

Supporting Information

for

Evidence and Isolation of Tetrahedral Intermediates Formed upon the Addition of Lithium Carbenoids to Weinreb Amides

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1. Instrumentation and General Methods

Melting Points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Shimadzu QP 1000 instrument (EI, 70 eV) and on a Bruker maXis 4G instrument (ESI-TOF, APCI, HRMS). ^1H , ^{13}C , ^{19}F and ^{15}N NMR spectra were recorded on a Bruker Avance III 400 spectrometer (400 MHz for ^1H , 100 MHz for ^{13}C , 376 MHz for ^{19}F and 40 MHz for ^{15}N) at 297 K using a directly detecting broadband observe (BBFO) probe. The centre of the (residual) solvent signal was used as an internal standard which was related to TMS with δ 7.26 ppm (^1H in CDCl_3), δ 7.16 ppm (^1H in C_6D_6), δ 77.00 ppm (^{13}C in CDCl_3) and δ 128.16 ppm (^{13}C in C_6D_6). ^{15}N NMR spectra were referenced against external nitromethane (0.0 ppm). For ^{19}F NMR spectra absolute referencing via the Ξ ratio was used. Spin-spin coupling constants (J) are given in Hz.

In nearly all cases, full and unambiguous assignment of all resonances could be performed by combined application of standard NMR techniques, such as APT, HSQC, HMBC, COSY and NOESY experiments.

All the reactions were carried out under inert atmosphere of argon. THF was distilled over Na / benzophenone. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar and TCI Europe. Solutions were evaporated under reduced pressure with a rotary evaporator.

Weinreb amides and *N*-acylpyrroles were prepared according to known procedures.¹

TLC was carried out on aluminium sheets pre-coated with silica gel 60F254 (Macherey-Nagel, Merck); the spots were visualised under UV light ($\lambda=254$ nm) and/or KMnO_4 (aq.) was used as revealing system.

2. Preparation of Neutral Aluminium Oxide Brockmann grade 3 (AloxN-BG3)

94 g of Aluminium Oxide Neutral (Brockmann grade 1, commercial) were put into a 500 mL flask and 6 g of distilled water were slowly added with a pipette on the glass surface. The flask was attached to a rotary evaporator and the mixture was stirred for 1 h at 20 °C *without* application of any reduced pressure. Once the mixture appeared homogeneous, the rotation was interrupted and the resulting AloxN-BG3 could be used as a normal stationary phase for liquid chromatography.

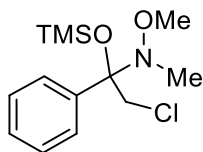
3. General Procedure for the Synthesis of *O*-TMS Hemiaminals

After the Starting Material (1.0 mmol, 1.0 equiv) was dissolved in dry THF (5 mL), the solution was brought at -78 °C in anhydrous conditions. After 5 minutes, the freshly distilled dihalomethane (3.0 equiv) was added and, after 2 minutes, the lithium base (2.8 equiv) was added dropwise with the syringe pump (flow: 0.200 mL/min). The mixture was allowed to stir at -78 °C for 45 minutes and, then, 1-(trimethylsilyl)imidazole (3 equiv) was added and the reaction was allowed to reach room temperature over 4 hours. The reaction was quenched with 5% NaHCO₃ solution (1 mL) and extracted with Et₂O (3 x 5 mL). The organic layer was washed with brine (5 mL), dried over Na₂SO₄, filtered and after removing the solvent under reduced pressure (bath 20 °C), the crude was purified by column chromatography on neutral alumina (grade III).

For the preparation of LTMP (0.5 M) employed for the generation of dihalocarbenoids, our previously described procedure has been used.² TMP (346 mg, 0.48 mL, 2.8 mmol, 2.8 equiv) was added to dry THF (3.4 mL) at 0°C, followed by MeLi-LiBr (1.5 M in diethyl ether, 1.67 mL, 2.8 mmol, 2.8 equiv). After stirring for 30 min, it was cannulated and used as described below.

4. Characterization of the Compounds

2-chloro-*N*-methoxy-*N*-methyl-1-phenyl-1-[(trimethylsilyl)oxy]ethanamine (**3**)



By following the General Procedure, starting from *N*-methoxy-*N*-methylbenzamide (0.165 g, 1.0 mmol, 1.0 equiv), ICH_2Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78°C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **3** was obtained in 82% yield (236 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

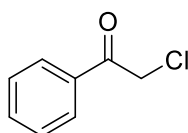
^1H NMR (400 MHz, C_6D_6) δ : 7.60 (m, 2H, Ph H-2,6), 7.20 (m, 2H, Ph H-3,5), 7.11 (m, 1H, Ph H-4), 4.05 (d, $J = 11.1$ Hz, 1H, CH_2Cl), 3.76 (d, $J = 11.1$ Hz, 1H, CH_2Cl), 3.24 (s, 3H, OCH_3), 2.22 (s, 3H, NCH_3), 0.39 (s, 9H, $\text{Si}(\text{CH}_3)_3$).

^{13}C NMR (100 MHz, C_6D_6) δ : 141.7 (Ph C-1), 128.1 (Ph C-3,4,5), 127.4 (Ph C-2,6), 96.0 (CCH_2Cl), 60.3 (OCH_3), 51.5 (CH_2Cl), 36.8 (NCH_3), 2.3 ($\text{Si}(\text{CH}_3)_3$).

^{15}N NMR (40 MHz, C_6D_6) δ : -207.4 (NCH_3).

HRMS (ESI), m/z : calcd. for $\text{C}_{13}\text{H}_{22}\text{ClNNaO}_2\text{Si}^+$: 310.1001 $[\text{M}+\text{Na}]^+$; found: 310.0998.

2-chloro-1-phenylethan-1-one (**4**)³



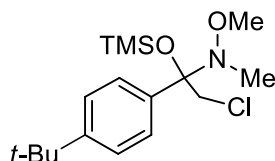
As reported in Table 1 of the manuscript, compound **4** could be isolated as a consequence of the degradation of the tetrahedral intermediate **3**.

^1H NMR (400 MHz, CDCl_3) δ : 7.92 (m, 2H, Ph H-2,6), 7.57 (m, 1H, Ph H-4), 7.47 (m, 2H, Ph H-3,5), 4.70 (s, 2H, CH_2).

^{13}C NMR (100 MHz, CDCl_3) δ : 190.8 ($\text{C}=\text{O}$), 134.0 (Ph C-1), 133.7 (Ph C-4), 128.6 (Ph C-2,6), 128.2 (Ph C-3,5), 46.0 (CH_2).

HRMS (ESI), m/z : calcd. for $\text{C}_8\text{H}_7\text{ClNa}^+$: 177.0078 $[\text{M}+\text{Na}]^+$; found: 177.0085.

2-chloro-*N*-methoxy-*N*-methyl-1-[4-(2-methyl-2-propanyl)phenyl]-1-[(trimethylsilyl)oxy]ethanamine (5)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-4-(2-methyl-2-propenyl)benzamide (0.221 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **5** was obtained in 95% yield (327 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

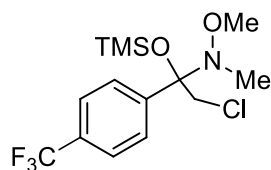
¹H NMR (400 MHz, CDCl₃) δ: 7.40 (m, 2H, Ph H-2,6), 7.33 (m, 2H, Ph H-3,5), 4.08 and 3.91 (AB-System, ²J_{AB} = 11.0 Hz, 2H, CH₂Cl), 3.61 (s, 3H, OCH₃), 2.28 (s, 3H, NCH₃), 1.31 (s, 9H, C(CH₃)₃), 0.29 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, CDCl₃) δ: 150.5 (Ph C-4), 138.1 (Ph C-1), 126.5 (Ph C-2,6), 124.6 (Ph C-3,5), 95.4 (CCH₂Cl), 60.4 (OCH₃), 51.0 (CH₂Cl), 36.7 (NCH₃), 34.4 (C(CH₃)₃), 31.4 (C(CH₃)₃), 2.1 (Si(CH₃)₃).

 ^{15}N NMR (40 MHz, CDCl_3) δ : -207.4 (NCH_3).

HRMS (ESI), m/z : calcd. for $C_{17}H_{30}ClNNaO_2Si^+$: 366.1627 $[M+Na]^+$; found: 366.1625.

2-chloro-*N*-methoxy-*N*-methyl-1-[4-(trifluoromethyl)phenyl]-1-[(trimethylsilyl)oxy]ethanamine (6)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide (0.233 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv.) was added. The desired product **6** was obtained in 84% yield (299 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.46 (m, 2H, Ph H-2,6), 7.40 (m, 2H, Ph H-3,5), 3.94 and 3.61 (AB-System, ²J_{AB} = 11.3 Hz, 2H, CH₂Cl), 3.20 (s, 3H, OCH₃), 2.07 (s, 3H, NCH₃), 0.35 (s, 9H, Si(CH₃)₃).

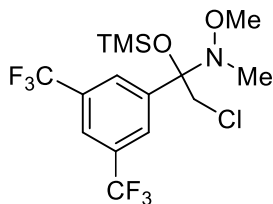
¹³C NMR (100 MHz, C₆D₆) δ: 145.6 (Ph C-1), 130.3 (q, ²J = 32.2 Hz, Ph C-4), 127.9 (Ph C-2,6), 125.1 (q, ³J = 3.8 Hz, Ph C-3,5), 125.0 (q, ¹J = 272.0 Hz, CF₃), 95.6 (CCH₂Cl), 60.3 (OCH₃), 51.0 (CH₂Cl), 36.7 (NCH₃), 2.1 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -208.9 (NCH₃).

¹⁹F NMR (376 MHz, C₆D₆): δ -62.2 (CF₃).

HRMS (APCI), *m/z*: calcd. for C₁₄H₂₂ClF₃NO₂Si⁺: 356.1055 [M+H]⁺; found: 356.1059.

1-[3,5-bis(trifluoromethyl)phenyl]-2-chloro-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (7)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-3,5-bis(trifluoromethyl)benzamide (0.301 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv.) was added. The desired product **7** was obtained in 89% yield (377 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 8.13 (s, 2H, Ph H-2,6), 7.78 (s, 1H, Ph H-4), 3.78 and 3.49 (AB-System, ²*J*_{AB} = 11.5 Hz, 2H, CH₂Cl), 3.11 (s, 3H, OCH₃), 1.99 (s, 3H, NCH₃), 0.26 (s, 9H, Si(CH₃)₃).

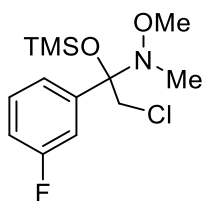
¹³C NMR (100 MHz, C₆D₆) δ: 144.9 (Ph C-1), 131.7 (q, ²*J* = 33.2 Hz, Ph C-3,5), 127.9 (m, Ph C-2,6), 124.1 (q, ¹*J* = 272.7 Hz, CF₃), 122.3 (sept, ³*J* = 3.8 Hz, Ph C-4), 95.3 (CCH₂Cl), 60.3 (OCH₃), 50.6 (CH₂Cl), 36.5 (NCH₃), 1.9 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -210.9 (NCH₃).

¹⁹F NMR (376 MHz, C₆D₆): δ -62.6 (CF₃).

HRMS (APCI), *m/z*: calcd. for C₁₅H₂₁ClF₆NO₂Si⁺: 424.0929 [M+H]⁺; found: 424.0935.

2-chloro-1-(3-fluorophenyl)-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (8)



By following the General Procedure, starting from 3-fluoro-*N*-methoxy-*N*-methylbenzamide (0.183 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **8** was obtained in 90% yield (275 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.43 (m, 1H, Ph H-2), 7.27 (m, 1H, Ph H-6), 6.95 (m, 1H, Ph H-5), 6.78 (m, 1H, Ph H-4), 3.97 and 3.63 (AB-System, ²J_{AB} = 11.2 Hz, 2H, CH₂Cl), 3.18 (s, 3H, OCH₃), 2.14 (s, 3H, NCH₃), 0.33 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 163.3 (d, ¹J = 244.5 Hz, Ph C-3), 144.6 (d, ³J = 7.1 Hz, Ph C-1), 129.6 (d, ³J = 7.9 Hz, Ph C-5), 123.1 (d, ⁴J = 2.9 Hz, Ph C-6), 115.0 (d, ²J = 21.2 Hz, Ph C-4), 114.8 (d, ²J = 23.1 Hz, Ph C-2), 95.6 (d, ⁴J = 2.1 Hz, CCH₂Cl), 60.3 (OCH₃), 51.2 (CH₂Cl), 36.7 (NCH₃), 2.2 (Si(CH₃)₃).

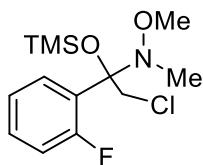
¹⁵N NMR (40 MHz, C₆D₆) δ: -208.4 (NCH₃).

¹⁹F NMR (376 MHz, C₆D₆): δ -113.2 (Ph 3-F).

IR (neat, ν: cm⁻¹): 1440.39, 1248.19, 1171.53, 1116.76, 1028.18, 993.88, 956.42, 839.66, 754.40.

HRMS (APCI), *m/z*: calcd. for C₁₃H₂₂ClFNO₂Si⁺: 306.1087 [M+H]⁺; found: 306.1087.

2-chloro-1-(2-fluorophenyl)-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (9)



By following the General Procedure, starting from 2-fluoro-*N*-methoxy-*N*-methylbenzamide (0.183 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv.) was added. The desired product **9** was obtained in 77% yield (235 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.82 (m, 1H, Ph H-6), 6.89 (m, 2H, Ph H-4,5), 6.78 (m, 1H, Ph H-3), 4.45 and 4.17 (AB-System, ²*J*_{AB} = 11.4 Hz, 1H, CH₂Cl), 3.23 (s, 3H, OCH₃), 2.23 (s, 3H, NCH₃), 0.39 (s, 9H, Si(CH₃)₃).

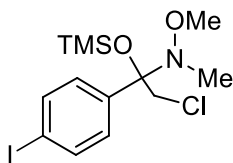
¹³C NMR (100 MHz, C₆D₆) δ: 159.6 (d, ¹*J* = 249.0 Hz, Ph C-2), 131.0 (d, ³*J* = 3.0 Hz, Ph C-6), 130.5 (d, ³*J* = 8.5 Hz, Ph C-4), 128.5 (Ph C-1), 123.9 (d, ⁴*J* = 3.5 Hz, Ph C-5), 116.3 (d, ²*J* = 24.0 Hz, Ph C-3), 95.2 (d, ³*J* = 7.1 Hz, CCH₂Cl), 60.4 (OCH₃), 49.2 (d, ⁴*J* = 5.6 Hz, CH₂Cl), 37.3 (NCH₃), 2.2 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -209.7 (NCH₃).

¹⁹F NMR (376 MHz, C₆D₆): δ -111.0 (Ph 2-F).

HRMS (APCI), *m/z*: calcd. for C₁₃H₂₂ClFNO₂Si⁺: 306.1087 [M+H]⁺; found: 306.1087.

2-chloro-1-(4-iodophenyl)-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (10)



By following the General Procedure, starting from 4-iodo-*N*-methoxy-*N*-methylbenzamide (0.291 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **10** was obtained in 86% yield (356 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

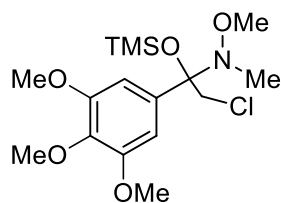
¹H NMR (400 MHz, C₆D₆) δ: 7.52 (m, 2H, Ph H-3,5), 7.14 (m, 2H, Ph H-2,6), 3.94 and 3.59 (AB-System, ²J_{AB} = 11.2 Hz, 2H, CH₂Cl), 3.18 (s, 3H, OCH₃), 2.11 (s, 3H, NCH₃), 0.34 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 141.4 (Ph C-1), 137.3 (Ph C-3,5), 129.5 (Ph C-2,6), 95.7 (CCH₂Cl), 94.3 (Ph C-4), 60.3 (OCH₃), 51.1 (CH₂Cl), 36.7 (NCH₃), 2.2 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -208.5 (NCH₃).

HRMS (APCI), *m/z*: calcd. for C₁₃H₂₂ClINO₂Si⁺: 414.0147 [M+H]⁺; found: 414.0145.

2-chloro-*N*-methoxy-*N*-methyl-1-(3,4,5-trimethoxyphenyl)-1-[(trimethylsilyl)oxy]ethanamine (11)



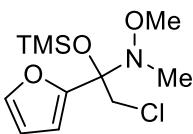
By following the General Procedure, starting from *N*,3,4,5-tetramethoxy-*N*-methylbenzamide (0.255 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **11** was obtained in 83% yield (312 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (300 MHz, C₆D₆) δ: 6.94 (s, 2H, Ph H-2,6), 4.08 (d, ²*J* = 10.9 Hz, 1H, CH₂Cl), 3.85 (m, 4H, CH₂Cl and Ph 4-OCH₃), 3.50 (s, 6H, Ph 3,5-OCH₃), 3.28 (s, 3H, N-OCH₃), 2.32 (s, 3H, NCH₃), 0.41 (s, 9H, Si(CH₃)₃).

¹³C NMR (75 MHz, C₆D₆) δ: 153.8, 139.3, 136.9, 128.1, 105.4, 96.1, 60.5, 60.3, 55.9, 51.6, 36.9, 2.2.

HRMS (ESI), *m/z*: calcd. for C₁₆H₂₉ClNO₅Si⁺: 378.1498 [M+H]⁺; found: 378.1497.

2-chloro-1-(2-furyl)-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (12**)**



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-2-furamide (0.155 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **12** was obtained in 79% yield (219 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

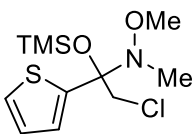
¹H NMR (400 MHz, C₆D₆) δ: 7.03 (dd, ³*J*_{Fu H-5, Fu H-4} = 1.8 Hz, ⁴*J*_{Fu H-5, Fu H-3} = 1.0 Hz, 1H, Fu H-5), 6.45 (dd, ³*J*_{Fu H-3, Fu H-4} = 3.2 Hz, ⁴*J*_{Fu H-3, Fu H-5} = 1.0 Hz, 1H, Fu H-3), 6.05 (dd, ³*J*_{Fu H-4, Fu H-3} = 3.2 Hz, ³*J*_{Fu H-4, Fu H-5} = 1.8 Hz, 1H, Fu H-4), 4.08 and 3.98 (AB-System, ²*J*_{AB} = 11.3 Hz, 2H, CH₂Cl), 3.21 (s, 3H, OCH₃), 2.35 (s, 3H, NCH₃), 0.32 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 153.4 (Fu C-2), 142.1 (Fu C-5), 110.6 (Fu C-4), 110.3 (Fu C-3), 93.3 (CCH₂Cl), 60.3 (OCH₃), 48.8 (CH₂Cl), 37.1 (NCH₃), 2.1 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -210.9 (NCH₃).

HRMS (ESI), *m/z*: calcd. For C₁₁H₂₁ClNO₃Si⁺: 278.0974 [M+H]⁺; found: 278.0975.

2-chloro-*N*-methoxy-*N*-methyl-1-(2-thienyl)-1-[(trimethylsilyl)oxy]ethanamine (13)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-2-thiophenecarboxamide (0.171 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **13** was obtained in 88% yield (259 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

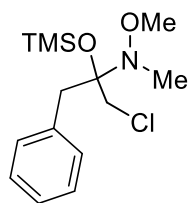
¹H NMR (400 MHz, C₆D₆) δ: 7.05 (dd, ³*J*_{Th H-3, Th H-4} = 3.6 Hz, ⁴*J*_{Th H-3, Th H-5} = 1.3 Hz, 1H, Th H-3), 6.89 (dd, ³*J*_{Th H-5, Fu H-4} = 5.1 Hz, ⁴*J*_{Th H-5, Th H-3} = 1.3 Hz, 1H, Th H-5), 6.75 (dd, ³*J*_{Th H-4, Th H-5} = 5.1 Hz, ³*J*_{Th H-4, Th H-3} = 3.6 Hz, 1H, Th H-4), 3.98 and 3.86 (AB-System, ²*J*_{AB} = 11.1 Hz, 1H, CH₂Cl), 3.24 (s, 3H, OCH₃), 2.34 (s, 3H, NCH₃), 0.34 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 146.2 (Th C-2), 126.9 (Th C-4), 125.8 (Th C-3), 125.7 (Th C-5), 95.1 (CCH₂Cl), 60.3 (OCH₃), 51.7 (CH₂Cl), 36.9 (NCH₃), 2.2 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -208.7 (NCH₃).

HRMS (APCI), *m/z*: calcd. for C₁₁H₂₁ClNO₂SSi⁺: 294.0745 [M+H]⁺; found: 294.0747.

1-chloro-*N*-methoxy-*N*-methyl-3-phenyl-2-[(trimethylsilyl)oxy]-2-propanamine (14**)**



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-2-phenylacetamide (0.179 g, 1.0 mmol, 1.0 equiv), ICH_2Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78°C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **14** was obtained in 82% yield (248 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

^1H NMR (400 MHz, C_6D_6) δ : 7.44 (m, 2H, Ph H-2,6), 7.19 (m, 2H, Ph H-3,5), 7.11 (m, 1H, Ph H-4), 3.66 (d, $^2J = 10.9$ Hz, 1H, CH_2Cl), 3.34 (s, 3H, OCH_3), 3.21 (d, $^2J = 10.9$ Hz, 1H, CH_2Cl), 3.01 and 2.82 (AB-System, $^2J_{\text{AB}} = 13.5$ Hz, 2H, CCH_2), 2.48 (s, 3H, NCH_3), 0.12 (s, 9H, $\text{Si}(\text{CH}_3)_3$).

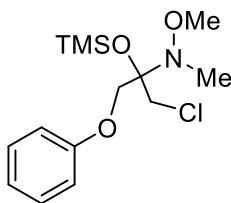
^{13}C NMR (100 MHz, C_6D_6) δ : 136.8 (Ph C-1), 131.1 (Ph C-2,6), 128.2 (Ph C-3,5), 127.1 (Ph C-4), 95.1 (CCH_2Cl), 59.7 (OCH_3), 45.3 (CH_2Cl), 41.5 (PhCH_2), 35.6 (NCH_3), 2.5 ($\text{Si}(\text{CH}_3)_3$).

^{15}N NMR (40 MHz, C_6D_6) δ : -213.6 (NCH_3).

IR (neat, ν : cm^{-1}): 1247.58, 1088.42, 1027.32, 965.12, 837.45, 754.56.

HRMS (APCI), m/z : calcd. for $\text{C}_{14}\text{H}_{25}\text{ClNO}_2\text{Si}^+$: 302.1338 $[\text{M}+\text{H}]^+$; found: 302.1341.

1-chloro-*N*-methoxy-*N*-methyl-3-phenoxy-2-[(trimethylsilyl)oxy]-2-propanamine (15)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-2-phenoxyacetamide (0.195 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **15** was obtained in 87% yield (276 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.09 (m, 2H, Ph H-3,5), 6.85 (m, 2H, Ph H-2,6), 6.83 (m, 1H, Ph H-4), 4.17 and 4.13 (AB-System, ²J_{AB} = 9.6 Hz, 2H, OCH₂), 3.90 and 3.70 (AB-System, ²J_{AB} = 11.4 Hz, 2H, CH₂Cl), 3.26 (s, 3H, OCH₃), 2.44 (s, 3H, NCH₃), 0.24 (s, 9H, Si(CH₃)₃).

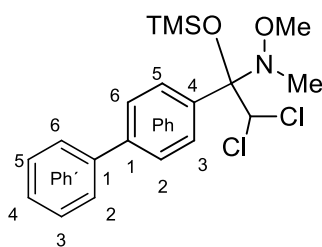
¹³C NMR (100 MHz, C₆D₆) δ: 158.8 (Ph C-1), 129.9 (Ph C-3,5), 121.5 (Ph C-4), 115.0 (Ph C-2,6), 93.2 (CCH₂Cl), 67.5 (OCH₂), 60.2 (OCH₃), 45.0 (CH₂Cl), 35.6 (NCH₃), 2.2 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -215.4 (NCH₃).

IR (neat, ν: cm⁻¹): 1236.53, 1119.14, 1080.09, 1010.17, 840.16, 751.30.

HRMS (APCI), *m/z*: calcd. for C₁₄H₂₅ClNO₃Si⁺: 318.1287 [M+H]⁺; found: 318.1291.

1-(4-biphenyl)-2,2-dichloro-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (16)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-4-biphenylcarboxamide (0.241 g, 1.0 mmol, 1.0 equiv), CH₂Cl₂ (255 mg, 0.19 mL, 3.0 mmol, 3.0 equiv), LTMP (0.5 M in THF, 5.6 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **16** was obtained in 83% yield (394 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

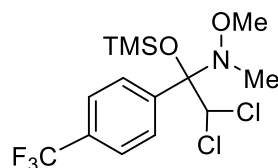
¹H NMR (400 MHz, C₆D₆) δ: 7.91 (m, 2H, Ph H-3,5), 7.53 (m, 2H, Ph H-2,6), 7.48 (m, 2H, Ph' H-2,6), 7.21 (m, 2H, Ph' H-3,5), 7.13 (m, 1H, Ph' H-4), 6.46 (s, 1H, CHCl₂), 3.43 (s, 3H, OCH₃), 2.31 (s, 3H, NCH₃), 0.35 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 141.9 (Ph C-1), 141.1 (Ph' C-1), 136.1 (Ph C-4), 130.5 (Ph C-3,5), 129.1 (Ph' C-3,5), 127.7 (Ph' C-4), 127.5 (Ph' C-2,6), 126.2 (Ph C-2,6), 98.3 (CCHCl₂), 76.0 (CHCl₂), 59.4 (OCH₃), 37.0 (NCH₃), 2.3 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -212.7 (NCH₃).

HRMS (ESI), *m/z*: calcd. for C₁₉H₂₆Cl₂NO₂Si⁺: 398.1104 [M+H]⁺; found: 398.1104.

2,2-dichloro-*N*-methoxy-*N*-methyl-1-[4-(trifluoromethyl)phenyl]-1-[(trimethylsilyl)oxy]ethanamine (17)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide (0.233 g, 1.0 mmol, 1.0 equiv), CH₂Cl₂ (255 mg, 0.19 mL, 3.0 mmol, 3.0 equiv), LTMP (0.5 M, 5.6 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **17** was obtained in 87% yield (325 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.73 (m, 2H, Ph H-2,6), 7.40 (m, 2H, Ph H-3,5), 6.32 (s, 1H, CHCl₂), 3.35 (s, 3H, OCH₃), 2.10 (s, 3H, NCH₃), 0.28 (s, 9H, Si(CH₃)₃).

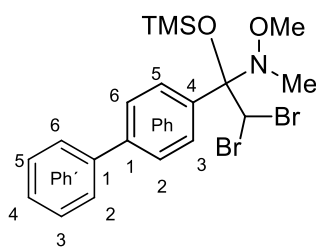
¹³C NMR (100 MHz, C₆D₆) δ: 140.9 (Ph C-1), 131.0 (q, ²*J* = 32.3 Hz, Ph C-4), 130.4 (Ph C-2,6), 125.0 (q, ¹*J* = 272.0 Hz, CF₃), 124.3 (q, ³*J* = 3.8 Hz, Ph C-3,5), 97.8 (CCHCl₂), 75.3 (CHCl₂), 59.4 (OCH₃), 36.8 (NCH₃), 2.1 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -213.9 (NCH₃).

¹⁹F NMR (376 MHz, C₆D₆): δ -62.3 (CF₃).

HRMS (ESI), *m/z*: calcd. for C₁₄H₂₁Cl₂F₃NO₂Si⁺: 390.0665 [M+H]⁺; found: 390.0663.

1-(4-biphenyl)-2,2-dibromo-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (18)



By following the General Procedure, starting from *N*-methoxy-*N*-methyl-4-biphenylcarboxamide (0.241 g, 1.0 mmol, 1.0 equiv), CH₂Br₂ (522 mg, 0.21 mL, 3.0 mmol, 3.0 equiv), LTMP (0.5 M, 5.6 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv.) was added. The desired product **18** was obtained in 92% yield (519 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

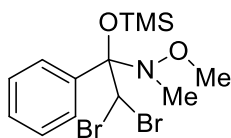
¹H NMR (400 MHz, C₆D₆) δ: 7.97 (m, 2H, Ph H-3,5), 7.55 (m, 2H, Ph H-2,6), 7.49 (m, 2H, Ph' H-2,6), 7.21 (m, 2H, Ph' H-3,5), 7.13 (m, 1H, Ph' H-4), 6.48 (s, 1H, CHBr₂), 3.47 (s, 3H, OCH₃), 2.31 (s, 3H, NCH₃), 0.36 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 141.9 (Ph C-1), 141.1 (Ph' C-1), 136.9 (Ph C-4), 130.6 (Ph C-3,5), 129.1 (Ph' C-3,5), 127.7 (Ph' C-4), 127.6 (Ph' C-2,6), 126.0 (Ph C-2,6), 97.3 (CCHBr₂), 59.4 (OCH₃), 52.8 (CHBr₂), 37.4 (NCH₃), 2.4 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -213.2 (NCH₃).

HRMS (ESI), *m/z*: calcd. for C₁₉H₂₆Br₂NO₂Si⁺: 486.0094 [M+H]⁺; found: 486.0092.

2,2-dibromo-*N*-methoxy-*N*-methyl-1-phenyl-1-[(trimethylsilyl)oxy]ethanamine (19)



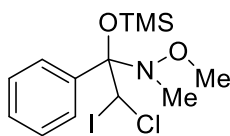
By following the General Procedure, starting from *N*-methoxy-*N*-methyl-4-biphenylcarboxamide (0.241 g, 1.0 mmol, 1.0 equiv), CH₂Br₂ (522 mg, 0.21 mL, 3.0 mmol, 3.0 equiv), LTMP (0.5 M in THF, 5.6 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product the desired product **19** was obtained in 85% yield (349 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.91 (m, 2H, Ph H-2,6), 7.23 (m, 2H, Ph H-3,5), 7.16 (m, 1H, Ph H-4), 6.44 (s, 1H, CHBr₂), 3.43 (s, 3H, OCH₃), 2.26 (s, 3H, NCH₃), 0.33 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 137.8 (Ph C-1), 130.1 (Ph C-2,6), 128.9 (Ph C-4), 127.2 (Ph C-3,5), 97.3 (CCHBr₂), 59.4 (OCH₃), 52.7 (CHBr₂), 37.3 (NCH₃), 2.3 (Si(CH₃)₃).

HRMS (ESI), *m/z*: calcd. for C₁₃H₂₂Br₂NO₂Si⁺: 409.9781 [M+H]⁺; found: 409.9782.

2-chloro2-iodo-*N*-methoxy-*N*-methyl-1-phenyl-1-[(trimethylsilyl)oxy]ethanamine (20)



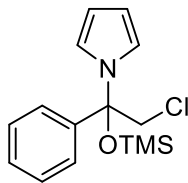
By following the General Procedure, starting from *N*-methoxy-*N*-methyl-4-biphenylcarboxamide (0.241 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), LTMP (0.5 M in THF, 5.6 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product the desired product **20** was obtained in 80% yield (331 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.89 (m, 2H, Ph H-2,6), 7.23 (m, 2H, Ph H-3,5), 7.16 (m, 1H, Ph H-4), 6.48 (s, 1H, CHClI), 3.40 (s, 3H, OCH₃), 2.27 (s, 3H, NCH₃), 0.35 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 138.9 (Ph C-1), 129.8 (Ph C-2,6), 128.9 (Ph C-4), 127.3 (Ph C-3,5), 97.6 (CCHClI), 59.3 (OCH₃), 40.8 (CHClI), 37.9 (NCH₃), 2.6 (Si(CH₃)₃).

HRMS (ESI), *m/z*: calcd. for C₁₃H₂₂ClINO₂Si⁺: 414.0147 [M+H]⁺; found: 414.0146.

1-{2-chloro-1-phenyl-1-[(trimethylsilyl)oxy]ethyl}-1*H*-pyrrole (21**)**



By following the General Procedure, starting from phenyl(1*H*-pyrrol-1-yl)methanone (0.171 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **21** was obtained in 80% yield (235 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.28 (m, 2H, Ph H-2,6), 7.08 (m, 2H, Ph H-3,5), 7.06 (m, 1H, Ph H-4), 6.68 (m, 2H, Py H-2,5), 6.22 (m, 2H, Py H-3,4), 3.77 and 3.74 (AB-System, ²*J*_{AB} = 11.7 Hz, 2H, CH₂Cl), -0.01 (s, 9H, Si(CH₃)₃).

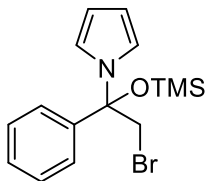
¹³C NMR (100 MHz, C₆D₆) δ: 142.8 (Ph C-1), 128.7 (Ph C-4), 128.1 (Ph C-3,5), 127.1 (Ph C-2,6), 120.2 (Py C-2,5), 109.2 (Py C-3,4), 89.1 (CCH₂Cl), 51.6 (CH₂Cl), 1.0 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -203.8 (Py N-1).

IR (neat, ν: cm⁻¹): 1553.23, 1251.47, 1115.07, 1091.23, 1072.00, 840.58, 724.32.

HRMS (ESI), *m/z*: calcd. for C₁₅H₂₁ClNOSi⁺: 294.1075 [M+H]⁺; found: 294.1075.

1-{2-bromo-1-phenyl-1-[(trimethylsilyl)oxy]ethyl}-1H-pyrrole (22)



By following the General Procedure, starting from phenyl(1H-pyrrol-1-yl)methanone (0.171 g, 1.0 mmol, 1.0 equiv), CH₂Br₂ (522 mg, 0.21, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **22** was obtained in 77% yield (260 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.27 (m, 2H, Ph H-2,6), 7.07 (m, 2H, Ph H-3,5), 7.06 (m, 1H, Ph H-4), 6.66 (m, 2H, Py H-2,5), 6.12 (m, 2H, Py H-3,4), 3.73 and 3.64 (AB-System, ²J_{AB} = 10.9 Hz, 2H, CH₂Br), -0.01 (s, 9H, Si(CH₃)₃).

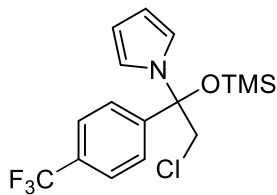
¹³C NMR (100 MHz, C₆D₆) δ: 143.0 (Ph C-1), 128.7 (Ph C-4), 128.1 (Ph C-3,5), 127.1 (Ph C-2,6), 120.2 (Py C-2,5), 109.2 (Py C-3,4), 88.4 (CCH₂Br), 40.9 (CH₂Br), 1.0 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -203.1 (Py N-1).

IR (neat, ν: cm⁻¹): 1509.59, 1248.45, 1141.60, 1112.04, 1082.68, 839.66.

HRMS (APCI), *m/z*: calcd. for C₁₅H₂₁BrNOSi⁺: 338.0570 [M+H]⁺; found: 338.0571.

1-{2-chloro-1-[4-(trifluoromethyl)phenyl]-1-[(trimethylsilyl)oxy]ethyl}-1H-pyrrole (23)



By following the General Procedure, starting from 1H-pyrrol-1-yl[4-(trifluoromethyl)-phenyl]methanone (0.239 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **23** was obtained in 85% yield (308 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.28 (m, 2H, Ph H-3,5), 7.15 (m, 2H, Ph H-2,6), 6.51 (m, 2H, Py H-2,5), 6.19 (m, 2H, Py H-3,4), 3.64 and 3.61 (AB-System, ²*J*_{AB} = 11.7 Hz, 2H, CH₂Cl), -0.04 (s, 9H, Si(CH₃)₃).

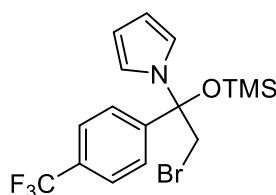
¹³C NMR (100 MHz, C₆D₆) δ: 146.6 (Ph C-1), 130.8 (q, ²*J* = 32.3 Hz, Ph C-4), 127.6 (Ph C-2,6), 125.1 (q, ³*J* = 3.7 Hz, Ph C-3,5), 124.8 (q, ¹*J* = 272.1 Hz, CF₃), 120.0 (Py C-2,5), 109.6 (Py C-3,4), 88.6 (CCH₂Cl), 50.9 (CH₂Cl), 0.8 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -205.3 (Py N-1).

¹⁹F NMR (376 MHz, C₆D₆): δ -62.3 (s, CF₃).

HRMS (APCI), *m/z*: calcd. for C₁₆H₂₀ClF₃NOSi⁺: 362.0949 [M+H]⁺; found: 362.0948.

1-{2-bromo-1-[4-(trifluoromethyl)phenyl]-1-[(trimethylsilyl)oxy]ethyl}-1H-pyrrole (24)



By following the General Procedure, starting from 1H-pyrrol-1-yl[4-(trifluoromethyl)phenyl]methanone (0.239 g, 1.0 mmol, 1.0 equiv), CH₂Br₂ (522 mg, 0.21 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **24** was obtained in 88% yield (358 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.29 (m, 2H, Ph H-3,5), 7.14 (m, 2H, Ph H-2,6), 6.49 (m, 2H, Py H-2,5), 6.18 (m, 2H, Py H-3,4), 3.61 and 3.48 (AB-System, ²J_{AB} = 10.9 Hz, 2H, CH₂Br), -0.03 (s, 9H, Si(CH₃)₃).

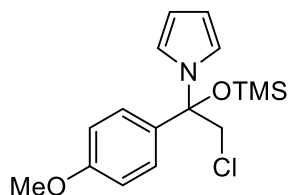
¹³C NMR (100 MHz, C₆D₆) δ: 146.9 (Ph C-1), 130.8 (q, ²J = 32.3 Hz, Ph C-4), 127.5 (Ph C-2,6), 125.1 (q, ³J = 3.7 Hz, Ph C-3,5), 124.8 (q, ¹J = 272.1 Hz, CF₃), 120.1 (Py C-2,5), 109.6 (Py C-3,4), 87.9 (CCH₂Br), 39.9 (CH₂Br), 0.8 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -204.6 (Py N-1).

¹⁹F NMR (376 MHz, C₆D₆): δ -62.3 (CF₃).

HRMS (ESI), *m/z*: calcd. for C₁₆H₂₀BrF₃NOSi⁺: 406.0444 [M+H]⁺; found: 406.0446.

1-{2-chloro-1-(4-methoxyphenyl)-1-[(trimethylsilyl)oxy]ethyl}-1H-pyrrole (25)



By following the General Procedure, starting from (4-methoxyphenyl)(1H-pyrrol-1-yl)methanone (0.201 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **25** was obtained in 76% yield (246 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.22 (m, 2H, Ph H-2,6), 6.76 (m, 2H, Py H-2,5), 6.68 (m, 2H, Ph H-3,5), 6.26 (m, 2H, Py H-3,4), 3.80 and 3.79 (AB-System, ²J_{AB} = 11.7 Hz, 2H, CH₂Cl), 3.26 (OCH₃), 0.01 (s, 9H, Si(CH₃)₃).

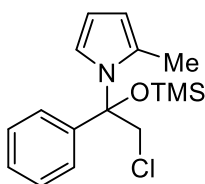
¹³C NMR (100 MHz, C₆D₆) δ: 160.3 (Ph C-4), 134.6 (Ph C-1), 128.6 (Ph C-2,6), 120.2 (Py C-2,5), 113.5 (Ph C-3,5), 109.1 (Py C-3,4), 89.0 (CCH₂Cl), 54.8 (OCH₃), 51.9 (CH₂Cl), 1.1 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -203.2 (Py N-1).

IR (neat, ν: cm⁻¹): 1509.71, 1249.38, 1141.63, 1112.21, 1083.80, 841.56, 497.00.

HRMS (APCI), *m/z*: calcd. for C₁₆H₂₃ClNO₂Si⁺: 324.1181 [M+H]⁺; found: 324.1185.

1-{2-chloro-1-phenyl-1-[(trimethylsilyl)oxy]ethyl}-2-methyl-1*H*-pyrrole (26)



By following the General Procedure, starting from (2-methyl-1*H*-pyrrol-1-yl)(phenyl)methanone (0.185 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv.) was added. The desired product **26** was obtained in 60% yield (185 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

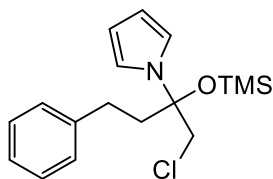
¹H NMR (400 MHz, C₆D₆) δ: 7.24 (m, 2H, Ph H-2,6), 7.07 (m, 2H, Ph H-3,5), 7.05 (m, 1H, Ph H-4), 6.78 (m, 1H, Py H-5), 6.23 (m, 1H, Py H-4), 6.00 (m, 1H, Py H-3), 3.82 and 3.78 (AB-System, ²*J*_{AB} = 11.4 Hz, 2H, CH₂Cl), 1.74 (s, 3H, CH₃), 0.02 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 143.3 (Ph C-1), 130.5 (Py C-2), 128.4 (Ph C-4), 128.0 (Ph C-3,5), 127.0 (Ph C-2,6), 118.2 (Py C-5), 110.7 (Py C-3), 107.7 (Py C-4), 89.0 (CCH₂Cl), 52.4 (CH₂Cl), 0.9 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -206.4 (Py N-1).

HRMS (ESI), *m/z*: calcd. for C₁₆H₂₂ClNNaOSi⁺: 330.1051 [M+Na]⁺; found: 330.1054.

1-{1-chloro-4-phenyl-2-[(trimethylsilyl)oxy]-2-butanyl}-1H-pyrrole (27)



By following the General Procedure, starting from 3-phenyl-1-(1*H*-pyrrol-1-yl)-1-propanone (0.199 g, 1.0 mmol, 1.0 equiv), ICH₂Cl (529 mg, 0.22 mL, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **27** was obtained in 79% yield (254 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 *v/v*, *n*-hexane/diethyl ether).

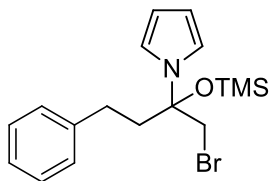
¹H NMR (400 MHz, C₆D₆) δ: 7.16 (m, 2H, Ph H-3,5), 7.08 (m, 1H, Ph H-4), 7.07 (m, 2H, Ph H-2,6), 6.69 (m, 2H, Py H-2,5), 6.29 (m, 2H, Py H-3,4), 3.53 (s, 2H, CH₂Cl), 2.51 (m, 2H, PhCH₂), 2.48 (m, 1H, PhCH₂CH₂), 2.19 (m, 1H, PhCH₂CH₂), 0.02 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 141.3 (Ph C-1), 128.9 (Ph C-3,5), 128.7 (Ph C-2,6), 126.5 (Ph C-4), 118.1 (Py C-2,5), 109.3 (Py C-3,4), 88.5 (CCH₂Cl), 49.8 (CH₂Cl), 40.2 (PhCH₂CH₂), 30.0 (PhCH₂), 1.2 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -204.5 (Py N-1).

HRMS (ESI), *m/z*: calcd. for C₁₇H₂₄ClNNaOSi⁺: 344.1208 [M+Na]⁺; found: 344.1209.

1-{1-bromo-4-phenyl-2-[(trimethylsilyl)oxy]-2-butan-1-yl}-1H-pyrrole (28)



By following the General Procedure, starting from 3-phenyl-1-(1*H*-pyrrol-1-yl)-1-propanone (0.199 g, 1.0 mmol, 1.0 equiv), CH₂Br₂ (522 mg, 0.21, 3.0 mmol, 3.0 equiv), MeLi-LiBr complex solution (1.5 M in diethyl ether, 1.87 mL, 2.8 mmol, 2.8 equiv), the reaction was stirred at -78 °C for 45 min, then 1-(trimethylsilyl)imidazole (421 mg, 0.44 mL, 3.0 mmol, 3.0 equiv) was added. The desired product **28** was obtained in 82% yield (300 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 *v/v*, *n*-hexane/diethyl ether).

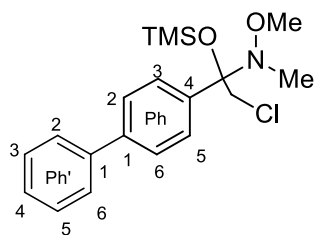
¹H NMR (400 MHz, C₆D₆) δ: 7.16 (m, 2H, Ph H-3,5), 7.09 (m, 3H, Ph H-2,4,6), 6.68 (m, 2H, Py H-2,5), 6.28 (m, 2H, Py H-3,4), 3.43 (s, 2H, CH₂Br), 2.51 (m, 3H, PhCH₂, PhCH₂CH₂), 2.24 (m, 1H, PhCH₂CH₂), -0.02 (s, 9H, Si(CH₃)₃).

¹³C NMR (100 MHz, C₆D₆) δ: 141.3 (Ph C-1), 128.9 (Ph C-3,5), 128.7 (Ph C-2,6), 126.5 (Ph C-4), 118.1 (Py C-2,5), 109.3 (Py C-3,4), 87.3 (CH₂Br), 40.9 (PhCH₂CH₂), 39.0 (CH₂Br), 30.1 (PhCH₂), 1.2 (Si(CH₃)₃).

¹⁵N NMR (40 MHz, C₆D₆) δ: -204.2 (Py N-1).

HRMS (ESI), *m/z*: calcd. for C₁₇H₂₅BrNOSi⁺: 366.0883 [M+H]⁺; found: 366.0888.

1-(4-biphenyl)-2-chloro-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine (29)



In a dry Schlenk flask $\text{Pd}_2(\text{dba})_3$ (4.6 mg, 0.005 mmol, 2.5 mol%) and $\text{P}(t\text{-Bu})_3$ (0.4 mg, 0.002 mmol, 10 mol%) were added to anhydrous toluene. Then, 2-chloro-1-(4-iodophenyl)-*N*-methoxy-*N*-methyl-1-[(trimethylsilyl)oxy]ethanamine **10** (0.19 mmol, 80 mg) was added to the mixture at -10°C . Phenyllithium [1.9 M in *n*-dibutyl ether, 0.57 mmol, 0.3 mL) was diluted with toluene to reach a concentration of 0.6 M and TMEDA (0.23 mmol, 0.034 mL) was added to it; this solution was slowly added over 2 h *via* a syringe pump. After the addition was completed, NaHCO_3 (aq. 5%) was added and the mixture was extracted 3 times with diethyl ether. The organic phases were collected and concentrated under reduced pressure. The desired product **29** was obtained in 65% yield (54 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

^1H NMR (400 MHz, C_6D_6) δ : 7.67 (m, 2H, Ph H-3,5), 7.54 (m, 2H, Ph H-2,6), 7.50 (m, 2H, Ph' H-2,6), 7.21 (m, 2H, Ph' H-3,5), 7.13 (m, 1H, Ph' H-4), 4.09 (d, $J = 11.1$ Hz, 1H, CH_2Cl), 3.82 (d, $J = 11.1$ Hz, 1H, CH_2Cl), 3.27 (s, 3H, OCH_3), 2.28 (s, 3H, NCH_3), 0.43 (s, 9H, $\text{Si}(\text{CH}_3)_3$).

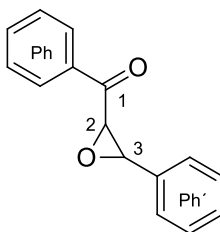
^{13}C NMR (100 MHz, C_6D_6) δ : 141.3 (Ph' C-1), 141.2 (Ph C-1), 140.8 (Ph C-4), 129.1 (Ph' C-3,5), 128.1 (Ph C-3,5), 127.6 (Ph' C-4), 127.5 (Ph' C-2,6), 127.0 (Ph C-2,6), 96.0 ($\underline{\text{C}}\text{CH}_2\text{Cl}$), 60.3 (OCH_3), 51.5 (CH_2Cl), 36.9 (NCH_3), 2.3 ($\text{Si}(\text{CH}_3)_3$).

^{15}N NMR (40 MHz, C_6D_6) δ : -207.6 (NCH_3).

IR (neat, ν : cm^{-1}): 1247.68, 1123.75, 1079.29, 1045.73, 841.23, 495.98.

HRMS (ESI), m/z : calcd. for $\text{C}_{19}\text{H}_{26}\text{ClNNaO}_2\text{Si}^+$: 386.1314 [$\text{M}+\text{Na}$] $^+$; found: 386.1312.

Phenyl(3-phenyl-2-oxiranyl)methanone (30)



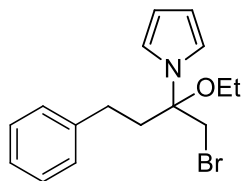
Compound **19** 2,2-dibromo-*N*-methoxy-*N*-methyl-1-phenyl-1-[(trimethylsilyl)oxy]ethanamine (100 mg, 0.25 mmol, 1.0 equiv) was dissolved in dry diethyl ether (5 mL) and the solution was cooled to -78 °C. After 5 minutes, benzaldehyde (0.037 mL, 0.24 mmol, 0.95 equiv) was added, followed by the dropwise addition of *t*-BuLi in *n*-pentane (1.7 M, 0.3 mL, 0.5 mmol, 2.0 equiv). The mixture was stirred at -78 °C for 1 h and, then slowly allowed to reach room temperature over 16 hours. The reaction was quenched with saturated NH₄Cl solution (1 mL) and extracted with Et₂O (3 x 5 mL). The organic layer was washed with brine (5 mL), dried over Na₂SO₄, filtered and after removing the solvent under reduced pressure, the crude was purified by column chromatography on silica gel to afford the desired product in 70% (53 mg) yield as a white solid (mp 82 °C, lit.⁴ 81-82 °C)

¹H NMR (400 MHz, C₆D₆) δ: 7.81 (m, 2H, Ph H-2,6), 7.10 (m, 1H, Ph H-4), 6.98 (m, 2H, Ph H-3,5), 7.07 („s“, 5H, Ph' H-2,6,4,5,6), 3.92 (s, 2H, H-2,3).

¹³C NMR (100 MHz, C₆D₆) δ: 192.4 (CO), 136.5 (Ph' C-1), 136.2 (Ph C-1), 133.5 (Ph C-4), 128.94 (Ph' C-4), 128.85 (Ph C-3,5, Ph' C-3,5), 128.5 (Ph C-2,6), 126.1 (Ph' C-2,6), 61.4 (C-2), 59.1 (C-3).

HRMS (ESI), *m/z*: calcd. for C₁₅H₁₃O₂⁺: 225.0910 [M+H]⁺; found: 225.0912.

1-{1-bromo-2-ethoxy-4-phenyl-2-butanyl}-1*H*-pyrrole (31**)**



1-{1-Bromo-4-phenyl-2-[(trimethylsilyl)oxy]-2-butanyl}-1*H*-pyrrole **28** (100 mg, 0.27 mmol, 1.0 equiv) was dissolved in dry DCM (5 mL) and the solution was cooled -78 °C. After 5 minutes, TMSOTf (0.06 mL, 0.32 mmol, 1.2 equiv) was added, followed by EtI (0.03 mL, 0.4 mmol, 1.5 equiv). The mixture was stirred at -78 °C for 1 h. The reaction was quenched with NaHCO₃ (aq. 5%, 1 mL) and extracted with DCM (3 x 5 mL). The organic layer was washed with brine (5 mL), dried over Na₂SO₄, filtered and the solvent was removed under reduced pressure. The desired product **31** was obtained in 71% yield (62 mg) as a colourless oil after chromatography on neutral alumina (grade III) (98:2 v/v, *n*-hexane/diethyl ether).

¹H NMR (400 MHz, C₆D₆) δ: 7.15 (m, 2H, Ph H-3,5), 7.08 (m, 1H, Ph H-4), 7.03 (m, 2H, Ph H-2,6), 6.66 (m, 2H, Py H-2,5), 6.32 (m, 2H, Py H-3,4), 3.44 and 3.41 (AB-System, ²*J*_{AB} = 11.2 Hz, 2H, CH₂Br), 2.98 – 2.84 (m, 2H, CH₂CH₃), 2.48 (m, 1H, PhCH₂CH₂), 2.40 (m, 2H, PhCH₂), 2.26 (m, 1H, PhCH₂CH₂), 0.93 (t, 3H, CH₃).

¹³C NMR (100 MHz, C₆D₆) δ: 141.2 (Ph C-1), 128.9 (Ph C-3,5), 128.7 (Ph C-2,6), 126.5 (Ph C-4), 118.4 (Py C-2,5), 109.4 (Py C-3,4), 89.4 (CCH₂Br), 57.9 (CH₂CH₃), 37.0 (PhCH₂CH₂), 35.9 (CH₂Br), 29.6 (PhCH₂), 15.2 (CH₃).

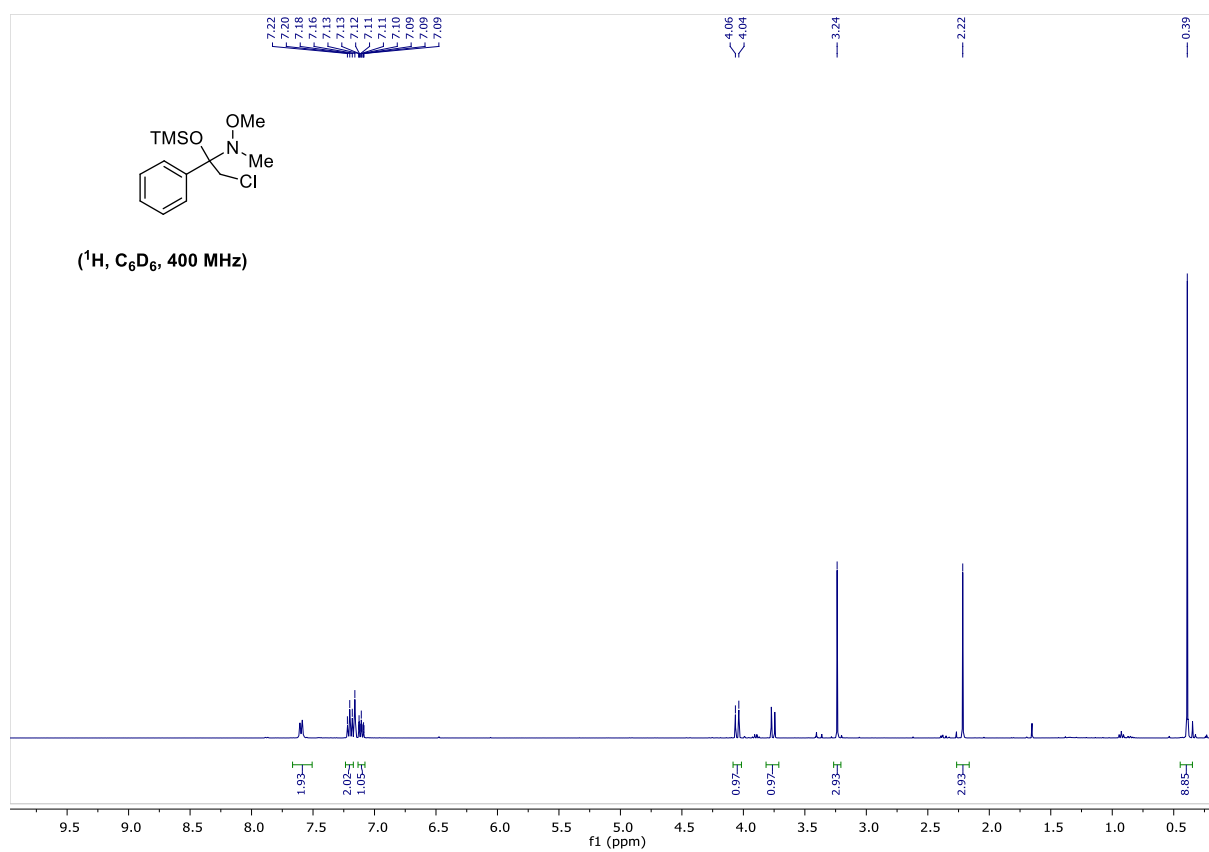
¹⁵N NMR (40 MHz, C₆D₆) δ: -209.4 (Py N-1).

HRMS (ESI), *m/z*: calcd. for C₁₇H₂₁BrNO⁺: 322.0801 [M+H]⁺; found: 322.0803

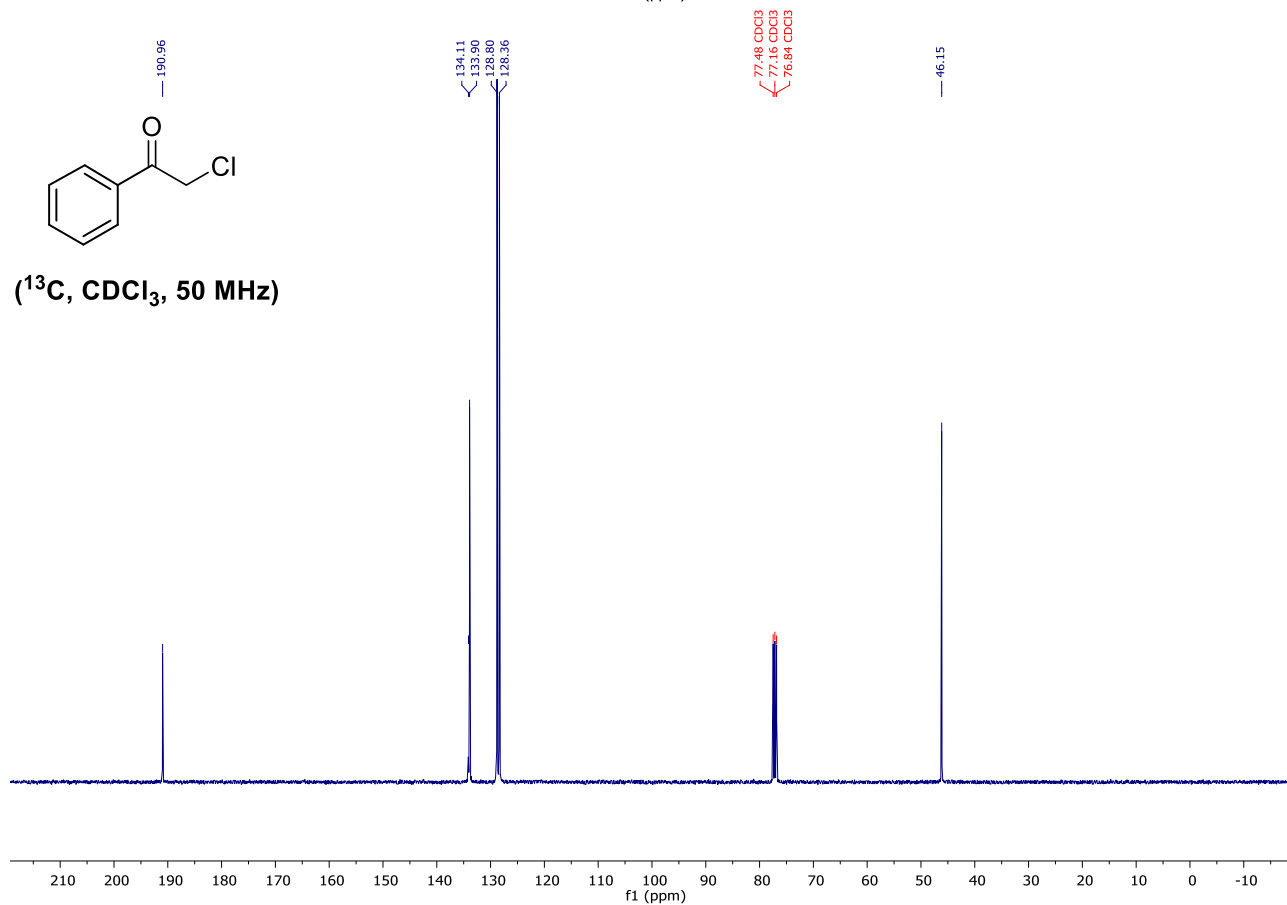
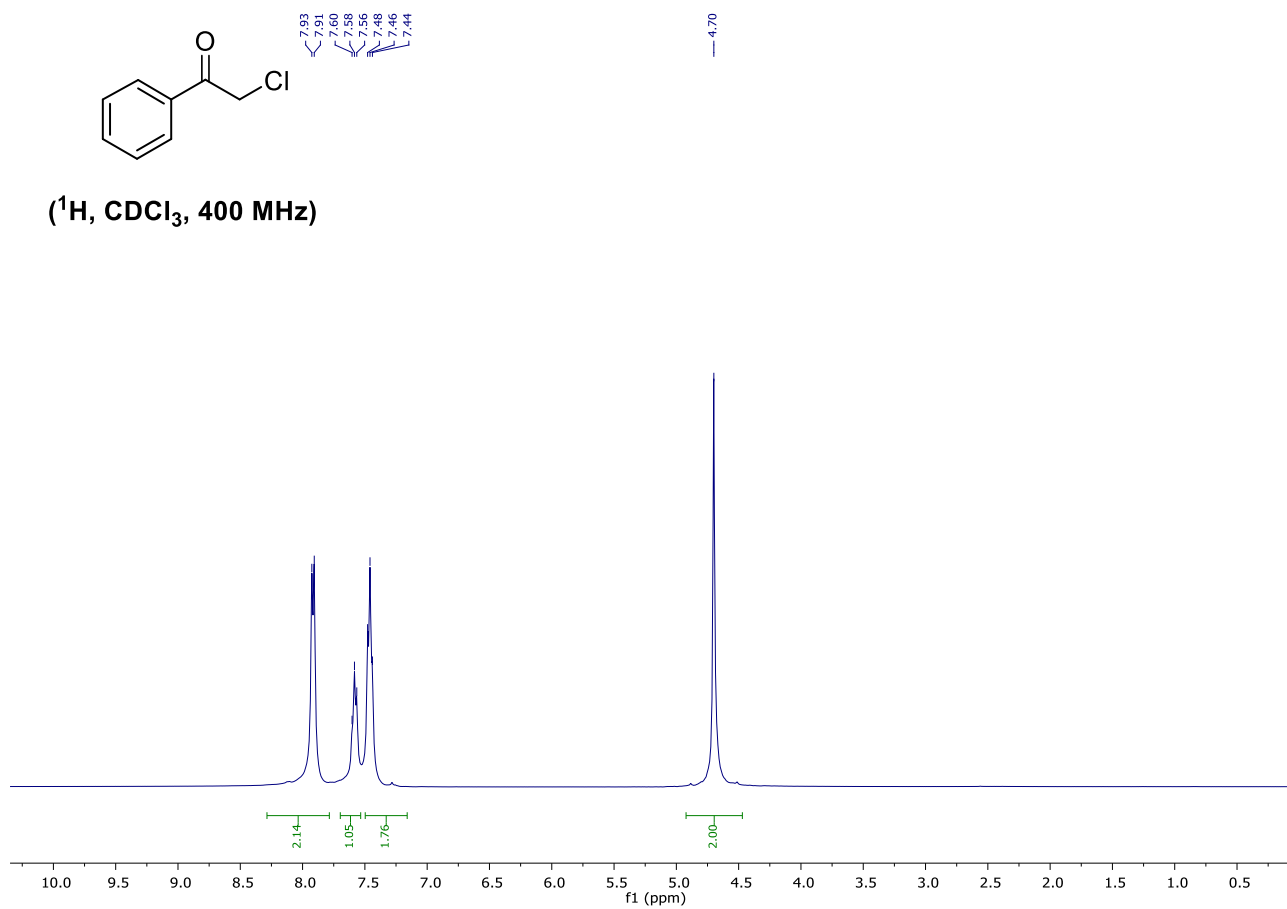
5. References

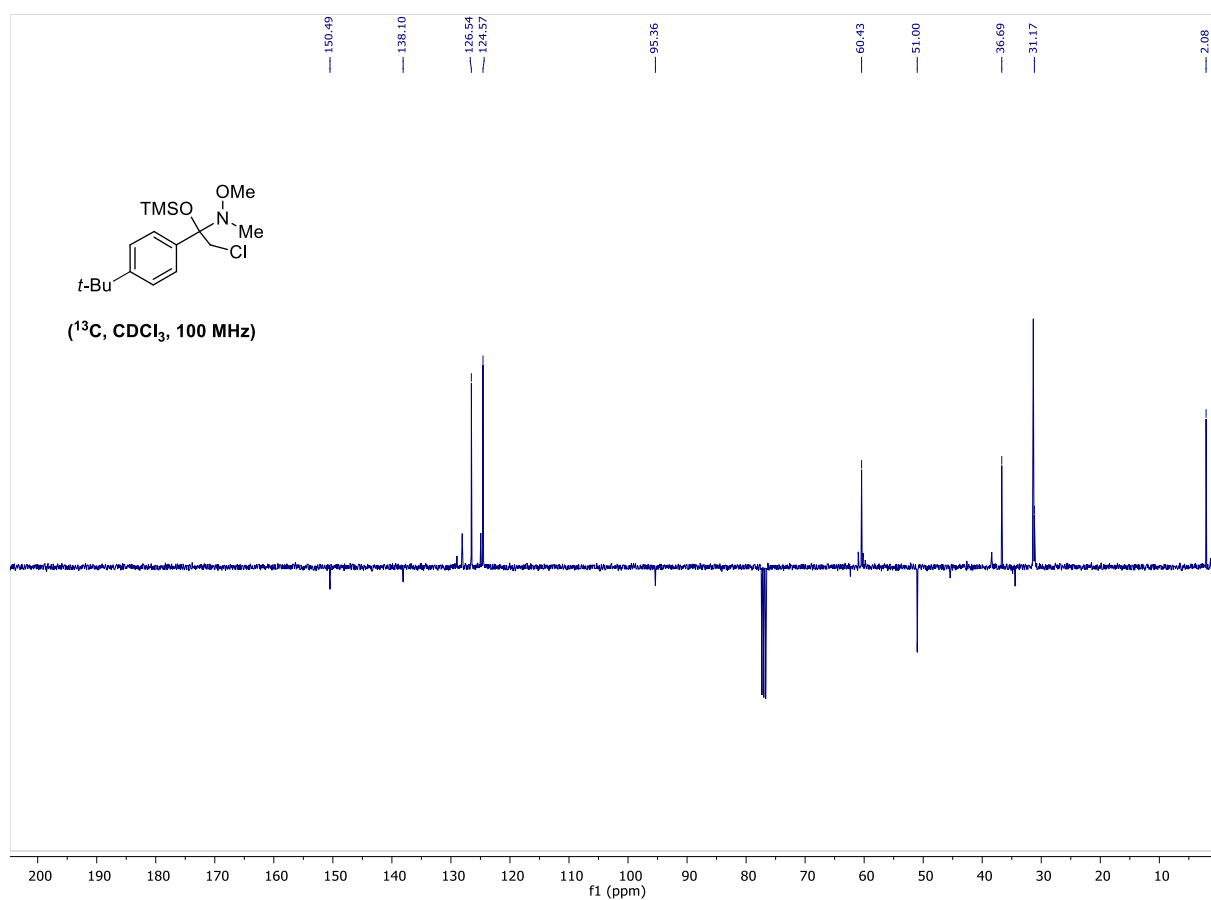
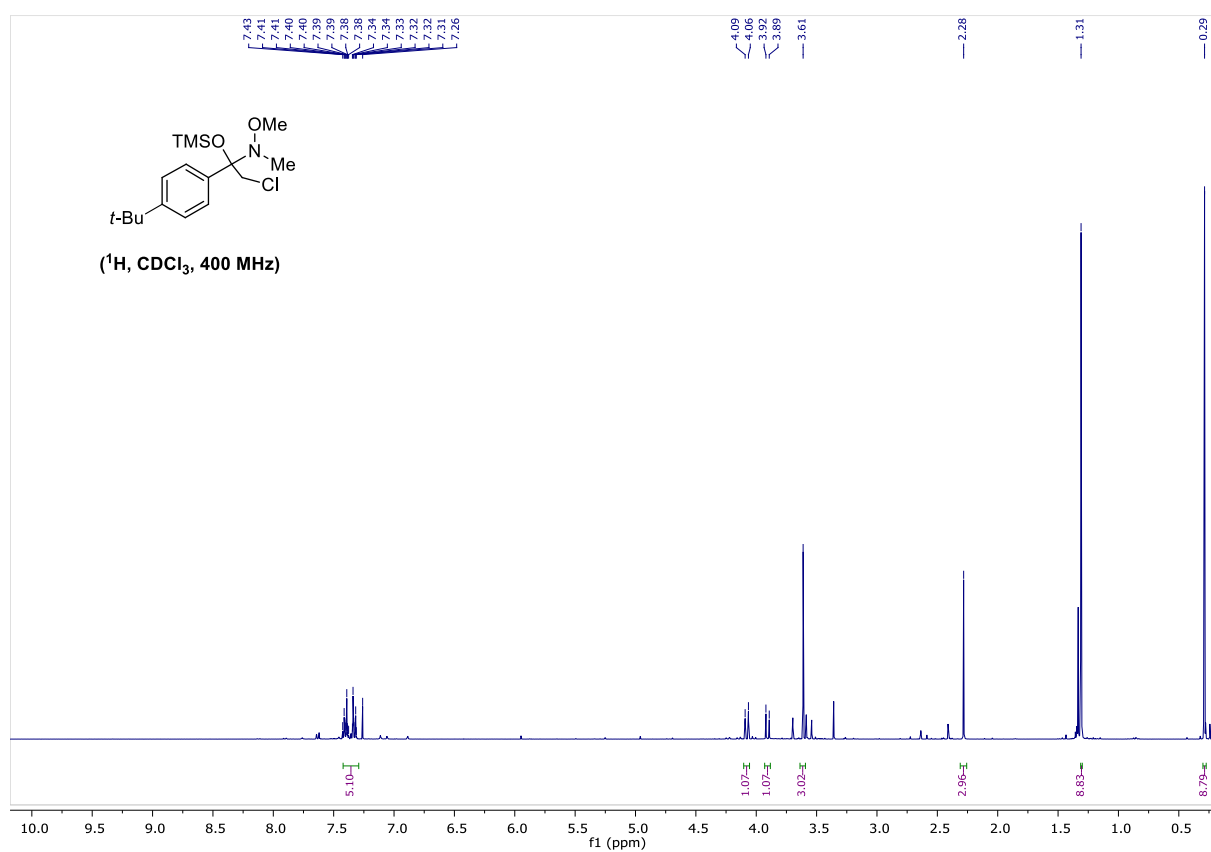
1. a) V. Pace, L. Castoldi, A. R. Alcantara and W. Holzer, *RSC Adv.*, 2013, **3**, 10158; b) A. D. Mamuye, L. Castoldi, U. Azzena, W. Holzer and V. Pace, *Org. Biomol. Chem.*, 2015, **13**, 1969; c) V. Pace, I. Murgia, S. Westermayer, T. Langer and W. Holzer, *Chem. Commun.*, 2016, **52**, 7584; d) D. A. Evans, G. Borg and K. A. Scheidt, *Angew. Chem. Int. Ed.*, 2002, **41**, 3188; e) S. Brandänge, E. Holmgren, H. Leijonmarck and B. Rodriguez, *Acta Chem. Scand.*, 1995, **49**, 922; f) S. Brandänge and B. Rodriguez, *Acta Chem. Scand.*, 1987, **B41**, 740.
2. V. Pace, L. Castoldi, A. D. Mamuye and W. Holzer, *Synthesis*, 2014, **46**, 2897.
3. V. Pace, L. Castoldi and W. Holzer, *Adv. Synth. Catal.*, 2014, **356**, 1761.
4. X.-L. Geng, Z. Wang, X.-Q. Li and C. Zhang, *J. Org. Chem.*, 2005, **70**, 9610.

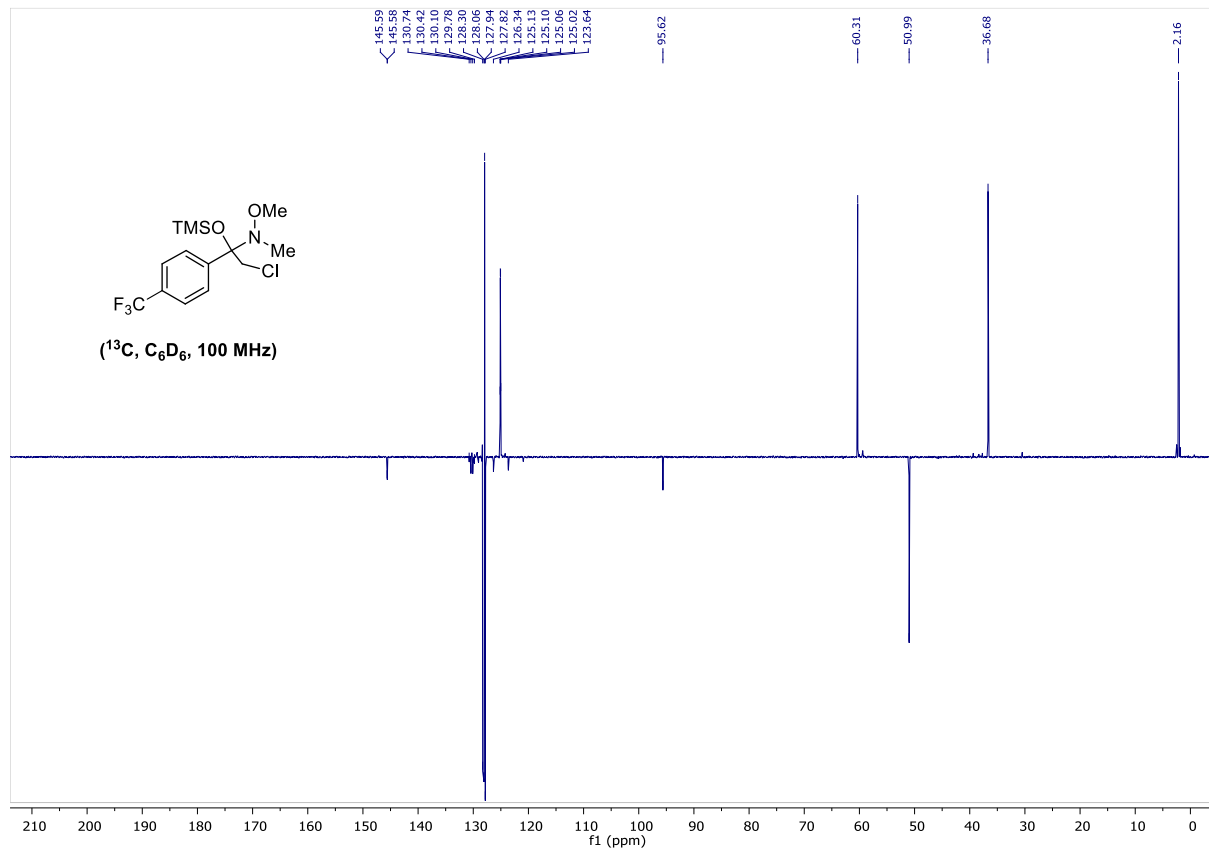
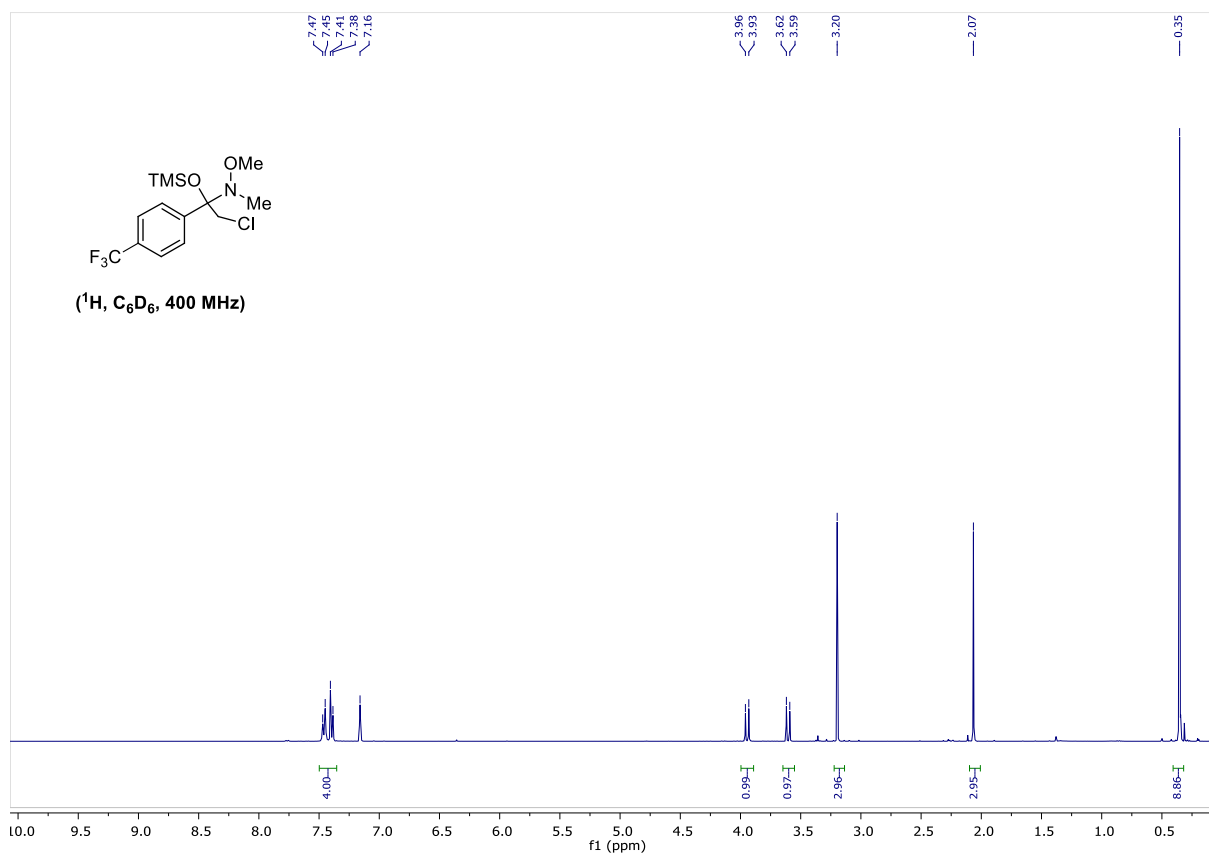
6. Copies of spectra

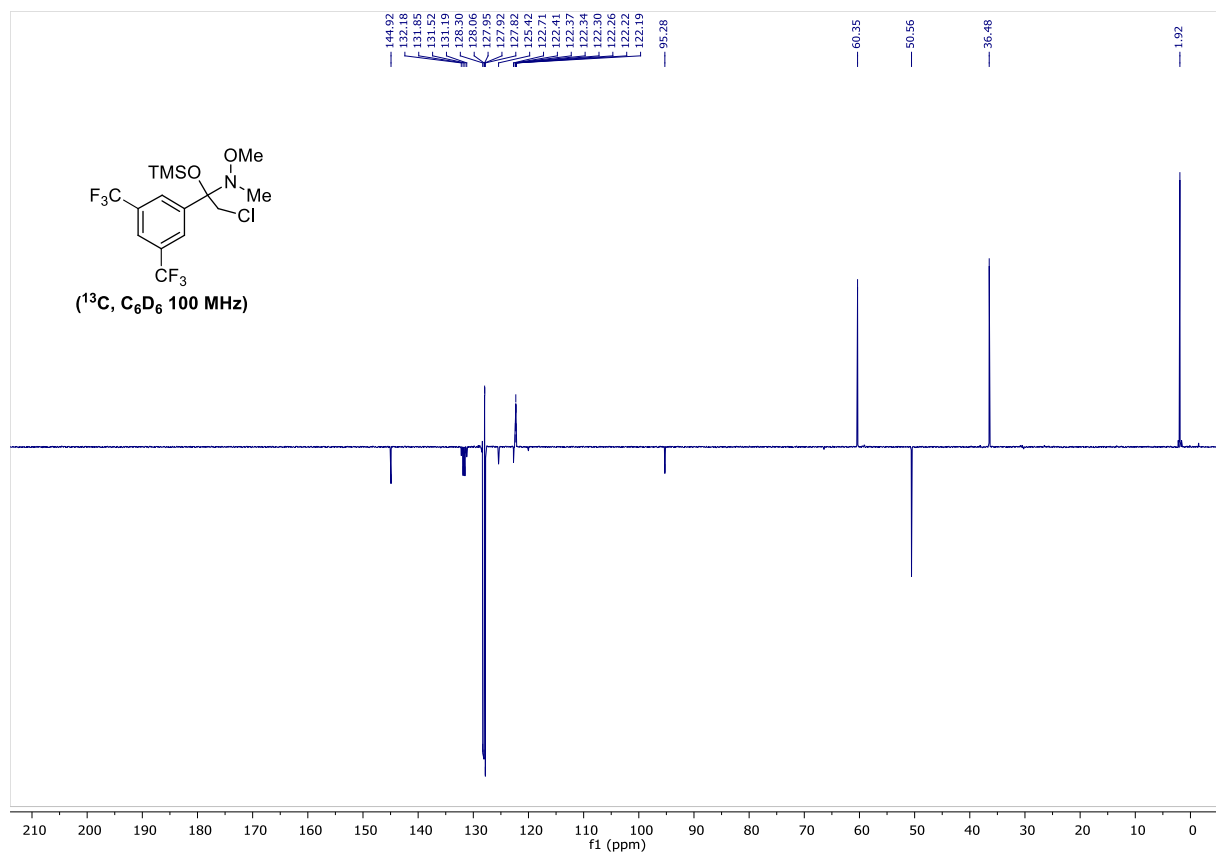
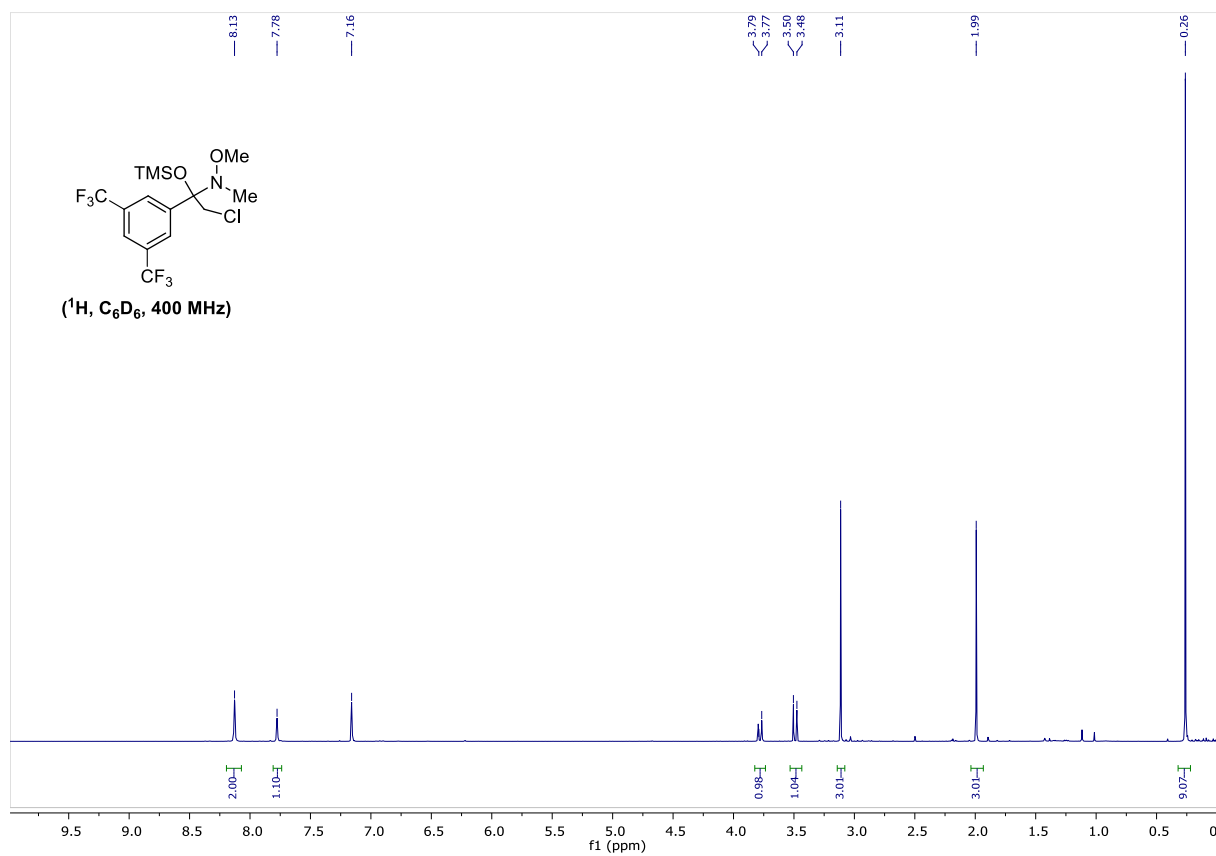


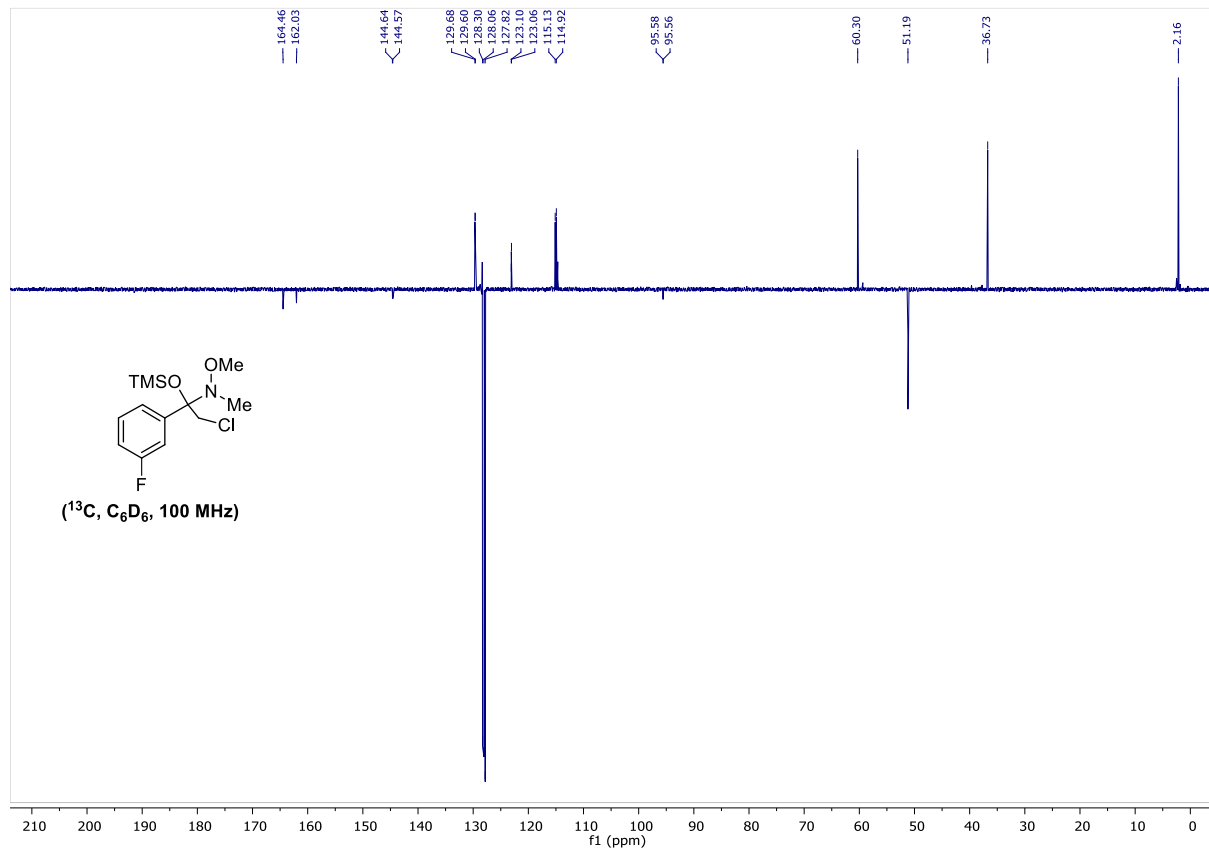
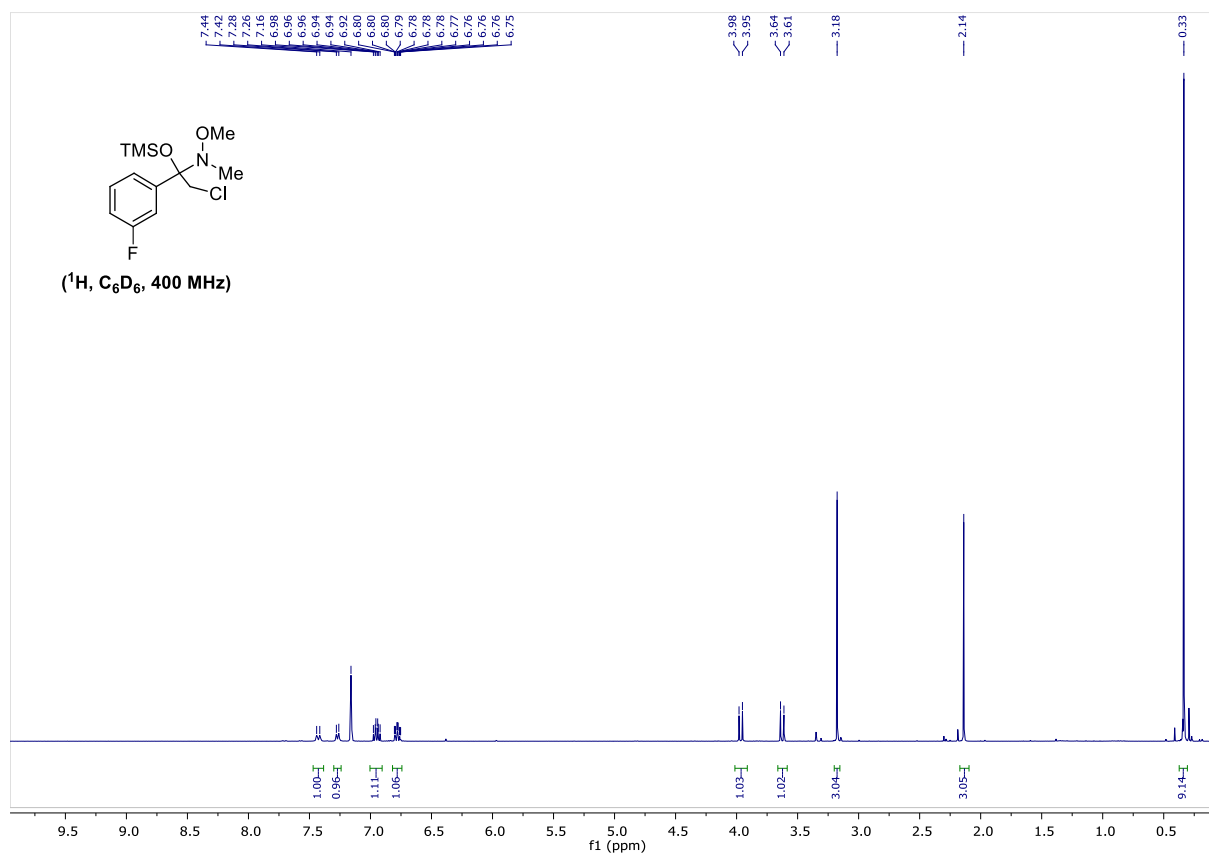
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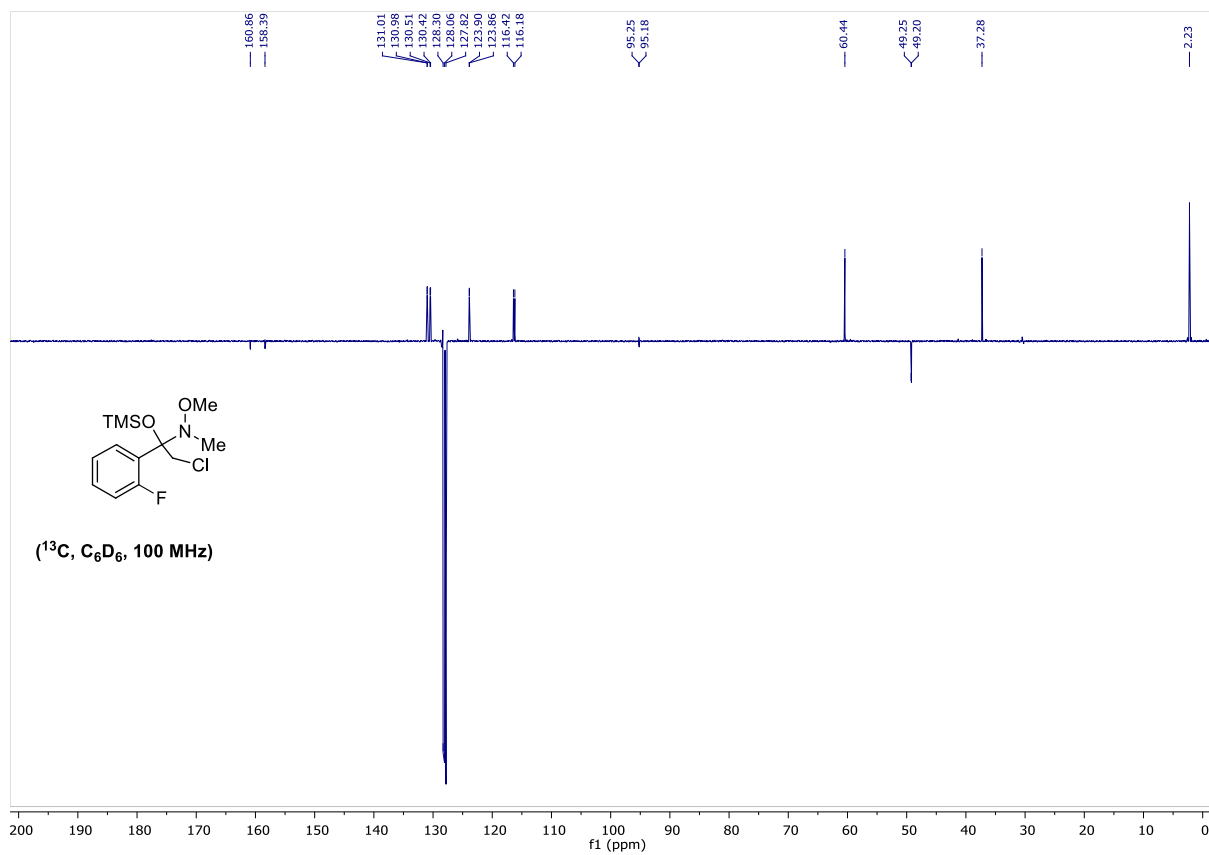
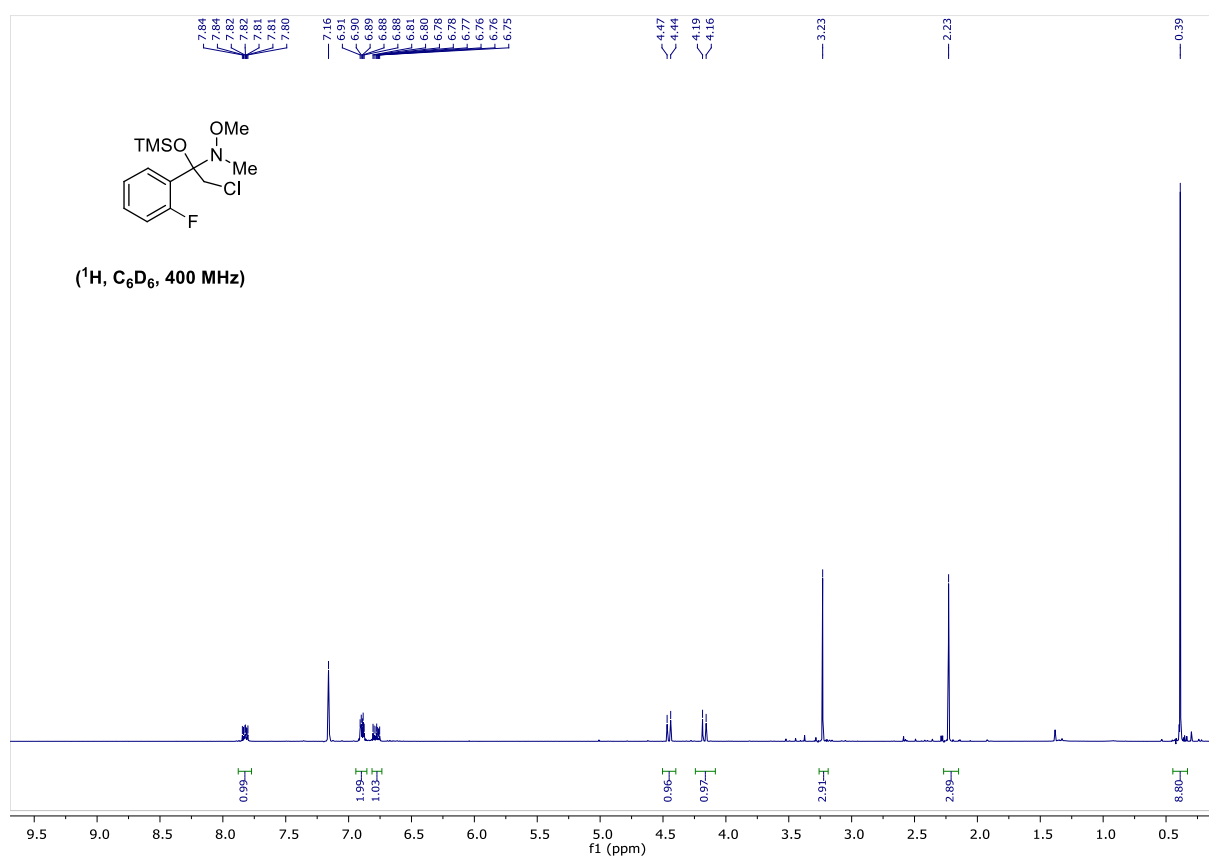


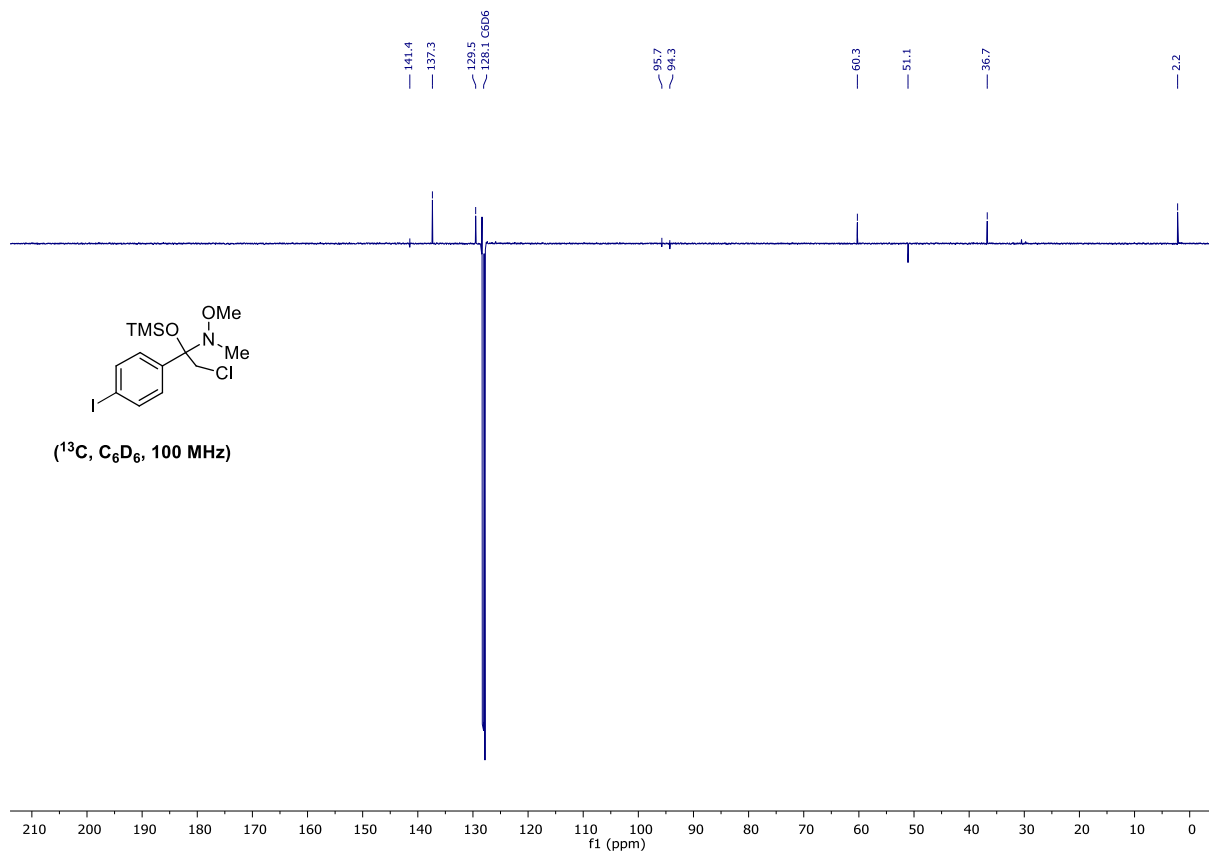
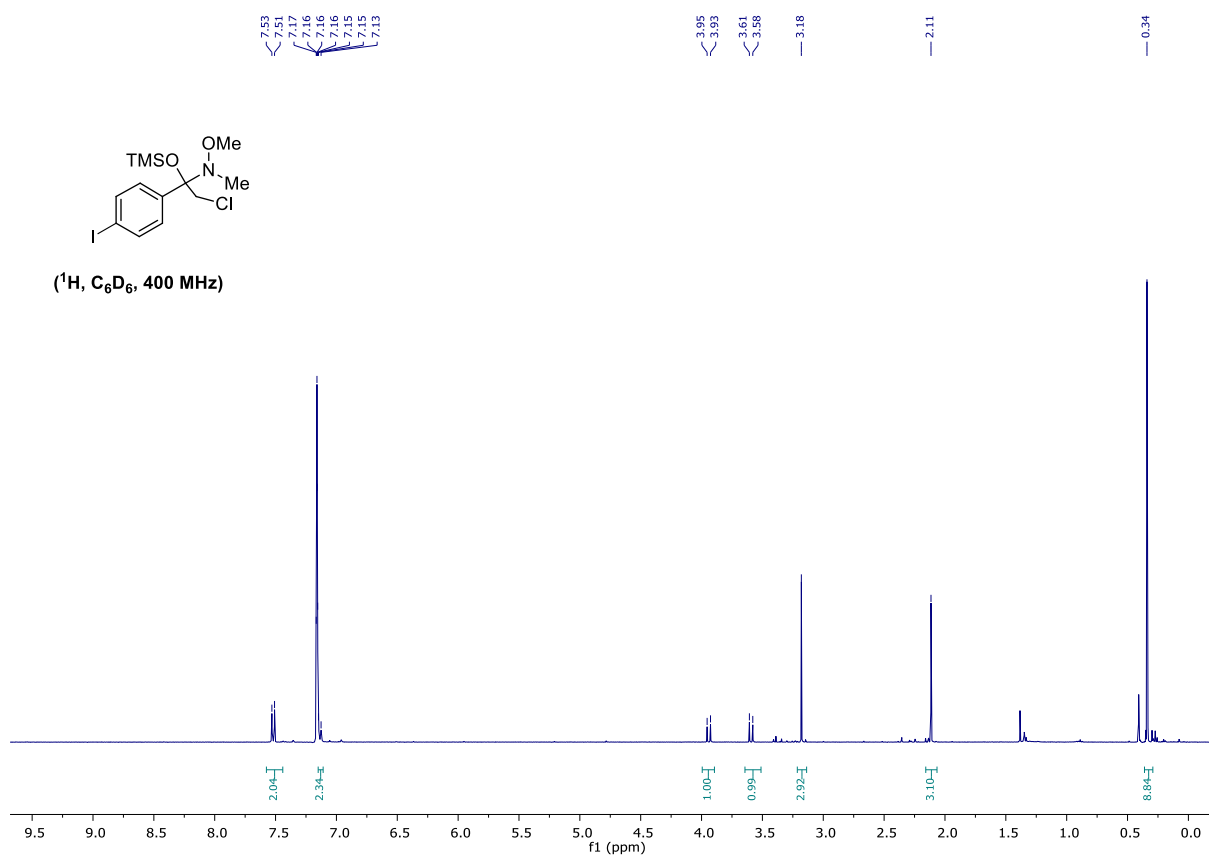












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