Supporting Information

Regioselective Oxidative Arylation of Indoles Bearing *N*-Alkyl Protecting Groups: Dual C-H Functionalization via a Concerted Metalation-Deprotonation Mechanism

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Materials

Reagents

Substrates, including indole, 5-cyanoindole, indole-5-carboxaldehyde, 5-nitroindole, 6-nitroindole, 7-azaindole, indole-6-carboxylic acid, *N*-methylindole, benzylchloride, methoxymethylchloride, 2-(trimethylsilyl)ethoxymethylchloride, 5-methoxyindole, 6-methoxyindole, acetic anhydride, methylindole-6-carboxylate, 7-methylindole, *o*-xylene, *o*-dichlorobenzene, *p*-xylene, *m*-xylene, and *p*-toluenesulfonylchloride were purchased from Sigma Aldrich. All the oxidants used were purchased from Acros Chemicals. Flash chromatography was performed on Silicycle silica gel (60Å, 40- 63 μm). All reagents were stored under an inert atmosphere before use.

$Pd(OAc)_2$

$Pd(OAc)_2$ was obtained from Precious Metals Online (http://www.precmet.com.au/). Upon receipt, it was then dried under vacuum at 100°C for approximately 6 hours.

$H_4PMo_{11}VO_{40}$ (HPMV)

14.4g molybdenum trioxide, 0.98g H_3PO_4 (85%), and 0.91g Vanadium Pentoxide (purchased from Wayne Pigment Corp., Milwaukee, WI) were added to 150ml H_20 and heated with stirring to 80°C for 6h. The precipitate is filtered, and the resulting solution is rotovapped and dried at 85°C under vacuum for 24h. The resulting crystals are orange.
(ref. *Applied Catalysis A: General* 270(2004), 101-111.) The orange product was further dehydrated by heating under vacuum at >115°C over-night. The resulting solid was slightly greener.

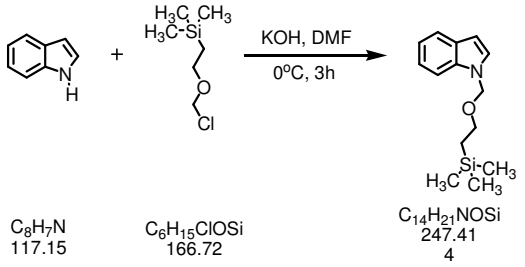
Instrumentation

Reactions were carried out in CEM Discover Microwave. This was the only microwave system that was amenable to the reaction. The formation of a silver mirror on the side of the reaction vial caused Biotage microwave systems to overheat, leading to explosions. Fortuitously, the positioning of the

infrared sensor below the reaction vial in the CEM system allowed for direct detection of the reaction's temperature, as the stir bar kept the surface of the glass free from silver precipitate.

GC/MS analysis was carried out on an Agilent Technologies 6890 GC System fixed with a 5973 Mass Selective Detector. NMR spectra were acquired using a Bruker Avance 300MHz spectrometer.

Synthesis of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole (4)



To a solution of potassium hydroxide (0.238g, 4.26mmol) in 10mL of DMF at 0°C was added a solution of indole (0.5g, 4.26mmol) in 5mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxy methylchloride (0.711g, 4.26mmol) in 5mL DMF and stirring is continued for 3h. The mixture was diluted with 30mL of water and extracted with three 30mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **4** 0.541g (52%). The NMR spectra matched with that previously published.[1]

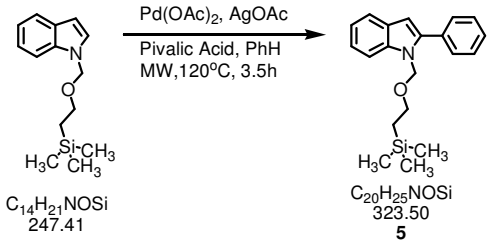
***R_f* -Value:** Hexane/Ethyl acetate (30:1 *v/v*) = 0.33

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.95 (t, ^3J = 7.50 Hz, 2H), 3.53 (t, ^3J = 9.00 Hz, 2H), 5.55 (s, 2H), 6.58 (dd, ^3J = 3.00 Hz, ^4J = 0.78 Hz, 1H), 7.18 – 7.33 (m, 3H), 7.56 (dd, ^3J = 9.00 Hz, ^4J = 0.78 Hz, 1H), 7.69 (m, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 19.15, 67.21, 77.04, 103.85, 111.39, 121.56, 122.35, 123.48, 129.47, 130.50, 137.80

LRMS EI (m/z): [M+] calc'd for $C_{14}H_{21}NOSi$ 247.14, observed 247.20 m/z

Synthesis of 2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (5)



A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.108g, 0.43mmol), palladium acetate (0.0097g, 0.043mmol), silver acetate (0.217g, 1.30mmol), 2,2-dimethylpropanoic acid (0.111g, 1.09mmol) in 4mL of benzene was microwave heated at 120^0C for 3.5h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **5** 0.097g (69%). The NMR spectra matched with that previously published.[1]

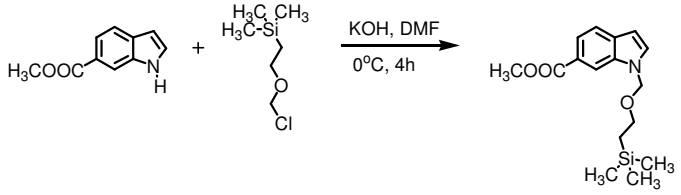
***R_f* -Value:** Hexane/Ethyl acetate (40:1 *v/v*) = 0.38

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.93 (t, ^3J =9.00 Hz, 2H), 3.55 (t, ^3J = 9.00 Hz, 2H), 5.52 (s, 2H), 6.66 (d, ^4J = 0.69 Hz, 1H)**,** 7.20 – 7.71 (m, 9H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 19.31, 67.25, 74.33, 104.58, 111.75, 121.95, 122.07, 123.65, 129.51, 129.77, 129.98, 130.99, 133.99, 139.70, 143.20

LRMS EI (m/z): [M+] calc'd for $C_{20}H_{25}NOSi$ 323.17, observed 323.20m/z

Synthesis of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole-6-carboxylate (7)



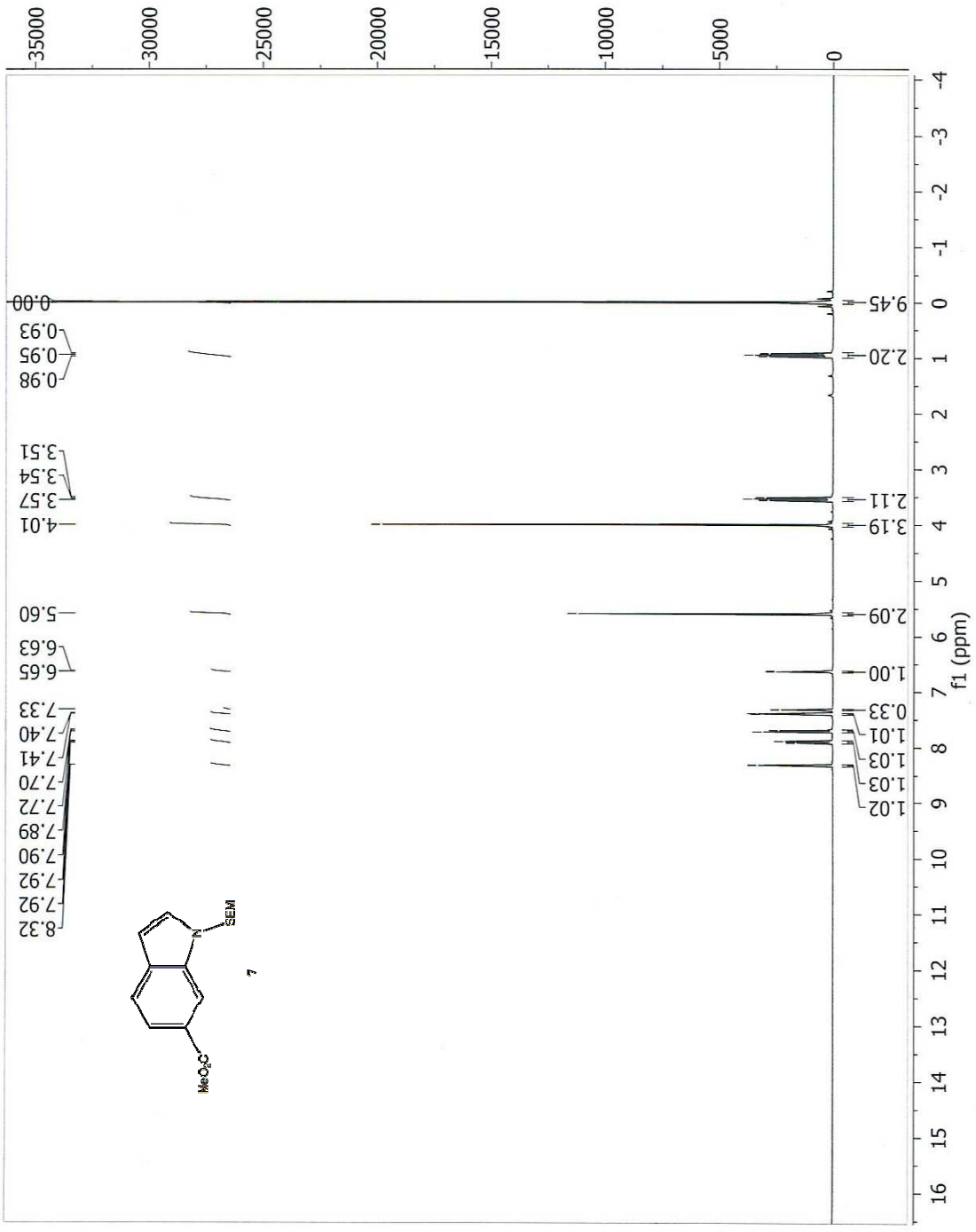
To a solution of potassium hydroxide (0.105g, 1.88mmol) in 6mL of DMF at 0°C was added a solution of methylindole-6-carboxylate (0.3g, 1.71mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.285g, 1.71mmol) in 2mL DMF and stirring is continued for 4h. The mixture was diluted with 40mL of water and extracted with three 40mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **7** 0.309g (59%).

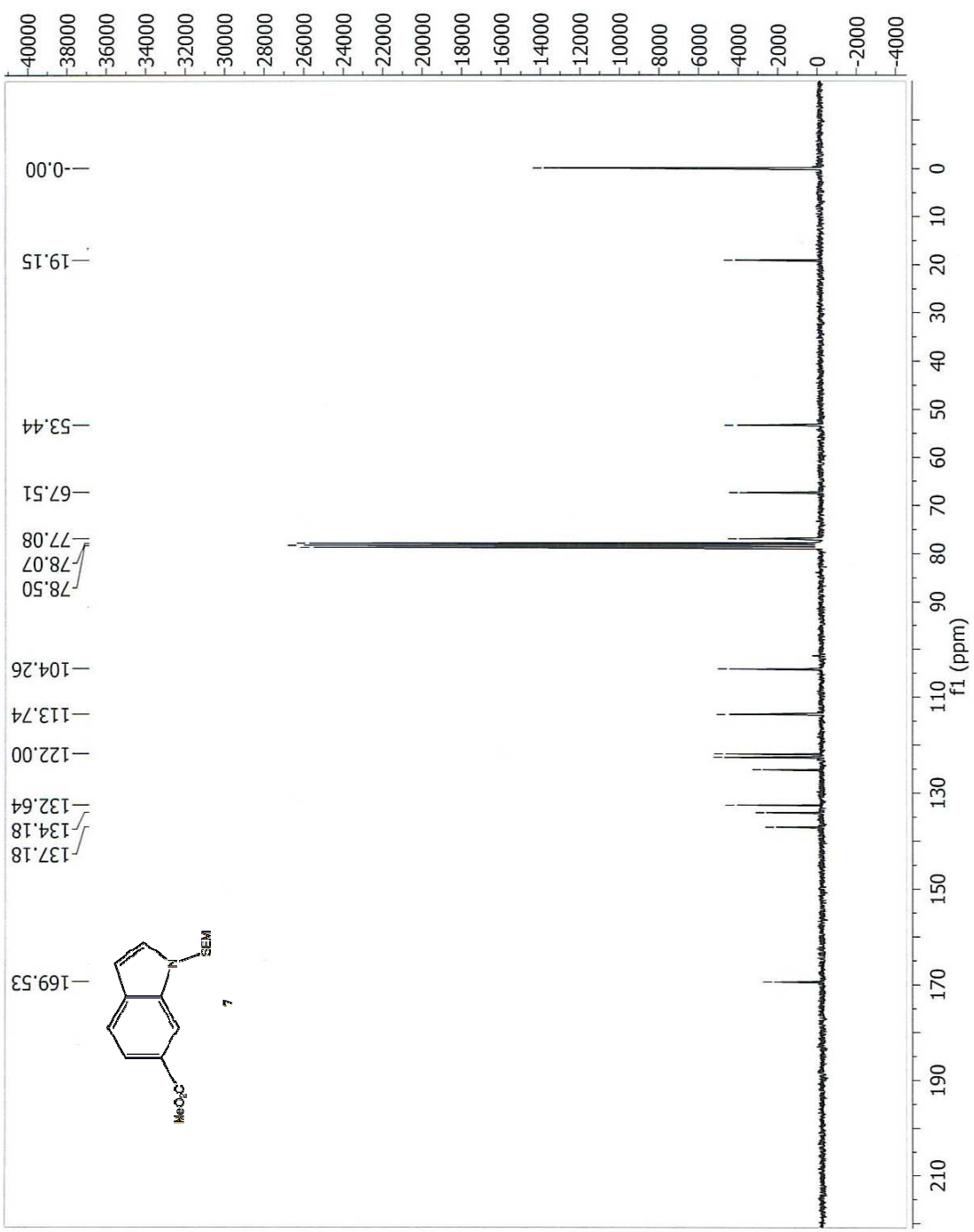
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.20

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.95 (t, ^3J =8.28 Hz, 2H), 3.54 (t, ^3J = 8.07 Hz, 2H), 4.01 (s, 3H), 5.60 (s, 2H), 6.63 (d, ^3J =3.15 Hz, 1H), 7.39 (d, ^3J =3.21 Hz, 1H), 7.70 (d, ^3J =8.34 Hz, 1H), 7.90 (dd, ^3J =8.31 Hz, ^4J = 1.26 Hz, 1H), 8.31 (s, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 19.15, 53.44, 67.51, 77.08, 104.26, 113.74, 122.00, 122.71, 125.26, 132.63, 134.17, 137.18, 169.53

LRMS EI (m/z): [M+] calc'd for $C_{16}H_{23}NO_3Si$ 305.14, observed 305.10 m/z


f1 (ppm)
SEM
MeO2C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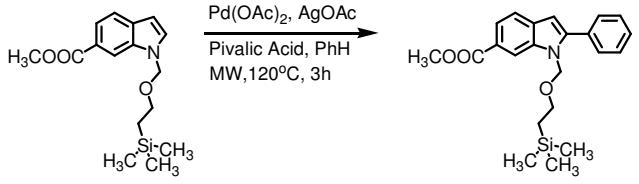
53.44
67.51
77.08
78.07
78.50
104.26
113.74
122.00
132.64
134.18
137.18
169.53
SEM
f1 (ppm)

Synthesis of 2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole-6-carboxylate (8)



$C_{16}H_{23}NO_3Si$
305.44

$C_{22}H_{27}NO_3Si$
381.54
8

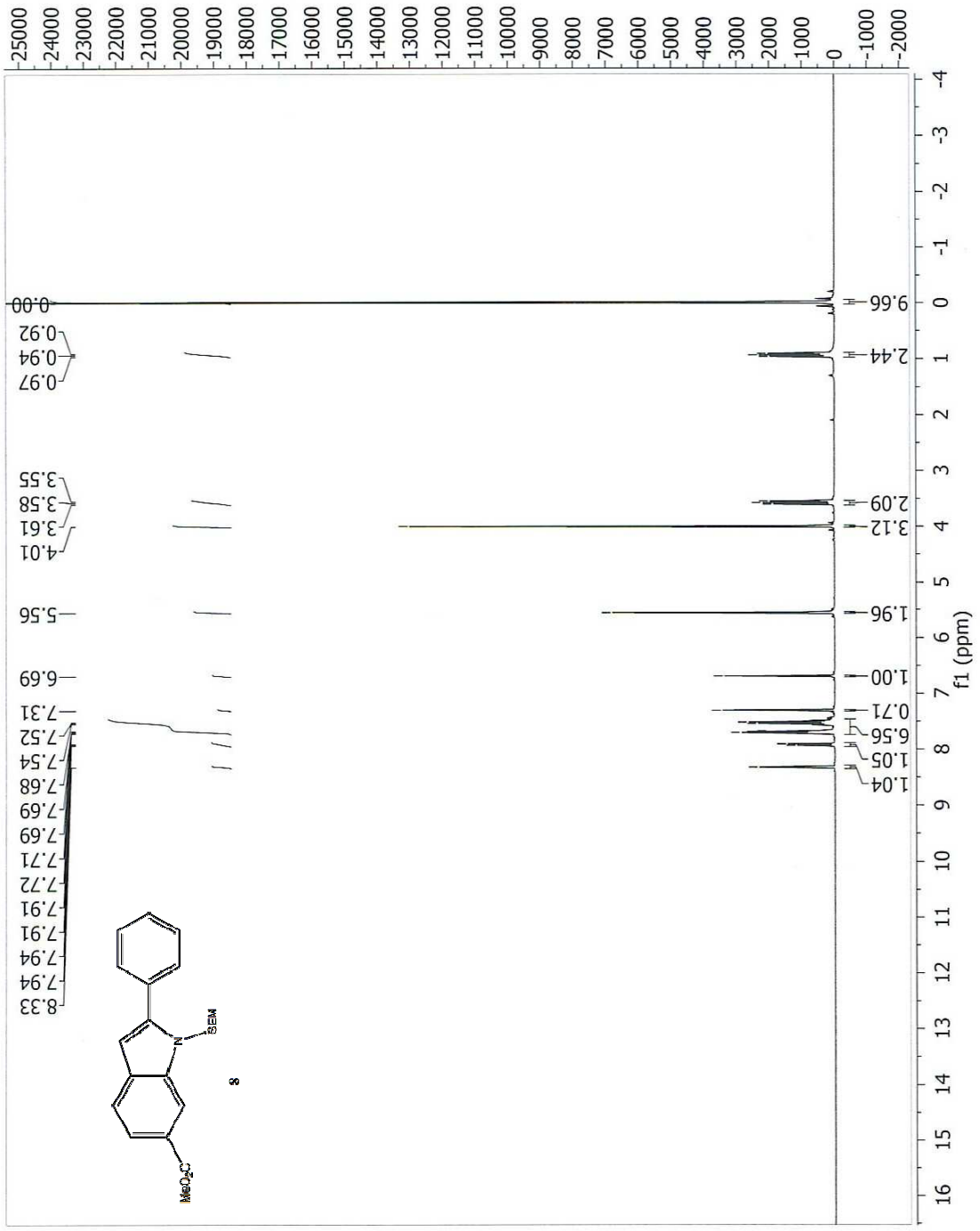
A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole-6-carboxylate (0.064g, 0.21mmol), palladium acetate (0.0047g, 0.021mmol), silver acetate (0.104g, 0.63mmol), 2,2-dimethylpropanoic acid (0.053g, 0.52mmol) in 5mL of benzene was microwave heated at 120°C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **8** 0.078g (97%).

***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.24

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.94 (t, ^3J =8.37 Hz, 2H), 3.58 (t, ^3J = 8.16 Hz, 2H), 4.01 (s, 3H), 5.56 (s, 2H), 6.69 (s, 1H), 7.52-7.71 (m, 6H), 7.91 (dd, ^3J =8.28 Hz, ^4J = 1.20 Hz, 1H), 8.33 (s, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 19.30, 53.44, 67.56, 104.84, 114.03, 121.51, 123.27, 125.16, 130.10, 130.14, 131.00, 133.48, 138.67, 146.32, 169.24

LRMS EI (m/z): [M+] calc'd for $C_{22}H_{27}NO_3Si$ 381.18, observed 381.20 m/z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7.94
7.94
7.91
7.91
7.72
7.71
7.69
7.69
7.68
7.54
7.52
7.31
6.69
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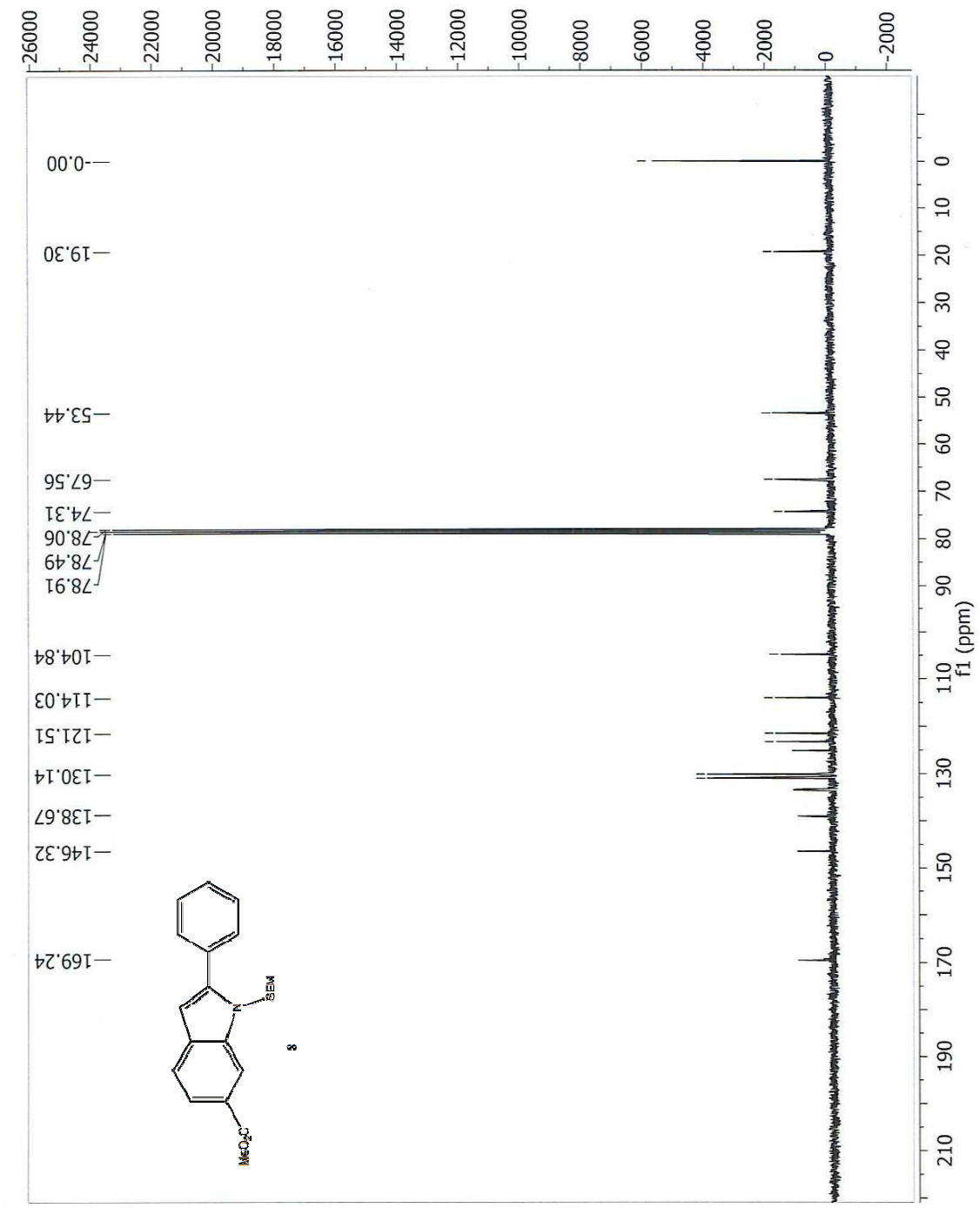
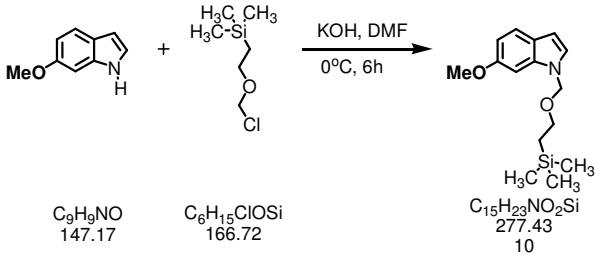
0.00
SEM
N
MeO2C
8


169.24
146.32
138.67
130.14
121.51
114.03
104.84
78.91
78.49
78.06
74.31
67.56
53.44
19.30
0.00
f1 (ppm)
SEM
MeO2C
8

Synthesis of 6-methoxy-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (10)



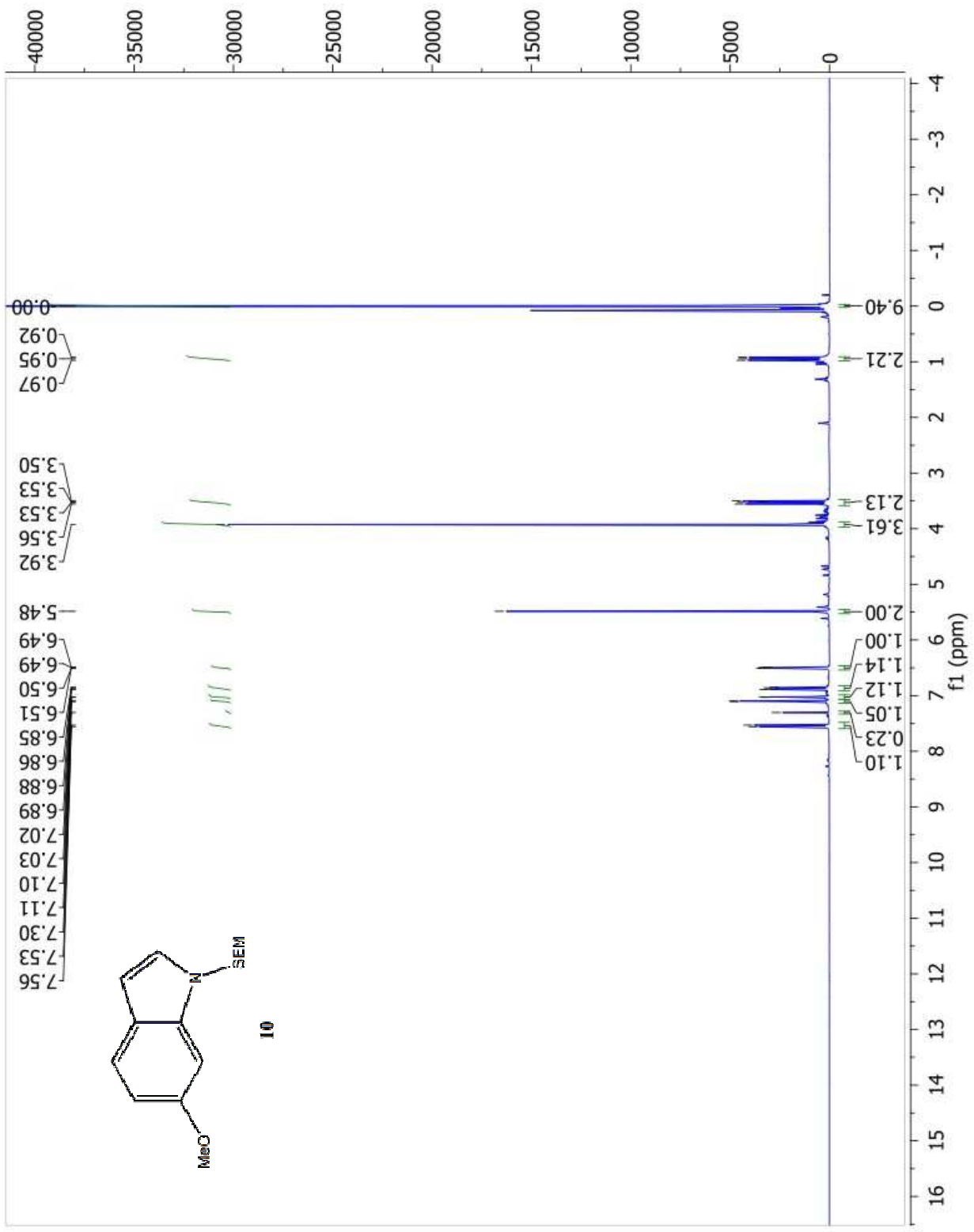
To a solution of potassium hydroxide (0.125g, 2.23mmol) in 10mL of DMF at 0°C was added a solution of 6-methoxyindole (0.3g, 2.03mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.339g, 2.03mmol) in 2mL DMF and stirring is continued for 6h. The mixture was diluted with 30mL of water and extracted with three 30mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **10** 0.350g (61%). The NMR spectra matched with that previously published.

***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.39

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.95 (t, ^3J = 8.28 Hz, 2H), 3.53 (t, ^3J = 8.04 Hz, 2H), 3.92 (s, 3H), 5.48 (s, 2H), 6.49 (d, ^3J = 3.15 Hz, 1H), 6.87 (dd, ^3J = 8.88 Hz, ^4J = 2.43 Hz, 1H), 7.03 (d, ^4J = 2.14 Hz, 1H), 7.10 (d, ^3J = 3.15 Hz, 1H), 7.53 (d, ^3J = 8.85 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.02, 19.13, 57.13, 67.10, 77.13, 95.04, 103.63, 111.61, 112.87, 124.67, 128.46, 138.48, 157.90

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{23}NO_2Si$ 277.15, observed 277.10 m/z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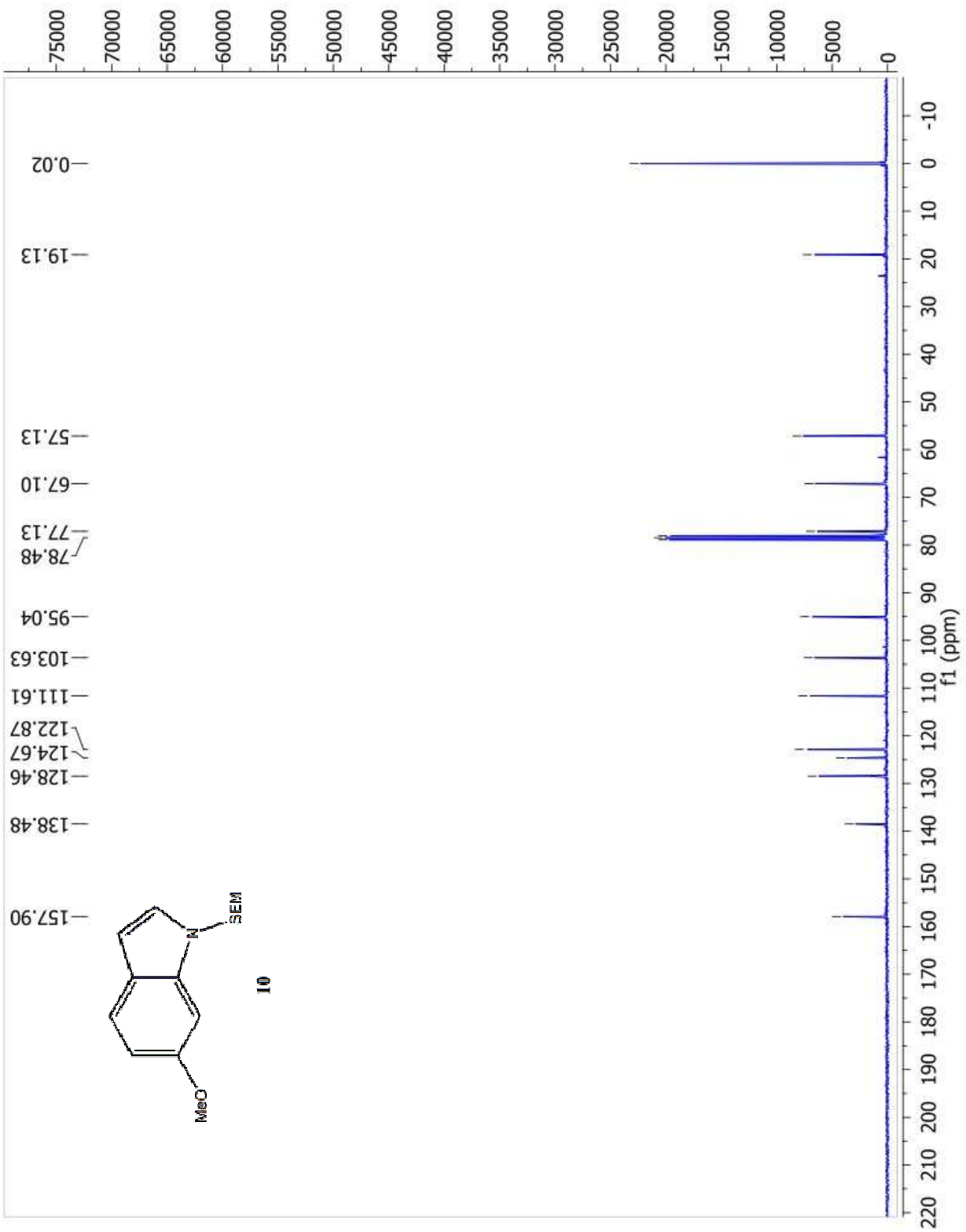
SEM
N
MeO
f1 (ppm)


157.90
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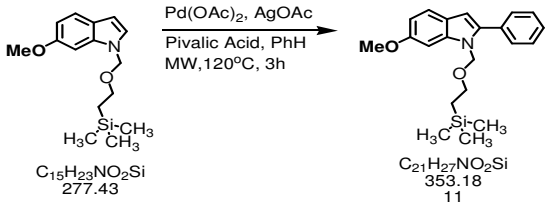
128.46
124.67
122.87
111.61
103.63
95.04
78.48
77.13
67.10
57.13
19.13
0.02
SEM
N
MeO
10
f1 (ppm)

Synthesis of 6-methoxy-2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (11)



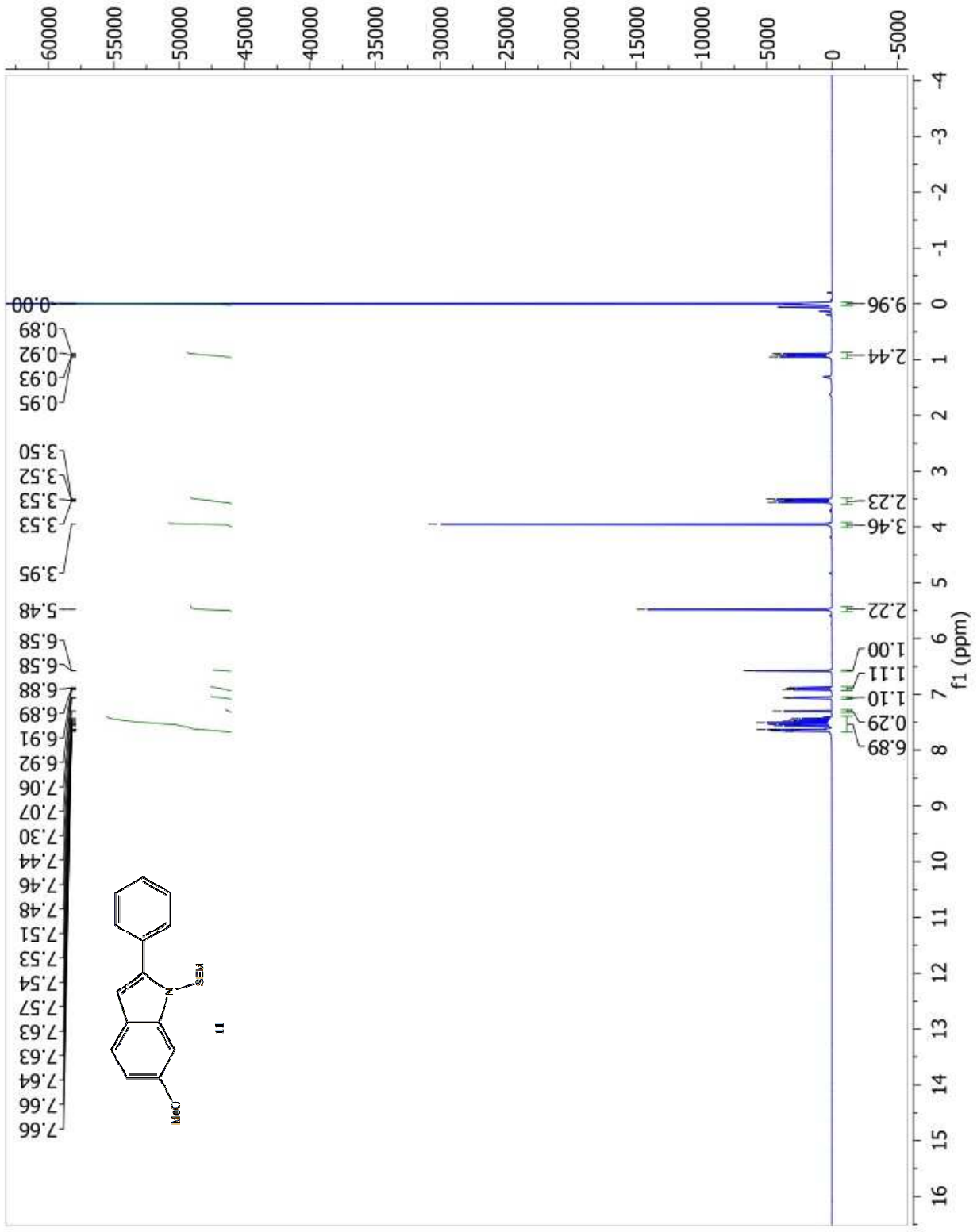
A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-6-methoxyindole (0.085g, 0.306mmol), palladium acetate (0.006g, 0.030mmol), silver acetate (0.152g, 0.920mmol), 2,2-dimethylpropanoic acid (0.078g, 0.76mmol) in 4mL of benzene was microwave heated at 120°C for 2h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **11** 0.061g (56%).

***R_f* -Value:** Hexane/Ethyl acetate (14:1 *v/v*) = 0.36

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.92 (t, ^3J =8.34 Hz, 2H), 3.53 (t, ^3J = 8.16 Hz, 2H), 3.93 (s, 3H), 5.48 (s, 2H), 6.58 (s, 1H), 6.90 (dd, ^3J =8.85 Hz, ^4J = 2.40 Hz, 1H), 7.07 (d, ^4J = 2.28 Hz, 1H), 7.44 – 7.66 (m, 6H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 19.26, 57.19, 67.12, 74.44, 95.73, 104.35, 111.76, 122.52, 124.01, 129.22, 129.95, 130.80, 134.13, 140.49, 142.19, 157.99

LRMS EI (m/z): [M+] calc'd for $C_{21}H_{27}NO_2Si$ 353.18, observed 353.20 m/z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0.00
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0.92
0.93
0.95
3.50
3.52
3.53
3.53
3.95
5.48
6.58
6.58
6.88
6.89
6.91
6.92
7.06
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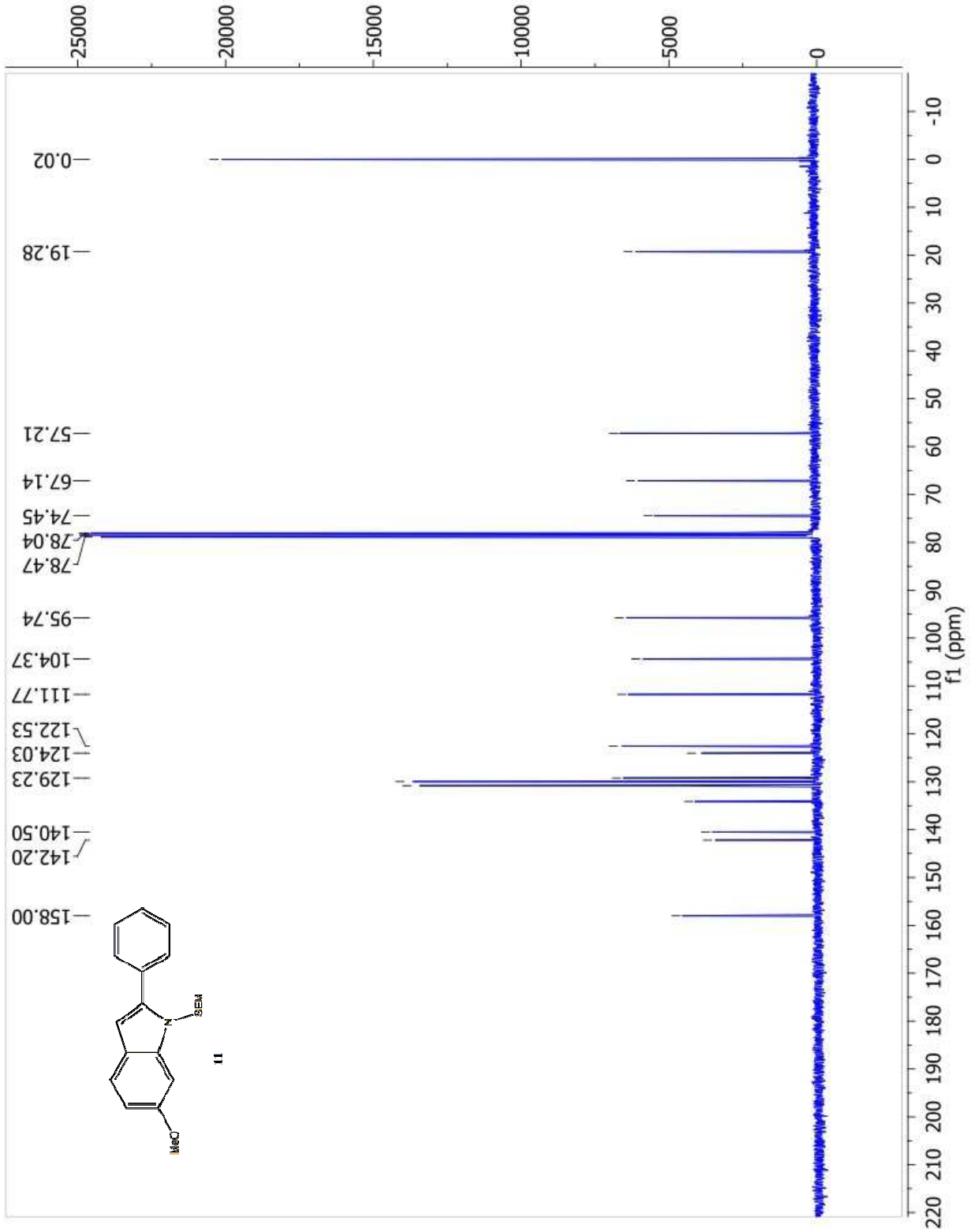
7.64
7.66
7.66
MeO
SEM
N
11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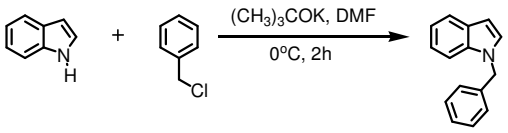
95.74
104.37
111.77
122.53
124.03
129.23
140.50
142.20
158.00
SEM
MeO
11
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
f1 (ppm)

Synthesis of *N*-benzylindole



C_8H_7N 117.15 | C_7H_7Cl 126.58 | $C_{15}H_{13}N$ 207.27

To a solution of potassium tert-butoxide (0.718g, 6.40mmol) in 10mL of DMF at 0°C was added a solution of indole (0.500g, 4.26mmol) in 5mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of benzylchloride (0.594g, 4.69mmol) in 5mL DMF and stirring is continued for 2h. The mixture was diluted with 30mL of water and extracted with three 30mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.677g (77%). The NMR spectra matched with that previously published.[2]

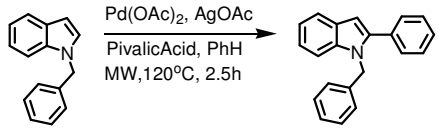
***R_f* -Value:** Hexane/Ethyl acetate (20:0.5 *v/v*) = 0.36

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.37 (s, 2H), 6.55 (dd, ^3J = 3.15 Hz, ^4J = 0.81 Hz 1H), 7.08-7.29 (m, 9H), 7.65 (m, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 50.06, 101.66, 109.67, 119.50, 120.95, 121.66, 126.75, 127.57, 128.24, 128.6, 128.74, 136.28, 137.53

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{13}N$ 207.10, observed 207.10 m/z

Synthesis of 1-benzyl-2-phenylindole (13)



$C_{15}H_{13}N$ 207.27 | $C_{21}H_{17}N$ 283.37 **13**

A magnetically stirred solution of *N*-benzylindole (0.100g, 0.48mmol), palladium acetate (0.010g, 0.048mmol), silver acetate (0.240g, 1.44mmol), 2,2-dimethylpropanoic acid (0.123g, 1.20mmol) in 4mL of benzene was microwave heated at 120^{0}C for 2.5h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of

ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **13** 0.077g (57%). The NMR spectra matched with that previously published.[3]

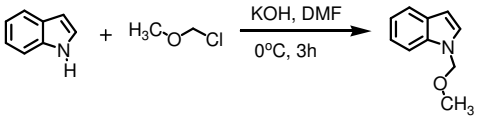
***R*$_f$ -Value:** Hexane/Ethyl acetate (40:1 *v/v*) = 0.38

^{1}H-NMR (300 MHz, CDCl$_3$): δ = 5.37 (s, 2H), 6.65 (d, 1H) 7.03 (d, ^3J = 6.00 Hz 2H), 7.13-7.43 (m, 11H), 7.67 (m, 1H)

^{13}C-NMR (75 MHz, CDCl$_3$): δ = 47.73, 102.31, 110.56, 120.16, 120.54, 121.90, 125.96, 127.15, 128.03, 128.55, 128.74, 129.21, 132.68, 137.96, 138.20, 141.82

LRMS EI (m/z): [M+] calc'd for $C_{21}H_{17}N$ 283.13, observed 283.10m/z

Synthesis of *N*-methoxymethylindole



C_8H_7N 117.15 | C_2H_5ClO 80.51 | $C_{10}H_{11}NO$ 161.20

To a solution of potassium hydroxide (0.238g, 4.26mmol) in 10mL of DMF at 0^{o}C was added a solution of indole (0.5g, 4.26mmol) in 5mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of methoxymethylchloride (0.343g, 4.26mmol) in 5mL DMF and stirring is continued for 3h. The mixture was diluted with 30mL of water and extracted with three 30mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.269g (40%). The NMR spectra matched with that previously published.[4]

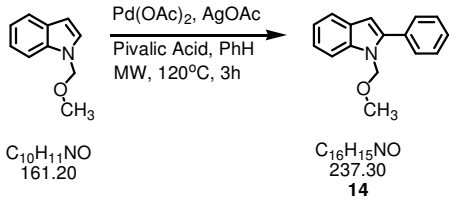
***R*$_f$ -Value:** Hexane/Ethyl acetate (20:1 *v/v*) = 0.30

^{1}H-NMR (300 MHz, CDCl$_3$): δ = 3.24 (s, 3H), 5.46 (s, 2H), 6.53 (d, ^3J = 3.00 Hz, 1H), 7.13 – 7.27 (m, 3H), 7.49 (d, ^3J = 9.00 Hz, 1H), 7.64 (d, ^3J = 6.00 Hz, 1H)

^{13}C-NMR (75 MHz, CDCl$_3$): δ = 55.86, 102.61, 109.86, 120.25, 120.98, 122.17, 128.10, 129.12, 136.34

LRMS EI (m/z): [M+] calc'd for $C_{10}H_{11}NO$ 161.08, observed 161.10 m/z

Synthesis of 1-methoxymethyl-2-phenyl-indole (14)



A magnetically stirred solution of 1-methoxymethylindole (0.064g, 0.397mmol), palladium acetate (0.008g, 0.039mmol), silver acetate (0.197g, 1.19mmol), 2,2-dimethylpropanoic acid (0.101g, 0.99mmol) in 10mL of benzene was microwave heated at 120^0C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **14** 0.053g (56%). The NMR spectra matched with that previously published.[5]

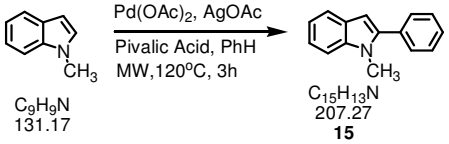
***R_f* -Value:** Hexane/Ethyl acetate (20:1 *v/v*) = 0.23

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.29 (s, 3H), 5.42 (s, 2H), 6.61 (s, 1H), 7.15-7.46 (m, 9H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 55.95, 74.74, 103.41, 110.22, 120.62, 120.78, 122.35, 128.17, 128.38, 128.61, 129.52, 132.44, 138.32, 141.85

LRMS EI (m/z): [M+] calc'd for $C_{16}H_{15}NO$ 237.12, observed 237.10 m/z

Synthesis of 1-methyl-2-phenylindole (15)



A magnetically stirred solution of *N*-methylindole (0.091g, 0.0698mmol), palladium acetate (0.015g, 0.069mmol), silver acetate (0.347g, 2.08mmol), 2,2-dimethylpropanoic acid (0.178g, 1.74mmol) in 4mL of benzene was microwave heated at 120^0C for 3h. After evaporation of the

solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **15** 0.043g (31%). The NMR spectra matched with that previously published.[1]

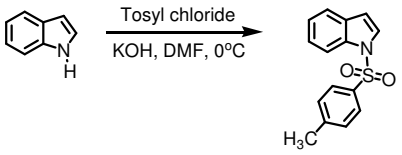
***R_f* -Value:** Hexane/Ethyl acetate (40:1 *v/v*) = 0.25

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.74 (s, 3H), 6.57 (s, 1H), 7.14-7.50 (m, 8H), 7.64 (d, ^3J = 6.0 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 31.17, 101.61, 109.59, 119.84, 120.45, 121.64, 127.84, 127.92, 128.48, 129.36, 132.81, 138.30, 141.55

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{13}N$ 207.10, observed 207.10 m/z

Synthesis of *N*-tosylindole



C_8H_7N
117.15

$C_{15}H_{13}NO_2S$
271.33

To a solution of KOH (0.1795g, 3.19mmol) in 30 mL of DMF at 0^{o}C was added a solution of indole (0.250g, 2.13mmol) in 5mL of DMF and the reaction mixture is stirred for 15 mins. After stirring for 15 mins a solution of tosyl chloride (0.447g, 2.34mmol) in 5mL DMF was added and stirring was continued for 15min. The mixture was then diluted with 30 mL of water and extracted with three 30 mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30 mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent was removed at reduced pressure and the crude product was purified by flash column chromatography to give pure (0.177g, 31%). The NMR spectra matched with that previously published.[6]

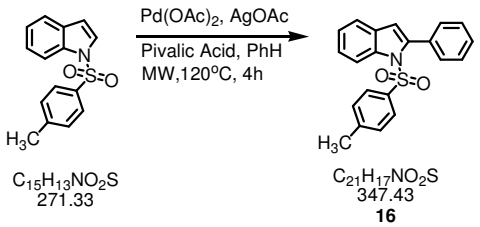
***R_f* -Value:** hexane/ethylacetate (9:1 *v/v*) = 0.46

^{1}H-NMR (400 MHz, $(CD_3)_2CO$): δ = 2.33 (s, 3H), 6.77 (d, ^3J = 3.64 Hz, 1H), 7.22 (t, ^3J = 6.92 Hz, 1H), 7.30-7.37 (m, 3H), 7.57 (d, ^3J = 7.72 Hz, 1H), 7.68 (d, ^3J = 2.96 Hz, 1H) 7.85 (d, ^3J = 8.40 Hz, 2H), 8.00 (d, ^3J = 8.44 Hz, 1H)

^{13}C-NMR (100 MHz, $(CD_3)_2CO$): δ = 20.54, 109.15, 113.45, 121.50, 123.39, 124.53, 126.68, 126.93, 130.03, 131.07, 134.92, 135.44, 145.50

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{13}NO_2S$ 271.06, observed 271.10 m/z

Synthesis of *N*-tosyl-2-phenylindole (16)



A magnetically stirred solution of *N*-tosylindole (0.089g, 0.33mmol), palladium acetate (0.0074g, 0.033mmol), silver acetate (0.164g, 0.98mmol), 2,2-dimethylpropanoic acid (0.084g, 0.82mmol) in 4mL of benzene was microwave heated at 120^0C for 4h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **16** 0.055g (49%). The NMR spectra matched with that previously published.[6]

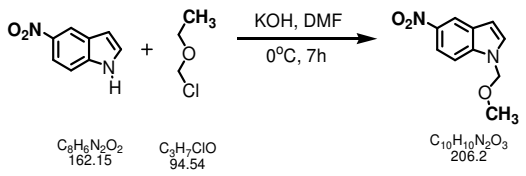
***R_f* -Value:** Hexane/Ether (9:1 *v/v*) = 0.32

^{1}H-NMR (300 MHz, $(CD_3)_2CO$): δ = 2.28 (s, 3H), 6.70 (s, 1H), 7.20 (d, ^3J = 8.08 Hz, 2H), 7.26-7.56 (m, 10H), 8.25 (d, ^3J = 8.24 Hz, 1H)

^{13}C-NMR (75 MHz, $(CD_3)_2CO$): δ = 20.53, 113.83, 116.41, 121.02, 124.82, 126.72, 127.56, 128.58, 129.50, 130.27

LRMS EI (m/z): [M+] calc'd for $C_{21}H_{17}NO_2S$ 347.09, observed 347.20 m/z

Synthesis of 1-methoxymethyl-5-nitroindole



Procedure:

To a solution of potassium hydroxide (0.097g, 1.74mmol) in 5mL of DMF at 0°C was added a solution of 5-nitroindole (0.097g, 1.74mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of methoxymethylchloride (0.127g, 1.58mmol) in 1mL DMF and stirring is continued for 7h. The mixture is then diluted with 30mL of water and extracted with three 40mL portions of ethyl acetate. The combined organic extracts are washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.266g (82%).

***R_f* -Value:** Hexane/Ethyl acetate (7:3 *v/v*) = 0.25

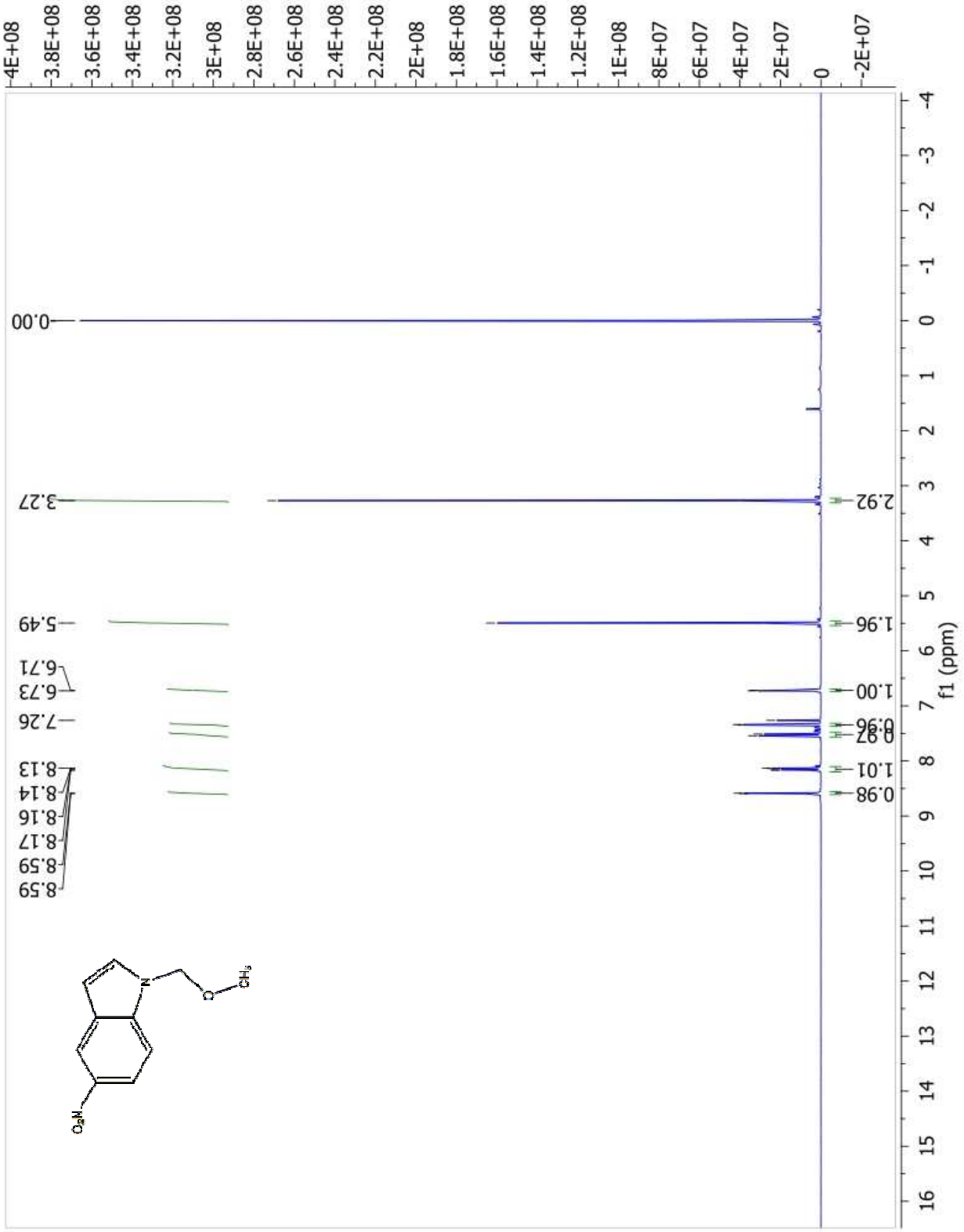
^{1}H-NMR (300 MHz, $CDCl_3$):

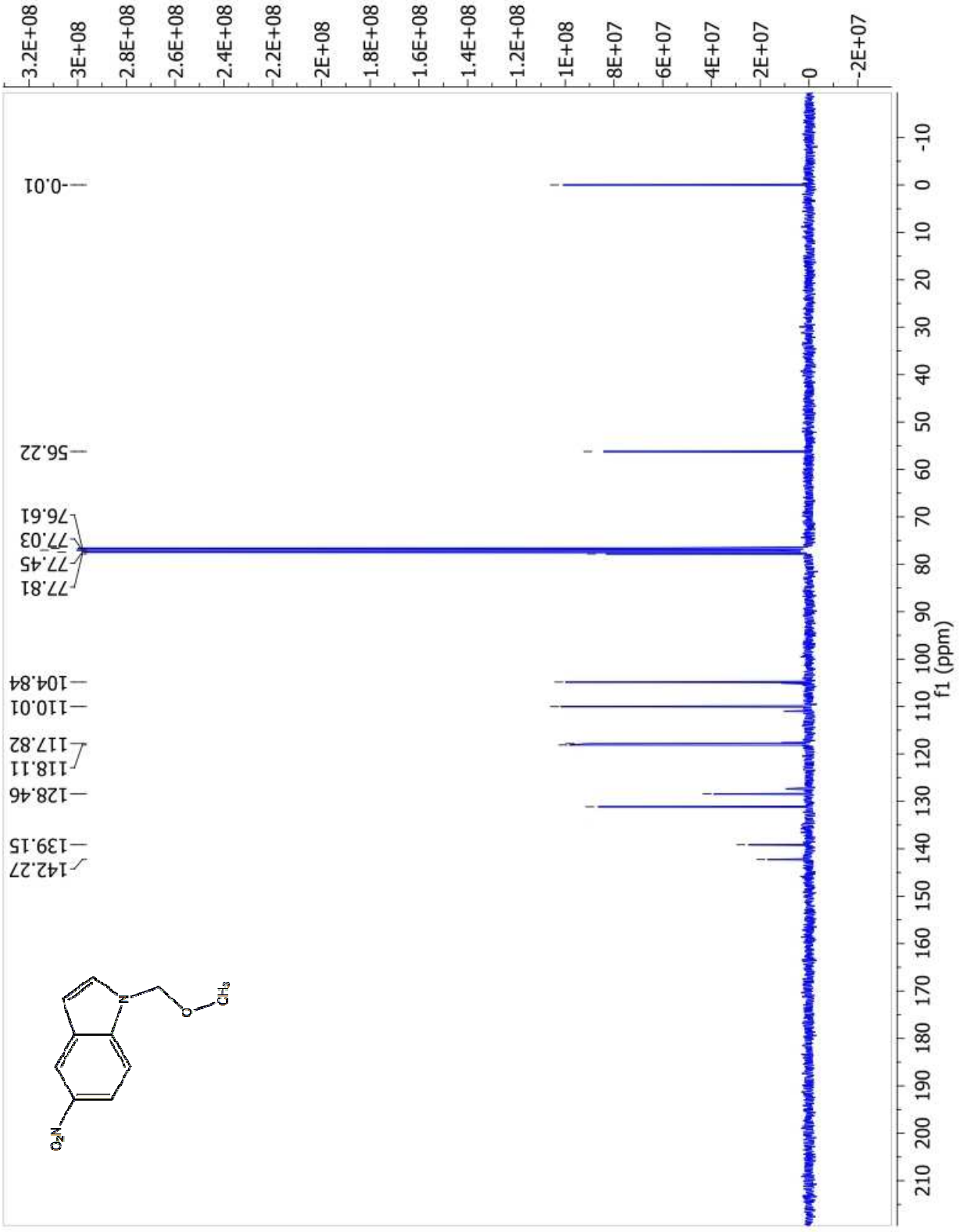
δ = 3.27 (s, 3H), 5.49 (s, 2H), 6.72 (d, ^3J = 3.33 Hz, 1H), 7.34 (d, ^3J = 3.33 Hz, 1H), 7.52 (d, ^3J = 9.09 Hz, 1H), 8.15 (dd, ^3J = 9.06 Hz ^4J =2.19 Hz, 1H), 8.58 (d, ^4J = 2.16 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$):

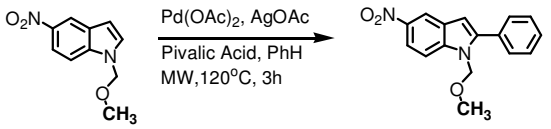
δ = 56.22, 77.81, 104.84, 110.01, 117.82, 118.11, 128.46, 131.15, 139.16, 142.27

LRMS EI (m/z): [M+] calc'd for $C_{10}H_{10}N_2O_3$ 206.06, observed 206.10 m/z


0.00
3.27
5.49
6.71
6.73
7.26
8.13
8.14
8.16
8.17
8.59
8.59
2.92
1.96
1.00
0.96
0.97
1.01
0.98
f1 (ppm)


-0.01
56.22
76.61
77.03
77.45
77.81
104.84
110.01
117.82
118.11
128.46
139.15
142.27
f1 (ppm)

Synthesis of 1-methoxymethyl-5-nitro-2-phenylindole (17)



$C_{10}H_{10}N_2O_3$
206.2

$C_{16}H_{14}N_2O_3$
282.29
17

Procedure:

A magnetically stirred solution of 1-[methoxymethyl]-5-nitroindole (0.095g, 0.460mmol), palladium acetate (0.010g, 0.046mmol), silver acetate (0.229g, 1.38mmol), 2,2-dimethylpropanoic acid (0.117g, 1.15mmol) in 4mL of benzene was microwave heated at 120^0C for 3h. After evaporation of the solvent the mixture is then diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts are washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **17** 0.088g (68%).

***R_f* -Value:** Hexane/Ethyl acetate (8:2 *v/v*) = 0.24

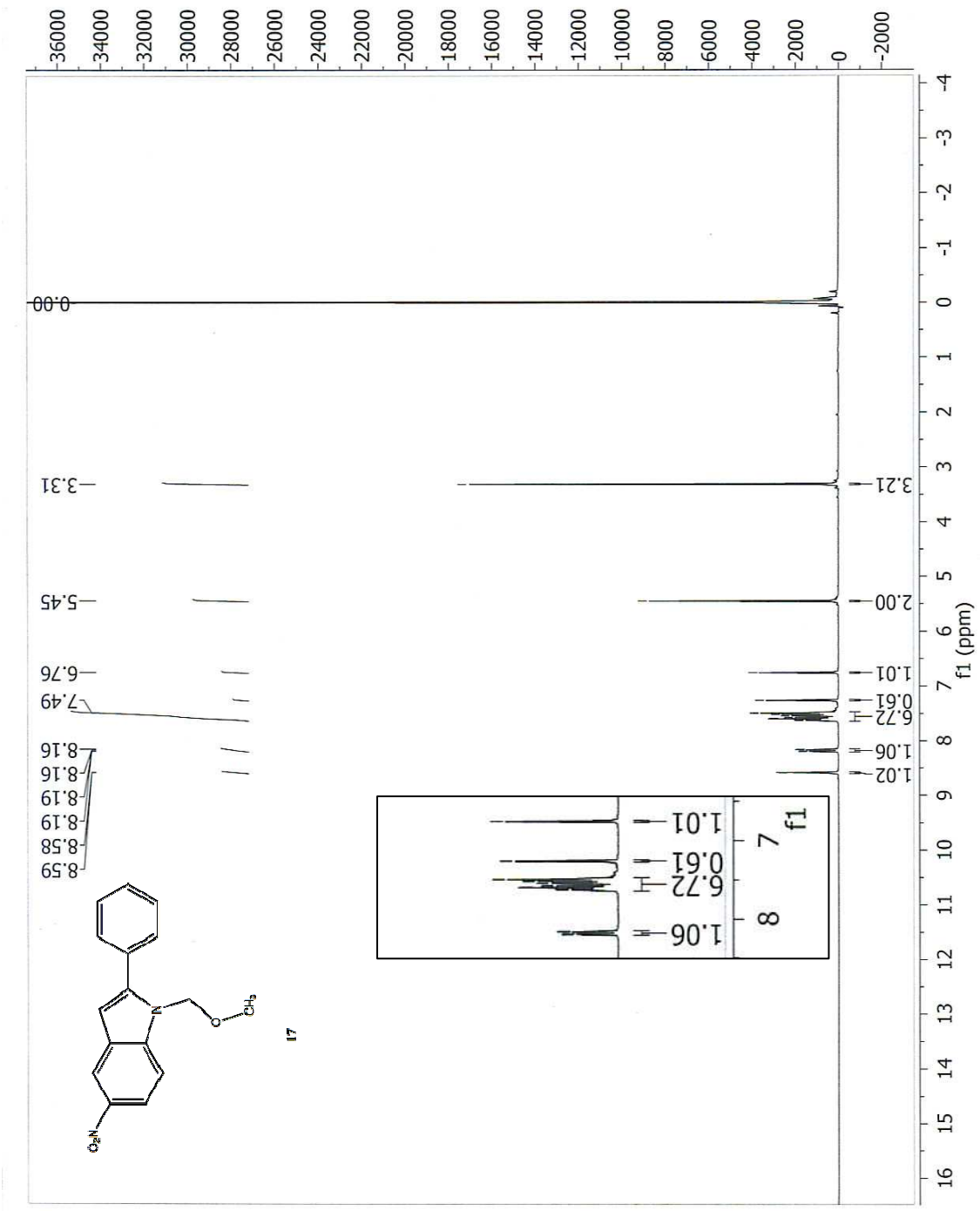
^{1}H-NMR (300 MHz, $CDCl_3$):

δ = 3.31 (s, 3H), 5.45 (s, 2H), 6.76 (s, 1H), 7.49-7.63 (m, 6H), 8.17 (dd, ^3J = 9.0 Hz, ^4J = 2.22 Hz, 1H), 8.58 (d, ^4J = 3.0 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 56.17, 74.94, 104.85, 110.28, 117.52, 117.85, 127.68, 128.84, 129.03, 129.50 131.09, 140.93, 142.53, 144.93

LRMS EI (m/z): [M+] calc'd for $C_{16}H_{14}N_2O_3$ 282.10, observed 282.10 m/z


f1 (ppm)
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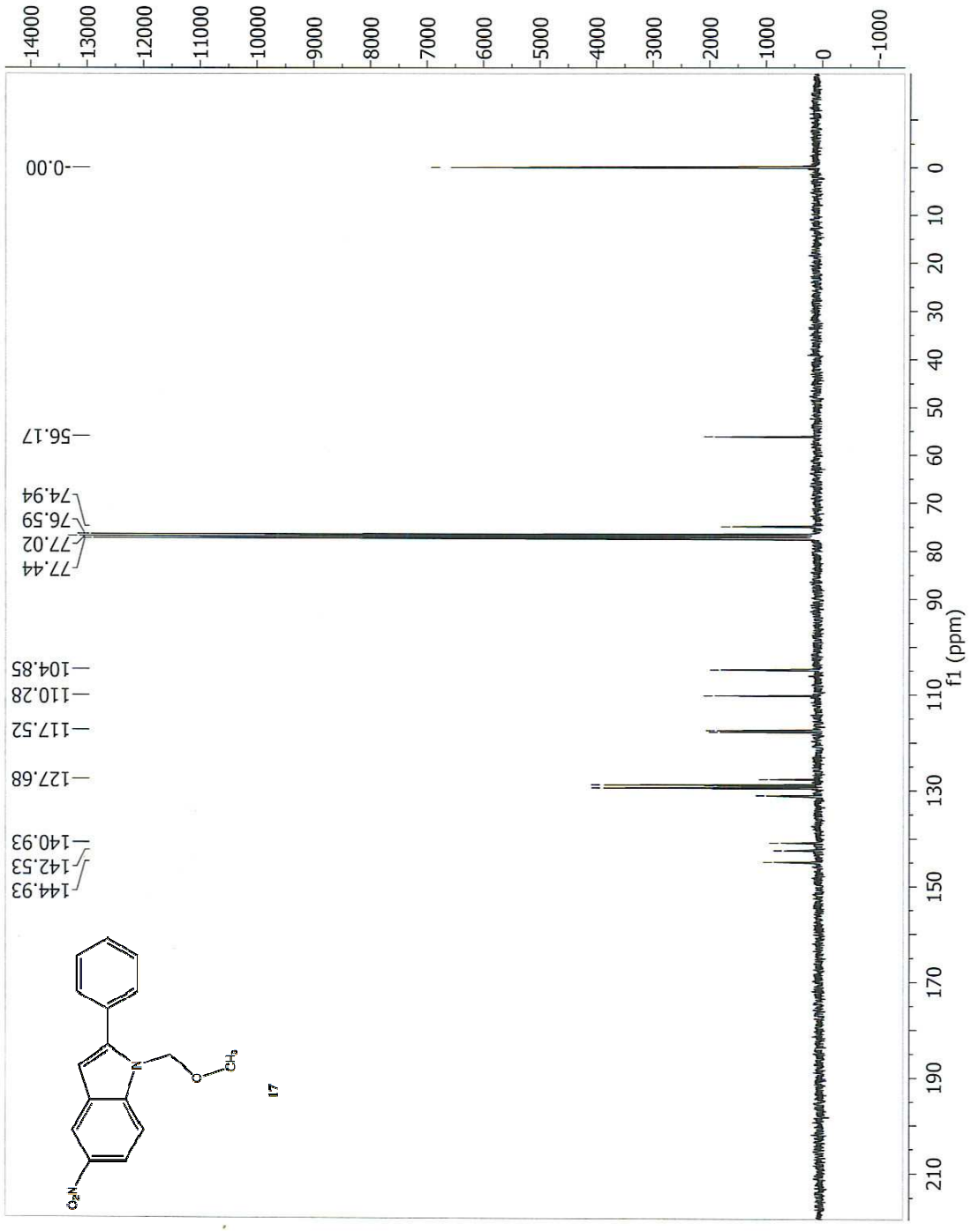
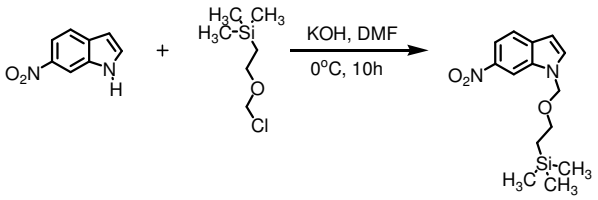
1.01
0.61
6.72
1.06
1.02
0.00
3.31
5.45
6.76
7.49
8.16
8.16
8.19
8.19
8.58
8.59
1.06
0.61
6.72
1.01
f1
17


144.93
142.53
140.93
127.68
117.52
110.28
104.85
77.44
77.02
76.59
74.94
56.17
0.00
f1 (ppm)
17

Synthesis of 6-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole



$C_8H_6N_2O_2$ 162.15 | $C_6H_{15}ClOSi$ 166.72 | $C_{14}H_{20}N_2O_3Si$ 292.41

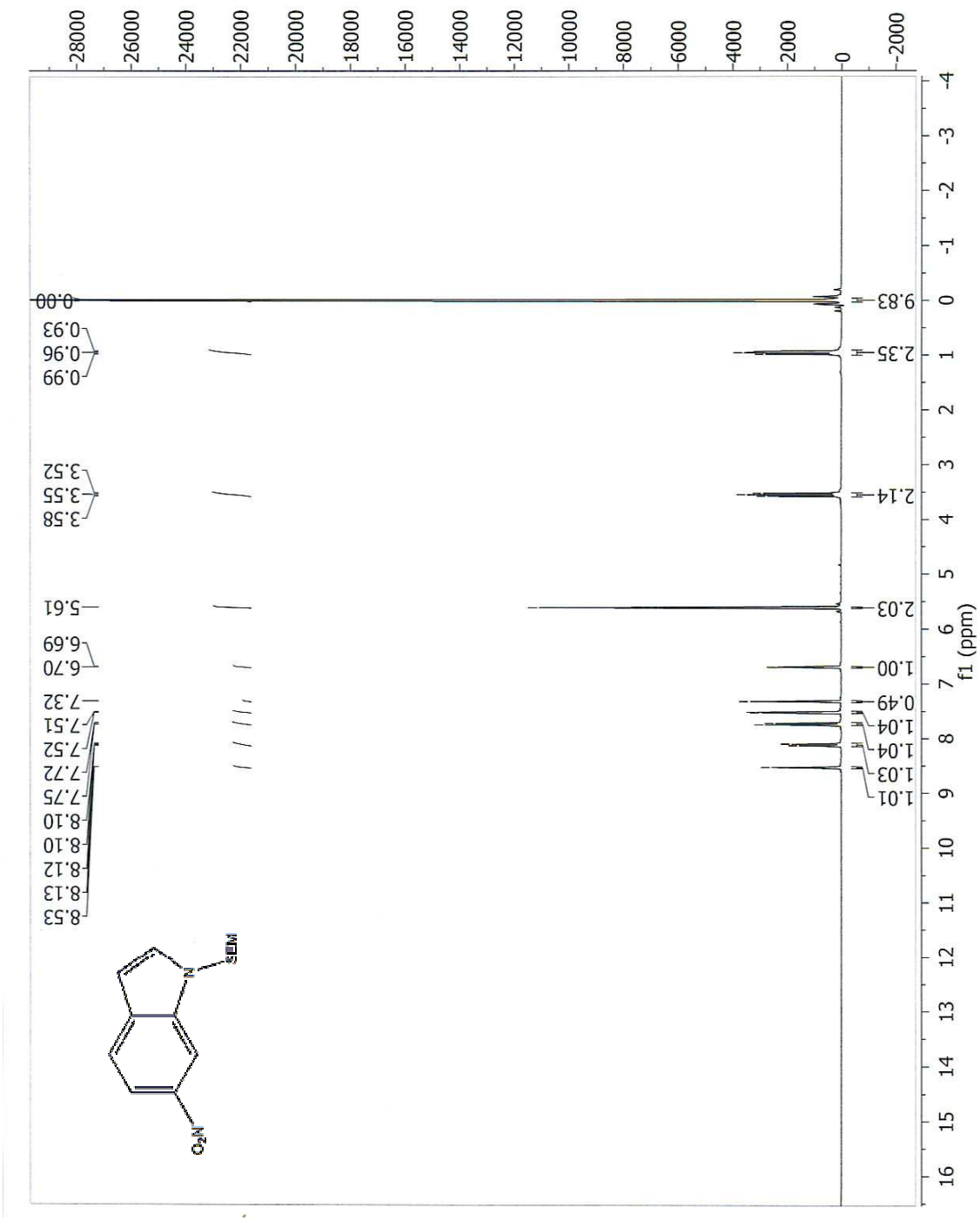
To a solution of potassium hydroxide (0.114g, 2.03mmol) in 8mL of DMF at 0°C was added a solution of 6-nitroindole (0.3g, 1.85mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.308g, 1.85mmol) in 2mL DMF and stirring is continued for 10h. The mixture was diluted with 30mL of water and extracted with three 30mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.206g (38%).

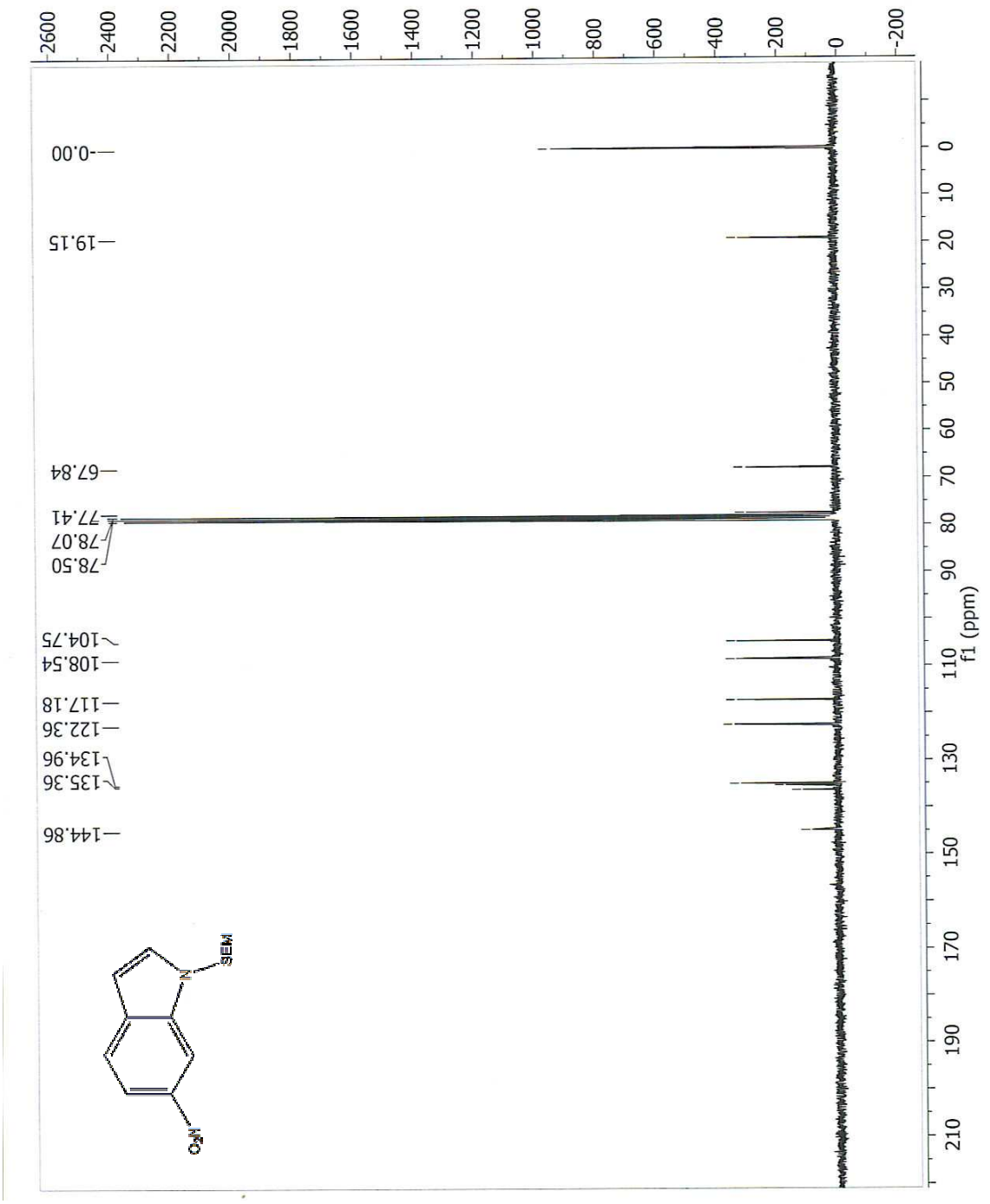
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.22

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.96 (t, ^3J =8.22 Hz, 2H), 3.55 (t, ^3J = 8.04 Hz, 2H), 5.61 (s, 2H), 6.69 (d, ^3J = 3.09 Hz, 1H), 7.51 (d, ^3J = 3.18 Hz, 1H), 7.73 (d, ^3J = 8.76 Hz, 1H), 8.11 (dd, ^3J =8.76 Hz, ^4J = 2.01 Hz, 1H), 8.52 (s, 1H)

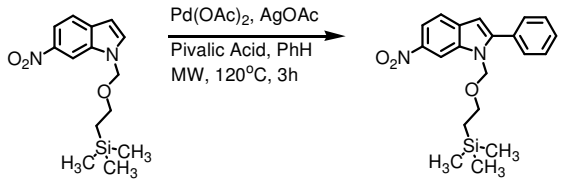
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 19.15, 67.84, 77.41, 104.75, 108.54, 117.18, 122.36, 134.96, 135.36, 136.35, 144.86

LRMS EI (m/z): [M+] calc'd for $C_{14}H_{20}N2O_3Si$ 292.12, observed 292.10 m/z


f1 (ppm)
SEM
N
O2N
0.00
0.93
0.96
0.99
3.52
3.55
3.58
5.61
6.69
6.70
7.32
7.51
7.52
7.72
7.75
8.10
8.10
8.12
8.13
8.53
1.01
1.03
1.04
1.04
0.49
1.00
2.03
2.14
2.35
9.83


-0.00
19.15
67.84
77.41
78.07
78.50
104.75
108.54
117.18
122.36
134.96
135.36
144.86
SEM
N
O
f1 (ppm)

Synthesis of 6-Nitro-2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (18)



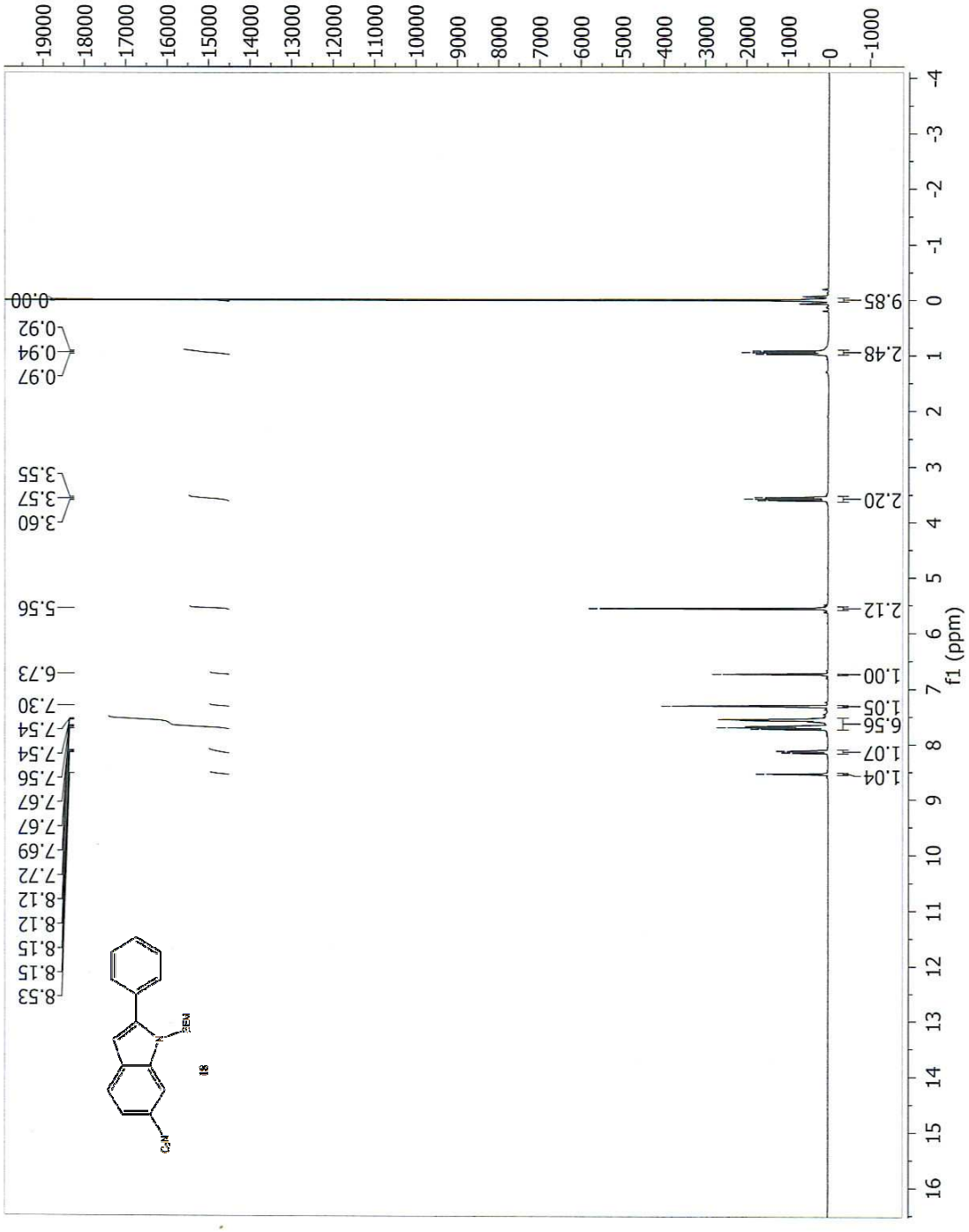
A magnetically stirred solution of 6-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.045g, 0.153mmol), palladium acetate (0.0034g, 0.015mmol), silver acetate (0.076g, 0.461mmol), 2,2-dimethylpropanoic acid (0.039g, 0.38mmol) in 4mL of benzene was microwave heated at 120°C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **18** 0.049g (88%).

***R_f* -Value:** Hexane/Ethyl acetate (10:1 *v/v*) = 0.38

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.94 (t, ^3J =8.37 Hz, 2H), 3.57 (t, ^3J = 8.07 Hz, 2H), 5.55 (s, 2H), 6.73 (s, 1H), 7.52-7.72 (m, 6H), 8.13 (dd, ^3J =8.73 Hz, ^4J = 1.98 Hz, 1H), 8.52 (d, 1H)

^{13}C-NMR (75MHz, $CDCl_3$): δ = 0.00, 19.29, 67.80, 74.52, 105.18, 108.81, 117.79, 121.78, 130.31, 130.66, 130.97, 132.64, 134.68, 138.20, 144.63, 148.91

LRMS EI (m/z): [M+] calc'd for $C_{20}H_{24}N_2O_3Si$ 368.16, observed 368.20 m/z


f1 (ppm)
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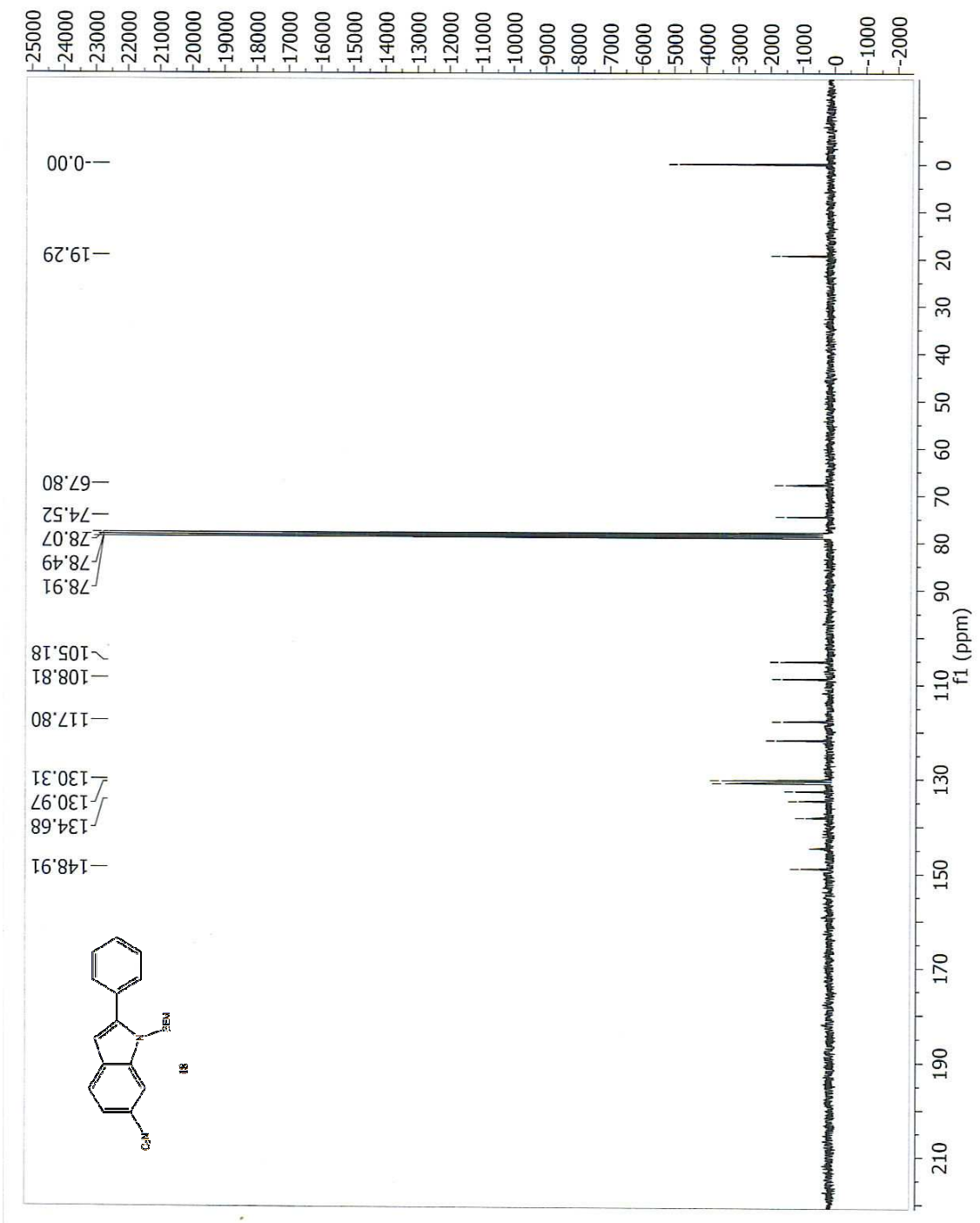
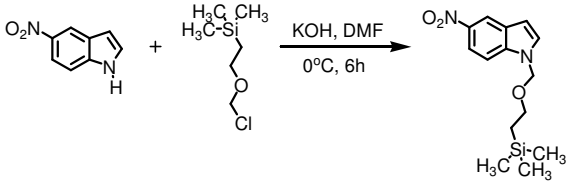
2.48
2.20
2.12
1.00
1.05
6.56
1.07
1.04
0.00
0.92
0.94
0.97
3.55
3.57
3.60
5.56
6.73
7.30
7.54
7.54
7.56
7.67
7.67
7.69
7.72
8.12
8.12
8.15
8.15
8.53
18


148.91
134.68
130.97
130.31
117.80
108.81
105.18
78.91
78.49
78.07
74.52
67.80
19.29
0.00
f1 (ppm)

Synthesis of 5-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole



$C_8H_6N_2O_2$ 162.15 | $C_6H_{15}ClOSi$ 166.72 | $C_{14}H_{20}N_2O_3Si$ 292.41

To a solution of potassium hydroxide (0.151g, 2.70mmol) in 8mL of DMF at 0°C was added a solution of 5-nitroindole (0.400g, 2.46mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.411g, 2.46mmol) in 2mL DMF and stirring is continued for 6h. The mixture was diluted with 50mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 50mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.452g (63%). The NMR spectra matched with that previously published.[1]

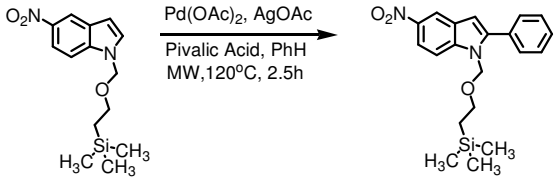
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.14

^{1}H-NMR (300 MHz, $CDCl_3$): δ = -0.06 (s, 9H), 0.89 (t, ^3J =8.19 Hz, 2H), 3.47 (t, ^3J =8.04 Hz, 2H), 5.52 (s, 2H), 6.71 (d, ^3J =3.27 Hz, 1H), 7.33 (d, ^3J =3.27 Hz, 1H), 7.52 (d, ^3J =9.06 Hz, 1H), 8.15 (dd, ^3J =9.06Hz, ^4J =2.19 Hz 1H), 8.59 (d, ^4J =2.16 Hz, 1H),

^{13}C-NMR (75 MHz, $CDCl_3$): δ = -1.48, 17.67, 66.33, 76.01, 104.70, 110.02, 117.74, 118.12, 128.37, 131.05, 139.14, 142.20

LRMS EI (m/z): [M+] calc'd for $C_{14}H_{20}N_2O_3Si$ 292.12, observed 292.10m/z

Synthesis of 5-nitro-2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (19)



$C_{14}H_{20}N_2O_3Si$ 292.41 | $C_{20}H_{24}N_2O_3Si$ 368.50 **19**

A magnetically stirred solution of 5-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.100g, 0.341mmol), palladium acetate (0.0076g, 0.034mmol), silver acetate (0.170g, 1.02mmol), 2,2-

dimethylpropanoic acid (0.0873g, 0.854mmol) in 4mL of benzene was microwave heated at 120^0C for 2.5h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **19** 0.096g (77%). The NMR spectra matched with that previously published.[1]

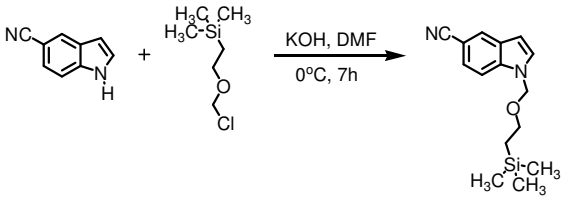
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.30

^{1}H-NMR (300 MHz, $CDCl_3$): δ = -0.06 (s, 9H), 0.86 (t, ^3J = 8.34 Hz, 2H), 3.47 (t, ^3J = 8.16 Hz, 2H), 5.49 (s, 2H), 6.74 (s, 1H), 7.49-7.63 (m, 6H), 8.16 (dd, ^3J = 9.06 Hz, ^4J = 2.22 Hz, 1H), 8.16 (d, ^4J = 2.16 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = -1.48, 17.80, 66.23, 73.10, 104.68, 110.35, 117.51, 117.75, 127.65, 128.79, 128.97, 129.55, 131.23, 140.91, 142.45, 144.87

LRMS EI (m/z): [M+] calc'd for $C_{20}H_{24}N_2O_3Si$ 368.15, observed 368.20m/z

Synthesis of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole-5-carbonitrile



To a solution of potassium hydroxide (0.127g, 2.27mmol) in 8mL of DMF at 0^oC was added a solution of 5-cyanoindole (0.294g, 2.06mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.343g, 2.06mmol) in 2mL DMF and stirring is continued for 7h. The mixture was diluted with 50mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 50mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.411g (73%). The NMR spectra matched with that previously published.[1]

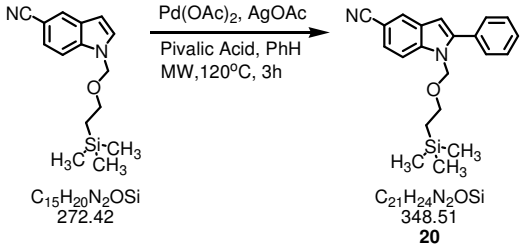
***R_f* -Value:** Hexane/Ethyl acetate (8:2 *v/v*) = 0.37

^{1}H-NMR (300 MHz, $CDCl_3$): δ = -0.06 (s, 9H), 0.88 (t, ^3J = 9.0 Hz, 2H), 3.46 (t, ^3J = 9.0 Hz, 2H), 5.50 (s, 2H), 6.60 (d, ^3J = 3.0 Hz, 1H), 7.29 (d, ^3J = 3.0 Hz, 1H), 7.45-7.53 (m, 2H), 7.98 (s, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 1.47, 19.14, 67.69, 77.30, 104.69, 104.88, 112.41, 122.08, 126.53, 127.98, 130.30, 131.68, 139.35

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{20}N_2OSi$ 272.13, observed 272.10 m/z

Synthesis of 5-cyano-2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (20)



A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole-5-carbonitrile (0.087g, 0.320mmol), palladium acetate (0.0071g, 0.032mmol), silver acetate (0.159g, 0.961mmol), 2,2-dimethylpropanoic acid (0.0817g, 0.799mmol) in 4mL of benzene was microwave heated at 120^{0}C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **20** 0.075g (68%). The NMR spectra matched with that previously published.[1]

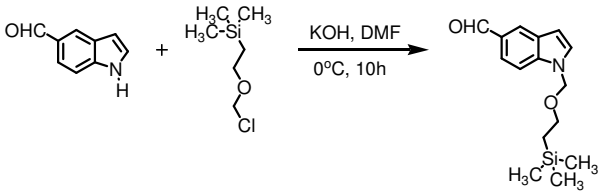
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.30

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.85 (t, ^3J = 8.4 Hz, 2H), 3.45 (t, ^3J = 8.0 Hz, 2H), 5.47 (s, 2H), 6.65 (s, 1H), 7.48-7.59 (m, 7H), 7.97 (d, ^4J = 0.63 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 17.80, 66.13, 72.94, 103.37, 103.75, 111.23, 120.63, 125.13, 125.89, 128.11, 128.75, 128.85, 129.57, 131.36, 139.63, 144.00

LRMS EI (m/z): [M+] calc'd for $C_{21}H_{24}N_2OSi$ 348.16, observed 348.20m/z

Synthesis of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole-5-carboxaldehyde



C_9H_7NO 145.16 | $C_6H_{15}ClOSi$ 166.72 | $C_{15}H_{21}NO_2Si$ 275.42

To a solution of potassium hydroxide (0.127g, 2.27mmol) in 8mL of DMF at 0°C was added a solution of indole-5-carboxaldehyde (0.300g, 2.06mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.343g, 2.06mmol) in 2mL DMF and stirring is continued for 10h. The mixture was diluted with 50mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 50mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.394g (69%). The NMR spectra matched with that previously published.[7]

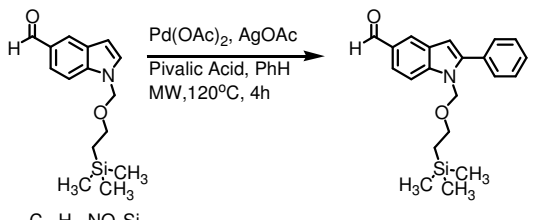
***R_f* -Value:** Hexane/Ethyl acetate (8:2 *v/v*) = 0.40

^{1}H-NMR (300 MHz, $CDCl_3$): δ = -0.06 (s, 9H), 0.89 (t, ^3J = 9.0 Hz, 2H), 3.48 (t, ^3J = 9.0 Hz, 2H), 5.52 (s, 2H), 6.68 (d, ^3J = 3.0 Hz, 1H), 7.27 (m, 1H), 7.58 (d, ^3J = 9.0 Hz, 1H), 7.81 (dd, ^3J = 9.0 Hz, ^4J = 1.3 Hz, 1H), 8.16 (s, 1H), 10.05 (s, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 17.69, 66.18, 75.80, 104.27, 110.56, 122.49, 126.15, 128.89, 129.83, 130.02, 139.70, 192.45

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{21}NO_2Si$ 275.13, observed 275.20 m/z

Synthesis of 2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole-5-carboxaldehyde (21)



$C_{15}H_{21}NO_2Si$ 275.42 → $C_{21}H_{25}NO_2Si$ 351.51 **21**

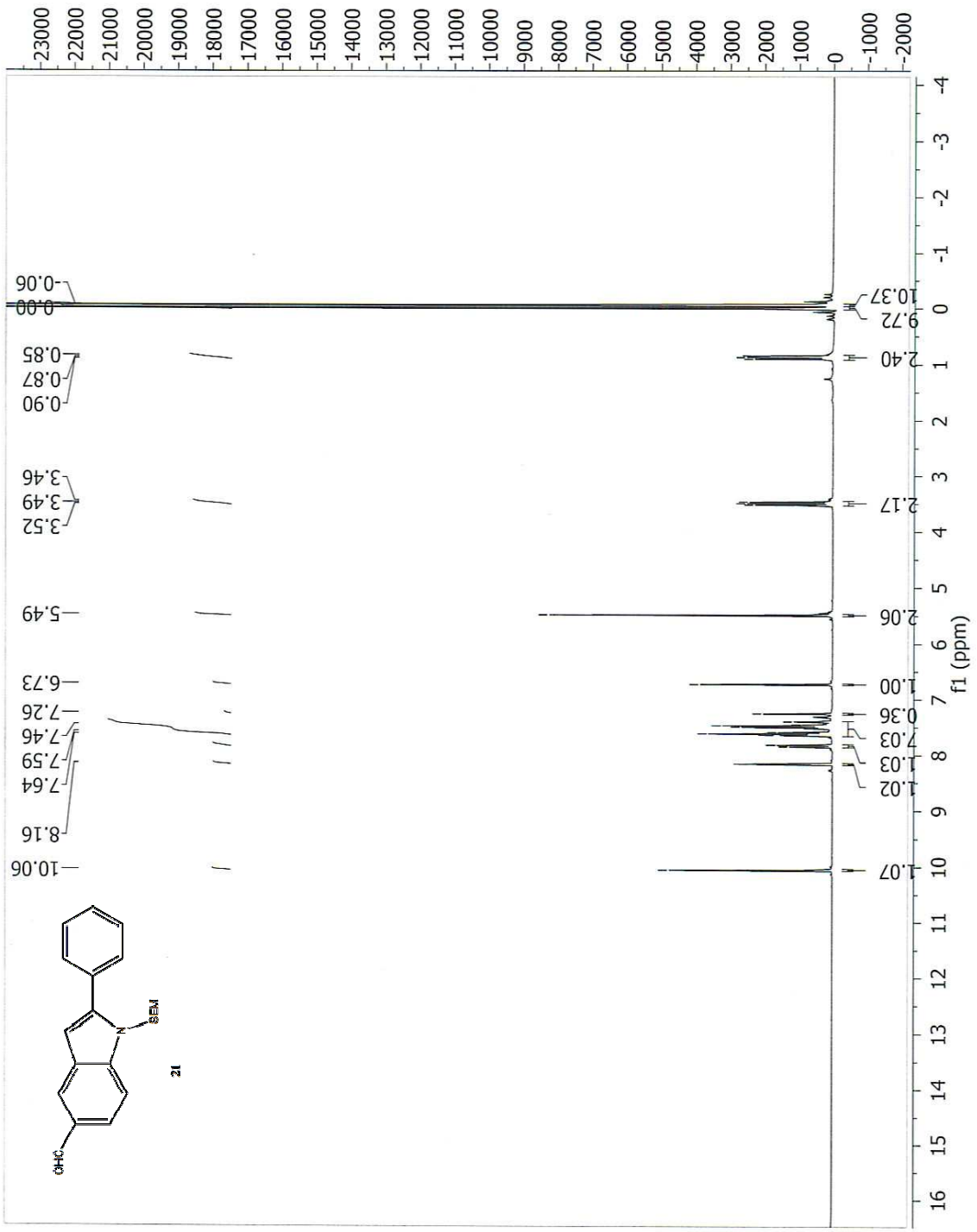
A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole-5-carboxaldehyde (0.090g, 0.329mmol), palladium acetate (0.0073g, 0.032mmol), silver acetate (0.164g, 0.987mmol), 2,2-dimethylpropanoic acid (0.084g, 0.823mmol) in 4mL of benzene was microwave heated at 120^0C for 4h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **21** 0.071g (67%).

***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.25

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.87 (t, ^3J = 8.3 Hz, 2H), 3.49 (t, ^3J = 8.1 Hz, 2H), 5.46 (s, 2H), 6.73 (s, 1H), 7.40-7.64 (m, 6H), 7.83 (dd, ^3J = 8.5 Hz, ^4J = 1.5 Hz, 1H), 8.15 (d, ^4J = 1.05 Hz, 1H), 10.06 (s, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 1.47, 19.29, 67.59, 74.44, 105.87, 112.37, 124.14, 126.93, 129.63, 130.14, 130.18, 131.02, 131.84, 133.11, 142.97, 145.10, 193.92

LRMS EI (m/z): [M+] calc'd for $C_{21}H_{25}NO_2Si$ 351.17, observed 351.20m/z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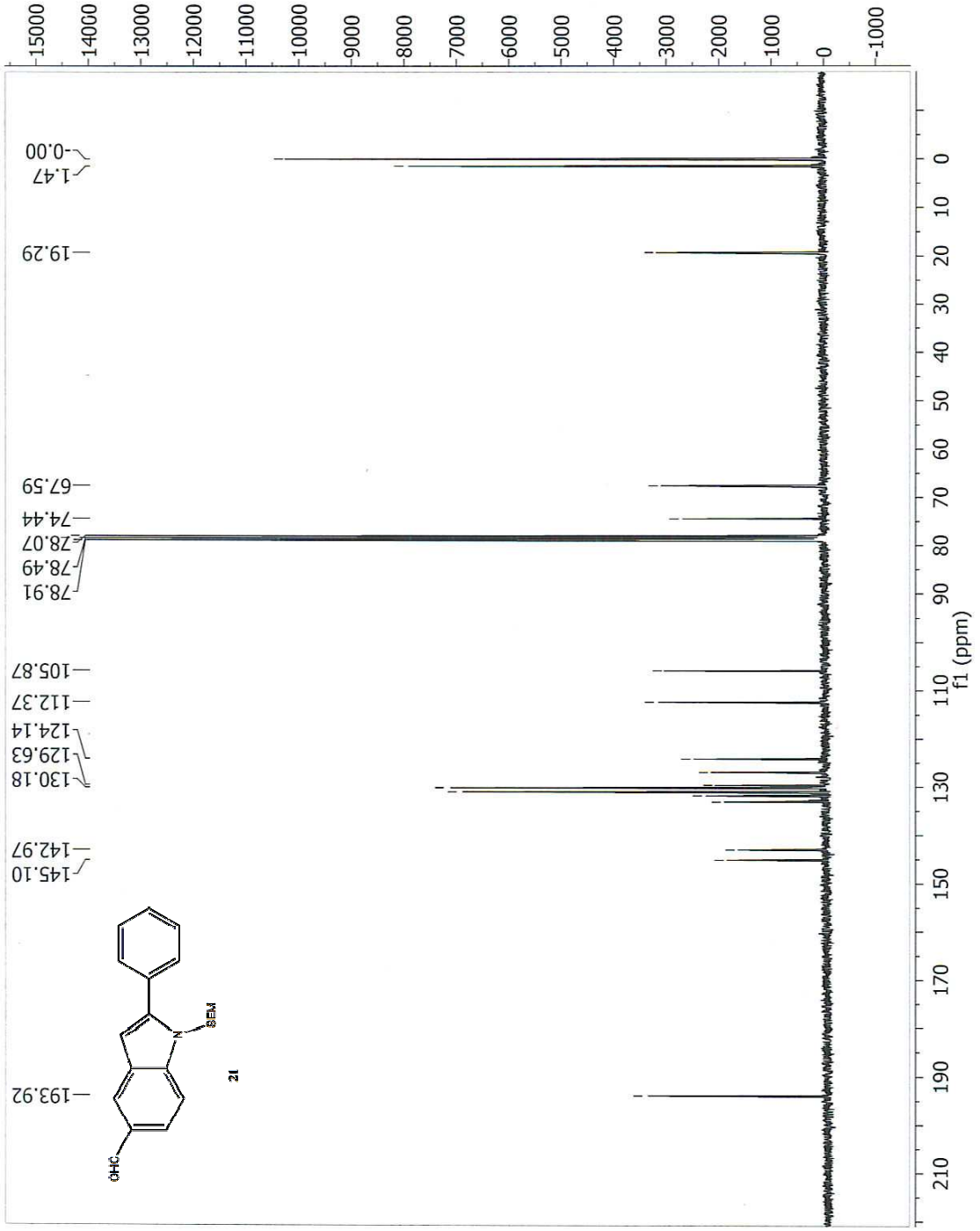
8.16
7.64
7.59
7.46
7.26
6.73
5.49
3.52
3.49
3.46
0.90
0.87
0.85
0.00
-0.06
10.37
9.72
2.40
2.17
2.06
1.00
0.36
7.03
1.03
1.02
1.07
f1 (ppm)
OHC
SEM
N
21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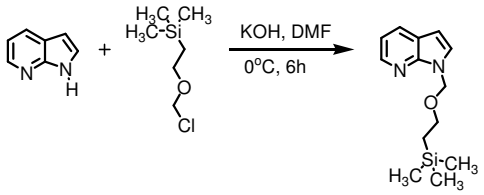
1.47
19.29
67.59
74.44
78.07
78.49
78.91
105.87
112.37
124.14
129.63
130.18
142.97
145.10
193.92
OHC
N
SEM
21
f1 (ppm)

Synthesis of 1-[2-(trimethylsilyl)-ethoxymethyl]-7-azaindole



$C_7H_6N_2$ 118.14 | $C_6H_{15}ClOSi$ 166.72 | $C_{13}H_{20}N_2OSi$ 248.40

To a solution of potassium hydroxide (0.208g, 3.72mmol) in 5mL of DMF at 0°C was added a solution of 7-azaindole (0.400g, 3.38mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.564g, 3.38mmol) in 1mL DMF and stirring is continued for 6h. The mixture was diluted with 50mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 50mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.513g (61%). The NMR spectra matched with that previously published.[1]

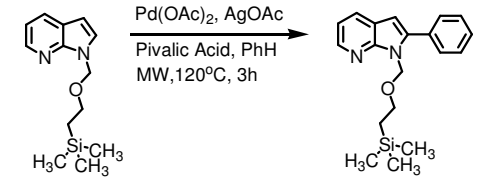
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.17

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 9H), 0.98 (t, ^3J = 8.2 Hz, 2H), 3.61 (t, ^3J = 8.2 Hz, 2H), 5.77 (s, 2H), 6.59 (d ^3J = 3.6 Hz, 1H), 7.16 (m, 1H), 7.42 (d ^3J =3.0 Hz, 1H), 7.99 (dd, ^3J =7.8 Hz ^4J =1.47 Hz, 1H), 8.41 (dd, ^3J =4.78 Hz ^4J =1.41 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 1.48, 19.21, 67.59, 74.29, 102.53, 117.79, 122.08, 129.35, 130.32, 144.65, 149.64

LRMS EI (m/z): [M+] calc'd for $C_{13}H_{20}N_2OSi$ 248.13, observed 248.10m/z

Synthesis of 2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-7-azaindole (22)



$C_{13}H_{20}N_2OSi$ 248.40 | $C_{19}H_{24}N_2OSi$ 324.49 **22**

A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-7-azaindole (0.090g, 0.364mmol), palladium acetate (0.0081g, 0.036mmol), silver acetate (0.181g, 1.09mmol), 2,2-

dimethylpropanoic acid (0.093g, 0.91mmol) in 4mL of benzene was microwave heated at 120^0C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **22** 0.085g (72%). The NMR spectra matched with that previously published.[1]

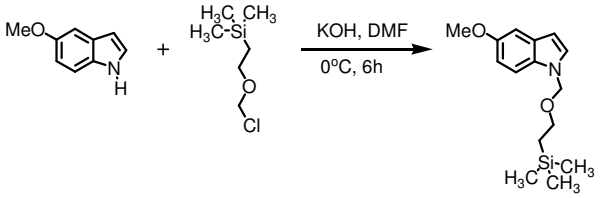
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.26

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 1.01(t, ^3J = 8.20 Hz, 2H), 3.78(t, ^3J = 8.20 Hz, 2H), 5.73 (s, 2H), 6.63 (s, 1H), 7.15 (dd, ^3J = 7.80 Hz, ^4J = 4.70 Hz, 1H), 7.46-7.55 (m, 3H), 7.84 (d, ^3J = 6.80 Hz, 2H), 7.93 (dd, ^3J = 7.70 Hz, ^4J = 1.40Hz, 1H), 8.39 (dd, ^3J = 4.80 Hz, ^4J = 1.50 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.0, 18.7, 66.9, 71.2, 101.20, 117.30, 120.90, 128.40, 128.80, 129.00, 129.70, 132.50, 142.40, 143.30, 150.00

LRMS EI (m/z): [M+] calc'd for $C_{19}H_{24}N_2OSi$ 324.17, observed 324.20 m/z

Synthesis of 5-methoxy-1-[2-(trimethylsilyl)-ethoxymethyl]-indole



To a solution of potassium hydroxide (0.125g, 2.23mmol) in 10mL of DMF at 0^oC was added a solution of 5-methoxyindole (0.3g, 2.03mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.339g, 2.03mmol) in 2mL DMF and stirring is continued for 6h. The mixture was diluted with 30mL of water and extracted with three 30mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.199g (35%). The NMR spectra matched with that previously published.[8]

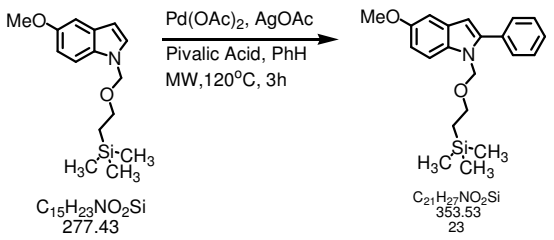
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.39

^{1}H-NMR (300 MHz, $CDCl_3$): δ = -0.07 (s, 9H), 0.87 (t, ^3J = 8.28 Hz, 2H), 3.45 (t, ^3J = 8.04 Hz, 2H), 3.85 (s, 3H), 5.44 (s, 2H), 6.44 (d, ^3J = 3.15 Hz, 1H), 6.89 (dd, ^3J = 8.88 Hz, ^4J = 2.43 Hz, 1H), 7.08 (d, ^4J = 2.14 Hz, 1H), 7.13 (d, ^3J = 3.15 Hz, 1H), 7.37 (d, ^3J = 8.85 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = -1.45, 17.68, 55.79, 65.67, 75.78, 101.95, 102.55, 110.71, 112.20, 128.58, 129.47, 131.53, 154.43

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{23}NO_2Si$ 277.15, observed 277.10 m/z

Synthesis of 5-methoxy-2-phenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (23)



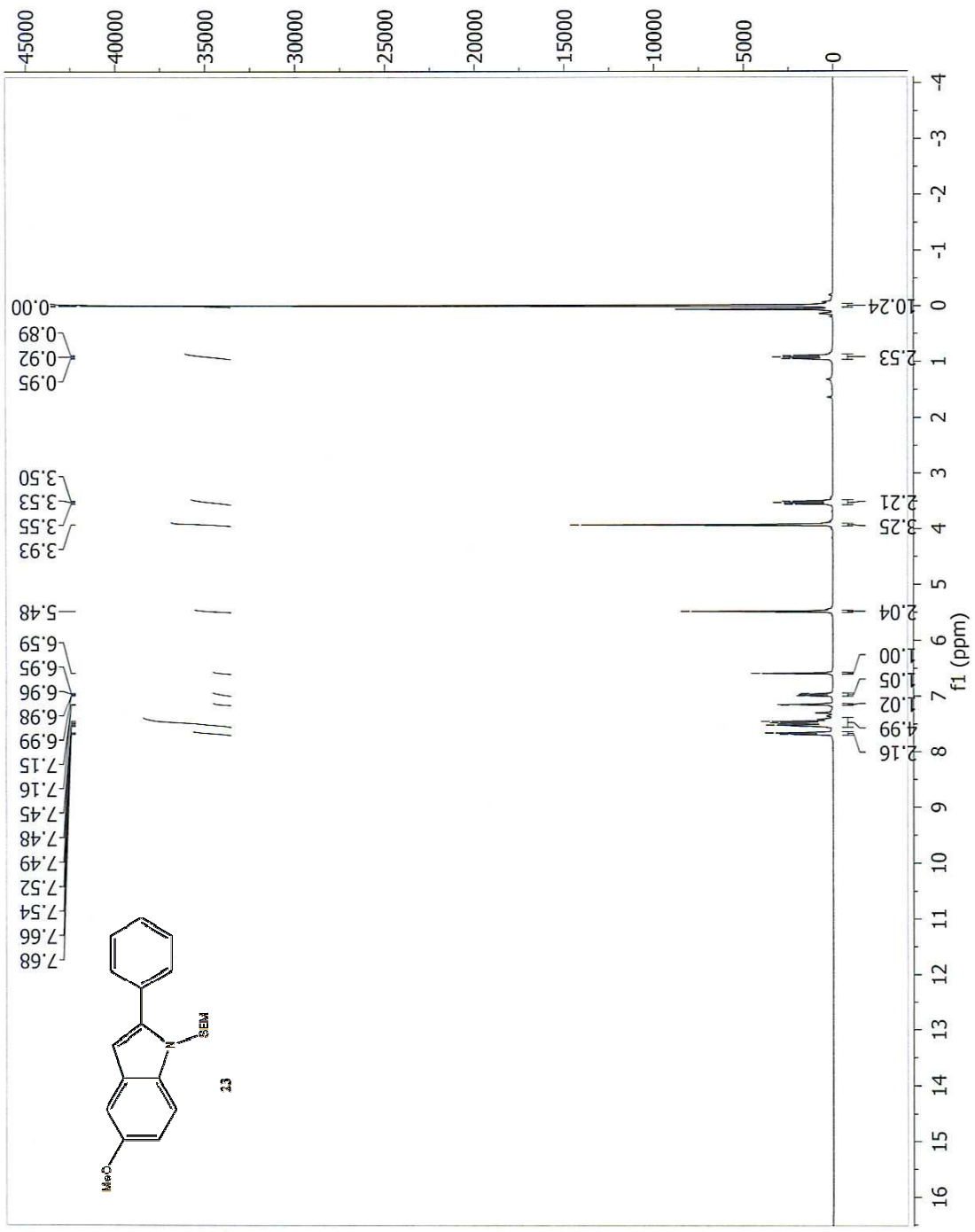
A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-5-methoxyindole (0.079g, 0.285mmol), palladium acetate (0.006g, 0.028mmol), silver acetate (0.142g, 0.855mmol), 2,2-dimethylpropanoic acid (0.072g, 0.71mmol) in 4mL of benzene was microwave heated at 120°C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **23** 0.048g (48%).

***R_f* -Value:** Hexane/Ethyl acetate (20:1 *v/v*) = 0.22

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.92 (t, ^3J =8.34 Hz, 2H), 3.53 (t, ^3J = 8.16 Hz, 2H), 3.93 (s, 3H), 5.48 (s, 2H), 6.59 (s, 1H), 6.97 (dd, ^3J =8.85 Hz, ^4J = 2.40 Hz, 1H), 7.15 (d, ^4J = 2.28 Hz, 1H), 7.42 – 7.54 (m, 4H), 7.67 (d, ^3J = 8.10 Hz, 2H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 1.45, 19.28, 57.26, 67.17, 74.46, 103.64, 104.28, 112.52, 113.66, 129.46, 129.97, 130.18, 130.89, 134.02, 134.88, 143.77, 156.20

LRMS EI (m/z): [M+] calc'd for $C_{21}H_{27}NO_2Si$ 353.18, observed 353.20 m/z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0.95
3.50
3.53
3.55
3.93
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6.95
6.96
6.98
6.99
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SEM
MeO
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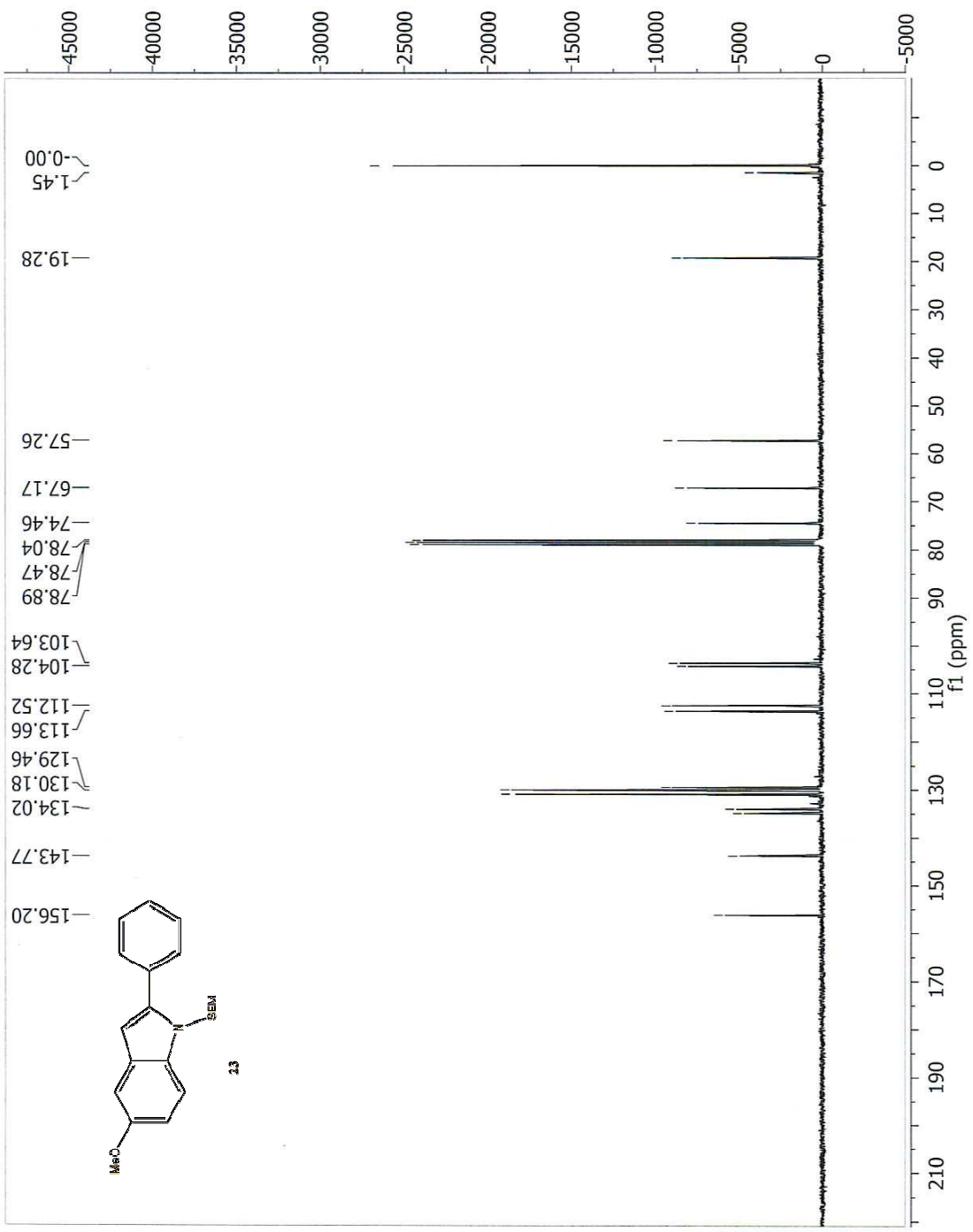
f1 (ppm)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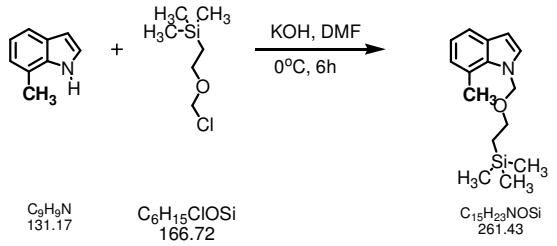
67.17
74.46
78.04
78.47
78.89
103.64
104.28
112.52
113.66
129.46
130.18
134.02
143.77
156.20
MeO
SEM
23
f1 (ppm)

Synthesis of 7-methyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole



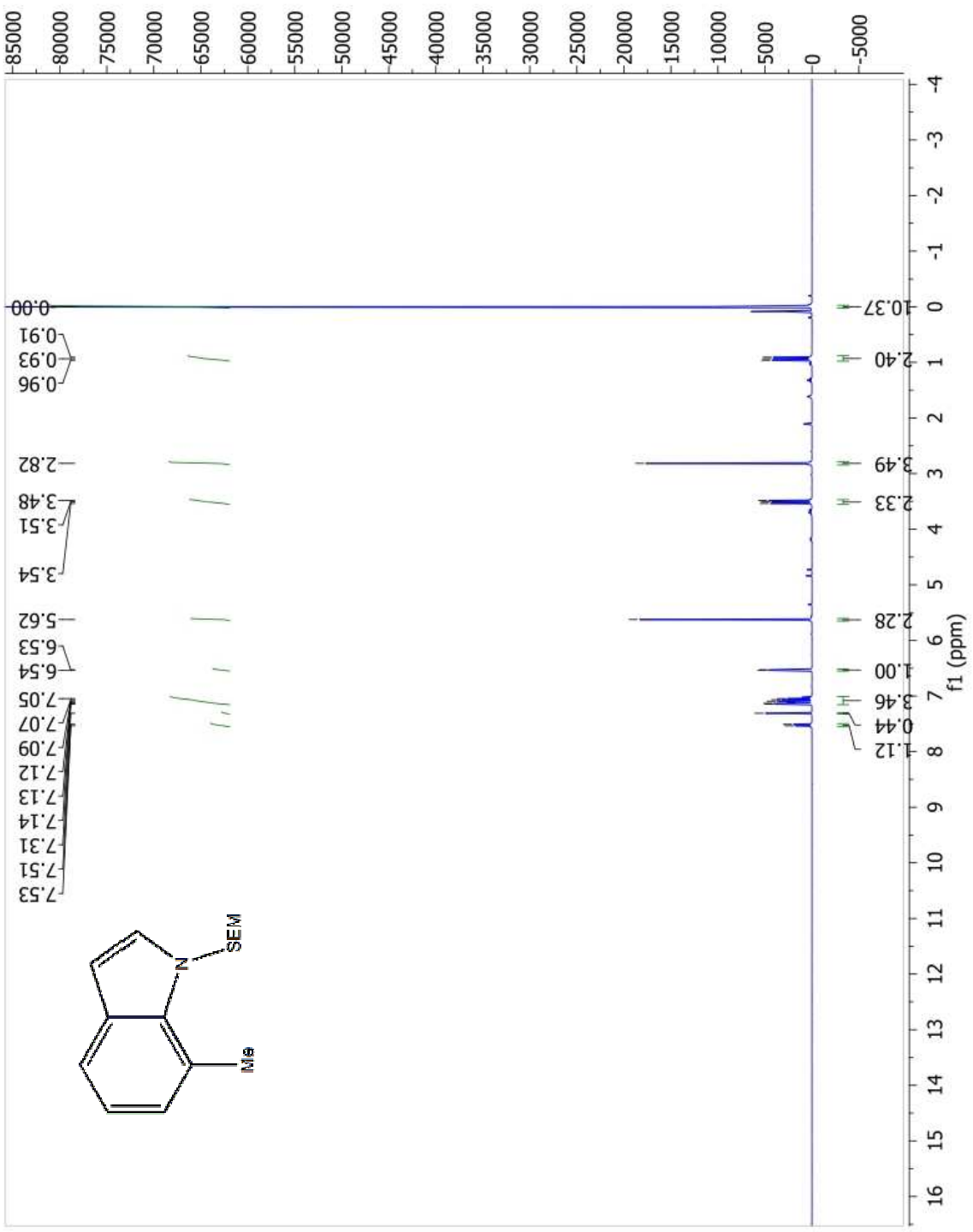
To a solution of potassium hydroxide (0.289g, 5.15mmol) in 10mL of DMF at 0°C was added a solution of 7-methylindole (0.616g, 4.69mmol) in 2mL of DMF and the reaction mixture is stirred for 15min. After stirring for 15mins add a solution of 2-(trimethylsilyl)ethoxymethylchloride (0.781g, 4.68mmol) in 2mL DMF and stirring is continued for 6h. The mixture was diluted with 30mL of water and extracted with three 30mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 30mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure 0.610g (50%). The NMR spectra matched with that previously published.[8]

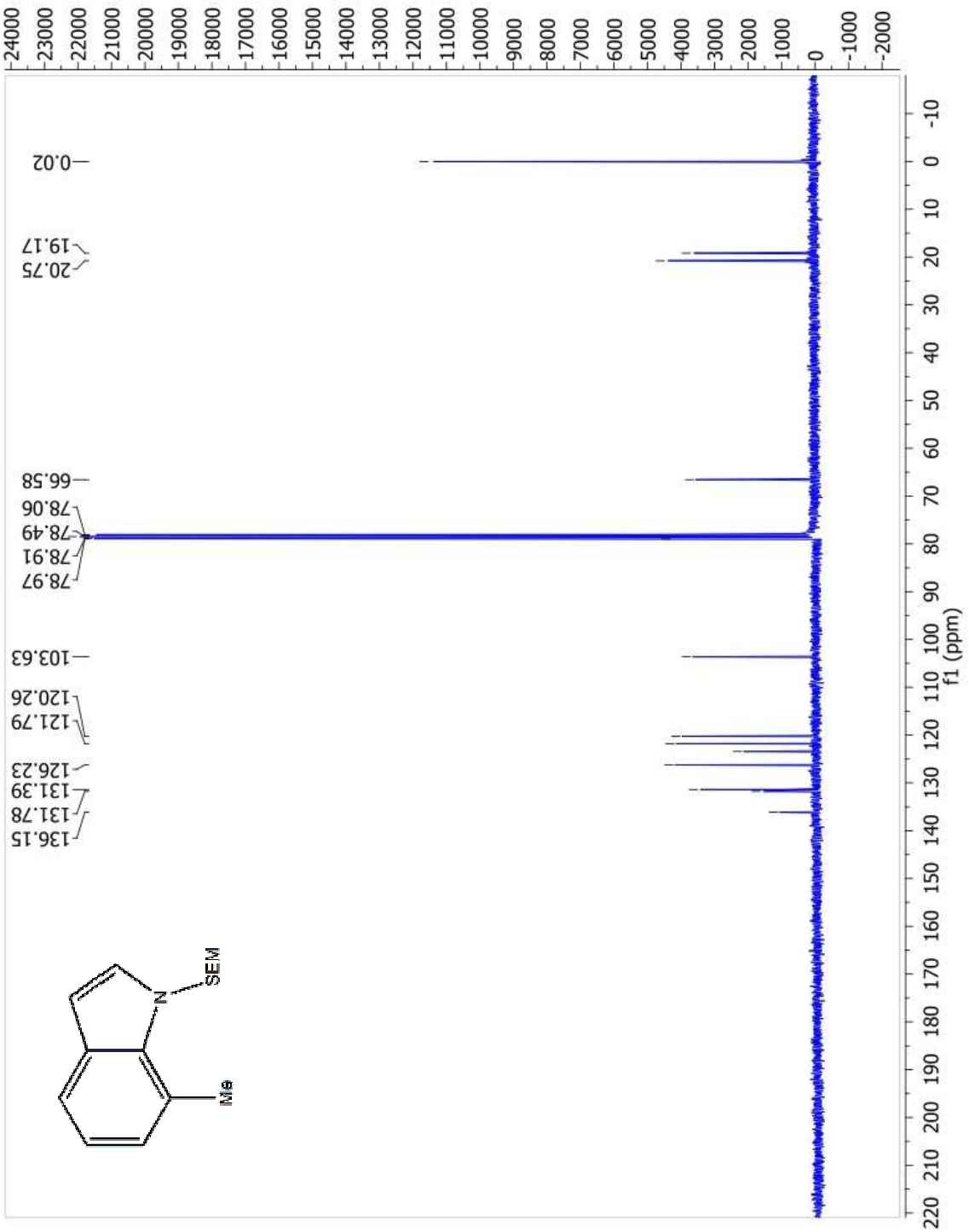
***R_f* -Value:** Hexane/Ethyl acetate (14:1 *v/v*) = 0.18

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.93 (t, ^3J = 9.0 Hz, 2H), 2.82 (s, 3H), 3.53 (t, ^3J = 8.04 Hz, 2H), 5.62 (s, 2H), 6.53 (d, ^3J = 3.0 Hz, 1H), 7.05-7.14 (m, 3H), 7.53 (d, ^3J = 6.0 Hz, 1H)

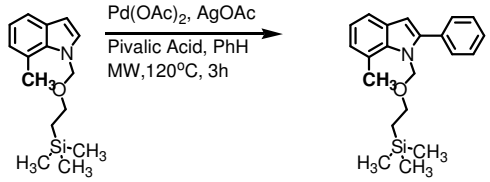
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 19.15, 20.73, 66.56, 103.61, 120.24, 121.78, 123.42, 126.22, 131.38, 131.77, 136.13

LRMS EI (m/z): [M+] calc'd for $C_{15}H_{23}NOSi$ 337.19, observed 261.10 m/z


SEM
N
Me
f1 (ppm)


SEM
N
Me
136.15
131.78
131.39
126.23
121.79
120.26
103.63
78.97
78.91
78.49
78.06
66.58
20.75
19.17
0.02
f1 (ppm)

Synthesis of 7-methyl-2-phenyl -1-[2-(trimethylsilyl)-ethoxymethyl]-indole (24)



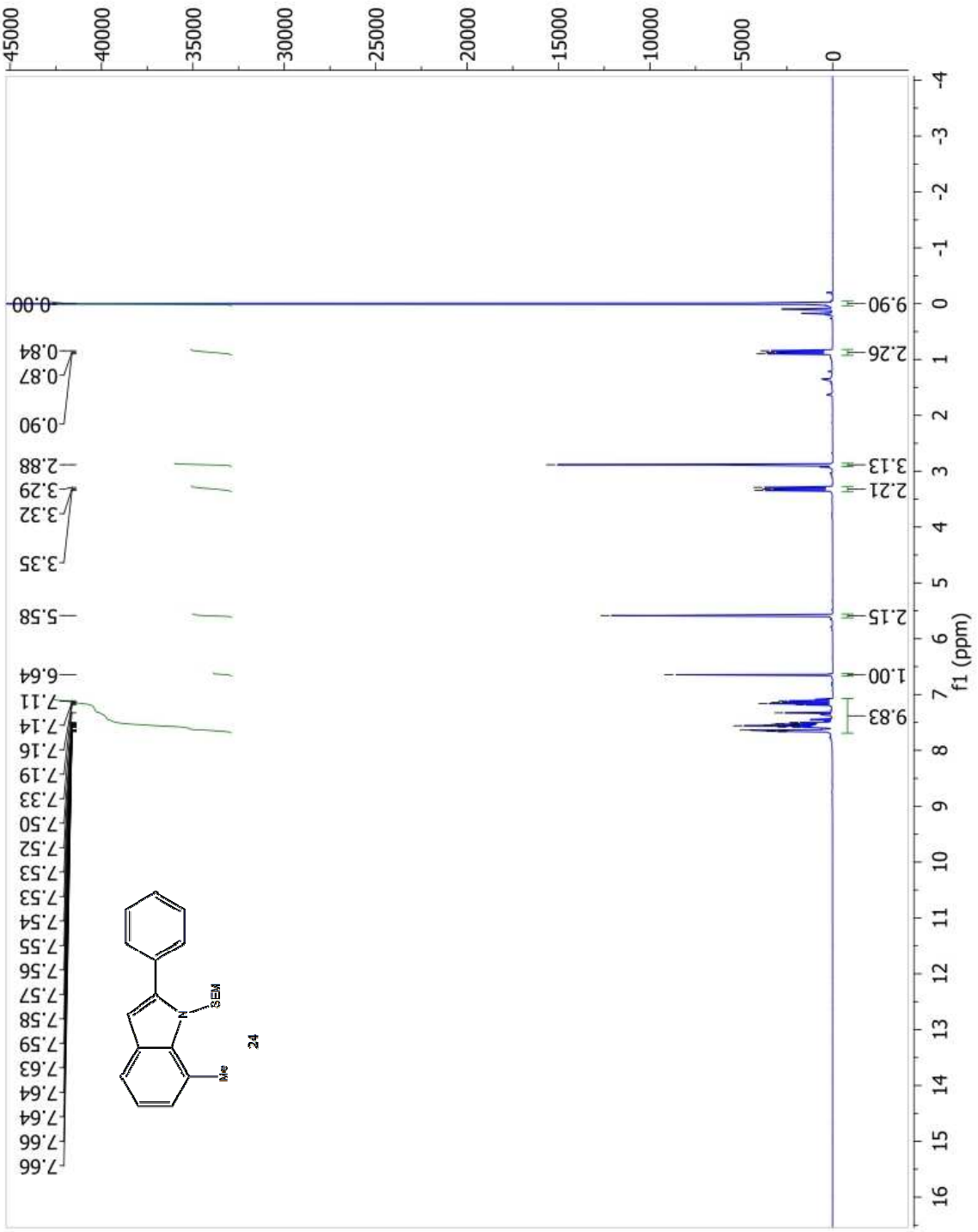
A magnetically stirred solution of 7-methyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.070g, 0.269mmol), palladium acetate (0.006g, 0.026mmol), silver acetate (0.134g, 0.806mmol), 2,2-dimethylpropanoic acid (0.068g, 0.665mmol) in 4mL of benzene was microwave heated at 120^0C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **24** 0.054g (61%).

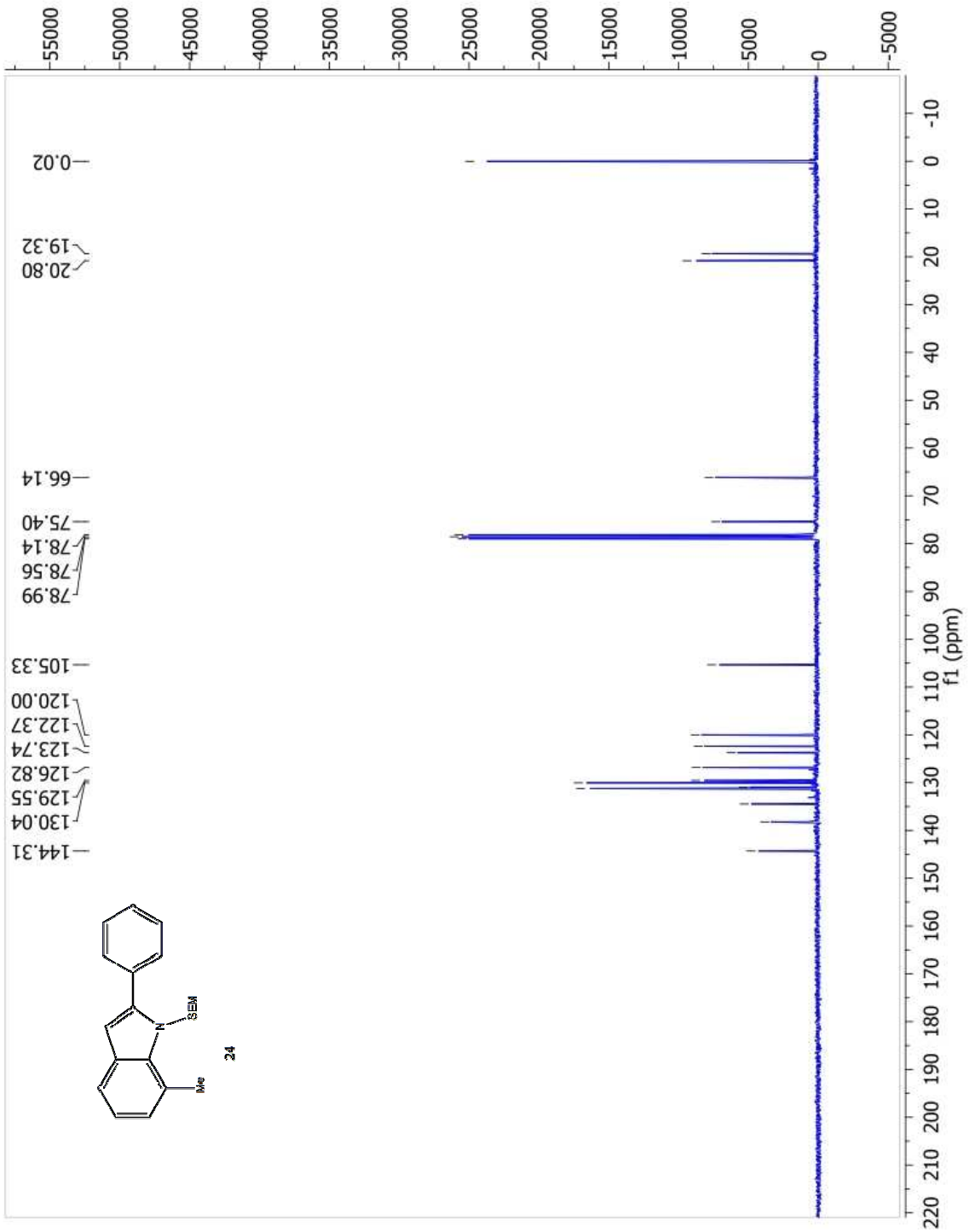
***R_f* -Value:** Hexane/Ethyl acetate (40:1 *v/v*) = 0.32

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.84 (t, ^3J = 9.0 Hz, 2H), 2.88 (s, 3H), 3.32 (t, ^3J = 8.04 Hz, 2H), 5.58 (s, 2H), 6.64 (s, 1H), 7.11-7.66 (m, 8H)

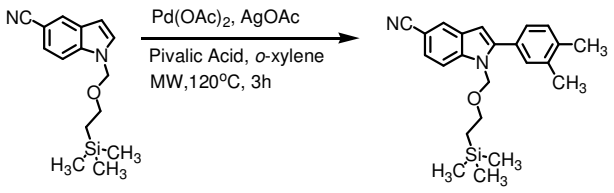
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.02, 19.32, 20.80, 66.14, 75.40, 105.33, 120.00, 122.37, 123.74, 126.82, 129.55, 130.04, 130.33, 131.38, 134.46, 138.20, 144.31

LRMS EI (m/z): [M+] calc'd for $C_{21}H_{27}NOSi$ 337.19, observed 337.20 m/z


24
SEM
Me
f1 (ppm)


144.31
130.04
129.55
126.82
123.74
122.37
120.00
105.33
78.99
78.56
78.14
75.40
66.14
20.80
19.32
0.02
SEM
Me
24
f1 (ppm)

Synthesis of 1-[2-(trimethylsilyl)-ethoxymethyl]-2-(3,4-dimethylphenyl)-indole-5-carbonitrile (25)



$C_{15}H_{20}N_2OSi$
Mol. Wt.: 272.42

$C_{23}H_{28}N_2OSi$
Mol. Wt.: 376.57

25

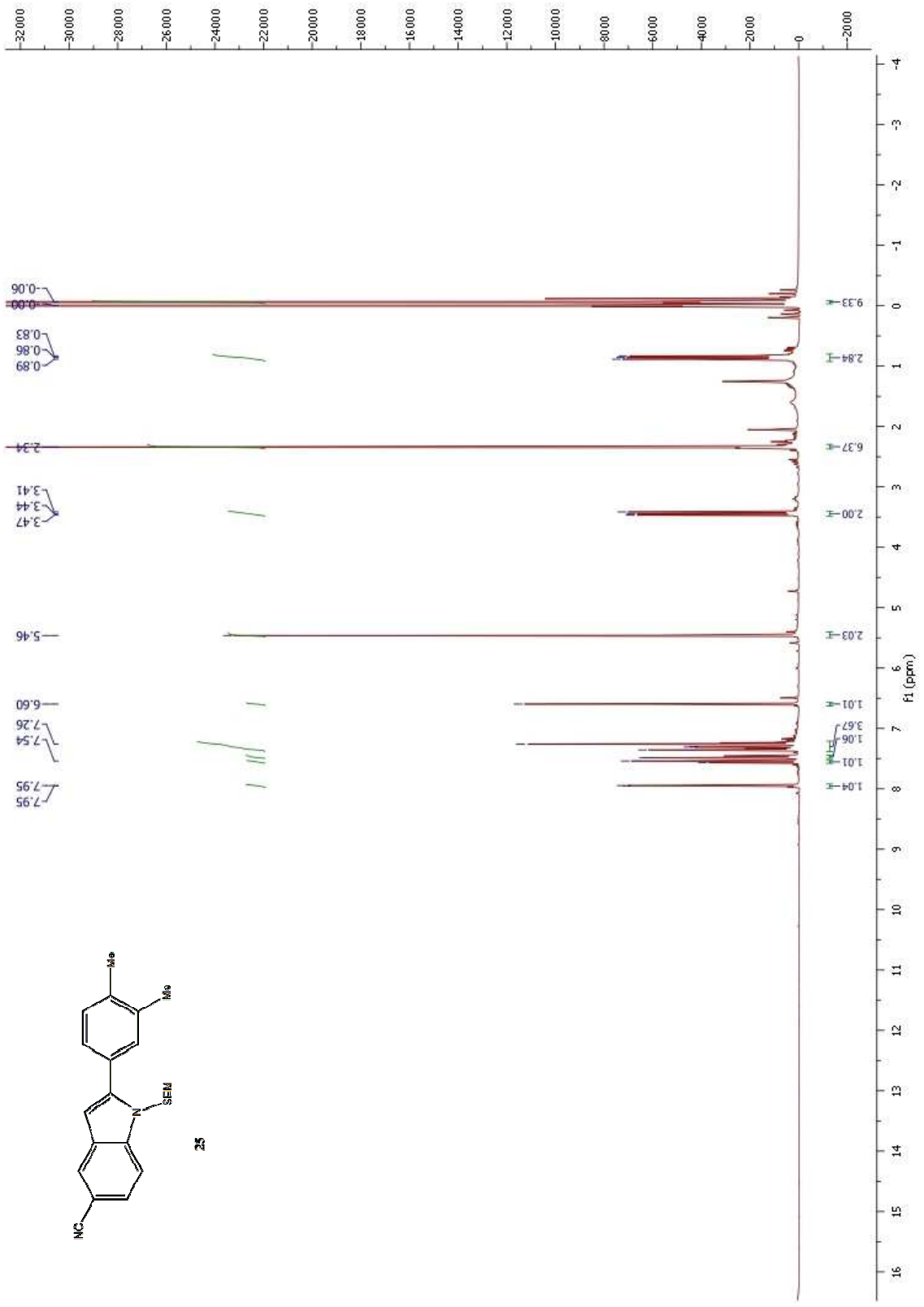
A magnetically stirred solution of 1-[2-(trimethylsilyl)-ethoxymethyl]-indole-5-carbonitrile (0.0400g, 0.147mmol), palladium acetate (0.0033g, 0.0147mmol), silver acetate (0.0732g, 0.441mmol), in 4mL of *o*-xylene was microwave heated at 120^0C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **25** 0.0420g (76%).

***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.28

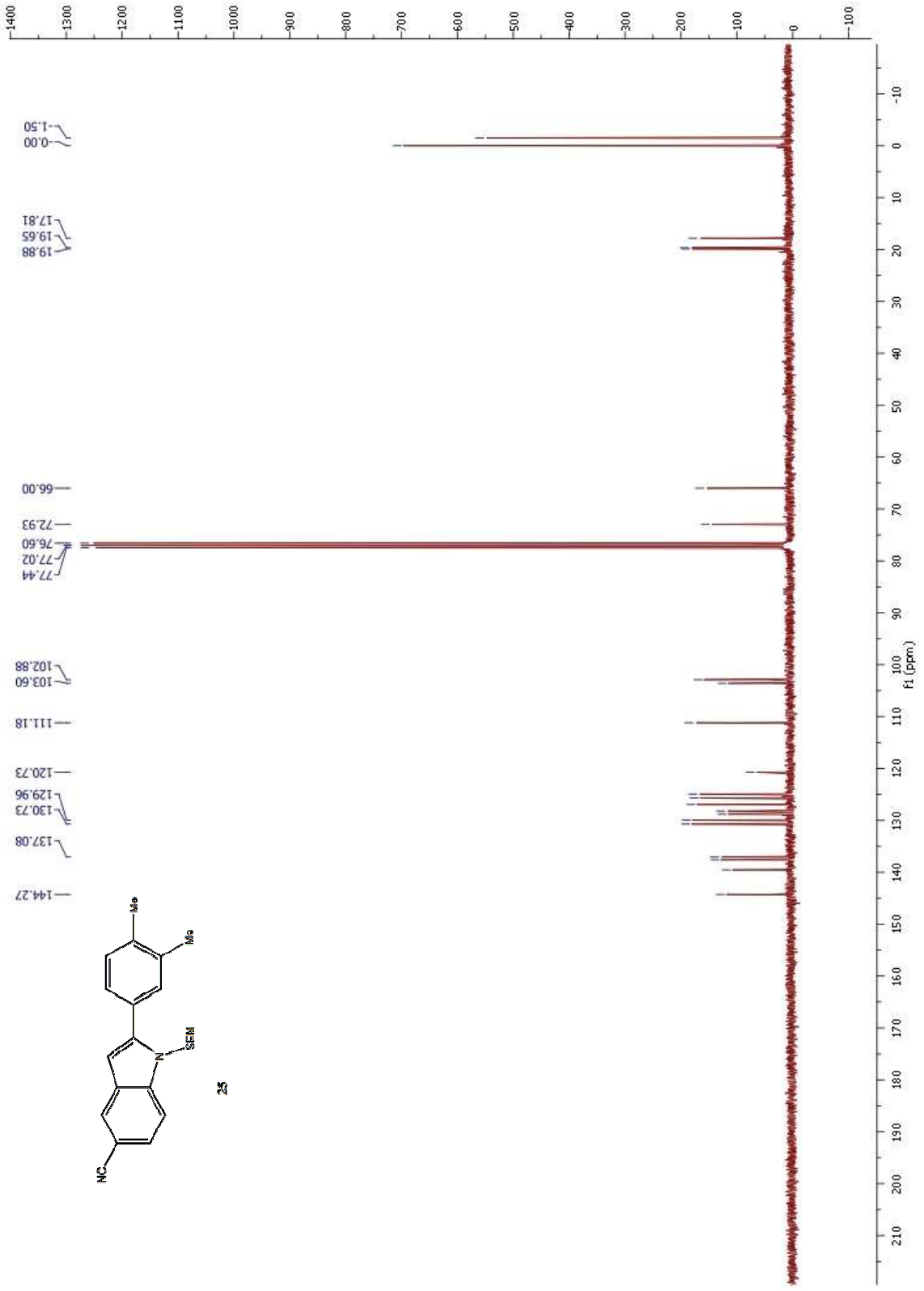
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 9H), 0.86 (t, ^3J =9.00 Hz, 2H), 2.34 (s, 6H), 3.44 (t, ^3J = 9.00 Hz, 2H), 5.46 (s, 2H), 6.60 (s, 1H), 7.23 – 7.36 (m, 4H), 7.47 (dd, ^3J =6.00 Hz, ^4J = 3.00 Hz, 1H), 7.55 (d, ^3J =9.00 Hz, 1H), 7.95 (dd, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 0.00, 17.81, 19.65, 19.88, 66.00, 72.93, 102.88, 103.60, 111.18, 120.73, 124.92, 125.71, 126.95, 128.19, 128.83, 129.96, 130.73, 137.08, 137.59, 139.53, 144.27

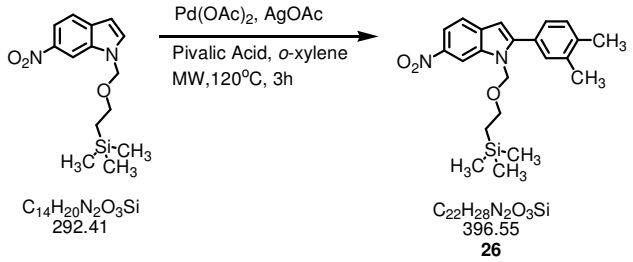
LRMS EI (m/z): [M+] calc'd for $C_{23}H_{28}N_2OSi$ 376.20, observed 377.03 m/z $[M+H]^+$


-0.06
0.00
0.83
0.86
0.89
2.34
3.41
3.44
3.47
5.46
6.60
7.26
7.54
7.95
7.95
9.33
2.84
6.37
2.00
2.03
1.01
3.67
1.06
1.01
1.04
f1 (ppm)
Me
Me
SEM
N
NC

25


-1.50
0.00
17.81
19.65
19.88
66.00
72.93
76.60
77.02
77.44
102.88
103.60
111.18
120.73
129.96
130.73
137.08
144.27
Me
Me
SEM
N
NC
25
f1 (ppm)

Synthesis of 6-Nitro-2-(3,4-dimethylphenyl)-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (26)



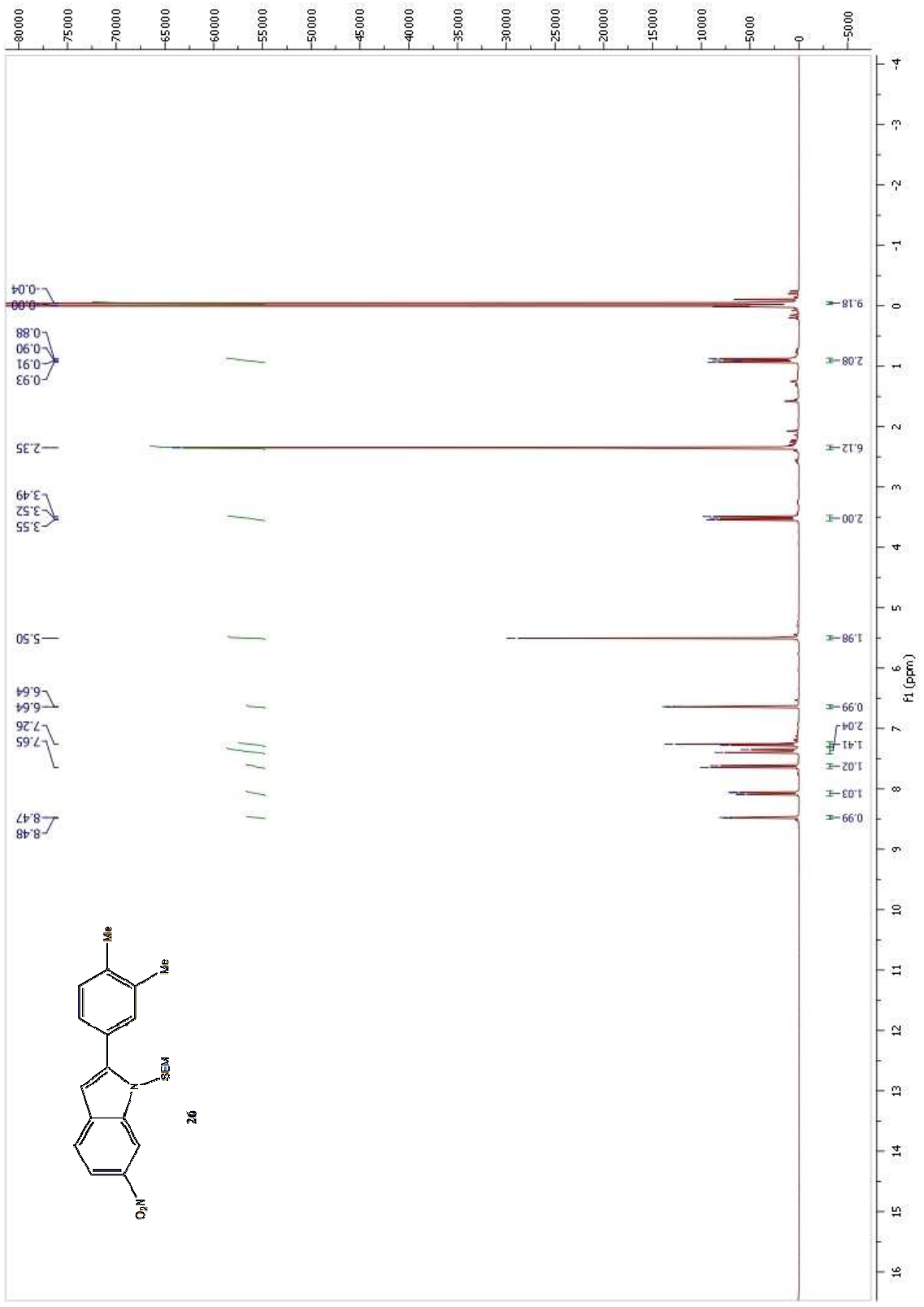
A magnetically stirred solution of 6-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.059g, 0.20mmol), palladium acetate (0.0045g, 0.020mmol), silver acetate (0.100g, 0.60mmol), 2,2-dimethylpropanoic acid (0.051g, 0.50mmol) in 4mL of *o*-xylene was microwave heated at 120°C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **26** 0.058g (73%).

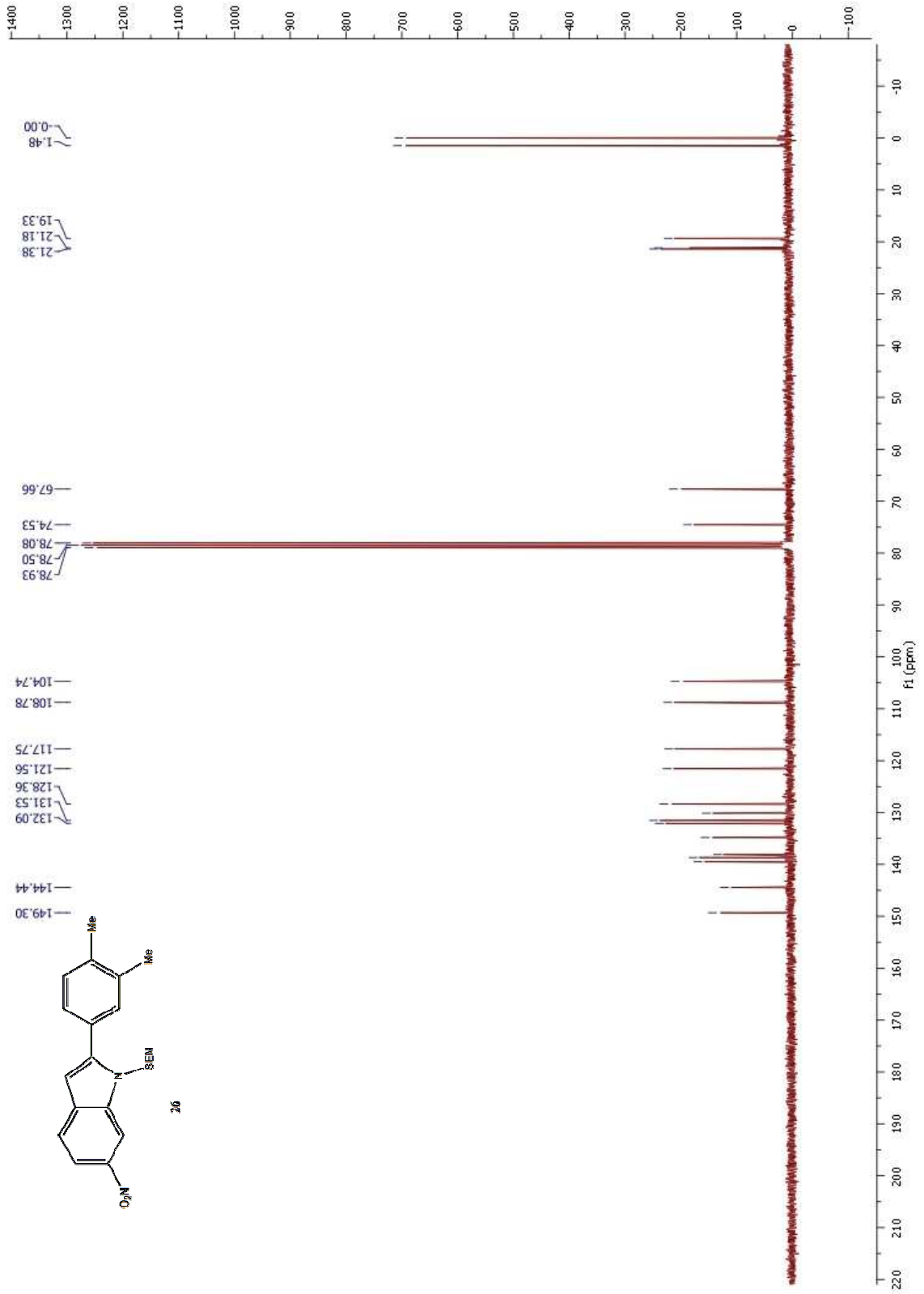
***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.33

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 9H), 0.91 (t, ^3J =6.00 Hz, 2H), 2.35 (s, 6H) 3.52 (t, ^3J = 9.00 Hz, 2H), 5.50 (s, 2H), 6.64 (s, 1H), 7.28 – 7.40 (m, 3H), 7.63 (d, ^3J = 9.00 Hz, 1H), 8.07 (dd, ^3J =9.00 Hz, ^4J = 1.20 Hz, 1H), 8.47 (dd, ^4J =3.00 Hz, 1H)

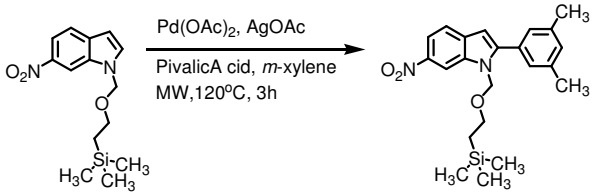
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 1.48, 19.33, 21.18, 21.38, 67.66, 74.53, 104.74, 108.78, 117.75, 121.56, 128.36, 130.13, 131.53, 132.09, 134.83, 138.11, 138.67, 139.50, 144.44, 149.30

LRMS EI (m/z): [M+] calc'd for $C_{22}H_{28}N_2O_3Si$ 396.19, observed 396.20 m/z


-0.04
0.00
0.88
0.90
0.91
0.93
2.35
3.49
3.52
3.55
5.50
6.64
6.64
7.26
7.65
8.47
8.48
9.18
2.08
6.12
2.00
1.98
0.99
2.04
1.41
1.02
1.03
0.99
f1 (ppm)
Me
Me
SEM
N
O2N
26


1.48
0.00
19.33
21.18
21.38
67.66
74.53
78.08
78.50
78.93
104.74
108.78
117.75
121.56
128.36
131.53
132.09
144.44
149.30
Me
Me
SEM
N
O2N
26
f1 (ppm)

Synthesis of 6-Nitro-2-(3,5-dimethylphenyl)-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (27)



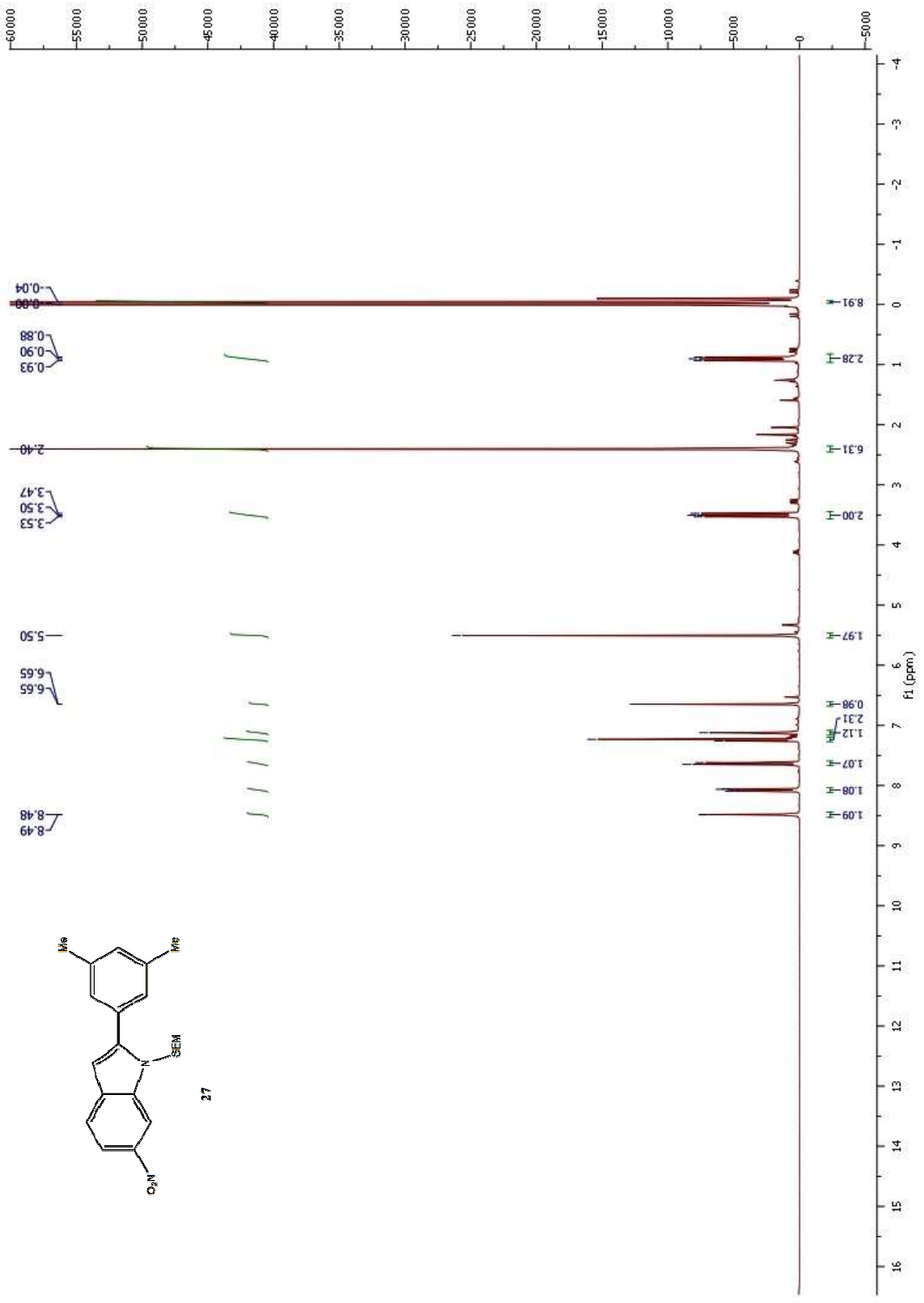
A magnetically stirred solution of 6-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.062g, 0.21mmol), palladium acetate (0.0047g, 0.021mmol), silver acetate (0.105g, 0.63mmol), 2,2-dimethylpropanoic acid (0.054g, 0.53mmol) in 4mL of *m*-xylene was microwave heated at 120°C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 50mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **27** 0.055g (65%).

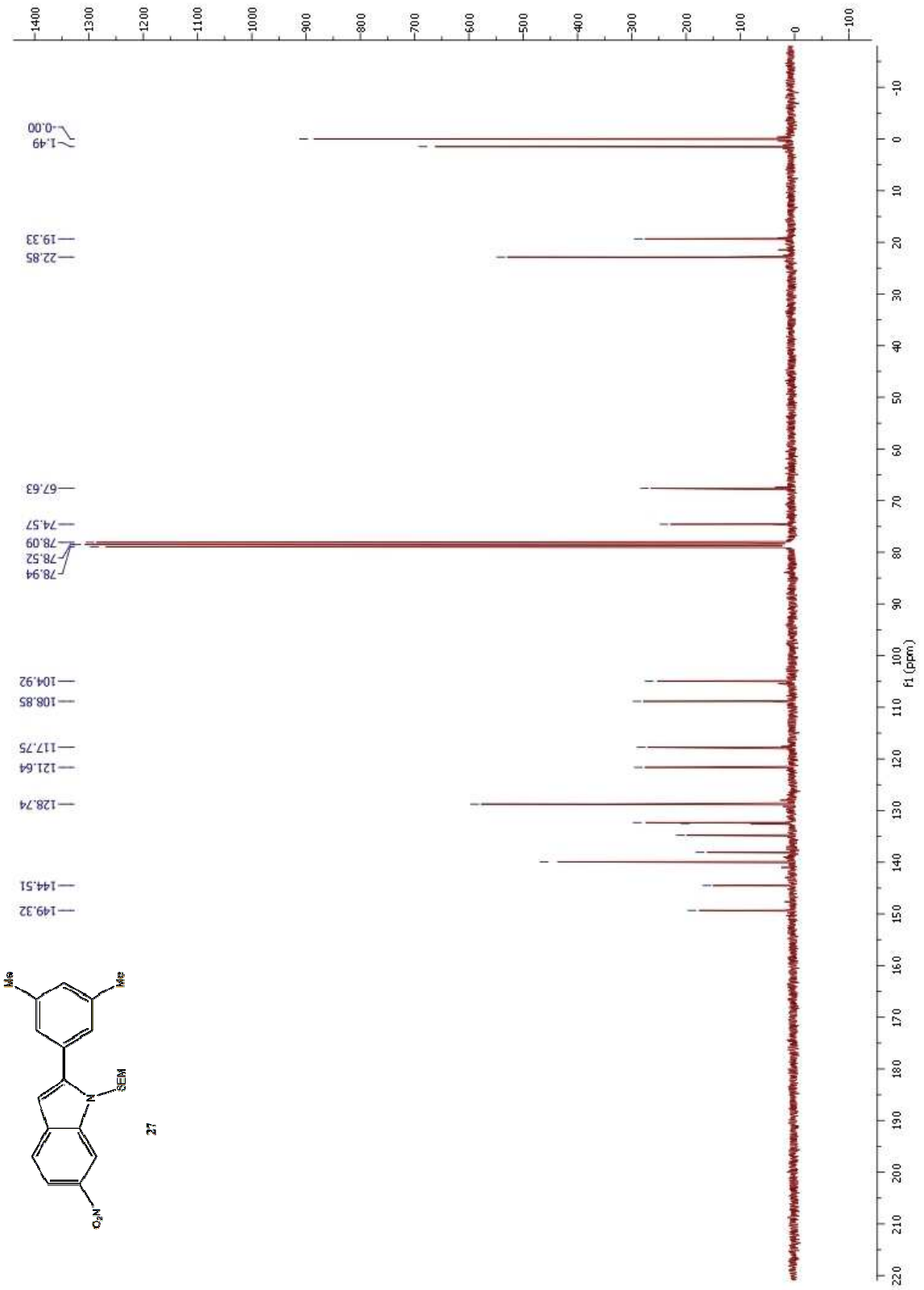
***R_f* -Value:** Hexane/Ethyl acetate (10:1 *v/v*) = 0.38

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 9H), 0.90 (t, ^3J =9.00 Hz, 2H), 2.40 (s, 6H) 3.50 (t, ^3J = 9.00 Hz, 2H), 5.50 (s, 2H), 6.65 (s, 1H), 7.12 (s, 1H), 7.24 (s, 2H), 7.64 (d, ^3J = 9.00 Hz, 1H), 8.07 (dd, ^3J =9.00 Hz, ^4J = 1.20 Hz, 1H), 8.48 (dd, ^4J =3.00 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 1.49, 19.33, 22.85, 67.63, 74.57, 104.92, 108.85, 117.75, 121.64, 128.74, 132.32, 132.51, 134.78, 138.09, 139.92, 144.51, 149.32

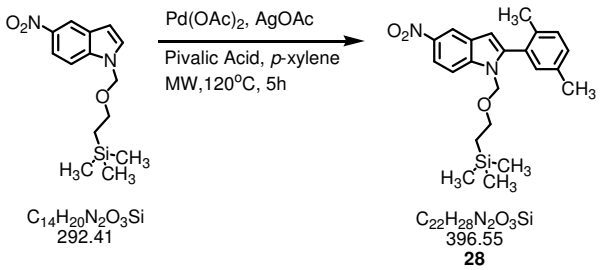
LRMS EI (m/z): [M+] calc'd for $C_{22}H_{28}N_2O_3Si$ 396.19, observed 396.20 m/z


Me
Me
SEM
N
O_2N
27


-0.00
1.49
19.33
22.85
67.63
74.57
78.09
78.52
78.94
104.92
108.85
117.75
121.64
128.74
144.51
149.32
f1 (ppm)
Me
Me
SEM
N
O2N

27

Synthesis of 5-nitro-2-(2,5-dimethylphenyl)-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (28)



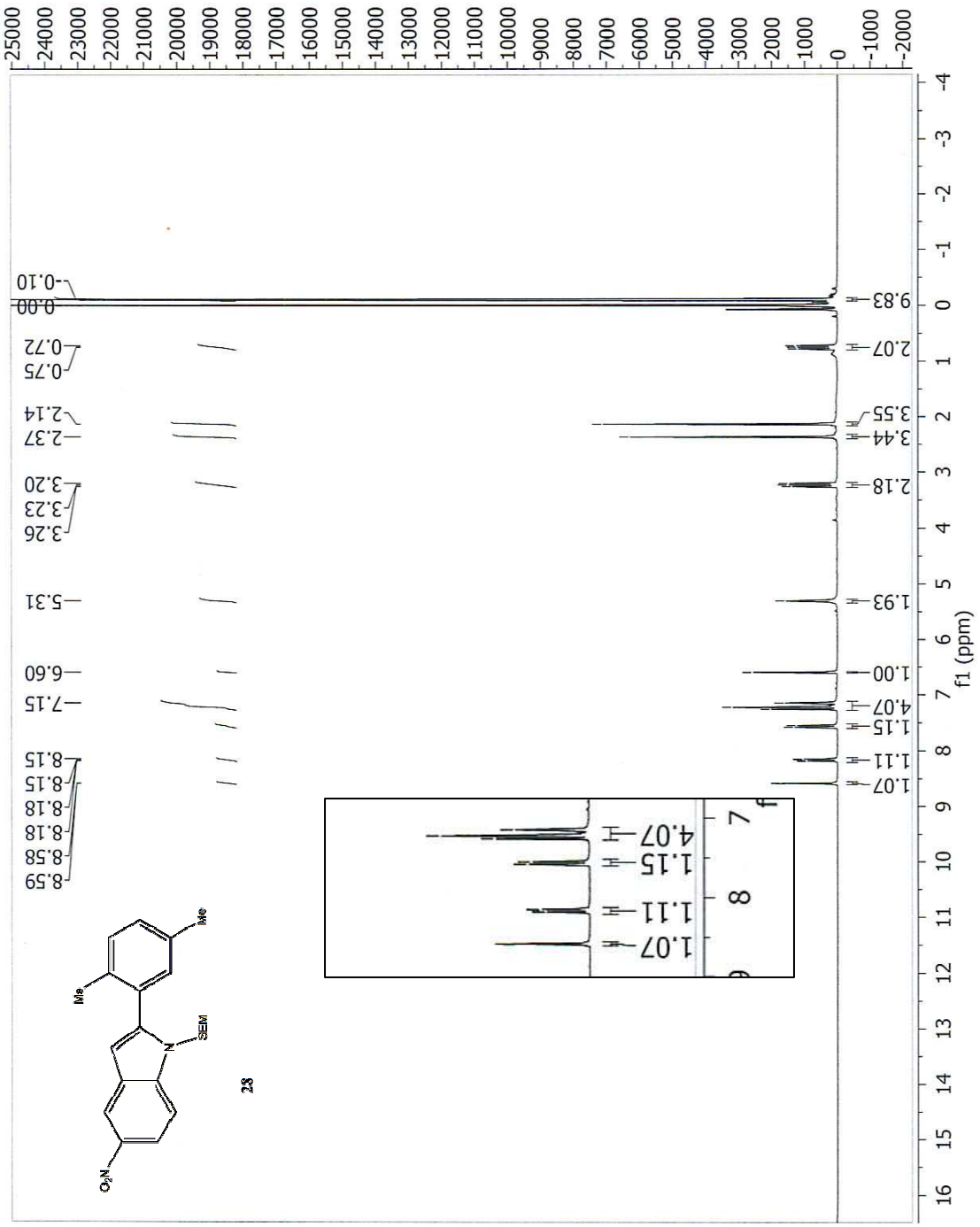
A magnetically stirred solution of 5-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.082g, 0.282mmol), palladium acetate (0.0063g, 0.028mmol), silver acetate (0.140g, 0.84mmol), 2,2-dimethylpropanoic acid (0.072g, 0.70mmol) in 4mL of *p*-xylene was microwave heated at 120^0C for 5h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **28** 0.024g (23%).

***R_f* -Value:** Hexane/Ethyl acetate (9:1 *v/v*) = 0.35

^{1}H-NMR (300 MHz, $CDCl_3$): δ = -0.10 (s, 9H), 0.72 (t, ^3J = 8.25 Hz, 2H), 3.23 (t, ^3J = 8.28 Hz, 2H), 2.14 (s, 3H), 2.37 (s, 3H), 5.31 (s, 2H), 6.60 (s, 1H), 7.15-7.26 (m, 3H), 7.56 (d, ^3J = 9.03 Hz, 1H), 8.16 (dd, ^3J = 9.03 Hz, ^4J = 2.22 Hz, 1H), 8.16 (d, ^4J = 2.16 Hz, 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 1.54, 19.26, 21.07, 22.43, 67.49, 74.63, 106.29, 112.10, 118.95, 119.03, 129.33, 131.76, 131.82, 132.05, 133.22, 136.20, 136.84, 141.34, 143.89, 145.10

LRMS EI (m/z): [M+] calc'd for $C_{22}H_{28}N_2O_3Si$ 396.19, observed 396.20 m/z


f1 (ppm)
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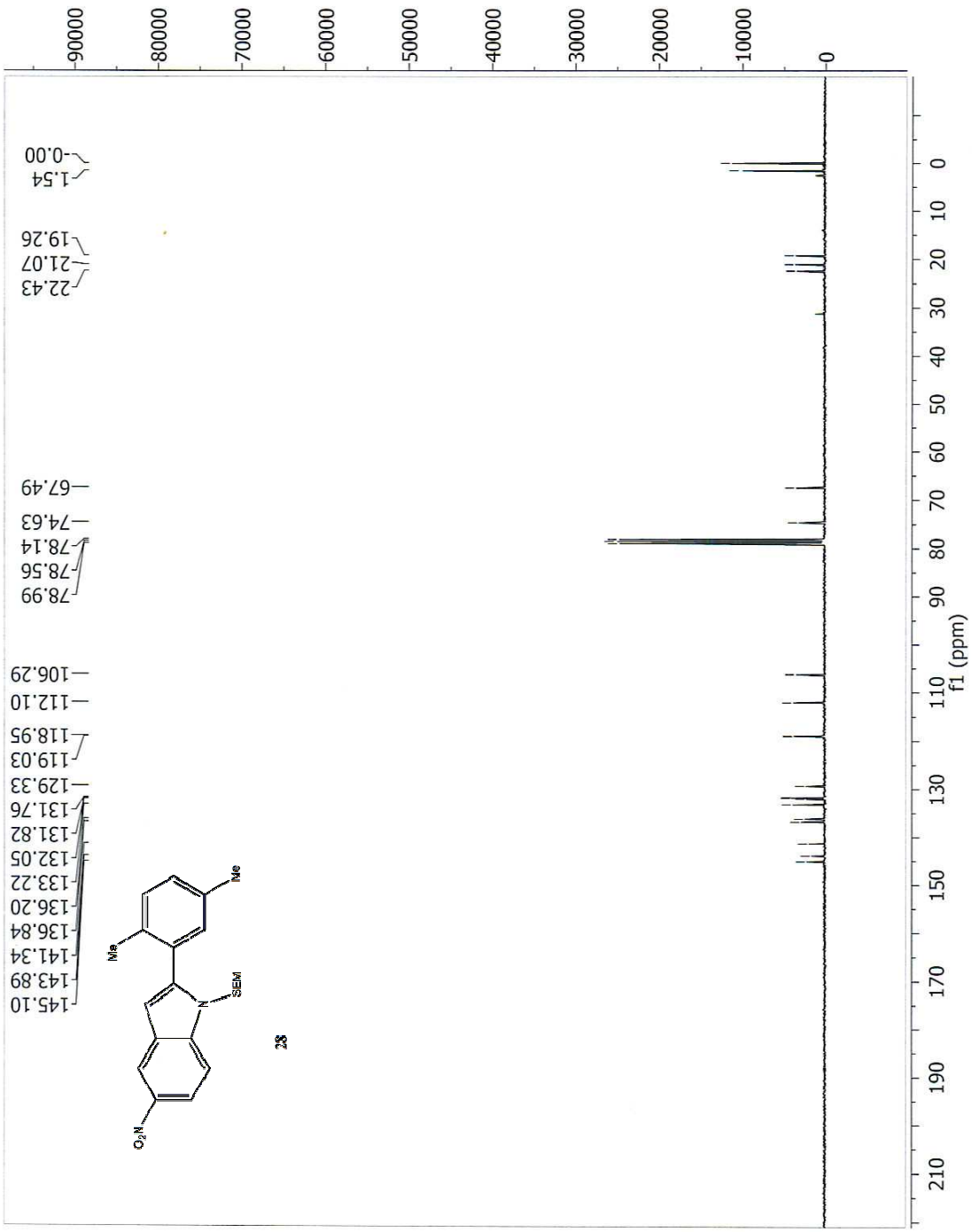
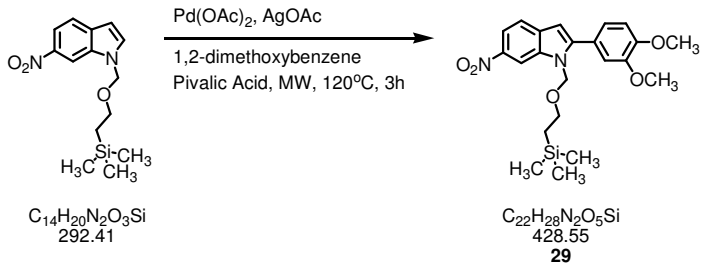
2.07
3.55
3.44
2.18
1.93
1.00
4.07
1.15
1.11
1.07
8.59
8.58
8.18
8.18
8.15
8.15
7.15
6.60
5.31
3.26
3.23
3.20
2.37
2.14
0.75
0.72
0.00
-0.10
Me
Me
SEM
N
O2N
23


-0.00
1.54
19.26
21.07
22.43
67.49
74.63
78.14
78.56
78.99
106.29
112.10
118.95
119.03
129.33
131.76
131.82
132.05
133.22
136.20
136.84
141.34
143.89
145.10
Me
Me
SEM
N
O2N
2s
f1 (ppm)

Synthesis of 6-Nitro-2-(3,4-dimethoxyphenyl)-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (29)



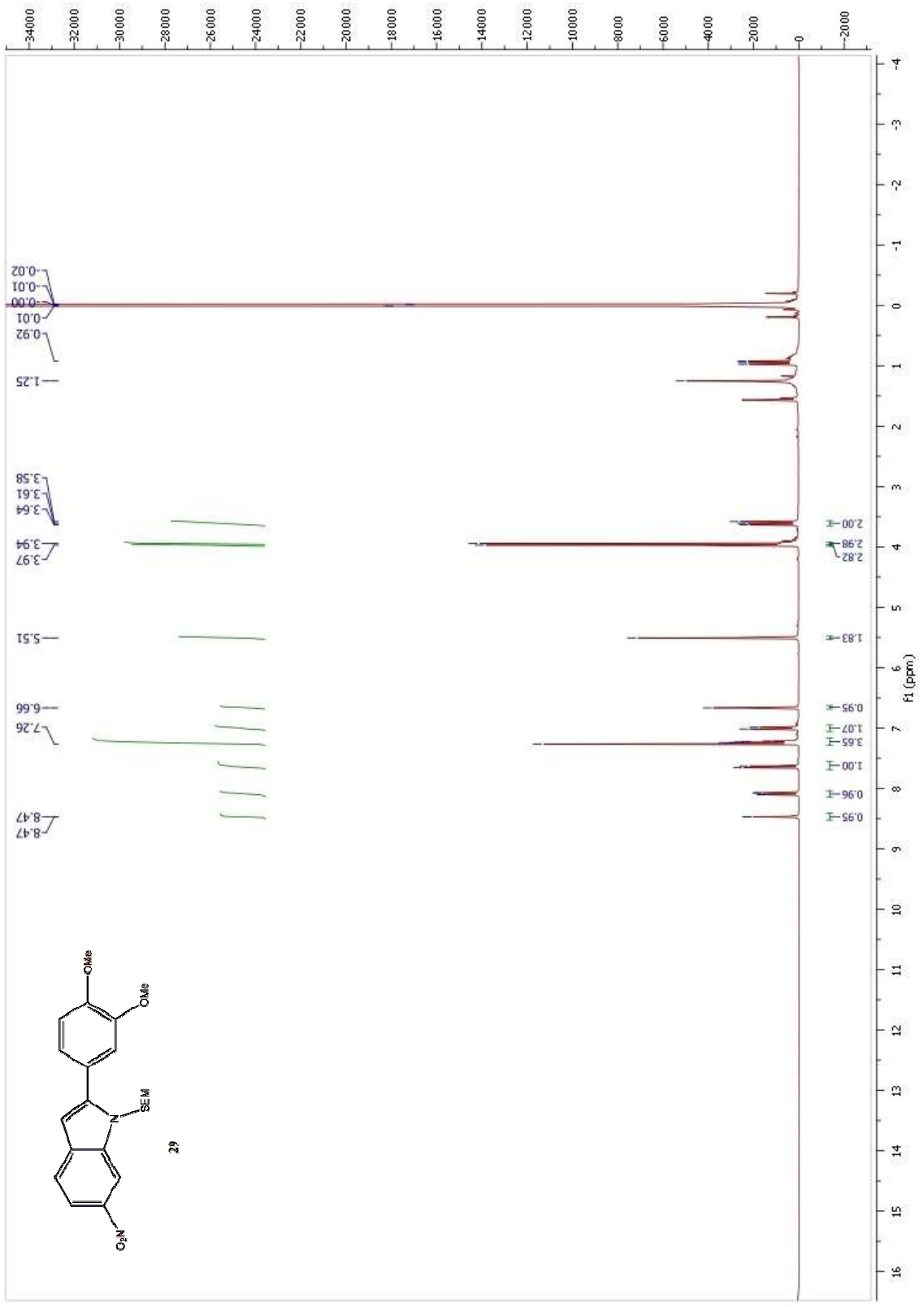
A magnetically stirred solution of 6-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.0400g, 0.1368mmol), palladium acetate (0.0033g, 0.0136mmol), silver acetate (0.0681g, 0.410mmol), 2,2-dimethylpropanoic acid (0.034g, 0.34mmol) in 4mL of 1,2-dimethoxybenzene was microwave heated at 120^0C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **29** 0.0082g (14%).

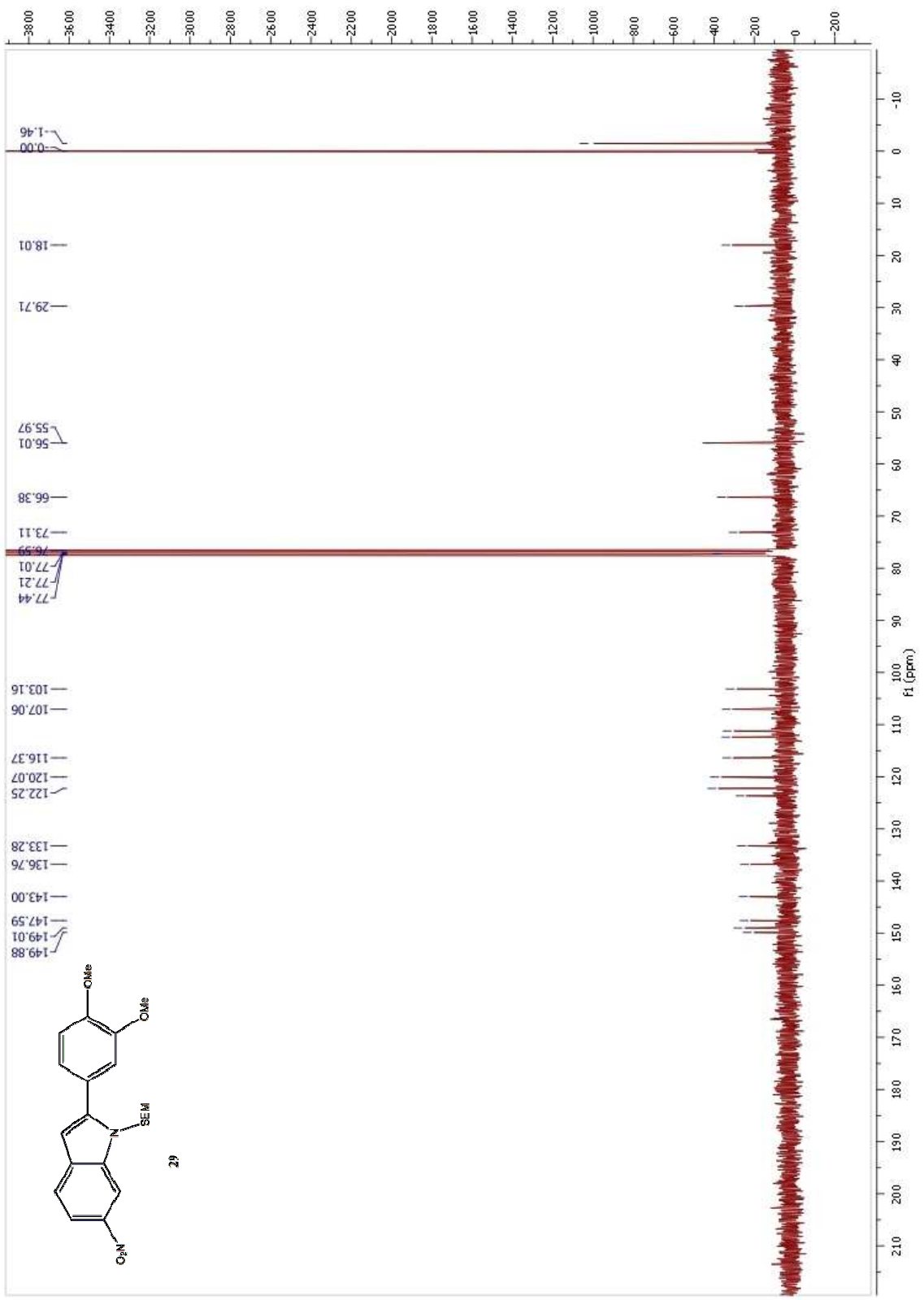
***R_f* -Value:** Hexane/Ethyl Acetate (8:2 *v/v*) = 0.18

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.92 (t, ^3J = 9.00 Hz, 2H), 3.61 (t, ^3J = 9.00 Hz, 2H), 3.94 (s, 3H), 3.97 (s, 3H), 5.51 (s, 2H), 6.66 (s, 1H), 7.00 (d, ^3J = 6.00 Hz, 1H), 7.21 – 7.24 (m, 2H), 7.64 (d, ^3J = 9.00 Hz, 1H), 8.09 (dd, ^3J = 9.00 Hz, ^4J = 3.00 Hz 1H), 8.09 (dd, ^4J = 3.00 Hz 1H)

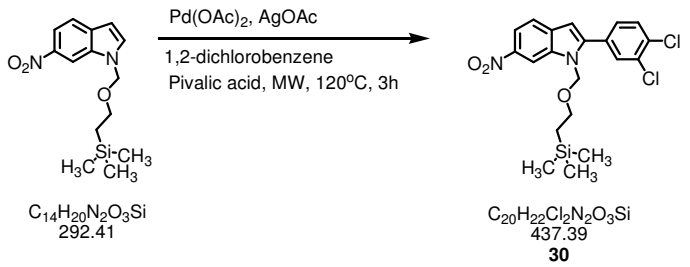
^{13}C-NMR (75 MHz, $CDCl_3$): δ = -1.46, 18.01, 29.71, 55.97, 56.01, 66.38, 73.11, 103.16, 107.06, 111.21, 112.40, 116.37, 120.07, 122.25, 123.66, 133.28, 136.76, 143.00, 147.59, 149.01, 149.88

LRMS EI (m/z): [M+] calc'd for $C_{22}H_{28}N_2O_5Si$ 428.18, observed 429.97 m/z $[M+H]^+$


OMe
OMe
N
SEM
O2N
29
f1 (ppm)


-1.46
0.00
18.01
29.71
55.97
56.01
66.38
73.11
76.99
77.01
77.21
77.44
103.16
107.06
116.37
120.07
122.25
133.28
136.76
143.00
147.59
149.01
149.88
OMe
OMe
SEM
N
O2N
29
f1 (ppm)

Synthesis of 6-Nitro-2-pentafluorophenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (30)



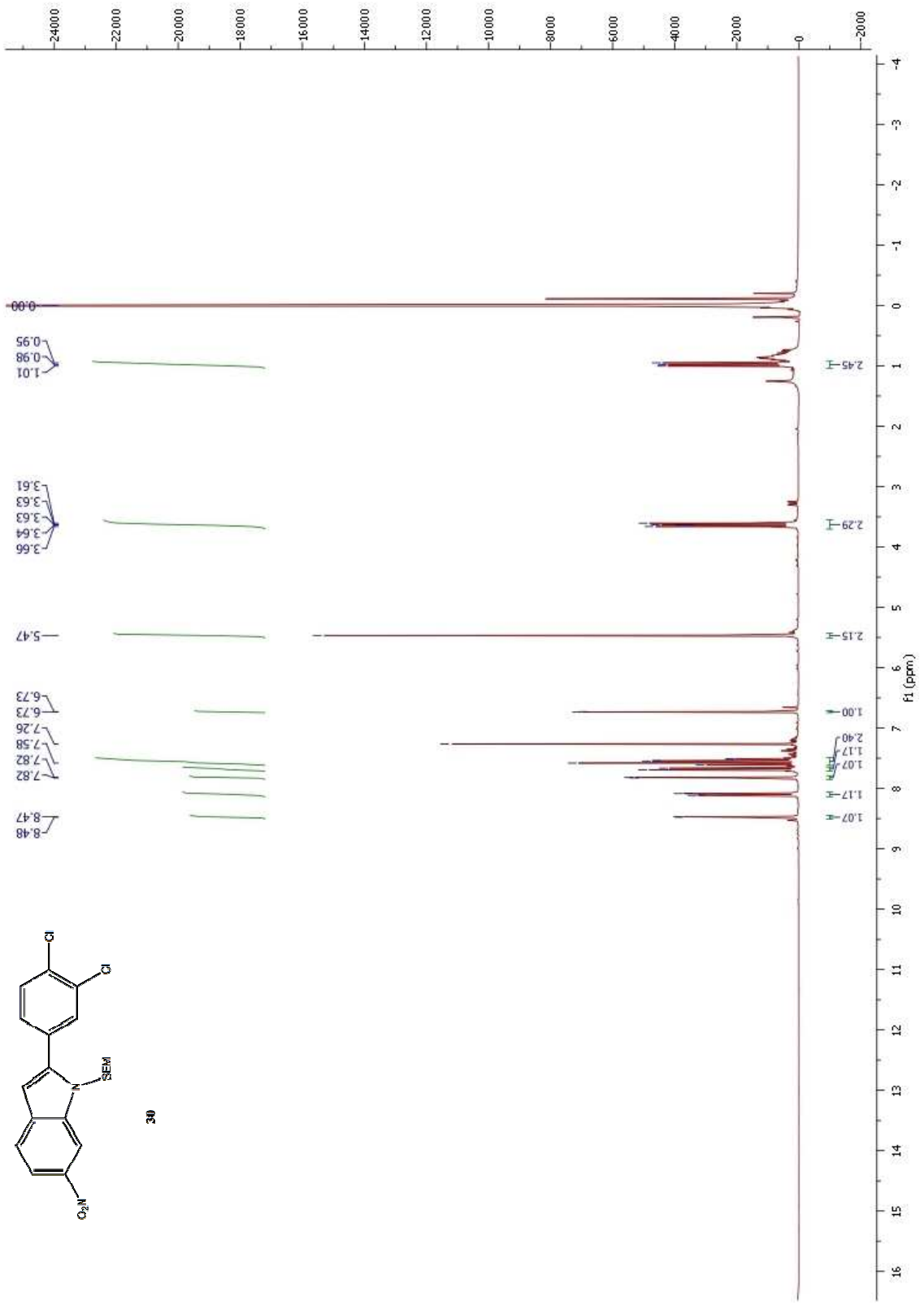
A magnetically stirred solution of 6-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.038g, 0.132mmol), palladium acetate (0.0029g, 0.0132mmol), silver acetate (0.065g, 0.391mmol), 2,2-dimethylpropanoic acid (0.033g, 0.33mmol) in 4mL of 1,2-dichlorobenzene was microwave heated at 120^0C for 3h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **30** 0.0371g (65%).

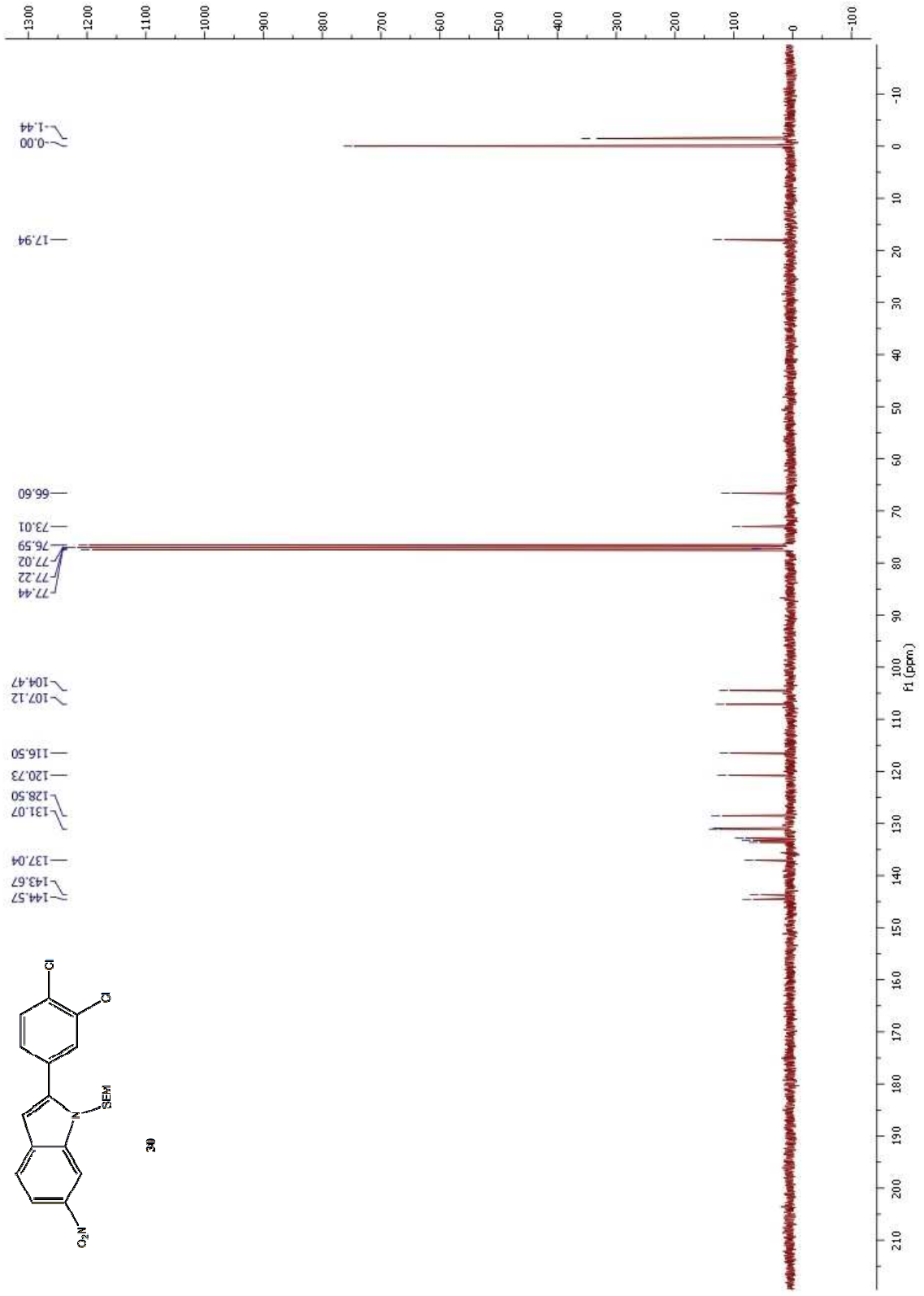
***R_f* -Value:** Hexane/Ethyl Acetate (9:1 *v/v*) = 0.20

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.98 (t, ^3J = 9.00 Hz, 2H), 3.63 (t, ^3J = 9.00 Hz, 2H), 5.47 (s, 2H), 6.73 (s, 1H), 7.51 – 7.58 (m, 2H), 7.67 (d, ^3J = 9.00 Hz, 1H), 7.82 (d, ^3J = 3.00 Hz, 1H), 8.10 (dd, ^3J = 6.00 Hz, ^4J = 3.00 Hz 1H), 8.47 (dd, ^4J = 3.00 Hz 1H)

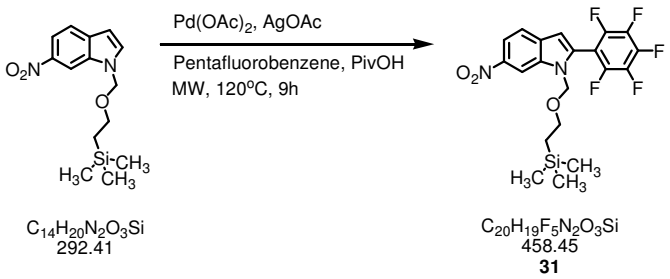
^{13}C-NMR (75 MHz, $CDCl_3$): δ = -1.44, 17.94, 66.60, 73.01, 104.47, 107.12, 116.50, 120.73, 128.50, 130.88, 131.07, 132.75, 133.21, 133.60, 137.04, 143.67, 144.57

LRMS EI (m/z): [M+] calc'd for $C_{20}H_{22}Cl_2N_2O_3Si$ 436.08, observed 438.02 m/z $[M+H]^+$


0.00
0.95
0.98
1.01
3.61
3.63
3.63
3.64
3.66
5.47
6.73
6.73
7.26
7.58
7.82
7.82
8.47
8.48
2.45
2.29
2.15
1.00
2.40
1.07
1.17
1.17
1.07
f1 (ppm)
Cl
Cl
SEM
N
O2N
30


-1.44
0.00
17.94
66.60
73.01
76.59
77.02
77.22
77.44
104.47
107.12
116.50
120.73
128.50
131.07
137.04
143.67
144.57
Cl
Cl
SEM
N
O2N
30
f1 (ppm)

Synthesis of 6-Nitro-2-pentafluorophenyl-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (31)



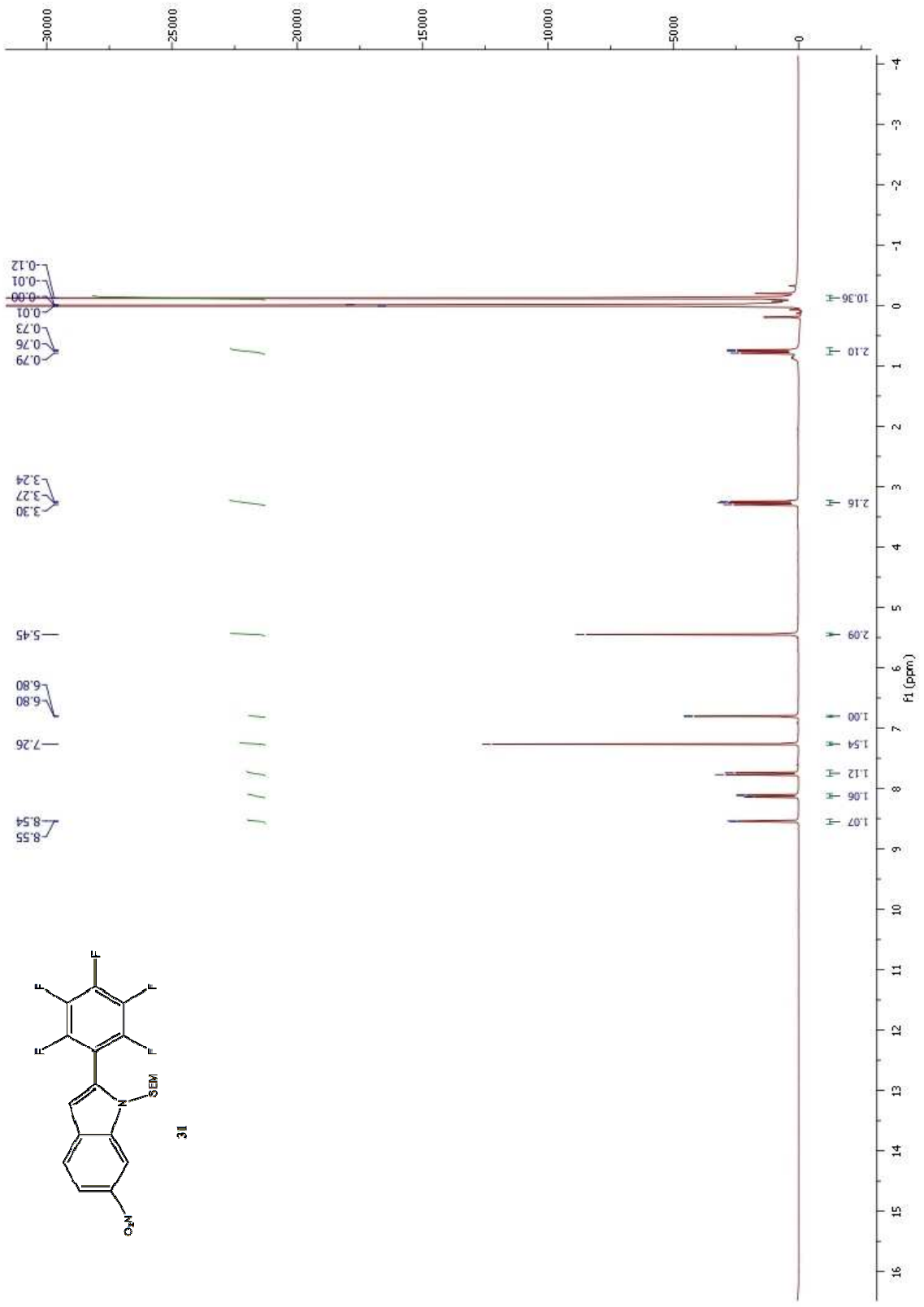
A magnetically stirred solution of 6-nitro-1-[2-(trimethylsilyl)-ethoxymethyl]-indole (0.0845g, 0.288mmol), palladium acetate (0.0064g, 0.0288mmol), silver acetate (0.143g, 0.864mmol), 2,2-dimethylpropanoic acid (0.073g, 0.72mmol) in 5mL of pentafluorobenzene was microwave heated at 120^0C for 9h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography to give pure **31** 0.058g (44%).

***R_f* -Value:** Hexane/Ethyl Acetate (10:1 *v/v*) = 0.39

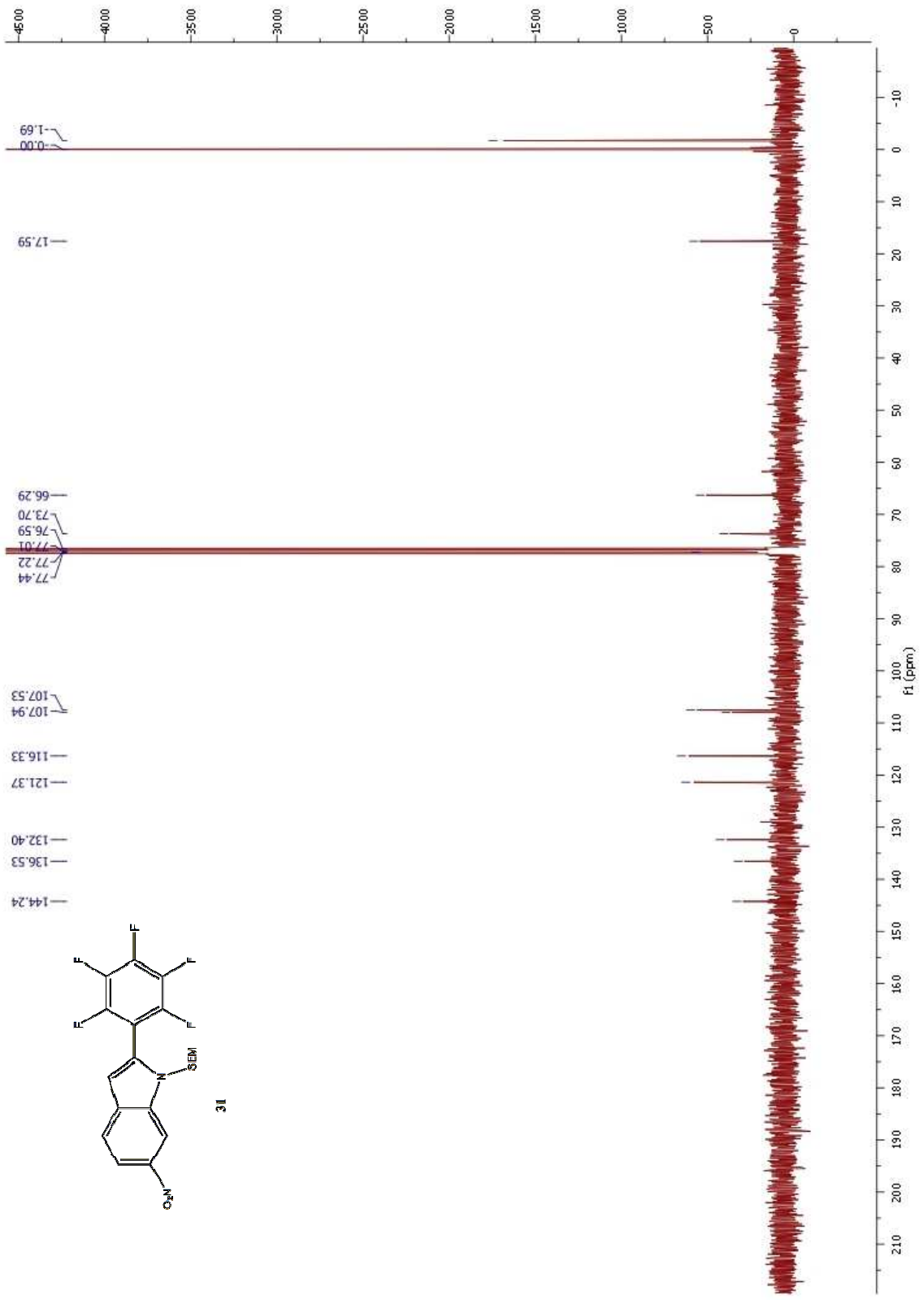
^{1}H-NMR (300 MHz, $CDCl_3$): δ = -0.12 (s, 9H), 0.76 (t, ^3J = 9.00 Hz, 2H), 3.27 (t, ^3J = 9.00 Hz, 2H), 5.45 (s, 2H), 6.80 (s, 1H), 7.75 (d, ^3J = 9.00 Hz, 1H), 8.12 (dd, ^3J = 9.00 Hz, ^4J = 3.00 Hz 1H), 8.54 (dd, ^4J = 3.00 Hz 1H)

^{13}C-NMR (75 MHz, $CDCl_3$): δ = -1.69, 17.59, 66.29, 73.70, 107.53, 107.94, 116.33, 121.37, 132.40, 136.53, 144.24

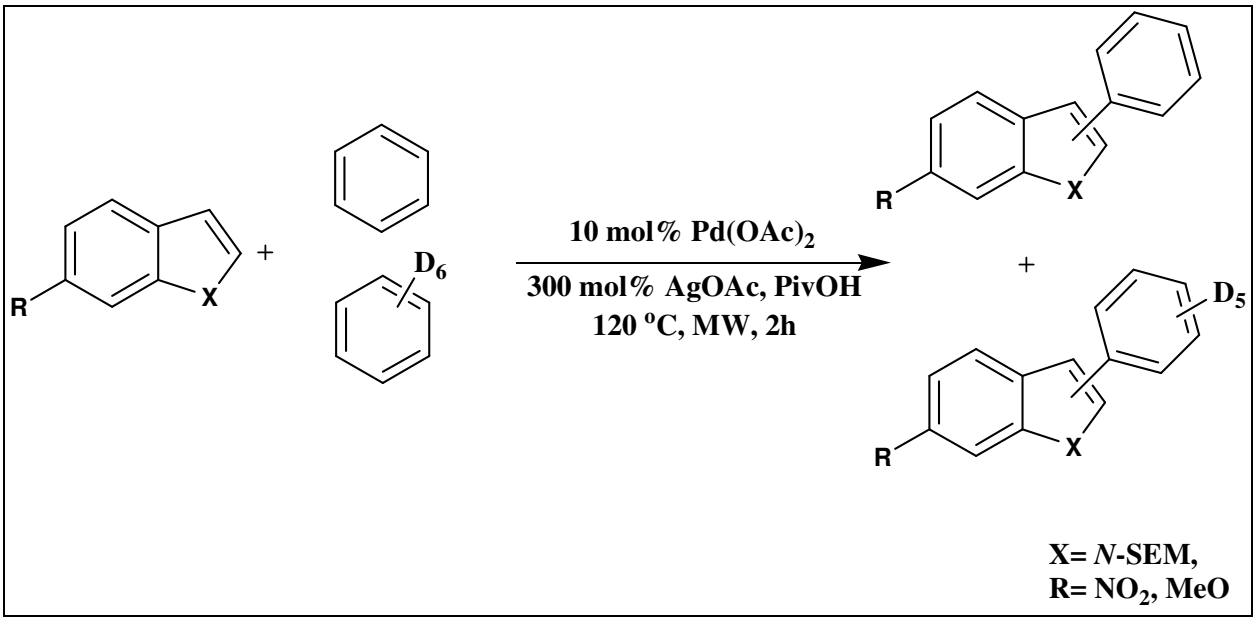
LRMS EI (m/z): [M+] calc'd for $C_{20}H_{19}F_5N_2O_3Si$ 458.11, observed 459.09 m/z $[M+H]^+$


30000
25000
20000
15000
10000
5000
0
-0.12
-0.01
0.00
0.01
0.73
0.76
0.79
3.24
3.27
3.30
5.45
6.80
6.80
7.26
8.54
8.55
10.36
2.10
2.16
2.09
1.00
1.54
1.12
1.06
1.07
f1 (ppm)
F
F
F
F
F
N
SEM
O2N

31


-1.69
0.00
17.59
66.29
73.70
76.59
77.01
77.22
77.44
107.53
107.94
116.33
121.37
132.40
136.53
144.24
F
F
F
F
F
SEM
N
O2N
31
f1 (ppm)

KIE experiments



A reaction was set up in a vial on a 0.2mmol scale of reactant, 10 mol% $Pd(OAc)_2$, 300 mol% AgOAc, PivOH (0eq, 0.5eq, 2.5eq, 30eq) with equimolar amounts of benzene (2.00mL, 22.5mmol) and benzene-d_6 (1.99mL, 22.5mmol) was microwave heated at 120 ^{0}C for 2h. The reaction was then cooled and an aliquot was removed and analyzed by GC/MS.

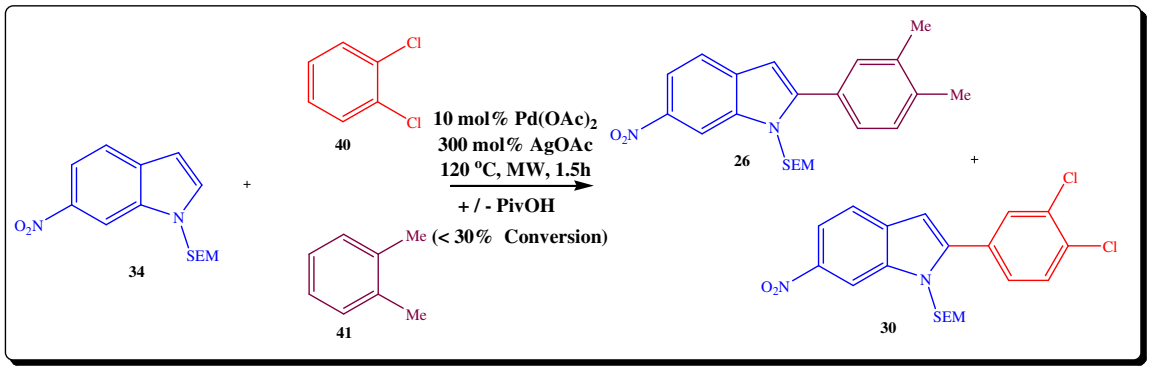
GC/MS Conditions:

J & W Scientific DB-1, capillary 25.0m x 200μm x 0.33μm, 1.3 mL/min, 40°C, hold 0.50min, 12°C/min to 320°C, hold 6.0min.

Substrate (R)	**PivOH (equiv)**	**Major (2-Ph) kH/kD**
NO_2, **34**	0	4.5
	0.5	5.0
	2.5	4.9
	30	4.3
OMe, **10**	0	4.6
	0.5	4.3
	2.5	4.1
	30	4.3

Competition Experiment's

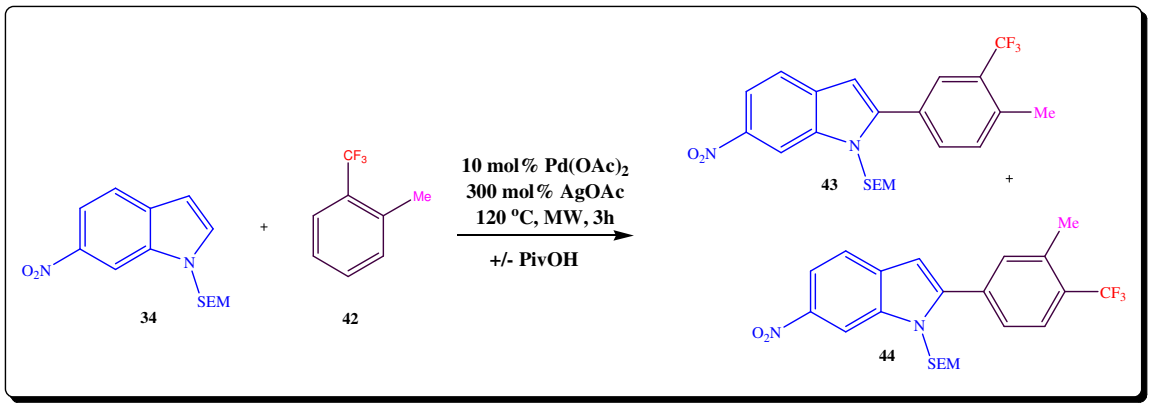
I)



A reaction was set up in a vial on a 0.2mmol scale of reactant **34**, 10 mol% $Pd(OAc)_2$, 300 mol% AgOAc, PivOH (0eq, 2.5eq, 10eq) with equimolar amounts of o-dichlorobenzene (2mL) and o-dimethylbenzene (2mL) was microwave heated at 120 ^{0}C for 1.5h. The reaction was then cooled and an aliquot was removed and analyzed by GC/MS.

PivOH	**26:30**
0 equiv	1.1:1
2.5 equiv	1.1:1
10 equiv	1.1:1

II)

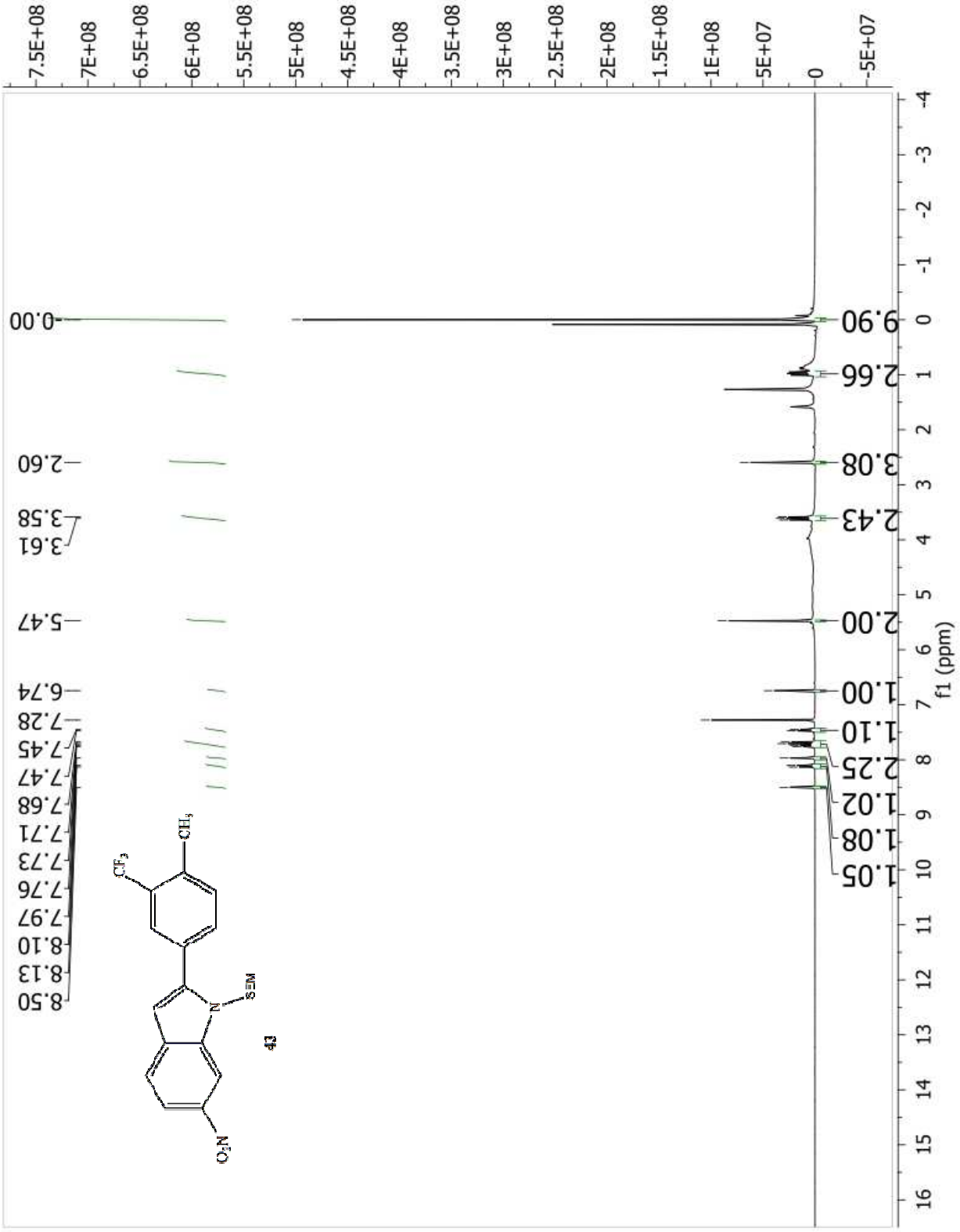


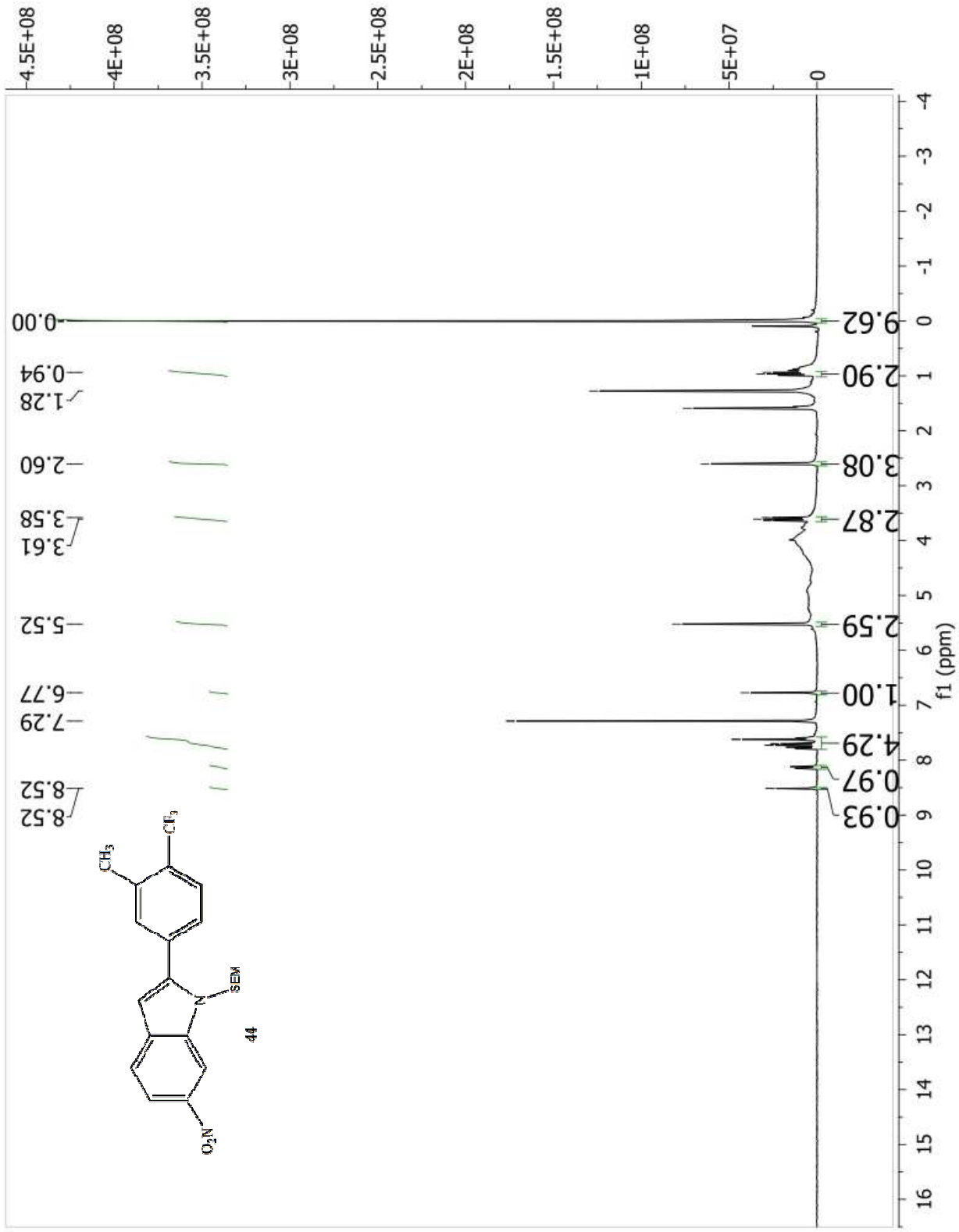
A reaction was set up in a vial on a 0.2mmol scale of reactant **34**, 10 mol% $Pd(OAc)_2$, 300 mol% AgOAc, PivOH (0eq, 2.5eq, 10eq) in 2-trifluoromethyltoluene **42** (5mL) was microwave heated at 120 ^{0}C for 1.5h. After evaporation of the solvent, the mixture was diluted with 40mL of water and extracted with three 60mL portions of ethyl acetate. The combined organic extracts were washed with two portions of 40mL of brine followed by two portions of 40mL of water and dried with anhydrous magnesium sulfate. After filtration, the solvent is removed at reduced pressure and crude product was purified by column chromatography (Hexane/Ethyl Acetate (14:1 *v/v*)) to give pure **43** and **44.**

PivOH	43:44
0 equiv	1.30:1
2.5 equiv	1.40:1
10 equiv	1.41:1

^{1}H-NMR (300 MHz, $CDCl_3$) 43: δ = 0.00 (s, 9H), 0.95 (t, ^3J = 9.00 Hz, 2H), 2.60 (s, 3H), 3.61 (t, ^3J = 9.00 Hz, 2H), 5.47 (s, 2H), 6.74 (s, 1H), 7.45 (d, ^3J = 6.00 Hz, 1H), 7.68 – 7.76 (m, 2H), 7.97 (s, 1H), 8.11 (dd, ^3J = 6.00 Hz, ^4J = 3.00 Hz, 1H), 8.50 (s, 1H)

^{1}H-NMR (300 MHz, $CDCl_3$) 44: δ = 0.00 (s, 9H), 0.95 (t, ^3J = 9.00 Hz, 2H), 2.60 (s, 3H), 3.61 (t, ^3J = 9.00 Hz, 2H), 5.52 (s, 2H), 6.77 (s, 1H), 7.29 – 7.73 (m, 4H), 7.97 (s, 1H), 8.11 (dd, ^3J = 6.00 Hz, ^4J = 3.00 Hz, 1H), 8.50 (s, 1H)


9.90
2.66
3.08
2.43
2.00
1.00
1.10
2.25
1.02
1.08
1.05
f1 (ppm)
0.00
2.60
3.58
3.61
5.47
6.74
7.28
7.45
7.47
7.68
7.71
7.73
7.76
7.97
8.10
8.13
8.50
CF3
CH3
TMS
O2N
43


9.62
2.90
3.08
2.87
2.59
1.00
4.29
0.97
0.93
8.52
8.52
7.29
6.77
5.52
3.61
3.58
2.60
1.28
0.94
0.00
f1 (ppm)
CH3
CF3
SEM
O2N
44

Computational Analysis

Indole Palladation Mechanism

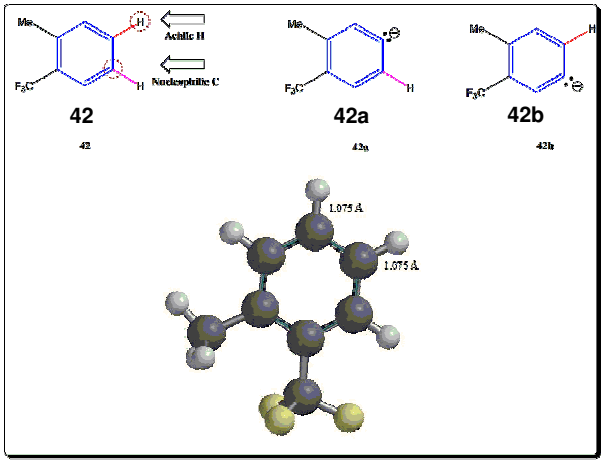
Density functional theory (DFT) calculations of the palladation of indole substrates were performed using the Gaussian 03 program. In all calculations, the spin-restricted method was employed. Wave function stability calculations were carried out to confirm that the calculated wave functions corresponded to the electronic ground state. The structures of all species were optimized using the B3LYP exchange-correlation functional with the mixed basis set (DZVP on Pd and TZVP on all other atoms). The Pd catalyst was modeled with two acetate ligands. Tight SCF convergence criteria (10−8 au) were used for all calculations. Harmonic frequency calculations with the analytic evaluation of force gradients (OPT = CalcAll) were used to determine the nature of the stationary points. Intrinsic reaction coordinate (IRC) calculations were used to confirm the reaction pathways through the CMD transition states. Free energies of species were evaluated at 298 K and 1 atm. Mayer bond orders were calculated using the AOMix program.

Computational Analysis of Arene 42

The computational analysis of substrate **42** and its anions were performed using Spartan'08 (wavefunction, Build 136) for Linux. Geometry optimizations were performed at the HF/6-31G* level, followed by subsequent single point energy calculations using B3LYP/6-31G* for computing the reliable electronic parameters. The lengths of C-H bonds *para* to the methyl group and trifluoromethyl group were computed to be identical (1.075 Å) and the computed molecular energies for trifluoromethyl benzene and its corresponding anions are listed in Table S1.

Entry	Energy (Kcal/mol)
42	-381902.79
42a	-381481.65
42b	-381480.98

Table S1. Molecular energies of trifluoromethyl benzene and anions



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