Supporting Information

for

C2-Alkylation of *N*-pyrimidylindole with vinylsilane via cobalt-catalyzed C–H bond activation

Zhenhua Ding and Naohiko Yoshikai*

Address: Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

Email: Naohiko Yoshikai - nyoshikai@ntu.edu.sg

* Corresponding author

Experimental details and characterization data of new compounds

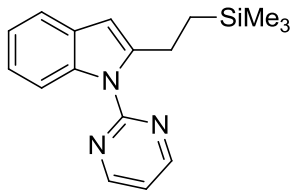
Contents

Materials and Methods

General. All reactions dealing with air or moisture-sensitive compounds were performed by standard Schlenk techniques in oven-dried reaction vessels under a nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AV-400 (400 MHz/100 MHz) NMR spectrometer. ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.0 ppm), respectively. Gas chromatographic (GC) analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and a capillary column, DB-5 (Agilent J&W, 0.25 mm i.d. x 30 m, 0.25 μm film thickness). High-resolution mass spectra (HRMS) were obtained with a Q-Tof Premier LC HR mass spectrometer.

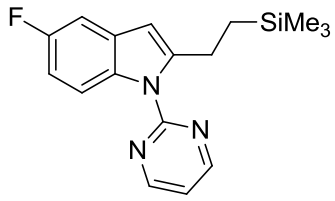
Materials. Unless otherwise noted, reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. THF was distilled over Na/benzophenone. Cyclohexylmagnesium bromide was prepared from bromocyclohexane and magnesium turnings in anhydrous THF and titrated before use. Sodium ethoxide was prepared from sodium and ethanol just before use. Anhydrous $CoBr_2$ (99%) was purchased from Aldrich. *N*-Pyrimidyl indoles were prepared according to the literature procedure [1,2].

C2-Alkylation of *N*-pyrimidyl indole with vinylsilane



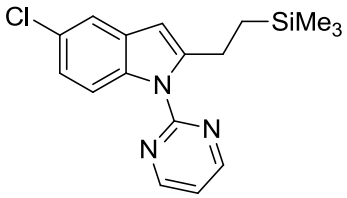
Typical Procedure: 1-(Pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3aa). In a Schlenk tube were placed 1-(pyrimidin-2-yl)-1*H*-indole (58.6 mg, 0.3 mmol), $CoBr_2$ (6.6 mg, 0.03 mmol), and bathocuproine (10.8 mg, 0.03 mmol), which were then dissolved in THF (1.3 mL). To the solution was added cyclohexylmagnesium bromide (0.60 M in THF, 0.3 mL, 0.18 mmol) at 0 °C. After stirring for 30 min at this temperature, vinyltrimethylsilane (66 μL, 0.45 mmol) was added. The reaction mixture was stirred at 60 °C for 12 h, and then quenched with saturated aqueous solution of NH_4Cl (1.5 mL). The resulting mixture was extracted with ethyl acetate (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude product by silica gel chromatography (eluent: hexane/EtOAc = 100/1) afforded the title compound as a colorless oil (61.2 mg, 69%). The 5 mmol scale reaction was performed according to a similar procedure by using a 100 mL Schlenk tube to afford the same product in 68% yield.

R_f 0.39 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, J = 4.8 Hz, 2 H), 8.24 (d, J = 8.0 Hz, 1 H), 7.54–7.52 (m, 1 H), 7.23–7.13 (m, 3 H), 6.50 (s, 1 H), 3.20–3.16 (m, 2 H), 0.86–0.82 (m, 2 H), 0.02 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 158.1, 145.0, 137.1, 129.4, 122.3, 121.7, 119.6, 117.0, 113.7, 105.1, 23.8, 16.5, −1.8; HRMS (ESI) Calcd for $C_{17}H_{21}N_3Si$ $[M + H]^+$ 296.1583, found 296.1584.

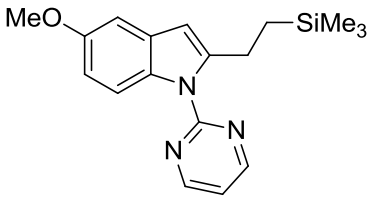


5-Fluoro-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3ba): 55% yield; colorless oil; R_f 0.37 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, J = 4.8 Hz, 2 H), 8.23–8.19 (m, 1 H), 7.18–7.14 (m, 2 H), 6.95–6.90 (m, 1 H), 6.45 (s, 1 H), 3.19–3.15 (m,

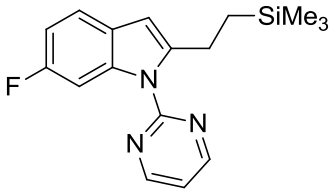
2 H), 0.85–0.81 (m, 2 H), 0.02 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9 (d, $^{1}J_{C\text{-}F}$ = 236 Hz), 158.2, 158.1, 146.8, 133.4, 130.1 (d, $^{3}J_{C\text{-}F}$ = 10.0 Hz), 117.1, 114.8 (d, $^{3}J_{C\text{-}F}$ = 9.1 Hz), 109.9 (d, $^{2}J_{C\text{-}F}$ = 24.8 Hz), 104.9, 104.8 (d, $^{2}J_{C\text{-}F}$ = 27.0 Hz), 24.1, 16.5, -1.8; HRMS (ESI) Calcd for $C_{17}H_{20}FN_3Si$ $[M + H]^+$ 314.1489, found 314.1491.



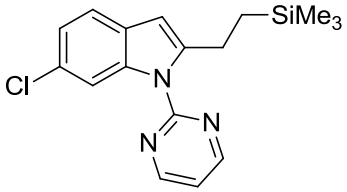
5-Chloro-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3ca): 39% yield; yellow oil; R_f 0.38 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.79 (d, *J* = 4.8 Hz, 2 H), 8.17 (d, *J* = 8.8 Hz, 1 H), 7.47 (d, *J* = 2.1 Hz, 1 H), 7.19–7.13 (m, 2 H), 6.43 (s, 1 H), 3.18–3.14 (m, 2 H), 0.84–0.80 (m, 2 H), 0.01 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.14, 158.09, 146.5, 135.4, 130.5, 127.1, 122.3, 119.1, 117.2, 114.9, 104.5, 24.0, 16.4, −1.8; HRMS (ESI) Calcd for $C_{17}H_{20}ClN_3Si$ $[M + H]^+$ 330.1193, found 330.1190.



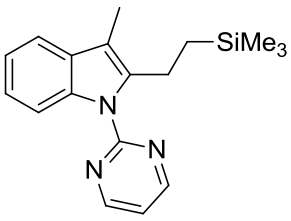
5-Methoxy-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3da): 62% yield; colorless oil; R_f 0.32 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.75 (d, *J* = 4.8 Hz, 2 H), 8.22 (d, *J* = 9.0 Hz, 1 H), 7.09 (t, *J* = 4.8 Hz, 1 H), 7.01 (d, *J* = 2.5 Hz, 1 H), 6.87–6.84 (m, 1 H), 6.43 (s, 1 H), 3.87 (s, 3 H), 3.21–3.17 (m, 2 H), 0.87–0.83 (m, 2 H), 0.03 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 157.9, 155.3, 145.8, 132.0, 130.1, 116.6, 114.9, 111.1, 105.1, 102.2, 55.7, 24.1, 16.6, −1.8; HRMS (ESI) Calcd for $C_{18}H_{23}N_3OSi$ $[M + H]^+$ 326.1689, found 326.1690.



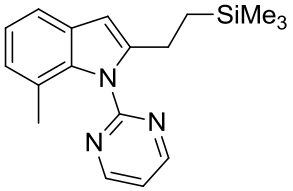
6-Fluoro-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3ea): 52% yield; colorless oil; R_f 0.47 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, J = 4.8 Hz, 2 H), 8.08–8.04 (m, 1 H), 7.44–40 (m, 1 H), 7.15 (t, J = 4.8 Hz, 1 H), 6.97–6.92 (m, 1 H), 6.46 (s, 1 H), 3.19–3.15 (m, 2 H), 0.85–0.81 (m, 2 H), 0.02 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0 (d, $^1J_{C\text{-}F}$ = 235 Hz), 158.2, 158.1, 145.5 (d, $^4J_{C\text{-}F}$ = 3.8 Hz), 137.1 (d, $^3J_{C\text{-}F}$ = 12.5 Hz), 125.6, 119.9 (d, $^3J_{C\text{-}F}$ = 9.9 Hz), 117.1, 109.8 (d, $^2J_{C\text{-}F}$ = 24.0 Hz), 104.8, 101.3 (d, $^2J_{C\text{-}F}$ = 28.4 Hz), 24.0, 16.5, −1.8; HRMS (ESI) Calcd for $C_{17}H_{20}FN_3Si$ $[M + H]^+$ 314.1489, found 314.1494.



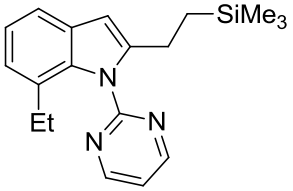
6-Chloro-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3fa): 43% yield; colorless oil; R_f 0.44 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (d, J = 4.8 Hz, 2 H), 8.29 (s, 1 H), 7.41 (d, J = 8.3 Hz, 1 H), 7.20–7.13 (m, 2 H), 6.45 (s, 1 H), 3.18–3.13 (m, 2 H), 0.83–0.79 (m, 2 H), 0.01 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 158.1, 145.9, 137.4, 128.1, 127.9, 122.2, 120.2, 117.3, 114.1, 104.8, 23.9, 16.5, −1.8; HRMS (ESI) Calcd for $C_{17}H_{20}ClN_3Si$ $[M + H]^+$ 330.1193, found 330.1192.



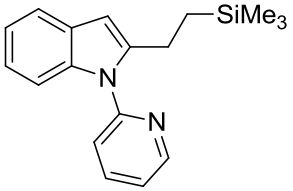
3-Methyl-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3ga): 42% yield; white solid; R_f 0.42 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77 (d, J = 4.8 Hz, 2 H), 8.26–8.24 (m, 1 H), 7.50–7.48 (m, 1 H), 7.22–7.20 (m, 2 H), 7.11 (t, J = 4.8 Hz, 1 H), 3.18–3.14 (m, 2 H), 2.29 (s, 3 H), 0.73–0.69 (m, 2 H), 0.01 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 158.0, 139.9, 136.1, 130.6, 122.5, 121.4, 117.8, 116.6, 113.5, 111.6, 20.4, 17.3, 8.7, −1.9; HRMS (ESI) Calcd for $C_{18}H_{23}N_3Si$ $[M + H]^+$ 310.1740, found 310.1743.



7-Methyl-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3ha): 71% yield; colorless oil; R_f 0.19 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (d, *J* = 4.8 Hz, 2 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 7.28 (t, *J* = 4.8 Hz, 1 H), 7.09 (t, *J* = 7.4 Hz, 1 H), 6.95 (d, *J* = 7.2 Hz, 1 H), 6.46 (s, 1 H), 2.74–2.69 (m, 2 H), 1.96 (s, 3 H), 0.82–0.78 (m, 2 H), −0.02 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 158.3, 144.9, 136.6, 129.6, 124.7, 121.4, 121.0, 119.0, 117.8, 102.3, 21.8, 19.9, 15.8, −1.9; HRMS (ESI) Calcd for $C_{18}H_{23}N_3Si$ $[M + H]^+$ 310.1740, found 310.1738.

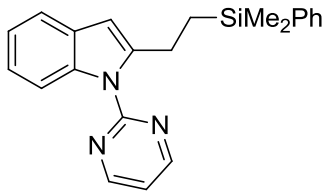


7-Ethyl-1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3ia): 58% yield; colorless oil; R_f 0.27 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (d, *J* = 4.8 Hz, 2 H), 7.44 (d, *J* = 6.9 Hz, 1 H), 7.30 (t, *J* = 4.8 Hz, 1 H), 7.13 (t, *J* = 7.5 Hz, 1 H), 7.02 (d, *J* = 7.3 Hz, 1 H), 6.47 (s, 1 H), 2.70–2.65 (m, 2 H), 2.30 (q, *J* = 7.5 Hz, 2 H), 0.98 (t, *J* = 7.5 Hz, 3 H), 0.81–0.76 (m, 2 H), −0.04 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 158.3, 145.1, 136.0, 129.9, 127.8, 122.5, 121.2, 119.2, 117.9, 102.5, 25.7, 21.9, 15.8, 13.9, −1.9; HRMS (ESI) Calcd for $C_{19}H_{25}N_3Si$ $[M + H]^+$ 324.1896, found 324.1892.

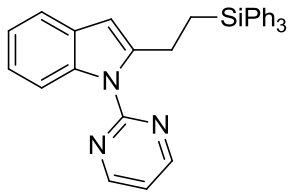


1-(Pyridin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (3ka): 80% yield; colorless oil; R_f 0.42 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69–8.67 (m, 1 H), 7.91–7.87 (m, 1 H), 7.62–7.60 (m, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.38–7.31 (m, 2 H), 7.17–7.14 (m, 2 H), 6.50

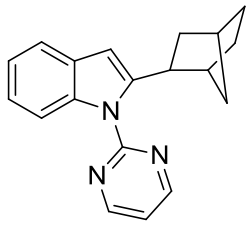
(s, 1 H), 2.92–2.88 (m, 2 H), 0.82–0.78 (m, 2 H), −0.02 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.6, 149.5, 144.2, 138.2, 137.3, 128.6, 121.9, 121.5, 120.9, 120.5, 119.9, 109.9, 101.7, 21.9, 15.9, −1.9; HRMS (ESI) Calcd for $C_{18}H_{22}N_2Si$ $[M + H]^+$ 295.1631, found 295.1631.



2-(2-(Dimethyl(phenyl)silyl)ethyl)-1-(pyrimidin-2-yl)-1*H*-indole (3ab): 50% yield; colorless oil; R_f 0.33 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (d, J = 4.8 Hz, 2 H), 8.29 (d, J = 8.0 Hz, 1 H), 7.57–7.55 (m, 3 H), 7.42–7.39 (m, 3 H), 7.26–7.22 (m, 2 H), 7.09 (t, J = 4.8 Hz, 1 H), 6.52 (s, 1 H), 3.27–3.23 (m, 2 H), 1.16–1.12 (m, 2 H), 0.34 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 158.0, 144.7, 139.0, 137.0, 133.6, 129.3, 128.9, 127.7, 122.4, 121.7, 119.6, 116.9, 113.8, 105.2, 23.9, 15.9, −3.2; HRMS (ESI) Calcd for $C_{22}H_{23}N_3Si$ $[M + H]^+$ 358.1740, found 358.1738.

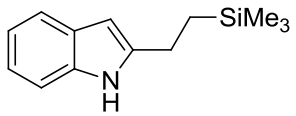


1-(Pyrimidin-2-yl)-2-(2-(triphenylsilyl)ethyl)-1*H*-indole (3ac): 31% yield; white solid; R_f 0.25 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, J = 4.8 Hz, 2 H), 8.36–8.34 (m, 1 H), 7.64–7.57 (m, 7 H), 7.50–7.41 (m, 9 H), 7.28–7.24 (m, 2 H), 7.07 (t, J = 4.8 Hz, 1 H), 6.58 (s, 1 H), 3.45–3.41 (m, 2 H), 1.84–1.80 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 157.9, 144.6, 137.0, 135.7, 134.8, 129.5, 129.3, 127.9, 122.5, 121.8, 119.7, 116.8, 113.9, 105.3, 24.1, 13.8; HRMS (ESI) Calcd for $C_{32}H_{27}N_3Si$ $[M + H]^+$ 482.2053, found 482.2051.



2-(Bicyclo[2.2.1]heptan-2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (3ad): 30% yield; colorless oil; R_f 0.33 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (d, J = 4.8 Hz, 2 H), 8.08–8.06 (m, 1 H), 7.56–7.53 (m, 1 H), 7.21–7.15 (m, 3 H), 6.49 (s, 1 H), 3.71–3.67 (m, 1 H), 2.38–2.29 (m, 2 H), 1.65–1.63 (m, 1 H), 1.58–1.53 (m, 4 H), 1.38–1.34 (m, 1 H), 1.27–1.24 (m, 1 H), 1.17–1.15 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 158.2, 146.9, 137.2, 129.1, 122.3, 121.5, 119.8, 117.3, 112.9, 103.3, 42.3, 40.6, 38.1, 36.8, 36.1, 29.7, 28.9; HRMS (ESI) Calcd for $C_{19}H_{19}N_3$ $[M + H]^+$ 290.1657, found 290.1655.

Removal of the pyrimidyl group



2-(2-(Trimethylsilyl)ethyl)-1*H*-indole (4aa): A mixture of 1-(pyrimidin-2-yl)-2-(2-(trimethylsilyl)ethyl)-1*H*-indole (**3aa**, 886 mg, 3 mmol) and freshly prepared sodium ethoxide (408 mg, 6 mmol) in DMSO (5 mL) was stirred at 100 ºC under nitrogen atmosphere for 20 h. After cooling to ambient temperature, the reaction mixture was extracted with EtOAc (2 × 20 mL), and the combined organic phase was dried over Na_2SO_4. After filtration and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel (hexane/EtOAc = 50/1) to yield the title product (554 mg, 85%) as a yellow solid.

R_f 0.38 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (brs, 1 H), 7.53 (d, *J* = 7.6 Hz, 1 H), 7.29 (d, *J* = 7.2 Hz, 1 H), 7.14–7.05 (m, 2 H), 6.25 (s, 1 H), 2.80–2.76 (m, 2 H), 1.01–0.96 (m, 2 H), 0.06 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 135.9, 128.8, 120.9, 119.7, 119.5, 110.2, 98.8, 22.5, 15.9, –1.8; HRMS (ESI) Calcd for $C_{13}H_{19}NSi$ $[M + H]^+$ 218.1365, found 218.1363

References

1. Ackermann, L.; Lygin, A. V. *Org. Lett.* **2011**, *13*, 3332–3335.

2. Ding, Z.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 4698–4701.

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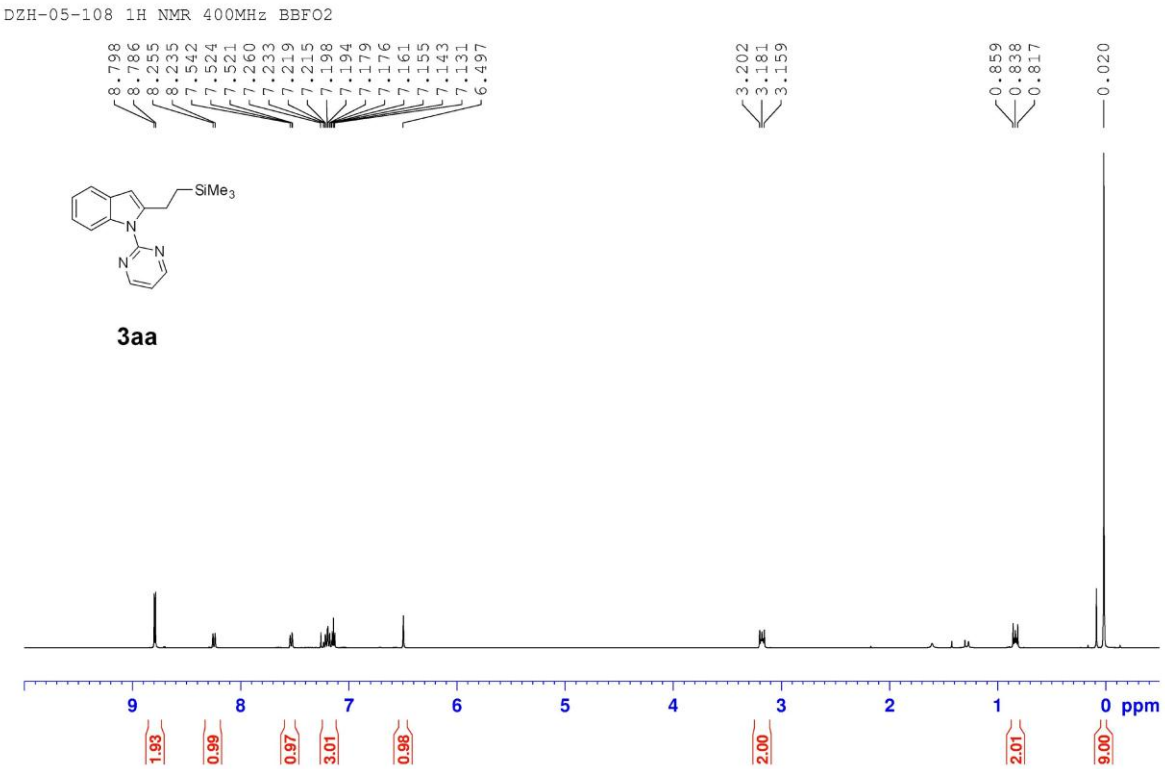
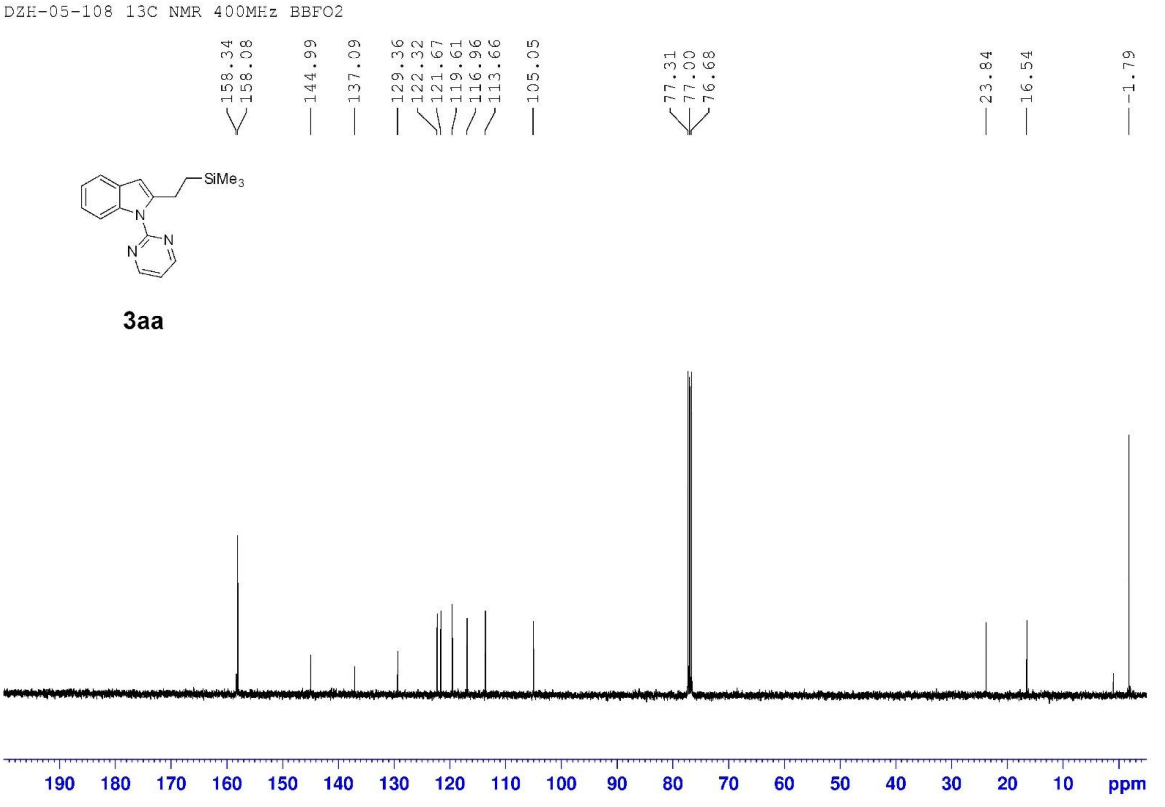
^{1}H and ^{13}C NMR spectra

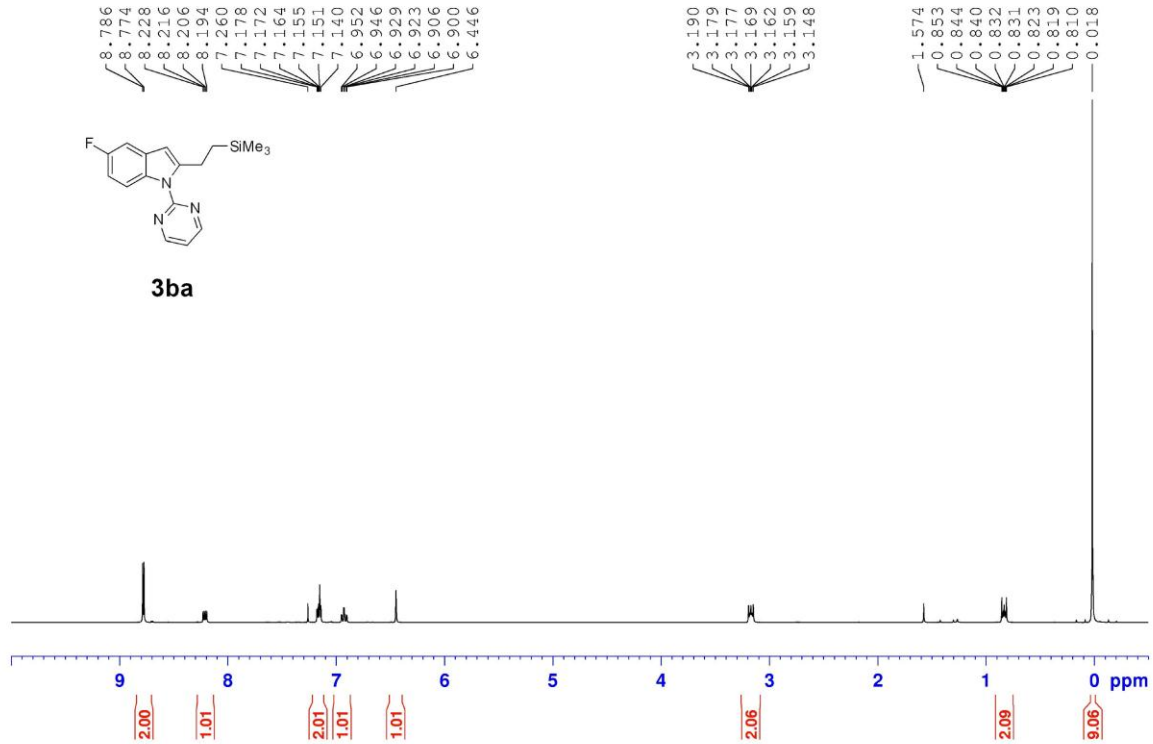


3aa



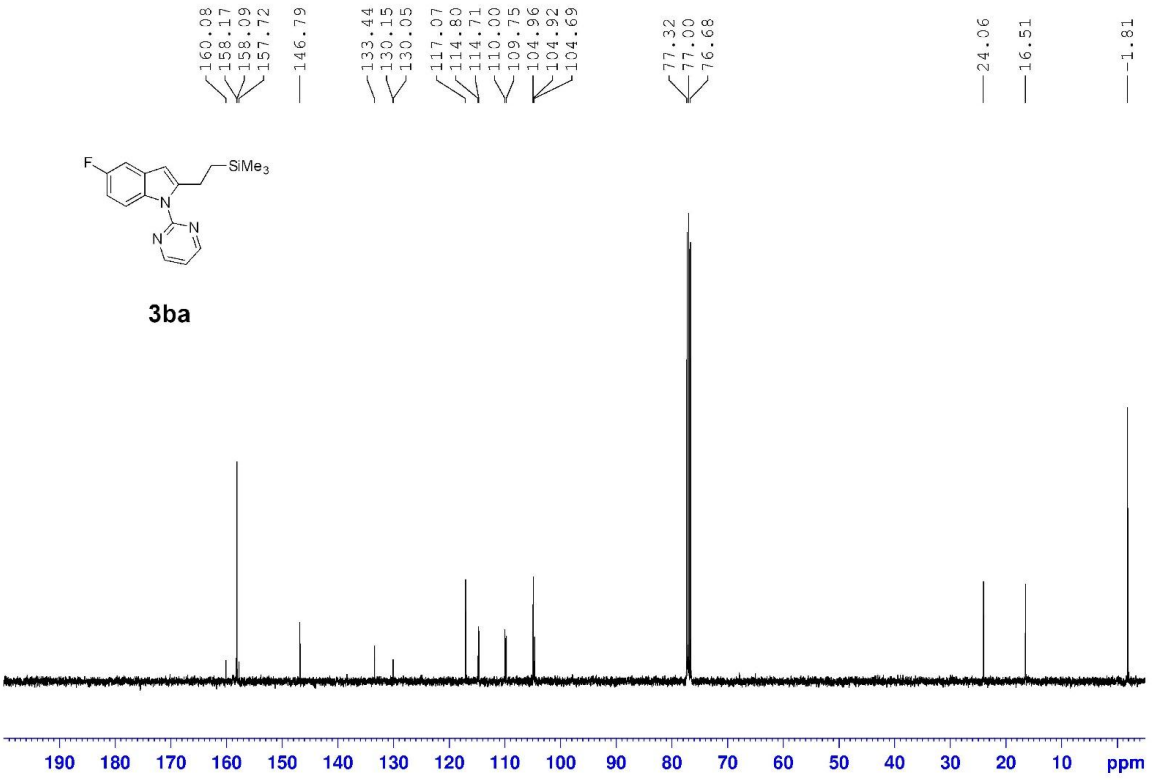
3aa

DZH-05-095 1H NMR CDCl3 BBOF1 400MHz



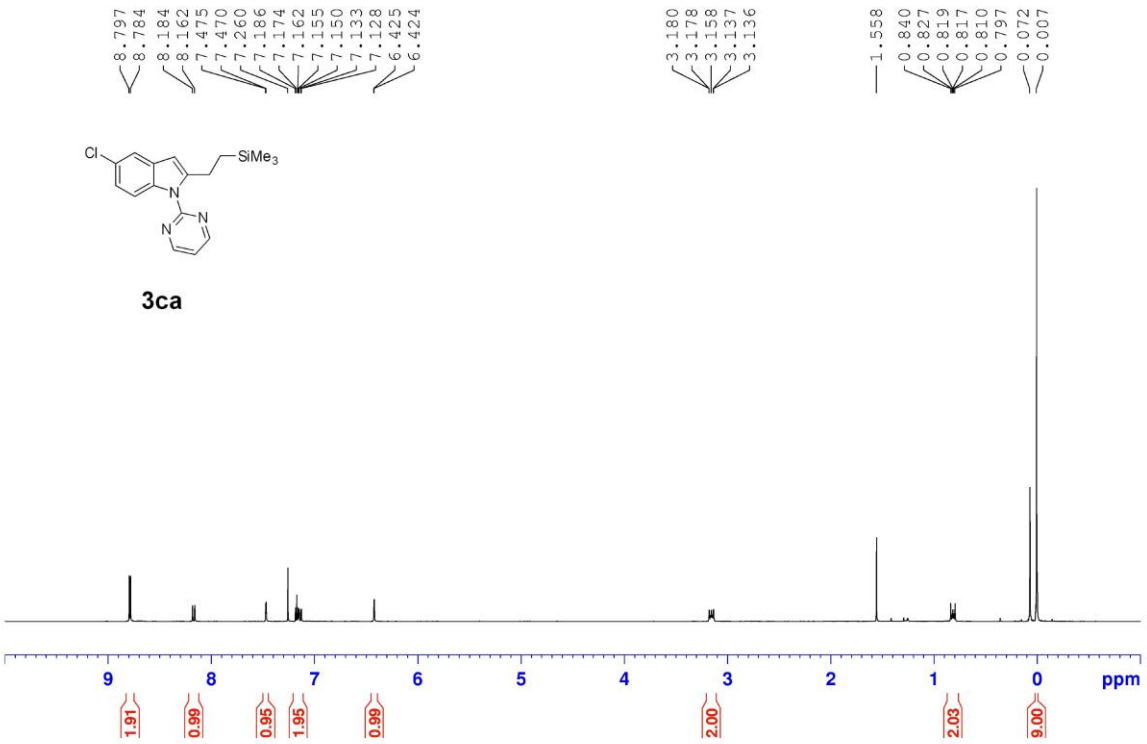
3ba

DZH-05-095 13C NMR CDCl3 BBOF1 400MHz



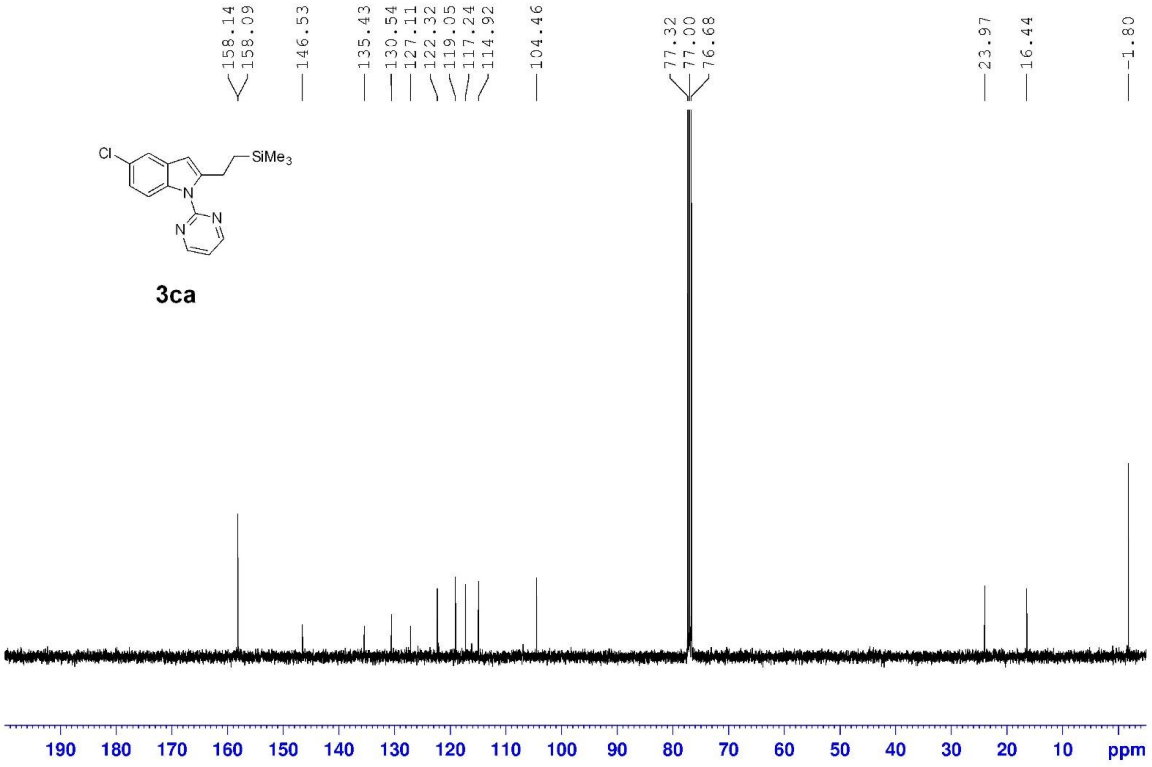
3ba

DZH-05-119 1H NMR CDCl3 BBOF1 400MHz



3ca

DZH-05-119 13C NMR CDCl3 BBOF1 400MHz



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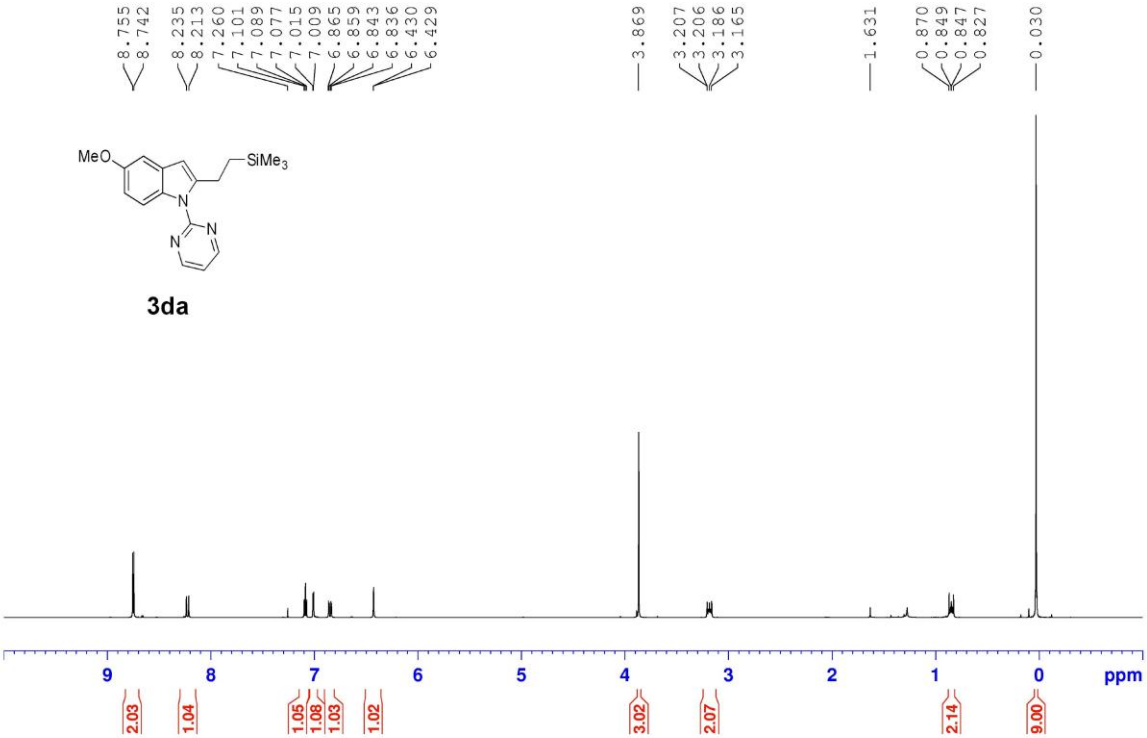
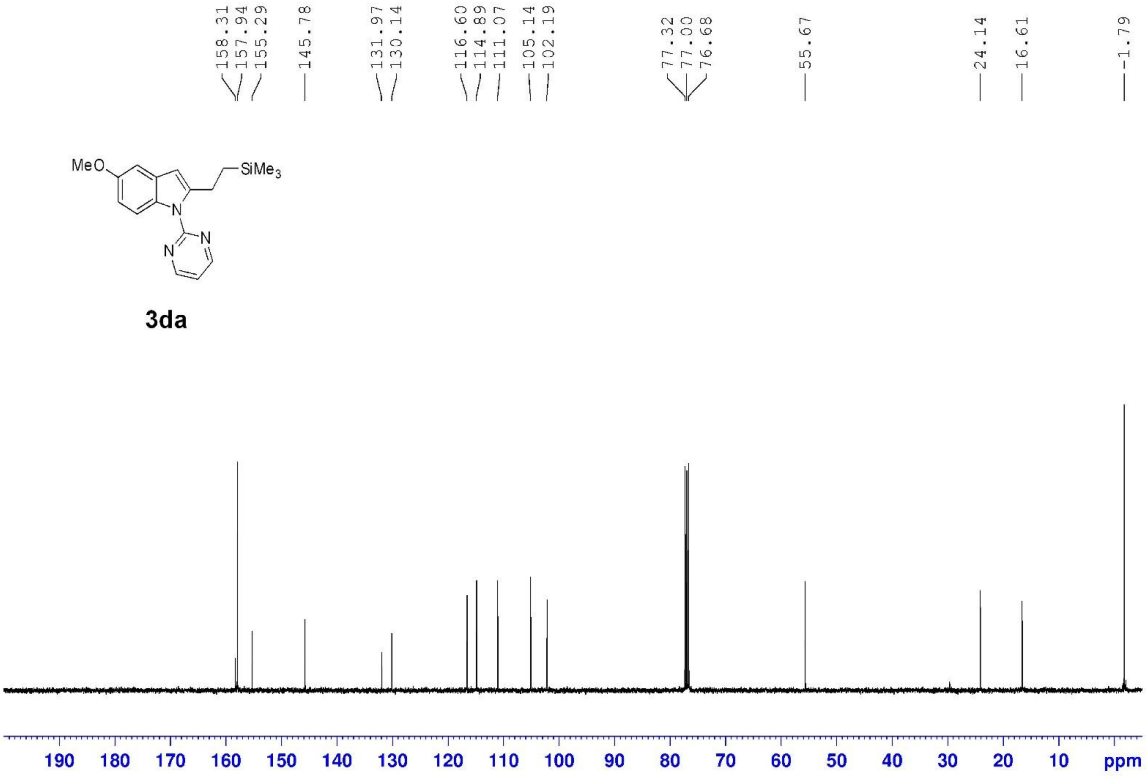
DZH-05-097-2 1H NMR CDCl3 BBOF1 400MHz



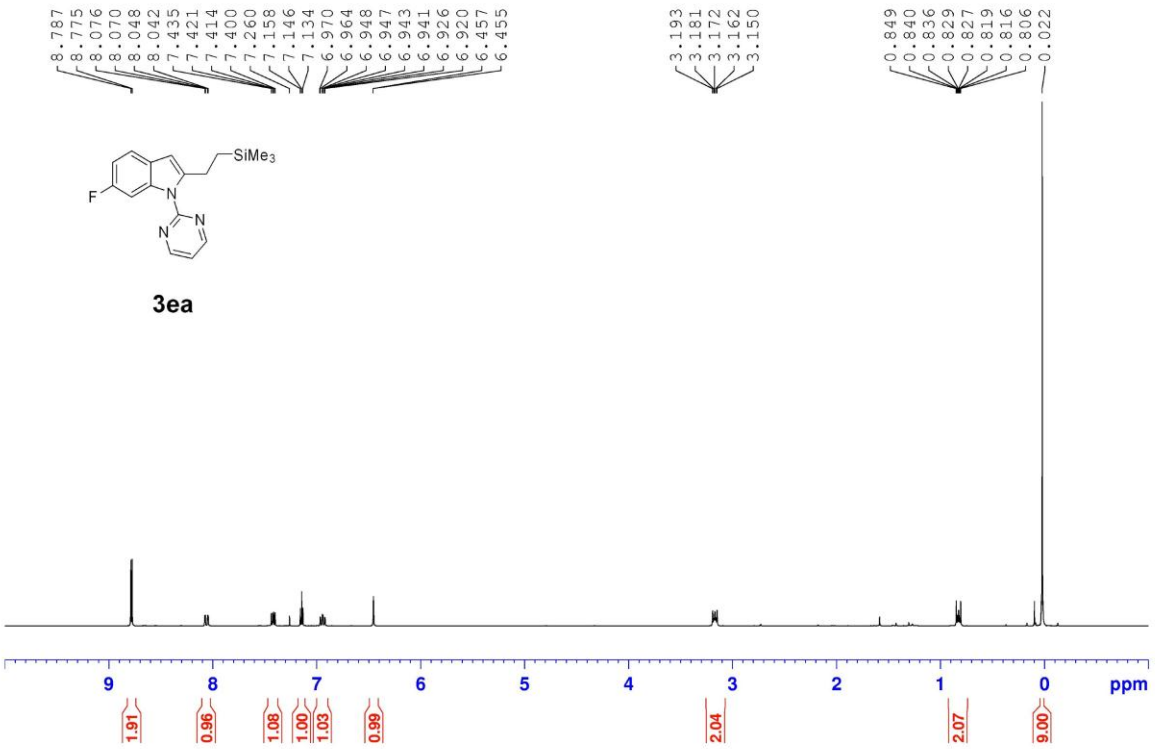
3da

DZH-05-097-2 13C NMR CDCl3 BBOF1 400MHz



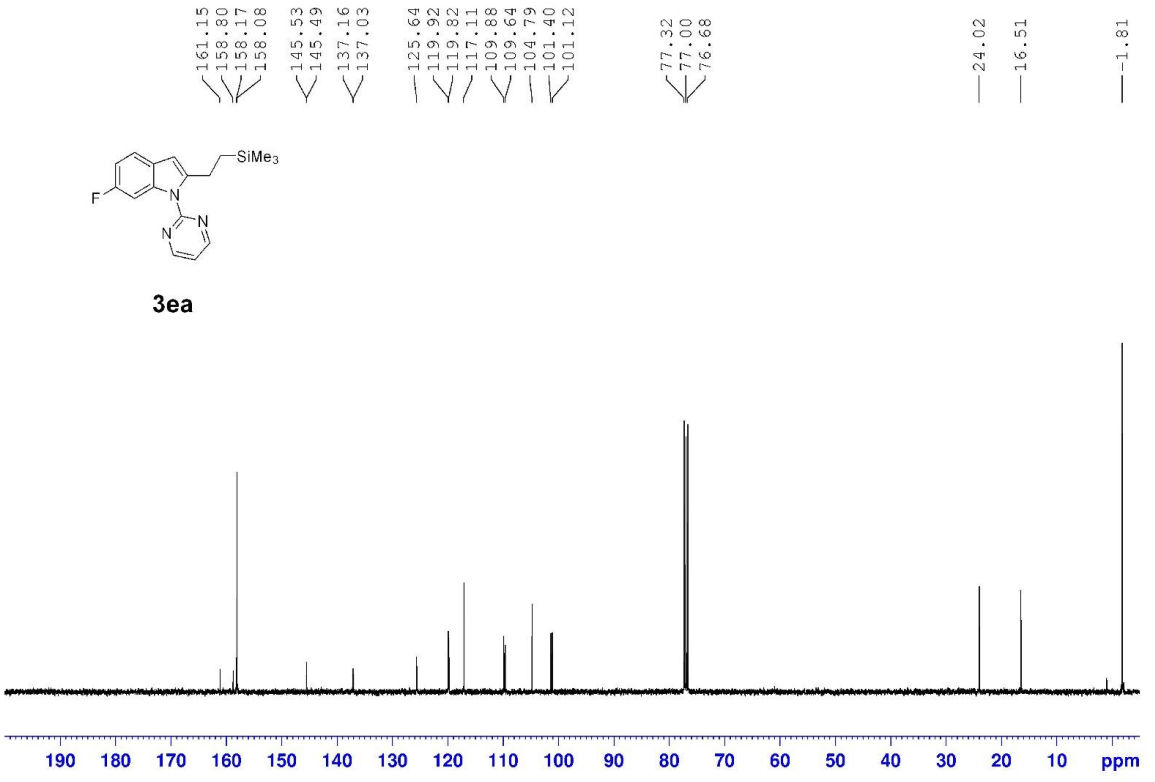
3da

DZH-05-112 1H NMR CDCl3 BBOF1 400MHz



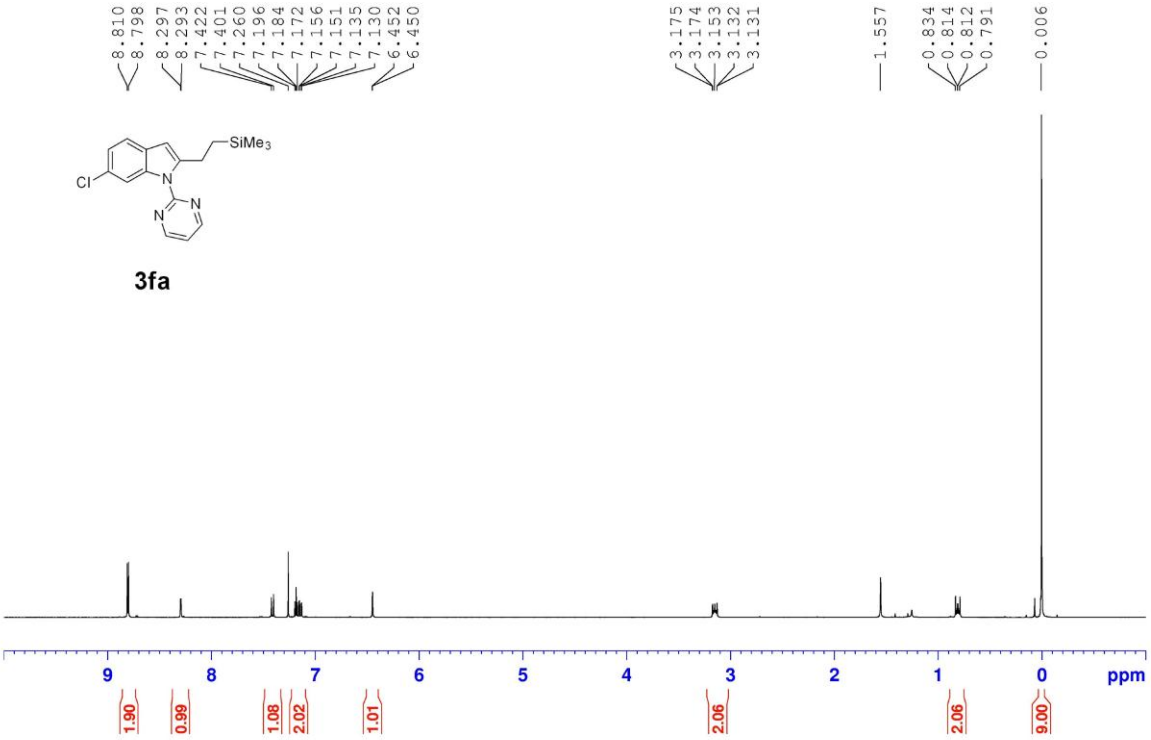
3ea

DZH-05-112 13C NMR CDCl3 BBOF1 400MHz



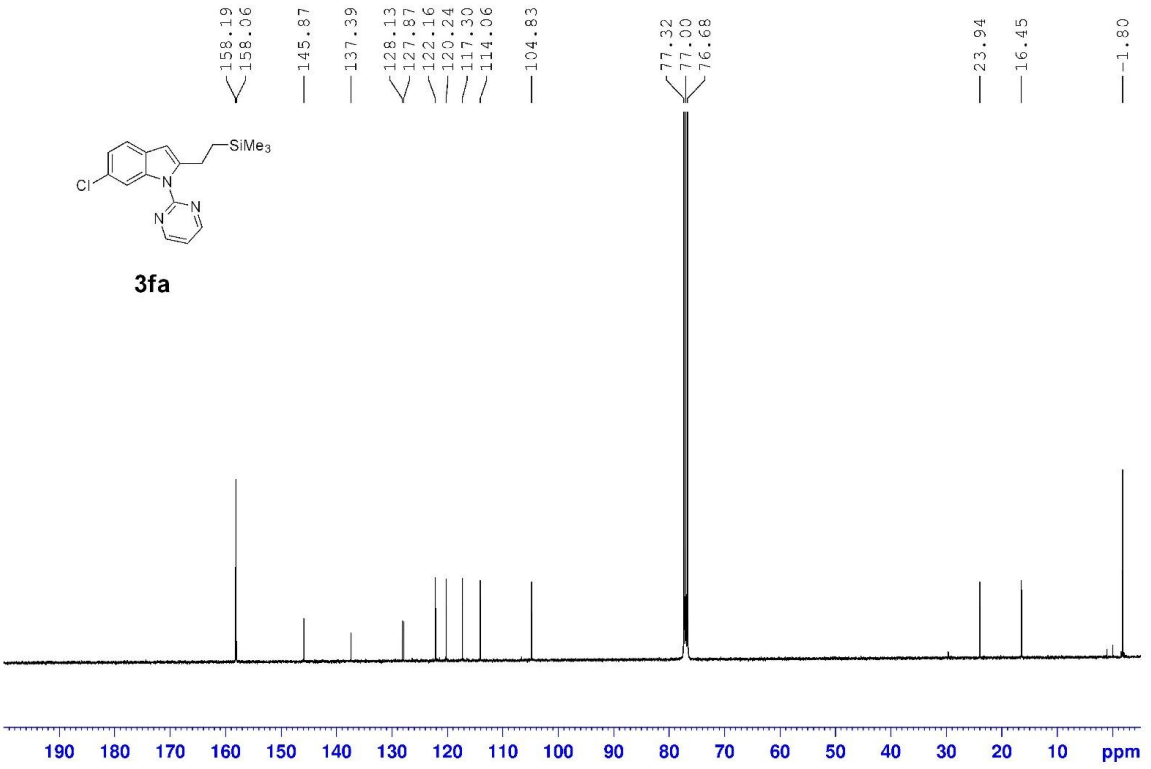
3ea

DZH-05-098 1H NMR CDCl3 BBOF1 400MHz



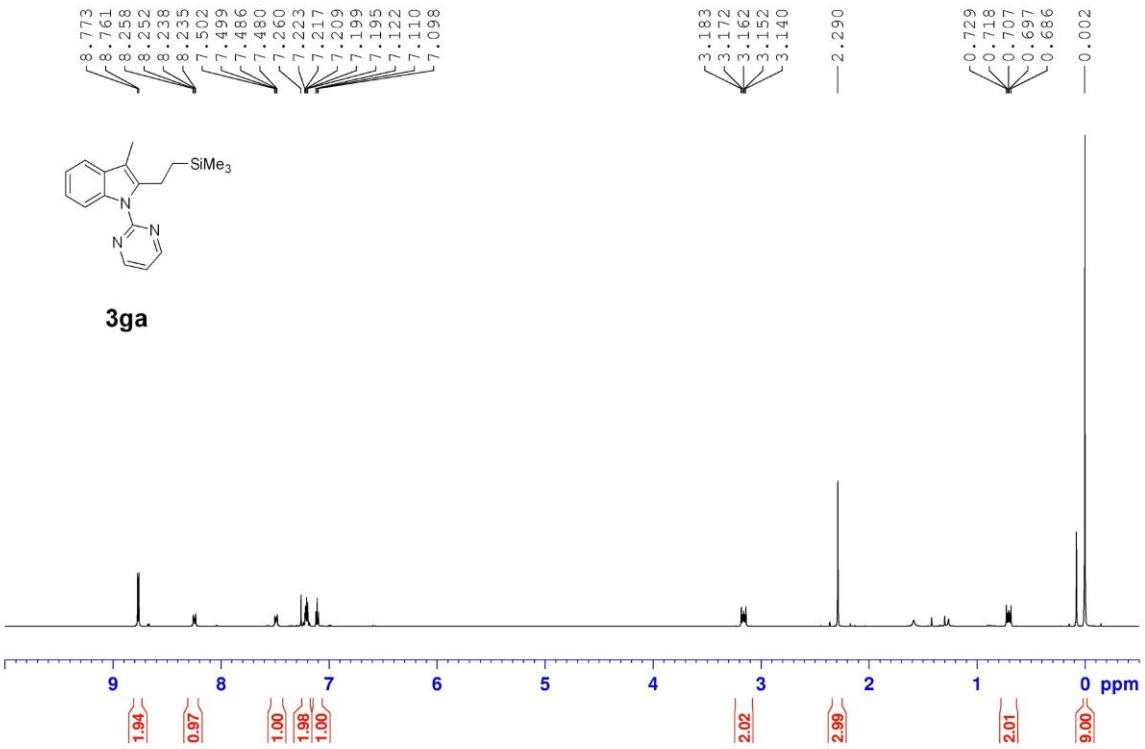
3fa

DZH-05-098 13C NMR CDCl3 BBOF1 400MHz



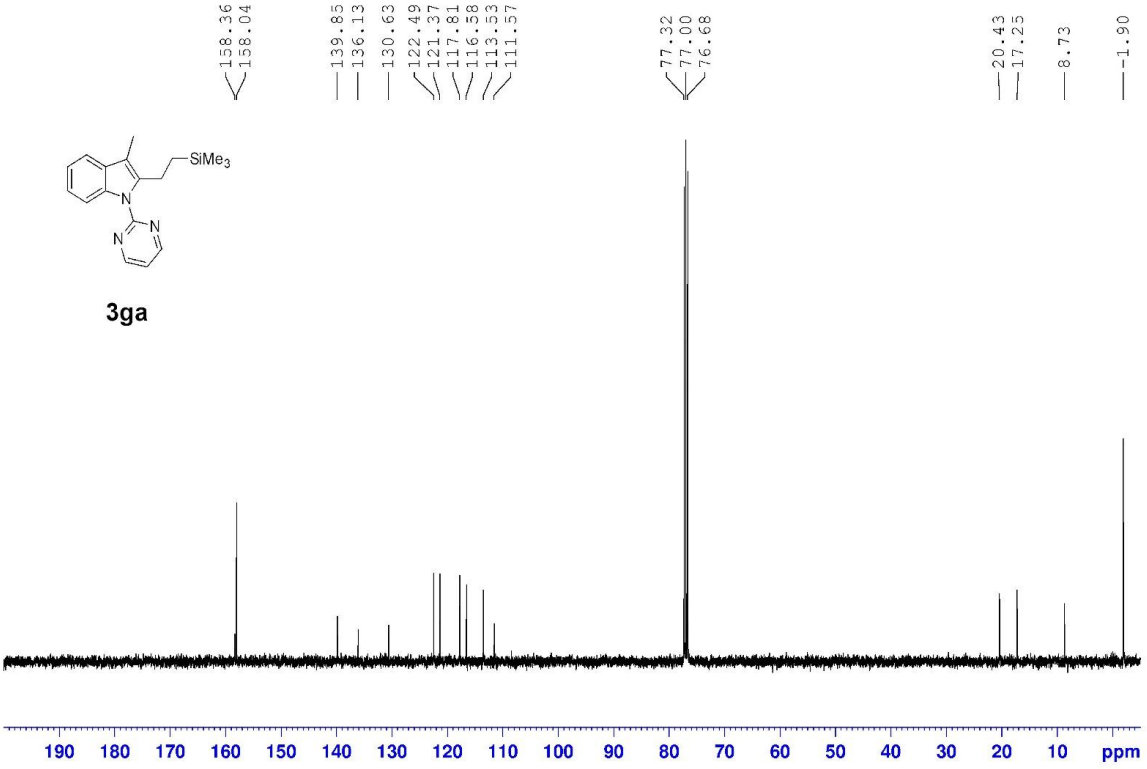
3fa

DZH-05-109 1H NMR 400MHz BBFO2



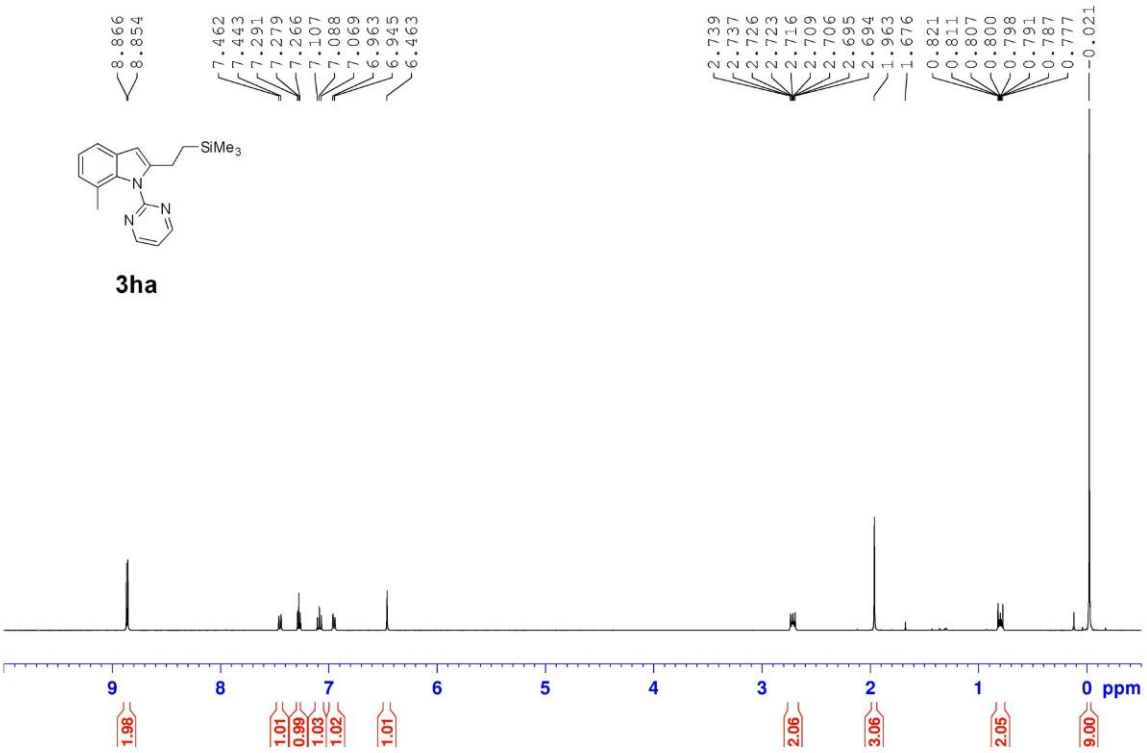
3ga

DZH-05-109 13C NMR CDCl3 BBOF1 400MHz



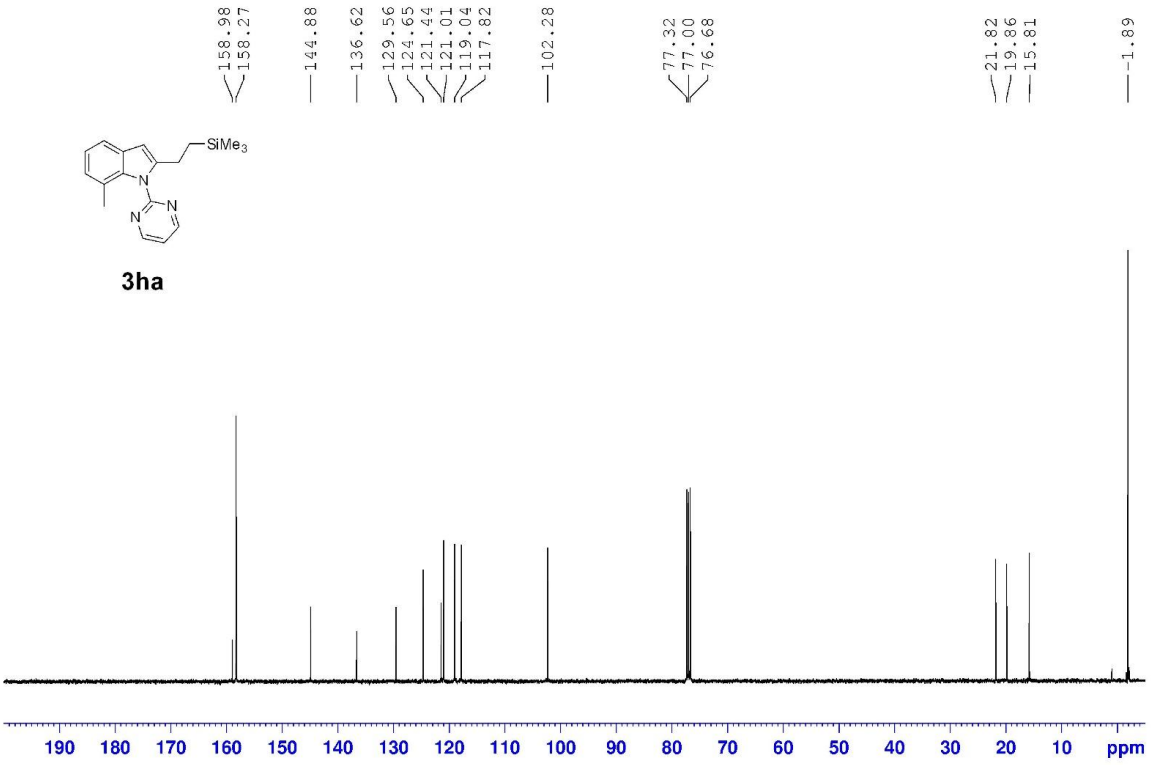
3ga

DZH-05-128 1H NMR CDCl3 BBOF1 400MHz



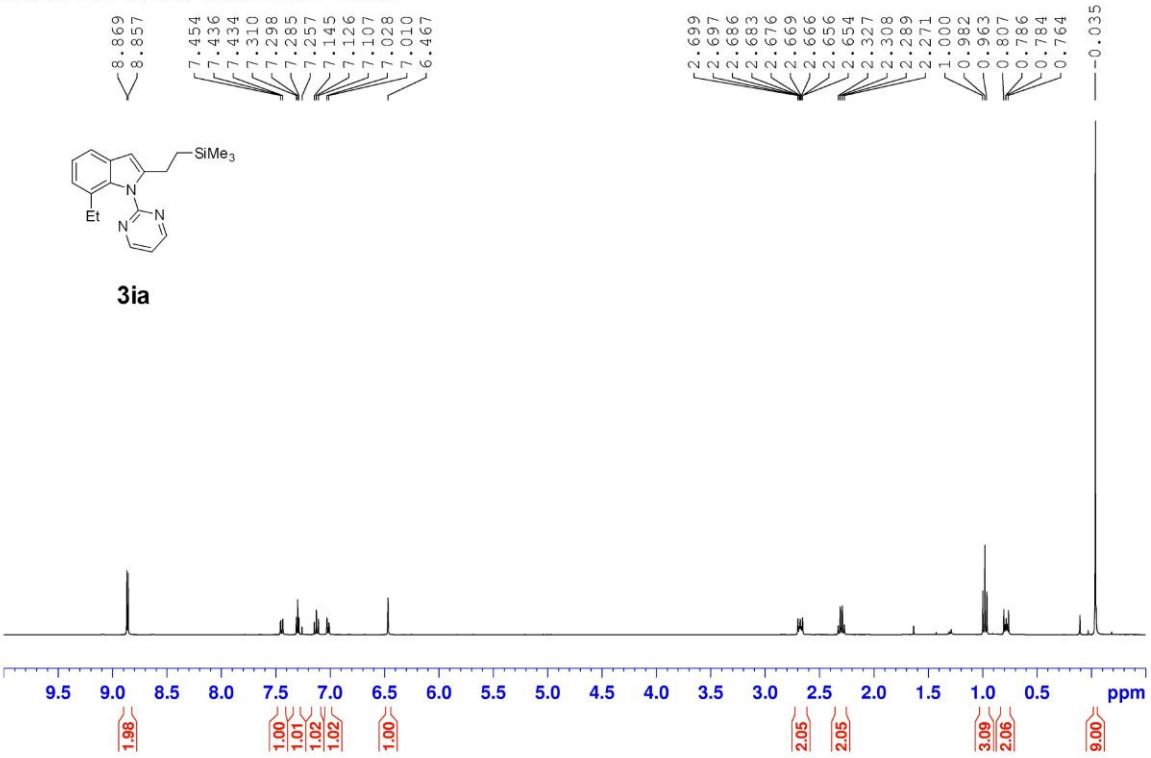
3ha

DZH-05-128 13C NMR CDCl3 BBOF1 400MHz



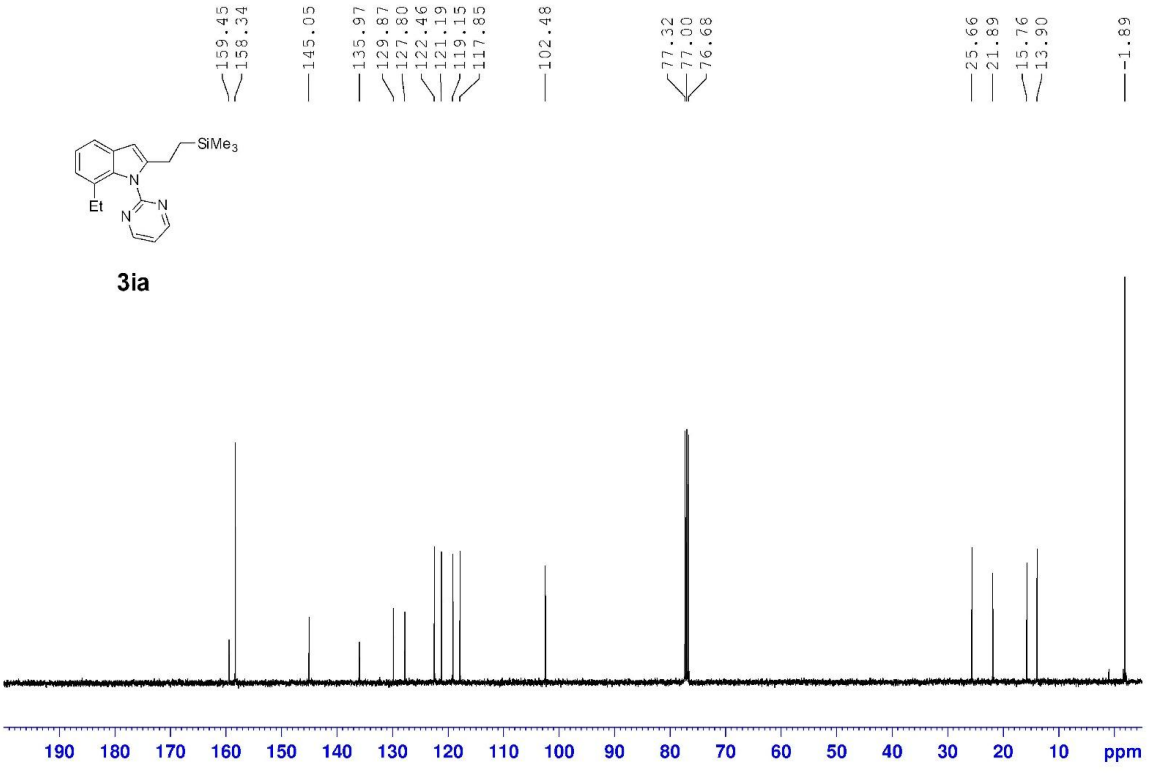
3ha

DZH-05-117 1H NMR CDCl3 BBOF1 400MHz



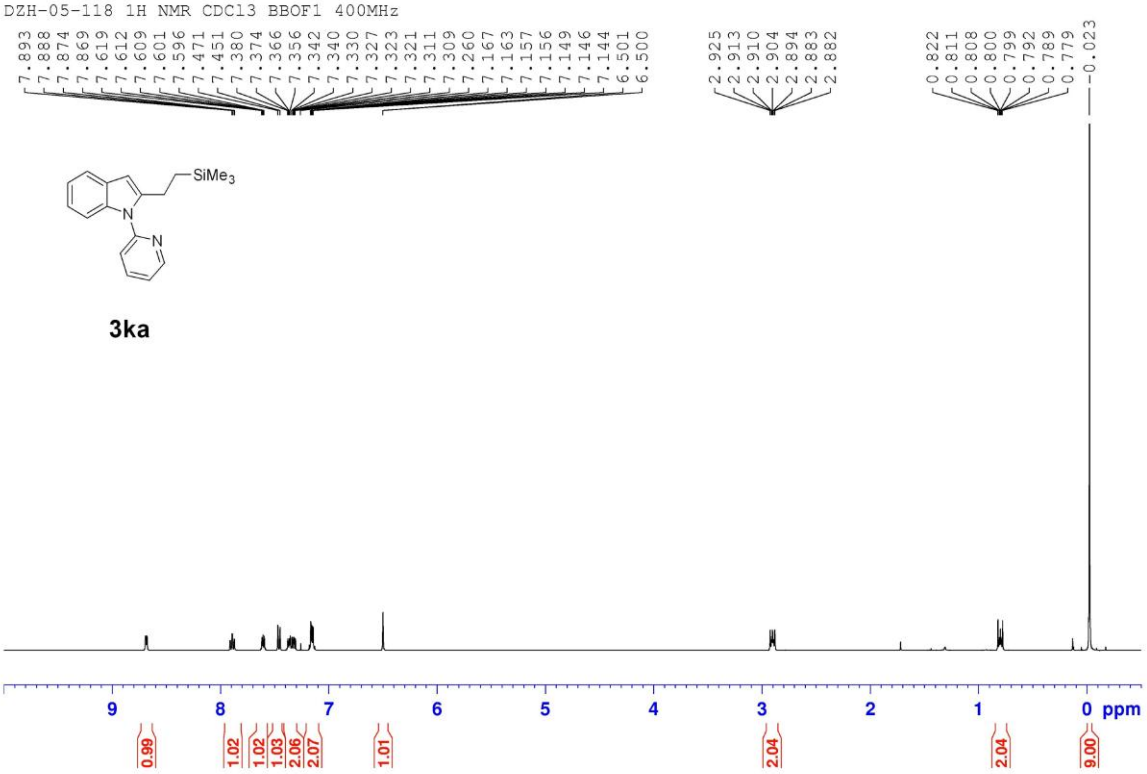
3ia

DZH-05-117 13C NMR CDCl3 BBOF1 400MHz



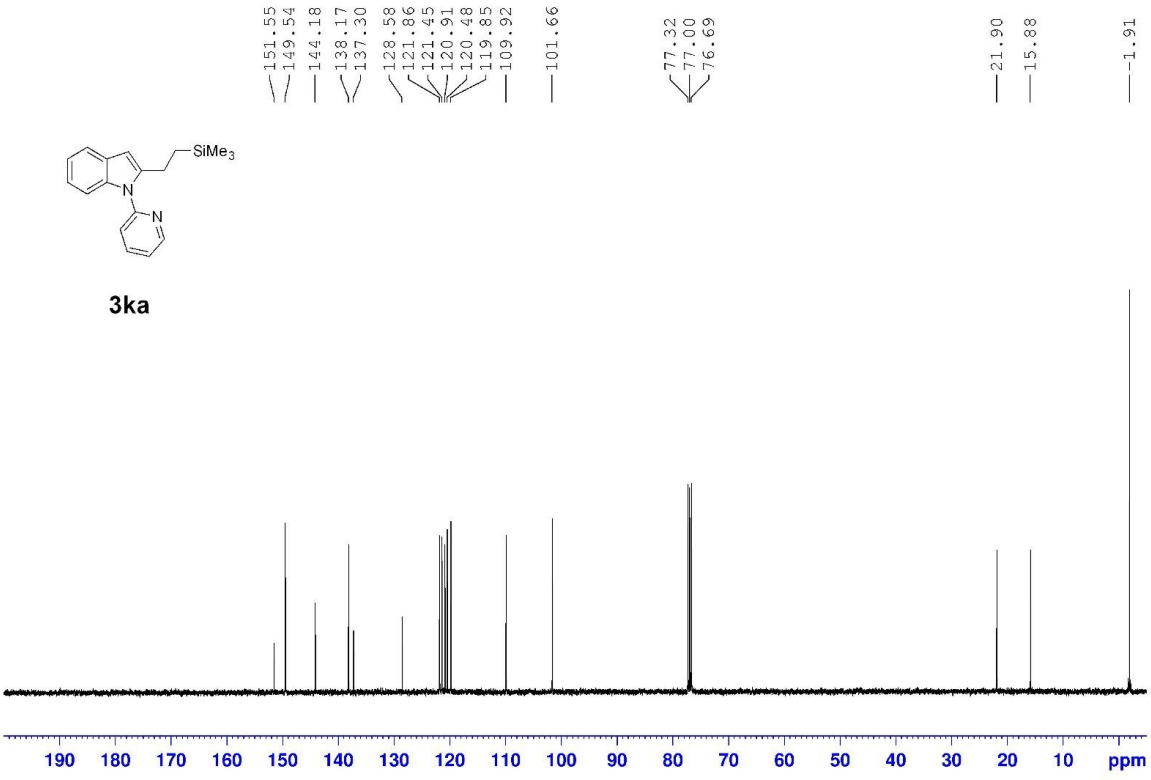
3ia

DZH-05-118 1H NMR CDCl3 BBOF1 400MHz



3ka

DZH-05-118 13C NMR CDCl3 BBOF1 400MHz



3ka

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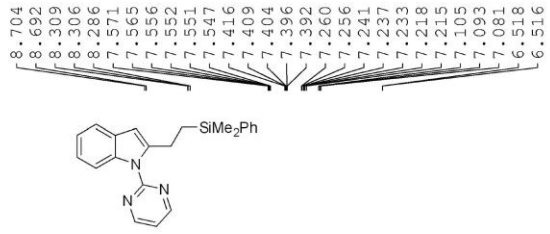
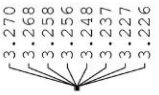
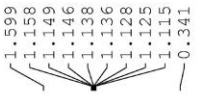
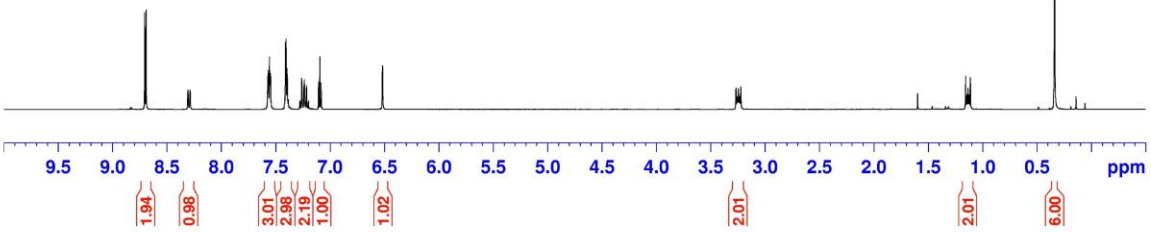


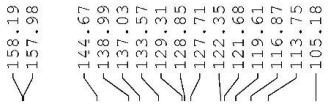


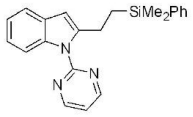


3ab

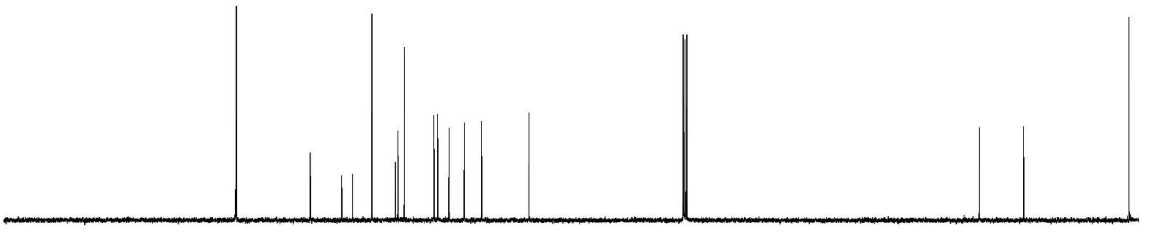


DZH-05-129 13C NMR CDCl3 BBOF1 400MHz





3ab



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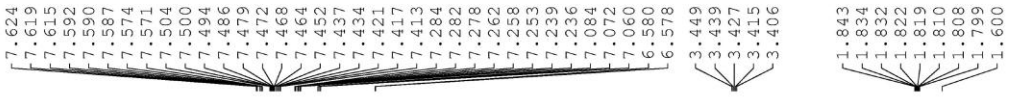
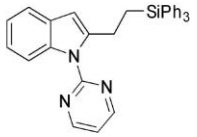
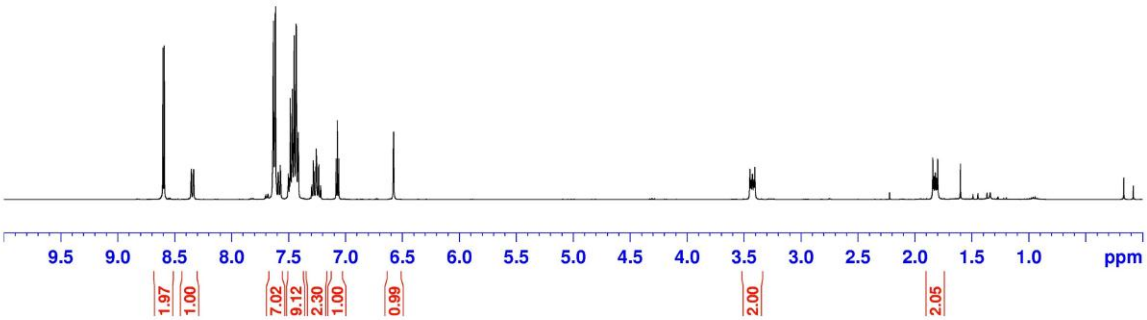




3ac



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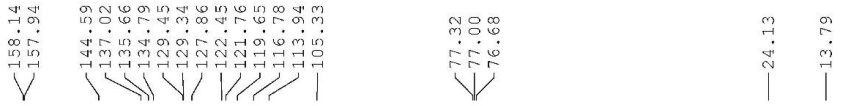

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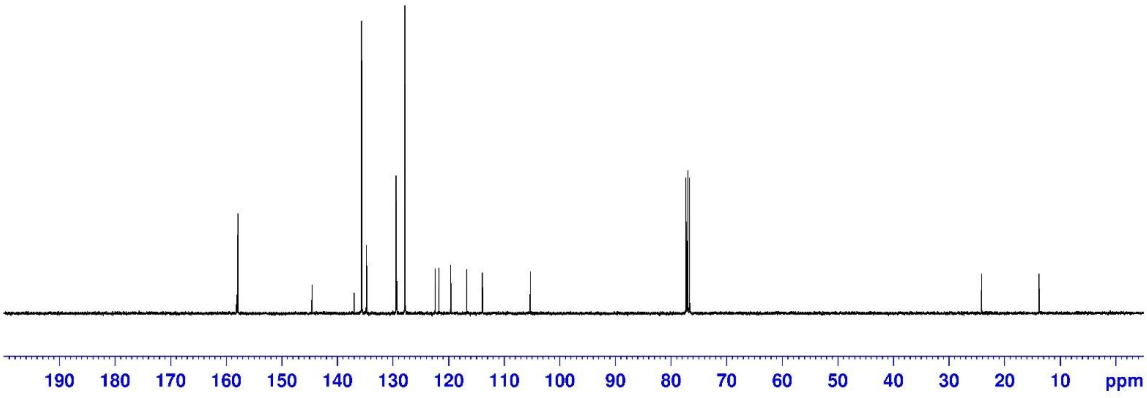

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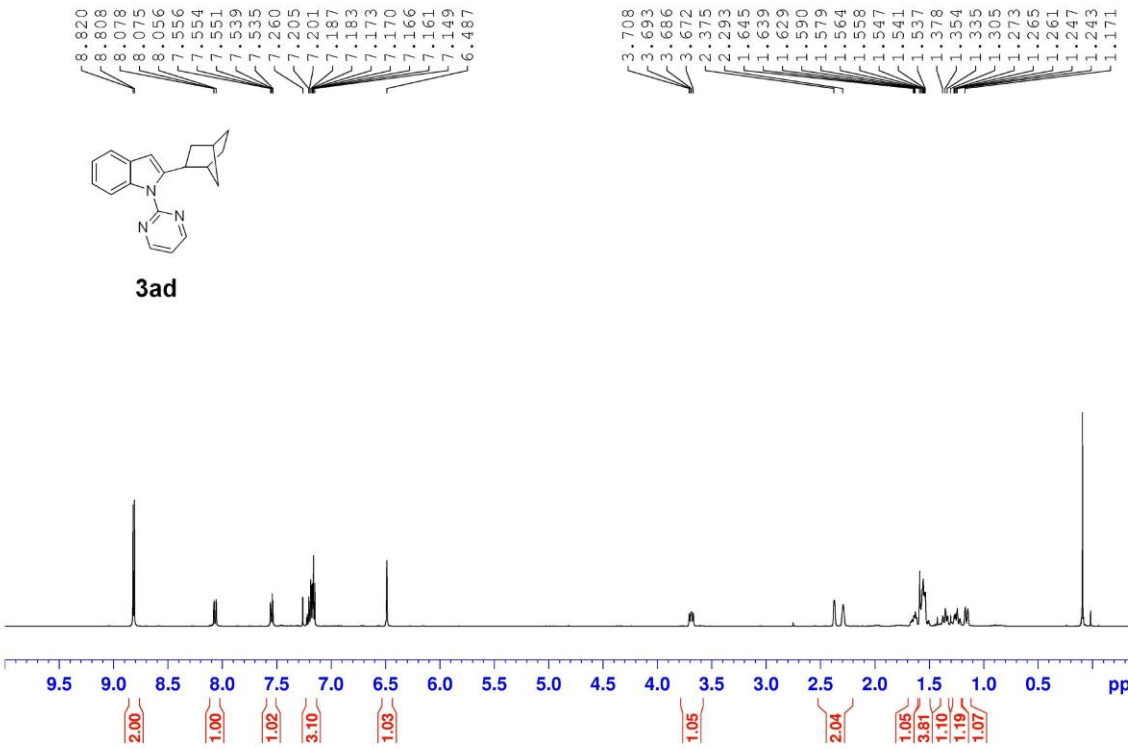
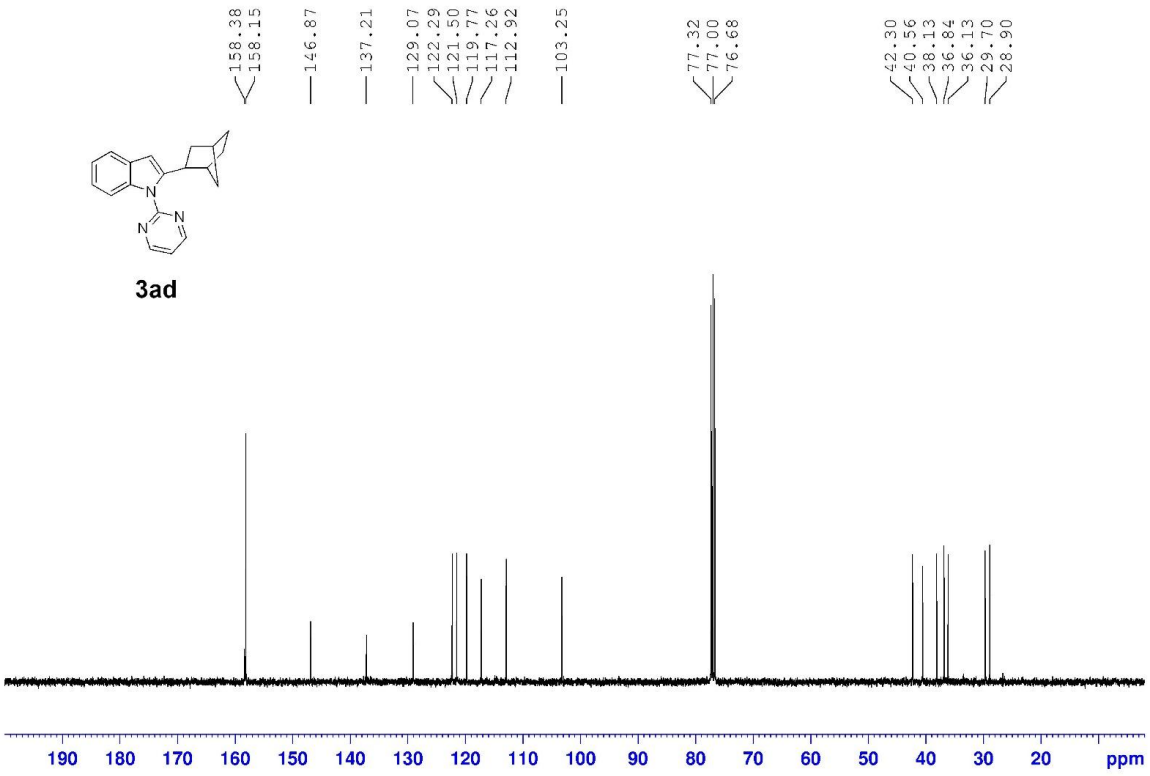


DZH-05-127 13C NMR CDCl3 BBOF1 400MHz



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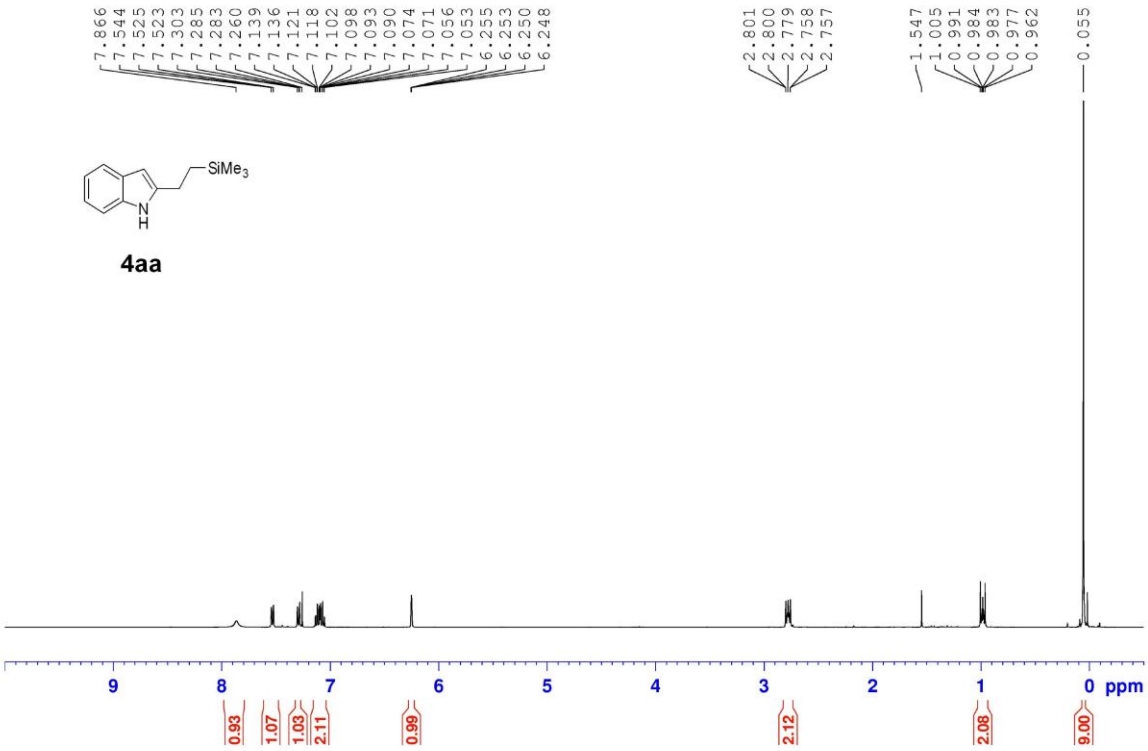

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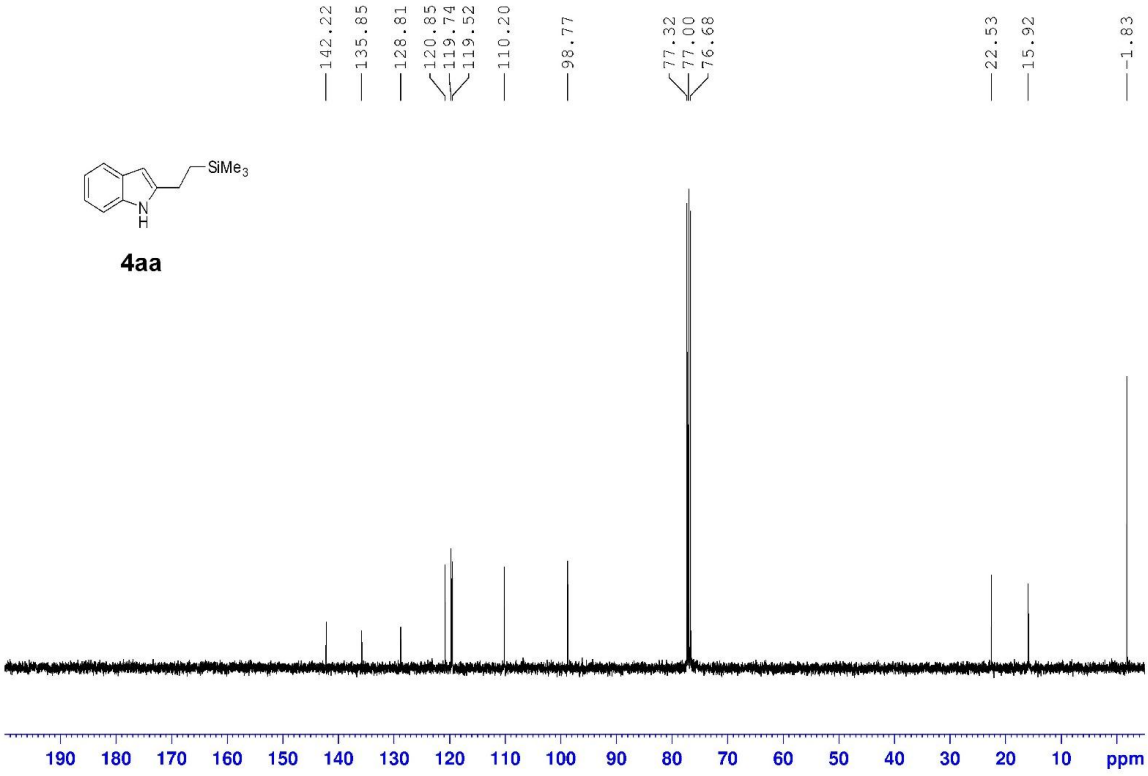

4aa