

Nickel-Catalyzed Cyanation of Unactivated Alkyl Sulfonates with Zn(CN)₂

Aiyou Xia, Peizhuo Lv, Xin Xie and Yuanhong Liu*

State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, People's Republic of China

Fax: (+86) 021-64166128, E-mail: yhliu@sioc.ac.cn

Contents:	Page
General Methods	S2
Synthesis of 1a-Ac , 1a-Bz , 1a-Ts and 1a with different protecting groups	S3
General procedure A for the synthesis of alkyl mesylates from alcohols	S7
General procedure B for the synthesis of alkyl mesylates from ketones	S7
Reaction of 1a under the standard conditions for alkyl halides reported in our previous paper	S23
1) Reaction of 1a under the standard conditions for alkyl chlorides reported in our previous paper	S23
2) Reaction of 1a under standard conditions for alkyl bromides reported in our previous paper	S24
Optimization studies for cyanation of secondary alkyl mesylates	S25
Nickel-catalyzed cyanation of secondary alkyl mesylates: synthesis of 2	S30
Reaction of 8a with Zn(CN) ₂ in the presence of n-Bu ₄ NX	S38
Optimization studies for cyanation of the primary alkyl mesylates	S39
Nickel-catalyzed cyanation of primary alkyl mesylates: synthesis of 9	S40
1 mmol scale reaction of 1a	S47
Reaction of 3a under the standard conditions for alkyl halides reported in our previous paper	S47
Mechanistic studies	S49
1) Reaction of 1a with <i>n</i> -Bu ₄ NI in the absence of Zn(CN) ₂	S49

2) Reaction of 1a in the presence of Zn(CN) ₂ with or without <i>n</i> -Bu ₄ NI	S49
3) Reaction of 3a under the standard conditions for alkyl mesylates	S50
4) Portionwise addition of 3a under the standard conditions for alkyl mesylates	S52
5) Reaction of 1a under the standard reaction conditions for 1 h	S52
6) Reaction of 1a with Zn(CN) ₂ in the presence of radical scavengers	S53
References	S54
NMR spectra	S56

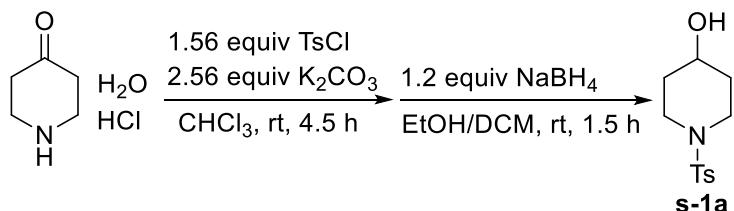
General Methods.

Unless noted, all reactions were carried out using a dry box technique under a nitrogen atmosphere. Tetrahydrofuran and toluene were distilled from sodium and benzophenone. 1,4-Dioxane was distilled from sodium. MeCN was dried using Innovative Technology Solvent Purifier. *N,N*-Dimethylformamide, XantPhos, dppf, PCy₃, *n*-Bu₄NI, Et₄NI and Cs₂CO₃ were purchased from J&K Chemical Company. NiCl₂·6H₂O, Mn, 4-aminopyridine and DABCO (triethylene diamine) were purchased from Alfa Aesar. NiCl₂(DME), NiI₂ and NiXantPhos were purchased from Strem. NiCl₂, DMAP, *n*-Bu₄NCl and *n*-Bu₄NBr were purchased from TCI. 2,2'-Bipyridine was purchased from Acros. Zinc powder (99% metals basis, 325 mesh) was purchased from Adamas. Before using, zinc powder was stirred with 1 M HCl aqueous solution, filtered and washed thoroughly with water, acetone and diethyl ether and dried under vacuum. Unless otherwise noted, all other reagents were purchased from commercial sources. 4-iodo-1-tosylpiperidine (**3a**) was prepared according to the published method.¹

¹H and ¹³C NMR spectra were recorded at room temperature in CDCl₃ (containing 0.03% TMS) solutions on Varian or Agilent XL-400 MHz spectrometer. ¹H NMR spectra was recorded with tetramethylsilane (0.00 ppm) or solvent residual peak (CDCl₃: 7.26 ppm) as internal reference; ¹³C NMR spectra was recorded with CDCl₃ (77.00 ppm) as internal reference. High-resolution mass spectra were obtained by using Waters Micromass GCT Premier or Agilent Technologies 6224 TOF LC/MS. The IR spectra were measured on a ThermoFisher Nicolet FT-IR spectrometer.

Synthesis of 1a-Ac, 1a-Bz, 1a-Ts and 1a with different protecting groups

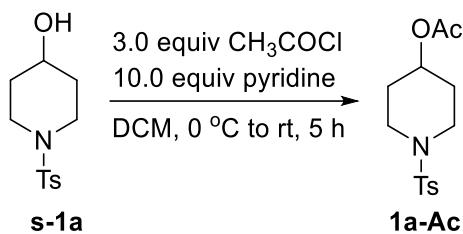
Synthesis of s-1a



To a solution of 4,4-piperidinediol hydrochloride (1.54 g, 10 mmol), K₂CO₃ (3.54 g, 25.6 mmol) in CHCl₃ (12 mL) and H₂O (12 mL) was added TsCl (2.97 g, 15.6 mmol) at room temperature under air. The mixture was stirred at room temperature for 4.5 h. After the starting material was completely consumed, the mixture was quenched with saturated NaHCO₃ solution, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 2:1 to dichloromethane) to afford the white solid which was used for the next step.

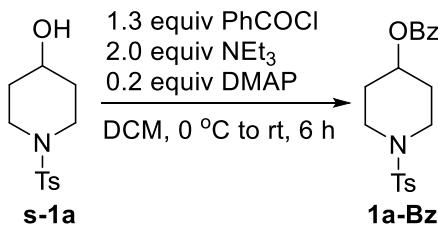
To a solution of the product above in EtOH (20 mL) and CH₂Cl₂ (20 mL) was added NaBH₄ (454.0 mg, 12 mmol) at room temperature under air. The mixture was stirred at room temperature for 1.5 h. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution. The mixture was then evaporated under the reduced pressure to remove most of EtOH, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: dichloromethane: ethyl acetate = 3:1) to afford 1-tosylpiperidin-4-ol (**s-1a**) in 63% isolated yield (1.61 g) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 3.71 (s, 1H), 3.33-3.27 (m, 2H), 2.82-2.76 (m, 2H), 2.43 (s, 3H), 2.07 (bs, 1H), 1.92-1.86 (m, 2H), 1.67-1.58 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 143.5, 132.9, 129.6, 127.5, 65.7, 43.2, 33.1, 21.4. The spectroscopic data is in agreement with that previously reported.²

Synthesis of 1a-Ac



To a solution of **s-1a** (766.0 mg, 3 mmol) in CH_2Cl_2 (10 mL) was added pyridine (2.4 mL, 30 mmol) at room temperature under air. The reaction mixture was then cooled down to 0 °C and acetyl chloride (0.64 mL, 9 mmol) was then added to the mixture. The mixture was warmed to room temperature and stirred for 5 h at room temperature. After the starting material was completely consumed, the mixture was quenched with water, extracted with CH_2Cl_2 , washed with 1M HCl and brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 1:2 to dichloromethane: ethyl acetate = 5:1) to afford 1-tosylpiperidin-4-yl acetate (**1a-Ac**) in 77% isolated yield (683.1 mg) as a white solid. M.p. 157-159 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 4.77-4.72 (m, 1H), 3.34-3.29 (m, 2H), 2.90-2.84 (m, 2H), 2.45 (s, 3H), 2.00 (s, 3H), 1.98-1.91 (m, 2H), 1.80-1.71 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 143.6, 133.1, 129.7, 127.6, 68.4, 43.4, 30.0, 21.5, 21.1. IR (neat): 2930, 1726, 1338, 1310, 1246, 1161, 1094, 1028, 977, 934, 896, 844, 816, 724 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_4\text{NaS}$ 320.0927; found 320.0927.

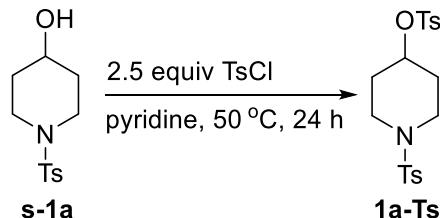
Synthesis of 1a-Bz



To a solution of **s-1a** (766.0 mg, 3 mmol) and DMAP (73.3 mg, 0.6 mmol) in CH_2Cl_2 (10 mL) was added NEt_3 (0.83 mL, 6 mmol) at room temperature under argon. The mixture was then placed at 0 °C and benzoyl chloride (0.45 mL, 3.9 mmol) was then added to the mixture. The mixture was warmed to room temperature and stirred for 6 h at room temperature. After

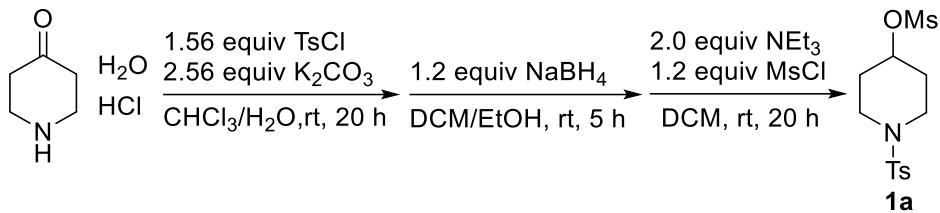
the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with CH₂Cl₂, washed with brine, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 1:1 to 1:4) to afford 1-tosylpiperidin-4-yl benzoate (**1a-Bz**) in 88% isolated yield (946.7 mg) as a white solid. M.p. 179-181 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.05-4.99 (m, 1H), 3.39-3.33 (m, 2H), 3.02-2.97 (m, 2H), 2.45 (s, 3H), 2.09-2.04 (m, 2H), 1.96-1.88 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 165.5, 143.6, 133.0, 130.0, 129.6, 129.4, 128.3, 127.6, 68.8, 43.3, 30.0, 21.5. IR (neat): 1715, 1448, 1334, 1299, 1276, 1163, 1155, 1021, 932, 816, 714, 651 cm⁻¹. HRMS (ESI-TOF) m/z: [M+Na]⁺ calcd for C₁₉H₂₁NO₄NaS 382.1084; found 382.1075.

Synthesis of **1a-Ts**



To a solution of TsCl (4.76 g, 25 mmol) in pyridine (40 mL) was added **s-1a** (2.55 g, 10 mmol) at room temperature under air. The mixture was heated to 50 °C (oil bath) and stirred for 24 h. After the starting material was completely consumed, the mixture was quenched with water. When most pyridine was evaporated under the reduced pressure, the residue was quenched with 1M HCl, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 2:1 to 1:1) to afford 1-tosylpiperidin-4-yl 4-methylbenzenesulfonate (**1a-Ts**) in 86% isolated yield (3.51 g) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.34-7.30 (m, 4H), 4.53-4.50 (m, 1H), 3.14-2.98 (m, 4H), 2.44 (s, 3H), 2.43 (s, 3H), 1.90-1.71 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 144.9, 143.8, 133.7, 132.9, 129.9, 129.7, 127.5, 127.5, 75.9, 42.2, 30.5, 21.5, 21.4. The spectroscopic data is in agreement with that previously reported.³

Synthesis of **1a**



To a solution of 4,4-piperidinediol hydrochloride (3.8 g, 25 mmol), K₂CO₃ (8.8 g, 64 mmol) in H₂O (30 mL) and CHCl₃ (30 mL) was added TsCl (7.4 g, 39 mmol) at room temperature under air. After stirring for 20 h, the mixture was extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 2:1 to dichloromethane) to afford a white solid which was used for the next step.

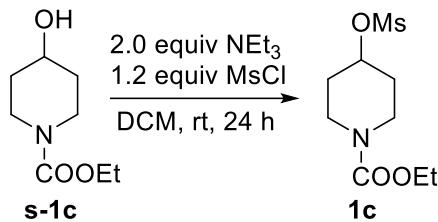
To a solution of the above product in CH₂Cl₂ (50 mL) and EtOH (50 mL) was added NaBH₄ (1.13 g, 30 mmol) by four portions in 15 min at room temperature under air. The mixture was stirred at room temperature for 5 h. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution. When most EtOH was evaporated under the reduced pressure, the residue was extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: dichloromethane to dichloromethane: ethyl acetate = 4:1) to afford the white solid which was used for the next step.

To a solution of the above product in CH₂Cl₂ (50 mL) were added NEt₃ (6.9 mL, 50 mmol) and MsCl (2.3 mL, 30 mmol) separately at room temperature under air. The mixture was stirred for 20 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 1:1 to dichloromethane to dichloromethane: ethyl acetate = 10:1) to afford 1-tosylpiperidin-4-yl methanesulfonate (**1a**) in 89% isolated yield (7.42 g) as a white solid. M.p. 175-177 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.64 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.79-4.74 (m, 1H), 3.17-3.08 (m, 4H), 2.98 (s, 3H), 2.45 (s, 3H), 2.10-1.94 (m, 4H); ¹³C NMR (100 MHz,

CDCl_3) δ 143.8, 132.8, 129.8, 127.5, 75.6, 42.4, 38.5, 30.9, 21.5. IR (neat): 1335, 1325, 1309, 1244, 1170, 1160, 1092, 949, 932, 816, 727, 708 IR (neat): 1715, 1448, 1334, 1299, 1276, 1163, 1155, 1021, 932, 816, 714, 651 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_5\text{NaS}_2$ 356.0597; found 356.0601.

General procedure A for the synthesis of alkyl mesylates from alcohols

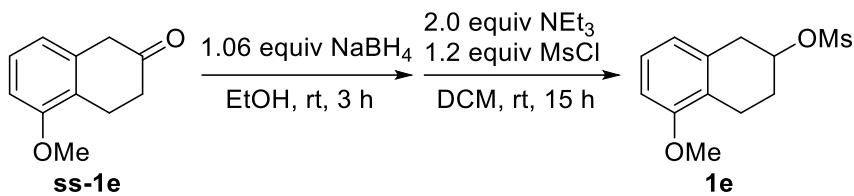
Typical procedure for the synthesis of **1c**.



To a solution of **s-1c** (1.73 g, 10 mmol) in CH_2Cl_2 (20 mL) were added NEt_3 (2.78 mL, 20 mmol) and MsCl (0.93 mL, 12 mmol) at room temperature under air. The mixture was stirred for 24 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2 , dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 2:1 to 1:1) to afford ethyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate (**1c**) in 98% isolated yield (2.46 g) as a light yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 4.93-4.87 (m, 1H), 4.14 (q, J = 7.2 Hz, 2H), 3.77-3.71 (m, 2H), 3.42-3.35 (m, 2H), 3.05 (s, 3H), 2.02-1.95 (m, 2H), 1.87-1.79 (m, 2H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.1, 77.2, 61.3, 40.2, 38.6, 31.4, 14.5. IR (neat): 2935, 1689, 1433, 1348, 1273, 1229, 1170, 940, 909, 877, 855, 767 IR (neat): 1715, 1448, 1334, 1299, 1276, 1163, 1155, 1021, 932, 816, 714, 651 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_9\text{H}_{17}\text{NO}_5\text{NaS}$ 274.0720; found 274.0724.

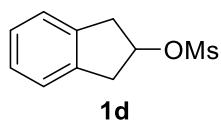
General procedure B for the synthesis of alkyl mesylates from ketones

Typical procedure for the synthesis of **1e**.



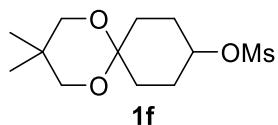
To a solution of **ss-1e** (1.23 g, 7 mmol) in EtOH (14 mL) was added NaBH₄ (279.9 mg, 7.4 mmol) by four portions in 15 min at room temperature under air. The mixture was stirred at room temperature for 3 h. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1 to 3:1) to afford the red oil which was used for the next step.

To a solution of the above product in CH₂Cl₂ (14 mL) were added NEt₃ (1.95 mL, 14 mmol) and MsCl (0.65 mL, 8.4 mmol) at room temperature under air. The mixture was stirred for 15 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1) to afford 5-methoxy-1,2,3,4-tetrahydronaphthalen-2-yl methanesulfonate (**1e**) in 57% isolated yield (1.02 g) over two steps as a light yellow solid. M.p. 79-81 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.12 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 5.16-5.10 (m, 1H), 3.81 (s, 3H), 3.21-3.16 (m, 1H), 3.11-3.01 (m, 4H), 2.94-2.86 (m, 1H), 2.78-2.70 (m, 1H), 2.15-2.07 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 156.9, 133.5, 126.7, 123.7, 121.2, 107.5, 77.6, 55.2, 38.7, 35.4, 28.3, 20.3. IR (neat): 2927, 1585, 1470, 1339, 1327, 1257, 1165, 1096, 1069, 980, 910, 881, 822, 771, 756 cm⁻¹. HRMS (ESI-TOF) m/z: [M+Na]⁺ calcd for C₁₂H₁₆O₄NaS 279.0662; found 279.0661.

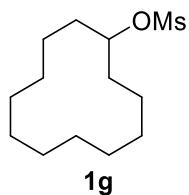


2,3-Dihydro-1H-inden-2-yl methanesulfonate (1d). General procedure A, 5 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether:

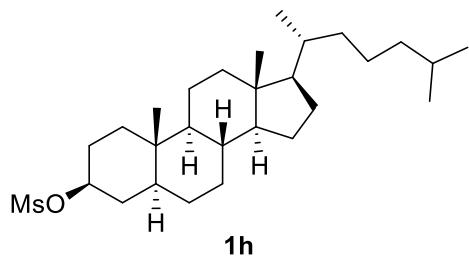
ethyl acetate = 8:1 to 5:1 to dichloromethane) to afford **1d** in 92% isolated yield (977.2 mg) as a light yellow solid. ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.19 (m, 4H), 5.53-5.48 (m, 1H), 3.35 (dd, *J* = 17.2, 6.4 Hz, 2H), 3.24 (dd, *J* = 17.2, 2.8 Hz, 2H), 3.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 139.0, 127.1, 124.6, 81.8, 40.1, 38.5. IR (neat): 3021, 1417, 1327, 1315, 1160, 1001, 944, 886, 797, 744, 731, 700 cm⁻¹. HRMS (EI-TOF) m/z: [M]⁺ calcd for C₁₀H₁₂O₃S 212.0502; found 212.0510.



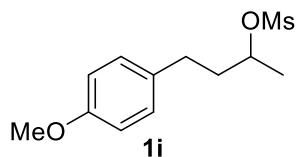
3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-9-yl methanesulfonate (1f). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1) to afford **1f** in 96% isolated yield (2.68 g) over two steps as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 4.85-4.80 (m, 1H), 3.51 (s, 2H), 3.48 (s, 2H), 3.02 (s, 3H), 2.02-1.95 (m, 2H), 1.93-1.89 (m, 4H), 1.85-1.79 (m, 2H), 0.97 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 96.2, 79.0, 70.2, 69.9, 38.6, 30.1, 28.1, 22.6. IR (neat): 2956, 1335, 1172, 1098, 938, 913, 898, 858, 755 cm⁻¹. HRMS (EI-TOF) m/z: [M]⁺ calcd for C₁₂H₂₂O₅S 278.1182; found 278.1179.



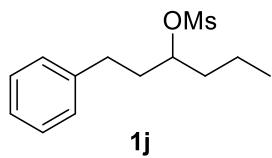
Cyclododecyl methanesulfonate (1g). General procedure A, 5 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1 to 15:1) to afford **1g** in 93% isolated yield (1.22 g) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 4.90-4.84 (m, 1H), 3.00 (s, 3H), 1.90-1.83 (m, 2H), 1.72-1.65 (m, 2H), 1.51-1.34 (m, 18H); ¹³C NMR (100 MHz, CDCl₃) δ 81.9, 38.6, 30.0, 23.9, 23.8, 23.1, 23.0, 20.5. IR (neat): 2930, 1469, 1337, 1167, 975, 930, 908, 876, 868, 833, 723 cm⁻¹. HRMS (EI-TOF) m/z: [M-Ms]⁺ calcd for C₁₂H₂₃O 183.1743; found 183.1746.



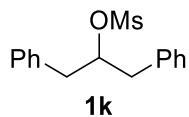
(3*S*,5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl methanesulfonate (1h). General procedure A, 3 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **1h** in 99% isolated yield (1.38 g) as a white solid. ^1H NMR (400 MHz, CDCl_3) δ 4.65-4.57 (m, 1H), 2.99 (s, 3H), 1.98-1.95 (m, 2H), 1.84-0.94 (m, 27H), 0.90-0.82 (m, 13H), 0.65-0.60 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 82.2, 56.3, 56.2, 54.0, 44.8, 42.5, 39.9, 39.4, 38.8, 36.7, 36.1, 35.7, 35.3, 35.2, 35.1, 31.8, 28.6, 28.4, 28.2, 27.9, 24.1, 23.8, 22.8, 22.5, 21.2, 18.6, 12.1, 12.0. The spectroscopic data is in agreement with that previously reported.⁴



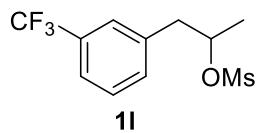
4-(4-Methoxyphenyl)butan-2-yl methanesulfonate (1i). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1) to afford **1i** in 96% isolated yield (2.48 g) over two steps as a light yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.11 (d, J = 8.4 Hz, 2H), 6.85-6.82 (m, 2H), 4.86-4.78 (m, 1H), 3.78 (s, 3H), 2.99 (s, 3H), 2.74-2.60 (m, 2H), 2.07-1.98 (m, 1H), 1.93-1.84 (m, 1H), 1.45 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.9, 132.6, 129.2, 113.9, 79.5, 55.2, 38.6, 38.5, 30.4, 21.2. IR (neat): 2937, 1608, 1511, 1335, 1240, 1169, 972, 916, 899, 831, 817, 805, 749 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4\text{NaS}$ 281.0818; found 281.0826.



1-Phenylhexan-3-yl methanesulfonate (1j). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **1j** in 77% isolated yield (1.97 g) over two steps as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.27 (t, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 7.6 Hz, 3H), 4.78-4.72 (m, 1H), 2.95 (s, 3H), 2.78-2.64 (m, 2H), 2.07-1.93 (m, 2H), 1.79-1.63 (m, 2H), 1.51-1.33 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 140.8, 128.3, 128.1, 125.9, 82.9, 38.4, 36.3, 35.9, 31.0, 18.0, 13.6. IR (neat): 2961, 1456, 1330, 1170, 969, 896, 751, 699 cm⁻¹. HRMS (EI-TOF) m/z: [M-OMs-H]⁺ calcd for C₁₂H₁₆ 160.1247; found 160.1240.

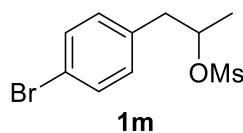


1,3-Diphenylpropan-2-yl methanesulfonate (1k). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford **1k** in 83% isolated yield (2.42 g) over two steps as a light yellow oil. M.p. 79-81 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.21 (m, 10H), 4.93-4.86 (m, 1H), 3.00 (d, *J* = 6.4 Hz, 4H), 2.15 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 136.5, 129.6, 128.6, 127.0, 85.9, 41.0, 37.0. IR (neat): 3029, 1453, 1342, 1170, 971, 896, 881, 755, 744, 700 cm⁻¹. HRMS (ESI-TOF) m/z: [M+Na]⁺ calcd for C₁₆H₁₈O₃NaS 313.0869; found 313.0861.



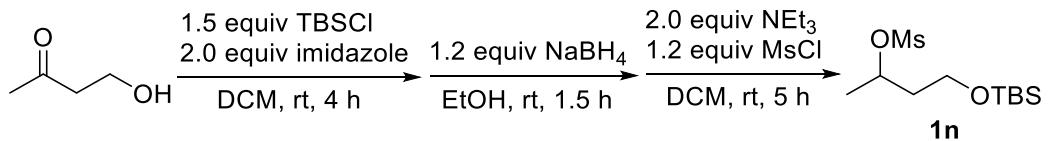
1-(3-(Trifluoromethyl)phenyl)propan-2-yl methanesulfonate (1l). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate: dichloromethane = 5:1:1) to afford **1l** in 85% isolated yield (2.41 g) over two steps as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.53-7.52 (m, 2H), 7.46-7.43 (m, 2H), 4.97-4.89 (m, 1H), 3.07-2.97 (m, 2H), 2.62 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H); ¹³C

¹H NMR (100 MHz, CDCl₃) δ 137.6, 133.0 (d, ⁴J_{C-F} = 1.5 Hz), 130.4 (q, ²J_{C-F} = 32.0 Hz), 128.9, 126.0 (q, ³J_{C-F} = 3.7 Hz), 123.9 (q, ¹J_{C-F} = 270.7 Hz), 123.6 (q, ³J_{C-F} = 3.7 Hz), 80.1, 42.2, 37.5, 20.8. IR (neat): 1363, 1346, 1328, 1168, 1127, 1073, 906, 889, 811, 704 cm⁻¹. HRMS (EI-TOF) m/z: [M-CH₃]⁺ calcd for C₁₀H₁₀O₃F₃S 267.0297; found 267.0309.



1-(4-Bromophenyl)propan-2-yl methanesulfonate (1m). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate: dichloromethane = 4:1:1) to afford **1m** in 89% isolated yield (2.60 g) over two steps as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 4.91-4.83 (m, 1H), 2.96-2.85 (m, 2H), 2.64 (s, 3H), 1.43 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 135.4, 131.4, 131.1, 120.7, 80.2, 42.0, 37.7, 20.9. IR (neat): 1487, 1370, 1343, 1330, 1171, 918, 906, 892, 841, 801, 786, 710 cm⁻¹. HRMS (EI-TOF) m/z: [M]⁺ calcd for C₁₀H₁₃O₃BrS 291.9763; found 291.9766.

Synthesis of 1n



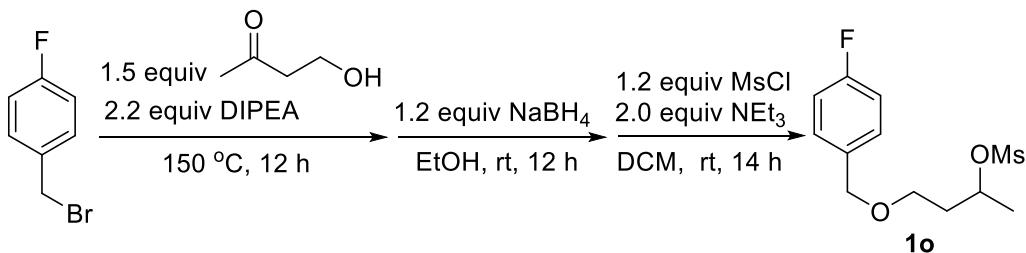
To a solution of 4-hydroxy-2-butanone (881.1 mg, 10 mmol) in CH₂Cl₂ (20 mL) were added imidazole (1.36 g, 20 mmol) and TBSCl (2.26 g, 15 mmol) at room temperature under air. The mixture was stirred for 4 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NaHCO₃ solution, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford the yellow oil which was used for the next step.

To a solution of the product above in EtOH (20 mL) was added NaBH₄ (454.0 mg, 12 mmol) by four portions in 15 min at room temperature under air. The mixture was stirred at

room temperature for 1.5 h. After the starting material was completely consumed, the mixture was quenched with saturated NaHCO_3 solution, extracted with ethyl acetate, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford the colourless oil which was used for the next step.

To a solution of the product above in CH_2Cl_2 (20 mL) were added NEt_3 (2.78 mL, 20 mmol) and MsCl (0.93 mL, 12 mmol) at room temperature under air. The mixture was stirred for 5 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NaHCO_3 solution, extracted with CH_2Cl_2 , dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford 4-((*tert*-butyldimethylsilyl)oxy)butan-2-yl methanesulfonate (**1n**) in 68% isolated yield (1.93 g) over three steps as a light yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 5.00-4.92 (m, 1H), 3.75-3.67 (m, 2H), 3.02 (s, 3H), 1.94-1.86 (m, 1H), 1.82-1.70 (m, 1H), 1.47 (d, J = 6.4 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 77.5, 58.4, 39.4, 38.0, 25.8, 21.6, 18.1, -5.5. IR (neat): 2930, 1352, 1255, 1175, 1086, 900, 834, 811, 775 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{11}\text{H}_{26}\text{O}_4\text{NaSiS}$ 305.1213; found 305.1218.

Synthesis of **1o**



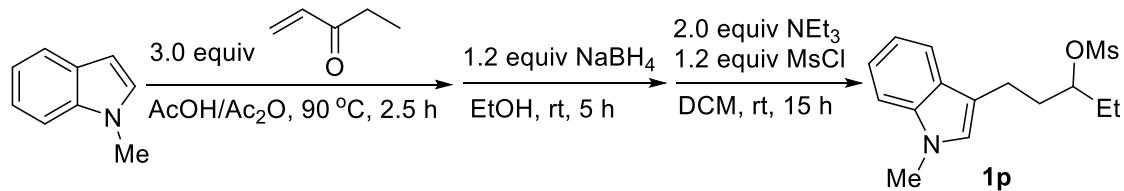
4-Fluorobenzyl bromide (1.89 g, 10 mmol), 4-hydroxy-2-butanone (1.32 g, 15 mmol) and DIPEA (3.64 mL, 22 mmol) were charged in a reaction vessel under Ar. The mixture was heated at 150 °C (oil bath) for 12 h. After the starting material was completely consumed, the mixture was quenched with 1 M HCl , extracted with ethyl acetate, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 8:1) to afford the

yellow oil which was used for the next step.

To a solution of the above product in EtOH (20 mL) was added NaBH₄ (454.0 mg, 12 mmol) by four portions in 15 min at room temperature under air. The mixture was stirred at room temperature for 12 h. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with ethyl acetate, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1 to 2:1) to afford the colourless oil which was used for the next step.

To a solution of the above product in CH₂Cl₂ (20 mL) were added NEt₃ (2.78 mL, 20 mmol) and MsCl (0.93 mL, 12 mmol) separately at room temperature under air. The mixture was stirred for 14 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1 to 3:1) to afford 4-((4-fluorobenzyl)oxy)butan-2-yl methanesulfonate (**1o**) in 52% isolated yield (1.44 g) over three steps as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.29 (m, 2H), 7.03 (t, *J* = 8.4 Hz, 2H), 5.03-4.95 (m, 1H), 4.46 (dd, *J* = 16.0 Hz, 11.6 Hz, 2H), 3.62-3.52 (m, 2H), 2.96 (s, 3H), 2.01-1.86 (m, 2H), 1.45 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.3 (d, ¹J_{C-F} = 244.0 Hz), 133.7 (d, ⁴J_{C-F} = 2.9 Hz), 129.5 (d, ³J_{C-F} = 8.2 Hz), 115.2 (d, ²J_{C-F} = 21.1 Hz), 77.3, 72.4, 65.7, 38.2, 36.6, 21.5. IR (neat): 2875, 1605, 1503, 1333, 1211, 1171, 1090, 900, 855, 815, 783, 720 cm⁻¹. HRMS (ESI-TOF) m/z: [M+Na]⁺ calcd for C₁₂H₁₇O₄FNaS 299.0724; found 299.0724.

Synthesis of **1p**



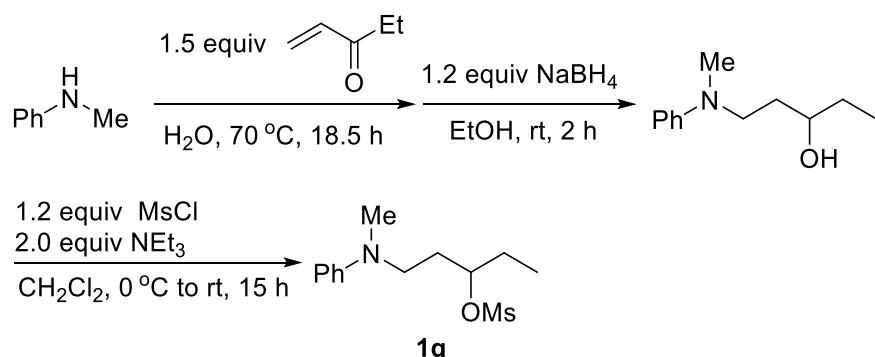
To a solution of 1-methylindole (1.31 g, 10 mmol) in AcOH (6 mL) and Ac₂O (2 mL) was added ethyl vinyl ketone (2.97 mL, 30 mmol) at room temperature under air. After stirring for

5 min at room temperature, the mixture was heated to 90 °C (oil bath) and stirred for 2.5 h. After the starting material was completely consumed, the mixture was cooled to 0 °C, quenched with water, added NaHCO₃ until the mixture was base, extracted with ethyl acetate, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford the yellow oil which was used for the next step.

To a solution of the above product in EtOH (20 mL) was added NaBH₄ (454.0 mg, 12 mmol) by four portions in 15 min at room temperature under air. The mixture was stirred at room temperature for 5 h. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with ethyl acetate, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1 to 2:1) to afford the yellow oil which was used for the next step.

To a solution of the above product in CH₂Cl₂ (20 mL) were added NEt₃ (2.78 mL, 20 mmol) and MsCl (0.93 mL, 12 mmol) separately at room temperature under air. The mixture was stirred for 15 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 1:1 to 1:3) to afford 1-(1-methyl-1*H*-indol-3-yl)pentan-3-yl methanesulfonate (**1p**) in 62% isolated yield (1.83 g) over three steps as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.22-7.19 (m, 1H), 7.11-7.07 (m, 1H), 6.88 (s, 1H), 4.79-4.73 (m, 1H), 3.70 (s, 3H), 2.96 (s, 3H), 2.92-2.78 (m, 2H), 2.15-1.99 (m, 2H), 1.86-1.71 (m, 2H), 0.98 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 136.9, 127.4, 126.3, 121.4, 118.6, 118.5, 113.2, 109.1, 84.5, 38.5, 34.3, 32.4, 27.3, 20.5, 9.0. IR (neat): 2927, 1480, 1342, 1326, 1172, 974, 901, 840, 737 cm⁻¹. HRMS (ESI-TOF) m/z: [M+Na]⁺ calcd for C₁₅H₂₁NO₃NaS 318.1134; found 318.1136.

Synthesis of **1q**

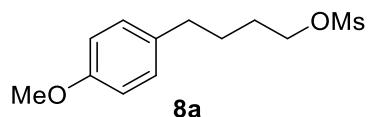


To a solution of *N*-Methylaniline (0.54 mL, 5 mmol) in H_2O (5 mL) was added ethyl vinyl ketone (630.9 mg, 7.5 mmol) at room temperature under air. The mixture was stirred for 18.5 h at 70°C (oil bath). After the starting material was completely consumed, the mixture was extracted with ethyl acetate, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 15:1 to 10:1) to afford the light yellow oil which was used for the next step.

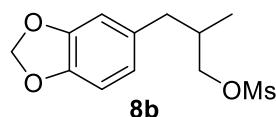
To a solution of the above product in EtOH (10 mL) was added NaBH_4 (226.9 mg, 6 mmol) at room temperature under air. The mixture was stirred at room temperature for 2 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 15:1 to 5:1) to afford the light yellow oil which was used for the next step.

To a solution of the above product (386.6 mg, 2 mmol) in CH_2Cl_2 (10 mL) were added NEt_3 (0.56 mL, 4 mmol) at room temperature under air. The mixture was placed at 0°C and MsCl (0.19 mL, 2.4 mmol) was then added to the mixture. The mixture was stirred for 15 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2 , washed with brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to 1-(methyl(phenyl)amino)pentan-3-yl methanesulfonate (**1q**) in 70% isolated yield (379.5 mg) as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.24-7.20 (m, 2H), 6.71-6.68

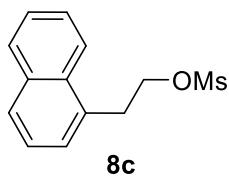
(m, 3H), 4.75-4.69 (m, 1H), 3.53-3.36 (m, 2H), 2.97 (s, 3H), 2.92 (s, 3H), 1.95-1.90 (m, 2H), 1.80-1.73 (m, 2H), 0.97 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.8, 129.1, 116.5, 112.4, 82.9, 48.5, 38.5, 38.3, 30.3, 27.6, 9.1. IR (neat): 2936, 1599, 1506, 1331, 1171, 903, 748, 692 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{22}\text{NO}_3\text{S}$ 272.1315; found 272.1317.



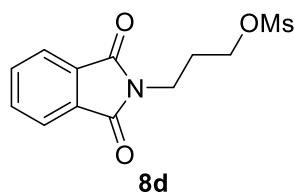
4-(4-Methoxyphenyl)butyl methanesulfonate (8a). General procedure A, 15 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford **8a** in 98% isolated yield (3.78 g) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.08 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 4.21 (t, J = 6.0 Hz, 2H), 3.77 (s, 3H), 2.97 (s, 3H), 2.59 (t, J = 7.2 Hz, 2H), 1.79-1.66 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.74, 133.5, 129.2, 113.7, 69.9, 55.1, 37.1, 34.1, 28.4, 27.3. The spectroscopic data is in agreement with that previously reported.⁵



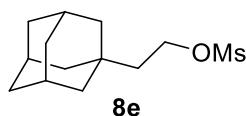
3-(Benzo[d][1,3]dioxol-5-yl)-2-methylpropyl methanesulfonate (8b). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate: dichloromethane = 4:1:1) to afford **8b** in 88% isolated yield (2.39 g) over two steps as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 6.73 (d, J = 7.6 Hz, 1H), 6.65 (s, 1H), 6.60 (d, J = 7.6 Hz, 1H), 5.92 (s, 2H), 4.09-4.00 (m, 2H), 3.00 (s, 3H), 2.69-2.64 (m, 1H), 2.46-2.41 (m, 1H), 2.17-2.09 (m, 1H), 0.98 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.2, 145.6, 132.5, 121.6, 108.9, 107.7, 100.5, 73.4, 38.2, 36.5, 34.6, 15.7. IR (neat): 2919, 1495, 1440, 1333, 1241, 1163, 1035, 963, 930, 851, 799, 749 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{16}\text{O}_5\text{NaS}$ 295.0611; found 295.0610.



2-(Naphthalen-1-yl)ethyl methanesulfonate (8c). General procedure A, 5 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1 to 3:1) to afford **8c** in 99% isolated yield (1.24 g) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.95 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.52-7.43 (m, 2H), 7.38-7.31 (m, 2H), 4.45 (t, *J* = 7.2 Hz, 2H), 3.45 (t, *J* = 7.2 Hz, 2H), 2.69 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 133.6, 131.9, 131.5, 128.8, 127.7, 127.2, 126.3, 125.6, 125.3, 122.9, 69.5, 36.9, 32.4. The spectroscopic data is in agreement with that previously reported.⁶

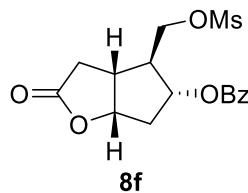


3-(1,3-Dioxoisindolin-2-yl)propyl methanesulfonate (8d). General procedure A, 20 mmol scale. The crude product was recrystallized with CH₂Cl₂/EtOH to afford **8d** in 81% yield (4.61 g) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.88-7.84 (m, 2H), 7.77-7.74 (m, 2H), 4.28 (t, *J* = 6.4 Hz, 2H), 3.85 (t, *J* = 6.4 Hz, 2H), 3.06 (s, 3H), 2.19-2.13 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 168.2, 134.1, 131.8, 123.3, 67.1, 37.3, 34.3, 28.1. IR (neat): 1702, 1347, 1174, 1058, 981, 926, 877, 832, 721, 711 cm⁻¹. HRMS (ESI-TOF) m/z: [M+Na]⁺ calcd for C₁₂H₁₃NO₅NaS 306.0407; found 306.0407.



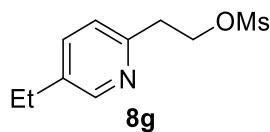
2-((3r,5r,7r)-Adamantan-1-yl)ethyl methanesulfonate (8e). General procedure A, 5 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford **8e** in 97% isolated yield (1.25 g) as a light yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 4.29 (t, *J* = 7.2 Hz, 2H), 3.00 (s, 3H), 1.97 (s,

3H), 1.73-1.70 (m, 3H), 1.65-1.62 (m, 3H), 1.57-1.54 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3) δ 66.7, 42.6, 42.2, 37.3, 36.7, 31.7, 28.3. IR (neat): 2898, 2846, 1451, 1351, 1170, 974, 949, 933, 840, 814, 789 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{22}\text{O}_3\text{NaS}$ 281.1182; found 281.1188.

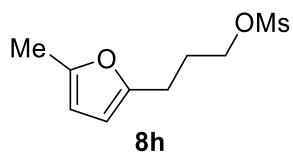


(3a*R*,4*S*,5*R*,6*aS*)-4-((Methylsulfonyloxy)methyl)-2-oxohexahydro-2*H*-cyclopenta[*b*]furan-5-yl benzoate (8f).

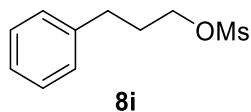
General procedure A, 3.6 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 1:3 to 1:5) to afford **8f** in 96% isolated yield (1.23 g) as a white solid. ^1H NMR (400 MHz, CDCl_3) δ 8.00-7.98 (m, 2H), 7.60-7.56 (m, 1H), 7.47-7.43 (m, 2H), 5.40-5.36 (m, 1H), 5.10-5.08 (m, 1H), 4.31 (d, $J = 5.6$ Hz, 2H), 3.06 (s, 3H), 2.99-2.89 (m, 2H), 2.60-2.48 (m, 3H), 2.39-2.35 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 175.9, 165.8, 133.4, 129.5, 129.1, 128.5, 83.9, 76.6, 68.5, 51.8, 40.2, 38.0, 37.3, 35.5. IR (neat): 1765, 1712, 1350, 1277, 1171, 1115, 978, 926, 718 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{18}\text{O}_7\text{NaS}$ 377.0665; found 377.0661.



2-(5-Ethylpyridin-2-yl)ethyl methanesulfonate (8g). General procedure A, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 1:1) to afford **8g** in 89% isolated yield (2.03 g) as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 8.38 (s, 1H), 7.46 (d, $J = 8.0$ Hz, 1H), 7.15 (d, $J = 8.0$ Hz, 1H), 4.63 (t, $J = 6.4$ Hz, 2H), 3.17 (t, $J = 6.4$ Hz, 2H), 2.91 (s, 3H), 2.61 (q, $J = 7.6$ Hz, 2H), 1.22 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 153.2, 148.5, 136.9, 135.4, 122.8, 68.9, 36.4, 25.0, 14.8. IR (neat): 2966, 1487, 1348, 1170, 954, 908, 803 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{10}\text{H}_{16}\text{NO}_3\text{S}$ 230.0845; found 230.0847.

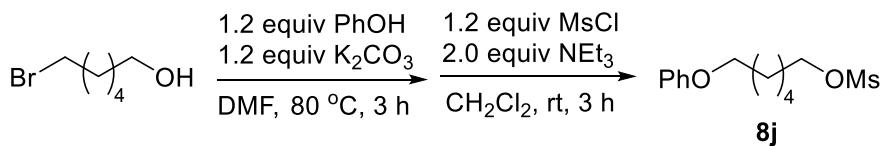


3-(5-Methylfuran-2-yl)propyl methanesulfonate (8h). General procedure B, 10 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1) to afford **8h** in 63% isolated yield (1.38 g) over two steps as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 5.91-5.85 (m, 2H), 4.25 (t, *J* = 6.4 Hz, 2H), 3.00 (s, 3H), 2.72 (t, *J* = 7.2 Hz, 2H), 2.24 (s, 3H), 2.10-2.03 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 151.9, 150.7, 106.3, 105.9, 69.0, 37.1, 27.6, 23.8, 13.4. IR (neat): 2922, 1566, 1350, 1170, 972, 941, 920, 830, 784 cm⁻¹. HRMS (EI-TOF) m/z: [M]⁺ calcd for C₉H₁₄O₄S 218.0607; found 218.0607.



3-Phenylpropyl methanesulfonate (8i). General procedure B, 20 mmol scale. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1) to afford **8i** in 56% isolated yield (2.40 g) over two steps as a light yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.31-7.17 (m, 5H), 4.21 (t, *J* = 6.0 Hz, 2H), 2.96 (s, 3H), 2.74 (t, *J* = 7.2 Hz, 2H), 2.10-2.03 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 140.2, 128.4, 128.3, 126.2, 69.1, 37.1, 31.4, 30.5. The spectroscopic data is in agreement with that previously reported.⁷

Synthesis of 8j

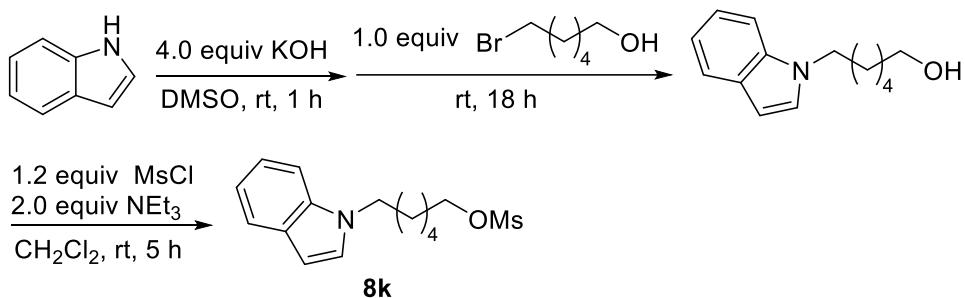


To a solution of PhOH (1.13g, 12 mmol) in DMF (30 mL) was added K₂CO₃ (1.66 g, 12 mmol) at room temperature under air. After stirring for 0.5 h, 6-bromo-1-hexanol (1.3 mL, 10 mmol) was added to the mixture. The mixture was then stirred at 80 °C (oil bath) for 3 h. After the starting material was completely consumed, the mixture was quenched with saturated NH₄Cl solution, extracted with ethyl acetate, washed with H₂O and brine, dried over anhydrous

Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford the product which was used for the next step.

To a solution of the above product in CH_2Cl_2 (30 mL) were added NEt_3 (2.78 mL, 20 mmol) and MsCl (0.93 mL, 12 mmol) at room temperature under air. The mixture was stirred for 3 h at room temperature. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford 6-phenoxyhexyl methanesulfonate (**8j**) in 86% isolated yield (2.33 g) over two steps as a light yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.29-7.25 (m, 2H), 6.94-6.87 (m, 3H), 4.22 (t, J = 6.4 Hz, 2H), 3.95 (t, J = 6.4 Hz, 2H), 2.97 (s, 3H), 1.82-1.72 (m, 4 H), 1.52-1.46 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.8, 129.3, 120.4, 114.3, 69.9, 67.3, 37.1, 28.9, 28.9, 25.4, 25.1. The spectroscopic data is in agreement with that previously reported.⁸

Synthesis of **8k**

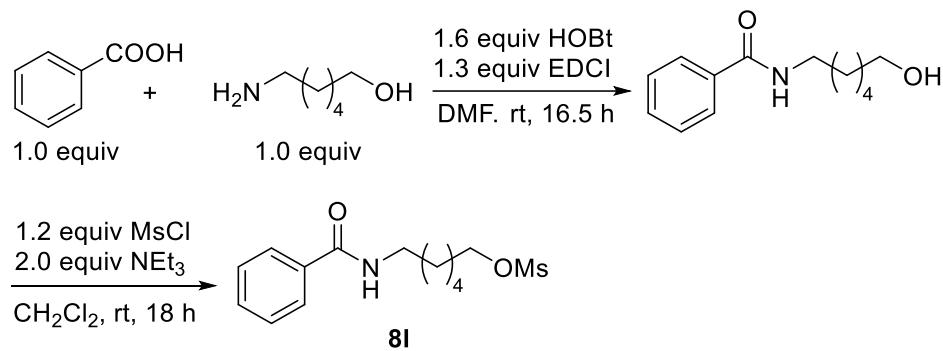


To a solution of indole (3.51 g, 30 mmol) in DMSO (50 mL) was added KOH (2.24 g, 40 mmol) at room temperature under air. After stirring for 1 h, 6-bromo-1-hexanol (1.3 mL, 10 mmol) was added to the mixture. The mixture was then stirred at room temperature for 18 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with H_2O and brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford

the product as a light yellow oil, which was used for the next step.

To a solution of the above product (434.6 mg, 2 mmol) in CH_2Cl_2 (20 mL) was added NEt_3 (0.56 mL, 4 mmol) at room temperature under air. The mixture was then stirred at 0 °C and MsCl (0.19 mL, 2.4 mmol) was added to the mixture. After addition, the mixture was then stirred at room temperature for 5 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2 , washed with H_2O and brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford 6-(1*H*-indol-1-yl)hexyl methanesulfonate (**8k**) in 93% isolated yield (550.1 mg) as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.19-7.15 (m, 1H), 7.09-7.04 (m, 2H), 6.46 (d, J = 3.2 Hz, 1H), 4.11-4.04 (m, 4H), 2.86 (s, 3H), 1.82-1.75 (m, 2H), 1.67-1.60 (m, 2H), 1.39-1.23 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 135.7, 128.4, 127.6, 121.2, 120.7, 119.0, 109.2, 100.7, 69.8, 45.9, 36.9, 29.8, 28.7, 26.1, 24.9. IR (neat): 2936, 2860, 1349, 1171, 946, 918, 740 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_3\text{NaS}$ 318.1134; found 318.1133.

Synthesis of **8l**



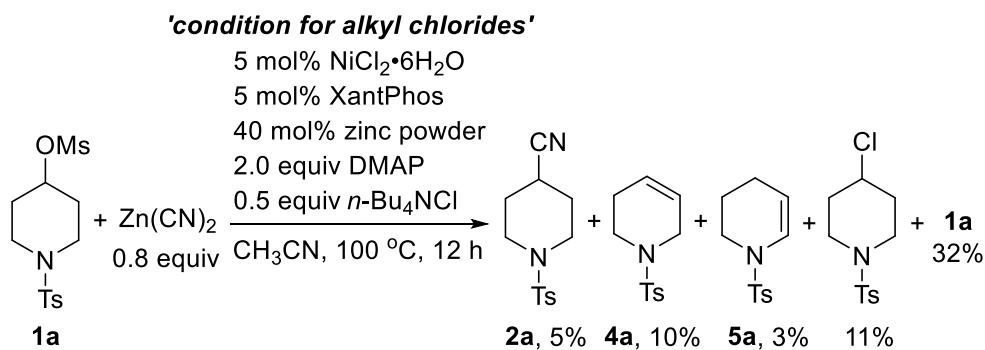
To a solution of benzoic acid (1.22 g, 10 mmol) and 6-amino-1-hexanol (1.32 mL, 10 mmol) in DMF (60 mL) was added EDCI (1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide) (2.02 g, 13 mmol) and HOBT (1-hydroxybenzotriazole) (2.16 g, 16 mmol) at room temperature under air. The mixture was then stirred at room temperature for 16.5 h. After the starting material was completely consumed, the mixture was quenched with H_2O , extracted with CH_2Cl_2 , washed with H_2O and brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent:

petroleum ether: ethyl acetate = 2:1 to ethyl acetate: methanol = 20:1 to 10:1) to afford the product as a white solid, which was used for the next step.

To a solution of the above product (442.6 mg, 2 mmol) in CH_2Cl_2 (10 mL) was added NEt_3 (0.56 mL, 4 mmol) at room temperature under air. The mixture was then stirred at 0 °C and MsCl (0.19 mL, 2.4 mmol) was added to the mixture. After addition, the mixture was then stirred at room temperature for 18 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2 , washed with H_2O and brine, dried over anhydrous Na_2SO_4 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 2:1 to 1:2) to afford 6-benzamidohexyl methanesulfonate (**8I**) in 91% isolated yield (542.4 mg) as a white solid. ^1H NMR (400 MHz, CDCl_3) δ 7.79-7.77 (m, 2H), 7.50-7.46 (m, 1H), 7.40 (t, J = 7.6 Hz, 2H), 6.66 (bs, 1H), 4.20 (t, J = 6.8 Hz, 2H), 3.42 (q, J = 6.8 Hz, 2H), 2.98 (s, 3H), 1.77-1.70 (m, 2H), 1.65-1.58 (m, 2H), 1.47-1.39 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.5, 134.5, 131.2, 128.3, 126.8, 69.9, 39.6, 37.1, 29.3, 28.8, 26.1, 24.9. IR (neat): 3330, 2936, 2857, 1629, 1532, 1345, 1163, 972, 954, 839, 686 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{NO}_4\text{NaS}$ 322.1084; found 322.1076.

Reaction of **1a** under the standard conditions for alkyl halides reported in our previous paper

1) Reaction of **1a** under the standard conditions for alkyl chlorides reported in our previous paper



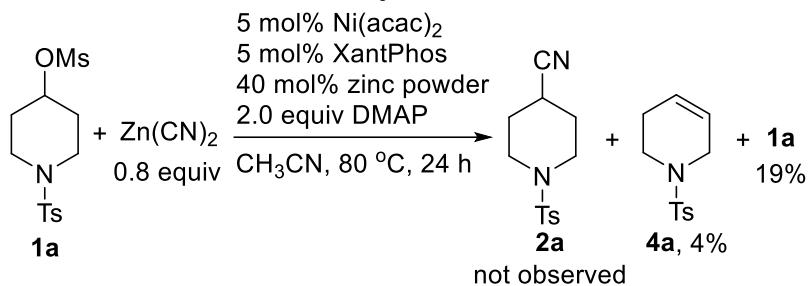
In a nitrogen-filled glove box, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (2.4 mg, 0.01 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (18.8 mg, 0.16 mmol), zinc powder (5.2 mg, 0.08 mmol), $n\text{-Bu}_4\text{NCl}$ (27.8 mg,

0.1 mmol), XantPhos (5.8 mg, 0.01 mmol), **1a** (66.7 mg, 0.2 mmol) and CH₃CN (0.4 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 12 h, the mixture was filtered through a pad of silica gel and washed with CH₂Cl₂. The solvent was evaporated under the reduced pressure and the yield were determined by ¹H NMR using 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) as an internal standard, the NMR yield of **2a** was 5%, the NMR yield of **4a** was 10%, the NMR yield of **5a** was 3%, the NMR yield of 4-chloro-1-tosylpiperidine was 11%, and **1a** was recovered in 32% yield.

The results indicated that under these conditions, trace of the desired product **2a** was formed.

2) Reaction of **1a** under standard conditions for alkyl bromides reported in our previous paper

'condition for alkyl bromides'



In a nitrogen-filled glove box, Ni(acac)₂ (2.6 mg, 0.01 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (18.8 mg, 0.16 mmol), zinc powder (5.2 mg, 0.08 mmol), XantPhos (5.8 mg, 0.01 mmol), **1a** (66.7 mg, 0.2 mmol) and CH₃CN (0.4 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 80 °C (oil bath) for 24 h, the mixture was filtered through a pad of silica gel and washed with CH₂Cl₂. The solvent was evaporated under the reduced pressure and the yield were determined by ¹H NMR using 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) as an internal standard, no desired product (**2a**) was observed, the NMR yield of **4a** was 4% and **1a** was recovered in 19% yield.

The results indicated that under these conditions, the desired product **2a** was not formed.

Optimization studies for cyanation of secondary alkyl mesylates

In a nitrogen-filled glove box, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1a** (133.4 mg, 0.4 mmol) and CH_3CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 10 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.

Table S1 Effects of substrate concentration and solvents

entry	substrate (M)	solvent	conversion (%)	2a	3a	4a	5a	6a
1	0.2	CH_3CN	97	88, 89 ^b	-	-	2	4
2	0.1	CH_3CN	74	69	-	-	-	4
3	0.2	THF	100	-	10	48	-	37
4	0.2	toluene	100	-	12	50	-	32
5	0.2	dioxane	100	69	-	-	14	17
6	0.2	DMF	100	83	-	-	6	-

^aYields were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

Table S2 Effects of catalysts

entry	Ni catalyst	conversion (%)	yield (%) ^a				
			2a	3a	4a	5a	6a
1	NiCl ₂ •6H ₂ O	97	88, 89 ^b	-	-	2	4
2	NiCl ₂ (DME)	100	72	-	5	-	17
3	NiCl ₂	97	60	-	5	-	31
4	NiI ₂	97	70	-	5	-	18

^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

Table S3 Effects of ligands

entry	x	ligand	conversion (%)	yield (%) ^a				
				2a	3a	4a	5a	6a
1	6	XantPhos	97	88, 89 ^b	-	-	2	4
2	6	NiXantPhos	98	87	-	1	1	5
3	6	dppf	95	74	-	-	7	12
4	6	2,2'-bpy	92	-	22	31	-	33
5	12	PCy ₃	94	-	21	35	-	34

^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

Table S4 Effects of basic additives

entry	y	basic additive	conversion (%)	2a	3a	4a	5a	6a
1	1.0	DMAP	97	88, 89 ^b	-	-	2	4
2	0.5	DMAP	98	89	-	-	3	4
3	0.25	DMAP	96	88	-	-	6	2
4	0.1	DMAP	98	84	-	-	7	4
5	1.0	Cs ₂ CO ₃	100	85	-	-	6	6
6	1.0	DABCO	98	74	-	4	6	5
7	1.0		96	82	-	-	3	8

^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

Table S5 Effects of additives of *n*-Bu₄NX derivatives

entry	z	additive	conversion (%)	2a	3a	4a	5a	6a
1	3.0	<i>n</i> -Bu ₄ NI	97	88, 89 ^b	-	-	2	4
2	2.0	<i>n</i> -Bu ₄ NI	86	72	-	2	2	7
3	3.0	<i>n</i> -Bu ₄ NBr	100	18	- ^c	18	-	34
4	3.0	<i>n</i> -Bu ₄ NCl	100	-	- ^d	13	-	-
5	3.0	Et ₄ NI	96	83	-	2	3	ca. 7
6	3.0	KI	57	41	-	2	2	-

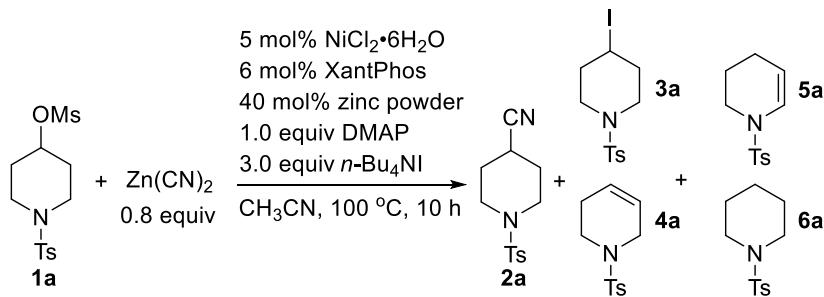
^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield. ^c4-Bromo-1-tosylpiperidine was formed in 28% yield. ^d4-Chloro-1-tosylpiperidine was formed in 84% yield.

Table S6 Effects of reducing agents and temperature

entry	z	reducing agent	t (°C)	conversion (%)	2a	3a	4a	5a	6a
1	40	zinc powder	100	97	88, 89 ^b	-	-	2	4
2	20	zinc powder	100	98	88	-	3	2	2
3	40	Mn	100	96	-	21	66	-	-
4	40	zinc powder	80	48	36	-	-	-	12

^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

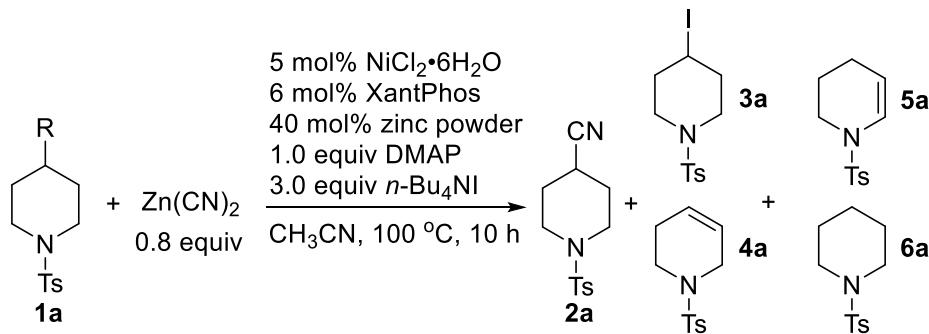
Table S7 Control experiments



entry	catalyst	DMAP (equiv)	zinc powder (mol%)	<i>n</i> -Bu ₄ NI (equiv)	XantPhos (mol%)	conversion (%)	2a	3a	4a	5a	6a
1	-	1.0	40	3.0	6	94	-	18	39	-	33
2	NiCl ₂ ·6H ₂ O	1.0	-	3.0	6	94	-	28	61	-	-
3	NiCl ₂ ·6H ₂ O	1.0	40	-	6	7	-	-	-	-	-
4	NiCl ₂ ·6H ₂ O	1.0	40	3.0	-	88	-	28	35	-	25
5	NiCl ₂ ·6H ₂ O	-	40	3.0	6	94	67	-	-	8	16
6	Ni(cod) ₂	1.0	-	3.0	6	94	43	17	34	-	-

^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Table S8 Effects of leaving groups

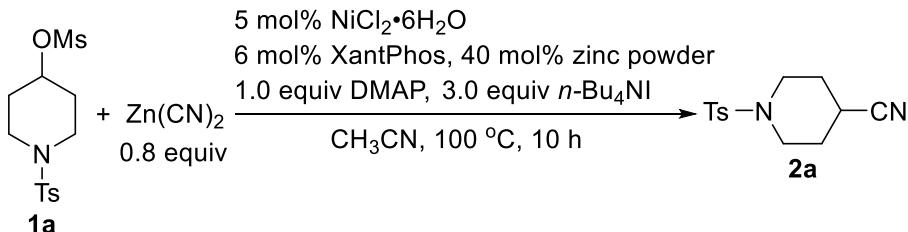


entry	R	conversion (%)	2a	3a	4a	5a	6a
1	OMs	97	88, 89 ^b	-	-	2	4
2	OTs	100	72	-	-	7	4
3	OAc	6	-	-	-	-	-
4	OBz	6	-	-	-	-	-

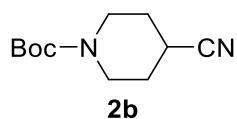
^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

Nickel-catalyzed cyanation of secondary alkyl mesylates

Typical procedure for nickel-catalyzed cyanation of **1a**

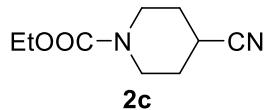


In a nitrogen-filled glove box, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1a** (133.4 mg, 0.4 mmol) and CH_3CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial (If the secondary alkyl mesylates is a liquid, it was added after CH_3CN). The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 10 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the yield were determined by ^1H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard. The NMR yield of **2a** was 88%. The residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1 to 2:1) to afford 1-tosylpiperidine-4-carbonitrile (**2a**) in 89% yield (94.0 mg) as a white solid. ^1H NMR (400 MHz, CDCl_3) 7.63 (d, $J = 8.4$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 3.16-3.05 (m, 4H), 2.75-2.70 (m, 1H), 2.44 (s, 3H), 2.03-1.88 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.9, 132.5, 129.7, 127.4, 120.3, 43.7, 27.7, 25.1, 21.4. The spectroscopic data is in agreement with that previously reported.⁹

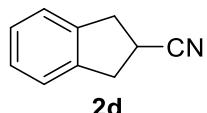


tert-Butyl 4-cyanopiperidine-1-carboxylate (2b**).** 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1b** (111.7 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1) to afford **2b** in 90% isolated yield (75.6 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3)

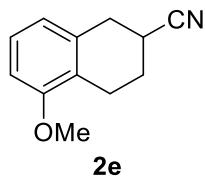
δ 3.69-3.63 (m, 2H), 3.36-3.30 (m, 2H), 2.84-2.78 (m, 1H), 1.95-1.74 (m, 4H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 154.4, 121.0, 80.0, 41.9, 28.4, 28.3, 26.2. The spectroscopic data is in agreement with that previously reported.¹⁰



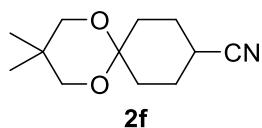
Ethyl 4-cyanopiperidine-1-carboxylate (2c). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1c** (100.5 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 3:1) to afford **2c** in 88% isolated yield (64.0 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 4.14 (q, $J = 7.2$ Hz, 2H), 3.73-3.67 (m, 2H), 3.44-3.37 (m, 2H), 2.87-2.81 (m, 1H), 1.94-1.76 (m, 4H), 1.26 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.0, 120.8, 61.4, 41.6, 28.2, 26.0, 14.4. IR (neat): 2919, 2854, 2239, 1690, 1429, 1267, 1219, 1122, 1030, 768 cm^{-1} . HRMS (EI-TOF) m/z: [M]⁺ calcd for $\text{C}_9\text{H}_{14}\text{N}_2\text{O}_2$ 182.1050; found 182.1051.



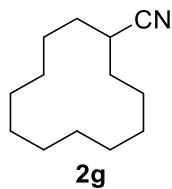
2,3-Dihydro-1H-indene-2-carbonitrile (2d). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1d** (84.9 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1 to 30:1) to afford **2d** in 77% isolated yield (44.2 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.24-7.19 (m, 4H), 3.38-3.23 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 139.6, 127.2, 124.4, 122.4, 37.3, 27.5. The spectroscopic data is in agreement with that previously reported.⁹



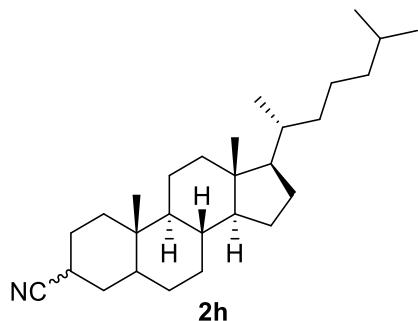
5-Methoxy-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (2e). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1e** (102.5 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **2e** in 62% isolated yield (46.4 mg) as white solid. ^1H NMR (400 MHz, CDCl_3) δ 7.12 (t, J = 8.0 Hz, 1H), 6.69 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 3.12-2.99 (m, 2H), 2.94-2.87 (m, 2H), 2.69-2.61 (m, 1H), 2.22-2.15 (m, 1H), 2.05-1.96 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.1, 133.5, 126.6, 123.5, 122.1, 120.8, 107.7, 55.2, 32.4, 25.9, 25.1, 21.2. The spectroscopic data is in agreement with that previously reported.⁹



3,3-Dimethyl-1,5-dioxaspiro[5.5]undecane-9-carbonitrile (2f). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1f** (111.3 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford **2f** in 82% isolated yield (68.5 mg) as a white solid. M.p. 62-64 °C. ^1H NMR (400 MHz, CDCl_3) δ 3.50 (s, 2H), 3.47 (s, 2H), 2.68-2.62 (m, 1H), 2.04-1.99 (m, 2H), 1.94-1.74 (m, 6H), 0.96 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 121.8, 95.8, 69.9, 69.7, 30.0, 29.9, 27.0, 25.4, 22.5. IR (neat): 2954, 2867, 2233, 1440, 1391, 1241, 1104, 910, 901 cm^{-1} . HRMS (EI-TOF) m/z: [M]⁺ calcd for $\text{C}_{12}\text{H}_{19}\text{NO}_2$ 209.1410; found 209.1405.

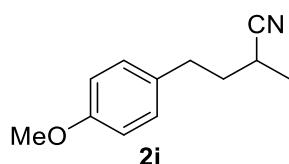


Cyclododecanecarbonitrile (2g). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1g** (105.0 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:1) to afford **2g** in 24% isolated yield (18.4 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 2.67-2.61 (m, 1H), 1.79-1.61 (m, 4H), 1.59-1.33 (m, 18H); ^{13}C NMR (100 MHz, CDCl_3) δ 123.2, 27.1, 26.4, 23.6, 23.4, 23.2, 23.1, 21.8. The spectroscopic data is in agreement with that previously reported.⁹

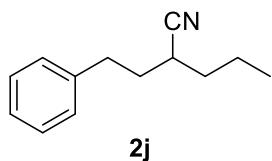


(8R,9S,10S,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthrene-3-carbonitrile (2h). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1h** (186.7 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The solvent was evaporated under the reduced pressure and the crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 5:1) to afford a mixture of two diastereoisomers in 33% yield (52.2 mg, isomer **A**) and 44% yield (69.4 mg, isomer **B**) as white solids, respectively. For isomer **A**: M.p. 166-168 °C. ^1H NMR (400 MHz, CDCl_3) δ 2.95 (s, 1H), 1.99-1.95 (m, 1H), 1.87-1.47 (m, 11H), 1.38-0.85 (m, 26H), 0.83-0.76 (m, 4H), 0.65 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 122.7, 56.3, 56.1, 53.8, 42.5, 42.3, 39.8,

39.5, 36.1, 35.9, 35.8, 35.3, 34.3, 31.6, 30.4, 28.2, 28.1, 28.0, 27.5, 24.2, 24.1, 23.8, 22.8, 22.5, 20.7, 18.6, 12.0, 11.8. IR (neat): 2931, 2866, 2847, 2239, 1469, 1443, 1380, 906, 736 cm^{-1} . HRMS (EI-TOF) m/z: [M]⁺ calcd for C₂₈H₄₇N 397.3703; found 397.3710. For isomer **B**: M.p. 141-143 °C. ¹H NMR (400 MHz, CDCl₃) δ 2.46-2.37 (m, 1H), 1.98-1.90 (m, 2H), 1.85-0.85 (m, 37H), 0.81 (s, 3H), 0.67-0.60 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 122.8, 56.3, 56.2, 54.0, 45.7, 42.5, 39.8, 39.4, 37.2, 36.1, 35.7, 35.4, 35.3, 31.8, 31.7, 28.4, 28.2, 28.1, 27.9, 25.6, 24.1, 23.8, 22.8, 22.5, 20.8, 18.6, 12.0, 12.0. IR (neat): 2928, 2865, 2236, 1465, 1383, 907, 733. HRMS (EI-TOF) m/z: [M]⁺ calcd for C₂₈H₄₇N 397.3703; found 397.3710.

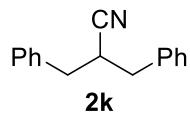


4-(4-Methoxyphenyl)-2-methylbutanenitrile (2i). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), CH₃CN (2.0 mL) and **1i** (103.3 mg, 0.4 mmol) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1 to 20:1) to afford **2i** in 71% isolated yield (54.0 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.11 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 3.78 (s, 3H), 2.84-2.77 (m, 1H), 2.72-2.64 (m, 1H), 2.60-2.51 (m, 1H), 1.96-1.87 (m, 1H), 1.83-1.74 (m, 1H), 1.31 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 158.0, 132.0, 129.2, 122.7, 113.9, 55.1, 35.8, 32.1, 24.6, 17.9. The spectroscopic data is in agreement with that previously reported.⁹

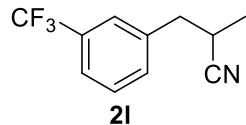


2-Phenylpentanenitrile (2j). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1j** (102.5 mg, 0.4 mmol) and

CH₃CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:1) to afford **2j** in 58% isolated yield (43.1 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.28 (m, 2H), 7.24-7.19 (m, 3H), 2.92-2.85 (m, 1H), 2.77-2.69 (m, 1H), 2.53-2.46 (m, 1H), 1.98-1.79 (m, 2H), 1.68-1.37 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 140.2, 128.5, 128.3, 126.3, 122.0, 34.2, 33.9, 33.2, 30.7, 20.3, 13.5. The spectroscopic data is in agreement with that previously reported.¹¹

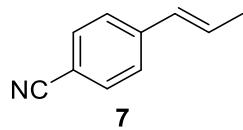


2-Benzyl-3-phenylpropanenitrile (2k). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1k** (116.2 mg, 0.4 mmol) and CH₃CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1 to 10:1) to afford **2k** in 71% isolated yield (63.2 mg) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.22 (m, 10H), 3.04-2.97 (m, 1H), 2.89 (d, *J* = 6.8 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 136.7, 129.0, 128.7, 127.2, 121.2, 37.8, 35.8. The spectroscopic data is in agreement with that previously reported.⁹

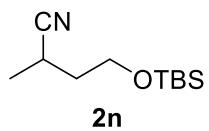


2-Methyl-3-(3-(trifluoromethyl)phenyl)propanenitrile (2l). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1l** (112.9 mg, 0.4 mmol) and CH₃CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:1) to afford **2l** in 81% isolated yield (69.1 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.56-7.54 (m, 1H), 7.49-7.46 (m, 3H), 3.01-2.84 (m, 3H), 1.35

(d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.7, 132.4, 131.0 (q, $^2J_{\text{C-F}} = 32.3$ Hz), 129.2, 125.7 (q, $^3J_{\text{C-F}} = 3.6$ Hz), 124.1 (q, $^3J_{\text{C-F}} = 3.6$ Hz), 123.9 (q, $^1J_{\text{C-F}} = 270.9$ Hz), 121.9, 39.6, 27.3, 17.5. IR (neat): 2241, 1451, 1325, 1202, 1163, 1119, 1098, 1073, 806, 793, 702, 663. HRMS (EI-TOF) m/z: $[\text{M}]^+$ calcd for $\text{C}_{11}\text{H}_{10}\text{F}_3\text{N}$ 213.0760; found 213.0762.

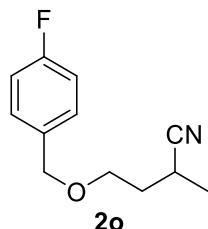


(E)-4-(Prop-1-en-1-yl)benzonitrile (7). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1m** (117.3 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:1) to afford **2l** in 31% isolated yield (17.5 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.56 (d, $J = 8.0$ Hz, 2H), 7.39 (d, $J = 8.0$ Hz, 2H), 6.44-6.34 (m, 2H), 1.92 (d, $J = 4.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 142.3, 132.3, 130.1, 129.7, 126.2, 119.1, 109.9, 18.6. The spectroscopic data is in agreement with that previously reported.¹²

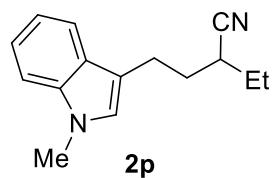


4-((tert-Butyldimethylsilyl)oxy)-2-methylbutanenitrile (2n). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), CH_3CN (2.0 mL) and **1n** (113.0 mg, 0.4 mmol) were stirred at 100 °C (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 2:1) to afford **2n** in 68% isolated yield (58.4 mg) as a light yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 3.76 (t, $J = 6.4$ Hz, 2H), 2.92-2.83 (m, 1H), 1.86-1.69 (m, 2H), 1.34 (d, $J = 7.2$ Hz, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 122.9, 59.6, 36.8, 25.8, 21.8, 18.2, 17.7, -5.6. IR (neat): 2953, 2930, 2856, 2239, 1461, 1255,

1096, 828, 811, 776 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{24}\text{NOSi}$ 214.1622; found 214.1625.



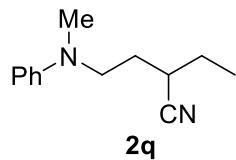
4-((4-Fluorobenzyl)oxy)-2-methylbutanenitrile (2o). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), CH_3CN (2.0 mL) and **1o** (110.5 mg, 0.4 mmol) were stirred at 100 $^\circ\text{C}$ (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **2o** in 70% isolated yield (58.1 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.28 (m, 2H), 7.06-7.01 (m, 2H), 4.48 (dd, J = 15.6 Hz, 7.6 Hz, 2H), 3.61 (t, J = 6.4 Hz, 2H), 2.93-2.84 (m, 1H), 1.92-1.80 (m, 2H), 1.33 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.3 (d, $^1J_{\text{C-F}} = 244.4$ Hz), 133.6 (d, $^4J_{\text{C-F}} = 2.9$ Hz), 129.4 (d, $^3J_{\text{C-F}} = 8.2$ Hz), 122.6, 115.2 (d, $^2J_{\text{C-F}} = 21.4$ Hz), 72.5, 66.8, 34.1, 22.4, 17.8. The spectroscopic data is in agreement with that previously reported.⁹



2-Ethyl-4-(1-methyl-1*H*-indol-3-yl)butanenitrile (2p). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1p** (118.2 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 100 $^\circ\text{C}$ (oil bath) for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **2p** in 27% isolated yield (24.7 mg) as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.58 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H),

7.11 (t, $J = 7.6$ Hz, 1H), 6.89 (s, 1H), 3.74 (s, 3H), 3.07-3.00 (m, 1H), 2.93-2.85 (m, 1H), 2.51-2.44 (m, 1H), 2.02-1.90 (m, 2H), 1.68-1.57 (m, 2H), 1.05 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.1, 127.4, 126.6, 122.2, 121.6, 118.8, 118.7, 112.7, 109.3, 32.6, 32.5, 25.4, 22.6, 11.5. IR (neat): 2931, 2231, 1613, 1472, 1377, 1326, 1247, 1012, 737 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2$ 227.1543; found 227.1540.

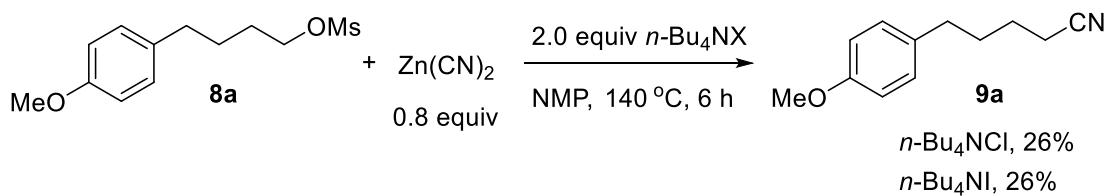
When the reaction was performed at 80 °C (oil bath) for 24 h, **2p** could be afforded in 53% isolated yield (47.7 mg) as a yellow oil.



2-Ethyl-4-(methyl(phenyl)amino)butanenitrile (2q). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1q** (108.6 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **2q** in 31% isolated yield (24.9 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.27-7.23 (m, 2H), 6.74-6.72 (m, 3H), 3.59-3.42 (m, 2H), 2.95 (s, 3H), 2.56-2.49 (m, 1H), 1.92-1.79 (m, 2H), 1.69-1.60 (m, 2H), 1.09 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.8, 129.3, 121.8, 116.8, 112.4, 50.4, 38.7, 30.9, 29.3, 25.7, 11.5. IR (neat): 2967, 2928, 2234, 1599, 1505, 1367, 1193, 748, 692 cm^{-1} . HRMS (ESI-TOF) m/z: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{N}_2$ 203.1543; found 203.1540.

When the reaction was performed at 100 °C (oil bath) for 10 h, **2q** could be afforded in 24% isolated yield (19.8 mg).

Reaction of **8a** with $\text{Zn}(\text{CN})_2$ in the presence of $n\text{-Bu}_4\text{NX}$



In a nitrogen-filled glove box, $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), $n\text{-Bu}_4\text{NCl}$ (222.3 mg, 0.8 mmol), **8a** (103.3 mg, 0.4 mmol) and NMP (0.4 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 140 °C (oil bath) for 6 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **9a** in 26% isolated yield (19.5 mg) as a colourless oil.

When $n\text{-Bu}_4\text{NI}$ (295.5 mg, 0.8 mmol) was used instead of $n\text{-Bu}_4\text{NCl}$, **9a** could be formed in 26% yield (19.4 mg) as a colourless oil.

Optimization studies for cyanation of the primary alkyl mesylates

In a nitrogen-filled glove box, $\text{NiCl}_2\cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **8a** (103.3 mg, 0.4 mmol) and CH_3CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 10 h or at 80 °C (oil bath) for 24 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.

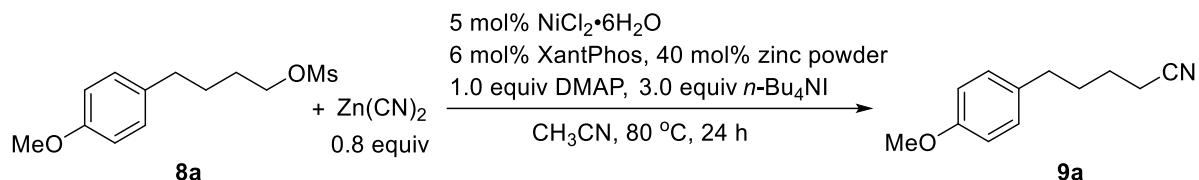
Table S9 Optimization studies for cyanation of the primary alkyl mesylates

entry	deviation from the conditions above	yield of 9a (%) ^a
1	none	39
2	no DMAP	17
3	2.0 equiv DMAP	41
4	2.0 equiv Cs ₂ CO ₃	29
5	2.0 equiv quinine, DBU or DABCO	trace
6	2.0 equiv DMAP, in DMF	21
7	2.0 equiv DMAP, 5 mol% NiCl ₂ (DME)	28
8	2.0 equiv DMAP, 6 mol% dppf	20
9	80 °C, 24 h	56, 54 ^b
10	60 °C, 29 h	36
11	2.0 equiv DMAP, 80 °C, 24 h	49
12	0.5 equiv DMAP, 80 °C, 24 h	54
13	no DMAP, 80 °C, 24 h	32
14	5 mol% NiCl ₂ , 80 °C, 24 h	15
15	5 mol% NiI ₂ , 80 °C, 24 h	24

^aYields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield.

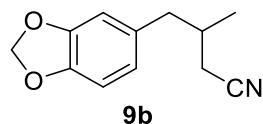
Nickel-catalyzed cyanation of primary alkyl mesylates

Typical procedure for Nickel-catalyzed cyanation of **8a**

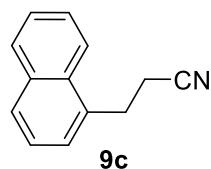


In a nitrogen-filled glove box, NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **8a** (103.3 mg, 0.4 mmol) and CH₃CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial (If the primary alkyl mesylate is a liquid, it was added after CH₃CN). The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 80 °C (oil bath) for 24 h, the mixture was filtered through a pad of silica gel and washed with CH₂Cl₂. The solvent was evaporated under the

reduced pressure and the yield were determined by ^1H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard. The NMR yield of **9a** was 56%. The residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1 to 10:1) to afford 5-(4-methoxyphenyl)pentanenitrile (**9a**) in 54% yield (41.1 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.08 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H), 2.59 (t, J = 6.8 Hz, 2H), 2.32 (t, J = 6.8 Hz, 2H), 1.78-1.62 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.8, 133.2, 129.2, 119.6, 113.8, 55.2, 34.0, 30.4, 24.7, 16.9. The spectroscopic data is in agreement with that previously reported.¹³

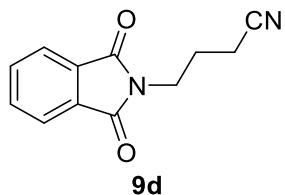


4-(Benzo[d][1,3]dioxol-5-yl)-3-methylbutanenitrile (9b). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **8b** (108.9 mg, 0.4 mmol) and CH_3CN (2.0 mL) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) to afford **9b** in 72% isolated yield (58.7 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 6.74 (d, J = 8.0 Hz, 1H), 6.64-6.60 (m, 2H), 5.93 (s, 2H), 2.62-2.52 (m, 2H), 2.29 (dd, J = 16.8 Hz, 5.6 Hz, 1H), 2.18 (dd, J = 16.4 Hz, 6.4 Hz, 1H), 2.12-2.03 (m, 1H), 1.10 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.7, 146.1, 132.6, 121.8, 118.5, 109.1, 108.2, 100.8, 41.6, 32.5, 23.4, 19.2. IR (neat): 2922, 2244, 1503, 1488, 1441, 1246, 1036, 927, 802 cm^{-1} . HRMS (EI-TOF) m/z: [M]⁺ calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_2$ 203.0941; found 203.0942.



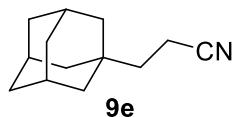
3-(Naphthalen-1-yl)propanenitrile (9c). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **8c** (100.1 mg, 0.4

mmol) and CH₃CN (2.0 mL) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1 to 10:1) to afford **9c** in 75% isolated yield (54.3 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.86 (t, *J* = 7.2 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.54-7.46 (m, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.35 (d, *J* = 6.8 Hz, 1H), 3.37 (t, *J* = 7.6 Hz, 2H), 2.69 (t, *J* = 7.6 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 133.8, 133.8, 131.0, 129.1, 128.0, 126.4, 125.8, 125.5, 122.5, 119.1, 28.6, 18.3. The spectroscopic data is in agreement with that previously reported.¹⁴



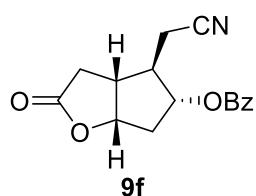
4-(1,3-Dioxoisoindolin-2-yl)butanenitrile (9d). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), NaHCO₃ (67.2 mg, 0.8 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **8d** (113.3 mg, 0.4 mmol) and CH₃CN (2.0 mL) were stirred at 80 °C (oil bath) for 24 h. The solvent was evaporated under the reduced pressure and the yield were determined by ¹H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard. The NMR yield of **9d** was 70%. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 3:1) to afford **9d** in 72% isolated yield (61.3 mg) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.88-7.83 (m, 2H), 7.77-7.72 (m, 2H), 3.82 (t, *J* = 6.8 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 2.12-2.05 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 168.1, 134.1, 131.7, 123.3, 118.7, 36.5, 24.6, 14.9. The spectroscopic data is in agreement with that previously reported.⁹

When 1.0 equiv DMAP was used instead of 2.0 equiv NaHCO₃, **9d** was formed in 50% NMR yield using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.

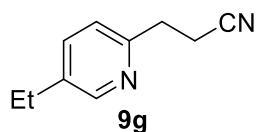


3-((3r,5r,7r)-Adamantan-1-yl)propanenitrile (9e). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, S42

0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **8e** (103.4 mg, 0.4 mmol) and CH₃CN (2.0 mL) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:1 to 2:1) to afford **9e** in 79% isolated yield (60.1 mg) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 2.29-2.25 (m, 2H), 1.98 (s, 3H), 1.73-1.70 (m, 3H), 1.63-1.60 (m, 3H), 1.50-1.46 (m, 8H); ¹³C NMR (100 MHz, CDCl₃) δ 120.8, 41.5, 39.3, 36.7, 32.0, 28.3, 10.8. The spectroscopic data is in agreement with that previously reported.¹⁵



(3aR,4R,5R,6aS)-4-(Cyanomethyl)-2-oxohexahydro-2H-cyclopenta[b]furan-5-yl benzoate (9f). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **8f** (141.7 mg, 0.4 mmol) and CH₃CN (2.0 mL) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 1:1) to afford **9f** in 67% isolated yield (76.9 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 5.25-5.21 (m, 1H), 5.10-5.08 (m, 1H), 2.99-2.92 (m, 1H), 2.88-2.82 (m, 1H), 2.70-2.53 (m, 4H), 2.48-2.42 (m, 1H), 2.33-2.28 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 175.6, 165.8, 133.5, 129.5, 128.9, 128.4, 117.3, 83.1, 78.1, 47.7, 42.3, 37.4, 35.0, 19.8. IR (neat): 2249, 1769, 1716, 1271, 1173, 906, 729, 712 cm⁻¹. HRMS (ESI-TOF) m/z: [M+Na]⁺ calcd for C₁₆H₁₅NO₄Na 308.0893; found 308.0893.

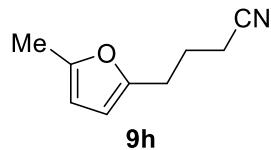


3-(5-Ethylpyridin-2-yl)propanenitrile (9g). 0.4 mmol scale. NiCl₂·6H₂O (9.5 mg, 0.04 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg,

0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (27.8 mg, 0.048 mmol), CH₃CN (2.0 mL) and **8g** (91.7 mg, 0.4 mmol) were stirred at 80 °C (oil bath) for 24 h. The solvent was evaporated under the reduced pressure and the yield were determined by ¹H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard. The NMR yield of **9g** was 68%. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1 to 3:1) to afford **9g** in 66% isolated yield (42.6 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 8.40 (s, 1H), 7.50-7.48 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 3.09 (t, *J* = 7.2 Hz, 2H), 2.82 (t, *J* = 7.2 Hz, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 154.3, 149.1, 137.7, 136.1, 122.6, 119.4, 32.8, 25.6, 16.8, 15.2. IR (neat): 2964, 2930, 2244, 1600, 1566, 1488, 1399, 1032, 845 cm⁻¹. HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for C₁₀H₁₃N₂ 161.1073; found 161.1074.

When the reaction was performed in the presence of 5% NiCl₂·6H₂O and 6% XantPhos instead of 10% NiCl₂·6H₂O and 12% XantPhos at 80 °C (oil bath) for 24 h, **9g** could be formed in 58% NMR yield using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.

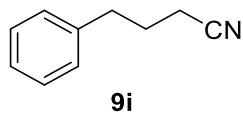
When the reaction was performed in the presence of 5% NiCl₂·6H₂O and 6% XantPhos instead of 10% NiCl₂·6H₂O and 12% XantPhos at 100 °C (oil bath) for 19 h, **9g** could be formed in 31% NMR yield using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.



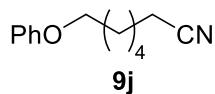
4-(5-Methylfuran-2-yl)butanenitrile (9h). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), CH₃CN (2.0 mL) and **8h** (87.3 mg, 0.4 mmol) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **9h** in 46% isolated yield (27.5 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.93-5.92 (m, 1H), 5.86-5.85 (m, 1H), 2.74 (t, *J* = 7.2 Hz, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 2.25 (s, 3H), 1.98 (quint, *J* = 7.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 151.3, 151.0, 119.3, 106.8, 105.9, 26.7, 24.1, 16.3, 13.4. IR (neat): 2922, 2244, 1569, 1434, 1217, 1020, 939, 783 cm⁻¹.

HRMS (EI-TOF) m/z: [M]⁺ calcd for C₉H₁₁NO 149.0835; found 149.0837.

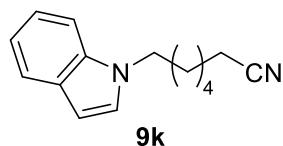
When the reaction was performed in the presence of 10% NiCl₂·6H₂O and 12% XantPhos instead of 5% NiCl₂·6H₂O and 6% XantPhos at 80 °C (oil bath) for 24 h, **9h** could be afforded in 54% isolated yield (32.1 mg) as a colourless oil.



4-Phenylbutanenitrile (9i). 0.4 mmol scale. NiCl₂·6H₂O (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), CH₃CN (2.0 mL) and **8i** (85.7 mg, 0.4 mmol) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:1 to 2:1) to afford **9i** in 54% isolated yield (31.2 mg) as a colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.17 (m, 5H), 2.77 (t, *J* = 7.2 Hz, 2H), 2.30 (t, *J* = 7.2 Hz, 2H), 1.97 (quint, *J* = 7.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 139.6, 128.6, 128.4, 126.4, 119.5, 34.3, 26.8, 16.3. The spectroscopic data is in agreement with that previously reported.⁹

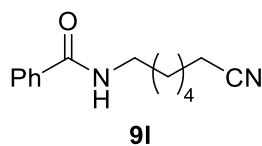


7-Phenoxyheptanenitrile (9j). 0.4 mmol scale. NiCl₂·6H₂O (9.5 mg, 0.04 mmol), DMAP (48.9 mg, 0.4 mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI (443.2 mg, 1.2 mmol), XantPhos (27.8 mg, 0.048 mmol), CH₃CN (2.0 mL) and **8j** (108.9 mg, 0.4 mmol) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1 to 10:1) to afford **9j** in 59% isolated yield (47.8 mg) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.24 (m, 2H), 6.95-6.87 (m, 3H), 3.95 (t, *J* = 6.4 Hz, 2H), 2.33 (t, *J* = 6.8 Hz, 2H), 1.82-1.76 (m, 2H), 1.71-1.63 (m, 2H), 1.53-1.49 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 158.9, 129.3, 120.5, 119.7, 114.3, 67.3, 28.9, 28.3, 25.3, 25.2, 17.0. IR (neat): 2937, 2242, 1599, 1585, 1496, 1472, 1243, 1172, 1032, 754, 692 cm⁻¹. HRMS (EI-TOF) m/z: [M]⁺ calcd for C₁₃H₁₇NO 203.1305; found 203.1307.



7-(1H-Indol-1-yl)heptanenitrile (9k). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (9.5 mg, 0.04 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (27.8 mg, 0.048 mmol), CH_3CN (2.0 mL) and **8k** (118.2 mg, 0.4 mmol) were stirred at 60 °C (oil bath) for 26 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **9k** in 66% isolated yield (59.9 mg) as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.21-7.17 (m, 1H), 7.10-7.05 (m, 2H), 6.47 (d, J = 2.8 Hz, 1H), 4.08 (t, J = 6.8 Hz, 2H), 2.22 (t, J = 6.8 Hz, 2H), 1.85-1.77 (m, 2H), 1.59-1.52 (m, 2H), 1.44-1.37 (m, 2H), 1.32-1.24 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 135.7, 128.4, 127.6, 121.2, 120.8, 119.6, 119.1, 109.2, 100.9, 46.0, 29.8, 28.1, 26.0, 25.0, 16.8. IR (neat): 2933, 2855, 2242, 1510, 1463, 1314, 764, 739 cm^{-1} . HRMS (ESI-TOF) m/z: [M+H]⁺ calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2$ 227.1543; found 227.1543.

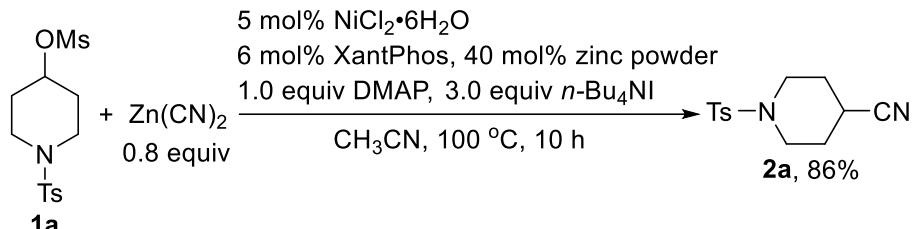
When the reaction was performed at 80 °C (oil bath) for 24 h, **9k** could be afforded in 14% isolated yield (12.6 mg) as a yellow oil.



N-(6-Cyanohexyl)benzamide (9l). 0.4 mmol scale. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (9.5 mg, 0.04 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (27.8 mg, 0.048 mmol), CH_3CN (2.0 mL) and **8l** (119.8 mg, 0.4 mmol) were stirred at 80 °C (oil bath) for 24 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 2:1 to 1:1) to afford **9l** in 56% isolated yield (52.0 mg) as a colourless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.79-7.77 (m, 2H), 7.50-7.46 (m, 1H), 7.42-7.38 (m, 2H), 6.74 (bs, 1H), 3.41 (q, J = 6.8 Hz, 2H), 2.31 (t, J = 7.2 Hz, 2H), 1.67-1.54 (m, 4H), 1.50-1.33 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3)

CDCl_3) δ 167.5, 134.5, 131.2, 128.3, 126.8, 119.7, 39.6, 29.2, 28.1, 25.9, 25.0, 16.8. IR (neat): 3327, 2928, 2857, 2244, 1636, 1537, 1489, 1306, 711, 694, 668 cm^{-1} . HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}$ 231.1492; found 231.1494.

1 mmol scale reaction of **1a**.

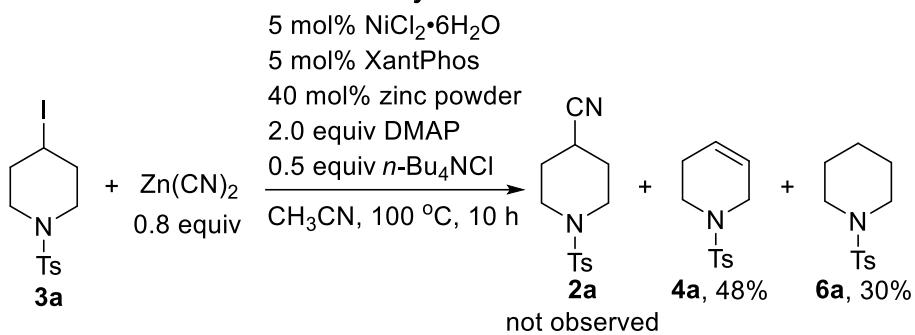


A sealable Schlenk tube was dried under vacuum using a heatgun, and evacuated and back-filled with argon for several times. Then $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (11.9 mg, 0.05 mmol), DMAP (122.2 mg, 1.0 mmol), $\text{Zn}(\text{CN})_2$ (93.9 mg, 0.8 mmol), zinc powder (26.2 mg, 0.4 mmol), $n\text{-Bu}_4\text{NI}$ (1.11 g, 3.0 mmol), XantPhos (34.7 mg, 0.06 mmol), **1a** (333.4 mg, 1.0 mmol) were added under argon. The tube was evacuated and refilled with argon for three times, and then acetonitrile (5.0 mL) was added via syringe. The Schlenk tube was sealed and immersed into an oil bath preheated at 100 °C. After stirring for 10 h, the mixture was cooled down to room temperature. Then the reaction mixture was filtered through a short pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 2:1) to afford **2a** in 86% yield (227.9 mg) as a white solid.

Reaction of **3a** under the standard conditions for alkyl halides reported in our previous paper

- 1) Reaction of **3a** under the standard conditions for alkyl chlorides reported in our previous paper

'condition for alkyl chlorides'

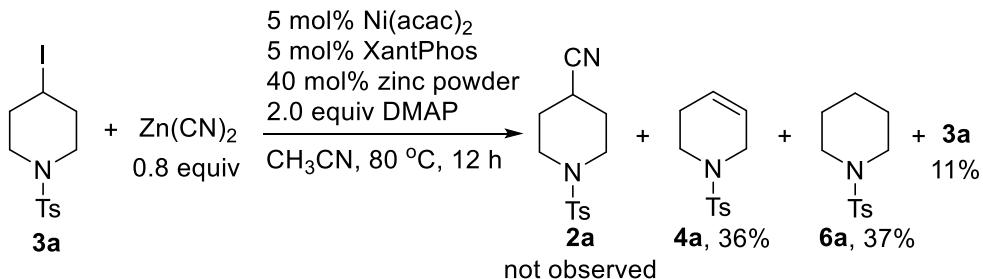


In a nitrogen-filled glove box, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (2.4 mg, 0.01 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (18.8 mg, 0.16 mmol), zinc powder (5.2 mg, 0.08 mmol), $n\text{-Bu}_4\text{NCl}$ (27.8 mg, 0.1 mmol), XantPhos (5.8 mg, 0.01 mmol), **3a** (73.0 mg, 0.2 mmol) and CH_3CN (0.4 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100°C (oil bath) for 10 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the yield were determined by ^1H NMR using 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) as an internal standard, no desired product (**2a**) was observed, the NMR yield of **4a** was 48%, the NMR yield of **6a** was 30%.

The results indicated that under these conditions, the desired product **2a** was not formed.

2) Reaction of **3a** under standard conditions for alkyl bromides reported in our previous paper

'condition for alkyl bromides'



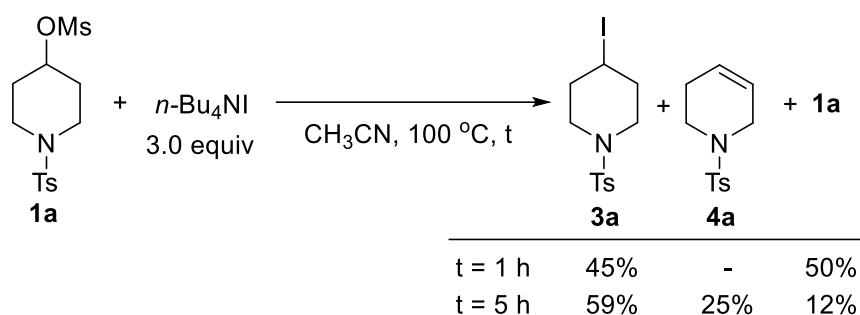
In a nitrogen-filled glove box, $\text{Ni}(\text{acac})_2$ (2.6 mg, 0.01 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (18.8 mg, 0.16 mmol), zinc powder (5.2 mg, 0.08 mmol), XantPhos (5.8 mg, 0.01 mmol), **3a** (73.0 mg, 0.2 mmol) and CH_3CN (0.4 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 80°C (oil bath) for 12 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure

and the yield were determined by ^1H NMR using 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) as an internal standard, no desired product (**2a**) was observed, the NMR yield of **4a** was 36%, the NMR yield of **6a** was 37%, and the NMR yield of unreacted **3a** was 11%.

The results indicated that under these conditions, the desired product **2a** was not formed.

Mechanistic studies:

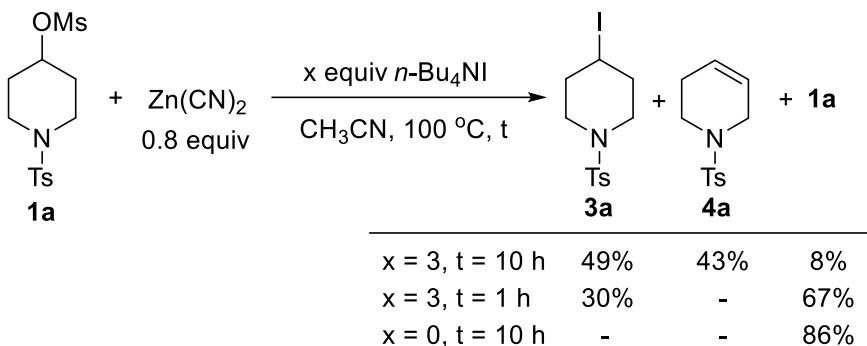
1) Reaction of **1a** with *n*-Bu₄NI in the absence of Zn(CN)₂



For $t = 1 \text{ h}$: In a nitrogen-filled glove box, *n*-Bu₄NI (221.6 mg, 0.6 mmol), **1a** (66.7 mg, 0.2 mmol) and CH₃CN (1 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 1 h, the mixture was filtered through a pad of silica gel and washed with CH₂Cl₂. The solvent was evaporated under the reduced pressure and the yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) as an internal standard, the NMR yield of **3a** was 45%, and the NMR yield of **1a** was 50%.

For $t = 5 \text{ h}$: In a nitrogen-filled glove box, *n*-Bu₄NI (443.2 mg, 1.2 mmol), **1a** (133.4 mg, 0.4 mmol) and CH₃CN (2 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 5 h, the mixture was filtered through a pad of silica gel and washed with CH₂Cl₂. The solvent was evaporated under the reduced pressure and the yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard, the NMR yield of **3a** was 59%, the NMR yield of **4a** was 25%, and **1a** was observed in 12% NMR yield.

2) Reaction of **1a** in the presence of Zn(CN)₂ with or without *n*-Bu₄NI

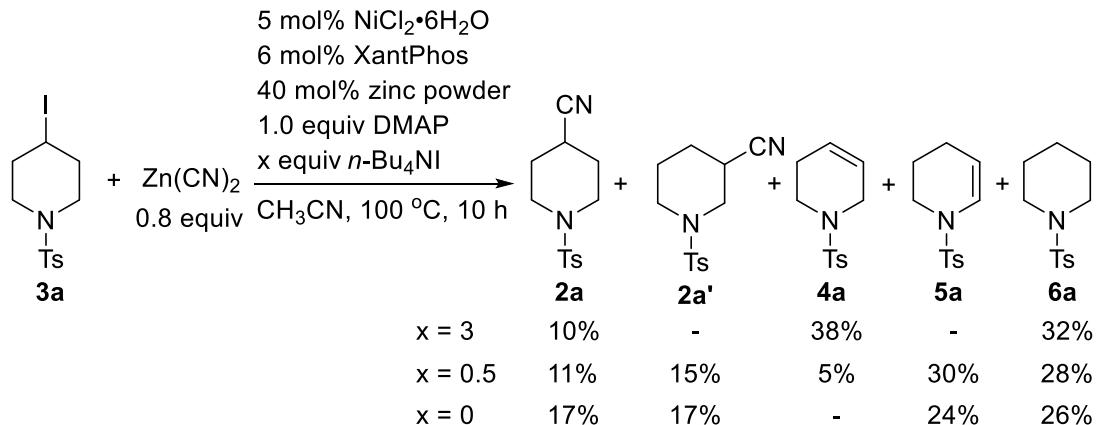


In a nitrogen-filled glove box, $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), **1a** (133.4 mg, 0.4 mmol) and CH_3CN (2 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 10 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard. The NMR yield of **3a** was 49%, the NMR yield of **4a** was 43%, and **1a** was observed in 8% NMR yield.

When the reaction was performed in the presence of 3.0 equiv $n\text{-Bu}_4\text{NI}$ for 1 h, **1a** was observed in 67% NMR yield, and **3a** was formed in 30% NMR yield using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.

When the reaction was performed without $n\text{-Bu}_4\text{NI}$ for 10 h, **1a** was recovered in 86% NMR yield using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.

3) Reaction of **3a** under the standard conditions for alkyl mesylates



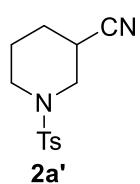
In a nitrogen-filled glove box, $\text{NiCl}_2\cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4

mmol), Zn(CN)₂ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), *n*-Bu₄NI, XantPhos (13.9 mg, 0.024 mmol), **3a** (146.1 mg, 0.4 mmol) and CH₃CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 10 h, the mixture was filtered through a pad of silica gel and washed with CH₂Cl₂. The solvent was evaporated under the reduced pressure.

When x = 3, *n*-Bu₄NI (443.2 mg, 1.2 mmol) was used; Using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard, the NMR yield of **4a** was 38% and the NMR yield of **6a** was 32%; The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 2:1) to afford **2a** in 10% isolated yield (10.8 mg) as a white solid.

When x = 0.5, *n*-Bu₄NI (73.9 mg, 0.2 mmol) was used; Using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard, the NMR yield of **4a** was 5%, the NMR yield of **5a** was 30% and the NMR yield of **6a** was 28%; The crude product was purified by preparative TLC on silica gel (eluent: petroleum ether: ethyl acetate = 2:1) to afford a mixture of **2a** and **2a'** (26.8 mg) in a ratio of 1:1.37. The yield of **2a** was 11% and the yield of **2a'** was 15%.

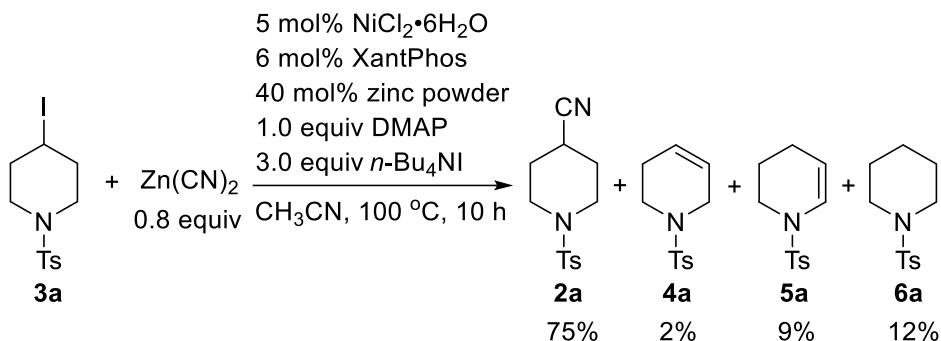
When x = 0, no *n*-Bu₄NI was used; Using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard, the NMR yield of **5a** was 24% and the NMR yield of **6a** was 26%; The crude product was purified by preparative TLC on silica gel (eluent: petroleum ether: ethyl acetate = 2:1) to afford a mixture of **2a** and **2a'** (35.0 mg) in a ratio of 1:1. The yield of **2a** was 17% and the yield of **2a'** was 17%.



1-tosylpiperidine-3-carbonitrile (2a'). ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.36-7.34 (m, 2H), 3.60-3.58 (m, 1H), 3.37-3.34 (m, 1H), 2.86-2.84 (m, 2H), 2.75-2.67 (m, 1H), 2.44 (s, 3H), 2.03-1.84 (m, 2H), 1.69-1.61 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 144.1, 132.8, 129.8, 127.5, 119.3, 47.6, 45.8, 27.3, 27.1, 23.0, 21.5. The spectroscopic data is in

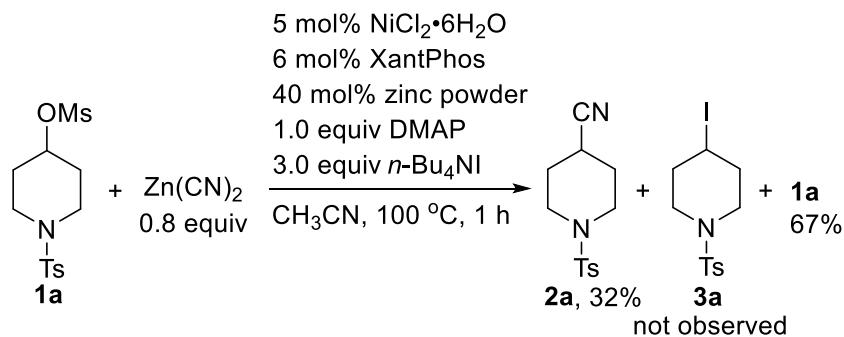
agreement with that previously reported.¹⁶

4) Portionwise addition of **3a** under the standard conditions for alkyl mesylates



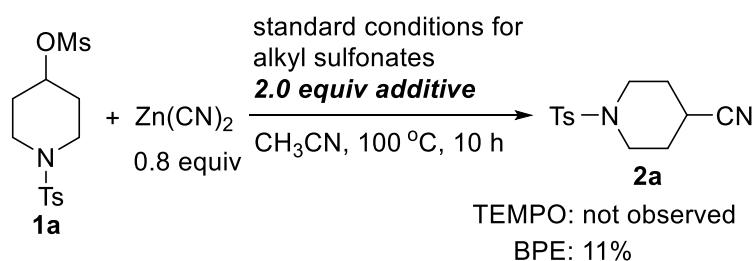
In a nitrogen-filled glove box, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **3a** (36.5 mg, 0.1 mmol) and CH_3CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial. The vial was taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 2 h, the mixture was cooled down. The vial was moved into glove box, and 0.1 mmol **3a** was added. The vial was taken outside the glove box again and stirred at 100 °C for 2 h. The above operation was repeated for next two times. After addition of the whole amounts of **3a**, the mixture was stirred for another 4 hours, then the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the yield were determined by ¹H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard, the NMR yield of **2a** was 75%, the NMR yield of **4a** was 2%, the NMR yield of **5a** was 9% and the NMR yield of **6a** was 12%.

5) Reaction of **1a** under the standard reaction conditions for 1 h



In a nitrogen-filled glove box, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1a** (133.4 mg, 0.4 mmol) and CH_3CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 1 h, the mixture was cooled down, filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure and the yield were determined by ^1H NMR using 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard. The NMR yield of desired product (**2a**) was 32%, the NMR yield of **1a** was 67% and alkyl iodide (**3a**) was not observed.

6) Reaction of **1a** with $\text{Zn}(\text{CN})_2$ in the presence of radical scavengers



In a nitrogen-filled glove box, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (4.8 mg, 0.02 mmol), DMAP (48.9 mg, 0.4 mmol), $\text{Zn}(\text{CN})_2$ (37.6 mg, 0.32 mmol), zinc powder (10.5 mg, 0.16 mmol), $n\text{-Bu}_4\text{NI}$ (443.2 mg, 1.2 mmol), XantPhos (13.9 mg, 0.024 mmol), **1a** (133.4 mg, 0.4 mmol), radical scavenger and CH_3CN (2.0 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. After the reaction mixture was stirred at 100 °C (oil bath) for 10 h, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2 . The solvent was evaporated under the reduced pressure.

When TEMPO (125.0 mg, 0.8 mmol) was used as the radical scavenger, no desired product (**2a**) was observed.

When BPE (1,1-diphenylethylene) (144.2 mg, 0.8 mmol) was used as the radical scavenger, **2a** could be observed in 11% NMR yield with 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard.

Reference:

- (1) Soulard, V.; Villa, G.; Vollmar, D. P.; Renaud, P. Radical Deuteration with D₂O: Catalysis and Mechanistic Insights. *J. Am. Chem. Soc.* **2018**, *140*, 155.
- (2) Weng, W.-Z.; Liang, H.; Zhang, B. Visible-Light-Mediated Aerobic Oxidation of Organoboron Compounds Using in Situ Generated Hydrogen Peroxide. *Org. Lett.* **2018**, *20*, 4979.
- (3) Anthore, L.; Zard, S. Z. A Convergent Radical Based Route to Trifluoromethyl Ketones and to α,β -Unsaturated Trifluoromethyl Ketones. *Org. Lett.* **2015**, *17*, 3058.
- (4) Sun, Q.; Cai, S.; Peterson, B. R. Practical Synthesis of 3 β -Amino-5-cholestene and Related 3 β -Halides Involving *i*-Steroid and Retro-*i*-Steroid Rearrangements. *Org. Lett.* **2009**, *11*, 567.
- (5) Liu, Y.; Cornella, J.; Martin, R. Ni-Catalyzed Carboxylation of Unactivated Primary Alkyl Bromides and Sulfonates with CO₂. *J. Am. Chem. Soc.* **2014**, *136*, 11212.
- (6) Kim, D. W.; Jeong, H.-J.; Lim, S. T.; Sohn, M.-H. Tetrabutylammonium Tetra(*tert*-Butyl Alcohol)-Coordinated Fluoride as a Facile Fluoride Source. *Angew. Chem. Int. Ed.* **2008**, *47*, 8404.
- (7) Romeiro, L. A. S.; da Silva Ferreira, M.; da Silva, L. L.; Castro, H. C.; Miranda, A. L. P.; Silva, C. L. M.; Noël, F.; Nascimento, J. B.; Araújo, C. V.; Tibiricá, E.; Barreiro, E. J.; Fraga, C. A. M. Discovery of LASSBio-772, a 1,3-benzodioxole *N*-phenylpiperazine derivative with potent alpha 1A/D-adrenergic receptor blocking properties. *Eur. J. Med. Chem.* **2011**, *46*, 3000.
- (8) Cho, W. S.; Kim, S. H.; Kim, D. J.; Mun, S.-d.; Kim, R.; Go, M. J.; Park, M. H.; Kim, M.; Lee, J.; Kim, Y. Zirconium complexes with pendant aryloxy groups attached to the metallocene moiety by ethyl or hexyl spacers. *Polyhedron* **2014**, *67*, 205.
- (9) Xia, A.; Xie, X.; Chen, H.; Zhao, J.; Zhang, C.; Liu, Y. Nickel-Catalyzed Cyanation of Unactivated Alkyl Chlorides or Bromides with Zn(CN)₂. *Org. Lett.* **2018**, *20*, 7735.
- (10) Ramirez, N. P.; König, B.; Gonzalez-Gomez, J. C. Decarboxylative Cyanation of Aliphatic Carboxylic Acids via Visible-Light Flavin Photocatalysis. *Org. Lett.* **2019**, *21*, 1368.

(11) Alazet, S.; West, M. S.; Patel, P.; Rousseaux, S. A. L. Synthesis of Nitrile-Bearing Quaternary Centers by an Equilibrium-Driven Transnitration and Anion-Relay Strategy. *Angew. Chem. Int. Ed.* **2019**, *58*, 10300.

(12) Rong, G.; Liu, D.; Lu, L.; Yan, H.; Zheng, Y.; Chen, J.; Mao, J. Iron-catalyzed decarboxylative methylation of α,β -unsaturated acids under ligand-free conditions. *Tetrahedron* **2014**, *70*, 5033.

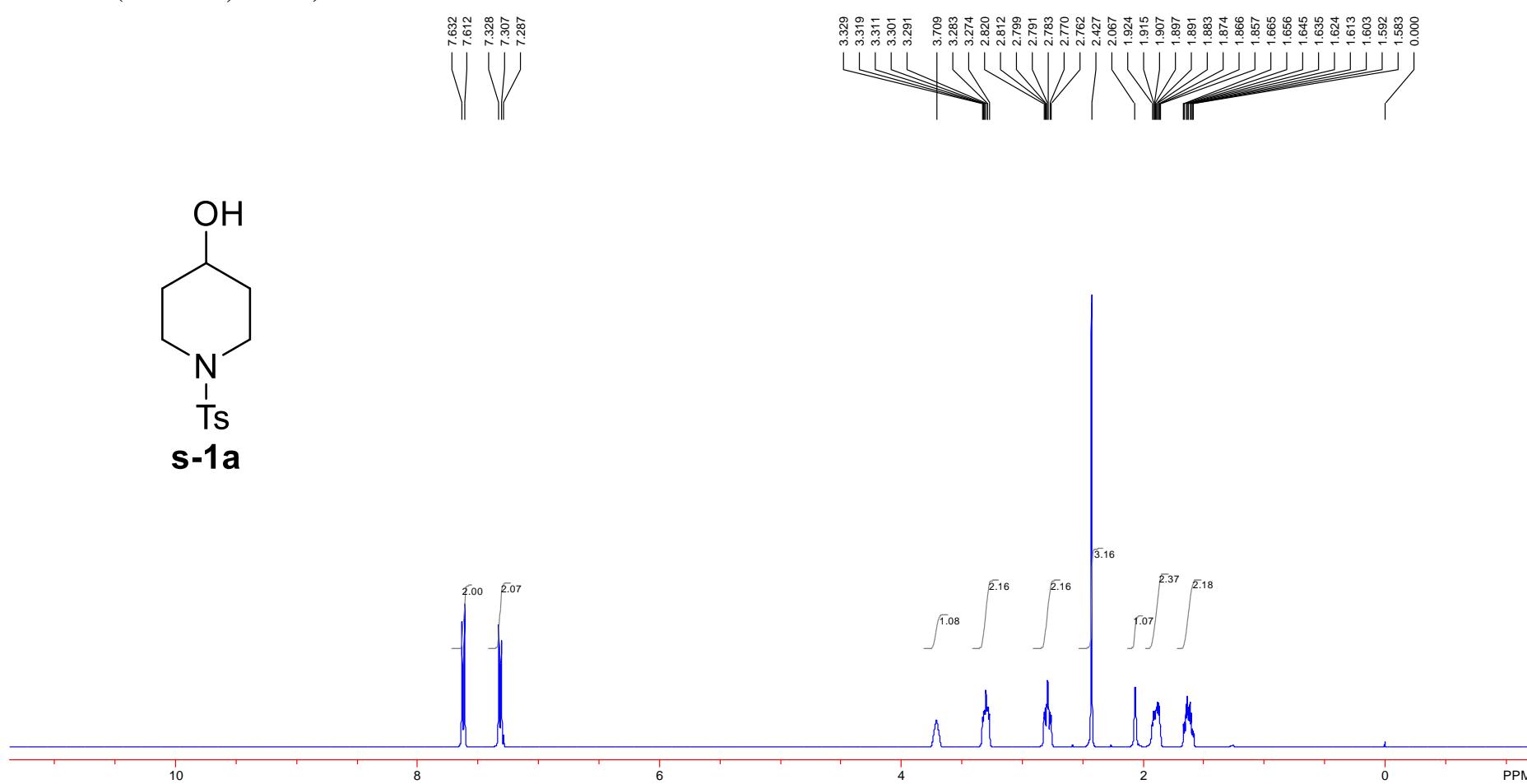
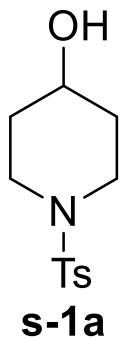
(13) Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. Suzuki-Miyaura Cross-Coupling Reactions of Primary Alkyltrifluoroborates with Aryl Chlorides. *J. Org. Chem.* **2009**, *74*, 3626.

(14) Iwata, Y.; Tanaka, Y.; Kubosaki, S.; Morita, T.; Yoshimi, Y. A strategy for generating aryl radicals from arylborates through organic photoredox catalysis: photo-Meerwein type arylation of electron-deficient alkenes. *Chem. Commun.* **2018**, *54*, 1257.

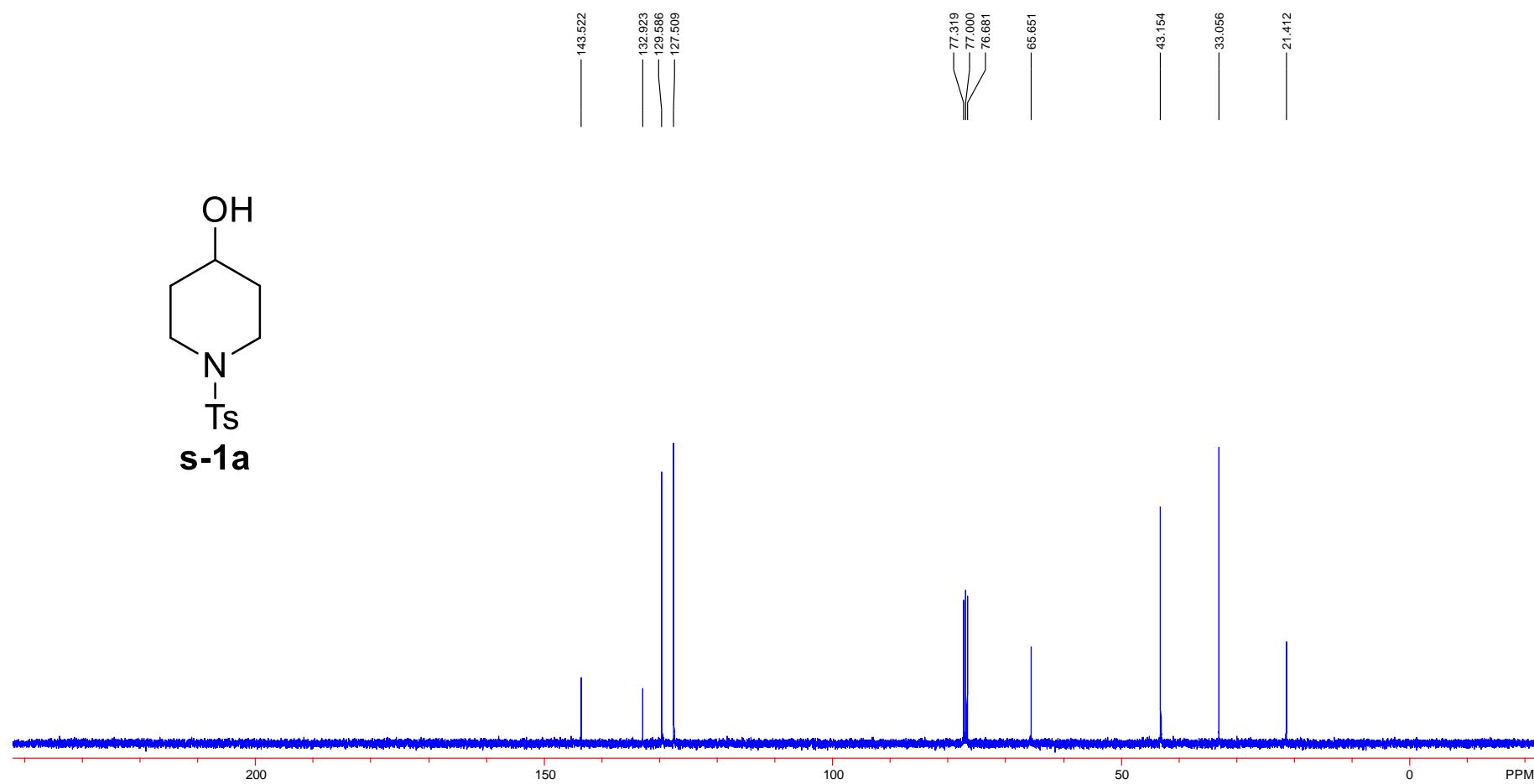
(15) Tanji, Y.; Hamaguchi, R.; Tsuji, Y.; Fujihara, T. Pd-Catalyzed intermolecular C-H bond arylation reactions: effect of bulkiness of carboxylate ligands. *Chem. Commun.* **2020**, *56*, 3843.

(16) Winkler, M.; Meischler, D.; Klempier, N. Nitrilase-Catalyzed Enantioselective Synthesis of Pyrrolidine- and Piperidinecarboxylic Acids. *Adv. Synth. Catal.* **2007**, *349*, 1475.

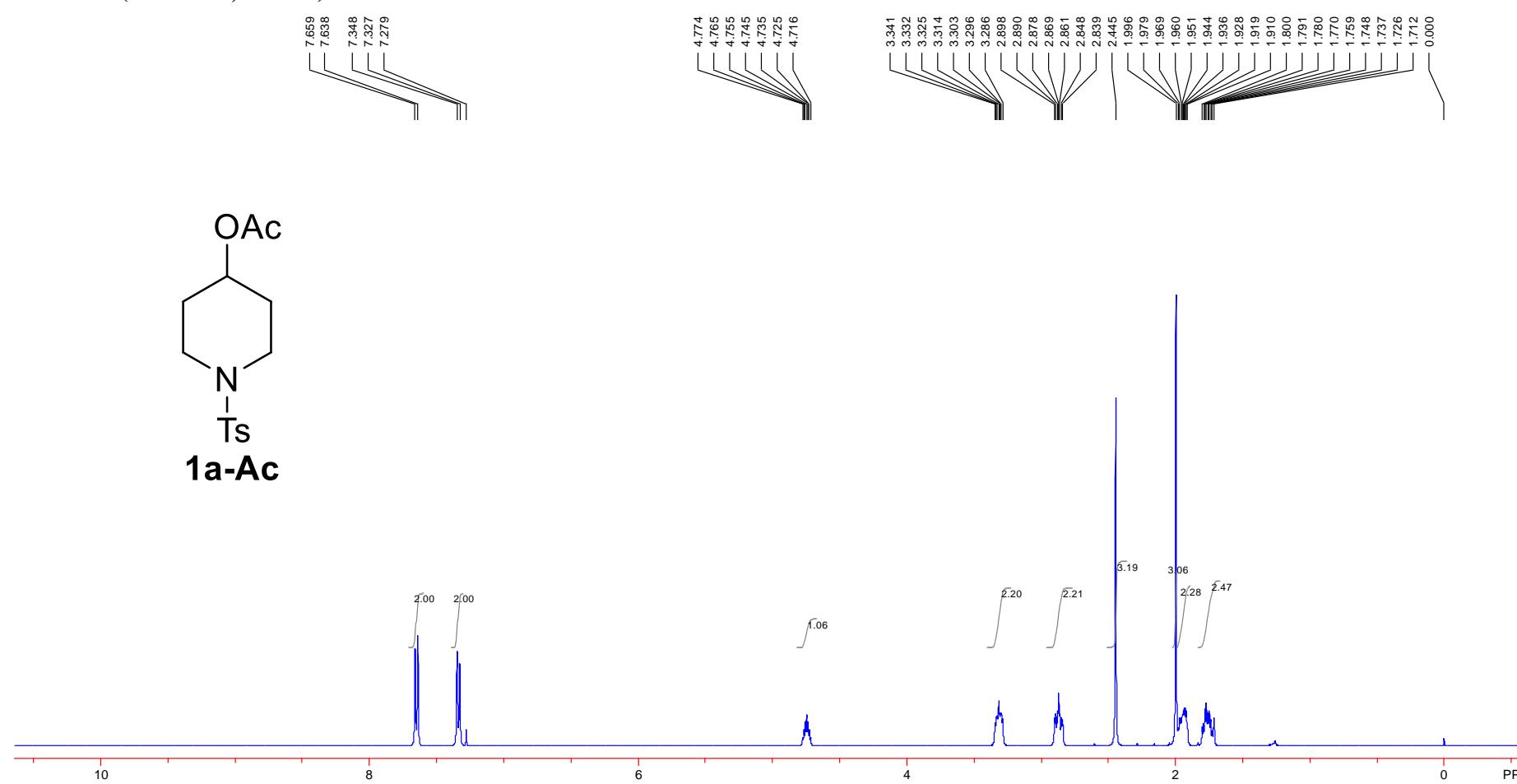
¹H NMR (400 MHz, CDCl₃)



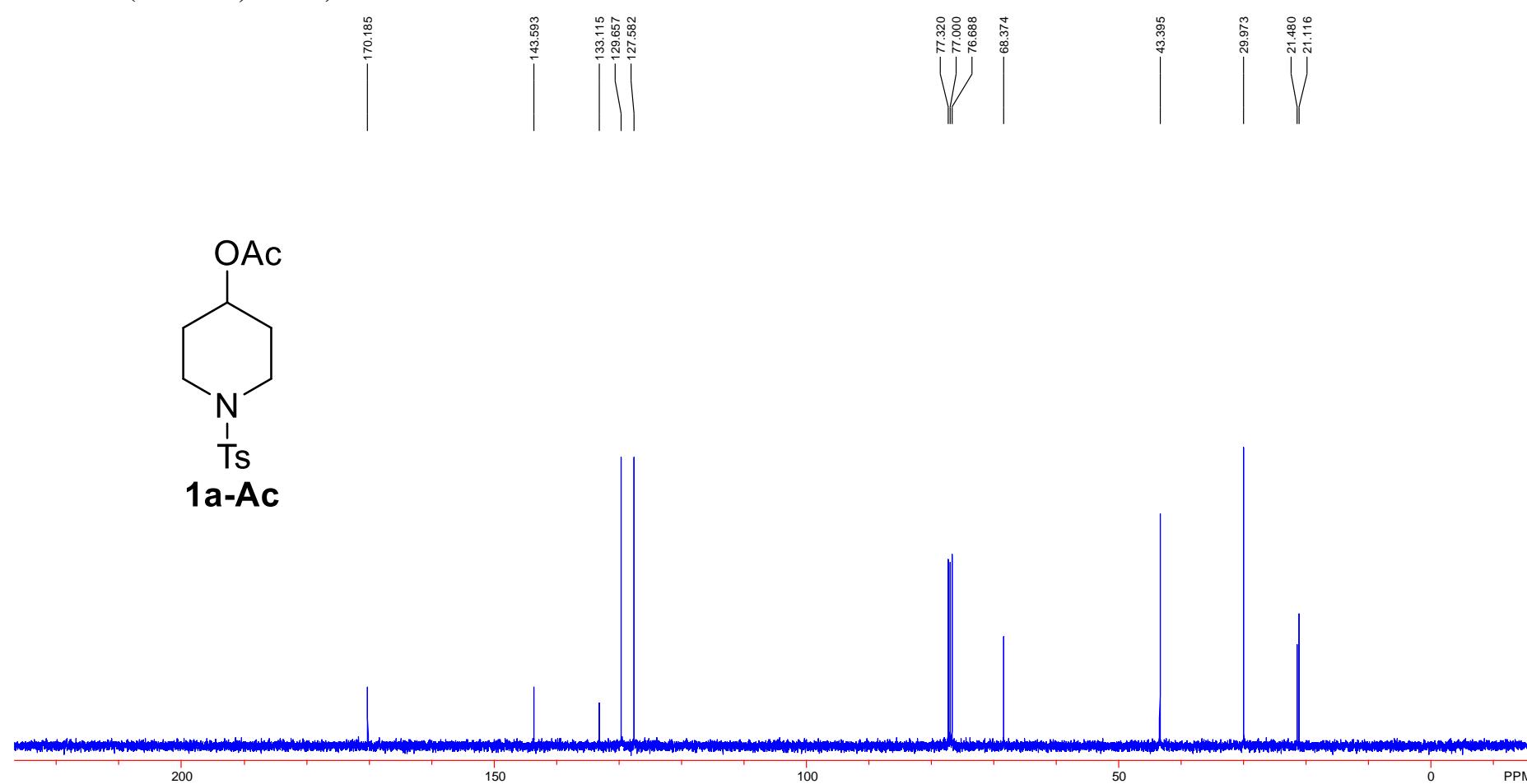
¹³C NMR (100 MHz, CDCl₃)



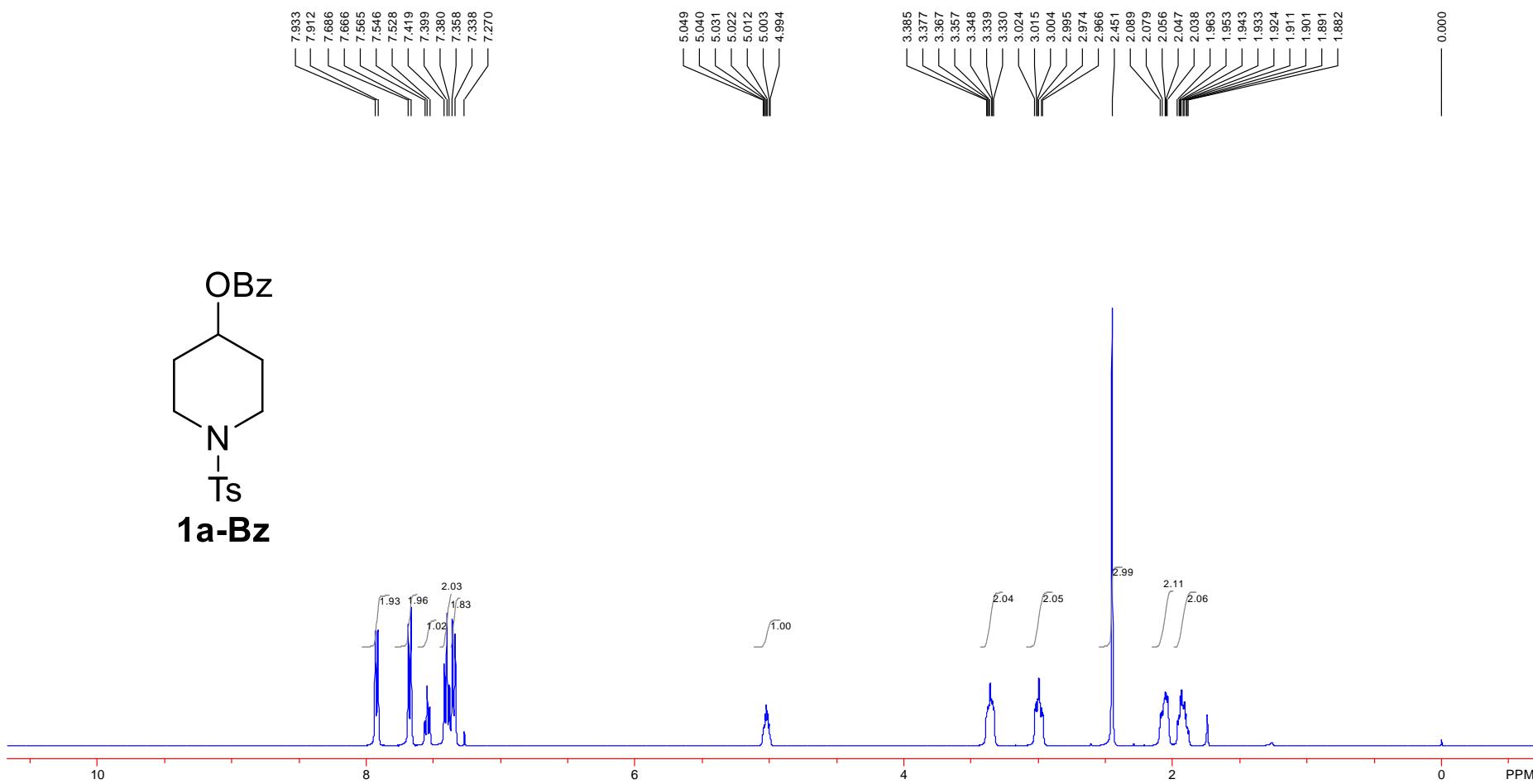
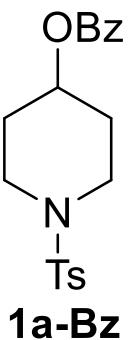
¹H NMR (400 MHz, CDCl₃)



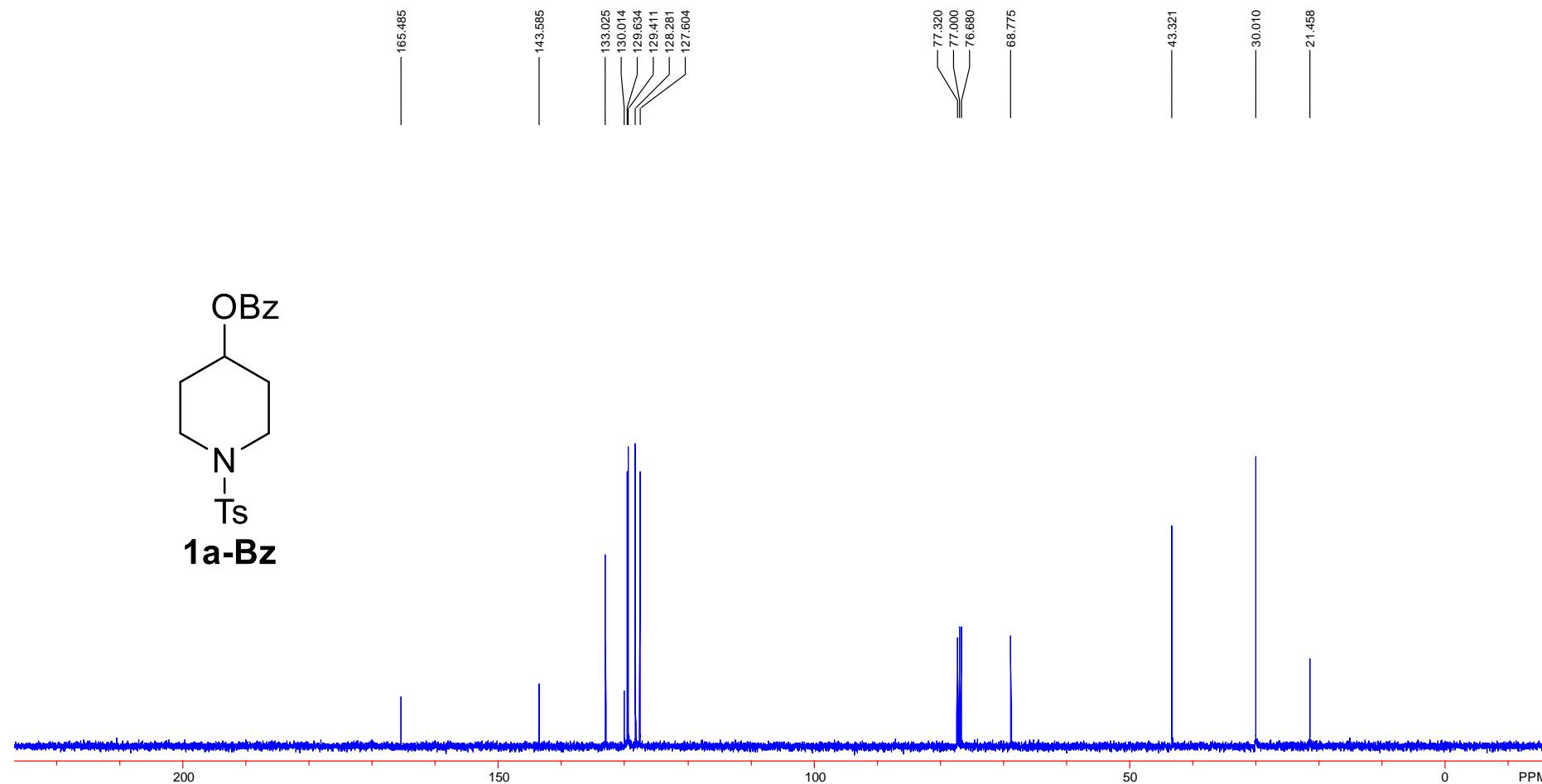
¹³C NMR (100 MHz, CDCl₃)



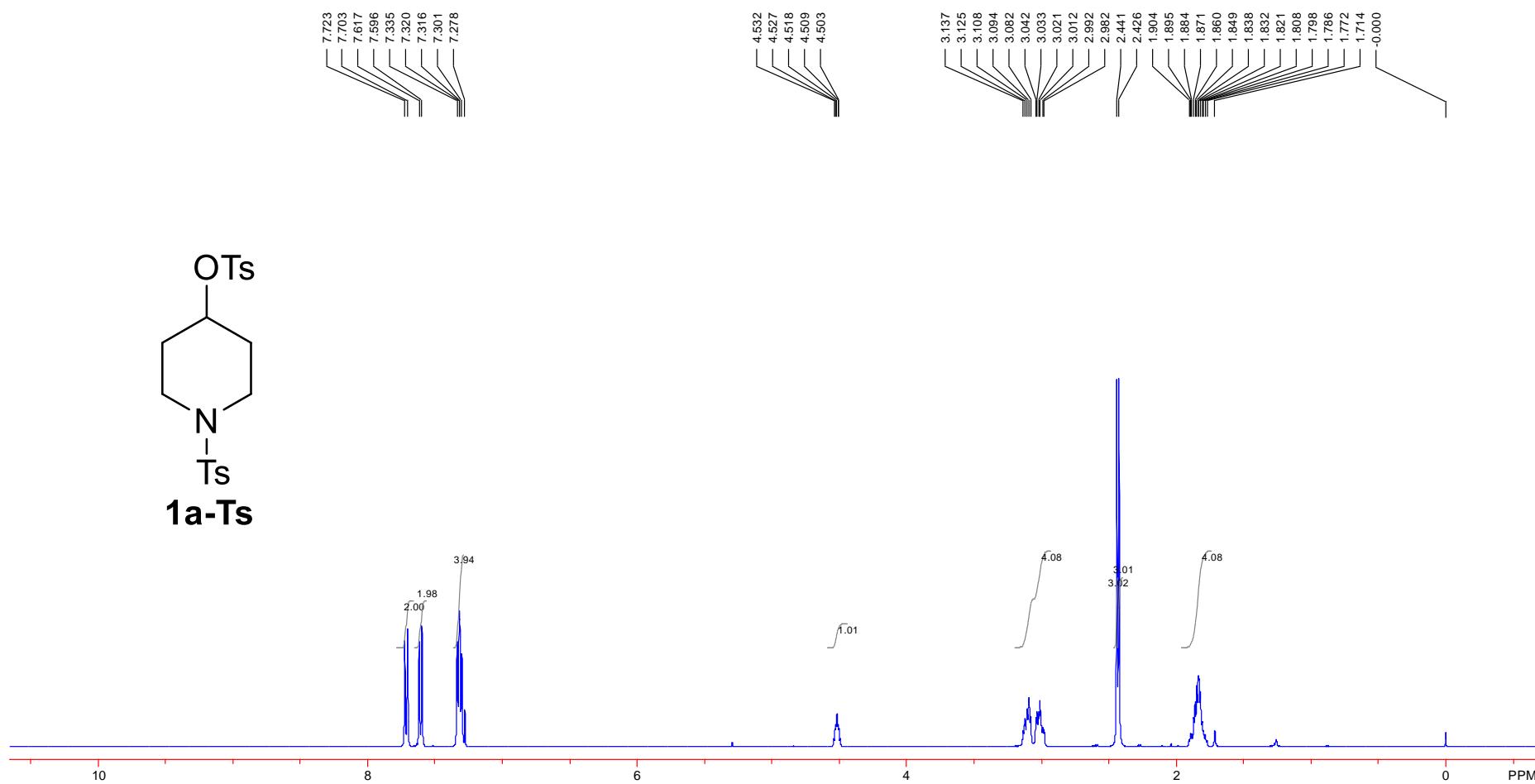
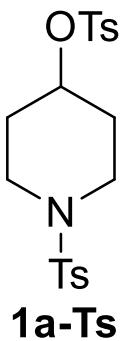
¹H NMR (400 MHz, CDCl₃)



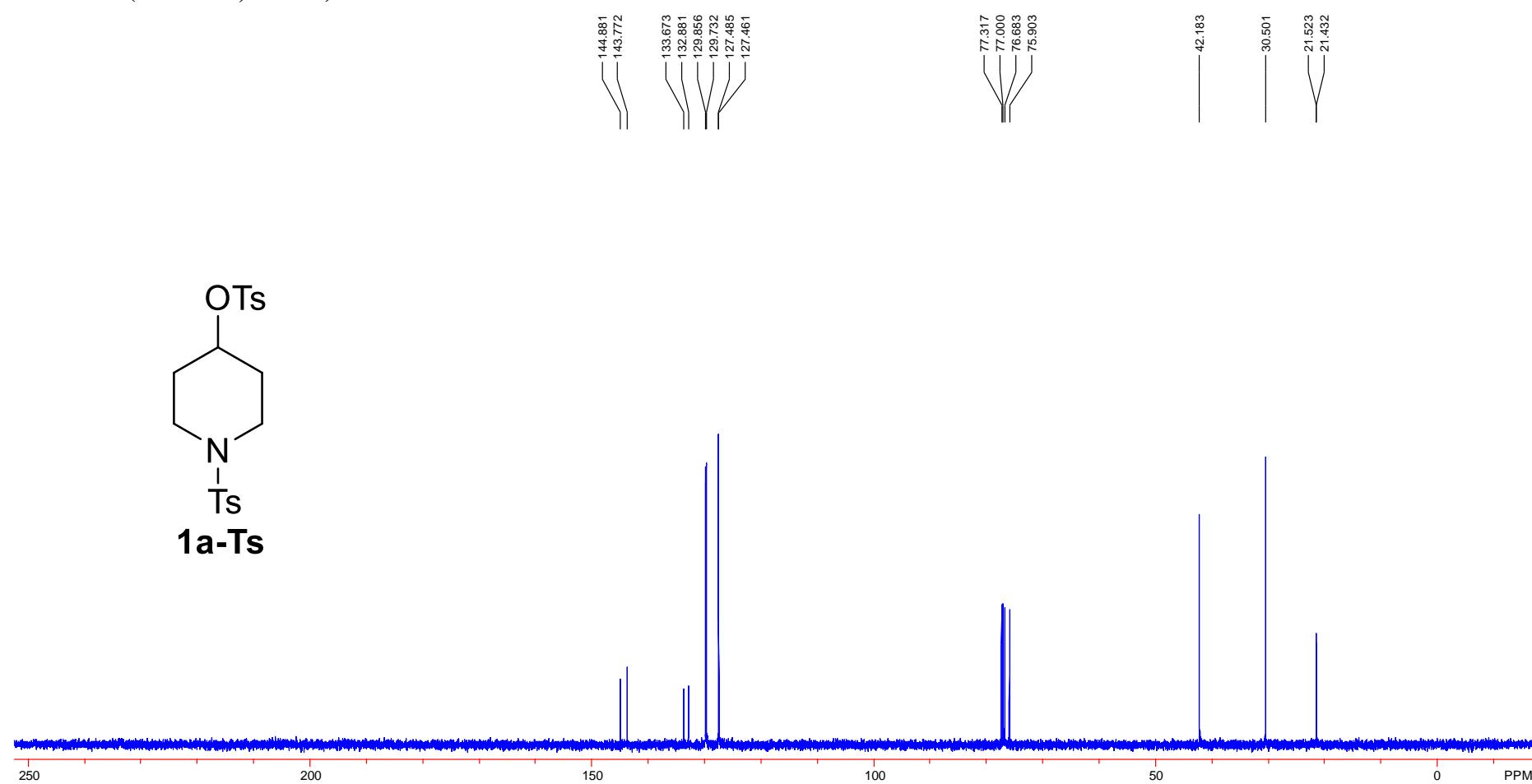
¹³C NMR (100 MHz, CDCl₃)



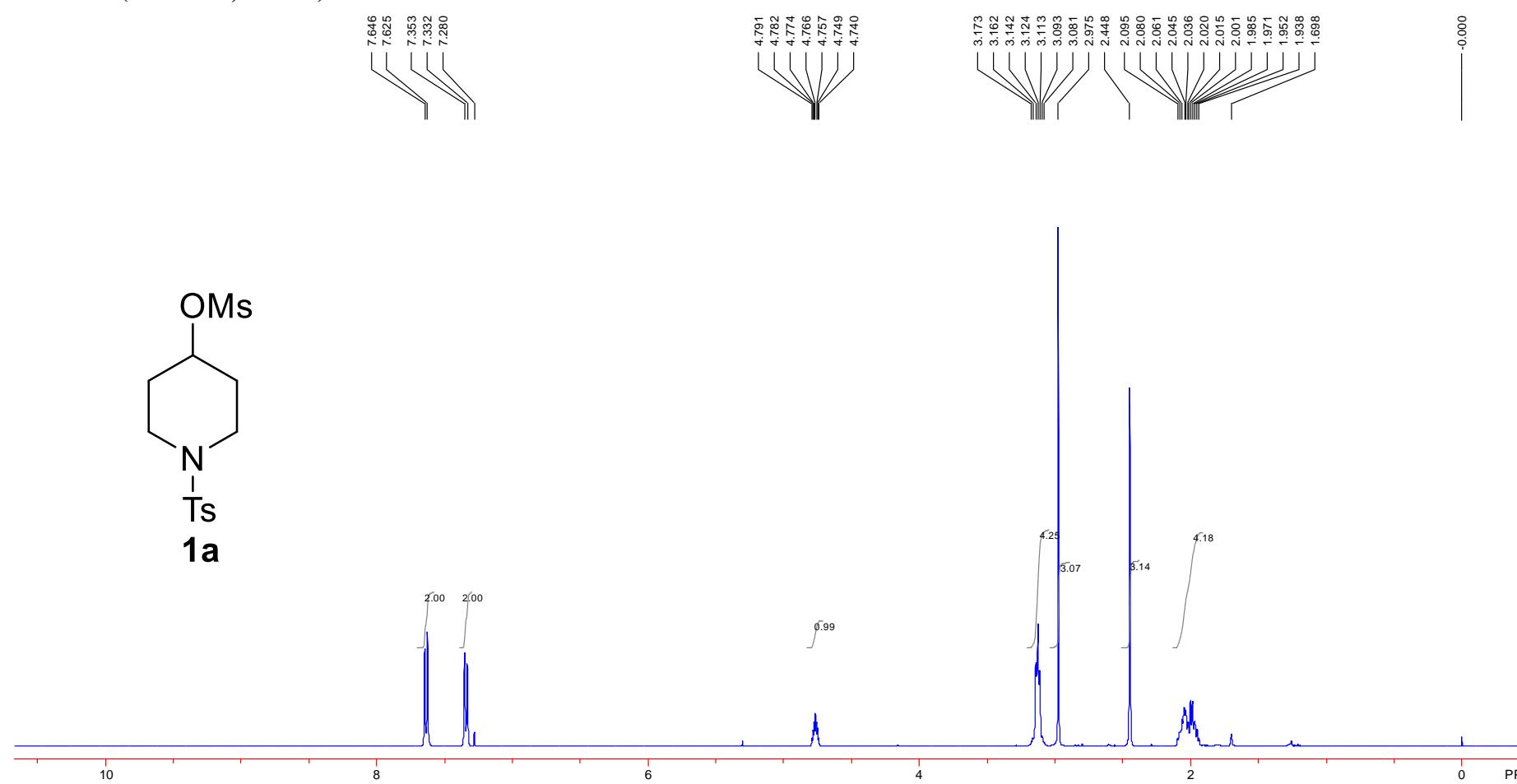
¹H NMR (400 MHz, CDCl₃)



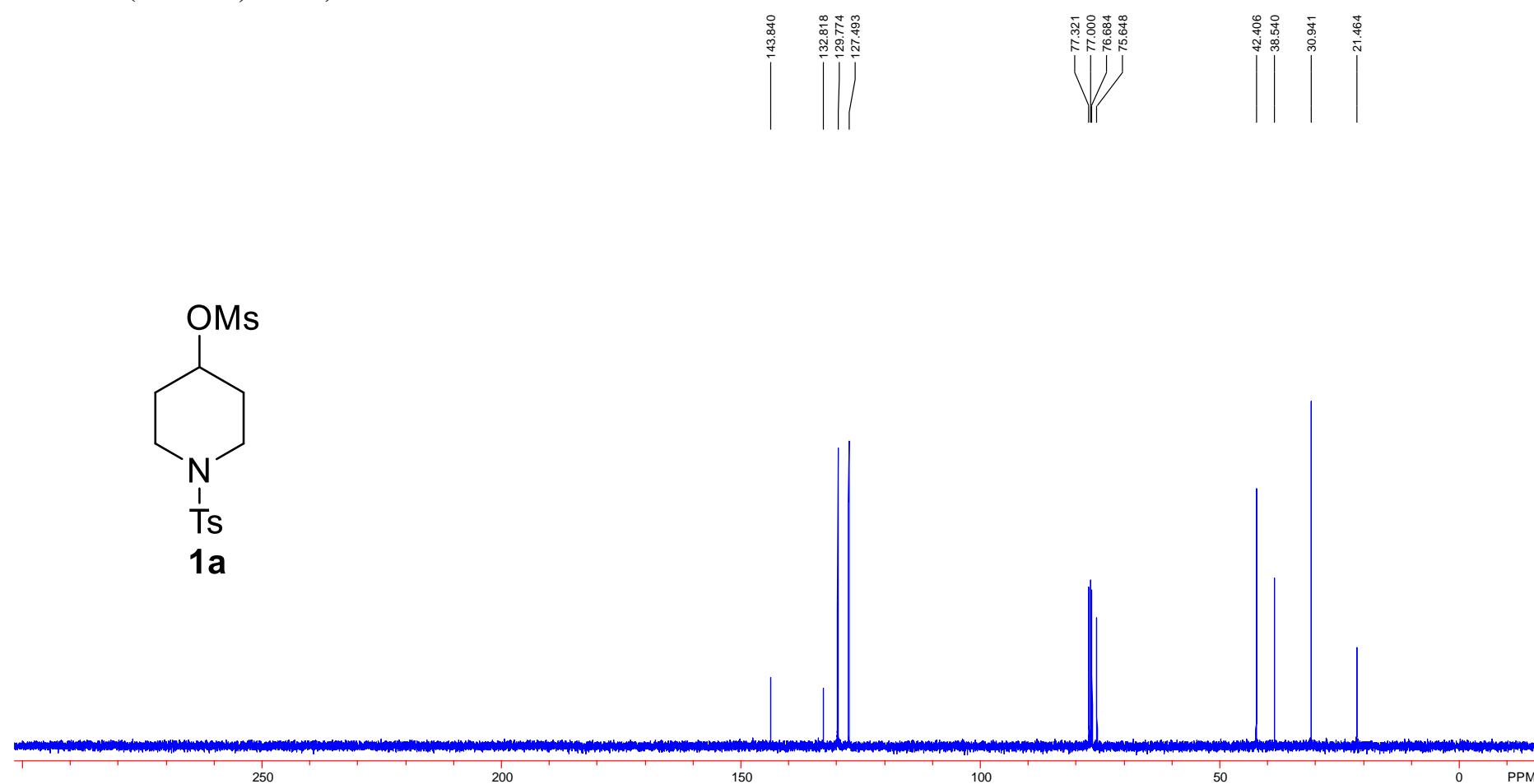
¹³C NMR (100 MHz, CDCl₃)



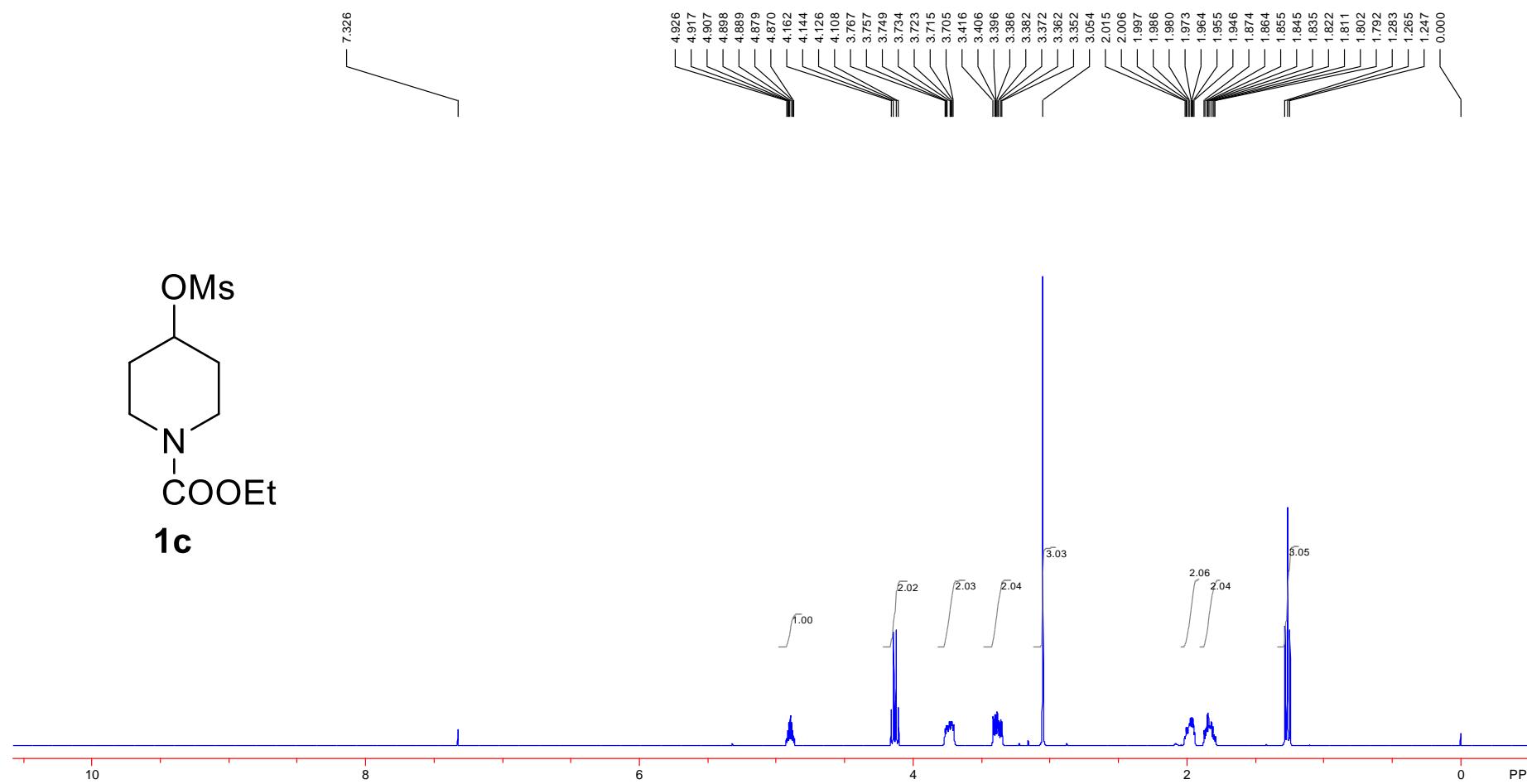
¹H NMR (400 MHz, CDCl₃)



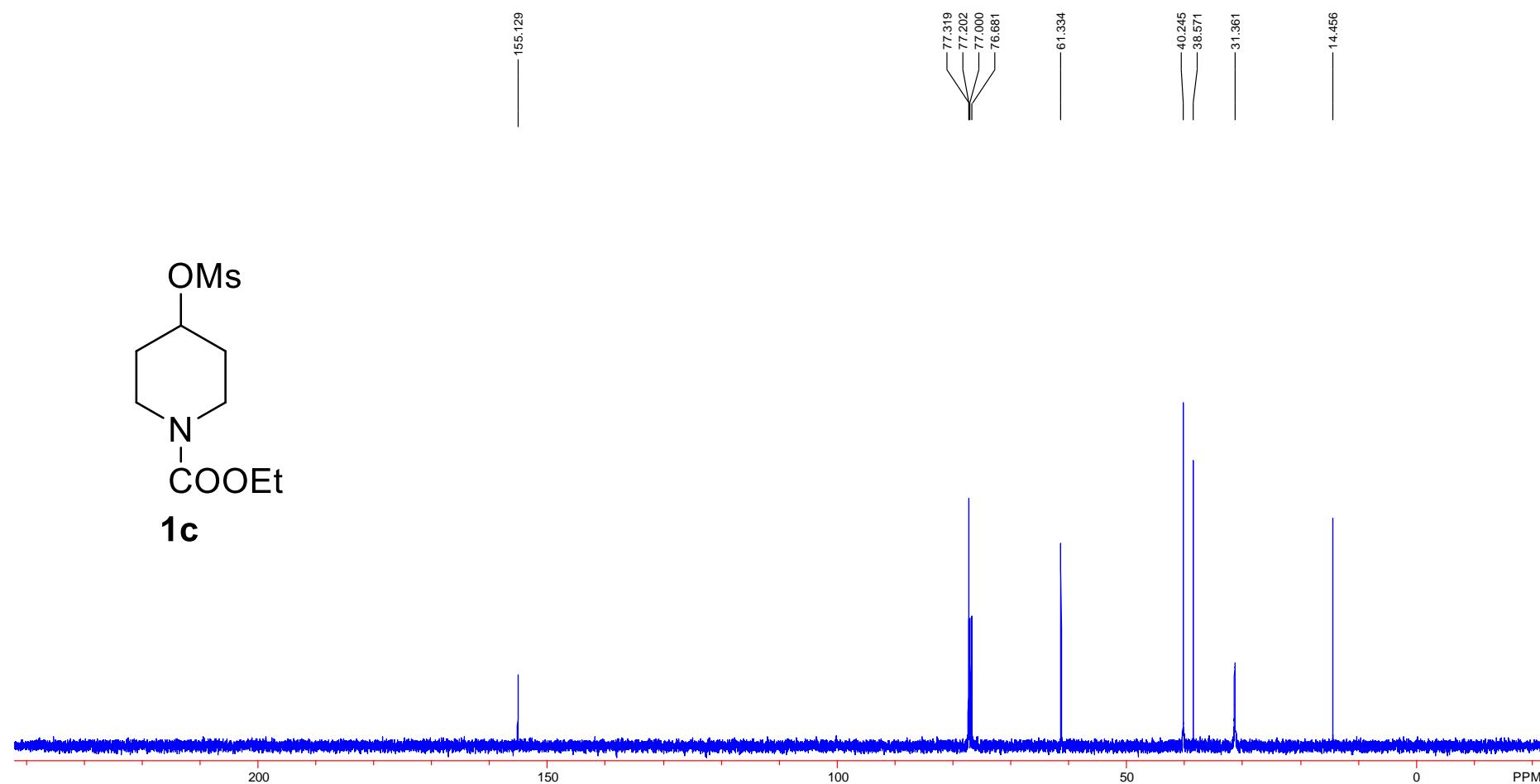
¹³C NMR (100 MHz, CDCl₃)



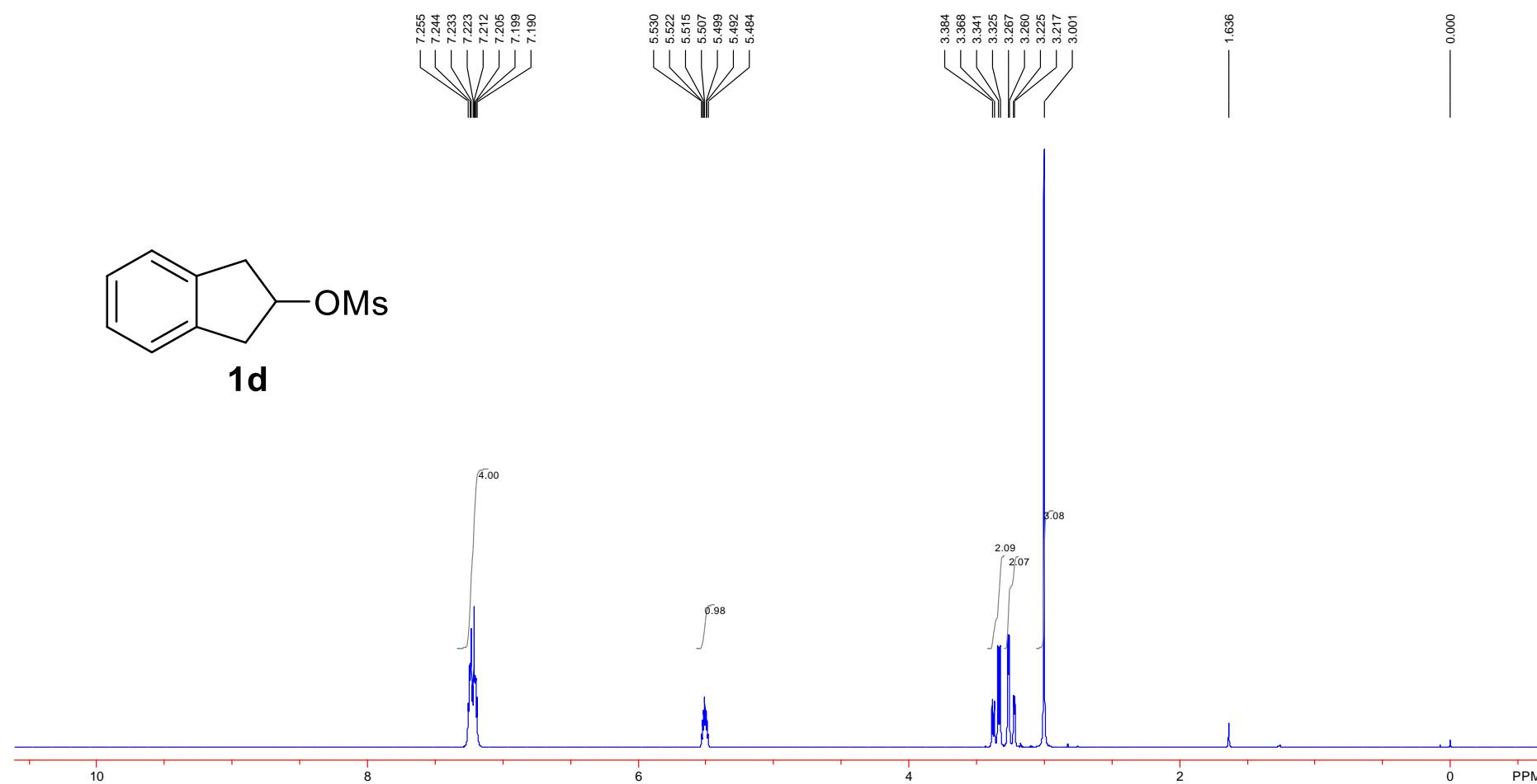
¹H NMR (400 MHz, CDCl₃)



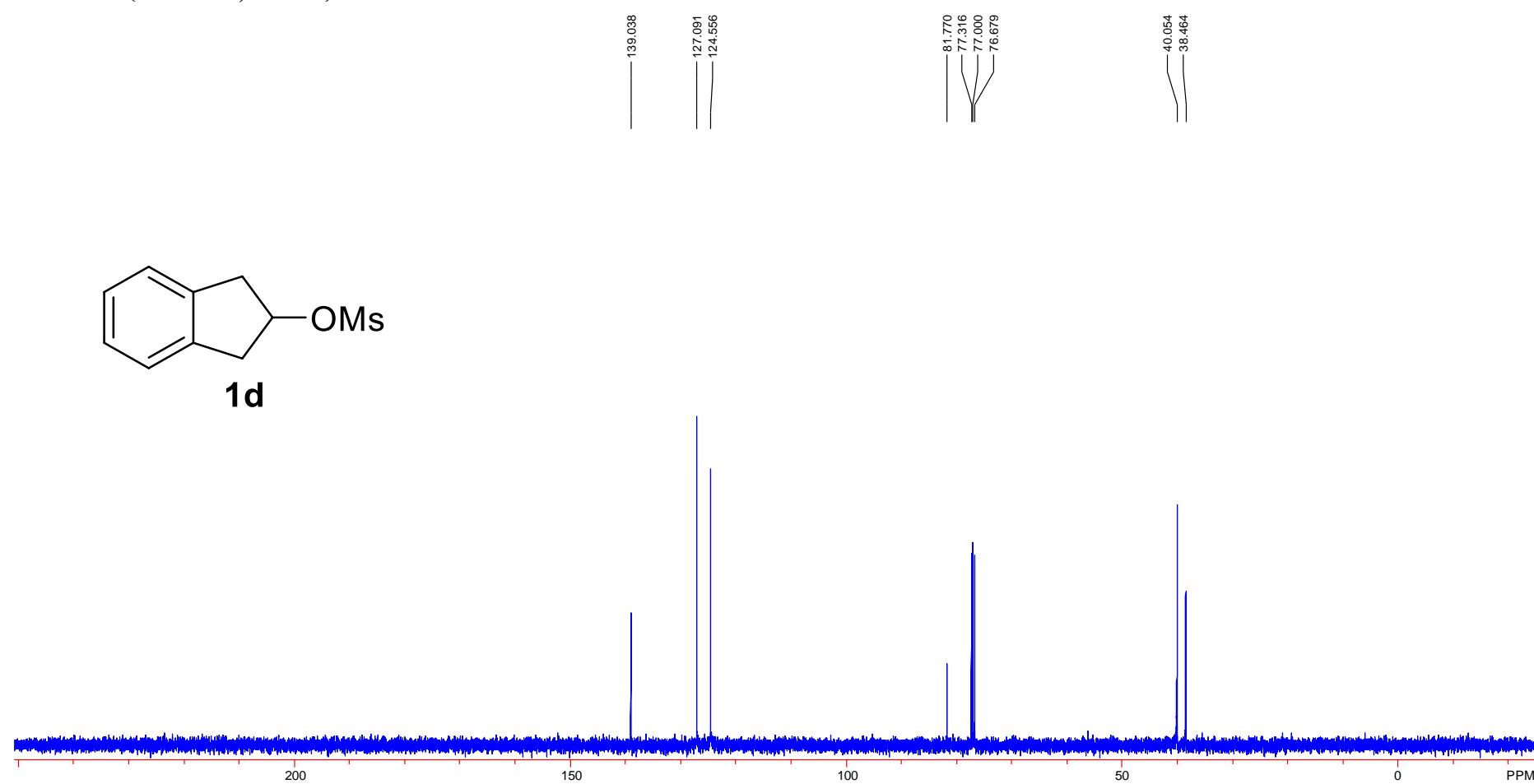
¹³C NMR (100 MHz, CDCl₃)



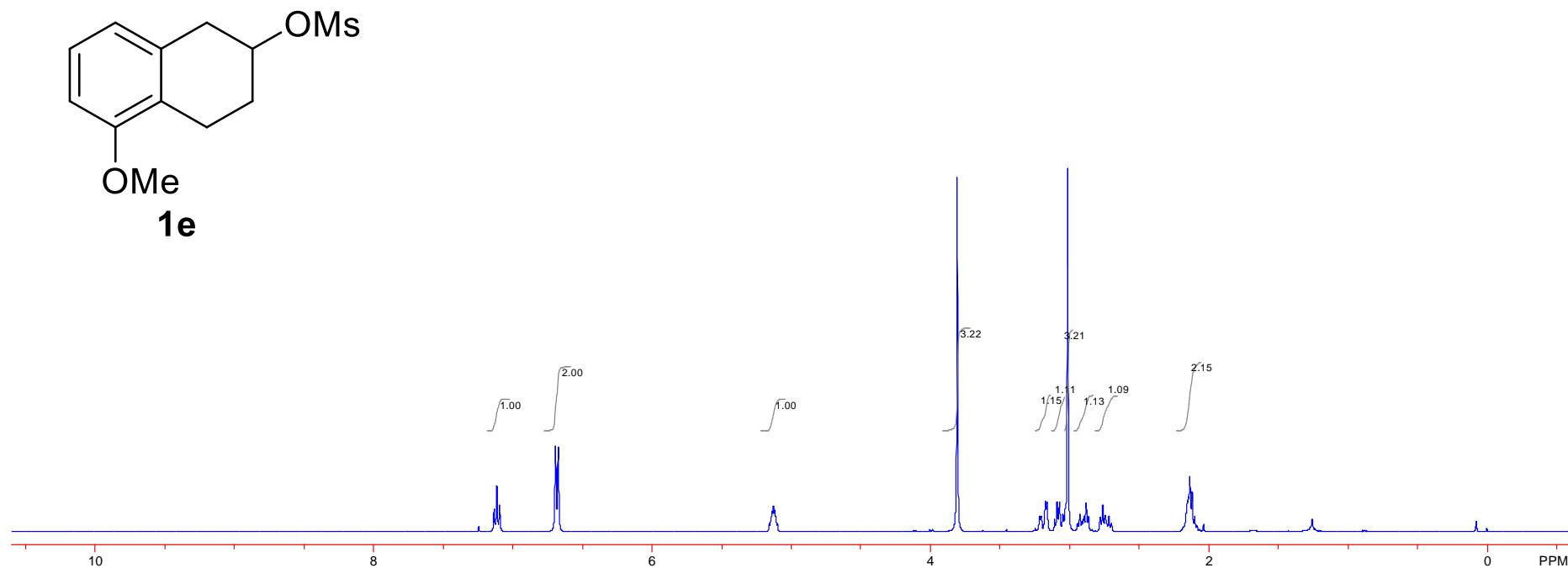
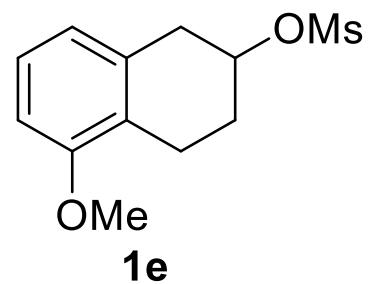
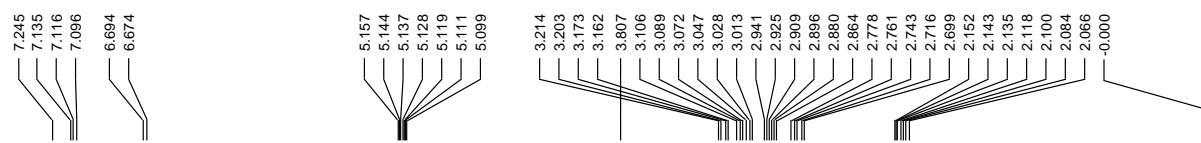
¹H NMR (400 MHz, CDCl₃)



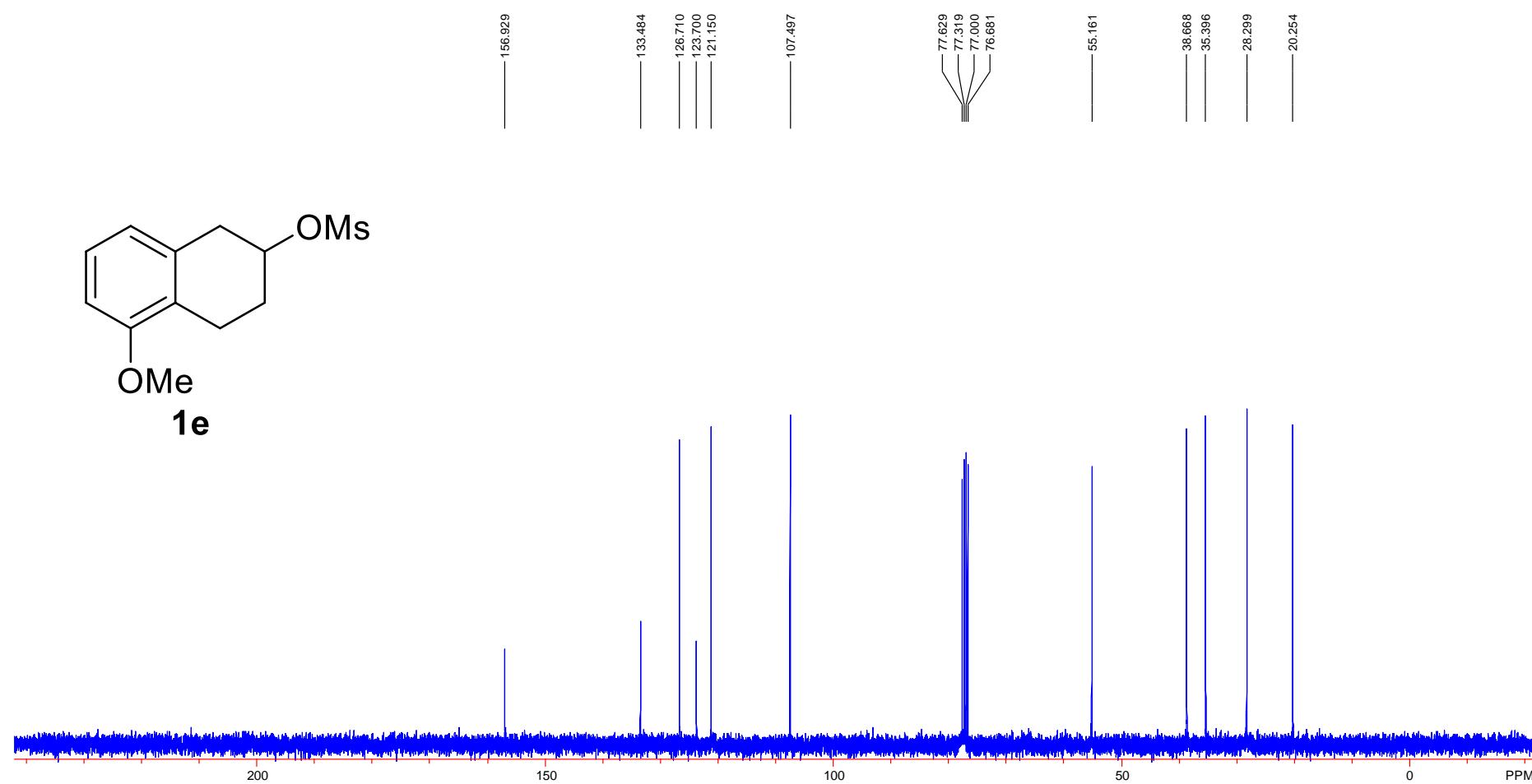
¹³C NMR (100 MHz, CDCl₃)



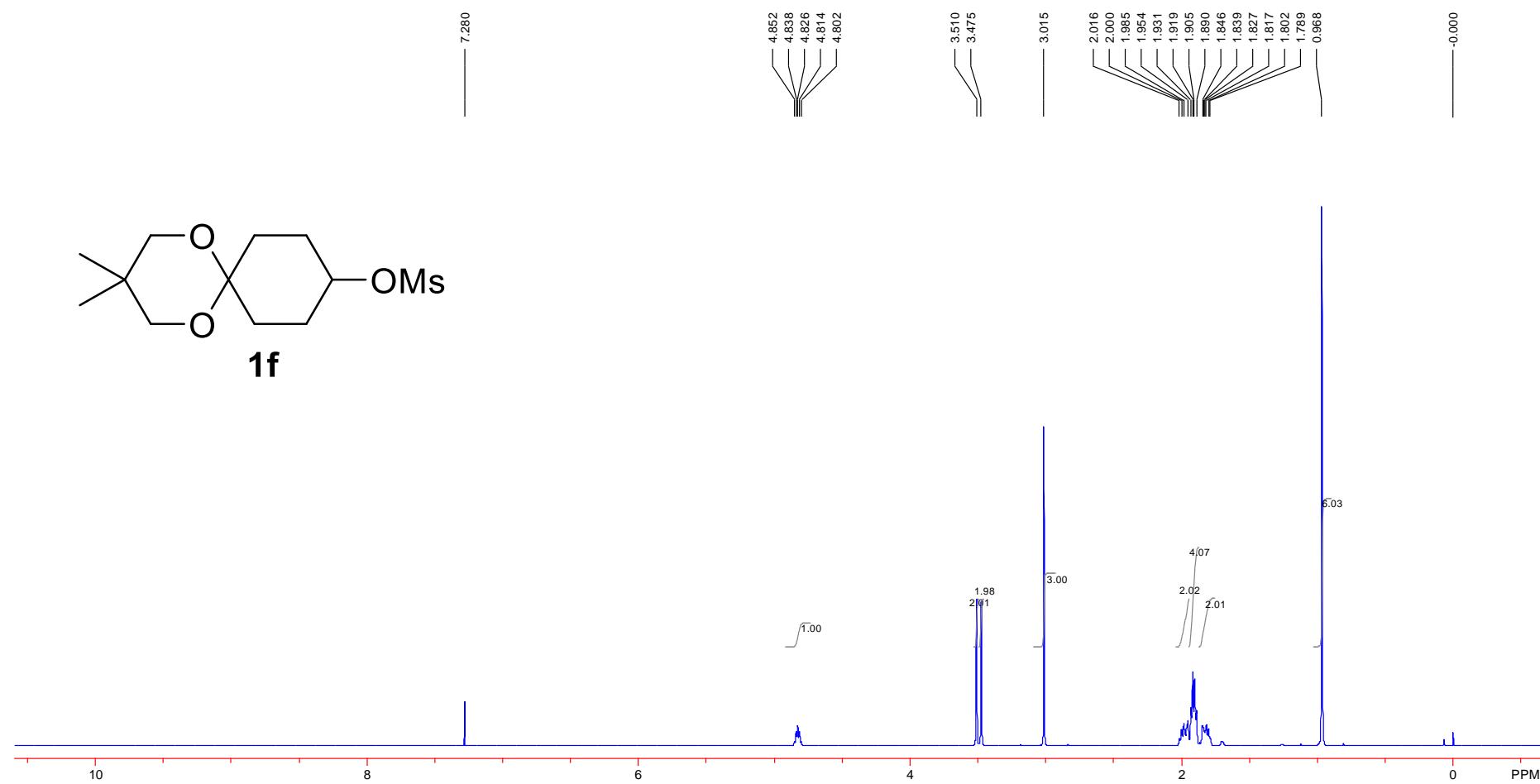
¹H NMR (400 MHz, CDCl₃)



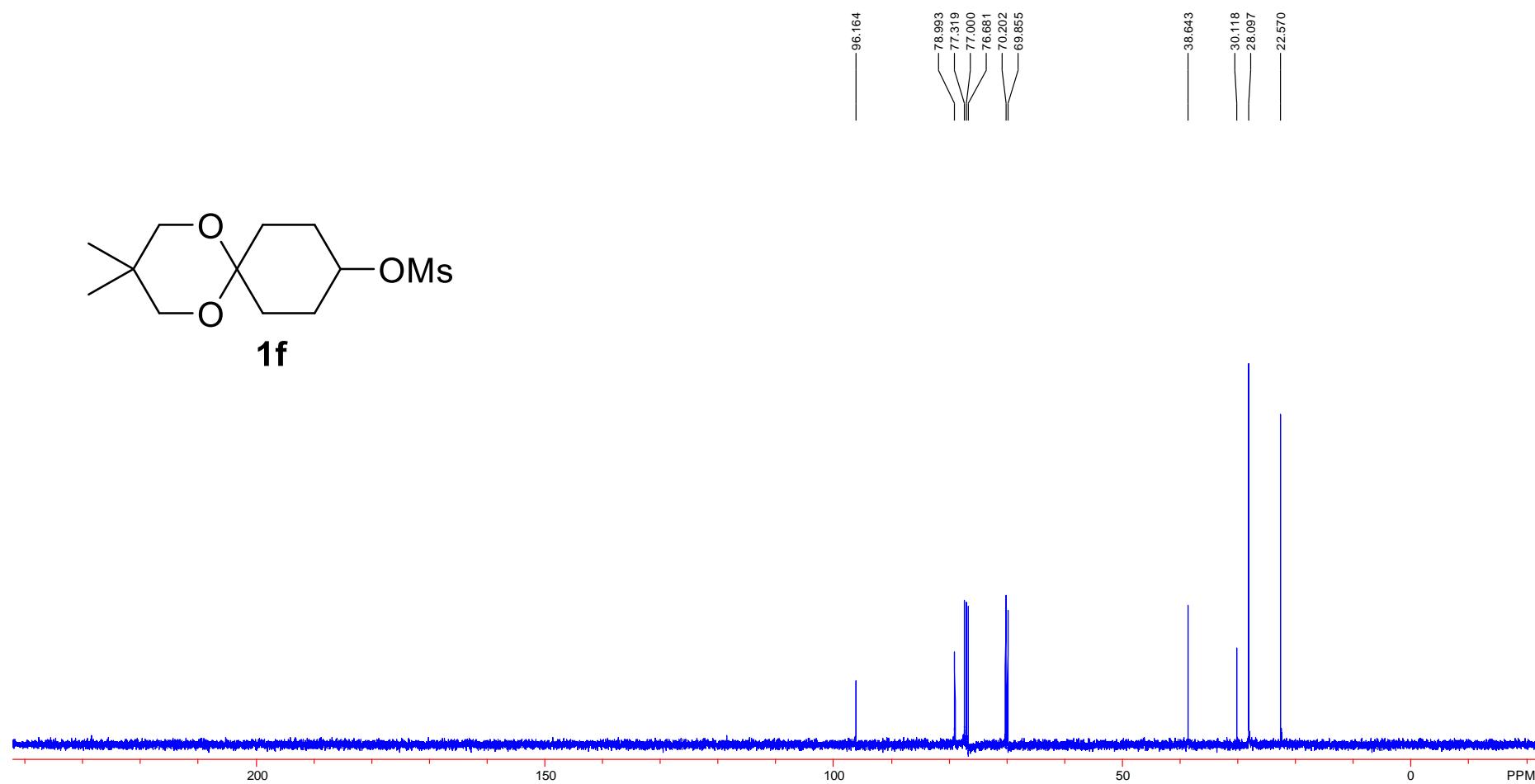
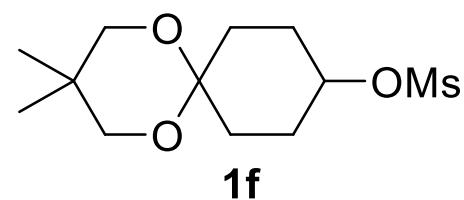
¹³C NMR (100 MHz, CDCl₃)



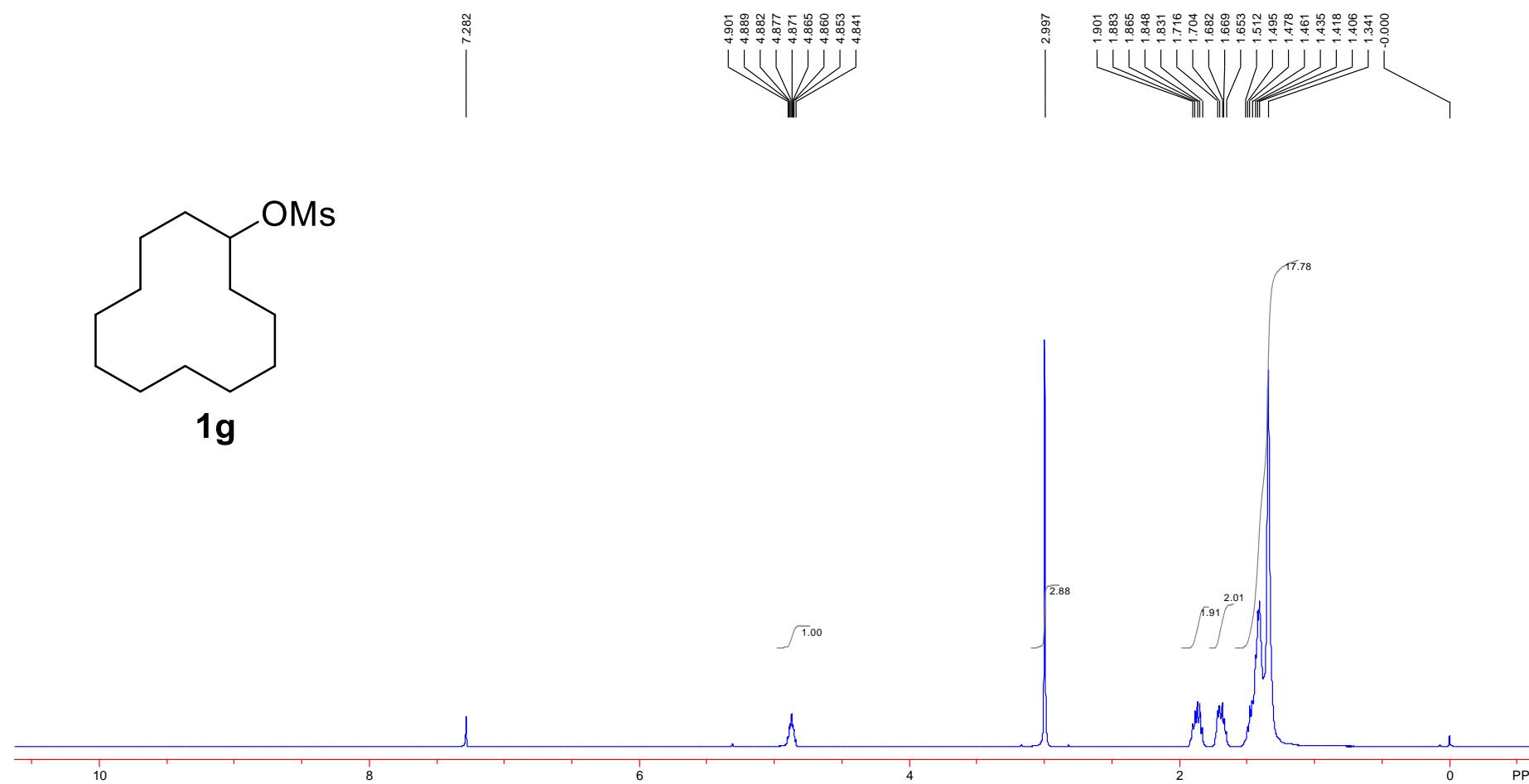
¹H NMR (400 MHz, CDCl₃)



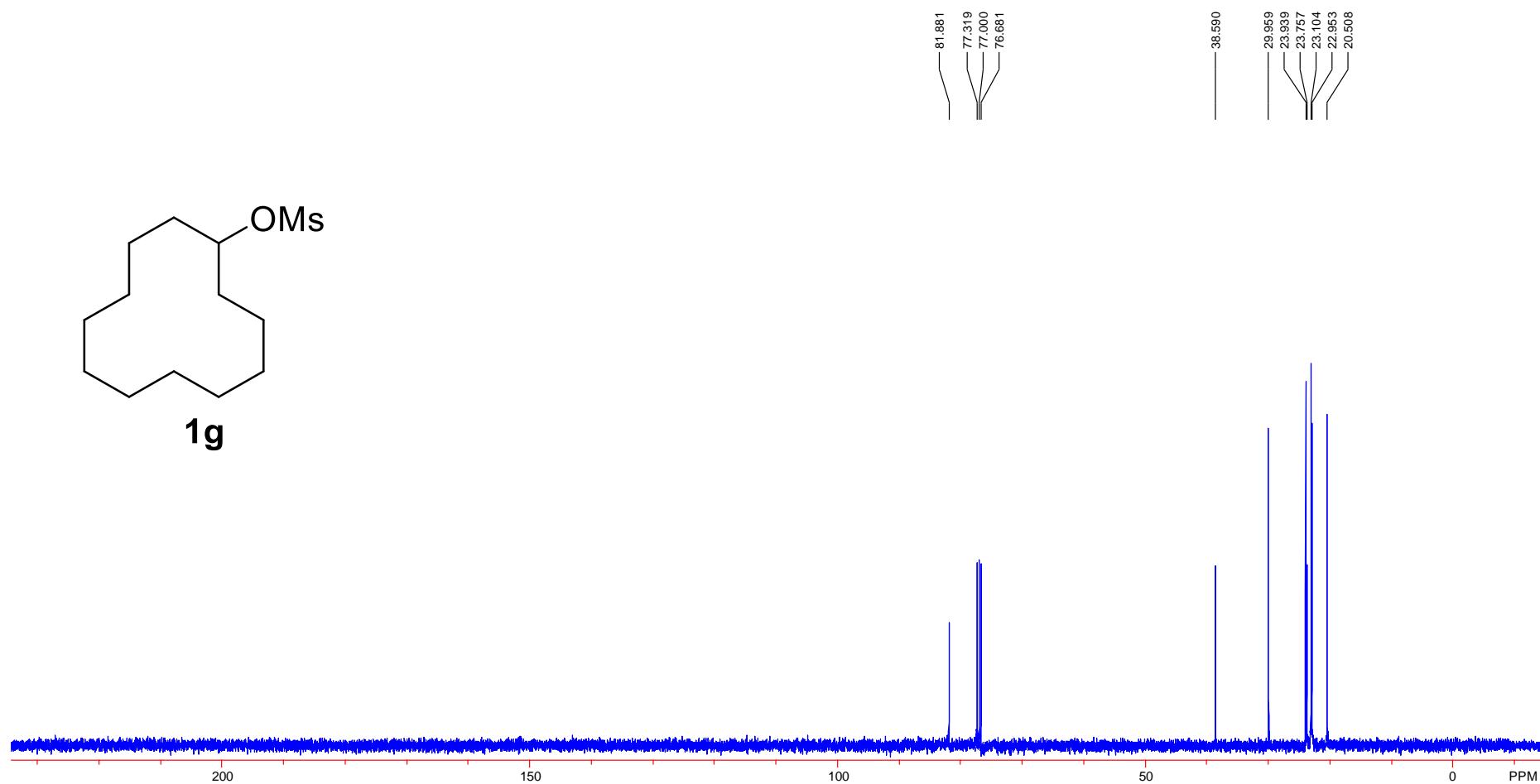
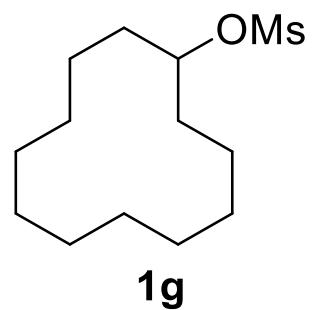
¹³C NMR (100 MHz, CDCl₃)



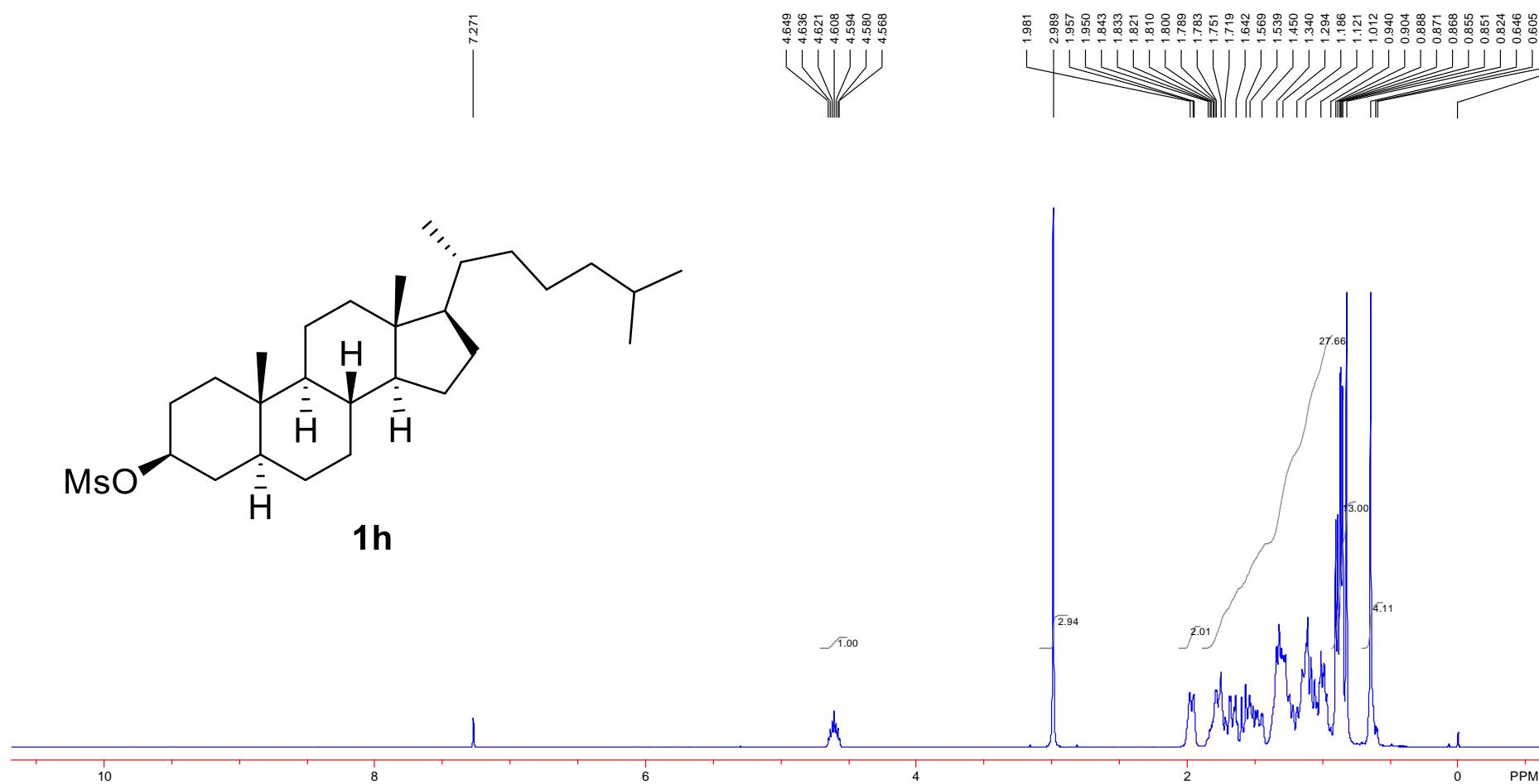
¹H NMR (400 MHz, CDCl₃)



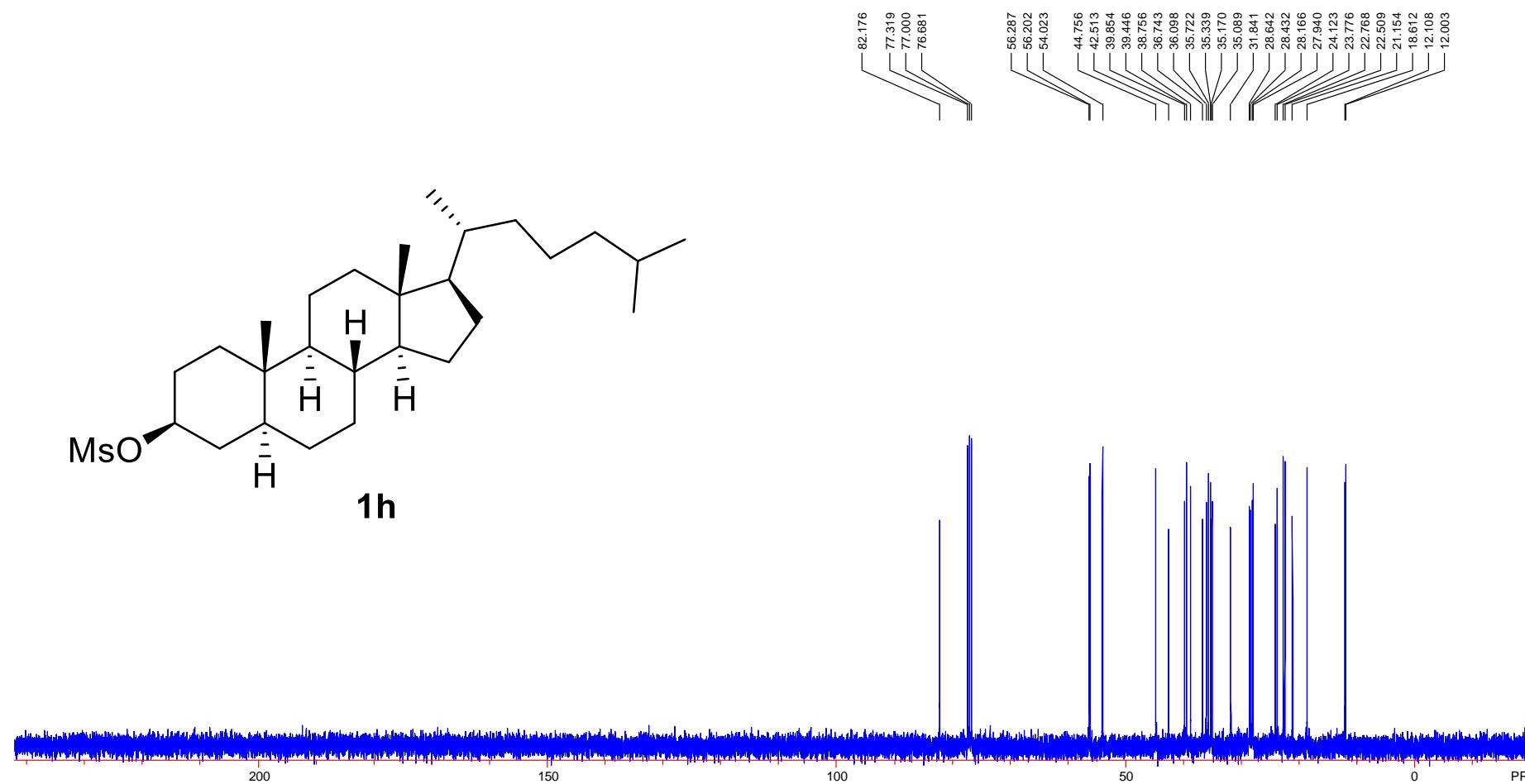
¹³C NMR (100 MHz, CDCl₃)



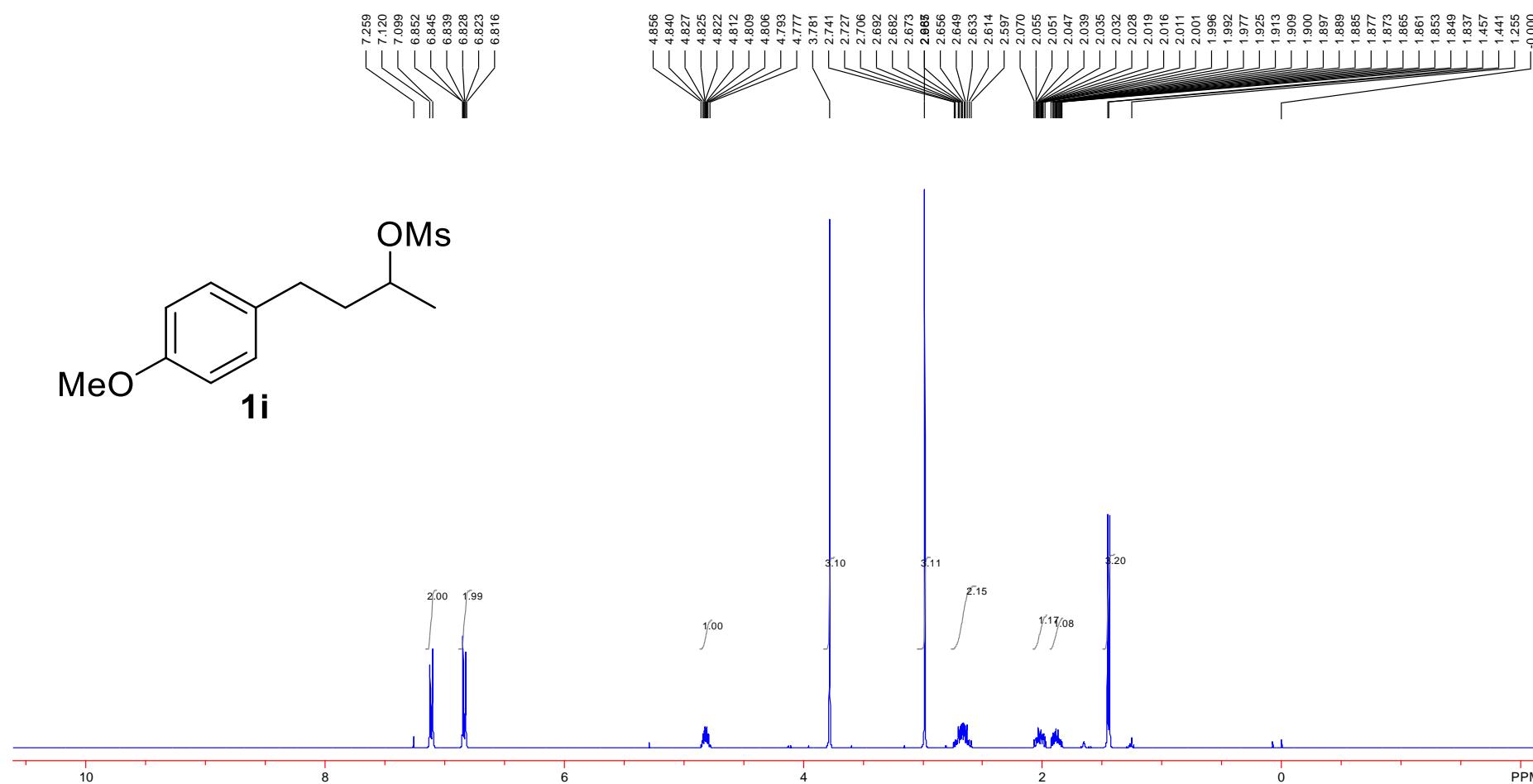
¹H NMR (400 MHz, CDCl₃)



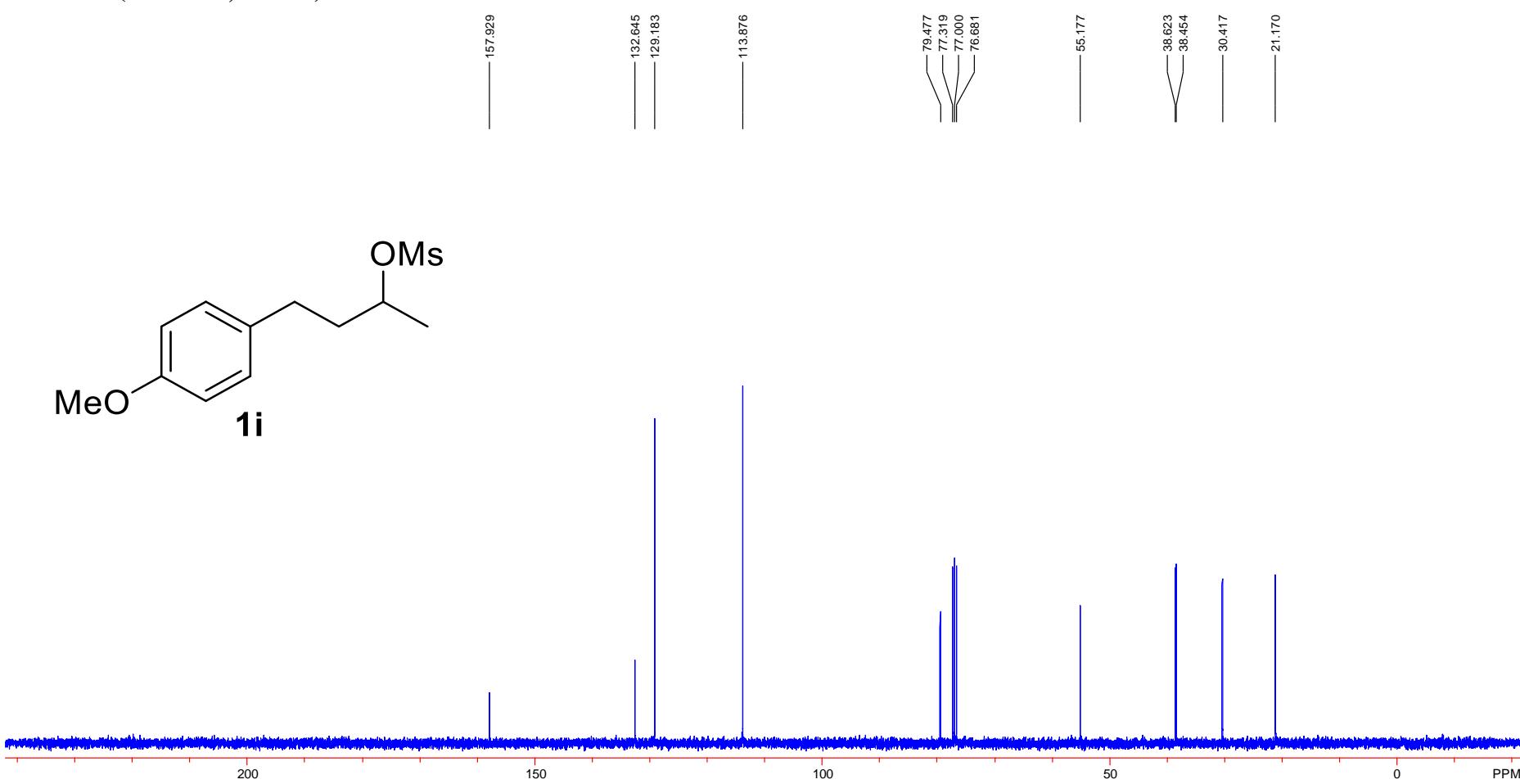
¹³C NMR (100 MHz, CDCl₃)



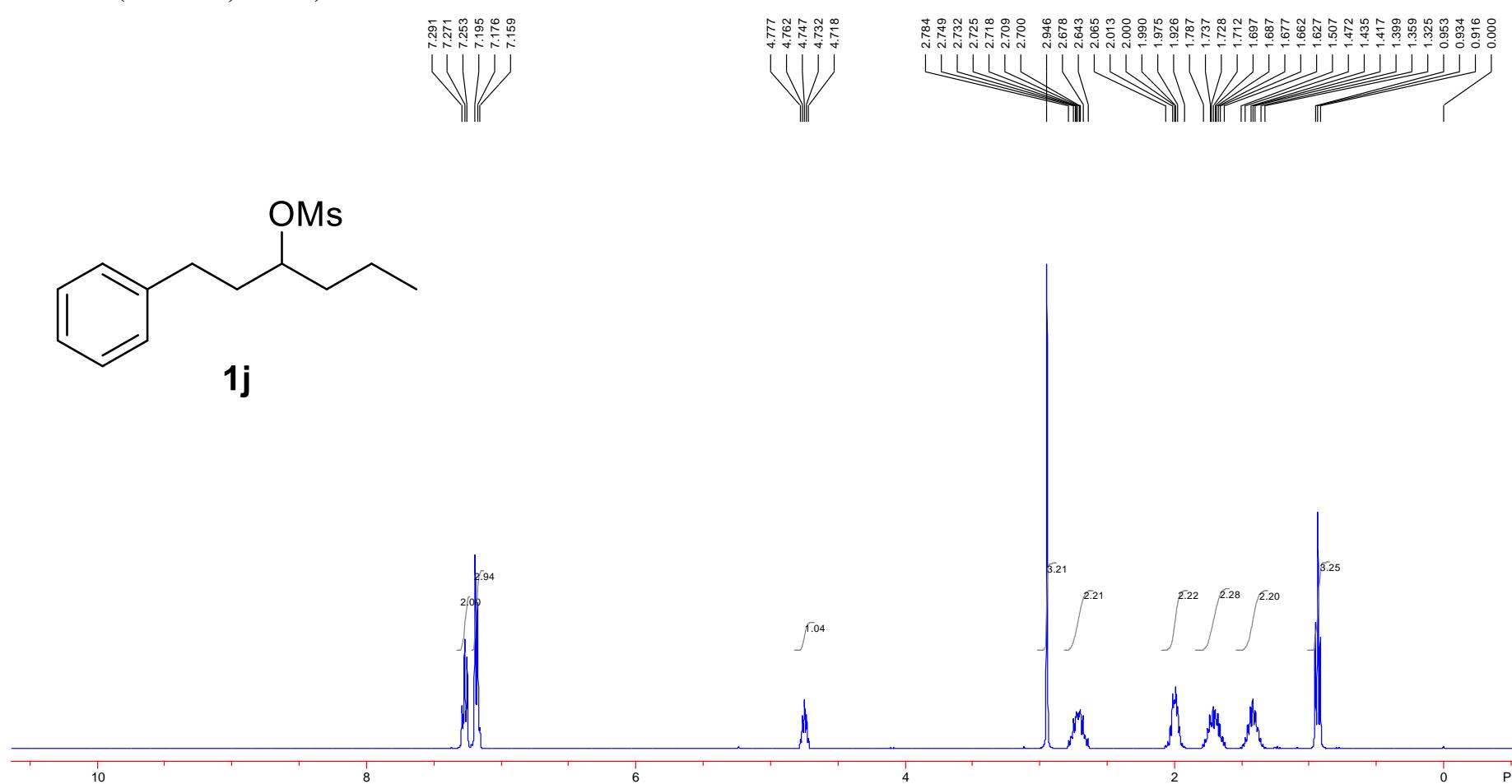
¹H NMR (400 MHz, CDCl₃)



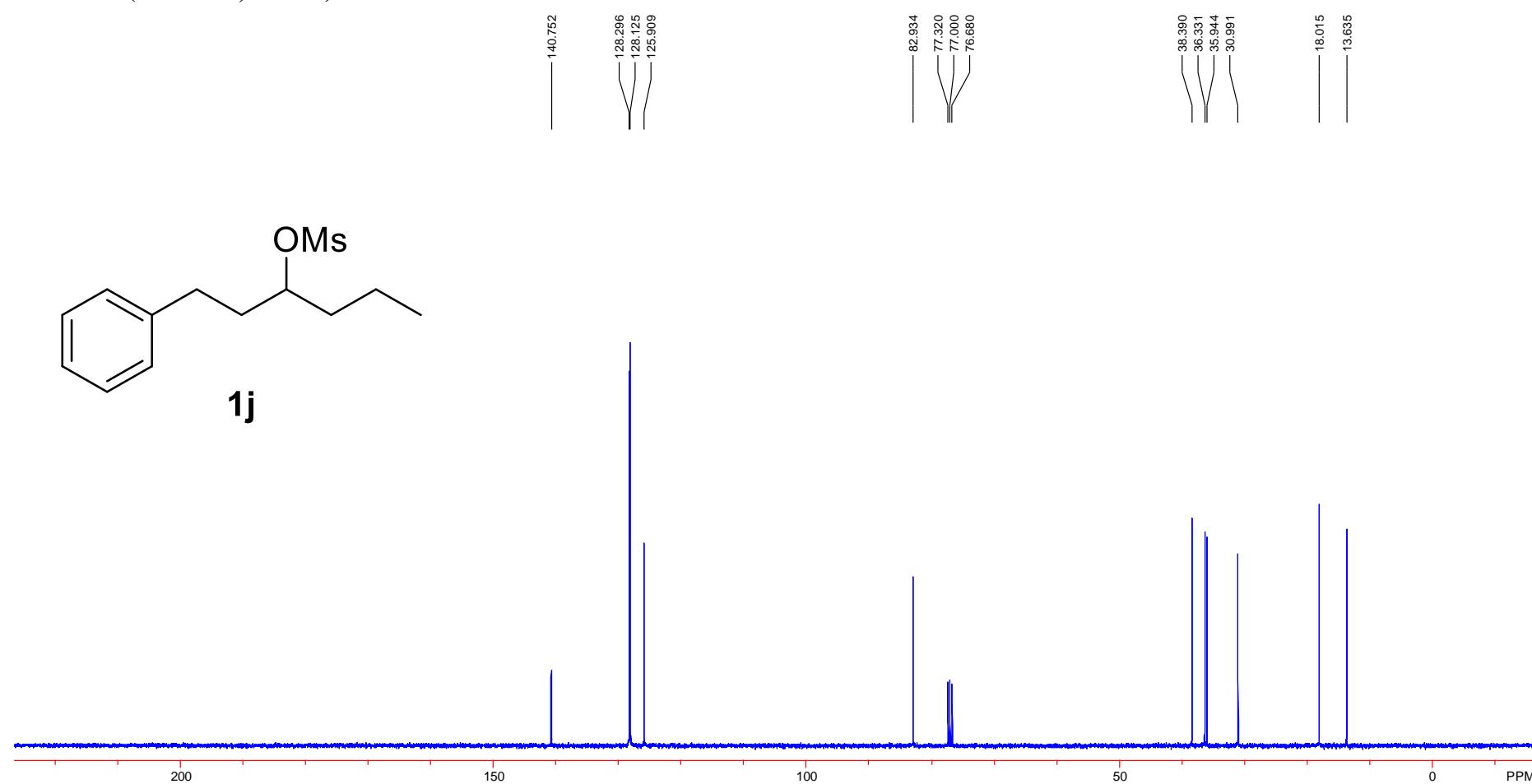
¹³C NMR (100 MHz, CDCl₃)



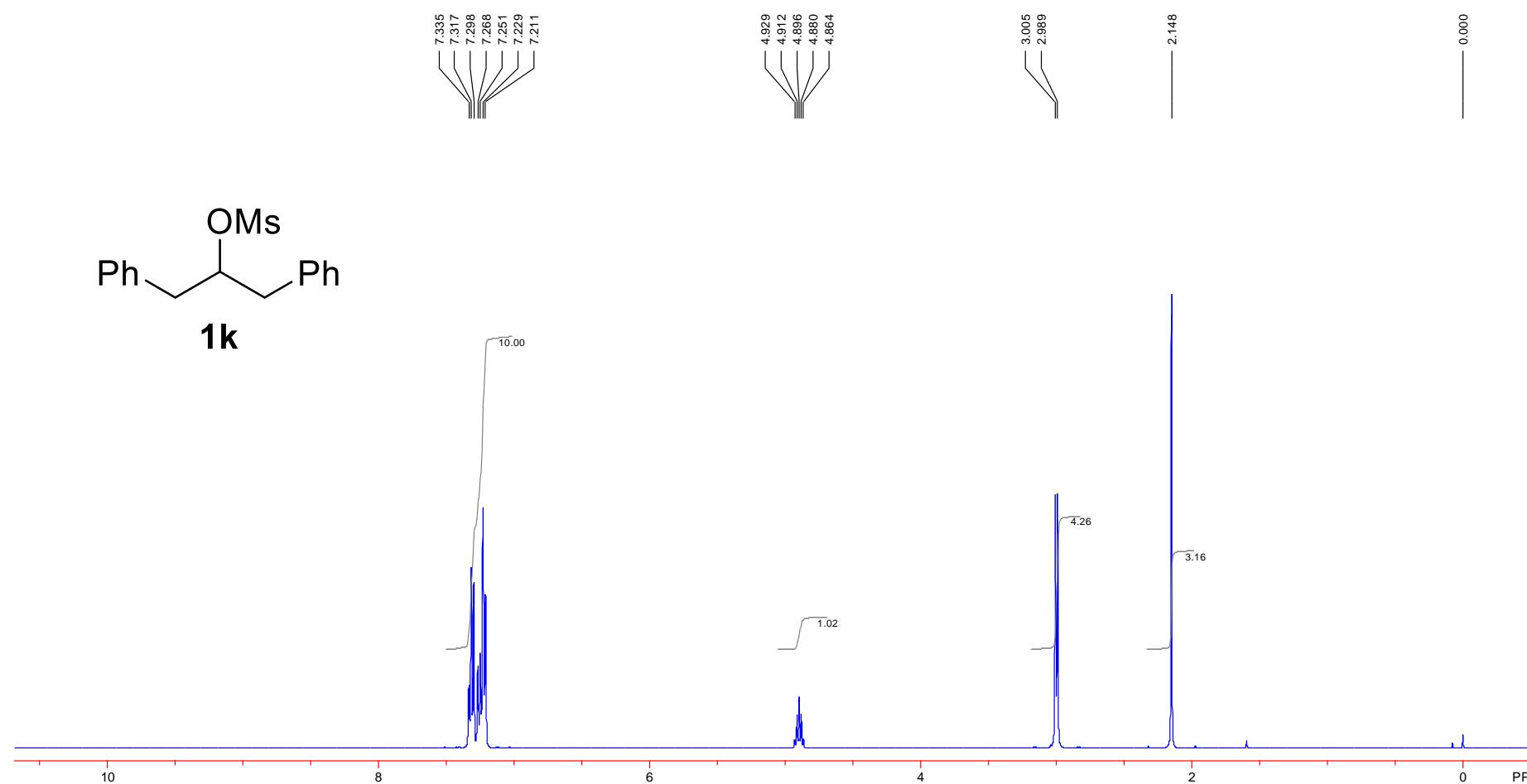
¹H NMR (400 MHz, CDCl₃)



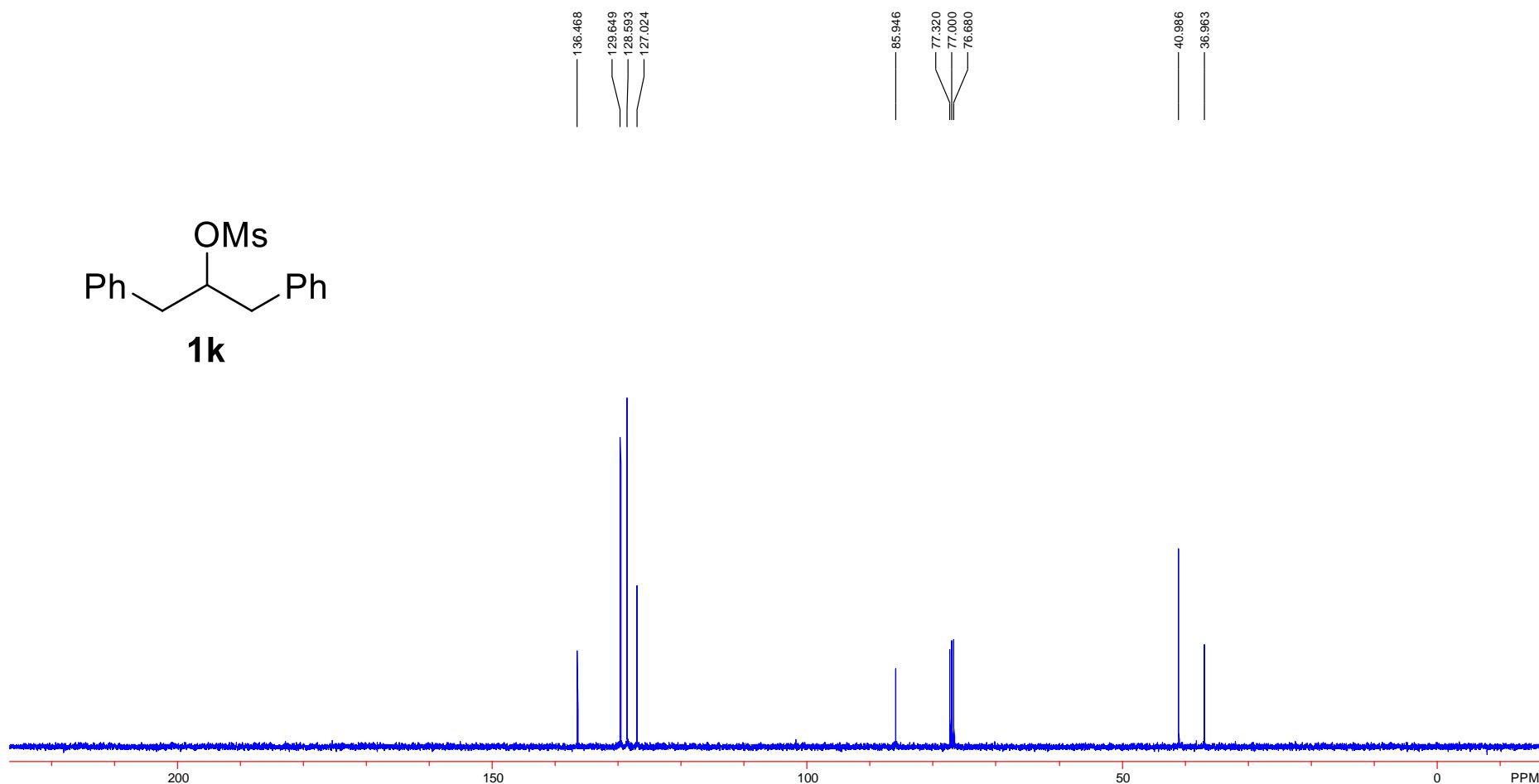
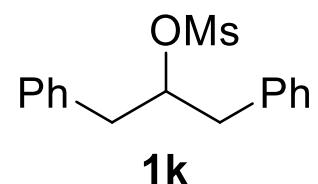
¹³C NMR (100 MHz, CDCl₃)



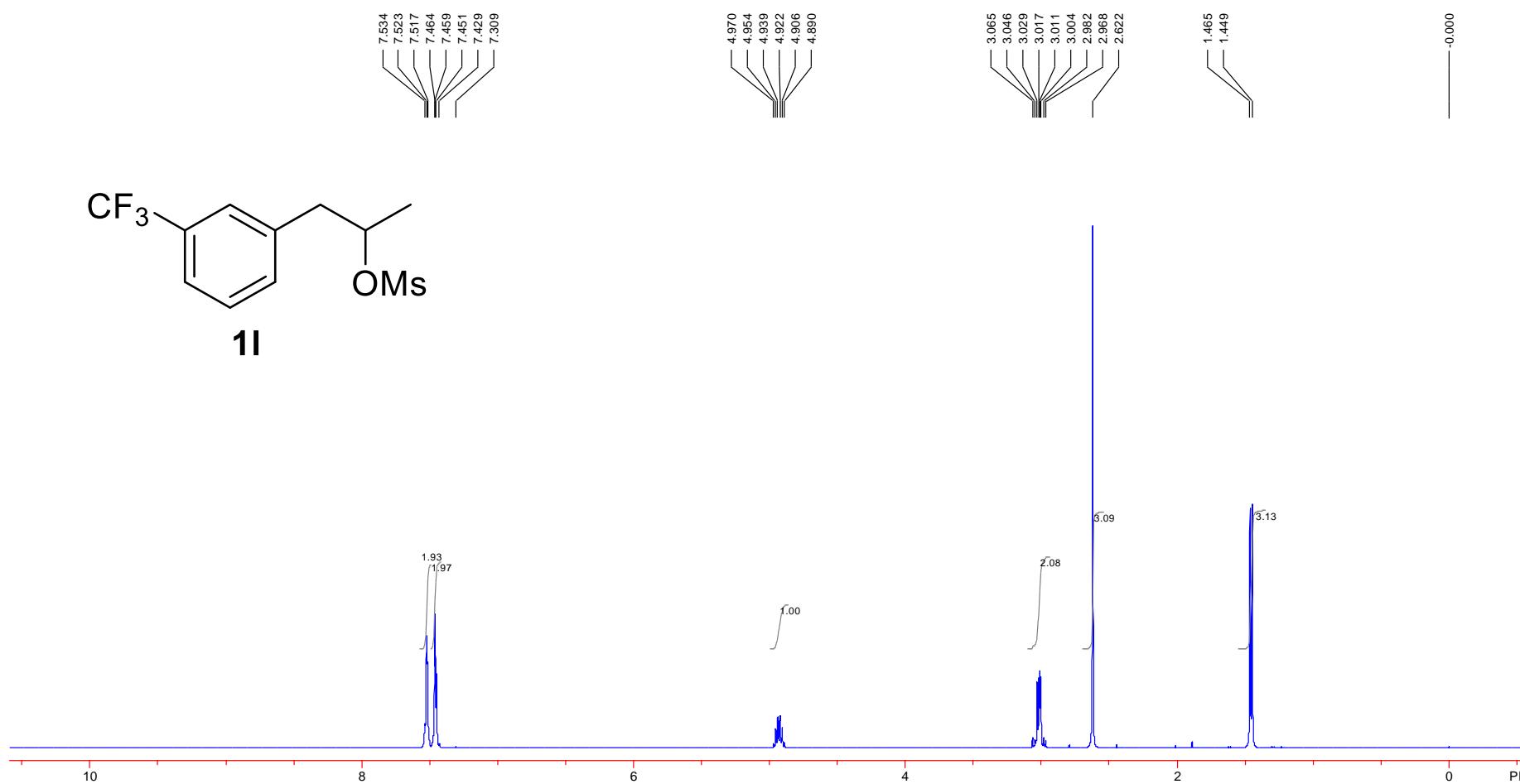
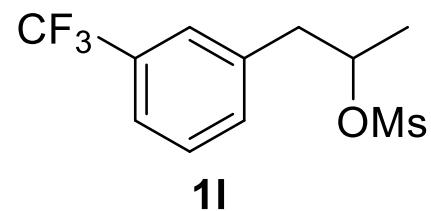
¹H NMR (400 MHz, CDCl₃)



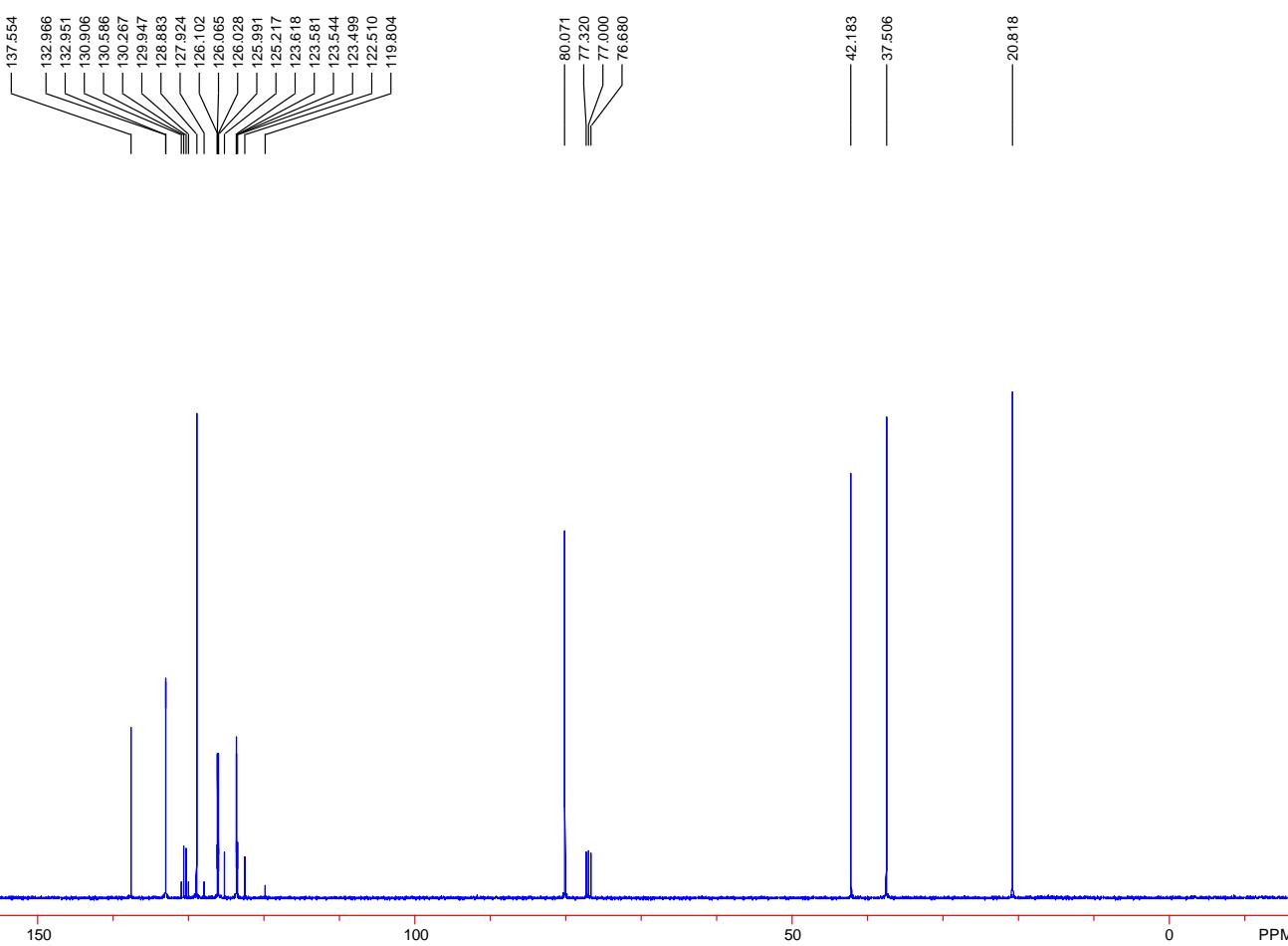
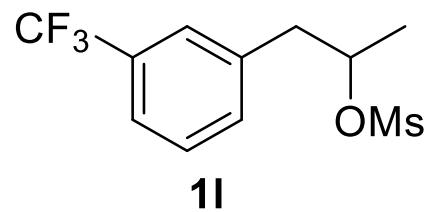
¹³C NMR (100 MHz, CDCl₃)



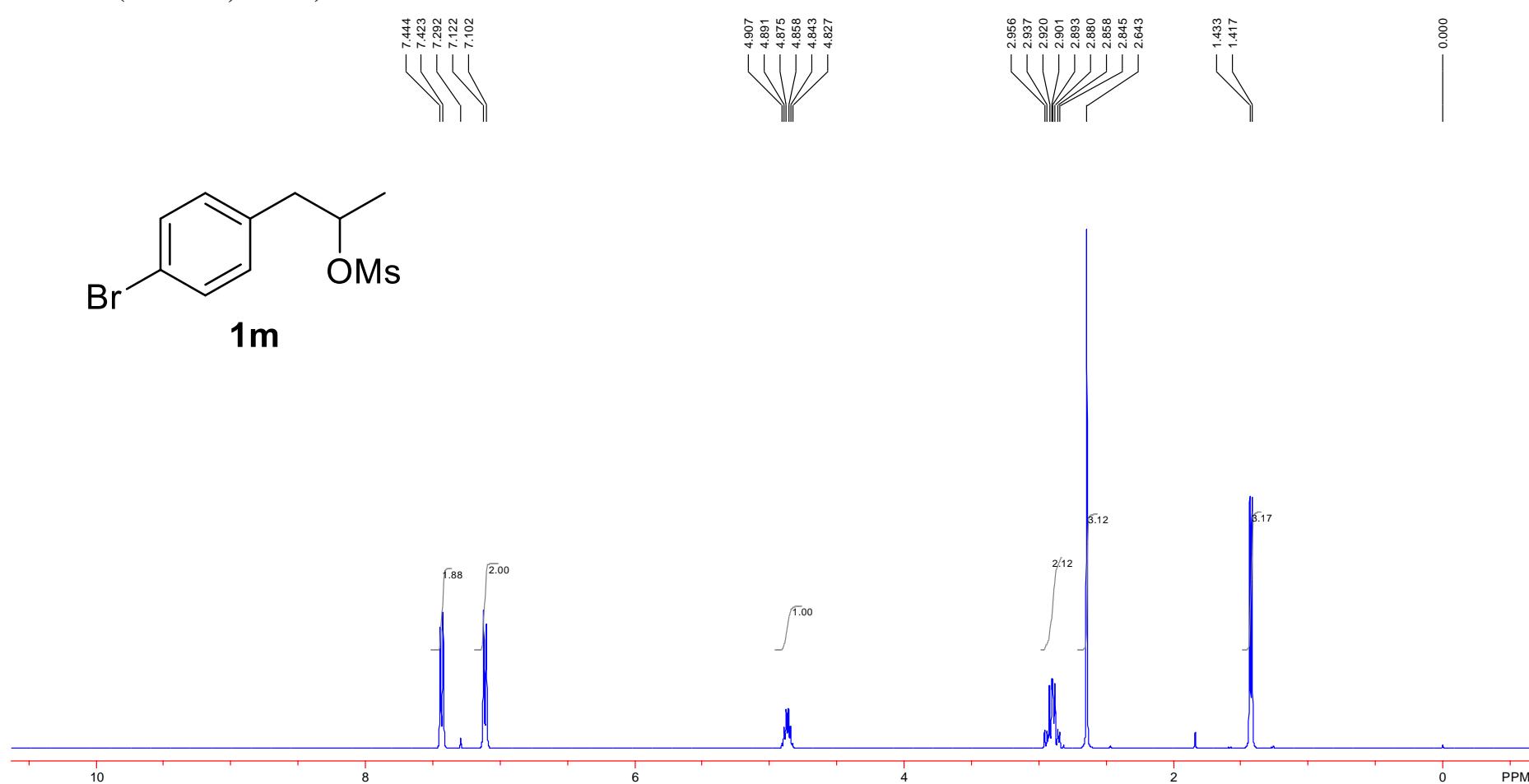
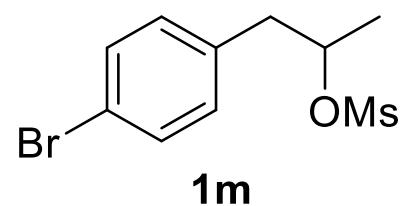
¹H NMR (400 MHz, CDCl₃)



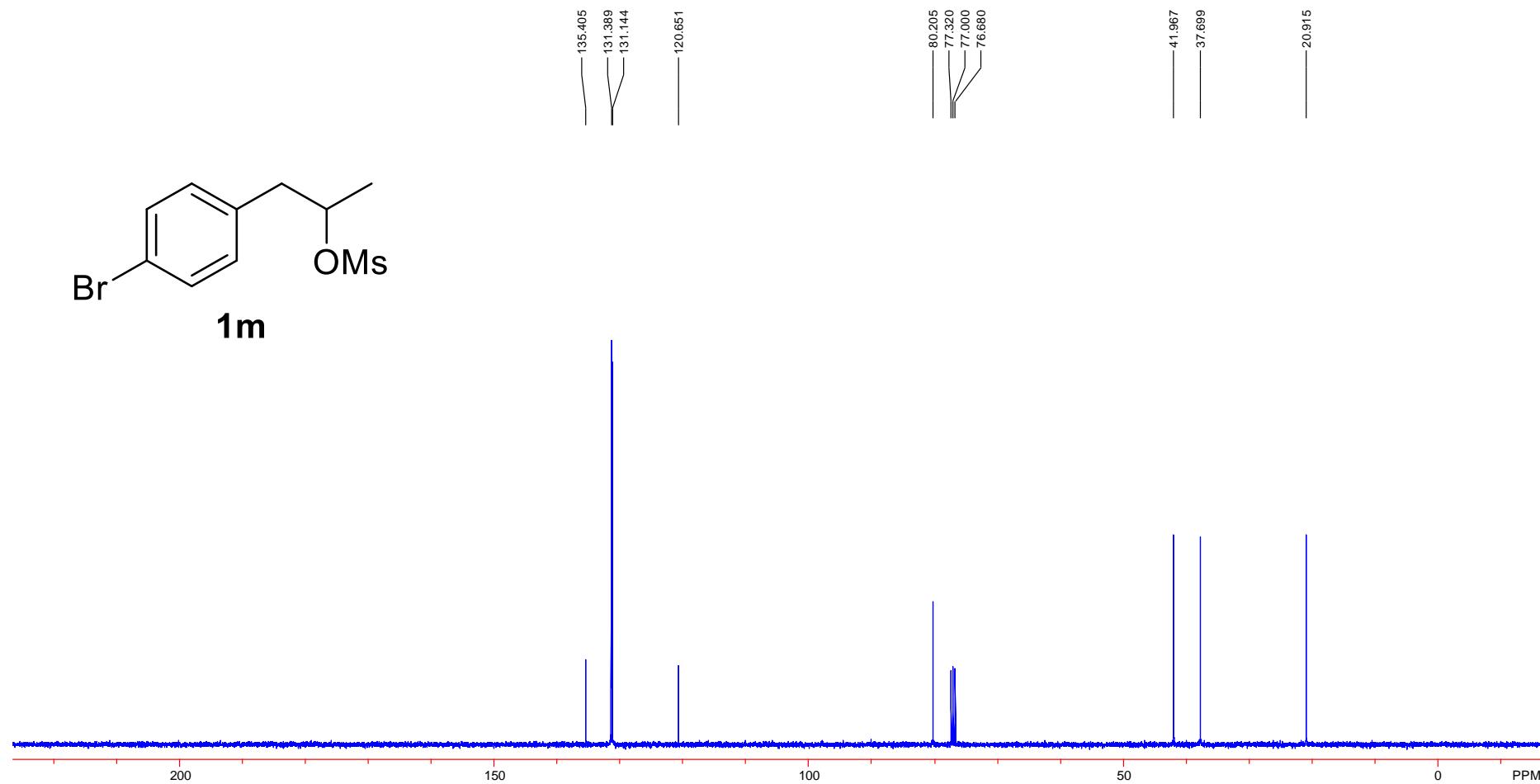
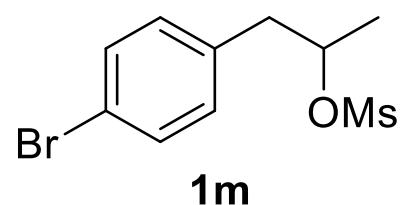
¹³C NMR (100 MHz, CDCl₃)



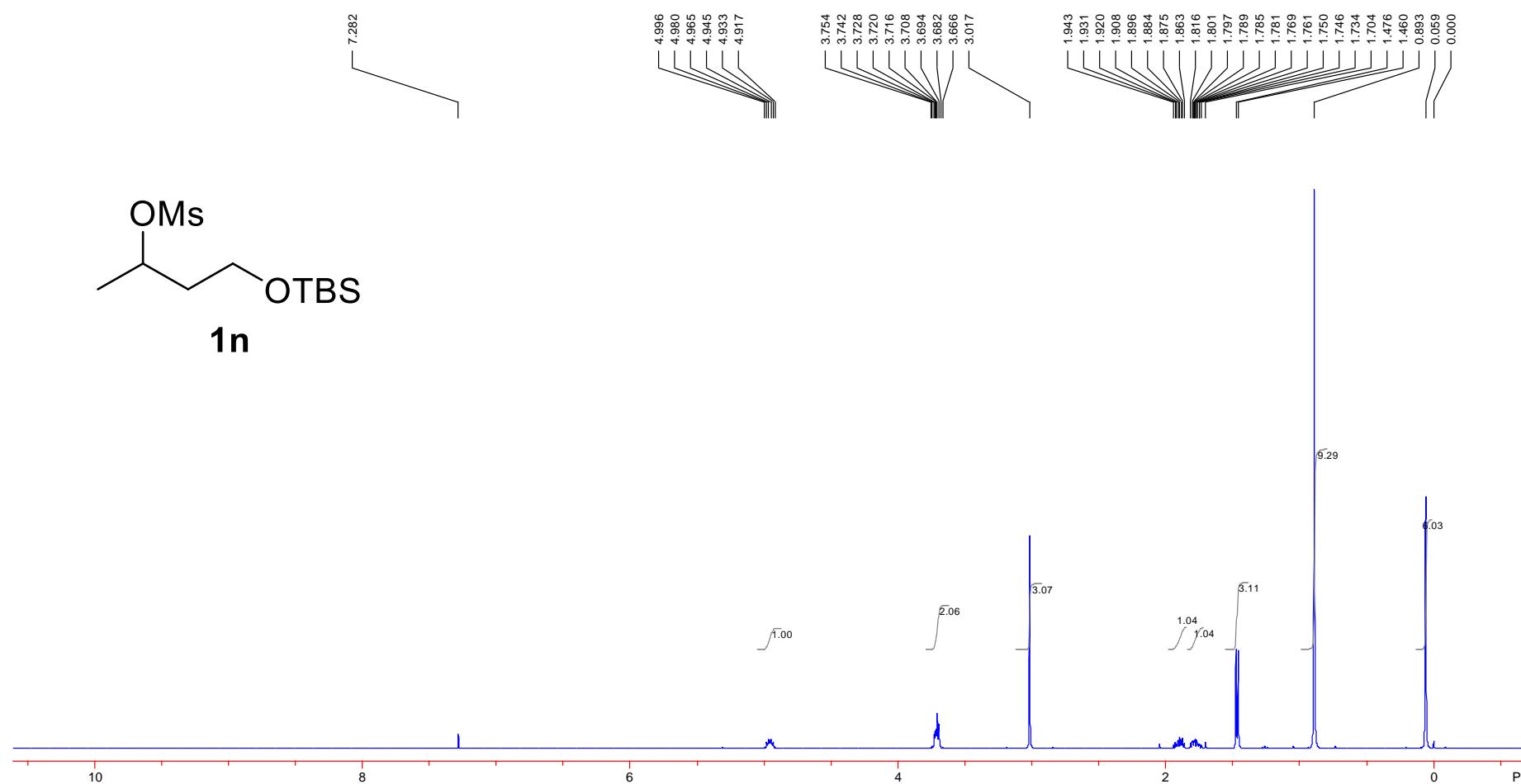
¹H NMR (400 MHz, CDCl₃)



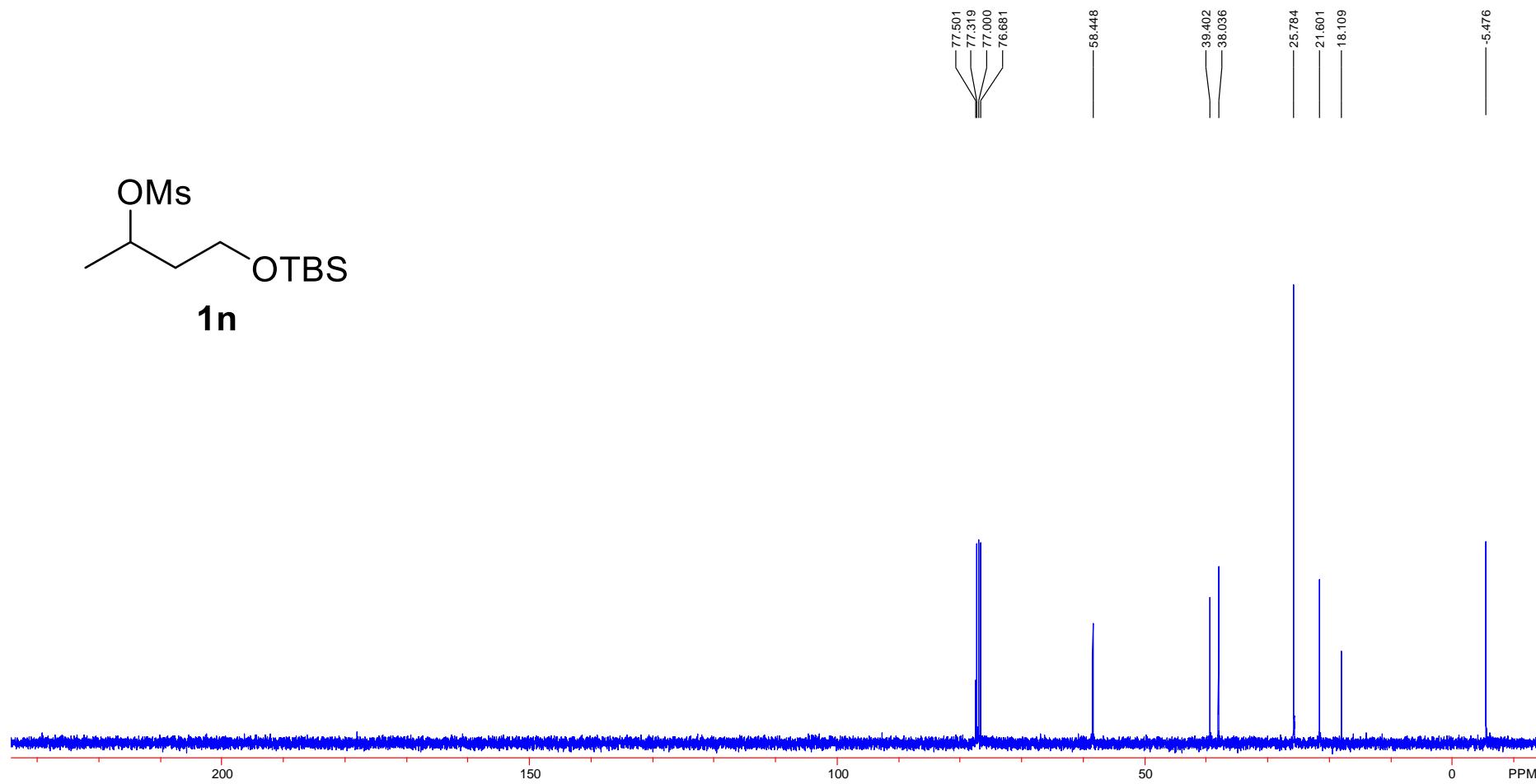
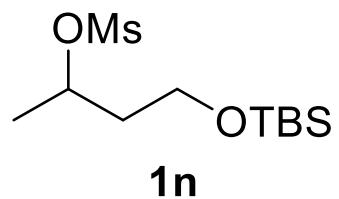
¹³C NMR (100 MHz, CDCl₃)



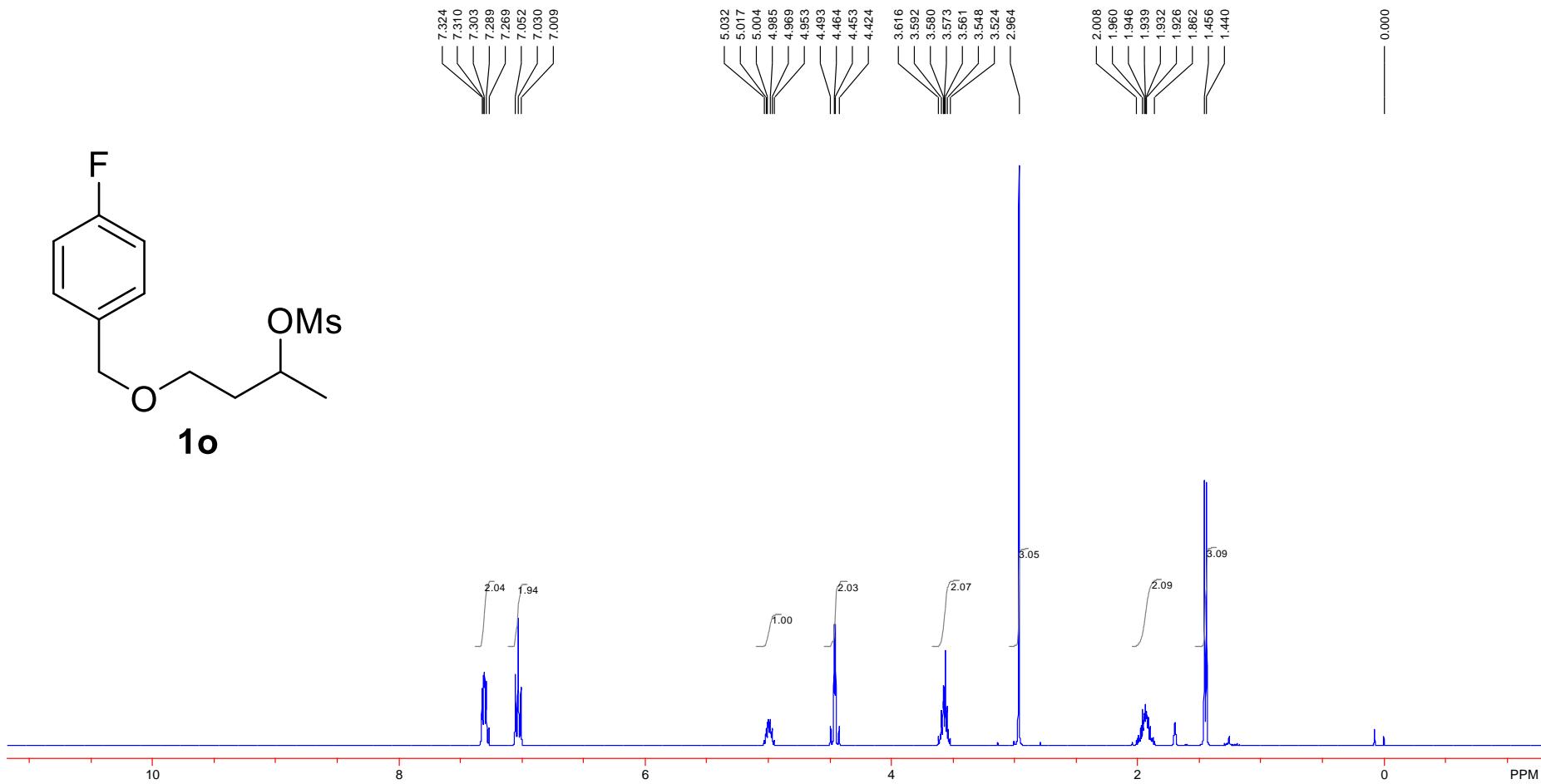
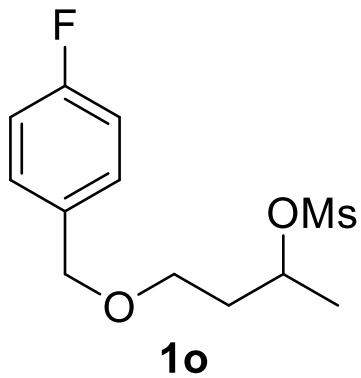
¹H NMR (400 MHz, CDCl₃)



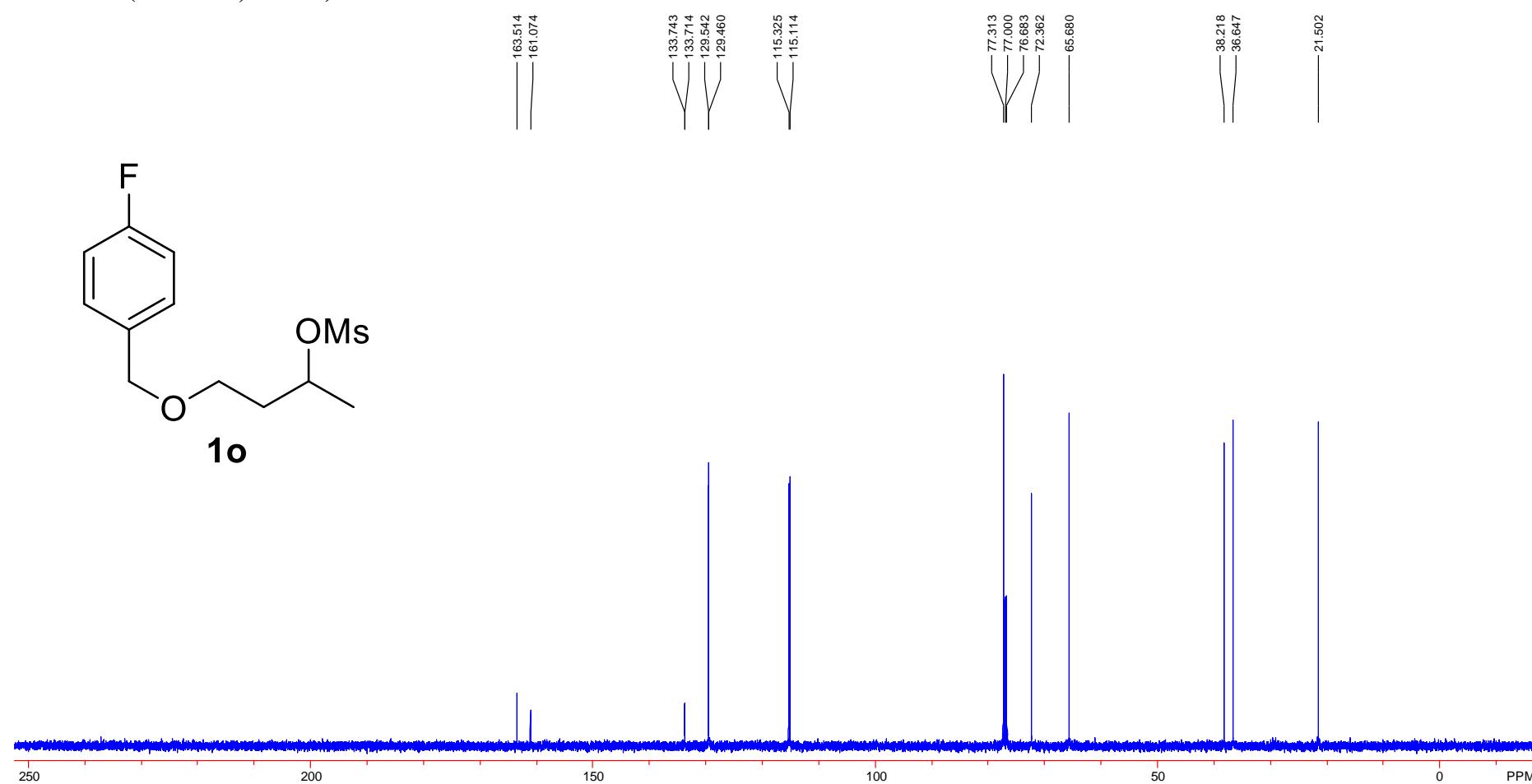
¹³C NMR (100 MHz, CDCl₃)



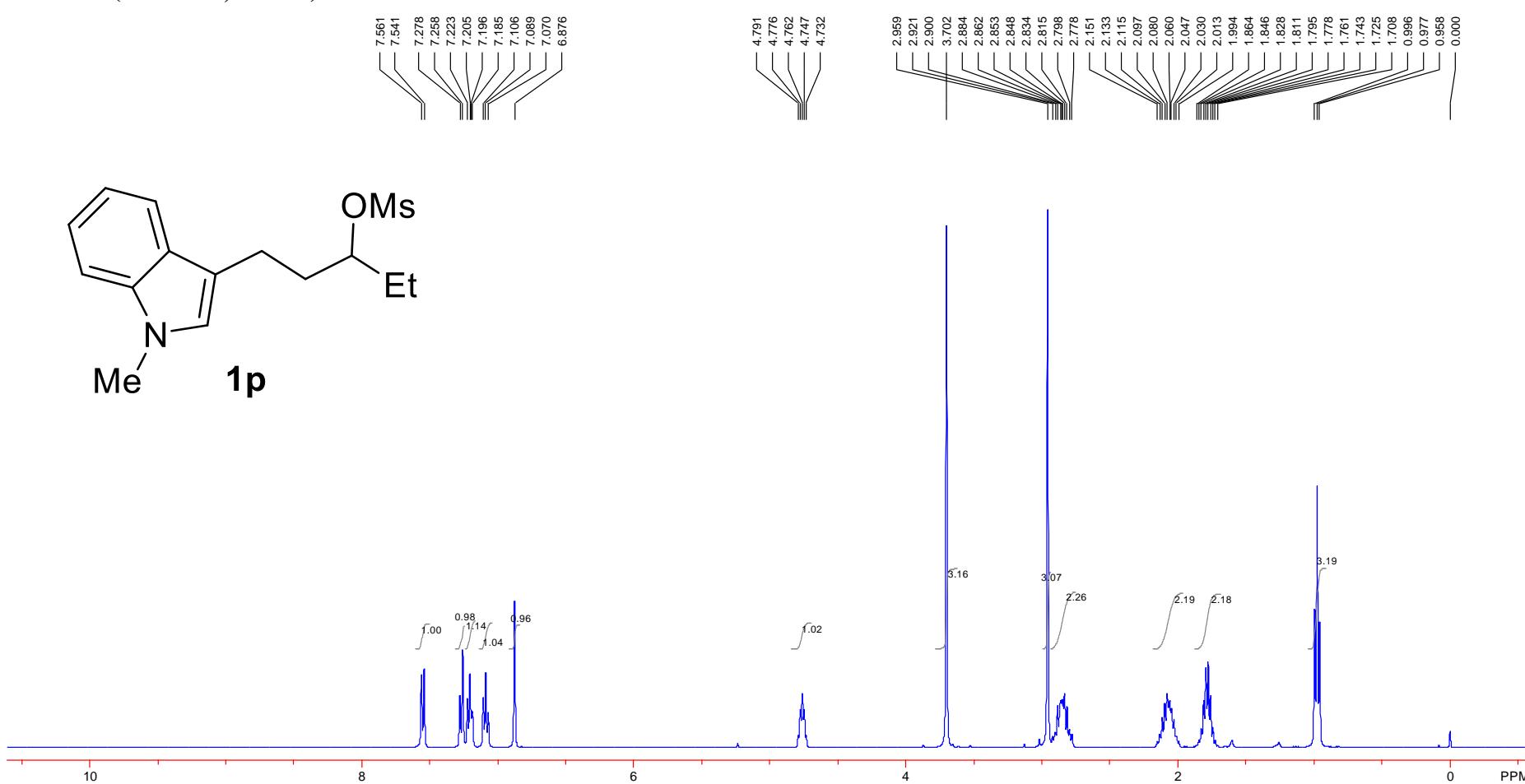
¹H NMR (400 MHz, CDCl₃)



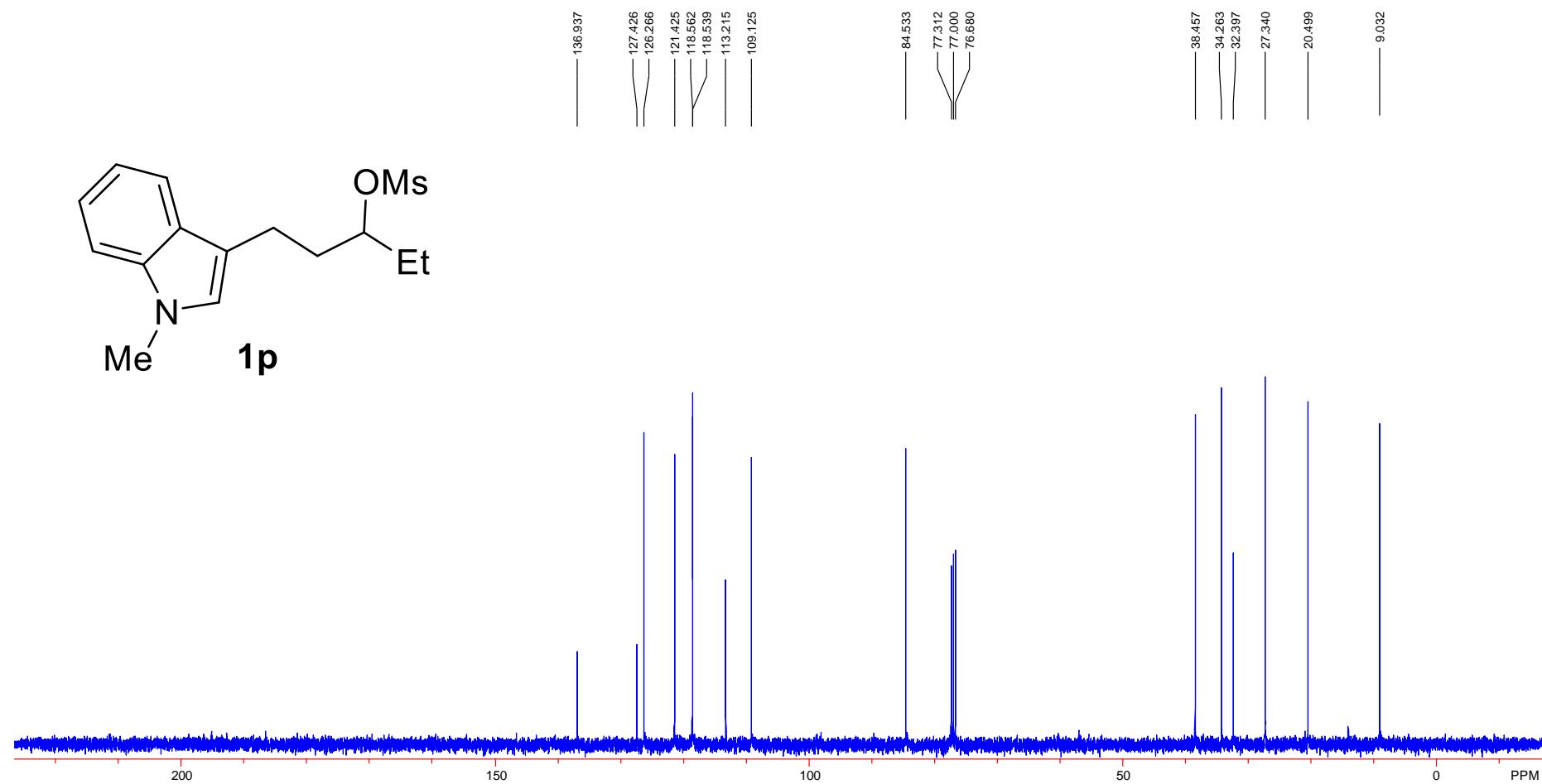
¹³C NMR (100 MHz, CDCl₃)



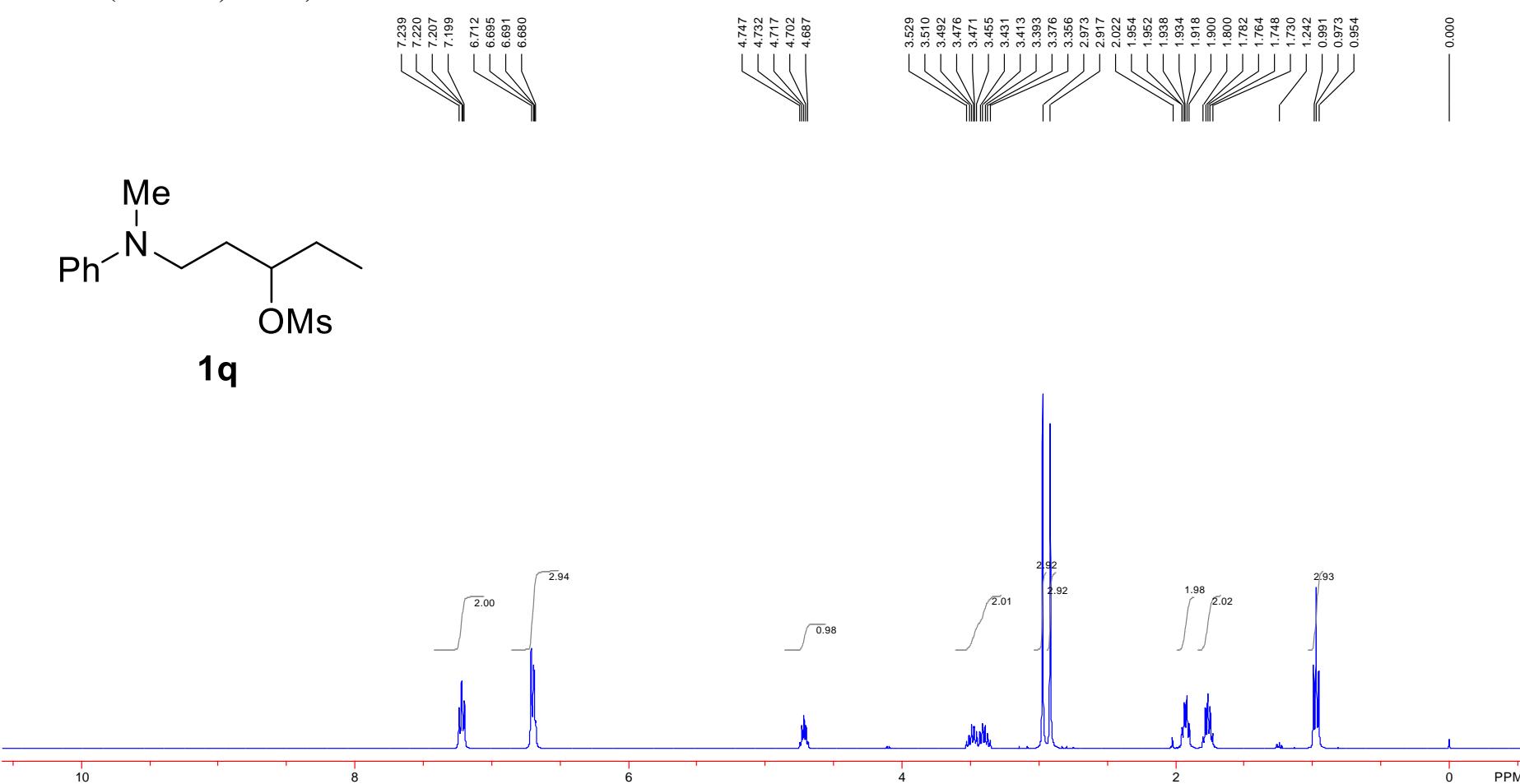
¹H NMR (400 MHz, CDCl₃)



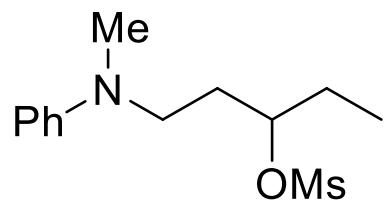
¹³C NMR (100 MHz, CDCl₃)



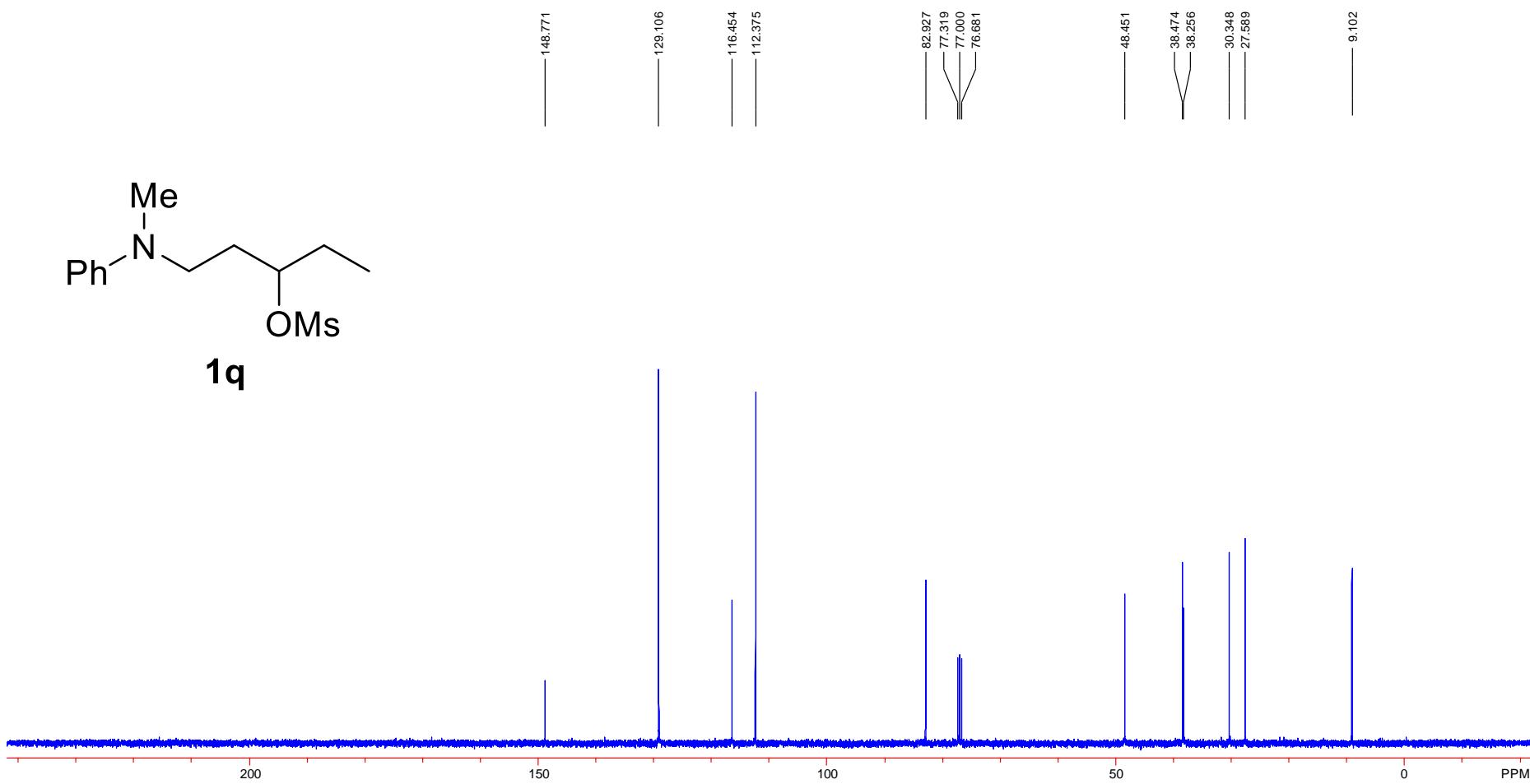
¹H NMR (400 MHz, CDCl₃)



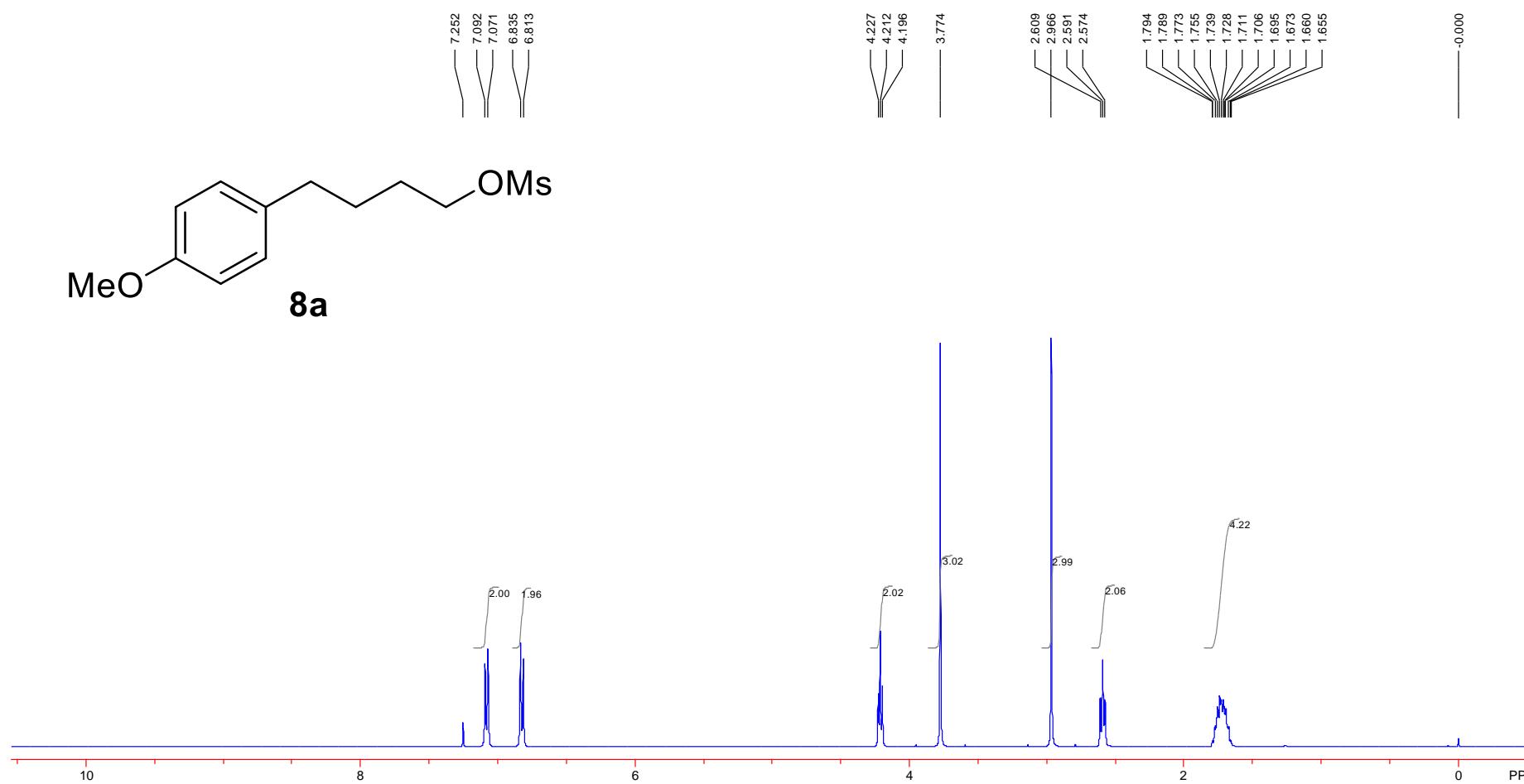
¹³C NMR (100 MHz, CDCl₃)



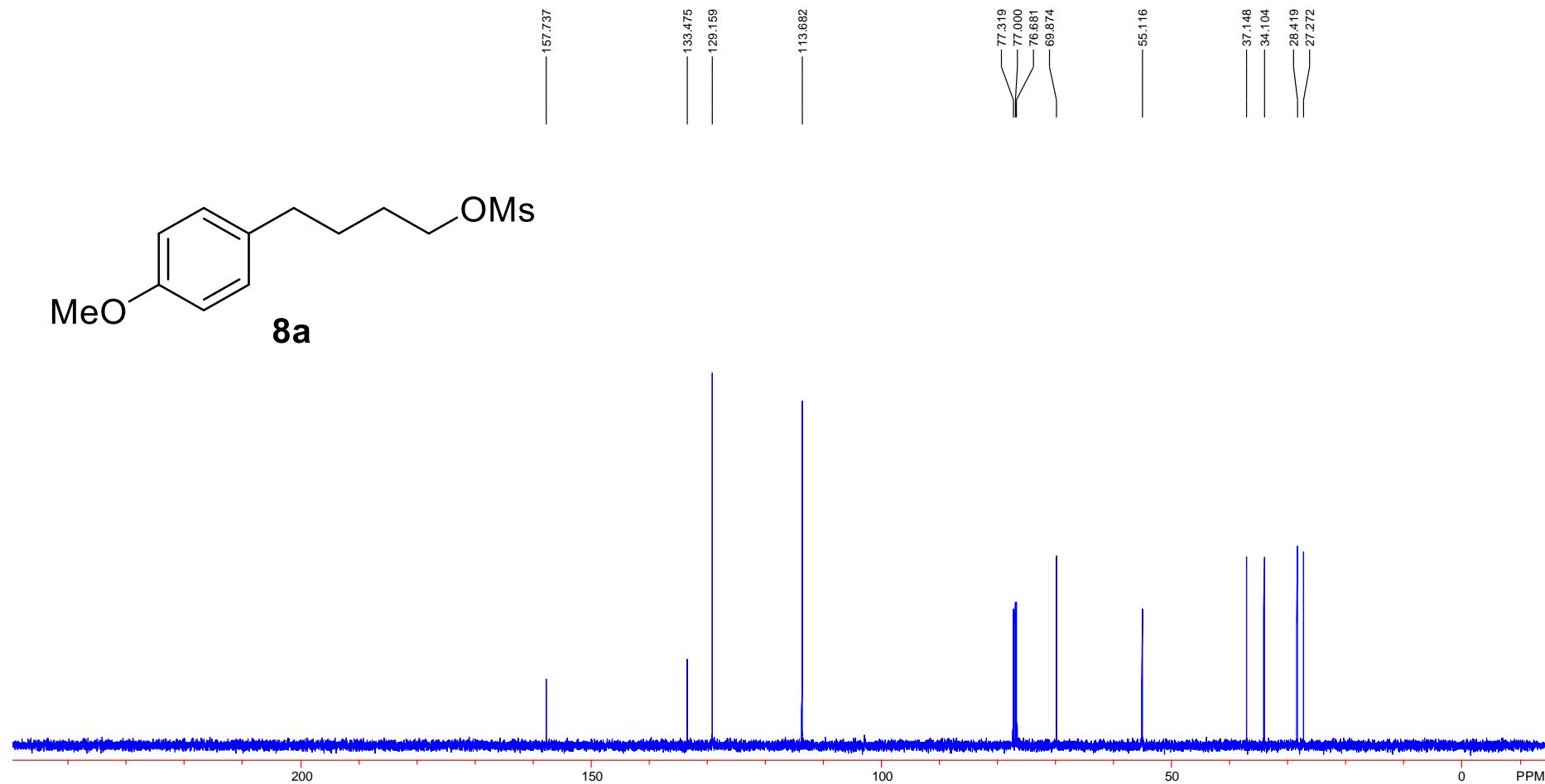
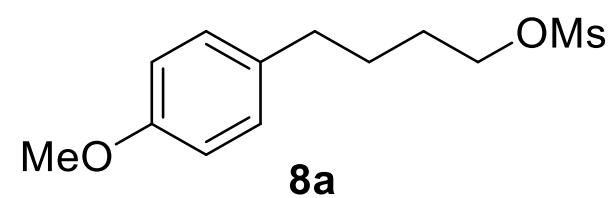
1q



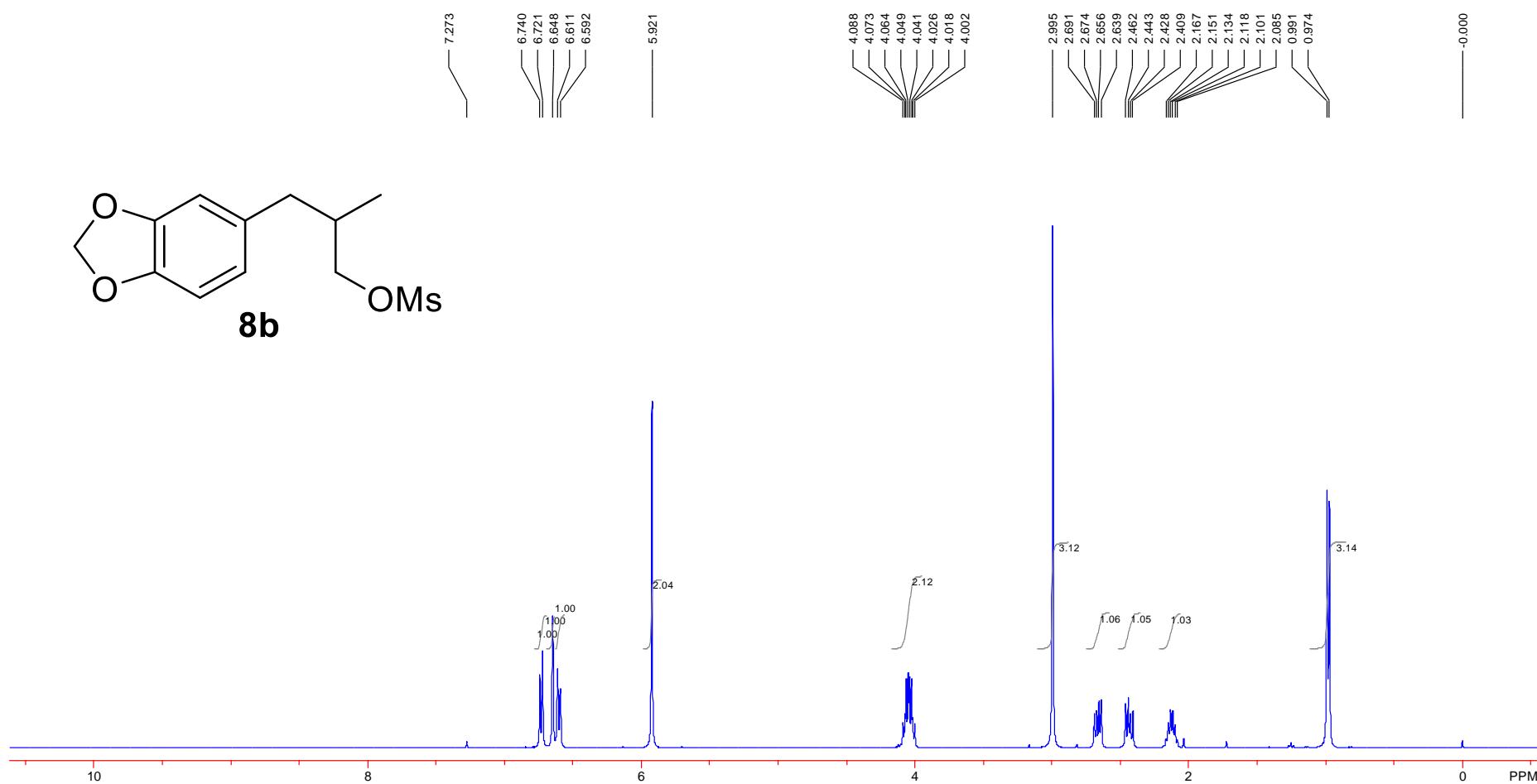
¹H NMR (400 MHz, CDCl₃)



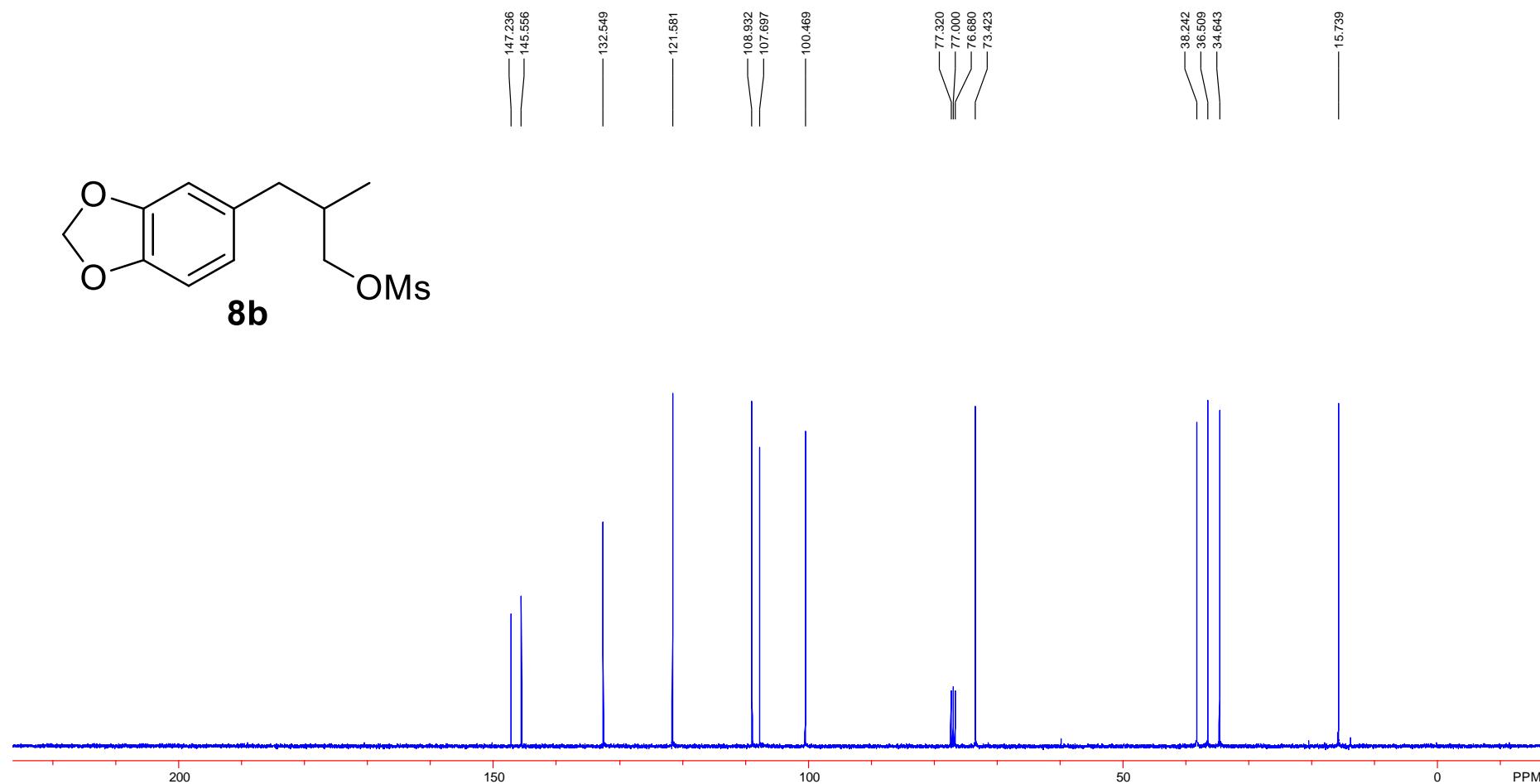
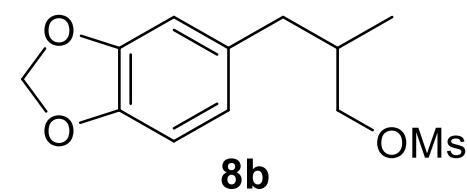
¹³C NMR (100 MHz, CDCl₃)



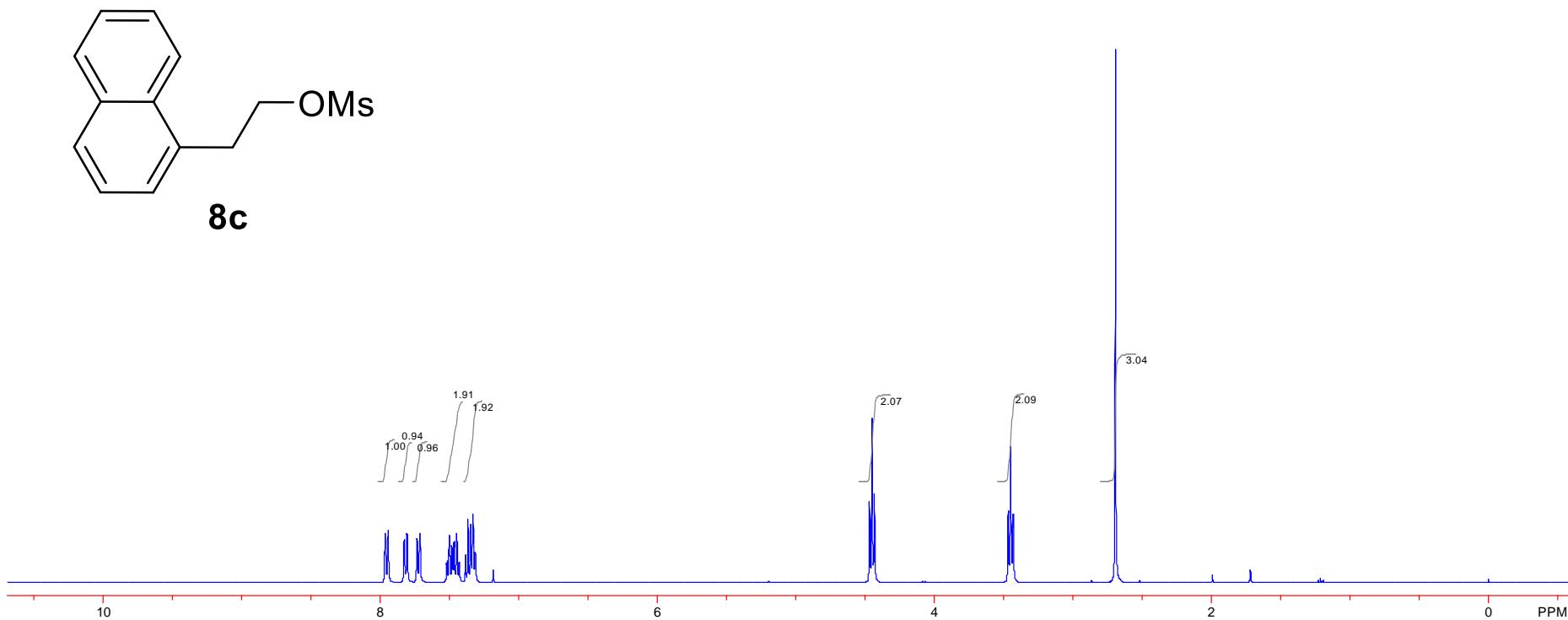
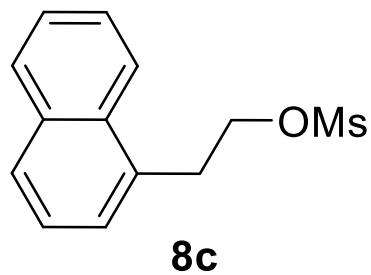
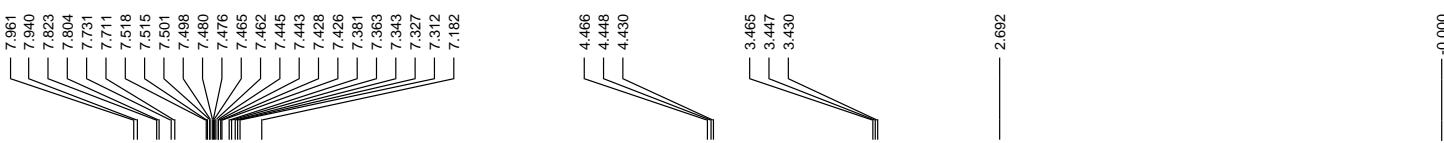
¹H NMR (400 MHz, CDCl₃)



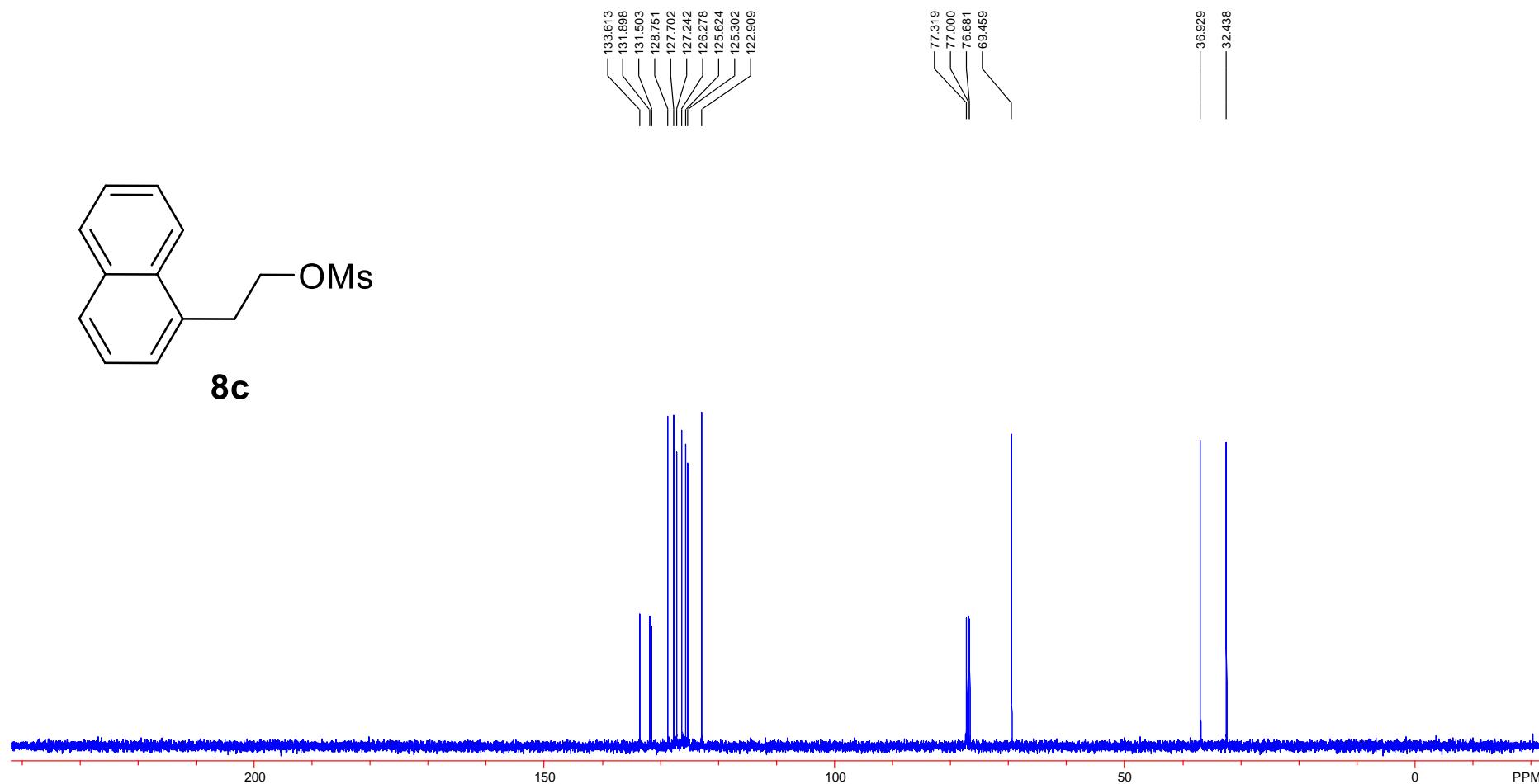
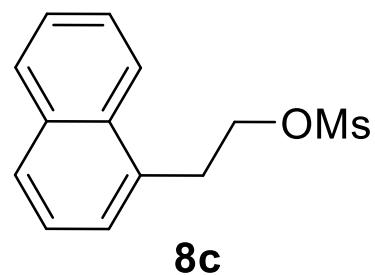
¹³C NMR (100 MHz, CDCl₃)



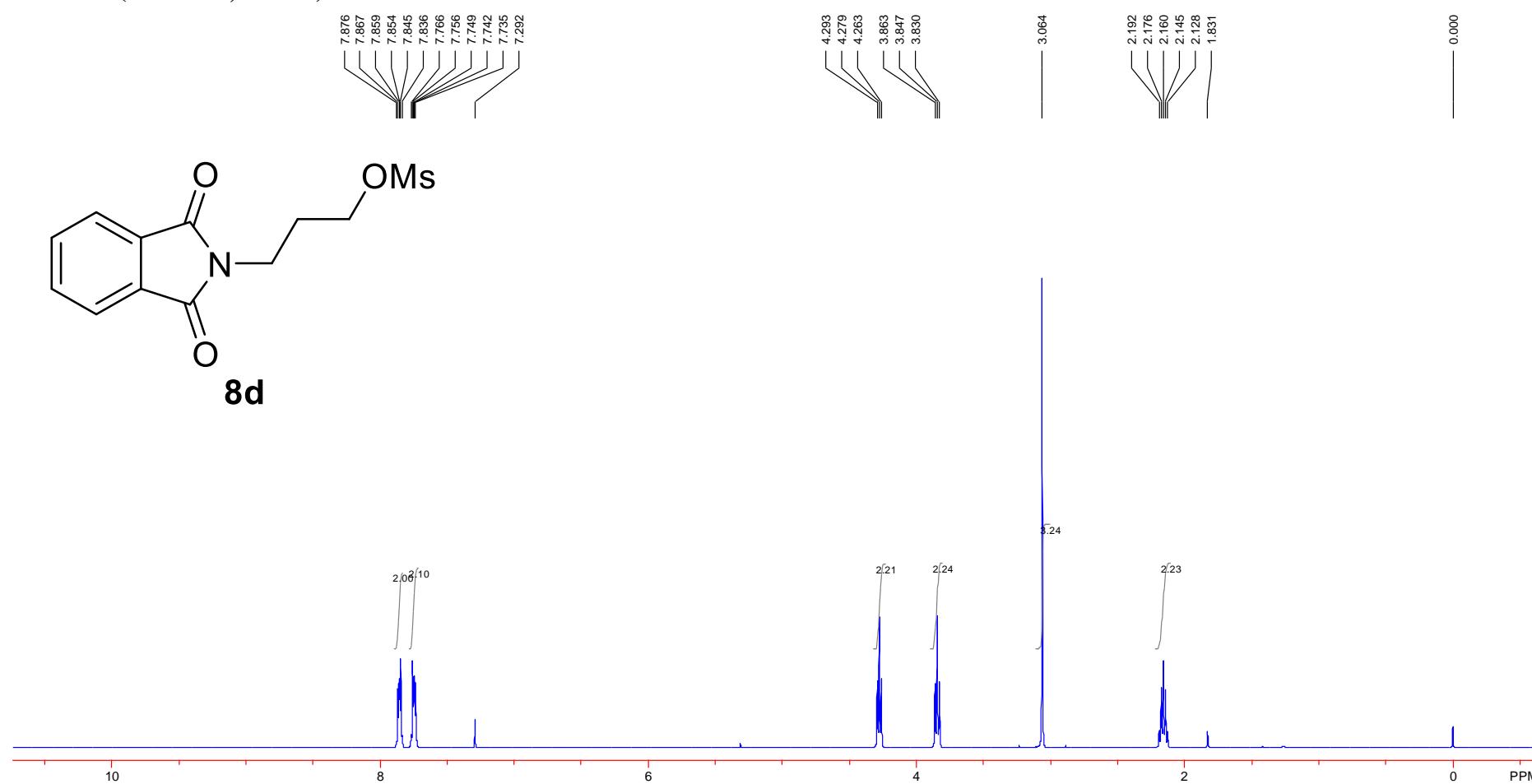
¹H NMR (400 MHz, CDCl₃)



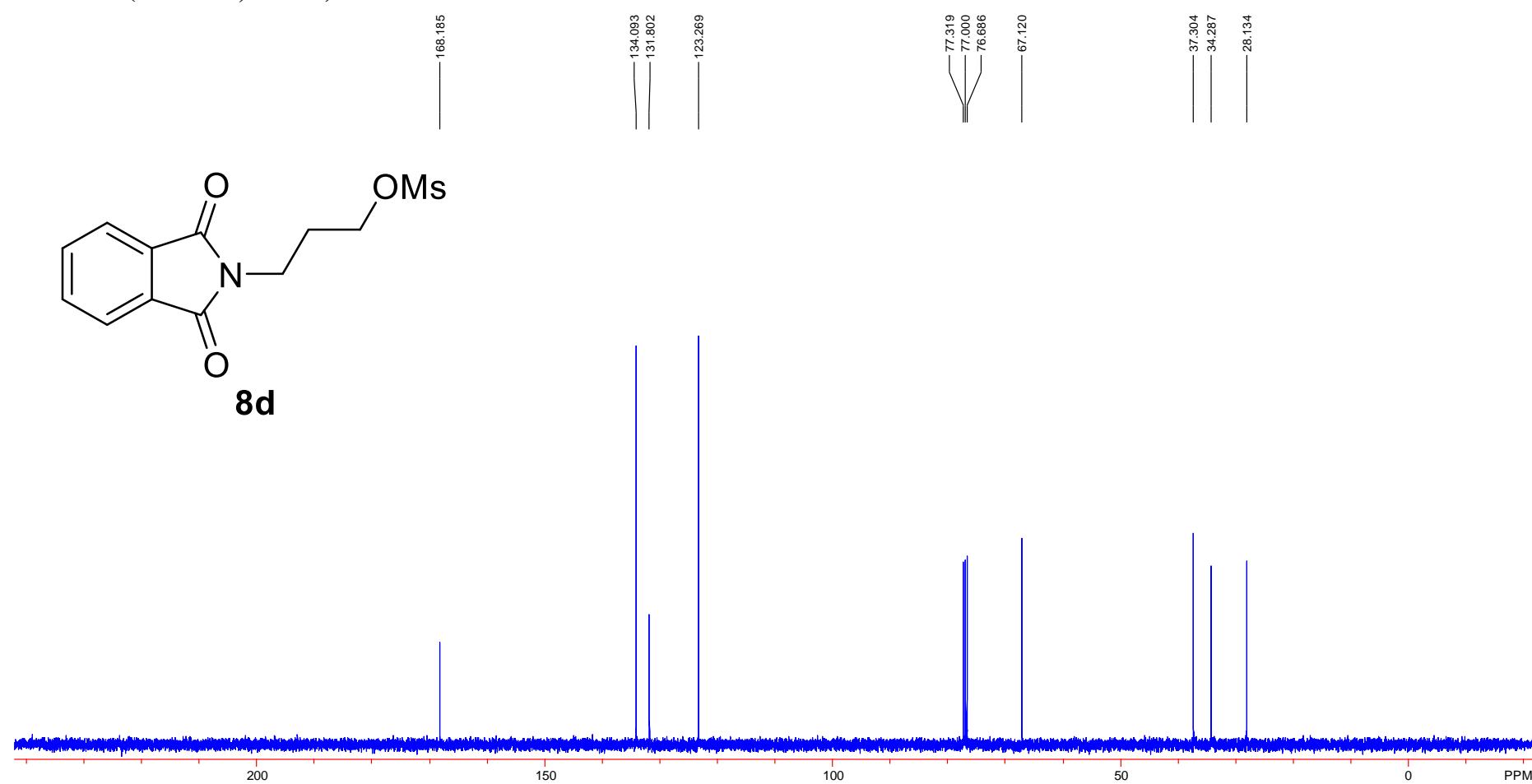
¹³C NMR (100 MHz, CDCl₃)



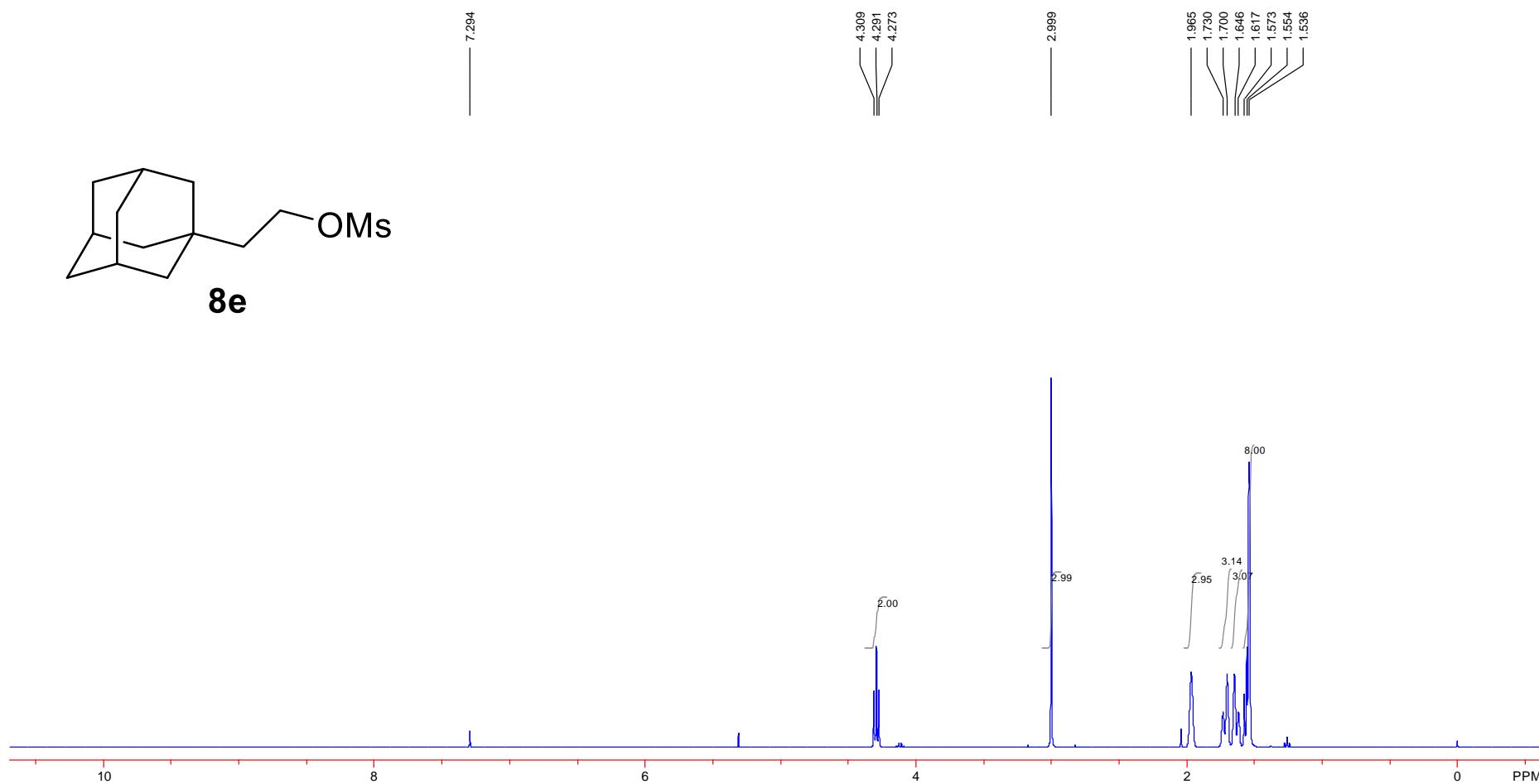
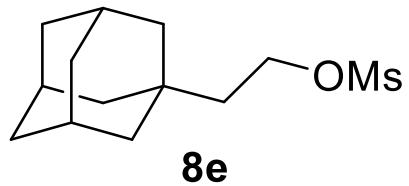
¹H NMR (400 MHz, CDCl₃)



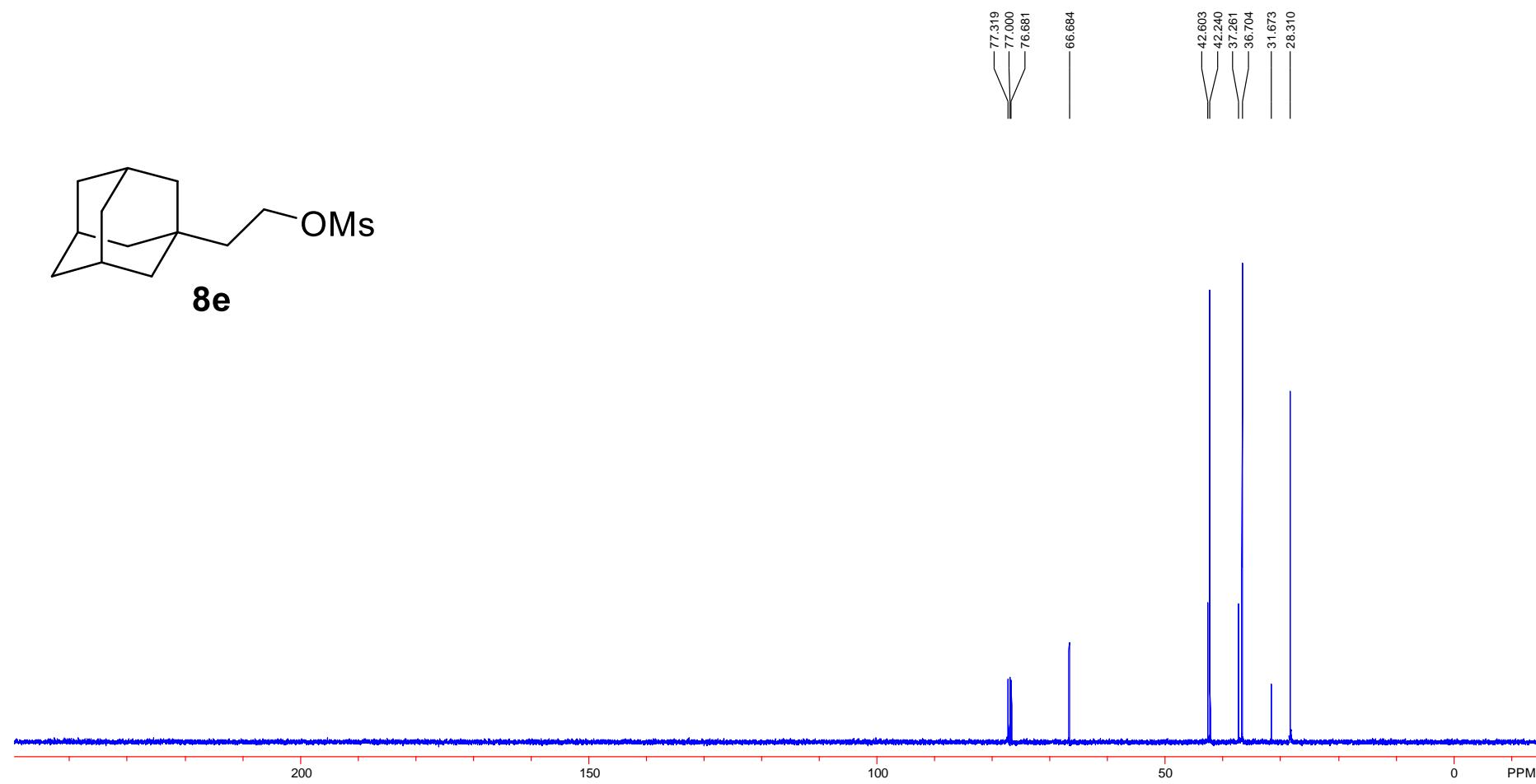
¹³C NMR (100 MHz, CDCl₃)



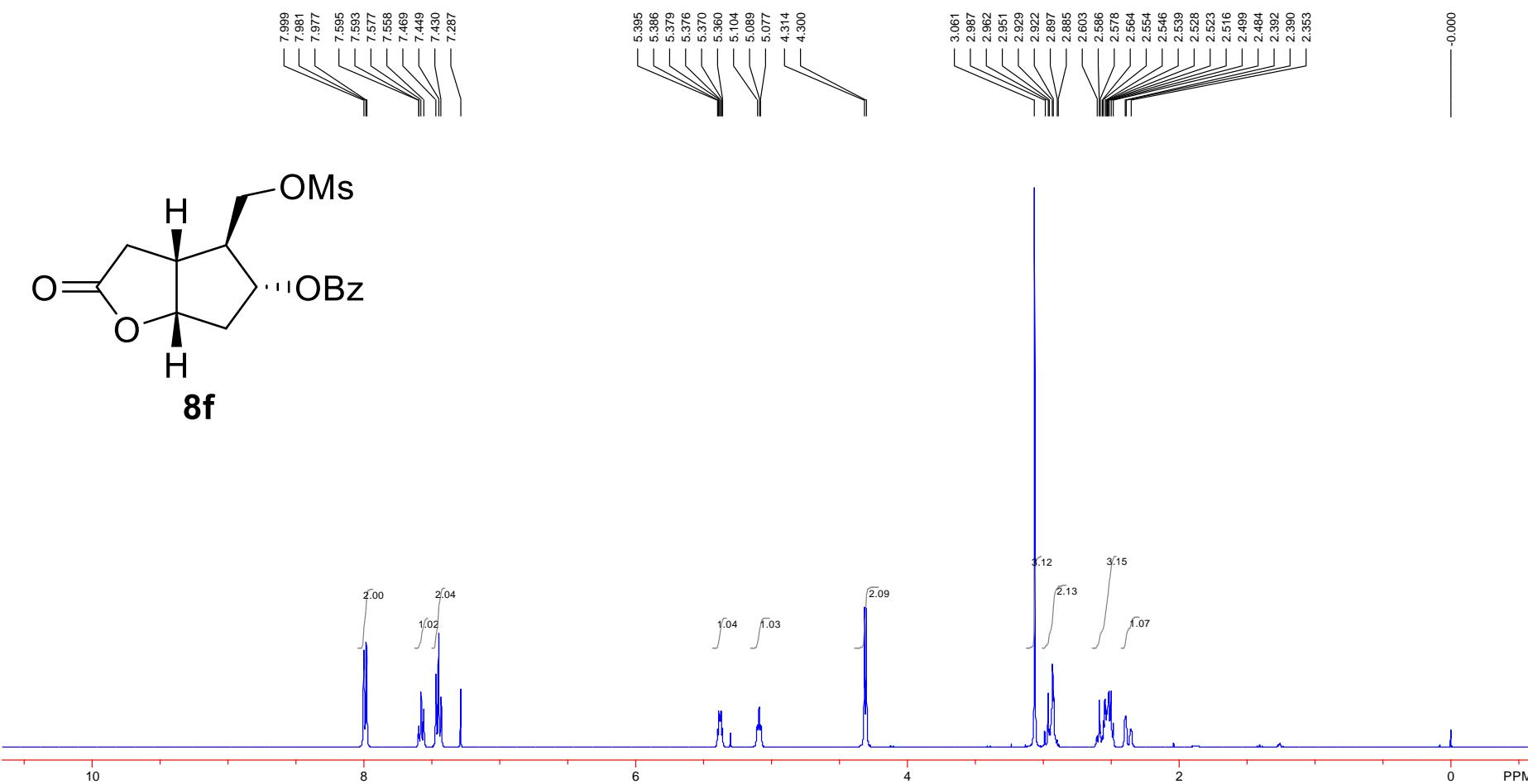
¹H NMR (400 MHz, CDCl₃)



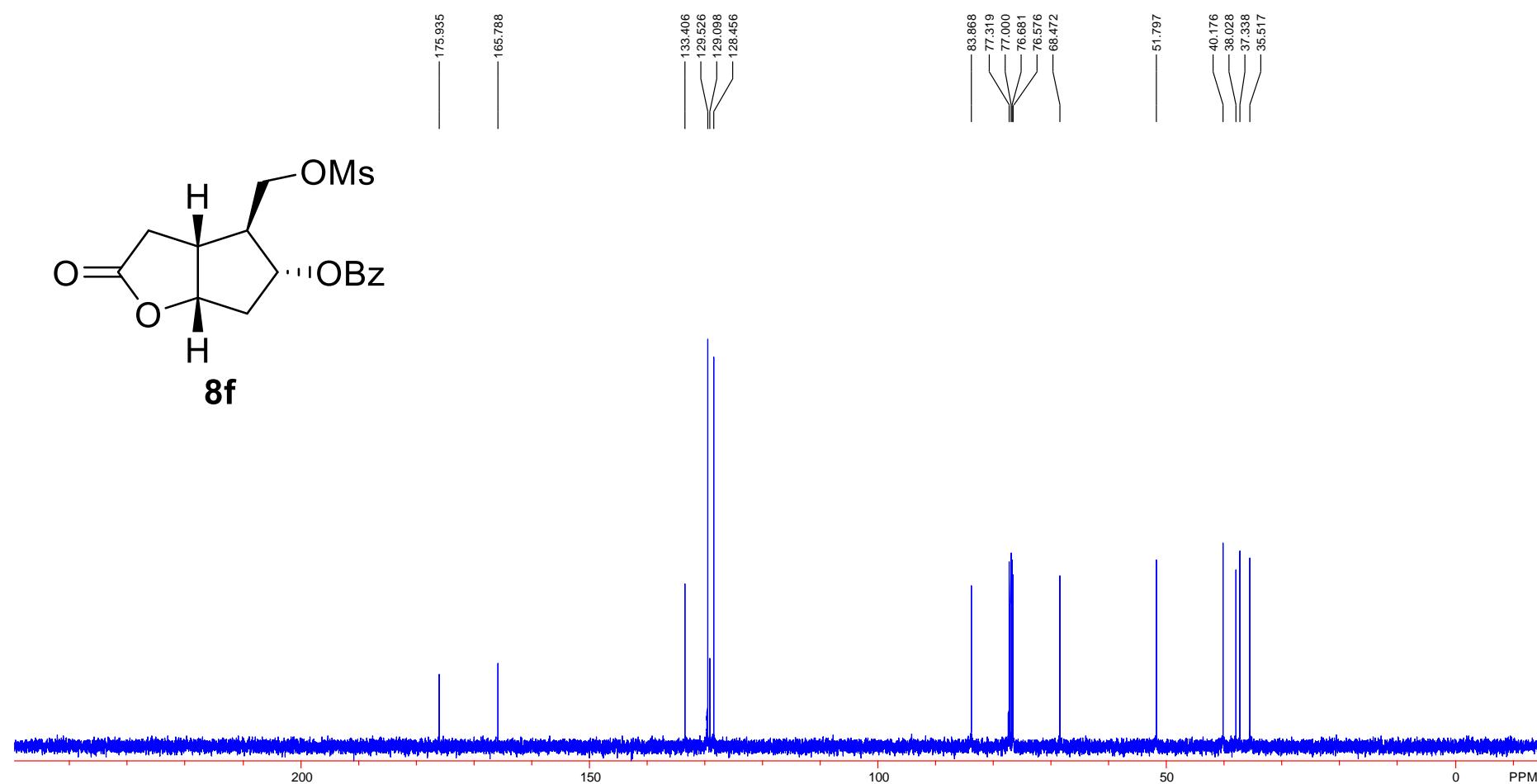
¹³C NMR (100 MHz, CDCl₃)



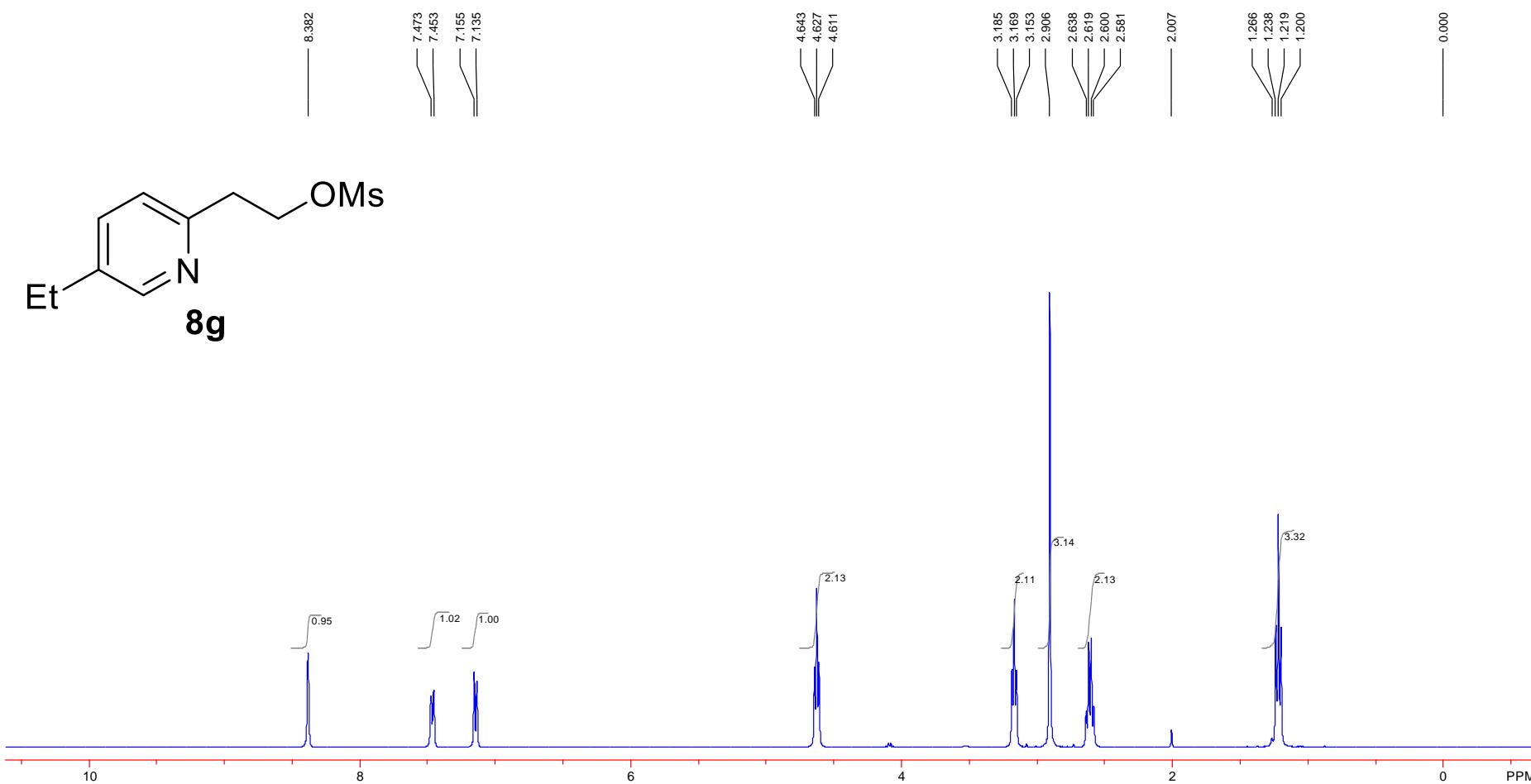
¹H NMR (400 MHz, CDCl₃)



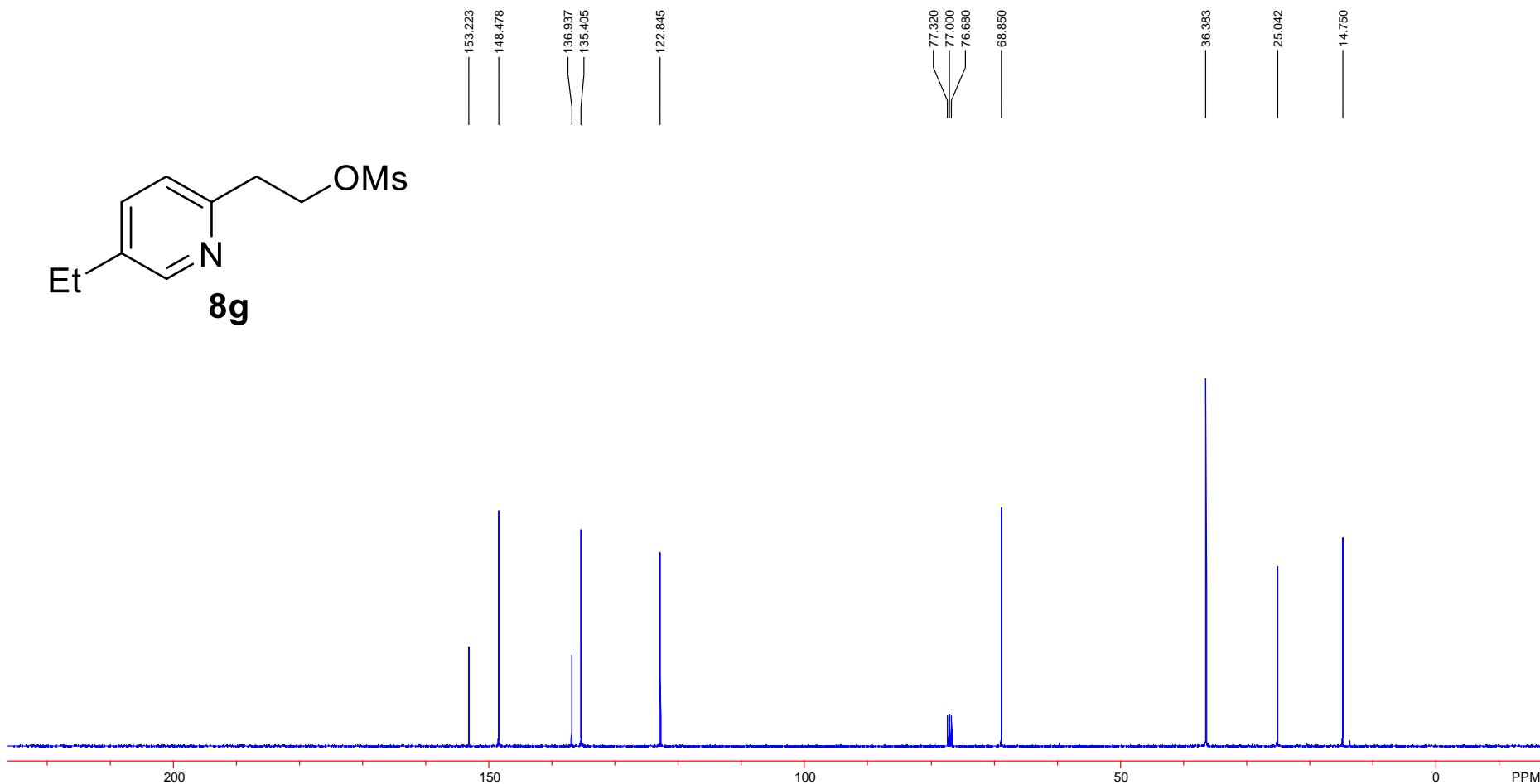
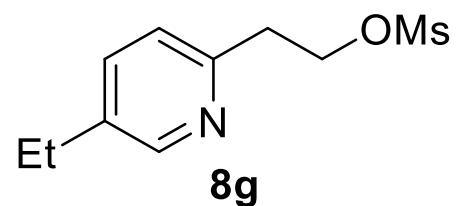
¹³C NMR (100 MHz, CDCl₃)



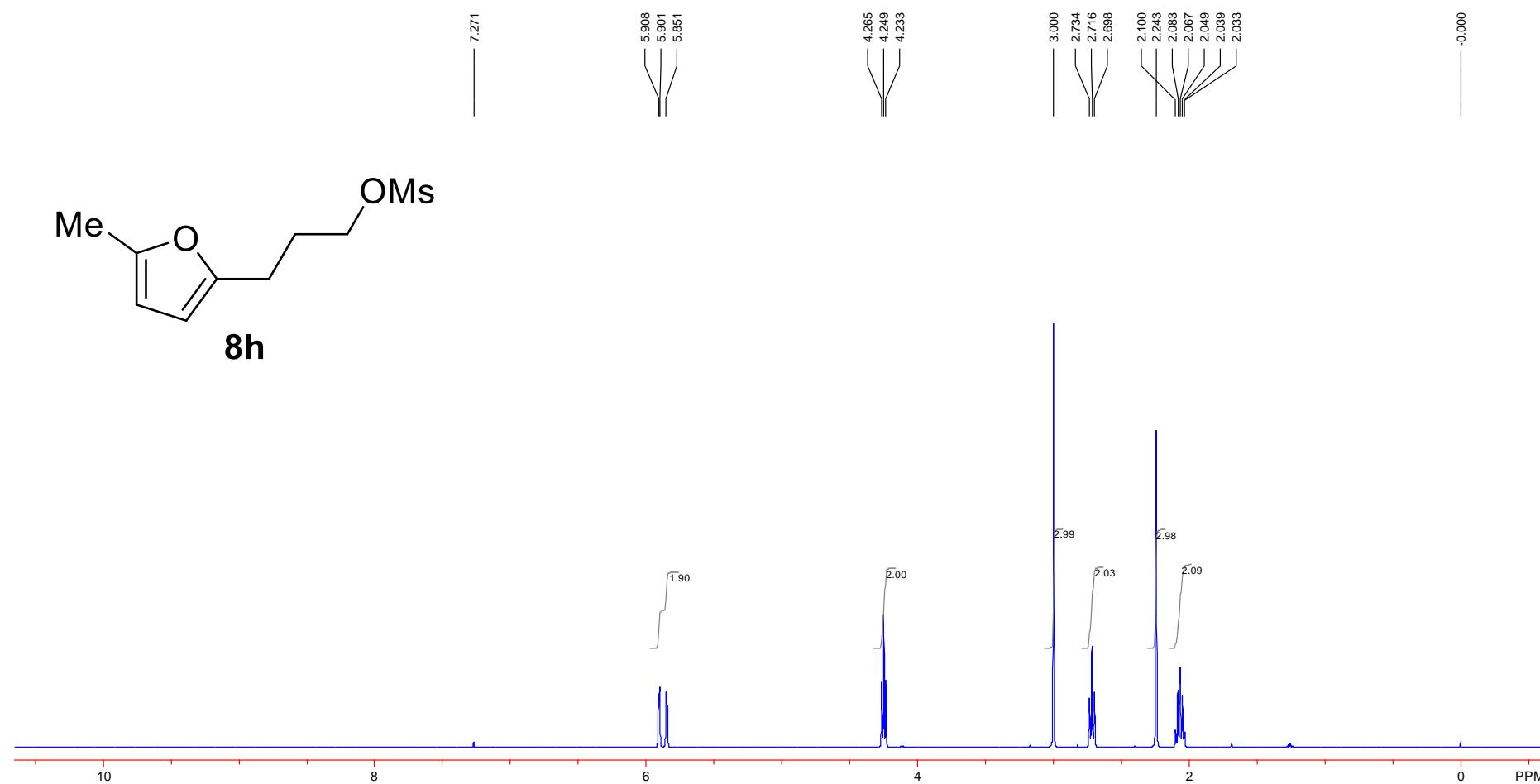
¹H NMR (400 MHz, CDCl₃)



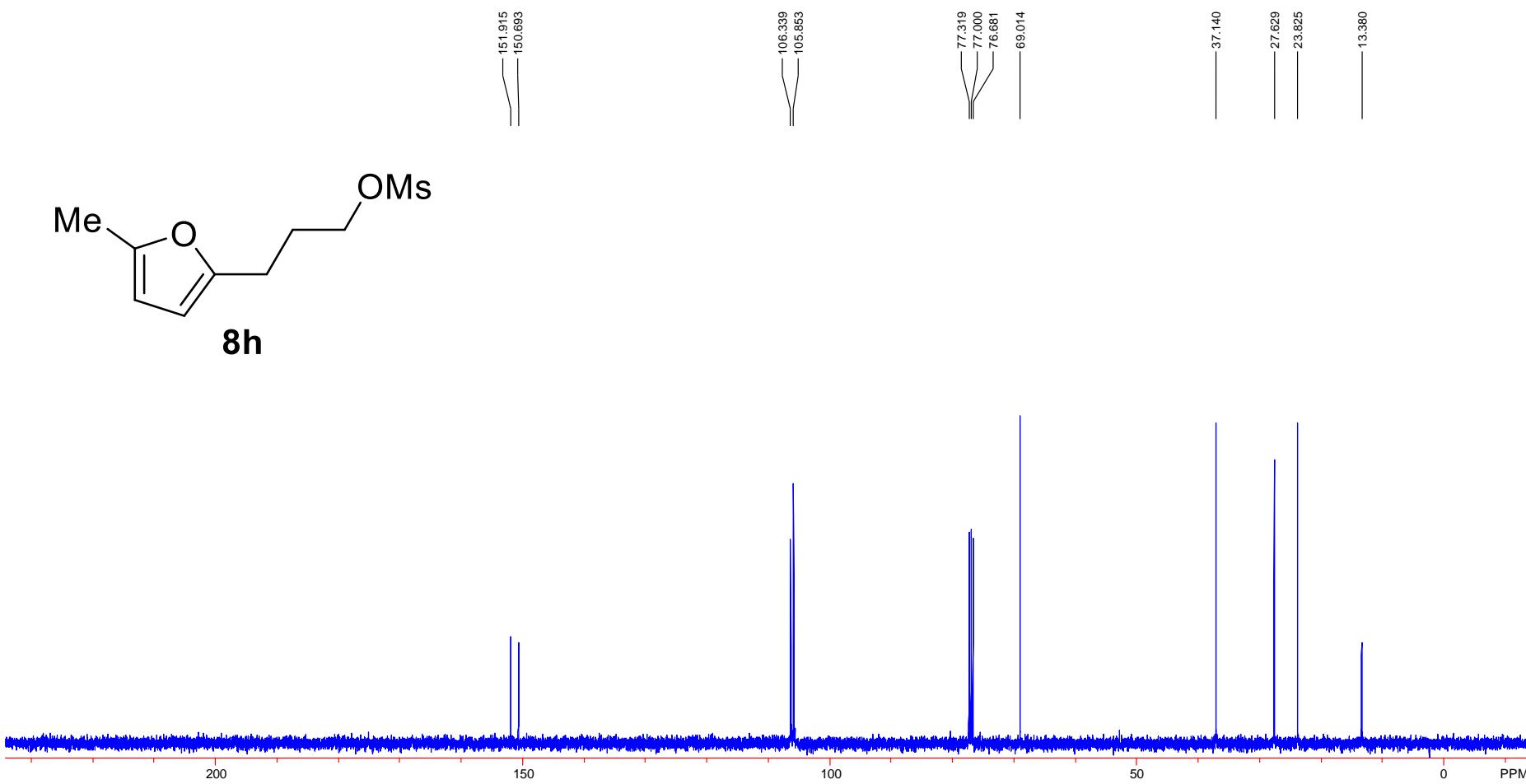
¹³C NMR (100 MHz, CDCl₃)



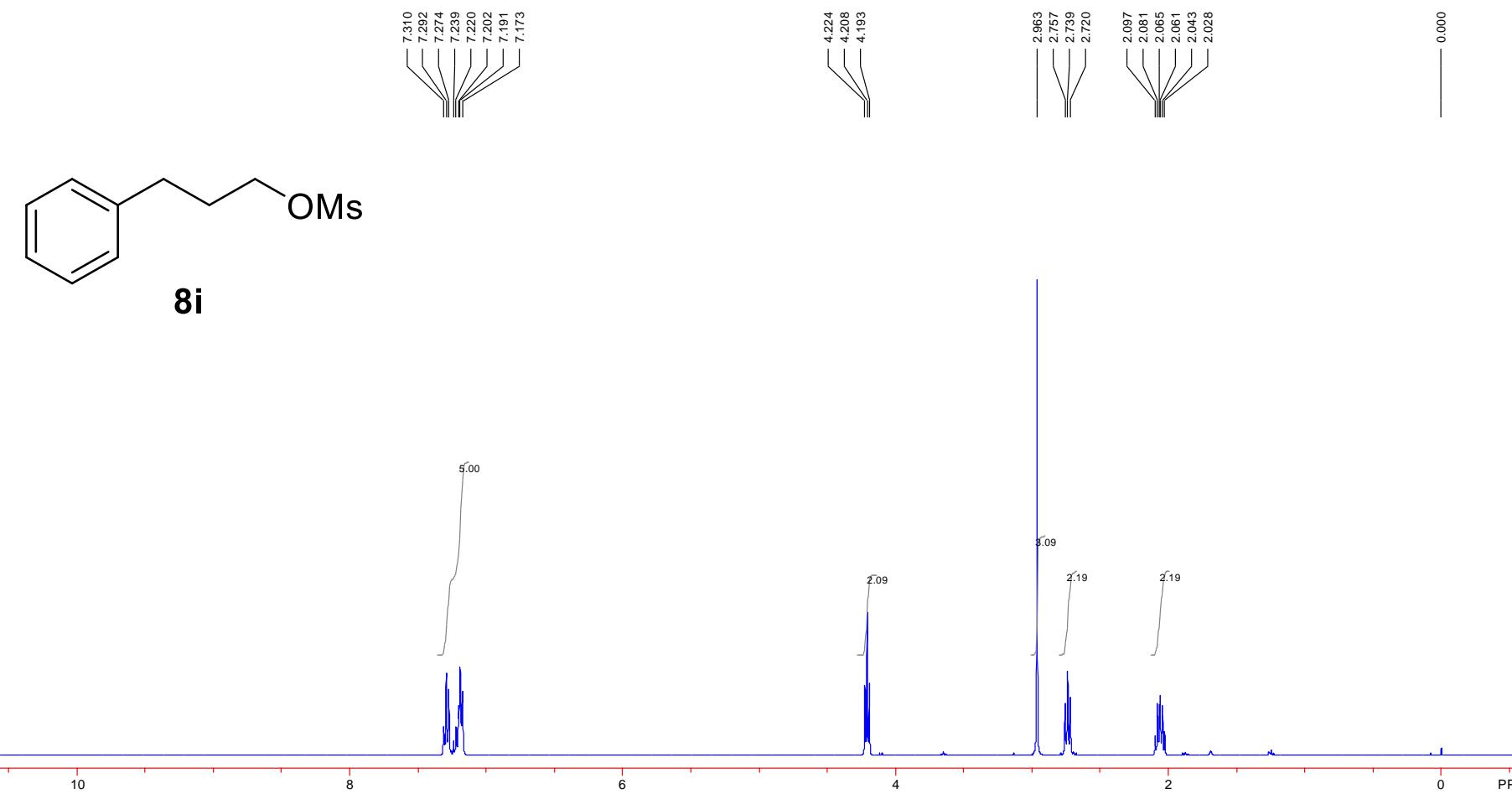
¹H NMR (400 MHz, CDCl₃)



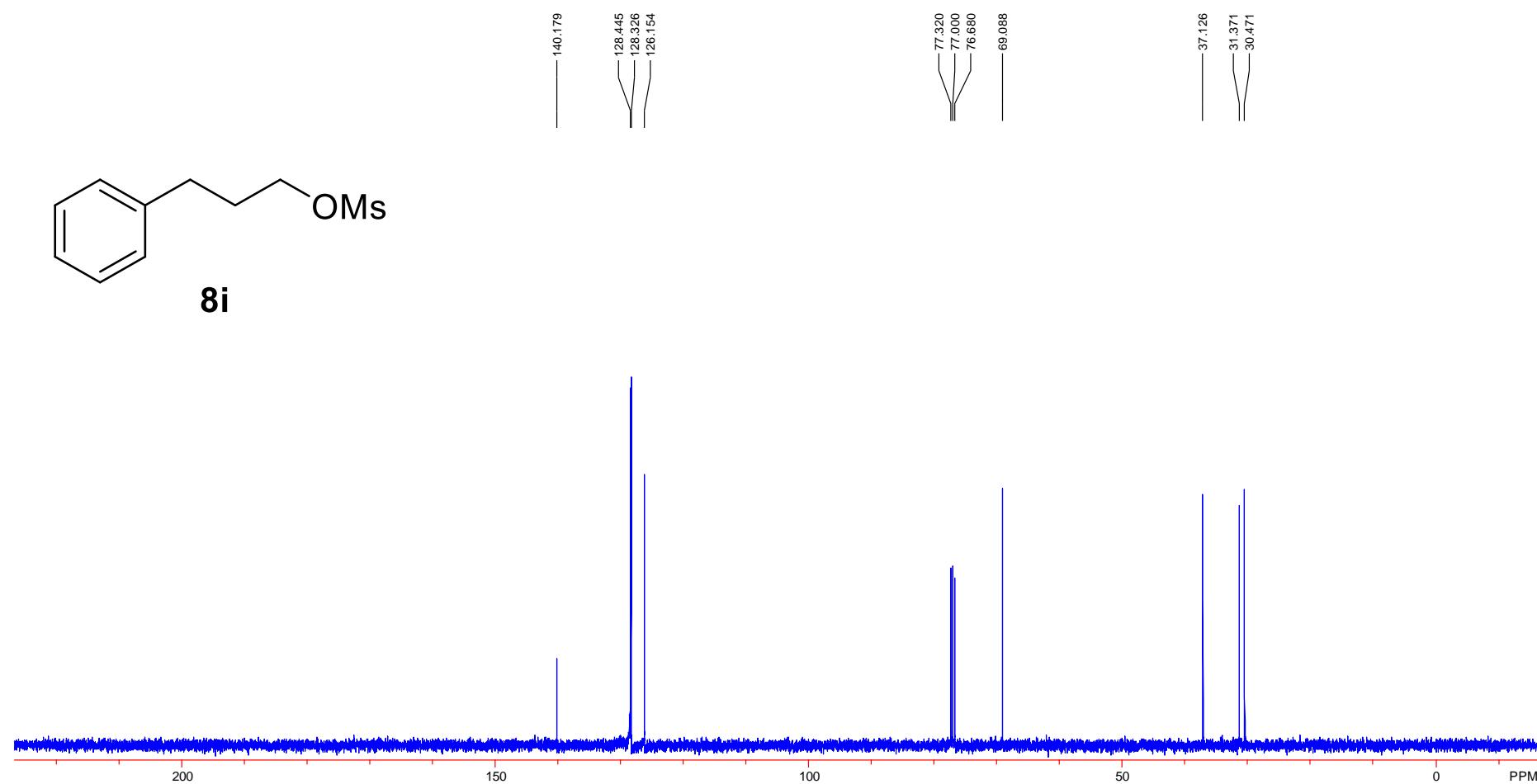
¹³C NMR (100 MHz, CDCl₃)



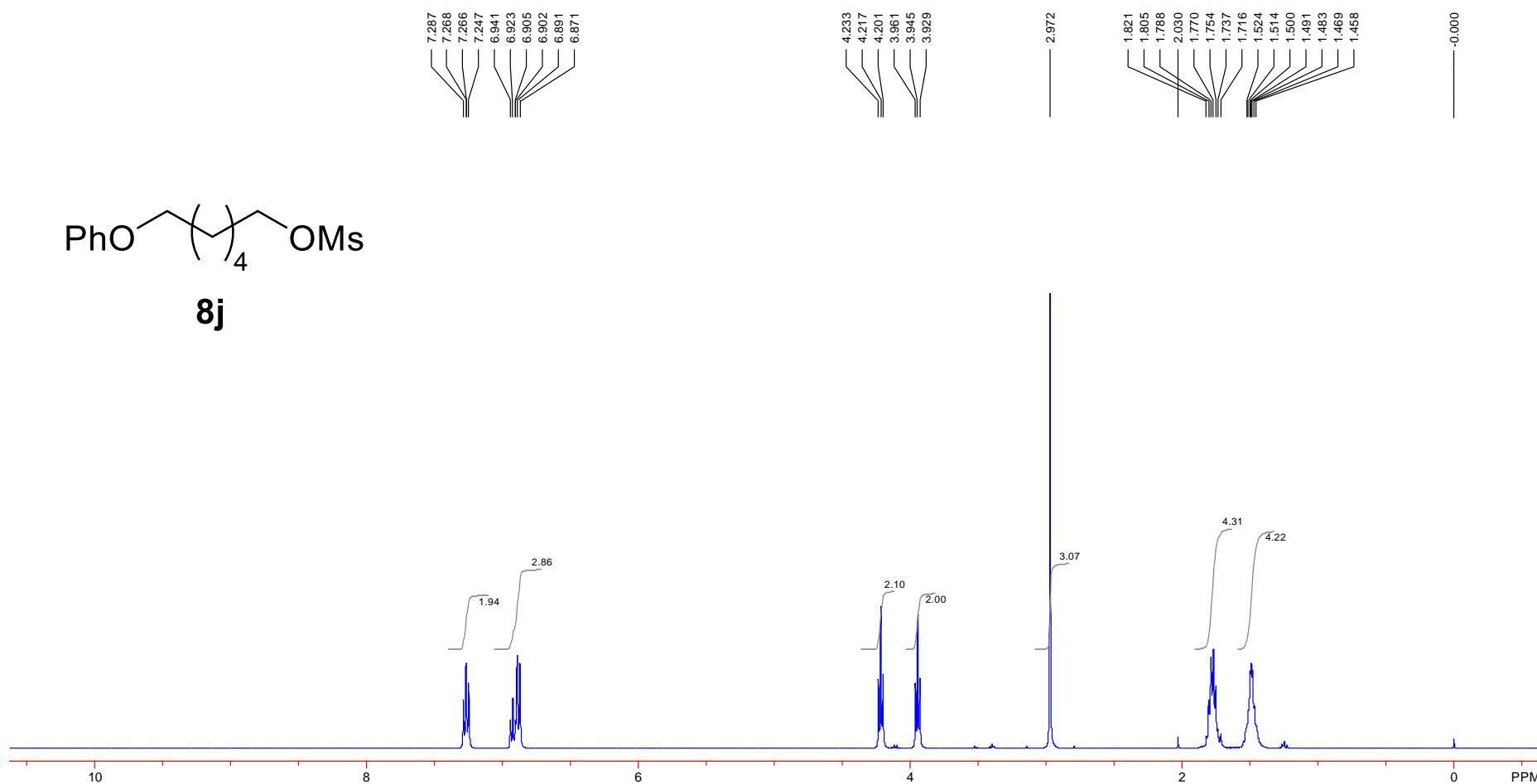
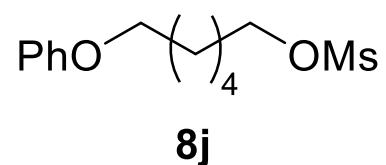
¹H NMR (400 MHz, CDCl₃)



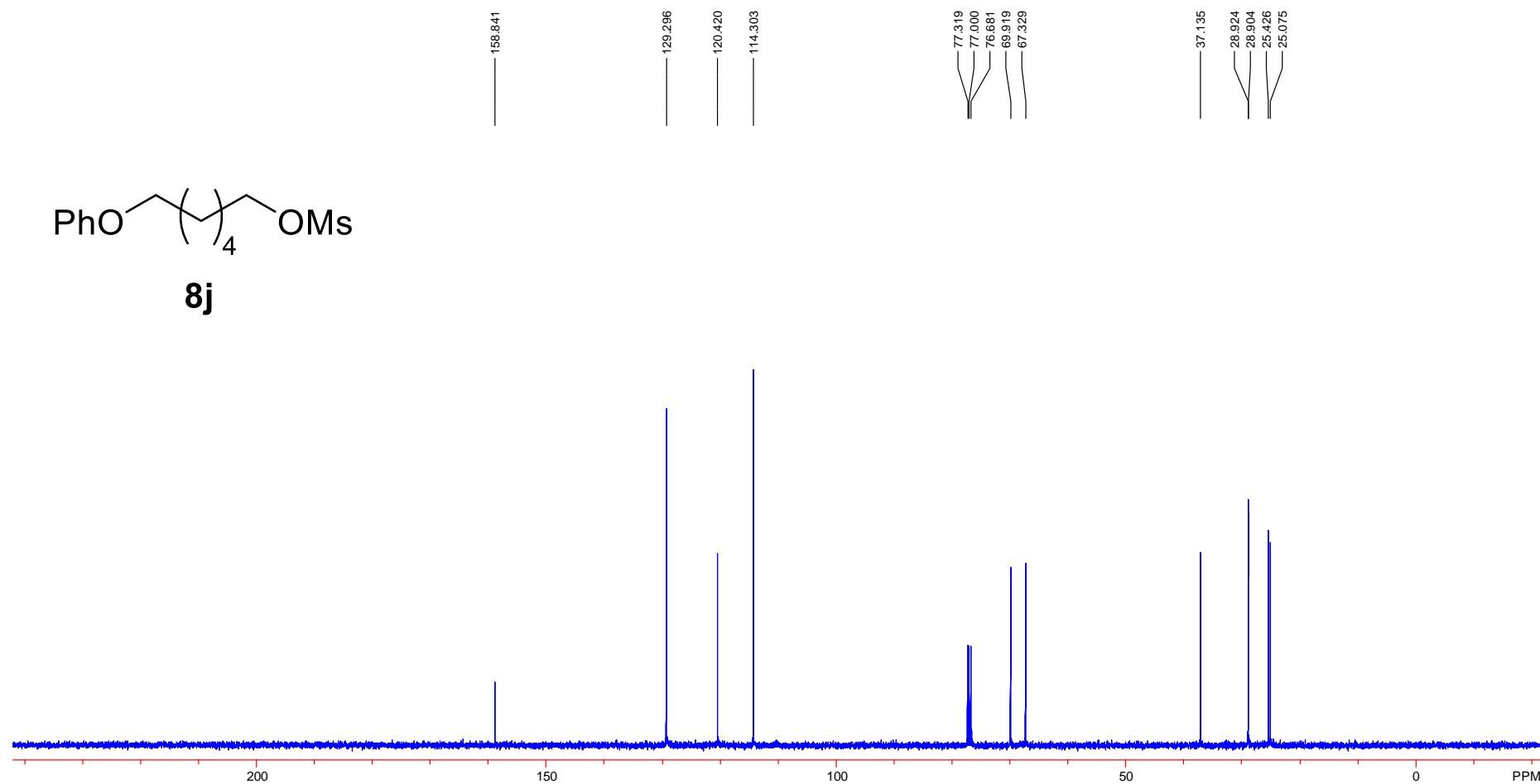
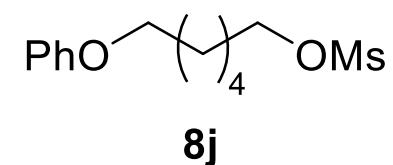
¹³C NMR (100 MHz, CDCl₃)



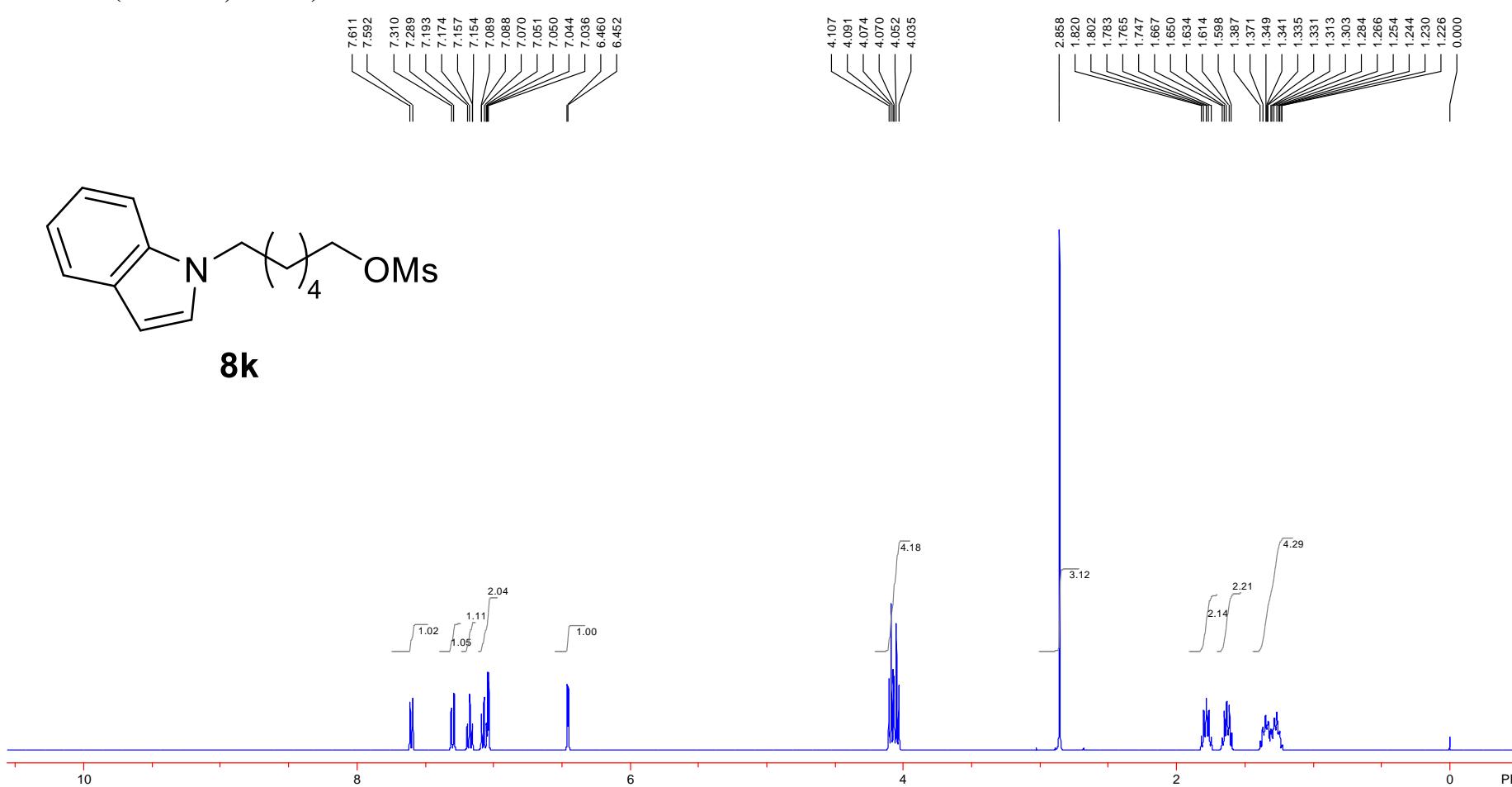
¹H NMR (400 MHz, CDCl₃)



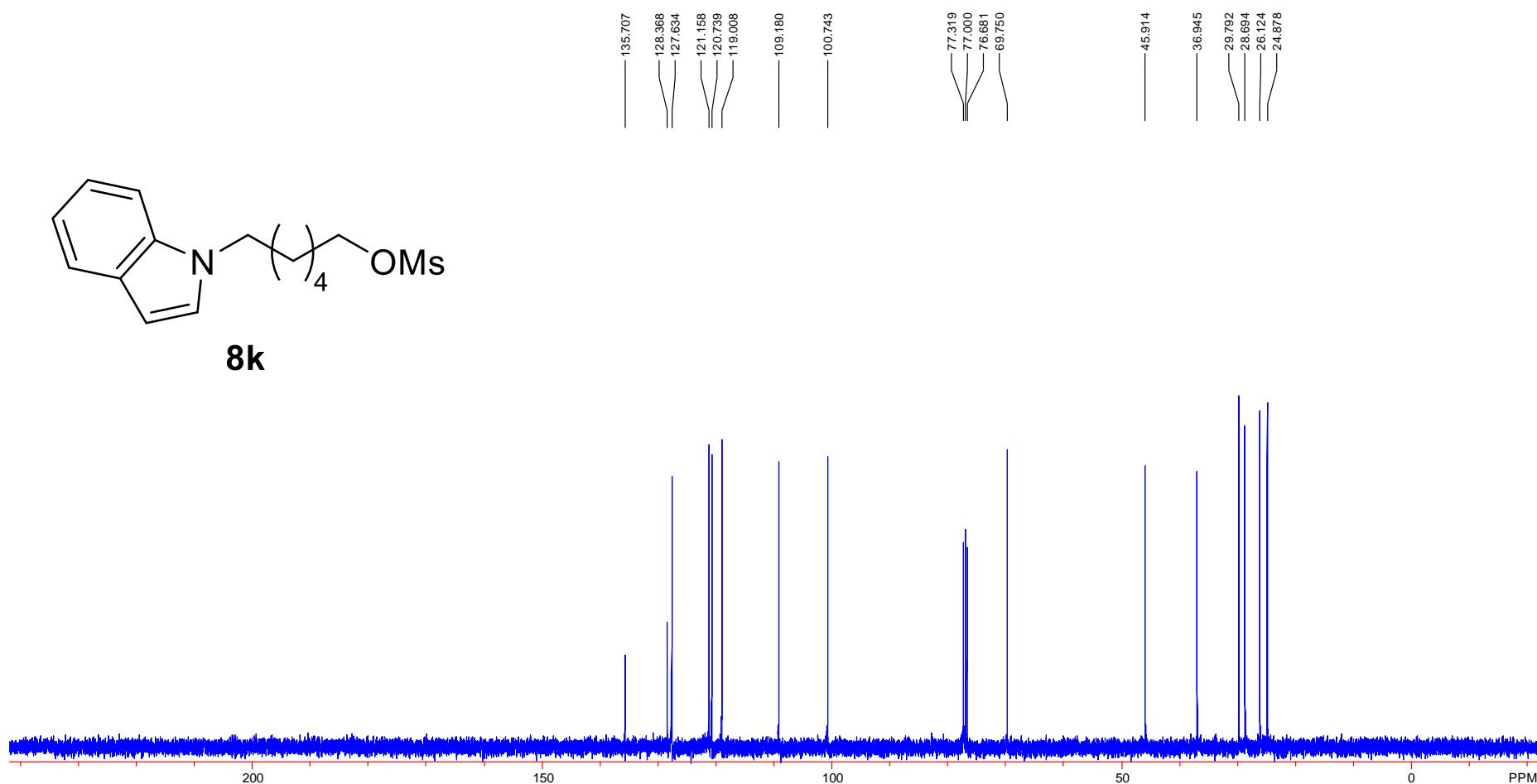
¹³C NMR (100 MHz, CDCl₃)



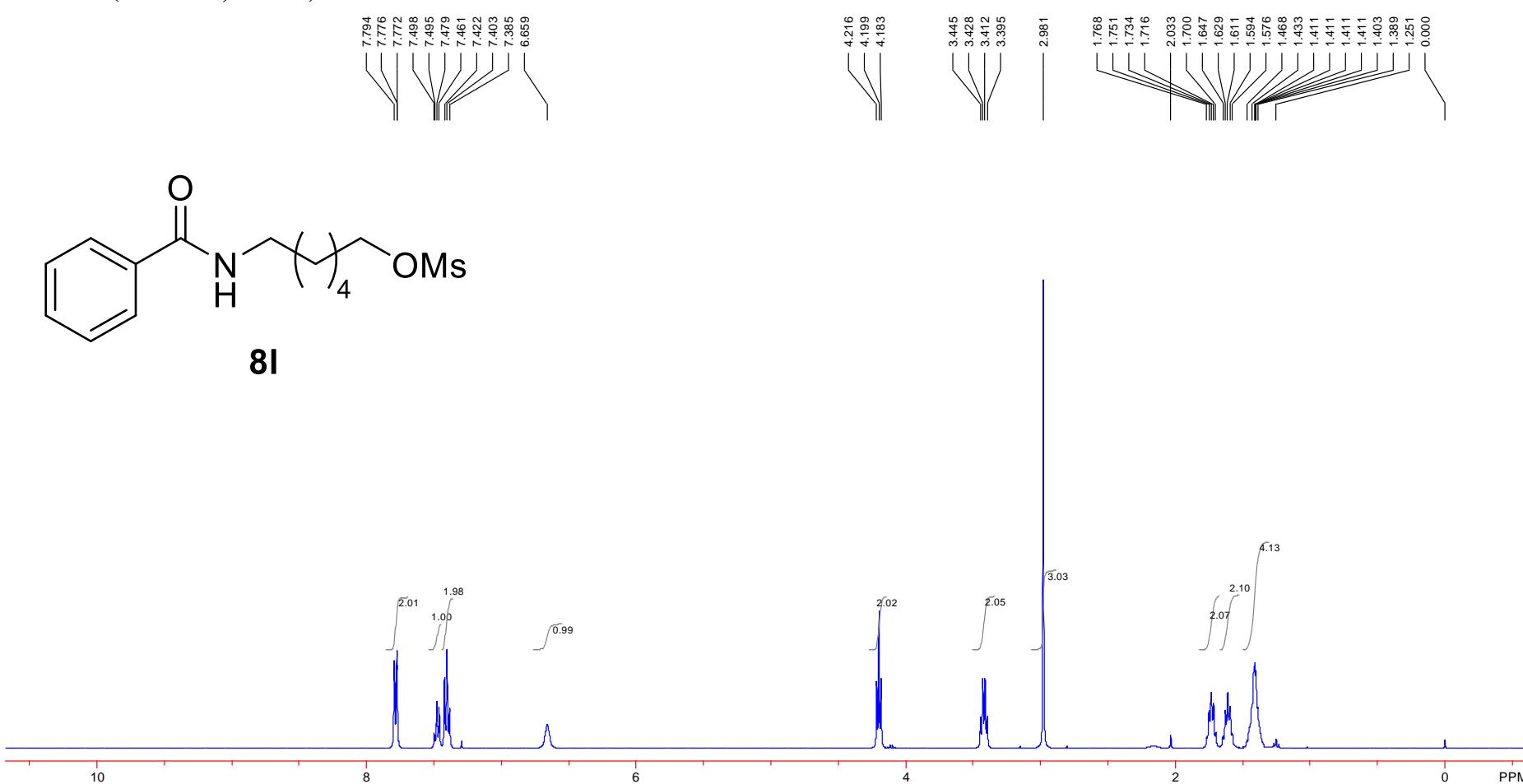
¹H NMR (400 MHz, CDCl₃)



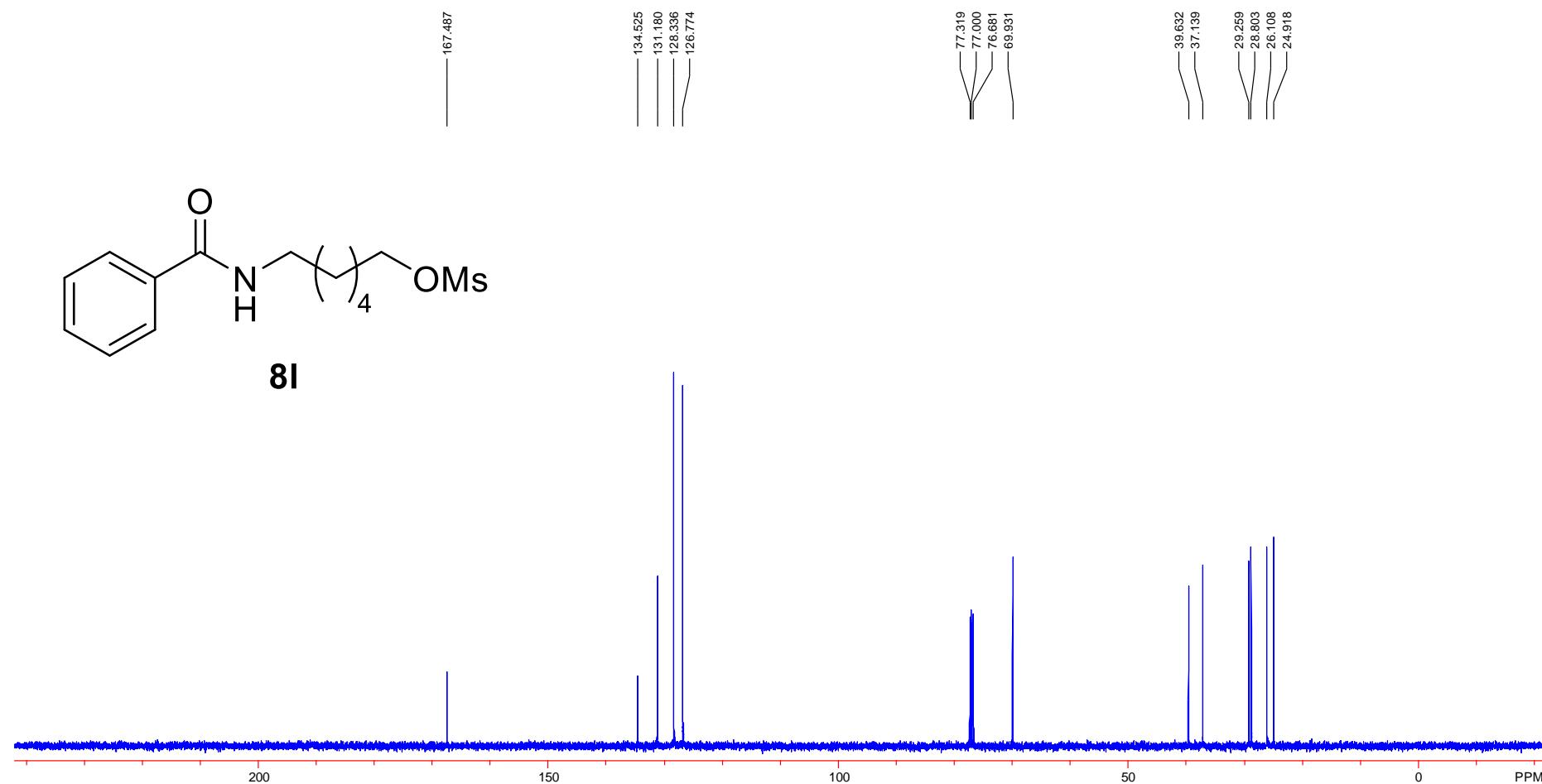
¹³C NMR (100 MHz, CDCl₃)



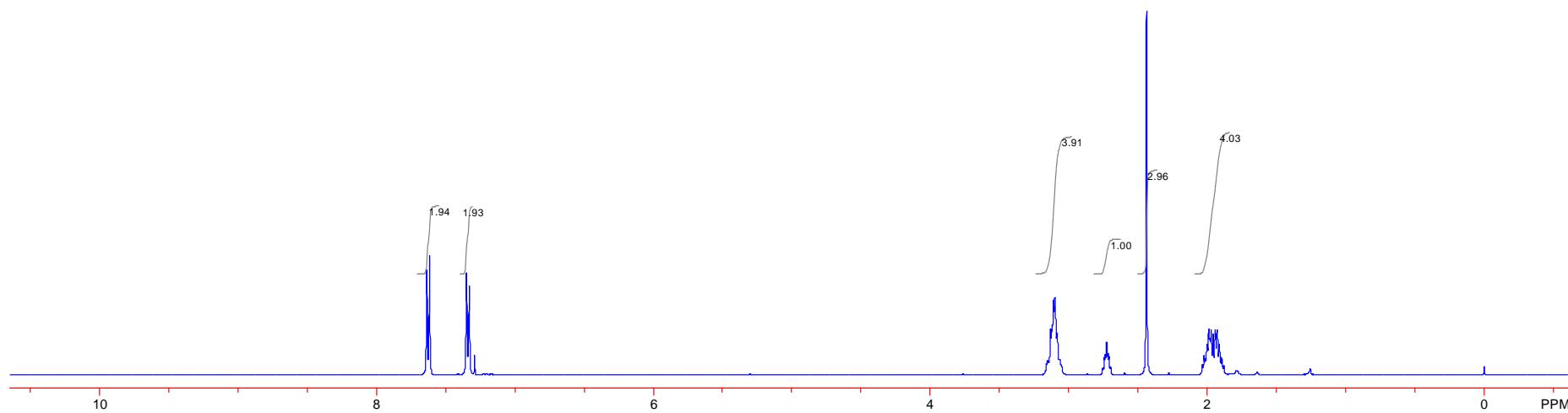
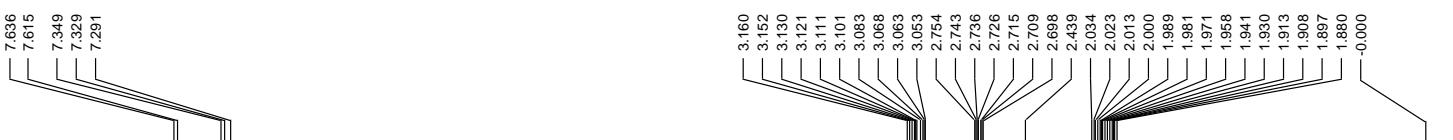
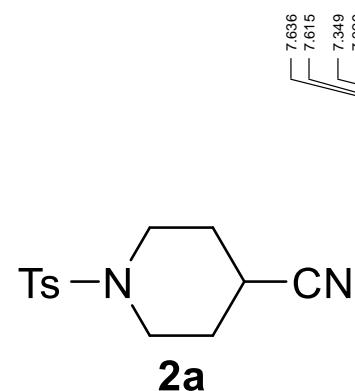
¹H NMR (400 MHz, CDCl₃)



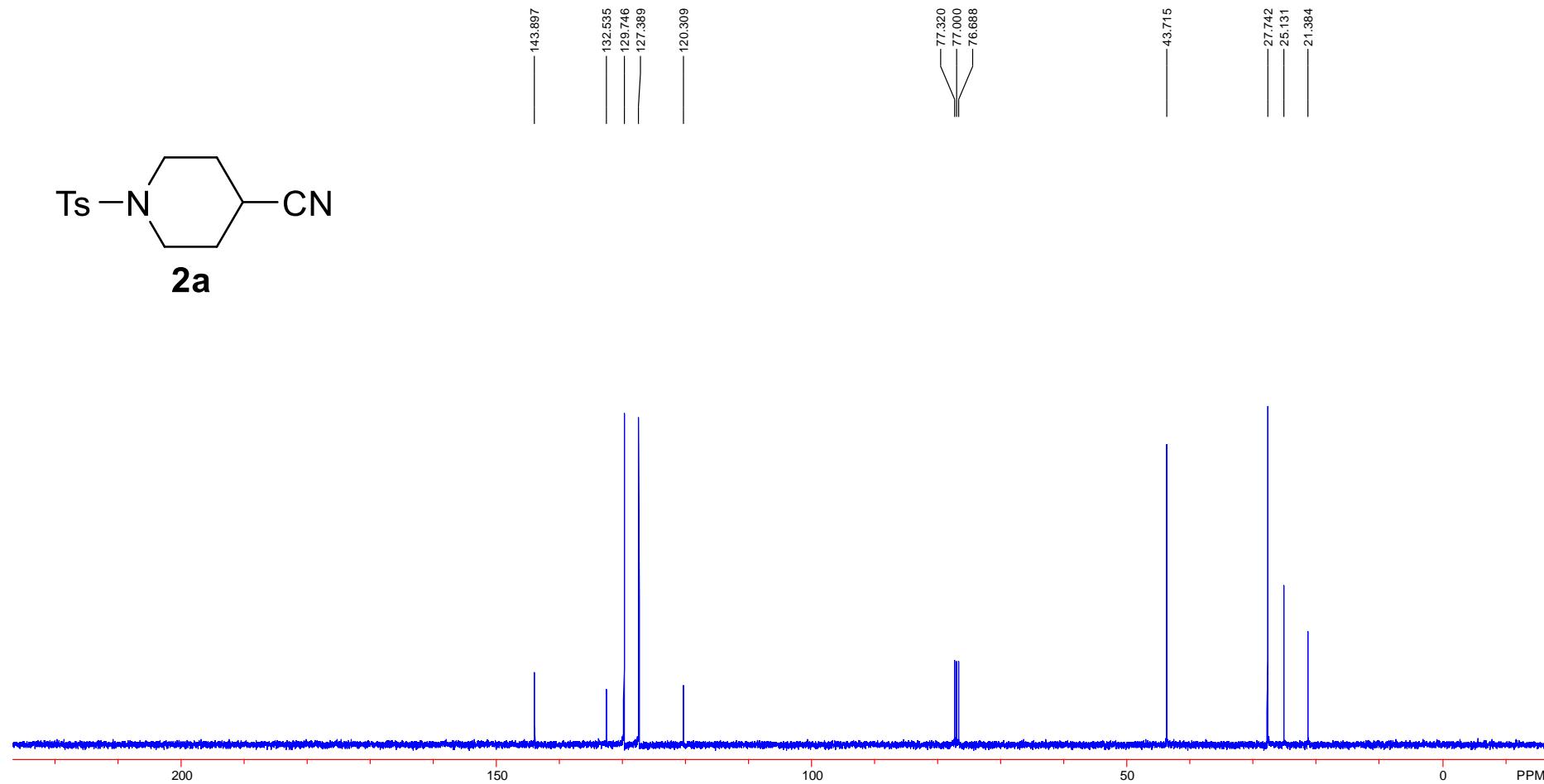
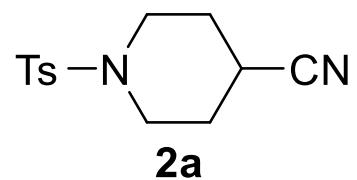
¹³C NMR (100 MHz, CDCl₃)



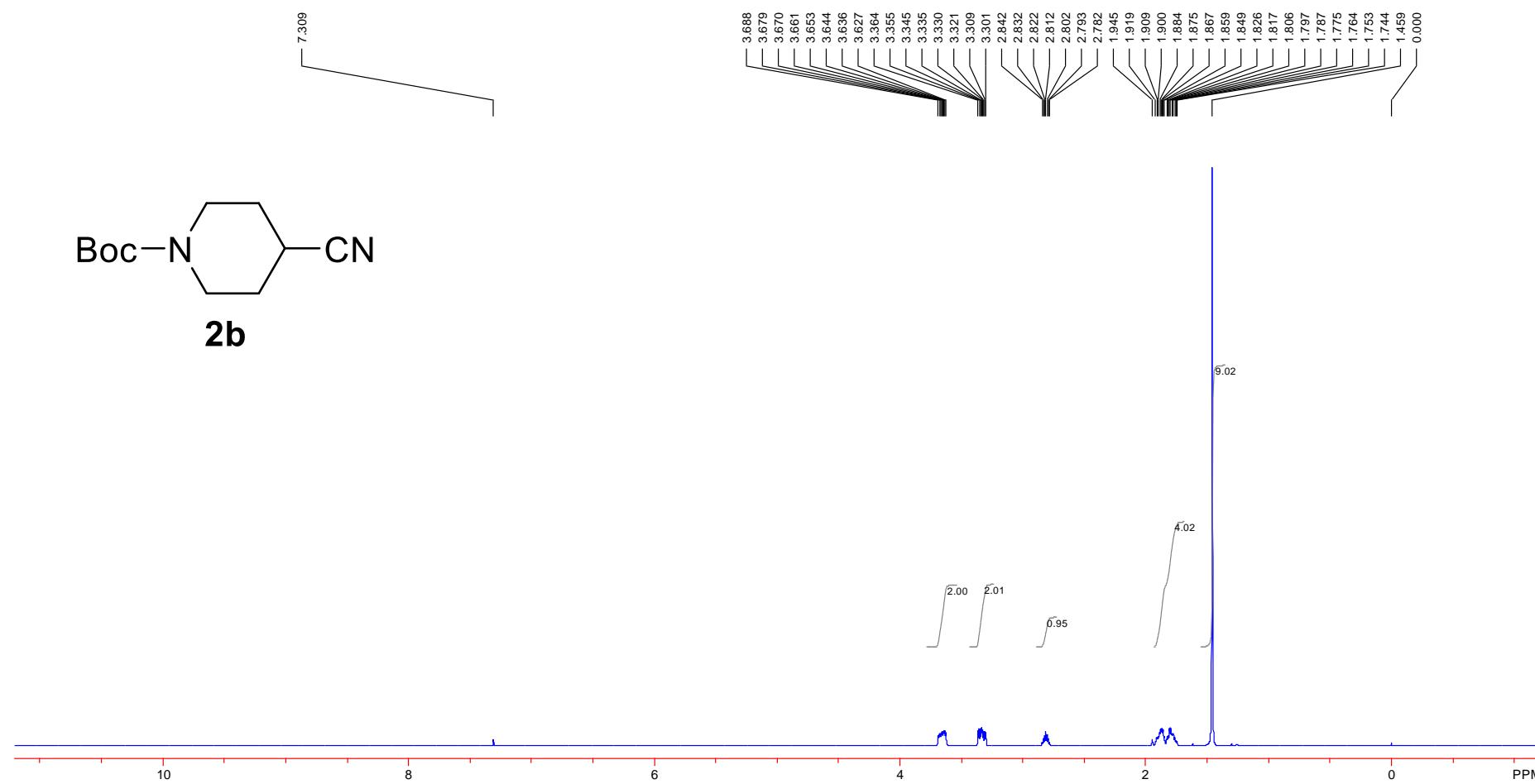
¹H NMR (400 MHz, CDCl₃)



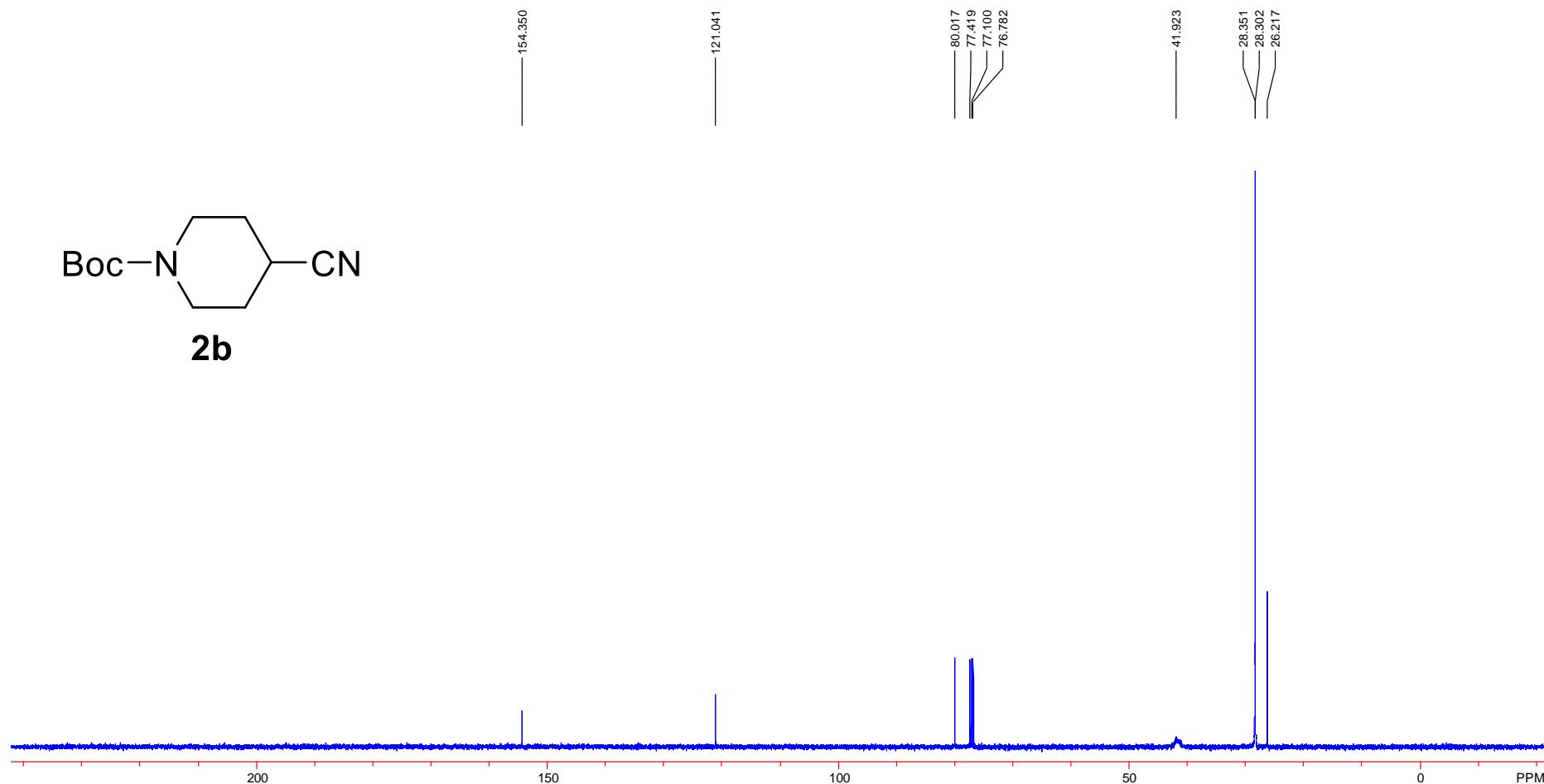
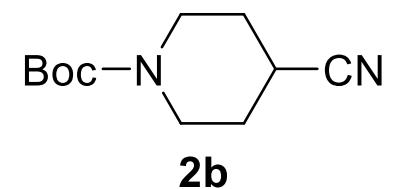
¹³C NMR (100 MHz, CDCl₃)



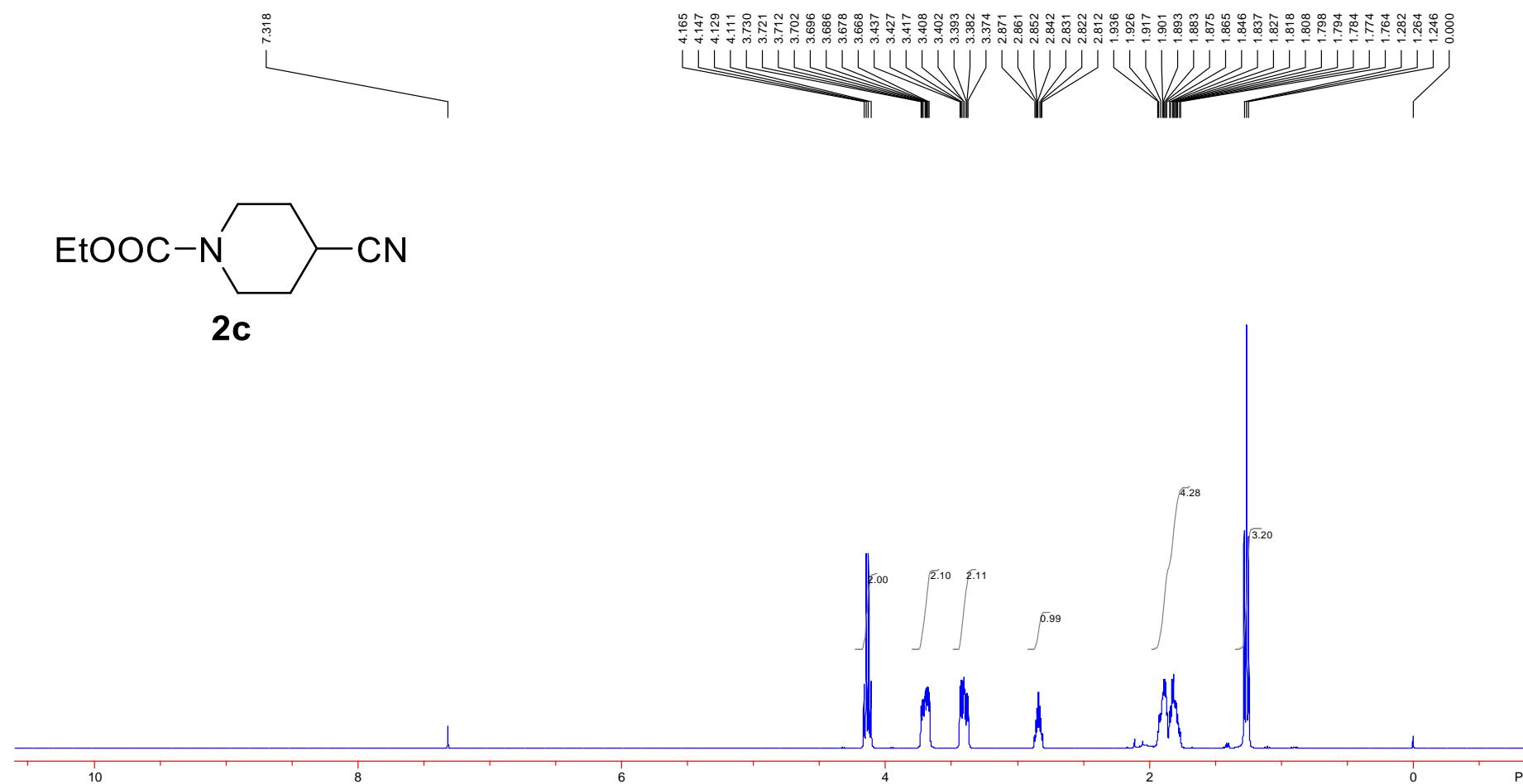
¹H NMR (400 MHz, CDCl₃)



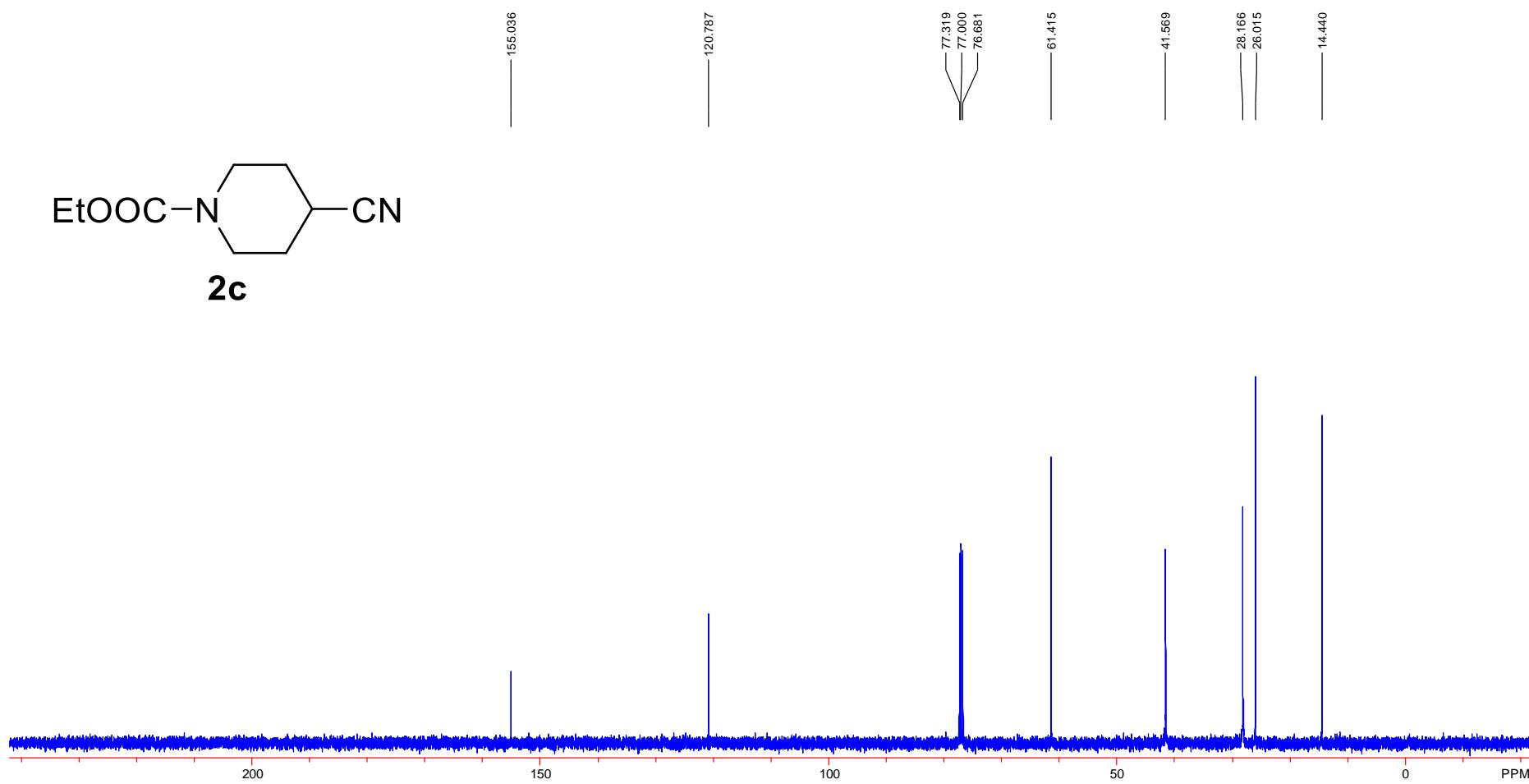
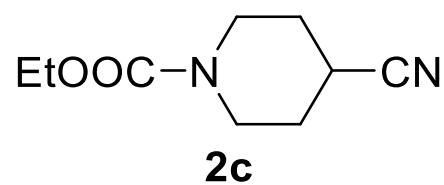
¹³C NMR (100 MHz, CDCl₃)



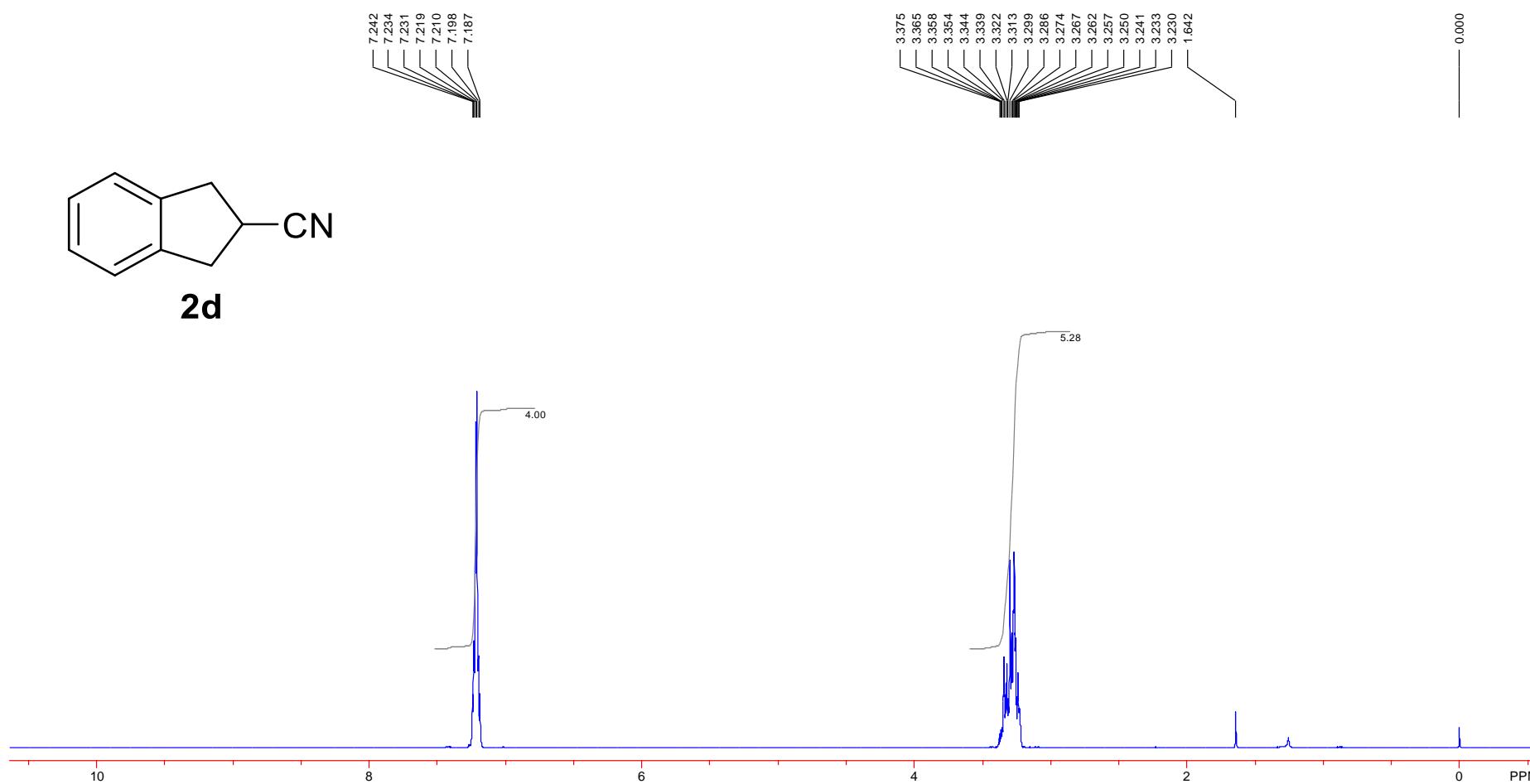
¹H NMR (400 MHz, CDCl₃)



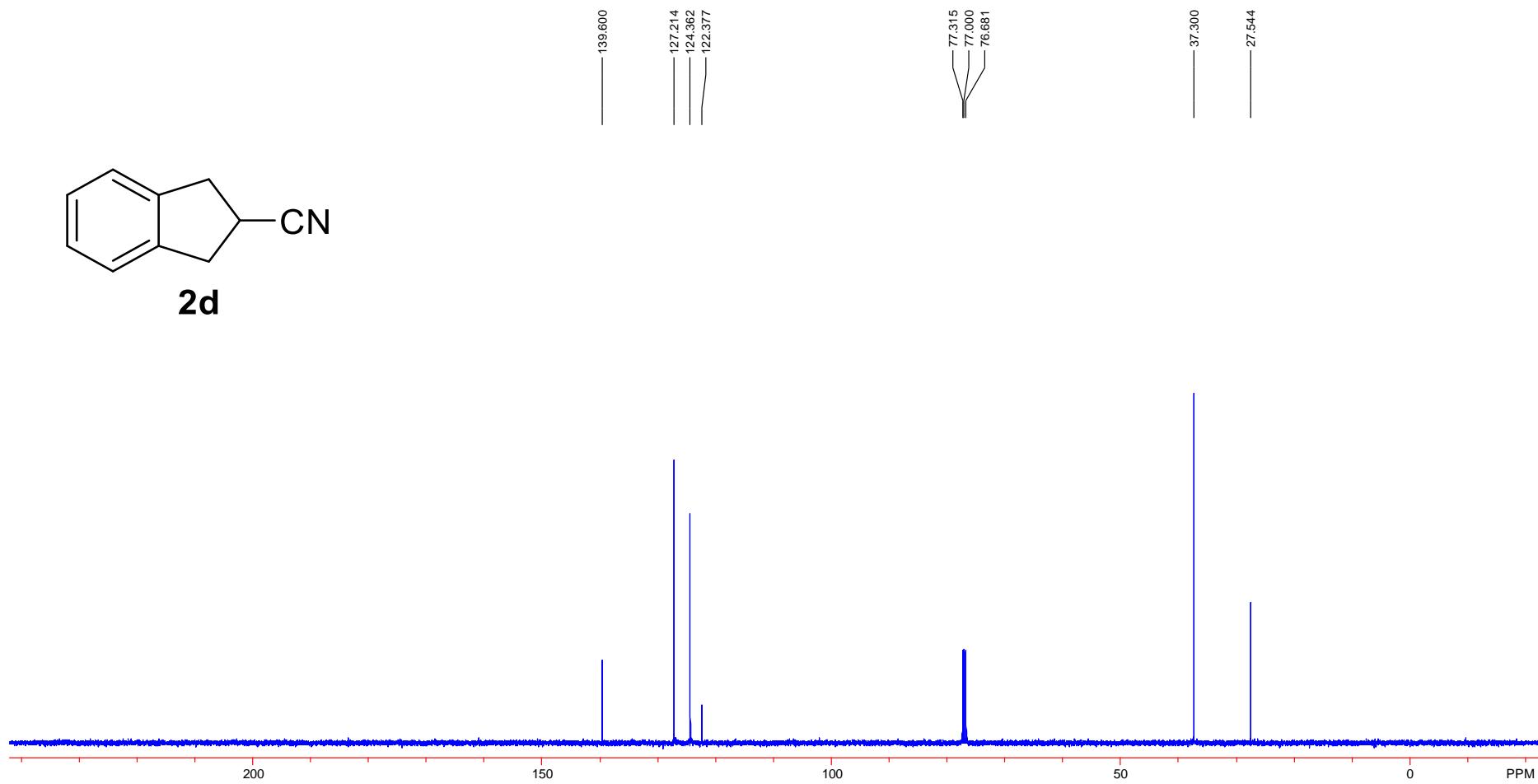
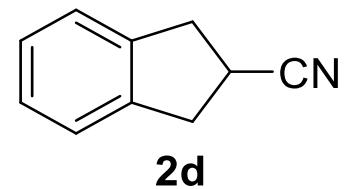
¹³C NMR (100 MHz, CDCl₃)



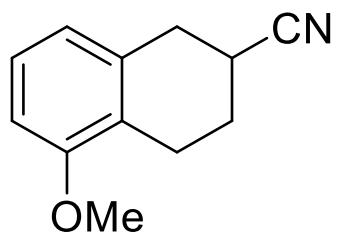
¹H NMR (400 MHz, CDCl₃)



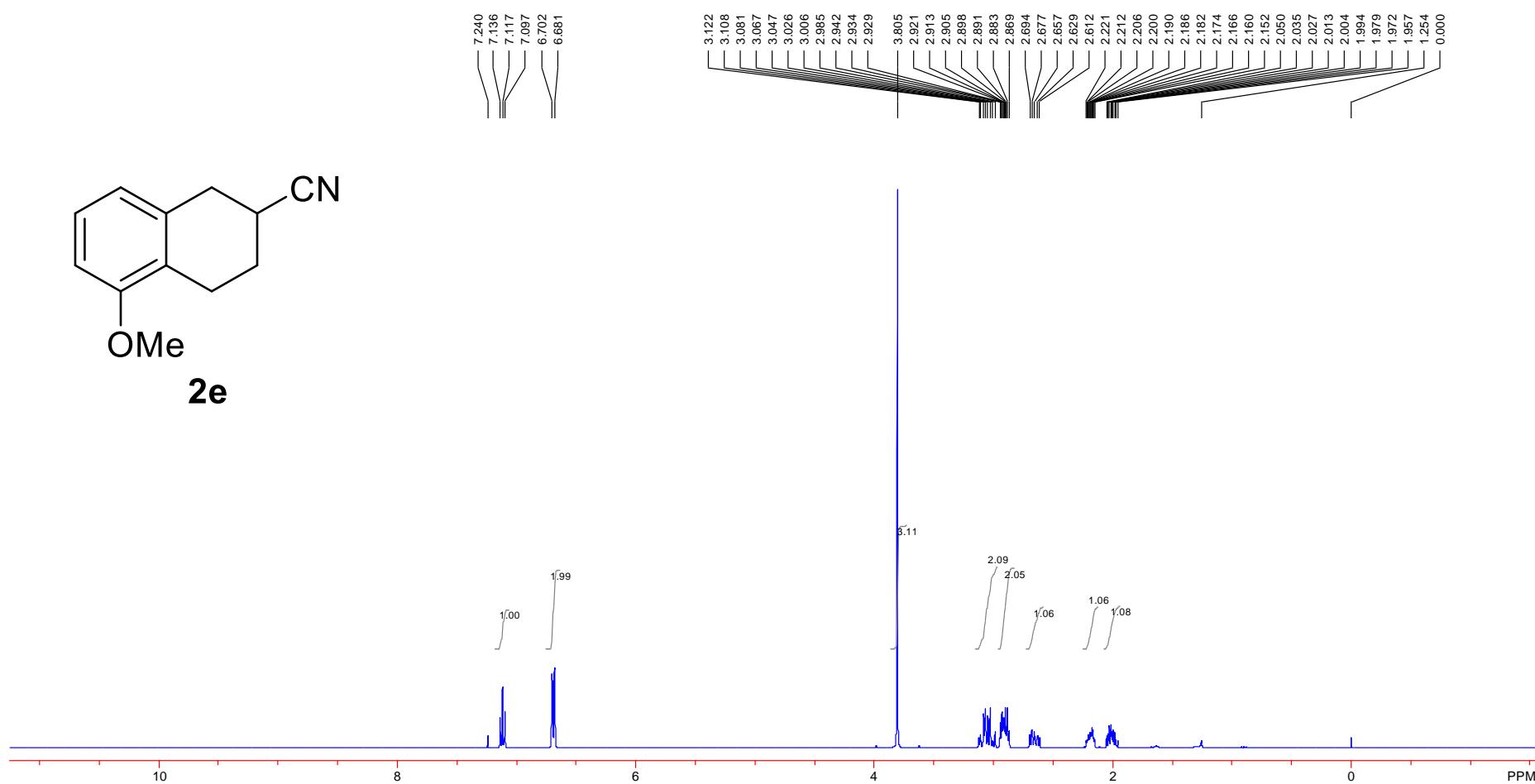
¹³C NMR (100 MHz, CDCl₃)



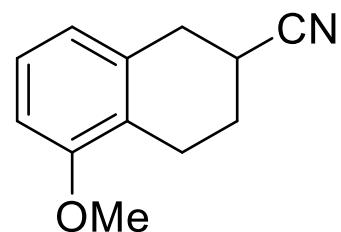
¹H NMR (400 MHz, CDCl₃)



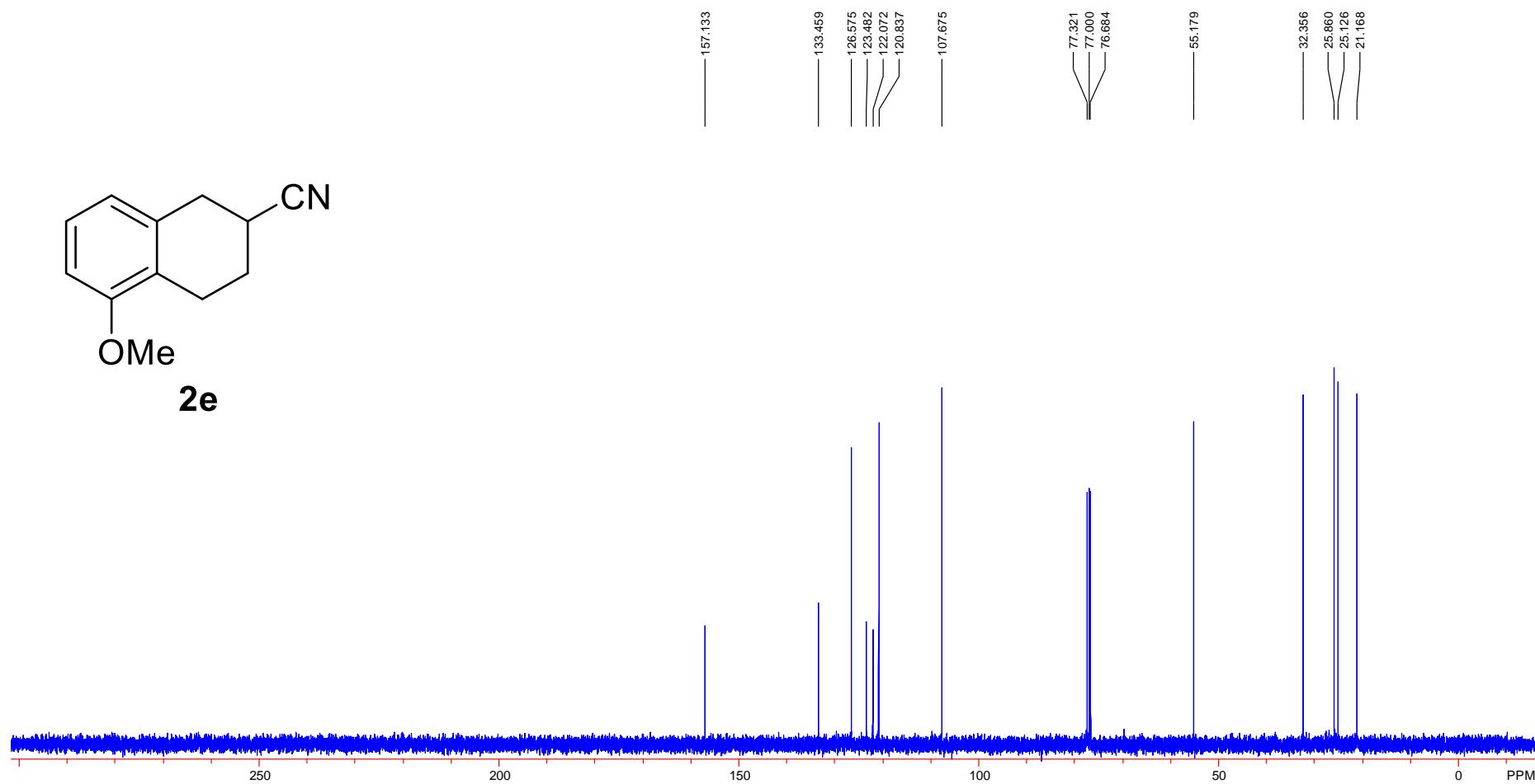
2e



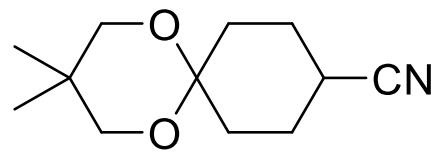
¹³C NMR (100 MHz, CDCl₃)



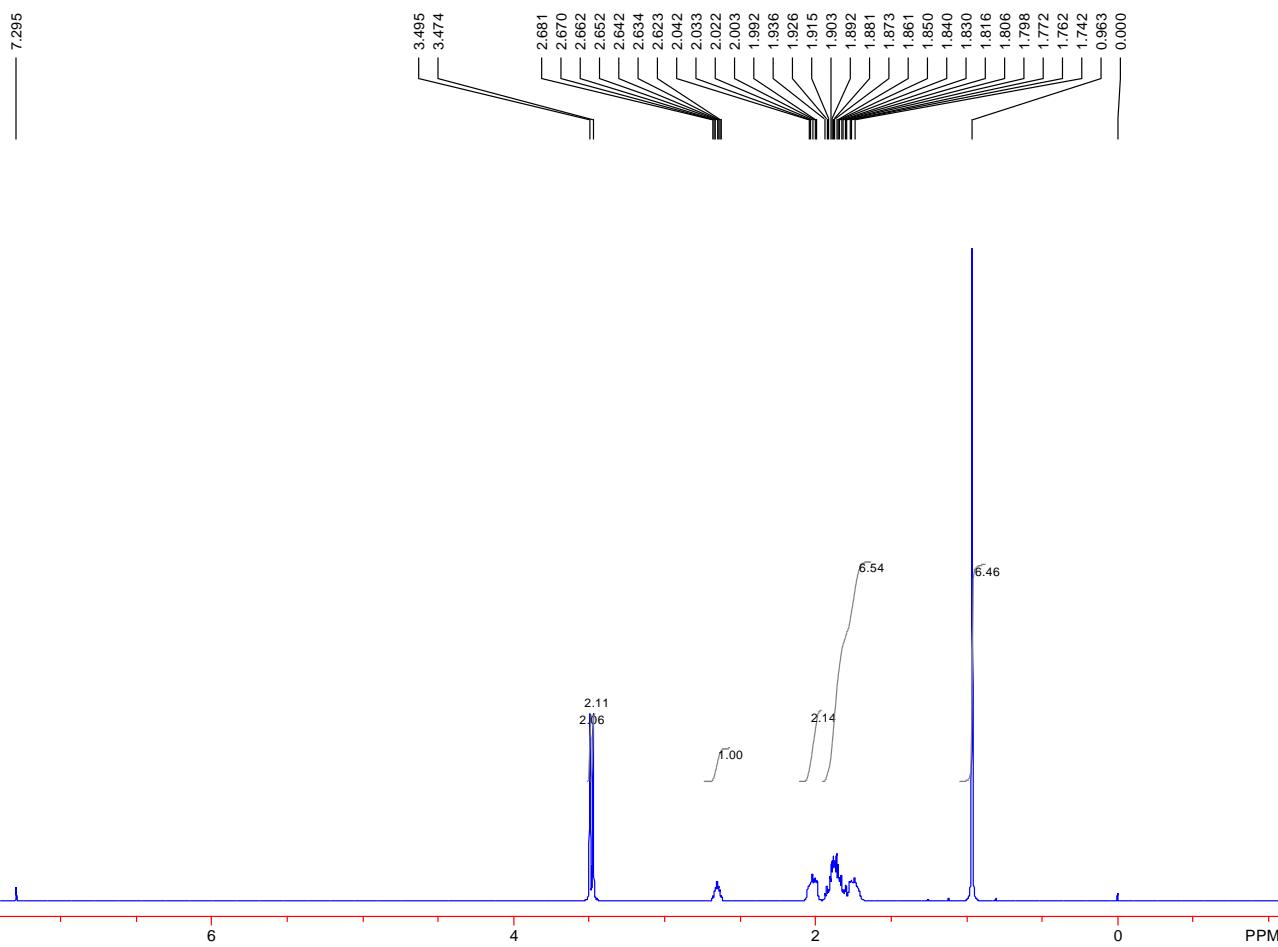
2e



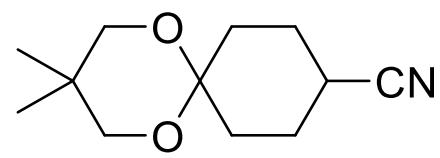
¹H NMR (400 MHz, CDCl₃)



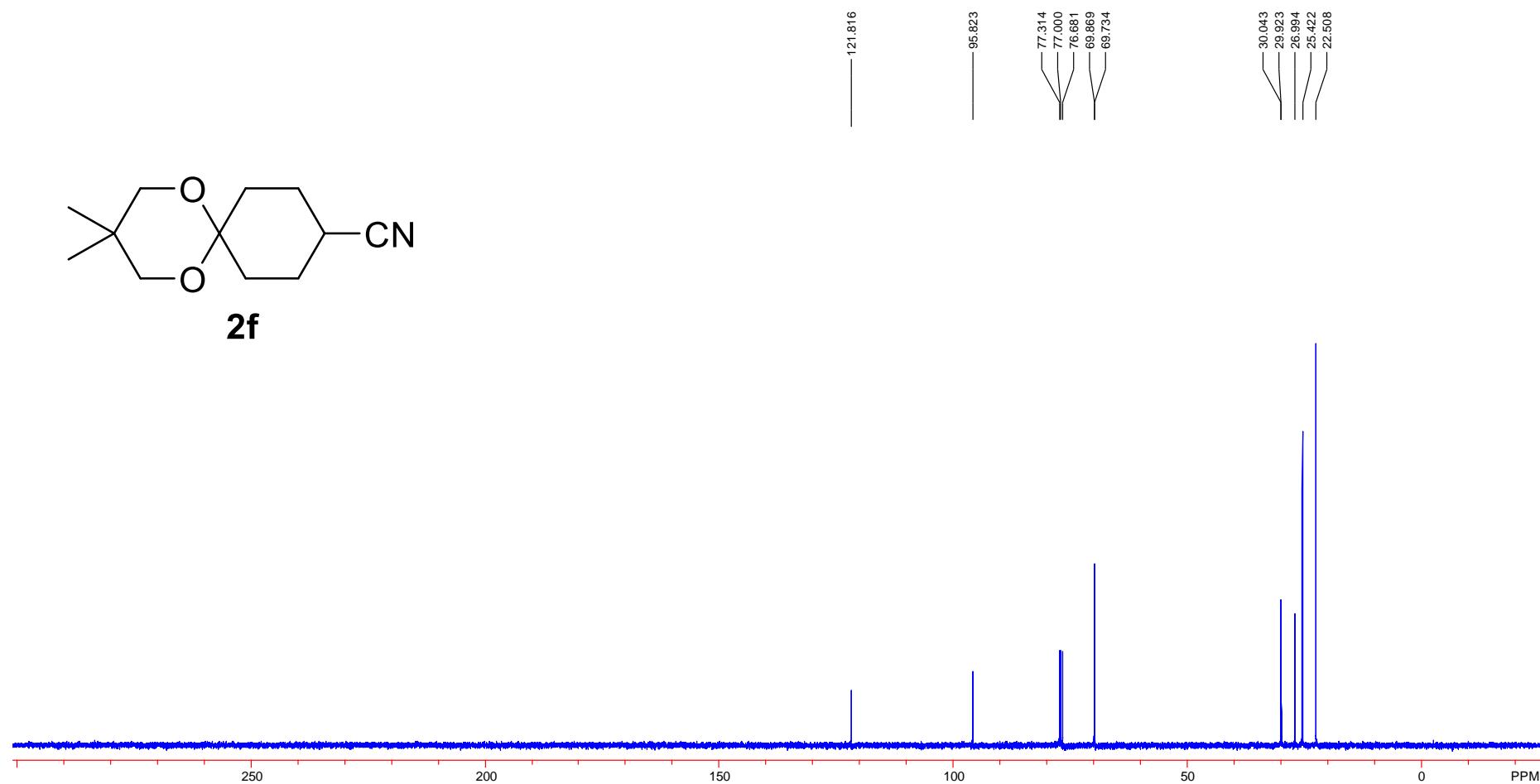
2f



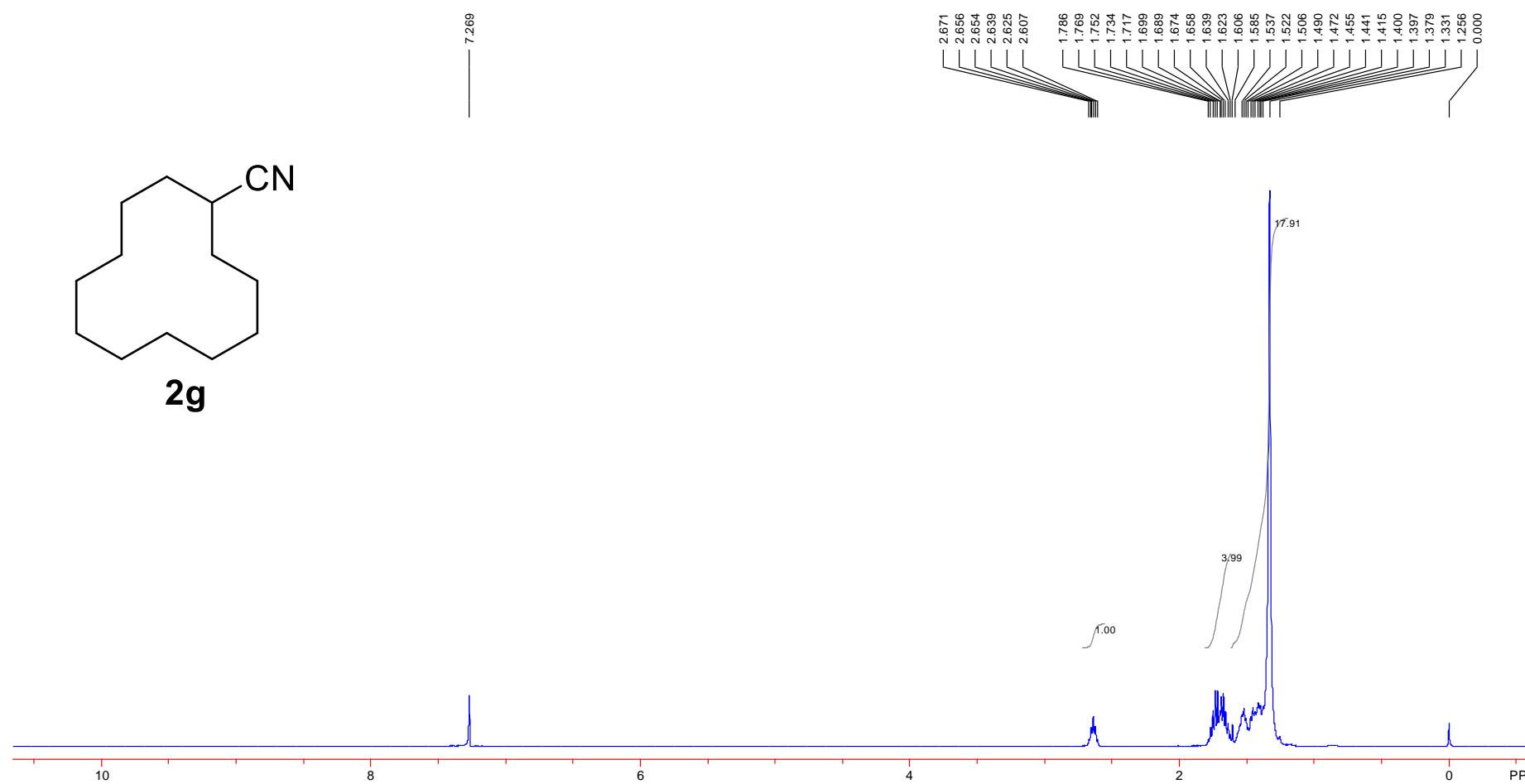
¹³C NMR (100 MHz, CDCl₃)



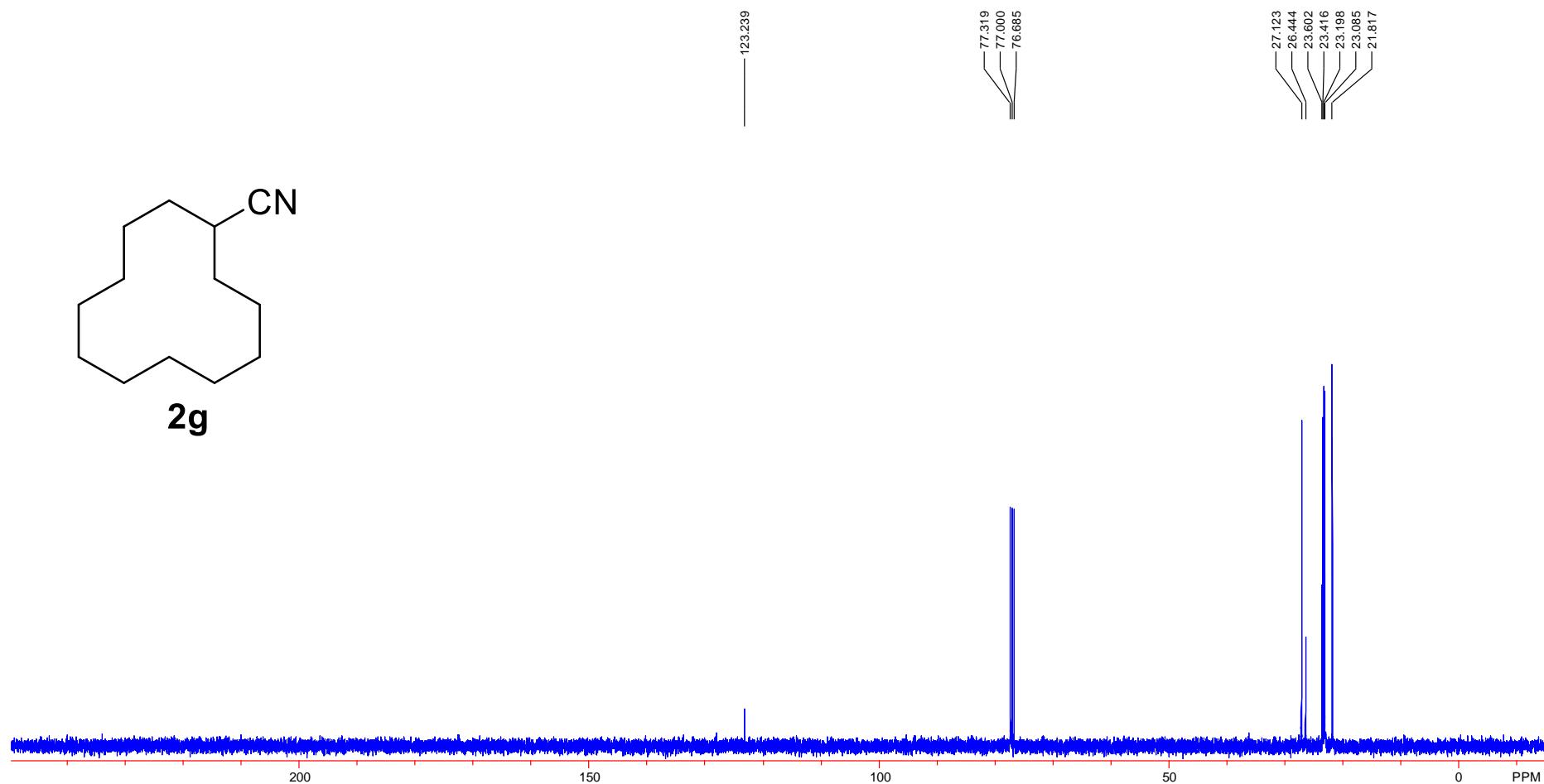
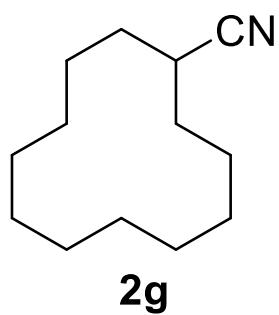
2f



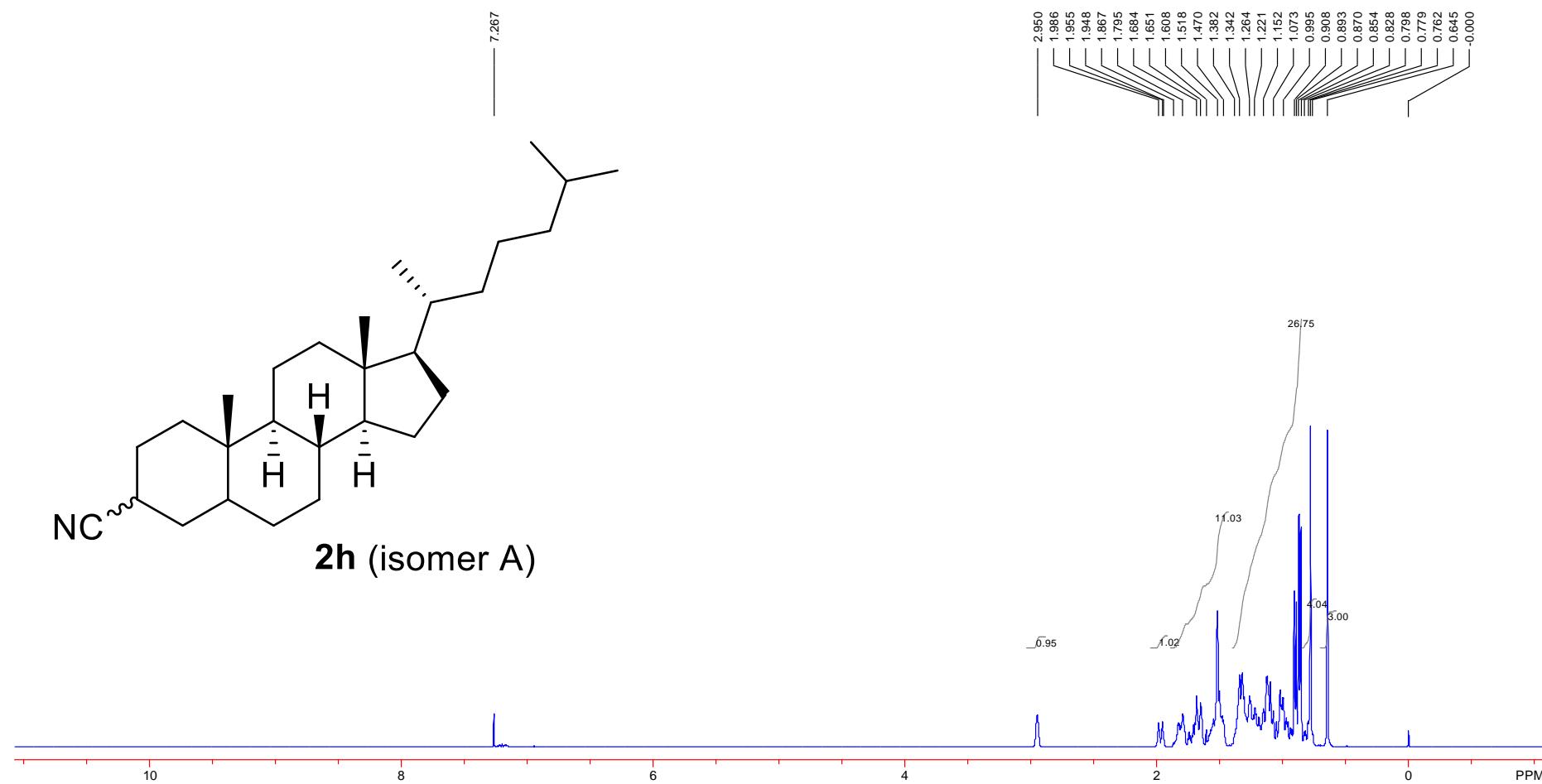
¹H NMR (400 MHz, CDCl₃)



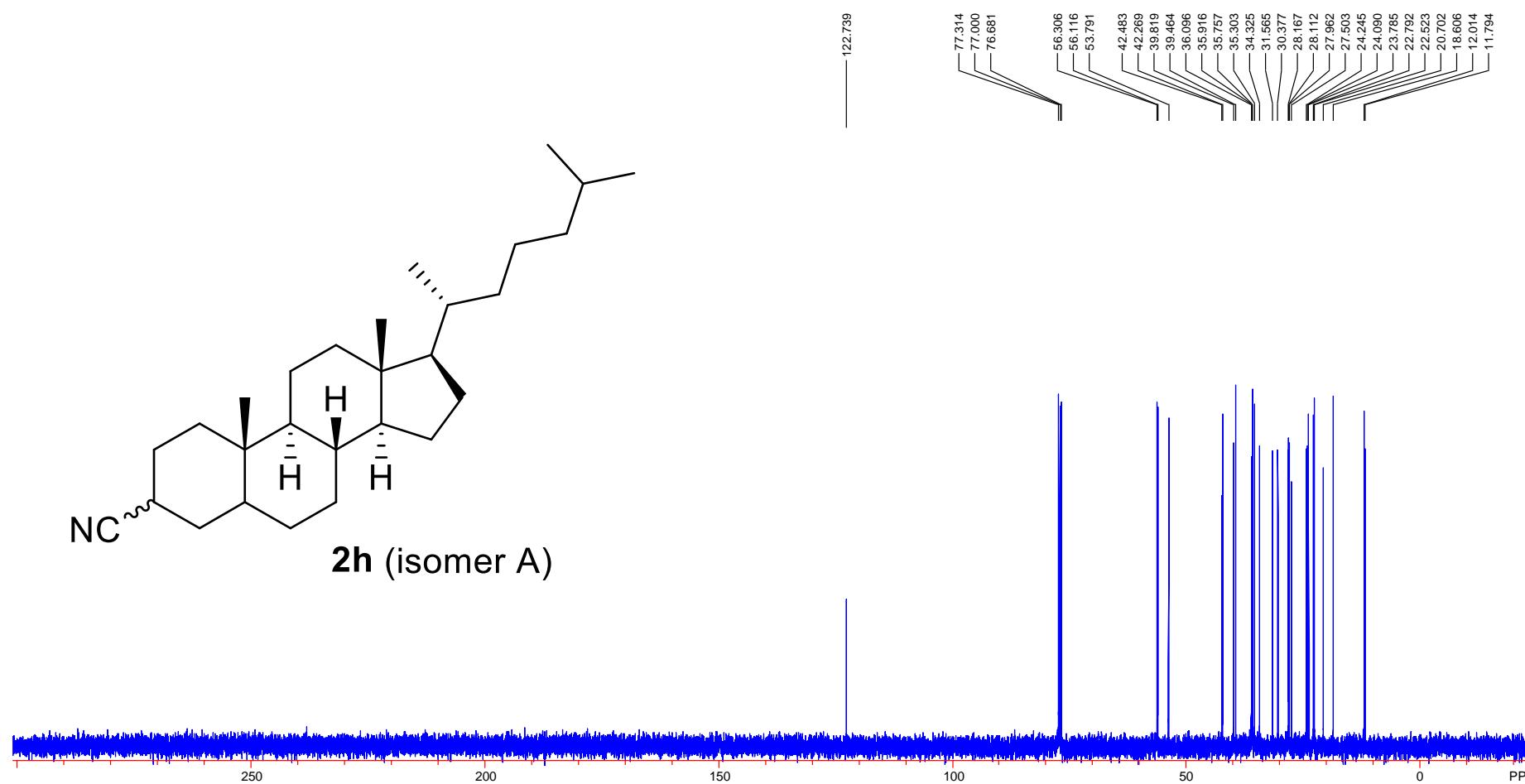
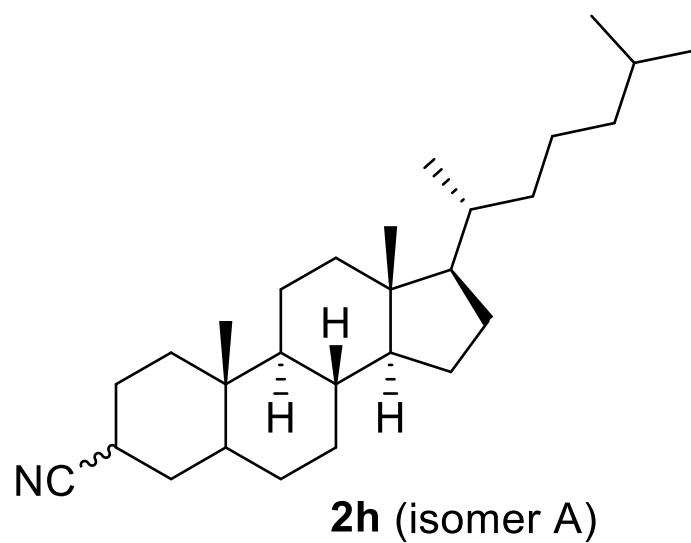
¹³C NMR (100 MHz, CDCl₃)



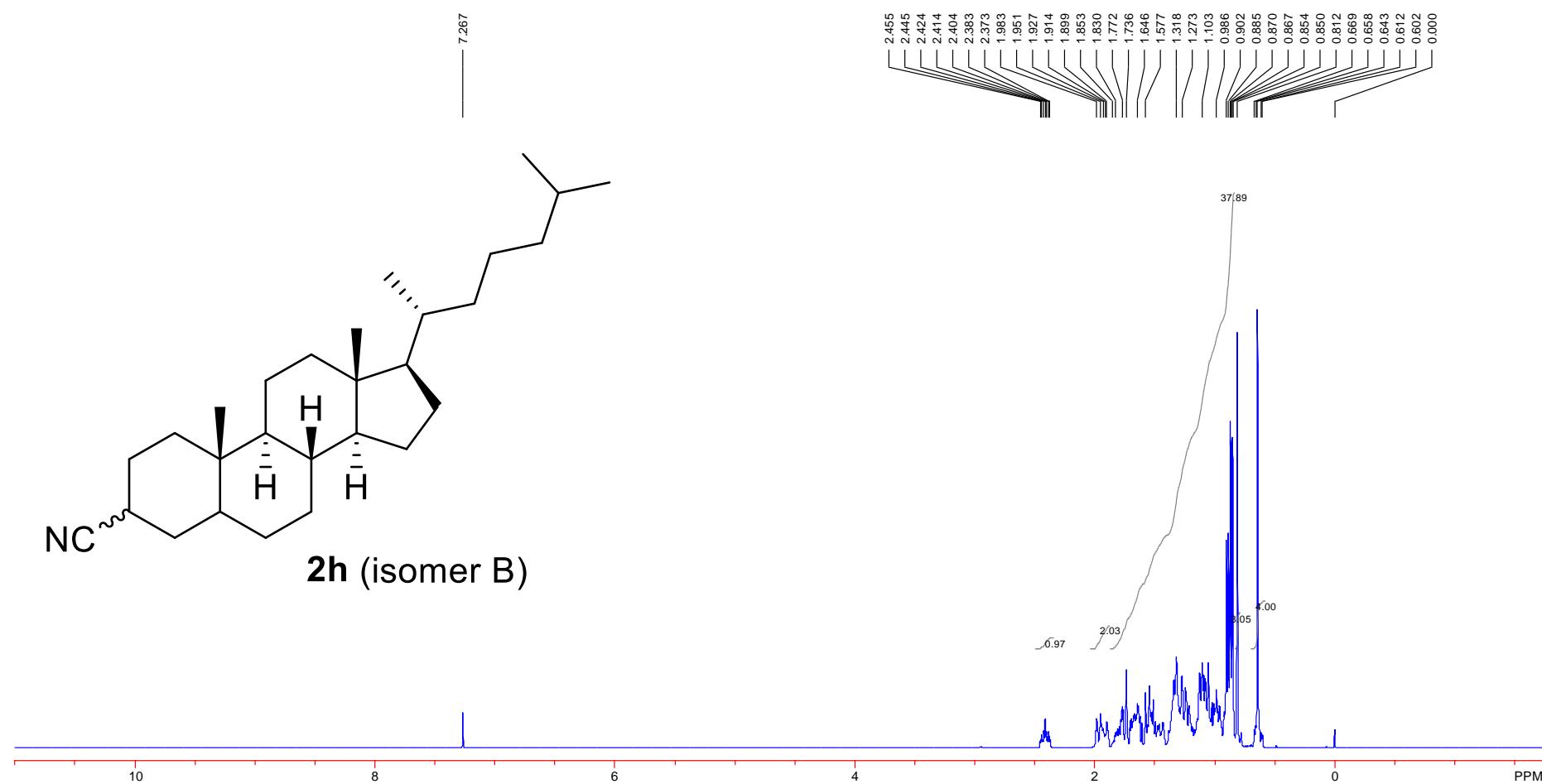
¹H NMR (400 MHz, CDCl₃)



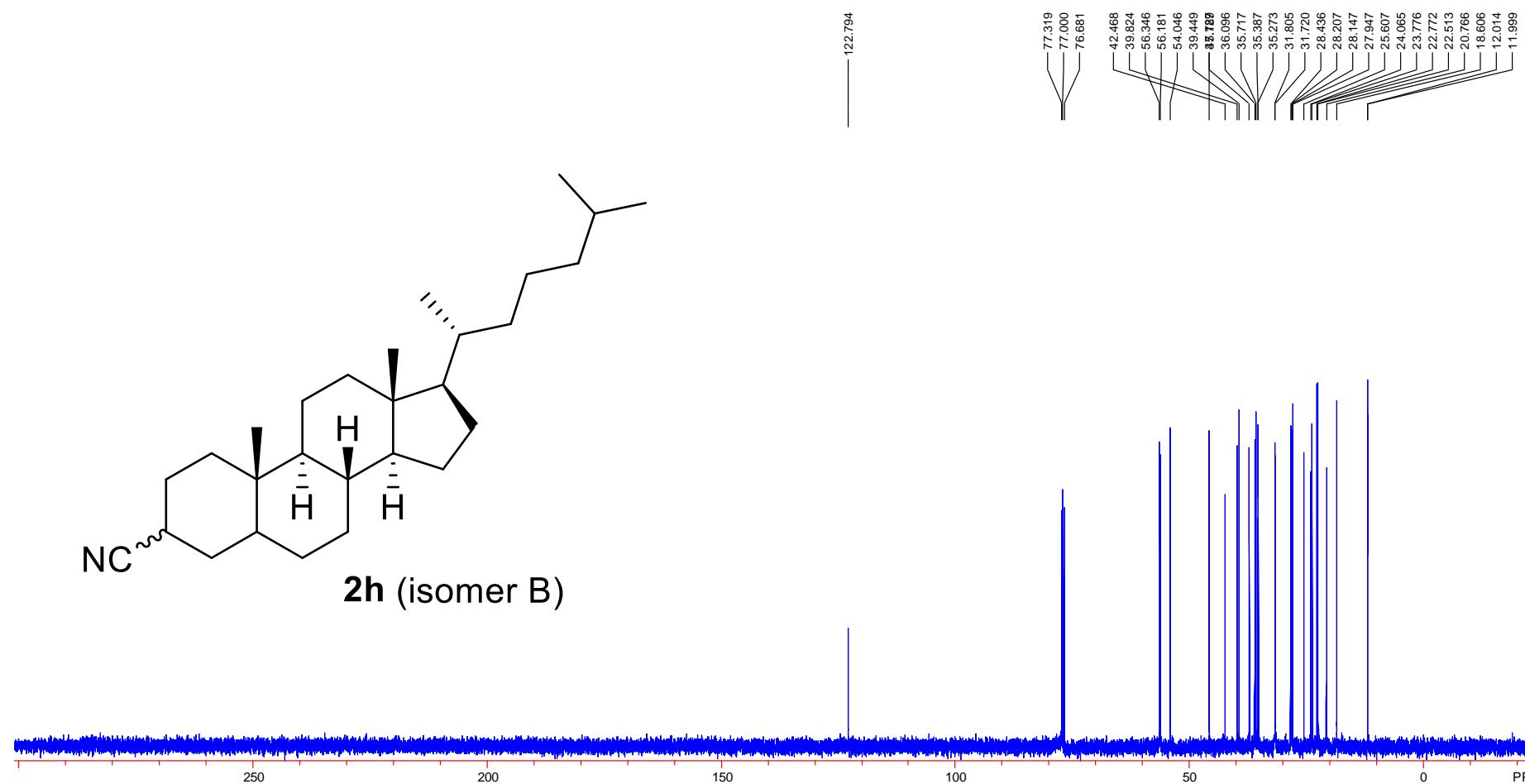
¹³C NMR (100 MHz, CDCl₃)



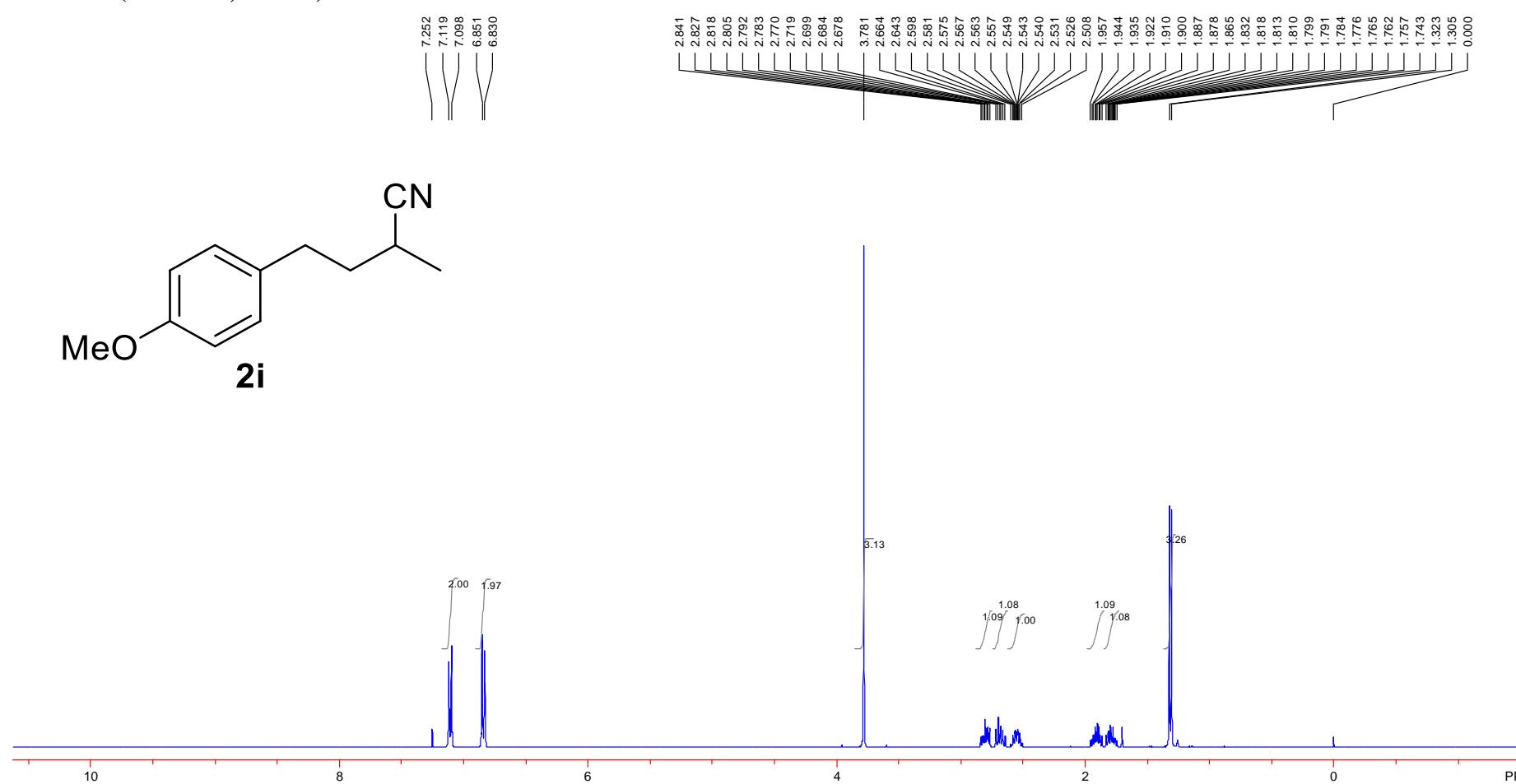
¹H NMR (400 MHz, CDCl₃)



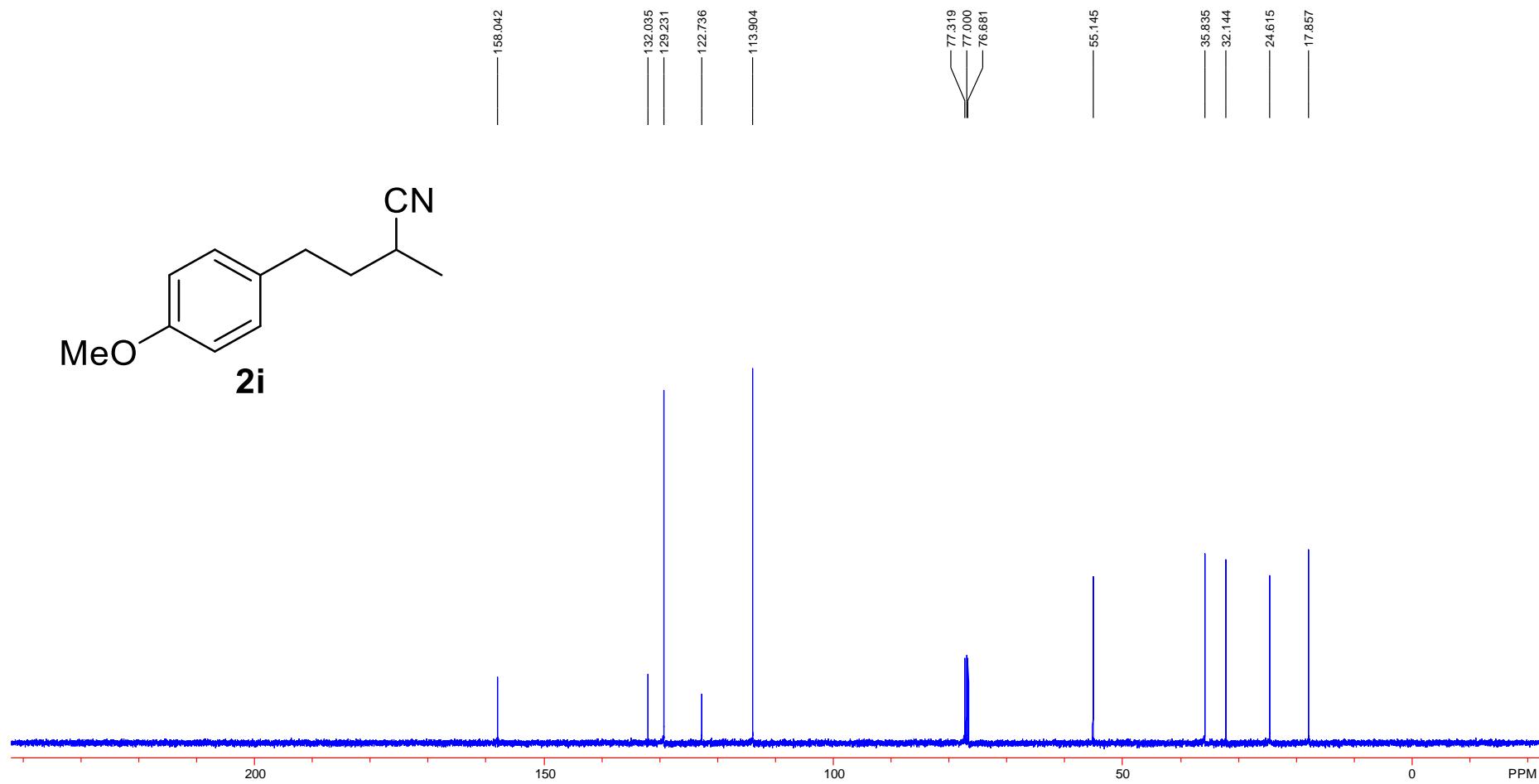
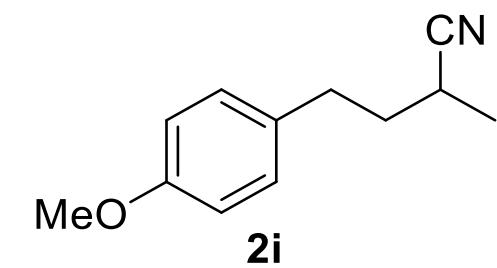
¹³C NMR (100 MHz, CDCl₃)



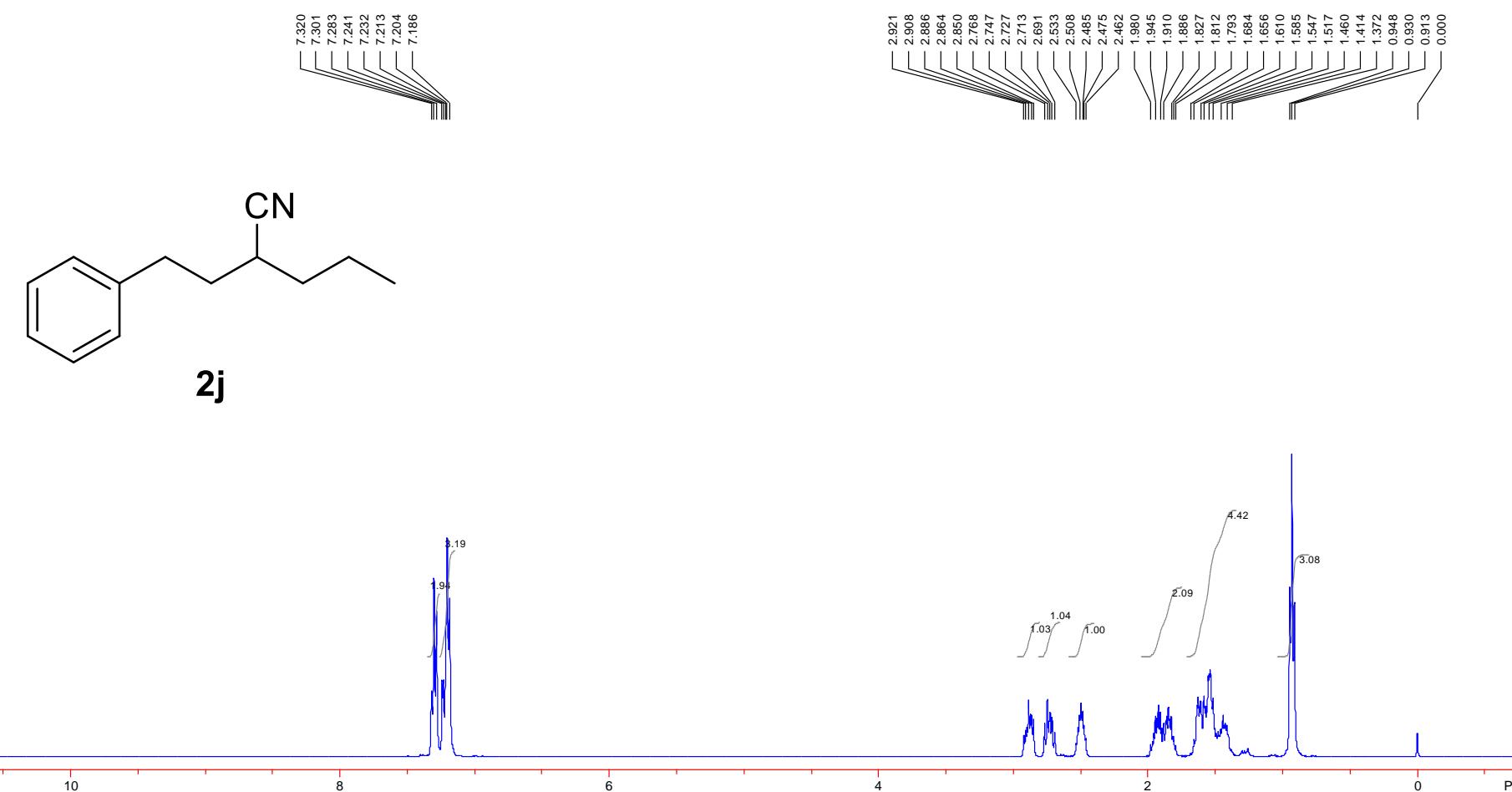
¹H NMR (400 MHz, CDCl₃)



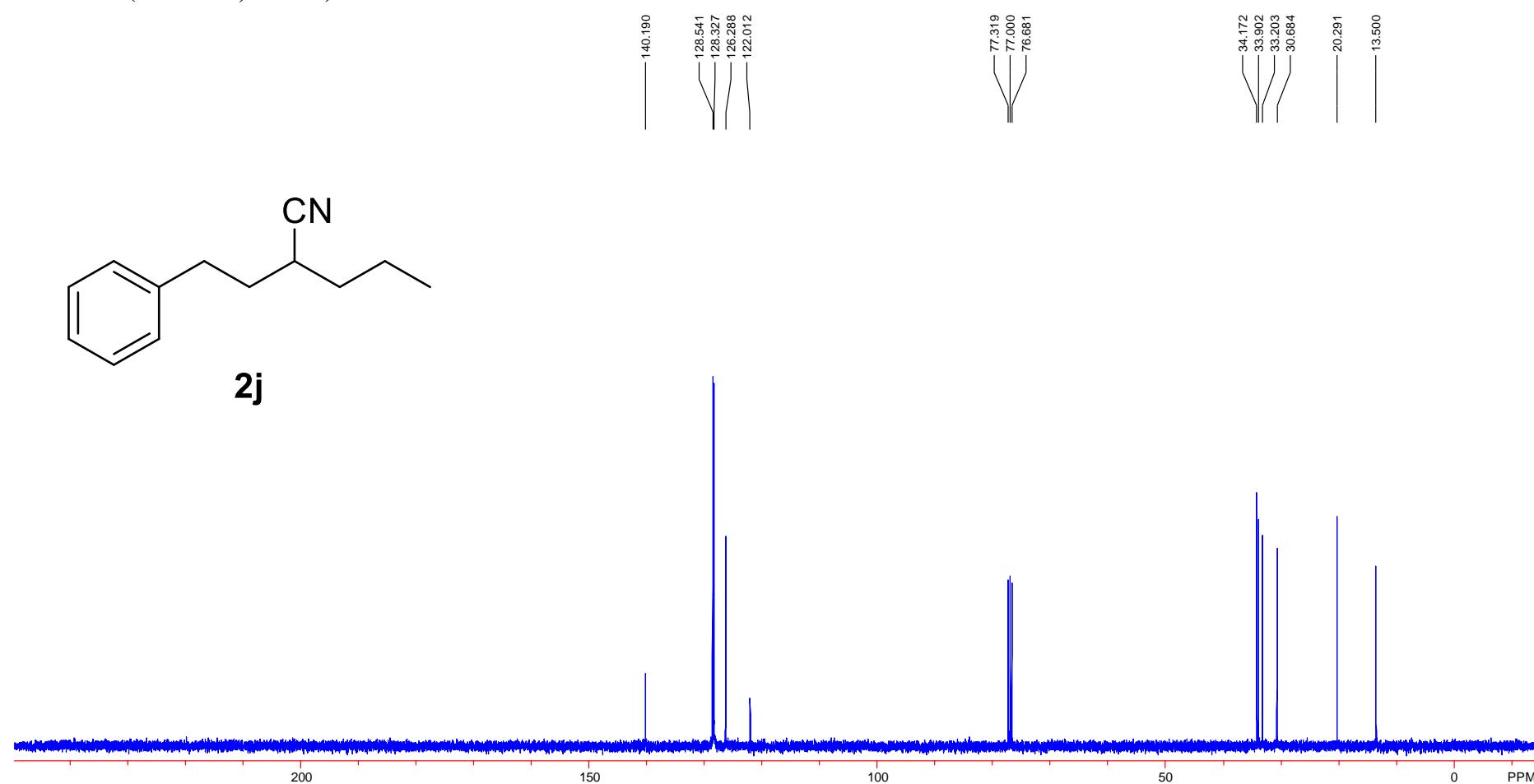
¹³C NMR (100 MHz, CDCl₃)



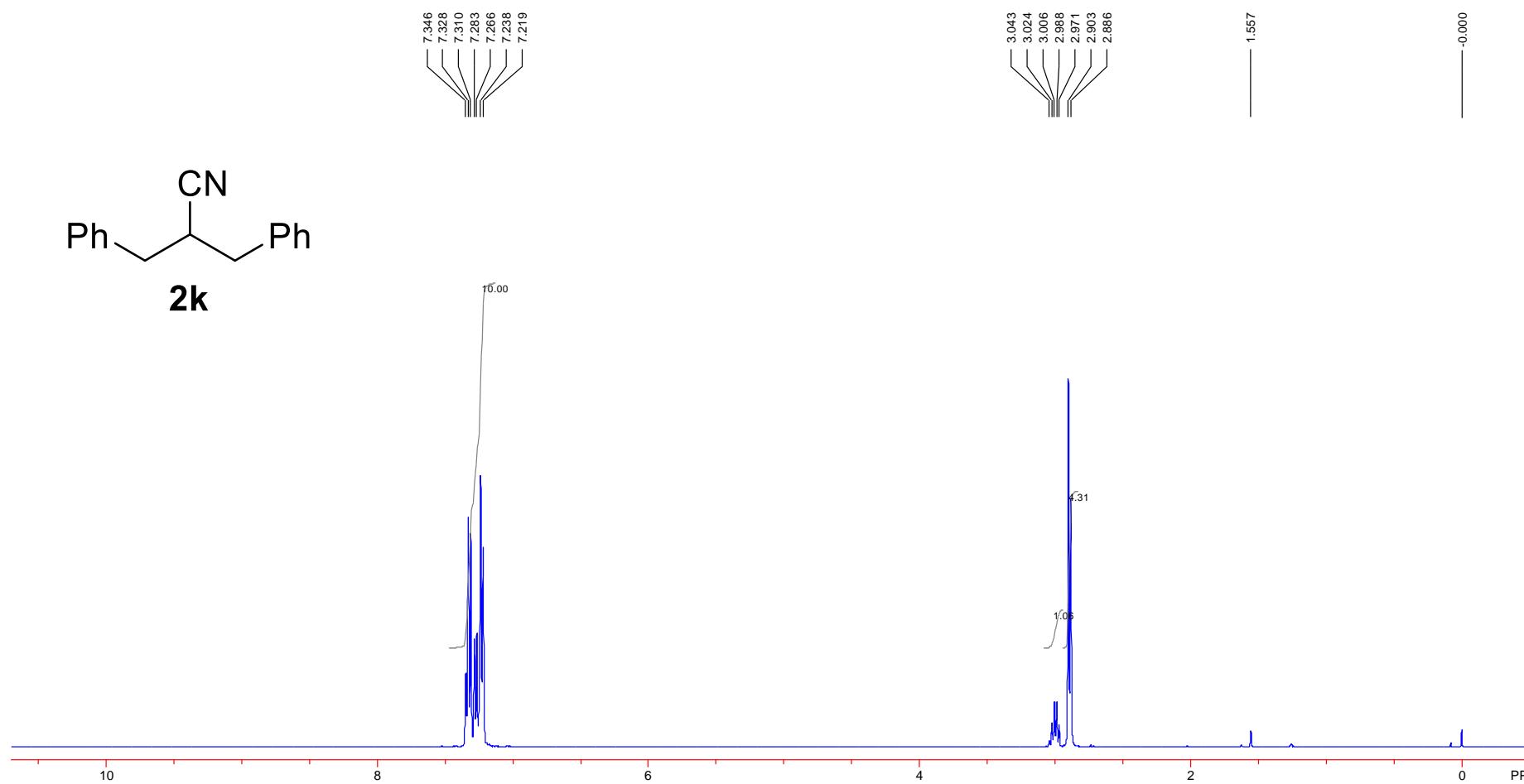
¹H NMR (400 MHz, CDCl₃)



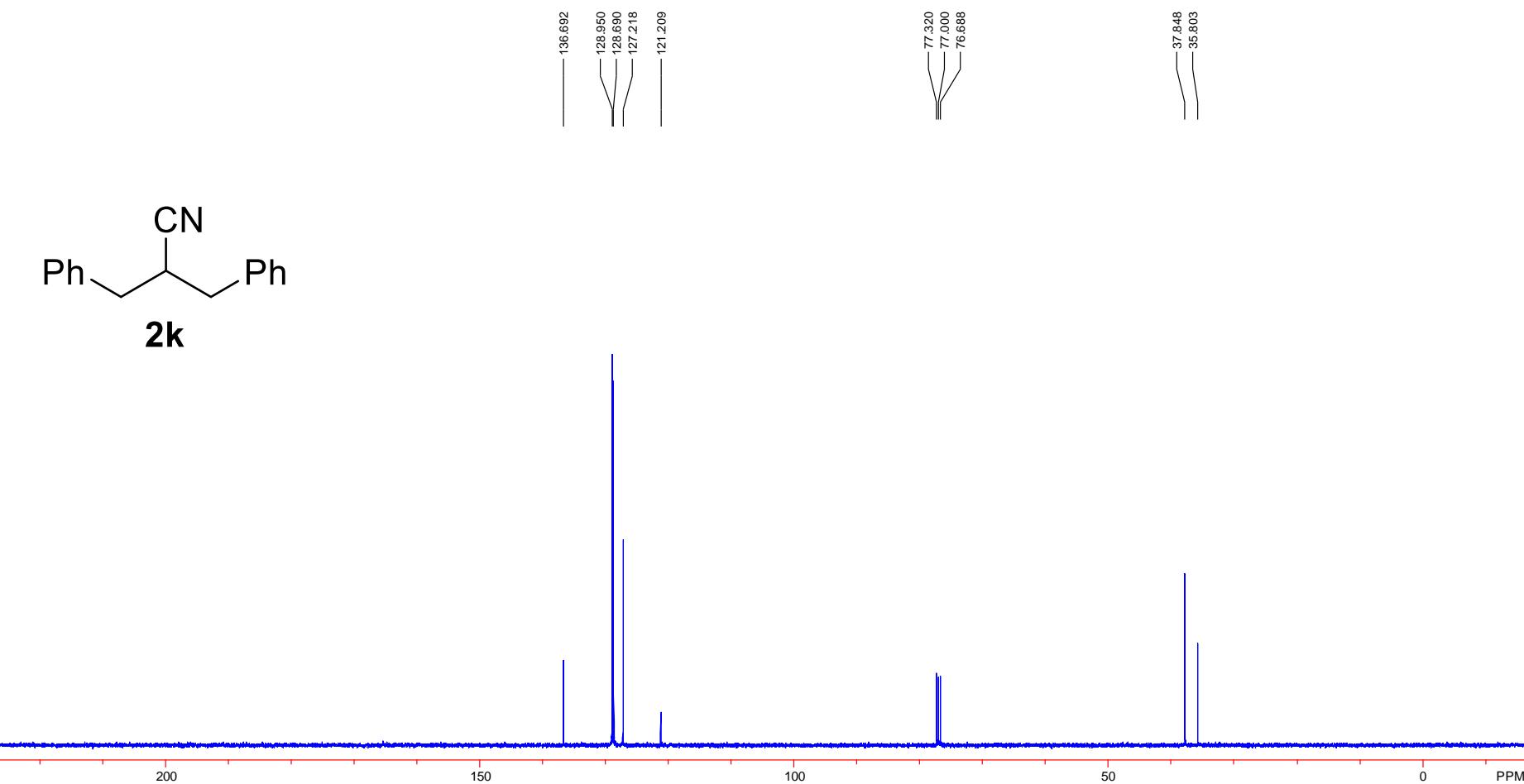
¹³C NMR (100 MHz, CDCl₃)



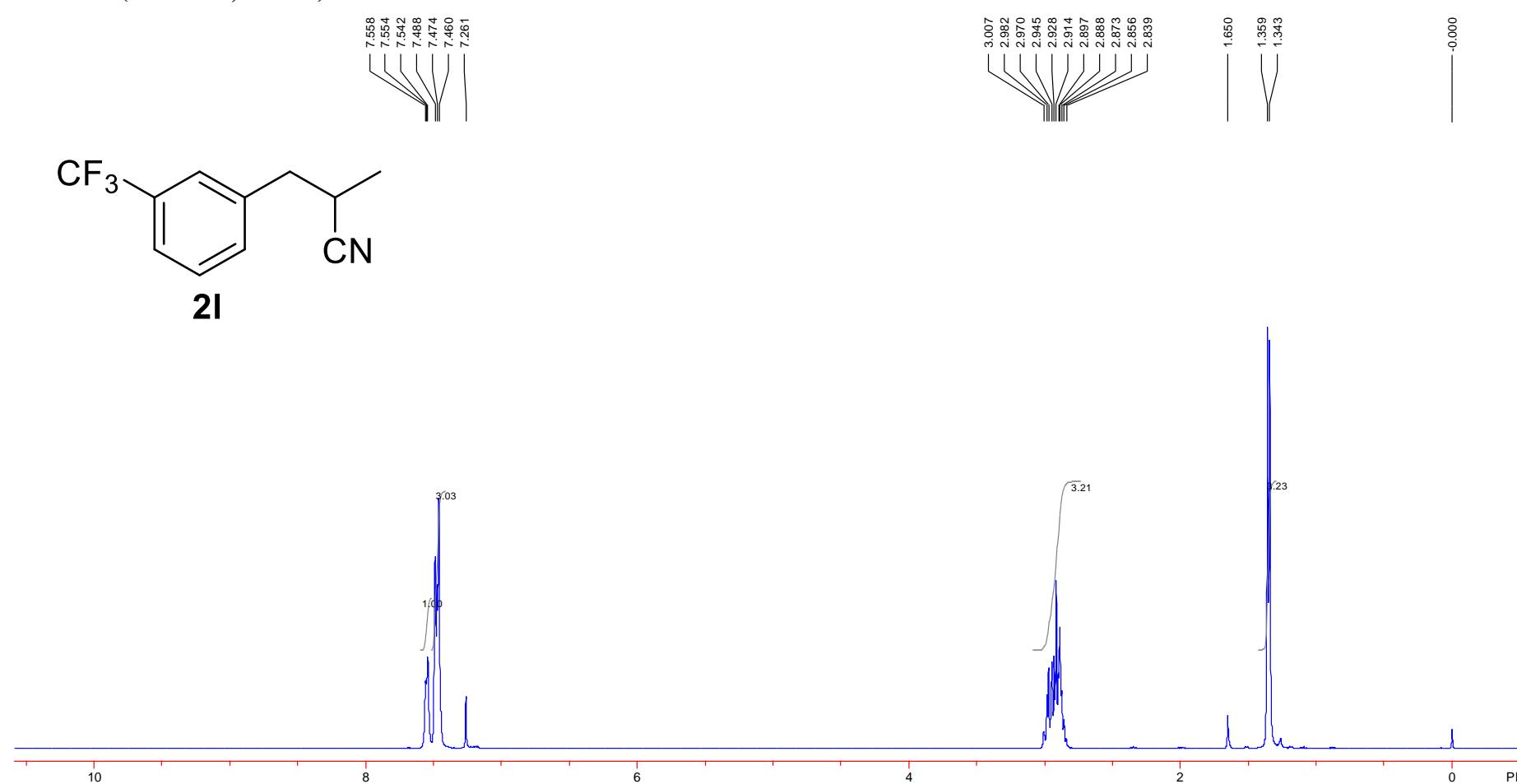
¹H NMR (400 MHz, CDCl₃)



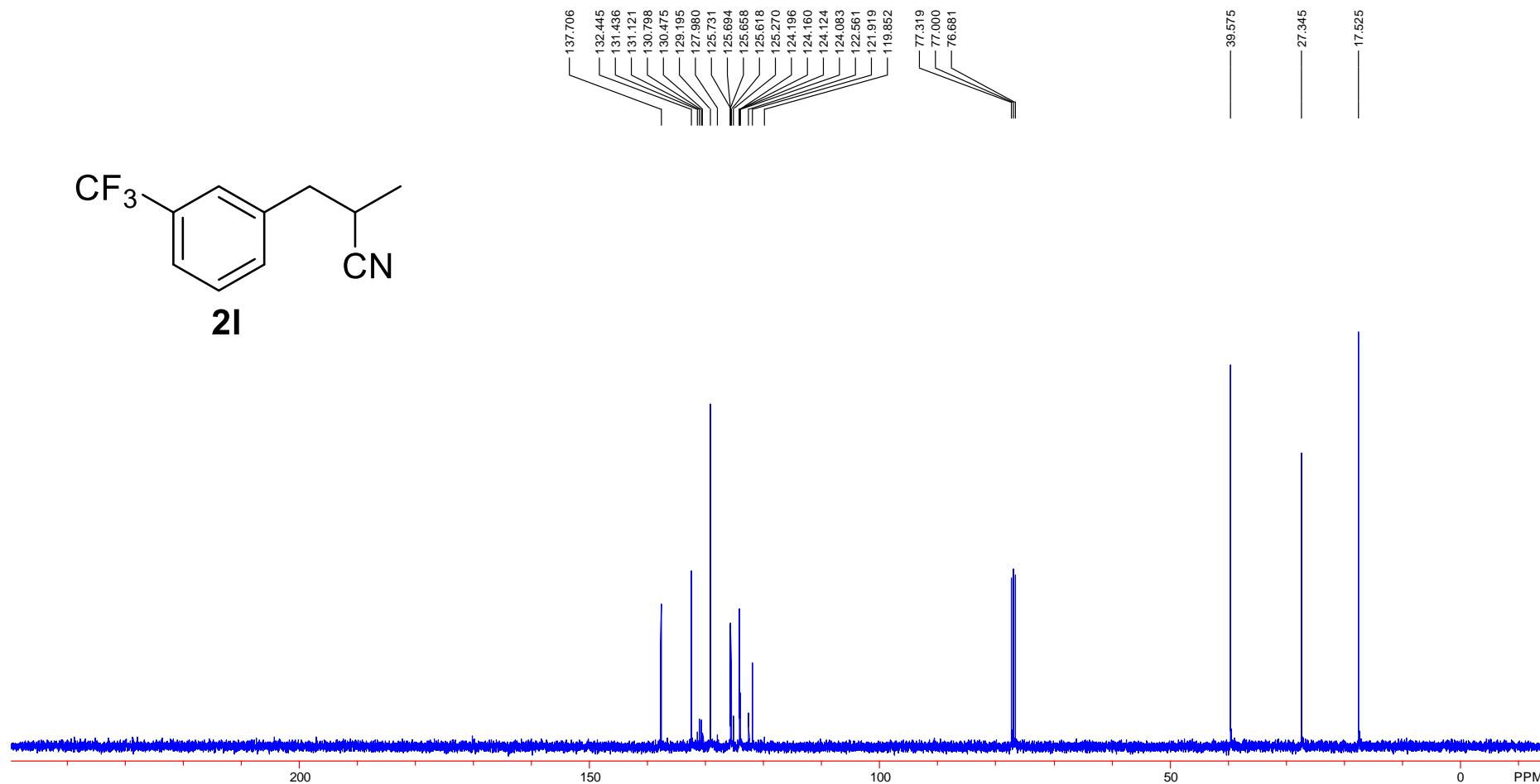
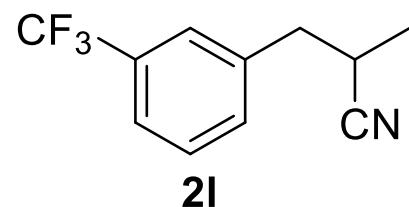
¹³C NMR (100 MHz, CDCl₃)



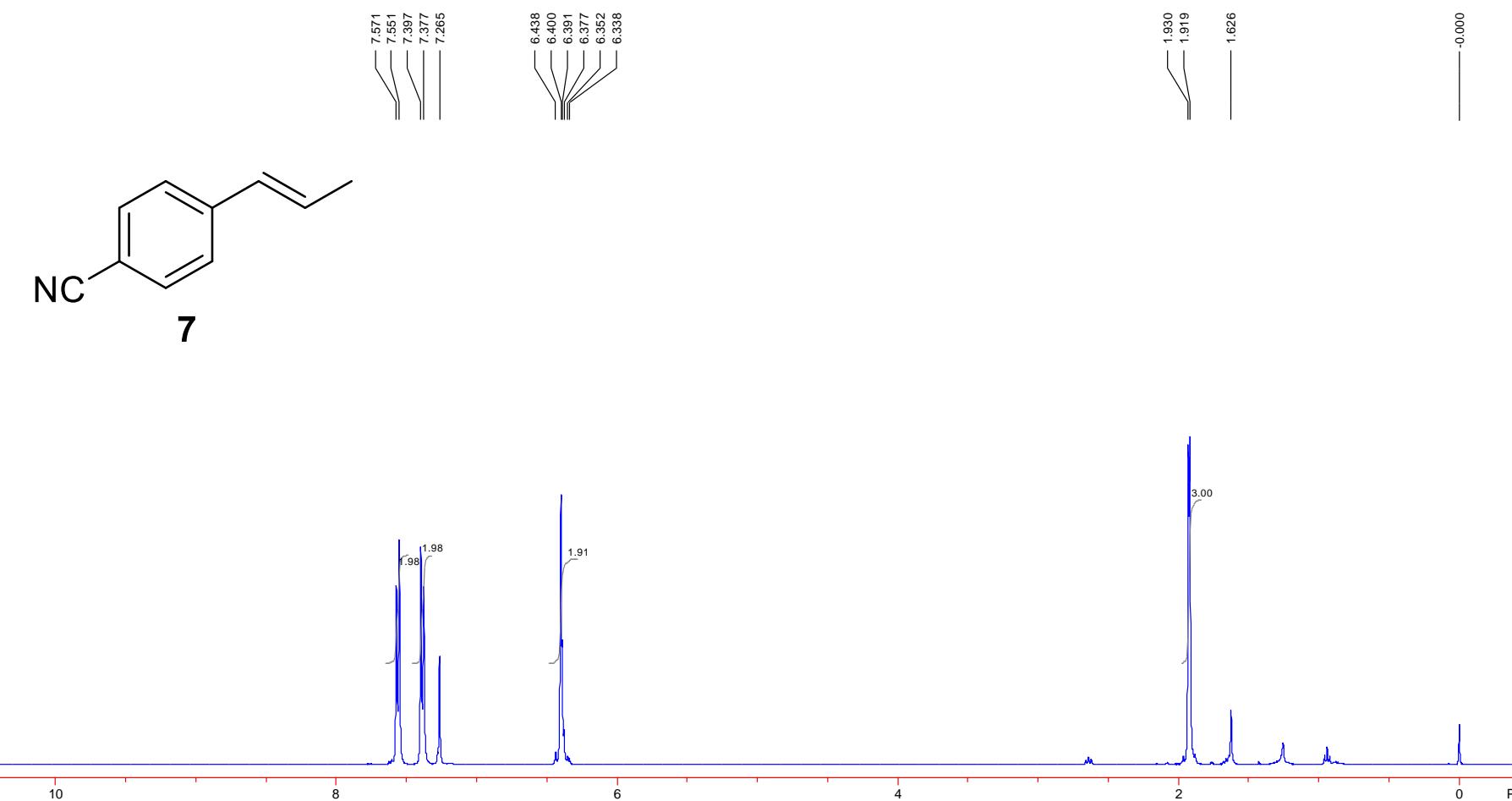
¹H NMR (400 MHz, CDCl₃)



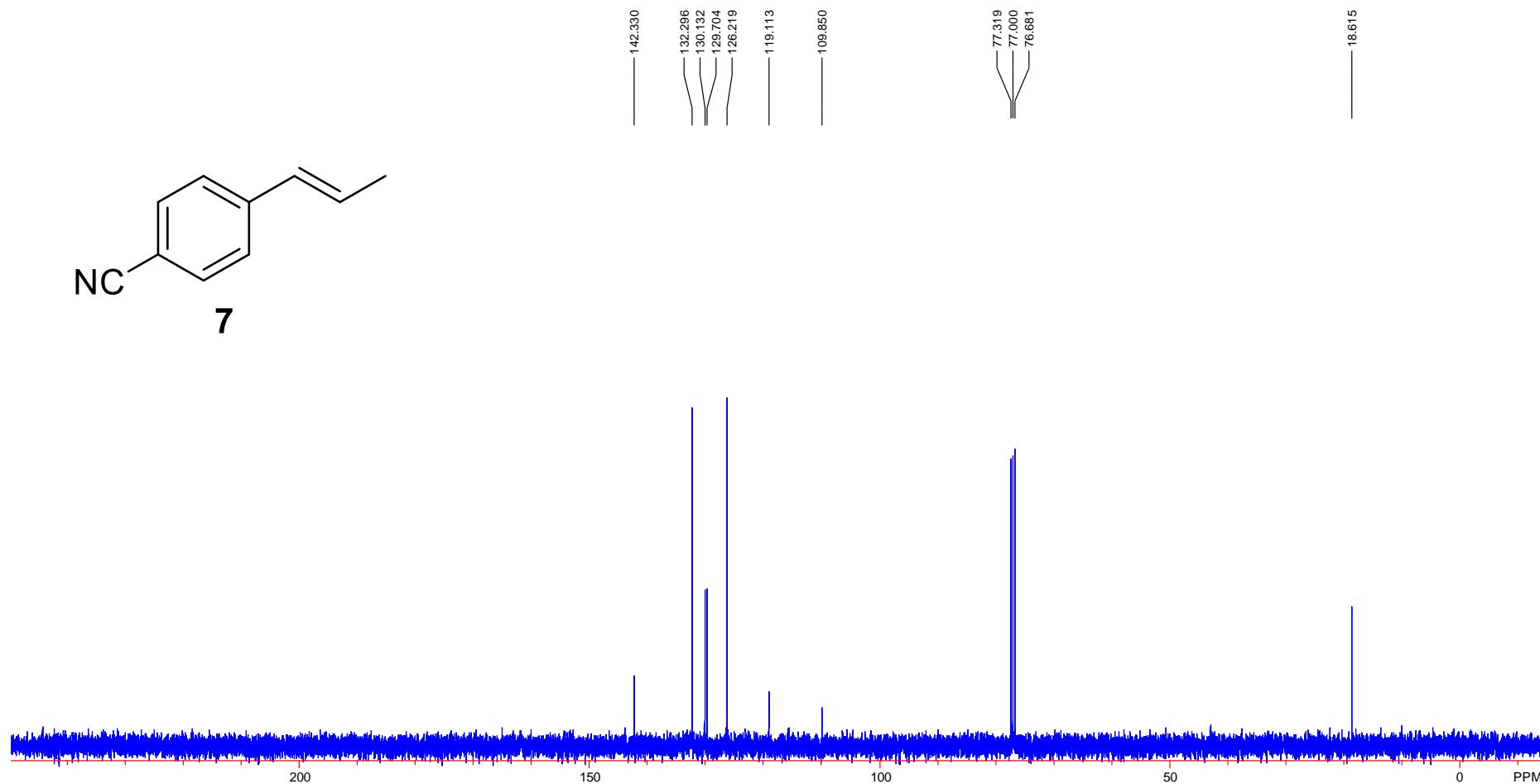
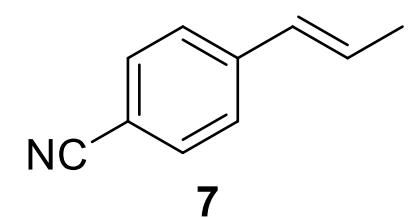
¹³C NMR (100 MHz, CDCl₃)



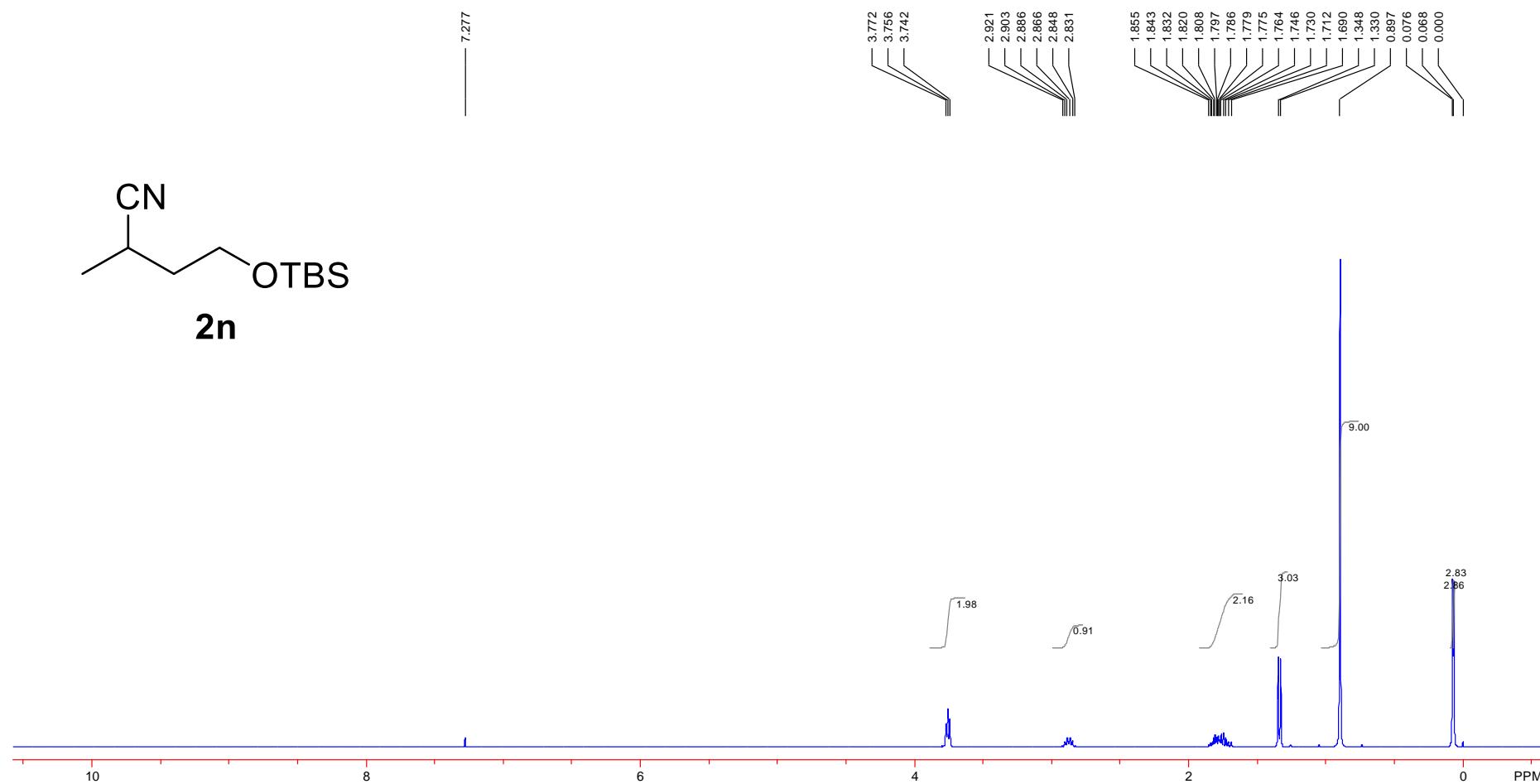
¹H NMR (400 MHz, CDCl₃)



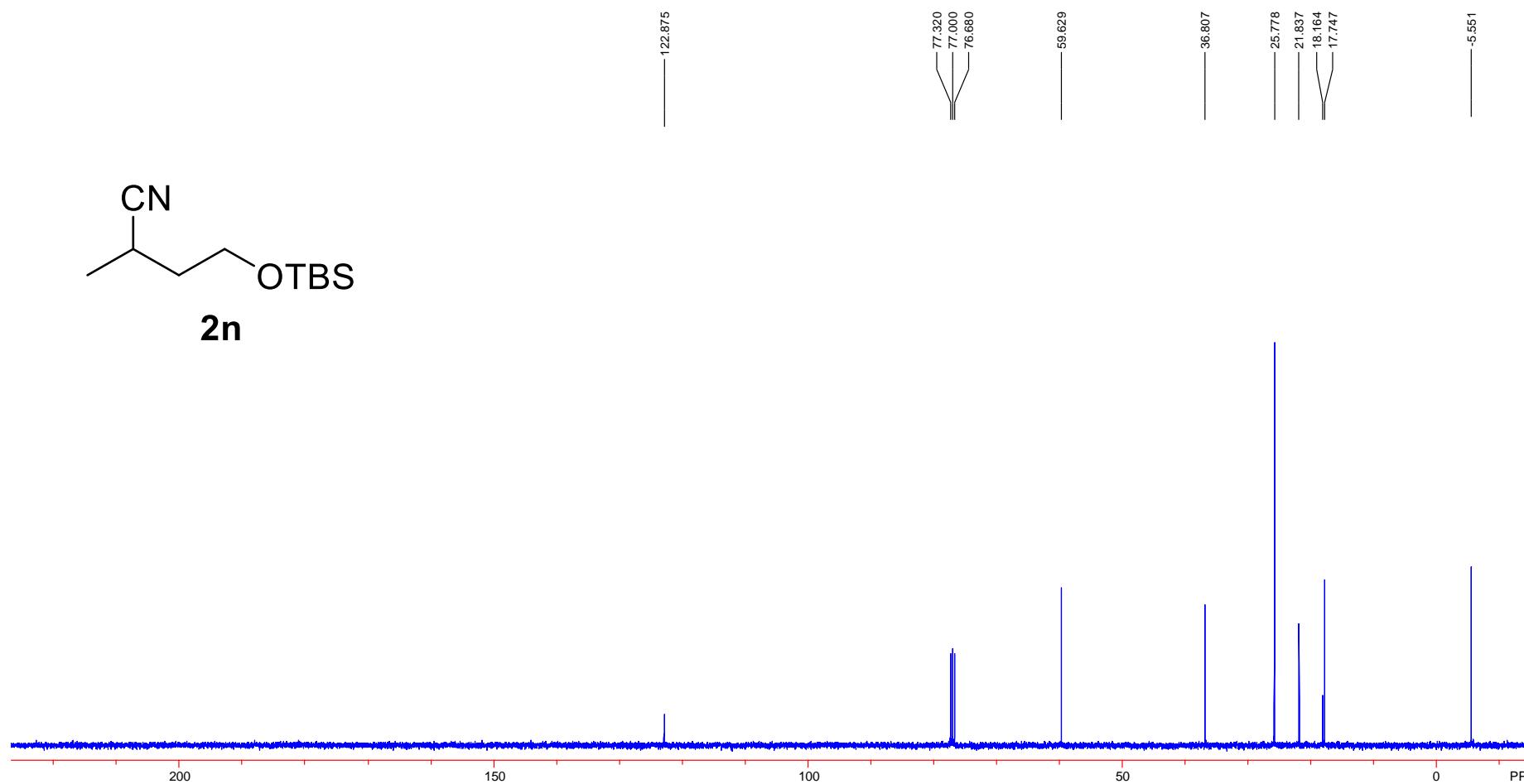
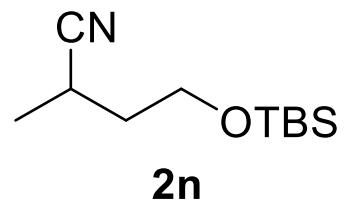
¹³C NMR (100 MHz, CDCl₃)



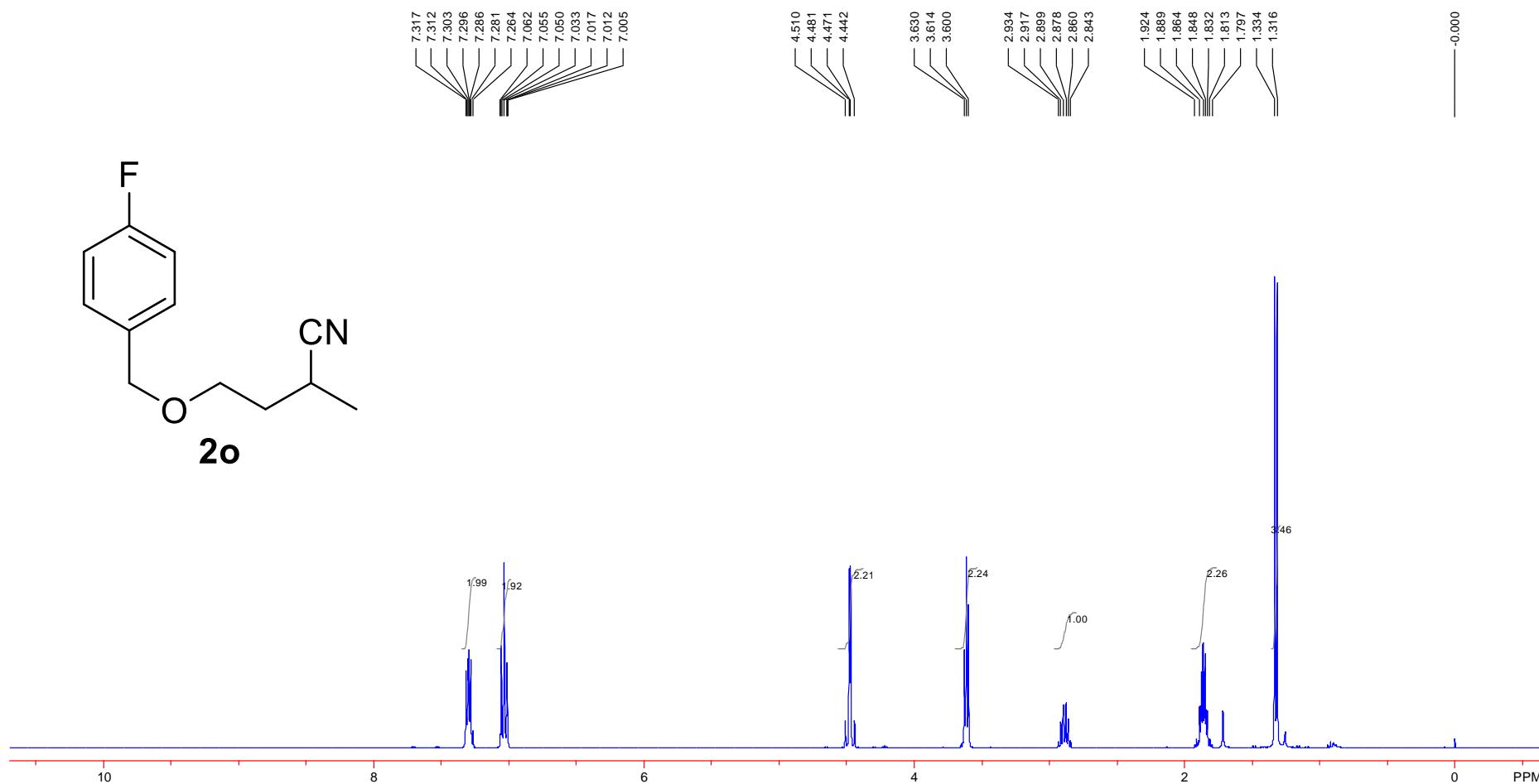
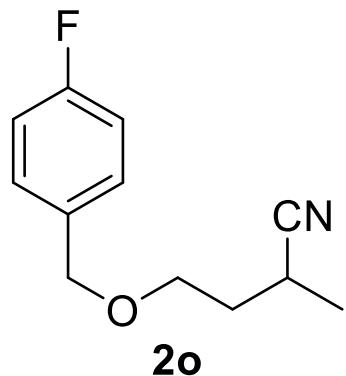
¹H NMR (400 MHz, CDCl₃)



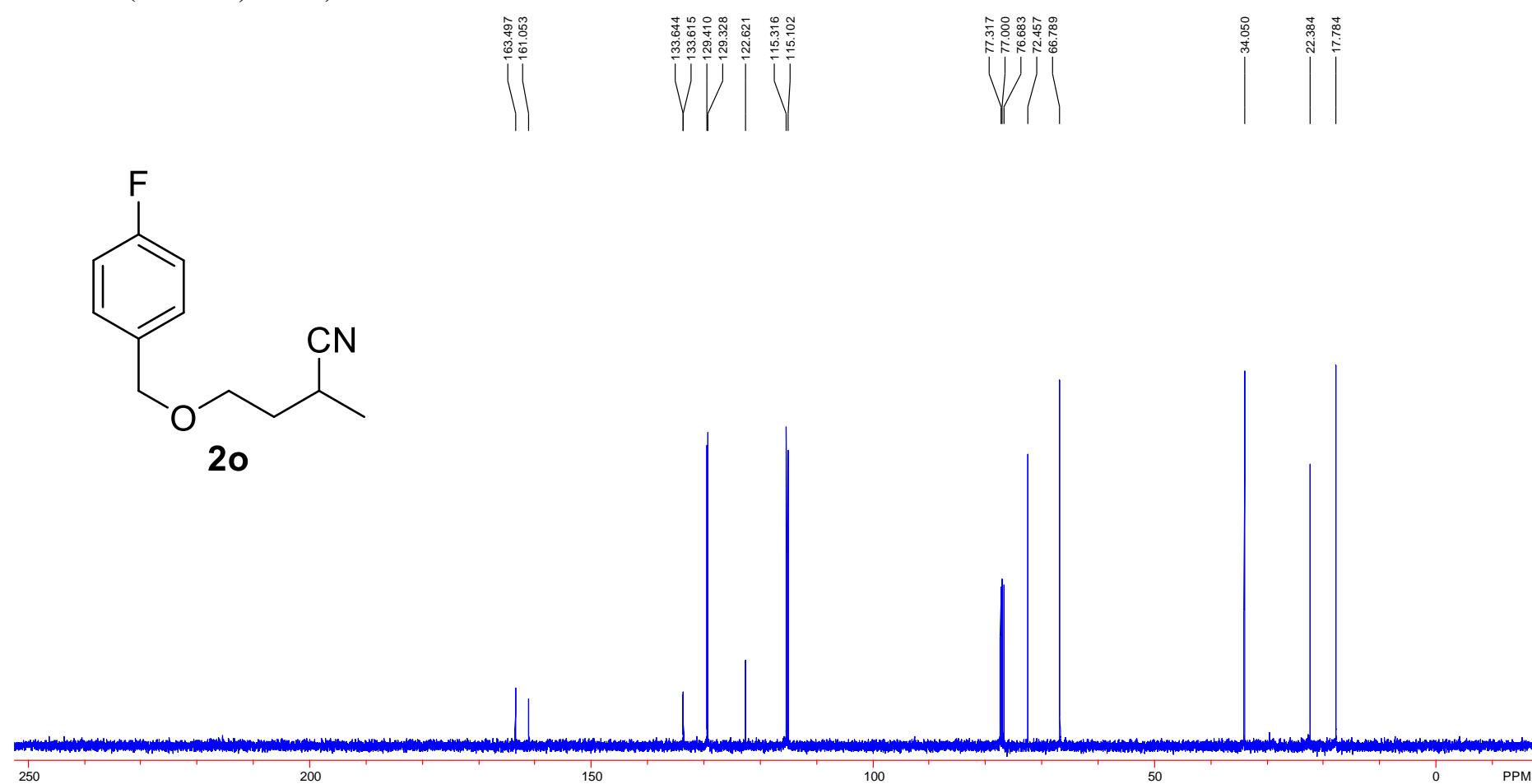
¹³C NMR (100 MHz, CDCl₃)



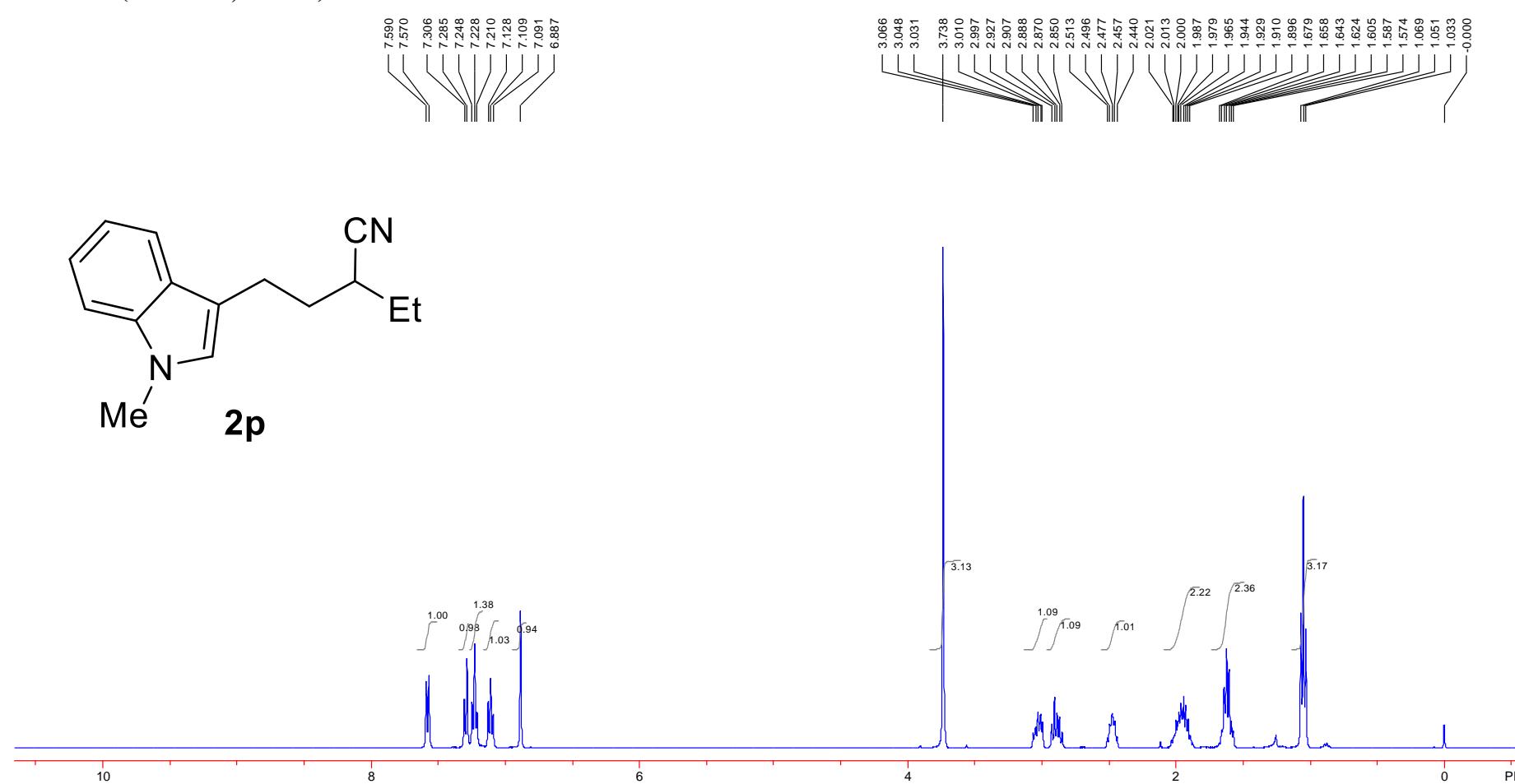
¹H NMR (400 MHz, CDCl₃)



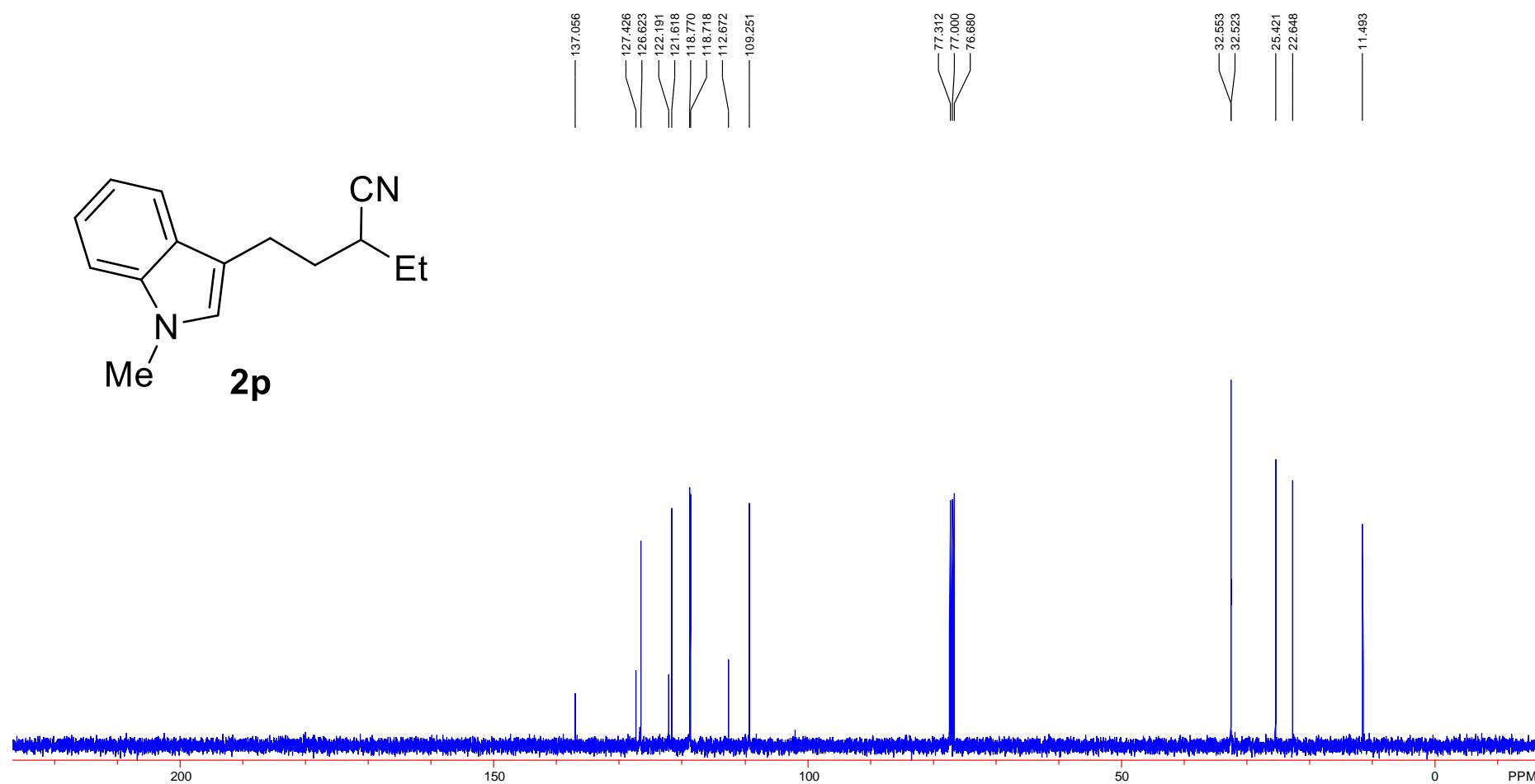
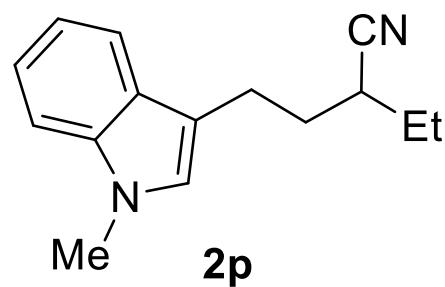
¹³C NMR (100 MHz, CDCl₃)



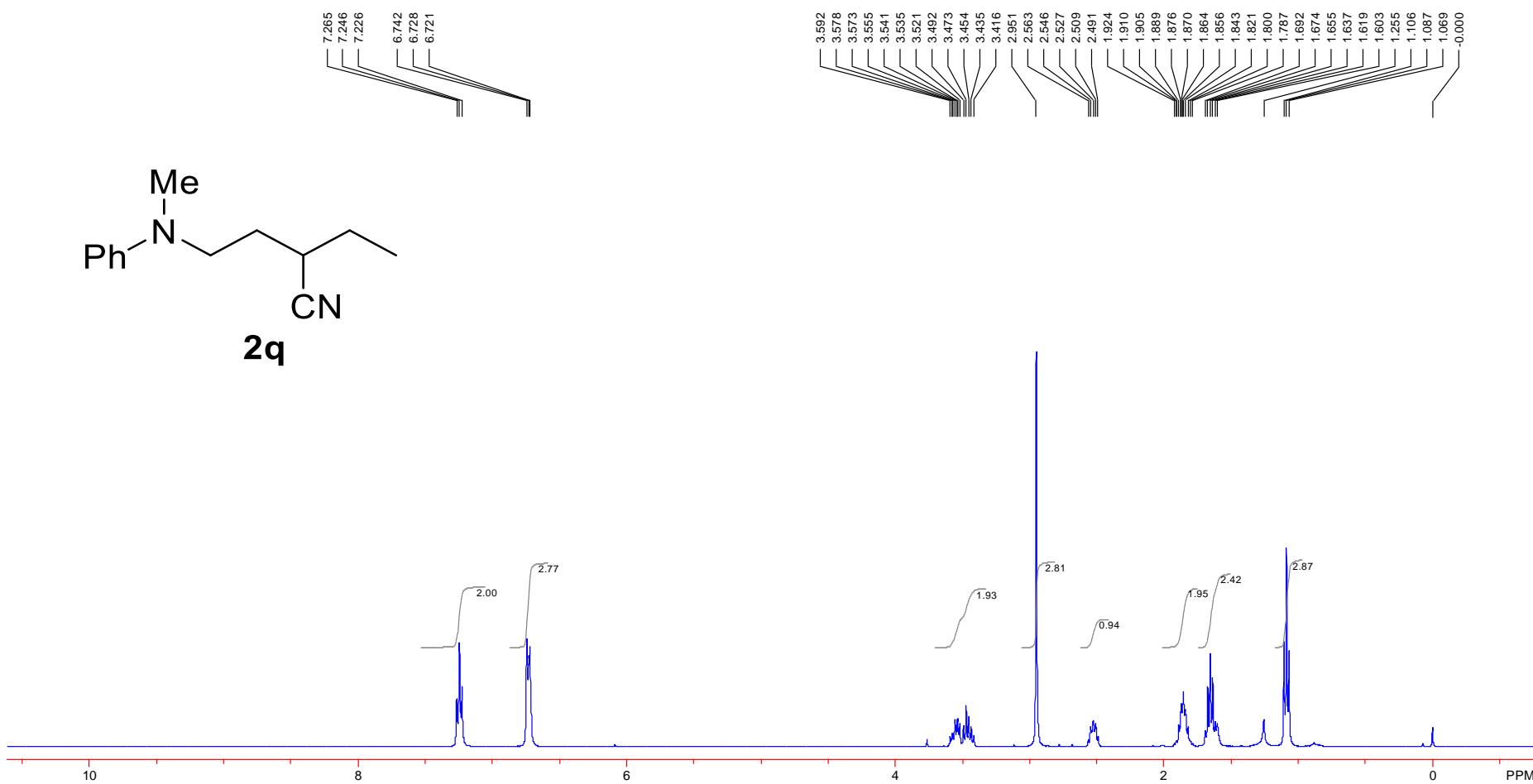
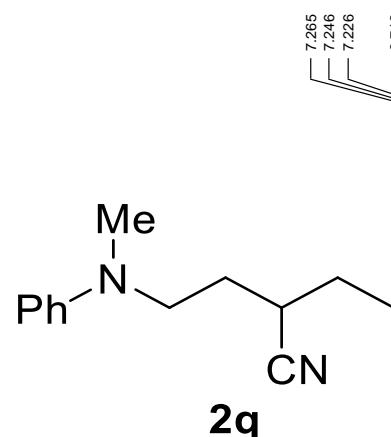
¹H NMR (400 MHz, CDCl₃)



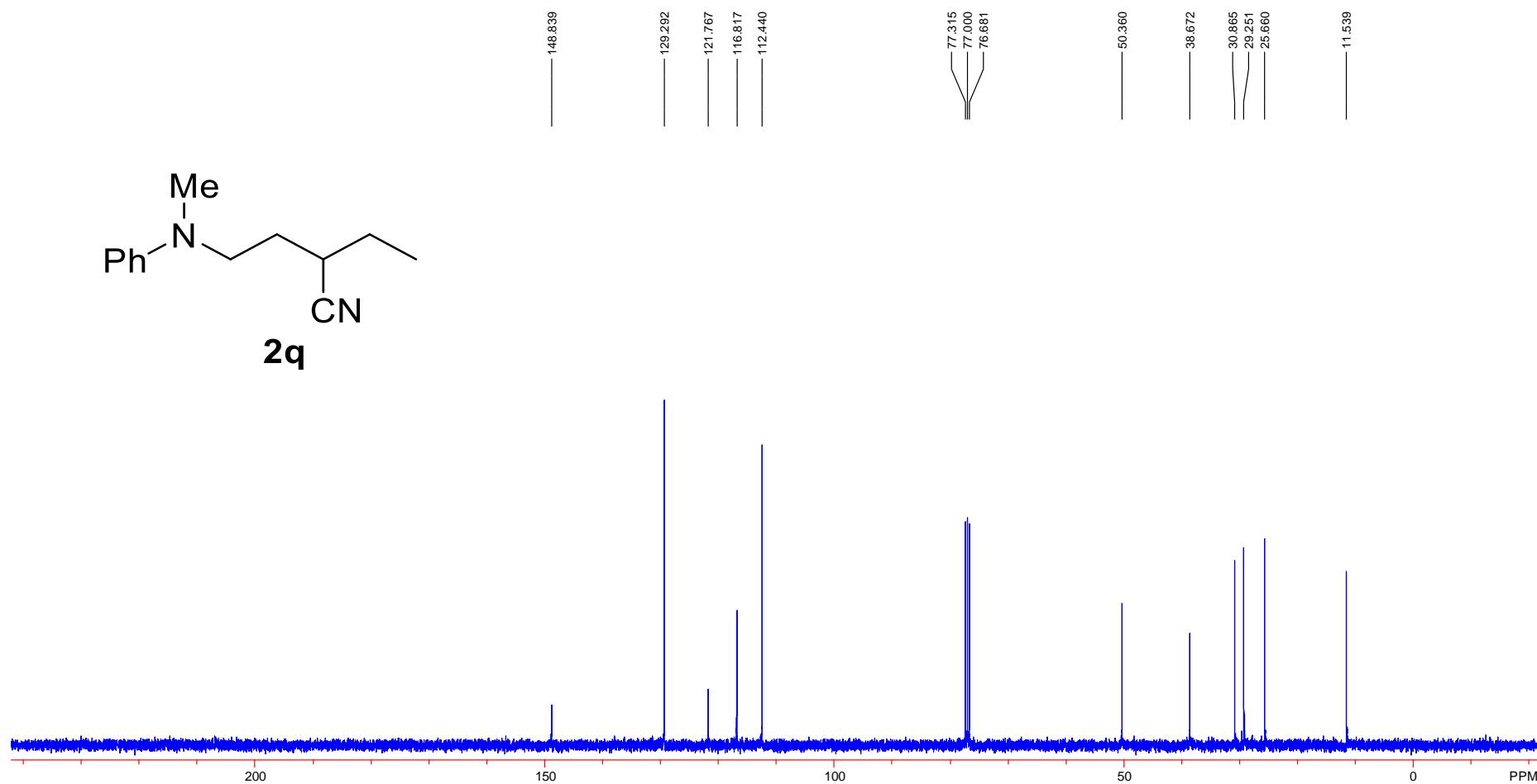
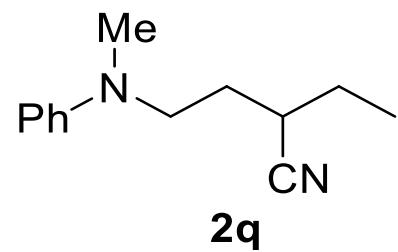
¹³C NMR (100 MHz, CDCl₃)



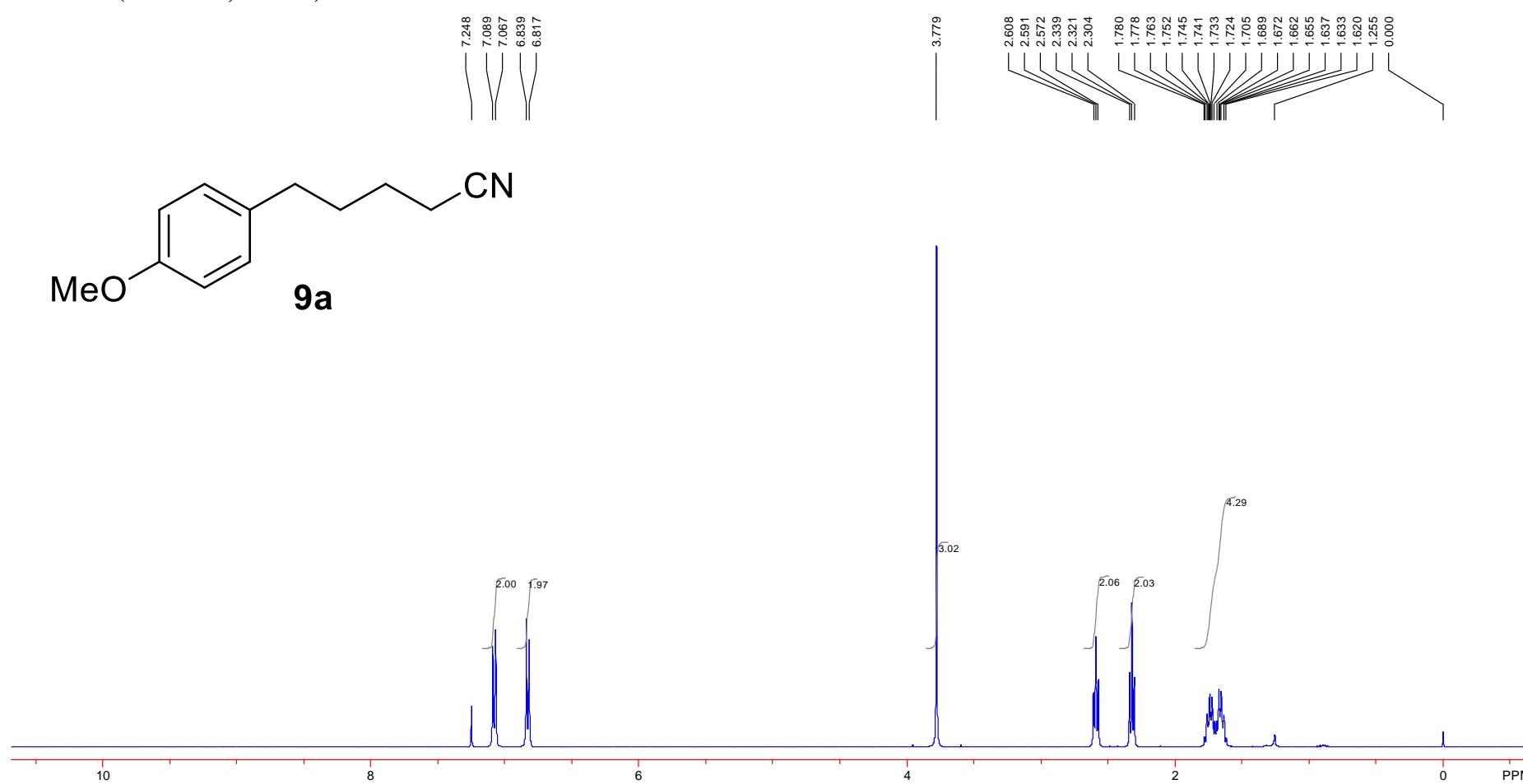
¹H NMR (400 MHz, CDCl₃)



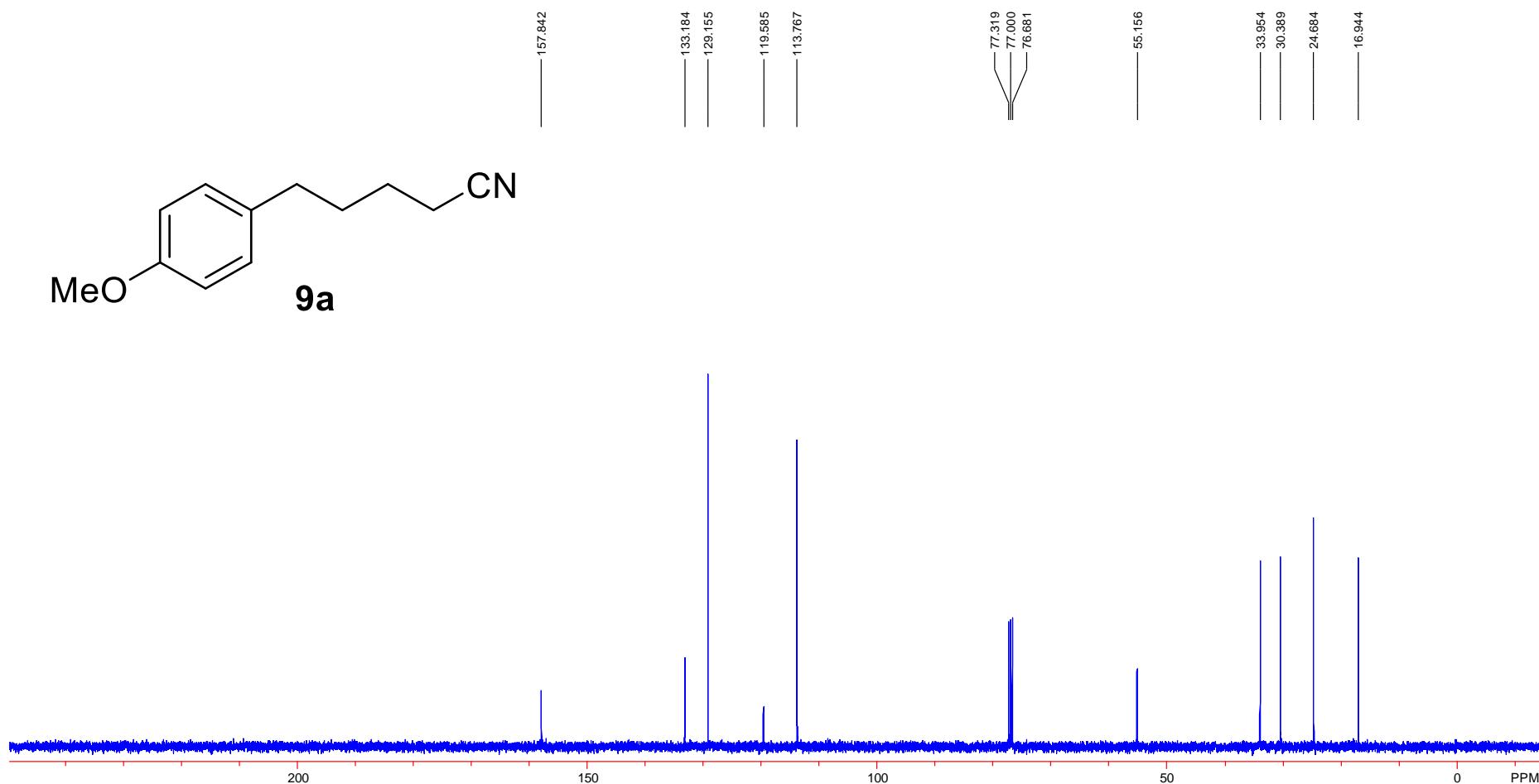
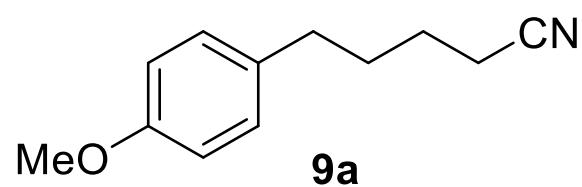
¹³C NMR (100 MHz, CDCl₃)



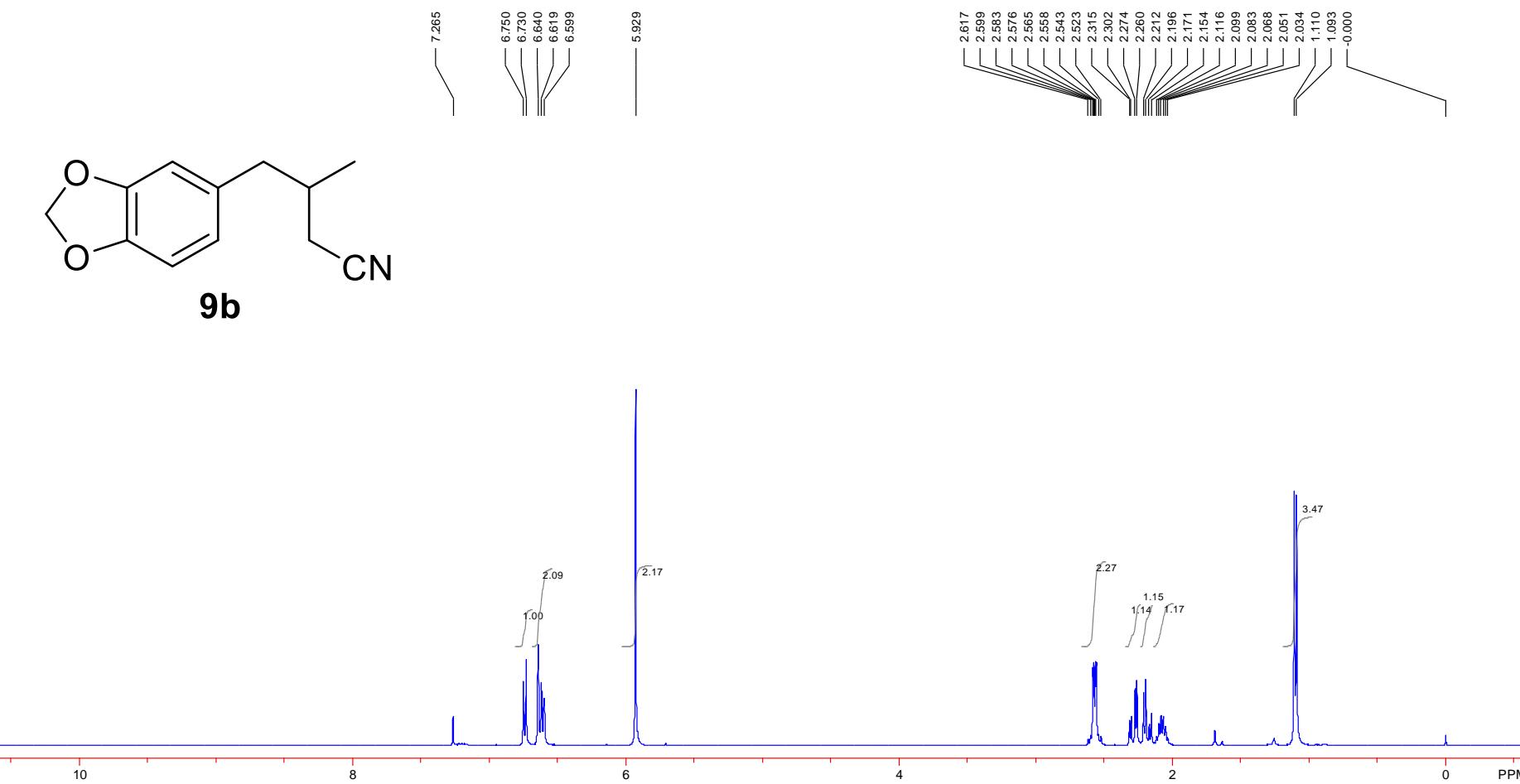
¹H NMR (400 MHz, CDCl₃)



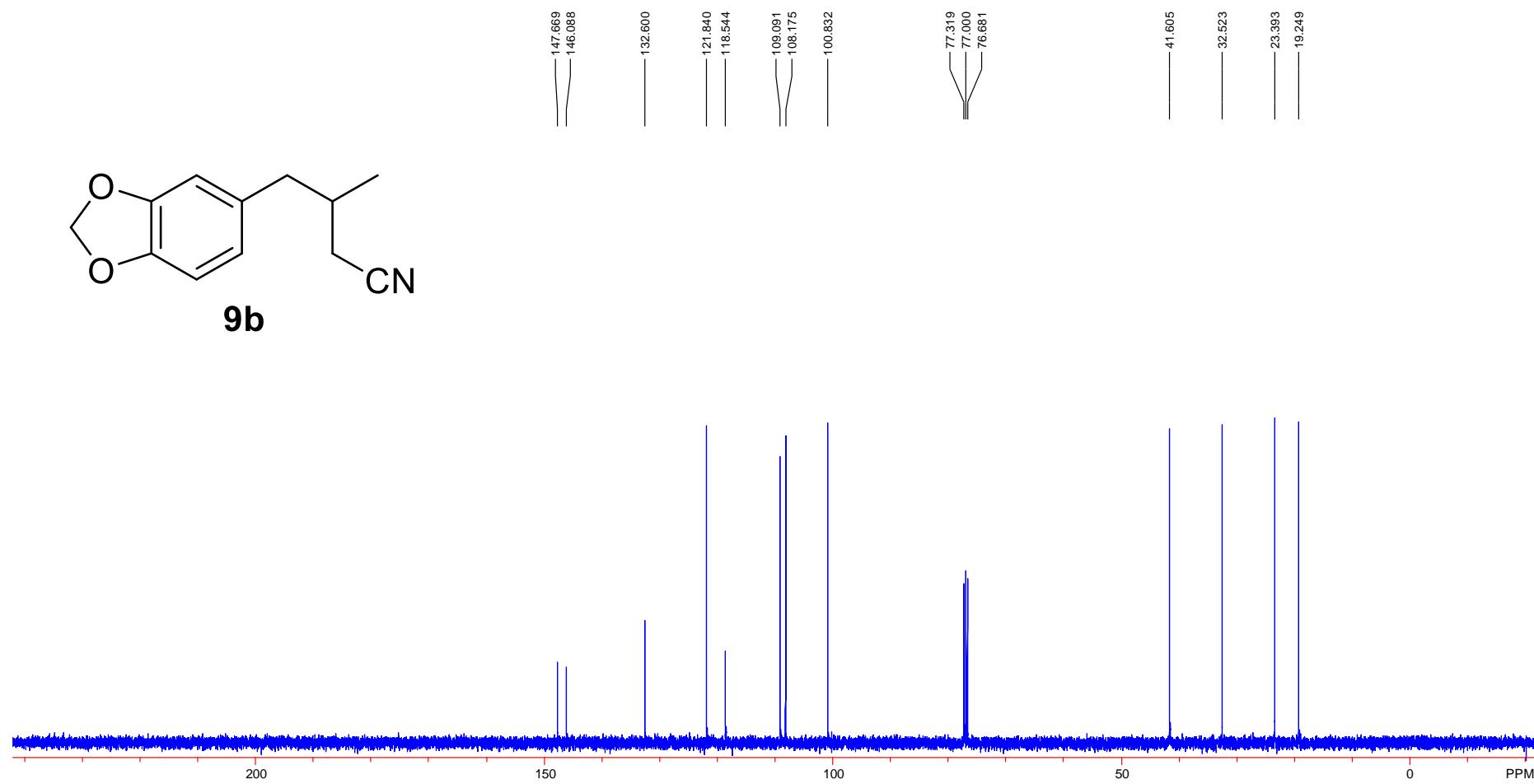
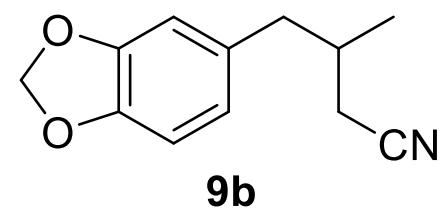
¹³C NMR (100 MHz, CDCl₃)



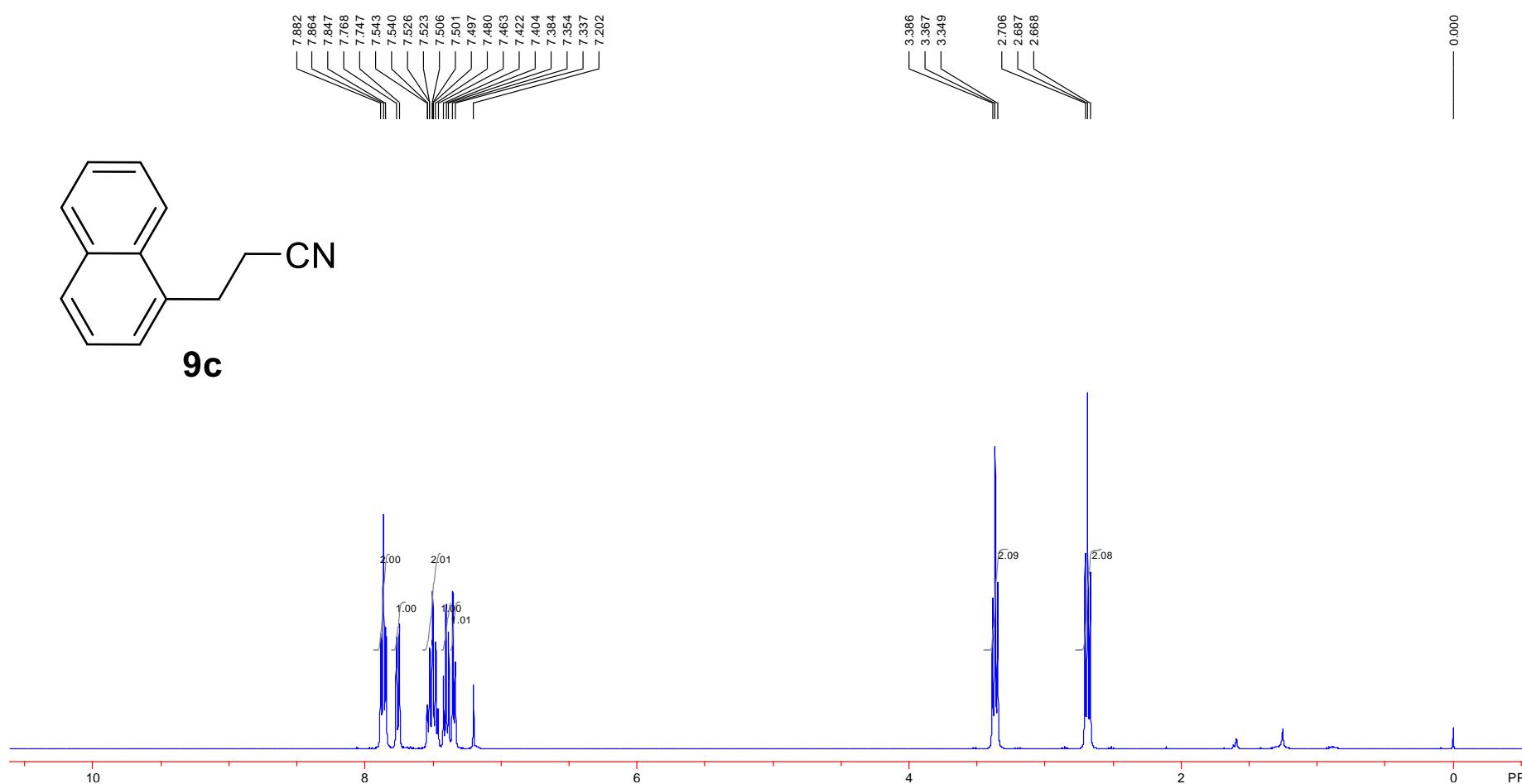
¹H NMR (400 MHz, CDCl₃)



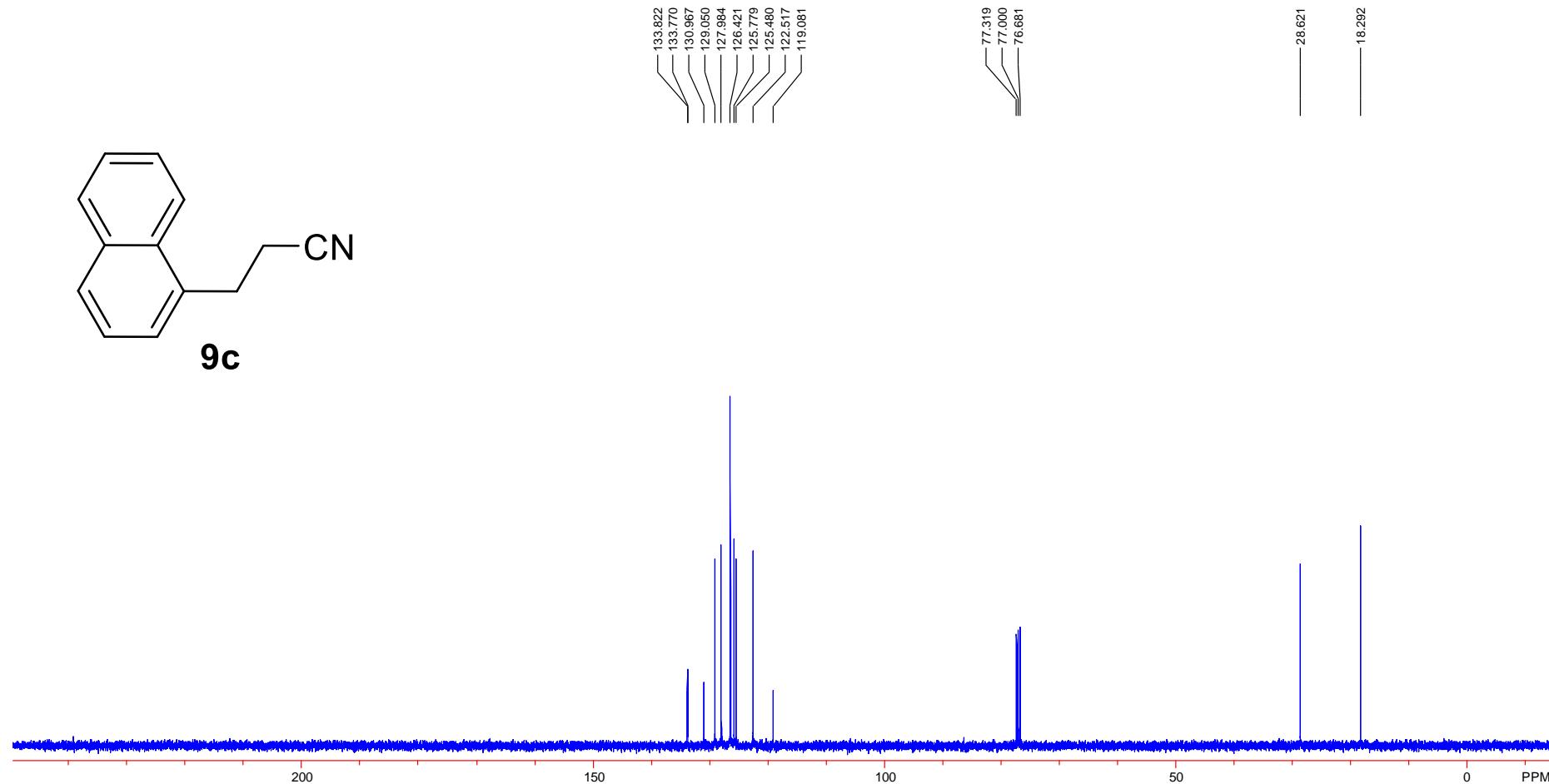
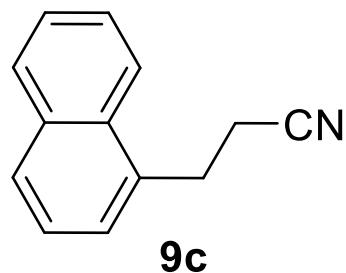
¹³C NMR (100 MHz, CDCl₃)



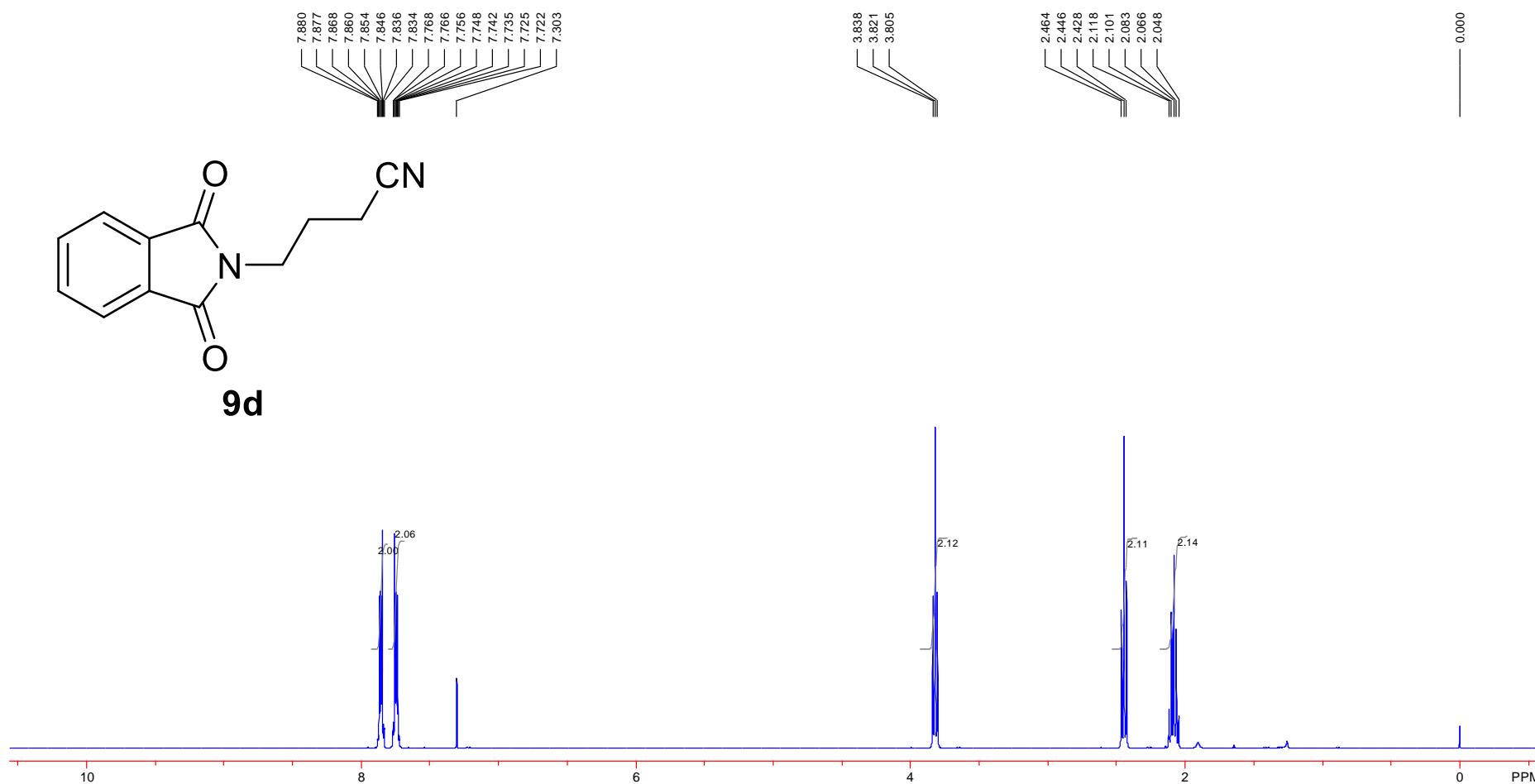
¹H NMR (400 MHz, CDCl₃)



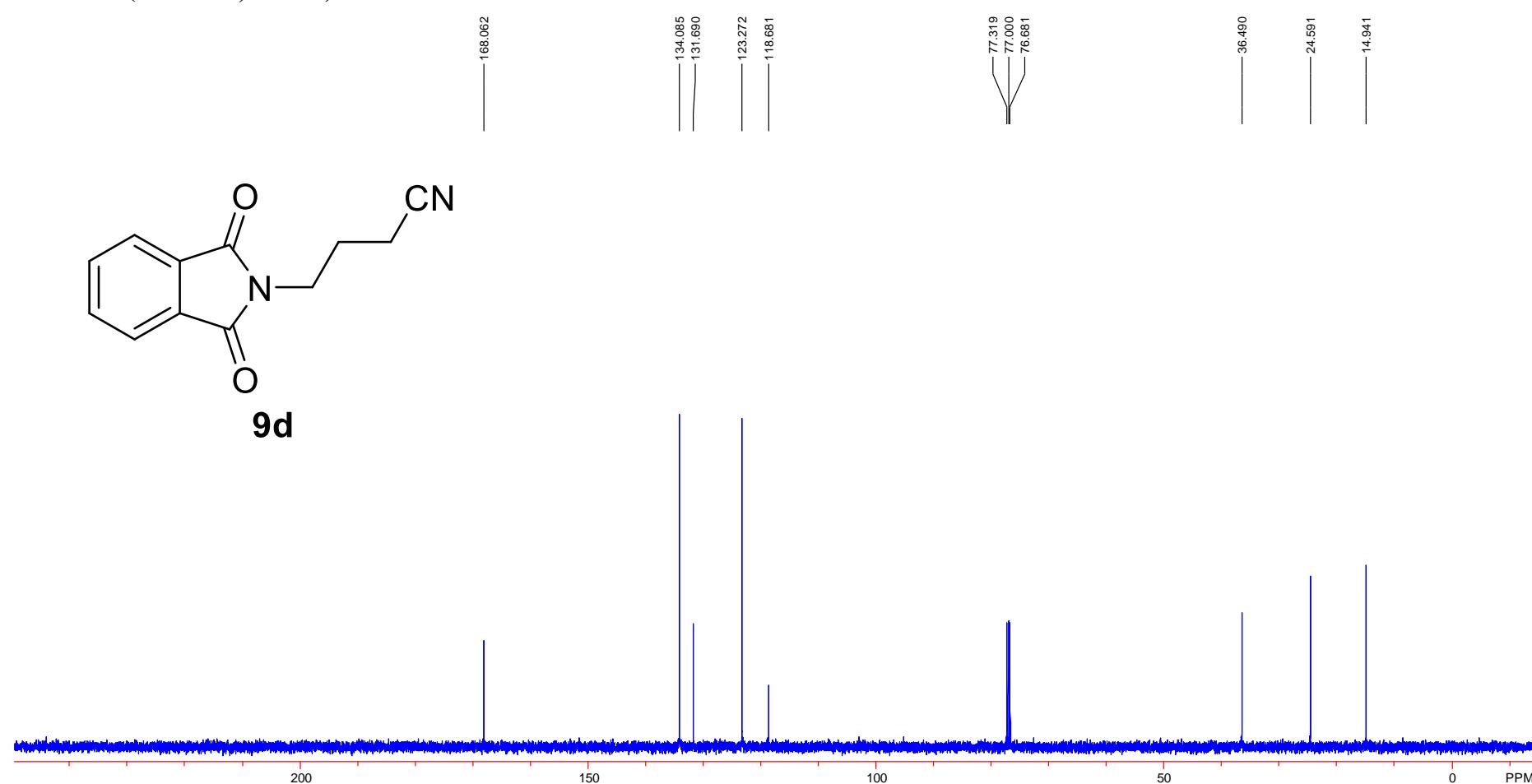
¹³C NMR (100 MHz, CDCl₃)



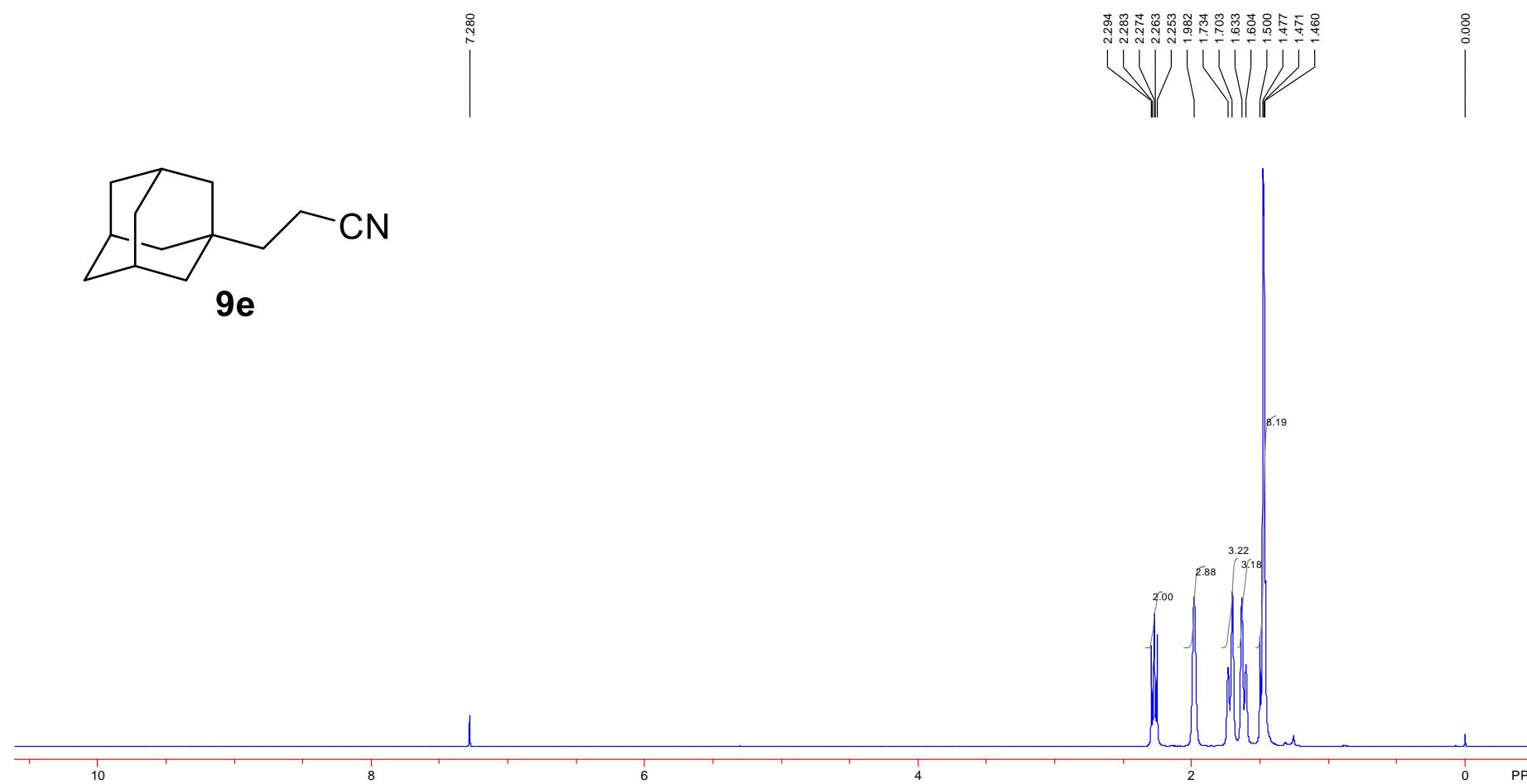
¹H NMR (400 MHz, CDCl₃)



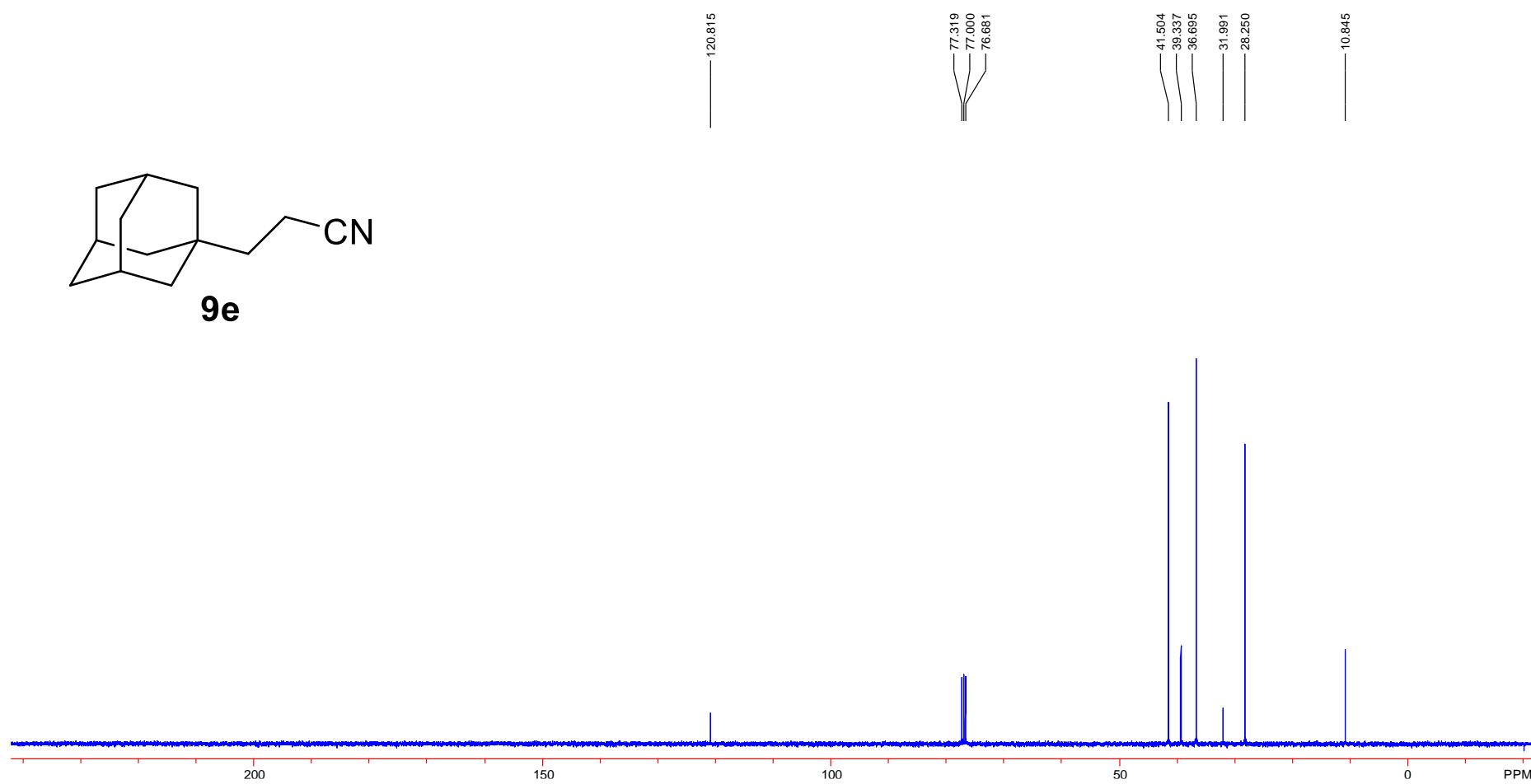
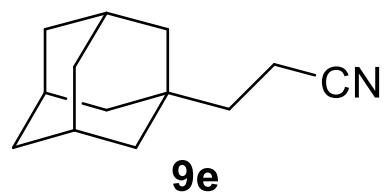
¹³C NMR (100 MHz, CDCl₃)



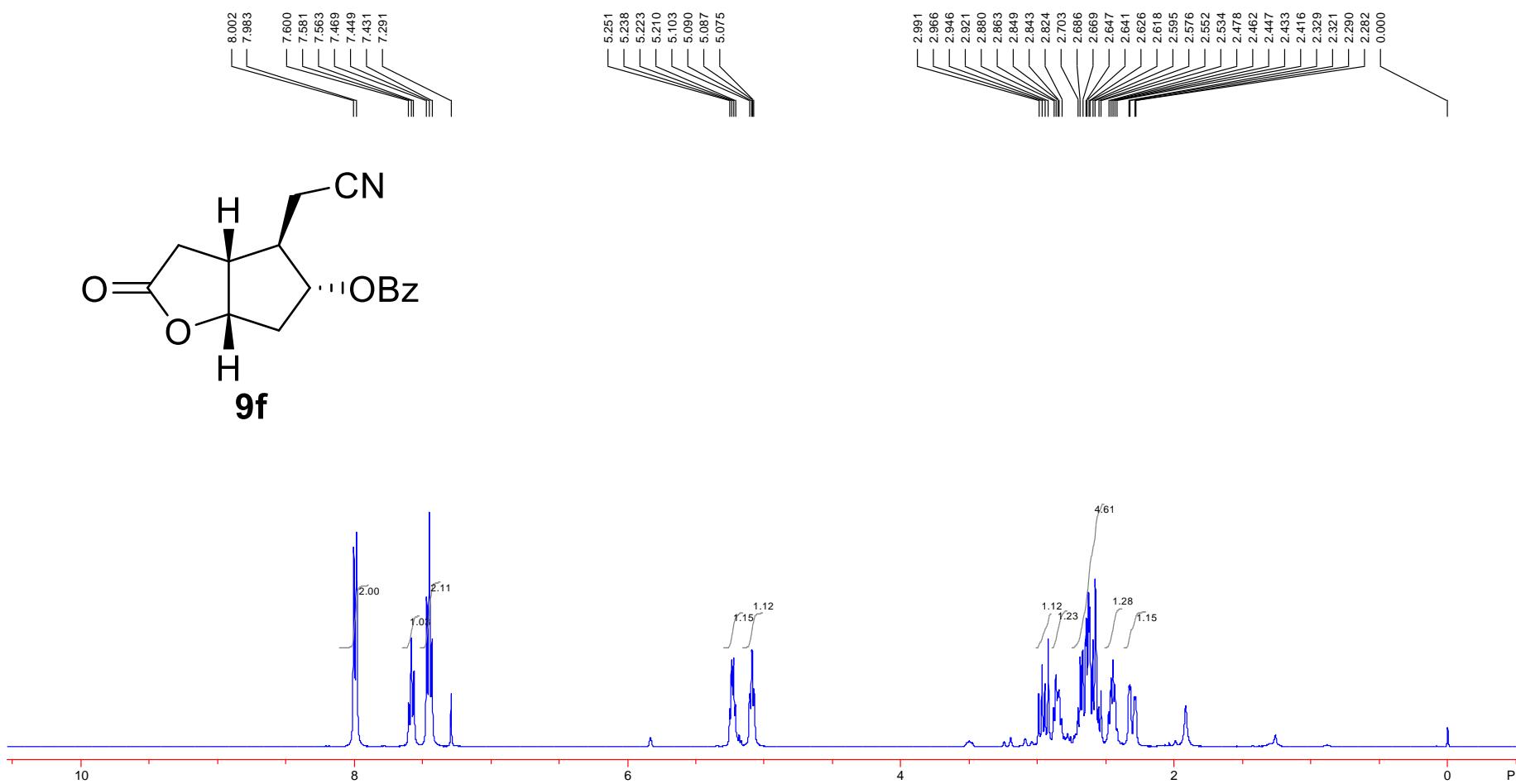
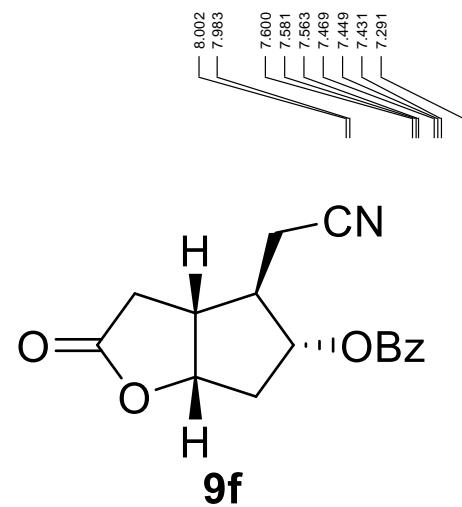
¹H NMR (400 MHz, CDCl₃)



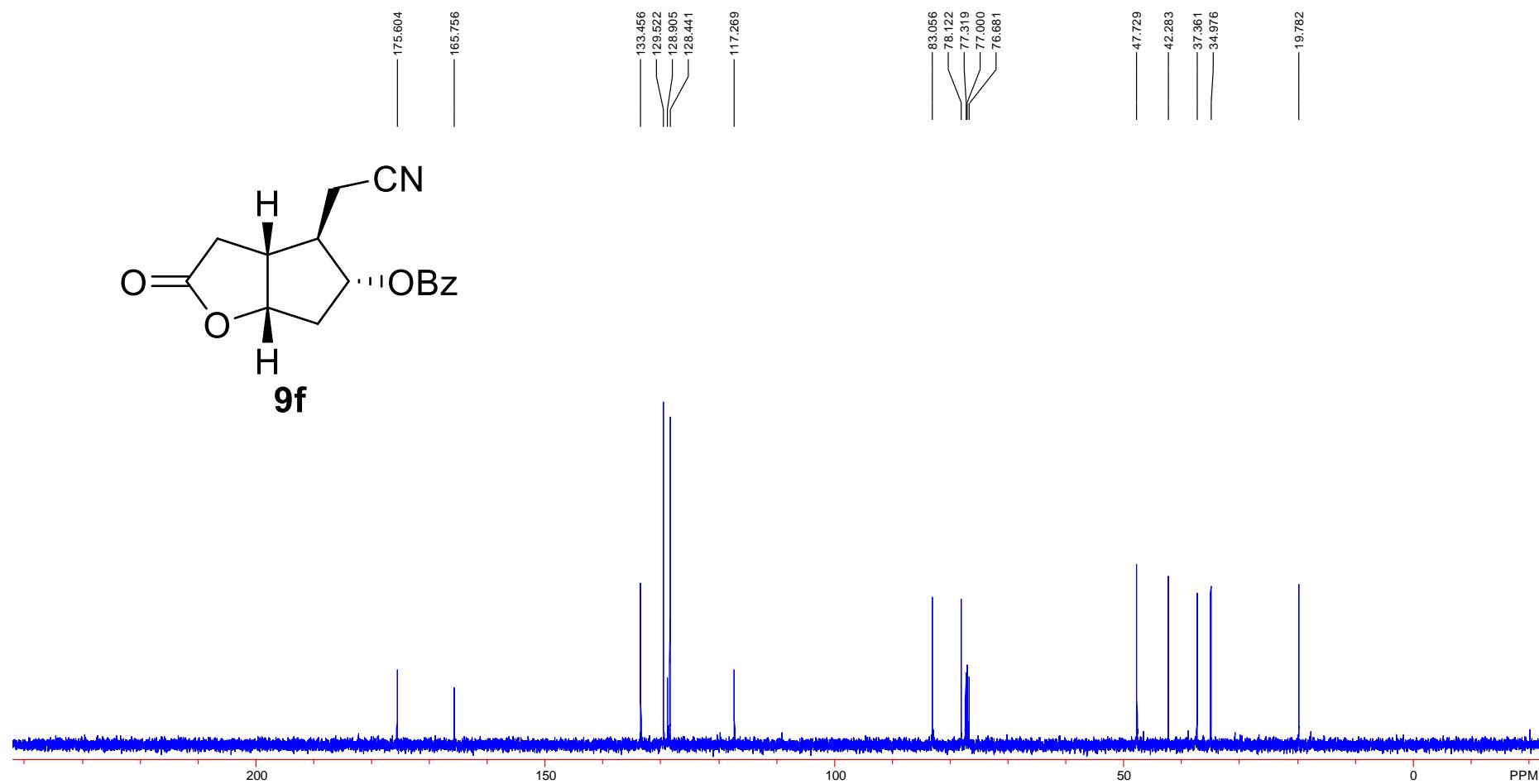
¹³C NMR (100 MHz, CDCl₃)



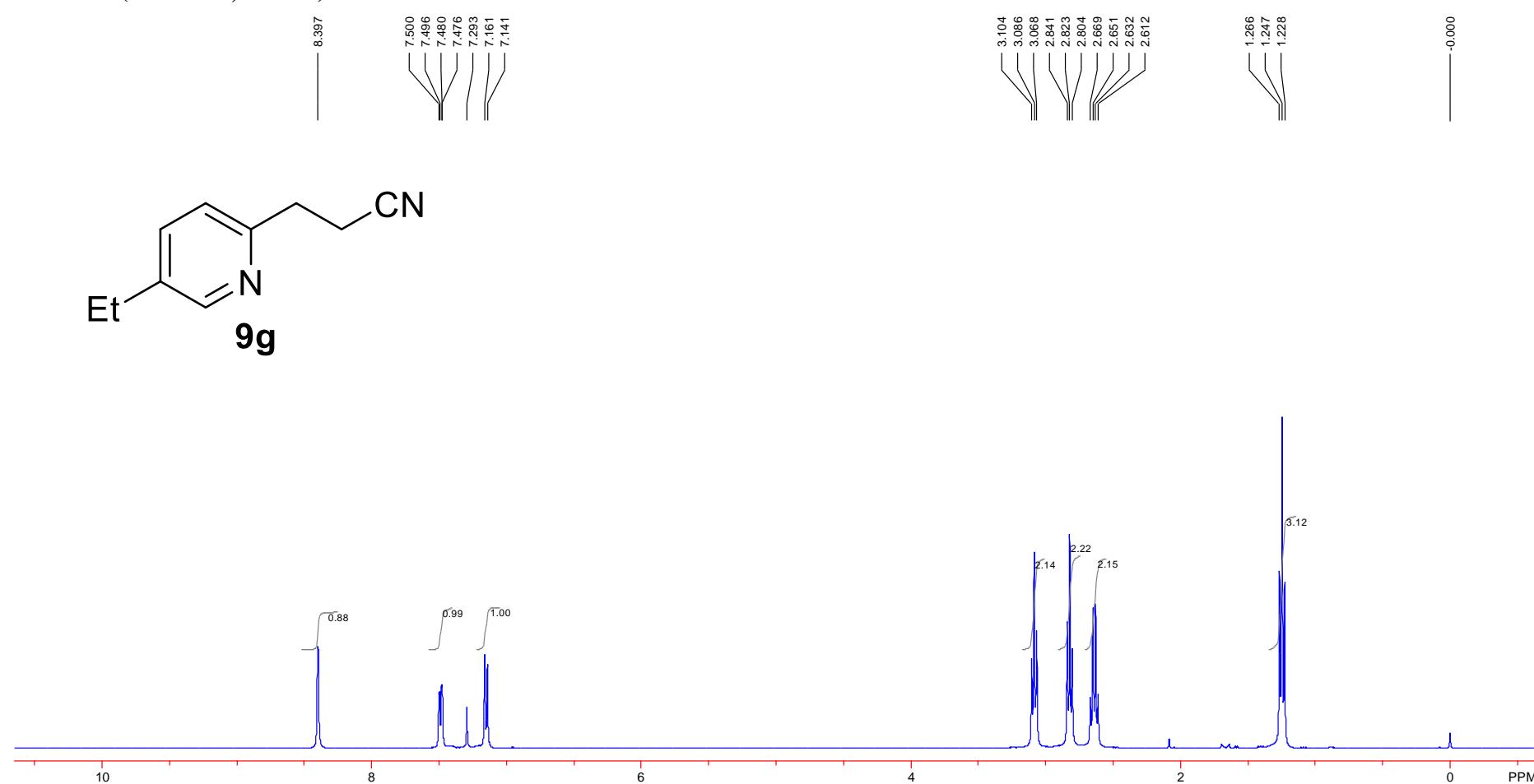
¹H NMR (400 MHz, CDCl₃)



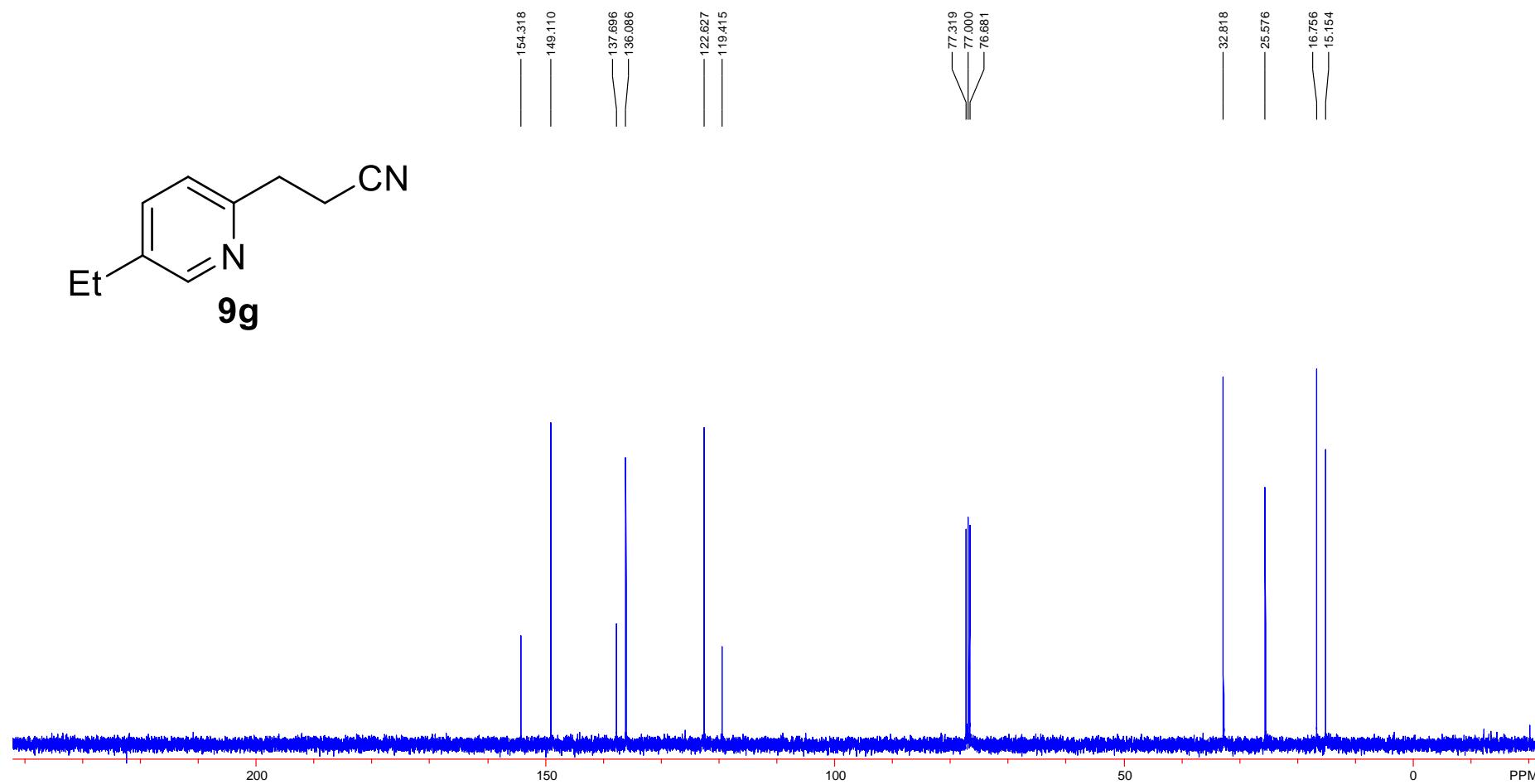
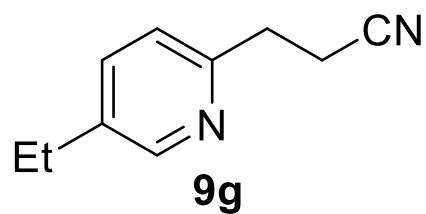
¹³C NMR (100 MHz, CDCl₃)



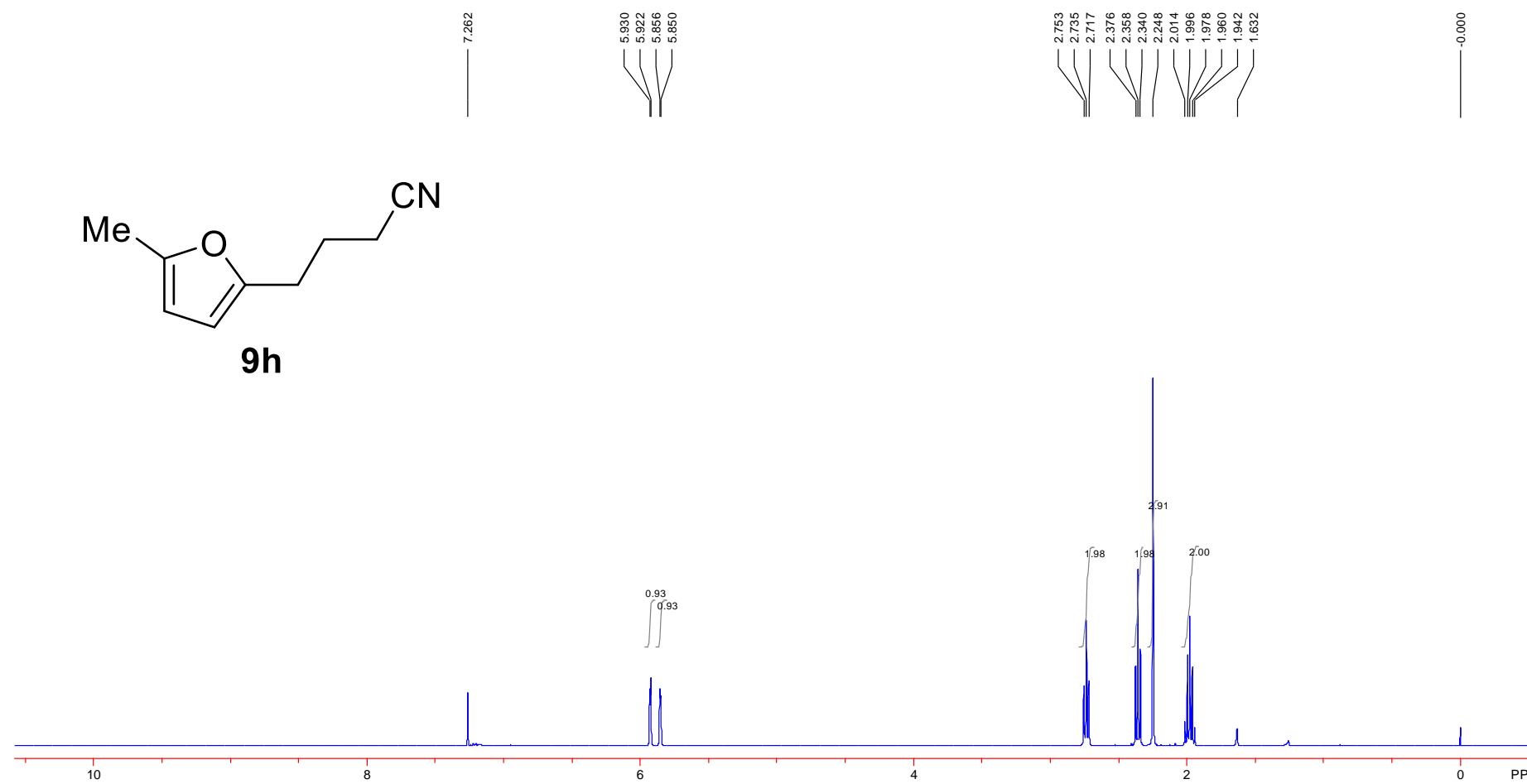
¹H NMR (400 MHz, CDCl₃)



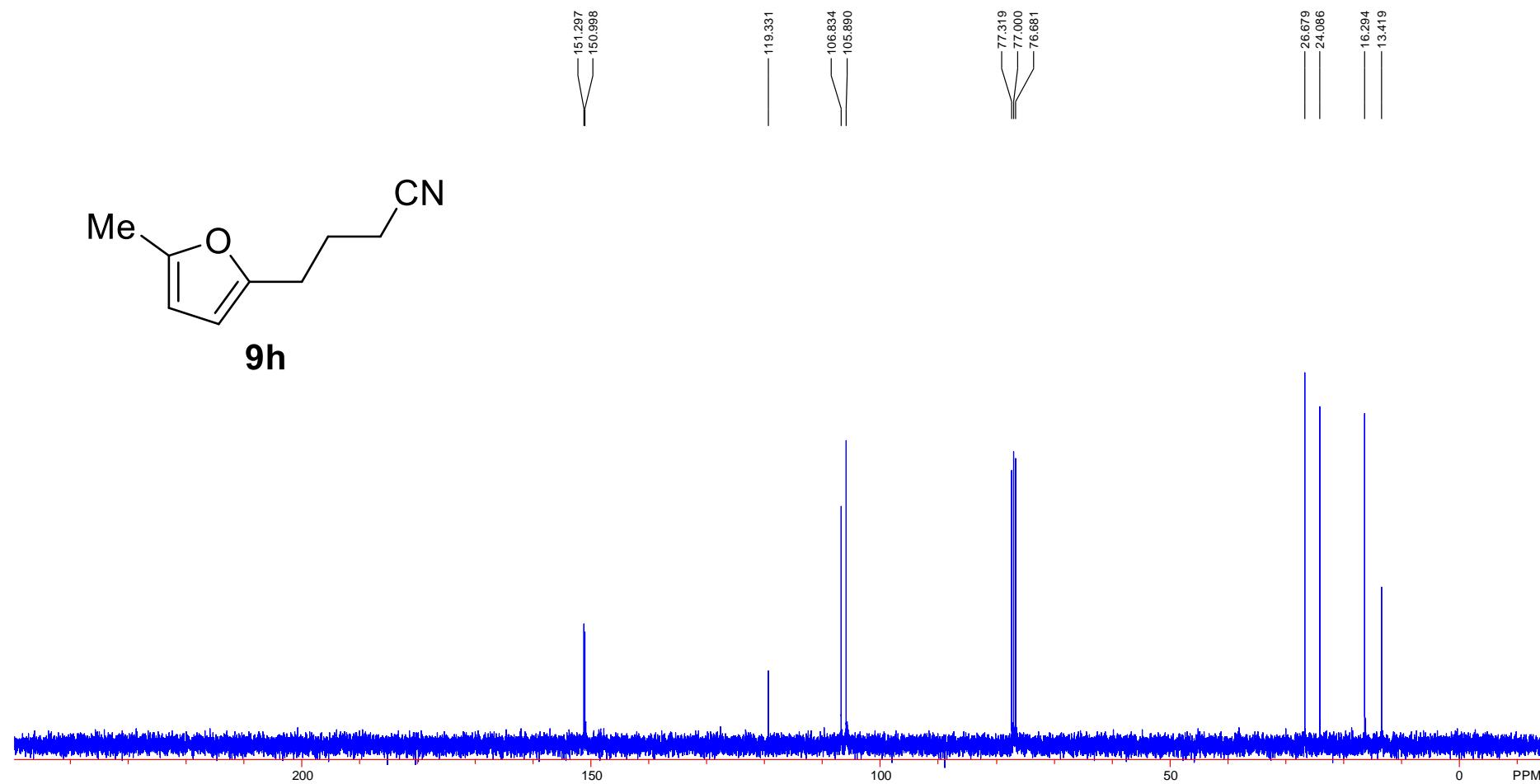
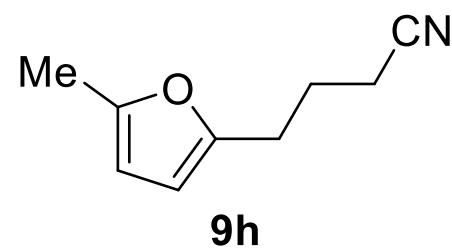
¹³C NMR (100 MHz, CDCl₃)



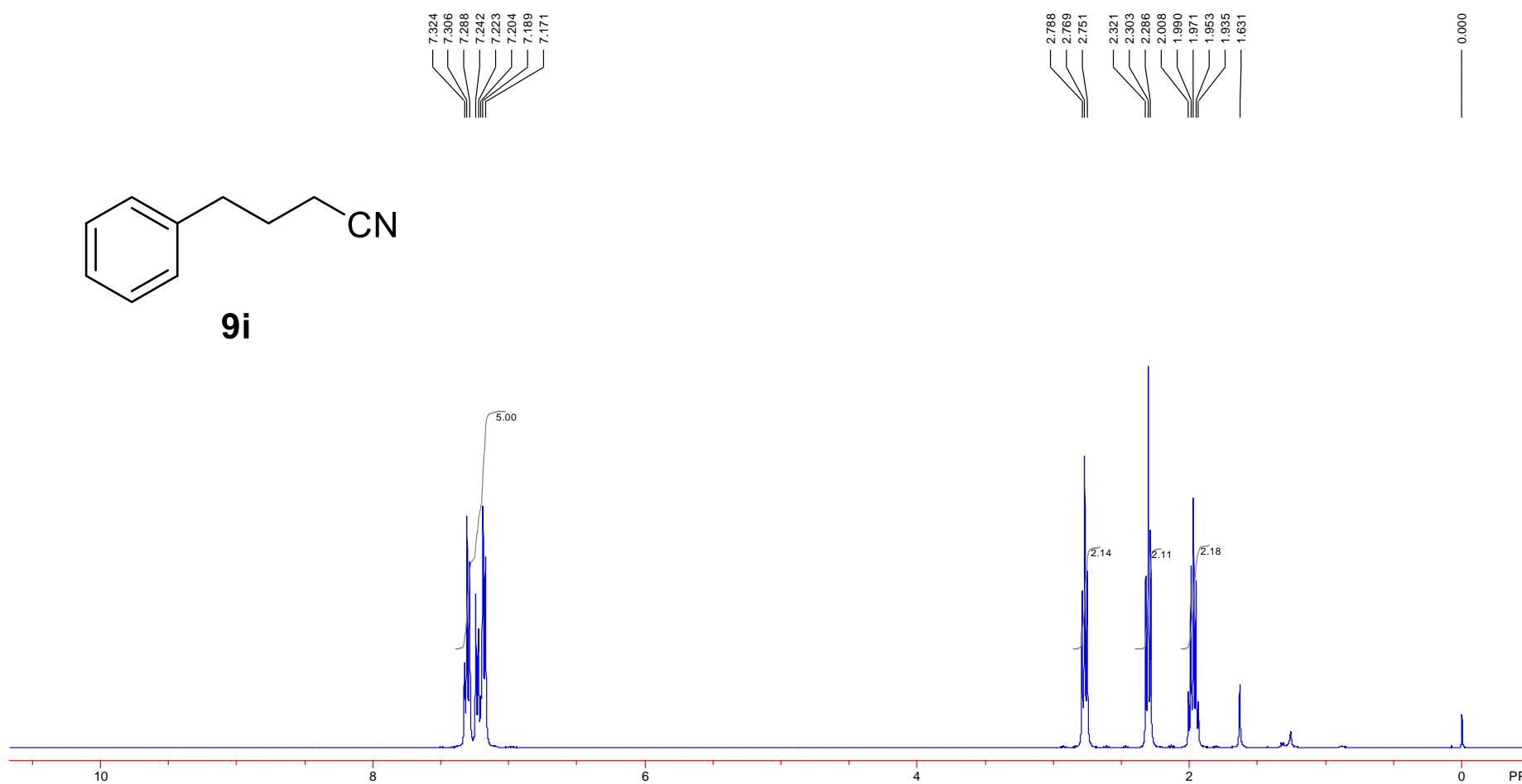
¹H NMR (400 MHz, CDCl₃)



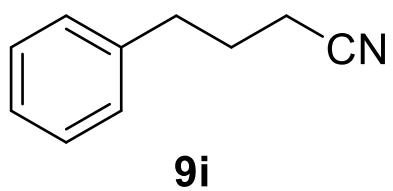
¹³C NMR (100 MHz, CDCl₃)



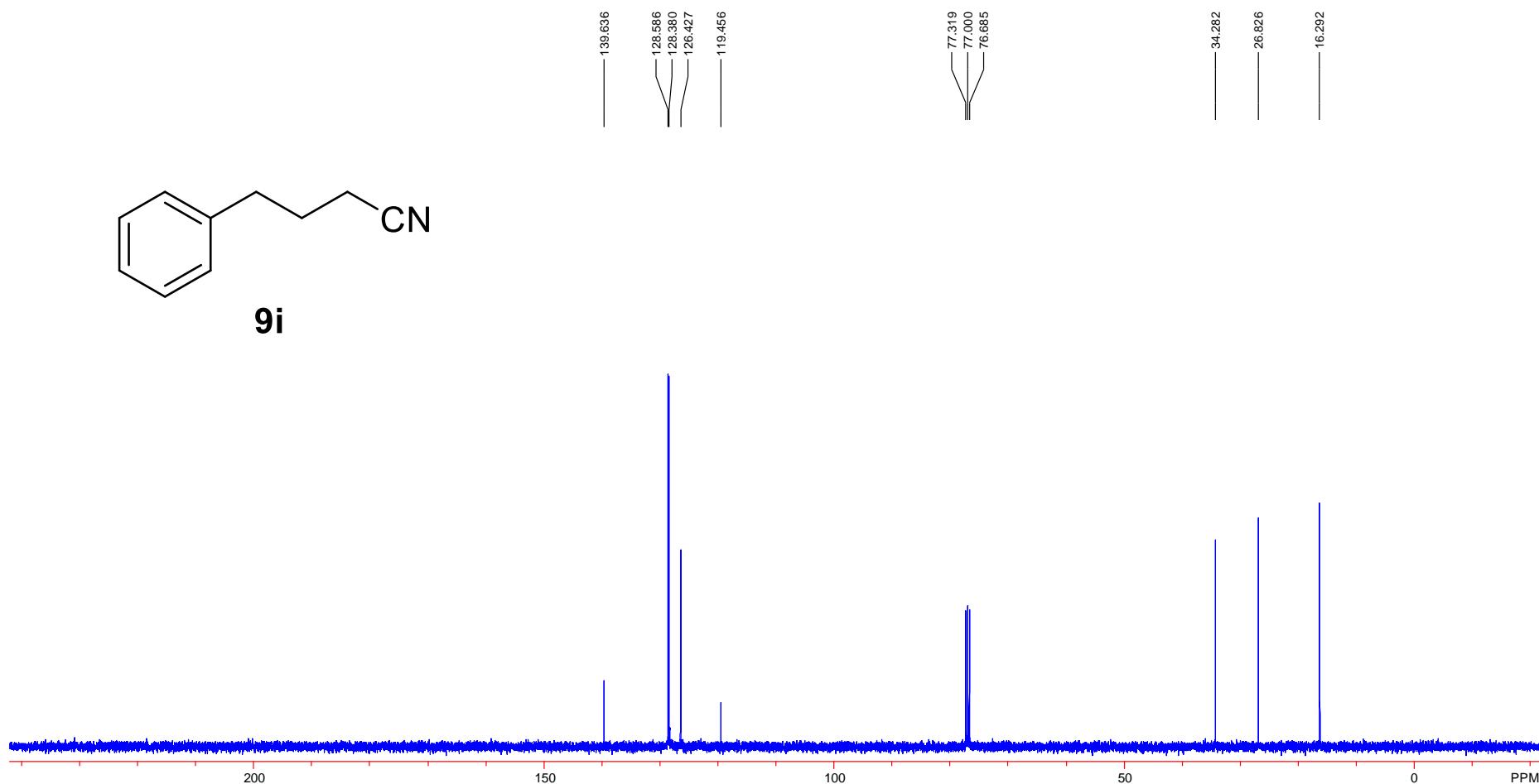
¹H NMR (400 MHz, CDCl₃)



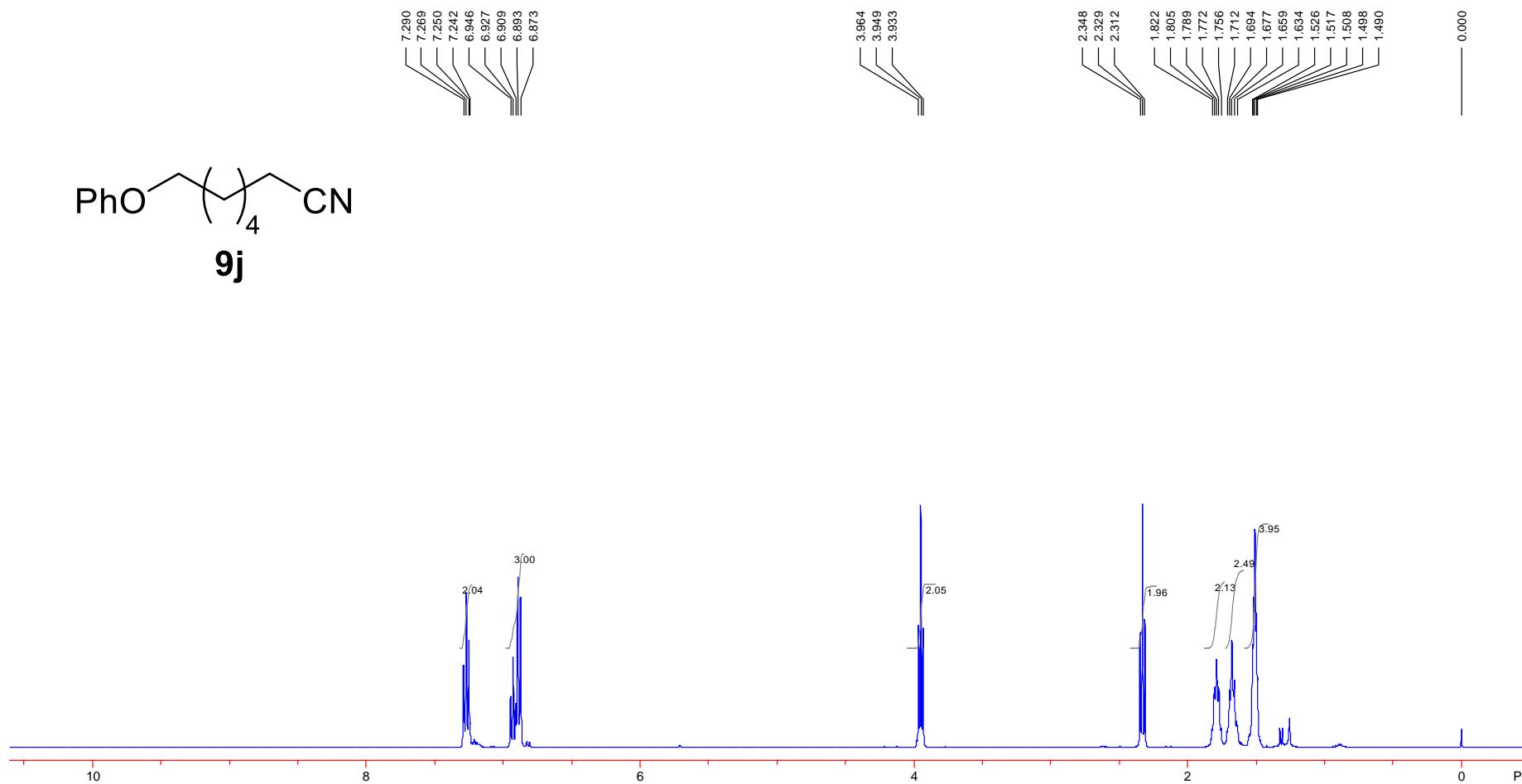
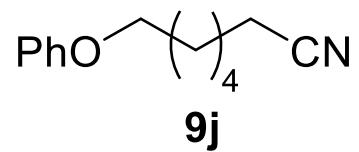
¹³C NMR (100 MHz, CDCl₃)



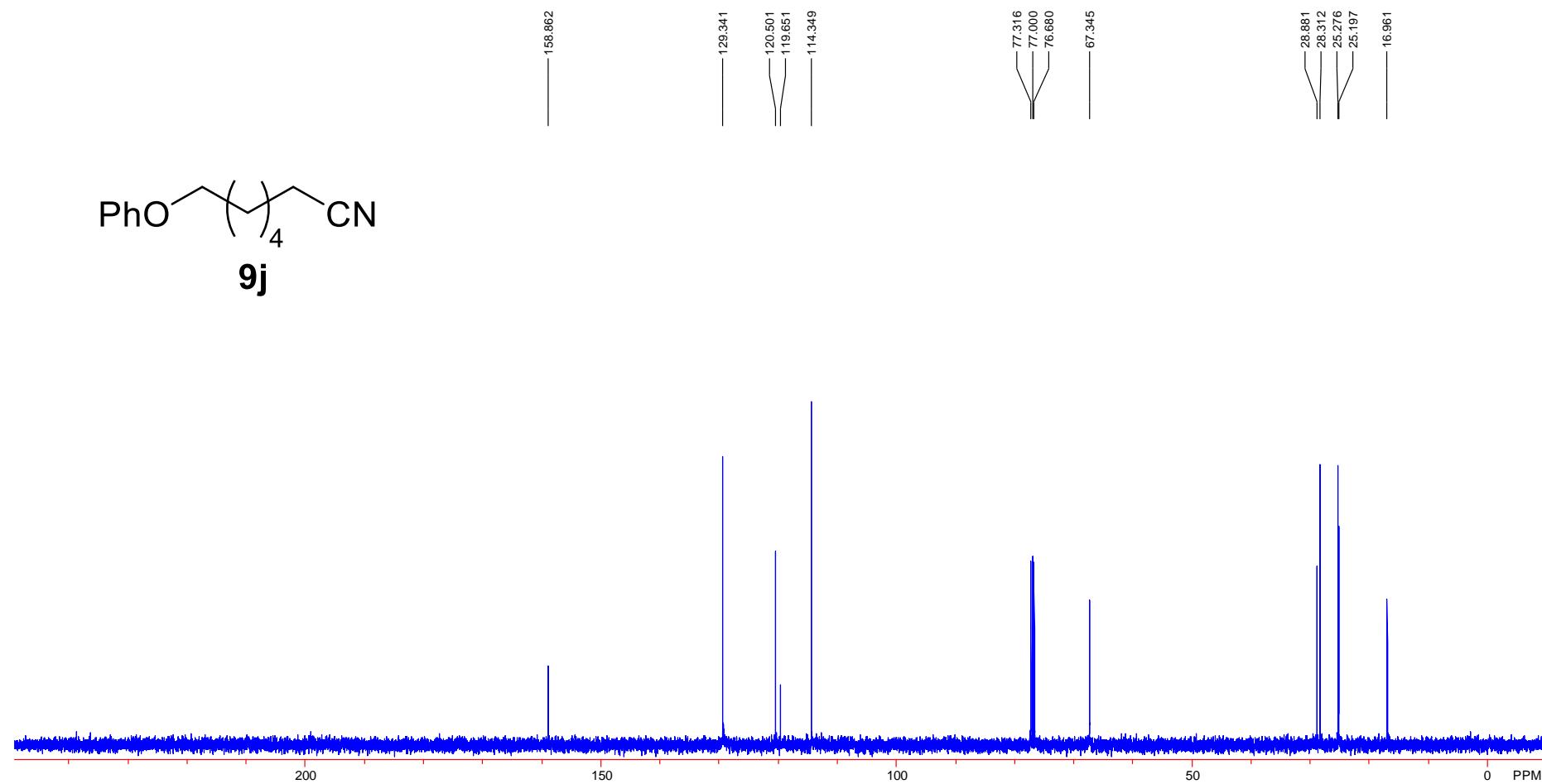
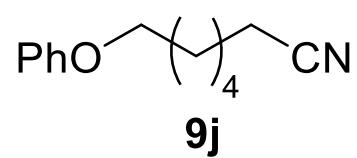
9i



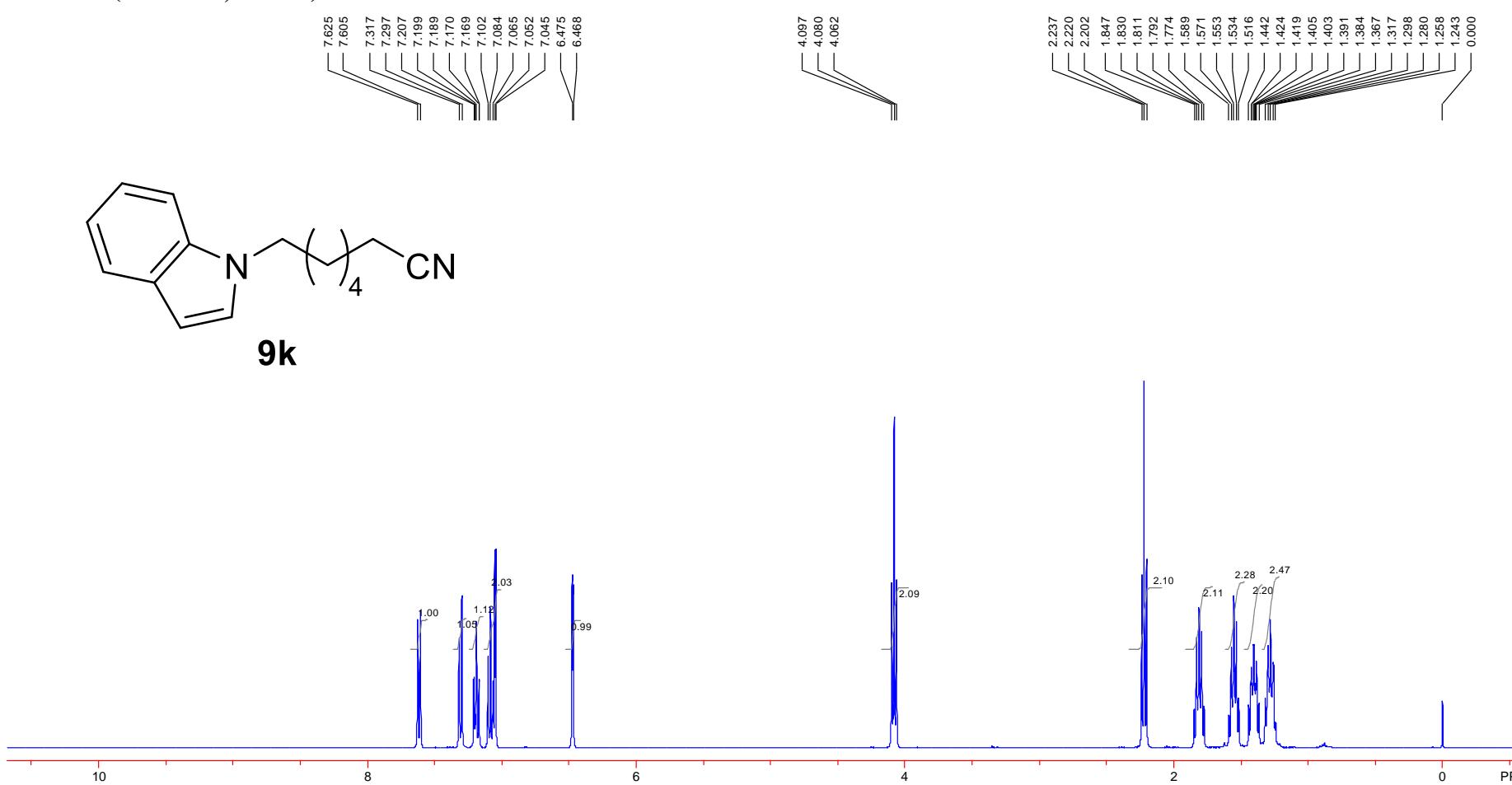
¹H NMR (400 MHz, CDCl₃)



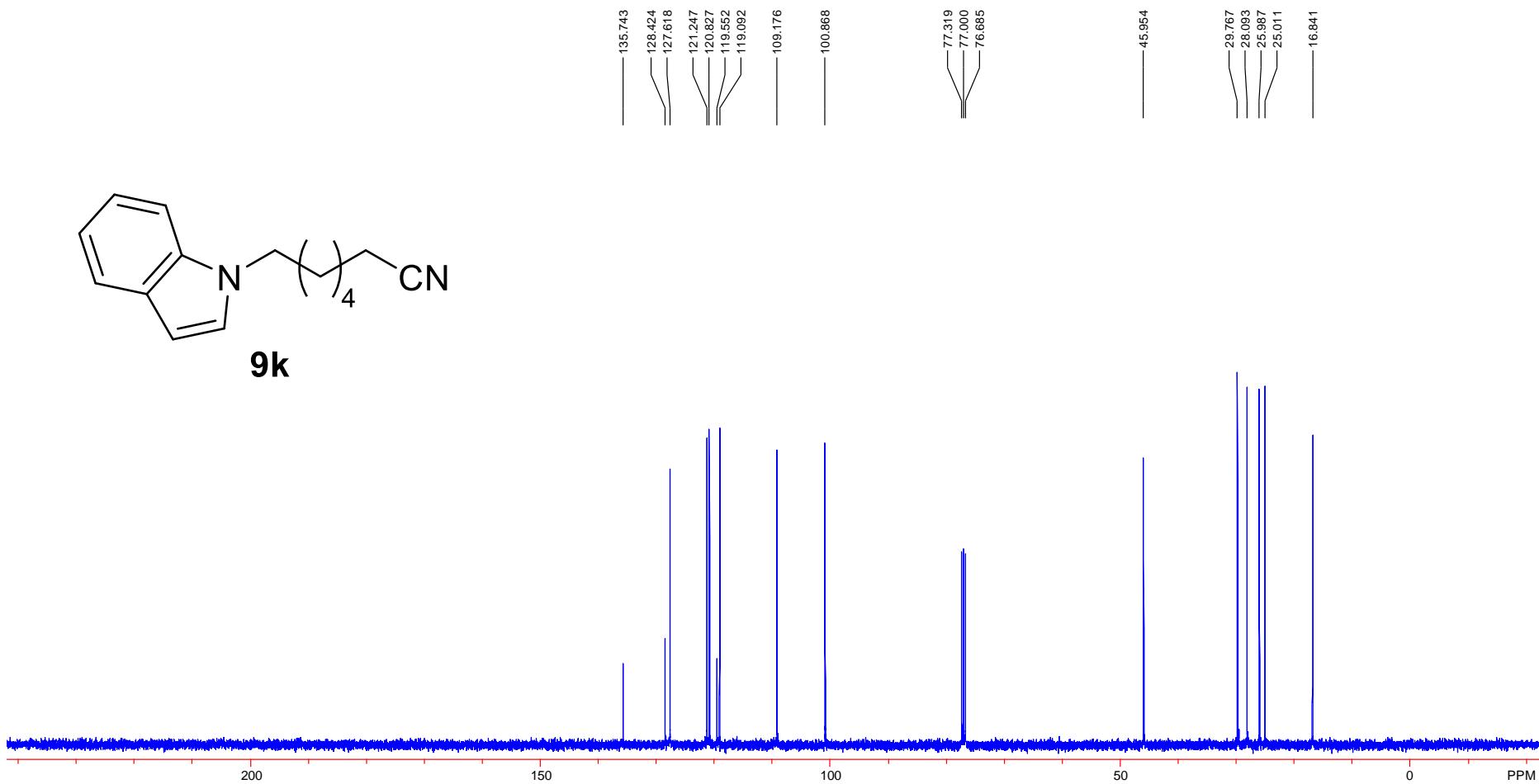
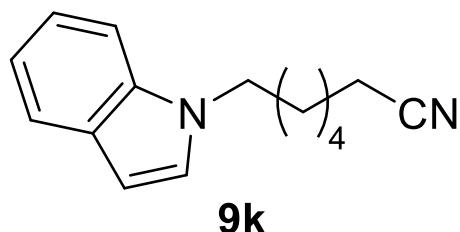
¹³C NMR (100 MHz, CDCl₃)



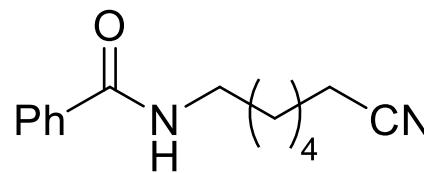
¹H NMR (400 MHz, CDCl₃)



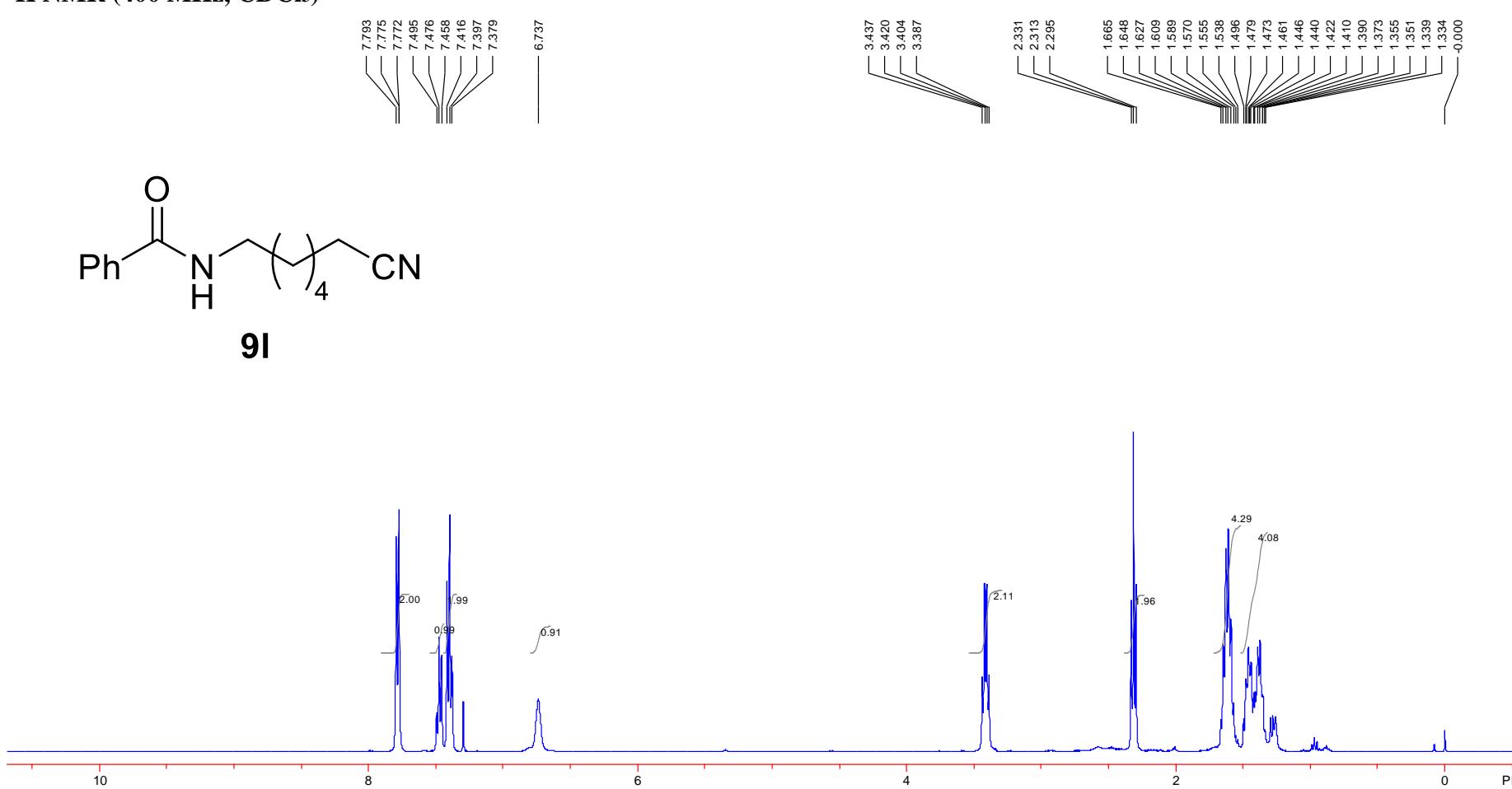
¹³C NMR (100 MHz, CDCl₃)



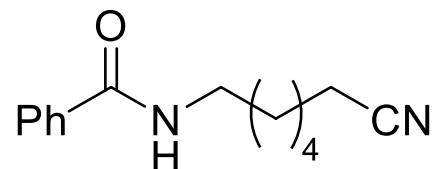
^1H NMR (400 MHz, CDCl_3)



91



¹³C NMR (100 MHz, CDCl₃)



9l

