Electronic Supplementary Information

Pd(II)-catalyzed *meta*-C–H bromination and chlorination of aniline and benzoic acid derivatives

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1. General Information

Unless otherwise noted, commercially available reagents were purchased from commercial suppliers (such as Adamas, J&K Chemical Co., Energy Chemical. etc), and used as received. Hexafluoroisopropanol (HFIP) was distilled before use. Unless otherwise noted, all reactions were run under argon and the indicated reaction temperature was that of the oil bath. The reaction vessels used for C–H functionalization were 50 mL Schlenk tube (Synthware). Purification of products was performed by flash chromatography (FC) using silica gel or preparative thin layer chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE III spectrometer (400 MHz and 101 MHz, respectively) and JEOL ECZ600S (600 MHz and 151 MHz, respectively). Chemical shifts are reported parts per million (ppm) referenced to $CDCl_3$ (δ 7.26 ppm), tetramethylsilane (TMS, δ 0.00 ppm), MeOH- *d*$_4$ (δ 3.31 ppm) for ^{1}H NMR; $CDCl_3$ (δ 77.16 ppm), MeOH-*d*$_4$ (δ 49.00 ppm) for ^{13}C NMR. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptaplet, m = multiplet, and br = broad. High-resolution mass spectra (HRMS) were obtained on an Impact II UHR-TOF mass spectrometry equipped with an ESI source from Bruker at Fujian Institute of Research on the Structure of Matter.

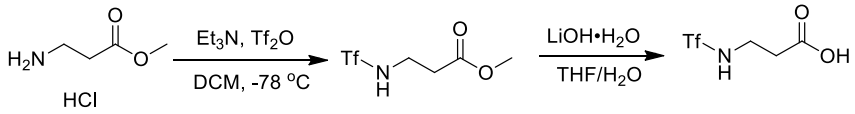
2. Experimental Section

2.1 Preparation and characterization of ligands and substrates

Preparation and characterization of ligands

***N*-TFA-β-Ala-OH** was synthesized following the literature procedures*(S1)*. β-Alanine (375 mg, 4.21 mmol) was suspended in dry tetrahydrofuran (3.5 ml) with stirring at -5 ^{o}C and trifluoroacetic anhydride (1 g, 4.76 mmol) was added dropwise. The colorless solution was allowed to warm to room temperature over 1 h and the solvent was reduced under reduced pressure. Water (0.5 ml) was added and the solution was lyophilized to yield a white foam. (775 mg, 99%). The sample was recrystallized from $CHCl_3$, light petroleum. ^{1}H NMR (400 MHz, MeOH-*d*$_4$) δ 3.53 (t, *J* = 6.9 Hz, 2H), 2.58 (t, *J* = 6.9 Hz, 2H). ^{19}F NMR (376 MHz, MeOH-*d*$_4$) δ -77.48. ^{13}C NMR (151 MHz, MeOH-*d*$_4$) δ 173.4, 157.7 (q, *J* = 37.1 Hz), 116.1 (q, *J* = 286.5 Hz), 35.4, 32.44.

***N*-Tf-β-Ala-OH**

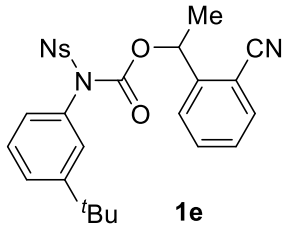


To a solution of β-alanine methyl ester hydrochloride (5.00 g, 35.8 mmol, Aldrich 05210) and triethylamine (10 mL, 71.6 mmol) in anhydrous CH_2Cl_2 (100 mL) was slowly added triflic anhydride (Tf_2O) (6.03 mL, 35.8 mmol) at -78 ℃. The reaction

mixture was allowed to warm up to room temperature and stirred for 14 h. The reaction mixture was concentrated under reduced pressure to leave red oil, which was filtered through a silica plug eluting with diethyl ether (200 mL). The filtrate was concentrated and the residue was purified by bulb to bulb distillation to give *N*-Tf-β-alanine methyl ester as colorless oil (7.20 g, 86% yield)*(S2)*. This compound (2.8 g, 12 mmol) was dissolved in THF (20 mL), H_2O (5 mL). The solution was cooled to 0 °C and LiOH·H_2O (1.5 g, 36 mmol) was added in batches. The mixture was warmed to room temperature gradually and stirred overnight. H_2O (30 mL) was then added and most of the organic solvent was removed under reduced pressure. The aqueous phase was extracted with Et_2O (30 mL × 2), and acidized to pH 1.0 with HCl (1N). The aqueous phase was extracted with EtOAc (15 mL × 4). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to *N*-Tf-β-Ala-OH (2.5g) in 95% yield. ^{1}H NMR (400 MHz, MeOH -d_4) δ 3.46 (t, *J* = 6.7 Hz, 2H), 2.57 (t, *J* = 6.7 Hz, 2H). ^{19}F NMR (376 MHz, MeOH -d_4) δ -79.51.^{13}C NMR (151 MHz, MeOH-d_4) δ 172.9, 120.1 (q, *J* = 320.9 Hz), 39.4, 34.5; HRMS (m/z, ESI-TOF): Calcd for $C_4H_6F_3NO_4S$ Na^+ [M+Na^+] 243.9862, found 243.9863.

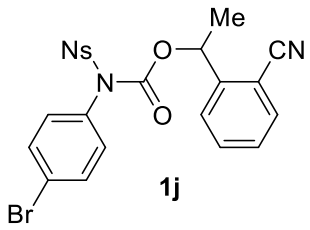
Preparation and characterization of substrates

All substrates ware synthesized following the literature procedures*(S3,S4)*.



1e

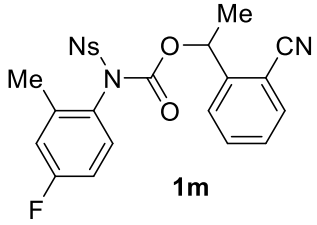
1-(2-cyanophenyl)ethyl(3-(tert-butyl)phenyl)((4-nitrophenyl)sulfonyl)carbamate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 9.2 Hz, 2H), 8.19 (d, *J* = 8.8 Hz, 2H), 7.56 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.54 – 7.51 (m, 1H), 7.48 (td, *J* = 7.6, 1.2 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H), 7.19 (t, *J* = 1.6 Hz, 1H), 7.12 – 7.07 (m, 2H), 6.04 (q, *J* = 6.8 Hz, 1H), 1.49 (d, *J* = 6.4 Hz, 3H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 151.0, 150.7, 144.3, 143.8, 135.0, 133.2, 133.0, 130.4, 129.2, 128.6, 126.9, 126.5, 126.5, 125.7, 124.1, 116.6, 110.4, 73.8, 34.9, 31.2, 21.5; HRMS (m/z, ESI-TOF): Calcd for $C_{26}H_{25}N_3O_6SNa^+$ [M+Na^+] 530.1356, found 530.1355.



1j

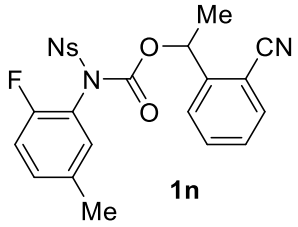
1-(2-cyanophenyl)ethyl(4-bromophenyl)((4-nitrophenyl)sulfonyl)carbamate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 8.8 Hz, 2H), 7.62 – 7.53 (m, 4H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.20 – 7.14 (m, 3H), 6.02 (q, *J* = 6.8 Hz, 1H), 1.52 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8, 150.6, 144.0, 143.4, 134.1, 133.3, 133.2, 132.9, 131.1, 130.4, 128.9, 126.0,

124.3, 124.2, 116.6, 110.6, 74.3, 21.2; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{16}{}^{79}BrN_3O_6SNa^+$ [M+Na^+] 551.9835, found 551.9834.



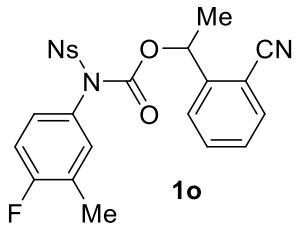
1m

1-(2-cyanophenyl)ethyl(4-fluoro-2-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: ^{1}H NMR (400 MHz, $CDCl_3$) rotamers appear in the NMR: δ 8.37 (m, 2H), 8.23 (m, 2H), 7.63 – 7.46 (m, 2H), 7.42 (d, *J* = 7.6 Hz, 0.39H), 7.40 – 7.33 (m, 0.65H), 7.16 (d, *J* = 7.8 Hz, 0.59H), 7.14 – 7.05 (m, 2H), 7.04 – 6.90 (m, 1.55H), 2.34 (s, 1.67H), 2.27 (s, 1.33H), 1.54 (d, *J* = 6.6 Hz, 1.68H), 1.49 (d, *J* = 6.6 Hz, 1.32H). ^{13}C NMR (101 MHz, $CDCl_3$) rotamers appear in the NMR: δ 163.0 (d, J_{C-F} = 248.9 Hz), 150.85, 150.81, 150.68, 150.55, 144.18, 144.16, 143.6, 143.5, 141.2 (d, J_{C-F} = 8.9 Hz), 141.1 (d, J_{C-F} = 8.9 Hz), 133.23, 133.19 (d, J_{C-F} = 14.5 Hz), 130.7, 130.6, 130.5 (d, J_{C-F} = 14.5 Hz), 130.4 (d, J_{C-F} = 8.2 Hz), 128.9, 128.7, 125.9, 125.7, 124.13, 124.11, 118.3 (d, J_{C-F} = 22.5 Hz), 118.1 (d, J_{C-F} = 22.4 Hz), 116.6, 116.5, 114.3 (d, J_{C-F} = 21.6 Hz), 114.1 (d, J_{C-F} = 22.7 Hz), 110.6, 110.5, 74.14, 74.06, 21.4, 21.3, 18.5, 18.45; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}FN_3O_6SNa^+$ [M+Na^+] 506.0793, found 506.0793.



1n

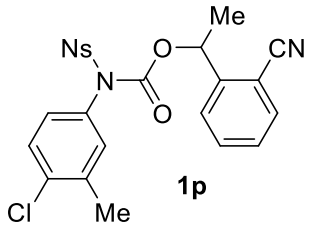
1-(2-cyanophenyl)ethyl(2-fluoro-5-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.22 (d, *J* = 8.8 Hz, 2H), 7.58 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.51 (td, *J* = 7.7, 1.4 Hz, 1H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.32 – 7.22 (m, 2H), 7.20 – 7.05 (m, 2H), 6.01 (q, *J* = 6.4 Hz, 1H), 2.40 (s, 3H), 1.48 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz,$CDCl_3$) δ 156.5 (d, J_{C-F} = 247.1 Hz), 150.8, 150.2, 144.0, 143.7, 135.0 (d, J_{C-F} = 3.9 Hz), 133.2, 133.1, 132.5 (d, J_{C-F} = 7.6 Hz), 132.3, 130.5 (d, J_{C-F} = 1.5 Hz), 128.7, 125.8, 123.9, 122.1 (d, J_{C-F} = 13.7 Hz), 116.5, 116.1 (d, J_{C-F} = 19.6 Hz), 110.3, 74.4, 21.5, 20.6; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}FN_3O_6SNa^+$ [M+Na^+] 506.0793, found 506.0793.



1o

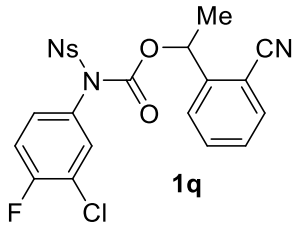
1-(2-cyanophenyl)ethyl(4-fluoro-3-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H), 8.17 (d, *J* = 9.2 Hz, 2H), 7.59 – 7.52 (m, 2H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.15 – 7.12 (m, 1H), 7.09 (d, *J* = 8.8 Hz, 1H), 7.07 – 7.03 (m, 1H),

6.02 (q, J = 6.4 Hz, 1H), 2.32 (d, J = 1.6 Hz, 3H), 1.53 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (d, J_{C-F} = 247.8 Hz), 150.9, 150.8, 144.2, 143.5, 133.2 (d, J_{C-F} = 7.9 Hz), 132.6 (d, J_{C-F} = 6.1 Hz), 130.5 (d, J_{C-F} = 3.5 Hz), 130.3, 128.8, 128.3 (d, J_{C-F} = 8.9 Hz), 126.7 (d, J_{C-F} = 19.4 Hz), 126.0, 124.1, 116.6, 116.1 (d, J_{C-F} = 24.0 Hz), 110.6, 74.2, 21.2, 14.6 (d, J_{C-F} = 3.3 Hz) ; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}FN_3O_6SNa^+$ [M+Na^+] 506.0793, found 506.0793.



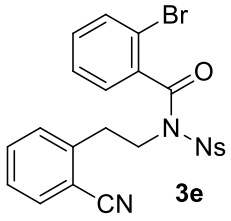
1p

1-(2-cyanophenyl)ethyl(4-chloro-3-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 9.2 Hz, 2H), 7.59 – 7.53 (m, 2H), 7.43 (d, J = 8.4 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.17 (d, J = 2.0 Hz, 1H), 7.03 (dd, J = 8.4, 2.4 Hz, 1H), 6.02 (q, J = 6.4 Hz, 1H), 2.41 (s, 3H), 1.53 (d, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8, 150.7, 144.1, 143.5, 137.9, 136.3, 133.3, 133.3, 133.2, 131.9, 130.3, 130.1, 128.8, 127.9, 126.0, 124.1, 116.6, 110.5, 74.3, 21.2, 20.2; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}{}^{35}ClN_3O_6SNa^+$ [M+Na^+] 522.0497, found 522.0492.



1q

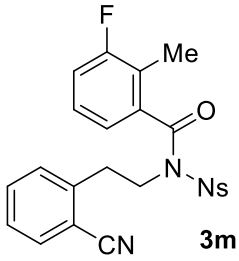
1-(2-cyanophenyl)ethyl(3-chloro-4-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 9.2 Hz, 2H), 8.16 (d, J = 8.8 Hz, 2H), 7.59 – 7.55 (m, 2H), 7.41 (td, J = 7.6, 1.2 Hz, 1H), 7.37 (dd, J = 6.4, 2.8 Hz, 1H), 7.28 – 7.18 (m, 3H), 6.03 (q, J = 6.4 Hz, 1H), 1.55 (d, J = 6.8 Hz, 3H). ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9 (d, J_{C-F} = 253.6 Hz), 150.9, 150.5, 143.8, 143.1, 133.3 (d, J_{C-F} = 6.6 Hz), 131.9, 131.4 (d, J_{C-F} = 4.0 Hz), 130.4, 129.7 (d, J_{C-F} = 7.9 Hz), 129.0, 126.1, 124.2, 122.1 (d, J_{C-F} = 19.1 Hz), 117.4 (d, J_{C-F} = 22.5 Hz), 116.6, 110.6, 74.6, 21.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{35}ClFN_3O_6SNa^+$ [M+Na^+] 526.0246, found 526.0246.



3e

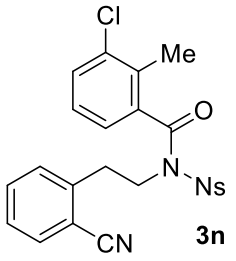
2-bromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.8 Hz, 2H), 8.19 (d, J = 8.8 Hz, 2H), 7.62 – 7.56 (m, 2H), 7.48 – 7.38 (m, 3H), 7.33 – 7.26 (m, 2H), 6.79 (dd, J = 1.6, 6.8 Hz, 1H), 4.11 (s, 2H), 3.28 (t, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 150.8, 143.6, 140.7, 135.2, 133.3, 133.2, 132.9, 132.0,

131.1, 130.6, 128.4, 127.9, 124.0, 118.7, 117.3, 113.0, 48.4, 35.3; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{16}{}^{79}BrN_3O_5SNa^+$ [M+Na$^+$] 535.9886, found 535.9885.



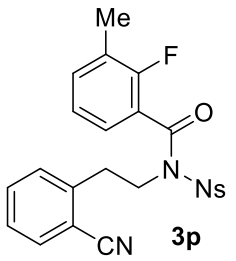
3m

N-(2-cyanophenethyl)-3-fluoro-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 – 8.36 (m, 2H), 8.18 – 8.08 (m, 2H), 7.65 – 7.51 (m, 2H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.20 – 7.06 (m, 2H), 6.68 (d, *J* = 6.8 Hz, 1H), 4.14 (t, *J* = 7.4 Hz, 2H), 3.26 (t, *J* = 7.5 Hz, 2H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4 (d, J_{C-F} = 3.4 Hz), 161.1 (d, J_{C-F} = 248.0 Hz), 150.9, 144.3, 140.7, 135.7 (d, J_{C-F} = 4.1 Hz), 133.3 (d, J_{C-F} = 8.2 Hz), 130.8, 130.3, 128.0, 127.7 (d, J_{C-F} = 8.5 Hz), 124.2, 122.8 (d, J_{C-F} = 19.2 Hz), 122.0 (d, J_{C-F} = 3.9 Hz), 117.7, 117.4 (d, J_{C-F} = 7.5 Hz), 112.9, 48.1, 35.1, 11.4 (d, J_{C-F} = 4.6 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}FN_3O_5SNa^+$ [M+Na$^+$] 490.0843, found 490.0841.



3n

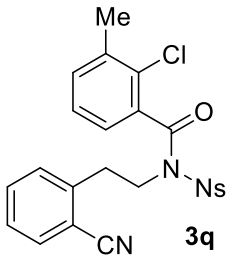
3-chloro-N-(2-cyanophenethyl)-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.7 Hz, 2H), 8.06 (d, *J* = 8.7 Hz, 2H), 7.62 – 7.52 (m, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.11 (t, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 4.13 (t, *J* = 7.5 Hz, 2H), 3.26 (t, *J* = 7.4 Hz, 2H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 150.8, 144.2, 140.7, 135.7, 135.6, 133.3, 133.2, 133.2, 131.5, 130.7, 130.2, 128.0, 127.2, 124.8, 124.2, 117.4, 113.0, 48.0, 35.1, 16.9. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}{}^{35}ClN_3O_5SNa^+$ [M+Na$^+$] 506.0548, found 506.0549.



3p

N-(2-cyanophenethyl)-2-fluoro-3-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.8 Hz, 2H), 8.12 (d, *J* = 8.8 Hz, 2H), 7.58 (td, *J* = 7.6, 0.8 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.30 – 7.27 (m, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.64 (t, *J* = 6.8 Hz, 1H), 4.24 (t, *J* = 6.8 Hz, 2H), 3.26 (t, *J* = 6.8 Hz, 2H), 2.21

(s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 156.4 (d, J_{C-F} = 246.4 Hz), 150.7, 144.05, 140.7, 134.67 (d, J_{C-F} = 5.5 Hz), 133.16 (d, J_{C-F} = 6.8 Hz), 131.3, 130.0, 127.8, 126.31 (d, J_{C-F} = 2.3 Hz), 125.73 (d, J_{C-F} = 16.8 Hz), 124.35 (d, J_{C-F} = 3.9 Hz), 124.0, 121.75 (d, J_{C-F} = 16.6 Hz), 117.2, 112.8, 47.99 (d, J_{C-F} = 1.8 Hz), 35.3, 14.33 (d, J_{C-F} = 3.8 Hz); HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}FN_3O_5SNa^+$ [M+Na^+] 490.0843, found 490.0843.

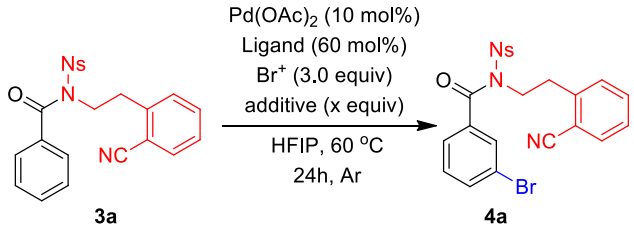


3q

2-chloro-N-(2-cyanophenethyl)-3-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 – 8.22 (m, 2H), 8.21 – 8.06 (m, 2H), 8.61 – 8.56 (m, 2H), 7.46 – 7.43 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 7.5 Hz, 1H), 4.11 (s, 2H), 3.28 (t, *J* = 7.0 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 150.9, 143.8, 140.9, 137.5, 133.6, 133.3, 133.2, 133.0, 131.2, 130.5, 130.0, 127.9, 127.2, 125.8, 124.0, 117.4, 113.1, 48.3, 35.4, 20.1. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}ClN_3O_5SNa^+$ [M+Na^+] 506.0548, found 506.0547.

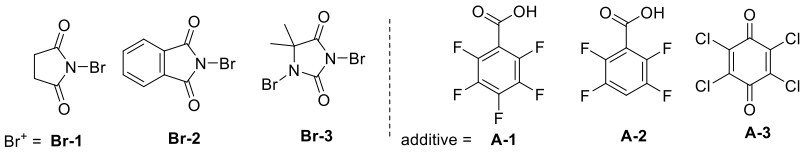
2.2 Reaction conditions screenings of benzoic acid derivatives.

Table S1. Optimization of reaction conditions of *meta*-bromination of benzoic acid.



Entry	ligand	"Br^+" (3 equiv)	additive (equiv)	T(°C)	yield (%)[a] (mono/di)
1	*N*-Ac-Gly-OH	**Br-1**	-	45	10% (1/-)
2	*N*-Ac-Gly-OH	**Br-1**	-	60	64% (4.8/1)
3	*N*-Ac-Gly-OH	**Br-1**	-	75	61% (3.7/1)
4	*N*-Ac-Gly-OH	**Br-1**	-	90	51% (4.1/1)
5	*N*-Ac-Gly-OH	**Br-2**	-	60	66% (3.7/1)
6	*N*-Ac-Gly-OH	**Br-3**	-	60	39% (12/1)
7	*N*-Ac-Gly-OH	**Br-2**	**A-2** (0.5)	60	82% (3.1/1)
8	*N*-Ac-Gly-OH	**Br-2**	**A-1** (0.25)	60	77% (4.1/1)
9	*N*-Ac-Gly-OH	**Br-2**	**A-1** (1)	60	87% (4.1/1)
10	*N*-Ac-Gly-OH	**Br-2**	**A-3** (1)	60	80% (2.5/1)
11	*N*-Ac-Gly-OH	**Br-2**	**A-1** (0.5)	60	-[b]
12	*N*-Formyl-Gly-OH	**Br-2**	**A-1** (0.5)	60	84% (3.9/1)
13	*N*-Tf-β-Ala-OH	**Br-2**	**A-1** (0.5)	60	38% (37.0/1)
14	*N*-TFA-β-Ala-OH	**Br-2**	**A-1** (0.5)	60	48% (23.0/1)
15	*N*-Tf-β-Ala-OH	**Br-2**	HOAc (2.0)	90	75% (4.4/1)
16	*N*-Tf-β-Ala-OH	**Br-2**	HOAc (5.0)	90	82% (7.2/1)
17	*N*-Tf-β-Ala-OH	**Br-2**	HOAc (10.0)	90	90% (83%, 5.4/1)[c]
18	*N*-Tf-β-Ala-OH	**Br-2**	HOAc (15.0)	90	88% (3.9/1)
19	*N*-Tf-β-Ala-OH	**Br-2**	HOAc (20.0)	90	82% (4.1/1)
20	*N*-Tf-β-Ala-OH	**Br-2**	TFA (2.0)	90	77% (8.6/1)
21	*N*-Tf-β-Ala-OH	**Br-2**	TFA (5.0)	90	67% (8.6/1)
22	*N*-Tf-β-Ala-OH	**Br-2**	TFA (10.0)	90	54% (8.0/1)
23	*N*-Tf-β-Ala-OH	**Br-2**	HOTf (0.5)	90	N.D.
24	*N*-Tf-β-Ala-OH	**Br-2**	HOTf (1.0)	90	N.D.
25	*N*-Tf-β-Ala-OH	**Br-2**	HOTf (2.0)	90	N.D.
26	*N*-Tf-β-Ala-OH	**Br-2**	HOTf (5.0)	90	N.D.
27	*N*-Tf-β-Ala-OH	**Br-2** (2.0 equiv)	**A-1** (5.0)	90	90% (86%, 4.1/1)[c]
28	*N*-Tf-β-Ala-OH	**Br-2** (1.5 equiv)	**A-1** (5.0)	90	85% (6.1/1)
29	*N*-Tf-β-Ala-OH	**Br-2**	**A-1** (5.0)	90	68% (7.5/1)

		(1.2 equiv)			
30	*N*-Tf-β-Ala-OH	**Br-2**	**A-1** (5.0)	90	94% (3.7/1)[d]
31	*N*-Tf-β-Ala-OH	**Br-2**	**A-1** (5.0)	90	95% (89%, 4.6/1)[c,e]

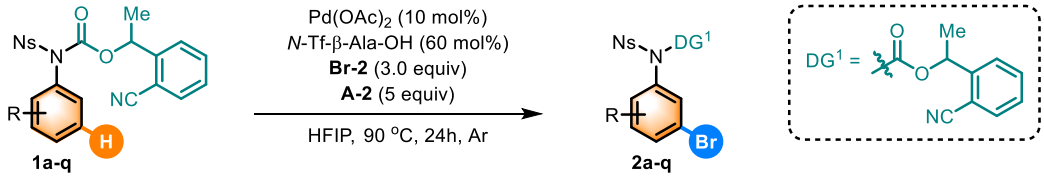


Reaction conditions: **3a** (0.1 mmol), $Pd(OAc)_2$ (10 mol%), ligand (60 mol%), Br^+ (3.0 equiv), additive (0.25-1 equiv), HFIP (1 mL), 60 ℃, 24 h, Ar. [a]Yield was determined by ^1H NMR with CH_2Br_2 as internal standard. [b]Without $Pd(OAc)_2$. [c]Isolated yield in parentheses. [d]18 h. [e]12 h.

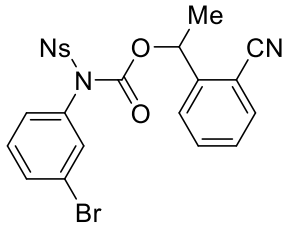
General procedure： **1** (0.10 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 10 mol%), ligand (60 mol%), **Br**$^+$ (3 equiv) and **Acid additive** (0.25-1 mmol) were dissolved in HFIP (1.0 mL) in a 50 mL Schlenk sealed tube. The reaction tube was capped, then evacuated briefly under vacuum and charged with argon (1 atm, balloon, × 3). The tube was then submerged into a preheated indicated oil bath at 90 ℃ to react for 24 h. The crude reaction mixture was diluted with EtOAc (10 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 20 mL of EtOAc. The filtrate was diluted in EtOAc and washed with saturated Na_2SO_3 and saturated NaCl aqueous solution. The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by preparative thin layer chromatography using DCM/Toluene as the eluent.

2.3 Experimental procedures and product characterization.

General procedure for *meta*-bromination of anilines

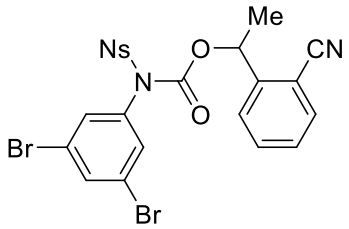


1 (0.10 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 10 mol%), *N*-Tf-*β*-Ala-OH (60 mol%), **Br-2** (3 equiv) and **A-2** (0.5 mmol) were dissolved in HFIP (1.0 mL) in a 50 mL Schlenk sealed tube. The reaction tube was capped, then evacuated briefly under vacuum and charged with argon (1 atm, balloon, × 3). The tube was then submerged into a preheated indicated oil bath at 90 °C to react for 24 h. The crude reaction mixture was diluted with EtOAc (10 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 20 mL of EtOAc. The filtrate was diluted in EtOAc and washed with saturated Na_2SO_3 and saturated NaCl aqueous solution. The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by preparative thin layer chromatography using DCM/Toluene or $CHCl_3$/Toluene (typically v/v = 1/500) as the eluent.



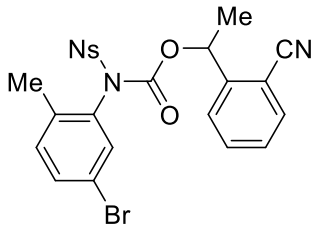
2a$_{mono}$

1-(2-cyanophenyl)ethyl(3-bromophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions and **A-1** as the additive on 0.1 mmol scale; 34.0 mg, 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.8 Hz, 2H), 8.18 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.59-7.53 (m, 2H), 7.43-7.35 (m, 3H), 7.26-7.22 (m, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 6.03 (q, *J* = 6.8 Hz, 1H), 1.53 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 150.6, 144.1, 143.5, 136.3, 133.4, 133.3, 132.7, 130.9, 130.5, 129.0, 128.5, 126.1, 124.3, 122.8, 116.7, 110.7, 74.5, 21.3; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{16}{}^{79}BrN_3O_6SNa^+$ [M+Na$^+$] 551.9835, found 551.9835.



2a$_{(m, m')di}$

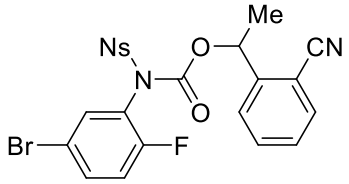
1-(2-cyanophenyl)ethyl(3,5-dibromophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions, **A-1** as the additive and **A-1** as the additive on 0.1 mmol scale; 17.9 mg, 29%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 – 8.36 (m, 2H), 8.17 (d, *J* = 6.0 Hz, 2H), 7.85 – 7.80 (m, 1H), 7.58 (td, *J* = 6.0, 0.8 Hz, 2H), 7.42 – 7.39 (m, 3H), 7.21 (d, *J* = 5.2 Hz, 1H), 6.03 (q, *J* = 4.4 Hz, 1H), 1.56 (d, *J* = 4.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 150.3, 143.7, 143.1, 136.8, 135.9, 133.5, 133.3, 131.7, 130.5, 129.1, 126.2, 124.3, 123.2, 116.6, 110.7, 74.8, 21.1; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br_2N_3O_6SNa^+$ [M+Na$^+$] 629.8941, found 629.8941.



2b

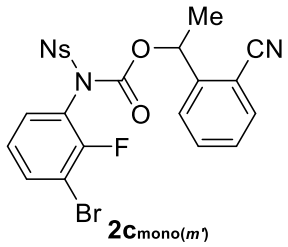
1-(2-cyanophenyl)ethyl(5-bromo-2-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions, *N*-TFA-β-Ala-OH as ligand and HOAc as additive on 0.1 mmol scale; 34.9 mg, 64%. ^{1}H NMR (600 MHz, $CDCl_3$) rotamers appear in the NMR: δ 8.42 – 8.37 (m, 2H), 8.27 – 8.21 (m, 2H), 7.61 – 7.58 (m, 1H), 7.57 – 7.50 (m, 2H), 7.41 (td, *J* = 7.6, 1.1 Hz, 0.45H), 7.37 (td, *J* = 7.6, 1.1 Hz, 0.55H), 7.28 – 7.25 (m, 1.6H), 7.17 – 7.11 (m, 1H), 7.08 (d, *J* = 7.9 Hz, 0.5H), 6.07 – 6.01 (m, 1H), 2.32 (s, 1.63H), 2.22 (s, 1.22H), 1.54 (d, *J* = 6.6 Hz, 1.73H), 1.51 (d, *J* = 6.6 Hz, 1.27H). ^{13}C NMR (151 MHz, $CDCl_3$)

δ 150.9, 150.9, 150.4, 150.2, 144.06, 144.0, 143.6, 143.5, 137.8, 137.6, 135.5, 135.5, 133.3, 133.2, 133.2, 133.1, 132.8, 132.7, 131.8, 131.6, 130.6, 128.9, 128.7, 126.0, 125.7, 124.2, 119.6, 119.4, 116.5, 116.5, 110.6, 110.4, 74.3, 74.1, 21.5, 21.4, 17.9, 17.9; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}{}^{79}BrN_3O_6SNa^+$ [M+Na$^+$] 565.9992, found 565.9988.



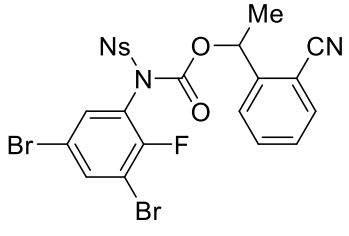
2c$_{mono(m)}$

1-(2-cyanophenyl)ethyl(5-bromo-2-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions and **A-1** as the additive on 0.1 mmol scale; 19.3 mg, 35%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 8.22 (d, J = 8.8 Hz, 2H), 7.64 – 7.53 (m, 4H), 7.39 (t, J = 7.6 Hz, 1H), 7.19 – 7.12 (m, 2H), 6.02 (q, J = 6.4 Hz, 1H), 1.51 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8 (d, J_{C-F} = 250.0 Hz), 151.0, 149.8, 143.5 (d, J_{C-F} = 30.8 Hz), 135.0, 134.96, 134.8, 133.3(d, J_{C-F} = 2.7 Hz), 130.6, 128.9, 125.9, 124.1, 123.9 (d, J_{C-F} = 15.4 Hz), 118.1 (d, J_{C-F} = 21.1 Hz), 116.9, 116.5, 110.4, 74.9, 21.4; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}BrFN_3O_6SNa^+$ [M+Na$^+$] 569.9741, found 569.9741.



2c$_{mono(m')}$

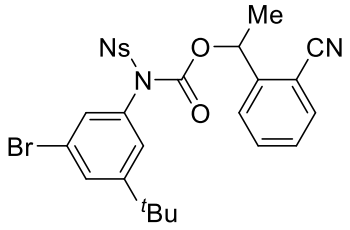
1-(2-cyanophenyl)ethyl(3-bromo-2-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions and **A-1** as the additive on 0.1 mmol scale; 13.8 mg, 25%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.8 Hz, 2H), 8.23 (d, J = 8.4 Hz, 2H), 7.72 (td, J = 6.4, 1.2 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.20 (t, J = 8.0 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.03 (q, J = 6.4 Hz, 1H), 1.50 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (d, J_{C-F} = 249.4 Hz), 151.0, 149.9, 143.5 (d, J_{C-F} = 32.8 Hz), 135.5, 133.3 (d, J_{C-F} = 4.5 Hz), 131.2, 130.6, 128.9, 125.9, 125.5, 124.1, 123.9 (d, J_{C-F} = 15.0 Hz), 116.5, 110.4, 110.0 (d, J_{C-F} = 20.4 Hz), 74.8, 21.4; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}BrFN_3O_6SNa^+$ [M+Na$^+$] 569.9741, found 569.9741.



2c$_{(m, m)di}$

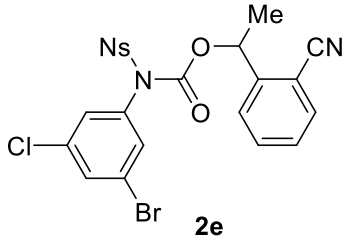
1-(2-cyanophenyl)ethyl(3,5-dibromo-2-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was

run with standard conditions and **A-1** as the additive on 0.1 mmol scale; 18.9 mg, 30%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 9.2 Hz, 2H), 8.22 (d, J = 8.8 Hz, 2H), 7.86 (dd, J = 5.6, 2.4 Hz, 1H), 7.62 – 7.54 (m, 3H), 7.41 (dd, J = 7.6, 0.8 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 6.03 (q, J = 6.8 Hz, 1H), 1.53 (d, J = 6.8 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1 (d, J_{C-F} = 244.6 Hz), 151.0, 149.5, 143.2 (d, J_{C-F} = 35.4 Hz), 137.7, 134.0, 133.4, 130.7, 129.0, 126.1, 124.6 (d, J_{C-F} = 16.0 Hz), 124.2, 124.16, 117.0, 116.6, 110.9 (d, J_{C-F} = 20.1 Hz), 110.5, 75.2, 21.3; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br_2FN_3O_6SNa^+$ [M+Na^+] 647.8846, found 647.8842.



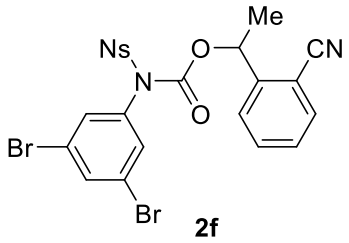
2d

1-(2-cyanophenyl)ethyl(3-bromo-5-(tert-butyl)phenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions at 60 ºC for 48 h and *N*-TFA-Gly-OH as ligand, HOAc as additive on 0.1 mmol scale; 43.4 mg, 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 9.2 Hz, 2H), 8.18 (d, J = 9.2 Hz, 2H), 7.63 (t, J = 1.6 Hz, 1H), 7.58 (dd, J = 7.6, 1.2 Hz, 1H), 7.53 (td, J = 7.6, 1.2 Hz, 1H), 7.38 (td, J = 7.6, 0.8 Hz, 1H), 7.25 (t, J = 1.6 Hz, 1H), 7.17 – 7.14 (m, 2H), 6.05 (q, J = 6.8 Hz, 1H), 1.52 (d, J = 6.8 Hz, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 150.8, 150.6, 144.0, 143.5, 135.9, 133.3, 133.1, 130.4, 130.3, 129.6, 128.8, 125.9, 125.7, 124.1, 122.4, 116.6, 110.5, 74.1, 35.1, 31.0, 21.2; HRMS (m/z, ESI-TOF): Calcd for $C_{26}H_{24}{}^{79}BrN_3O_6SNa^+$ [M+Na^+] 608.0461, found 608.0459.



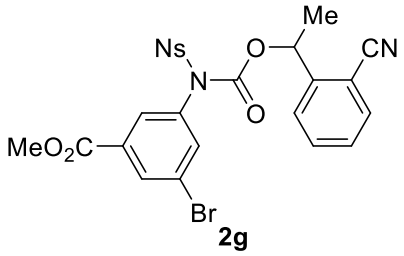
2e

1-(2-cyanophenyl)ethyl(3-bromo-5-chlorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions at 100 ºC for 48 h, and *N-TFA*-Gly-OH as ligand on 0.1 mmol scale; 37.9 mg, 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 8.8 Hz, 2H), 7.66 (t, J = 2.0 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.41 (td, J = 7.6, 0.8 Hz, 1H), 7.35 (t, J = 1.6 Hz, 1H), 7.26 (t, J = 1.6 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 6.04 (q, J = 6.8 Hz, 1H), 1.56 (d, J = 6.8 Hz, 3H).;^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 150.2, 143.7, 143.1, 136.6, 135.8, 133.4, 133.3, 133.1, 131.1, 130.4, 129.0, 128.9, 126.1, 124.3, 122.9, 116.6, 110.7, 74.7, 21.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br^{35}ClN_3O_6SNa^+$ [M+Na^+] 585.9446, found 585.9444.



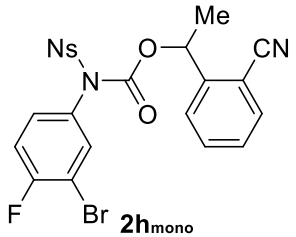
2f

1-(2-cyanophenyl)ethyl(3-bromo-5-chlorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions at 100 ºC for 48 h, and *N*-TFA-Gly-OH as ligand on 0.1 mmol scale; 38.9 mg, 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 – 8.36 (m, 2H), 8.17 (d, *J* = 6.0 Hz, 2H), 7.85 – 7.80 (m, 1H), 7.58 (td, *J* = 6.0, 0.8 Hz, 2H), 7.42 – 7.39 (m, 3H), 7.21 (d, *J* = 5.2 Hz, 1H), 6.03 (q, *J* = 4.4 Hz, 1H), 1.56 (d, *J* = 4.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 150.3, 143.7, 143.1, 136.8, 135.9, 133.5, 133.3, 131.7, 130.5, 129.1, 126.2, 124.3, 123.2, 116.6, 110.7, 74.8, 21.1; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br_2N_3O_6SNa^+$ [M+Na$^+$] 629.8941, found 629.8937.



2g

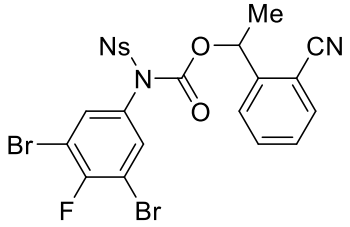
methyl-3-bromo-5-(N-((1-(2-cyanophenyl)ethoxy)carbonyl)-4-nitrophenylsulfonamido)benzoate: The corresponding reaction was run with standard conditions at 100 ºC for 48 h, and *N*-TFA-Gly-OH as ligand on 0.1 mmol scale; 38.9 mg, 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.30 (t, *J* = 1.6 Hz, 1H), 8.18 (d, *J* = 8.8 Hz, 2H), 7.87 (t, *J* = 2.0 Hz, 1H), 7.64 (t, *J* = 2.0 Hz, 1H), 7.60 – 7.54 (m, 2H), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 6.03 (q, *J* = 6.8 Hz, 1H), 3.96 (s, 3H), 1.54 (d, *J* = 6.8 Hz, 3H).;^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 151.0, 150.3, 143.7, 143.1, 136.8, 136.2, 134.1, 133.4, 133.3, 133.1, 130.5, 129.3, 129.0, 126.1, 124.3, 122.8, 116.6, 110.6, 74.7, 52.9, 21.1; HRMS (m/z, ESI-TOF): Calcd for $C_{24}H_{18}{}^{79}BrN_3O_8SNa^+$ [M+Na$^+$] 609.9890, found 609.9888.



2h$_{mono}$

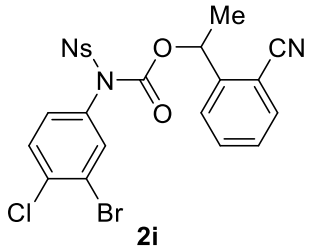
1-(2-cyanophenyl)ethyl(3-bromo-4-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 42.7 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 9.2 Hz, 2H), 7.60 – 7.55 (m, 2H), 7.50 – 7.48 (m, 2H), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H), 7.25 - 7.21 (m, 3H), 6.03 (q, *J* = 6.8 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 3H).;^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9 (d, $J_{C\text{-}F}$ = 250.6 Hz), 150.7 (d, $J_{C\text{-}F}$ =

39.1 Hz), 143.8, 143.1, 134.68, 134.67, 133.3 (d, J_{C-F} = 4.8 Hz), 131.6 (d, J_{C-F} = 3.9 Hz), 130.4, 130.3, 129.0, 126.1, 124.2, 117.2 (d, J_{C-F} = 23.7 Hz), 116.6, 110.7, 109.8 (d, J_{C-F} = 22.6 Hz), 74.5, 21.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}BrFN_3O_6SNa^+$ [M+Na$^+$] 569.9741, found 569.9741.



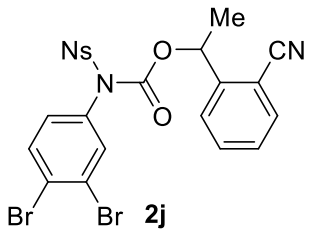
2h$_{(m,\ m')di}$

1-(2-cyanophenyl)ethyl(3,5-dibromo-4-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 12.7 mg, 20%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 8.16 (d, J = 8.8 Hz, 2H), 7.61 – 7.58 (m, 2H), 7.47 (d, J = 5.6 Hz, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.27– 7.22 (m, 1H), 6.03 (q, J = 6.8 Hz, 1H), 1.58 (d, J = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.8 (d, J_{C-F} = 249.8 Hz), 151.0, 150.3, 143.6, 142.9, 133.8, 133.4 (d, J_{C-F} = 2.7 Hz), 131.9 (d, J_{C-F} = 4.7 Hz), 130.4, 129.1, 126.2, 124.3, 116.6, 110.8, 110.3 (d, J_{C-F} = 23.7 Hz), 74.8, 20.8; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br_2FN_3O_6SNa^+$ [M+Na$^+$] 647.8846, found 647.8847.



2i

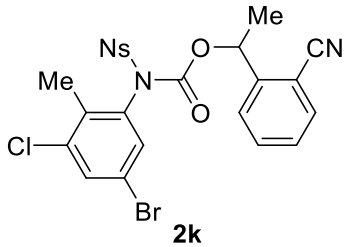
1**-(2-cyanophenyl)ethyl(3-bromo-4-chlorophenyl)((4-nitrophenyl)sulfonyl)carbamate**: The corresponding reaction was run with standard conditions at 100 °C for 48 h on 0.1 mmol scale; 37.3 mg, 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.8 Hz, 2H), 8.16 (d, J = 8.8 Hz, 2H), 7.60 – 7.54 (m, 4H), 7.41 (td, J = 7.6, 1.2 Hz, 1H), 7.23 – 7.19 (m, 2H), 6.03 (q, J = 6.8 Hz, 1H), 1.55 (d, J = 6.4 Hz, 3H).;^{13}C NMR (101 MHz, $CDCl_3$) δ 150.9, 150.4, 143.7, 143.1, 136.7, 134.6, 134.1, 133.4, 133.3, 131.0, 130.4, 129.5, 129.0, 126.1, 124.2, 123.1, 116.6, 110.7, 74.6, 21.0.;^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 150.2, 143.7, 143.1, 136.6, 135.8, 133.4, 133.3, 133.1, 131.1, 130.4, 129.0, 128.9, 126.1, 124.3, 123.1, 116.6, 110.7, 74.7, 21.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br^{35}ClN_3O_6SNa^+$ [M+Na$^+$] 585.9446, found 585.9442.



2j

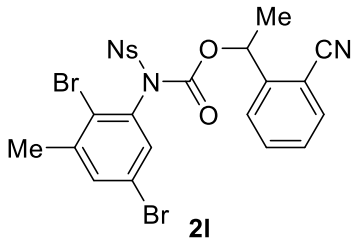
1-(2-cyanophenyl)ethyl(3,4-dibromophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard

conditions at 100 ºC for 48 h on 0.1 mmol scale; 37.9 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.58 (t, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.12 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.03 (q, *J* = 6.8 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 150.9, 150.3, 143.7, 143.1, 134.8, 134.5, 134.4, 133.4, 133.3, 130.4, 129.6, 129.0, 127.0, 126.1, 125.5, 124.2, 116.6, 110.7, 74.6, 21.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br_2N_3O_6SNa^+$ [M+Na$^+$] 629.8941, found 629.8932.



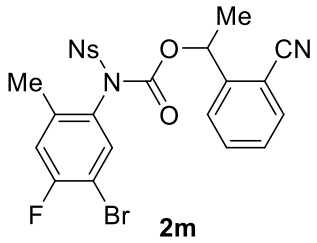
2k

1-(2-cyanophenyl)ethyl(5-bromo-3-chloro-2-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 53.2 mg, 92%. ^{1}H NMR (600 MHz, $CDCl_3$): (rotamers appear in the NMR) δ 8.40 (dd, *J* = 19.2, 9.0 Hz, 2H), 8.23 (dd, *J* = 19.8, 9.0 Hz, 2H), 7.69 (d, *J* = 2.0 Hz, 0.4H), 7.67 (d, *J* = 2.0 Hz, 0.5H), 7.60 (ddd, *J* = 7.8, 3.6, 1.2 Hz, 1H), 7.56 (dtd, *J* = 14.4, 7.8, 1.2 Hz, 1H), 7.43 (td, *J* = 7.6, 1.1 Hz, 0.46H), 7.39 (td, *J* = 7.6, 1.1 Hz, 0.56H), 7.22 (d, *J* = 1.9 Hz, 0.40H), 7.15 (t, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 2.0 Hz, 0.52H), 6.08 – 6.01 (m, 1H), 2.32 (s, 1.65H), 2.19 (s, 1.35fH), 1.56 – 1.52 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.0, 151.0, 150.1, 150.1, 143.7, 143.7, 143.2, 143.2, 136.9, 136.8, 136.7, 136.4, 136.2, 136.2, 133.7, 133.6, 133.3, 133.2, 130.7, 130.7, 130.5, 129.0, 128.9, 126.0, 125.9, 124.2, 19.2, 119.0, 116.5, 116.4, 110.7, 110.6, 74.6, 74.5, 21.3, 21.2, 15.9, 15.8; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br^{35}ClN_3O_6SNa^+$ [M+Na$^+$] 599.9602, found 599.9602.



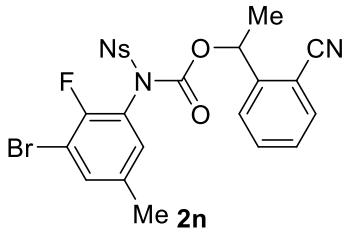
2l

1-(2-cyanophenyl)ethyl(2,5-dibromo-3-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 55.6 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) (rotamers appear in the NMR) δ 8.40 – 8.37 (m, 2H), 8.33 – 8.27 (m, 2H), 7.64 – 7.57 (m, 1H), 7.57 – 7.49 (m, 2H), 7.46 (d, *J* = 2.1 Hz, 0.43H), 7.43 – 7.35 (m, 1.52H), 7.21 (d, *J* = 7.9 Hz, 0.44H), 7.13 (d, *J* = 7.9 Hz, 0.55H), 6.07 – 6.00 (m, 1H), 2.48 (s, 1.64H), 2.41 (s, 1.31H), 1.56 – 1.47 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 151.0, 149.8, 149.7, 143.9, 143.8, 143.5, 143.4, 142.1, 141.9, 135.6, 135.6, 135.0, 133.3, 133.3, 133.2, 133.1, 132.1, 131.9, 131.2, 131.2, 128.8, 126.4, 126.1, 126.0, 126.0, 123.9, 120.8, 120.7, 116.5, 110.4, 110.3, 74.8, 74.6, 23.7, 23.6, 21.7, 21.4; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br_2N_3O_6SNa^+$ [M+Na$^+$] 643.9097, found 643.9087.



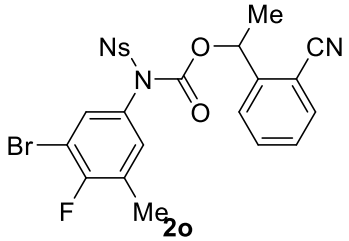
2m

1-(2-cyanophenyl)ethyl(5-bromo-4-fluoro-2-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions at 100 ºC for 48 h and HOAc as additive on 0.1 mmol scale; 36.1 mg, 64%. ^{1}H NMR (400 MHz, $CDCl_3$) (rotamers appear in the NMR): δ 8.40 (dd, *J* = 13.6, 8.8 Hz, 2H), 8.23 (dd, *J* = 14.8, 8.8 Hz, 2H), 7.61 – 7.52 (m, 2H), 7.44 – 7.37 (m, 1H), 7.31 (d, *J* = 6.3 Hz, 0.49H), 7.21 (d, *J* = 6.3 Hz, 0.52H), 7.19 – 7.13 (m, 2H), 6.07 – 6.00 (m, 1H), 2.32 (s, 1.68H), 2.23 (s, 1.29H), 1.56 – 1.52 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.56 (d, J_{C-F} = 251.7 Hz), 159.53 (d, J_{C-F} = 251.7, Hz), 151.0 (d, J_{C-F} = 5.6 Hz), 150.3 (d, J_{C-F} = 14.7 Hz), 143.9, 143.85, 143.3, 143.2, 140.6 (d, J_{C-F} = 8.0 Hz), 140.4 (d, J_{C-F} = 8.2 Hz), 133.7, 133.6, 133.33, 133.29, 133.2, 131.1, 130.63, 130.6, 129.0, 128.9, 126.1, 125.8, 124.2, 118.9 (d, J_{C-F} = 23.3 Hz) 118.8 (d, J_{C-F} = 23.1 Hz), 116.52, 116.42, 110.7, 110.5, 106.5 (d, J_{C-F} = 22.3 Hz), 106.3 (d, J_{C-F} = 22.5 Hz), 106.2, 74.5, 74.3, 21.26, 21.18, 18.3, 18.2; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}BrFN_3O_6SNa^+$ [M+Na$^+$] 583.9898, found 583.9894.



2n

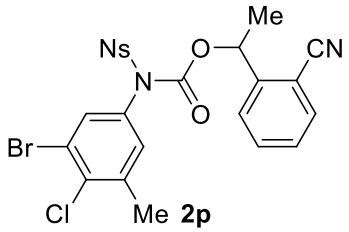
1-(2-cyanophenyl)ethyl(3-bromo-2-fluoro-5-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 55.1 mg, 98%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.8 Hz, 2H), 8.22 (d, *J* = 8.8 Hz, 2H), 7.60 – 7.51 (m, 3H), 7.38 (td, *J* = 7.6, 0.4 Hz, 1H), 7.22 (d, *J* = 5.6 Hz, 1H), 7.15 (d, *J* = 6.4 Hz, 1H), 6.01 (q, *J* = 6.4 Hz, 1H), 2.40 (s, 3H), 1.50 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.6 (d, J_{C-F} = 246.8 Hz), 151.0, 150.0, 143.8, 143.5, 135.9, 135.8, 133.3 (d, J_{C-F} = 7.7 Hz), 131.7, 130.7, 128.9, 126.0, 124.1, 123.2 (d, J_{C-F} = 14.6 Hz), 116.6, 110.4, 109.4 (d, J_{C-F} = 20.0 Hz), 74.8, 21.5, 20.6; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}BrFN_3O_6SNa^+$ [M+Na$^+$] 583.9898, found 583.9898.



2o

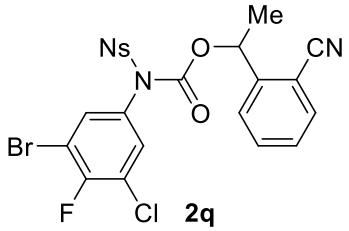
1-(2-cyanophenyl)ethyl(3-bromo-4-fluoro-5-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was

run with standard conditions on 0.1 mmol scale; 55.3 mg, 98%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 8.8 Hz, 2H), 7.61 – 7.55 (m, 2H), 7.41 (td, J = 7.6, 1.2 Hz, 1H), 7.28 (dd, J = 5.6, 2.4 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 7.11 (dd, J = 6.0, 2.8 Hz, 1H), 6.02 (q, J = 6.4 Hz, 1H), 2.36 (d, J = 2.4 Hz, 3H), 1.55 (d, J = 6.4 Hz, 3H);^{13}C NMR (151 MHz, $CDCl_3$) δ 158.5 (d, $J_{C\text{-}F}$ = 248.4 Hz), 150.8, 150.6, 143.9, 143.2, 133.3 (d, $J_{C\text{-}F}$ = 5.3 Hz), 131.8 (d, $J_{C\text{-}F}$ = 5.0 Hz), 131.7, 130.9 (d, $J_{C\text{-}F}$ = 4.1 Hz), 130.4, 128.9, 127.8 (d, $J_{C\text{-}F}$ = 19.7 Hz), 126.1, 124.2, 116.6, 110.7, 109.4 (d, $J_{C\text{-}F}$ = 23.3 Hz), 74.5, 21.0, 15.1 (d, $J_{C\text{-}F}$ = 2.7 Hz); HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}BrFN_3O_6SNa^+$ [M+Na$^+$] 583.9898, found 583.9895.



2p

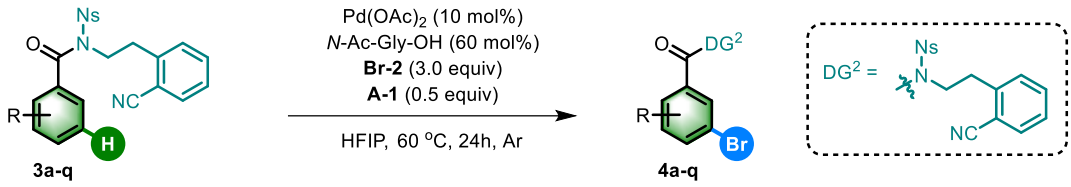
1-(2-cyanophenyl)ethyl(3-bromo-4-chloro-5-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions at 100 ºC for 48 h on 0.1 mmol scale; 45.2 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 8.16 (d, J = 9.2 Hz, 2H), 7.61 – 7.55 (m, 2H), 7.41 (td, J = 7.6, 1.2 Hz, 1H), 7.37 (d, J = 2.4 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.17 (dd, J = 2.4, 0.4 Hz, 1H), 6.03 (q, J = 6.4 Hz, 1H), 2.49 (s, 3H), 1.55 (d, J = 6.4 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.0, 150.5, 144.0, 143.3, 139.7, 136.7, 133.4, 133.4, 133.3, 131.9, 130.9, 130.5, 129.0, 126.2, 124.3, 123.5, 116.7, 110.8, 74.6, 21.9, 21.1; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br^{35}ClN_3O_6SNa^+$ [M+Na$^+$] 599.9602, found 599.9601.



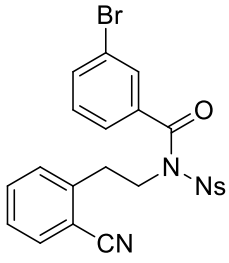
2q

1-(2-cyanophenyl)ethyl(3-bromo-5-chloro-4-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions at 100 ºC for 48 h and *N*-TFA-Gly-OH as ligand, on 0.1 mmol scale; 36.1 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 8.16 (d, J = 8.4 Hz, 2H), 7.59 (t, J = 7.2 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.35 – 7.33 (m, 1H), 7.25 (s, 1H), 6.04 (q, J = 6.4 Hz, 1H), 1.58 (d, J = 6.8 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.1 (d, $J_{C\text{-}F}$ = 251.4 Hz), 151.1, 150.3, 143.7, 142.9, 133.4, 133.1, 131.6 (d, $J_{C\text{-}F}$ = 5.3 Hz), 131.1, 130.5, 129.2, 126.3, 124.4, 123.0 (d, $J_{C\text{-}F}$ = 20.0 Hz), 116.7, 110.9, 110.7 (d, $J_{C\text{-}F}$ = 22.5 Hz), 74.9, 20.9; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br^{35}ClFN_3O_6SNa^+$ [M+Na$^+$] 603.9351, found 603.9342.

General procedure for *meta*-bromination of benzoic acids

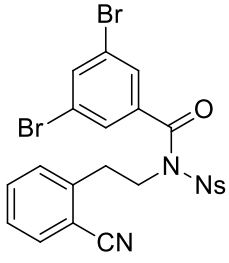


3 (0.10 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 10 mol%), *N*-Ac-Gly-OH (60 mol%), **Br-2** (3 equiv) and **A-1** (0.05 mmol) were dissolved in HFIP (1.0 mL) in a 50 mL Schlenk sealed tube. The reaction tube was capped, then evacuated briefly under vacuum and charged with argon (1 atm, balloon, × 3). The tube was then submerged into a preheated indicated oil bath at 60 °C to react for 24 h. The crude reaction mixture was diluted with EtOAc (10 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 20 mL of EtOAc. The filtrate was diluted in EtOAc and washed with saturated Na_2SO_3 and saturated NaCl aqueous solution. The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by preparative thin layer chromatography using DCM/Toluene as the eluent.



4a$_{mono}$

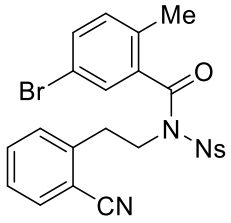
3-bromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 34.5 mg, 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.0 Hz, 2H), 8.15 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.32 – 7.22 (m, 3H), 7.10 (s, 1H), 4.26 (t, *J* = 6.4 Hz, 2H), 3.22 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 150.7, 143.9, 140.5, 135.3, 135.1, 133.2, 131.0, 130.6 , 130.1, 128.0, 126.0, 124.3, 122.6, 117.2, 112.8, 48.3, 34.9; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{16}{}^{79}BrN_3O_5SNa^+$ [M+Na$^+$] 535.9886, found 535.9891.



4a$_{(m, m')di}$

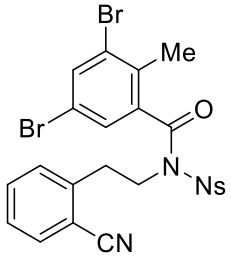
3,5-dibromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 11.8 mg, 20%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J*

= 8.8 Hz, 2H), 8.11 (d, *J* = 9.2 Hz, 2H), 7.78 – 7.74 (m, 1H), 7.60 – 7.56 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 2.0 Hz, 2H), 4.25 (t, *J* = 6.8 Hz, 2H), 3.23 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 150.9, 143.7, 140.4, 137.4, 136.7, 133.2, 131.1, 130.1, 129.2, 128.1, 124.4, 123.1, 123.1, 117.2, 112.9, 48.1, 34.7; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br_2N_3O_5SNa^+$ [M+Na^+] 613.8991, found 613.8987.



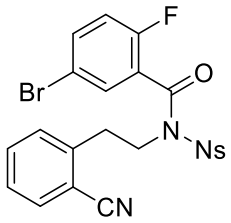
4b$_{mono}$

5-bromo-N-(2-cyanophenethyl)-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 40.7 mg, 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 7.65 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.59 (td, *J* = 7.6, 1.2 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.56 (d, *J* = 2.0 Hz, 1H), 4.19 (t, *J* = 6.8 Hz, 2H), 3.29 (t, *J* = 7.2 Hz, 2H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 150.8, 144.2, 140.6, 135.5, 134.1, 133.7, 133.3, 133.2, 132.4, 130.9, 130.0, 129.0, 128.0, 124.2, 119.1, 117.3, 112.9, 47.9, 35.0, 18.6; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}{}^{79}BrN_3O_5SNa^+$ [M+Na^+] 550.0043, found 550.0040.



4b$_{(m,\ m')di}$

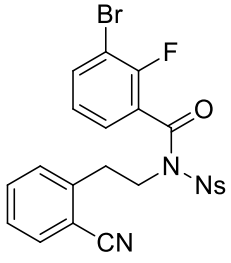
3,5-dibromo-N-(2-cyanophenethyl)-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 6.6 mg, 11%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.8 Hz, 2H), 7.99 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.60 (td, *J* = 7.6, 1.2 Hz, 1H), 7.44 – 7.41 (m, 2H), 6.62 (d, *J* = 2.0 Hz, 1H), 4.19 (s, 2H), 3.31 (t, *J* = 7.6 Hz, 2H), 2.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 150.9, 143.9, 140.5, 136.8, 136.7, 134.1, 133.3, 133.3, 130.8, 129.9, 128.1, 128.0, 126.9, 124.3, 119.4, 117.4, 113.0, 47.8, 34.9, 19.6; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br_2N_3O_5SNa^+$ [M+Na^+] 627.9148, found 627.9146.



4c$_{mono\ (m)}$

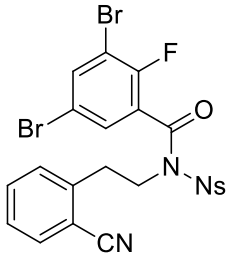
5-bromo-N-(2-cyanophenethyl)-2-fluoro-N-((4-

nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 12.3 mg, 23%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.4 Hz, 2H), 8.14 (d, *J* = 8.4 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.49 – 7.43 (m, 2H), 6.95 (t, *J* = 9.2 Hz, 1H), 6.61 (dd, *J* = 5.6, 2.4 Hz, 1H), 4.25 (t, *J* = 5.6 Hz, 2H), 3.27 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 156.8 (d, J_{C-F} = 249.0 Hz), 150.9, 143.7, 140.3, 136.2 (d, J_{C-F} = 8.2 Hz), 133.3 (d, J_{C-F} = 2.8 Hz), 131.6, 131.5 (d, J_{C-F} = 2.7 Hz), 130.1, 128.0, 124.2, 123.7 (d, J_{C-F} = 17.3 Hz), 117.8 (d, J_{C-F} = 22.5 Hz), 117.3 (d, J_{C-F} = 3.3 Hz), 117.1, 112.8, 48.0 (d, J_{C-F} = 2.1 Hz), 35.3; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}BrFN_3O_5SNa^+$ [M+Na^+] 553.9792, found 553.9790.



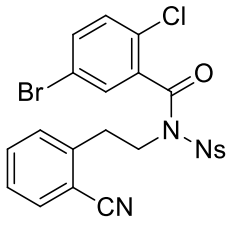
4cmono (*m'*)

3-bromo-N-(2-cyanophenethyl)-2-fluoro-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 18.0 mg, 34%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.67 – 7.57 (m, 3H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.96 – 6.92 (m, 1H), 4.23 (t, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 7.2 Hz, 2H): ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 154.5 (d, J_{C-F} = 248.1 Hz), 150.8, 143.6, 140.6, 136.4, 133.2 (d, J_{C-F} = 13.1 Hz), 131.2, 129.8, 128.1, 128.07, 127.9, 125.7 (d, J_{C-F} = 4.2 Hz), 124.3, 123.6 (d, J_{C-F} = 17.2 Hz), 117.3, 112.9, 109.6 (d, J_{C-F} = 20.5 Hz), 47.9, 35.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}BrFN_3O_5SNa^+$ [M+Na^+] 553.9792, found 553.9788.



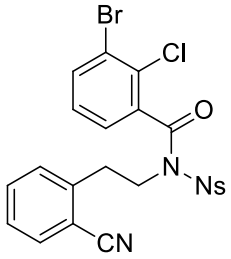
4c(*m, m'*)di

3,5-dibromo-N-(2-cyanophenethyl)-2-fluoro-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 9.0 mg, 15%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.0 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.81 – 7.76 (m, 1H), 7.65 – 7.60 (m, 2H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 6.71 (dd, *J* = 5.2, 2.4 Hz, 1H), 4.23 (s, 2H), 3.29 (t, *J* = 6.8 Hz, 2H);^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 153.7 (d, J_{C-F} = 248.3 Hz), 150.9, 143.4, 140.3, 138.6, 133.3 (d, J_{C-F} = 8.3 Hz), 131.4, 130.5, 130.47, 130.0, 128.1, 124.7 (d, J_{C-F} = 19.4 Hz), 124.3, 117.5 (d, J_{C-F} = 4.1 Hz), 117.2, 112.9, 110.7 (d, J_{C-F} = 22.2 Hz), 47.9, 35.1; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br_2FN_3O_5SNa^+$ [M+Na^+] 631.8897, found 631.8898.



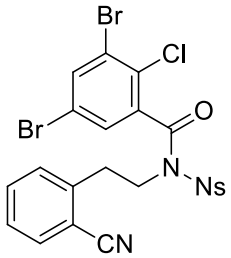
4d$_{\text{mono }(m)}$

5-bromo-2-chloro-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 27.6 mg, 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.8 Hz, 2H), 8.17 (d, *J* = 8.8 Hz, 2H), 7.66 – 7.62 (m, 2H), 7.52 – 7.44 (m, 3H), 7.18 (d, *J* = 8.4 Hz, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 4.16 (s, 2H), 3.30 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 150.9, 143.5, 140.3, 135.0, 134.6, 133.4, 133.3, 131.5, 131.1, 131.0, 130.5, 129.0, 128.1, 124.0, 121.0 117.1, 113.0, 48.3, 35.3; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br^{35}ClN_3O_5SNa^+$ [M+Na^+] 569.9497, found 569.9500.



4d$_{\text{mono }(m')}$

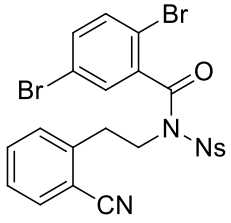
3-bromo-2-chloro-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 6.7 mg, 12%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 9.2 Hz, 2H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.71 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.63 – 7.59 (m, 2H), 7.48 – 7.46 (m, 1H), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H), 7.16 (t, *J* = 8.0 Hz, 1H), 6.93 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.12 (s, 2H), 3.31 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 150.9, 143.4, 140.7, 135.7, 135.2, 133.2, 133.1, 131.0, 130.4, 130.3 , 128.3, 127.9, 127.2, 124.0, 123.7, 117.4, 113.0, 48.1, 35.1; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br^{35}ClN_3O_5SNa^+$ [M+Na^+] 569.9497, found 569.9492.



4d$_{(m,\ m')\text{di}}$

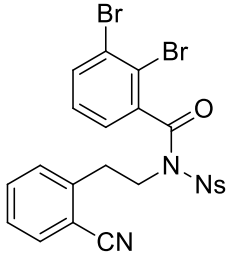
3,5-dibromo-2-chloro-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 7.0 mg, 11%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 2.0 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.45 (td, *J* = 7.6, 1.2 Hz, 1H), 6.67 (d, *J* = 2.0 Hz, 1H), 4.12 (s, 2H), 3.32 (t, *J* = 7.2 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 151.0, 143.2, 140.3, 137.9, 136.0, 133.3, 131.3, 130.3, 129.8, 129.6, 128.1, 124.5, 124.1, 121.1, 117.2,

113.0, 48.1, 35.1; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br_2{}^{35}ClN_3O_5SNa^+$ [M+Na^+] 647.8602, found 647.8605.



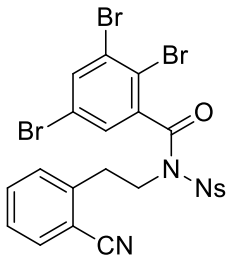
4e$_{mono\ (m)}$

2,5-dibromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 29.0 mg, 49%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.21 (d, *J* = 8.8 Hz, 2H), 7.64 (td, *J* = 7.6, 1.2 Hz, 1H), 7.51 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.46 (td, *J* = 7.6, 0.8 Hz, 1H), 7.41 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 4.13 (s, 2H), 3.31 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 150.9, 143.3, 140.3, 136.7, 135.0, 134.3, 133.4, 133.3, 131.4, 131.1, 130.7 128.1, 124.0, 121.7, 117.4, 117.1, 113.0, 48.5, 35.3; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br_2N_3O_5SNa^+$ [M+Na^+] 613.8991, found 613.8990.



4e$_{mono\ (m')}$

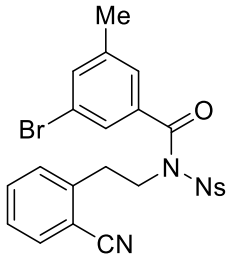
2,3-dibromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 8.3 mg, 14%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.62 – 7.59 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 4.09 (brs, 2H), 3.31 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 150.9, 143.3, 140.7, 137.6, 135.4, 133.2, 133.1, 130.9, 130.4, 129.0, 127.9, 127.0, 126.2, 124.0, 121.4, 117.4, 113.0, 48.3, 35.1; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br_2N_3O_5SNa^+$ [M+Na^+] 613.8991, found 613.8991.



4e$_{(m, m')di}$

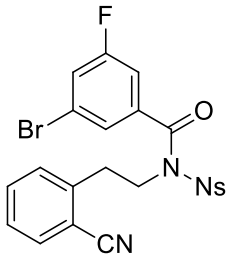
2**,3,5-tribromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide**: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 8.7 mg, 13%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.14 (d, *J* = 8.8 Hz, 2H), 7.83 (d, *J* = 2.0 Hz, 1H), 7.67 – 7.62 (m, 2H),

7.51 (d, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 6.66 (d, J = 2.0 Hz, 1H), 4.11 (s, 2H), 3.33 (t, J = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 151.0, 143.1, 140.3, 138.5, 137.7, 133.3, 131.2, 130.5, 129.7, 128.1, 127.1, 124.1, 121.9, 120.3, 117.2, 113.0, 48.3, 35.1; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{75}Br_3N_3O_5SNa^+$ [M+Na^+] 691.8096, found 691.8094.



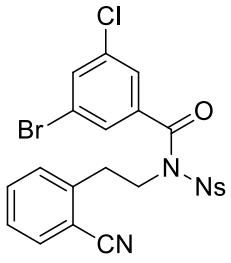
4f

3-bromo-N-(2-cyanophenethyl)-5-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions for 16 h and chloranil (0.1 mmol) as additive on 0.1 mmol scale; 34.5 mg, 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.4 Hz, 2H), 8.16 (d, J = 8.4 Hz, 2H), 7.57 – 7.53 (m, 2H), 7.44 (s, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 6.95 (s, 1H), 6.91 (s, 1H), 4.27 (t, J = 6.8 Hz, 2H), 3.21 (t, J = 6.8 Hz, 2H), 2.32 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 150.7, 144.0, 140.8, 140.5, 135.6, 135.1, 133.2, 133.2, 131.0, 130.2, 127.9, 127.5, 126.7, 124.2, 122.4, 117.2, 112.8, 48.3, 34.9, 21.1; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}{}^{79}BrN_3O_5SNa^+$ [M+Na^+] 550.0043, found 550.0040.



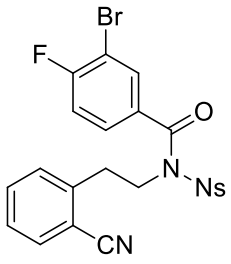
4g

3-bromo-N-(2-cyanophenethyl)-5-fluoro-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions for 48 h and chloranil (0.1 mmol) as additive on 0.1 mmol scale; 31.5 mg, 59%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.8 Hz, 2H), 8.14 (d, J = 9.2 Hz, 2H), 7.59 – 7.56 (m, 2H), 7.43 – 7.33 (m, 3H), 6.97 (s, 1H), 6.87 (d, J = 7.6 Hz, 1H), 4.24 (t, J = 6.8 Hz, 2H), 3.23 (t, J = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (d, $J_{C\text{-}F}$ = 2.7 Hz), 161.9 (d, $J_{C\text{-}F}$ = 253.0 Hz), 150.9, 143.7, 140.4, 136.7, 136.6, 133.2 (d, $J_{C\text{-}F}$ = 3.4 Hz), 131.0, 130.1, 128.1, 126.4 (d, $J_{C\text{-}F}$ = 3.5 Hz), 124.4, 123.0 (d, $J_{C\text{-}F}$ = 9.1 Hz), 122.7 (d, $J_{C\text{-}F}$ = 23.7 Hz), 117.2, 113.8 (d, $J_{C\text{-}F}$ = 23.4 Hz), 112.9, 48.1, 34.8; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}BrFN_3O_5SNa^+$ [M+Na^+] 553.9792, found 553.9790.



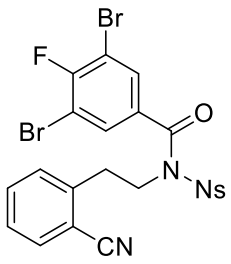
4h

3-**bromo-5-chloro-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide**: The corresponding reaction was run with standard conditions for 48 h and chloranil (0.1 mmol) as additive on 0.1 mmol scale; 34.9 mg, 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.8 Hz, 2H), 8.12 (d, J = 8.8 Hz, 2H), 7.63 (t, J = 1.6 Hz, 1H), 7.59 – 7.56 (m, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.08 (t, J = 1.6 Hz, 1H), 7.02 (t, J = 1.6 Hz, 1H), 4.25 (t, J = 6.8 Hz, 2H), 3.23 (t, J = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 150.9, 143.7 140.4 136.5, 135.5, 134.7, 133.3 131.1, 130.1, 128.7, 128.1 126.4 124.4, 123.0, 117.3, 112.9, 48.1, 34.8; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br^{35}ClN_3O_5SNa^+$ [M+Na$^+$] 569.9497, found 569.9493.



4i$_{mono}$

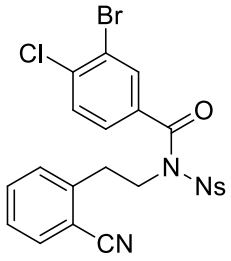
3-bromo-N-(2-cyanophenethyl)-4-fluoro-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 33.0 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.8 Hz, 2H), 8.13 (d, J = 8.8 Hz, 2H), 7.56 (t, J = 8.0 Hz, 2H), 7.39 (t, J = 7.6 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.31 (d, J = 8.0 Hz, 1H), 7.15 (t, J = 8.4 Hz, 1H), 4.21 (t, J = 7.2 Hz, 2H), 3.21 (t, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 161.4 (d, J_{C-F} = 254.0 Hz), 150.8, 143.8, 140.5, 133.86, 133.8, 133.2 (d, J_{C-F} = 2.9 Hz), 131.1 (d, J_{C-F} = 4.0 Hz), 130.9, 130.0, 129.2 (d, J_{C-F} = 8.3 Hz), 128.0, 124.4, 117.3, 116.7 (d, J_{C-F} = 23.1 Hz), 112.8, 109.7 (d, J_{C-F} = 21.8 Hz), 48.2, 34.7; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}BrFN_3O_5SNa^+$ [M+Na$^+$] 553.9792, found 553.9789.



4i$_{(m, m')di}$

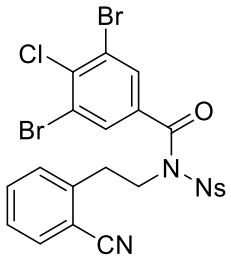
3,5-dibromo-N-(2-cyanophenethyl)-4-fluoroN-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard

conditions, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 6.5 mg, 11%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.4 Hz, 2H), 8.10 (d, J = 8.8 Hz, 2H), 7.60 – 7.55 (m, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.35 – 7.31 (m, 3H), 4.20 (t, J = 6.8 Hz, 2H), 3.22 (t, J = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 158.2 (d, J_{C-F} = 252.7 Hz), 150.9, 143.6, 140.4, 133.2 (d, J_{C-F} = 1.9 Hz), 132.4, 131.9 (d, J_{C-F} = 4.8 Hz), 131.0, 130.0, 128.1, 124.5, 117.2, 112.9, 110.3 (d, J_{C-F} = 23.1 Hz), 48.0, 34.5; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br_2FN_3O_5SNa^+$ [M+Na$^+$] 631.8897, found 631.8895.



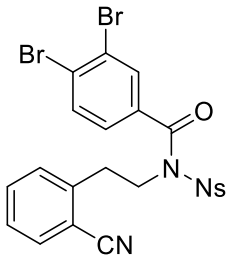
4j$_{mono}$

3-bromo-4-chloro-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions for 48 h, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 31.9 mg, 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 9.2 Hz, 2H), 8.12 (d, J = 8.8 Hz, 2H), 7.58 – 7.54 (m, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.40 (td, J = 7.6, 0.8 Hz, 1H), 7.34 (d, J = 2.0 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.26 (dd, J = 8.0, 2.0 Hz, 1H), 4.21 (t, J = 6.8 Hz, 2H), 3.22 (t, J = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 150.8, 143.8, 140.5, 139.0, 133.4, 133.2, 133.1, 130.9, 130.4, 130.0, 128.0, 127.7, 124.4, 122.9, 117.3, 112.8, 48.1, 34.6; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br^{35}ClN_3O_5SNa^+$ [M+Na$^+$] 569.9497, found 569.9493.



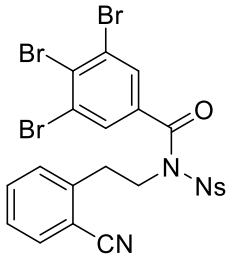
4j$_{(m, m')di}$

3,5-dibromo-4-chloro-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions for 48 h, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 8.8 mg, 14%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.8 Hz, 2H), 8.09 (d, J = 9.2 Hz, 2H), 7.60 – 7.55 (m, 2H), 7.41 (td, J = 7.6, 0.8 Hz, 1H), 7.38 (s, 2H), 7.33 (d, J = 7.6 Hz, 1H), 4.21 (t, J = 6.8 Hz, 2H), 3.22 (t, J = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 150.9, 143.5, 140.4, 139.2, 134.1, 133.2, 131.6, 131.0, 129.9, 128.1, 124.5, 123.8, 117.3, 112.9, 47.9, 34.5; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br_2{}^{35}ClN_3O_5SNa^+$ [M+Na$^+$] 647.8602, found 647.8602.



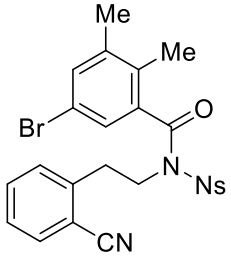
4k$_{mono}$

3,4-dibromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions for 48 h, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 35.7 mg, 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 9.2 Hz, 2H), 8.11 (d, J = 8.8 Hz, 2H), 7.66 (d, J = 8.4 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.40 (t, J = 7.6 Hz, 1H), 7.33 – 7.30 (m, 2H), 7.16 (dd, J = 8.0, 2.0 Hz, 1H), 4.20 (t, J = 7.2 Hz, 2H), 3.22 (t, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 150.8, 143.8, 140.5, 134.1, 133.8, 133.2, 132.9, 130.9, 130.0, 129.7, 128.0, 127.5, 125.3, 124.4, 117.3, 112.9, 48.1, 34.6; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{79}Br_2N_3O_5SNa^+$ [M+Na^+] 613.8991, found 613.8993.



4k$_{(m,\ m')di}$

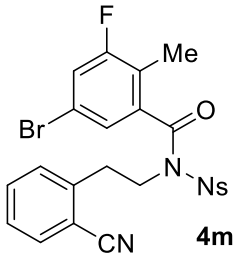
3,4,5-tribromo-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions for 48 h, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 8.1 mg, 12%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.8 Hz, 2H), 8.09 (d, J = 8.8 Hz, 2H), 7.60 – 7.55 (m, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.35 (s, 2H), 7.33 (d, J = 7.6 Hz, 1H), 4.21 (t, J = 6.8 Hz, 2H), 3.22 (t, J = 6.8 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.5, 150.9, 143.6, 140.4, 134.8, 133.2, 132.3, 131.2, 131.0, 130.0, 128.1, 126.4, 124.5, 117.3, 112.9, 47.9, 34.5; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}Br_3N_3O_5SNa^+$ [M+Na^+] 691.8096, found 691.8097.



4l

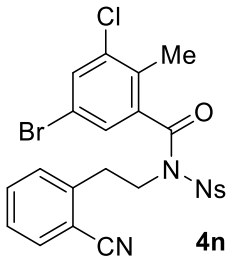
5-**bromo-N-(2-cyanophenethyl)-2,3-dimethyl-N-((4-nitrophenyl)sulfonyl)benzamide**: The corresponding reaction was run with standard conditions for 16 h without adding **A-1** on 0.1 mmol scale; 38.6 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.8 Hz, 2H), 8.03 (t, J = 8.8 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.34 (s, 1H), 6.44 (s, 1H), 4.17

(s, 2H), 3.30 (t, J = 7.2 Hz, 2H), 2.23 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 150.8, 144.2, 140.6, 140.4, 135.7, 134.6, 133.3, 133.2, 132.5, 130.8, 130.0, 128.0, 126.4, 124.1, 118.9, 117.4, 112.9, 47.9, 35.0, 19.9, 16.0; HRMS (m/z, ESI-TOF): Calcd for $C_{24}H_{20}{}^{79}BrN_3O_5SNa^+$ [M+Na^+] 564.0199, found 564.0196.



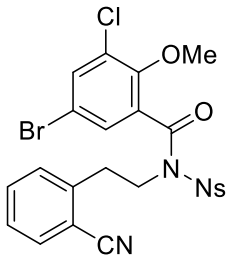
4m

5-bromo-N-(2-cyanophenethyl)-3-fluoro-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 39.5 mg, 72%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.9 Hz, 2H), 8.04 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.49 – 7.35 (m, 2H), 7.26 (d, J = 8.6 Hz, 1H), 6.43 (s, 1H), 4.19 (t, J = 7.3 Hz, 2H), 3.29 (t, J = 7.2 Hz, 2H), 1.99 (d, J = 2.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9 (d, $J_{C\text{-}F}$ = 3.6 Hz), 160.9 (d, $J_{C\text{-}F}$ = 252.6 Hz), 151.0, 144.1, 140.6, 137.2 (d, $J_{C\text{-}F}$ = 4.9 Hz), 133.4, 130.9, 130.0, 128.1, 124.9, 124.84, 124.4, 122.3 (d, $J_{C\text{-}F}$ = 19.2 Hz), 121.0 (d, $J_{C\text{-}F}$ = 26.0 Hz), 119.4 (d, $J_{C\text{-}F}$ = 9.8 Hz), 117.4, 113.0, 48.0, 35.0, 11.4 (d, $J_{C\text{-}F}$ = 4.2 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}BrFN_3O_5SNa^+$ [M+Na^+] 567.9949, found 567.9947.



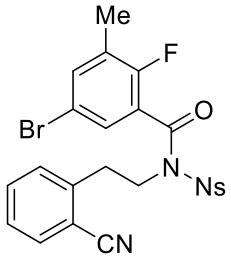
4n

5-bromo-3-chloro-N-(2-cyanophenethyl)-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 42.0 mg, 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.9 Hz, 2H), 8.00 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 7.7 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.42 (t, J = 7.7 Hz, 2H), 6.55 (s, 1H), 4.18 (s, 2H), 3.29 (t, J = 7.2 Hz, 2H), 2.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 150.9, 144.0, 140.6, 137.0, 136.7, 133.8, 133.4, 133.3, 132.6, 130.9, 130.0, 128.1, 127.5, 124.4, 119.4, 117.5, 113.0, 47.9, 35.0, 16.8. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br^{35}ClN_3O_5SNa^+$ [M+Na^+] 583.9653, found 583.9655.



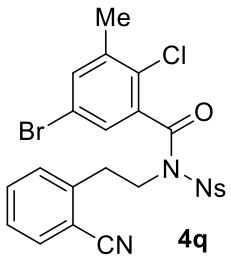
4o

5-bromo-3-chloro-N-(2-cyanophenethyl)-2-methoxy-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 47.9 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.4 Hz, 2H), 8.14 (d, *J* = 8.8 Hz, 2H), 7.64 – 7.58 (m, 3H), 7.45 – 7.40 (m, 2H), 6.64 (d, *J* = 2.0 Hz, 1H), 4.15 (t, *J* = 6.4 Hz, 2H), 3.54 (s, 3H), 3.25 (t, *J* = 6.8 Hz, 2H);^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 151.2, 150.8, 143.8, 140.5, 135.5, 133.3, 133.2, 131.5, 131.0, 130.2, 129.3, 129.0, 128.0, 124.1, 117.2, 117.1, 113.0, 62.2, 48.1, 35.1; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br^{35}ClN_3O_6SNa^+$ [M+Na$^+$] 599.9602, found 599.9602.



4p

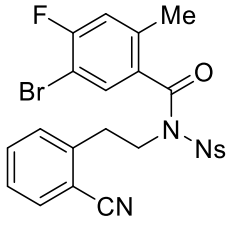
5-bromo-N-(2-cyanophenethyl)-2-fluoro-3-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 33.9 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.4 Hz, 2H), 8.14 (d, *J* = 8.4 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.40 (dd, *J* = 6.4, 1.2 Hz, 1H), 6.39 (dd, *J* = 5.2, 2.4 Hz, 1H), 4.25 (s, 2H), 3.27 (t, *J* = 6.4 Hz, 2H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 155.3 (d, $J_{C\text{-}F}$ = 246.7 Hz), 150.8, 143.8, 140.4, 137.2 (d, $J_{C\text{-}F}$ = 5.4 Hz), 133.3, 131.6, 130.1, 128.7 (d, $J_{C\text{-}F}$ = 2.5 Hz), 128.2, 128.0, 124.1, 123.2 (d, $J_{C\text{-}F}$ = 18.3 Hz), 117.1, 116.7 (d, $J_{C\text{-}F}$ = 3.4 Hz), 112.8, 48.1, 35.4, 14.3 (d, $J_{C\text{-}F}$ = 3.5 Hz) ; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}BrFN_3O_5SNa^+$ [M+Na$^+$] 567.9949, found 567.9949.



4q

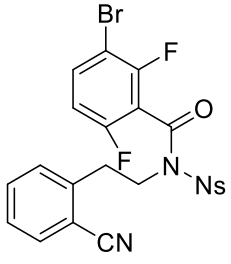
5-bromo-2-chloro-N-(2-cyanophenethyl)-3-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 43.0 mg, 76%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 8.9 Hz, 2H), 7.63 (t, *J* = 6.8 Hz, 2H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.48 – 7.40 (m, 2H), 6.36 (s, 1H), 4.13 (s, 2H), 3.29 (t, *J* = 6.7 Hz, 2H), 2.28 (s,

3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 151.0, 143.5, 140.4, 139.5, 135.7, 134.8, 133.5, 133.4, 131.5, 130.6, 129.0, 128.3, 128.2, 124.0, 120.6, 117.2, 113.0, 48.4, 35.4, 20.0. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br^{35}ClN_3O_5SNa^+$ [M+Na^+] 583.9653, found 583.9649.



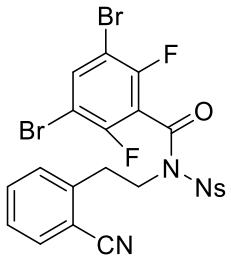
4r

5-bromo-N-(2-cyanophenethyl)-4-fluoro-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 35.6 mg, 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 9.2 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.60 (td, *J* = 7.6, 1.2 Hz, 1H), 7.44 – 7.39 (m, 2H), 6.97 (d, *J* = 9.2 Hz, 1H), 6.68 (d, *J* = 6.8 Hz, 1H), 4.19 (t, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 7.2 Hz, 2H), 2.11 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 159.9 (d, $J_{C\text{-}F}$ = 251.3 Hz), 150.8, 144.1, 140.5, 137.8 (d, $J_{C\text{-}F}$ = 7.8 Hz), 133.3 (d, $J_{C\text{-}F}$ = 1.4 Hz), 131.55, 131.5, 131.3 (d, $J_{C\text{-}F}$ = 3.8 Hz), 130.8, 129.9, 128.0, 124.3, 118.8 (d, $J_{C\text{-}F}$ = 22.5 Hz), 117.3, 112.9, 105.9 (d, $J_{C\text{-}F}$ = 21.6 Hz), 47.9, 34.9, 18.9; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}BrFN_3O_5SNa^+$ [M+Na^+] 567.9949, found 567.9948.



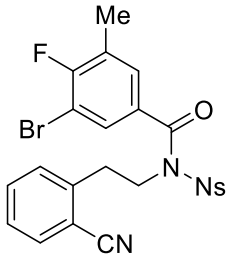
4s$_{mono}$

5-bromo-N-(2-cyanophenethyl)-2,5-difluoro-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 28.1 mg, 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.8 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.58 (m, 3H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 6.89 (t, *J* = 8.4 Hz, 1H), 4.23 (t, *J* = 7.2 Hz, 2H), 3.31 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 157.8 (dd, $J_{C\text{-}F}$ = 251.6, 5.7 Hz), 155.0 (dd, $J_{C\text{-}F}$ = 250.3, 7.2 Hz), 150.9, 143.5, 140.4, 135.82 (d, $J_{C\text{-}F}$ = 8.3 Hz), 133.3, 133.1, 131.1, 129.6, 128.0, 124.4, 117.5, 113.3 (dd, $J_{C\text{-}F}$ = 21.8, 3.9 Hz), 112.6, 104.5 (dd, $J_{C\text{-}F}$ = 20.9, 4.2 Hz), 47.7, 34.6; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{14}{}^{79}BrF_2N_3O_5SNa^+$ [M+Na^+] 571.9698, found 571.9699.



4s$_{(m, m')di}$

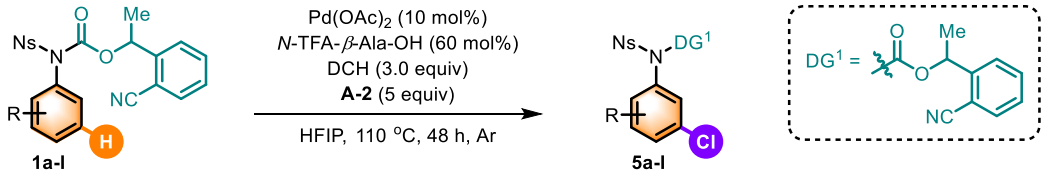
3,5-dibromo-N-(2-cyanophenethyl)-2,6-difluoro-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 6.8 mg, 11%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 8.8 Hz, 2H), 7.86 (td, J = 7.2, 0.8 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.46 (d, J = 7.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 4.23 (t, J = 7.6 Hz, 2H), 3.31 (t, J = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 154.2 (dd, J_{C-F} = 250.8, 6.0 Hz), 151.0, 143.2, 140.3, 138.0, 133.4, 133.1, 131.1, 129.5, 128.0, 124.6, 117.5, 112.7, 105.3 (dd, J_{C-F} = 22.7, 3.7 Hz), 47.7, 34.5; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{13}{}^{79}Br_2F_2N_3O_5SNa^+$ [M+Na$^+$] 649.8803, found 649.8805.



4t

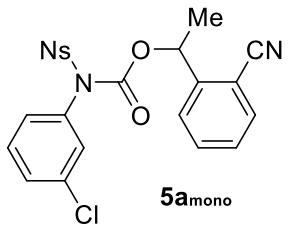
3-bromo-N-(2-cyanophenethyl)-4-fluoro-5-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions, Fomyl-Gly-OH as ligand on 0.1 mmol scale; 32.6 mg, 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.8 Hz, 2H), 8.14 (d, J = 8.8 Hz, 2H), 7.57 – 7.53 (m, 2H), 7.39 (t, J = 8.0 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.15 – 7.11 (m, 2H), 4.22 (t, J = 7.2 Hz, 2H), 3.20 (t, J = 7.2 Hz, 2H), 2.31(s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 159.9 (d, J_{C-F} = 252.1 Hz), 150.8, 143.9, 140.5, 133.2 (d, J_{C-F} = 5.1 Hz), 131.0, 130.4, 130.37, 130.32, 130.1, 127.9, 127.2 (d, J_{C-F} = 19.1 Hz), 124.3, 117.2, 112.8, 109.4 (d, J_{C-F} = 22.7 Hz), 48.2, 34.7, 15.0 (d, J_{C-F} = 3.0 Hz) ; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}BrFN_3O_5SNa^+$ [M+Na$^+$] 567.9949, found 567.9952.

General procedure for *meta*-chlorination of anilines



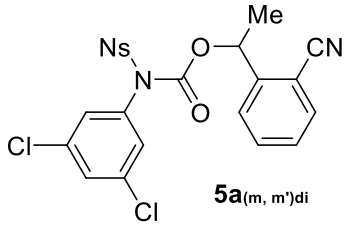
1 (0.10 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 10 mol%), *N*-TFA-*β*-Ala-OH (60 mol%), DCH (3 equiv) and **A-2** (0.5 mmol) were dissolved in HFIP (1.0 mL) in a 50 mL Schlenk sealed tube. The reaction tube was capped, then evacuated briefly under vacuum and charged with argon (1 atm, balloon, × 3). The reaction tube was

capped, then evacuated briefly under vacuum and charged with argaon (1 atm, balloon, × 3) The tube was then submerged into a preheated indicated oil bath at 110 °C to react for 48 h. The crude reaction mixture was diluted with EtOAc (10 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 20 mL of EtOAc. The filtrate was diluted in EtOAc and washed with saturated Na_2SO_3 and saturated NaCl aqueous solution. The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by preparative thin layer chromatography using DCM/Toluene as the eluent.



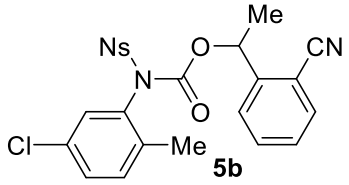
5amono

1-(2-cyanophenyl)ethyl(3-chlorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 28.8 mg, 59%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.18 (d, *J* = 8.9 Hz, 2H), 7.61-7.47 (m, 3H), 7.46-7.36 (m, 2H), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.23 – 8.14 (m, 2H), 7.61 – 7.47 (m, 3H), 7.46 – 7.36 (m, 2H), 7.28 (t, *J* = 1.9 Hz, 1H), 7.23 – 7.15 (m, 2H), 6.03 (q, *J* = 6.6 Hz, 1H), 1.53 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 150.6, 144.1, 143.5, 136.1, 135.2, 133.4, 133.3, 130.6, 130.5, 130.4, 129.9, 129.0, 128.0, 126.1, 124.3, 116.7, 110.6, 74.5, 21.3; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{16}{}^{35}ClN_3O_6SNa^+$ [M+Na^+] 508.0341, found 508.0345.



5a(m, m')di

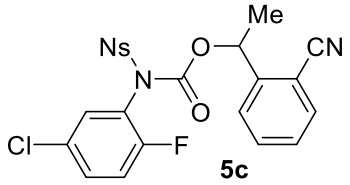
1-(2-cyanophenyl)ethyl(3,5-dichlorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 9.7 mg, 19%. ^{1}H NMR (600 MHz, $CDCl_3$) δ8.38 (d, *J* = 9.0 Hz, 2H), 8.17 (d, *J* = 9.0 Hz, 2H), 7.60 – 7.57 (m, 2H), 7.51 (t, *J* = 1.8 Hz, 1H), 7.41 (td, *J* = 7.8, 1.2 Hz, 1H), 7.23 – 7.19 (m, 3H), 6.03 (q, *J* = 6.6 Hz, 1H), 1.56 (d, *J* = 6.6 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.0, 150.2, 143.7, 143.1, 136.5, 135.7, 133.3, 133.3, 130.4, 129.0, 128.4, 126.1, 124.3, 116.6, 110.7, 74.7, 21.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{35}Cl_2N_3O_6SNa^+$ [M+Na^+] 541.9951, found 541.9950.



5b

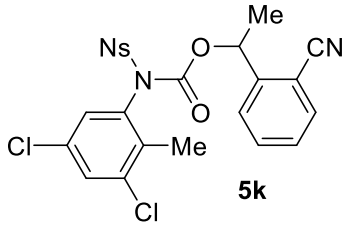
1-(2-cyanophenyl)ethyl(5-chloro-2-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions and HOAc as additive on 0.1 mmol scale; 32.7 mg, 65%. ^{1}H NMR (600

MHz, $CDCl_3$) two rotamers exist: δ 8.42 – 8.3.7 (m, 2H), 8.27 – 8.22 (m, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.53 (dtd, *J* = 18.0, 7.8, 1.2 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.33 – 7.30 (m, 1H), 7.15 – 7.11 (m, 1H), 7.09 (d, *J* = 7.8 Hz, 0.56H), 7.02 (d, *J* = 2.0 Hz, 0.51H), 6.07 – 6.01 (m, 1H), 2.33 (s, 1.72H), 2.24 (s, 1.28H), 1.52 (dd, *J* = 39.6, 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.9, 150.9, 150.4, 150.3, 144.1, 144.0, 143.6, 143.5, 137.3, 137.1, 135.3, 133.3, 133.2, 133.1, 132.5, 132.3, 132.2, 132.0, 130.8, 130.6, 130.4, 130.3, 129.0, 128.9, 128.8, 128.8, 126.0, 125.7, 124.2, 116.5, 116.5, 110.6, 110.4, 74.3, 74.2, 21.5, 21.3, 17.9, 17.8; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}{}^{35}ClN_3O_6SNa^+$ [M+Na^+] 522.0497, found 522.0495.



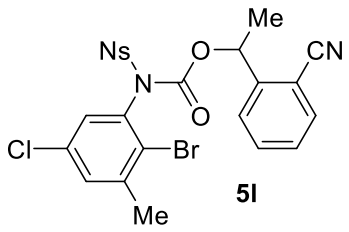
5c

1-(2-cyanophenyl)ethyl(5-chloro-2-fluorophenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions and *N*-TFA-Gly-OH as ligand on 0.1 mmol scale; 22.2 mg, 44%. ^1H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.4 Hz, 2H), 8.22 (d, *J* = 9.0 Hz, 2H), 7.60 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.54 (td, *J* = 7.8, 1.2 Hz, 1H), 7.49 – 7.47 (m, 1H), 7.45 (dd, *J* = 6.6, 3.0 Hz, 1H), 7.40 (td, *J* = 7.8, 1.2 Hz, 1H), 7.21 – 7.18 (m, 2H), 6.01 (q, *J* = 6.6 Hz, 1H), 1.51 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.3 (d, $J_{C\text{-}F}$ = 250.1 Hz), 151.0, 149.9, 143.7, 143.4, 133.4, 132.1, 132.0 (d, $J_{C\text{-}F}$ = 5.4 Hz), 130.7, 130.0 (d, $J_{C\text{-}F}$ = 3.5 Hz), 128.9, 126.0, 124.1, 123.7 (d, $J_{C\text{-}F}$ = 15.2 Hz), 117.7 (d, $J_{C\text{-}F}$ = 21.2 Hz), 116.6, 110.5, 74.9, 21.4; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{35}ClFN_3O_6SNa^+$ [M+Na^+] 526.0246, found 526.0246.



5k

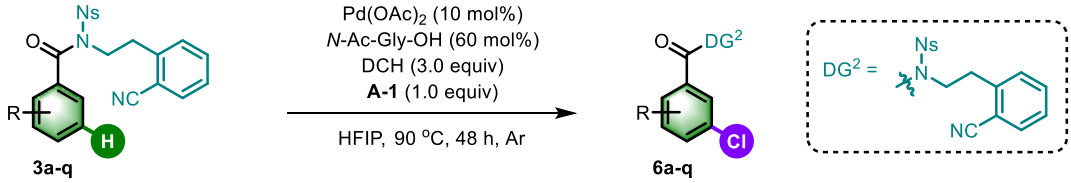
1-(2-cyanophenyl)ethyl(3,5-dichloro-2-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 31.4 mg, 59%. ^1H NMR (600 MHz, $CDCl_3$) two rotamers exist: δ 8.40 (dd, *J* = 20.4, 9.0 Hz, 2H), 8.23 (dd, *J* = 20.4, 9.0 Hz, 2H), 7.61 – 7.52 (m, 3H), 7.41 (dtd, *J* = 21.6, 7.2, 0.6 Hz, 1H), 7.16 (dd, *J* = 7.8, 2.4 Hz, 1H), 7.09 (d, *J* = 2.0 Hz, 0.46H), 6.99 (d, *J* = 2.1 Hz, 0.54H), 6.07 – 6.02 (m, 1H), 2.33 (s, 4H), 2.21 (s, 1.68H), 1.54 (m, 1.33H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.0, 151.0, 150.1, 150.1, 143.7, 143.7, 143.2, 143.2, 136.7, 136.6, 136.2, 136.0, 136.0, 135.9, 133.3, 133.3, 133.3, 132.2, 132.0, 130.9, 130.9, 130.7, 129.0, 128.9, 127.9, 127.7, 126.0, 125.9, 124.2, 116.5, 116.4, 110.7, 110.6, 74.6, 74.5, 21.2, 21.2, 15.8, 15.7; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{35}Cl_2N_3O_6SNa^+$ [M+Na^+] 556.0107, found 556.0107.



5l

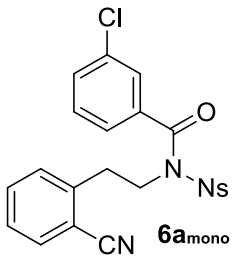
1-(2-cyanophenyl)ethyl(2-bromo-5-chloro-3-methylphenyl)((4-nitrophenyl)sulfonyl)carbamate: The corresponding reaction was run with standard conditions and *N*-Tf-β-Ala-OH as ligand on 0.1 mmol scale; 38.5 mg, 66%. ^{1}H NMR (600 MHz, CDCl3) two rotamers exist: δ 8.38 (dd, *J* = 14.4, 9.0 Hz, 2H), 8.23 (dd, *J* = 13.8, 8.4 Hz, 2H), 7.60 (td, *J* = 7.2, 0.6 Hz, 1H), 7.52 (dtd, *J* = 13.2, 7.7, 1.2 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.32 (d, *J* = 2.4 Hz, 0.46H), 7.28 (d, *J* = 2.4 Hz, 0.48H), 7.21 (d, *J* = 7.8 Hz, 0.47H), 7.13 (d, *J* = 7.8 Hz, 0.60H), 6.06 – 6.01 (m, 1H), 2.48 (s, 1.68H), 2.42 (s, 1.32H), 1.53 (dd, *J* = 10.8, 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.1, 151.0, 149.9, 149.8, 144.0, 143.9, 143.6, 143.5, 141.8, 141.7, 135.6, 135.5, 133.4, 133.4, 133.3, 133.3, 133.3, 133.2, 132.2, 131.3, 131.3, 129.3, 129.2, 128.9, 126.5, 126.1, 125.3, 124.0, 116.6, 110.5, 110.4, 74.9, 74.7, 23.9, 23.8, 21.8, 21.5; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{79}Br^{35}ClN_3O_6SNa^+$ [M+Na$^+$] 599.9602, found 599.9597.

General procedure for *meta*-chlorination of benzoic acids



3a-q **6a-q**

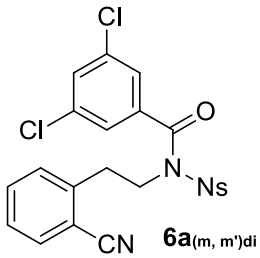
3 (0.10 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 10 mol%), *N*-Ac-Gly-OH (60 mol%), DCH (3 equiv) and **A-1** (0.1 mmol) were dissolved in HFIP (1.0 mL) in a 50 mL Schlenk sealed tube. The reaction tube was capped, then evacuated briefly under vacuum and charged with argon (1 atm, balloon, × 3). The tube was then submerged into a preheated indicated oil bath at 90 °C to react for 48 h. The crude reaction mixture was diluted with EtOAc (10 mL) and filtered through a short pad of Celite. The sealed tube and Celite pad were washed with an additional 20 mL of EtOAc. The filtrate was diluted in EtOAc and washed with saturated Na_2SO_3 and saturated NaCl aqueous solution. The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by preparative thin layer chromatography using DCM/Toluene as the eluent.



6amono

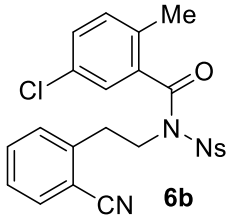
3-chloro-N-(2-cyanophenethyl)-N-(4-

nitrophenylsulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 29.5 mg, 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.9 Hz, 2H), 8.16 (d, *J* = 8.9 Hz, 2H), 7.59 - 7.51 (m, 2H), 7.50 - 7.44 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.36 - 7.28 (m, 2H), 7.17 (d, *J* = 7.7 Hz, 1H), 6.99 (t, *J* = 1.6 Hz, 1H), 4.25 (t, *J* = 6.9 Hz, 2H), 3.21 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 150.9, 144.1, 140.6, 135.2, 134.9, 133.3, 133.3, 132.3, 131.1, 130.3, 130.0, 128.1, 127.9, 125.7, 124.4, 117.3, 112.9, 48.4, 35.0; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{17}{}^{35}ClN_3O_5S^+$ [M+H$^+$] 470.0572, found 470.0580.



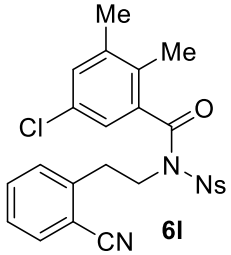
6a(m, m')di

3,5-dichloro-N-(2-cyanophenethyl)-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 4.7 mg, 9%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.39 (d, *J* = 9.0 Hz, 2H), 8.13 (d, *J* = 9.0 Hz, 2H), 7.59 – 7.56 (m, 2H), 7.47 (t, *J* = 1.8 Hz, 1H), 7.41 (td, *J* = 7.8, 1.2 Hz, 1H), 7.34 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.95 (d, *J* = 1.8 Hz, 2H), 4.24 (t, *J* = 6.6 Hz, 2H), 3.23 (t, *J* = 6.6 Hz, 2H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 151.0, 143.8, 140.4, 136.4, 135.6, 133.3, 133.3, 132.1, 131.2, 130.2, 128.1, 126.0, 124.5, 117.3, 113.0, 48.2, 34.9; HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{15}{}^{35}Cl_2N_3O_5SNa^+$ [M+Na$^+$] 526.0002, found 526.0000.



6b

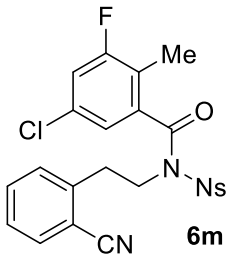
5-chloro-N-(2-cyanophenethyl)-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 35.0 mg, 72%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (d, *J* = 9.0 Hz, 2H), 8.07 (d, *J* = 9.0 Hz, 2H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.59 (td, *J* = 8.4, 2.4 Hz, 1H), 7.42 (td, *J* = 7.8, 1.2 Hz, 1H), 7.39 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.29 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 6.40 (d, *J* = 2.4 Hz, 1H), 4.17 (s, 2H), 3.27 (t, *J* = 7.2 Hz, 2H), 2.05 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.3, 150.9, 144.2, 140.6, 135.1, 133.5, 133.4, 133.3, 132.2, 131.6, 131.0, 130.8, 130.2, 128.1, 126.3, 124.2, 117.4, 113.0, 48.0, 35.1, 18.5; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{18}{}^{35}ClN_3O_5SNa^+$ [M+Na$^+$] 506.0548, found 506.0548.



6l

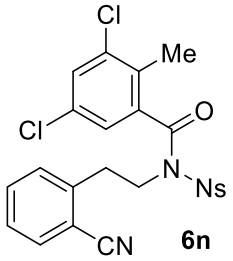
5-chloro-N-(2-cyanophenethyl)-2,3-dimethyl-N-((4-

nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 43.7 mg, 88%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (d, *J* = 9.0 Hz, 2H), 8.06 (d, *J* = 9.0 Hz, 2H), 7.61 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.58 (td, *J* = 7.8, 1.2 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.18 (d, *J* = 1.2 Hz, 1H), 6.29 (d, *J* = 2.4 Hz, 1H), 4.14 (s, 2H), 3.26 (t, *J* = 7.2 Hz, 2H), 2.21 (s, 3H), 1.93 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.8, 150.8, 144.3, 140.7, 140.3, 135.4, 133.3, 133.3, 131.9, 131.8, 131.2, 130.9, 130.2, 128.0, 124.2, 123.7, 117.4, 113.0, 48.1, 35.1, 20.0, 15.9; HRMS (m/z, ESI-TOF): Calcd for $C_{24}H_{20}{}^{35}ClN_3O_5SNa^+$ [M+Na$^+$] 520.0704, found 520.0704.



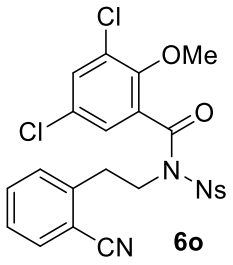
6m

5-chloro-N-(2-cyanophenethyl)-3-fluoro-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 26.2 mg, 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.9 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 8.2 Hz, 2H), 7.12 (dd, *J* = 8.9, 2.0 Hz, 1H), 6.31 (s, 1H), 4.15 (d, *J* = 7.6 Hz, 2H), 3.28 (t, *J* = 7.2 Hz, 2H), 1.98 (d, *J* = 2.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (d, $J_{C\text{-}F}$ = 3.7 Hz), 160.9 (d, $J_{C\text{-}F}$ = 251.7 Hz), 151.0, 144.1, 140.5, 136.8 (d, $J_{C\text{-}F}$ = 5.2 Hz), 133.37 (d, $J_{C\text{-}F}$ = 2.6 Hz), 132.4 (d, $J_{C\text{-}F}$ = 10.7 Hz), 131.0, 130.1, 128.2, 124.4, 122.1 (d, $J_{C\text{-}F}$ = 3.9 Hz), 121.8, 121.6, 118.2 (d, $J_{C\text{-}F}$ = 26.1 Hz), 117.4, 113.0, 48.0, 35.1, 11.2 (d, $J_{C\text{-}F}$ = 4.1 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{35}ClFN_3O_5SNa^+$ [M+Na$^+$] 524.0454, found 524.0453.



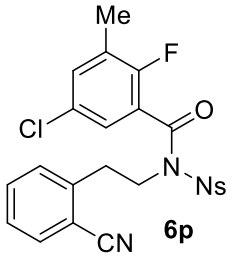
6n

3,5-dichloro-N-(2-cyanophenethyl)-2-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 26.7 mg, 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.6 Hz, 2H), 8.03 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.45 – 7.37 (m, 3H), 6.43 (d, *J* = 2.1 Hz, 1H), 4.16 (s, 2H), 3.29 (t, *J* = 7.2 Hz, 2H), 2.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 151.0, 144.0, 140.6, 136.6, 136.5, 133.4, 133.4, 132.2, 132.0, 131.1, 130.9, 130.1, 128.2, 124.8, 124.4, 117.4, 113.1, 48.0, 35.0, 16.6. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{35}Cl_2N_3O_5SNa^+$ [M+Na$^+$] 540.0158, found 540.0155.



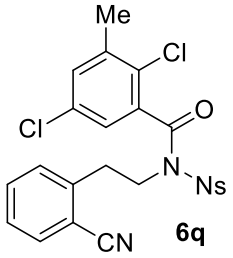
6o

3,5-dichloro-N-(2-cyanophenethyl)-2-methoxy-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 27.4 mg, 51%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, *J* = 9.0 Hz, 2H), 8.15 (d, *J* = 9.0 Hz, 2H), 7.62 – 7.60 (m, 2H), 7.45 – 7.42 (m, 3H), 6.47 (d, *J* = 2.4 Hz, 1H), 4.14 (s, 2H), 3.50 (s, 3H), 3.25 (t, *J* = 7.2 Hz, 2H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ166.4, 150.9, 150.7, 143.9, 140.6, 133.3, 133.3, 132.7, 131.2, 131.1, 130.2, 130.2, 129.1, 128.0, 126.2, 124.1, 117.3, 113.1, 62.3, 48.1, 35.2; HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{35}Cl_2N_3O_6SNa^+$ [M+Na^+] 556.0107, found 556.0107.



6p

5-chloro-N-(2-cyanophenethyl)-2-fluoro-3-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 21.2 mg, 42%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 9.0 Hz, 2H), 8.14 (d, *J* = 9.0 Hz, 2H), 7.62 (td, *J* = 7.8, 1.2 Hz, 1H), 7.55 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.43 (td, *J* = 7.8, 1.2 Hz, 1H), 7.24 (ddd, *J* = 6.0, 2.4, 0.6 Hz, 1H), 6.25 (dd, *J* = 5.4, 2.4 Hz, 1H), 4.24 (s, 2H), 3.26 (t, *J* = 6.0 Hz, 2H), 2.21 (d, *J* = 1.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.3, 154.8 (d, $J_{C\text{-}F}$ = 246.3 Hz), 150.9, 143.9, 140.5, 134.3 (d, $J_{C\text{-}F}$ = 5.4 Hz), 133.3 (d, $J_{C\text{-}F}$ = 9.5 Hz), 131.6, 130.2, 129.5 (d, $J_{C\text{-}F}$ = 3.5 Hz), 128.0, 127.8 (d, $J_{C\text{-}F}$ = 18.6 Hz), 125.9, 125.86, 124.2, 122.9(d, $J_{C\text{-}F}$ = 18.5 Hz), 117.2, 112.9, 48.1, 35.5, 14.5 (d, $J_{C\text{-}F}$ = 3.5 Hz); HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{35}ClFN_3O_5SNa^+$ [M+Na^+] 524.0454, found 524.0454.



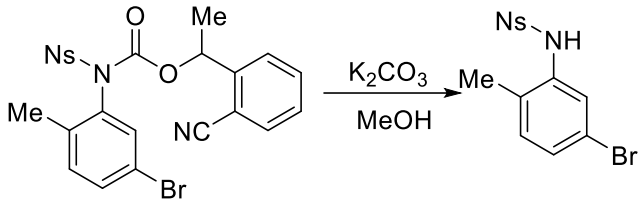
6q

2,5-dichloro-N-(2-cyanophenethyl)-3-methyl-N-((4-nitrophenyl)sulfonyl)benzamide: The corresponding reaction was run with standard conditions on 0.1 mmol scale; 25.1 mg, 48%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.6 Hz, 2H), 8.18 (d, *J* = 8.7 Hz, 2H), 7.69 – 7.58 (m, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.28 (s, 1H), 6.23 (d, *J* = 2.5 Hz, 1H), 4.14 (s, 2H), 3.30 (t, *J* = 6.7 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 151.0, 143.6, 140.5, 139.2, 134.5, 133.4, 133.4, 132.9, 132.8, 131.5, 130.6, 128.3, 128.2, 125.6, 124.0, 117.2,

113.1, 48.4, 35.4, 20.1. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{17}{}^{35}Cl_2N_3O_5SNa^+$ [M+Na^+] 540.0158, found 540.0156.

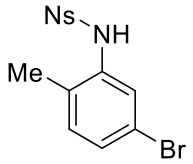
2.4 Removal of the directing group and diversification of *meta*-brominated aniline

Removal of the directing group



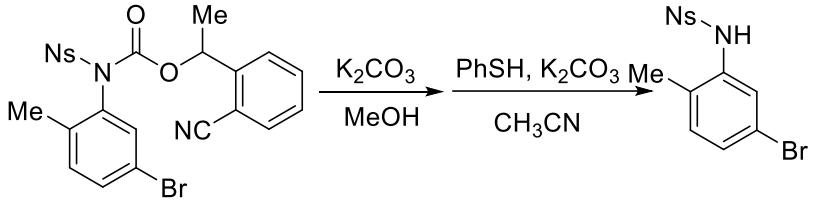
2b **7b**

To a solution of **2b** (54.4 mg,0.1 mmol) in MeOH (1 mL) was added K_2CO_3 (41 mg, 0.3 mmol, 3.0 equiv) at 50 ºC. After stirring for 24 h, solvent was removed under reduced pressure and 1N HCl (5 mL) was added. The aqueous phase was extracted with EtOAc (5 mL × 3). The combined organic layer was dried over Na_2SO_4. After removal of the solvent, the residue was purified by flash silica gel chromatography to give **7b** (29.3 mg, 79%) as white solid.



7b

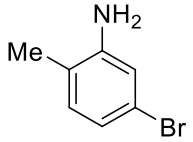
N-(5-bromo-2-methylphenyl)-4-nitrobenzenesulfonamide: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 – 8.30 (m, 2H), 7.94 – 7.92 (m, 2H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.25 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.99 (d, *J* = 7.8, 1H), 6.52 (s, 1H), 1.94 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.5, 145.0, 134.7, 132.4, 130.4, 130.2, 128.5, 127.4, 124.5, 120.2, 17.4; HRMS (m/z, ESI-TOF): Calcd for $C_{13}H_{11}{}^{79}BrN_2O_4S$ [M-H^+] 368.9550, found 368.9549.



2b **8b**

To a solution of **2b** (54.4 mg, 0.1 mmol) in MeOH (1 mL) was added K_2CO_3 (41 mg, 0.3 mmol, 3.0 equiv) at 50 ºC. After stirring for 24 h, solvent was removed under reduced pressure. The residue was added DMSO (100 μL), PhSH (72 μL, 0.65 mmol, 6.5 equiv) and K_2CO_3 (55.3 mg, 0.4 mmol, 4.0 equiv) in acetonitrile (2 mL)**.** The mixture was then heated at 100 ℃ for 24h. When finished, the reaction was quenched

and diluted with sat. NH_4Cl, and extracted with EtOAc (3 x 5 mL); the organic phase was dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash chromatography with petroleum ether/EtOAc (10:1) to give **8b** (14.9 mg, 80%)*(S5)*.

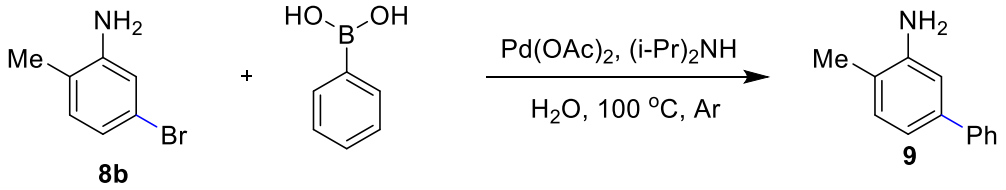


8b

5-bromo-2-methylaniline*(S6)* ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.89 (d, *J* = 7.8 Hz, 1H), 6.81 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.79 (d, *J* = 2.4 Hz, 1H), 3.63 (brs, 2H), 2.09 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.1, 131.8, 121.3, 121.2, 120.1, 117.4, 17.0.

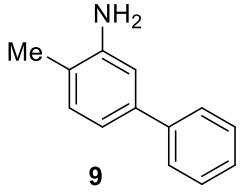
Diversification of *meta*-Brominated aniline

Arylation*(S7)*



8b **9**

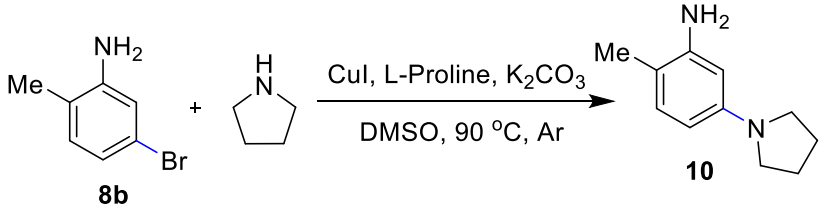
A mixture of **8b** (37.2 mg, 0.2 mmol, 1.0 equiv), arylboronic acid (36.6 mg, 0.3 mmol, 1.5 equiv), (i-Pr)$_2$NH (56 µL, 0.3 mmol, 2.0 equiv), $Pd(OAc)_2$ (1.0 mg, 0.004 mmol, 2 mol%), H_2O (0.5 mL) was stirred at 100 °C for 4h. The reaction mixture was added to brine (10 mL) and extracted with ethyl acetate (3 × 10 mL). The solvent was concentrated under vacuum and purified by flash silica gel chromatography to yield **9** (34.7 mg, 95%).



9

4-methyl-[1,1'-biphenyl]-3-amine*(S8)* ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 – 7.57 (m, 2H), 7.44 – 7.42 (m, 2H), 7.35 – 7.32 (m, 1H), 7.14 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.98 – 6.97 (m, 1H), 6.92 (s, 1H), 3.49 (brs, 2H), 2.22 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.9, 141.5, 140.3, 131.0, 128.8, 127.1, 121.7, 117.7, 113.8, 17.2.

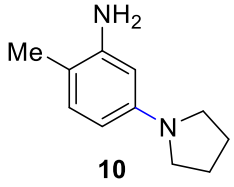
Amination*(S9)*



8b **10**

A mixture of **8b** (279.1 mg, 1.5 mmol, 1.0 equiv), tetrahydropyrrole (184 µL, 2.25 mmol, 1.5 equiv), K_2CO_3 (414.6 mg, 3 mmol, 2.0 equiv), CuI (28.6 mg, 0.15 mmol, 10

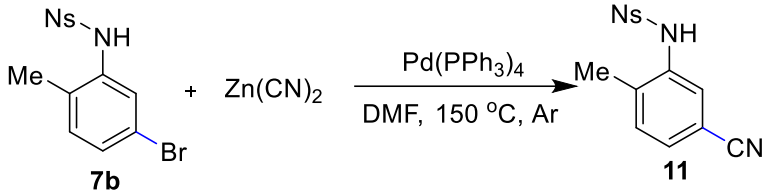
mol%), L-proline (34.5 mg, 0.3 mmol, 20 mol%) in 1 mL of DMSO was heated at 90 ℃ for 29 h. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuum. The residual oil was loaded on a silica gel column and eluted with 1/10 ethyl acetate/petroleum ether to afford **10** (193.0 mg, 73%).



10

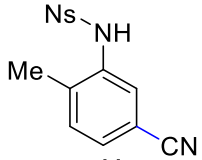
2-methyl-5-(pyrrolidin-1-yl)aniline: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.97 (d, *J* = 8.4 Hz, 1H), 6.08 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.02 (d, *J* = 2.4 Hz, 1H), 3.58 (brs, 2H), 3.31 – 3.29 (m, 4H), 2.16 (s, 3H), 2.05 – 2.03 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.9, 145.3, 131.1, 110.1, 103.1, 98.9, 47.9, 25.5, 16.5; HRMS (m/z, ESI-TOF): Calcd for $C_{11}H_{17}N_{29}^+$ [M+H$^+$] 177.1386, found 177.1387.

Cyanation*(S10)*



7b **11**

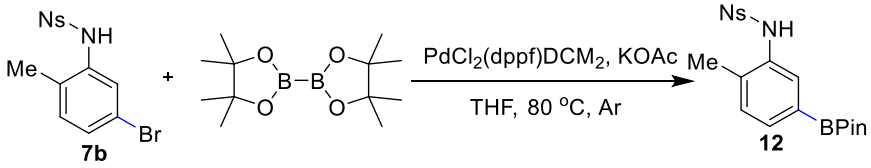
To a mixture of **7b** (37.1 mg, 0.1 mmol, 1.0 equiv), $Zn(CN)_2$ (23.5 mg, 0.2 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol, 10 mol%) in DMF (1 mL) was stirred at 150 °C for 24 h. After The reaction was cooled to room temperature when completed, and it was diluted with EtOAc, washed with H_2O and saturated NaCl aqueous solution. The combined organic layers was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by flash silica gel chromatography to yield **11** (21.2 mg, 67%).



11

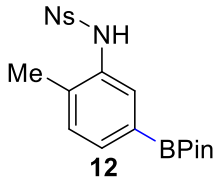
N-(5-cyano-2-methylphenyl)-4-nitrobenzenesulfonamide: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.2 Hz, 2H), 7.97 (d, *J* = 7.2 Hz, 2H), 7.65 (d, *J* = 1.2 Hz, 1H), 7.42 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.26 (d, *J* = 7.8 Hz, 1H), 6.95 (s, 1H), 2.12 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.6, 145.0, 137.2, 134.7, 132.2, 130.4, 128.5, 127.4, 124.7, 118.0, 111.4, 18.3; HRMS (m/z, ESI-TOF): Calcd for $C_{14}H_{11}N_3O_4SNa^+$ [M+Na$^+$] 340.0362, found 340.0369.

Borylation*(S11)*



7b **12**

A mixture of **7b** (37.1 mg, 0.1 mmol, 1.0 equiv), B_2Pin_2 (30.5 mg, 0.12 mmol, 1.2 equiv) and KOAc (29.4 mg, 0.3 mmol, 3.0 equiv) in THF (6 mL) was purged with Ar. $PdCl_2$(dppf)-DCM (8.1 mg, 0.01 mmol, 10 mol%) was added. The mixture was purged for another 5 minutes then was heated in 80 °C under nitrogen for 24 hours. The mixture was allowed to cool to room temperature and was filtered through celite washed with EtOAc. The solvents were removed under reduced pressure and the residue was purified by silica gel chromatography to yield **12** (32.2 mg, 77%).



12

N-(2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-4-nitrobenzenesulfonamide: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 – 8.26 (m, 2H), 7.89 – 7.87 (m, 2H), 7.57 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.39 (s, 1H), 7.16 (d, *J* = 7.2, 1H), 6.51 (s, 1H), 2.10 (s, 3H), 1.29 (s, 12H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.3, 145.3, 137.4, 134.1, 132.9, 132.6, 130.9, 128.8, 124.3, 84.1, 24.9, 18.2; HRMS (m/z, ESI-TOF): Calcd for $C_{19}H_{23}BN_2O_6SNa^+$ [M+Na^+] 441.1262 found 441.1269.

2.5 References

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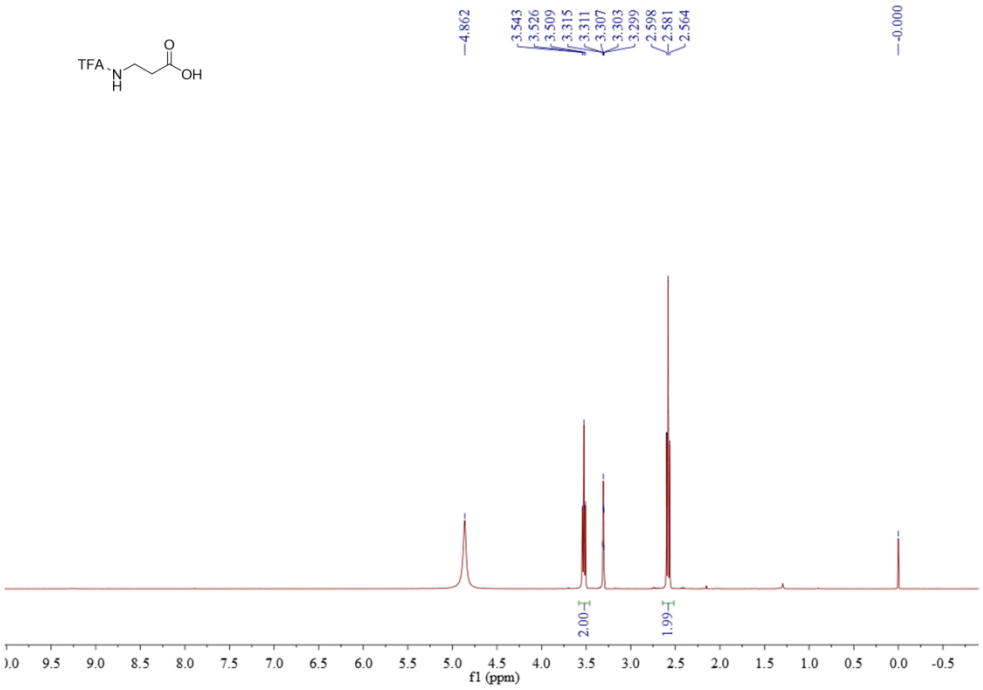
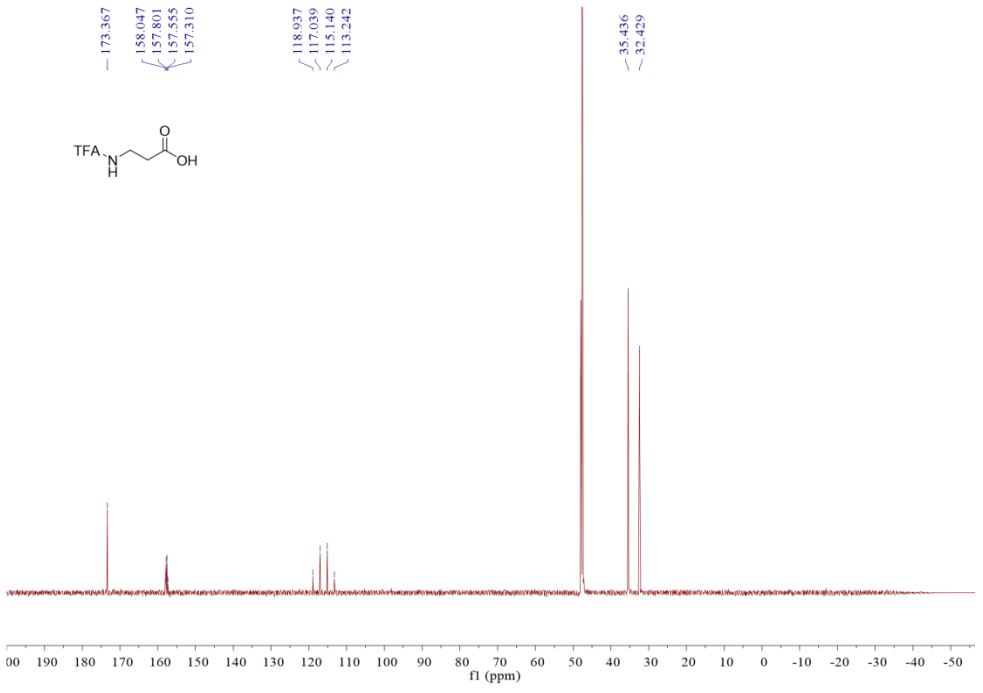
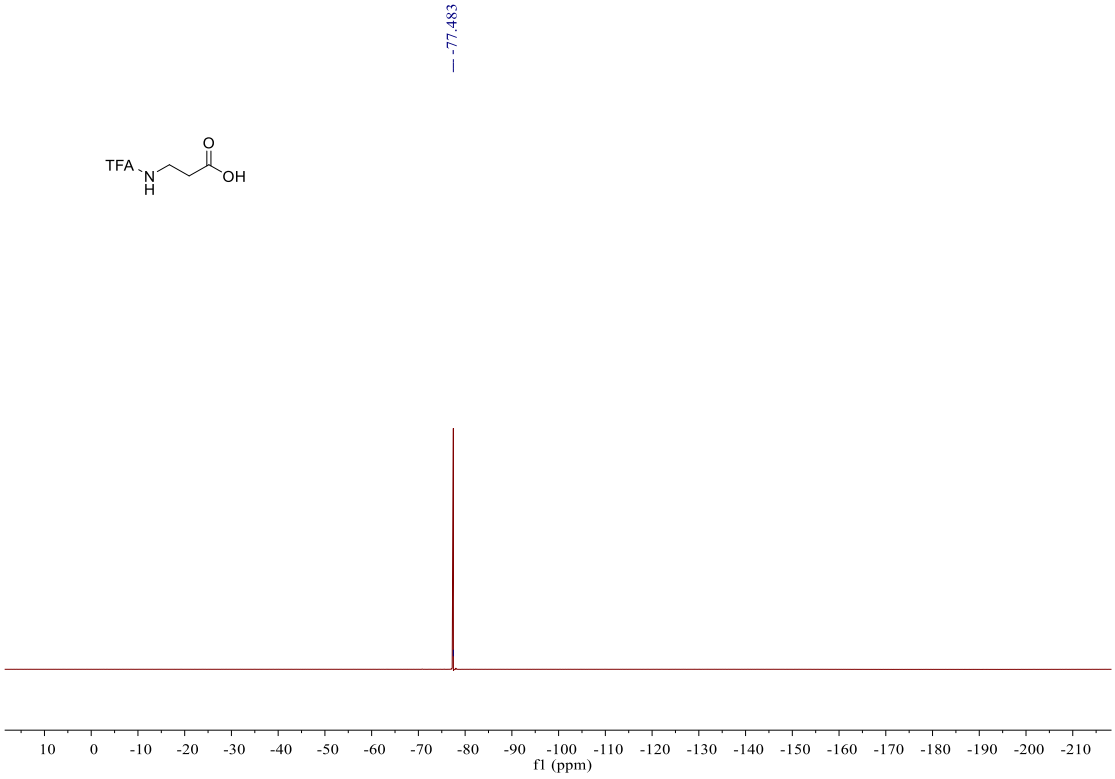
3. NMR Spectra of Compounds





^{1}H, and ^{13}C NMR spectra for *N*-TFA-β-Ala-OH



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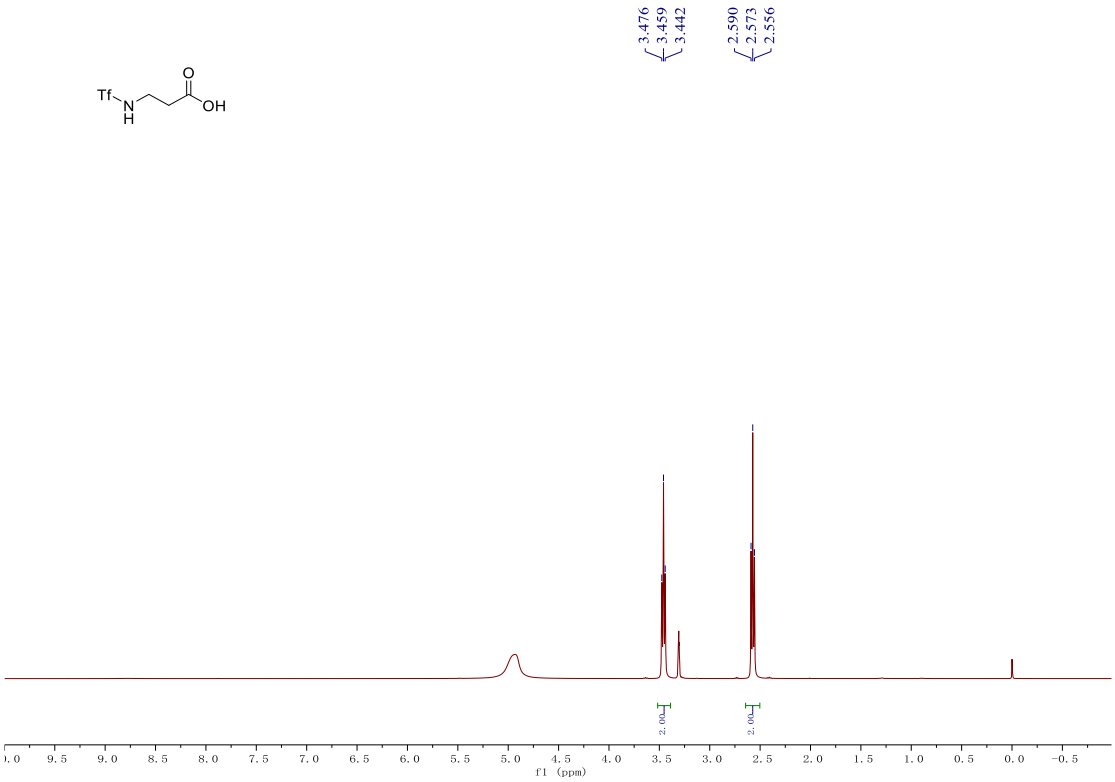

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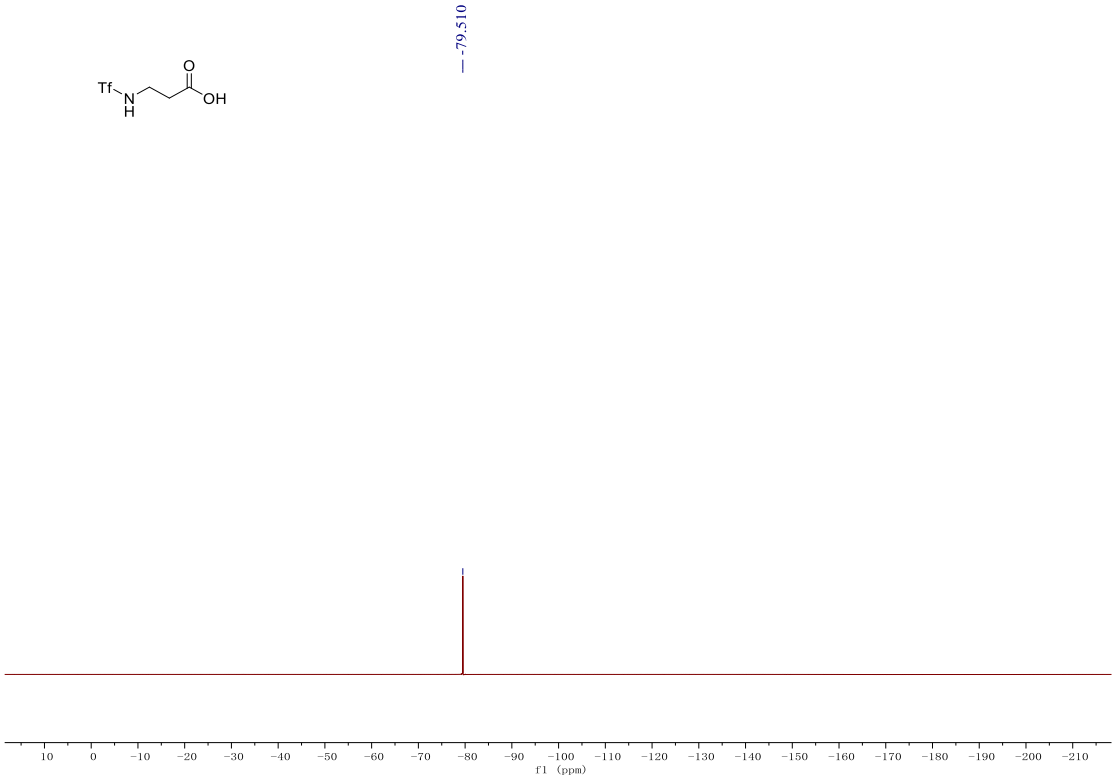

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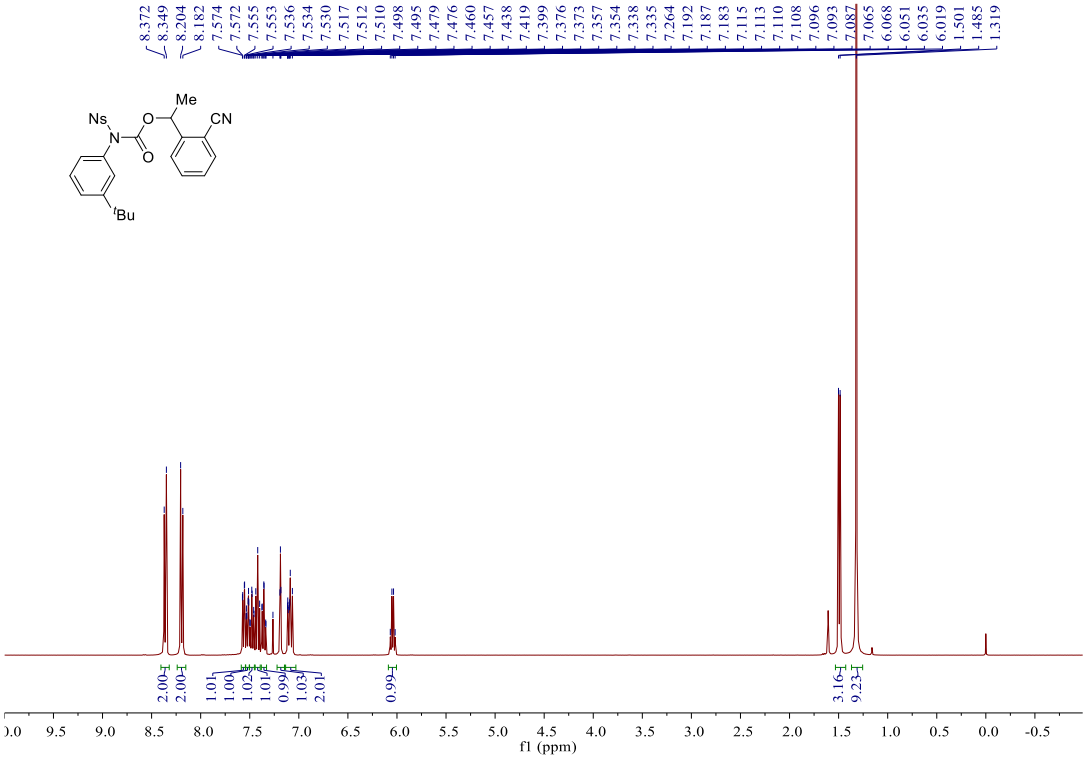
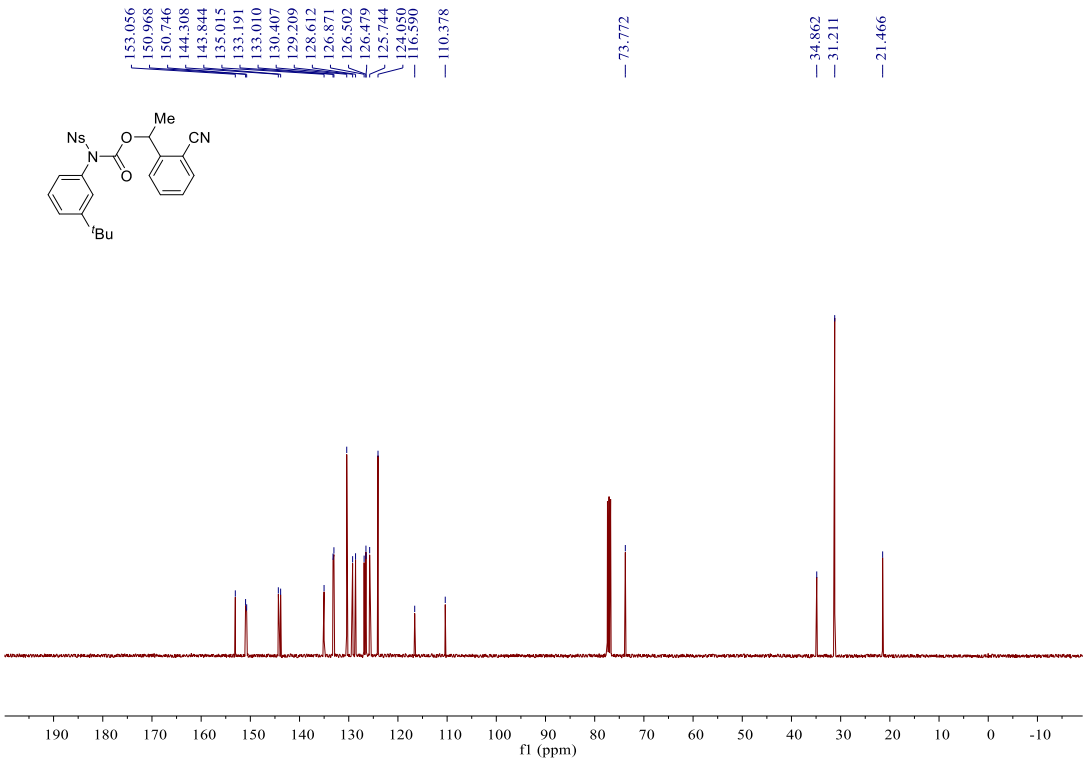
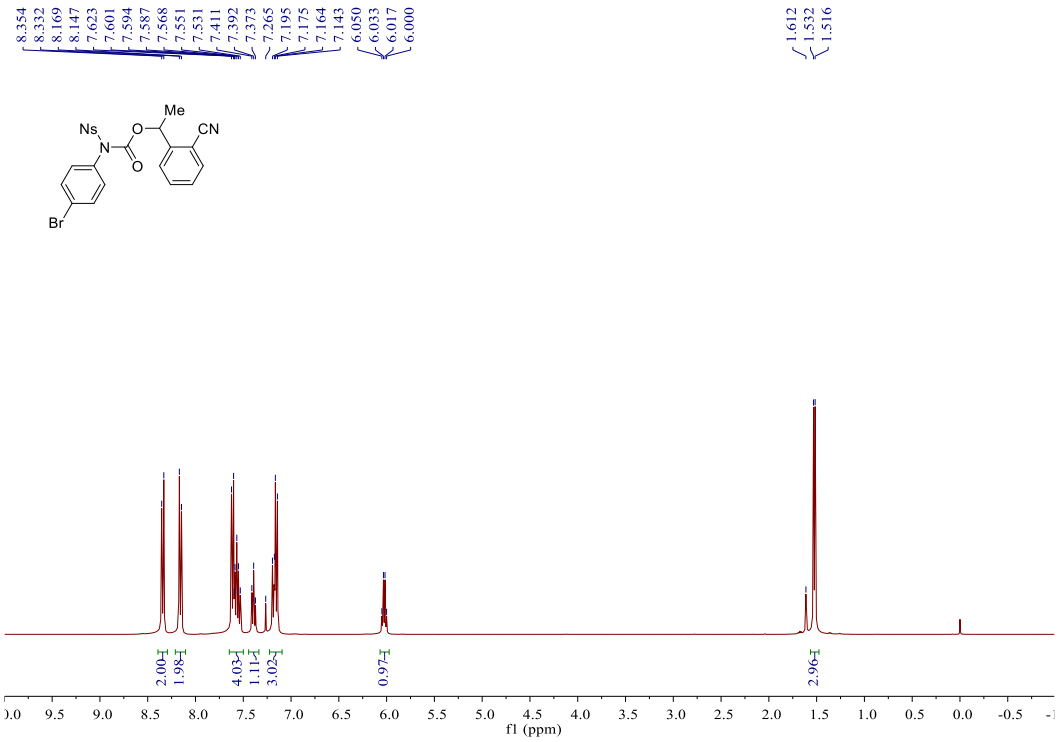
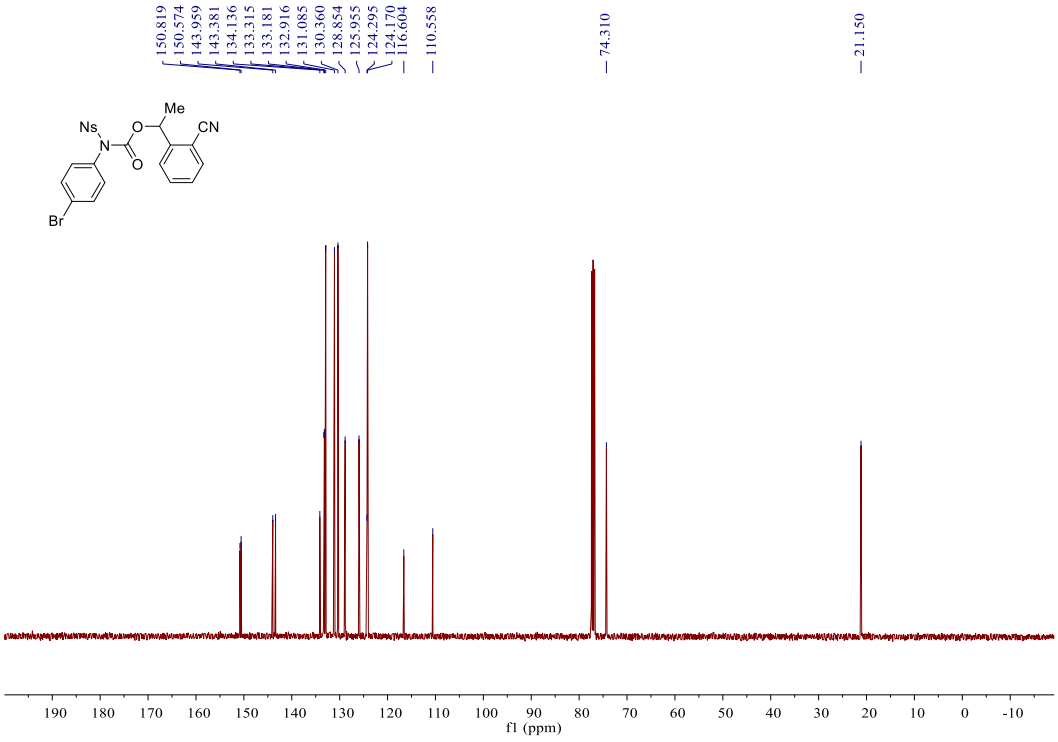


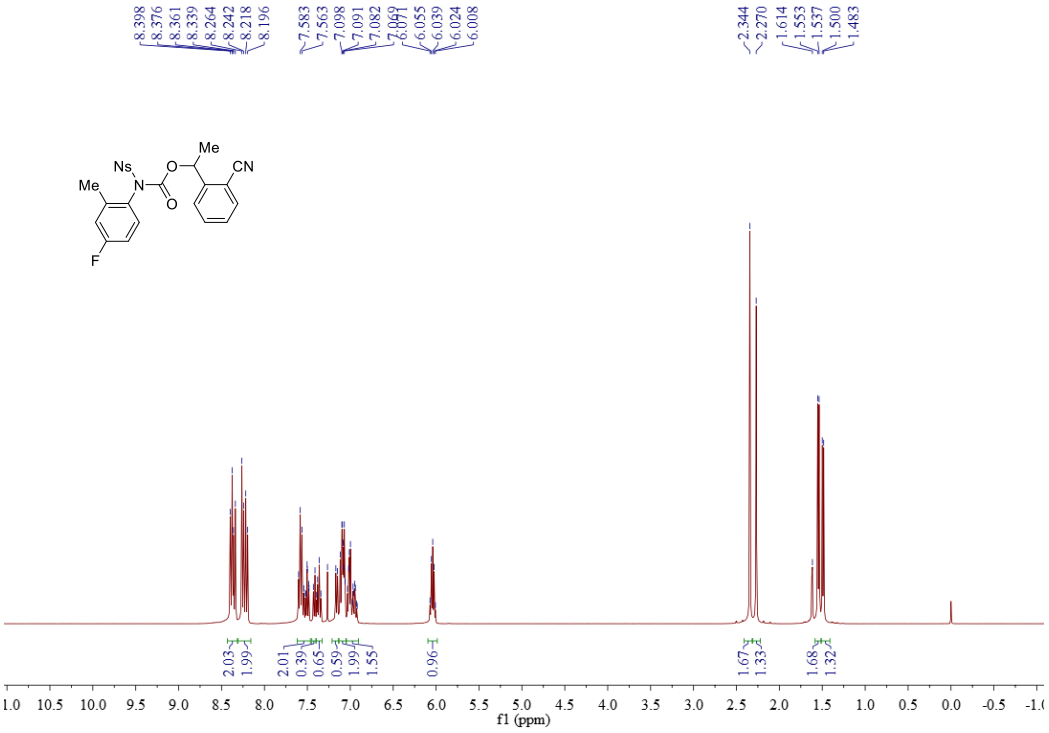


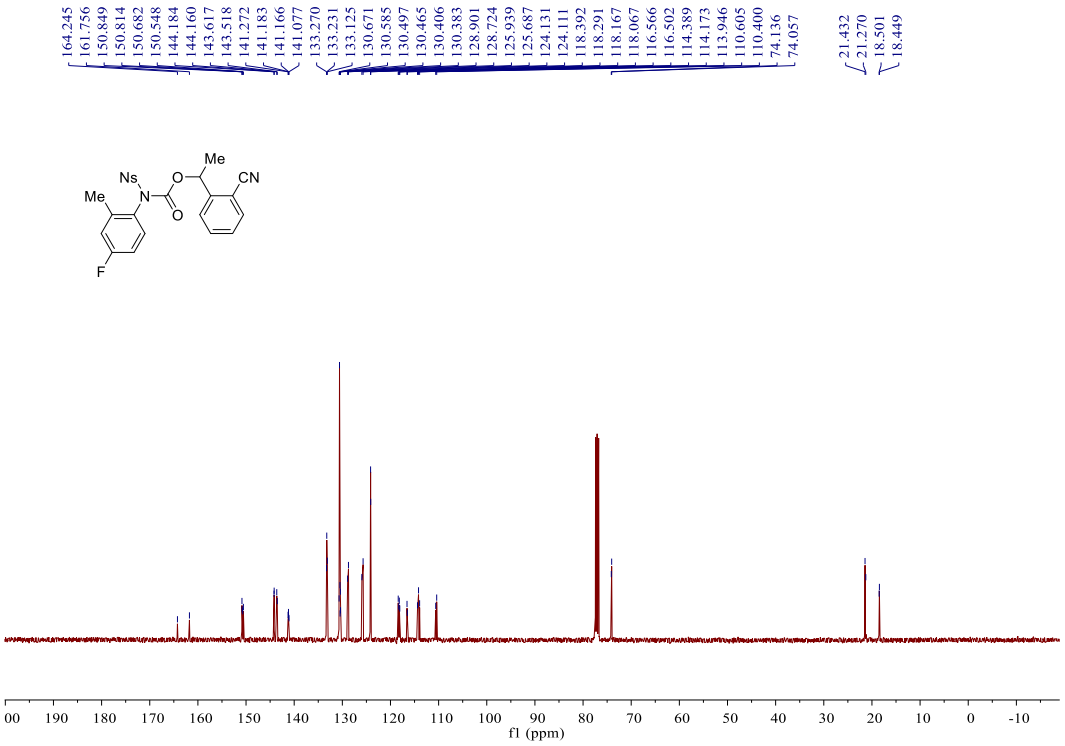
^{1}H and ^{13}C NMR spectra for **1e**





^{1}H and ^{13}C NMR spectra for **1j**





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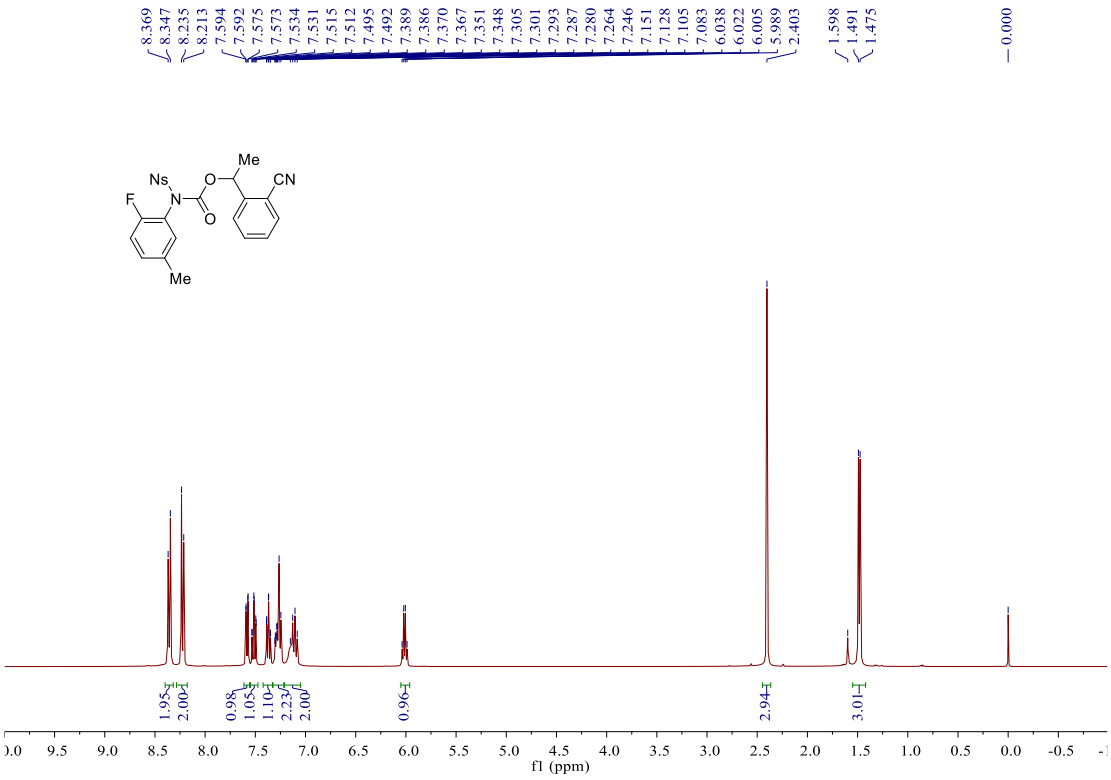

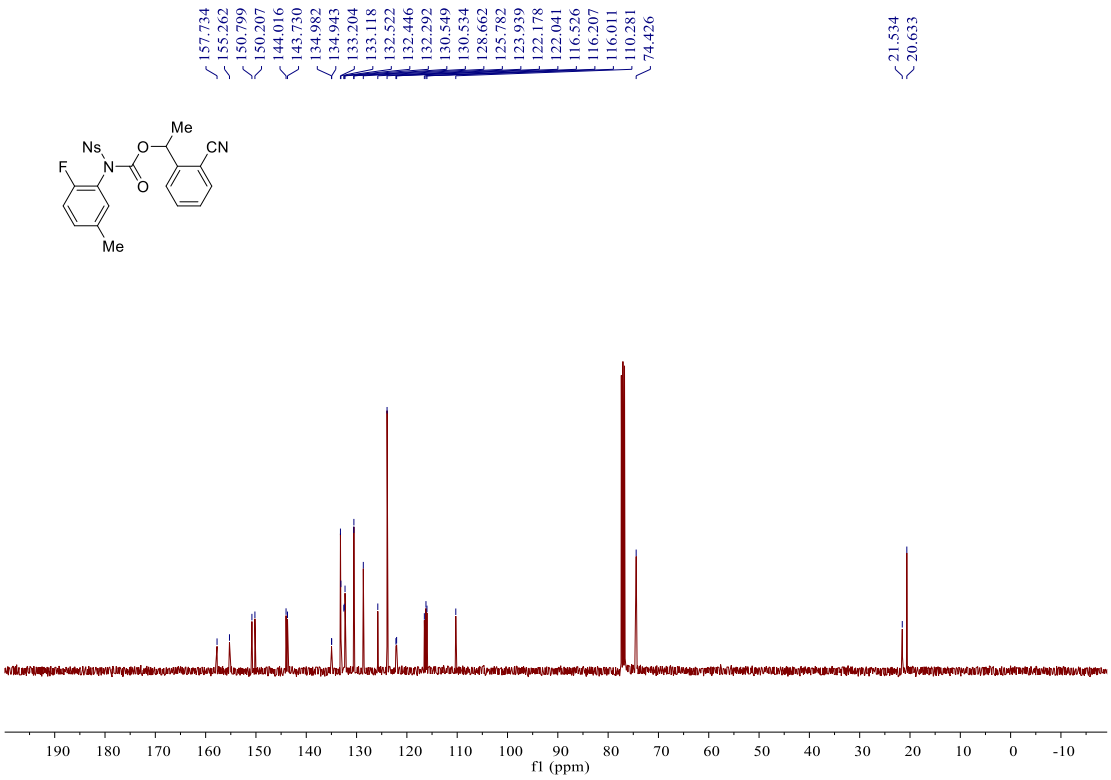

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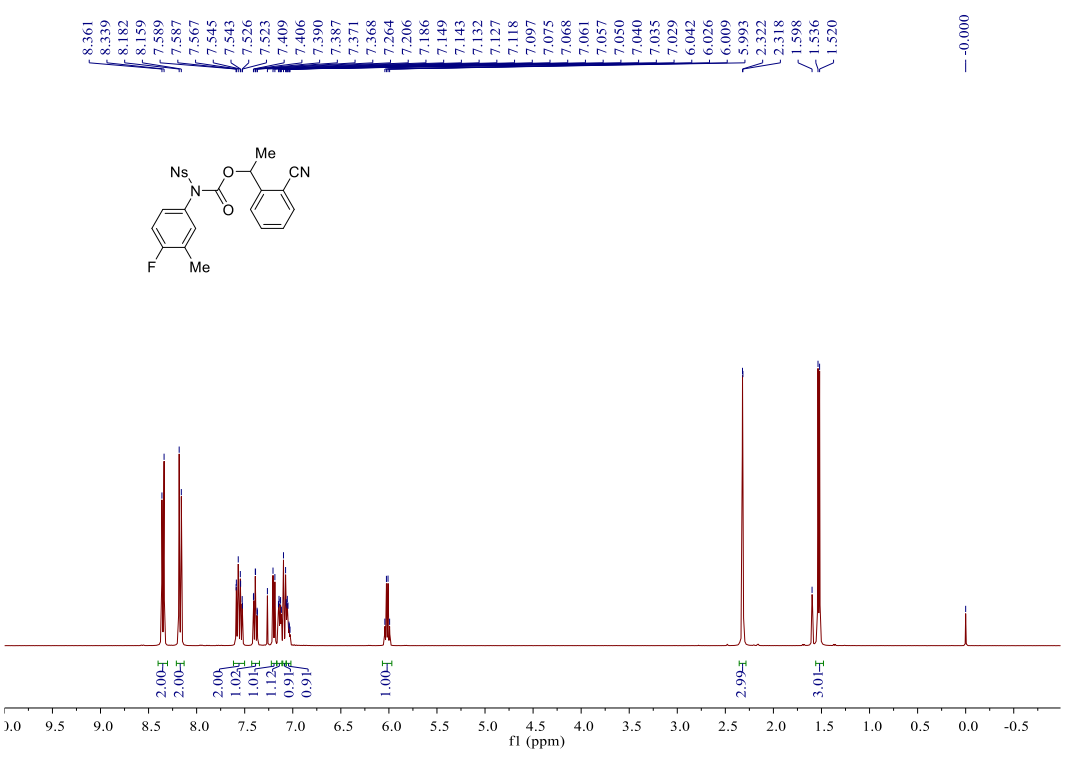

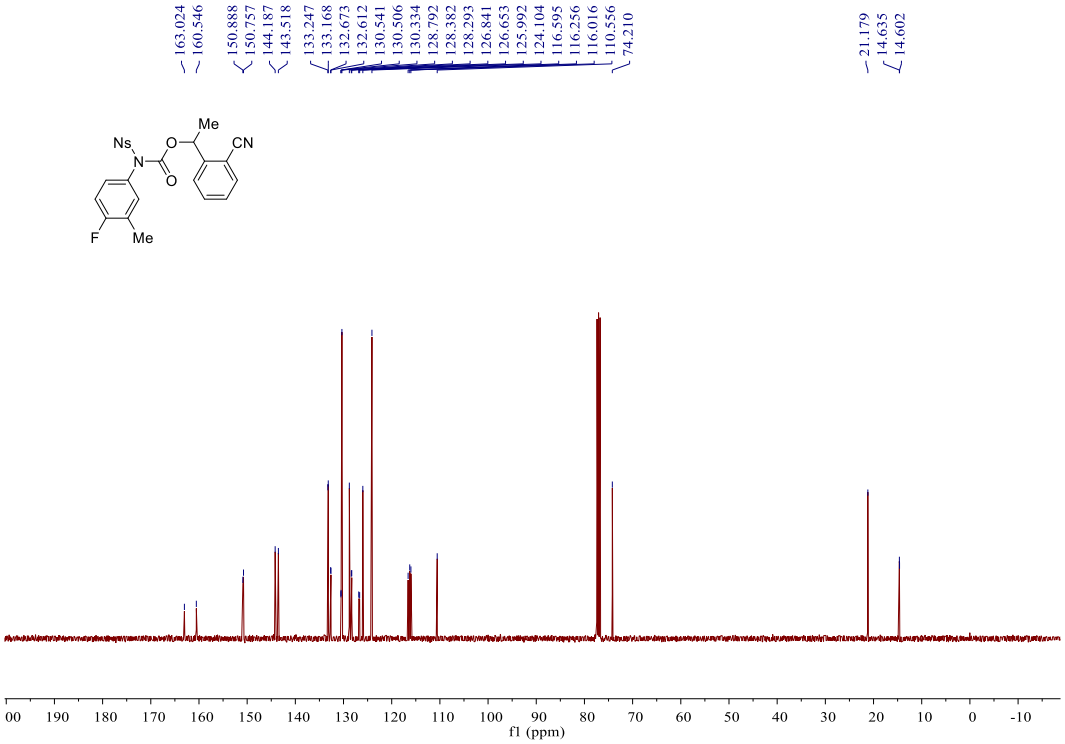

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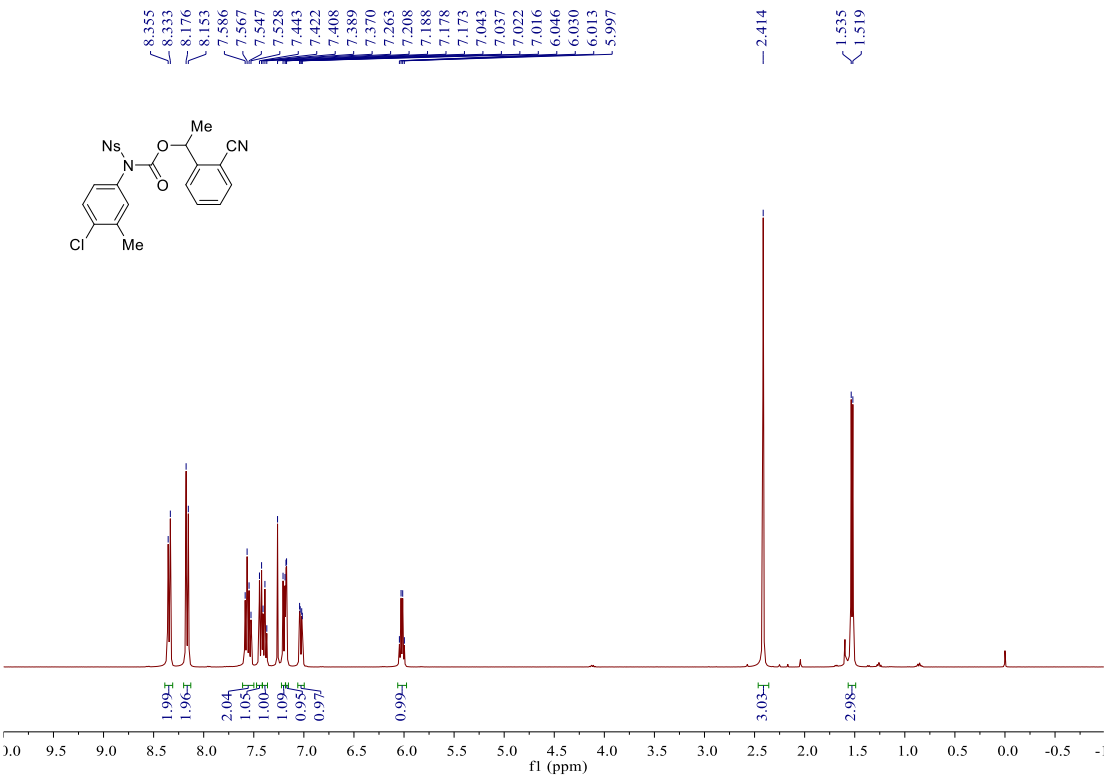

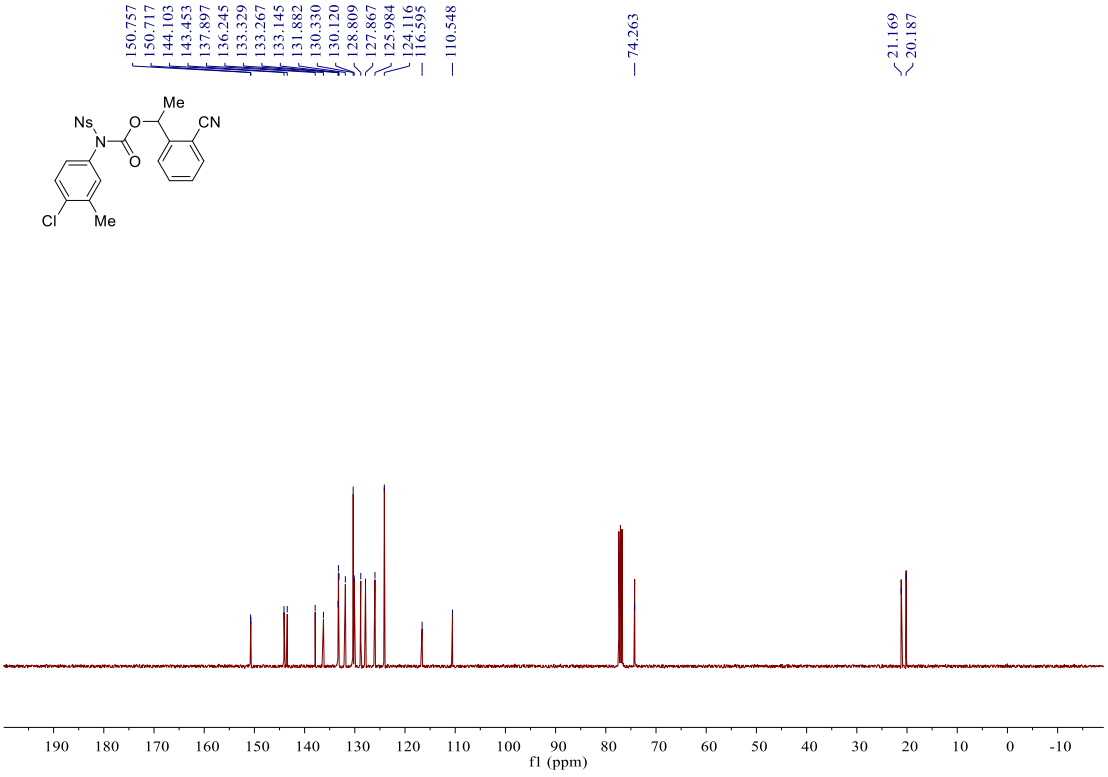

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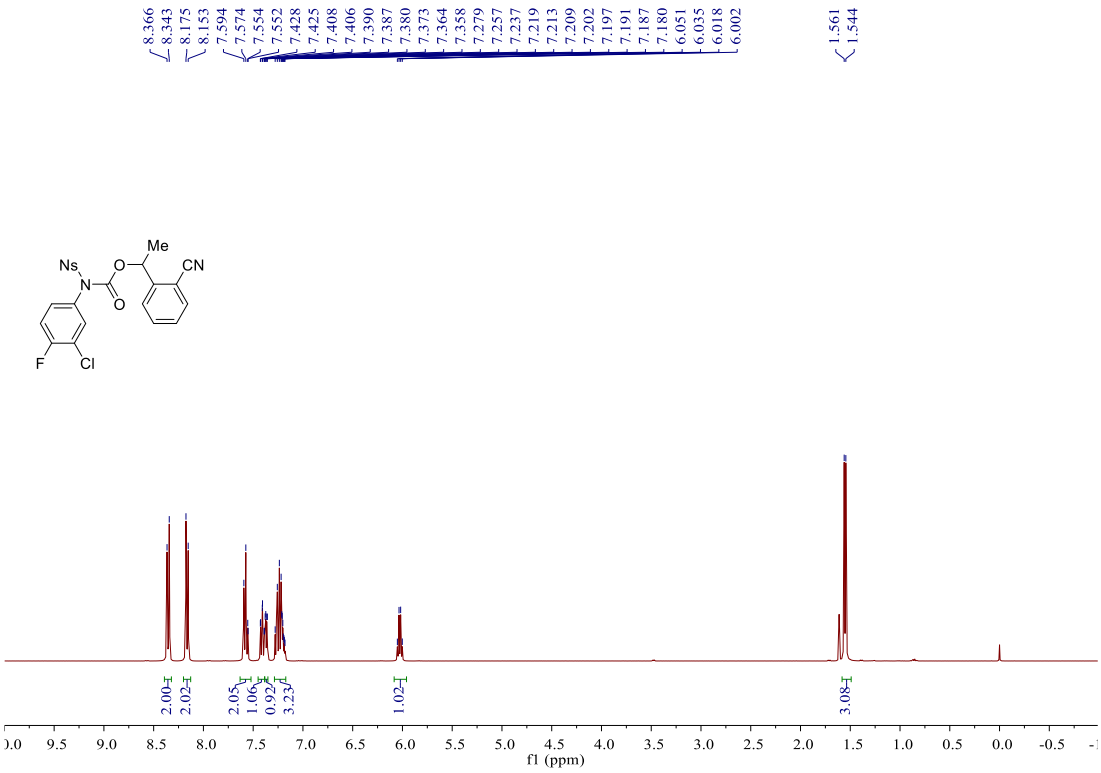

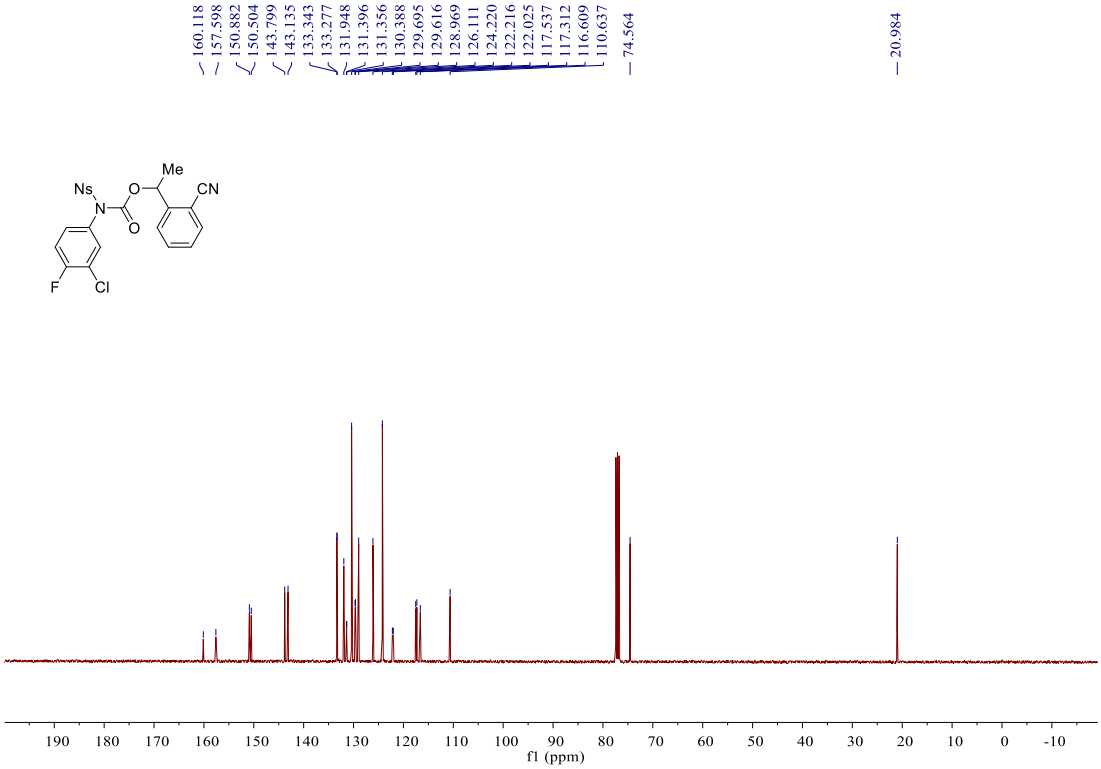

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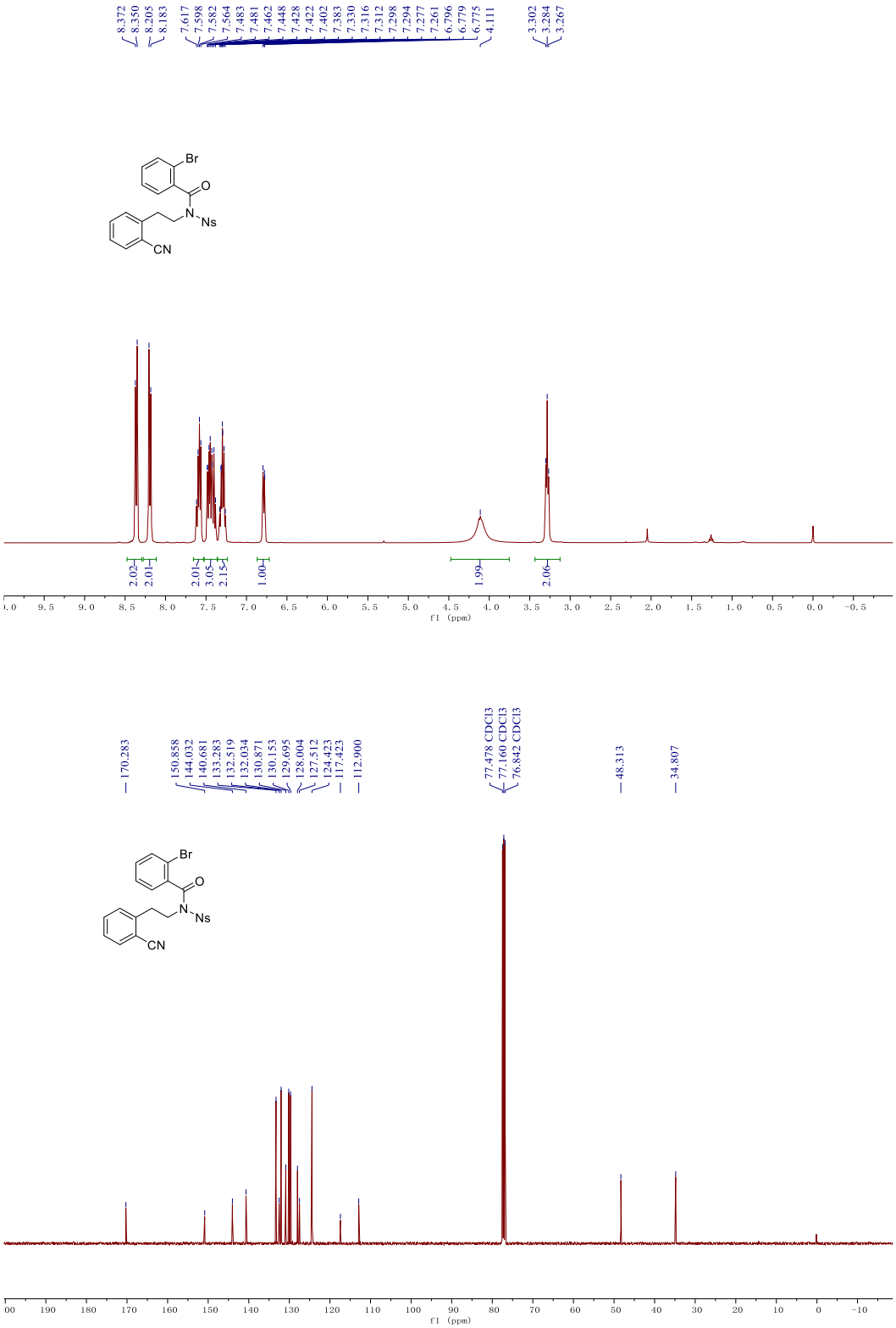

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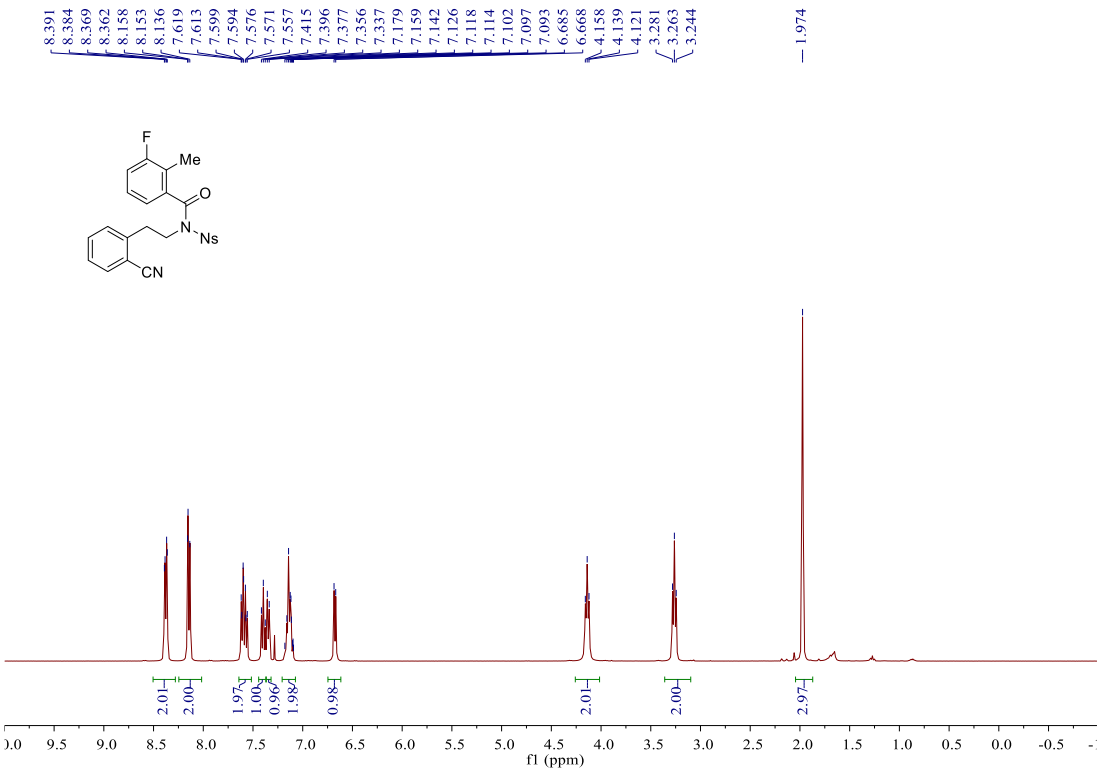

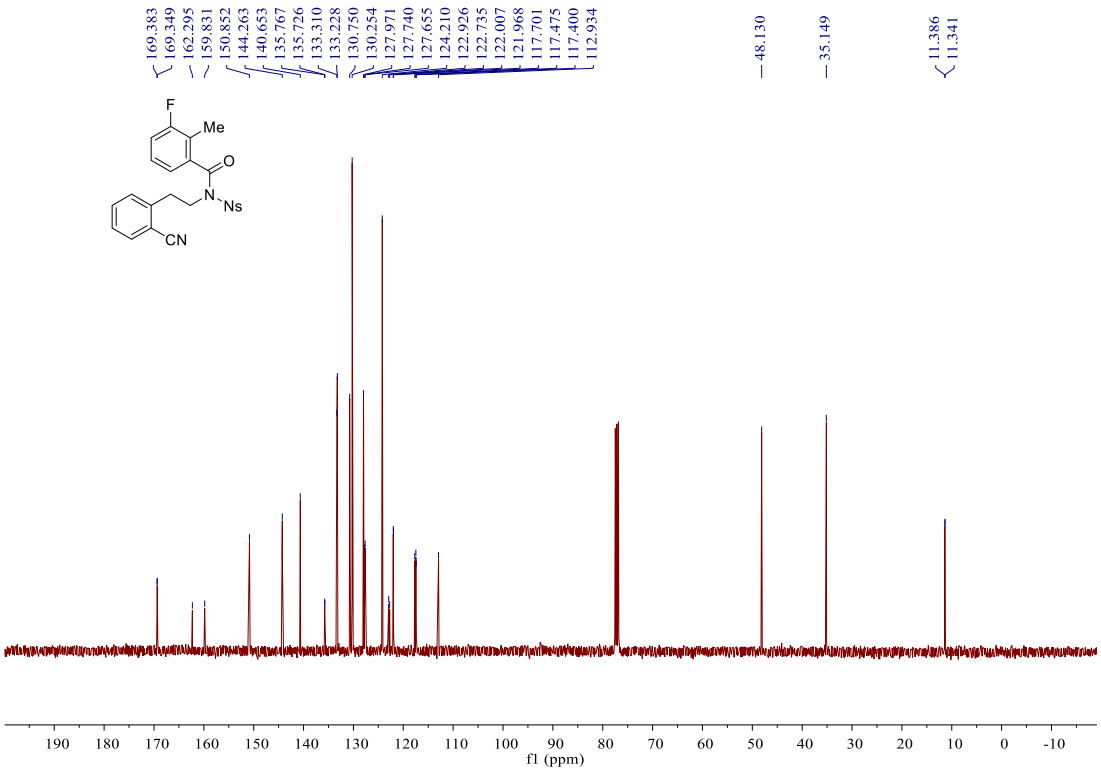

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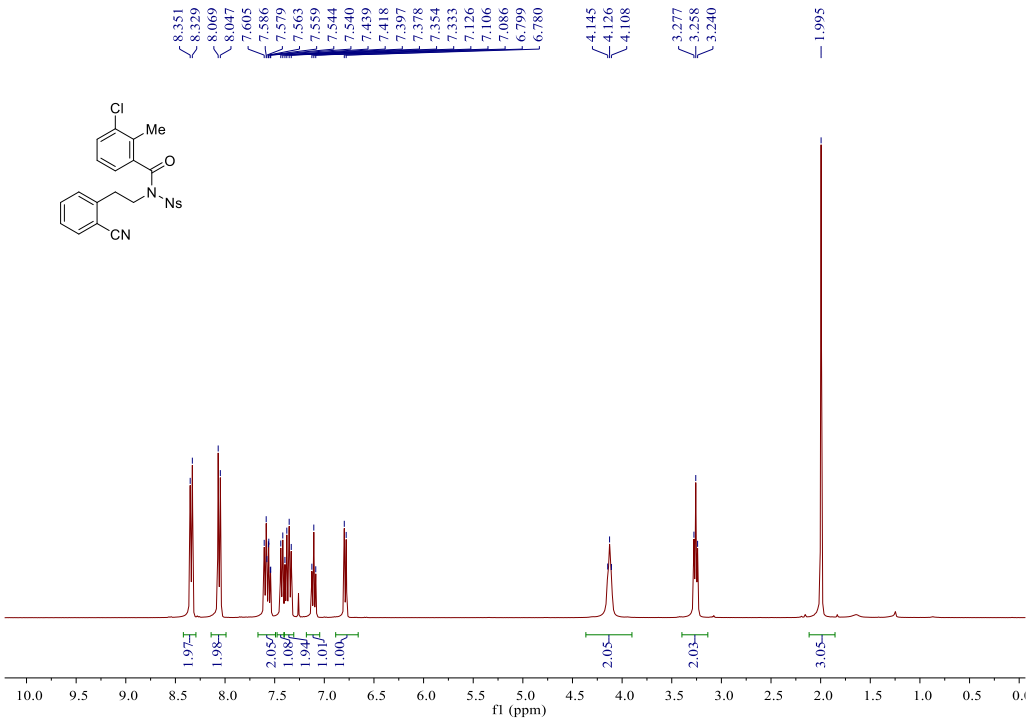

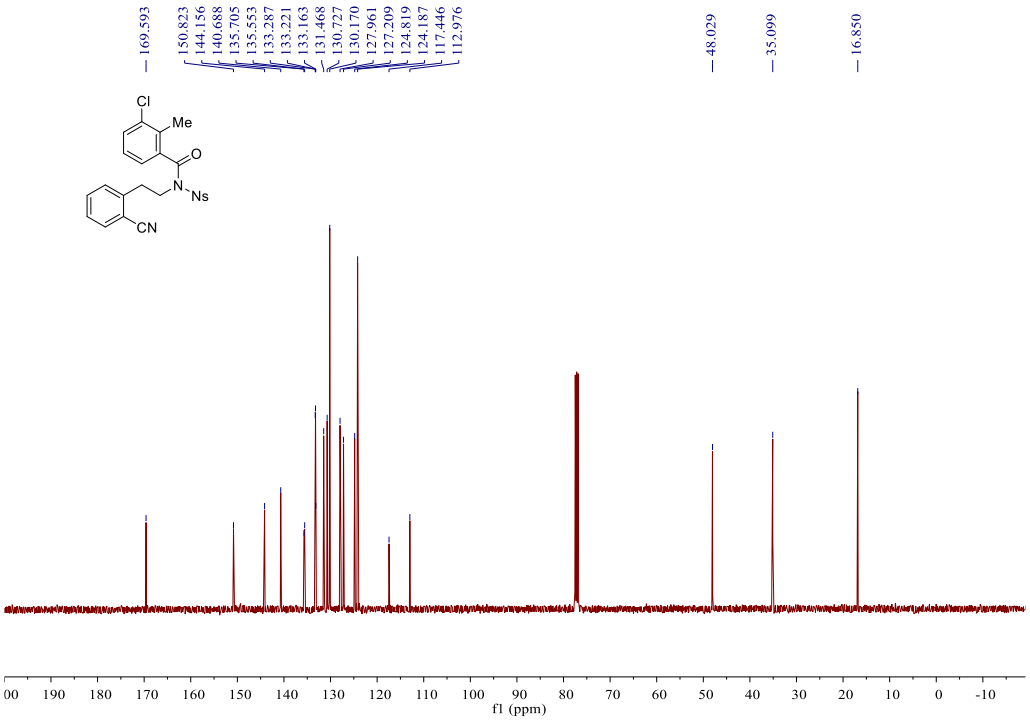

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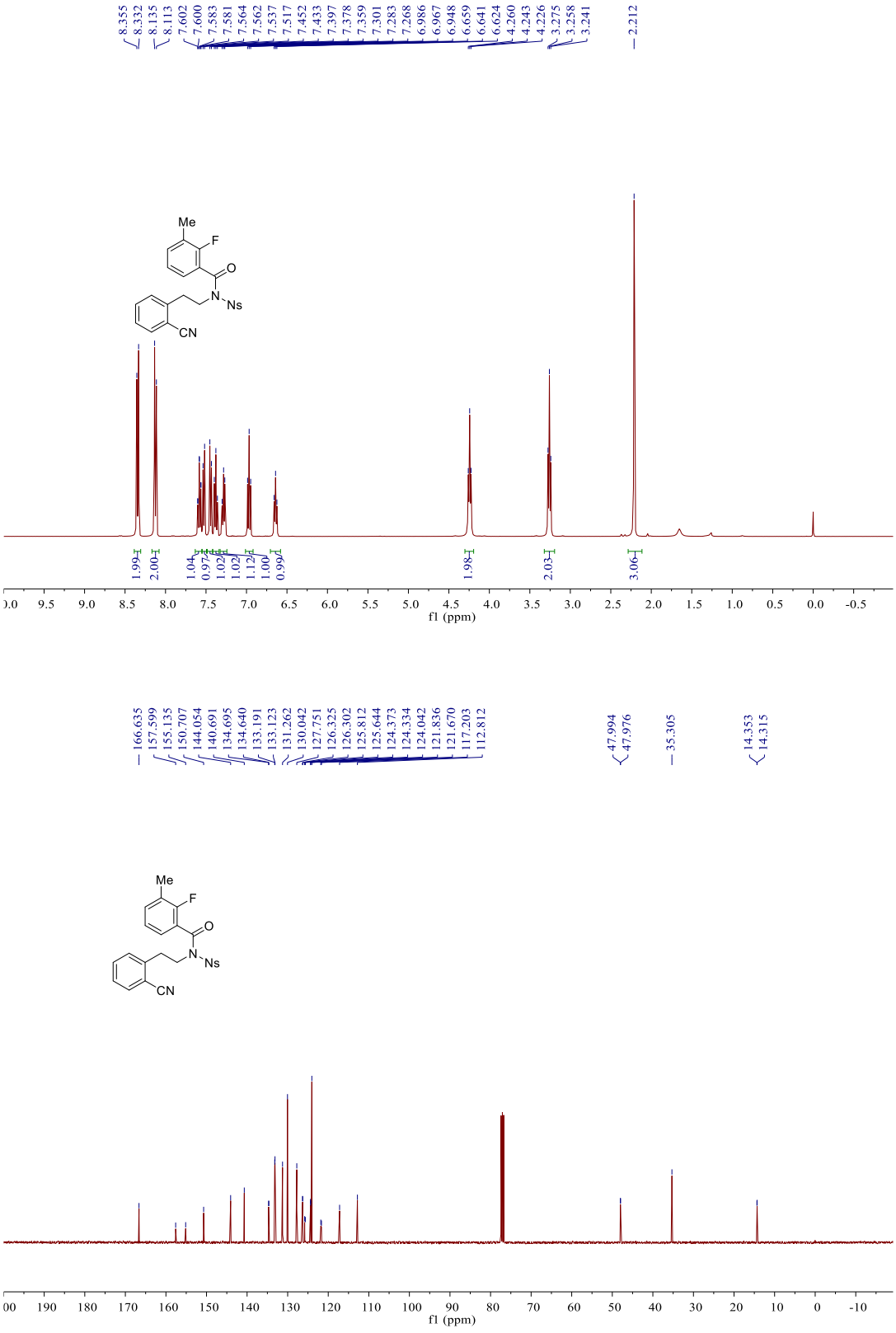

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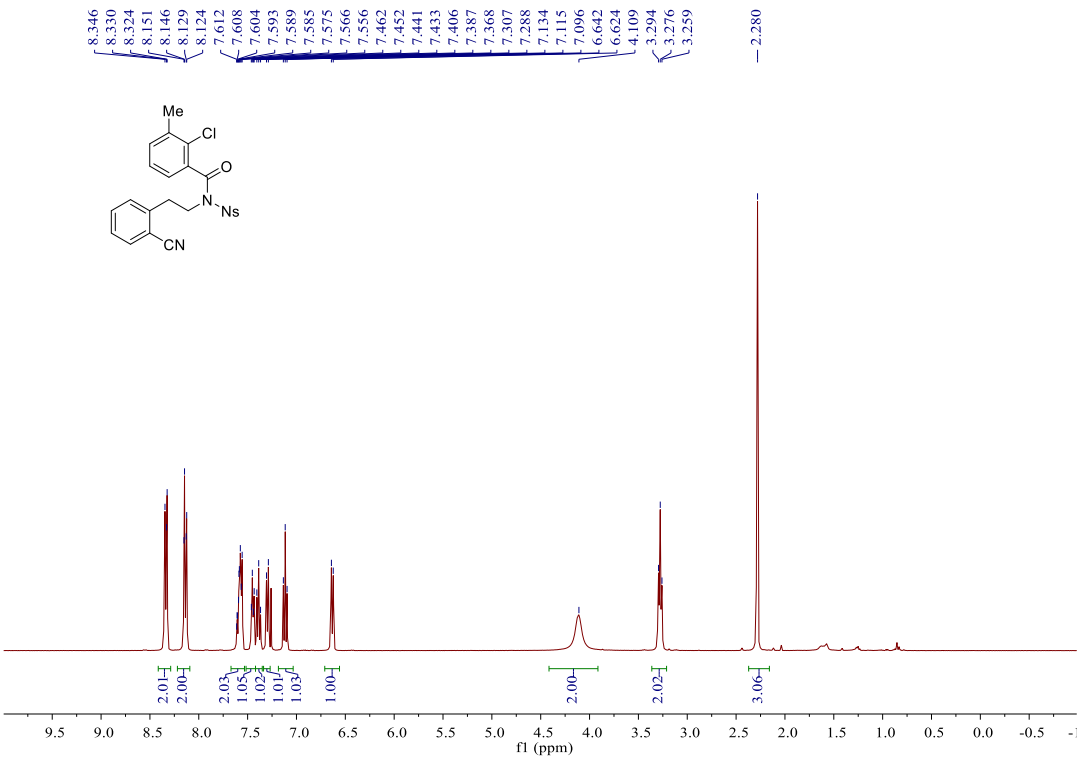
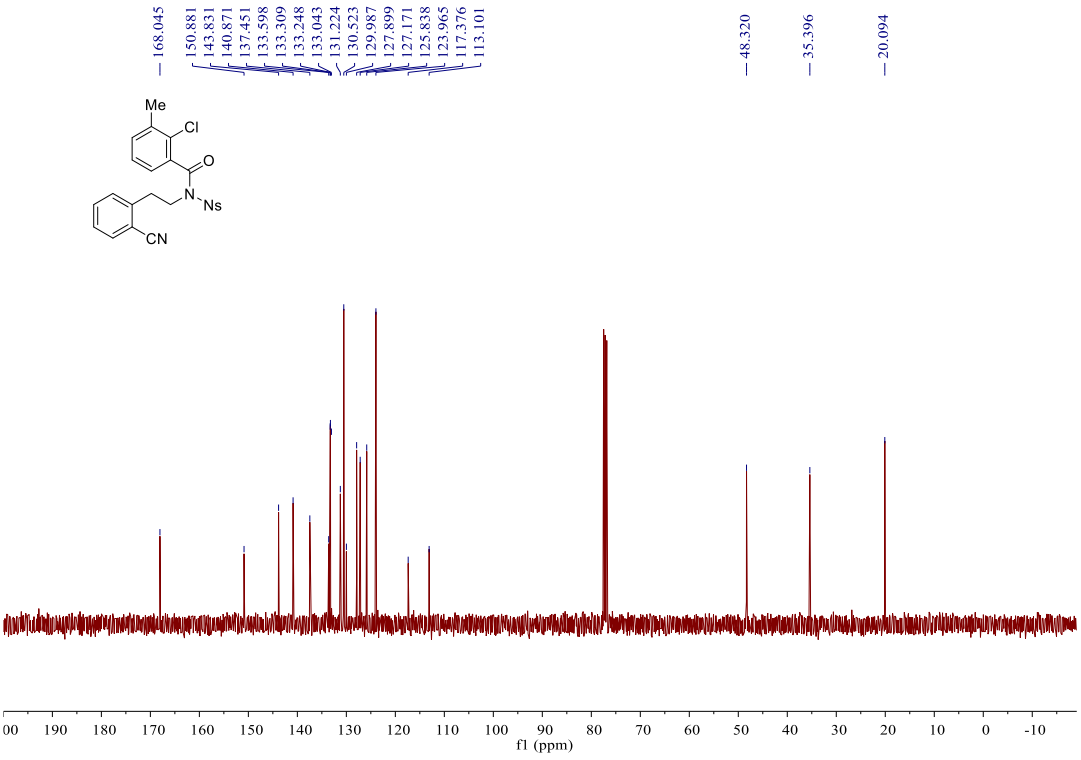
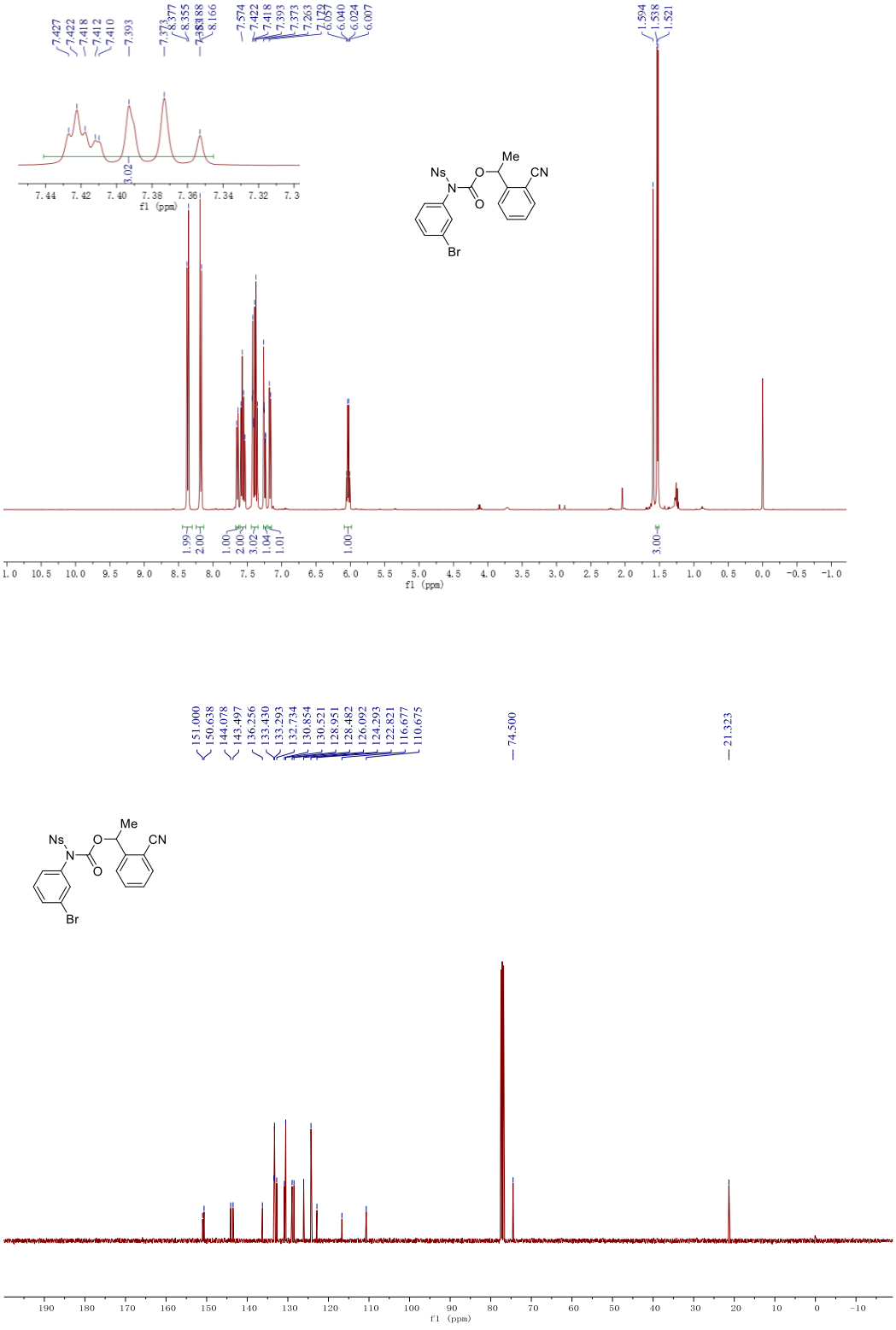
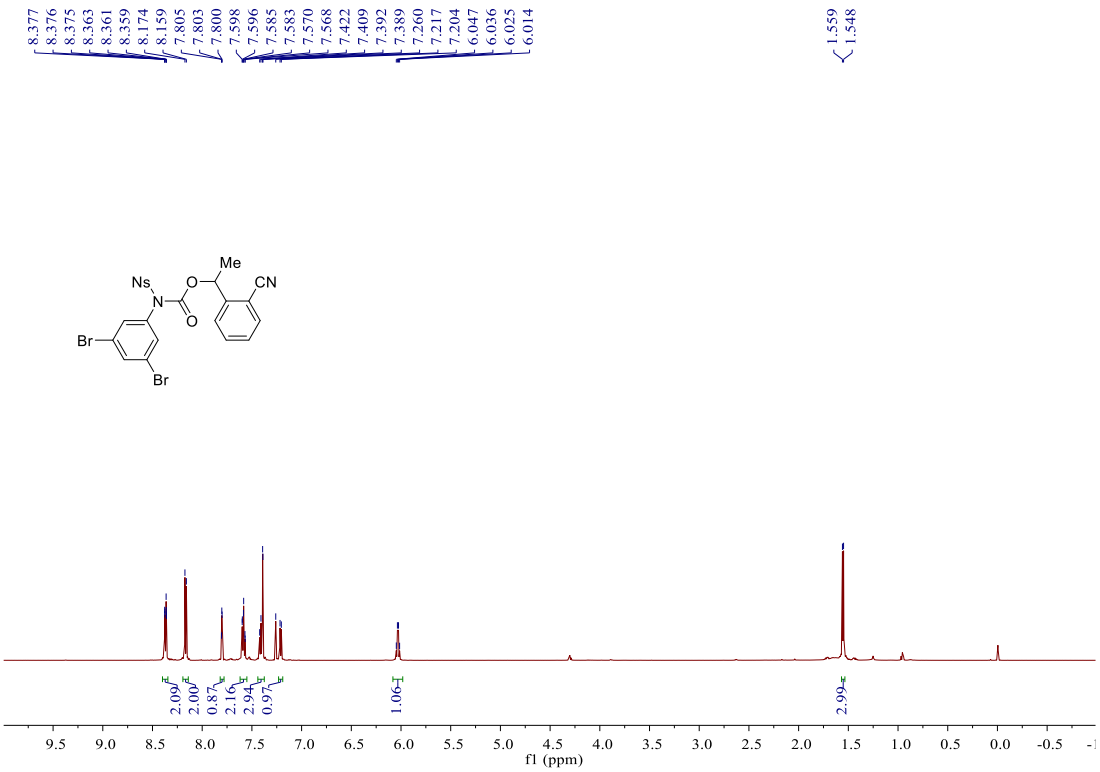


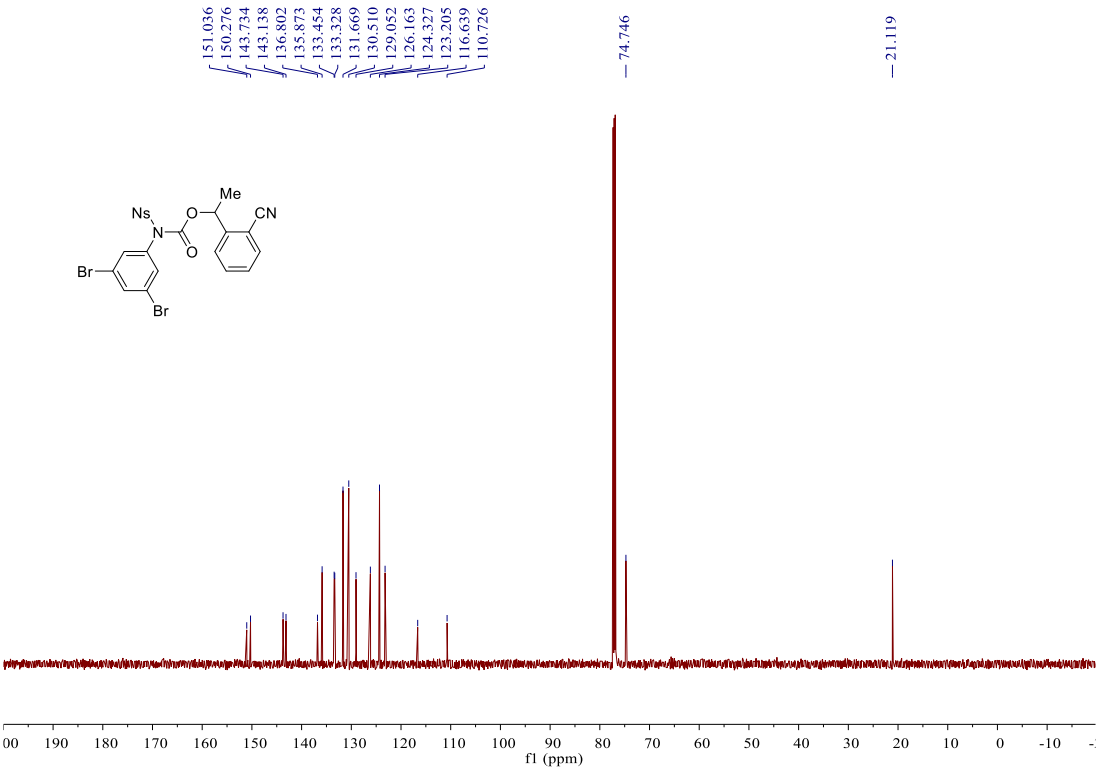


^{1}H and ^{13}C NMR spectra for **3q**

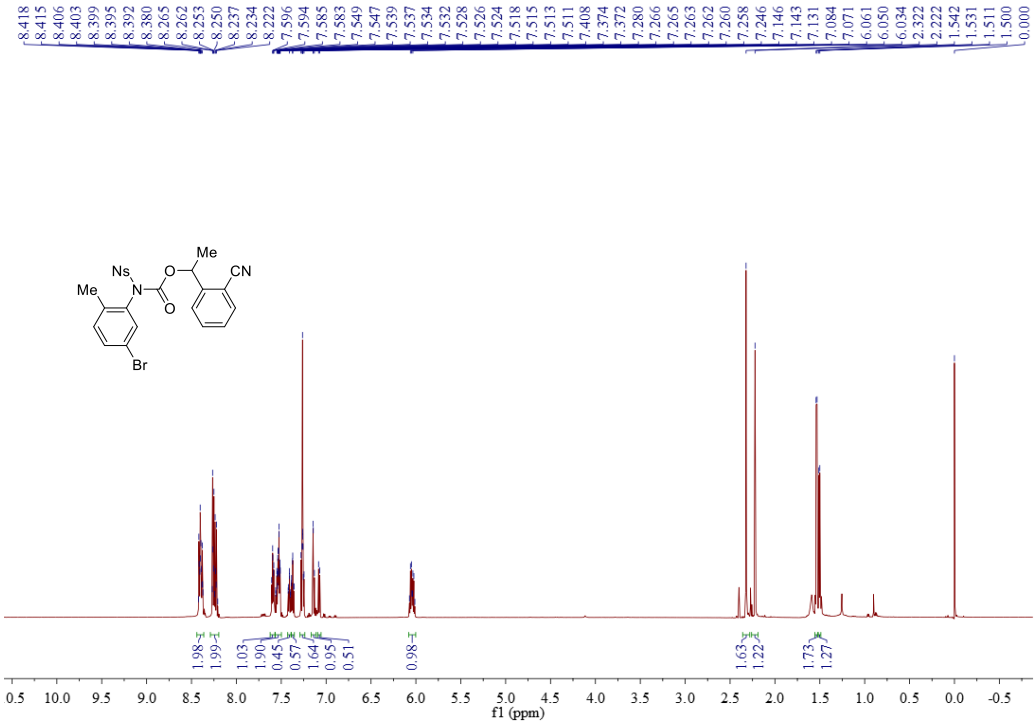


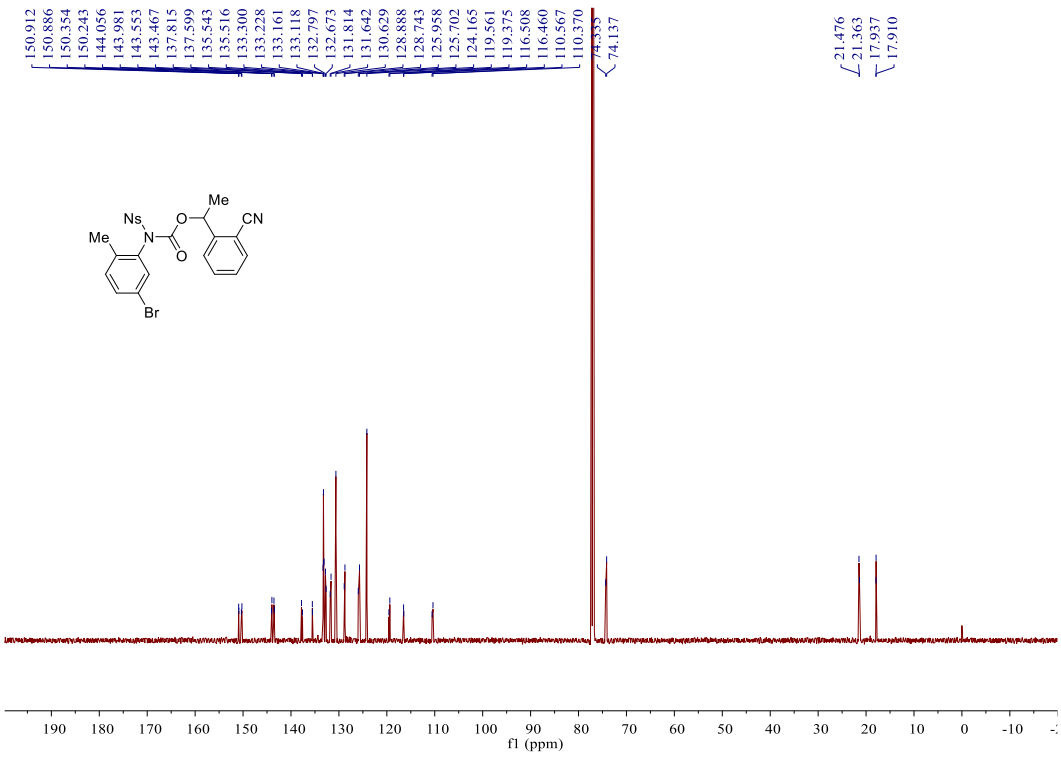
^{1}H and ^{13}C NMR spectra for **2a$_{mono}$**



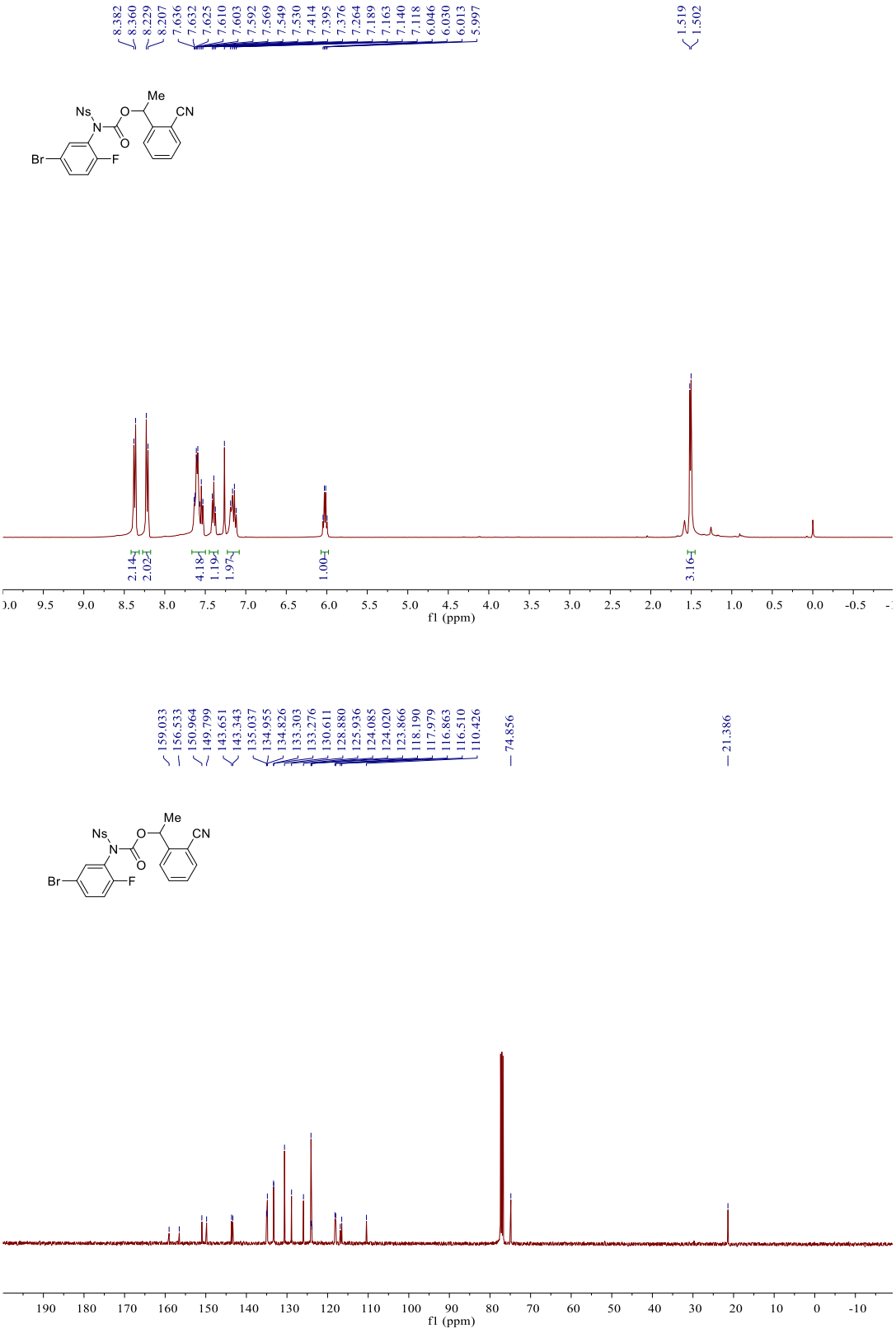


^{1}H and ^{13}C NMR spectra for **2a$_{(m,\ m')di}$**

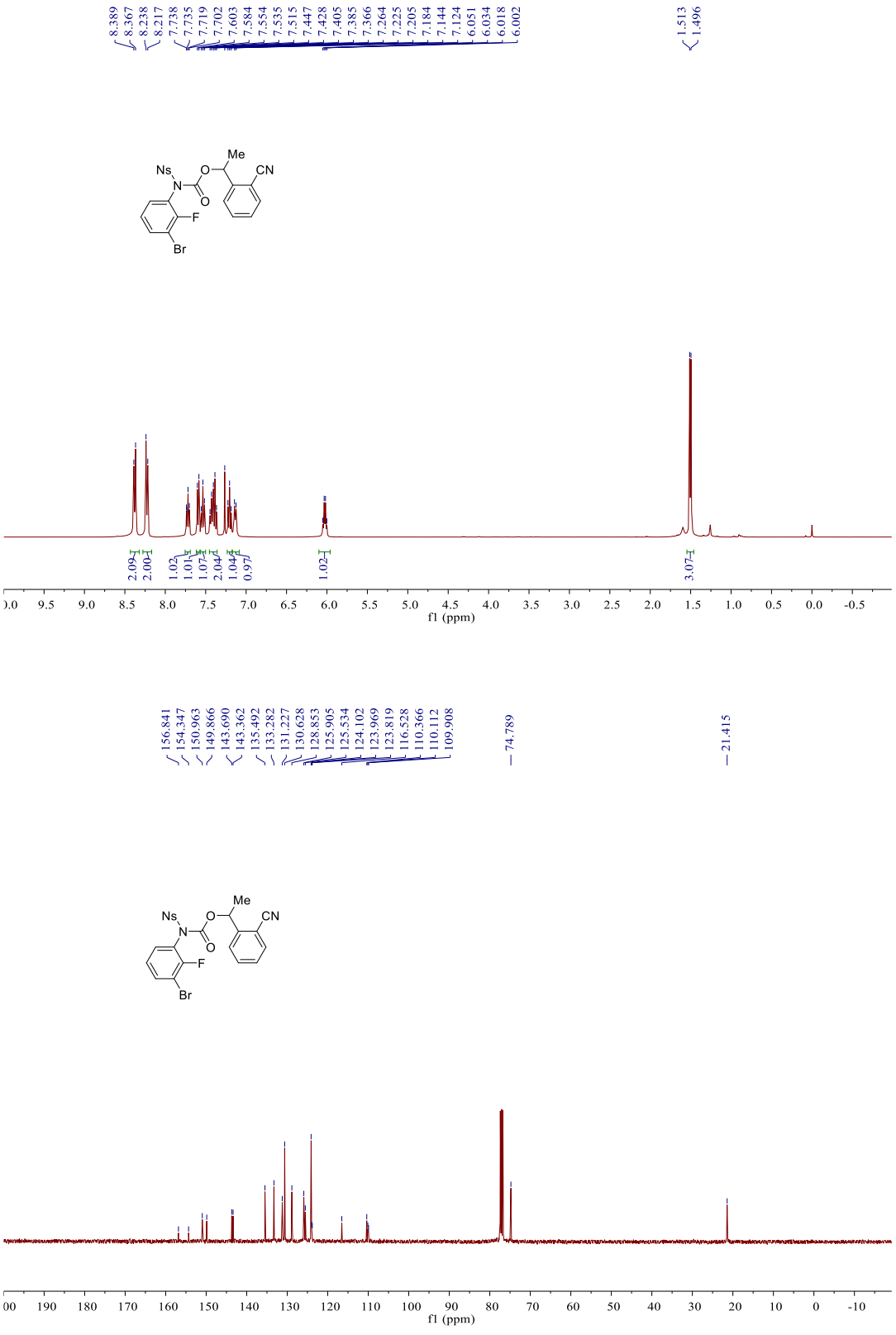




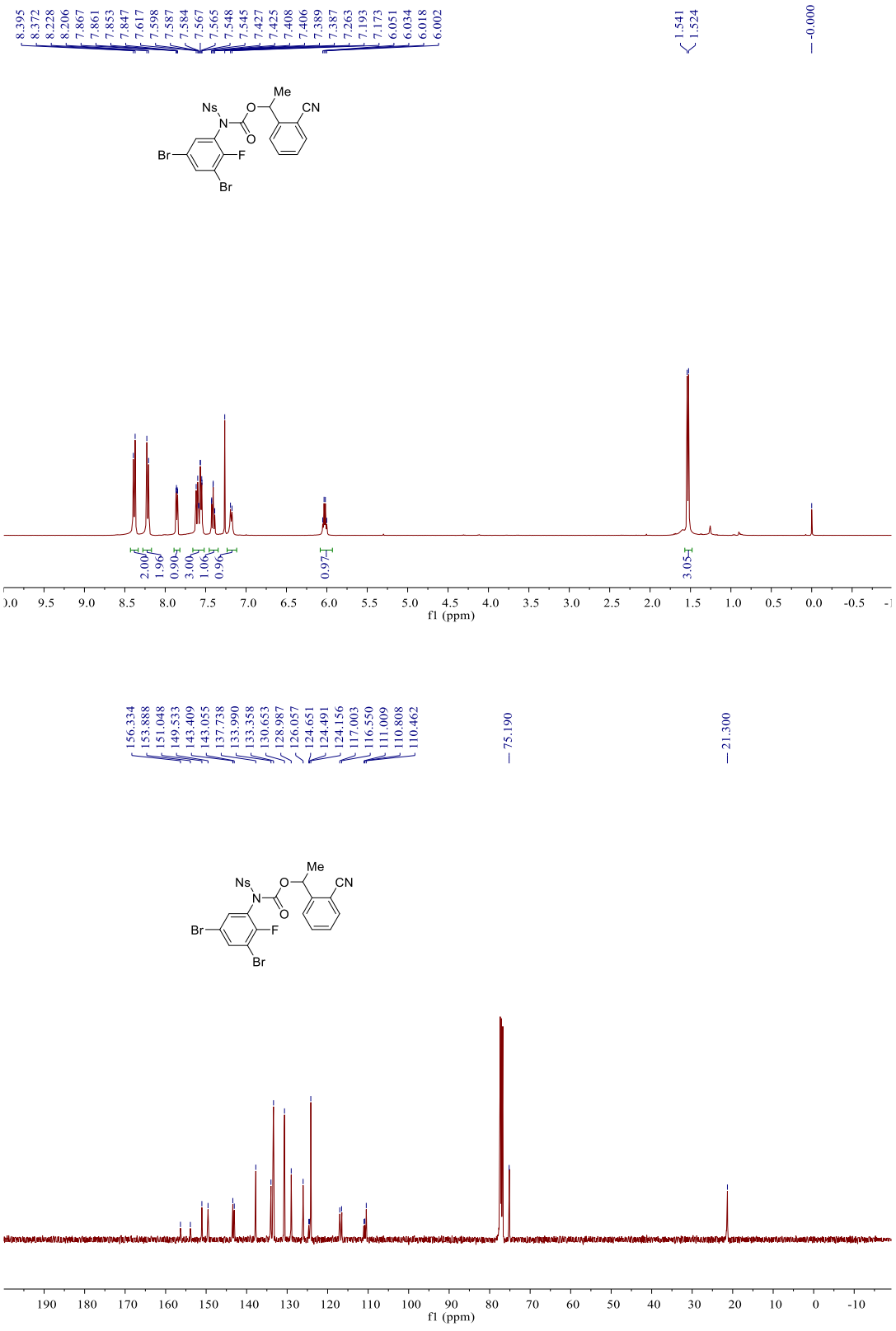
^{1}H and ^{13}C NMR spectra for **2b**



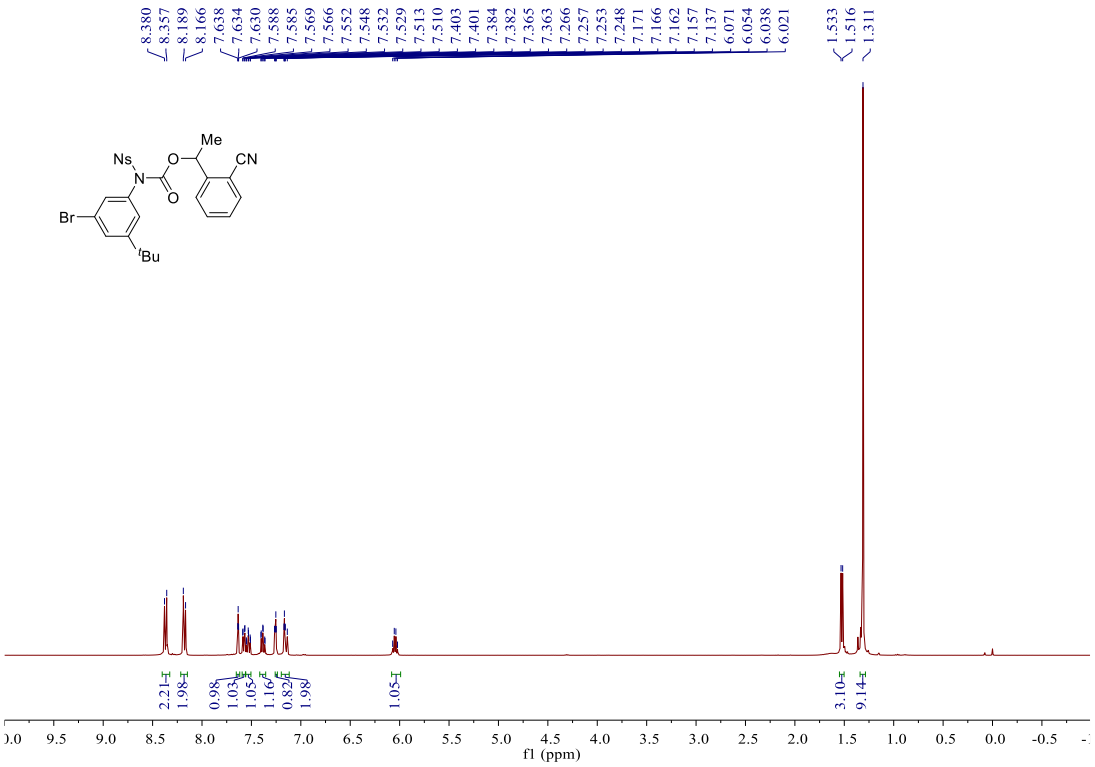
^{1}H and ^{13}C NMR spectra for **2c$_{mono(m)}$**

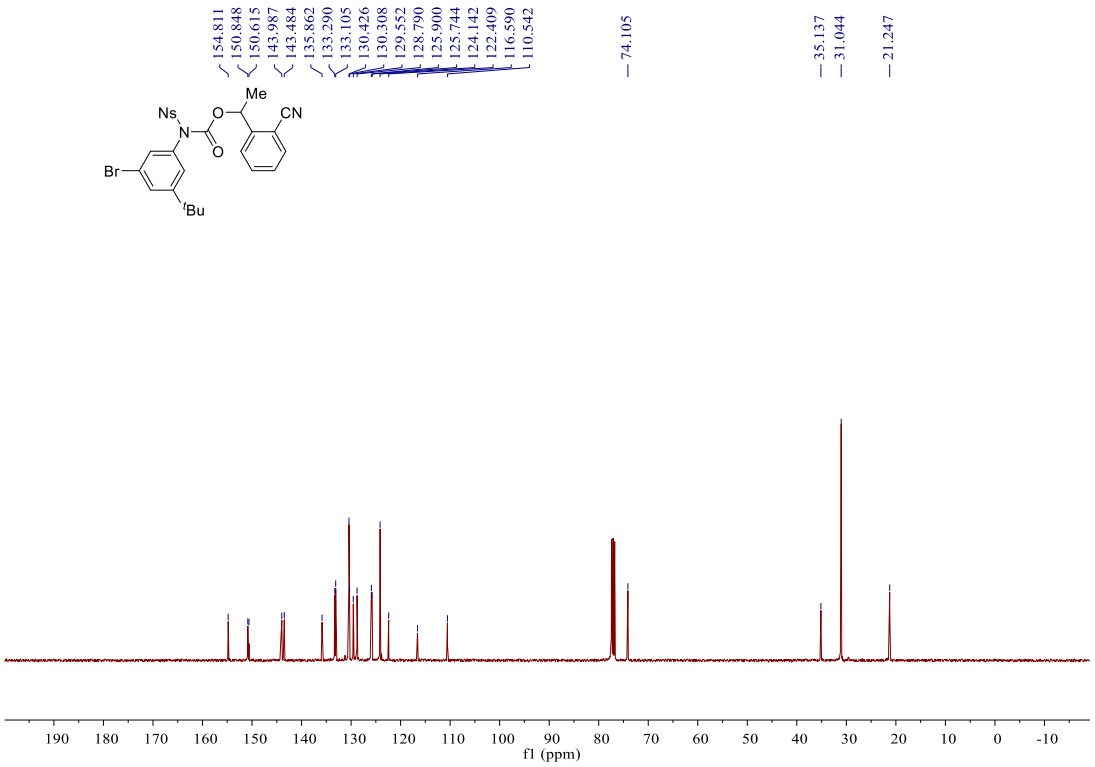


^{1}H and ^{13}C NMR spectra for **2c**$_{\mathbf{mono(m')}}$



^{1}H and ^{13}C NMR spectra for **2c$_{(m, m)di}$**





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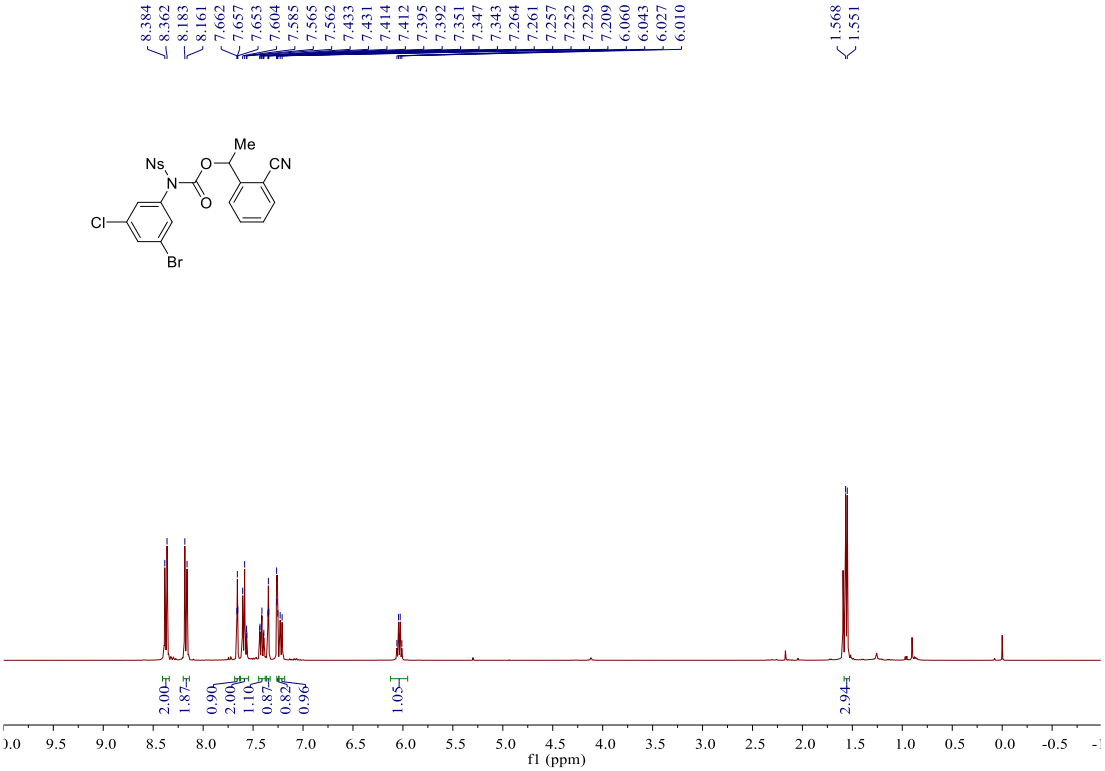

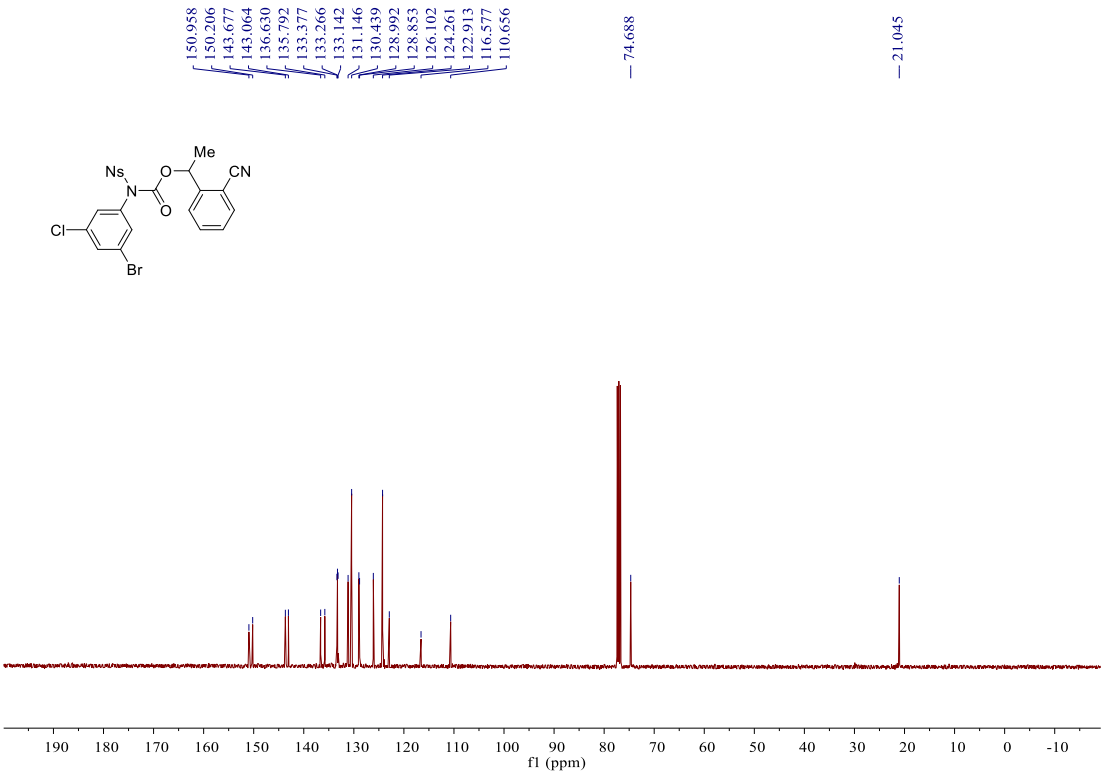

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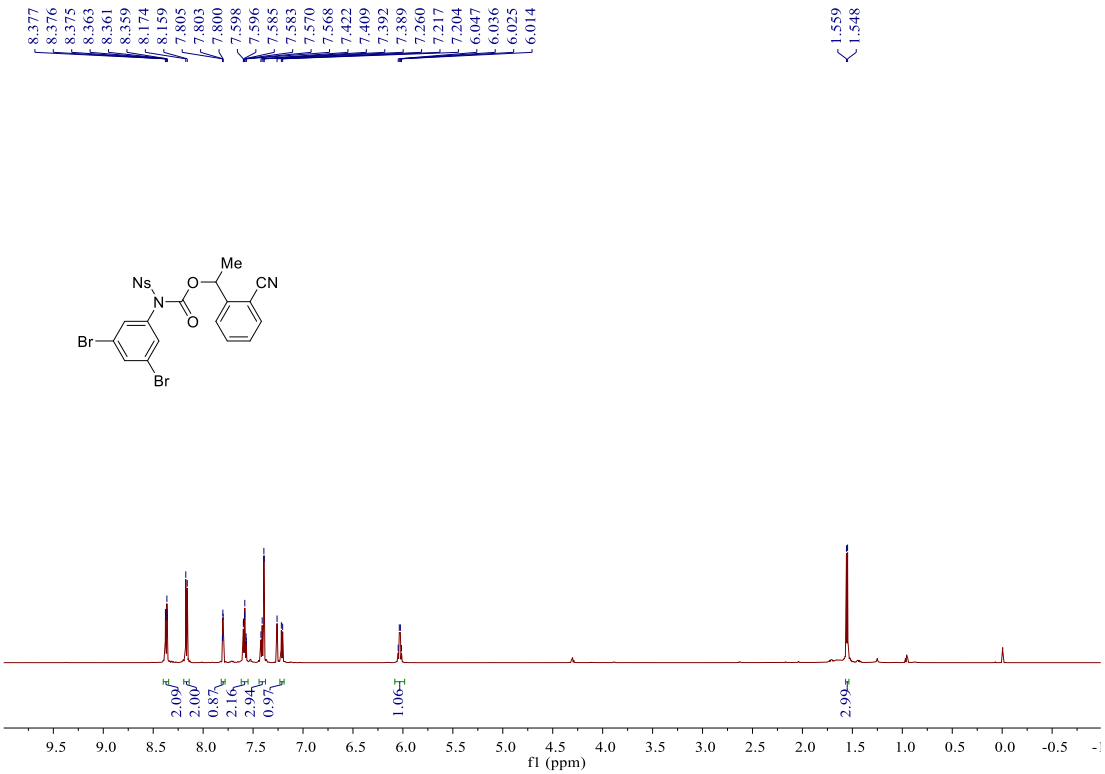
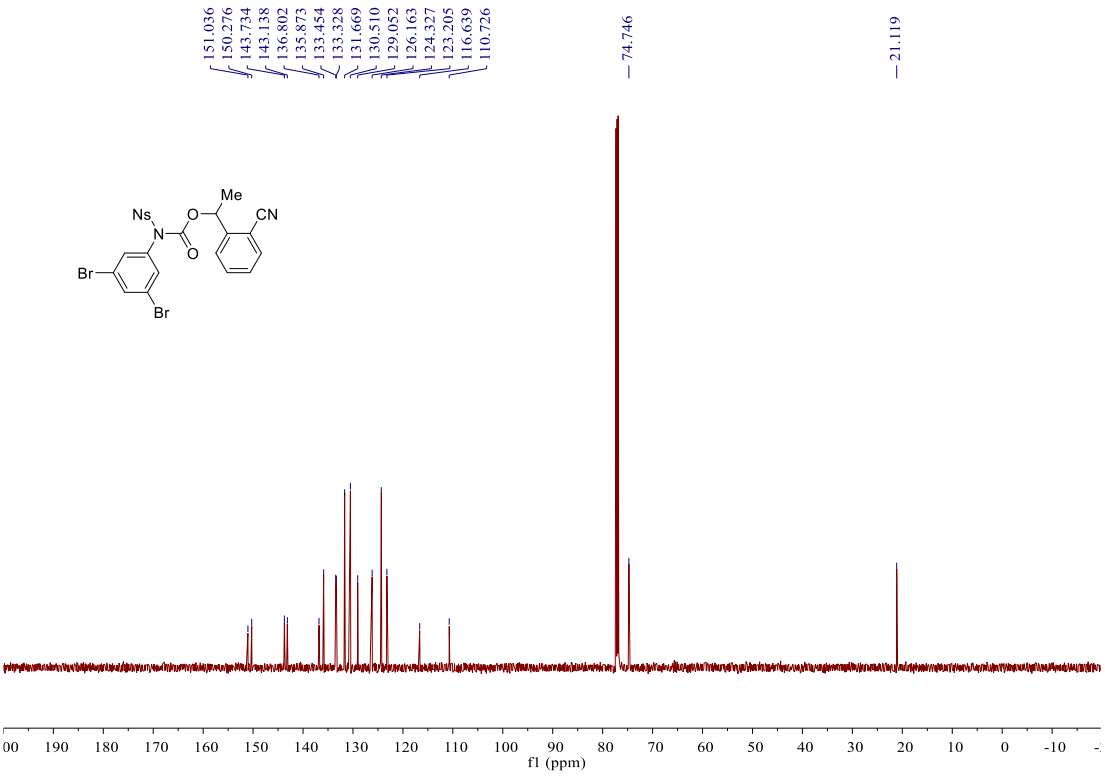
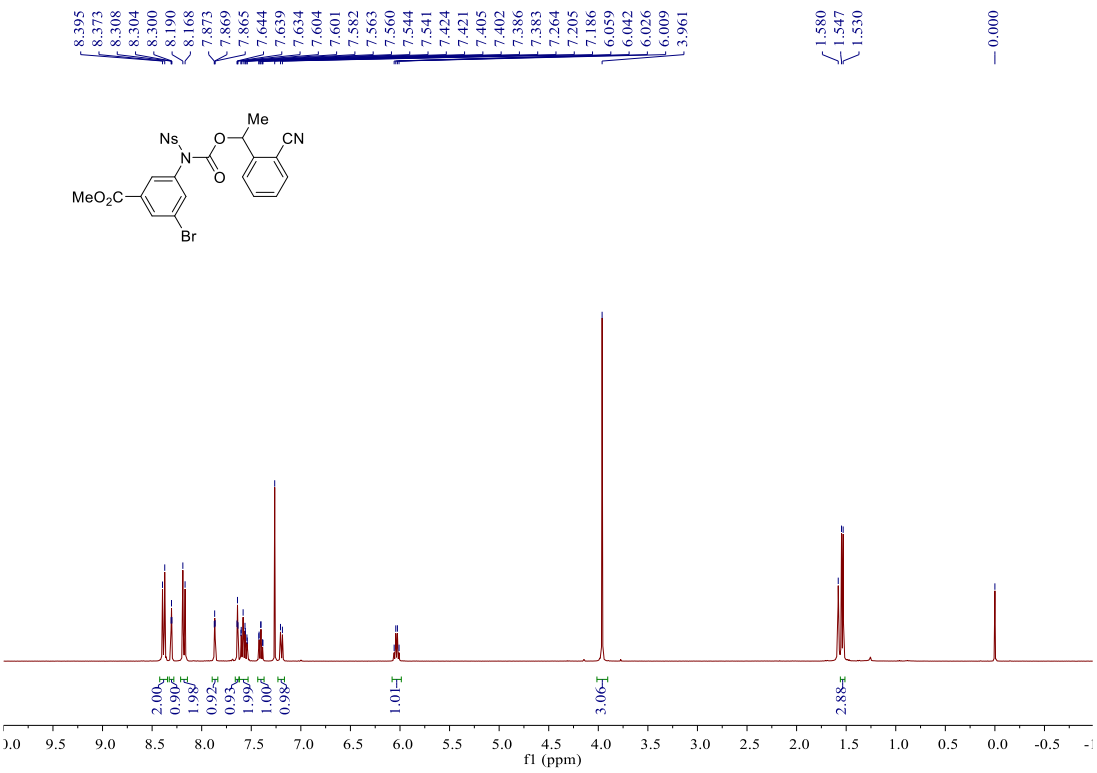
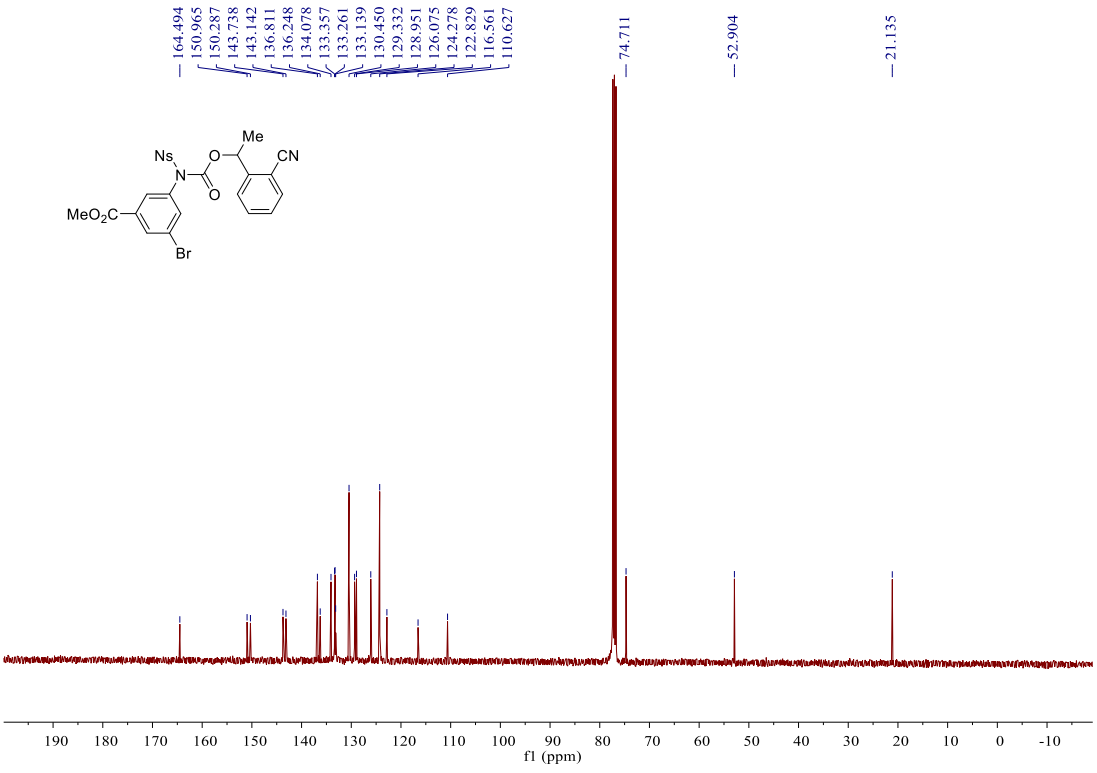


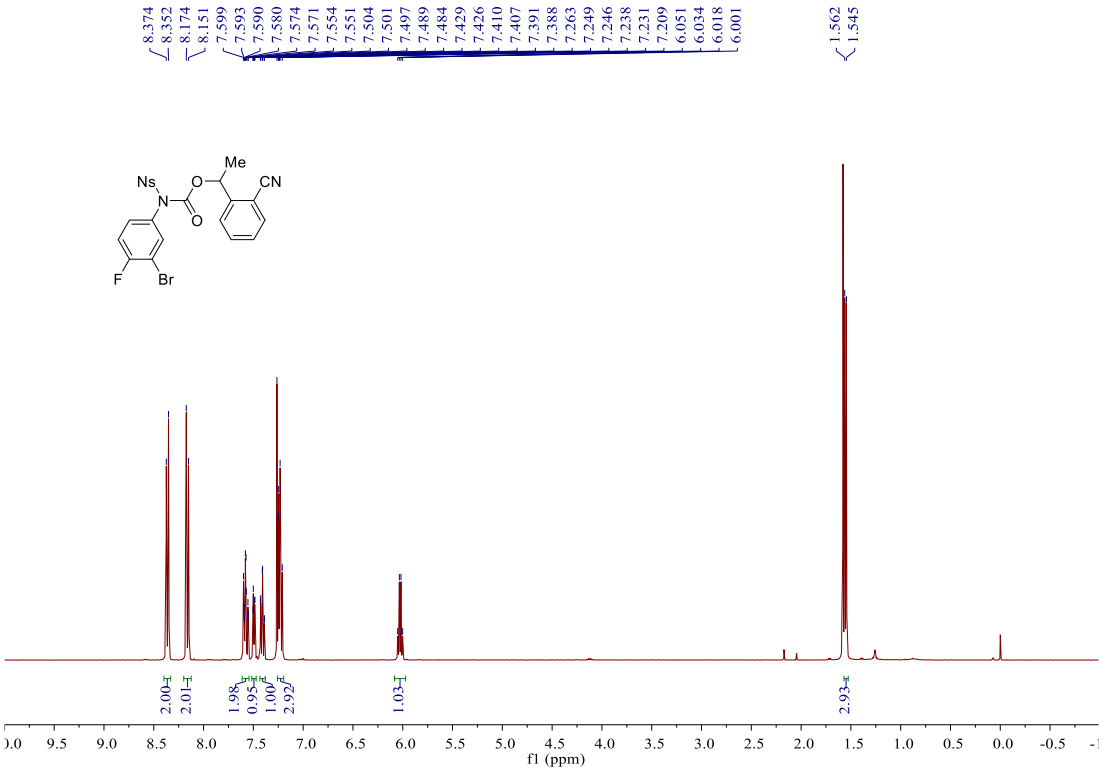


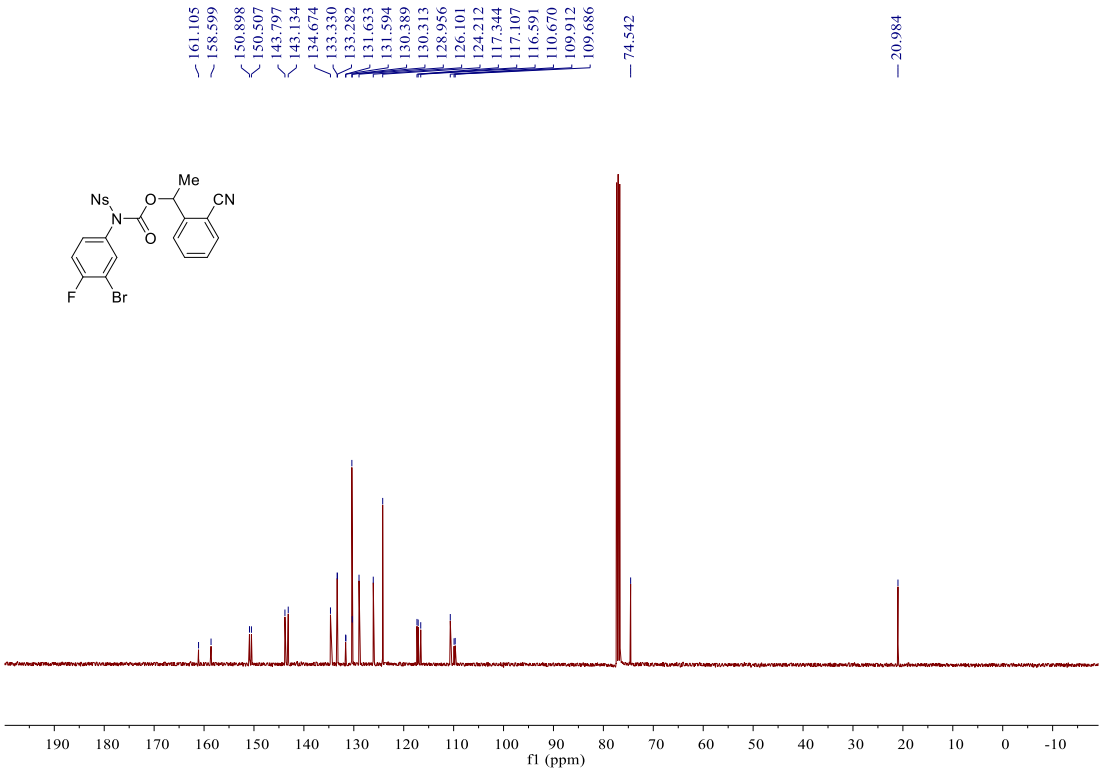
^{1}H and ^{13}C NMR spectra for **2f**



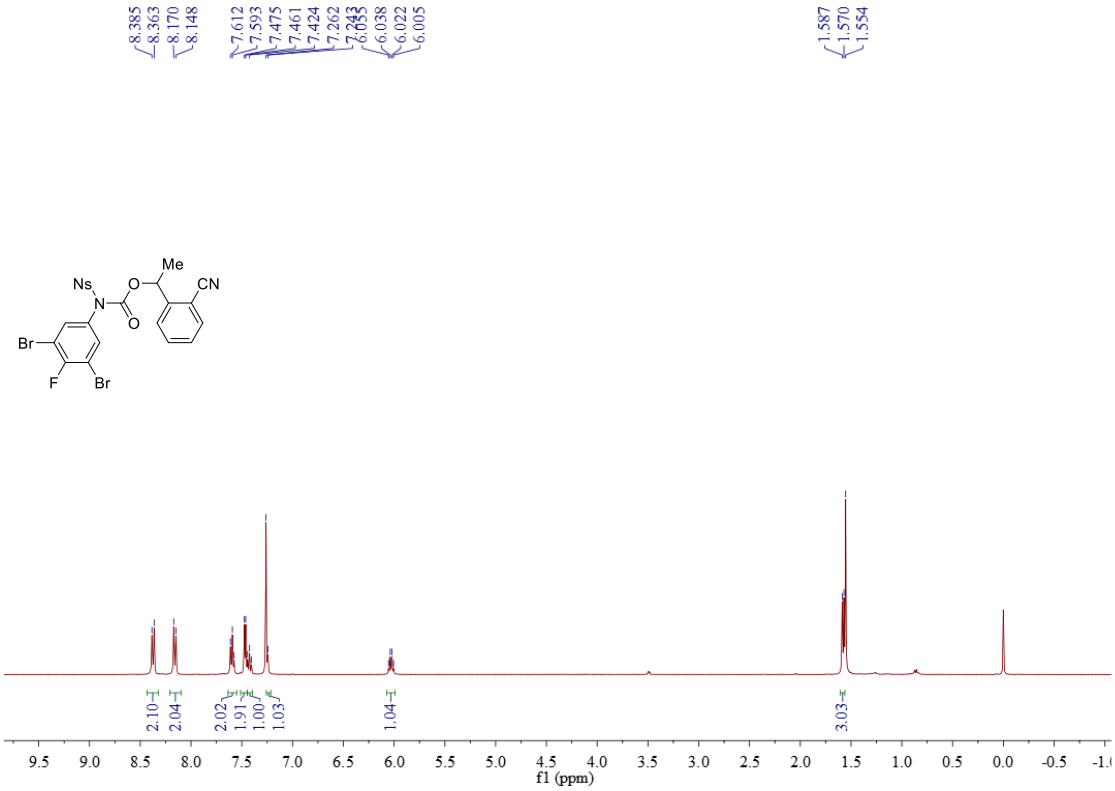


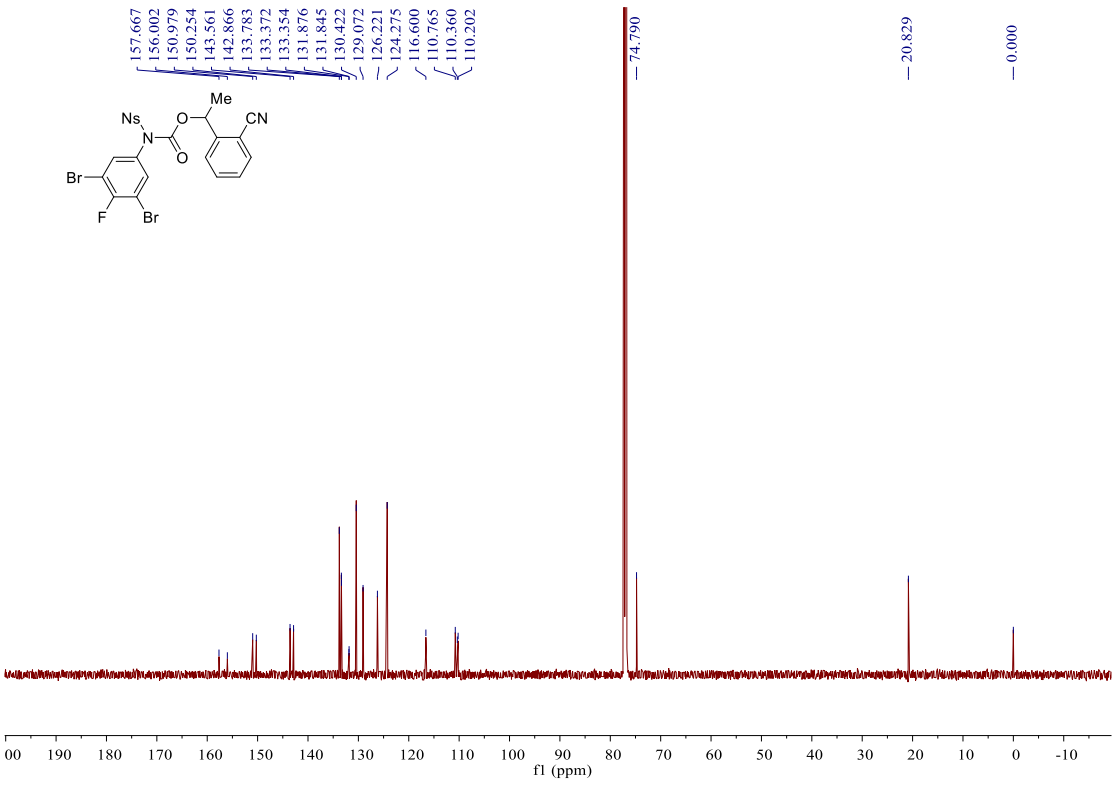
^{1}H and ^{13}C NMR spectra for **2g**



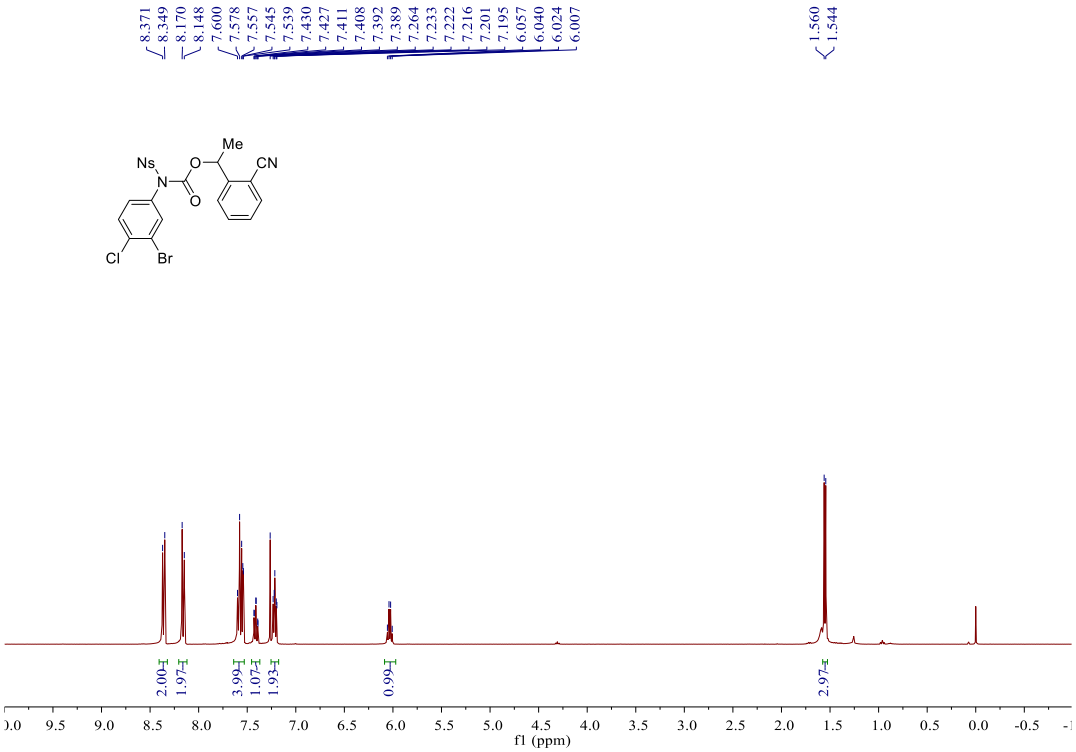


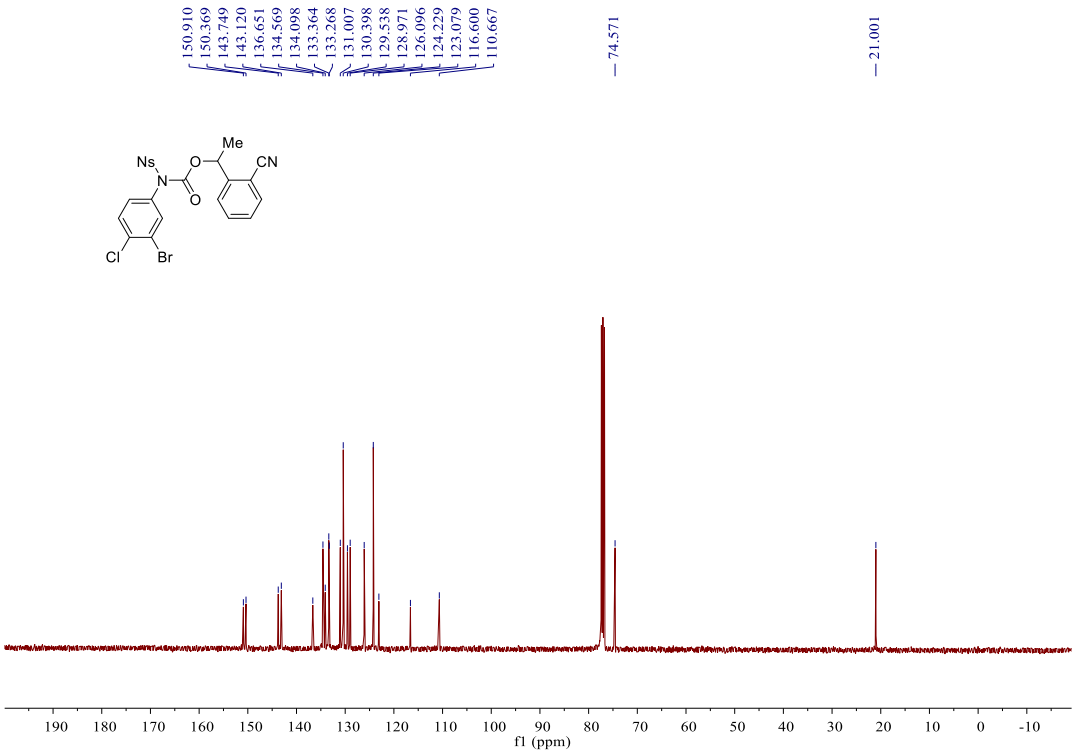
^{1}H and ^{13}C NMR spectra for **2h$_{mono}$**



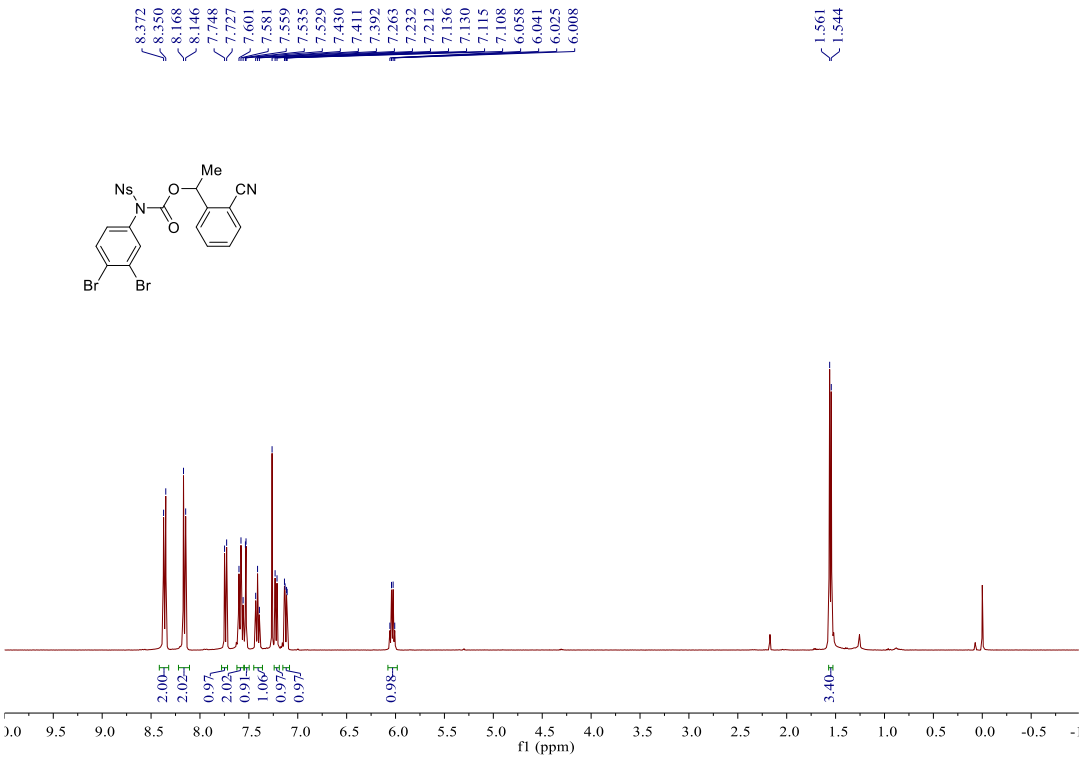


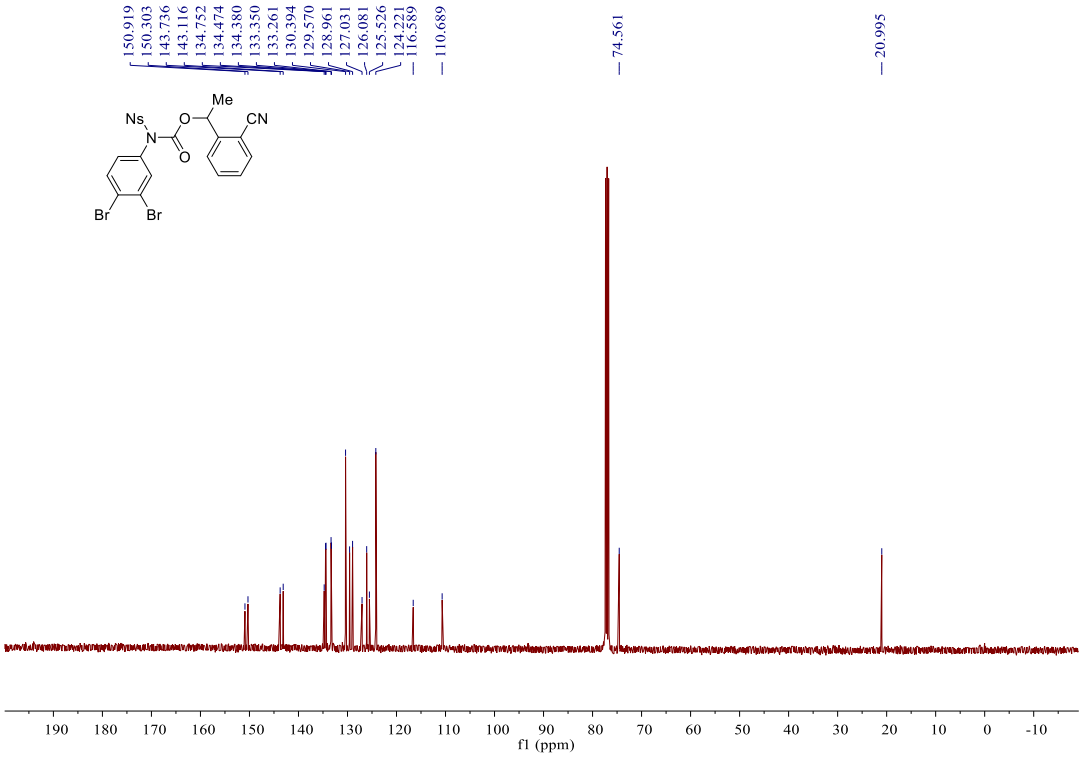
^{1}H and ^{13}C NMR spectra for **2h$_{(m, m')di}$**



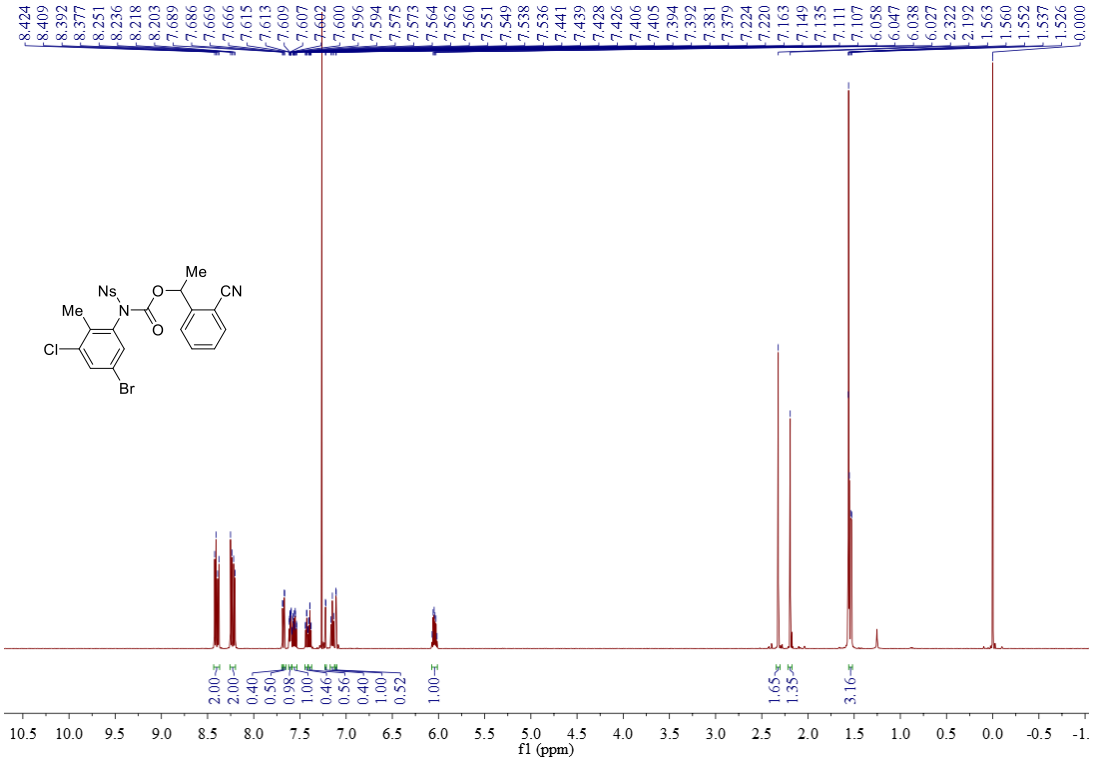


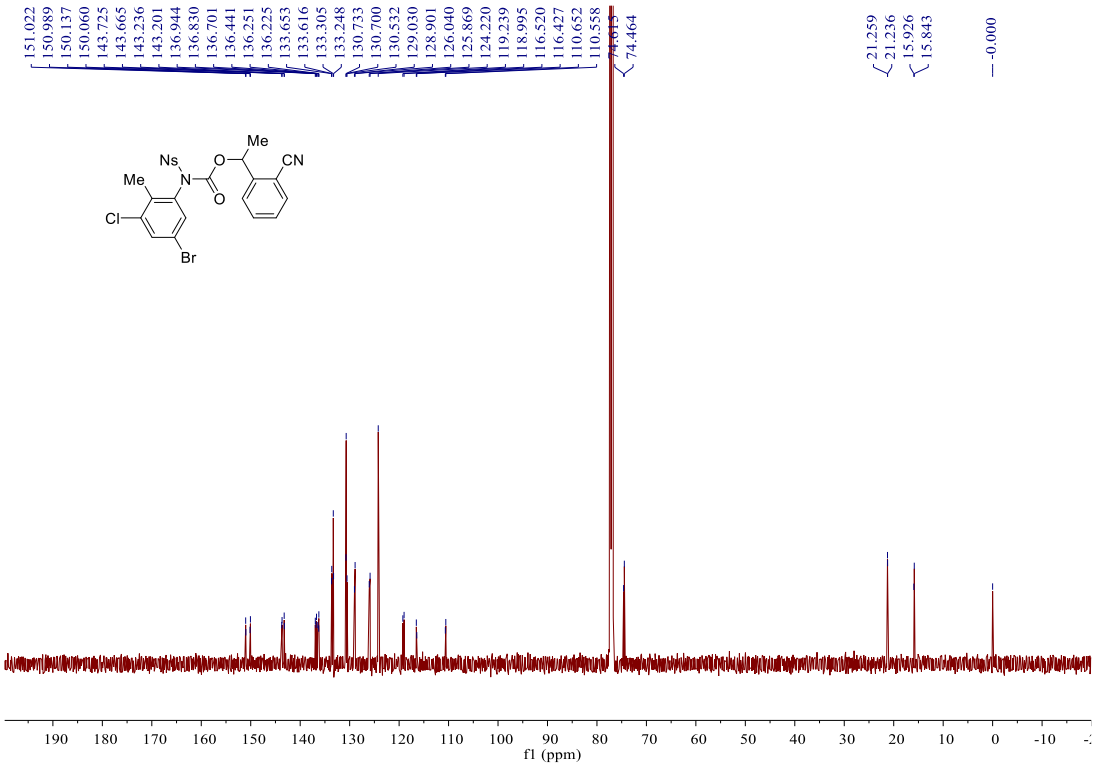
^{1}H and ^{13}C NMR spectra for **2i**



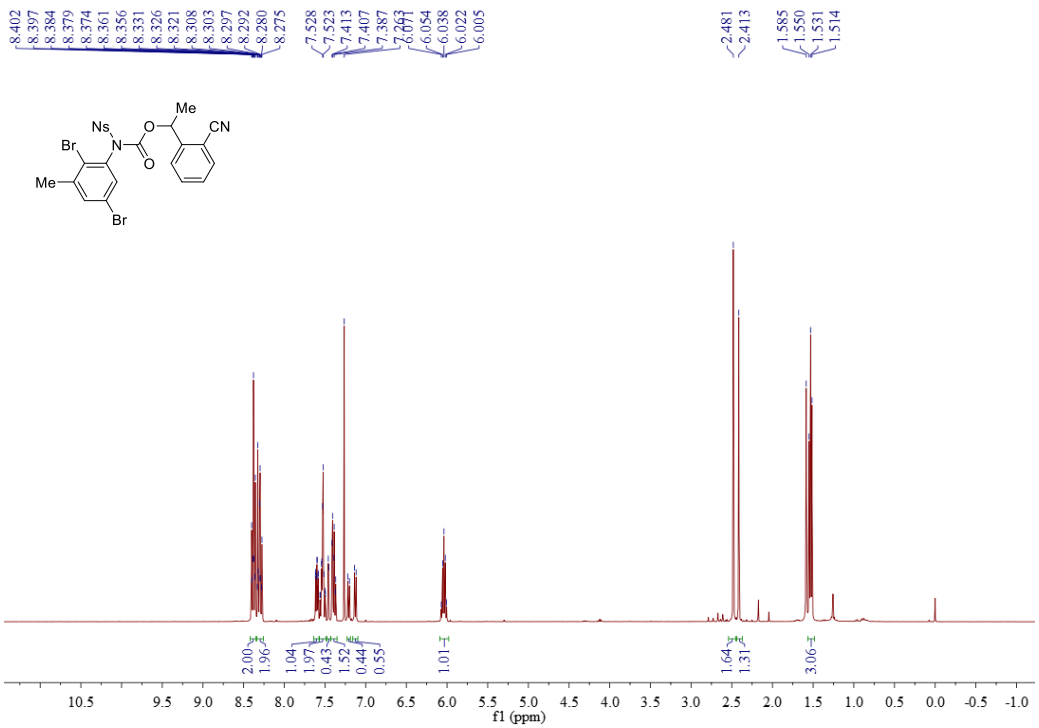


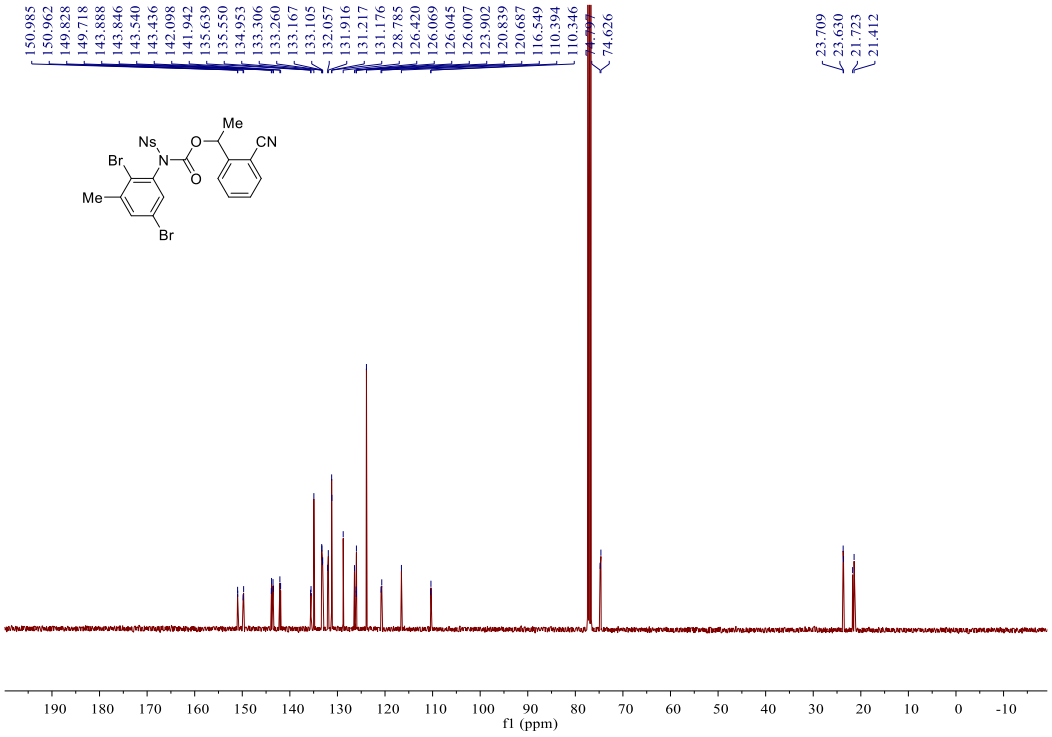
^{1}H and ^{13}C NMR spectra for **2j**



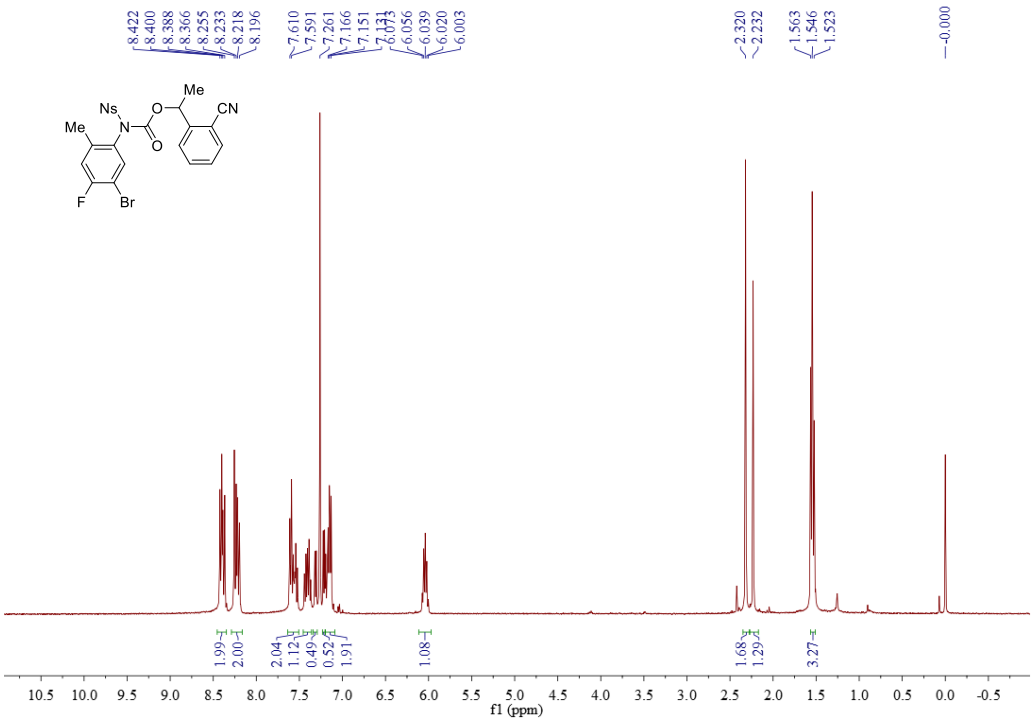


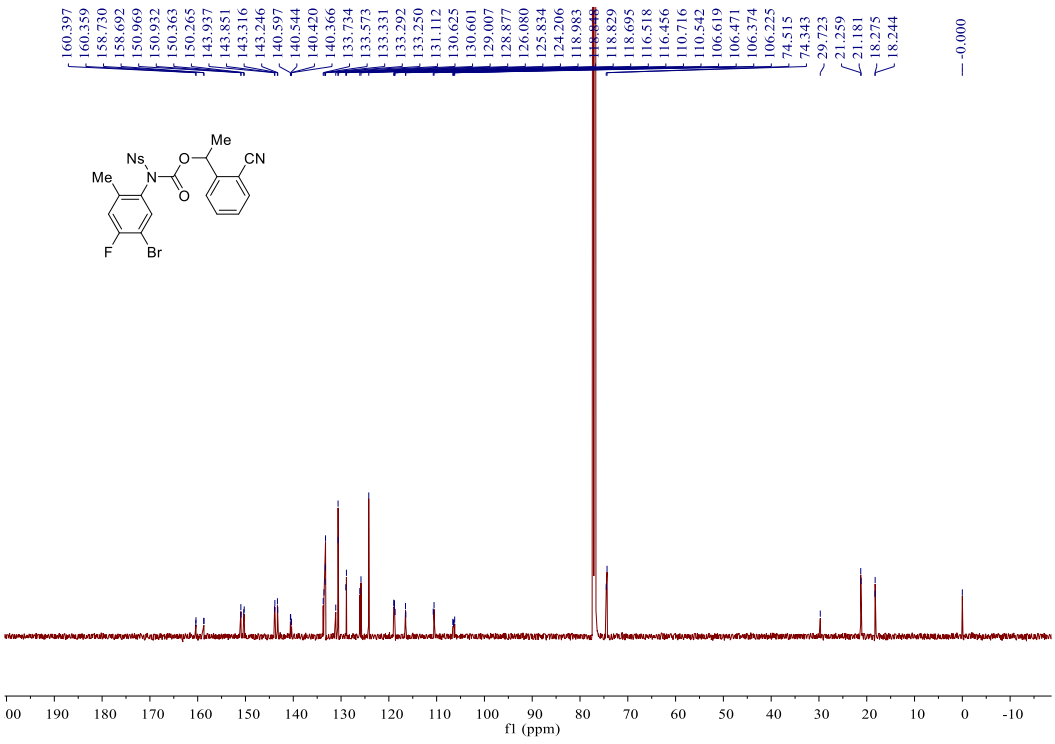
^{1}H and ^{13}C NMR spectra for **2k**



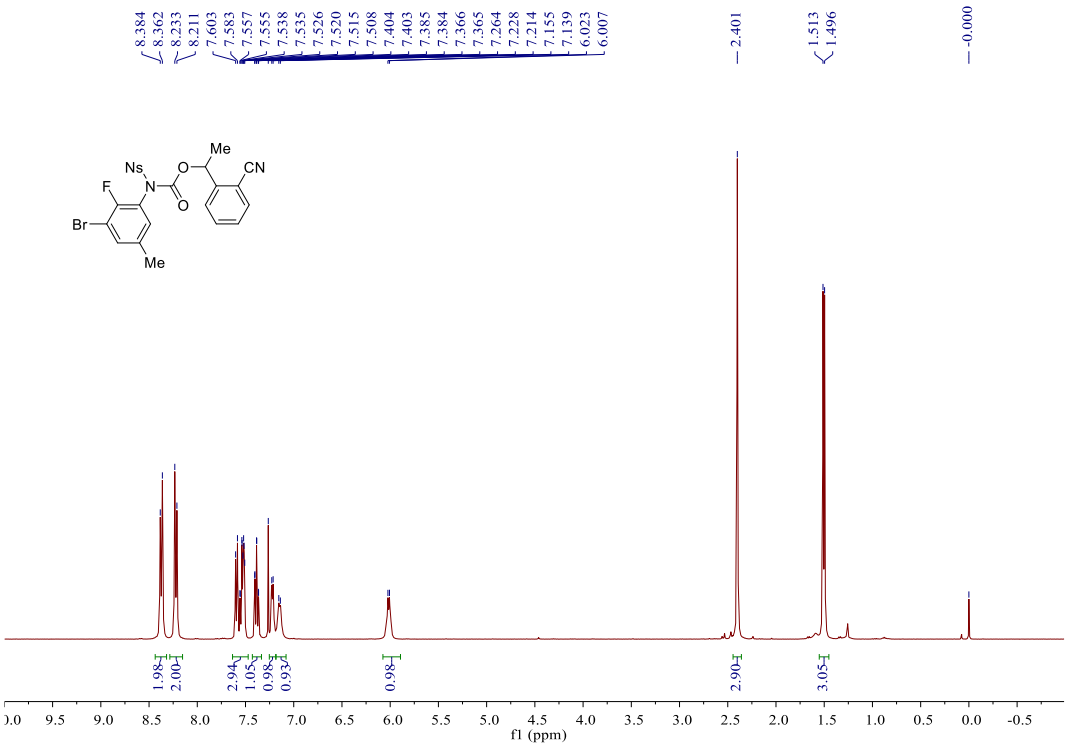


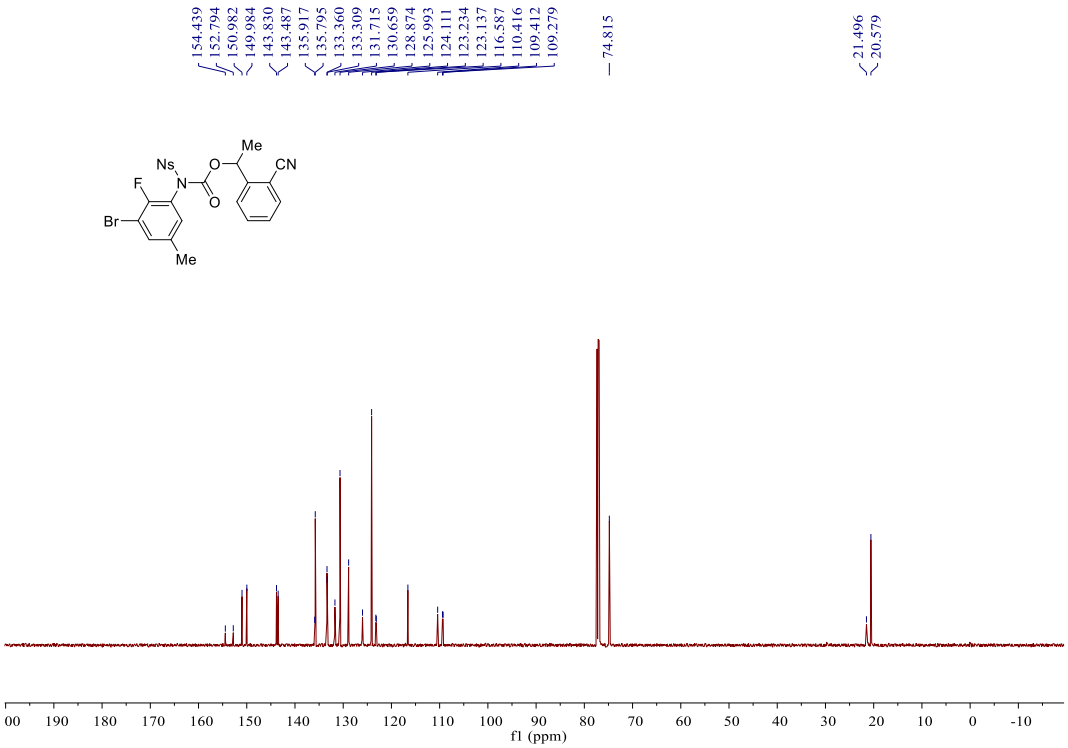
^{1}H and ^{13}C NMR spectra for **2l**



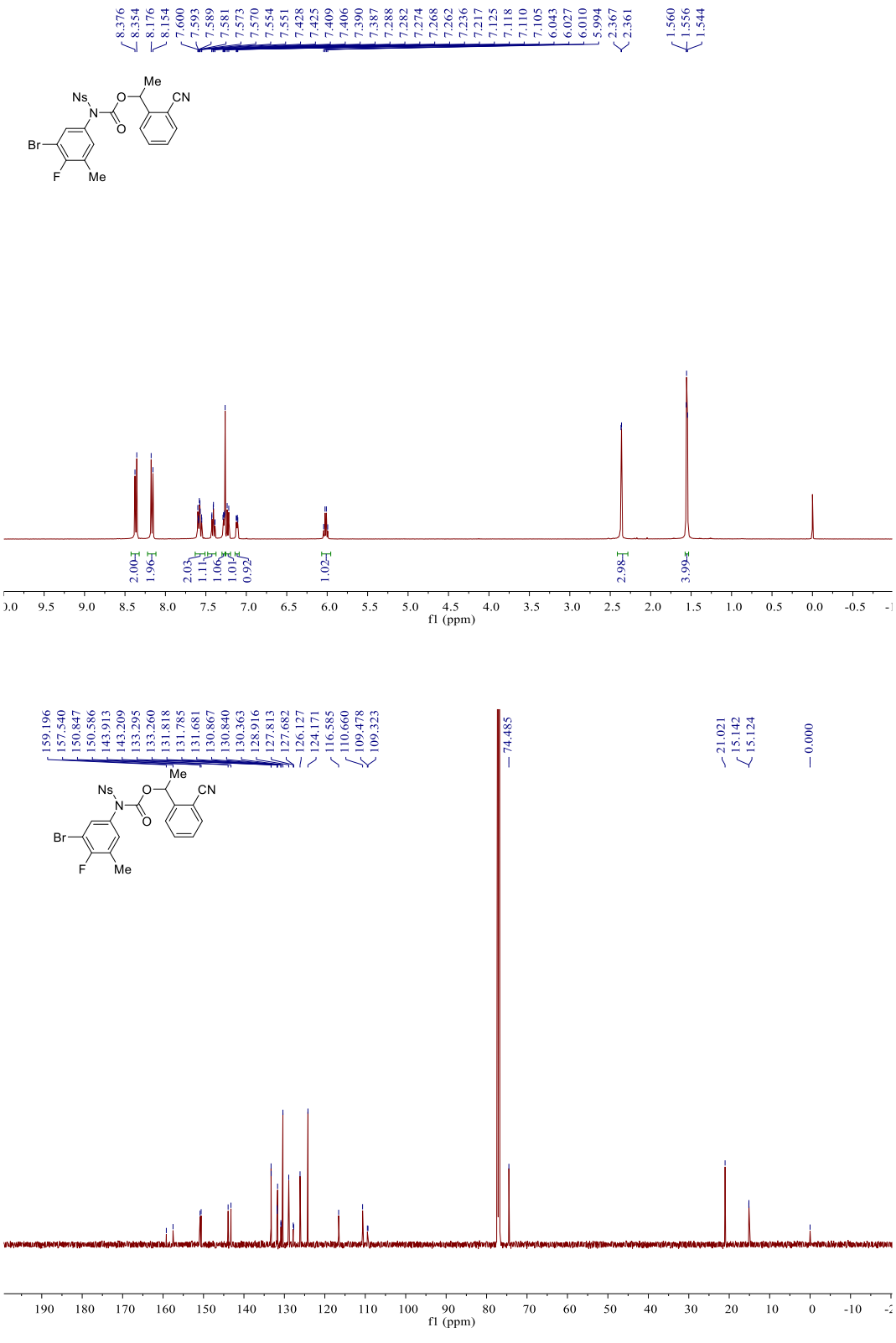


^{1}H and ^{13}C NMR spectra for **2m**

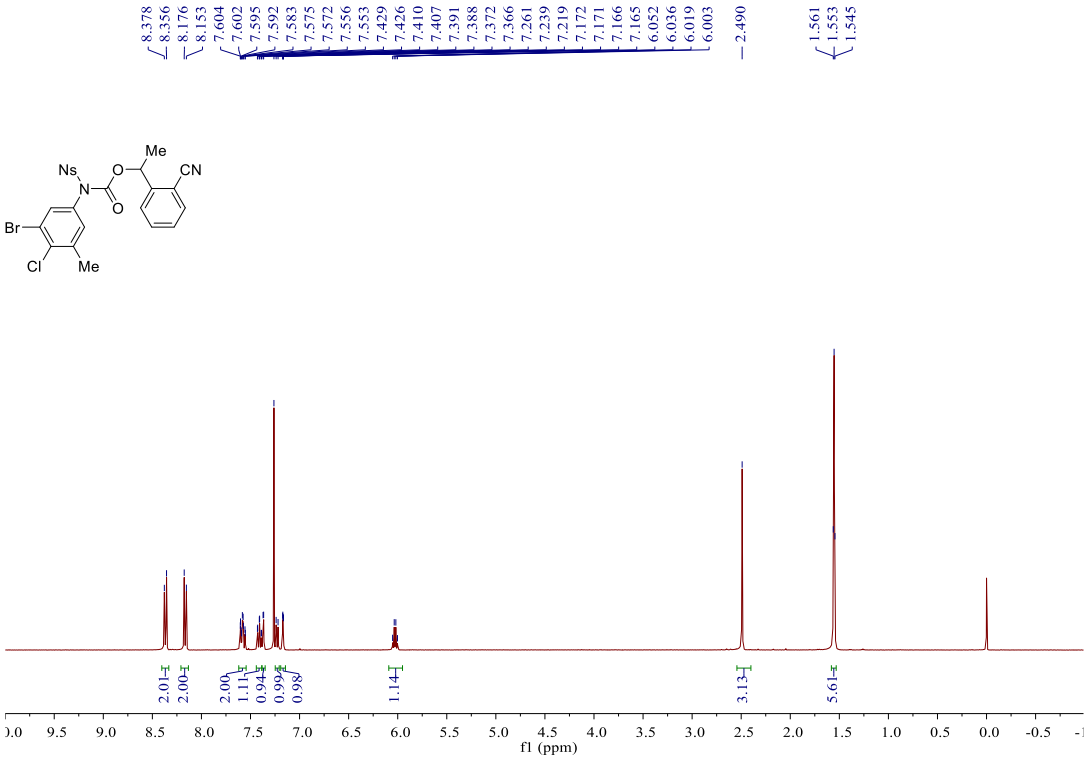


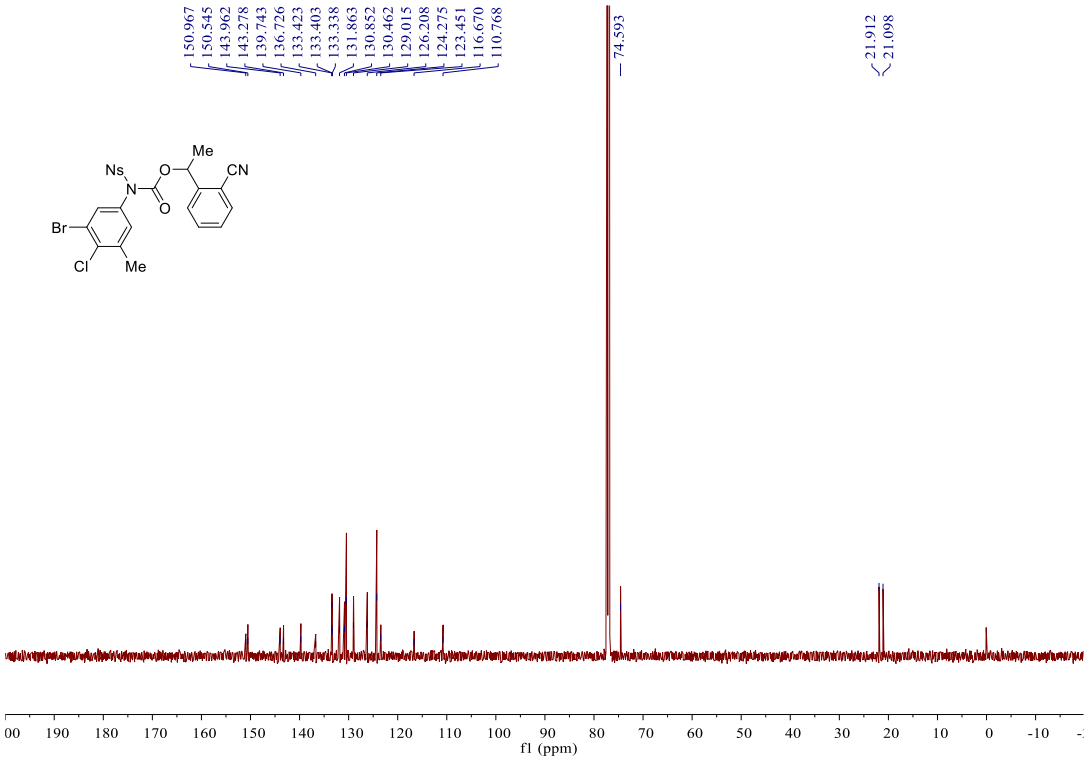


^{1}H and ^{13}C NMR spectra for **2n**

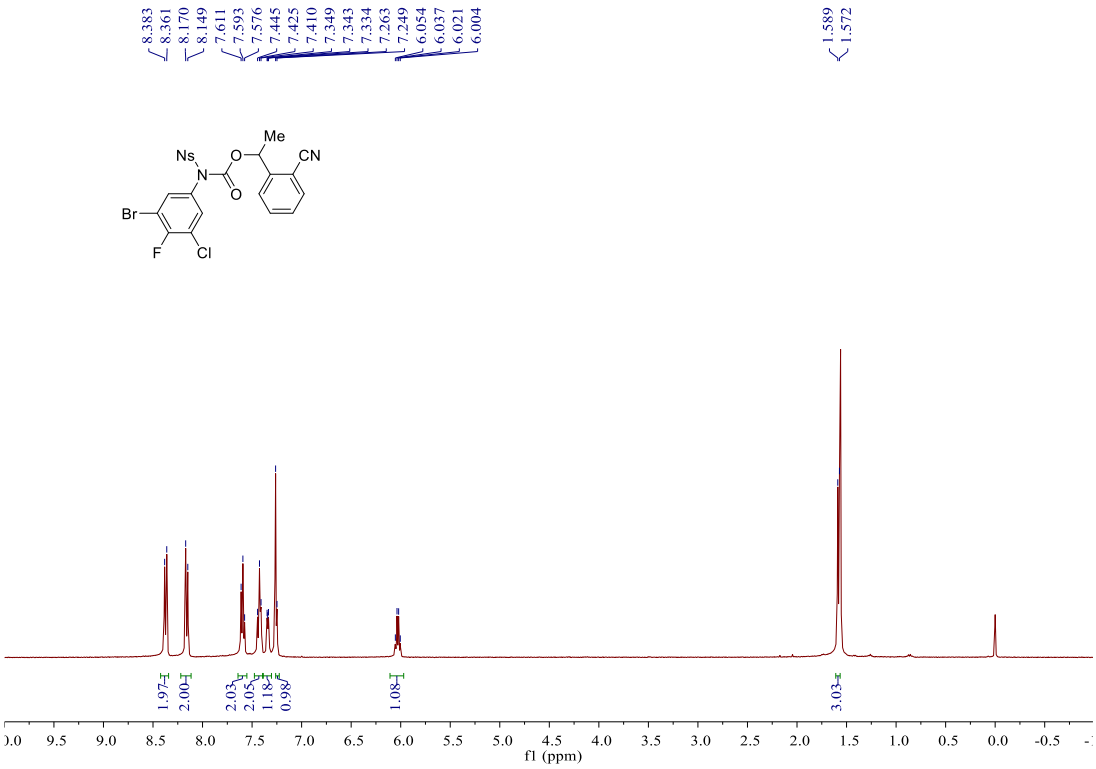


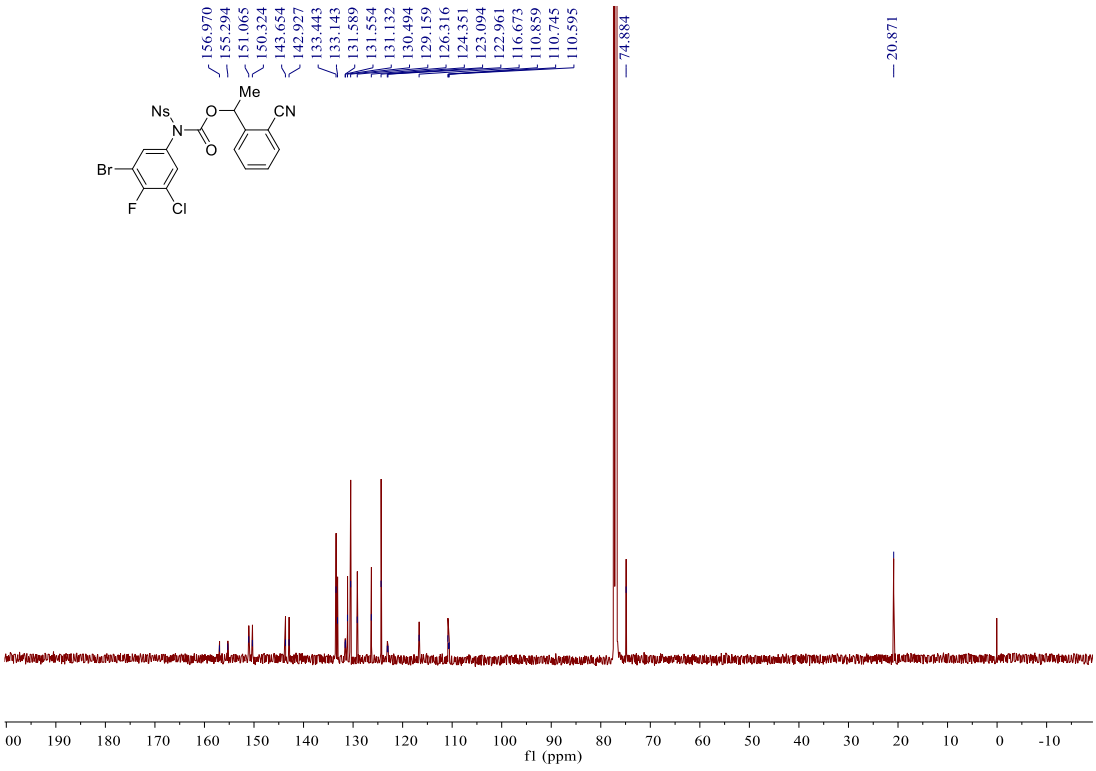
^{1}H and ^{13}C NMR spectra for **2o**



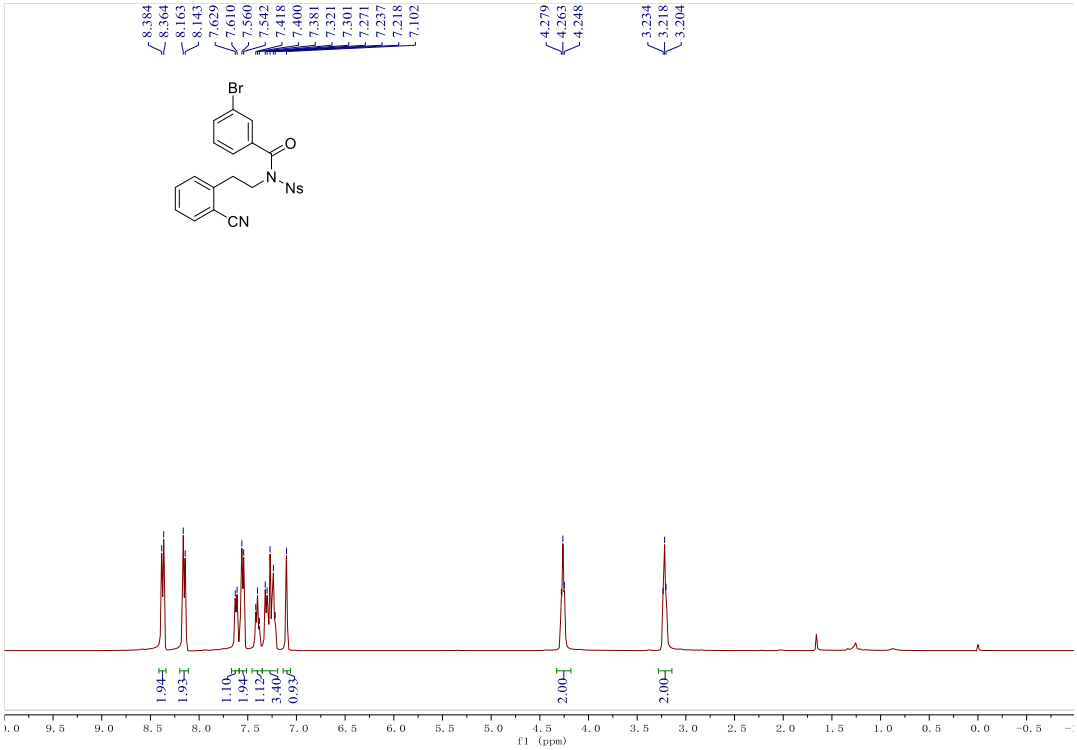


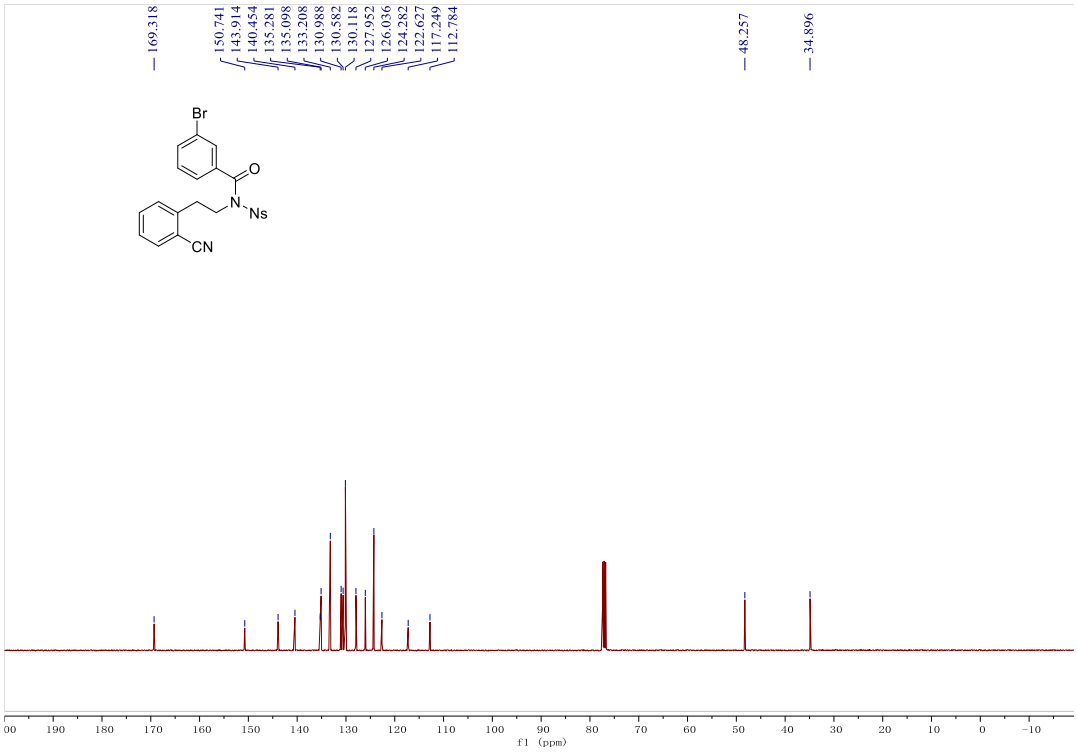
^{1}H and ^{13}C NMR spectra for **2p**



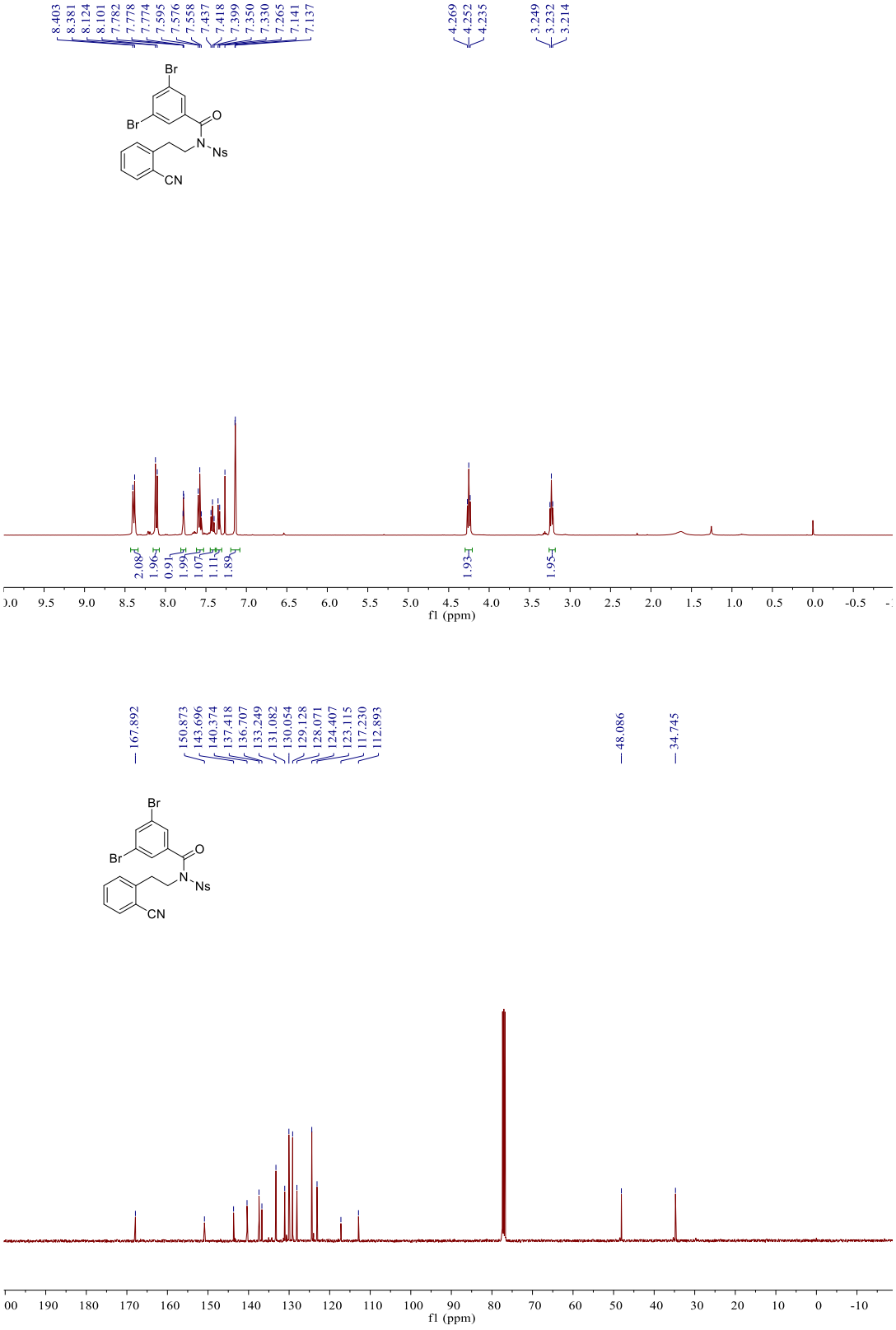


^{1}H and ^{13}C NMR spectra for **2q**

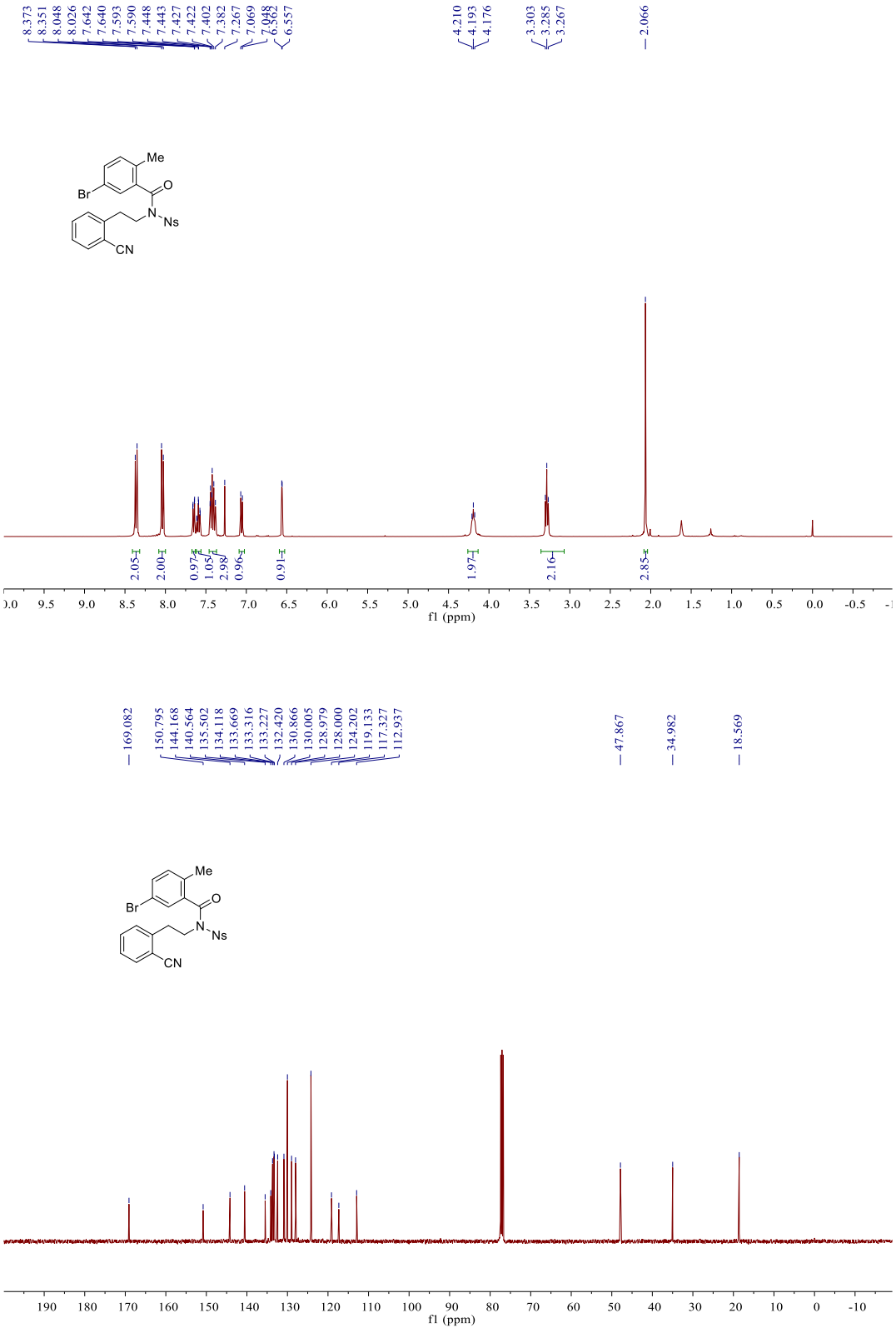




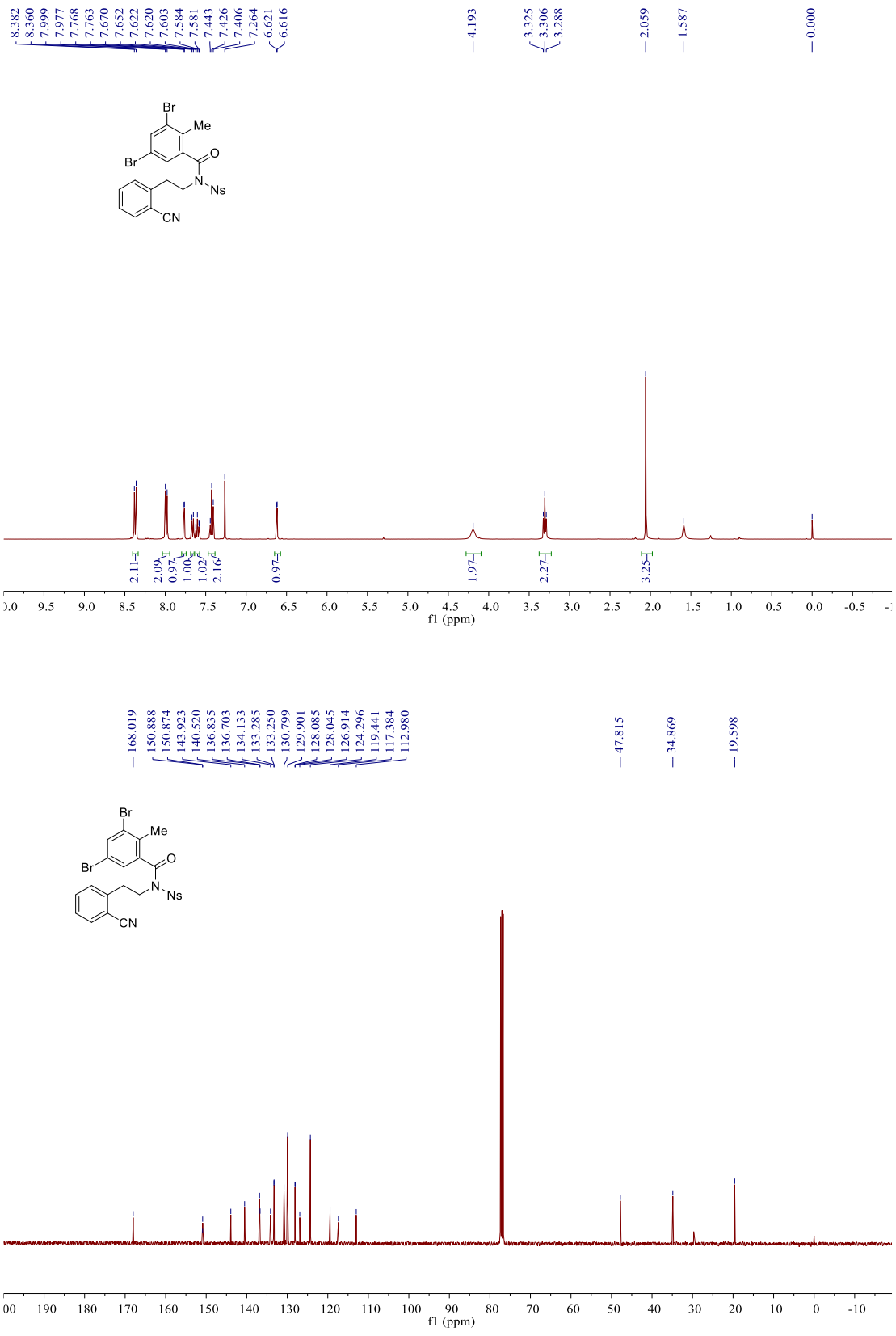
^{1}H and ^{13}C NMR spectra for **4a$_{mono}$**



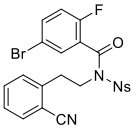
^{1}H and ^{13}C NMR spectra for **4a$_{(m,\ m')di}$**

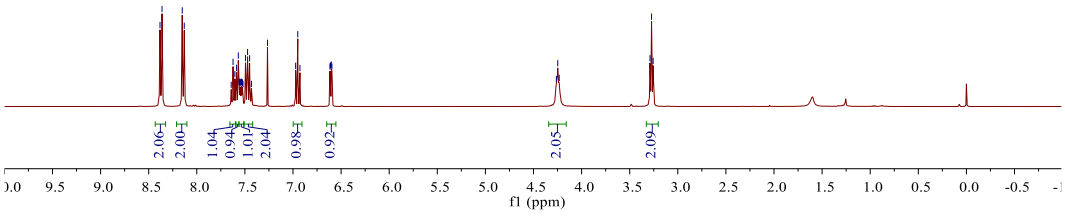


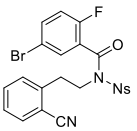
^{1}H and ^{13}C NMR spectra for **4b$_{mono}$**

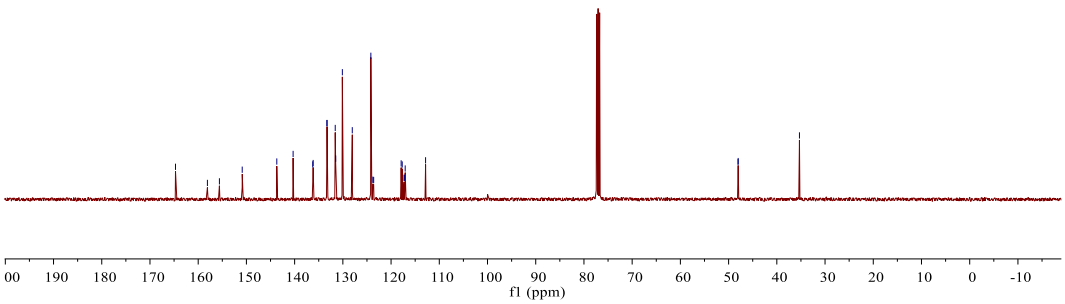


^{1}H and ^{13}C NMR spectra for **4b**$_{\mathbf{(m,\ m')di}}$

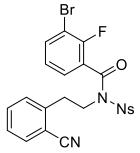


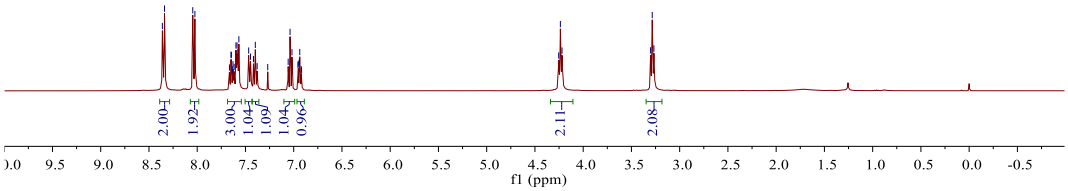


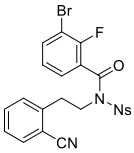


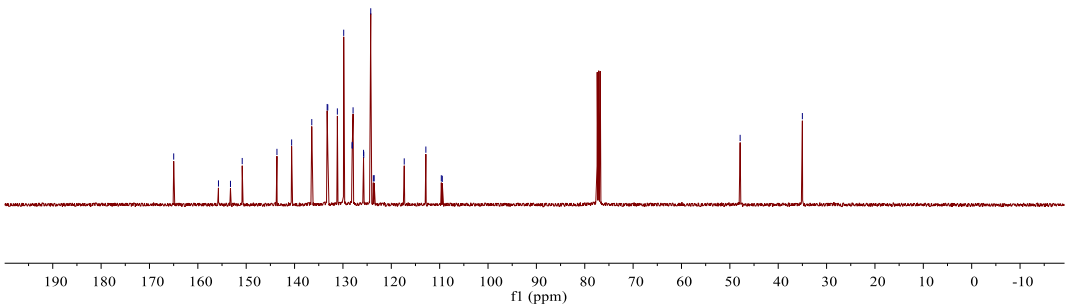


^{1}H and ^{13}C NMR spectra for **4c$_{\text{mono (m)}}$**

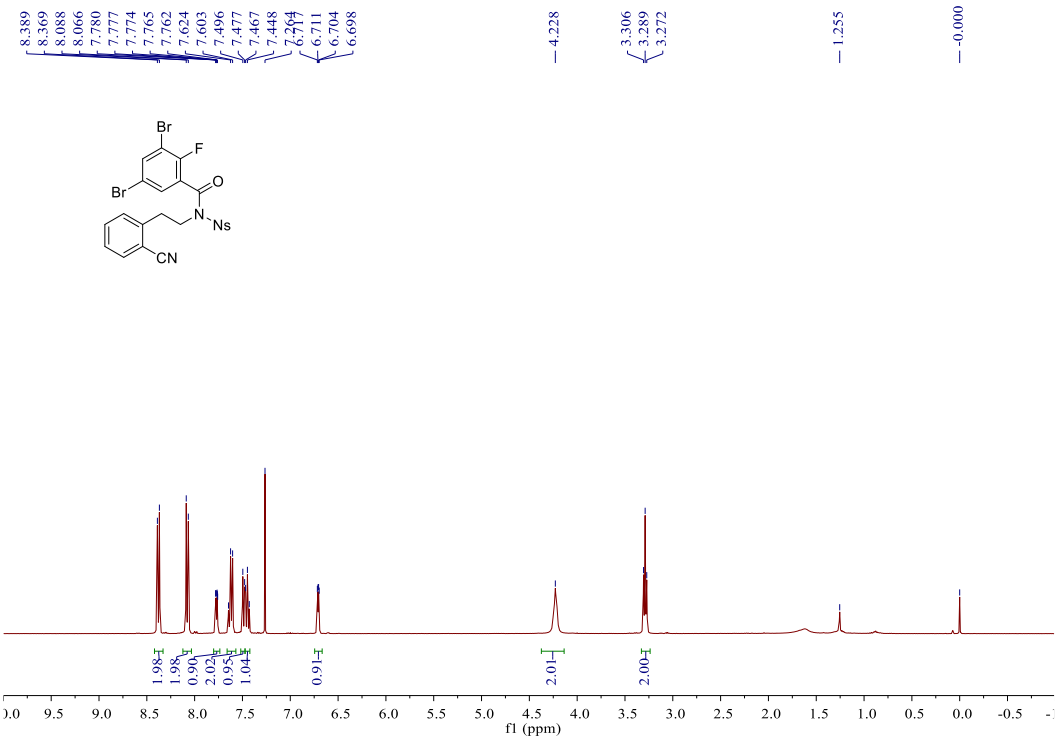


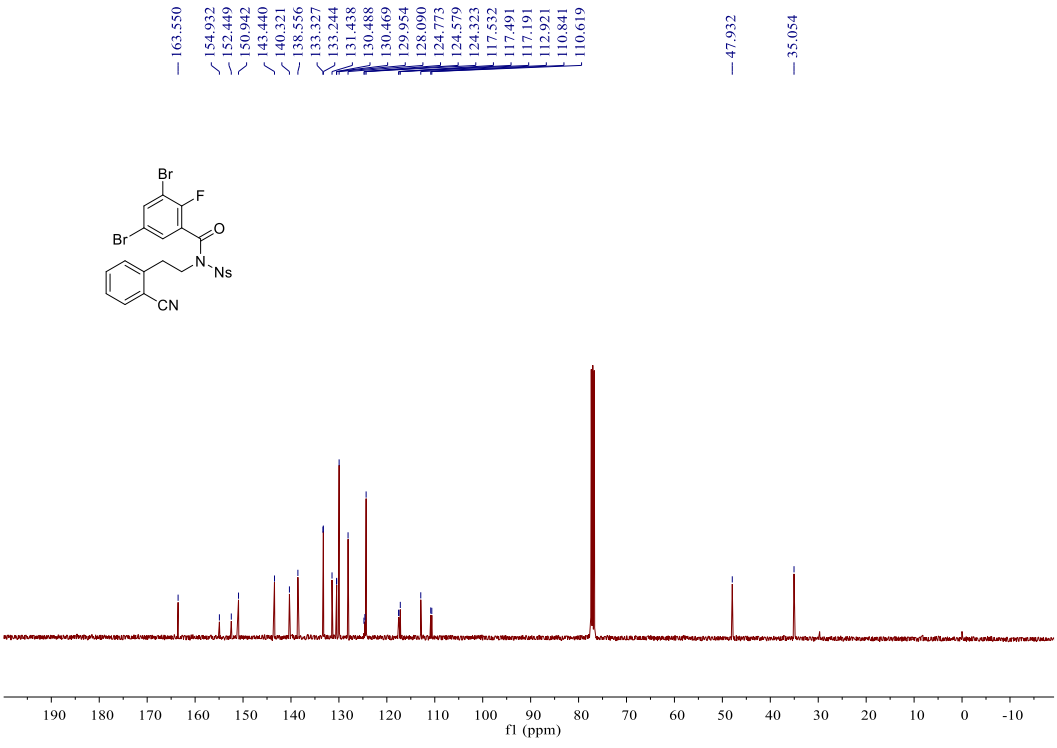




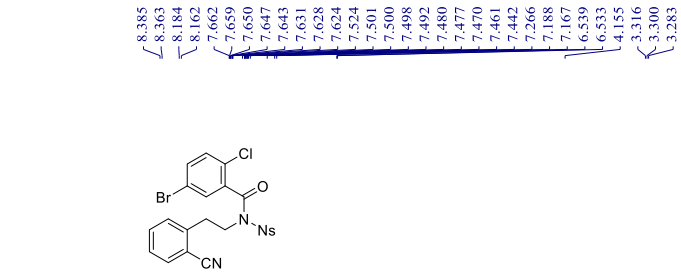


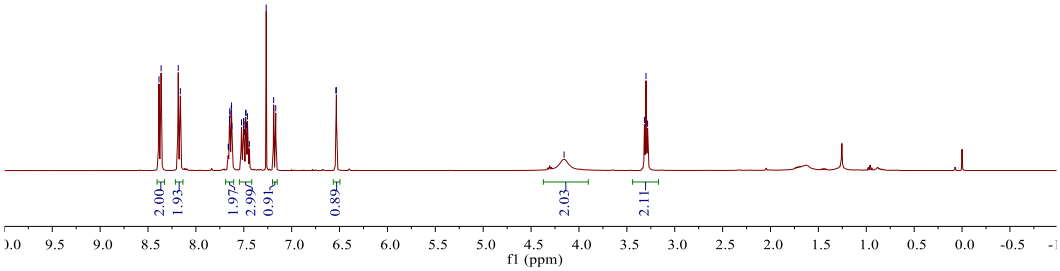
^{1}H and ^{13}C NMR spectra for **4c**$_{\text{mono (m')}}$

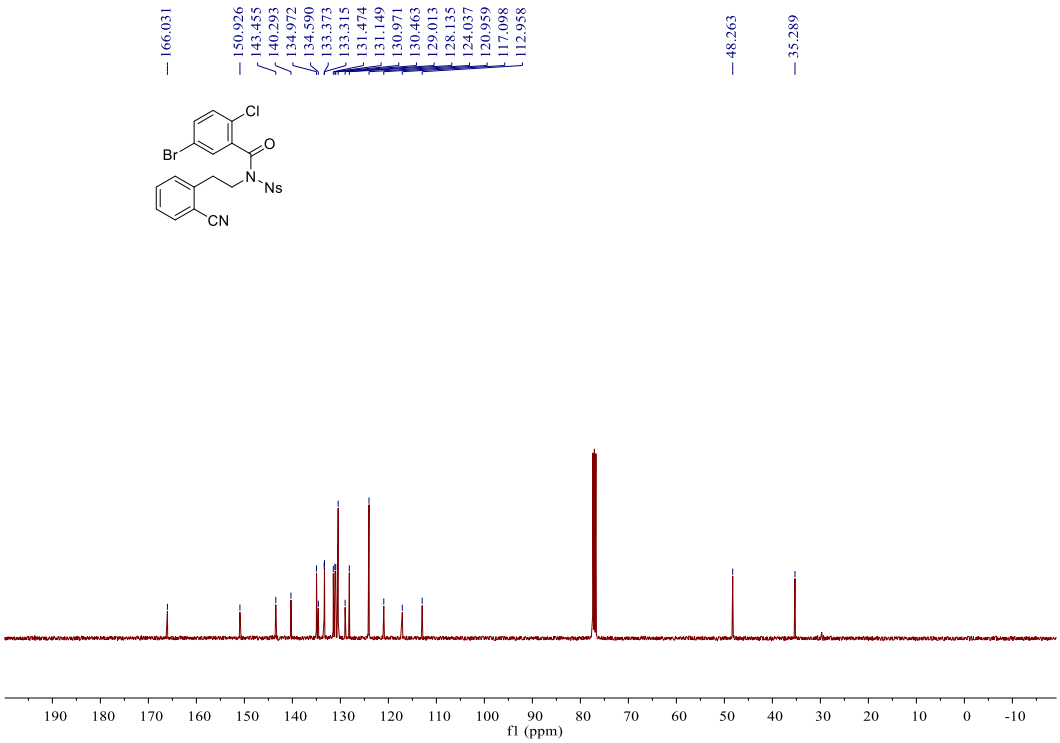




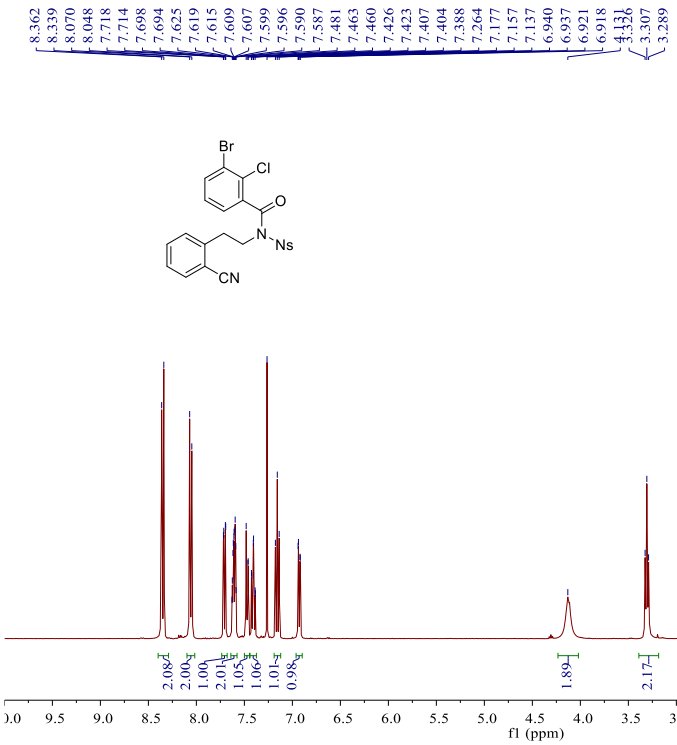
^{1}H and ^{13}C NMR spectra for **4c$_{(m, m')di}$**

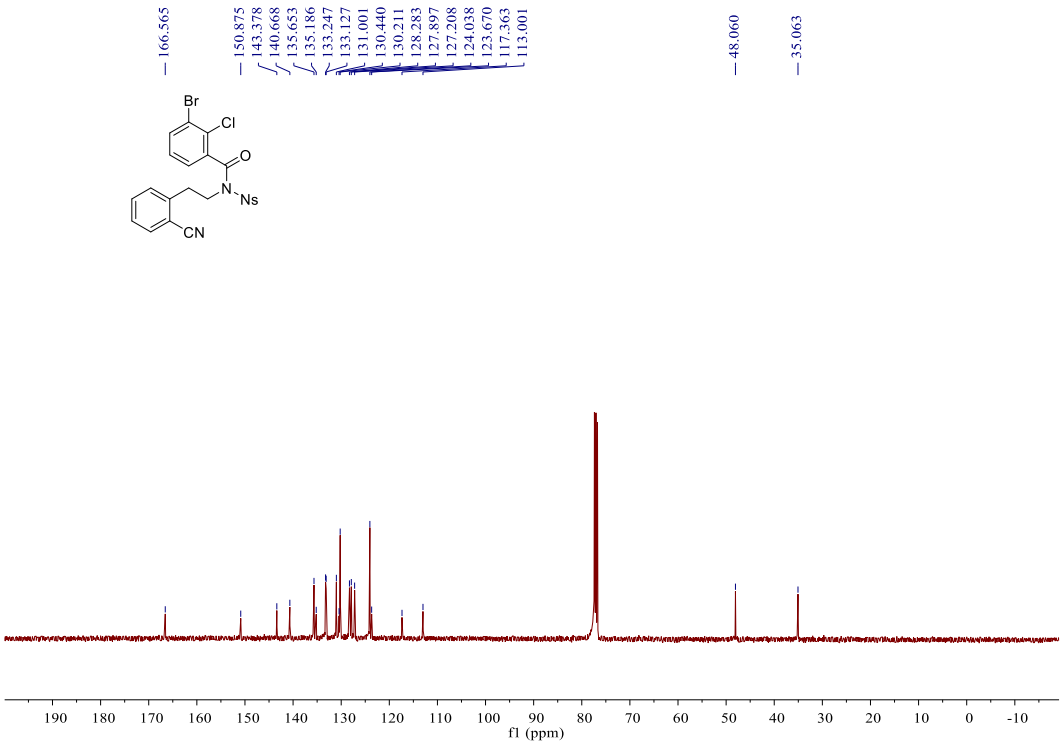




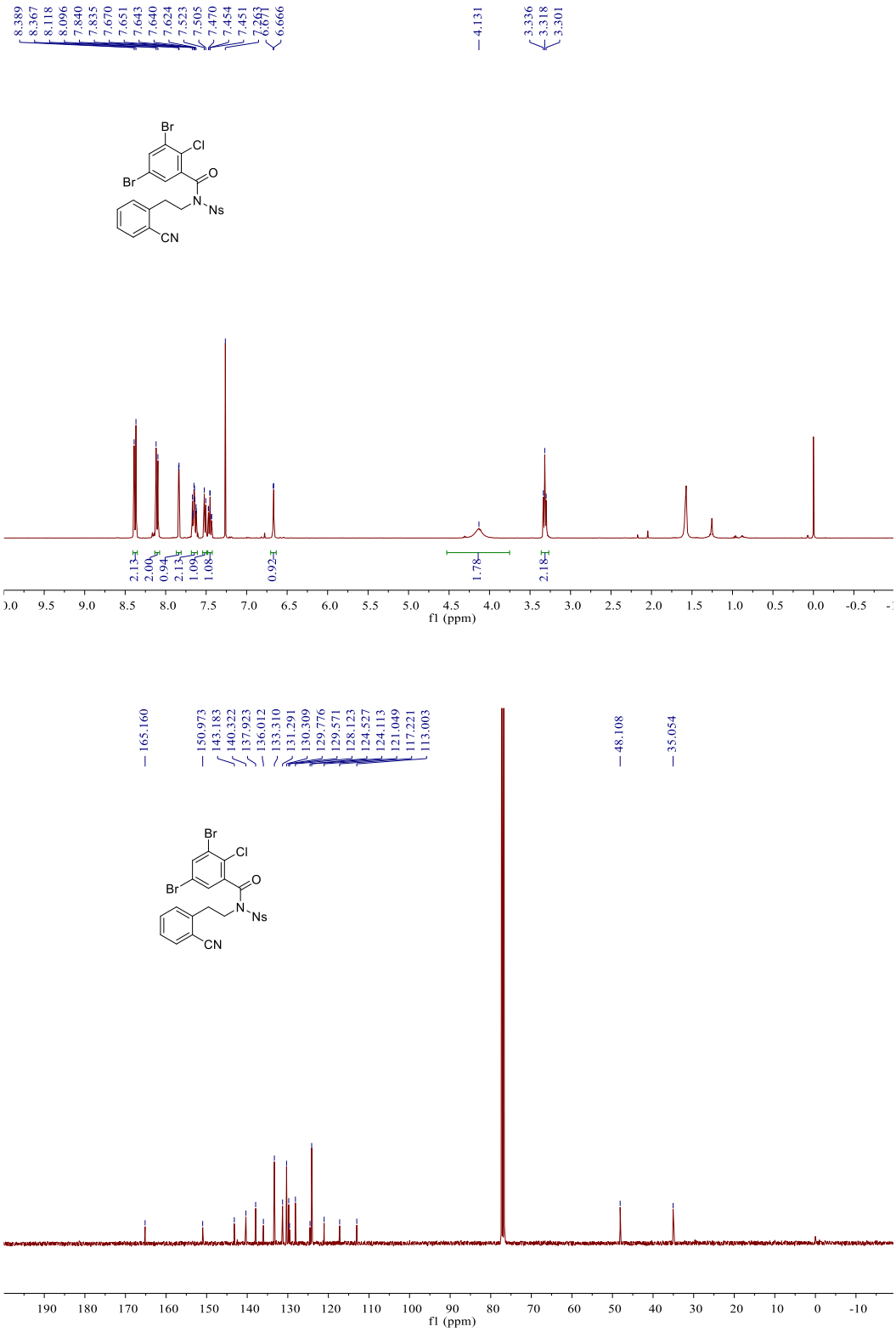


^{1}H and ^{13}C NMR spectra for **4d**$_{\text{mono (m)}}$

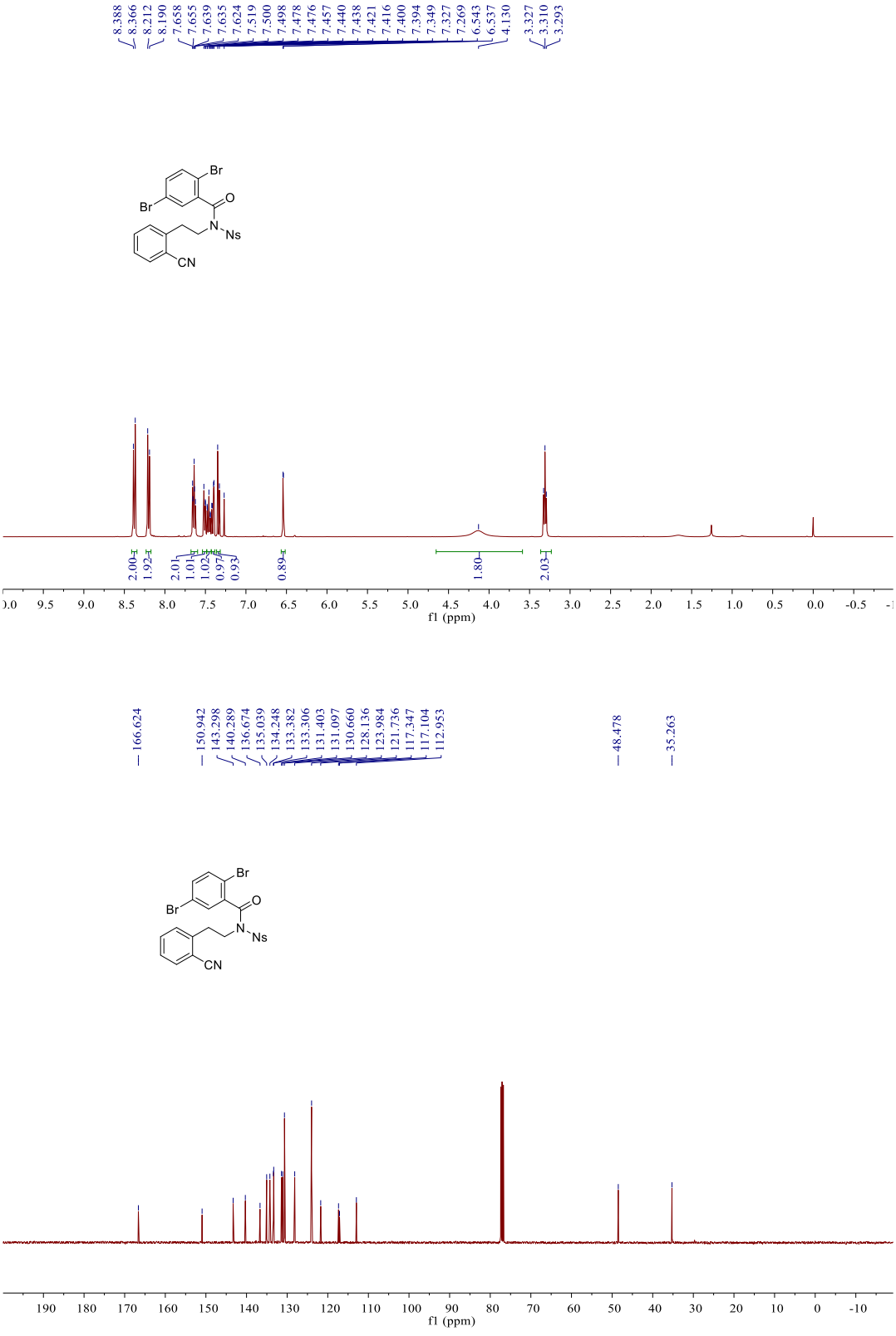




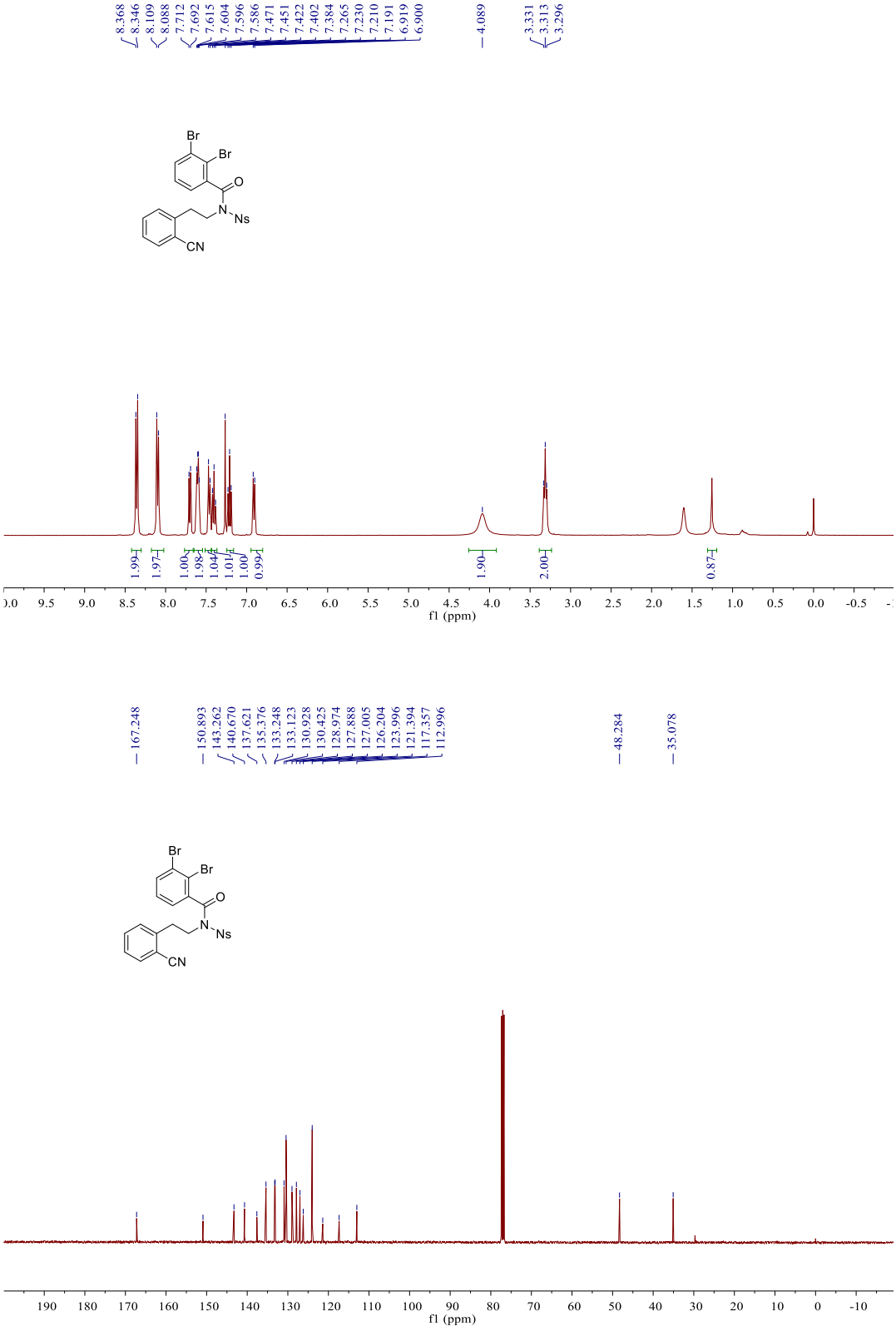
^{1}H and ^{13}C NMR spectra for **4d**$_{\text{mono (m')}}$



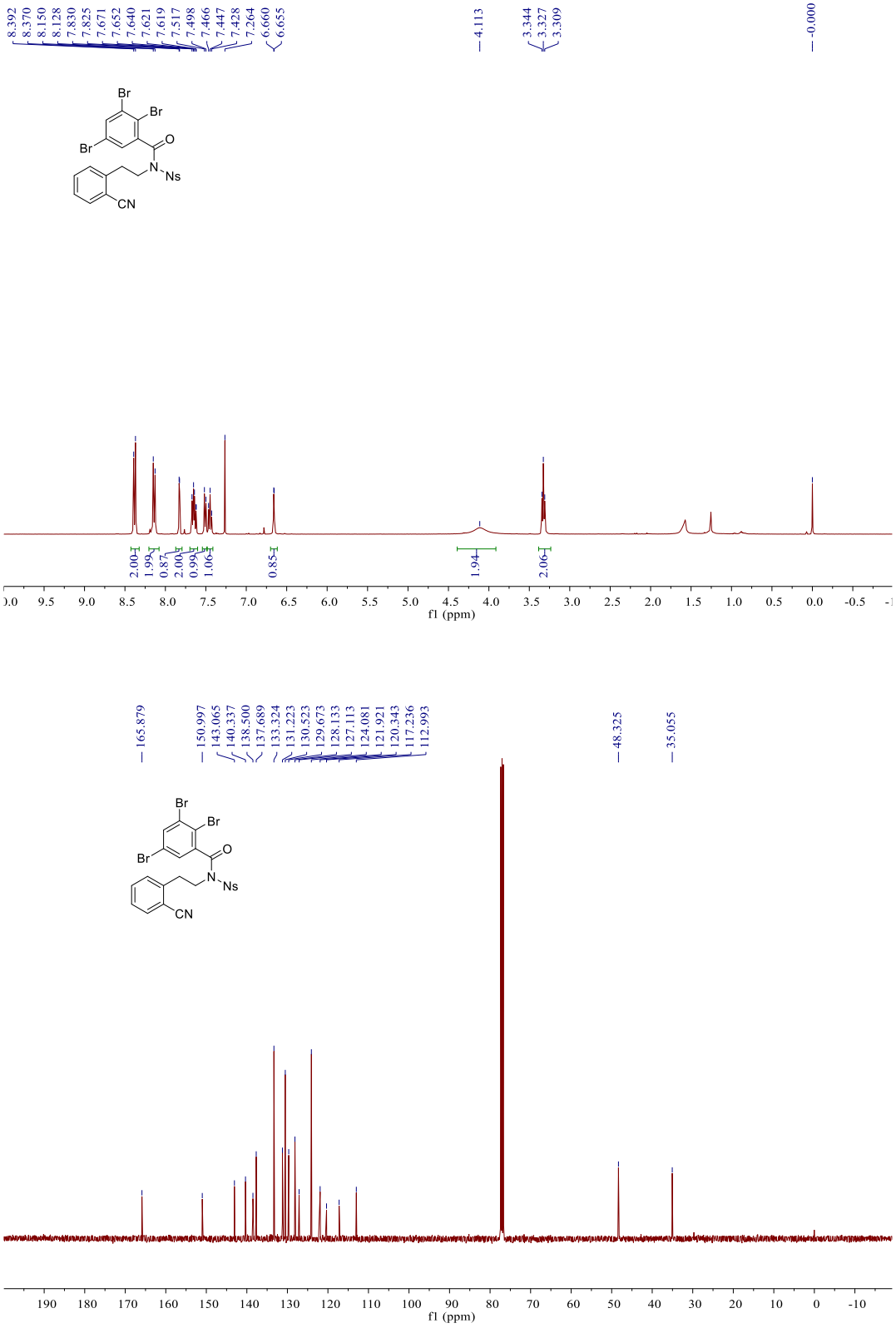
^{1}H and ^{13}C NMR spectra for **4d**$_{(m,\ m')di}$



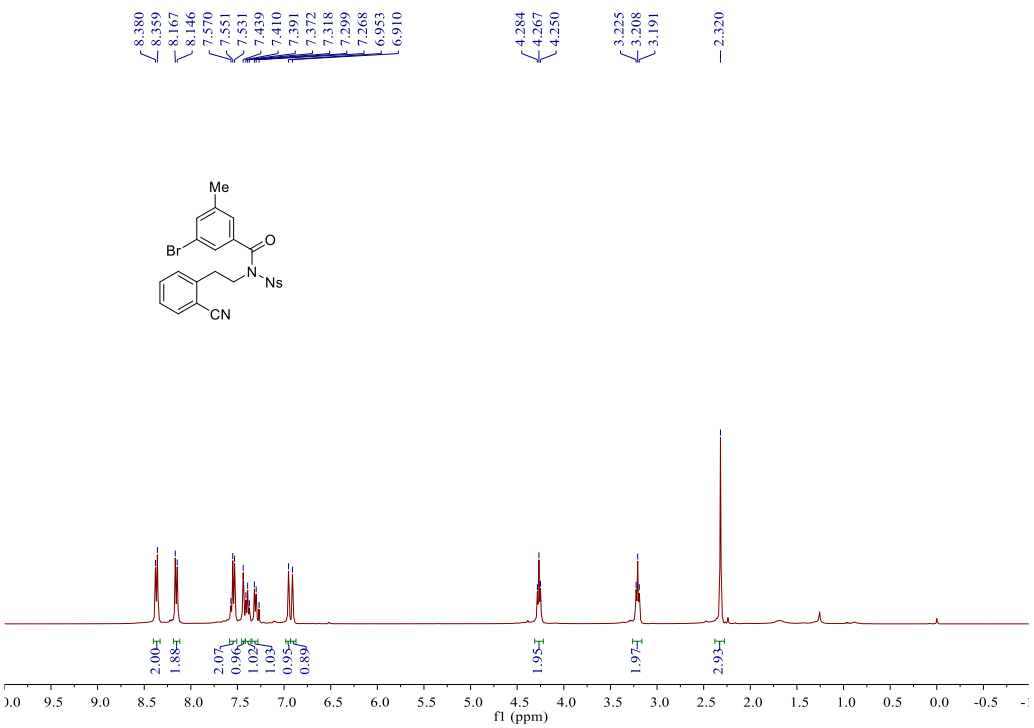
^{1}H and ^{13}C NMR spectra for **4e**$_{\text{mono (m)}}$

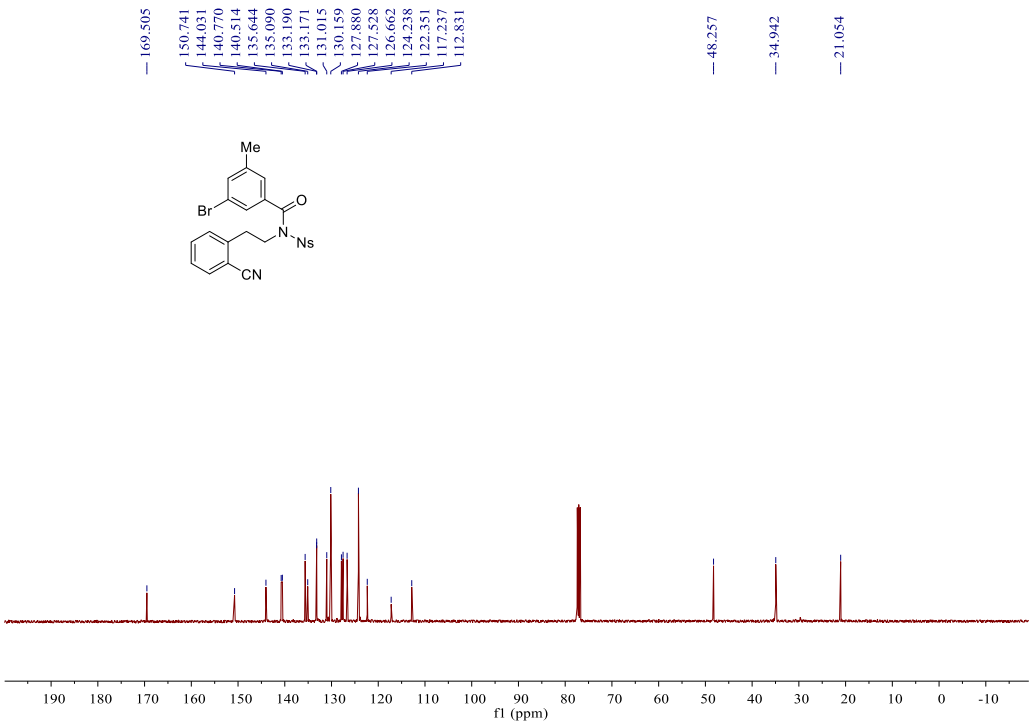


^{1}H and ^{13}C NMR spectra for **4e**$_{\text{mono (m')}}$

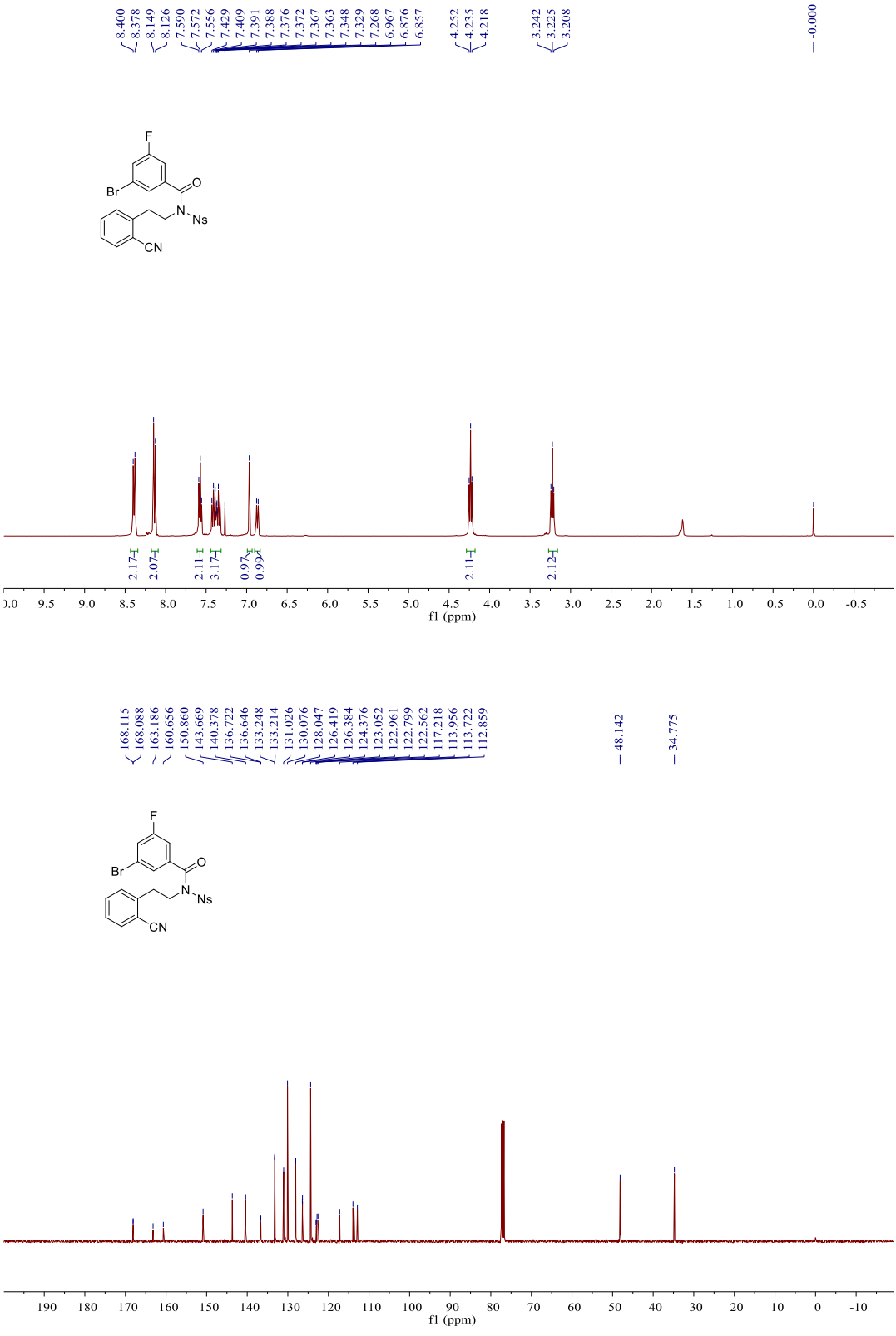


^{1}H and ^{13}C NMR spectra for **4e**$_{\textbf{(m, m')di}}$

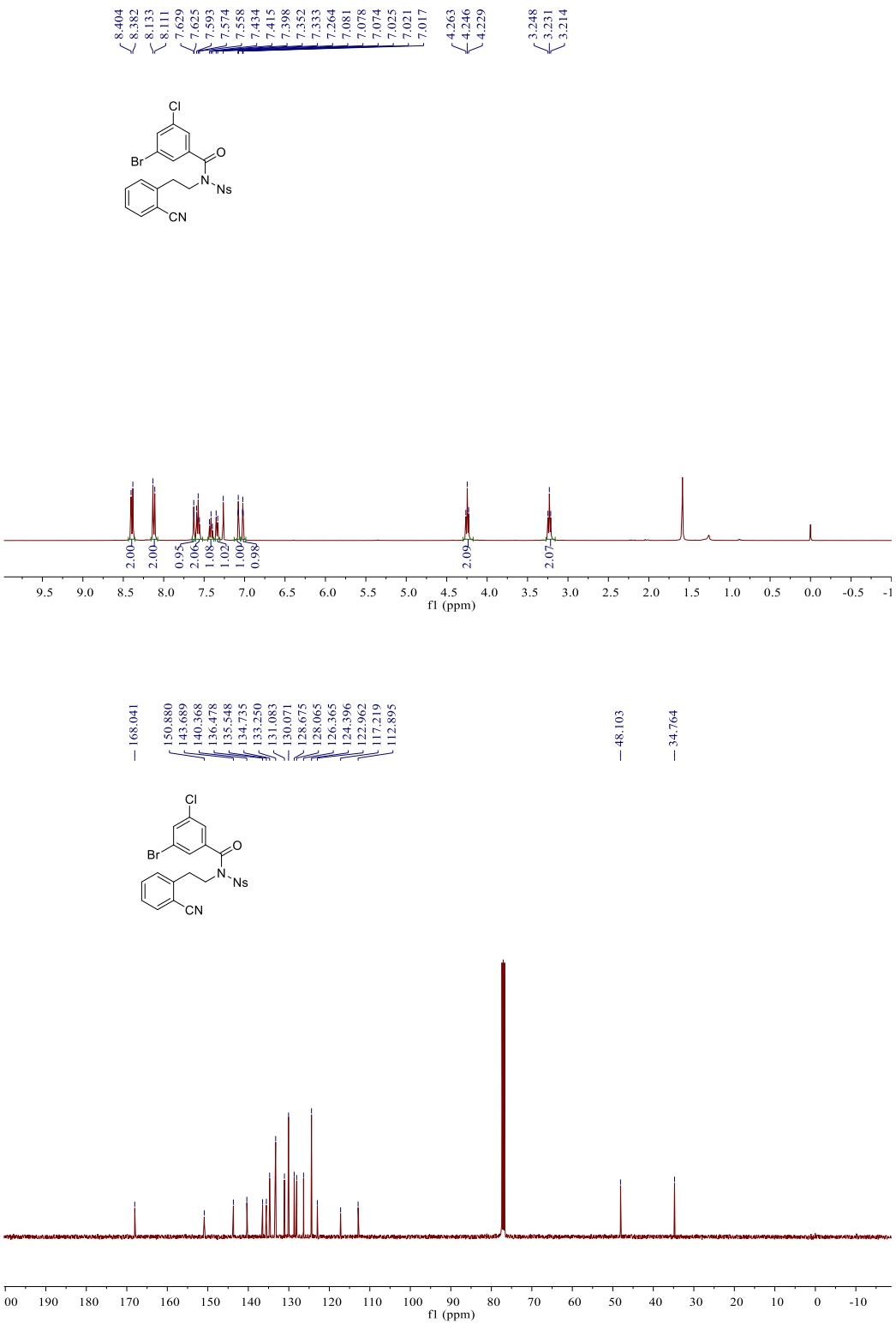




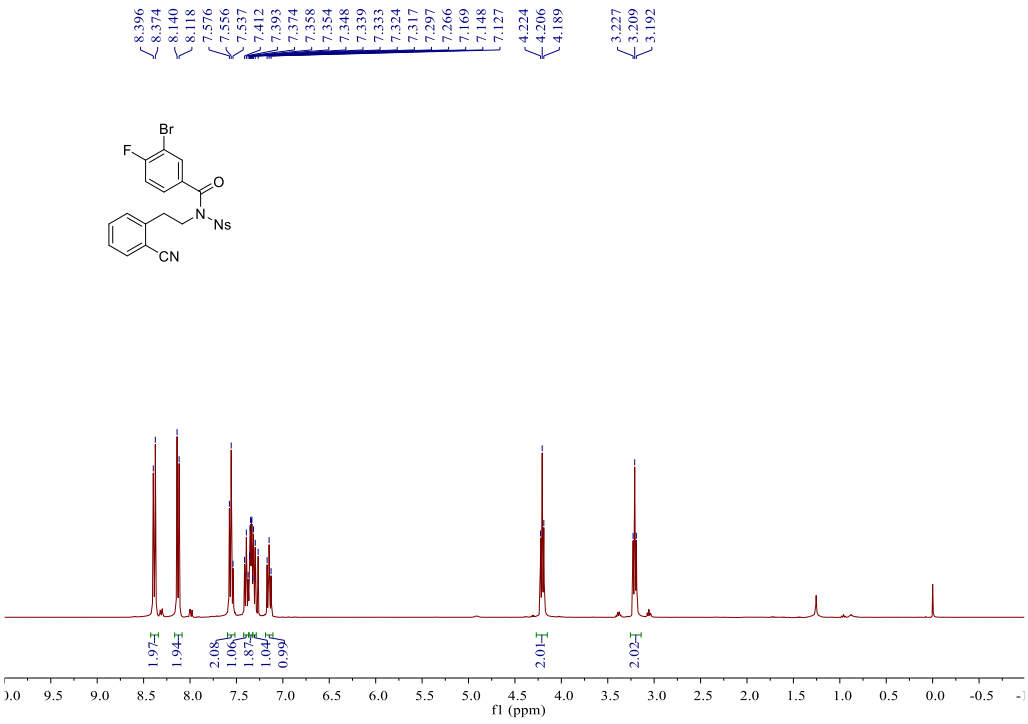
^{1}H and ^{13}C NMR spectra for **4f**

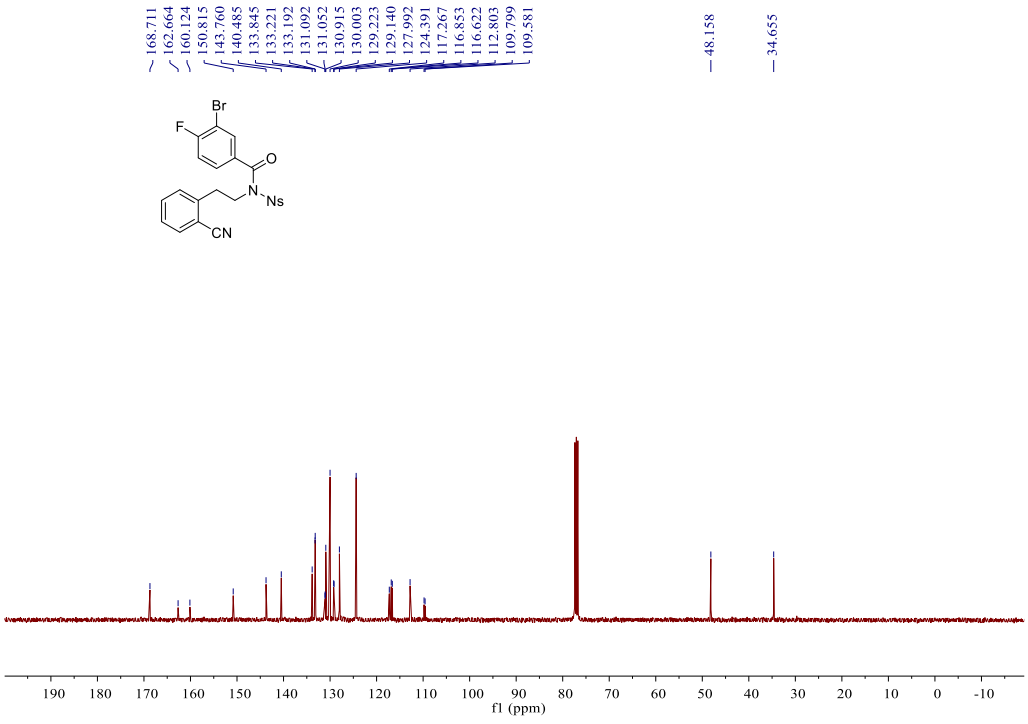


^{1}H and ^{13}C NMR spectra for **4g**

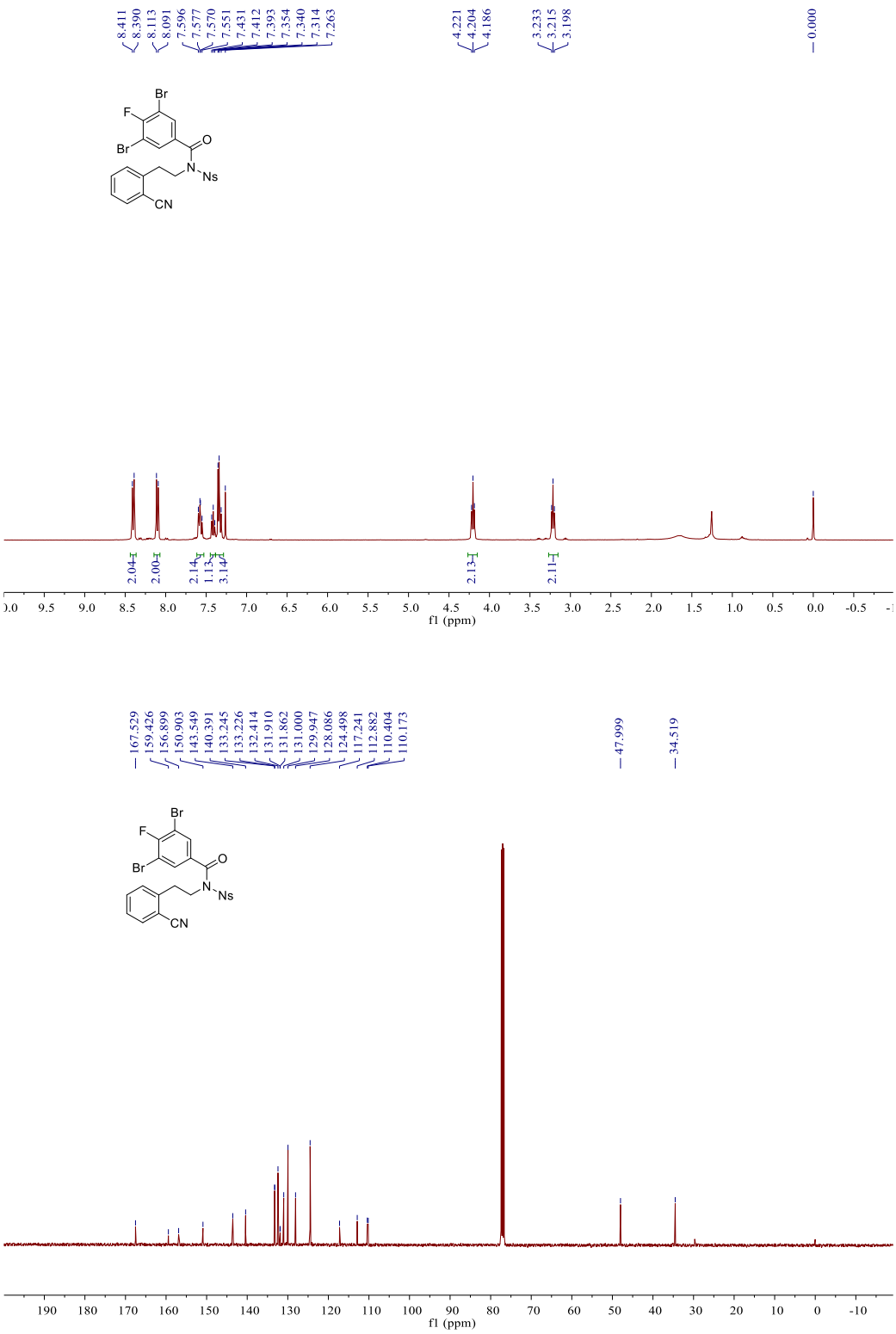


^{1}H and ^{13}C NMR spectra for **4h**

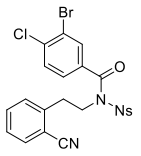


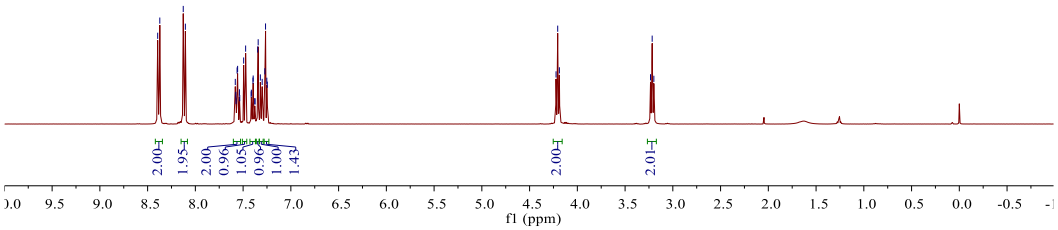


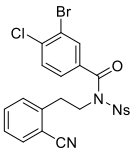
^{1}H and ^{13}C NMR spectra for **4i$_{mono}$**

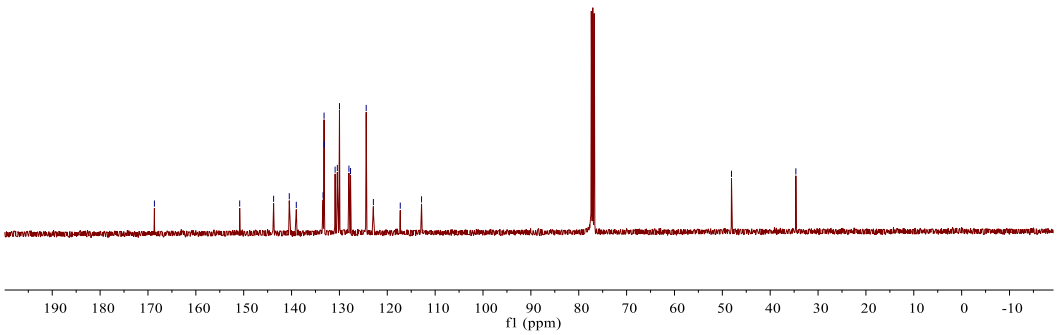


^{1}H and ^{13}C NMR spectra for **4i$_{(m,\ m')di}$**

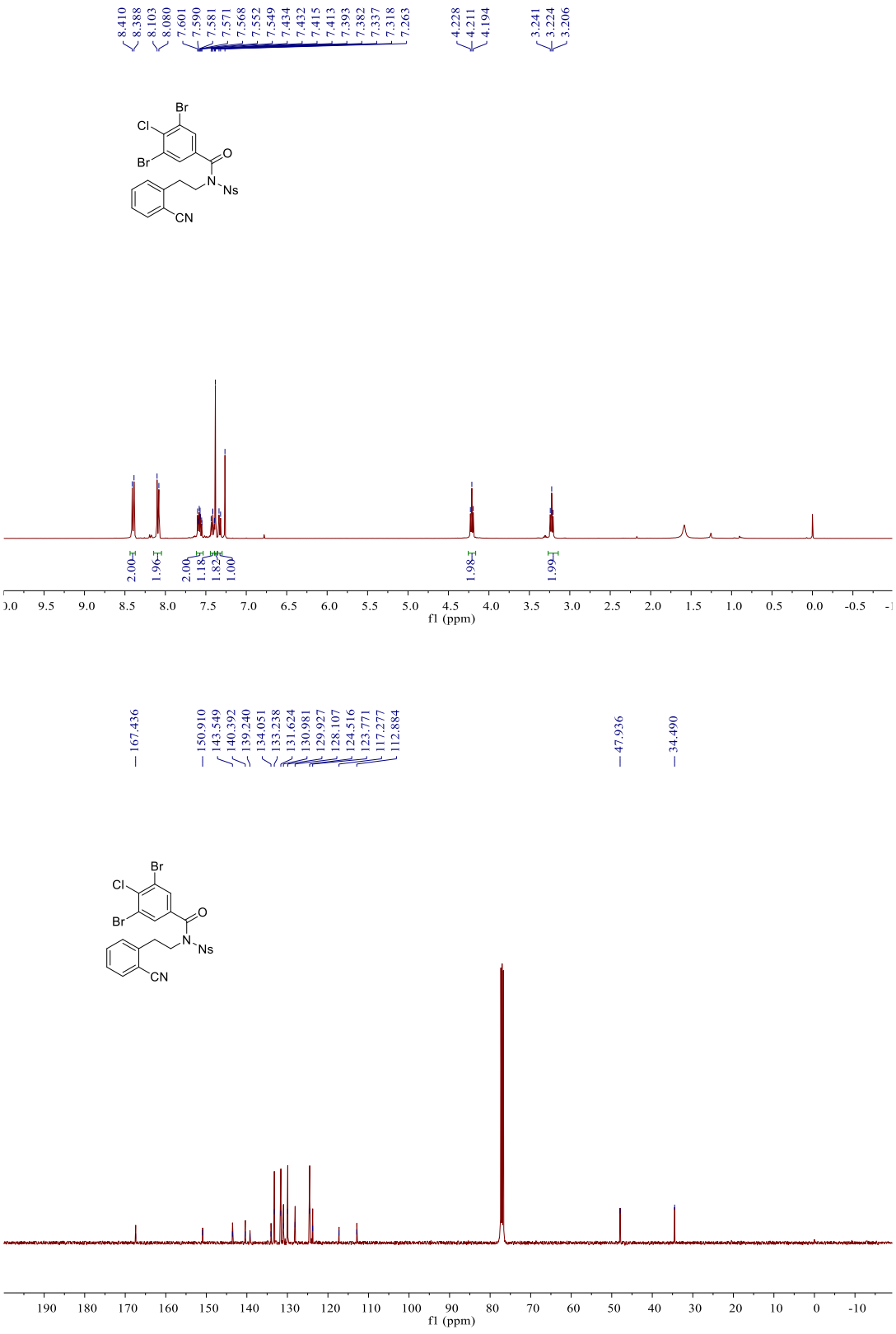




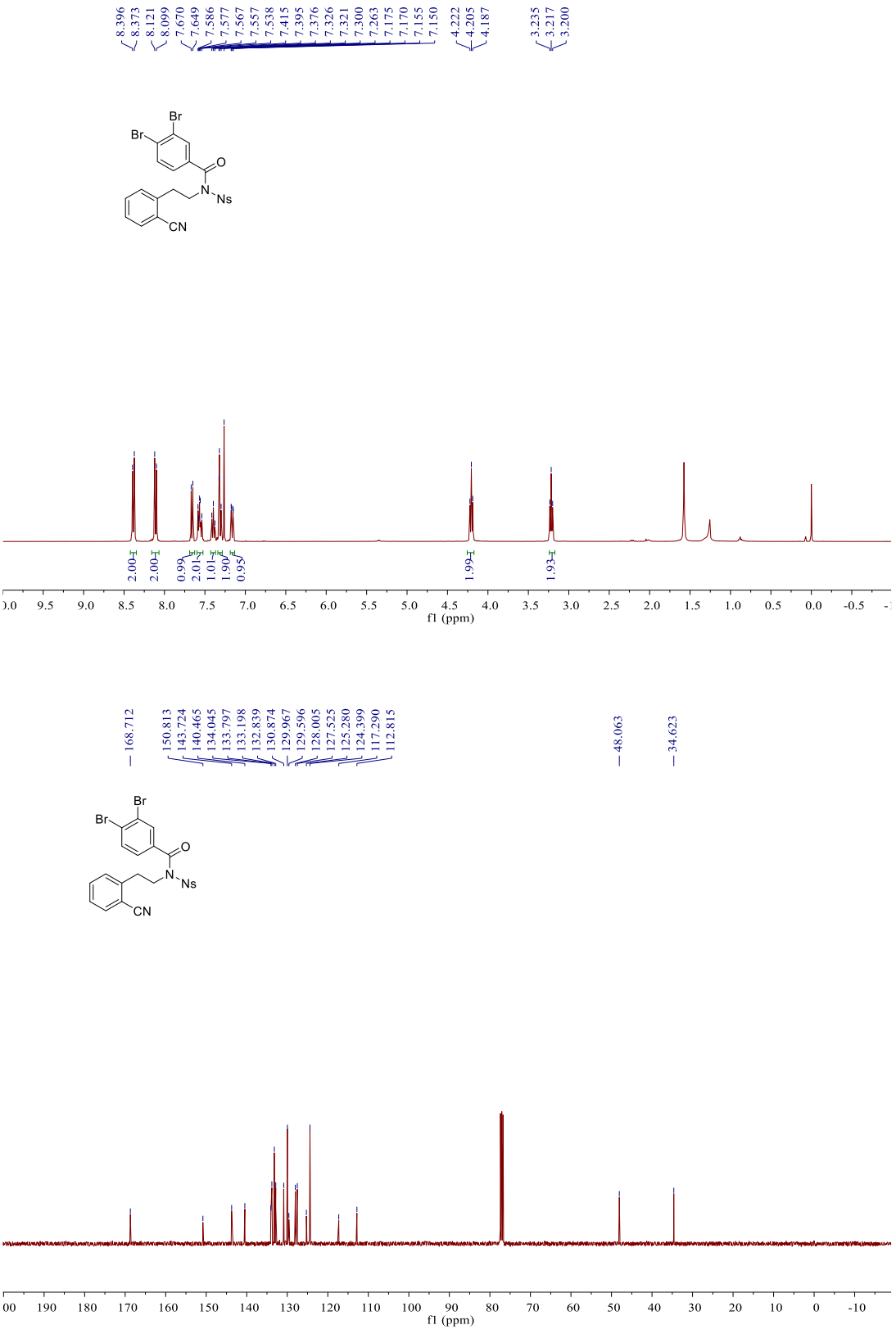




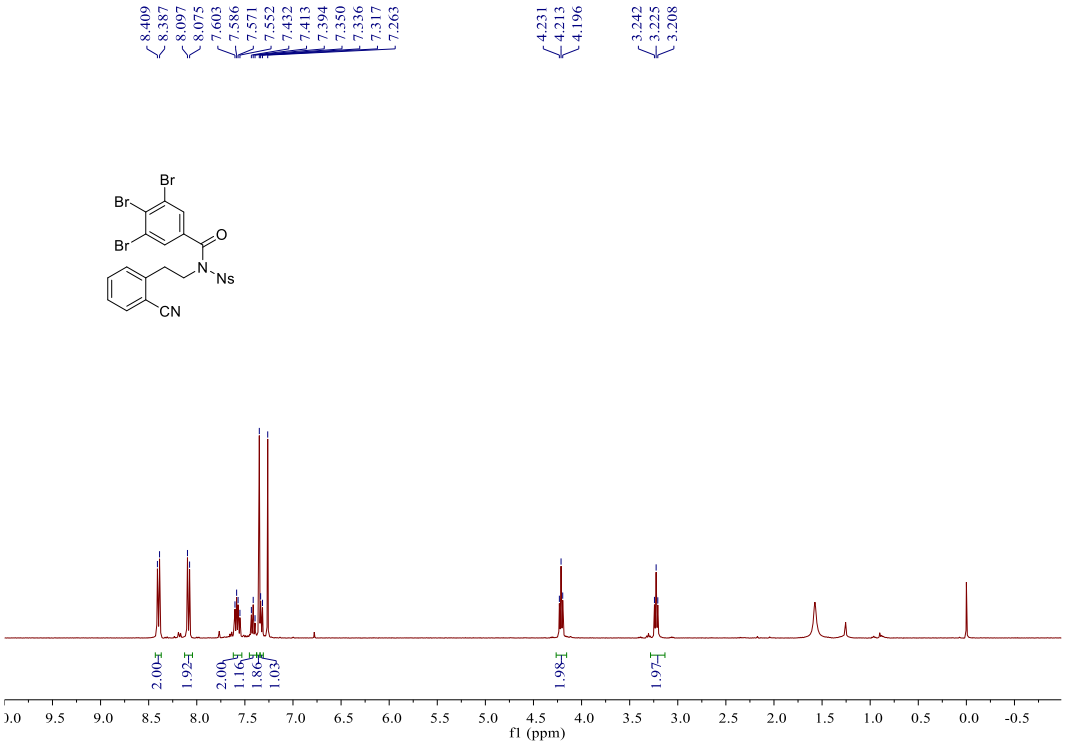
^{1}H and ^{13}C NMR spectra for **4j$_{mono}$**

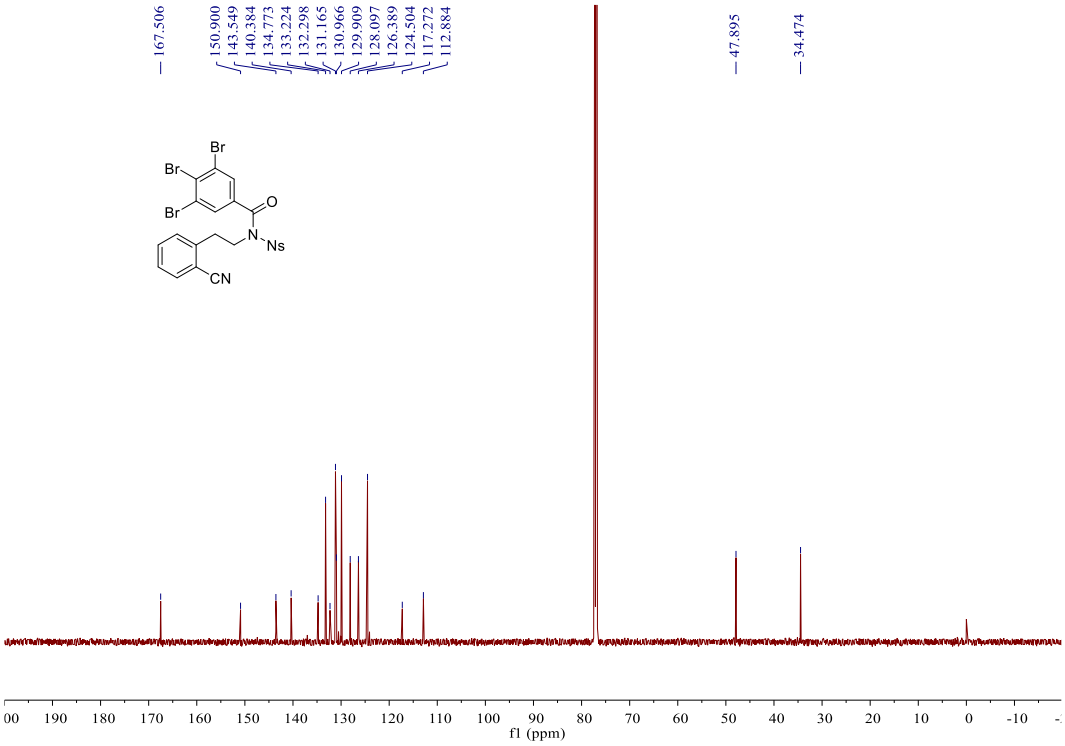


^{1}H and ^{13}C NMR spectra for **4j$_{(m, m')di}$**

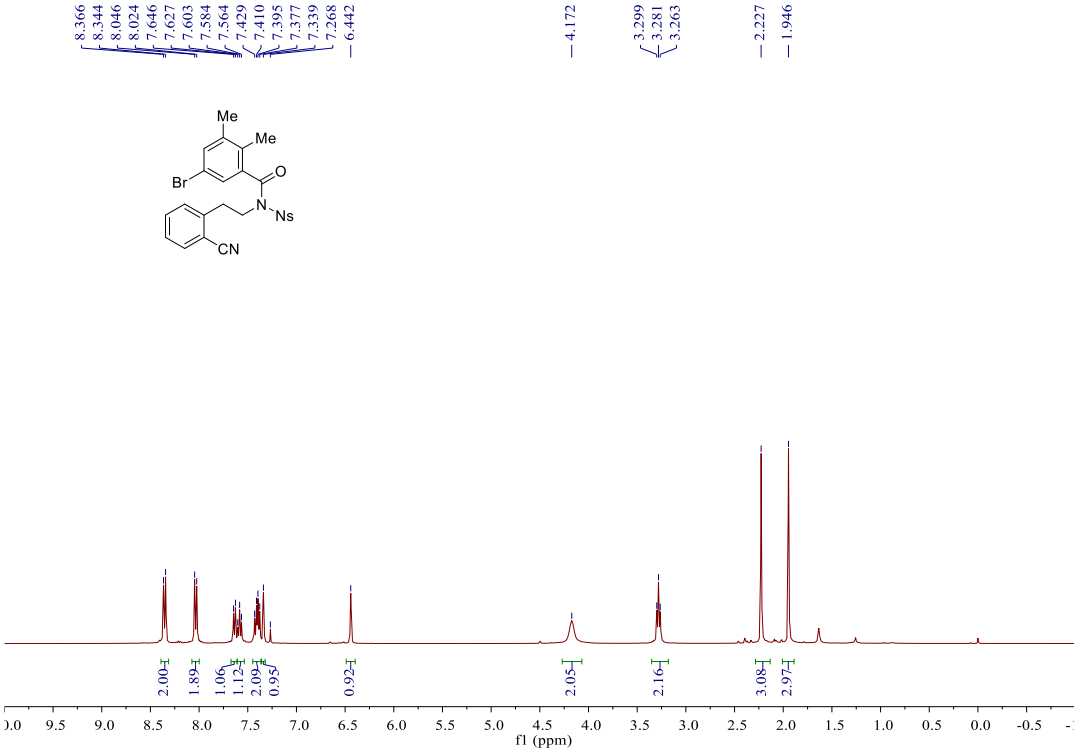


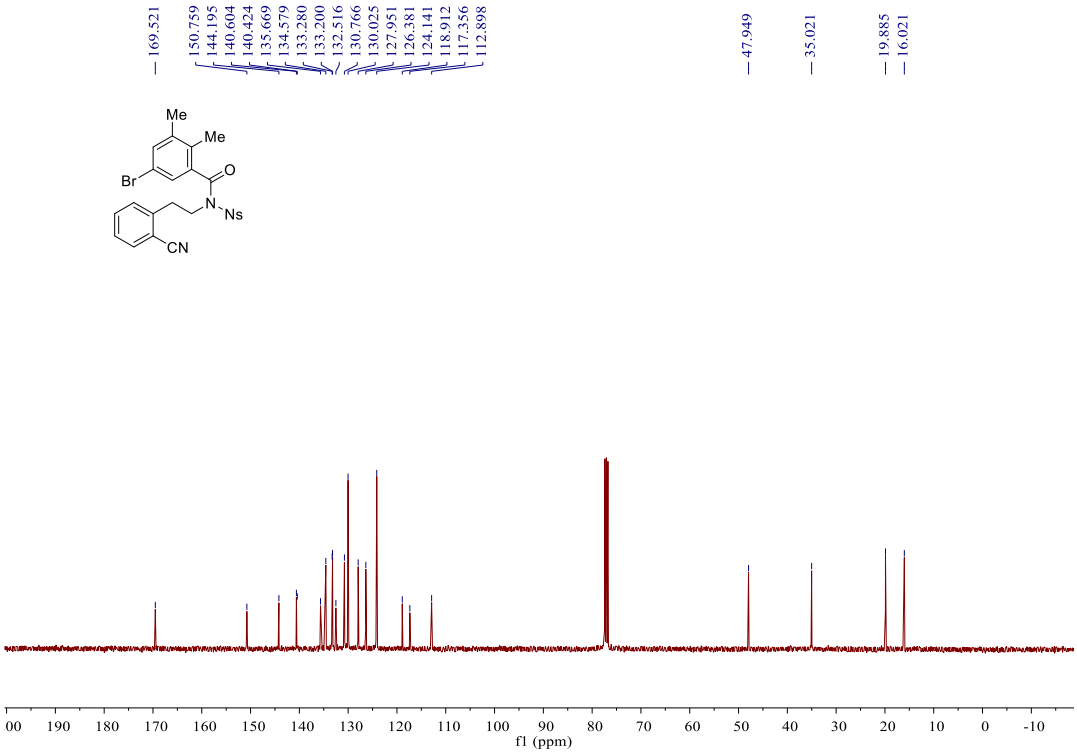
^{1}H and ^{13}C NMR spectra for **4k$_{mono}$**



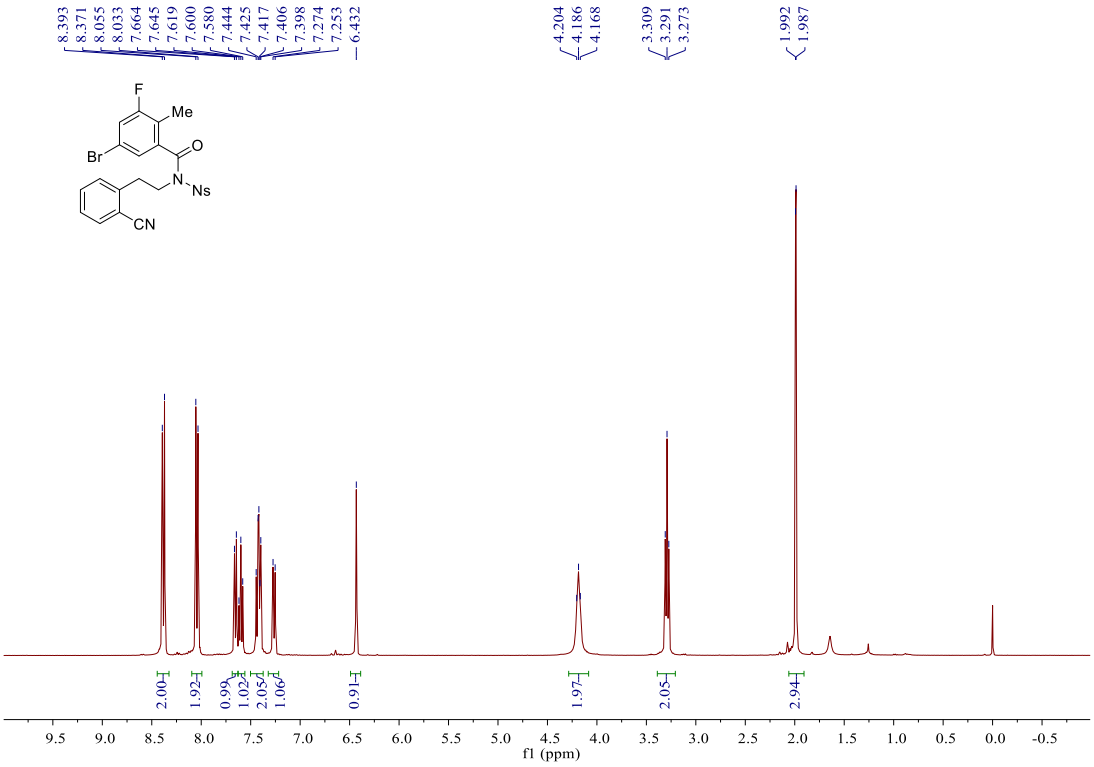


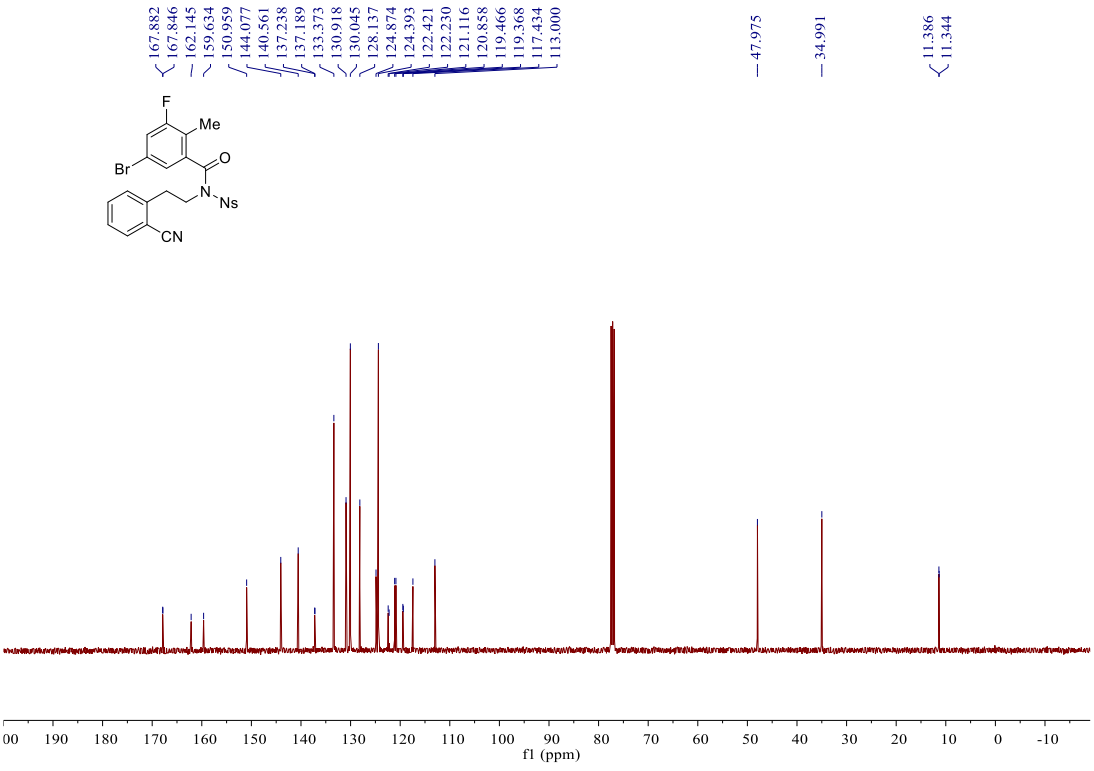
^{1}H and ^{13}C NMR spectra for **4k**$_{(m, m')di}$



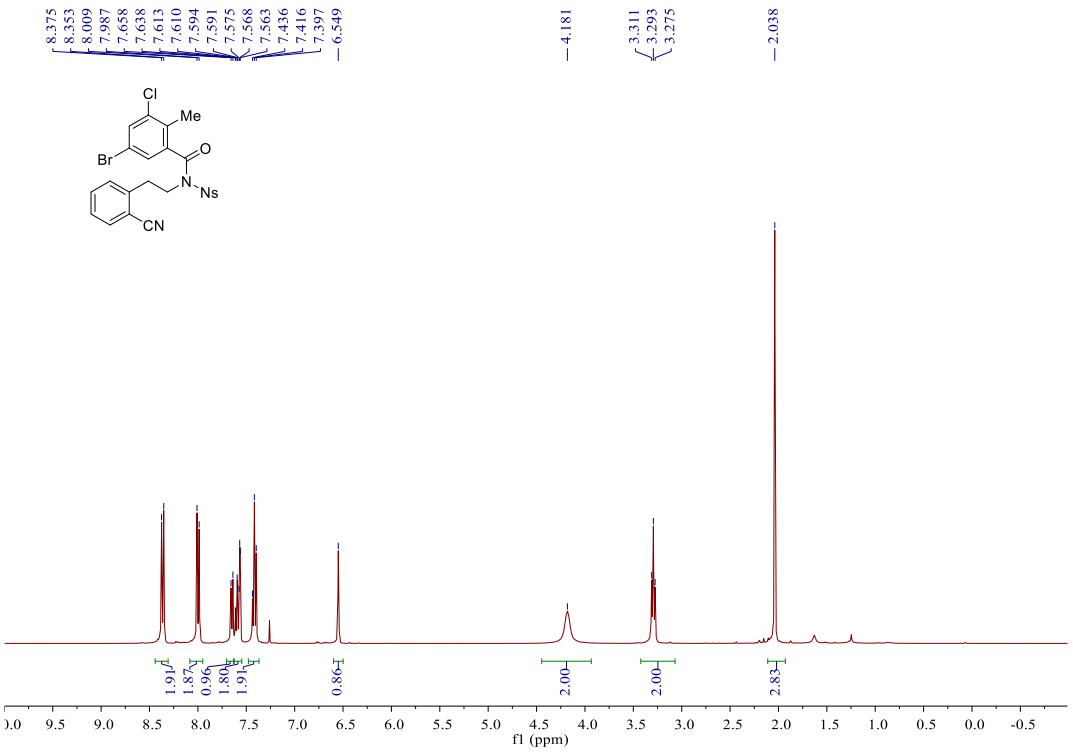


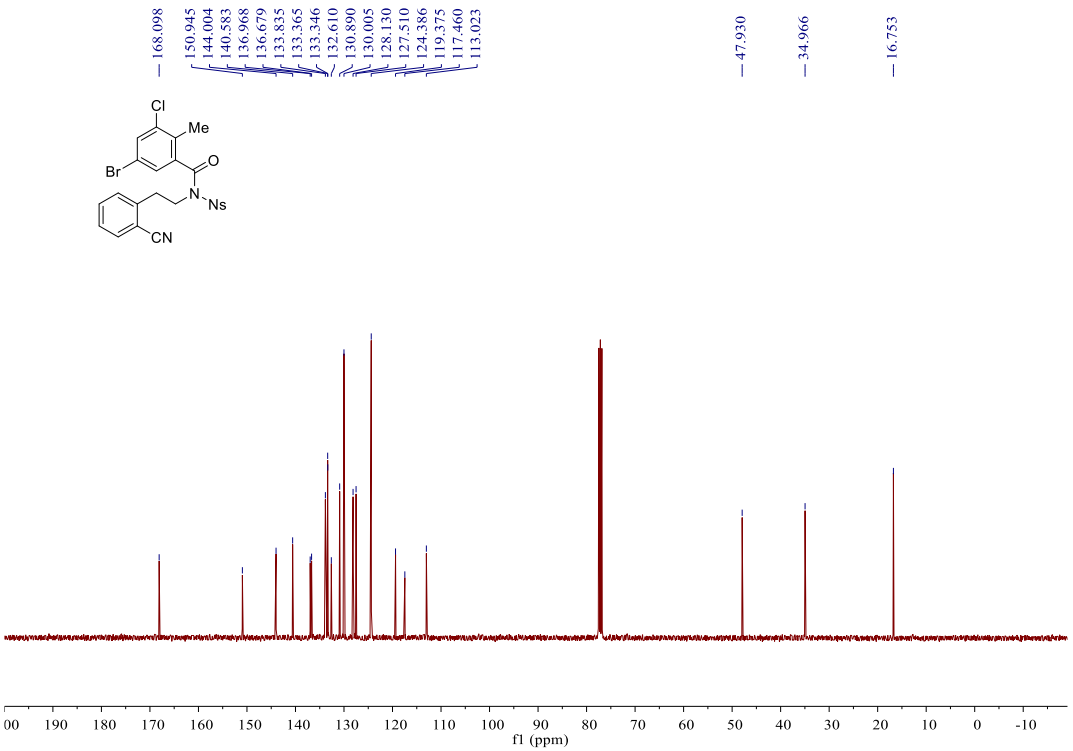
^{1}H and ^{13}C NMR spectra for **4l**



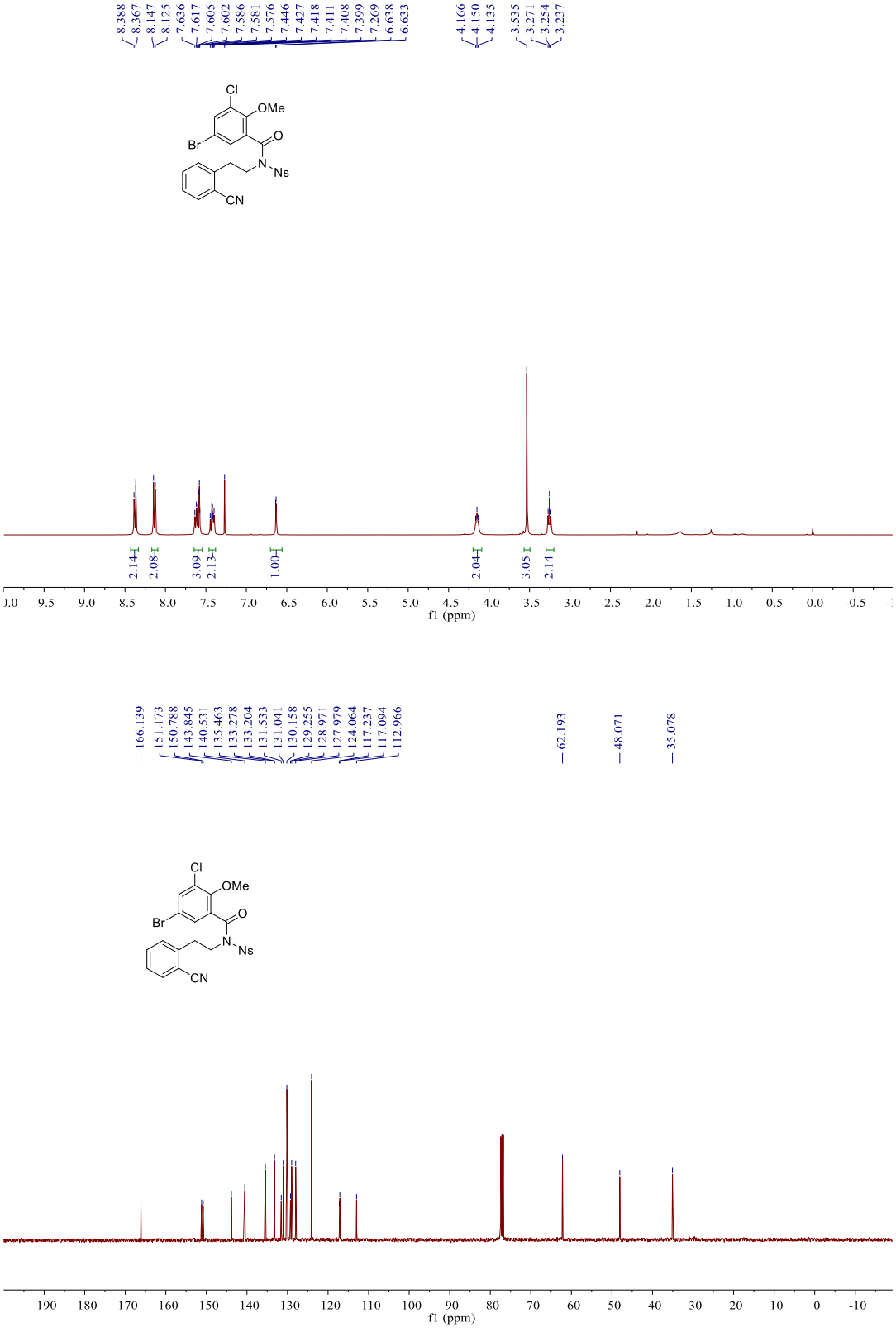


^{1}H and ^{13}C NMR spectra for **4m**

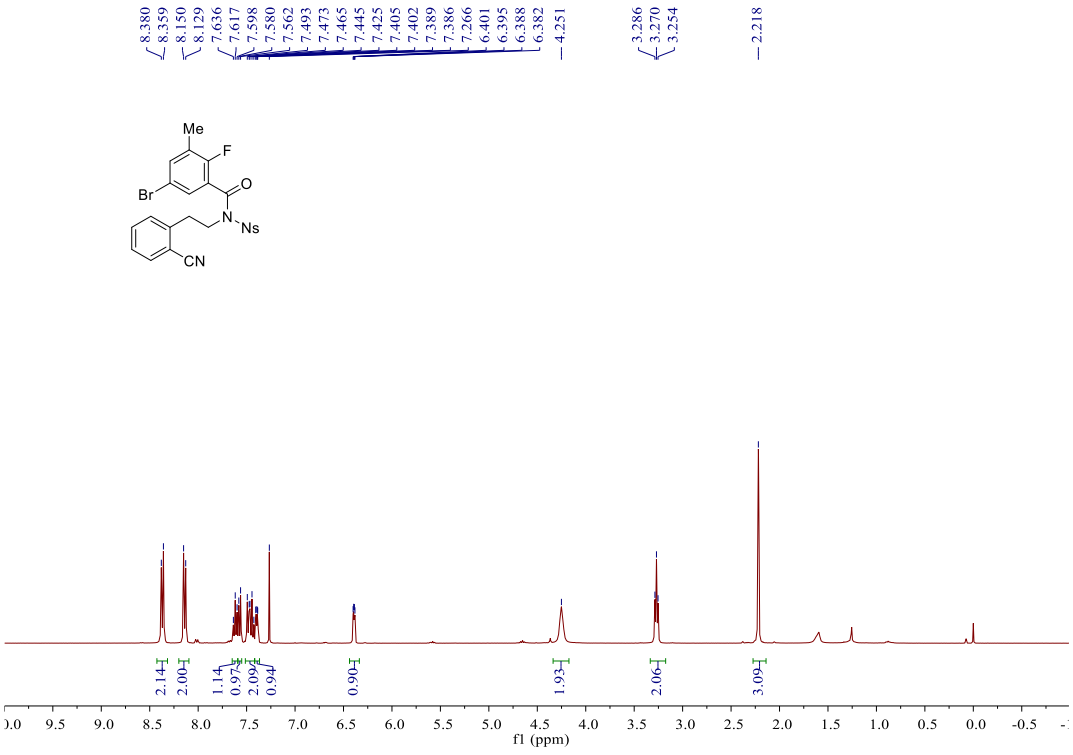


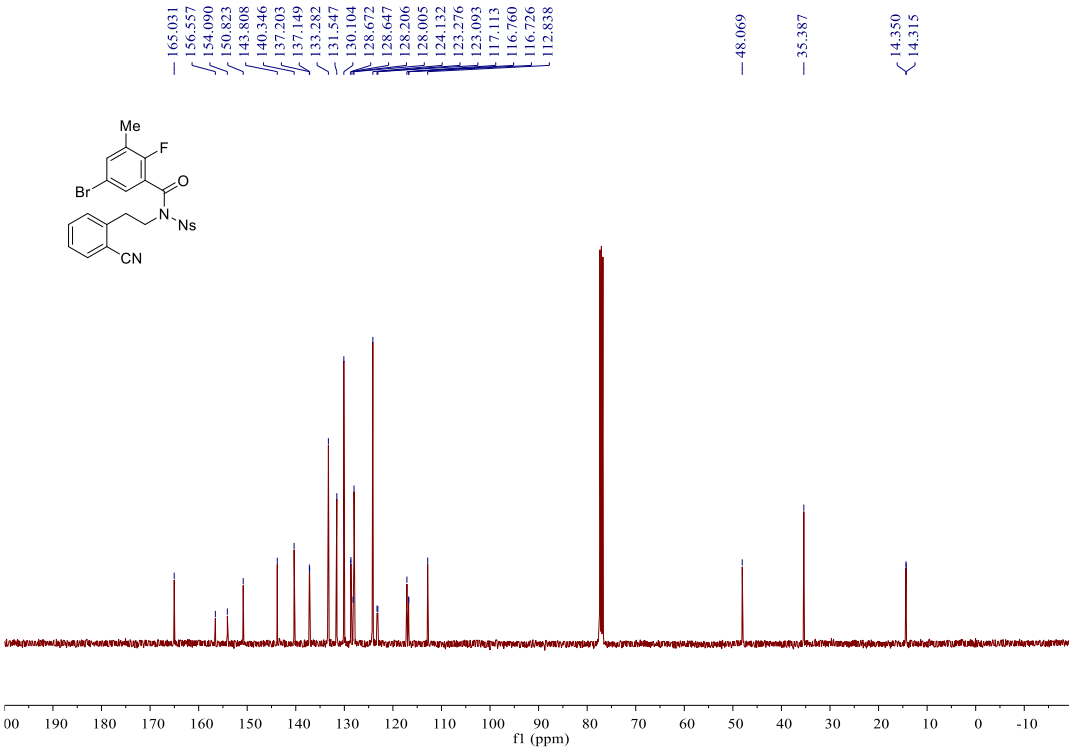


^{1}H and ^{13}C NMR spectra for **4n**

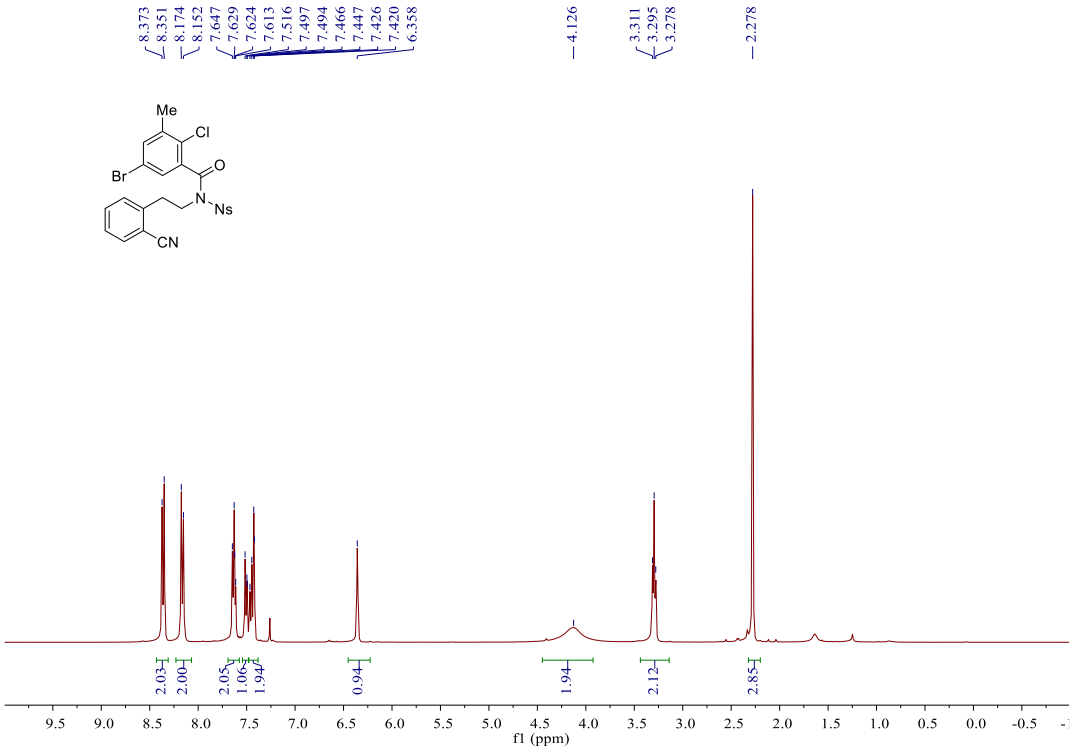


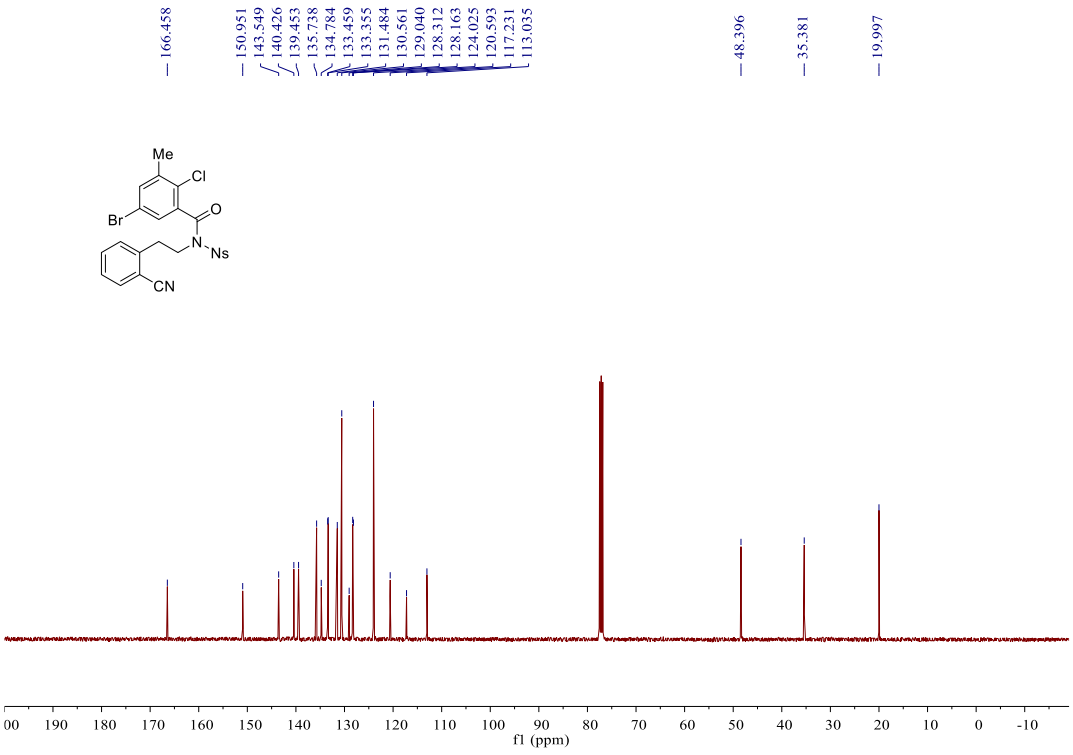
^{1}H and ^{13}C NMR spectra for **4o**



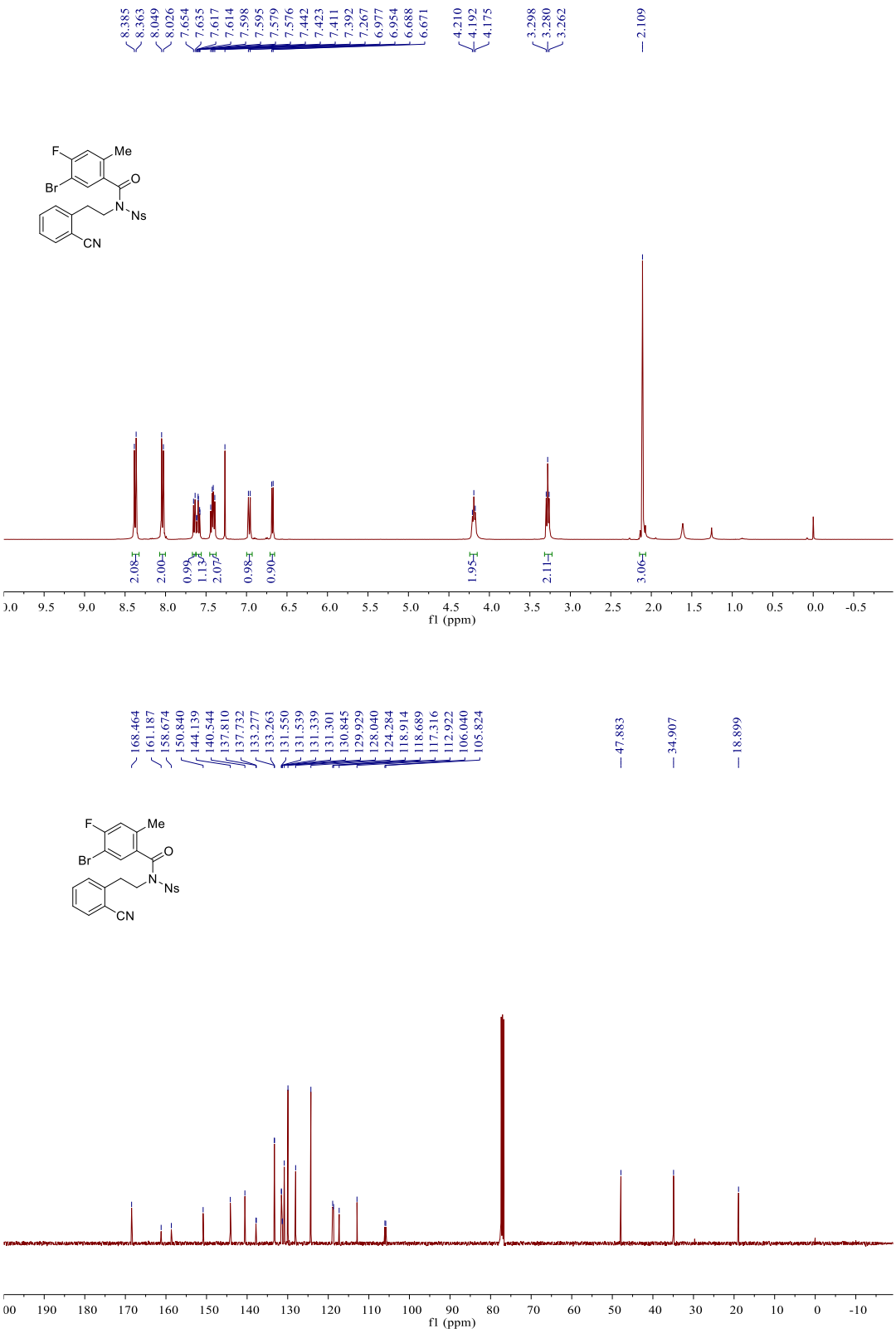


^{1}H and ^{13}C NMR spectra for **4p**

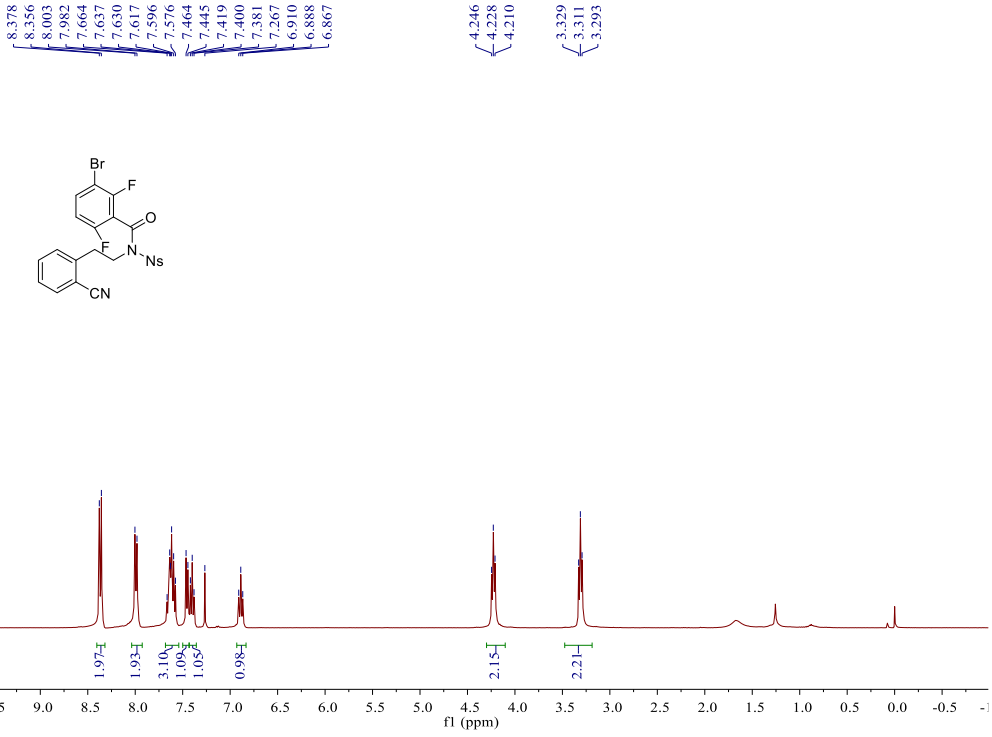


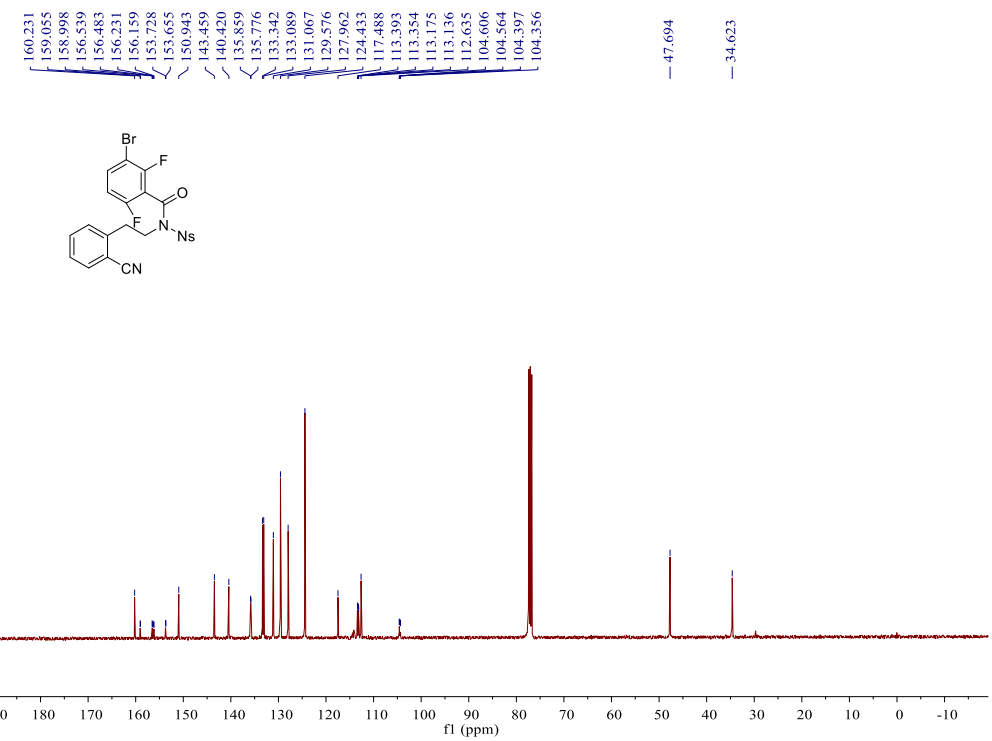


^{1}H and ^{13}C NMR spectra for **4q**

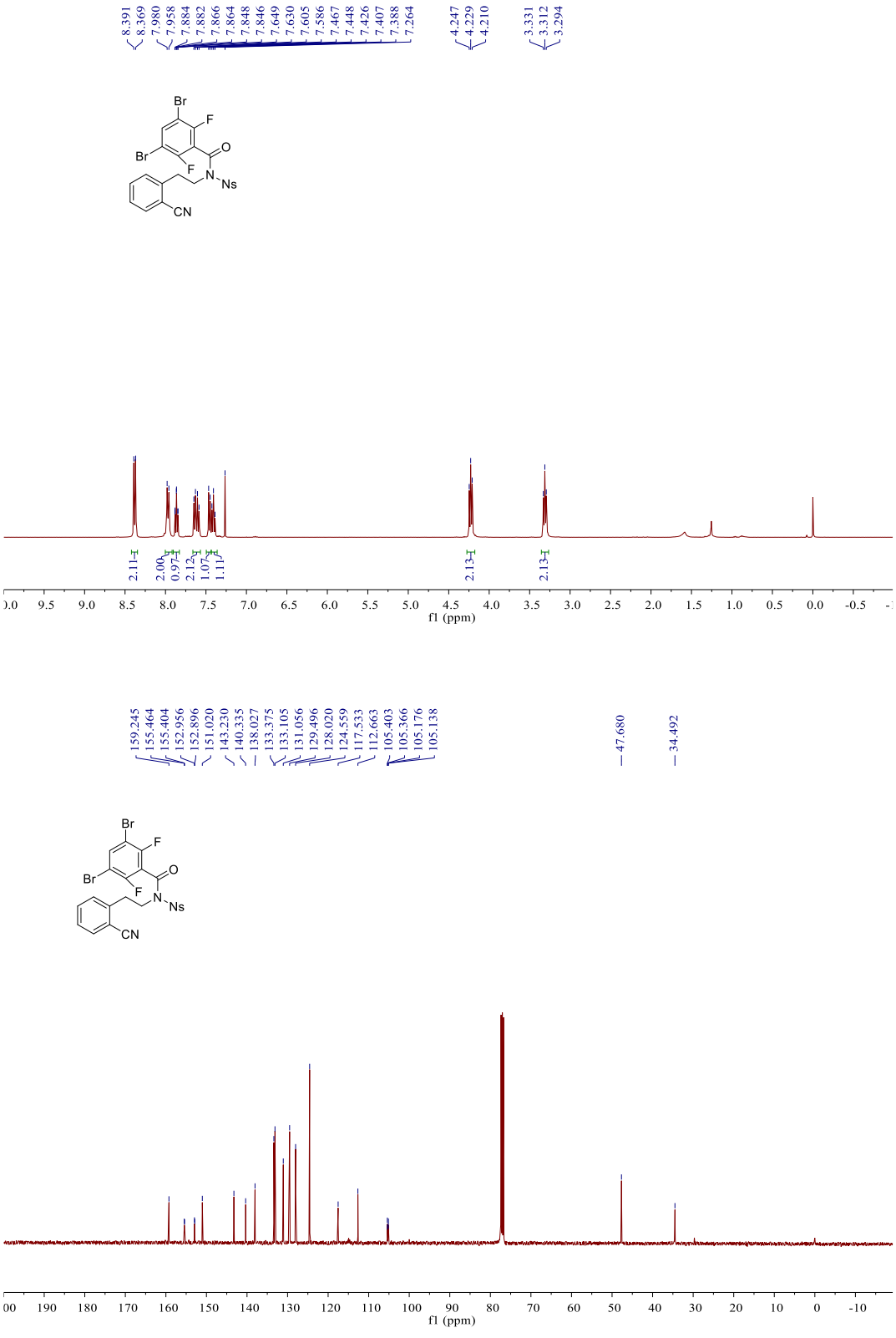


^{1}H and ^{13}C NMR spectra for **4r**

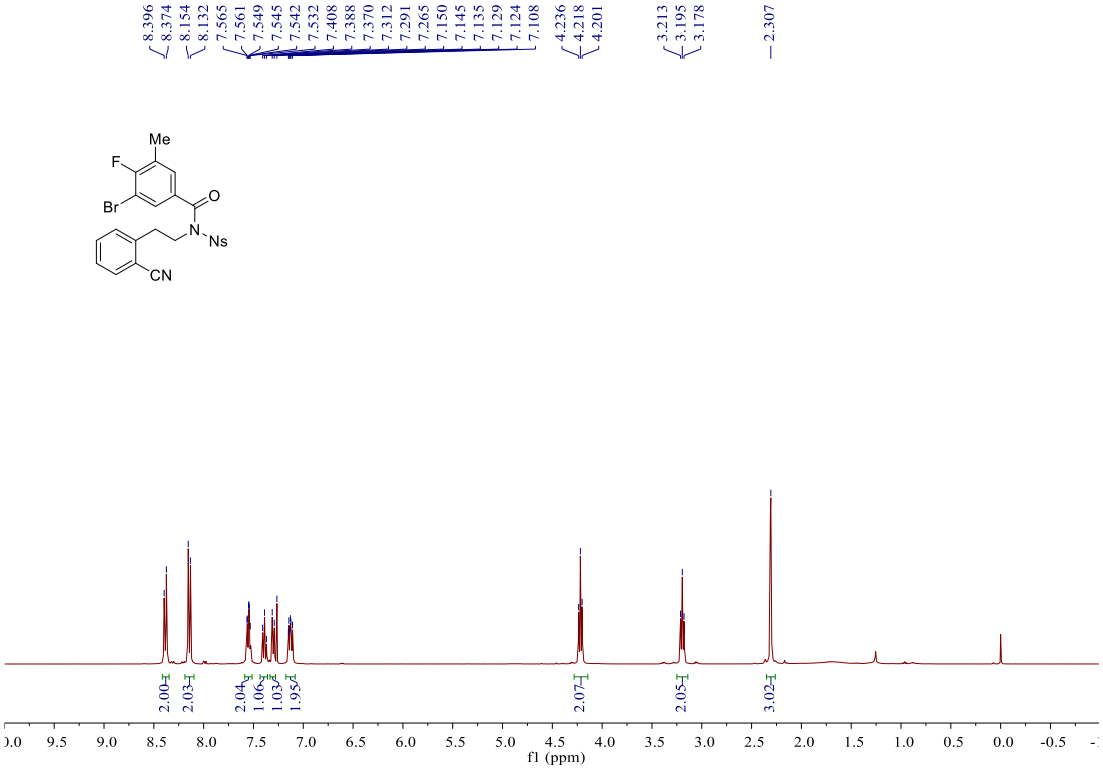


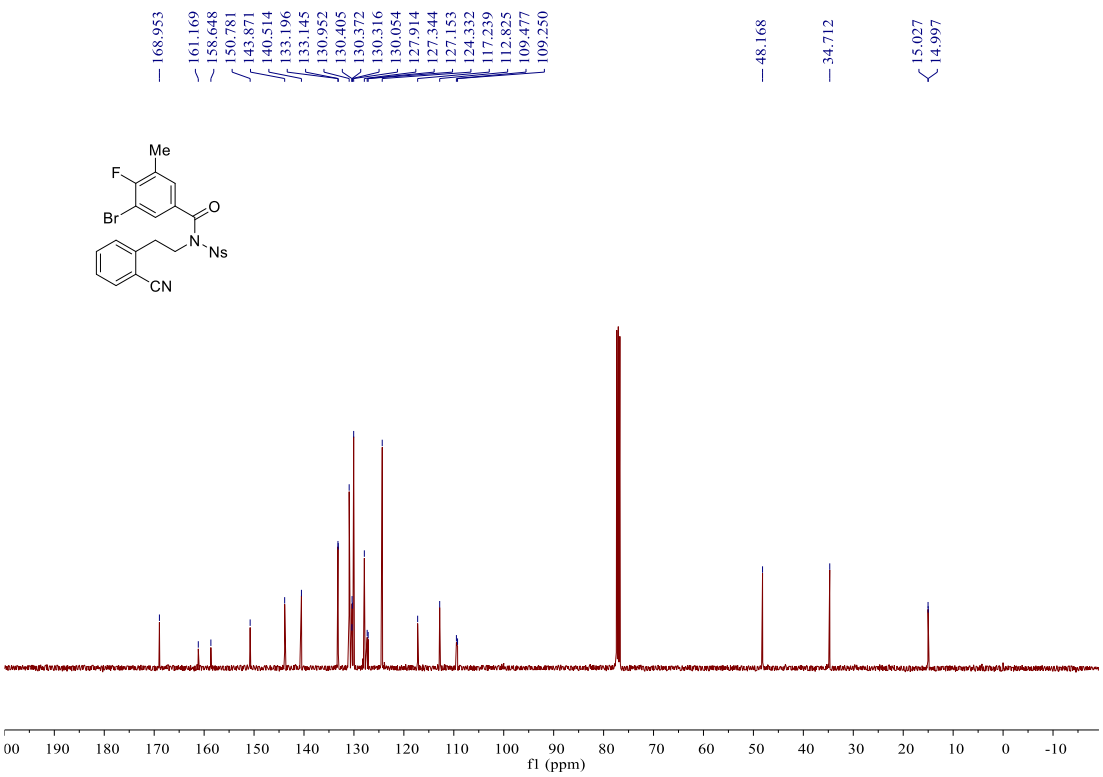


^{1}H and ^{13}C NMR spectra for **4s$_{mono}$**

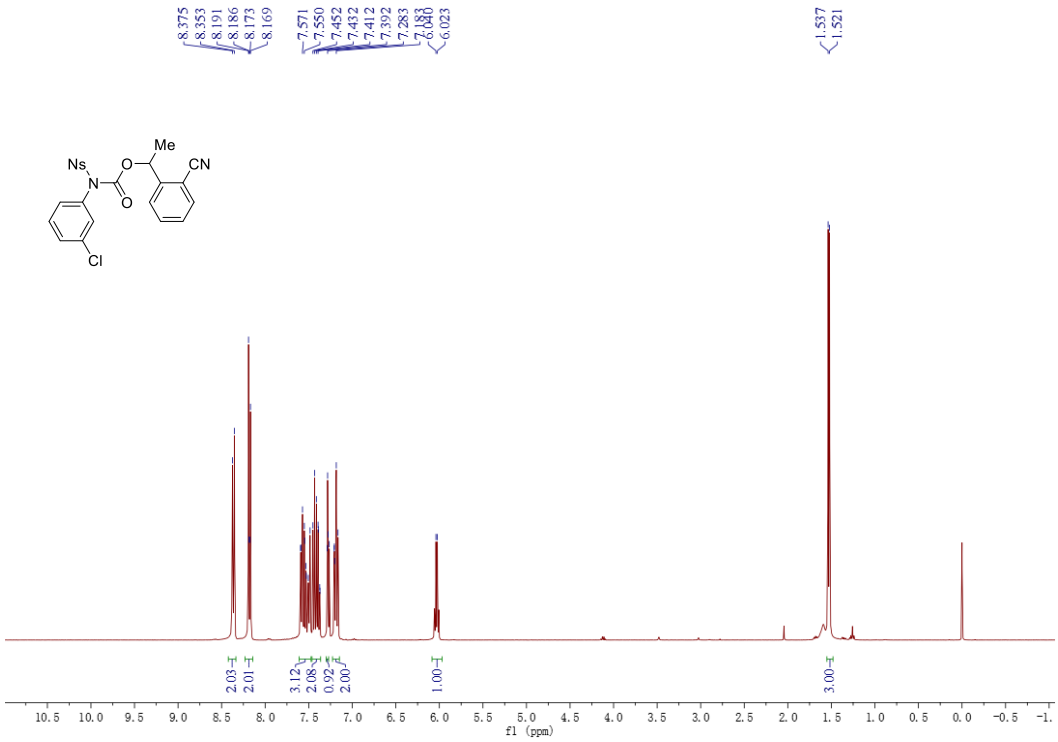


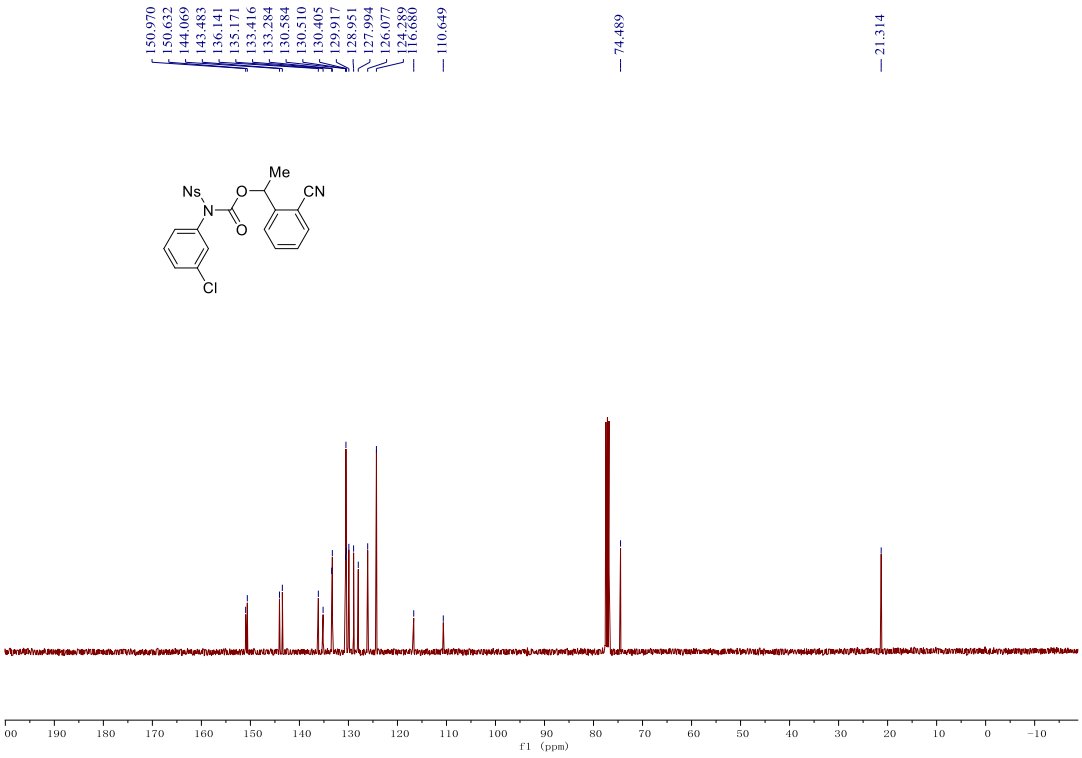
^{1}H and ^{13}C NMR spectra for **4s$_{(m, m')di}$**



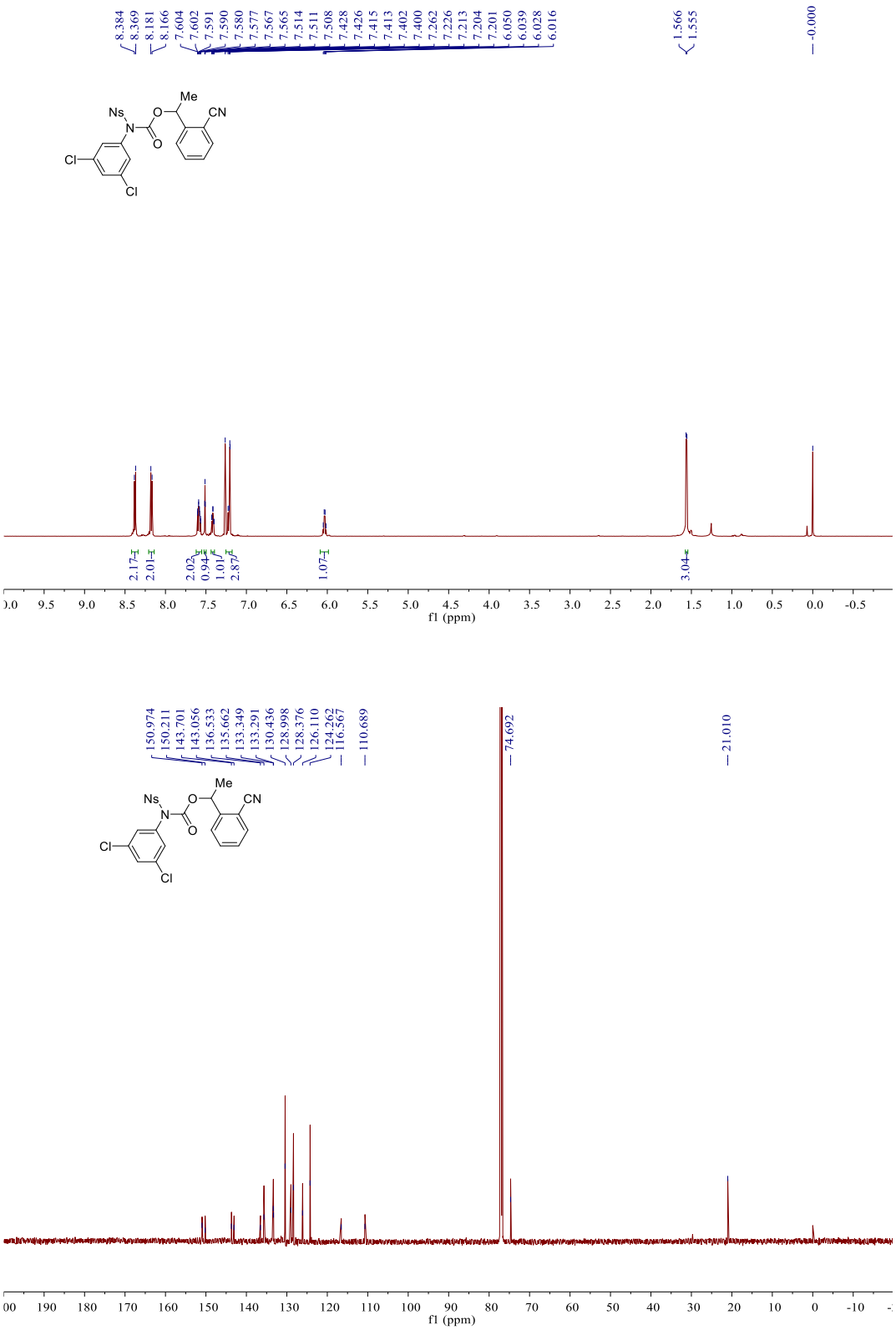


^{1}H and ^{13}C NMR spectra for **4t**

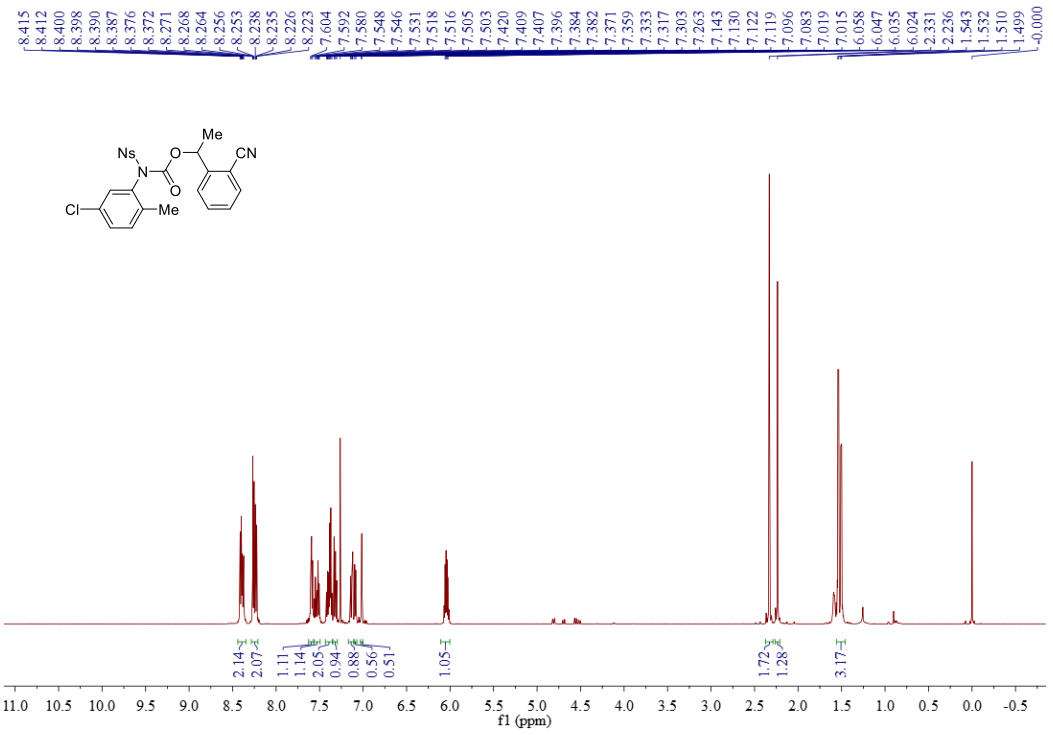


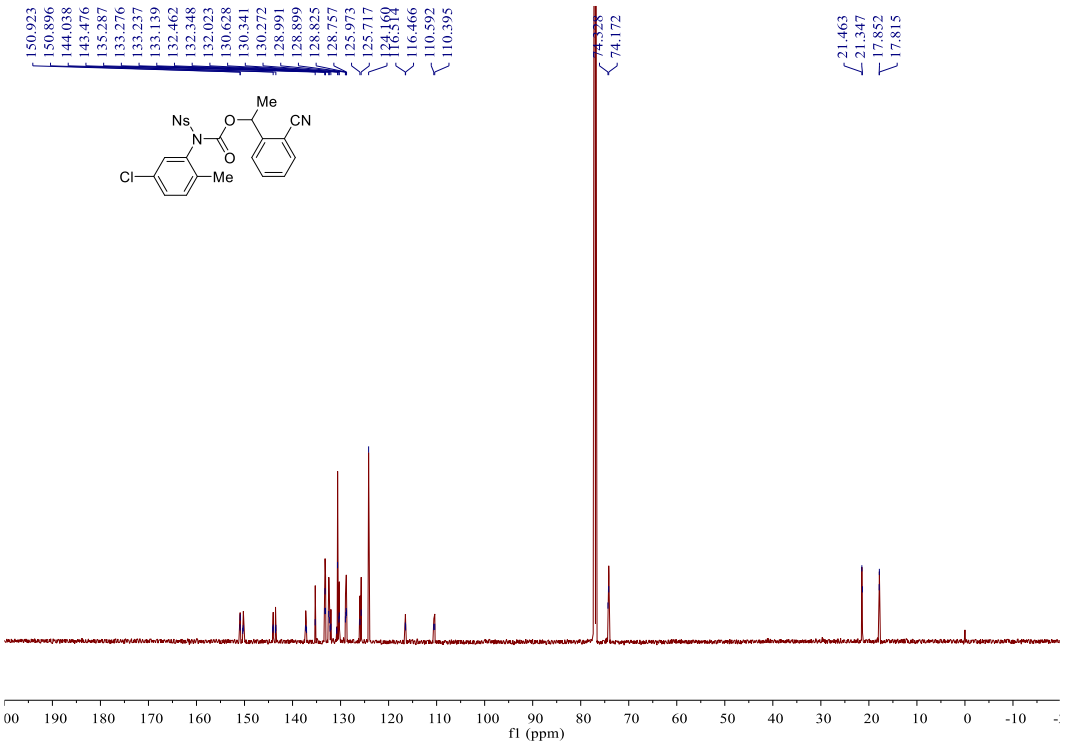


^{1}H, ^{13}C NMR spectra for **5a**$_{mono}$

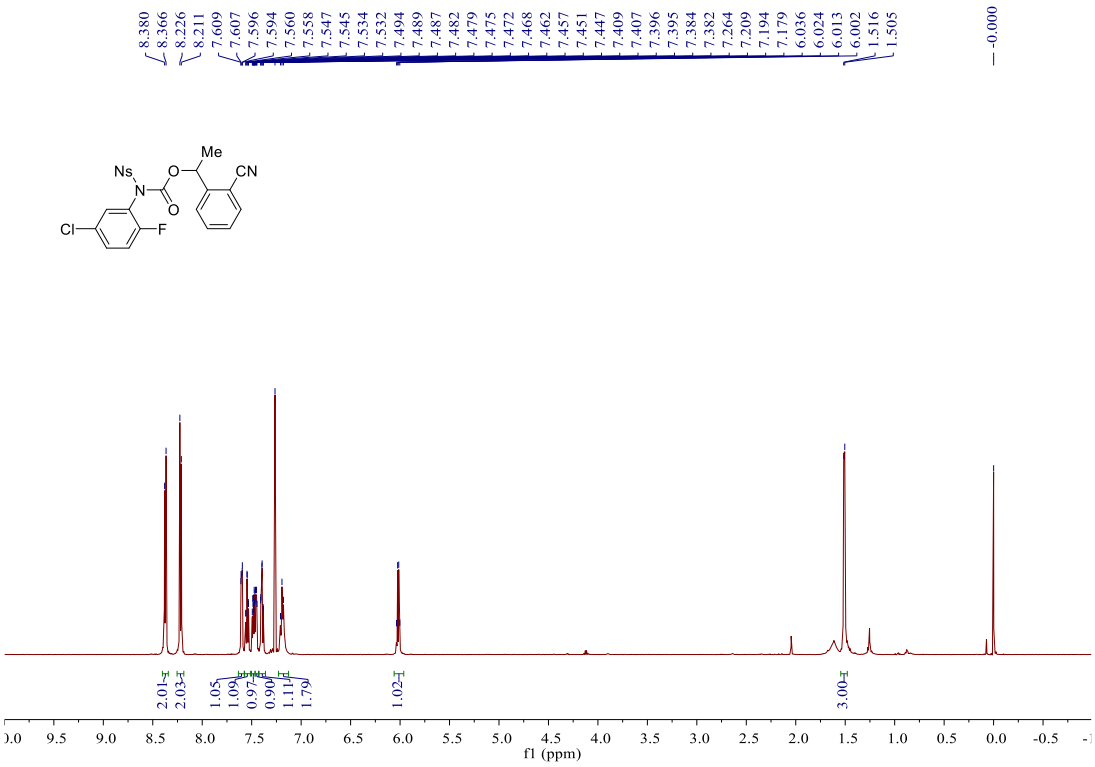


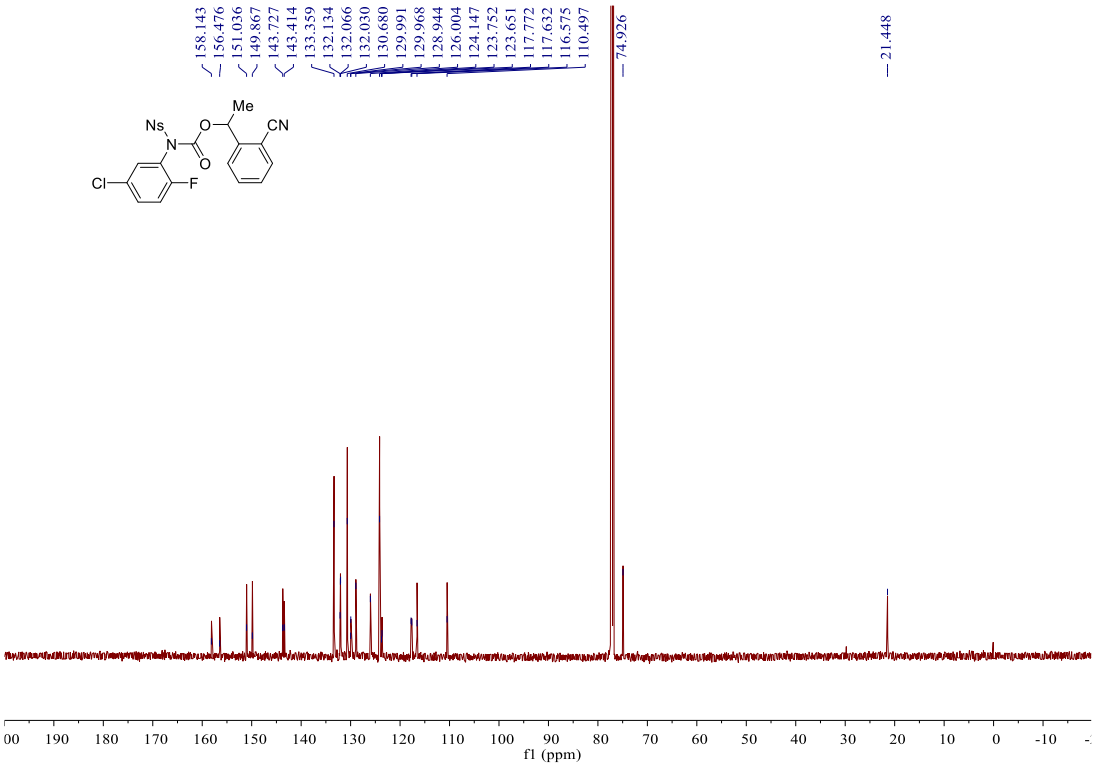
^{1}H and ^{13}C NMR spectra for **5a$_{(m,\ m')di}$**



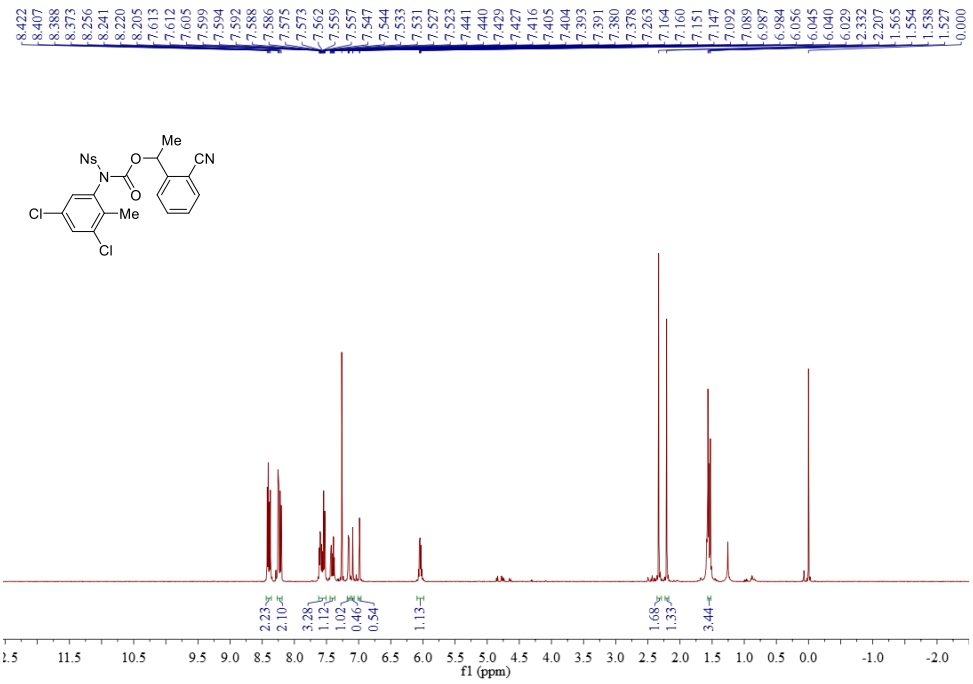


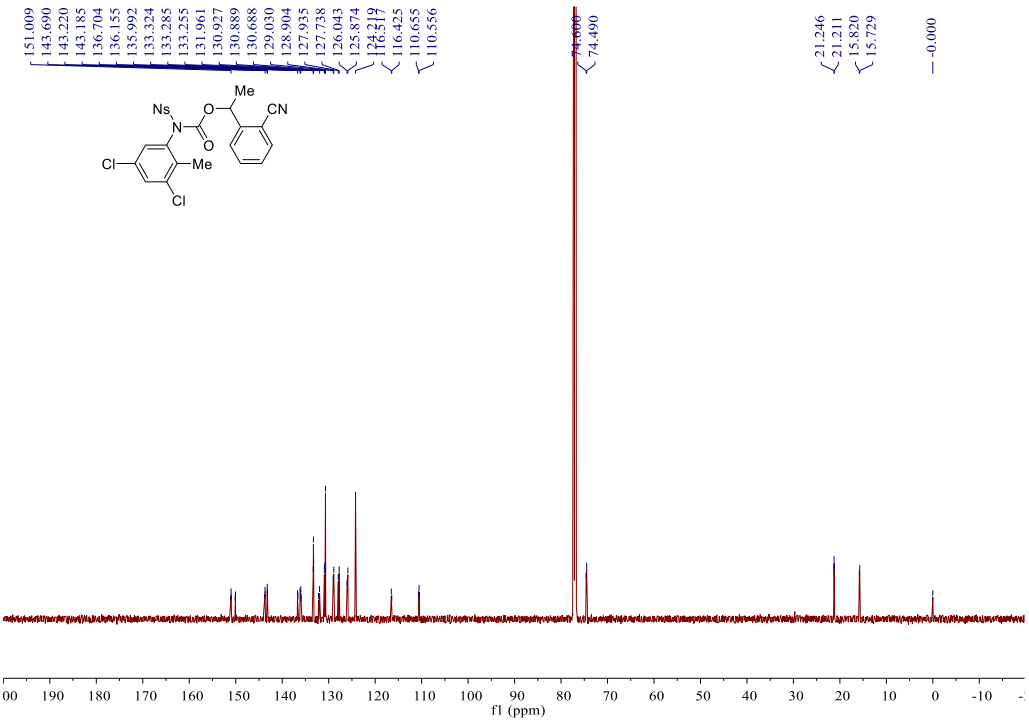
^{1}H and ^{13}C NMR spectra for **5b**



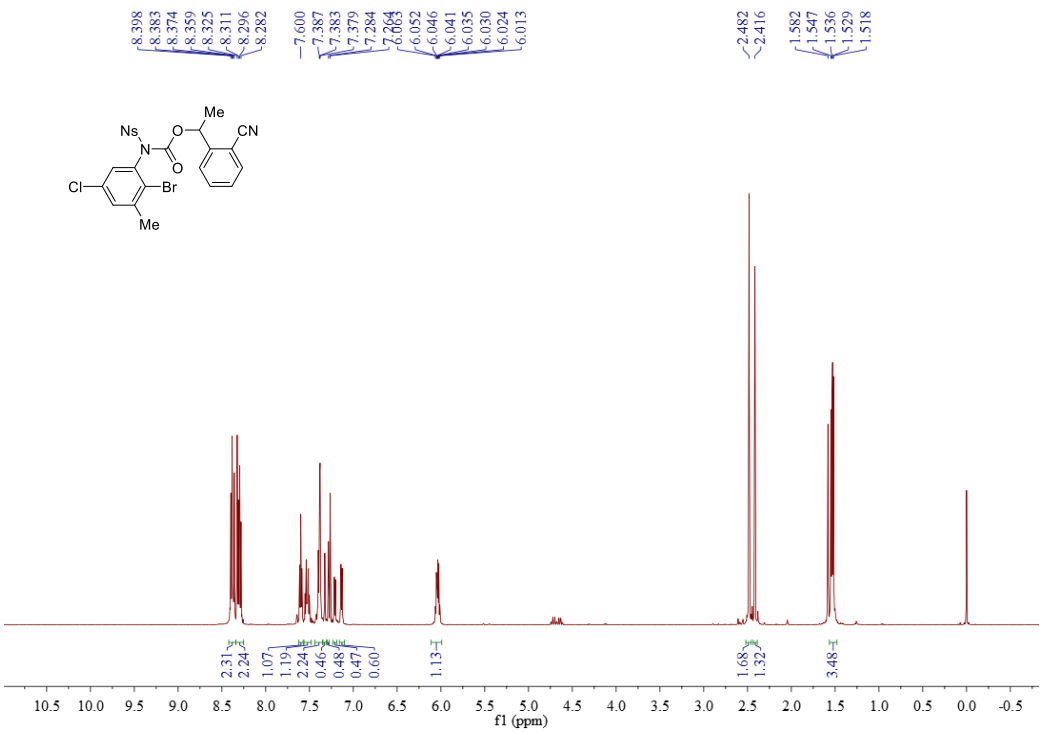


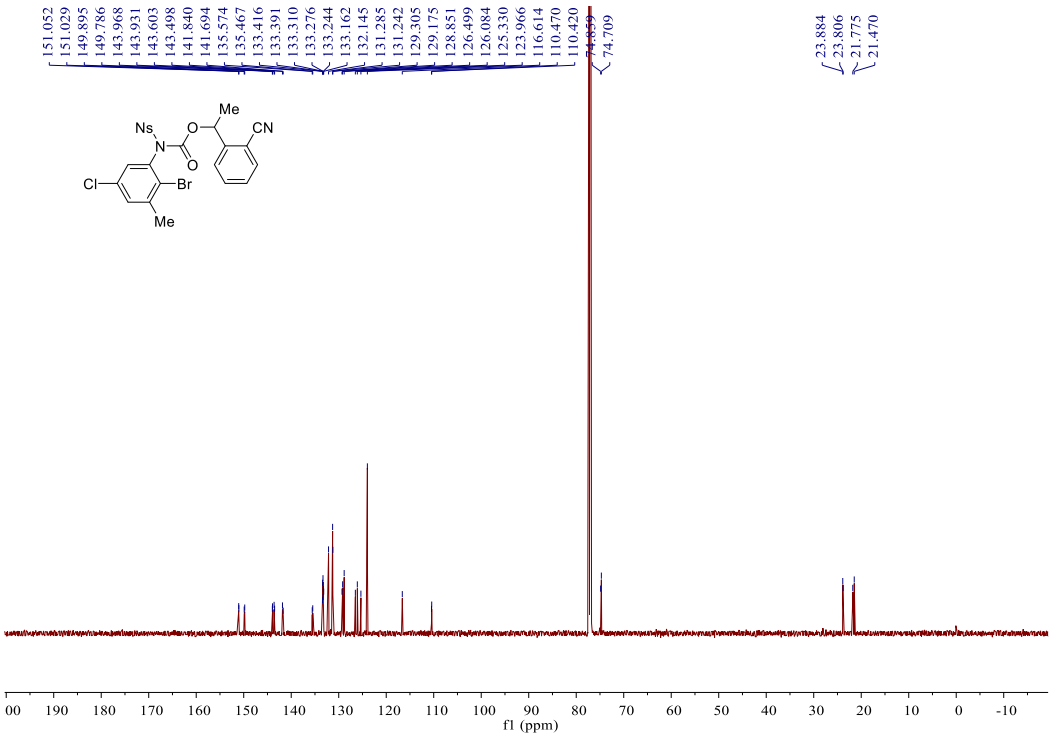
^{1}H and ^{13}C NMR spectra for **5c**



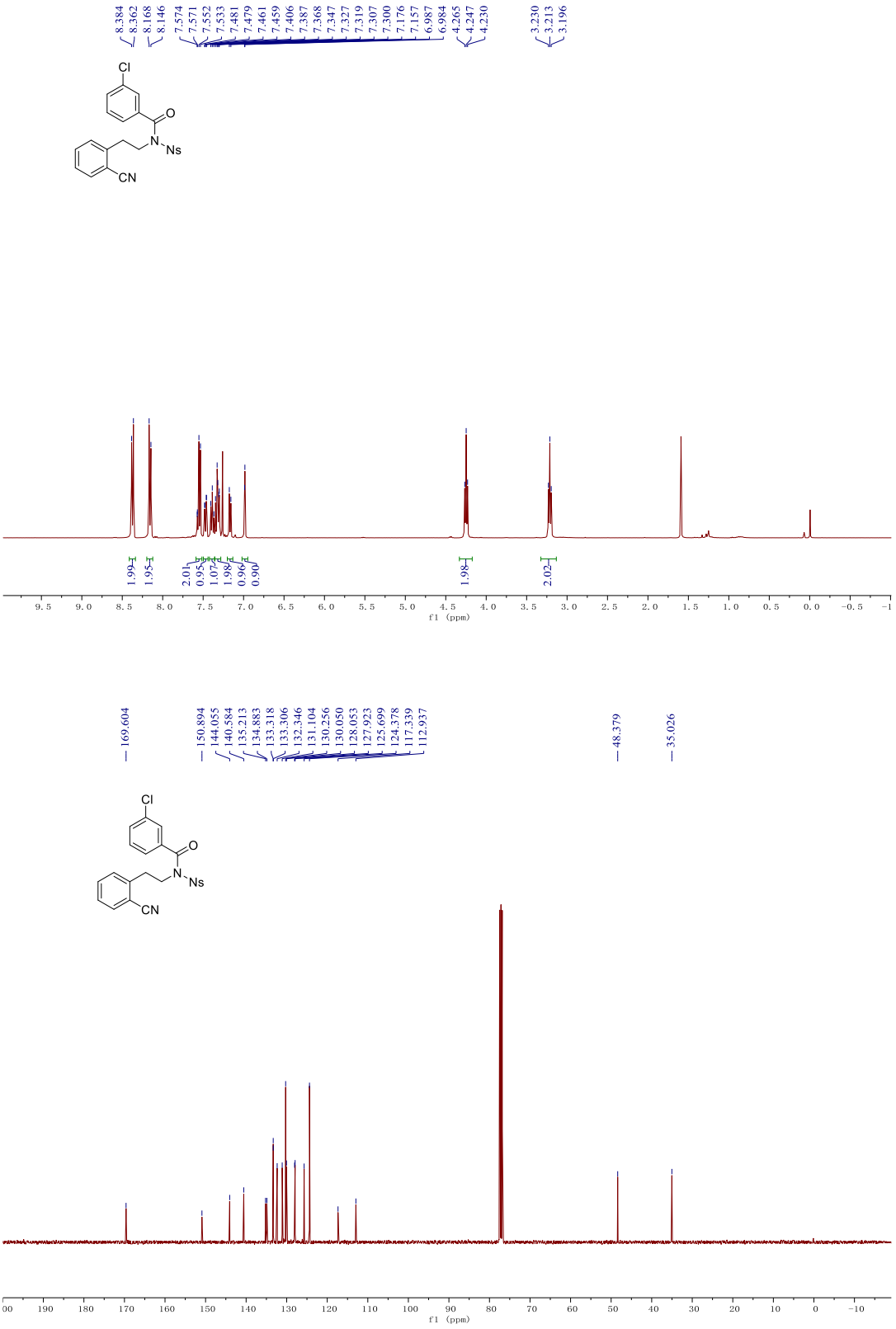


^{1}H and ^{13}C NMR spectra for **5k**

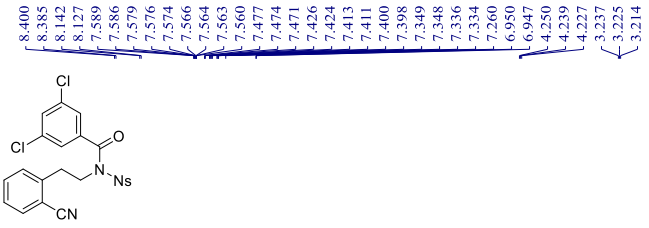


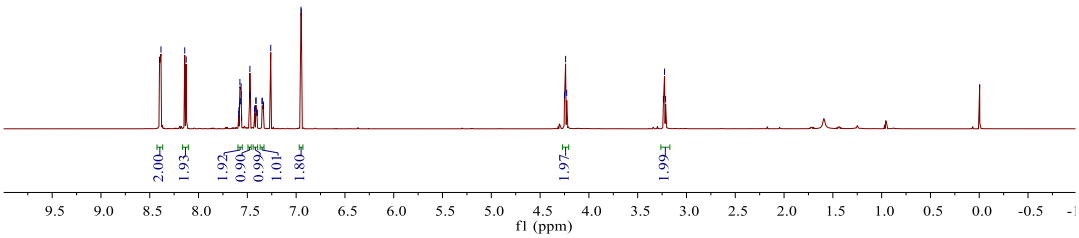


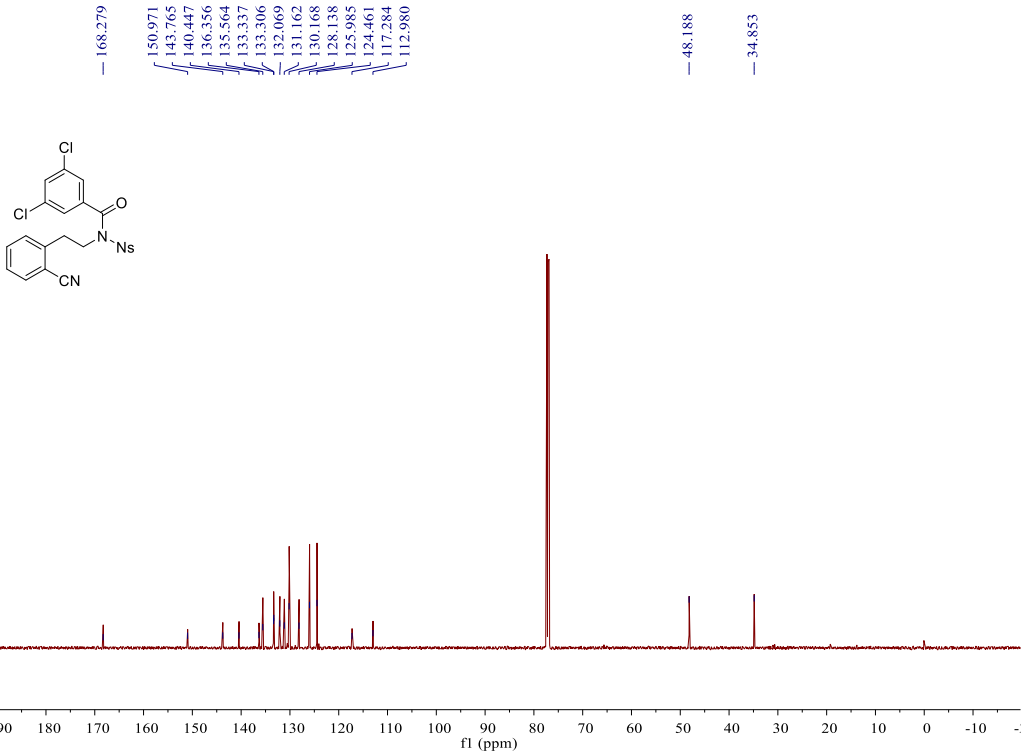
^{1}H and ^{13}C NMR spectra for **5l**



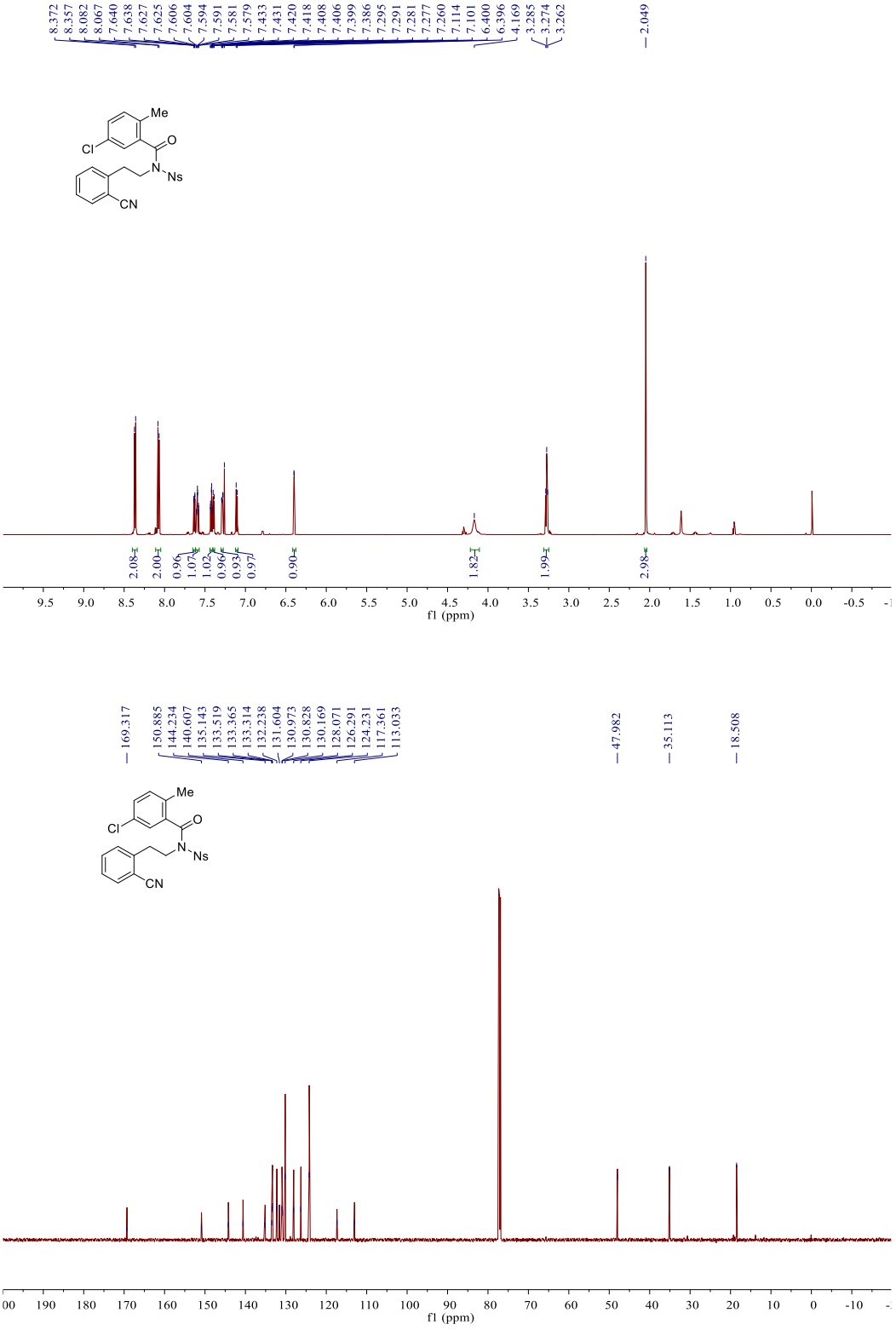
^{1}H and ^{13}C NMR spectra for **6a**$_{mono}$



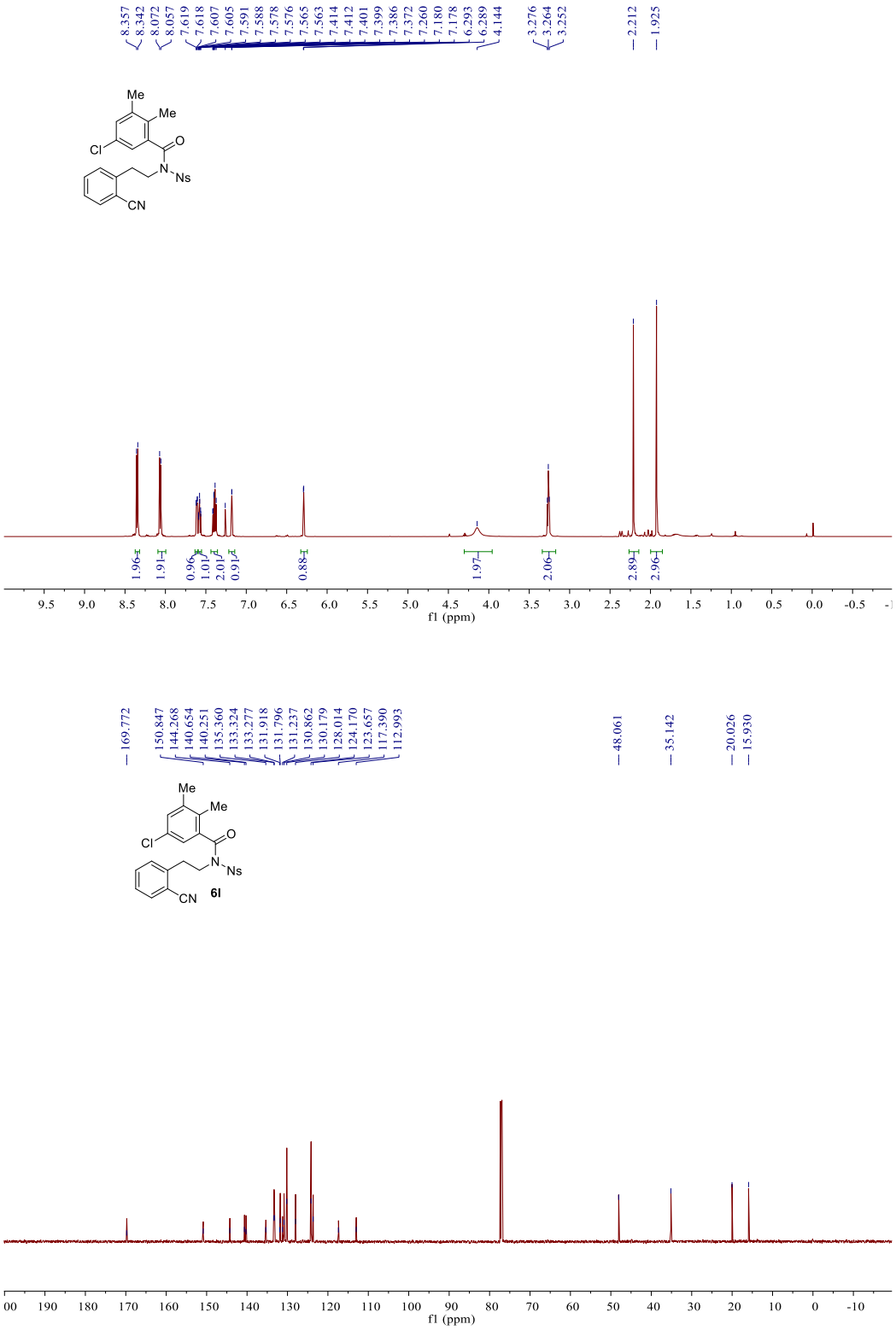




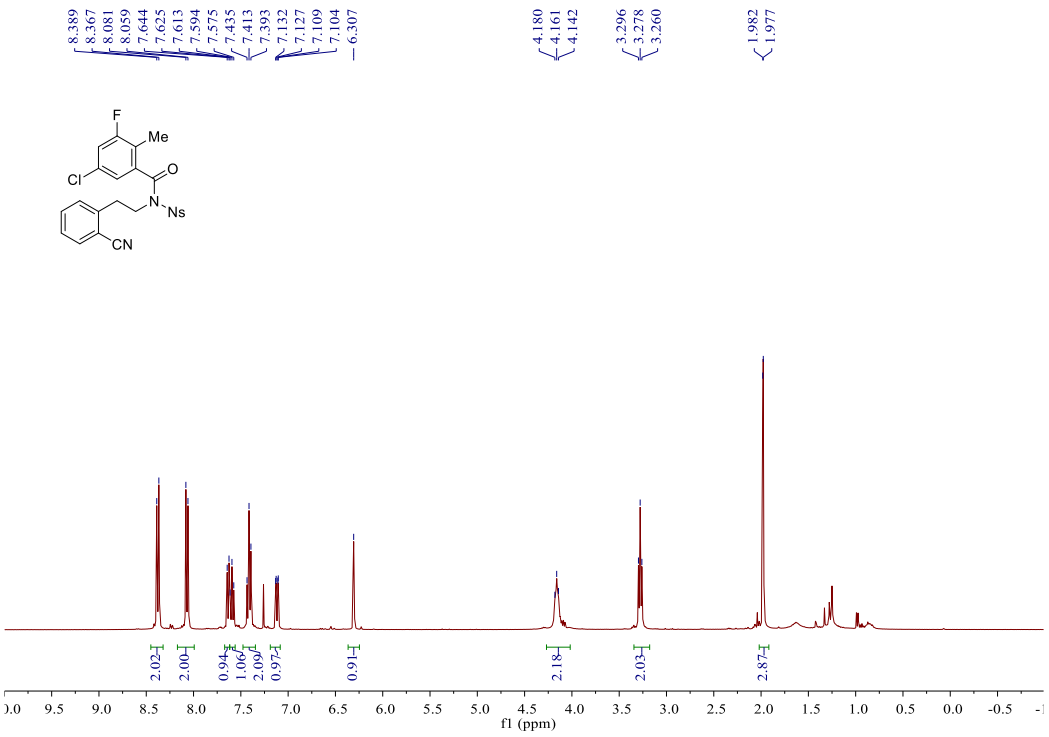
^{1}H and ^{13}C NMR spectra for **6a$_{(m, m')di}$**

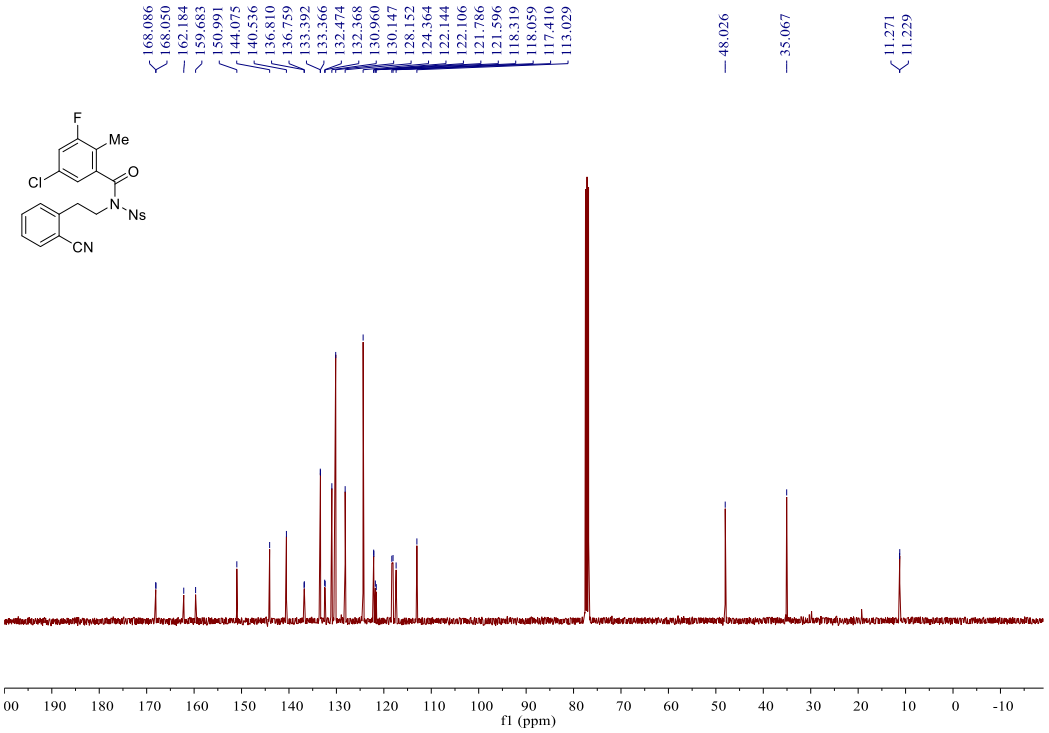


^{1}H and ^{13}C NMR spectra for **6b**

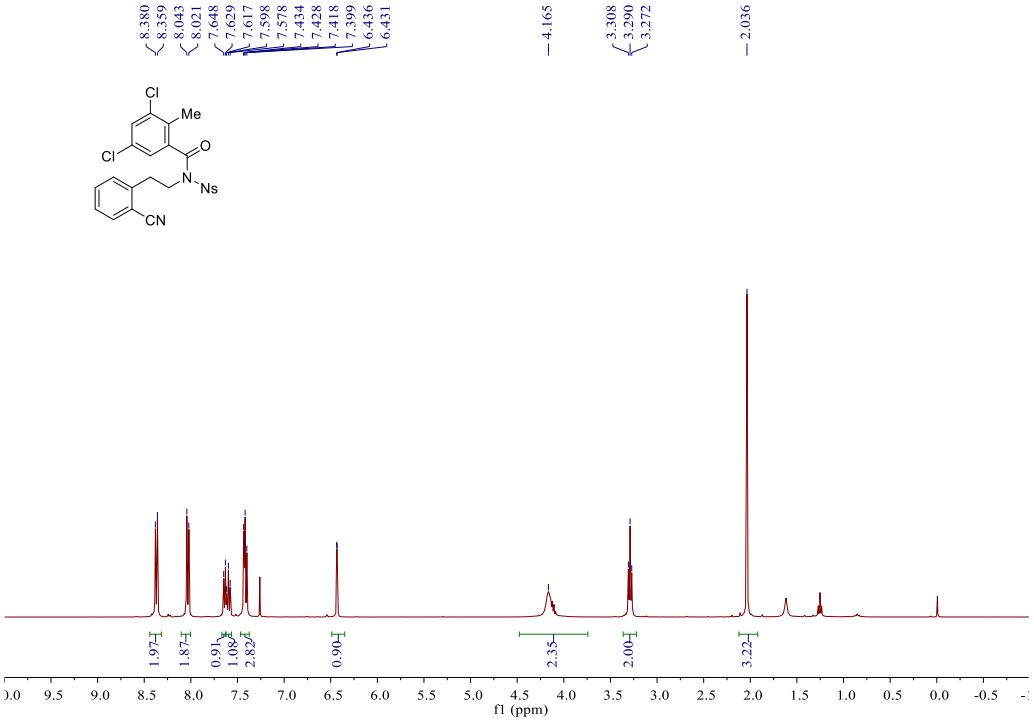


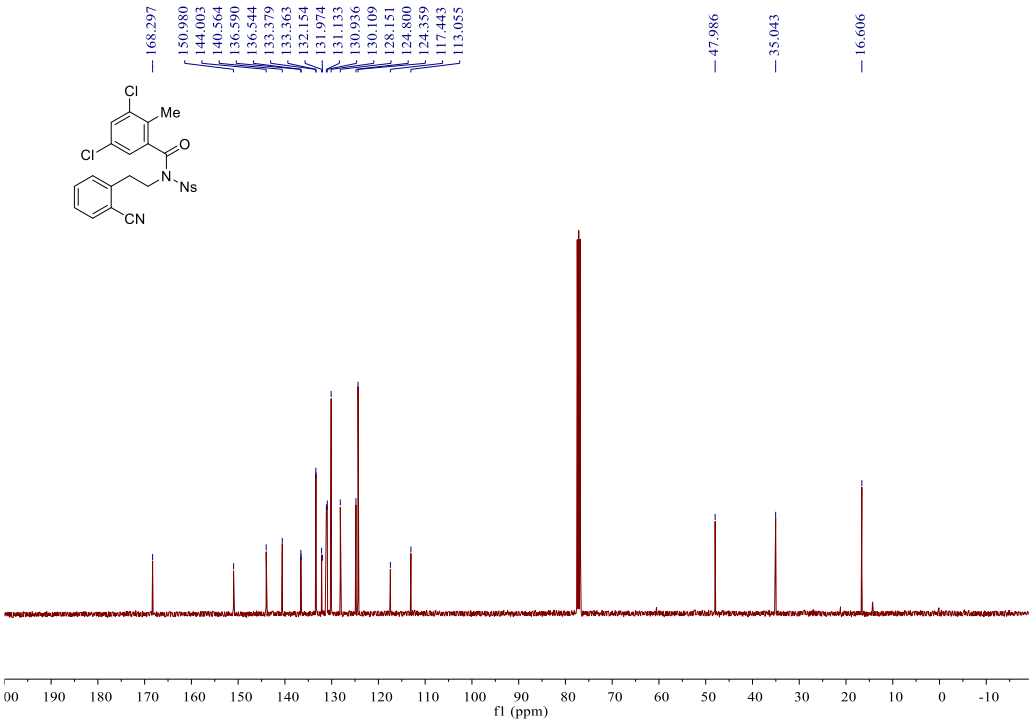
^{1}H and ^{13}C NMR spectra for **6l**



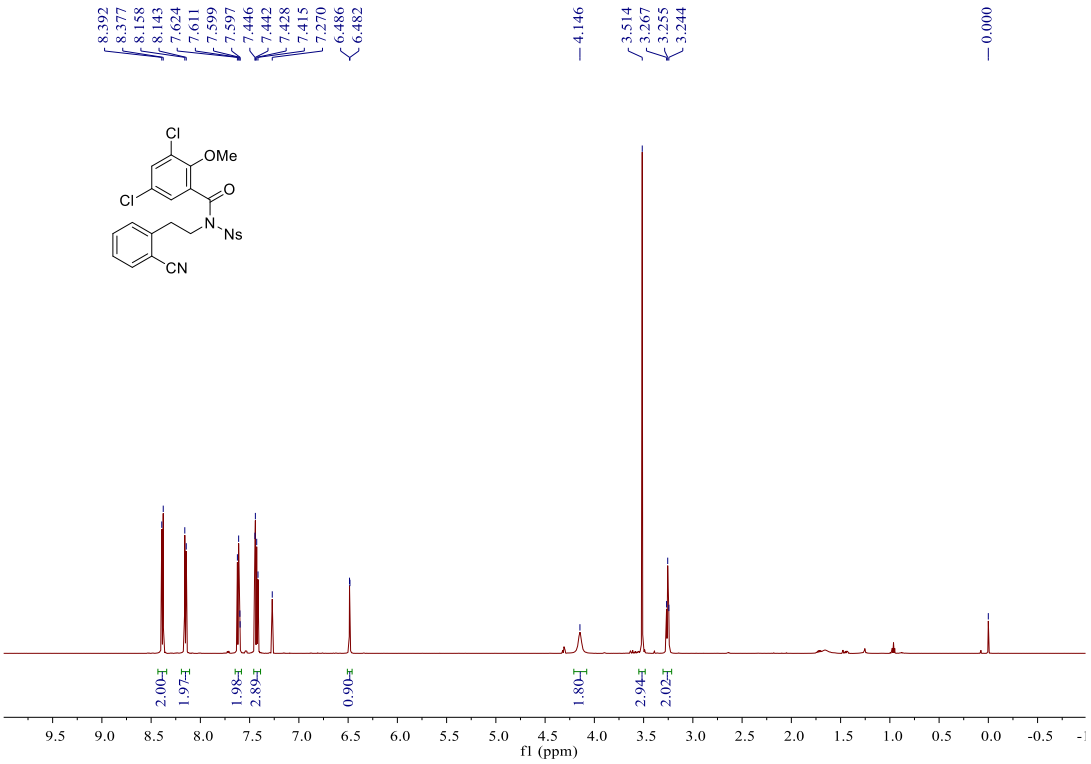


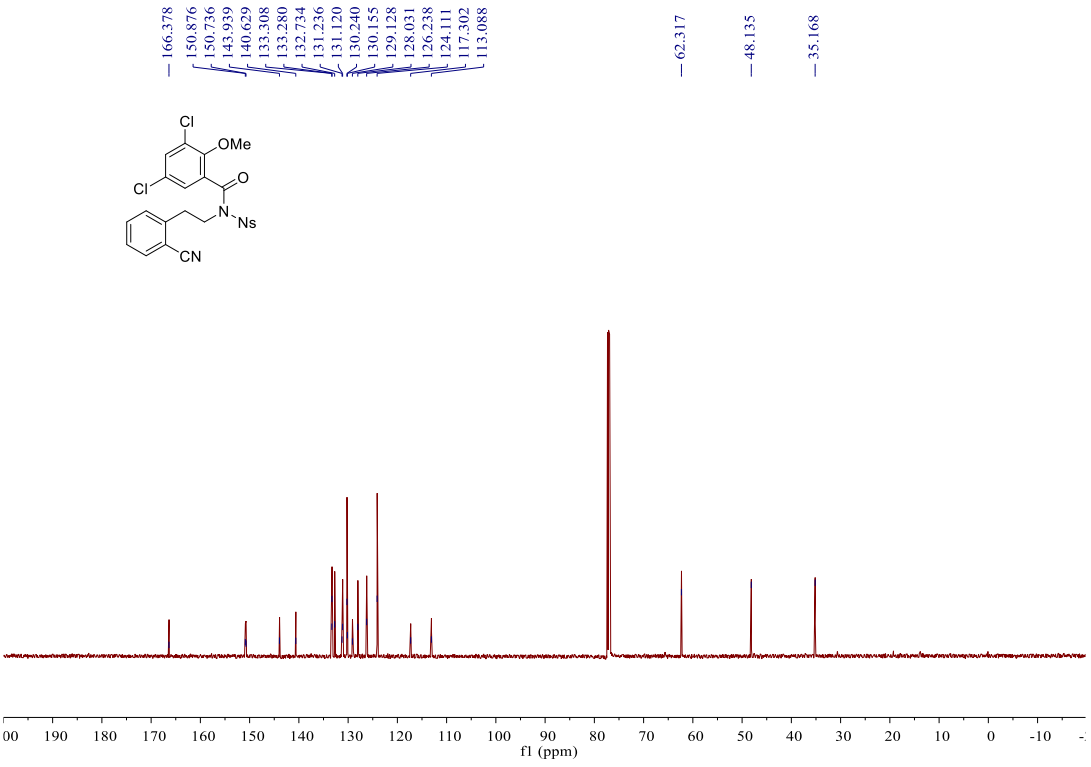
^{1}H and ^{13}C NMR spectra for **6m**



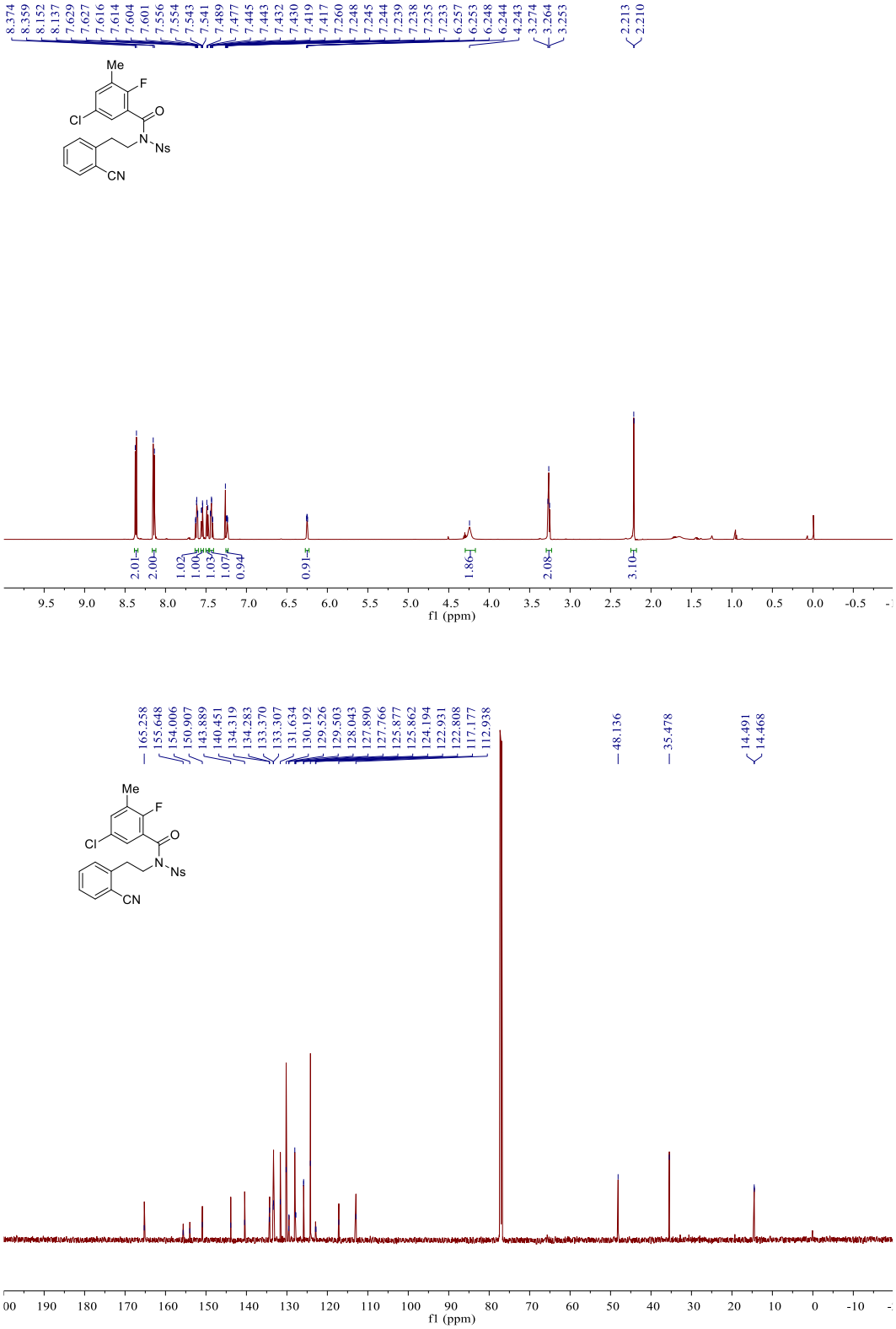


^{1}H and ^{13}C NMR spectra for **6n**

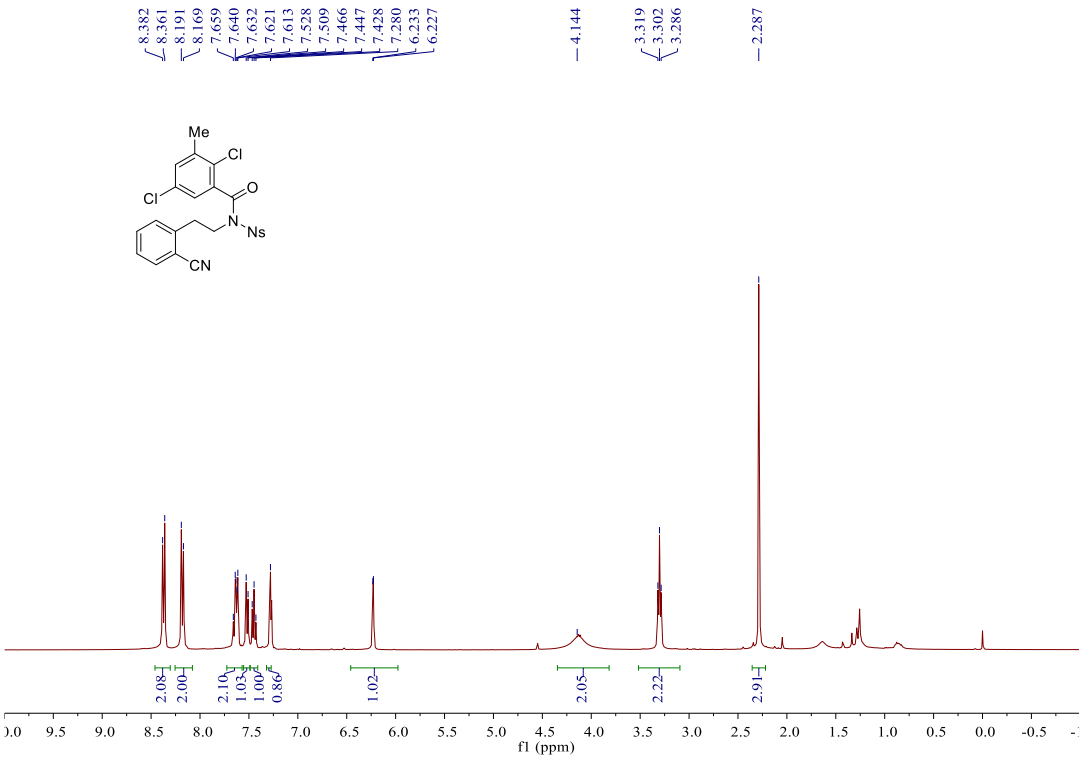


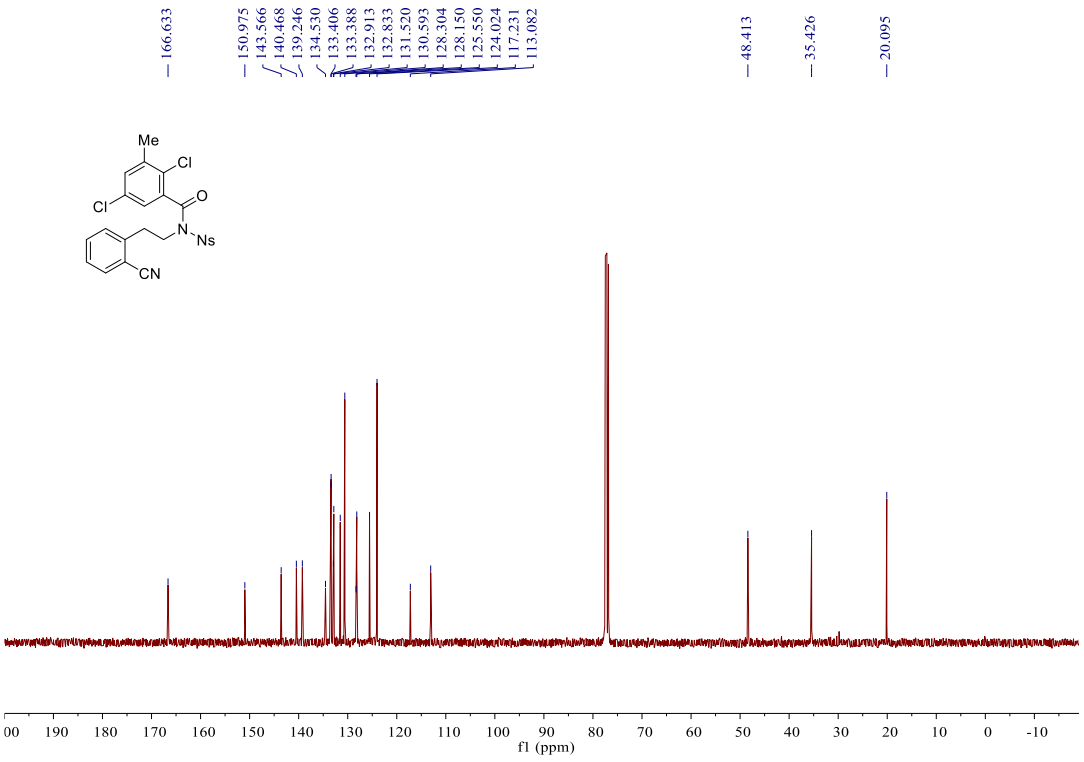


^{1}H and ^{13}C NMR spectra for **6o**

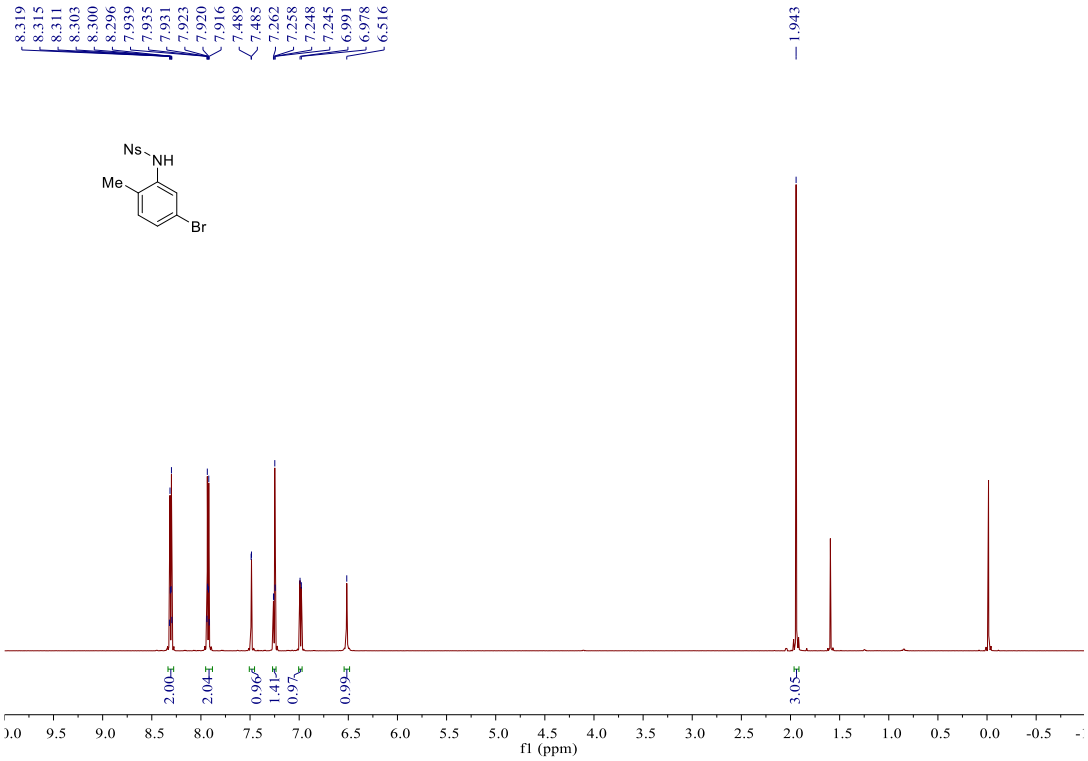


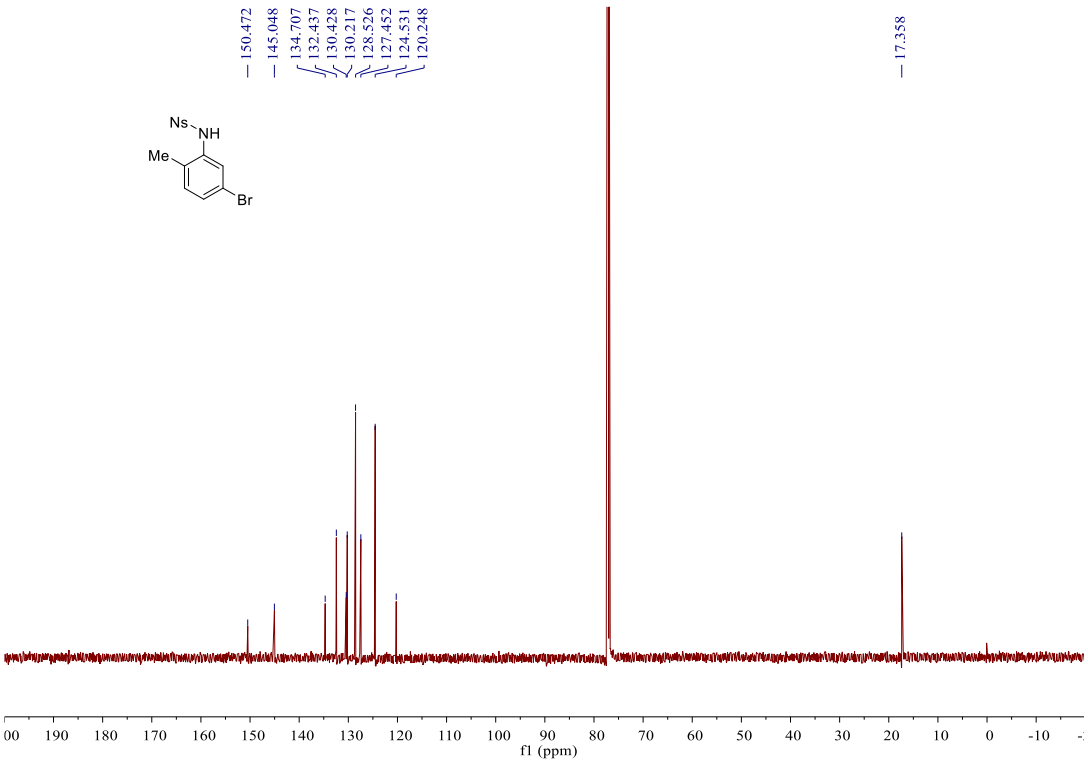
^{1}H and ^{13}C NMR spectra for **6p**



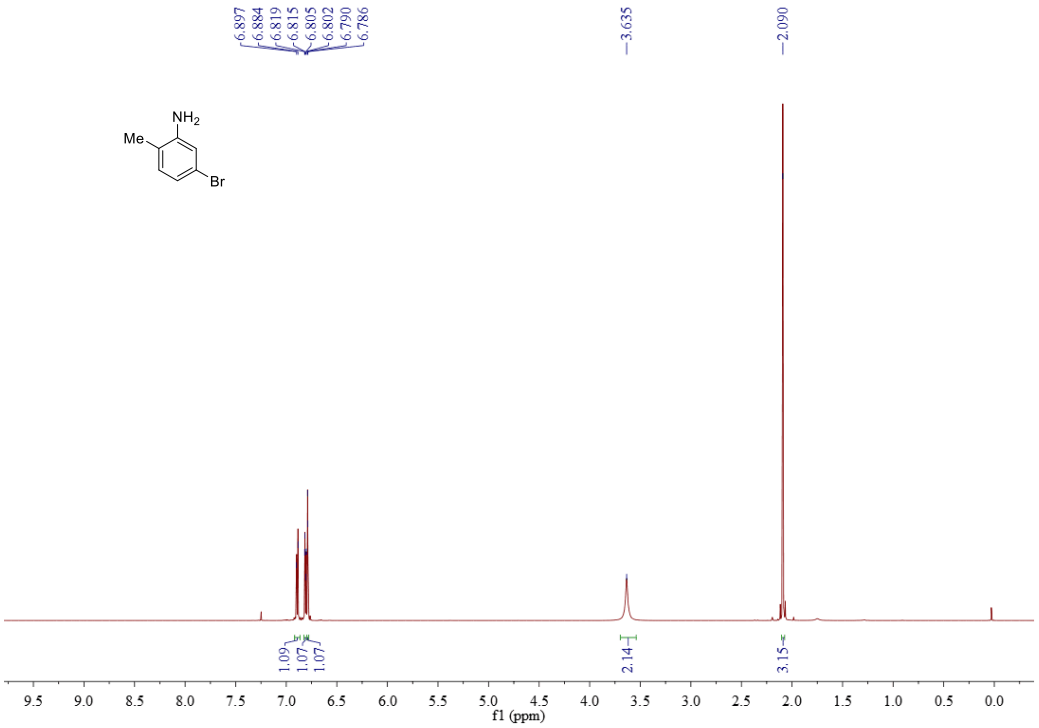


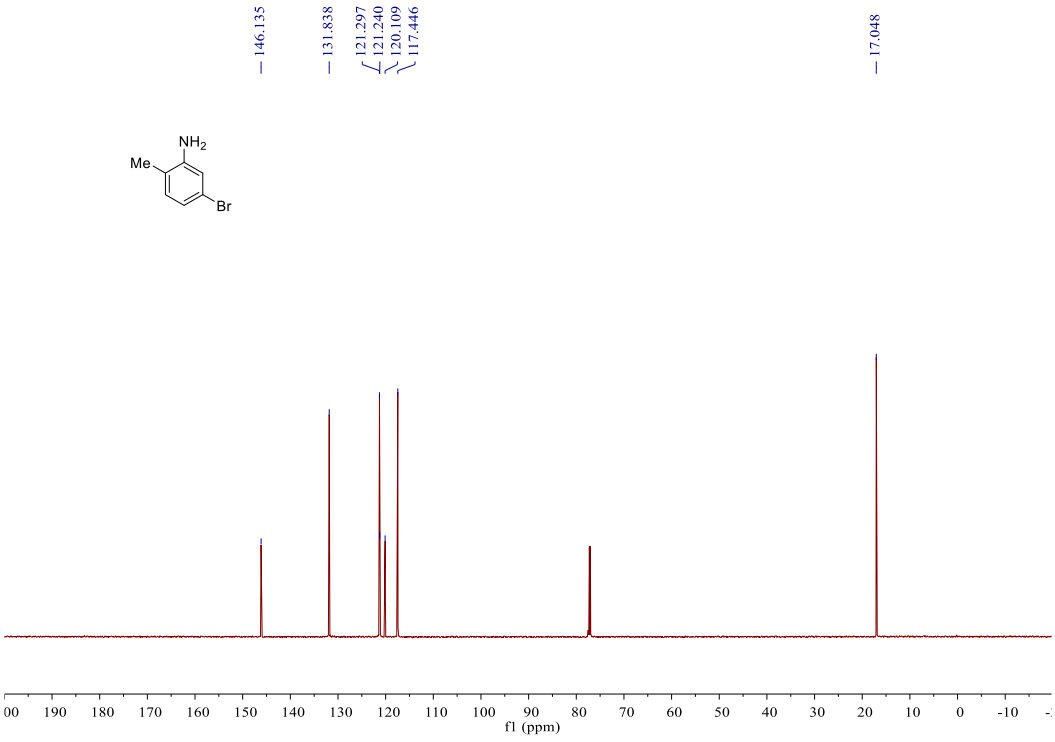
^{1}H and ^{13}C NMR spectra for **6q**



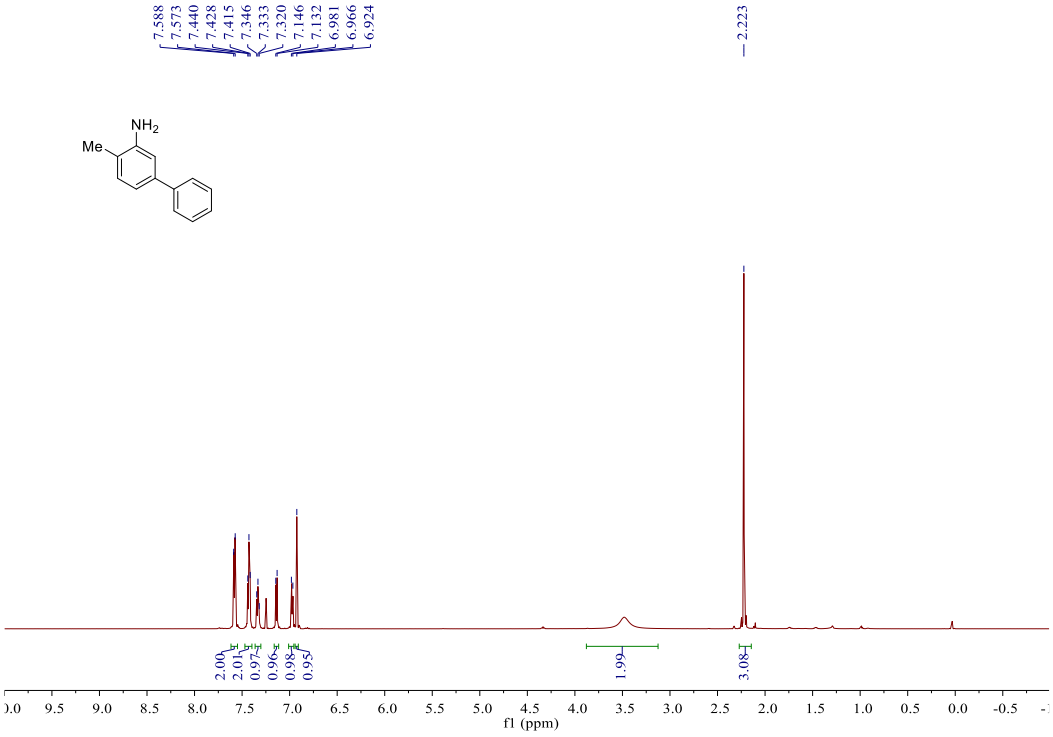


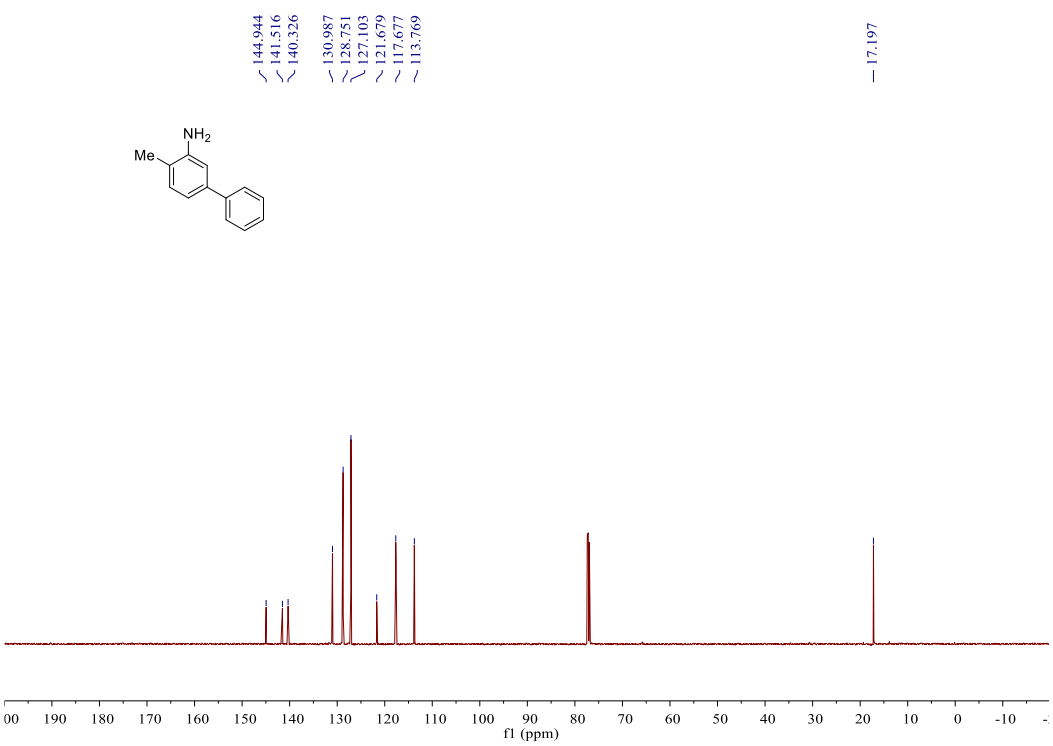
^{1}H and ^{13}C NMR spectra for **7b**



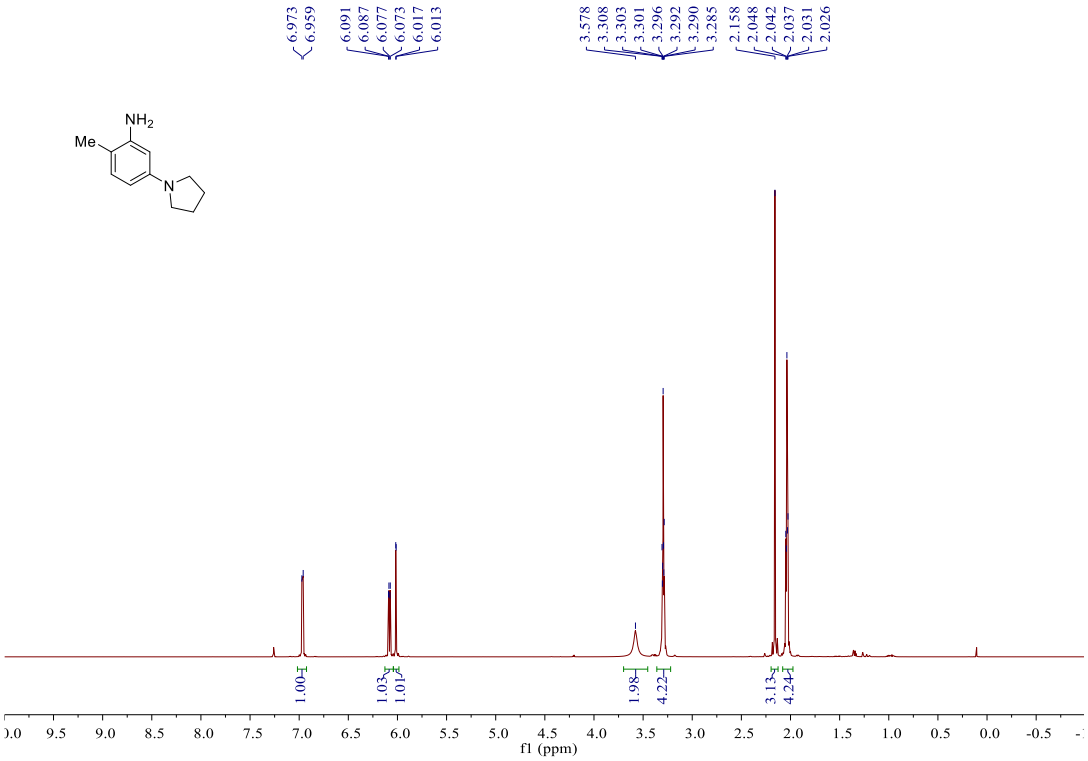


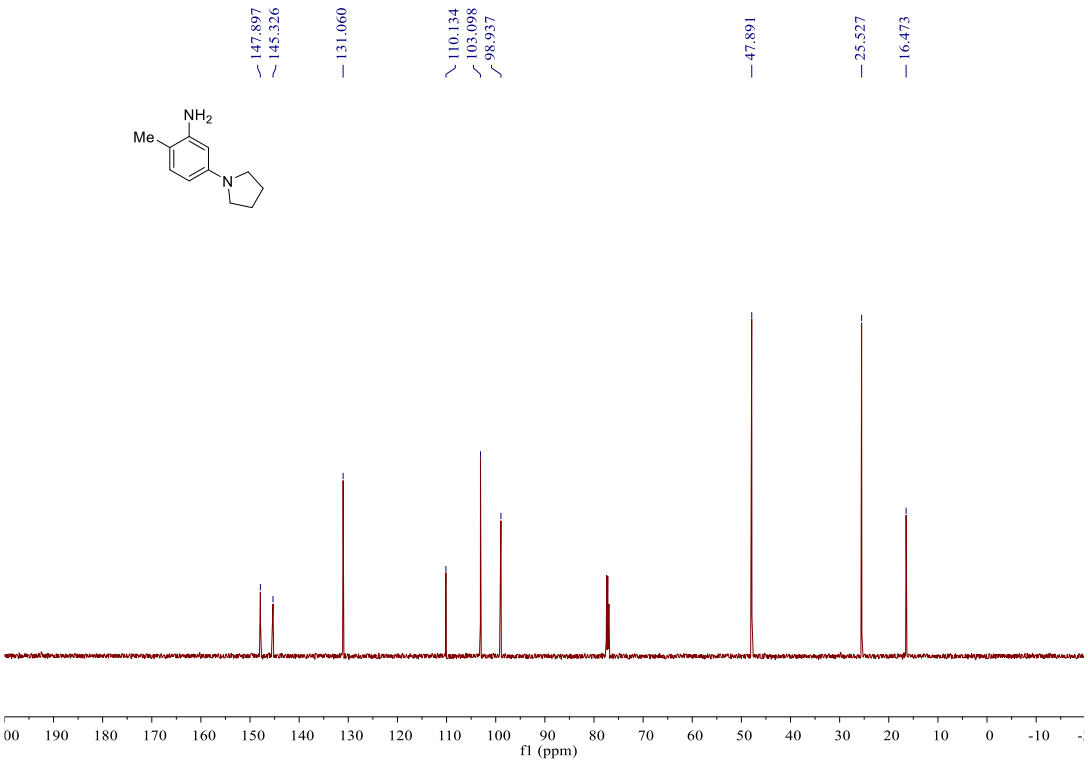
^{1}H and ^{13}C NMR spectra for **8b**



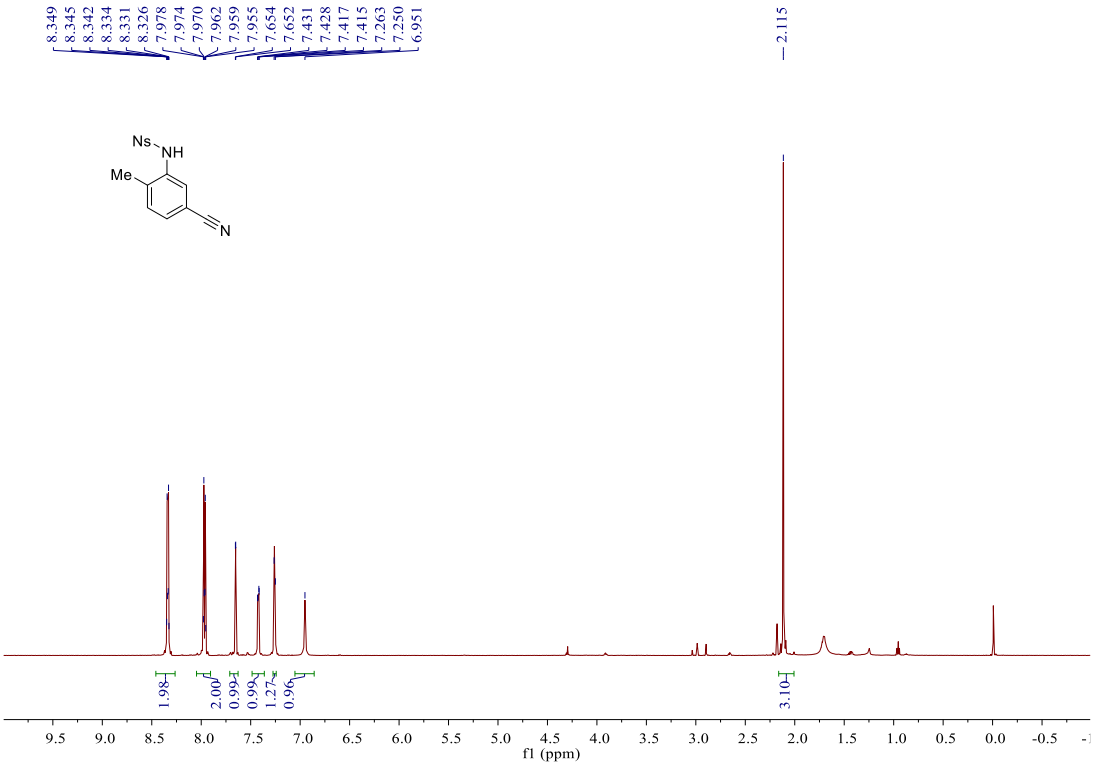


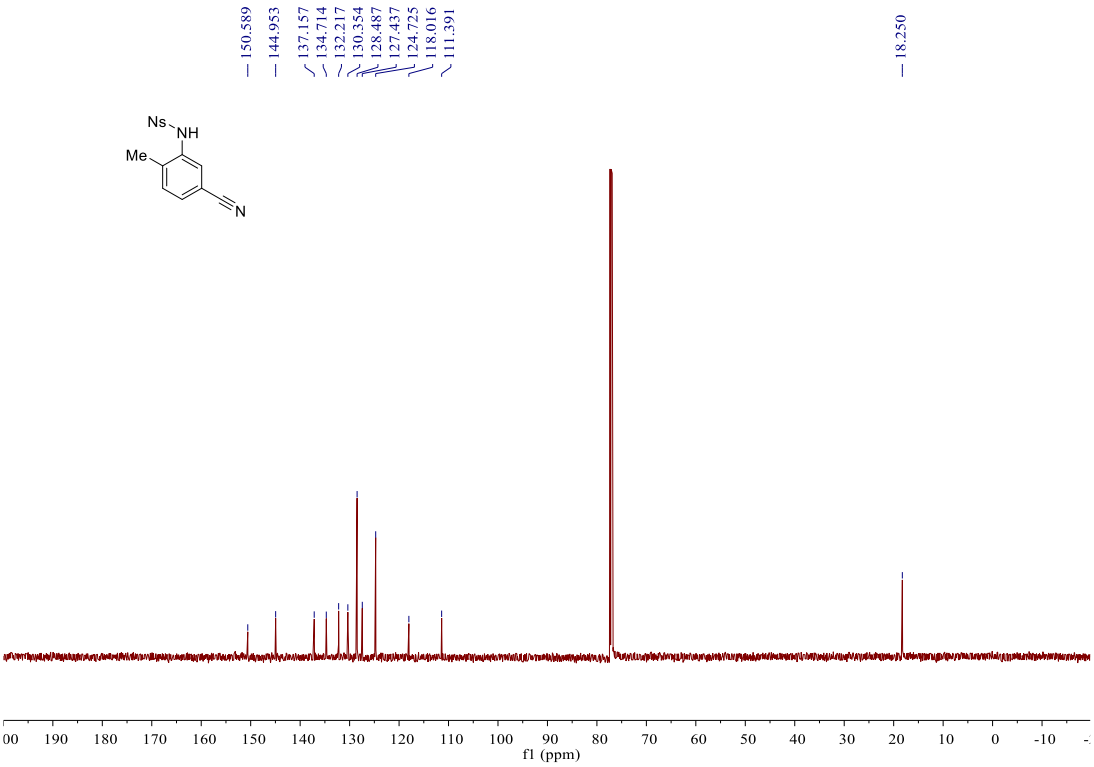
^{1}H and ^{13}C NMR spectra for **9**



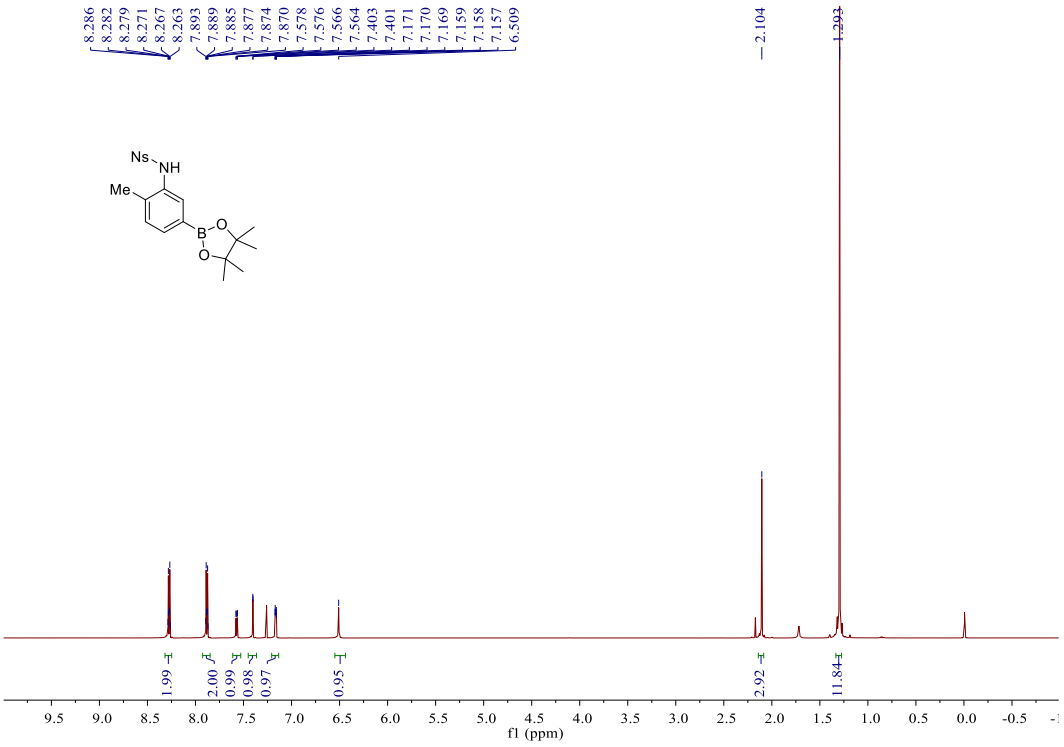


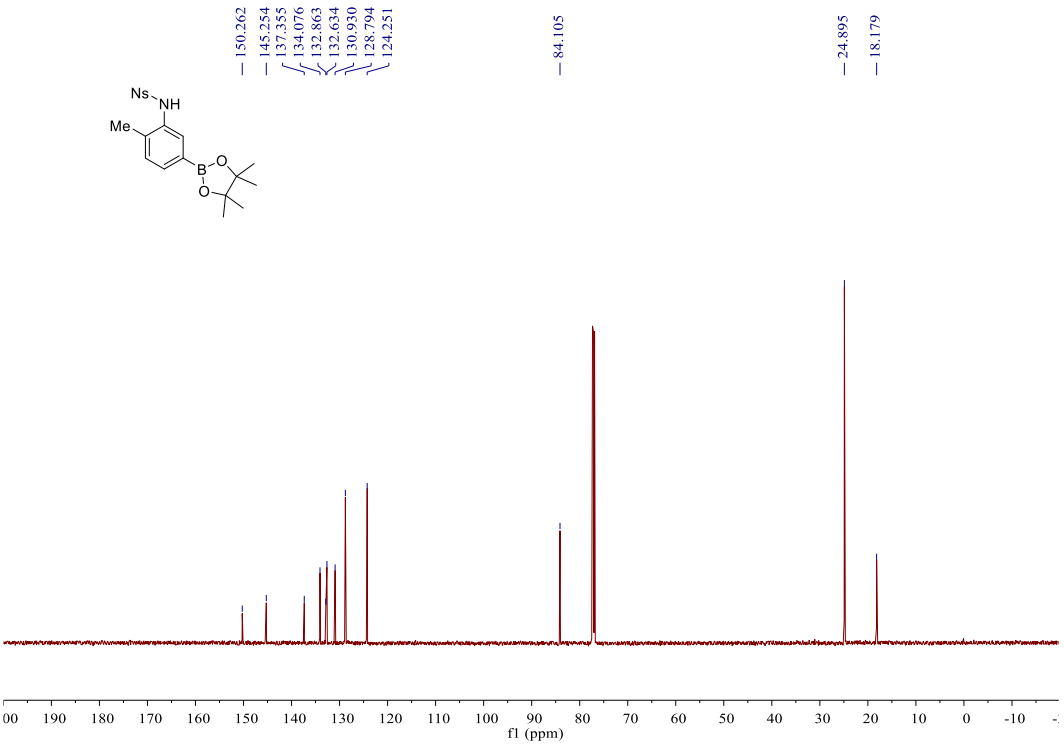
^{1}H and ^{13}C NMR spectra for **10**





^{1}H and ^{13}C NMR spectra for **11**





^{1}H and ^{13}C NMR spectra for **12**