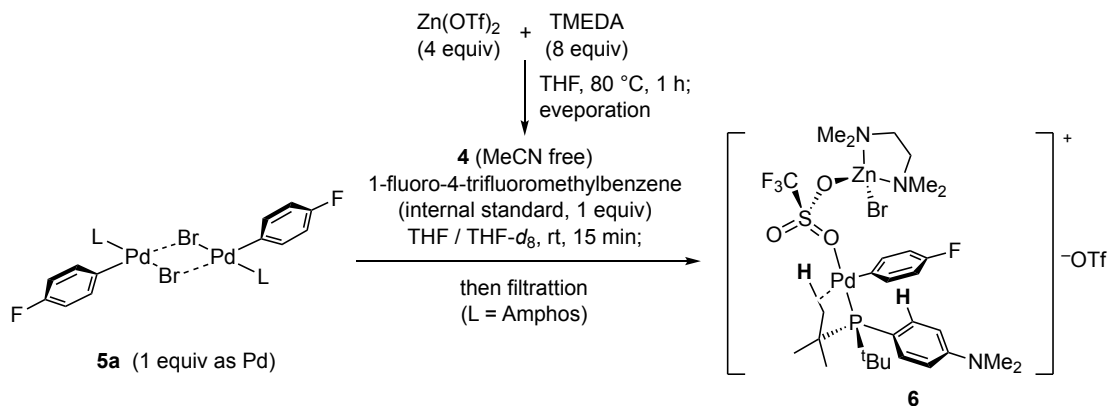


entry	organoboron	additive	time (h)	yield of 3 (%)	yield of S4 (%)
1	PhBF ₃ K (2a)	4 (3.9 equiv/Zn)	3	65	18
2	PhB(OH) ₂ (2b)	4 (3.9 equiv/Zn)	3	47	31
3	(PhBO) ₃ (2c)	4 (3.9 equiv/Zn)	3	53	30
4	PhBpin (2d)	4 (3.9 equiv/Zn)	3	8	4
5	PhBF ₃ K (2a)	4 (3.9 equiv/Zn) Amphos (3 equiv)	1	93	0
6	PhBF ₃ K (2a)	4 (3.9 equiv/Zn) 4-BrC ₆ H ₄ OCF ₃ (3 equiv)	1	88	6
7	PhBF ₃ K (2a)	AgOTf (2 equiv)	3	95	0
8	PhB(OH) ₂ (2b)	AgOTf (2 equiv)	3	67	0
9	PhBF ₃ K (2a)	AgBF ₄ (2 equiv)	3	>99	0
10	(PhBO) ₃ (2c)	AgBF ₄ (2 equiv)	3	>99	0
11	PhBpin (2d)	AgBF ₄ (2 equiv)	3	8	4
12	PhBF ₃ K (2a)	none	3	0	0
13	PhB(OH) ₂ (2b)	none	3	32	3

^aYields were determined by ¹⁹F NMR analysis.

Stoichiometric reactions of intermediate

Preparation of 6. To a 4 mL capped vial equipped with a magnetic stir bar were added $\text{Zn}(\text{OTf})_2$ (58.2 mg, 0.160 mmol, 4 equiv) and THF (1 mL). To this solution was added TMEDA (47.7 μL , 0.320 mmol, 8 equiv), and the suspension was stirred for 1 h at 80 $^\circ\text{C}$. After stirring, the solvents were removed under reduced pressure, and the residue was dried under vacuum. Then the vial that contains zinc complex **4** (MeCN free, see the next paragraph for details) was taken into a glovebox. To this vial was added a solution of palladium complex **5a** (21.9 mg, 40.0 μmol , 1 equiv) in THF (2.0 mL), and the mixture was stirred for 15 min at room temperature. During stirring, most of **4** dissolved to afford a pale brown suspension (For the analysis of the insoluble solid, see “**Solid IR analysis of the zinc hydroxide oligomer**” and Supplementary Fig. 9). After passing the mixture through a membrane filter (0.2 μm , GE Healthcare Life Science, 6779-1302) using a syringe, to the filtrate was added 1-fluoro-4-trifluoromethylbenzene (5.1 μL , 40 μmol , 1.0 equiv) as an internal standard, which was used as a stock solution (**stock solution A: 6** in THF). The concentration of **6** in the resultant solution varied (typically 18–19 mmol/L, 90–95% yields from **5a**) and thus was estimated every time when prepared by ^{19}F NMR analysis. To an NMR tube were added **stock solution A** (**6** in THF, 200 μL), THF (200 μL), and THF- d_8 (200 μL). After stirring the solution with a vortex mixer for 15 sec, ^{19}F NMR measurement was conducted. The concentration of **6** were determined by comparison of integrated values of the signal that corresponds to **6** (δ –121.5 ppm) with that of 1-fluoro-4-trifluoromethylbenzene (δ –108.6 ppm for ArF).

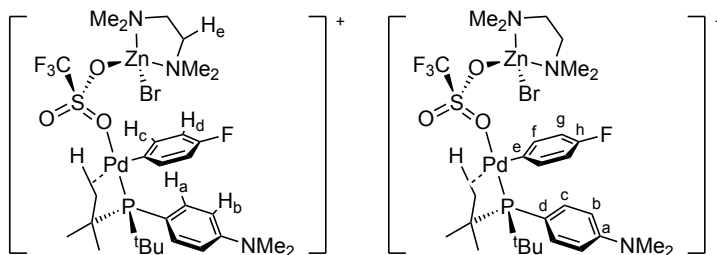


The use of four equivalent of **4** (MeCN free) was necessary for complete conversion from **5a** to **6**. For the effect of the amount of **4** (MeCN free), see Supplementary Table 7. Although the structure of zinc complex **4** (MeCN free) is not elucidated from SC-XRD analysis, we assumed that it has a similar trinuclear structure as that of **4** (recrystallized from MeCN) from the comparison of EXAFS of them. A part of **5a** remained when **4** prepared with MeCN (see Page 10) was used instead of **4** (MeCN free) probably because the Lewis basicity of the tiny amount of

remained acetonitrile impeded the Zn–Br interaction. The structure of **6** was estimated by XAS, NMR, and theoretical calculation, as described in the main text. We considered that the counter anion would be triflate based on the reaction's stoichiometry but was not experimentally confirmed.

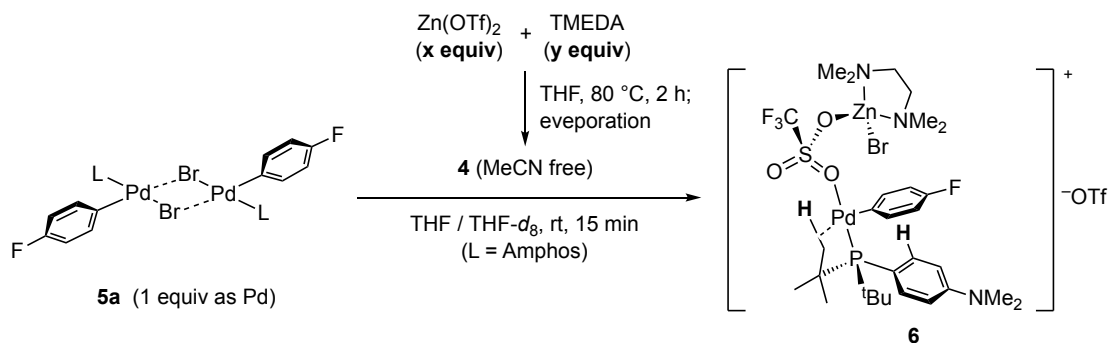
For ^1H , $^{13}\text{C}\{^1\text{H}\}$, ^{19}F , and ^{31}P NMR analysis for structural characterization, the corresponding solution of **6** in THF- d_8 (1 mL) was prepared with a 20 μmol of **5a** in the absence of 1-fluoro-4-trifluoromethylbenzene (**stock solution B**: **6** in THF- d_8). We did not fully identify the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum because the solution contains a large amount of TMEDA trifluoromethanesulfonic acid salt that complicated the characterization of signals in the aliphatic region;

^1H NMR (THF- d_8) δ 7.78–7.73 (H_a , AA'BB', 2H), 7.67–7.64 (H_c , AA'BB', 2H), 6.87–6.81 ($\text{H}_b + \text{H}_d$, m, 4H), 3.12 (NMe_2 of TMEDA ligand, s, 12H), 2.98 (NMe_2 of Amphos ligand, s, 6H), 1.30 (^tBu , s, 9H), 1.27 (^tBu , s, 9H) (The excess integrals of the signal at δ 2.66 were



presumably indicate their overlapping with that correspond to H_c in **6** and TMEDA triflic acid salt. Any significant signal in the high magnetic field (from δ 0 to -20 ppm) was not observed.); $^{13}\text{C}\{^1\text{H}\}$ NMR for aromatic region (THF- d_8) δ 162.7 (C_h , d, $J_{\text{C-F}} = 242.2$ Hz, 1C), 152.8 (C_a , 1C), 139.2 (C_f , 2C), 136.7 (C_c , d, $J_{\text{C-P}} = 9.6$ Hz, 2C), 136.3 (C_e , d, $J_{\text{C-P}} = 10.6$ Hz, 1C), 121.9 (CF_3 in OTf, q, $J_{\text{C-F}} = 320.4$ Hz, 1C), 114.8 (C_g , d, $J_{\text{C-F}} = 19.1$ Hz, 2C), 113.2 (C_d , d, $J_{\text{C-P}} = 37.1$ Hz, 1C), 111.8 (C_b , d, $J_{\text{C-P}} = 10.6$ Hz, 2C); ^{19}F NMR (THF- d_8) δ -79.0 (3F, OTf), -121.5 (1F, ArF) (the excess integral of the signal at δ -79.0 indicates the presence of TMEDA trifluoromethanesulfonic acid salt in the solution); ^{31}P NMR (THF- d_8) δ 51.2. Signals in the ^1H spectrum and the ^{13}C NMR spectrum in the aromatic region were assigned by combination use of 2D NMR technique. All NMR spectra obtained for characterization, including ^1H , $^{13}\text{C}\{^1\text{H}\}$, ^{19}F , ^{31}P , ^1H - ^1H COSY, HMQC, and HMBC measurements, are shown in the NMR spectra section. Unfortunately, the mass peak that corresponds to **6** was not detected by ESI-MS analysis even at lower ionization temperature (40°C).

Supplementary Table 7. Optimization of the amount of zinc complex.



entry	$\text{Zn}(\text{OTf})_2$ (x equiv)	TMEDA (y equiv)	Ratio of 5a : 6 ^a
1	1.2	1.2	75:25
2	2.4	2.4	56:44
3	4.0	4.0	11:89
4	1.2	2.4	71:29
5	2.4	4.8	23:77
6	4.0	8.0	0:100

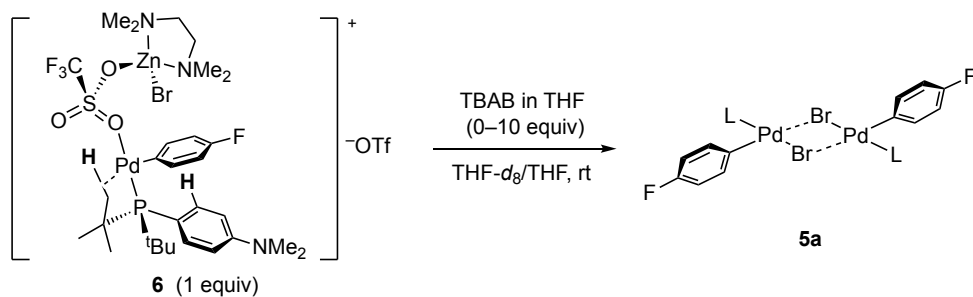
^aRatios were determined by ^{19}F NMR analysis comparing integrated values of the signal that corresponds to **5a** ($\delta -124.8$ ppm) with that of **6** ($\delta -121.5$ ppm).

Regeneration of 5a from 6 with TBAB (Fig. 3A). To confirm the reversibility of the debromination process, we treated **6** with a bromide.

To an NMR tube were added **stock solution A** (**6** in THF, 18.2 mmol/L, 200 μL , 3.64 μmol , 1 equiv) and THF- d_8 (600 μL) in a glovebox filled with argon gas. The NMR tube was sealed with a rubber septum and taken out from the glovebox. To the NMR tube was added an appropriate amount of TBAB solutions (184 mmol/L in THF, 20 μL for 3.68 μmol (1 equiv)) via a syringe at room temperature. After stirring the solution with a vortex mixer for 1 min, ^{19}F NMR measurement was conducted. The yields were determined by comparison of integrated values of the signal that corresponds to **6** ($\delta -121.5$ ppm) or **5a** ($\delta -124.8$ ppm) with that of 1-fluoro-4-trifluoromethylbenzene ($\delta -108.6$ ppm for ArF).

As shown in the data summarized in Supplementary Table 8, the addition of an excess amount of TBAB to **6** afforded **5a**, indicating **6** formed by bromide abstraction of **5a** with zinc complex **4**. The addition of a less amount of TBAB (1–4 equiv) did not cause the regeneration of **5a**, suggesting that a part of zinc species derived from **4** dissolved in the stock solution and reacted with TBAB preference to **6**.

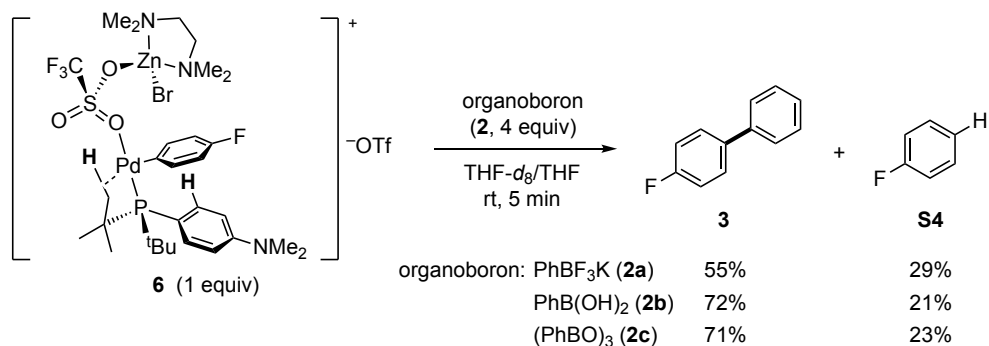
Supplementary Table 8. Reaction of 6 with TBAB to regenerate 5a.



entry	TBAB (equiv)	Recovery of 6 (%) ^a	Yield of 5a (%) ^a
1	0	92	11
2	1	88	10
3	2	95	10
4	3	>99	0
5	4	>99	0
6	10	0	99

^aYields were determined by ¹⁹F NMR analysis.

Reactions of stock solution A (6 in THF) with organoborons 2a–c (Fig. 3A).



To a 4 mL capped vial were added organoboron **2** (**2a**: 2.9 mg, 16 μmol, 4 equiv; **2b**: 2.0 mg, 16 μmol, 4 equiv; **2c**: 5.0 mg, 16 μmol, 4 equiv), THF (200 μL), THF-*d*₈ (200 μL), and **stock solution A** (**6** in THF, 18.2 mmol/L, 200 μL, 3.64 μmol, 1 equiv), sequentially, in a glovebox filled with argon gas. After stirring the mixture for 5 min at room temperature, the suspension was transferred into an NMR tube, and then ¹⁹F NMR measurement was conducted. The yields were determined by comparison of integrated values of the signal that corresponds to **3** (δ –117.1 ppm) or **S4** (δ –114.2 ppm) with that of 1-fluoro-4-trifluoromethylbenzene (δ –108.6 ppm for ArF).

Time course studies (Fig. 3B)

Time course study for the reaction of stock solution A (6 in THF) with 2c. For time course study with ^{19}F NMR analysis, we employed triphenylboroxine (**2c**) as an organoborons because of its sufficient solubility to THF and the reactivity as shown in Fig. 3B.

To a 4 mL capped vial were added **2c** (74.8 mg, 0.240 mmol) and THF (1.5 mL), and stirred for 3 min to afford a clear solution (**stock solution 2c**).

To an NMR tube capped with a septum was added **stock solution A** (**6**: 4 μmol , 1 equiv; 1-fluoro-4-trifluoromethylbenzene: 8 μmol , 2 equiv; THF: 200 μL) and THF- d_8 (200 μL). After cooled to $-78\text{ }^{\circ}\text{C}$ with a dry ice-acetone bath, to this was added **stock solution 2c** (**2c**: 48 μmol , 12 equiv; THF: 300 μL). The solution was vigorously mixed with a vortex mixer for 10 sec before the temperature of the mixture rose. The NMR tube was quickly cleaned with a KimWipe[®] and then introduced into a probe of the NMR spectrometer pre-cooled to $-50\text{ }^{\circ}\text{C}$. ^{19}F NMR analysis of this solution at $-50\text{ }^{\circ}\text{C}$ showed no conversion of **6**. Then, temperature of the NMR spectrometer was set at $-30\text{ }^{\circ}\text{C}$ and conducted acquisition of ^{19}F NMR signals every 1 min for over 15 min. This experiment was conducted three times repeatedly.

Supplementary Table 9. Time-dependent yields of 3 of the reaction of 6 with 2c

time (min)	1st (%)	2nd (%)	3rd (%)	average yield with standard deviation (%)
1	4.7	4.6	2.6	3.9 ± 1.2
2	10.5	14.6	11.6	12.2 ± 2.1
3	24.3	23.3	24.5	24.0 ± 0.6
4	31.7	31.7	33.7	32.4 ± 1.2
5	36.7	37.5	39.3	37.8 ± 1.3
6	40.9	40.2	42.9	41.4 ± 1.4
7	43.4	42.5	45.8	43.9 ± 1.7
8	46.0	45.0	49.0	46.7 ± 2.1
9	47.3	45.5	51.1	48.0 ± 2.9
10	49.0	47.3	51.7	49.3 ± 2.2
11	50.5	49.0	53.9	51.1 ± 2.5
12	51.5	49.9	54.9	52.1 ± 2.5
13	51.2	50.2	55.7	52.4 ± 3.0
14	53.7	51.1	56.0	53.6 ± 2.4

Time course study for the reaction of cationic complexes 5b and 5c with 2c. To a 4 mL capped vial were added **5a** (10.9 mg, 20.0 μmol), 1-fluoro-4-trifluoromethylbenzene (5.1 μL , 40 μmol), THF- d_8 (1.0 mL), and THF (1.0 mL), and stirred for 10 min to afford a clear solution (**stock solution 5a**).

To an NMR tube capped with a septum were added silver salts (silver(I) triflate (AgOTf): 2.5 mg, 9.7 μmol , 2.4 equiv; silver(I) tetrafluoroborate (AgBF₄): 1.9 mg, 9.8 μmol , 2.5 equiv; THF: 400 μL) and **stock solution 5a** (**5a**: 4 μmol , 1 equiv; 1-fluoro-4-trifluoromethylbenzene: 8 μmol , 2 equiv; THF: 200 μL ; THF- d_8 : 200 μL). After cooled to $-78\text{ }^{\circ}\text{C}$ with a dry ice-acetone bath, to this was added **stock solution 2c** (**2c**: 48 μmol , THF: 300 μL). The solution was vigorously mixed with a vortex mixer for 10 sec before the temperature of the mixture rose. The NMR tube was quickly cleaned with a KimWipe[®] and then introduced into a probe of the NMR spectrometer pre-cooled to $-50\text{ }^{\circ}\text{C}$. ¹⁹F NMR analysis of this solution at $-50\text{ }^{\circ}\text{C}$ showed complete changes of **5a** to cationic palladium complexes **5b** and **5c** but no formation of **3**. Then, temperature of the NMR spectrometer was set at $-30\text{ }^{\circ}\text{C}$ and conducted acquisition of ¹⁹F NMR signals every 1 min for over 15 min. This experiment was conducted three times repeatedly.

Supplementary Table 10. Time-dependent yields of 3 of the reaction of 5b with 2c

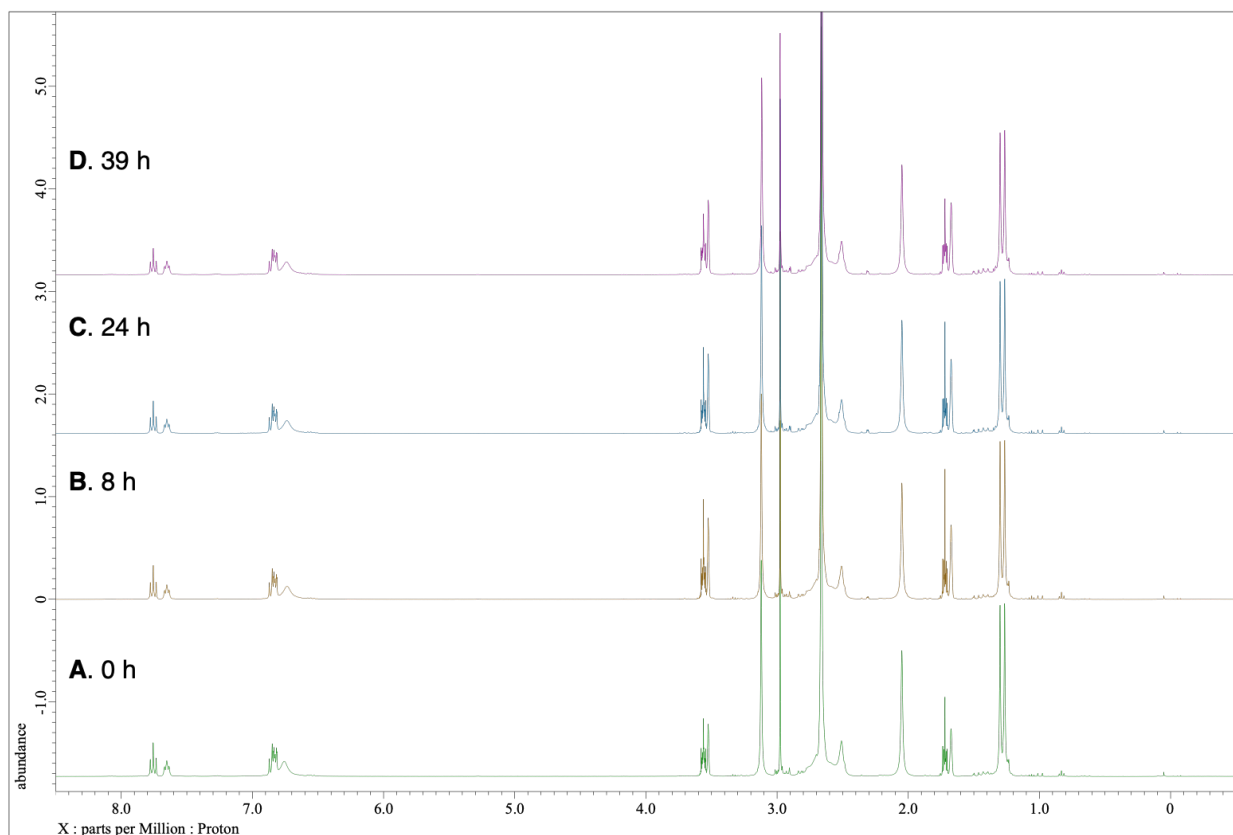
time (min)	1st (%)	2nd (%)	3rd (%)	average yield with standard deviation (%)
1	15.4	19.3	25.3	21.9 $\pm$ 5.7
2	19.8	25.1	32.1	27.6 $\pm$ 6.8
3	23.5	31.0	34.9	30.9 $\pm$ 6.4
4	26.4	34.4	38.7	33.6 $\pm$ 6.4
5	27.8	35.6	40.1	35.8 $\pm$ 7.0
6	30.6	39.5	42.0	37.7 $\pm$ 6.2
7	31.4	40.4	42.8	38.5 $\pm$ 6.2
8	32.5	41.2	43.4	39.6 $\pm$ 6.2
9	34.9	43.0	44.5	41.2 $\pm$ 5.5
10	33.9	44.3	46.6	41.6 $\pm$ 6.7
11	35.7	44.3	46.1	42.4 $\pm$ 5.8
12	35.5	45.3	47.4	43.1 $\pm$ 6.6
13	37.4	46.3	48.3	44.0 $\pm$ 5.8
14	37.8	46.4	48.6	44.4 $\pm$ 5.8

Supplementary Table 11. Time-dependent yields of 3 of the reaction of 5c with 2c

time (min)	1st (%)	2nd (%)	3rd (%)	average yield with standard deviation (%)
1	23.5	24.9	21.5	23.3 ± 1.7
2	33.5	35.3	32.2	33.6 ± 1.6
3	40.5	43.6	40.9	41.6 ± 1.7
4	45.8	52.6	49.1	49.2 ± 3.4
5	49.2	57.9	54.3	53.8 ± 4.4
6	53.5	62.5	59.5	58.5 ± 4.6
7	56.9	64.7	62.9	61.5 ± 4.1
8	59.8	68.8	68.5	65.7 ± 5.1
9	63.2	70.7	69.2	67.7 ± 4.0
10	63.6	74.5	71.9	70.0 ± 5.7
11	65.2	76.0	74.4	71.9 ± 5.8
12	66.9	78.3	76.8	74.0 ± 6.2
13	68.8	79.7	79.5	76.0 ± 6.2
14	70.2	81.3	80.1	77.2 ± 6.1

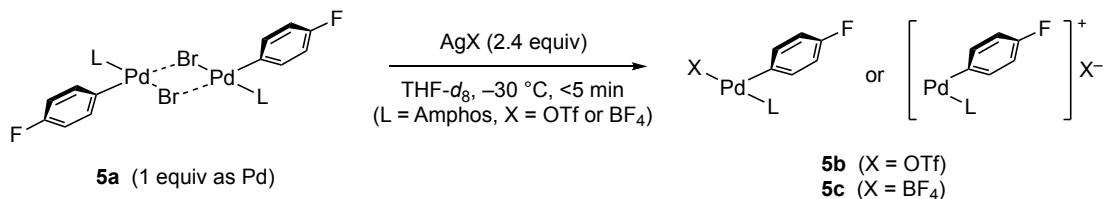
Stability tests of cationic arylpalladium(II) complexes

Stability test of 6. To an NMR tube was added **stock solution B** (**6** in THF, 1 mL) in a glovebox filled with argon gas. After capping the NMR tube, ^1H NMR data acquisition of this solution was conducted at 23 °C several times during 39 h, which showed no significant spectral change (Supplementary Fig. 4).



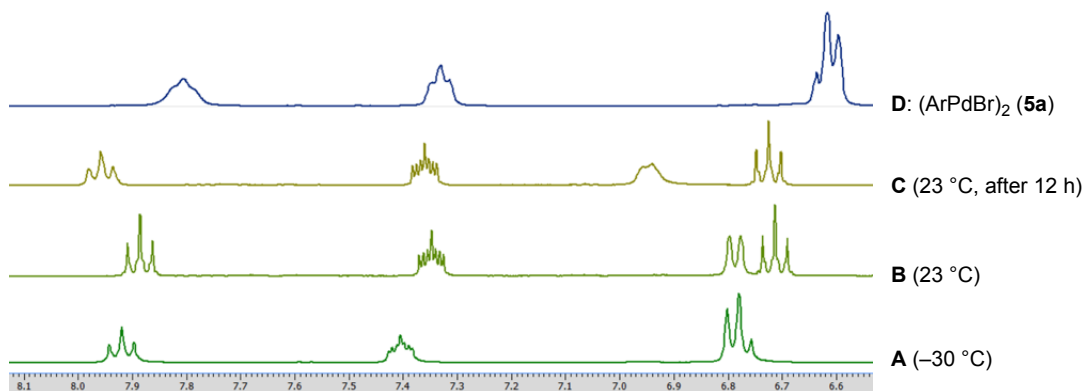
Supplementary Fig. 4. Time course of ^1H NMR spectra of 6. A, Just after the preparation. B, After 8 h. C, After 24 h. D, After 39 h at 23 °C under argon atmosphere.

NMR analysis of related cationic complexes **5b and **5c** and their stability tests.** We generated cationic palladium(II) species with silver salts at lower temperature than that for **6** to avoid their thermal decomposition.

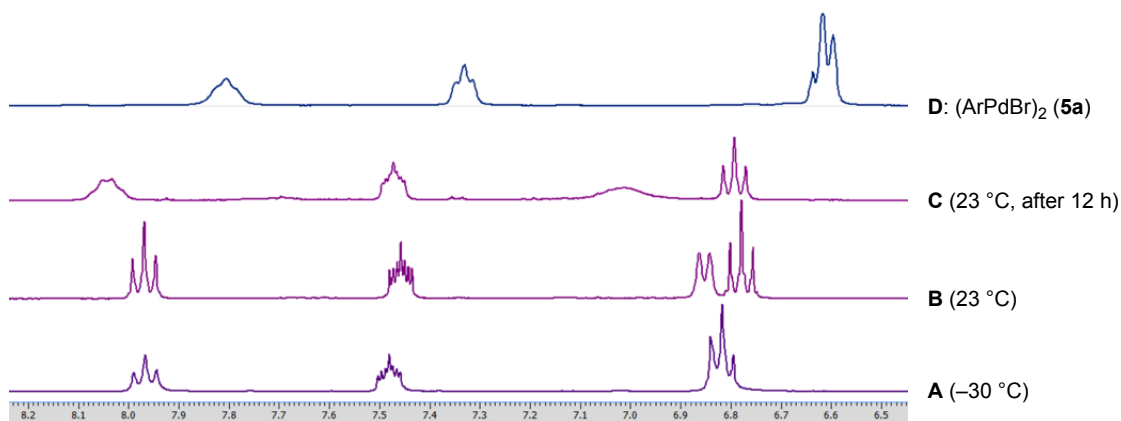


To an NMR tube capped with a septum were added silver salts (AgOTf: 6.2 mg, 24 μmol , 2.4 equiv; AgBF₄: 4.7 mg, 24 μmol , 2.4 equiv) and THF-*d*₈ (0.4 mL) in a glovebox. The NMR tube was taken out from the glovebox and cooled to $-78\text{ }^\circ\text{C}$ with a dry ice-acetone bath followed by the slow addition of a solution of **5a** (5.5 mg, 10 μmol , 1 equiv) in THF-*d*₈ at $-78\text{ }^\circ\text{C}$. The suspension was vigorously mixed with a vortex mixer for 10 sec before the temperature of the mixture rose. The NMR tube was quickly cleaned with a KimWipe® and then introduced into a probe of the NMR spectrometer pre-cooled to $-30\text{ }^\circ\text{C}$.

¹H NMR data acquisition of each mixture was conducted at $-30\text{ }^\circ\text{C}$, $23\text{ }^\circ\text{C}$, and 12 h later at $23\text{ }^\circ\text{C}$. The corresponding NMR spectra are shown in Supplementary Figs. 5 and 6, indicating the dissociation of the bromide completed within a few minutes at $-30\text{ }^\circ\text{C}$. Changes in ¹H NMR spectrum were observed when increasing temperature from $-30\text{ }^\circ\text{C}$ to $23\text{ }^\circ\text{C}$, showing their complete conversion, although the products were not identified.



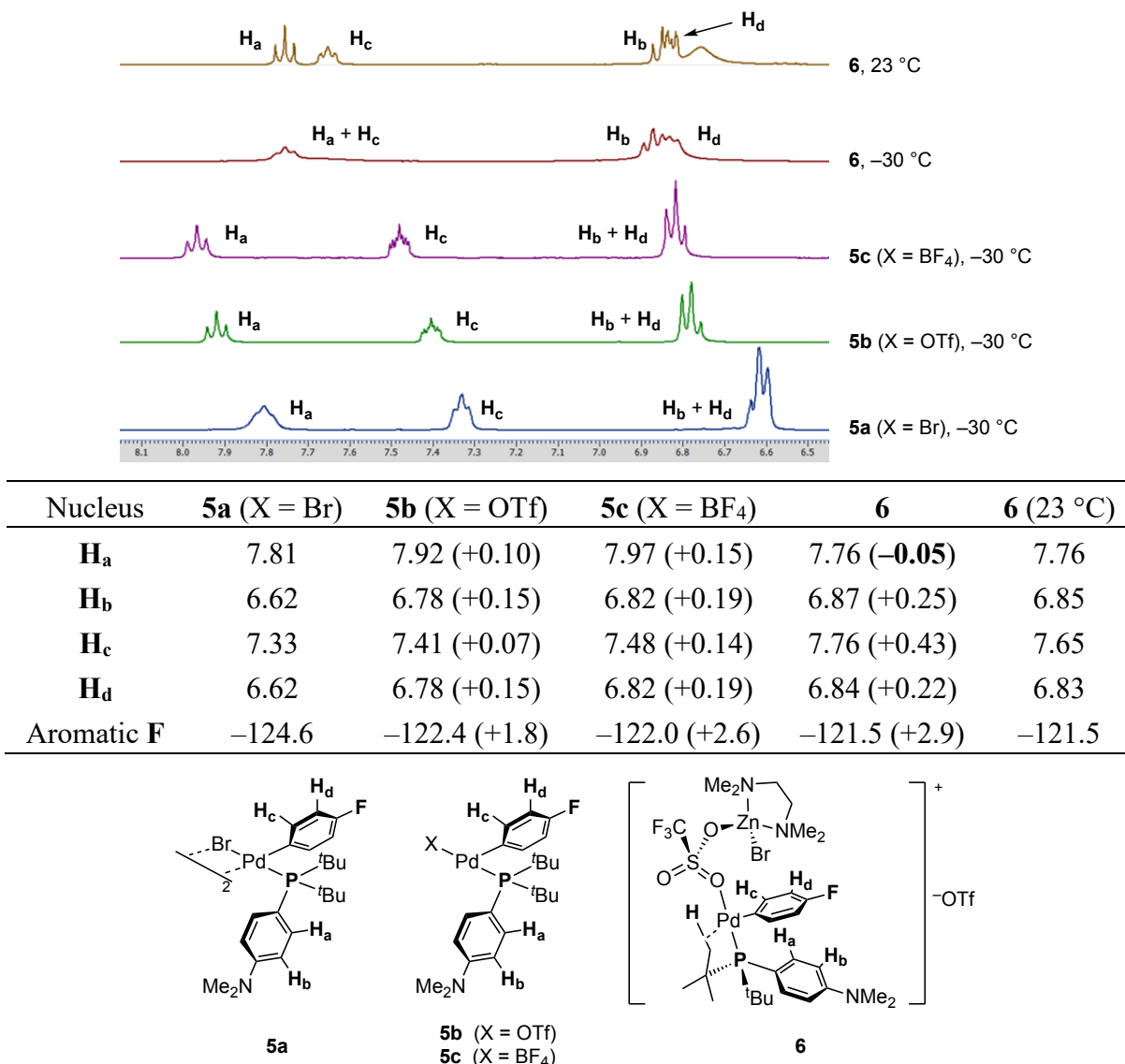
Supplementary Fig. 5. Enlarged ^1H NMR spectra of the aromatic field of **5b and **5a**.** Spectra of **5b** obtained at $-30\text{ }^\circ\text{C}$ (**A**), at $23\text{ }^\circ\text{C}$ (**B**), and after 12 h at $23\text{ }^\circ\text{C}$ (**C**) under argon atmosphere and that of **5a** obtained at $-30\text{ }^\circ\text{C}$ (**D**).



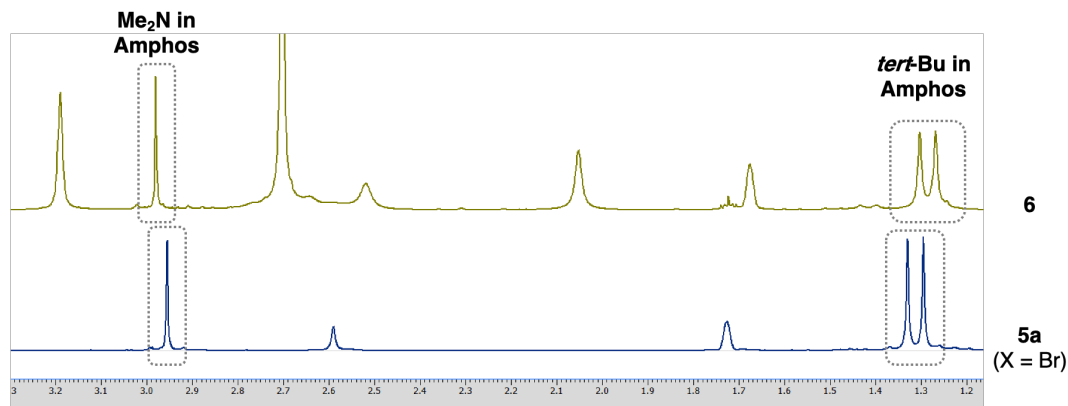
Supplementary Fig. 6. Enlarged ^1H NMR spectra of the aromatic field of **5c and **5a**.** Spectra of **5c** obtained at $-30\text{ }^\circ\text{C}$ (**A**), at $23\text{ }^\circ\text{C}$ (**B**), and after 12 h at $23\text{ }^\circ\text{C}$ (**C**) under argon atmosphere and that of **5a** obtained at $-30\text{ }^\circ\text{C}$ (**D**).

Comparison of ^1H NMR spectra of **6** and **5a–c** (Fig. 3C)

We compared the ^1H NMR spectra of these complexes to obtain information on the chemical structures and differences in the electrostatic properties of the complexes. The ^1H NMR signals were corrected at room temperature and $-30\text{ }^\circ\text{C}$ in $\text{THF-}d_8$ because of the smooth degradation of **5b** and **5c** at room temperature (Supplementary Figs. 5 and 6).¹³ The results are summarized in Supplementary Figs. 7 and 8.



Supplementary Fig. 7. Enlarged aromatic region ^1H NMR spectra of **6 and **5a–c**.** Spectra and selected chemical shifts (δ , ppm) of **5a–c** at $-30\text{ }^\circ\text{C}$, **6** at $-30\text{ }^\circ\text{C}$, and **6** at $23\text{ }^\circ\text{C}$. The differences of the chemical shifts from **5a** are shown in the parentheses.



Supplementary Fig. 8. Enlarged aliphatic region ^1H NMR spectra of **6 and **5a**.** Spectra were obtained at room temperature. The signal that corresponds to *tert*-butyl groups of **6** is broadened compared to that of **5a**.

Consideration of the hydroxy group of **4** as a base

We concluded the zinc-mediated SMC reaction occurs in the absence of a base because the addition of several Lewis acids, such as $\text{Zn}(\text{OTf})_2$ and $\text{In}(\text{OTf})_3$, promoted the reaction to afford the products in moderate to high yields (Supplementary Table 2). However, the most effective agent, **4**, has a hydroxy group and could serve as a base that promotes transmetalation with organoborons. Possible roles of the hydroxy group could be estimated as below;

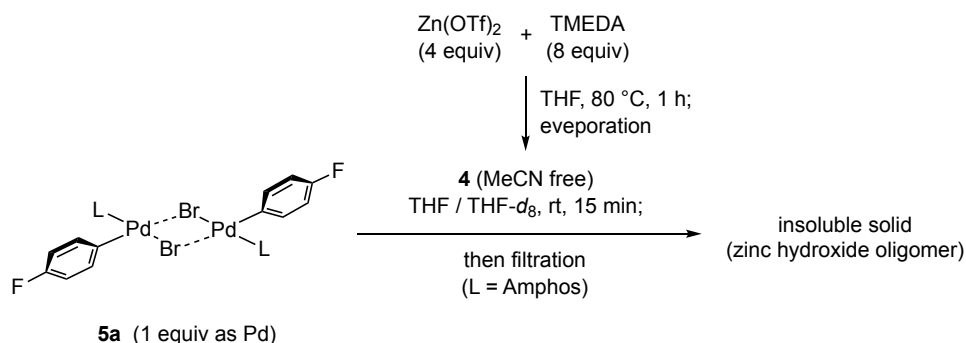
Case 1. Transmetalation with organoborons to afford organozinc intermediates.

Case 2. Free base to form organoborate.

Case 3. Anion exchange with **5a** to afford a palladium(II) hydroxide intermediate.

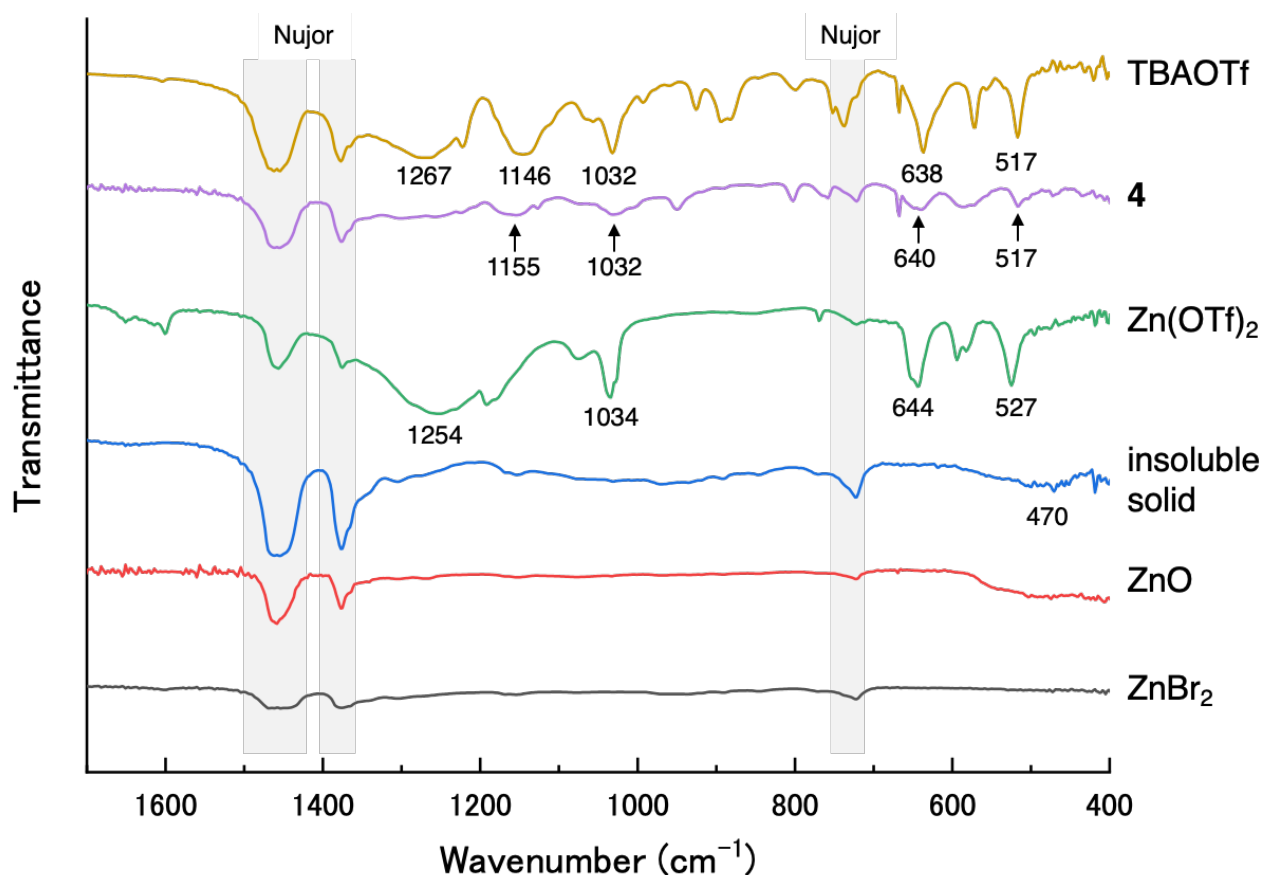
Among the cases, **Case 3** could be denied by the XAS analysis (see: **Consideration of other possible structures** and Supplementary Fig. 19). To address other possibilities, we conducted several additional experiments.

Solid IR analysis of the zinc hydroxide oligomer. To reveal the fate of the hydroxy group under the stoichiometric conditions, we isolated the insoluble byproduct formed in the generation of **6** by filtration and performed IR analysis to obtain structural information.



To a 4 mL capped vial equipped with a magnetic stir bar were added Zn(OTf)_2 (58.2 mg, 0.160 mmol, 4 equiv) and THF (1 mL). To this solution was added TMEDA (47.7 μL , 0.320 mmol, 8 equiv), and the suspension was stirred for 1 h at 80 °C. After stirring, the solvents were removed under reduced pressure, and the residue was dried under vacuum. Then the vial that contains zinc complex **4** was taken into a glovebox. To this vial was added a solution of palladium complex **5a** (21.9 mg, 40.0 μmol , 1 equiv) in THF (2.0 mL), and the mixture was stirred for 15 min at room temperature. During stirring, most of **4** dissolved to afford a pale brown suspension. The insoluble solid was corrected by filtration, washed with THF (3 mL), and dried under vacuum to give a white solid (38.0 mg), presumably containing the zinc residue and TMEDA trifluoromethanesulfonic acid salt. The white solid was suspended in MeCN (2 mL) and stirred for 2 min at room temperature. The insoluble solid was again corrected by filtration and dried under vacuum to give a white solid (**insoluble solid**, 6.1 mg). For IR analysis, a small amount of the sample (less than 0.2 mg) was suspended with Nujol and sandwiched between KBr plates. Infrared (IR) spectra were measured by transmission mode on a Shimadzu IRPrestige-21 spectrometer. For the comparison, we subjected the same analysis with ZnBr_2 , ZnO , Zn(OTf)_2 , **4**, and TBAOTf. The spectra are summarized in Supplementary Fig. 9.

IR spectra of TBAOTf, **4**, and Zn(OTf)_2 showed characteristic signals both in the stretching (1270–1030 cm^{-1}) and scissoring (650–510 cm^{-1}) regions that correspond to the triflate groups.⁷ In contrast, these signals disappeared in the spectra of **insoluble solid**, indicating the absence of a triflate group. Instead, a broad weak signal (470 cm^{-1}) appeared, which is also observed in the spectrum of ZnO . Considering that ZnO could form from zinc hydroxide via spontaneous dehydration, we assume that the hydroxy group in **4** is captured by the excess amount of unreacted **4** under the stoichiometric conditions to form zinc dihydroxide complex followed by dehydrative oligomerization to afford insoluble zinc oxide. Based on this consideration, we conclude that the hydroxy group is not involved in the following transmetalation process under the conditions, denying **Case 2**.



Supplementary Fig. 9. IR spectra of the insoluble byproduct and related compounds. The digits written on the spectra are the peak top wavenumber of the characteristic signals.

NMR experiments of the mixture of **4 with **2c**.** The transmetalation of organoborons with zinc(II) salts that afford organozinc species (**Case 1**) is a potential alternative pathway.^{8,9} To confirm the possibility, NMR analysis of the mixture of **4** and an organoboron was performed, in which (PhBO)₃ (**2c**) was employed because of the high solubility to THF. The results are summarized in Supplementary Fig. 10. Samples for ¹H NMR analysis were prepared as shown below;

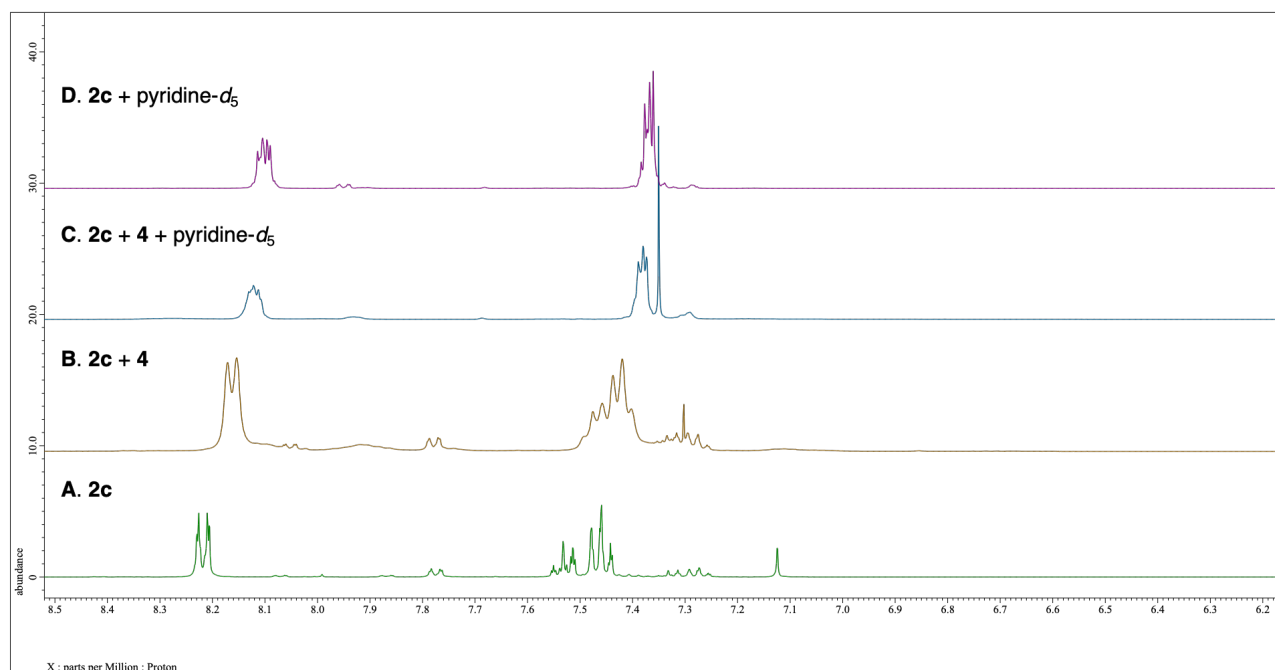
Solution A: To an NMR tube with a screwcap were added **2c** (31.2 mg, 0.100 mmol) and THF-*d*₈ (0.8 mL) were added in a glovebox.

Solution B: To an NMR tube with a screwcap were added **2c** (31.2 mg, 0.100 mmol), **4** (27.6 mg, 79.4 μmol/Zn), and THF-*d*₈ (0.8 mL) were added in a glovebox.

Solution C: To an NMR tube with a screwcap were added **2c** (31.2 mg, 0.100 mmol), **4** (27.6 mg, 79.4 μmol/Zn), THF-*d*₈ (0.8 mL), and pyridine-*d*₈ (0.2 mL) were sequentially added in a glovebox.

Solution D: To an NMR tube with a screwcap were added **2c** (31.2 mg, 0.100 mmol), THF-*d*₈ (0.8 mL), and pyridine-*d*₅ (0.2 mL) were added in a glovebox.

A slightly high magnetic field shift was observed when we added **4** to a solution of **2c** (Supplementary Fig. 10, **A** to **B**), indicating an interaction between the reagents. To confirm that the NMR change is a reversible process, we further added pyridine-*d*₅ to the solution, which showed again a slightly high magnetic field shift (**B** to **C**). The chemical shift of the mixture was not identical to **2c**, probably due to a weak interaction between **2c** and pyridine-*d*₅. Indeed, we also subjected NMR analysis of the mixture of **2c** and pyridine-*d*₅ (**D**), affording a similar spectrum to the mixture **C**. These results indicate the reversibility of the interaction between **4** and **2c**. Moreover, more anionic organometallic species, which could show significant high magnetic field shifts, was not observed between δ 7.0–6.0 ppm. Based on the results, we consider that the addition of **4** does not cause the cleavage of carbon–boron bond and therefore the generation of arylzinc species, denying **Case 1**.



Supplementary Fig. 10. ¹H NMR spectra of the mixtures of **4** and **2c**. Spectra were obtained at 23 °C in THF-*d*₈. **A.** **2c**. **B.** A solution **A** with **4**. **C.** A solution of **C** with pyridine-*d*₅. **D.** A solution of **2c** and pyridine-*d*₅.

Supplementary Method 3: XAS experiment

General method

Unless otherwise noted, X-ray absorption spectroscopy (XAS) experiments were performed at SPring-8 BL14B2 beamline using Si(311) double-crystal monochromatized synchrotron radiation. All XAS experiments were carried out using transmission mode with quick scan technique (QXAFS). Ionization chambers were used to measure the intensities of the incident (I_0) and transmitted (I) X-ray. E_0 value was defined as a fraction of the edge step of the normalized $\mu(E)$ spectrum. E_0 values of Pd foil, CsBr, and Zn foil were set to the following values for photon energy calibration (Pd: 24350 eV, Br: 13474 eV, Zn: 9659 eV).

XAS analyses were conducted using Demeter package, a comprehensive system for processing and analysing X-ray absorption spectroscopy data.^{10–12} Background removal and normalization of raw data were performed by cubic spline method using Athena software. The extracted extended X-ray absorption fine structure (EXAFS) oscillation was Fourier transformed with k^3 -weight, and curve-fitting was conducted in r -space using Artemis software. Single scattering paths were calculated using FEFF 6 code¹³ built in this package with the molecular geometries obtained from SC-XRD analysis or DFT calculation. The intrinsic loss factor ($S_0^2 = 1$) and the coordination number (CN) were fixed. Other EXAFS parameters, including bond length difference (ΔR), absorption edge energy correction (ΔE_0), and Debye–Waller factor (σ^2), were based on a fitting result, unless otherwise noted.

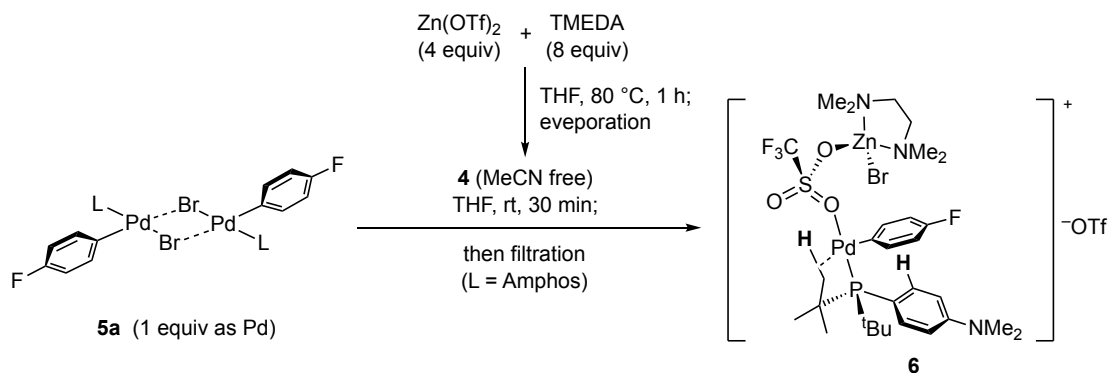
Preparation of solid sample

A mixture of a reagent and an appropriate amount of boron nitride were ground using an agate mortar over 45 min in a glovebox filled with argon gas. The resulting powder was pelletized using a tablet press (JASCO Corporation, $\phi = 10$ mm) and a hydraulic press (RIKEN KIKI Co., Ltd., CMD-5PA with the pressure ranging between 10 and 15 MPa). The thus-prepared pellets were packed in a gas barrier bag (thickness: 60 μm), taken out from the glovebox, and subjected to XAS measurement.

Preparation of liquid sample

A reagent (80.0 μmol) was dissolved in THF (1.0 mL) in a glovebox filled with argon gas. An aliquot of the solution (ca. 80 mmol/L) was transferred to an own-made liquid cell (for Pd: path length = 20 mm, PEEK; for Br: path length = 10 mm, PEEK; for Zn: path length = 6.5 mm, borosilicate glass) with PTFE windows (NITOFLO[®] No.900UL, 50 μm thickness). The cell was taken out from the glovebox and subjected to XAS measurement.

In-situ XAS experiment for observation of reactive intermediate **6**

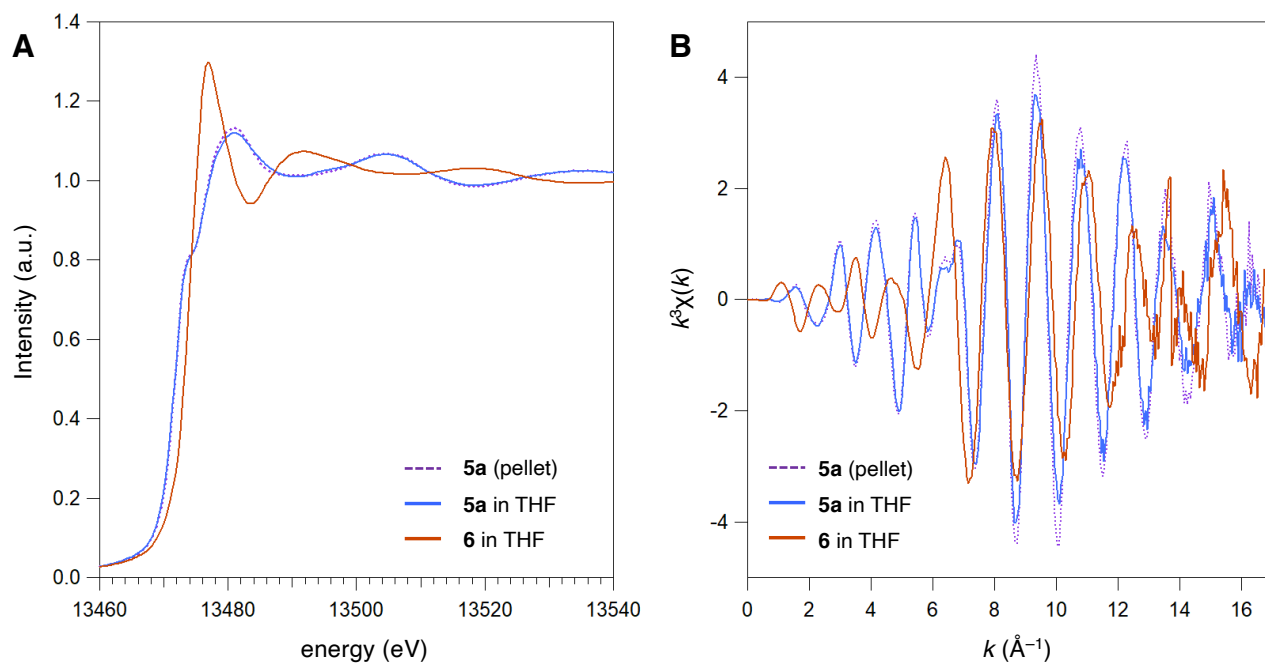


To a 4 mL capped vial equipped with a magnetic stir bar were added Zn(OTf)₂ (58.2 mg, 0.160 mmol, 4 equiv) and THF (1.0 mL). To this solution was added TMEDA (47.7 μ L, 0.320 mmol, 8 equiv), and the suspension was stirred for 1 h at 80 °C with an aluminium heat block. After stirring, the solvents were removed under reduced pressure, and the residue was dried under vacuum. The resulting zinc complex **4** was stored under argon atmosphere and taken to the radiation facility.

The vial that contains zinc complex **4** and a magnetic stir bar was taken into a glovebox filled with argon gas at the radiation facility. To this vial was added a solution of palladium complex **5a** (21.9 mg, 40.0 μ mol, 1 equiv) in THF (1.0 mL), and the mixture was stirred for 30 min at room temperature. After passing the mixture through a membrane filter (0.2 μ m, GE Healthcare Life Science, 6779-1302) using a syringe, an aliquot of the clear brown solution was transferred to an own-made liquid cell (for Pd: path length = 20 mm, PEEK; for Br: path length = 10 mm, PEEK; for Zn: path length = 6.5 mm, borosilicate glass) with PTFE film windows (50 μ m thickness, NITOFLO[®] No.900UL). The cell containing the reaction mixture was taken out from the glovebox, and immediately subjected to XAS measurement.

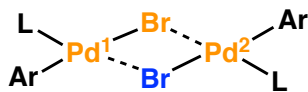
We confirmed the structure of **5a** in THF by comparing the solution state XAS data with the solid-state counterpart. Br-K and Pd-K edge X-ray absorption near edge structure (XANES) spectrum and Fourier-transformed EXAFS of **5a** in THF were almost identical to those in the solid state (Supplementary Figs. 11 and 14). In addition, a characteristic peak corresponding to Br–Br scattering (3.1 Å) was observed on Br-K edge EXAFS (Fig. 4A, Supplementary Table 12, and Supplementary Fig. 12), indicating the dimer structure remains unchanged even in the solution state. A peak corresponding to Pd–Pd scattering did not observed on Pd-K edge EXAFS (Fig. 4B), probably due to the large Debye–Waller factor, implying the dynamic turbulence of Pd–Pd distance in powder and solution state. The relatively large ΔR value of Pd–S scattering (-0.196 ± 0.038 Å), which was derived from the curve fitting, is probably attributed to the conformational isomerism between η^1 - and η^2 -coordination modes of the triflate (Supplementary Table 14).

Br-K edge XAS data (Supplementary Figs. 11–13 and Supplementary Tables 12 and 13)

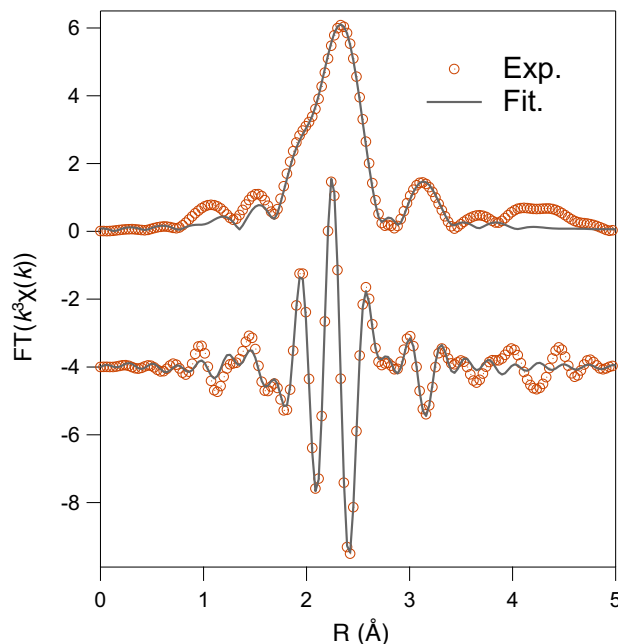


Supplementary Fig. 11. Br-K edge XAS data of 5a and 6. A, XANES spectra. B, k^3 -weighted EXAFS oscillation.

Supplementary Table 12. Parameters obtained from the curve-fitting analysis of Br-K edge EXAFS of 5a in r -space. k -range: 3–13 $\text{\AA}^{-1}$, r -range: 1.7–3.5 $\text{\AA}$, $S_0^2 = 1.00$, Number of variable parameters = 4. ^aAbsorption edge energy correction. ^bDebye–Waller factor. ^cBond length obtained from SC-XRD experiment (fixed parameter). ^dReduced χ -squared value. ^eGoodness-of-Fit index.

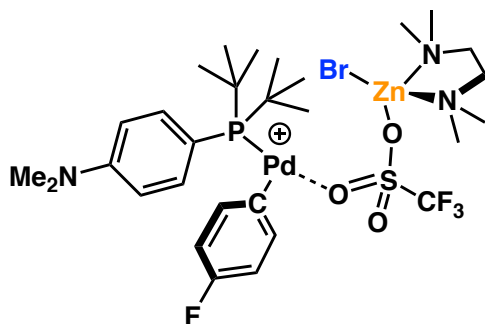


Scattering path	ΔE_0 (eV) ^a	σ^2 ($10^{-3} \text{\AA}^2$) ^b	R_{XRD} ($\text{\AA}$) ^c	χ_v^{2d}	R factor (%) ^e
Br–Pd ¹	2.90 ± 0.277	6.05 ± 0.103	2.507	51.61	0.295
Br–Pd ²	2.90 ± 0.277	6.05 ± 0.103	2.557		
Br–Br	3.97 ± 1.20	8.37 ± 0.678	3.359		

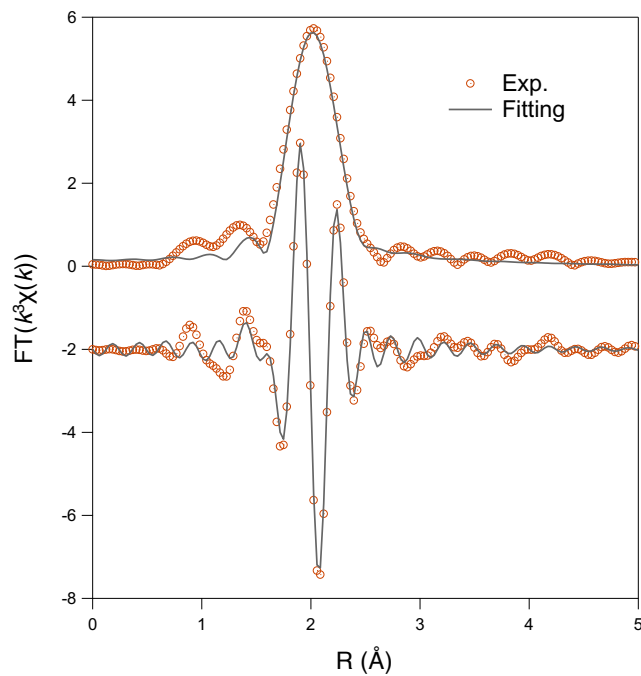


Supplementary Fig. 12. Plots of the fitted curve for Br-K edge EXAFS of 5a in THF solution in *r*-space: magnitude and its imaginary part. The scattering paths were calculated using the coordinates derived from the corresponding CIF file (CCDC: 2073816) generated through SC-XRD analysis.

Supplementary Table 13. Parameters obtained from the curve-fitting analysis of Br-K edge EXAFS of 6 in *r*-space. *k*-range: 3–13 Å⁻¹, *r*-range: 1.2–2.8 Å, *S*₀² = 1.00, Number of variable parameters = 3. ^aAbsorption edge energy correction. ^bDebye–Waller factor. ^cBond length difference. ^dReduced χ -squared value. ^eGoodness-of-Fit index.

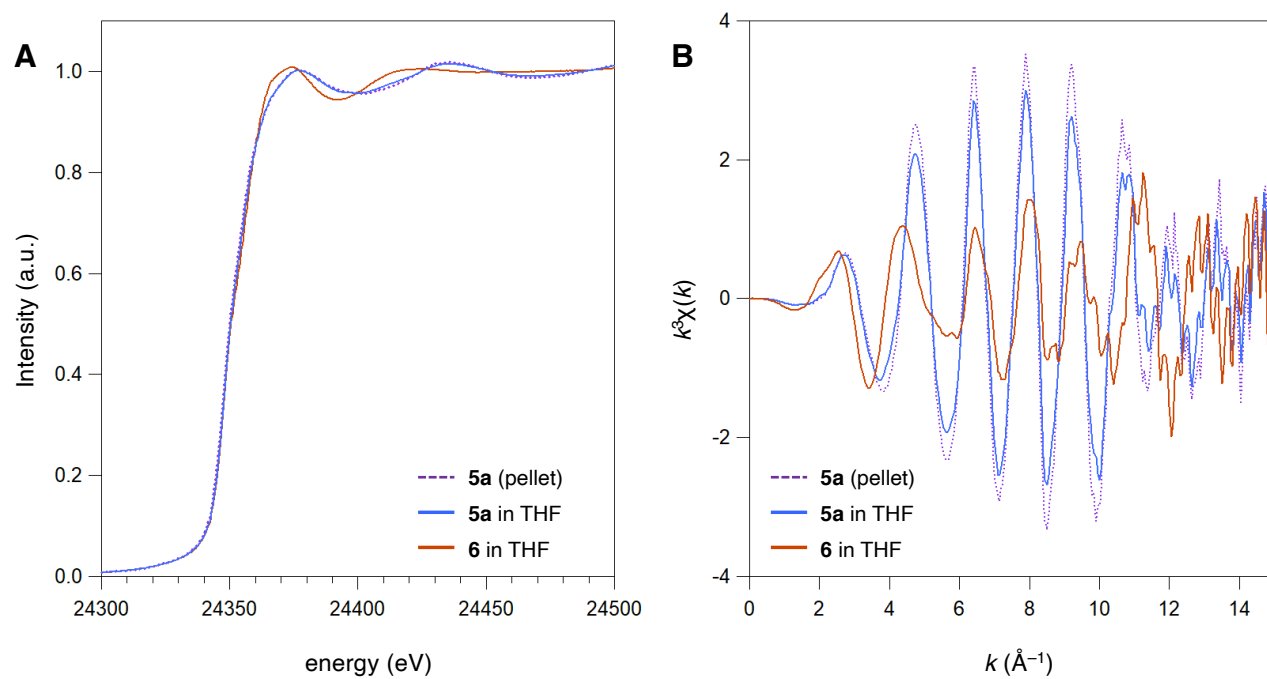


scattering path	ΔE_0 (eV) ^a	σ^2 (10 ⁻³ Å ²) ^b	ΔR (Å) ^c	R_{DFT} (Å)	χ^2 ^d	<i>R</i> factor (%) ^e
Br–Zn	4.23 ± 2.36	4.26 ± 0.31	+0.034 ± 0.008	2.308	238.80	2.09



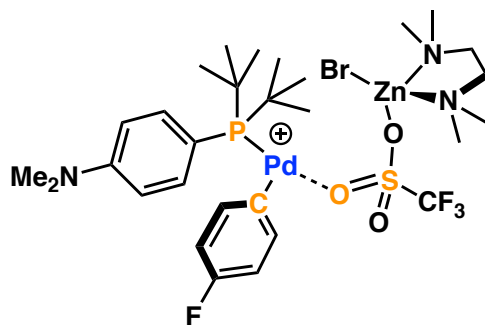
Supplementary Fig. 13. Plots of the fitted curve for Br-K edge EXAFS of 6 in THF solution in r -space: magnitude and its imaginary part.

Pd-K edge XAS data (Supplementary Fig. 14 and Supplementary Table 14)



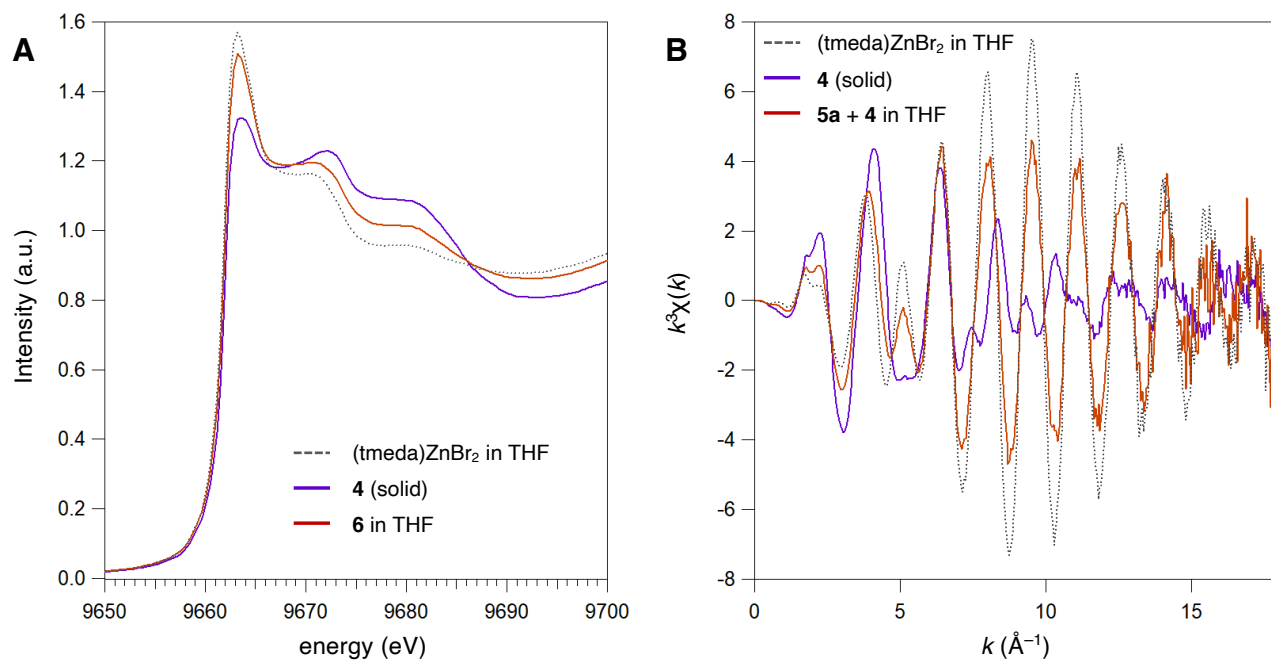
Supplementary Fig. 14. Pd-K edge XAS data of 5a and 6. A, XANES spectra. B, k^3 -weighted EXAFS oscillation.

Supplementary Table 14. Parameters obtained from the curve-fitting analysis of Pd-K edge EXAFS of **6 in *r*-space.** *k*-range: 3–14 Å⁻¹, *r*-range: 1.2–3.0 Å, *S*₀² = 1.00, Number of variable parameters = 8. ^aAbsorption edge energy correction. ^bDebye–Waller factor. ^cBond length difference. ^dReduced χ -squared value. ^eGoodness-of-Fit index.



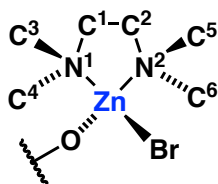
scattering path	ΔE_0 (eV) ^a	σ^2 (10 ⁻³ Å ²) ^b	ΔR (Å) ^c	R_{DFT} (Å)	χ^2_{v} ^d	<i>R</i> factor (%) ^e
Pd–C	-2.39 ± 6.28	2.53 ± 1.30	$+0.034 \pm 0.013$	1.961	117.40	1.28
Pd–O	-2.39 ± 6.28	2.53 ± 1.30	$+0.007 \pm 0.027$	2.181		
Pd–P	2.78 ± 5.95	6.60 ± 2.54	$+0.035 \pm 0.032$	2.277		
Pd–S	-3.09 ± 6.64	6.75 ± 1.70	-0.196 ± 0.038	3.238		

Zn-K edge XAS data (Supplementary Figs. 15, 16 and Supplementary Table 15)

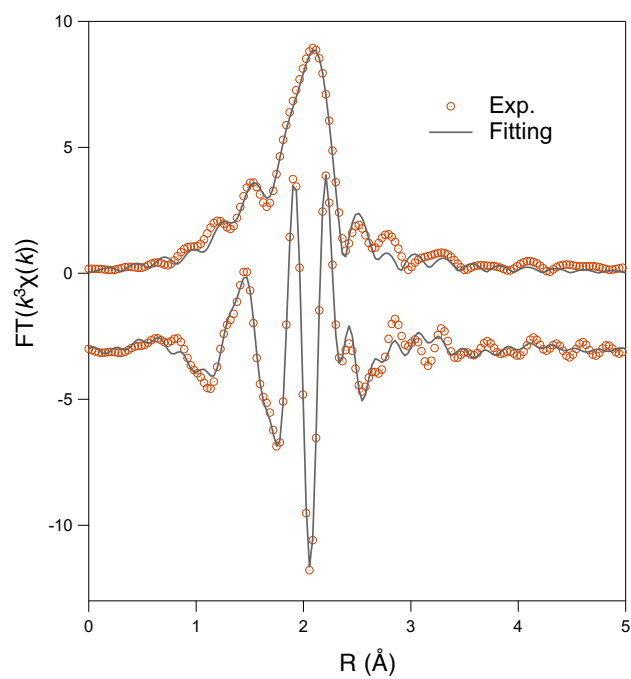


Supplementary Fig. 15. Zn-K edge XAS data of (tmeda)ZnBr₂, 4, and 6. A, XANES spectra. B, k^3 -weighted EXAFS oscillation.

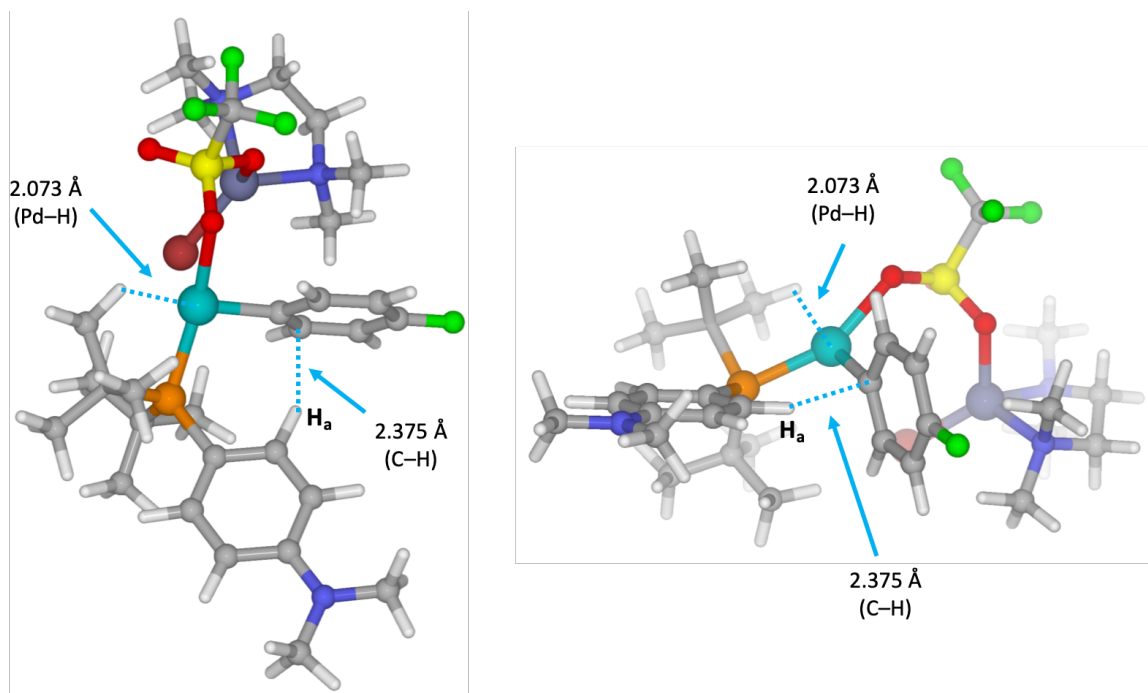
Supplementary Table 15. Parameters obtained from the curve-fitting analysis of Zn-K edge EXAFS of 6 in *r*-space. *k*-range: 3–15 Å^{−1}, *r*-range: 1.0–3.0 Å, *S*₀² = 1.00, Number of variable parameters = 7. ^aAbsorption edge energy correction. ^bDebye–Waller factor. ^cBond length difference. ^dReduced χ -squared value. ^eGoodness-of-Fit index.



scattering path	ΔE_0 (eV) ^a	σ^2 (10 ^{−3} Å ²) ^b	ΔR (Å) ^c	R_{DFT} (Å)	χ^2_{v} ^d	<i>R</i> factor (%) ^e
Zn–O	5.55 ± 2.42	9.24 ± 2.98	−0.058 ± 0.035	1.989	24.48	1.31
Zn–N ¹	5.55 ± 2.42	9.24 ± 2.98	−0.017 ± 0.027	2.106		
Zn–N ²	5.55 ± 2.42	9.24 ± 2.98	−0.017 ± 0.027	2.110		
Zn–Br	1.66 ± 2.99	3.26 ± 0.23	+0.029 ± 0.007	2.308		
Zn–C ¹	5.55 ± 2.42	9.24 ± 2.98	+0.004 ± 0.042	2.811		
Zn–C ²	5.55 ± 2.42	9.24 ± 2.98	+0.004 ± 0.042	2.853		
Zn–C ³	5.55 ± 2.42	9.24 ± 2.98	+0.004 ± 0.042	2.939		
Zn–C ⁴	5.55 ± 2.42	9.24 ± 2.98	+0.004 ± 0.042	2.940		
Zn–C ⁵	5.55 ± 2.42	9.24 ± 2.98	+0.004 ± 0.042	2.967		
Zn–C ⁶	5.55 ± 2.42	9.24 ± 2.98	+0.004 ± 0.042	3.002		



Supplementary Fig. 16. Plots of the fitted curve for Zn-K edge EXAFS of 6 in THF solution in r -space: magnitude and its imaginary part.

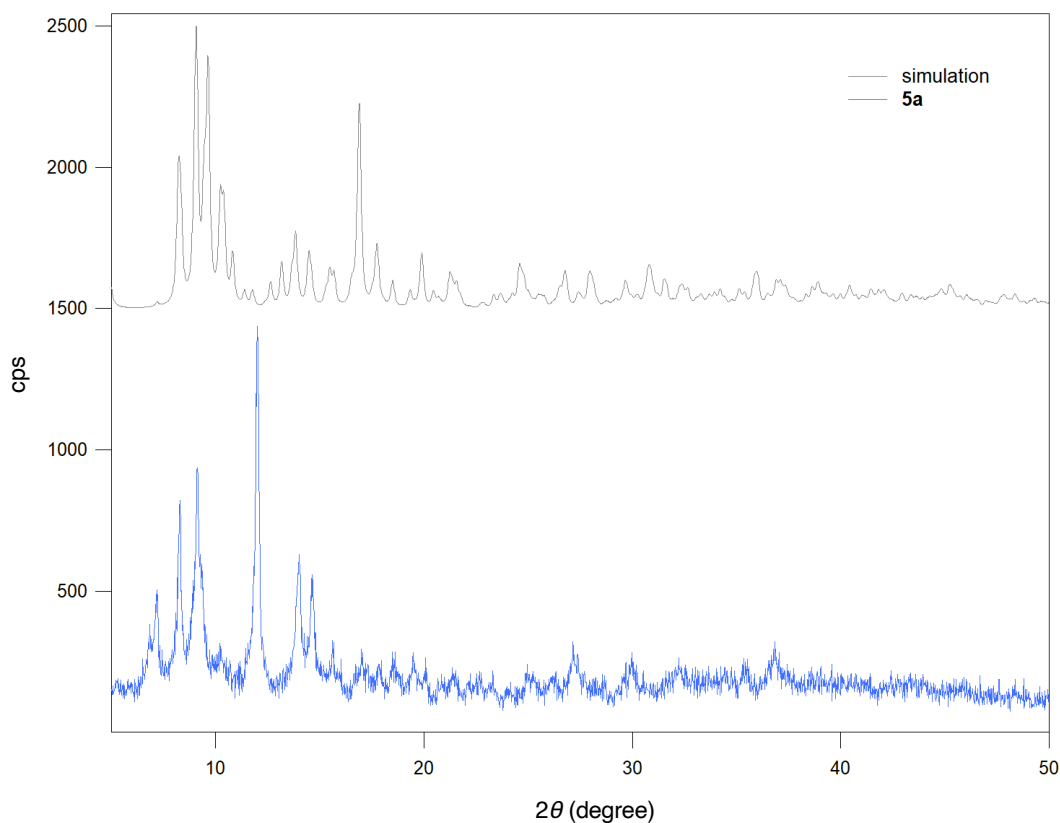


Supplementary Fig. 17. The views of the optimized structure of **6** obtained by DFT calculation. Hydrogen **H_a** indicates the aromatic hydrogen atom at the *ortho*-position of the phosphine atom is directed into the centre of the fluorophenyl group.

Powder XRD data of **5a** after grinding

The palladium complex **5a** was ground using an agate mortar over 15 min in a glovebox filled with argon gas. The resulting powder was loaded on a glass sample holder, and powder XRD measurement was conducted using the $\theta/2\theta$ scan with the continuous scanning mode (scan speed: $4^\circ/\text{min}$, scan step: 0.02°). The simulated XRD pattern was obtained using Mercury software with the corresponding CIF file (CCDC: 2073816) generated through SC-XRD analysis (FWHM = 0.02).

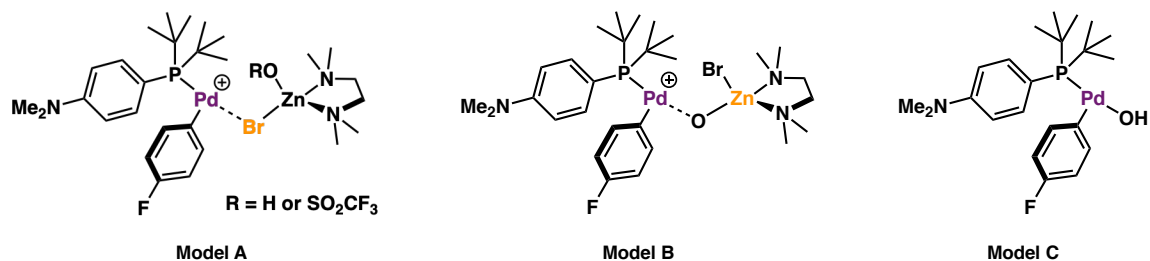
To obtain the information about the crystal structure of **5a** which was subjected to XAS experiments, powder XRD measurement was carried out using a powder sample ground for 15 min (Supplementary Fig. 18). Although some of peaks matched with the simulated XRD pattern, the experimental powder XRD pattern was basically not identical to the simulated one from SC-XRD measurement. This result indicated that the crystal structure of the powder sample is different from that of single crystal. Considering the Br–Br scattering was observed on Br–K edge EXAFS spectrum (Fig. 4A), this difference would be attributed to the change of the packing structure.



Supplementary Fig. 18. Experimental and simulated powder XRD data of **5a after grinding.**

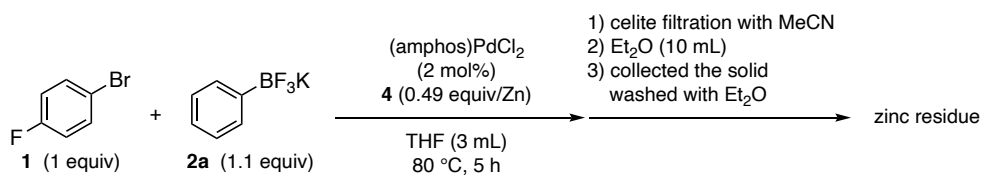
Consideration of other possible structures

The bromine activated model structure (Supplementary Fig. 19, Model A) could be ruled out because of the absence of a Fourier peak which corresponds to Br–Pd scattering on Br–K edge EXAFS (Fig. 4A). It was possible to consider the local structure of **6** as a Pd/Zn binuclear complex bridged by oxygen atom (Model B). Namely, the third peak of Pd–K edge EXAFS might be assigned as a scattering of the remote Pd–(O)–Zn. To verify the possibility, a curve fitting of EXAFS was also conducted with the same manner, resulted in poor conversion of fitting parameters, which suggests that this model structure could be ruled out. A fitting using the hydroxy palladium model structure (Model C) was also performed, but the third peak was not observed from the simulated spectrum based on FEFF calculation.



Supplementary Fig. 19. Other possible intermediates.

Analysis of the Zn residue after catalytic reaction on Zn–K edge XAS experiment

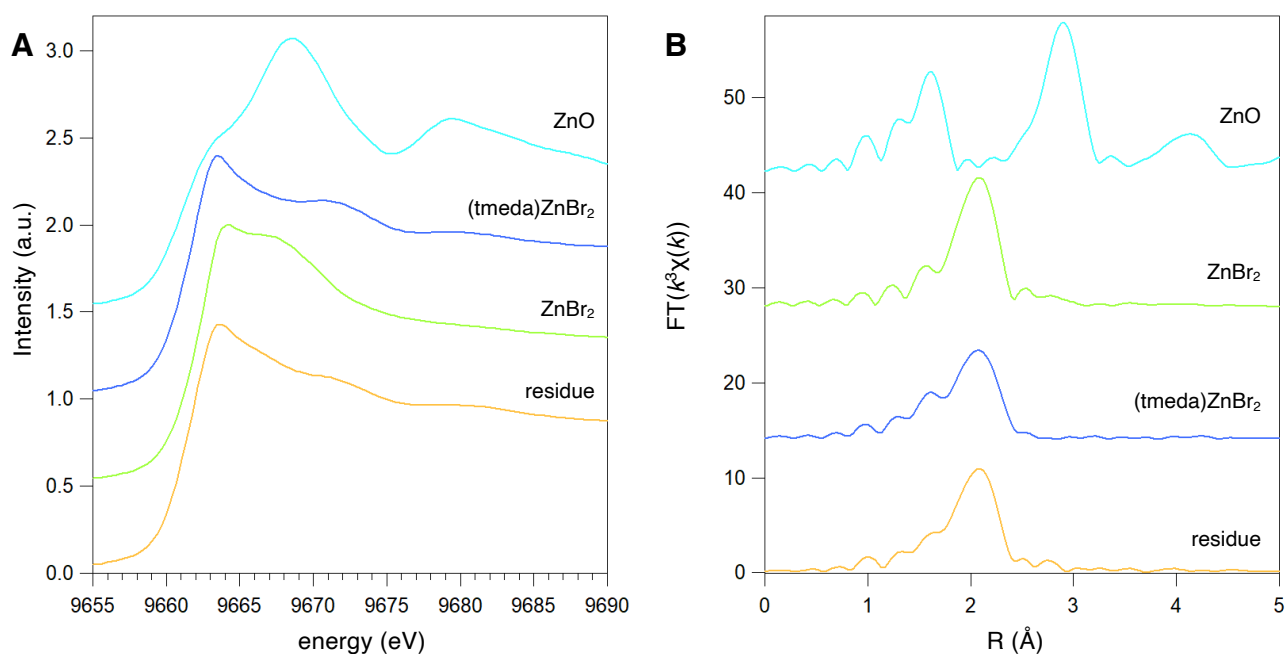


This experiment was performed at KEK Photon Factory BL-12C beamline using Si(111) double-crystal monochromatized synchrotron radiation.

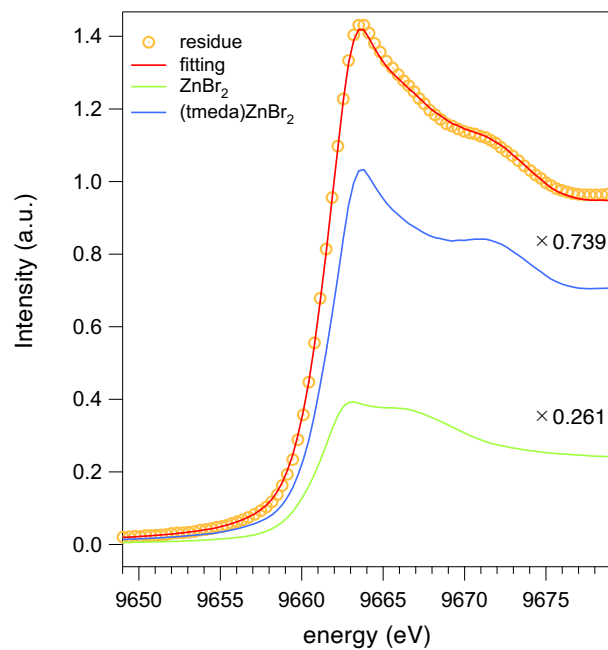
To a 4 mL capped vial equipped with a magnetic stir bar were added PdCl₂(amphos)₂ (4.2 mg, 6.0 μmol, 2 mol%), **4** (50.9 mg, 0.146 mmol/Zn, 0.49 equiv/Zn), **2a** (60.7 mg, 0.33 mmol, 1.1 equiv), THF (3.0 mL), and **1** (32.8 μL, 0.300 mmol, 1 equiv) sequentially in a glovebox filled with argon gas. The reaction vial was taken out from the glovebox and stirred for 5 h at 80 °C with an aluminium heat block. After cooling to room temperature, the mixture was passed through a short pad of Celite®, and washed with MeCN (ca. 10 mL) and Et₂O (ca. 10 mL), successively. The filtrate was concentrated under reduced pressure, and the resulting precipitate was washed with

Et₂O (ca. 10 mL). After dried under high vacuum, the solid residue (47.2 mg, pale colour solid) was subjected to XAS experiment.

To reveal the fate of zinc complex **4**, Zn-K edge XAS analysis of the residual solid after the SMC reaction was conducted. Since XANES and EXAFS spectra of the residue resembled those of ZnBr₂, it was found that **4** was converted to rather ZnBr₂ not ZnO, as expected from the *in-situ* XAS experiments (Supplementary Fig. 20). Linear combination fitting analysis was also carried out in the range ranging between E_0-10 and E_0+20 eV using ZnBr₂ and (tmeda)ZnBr₂ as references to find that the residue was composed of the mixture of ZnBr₂ and (tmeda)ZnBr₂ in the ratio of 26:74 (Supplementary Fig. 21).



Supplementary Fig. 20. Zn-K edge XAS data of the residue after reaction and references. A, XANES spectra. **B,** EXAFS.



Supplementary Fig. 21. Linear combination fitting analysis of the residue after reaction on Zn-K edge XANES spectrum.

Supplementary Method 4: Computational studies

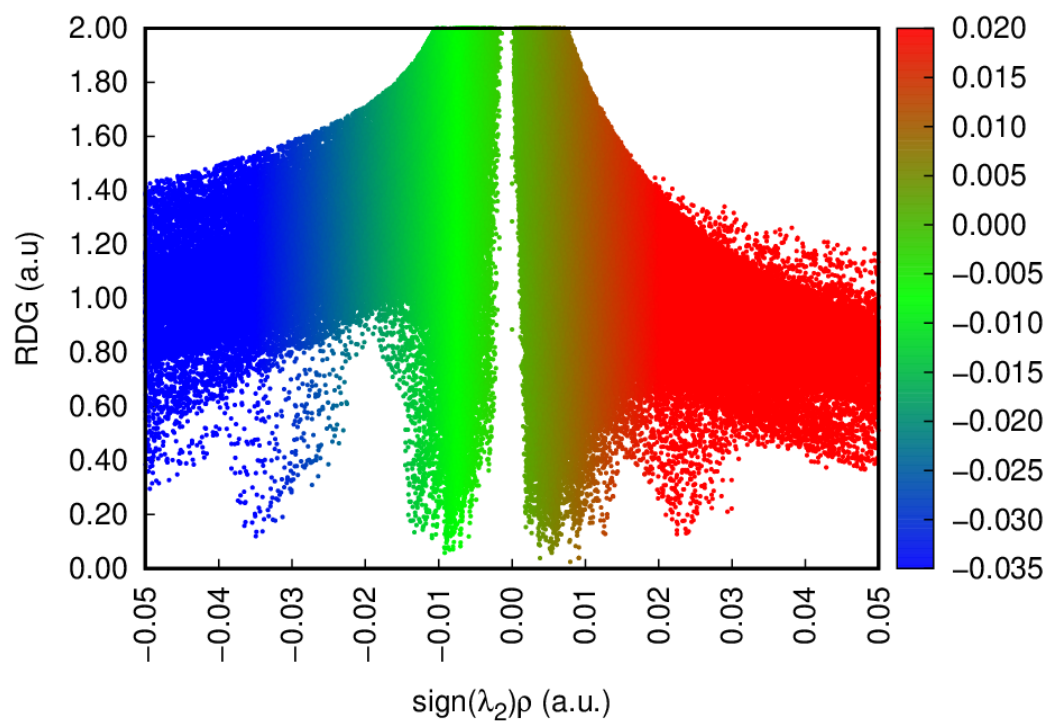
General method

We performed calculations of each element steps in the zinc-mediated SMC reaction to elucidate the reaction mechanism using 4-fluorobromobenzene (**1**) and potassium phenyl(trifluoro)borate (**2a**) as a model compound. All calculations were performed at RIKEN on Hokusai Big Waterfall (BW) using Gaussian 16 (revision C.01) program package.¹⁴ Geometry optimization and transition state (TS) calculations were carried out by the DFT method at B3PW91-D3 level of theory^{15–19} with a def2-SVP basis set^{20,21} for all atoms in the gas phase. Harmonic frequency calculations were conducted at the same level of theory on the optimized geometries to check all the stationary points as either minima or first-order saddle points. Intrinsic reaction coordinate (IRC) calculations²² were carried out to confirm the transition states connecting the correct reactants and products on the potential energy surface. The zero-point energy (ZPE) and thermal energy corrections were calculated using vibrational frequencies. The self-consistent field energies (298.15 K, 1 atm) were corrected at B3PW91-D3 level of theory in THF using IEF-PCM solvation model²³ with a def2-TZVP basis set^{20,21} for all atoms. Computed structures are illustrated using VESTA²⁴ or CYL-view²⁵.

Summary: B3PW91-D3/def2-TZVP/IEF-PCM(THF)//B3PW91-D3/def2-SVP/gas phase

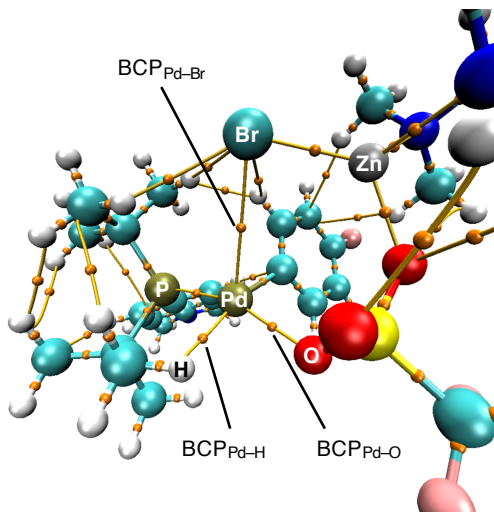
Electron density analyses

Electron density analyses for the optimized coordinates were conducted with the electron density at the B3PW91-D3/aug-cc-pVDZ,LanL2DZ(for Pd)/IEF-PCM(THF) level of theory as the SCF energy correction using Multiwfn program.²⁶ The wavefunction files in a formatted gaussian checkpoint (fchk) file format were generated using Gaussian 16. Qualitative non-covalent interactions (NCIs) in the computed structures were visualized with the non-covalent interaction index.²⁷ The following thresholds were applied to generate the NCI isosurface; $\text{sign}(\lambda_2)\rho$ ranging from -0.50 to 0.50 a.u. and reduced density gradient (RDG) = 0.40 a.u. The surfaces were coloured on a blue-green-red (BGR) scale using VMD program²⁸ according to values of $\text{sign}(\lambda_2)\rho$ ranging from -0.035 to 0.02 a.u. The blue and green regions indicate strong and weak attractive interactions, respectively. QTAIM analyses and Wiberg bond indexes (WBIs) calculation were conducted with the corresponding fchk files. The obtained bond paths and the bond critical points (BCPs) were visualized using VMD program. Natural bond orbital (NBO) calculation was performed by NBO 7.0.7 programs²⁹ at Research Center for Computational Science, National Institutes of Natural Science (NINS), Okazaki Research Facilities. The reference molecular orbitals were calculated for the optimized coordinates at the same level of theory.



Supplementary Fig. 22. Plots of the non-covalent interaction index of 6.

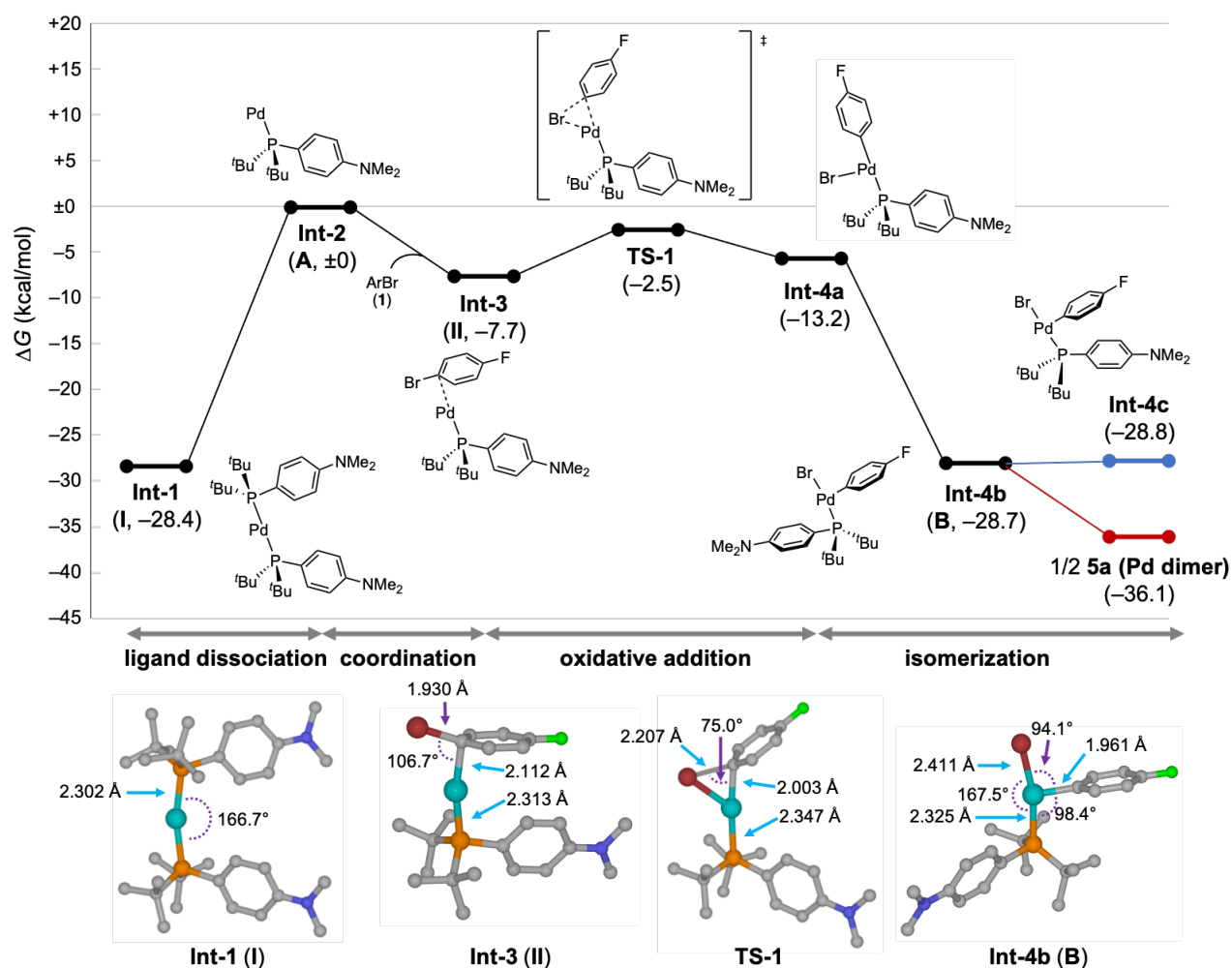
Supplementary Table 16. Summary of the electronic properties at BCPs of 6. $\rho_{\text{bcp}}(r)$: electron density, $\nabla^2\rho_{\text{bcp}}(r)$: Laplacian of electron density, $G(r)$: kinetic energy density, $H(r)$: total energy density, WBI: Wiberg bond index.^{30,31}



BCP	$\rho_{\text{bcp}}(r)$ ($\text{e}\text{\AA}^{-3}$)	$\nabla^2\rho_{\text{bcp}}(r)$ ($\text{e}\text{\AA}^{-5}$)	$G(r)/\rho_{\text{bcp}}(r)$ (he^{-1})	$H(r)/\rho_{\text{bcp}}(r)$ (he^{-1})	WBI
Pd–O	0.434	+8.11	1.40	−0.0868	0.476
Pd–H	0.252	+3.16	1.02	−0.138	0.167
Pd–Br	0.0605	+0.511	0.543	0.0480	0.091

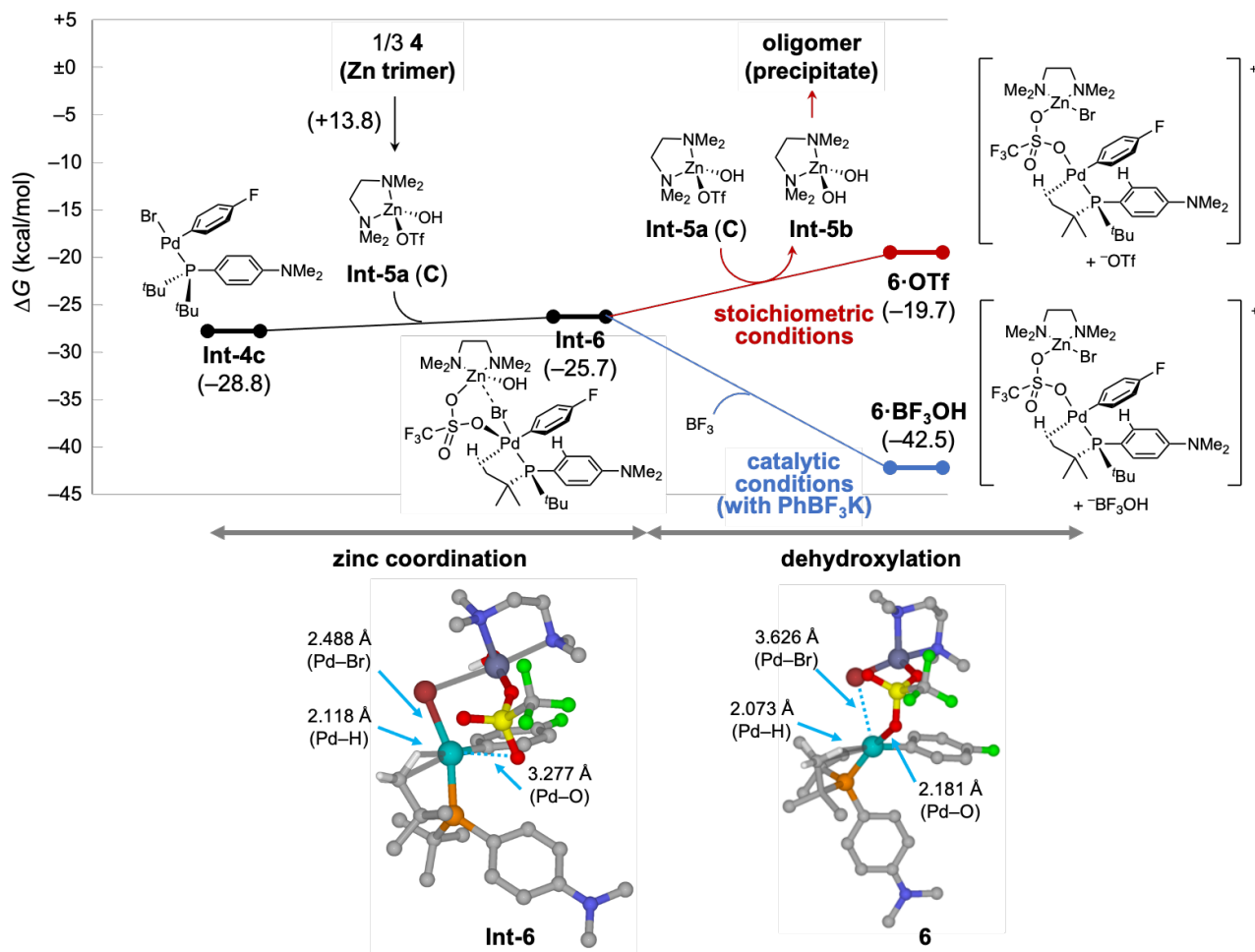
Energy profiles of Zn-mediated SMC reaction

Oxidative addition. We set the catalytically active species (amphos)Pd species (**Int-2**, **A** in Fig. 6) as the zero point. The dissociation of one equivalent of Amphos from **Int-1** (**I** in Fig. 6) is considered to be a starting point when $\text{PdCl}_2(\text{amphos})_2$ was used as a precatalyst. This process is endergonic with a considerable energy difference (+28.4 kcal/mol), suggesting **Int-1** is a resting state of this reaction. After coordination of **1** to form **Int-3** (**II**), oxidative addition proceeds with an endothermal energy of 5.2 kcal/mol followed by isomerization of the ligands to afford palladium dimer **5a**. This result is consistent with that preparation of **5a** from **1** can be conducted at room temperature. The calculation also revealed that the aryl palladium complexes can exist as a monomer **Int-4b** (**B**) or its conformational isomer **Int-4c** with small energy barriers.



Supplementary Fig. 23. Energy profile for oxidative addition. Selected optimized structures with the bond length and angles are shown.

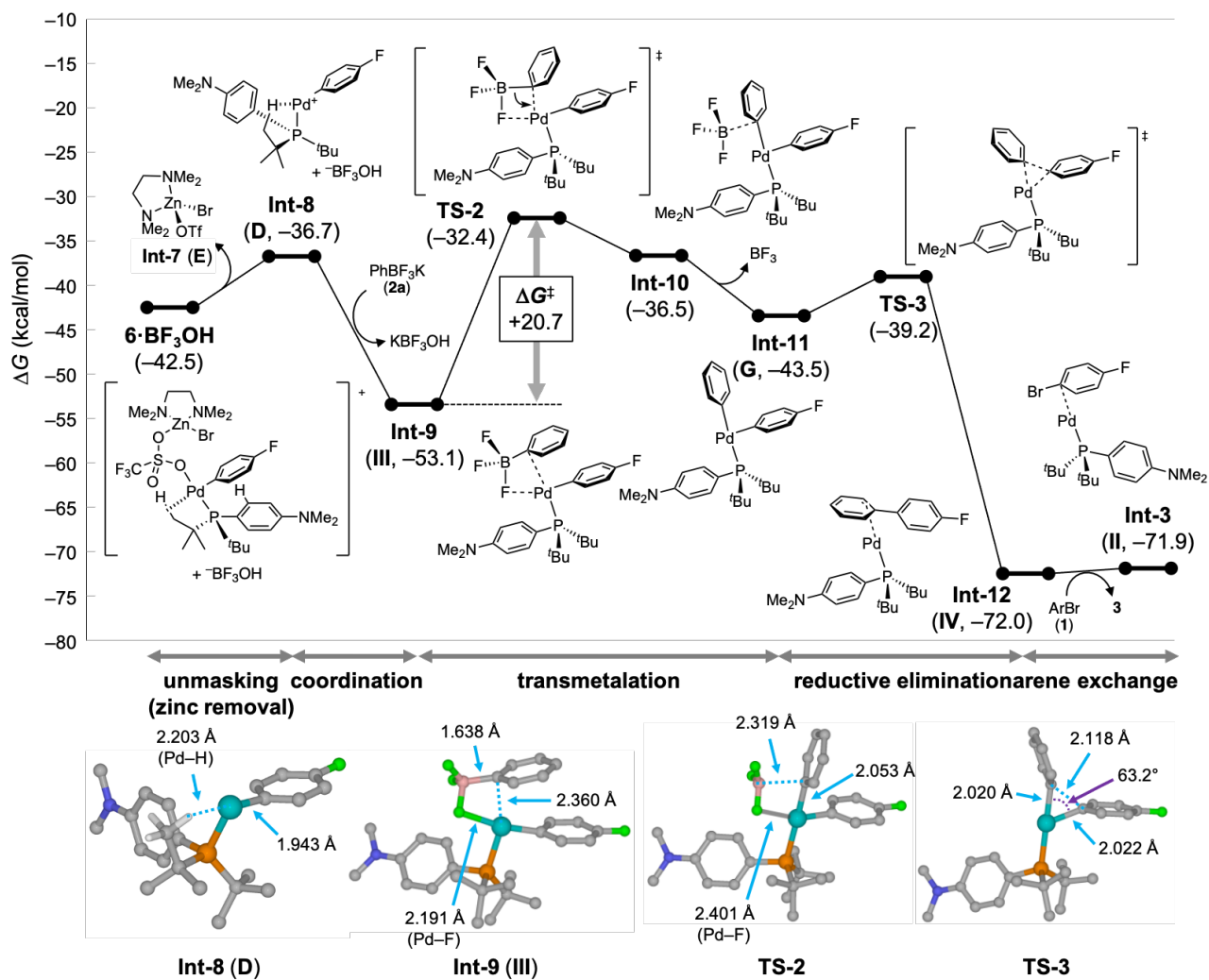
Generation of intermediate 6. We calculated several pathways between **5a** and **6** and found that palladium–zinc hydroxy complex **Int-6**, where the zinc moiety behaves as a bidentate ligand via the triflate and bromide moieties, is a plausible intermediate. First, zinc monomer **Int-5a** (**C**), formed by monomerization of **4**, binds to **Int-4c** to afford **Int-6**. Although the monomerization of zinc trimer **4** is an endergonic (+13.8 kcal/mol), the energy gap between **Int-4c** and **Int-6** is small (+3.1 kcal/mol). Following dehydroxylation from the zinc centre occurs to give bimetallic intermediate **6**. In the stoichiometric reaction conditions, remaining **Int-5a** could abstract the hydroxy group as four equivalents of **4** was used for the quantitative conversion. Although this step is uphill (+6.0 kcal/mol) to produce **6·OTf**, byproduct **Int-5b** could oligomerize to afford a precipitate, being this process irreversible. In the catalytic conditions, boron trifluoride (BF₃), formed at the initiation of the palladium catalyst and transmetalation with **2a**, could be a preferable acceptor of the hydroxy group. The dehydroxylation with BF₃ is favourable in free energy (–16.8 kcal/mol) and proceeds to give **6·BF₃OH** bearing hydroxy(trifluoro)borate as a counter anion. We employed **6·BF₃OH** for the following calculation study.



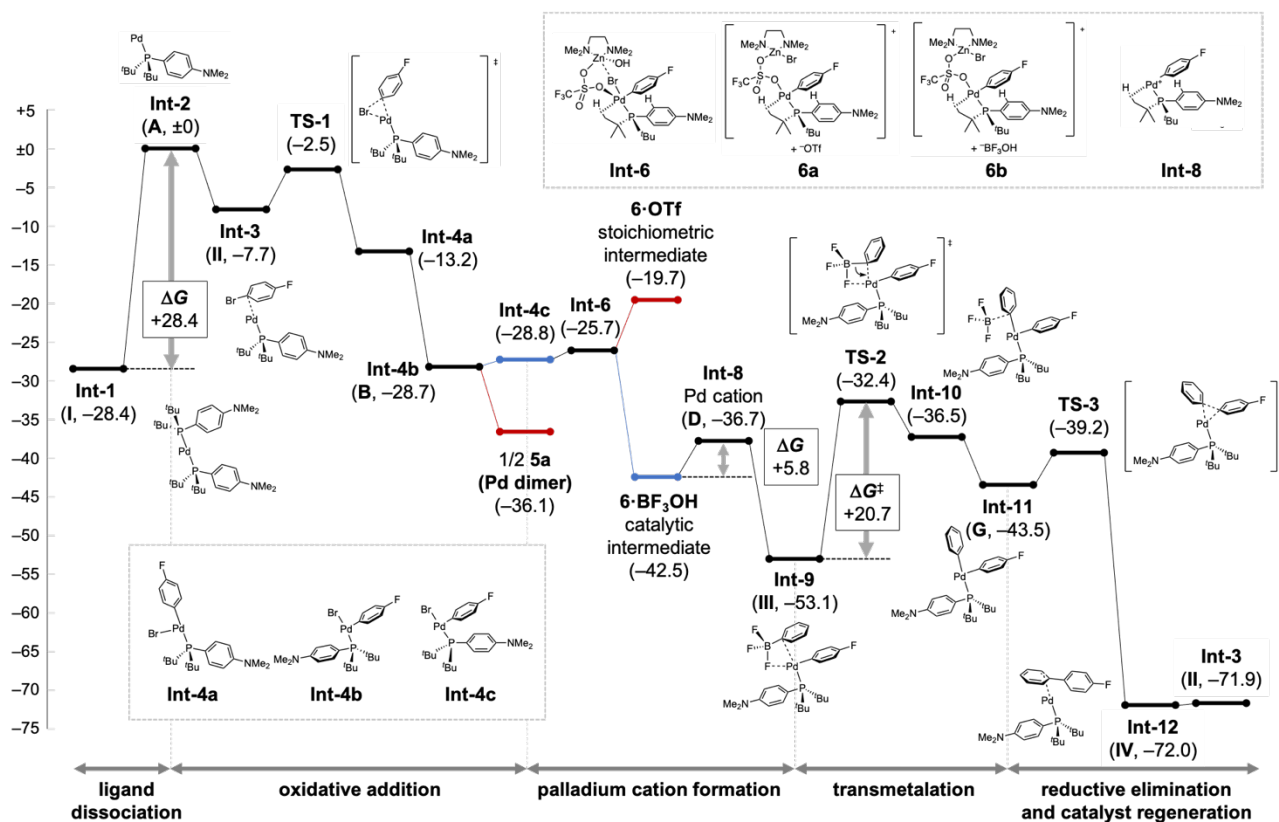
Supplementary Fig. 24. Energy profile for formation of intermediate **6**. Selected optimized structures with the bond length and angles are shown.

Transmetalation and reductive elimination. Based on the calculation, we assumed that generation of naked cationic palladium complex **Int-8 (D)**, active species for the base-independent transmetalation with organoborons, forms by removal of the zinc moiety from **6·BF₃OH**. This liberation step is endergonic but not a high energy process (+5.7 kcal/mol), supporting that transmetalation-active species predominantly exists as **6**. The following coordination of **2a** is preferable (−16.4 kcal/mol) to afford relatively stable species **Int-9 (III)**. The barrier for the transmetalation (**TS-2**) was estimated to be 20.7 kcal/mol, which is not too high to occur the reaction without heating conditions. Although the transmetalation followed by liberation of BF₃ is thermodynamically unfavoured (+9.6 kcal/mol from **Int-9** to **Int-11**), the following reductive elimination smoothly takes place via the transition state **TS-3** with an energy barrier of only 4.3 kcal/mol to give **3** and regenerate **Int-3 (II)**, −28.4 kcal/mol from **Int-11**. Overall, this catalytic

transformation is thermodynamically favourable, and the activation free energy for the whole catalytic cycle is 20.7 kcal/mol for transmetalation, which is consistent that the stoichiometric reaction of palladium complexes **5a** or **6** with organoborons **2** proceeds without heating.



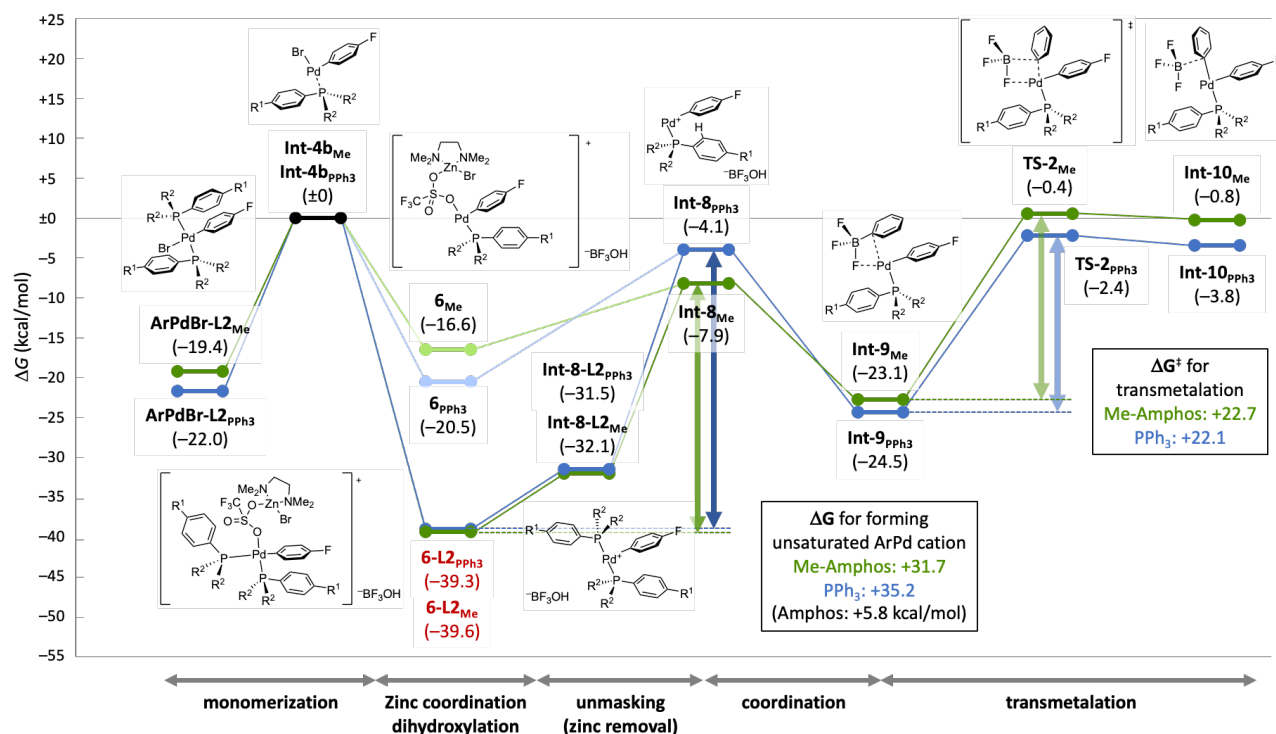
Supplementary Fig. 25. Energy profile for formation of biaryl **3** from intermediate **6**. Selected optimized structures with the bond length and angles are shown.



Supplementary Fig. 26. Summary of energy profile of the zinc-mediated SMC reaction. The reagents and products are omitted for clarity.

Consideration on ligand effect. To gain insight into the contribution of the agostic interaction (Figs. 4H and 4I) for the ligand effect, we conducted DFT analysis. We selected **Me-Amphos**, an Amphos derivative having methyl groups instead of *tert*-butyl groups, as a model ligand that cannot form the agostic interaction due to the small substituents. For the comparison, we also investigated the energy profile with triphenylphosphine (PPh₃). As shown in Supplementary Fig. 2, the reaction using dimethylphenylphosphine (PhPMe₂, a derivative of Me-Amphos) or PPh₃ gave poor yields (1%, 13%, respectively). The results are summarized in Supplementary Fig. 27.

We found that the use of a sterically non-hindered ligand, such as Me-Amphos or PPh₃, is difficult to generate a coordinatively unsaturated cation complex (**Int-8**). A significant difference in the relative Gibbs free energies for generation of **Int-8** or the transmetalation (**TS-2**) was not observed; however, dual binding of the small ligand occurs and considerably stabilizes the intermediates, including Pd/Zn binuclear complexes (**6-L2**) and (diphosphine)arylpalladium cation complexes (**Int-8-L2**). The stabilization causes high energy barrier (>30 kcal/mol) to form **Int-8**, prohibiting an efficient conversion. Based on these results, we considered that the agostic interaction would contribute to avoiding the dual ligand binding and stabilize coordinatively unsaturated cation complexes, such as **6** and **Int-8**.



Supplementary Fig. 27. Ligand effect on energy profile of the zinc-mediated SMC reaction.

Supplementary Table 17. Calculated energies and thermochemical parameters of the optimized structures. Imaginary frequencies (cm^{-1}) of the structures for the transition states are shown in the parenthesis.

structure	E (hartree)	H (hartree)	TS (hartree)	G (hartree)
Int-1	-2170.916987	-2170.916043	0.131524	-2171.047566
Int-2	-1150.302168	-1150.301224	0.071876	-1150.373099
ArBr (1)	-2904.973787	-2904.972843	0.039549	-2905.012392
Int-3	-4055.306943	-4055.305999	0.091751	-4055.397750
TS-1 (-135.52 cm^{-1})	-4055.299579	-4055.298635	0.090805	-4055.389440
Int-4a	-4055.319299	-4055.318354	0.088182	-4055.406537
Int-4b	-4055.343524	-4055.342580	0.088694	-4055.431274
Int-4c	-4055.342505	-4055.341561	0.089893	-4055.431453
5a	-8107.625382	-8107.624438	0.168392	-8107.792830
4	-9493.235740	-9493.234796	0.153048	-9493.387843
Int-5a	-3164.369945	-3164.369001	0.071594	-3164.440595
Int-6	-7219.730946	-7219.730002	0.137010	-7219.867012
Int-5b	-2278.674346	-2278.673402	0.056083	-2278.729485
6	-7140.677001	-7140.676057	0.144787	-7140.820843
^-OTf	-961.641641	-961.640697	0.039733	-961.680430
$^-\text{BF}_3\text{OH}$	-399.988415	-399.987471	0.034772	-400.022243
Int-7	-5662.772770	-5662.771826	0.070763	-5662.842589
Int-8	-1480.953034	-1480.952090	0.084344	-1481.036434
PhBF ₃ K (2a)	-1156.104900	-1156.103955	0.048350	-1156.152305
KBF ₃ OH	-1000.410680	-1000.409736	0.040424	-1000.450160
Int-9	-2037.266573	-2037.265629	0.104074	-2037.369703
TS-2 (-108.93 cm^{-1})	-2037.231869	-2037.230925	0.105767	-2037.336692
Int-10	-2037.233891	-2037.232947	0.110301	-2037.343248
BF ₃	-324.569792	-324.568848	0.030638	-324.599486
Int-11	-1712.658319	-1712.657375	0.097509	-1712.754884
TS-3 (-203.99 cm^{-1})	-1712.652549	-1712.651605	0.096585	-1712.748189
Int-12	-1712.704416	-1712.703472	0.096953	-1712.800426
3	-562.370237	-562.369293	0.045557	-562.414850

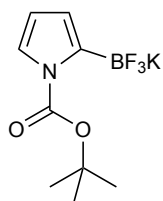
Supplementary Table 18. Calculated energies and thermochemical parameters of the optimized structures for Supplementary Fig. 27. Imaginary frequencies (cm^{-1}) of the structures for the transition states are shown in the parenthesis.

structure	E (hartree)	H (hartree)	TS (hartree)	G (hartree)
ArPdBr-L2 _{Me}	-4606.246620	-4606.245675	0.105443	-4606.351118
Int-4b _{Me}	-3819.631780	-3819.630835	0.078261	-3819.709097
6 _{Me}	-6908.051061	-6908.050117	0.120456	-6908.170573
6-L2 _{Me}	-7694.671660	-7694.670716	0.140764	-7694.811480
Int-8-L2 _{Me}	-2031.855644	-2031.854700	0.102284	-2031.956984
Int-8 _{Me}	-1245.242511	-1245.241567	0.072612	-1245.314179
Int-9 _{Me}	-1801.555272	-1801.554328	0.091371	-1801.645699
TS-2 _{Me} (-63.22 cm^{-1})	-1801.515389	-1801.514445	0.093850	-1801.608295
Int-10 _{Me}	-1801.516106	-1801.515162	0.094482	-1801.609644
ArPdBr-L2 _{PPh3}	-5105.141003	-5105.140059	0.116487	-5105.256546
Int-4b _{PPh3}	-4069.080685	-4069.079740	0.080789	-4069.160529
6 _{PPh3}	-7157.506515	-7157.505571	0.122513	-7157.628084
6-L2 _{PPh3}	-8193.567731	-8193.566787	0.152217	-8193.719004
Int-8-L2 _{PPh3}	-2530.751612	-2530.750668	0.113262	-2530.863931
Int-8 _{PPh3}	-1494.683039	-1494.682095	0.077221	-1494.759316
Int-9 _{PPh3}	-2051.003188	-2051.002244	0.096870	-2051.099113
TS-2 _{PPh3} (-95.01 cm^{-1})	-2050.965305	-2050.964361	0.099612	-2051.063973
Int-10 _{PPh3}	-2050.968036	-2050.967092	0.099176	-2051.066268

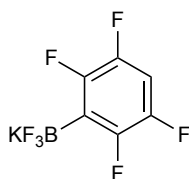
Supplementary Method 5: Synthetic procedure and characterization data

Synthesis of potassium organo(trifluoro)borates

Preparation of potassium organo(trifluoro)borates was conducted according to the reported procedure.³²

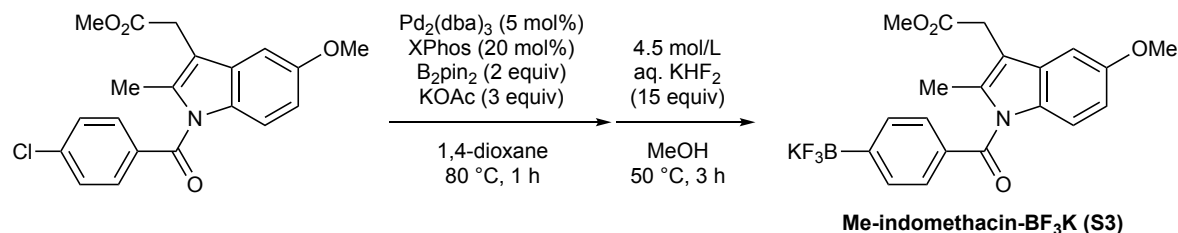


Potassium *N*-butoxycarbonylpyrrol-2-yl(trifluoro)borate (S1). Prepared from *N*-butoxycarbonylpyrrol-2-ylboronic acid (405.1 mg, 1.92 mmol); Yield: 73.7% (387 mg, 1.42 mmol); White solid (mp: 172–173 °C); ¹H NMR (DMSO-*d*₆) δ 7.08–7.07 (m, 1H), 5.99–5.94 (m, 2H), 1.50 (s, 9H); ¹³C{¹H} NMR (DMSO-*d*₆) δ 150.4 (1C), 120.5 (1C), 116.5 (1C), 110.0 (1C), 81.1 (1C), 27.6 (3C) (the signal for the carbon that is attached to the boron atom was not observed); ¹⁹F NMR (DMSO-*d*₆) δ –135.7; ¹¹B NMR (DMSO-*d*₆) δ 0.7. The chemical shifts were consistent with those reported in the literature.²³



Potassium 2,3,5,6-tetrafluorophenyl(trifluoro)borate (S2). Prepared from 2,3,5,6-tetrafluorophenylboronic acid (150 mg, 0.774 mmol); Yield: 40.4% (80.0 mg, 0.313 mmol); White solid (mp: 288 °C, decomp.); ¹H NMR (DMSO-*d*₆) δ 7.38–7.29 (m, 1H); ¹³C{¹H} NMR (DMSO-*d*₆) δ 147.3 (dm, ¹*J*_{C-F} = 240.2 Hz, 2C), 144.9 (dm, ¹*J*_{C-F} = 236.7 Hz, 2C), 103.3 (t, ²*J*_{C-F} = 23.3 Hz, 1C), 102.1 (t, ²*J*_{C-F} = 22.9 Hz, 1C); ¹⁹F NMR (DMSO-*d*₆) δ –132.6 (q, *J*_{F-B} = 42.7 Hz, 3F), –132.0 (d, *J*_{F-F} = 11.2 Hz, 2F), –141.9 – –142.1 (m, 2F); ¹¹B NMR (DMSO-*d*₆) δ 0.5 (q, *J*_{B-F} = 45.0 Hz, 1B); IR (ZnSe, cm^{–1}) 1462, 1256, 1169, 1049, 1007, 966, 899, 851, 831, 716; HRMS (ESI[–]) *m/z* 217.0059 (217.0054 calcd for C₆HBF₇[–], [M–K][–]).

Synthesis of potassium Me-indomethacin(trifluoro)borate (S3)



To a round-bottom flask equipped with a magnetic stir bar were added indomethacin methyl ester (3.00 g, 8.07 mmol, 1 equiv), B₂pin₂ (4.10 g, 16.1 mmol, 2.0 equiv), Pd₂(dba)₃ (366 mg, 0.400 mmol, 0.05 equiv), XPhos (768 mg, 1.61 mmol, 0.20 equiv), KOAc (2.38 g, 24.3 mmol, 3.0 equiv), and 1,4-dioxane (32.3 mL). The mixture was stirred for 1 h at 80 °C with an oil bath and then cooled to room temperature. To this was added saturated aqueous ammonium chloride (ca. 20 mL), and the mixture was extracted with EtOAc (ca. 30 mL × 3). The combined organic extract was dried over Na₂SO₄. After filtration, the filtrate was concentrated under reduced pressure to give a crude mixture that contained **Me-indomethacin-Bpin**.

To a solution of the crude mixture in MeOH (323 mL) was added an aqueous solution of KHF₂ (4.5 mol/L, 26.9 mL, 121 mmol, 15 equiv). The mixture was stirred for 3 h at 50 °C and then cooled to room temperature. The solvents were removed under reduced pressure, and the residue was dried under vacuum. The residue was suspended in acetone (ca. 300 mL) and irradiated with an ultrasonic wave for 1 min. After passing the mixture through a pad of Celite[®] and washing with acetone, the filtrate was concentrated under reduced pressure until a white precipitate was observed. To this suspension was added Et₂O (150 mL) to promote the precipitation. The insoluble solid was collected by filtration, washed with Et₂O, and dried under vacuum to give **S3** (3.23 g, 7.29 mmol, 90.3%) as a white solid;

mp: 245 °C (decompose); TLC: *R*_f = 0.59 (CHCl₃/MeOH = 2/1); ¹H NMR (DMSO-*d*₆) δ 7.50 (d, *J*_{H-H} = 8.3 Hz, 2H), 7.40 (d, *J*_{H-H} = 7.9 Hz, 2H), 7.00 (d, *J*_{H-H} = 2.4 Hz, 1H), 6.83 (d, *J*_{H-H} = 8.7 Hz, 1H), 6.67 (dd, *J*_{H-H} = 9.1, 2.0 Hz, 1H), 3.78 (s, 2H), 3.75 (s, 3H), 3.63 (s, 3H), 2.24 (s, 3H); ¹³C{¹H} NMR (DMSO-*d*₆) δ 171.2 (1C), 169.9 (1C), 155.2 (1C), 135.6 (1C), 131.8 (1C), 131.6 (2C), 130.5 (1C), 130.1 (1C), 127.2 (2C), 114.3 (1C), 111.6 (1C), 111.1 (1C), 101.3 (1C), 55.3 (1C), 51.8 (1C), 29.2 (1C), 12.9 (1C) (the signal for the carbon that is attached to the boron atom was not observed); ¹⁹F NMR (DMSO-*d*₆) δ -139.7 (m, 3F); ¹¹B NMR (DMSO-*d*₆) δ 1.8 (s, 1B); IR (ZnSe, cm⁻¹) 1377, 1204, 1175, 995, 968, 957, 939, 914, 827, 799; HRMS (ESI⁻) *m/z* 404.1279 (404.1275 calcd for C₂₀H₁₈¹¹BF₃NO₄⁻, [M-K]⁻).

Procedures for zinc-mediated SMC reaction

Zinc-mediated SMC with aryl bromides. To a 4 mL capped vial equipped with a magnetic stir bar were added aryl bromide (0.200 mmol, 1 equiv), organo(trifluoro)borate (0.220 mmol, 1.1 equiv), PdCl₂(amphos)₂ (2.8 mg, 4.0 μmol, 0.02 equiv), **4** (54.2 mg, 0.156 mmol/Zn, 0.78 equiv/Zn), and THF (1.0 mL). The mixture was stirred for time as indicated at 80 °C and then cooled to room temperature. The mixture was poured into saturated aqueous sodium hydrogen carbonate (ca. 2 mL), and the mixture was extracted with EtOAc (ca. 3 mL × 3). The combined organic extract was dried over Na₂SO₄. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to give the corresponding products. Further purification was conducted with GPC or HPLC when required.

Zinc-mediated SMC with aryl chlorides. To a 4 mL capped vial equipped with a magnetic stir bar were added aryl chloride (0.200 mmol, 1 equiv), potassium aryl(trifluoro)borate (0.220 mmol, 1.1 equiv), (cod)Pd(CH₂TMS)₂ (3.1 mg, 8.0 μmol, 0.04 equiv), XPhos (9.5 mg, 20 μmol, 0.1 equiv), **4** (54.2 mg, 0.156 mmol/Zn, 0.78 equiv/Zn), and CPME (1.0 mL). The mixture was stirred for time as indicated at 120 °C and then cooled to room temperature. The mixture was poured into saturated aqueous sodium hydrogen carbonate (ca. 2 mL), and the mixture was extracted with EtOAc (ca. 3 mL × 3). The combined organic extract was dried over Na₂SO₄. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to give the corresponding products. Further purification was conducted with GPC or HPLC when required.

Comparing reaction conditions for SMC reactions

To evaluate the synthetic utility of the zinc-mediated SMC reaction, we attempted to synthesize some products under the reported conditions for cross-coupling reaction of organohalides and potassium organo(trifluoro)borates (Supplementary Table. 19). As representatives, we selected two types of conditions for the comparison with the newly developed method (**condition 1**): One is the condition using an aqueous solvent that was efficient to use functionalized potassium aryl(trifluoro)borates and alkynylborates (**condition 2**).^{33,34} The addition of water is reported to be effective for releasing transmetalation-active organoboronic acids from organo(trifluoro)borates³⁵ and organoboronic acid esters.³⁶ The other was reported that was suitable to use potassium heteroaryl(trifluoro)borates (**condition 3**).³⁷ The detailed procedures are shown below.

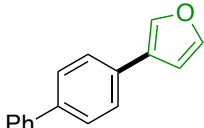
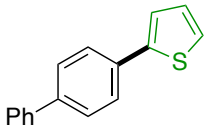
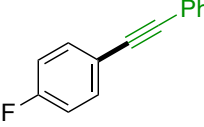
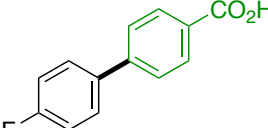
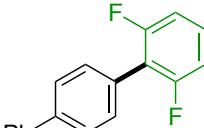
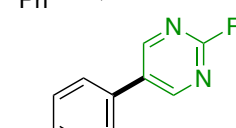
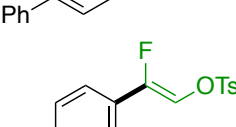
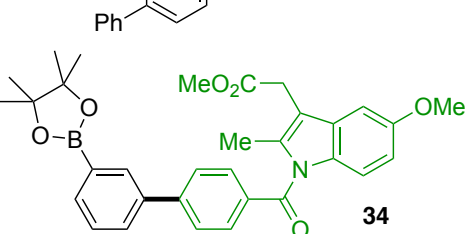
Condition 2: To a 4 mL capped vial equipped with a magnetic stir bar were added aryl bromide (0.200 mmol, 1 equiv), organo(trifluoro)borate (0.220 mmol, 1.1 equiv), PdCl₂(dppf)₂·CH₂Cl₂ (14.7 mg, 18.0 μmol, 0.09 equiv), K₂CO₃ (82.9 mg, 0.600 mmol, 3 equiv), THF (2 mL), and H₂O

(50 μ L). The mixture was stirred for time as indicated for 16 h at 80 $^{\circ}$ C with an aluminium heat block and then cooled to room temperature. After cooling to room temperature, to the reaction mixture was added saturated aqueous NaHCO_3 (ca. 1 mL), Et_2O (ca. 1 mL), and PhCF_3 (for ^{19}F NMR, 12.3 μ L, 0.100 mmol) or 1,1,2,2-tetrachloroethane (for ^1H NMR, 10.5 μ L, 0.100 mmol) as an internal standard. After vigorous stirring, a portion of the organic phase (ca. 0.4 mL) was transferred into an NMR tube, followed by dilution with CDCl_3 (ca. 0.4 mL). ^1H or ^{19}F NMR measurement was performed to determine the yield of products.

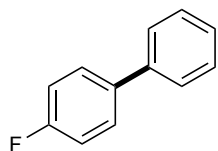
Condition 3: To a 4 mL capped vial equipped with a magnetic stir bar were added aryl bromide (0.200 mmol, 1 equiv), organo(trifluoro)borate (0.220 mmol, 1.1 equiv), $\text{Pd}(\text{OAc})_2$ (0.9 mg, 4 μ mol, 0.02 equiv), RuPhos (3.7 mg, 7.9 μ mol, 0.04 equiv), Na_2CO_3 (42.4 mg, 0.400 mmol, 2 equiv), and EtOH (1 mL). The mixture was stirred for time as indicated for 3 h at 85 $^{\circ}$ C with an aluminium heat block and then cooled to room temperature. After cooling to room temperature, to the reaction mixture was added saturated aqueous NaHCO_3 (ca. 1 mL), Et_2O (ca. 1 mL), and PhCF_3 (for ^{19}F NMR, 12.3 μ L, 0.100 mmol) or 1,1,2,2-tetrachloroethane (for ^1H NMR, 10.5 μ L, 0.100 mmol) as an internal standard. After vigorous stirring, a portion of the organic phase (ca. 0.4 mL) was transferred into an NMR tube, followed by dilution with CDCl_3 (ca. 0.4 mL). ^1H or ^{19}F NMR measurement was performed to determine the yield of products.

First, we examined cross-coupling reactions with potassium heteroaryl(trifluoro)borates and an alkynyl(trifluoro)borate under these conditions and found to provide **20**, **23**, **27** in high yields without a considerable difference. In contrast, we found significant differences when we used organoborates having base-sensitive functional groups. For example, 4-carboxyphenyl(trifluoro)borate did not participate in the conventional conditions, and the coupling product **14** was not observed. The use of potassium 2,6-difluorophenyl(trifluoro)borate and (*Z*)-(1-fluoro-2-tosyloxy)ethen-1-yl(trifluoro)borate under the **conditions 2** or **3** gave the products **16** and **26** in low yields, probably because protodeborylation predominantly occurred under the basic conditions. Similar results were obtained when potassium (2-fluoropyrimidin-5-yl)(trifluoro)borate was used as a substrate, affording a trace amount of product **22** under **condition 3**. The low efficiency would be caused by defluorinative $\text{S}_{\text{N}}\text{Ar}$ reaction with nucleophilic solvents under basic conditions. Another example is the synthesis of **34** with 2-(3-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. The product was obtained under **conditions 2** and **3** in moderate yields, probably due to overreaction with the pinacolboron moiety, while **condition 1** showed a high yield. This preliminary comparison indicates the broad applicability of the zinc-mediated non-basic conditions for cross-coupling reactions.

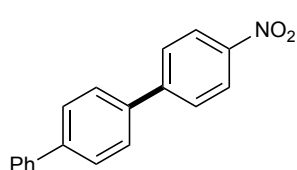
Supplementary Table 19. Comparison of SMC reactions' ability to obtain representative products under three types of conditions.

$\text{R}^1\text{-Br} + \text{KF}_3\text{B-R}^2 \xrightarrow{\text{conditions}} \text{R}^1\text{-R}^2$ (1 equiv) (1.1 equiv)		condition 1: Same as Fig. 7 condition 2: PdCl₂(dppf)·CH₂Cl₂ (9 mol%) K₂CO₃ (3 equiv), THF (0.1 mol/L) H₂O (5 mmol/L), 80 °C, 12 h condition 3: Pd(OAc)₂ (2 mol%) RuPhos (4 mol%), Na₂CO₃ (2 equiv) EtOH (0.18 mol/L), 85 °C, 3 h		
Product		condition 1 (isolated yield)	condition 2 (¹ H or ¹⁹ F NMR yield)	condition 3 (¹ H or ¹⁹ F NMR yield)
	20	75%	82%	>99%
	23	96%	78%	99%
	27	67%	90%	94%
	14	80%	not observed	not observed
	16	93%	7%	8%
	22	97%	not observed	2%
	26	82% (1 mmol scale)	14%	6%
	34	81%	23%	48%

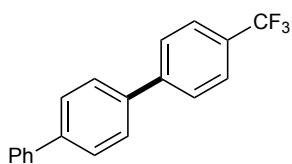
Characterization data



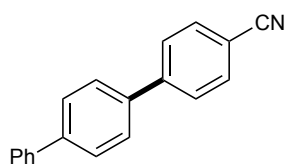
4-Fluorobiphenyl (3). Prepared from 4-fluorobromobenzene (**1**, 21.9 μL , 0.200 mmol) and potassium phenyl(trifluoro)borate (**2a**, 40.5 mg, 0.22 mmol), or chlorobenzene (20.3 μL , 0.200 mmol) and potassium 4-fluorophenyl(trifluoro)borate (44.4 mg, 0.220 mmol); Reaction time: 3 h (with **1**), 6 h (with chlorobenzene); Yield: 86.8% (from **1**: 29.9 mg, 0.174 mmol), 70.8% (from chlorobenzene: 24.4 mg, 0.142 mmol); White solid (mp: 73–74 $^{\circ}\text{C}$); TLC: R_f = 0.48 (*n*-hexane); ^1H NMR (CDCl_3) δ 7.57–7.52 (m, 4H), 7.45–7.41 (m, 2H), 7.34 (tt, $J_{\text{H-H}}$ = 7.5, 2.0 Hz, 1H), 7.12 (AA'BB'X, $J_{\text{H-H}}$ = 8.9, 2.2 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 162.6 (d, $J_{\text{C-F}}$ = 246.1 Hz, 1C), 140.4 (1C), 137.5 (d, $J_{\text{C-F}}$ = 2.9 Hz, 1C), 129.0 (2C), 128.9 (d, $J_{\text{C-F}}$ = 7.7 Hz, 2C), 127.4 (1C), 127.2 (2C), 115.8 (d, $J_{\text{C-F}}$ = 21.0 Hz, 2C); ^{19}F NMR (CDCl_3) δ –115.8 (m, 1F). The chemical shifts were consistent with those reported in the literature.³⁸



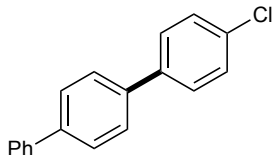
4-Nitro-1,1':4',1''-terphenyl (7). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 4-nitrophenyl(trifluoro)borate (50.4 mg, 0.220 mmol); Reaction time: 3 h; Yield: 84.1% (46.3 mg, 0.168 mmol); White solid (mp: 214–216 $^{\circ}\text{C}$); TLC: R_f = 0.70 (*n*-hexane/EtOAc = 4/1); ^1H NMR (CDCl_3) δ 8.34–8.31 (m, 2H), 7.82–7.78 (m, 2H), 7.75–7.71 (m, 4H), 7.67–7.64 (m, 2H), 7.51–7.47 (m, 2H), 7.42–7.38 (AA'BB'C, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 147.3 (1C), 147.2 (1C), 142.0 (1C), 140.3 (1C), 137.7 (1C), 129.1 (2C), 128.02 (2C), 127.99 (1C), 127.96 (2C), 127.8 (2C), 127.3 (2C), 124.4 (2C); IR (ZnSe, cm^{-1}) 1738, 1510, 1478, 1339, 1217, 1192, 855, 831, 772, 747; HRMS (ESI^+) m/z 276.1018 (276.1019 calcd for $\text{C}_{18}\text{H}_{14}\text{NO}_2^+$, $[\text{M}+\text{H}]^+$).



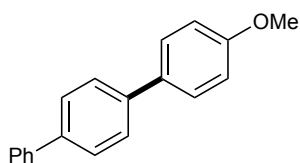
4-Trifluoromethyl-1,1':4',1''-terphenyl (8). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium trifluoro(4-trifluoromethylphenyl)borate (55.4 mg, 0.220 mmol); Reaction time: 17 h; Yield: 94.0% (56.1 mg, 0.188 mmol); White solid (mp: 207–209 $^{\circ}\text{C}$); TLC: R_f = 0.62 (*n*-hexane/EtOAc = 19/1); ^1H NMR (CDCl_3) δ 7.76–7.63 (m, 10H), 7.50–7.46 (AA'BB', 2H), 7.41–7.37 (AA'BB'C, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 144.4 (1C), 141.3 (1C), 140.6 (1C), 138.8 (1C), 129.6 (q, $^2J_{\text{C-F}}$ = 32.6 Hz, 1C), 129.1 (2C), 127.9 (2C), 127.83 (2C), 127.79 (1C), 127.5 (2C), 127.3 (2C), 126.0 (q, $^3J_{\text{C-F}}$ = 3.8 Hz, 2C), 124.5 (q, $^1J_{\text{C-F}}$ = 273.0 Hz, 1C); ^{19}F NMR (CDCl_3) δ –62.2; IR (ZnSe, cm^{-1}) 1325, 1289, 1159, 1113, 1072, 1013, 829, 768, 739, 691; HRMS (ESI^+) m/z 299.1042 (299.1042 calcd for $\text{C}_{19}\text{H}_{14}\text{F}_3^+$, $[\text{M}+\text{H}]^+$).



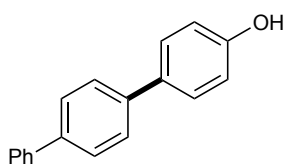
4-Cyano-1,1':4',1''-terphenyl (9). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 4-cyanophenyl(trifluoro)borate (46.0 mg, 0.220 mmol); Reaction time: 3 min; Yield: 87.1% (44.5 mg, 0.174 mmol); White solid (mp: 197–200 °C); TLC: R_f = 0.52 (*n*-hexane/EtOAc = 4/1); ^1H NMR (CDCl_3) δ 7.77–7.62 (m, 10H), 7.49–7.45 (m, 2H), 7.41–7.37 (AA'BB'C, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 145.3 (1C), 141.7 (1C), 140.3 (1C), 138.1 (1C), 132.8 (2C), 129.1 (2C), 128.0 (2C), 127.9 (1C), 127.8 (2C), 127.7 (2C), 127.2 (2C), 119.1 (1C), 111.1 (1C). The chemical shifts were consistent with those reported in the literature.³⁹



4-Chloro-1,1':4',1''-terphenyl (10). Prepared from 4-bromobiphenyl (46.6 mg, 0.220 mmol) and potassium 4-chlorophenyl(trifluoro)borate (48.1 mg, 0.220 mmol); Reaction time: 17 h; Yield: 83.9% (44.4 mg, 0.168 mmol); White solid (mp: 224–225 °C); TLC: R_f = 0.70 (*n*-hexane/EtOAc = 19/1); ^1H NMR (CDCl_3) δ 7.69–7.62 (m, 6H), 7.58–7.55 (AA'BB', 2H), 7.48–7.41 (m, 4H), 7.39–7.35 (AA'BB'C, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 140.70 (1C), 140.66 (1C), 139.3 (1C), 139.0 (1C), 133.6 (1C), 129.2 (2C), 129.0 (2C), 128.5 (2C), 127.8 (2C), 127.7 (1C), 127.5 (2C), 127.2 (2C). The chemical shifts were consistent with those reported in the literature.⁴⁰

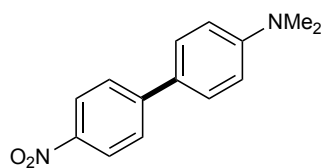


4-Methoxy-1,1':4',1''-terphenyl (11). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 4-methoxyphenyl(trifluoro)borate (47.1 mg, 0.220 mmol); Reaction time: 17 h; Yield: 82.0% (42.7 mg, 0.164 mmol); White solid (mp: 226–227 °C); TLC: R_f = 0.48 (*n*-hexane/EtOAc = 19/1); ^1H NMR (CDCl_3) δ 7.67–7.62 (m, 6H), 7.61–7.57 (m, 2H), 7.48–7.44 (m, 2H), 7.38–7.33 (AA'BB'C, 1H), 7.01–6.99 (AA'BB', 2H), 3.87 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 159.4 (1C), 140.9 (1C), 139.9 (1C), 139.7 (1C), 133.4 (1C), 129.0 (2C), 128.2 (2C), 127.7 (2C), 127.4 (1C), 127.22 (2C), 127.18 (2C), 114.4 (2C), 55.5 (1C). The chemical shifts were consistent with those reported in the literature.⁴¹

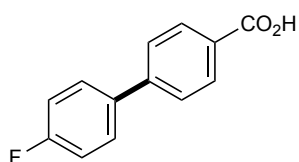


4-Hydroxy-1,1':4',1''-terphenyl (12). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 4-hydroxyphenyl(trifluoro)borate (44.0 mg, 0.220 mmol) or 4-hydroxyphenylboronic acid (41.4 mg, 0.300 mmol); Reaction time: 3 h; Yield: 24.8% (from potassium 4-hydroxyphenyl(trifluoro)borate, 12.2 mg, 49.5 μmol), 73.1% (from 4-hydroxyphenylboronic acid, 36.0 mg, 0.146 mmol); White solid (mp: 264–267 °C); TLC: R_f = 0.28 (*n*-hexane/EtOAc = 3/1); ^1H NMR ($\text{DMSO}-d_6$) δ 9.59 (s, 1H), 7.66–7.72 (m, 6H), 7.54 (d, $J_{\text{H-H}}$ = 8.7 Hz, 2H), 7.47 (t, $J_{\text{H-H}}$ = 7.7 Hz, 2H), 7.36 (t, $J_{\text{H-H}}$ = 7.5 Hz, 1H), 6.87 (d, $J_{\text{H-H}}$ = 8.3 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{DMSO}-$

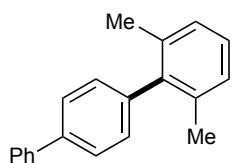
d_6) δ 157.3 (1C), 139.7 (1C), 139.2 (1C), 138.0 (1C), 130.3 (1C), 129.0 (2C), 127.7 (2C), 127.4 (1C), 127.1 (2C), 126.5 (2C), 126.4 (2C), 115.8 (2C). The chemical shifts were consistent with those reported in the literature.⁴¹



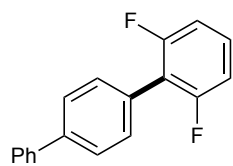
4-Dimethylamino-4'-nitrobiphenyl (13). Prepared from 1-bromo-*N,N*-dimethylaniline (80.0 mg, 0.400 mmol) and potassium 4-nitrophenyl(trifluoro)borate (101 mg, 0.441 mmol); Reaction time: 13 h; Yield: 98.8% (95.8 mg, 0.395 mmol); Yellow solid (mp: 237–240 °C); TLC: R_f = 0.50 (*n*-hexane/EtOAc = 4/1); ^1H NMR (CDCl_3) δ 8.26–8.23 (AA'BB', 2H), 7.70–7.67 (AA'BB', 2H), 7.59–7.55 (AA'BB', 2H), 6.82–6.79 (AA'BB', 2H), 3.04 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 151.1 (1C), 147.8 (1C), 146.0 (1C), 128.3 (2C), 126.3 (2C), 126.0 (1C), 124.4 (2C), 112.7 (2C), 44.5 (2C). The chemical shifts were consistent with those reported in the literature.⁴²



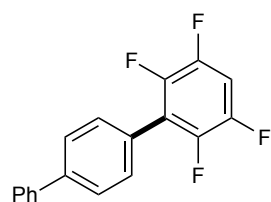
4-Carboxy-4'-fluorobiphenyl (14). Prepared from 4-fluorobromobenzene (**1**, 21.9 μL , 0.200 mmol) and potassium 4-carboxyphenyl(trifluoro)borate (50.2 mg, 0.220 mmol); Reaction time: 7 h; Yield: 79.6% (34.4 mg, 0.159 mmol); White solid (mp: 236–239 °C); TLC: R_f = 0.48 ($\text{CHCl}_3/\text{MeOH}$ = 9/1); ^1H NMR ($\text{DMSO}-d_6$) δ 13.06 (bs, 1H), 8.01 (d, $J_{\text{H-H}}$ = 7.5 Hz, 2H), 7.81–7.77 (m, 4H), 7.36–7.31 (AA'BB', 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{DMSO}-d_6$) δ 167.1 (1C), 162.4 (d, $^1J_{\text{C-F}}$ = 246.0 Hz, 1C), 143.2 (1C), 135.5 (d, $^4J_{\text{C-F}}$ = 2.8 Hz, 1C), 130.0 (2C), 129.6 (1C), 129.1 (d, $^3J_{\text{C-F}}$ = 8.6 Hz, 2C), 126.8 (2C), 116.0 (d, $^2J_{\text{C-F}}$ = 21.9 Hz, 2C); ^{19}F NMR ($\text{DMSO}-d_6$) δ –114.1 (m, 1F). The chemical shifts were consistent with those reported in the literature.⁴³



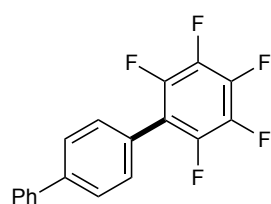
2,6-Dimethyl-1,1':4,1''-terphenyl (15). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 2,6-dimethylphenyl(trifluoro)borate (46.7 mg, 0.220 mmol); Reaction time: 3 h; Yield: 95.4% (49.3 mg, 0.191 mmol); White solid (mp: 87–90 °C); TLC: R_f = 0.29 (*n*-hexane); ^1H NMR (CDCl_3) δ 7.65–7.68 (m, 4H), 7.46 (d, $J_{\text{H-H}}$ = 7.5 Hz, 2H), 7.38–7.34 (AA'BB'C, 1H), 7.12–7.24 (m, 5H), 2.08 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 141.7 (1C), 141.1 (1C), 140.3 (1C), 139.5 (1C), 136.4 (1C), 129.7 (2C), 129.0 (2C), 127.5 (2C), 127.4 (1C), 127.3 (2C+2C), 127.2 (2C), 21.1 (2C). The chemical shifts were consistent with those reported in the literature.⁴⁴



2,6-Difluoro-1,1':4',1''-terphenyl (16). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 2,6-difluorophenyl(trifluoro)borate (48.4 mg, 0.220 mmol); Reaction time: 4 h; Yield: 92.8% (49.4 mg, 0.186 mmol); White solid (mp: 198.5–198.9 °C); TLC: R_f = 0.50 (*n*-hexane/EtOAc = 19/1); ^1H NMR (CDCl_3) δ 7.70–7.63 (m, 4H), 7.61–7.55 (m, 2H), 7.48–7.42 (m, 2H), 7.39–7.27 (m, 2H), 7.05–6.97 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 160.3 (dd, $^1J_{\text{C-F}}$ = 248.4 Hz, $^3J_{\text{C-F}}$ = 7.2 Hz, 2C), 141.2 (1C), 140.8 (1C), 130.9 (2C), 129.1 (t, $^2J_{\text{C-F}}$ = 10.6 Hz, 1C), 129.0 (2C), 128.3 (1C), 127.7 (1C), 127.4 (2C), 127.2 (2C), 118.3 (t, $^2J_{\text{C-F}}$ = 18.6 Hz, 1C), 111.9 (dd, $^2J_{\text{C-F}}$ = 19.1 Hz, $^4J_{\text{C-F}}$ = 6.7 Hz, 2C); ^{19}F NMR (CDCl_3) δ –114.4; IR (ZnSe, cm^{-1}) 1728, 1717, 1460, 1445, 1366, 1273, 1228, 1217, 991, 727; HRMS (ESI $^+$) m/z 267.0977 (267.0980 calcd for $\text{C}_{18}\text{H}_{13}\text{F}_2^+$, $[\text{M}+\text{H}]^+$).



2,3,5,6-Tetrafluoro-1,1':4',1''-terphenyl (17). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 2,3,5,6-tetrafluorophenyl(trifluoro)borate (**S2**, 56.3 mg, 0.220 mmol); Reaction time: 15 h; Yield: 78.7% (47.6 mg, 0.158 mmol); White solid (mp: 174–177 °C); TLC: R_f = 0.62 (*n*-hexane/EtOAc = 19/1); ^1H NMR (CDCl_3) δ 7.74–7.71 (AA'BB', 2H), 7.66–7.63 (AA'BB', 2H), 7.57–7.54 (AA'BB', 2H), 7.50–7.46 (AA'BB', 2H), 7.41–7.37 (AA'BB'C, 1H), 7.08 (tt, $^2J_{\text{H-F}}$ = 9.6 Hz, $^3J_{\text{H-F}}$ = 7.2 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 146.4 (dm, $^1J_{\text{C-F}}$ = 254.8 Hz, 2C), 143.9 (dm, $^1J_{\text{C-F}}$ = 254.8 Hz, 2C), 142.2 (1C), 140.4 (1C), 130.7 (2C), 129.1 (2C), 128.0 (1C), 127.5 (2C), 127.4 (2C), 126.5 (1C), 121.3 (t, $^2J_{\text{C-F}}$ = 15.4 Hz, 1C), 105.0 (t, $^2J_{\text{C-F}}$ = 23.0 Hz, 1C); ^{19}F NMR (CDCl_3) δ –138.9 – –139.0 (m, 2F), –143.6 – –143.8 (m, 2F). The chemical shifts were consistent with those reported in the literature.⁴⁵

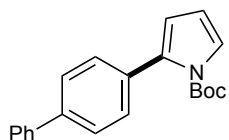


2,3,4,5,6-Pentafluoro-1,1':4',1''-terphenyl (18). We prepared potassium pentafluorophenyl(trifluoro)borate for the SMC reaction without precise purification because we could not isolate it in a pure form.

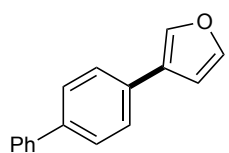
To a 4 mL capped vial equipped with a magnetic stir bar were added pentafluorophenylboronic acid (127 mg, 0.599 mmol, 3.0 equiv), KHF_2 (155 mg, 1.98 mmol, 10 equiv), MeOH (1.2 mL), and water (60 μL). The mixture was stirred for 1 h at room temperature. After removal of the solvents under reduced pressure, the residue was dried under high vacuum. The residue was suspended in acetone (ca. 2 mL), added magnesium sulfate (100 mg), and irradiated with an ultrasonic wave for 1 min. After passing the mixture through a glass filter and washing with acetone (ca. 10 mL), the filtrate was concentrated under reduced pressure to give a white solid containing potassium pentafluorophenyl(trifluoro)borate with impurities, probably including fluorinated inorganic compounds such as KHF_2 .

To a 4 mL capped vial equipped with a magnetic stir bar were added the crude mixture, **1** (46.6 mg, 0.200 mmol, 1 equiv), PdCl₂(amphos)₂ (2.8 mg, 4.0 μmol, 0.02 equiv), **4** (54.2 mg, 0.156 mmol, 0.78 equiv/Zn), and THF (2.0 mL). The mixture was stirred for 24 h at 80 °C and then cooled to room temperature. The mixture was poured into saturated aqueous sodium hydrogen carbonate (ca. 2 mL), and the mixture was extracted with EtOAc (ca. 3 mL × 3). The combined organic extract was dried over Na₂SO₄. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography followed by GPC to give **10** (50.5 mg, 0.158 mmol, 79.0%) as a white solid (mp: 129.7–193.4 °C);

TLC: *R*_f = 0.62 (*n*-hexane/EtOAc = 19/1); ¹H NMR (CDCl₃) δ 7.72–7.70 (AA'BB', 2H), 7.64–7.62 (AA'BB', 2H), 7.51–7.45 (m, 4H), 7.40–7.36 (AA'BB'C, 1H); ¹³C{¹H} NMR (CDCl₃) δ 144.4 (dm, ¹*J*_{C-F} = 248.2 Hz, 2C), 142.4 (1C), 140.6 (dm, ¹*J*_{C-F} = 250.1 Hz, 1C), 140.3 (1C), 138.1 (dm, ¹*J*_{C-F} = 252.9 Hz, 2C), 130.7 (2C), 129.1 (2C), 128.0 (1C), 127.6 (2C), 127.4 (2C), 125.4 (1C), 115.8 (t, ²*J*_{C-F} = 18.2 Hz, 1C); ¹⁹F NMR (CDCl₃) δ –143.0 – –143.1 (m, 2F), –155.3 – –155.4 (t, ³*J*_{F-F} = 19.4 Hz, 1F), –161.9 – –162.1 (m, 2F). The chemical shifts were consistent with those reported in the literature.⁴⁵

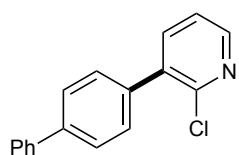


2-(Biphenyl-4-yl)-1-butoxycarbonylpyrrole (19). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium (1-butoxycarbonylpyrrol-2-yl)difluorophenyl(trifluoro)borate (**S1**, 60.1 mg, 0.220 mmol); Reaction time: 3 h; Yield: 60.1% (38.4 mg, 0.120 mmol); White solid (mp: 109–113 °C); TLC: *R*_f = 0.30 (*n*-hexane/EtOAc = 9/1); ¹H NMR (CDCl₃) δ 7.62 (d, *J*_{H-H} = 7.9 Hz, 2H), 7.58 (d, *J*_{H-H} = 7.9 Hz, 2H), 7.46–7.41 (m, 4H), 7.37–7.33 (m, 2H), 6.24 (d, *J*_{H-H} = 3.2 Hz, 2H), 1.38 (s, 9H); ¹³C{¹H} NMR (CDCl₃) δ 149.6 (1C), 141.1 (1C), 140.1 (1C), 134.9 (1C), 133.6 (1C), 129.7 (2C), 129.0 (2C), 127.4 (1C), 127.2 (2C), 126.5 (2C), 122.9 (1C), 114.7 (1C), 110.8 (1C), 83.9 (1C), 27.8 (3C); IR (ZnSe, cm⁻¹) 1744, 1323, 1301, 1138, 970, 844, 768, 756, 742, 700; HRMS (ESI⁺) *m/z* 320.1645 (320.1645 calcd for C₂₁H₂₂NO₂⁺, [M+H]⁺).



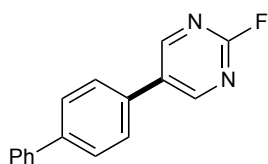
3-(Biphenyl-4-yl)furan (20). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 3-furanyl(trifluoro)borate (38.3 mg, 0.220 mmol); Reaction time: 3 h; Yield: 75.4% (33.2 mg, 0.151 mmol); White solid (mp: 157–160 °C); TLC: *R*_f = 0.36 (*n*-hexane/EtOAc = 50/1); ¹H NMR (CDCl₃) δ 7.78 (dd, *J*_{H-H} = 1.4, 1.4 Hz, 1H), 7.63–7.61 (m, 4H), 7.58–7.55 (m, 2H), 7.50 (dd, *J*_{H-H} = 2.0, 2.0 Hz, 1H), 7.47–7.43 (m, 2H), 7.35 (AA'BB'C, *J*_{H-H} = 7.3, 2.0 Hz, 1H), 6.74 (dd, *J*_{H-H} = 1.8, 0.8 Hz, 1H); ¹³C{¹H} NMR (CDCl₃) δ 143.9 (1C), 140.9 (1C), 140.0 (1C), 138.8 (1C), 131.6 (1C), 129.0 (2C), 127.7 (2C), 127.5 (1C), 127.1 (2C), 126.4 (2C), 126.3 (1C), 109.0 (1C); IR (ZnSe, cm⁻¹)

1161, 1053, 871, 839, 790, 760, 719, 691; HRMS (ESI⁺) m/z 221.0961 (221.0961 calcd for C₁₆H₁₃O⁺, [M+H]⁺).



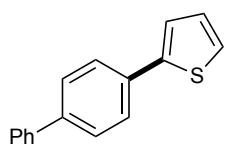
2-Chloro-3-(biphenyl-4-yl)pyridine (21). Prepared from 4-bromobiphenyl

(46.6 mg, 0.200 mmol) and potassium (2-chloropyridin-3-yl) (trifluoro)borate (87.8 mg, 0.400 mmol); Reaction time: 3 h; Yield: 45.9% (2 mol% of cat. Pd was used, 24.4 mg, 91.8 μ mol), 78.6% (5 mol% of cat. Pd was used, 41.8 mg, 0.157 mmol); White solid (mp: 103–104 °C); TLC: R_f = 0.39 (*n*-hexane/EtOAc = 4/1); ¹H NMR (CDCl₃) δ 8.42 (dd, J_{H-H} = 4.9, 2.0 Hz, 1H), 7.73 (dd, J_{H-H} = 7.5, 2.0 Hz, 1H), 7.71–7.69 (AA'BB', 2H), 7.66–7.64 (AA'BB', 2H), 7.55–7.54 (AA'BB', 2H), 7.49–7.46 (AA'BB', 2H), 7.40–7.36 (AA'BB'C, 1H), 7.34 (dd, J_{H-H} = 7.5, 4.8 Hz, 1H); ¹³C{¹H} NMR (CDCl₃) δ 150.0 (1C), 148.6 (1C), 141.4 (1C), 140.6 (1C), 139.8 (1C), 136.9 (1C), 136.6 (1C), 129.9 (2C), 129.1 (2C), 127.8 (1C), 127.4 (2C), 127.3 (2C), 122.8 (1C); IR (ZnSe, cm⁻¹) 1482, 1383, 999, 844, 808, 789, 768, 731, 698, 664; HRMS (ESI⁺) m/z 266.0732 (266.0731 calcd for C₁₇H₁₃³⁵ClN⁺, [M+H]⁺).



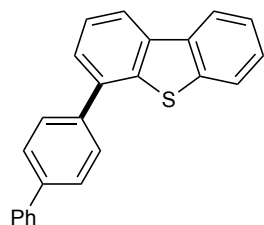
5-(Biphenyl-4-yl)-2-fluoropyrimidine (22). Prepared from 4-

bromobiphenyl (46.6 mg, 0.200 mmol) and potassium (2-fluoropyrimidin-5-yl)(trifluoro)borate (44.9 mg, 0.220 mmol); Reaction time: 18 h; Yield: 96.5% (48.3 mg, 0.193 mmol); White solid (mp: 160–161 °C); TLC: R_f = 0.76 (*n*-hexane/EtOAc = 1/1); ¹H NMR (CDCl₃) δ 8.87 (d, ⁴ J_{H-F} = 1.8 Hz, 2H), 7.77–7.74 (AA'BB', 2H), 7.65–7.62 (m, 4H), 7.51–7.47 (AA'BB', 2H), 7.43–7.38 (AA'BB'C, 1H); ¹³C{¹H} NMR (CDCl₃) δ 162.6 (d, ¹ J_{C-F} = 221.3 Hz, 1C), 158.9 (d, ³ J_{C-F} = 11.5 Hz, 2C), 142.2 (1C), 140.0 (1C), 132.7 (d, ⁴ J_{H-F} = 4.8 Hz, 1C), 132.0 (1C), 129.1 (2C), 128.3 (2C), 128.1 (1C), 127.4 (2C), 127.2 (2C); ¹⁹F NMR (CDCl₃) δ -47.5; IR (ZnSe, cm⁻¹) 1572, 1435, 1416, 1300, 872, 843, 787, 770, 727, 692; HRMS (ESI⁺) m/z 251.0981 (251.0979 calcd for C₁₆H₁₂FN₂⁺, [M+H]⁺).

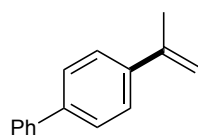


2-(Biphenyl-4-yl)thiophene (23). Prepared from 4-bromobiphenyl (46.6 mg,

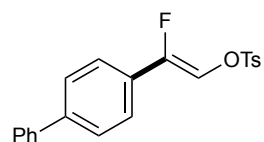
0.200 mmol) and potassium 2-thienyl(trifluoro)borate (41.8 mg, 0.220 mmol); Reaction time: 3 h; Yield: 96.3% (45.5 mg, 0.193 mmol); White solid (mp: 178–179 °C); TLC: R_f = 0.44 (*n*-hexane/EtOAc = 19/1); ¹H NMR (CDCl₃) δ 7.71–7.68 (m, 2H), 7.64–7.60 (m, 4H), 7.48–7.43 (m, 2H), 7.38–7.34 (m, 2H), 7.30 (dd, J_{H-H} = 5.1, 1.2 Hz, 1H), 7.11 (dd, J_{H-H} = 5.5, 3.6 Hz, 1H); ¹³C{¹H} NMR (CDCl₃) δ 144.2 (1C), 140.7 (1C), 140.4 (1C), 133.6 (1C), 129.0 (2C), 128.3 (1C), 127.7 (2C), 127.6 (1C), 127.1 (2C), 126.5 (2C), 125.1(1C), 123.3 (1C). The chemical shifts were consistent with those reported in the literature.⁴⁶



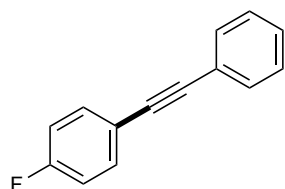
2-(Biphenyl-4-yl)dibenzothiophene (24). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium dibenzothiophene-2-yl (trifluoro)borate (63.8 mg, 0.200 mmol); Reaction time: 4 h; Yield: 97.6% (65.7 mg, 0.195 mmol); White solid (mp: 153–155 °C); TLC: R_f = 0.54 (*n*-hexane/EtOAc = 9/1); ^1H NMR (CDCl_3) δ 8.23–8.17 (m, 2H), 7.87–7.83 (m, 3H), 7.78–7.75 (m, 2H), 7.71–7.69 (m, 2H), 7.61–7.47 (m, 6H), 7.41–7.37 (AA'BB'C, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 140.9 (1C), 140.8 (1C), 139.7 (1C), 139.6 (1C), 138.6 (1C), 136.7 (1C), 136.4 (1C), 135.9 (1C), 129.0 (2C), 128.8 (2C), 127.6 (2C+1C), 127.3 (2C), 127.01 (1C), 126.97 (1C), 125.3 (1C), 124.5 (1C), 122.8 (1C), 121.9 (1C), 120.7 (1C); IR (ZnSe, cm^{-1}) 1730, 1715, 1439, 1377, 1364, 845, 743, 729, 656, 642; HRMS (ESI^+) m/z 337.1046 (337.1045 calcd for $\text{C}_{24}\text{H}_{17}^{32}\text{S}^+$, $[\text{M}+\text{H}]^+$).



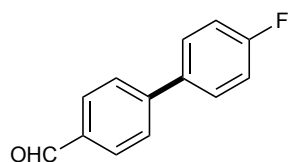
4-(1-Propen-2-yl)biphenyl (25). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and potassium 1-propen-2-yl(trifluoro)borate (32.6 mg, 0.200 mmol); Reaction time: 7 h; Yield: 96.5% (37.5 mg, 0.193 mmol); White solid (mp: 113–116 °C); TLC: R_f = 0.60 (*n*-hexane/EtOAc = 19/1); ^1H NMR (CDCl_3) δ 7.61–7.54 (m, 6H), 7.46–7.24 (m, 2H), 7.37–7.33 (AA'BB'C, 1H), 5.44 (dq, $J_{\text{H-H}} = 1.6, 0.8$ Hz, 1H), 5.12 (dq, $J_{\text{H-H}} = 1.6, 1.6$ Hz, 1H), 2.19 (dd, $J_{\text{H-H}} = 1.6, 0.8$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 142.9 (1C), 140.9 (1C), 140.4 (1C), 140.2 (1C), 128.9 (2C), 127.4 (1C), 127.2 (2C), 127.1 (2C), 126.1 (2C), 112.6 (1C), 22.0 (1C). The chemical shifts were consistent with those reported in the literature.⁴⁷



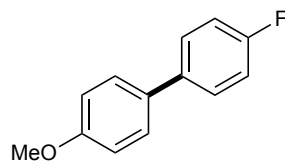
(Z)-2-(Biphenyl-4-yl)-2-fluoroethenyl 4-methylbenzenesulfonate (26). Prepared from 4-bromobiphenyl (233 mg, 1.00 mmol) and potassium (Z)-(1-fluoro-2-tosyloxy)ethen-1-yl(trifluoro)borate (354 mg, 1.10 mmol); Reaction time: 3 h; Yield: 82.1% (303 mg, 0.821 mmol); White solid (mp: 139–140 °C); TLC: R_f = 0.34 (*n*-hexane/EtOAc = 4/1); ^1H NMR (acetone- d_6) δ 7.94 (dt, $J_{\text{H-H}} = 8.7, 1.8$ Hz, 2H), 7.73–7.71 (AA'BB', 2H), 7.69–7.66 (AA'BB', 2H), 7.64–7.61 (AA'BB', 2H), 7.54–7.52 (AA'BB', 2H), 7.49–7.45 (AA'BB', 2H), 7.39 (AA'BB'C, 1H), 7.20 (d, $J_{\text{H-F}} = 20.2$ Hz, 1H), 2.47 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (acetone- d_6) δ 152.0 (d, $^1J_{\text{C-F}} = 251.6$ Hz, 1C), 147.0 (1C), 143.3 (1C), 140.6 (1C), 133.0 (1C), 131.1 (2C), 129.8 (2C), 129.0 (2C), 128.8 (1C), 128.5 (d, $^2J_{\text{C-F}} = 23.9$ Hz, 1C), 128.1 (d, $^4J_{\text{C-F}} = 1.9$ Hz, 2C), 127.7 (2C), 125.3 (d, $^3J_{\text{C-F}} = 6.7$ Hz, 2C), 119.8 (d, $^2J_{\text{C-F}} = 13.3$ Hz, 1C), 21.6 (1C); ^{19}F NMR (acetone- d_6) δ -132.2 (d, $J_{\text{H-F}} = 19.7$ Hz, 1F). The chemical shifts were consistent with those reported in the literature.⁴⁸



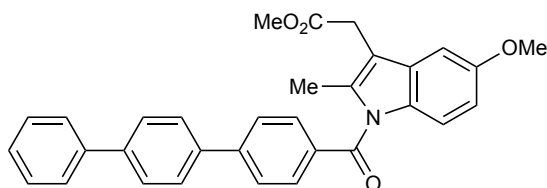
1-(4-Fluorophenyl)-2-phenylethyne (27). Prepared from 4-fluorobromobenzene (**1**, 21.0 μ L, 0.200 mmol) and potassium 2-phenylethynyl(trifluoro)borate (45.8 mg, 0.220 mmol); Reaction time: 3 h; Yield: 66.5% (26.1 mg, 0.133 mmol); White solid (mp: 109–110 $^{\circ}$ C); TLC: R_f = 0.33 (*n*-hexane); ^1H NMR (CDCl_3) δ 7.55–7.49 (m, 4H) 7.38–7.33 (m, 3H), 7.08–7.02 (AA'BB'X, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 162.7 (d, $J_{\text{C-F}}$ = 249.9 Hz, 1C), 133.7 (d, $J_{\text{C-F}}$ = 8.6 Hz, 2C), 131.7 (2C), 128.6 (2C), 128.5 (1C), 123.3 (1C), 119.5 (d, $J_{\text{C-F}}$ = 3.8 Hz, 1C), 115.8 (d, $J_{\text{C-F}}$ = 22.9 Hz, 2C), 89.2 (1C), 88.5 (1C); ^{19}F NMR (CDCl_3) δ –110.9 (m, 1F). The chemical shifts were consistent with those reported in the literature.⁴⁹



4-Fluoro-4'-formylbiphenyl (28). Prepared from 4-chlorobenzaldehyde (28.1 mg, 0.200 mmol) and potassium phenyl(trifluoro)borate (**2a**, 40.5 mg, 0.220 mmol); Reaction time: 4 h; Yield: 86.4% (34.6 mg, 0.173 mmol); White solid (mp: 76–77 $^{\circ}$ C); TLC: R_f = 0.28 (*n*-hexane/EtOAc = 9/1); ^1H NMR (CDCl_3) δ 10.06 (s, 1H), 7.97–7.94 (m, 2H), 7.72–7.69 (m, 2H), 7.64–7.58 (m, 2H), 7.21–7.15 (AA'BB'X, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 192.0 (1C), 163.3 (d, $^1J_{\text{C-F}}$ = 248.8 Hz, 1C), 146.3 (1C), 136.0 (d, $^4J_{\text{C-F}}$ = 2.9 Hz, 1C), 135.3 (1C), 130.5 (2C), 129.2 (d, $^3J_{\text{C-F}}$ = 7.7 Hz, 2C), 127.7 (2C), 116.2 (d, $^2J_{\text{C-F}}$ = 21.0 Hz, 2C); ^{19}F NMR (CDCl_3) δ –113.5 (m, 1F). The chemical shifts were consistent with those reported in the literature.⁵⁰

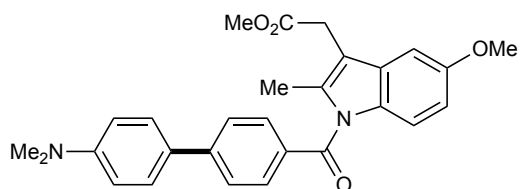


4-Fluoro-4'-methoxybiphenyl (29). Prepared from 4-chloroanisole (24.2 μ L, 0.200 mmol) and potassium 4-fluorophenyl (trifluoro)borate (44.4 mg, 0.220 mmol); Reaction time: 6 h; Yield: 65.0% (26.3 mg, 0.130 mmol); White solid (mp: 87–90 $^{\circ}$ C); TLC: R_f = 0.40 (*n*-hexane/EtOAc = 19/1); ^1H NMR (CDCl_3) δ 7.52–7.45 (m, 4H), 7.13–7.07 (m, 2H), 6.99–6.95 (m, 2H), 3.85 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 162.3 (d, $J_{\text{C-F}}$ = 244.1 Hz, 1C), 159.3 (1C), 137.2 (d, $J_{\text{C-F}}$ = 2.9 Hz, 1C), 133.0 (1C), 128.4 (d, $J_{\text{C-F}}$ = 8.6 Hz, 2C), 128.2 (2C), 115.7 (d, $J_{\text{C-F}}$ = 21.0 Hz, 2C), 114.4 (2C), 55.5 (1C); ^{19}F NMR (CDCl_3) δ –116.7 (m, 1F). The chemical shifts were consistent with those reported in the literature.³⁹



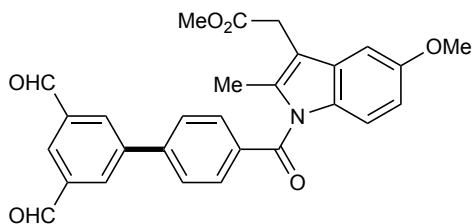
4-Biphenylmethylindomethacin (30). Prepared from 4-bromobiphenyl (46.6 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 4 h; Yield: 92.5% (90.6 mg, 0.185 mmol); White solid (mp: 198–201 $^{\circ}$ C); TLC: R_f = 0.48 (*n*-hexane/EtOAc = 2/1); ^1H NMR (CDCl_3) δ 7.83–7.72 (m, 8H), 7.67–7.65 (m, 2H), 7.48 (dd, $J_{\text{H-H}}$

= 7.6, 7.6 Hz, 2H), 7.41–7.39 (m, 1H), 6.98–6.96 (m, 2H), 6.68 (dd, $J_{H-H} = 9.1, 2.5$ Hz, 1H), 3.85 (s, 3H), 3.72 (s, 3H), 3.70 (s, 2H), 2.44 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 171.6 (1C), 169.4 (1C), 156.1 (1C), 145.3 (1C), 141.4 (1C), 140.5 (1C), 138.6 (1C), 136.3 (1C), 134.3 (1C), 131.2 (1C), 130.7 (2C+1C), 129.1 (2C), 127.9 (2C), 127.8 (2C+1C), 127.3 (2C), 127.3 (2C), 115.3 (1C), 112.3 (1C), 111.7 (1C), 101.3 (1C), 55.9 (1C), 52.3 (1C), 30.4 (1C), 13.5 (1C); IR (ZnSe, cm^{-1}) 1726, 1659, 1483, 1445, 1433, 1362, 1337, 1279, 1225, 756; HRMS (ESI^+) m/z 490.2015 (490.2013 calcd for $\text{C}_{32}\text{H}_{28}\text{NO}_4^+$, $[\text{M}+\text{H}]^+$).



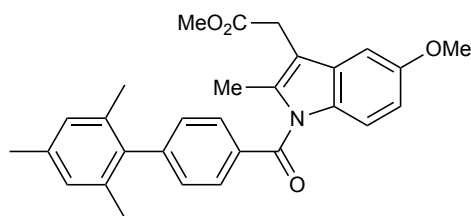
4-Dimethylaminophenyl-methylindomethacin (31).

Prepared from 1-bromo-*N,N*-dimethylaniline (40.0 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 4 h; Yield: 92.5% (84.5 mg, 0.185 mmol); White solid (mp: 152–155 °C); TLC: $R_f = 0.25$ (*n*-hexane/EtOAc = 3/1); ^1H NMR (CDCl_3) δ 7.76–7.74 (AA'BB', 2H), 7.68–7.66 (AA'BB', 2H), 7.61–7.58 (AA'BB', 2H), 6.98–6.96 (m, 2H), 6.83–6.80 (AA'BB', 2H), 6.67 (dd, $J_{H-H} = 9.1, 2.5$ Hz, 1H), 3.84 (s, 3H), 3.71 (s, 3H), 3.69 (s, 2H), 3.03 (s, 6H), 2.43 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 171.6 (1C), 169.4 (1C), 155.9 (1C), 150.7 (1C), 145.8 (1C), 136.2 (1C), 132.4 (1C), 131.2 (1C), 130.7 (2C), 130.5 (1C), 128.0 (2C), 126.9 (1C), 125.9 (2C), 115.1 (1C), 112.6 (2C), 111.9 (1C), 111.5 (1C), 101.1 (1C), 55.8 (1C), 52.2 (1C), 40.4 (2C), 30.3 (1C), 13.3 (1C); IR (ZnSe, cm^{-1}) 1732, 1672, 1601, 1364, 1310, 1263, 1219, 1204, 1171, 812; HRMS (ESI^+) m/z 457.2118 (457.2122 calcd for $\text{C}_{28}\text{H}_{29}\text{N}_2\text{O}_4^+$, $[\text{M}+\text{H}]^+$).



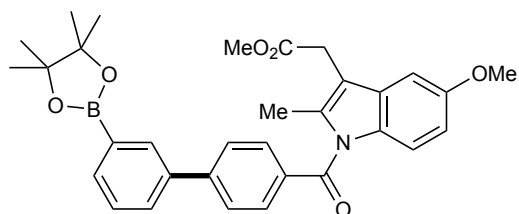
3,5-Diformylphenyl-methylindomethacin (32). Prepared

from 1-bromo-3,5-diformylbenzene (42.6 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 4 h; Yield: 99.9% (93.8 mg, 2.00 mmol); White solid (mp: 135–138 °C); TLC: $R_f = 0.56$ (*n*-hexane/EtOAc = 1/1); ^1H NMR (CDCl_3) δ 10.21 (s, 2H), 8.44–8.42 (m, 3H), 7.89–7.86 (AA'BB', 2H), 7.82–7.80 (AA'BB', 2H), 6.98 (d, $J_{H-H} = 2.5$ Hz, 1H), 6.92 (d, $J_{H-H} = 9.1$ Hz, 1H), 6.68 (dd, $J_{H-H} = 9.1, 2.5$ Hz, 1H), 3.85 (s, 3H), 3.72 (s, 3H), 3.70 (s, 2H), 2.43 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 190.9 (2C), 171.5 (1C), 168.8 (1C), 156.1 (1C), 142.5 (1C), 141.8 (1C), 137.8 (2C), 136.1 (1C), 135.7 (1C), 133.0 (2C), 130.9 (1C), 130.8 (2C+1C+1C), 127.6 (2C), 115.1 (1C), 112.6 (1C), 111.7 (1C), 101.4 (1C), 55.8 (1C), 52.3 (1C), 30.2 (1C), 13.5 (1C); IR (ZnSe, cm^{-1}) 1728, 1697, 1659, 1435, 1319, 1233, 1192, 1171, 1155, 650; HRMS (ESI^+) m/z 470.1598 (470.1598 calcd for $\text{C}_{28}\text{H}_{24}\text{NO}_6^+$, $[\text{M}+\text{H}]^+$).



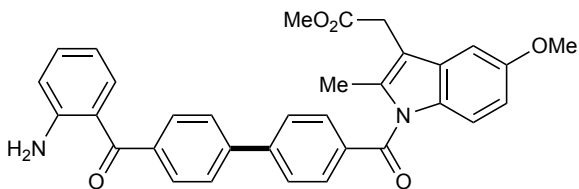
2,4,6-Trimethylphenyl-methylindomethacin (33).

Prepared from 1-bromomesitylene (30.6 μ L, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 3 h; Yield: 92.6% (84.4 mg, 0.185 mmol); White solid (mp: 129–131 $^{\circ}$ C); TLC: R_f = 0.58 (*n*-hexane/EtOAc = 3/1); ^1H NMR (CDCl_3) δ 7.77–7.75 (AA'BB', 2H), 7.29–7.26 (m, 2H), 6.97–6.94 (m, 4H), 6.67 (dd, J = 9.1, 2.7 Hz, 1H), 3.85 (s, 3H), 3.71 (s, 3H), 3.69 (s, 2H), 2.41 (s, 3H), 2.35 (s, 3H), 2.03 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 171.5 (1C), 169.7 (1C), 156.1 (1C), 146.3 (1C), 137.8 (1C), 137.4 (1C), 136.1 (1C), 135.5 (2C), 134.1 (1C), 131.2 (1C), 130.7 (1C), 130.0 (2C+2C), 128.4 (2C), 115.2 (1C), 112.3 (1C), 111.6 (1C), 101.2 (1C), 55.8 (1C), 52.3 (1C), 30.3 (1C), 21.2 (1C), 20.8 (2C), 13.4 (1C); IR (ZnSe, cm^{-1}) 1736, 1667, 1605, 1474, 1456, 1433, 1358, 1327, 1263, 1223; HRMS (ESI^+) m/z 478.1989 (478.1989 calcd for $\text{C}_{29}\text{H}_{29}\text{NO}_4\text{Na}^+$, $[\text{M}+\text{Na}]^+$).



3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl-methylindomethacin (34).

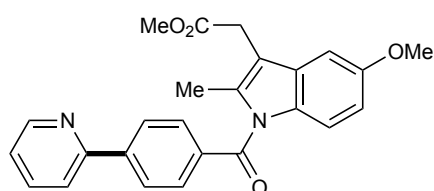
Prepared from 2-(3-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (56.6 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 3 h; Yield: 81.2% (87.7 mg, 0.163 mmol); White solid (mp: 57–60 $^{\circ}$ C); TLC: R_f = 0.50 (*n*-hexane/EtOAc = 2/1); ^1H NMR (CDCl_3) δ 8.10 (s, 1H), 7.86 (ddd, $J_{\text{H-H}}$ = 7.5, 1.1, 1.1 Hz, 1H), 7.80–7.73 (m, 5H), 7.50 (dd, $J_{\text{H-H}}$ = 7.5, 7.5 Hz, 1H), 6.97 (d, $J_{\text{H-H}}$ = 2.6 Hz, 1H), 6.94 (d, $J_{\text{H-H}}$ = 8.9 Hz, 1H), 6.68 (dd, $J_{\text{H-H}}$ = 8.9, 2.6 Hz, 1H), 3.85 (s, 3H), 3.71 (s, 3H), 3.69 (s, 2H), 2.42 (s, 3H), 1.38 (s, 12H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 171.6 (1C), 169.4 (1C), 156.0 (1C), 145.7 (1C), 139.2 (1C), 136.2 (1C), 134.9 (1C), 134.2 (1C), 133.7 (1C), 131.1 (1C), 130.7 (1C), 130.5 (2C), 130.2 (1C), 128.6 (1C), 127.6 (2C), 115.2 (1C), 112.2 (1C), 111.6 (1C), 101.3 (1C), 84.2 (2C), 55.5 (1C), 52.3 (1C), 30.3 (1C), 25.0 (4C), 13.5 (1C) (the signal for the carbon that is attached to the boron atom was not observed); ^{11}B NMR (CDCl_3) δ 29.7; IR (ZnSe, cm^{-1}) 1680, 1356, 1316, 1289, 1260, 1225, 1165, 1142, 1069, 708; HRMS (ESI^+) m/z 540.2548 (540.2552 calcd for $\text{C}_{32}\text{H}_{35}^{11}\text{BNO}_6^+$, $[\text{M}+\text{H}]^+$).



4-(2-Aminophenylcarbonyl)phenyl-methylindomethacin (35).

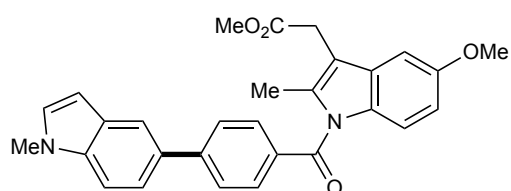
Prepared from 2-amino-4'-bromobenzophenone (55.2 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 4 h; Yield: 65.9% (70.2 mg, 0.132 mmol); White solid (mp: 152–154 $^{\circ}$ C); TLC: R_f = 0.26 (*n*-hexane/EtOAc = 2/1); ^1H NMR (CDCl_3) δ 7.85–7.70 (m, 8H), 7.50 (dd, $J_{\text{H-H}}$ = 8.2, 1.8 Hz, 1H), 7.35–7.30 (m, 1H), 6.98–6.95 (m, 2H), 6.78 (d,

$J_{\text{H-H}} = 8.2$ Hz, 1H), 6.68 (dd, $J_{\text{H-H}} = 9.1, 2.7$ Hz, 1H), 6.66–6.62 (m, 1H), 6.13 (bs, 2H), 3.85 (s, 3H), 3.71 (s, 3H), 3.70 (s, 2H), 2.43 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 198.6 (1C), 171.6 (1C), 169.2 (1C), 156.1 (1C), 151.2 (1C), 144.7 (1C), 142.4 (1C), 140.0 (1C), 136.3 (1C), 135.0 (1C), 134.6 (2C), 131.1 (1C), 130.8 (1C), 130.7 (2C), 130.1 (2C), 127.7 (2C), 127.2 (2C), 118.2 (1C), 117.3 (1C), 115.8 (1C), 115.2 (1C), 112.4 (1C), 111.7 (1C), 101.4 (1C), 55.9 (1C), 52.4 (1C), 30.4 (1C), 13.6 (1C); IR (ZnSe, cm^{-1}) 1732, 1607, 1582, 1476, 1366, 1329, 1231, 1217, 833, 750; HRMS (ESI^+) m/z 533.2071 (533.2071 calcd for $\text{C}_{33}\text{H}_{29}\text{N}_2\text{O}_5^+$, $[\text{M}+\text{H}]^+$).



2-Pyridyl-methylindomethacin (36). Prepared from 2-bromopyridine (31.6 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 3 h; Yield: 86.5% (71.7 mg, 0.173 mmol); White solid (mp: 97–100 °C); TLC: $R_f = 0.18$ (n -hexane/EtOAc = 2/1); ^1H NMR (CDCl_3) δ 8.75 (ddd, $J_{\text{H-H}} =$

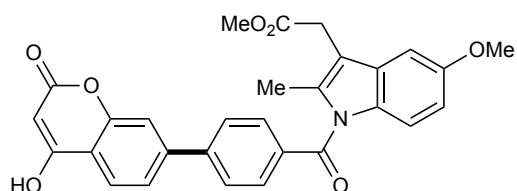
3.2, 1.7, 1.7 Hz, 1H), 8.15–8.12 (AA'BB', 2H), 7.85–7.81 (m, 4H), 7.34–7.30 (m, 1H), 6.97–6.94 (m, 2H), 6.65 (dd, $J_{\text{H-H}} = 8.8, 2.5$ Hz, 1H), 3.83 (s, 3H), 3.71 (s, 3H), 3.68 (s, 2H), 2.42 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 171.5 (1C), 169.2 (1C), 156.1 (1C), 156.0 (1C), 150.1 (1C), 143.6 (1C), 137.2 (1C), 136.2 (1C), 135.8 (1C), 131.1 (1C), 130.7 (1C), 130.4 (2C), 127.3 (2C), 123.2 (1C), 121.2 (1C), 115.3 (1C), 112.4 (1C), 111.7 (1C), 101.3 (1C), 55.8 (1C), 52.3 (1C), 30.3 (1C), 13.5 (1C); IR (ZnSe, cm^{-1}) 1728, 1659, 1433, 1360, 1335, 1306, 1269, 1217, 1146, 752; HRMS (ESI^+) m/z 415.1648 (415.1652 calcd for $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_4^+$, $[\text{M}+\text{H}]^+$).



1-Methylindol-5-yl-methylindomethacin (37).

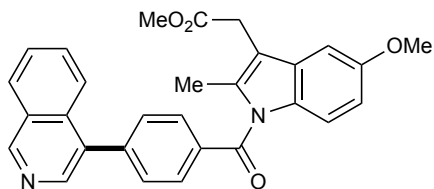
Prepared from 5-bromo-1-methylindole (42.0 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 3 h; Yield: 91.1% (85.0 mg, 0.182 mmol); White solid (mp: 150–153 °C); TLC: $R_f = 0.38$ (n -hexane/EtOAc =

2/1); ^1H NMR (CDCl_3) δ 7.93 (d, $J_{\text{H-H}} = 1.6$ Hz, 1H), 7.81–7.76 (m, 4H), 7.55 (dd, $J_{\text{H-H}} = 8.5, 2.0$ Hz, 1H), 7.42 (d, $J_{\text{H-H}} = 8.7$ Hz, 1H), 7.12 (d, $J_{\text{H-H}} = 3.2$ Hz, 1H), 7.01–6.98 (m, 2H), 6.68 (dd, $J_{\text{H-H}} = 8.9, 2.4$ Hz, 1H), 6.57 (d, $J_{\text{H-H}} = 2.4$ Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.71 (s, 3H), 3.70 (s, 2H), 2.44 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 171.6 (1C), 169.5 (1C), 155.9 (1C), 147.3 (1C), 136.9 (1C), 136.3 (1C), 133.0 (1C), 131.2 (1C), 131.1 (1C), 130.6 (2C+1C), 130.0 (1C), 129.1 (1C), 127.4 (2C), 121.2 (1C), 119.9 (1C), 115.2 (1C), 112.0 (1C), 111.6 (1C), 109.9 (1C), 101.7 (1C), 101.2 (1C), 55.8 (1C), 52.2 (1C), 33.1 (1C), 30.3 (1C), 13.4 (1C); IR (ZnSe, cm^{-1}) 1736, 1441, 1360, 1327, 1233, 1169, 1150, 801, 710, 608; HRMS (ESI^+) m/z 467.1965 (467.1965 calcd for $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_4^+$, $[\text{M}+\text{H}]^+$).



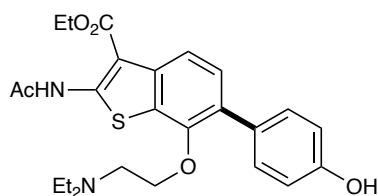
4-Hydroxy-2-oxo-2H-chromen-7-yl-methylindomethacin (38). Prepared from 7-bromo-4-hydroxy-2H-chromen-2-one (48.2 mg, 0.200 mmol) and **S3** (97.5 mg, 0.220 mmol); Reaction time: 5 h; Yield: 94.8% (94.3 mg, 1.90 mmol); White solid (mp:

198–201 °C); TLC: R_f = 0.74 ($\text{CHCl}_3/\text{MeOH}$ = 4/1); ^1H NMR ($\text{DMSO}-d_6$) δ 8.16 (d, $J_{\text{H-H}}$ = 2.3 Hz, 1H), 8.09–8.07 (m, 1H), 7.96–7.94 (AA'BB', 2H), 7.78–7.76 (AA'BB', 2H), 7.52 (d, $J_{\text{H-H}}$ = 9.1 Hz, 1H), 7.04 (d, $J_{\text{H-H}}$ = 2.3 Hz, 1H), 6.96 (d, $J_{\text{H-H}}$ = 9.1 Hz, 1H), 6.72 (dd, $J_{\text{H-H}}$ = 9.1, 2.3 Hz, 1H), 5.68–5.60 (m, 1H), 3.81 (s, 2H), 3.76 (s, 3H), 3.64 (s, 3H), 2.27 (s, 3H) (the signal for the proton of the hydroxy group was not observed); $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{DMSO}-d_6$) δ 171.1 (1C), 168.6 (1C), 165.7 (1C), 161.8 (1C), 155.5 (1C), 153.6 (1C), 142.9 (1C), 135.5 (1C), 134.4 (1C), 134.2 (1C), 131.3 (1C), 130.5 (1C), 130.3 (1C), 130.2 (2C), 127.1 (2C), 121.4 (1C), 117.4 (1C), 116.5 (1C), 114.6 (1C), 112.5 (1C), 111.4 (1C), 101.6 (1C), 91.3 (1C), 55.4 (1C), 51.9 (1C), 29.2 (1C), 13.2 (1C); IR (ZnSe , cm^{-1}) 1721, 1674, 1543, 1304, 1273, 1258, 1244, 1223, 1186, 1169; HRMS (ESI^-) m/z 496.1389 (496.1391 calcd for $\text{C}_{29}\text{H}_{22}\text{NO}_7^-$, $[\text{M}-\text{H}]^-$).



4-Isoquinolinyl-methylindomethacin (39). Prepared from 4-bromoisoquinoline (41.6 mg, 0.200 mmol) and **S3** (97.5 mg, 0.22 mmol); Reaction time: 3 h; Yield: 73.6% (68.4 mg, 0.147 mmol); White solid (mp: 70–73 °C); TLC: R_f = 0.30 (n -hexane/ EtOAc = 1/1); ^1H NMR (CDCl_3) δ 9.32 (bs, 1H), 8.56

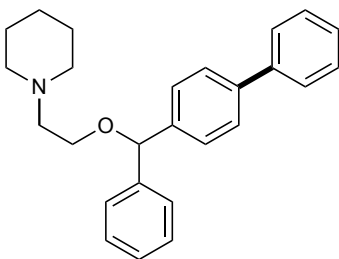
(br, 1H), 8.09 (d, $J_{\text{H-H}}$ = 7.5 Hz, 1H), 7.91–7.88 (m, 3H), 7.76–7.65 (m, 4H), 7.05 (d, $J_{\text{H-H}}$ = 8.6 Hz, 1H), 6.99 (d, $J_{\text{H-H}}$ = 2.3 Hz, 1H), 6.73 (dd, $J_{\text{H-H}}$ = 8.6, 2.3 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 3H), 3.71 (s, 2H), 2.46 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 171.5 (1C), 169.1 (1C), 156.1 (1C), 152.9 (1C), 142.9 (1C), 141.8 (1C), 136.1 (1C), 135.2 (1C), 133.8 (1C), 132.1 (1C), 131.2 (1C), 131.1 (1C), 130.8 (1C), 130.6 (2C), 130.2 (2C), 128.5 (1C), 128.2 (1C), 127.6 (1C), 124.3 (1C), 115.2 (1C), 112.5 (1C), 111.7 (1C), 101.4 (1C), 55.8 (1C), 52.3 (1C), 30.3 (1C), 13.6 (1C); IR (ZnSe , cm^{-1}) 1732, 1680, 1476, 1356, 1314, 1219, 1165, 1144, 787, 752; HRMS (ESI^+) m/z 465.1806 (465.1809 calcd for $\text{C}_{29}\text{H}_{25}\text{N}_2\text{O}_4^+$, $[\text{M}+\text{H}]^+$).



TMD-512 (40). Prepared from ethyl 2-acetylthio-6-bromo-7-[2-(N,N -diethylamino)ethoxy]benzoate (91.5 mg, 0.200 mmol) and potassium 4-hydroxyphenyl(trifluoroborate) (44.0 mg, 0.220 mmol); Reaction time: 3 h; Yield: 56.0% (52.7 mg, 0.0112 mmol); White solid (mp:

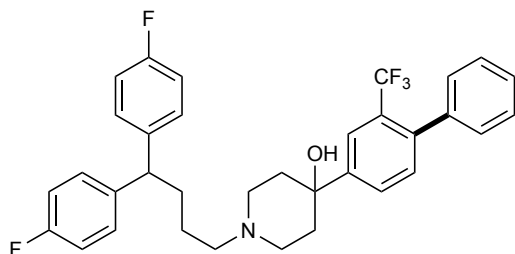
185–188 °C); TLC: R_f = 0.24 ($\text{CHCl}_3/\text{MeOH}$ = 9/1); ^1H NMR (CDCl_3) δ 11.75 (bs, 1H), 8.03 (d,

$J_{\text{H-H}} = 8.7$ Hz, 1H), 7.48–7.45 (AA'BB', 2H), 7.38 (d, $J_{\text{H-H}} = 8.3$ Hz, 1H), 6.88–6.85 (AA'BB', 2H), 4.50 (q, $J_{\text{H-H}} = 7.1$ Hz, 2H), 3.87 (t, $J_{\text{H-H}} = 6.3$ Hz, 2H), 2.89 (t, $J_{\text{H-H}} = 6.3$ Hz, 2H), 2.68 (q, $J_{\text{H-H}} = 7.0$ Hz, 4H), 2.37 (s, 3H), 1.52 (t, $J_{\text{H-H}} = 7.3$ Hz, 3H), 1.06 (t, $J_{\text{H-H}} = 7.1$ Hz, 6H) (the signal for the proton of the acidic group was not observed); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 168.2 (1C), 166.9 (1C), 155.7 (1C), 153.0 (1C), 150.6 (1C), 134.7 (1C), 130.6 (2C), 130.1 (1C), 129.3 (1C), 128.8 (1C), 128.4 (1C), 119.3 (1C), 115.7 (2C), 106.8 (1C), 70.4 (1C), 61.3 (1C), 52.2 (1C), 47.4 (2C), 24.2 (1C), 14.6 (1C), 11.2 (2C). The chemical shifts were consistent with those reported in the literature.⁵



Phenyl-cloperastine (41). Prepared from cloperastine (33.2 mg, 0.101 mmol) and potassium phenyl(trifluoro)borate (**2a**, 20.4 mg, 0.111 mmol); Reaction time: 6 h; Purified with silica-gel column chromatography followed by GPC.; Yield: 41.3% (15.5 mg, 41.7 μmol); White solid (mp: 57–60 °C); TLC: $R_f = 0.30$ ($\text{CHCl}_3/\text{MeOH} = 19/1$); ^1H NMR (CDCl_3) δ 7.56–7.52 (m, 4H), 7.43–7.37 (m, 6H),

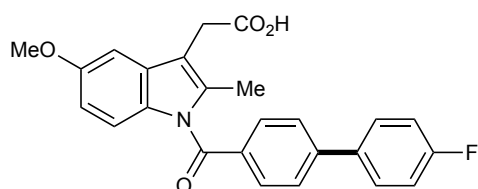
7.35–7.30 (m, 3H), 7.27–7.23 (m, 1H), 5.42 (s, 1H), 3.65 (t, $J = 6.3$ Hz, 2H), 2.70 (t, $J = 6.1$ Hz, 2H), 2.50 (bs, 4H), 1.60 (tt, $J_{\text{H-H}} = 5.5, 5.5$ Hz, 4H), 1.44 (dd, $J_{\text{H-H}} = 6.3, 5.1$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 142.3 (1C), 141.5 (1C), 141.1 (1C), 140.5 (1C), 128.9 (2C), 128.6 (2C), 127.7 (1C), 127.6 (2C), 127.4 (1C), 127.3 (2C), 127.25 (2C), 127.17 (2C), 83.9 (1C), 67.1 (1C), 58.7 (1C), 55.1 (2C), 26.0 (2C), 24.3 (1C); IR (ZnSe, cm^{-1}) 1485, 1298, 1098, 1072, 1040, 1007, 756, 739, 694, 650; HRMS (ESI⁺) m/z 372.2313 (372.2323 calcd for $\text{C}_{26}\text{H}_{30}\text{NO}^+$, $[\text{M}+\text{H}]^+$).



Phenyl-penfluridol (42). Prepared from penfluridol (52.4 mg, 0.100 mmol) and potassium phenyl(trifluoro)borate (**2a**, 20.2 mg, 0.110 mmol) with (cod)Pd(CH_2TMS)₂ (3.9 mg, 10 μmol , 10 mol%) and XPhos (5.7 mg, 12 μmol , 12 mol%); Reaction time: 6 h; Purified with silica-gel column chromatography

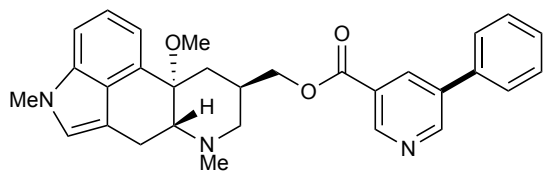
followed by HPLC. Column: COSMOSIL C₁₈-AR-II (10 $\times$ 250 mm); Eluent: MeCN (0.1% TFA) : H₂O (0.1% TFA) = 50 : 50; Flow rate: 5.0 mL/min; Wavelength of UV detection: 254 nm; Retention time: 14.7 min; Yield: 69.7% (39.4 mg, 69.7 μmol); White solid (mp: 45–48 °C); TLC: $R_f = 0.30$ ($\text{CHCl}_3/\text{MeOH} = 19/1$); ^1H NMR (CDCl_3) δ 7.90 (d, $J_{\text{H-H}} = 1.6$ Hz, 1H), 7.67 (dd, $J_{\text{H-H}} = 8.1, 1.6$ Hz, 1H), 7.41–7.36 (m, 3H), 7.31–7.30 (m, 3H), 7.20–7.15 (m, 4H), 7.00–6.94 (AA'BB'X, 4H), 3.89 (t, $J_{\text{H-H}} = 7.7$ Hz, 1H), 2.80 (d, $J_{\text{H-H}} = 11.5$ Hz, 2H), 2.47–2.37 (m, 4H), 2.18 (td, $J_{\text{H-H}} = 13.0, 4.0$ Hz, 2H), 2.04 (dd, $J_{\text{H-H}} = 15.6, 7.9$ Hz, 2H), 1.78–1.75 (m, 2H), 1.54–1.46 (m, 2H) (the signal for the proton of the hydroxy group was not observed); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ

161.5 (d, $^1J_{C-F}$ = 245.0 Hz, 2C), 148.0 (1C), 140.7 (d, $^4J_{C-F}$ = 2.9 Hz, 2C), 140.2 (1C), 139.8 (1C), 132.3 (1C), 129.3 (d, $^3J_{C-F}$ = 8.6 Hz, 4C), 129.1 (2C), 128.5 (q, $^2J_{C-F}$ = 29.9 Hz, 1C), 127.9 (2C), 127.8 (1C), 127.7 (1C), 124.3 (q, $^1J_{C-F}$ = 274.2 Hz, 1C), 122.6 (q, $^3J_{C-F}$ = 5.4 Hz, 1C), 115.5 (d, $^2J_{C-F}$ = 20.9 Hz, 4C), 71.5 (1C), 58.8 (1C), 50.0 (2C), 49.6 (2C), 38.7 (1C), 34.1 (1C), 25.7 (1C); ^{19}F NMR (CDCl_3) δ -56.6 (s, 3F), -116.9 (m, 2F); IR (ZnSe, cm^{-1}) 1505, 1314, 1262, 1221, 1121, 1071, 1036, 824, 801, 702; HRMS (ESI^+) m/z 566.2474 (566.2477 calcd for $\text{C}_{34}\text{H}_{33}\text{F}_5\text{NO}^+$, $[\text{M}+\text{H}]^+$).



4-Fluorophenyl-indomethacin (43). Prepared from indomethacin (35.8 mg, 0.100 mmol) and potassium 4-fluorophenyl(trifluoro)borate (30.3 mg, 0.150 mmol) with (cod) $\text{Pd}(\text{CH}_2\text{TMS})_2$ (3.9 mg, 10 μmol , 10 mol%) and XPhos (5.7 mg, 12 μmol , 12 mol%); Reaction time: 6 h;

Yield: 55.8% (23.3 mg, 55.8 μmol); White solid (mp: 161–164 $^\circ\text{C}$); TLC: R_f = 0.48 ($\text{CHCl}_3/\text{MeOH}$ = 9/1); ^1H NMR (CDCl_3) δ 7.81–7.78 (m, 2H), 7.68–7.61 (m, 4H), 7.20–7.15 (AA'BB'X, 2H), 6.97 (d, J_{H-H} = 2.8 Hz, 1H), 6.94 (d, J = 8.7 Hz, 1H), 6.67 (dd, J_{H-H} = 8.9, 2.8 Hz, 1H), 3.84 (s, 3H), 3.73 (s, 2H), 2.43 (s, 3H) (the signal for the hydrogen of the carboxy group was not observed); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 176.4 (1C), 169.3 (1C), 163.3 (d, $^1J_{C-F}$ = 247.9 Hz, 1C), 156.1 (1C), 144.8 (1C), 136.6 (1C), 135.9 (d, $^4J_{C-F}$ = 2.9 Hz, 1C), 134.2 (1C), 131.1 (1C), 130.7 (2C), 130.6 (1C), 129.2 (d, $^3J_{C-F}$ = 8.7 Hz, 2C), 127.4 (2C), 116.2 (d, $^2J_{C-F}$ = 21.9 Hz, 2C), 115.3 (1C), 111.8 (1C), 111.7 (1C), 101.2 (1C), 55.9 (1C), 30.1 (1C), 13.5 (1C); ^{19}F NMR (CDCl_3) δ -113.6 (m, 1F); IR (ZnSe, cm^{-1}) 1709, 1688, 1479, 1370, 1314, 1217, 1198, 1074, 824, 801; HRMS (ESI^+) m/z 418.1442 (418.1449 calcd for $\text{C}_{25}\text{H}_{21}\text{FNO}_4^+$, $[\text{M}+\text{H}]^+$).



Phenyl-nicergoline (44). Prepared from nicergoline (48.4 mg, 0.100 mmol) and potassium phenyl(trifluoro)borate (**2a**, 20.2 mg, 0.100 mmol) with $\text{PdCl}_2(\text{amphos})_2$ (3.5 mg, 4.9 μmol , 4.9 mol%);

Reaction time: 24 h; Purified with silica-gel column chromatography followed by HPLC. Column: COSMOSIL C_{18} -MS-II (10 $\times$ 250 mm); Eluent: $\text{MeOH} : \text{MeCN} : \text{aq. KH}_2\text{PO}_4$ (50 mmol/L, pH = 7 adjusted with Et_3N) = 30 : 30 : 40; Flow rate: 5.0 mL/min; Wavelength of UV detection: 288 nm; Retention time: 19.7 min; Yield: 82.0% (39.5 mg, 0.0820 mmol); White solid (mp: 163–166 $^\circ\text{C}$); TLC: R_f = 0.35 ($\text{CHCl}_3/\text{MeOH}$ = 19/1); ^1H NMR (CDCl_3) δ 9.21 (d, J_{H-H} = 2.0 Hz, 1H), 9.03 (d, J_{H-H} = 2.0 Hz, 1H), 8.51 (t, J_{H-H} = 2.4 Hz, 1H), 7.65–7.62 (m, 2H), 7.54–7.50 (m, 2H), 7.47–7.43 (m, 1H), 7.24–7.18 (m, 2H), 7.07 (d, J_{H-H} = 2.4 Hz, 1H), 6.80 (d, J_{H-H} = 1.6 Hz, 1H), 4.44 (dd, J_{H-H} = 10.9, 4.8 Hz, 1H), 4.33 (dd, J_{H-H} = 10.9, 7.5 Hz, 1H), 3.78 (s, 3H), 3.27–3.19 (m,

2H), 3.07–2.98 (m, 5H), 2.73–2.64 (m, 1H), 2.49 (s, 3H), 2.38–2.37 (m, 1H), 2.12 (t, $J_{\text{H-H}} = 10.9$ Hz, 1H), 1.41 (t, $J_{\text{H-H}} = 13.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ 165.4 (1C), 152.0 (1C), 149.4 (1C), 136.71 (1C), 136.68 (1C), 135.4 (1C), 135.2 (1C), 129.7 (1C), 129.4 (2C), 128.8 (1C), 127.3 (2C), 126.4 (1C), 126.2 (1C), 123.4 (1C), 121.6 (1C), 115.1 (1C), 110.3 (1C), 109.1 (1C), 73.7 (1C), 70.1 (1C), 68.4 (1C), 60.8 (1C), 49.6 (1C), 44.0 (1C), 32.9 (1C), 31.6 (1C), 30.3 (1C), 22.4 (1C); IR (ZnSe, cm^{-1}) 1713, 1470, 1306, 1246, 1234, 1071, 1049, 937, 747, 700; HRMS (ESI^+) m/z 482.2437 (482.2438 calcd for $\text{C}_{30}\text{H}_{32}\text{N}_3\text{O}_3^+$, $[\text{M}+\text{H}]^+$).

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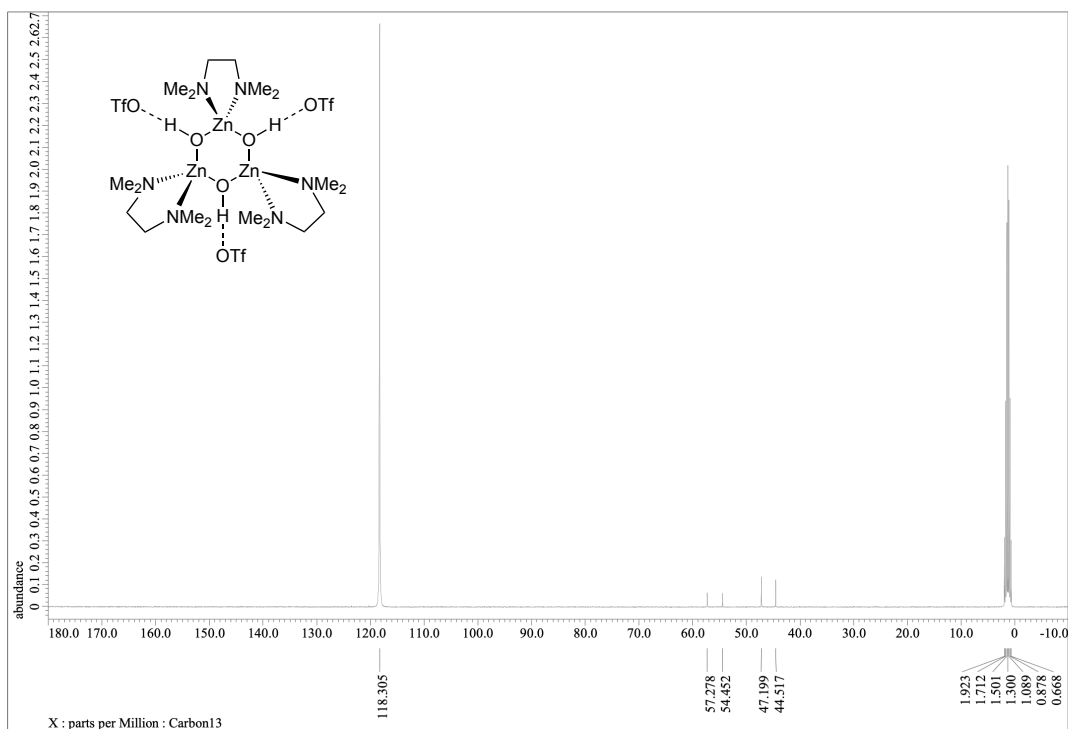
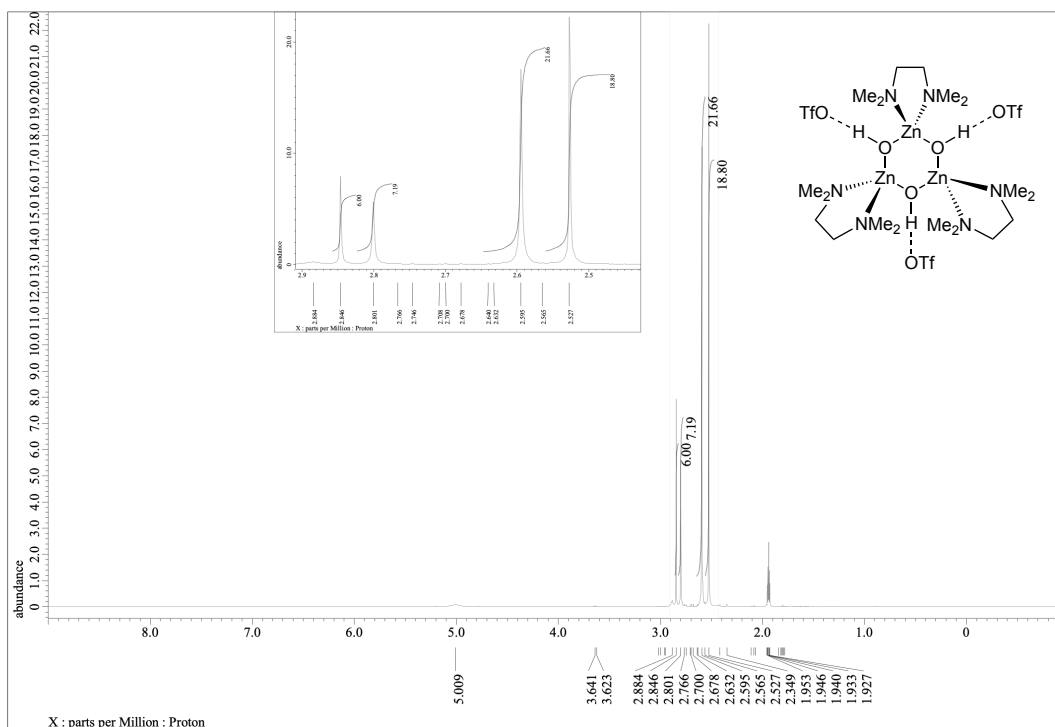
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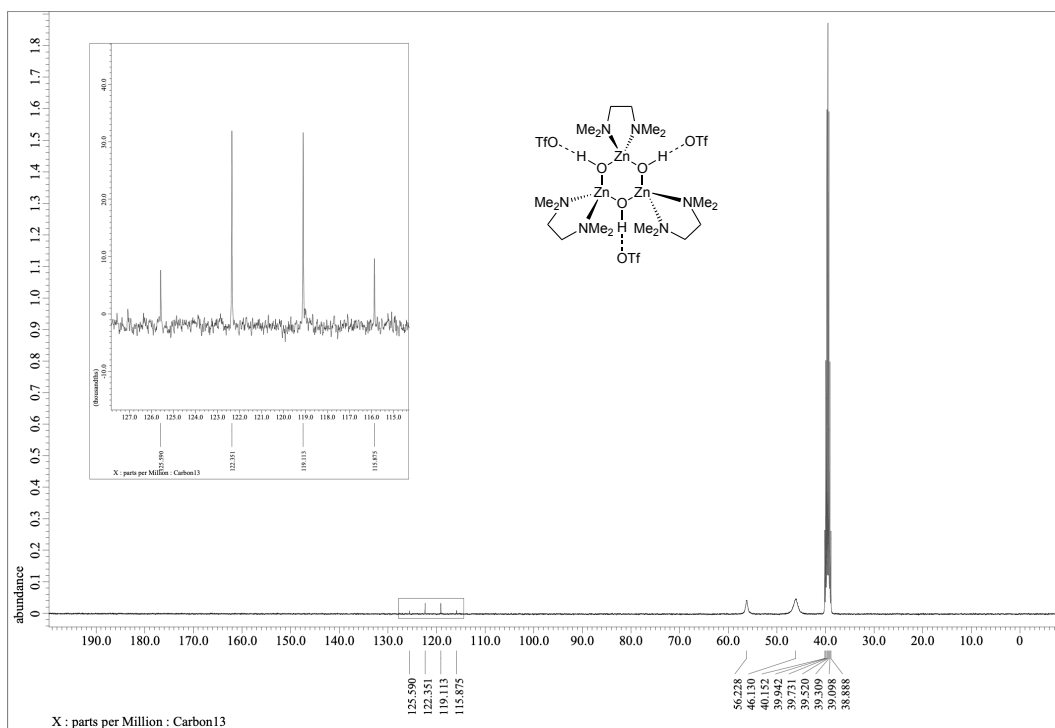
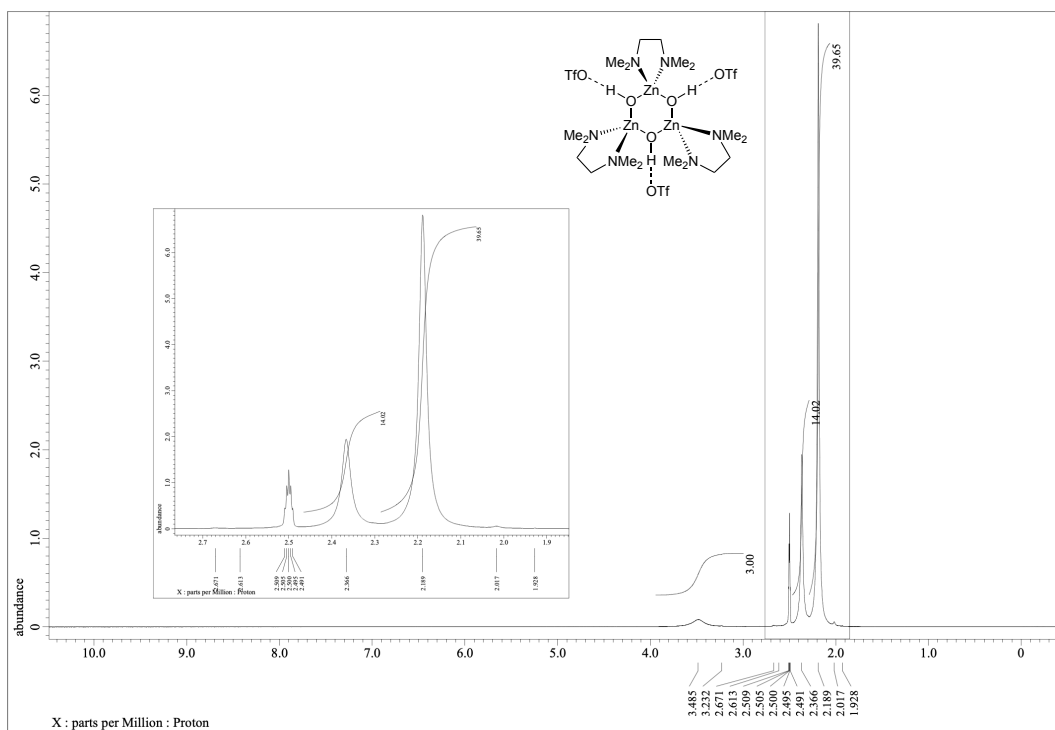
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NMR spectra

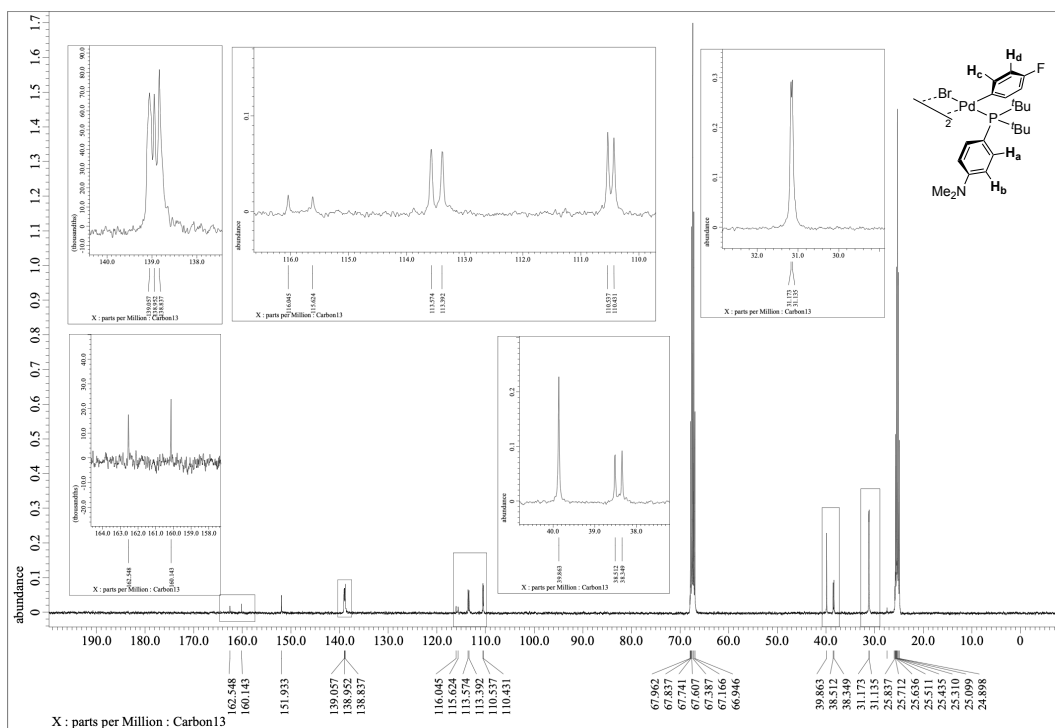
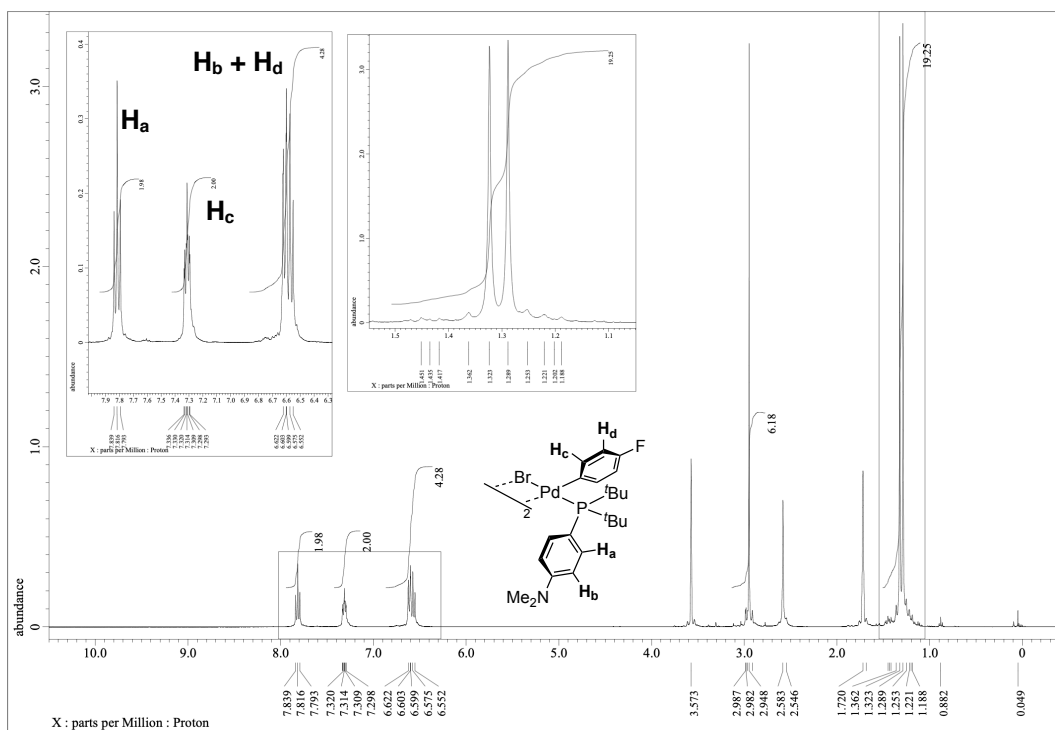
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4** ($\text{MeCN-}d_3$)



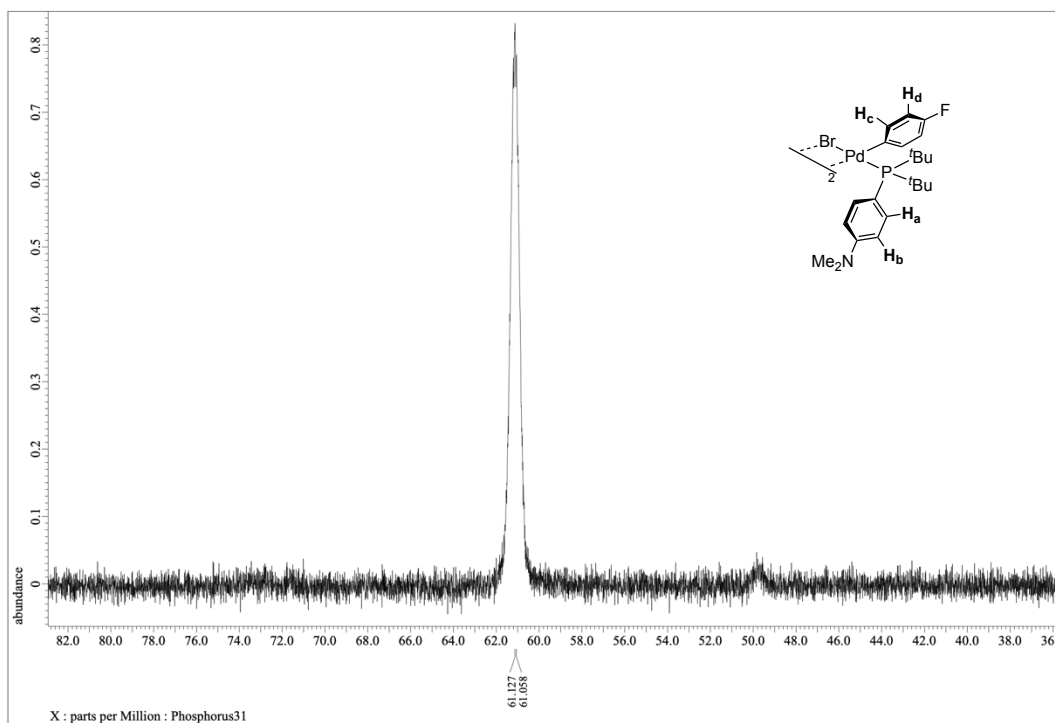
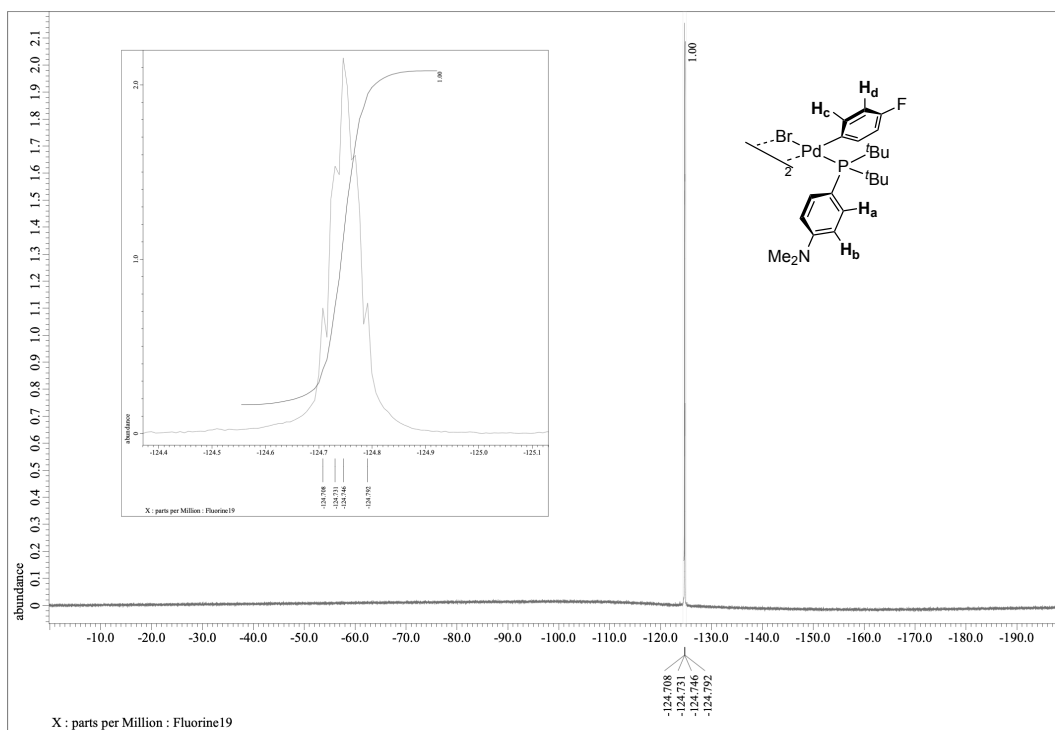
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4** (DMSO- d_6)



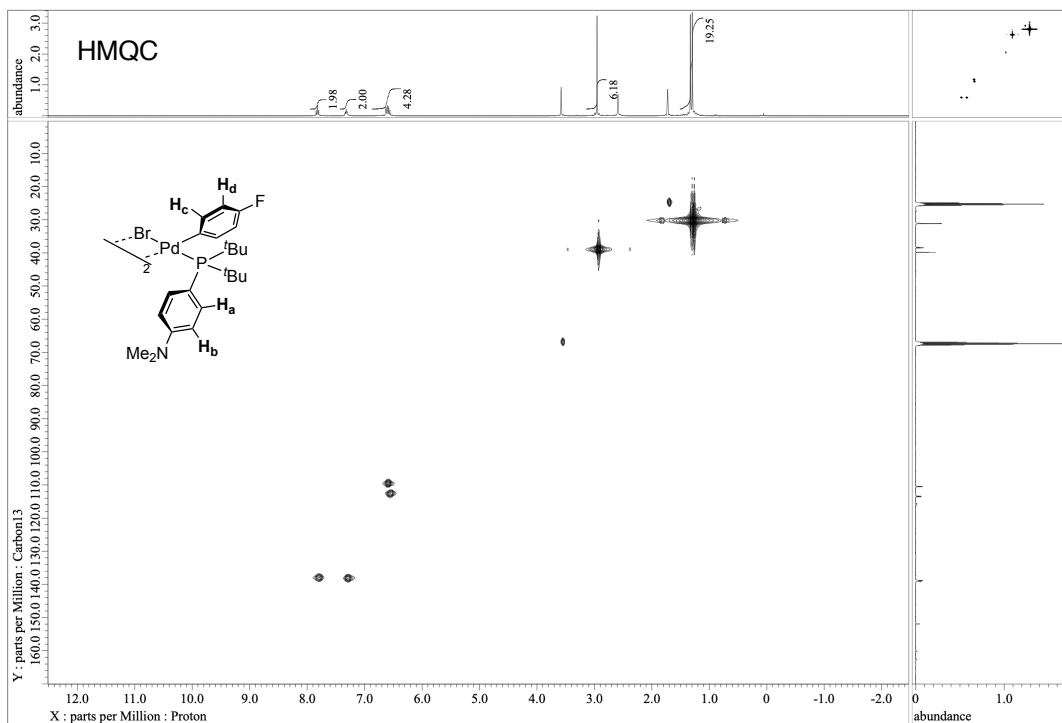
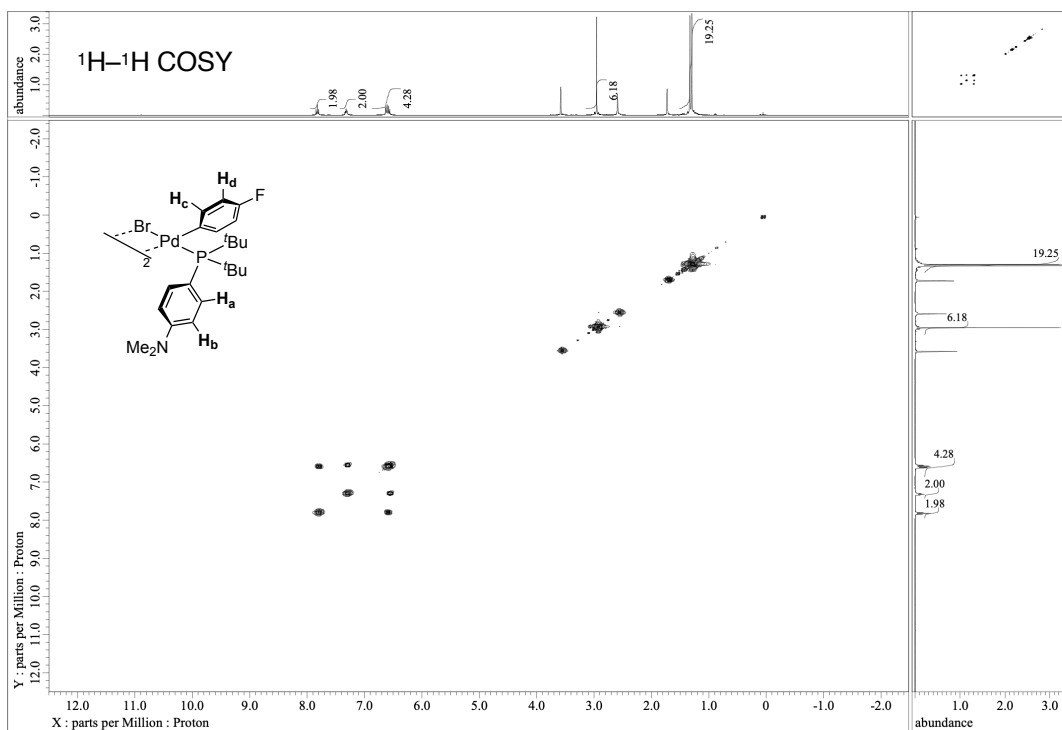
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **5a** (THF- d_8)

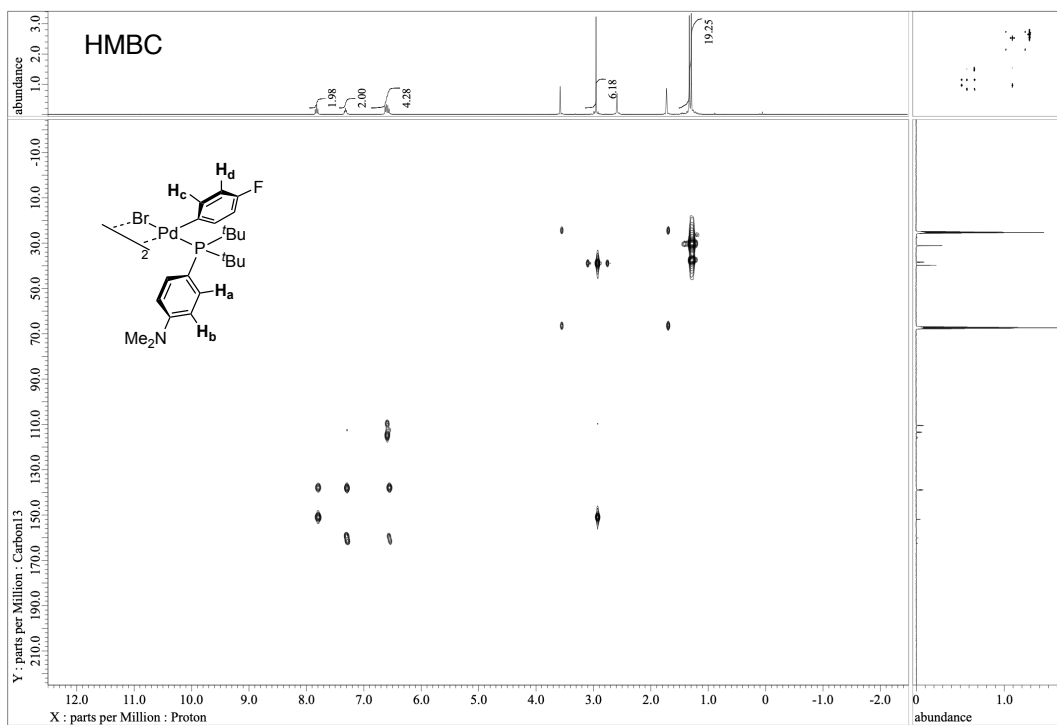


^{19}F NMR (373 MHz) and ^{31}P NMR (127 MHz) spectra of **5a** ($\text{THF-}d_8$)

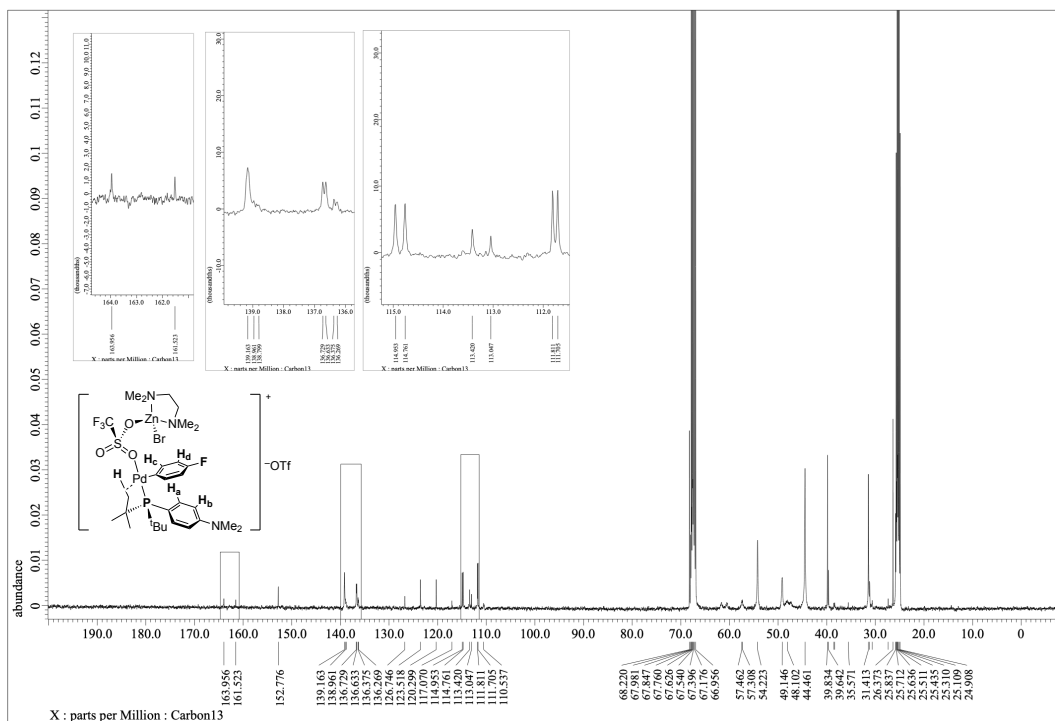
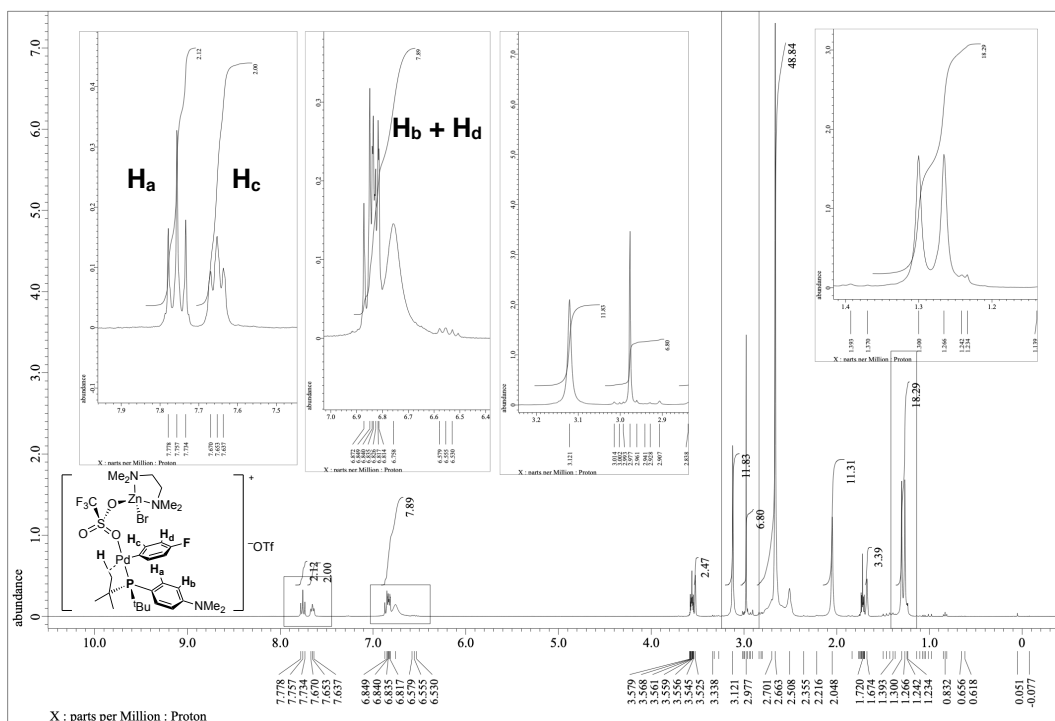


^1H - ^1H COSY, HMQC, and HMBC spectra of **5a** (THF- d_8)

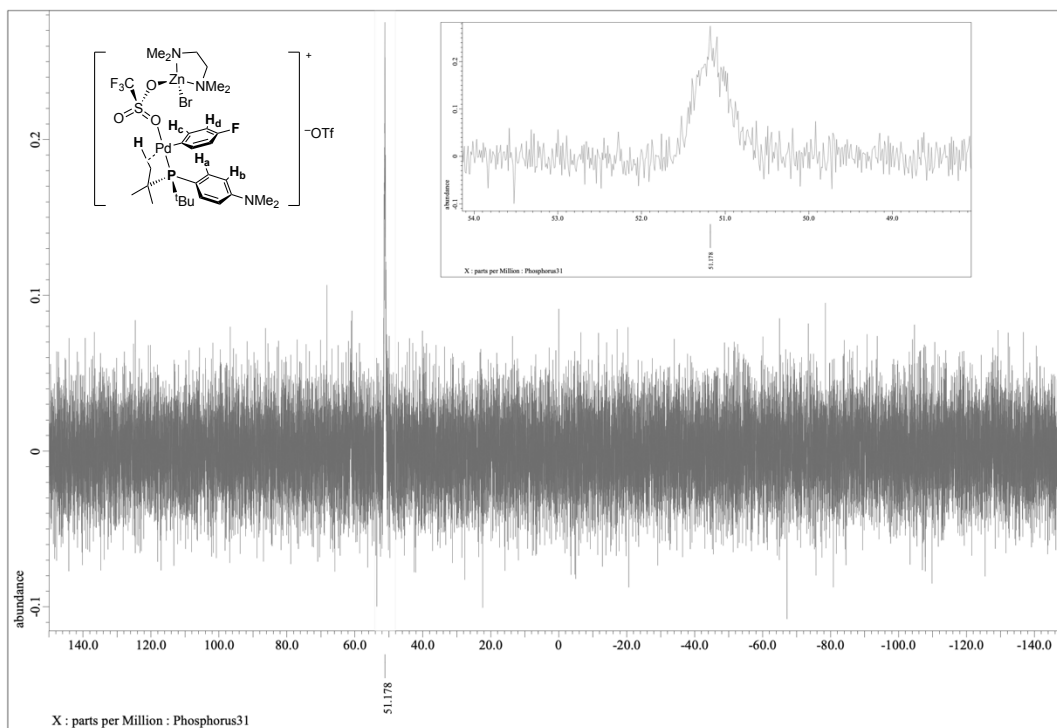
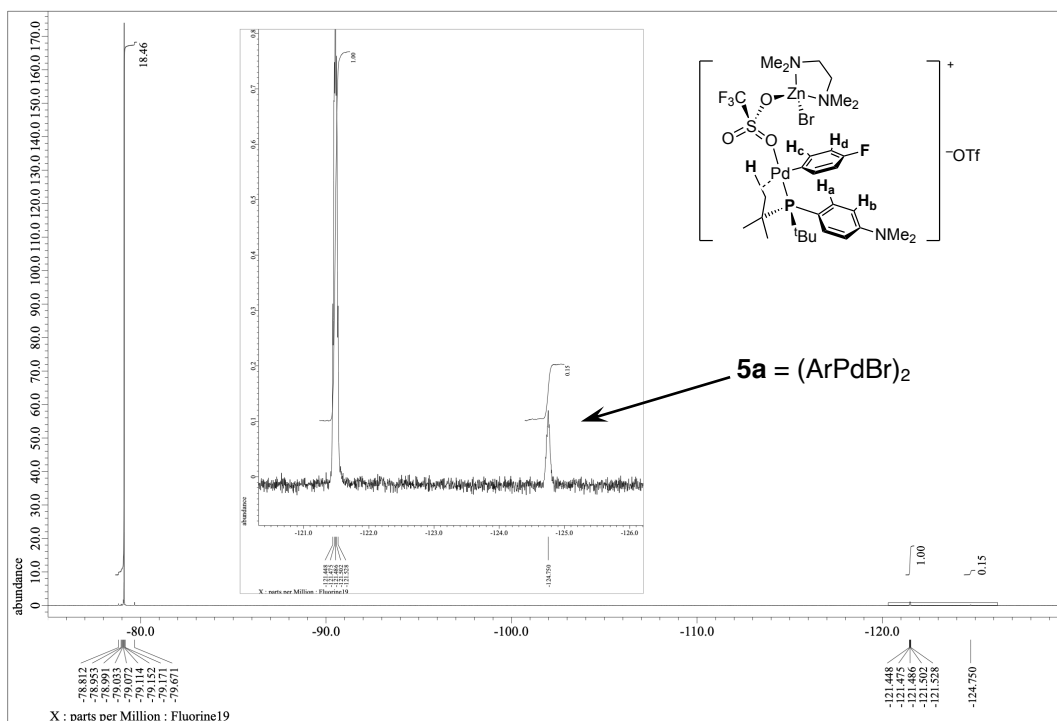




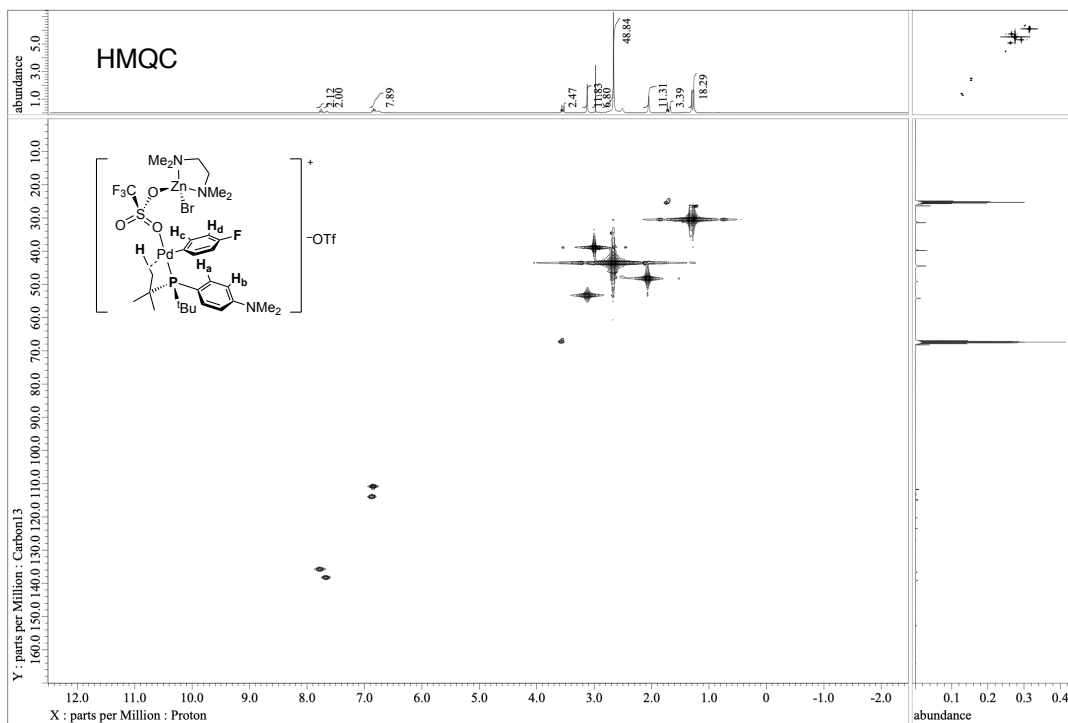
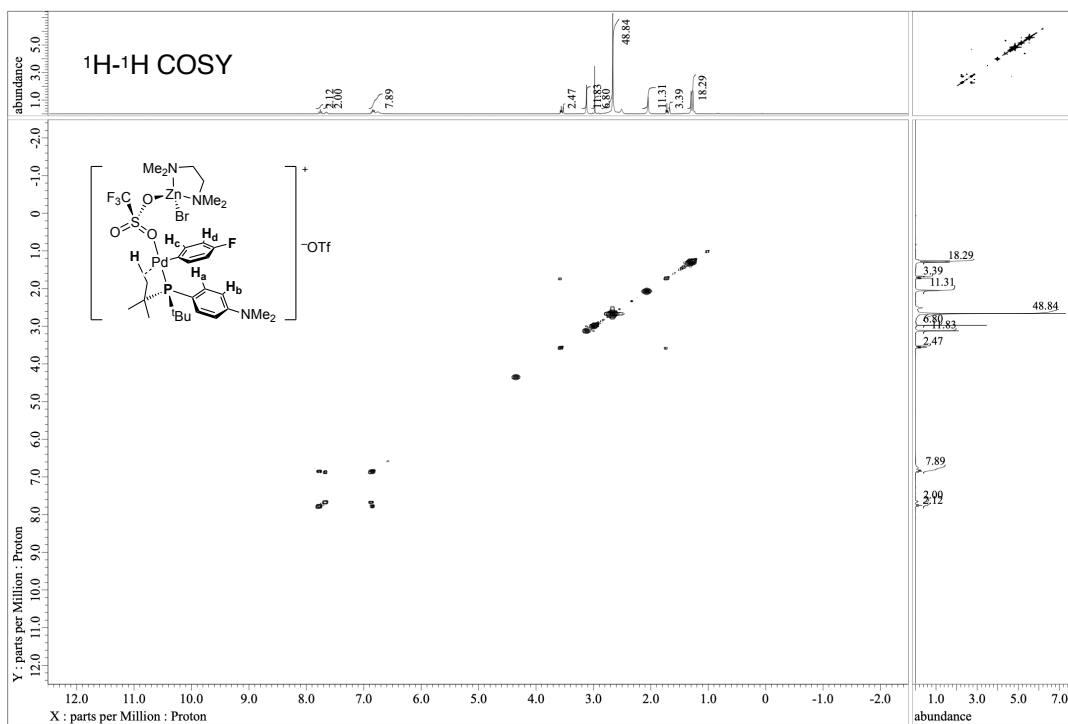
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **6** (THF- d_8)

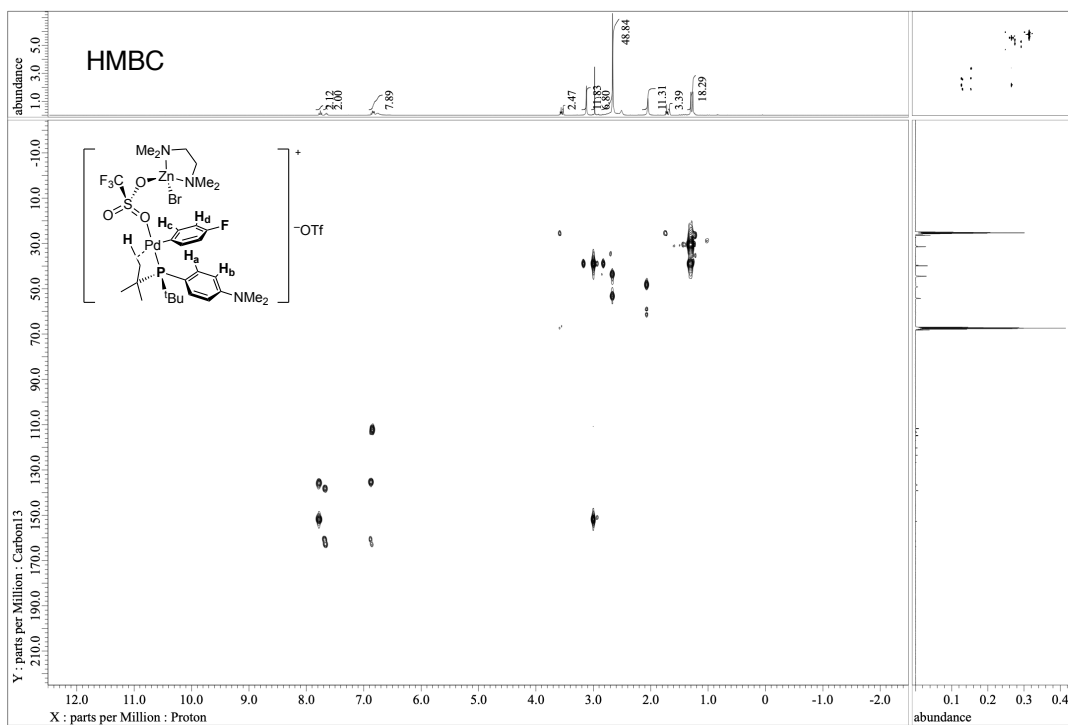


^{19}F NMR (373 MHz) and ^{31}P NMR (127 MHz) spectra of **6** (THF- d_8)

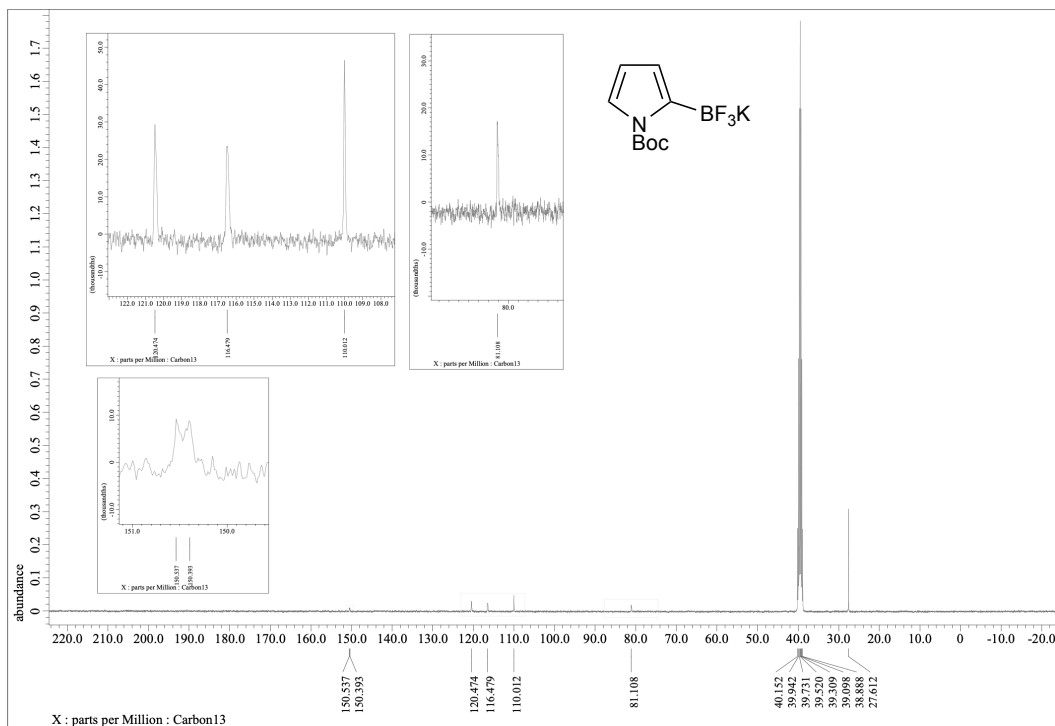
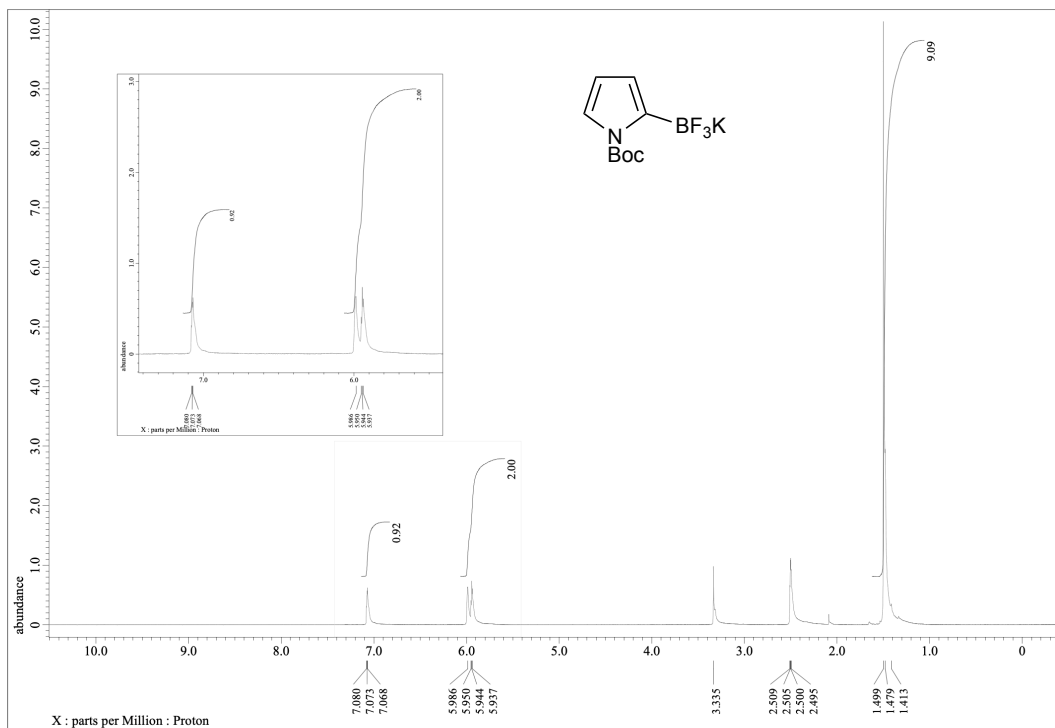


^1H - ^1H COSY, HMQC, and HMBC spectra of **6** (THF- d_8)

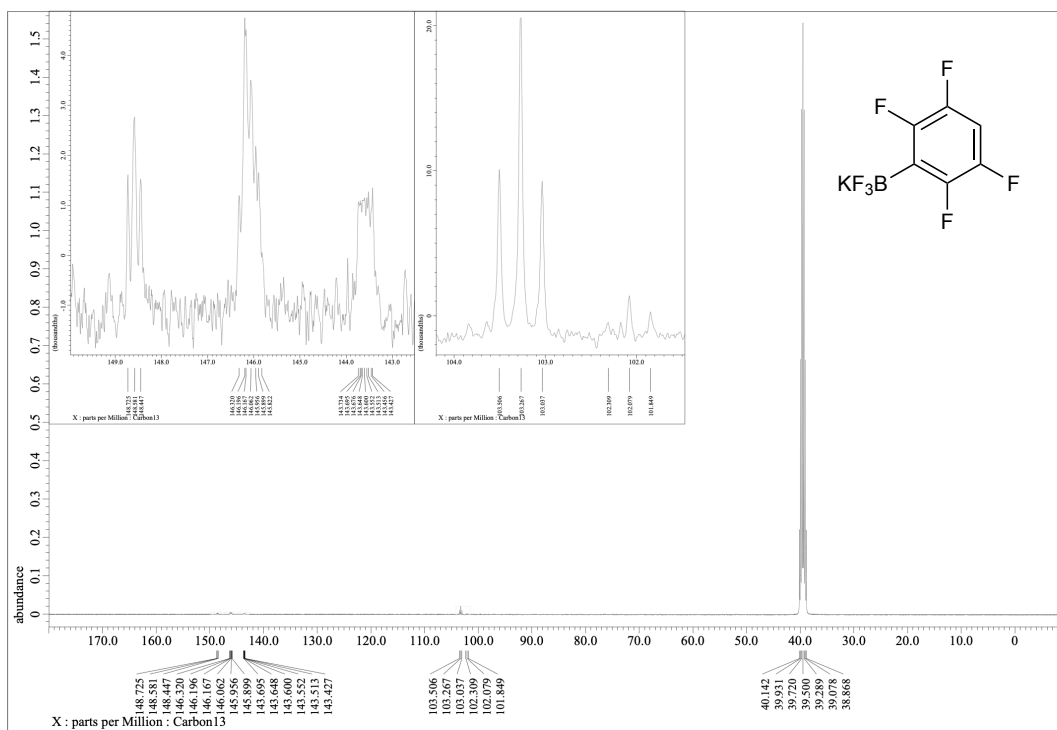
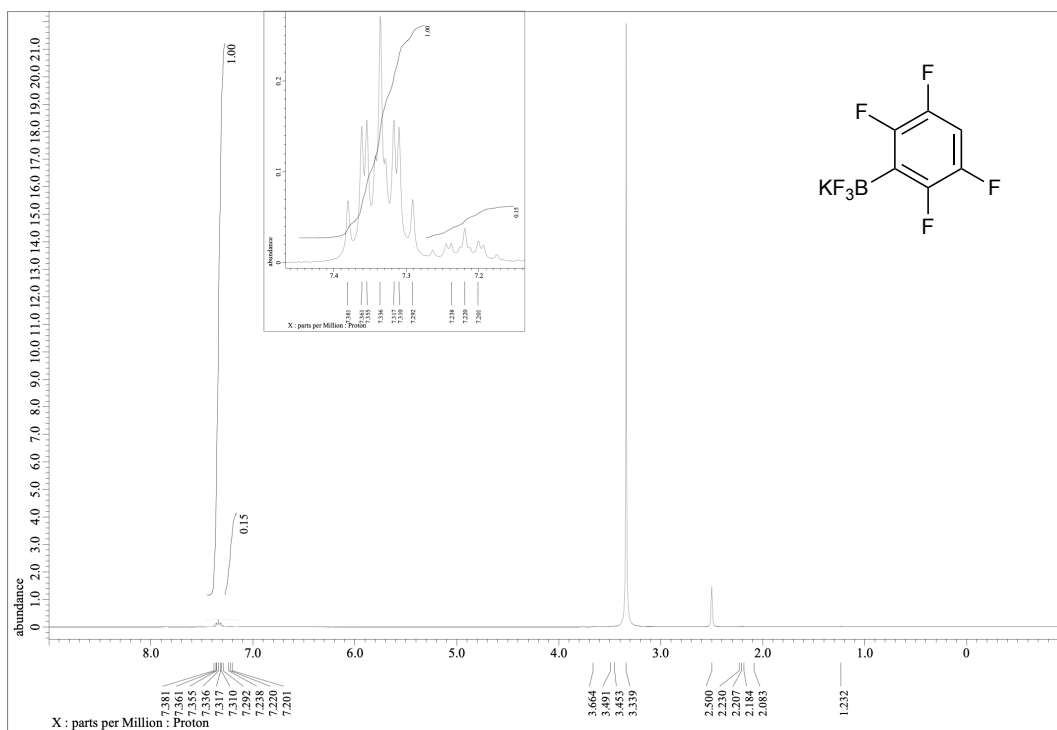




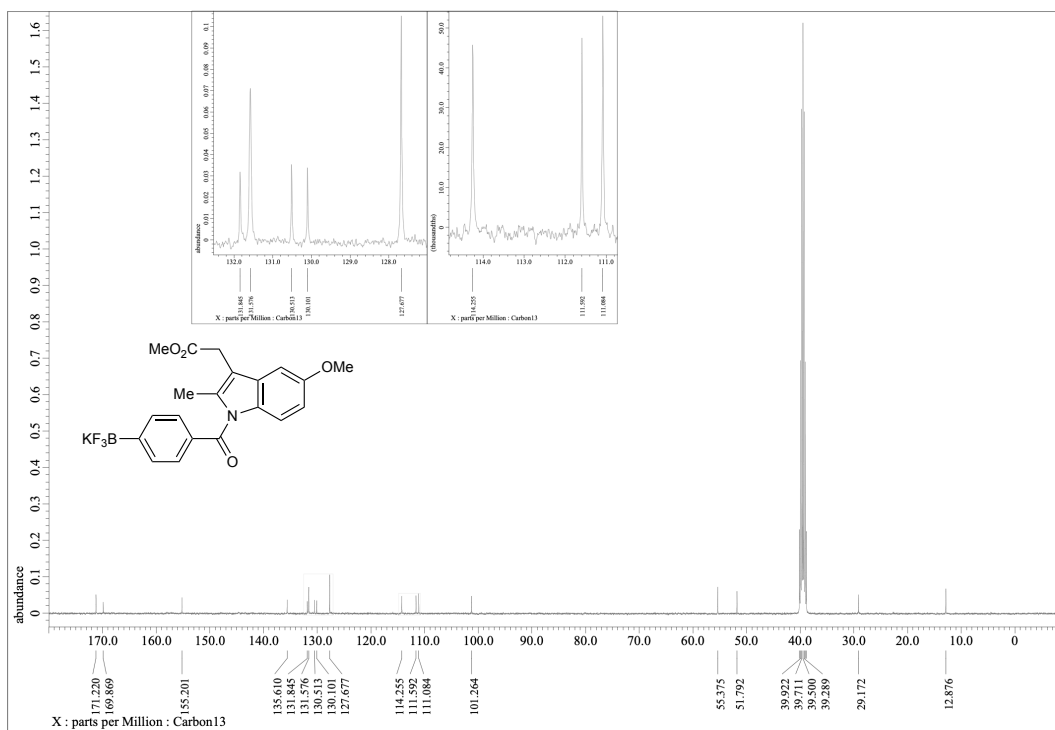
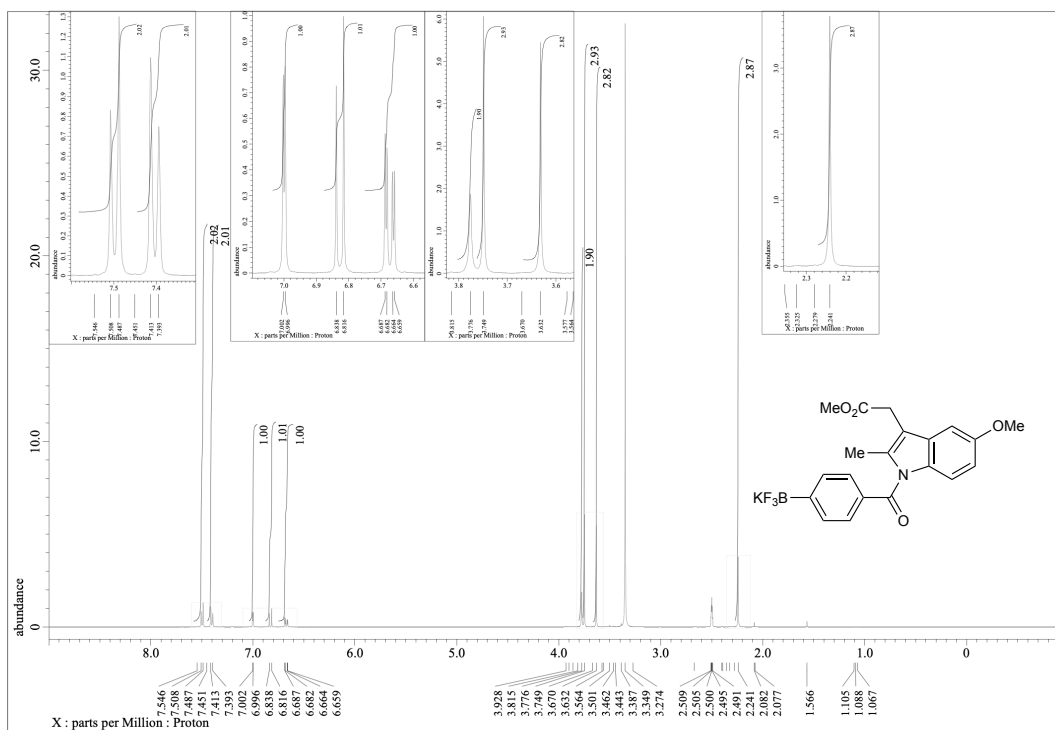
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **S1** ($\text{DMSO-}d_6$)



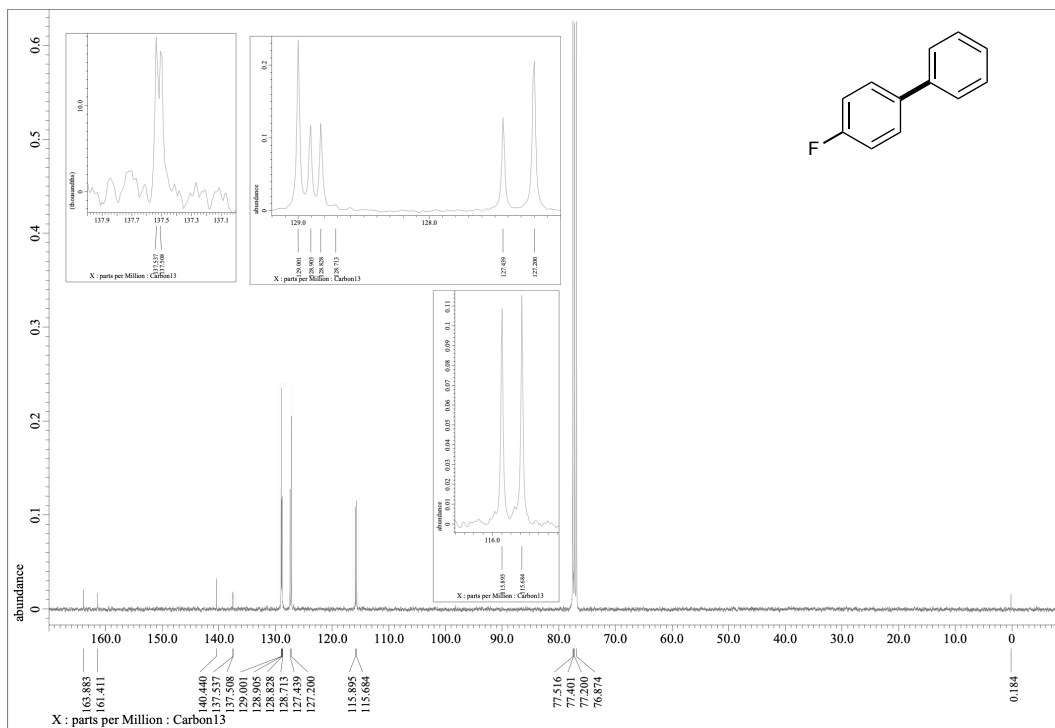
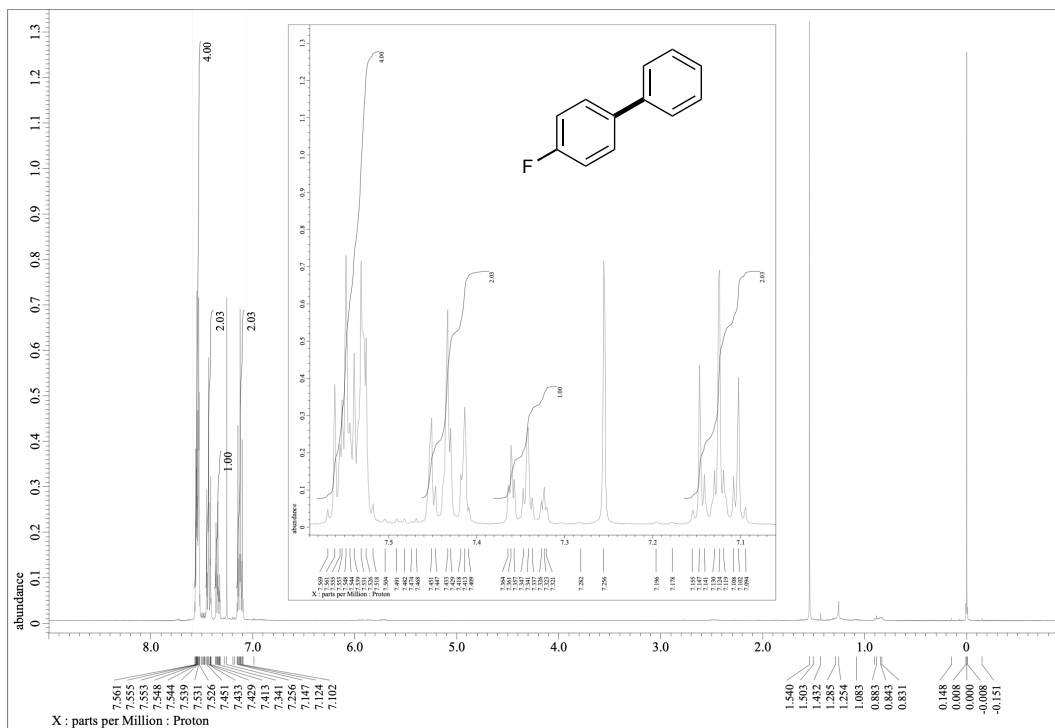
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **S2** (DMSO-*d*₆)



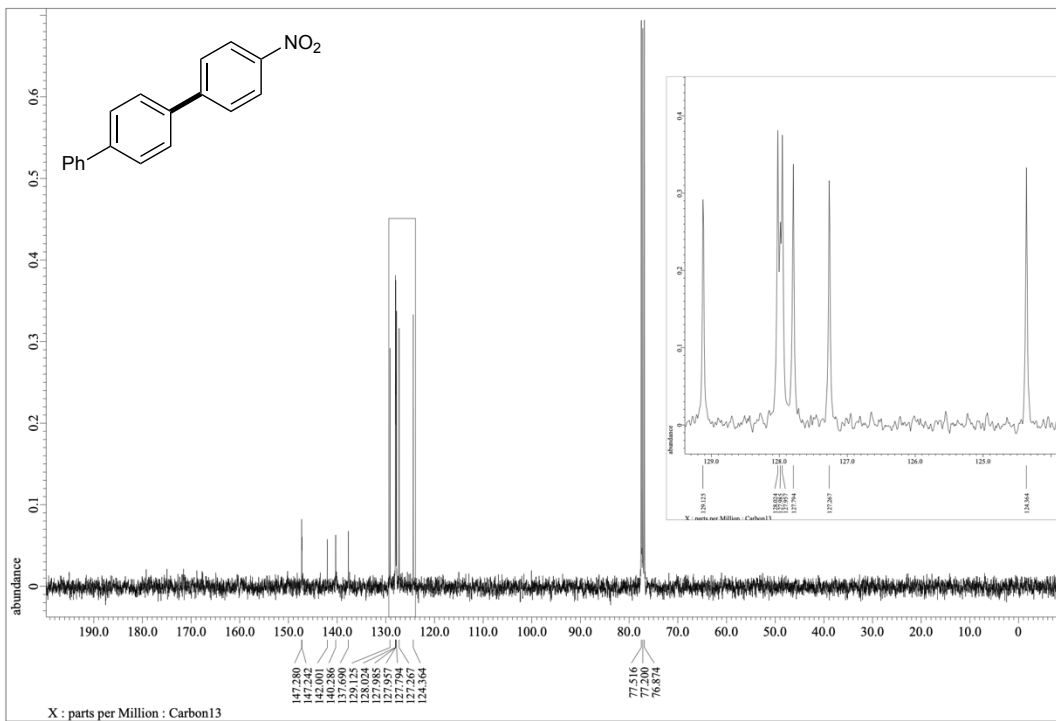
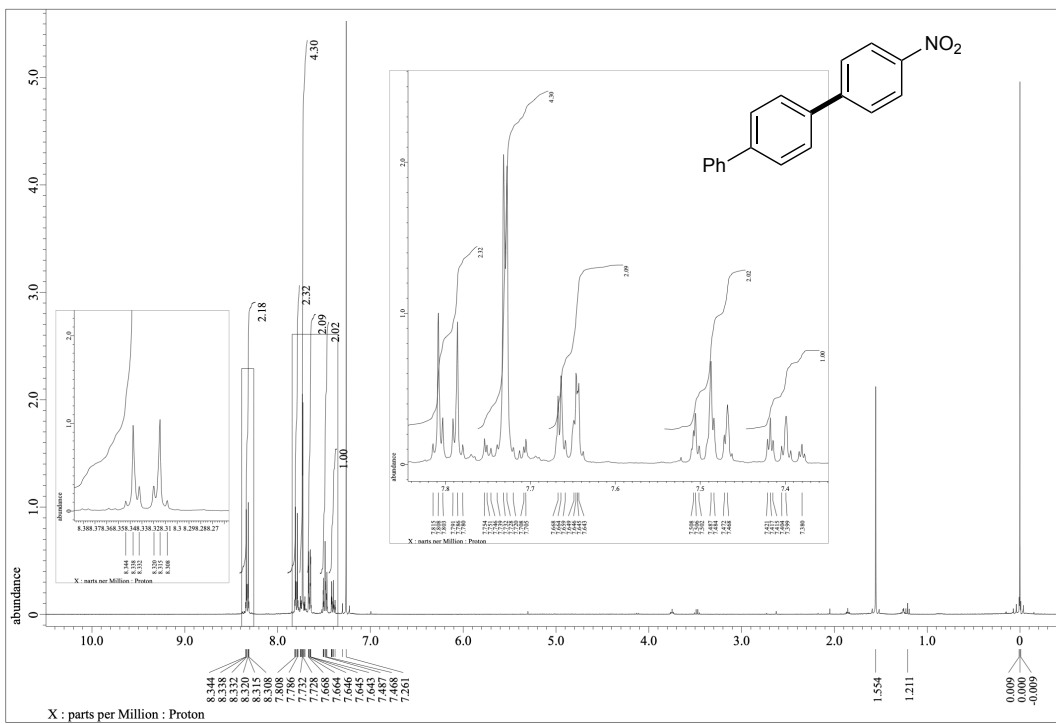
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **S3** ($\text{DMSO}-d_6$)



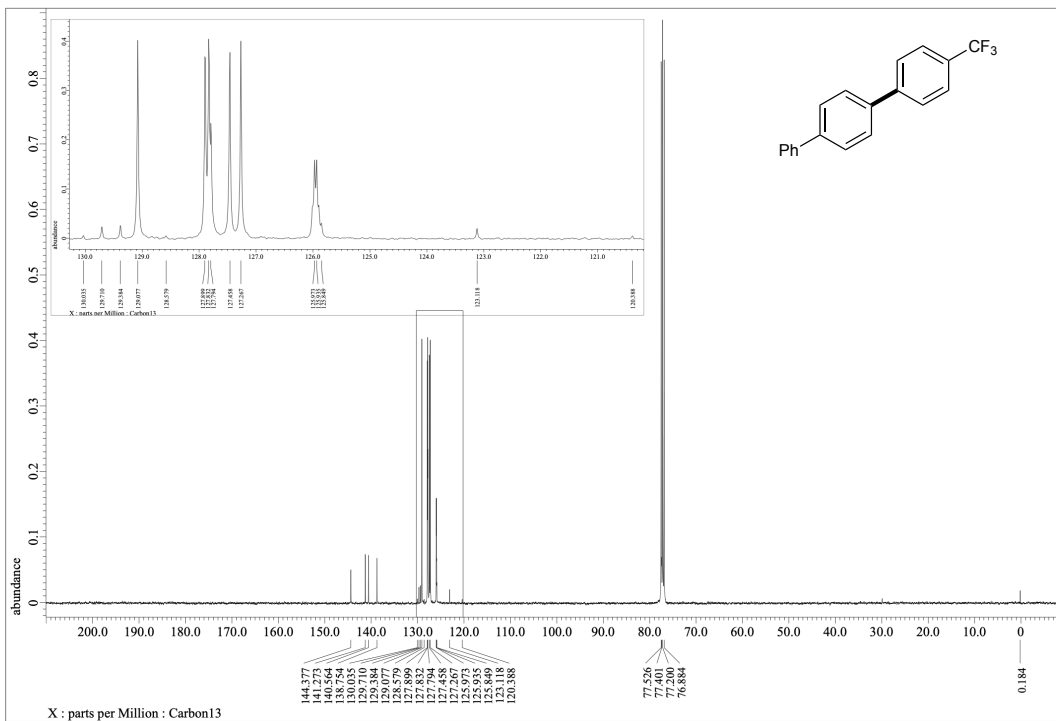
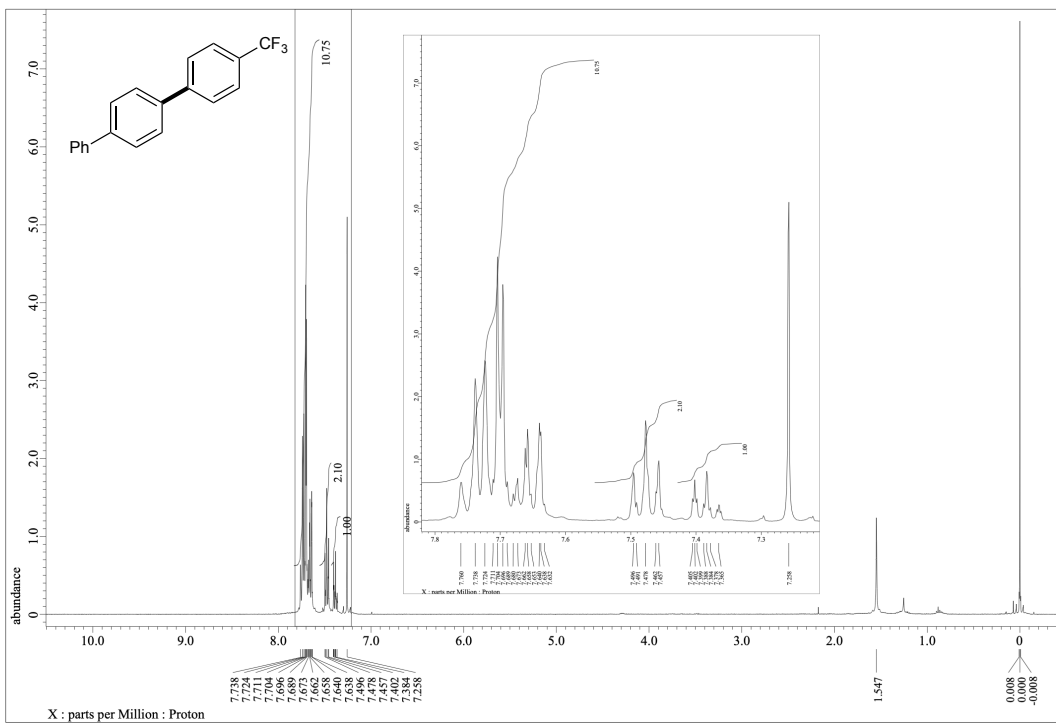
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3** (CDCl_3)



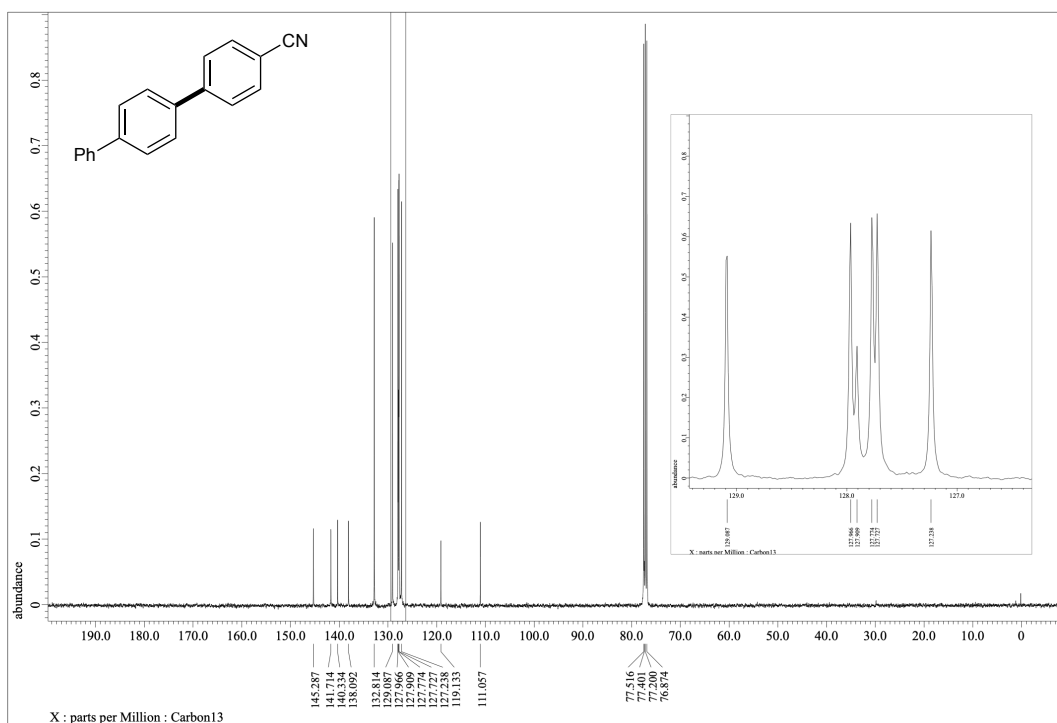
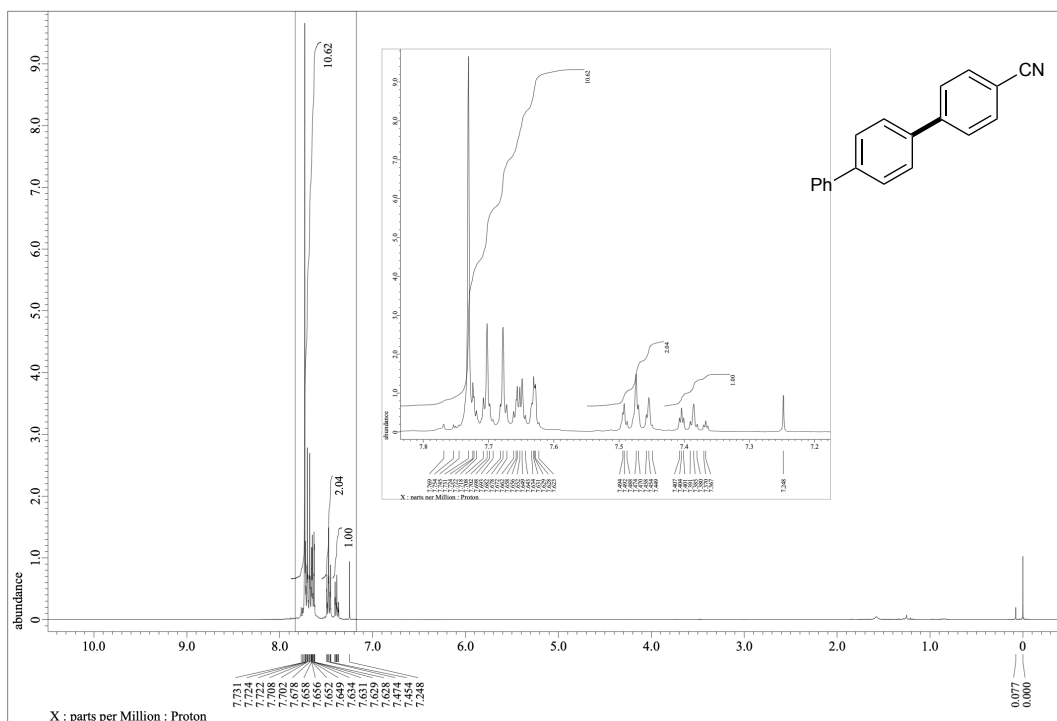
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **7** (CDCl₃)



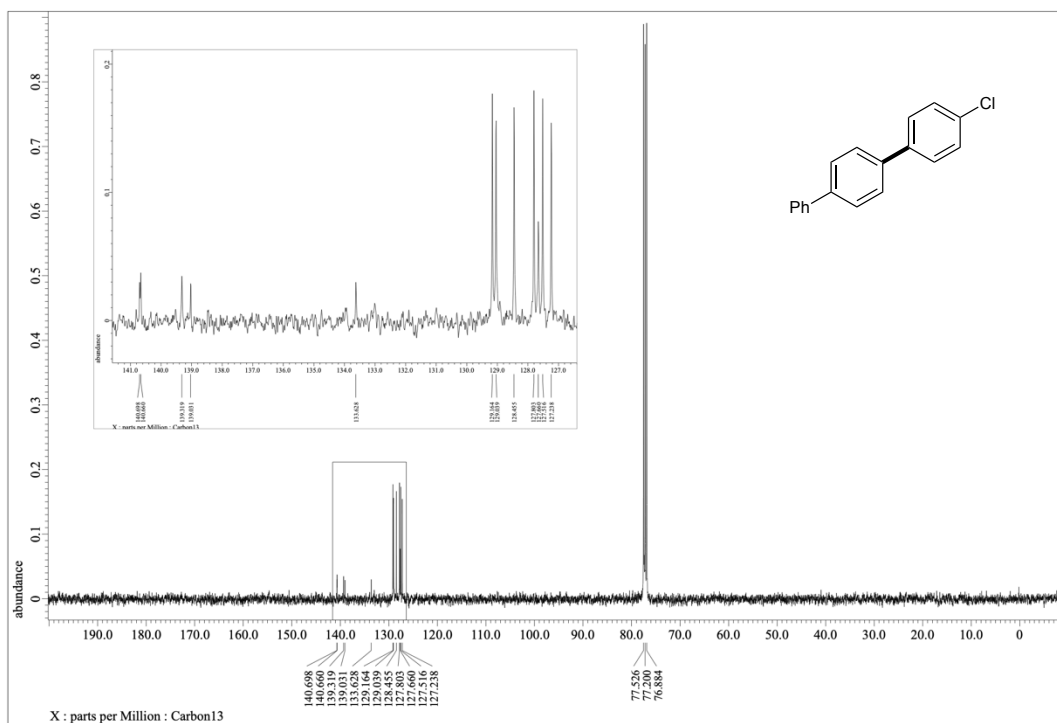
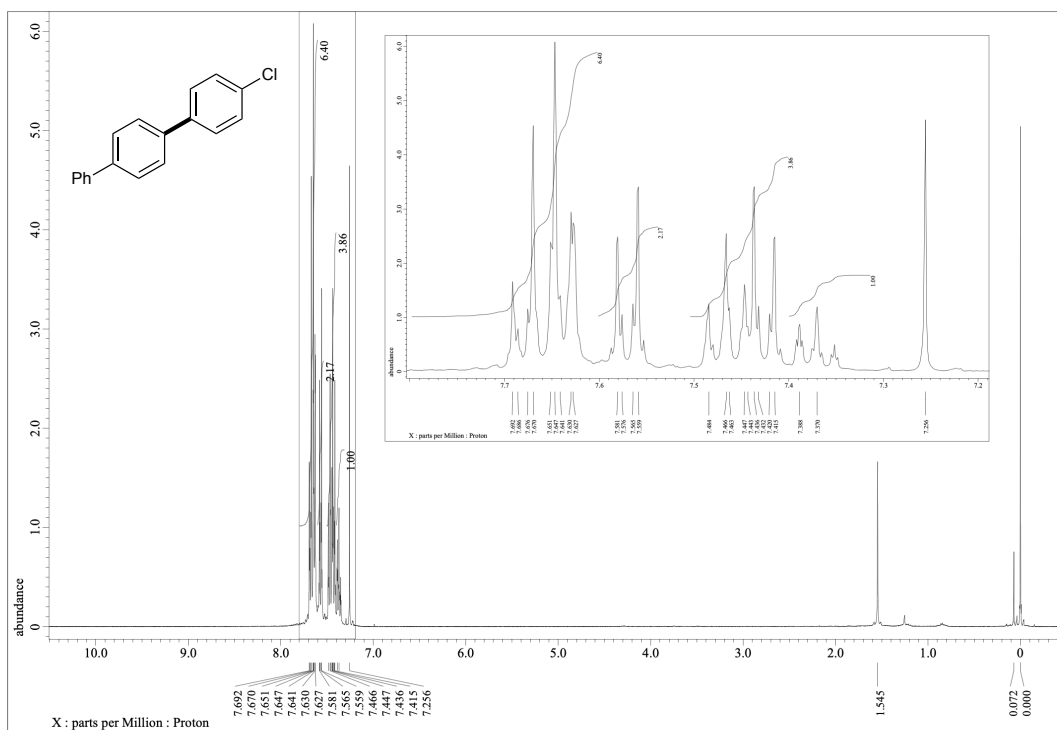
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **8** (CDCl₃)



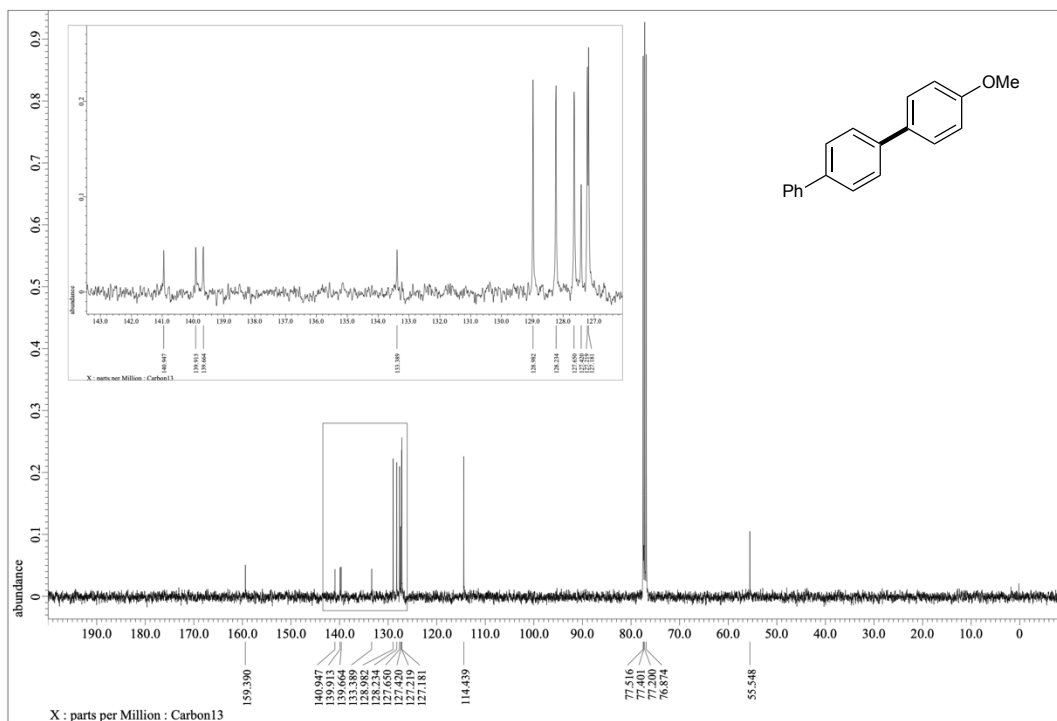
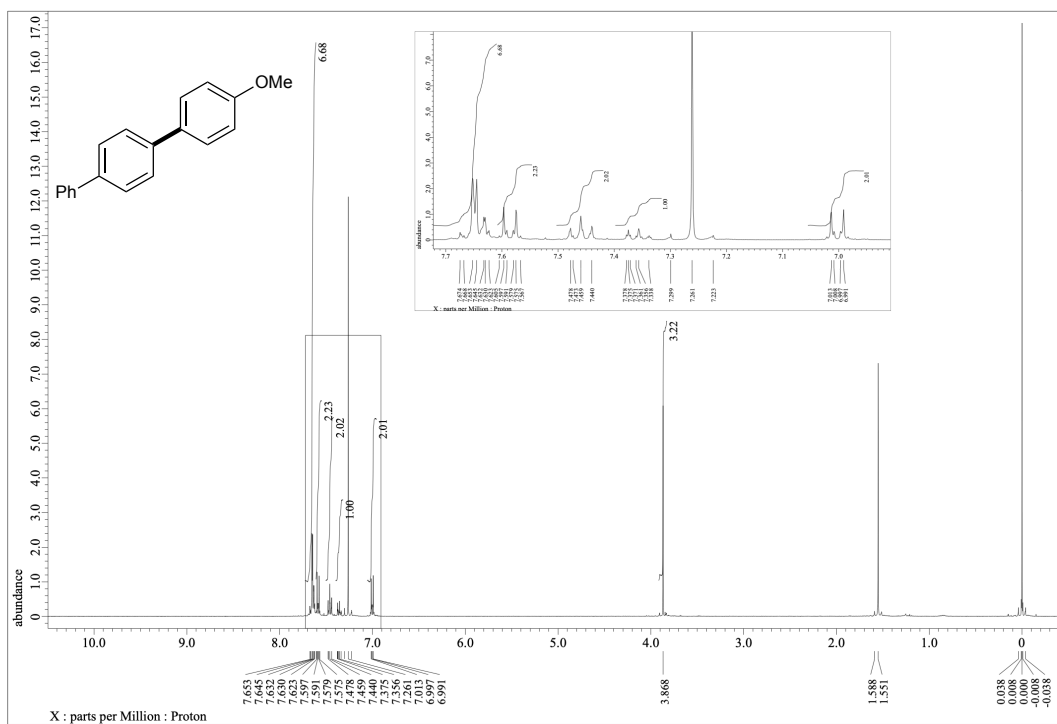
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **9** (CDCl_3)



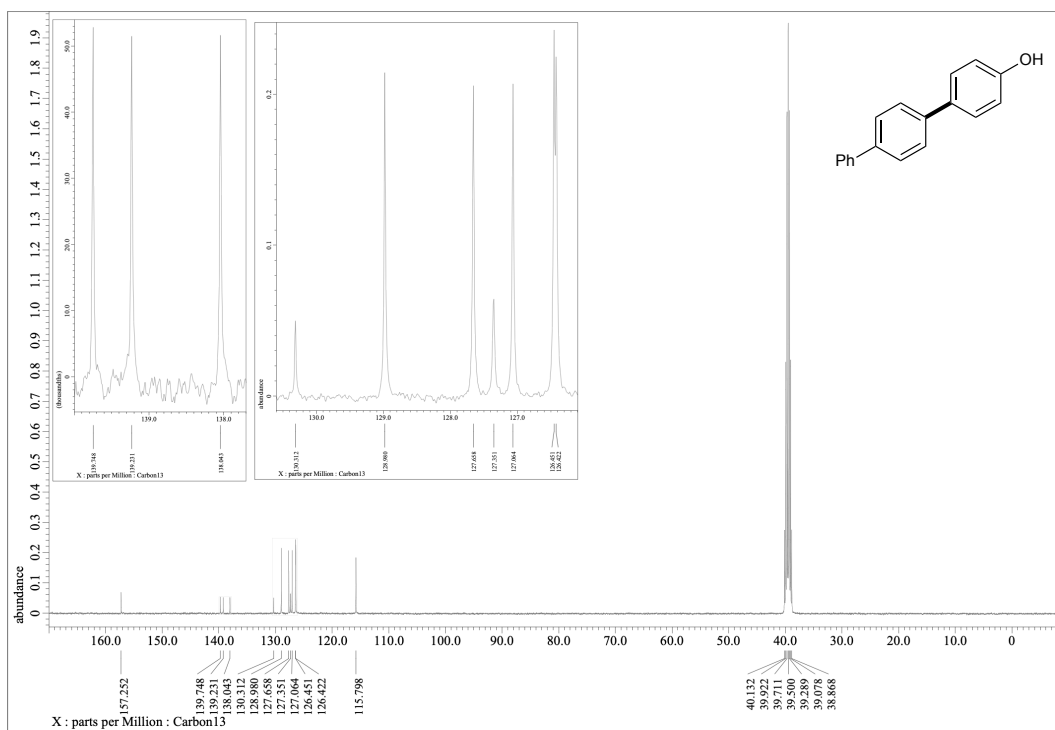
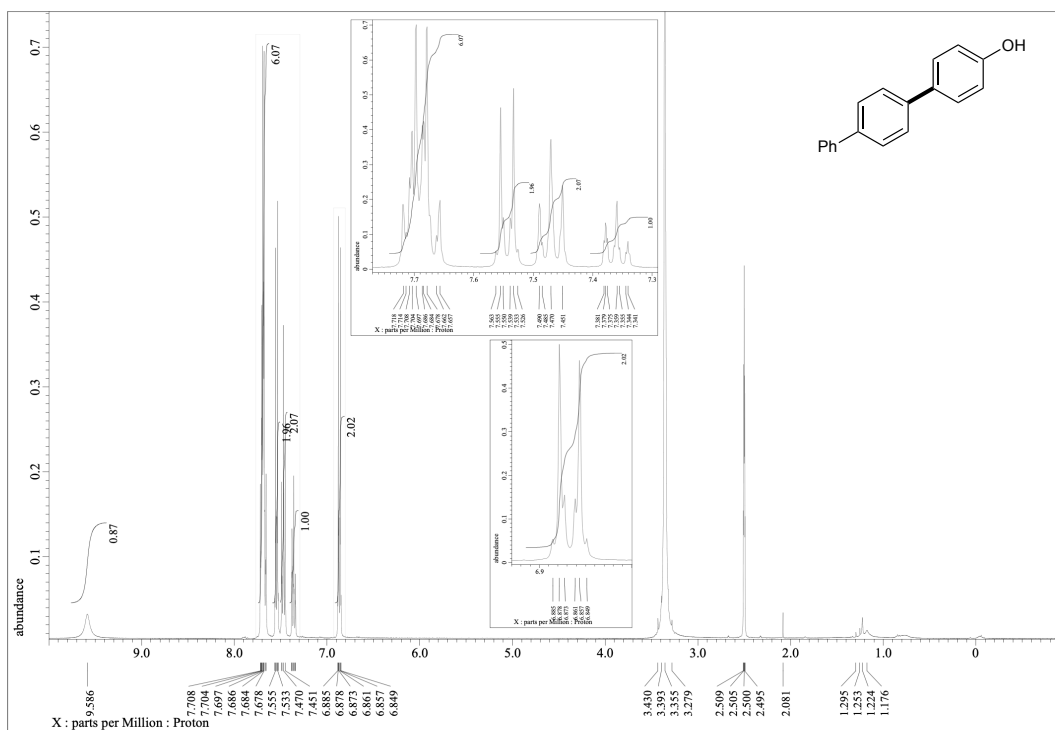
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **10** (CDCl_3)



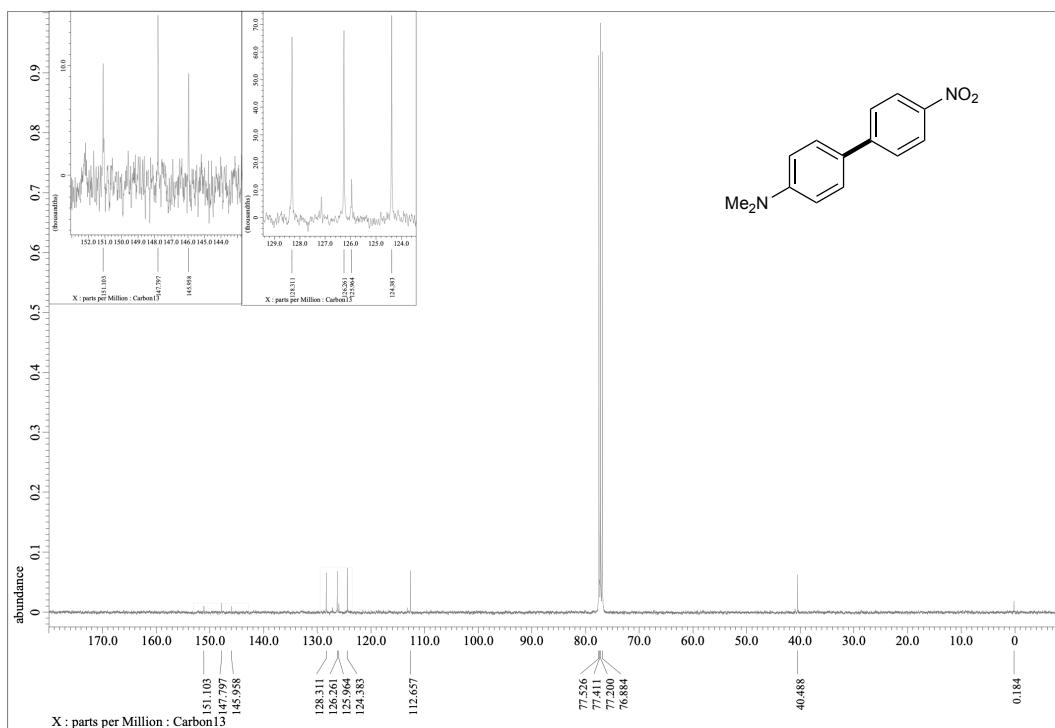
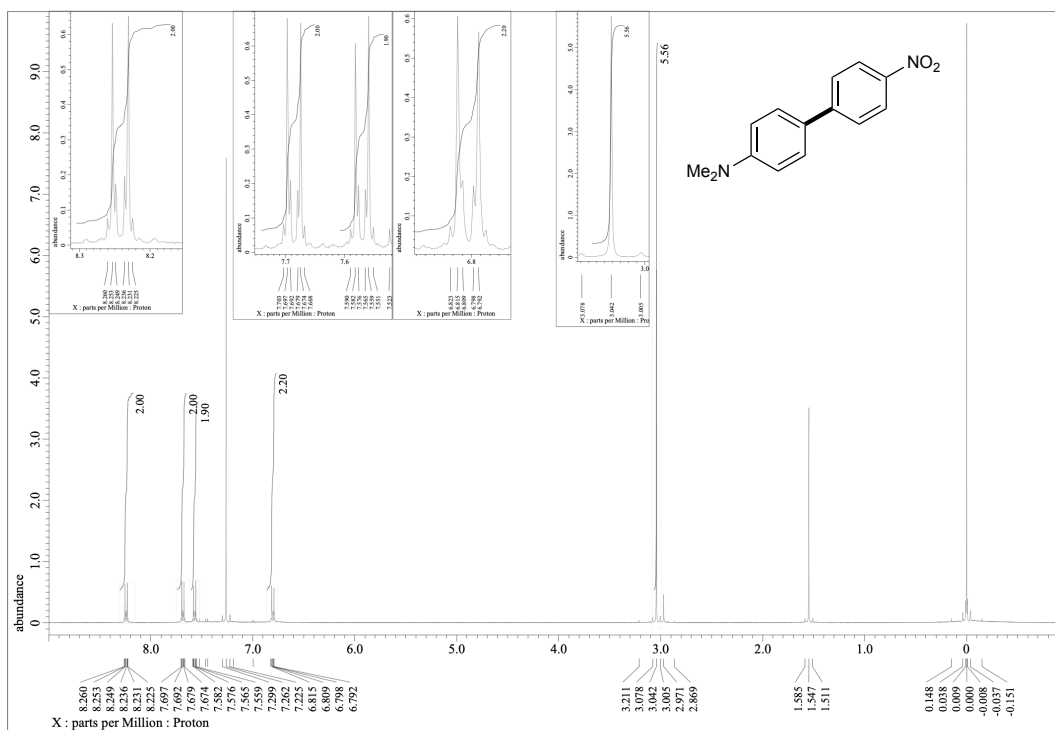
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **11** (CDCl_3)



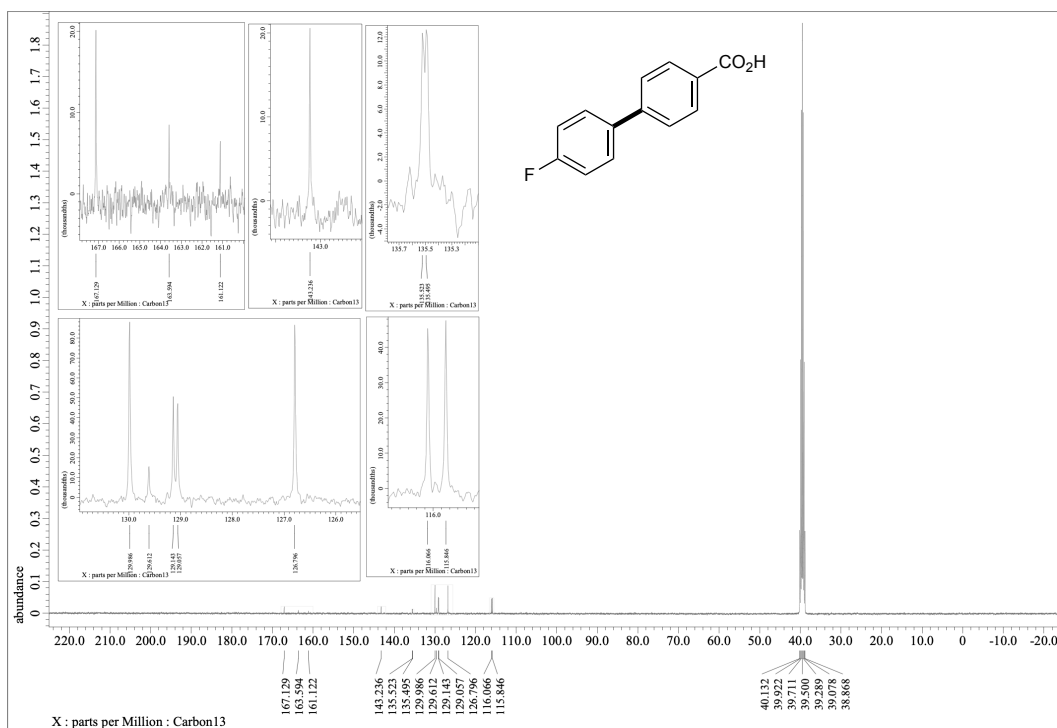
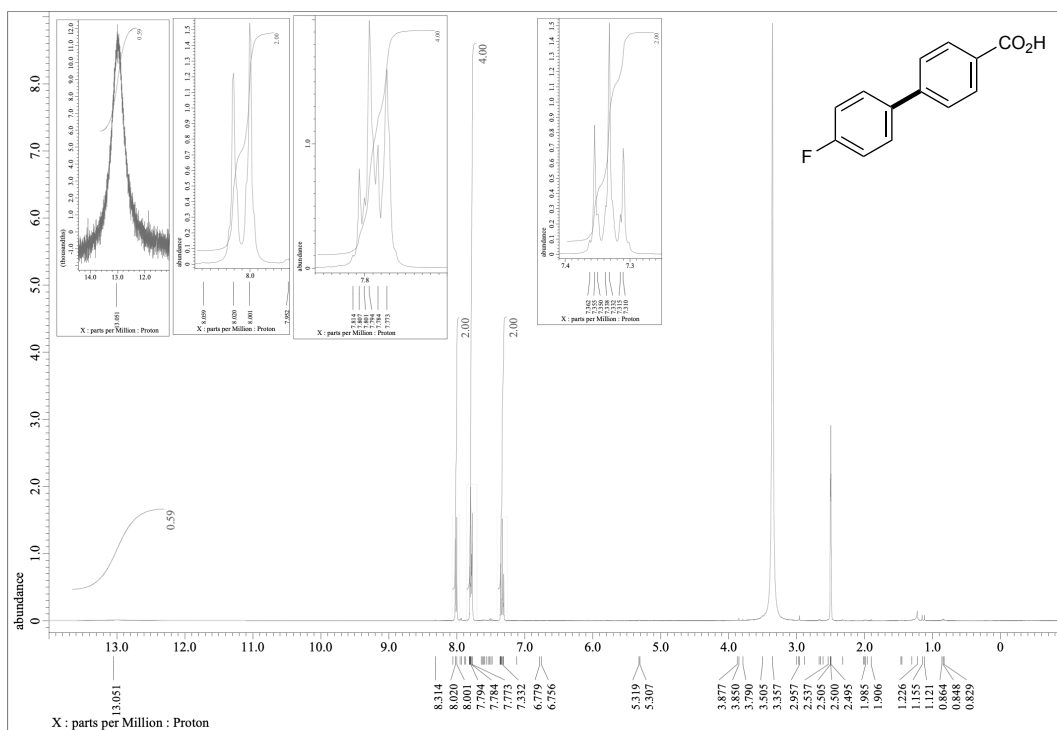
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **12** (DMSO- d_6)



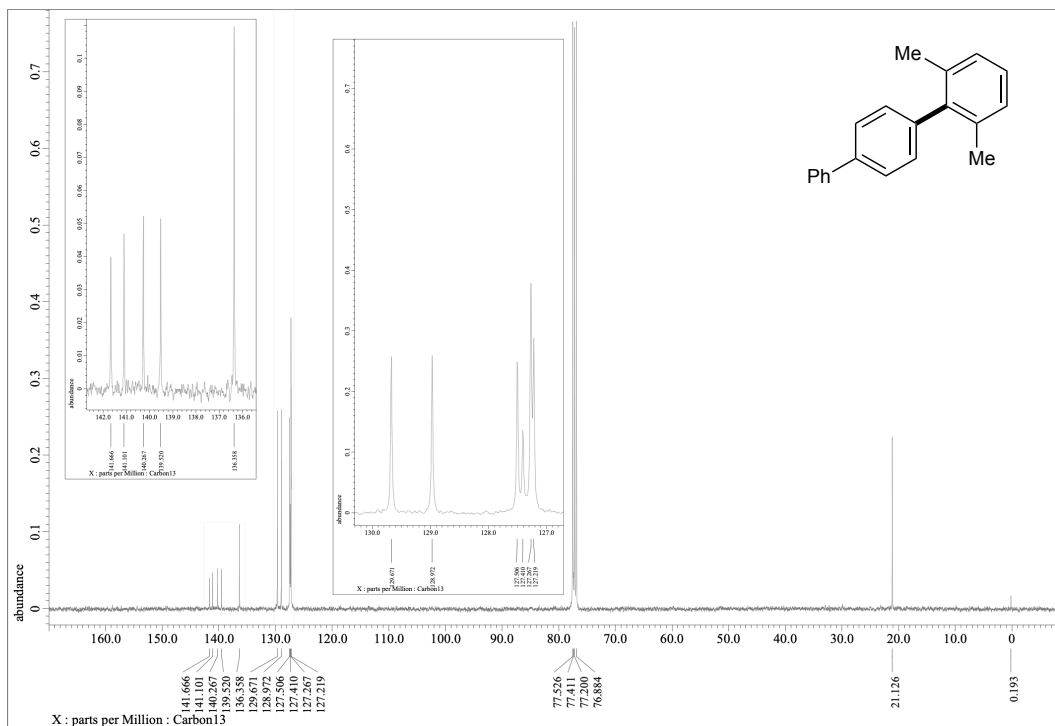
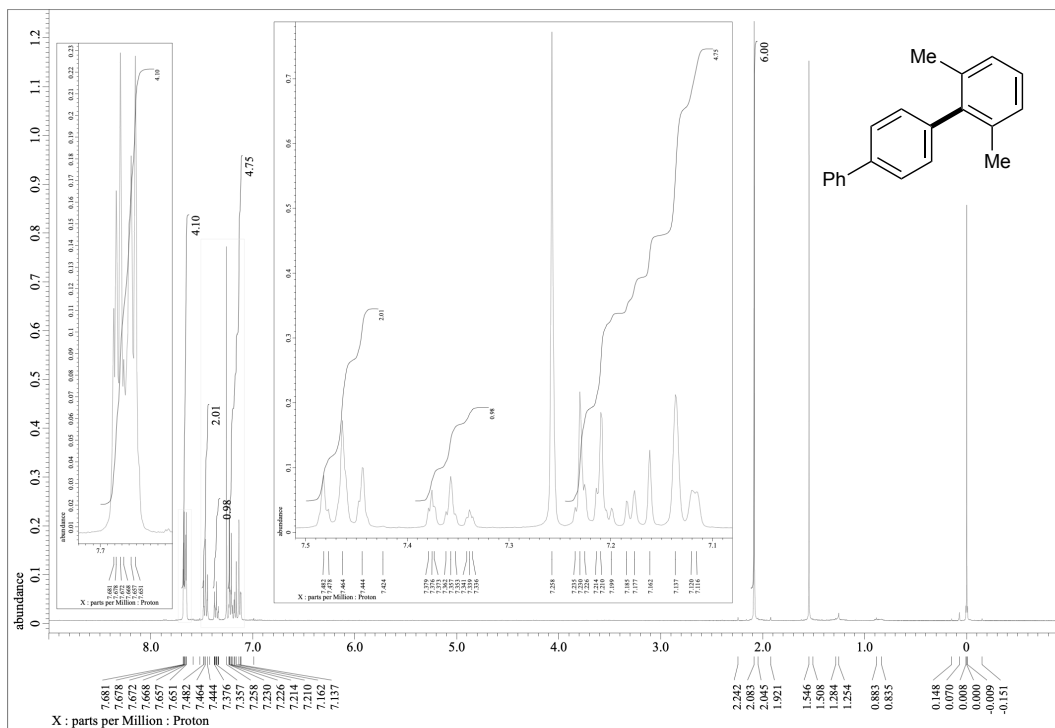
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **13** (CDCl_3)

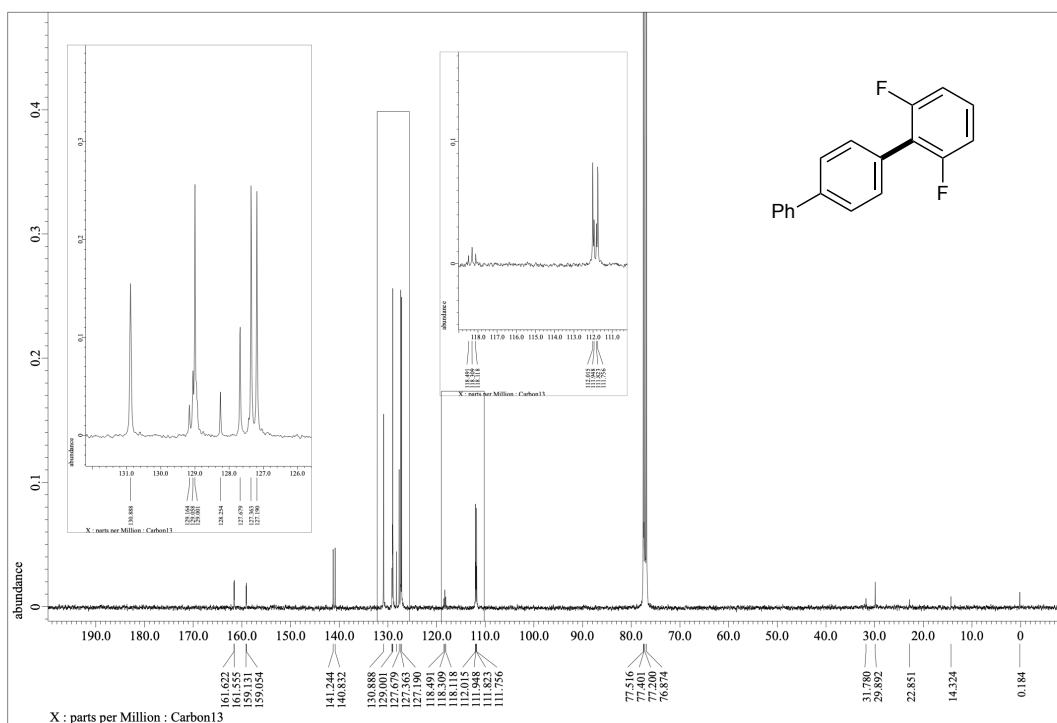
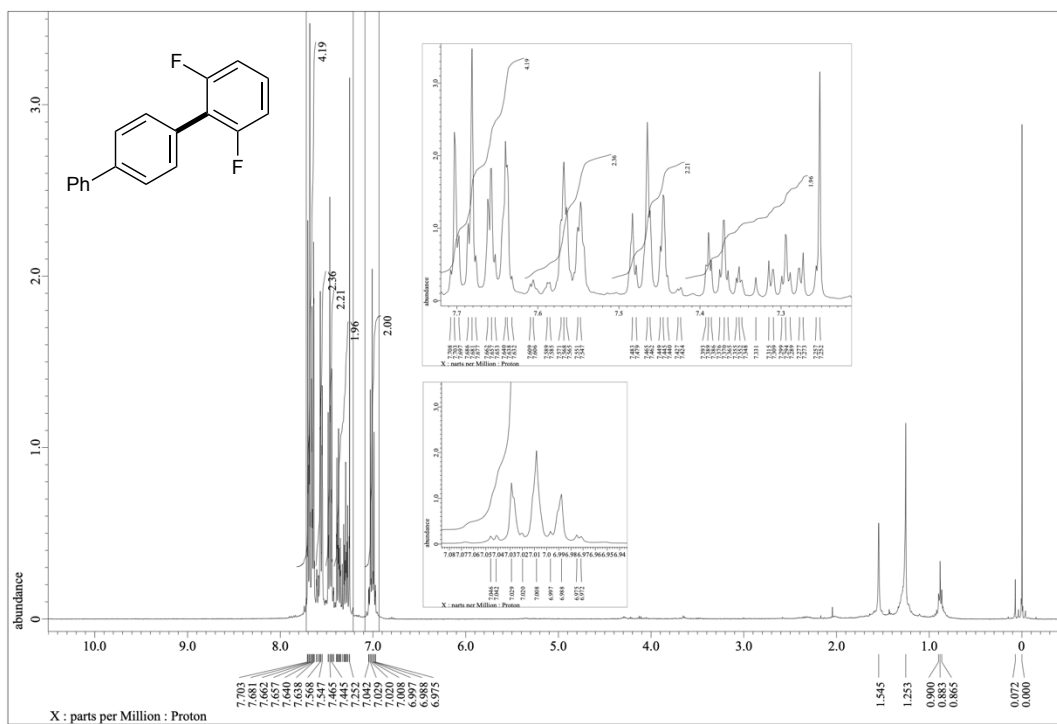


^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **14** (DMSO- d_6)

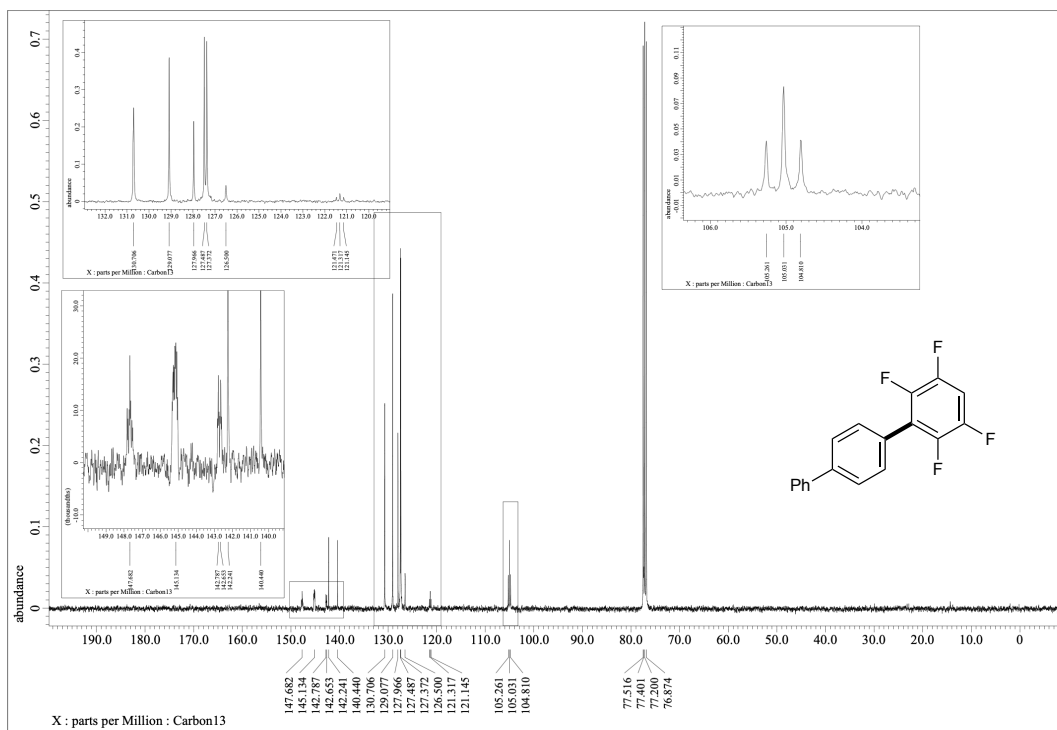
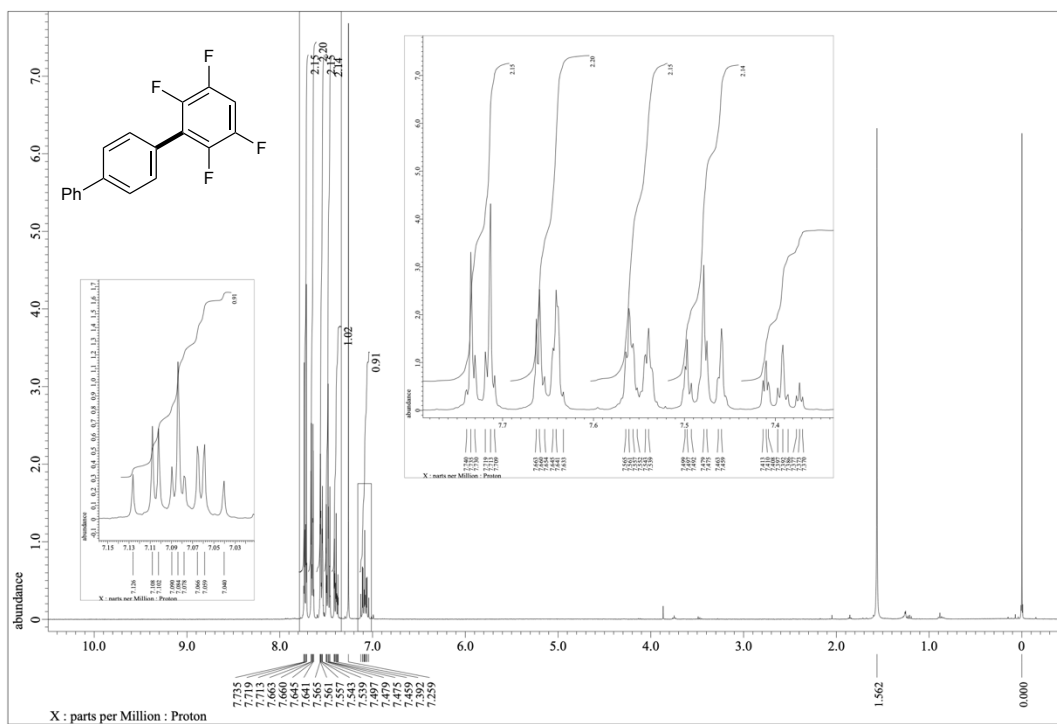


^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **15** (CDCl_3)

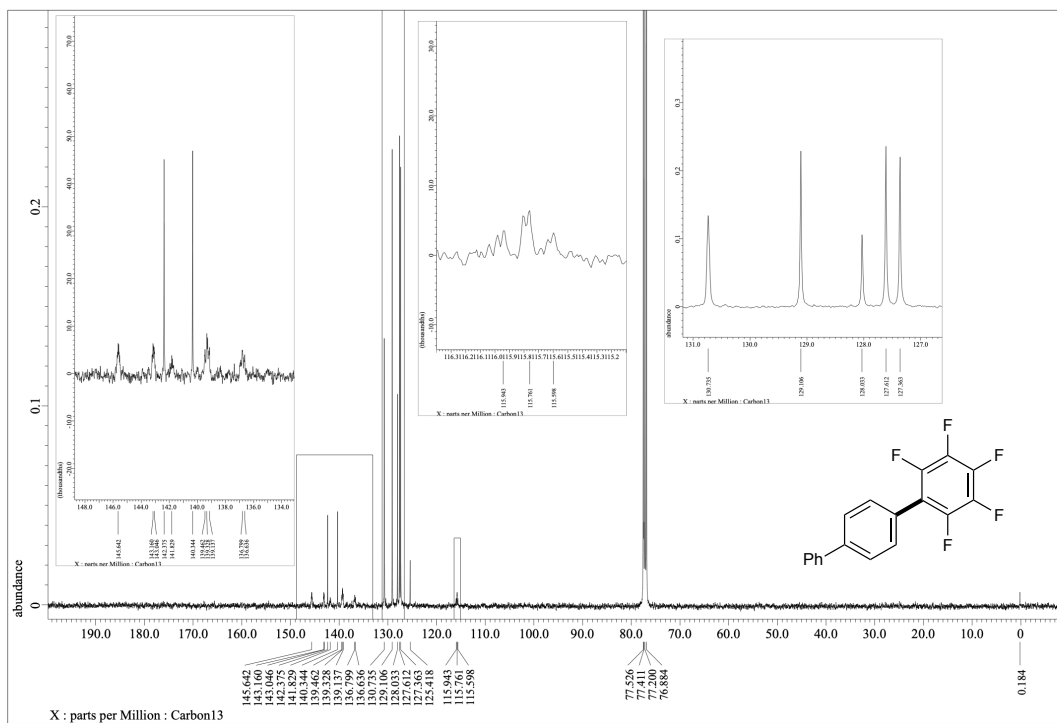
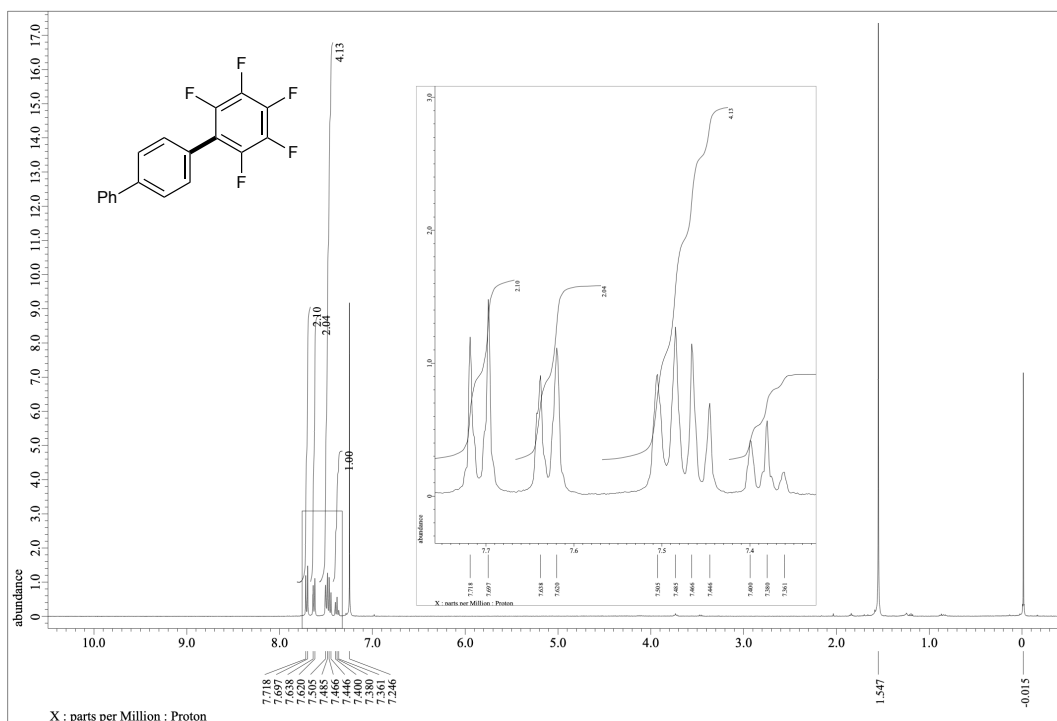


¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **16** (CDCl₃)

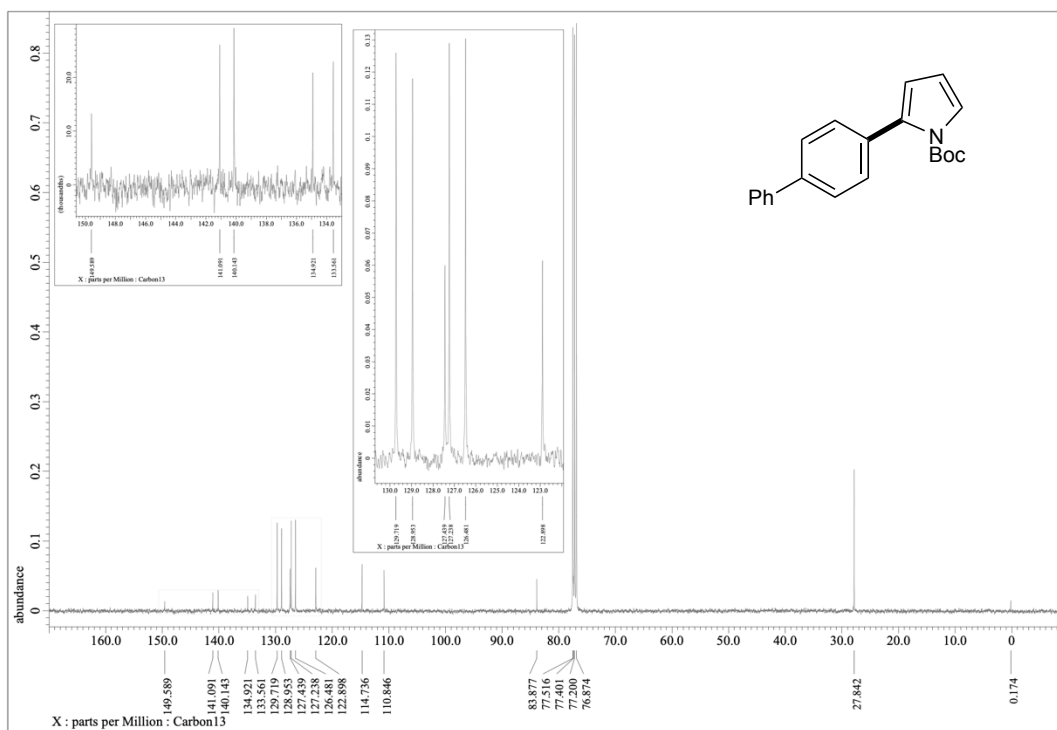
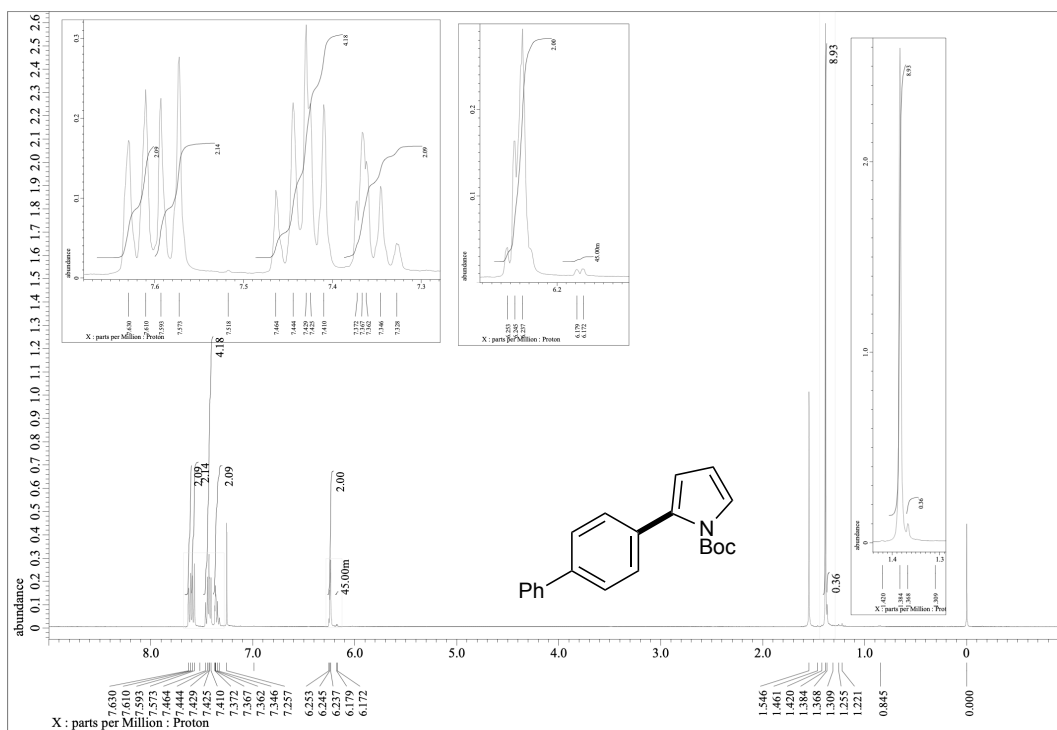
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **17** (CDCl₃)



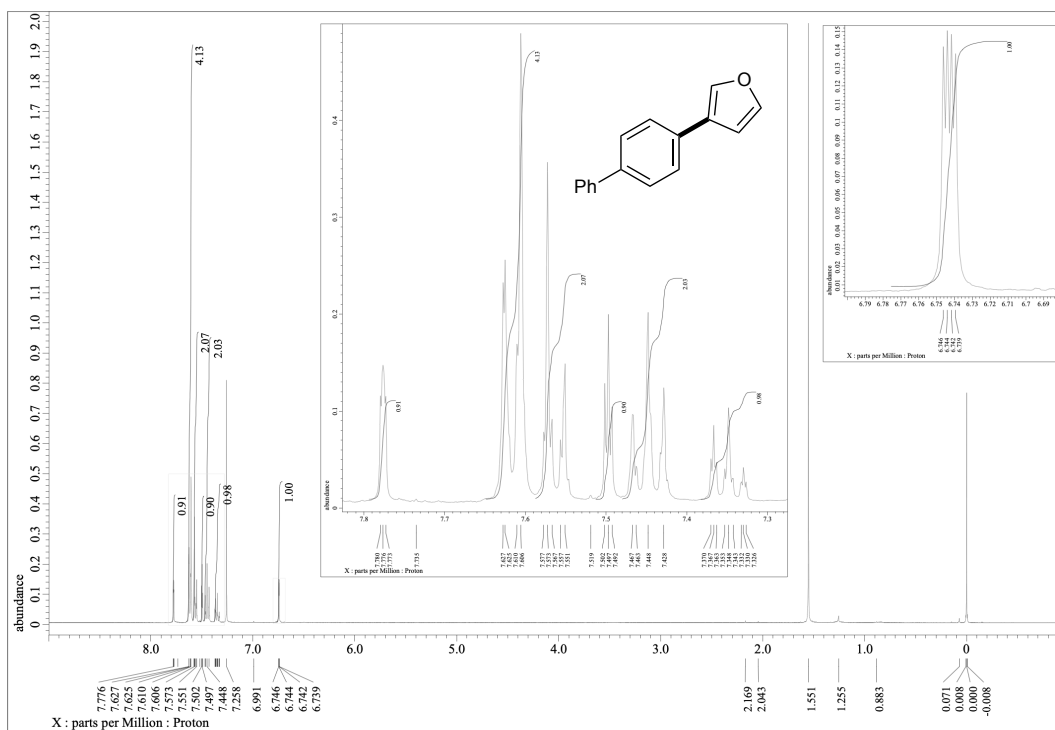
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **18** (CDCl_3)



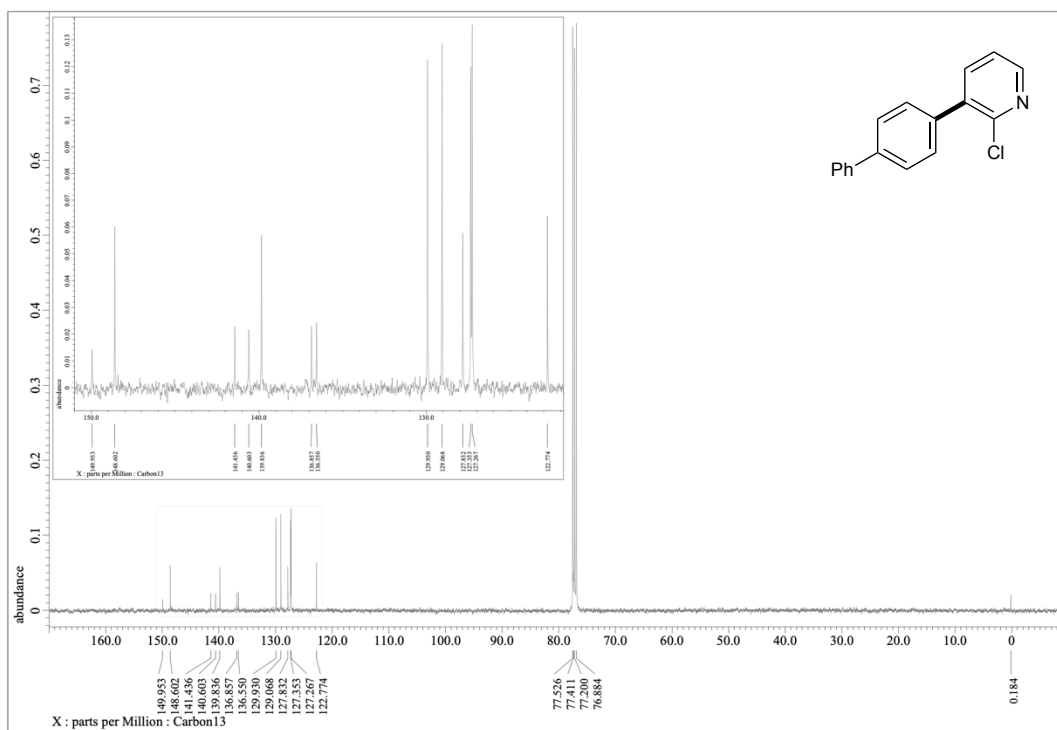
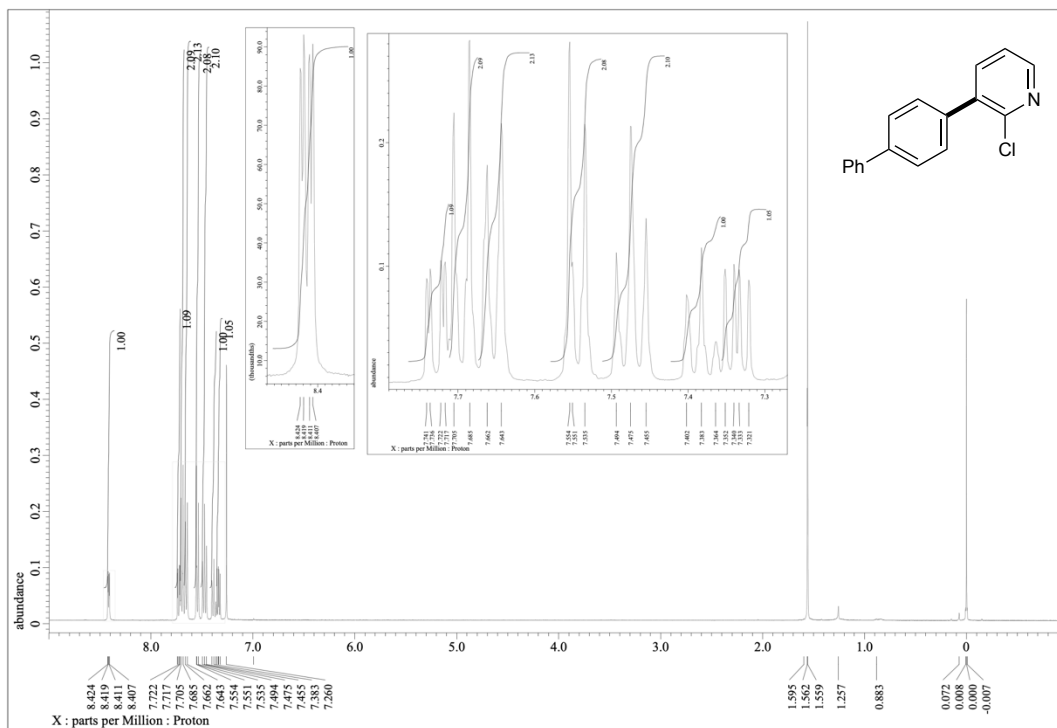
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **19** (CDCl₃)



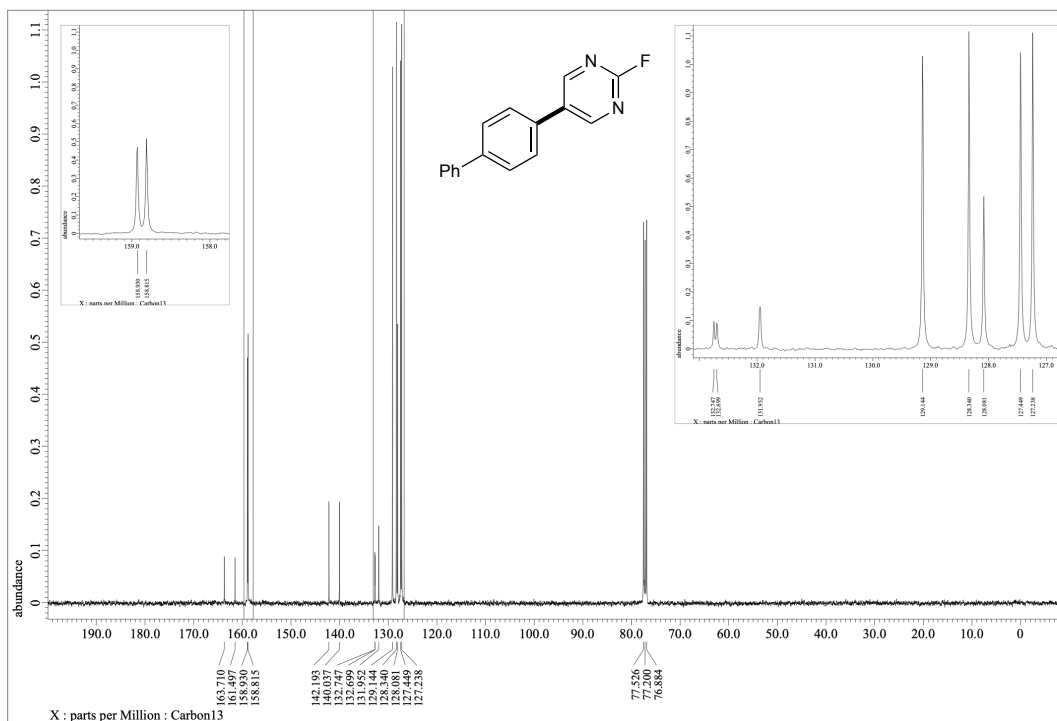
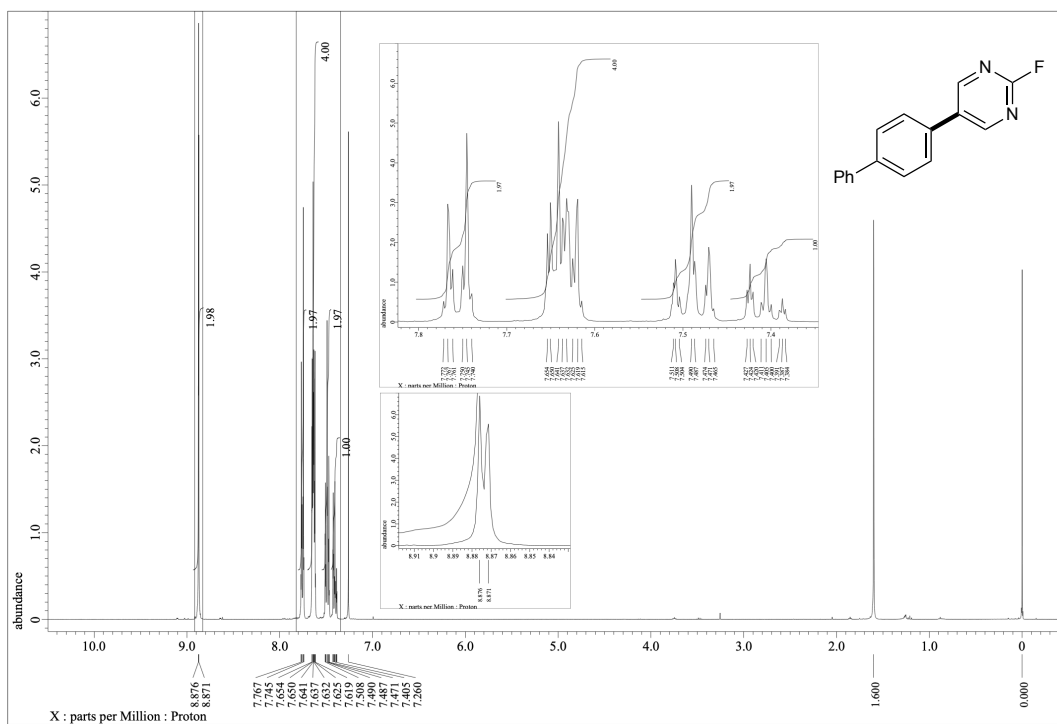
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **20** (CDCl_3)



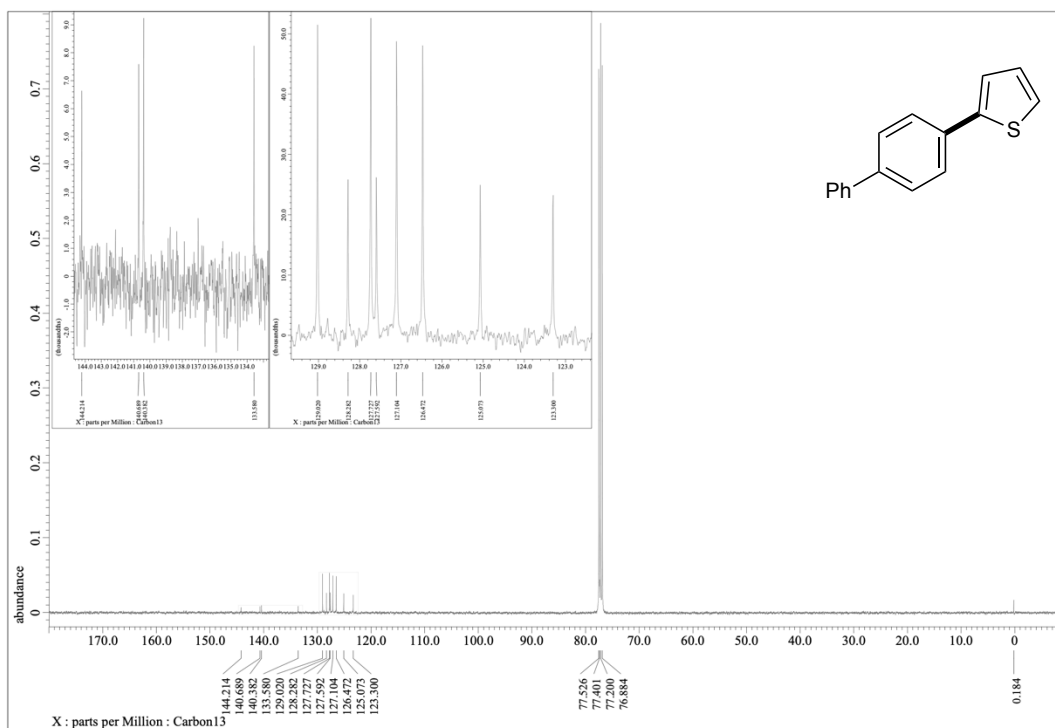
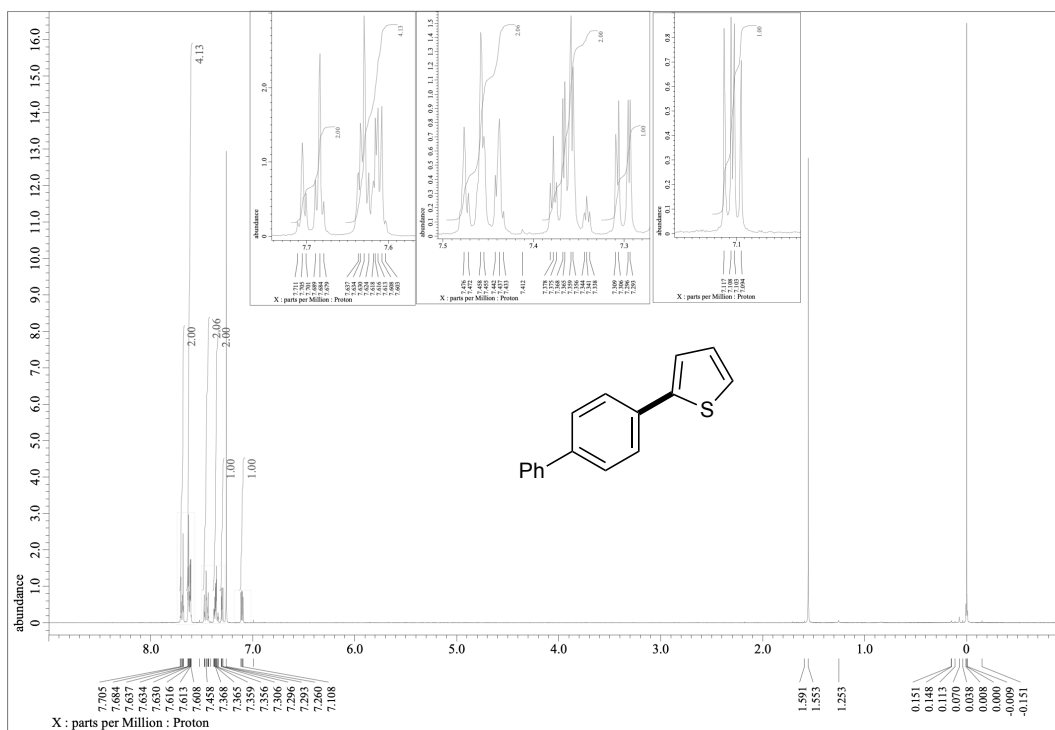
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **21** (CDCl₃)



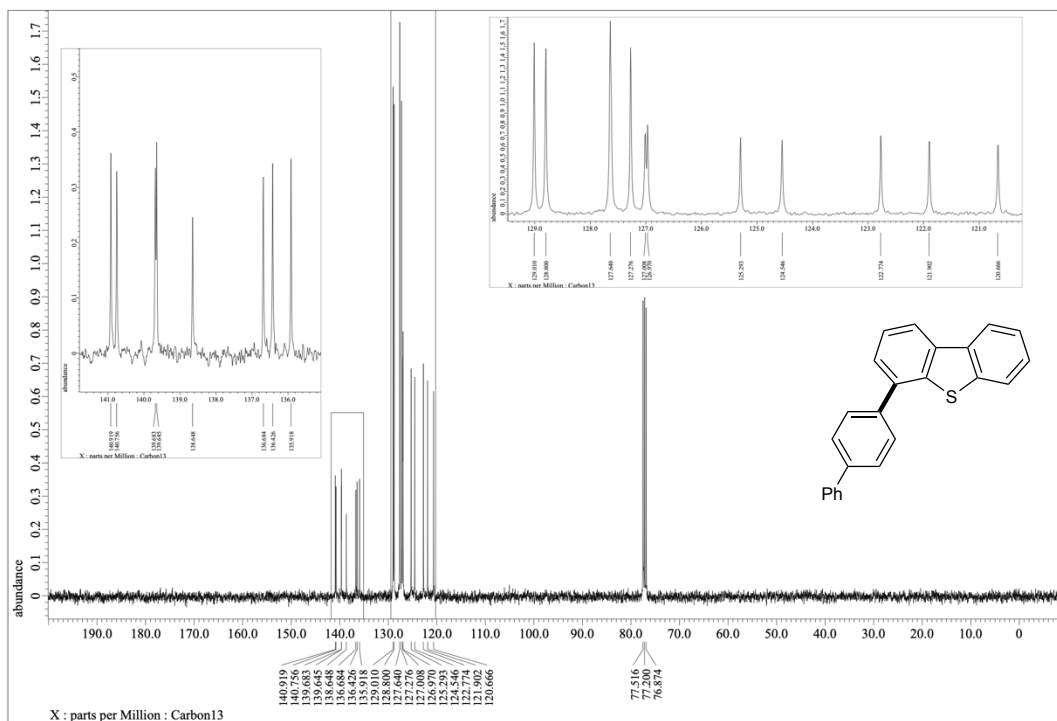
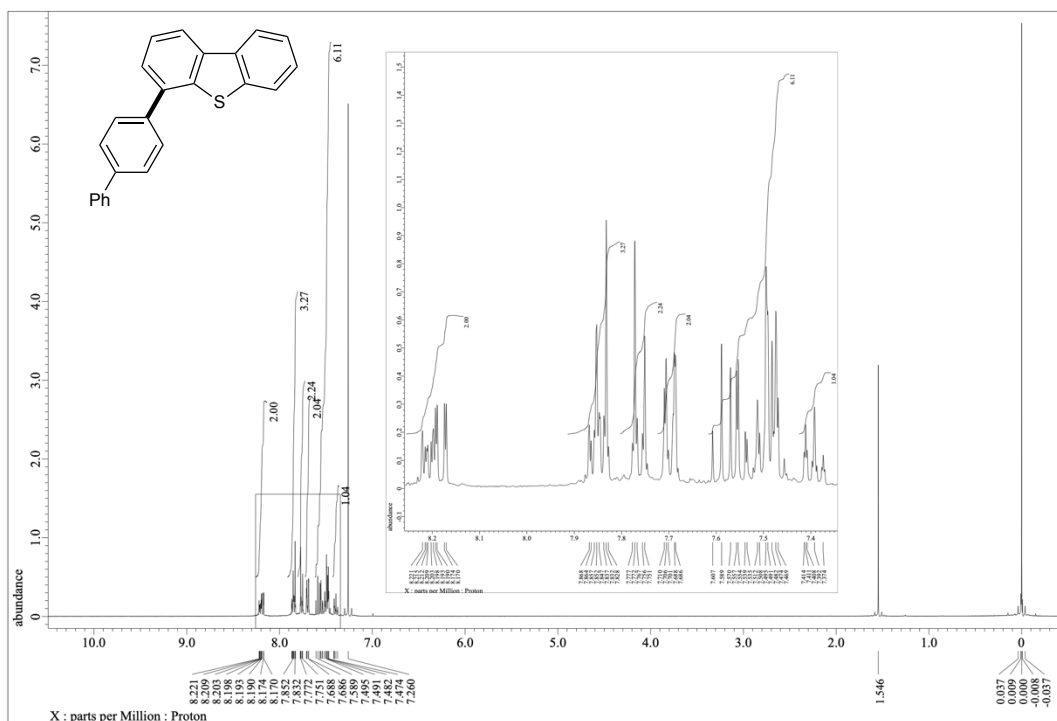
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **22** (CDCl_3)



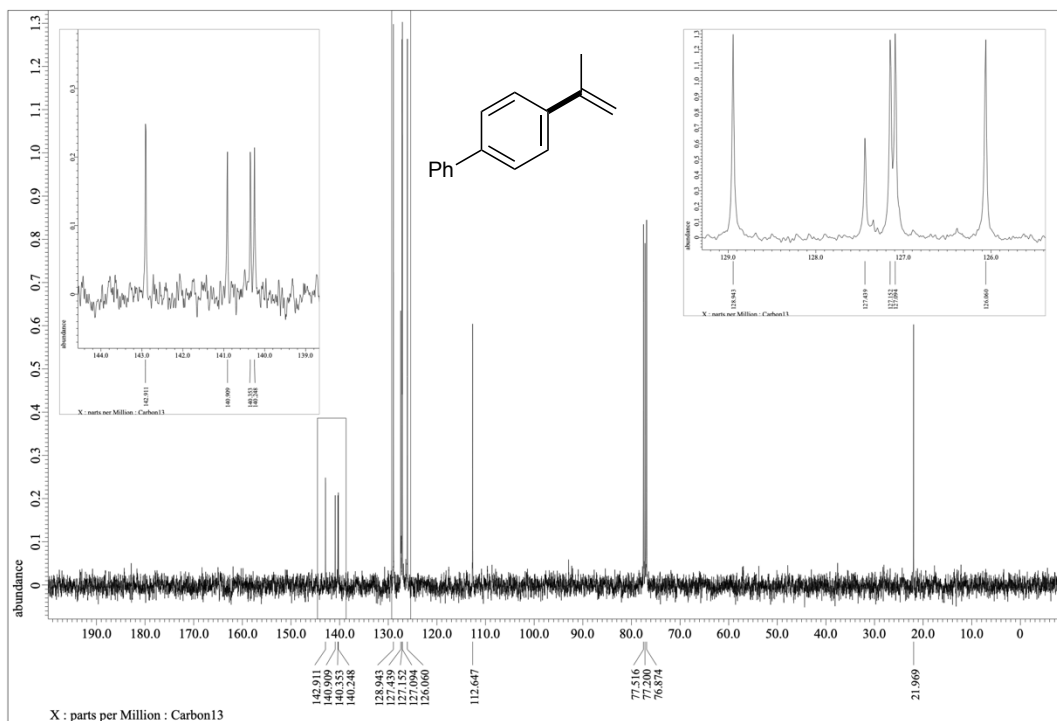
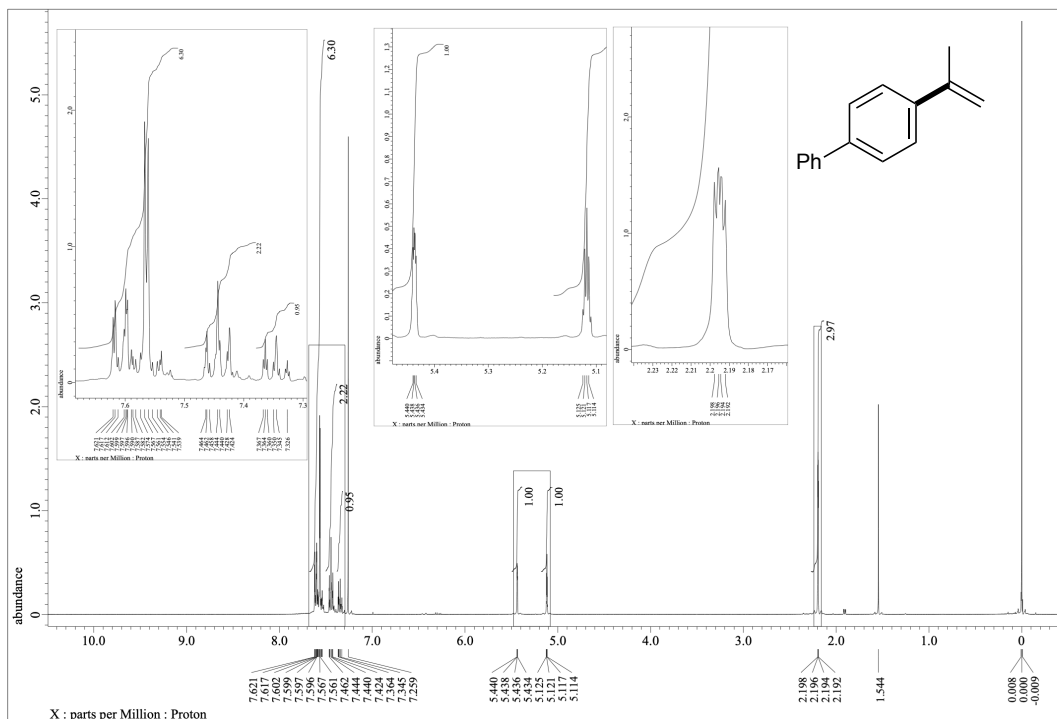
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **23** (CDCl_3)



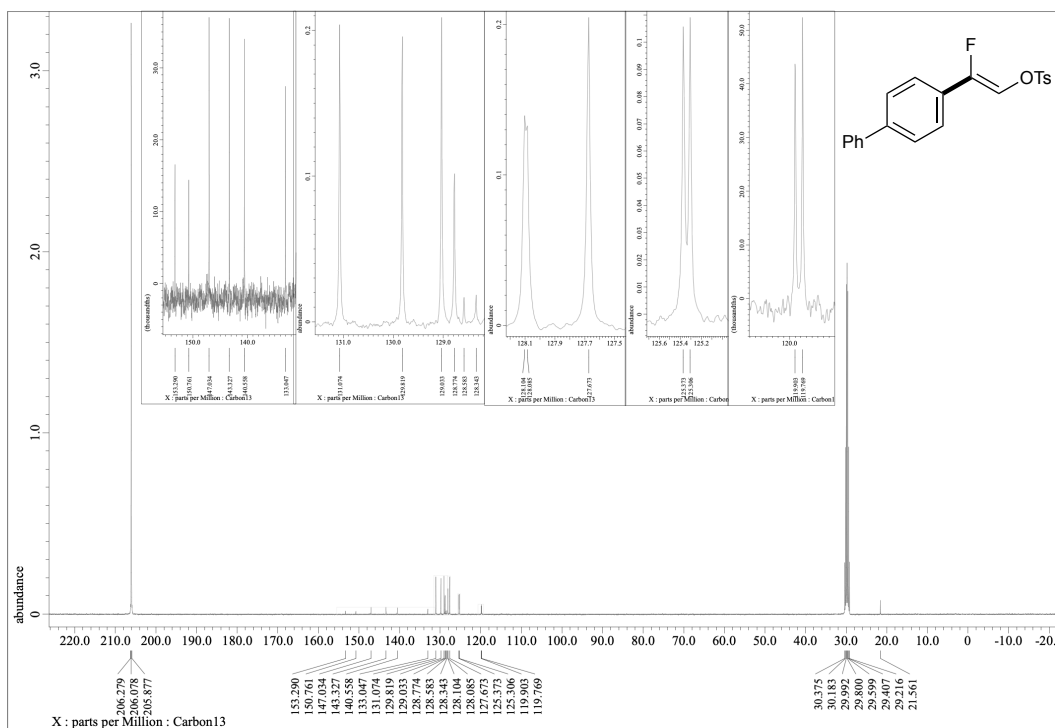
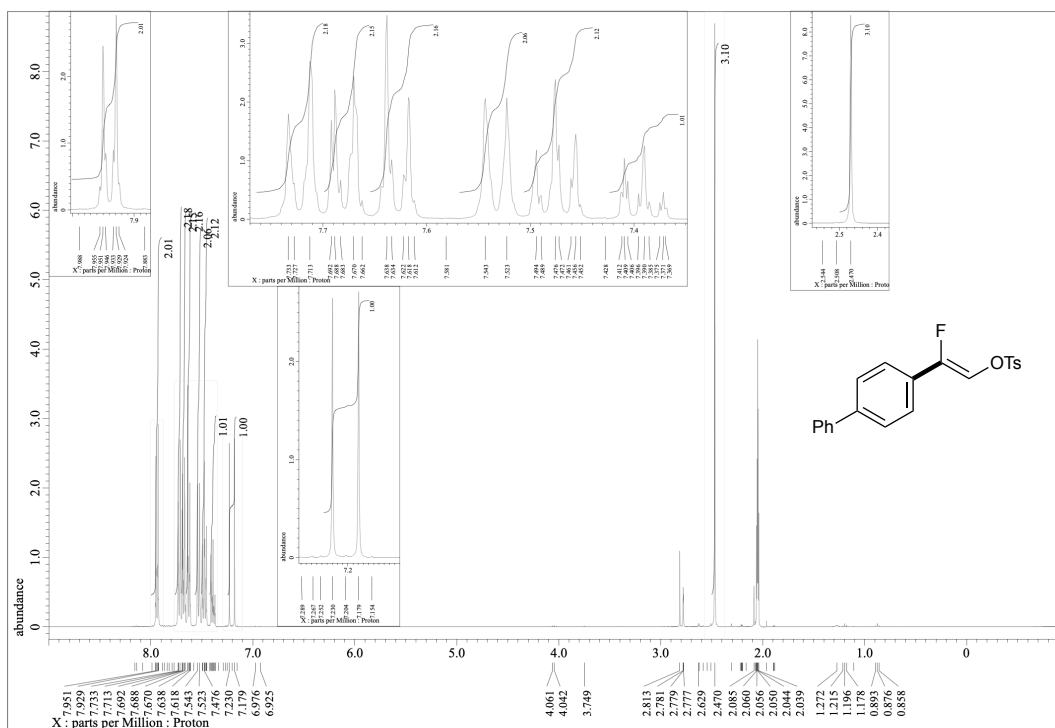
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **24** (CDCl_3)



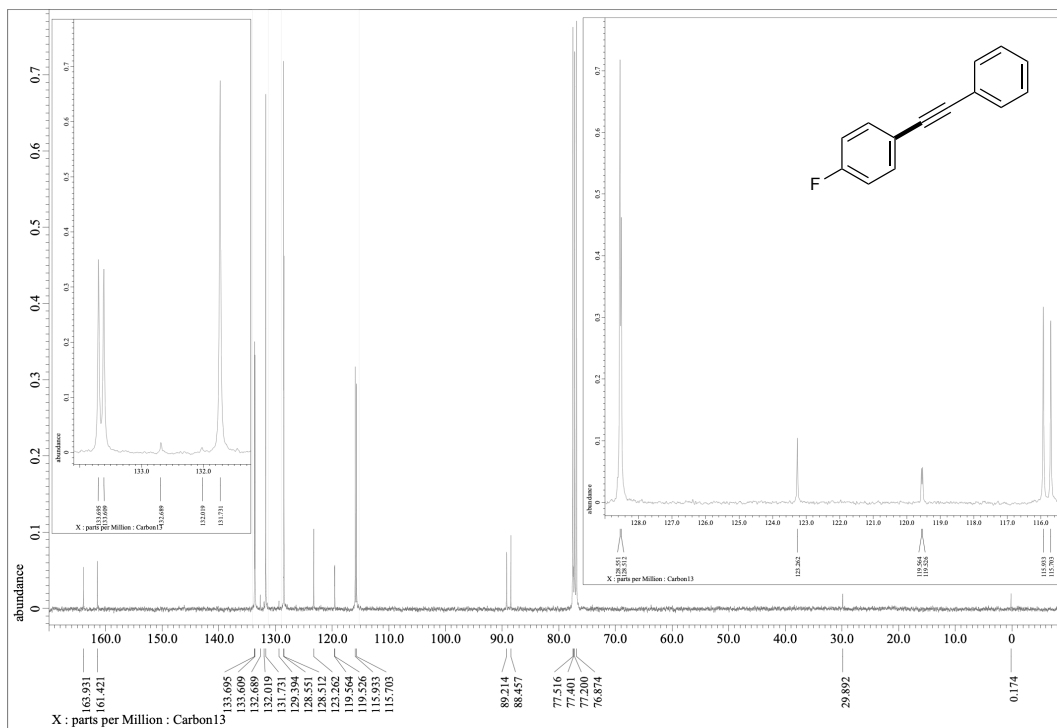
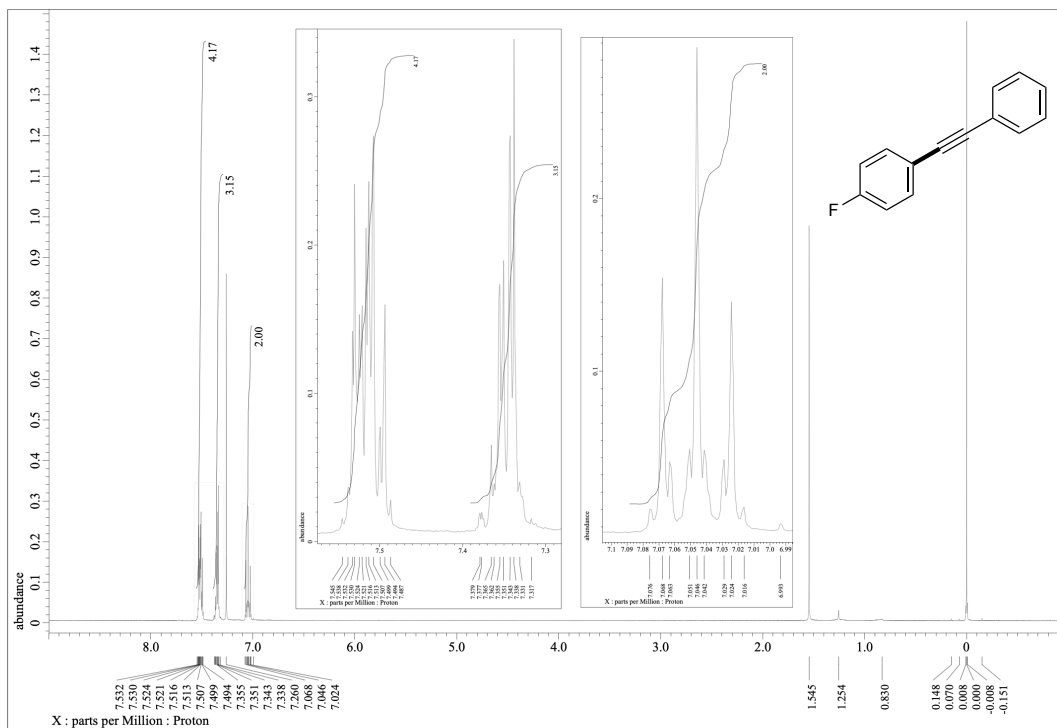
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **25** (CDCl_3)



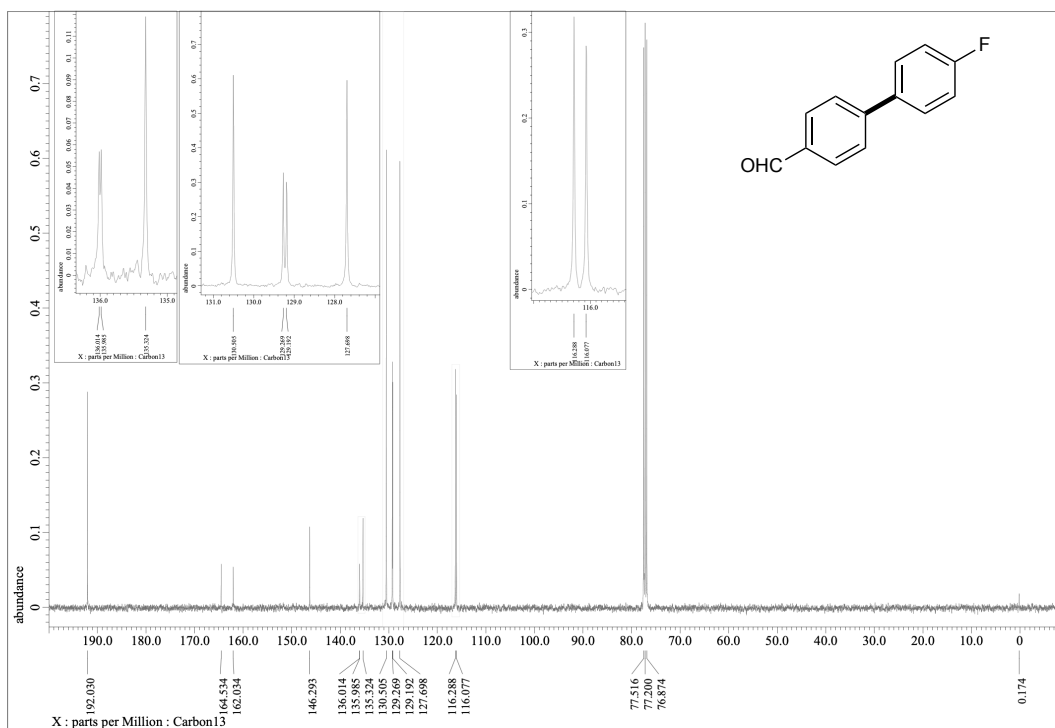
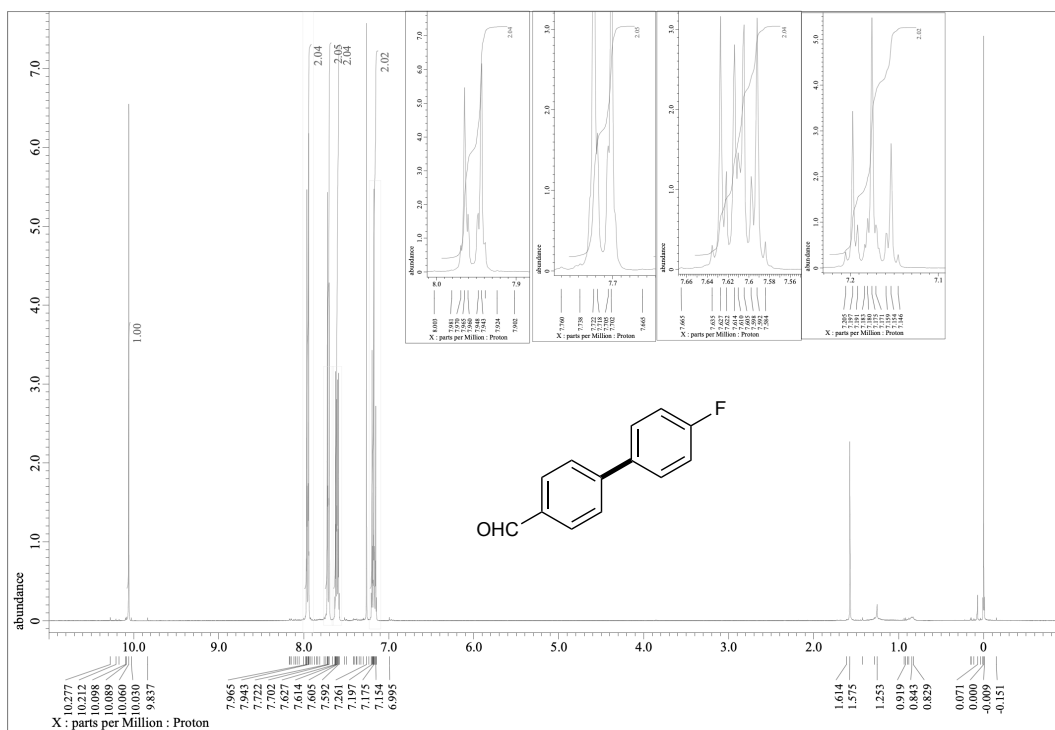
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **26** (acetone-*d*₆)



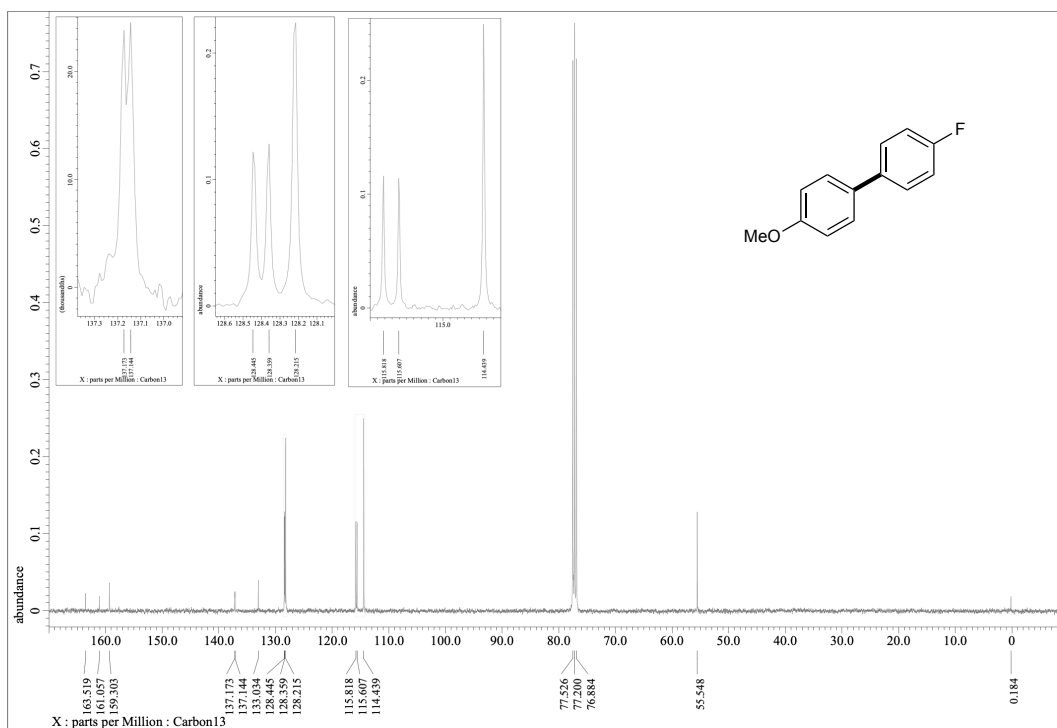
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **27** (CDCl_3)



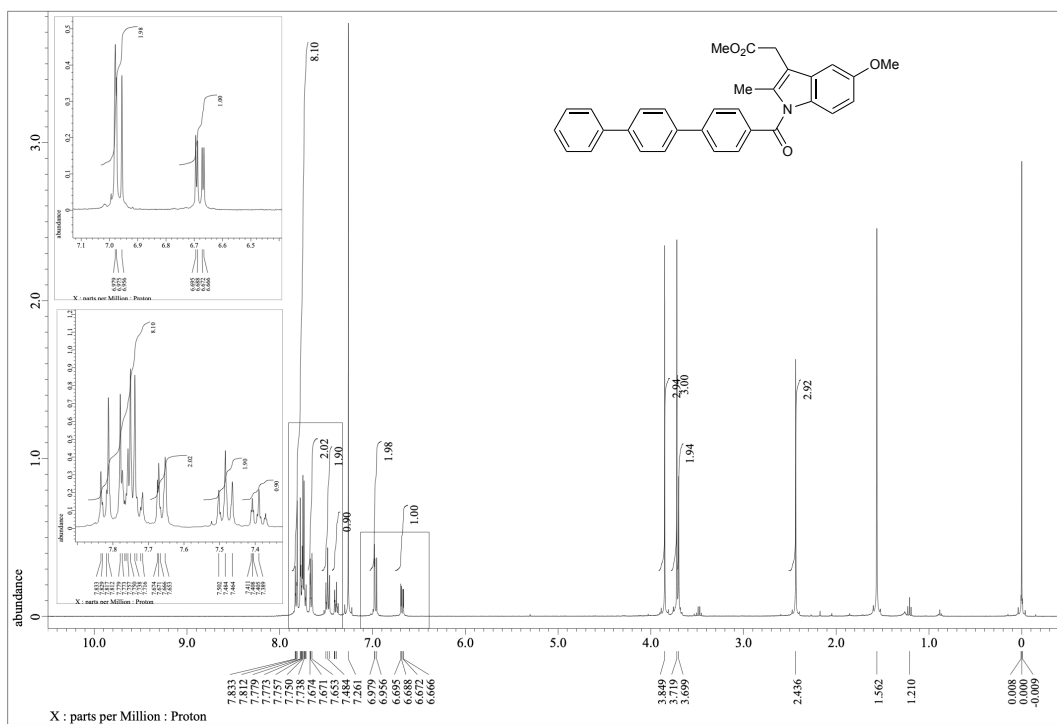
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **28** (CDCl_3)



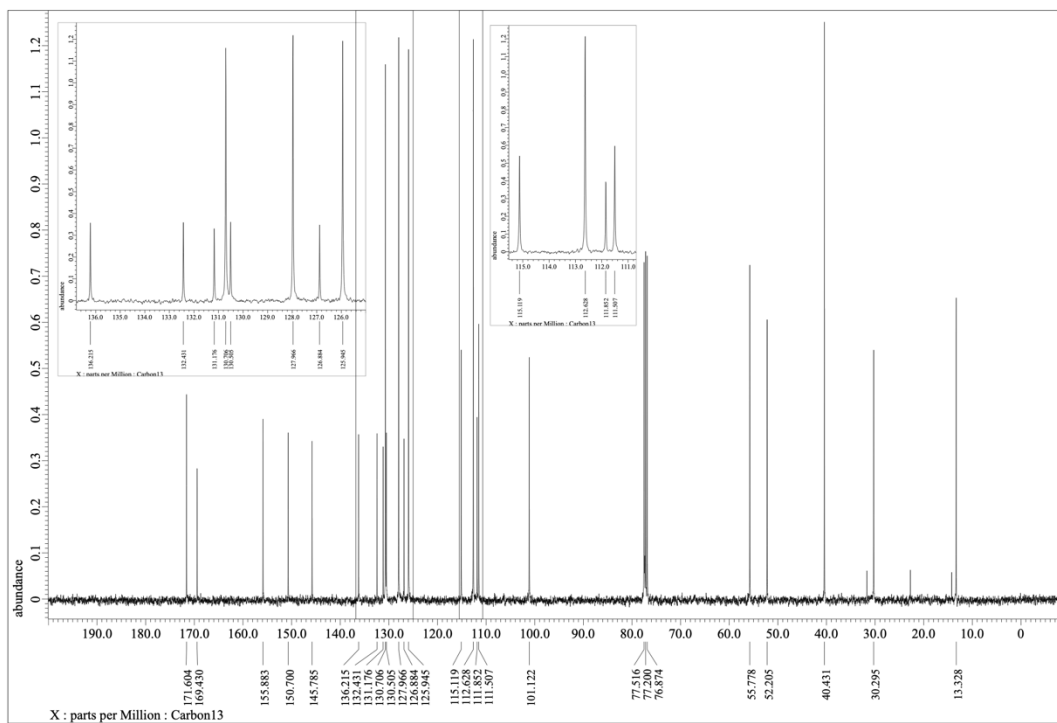
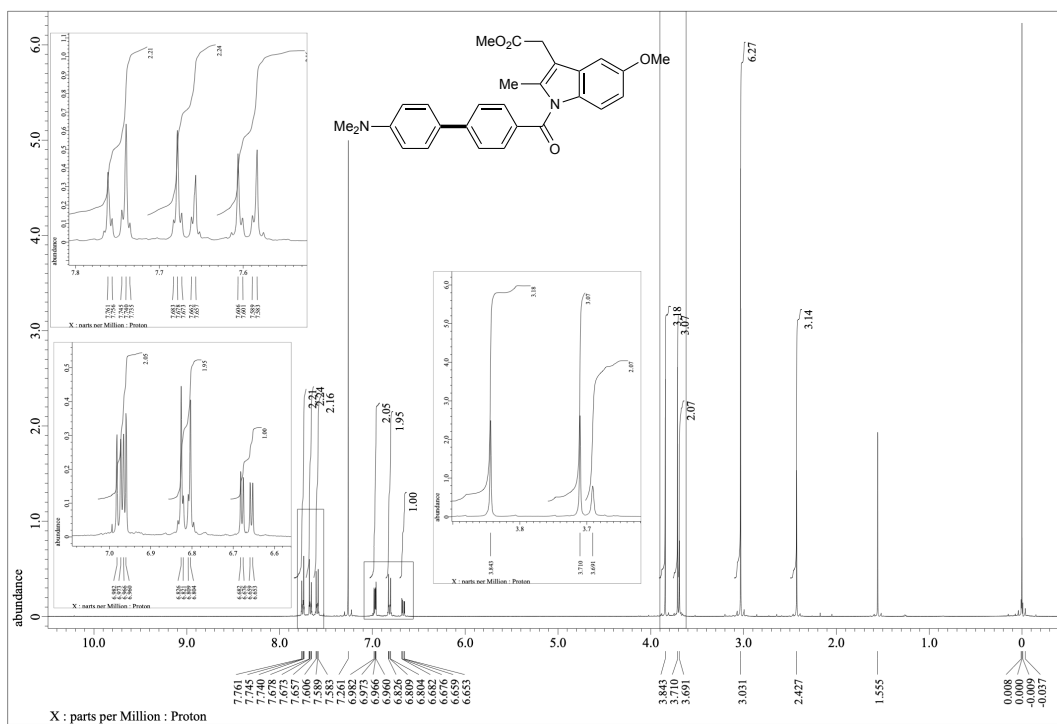
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **29** (CDCl₃)



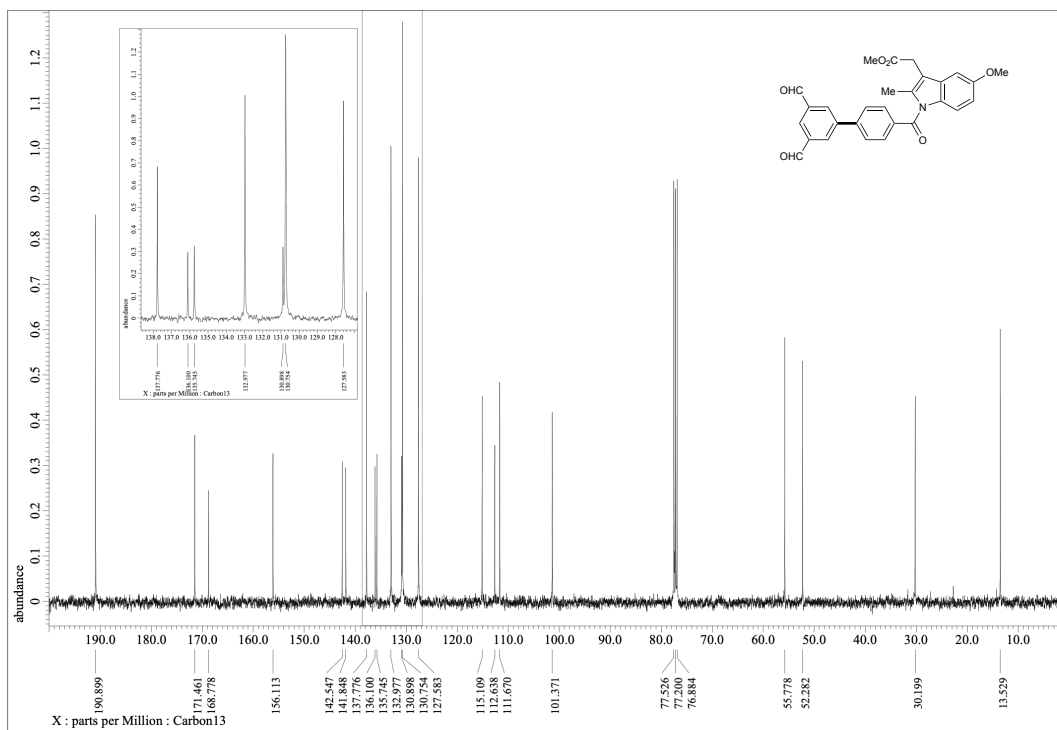
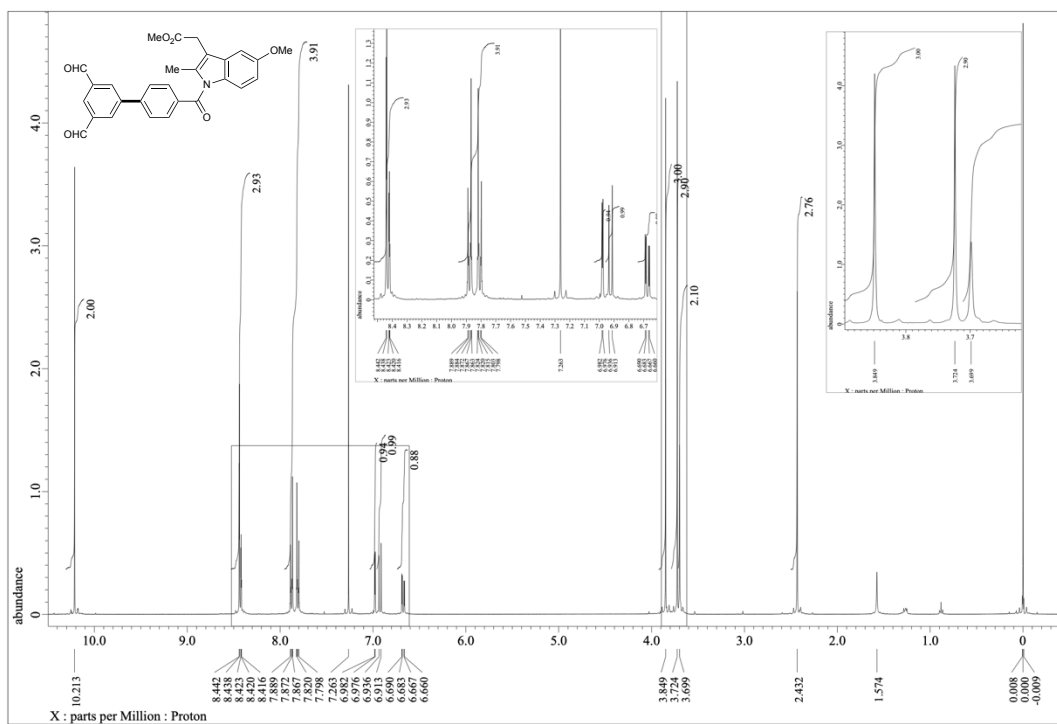
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **30** (CDCl_3)



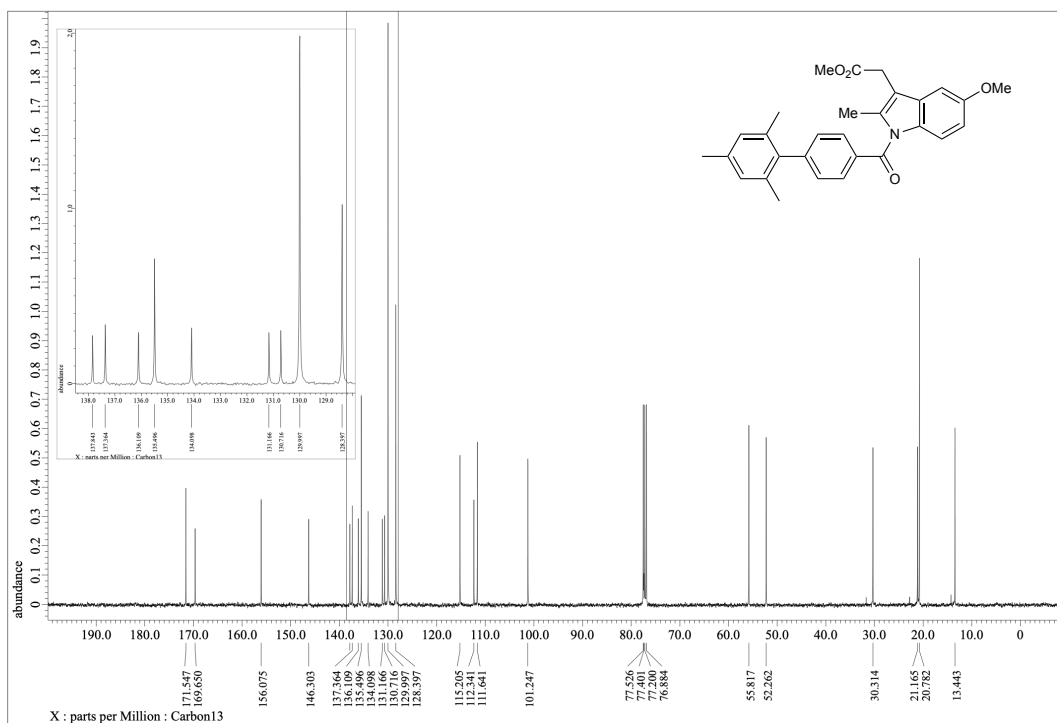
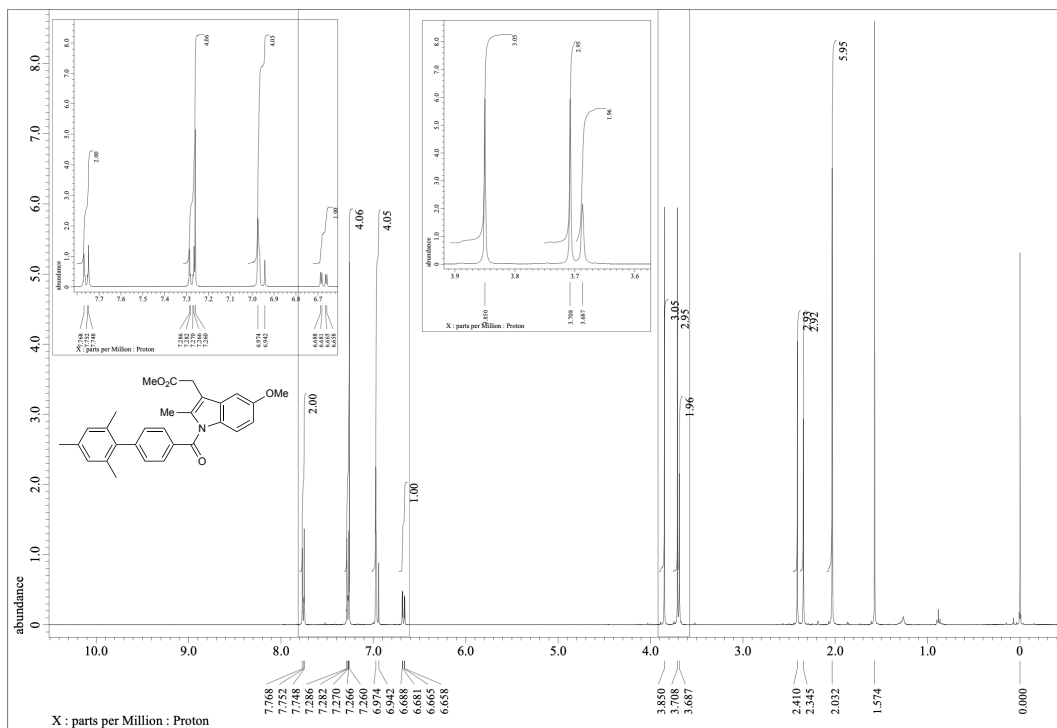
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **31** (CDCl_3)



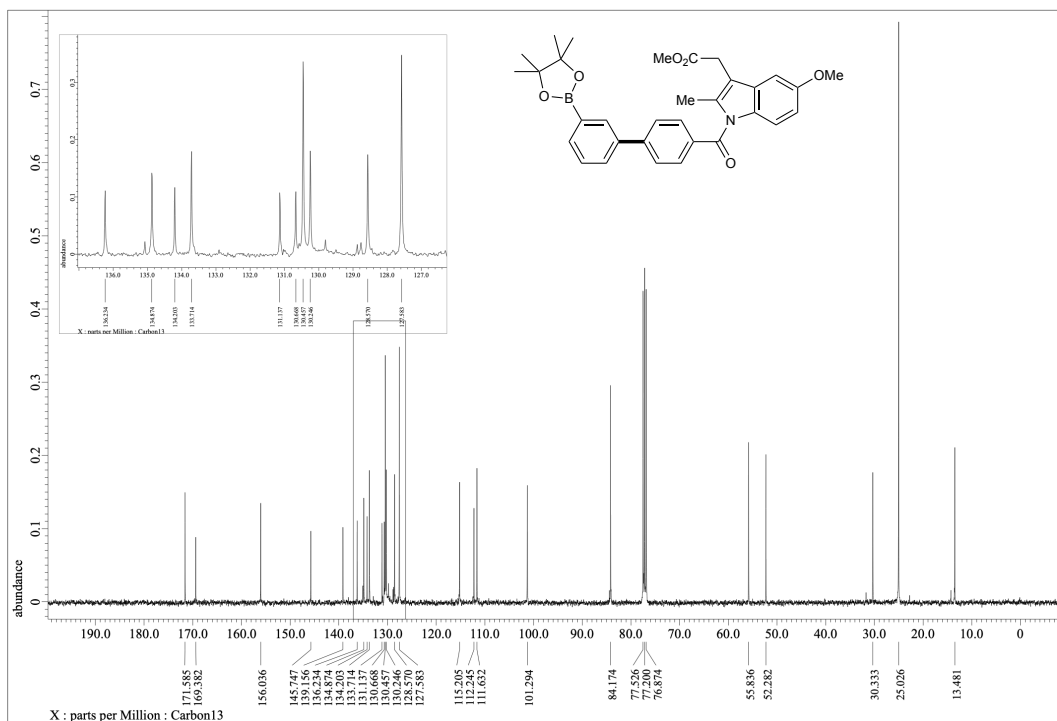
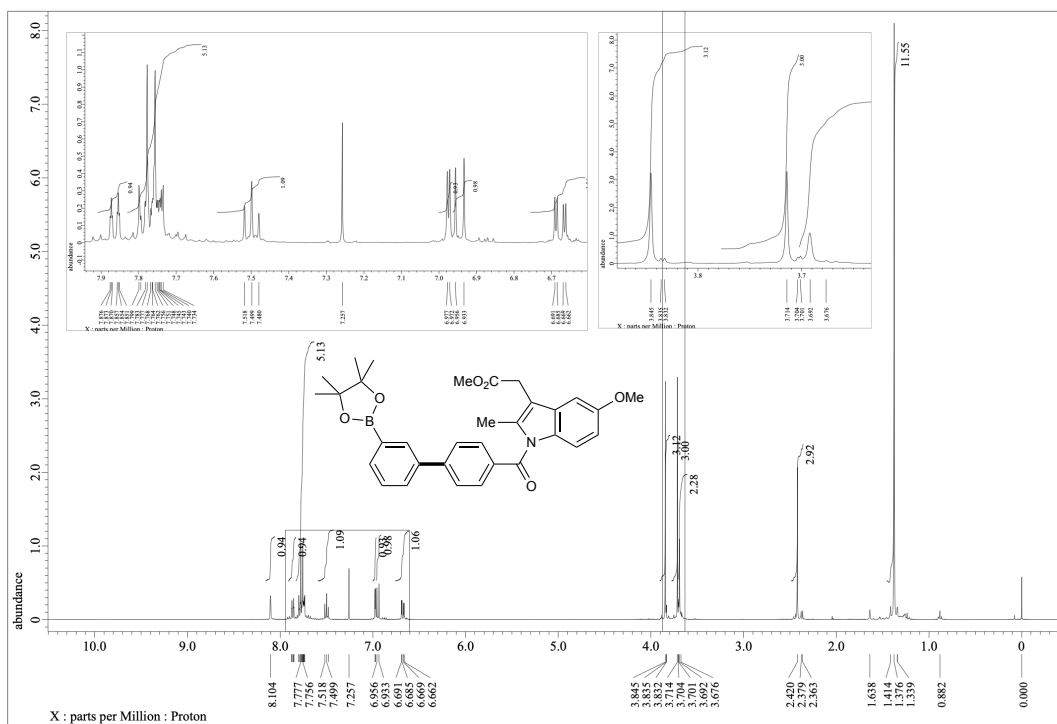
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **32** (CDCl₃)



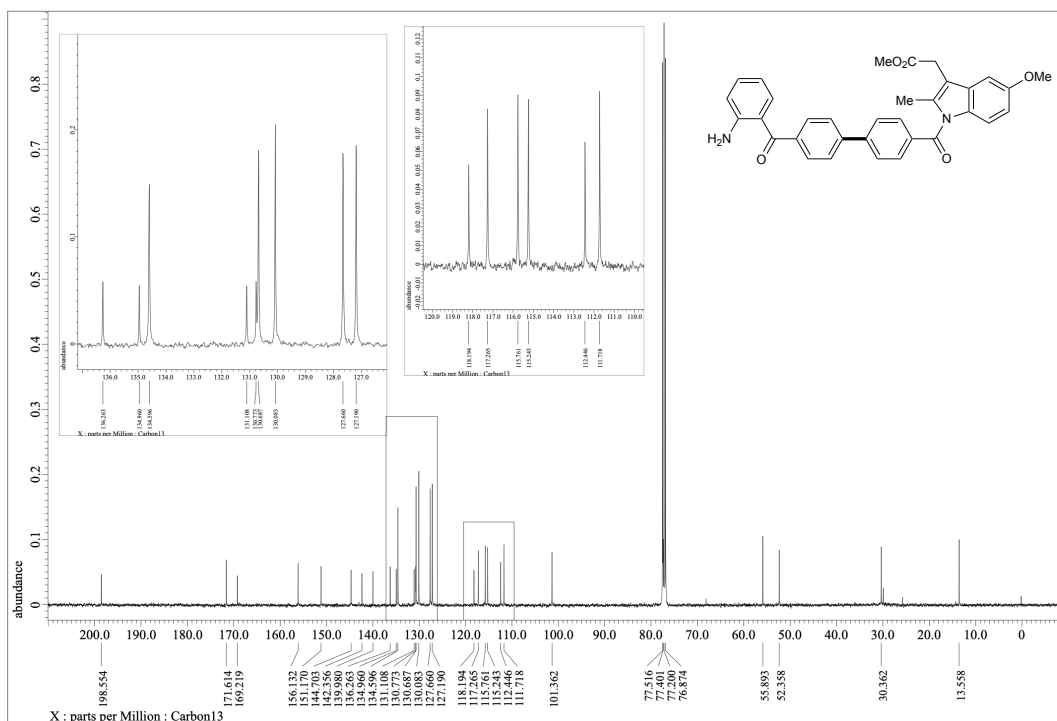
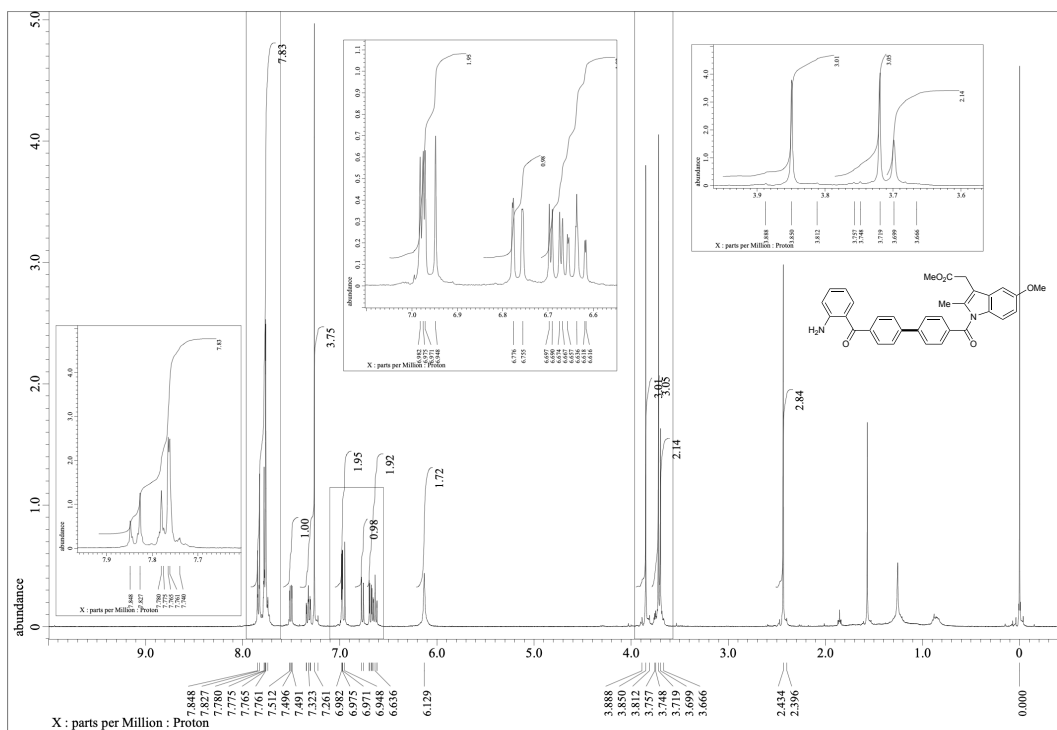
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **33** (CDCl_3)

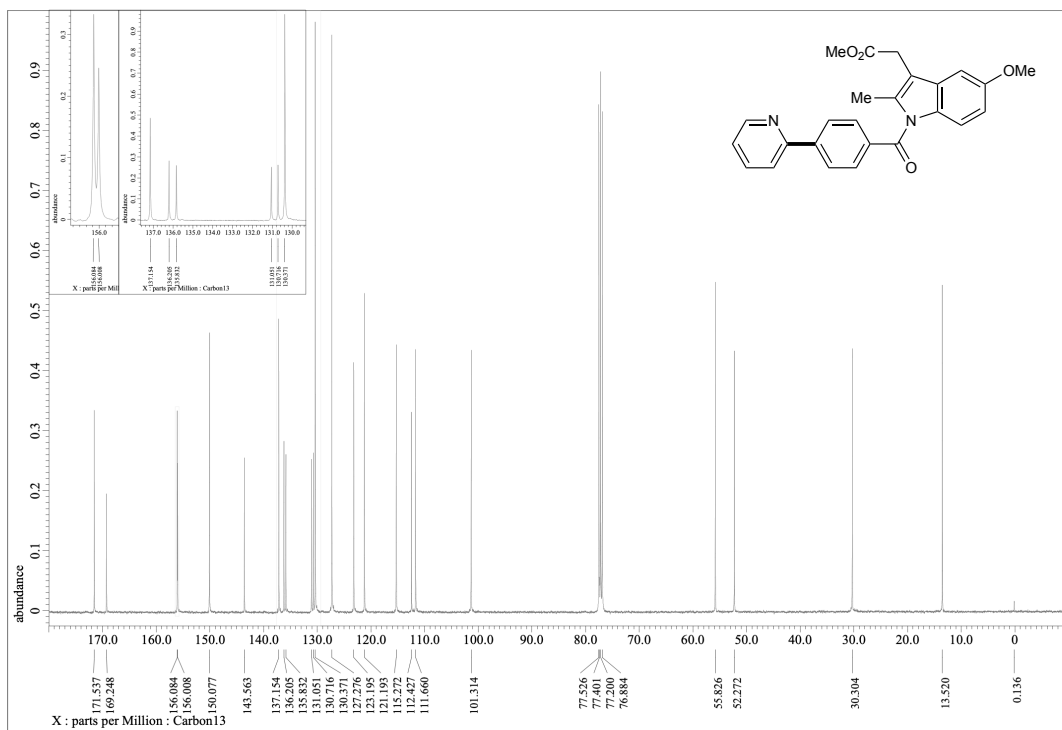
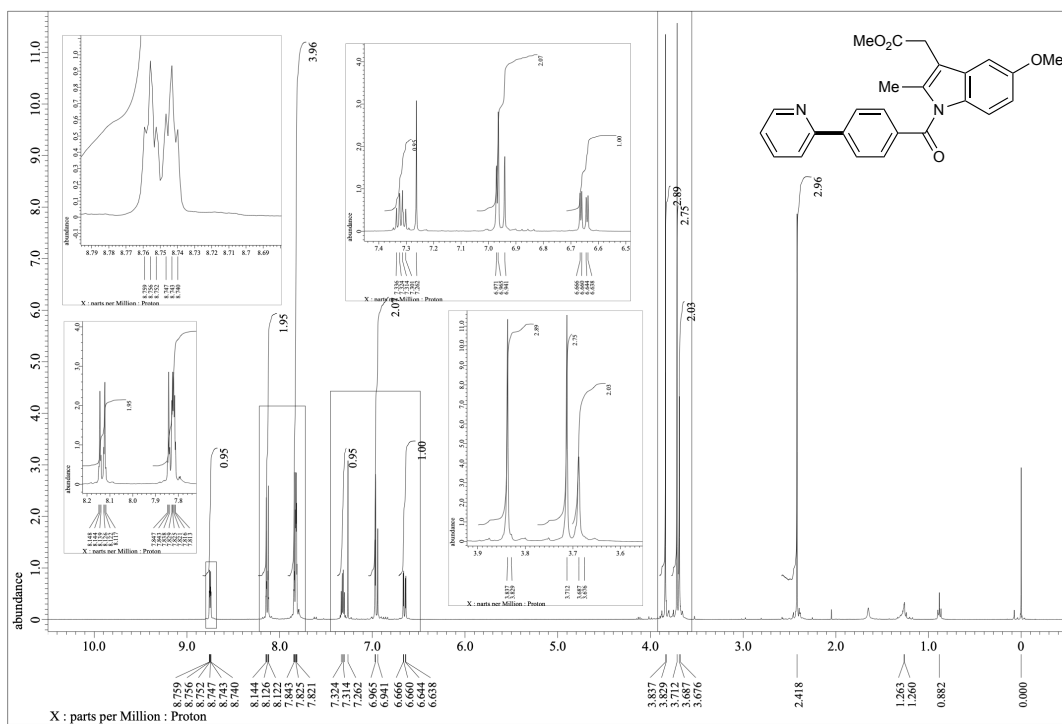


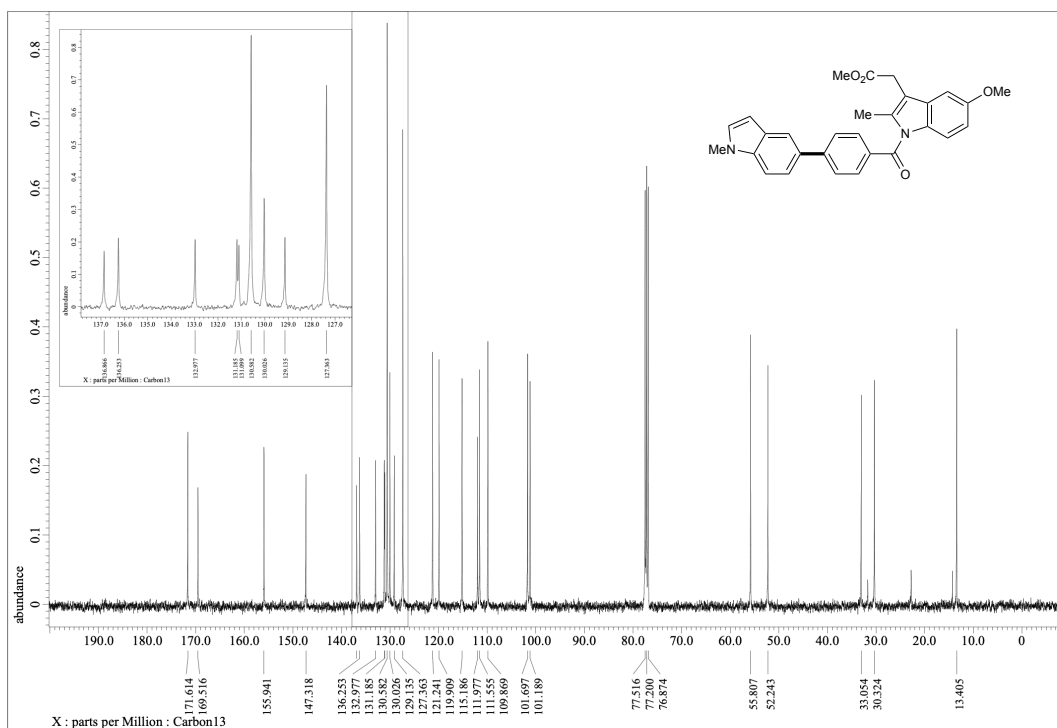
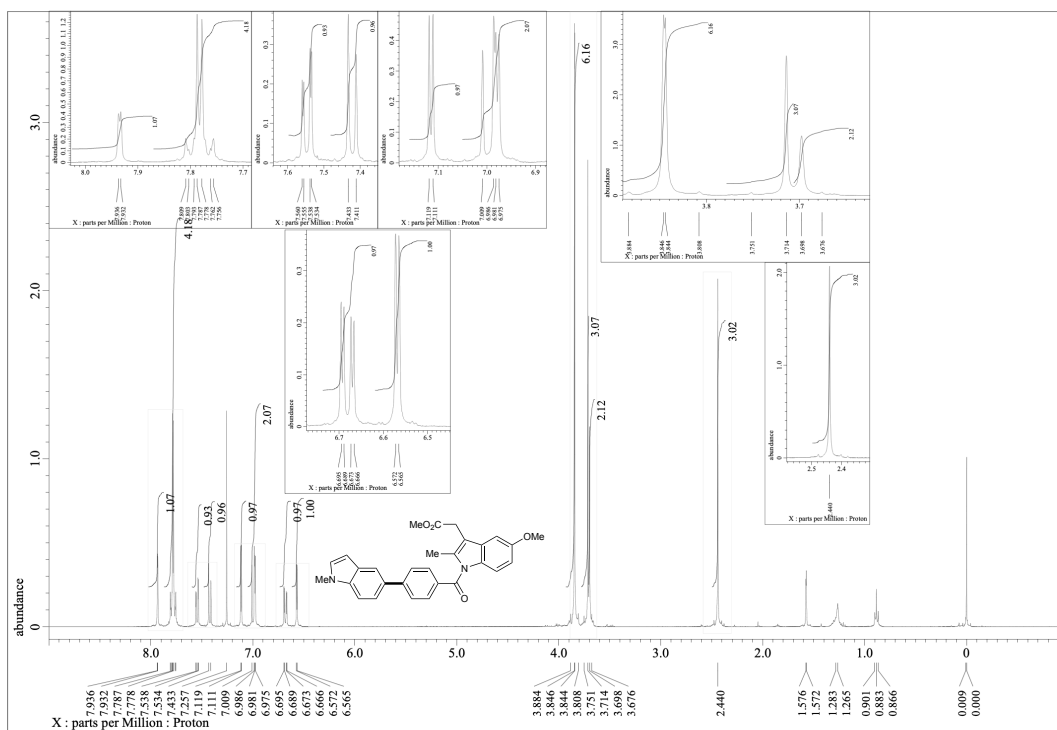
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **34** (CDCl_3)



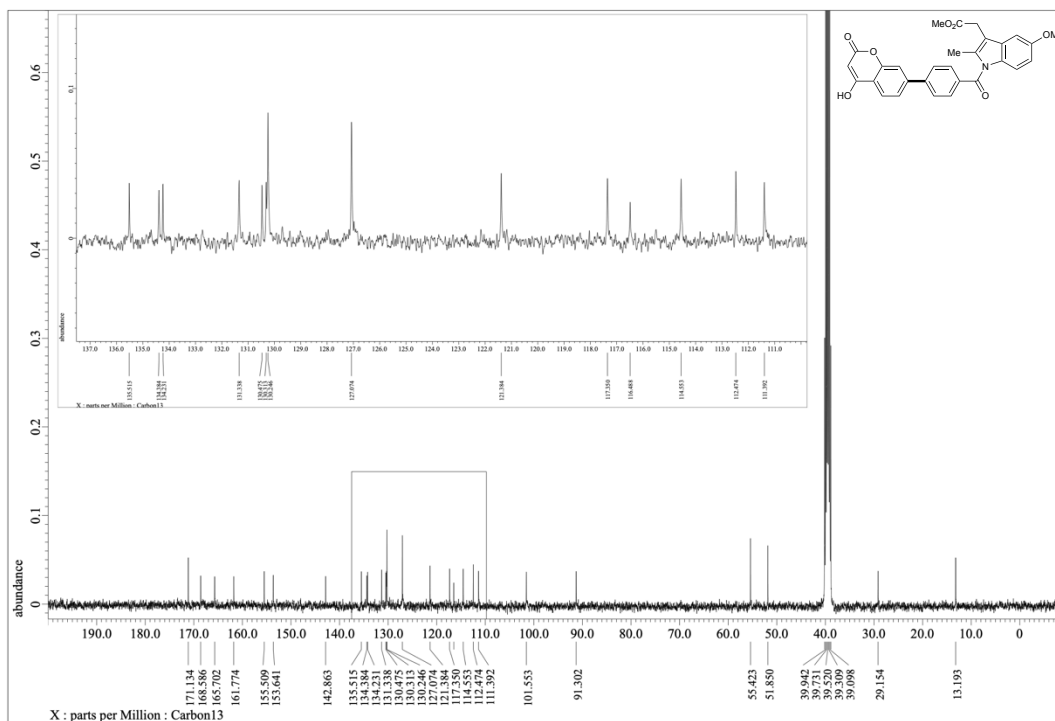
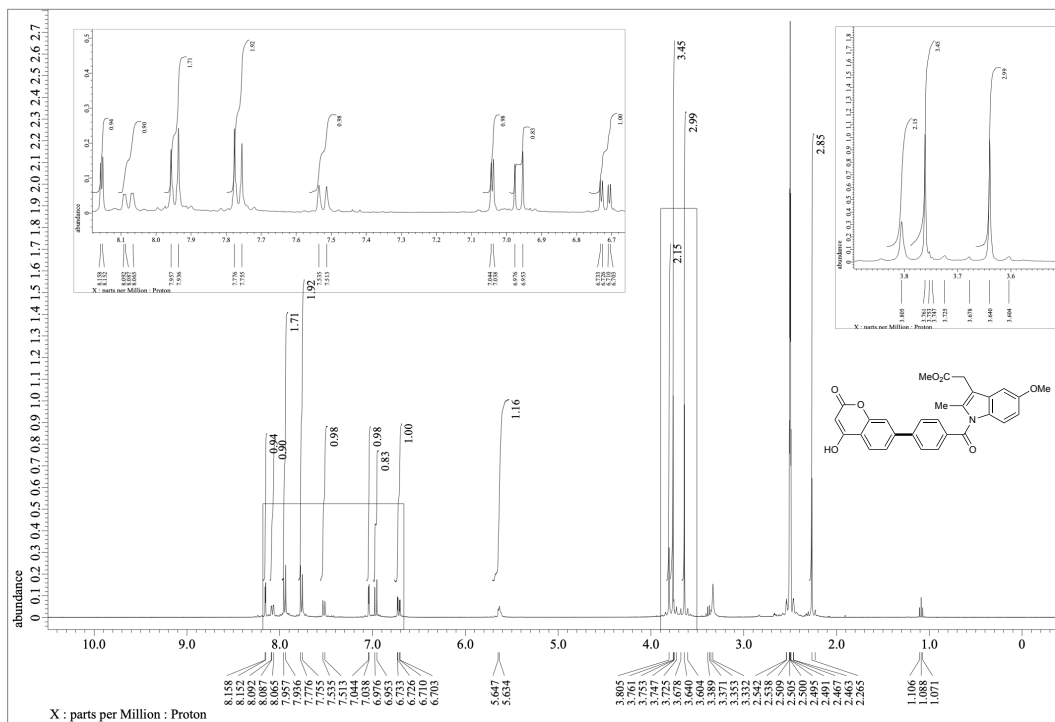
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **35** (CDCl_3)



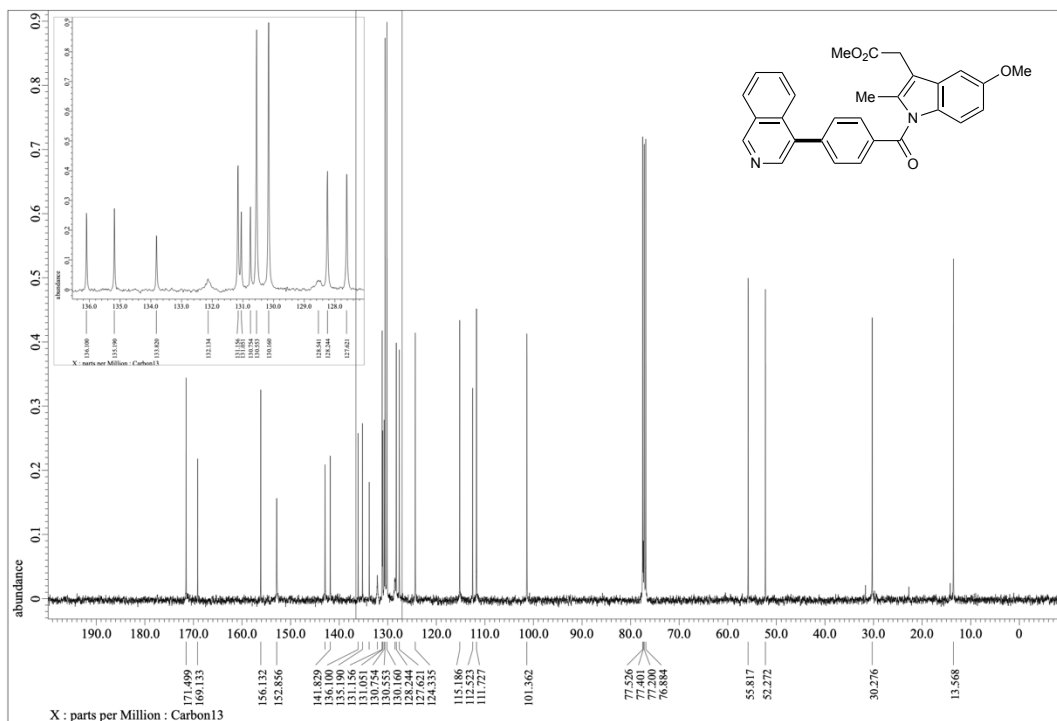
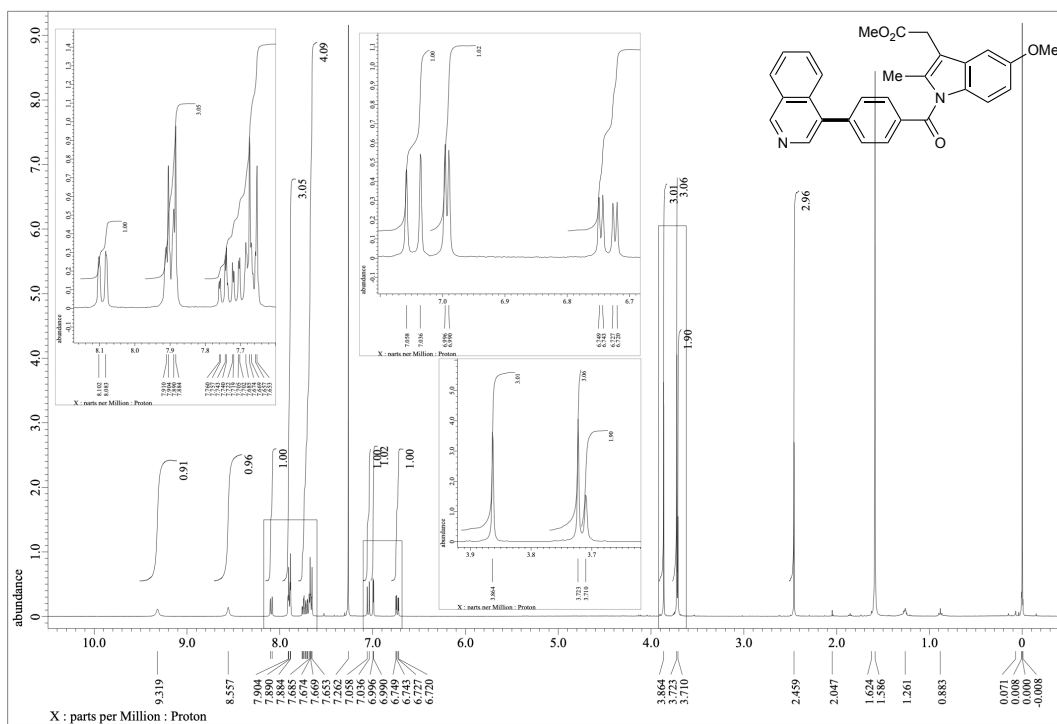
¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **36** (CDCl₃)

¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra of **37** (CDCl₃)

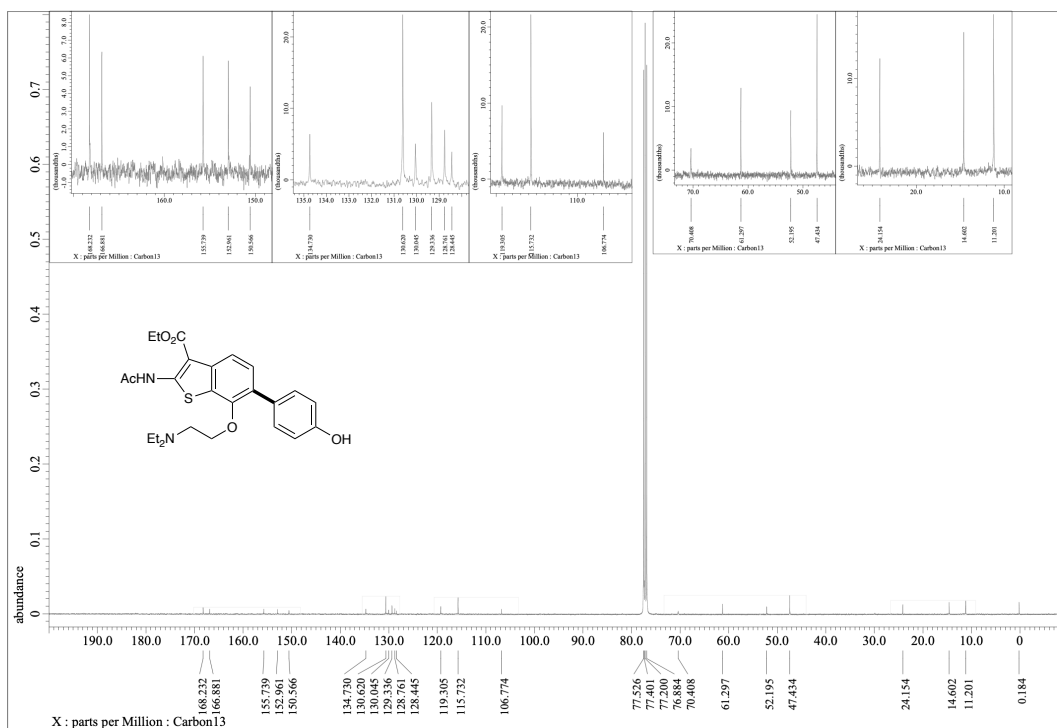
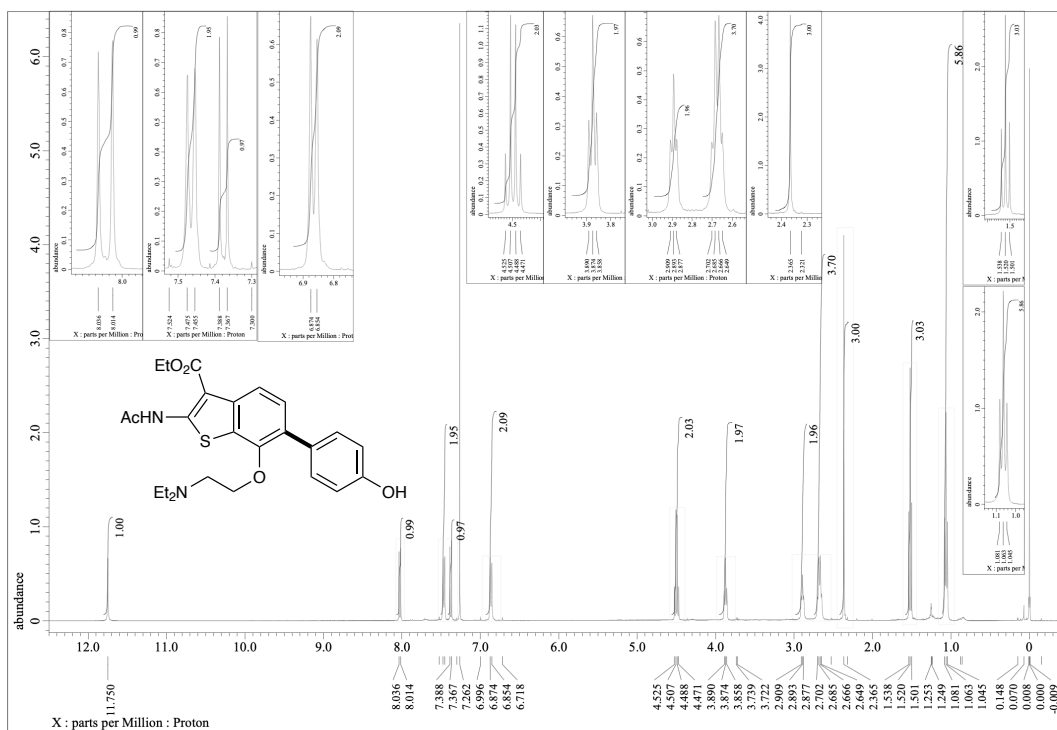
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **38** (DMSO- d_6)



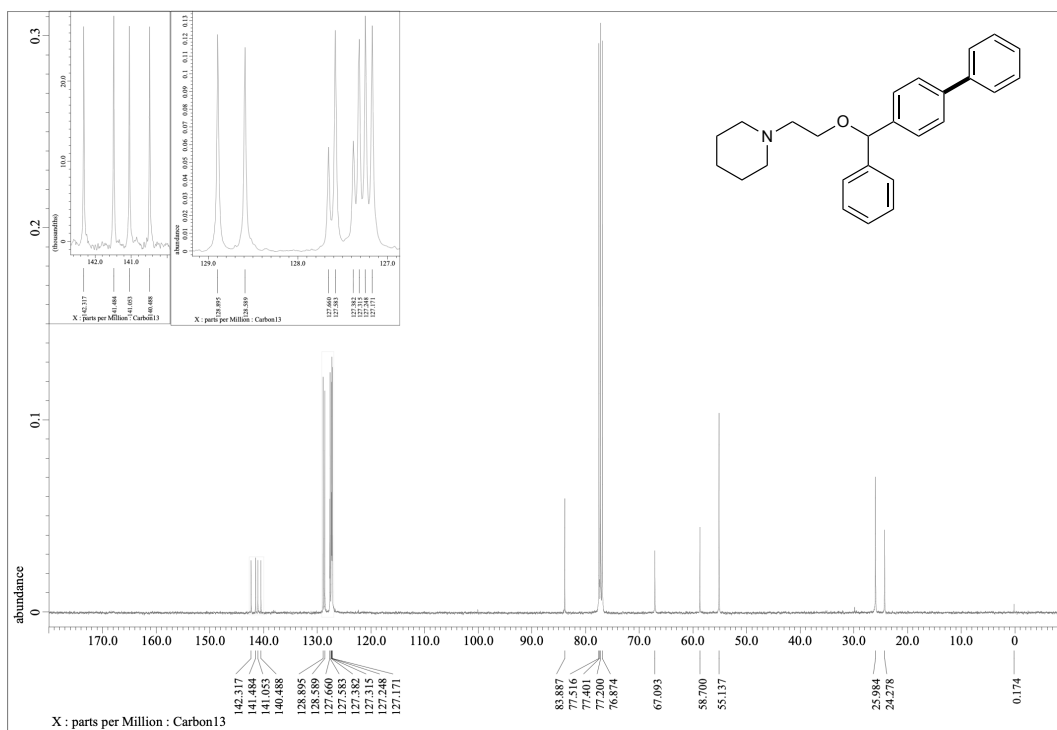
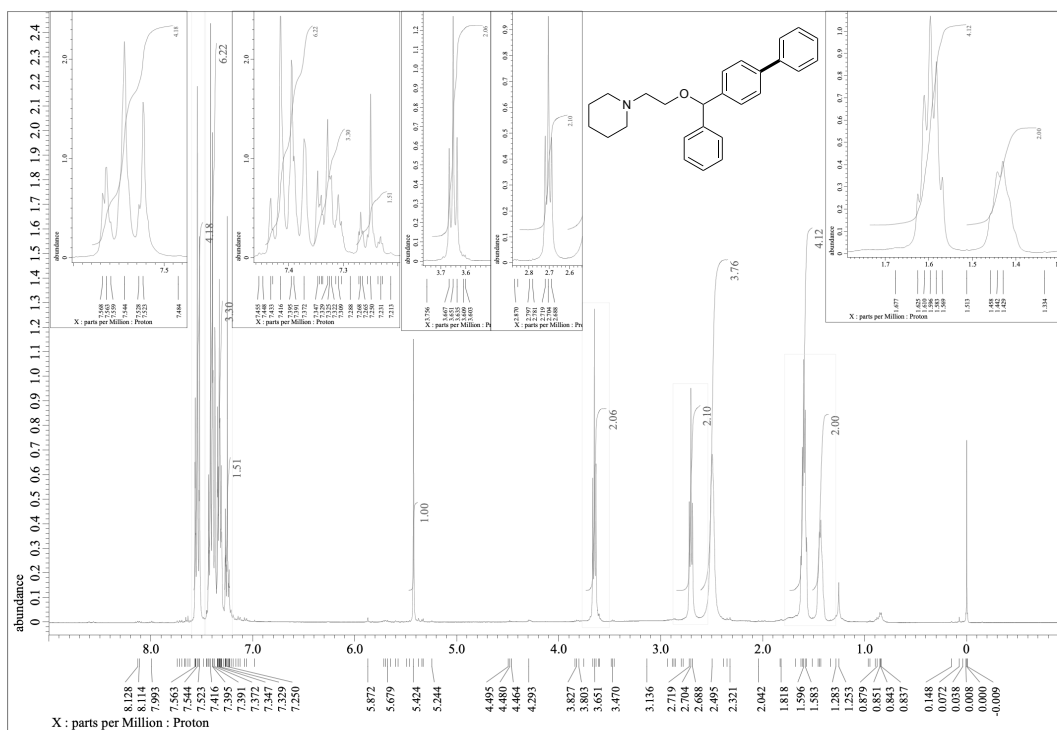
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **39** (CDCl_3)



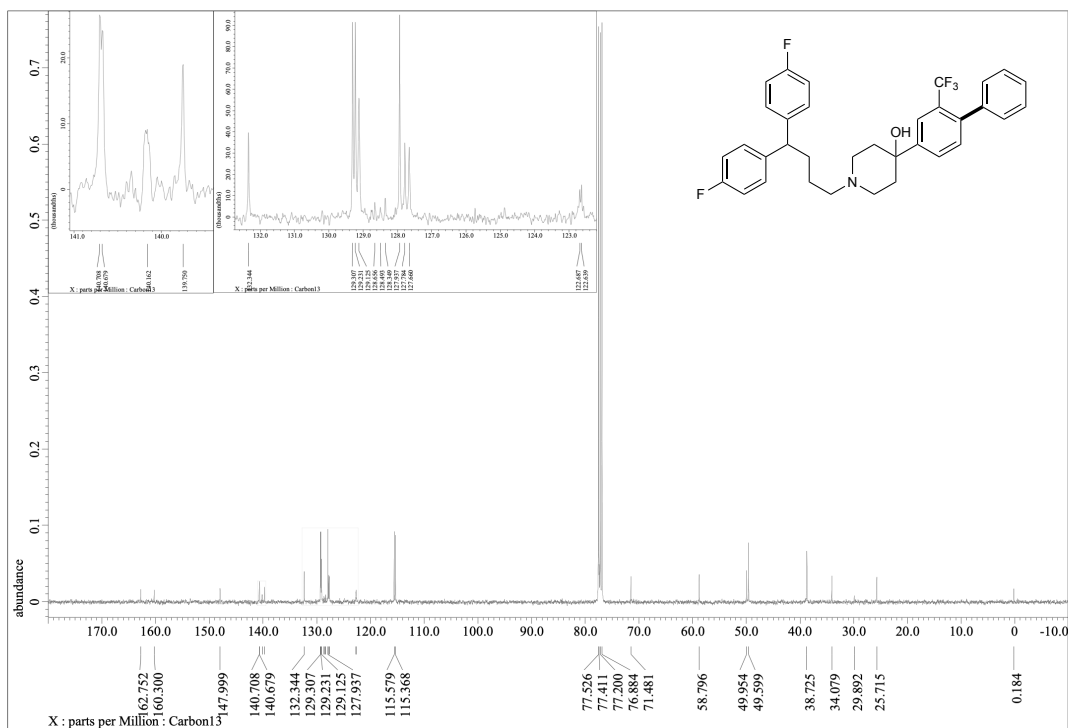
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **40** (CDCl_3)



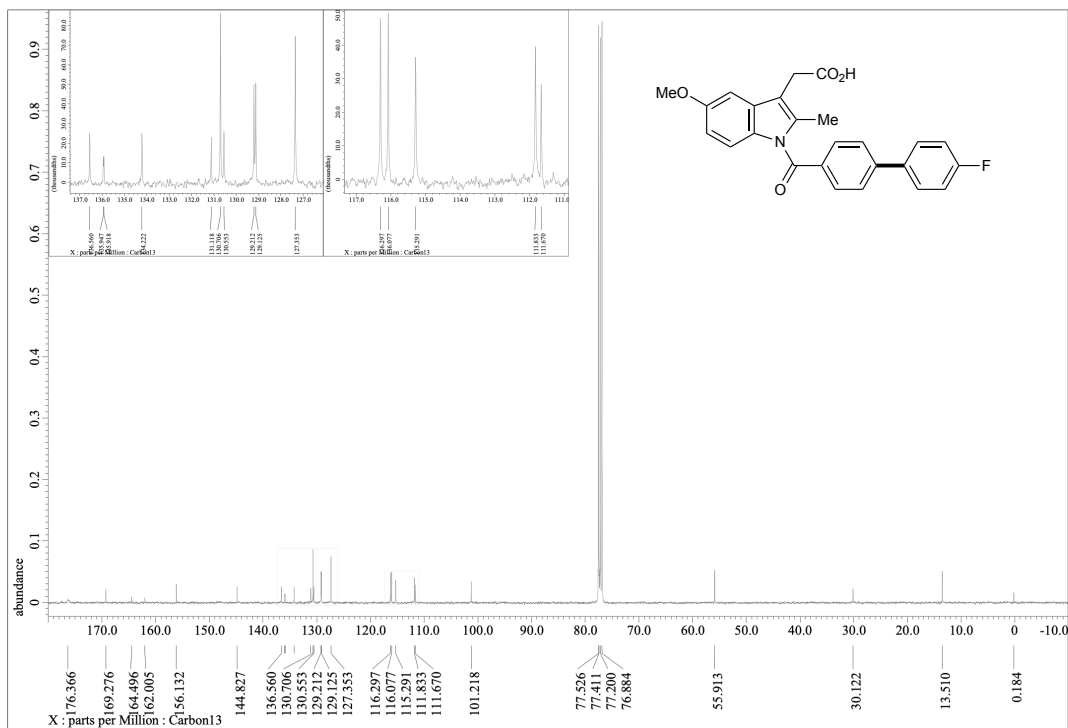
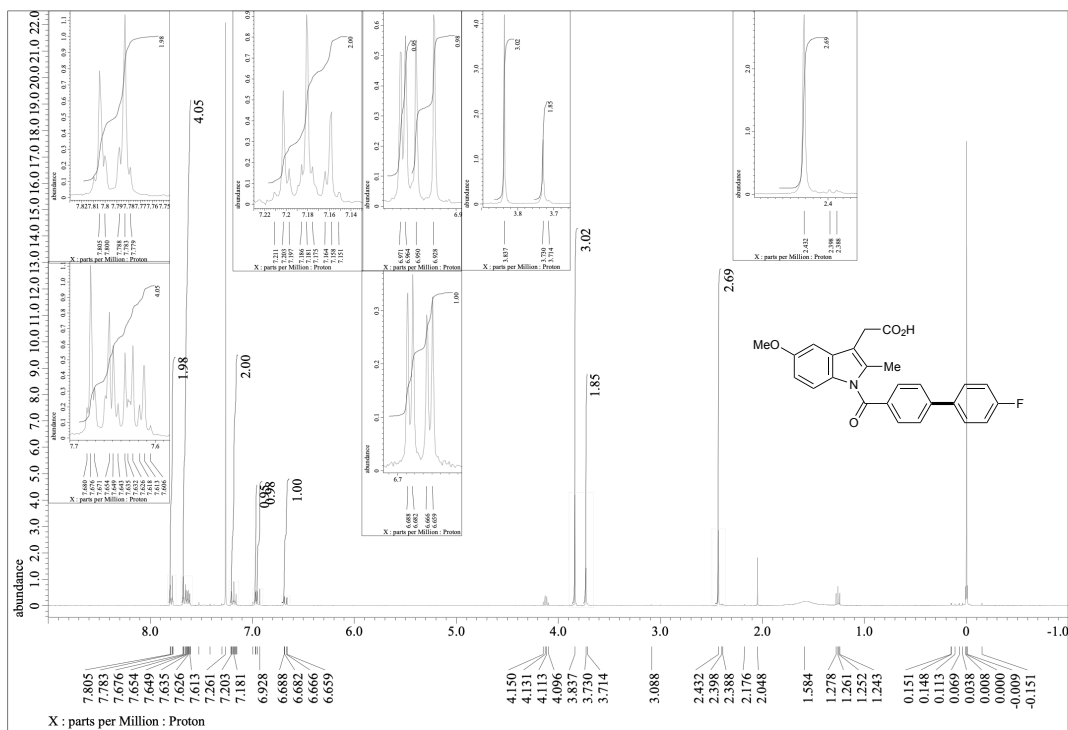
^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **41** (CDCl_3)



^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **42** (CDCl_3)



^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **43** (CDCl_3)



^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **44** (CDCl_3)

