Copper-Catalyzed Remote (δ) C(sp^3)-H Bond Amination: A Practical Strategy to Construct Pyrrolidine Derivatives

Supporting Information

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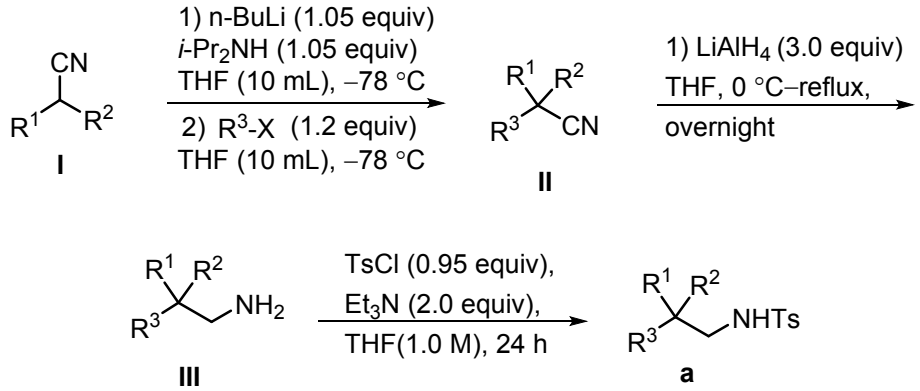
Instrumentation and Chemical

NMR spectra were recorded on Bruker 400 and 600 M spectrometers, operating at 400 and 600 MHz for ^{1}H NMR and 100 and 125 MHz for ^{13}C NMR spectrophotometer using $CDCl_3$ and TMS as the internal standard. Chemical shift values for ^{1}H and ^{13}C are referenced to residual solvent peaks ($CHCl_3$ in $CDCl_3$: 7.26 ppm for ^{1}H, 77.00 ppm for ^{13}C; Chemical shifts are reported in δ ppm. All coupling constants (*J* values) were reported in Hertz (Hz). Data for ^{1}H-NMR spectra are reported as follows: chemical shift (ppm, referenced to TMS; s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet), coupling constant (Hz), and integration. Column chromatography was performed on silica gel 200-300 mesh. High-resolution mass spectra (HRMS) were recorded on

electron-spray ionization (ESI) technique.

All reactions were carried out under nitrogen atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. CuI was purchased from Energy Chemical Reagent Co., Ltd., $PhI(OTFA)_2$ was purchased from Beijing Innochem Science & Technology Co., Ltd. DCE was freshly distilled over CaH_2 under N_2.

General Procedure: Preparation of sulfonamides



n-BuLi in hexane (2.5 M, 20 mmol, 80 mL) was added dropwise to a solution of *i*-Pr_2NH (21.0 mmol, 3.5 mL) in THF (10 mL) at –78 ºC and stirred for 1 h. Then alkyl nitrile **I** (20 mmol) was added dropwise to the resulting LDA solution at –78 ºC and stirred at this temperature for 1 h. Alkyl halide (30 mmol) was then added dropwise to the solution at –78 ºC. After the addition, the mixture was warmed to room temperature and stirred overnight. After down, the mixture was quenched with saturated aqueous NH_4Cl, and extracted with EtOAc (20 mL × 3). Combined extracts were washed with water, brine solution and dried over anhydrous Na_2SO_4. Solvent was evaporated in Rota-evaporator. The residue was purified by silica gel chromatography (2%–10% EtOAc/petroleum ether) to provide corresponding nitrile **II**.

$LiAlH_4$ (2.28 g, 60 mmol, 3.0 equiv) was slowly added to the solution of crude nitrile in THF (30mL) at room temperature. Then the mixture was heated to 70 ℃ for 24 hours. After that, the reaction was cooled down, the $Na_2SO_4 \cdot 10H_2O$ was added slowly until the mixture was clear to quench the reaction, filtered, solid was washed

with Et_2O, the combined ether solution was concentrated in vacuo to give the desired amide **III**.

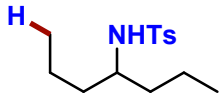
To a solution of amide **III** (10 mmol, 1.0 equiv) in dichloromethane (20 mL) was added triethylamine (1.67 mL, 12 mmol, 1.2 equiv) at 0 ° C. Tosyl chloride (1.89 g, 9.5 mmol, 0.95 equiv) was added portion wise. Then the mixture was stirring for 24 hours at room temperature. Then the mixture was quenched by water (20 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (20mL × 2). The combined organic phase was washed with brine (30 mL), and then dried over Na_2SO_4. Evaporation and column chromatography on silica gel (ethyl acetate/hexane = 1:100-1:5 as eluent) afforded corresponding sulfonamides **a** as colorless solid.

Sulfonamide substrates **6a**, **8a, 10a**, **11a**, **13a**, **14a**,, **17a**, **18a**, **24a, 25a** were prepared according to the general procedures.

Characterization Data for Sulfonamides

Sulfonamides **1a**,[1] **2a**,[2] **3a**,[3] **4a**,[2] **5a**,[2] **7a**,[4] **9a**,[3] **12a**,[5] **15a**,[3] **16a**,[3] **19a**,[4] **20a**,[4] **21a**,[4] **22a**,[4] **23a**,[6] **24a**,[7] can be found in literatures.

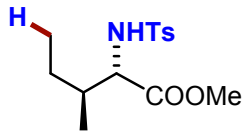
***N*-(heptan-4-yl)-4-methylbenzenesulfonamide (1a)**



1a

White solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.75 (s, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 4.13 (d, *J* = 8.1 Hz, 1H), 3.20–3.27 (m, 1H), 2.39 (s, 3H), 1.09–1.36 (m, 8H), 0.75 (t, *J* = 6.9 Hz, 6H).

Methyl tosyl-*L*-isoleucinate (2a)

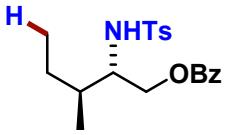


L-isoleu-**2a**

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 5.05 (d, *J* = 9.9 Hz, 1H), 3.78 (dd, *J* = 9.9, 5.4 Hz, 1H), 3.43 (s, 3H),

2.42 (s, 3H), 1.72–1.78 (m, 1H), 1.38–1.44 (m, 1H), 1.11–1.18 (m, 1H), 0.9 (d, *J* = 6.9 Hz, 3H), 0.86 (t, *J* = 7.5 Hz, 3H).

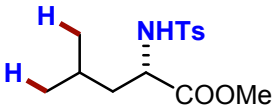
(2*S*,3*S*)-3-methyl-2-((4-methylphenyl)sulfonamido)pentyl benzoate (3a)



L-isoleu-**3a**

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.2 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 4.77 (t, *J* = 6.6 Hz, 1H), 4.31 (dd, *J* = 9.9, 5.4 Hz, 1H), 4.13 (dd, *J* = 7.8, 3.9 Hz, 1H), 3.51–3.55 (m, 1H), 2.30 (s, 3H), 1.71–1.1.75 (m, 1H), 1.13–1.20 (m, 1H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.90 (t, *J* = 7.8 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 166.42, 143.18, 137.88, 133.15, 129.63, 129.58, 128.30, 126.82, 63.94, 57.02, 37.42, 25.49, 21.45, 14.75, 11.57.

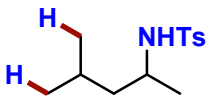
Methyl tosyl-L-leucinate (4a)



L-leu-**4a**

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 4.96 (d, *J* = 9.9 Hz, 1H), 3.93 (ddd, *J* = 9.9, 8.4, 6.3 Hz, 1H), 3.44 (s, 3H), 2.42 (s, 3H), 1.84–1.72 (m, 1H), 1.53–1.42 (m, 2H), 0.89 (dd, *J* = 12.0, 6.6 Hz, 6H).

***N*-(4-methylpentan-2-yl)-4-methyl- benzenesulfonamide (5a)**

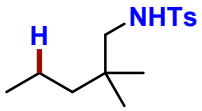


5a

White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) 7.76 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.08 (d, *J* = 8.1 Hz, 1H), 3.31–3.38 (m, 1H), 2.43 (s, 3H), 1.25 (ddd, *J* = 13.8, 8.1, 6.3 Hz, 1H), 1.14 (ddd, *J* = 13.8, 8.1, 6.3 Hz, 1H), 1.02 (d, *J* = 6.3 Hz, 3H), 0.80

(d, J = 6.6 Hz, 3H), 0.73 (d, J = 6.6 Hz, 3H).

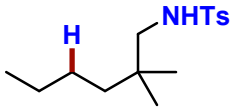
***N*-(2,2-dimethylpentyl)-4-methylbenzenesulfonamide (6a)**



6a

White solid. mp: 65-66 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.37 (t, J = 6.6 Hz, 1H), 2.68 (d, J = 6.9 Hz, 2H), 2.43 (s, 3H), 1.11–1.18 (m, 4H), 0.84 (t, J = 6.6 Hz, 3H), 0.82 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.24, 137.02, 129.64, 127.07, 52.99, 41.92, 33.76, 24.89, 21.49, 16.88, 14.7. **IR** (thin film, cm^{-1}): 3355, 2948, 2830, 1418. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{14}H_{23}NNaO_2S$, 292.1342; found, 292.1341.

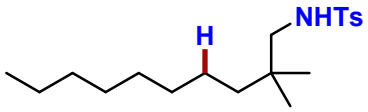
***N*-(2,2-Dimethylhexyl)-4-methylbenzenesulfonamide (7a)**



7a

White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.30 (t, J = 6.9 Hz, 1H), 2.68 (d, J = 6.9 Hz, 2H), 2.43 (s, 3H), 1.19–1.25 (m, 2H), 1.09–1.1.17 (m, 4H), 0.84 (t, J = 7.2 Hz, 3H), 0.82 (s, 6H).

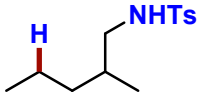
***N*-(2,2-dimethyldectyl)-4-methylbenzenesulfonamide (8a)**



8a

White solid. **mp**: 41-42 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.2 Hz, 2H), 4.30 (br s, 1H), 2.68 (d, J = 6.8 Hz, 2H), 2.43 (s, 3H), 1.25–1.30 (m, 2H), 1.15–1.23 (m, 8H), 1.10–1.14 (m, 4H), 0.88 (t, J = 7.1 Hz, 3H), 0.82 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.15, 137.05, 129.62, 127.07, 52.98, 39.51, 33.67, 31.85, 30.35, 29.53, 29.28, 24.88, 23.64, 22.63, 21.47, 14.07. **IR** (thin film, cm^{-1}): 3357, 2946, 2834, 1457. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{19}H_{33}NNaO_2S$, 362.2124; found, 362.2127.

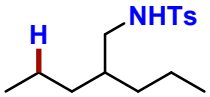
***N*-(2-methylpentyl)-4-methyl- benzenesulfonamide (9a)**



9a

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.38 (t, *J* = 5.4 Hz, 1H), 2.84 (ddd, *J* = 12.3, 8.1, 5.4 Hz, 1H), 2.72 (ddd, *J* = 12.3, 8.1, 5.4 Hz, 1H), 2.43 (s, 3H), 1.53 – 1.58 (m, 1H), 1.17–1.31 (m, 3H), 1.10 – 1.06 (m, 1H), 0.85 (d, *J* = 8.1 Hz, 3H), 0.83 (t, *J* = 6.9 Hz, 3H).

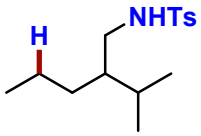
***N*-(2-propylpentyl)-4-methyl- benzenesulfonamide (10a)**



10a

White solid. **mp**: 86-87 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.21 (t, *J* = 6.3 Hz, 1H), 2.85 (t, *J* = 6.3 Hz, 2H), 2.43 (s, 3H), 1.41–1.45 (m, 1H), 1.16–1.23 (m, 8H), 0.83 (t, *J* = 6.6 Hz, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.28, 137.04, 129.64, 127.11, 46.17, 37.32, 33.72, 21.49, 19.61, 14.23. **IR** (thin film, cm^{-1}): 3348, 2951, 2834, 1457. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{15}H_{25}NNaO_2S$, 306.1498; found, 306.1505.

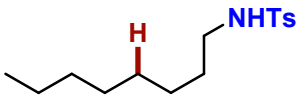
***N*-(2-isopropylpentyl)-4-methylbenzenesulfonamide (11a)**



11a

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.22 (br s, 1H), 2.82–2.89 (m, 2H), 2.43 (s, 3H), 1.65–1.70 (m, 1H), 1.12 – 1.27 (m, 4H), 1.05–1.09 (m, 1H), 0.83 (t, *J* = 6.9 Hz, 3H), 0.79 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.26, 137.00, 129.64, 127.11, 44.13, 43.65, 30.52, 28.04, 21.49, 20.58, 19.43, 18.80, 14.26. **IR** (thin film, cm^{-1}): 3351, 2946, 2834, 1661. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{15}H_{25}NNaO_2S$, 306.1498; found, 306.1506.

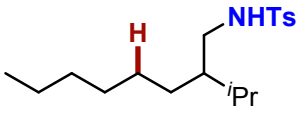
***N*-octyl4-methylbenzenesulfonamide (12a)**



12a

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.23 (br s, 1H), 2.93 (dd, *J* = 12.3, 6.7 Hz, 2H), 2.43 (s, 3H), 1.41–1.46 (m, 2H), 1.20–1.30 (m, 10H), 0.87 (t, *J* = 7.1 Hz, 3H).

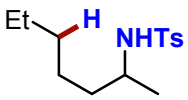
***N*-(2-isopropyloctyl)-4-methylbenzenesulfonamide (13a)**



13a

White solid. **mp**: 34-35 ºC;**^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 4.20 (t, *J* = 6.1 Hz, 1H), 2.82–2.90 (m, 2H), 2.43 (s, 3H), 1.68 (sext, *J* = 6.4 Hz, 1H), 1.22–1.26 (m, 3H), 1.15–1.21 (m, 6H), 1.10–1.12 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.79 (t, *J* = 6.7 Hz, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.21, 136.94, 129.62, 127.11, 44.05, 43.84, 31.74, 29.53, 28.23, 28.01, 27.39, 22.60, 21.48, 19.40, 18.85, 14.05. **IR** (thin film, cm^{-1}): 3357, 2948, 2830, 1455. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{18}H_{31}NNaO_2S$, 348.1968; found, 348.1971.

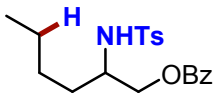
***N*-(heptan-2-yl)-4-methylbenzenesulfonamide (14a)**



14a

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 4.28 (d, *J* = 7.6 Hz, 1H), 3.26–3.32 (m, 1H), 2.42 (s, 3H), 1.29–1.37 (m, 2H), 1.07–1.24 (m, 6H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.08, 138.22, 129.55, 127.00, 49.93, 37.37, 31.36, 25.11, 22.43, 21.74, 21.46, 13.90. **IR** (thin film, cm^{-1}): 3361, 2946, 2834, 1416. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{14}H_{23}NNaO_2S$, 292.1342; found, 292.1337.

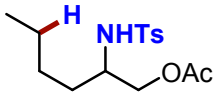
2-((4-methylphenyl)sulfonamido)hexyl benzoate (15a)



15a

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 4.65 (d, *J* = 8.7, 1H), 4.26 (dd, *J* = 8.7, 5.7 Hz, 1H), 4.13 (dd, *J* = 8.7, 5.7 Hz, 1H), 3.58–3.63 (m, 1H), 2.33 (s, 3H), 1.54–1.60 (m, 2H), 1.23–1.29 (m, 4H), 0.83 (t, *J* = 6.9 Hz, 3H).

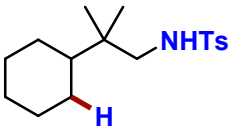
2-((4-methylphenyl)sulfonamido)hexyl acetate (16a)



16a

Colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.61 (d, *J* = 8.4 Hz, 1H), 3.98 (dd, *J* =8.4, 5.4 Hz, 1H), 3.89 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.42–3.50 (m, 1H), 2.42 (s, 3H), 1.95 (s, 3H), 1.36–1.48 (m, 2H), 1.17–1.27 (m, 4H), 0.80 (t, *J* = 6.6 Hz, 3H).

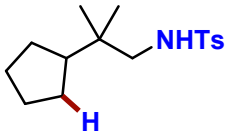
***N*-(2-cyclohexyl-2-methylpropyl)-4-methylbenzenesulfonamide (17a)**



17a

White solid. **mp**: 140-141 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.25 (t, *J* = 5.4 Hz, 1H), 2.72 (d, *J* = 6.9 Hz, 2H), 2.43 (s, 3H), 1.72 (d, *J* = 12.9 Hz, 2H), 1.62 (d, *J* = 12.6 Hz, 1H), 1.56 (d, *J* = 12.9 Hz, 2H), 1.01–1.17 (m, 5H), 0.85–0.92 (m, 2H), 0.79 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.18, 136.93, 129.62, 127.07, 51.70, 43.66, 35.98, 26.90, 26.85, 26.47, 22.60, 21.47. **IR** (thin film, cm^{-1}): 3353, 2944, 2834，1422, 1118. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{17}H_{27}NNaO_2S$, 332.1655; found, 332.1655.

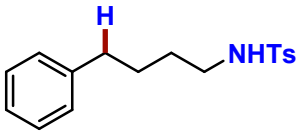
***N*-(2-cyclopentyl-2-methylpropyl)-4-methylbenzenesulfonamide (18a)**



18a

White solid. **mp**: 93-94 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.0 1Hz, 2H), 4.32 (t, *J* = 6.6 Hz, 1H), 2.70 (d, *J* = 6.9 Hz, 2H), 2.43 (s, 3H), 1.67–1.73 (m, 1H), 1.46–1.55 (m, 6H), 1.14–1.19 (m, 2H), 0.80 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.24, 136.98, 129.65, 127.06, 53.13, 46.83, 35.55, 26.64, 25.48, 22.32, 21.51. **IR** (thin film, cm^{-1}): 3357, 2946, 2834，1453，1034. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{16}H_{25}NNaO_2S$, 318.1498; found, 318.1490.

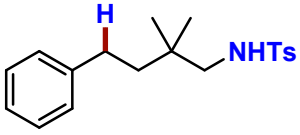
***N*-(4-phenylbutyl)-4-methyl- benzenesulfonamide (19a)**



19a

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 3H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 2H), 4.24–4.29 (m, *J* = 5.8 Hz, 1H), 2.95 (dt, *J* = 10.2, 6.9 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.42 (s, 3H), 1.56–1.61 (m, 2H), 1.45–1.50 (m, 2H).

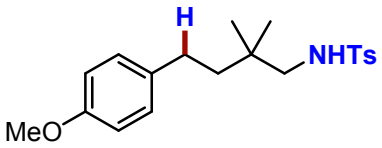
***N*-(2,2-Dimethyl-4-phenylbutyl)-4-methylbenzenesulfonamide (20a)**



20a

White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 2H), 4.34 (t, *J* = 6.9 Hz, 1H), 2.74 (d, *J* = 6.9 Hz, 2H), 2.49 (ddd, *J* = 8.7, 5.1, 3.9 Hz, 2H), 2.42 (s, 3H), 1.49 (ddd, *J* = 8.7, 5.1, 3.9 Hz, 2H), 0.92 (s, 6H).

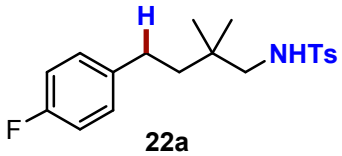
***N*-(4-(4-Methoxyphenyl)-2,2-dimethylbutyl)-4-methylbenzenesulfonamide (21a)**



21a

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.34 (t, *J* = 6.6 Hz, 1H), 3.78 (s, 3H), 2.73 (d, *J* = 6.9 Hz, 2H), 2.44 (ddd, *J* = 8.7, 5.1, 3.6 Hz, 1H), 2.42 (s, 3H), 1.46 (ddd, *J* = 8.7, 5.1, 3.6, 1H), 0.91 (s, 6H).

***N*-(4-(4-Fluorophenyl)-2,2-dimethylbutyl)-4-methylbenzenesulfonamide (22a)**

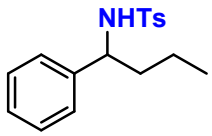


22a

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.08 (dd, *J* = 8.4, 5.6 Hz, 2H), 6.93 (t, *J* = 8.7 Hz, 2H), 4.47 (t, *J* = 8.7 Hz, 2H), 2.73 (d, *J* = 6.9 Hz, 2H), 2.47 (ddd, *J* = 8.7, 5.1, 3.6 Hz, 1H), 2.42 (s, 3H), 1.47 (ddd, *J* = 8.7, 5.1, 3.6 Hz, 1H), 0.92 (d, *J* = 5.1 Hz, 6H).

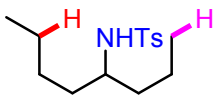
***N*-(1-phenylbutyl)-4-methyl-benzenesulfonamide (23a)**

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.1 Hz, 2H), 7.14–7.15 (m, 3H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.99–7.00 (m, 2H), 4.84 (d, *J* = 7.1 Hz, 1H), 4.27 (q, *J* = 7.3 Hz, 1H), 2.35 (s, 3H), 1.72–1.78 (m, 1H), 1.62–1.68 (m, 1H), 1.2–1.30 (m, 1H), 1.20–1.09 (m, 1H), 0.83 (t, *J* = 7.4 Hz, 3H).



23a

***N*-(octan-4-yl)-4-methyl- benzenesulfonamide (24a)**

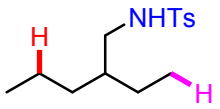


24a

White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* =

8.1 Hz, 2H), 4.11 (d, *J* = 8.4 Hz, 1H), 1.33–1.39 (m, 2H), 1.24–1.30 (m, 3H), 1.11–1.19 (m, 4H), 1.04–1.09 (m, 1H), 0.78 (t, *J* = 7.2 Hz, 6H).

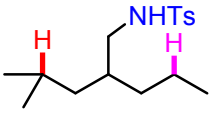
***N*-(2-ethylpentyl)-4-methylbenzenesulfonamide (25a)**



25a

White solid. **mp**: 48-49 ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = k8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.19–4.23 (m, 2H), 2.84–2.86 (m, 2H), 2.43 (s, 3H), 1.33–1.40 (m, 1H), 1.24–1.29 (m, 2H), 1.16–1.23 (m, 4H), 0.84 (t, *J* = 6.6 Hz, 3H), 0.79 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.22, 136.95, 129.61, 127.07, 45.72, 38.91, 33.18, 23.82, 21.47, 19.59, 14.20, 10.63. **IR** (thin film, cm^{-1}): 3353, 2944, 2834, 1459, 1036. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{14}H_{23}NNaO_2S$, 292.1342; found, 292.1351.

***N*-(4-methyl-2-propylpentyl)-4-methyl-benzenesulfonamide (26a)**



26a

White solid. **mp**: 59-61ºC; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.46 (br s, 1H), 2.80–2.85 (m, 2H), 2.43 (s, 3H), 1.47–1.53 (m, 2H), 1.15–1.20 (m, 4H), 1.02–1.04 (m, 2H), 0.82 (t, *J* = 6.3 Hz, 3H), 0.79 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.27, 137.00, 129.63, 127.10, 46.29, 41.15, 35.10, 33.91, 25.06, 22.69, 21.48, 19.42, 14.23. **IR** (thin film, cm^{-1}): 3369, 2951, 2834, 1455. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{16}H_{27}NNaO_2S$, 320.1655; found, 320.1658.

Procedures for Copper-Catalyzed Remote (δ) C(sp^3)-H Bond Amination

Procedure A:1a (26.9 mg, 0.10 mmol), $Cu(OTf)_2$ (10 mol%, 3.6 mg, 0.01 mmol), $PhI(OTFA)_2$ (2.0 equiv, 86.0 mg, 0.2 mmol) were weighed in the air and charged into an oven-dried 25 mL Schlenk tube. After addition of 1.0 mL DCE, the sealed tube

was placed in a 100 ℃ parallel synthesizer and stirred for 10 h. After completion, the reaction mixture was cooled down to room temperature and the solvent was removed under reduced pressure. Flash Silica gel column purification (2% EtOAc/ petroleum ether) of the crude product provided **2a** (21.4 mg, 0.08mmol) in 80% isolated yield.

Procedure B: Changed: $PhI(OTFA)_2$ (3.0 equiv, 129.0 mg, 0.3 mmol). Other process is the same as the **Procedure A.**

Procedure C: Changed: $PhI(OTFA)_2$ (2.5 equiv, 107.5 mg, 0.25 mmol). Other process is the same as the **Procedure A.**

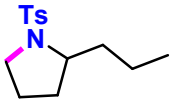
Procedure D: Changed: CuI (10 mol%, 1.9 mg, 0.01 mmol). Other process is the same as the **Procedure A.**

Procedure E: Changed: Changed: $PhI(OTFA)_2$ (4.0 equiv, 172.0 mg, 0.4 mmol). Other process is the same as the **Procedure A.**

Characterization Data for Pyrrolidines

Compound **1b**,[3] **2b**,[2] **3b**,[3] **4b**,[2] **5b**,[2] **6b**,[8] **7b**,[4] **9b**,[3] **12b**,[9] **14b**,[10] **15b**,[3] **16b**,[3] **19b**,[4] **20b**,[4] **21b**,[4] **22b**,[4] **23b,**[4] **24b**,[11] can be found in the literature.

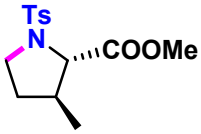
2-propyl-1-tosylpyrrolidine (1b)



1b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 3.61 (ddt, *J* = 9.0, 6.9, 4.8 Hz, 1H), 3.37 (ddd, *J* = 10.5, 7.2, 5.1 Hz, 1H), 3.19 (ddd, *J* = 10.5, 7.2, 5.2 Hz, 1H), 2.43 (s, 3H), 1.73–1.84 (m, 2H), 1.53–1.58 (m, 3H), 1.41–1.50 (m, 2H), 1.34 (sext, *J* = 7.2 Hz, 2H), 0.94 (t, *J* = 7.2 Hz, 3H).

(2S,3S)-Methyl 3-methyl-2-carboxylate 1-tosylpyrrolidine (2b)

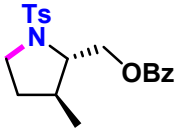


2b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 3.80 (d, *J* = 5.4 Hz, 1H), 3.75 (s, 3H), 3.41–3.47 (m, 2H), 2.43 (s, 3H),

2.36 (quint, J = 6.3 Hz, 1H), 2.04 (sext, J = 6.3 Hz, 1H), 1.36 (sext, J = 6.6 Hz, 1H), 0.93 (d, J = 6.9 Hz, 3H).

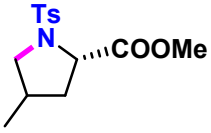
((2S,3S)-3-methyl-2-methyl benzoate)-1-tosylpyrrolidine (3b)



3b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.02 (d, J = 8.1 Hz, 2H), 7.77 (d, J = 8.1 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 4.52 (dd, J = 11.2, 3.9 Hz, 1H), 4.43 (dd, J = 11.2, 6.7 Hz, 1H), 3.56 (dt, J = 6.7, 3.9 Hz, 1H), 3.44 (ddd, J = 10.3, 6.9, 6.1 Hz, 1H), 3.38 (ddd, J = 10.3, 6.9, 6.1 Hz, 1H), 2.41 (s, 3H), 2.19–2.24 (m, 1H), 2.00 (sext, J = 6.6 Hz, 1H), 1.21–1.27 (m, 1H), 0.68 (d, J = 6.9 Hz, 3H).

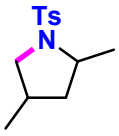
methyl (2S)-4-methyl- -2-carboxylate-1-tosylpyrrolidine (4b)



4b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.2 Hz, 1/2×4H, 1/2×4H), 4.34 (dd, J = 9.1, 2.9 Hz, 1H), 4.26 (t, J = 8.3 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.56–3.59 (m, 1/2×2H, 1/2×2H), 2.97 (t, J = 9.9 Hz,1H), 2.80 (t, J = 8.8 Hz, 1H), 2.43 (s, 1/2×6H, 1/2×6H), 2.31–2.35 (m, 1H), 2.07 (ddd, J = 12.8, 6.2, 2.9 Hz, 1H), 1.92–1.98 (m, 1H), 1.57–1.66 (m, 3H), 0.99 (d, J = 6.6 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H).

2,4-dimethyl-1-tosylpyrrolidine (5b)

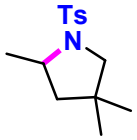


5b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 2/5×3H, 3/5×3H), 7.31 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 3.73–3.78 (m, 2/5×1H), 3.58–3.62 (m, 3/5×1H), 3.51–3.57 (m, 2H), 2.91 (t, J = 10.7 Hz, 3/5×1H), 2.58 (t, J = 9.3 Hz,

2/5×1H). 2.43 (s, 2/5×5H, 3/5×5H), 2.31–2.38 (m, 1H), 2.04–2.08 (m, 1H), 1.54–1.60 (m, 2H), 1.40 (d, J = 6.2 Hz, 3H), 1.30 (d, J = 6.4 Hz, 2H), 1.25–1.29 (m, 1H), 1.11–1.16 (m, 1H), 0.92 (t, J = 6.2 Hz, 3H), 0.84 (d, J = 6.4 Hz, 2H).

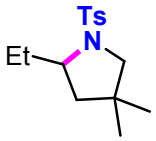
(*R*)-2,4,4-trimethyl-1-tosylpyrrolidine (6b)



6b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 3.64 (sext, J = 6.8 Hz 1H), 3.17 (d, J = 10.4 Hz, 1H), 3.07 (d, J = 10.4 Hz, 1H), 2.42 (s, 3H), 1.73 (dd, J = 12.5, 7.2 Hz, 1H), 1.41 (d, J = 6.1 Hz, 4H), 1.04 (s, 3H), 0.55 (s, 3H).

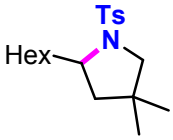
2-ethyl-4,4-dimethyl-1-tosylpyrrolidine (7b)



7b

Colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 3.54 (ddt, J = 9.5, 9.2, 3.2 Hz, 1H), 3.12 (d, J = 10.6 Hz, 1H), 3.10 (d, J = 10.6 Hz, 1H), 2.42 (s, 3H), 2.06–2.16 (m, 1H), 1.68 (dd, J = 12.5, 7.2 Hz, 1H), 1.51–1.60 (m, 1H), 1.42 (dd, J = 12.5, 8.8 Hz, 1H), 1.02 (s, 3H), 0.85 (t, J = 7.5 Hz, 3H), 0.53 (s, 3H).

2-hexyl-4,4-dimethyl-1-tosylpyrrolidine (8b)

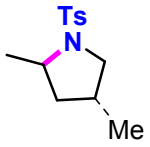


8b

Yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 3.54–3.59 (m, 1H), 3.12 (q, J = 10.6 Hz, 2H), 2.42 (s, 3H), 2.08–2.13 (m, 1H), 1.70 (dd, J = 12.5, 7.2 Hz, 1H), 1.49–1.55 (m, 1H), 1.43 (dd, J = 12.5, 8.8 Hz, 1H), 1.19 –1.31 (m, 8H), 1.02 (s, 3H), 0.89 (t, J = 6.9 Hz, 3H), 0.54 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.97, 135.76, 129.42, 127.37, 61.34, 60.38, 46.22, 37.32,

36.35, 31.80, 29.22, 26.46, 25.87, 25.64, 22.56, 21.46, 14.04. **IR** (thin film, cm^{-1}): 3369, 2951, 2836. **HRMS–ESI** (*m/z*): $[M+H]^+$ calcd. for $C_{19}H_{32}NO_2S$, 338.2148; Found: 338.2149.

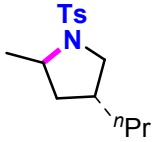
2,4-dimethyl-1-tosylpyrrolidine (9b)



9b (**5b**)

Colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 1/2×4H, 1/2×4H), 7.31 (d, *J* = 8.1 Hz, 1/2×4H, 1/2×4H), 3.73–3.78 (m, 1H), 3.51–3.64 (m, 3H), 2.91 (t, *J* = 10.7 Hz, 1H), 2.58 (t, *J* = 9.3 Hz, 1H). 2.43 (s, 1/2×6H, 1/2×6H), 2.32–2.40 (m, 1H), 2.03–2.09 (m, 1H), 1.54–1.62 (m, 2H), 1.40 (d, *J* = 6.2 Hz, 3H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.24–1.29 (m, 1H), 1.09–1.17 (m, 1H), 0.91 (t, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H).

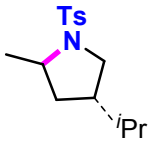
2-methyl-4-propyl-1-tosylpyrrolidine (10b)



10b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 1/2×4H, 1/2×4H), 7.31 (d, *J* = 7.8 Hz, 1/2×4H, 1/2×4H), 3.73–3.77 (m, 1H), 3.54–3.59 (m, 3H), 2.93 (t, *J* = 10.8 Hz, 1H), 2.60 (t, *J* = 9.4 Hz, 1H), 2.43 (s, 6H), 2.1–2.28 (m, 1H), 2.04–2.08 (m, 1H), 1.57–1.62 (m, 2H), 1.43–1.49 (m, 1H), 1.38 (d, *J* = 6.1 Hz, 3H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.18–1.24 (m, 6H), 1.07–1.15 (m, 3H), 0.83 (t, *J* = 7.1 Hz, 3H), 0.82 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.08, 135.42, 134.68, 129.54, 129.49, 127.48, 127.39, 56.84, 55.77, 54.62, 54.34, 41.47, 39.53, 37.77, 36.57 , 34.95, 34.76, 23.36, 22.75, 21.47, 21.28, 21.22, 14.03, 14.00. **IR** (thin film, cm^{-1}): 3356, 2948, 2834. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{15}H_{23}NNaO_2S$, 304.1342; Found: 304.1350.

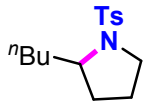
4-isopropyl-2-methyl-1-tosylpyrrolidine (11b)



11b

Yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 1/2×4H, 1/2×4H), 7.31 (d, *J* = 7.5 Hz, 1/2×4H, 1/2×4H), 3.77–3.82 (m, 1H), 3.54–3.60 (m, 3H), 2.98 (t, *J* = 10.7 Hz, 1H), 2.61 (t, *J* = 9.8 Hz, 1H), 2.44 (s, 3H), 2.43 (s, 3H), 2.03–2.09 (m, 1H), 1.93–2.01 (m, 1H), 1.56–1.59 (m, 1H), 1.38 (d, *J* = 6.1 Hz, 3H), 1.31–1.35 (m, 1H), 1.29 (d, *J* = 6.5 Hz, 3H), 1.19–1.26 (m, 2H), 1.15–1.18 (m, 2H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 6.5 Hz, 3H), 0.79 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.08, 135.38, 134.58, 129.54, 29.49, 127.44, 127.34, 57.10, 56.09, 53.54, 53.26, 45.32, 44.13, 40.04, 37.73, 31.79, 31.46, 23.45, 22.58, 21.47, 21.42, 21.26, 21.14, 20.95. **IR** (thin film, cm^{-1}): 3367, 2951, 2832, 1665. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{15}H_{23}NNaO_2S$, 304.1342; Found: 304.1349.

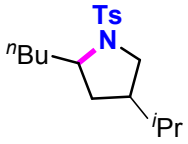
2-butyl-1-tosylpyrrolidine (12b)



12b

Yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 3.57–3.61 (m, 1H), 3.35–3.39 (m, 1H), 3.16–3.20 (m, 1H), 2.43 (s, 3H), 1.80–1.86 (m, 1H), 1.73–1.79 (m, 1H), 1.53–1.57 (m, 2H), 1.42–1.50 (m, 2H), 1.25–1.37 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H).

2-butyl-4-isopropyl-1-tosylpyrrolidine (13b)

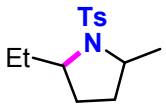


13b

Yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 1/2×4H, 1/2×4H), 7.31 (d, *J* = 8.1 Hz, 1/2×4H, 1/2×4H), 3.59–3.64 (m, 2H), 3.49–3.56 (m, 2H), 2.90 (t, *J* = 11.2 Hz, 1H), 2.62 (t, *J* = 9.9 Hz, 1H), 2.44 (s, 3H), 2.43 (s, 3H), 1.97–2.07 (m,

2H), 1.86–1.95 (m, 1H), 1.73–1.81 (m, 1H), 1.68 (dd, *J* = 12.3, 6.1 Hz, 1H), 1.03–1.59 (m, 15H), 0.91 (t, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 3.7 Hz, 3H), 0.78 (d, *J* = 3.7 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.08, 143.06, 135.71, 134.62, 129.56, 129.50, 127.55, 127.35, 61.28, 60.81, 53.55, 53.08, 45.62, 44.48, 37.31, 36.53, 36.39, 34.91, 32.03, 31.45, 28.56, 27.80, 22.68, 22.61, 21.49, 21.42, 21.32, 21.18, 21.05, 14.07, 14.06. **IR** (thin film, cm^{-1}): 3363, 2948, 2836. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{18}H_{29}NNaO_2S$, 346.1811; Found: 346.1815.

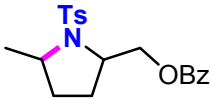
2-ethyl-5-methyl-1-tosylpyrrolidine (14b)



14b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2/5×3H), 7.72 (d, *J* = 8.0 Hz, 3/5×3H), 7.29 (d, *J* = 8.0 Hz, 2/5×3H), 7.26 (d, *J* = 8.0 Hz, 3/5×3H), 4.03 (qunit, *J* = 6.4 Hz, 1H), 3.73–3.76 (m, 1H), 3.67 (sext, *J* = 6.3 Hz, 3/5×1H), 3.49–3.54 (m, 3/5×1H), 2.42 (s, 2H), 2.41 (s, 3H), 1.84–2.08 (m, 2/5×4H, 3/5×4H), 1.67–1.70 (m, 1H), 1.41–1.59 (m, 2/5×6H, 3/5×6H), 1.32 (d, *J* = 6.4 Hz, 2H), 1.19 (d, *J* = 6.4 Hz, 3H), 0.93 (t, *J* = 7.5 Hz, 2H), 0.80 (t, *J* = 7.4 Hz, 3H).

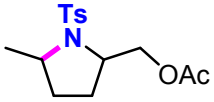
(5-methyl methyl benzoate)-1-tosylpyrrolidinel (15b)



15b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.1 Hz, 2H), 7.83 (d, *J* = 7.1 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.53–7.58 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 4.48–4.53 (m, 2H), 4.36–4.39 (m, 2H), 4.21–4.24 (m, 1H), 4.14 (quint, *J* = 6.6 Hz, 1H), 3.98–4.03 (m, 1H), 3.71 (sext, *J* = 6.5 Hz, 1H), 2.43 (s, 3H), 2.27 (s, 3H), 2.16–2.22 (m, 2H), 1.88–1.92 (m, 1H), 1.78–1.84 (m, 1H), 1.68–1.73 (m, 1H), 1.56–1.61 (m, 3H), 1.38 (d, *J* = 6.3 Hz, 3H), 1.29 (d, *J* = 6.4 Hz, 3H).

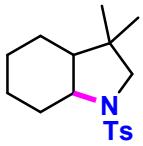
(5-methyl methyl acetate)-1-tosylpyrrolidine (16b)



16b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (t, *J* = 8.8 Hz, 2/5×4H, 3/5×4H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 4.25–4.29 (m, 1H), 4.20 (dd, *J* = 11.0, 4.8 Hz, 1H), 4.13 (dd, *J* = 11.0, 7.2 Hz, 1H), 4.03–4.09 (m, 3H), 3.88 (hept, *J* = 3.9 Hz 1H), 3.68 (sext, *J* = 6.3 Hz, 1H), 2.43 (s, 3H), 2.42 (s, 3H), 2.03–2.15 (m, 2H), 2.08 (s, 3H), 1.95 (s, 3H), 1.79–1.82 (m, 1H), 1.65–1.70 (m, 2H), 1.48–1.55 (m, 2/5×3H, 3/5×3H), 1.35 (d, *J* = 6.3 Hz, 3H), 1.22 (d, *J* = 6.4 Hz, 3H).

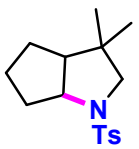
3,3-dimethyl-1-tosyloctahydro-*1H*-indole (17b)



17b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 3.54 (m, 1H), 3.31 (d, *J* = 10.6 Hz, 1H), 3.06 (d, *J* = 10.6 Hz, 1H), 2.51 (m, 1H), 2.43 (s, 3H), 1.66–1.68 (m, 1H), 1.49–1.59 (m, 3H), 1.11–1.26 (m, 2H), 0.90 (s, 3H), 0.46 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.10, 134.21, 129.42, 127.53, 60.38, 58.90, 47.79, 38.95, 28.86, 27.05, 24.65, 24.36, 21.87, 21.52, 20.32. **IR** (thin film, cm^{-1}): 3361, 2946, 2832, 1457. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{17}H_{25}NNaO_2S$, 330.1498; Found: 330.1501.

3,3-dimethyl-1-tosyloctahydrocyclopenta[*b*]pyrrole (18b)

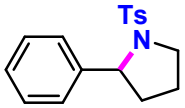


18b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.02–4.05 (m, 1H), 3.14 (d, *J* = 10.4 Hz, 1H), 3.08 (d, *J* = 10.4 Hz, 1H), 2.42 (s, 3H), 2.01 (q, *J* = 8.0 Hz, 1H), 1.97 (q, *J* = 6.3 Hz, 2H), 1.72–1.75(m, 1H), 1.54–1.58 (m, 1H), 1.39–1.46 (m, 2H), 0.95 (s, 3H), 0.54 (s, 3H). **^{13}C NMR** (150

MHz, $CDCl_3$) δ 142.94, 136.10, 129.44, 127.26, 65.33, 59.56, 55.75, 39.55, 34.90, 28.08, 27.38, 26.01, 21.93, 21.50. **IR** (thin film, cm^{-1}): 3363, 2948, 2834. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{16}H_{23}NNaO_2S$, 316.1342; Found: 316.1331.

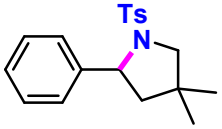
2-phenyl-1-tosylpyrrolidine (19b)



19b

Colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.26–7.30 (m, , 6H), 7.19–7.24 (m, 1H), 4.79 (dd, *J* = 7.9, 3.6 Hz, 1H), 3.56–3.6 (m, 1H), 3.39–3.45 (m, 1H), 2.42 (s, 3H), 1.94–2.04 (m, 1H), 1.77–1.90 (m, 2H), 1.62–1.70 (m, 1H).

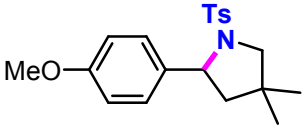
4,4-dimethyl-2-phenyl-1-tosylpyrrolidine (20b)



20b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 2H), 7.20–7.26 (m, 7H), 4.70 (t, *J* = 8.2 Hz, 2H), 3.44 (d, *J* = 10.4 Hz, 1H), 3.34 (d, *J* = 10.4 Hz, 1H), 2.40 (s, 3H), 2.02 (dd, *J* = 12.8, 7.4 Hz, 1H), 1.72 (dd, *J* = 12.8, 9.8 Hz, 1H), 1.05 (s, 3H), 0.76 (s, 3H).

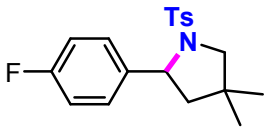
2-(4-Methoxyphenyl)-4,4-dimethyl-1-tosylpyrrolidine (21b)



21b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.79 (d, *J* = 8.1 Hz, 2H), 4.65 (t, *J* = 8.3 Hz, 1H), 3.79 (s, 3H), 3.43 (d, *J* = 10.3 Hz, 1H), 3.32 (d, *J* = 10.3 Hz, 1H), 2.40 (s, 3H), 1.98 (dd, *J* = 12.7, 7.2 Hz, 1H), 1.71 (t, *J* = 11.1Hz, 1H), 1.05 (s, 3H), 0.77 (s, 3H).

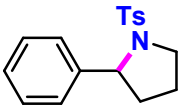
2-(4-Fluorophenyl)-4,4-dimethyl-1-tosylpyrrolidine (22b)



22b

Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 2H), 7.23 (d = 7.7 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 6.94 (t, *J* = 8.3 Hz, 2H), 4.67 (t, *J* = 8.3 Hz, 1H), 3.43 (d, *J* = 10.4 Hz, 1H), 3.33 (d, *J* = 10.4 Hz, 1H), 2.41 (s, 3H), 2.00 (dd, *J* = 12.8, 7.3 Hz, 1H), 1.69 (d, *J* = 12.8, 9.9 Hz, 1H), 1.05 (s, 3H), 0.75 (s, 3H).

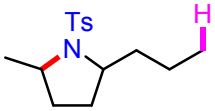
2-phenyl-1-tosylpyrrolidine (23b)



23b (19b)

Colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.8 Hz, 2H), 7.18–7.22 (m, 6H), 7.15–7.16 (m, 1H), 4.72 (dd, *J* = 8.0, 3.5 Hz, 1H), 3.52–3.55 (m, 1H), 3.33–3.38 (m, 1H), 2.35 (s, 3H), 1.89–1.93 (m, 1H), 1.72–1.80 (m, 2H), 1.58–1.61 (m, 1H).

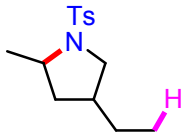
2-methyl-5-propyl-1-tosylpyrrolidine (24b)



24b

White Solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 4.01 (quint, *J* = 7.1 Hz, 1H), 3.80–3.83 (m, 1H), 3.66 (sext, *J* = 6.4 Hz, 1H), 3.55–3.60 (m, 1H), 2.43 (s, 3H), 2.41 (s, 3H), 2.02–2.09 (m, 1H), 1.95–2.01 (m, 1H), 1.80–1.89 (m, 2H), 1.67 (dd, *J* = 12.2, 6.8 Hz, 1H), 1.41–1.62 (m, 6H), 1.34–1.39 (m, 2H), 1.31 (d, *J* = 6.2 Hz, 3H), 1.28–1.30 (m, 1H), 1.19–1.25 (m, 2H), 1.18 (d, *J* = 6.5 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H).

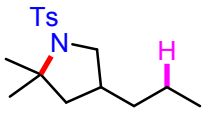
4-ethyl-2-methyl-1-tosylpyrrolidine (25b)



25b

Yellow Oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.8 Hz, 1/2×4H, 1/2×4H), 7.31 (d, *J* = 7.8 Hz, 1/2×4H, 1/2×4H), 3.76 (quint, *J* = 6.8 Hz 1H), 3.54–3.58 (m, 3H), 2.94 (t, *J* = 10.7 Hz, 1H), 2.61 (t, *J* = 9.4 Hz, 1H), 2.43 (s, 6H), 2.13–2.21 (m, 1H), 2.08 (quint, *J* = 6.4 Hz, 1H), 1.60 (dd, *J* = 12.2, 6.1 Hz, 1H), 1.41–1.43 (m, 1H), 1.39 (d, *J* = 6.1 Hz, 3H), 1.30 (d, *J* = 6.3 Hz, 3H), 1.23–1.27 (m, 3H), 1.12–1.19 (m, 3H), 0.82 (t, *J* = 6.9 Hz, 3H), 0.80 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.08, 135.35, 134.67, 129.55, 129.49, 127.47, 127.40, 56.90, 55.84, 54.46, 54.16, 41.12, 39.69, 39.17, 38.53, 25.67, 25.56, 23.34, 22.76, 21.48, 12.51, 12.41. **IR** (thin film, cm^{-1}): 3361, 2948, 2832. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{14}H_{21}NNaO_2S$, 290.1185; Found: 290.1197.

2,2-dimethyl-4-propyl-1-tosylpyrrolidine (26b)

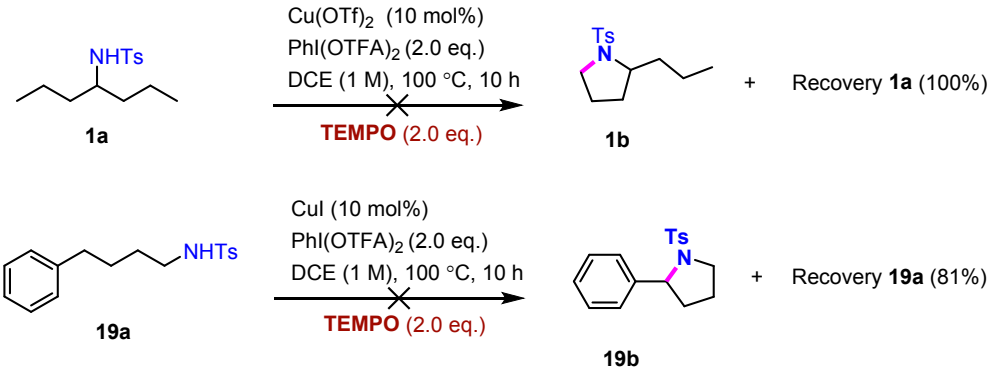


26b

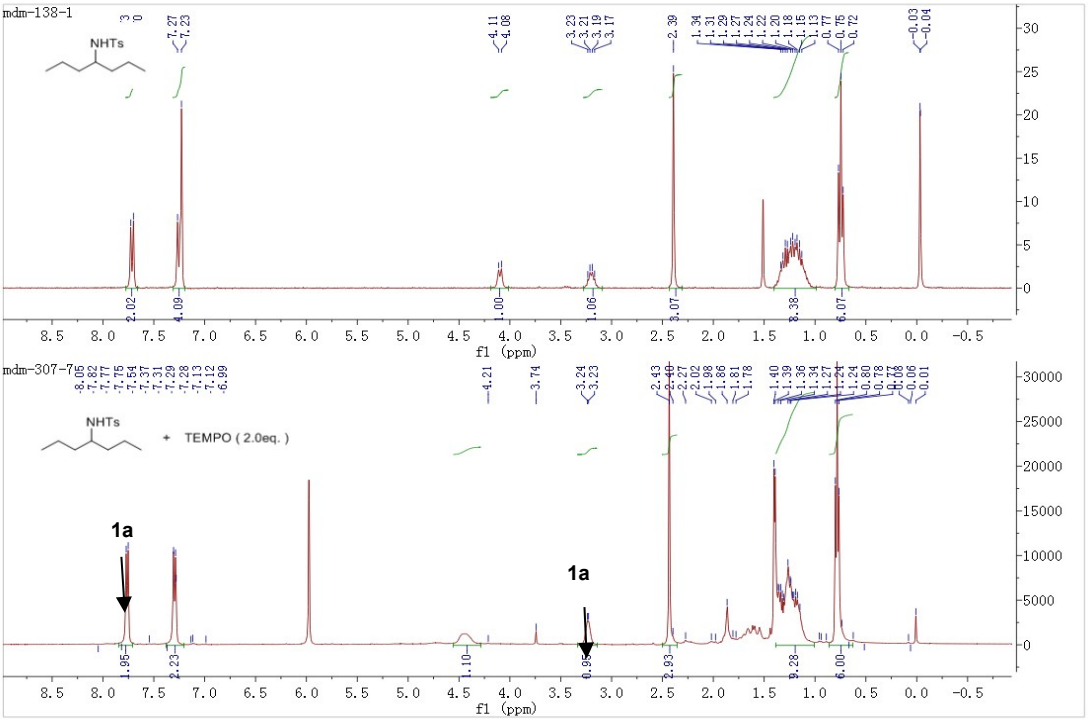
Colourless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 3.64 (t, *J* = 8.1 Hz, 1H), 2.77 (t, *J* = 9.6 Hz, 1H), 2.42 (s, 3H), 2.16–2.22 (m, 1H), 1.88 (dd, *J* = 12.1, 6.2 Hz, 1H), 1.46 (s, 3H), 1.43 (s, 3H), 1.23–1.28 (m, 4H), 0.88 (t, *J* = 6.4 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.46, 138.66, 129.33, 127.13, 65.61, 54.75, 49.60, 35.44, 35.17, 29.01, 28.46, 21.45, 21.29, 14.16. **IR** (thin film, cm^{-1}): 3357, 2946, 2836. **HRMS–ESI** (*m/z*): $[M+Na]^+$ calcd. for $C_{16}H_{25}NNaO_2S$, 318.1498; Found: 318.1501.

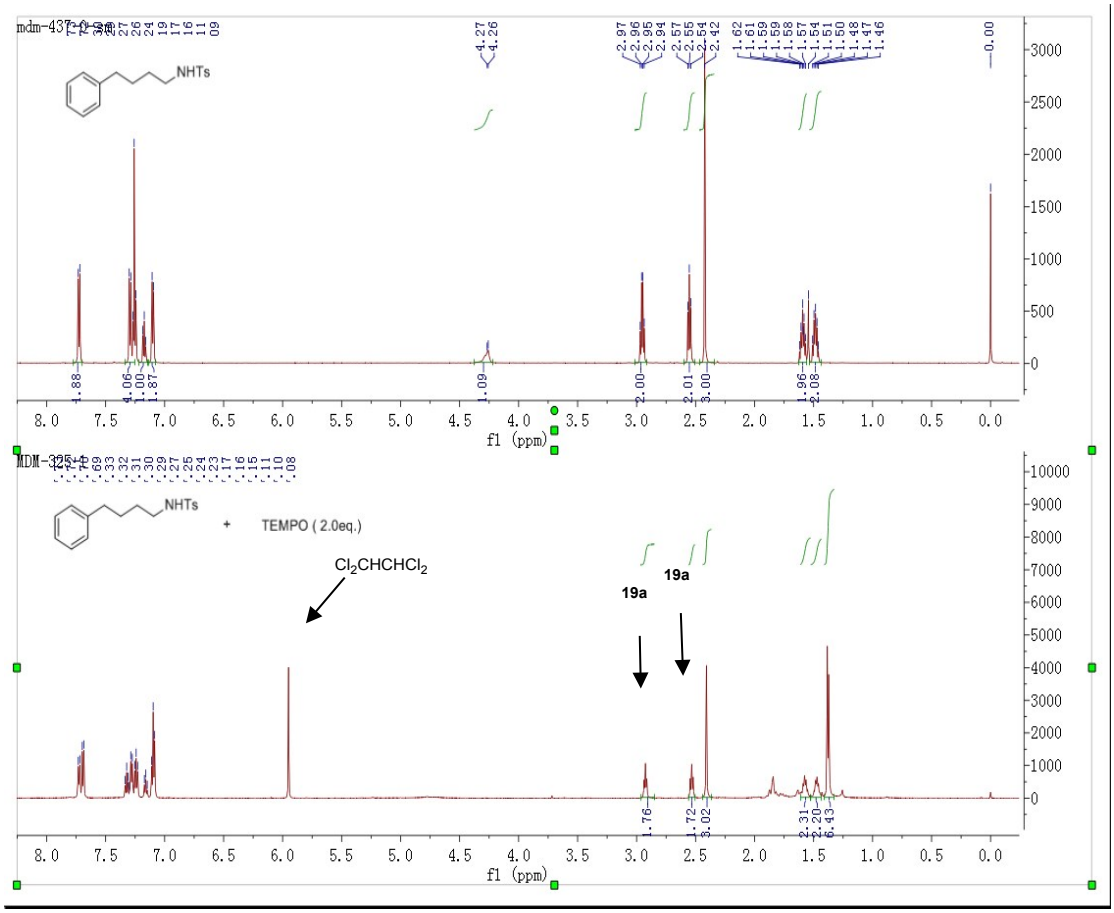
Mechanism Study

1. TEMPO Control Experiments

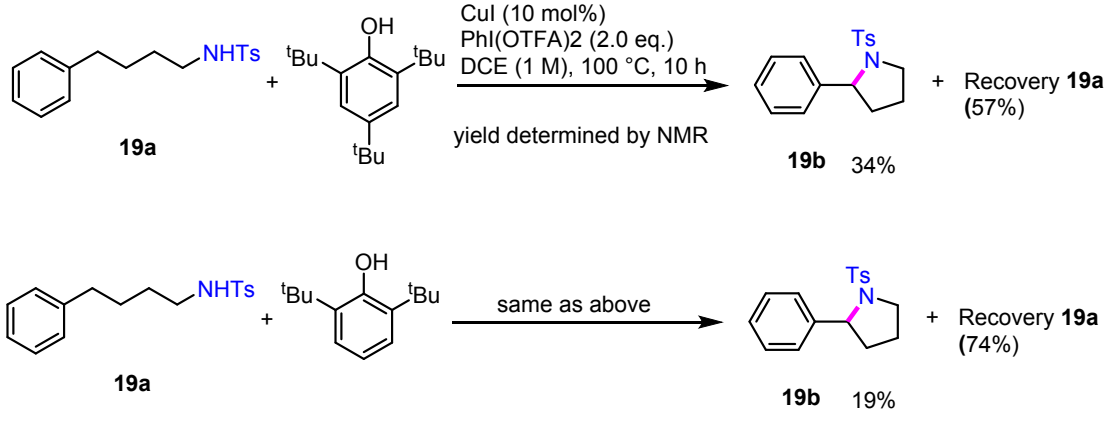


When 2.0 equiv of TEMPO was added under the standarder reaction condition, the reaction does not proceed at all, only the starting materials was detected form the crude ^{1}H NMR.

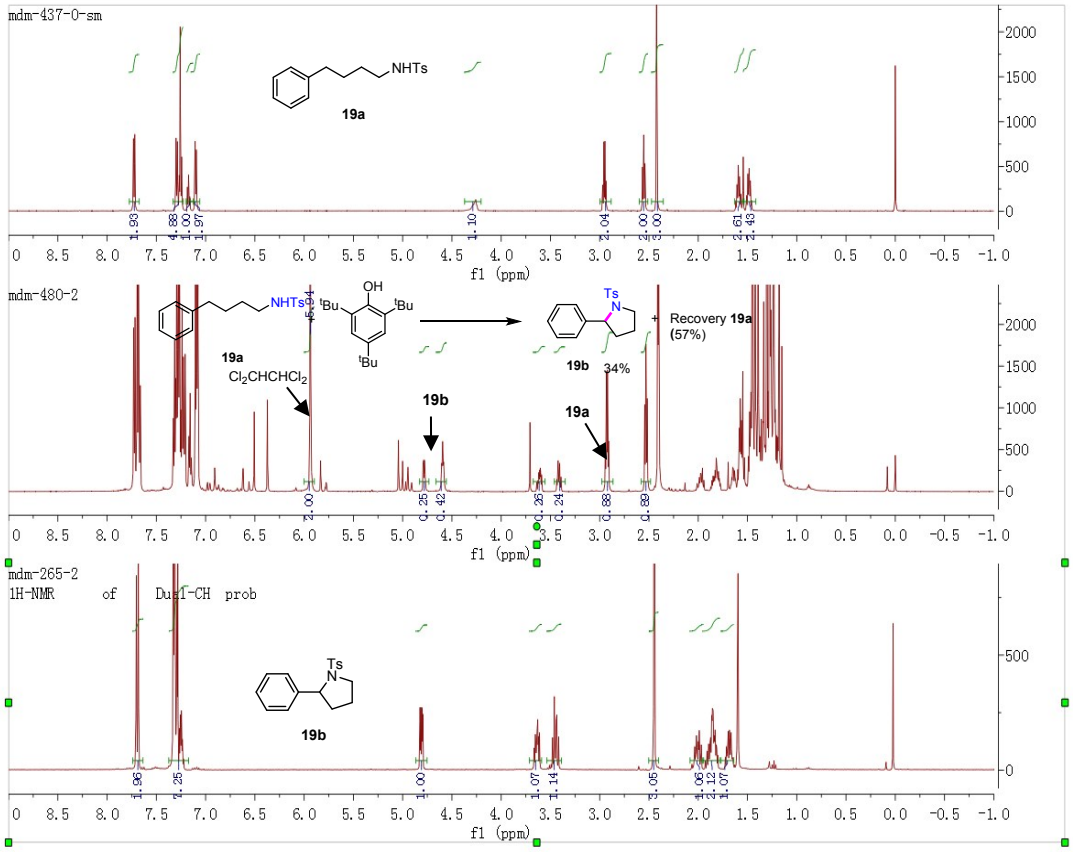




2. Radical capture experiments



The reaction yield was decreased significantly in the presence of 1.0 equiv 2,6-*di*-*tert*-butylphenol or 2, 4, 6-*tri*-*tert*-butylphenol.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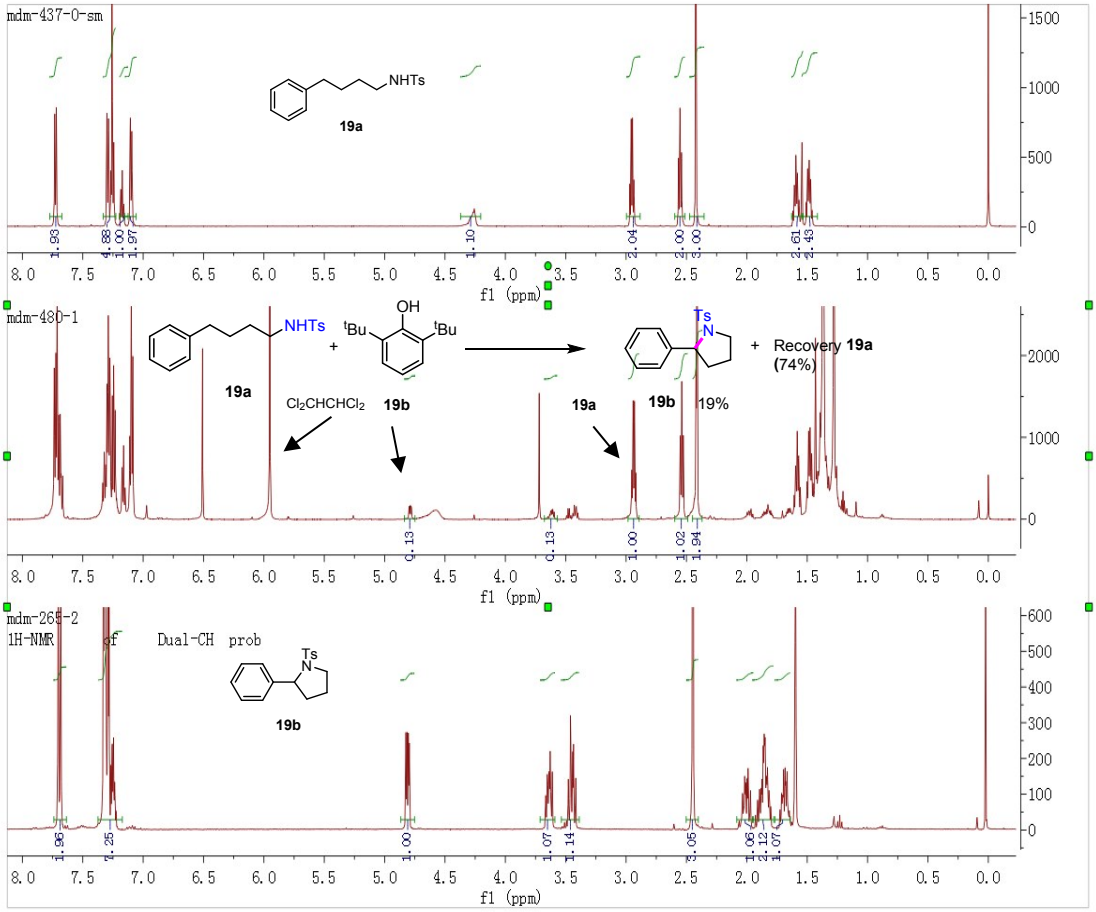
NHTs
19a
mdm-480-2
NHTs
OH
tBu
tBu
tBu
Ts
N
+ Recovery 19a
(57%)
19a
Cl2CHCHCl2
19b
19b 34%
19a
mdm-265-2
1H-NMR of Dual-CH prob
Ts
N
19b
f1 (ppm)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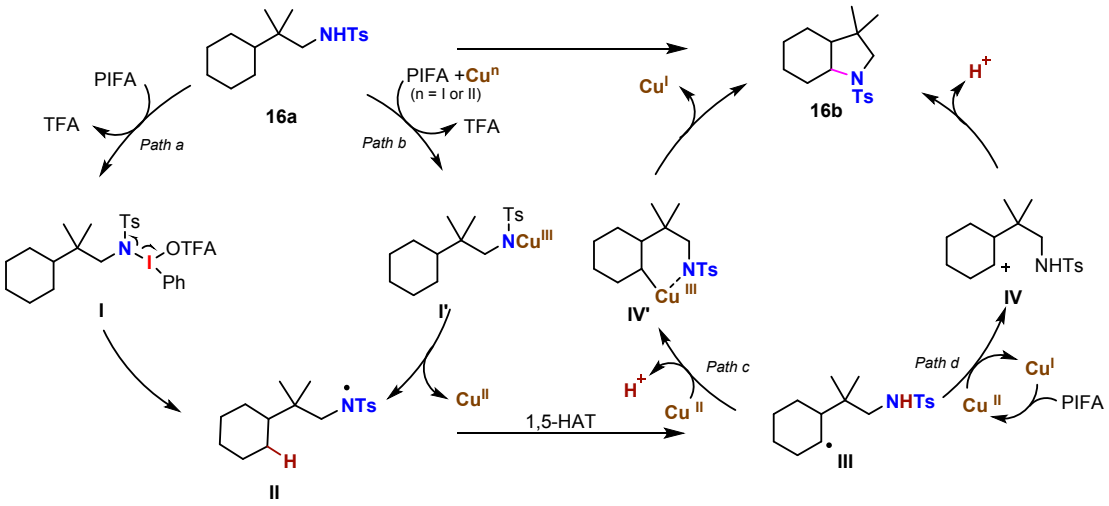
NHTs
19a
mdm-480-1
NHTs
+
OH
tBu
tBu
Ts
N
+ Recovery 19a
(74%)
19a
Cl2CHCHCl2
19b
19a
19b 19%
mdm-265-2
1H-NMR of Dual-CH prob
Ts
N
19b
f1 (ppm)

Proposed Mechanisms:



The reaction is initiated by generation of a polarized aminyl radical II followed by two possible ways. Direct oxidation of sulphonamides (**16a**) with PIFA generating the amido-λ^3-iodane **I**,[17] which underwent the homolysis of nitrogen-iodine bond forming the *N*−centered radical **II**. Or through formation of Cu(III) −sulphonamide intermediate **I'** followed by homolysis of the *N*−Cu bond. A subsequent 1,5−HAT of C−H bond by a polarized aminyl radical formed a carbon radical (**III**), which also followed by two possible pathways. One is the single-electron oxidation of carbon radical to give carbon cation (**IV**), which was captured by sulphonamide group to afford the cyclization product (**16b**) (Path a). Another is the oxidation addition of carbon radical by Cu(II) catalyst to generate Cu(III) −sulphonamide intermediate **IV'**, after reductive elimination to give the cyclization product (**16b**) (Path b).

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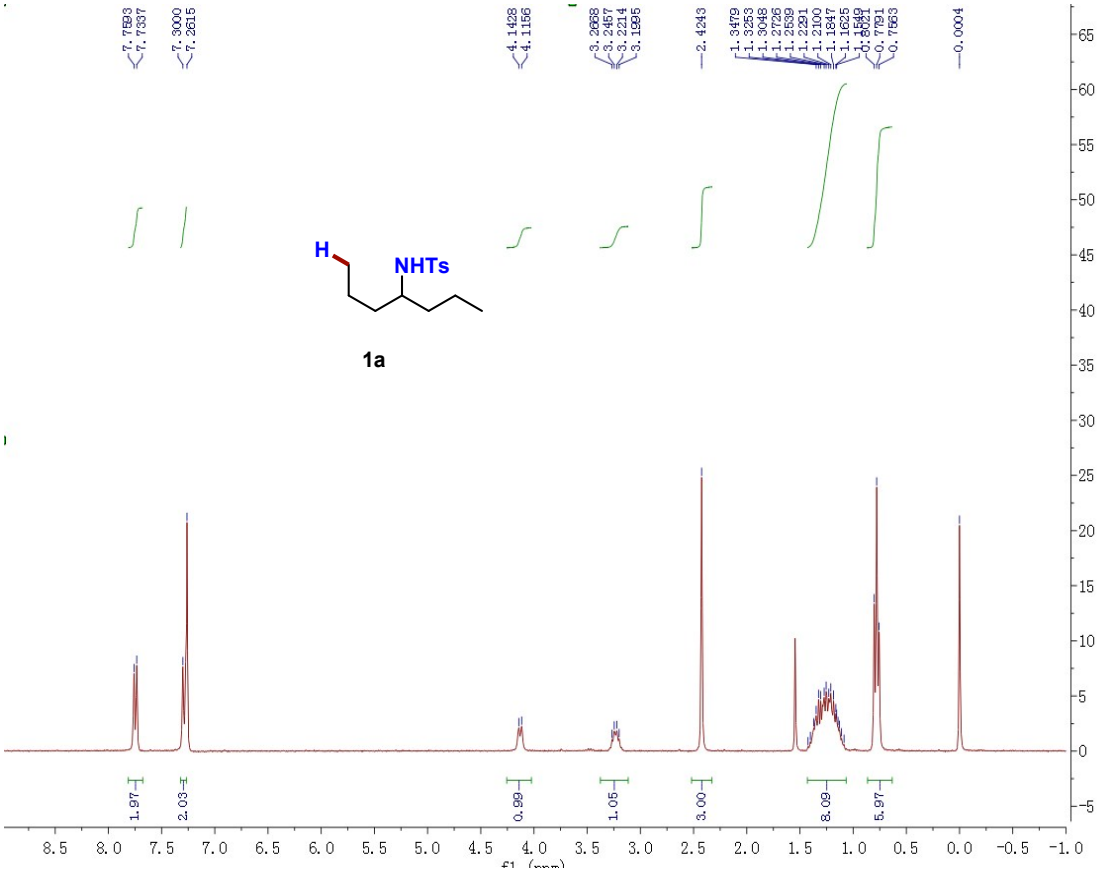
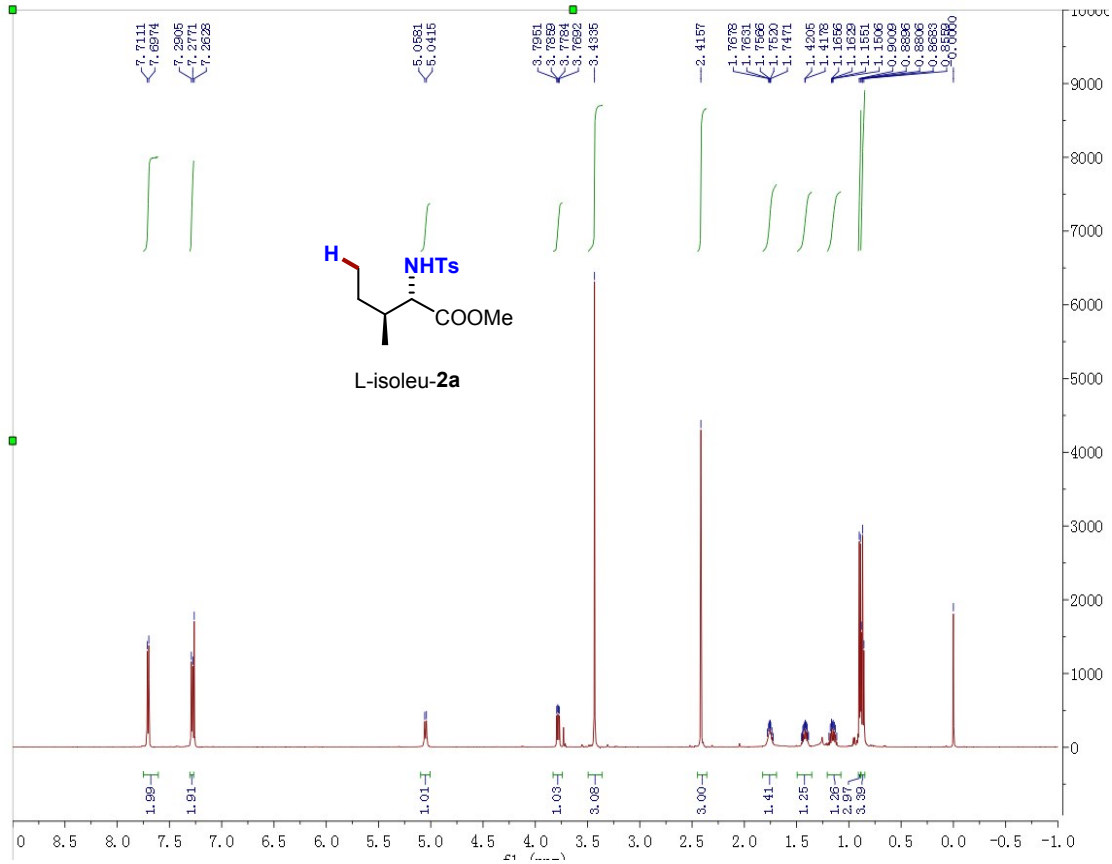
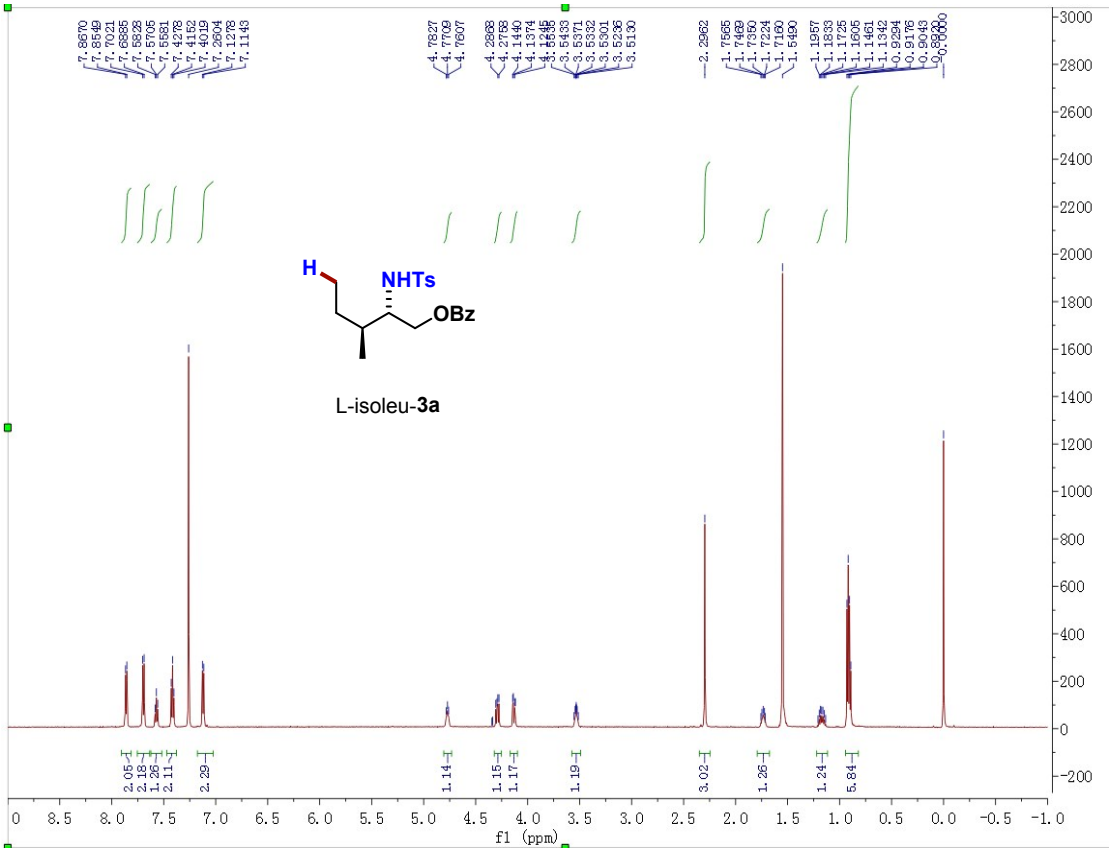
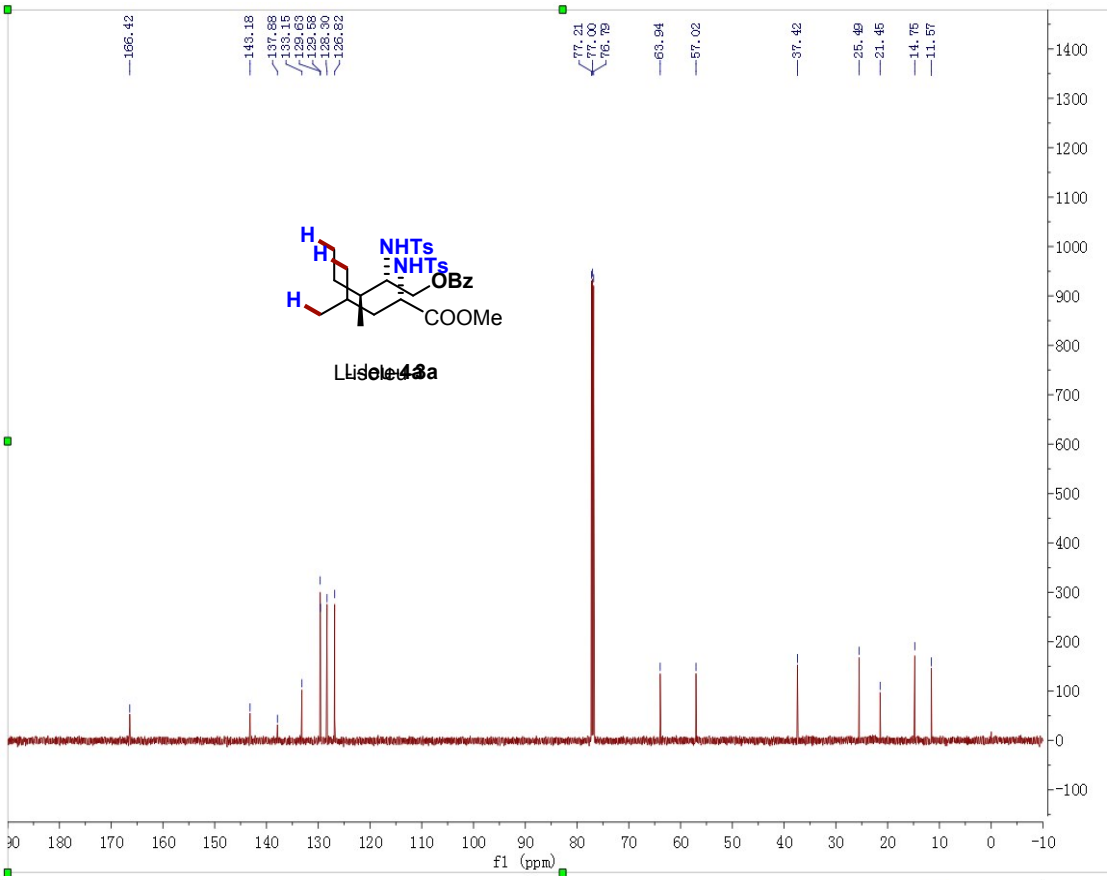
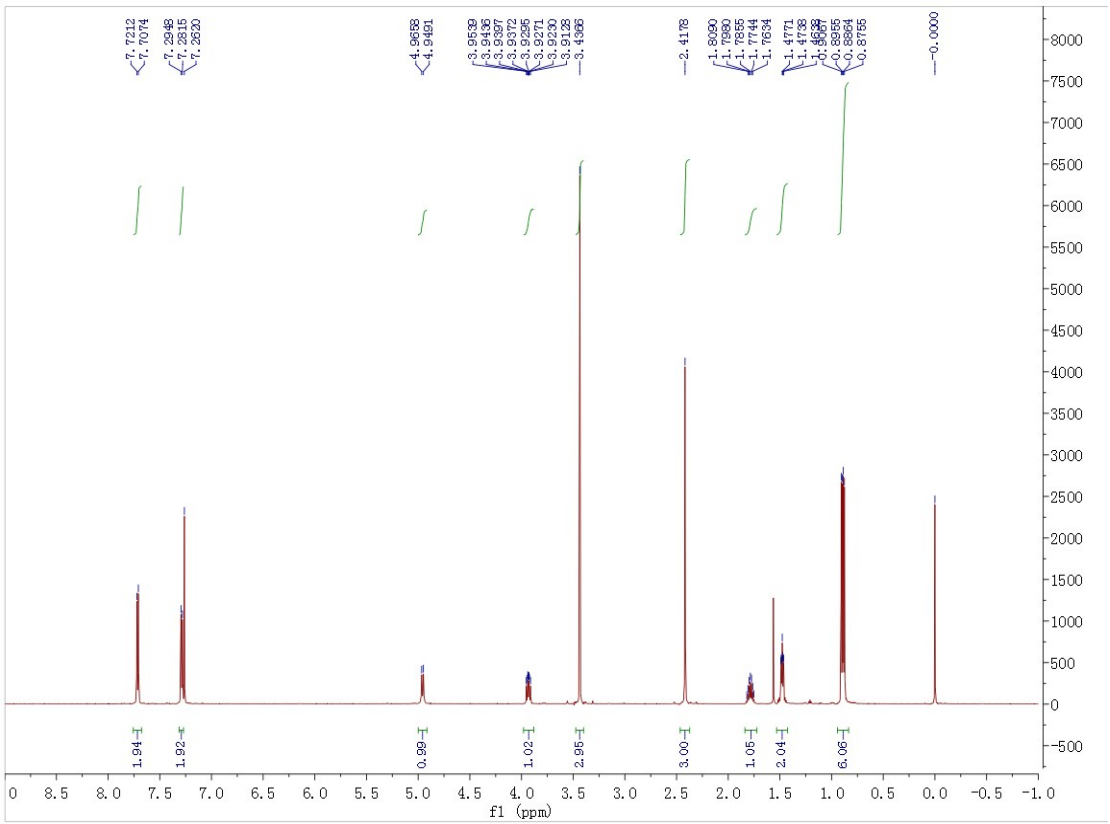
NMR Spectra




H
NHTs
COOMe
L-isoleu-2a


H
NHTs
OBz
L-isoleu-3a
f1 (ppm)


166.42
143.18
137.88
133.15
129.63
129.58
128.30
126.82
77.21
77.00
76.79
63.94
57.02
37.42
25.49
21.45
14.75
11.57
H
H
NHTs
NHTs
OBz
H
COOMe
f1 (ppm)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7.2815
7.2630
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4.9491
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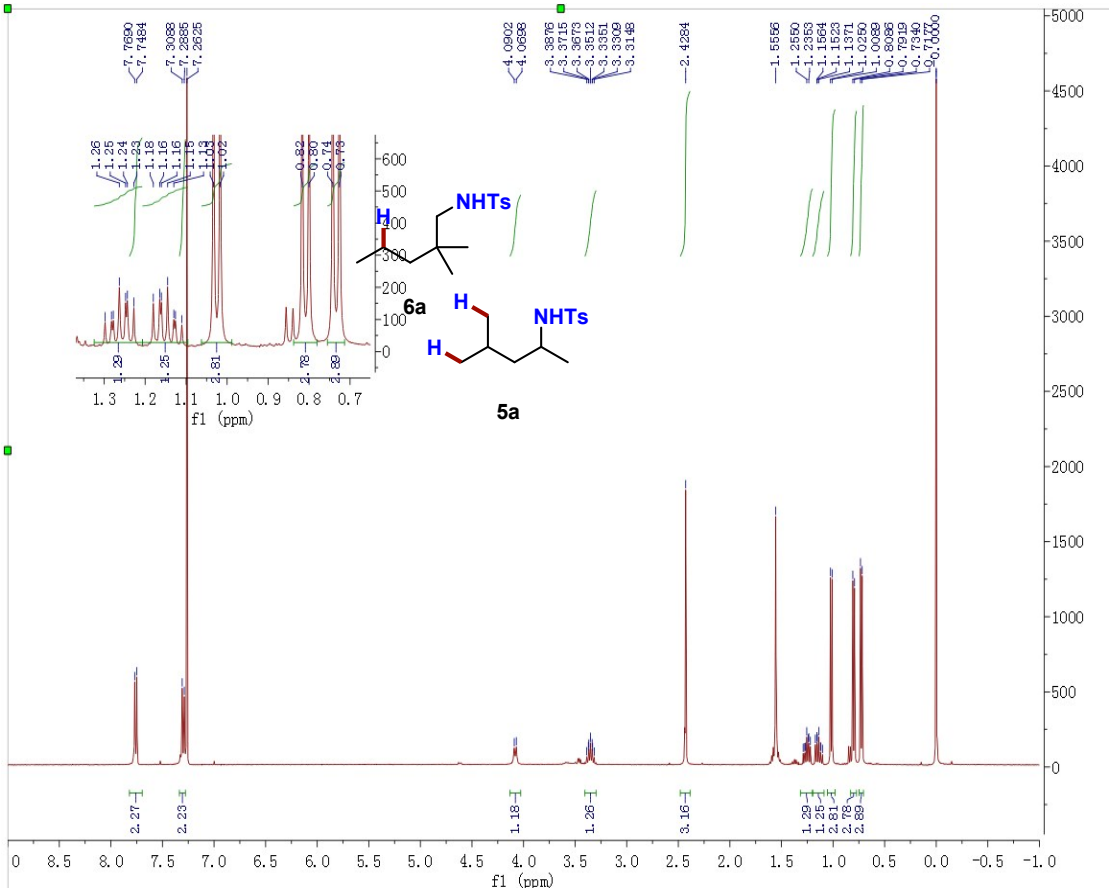
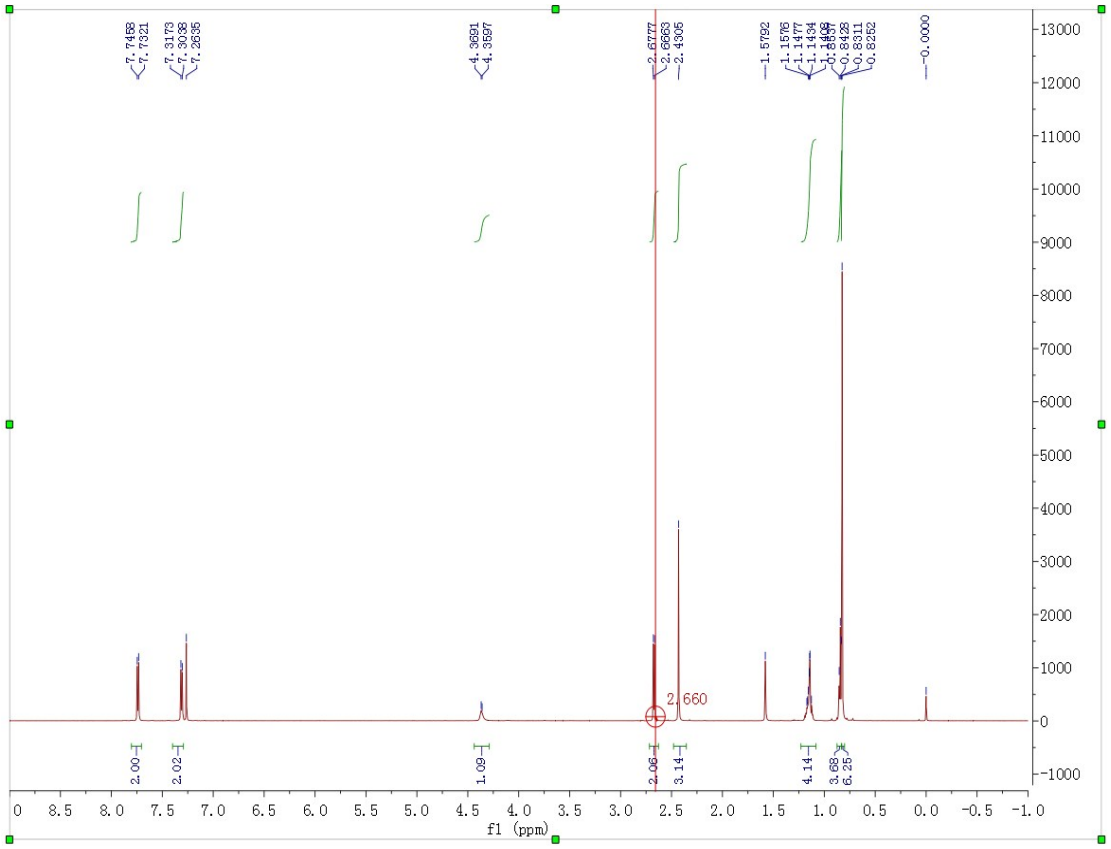
3.9372
3.9295
3.9271
3.9230
3.9128
3.4366
2.4178
1.8090
1.7990
1.7855
1.7744
1.7634
1.4771
1.4738
0.8955
0.8864
0.8755
-0.0000
1.94
1.92
0.99
1.02
2.95
3.00
1.05
2.04
6.06
f1 (ppm)


NHTs
H
6a
H
H
NHTs
5a
f1 (ppm)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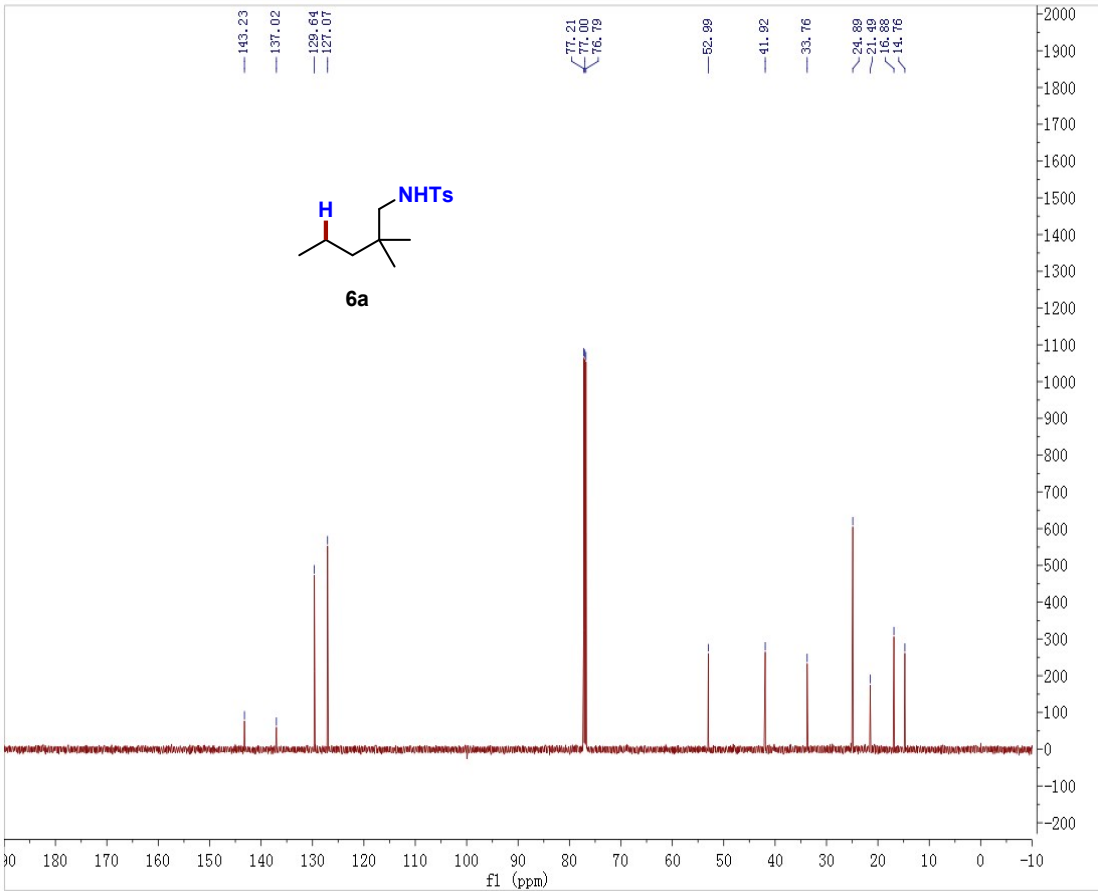
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77.21
77.00
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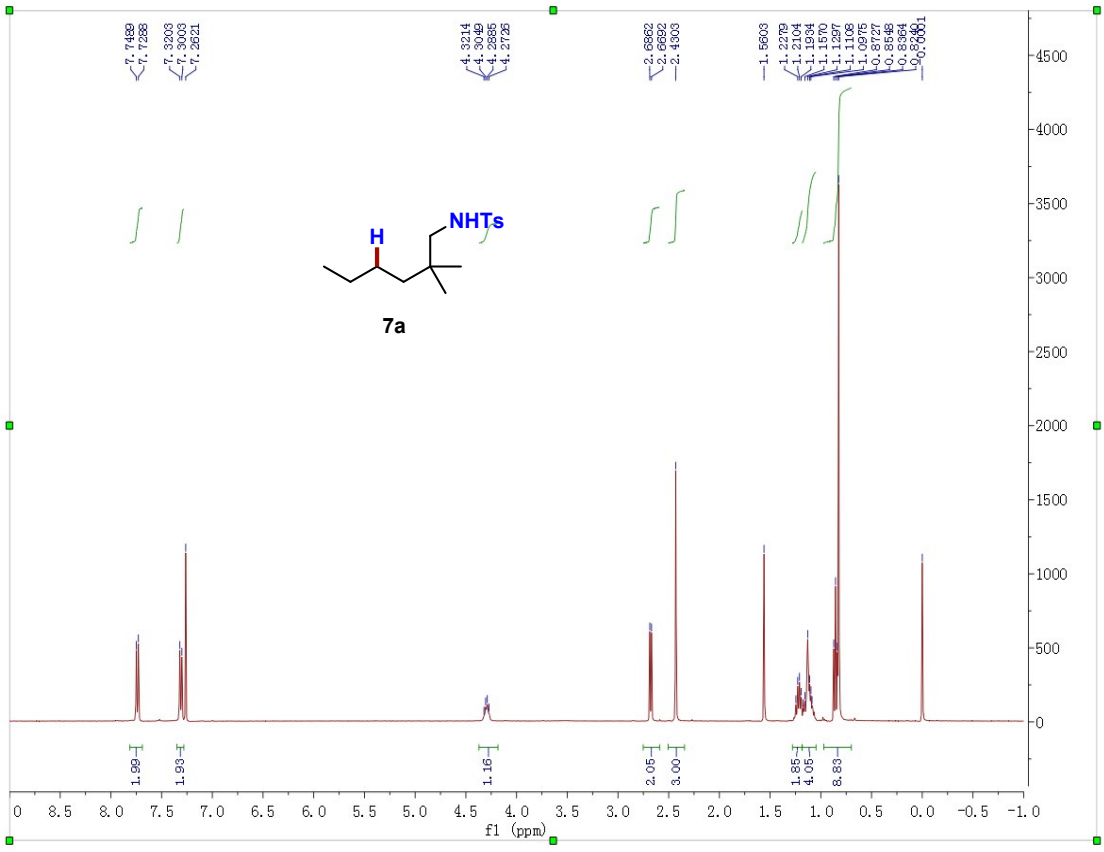
NHTs
H
6a
f1 (ppm)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1.2104
1.1934
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1.1108
1.0975
0.8727
0.8548
0.8364
0.8240
0.0001
NHTs
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7a
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3.00
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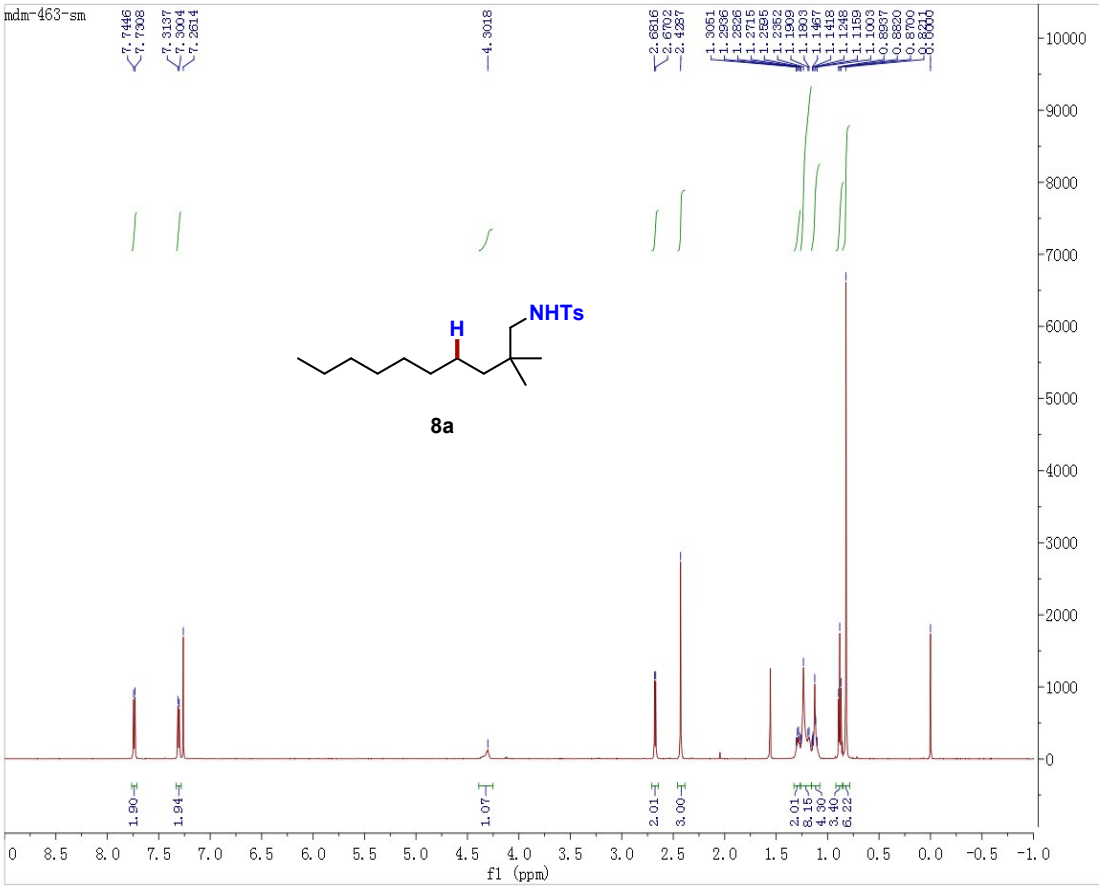
8.83
f1 (ppm)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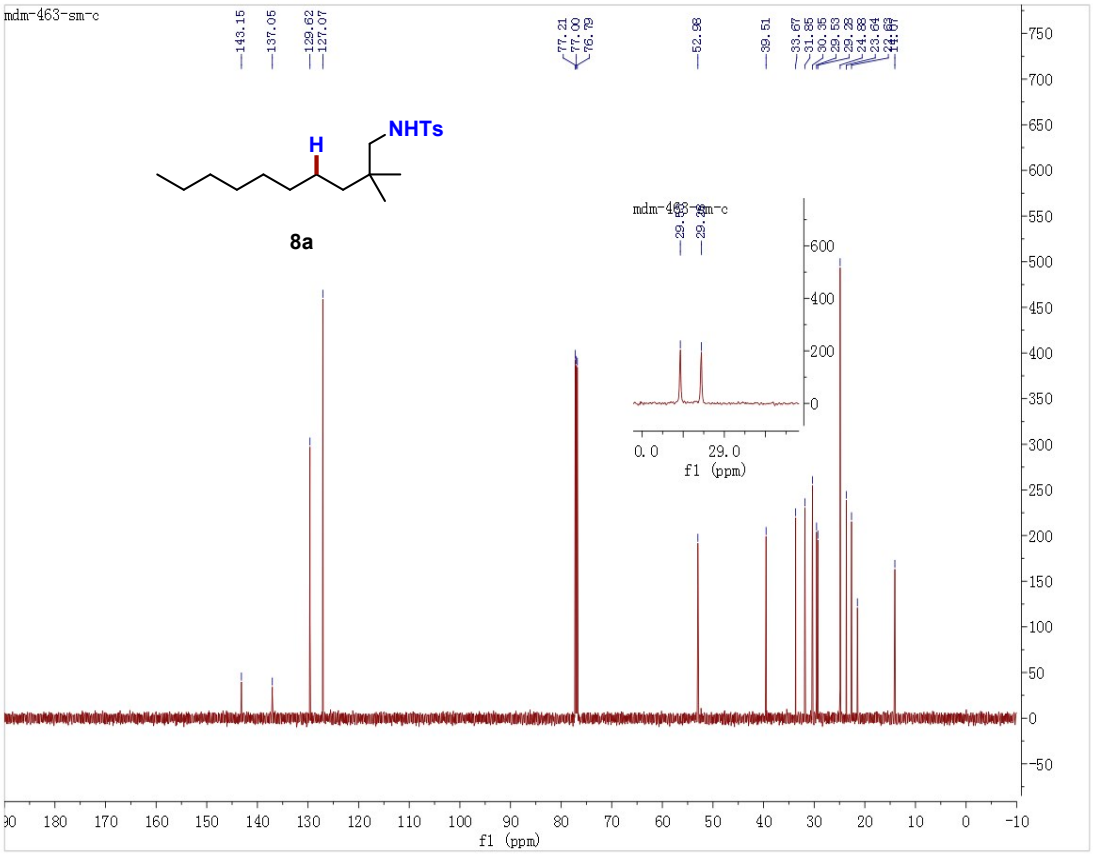
H
8a
f1 (ppm)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NHTs
H
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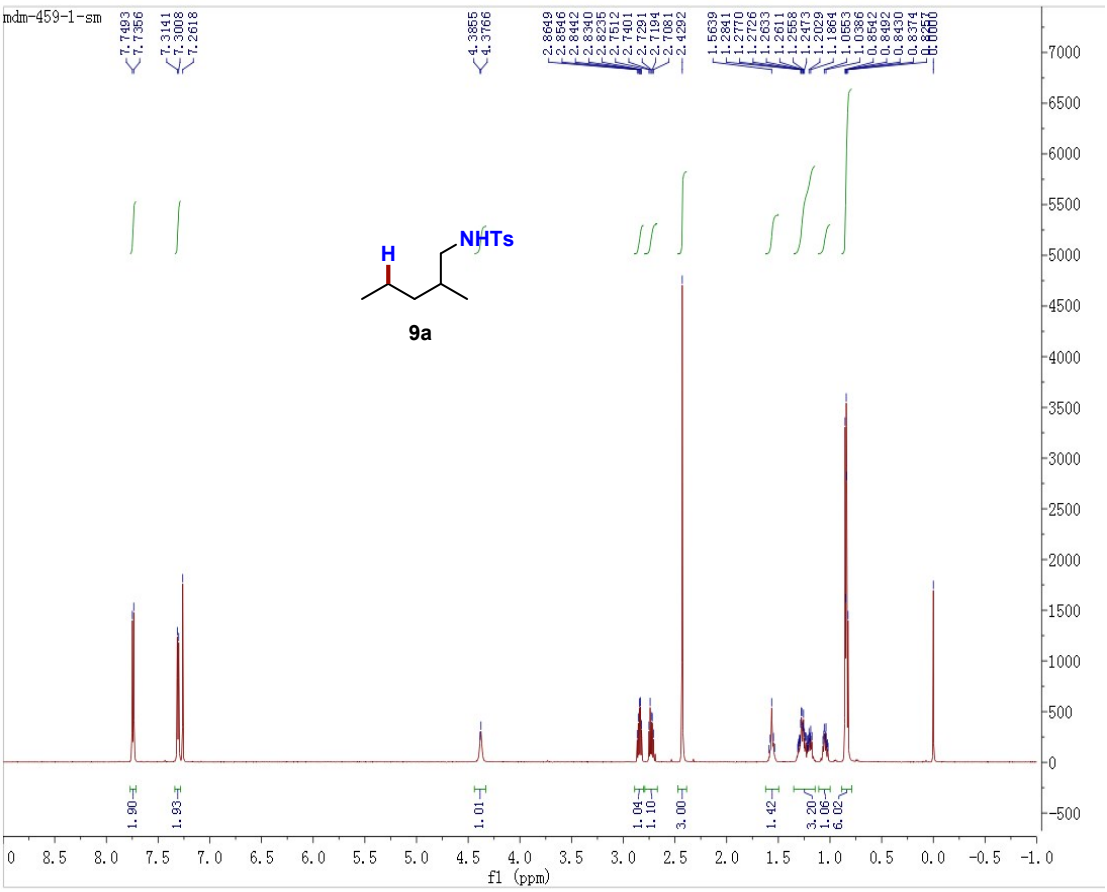
f1 (ppm)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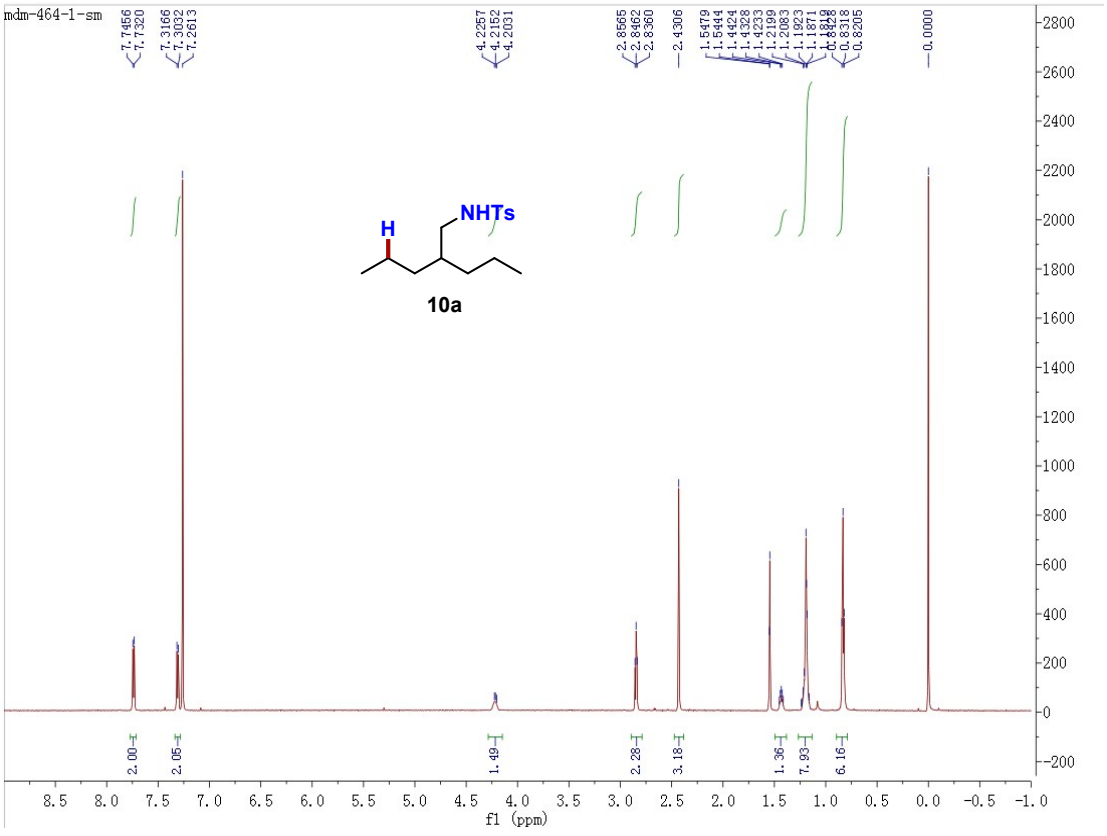
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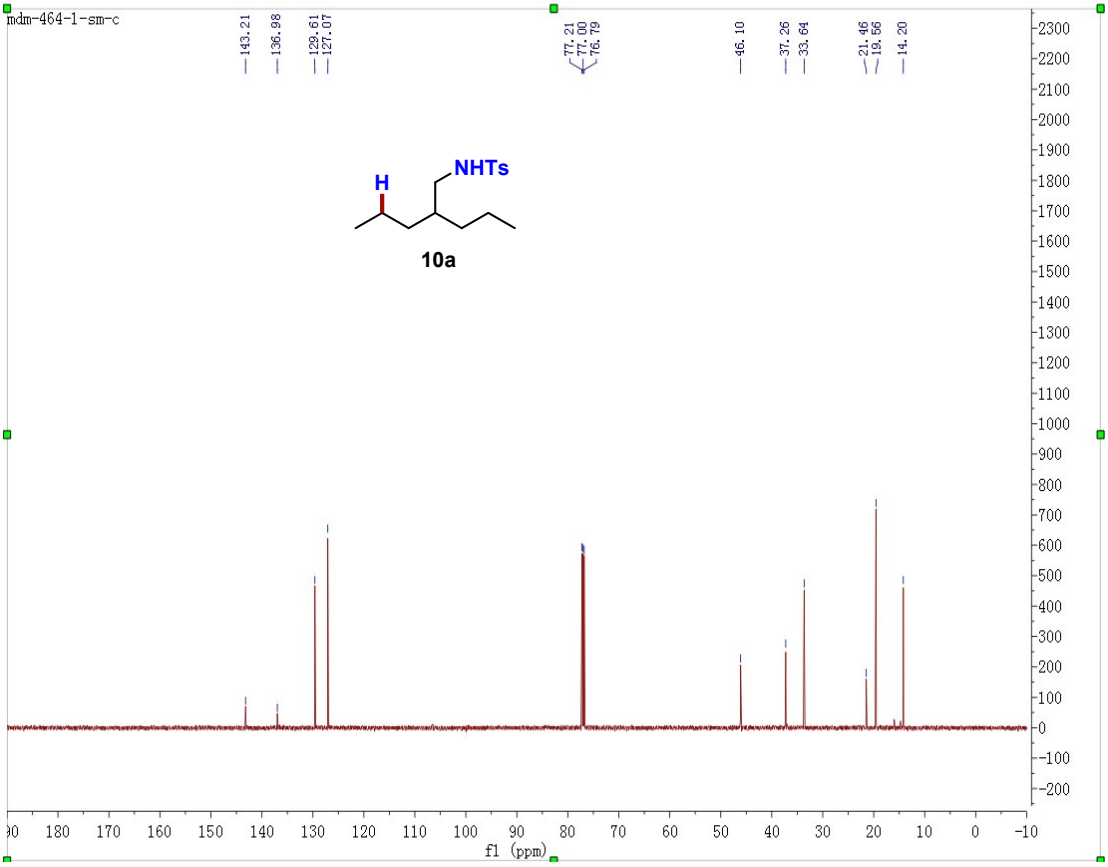
H
10a
f1 (ppm)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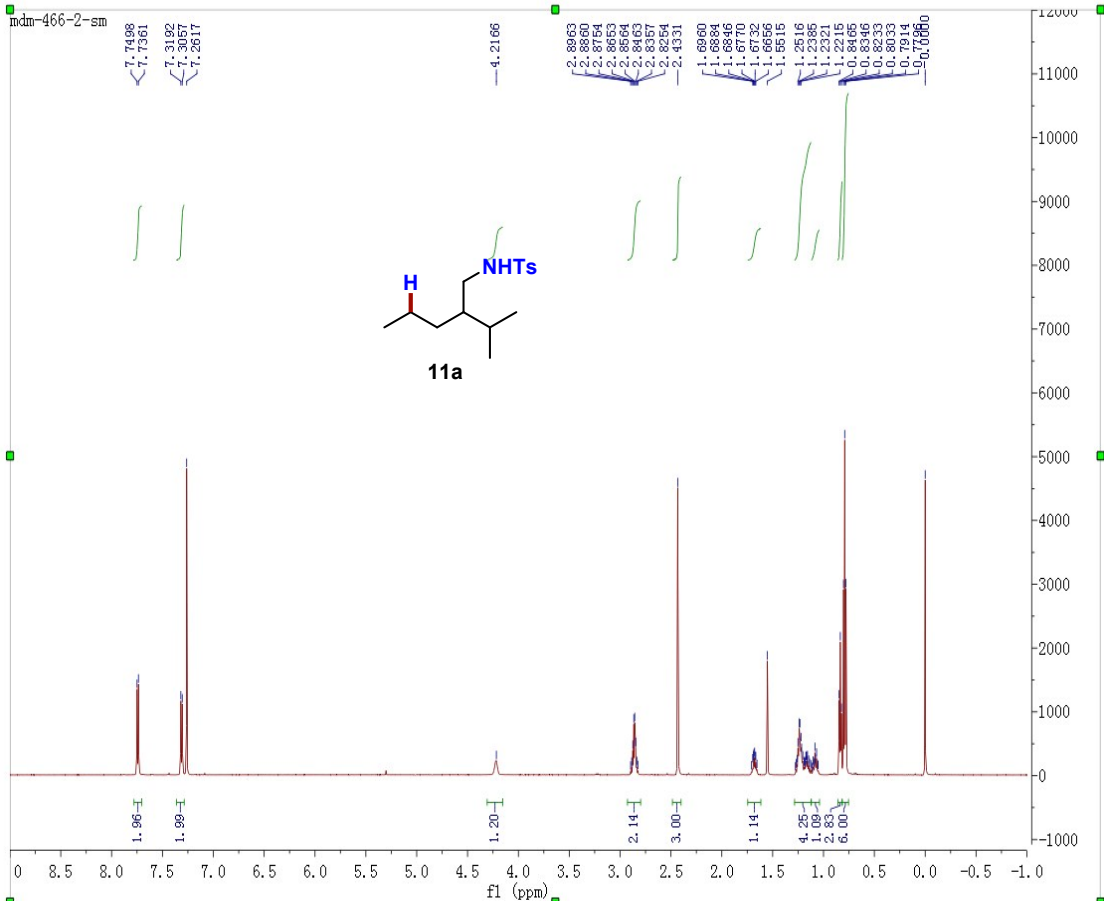
14.20
H
NHTs
10a
f1 (ppm)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1.2516
1.2385
1.2321
1.2215
0.8465
0.8346
0.8233
0.8033
0.7914
0.7860
0.0000
H
NHTs
11a
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1.20
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3.00
1.14
4.25
1.09
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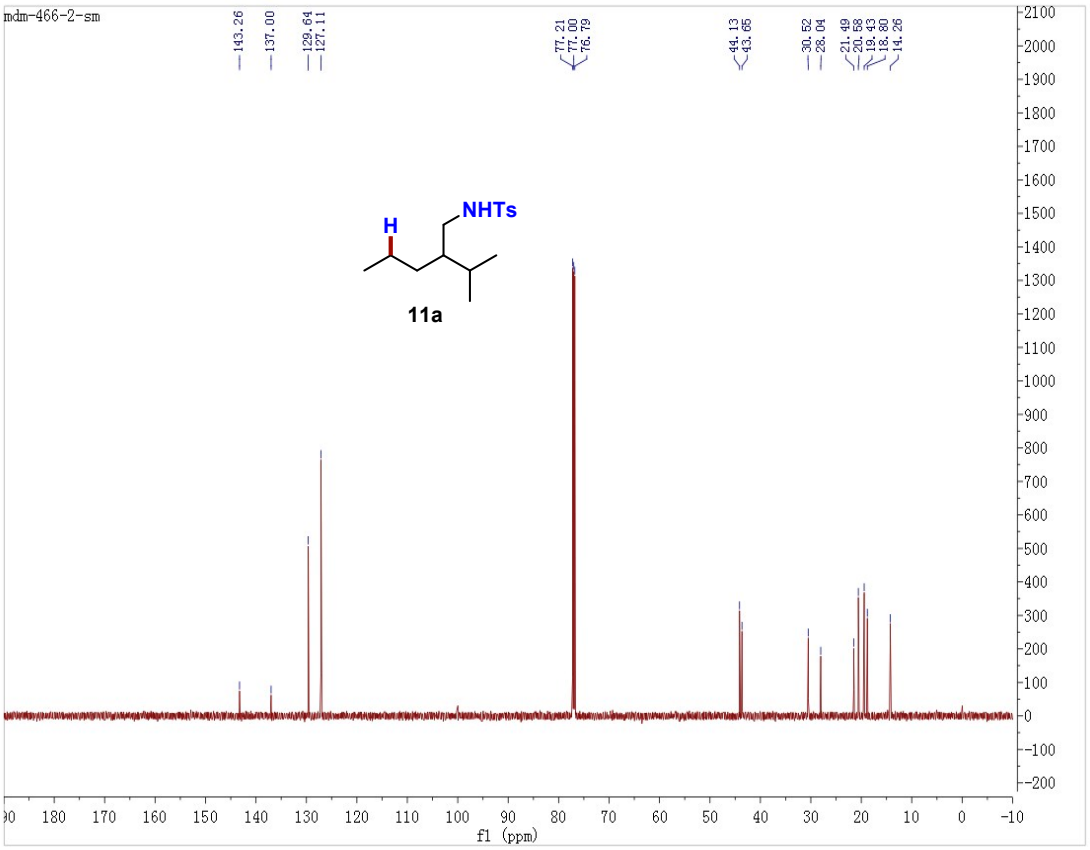
6.00
f1 (ppm)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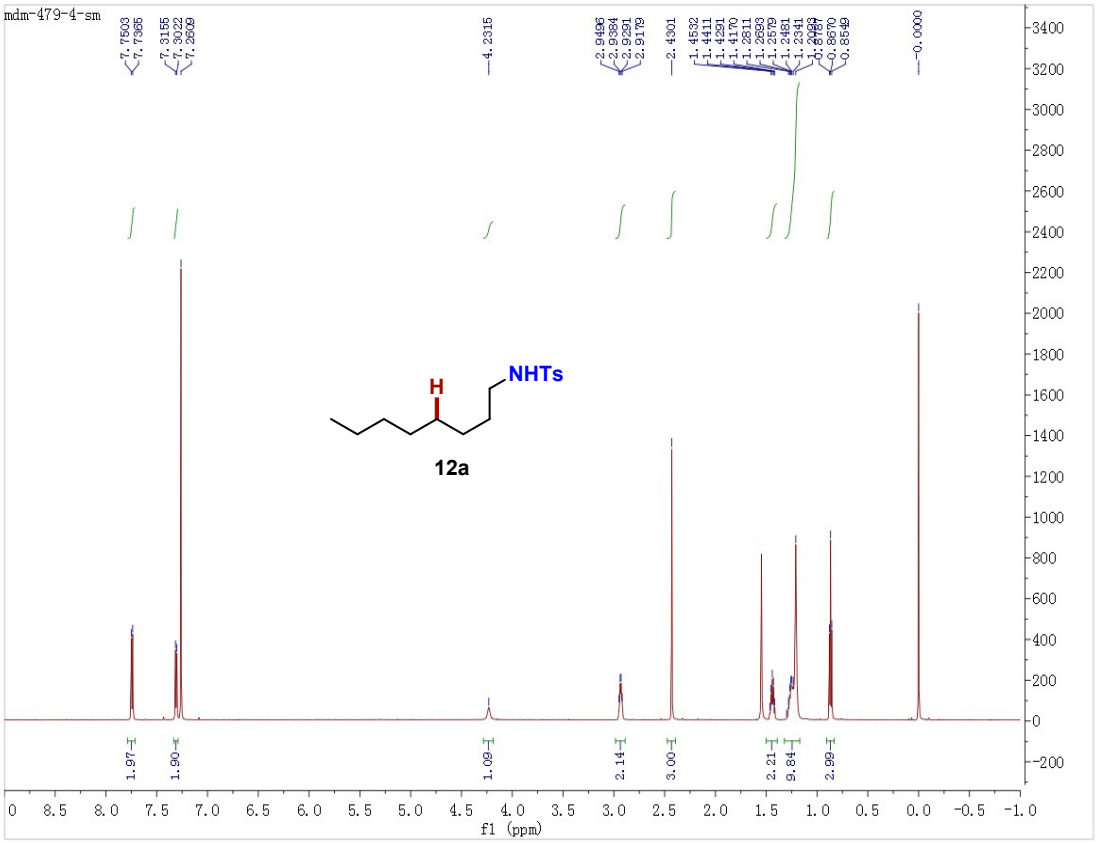
14.26
NHTs
H
11a
f1 (ppm)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1.4291
1.4170
1.2931
1.2693
1.2579
1.2481
1.2341
0.8787
0.8670
0.8549
0.0000
NHTs
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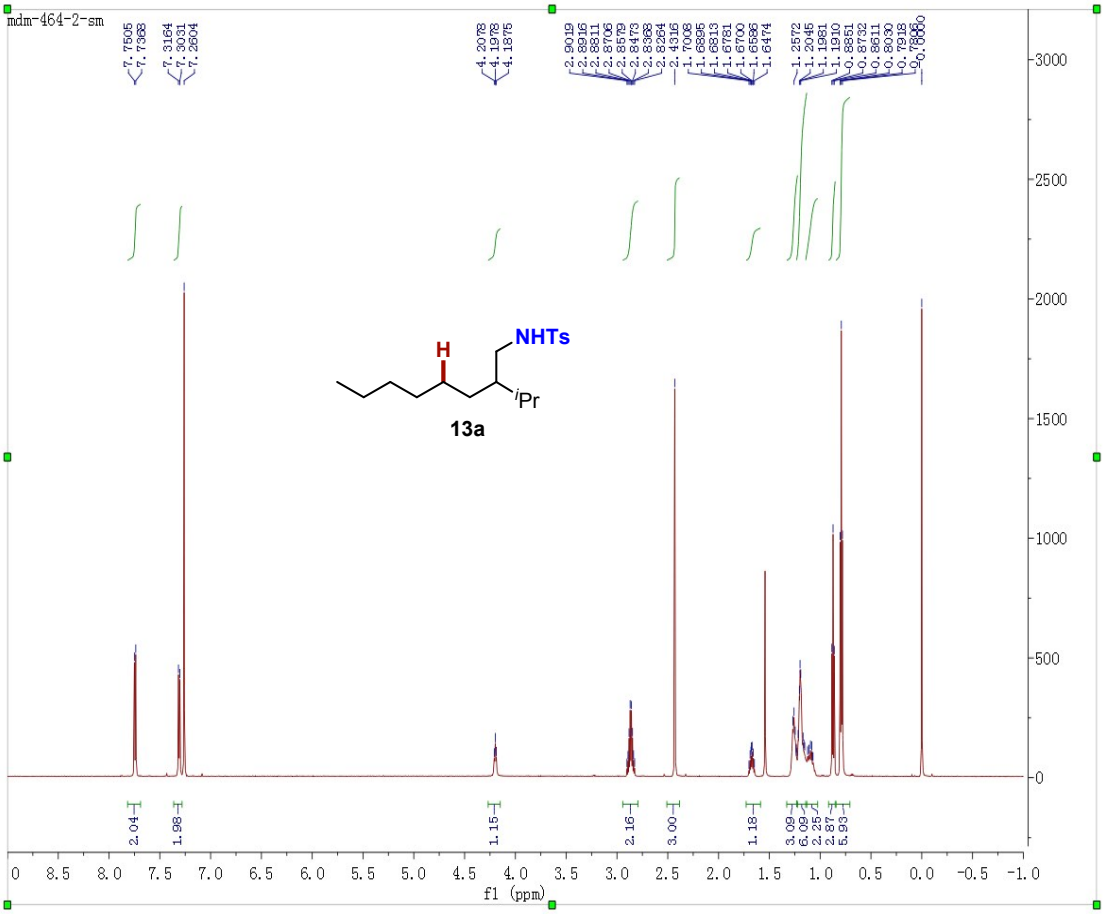
3.00
2.21
9.84
2.99
f1 (ppm)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NHTs
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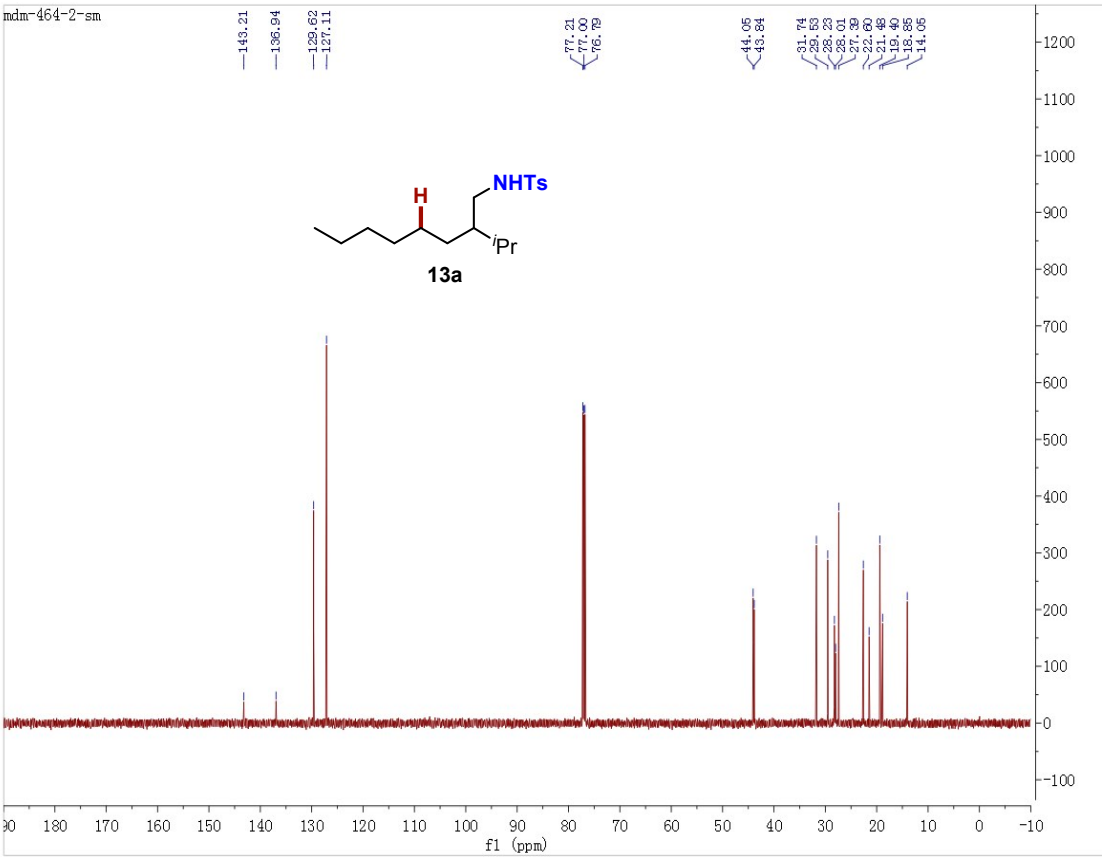
iPr
13a
f1 (ppm)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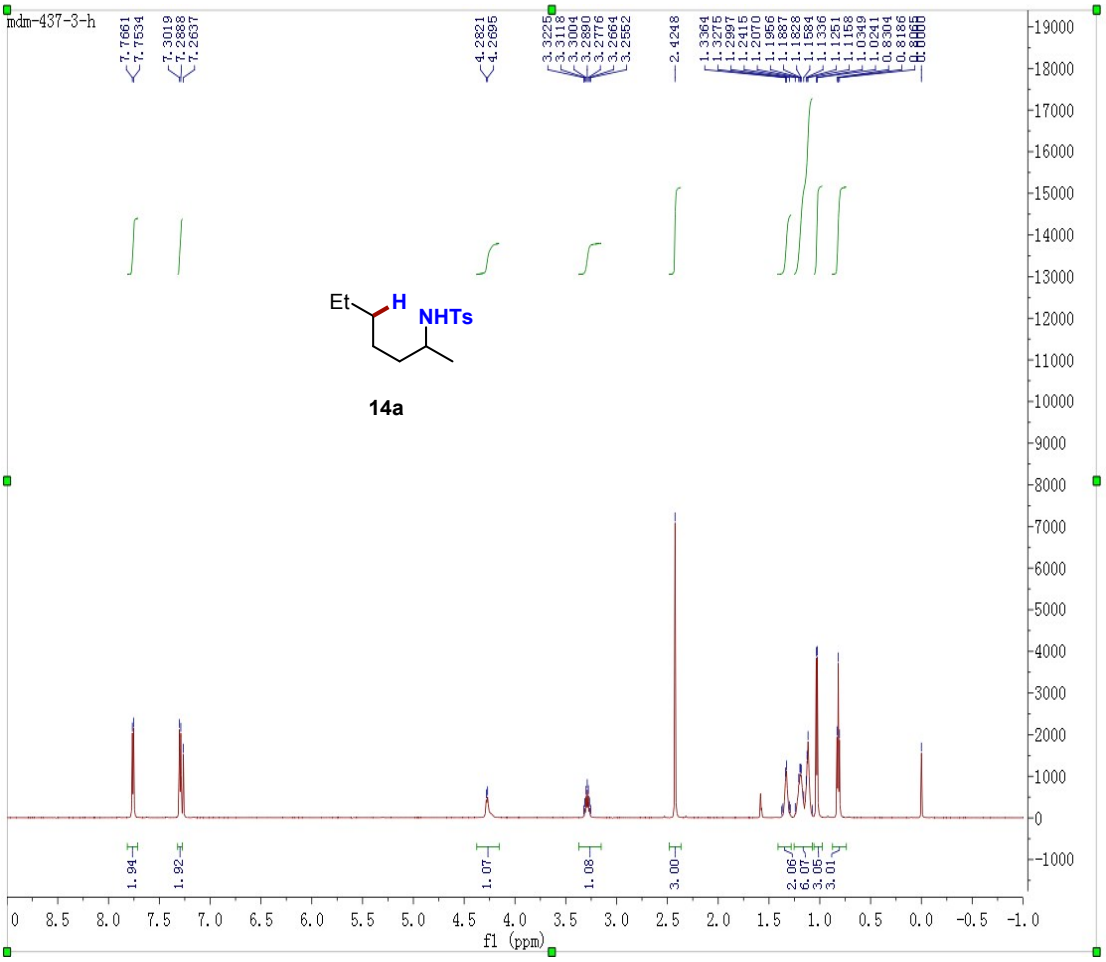
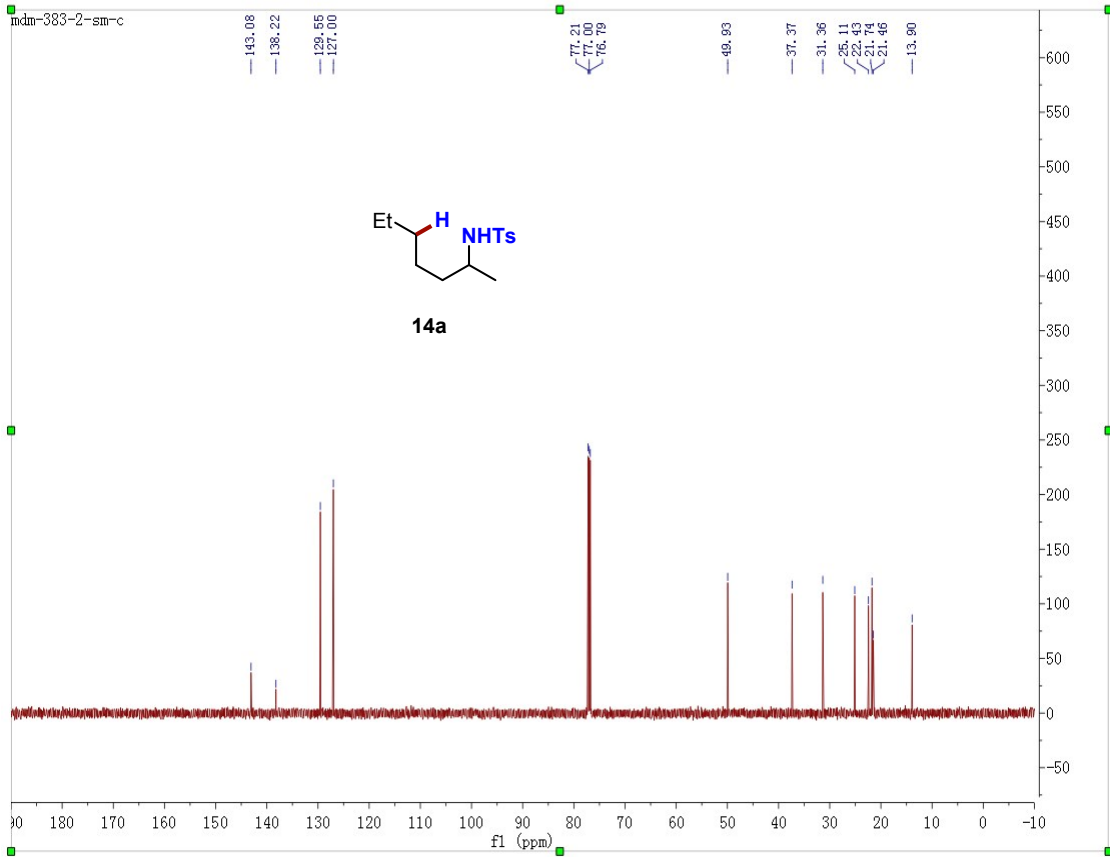
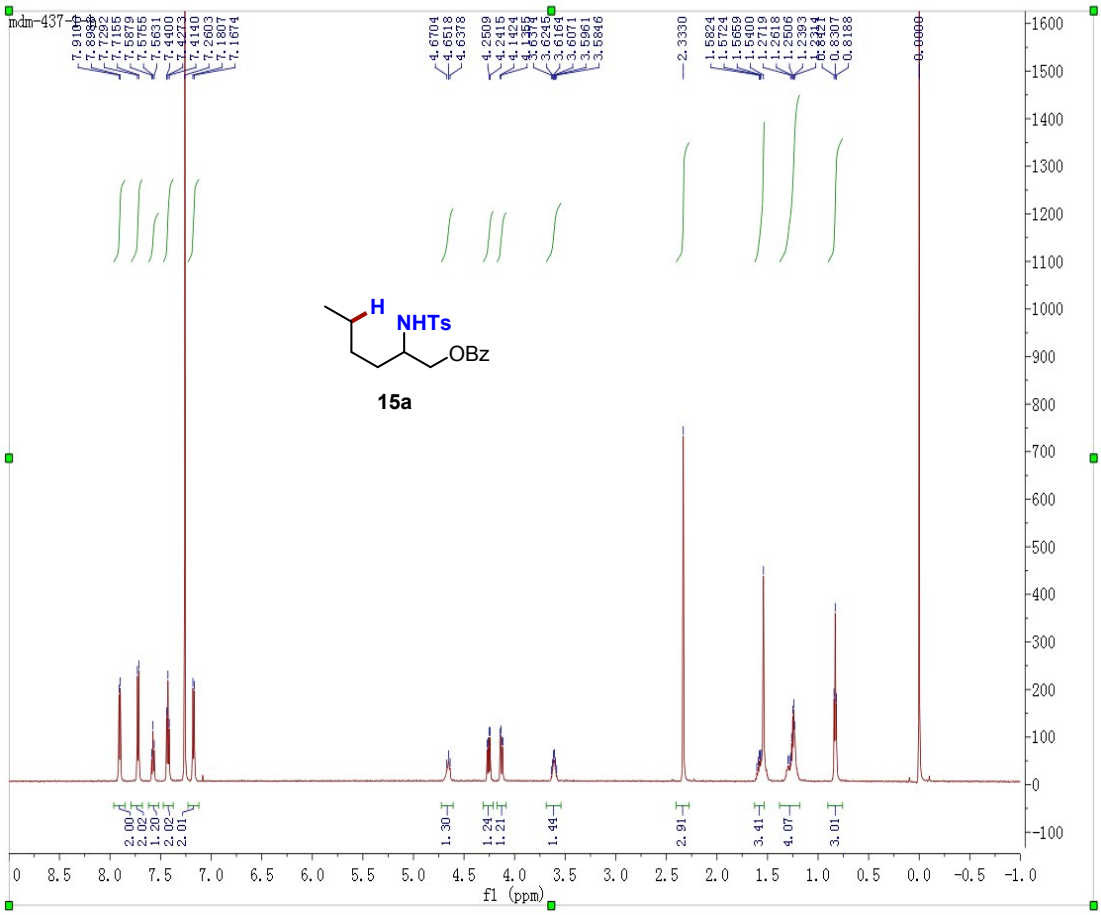
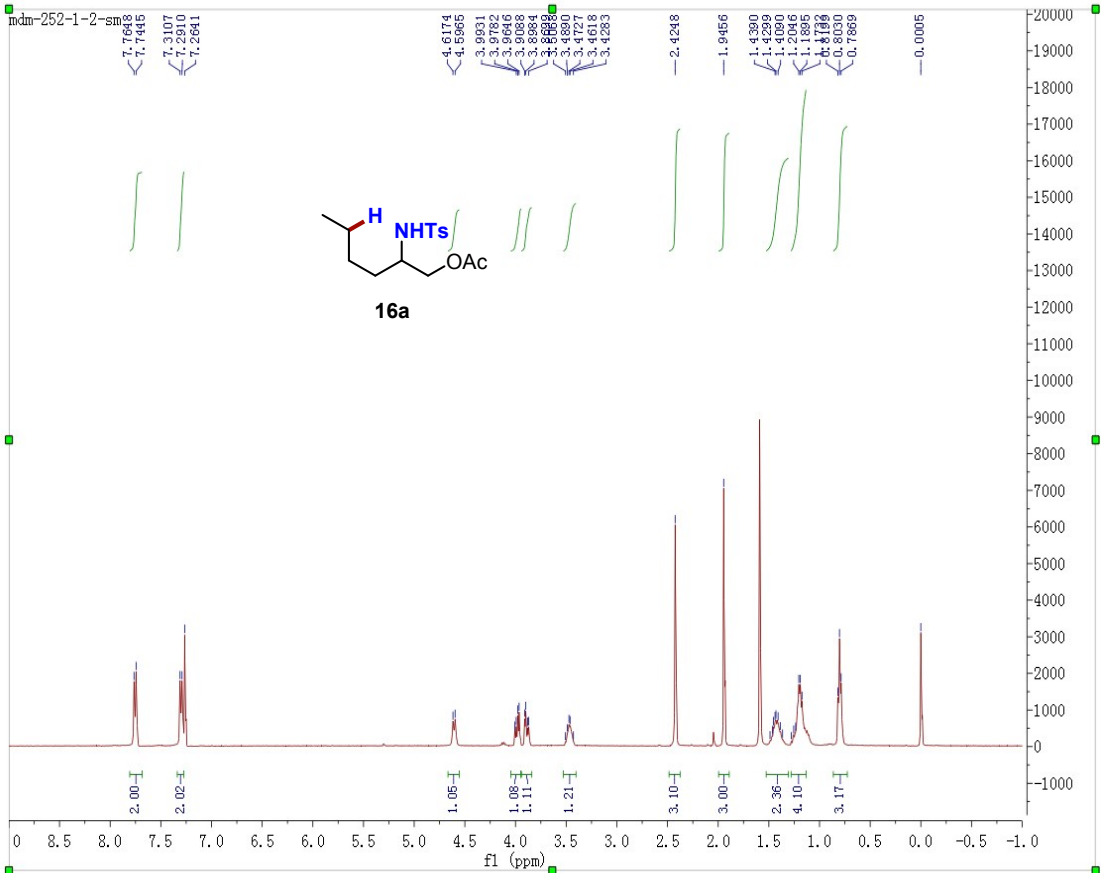
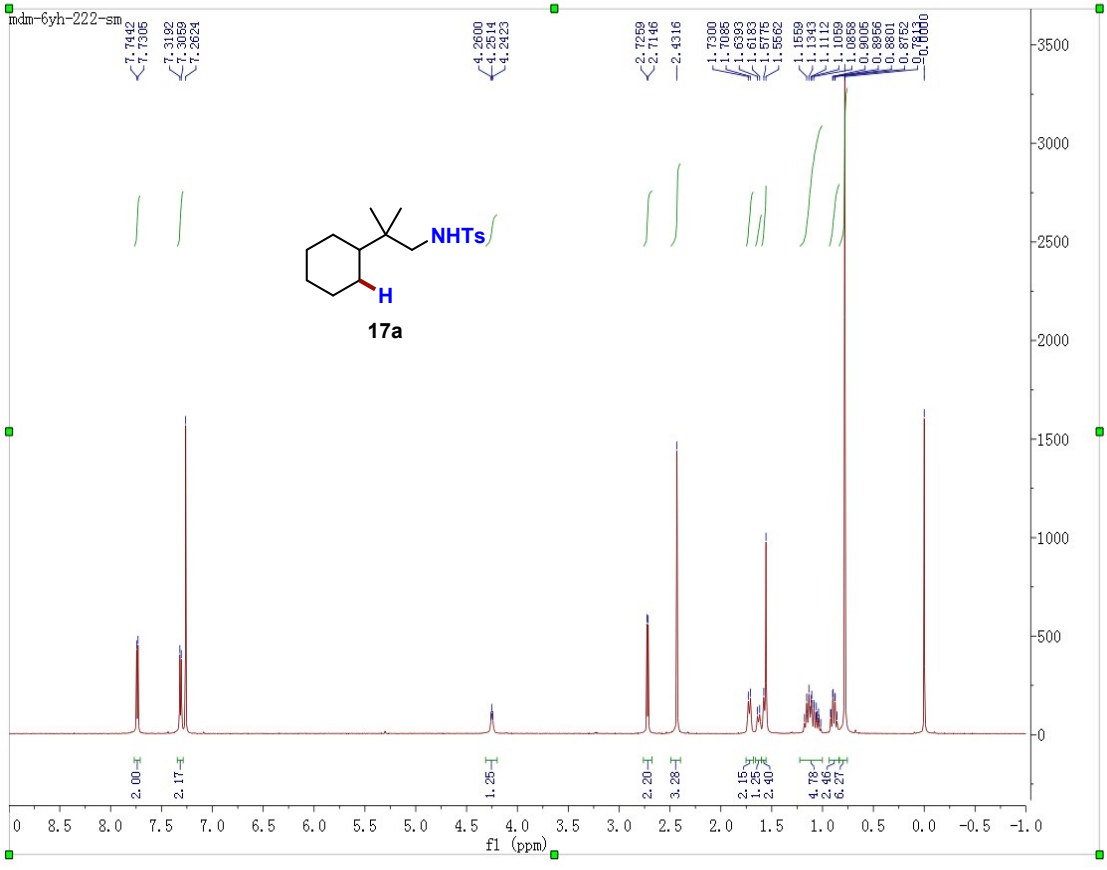
NHTs
H
iPr
13a
f1 (ppm)

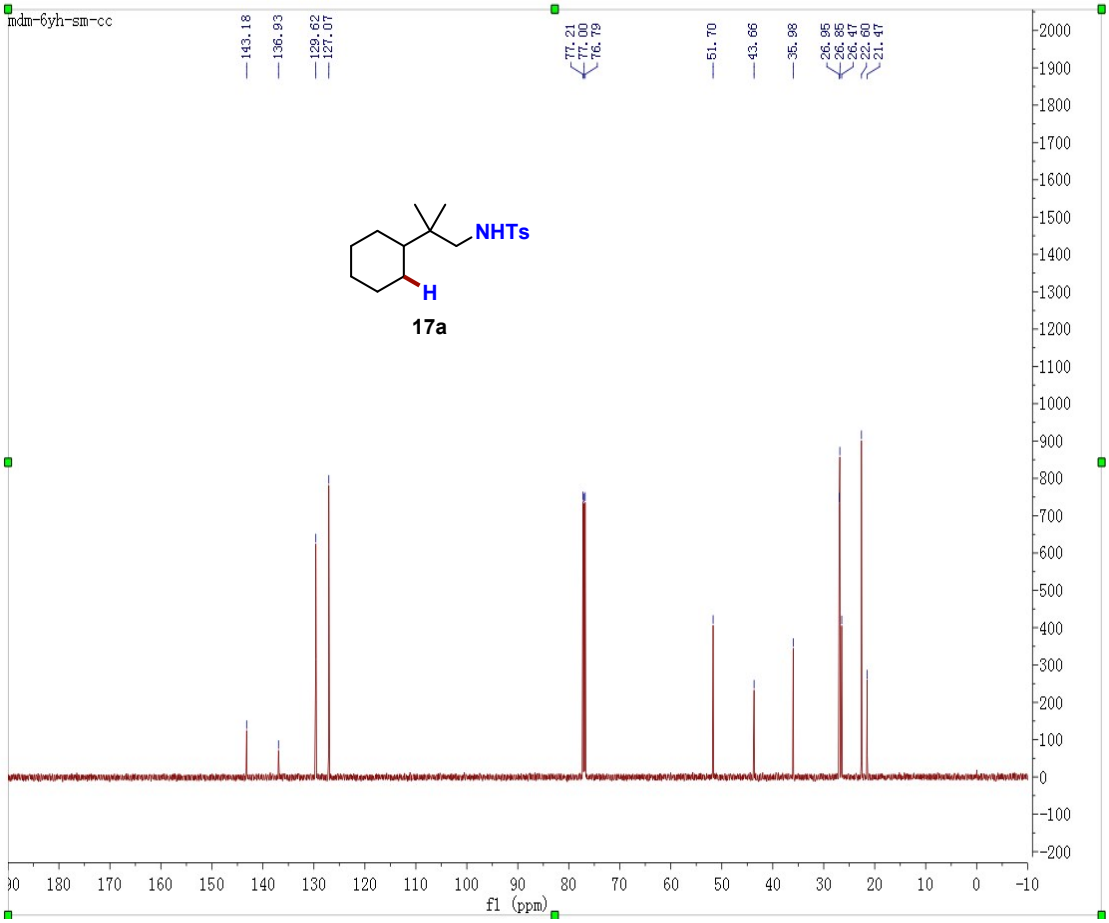

mdm-437-3-h
Et
H
NHTs
14a
f1 (ppm)

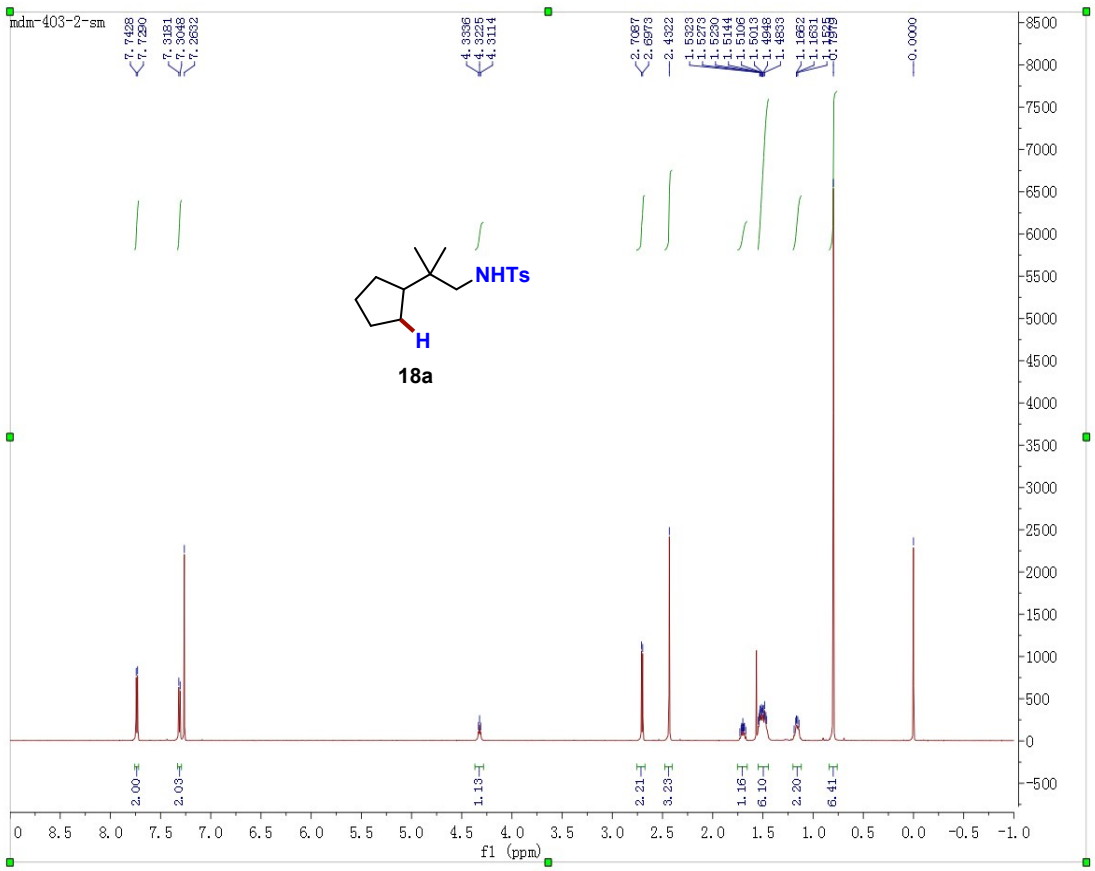

mdm-383-2-sm-c
Et
H
NHTs
14a
f1 (ppm)

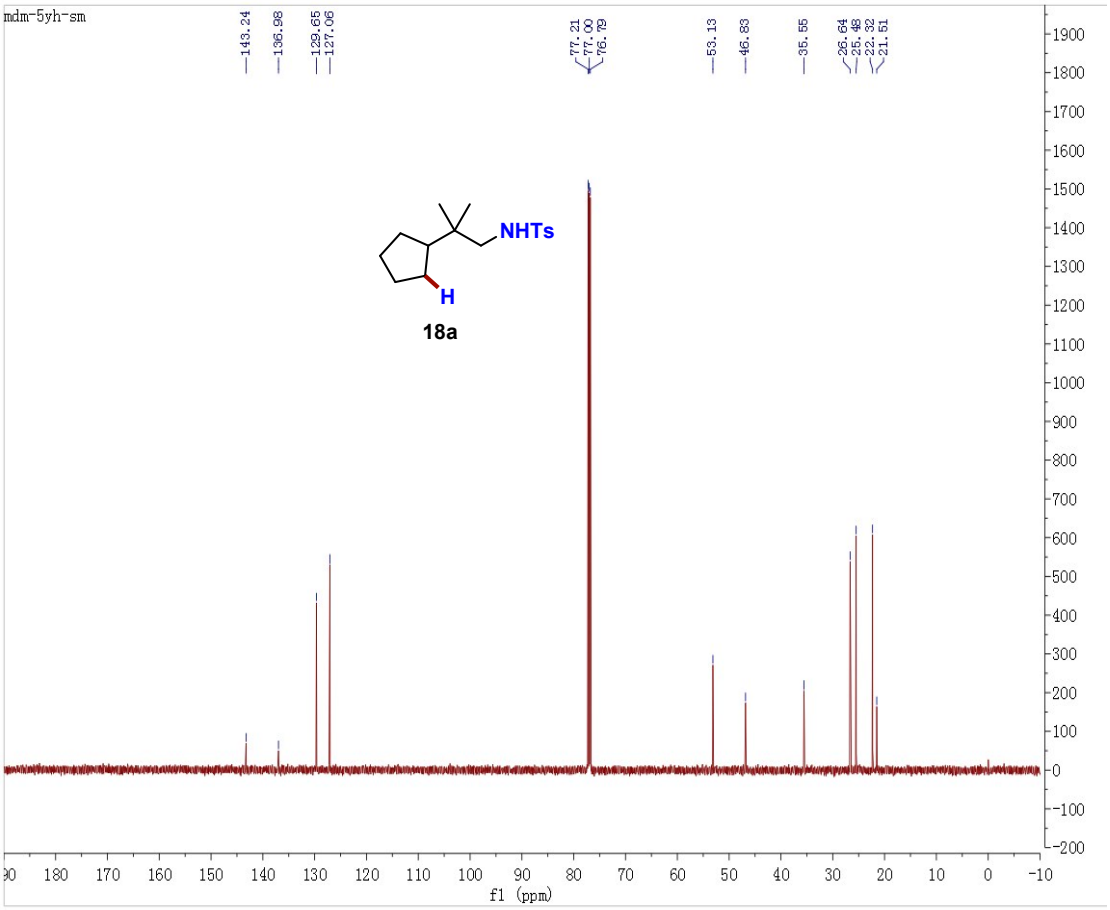

mdm-437-1
NHTs
OBz
15a
f1 (ppm)

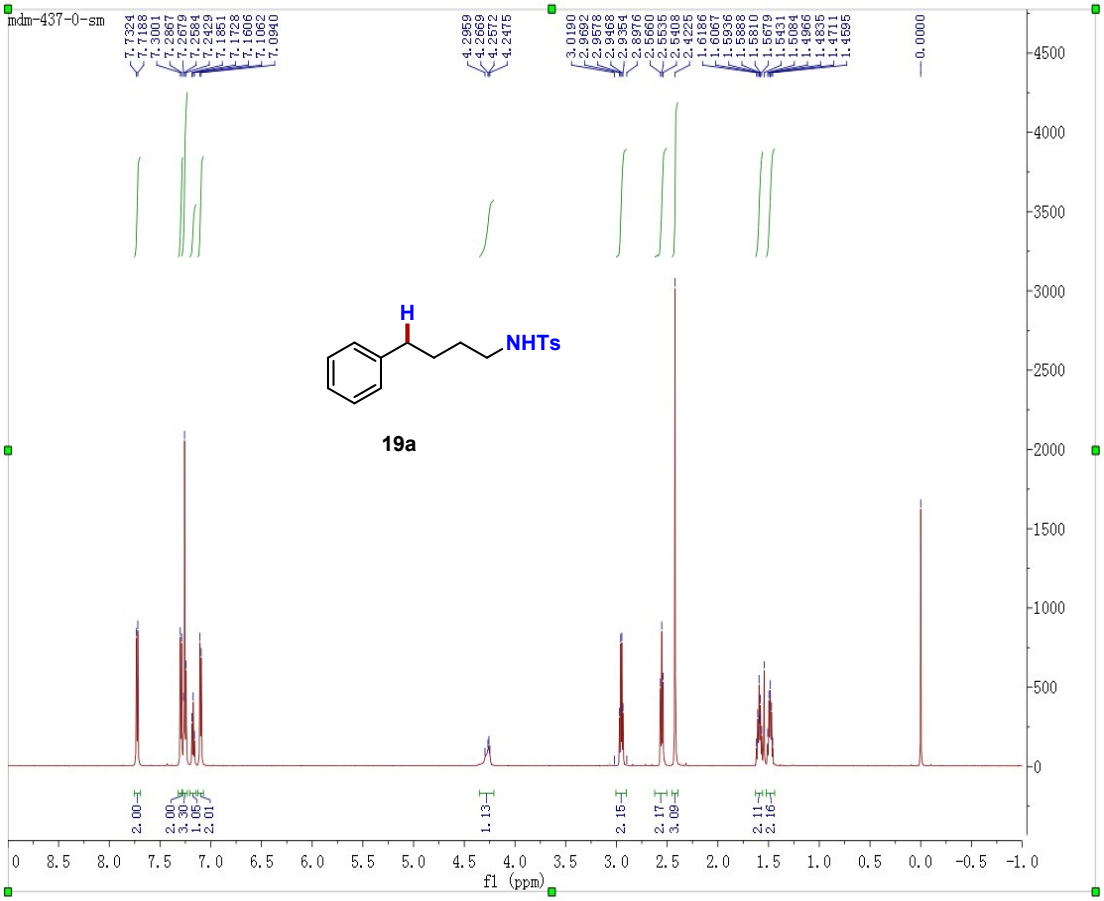

mdm-252-1-2-sm
H
NHTs
OAc
16a
f1 (ppm)

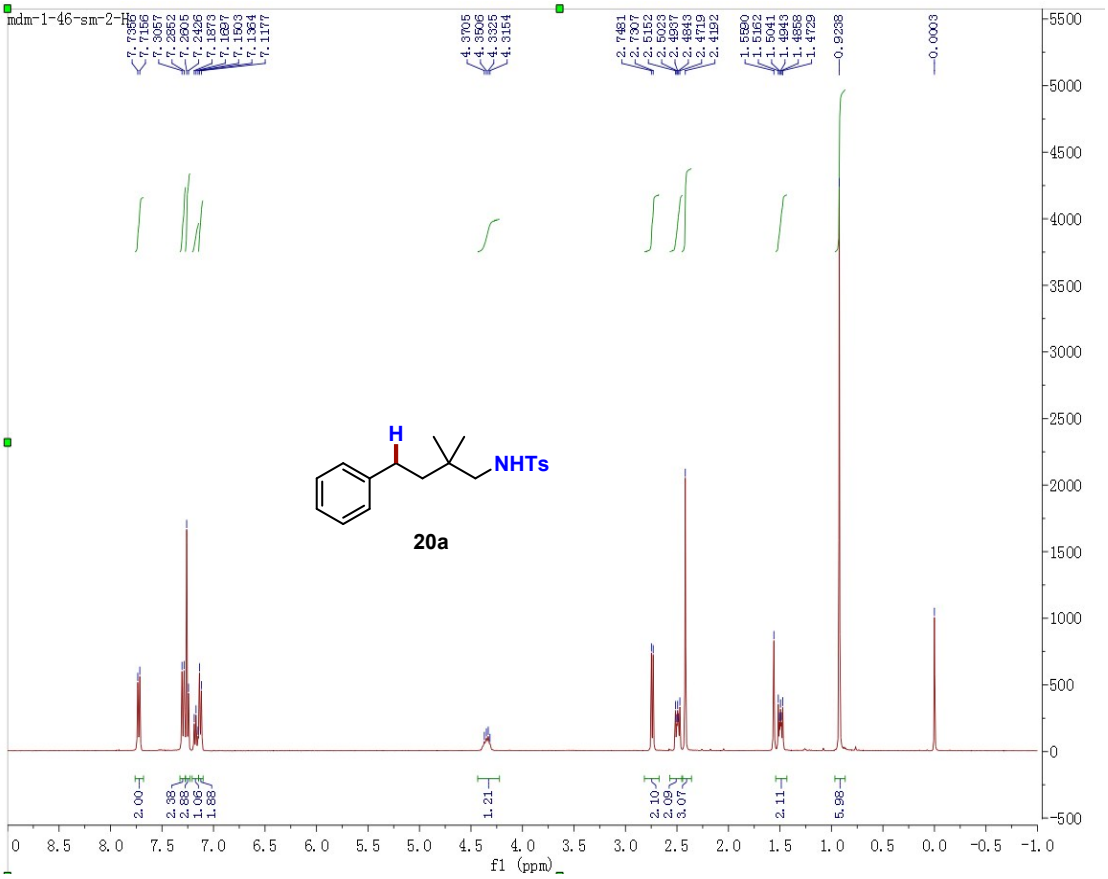

mdm-6yh-222-sm
NHTs
H
17a
f1 (ppm)

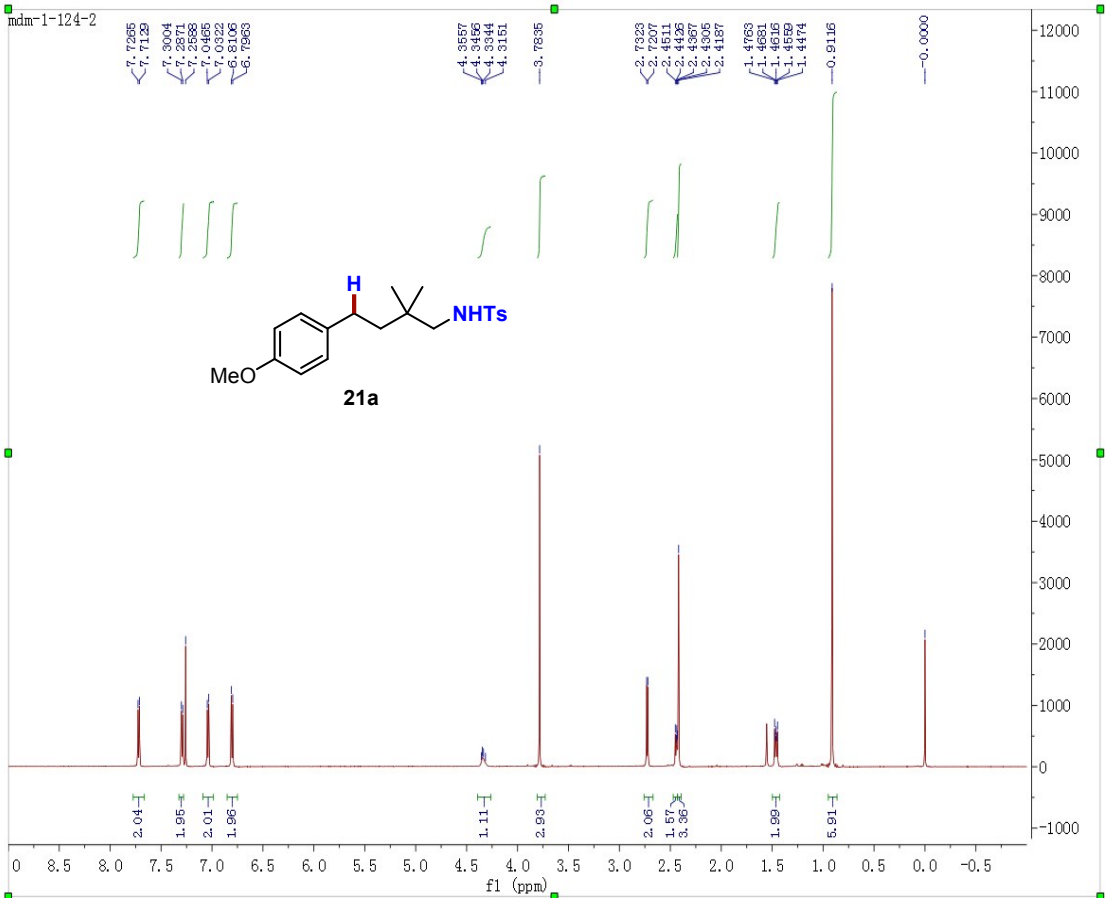

mdm-6yh-sm-cc
143.18
136.93
129.62
127.07
77.21
77.00
76.79
51.70
43.66
35.98
26.95
26.85
26.47
22.60
21.47
NHTs
H
17a
f1 (ppm)

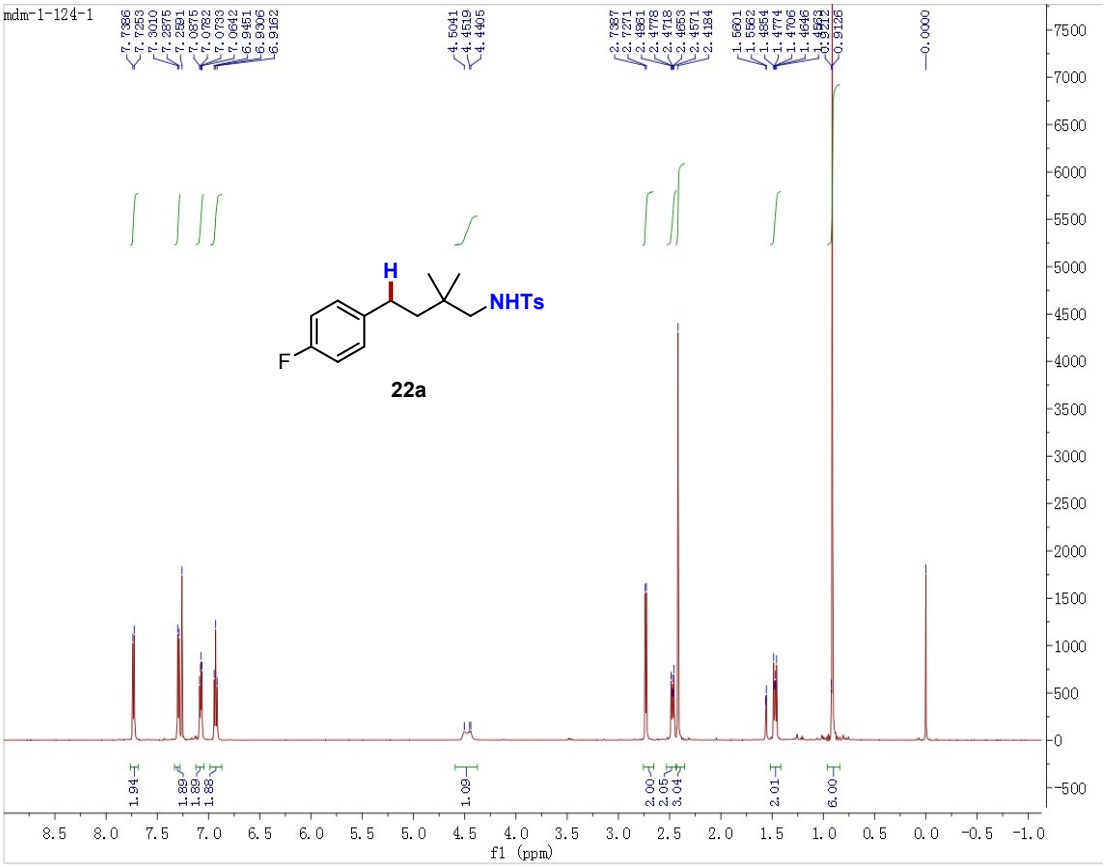

mdm-403-2-sm
7.7428
7.7290
7.3181
7.3048
7.2632
4.3336
4.3225
4.3114
2.7067
2.6973
2.4322
1.5323
1.5273
1.5230
1.5144
1.5106
1.5013
1.4948
1.4833
1.1662
1.1631
0.1979
0.0000
NHTs
H
18a
2.00
2.03
1.13
2.21
3.23
1.16
6.10
2.20
6.41
f1 (ppm)

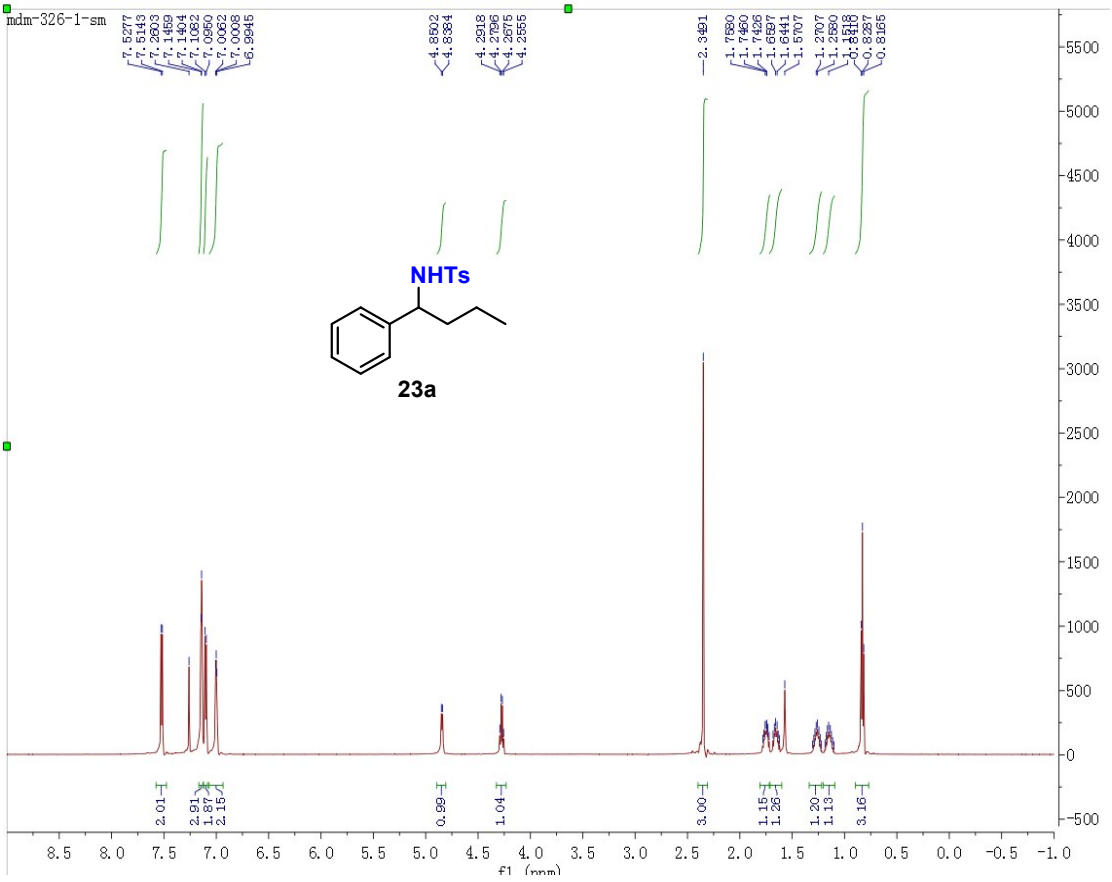

mdm-5yh-sm
143.24
136.98
129.65
127.06
77.21
77.00
76.79
53.13
46.83
35.55
26.64
25.48
22.32
21.51
NHTs
H
18a
f1 (ppm)

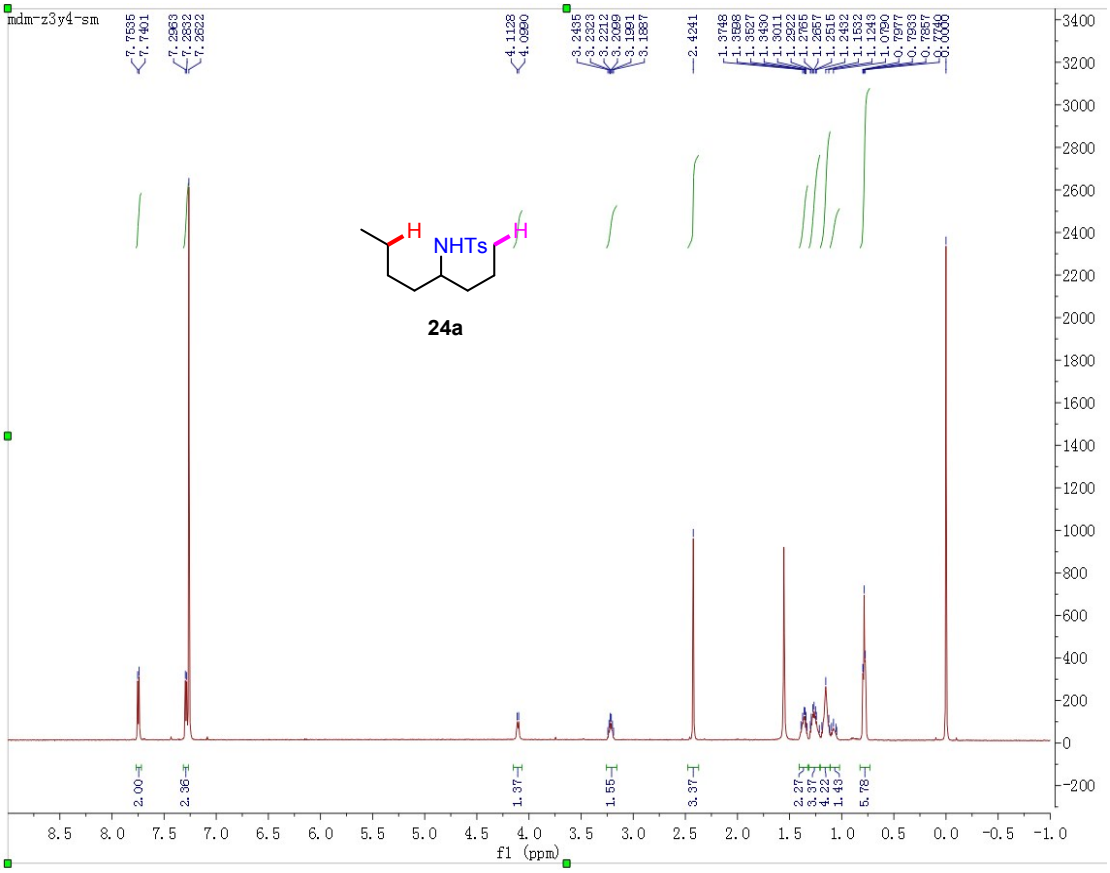

mdm-437-0-sm
7.7324
7.7188
7.3001
7.2867
7.2679
7.2584
7.2429
7.1851
7.1728
7.1606
7.1062
7.0940
4.2959
4.2669
4.2572
4.2475
3.0190
2.9692
2.9578
2.9468
2.9364
2.8976
2.5660
2.5535
2.5408
2.4225
1.6186
1.6067
1.5936
1.5888
1.5810
1.5679
1.5431
1.5084
1.4966
1.4835
1.4711
1.4595
0.0000
H
NHTs
19a
2.00
2.00
3.30
1.05
2.01
1.13
2.15
2.17
3.09
2.11
2.16
f1 (ppm)

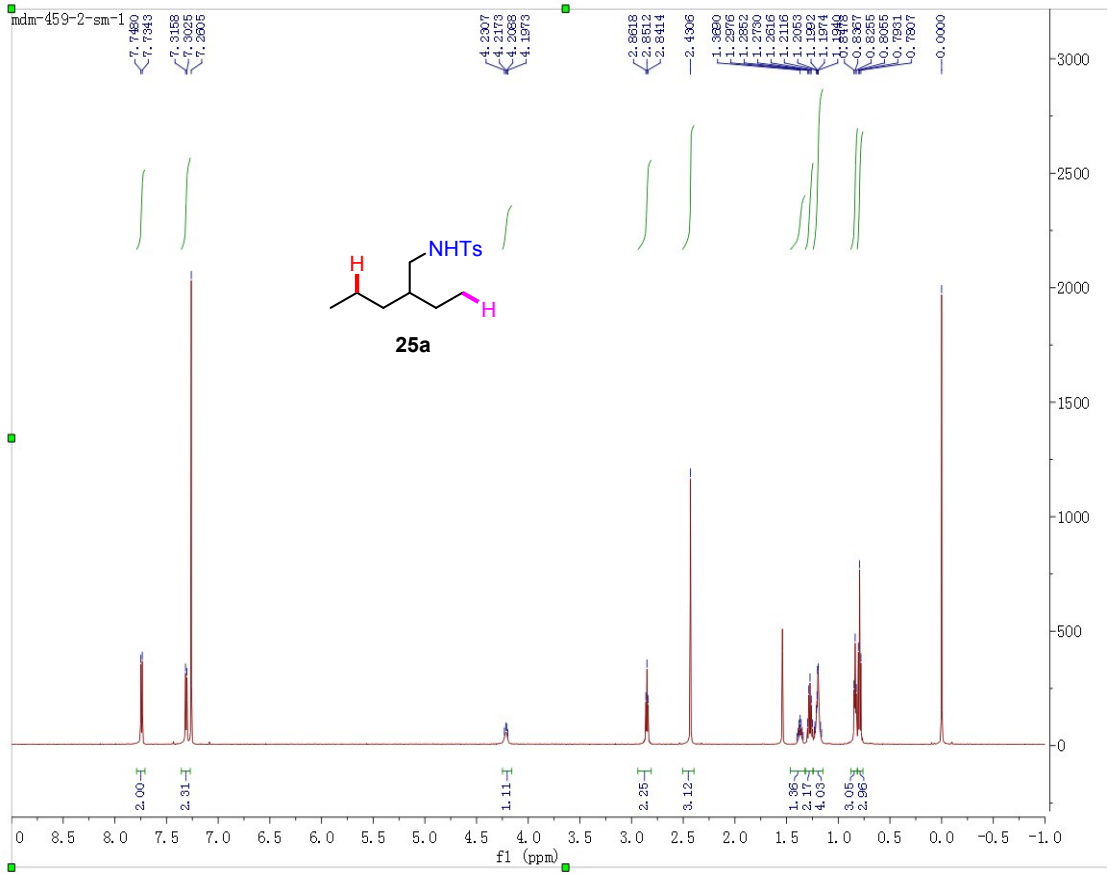

mdm-1-46-sm-2-H
H
NHTs
20a
f1 (ppm)

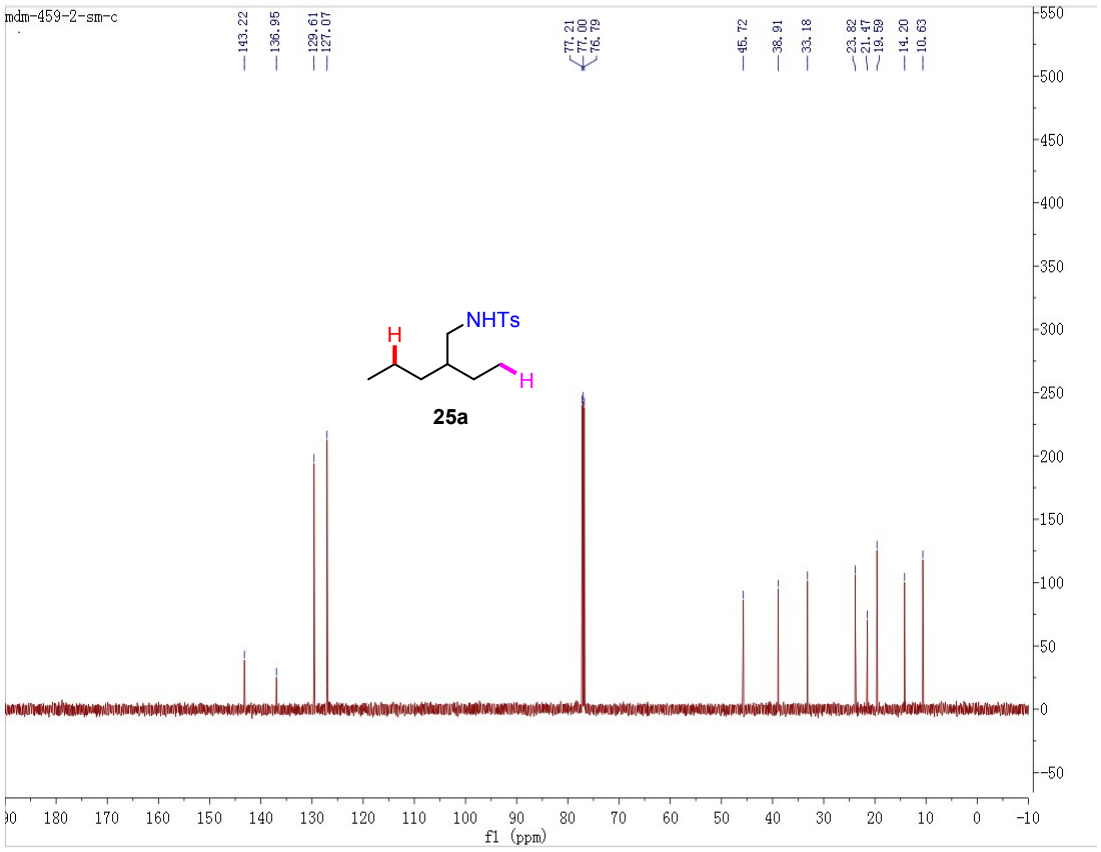

mdm-1-124-2
H
NHTs
MeO
21a
f1 (ppm)


mdm-1-124-1
H
NHTs
F
22a
f1 (ppm)

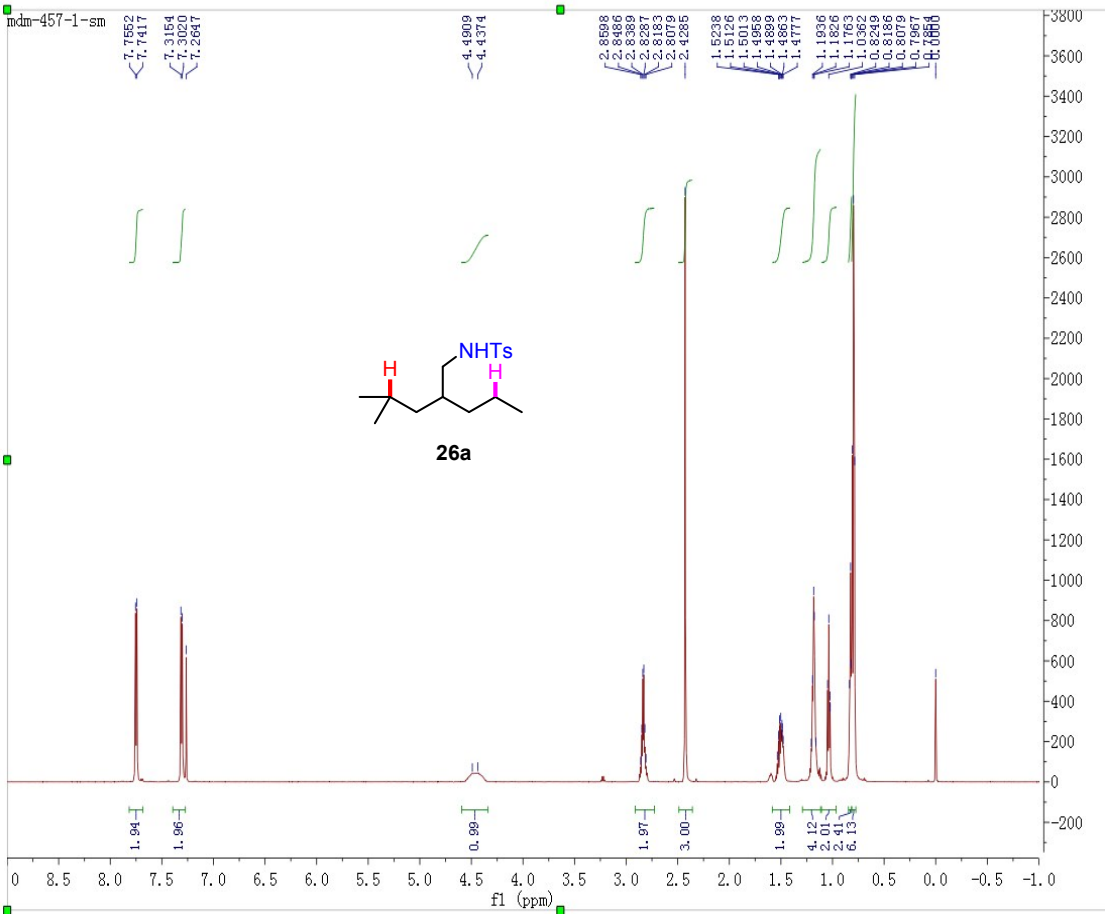

mdm-326-1-sm
NHTs
23a
f1 (ppm)


mdm-z3y4-sm
NHTs
H
H
24a
f1 (ppm)

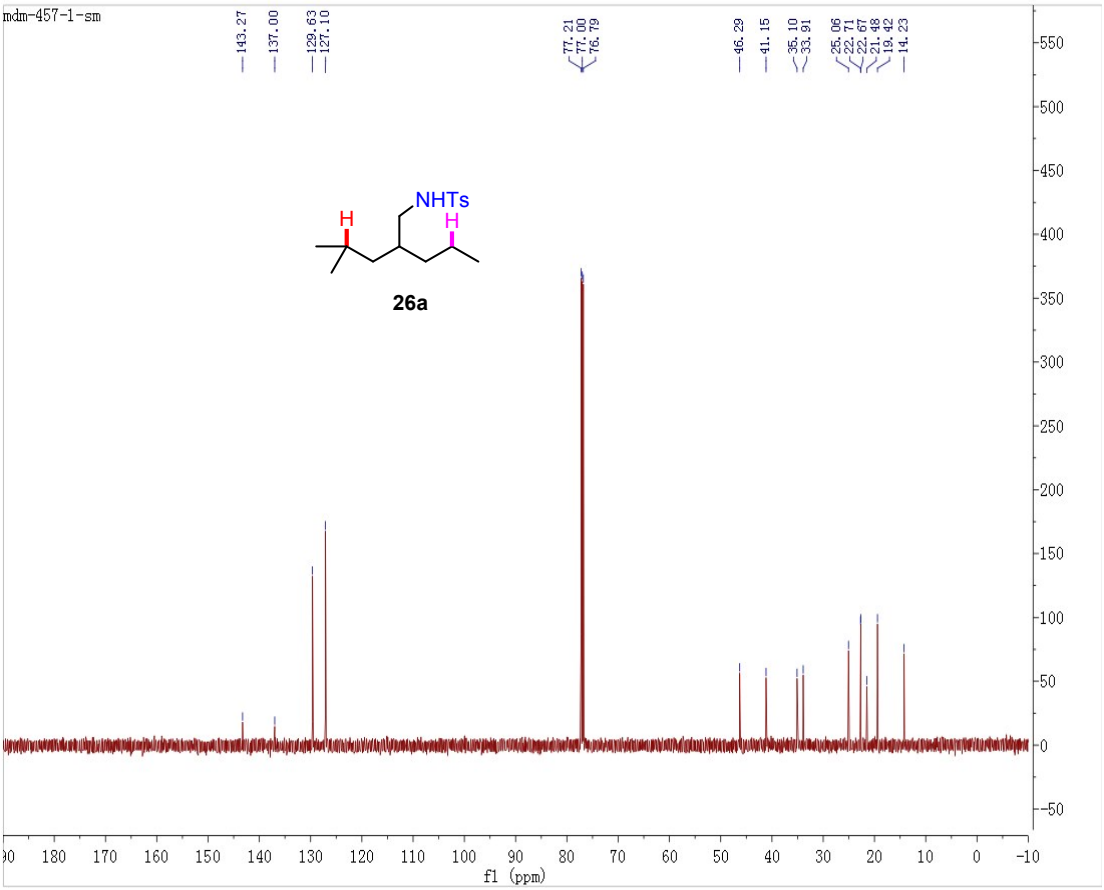

mdm-459-2-sm-1
NHTs
H
H
25a
f1 (ppm)

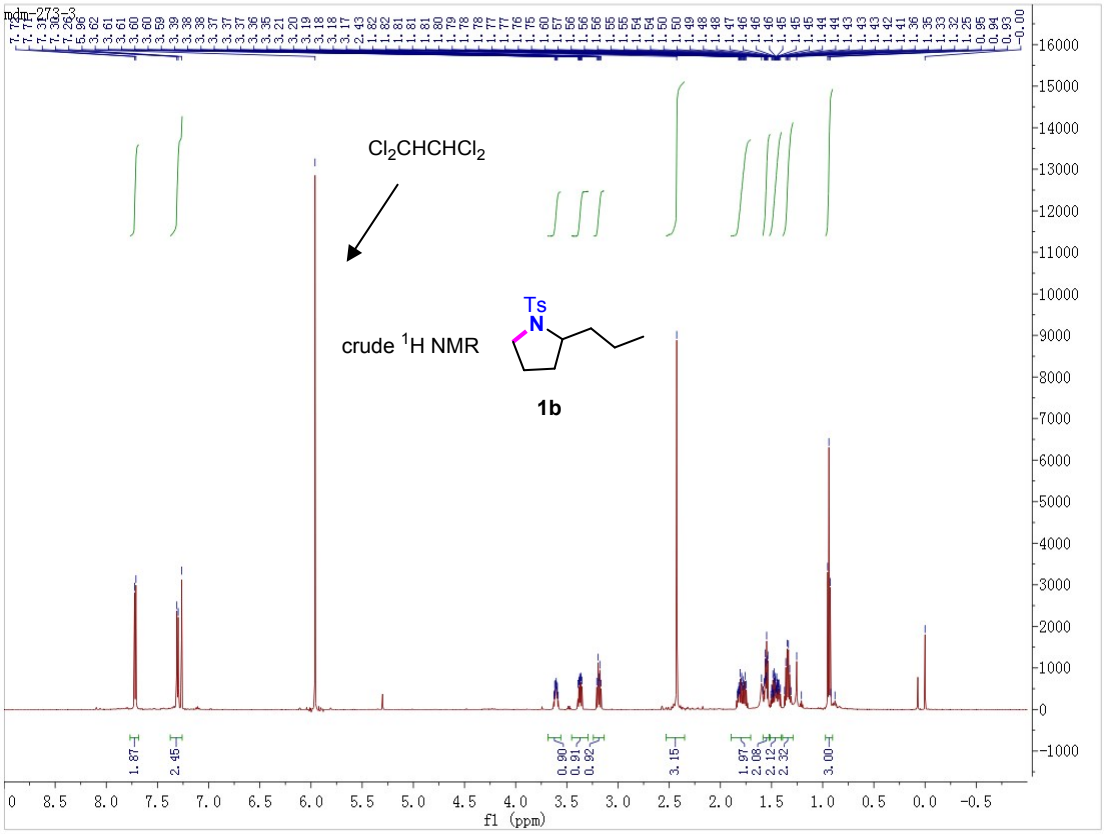

mdm-459-2-sm-c
143.22
136.95
129.61
127.07
77.21
77.00
76.79
45.72
38.91
33.18
23.82
21.47
19.59
14.20
10.63
NHTs
H
H
f1 (ppm)

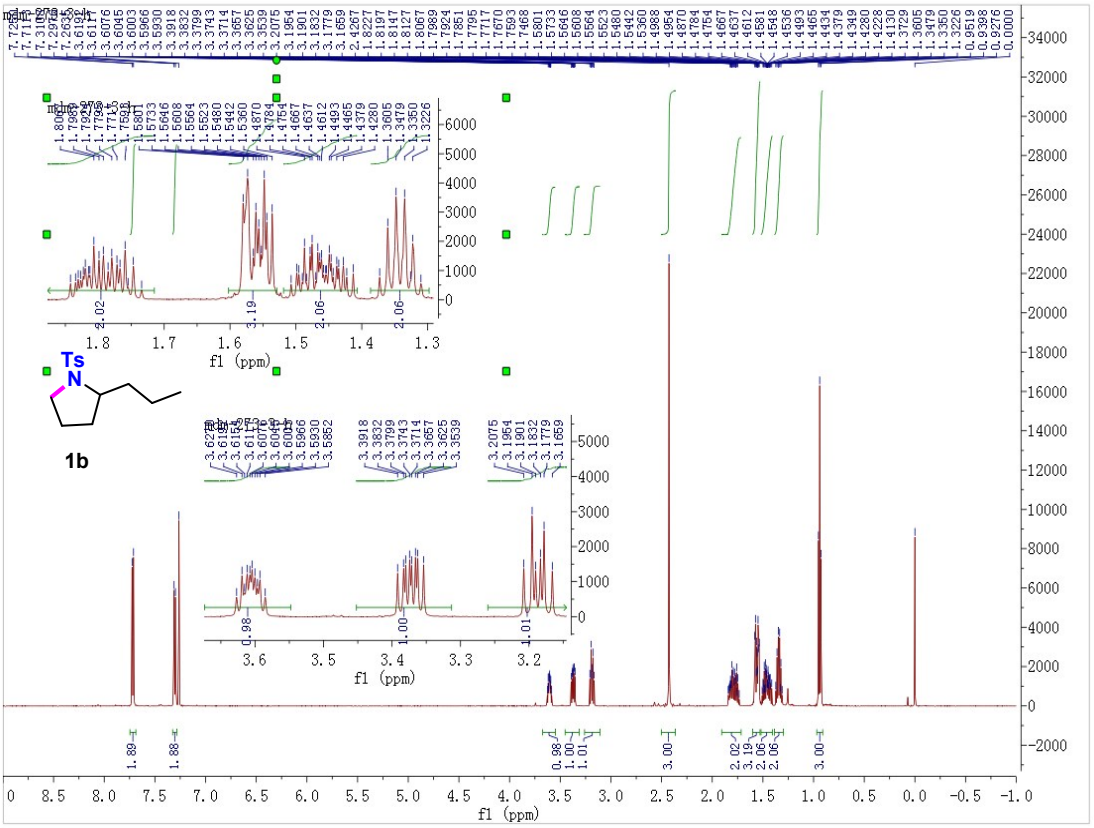
25a

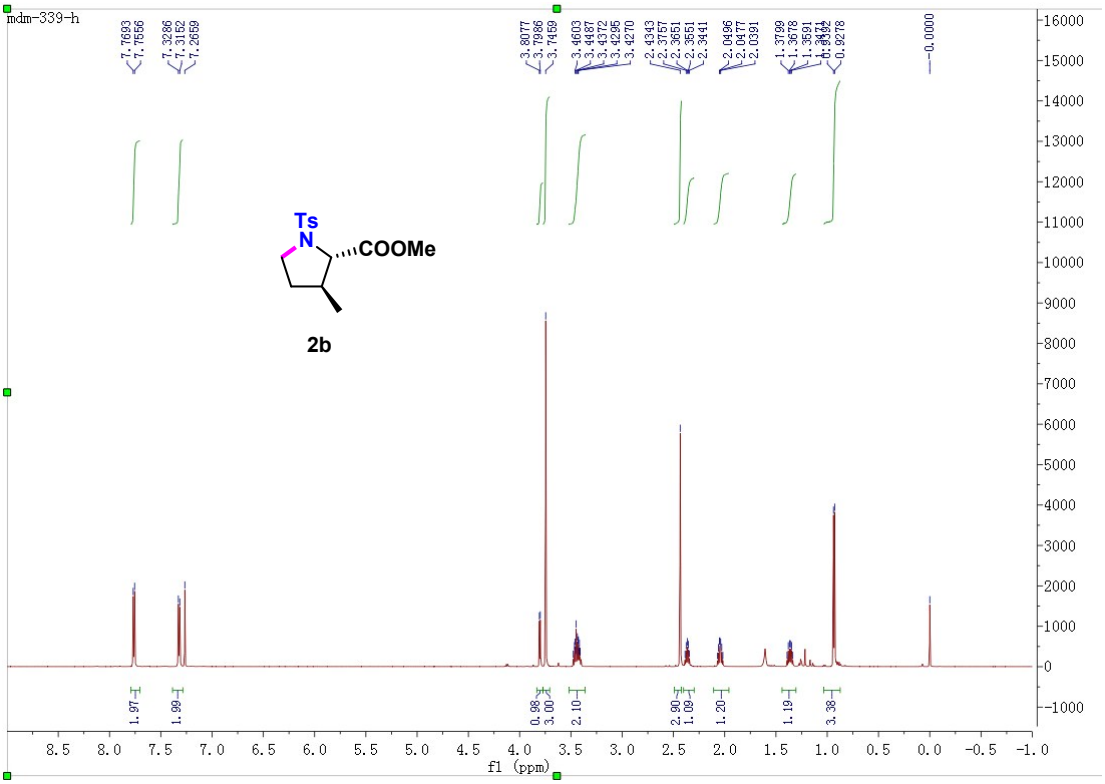

mdm-457-1-sm
7.7552
7.7417
7.3154
7.3020
7.2647
4.4909
4.4374
2.8598
2.8486
2.8389
2.8287
2.8183
2.8079
2.4285
1.5238
1.5126
1.5013
1.4958
1.4899
1.4863
1.4777
1.1936
1.1826
1.1753
1.1362
1.0249
0.8186
0.8079
0.7967
0.7854
0.0000
NHTs
H
H
1.94
1.96
0.99
1.97
3.00
1.99
4.12
2.01
2.41
6.13
f1 (ppm)

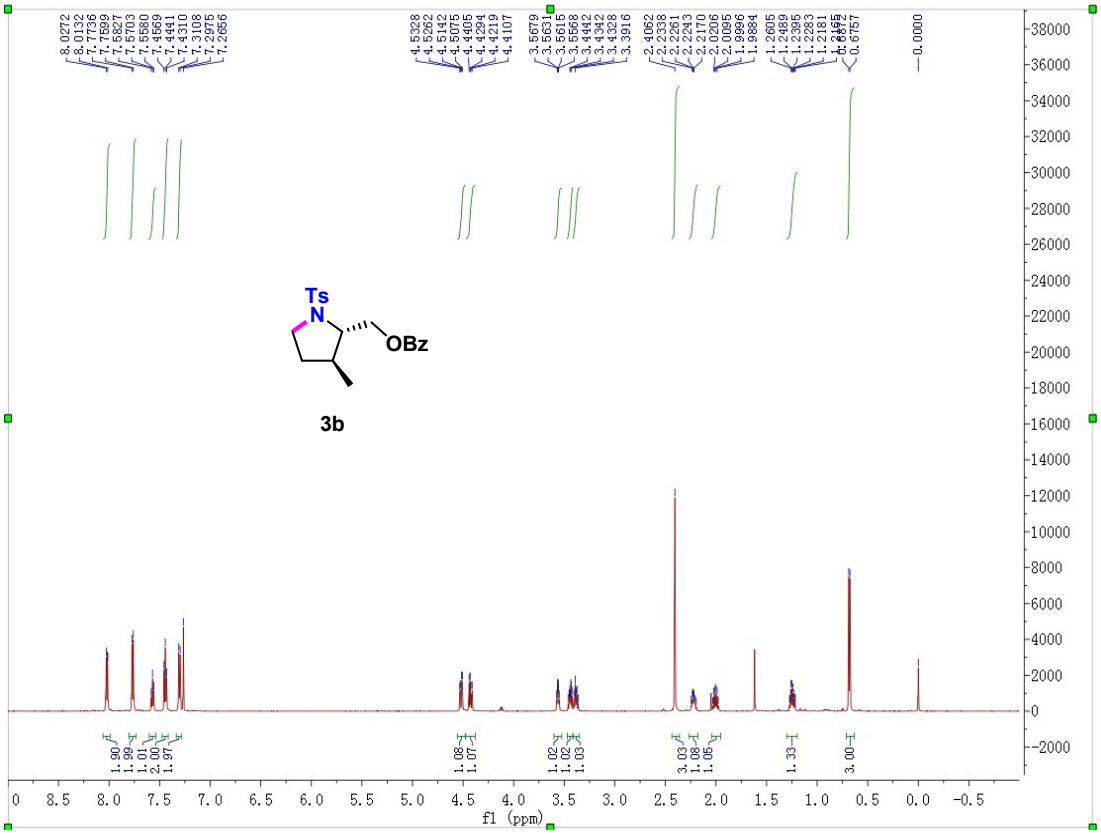
26a

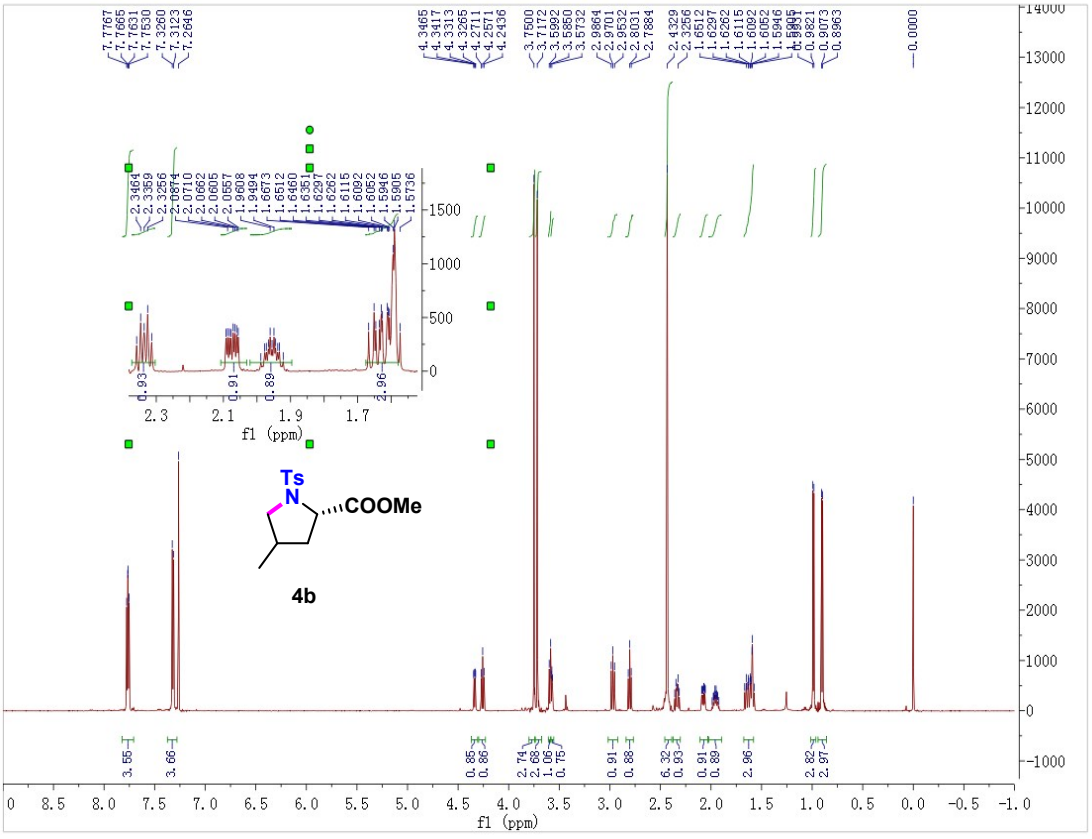

mdm-457-1-sm
143.27
137.00
129.63
127.10
77.21
77.00
76.79
46.29
41.15
35.10
33.91
25.06
22.71
22.67
21.48
19.42
14.23
NHTs
H
H
26a
f1 (ppm)

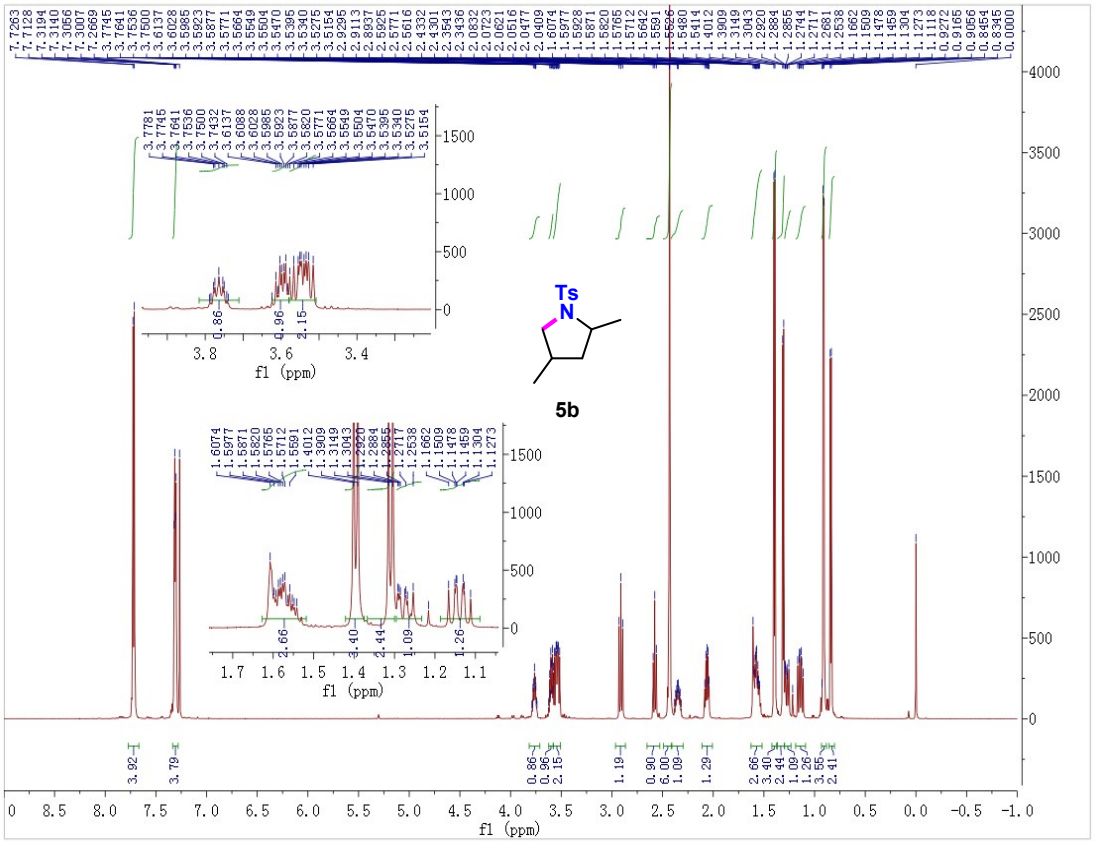

mdm-273
Cl2CHCHCl2
crude 1H NMR
Ts
N
1b
1.87
2.45
0.90
0.91
0.92
3.15
1.97
2.08
2.12
2.32
3.00
f1 (ppm)

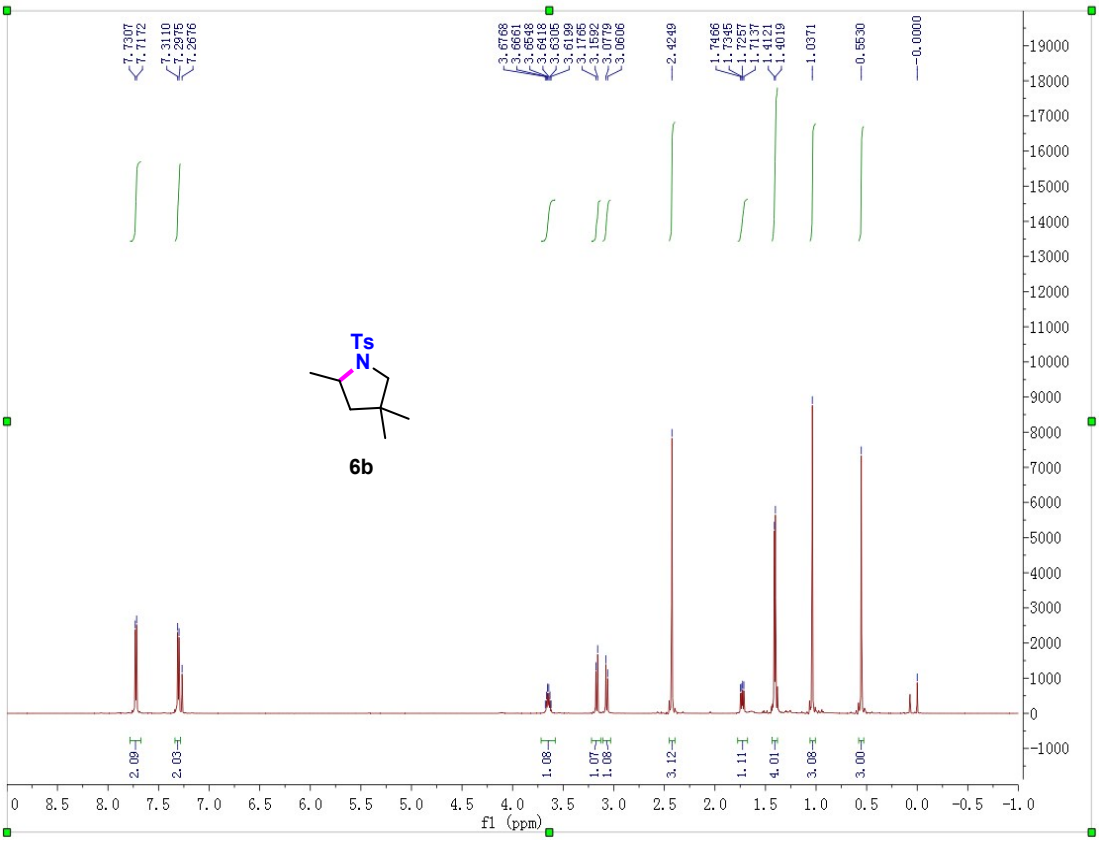

Ts
N
1b
f1 (ppm)

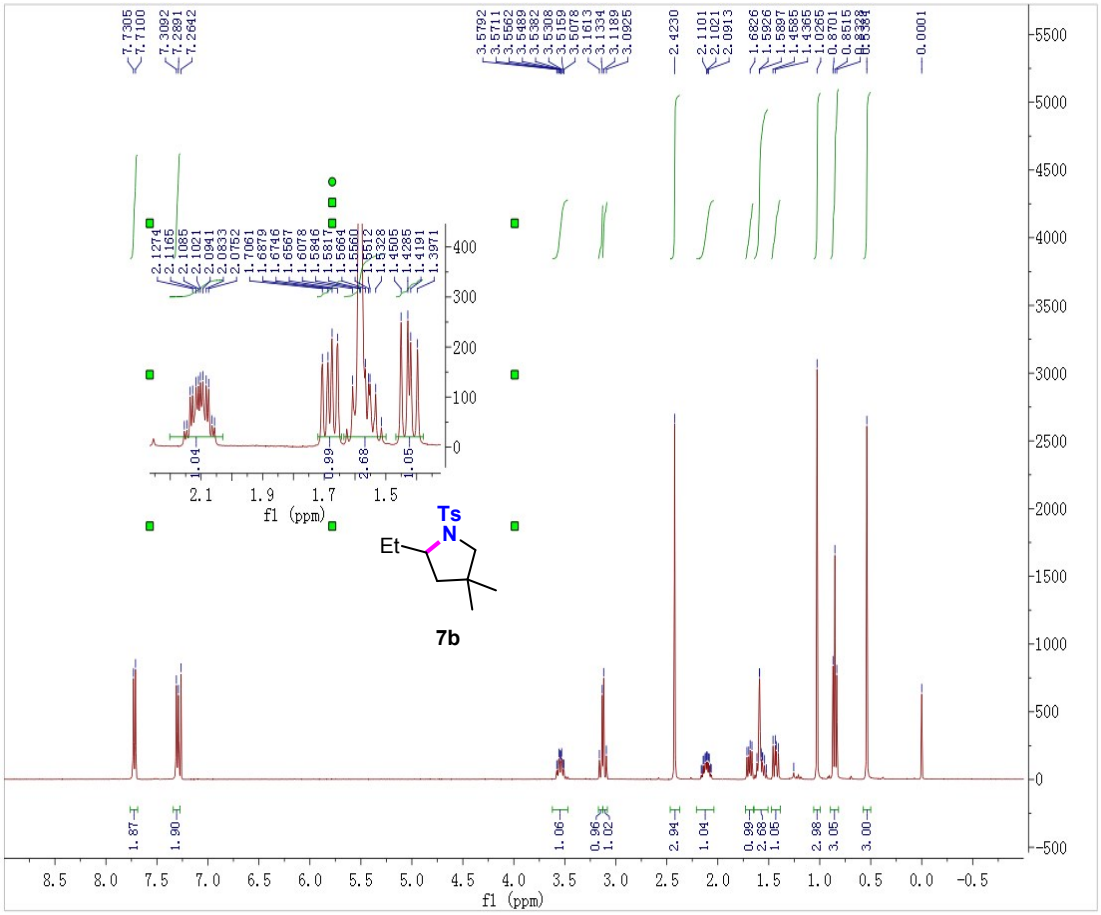

mdm-339-h
Ts
N
COOMe
2b
f1 (ppm)

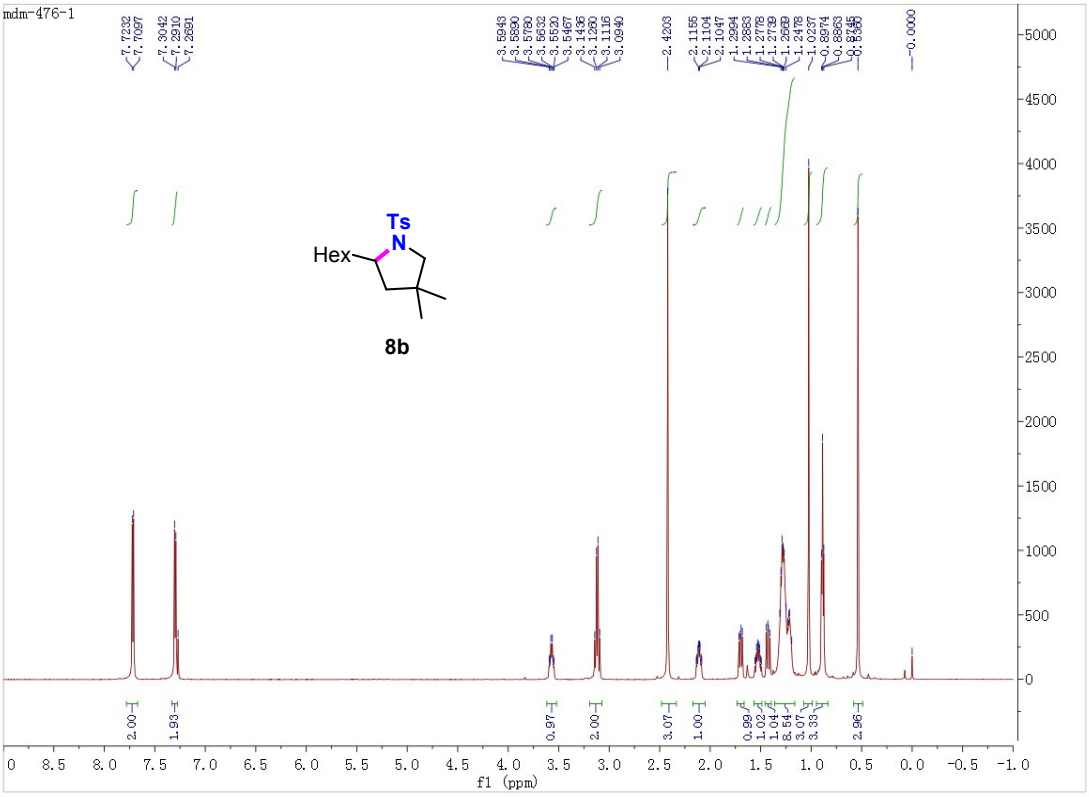

Ts
N
OBz
3b
f1 (ppm)

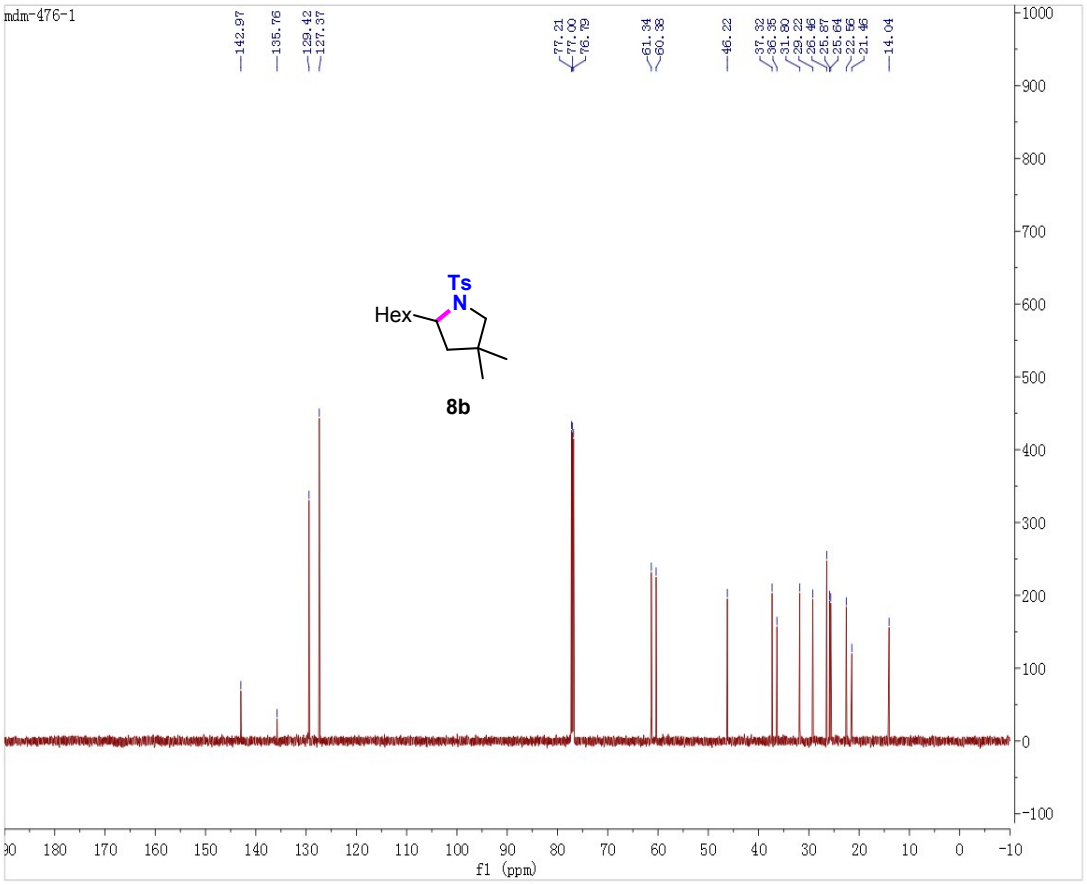

Ts
N
COOMe
4b
f1 (ppm)

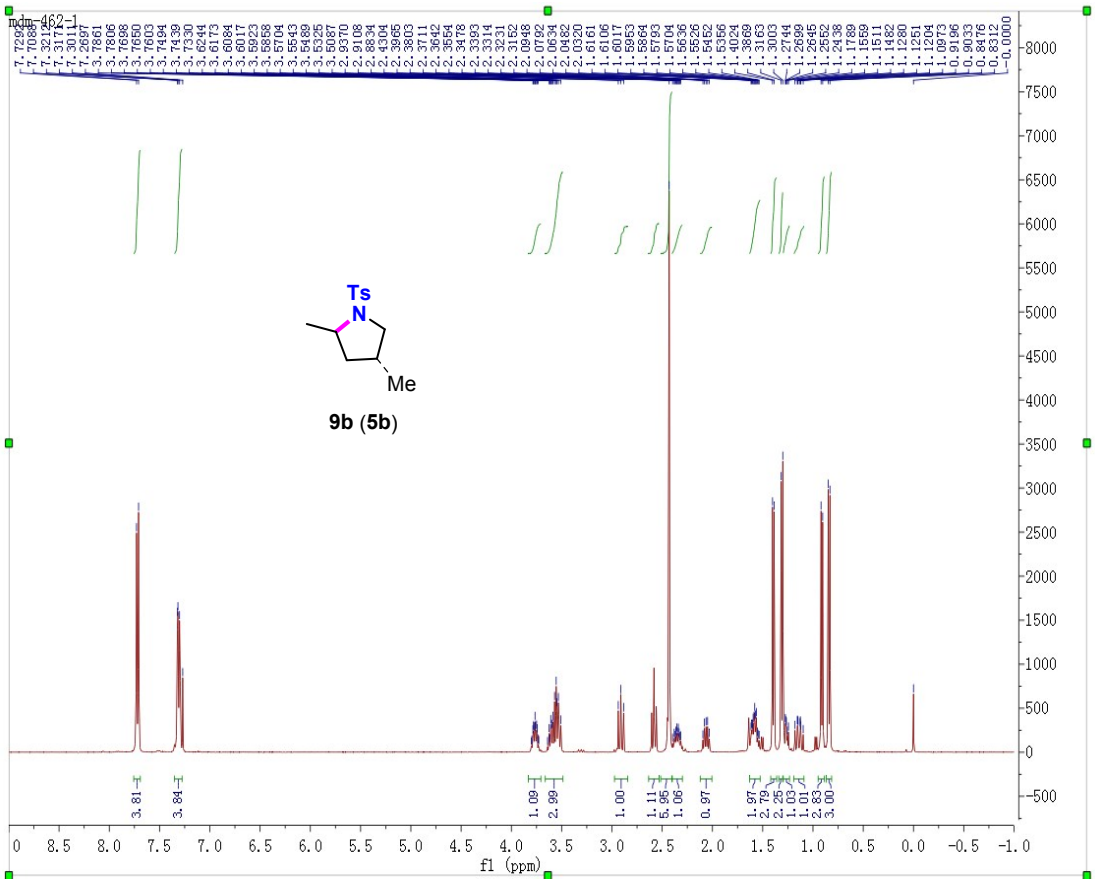

Ts
N
5b
f1 (ppm)

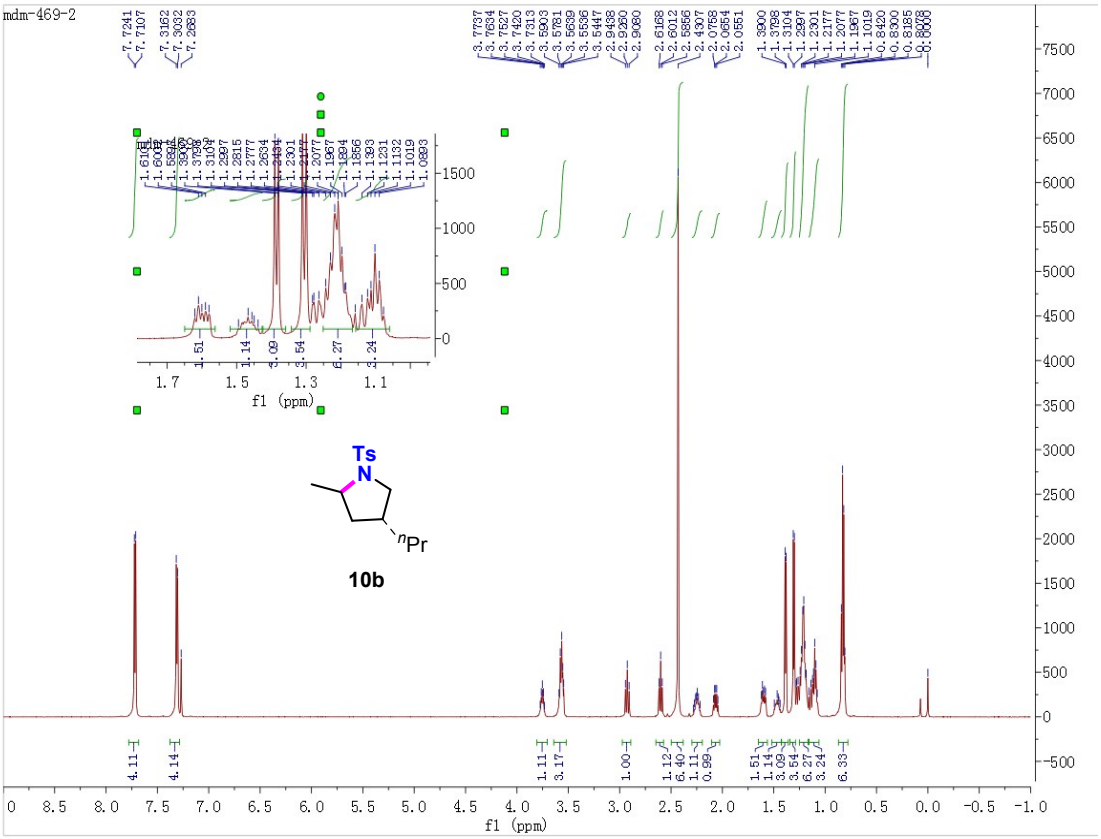

Ts
N
6b
f1 (ppm)

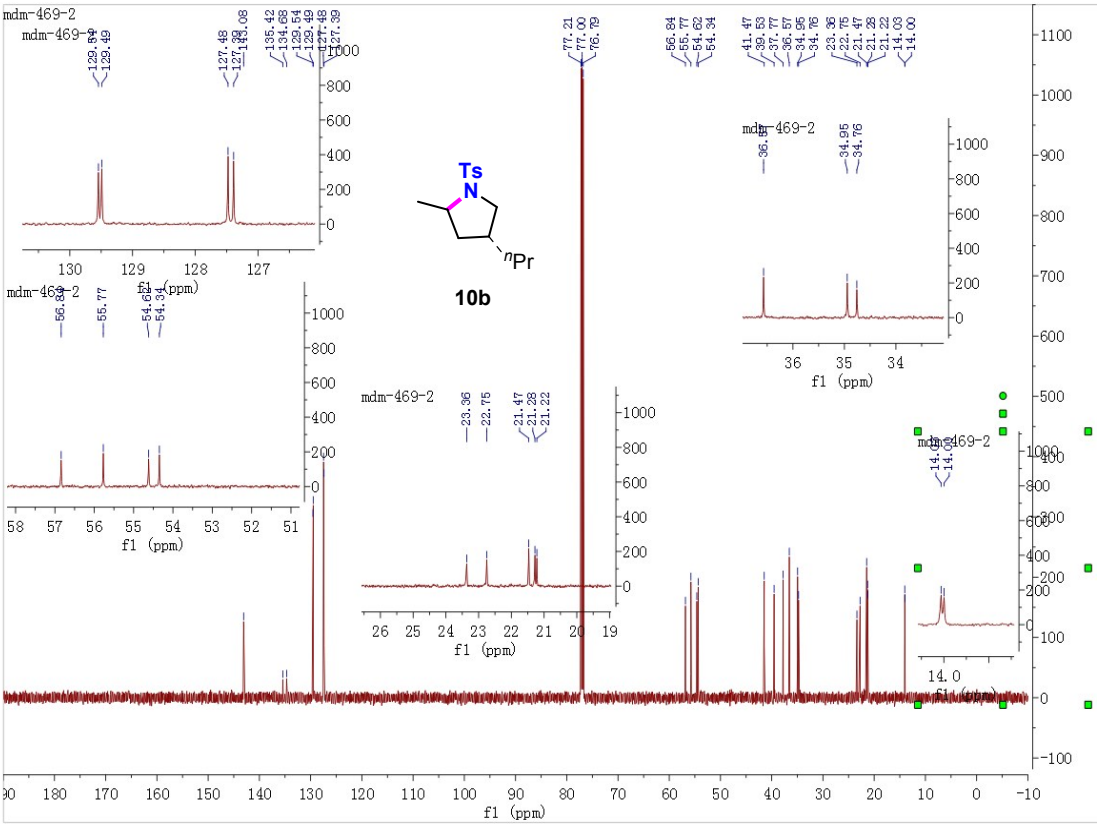

Ts
N
Et
7b
f1 (ppm)

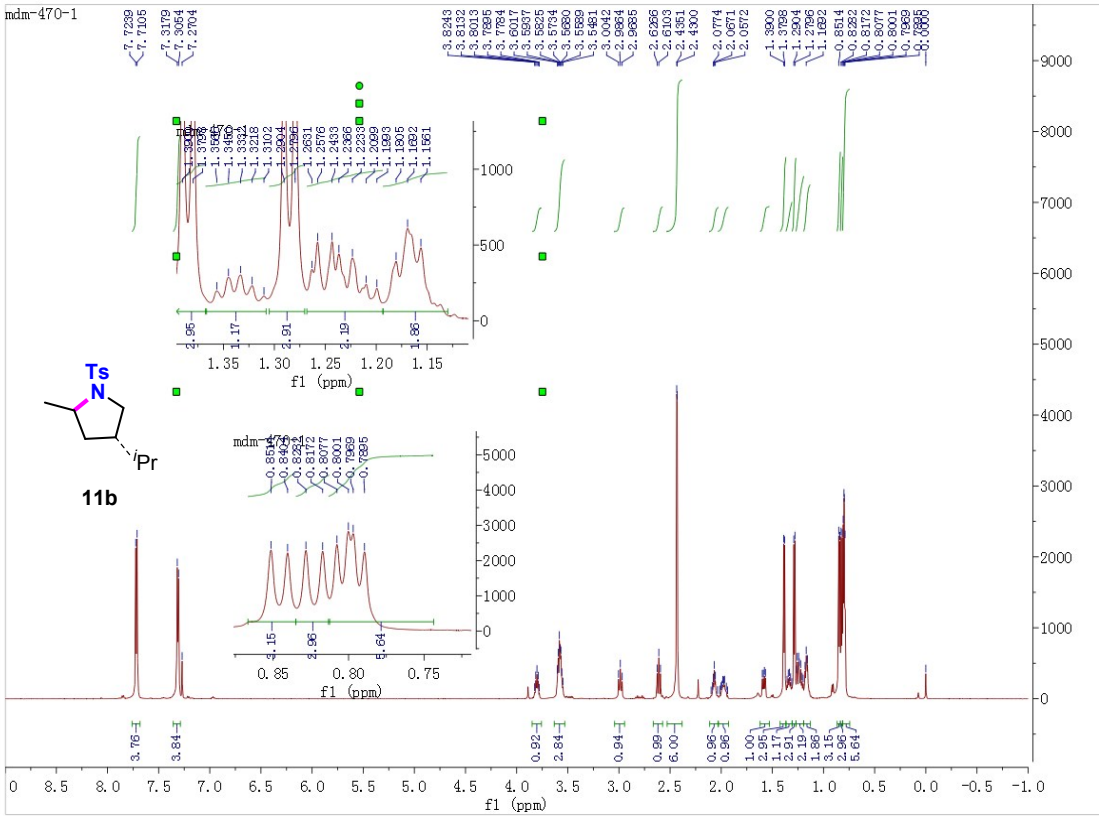

mdm-476-1
Ts
N
Hex
8b
f1 (ppm)

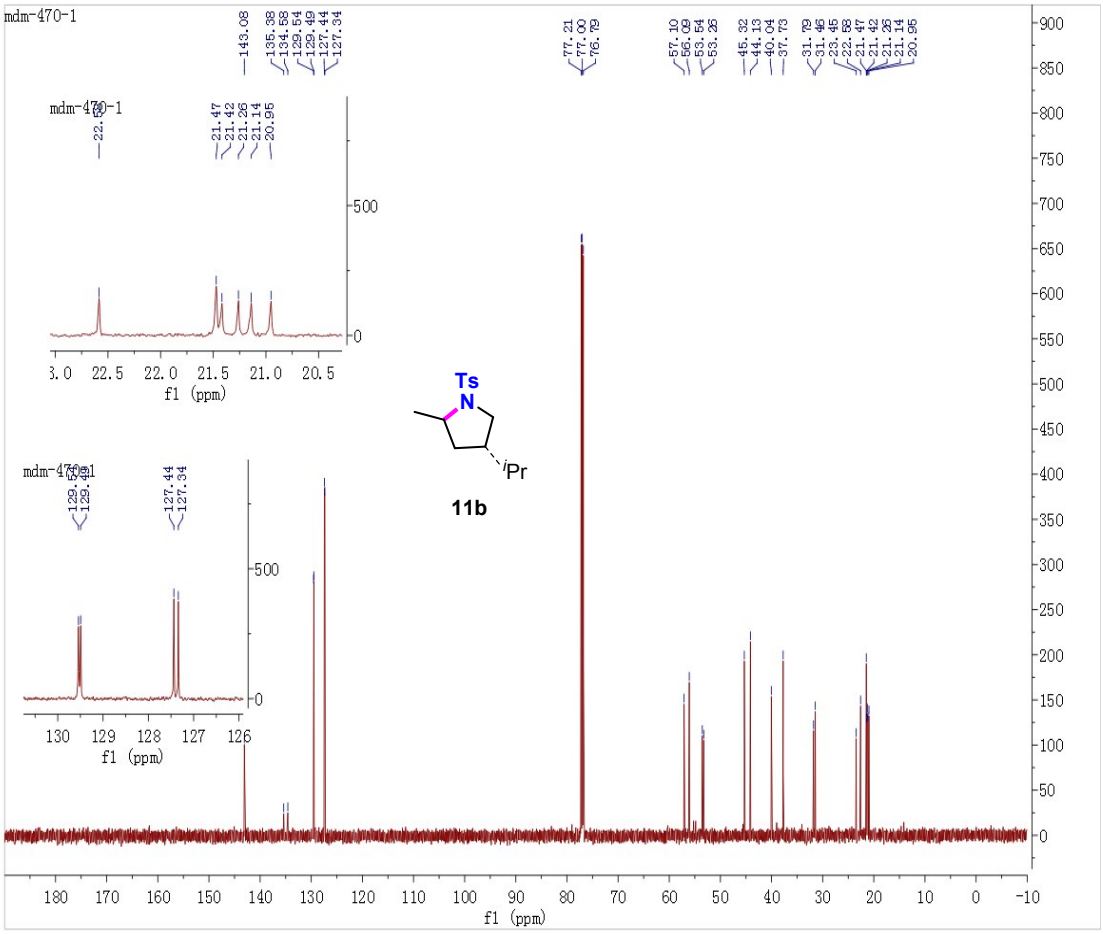

mdm-476-1
142.97
135.76
129.42
127.37
77.21
77.00
76.79
61.34
60.38
46.22
37.32
36.35
31.80
29.22
26.46
25.87
25.64
22.56
21.46
14.04
Ts
N
Hex
8b
f1 (ppm)

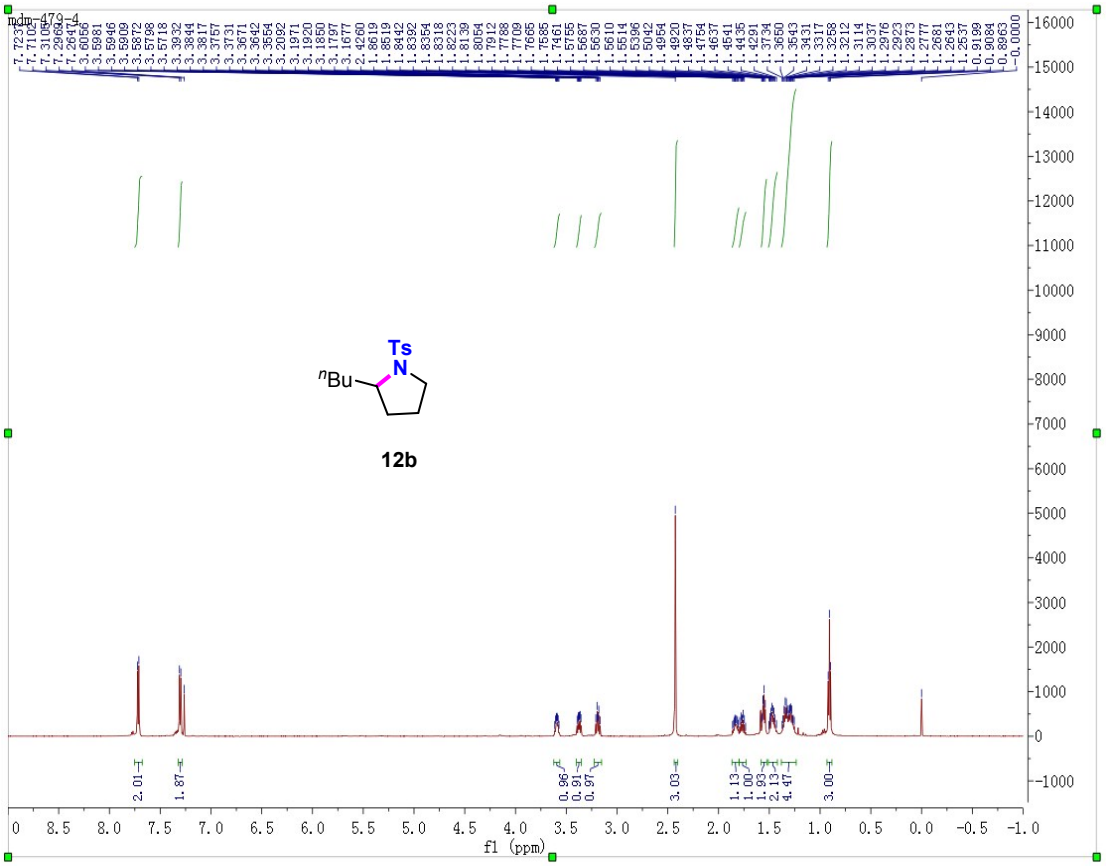

mdm-462-1
Ts
N
Me
9b (5b)
3.81
3.84
1.09
2.99
1.00
1.11
5.05
1.06
0.97
1.97
2.79
2.25
1.01
2.83
3.00
f1 (ppm)

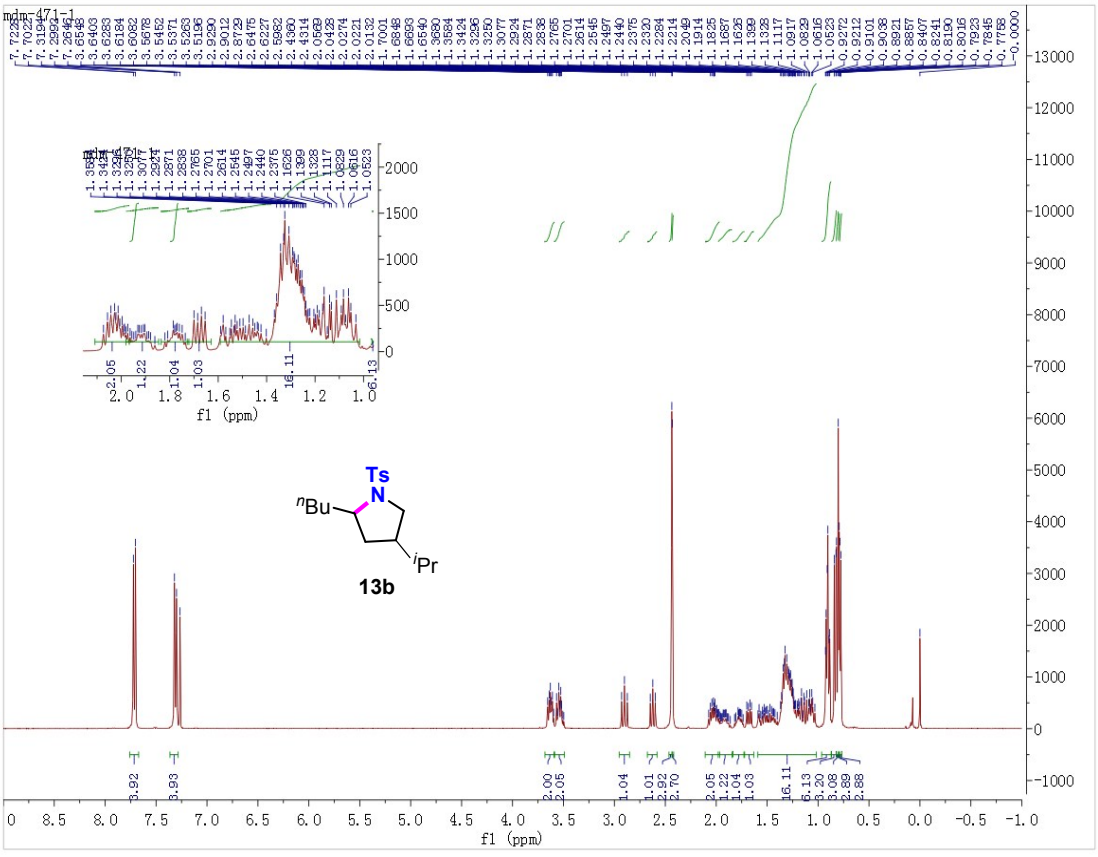

mdm-469-2
Ts
N
nPr
10b
f1 (ppm)

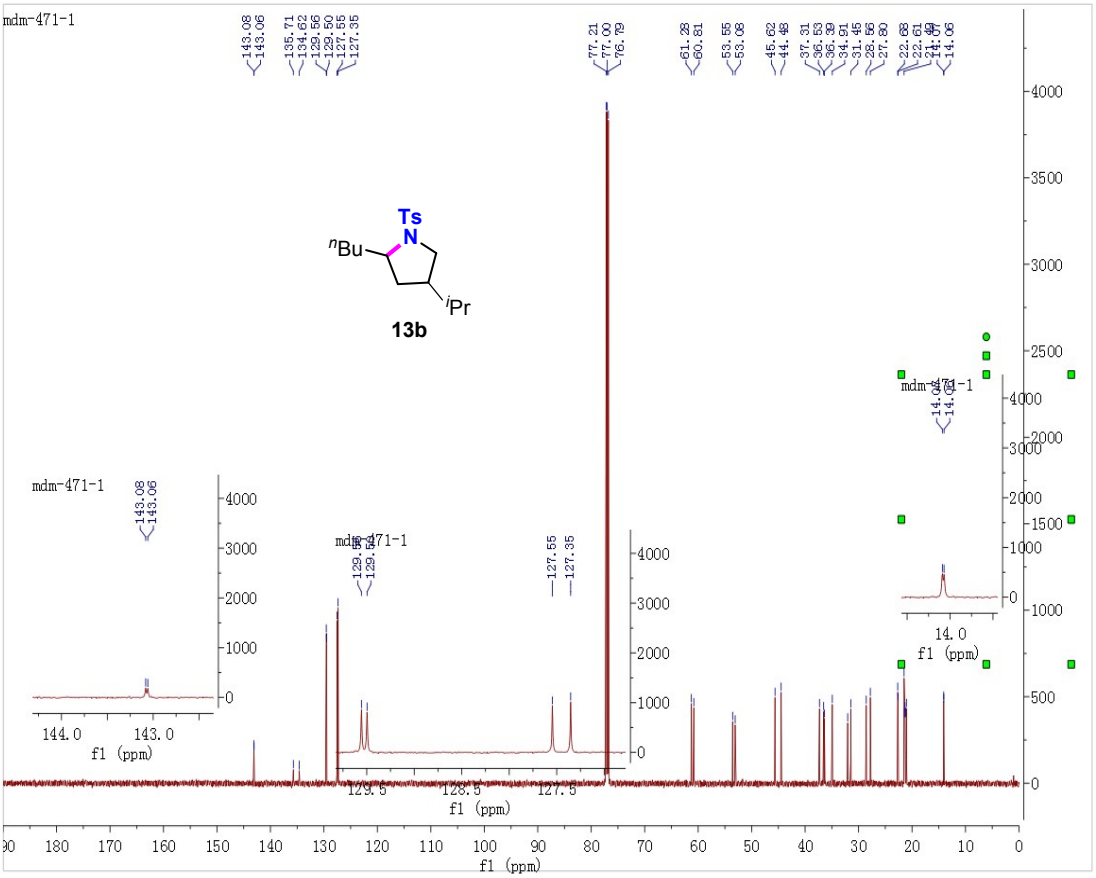

mdm-469-2
Ts
N
nPr
10b
f1 (ppm)

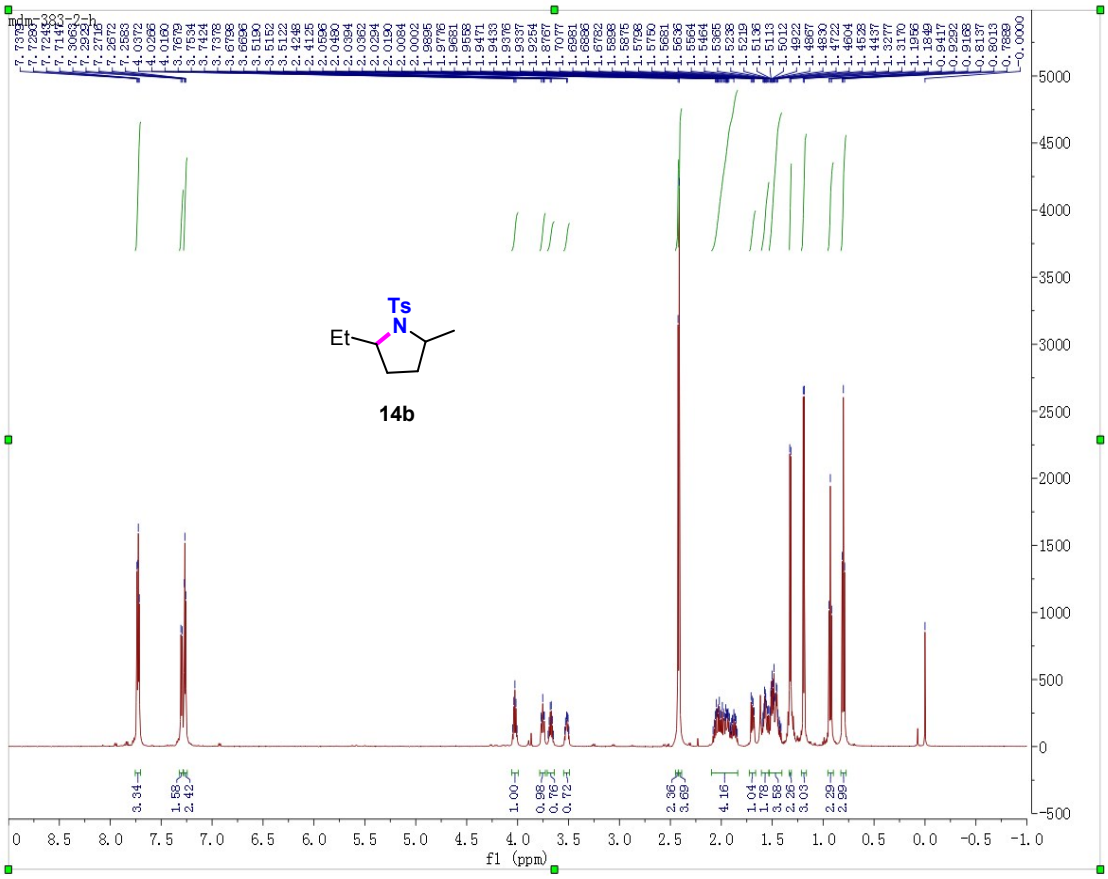

mdm-470-1
Ts
N
iPr
11b
f1 (ppm)

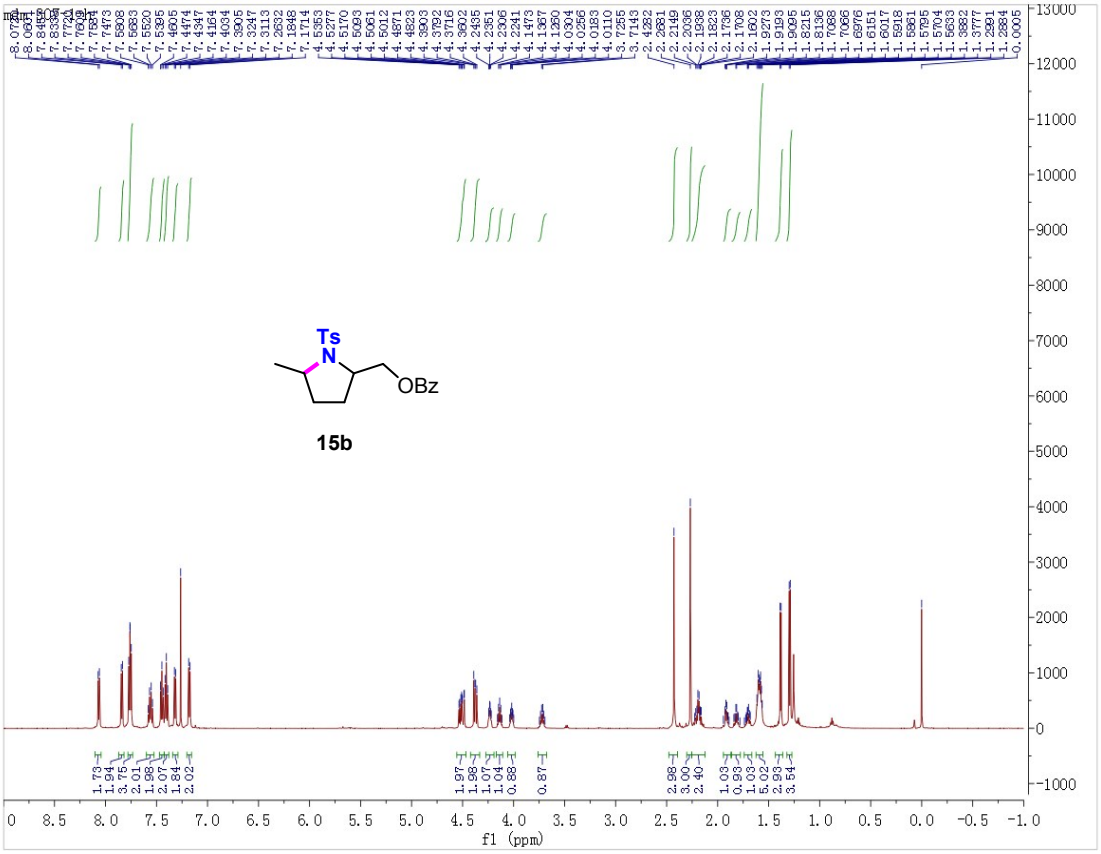

mdm-470-1
Ts
N
iPr
11b
f1 (ppm)

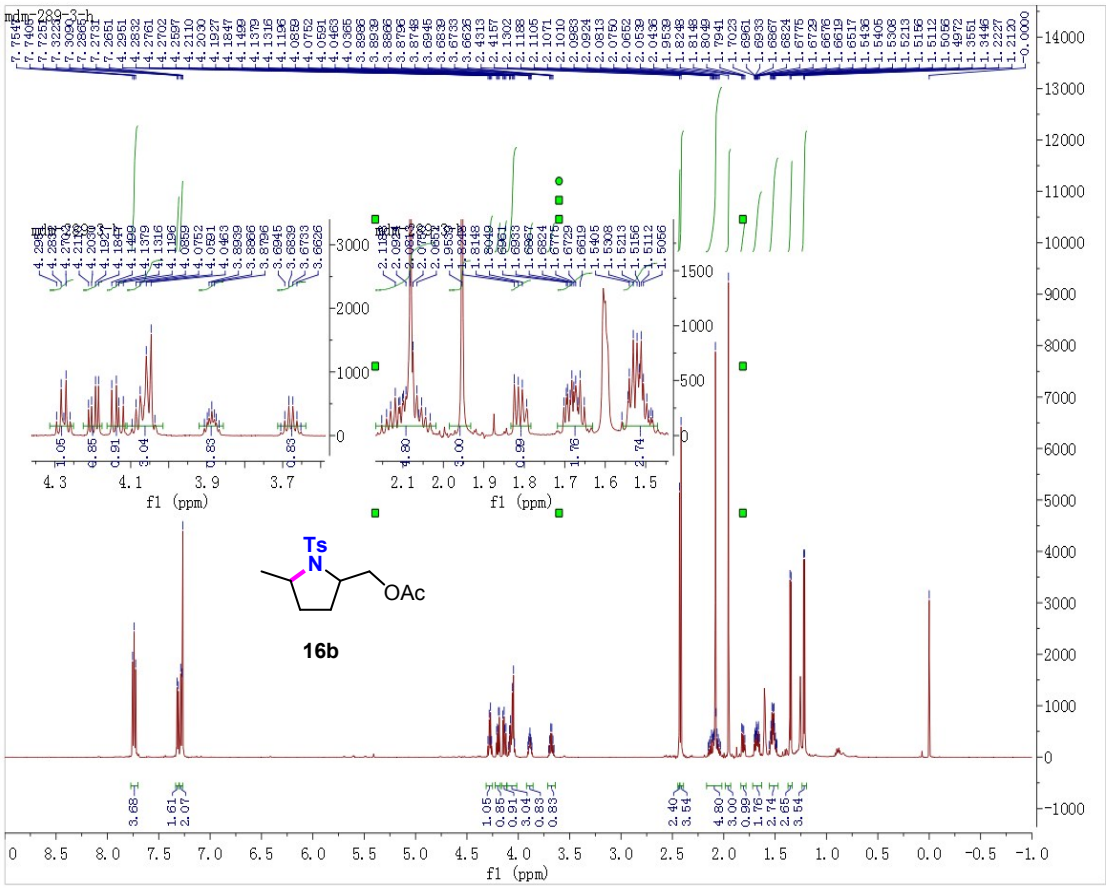

mdm-479-1
Ts
N
nBu
12b
f1 (ppm)

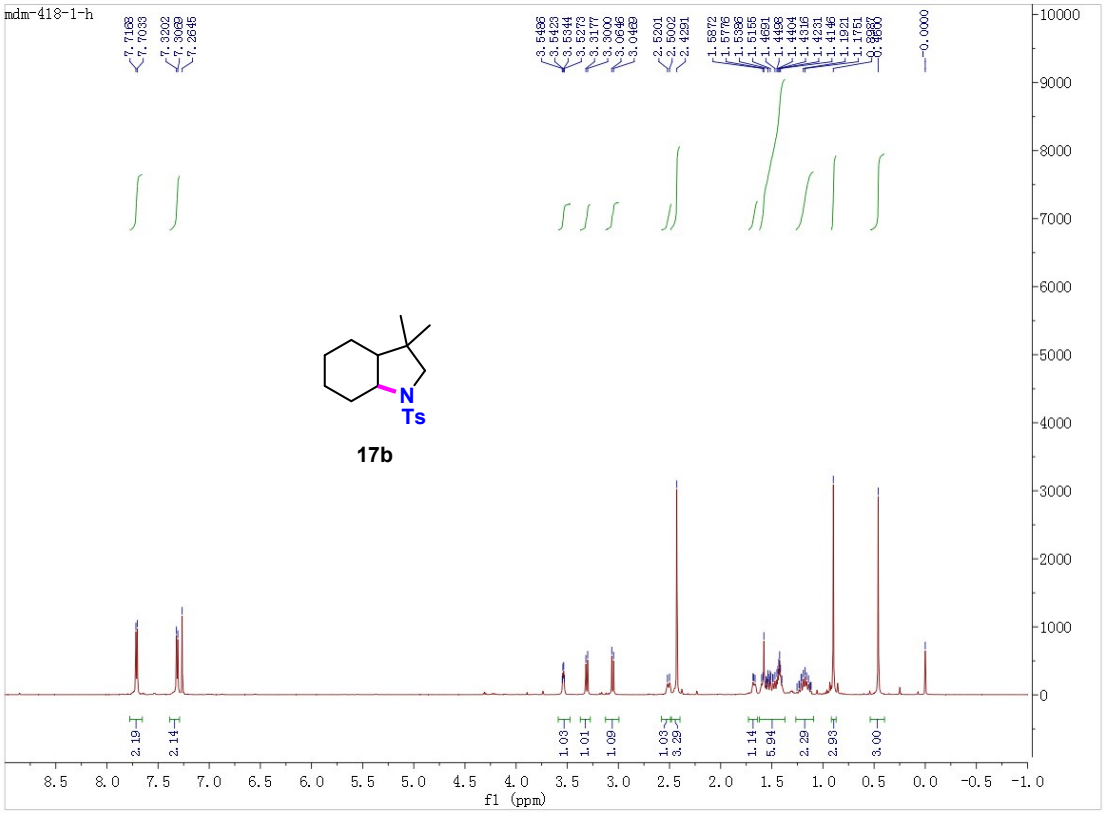

mdm-471-1
Ts
N
nBu
iPr
13b
f1 (ppm)

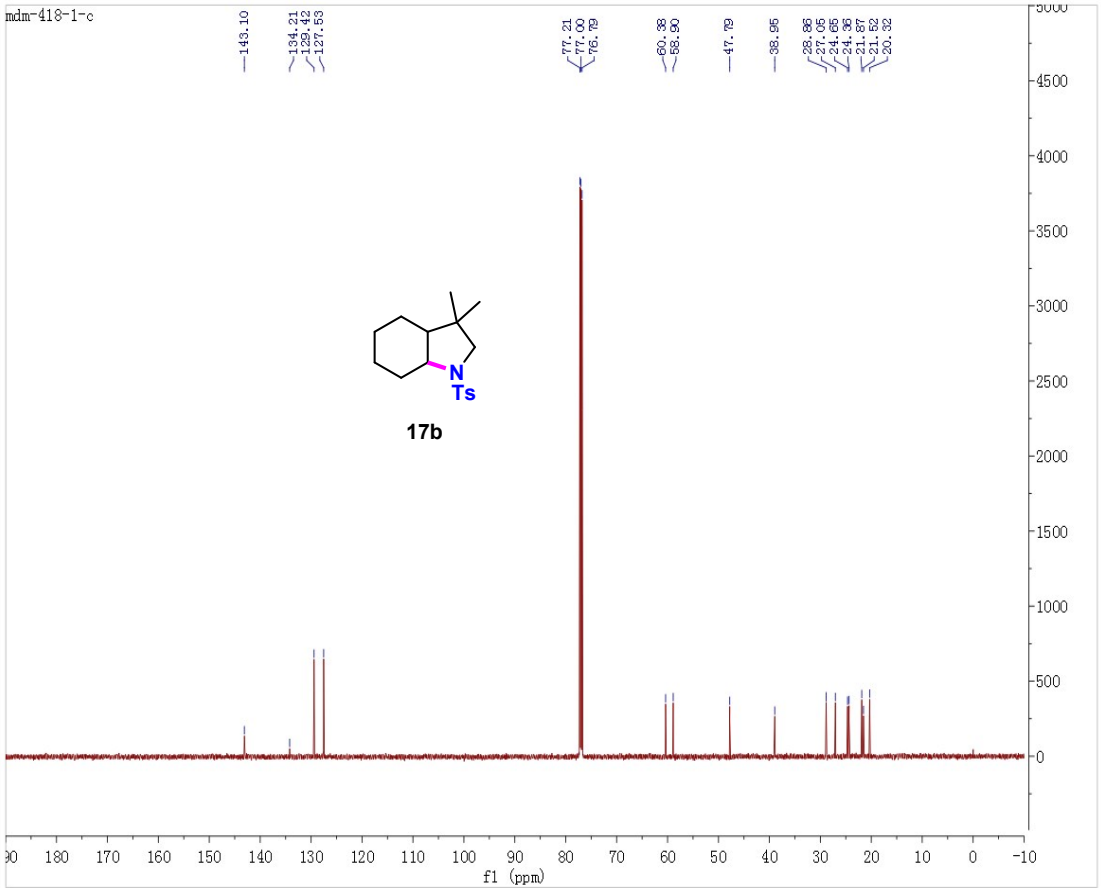

mdm-471-1
Ts
N
nBu
iPr
13b
f1 (ppm)

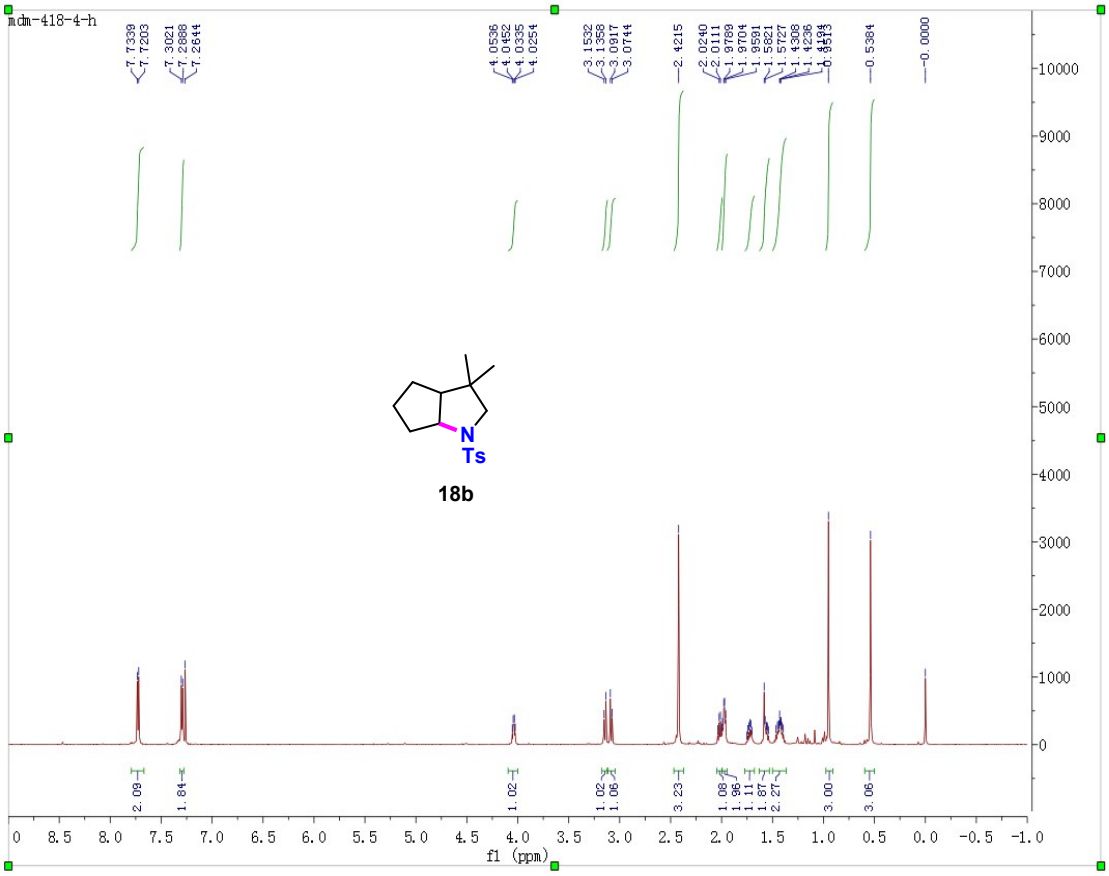

Ts
N
Et
14b
f1 (ppm)

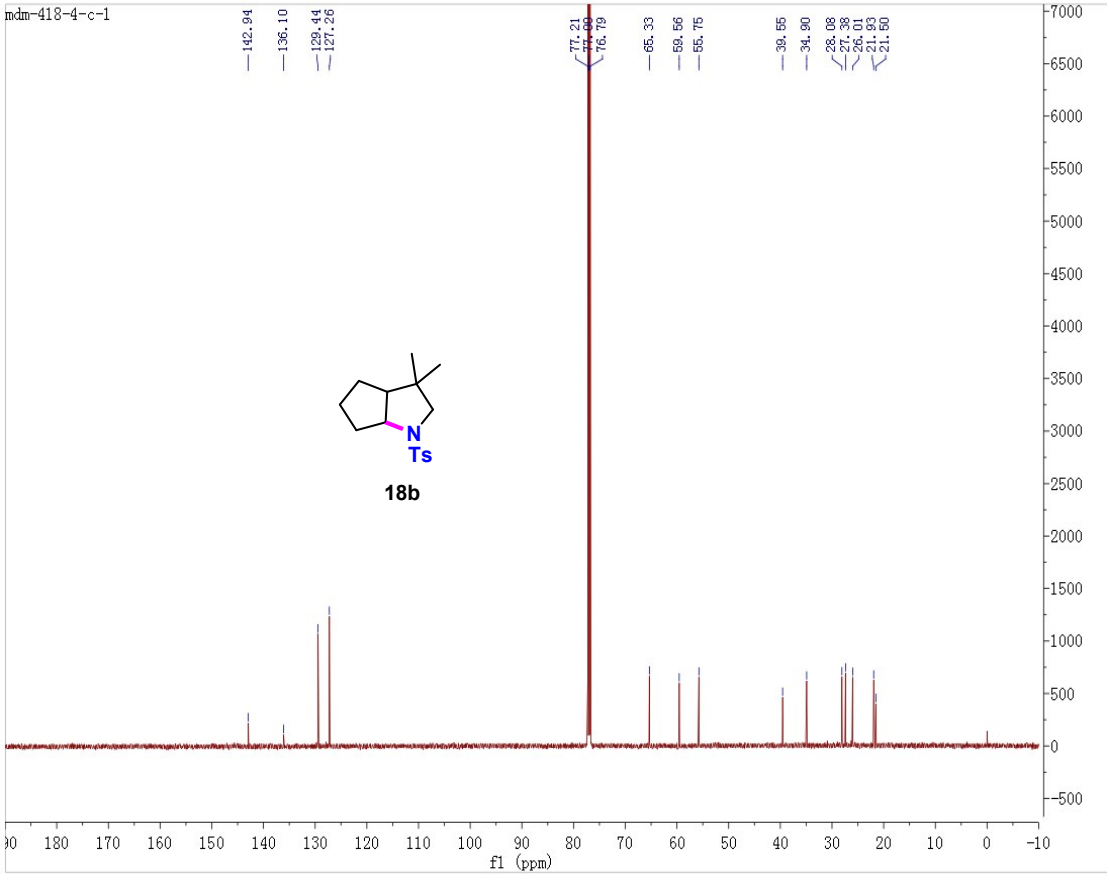

Ts
N
OBz
15b
f1 (ppm)

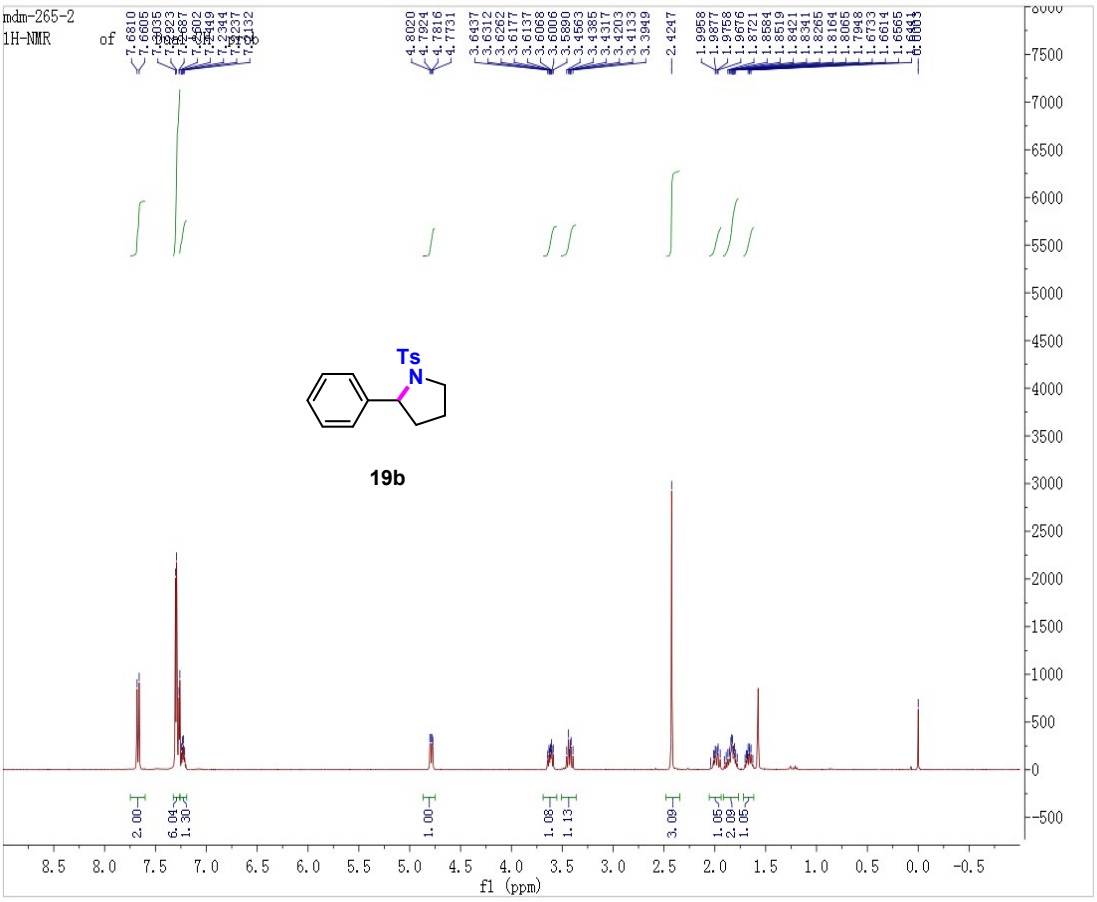

Ts
N
OAc
16b
f1 (ppm)

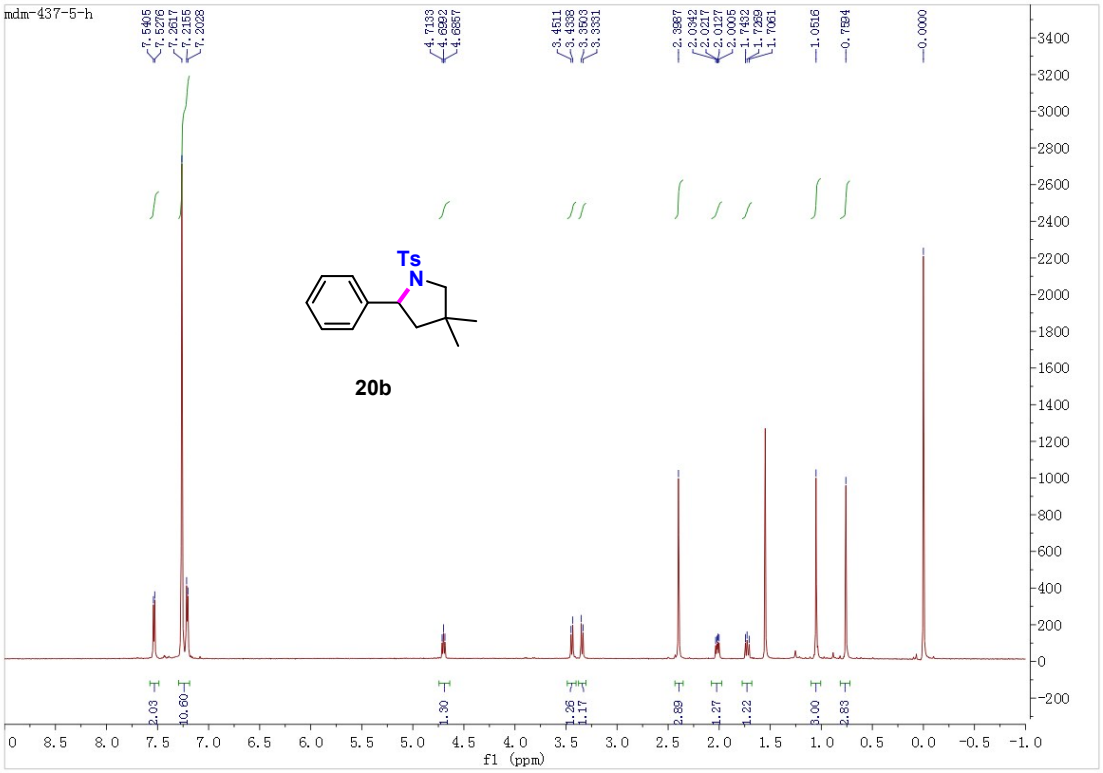

mdm-418-1-h
N
Ts
17b
f1 (ppm)

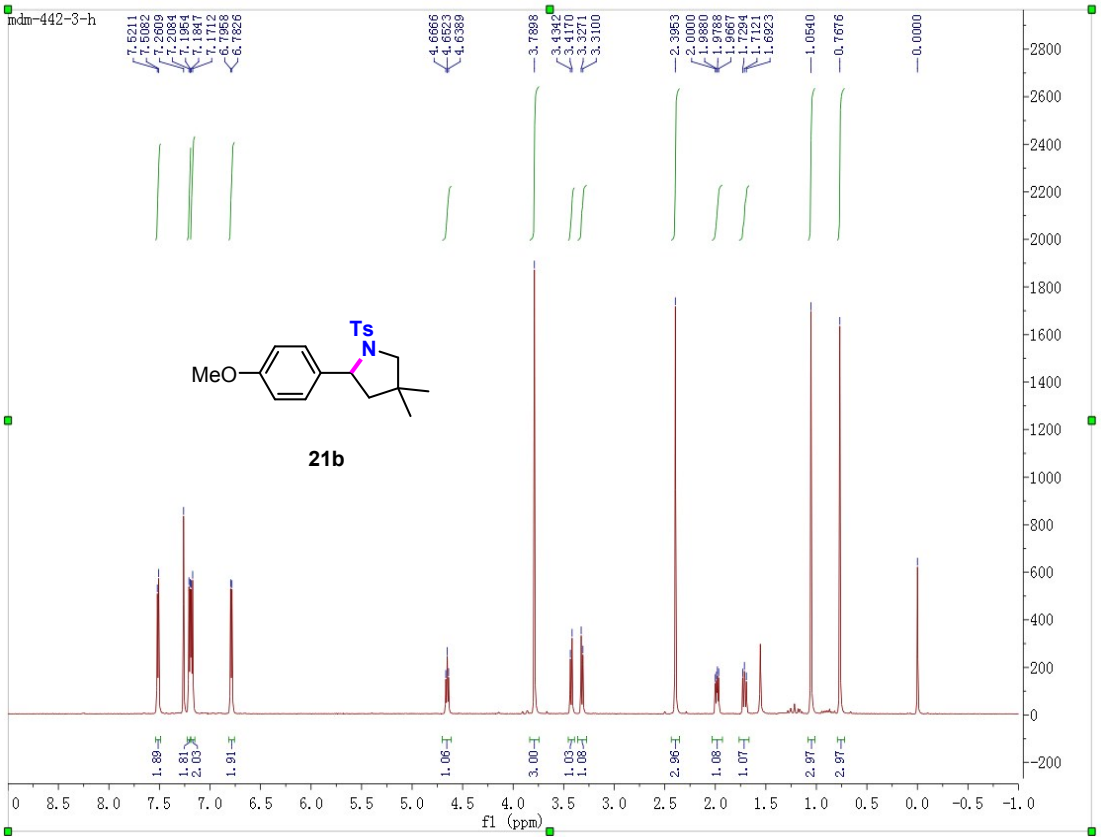

mdm-418-1-c
N
Ts
17b
f1 (ppm)

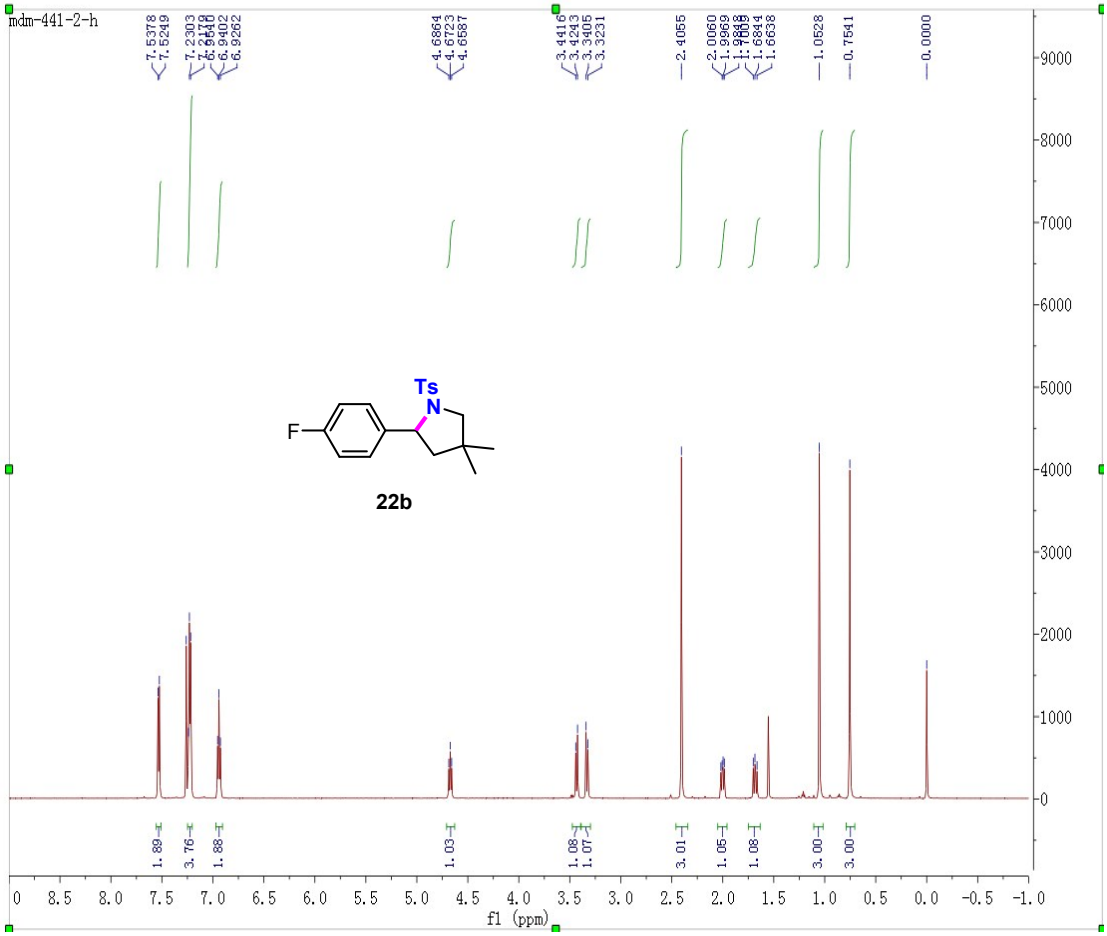

mdm-418-4-h
7.7339
7.7203
7.3021
7.2888
7.2644
4.0536
4.0452
4.0335
4.0254
3.1532
3.1358
3.0917
3.0744
2.4215
2.0240
2.0111
1.9789
1.9704
1.9591
1.5821
1.5727
1.4298
1.4194
0.9513
0.5384
-0.0000
N
Ts
18b
f1 (ppm)

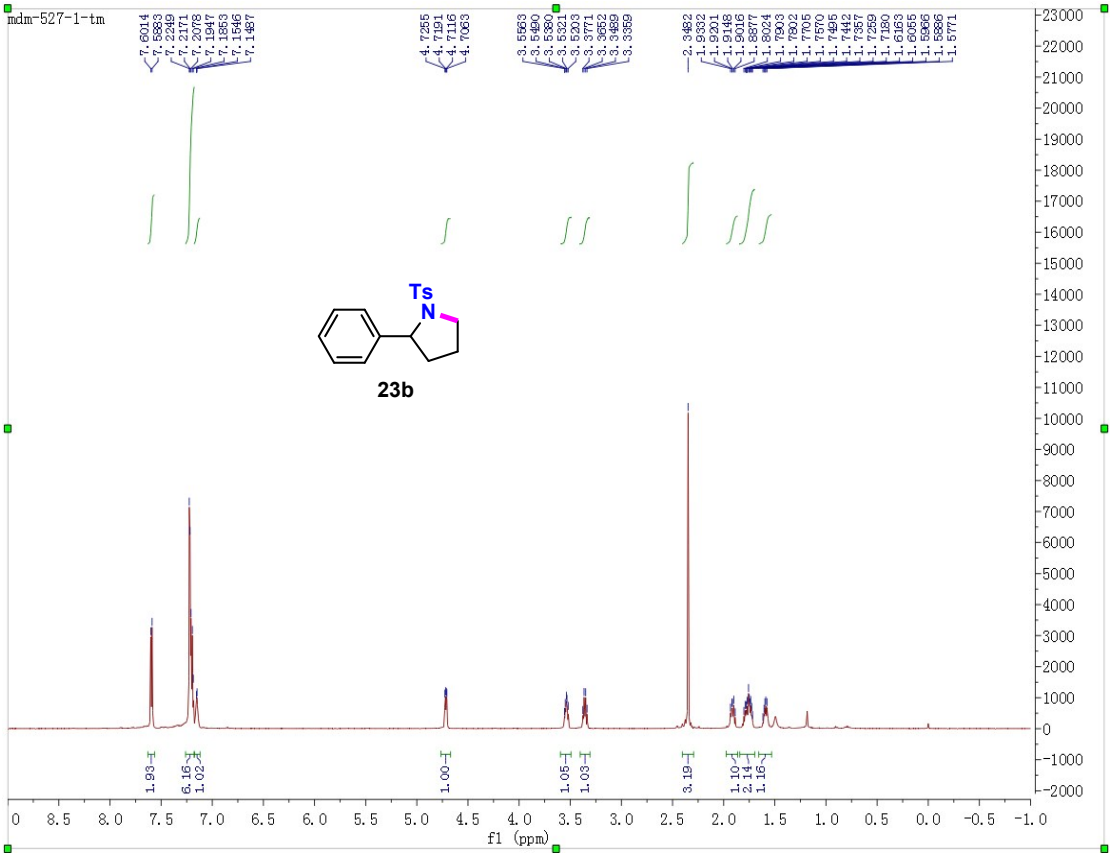

mdm-418-4-c-1
142.94
136.10
129.44
127.26
77.21
77.00
76.79
65.33
59.56
55.75
39.55
34.90
28.08
27.38
26.01
21.93
21.50
N
Ts
18b
f1 (ppm)

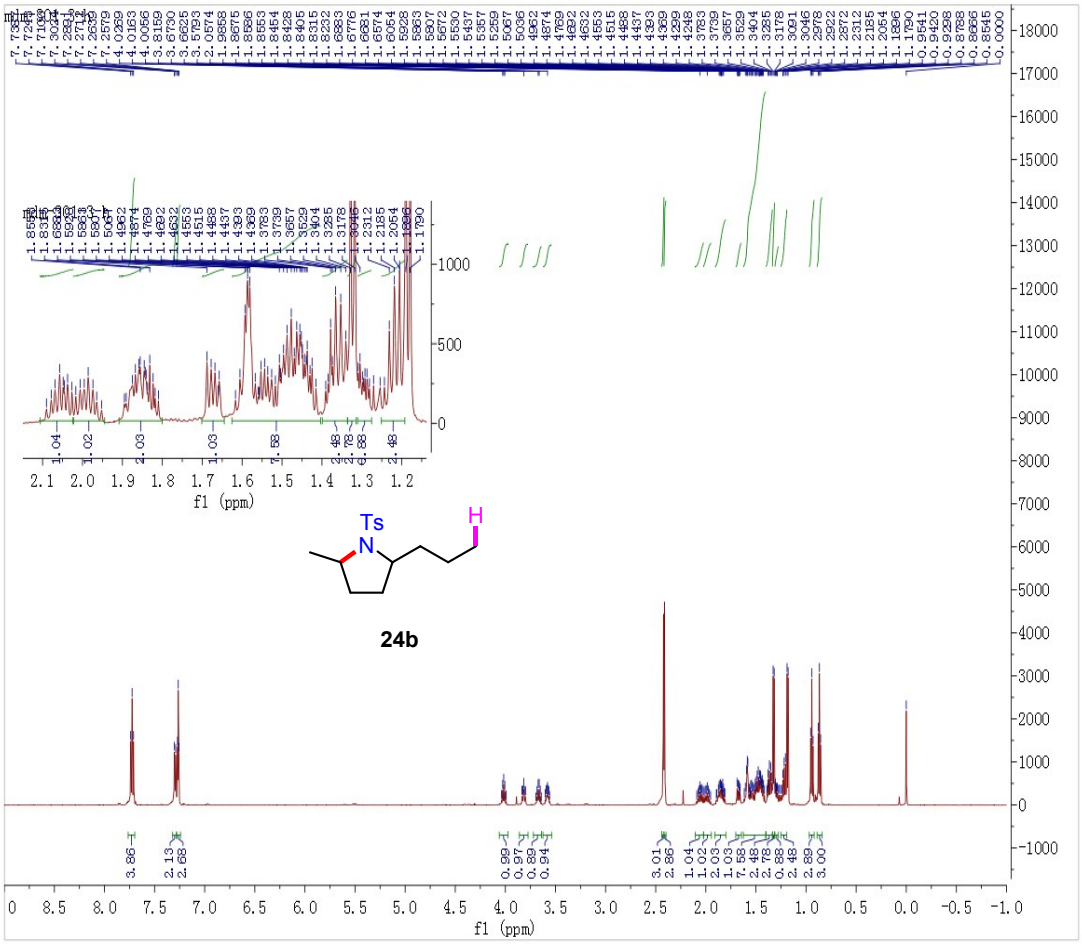

mdm-265-2
1H-NMR
Ts
N
19b
f1 (ppm)

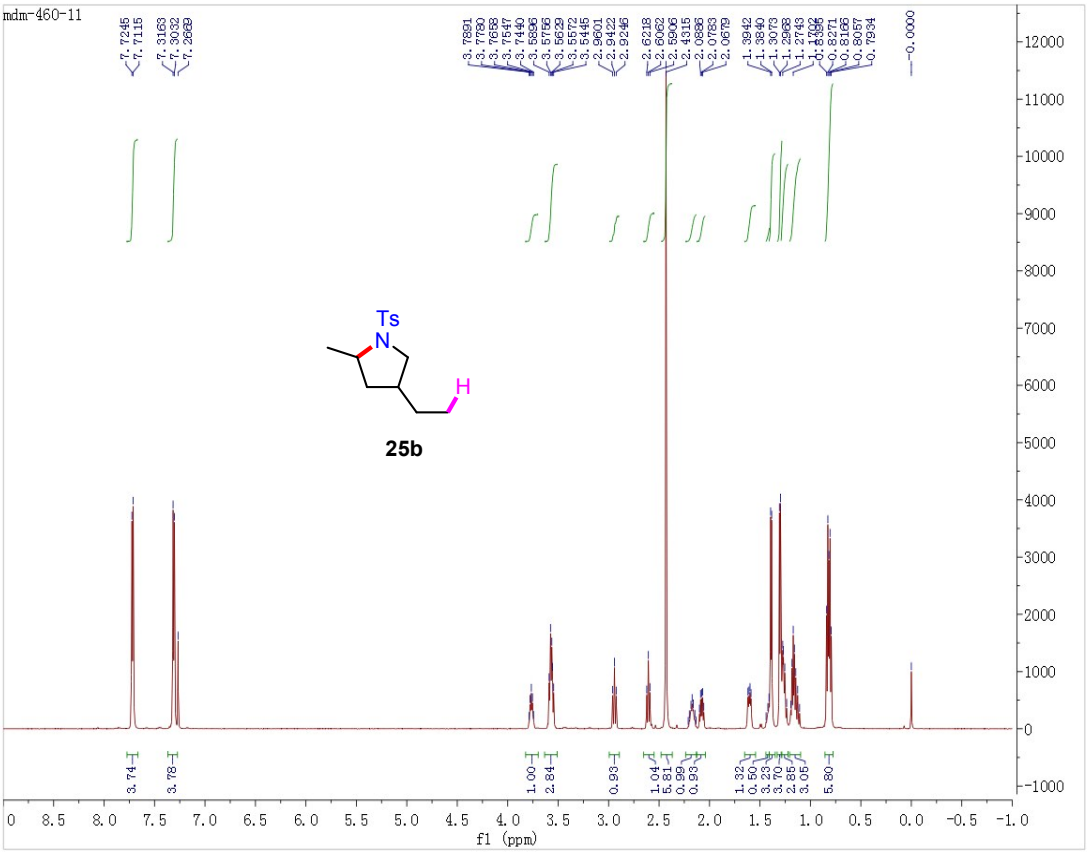

mdm-437-5-h
Ts
N
20b
f1 (ppm)

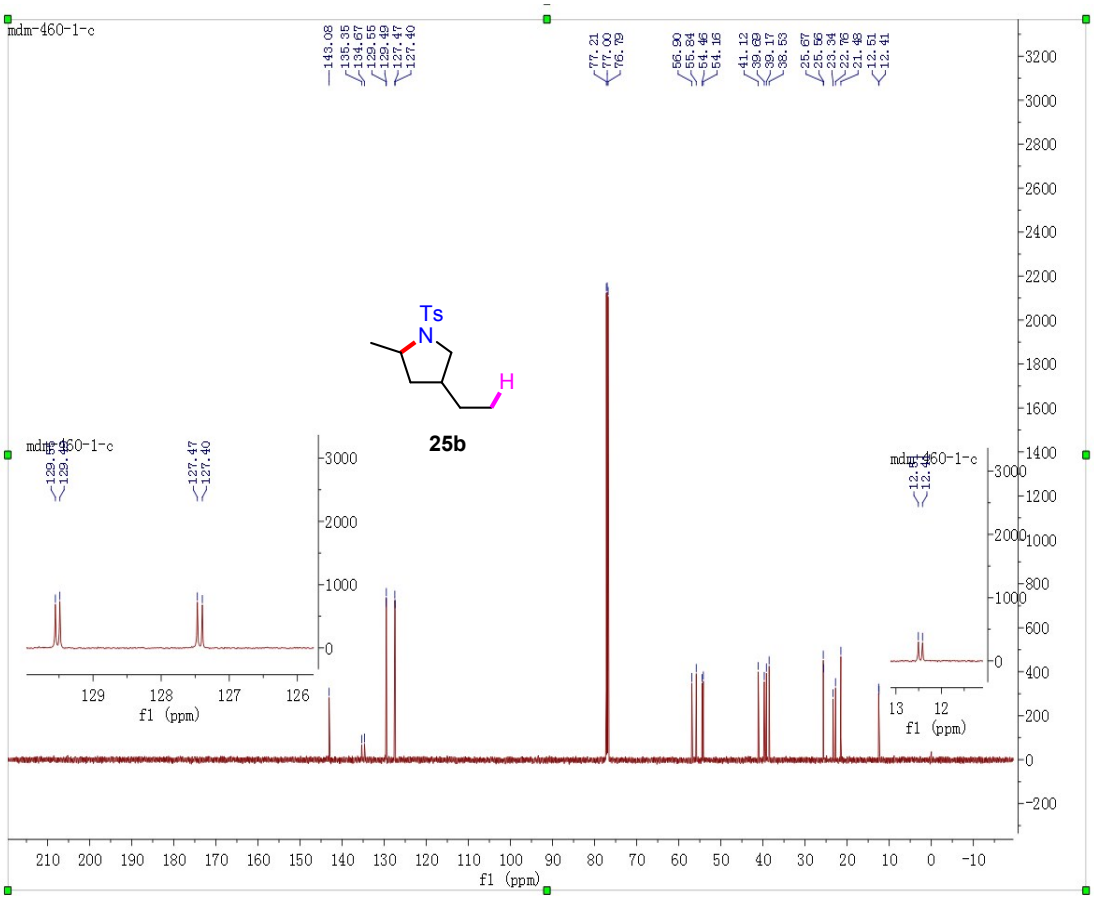

mdm-442-3-h
Ts
N
MeO
21b
f1 (ppm)

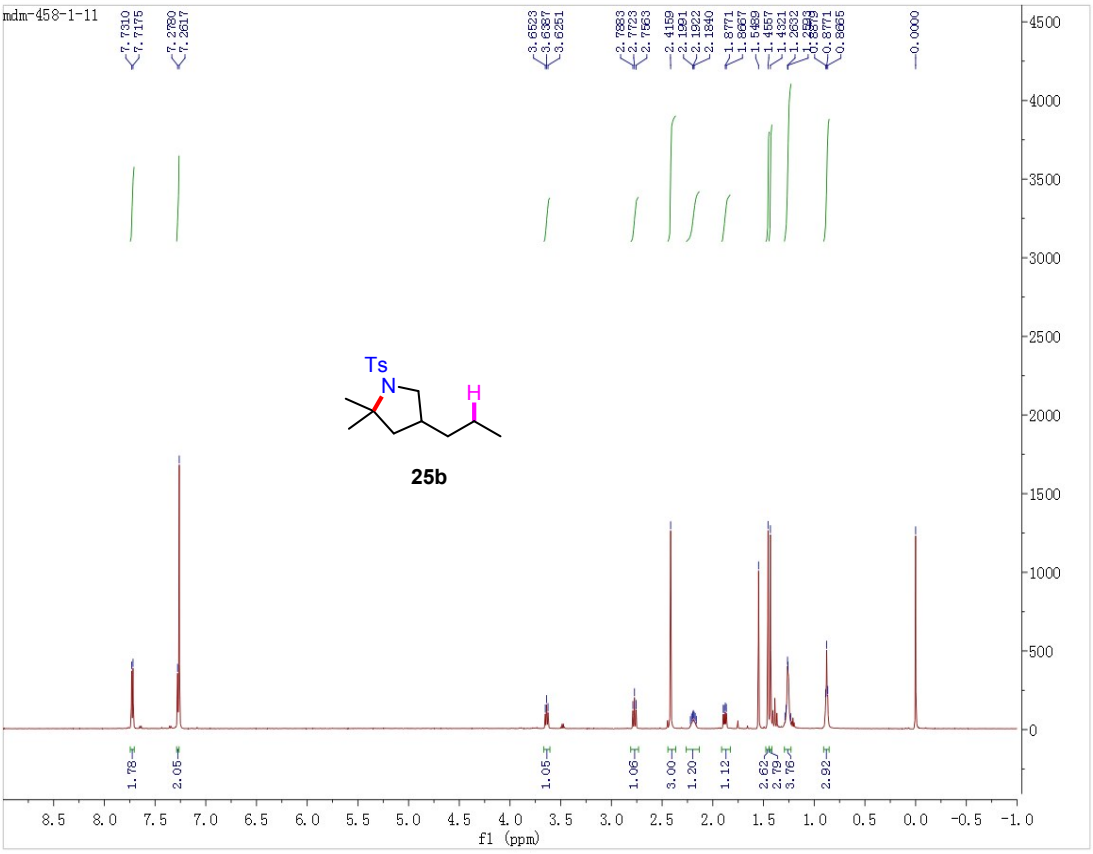

mdm-441-2-h
Ts
N
F
22b
f1 (ppm)

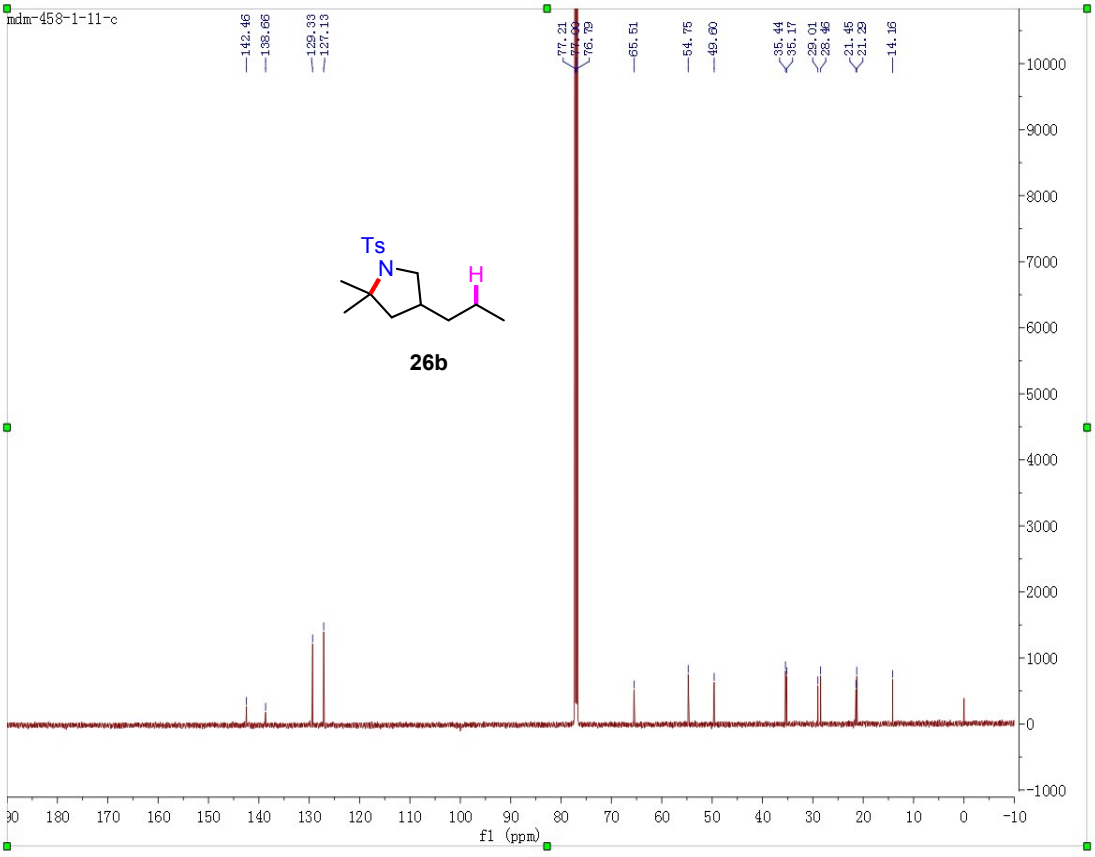

mdm-527-1-tm
Ts
N
23b
f1 (ppm)

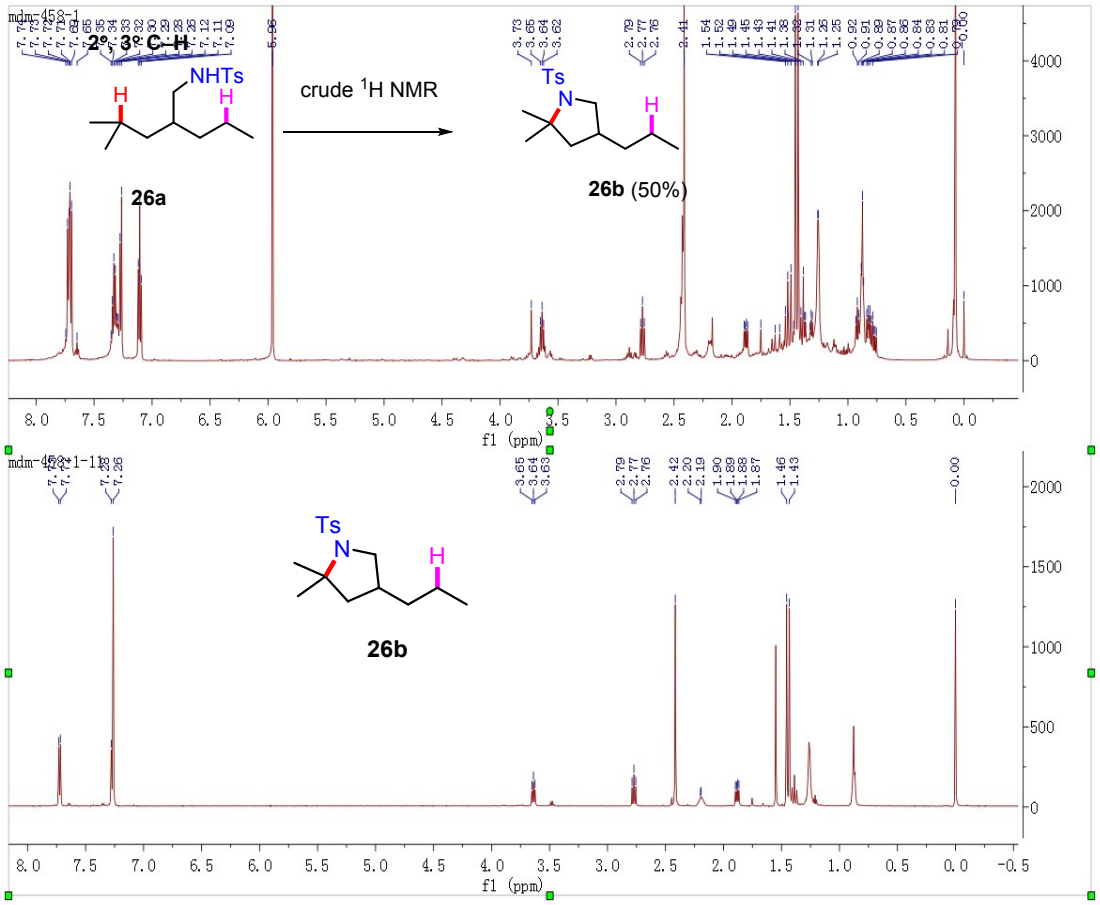

Ts
N
H
24b
f1 (ppm)


mdm-460-11
Ts
N
H
25b
f1 (ppm)


mdm-460-1-c
Ts
N
H
25b
f1 (ppm)


mdm-458-1-11
Ts
N
H
25b
f1 (ppm)


mdm-458-1-11-c
Ts
N
H
26b
f1 (ppm)


2°, 3° C–H
NHTs
H
H
26a
crude ^{1}H NMR
Ts
N
H
26b (50%)
f1 (ppm)
Ts
N
H
26b
f1 (ppm)