Supporting Information

N-Silyl Protecting Groups for Labile Aziridines:

Application Toward the Synthesis of *N*-H Aziridinomitosenes

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5-(3,6-Bis(tert-butyldimethylsilyloxy)hex-4-ynyl)-2-((2S,3R)-3-(iodomethyl)aziridin-2-yl)oxazole (6)

A solution of the *N*-trityl analog of **6**[1] (746 mg, 0.896 mmol) and triethylsilane (0.57 mL, 3.58 mmol) in 15 mL of anhydrous CH_2Cl_2 was cooled to 0 °C, and trifluoroacetic acid (0.35 mL, 4.48 mmol) was added dropwise. The yellow color of the resulting solution gradually faded over 5 min. After 1 h at 0 °C, NEt*i*Pr$_2$ (1.1 mL, 6.31 mmol) was added. The colorless reaction mixture was poured into 50 mL of water and extracted with 3x20 mL of CH_2Cl_2. The combined organic extract was dried (Na_2SO_4), concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (6:1 hexanes/acetone eluent) to give 505 mg (95%) of the product as a colorless oil. HRMS calcd for $C_{24}H_{43}IN_2NaO_3Si_2$: 613.1755, found (ESI) *m/z*= 613.1748, error= 1 ppm ($M+Na^+$); IR (neat, cm^{-1}) 3227, N-H; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.68 (1H, s) 4.45-4.38 (1H, m) 4.305 (1H, d, *J*= 1.65 Hz) 4.303 (1H, d, 1.65 Hz) 3.56-3.32 (1.6H, m) 3.31-3.21 (1.4H, m) 3.02-2.86 (0.6H, m) 2.85-2.68 (2.4 H, m) 2.06-1.93 (2H, m) 1.66-1.8 (0.6H, m) 1.4-1.1 (0.4H, m) 0.91 (9H, s) 0.90 (9H, s) 0.14 (3H, s) 0.12 (6H, s) 0.10 (3H, s); ^{13}C NMR (75.5 MHz, $CDCl_3$, ppm) δ 158.9, 153.0 (broad singlet), 122.8 (broad singlet), 85.3, 83.2, 61.7, 51.7, 40.7 (broad singlet), 39.1 (broad singlet), 36.11, 36.08, 35.0 (broad singlet), 25.8, 21.3, 18.3, 18.2, 4.1 (broad singlet), 1.7 (broad singlet), -4.4, -5.1, -5.1. The NMR spectra were complicated by inversion of the aziridine nitrogen and the 1:1 mixture of diasteromers.

5-(3,6-Bis(*tert*-butyldimethylsilyloxy)hex-4-ynyl)-2-((*2S,3R*)-1-(*tert*-butyldiphenylsilyl)-3-(iodomethyl)aziridin-2-yl)oxazole (7a)

To a solution of aziridine **6** (37.8 mg, 0.064 mmol) and NEtiPr$_2$ (44 μL, 0.252 mmol) in 3 mL CH_2Cl_2 at 0 °C was added *tert*-butyldiphenylsilyl triflate[2] (0.34 mL, 0.963 mmol). After stirring

at 0 °C for 1 h, the colorless solution was poured into 30 mL of ether and washed with 10 mL H_2O and then 10 mL brine. The organic phase was dried (Na_2SO_4), concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (100:10:1 hexanes/ether/triethylamine eluent) to give 48.7 mg (92% yield) of the product (*ca.* 1:1 mixture of diastereomers) as a colorless oil. HRMS calcd for $C_{40}H_{62}IN_2O_3Si_3$: 829.31131, found (FAB) *m/z*= 829.3112, error= 0.1 ppm ($M+H^+$); IR (neat, cm^{-1}) 1571, oxazole; 500 MHz NMR ($CDCl_3$, ppm) δ 7.66-7.63 (2H, m) 7.62-7.59 (2H, m) 7.48-7.33 (6H, m) 6.77 (0.5H, s) 6.76 (0.5H, s) 4.48-4.42 (1H, m) 4.34 (1H, d, J= 1.6 Hz) 4.33 (1H, d, J= 1.6 Hz) 3.58-3.54 (1H, m) 3.32 (0.5H, dd, J= 9.8, 9.8 Hz) 3.30 (0.5H, dd, J= 9.8, 9.8 Hz) 2.96 (0.5H, d, J= 4.6 Hz) 2.95 (0.5H, d, J= 4.6 Hz) 2.84-2.79 (2H, m) 2.47-2.42 (1H, m) 2.06-1.96 (2H, m) 1.14 (9H, s) 0.91 (13.5H, s) 0.90 (4.5H, s) 0.15 (1.5H, s) 0.14 (1.5H, s) 0.12 (3H, s) 0.11 (3H, s) 0.10 (1.5H, s) 0.09 (1.5H, s); ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 159.9, 152.5, 152.5, 136.1, 136.0, 131.6, 131.2, 130.0, 129.9, 127.8, 127.8, 123.1, 123.1, 85.5, 83.2, 61.8, 61.7, 51.7, 40.2, 36.3, 34.9, 27.4, 25.8, 21.3, 19.0, 18.2, 18.2, 5.0, -4.4, -5.0, -5.1.

***tert*-Butyltris(3-(trifluoromethyl)phenyl)silane (15)**

To a 3-necked 100 mL flask equipped with a stopper, a reflux condenser, and an addition funnel was placed *n*BuLi (1.58 M solution in hexanes, 11.6 mL, 18.3 mmol). The flask was cooled (-15 °C, dry ice/ethylene glycol) and 3-bromobenzotrifluoride (2.55 mL, 18.3 mmol) in 10 mL ether was added dropwise via the addition funnel. After stirring at -15 °C for 4 h, *t*BuSiCl_3 (1.00 g, 5.22 mmol) in 8 mL ether was added dropwise via the addition funnel. The cold bath was removed and the reaction was stirred at rt for 37 h. 20 mL of ice-cold water was added to the now yellow suspension. The phases were separated and the aqueous phase was extracted with 3x50 mL $CHCl_3$, the combined organic extracts were dried ($MgSO_4$), concentrated, and the

yellow solid was recrystallized from EtOAc to provide the desired product (2.364 g, 87%) as a white crystalline solid, mp 151-152 °C. HRMS calcd for $C_{21}H_{12}F_9Si$: 463.0559, found (EI) *m/z*= 463.0556, error= 1 ppm (M-$C_4H_9^+$); IR (neat, cm^{-1}) 1600, aromatic C=C; 300 MHz NMR ($CDCl_3$, ppm) δ 7.80 (3H, s) 7.75-7.66 (6H, m) 7.53 (3H, t, *J*= 7.7 Hz) 1.20 (9H, s); ^{13}C NMR (75.5 MHz, $CDCl_3$, ppm) δ 139.7 (q, $^4J_{CF}$ = 1.1 Hz), 134.6, 132.5 (q, $^3J_{CF}$ = 3.9 Hz), 130.5 (q, $^2J_{CF}$ = 32.1 Hz), 128.6, 126.9 (q, $^3J_{CF}$ = 3.9 Hz), 124.2 (q, $^1J_{CF}$ = 272.6 Hz), 28.7, 18.9.

_N_-Benzyl(*tert*-butyl)bis(3-(trifluoromethyl)phenyl)silanamine (17)

To silane **15** (910 mg, 1.748 mmol) in 15 mL CH_2Cl_2 at 0 °C was added TfOH (0.180 mL, 2.04 mmol) dropwise. The solution was allowed to slowly warm to rt and, after stirring for 3 h, the solution was transferred via cannula to benzylamine (0.16 mL, 1.457 mmol) and NEt_3 (0.61 mL, 4.37 mmol) in 5 mL CH_2Cl_2 at 0 °C. The solution was stirred at rt for 3 h, poured into 60 mL of ether, washed with 30 mL H_2O, 30 mL brine, dried ($MgSO_4$), and concentrated via rotary evaporation. The resulting brown oil was purified via flash column chromatography on silica gel (1% NEt_3 in hexane) to yield 0.567 g (81%) of **17** as a clear colorless oil. HRMS calcd for $C_{21}H_{16}F_6NSi$: 424.0956, found (EI) *m/z*= 424.0961, error= 1 ppm (M-$C_4H_9^+$); IR (neat, cm^{-1}) 3417, N-H; 300 MHz NMR ($CDCl_3$, ppm) δ 7.98 (2H, s) 7.88 (2H, d, *J*= 7.3) 7.68 (2H, d, *J*= 7.9 Hz) 7.51 (2H, t, *J*= 7.6 Hz) 7.34-7.20 (5H, m) 3.91 (2H, d, J= 7.6 Hz) 1.39 (1H, t, J= 7.6 Hz) 1.06 (9H, s). ^{13}C NMR (75.5 MHz, $CDCl_3$, ppm) δ 143.0, 139.2-139.1 (m), 135.9, 132.3 (q, $^3J_{CF}$ = 3.3 Hz), 130.3 (q, $^2J_{CF}$ = 31.5 Hz), 128.7, 128.4, 127.2, 127.1, 126.6 (q, $^2J_{CF}$ = 3.3 Hz), 124.6 (q, $^1J_{CF}$ = 272.0 Hz), 46.8, 27.5, 18.7.

***N*-Benzyl(*tert*-butyl)diphenylsilanamine (19)**

tert-Butyl(chloro)diphenylsilane (1.2 mL, 4.58 mmol) was added to benzylamine (0.5 mL, 4.58 mmol) and NEt_3 (0.96 mL, 6.87 mmol) in 10 mL CH_3CN at rt. After stirring for 2 h, the now cloudy solution was poured into 50 mL ether, washed with 25 mL H_2O and 25 mL brine, dried ($MgSO_4$) and concentrated via rotary evaporation. The resulting colorless oil was purified via flash column chromatography on silica gel (1% NEt_3 in hexanes eluent) to yield 1.555 g (98%) of product as a clear colorless oil that solidified upon standing, mp 32-34 °C. HRMS calcd for $C_{23}H_{27}NSi$: 345.1913, HRMS calcd for $C_{19}H_{18}NSi$: 288.1209, found (EI) *m/z*= 288.1204, error= 2 ppm ($M-C_4H_9^+$); IR (neat, cm^{-1}) 3398, N-H; 300 MHz NMR ($CDCl_3$, ppm) δ 7.78-7.71 (4H, m) 7.42-7.18 (11H, m) 3.96 (2H, d, J= 7.6 Hz) 1.30-1.18 (1H, m) 1.06 (9H, s); ^{13}C NMR (75.5 MHz, $CDCl_3$, ppm) δ 144.0, 136.2, 135.4, 129.5, 128.6, 127.9, 127.3, 126.8, 46.9, 27.8, 19.0.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to methyl chloroformate. To a solution of *N*-silyl benzylamine **17** (43.0 mg, 0.089 mmol) and NEt_3 (31 μL, 0.222 mmol) in 1.0 mL CH_2Cl_2 at rt was added methyl chloroformate (14 μL, 0.179 mmol). After stirring at rt for 6 hours, the solution was poured into 15 mL brine and extracted with 3x15 mL ether. The combined ether extracts were dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 41.0 mg of **17** (95% recovery). The same protocol applied to silylamine **18** (57.8 mg) and **19** (59.0 mg) led to 93% and 89% recovery, respectively.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to MeI. To a solution of *N*-silyl benzylamine **17** (32.9 mg, 0.0683 mmol) and $NEtiPr_2$ (30 μL, 0.171 mmol) in 1.0 mL CH_2Cl_2 at rt was added MeI (8.5 μL, 0.137 mmol). The solution was stirred at rt, a white precipitate formed after 2 h, and, after 6 h total stirring, the

solution was poured into 15 mL brine and extracted with 3x15 mL ether. The combined ether extracts were dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 30.7 mg of **17** (93% recovery). The same protocol applied to silylamine **18** (57.8 mg) and **19** (60.9 mg) led to 93% and 97% recovery, respectively.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to acetic anhydride. To a solution of *N*-silyl benzylamine **17** (37.8 mg, 0.0785 mmol) and NEt_3 (12 μL, 0..0863 mmol) in 0.5 mL CH_2Cl_2 at rt was added acetic anhydride (7.4 μL, 0.0785 mmol). After stirring at rt for 6 hours, the solution was poured into 15 mL brine and extracted with 3x15 mL ether. The combined ether extracts were dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 36.8 mg of **17** (97% recovery). The same protocol applied to silylamine **18** (80.4 mg) and **19** (50.0 mg) led to 95% and 99% recovery, respectively.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to aqueous THF solutions. A solution of *N*-silyl benzylamine **17** (36.3 mg), 0.8 mL THF, and 0.2 mL H_2O was stirred at rt for 6 hours, after which time the solution was poured into 15 mL brine and extracted with 3x15 mL ether. The combined ether extracts were dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 31.1 mg of **17** (86% recovery). The same protocol applied to silylamine **18** (59.1) and **19** (53.1) led to 94% and 88% recovery, respectively.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to ethanolic $NaBH_4$. To a solution of *N*-silyl benzylamine **17** (41.5 mg, 0.0862 mmol) in 1 mL EtOH at 0 °C was added $NaBH_4$ (3.0 mg, 0.0776 mmol). After stirring at 0 °C for 2 hours, the solution was poured into 15 mL brine and extracted with 3x15 mL ether. The

combined ether extracts were dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 40.4 mg of **17** (97% recovery). The same protocol applied to silylamine **18** (56.1 mg) and **19** (55.0) led to 98% and 82% recovery, respectively.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamines to CD_3OD. *Circa* 10 mg of the silyl amine was dissolved in 0.6 mL of CD_3OD and the extent of solvolysis was monitored by integration of the signals corresponding to the benzylic protons of the silyl amines (**17**: δ 3.89 ppm, **18**: δ 3.89 ppm, and **19**: δ 3.90 ppm) and benzylamine (δ 3.76 ppm) on regular intervals. After 7 days at rt, **17** displayed 22% solvolysis (δ 3.89 ppm, 2H; δ 3.76 ppm 0.56H) s; while **18** underwent 9% solvolysis (δ 3.89 ppm, 2H; δ 3.76 ppm 0.21H) after 8 days; and, finally, **19** displayed 22% solvolysis (δ 3.90 ppm, 2H; δ 3.76 ppm, 0.58H) after 7.5 hours.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to nBuLi. To a solution of *N*-silyl benzylamine **17** (39.3 mg, 0.0816 mmol) in 1.0 mL THF at 0 °C was added *n*BuLi (1.6 M solution in hexanes, 51 μL, 0.0816 mmol), upon which time the formerly clear solution immediately became purple. The color faded over *ca.* 2 min and the solution was stirred at 0 °C for 1 h. 25 mL of ice-cold water was added and the aqueous phase was extracted with 3x25 mL ether. The combined ether extracts were dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 39.0 mg of **17** (99% recovery). The same protocol applied to silylamine **18** (92.6 mg, 0.1499 mmol) and **19** (51.7 mg, 0.150 mmol) led to 86% and 95% recovery, respectively.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to LDA. To a solution of *N*-silyl benzylamine **17** (36.3 mg, 0.0754 mmol) in 1.0 mL THF at 0 °C was added LDA (1.0 M solution in hexanes/THF, 0.15 mL, 0.151 mmol),

upon which time the clear solution turned pink. After stirring for 2 h, 25 mL of ice-cold water was added and the aqueous phase was extracted with 3x25 mL ether. The combined ether extracts were dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 36.2 mg of **17** (99% recovery). The protocol applied to **18** (108.2 mg, 0.1752 mmol) and **19** (58.8 mg, 0.1702 mmol) led to 89% and 95% recovery, respectively.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to refluxing NaOH/MeOH. A solution of *N*-silyl benzylamine **19** (54.2 mg) in 1.0 mL of 20% NaOH in MeOH was refluxed for 16 h, at which time it was cooled to rt and poured into 10 mL H_2O and the aqueous phase was extracted with 3x10 mL ether. The combined ether extracts were washed with 10 mL brine dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 44.8 mg of **19** (83% recovery). The same protocol applied to silylamines **17** and **18** led to no recovery of starting material.

Representative Procedure—*N*-Silyl benzylamine stability studies. Exposure of *N*-silyl benzylamine 17 to 1% NaOH in MeOH. A solution of *N*-silyl benzylamine **17** (39.5 mg) in 1.0 mL of 1% NaOH in MeOH was stirred at rt for 1 h, at which time it was poured into 10 mL H_2O and the aqueous phase was extracted with 3x10 mL ether. The combined ether extracts were washed with 10 mL brine dried (Na_2SO_4), concentrated, and purified via flash column chromatography (1% NEt_3 in hexane) to yield 35.8 mg of **17** (91% recovery). The same protocol applied to silylamine **18** led to 78% recovery of starting material.

5-(3,6-Bis(*tert*-butyldimethylsilyloxy)hex-4-ynyl)-2-((*2S,3R*)-1-(*tert*-butylbis(3-(trifluoromethyl)phenyl)silyl)-3-(iodomethyl)aziridin-2-yl)oxazole (21a)

To silane **15** (391 mg, 0.751 mmol) in 3 mL CH_2Cl_2 at 0 °C was added TfOH (73 μL, 0.8258 mmol) dropwise. After 3 h at 0 °C, the solution was transferred via cannula to aziridine **6** (293.2

mg, 0.496 mmol) and $NEtiPr_2$ (0.32 mL, 1.99 mmol) in 3 mL CH_2Cl_2 at 0 °C. After stirring at 0 °C for 15 min and at rt for 2 h, the solution was poured into 100 mL of ether, then washed with 25 mL H_2O and 25 mL brine. The organic extract was dried (Na_2SO_4) and concentrated via rotary evaporation. The resulting brown oil was purified via flash column chromatography on silica gel (1% NEt_3 in 8:1 hexane/ether eluent) to yield 0.398 g (83%) of product (*ca.* 1:1 mixture of diastereomers) as a pale brown syrup. HRMS calcd for $C_{42}H_{59}F_6IN_2NaO_3Si_3$: 987.2680, found (ESI) *m/z*= 987.2673, error= 1 ppm ($M+Na^+$); IR (neat, cm^{-1}) 1573, oxazole; 300 MHz NMR ($CDCl_3$, ppm) δ 7.89 (2H, s) 7.72-7.68 (4H, m) 7.59-7.48 (2H, m) 6.781 (0.5H, s) 6.778 (0.5H, s) 4.49-4.40 (1H, m) 4.34 (1H, d, J= 2.0 Hz) 4.33 (1H, d, J= 1.8 Hz) 3.60-3.47 (1H, m) 3.33 (0.5H, dd, J= 9.2, 9.2 Hz) 3.31 (0.5H, dd, J= 9.3, 9.3 Hz) 2.960 (0.5H, d, J= 4.7 Hz) 2.956 (0.5H, d, J= 4.7 Hz) 2.86-2.79 (2H, m) 2.53-2.46 (1H, m) 2.05-1.96 (2H, m) 1.16 (9H, s) 0.901 (13.5H, s) 0.898 (4.5H, s) 0.14 (1.5H, s) 0.13 (1.5H, s) 0.113 (3H, s) 0.109 (3H, s) 0.103 (1.5H, s) 0.095 (1.5H, s);^{13}C NMR (75.5 MHz, $CDCl_3$, ppm) δ 159.0, 153.0, 152.9, 139.2, 139.1, 132.3-132.1, 130.5 (q, $^2J_{CF}$ = 32.6 Hz), 128.4, 128.3, 127.2 (q, $^3J_{CF}$ = 3.7 Hz) 127.1 (q, $^3J_{CF}$ = 3.8 Hz), 124.1 (q, $^1J_{CF}$ = 273.2 Hz), 124.0 (q, $^4J_{CF}$ = 272.7 Hz), 123.2, 123.1, 85.4, 83.2, 61.8, 61.7, 51.7, 40.5, 36.2, 35.1, 27.3, 25.8, 21.3, 19.0, 18.3, 18.2, 3.9, -4.4, -5.04, -5.06, -5.13.

2-((*2S,3R*)-1-(Bis(3,5-bis(trifluoromethyl)phenyl)(*tert*-butyl)silyl)-3-(iodomethyl)aziridin-2-yl)-5-(3,6-bis(*tert*-butyldimethylsilyloxy)hex-4-ynyl)oxazole (21b)

To silane **16** (319 mg, 0.542 mmol) in 1 mL CH_2Cl_2 at 0 °C was added TfOH (53 μL, 0.596 mmol) dropwise. After 3 h at 0 °C, the solution was transferred via cannula to aziridine **6** (222.3 mg, 0.3764 mmol) and $NEtiPr_2$ (0.25 mL, 1.51 mmol) in 3 mL CH_2Cl_2 at 0 °C. After stirring at 0 °C for 15 min and at rt for 2 h, the solution was poured into 100 mL of ether, then washed with 25 mL H_2O and 25 mL brine. The organic extract was dried (Na_2SO_4) and concentrated via

rotary evaporation. The resulting brown oil was purified via flash column chromatography on silica gel (1% NEt_3 in 12:1 hexane/ether eluent) to yield 0.279 g (67%) of product (*ca.* 1:1 mixture of diastereomers) as a clear syrup. HRMS calcd for $C_{44}H_{57}F_{12}IN_2NaO_3Si_3$: 1123.2428, found (ESI) *m/z*= 1123.2424, error= 0.4 ppm ($M+Na^+$); IR (neat, cm^{-1}) 1557, oxazole; 300 MHz NMR ($CDCl_3$, ppm) δ 8.11-7.94 (6H, m) 6.80 (0.5H, s) 6.79 (0.5H, s) 4.49-4.40 (1H, m) 4.34 (1H, d, J= 1.5 Hz) 4.33 (1H, d, J= 1.8 Hz) 3.54-3.46 (1H, m) 3.36-3.27 (1H, m) 3.02 (0.5H, d, J= 4.7 Hz) 3.01 (0.5H, d, J= 4.7 Hz) 2.87-2.78 (2H, m) 2.64-2.56 (1H, m) 2.24-1.95 (2H, m) 1.19 (9H, s) 0.898 (9H, s) 0.896 (9H, s) 0.14 (1.5H, s) 0.13 (1.5H, s) 0.110 (3H, s) 0.107 (3H, s) 0.10 (1.5H, s) 0.09 (1.5H, s);^{13}C NMR (75.5 MHz, $CDCl_3$, ppm) δ 158.4, 153.6, 153.6, 134.2, 134.1, 131.7 (q, $^2J_{CF}$ = 33.3 Hz), 131.6 (q, $^2J_{CF}$ = 33.3 Hz), 125-124.6 (m), 123.5, 123.4, 123.3 (q, $^1J_{CF}$ = 273.1 Hz), 85.6, 83.5, 61.9, 51.9, 41.2, 36.3, 35.6, 27.3, 26.0, 26.0, 21.5, 21.4, 19.3, 18.5, 18.4, 3.2, -4.2, -4.9, -4.9.

Representative Procedure—Cycloaddition of *N*-silyl aziridinomitosene precursors. (1S,2S,8R and 8S)-8-tert-butyldimethylsilyloxy-9-tert-butyldimethylsilyloxymethyl-1,2-(*N*-tert-butyldiphenylsilylaziridino)-2,3,5,6,7,8-hexahydro-5-oxo-1H-pyrrolo[1,2-a]indole (9). Following the general previously published procedure,[1] AgOTf (140 mg, 0.545 mmol) and iodide **7a** (298 mg, 0.359 mmol) in 4 mL CH_3CN was stirred under N_2 at 70 °C for 3 h. The cooled reaction mixture was transferred *via* cannula dropwise over 5 min into a stirred suspension of $BnMe_3N^+CN^-$ (188 mg, 1.07 mmol) in 3 mL of anhydrous CH_3CN at rt. After stirring at rt for 30 min, the brown solution was poured into 50 mL of ether, washed with water and brine, dried (Na_2SO_4), and purified by flash chromatography on silica gel (100:20:1 hexane/ethyl acetate/triethylamine eluent) to give 144 mg of the crude product as a tan oil. A 72 mg fraction of the crude product was purified by preparative TLC on silica gel pretreated with

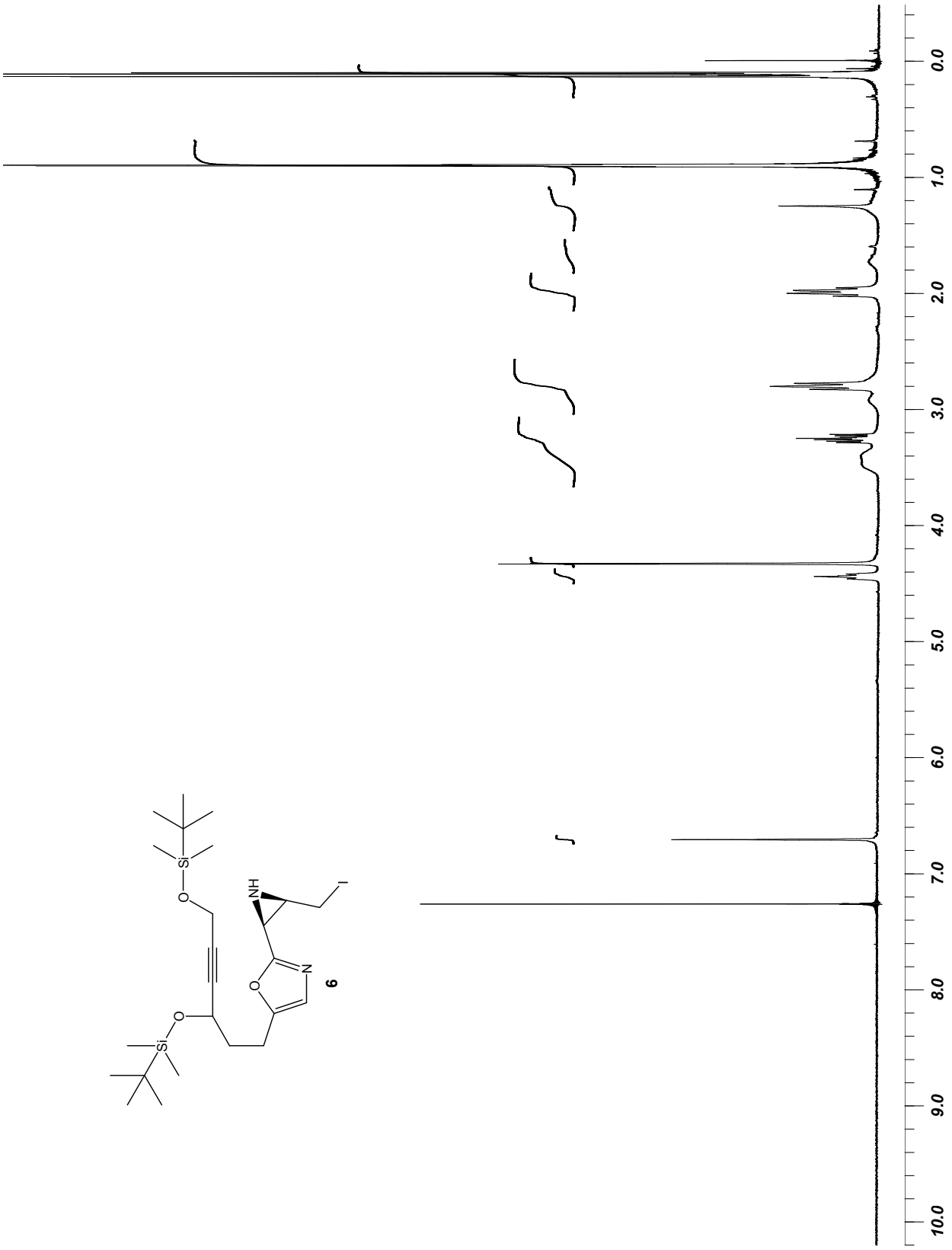
triethylamine (5 min in a chamber saturated with triethylamine vapor, 20x20x0.1 cm, 5:1 hexanes/ethyl acetate eluent) to give 51 mg (41%) of the pure product (*ca.* 1:1 mixture of diastereomers) as a pale tan oil. HRMS calcd for $C_{40}H_{61}N_2O_3Si_3$: 701.39901, found (FAB) *m/z*= 701.3984, error= 1 ppm ($M+H^+$); IR (neat, cm^{-1}) 1652, C=O; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.62-7.56 (4H, m) 7.44-7.39 (2H, m) 7.38-7.32 (4H, m) 5.03 (0.5H, dd, *J*= 6.0, 3.8 Hz) 5.00 (0.5H, dd, *J*= 5.4, 3.4 Hz) 4.78 (0.5H, AB q, *J*= 12.1 Hz) 4.73 (1H, s) 4.72 (0.5H, AB q, *J*= 12.1 Hz) 4.33 (1H, d, *J*= 13.2 Hz) 4.03 (0.5H, dd, *J*= 13.2, 3.6 Hz) 4.02 (0.5H, dd, *J*= 13.2, 3.4 Hz) 3.25 (0.5H, d, *J*= 3.9 Hz) 3.22-3.18 (1.5H, m) 2.80-2.70 (1H, m) 2.37-2.28 (1H, m) 2.27-2.19 (1H, m) 2.13-2.04 (1H, m) 1.14 (4.5H, s) 1.13 (4.5H, s) 0.95 (4.5H, s) 0.89 (4.5H, s) 0.82 (4.5H, s) 0.81 (4.5H, s) 0.18 (1.5H, s) 0.16 (1.5H, s) 0.15 (1.5H, s) 0.13 (1.5H, s) 0.01 (1.5H, s) -0.01 (1.5H, s) -0.03 (1.5H, s) -0.05 (1.5H, s); ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 187.8, 187.7, 143.2, 142.9, 137.0, 136.3, 135.8, 135.8, 135.8, 135.8, 132.6, 132.5, 132.5, 132.3, 129.8, 129.7, 129.7, 129.7, 127.8, 127.7, 127.7, 127.7, 123.2, 123.2, 115.7, 115.7, 64.9, 64.2, 57.9, 57.8, 50.3, 50.2, 41.0, 40.9, 34.7, 34.5, 34.4, 34.0, 33.9, 33.5, 27.7, 27.6, 26.0, 26.0, 25.9, 19.3, 19.3, 18.4, 18.3, 18.2, 18.1, -4.0, -4.2, -4.3, -4.4, -5.2, -5.4, -5.4, -5.4.

TBAF deprotection of *N*-silyl aziridinomitosene precursors to generate (1S,2S,8R and 8S)-1,2-Aziridino-8-tert-butyldimethylsilyloxy-9-tert-butyldimethylsilyloxymethyl-2,3,5,6,7,8-hexahydro-5-oxo-1H-pyrrolo[1,2-a]indole (24). 1.0 equivalents of TBAF (1.0 M solution in THF) was added to a solution of the silyl aziridine (**9**, **23a**, or **23b**) in THF at 0 °C. The tan solution was stirred at 0 °C for 1 h, poured into brine, and extracted with ether. The combined organic phase was dried (Na_2SO_4) and concentrated by rotary evaporation. The residue was purified by preparative TLC on silica gel pretreated with NEt_3 for 5 min in a chamber saturated with NEt_3 vapor (20x20x0.1 cm, 1:3 hexane/EtOAc eluent) to give the product (ca. 1:1 mixture

of diastereomers) as a colorless oil (26% from **7a**, 32% from **21a**, and 18% from **21b**). HRMS calc for $C_{24}H_{43}N_2O_3Si_2$: 463.28123, found (FAB) *m/z*= 463.2790, error= 5 ppm ($M+H^+$); IR (neat, cm^{-1}) 3250, N-H; 1644, C=O; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 5.01-4.94 (1H, m) 4.84-4.70 (2H, m) 4.41-4.36 (0.6H, m) 4.32-4.27 (0.4H, m) 4.25-4.19 (0.6H, m) 4.16-4.10 (0.4H, m) 3.65-3.60 (0.4H, m) 3.50-3.44 (0.4H, m) 3.38-3.30 (1.2H, m) 2.77-2.63 (1H, m) 2.38-2.27 (1H, m) 2.27-2.15 (1H, m) 2.11-2.00 (1H, m) 1.09-1.01 (0.6H, m) 0.94 (9H, s) 0.91-0.89 (9H, m) 0.29-0.24 (0.4H, m) 0.17-0.10 (12H, m); ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ 187.8, 187.7, 187.7, 187.6, 143.0, 143.0, 141.2, 141.1, 137.3, 137.2, 137.1, 136.7, 123.2, 116.7, 116.6, 116.3, 116.2, 65.0, 65.0, 64.8, 64.5, 58.6, 58.5, 58.1, 57.9, 49.9, 49.8, 49.7, 39.9, 39.9, 38.4, 38.2, 34.9, 34.8, 34.7, 34.5, 34.5, 34.4, 34.3, 32.4, 32.1, 32.0, 26.0, 26.0, 25.9, 18.4, 18.4, 18.1, -4.1, -4.1, -4.4, -5.2, -5.2, -5.2, -5.3. The NMR spectra were complicated by inversion of the aziridine nitrogen (3:2 invertomer ratio, based on integration of N-H signals at 1.09-1.01 ppm and 0.29-0.24 ppm) and the 1:1 mixture of diasteromers. Addition of ca. 2 mg of powdered 4 Å molecular sieves to the NMR tube served to sharpen the signals.

References

1. Vedejs, E.; Naidu, B. N.; Klapars, A.; Warner, D. L.; Li, V. S.; Na, Y.; Kohn, H. *J. Am. Chem. Soc.* **2003**, *125*, 15796-15806.
2. Bassindale, A. R.; Stout, T. *J. Organomet. Chem.* **1984**, *271*, C1-C3.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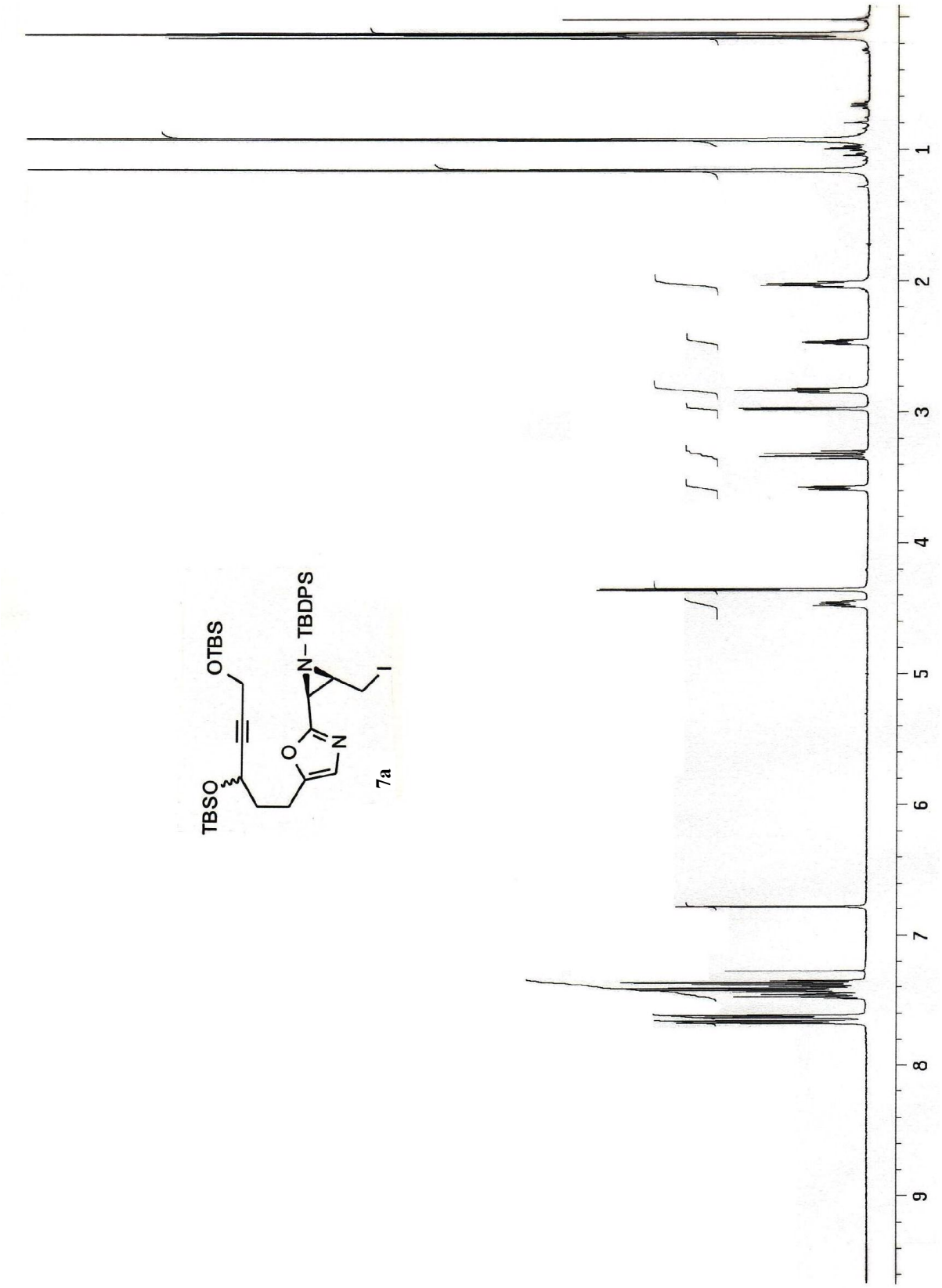
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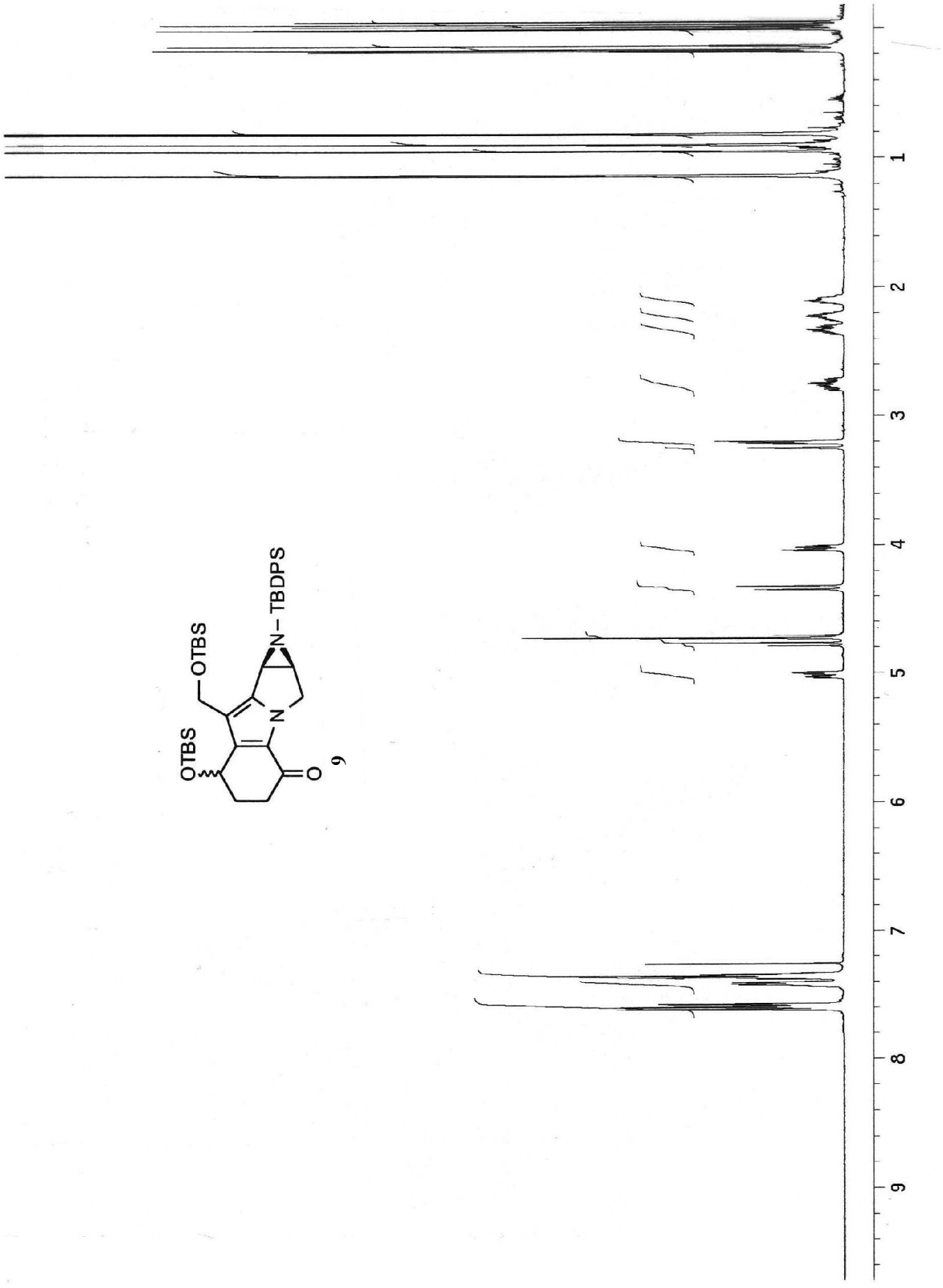
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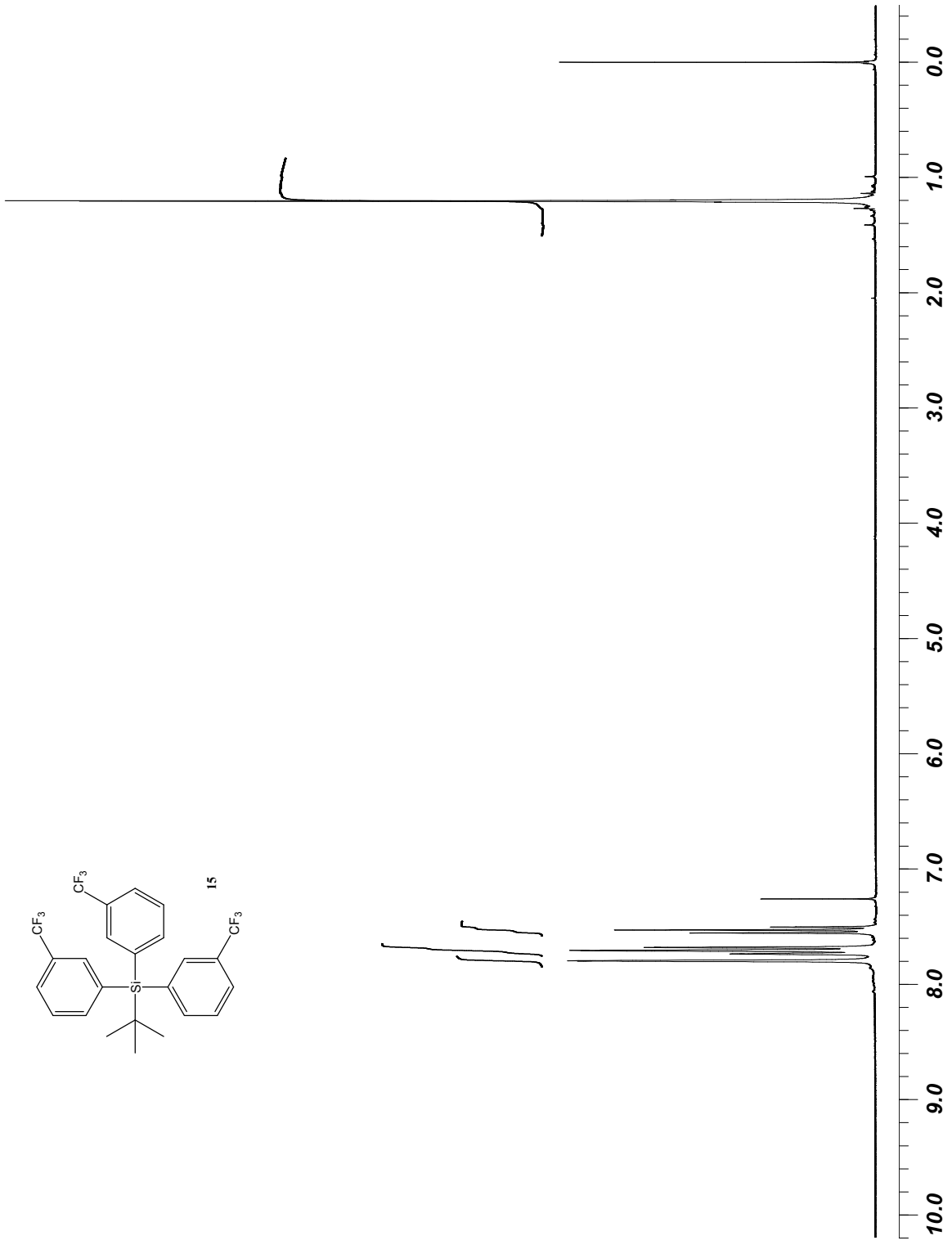
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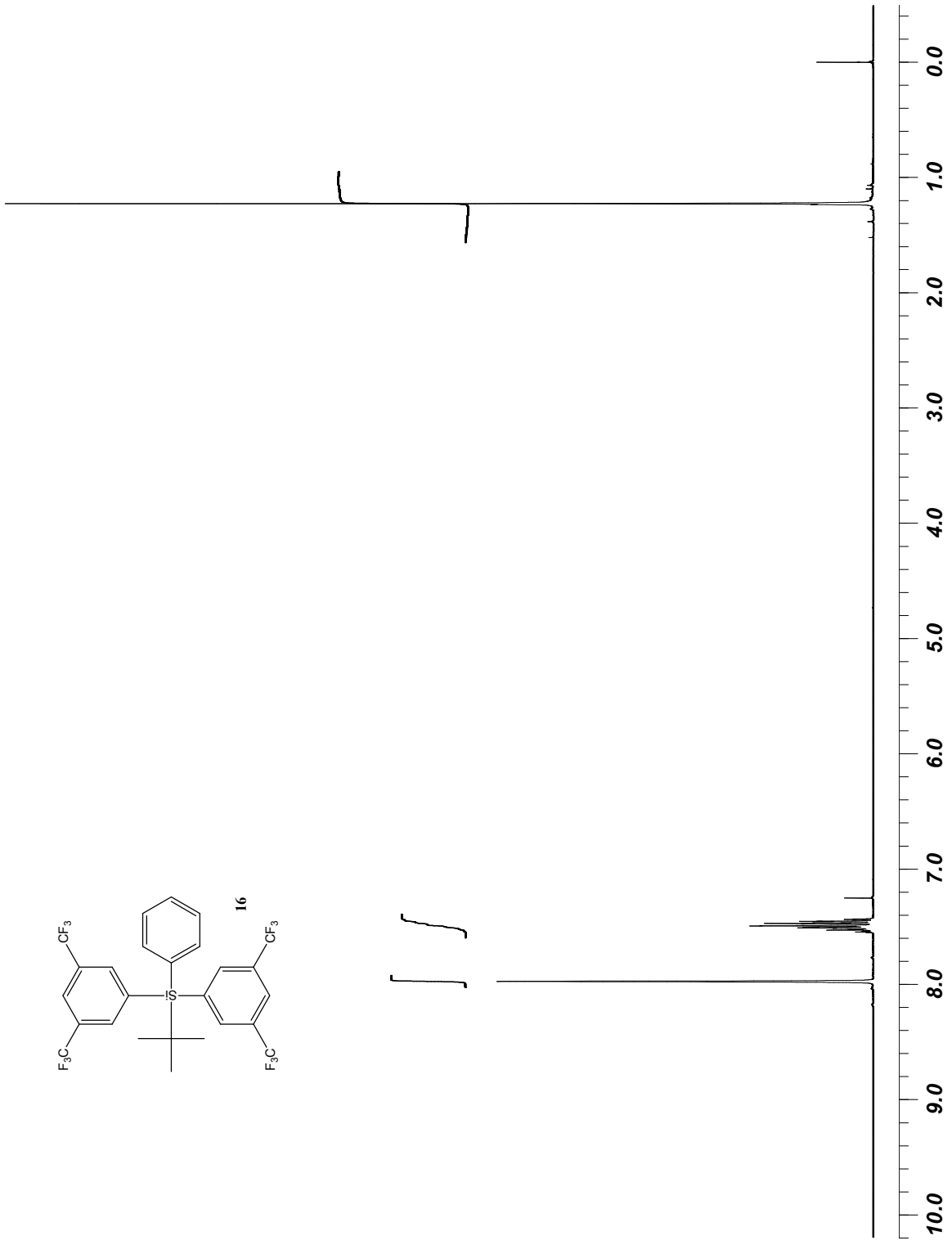
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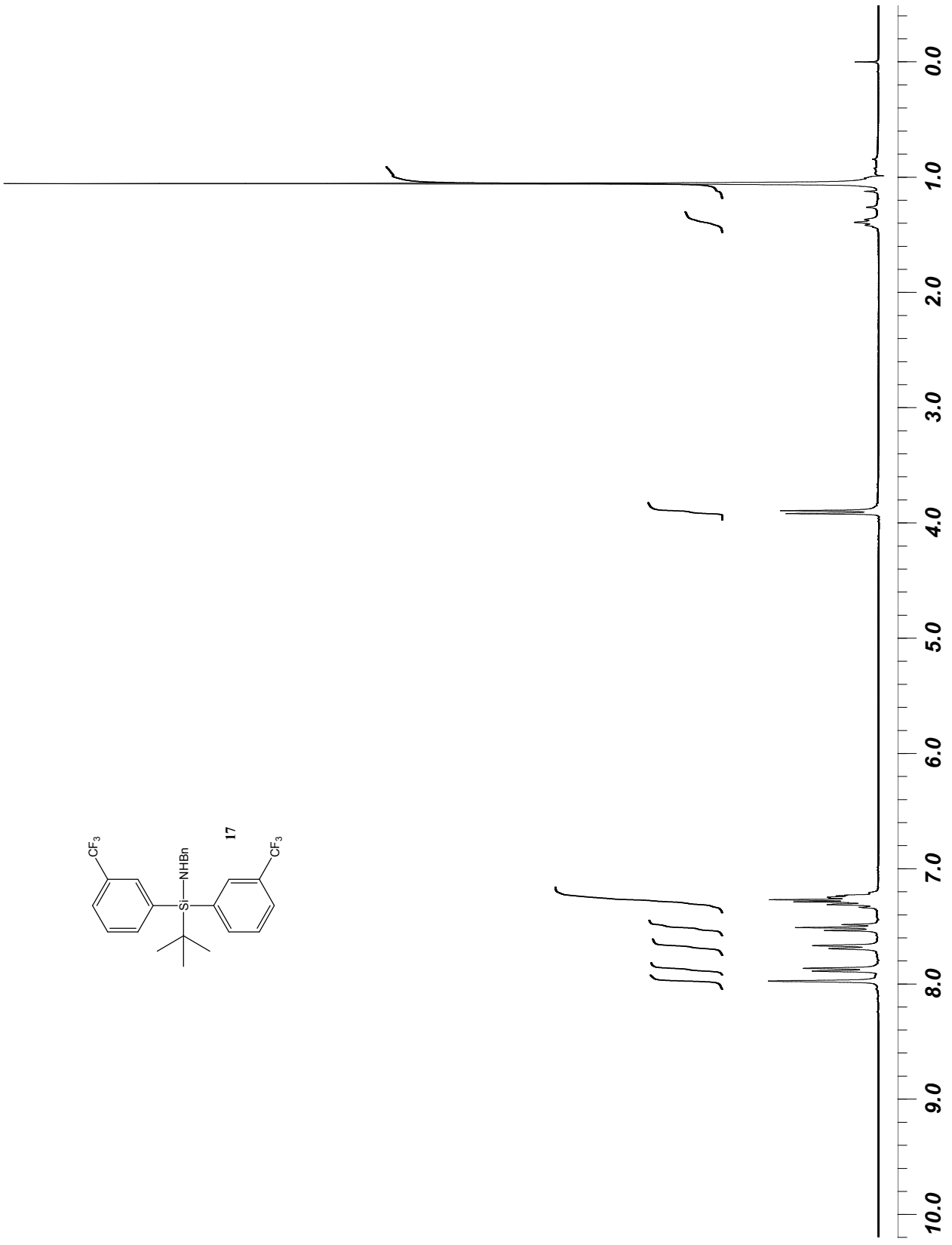
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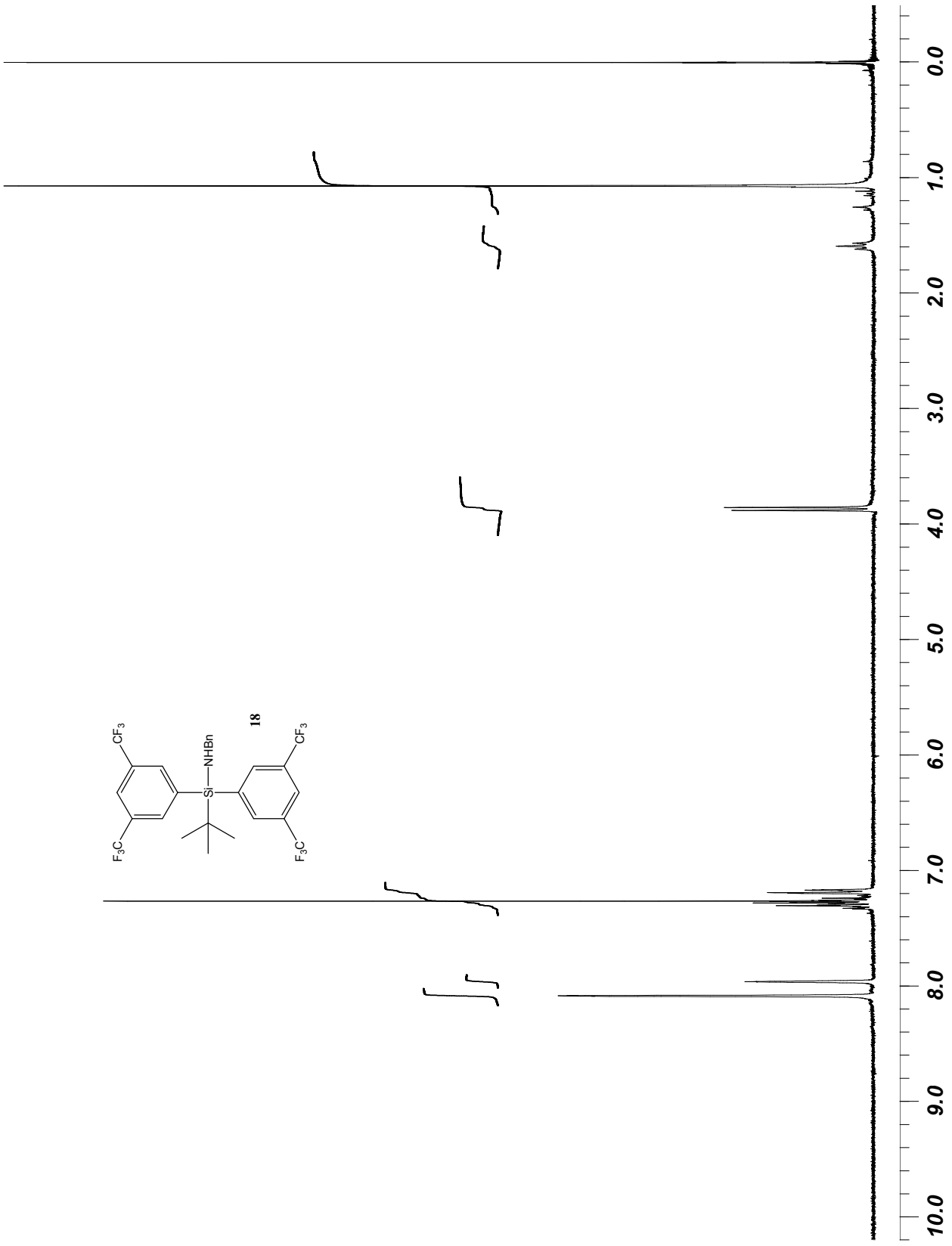
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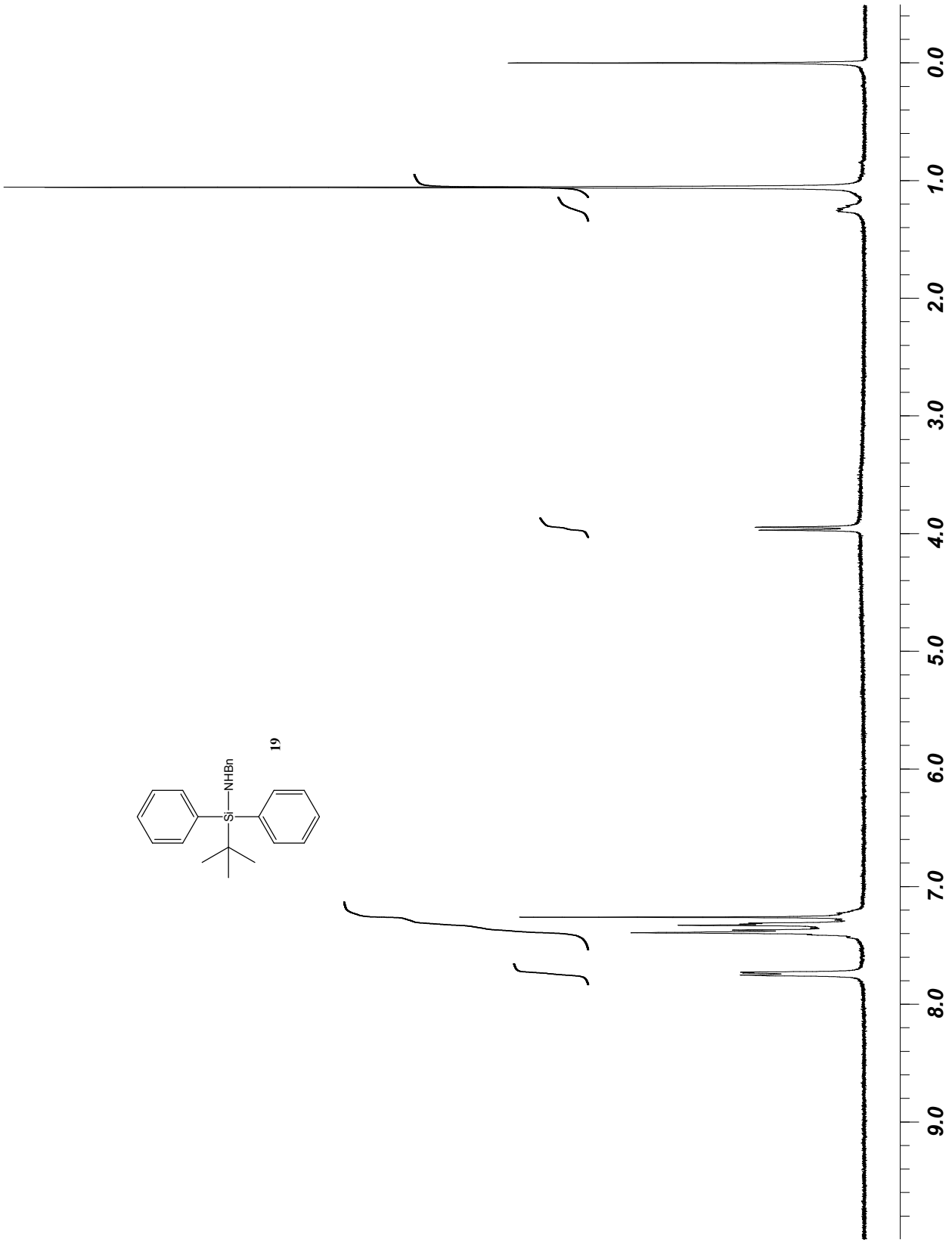
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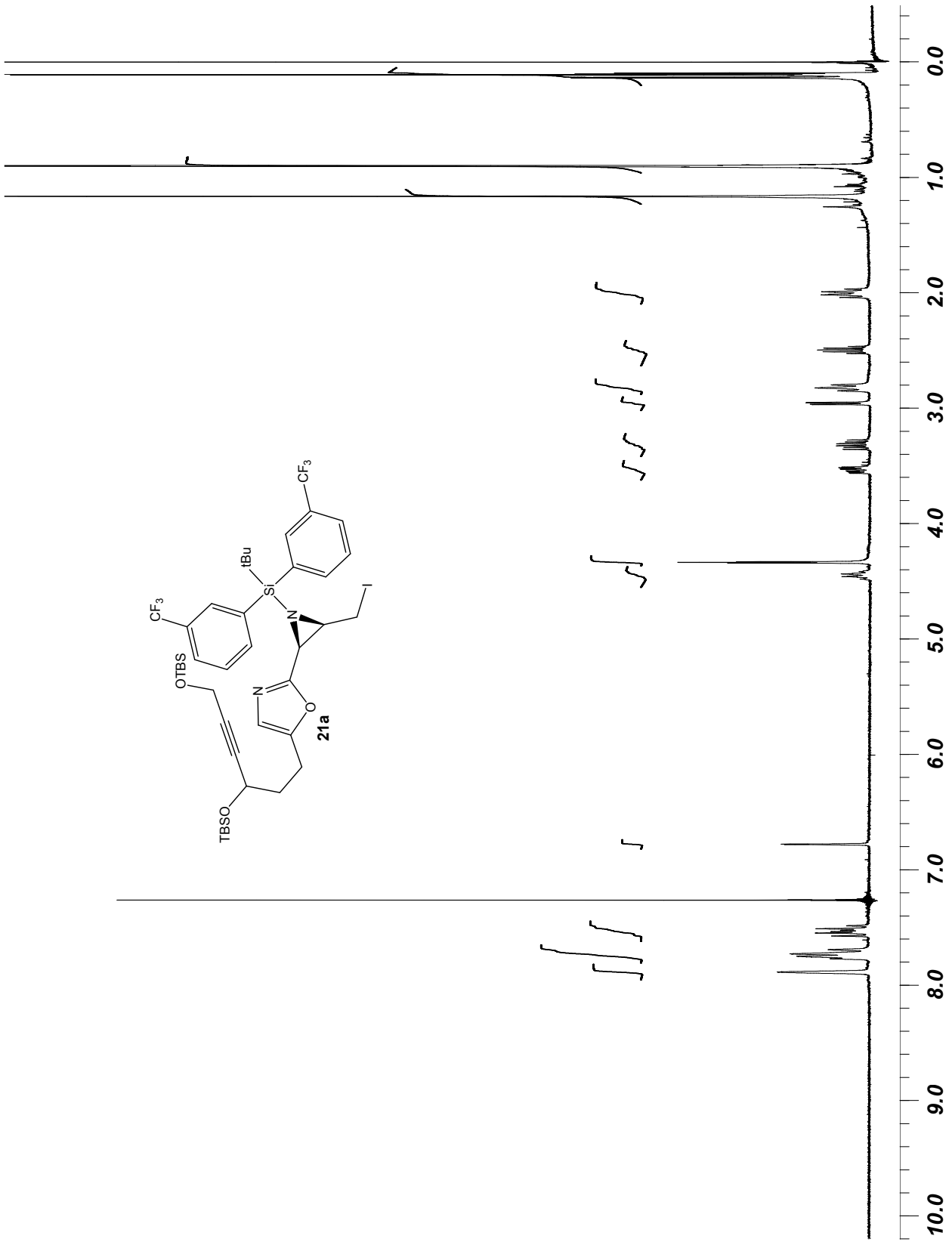
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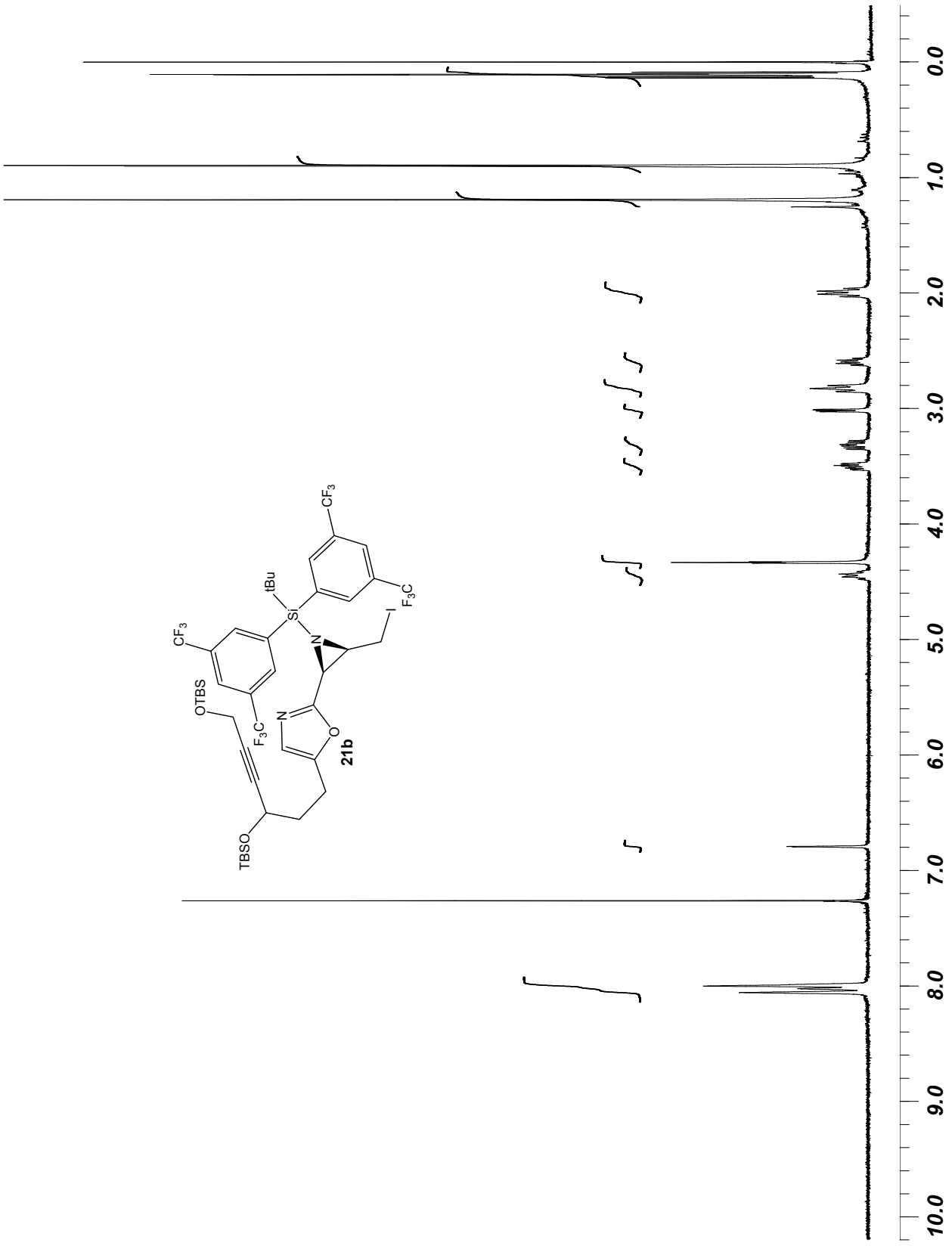
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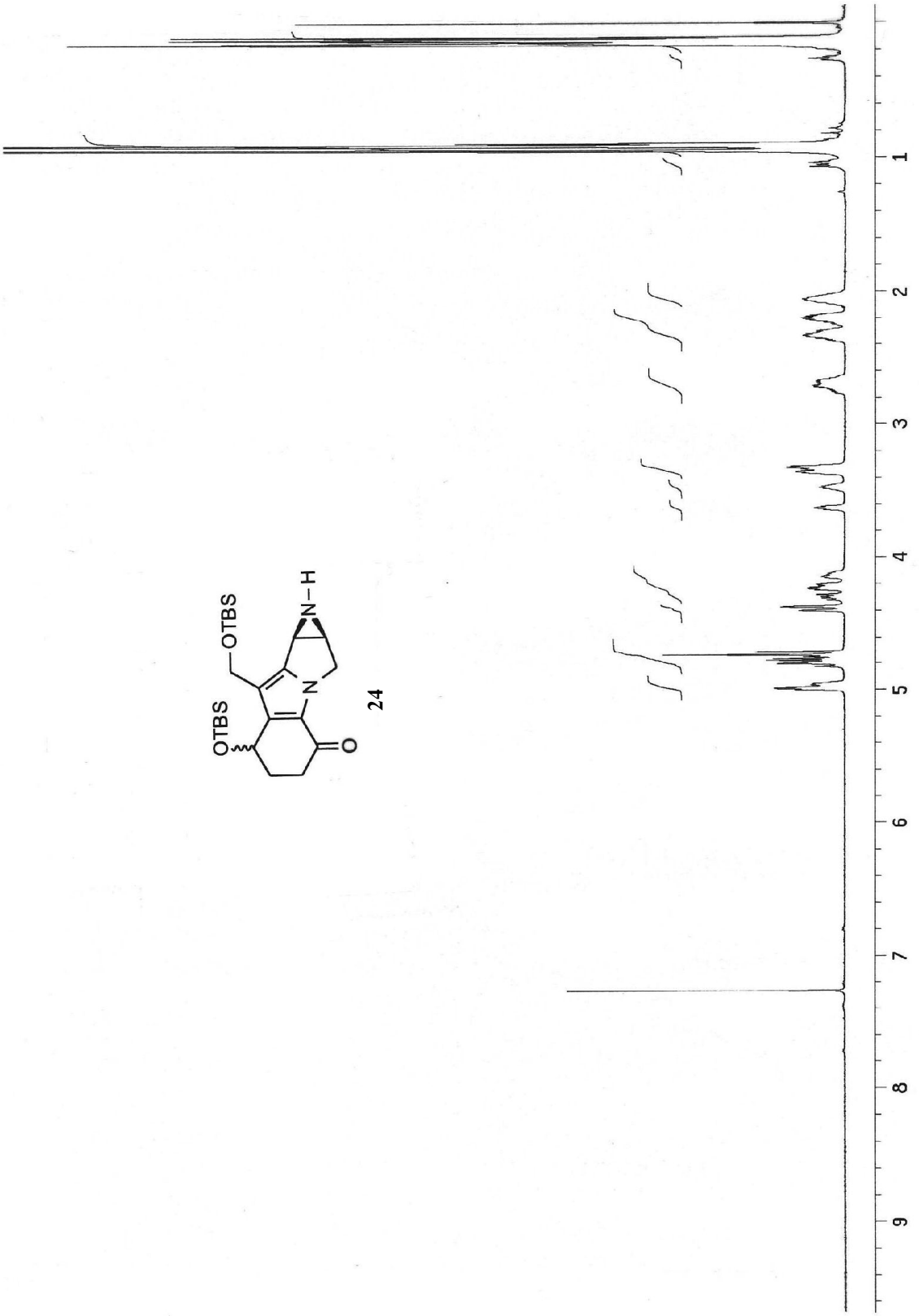
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