

Supplementary Information

Synthesis of a Bcl9 alpha-helix mimetic for inhibition of PPIs by a combination of electrooxidative phenol coupling and Pd-catalyzed cross coupling

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1. General aspects

All commercially available chemicals were purchased from Acros Organics, Alfa Aesar, Fluka, Fisher Scientific, Fluorochem, Merck, Sigma Aldrich or VWR. They were used without further purification.

Oxygen and moisture sensitive reactions were performed under inert conditions using standard Schlenk techniques. The reactions were carried out under argon or nitrogen atmosphere using anhydrous dry and degassed solvents. Procedure for degassing of solvents: The solvent was transferred into a flame dried Schlenk flask under inert gas (argon or nitrogen) atmosphere and the inert gas was bubbled through the solvent via cannula in an ultrasonication bath for 15 min.

Solvents

The commercially available solvents were used without further purification, unless otherwise specified below. Anhydrous solvents were purchased in *extra dry grade* from Sigma Aldrich or Acros Organics or prepared according to the standard procedures listed below. The anhydrous solvents were stored over activated molecular sieves in brown glass bottles equipped with a Schlenk adapter under argon. The 3 Å and 4 Å molecular sieves were activated at 200 °C under vacuum (oil pump, 0.01 – 0.03 mbar) for 2 d.

Acetic acid (AcOH): AcOH was purchased from Acros Organics and used without further purification.

Acetonitrile (MeCN): anhydrous MeCN was purchased from Alfa Aesar as extra dry solvent (99.8 %, H₂O <50 ppm, in ChemSeal™ bottle). It was stored over 3 Å molecular sieves under argon in a brown bottle.

MeCN for HPLC measurements and purifications was purchased from VWR in HPLC/UHPLC-MS grade in 2.5 L brown bottles.

Chloroform: was purchased from VWR Chemicals in 2.5 L brown bottles and distilled in a rotary evaporator to remove the stabilisers. Chloroform was stored in brown bottles.

Cyclohexane: Cyclohexane was purchased from VWR in 5 L metal bottles and used without further purification.

Dichloromethane (DCM): DCM was purchased from Fisher Chemicals in 5 L plastic bottles and used without further purification.

DCM stabilized with EtOH was first dried with P₄O₁₀, distilled, then heated under reflux over CaH₂ and distilled. It was stored in a brown glass bottle over 4 Å molecular sieves under argon.

1,2-Dimethoxyethane (1,2-DME): 1,2-DME was purchased from Sigma-Aldrich in 1 L glass bottles and used directly in the reactions.

Anhydrous 1,2-DME was prepared by filtering through an alox-column (Pure Solv by Innovative Technology) and it was stored over 4 Å molecular sieves in brown glass bottles under argon.

N,N-Dimethylformamide (DMF): DMF was purchased from Merck-Schuchardt in brown glass bottles and used without further purification.

Anhydrous DMF was purchased from Sigma Aldrich as *extra dry solvent* (99.8 %, H₂O <50 ppm, in Sure/Seal™) and transferred into a brown glass bottle and stored over 4 Å molecular sieves under argon atmosphere.

N,N-Dimethylacetamide: anhydrous *N,N*-Dimethylacetamide was purchased from Sigma Aldrich as *extra dry solvent* (99.8 %, H₂O <50 ppm, in Sure/Seal™) and transferred into a brown glass bottle and stored over 4 Å molecular sieves under argon atmosphere.

1,4-Dioxane: 1,4-Dioxane was purchased from Acros Organics in a 2.5 L glass bottle and used without further purification.

Anhydrous 1,4-Dioxane was purchased from Sigma Aldrich as *extra dry solvent* (99.8 %, H₂O <50 ppm, in Sure/Seal™) and transferred into a brown glass bottle and stored over 4 Å molecular sieves under argon atmosphere.

Ethanol (EtOH): EtOH was purchased in 25 L plastic cans from Merck and used without further purification.

Ethyl acetate (EtOAc): EtOAc was purchased from Fisher Chemicals in 5 L plastic bottles and used without further purification.

1,1,1,3,3,3-Hexafluoroisopropan-2-ol (HFIP): HFIP was purchased from Fluorochem in 1 L brown glass bottles and used without further purification.

Triethylamine (Et₃N): Et₃N was purchased from Sigma Aldrich in 2.5 L brown glass bottle.

Et₃N was dried by heating under reflux over CaH₂, distilled and stored under argon atmosphere over 4 Å molecular sieves in a brown bottle.

Tetrahydrofuran (THF): The commercially available THF was distilled in a rotary evaporator to remove the stabilisers and stored over KOH in brown glass bottles.

THF was dried by heating under reflux under argon atmosphere over sodium and benzophenone, distilled and stored over 4 Å molecular sieves in a brown glass bottle under argon atmosphere.

Analytical Methods

Gas chromatography (GC-MS)

Gas chromatography was performed on an Agilent Technologies 7890A (G3440A) GC system equipped with an Agilent Technologies 7683 Series autosampler and an Agilent Technologies 7683B Series injector. The detection was carried out with coupled mass detector (Agilent Technologies 5975C inert mass sensitive detector with triple-axis detector (MSD, EI, 70 eV; transfer line: 300 °C; MS source: 240 °C; MS quad: 180 °C).

Column: Agilent Technologies J&W GC-column HP-5MS (5%-phenyl) methylpolysiloxane; length: 30 m; inner-diameter: 0.250 mm; film: 0.25 µm. Flow: Constant helium flow rate.

MV_50: 0.0 – 1.0 min, isocratic, 50 °C; 1.0 – 6.25 min, linear 50 °C to 300 °C (40 °C min⁻¹); 6.25 – 11.25 isocratic, 300 °C; solvent delay 4.0 min.

MV_100: 0.0 – 1.0 min, isocratic, 100 °C; 1.0 – 5.0 min, linear 50 °C to 300 °C (50 °C min⁻¹); 5.0 – 17.0 isocratic, 300 °C; solvent delay 3.0 min.

High-performance liquid chromatography (HPLC)

Analytical HPLC analysis was performed on an Agilent Technologies 1260 Infinity system coupled with UV detector (Agilent Technologies 1200 Series) and mass detector (Agilent Technologies 6120 Quadrupole LC/MS).

Column: C-18-Reversed-Phase column of the type Poroshell® 120 SB-C18, 3.0 x 100 mm, 2.7 µm by Agilent Technologies.. Flow: Constant flow rate 0.7 mL/min, T = 35 °C.

MV_general: 0.0 – 0.1 min, isocratic, 2 % MeCN (98 % H₂O + 0.05 % TFA); 0.1 – 8.0 min, linear, 2 % to 100 % MeCN (98 % to 0 % H₂O + 0.05 % TFA); 8.0 – 11.1 min, isocratic, 100 % MeCN; 11.1 – 11.3 min, linear, 100 % to 2 % MeCN (0 % to 98 % H₂O + 0.05 % TFA); 11.3 – 12.0 min, isocratic, 2 % MeCN (98 % H₂O + 0.05 % TFA).

MV_70: 0.0 – 0.1 min, isocratic, 70 % MeCN (30 % H₂O + 0.05 % TFA); 0.1 – 8.0 min, linear, 70 % to 100 % MeCN (30 % to 0 % H₂O + 0.05 % TFA); 8.0 – 11.1 min, isocratic, 100 % MeCN; 11.1 – 11.3 min, linear, 100 % to 70 % MeCN (0 % to 30 % H₂O + 0.05 % TFA); 11.3 – 12.0 min, isocratic, 70 % MeCN (30 % H₂O + 0.05 % TFA).

High-resolution mass spectrometry (HRMS)

HRMS measurements were performed by Prof. Robert Saf and Ing. Karin Bartl (TU Graz – ICTM) on a Waters GCT Premier-system with EI ionisation source with a potential of E = 70 eV or a MALDI-TOF/TOF (Bruker Ultraflex Extreme) with nanostructured laser desorption ionisation (naldi) plates (Bruker MSP 96 NALDI target plate).

Melting point

Melting points were measured using the melting-point apparatus “Mel-Temp[®]” from Electrothermal with a microscope output for visual observation. For correct determination of the melting points was the heating rate kept 0.5 °C/min.

Nuclear magnetic resonance

NMR measurements were performed on a Bruker Avance III 300 MHz FT NMR spectrometer (300.36 MHz (¹H), 75.53 MHz (¹³C)) and a Varian Unity Inova 500 spectrometer (¹H: 499.87 MHz; ¹³C: 125.69 MHz, ¹⁹F: 470.32 MHz). Chemical shifts [δ] = ppm were referenced to residual protonated solvent signals of: DMSO-d₆: δ = 2.50 ppm (¹H); 39.52 ppm (¹³C), MeOD: δ = 3.31 ppm (¹H); 49.00 ppm (¹³C) and CDCl₃: δ = 7.26 ppm (¹H); 77.16 ppm (¹³C)^[54]. The signal abbreviation: s (singlet), br s (broad singlet), d (doublet), dd (doublet of doublet), dtd (doublet of triplet of doublet), t (triplet), q (quadruplet), m (multiplet). The abbreviation C_q is used for quaternary carbon atoms and C^{Ar} for carbon in aromatic ring. The signals were assigned by 2D-COSY, APT and 2D-HSQC experiments.

Thin layer chromatography

Thin layer chromatography was performed on silica gel plates from Merck (silica gel 60 F₂₅₄ aluminium sheets 20x20 cm). UV-detection and staining with reagent solutions following

developing in a hot air stream using a heat gun were used. The UV-detection was carried out at two wavelengths $\lambda = 254$ and 366 nm. The staining was performed by standard detection solutions.

CAM: 50.0 g $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}\cdot 4\text{H}_2\text{O}$, 2.00 g $\text{Ce}(\text{SO}_4)_2$ and 50.0 mL conc. H_2SO_4 were dissolved in 400 mL H_2O .

Ninhydrin: 1.50 g ninhydrin were dissolved in 100 mL *n*-butanol. 3.00 mL AcOH were added.

KMnO₄: 1.50 g of KMnO_4 and 10.0 g K_2CO_3 were dissolved in 200 mL H_2O . 1.25 mL 10% NaOH were added.

Vanillin: 15 g vanillin were dissolved in 250 mL ethanol and 2.5 mL conc. H_2SO_4

Column chromatography

Silica gel (SiO_2) (Acros Organics, SiO_2 for chromatography 0.035 – 0.070 mm, 60 Å, nitrogen flushed) was used for preparative column chromatography. The eluent was chosen based on a R_f -value from TLC in the range between $R_f = 0.2 - 0.3$ of the desired compounds. The crude products, which were not soluble in the mobile phase, were dissolved in DCM and the 1.5 – 2.0 fold amount of Celite[®]545 was added. The solvent was then removed under reduced pressure. The residue was dried under vacuum and transferred on top of the packed column.

Semi-preparative HPLC

Semi-preparative HPLC separations were carried out on a Thermo Scientific Dionex Ulti Mate 3000 Instrument with UV-detection at $\lambda = 254$ and automatic fractions collector.

Column: Macherey-Nagel VP 125/21 Nucleodur 100-5 C18 ec column. Flow: Constant flow rate 12 mL/min, $T = 30$ °C.

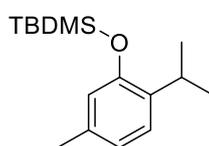
Prep_10to100_+0.1: 0.0 – 2.0 min, isocratic, 10 % CH_3CN (90 % H_2O + 0.1 % TFA); 2.0 – 10.0 min, linear, 10 to 100 % CH_3CN (90 % to 0 % H_2O + 0.1 % TFA); 10.0 – 12.0 min, isocratic, 100 % CH_3CN ; 12.0 – 12.5 min, linear, 100 to 10 % CH_3CN (0 % to 90 % H_2O + 0.1 % TFA); 12.5 – 14.0 min, isocratic, 10 % CH_3CN (90 % H_2O + 0.1 % TFA).

Hydrogenation

Hydrogenations under high pressure were performed using an H-Cube™ (HC-2.SS from Thales Nanotechnology Inc.) flow reactor. A 10 % Pd/C cartridge (Thales Nanotechnology Inc., THS 01111, 10% Pd/C), or a Raney-Nickel cartridge (Thales Nanotechnology Inc., THS 01112, Ra-Ni) were used for hydrogenation in the range of 1 to 70 bar and 25 to 70 °C.

2. Experimental section

tert-Butyl-(2-isopropyl-5-methylphenoxy)-dimethylsilane (**2**)



2

In a 250 mL round bottom flask 2.00 g thymol (13.3 mmol, 1 eq.) and 2.38 g imidazole (34.7 mmol, 2.6 eq.) were dissolved in 60 mL abs. DCM. 3.05 g TBDMSCl (20.3 mmol, 1.5 eq.) were slowly added to the stirring solution. The reaction mixture was stirred overnight at RT. The final suspension was washed with 100 mL H₂O, then with a sat. NaHCO₃ solution and again with 100 mL H₂O. The organic phase was dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via Kugelrohr distillation (70 °C, 0.01 mbar).

Yield: 3.05 g (87 %), colorless oil, C₁₆H₂₈OSi [264.48 g/mol].

¹H NMR (300 MHz, CDCl₃) δ = 7.10 (d, ³J (H,H) = 7.7 Hz, 1H, C^{Ar}H), 6.76 (d, ³J (H,H) = 7.6 Hz, 1H, C^{Ar}H), 6.60 (s, 1H, C^{Ar}H), 3.39-3.15 (m, 1H, CH), 2.28 (s, 3H, C^{Ar}-CH₃), 1.19 (d, ³J = (H,H) 6.9 Hz, 6H, CH-(CH₃)₂), 1.03 (s, 9H, C-(CH₃)₃), 0.25 (s, 6H, Si-(CH₃)₂) ppm (Figure S3)

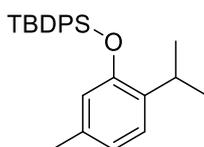
¹³C NMR (76 MHz, CDCl₃) δ = 152.7 (C_q, C^{Ar}), 136.2 (C_q, C^{Ar}), 136.1 (C_q, C^{Ar}), 126.1 (C^{Ar}), 122.0 (C^{Ar}), 119.3 (C^{Ar}), 26.4 (CH-(CH₃)₂), 26.0 (C-(CH₃)₃), 23.1 (CH-(CH₃)₂), 21.2 (C^{Ar}-CH₃), 18.4 (C-(CH₃)₃), -3.9 (Si-(CH₃)₂) ppm (Figure S3)

GC-MS (EI, 70 eV; MT_50_S): $t_R = 5.57$ min; m/z (%) = 264 (14) [M^+], 249 (2) [$M^+ - CH_3$], 207(100) [$M^+ - iPr$], 149 (8) [$M^+ - tBu$]

TLC $R_f = 0.57$ (cyclohexane, UV)

HRMS (EI): calcd for [M^+]: 264.1909; found: 264.1916

tert-Butyl-(2-isopropyl-5-methylphenoxy)-diphenylsilane (**4**)



4

In a 250 mL round bottom flask 2.00 g thymol (13.3 mmol, 1 eq.), 2.38 g imidazole (34.7 mmol, 2.6 eq.) were dissolved in 60 mL abs. DCM. 5.28 mL TBDMSCl (20.3 mmol, 1.5 eq.) were slowly added to the stirring solution. The reaction mixture was stirred overnight at RT. The final suspension was washed with 100 mL H₂O, then with a sat NaHCO₃ solution and again with 100 mL H₂O. The organic phase was dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (50 g SiO₂, eluent: cyclohexane/EtOAc = 100/1).

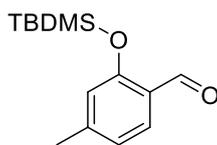
Yield: 4.69 g (91 %), colorless solid, C₂₆H₃₂OSi [388.63 g/mol].

¹H NMR (300 MHz, CDCl₃) $\delta = 7.74$ (d, 3J (H,H) = 6.3 Hz, 4H, C^{Ar}H), 7.52 – 7.30 (m, 6H, C^{Ar}H), 7.13 (d, 3J (H,H) = 7.7 Hz, 1H, C^{Ar}H), 6.69 (d, 3J (H,H) = 7.6 Hz, 1H, C^{Ar}H), 6.25 (s, 1H, C^{Ar}H), 3.66 – 3.48 (m, 1H, CH-(CH₃)₂), 1.95 (s, 3H, C^{Ar}CH₃), 1.31 (d, 3J (H,H) = 6.9 Hz, 6H, CH-(CH₃)₂), 1.12 (s, 9H, C-(CH₃)₃) ppm (Figure S4)

¹³C NMR (76 MHz, CDCl₃) $\delta = 152.6$ (C_q, C^{Ar}), 135.8 (C_q, C^{Ar}), 135.6 (C_q, C^{Ar}), 135.5 (C^{Ar}), 133.2 (C_q, C^{Ar}), 129.9 (C^{Ar}), 127.9 (C^{Ar}), 125.8 (C^{Ar}), 121.8 (C^{Ar}), 119.7 (C^{Ar}), 26.8 (C-(CH₃)₃), 26.7 (C-(CH₃)₃), 23.2 (CH-(CH₃)₂), 21.0 (CH-(CH₃)₂), 19.7 (C^{Ar}CH₃) ppm (Figure S4)

HRMS (EI): calcd for [M^+]: 388.2222; found: 388.2232

2-((*tert*-Butyldimethylsilyl)oxy)-4-methylbenzaldehyde (**S1**)



S1

In a flame dried 250 mL round bottom flask equipped with a Schlenk adapter 3.00 g 2-hydroxy-4-methylbenzaldehyde (22.1 mmol, 1.00 eq.) and 3.01 g imidazole (44.3 mmol, 2.01 eq.) were dissolved in 100 mL abs. DCM. Then 4.33 g *tert*-butylchlorodimethylsilane (28.7 mmol, 1.30 eq.) were added to the solution. The reaction mixture was stirred at RT and during the reaction, a white precipitate formed. After full conversion was detected by TLC (after 16 h) the reaction mixture was quenched by the addition of 100 mL H₂O. The phases were separated and the aqueous phase was extracted with DCM (3 x 100 mL). The combined organic phases were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The excess of TBDMSCl was removed via Kugelrohr distillation (60 °C, 0.12 mbar) and the crude product was purified via column chromatography (120 g SiO₂, eluent: cyclohexane/EtOAc = 20/1).

Yield: 4.39 g (79 %), colourless oil, C₁₄H₂₂O₂Si [250.41 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 10.39 (s, 1H, CHO), 7.70 (d, ³J = 7.9 Hz, 1H, C^{Ar}H), 6.84 (d, ³J = 7.8 Hz, 1H, C^{Ar}H), 6.67 (s, 1H, C^{Ar}H), 2.35 (s, 3H, C^{Ar}-CH₃), 1.02 (s, 9H, C-(CH₃)₃), 0.27 (s, 6H, Si-(CH₃)₂) ppm (Figure S5)

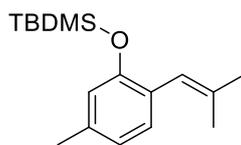
¹³C NMR (76 MHz, CDCl₃) δ = 189.9 (CHO), 159.1 (C_q, C^{Ar}), 147.2 (C_q, C^{Ar}), 128.4 (C^{Ar}), 125.2 (C_q, C^{Ar}), 122.8 (C^{Ar}), 120.8 (C^{Ar}), 25.8 (C-(CH₃)₃), 22.2 (C^{Ar}-CH₃), 18.5 (C-(CH₃)₃), -4.2 (Si-(CH₃)₂) ppm (Figure S5)

HPLC-MS (ESI+, 5_100_Poroshell120-C18EC): *t_R* = 6.12 min; *m/z* (%) = 251 [M+H⁺]

TLC R_f = 0.60 (cyclohexane/EtOAc = 20/1, UV)

HRMS (EI): calcd for [M⁺-*t*Bu]: 193.0685; found: 193.0682

tert-Butyldimethyl(5-methyl-2-(2-methylprop-1-en-1-yl)phenoxy)silane (**S2**)



S2

In a flame dried 250 mL round bottom flask equipped with a Schlenk adapter 6.73 g isopropyltriphenylphosphonium iodide (15.6 mmol, 1.30 eq) were suspended in 100 mL abs. THF. 5.75 mL *n*-BuLi (2.50M in hexane) (14.4 mmol, 1.20 eq) were added slowly to the vigorously stirred reaction mixture at RT. After the addition, the dark orange suspension was stirred at RT for 1 h. The reaction mixture was cooled down to -78 °C in an acetone/dry ice bath and a solution of 3.01 g 2-((*tert*-butyldimethylsilyl)oxy)-4-methylbenzaldehyde (**S1**) (12.0 mmol, 1.00 eq) in 5 mL abs. THF was added. The reaction mixture was stirred at -78 °C for 10 min and then the reaction was allowed to warm up to RT. After 11 h, the reaction mixture was concentrated in vacuum and diluted with 90 mL DCM. The resulting orange suspension was washed with 90 mL H₂O. The aqueous phase was extracted with DCM (2 x 90 mL). The combined organic phases were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via SiO₂ filtration (100 g SiO₂, eluent: cyclohexane).

Yield: 2.95 g (89 %), colorless oil, C₁₇H₂₈OSi [276.50 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 7.05 (d, ³*J* (H,H) = 7.7 Hz, 1H, C^{Ar}H), 6.74 (d, ³*J* (H,H) = 7.5 Hz, 1H, C^{Ar}H), 6.62 (s, 1H, C^{Ar}H), 6.24 (s, 1H, C^{Ar}-CH) 2.29 (s, 3H, C^{Ar}-CH₃), 1.88 (s, 3H, CH₃), 1.77 (s, 3H, CH₃), 1.00 (s, 9H, C-(CH₃)₃), 0.14 (s, 6H, Si-(CH₃)₂) ppm (Figure S6)

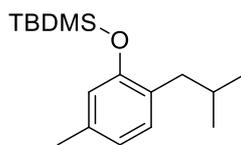
¹³C NMR (76 MHz, CDCl₃) δ = 153.3 (C_q, C^{Ar}), 137.2 (C_q, C^{Ar}), 134.2 (C-(CH₃)₂), 130.3 (C^{Ar}), 127.6 (C_q, C^{Ar}), 122.0 (CH), 121.8 (C^{Ar}), 120.5 (C^{Ar}), 26.5 (C-(CH₃)₂), 25.9 (C-(CH₃)₃), 21.3 (C^{Ar}-CH₃), 19.5 (C-(CH₃)₂), 18.4 (C-(CH₃)₃), -4.3 (Si-(CH₃)₂) ppm (Figure S6)

GC-MS (EI, 70 eV; MT_50_S): *t*_R = 5.93 min; *m/z* (%) = 276 (14) [M⁺], 261 (2) [M⁺-CH₃], 219 (100) [M⁺-*t*Bu]

TLC R_f = 0.28 (cyclohexane, UV)

HRMS (EI): calcd for [M⁺]: 276.1909; found: 276.1913

tert-Butyl(2-isobutyl-5-methylphenoxy)dimethylsilane (**6**)



6

The reduction of the double bond was performed using a H-CubeTM flow reactor with a 10 % Pd/C cartridge (THS01111). A solution of 2.30 g *tert*-butyldimethyl(5-methyl-2-(2-methylprop-1-en-1-yl)phenoxy)silane (**5**) (8.31 mmol, 1.00 eq.) in 170 ml MeOH was reduced in a continuous flow of hydrogen (flow: 1 mL/min, 60 °C, pressure: 52.5 bar). Then the solvent was removed under reduced pressure and the product was used without further purification.

Yield: 2.06 g (89 %), colorless oil, C₁₇H₃₀OSi [278.51 g/mol]

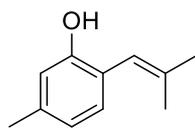
¹H NMR (300 MHz, CDCl₃) δ = 6.96 (d, ³J (H,H) = 7.5 Hz, 1H, C^{Ar}H), 6.68 (d, ³J (H,H) = 7.5 Hz, 1H, C^{Ar}H), 6.59 (s, 1H, C^{Ar}H), 2.40 (d, ³J (H,H) = 7.1 Hz, 1H, C^{Ar}-CH₂) 2.27 (s, 3H, C^{Ar}-CH₃), 1.87 (m, 1H, CH-(CH₃)₂), 1.01 (s, 9H, C-(CH₃)₃), 0.88 (d, ³J (H,H) = 6.6 Hz, 6H, CH-(CH₃)₂), 0.23 (s, 6H, Si-(CH₃)₂) ppm (Figure S7)

¹³C NMR (76 MHz, CDCl₃) δ = 153.7 (C_q, C^{Ar}), 136.5 (C_q, C^{Ar}), 131.1 (C^{Ar}), 129.3 (C_q, C^{Ar}), 121.5 (C^{Ar}), 119.3 (C^{Ar}), 39.7 (CH₂), 28.9 (CH-(CH₃)₂), 26.0 (C-(CH₃)₃), 22.7 (CH-(CH₃)₂), 21.3 (C^{Ar}-CH₃), 18.4 (C-(CH₃)₃), -3.9 (Si-(CH₃)₂) ppm (Figure S7)

GC-MS (EI, 70 eV; MT_50_S): *t*_R = 5.78 min; *m/z* (%) = 278 (50) [M⁺], 263 (5) [M⁺-CH₃], 235 (12) [M⁺-*i*Pr], 221 (100) [M⁺-*t*Bu]

HRMS (EI): calcd for [M⁺]: 278.2066; found: 278.2068

5-Methyl-2-(2-methylprop-1-en-1-yl)phenol (**S3**)



S3

In a 250 mL flame dried Schlenk flask 5.00 g 2-hydroxy-4-methylbenzaldehyde (36.7 mmol, 1 eq.) were dissolved in 50 mL abs. THF under an argon and the solution was cooled to 0 °C. 45.9 mL 2.0M *i*PrMgCl (91.8 mmol, 2.5 eq.) were slowly added at 0 °C. After full addition the reaction mixture was allowed to warm up to RT and stirred for 2 h. The reaction mixture was quenched by addition of 30 mL sat. NH₄Cl solution, neutralized with 150 mL 1.0M HCl aq. solution and extracted with DCM (3 x 100 ml). The combined organic phases were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The residue was dissolved in 30 mL toluene in a 120 mL ace pressure tube and stirred at 170 °C for 2 d. The reaction mixture was cooled down and the solvent was removed using rotary evaporator. The crude product was purified via column chromatography (150 g SiO₂, eluent: cyclohexane/EtOAc = 50/1).

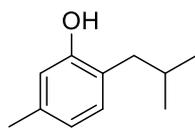
Yield: 4.97 g (83 %), colorless oil, C₁₁H₁₄O₂ [178.23 g/mol].

¹H NMR (300 MHz, CDCl₃) δ = 6.93 (d, ³*J* (H,H) = 7.5 Hz, 1H, C^{Ar}H), 6.80 – 6.62 (m, 2H, C^{Ar}H), 6.09 (s, 1H, C^{Ar}-CH), 4.96 (s, 1H, OH), 2.30 (s, 3H, C^{Ar}-CH₃), 1.93 (s, 3H, C-CH₃), 1.68 (s, 3H, C-CH₃) ppm (Figure S8)

¹³C NMR (76 MHz, CDCl₃) δ = 152.8 (C_q, C^{Ar}), 140.3 (C_q, C^{Ar}), 138.4 (C_q, C-(CH₃)₂), 129.7 (C^{Ar}), 121.9 (C^{Ar}), 121.1 (C^{Ar}), 118.8 (C^{Ar}-CH), 115.6 (C_q, C^{Ar}), 26.0 (C-(CH₃)₂), 21.3 (C^{Ar}-CH₃), 19.6 (C-(CH₃)₂) ppm (Figure S8)

TLC: R_f = 0.39 (cyclohexane/EtOAc = 20/1, UV)

2-Isobutyl-5-methylphenol (**8**)



8

In a 250 mL flame dried Schlenk flask 4.97 g 5-methyl-2-(2-methylprop-1-en-1-yl)phenol (**S3**) (30.7 mmol, 1 eq.) were dissolved in MeOH under argon and 650 mg 10 % Pd/C (614 μ mol, 0.02 eq) were added under an argon. After ensuring hydrogen atmosphere by evacuation and flushing with hydrogen from a balloon the reaction mixture was vigorously stirred at RT for 24 h. After detection of full conversion by GC-MS the catalyst was removed by filtration through a pad of Celite[®] (3 g) under argon atmosphere. The solvent was removed under reduced pressure. The crude product was purified via Kugelrohr distillation (120 °C, 0.37 mbar).

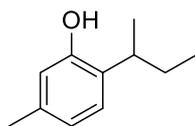
Yield: 4.63 g (93 %), colorless oil, C₁₁H₁₄O₂ [178.23 g/mol].

¹H NMR (300 MHz, CDCl₃) δ = 6.97 (d, ³J (H,H) = 7.6 Hz, 1H, C^{Ar}H), 6.69 (d, ³J (H,H) = 7.4 Hz, 1H, C^{Ar}H), 6.60 (s, 1H, C^{Ar}H), 4.63 (s, 1H, OH), 2.45 (d, ³J (H,H) = 7.2 Hz, 2H, C^{Ar}-CH₂), 2.29 (s, 3H, C^{Ar}-CH₃), 2.01 – 1.84 (m, 1H, CH), 0.94 (d, ³J (H,H) = 6.6 Hz, 6H, CH-(CH₃)₂) ppm (Figure S9)

¹³C NMR (76 MHz, CDCl₃) δ = 153.6 (C_q, C^{Ar}), 137.2 (C_q, C^{Ar}), 131.2 (C^{Ar}), 124.4 (C_q, C^{Ar}), 121.5 (C^{Ar}), 116.1 (C^{Ar}), 39.1 (C^{Ar}-CH₂), 29.1 (CH), 22.5 (CH-(CH₃)₂), 21.1 (C^{Ar}-CH₃) ppm (Figure S9)

TLC: R_f = 0.56 (cyclohexane/EtOAc = 5/1, UV)

2-(*sec*-Butyl)-5-methylphenol (**10**)



10

In a 250 mL flame dried Schlenk flask 3.00 g 1-(2-hydroxy-4-methylphenyl)ethan-1-one (20.0 mmol, 1 eq.) were dissolved in 50 mL abs. THF under argon and the solution was cooled

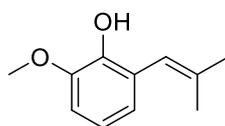
to 0 °C. 20 mL 3M EtMgBr in THF (60 mmol, 3 eq.) were slowly added at 0 °C. After full addition the reaction mixture was allowed to warm up to RT and stirred for 2 h. The reaction mixture was quenched by addition of 25 mL sat. NH₄Cl solution, neutralized with 100 mL 1M HCl aq. solution and extracted with DCM (3x50 ml). The combined organic phases were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The residue was purified via Kugelrohr distillation (100 °C, 0.17 mbar). The 2.08 g distillate (12.8 mmol, 1 eq.) were dissolved in 50 mL MeOH in a 100 mL Schlenk flask under argon and 272 mg 10 % Pd/C (257 μmol, 0.02 eq.) were added under argon contracurrent. After ensuring hydrogen atmosphere by evacuation and flushing with hydrogen from a balloon the reaction mixture was vigorously stirred at RT for 22 h. After detection of full conversion by GC-MS the catalyst was removed by filtration through a pad of Celite[®] (2 g) under argon atmosphere. The solvent was removed under reduced pressure. The product was used without further purification.

Yield: 2.07 g (63 %), colorless oil, C₁₁H₁₄O₂ [178.23 g/mol].

¹H NMR (300 MHz, CDCl₃) δ = 7.04 (d, ³J (H,H) = 7.7 Hz, 1H, C^{Ar}H), 6.74 (d, ³J (H,H) = 7.5 Hz, 1H, C^{Ar}H), 6.59 (s, 1H, C^{Ar}H), 4.66 (s, 1H, OH), 3.06 – 2.77 (m, 1H, C^{Ar}-CH), 2.28 (s, 3H, C^{Ar}-CH₃), 1.80 – 1.45 (m, 2H, CH-CH₂-CH₃), 1.23 (d, ³J (H,H) = 6.9 Hz, 1H, CH-CH₃), 0.88 (t, ³J (H,H) = 7.4 Hz, 1H, CH₂-CH₃) ppm (Figure S10)

¹³C NMR (76 MHz, CDCl₃) δ = 153.0 (C_q, C^{Ar}), 136.6 (C_q, C^{Ar}), 130.3 (C_q, C^{Ar}), 127.1 (C^{Ar}), 121.8 (C^{Ar}), 116.2 (C^{Ar}), 33.9 (C^{Ar}-CH), 30.0 (CH-CH₂-CH₃), 21.0 (C^{Ar}-CH₃), 20.7 (CH-CH₃), 12.3 (CH₂-CH₃) ppm (Figure S10)

2-Methoxy-6-(2-methylprop-1-en-1-yl)phenol (**S4**)



S4

In a 250 mL flame dried Schlenk flask 4.56 g 2-hydroxy-3-methoxybenzaldehyde (30.0 mmol, 1 eq.) were dissolved in 50 mL abs. THF under argon and the solution was cooled to 0 °C. 37.5 mL of 2M *i*PrMgCl in THF (75 mmol, 2.5 eq.) were slowly added at 0 °C. After full addition the reaction mixture was allowed to warm up to RT and stirred for 2 h. The reaction mixture was quenched by addition of 25 mL sat. NH₄Cl solution, neutralized by 100 mL 1M HCl aq. solution and extracted with DCM (2x50 ml). The combined organic phases were dried

over Na₂SO₄ and the solvent was removed under reduced pressure. The residue was dissolved in 30 mL toluene in a 120 mL ace pressure tube and stirred at 170 °C for 16 h. The reaction mixture was cooled down and the solvent was removed using a rotary evaporator. The crude product was purified via column chromatography (120 g SiO₂, eluent: cyclohexane/EtOAc = 20/1).

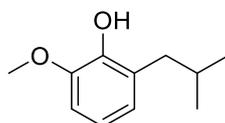
Yield: 3.78 g (70 %), colorless oil, C₁₁H₁₄O₂ [178.23 g/mol].

¹H NMR (300 MHz, CDCl₃) δ = 6.90 – 6.66 (m, 3H, C^{Ar}H), 6.30 (s, 1H, C^{Ar}-CH), 5.70 (s, 1H, OH), 3.89 (s, 3H, O-CH₃), 1.94 (s, 3H, C-CH₃), 1.80 (s, 3H, C-CH₃) ppm (Figure S11)

¹³C NMR (76 MHz, CDCl₃) δ = 146.6 (C_q, C^{Ar}), 143.1 (C_q, C^{Ar}), 137.0 (C_q, C-(CH₃)₂), 125.2 (C_q, C^{Ar}), 122.7 (C^{Ar}), 119.6 (C^{Ar}-CH), 119.1 (C^{Ar}), 108.9 (C^{Ar}), 56.2 (O-CH₃), 26.6 (C-CH₃), 19.8 (C-CH₃) ppm (Figure S11)

TLC: R_f = 0.39 (DCM/MeOH = 5/1, UV)

2-Isobutyl-6-methoxyphenol (**12**)



12

In a 250 mL Schlenk flask 3.60 g 2-methoxy-6-(2-methylprop-1-en-1-yl)phenol (**S4**) (20.1 mmol, 1 eq.) were dissolved in 70 mL MeOH under argon and 425 mg 10 % Pd/C (402 μmol, 0.02 eq) were added under an argon contracurrent. After ensuring hydrogen atmosphere by evacuation and flushing with hydrogen from balloon the reaction mixture was vigorously stirred at RT for 24 h. After detection of full conversion by GC-MS the catalyst was removed by filtration through a pad of Celite[®] (2 g) under argon atmosphere. The solvent was removed under reduced pressure. The product was used without further purification.

Yield: 3.50 g (97 %), colorless solid, C₁₁H₁₄O₂ [178.23 g/mol].

¹H NMR (300 MHz, CDCl₃) δ = 6.83 – 6.64 (m, 3H, C^{Ar}H), 5.66 (s, 1H, OH), 3.88 (s, 3H, O-CH₃), 2.52 (d, ³J (H,H) = 7.2 Hz, 2H, C^{Ar}-CH₂), 2.06 – 1.87 (m, 1H, CH), 0.93 (d, ³J (H,H) = 6.6 Hz, 6H, CH-(CH₃)₂) ppm (Figure S12)

^{13}C NMR (76 MHz, CDCl_3) δ = 146.4 (C_q , C^{Ar}), 143.9 (C_q , C^{Ar}), 127.8 (C_q , C^{Ar}), 123.6 (C^{Ar}), 119.0 (C^{Ar}), 108.3 (C^{Ar}), 56.1 (O- $\underline{\text{C}}\text{H}_3$), 39.1 (C^{Ar} - $\underline{\text{C}}\text{H}_2$), 28.9 (CH), 22.7 (CH-($\underline{\text{C}}\text{H}_3$) $_2$) ppm (Figure S12)

$\text{m.p.}^{\text{exp}} = 33\text{-}34^\circ\text{C}$

General Protocol for the Anodic Cross-Coupling Reactions in a Beaker-Type Cell – GP1

A solution of phenol **A** (1.9 mmol, 1 eq.), phenol **B** (1.9 – 3.8 mmol, 1 – 2 eq.) and tetrabutylammonium tetrafluoroborate ($[\text{TBA}][\text{BF}_4]$) (740 mg, 2.25 mmol) in 25 mL 1,1,1,3,3,3-hexafluoropropan-2-ol was transferred into an undivided beaker-type cell equipped with a boron-doped diamond (BDD) anode and cathode. A constant current electrolysis with a current density of 5.9 or 7.2 mA/cm^2 was performed at room temperature. After application of 2.2 F per mole **A** the electrolysis was stopped, and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (Figure S1).

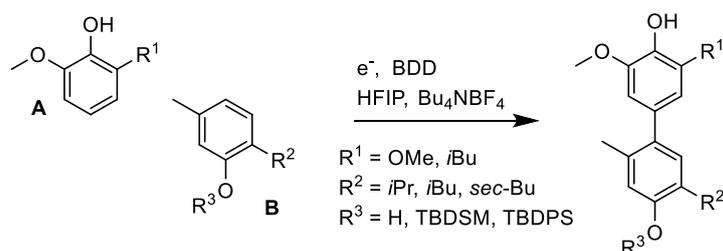


Figure S1. Anodic Cross-Coupling Reactions.

The experiments were carried out in a 25 mL beaker-type cell which consists of a simple glass beaker. The cells were homemade by the university's mechanical shop (JGU Mainz, Germany). The cell is capped with a teflon plug, which allows the precise alignment of the used BDD electrodes (Figure S2) (active used surface 2.0 cm x 4.5 cm, 8 mm distance between electrodes).

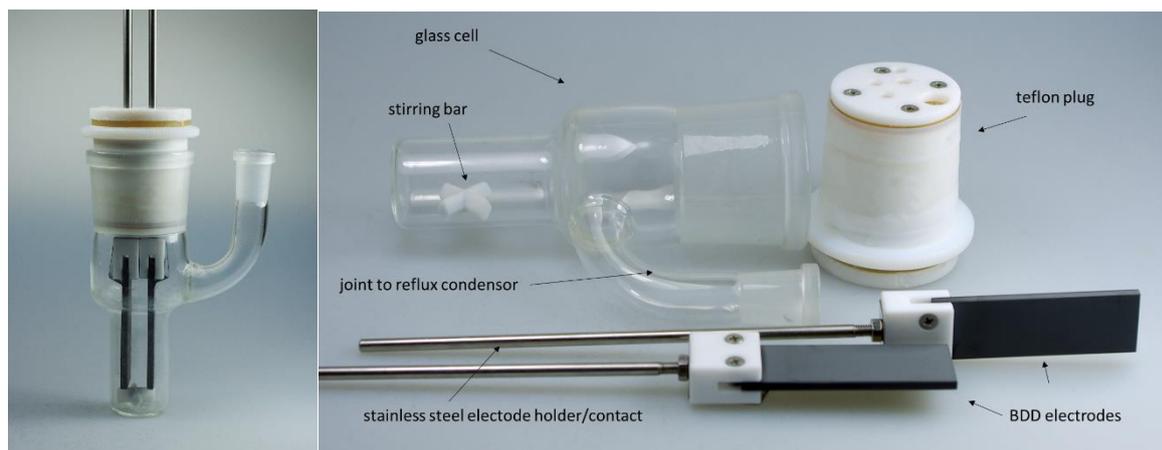
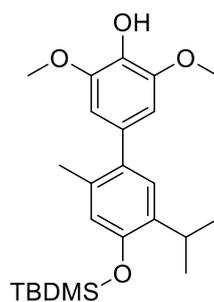


Figure S2. Electrolysis set up.

3,5-Dimethoxy-4'-(((1,1-dimethylethyl)dimethylsilyl)oxy)-4-hydroxy-2'-methyl-5'-(1-methylethyl)-biphenyl (**3**)



3

According to the general protocol **GP1**, 293 mg 2,6-dimethoxyphenol (**1**) (1.9 mmol, 1.0 eq.), 1.00 g *tert*-Butyl(2-isopropyl-5-methylphenoxy)-dimethylsilane (**2**) (3.8 mmol, 2.0 eq.) and 740 mg [TBA][BF₄] (2.25 mmol, 0.09 M) were dissolved in 25 mL HFIP and transferred into a beaker-type cell. After 2.2 F were passed in a constant current electrolysis with a current density of 5.9 mA/cm² at room temperature the electrolysis was stopped. The solvent was removed under reduced pressure. The crude product was purified via column chromatography (50 g SiO₂, eluent: cyclohexane/EtOAc = 4/1).

Yield: 213 mg (27 %), colorless oil, C₂₄H₃₆O₄Si [416.63 g/mol]

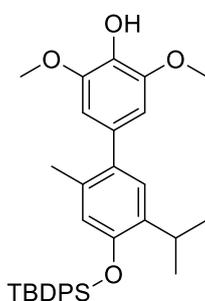
¹H NMR (300 MHz, CDCl₃) δ = 7.06 (s, 1H, C^{Ar}H), 6.67 (s, 1H, C^{Ar}H), 6.53 (s, 2H, C^{Ar}H), 5.49 (bs, 1H, OH), 3.90 (s, 6H, OCH₃), 3.38-3.20 (m, 1H, CH), 2.21 (s, 3H, C^{Ar}-CH₃), 1.22 (d, ³J = 6.9 Hz, 6H, CH-(CH₃)₂), 1.04 (s, 9H, C-(CH₃)₃), 0.29 (s, 6H, Si-CH₃) ppm (Figure S13)

^{13}C NMR (76 MHz, CDCl_3) δ = 152.0 (C_q , C^{Ar}), 146.7 (C_q , C^{Ar}), 136.4 (C_q , C^{Ar}), 135.0 (C_q , C^{Ar}), 133.6 (C_q , C^{Ar}), 133.4 (C_q , C^{Ar}), 127.7 (C^{Ar}), 119.9 (C^{Ar}), 106.5 (C^{Ar}), 56.5 (O-CH₃), 26.6 ($\text{CH}-(\text{CH}_3)_2$), 25.9 (C-(CH_3)₃), 23.1 ($\text{CH}-(\text{CH}_3)_2$), 20.4 ($\text{C}^{\text{Ar}}-\text{CH}_3$), 18.4 ($\text{C}-(\text{CH}_3)_3$), -3.9 (Si-(CH₃)₂) ppm (Figure S13)

TLC R_f = 0.28 (DCM, UV)

HRMS (MALDI): calcd for [M^+]: 416.2383; found: 416.2389

3,5-Dimethoxy-4'-(((1,1-dimethylethyl)diphenylsilyl)oxy)-4-hydroxy-2'-methyl-5'-(1-methylethyl)-biphenyl (**5**)



5

According to the general protocol **GPI**, 293 mg 2,6-dimethoxyphenol (**1**) (1.9 mmol, 1.0 eq.), 739 mg *tert*-butyl(2-isopropyl-5-methylphenoxy)-diphenylsilane (**4**) (1.9 mmol, 1.0 eq.) and 740 mg [TBA][BF₄] (2.25 mmol, 0.09 M) were dissolved in 25 mL HFIP and transferred into a beaker-type cell. After 2.2 F were passed in a constant current electrolysis with a current density of 5.9 mA/cm² at room temperature the electrolysis was stopped. The solvent was removed under reduced pressure. The crude product was purified via column chromatography (50 g SiO₂, eluent: cyclohexane/EtOAc = 4/1).

Yield: 245 mg (23 %), colorless solid, C₃₄H₄₀O₄Si [540.78 g/mol]

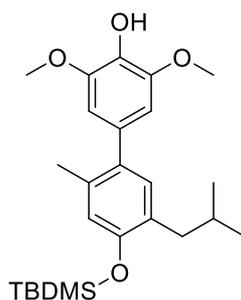
^1H NMR (300 MHz, CDCl_3): δ = 7.77 (d, 3J (H,H) = 6.2 Hz, 4H, $\text{C}^{\text{Ar}}\text{H}$), 7.52 – 7.33 (m, 6H, $\text{C}^{\text{Ar}}\text{H}$), 7.08 (s, 1H, $\text{C}^{\text{Ar}}\text{H}$), 6.49 (s, 2H, $\text{C}^{\text{Ar}}\text{H}$), 6.31 (s, 1H, $\text{C}^{\text{Ar}}\text{H}$), 5.46 (s, 1H, OH), 3.88 (s, 6H, O-CH₃), 3.68 – 3.52 (m, 1H, $\text{C}^{\text{Ar}}-\text{CH}$), 1.85 (s, 3H, $\text{C}^{\text{Ar}}-\text{CH}_3$), 1.33 (d, 3J (H,H) = 6.9 Hz, 6H, CH-(CH₃)₂), 1.13 (s, 9H, C-(CH₃)₃) ppm (Figure S14)

^{13}C -NMR (76 MHz, CDCl_3): δ = 151.7 (C_q , C^{Ar}), 146.7 (C_q , C^{Ar}), 135.7 (C_q , C^{Ar}), 135.7 (C^{Ar}), 134.8 (C_q , C^{Ar}), 133.6 (C_q , C^{Ar}), 133.5 (C_q , C^{Ar}), 133.1 (C_q , C^{Ar}), 133.1 (C_q , C^{Ar}), 130.0 (C^{Ar}),

127.9 (C^{Ar}), 127.4 (C^{Ar}), 120.4 (C^{Ar}), 106.5 (C^{Ar}), 56.5 (O-CH₃), 26.9 (C^{Ar}-CH), 26.8 (C-(CH₃)₃), 23.2 (CH-(CH₃)₂), 20.2 (C^{Ar}-CH₃), 19.8 (C-(CH₃)₃) ppm (Figure S14)

HRMS (EI): calcd for [M⁺]: 540.2696; found: 540.2701

3,5-Dimethoxy-4'-(((1,1-dimethylethyl)dimethylsilyl)oxy)-4-hydroxy-2'-methyl-5'-(1-methylethyl)-biphenyl (**7**)



7

According to the general protocol **GPI** 293 mg 2,6-dimethoxyphenol (**1**) (1.9 mmol, 1.0 eq.), 1.06 g *tert*-butyl(2-isobutyl-5-methylphenoxy)dimethylsilane (**6**) (3.8 mmol, 2.0 eq.) and 740 mg [TBA][BF₄] (2.25 mmol, 0.09 M) were dissolved in 25 mL HFIP and transferred into a beaker-type cell. After 2.2 F were passed in a constant current electrolysis with a current density of 7.2 mA/cm² at room temperature the electrolysis was stopped. The solvent was removed under reduced pressure. The crude product was purified via column chromatography (50 g SiO₂, eluent: cyclohexane/EtOAc = 4/1).

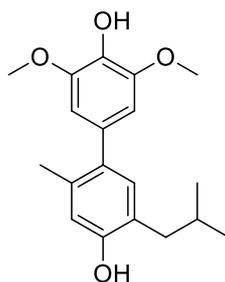
Yield: 220 mg (27 %), colorless solid, C₂₅H₃₈O₄Si [430.66 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 6.96 (s, 1H, C^{Ar}H), 6.66 (s, 1H, C^{Ar}H), 6.52 (s, 2H, C^{Ar}H), 5.48 (s, 1H, OH), 3.90 (s, 6H, O-CH₃), 2.44 (d, ³J (H,H) = 7.0 Hz, 2H, C^{Ar}-CH₂), 2.22 (s, 3H, C^{Ar}-CH₃), 1.97 – 1.80 (m, 1H, CH-(CH₃)₂), 1.04 (s, 9H, C-(CH₃)₃), 0.92 (d, ³J (H,H) = 6.6 Hz, 6H, CH-(CH₃)₂), 0.27 (s, 6H, Si-(CH₃)₂) ppm (Figure S15)

¹³C NMR (76 MHz, CDCl₃) δ = 152.9 (C_q, C^{Ar}), 146.7 (C_q, C^{Ar}), 134.6 (C_q, C^{Ar}), 133.7 (C_q, C^{Ar}), 133.5 (C_q, C^{Ar}), 133.4 (C_q, C^{Ar}), 132.6 (C^{Ar}), 129.7 (C_q, C^{Ar}), 120.0 (C^{Ar}), 106.5 (C^{Ar}), 56.5 (O-CH₃), 39.6 (C^{Ar}-CH₂), 29.0 (CH-(CH₃)₂), 26.0 (C-(CH₃)₃), 22.7 (CH-(CH₃)₂), 20.5 (C^{Ar}-CH₃), 18.4 (C-(CH₃)₃), -3.9 (Si-(CH₃)₂) ppm (Figure S15)

HRMS (EI): calcd for [M⁺]: 430.2539; found: 430.2540

5-Isobutyl-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**9**)



9

According to the general protocol **GP1** 308 mg 2,6-dimethoxyphenol (**1**) (2.0 mmol, 1.0 eq.), 492 mg 2-isobutyl-5-methylphenol (**8**) (2.85 mmol, 1.5 eq.) and 740 mg [TBA][BF₄] (2.25 mmol, 0.09 M) were dissolved in 25 mL HFIP and transferred into a beaker-type cell. After 2.2 F were passed in a constant current electrolysis with a current density of 5.9 mA/cm² at room temperature the electrolysis was stopped. The solvent was removed under reduced pressure. The crude product was purified via column chromatography (30 g SiO₂, eluent: cyclohexane/EtOAc = 5/1 → 4/1).

Yield: 405 mg (64 %), colorless solid, C₁₉H₂₄O₄ [316.40 g/mol].

¹H NMR (300 MHz, CDCl₃): δ = 6.95 (s, 1H, C^{Ar}H), 6.68 (s, 1H, C^{Ar}H), 6.51 (s, 2H, C^{Ar}H), 5.51 (s, 1H, OH), 4.74 (s, 1H, OH), 3.89 (s, 6H, O-CH₃), 2.48 (d, ³J (H,H) = 7.1 Hz, 2H, C^{Ar}-CH₂), 2.21 (s, 3H, C^{Ar}-CH₃), 1.94 (m, 1H; CH), 0.96 (d, ³J (H,H) = 6.6 Hz, 6H; CH-(CH₃)₂) ppm (Figure S16)

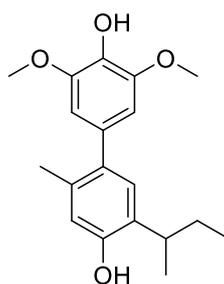
¹³C-NMR (76 MHz, CDCl₃): δ = 152.7 (C_q, C^{Ar}), 146.6 (C_q, C^{Ar}), 134.5 (C_q, C^{Ar}), 134.3 (C_q, C^{Ar}), 133.5 (C_q, C^{Ar}), 133.1 (C_q, C^{Ar}), 124.7 (C_q, C^{Ar}), 132.5 (C^{Ar}), 116.9 (C^{Ar}), 166.4 (C^{Ar}), 56.4 (O-CH₃), 38.9 (C^{Ar}-CH₂), 29.1 (C^{Ar}-CH₃), 22.6 (CH-(CH₃)₂) ppm (Figure S16)

TLC: R_f = 0.26 (cyclohexane/EtOAc = 3/1, UV)

mp = 135 - 137 °C

HRMS (EI): calcd for [M⁺]: 316.1675; found: 316.1683

5-(*sec*-Butyl)-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**11**)



11

According to the general protocol **GP1** 293 mg 2,6-dimethoxyphenol (**1**) (1.9 mmol, 1.0 eq.), 467 mg 2-(*sec*-butyl)-5-methylphenol (**10**) (2.85 mmol, 1.5 eq.) and 740 mg [TBA][BF₄] (2.25 mmol, 0.09 M) were dissolved in 25 mL HFIP and transferred into a beaker-type cell. After 2.2 F were passed in a constant current electrolysis with a current density of 5.9 mA/cm² at room temperature the electrolysis was stopped. The solvent was removed under reduced pressure. The crude product was purified via column chromatography (30 g SiO₂, eluent: cyclohexane/EtOAc = 5/1 → 4/1).

Yield: 414 mg (69 %), colorless oil, C₁₉H₂₄O₄ [316.40 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 7.01 (s, 1H, C^{Ar}H), 6.67 (s, 1H, C^{Ar}H), 6.51 (s, 2H, C^{Ar}H), 5.52 (s, 1H, OH), 4.83 (s, 1H, OH), 3.90 (s, 6H, O-CH₃), 3.03 – 2.86 (m, 1H, C^{Ar}-CH), 2.20 (s, 3H, C^{Ar}-CH₃), 1.76 – 1.55 (m, 2H, CH-CH₂), 1.25 (d, ³J(H,H) = 6.9 Hz, 3H, CH-CH₃), 0.91 (t, ³J(H,H) = 7.3 Hz, 3H, CH₂-CH₃) ppm (Figure S17)

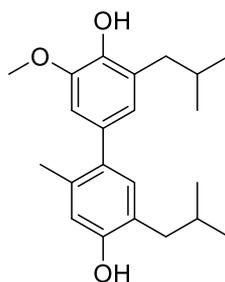
¹³C NMR (76 MHz, CDCl₃) δ = 152.3 (C_q, C^{Ar}), 146.7 (C_q, C^{Ar}), 135.0 (C_q, C^{Ar}), 133.9 (C_q, C^{Ar}), 133.6 (C_q, C^{Ar}), 133.4 (C_q, C^{Ar}), 130.7 (C_q, C^{Ar}), 128.7 (C^{Ar}), 117.1 (C^{Ar}), 106.5 (C^{Ar}), 56.5 (O-CH₃), 34.1 (C^{Ar}-CH), 30.0 (CH-CH₂), 20.6 (C^{Ar}-CH₃), 20.2 (CH-CH₃), 12.4 (CH₂-CH₃) ppm (Figure S17)

TLC: R_f = 0.26 (cyclohexane/EtOAc = 3/1, UV)

mp = 128 - 131 °C

HRMS (ED): calcd for [M⁺]: 316.1675; found: 316.1680

3',5-Diisobutyl-5'-methoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**13**)



13

According to the general protocol **GP1** 343 mg 2-isobutyl-6-methoxyphenol (**12**) (1.9 mmol, 1.0 eq.), 624 mg 2-isobutyl-5-methylphenol (**8**) (3.8 mmol, 2.0 eq.) and 740 mg [TBA][BF₄] (2.25 mmol, 0.09 M) were dissolved in 25 mL HFIP and transferred into a beaker-type cell. After 2.2 F were passed in a constant current electrolysis with a current density of 5.9 mA/cm² at room temperature the electrolysis was stopped. The solvent was removed under reduced pressure. The crude product was purified via column chromatography (50 g SiO₂, eluent: cyclohexane/EtOAc = 20/1 → 10/1). The product was contaminated with 42 % of the homo coupled product of 2-isobutyl-6-methoxyphenol, which was removed after nonaflation.

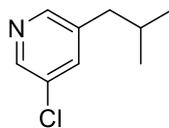
Yield: 181 mg (27 %), colorless oil, C₂₂H₃₀O₃ [342.48 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 6.95 (s, 1H, C^{Ar}H), 6.88 (s, 1H, C^{Ar}H), 6.69 – 6.63 (m, 2H, C^{Ar}H), 3.89 (s, 3H, O-CH₃), 2.51 – 2.40 (m, 4H, 2 C^{Ar}-CH₂), 2.22 (s, 3H, C^{Ar}-CH₃), 2.02 – 1.87 (m, 2H, 2 CH₂-CH), 0.99 – 0.86 (m, 12H, 2 CH-(CH₃)₂) ppm (Figure S18)

TLC: R_f = 0.39 (cyclohexane/EtOAc = 5/1, UV and CAM)

HRMS (EI): calcd for [M⁺]: 342.2195; found: 342.2193

3-Chloro-5-isobutylpyridine (**15**)



15

A flame dried three-neck 500 mL round bottom flask equipped with argon inlet was charged with 400 mL abs. THF, 25 mL abs. NMP, 11.3 g 3,5-dichloropyridine (**14**) (76.2 mmol, 1.00 eq) and 1.36 g Fe(acac)₃ (3.85 mmol, 0.05 eq). The obtained red solution was cooled down to 0 °C in an ice bath and 37 mL *i*PrMgCl 2.06M in THF (76.2 mmol, 1.00 eq) were added over 20 min. The solution was allowed to warm up to RT and the reaction was monitored via GC-MS. After 5 h, the conversion was not increasing further and the catalyst was removed by filtration through a pad of silica (eluted with 400 mL EtOAc). The yellowish filtrate was concentrated *in vacuo* to a volume of 30 mL, washed with sat. NaHCO₃ solution (3x30 mL) and dried over Na₂SO₄. The crude product was again concentrated *in vacuo* and purified via column chromatography (500 g SiO₂, eluent: cyclohexane/EtOAc = 10/1).

Yield: 6.85 g (53 %) clear liquid, C₉H₁₂ClN [169.65 g/mol]

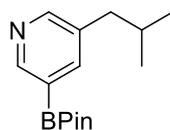
¹H NMR (300 MHz, CDCl₃) δ = 8.40 (d, ⁴*J* (H,H) = 2.0 Hz, 1H, C^{Ar}H), 8.28 (d, ⁴*J* (H,H) = 1.3 Hz, 1H, C^{Ar}H), 7.45 (s, 1H, C^{Ar}H), 2.46 (d, ³*J* (H,H) = 7.2 Hz, 2H, C^{Ar}-CH₂), 1.86 (m, 1H, CH₂-CH), 0.91 (d, ³*J* (H,H) = 6.4 Hz, 6H, CH-(CH₃)₂) ppm (Figure S19)

¹³C NMR (76 MHz, CDCl₃) δ = 148.4 (C^{Ar}), 146.3 (C^{Ar}), 138.3 (C_q, C^{Ar}), 136.3 (C^{Ar}), 131.8 (C_q, C^{Ar}), 42.0 (C^{Ar}-CH₂), 30.0 (CH₂-CH), 22.3 (CH-(CH₃)₂) ppm (Figure S19)

GC-MS (EI, 70 eV; MT_50_S): *t*_R = 4.60 min; *m/z* (%) = 169 (44) [M⁺], 127 (100) [M⁺-C₃H₇]

TLC R_f = 0.30 (cyclohexane/EtOAc = 10/1, UV)

3-Isobutyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**16**)



16

A flame dried round bottom flask with Schlenk adapter was charged with 3.01 g 3-chloro-5-isobutylpyridine (**15**) (17.7 mmol, 1.00 eq), 4.96 g bis(pinacolato)diboron (19.5 mmol, 1.10 eq), 98.0 mg Pd₂dba₃ (0.11 mmol, 0.6 mol%) and 143 mg XPhos (0.30 mmol, 1.7 mol%). The round bottom flask was evacuated and flushed with argon (3x). Then, 30 mL abs., degassed 1,4-dioxane were added. The obtained brown-red suspension was stirred overnight at 105 °C. After full conversion was detected by GC-MS, the solvent was removed under reduced pressure. The crude product was dissolved in 100 mL EtOAc, washed with H₂O (100 mL) and the aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were dried over Na₂SO₄, the solvent was removed under reduced pressure and the crude product was further purified via Kugelrohr-distillation (125 °C, 0.1 mbar).

Yield: 4.31 g (93 %) colourless solid, C₁₅H₂₄BNO₂ [261.17 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 8.77 (d, ⁴J (H,H) = 1.3 Hz, 1H, C^{Ar}H), 8.45 (d, ⁴J (H,H) = 1.9 Hz, 1H, C^{Ar}H), 7.84 (s, 1H, C^{Ar}H), 2.46 (d, ³J (H,H) = 7.1 Hz, 2H, C^{Ar}-CH₂), 1.88 (m, 1H, CH₂-CH), 1.34 (s, 12H, C_q-(CH₃)₂), 0.90 (d, ³J (H,H) = 6.6 Hz, 6H, CH-(CH₃)₂) ppm (Figure S20)

¹³C NMR (76 MHz, CDCl₃) δ = 153.0 (C^{Ar}), 152.6 (C^{Ar}), 142.9 (C^{Ar}), 136.1 (C_q, C^{Ar}), 84.3 (O-C_q), 42.4 (C^{Ar}-CH₂), 30.2 (CH₂-CH), 25.0 (C_q-(CH₃)₂), 22.3 (CH-(CH₃)₂) ppm (Figure S20)

GC-MS (EI, 70 eV; MT_50_S): *t_R* = 6.28 min; *m/z* (%) = 261 (65) [M⁺], 246 (100) [M⁺-CH₃], 218 (42) [M⁺-C₃H₇], 162 (67) [M⁺-C₆H₁₂O]

m.p.^{exp} = 70-72 °C

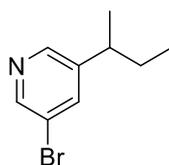
sec-Butylzinc(II) iodide (**S5**)



S5

A flame dried and argon flushed 2-neck round bottom flask was charged with 4.27 g Zn dust (65.4 mmol, 2.01 eq) and subsequently evacuated, heated and flushed with argon (3x). The Zn dust was suspended in 10 mL abs. THF and 140 μ L 1,2-dibromoethane (1.63 mmol, 0.05 eq). The suspension was heated to reflux and cooled down to RT three times before 207 μ L TMSCl (1.63 mmol, 0.05 eq) were added. This suspension was stirred for 10 min and a solution of 3.8 mL 2-iodobutane (32.6 mmol, 1.00 eq) in 8 mL abs. THF was added over 15 min. After the addition was finished, the reaction was stirred at RT for 2 h. The concentration of *sec*-butylzinc(II) iodide was not determined.

3-Bromo-5-(*sec*-butyl)pyridine (**18**)



18

A flame dried 100 mL round bottom flask with Schlenk adapter was charged with 6.44 g 3,5-dibromopyridine (**17**) (27.2 mmol, 1.00 eq), 221 mg PdCl₂(dppf) (0.302 mmol, 0.01 eq) and 20 mL abs. THF were added. The orange coloured suspension changed the colour to black upon addition of 20 mL of the *sec*-butylzinc(II) iodide solution (**S5**) (27.2 mmol, 1.00 eq). The solution was stirred overnight at 70 °C. After full conversion was detected by GC-MS, the reaction mixture was cooled to RT. The solvent was removed under reduced pressure and the crude product was purified via column chromatography (500 g SiO₂, eluent: cyclohexane/EtOAc = 9/1).

Yield: 1.98 g (34 %) pale yellow liquid, C₉H₁₂BrN [214.11 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 8.65 (s, 1H, C^{Ar}H), 8.42 (d, ⁴J (H,H) = 5.0 Hz, 1H, C^{Ar}H), 7.13 (d, ⁴J (H,H) = 5.0 Hz, 1H, C^{Ar}H), 3.20-3.04 (m, 1H, C^{Ar}-CH), 1.73-1.49 (m, 2H, CH-CH₂),

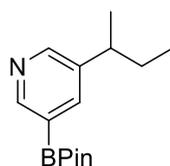
1.21 (d, $^3J(\text{H,H}) = 6.9$ Hz, 3H, CH-CH₃), 0.87 (t, $^3J(\text{H,H}) = 7.4$ Hz, 3H, CH₂-CH₃) ppm (Figure S21)

$^{13}\text{C NMR}$ (76 MHz, CDCl₃) $\delta = 155.3$ (C_q, C^{Ar}), 152.1 (C^{Ar}), 148.5 (C^{Ar}), 123.6 (C_q, C^{Ar}), 122.5 (C^{Ar}), 39.5 (C^{Ar}-CH), 29.5 (CH-CH₂), 20.0 (CH-CH₃), 11.9 (CH₂-CH₃) ppm (Figure S21)

GC-MS (EI, 70 eV; MT_50_S): $t_R = 4.92$ min; m/z (%) = 215 (64) [M⁺], 213 (63) [M⁺], 186 (100) [M⁺-C₂H₅], 104 (100) [M⁺-C₂H₅Br]

TLC $R_f = 0.32$ (cyclohexane/EtOAc = 9/1, UV)

3-(*sec*-Butyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**19**)



19

In a flame dried round bottom flask with Schlenk adapter 1.61 g 3-bromo-5-(*sec*-butyl)pyridine (**18**) (7.51 mmol, 1.00 eq) were dissolved in 15 mL abs. THF. The solution was cooled down to 0 °C in an ice bath and 7.0 mL *i*PrMgCl·LiCl (1.3 M in THF) (9.10 mmol, 1.21 eq) were added. The metal-halogen exchange was monitored by GC-MS. Due to insufficient conversion (83 % after 2.5 h) another 1.20 mL *i*PrMgCl·LiCl (1.3M in THF) (1.56 mmol, 0.21 eq) were added. After one additional hour of stirring, the metal-halogen exchange was completed and 1.9 mL PinBO*i*Pr (9.3 mmol, 1.24 eq) were added. The reaction mixture was allowed to warm up to RT and was stirred overnight. The reaction was quenched by the addition of 50 mL sat. NH₄Cl solution. The phases were separated and the aqueous phase was extracted with DCM (5 x 50 mL). The combined organic layers were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via Kugelrohr-distillation (150 °C, 0.08 mbar).

Yield: 981 mg (50 %) beige solid, C₁₅H₂₄BNO₂ [261.17 g/mol]

$^1\text{H NMR}$ (300 MHz, CDCl₃) $\delta = 8.82$ (s, 1H, C^{Ar}H), 8.53 (d, $^4J(\text{H,H}) = 5.3$ Hz, 1H, C^{Ar}H), 7.15 (d, $^4J(\text{H,H}) = 5.2$ Hz, 1H, C^{Ar}H), 3.50-3.28 (m, 1H, C^{Ar}-CH), 1.69-1.44 (m, 2H, CH-CH₂),

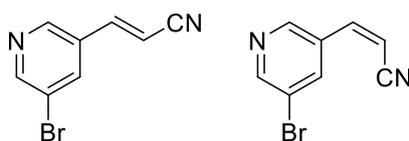
1.34 (s, 12H, C_q-(CH₃)₂), 1.20 (d, ³J (H,H) = 6.9 Hz, 3H, CH-CH₃), 0.82 (t, ³J (H,H) = 7.3 Hz, 3H, CH₂-CH₃) ppm (Figure S22)

¹³C NMR (76 MHz, CDCl₃) δ = 163.7 (C_q, C^{Ar}), 156.1 (C^{Ar}), 151.5 (C^{Ar}), 120.6 (C^{Ar}), 83.9 (O-C_q), 38.3 (C^{Ar}-CH), 31.3 (CH-CH₂), 25.0 (C_q-(CH₃)₂), 20.9 (CH-CH₃), 12.1 (CH₂-CH₃) ppm (Figure S22)

GC-MS (EI, 70 eV; MT_50_S): t_R = 6.18 min; m/z (%) = 261 (10) [M⁺], 246 (12) [M⁺-CH₃], 161 (100) [M⁺-C₆H₁₂O], 146 (36) [M⁺-C₆H₁₂O₂]

m.p.^{exp} = 88-90 °C

(*E,Z*)-3-(5-Bromopyridin-3-yl)acrylonitrile (**20**)



20

A flame dried and argon flushed Schlenk-flask was charged with 2.37 g 3,5-dibromopyridine (**17**) (10.0 mmol, 1 eq.), 2.07 g K₂CO₃ (15.0 mmol, 1.5 eq.), 48.9 mg Pd(OAc)₂ (200 μmol, 0.02 eq.) and 35 mL degassed DMF. 660 μL acrylonitrile (531 mg, 10.0 mmol, 1 eq.) were added to the pale yellow suspension. The reaction mixture was stirred at 90 °C under argon atmosphere for 16 h. The reaction was cooled down, diluted with 100 mL H₂O. The resulting solution was extracted with DCM (3 x 70 mL). The organic phase was dried over Na₂SO₄, filtered and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (75 g SiO₂, 3.0 x 20 cm, eluent: cyclohexane/EtOAc = 4/1 → 2/1). The received mixture of stereoisomers was directly used in the subsequent reduction.

Yield: 1.08 g (*E/Z* = 3.2/1, 58 %), colorless powder, C₈H₅BrN₂ [209.05 g/mol].

(*E*)-3-(5-bromopyridin-3-yl)acrylonitrile

¹H NMR (300 MHz, CDCl₃) δ 8.71 (s, 1H, C^{Ar}H), 8.60 (s, 1H, C^{Ar}H), 7.92 (s, 1H, C^{Ar}H), 7.35 (d, ³J (H,H) = 16.7 Hz, 1H, C^{Ar}-CH), 5.99 (d, ³J (H,H) = 16.7 Hz, 1H, CH-CH) ppm (Figure S23)

¹³C NMR (76 MHz, CDCl₃) δ 153.0 (C^{Ar}), 147.0 (C^{Ar}), 145.5 (C^{Ar}-CH), 136.0 (C^{Ar}), 130.9 (C_q, C^{Ar}), 121.4 (C_q, C^{Ar}), 116.9 (CH-CN), 100.6 (CH-CH) ppm (Figure S23)

GC-MS: (EI, 70 eV; MT_50_S): t_R = 5.80 min; m/z (%): 210 (100) [M⁺], 208 (100) [M⁺], 184 (18) [M⁺-CN], 182 (18) [M⁺-CN], 129 (47) [M⁺- Br]

TLC: R_f = 0.43 (cyclohexane/EtOAc = 2/1, UV)

m.p.^{exp} = 131 – 133 °C

HRMS (DI-EI) calcd (m/z) for [C₈H₅⁷⁹BrN₂⁺]: 207.9628; found: 207.9639

(Z)-3-(5-bromopyridin-3-yl)acrylonitrile

¹H NMR (300 MHz, CDCl₃) δ 8.82 – 8.65 (m, 2H, C^{Ar}H), 8.43 (s, 1H, C^{Ar}H), 7.10 (d, ³J (H,H) = 12.1 Hz, 1H, C^{Ar}-CH), 5.67 (d, ³J (H,H) = 12.1 Hz, 1H; CH-CH) ppm (Figure S24)

¹³C NMR (76 MHz, CDCl₃) δ 152.8 (C^{Ar}), 148.7 (C^{Ar}), 143.6 (C^{Ar}-CH), 137.4 (C^{Ar}), 130.9 (C_q, C^{Ar}), 121.2 (C_q, C^{Ar}), 116.2 (CH-CN), 99.5 (CH-CH) ppm (Figure S24)

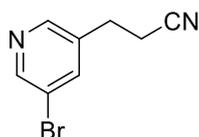
GC-MS: (EI, 70 eV; MT_50_S): t_R = 5.80 min; m/z (%): 210 (100) [M⁺], 208 (100) [M⁺], 184 (17) [M⁺-CN], 182 (17) [M⁺-CN], 129 (44) [M⁺- Br]

TLC: R_f = 0.26 (cyclohexane/EtOAc = 2/1, UV)

m.p.^{exp} = 96 – 99 °C

HRMS (DI-EI) calcd (m/z) for [C₈H₅⁷⁹BrN₂⁺]: 207.9636; found: 207.9639

3-(5-Bromopyridin-3-yl)propanenitrile (**21**)



21

In a 250 mL round-bottom 2.83 g (*E,Z*)-3-(5-bromopyridin-3-yl)acrylonitrile (**20**) (13.5 mmol, 1 eq.), 15.1 g *p*-tosyl hydrazide (81.2 mmol, 6 eq.) and 6.68 g NaOAc (81.2 mmol, 6 eq.) were suspended in 80 mL THF. The suspension was stirred at 70 °C for 24 h. The solvent was removed under reduced pressure and the residue was diluted with 100 mL DCM and extracted

with 150 mL sat. NaHCO₃ solution. The aqueous phase was extracted with DCM (2 x 50 mL). The collected organic phase was dried over Na₂SO₄ and the solvent removed under reduced pressure. The crude product was purified via column chromatography (350 g SiO₂, 5.0 x 35 cm, eluent: cyclohexane/EtOAc = 3/1 → 2/1).

Yield: 2.46 g (86 %), colorless oil, C₈H₇BrN₂ [211.06 g/mol].

¹H NMR (300 MHz, CDCl₃) δ 8.61 (d, ⁴J (H,H) = 1.5 Hz, 1H, C^{Ar}H), 8.44 (s, 1H, C^{Ar}H), 7.75 (s, 1H, C^{Ar}H), 2.96 (t, ³J (H,H) = 7.2 Hz, 2H, C^{Ar}-CH₂), 2.66 (t, ³J (H,H) = 7.2 Hz, 2H; CH₂-CH₂) ppm (Figure S25)

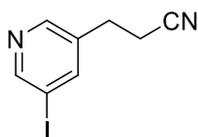
¹³C NMR (76 MHz, CDCl₃) δ 150.2 (C^{Ar}), 147.9 (C^{Ar}), 138.6 (C^{Ar}), 135.2 (C_q, C^{Ar}), 121.0 (C_q, C^{Ar}), 118.2 (CH₂-CN), 28.5 (C^{Ar}-CH₂), 19.0 (CH₂-CH₂) ppm (Figure S25)

GC-MS: (EI, 70 eV; MT_50_S): t_R = 5.82 min; m/z (%): 212 (46) [M⁺], 210 (46) [M⁺], 172 (100) [M⁺-CH₂CN], 170 (100) [M⁺-CH₂CN]

TLC: R_f = 0.29 (cyclohexane/EtOAc = 1/1, UV and CAM)

HRMS (DI-EI) calcd (m/z) for [C₈H₇⁷⁹BrN₂⁺]: 209.9793; found: 209.9777

3-(5-Iodopyridin-3-yl)propanenitrile (**22**)



22

A flame dried round-bottom flask was charged with 351 mg 3-(5-bromopyridin-3-yl)propanenitrile (**21**) (1.66 mmol, 1 eq), which was dissolved in 10 mL abs., degassed 1,4-dioxane. 35 μL *N,N*-dimethyl ethylene diamine (29.2 mg, 332 μmol, 0.2 eq), 998 mg NaI (6.65 mmol, 4.0 eq.) and 31.5 mg CuI (166 μmol, 0.1 eq.) were added. The suspension was stirred at 110 °C until full conversion was observed after 48 h (GC-MS). The reaction mixture was cooled down to RT and 10 mL sat. NH₄Cl solution were added. The resulting blue suspension was diluted with 10 mL H₂O and extracted with DCM (3 x 20 mL). The combined organic phases were dried over Na₂SO₄, filtered and the solvent was removed under reduced

pressure. The crude product was purified via column chromatography (15 g SiO₂, 1.5 x 20 cm, eluent: cyclohexane/EtOAc = 2/1 → 6/5).

Yield: 386 mg (90 %), pale yellow oil, C₈H₇BrIN₂ [257.97 g/mol].

¹H NMR (300 MHz, CDCl₃) δ 8.76 (s, 1H, C^{Ar}H), 8.45 (s, 1H, C^{Ar}H), 7.93 (s, 1H, C^{Ar}H), 2.92 (t, ³J (H,H) = 7.2 Hz, 2H, C^{Ar}-CH₂), 2.65 (t, ³J (H,H) = 7.2 Hz, 2H, CH₂-CH₂) ppm (Figure S26)

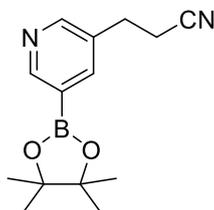
¹³C NMR (76 MHz, CDCl₃) δ 155.0 (C^{Ar}), 148.2 (C^{Ar}), 144.2 (C^{Ar}), 135.5 (C_q, C^{Ar}), 118.2 (CH₂-CN), 93.7 (C_q, C^{Ar}), 28.4 (C^{Ar}-CH₂), 19.0 (CH₂-CH₂) ppm (Figure S26)

GC-MS: (EI, 70 eV; MT_50_S): t_R = 6.20; m/z (%): 258 (100) [M⁺], 218 (82) [M⁺-CH₂CN], 131 (14) [M⁺-I]

TLC: R_f = 0.38 (cyclohexane/EtOAc = 1/1, UV)

HRMS (DI-EI) calcd (m/z) for [M⁺]: 257.9654; found: 257.9662

3-(5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)propanenitrile (**23**)



23

A flame dried Schlenk flask was charged with 386 mg 3-(5-iodopyridin-3-yl)propanenitrile (**22**) (1.50 mmol, 1 eq.), which was dissolved in 5 mL absolute THF. The reaction mixture was cooled to -78 °C and 1.33 mL *i*PrMgCl·LiCl (1.24M in THF) (1.65 mmol, 1.1 eq.) were slowly added. The reaction mixture was stirred at -78 °C until full conversion (4 h, GC-MS) was observed. 333 μL PinBO*i*Pr (307 mg, 1.65 mmol, 1.1 eq.) were added. The reaction mixture was slowly warmed up to RT and stirred for 2 h. The reaction was quenched by addition of 5 mL sat. NH₄Cl solution, then diluted with 10 mL H₂O and extracted with DCM (3 x 20 mL). The combined organic phases were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The residue was purified via Kugelrohr-distillation (150 °C, 8·10⁻² mbar).

Yield: 240 mg (62 %), colorless solid, C₁₄H₁₉BN₂O₂ [258.13 g/mol].

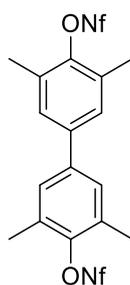
¹H NMR (300 MHz, CDCl₃) δ 8.86 (s, 1H, C^{Ar}H), 8.57 (d, ⁴J (H,H) = 1.8 Hz, 1H, C^{Ar}H), 7.94 (s, 1H, C^{Ar}H), 2.97 (t, ³J (H,H) = 7.4 Hz, 2H, C^{Ar}-CH₂), 2.65 (t, ³J (H,H) = 7.4 Hz, 2H, CH₂-CH₂), 1.34 (s, 12H, C_q-(CH₃)₂) ppm (Figure S27)

¹³C NMR (76 MHz, CDCl₃) δ 154.2 (C^{Ar}), 151.6 (C^{Ar}), 142.3 (C^{Ar}), 132.9 (C_q, C^{Ar}), 118.5 (CH₂-CN), 84.5 (O-C_q), 28.9 (C^{Ar}-CH₂), 25.0 (C_q-CH₃), 19.1 (CH₂-CH₂) ppm (Figure S27)

GC-MS: (EI, 70 eV; MT_50_S): t_R = 6.90; m/z (%): 257 (97) [M⁺], 243 (45) [M⁺-CH₃], 173 (32) [M⁺-C₆H₁₂], 159 (100) [M⁺-C₆H₁₁O]

HRMS (DI-EI) calcd (m/z) for [M⁺-H]: 257.1464; found: 257.1469

3,3',5,5'-Tetramethyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**26**)



26

A 10 mL flame dried Schlenk flask was charged with 97.3 mg 3,3,5,5'-tetramethylbiphenyl-4,4'-diol (**25**) (0.402 mmol, 1.00 eq), 2 mL abs. DCM, 0.18 mL abs. Et₃N and 163 μL nonafluorobutanesulfonyl fluoride (0.908 mmol, 2.26 eq). The beige solution was stirred overnight at RT, then and after that quenched by the addition of 13 mL DCM and 15 mL H₂O. The phases were separated and the aqueous phase was extracted with DCM (3 x 15 mL). The combined organic layers were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (50 g SiO₂, eluent: cyclohexane/EtOAc = 8/1).

Yield: 200 mg (62 %) colourless solid, C₂₄H₁₆F₁₈O₆S₂ [806.48 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 7.27 (s, 4H, C^{Ar}H), 2.45 (s, 12H, C^{Ar}-CH₃) ppm (Figure S28)

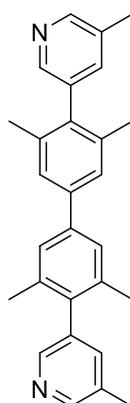
^{13}C NMR (76 MHz, CDCl_3) δ = 146.6 (C_q , C^{Ar}), 139.7 (C_q , C^{Ar}), 132.3 (C_q , C^{Ar}), 128.8 (C^{Ar}), 17.5 ($\text{C}^{\text{Ar}}\text{-CH}_3$) ppm (Figure S28)

TLC R_f = 0.74 (cyclohexane/EtOAc = 8/1, UV)

m.p.^{exp} = 74-75 °C

HRMS (EI): calcd. for $[M^+]$: 806.0101; found: 806.0140

5,5'-(3,3',5,5'-Tetramethyl-[1,1'-biphenyl]-4,4'-diyl) bis(3-methylpyridine) (**28**)



28

A flame dried Schlenk flask was charged with 77.5 mg **26** (0.0961 mmol, 1.00 eq), 47.2 mg 5-methylpyridine-3-boronic acid (**27**) (0.215 mmol, 2.24 eq), 174 mg K_3PO_4 (0.819 mmol, 8.52 eq) and 13.0 mg $\text{PdCl}_2(\text{dppf})\cdot\text{DCM}$ (0.0159 mg, 16.6 mol%). The Schlenk flask was subsequently evacuated and flushed with nitrogen (3x). Then, 2 mL abs., degassed 1,2-DME were added and the resulting suspension was heated to 80 °C. After 5.5 h full conversion was detected via TLC and after cooling to RT the catalyst was removed by filtration through a pad of SiO_2 (eluted with 100 mL MeOH). The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (15 g SiO_2 , eluent: cyclohexane/EtOAc = 2/1).

Yield: 23.9 mg (63 %) brownish solid, $\text{C}_{28}\text{H}_{28}\text{N}_2$ [392.55 g/mol]

^1H NMR (300 MHz, CDCl_3) δ = 8.46 (s, 2H, $\text{C}^{\text{Ar}}\text{H}$), 8.29 (s, 2H, $\text{C}^{\text{Ar}}\text{H}$), 7.38 (s, 4H, $\text{C}^{\text{Ar}}\text{H}$), 7.37 (s, 2H, $\text{C}^{\text{Ar}}\text{H}$), 2.41 (s, 6H, $\text{C}^{\text{Pyr}}\text{-CH}_3$), 2.11 (s, 12H, $\text{C}^{\text{Ar}}\text{-CH}_3$) ppm (Figure S29)

^{13}C NMR (76 MHz, CDCl_3) δ = 148.9 (C^{Ar}), 147.4 (C^{Ar}), 140.5 (C_q , C^{Ar}), 137.4 (C^{Ar}), 137.2 (C_q , C^{Ar}), 136.9 (C_q , C^{Ar}), 133.0 (C_q , C^{Ar}), 126.4 (C^{Ar}), 21.2 ($\text{C}^{\text{Pyr}}\text{-CH}_3$), 18.6 ($\text{C}^{\text{Ar}}\text{-CH}_3$) ppm (Figure S29)

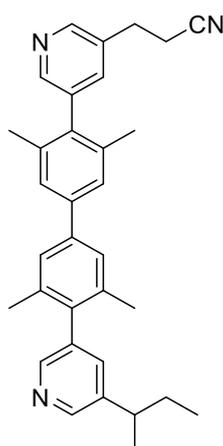
GC-MS (EI, 70 eV; MT_50_S): t_R = 7.96 min; m/z (%) = 392 (100) [M^+], 377 (5) [$\text{M}^+\text{-CH}_3$]

TLC R_f = 0.28 (cyclohexane/EtOAc = 1/2, UV)

m.p.^{exp} = 75-78 °C

HRMS (EI): calcd for [M^+]: 392.2252; found: 392.2250

3-(5-(4'-(5-(*sec*-Butyl)pyridin-3-yl)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-4-yl)pyridin-3-yl)propanenitrile (**29**)



29

A 13 mL glass vial was charged with 499 mg **26** (619 μmol , 1.00 eq), 162 mg **19** (619 μmol , 1.00 eq), 14.2 mg $\text{Pd}(\text{OAc})_2$ (63.2 μmol , 10 mol%), 53.6 mg SPhos (131 μmol , 21 mol%) and 407 mg K_3PO_4 (1.92 mmol, 3.10 eq). The starting materials were transferred into a glovebox and suspended in 13 mL abs., degassed 1,2-DME in a 20 ml screw cap vial. The obtained brown-orange suspension was stirred for 13 h at 80 °C until full consumption of the boronic acid ester was observed via HPLC-MS. The solvent was removed under reduced pressure and the crude product was purified via column chromatography (50 g SiO_2 , eluent: cyclohexane/EtOAc = 5/1). The teraryl nonaflate was isolated as a yellow solid and directly used in the second coupling. Therefore, a 5 mL glass vial was charged with 63.8 mg (99.4 μmol , 1.00 eq) teraryl nonaflate, 52.2 mg (20.2 μmol , 2.03 eq) **23**, 4.1 mg (10 μmol , 10 mol%) SPhos, 1.1 mg (4.9 μmol , 5 mol%) $\text{Pd}(\text{OAc})_2$ and transferred into a glovebox. 63.3 mg (298 μmol ,

3.00 eq) K_3PO_4 and 1.6 mL abs., degassed DME were added and the mixture was stirred at 80 °C. After 13 h, the reaction was cooled to RT. The catalyst was removed by filtration through a pad of silica gel (eluted with 10 mL EtOAc) and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (15 g SiO_2 , eluent: cyclohexane/EtOAc = 1/3).

Yield: 47.0 mg (16 %) colourless solid, $C_{33}H_{35}N_3$ [473.66 g/mol]

1H NMR (300 MHz, methanol- d_4) δ = 8.55 (s, 1H, $C^{Ar}H$), 8.52 (s, 1H, $C^{Ar}H$), 8.31 (s, 1H, $C^{Ar}H$), 8.20 (s, 1H, $C^{Ar}H$), 7.71 (s, 1H, $C^{Ar}H$), 7.54 (d, 4J = 5.1 Hz, 1H, $C^{Ar}H$), 7.48 (s, 2H, $C^{Ar}H$), 7.47 (s, 2H, $C^{Ar}H$), 3.09 (t, 3J = 6.9 Hz, 2H, $C^{Pyr}-\underline{CH_2}-CH_2-CN$), 2.88 (t, 3J = 6.9 Hz, 2H, $C^{Pyr}-\underline{CH_2}-CH_2-CN$), 2.45 (m, 1H, $C^{Pyr}-\underline{CH}$), 2.12 (s, 6H, $C^{Ar}-\underline{CH_3}$), 2.06 (s, 6H, $C^{Ar}-\underline{CH_3}$), 1.71-1.47 (m, 2H, $C^{Pyr}-\underline{CH}-\underline{CH_2}$), 1.17 (d, 3J = 6.8 Hz, 3H, $C^{Pyr}-\underline{CH}-\underline{CH_3}$), 0.83 (t, 3J = 7.36 Hz, 3H, $C^{Pyr}-\underline{CH}-CH_2-\underline{CH_3}$) ppm (Figure S30)

^{13}C NMR (76 MHz, $CDCl_3$) δ = 158.5 (C_q , C^{Ar}), 150.1 (C^{Ar}), 149.0 (C^{Ar}), 148.8 (C^{Ar}), 141.9 (C_q , C^{Ar}), 141.8 (C_q , C^{Ar}), 139.5 (C^{Ar}), 138.2 (C_q , C^{Ar}), 138.0 (C_q , C^{Ar}), 137.9 (C_q , C^{Ar}), 137.7 (C_q , C^{Ar}), 136.5 (C_q , C^{Ar}), 127.3 (C^{Ar}), 123.2 (C^{Ar}), 120.2 (CN), 38.2 ($C^{Ar}-\underline{CH}$), 30.8 ($C^{Ar}-\underline{CH}-\underline{CH_2}$), 29.3 ($C^{Ar}-\underline{CH_2}$), 21.2 ($C^{Ar}-\underline{CH_3}$), 20.7 ($\underline{CH}-\underline{CH_3}$), 19.3 ($\underline{CH_2}-CN$), 12.5 ($\underline{CH_2}-\underline{CH_3}$) ppm (Figure S30)

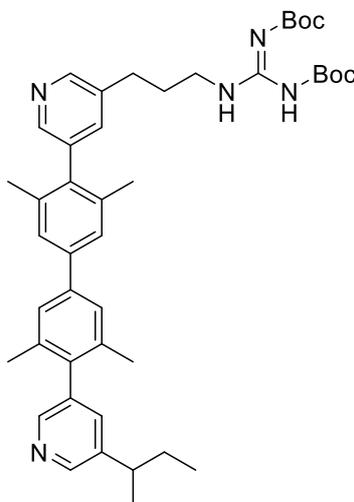
HPLC-MS (Poroshell, ESI⁺, MV_general): t_R = 4.87 min; m/z: 475 [$M+H^+$]

TLC R_f = 0.16 (cyclohexane/EtOAc = 1/3, UV)

m.p.^{exp} = 87-88 °C

HRMS (EI): calcd for [M^+]: 473.2831; found: 473.2830

3-(5-(4'-(5-(*sec*-Butyl)pyridin-3-yl)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-4-yl)pyridin-3-yl)propyl-*N,N'*-di-Boc-guanidine (**30**)



In a 50 mL round bottom flask 47 mg **29** (99.2 μmol , 1.00 eq) were dissolved in 1 mL MeOH and 2 drops of NH_3 (25 % (v/v) in H_2O). After vacuum degassing (3x evacuating and flushing with N_2), a spatula tip of Raney[®]-Nickel (Raney[®] 2800 slurry in H_2O) was added. A H_2 filled balloon was connected, the reaction atmosphere was saturated with H_2 (5x evacuated and flushed with H_2) and this mixture was stirred at RT for 24 h. The hydrogenation catalyst was filtered off under inert conditions with a fritted Schlenk funnel filled with a pad of Celite[®] and the solvent was removed under reduced pressure. The colourless solid was dissolved in 8 mL DMF and 30.9 mg *N,N'*-di-boc-1*H*-pyrazole-1-carboximidine (**24**) (99.6 μmol , 1.00 eq) were added. The colourless solution was stirred at RT for 4 h. Then, the solvent was removed under reduced pressure and the crude product was purified via column chromatography (10 g SiO_2 , eluent: cyclohexane/EtOAc = 1/2).

Yield: 11.3 mg (16 %) greyish solid, $\text{C}_{44}\text{H}_{57}\text{N}_5\text{O}_4$ [719.97 g/mol]

^1H NMR (300 MHz, CDCl_3) δ = 11.51 (bs, 1, NH), 8.57 (d, $^4J = 5.2$ Hz, 1H, C^{ArH}), 8.48 (d, 4J (H,H) = 1.2 Hz, 1H, C^{ArH}), 8.43 (bs, 1H, NH), 8.33 (d, 4J (H,H) = 1.2 Hz, 1H, C^{ArH}), 8.29 (s, 1H, C^{ArH}), 7.41 (s, 2H, C^{ArH}), 7.39 (s, 2H, C^{ArH}), 7.29 (d, $^4J = 5.3$ Hz, 1H, C^{ArH}), 3.58-3.45 (m, 2H, $\text{C}^{\text{Pyr}}\text{-CH}_2\text{-CH}_2\text{-CH}_2$), 2.76 (t, $^3J = 7.6$ Hz, 2H, $\text{C}^{\text{Pyr}}\text{-CH}_2\text{-CH}_2$), 2.48-2.30 (m, 1H, $\text{C}^{\text{Pyr}}\text{-CH-CH}_2$), 2.11 (s, 6H, $\text{C}^{\text{Ar}}\text{-CH}_3$), 2.06 (s, 6H, $\text{C}^{\text{Ar}}\text{-CH}_3$), 2.01-1.90 (m, 2H, $\text{C}^{\text{Pyr}}\text{-CH}_2\text{-CH}_2\text{-CH}_2$), 1.50 (s, 18H, CH_3^{Boc}), 1.31-1.19 (m, 2H, $\text{C}^{\text{Pyr}}\text{-CH-CH}_2$), 1.12 (d, $^3J = 6.8$ Hz, 3H, $\text{C}^{\text{Pyr}}\text{-CH-CH}_3$), 0.81 (t, $^3J = 7.6$ Hz, 3H, $\text{C}^{\text{Pyr}}\text{-CH-CH}_2\text{-CH}_3$) ppm (Figure S31)

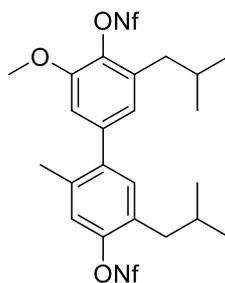
¹³C NMR (126 MHz, CDCl₃) δ = 174.2 (C_q^{Guanidine}), 163.8 (C=O), 156.4 (C_q, C^{Ar}), 155.6 (C_q, C^{Ar}), 153.6 (C=O), 150.1 (C^{Ar}), 148.6 (C^{Ar}), 148.2 (C^{Ar}), 147.9 (C^{Ar}), 140.5 (C_q, C^{Ar}), 140.3 (C_q, C^{Ar}), 137.2 (C_q, C^{Ar}), 137.1 (C^{Ar}), 137.0 (C^{Ar}), 136.9 (C_q, C^{Ar}), 136.6 (C_q, C^{Ar}), 136.4 (C_q, C^{Ar}), 135.9 (C_q, C^{Ar}), 135.6 (C_q, C^{Ar}), 126.5 (C^{Ar}), 121.3 (C^{Ar}), 83.4 (C_q, C^{tBu}), 79.5 (C_q, C^{tBu}), 40.4 (C^{Pyr}-CH₂-CH₂-CH₂), 36.8 (C^{Pyr}-CH), 30.7 (C^{Pyr}-CH₂-CH₂), 30.4 (C^{Pyr}-CH₂), 30.0 (C^{Pyr}-CH-CH₂), 28.5 (CH₃^{Boc}), 28.2 (CH₃^{Boc}), 21.3 (C^{Ar}-CH₃), 21.2 (C^{Ar}-CH₃), 20.8 (CH-CH₃), 12.2 (CH₂-CH₃) ppm (Figure S31)

TLC R_f = 0.32 (cyclohexane/EtOAc = 1/2, UV)

m.p.^{exp} = 78-80°C

HRMS (MALDI): calcd for [M+Na⁺]: 742.4308; found: 742.4281

3',5-Diisobutyl-5'-methoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**31**)



31

A 20 mL flame dried Schlenk flask was charged with 155 mg 3',5-diisobutyl-5'-methoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**13**) (contaminated with 42 % of homocoupled product) (453 μmol, 1.0 eq), 157 μL abs. Et₃N (1.13 mmol, 2.5 eq) and 5 mL abs. DCM. Then 179 μL NfF (997 μmol, 2.2 eq) were slowly added and the reaction was stirred at RT for 16 h. The reaction mixture was diluted with 5 mL DCM and subsequently washed with 5 mL 1M HCl aq. solution, 5 mL sat. NaHCO₃ solution and 5 mL sat. NaCl solution. The organic phase was dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (10 g SiO₂, eluent: cyclohexane/EtOAc = 75/1).

Yield: 78 mg (19 %), colorless oil, C₃₀H₂₈F₁₈O₇S₂ [906.64 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 7.15 (s, 1H, C^{Ar}H), 7.12 (s, 1H, C^{Ar}H), 6.76 (s, 1H, C^{Ar}H), 6.74 (s, 1H, C^{Ar}H), 3.91 (s, 3H, O-CH₃), 2.68 – 2.49 (m, 4H, 2 C^{Ar}-CH₂), 2.25 (s, 3H, C^{Ar}-CH₃), 2.02 – 1.86 (m, 2H, 2 CH₂-CH), 1.01 – 0.82 (m, 12H, 2 CH-(CH₃)₂) ppm (Figure S32)

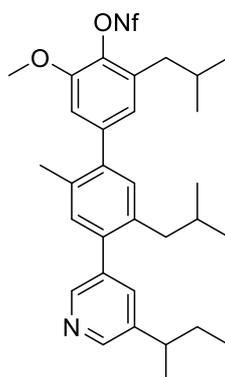
¹³C NMR (76 MHz, CDCl₃) δ 151.1 (C_q, C^{Ar}), 147.7 (C_q, C^{Ar}), 140.9 (C_q, C^{Ar}), 140.6 (C_q, C^{Ar}), 137.3 (C_q, C^{Ar}), 135.7 (C_q, C^{Ar}), 135.6 (C_q, C^{Ar}), 133.0 (C^{Ar}), 131.9 (C_q, C^{Ar}), 123.9 (C^{Ar}), 122.9 (C^{Ar}), 111.6 (C^{Ar}), 56.3 (O-CH₃), 39.4 (C^{Ar}-CH₂), 39.1 (C^{Ar}-CH₂), 29.4 (CH₂-CH), 29.2 (CH₂-CH), 22.4 (CH-(CH₃)₂), 20.3 (CH-(CH₃)₂) ppm (Figure S32)

HPLC-MS (Poroshell, ESI⁺, MV_70): t_R = 10.10 min

TLC: R_f = 0.17 (cyclohexane/EtOAc = 50/1, UV and CAM)

HRMS (EI): calcd for [M⁺]: 906.0689; found: 906.1045

4'-(5-(*sec*-butyl)pyridin-3-yl)-3,5'-diisobutyl-5-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl
1,1,2,2,3,3,4,4,4,4-nonafluorobutane-1-sulfonate (**32**)



32

A 25 mL flame dried Schlenk flask was charged with 560 mg **31** (618 μmol, 1.0 eq.), 161 mg **19** (618 μmol, 1.0 eq.), 35.7 mg Pd(PPh₃)₄ (30.9 μmol, 0.05 eq.), 262 mg K₃PO₄ (1.24 mmol, 2.00 eq.) and 5 mL abs. degassed 1,2-DME. The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was cooled down to RT and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (50 g SiO₂, eluent: cyclohexane/EtOAc = 5/1).

Yield: 191 mg (42 %), colorless oil, C₃₅H₄₀F₉NO₄S [741.75 g/mol]

A 10 mL flame dried Schlenk flask was charged with 105 mg **32** (141 μmol , 1.0 eq.), 43.9 mg **23** (170 μmol , 1.2 eq.), 5.50 mg SPhos Pd G3 (7.05 μmol , 0.05 eq.), 91.7 mg Cs_2CO_3 (282 μmol , 2.00 eq.) and 2 mL abs. degassed DMF. The reaction mixture was stirred at 90 °C for 20 h. The reaction mixture was cooled down to RT and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (10 g SiO_2 , eluent: cyclohexane/EtOAc = 1/1 \rightarrow 1/3).

Yield: 44 mg (54 %), colorless oil, $\text{C}_{39}\text{H}_{47}\text{N}_3\text{O}$ [573.83 g/mol]

^1H NMR (500 MHz, CDCl_3) δ = 8.54 (dd, $^3,^4J(\text{H,H}) = 5.0, 3.5$ Hz, 1H, C^{ArH}), 8.49 (d, $^4J(\text{H,H}) = 1.7$ Hz, 1H, C^{ArH}), 8.46 (s, 1H, C^{ArH}), 8.36 (d, $^3J(\text{H,H}) = 6.4$ Hz, 1H, C^{ArH}), 7.54 (s, 1H, C^{ArH}), 7.24 (d, $^3J(\text{H,H}) = 5.2$ Hz, 1H, C^{ArH}), 7.19 (d, $^3J(\text{H,H}) = 5.7$ Hz, 1H, C^{ArH}), 7.01 (d, $^3J(\text{H,H}) = 4.0$ Hz, 1H, C^{ArH}), 6.93 (s, 1H, C^{ArH}), 6.84 (s, 1H, C^{ArH}), 3.74 (s, 3H, O- $\underline{\text{CH}_3}$), 3.05 (t, $^3J(\text{H,H}) = 7.2$ Hz, 2H, $\underline{\text{CH}_2}$ - $\underline{\text{CH}_2}$ -CN), 2.71 (t, $^3J(\text{H,H}) = 7.2$ Hz, 2H, CH_2 - $\underline{\text{CH}_2}$ -CN), 2.64 – 2.48 (m, 1H, C^{Ar} - $\underline{\text{CH}}$), 2.37 (d, $^3J(\text{H,H}) = 7.2$ Hz, 2H, C^{Ar} - $\underline{\text{CH}_2}$), 2.35 – 2.29 (m, 4H, C^{Ar} - $\underline{\text{CH}_3}$, C^{Ar} - $\underline{\text{CHH}}$), 2.25 – 2.16 (m, 1H, C^{Ar} - $\underline{\text{CHH}}$), 1.80 – 1.45 (m, 4H, 2 CH_2 - $\underline{\text{CH}}$, CH - $\underline{\text{CH}_2}$), 1.22 – 1.06 (m, 3H, CH - $\underline{\text{CH}_3}$), 0.84 – 0.69 (m, 15H, CH - $(\underline{\text{CH}_3})_2$, CH_2 - $\underline{\text{CH}_3}$) ppm (Figure S34)

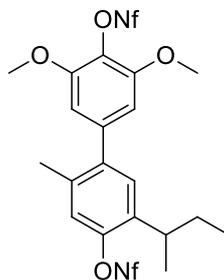
^{13}C NMR (126 MHz, CDCl_3) δ = 156.9 (C_q , C^{Ar}), 155.1 (C_q , C^{Ar}), 154.7 (C_q , C^{Ar}), 150.8 (C_q , C^{Ar}), 150.6 (C_q , C^{Ar}), 150.5 (C^{Ar}), 148.8 (C_q , C^{Ar}), 148.7 (C_q , C^{Ar}), 147.8 (C^{Ar}), 142.6 (C^{Ar}), 141.4 (C_q , C^{Ar}), 141.3 (C_q , C^{Ar}), 141.2 (C^{Ar}), 138.2 (C_q , C^{Ar}), 137.6 (C_q , C^{Ar}), 137.3 (C_q , C^{Ar}), 136.7 (C_q , C^{Ar}), 136.6 (C_q , C^{Ar}), 136.6 (C_q , C^{Ar}), 133.6 (C^{Ar}), 132.7 (C_q , C^{Ar}), 132.7 (C^{Ar}), 132.4 (C^{Ar}), 132.4 (C^{Ar}), 132.4 (C_q , C^{Ar}), 130.9 (C^{Ar}), 130.8 (C^{Ar}), 125.3 (C_q , C^{Ar}), 123.6 (C^{Ar}), 120.8 (C_q , C^{Ar}), 120.7 (C_q , C^{Ar}), 118.6 (C_q , CN), 109.6 (C^{Ar}), 55.9 (O- $\underline{\text{CH}_3}$), 42.4 (C^{Ar} - $\underline{\text{CH}_2}$), 42.1 (C^{Ar} - $\underline{\text{CH}_2}$), 42.1 (C^{Ar} - $\underline{\text{CH}_2}$), 37.0 (C^{Ar} - $\underline{\text{CH}}$), 36.3 (C^{Ar} - $\underline{\text{CH}}$), 31.6 (CH - $\underline{\text{CH}_2}$), 29.8 (CH_2 - $\underline{\text{CH}}$), 29.3 (CH - $\underline{\text{CH}_2}$), 29.2 (CH_2 - $\underline{\text{CH}}$), 29.1 (CH_2 - $\underline{\text{CH}}$), 29.0 (CH_2 - $\underline{\text{CH}}$), 25.0 ($\underline{\text{CH}_2}$ - $\underline{\text{CH}_2}$ -CN), 22.6 (CH - $(\underline{\text{CH}_3})_2$), 22.5 (CH - $(\underline{\text{CH}_3})_2$), 20.7 (CH - $\underline{\text{CH}_3}$), 20.3 (C^{Ar} - $\underline{\text{CH}_3}$), 20.2 (CH - $\underline{\text{CH}_3}$), 19.3 ($\underline{\text{CH}_2}$ - $\underline{\text{CH}_2}$ -CN), 12.5 (CH_2 - $\underline{\text{CH}_3}$), 12.1 (CH_2 - $\underline{\text{CH}_3}$) ppm (Figure S34)

HPLC-MS (Poroshell, ESI⁺, MV_general): $t_{\text{R}} = 6.10$ min; m/z: 574 [$M+\text{H}^+$]

TLC: $R_f = 0.26$ (EtOAc, UV)

HRMS (EI): calcd for [M^+]: 573.3719; found: 573.3721

5-(*sec*-Butyl)-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**34**)



34

A 25 mL flame dried Schlenk flask was charged with 515 mg 5-(*sec*-butyl)-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**11**) (1.63 mmol, 1.0 eq), 567 μ L abs. Et₃N (4.07 mmol, 2.5 eq) and 8 mL abs. DCM. Then 645 μ L NfF (3.57 mmol, 2.2 eq) were slowly added and the reaction was stirred at RT for 16 h. The reaction mixture was diluted with 15 mL DCM and subsequently washed with 15 mL 1M HCl aq. solution, 15 mL sat. NaHCO₃ solution and 15 mL sat. NaCl solution. The organic phase was dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (20 g SiO₂, eluent: cyclohexane/EtOAc = 40/1).

Yield: 1.34 g (93 %), colorless oil, C₂₇H₂₂F₁₈O₈S₂ [880.56 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 7.16 (s, 1H, C^{Ar}H), 7.14 (s, 1H, C^{Ar}H), 6.51 (s, 2H, C^{Ar}H), 3.90 (s, 6H, O-CH₃), 3.11 – 2.97 (m, 1H, C^{Ar}-CH), 2.25 (s, 3H, C^{Ar}-CH₃), 1.62 (t, ³J (H,H) = 7.3 Hz, 2H, CH-CH₂), 1.26 (d, ³J (H,H) = 6.8 Hz, 3H, CH-CH₃), 0.88 (t, ³J (H,H) = 7.3 Hz, 3H, CH₂-CH₃) ppm (Figure S35)

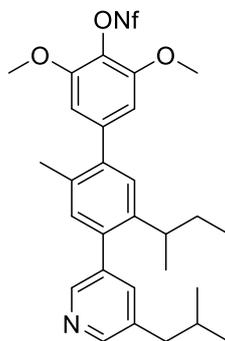
¹³C NMR (76 MHz, CDCl₃) δ = 152.3 (C_q, C^{Ar}), 147.0 (C_q, C^{Ar}), 141.7 (C_q, C^{Ar}), 141.5 (C_q, C^{Ar}), 137.8 (C_q, C^{Ar}), 135.2 (C_q, C^{Ar}), 129.0 (C^{Ar}), 127.6 (C_q, C^{Ar}), 122.8 (C^{Ar}), 106.1 (C^{Ar}), 56.6 (O-CH₃), 34.1 (C^{Ar}-CH), 30.6 (CH-CH₂), 21.1 (CH-CH₃), 20.2 (C^{Ar}-CH₃), 12.2 (CH₂-CH₃) ppm (Figure S35)

TLC: R_f = 0.22 (cyclohexane/EtOAc = 40/1, UV and CAM)

m.p.^{exp} = 63-65 °C

HRMS (EI): calcd for [M⁺]: 880.0469; found: 880.0488

5'-(*sec*-Butyl)-4'-(5-isobutylpyridin-3-yl)-3,5-dimethoxy-2'-methyl-[1,1'-biphenyl]-4-yl
1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (**35**)



35

A 20 mL flame dried Schlenk flask was charged with 440 mg **34** (500 μ mol, 1.0 eq.), 137 mg **16** (525 μ mol, 1.05 eq.), 18.3 mg Pd(dppf)Cl₂ (25.0 μ mol, 0.05 eq.), 325 mg Cs₂CO₃ (1.00 mmol, 2.00 eq.) and 5 mL abs. degassed 1,4-dioxane. The reaction mixture was stirred at 80 °C for 16 h. The reaction mixture was cooled down to RT, diluted with 20 mL DCM and washed with 20 mL H₂O. The aqueous phase was extracted with 20 mL DCM. The combined organic phases were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (25 g SiO₂, eluent: cyclohexane/EtOAc = 4/1).

Yield: 218 mg (61 %), colorless oil, C₃₂H₃₄F₉NO₅S [715.67 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 8.42 (s, 2H, C^{Ar}H), 7.40 (s, 1H, C^{Ar}H), 7.19 (s, 1H, C^{Ar}H), 7.10 (s, 1H, C^{Ar}H), 6.60 (s, 2H, C^{Ar}H), 3.91 (s, 6H, O-CH₃), 2.78 – 2.62 (m, 1H), 2.55 (d, ³J (H,H) = 7.0 Hz, 2H), 2.28 (s, 3H, C^{Ar}-CH₃), 2.00 – 1.83 (m, 1H, C^{Ar}-CH), 1.65 – 1.45 (m, 2H, C^{Ar}-CH₂), 1.17 (d, ³J (H,H) = 6.8 Hz, 3H, CH-CH₃), 0.96 (d, ³J (H,H) = 6.5 Hz, 6H, CH₂-(CH₃)₂), 0.73 (t, ³J (H,H) = 7.3 Hz, 3H) ppm (Figure S36)

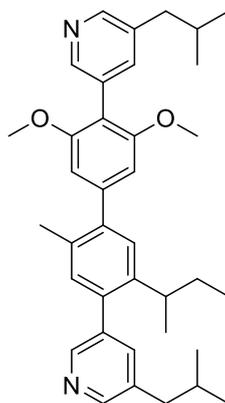
¹³C NMR (76 MHz, CDCl₃) δ = 152.1 (C_q, C^{Ar}), 149.1 (C^{Ar}), 147.6 (C^{Ar}), 143.5 (C_q, C^{Ar}), 142.8 (C_q, C^{Ar}), 141.3 (C_q, C^{Ar}), 138.0 (C_q, C^{Ar}), 137.4, 136.7 (C_q, C^{Ar}), 136.1 (C_q, C^{Ar}), 132.4 (C_q, C^{Ar}), 132.0 (C^{Ar}), 127.2 (C^{Ar}), 106.2 (C^{Ar}), 56.5 (O-CH₃), 42.4 (C^{Ar}-CH₂), 36.4 (C^{Ar}-CH), 31.3 (CH-CH₂), 30.2 (CH₂-CH), 22.4 (CH-CH₃), 22.3 (CH₂-(CH₃)₂), 20.0 (C^{Ar}-CH₃), 12.4 (CH₂-(CH₃)₂) ppm (Figure S36)

HPLC-MS (Poroshell, ESI⁺, MV_general): t_R = 8.44 min; m/z: 716 [M+H⁺]

TLC: R_f = 0.21 (cyclohexane/EtOAc = 4/1, UV and CAM)

HRMS (EI): calcd for [M^+]: 715.2014; found: 715.2023

5,5'-(5-(*sec*-Butyl)-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl)bis(3-isobutylpyridine)
(36)



36

A 10 mL flame dried Schlenk flask was charged with 125 mg **35** (175 μ mol, 1.0 eq.), 54.8 mg **16** (210 μ mol, 1.2 eq.), 6.83 mg SPhos Pd G3 (8.75 μ mol, 0.05 eq.), 114 mg Cs_2CO_3 (350 μ mol, 2.00 eq.) and 2 mL abs. degassed DMF. The reaction mixture was stirred at 90 $^\circ\text{C}$ for 18 h. The reaction mixture was cooled down to RT and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (10 g SiO_2 , eluent: cyclohexane/EtOAc = 2/1).

Yield: 89 mg (92 %), colorless oil, $\text{C}_{37}\text{H}_{46}\text{N}_2\text{O}_2$ [550.79 g/mol]

^1H NMR (300 MHz, CDCl_3) δ = 8.51 (d, 3J (H,H) = 1.7 Hz, 1H), 8.47 – 8.38 (m, 2H), 8.34 (d, 3J (H,H) = 1.8 Hz, 1H), 7.56 (s, 1H), 7.43 (s, 1H), 7.28 (s, 1H), 7.12 (s, 1H), 6.65 (s, 2H), 3.77 (s, 6H), 2.80 – 2.65 (m, 1H), 2.55 (t, 3J (H,H) = 6.8 Hz, 4H), 2.36 (s, 3H), 1.99 – 1.82 (m, 2H), 1.70 – 1.46 (m, 2H), 1.20 (d, 3J (H,H) = 6.8 Hz, 3H), 1.04 – 0.87 (m 12H), 0.75 (t, 3J (H,H) = 7.3 Hz, 3H) ppm (Figure S37)

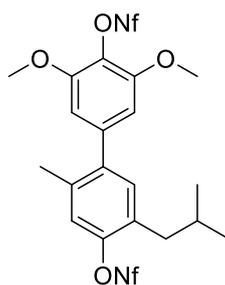
^{13}C NMR (76 MHz, CDCl_3) δ = 157.5 (C_q , C^{Ar}), 149.5 (C^{Ar}), 149.0 (C^{Ar}), 148.5 (C^{Ar}), 147.7 (C^{Ar}), 143.5 (C_q , C^{Ar}), 143.3 (C_q , C^{Ar}), 142.2 (C_q , C^{Ar}), 139.5 (C^{Ar}), 137.6 (C_q , C^{Ar}), 137.5 (C^{Ar}), 136.8 (C_q , C^{Ar}), 136.1 (C_q , C^{Ar}), 135.5 (C_q , C^{Ar}), 132.6 (C_q , C^{Ar}), 132.0 (C^{Ar}), 129.3 (C_q , C^{Ar}), 127.3 (C^{Ar}), 105.6 (C^{Ar}), 56.1 (O- $\underline{\text{C}}\text{H}_3$), 42.5 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}_2$), 42.4 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}_2$), 36.5 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}$), 31.3 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}_2$), 30.2 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}$), 30.2 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}$), 22.5 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}_3$), 22.4 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}_3$), 20.1 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}_3$), 12.5 ($\text{C}^{\text{Ar}}-\underline{\text{C}}\text{H}_3$) ppm (Figure S37)

HPLC-MS (Poroshell, ESI⁺, MV_general): t_R = 6.37 min; m/z: 551 [M+H⁺]

TLC: R_f = 0.20 (cyclohexane/EtOAc = 4/1, UV and CAM)

HRMS (EI): calcd for [M⁺]: 550.3559; found: 550.3557

5-Isobutyl-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**37**)



37

A 25 mL flame dried Schlenk flask was charged with 408 mg 5-isobutyl-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**9**) (1.29 mmol, 1.0 eq), 449 μ L abs. Et₃N (3.23 mmol, 2.5 eq) and 6 mL abs. DCM. Then 510 μ L NfF (2.84 mmol, 2.2 eq) were slowly added and the reaction was stirred at RT for 16 h. The reaction mixture was diluted with 15 mL DCM and subsequently washed with 15 mL 1M HCl aq. solution, 15 mL sat. NaHCO₃ solution and 15 mL sat. NaCl solution. The organic phase was dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (20 g SiO₂, eluent: cyclohexane/EtOAc = 40/1).

Yield: 1.03 g (91 %), colorless solid, C₂₇H₂₂F₁₈O₈S₂ [880.56 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 7.16 (s, 1H, C^{Ar}H), 7.13 (s, 1H, C^{Ar}H), 6.51 (s, 2H, C^{Ar}H), 3.90 (s, 6H, O-CH₃), 2.58 (d, ³J (H,H) = 7.1 Hz, 2H, C^{Ar}-CH₂), 2.26 (s, 3H, C^{Ar}-CH₃), 2.02 – 1.82 (m, 1H, CH₂-CH), 0.94 (d, ³J (H,H) = 6.6 Hz, 6H, CH-(CH₃)₂) ppm (Figure S38)

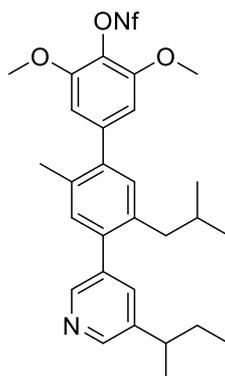
¹³C NMR (76 MHz, CDCl₃) δ = 152.3 (C_q, C^{Ar}), 147.8 (C_q, C^{Ar}), 141.2 (C_q, C^{Ar}), 141.1 (C_q, C^{Ar}), 135.6 (C_q, C^{Ar}), 132.9 (C_q, C^{Ar}), 131.9 (C^{Ar}), 127.6 (C_q, C^{Ar}), 122.9 (C^{Ar}), 106.1 (C^{Ar}), 56.6 (O-CH₃), 39.1 (C^{Ar}-CH₂), 29.4 (CH₂-CH), 22.4 (CH-(CH₃)₂), 20.3 (C^{Ar}-CH₃) ppm (Figure S38)

TLC: R_f = 0.21 (cyclohexane/EtOAc = 40/1, UV and CAM)

m.p.^{exp} = 56-57 °C

HRMS (EI): calcd for [*M*⁺]: 880.0469; found: 880.0497

4'-(5-(*sec*-Butyl)pyridin-3-yl)-5'-isobutyl-3,5-dimethoxy-2'-methyl-[1,1'-biphenyl]-4-yl
1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (**38**)



38

A 10 mL flame dried Schlenk flask was charged with 110 mg **37** (125 μ mol, 1.0 eq.), 35.9 mg **19** (138 μ mol, 1. eq.), 4.58 mg Pd(dppf)Cl₂ (6.25 μ mol, 0.05 eq.), 81.2 mg Cs₂CO₃ (250 μ mol, 2.00 eq.) and 3 mL abs. degassed 1,4-dioxane. The reaction mixture was stirred at 80 °C for 16 h. The reaction mixture was cooled down to RT and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (25 g SiO₂, eluent: cyclohexane/EtOAc = 5/1 \rightarrow 4/1).

Yield: 56 mg (63 %), colorless oil, C₃₂H₃₄F₉NO₅S [715.67 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 8.60 – 8.47 (m, 1H, C^{Ar}H), 8.34 (d, ⁴*J* (H,H) = 3.5 Hz, 1H, C^{Ar}H), 7.26 – 7.19 (m, 1H, C^{Ar}H), 7.13 (d, ⁴*J* (H,H) = 2.7 Hz, 1H, C^{Ar}H), 6.99 (s, 1H, C^{Ar}H), 6.63 (d, ⁴*J* (H,H) = 1.1 Hz, 2H, C^{Ar}H), 3.93 (s, 6H, O-CH₃), 2.64 – 2.41 (m, 1H, C^{Ar}-CH), 2.37 – 2.11 (m, 5H, C^{Ar}-CH₃, C^{Ar}-CH₂), 1.79 – 1.45 (m, 3H, CH-CH₂, CH₂-CH), 1.14 (dd, ^{2,3}*J* (H,H) = 30.7, 6.8 Hz, 3H, CH-CH₃), 0.90 – 0.60 (m, 9H, CH₂-CH₃, CH-(CH₃)₂) ppm (Figure S39)

¹³C NMR (76 MHz, CDCl₃) δ = 155.0 (C_q, C^{Ar}), 154.6 (C_q, C^{Ar}), 152.1 (C_q, C^{Ar}), 150.8 (C^{Ar}), 150.6 (C^{Ar}), 149.0 (C^{Ar}), 148.9 (C^{Ar}), 142.7 (C_q, C^{Ar}), 140.5 (C_q, C^{Ar}), 140.5 (C_q, C^{Ar}), 137.8 (C_q, C^{Ar}), 137.5 (C_q, C^{Ar}), 137.2 (C_q, C^{Ar}), 137.2 (C_q, C^{Ar}), 136.4 (C_q, C^{Ar}), 136.4 (C_q, C^{Ar}), 132.8 (C^{Ar}), 132.5 (C^{Ar}), 132.2 (C_q, C^{Ar}), 130.7 (C^{Ar}), 130.6 (C^{Ar}), 127.4 (C_q, C^{Ar}), 120.8 (C^{Ar}), 120.7 (C^{Ar}), 106.3 (C^{Ar}), 56.5 (O-CH₃), 42.1 (C^{Ar}-CH₂), 37.0 (C^{Ar}-CH), 36.4 (C^{Ar}-CH), 31.5

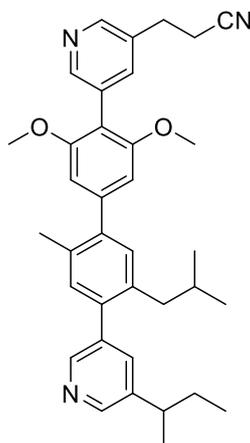
(CH-CH₂), 29.3 (CH-CH₂), 29.2 (CH₂-CH), 29.1 (CH₂-CH), 22.6 (C^{Ar}-CH₃), 22.5 (CH-CH₃), 20.7 (CH-CH₃), 20.1 (CH-(CH₃)₂), 20.0 (CH-(CH₃)₂), 12.5 (CH₂-CH₃), 12.1 (CH₂-CH₃) ppm (Figure S39)

HPLC-MS (Poroshell, ESI⁺, MV_general): t_R = 8.49 min; m/z: 716 [M+H⁺]

TLC: R_f = 0.19 (cyclohexane/EtOAc = 4/1, UV and CAM)

HRMS (EI): calcd for [M⁺]: 715.2014; found: 715.2021

3-(5-(4'-(5-(*sec*-Butyl)pyridin-3-yl)-5'-isobutyl-3,5-dimethoxy-2'-methyl-[1,1'-biphenyl]-4-yl)pyridin-3-yl)propanenitrile (**39**)



39

A 10 mL flame dried Schlenk flask was charged with 52 mg **38** (72.7 μmol, 1.0 eq.), 20.6 mg **23** (210 μmol, 1.1 eq.), 2.8 mg SPhos Pd G3 (3.64 μmol, 0.05 eq.), 71.0 mg Cs₂CO₃ (218 μmol, 3.00 eq.) and 2 mL abs. degassed DMF. The reaction mixture was stirred at 90 °C for 18 h. The reaction mixture was cooled down to RT and the solvent was removed under reduced pressure. The crude product was purified via semi-preparative column chromatography (Prep_10to100_+0.1).

Yield: 23 mg (69 %), colorless oil, C₃₆H₄₁N₃O₂ [547.74 g/mol]

¹H NMR (300 MHz, CDCl₃) δ = 8.88 – 8.74 (m, 3H, C^{Ar}H), 8.56 (d, ⁴J (H,H) = 6.2 Hz, 1H, C^{Ar}H), 8.42 (s, 1H, C^{Ar}H), 7.81 (d, ⁴J (H,H) = 5.9 Hz, 1H, C^{Ar}H), 7.23 (d, ⁴J (H,H) = 2.3 Hz, 1H, C^{Ar}H), 7.00 (s, 1H, C^{Ar}H), 6.66 (d, ⁴J (H,H) = 1.5 Hz, 2H, C^{Ar}H), 3.84 (s, 6H, O-CH₃), 3.22 (t, ³J (H,H) = 6.7 Hz, 2H, CH₂-CH₂-CN), 2.90 – 2.69 (m, 3H, CH₂-CH₂-CN, C^{Ar}-CH), 2.41 –

2.25 (m, 4H, C^{Ar}-CH₃, C^{Ar}-CHH), 2.19 – 2.02 (m, 1H, C^{Ar}-CHH), 1.81 – 1.52 (m, 3H, CH₂-CH, CH-CH₂), 1.35 – 1.12 (m, 3H, CH-CH₃), 0.96 – 0.66 (m, 9H, CH-(CH₃)₂, CH₂-CH₃) ppm (Figure S40)

¹³C NMR (76 MHz, CDCl₃) δ = 166.2 (C_q, C^{Ar}), 165.9 (C_q, C^{Ar}), 162.7 (C_q, C^{Ar}), 162.3 (C_q, C^{Ar}), 157.1 (C_q, C^{Ar}), 147.2 (C^{Ar}), 145.3 (C^{Ar}), 143.5 (C^{Ar}), 142.7 (C_q, C^{Ar}), 142.6 (C_q, C^{Ar}), 142.4 (C_q, C^{Ar}), 142.3 (C_q, C^{Ar}), 141.0 (C_q, C^{Ar}), 140.9 (C_q, C^{Ar}), 140.1 (C^{Ar}), 140.0 (C^{Ar}), 139.4 (C_q, C^{Ar}), 137.3 (C^{Ar}), 137.0 (C^{Ar}), 136.5 (C^{Ar}), 134.2 (C_q, C^{Ar}), 133.4 (C_q, C^{Ar}), 133.1 (C_q, C^{Ar}), 133.0 (C_q, C^{Ar}), 132.3 (C^{Ar}), 132.0 (C^{Ar}), 131.0 (C_q, C^{Ar}), 124.1 (C^{Ar}), 124.0 (C^{Ar}), 118.5 (C_q, CN), 117.9 (C_q, C^{Ar}), 114.6 (C_q, C^{Ar}), 110.1 (C_q, C^{Ar}), 105.4 (C^{Ar}), 56.2 (O-CH₃), 42.0 (C^{Ar}-CH₂), 38.3 (C^{Ar}-CH), 37.5 (C^{Ar}-CH), 31.5 (CH-CH₂), 29.6 (CH₂-CH), 29.4 (CH₂-CH), 28.8 (CH-CH₂), 28.6 (CH-CH₂-CN), 22.5 (C^{Ar}-CH₃), 22.2 (CH-CH₃), 20.2 (CH-(CH₃)₂), 20.1 (CH-CH₃), 20.0 (CH-(CH₃)₂), 18.8 (CH-CH₂-CN), 12.3 (CH₂-CH₃), 12.0 (CH₂-CH₃) ppm (Figure S40)

HPLC-MS (Poroshell, ESI⁺, MV_general): t_R = 5.45 min; m/z: 548 [M+H⁺]

TLC: R_f = 0.31 (EtOAc, UV)

HRMS (EI): calcd for [M⁺]: 547.3199; found: 547.3198

3. Spectra

^1H and ^{13}C spectra of *tert*-butyl(2-isopropyl-5-methylphenoxy)-dimethylsilane (**2**)

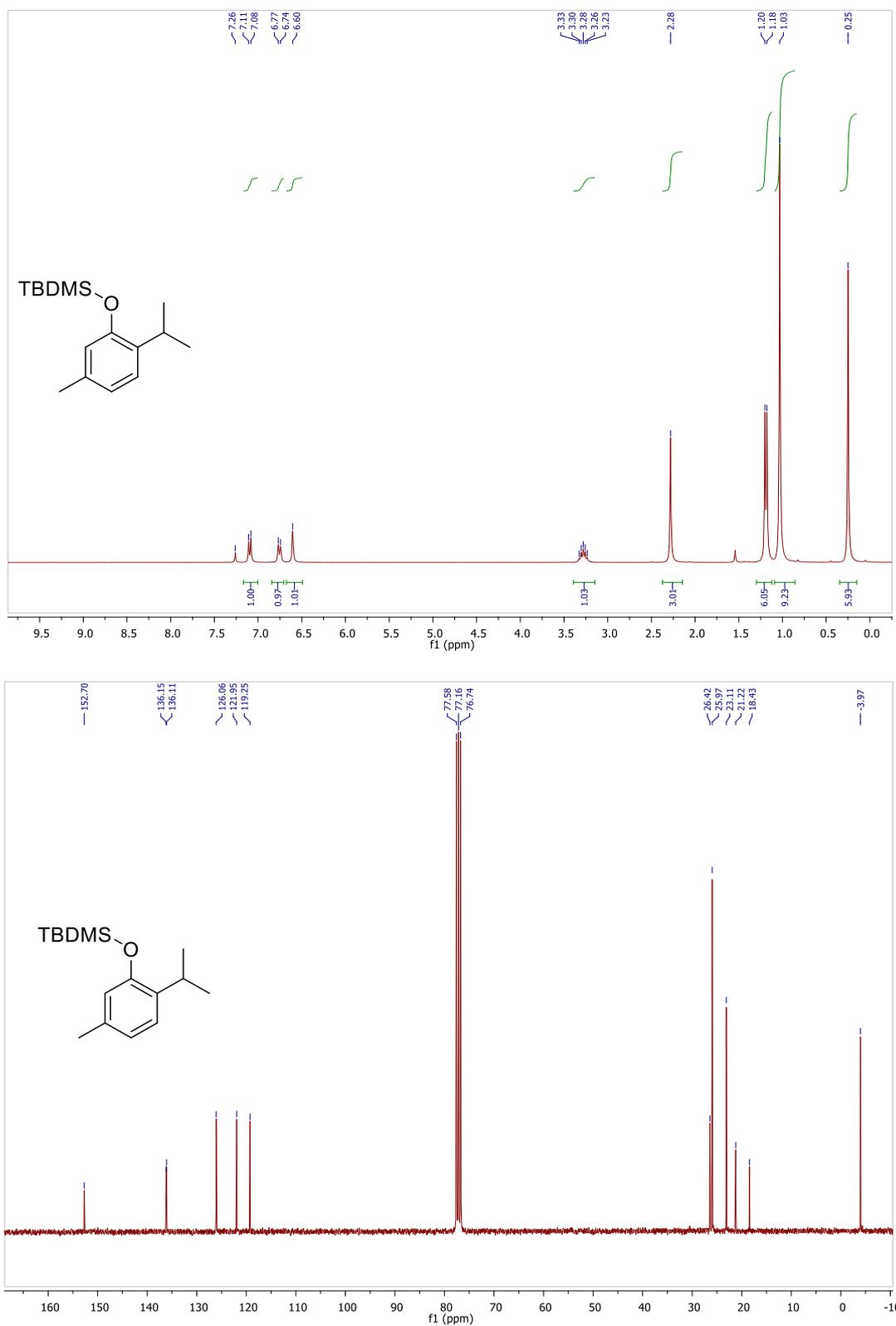


Figure S3. NMR spectra of compound **2**.

^1H and ^{13}C spectra of *tert*-butyl(2-isopropyl-5-methylphenoxy)-diphenylsilane (**4**)

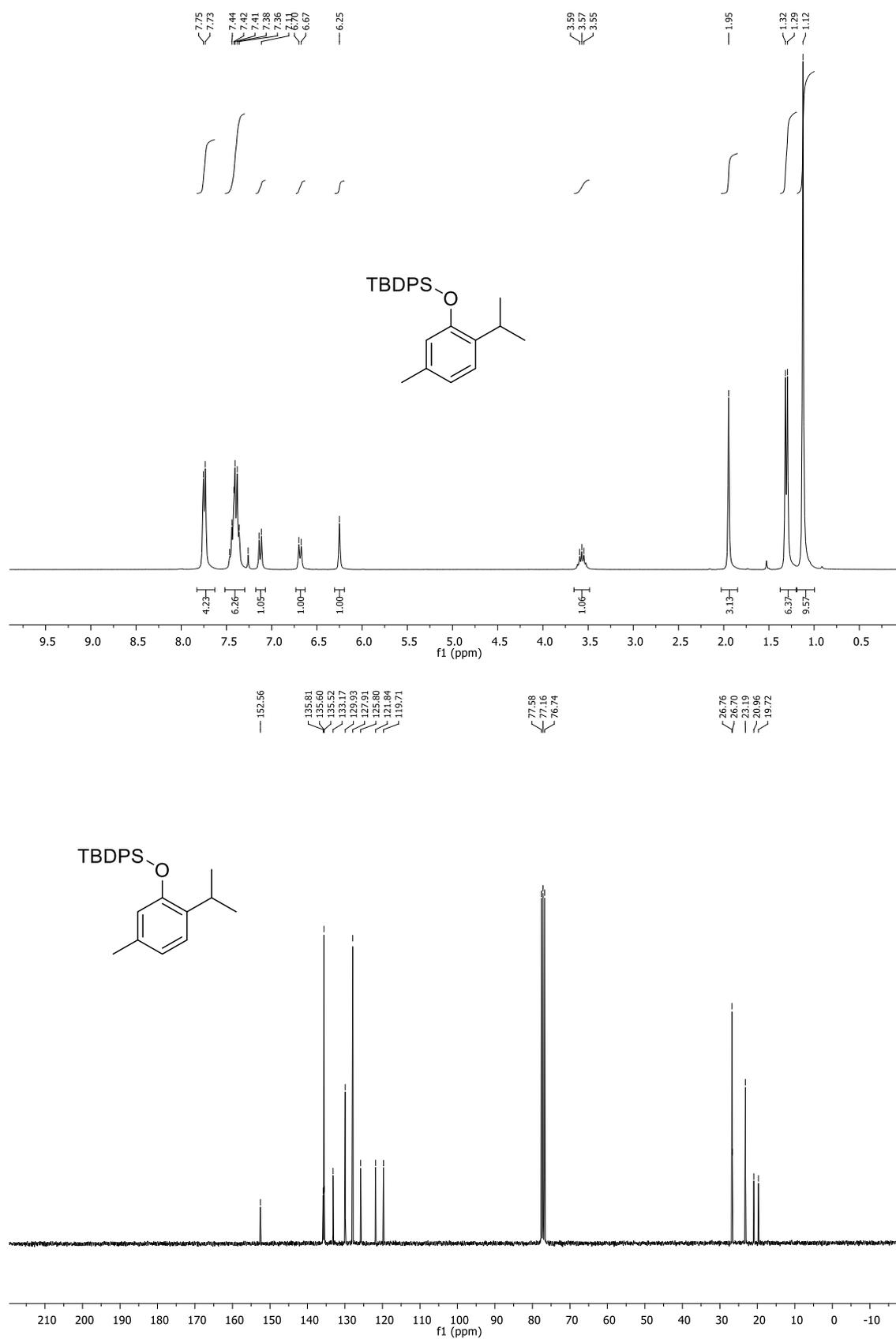


Figure S4. NMR spectra of compound **4**.

^1H and ^{13}C spectra of 2-((*tert*-butyldimethylsilyl)oxy)-4-methylbenzaldehyde (**S1**)

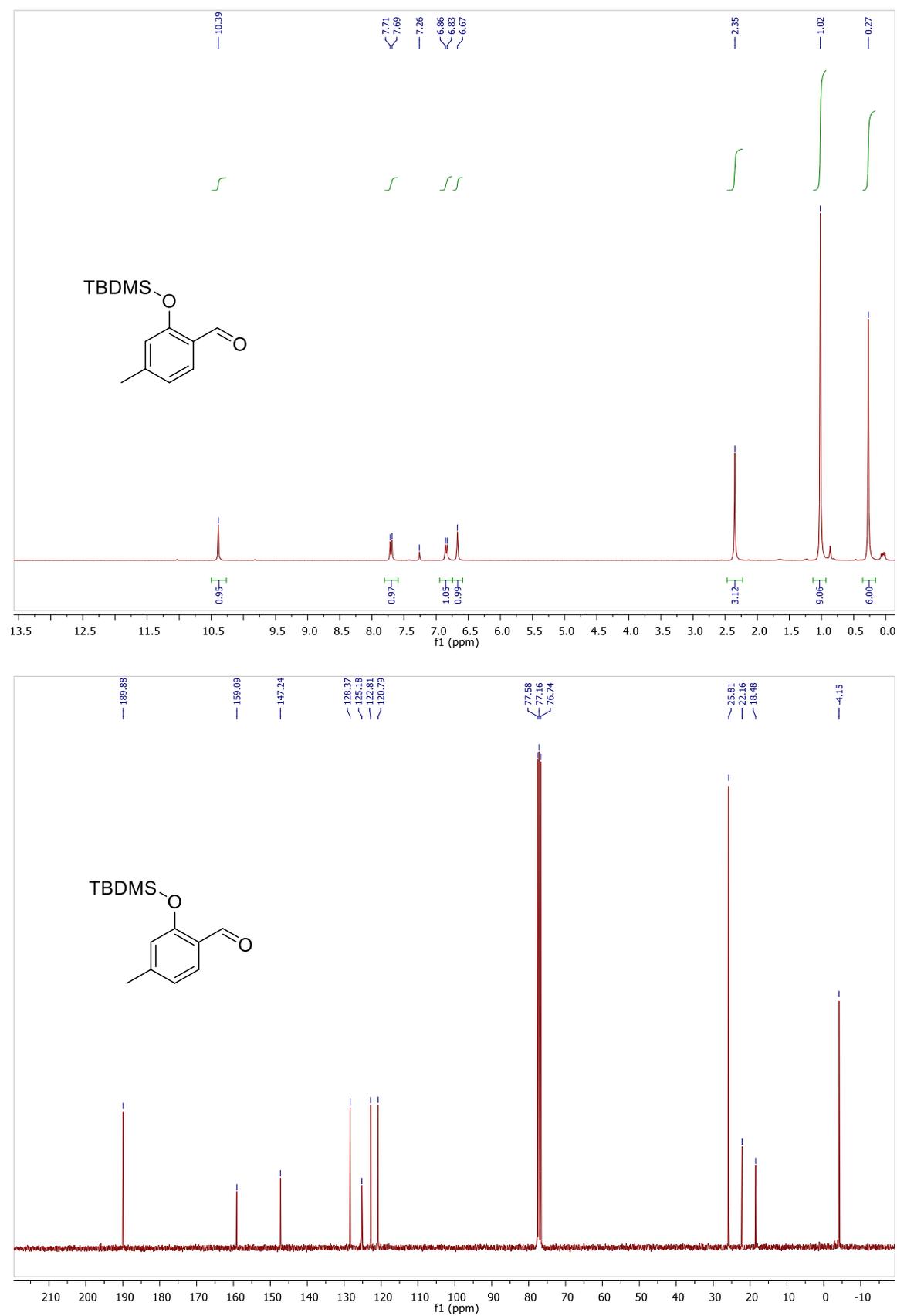


Figure S5. NMR spectra of compound **S1**.

^1H and ^{13}C spectra of *tert*-butyldimethyl(5-methyl-2-(2-methylprop-1-en-1-yl)phenoxy)silane (S2)

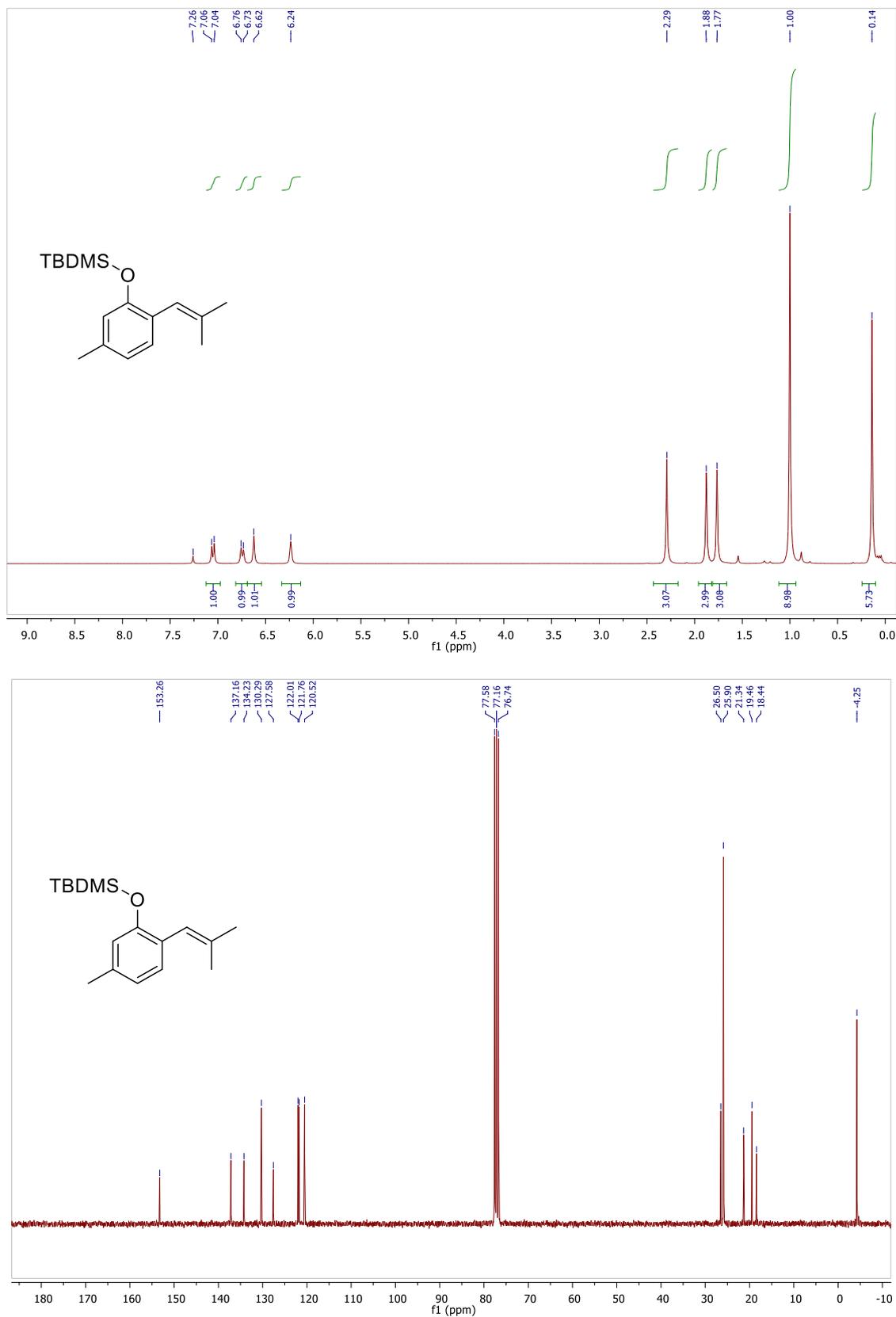


Figure S6. NMR spectra of compound S2.

^1H and ^{13}C spectra of *tert*-butyl(2-isobutyl-5-methylphenoxy)dimethylsilane (**6**)

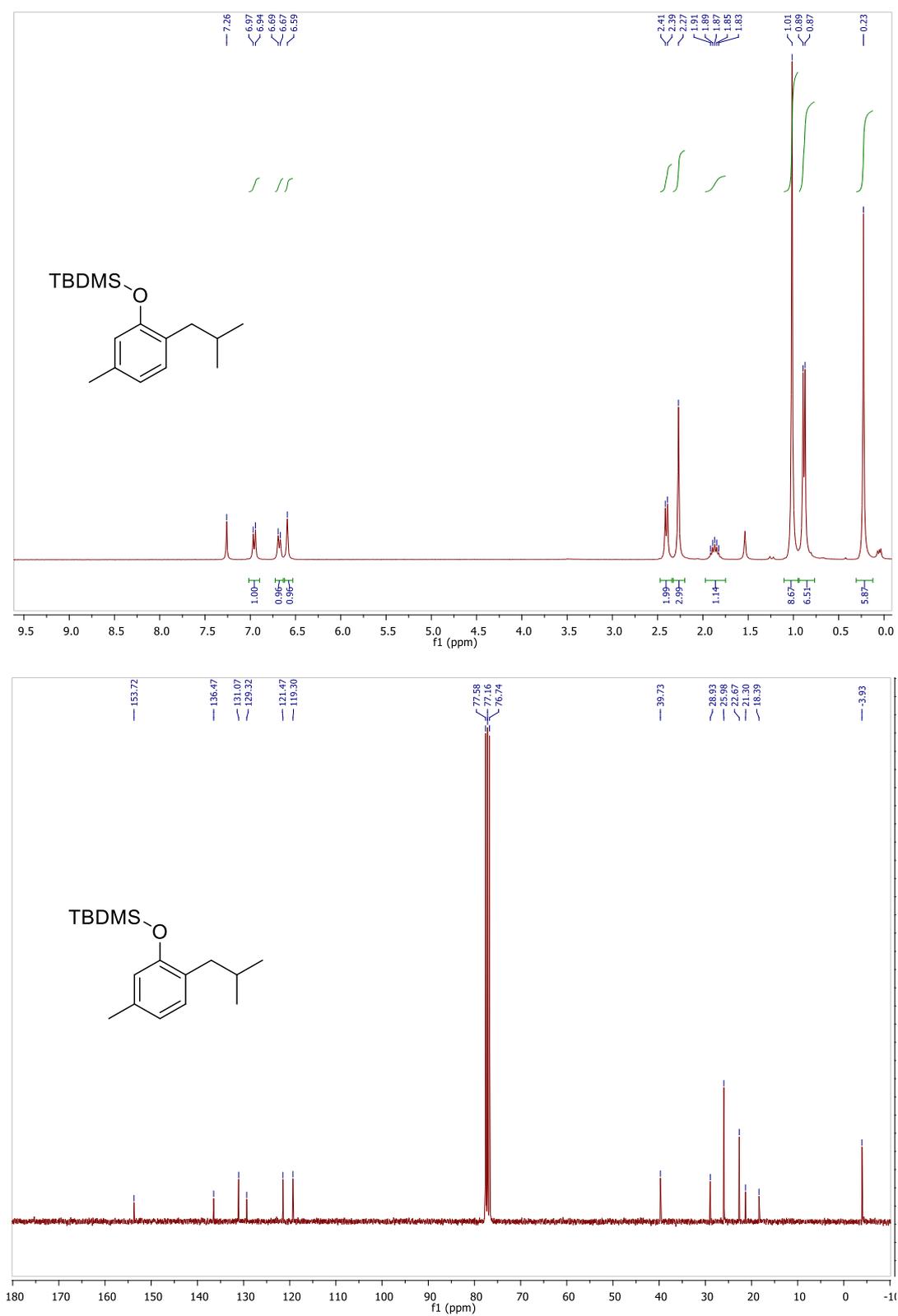


Figure S7. NMR spectra of compound **6**.

^1H and ^{13}C spectra of 5-methyl-2-(2-methylprop-1-en-1-yl)phenol (**S3**)

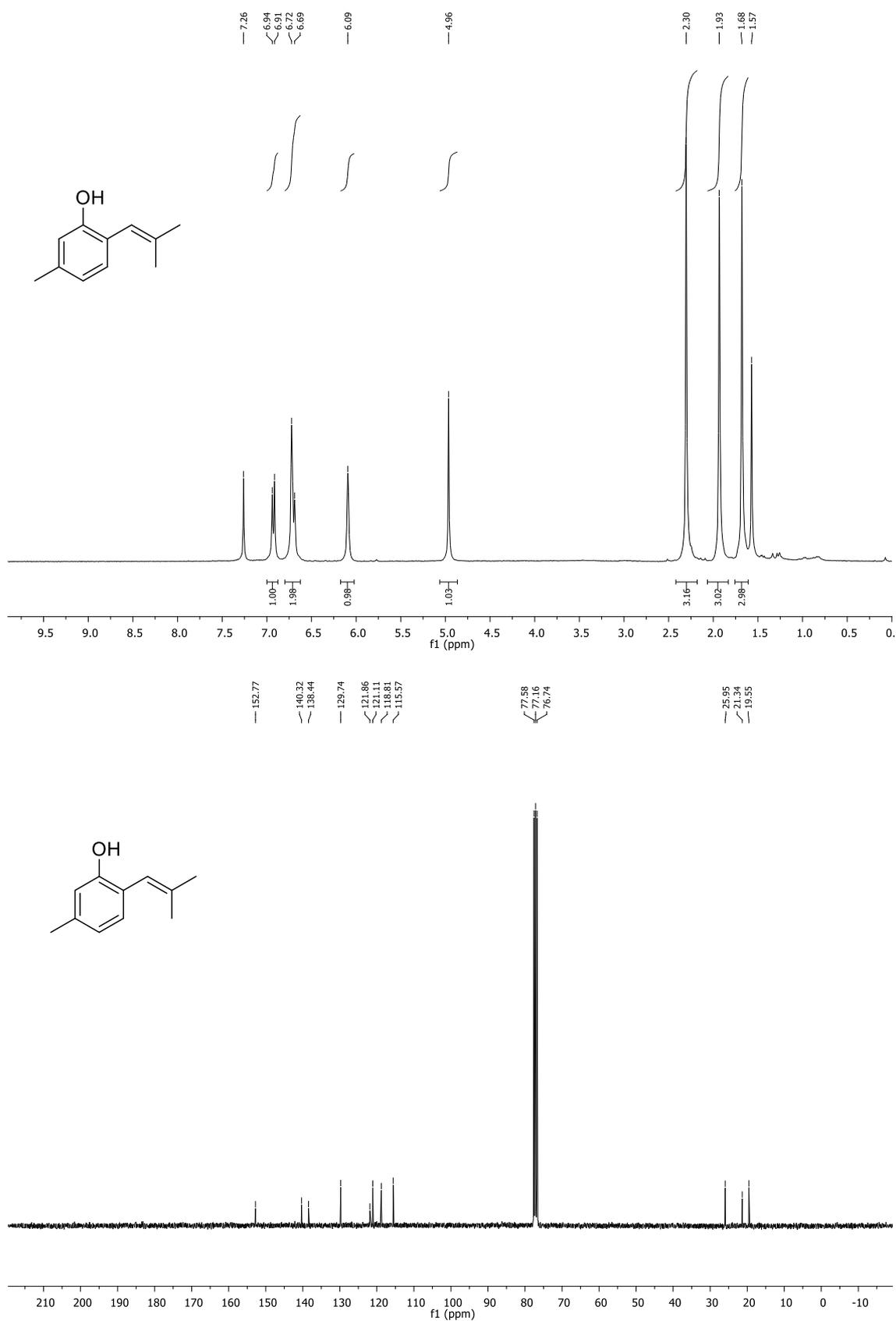


Figure S8. NMR spectra of compound **S3**.

^1H and ^{13}C spectra of 2-isobutyl-5-methylphenol (**8**)

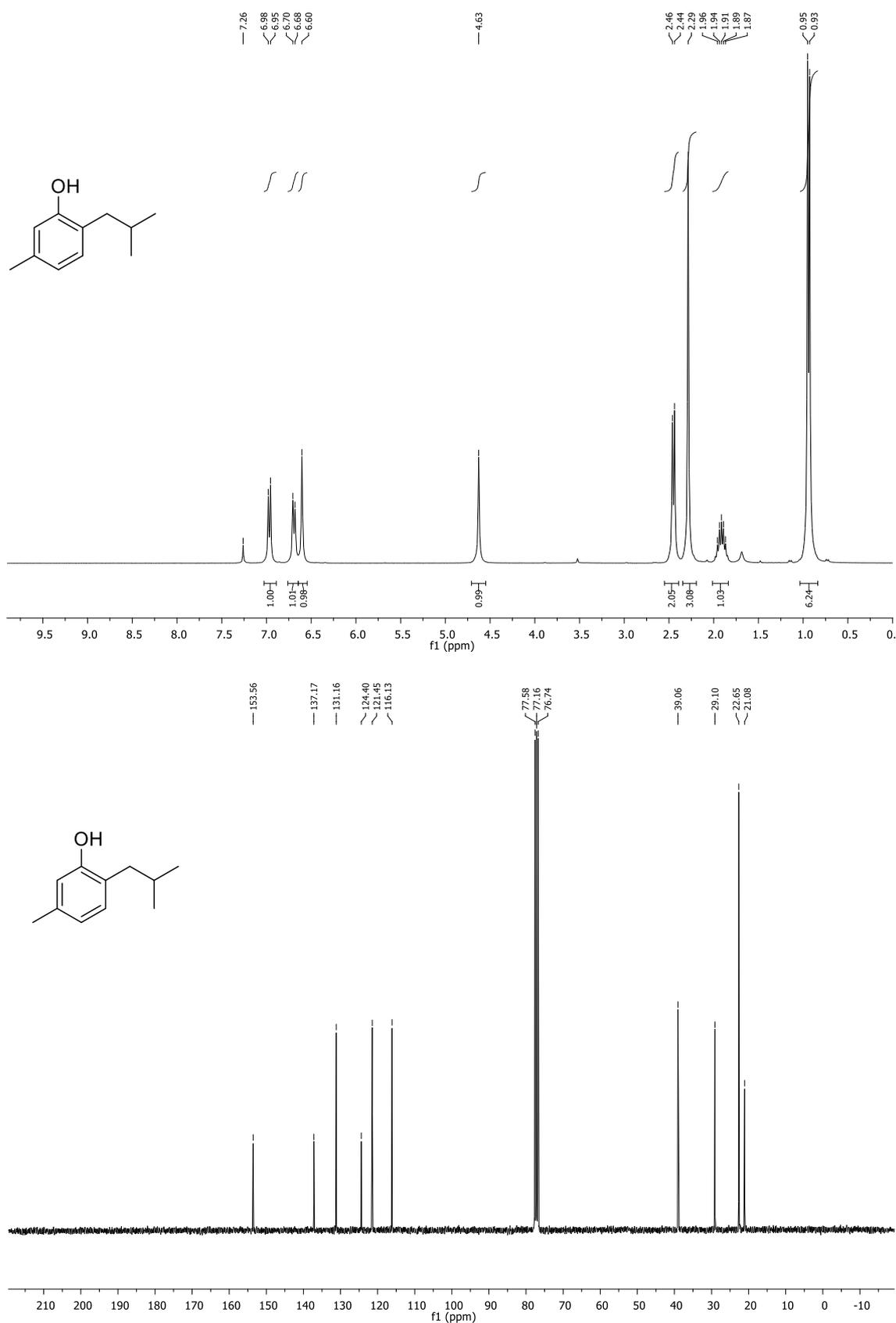


Figure S9. NMR spectra of compound **8**.

^1H and ^{13}C spectra of 2-(*sec*-butyl)-5-methylphenol (**10**)

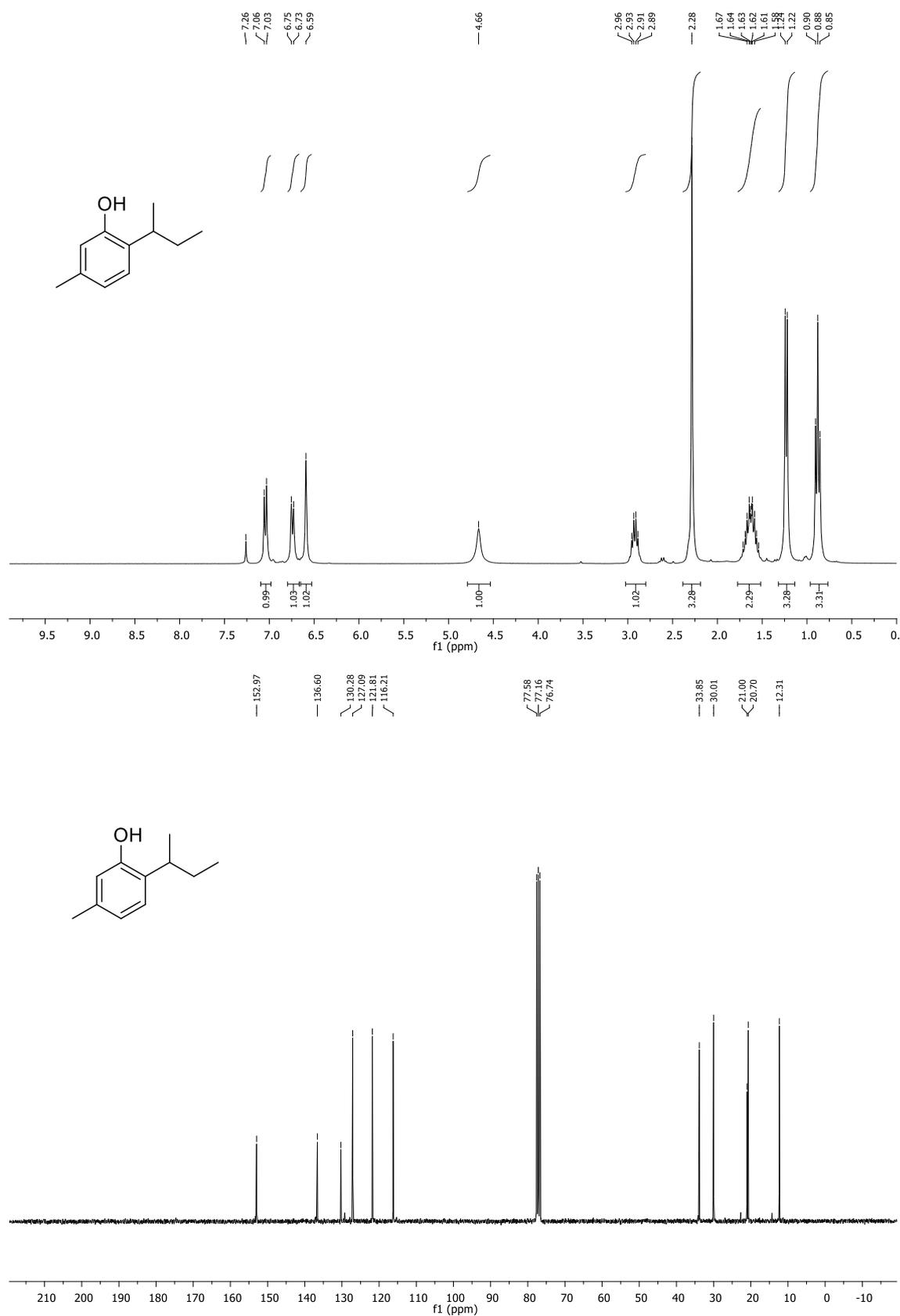


Figure S10. NMR spectra of compound **10**.

^1H and ^{13}C spectra of 2-methoxy-6-(2-methylprop-1-en-1-yl)phenol (**S4**)

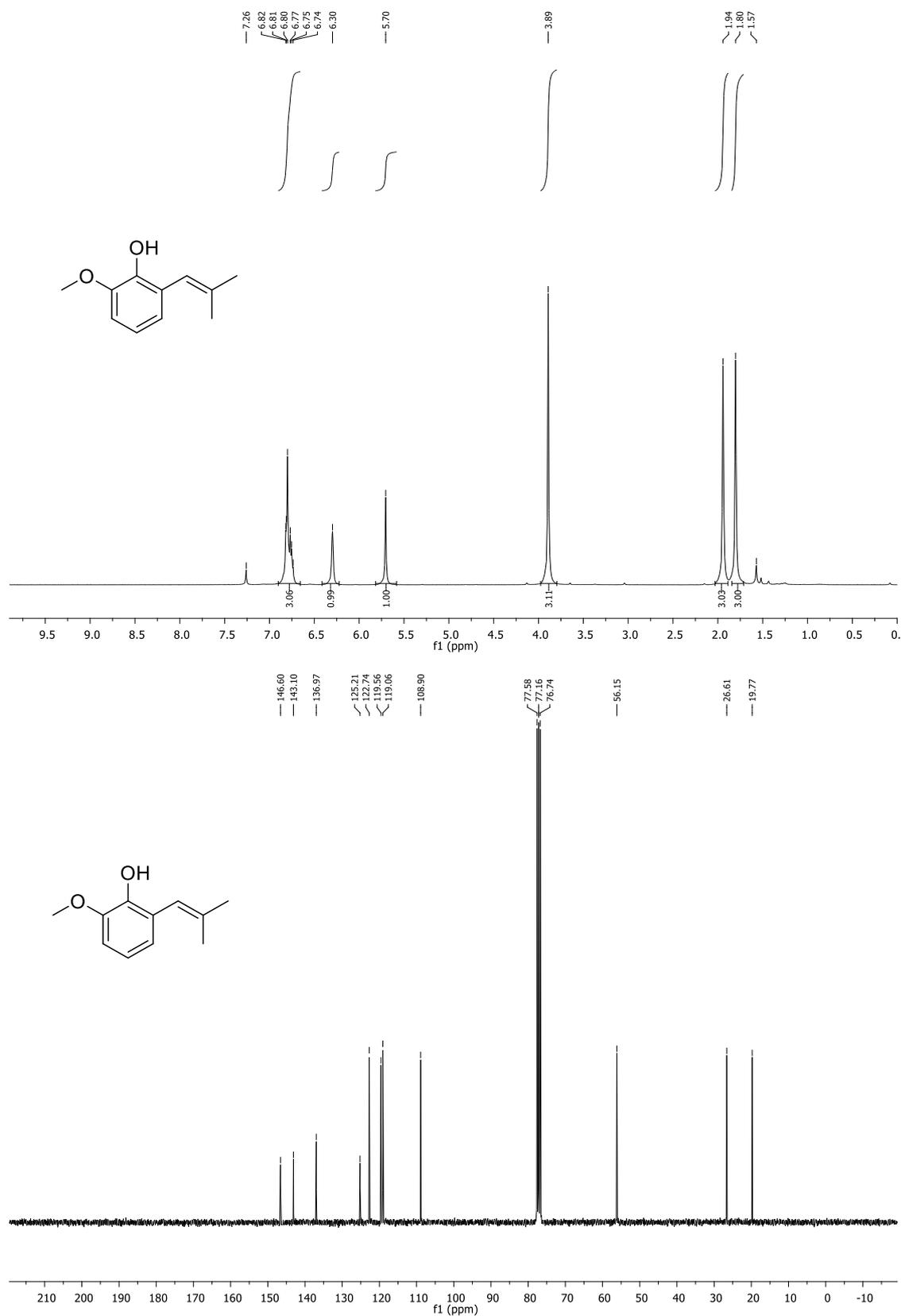


Figure S11. NMR spectra of compound **S4**.

^1H and ^{13}C spectra of 2-isobutyl-6-methoxyphenol (**12**)

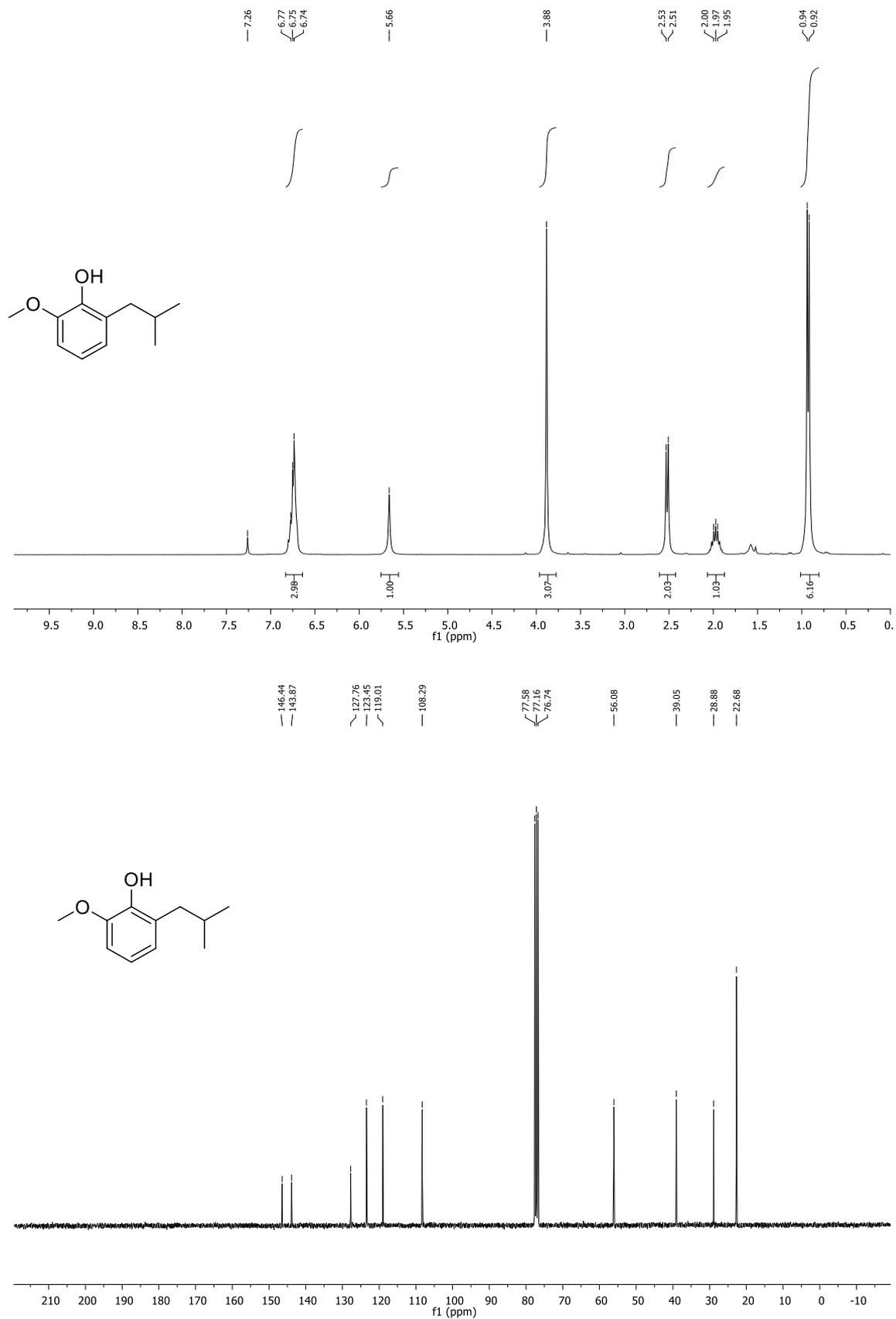


Figure S12. NMR spectra of compound **12**.

^1H and ^{13}C spectra of 3,5-dimethoxy-4'-(((1,1-dimethylethyl)dimethylsilyl)oxy)-4-hydroxy-2'-methyl-5'-(1-methylethyl)-biphenyl (**3**)

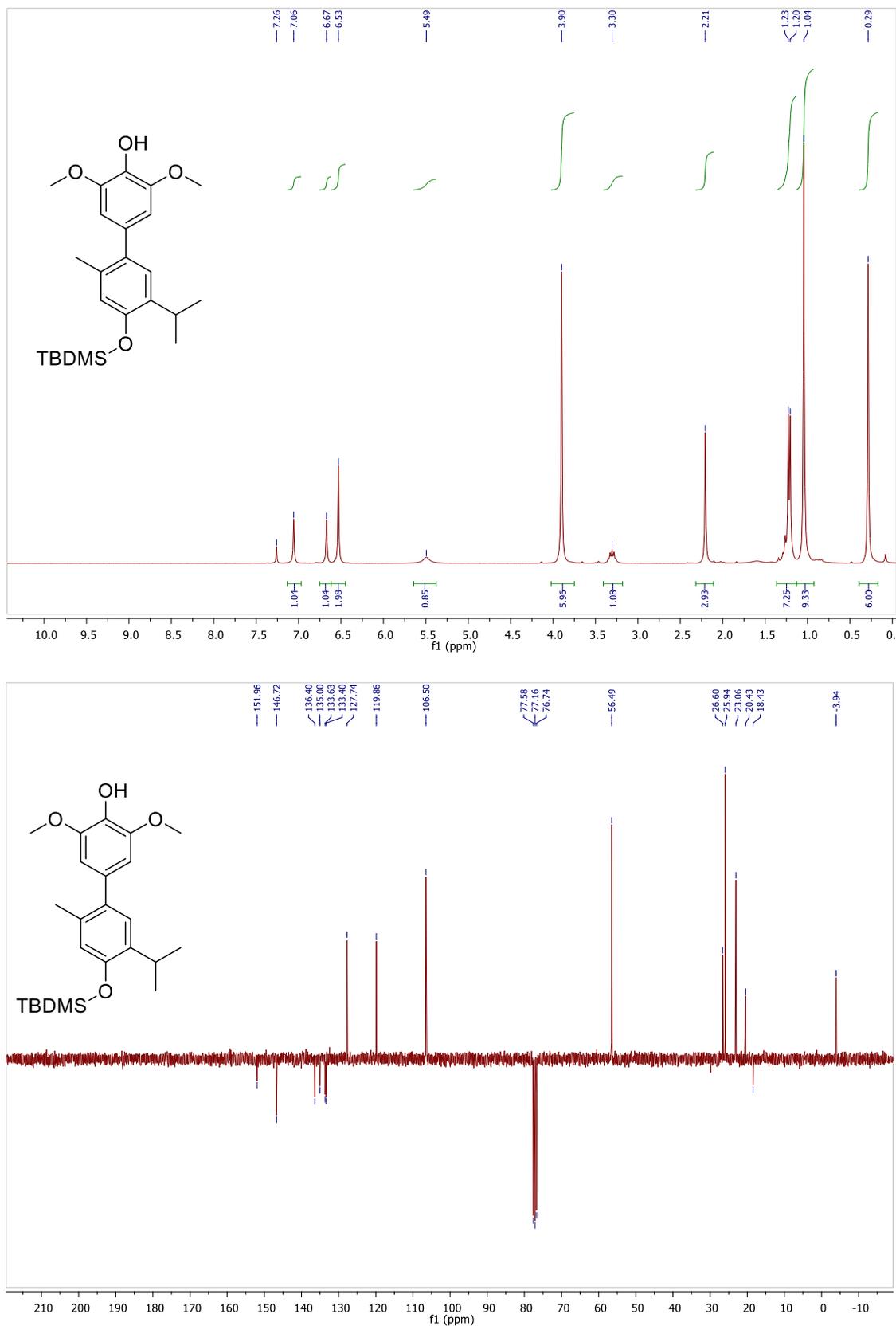


Figure S13. NMR spectra of compound **3**.

^1H and ^{13}C spectra of 3,5-dimethoxy-4'-(((1,1-dimethylethyl)diphenylsilyl)oxy)-4-hydroxy-2'-methyl-5'-(1-methylethyl)-biphenyl (**5**)

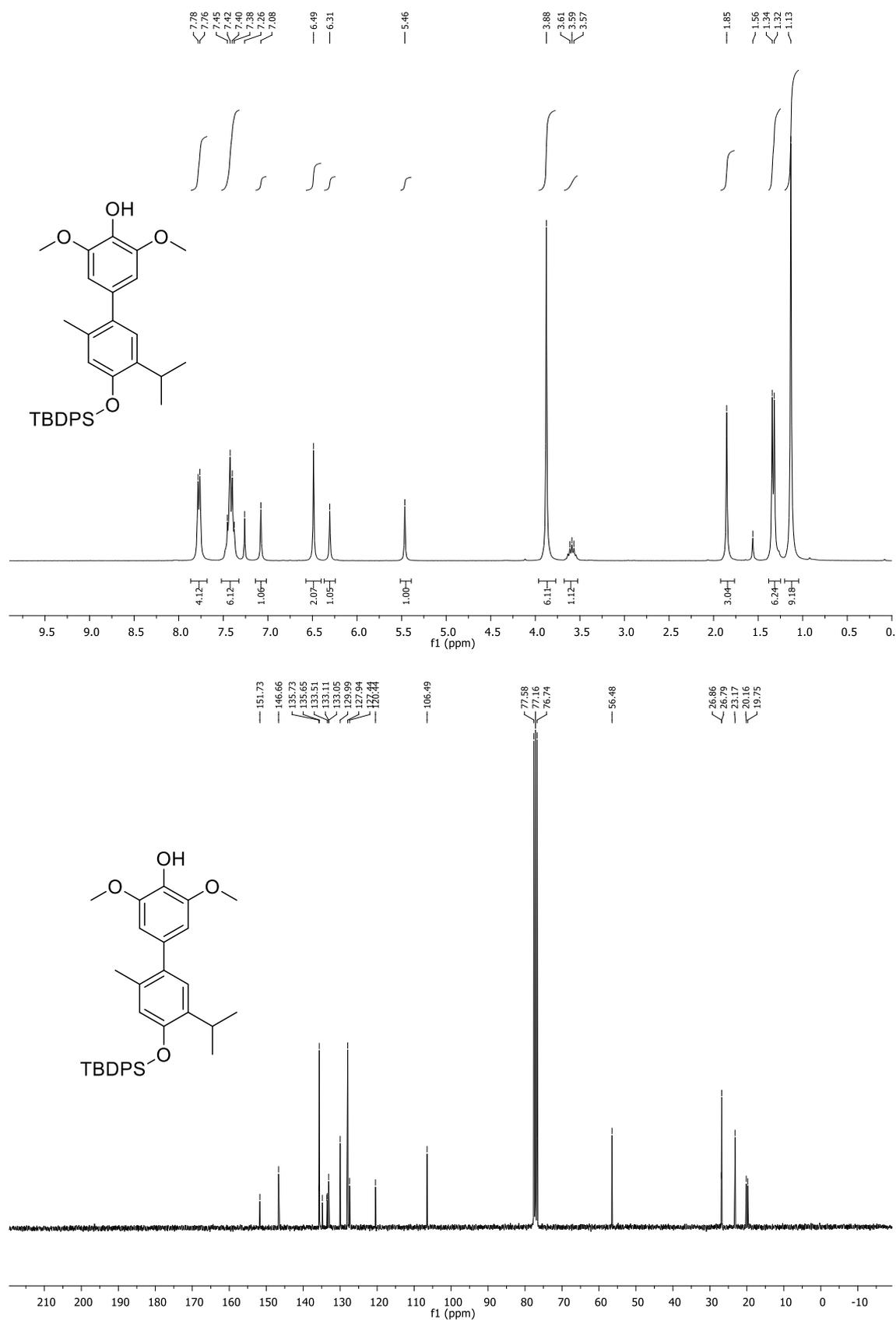


Figure S14. NMR spectra of compound **5**.

^1H and ^{13}C spectra of 3,5-dimethoxy-4'-(((1,1-dimethylethyl)dimethylsilyl)oxy)-4-hydroxy-2'-methyl-5'-(1-methylethyl)-biphenyl (**7**)

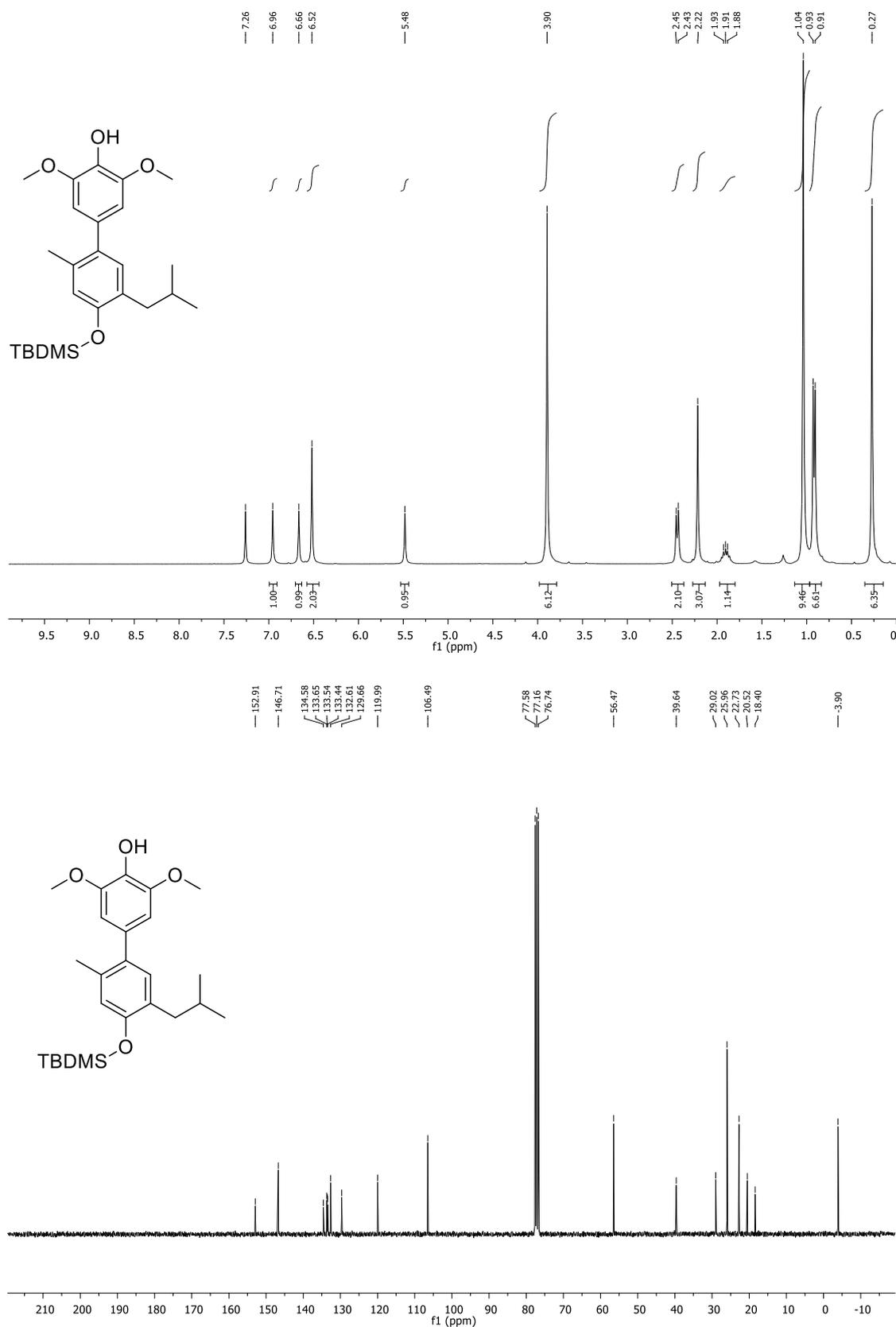


Figure S15. NMR spectra of compound **7**.

^1H and ^{13}C spectra of 5-isobutyl-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**9**)

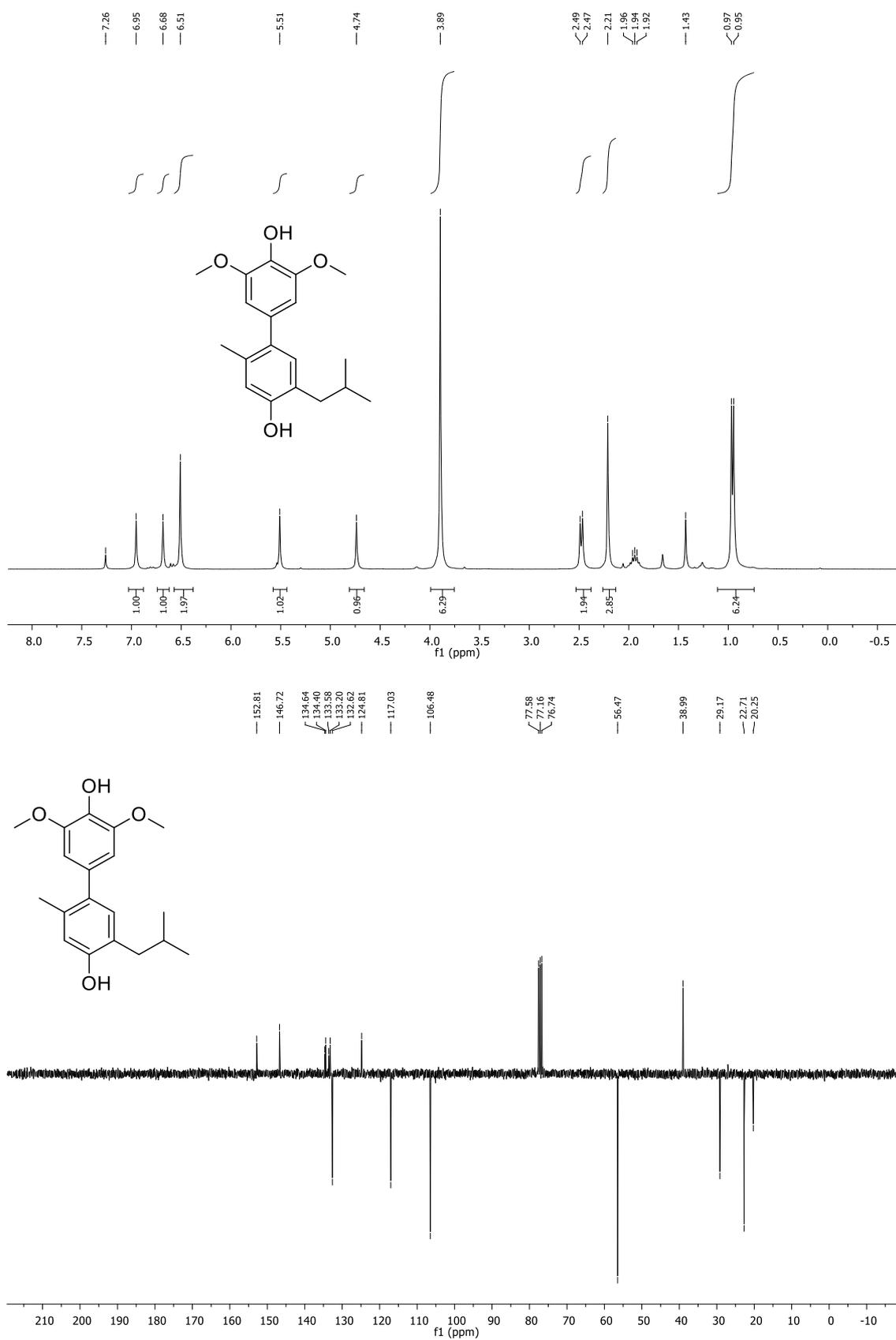


Figure S16. NMR spectra of compound **9**.

^1H and ^{13}C spectra of 5-(*sec*-butyl)-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**11**)

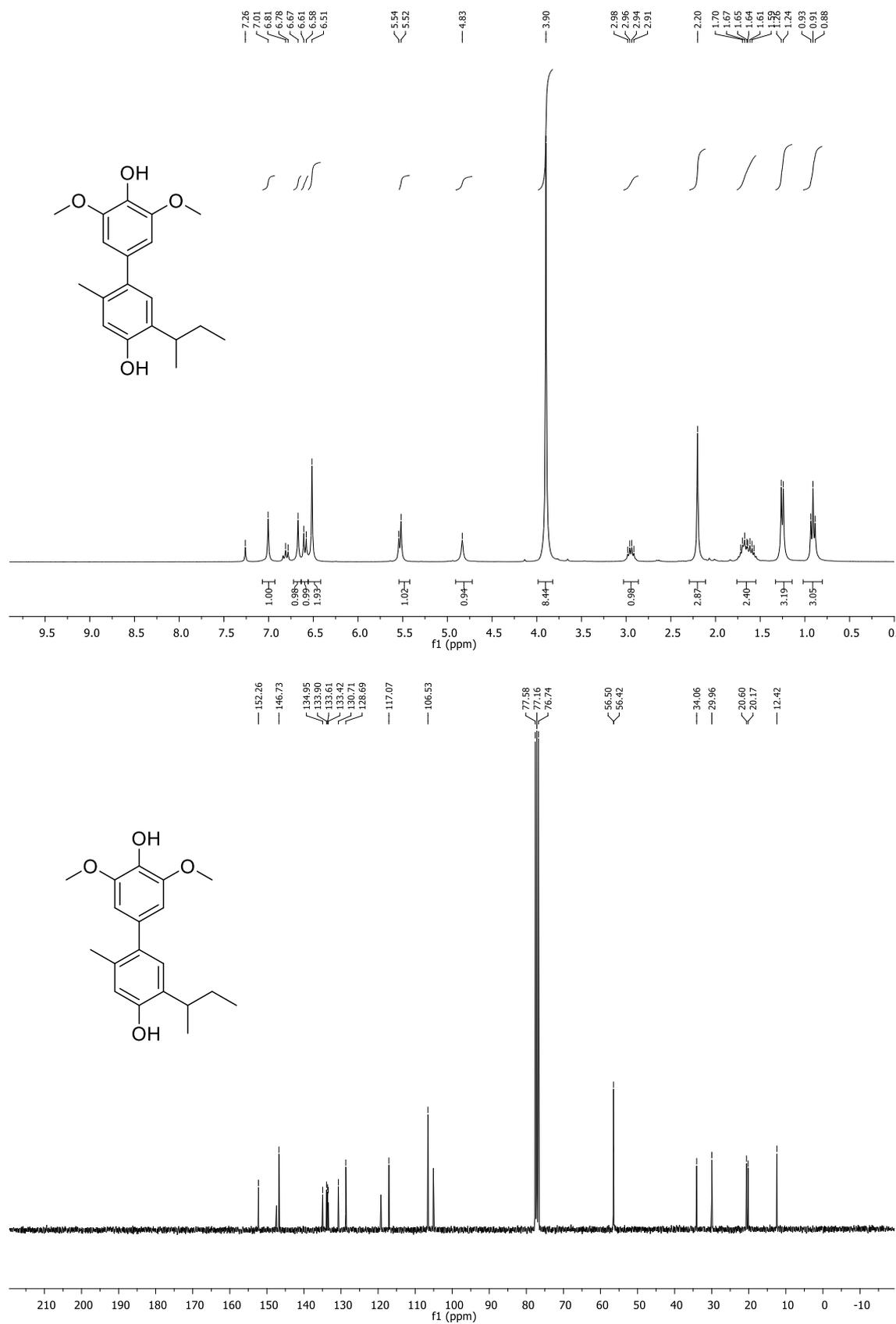


Figure S17. NMR spectra of compound **11**.

^1H and ^{13}C spectra of mixture of 3',5'-diisobutyl-5'-methoxy-2-methyl-[1,1'-biphenyl]-4,4'-diol (**13**) and 3,3'-diisobutyl-5,5'-dimethoxy-[1,1'-biphenyl]-4,4'-diol

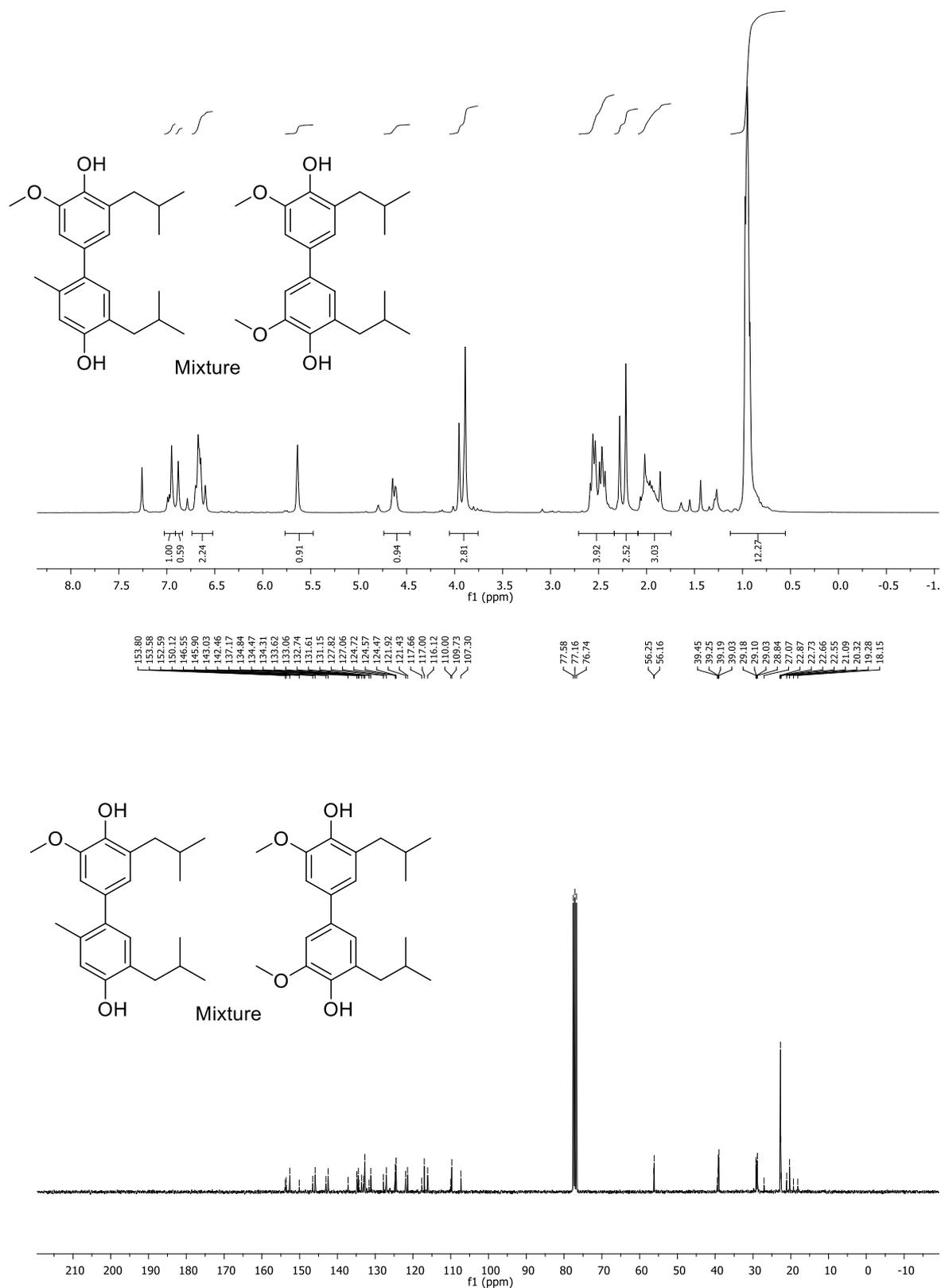


Figure S18. NMR spectra of compound **13**.

^1H and ^{13}C spectra of 3-chloro-5-isobutylpyridine (**15**)

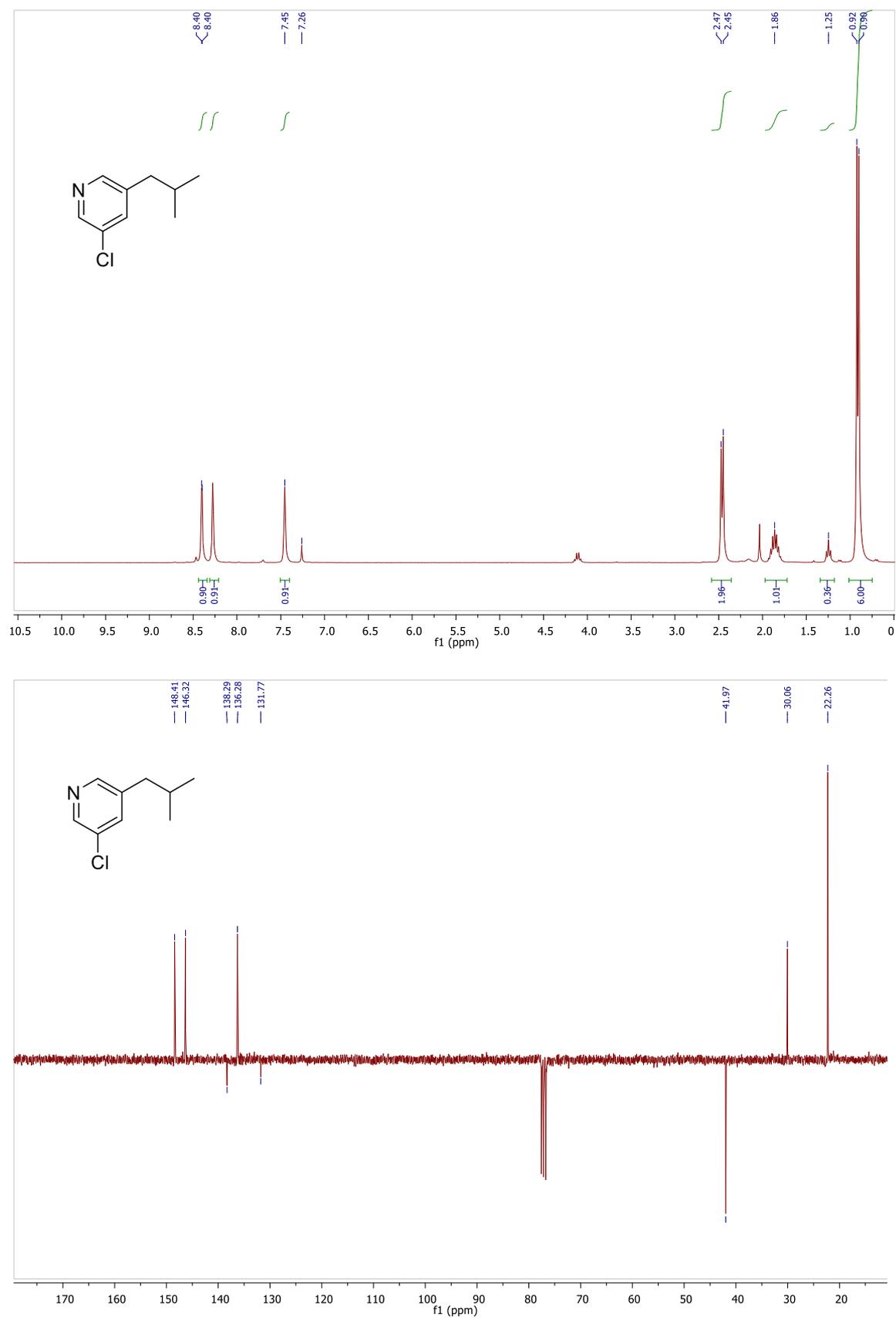


Figure S19. NMR spectra of compound **15**.

^1H and ^{13}C spectra of 3-isobutyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**16**)

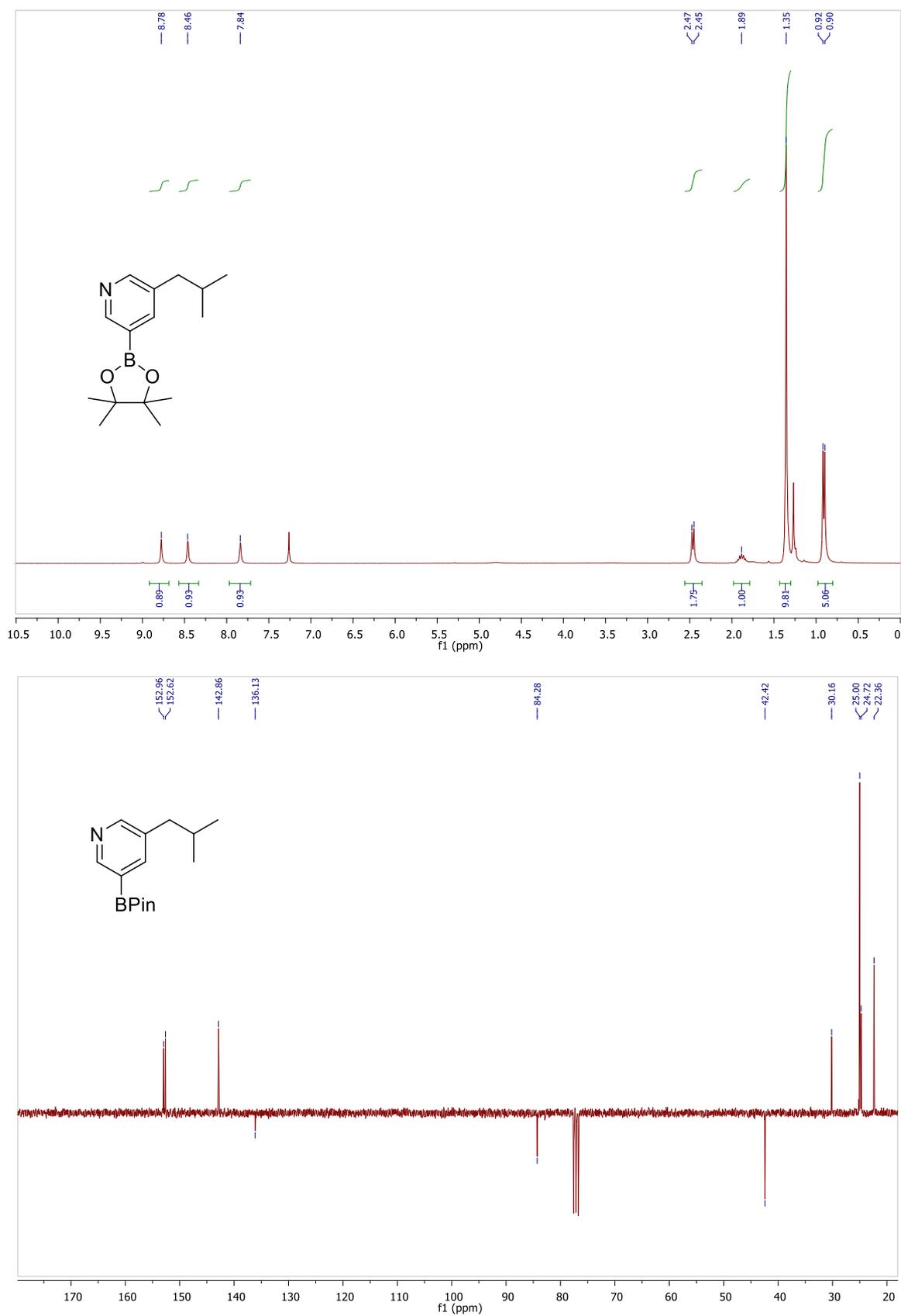


Figure S20. NMR spectra of compound **16**.

^1H and ^{13}C spectra of 3-bromo-5-(*sec*-butyl)pyridine (**18**)

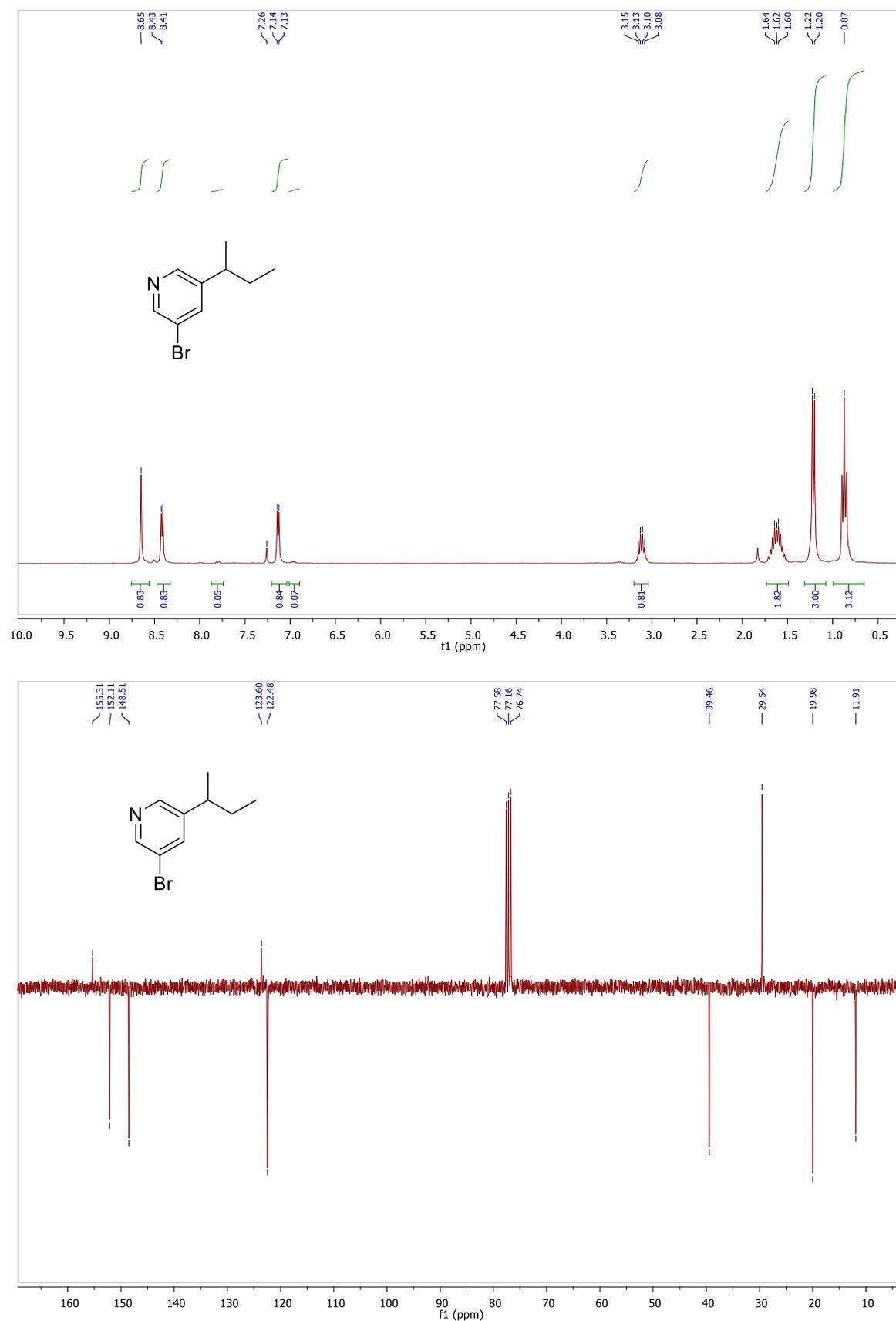


Figure S21. NMR spectra of compound **18**.

^1H and ^{13}C spectra of 3-(*sec*-butyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (19)

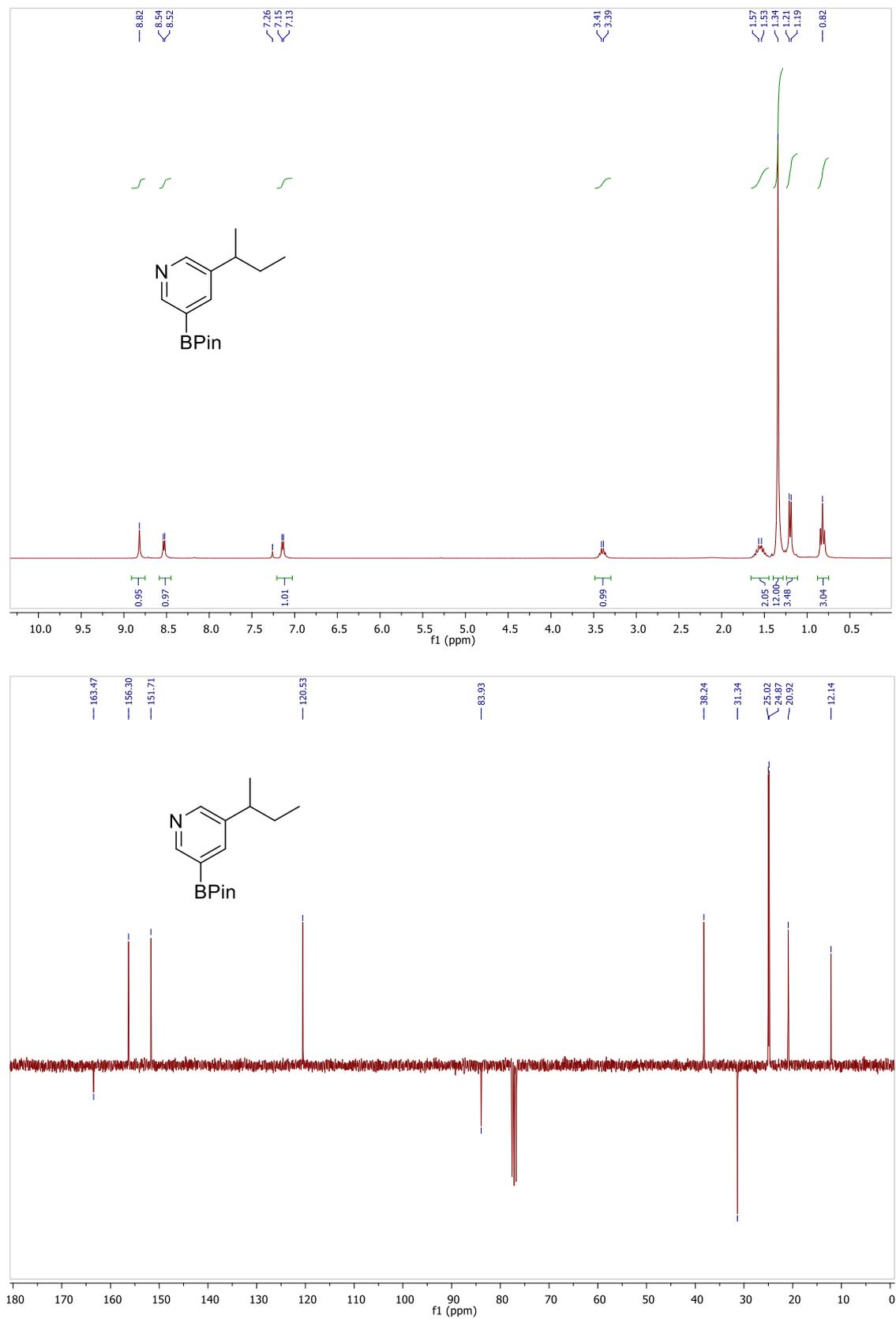


Figure S22. NMR spectra of compound 19.

^1H and ^{13}C spectra of *E*-3-(5-bromopyridin-3-yl)acrylonitrile (**20**)

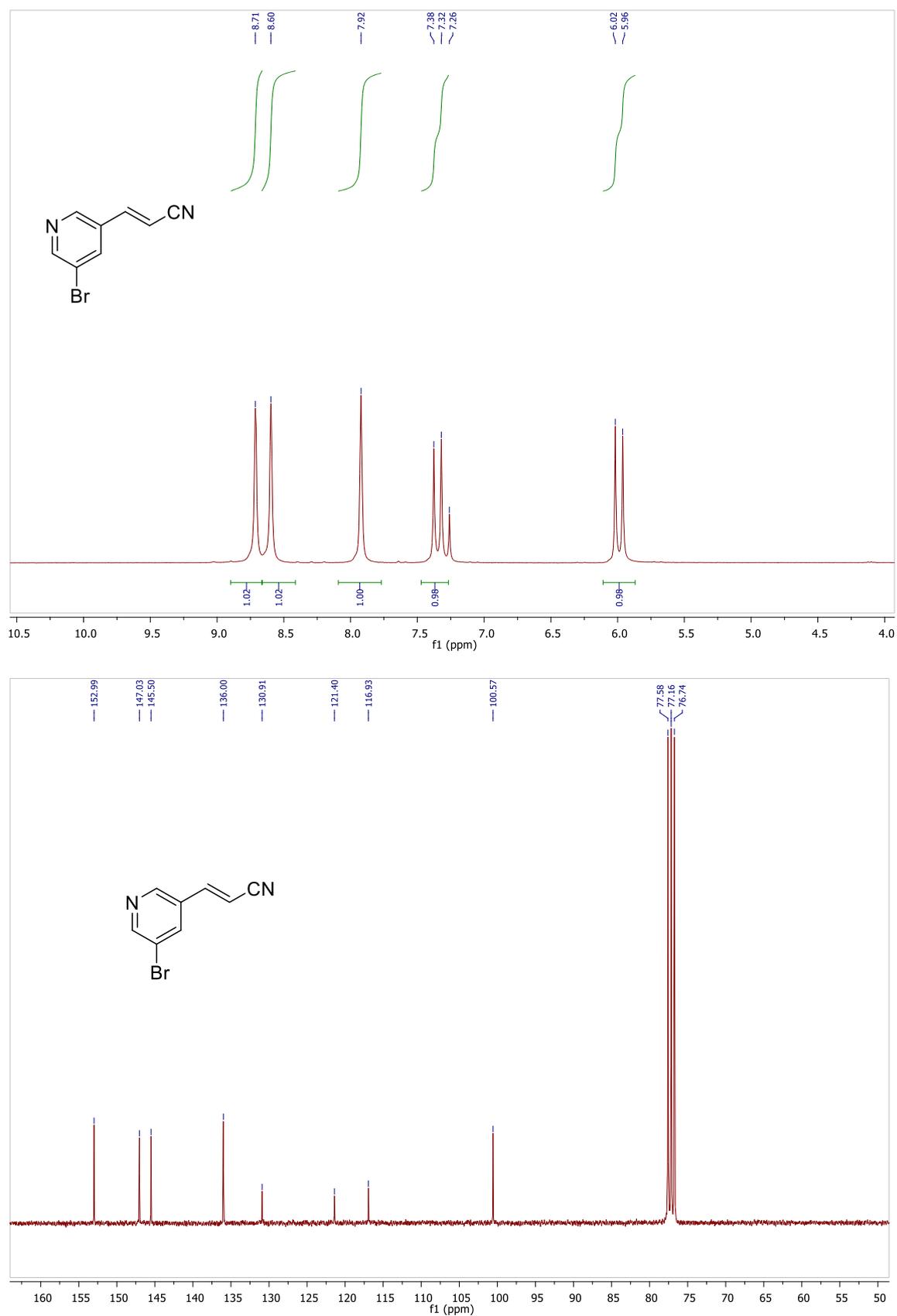


Figure S23. NMR spectra of compound (*E*)-**20**.

^1H and ^{13}C spectra of *Z*-3-(5-bromopyridin-3-yl)acrylonitrile (**20**)

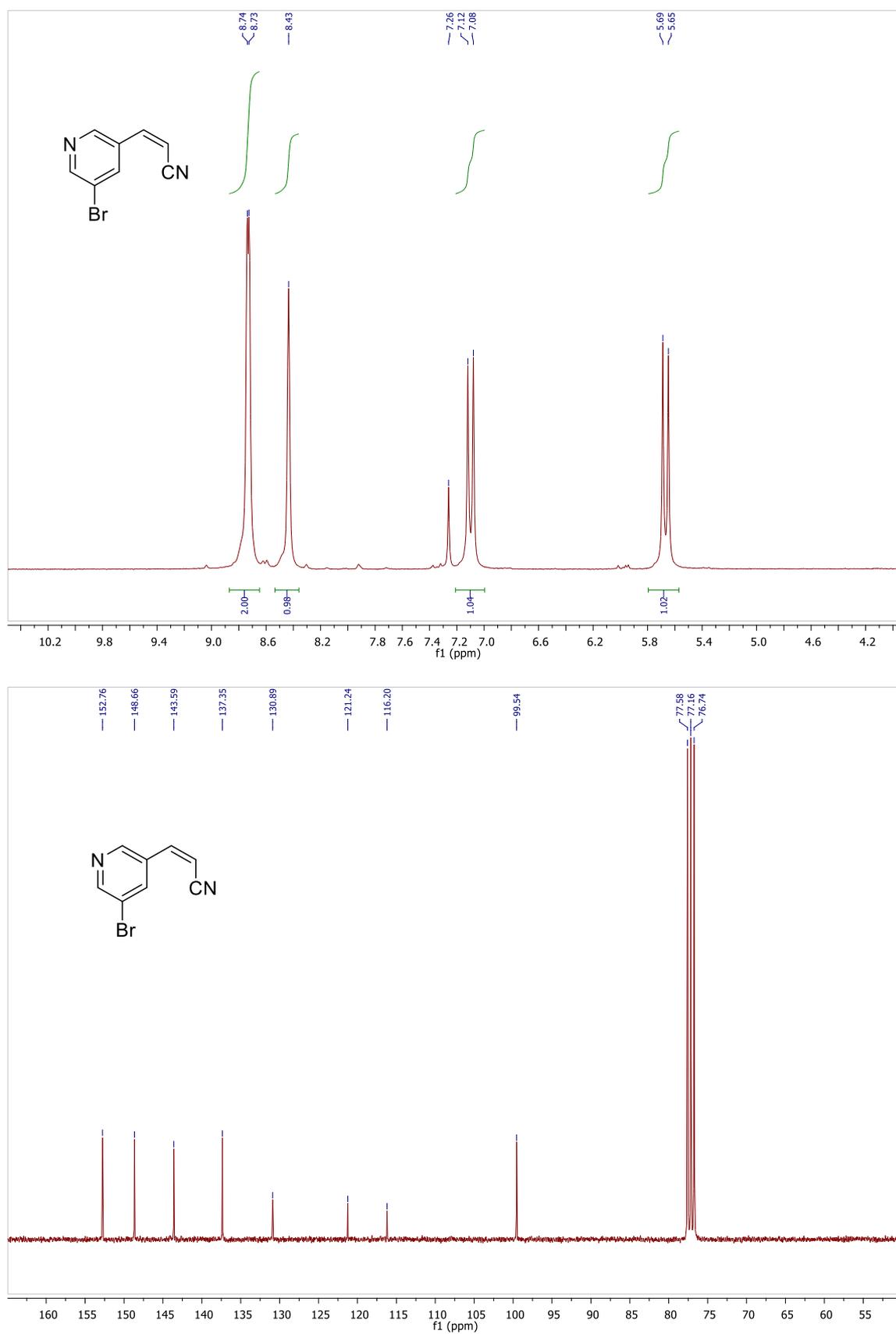


Figure S24. NMR spectra of compound (*Z*)-20.

^1H and ^{13}C spectra of 3-(5-Bromopyridin-3-yl)propanenitrile (**21**)

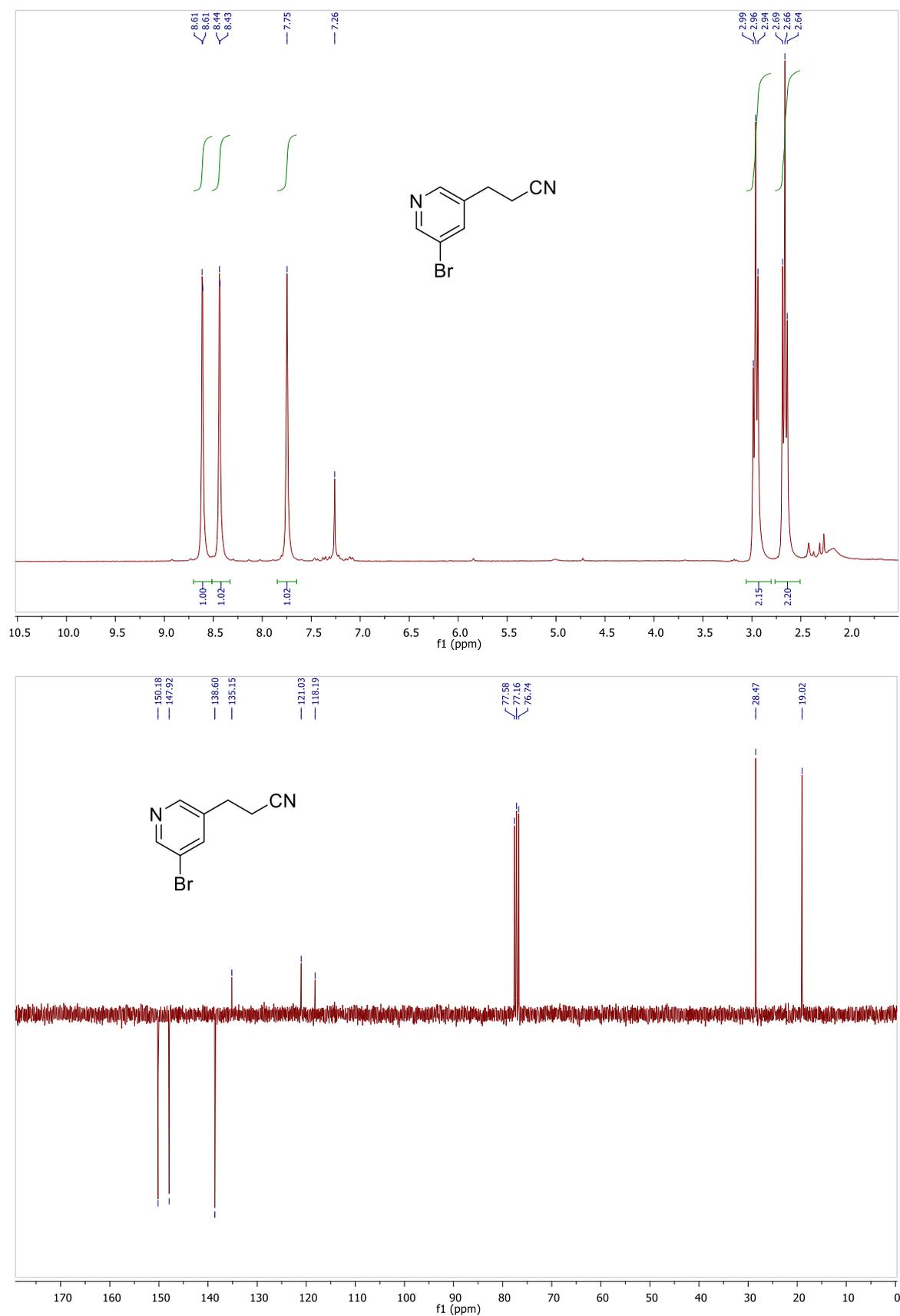


Figure S25. NMR spectra of compound **21**.

^1H and ^{13}C spectra of 3-(5-iodopyridin-3-yl)propanenitrile (**22**)

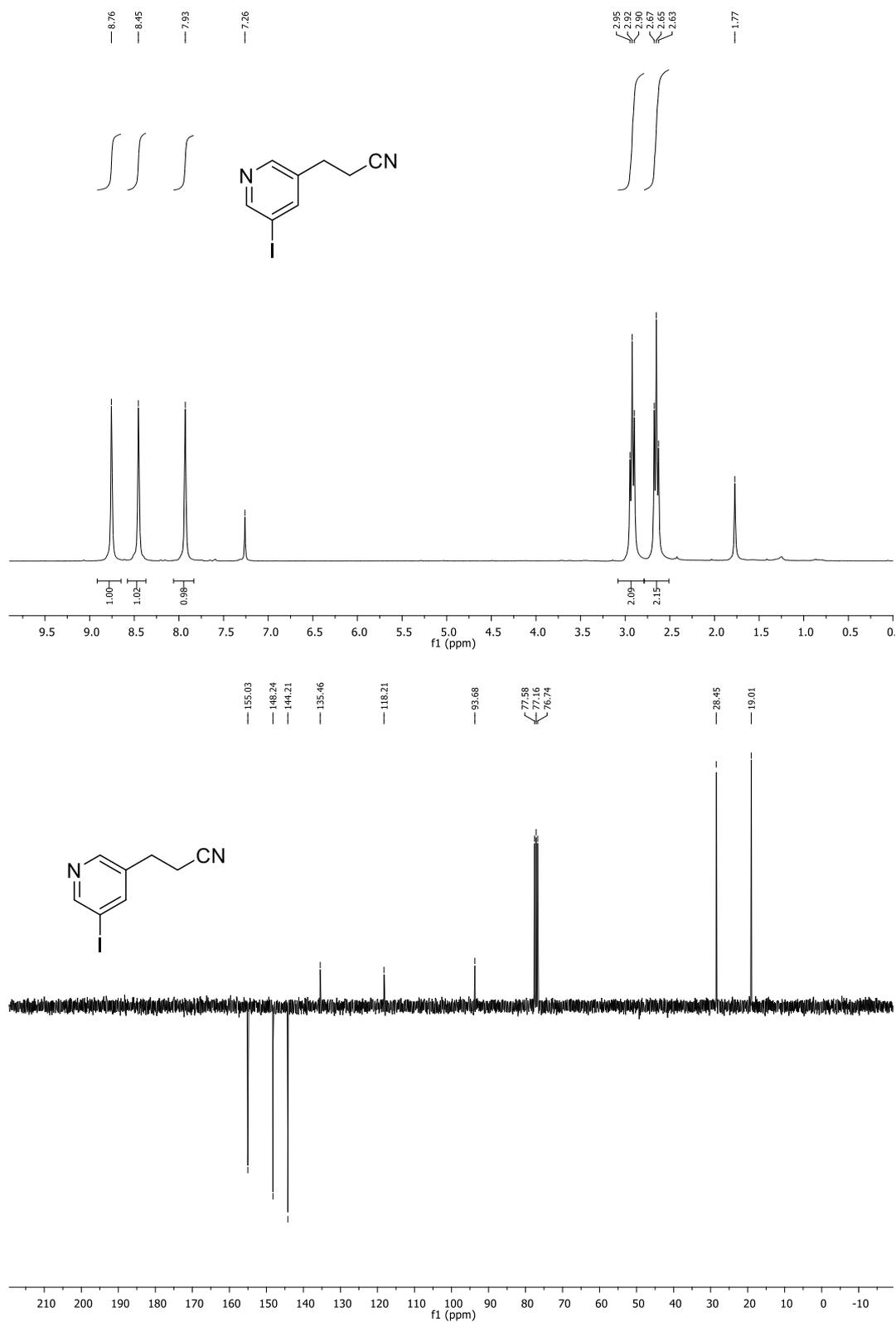


Figure S26. NMR spectra of compound **22**.

^1H and ^{13}C spectra of 3-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)propanenitrile (**23**)

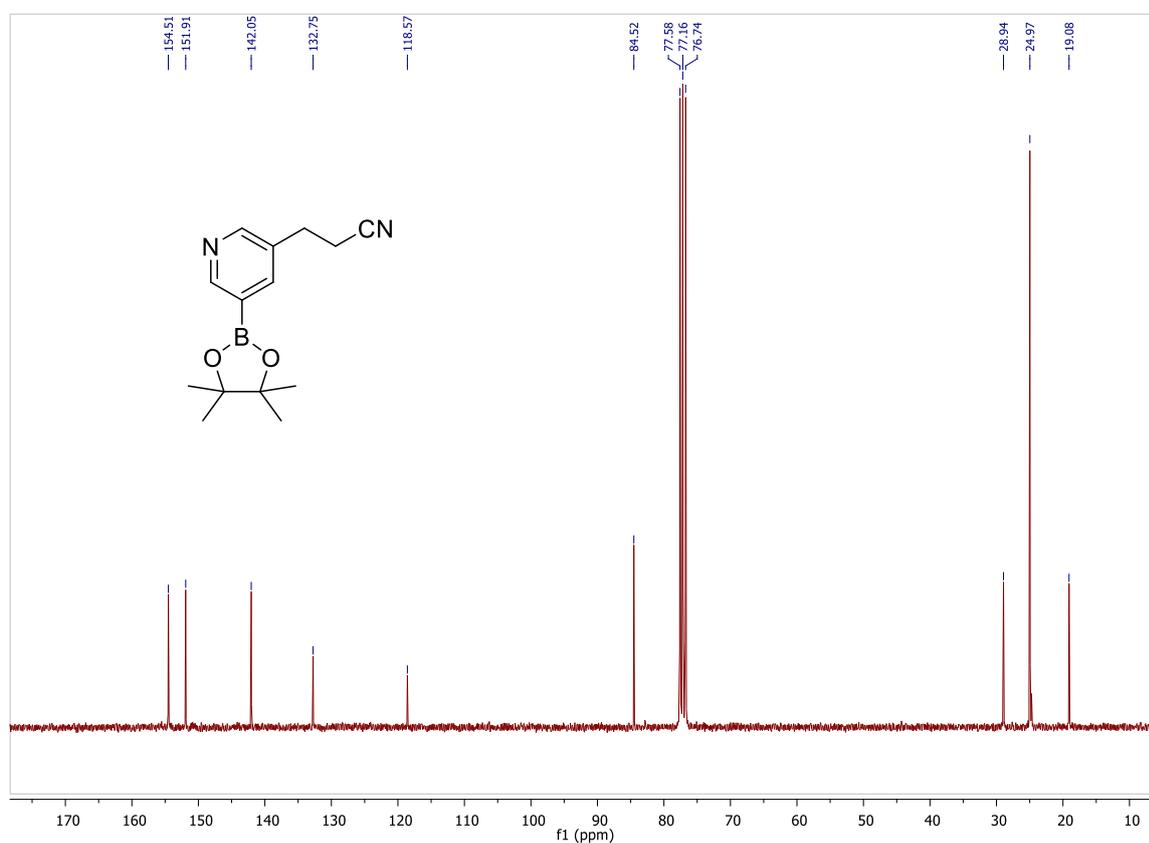
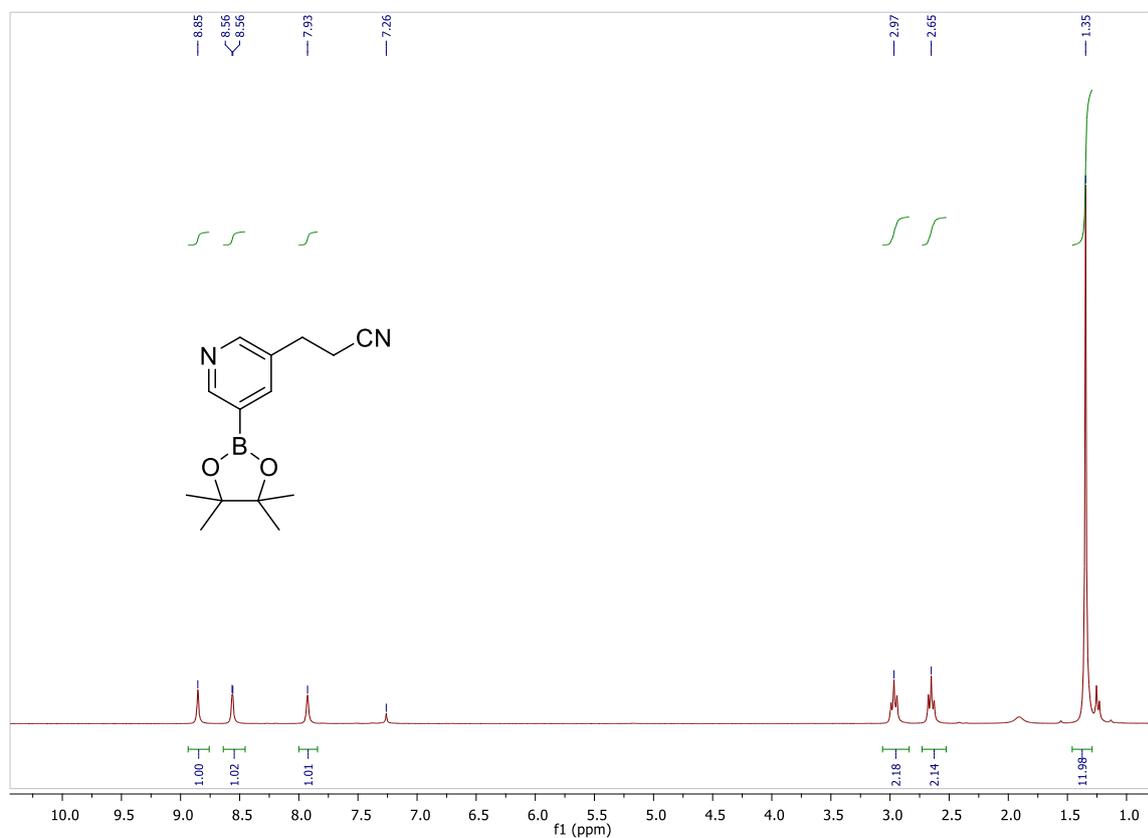


Figure S27. NMR spectra of compound **23**.

^1H and ^{13}C spectra of 3,3',5,5'-tetramethyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**26**)

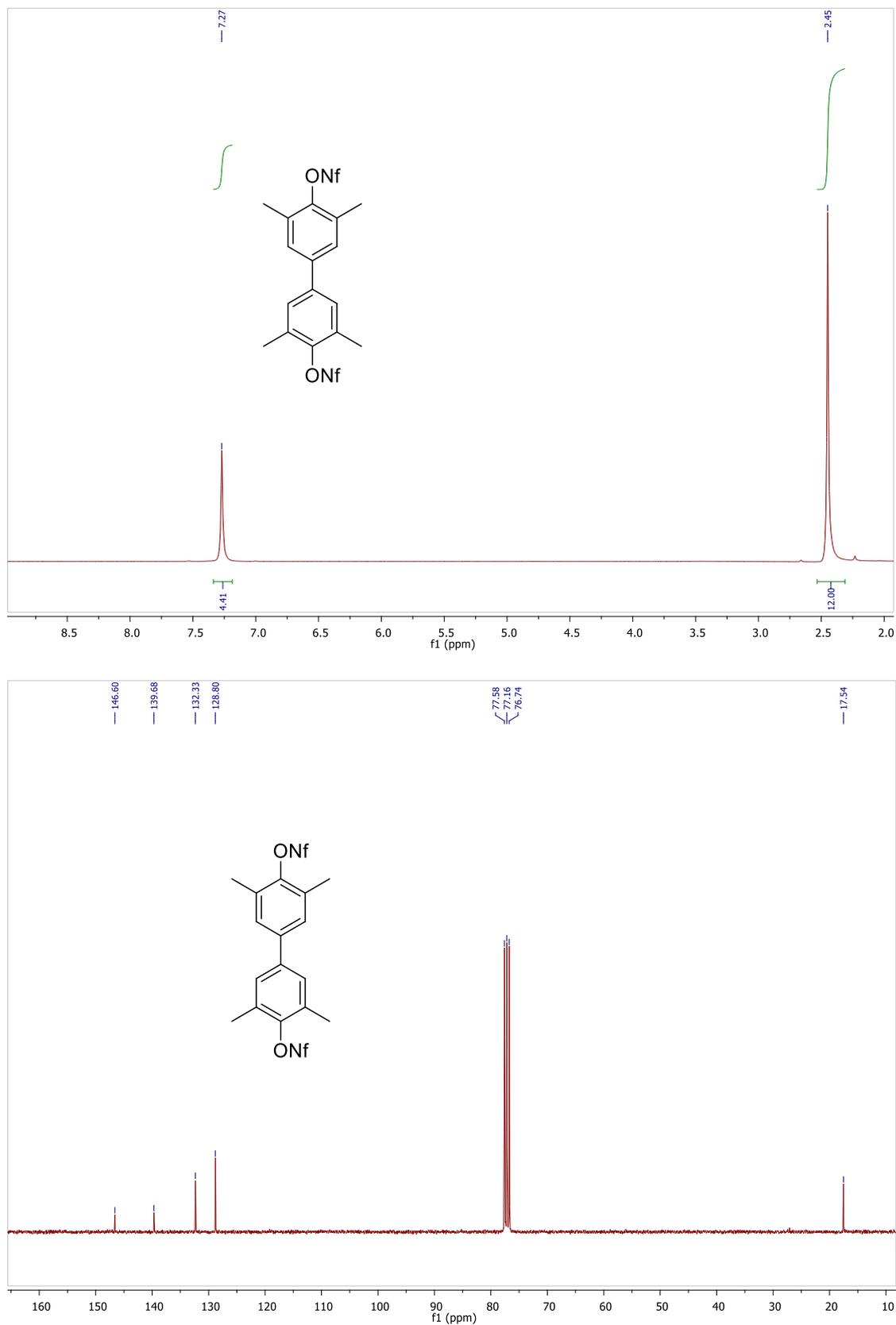


Figure S28. NMR spectra of compound **26**.

^1H and ^{13}C spectra of 5,5'-(3,3',5,5'-tetramethyl-[1,1'-biphenyl]-4,4'-diyl) bis(3-methylpyridine)
(28)

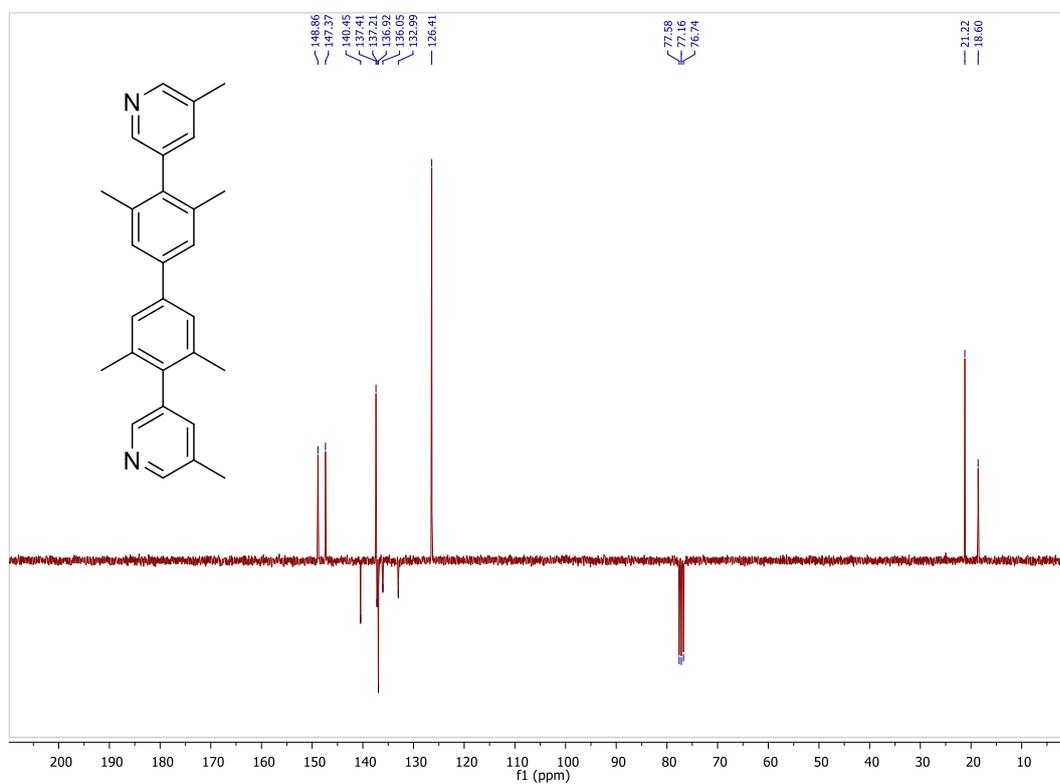
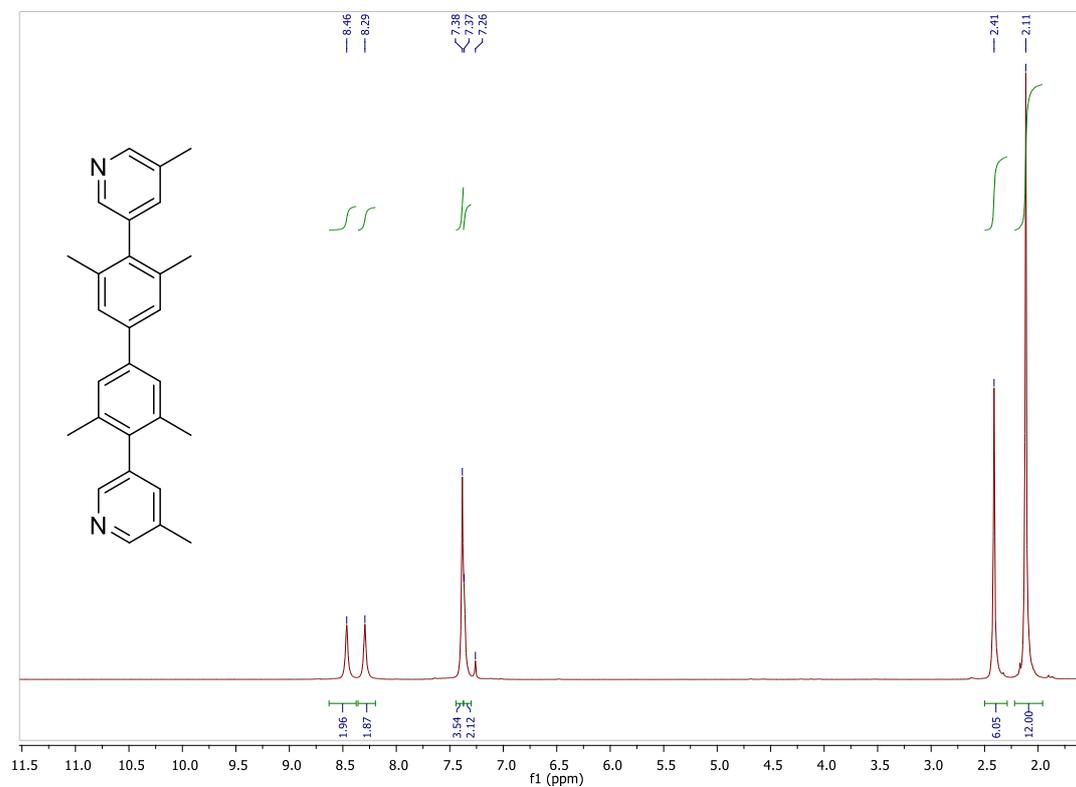


Figure S29. NMR spectra of compound 28.

^1H and ^{13}C spectra of 3-(5-(4'-(5-(*sec*-butyl)pyridin-3-yl)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-4-yl)pyridin-3-yl)propanenitrile (**29**)

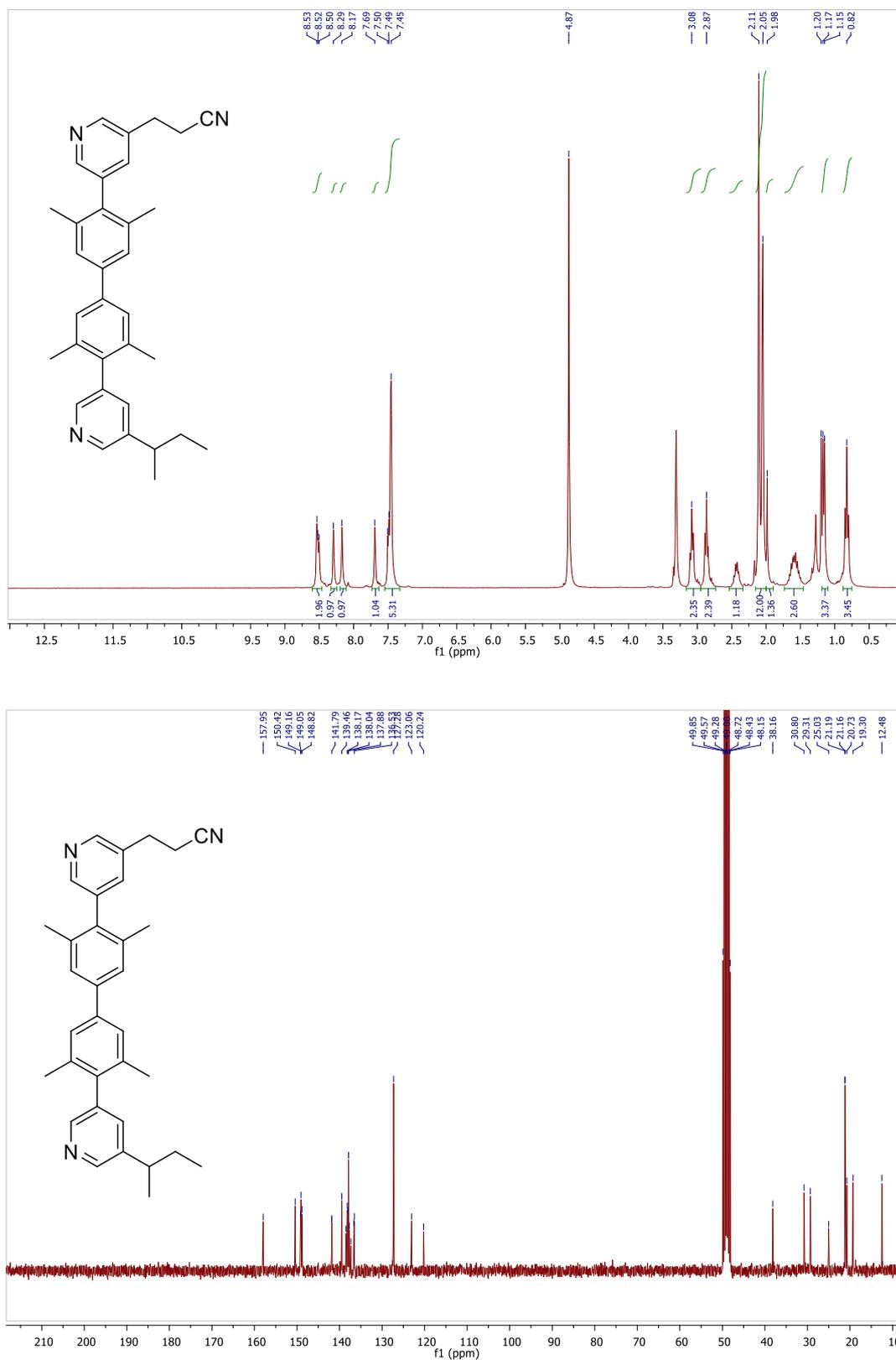


Figure S30. NMR spectra of compound **29**.

^1H and ^{13}C spectra of 3-(5-(4'-(5-(*sec*-butyl)pyridin-3-yl)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-4-yl)pyridin-3-yl)propyl-*N,N'*-di-boc-guanidine (**30**)

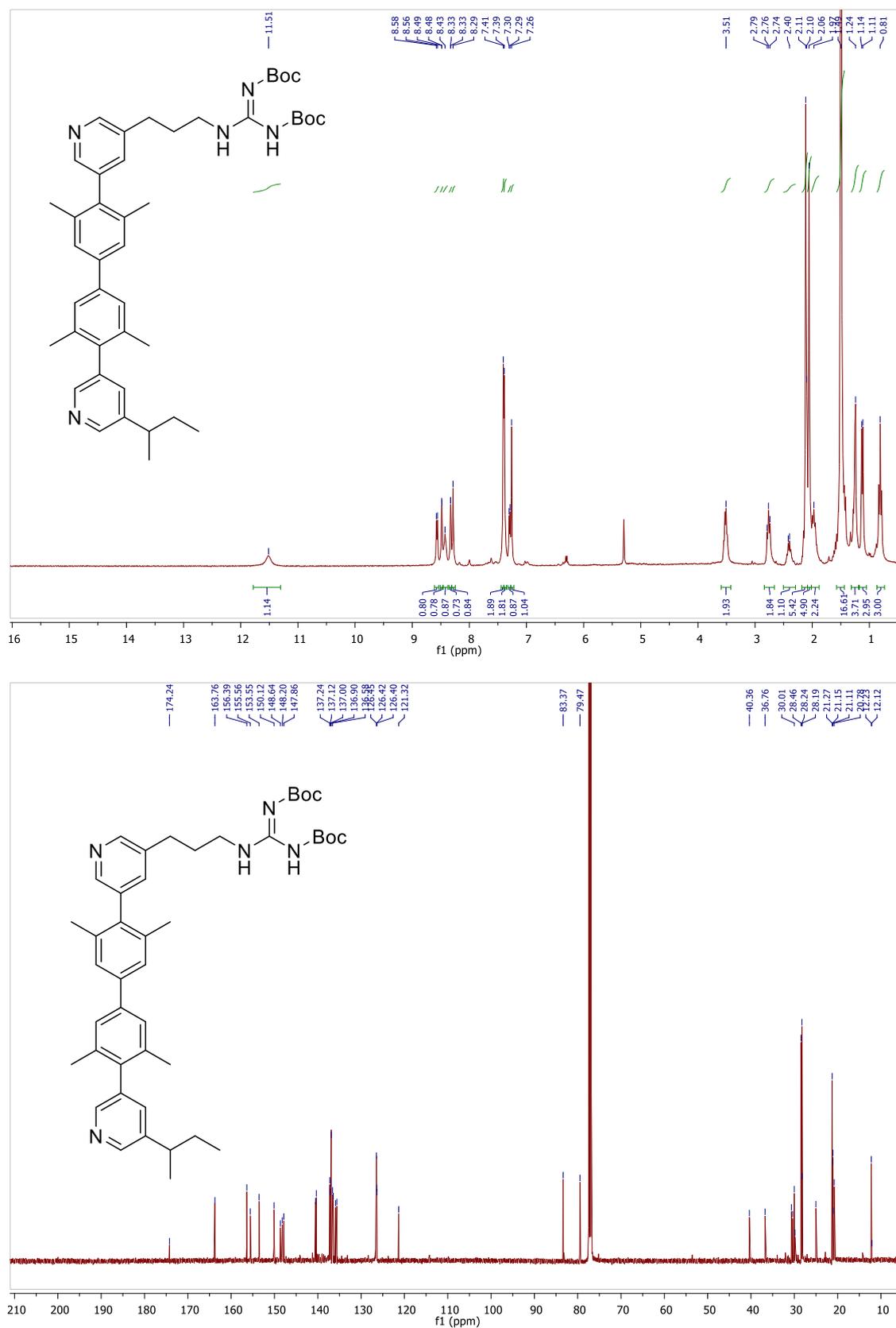


Figure S31. NMR spectra of compound **30**.

^1H and ^{13}C spectra of 3',5-diisobutyl-5'-methoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**31**)

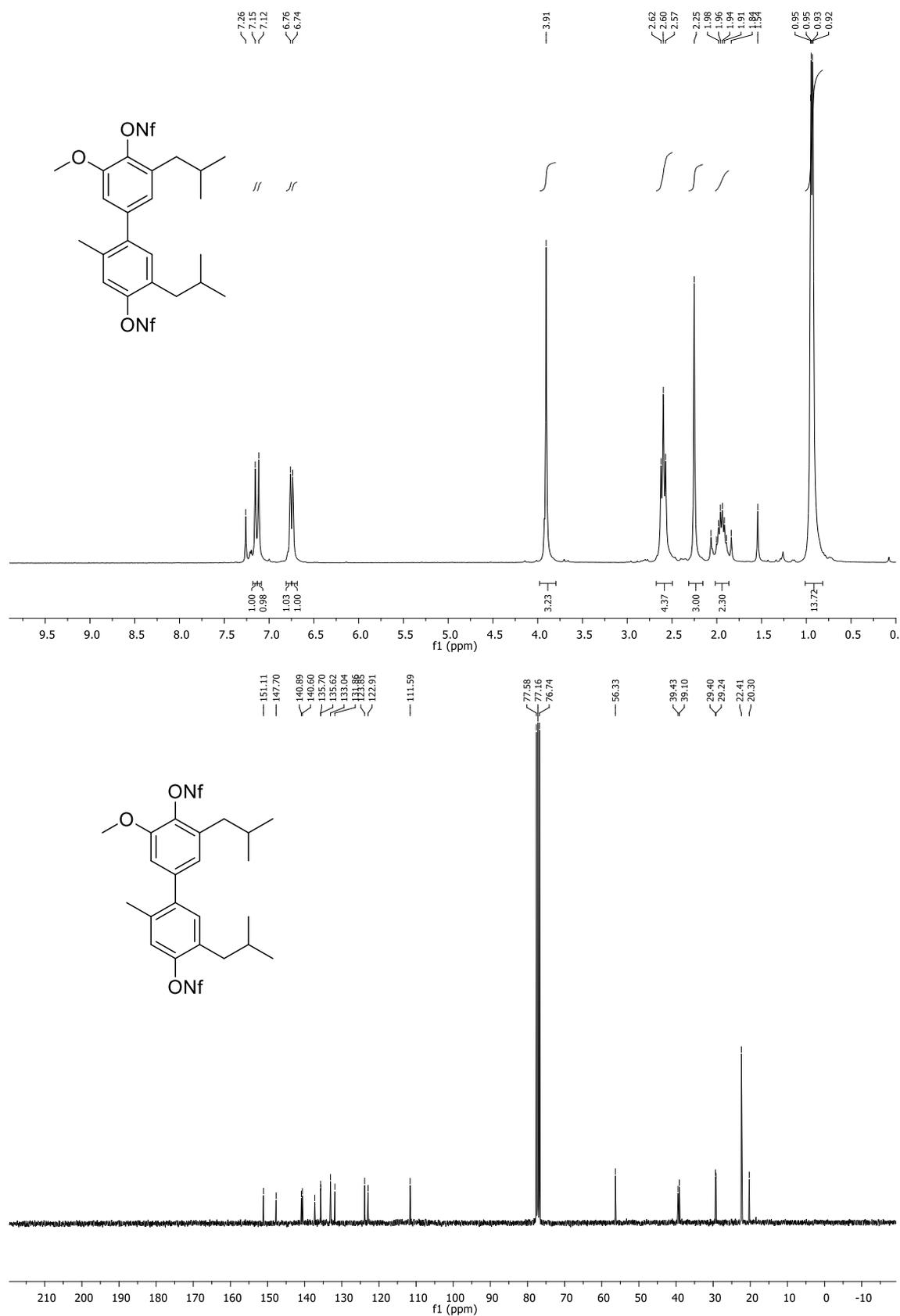


Figure S32. NMR spectra of compound **31**.

^1H and ^{13}C spectra of 4'-(5-(*sec*-butyl)pyridin-3-yl)-3,5'-diisobutyl-5-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (**32**)

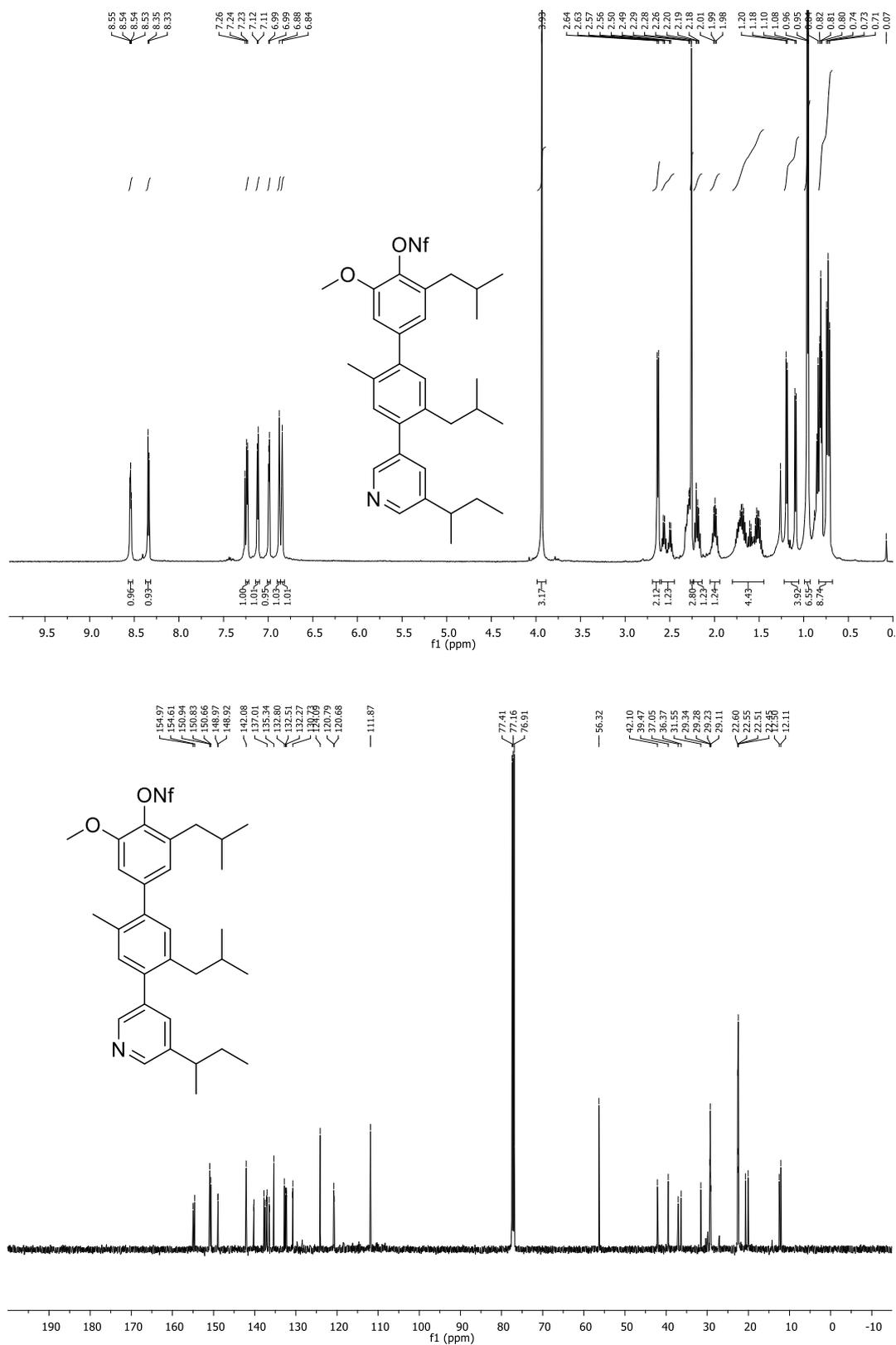


Figure S33. NMR spectra of compound **32**.

^1H and ^{13}C spectra of 3-(5-(4'-(5-(*sec*-butyl)pyridin-3-yl)-3,5'-diisobutyl-5-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl)pyridin-3-yl)propanenitrile (**33**)

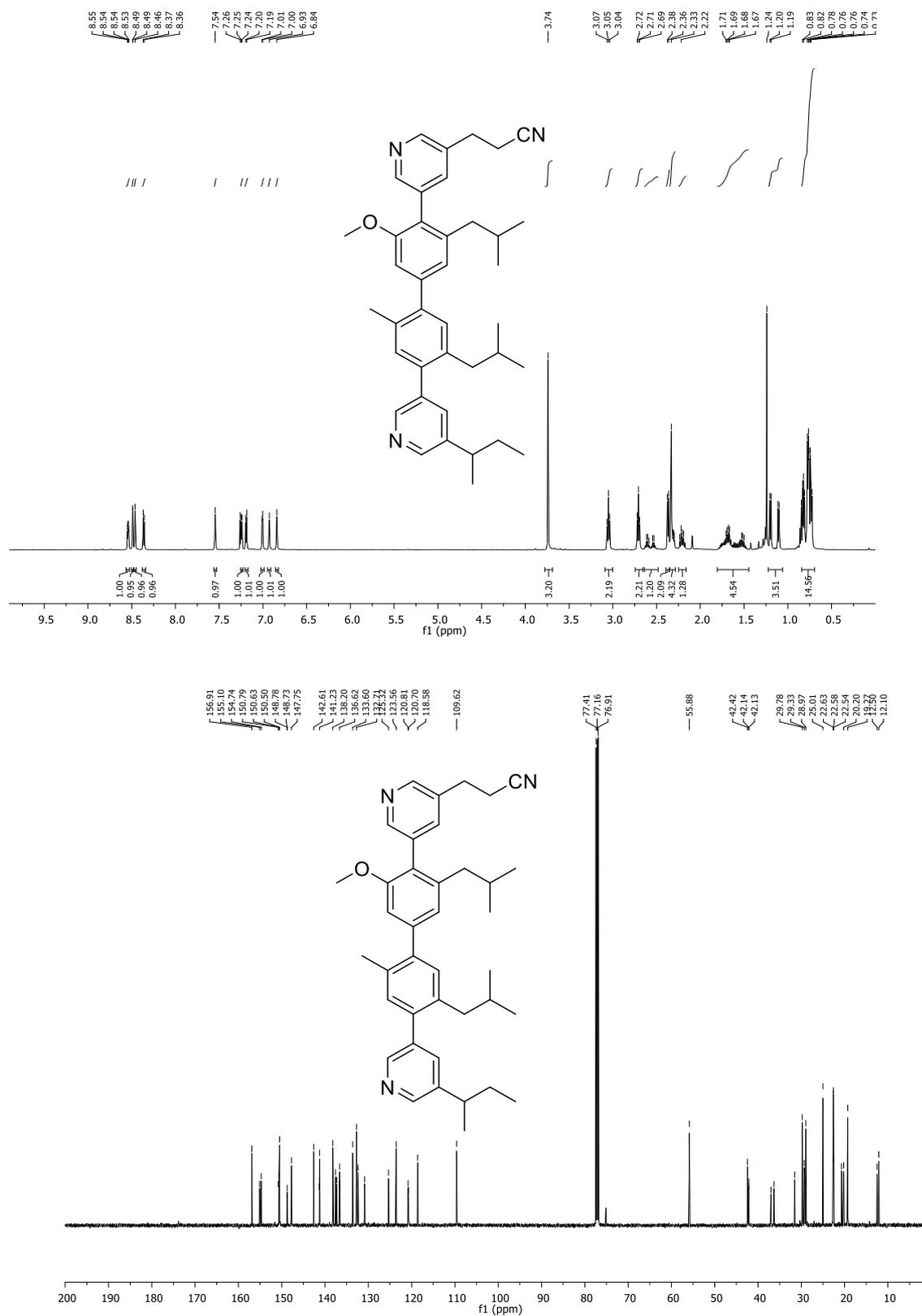


Figure S34. NMR spectra of compound **33**.

^1H and ^{13}C spectra of 5-(*sec*-butyl)-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**34**)

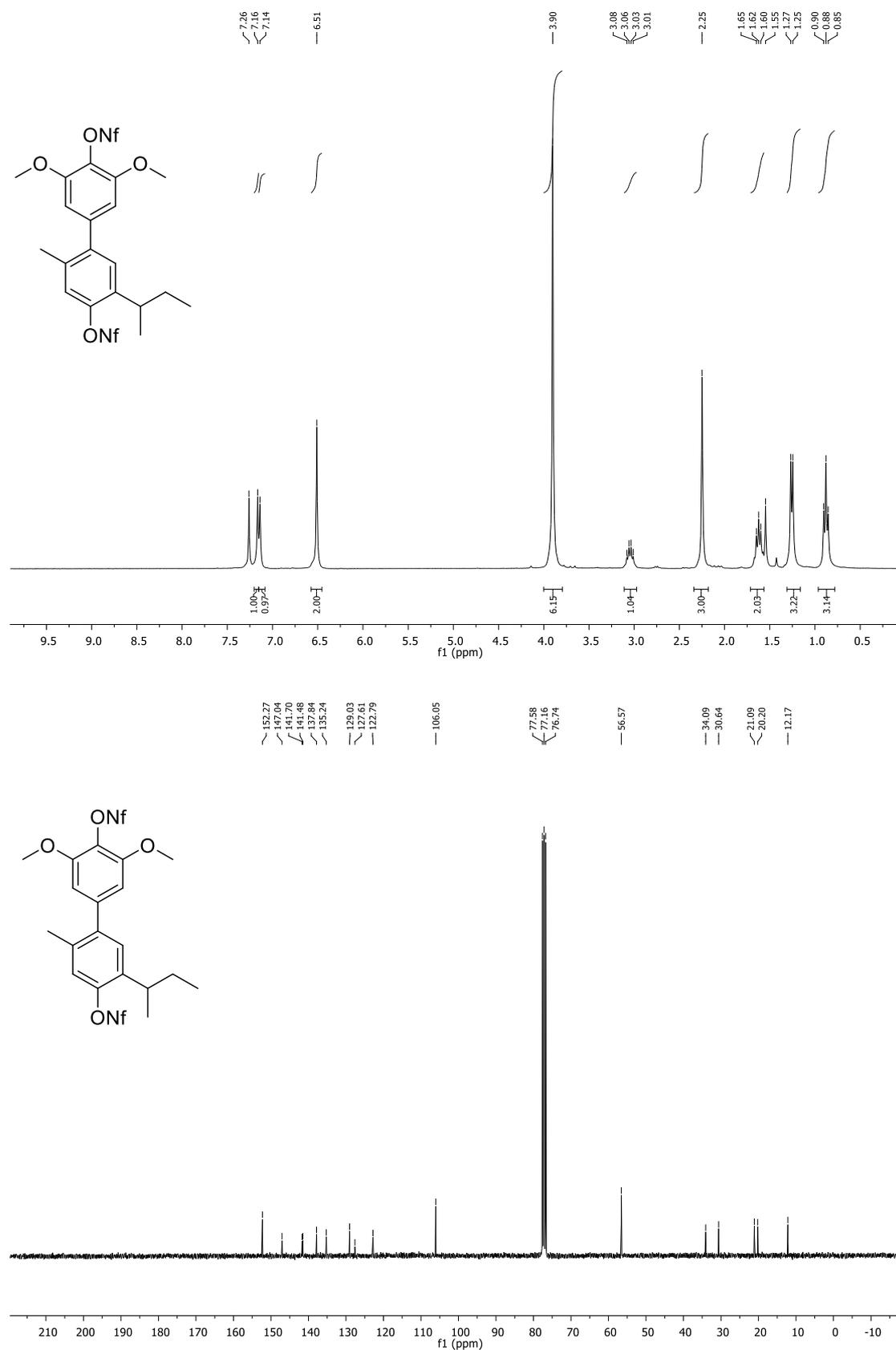


Figure S35. NMR spectra of compound **34**.

^1H and ^{13}C spectra of 5'-(*sec*-butyl)-4'-(5-isobutylpyridin-3-yl)-3,5-dimethoxy-2'-methyl-[1,1'-biphenyl]-4-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (**35**)

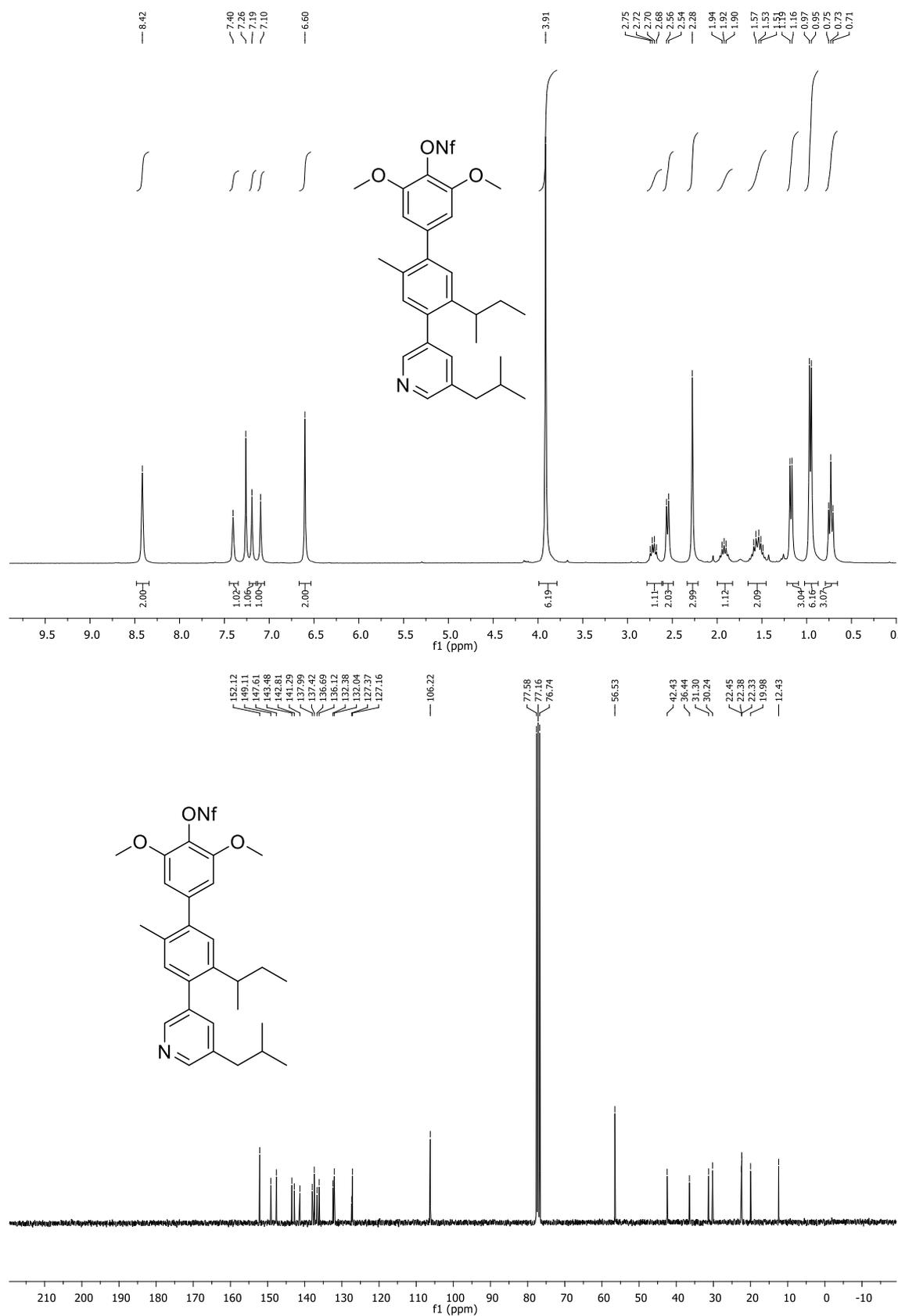


Figure S36. NMR spectra of compound **35**.

^1H and ^{13}C spectra of 5,5'-(5-(*sec*-butyl)-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl)bis(3-isobutylpyridine) (**36**)

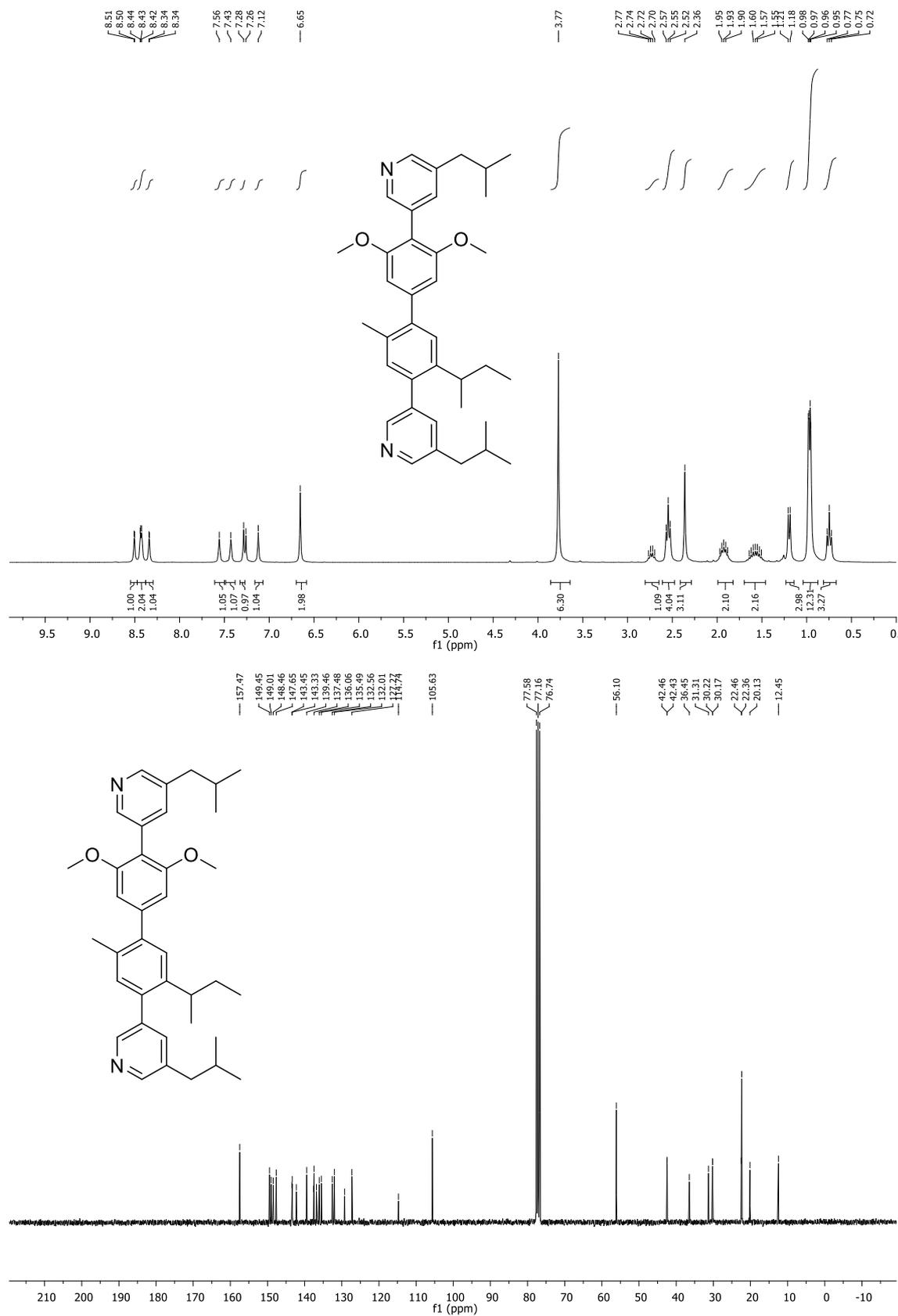


Figure S37. NMR spectra of compound **36**.

^1H and ^{13}C spectra of 5-isobutyl-3',5'-dimethoxy-2-methyl-[1,1'-biphenyl]-4,4'-diyl bis(1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate) (**37**)

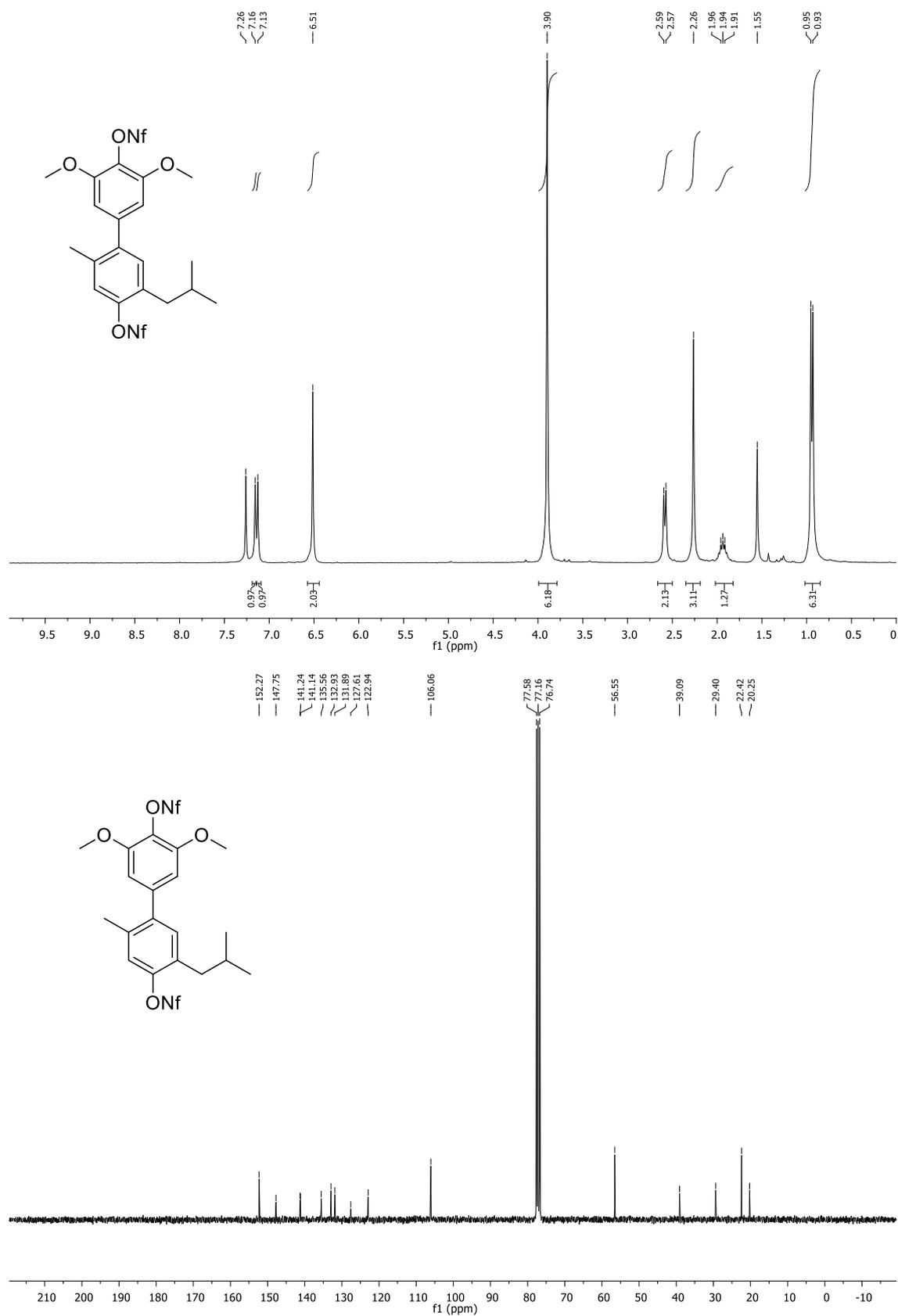


Figure S38. NMR spectra of compound **37**.

^1H and ^{13}C spectra of 4'-(5-(*sec*-butyl)pyridin-3-yl)-5'-isobutyl-3,5-dimethoxy-2'-methyl-[1,1'-biphenyl]-4-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (**38**)

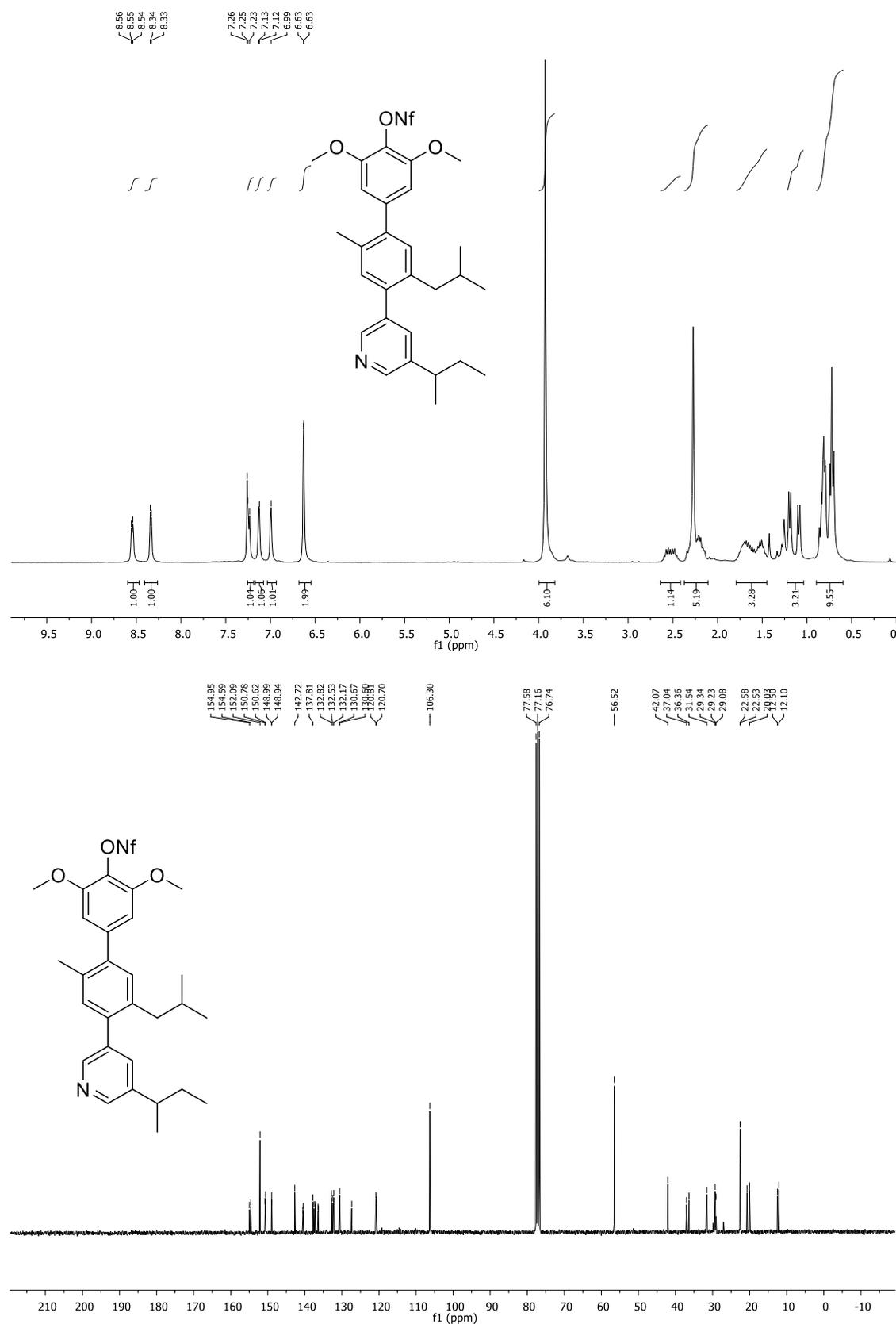


Figure S39. NMR spectra of compound **38**.

^1H and ^{13}C spectra of 3-(5-(4'-(5-(*sec*-butyl)pyridin-3-yl)-5'-isobutyl-3,5-dimethoxy-2'-methyl-[1,1'-biphenyl]-4-yl)pyridin-3-yl)propanenitrile (**39**)

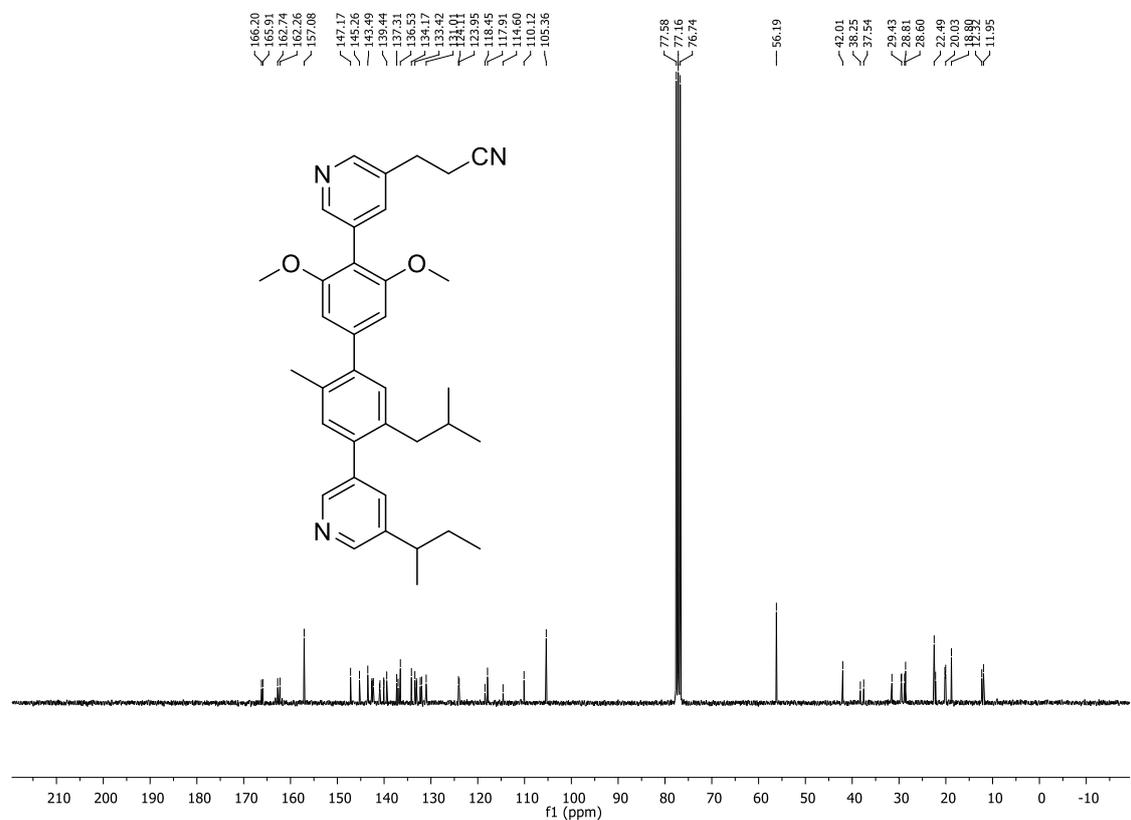
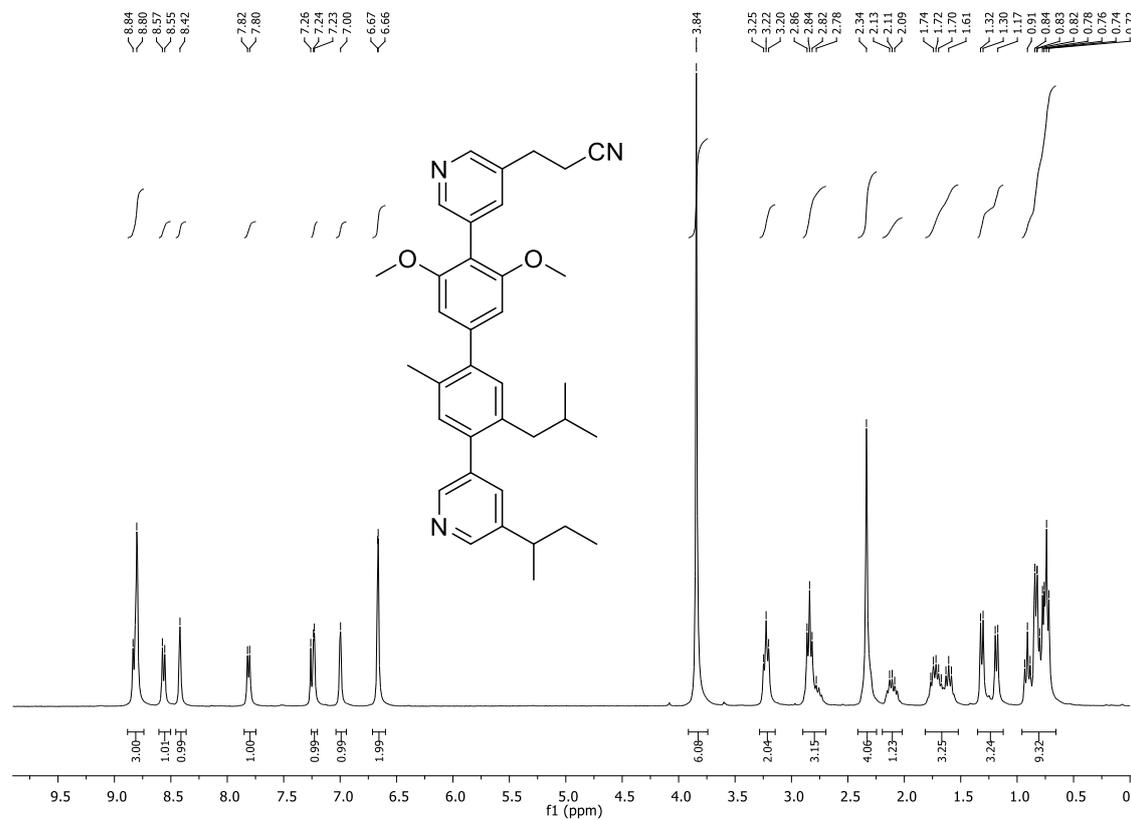


Figure S40. NMR spectra of compound **39**.