Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Highly effective and selective $FeBr_3$-promoted deuterium bromination/cyclization of 1,n-enynes

Supporting Information

Table of Contents

General remarks

All the manipulations were performed in air, unless mentioned otherwise. THF, toluene, and hexane were purchased from J&K Chemicals and used without further purification. The following chemicals were purchased and used as received: $FeBr_3$ (99%, Sigma-Aldrich), D_2O (Energy Chemicals), DCE (J&K Chemical and *de*-water). All enynes were prepared by literature report procedures[1].

^1H, ^{13}C, ^9F NMR spectra were recorded using Bruker 400 MHz, 500 MHz and 600 MHz NMR, Agilent Technologies 600 MHz NMR spectrometer. ^1H NMR and ^{13}C NMR spectra were referenced to resonances of the residual protons in the deuterated solvents. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, dt = doublet of triplets, br = broad singlet and m = multiplet. HR-MS analyses were performed at a Thermo Scientific Exactive-TOF (ESI ionization source).

General procedure for evaluation of conditions.

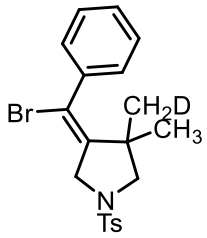
In a 4-mL screw-capped vial, **1a** (67.8 mg, 0.2 mmol), $FeBr_3$ (70.9 mg, 0.24 mol), solvent (0.5 mL) and a magnetic stirring bar were added under air. Then D_2O (4.8 mg, 0.24 mmol) were added. The vial was sealed with a cap containing a PTFE septum, then transferred to an oil bath at 80 ^oC. The reaction mixture was stirred at 80 ^oC for 1 h and the resulting solution was concentrated in vacuum. Conversions and Z/E ratio were determined by NMR analysis with crude reaction mixture.

General procedure for deuterium bromination/cyclization of enynes

In a 4-mL screw-capped vial, **1a** (101.7 mg, 0.3 mmol), $FeBr_3$ (106.4 mg, 0.36 mol), solvent (0.5 mL) and a magnetic stirring bar were added under air. Then D_2O (7.2 mg, 0.36 mmol) were added. The vial was sealed with a cap containing a PTFE septum, then transferred to an oil bath at 80 ^oC. The reaction mixture was stirred at 80 ^oC for 1 h and the resulting solution was concentrated in vacuum. The crude product was purified by column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:70 - 1:2) as eluent, and data for characterization of the products are listed below.

Characterization data of heterocyclic alkenyl bromide

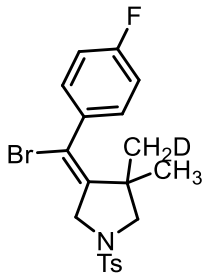
(*Z*)-4-(bromo(phenyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2a)



2a

The title compound was isolated (112.5 mg, 89%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^1H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.30 (m, 3H), 7.21 (dd, *J* = 7.4, 2.2 Hz, 2H), 4.00 (s, 2H), 3.03 (s, 2H), 2.47 (s, 3H), 0.90 (s, 3H), 0.89 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.5, 144.0, 139.6, 132.1, 129.9, 129.0, 128.8, 128.3, 128.1, 115.8, 63.2, 56.6, 44.2, 26.1, 25.8 (t, *J* = 19.6 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{22}DBrNO_2S^+$: 426.0690, found 420.0692.

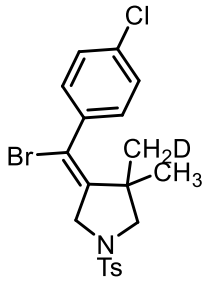
(*Z*)-4-(bromo(4-fluorophenyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2b)



2b

The title compound was isolated (92.3 mg, 70%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 6.0 Hz, 2H), 7.39 (d, *J* = 6.0 Hz, 2H), 7.21 – 7.19 (m, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 3.99 (s, 2H), 3.03 (s, 2H), 2.47 (s, 3H), 0.90 (s, 3H), 0.89 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.7 (d, *J* = 249.6 Hz), 145.5, 144.0, 135.8 (d, *J* = 3.8 Hz), 132.2, 131.0 (d, *J* = 8.2 Hz), 129.9, 128.2, 115.5 (d, *J* = 21.8 Hz), 114.7, 63.1, 56.5, 44.1, 26.1, 25.8 (t, *J* = 18.1 Hz), 21.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ -111.68. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{21}DBrFNO_2S^+$: 439.0596, found 439.0594.

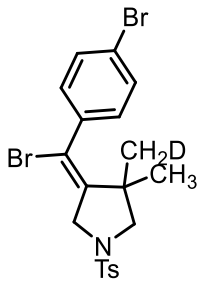
(*Z*)-4-(bromo(4-chlorophenyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2c)



2c

The title compound was isolated (94.3 mg, 69%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.29 (dd, *J* = 8.7, 2.4 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 3.98 (s, 2H), 3.02 (s, 2H), 2.46 (s, 3H), 0.91 (s, 3H), 0.89 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.5, 144.0, 138.1, 134.8, 132.0, 130.4, 129.9, 128.7, 128.2, 114.3, 63.2, 56.6, 44.2, 26.2, 25.9 (t, *J* = 19.2 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{21}DBrClNO_2S^+$: 455.0300, found 455.0298.

(*Z*)-4-(bromo(4-bromophenyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2d)

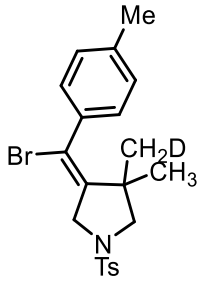


2d

The title compound was isolated (115.6 mg, 77%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.49 – 7.42 (m, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.12 – 7.05 (m, 2H), 3.97 (s, 2H), 3.02 (s, 2H), 2.46 (s, 3H), 0.91 (s, 3H), 0.90 (d, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.5, 144.0, 138.5, 132.0, 131.6,

130.7, 129.9, 128.2, 123.1, 114.3, 63.2, 56.6, 44.2, 26.2, 25.9 (t, *J* = 20.2 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{21}DBr_2NO_2S^+$: 498.9795, found 498.9795.

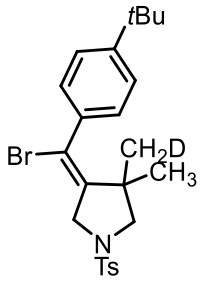
(*Z*)-4-(bromo(*p*-tolyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2e)



2e

The title compound was isolated (86.2 mg, 66%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.69 (m, 2H), 7.42 – 7.35 (m, 2H), 7.17 – 7.05 (m, 4H), 3.98 (s, 2H), 3.02 (s, 2H), 2.47 (s, 3H), 2.34 (s, 3H), 1.60 (s, 3H), 0.91 (s, 3H), 0.90 (d, *J* = 7.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 144.0, 138.9, 136.9, 132.2, 129.9, 129.0, 128.9, 128.2, 116.2, 63.3, 56.6, 44.2, 26.2, 21.6 (d, *J* = 31.2 Hz). HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{24}DBrNO_2S^+$: 435.0847, found 435.0845.

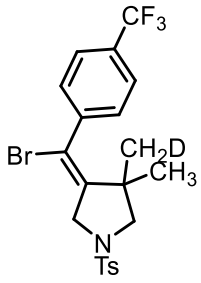
(*Z*)-4-(bromo(4-*(tert*-butyl)phenyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2f)



2f

The title compound was isolated (87.3 mg, 61%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 3.99 (s, 2H), 3.03 (s, 2H), 2.47 (s, 3H), 1.30 (s, 9H), 0.90 (s, 3H), 0.90 (d, *J* = 10.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.1, 144.4, 143.9, 136.7, 132.3, 129.9, 128.7, 128.2, 125.2, 116.3, 63.3, 56.6, 44.2, 34.8, 31.4, 26.2, 25.9 (t, *J* = 19.6 Hz), 21.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{30}DBrNO_2S^+$: 477.1316, found 477.1314.

(*Z*)-4-(bromo(4-(trifluoromethyl)phenyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2g)

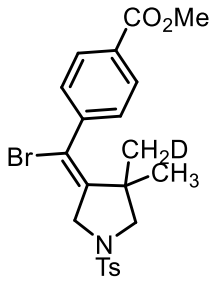


2g

The title compound was isolated (121.8 mg, 83%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz,

2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 4.01 (s, 2H), 3.05 (s, 2H), 2.48 (s, 3H), 0.91 (s, 3H), 0.90 (d, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.0, 144.1, 143.1, 132.0, 131.0 (q, *J* = 32.3 Hz), 130.0, 129.6, 128.2, 125.4 (q, *J* = 3.8 Hz), 125.2, 122.5, 113.6, 63.2, 56.6, 44.3, 26.2, 25.9 (t, *J* = 19.2 Hz), 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.77. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{21}DBrF_3NO_2S^+$: 489.0564, found 489.0563.

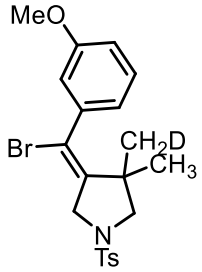
Methyl (*Z*)-4-(bromo(4-methyl-4-(methyl-*d*)-1-tosylpyrrolidin-3-ylidene)methyl)benzoate (2h)



2h

The title compound was isolated (128 mg, 89%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 4:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.97 (m, 2H), 7.76 – 7.71 (m, 2H), 7.38 (d, *J* = 7.9 Hz, 2H), 7.31 – 7.27 (m, 2H), 4.00 (s, 2H), 3.90 (s, 3H), 3.03 (s, 2H), 2.46 (s, 3H), 0.89(s, 3H), 0.88 (d, *J* = 10.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4, 145.6, 144.03, 144.01, 132.1, 130.4, 129.9, 129.6, 129.2, 128.1, 114.1, 63.2, 56.6, 52.4, 44.2, 26.1, 25.9 (t, *J* = 19.6 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{24}DBrNO_4S^+$: 479.0745, found 479.0745.

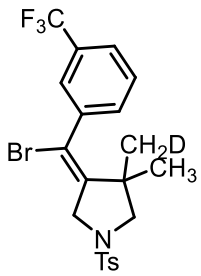
(*Z*)-4-(bromo(3-methoxyphenyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2i)



2i

The title compound was isolated (79.9 mg, 59%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.24 (dd, *J* = 15.3, 7.4 Hz, 1H), 6.88 – 6.77 (m, 2H), 6.74 (dd, *J* = 2.7, 1.6 Hz, 1H), 3.99 (s, 2H), 3.78 (s, 3H), 3.03 (s, 2H), 2.47 (s, 3H), 0.93(s, 3H), 0.93 (d, *J* = 7.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 144.5, 144.0, 140.8, 132.1, 129.9, 129.4, 128.2, 121.5, 115.6, 114.6, 114.5, 63.2, 56.5, 55.4, 44.2, 26.1, 25.8 (t, *J* = 20.2 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{24}DBrNO_3S^+$: 451.0796, found 451.0795.

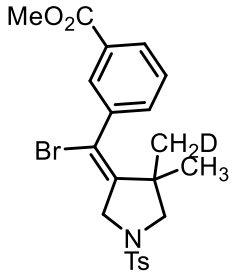
(Z)-4-(bromo(3-(trifluoromethyl)phenyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2j)



2j

The title compound was isolated (91 mg, 62%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.60 – 7.54 (m, 1H), 7.49 – 7.43 (m, 2H), 7.43 – 7.35 (m, 3H), 4.00 (s, 2H), 3.03 (s, 2H), 2.46 (s, 3H), 0.88 (s, 3H), 0.88 (d, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.2, 144.1, 140.3, 132.4, 132.0, 130.8 (q, *J* = 32.3 Hz), 129.9, 129.0, 128.1, 126.0 (q, *J* = 4.0 Hz), 125.5 (q, *J* = 4.0 Hz), 123.7 (q, *J* = 273.7 Hz), 113.5, 63.2, 56.6, 44.2, 26.1, 25.9 (t, *J* = 19.2 Hz), 21.7. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{21}DBrF_3NO_2S^+$: 489.0564, found 489.0563.

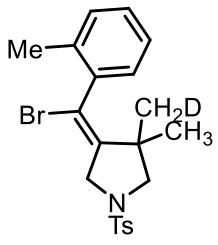
Methyl (*Z*)-3-(bromo(4-methyl-4-(methyl-*d*)-1-tosylpyrrolidin-3-ylidene)methyl)benzoate (2k)



2k

The title compound was isolated (93.4 mg, 67%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (td, *J* = 4.3, 3.5, 1.9 Hz, 1H), 7.89 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.34 (m, 4H), 4.00 (s, 2H), 3.90 (s, 3H), 3.02 (s, 2H), 2.47 (s, 3H), 0.89 (s, 3H), 0.88 (d, *J* = 7.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 145.6, 144.1, 139.9, 133.4, 131.9, 130.4, 130.2, 130.0, 129.9, 128.6, 128.1, 114.3, 63.2, 56.6, 52.4, 44.2, 26.3, 25.9 (t, *J* = 19.2 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{24}DBrNO_4S^+$: 479.0745, found 479.0745.

(*Z*)-4-(bromo(*o*-tolyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2l)

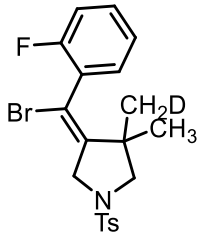


2l

The title compound was isolated (84.9 mg, 65%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.27-7.21 (m, 1H), 6.86 - 6.79 (m, 2H), 6.75 - 6.74 (m, 1H), 3.99 (s, 2H), 3.78 (s, 3H), 3.03 (s, 2H), 2.47 (s, 3H), 0.93 (s, 3H), 0.92 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 144.3, 143.9, 140.7, 132.0, 129.8, 129.3, 128.1, 121.4, 115.5, 114.5, 114.4, 63.2, 56.4, 55.3,

44.1, 26.0, 25.7 (t, *J* = 20.2 Hz), 21.6. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{24}DBrNO_2S^+$: 435.0847, found 435.0847.

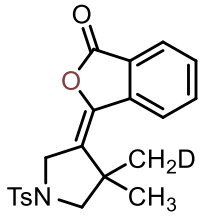
(*Z*)-4-(bromo(2-fluorophenyl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2m)



2m

The title compound was isolated (109.4 mg, 83%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.33 (tdd, *J* = 7.5, 5.3, 2.1 Hz, 1H), 7.18 (td, *J* = 7.4, 2.1 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.04 (t, *J* = 8.9 Hz, 1H), 4.12 (d, *J* = 15.5 Hz, 1H), 3.89 (d, *J* = 15.5 Hz, 1H), 3.15 (d, *J* = 8.9 Hz, 1H), 2.92 (d, *J* = 8.9 Hz, 1H), 2.47 (s, 3H), 1.01-0.79 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2 (d, *J* = 249.2 Hz), 147.3, 144.1, 132.0, 131.22, 131.20, 131.15, 130.0, 128.1, 127.1 (d, *J* = 16.3 Hz), 124.1 (d, *J* = 3.6 Hz), 116.1 (d, *J* = 21.4 Hz), 108.4, 63.0, 56.4, 44.2, 26.8, 23.8, 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.01. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{21}DBrFNO_2S^+$: 439.0596, found 439.0594.

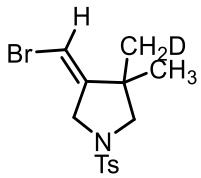
(*Z*)-3-(4-methyl-4-(methyl-*d*)-1-tosylpyrrolidin-3-ylidene)isobenzofuran-1(3*H*)-one (2n)



2n

The title compound was isolated (78.4 mg, 68%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.77 – 7.68 (m, 3H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 2H), 4.18 (s, 2H), 3.12 (s, 2H), 2.44 (s, 3H), 1.50 (s, 3H), 1.49 (d, *J* = 7.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 144.3, 140.2, 136.3, 134.4, 131.2, 130.2, 129.9, 129.6, 128.4, 126.2, 126.1, 124.1, 63.9, 53.1, 41.3, 25.1, 24.8 (t, *J* = 20.2 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{21}DNO_4S^+$: 385.1327, found 385.1326.

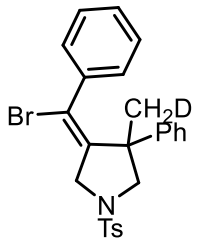
4-(bromomethylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2o)



2o

The title compound was isolated (54.9 mg, 53%, *Z*/*E* = 2:1) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.3, 2.5 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.86, 5.64 (s, 1H), 3.66 (d, *J* = 1.9 Hz), 3.58 (d, *J* = 1.9 Hz, 2H), 2.83 (d, *J* = 10.6 Hz, 2H), 2.43 (s, 3H), 1.08 (s, 3H), 1.11 – 1.01 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.0, 137.4, 133.3, 129.9, 127.7, 124.8, 113.8, 54.3, 50.9, 49.1, 26.5, 26.1 (t, *J* = 19.6 Hz), 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{14}H_{18}DBrNO_2S^+$: 345.0377, found 345.0378.

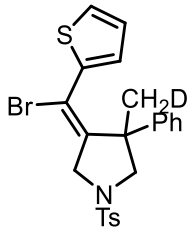
(*Z*)-4-(bromo(phenyl)methylene)-3-(methyl-*d*)-3-phenyl-1-tosylpyrrolidine (2p)



2p

The title compound was isolated (104.4 mg, 72%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.13 (dt, *J* = 4.8, 2.7 Hz, 3H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.03 – 6.96 (m, 4H), 6.79 – 6.70 (m, 2H), 4.22 (d, *J* = 3.0 Hz, 2H), 3.50 (d, *J* = 9.3 Hz, 1H), 3.29 (d, *J* = 9.3 Hz, 1H), 2.48 (s, 3H), 1.30 – 1.25 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.2, 144.7, 144.0, 138.9, 132.3, 129.9, 128.7, 128.31, 128.29, 128.1, 127.8, 126.8, 126.5, 117.9, 65.4, 57.3, 50.9, 23.9, 23.6 (t, *J* = 21.1 Hz), 21.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{25}H_{23}DBrNO_2S^+$: 483.0841, found 483.0841.

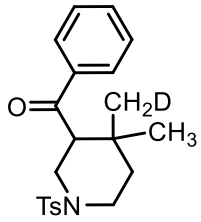
(*Z*)-4-(bromo(thiophen-2-yl)methylene)-3-(methyl-d)-3-phenyl-1-tosylpyrrolidine (2q)



2q

The title compound was isolated (71.8 mg, 56%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.68 (m, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.26 (m, 1H), 7.19 (dd, *J* = 3.1, 1.4 Hz, 1H), 7.02 – 6.88 (m, 1H), 3.97 (s, 2H), 3.03 (s, 2H), 2.47 (s, 3H), 0.96 (s, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3, 144.0, 139.2, 132.1, 129.9, 128.4, 128.2, 125.8, 125.1, 110.3, 63.2, 56.6, 44.3, 26.0, 25.7 (m) , 21.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{20}DBrNO_2S_2^+$: 427.0254, found 427.0255.

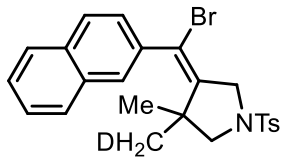
(4-methyl-4-(methyl-d)-1-tosylpiperidin-3-yl)(phenyl)methanone (2r)



2r

The title compound was isolated (80.9 mg, 62%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 2H), 7.68 – 7.61 (m, 2H), 7.60 – 7.55 (m, 1H), 7.49 – 7.43 (m, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 3.73 – 3.59 (m, 2H), 2.82 – 2.73 (m, 1H), 2.55 – 2.47 (m, 1H), 2.44 (s, 3H), 1.76 (td, *J* = 13.2, 4.7 Hz, 1H), 1.49 – 1.41 (m, 1H), 0.85 (s, 3H), 0.84 (d, *J* = 21.3 Hz, 5H). 0.83 (d, *J* = 24.0 Hz, 1H) ^{13}C NMR (151 MHz, $CDCl_3$) δ 201.5, 143.7, 138.30, 138.26, 133.5, 133.3, 129.9, 128.8, 128.4, 127.8, 50.9, 50.6 – 49.7 (m).44.6, 42.5, 40.0, 32.5, 31.2, 21.7, 19.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{24}DNO_3SNa^+$: 395.1510, found 395.1504.

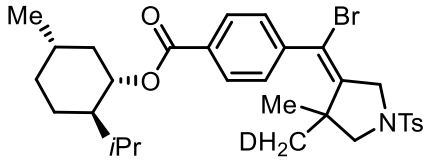
(*Z*)-4-(bromo(naphthalen-2-yl)methylene)-3-methyl-3-(methyl-*d*)-1-tosylpyrrolidine (2s)



2s

The title compound was isolated (60.8 mg, 43%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 3H), 7.78 – 7.74 (m, 2H), 7.70 (d, *J* = 1.9 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.30 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.06 (s, 2H), 3.05 (s, 2H), 2.48 (s, 3H), 0.93 (s, 3H), 0.92 (d, *J* = 10.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.1, 144.0, 137.0, 133.1, 132.7, 132.3, 130.0, 128.4, 128.31, 128.26, 128.2, 127.9, 127.1, 126.8, 126.7, 116.1, 63.3, 56.7, 44.3, 29.8, 26.3, 21.8. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{23}DNO_3SBrNa^+$: 493.0666, found 493.0665.

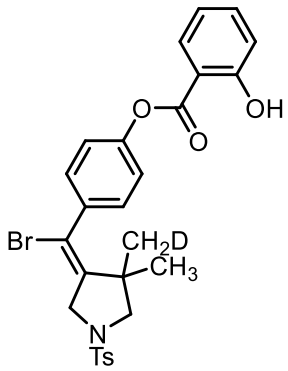
(1*S*, 2*R*, 5*R*)-2-isopropyl-5-methylcyclohexyl 4-((*Z*)-bromo(4-methyl-4-(methyl-*d*)-1-tosyl pyrrolidin-3-ylidene)methyl)benzoate (2t)



2t

The title compound was isolated (114.1 mg, 63%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.92 (td, *J* = 10.9, 4.4 Hz, 1H), 4.01 (s, 2H), 3.04 (s, 2H), 2.47 (s, 3H), 2.10 (d, *J* = 11.7 Hz, 1H), 1.94 (td, *J* = 7.0, 2.9 Hz, 1H), 1.72 (dt, *J* = 11.6, 2.9 Hz, 2H), 1.56 – 1.52 (m, 2H), 1.15 – 1.05 (m, 2H), 0.91 (dd, *J* = 6.8, 3.4 Hz, 12H), 0.78 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 145.5, 144.0, 143.8, 132.2, 131.1, 129.9, 129.6, 129.1, 128.2, 114.3, 75.3, 63.2, 56.6, 47.3, 44.3, 41.1, 34.4, 31.6, 29.8, 26.6, 26.2 (dd, *J* = 7.6, 3.0 Hz), 23.7, 22.1, 21.7, 20.9, 16.5.

(*Z*)-4-(bromo(4-methyl-4-(methyl-*d*)-1-tosylpyrrolidin-3-ylidene)methyl)phenyl 2-hydroxybenzoate (2u)

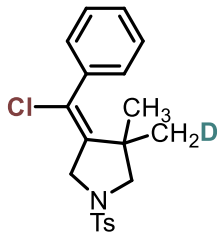


2u

The title compound was isolated (113.7 mg, 68%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.4 (s, 1H), 8.04 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.76 (d, *J* = 6.0 Hz, 2H), 7.56 – 7.53 (m, 1H), 7.39 (d, *J* = 9.0 Hz, 2H), 7.31 – 7.30 (m, 2H), 7.20 (d, *J* = 7.2 Hz, 2H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.99 – 6.96 (m, 1H), 4.01 (s, 2H), 3.05 (s, 2H), 2.47 (s, 3H), 0.95 (s, 3H), 0.93 (d, *J* = 10.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 162.4, 150.2,

145.6, 144.0, 137.8, 136.8, 132.2, 130.5, 130.4, 129.9, 128.2, 121.7, 119.7, 118.0, 114.5, 111.7, 63.3, 56.6, 44.3, 26.3, 26.0 (t, *J* = 18.8 Hz), 21.7.

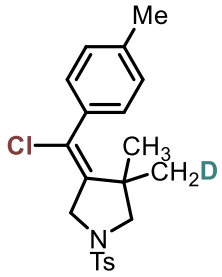
(*Z*)-4-(chloro(phenyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2aa)



2aa

The title compound was isolated (91.4 mg, 81%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.34 – 7.31 (m, 3H), 7.24 – 7.21 (m, 2H), 4.05 (s, 2H), 3.00 (s, 2H), 2.46 (s, 3H), 0.91 (s, 3H), 0.90 (d, *J* = 10.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.0, 141.9, 137.8, 132.1, 129.9, 129.2, 129.0, 128.4, 128.2, 125.3, 63.1, 54.0, 43.2, 26.1, 25.9 (t, *J* = 19.6 Hz), 21.7.

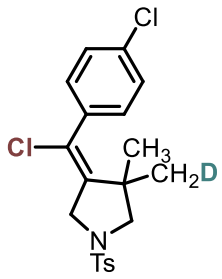
(*Z*)-4-(chloro(p-tolyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2ab)



2ab

The title compound was isolated (63.2 mg, 54%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.15 – 7.09 (m, 4H), 4.03 (s, 2H), 2.99 (s, 2H), 2.47 (s, 3H), 2.35 (s, 3H), 0.91 (s, 3H), 0.90 (d, *J* = 10.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 141.7, 139.0, 135.1, 132.3, 129.9, 129.12, 129.06, 128.2, 125.6, 63.1, 54.0, 43.3, 29.8, 26.2, 25.8 (t, *J* = 20.2 Hz), 21.8, 21.4.

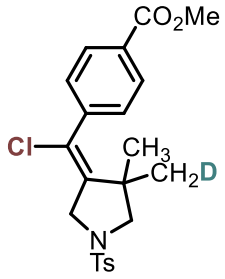
(*Z*)-4-(chloro(4-chlorophenyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2ac)



2ac

The title compound was isolated (93.5 mg, 76%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 7.9 Hz, 2H), 7.33 – 7.29 (m, 2H), 7.18 – 7.15 (m, 2H), 4.02 (s, 2H), 2.99 (s, 2H), 2.46 (s, 3H), 0.91 (s, 3H), 0.90 (d, *J* = 10.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.0, 142.8, 136.3, 135.0, 132.1, 130.6, 129.9, 128.7, 128.2, 124.0, 63.0, 54.0, 43.3, 26.2,25.9 (t, *J* = 21.1 Hz), 21.7.

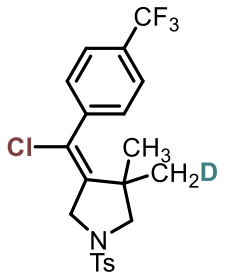
methyl (*Z*)-4-(chloro(4-methyl-4-(methyl-d)-1-tosylpyrrolidin-3-ylidene)methyl)benzoate (2ad)



2ad

The title compound was isolated (101.6 mg, 78%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 20:1).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.97 (m, 2H), 7.75 – 7.70 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.32 – 7.29 (m, 2H), 4.04 (s, 2H), 3.90 (s, 3H), 2.99 (s, 2H), 2.45 (s, 3H), 0.89 (s, 3H), 0.88 (d, *J* = 10.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 144.0, 142.9, 142.2, 132.0, 130.5, 130.0, 129.6, 129.3, 128.1, 123.8, 63.0, 54.0, 52.4, 43.2, 26.1, 25.8 (t, *J* = 18.9 Hz), 21.6.

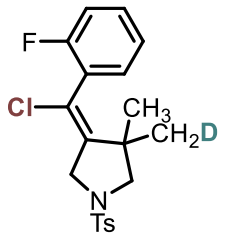
(*Z*)-4-(chloro(4-(trifluoromethyl)phenyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2ae)



2ae

The title compound was isolated (121.2 mg, 91%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.38 (dd, *J* = 12.3, 7.9 Hz, 4H), 4.06 (s, 2H), 3.01 (s, 2H), 2.47 (s, 3H), 0.91 (s, 3H), 0.90 (d, *J* = 10.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.1, 143.4, 141.4 (d, *J* = 1.8 Hz), 132.1, 131.1 (q, *J* = 32.7 Hz), 130.0, 129.7, 128.2, 125.5 (q, *J* = 3.6 Hz), 123.8 (q, *J* = 272.5 Hz), 123.4, 63.0, 54.0, 43.3, 26.2, 26.0 (t, *J* = 20.2 Hz), 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.76.

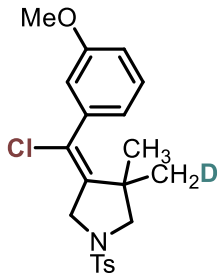
(*Z*)-4-(chloro(2-fluorophenyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2af)



2af

The title compound was isolated (70.9 mg, 60%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.40 – 7.33 (m, 3H), 7.23 – 7.18 (m, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.06 (t, *J* = 8.9 Hz, 1H), 4.17 (d, *J* = 15.6 Hz, 1H), 3.94 (d, *J* = 15.6 Hz, 1H), 3.12 (d, *J* = 8.9 Hz, 1H), 2.89 (d, *J* = 8.9 Hz, 1H), 2.47 (s, 3H), 1.02 (d, *J* = 10.6 Hz)+ 0.78 (d, *J* = 10.0 Hz) (5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6 (d, *J* = 248.9 Hz), 144.7, 144.0, 132.2, 131.5 (d, *J* = 2.3 Hz), 131.4 (d, *J* = 7.6 Hz), 130.0, 128.1, 125.4 (d, *J* = 15.9 Hz), 124.1 (d, *J* = 4.1 Hz), 118.75, 116.1 (d, *J* = 21.3 Hz), 62.9, 53.9, 43.4, 43.3, 29.8, 26.9, 26.5 (t, *J* = 18.9 Hz), 23.9, 23.60 (t, *J* = 18.9 Hz), 21.7. ^{19}F NMR (377 MHz, $CDCl_3$) δ -112.47.

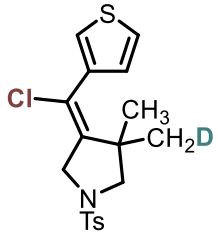
(*Z*)-4-(chloro(3-methoxyphenyl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2ag)



2ag

The title compound was isolated (70.0 mg, 55%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 30:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 7.9 Hz, 2H), 7.23 (dd, *J* = 8.0, 3.5 Hz, 1H), 6.87 (ddd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 6.82 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.76 (dd, *J* = 2.6, 1.4 Hz, 1H), 4.04 (s, 2H), 3.78 (s, 3H), 3.00 (s, 2H), 2.46 (s, 3H), 0.94 (s, 3H), 0.93 (d, *J* = 10.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.3, 144.0, 141.8, 139.0, 132.2, 129.9, 129.4, 128.2, 125.0, 121.6, 114.8, 114.6, 63.1, 55.4, 54.0, 43.4, 26.1, 25.8 (t, *J* = 18.1 Hz), 21.7.

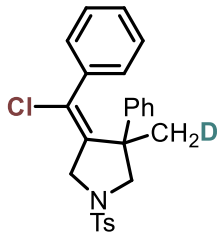
(*Z*)-4-(chloro(thiophen-3-yl)methylene)-3-methyl-3-(methyl-d)-1-tosylpyrrolidine (2ah)



2ah

The title compound was isolated (50.4 mg, 44%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 – 7.71 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.28 (dt, *J* = 4.5, 2.2 Hz, 1H), 7.22 (dd, *J* = 3.0, 1.3 Hz, 1H), 6.96 (dd, *J* = 5.0, 1.4 Hz, 1H), 4.02 (s, 2H), 3.00 (s, 2H), 2.46 (s, 3H), 0.96 (s, 3H), 0.95 (d, *J* = 10.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 143.5, 137.5, 132.2, 129.9, 128.3, 128.2, 125.9, 125.6, 120.2, 63.1, 54.1, 43.4, 29.8, 26.0, 25.7 (t, *J* = 18.9 Hz), 21.8.

(*Z*)-4-(chloro(phenyl)methylene)-3-(methyl-d)-3-phenyl-1-tosylpyrrolidine (2ai)



2ai

The title compound was isolated (67.0 mg, 51%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 – 7.69 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.18 – 7.13 (m, 3H), 7.12 – 7.09 (m, 1H), 7.07 – 7.04 (m, 2H), 7.02 (t, *J* = 7.7 Hz, 2H), 6.82 – 6.77 (m, 2H), 4.30 – 4.23 (m, 2H), 3.48 (d, *J* = 9.3 Hz, 1H), 3.24 (d, *J* = 9.3 Hz, 1H), 2.47 (s, 3H), 1.28 (d, *J* = 9.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.9, 144.0, 142.4, 137.2, 132.3, 129.9, 128.8, 128.5, 128.3, 128.1, 127.8, 127.2, 126.8, 126.5, 65.2, 54.8, 50.3, 29.8, 23.8, 23.6 (t, *J* = 20.2 Hz), 21.8.

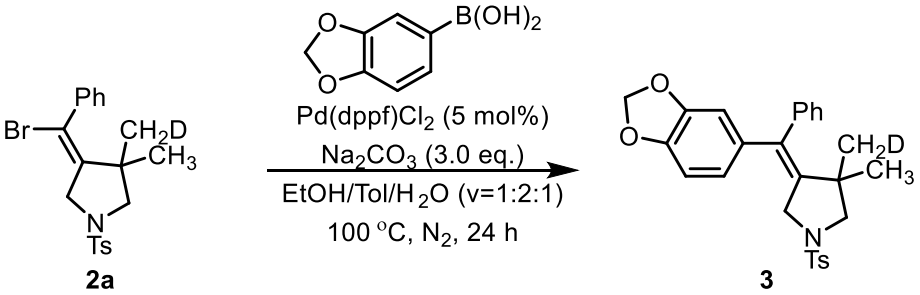
Gram-scale reaction

In a 50-mL round bottle, **1a** (1.01 g, 3 mmol), $FeBr_3$ (1.06 g, 3.6 mmol), solvent (10 mL) and a magnetic

stirring bar were added under air. Then D_2O (72 mg, 3.6 mmol) were added. The vial was sealed with a cap containing a PTFE septum, then transferred to an oil bath at 80 °C. The reaction mixture was stirred at 80 °C for 2 h and the resulting solution was concentrated in vacuum. The crude product was purified by column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:70-1:10) as eluent, and the desired product **2a** were obtained with 85% yield (1.07 g).

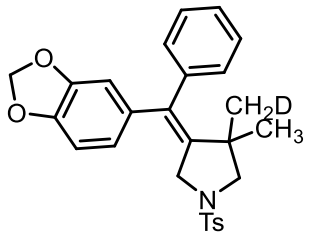
Transformation of alkenyl bromide

Procedure of Suzuki coupling of 2a with benzo[*d*][1,3]dioxol-5-ylboronic acid



2a **3**

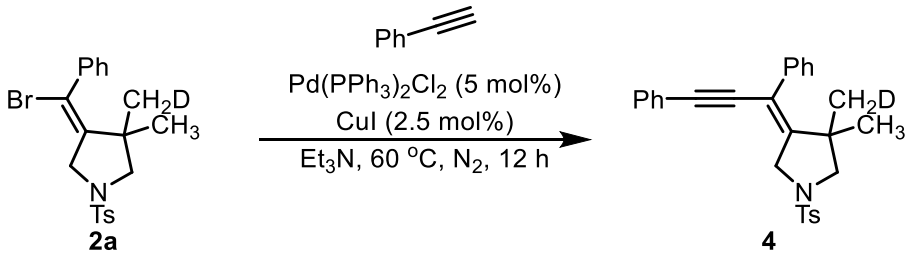
Prepared according to a previous reported method[2]. In a 10-mL Shrek tube, **2a** (84.2 mg, 0.2 mmol), benzo[*d*][1,3]dioxol-5-ylboronic acid (39.8 mg, 0.24 mmol), $Pd(dppf)Cl_2$ (7.31 mg, 0.01 mmol), Na_2CO_3 (63.6 mg, 0.6 mmol), EtOH/toluene/H_2O (v = 1:2:1, 1 mL) and a magnetic stirring bar were added under N_2. The Shrek tube was transferred to an oil bath at 100 °C. The reaction mixture was stirred at 100 °C for 24 h and the resulting solution was concentrated in vacuum. The crude product was purified by column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:20) as eluent, and data for characterization of the product **3** listed below.



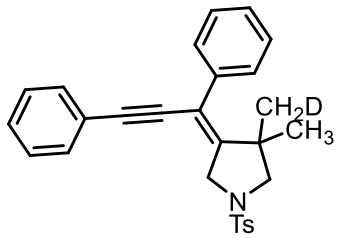
3

The title compound was isolated (70.3 mg, 76%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.27 – 7.23 (m, 2H), 7.22 – 7.18 (m, 1H), 7.13 – 7.09 (m, 2H), 6.71 (d, *J* = 8.6 Hz, 1H), 6.57 – 6.51 (m, 2H), 5.92 (s, 2H), 3.84 (s, 2H), 2.96 (s, 2H), 2.47 (s, 3H), 0.93 (s, 3H), 0.91 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.8, 146.5, 143.7, 141.4, 141.1, 136.8, 136.2, 132.4, 129.8, 128.9, 128.1, 128.0, 127.0, 120.9, 110.1, 108.6, 108.2, 101.1, 62.9, 52.8, 42.7, 26.79, 26.77, 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{27}H_{26}DNO_4S^+$: 485.1616, found 485.1612.

Procedure of Sonogashira coupling of 2a with phenylacetylene



Prepared according to a previous reported method[3]. In a 10-mL Shrek tube, **2a** (84.2 mg, 0.2 mmol), $Pd(PPh_3)Cl_2$ (7.02 mg, 0.01 mmol), CuI (0.95 mg, 0.005 mmol), Et_3N (1 mL) and a magnetic stirring bar were added under N_2. Then phenylacetylene (40.85 mg, 0.4 mmol) was added through a syringe. The Shrek tube was transferred to an oil bath at 60 °C. The reaction mixture was stirred at 60 °C for 12 h and the resulting solution was concentrated in vacuum. The crude product was purified by column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:50) as eluent, and data for characterization of the product **4** listed below.



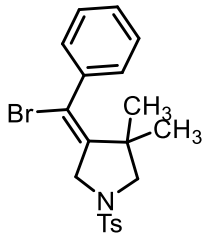
4

The title compound was isolated (75.3 mg, 85%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.9 Hz, 2H), 7.37 (d, *J* = 7.1 Hz, 4H), 7.35 – 7.28 (m, 5H), 7.27 – 7.22 (m, 3H), 4.26 (s, 2H), 3.01 (s, 2H), 2.46 (s, 3H), 0.94 (d, *J* = 10.7 Hz, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 143.9, 137.5, 132.5, 131.5, 129.9, 129.2, 128.5, 128.4, 128.3, 128.2, 127.8, 123.2, 117.6, 95.8, 88.8, 63.1, 54.5, 43.3, 26.30, 26.28, 21.7. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{28}H_{27}DNO_2S^+$: 443.1898, found 443.1896.

Procedure of hydrobromination/cyclization of enynes with H_2O

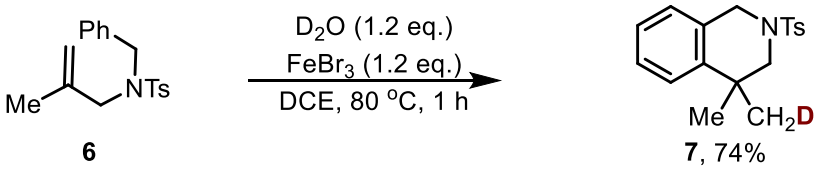
In a 4-mL screw-capped vial, **1a** (101.8 mg, 0.3 mmol), $FeBr_3$ (106.4 mg, 0.36 mol), DCE (1 mL) and a magnetic stirring bar were added under air. Then H_2O (6.5 mg, 0.36 mmol) were added. The vial was sealed with a cap containing a PTFE septum, then transferred to an oil bath at 80 °C. The reaction mixture was stirred at 80 °C for 1 h and the resulting solution was concentrated in vacuum. The crude product was purified by column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:50) as eluent, and data for characterization of the products are listed below.

Characterization data of product 2a'



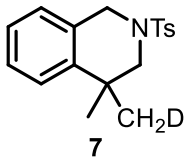
2a'

The title compound was isolated (110.9 mg, 88%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 70:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.31 (dd, *J* = 5.1, 2.0 Hz, 3H), 7.23 – 7.18 (m, 2H), 4.00 (s, 2H), 3.03 (s, 2H), 2.47 (s, 3H), 0.90 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 144.0, 139.7, 132.1, 129.9, 129.1, 128.8, 128.3, 128.2, 115.9, 63.3, 56.6, 44.2, 26.2, 21.8.



6 **7**, 74%

In a 4-mL screw-capped vial, $FeBr_3$ (70.9 mg, 0.24 mol), **6** (63.0 mg, 0.2 mmol), DCE (1.0 mL) and a magnetic stirring bar were added under air. Then D_2O (4.8 mg, 0.24 mmol) were added. The vial was sealed with a cap containing a PTFE septum, then transferred to an oil bath at 80 °C. The reaction mixture was stirred at 80 °C for 1 h and the resulting solution was concentrated in vacuum. The crude product was purified by column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:50) as eluent, and data for characterization of the product **7** is listed below.



7

The title compound was isolated (46.8 mg, 74%) as a white solid after flash chromatography on silica gel (Hexane/EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.69 (m, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.30 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.19 (td, *J* = 7.6, 1.4 Hz, 1H), 7.12 (td, *J* = 7.5, 1.3 Hz, 1H), 7.00 (dd, *J* = 7.7, 1.3 Hz, 1H), 4.21 (s, 2H), 3.02 (s, 2H), 2.43 (s, 3H), 1.34 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 142.7, 133.1, 130.5, 129.8, 127.9, 127.2, 126.3, 126.2, 125.9, 56.1, 48.6, 35.5, 28.5, 28.5-28.1 (m), 21.6.

Crystal structure of 2d and 2k

Single crystal of product **2d** and **2k** was obtained through slow evaporation of a mix solution in n-hexane and dichloromethane at room temperature. X-ray data was collected with a Bruker APEX-II CCD diffractometer.

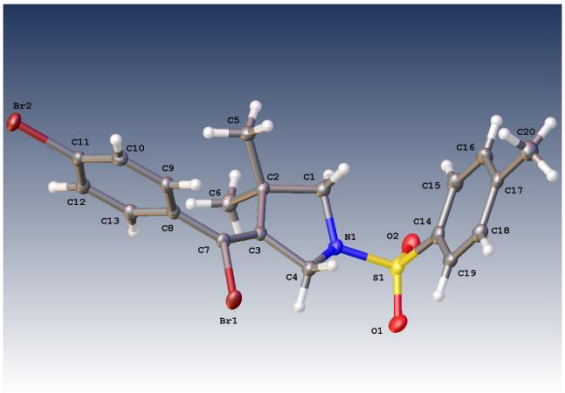


Table 1 Crystal data and structure refinement for 2d.

Identification code	2d
Empirical formula	$C_{20}H_{21}Br_2NO_2S$
Formula weight	499.26
Temperature/K	100.00
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	24.3597(8)
b/Å	6.0092(2)
c/Å	13.7493(5)
α/°	90
β/°	97.850(2)
γ/°	90
Volume/Å^3	1993.79(12)
Z	4
ρ_{calc}g/cm^3	1.663
μ/mm^{-1}	6.252
F(000)	1000.0
Crystal size/mm^3	0.1 × 0.1 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	7.326 to 144.166
Index ranges	-30 ≤ h ≤ 30, -7 ≤ k ≤ 7, -16 ≤ l ≤ 16
Reflections collected	50364
Independent reflections	3920 [R_{int} = 0.0546, R_{sigma} = 0.0293]
Data/restraints/parameters	3920/0/238
Goodness-of-fit on F^2	1.221
Final R indexes [I>=2σ (I)]	R_1 = 0.0293, wR_2 = 0.0734
Final R indexes [all data]	R_1 = 0.0294, wR_2 = 0.0734
Largest diff. peak/hole / e Å^{-3}	1.04/-0.71

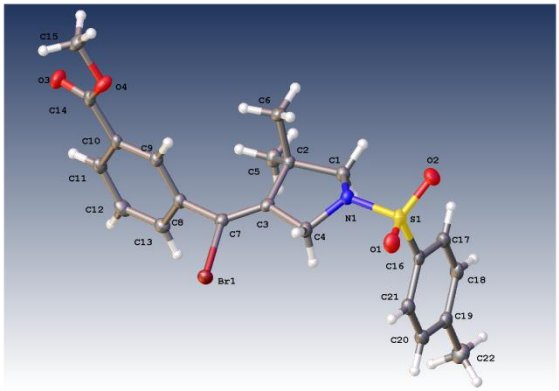


Table 1 Crystal data and structure refinement for 2k.

Identification code	2k
Empirical formula	$C_{22}H_{24}BrNO_4S$
Formula weight	478.39
Temperature/K	101.00
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	26.5945(8)
b/Å	6.1407(2)
c/Å	13.3679(4)
α/°	90
β/°	103.4980(10)
γ/°	90
Volume/Å^3	2122.79(11)
Z	4
ρ_{calc}g/cm^3	1.497
μ/mm^{-1}	3.797
F(000)	984.0
Crystal size/mm^3	0.1 × 0.1 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	10.262 to 144.314
Index ranges	-32 ≤ h ≤ 32, -7 ≤ k ≤ 7, -16 ≤ l ≤ 14
Reflections collected	36287
Independent reflections	4094 [R_{int} = 0.0524, R_{sigma} = 0.0326]
Data/restraints/parameters	4094/0/266
Goodness-of-fit on F^2	1.108
Final R indexes [I>=2σ (I)]	R_1 = 0.0370, wR_2 = 0.0929
Final R indexes [all data]	R_1 = 0.0373, wR_2 = 0.0930
Largest diff. peak/hole / e Å^{-3}	1.59/-0.66

References

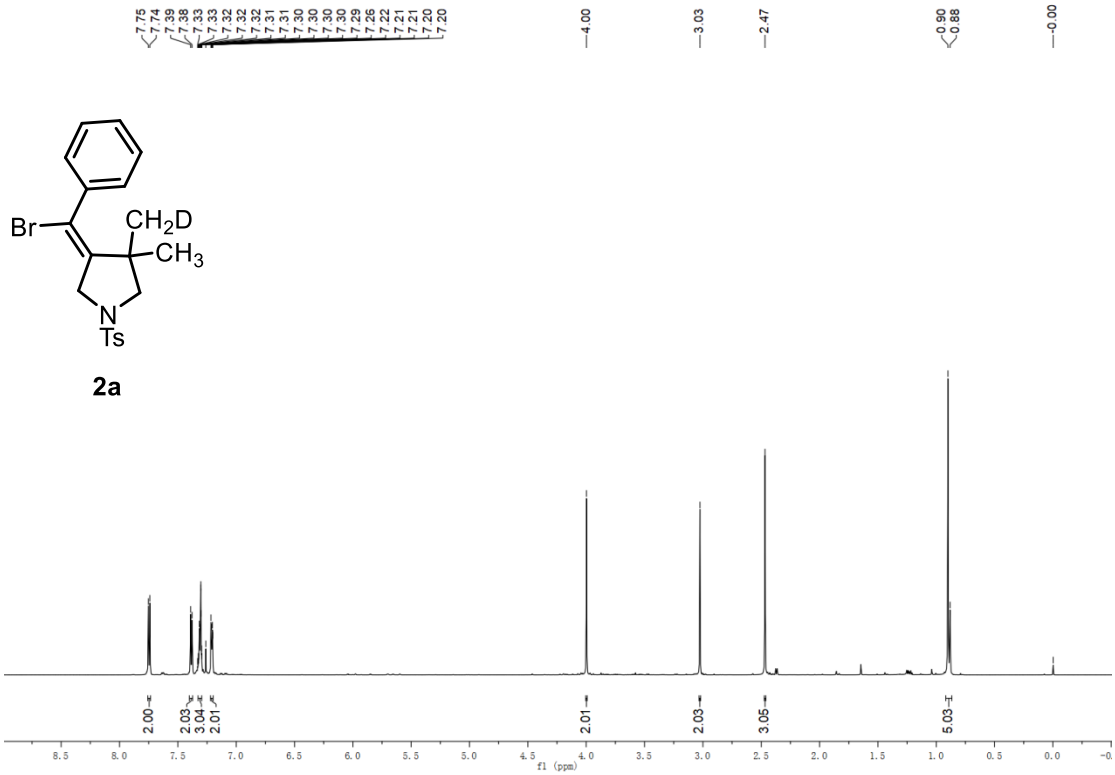
(1) a) M. Gerdin, S. K. Nadakudity, C. Worch, C. Moberg, *Adv. Synth. Catal.* **2010**, *352*, 2559; b) T. Xi, X. Chen, H. Zhang, Z. Lu, *Synthesis,* **2016**, *48*, 2837; c) J. H. Park, Y. Cho, Y. K. Chung, *Angew. Chem. Int. Ed.* **2010**, *49*, 5138; d) Y.-T. He, Q. Wang, J. Zhao, X.-Z. Wang, Y.-F. Qiu, Y.-C. Yang, J.-Y. Hu, X.-Y. Liu, Y. -M. Liang, *Adv. Synth. Catal.* **2015**, *357*, 3069; e) A. Gansäuer, M. Otte, L. Shi, *J. Am. Chem. Soc.* **2011**, *133*, 416; f) J. Huang, X. Hu, F. Chen, J. Gui, W. Zeng, *Org. Biomol. Chem.,* **2019**, *17*, 7042; g) K. R. Strom, A. C. Impastato, K. J. Moy, A. J. Landreth, J. K. Snyder, *Org. Lett.* **2015**, *17*, 2126; h) Y. Zhang, Y. -J. Wang, Q. Zou, X. -Y. Liu, Z. Chen, *Org. Lett*. **2022**, 24, 8153.

(2) R. Ebule, S. Liang, G. B. Hammond, B. Xu, *ACS Catal*. **2017**, *7*, 6798

(3) K. Takahashi, K. Fukushima, M. Seto, A. Togashi, Y. Arai, M. Tsubuki, T. Honda, *J. Org. Chem.* **2018**, *83*, 10636.

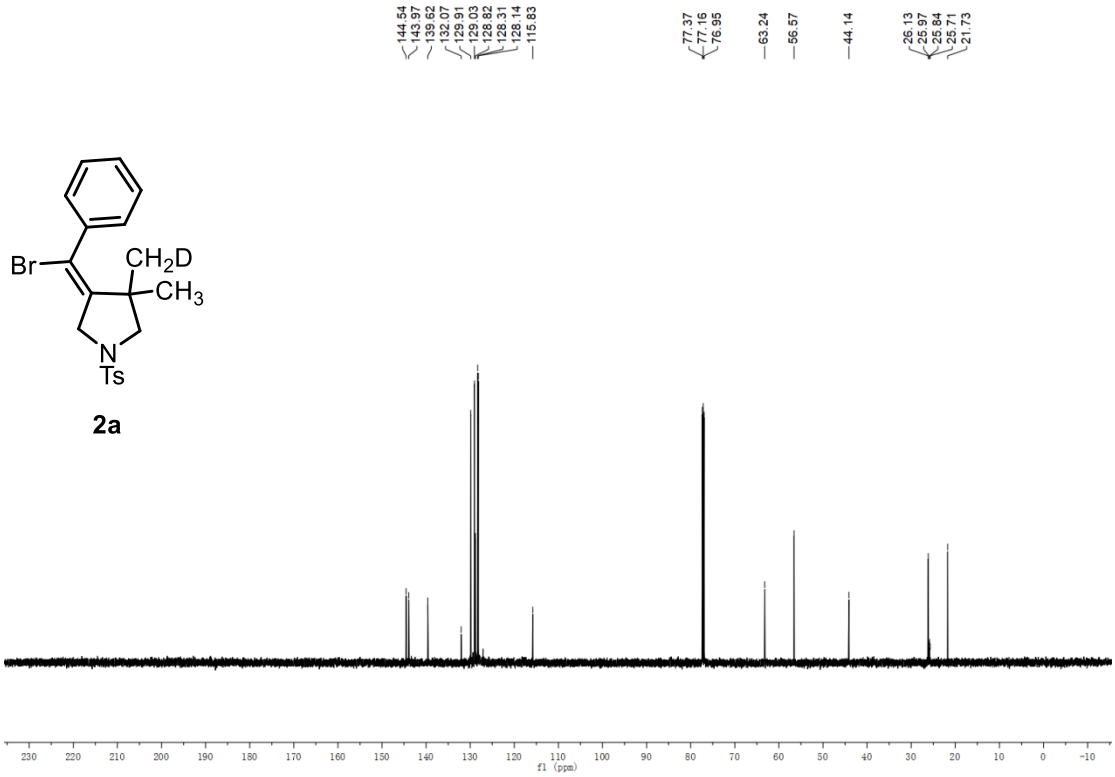
NMR spectra

^{1}H NMR of **2a** (600 MHz, $CDCl_3$)



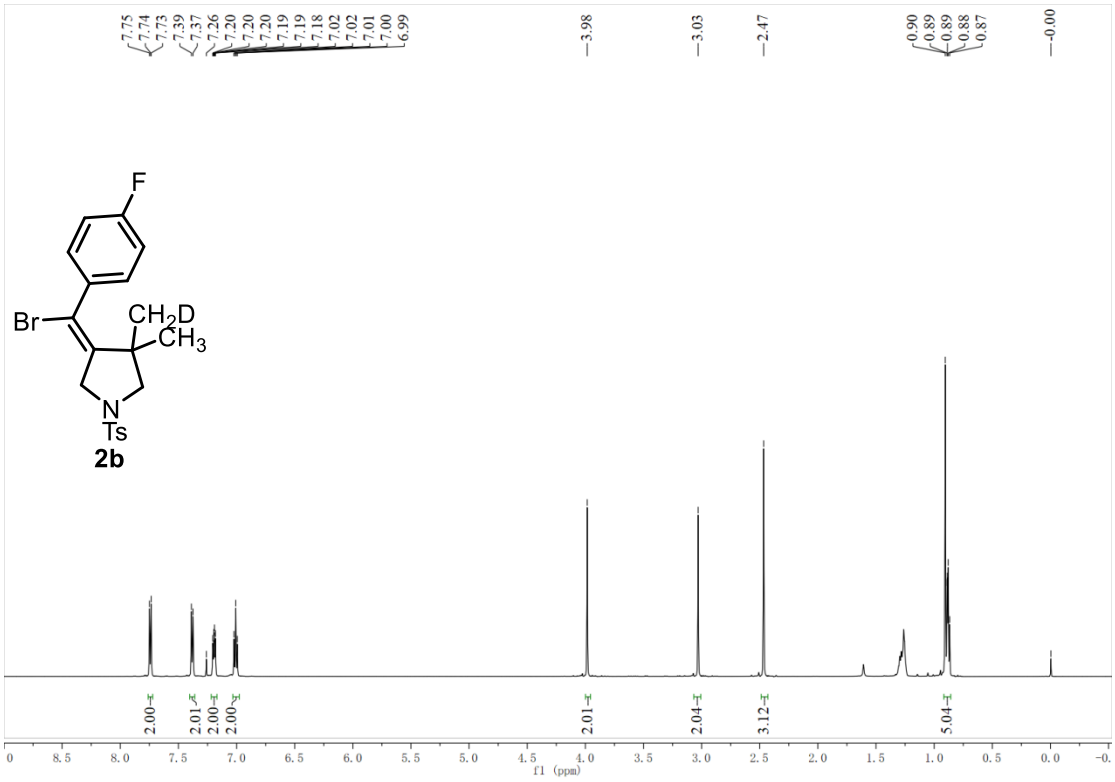
2a

^{13}C NMR of **2a** (151 MHz, $CDCl_3$)

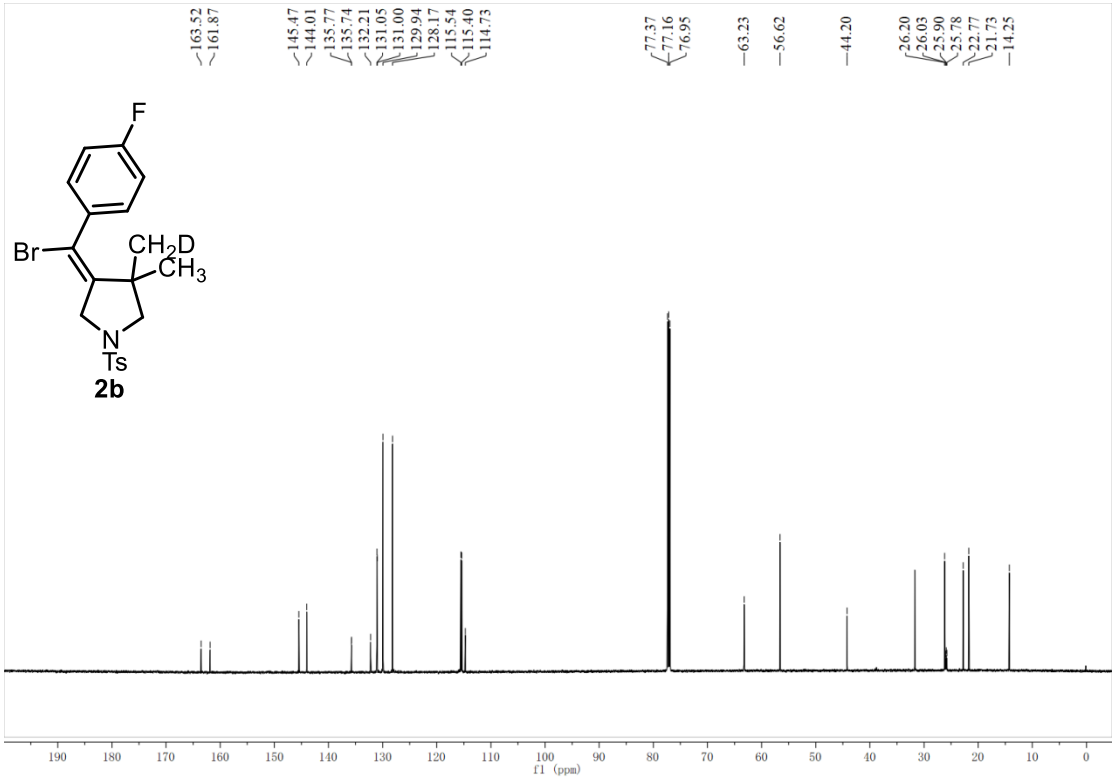


2a

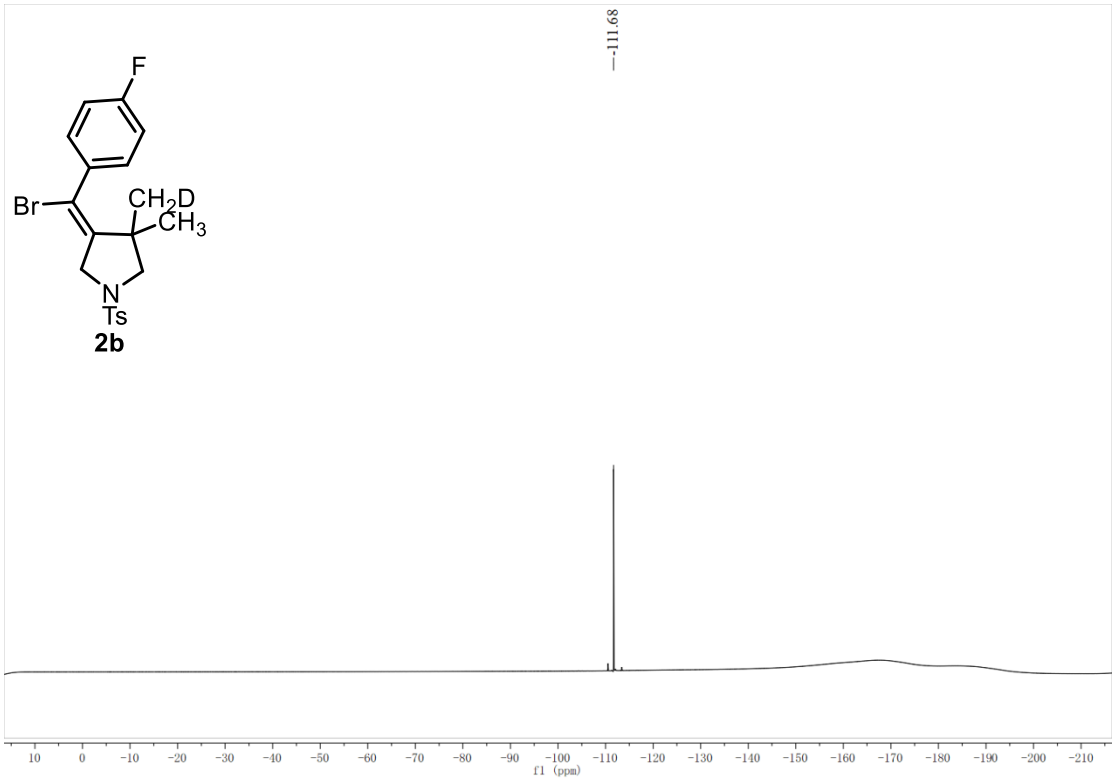
^{1}H NMR of **2b** (600 MHz, $CDCl_3$)



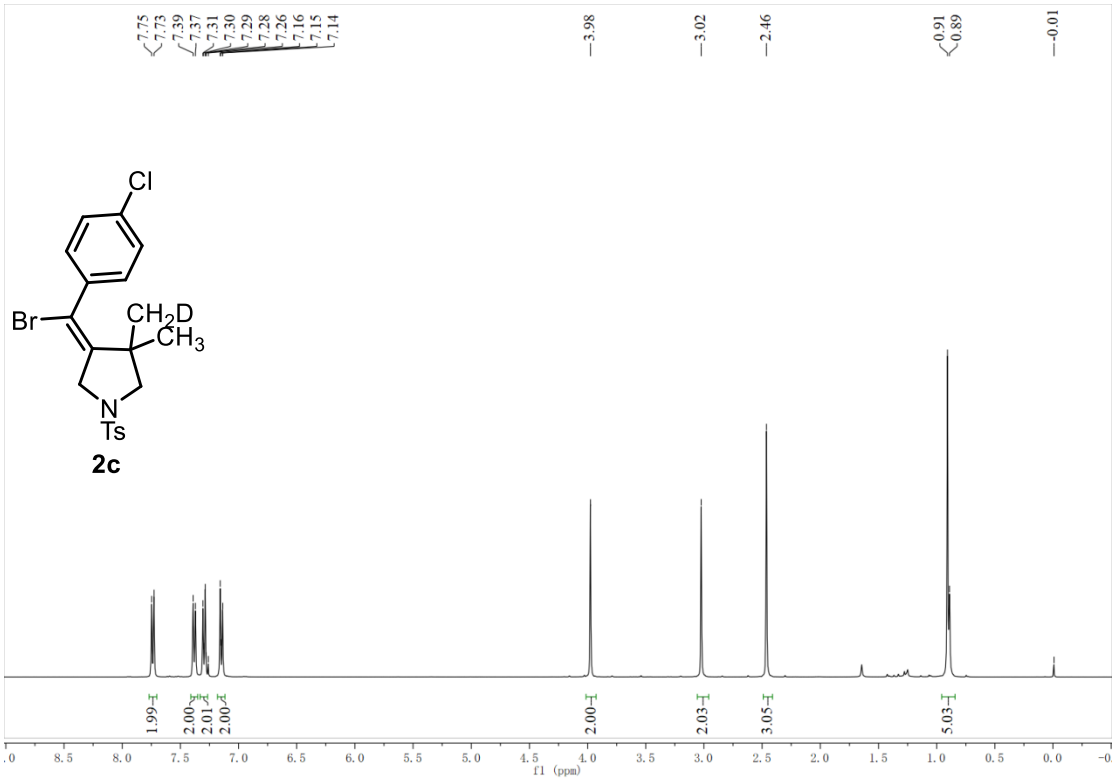
^{13}C NMR of **2b** (151 MHz, $CDCl_3$)



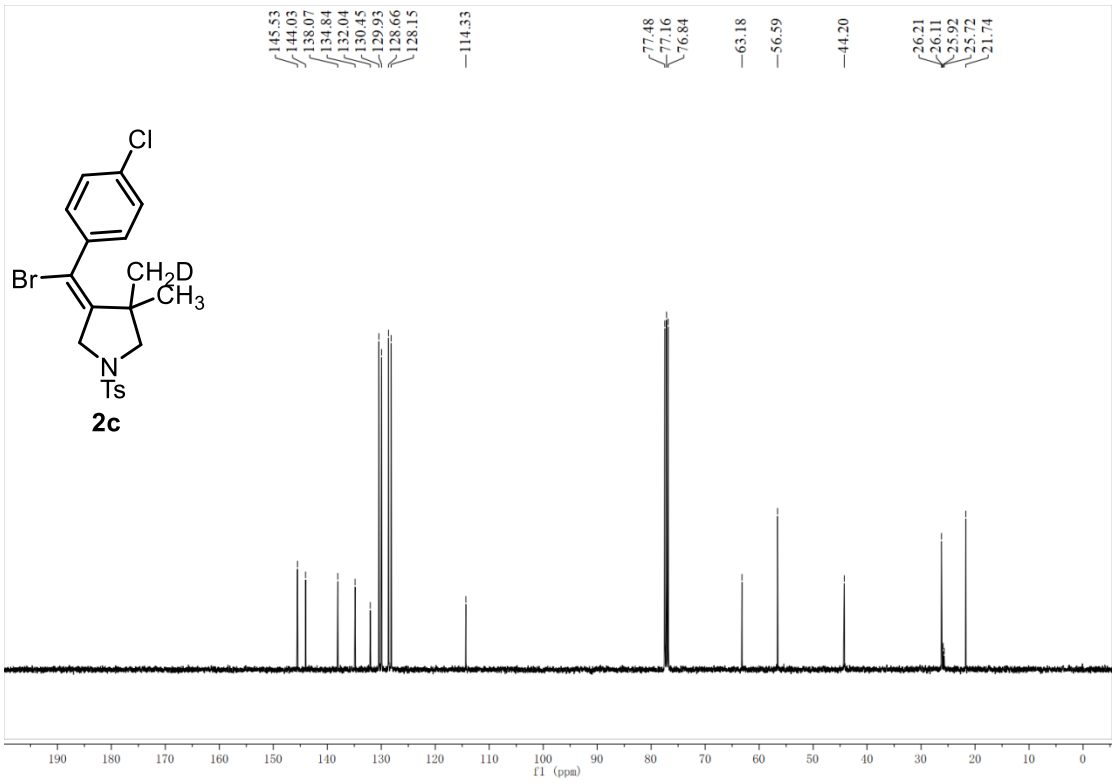
^{19}F NMR of **2b** (565 MHz, $CDCl_3$)



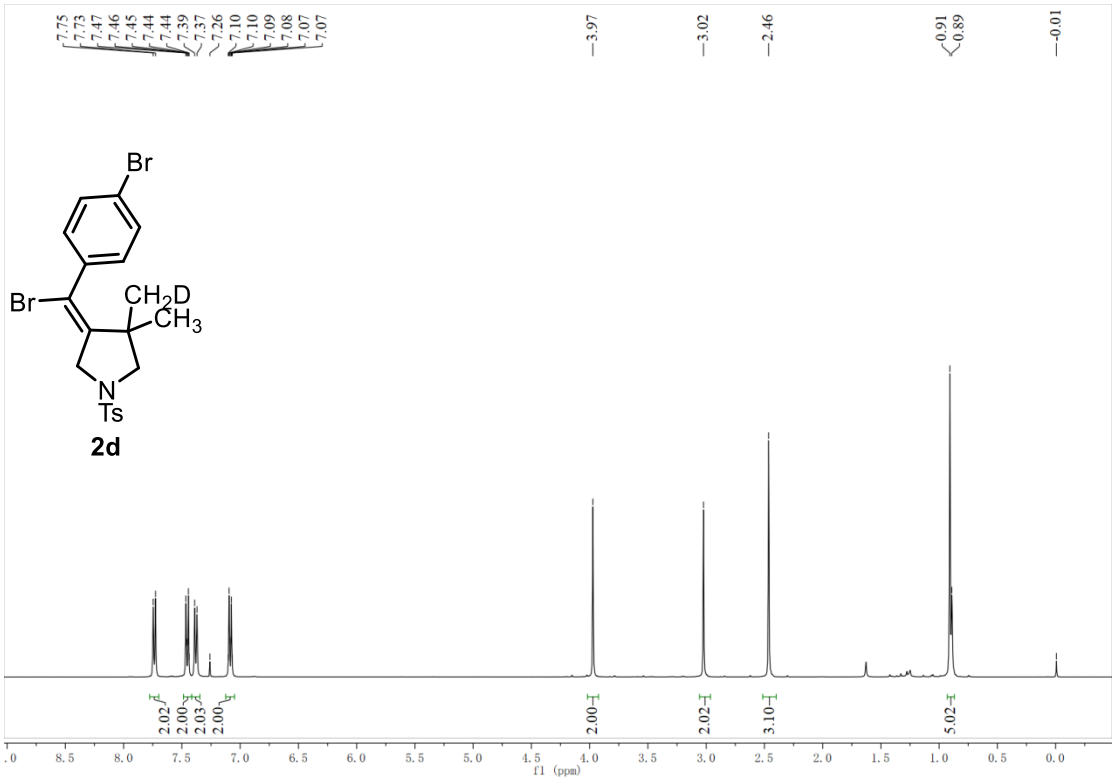
^{1}H NMR of **2c** (400 MHz, $CDCl_3$)



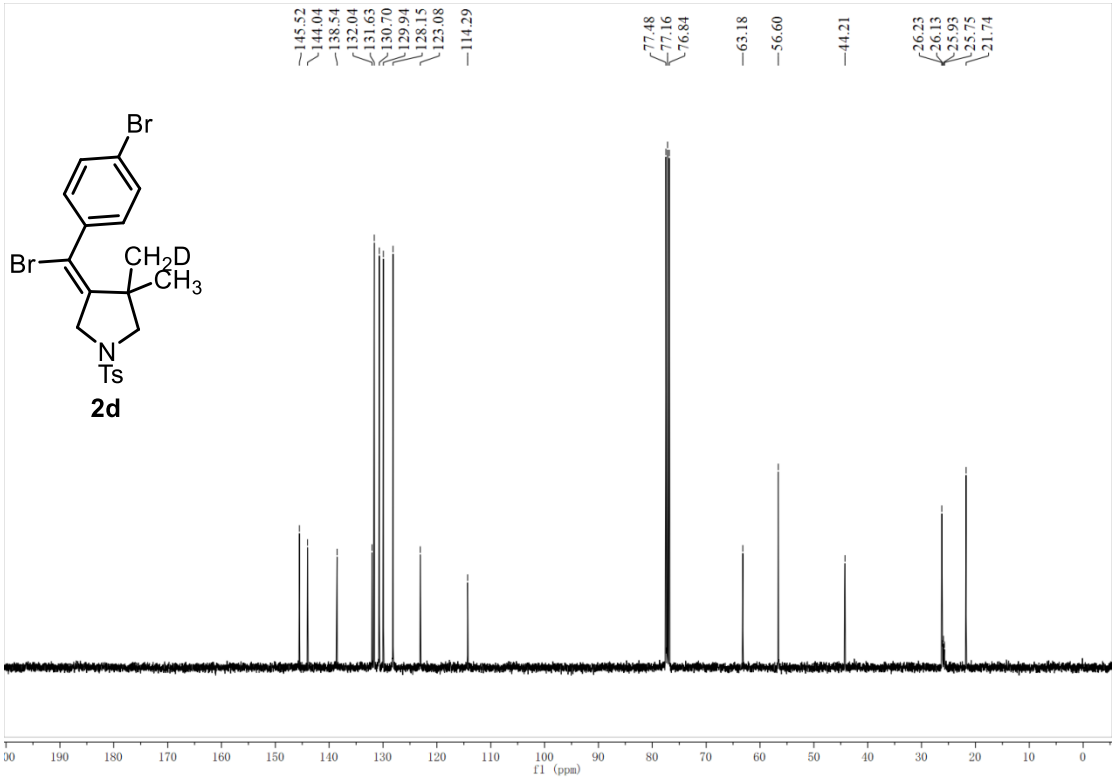
^{13}C NMR of **2c** (101 MHz, $CDCl_3$)



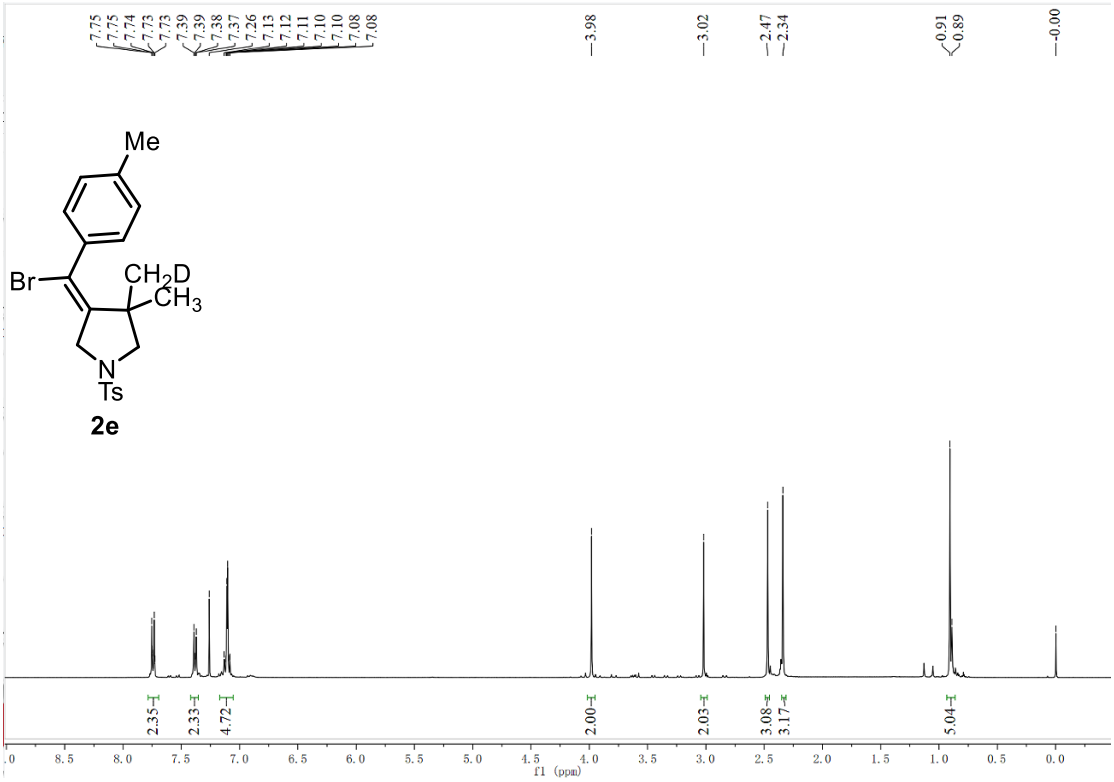
^{1}H NMR of **2d** (400 MHz, $CDCl_3$)



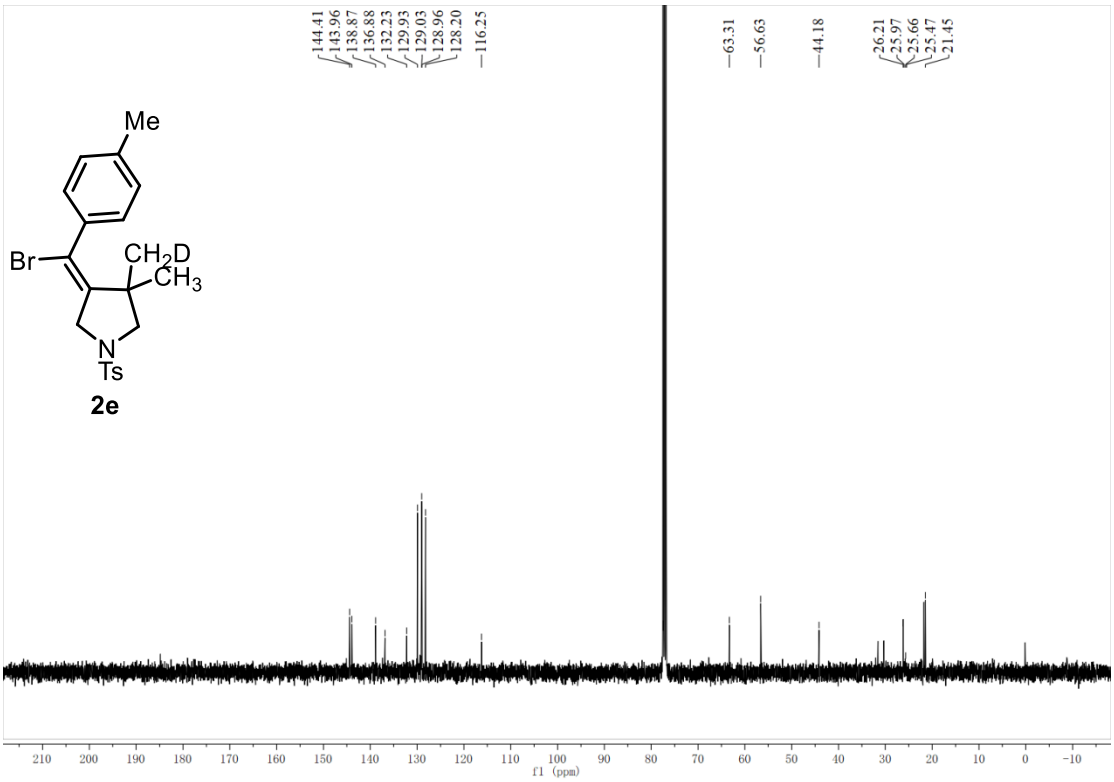
^{13}C NMR of **2d** (101 MHz, $CDCl_3$)



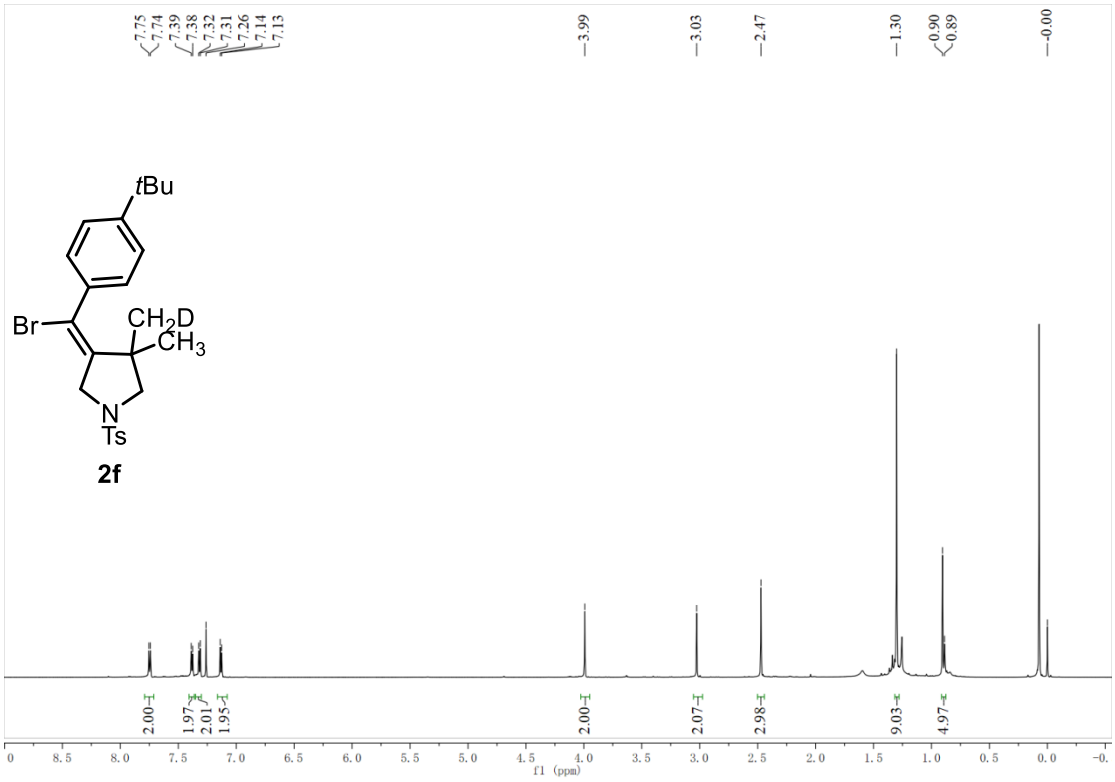
^{1}H NMR of **2e** (400 MHz, $CDCl_3$)



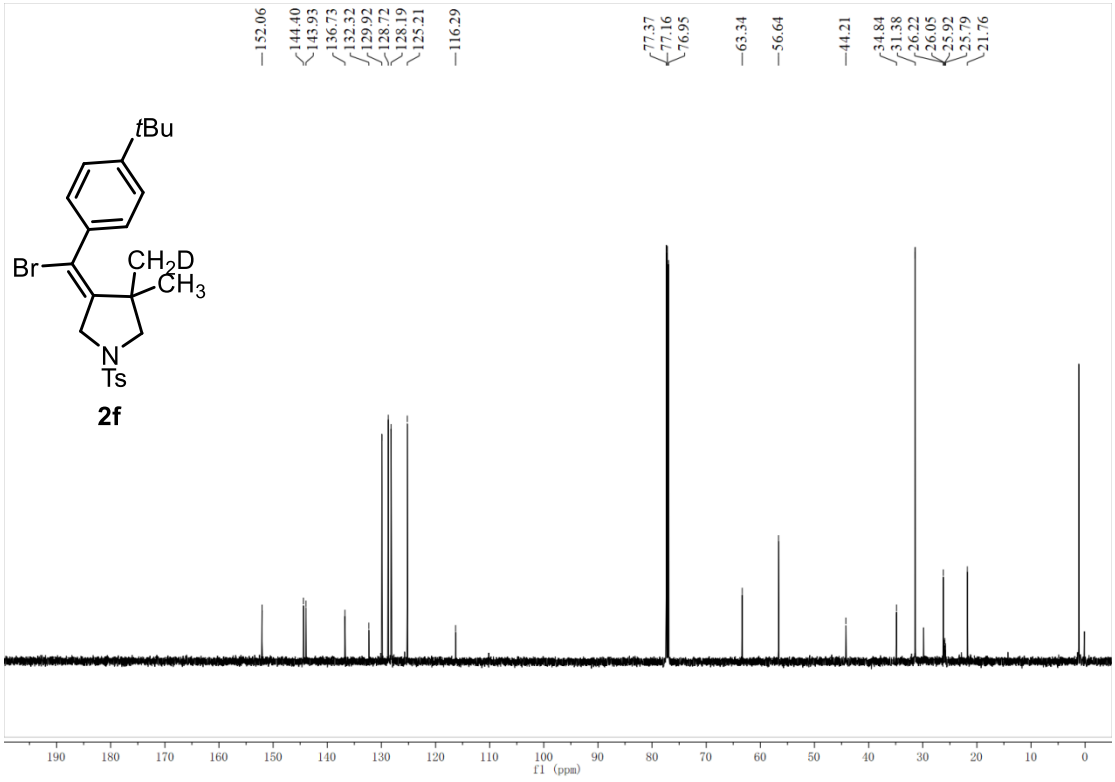
^{13}C NMR of **2e** (101 MHz, $CDCl_3$)



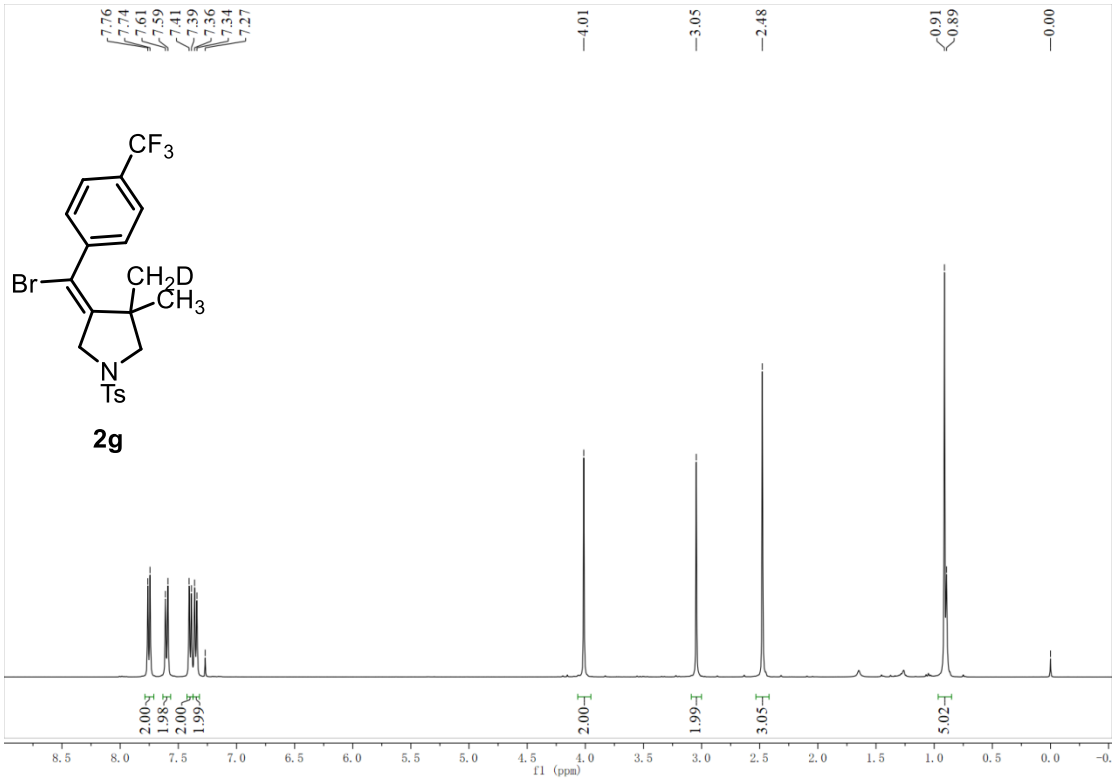
^{1}H NMR of **2f** (600 MHz, $CDCl_3$)



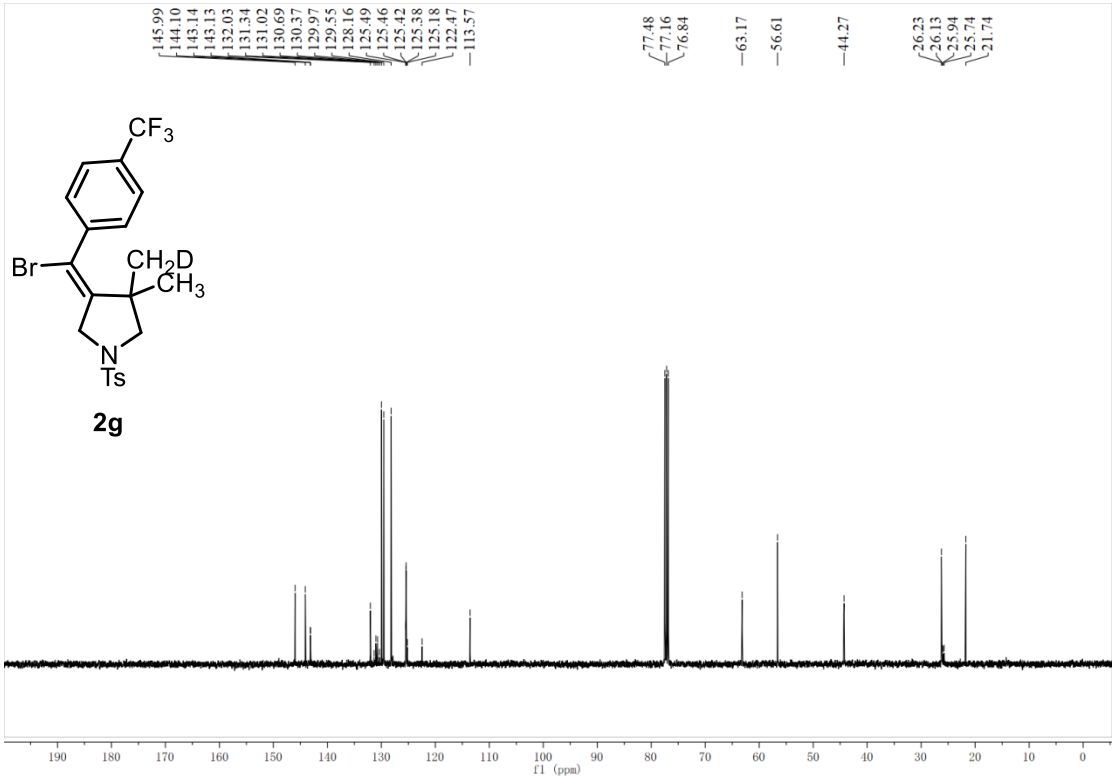
^{13}C NMR of **2f** (151 MHz, $CDCl_3$)



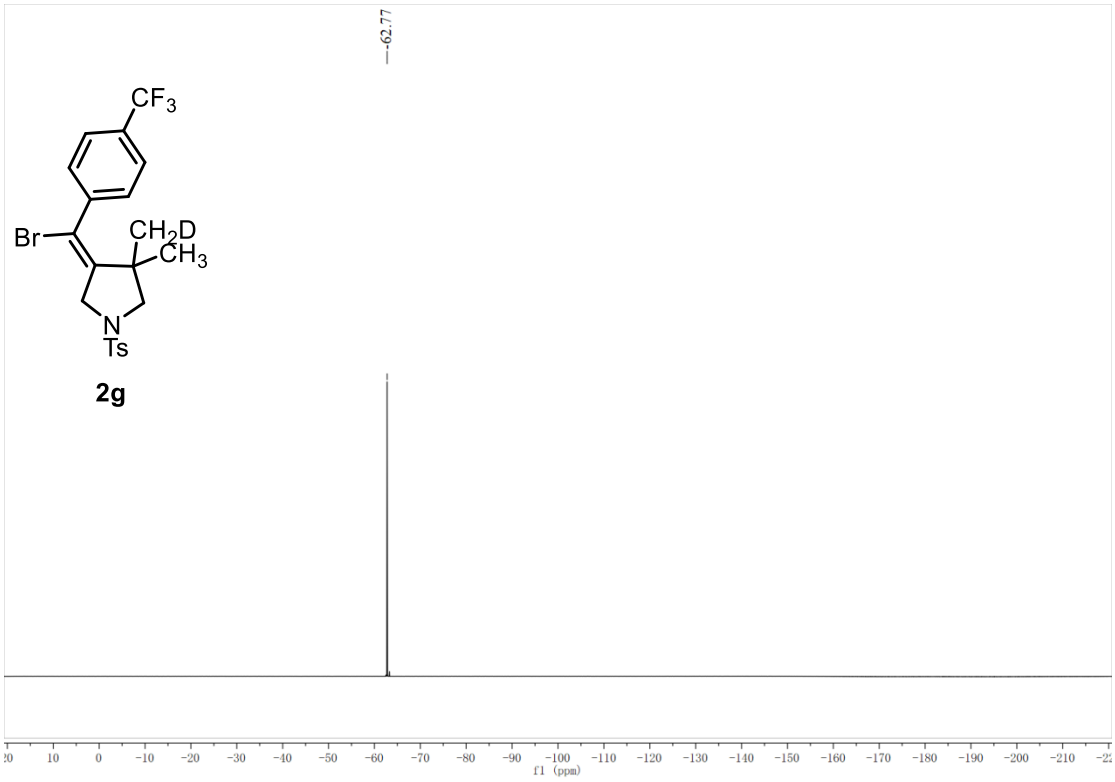
^{1}H NMR of **2g** (400 MHz, $CDCl_3$)



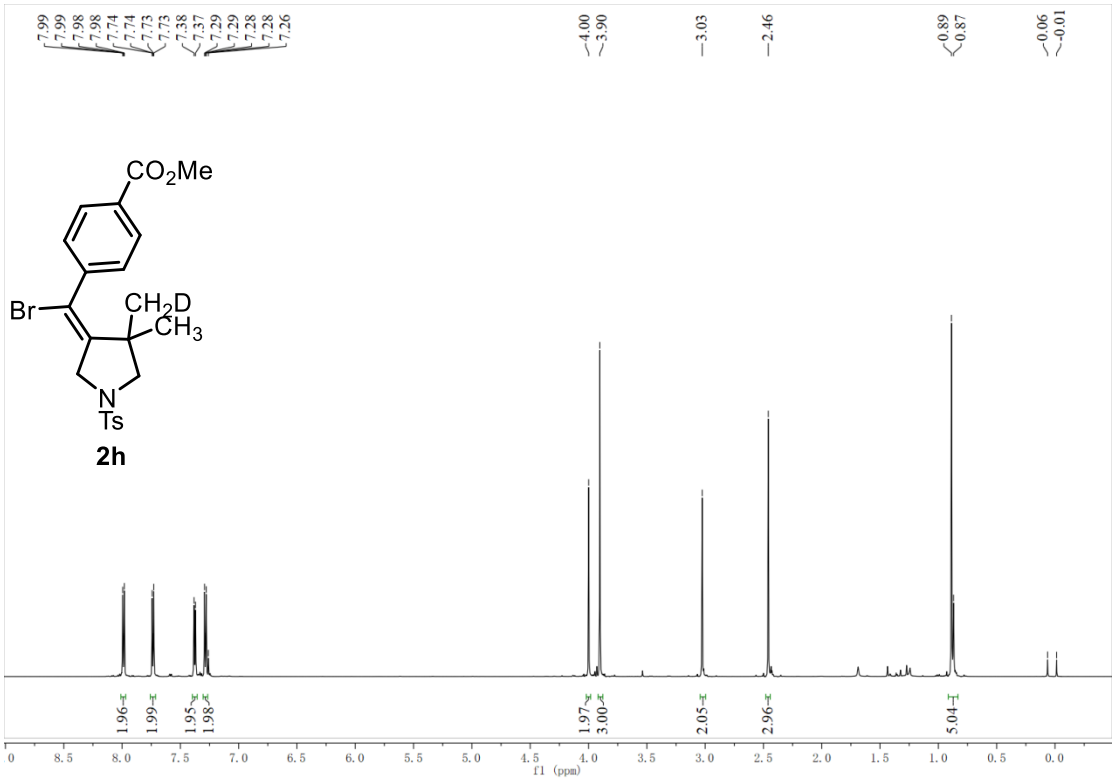
^{13}C NMR of **2g** (101 MHz, $CDCl_3$)



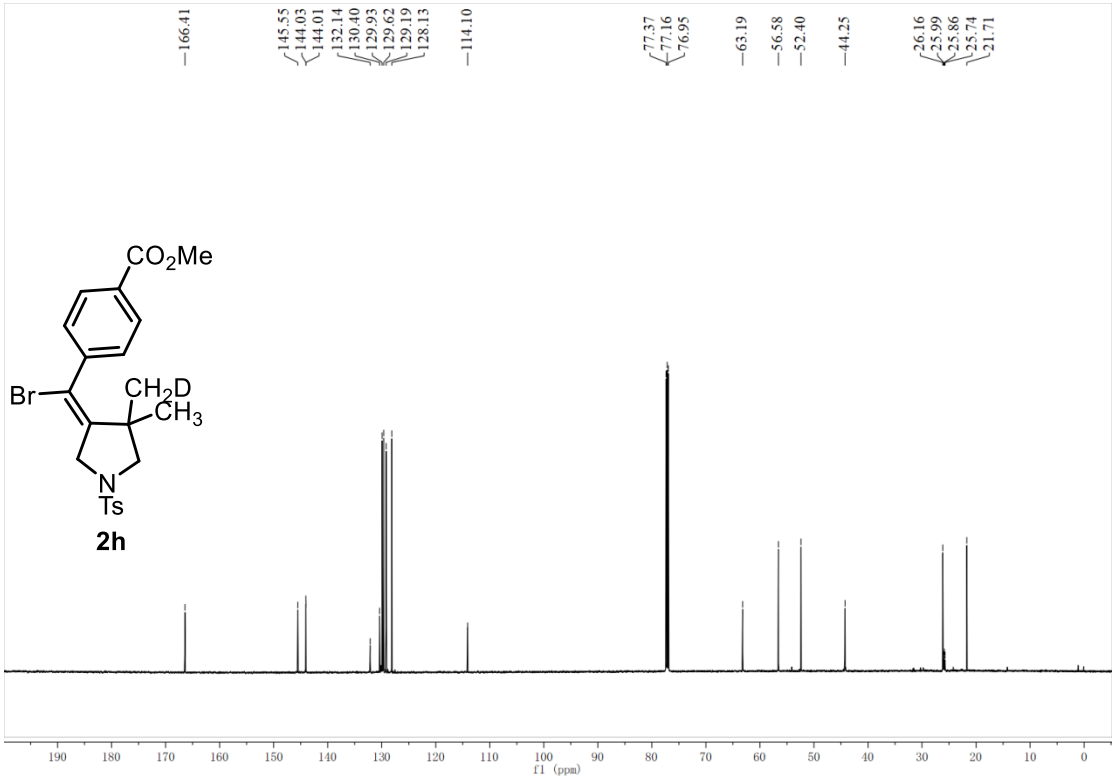
^{19}F NMR of **2g** ($CDCl_3$)



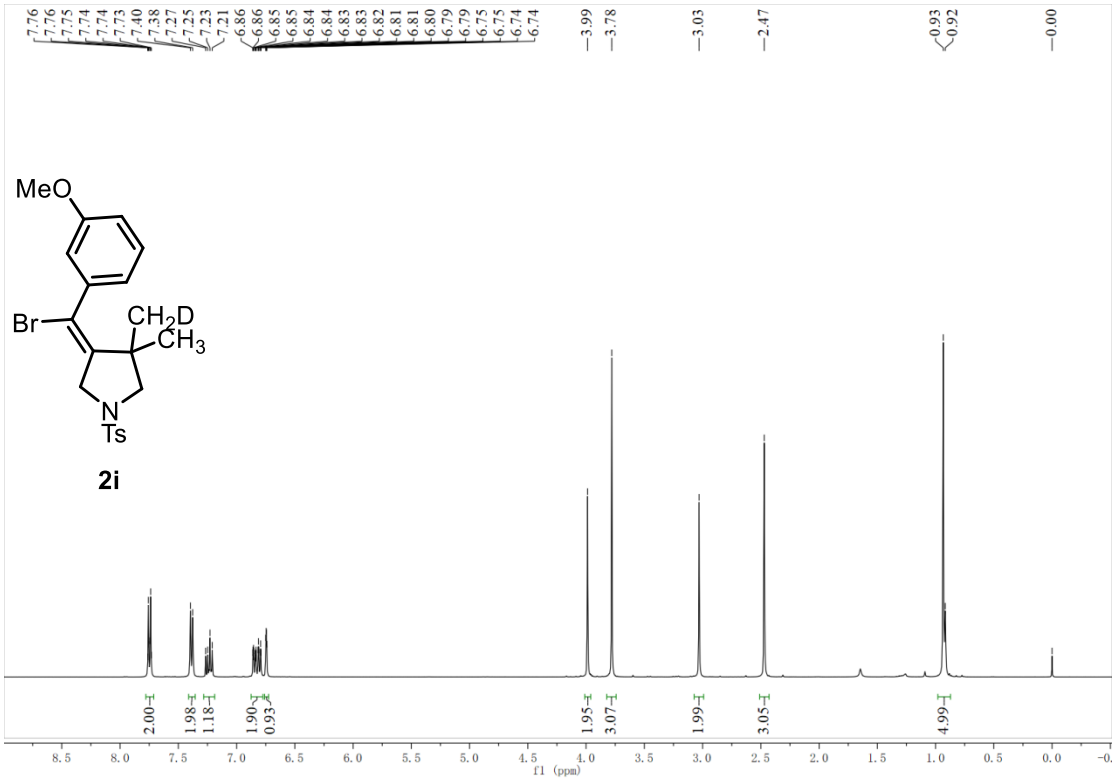
^{1}H NMR of **2h** (600 MHz, $CDCl_3$)



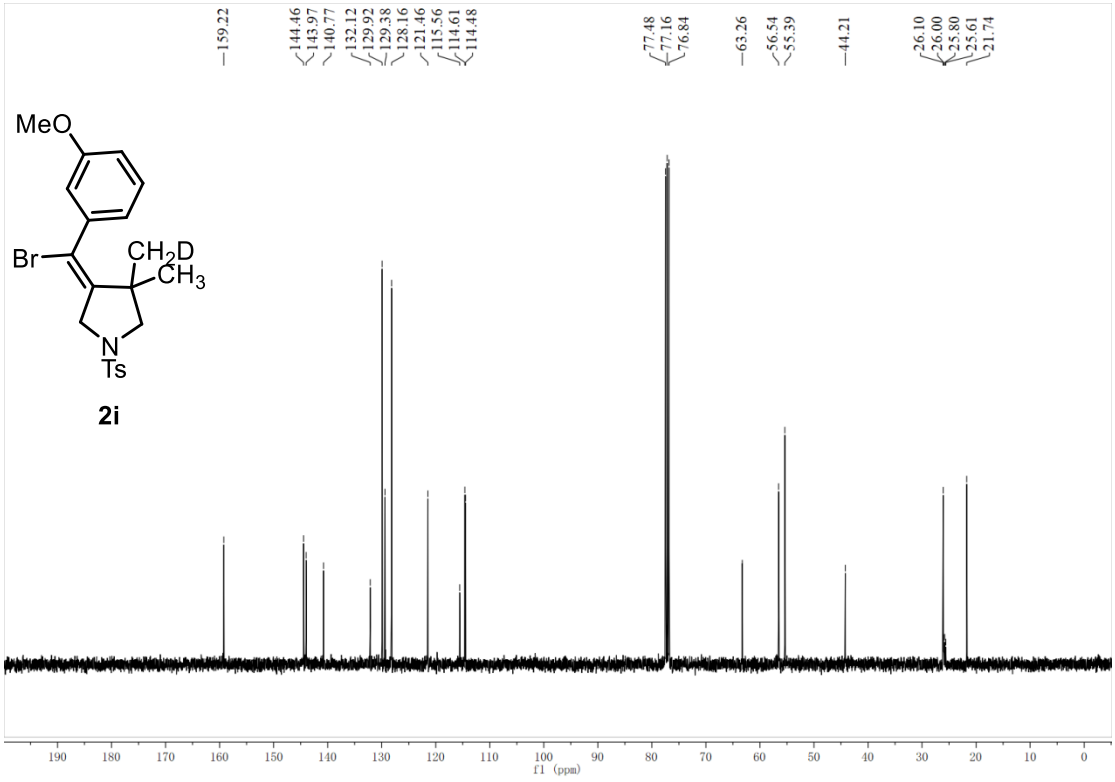
^{13}C NMR of **2h** (151 MHz, $CDCl_3$)



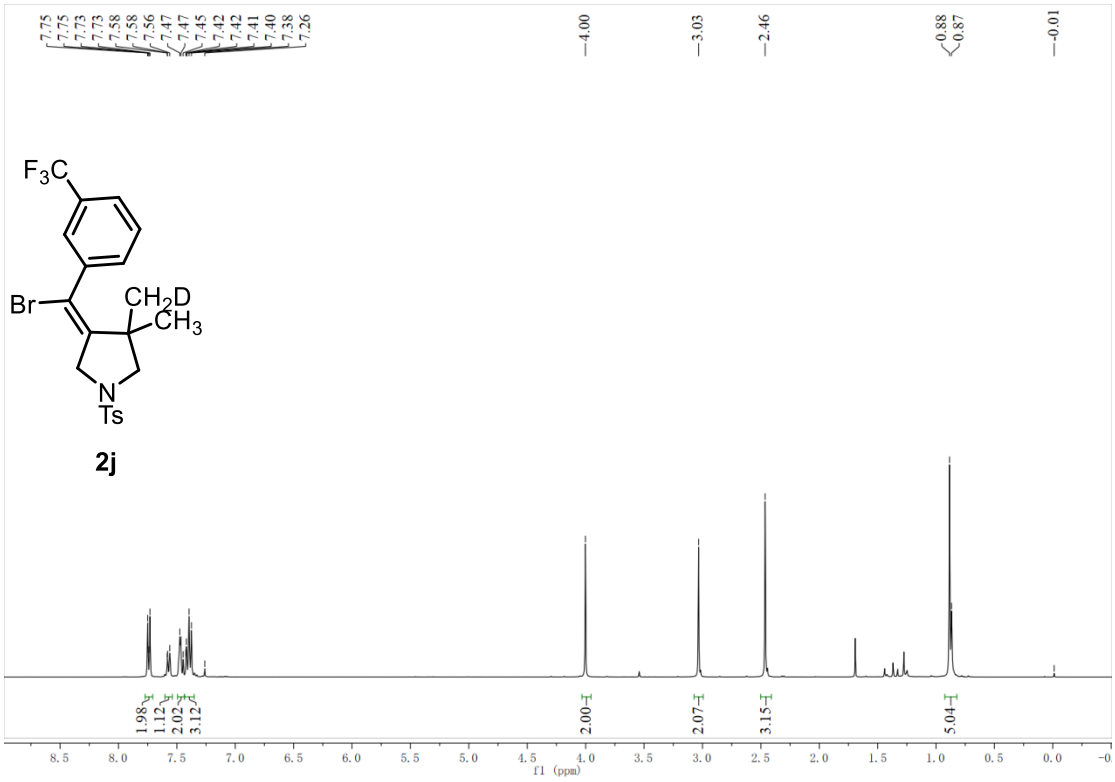
^{1}H NMR of **2i** (400 MHz, $CDCl_3$)



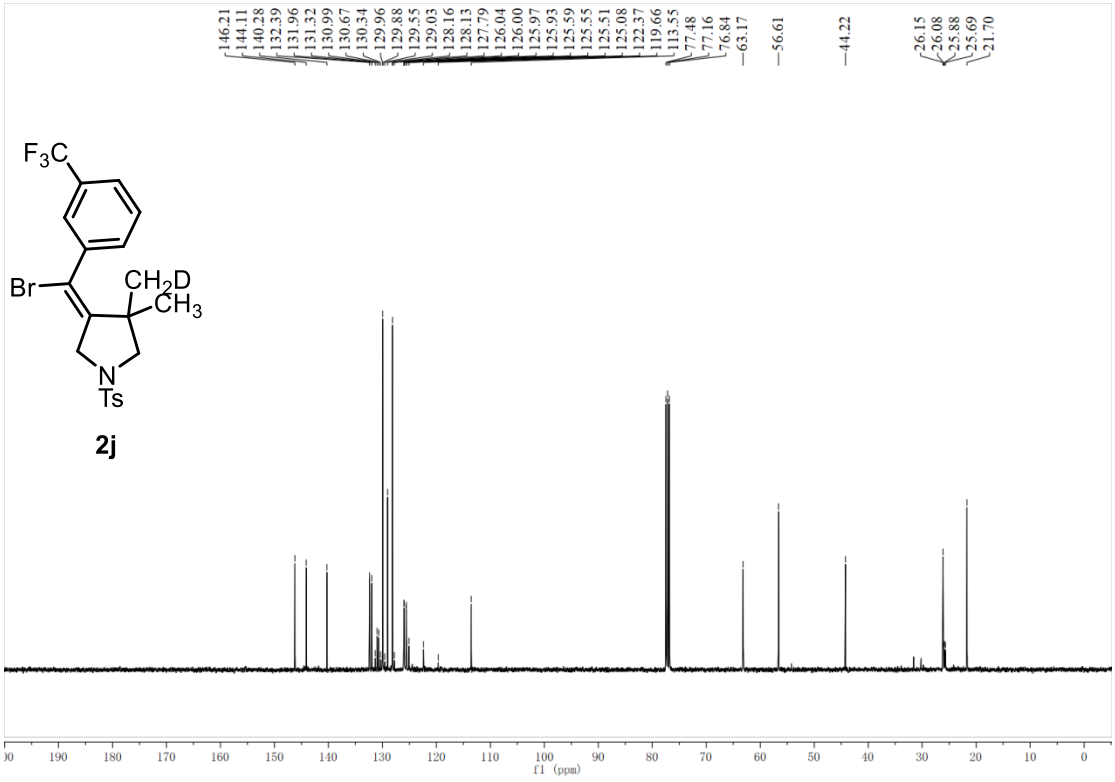
^{13}C NMR of **2i** (101 MHz, $CDCl_3$)



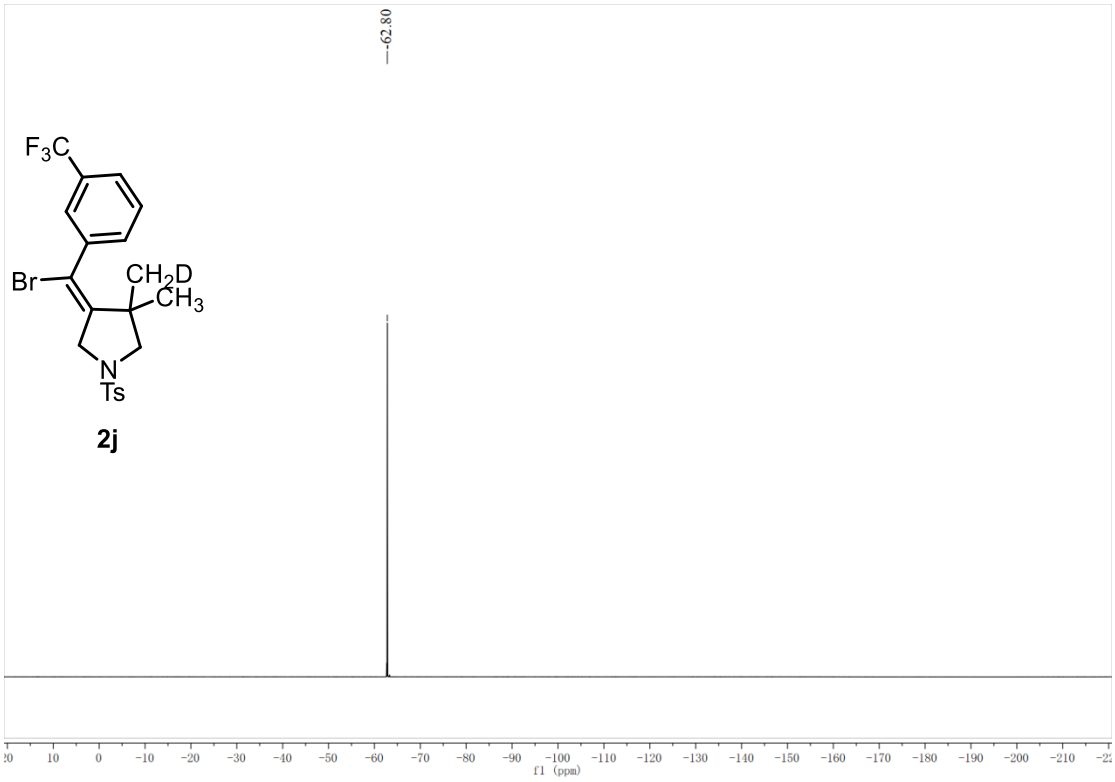
^{1}H NMR of **2j** (400 MHz, $CDCl_3$)



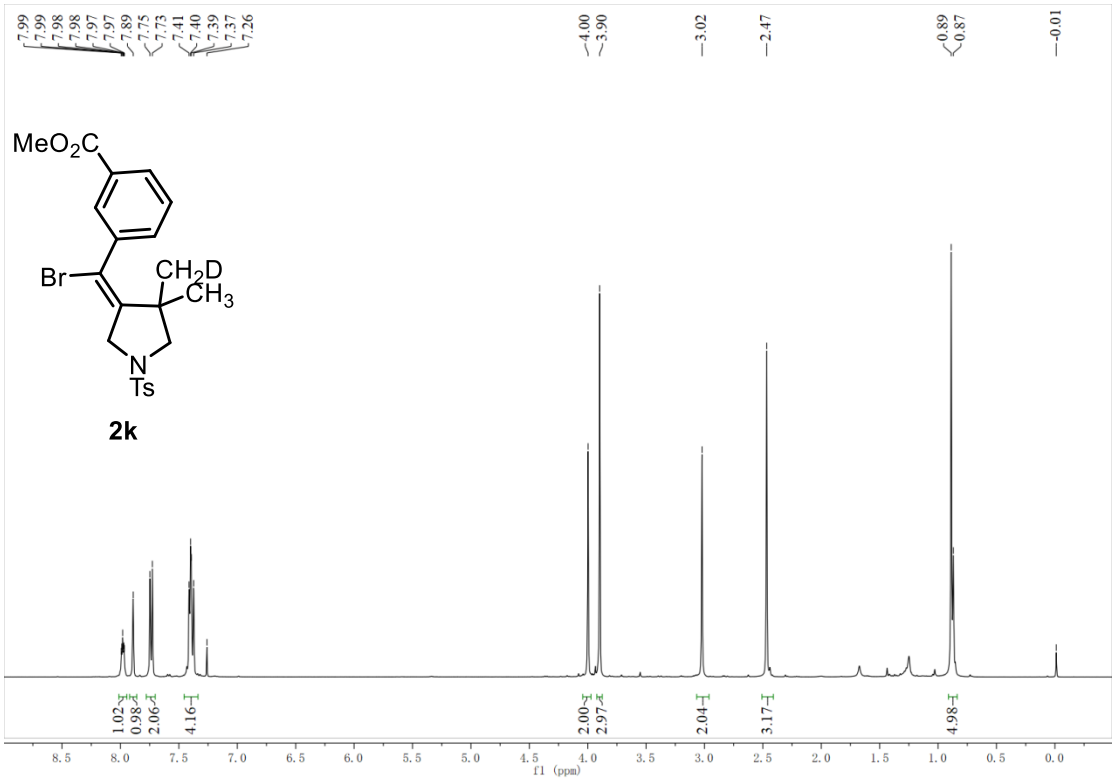
^{13}C NMR of **2j** (101 MHz, $CDCl_3$)



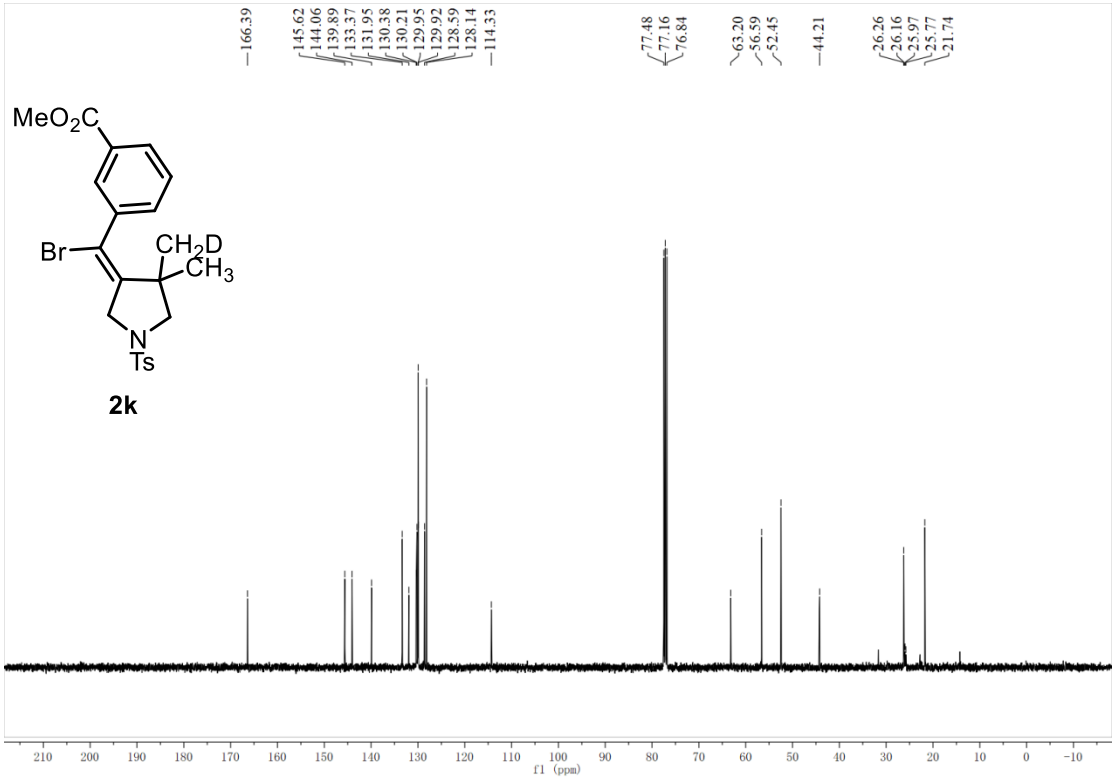
^{19}F NMR of **2j** (565 MHz, $CDCl_3$)



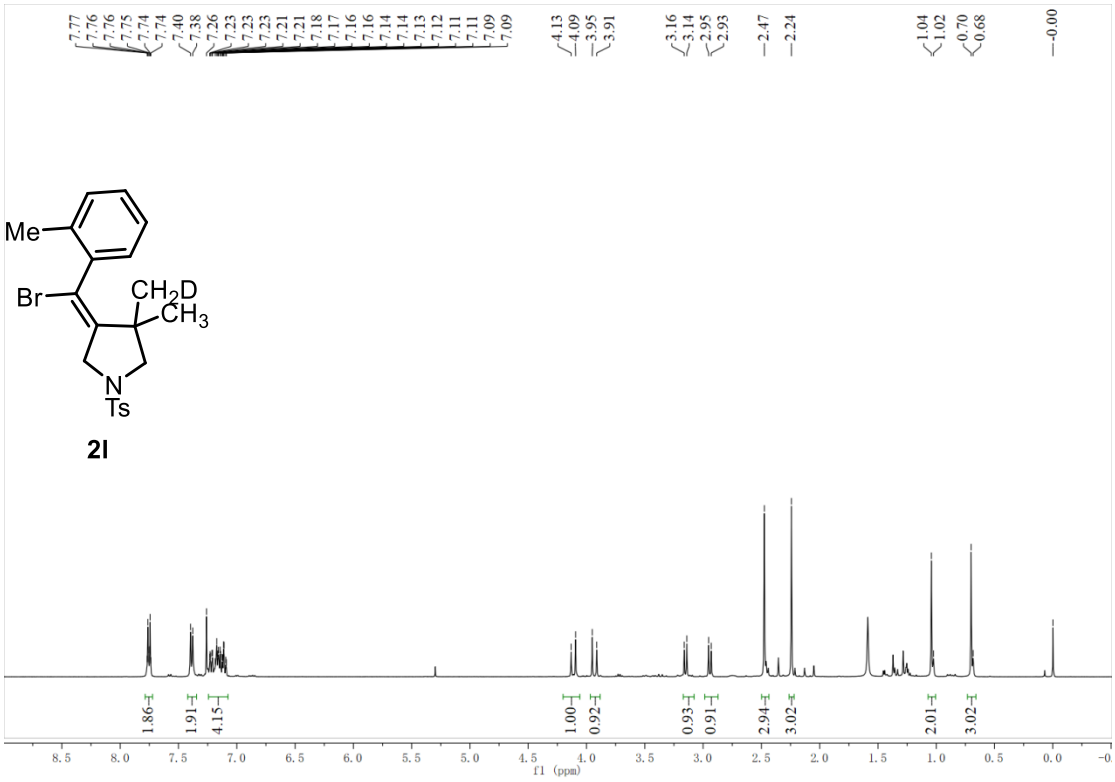
^{1}H NMR of **2k** (400 MHz, $CDCl_3$)



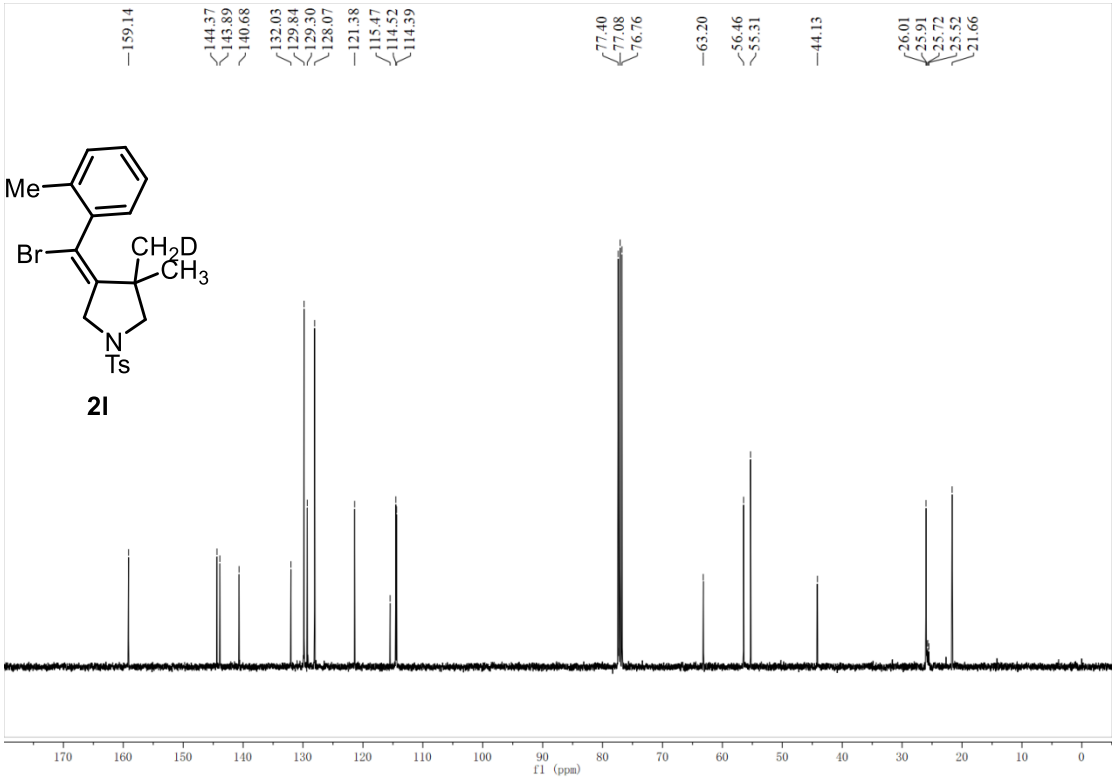
^{13}C NMR of **2k** (101 MHz, $CDCl_3$)



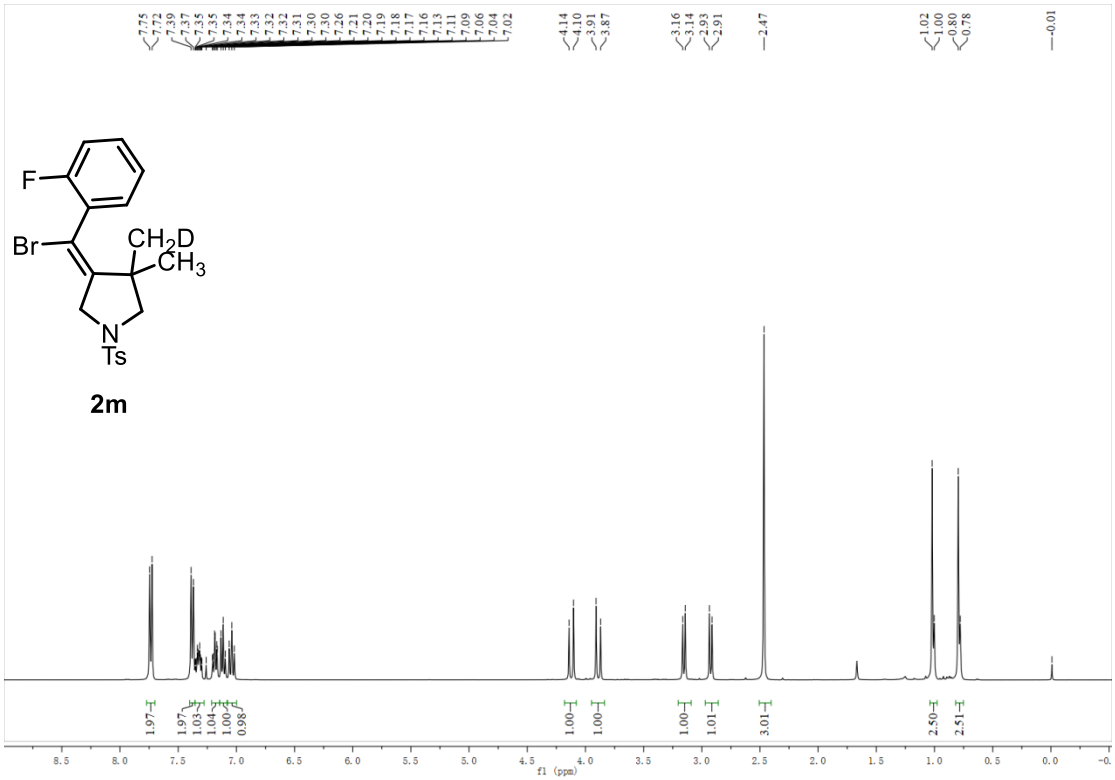
^{1}H NMR of **2l** (400 MHz, $CDCl_3$)



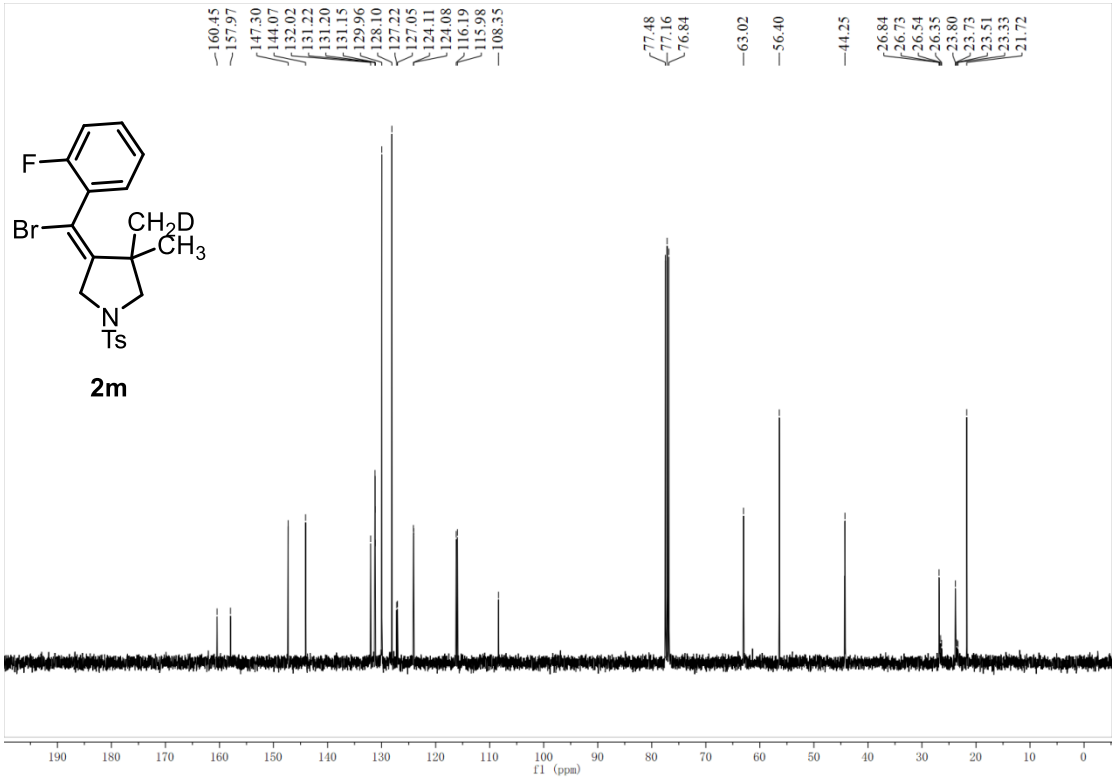
^{13}C NMR of **2l** (151 MHz, $CDCl_3$)



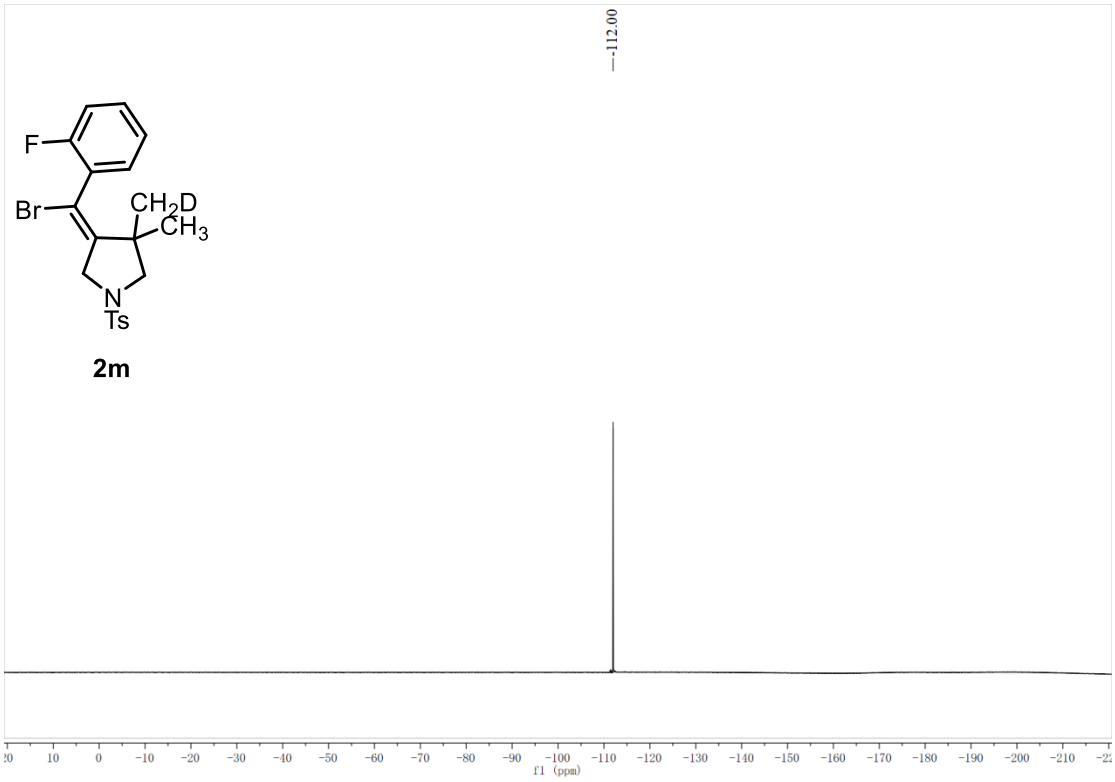
^{1}H NMR of **2m** (400 MHz, $CDCl_3$)



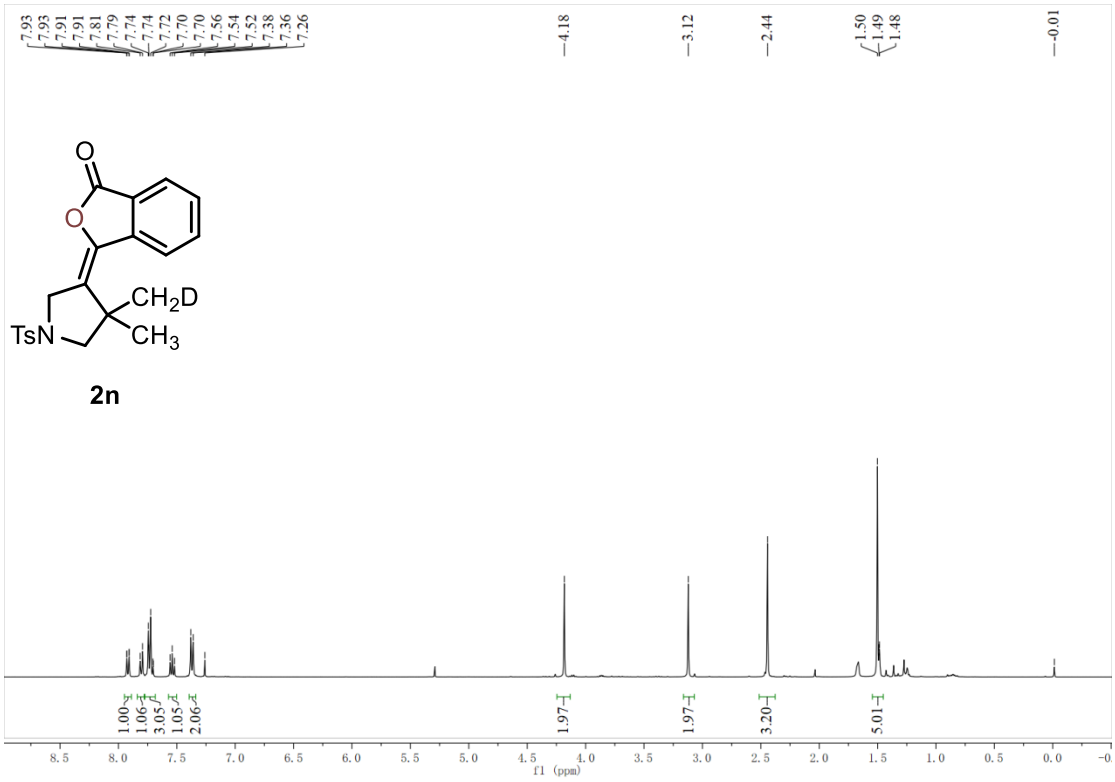
^{13}C NMR of **2m** (101 MHz, $CDCl_3$)



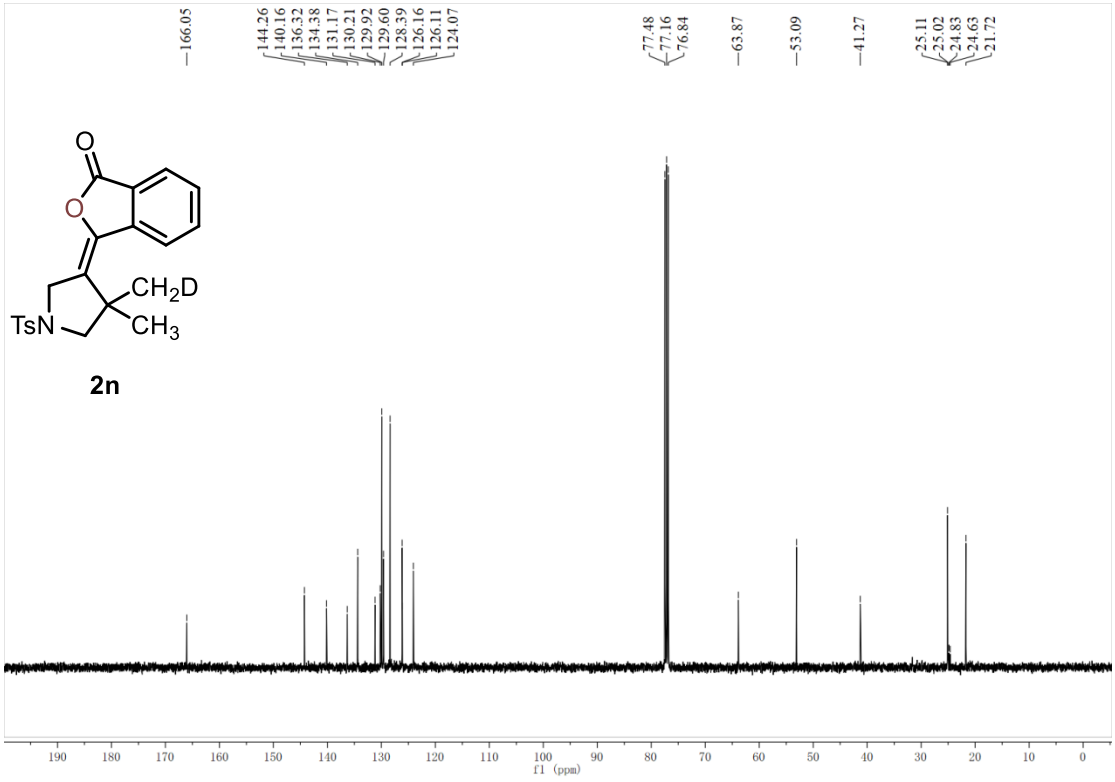
^{19}F NMR of **2m** (376 MHz, $CDCl_3$)



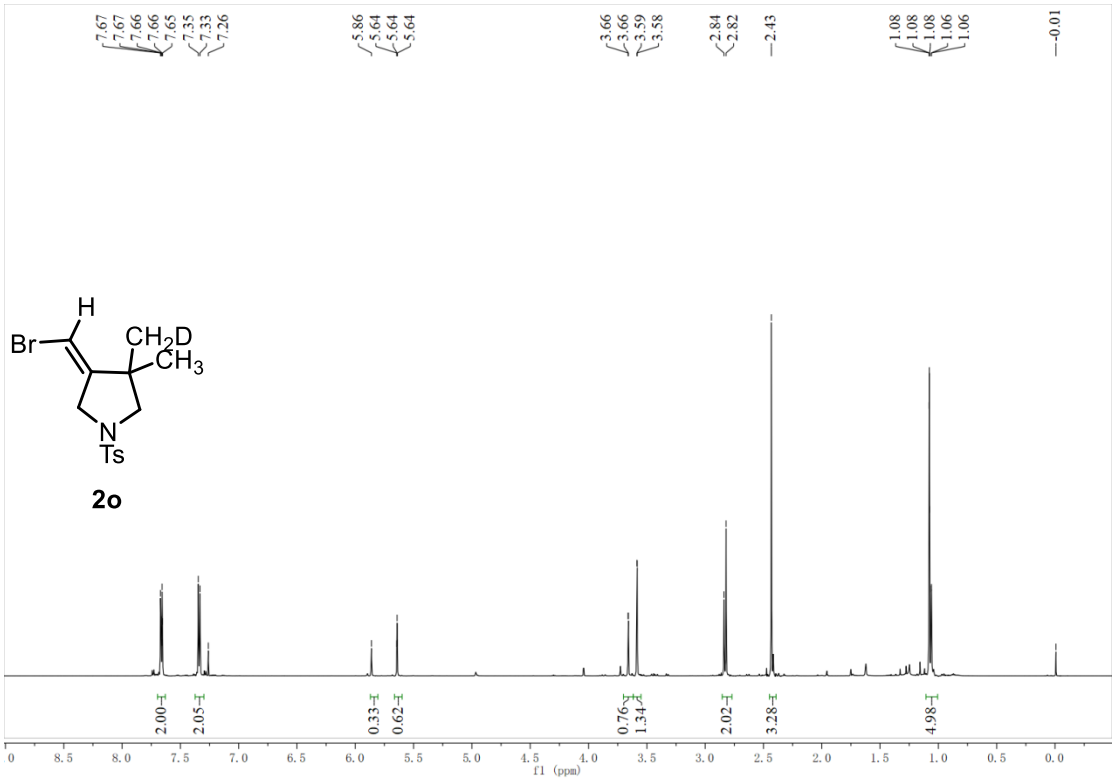
^{1}H NMR of **2n** (400 MHz, $CDCl_3$)



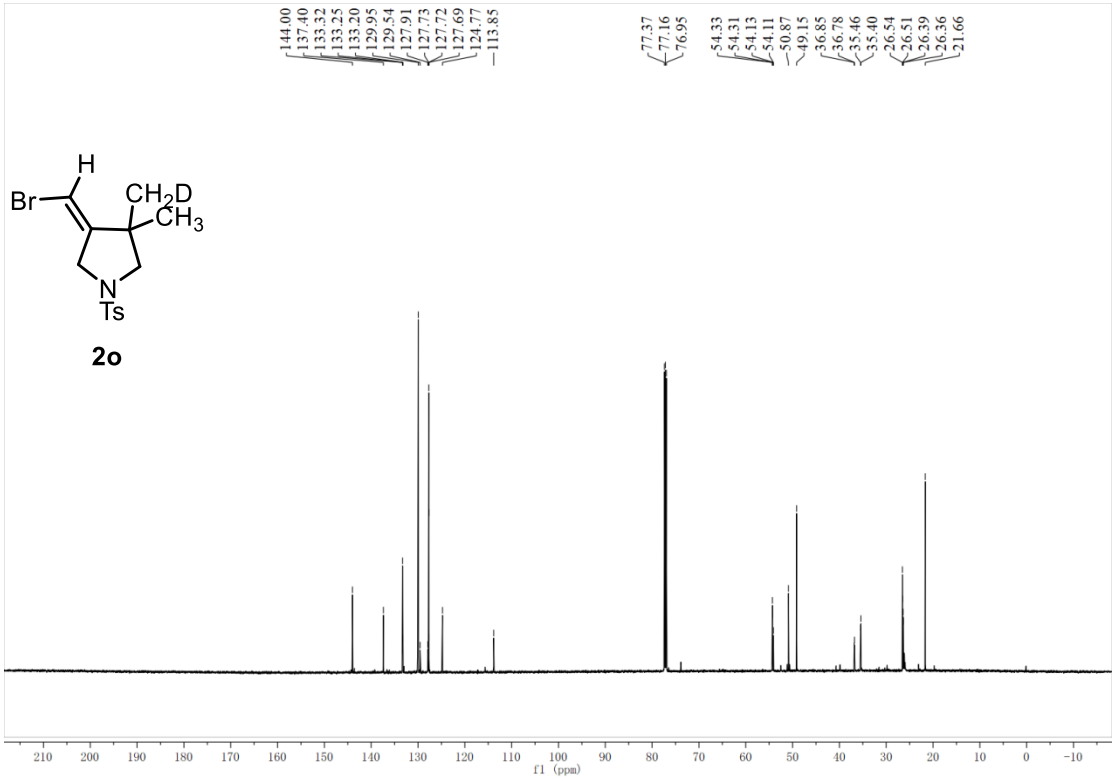
^{13}C NMR of **2n** (101 MHz, $CDCl_3$)



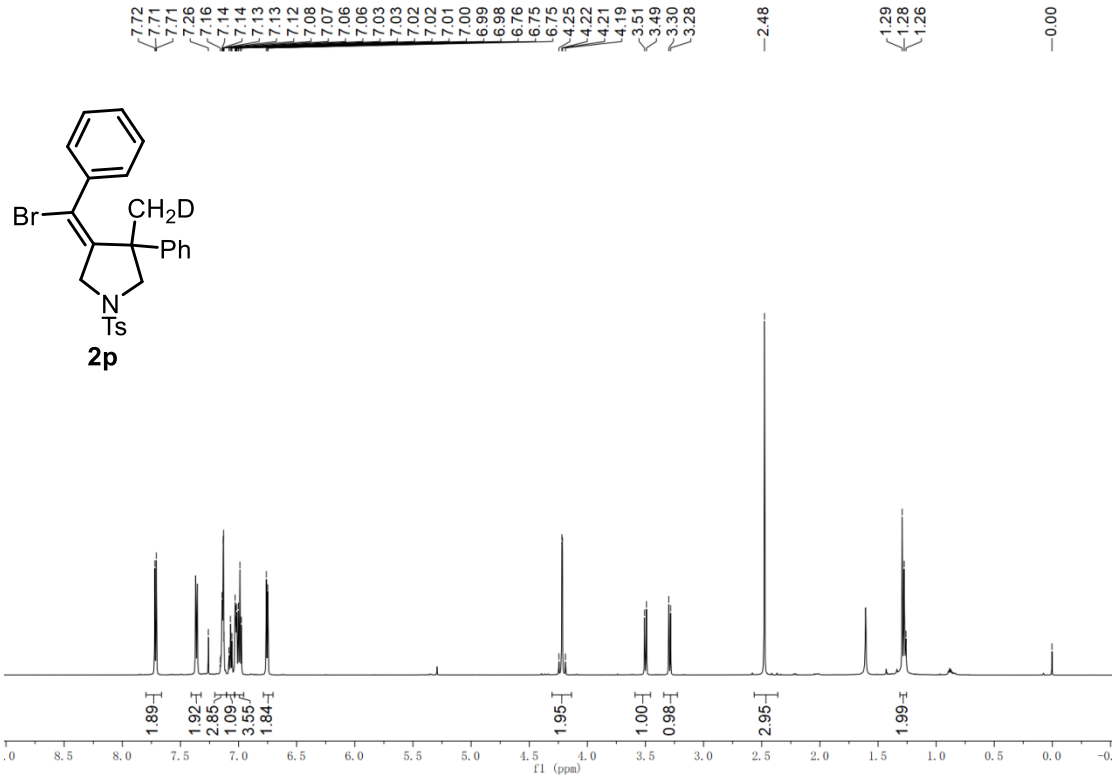
^{1}H NMR of **2o** (600 MHz, $CDCl_3$)



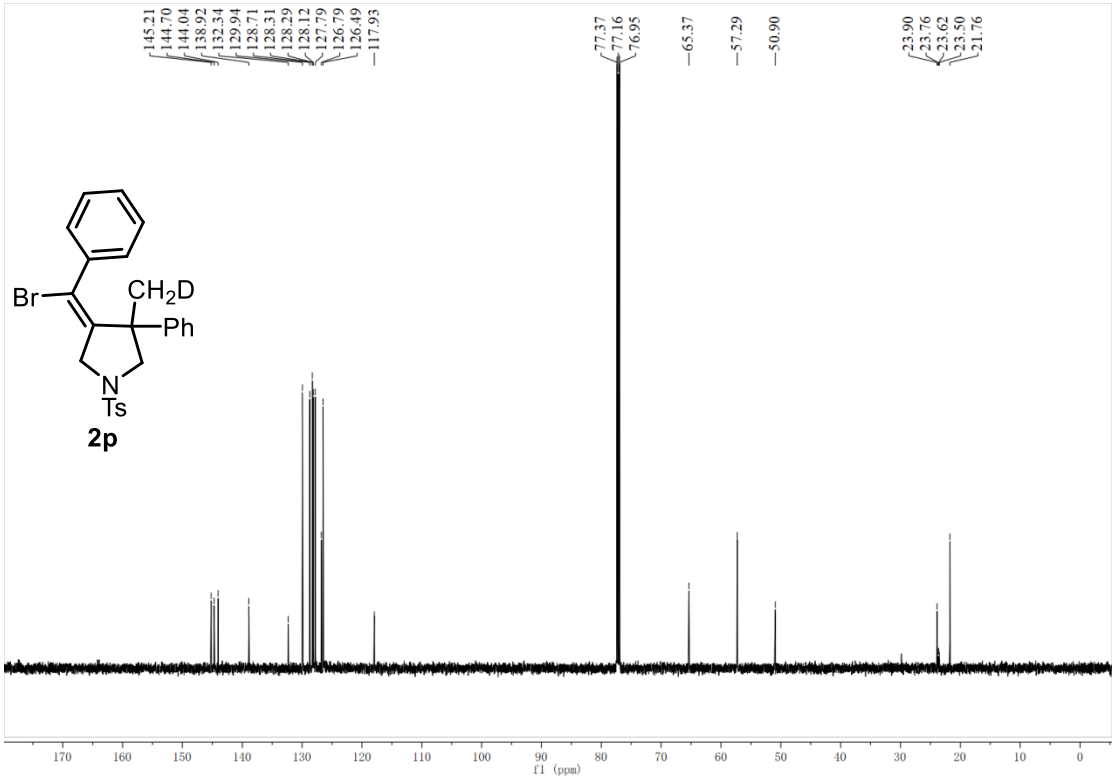
^{13}C NMR of **2o** (151 MHz, $CDCl_3$)



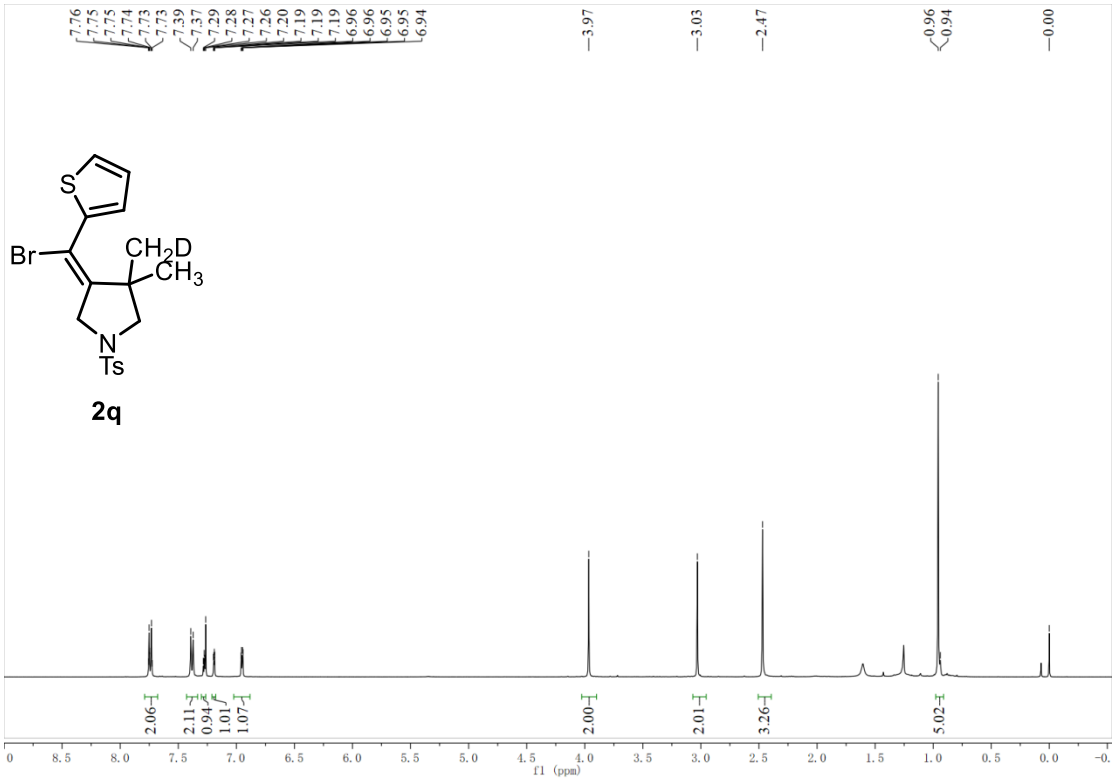
^{1}H NMR of **2p** (600 MHz, $CDCl_3$)



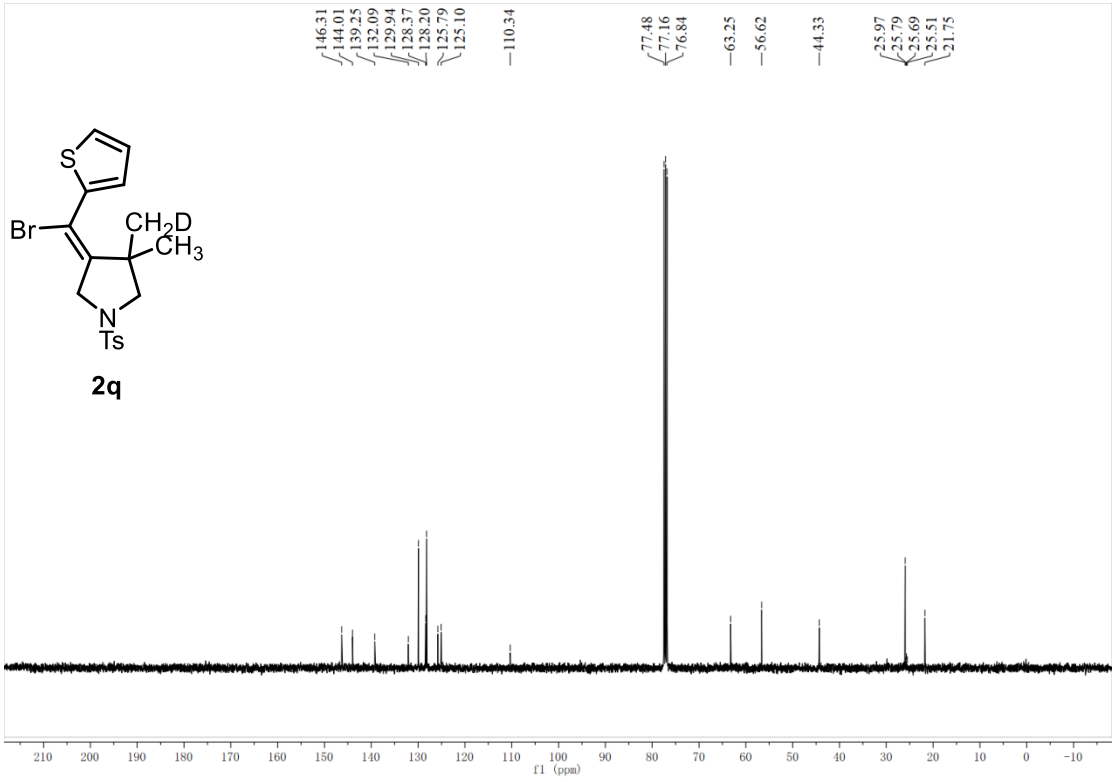
^{13}C NMR of **2p** (151 MHz, $CDCl_3$)



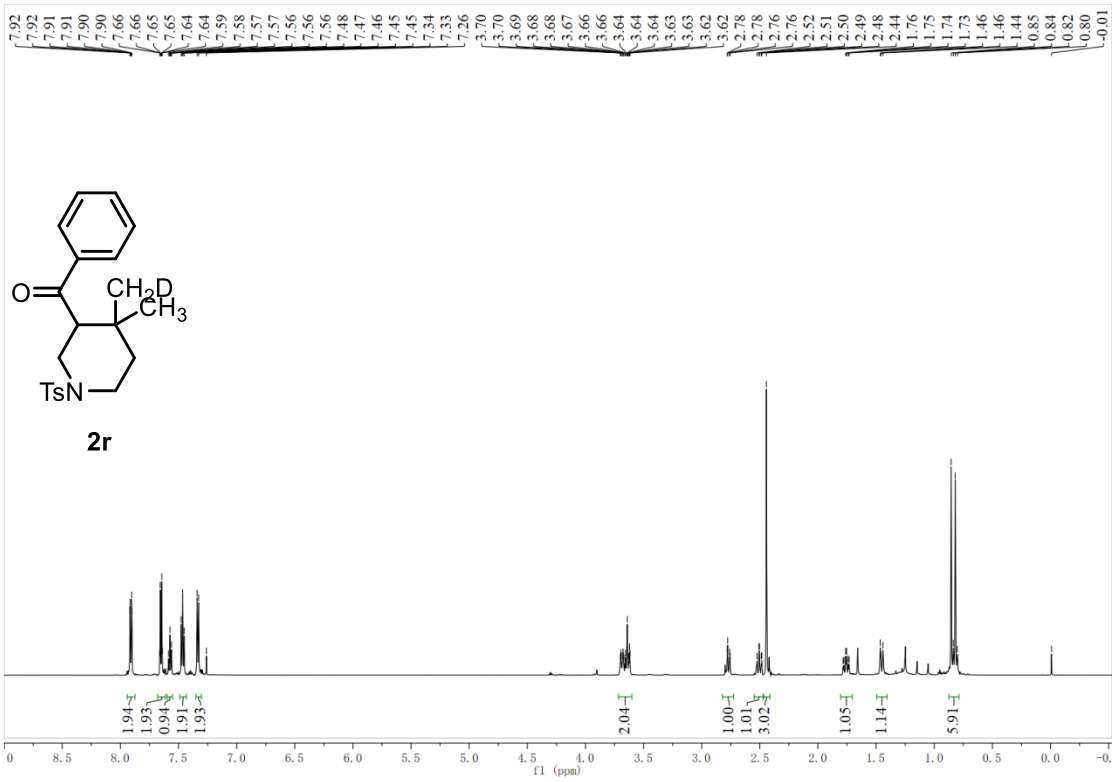
^{1}H NMR of **2q** (600 MHz, $CDCl_3$)



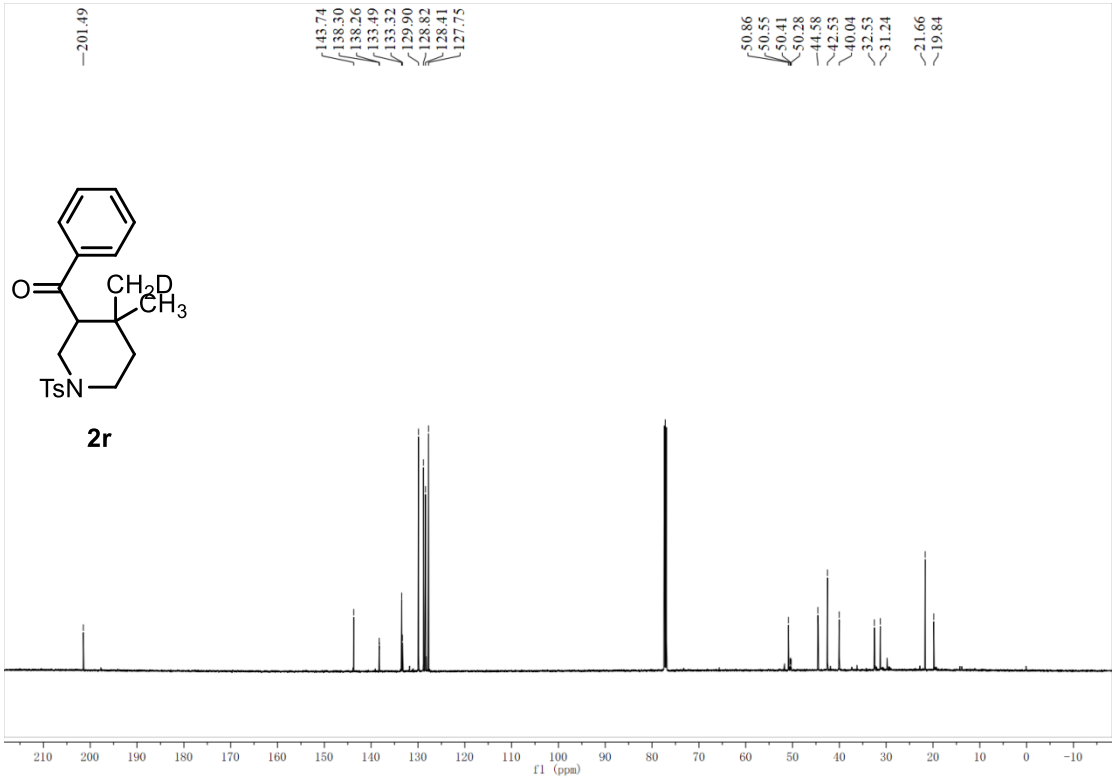
^{13}C NMR of **2q** (151 MHz, $CDCl_3$)



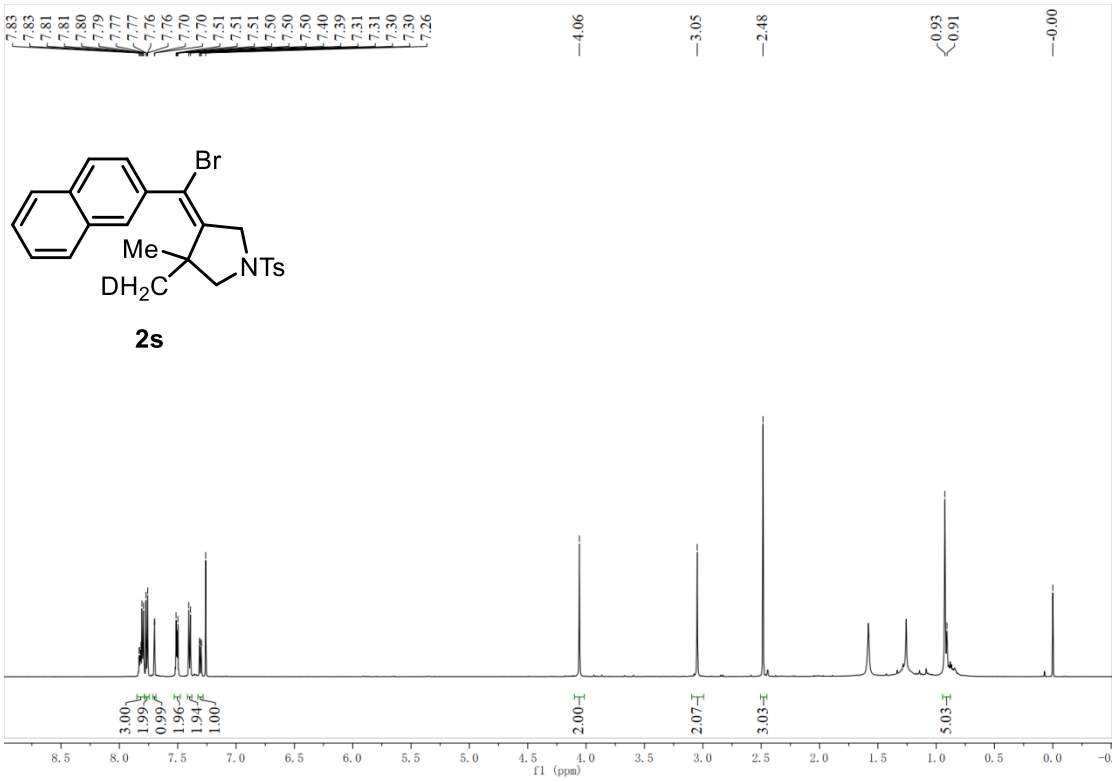
^{1}H NMR of **2r** (600 MHz, $CDCl_3$)



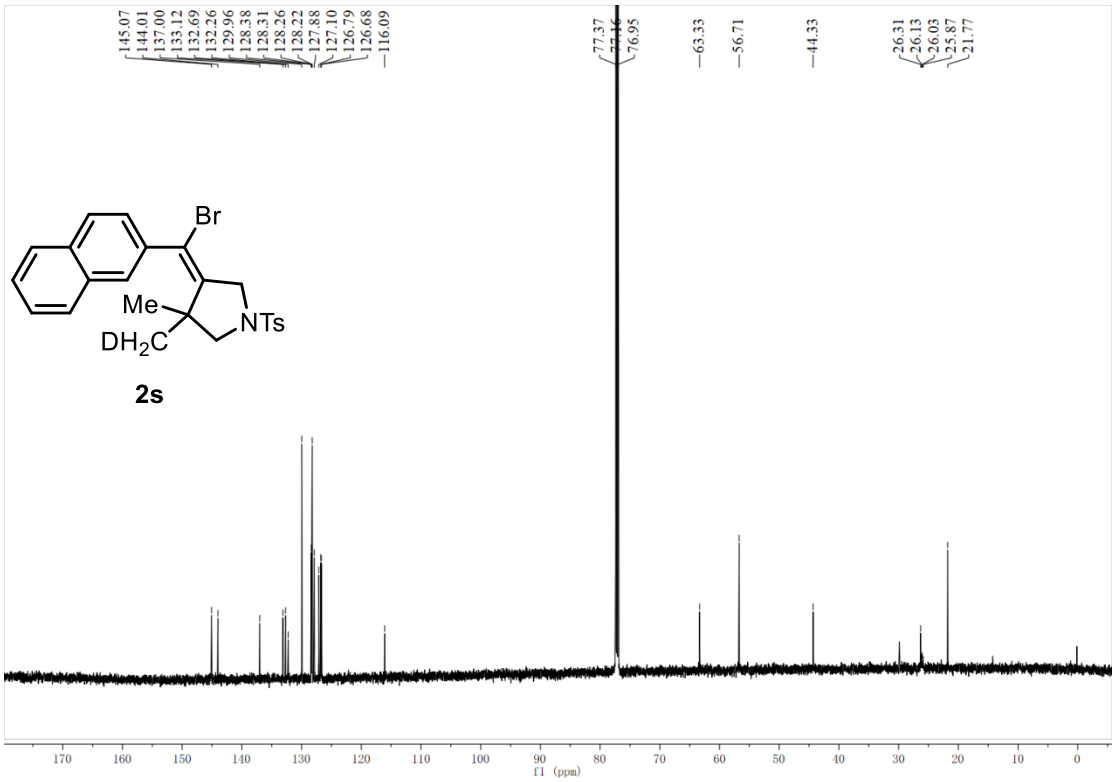
^{13}C NMR of **2r** (151 MHz, $CDCl_3$)



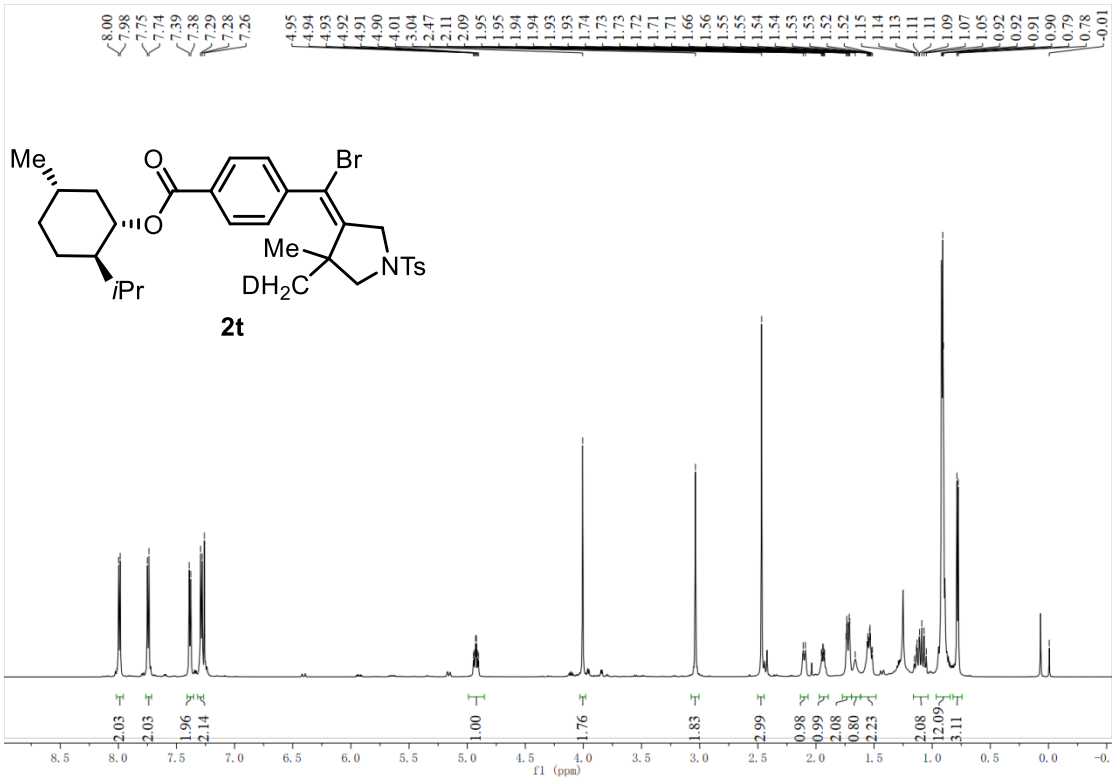
^{1}H NMR of **2s** (600 MHz, $CDCl_3$)



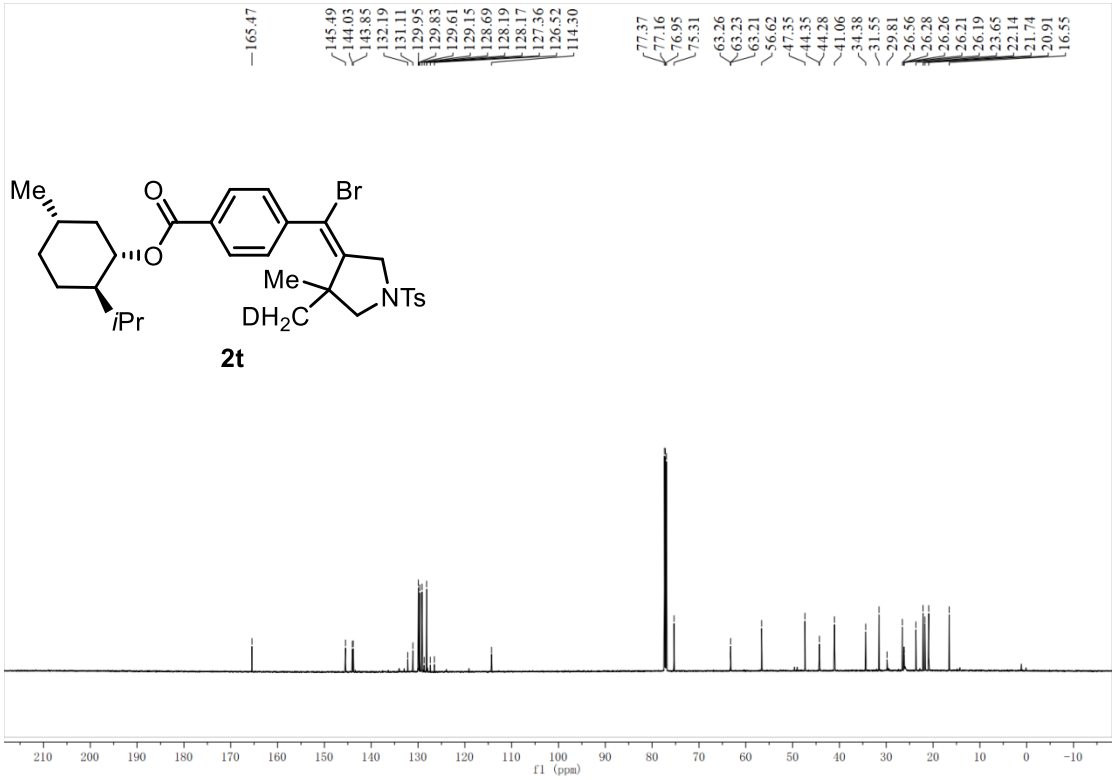
^{13}C NMR of **2s** (151 MHz, $CDCl_3$)



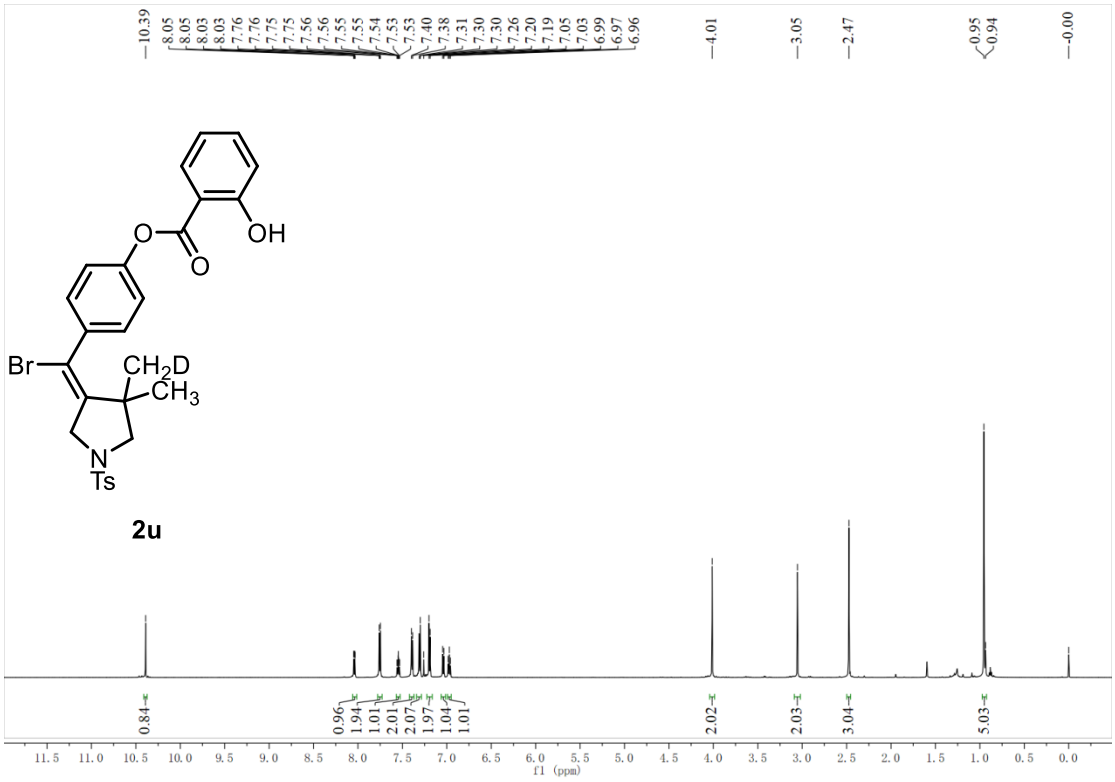
^{1}H NMR of **2t** (600 MHz, $CDCl_3$)



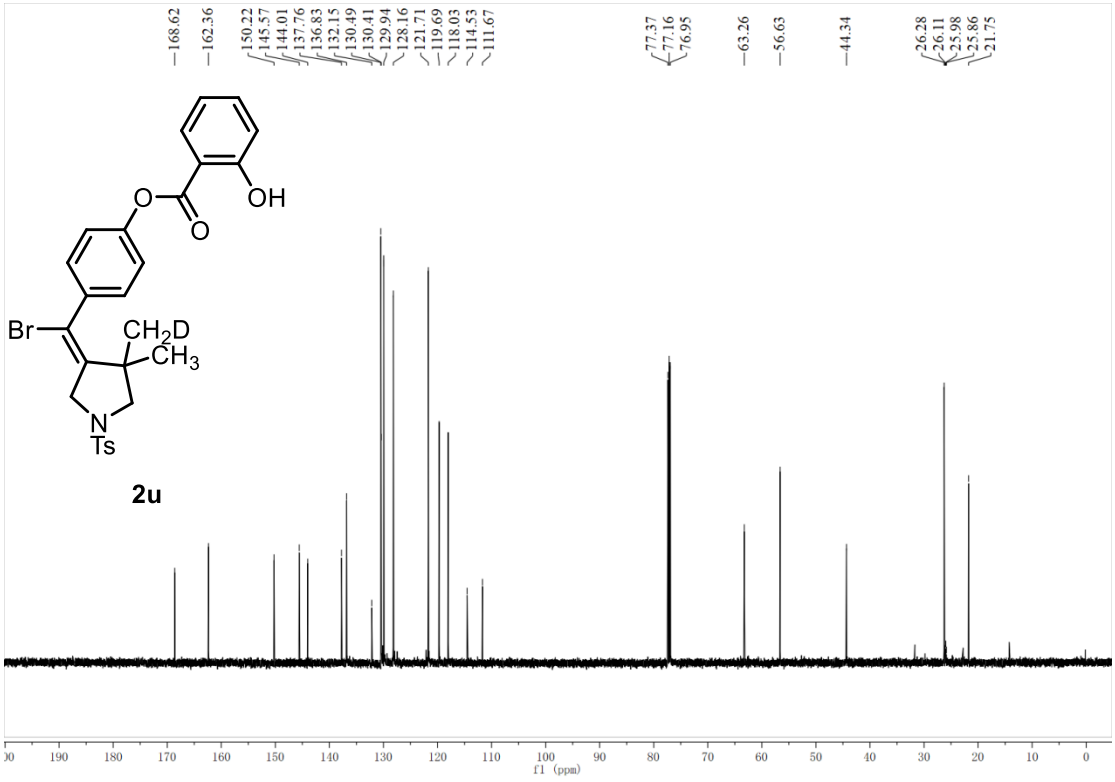
^{13}C NMR of **2t** (151 MHz, $CDCl_3$)



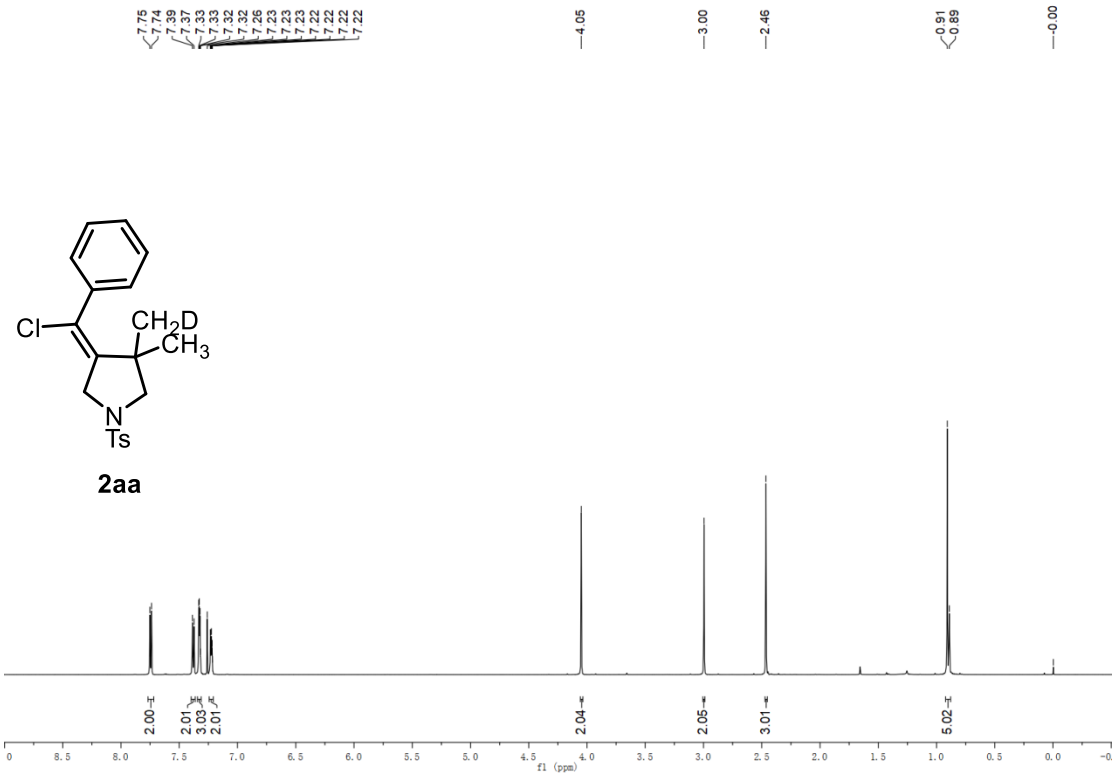
^{1}H NMR of **2u** (400 MHz, $CDCl_3$)



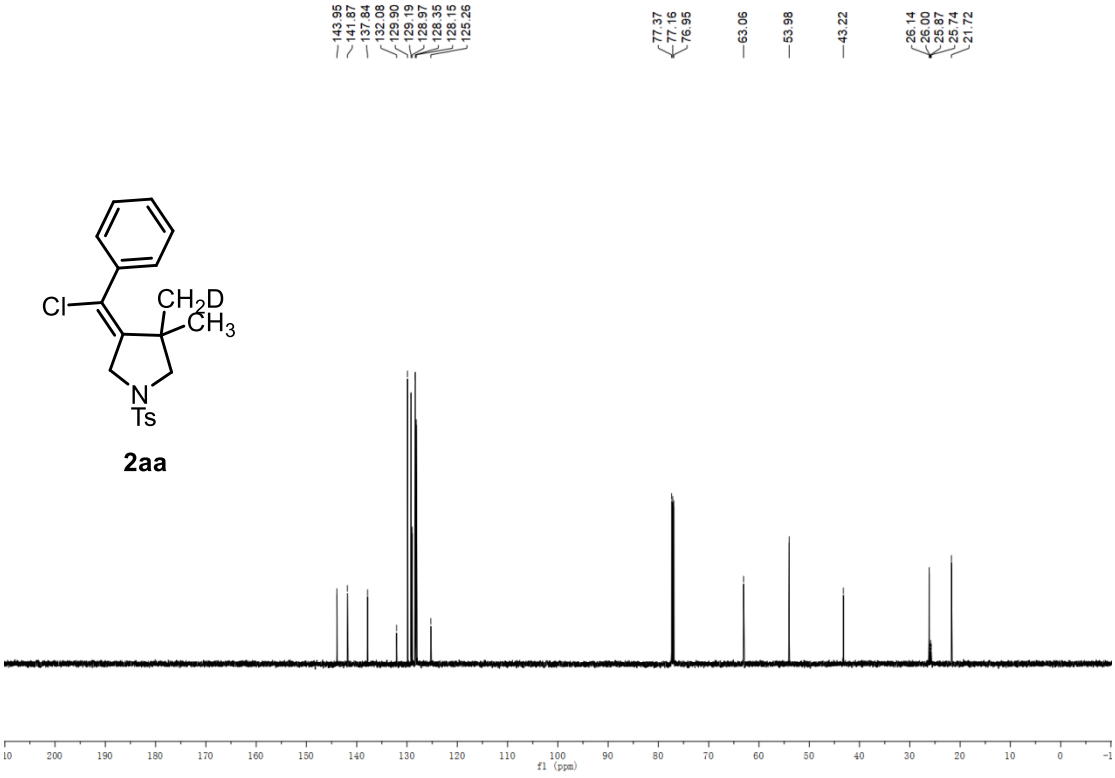
^{13}C NMR of **2u** (101 MHz, $CDCl_3$)



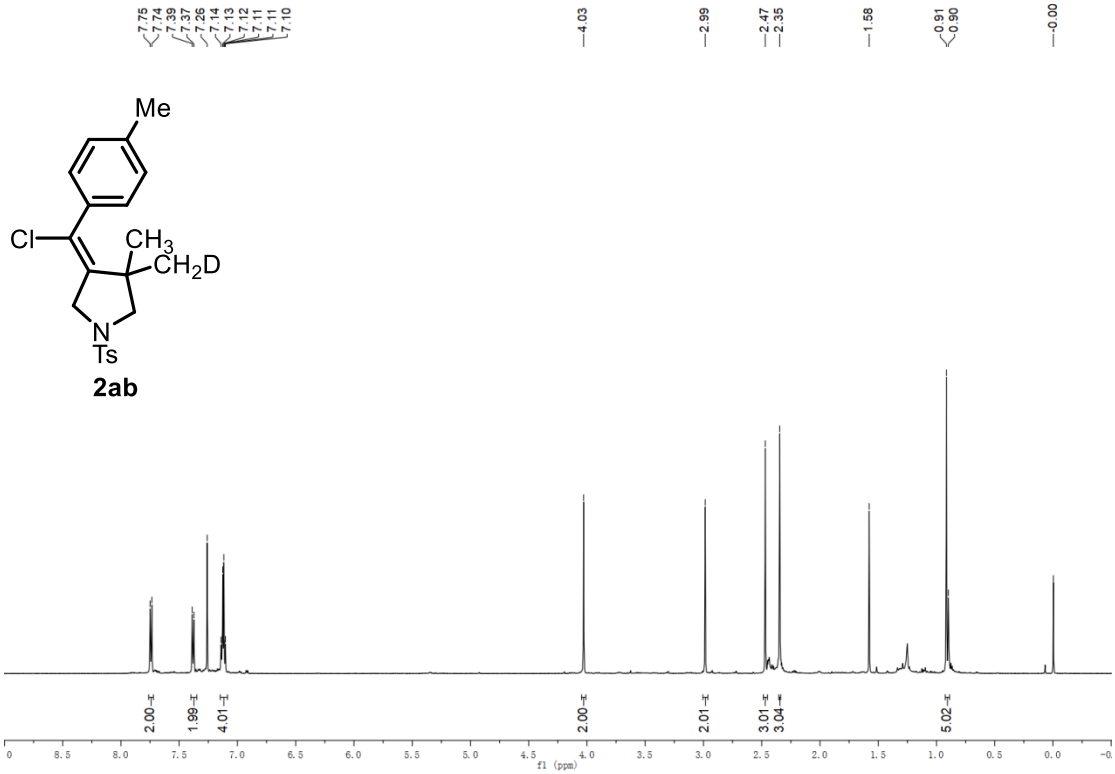
^{1}H NMR of **2aa** (600 MHz, $CDCl_3$)



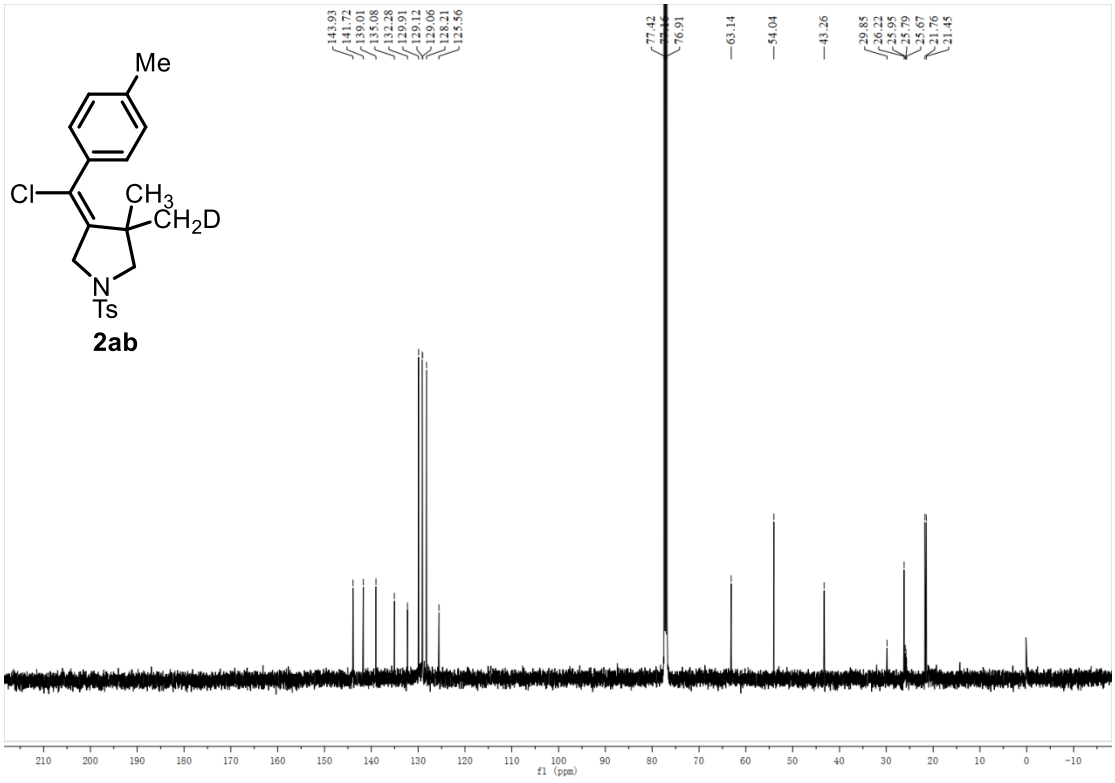
^{13}C NMR of **2aa** (151 MHz, $CDCl_3$)



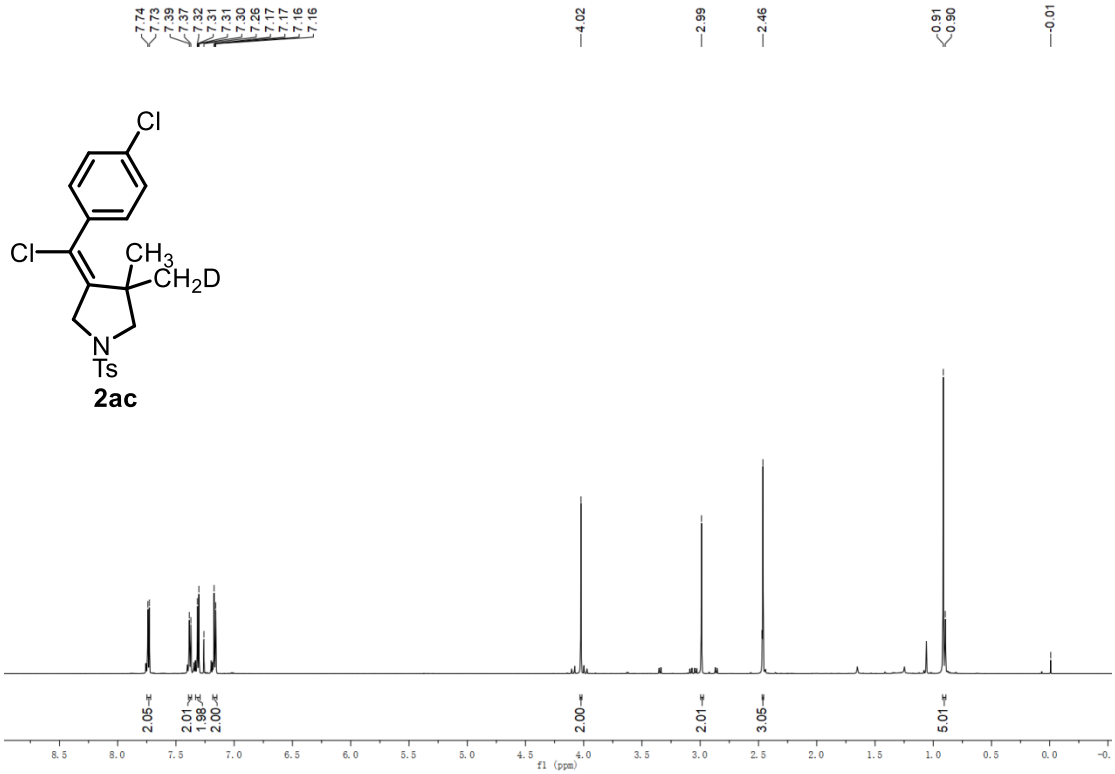
^{1}H NMR of **2ab** (600 MHz, $CDCl_3$)



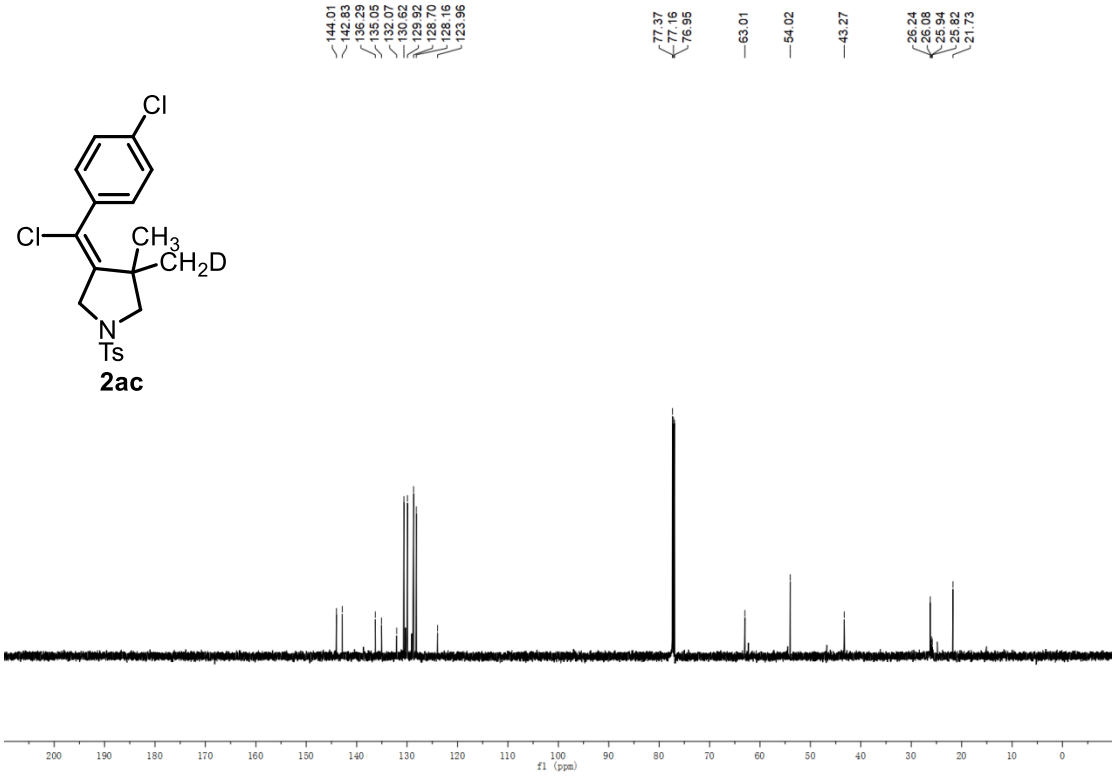
^{13}C NMR of **2ab** (126 MHz, $CDCl_3$)



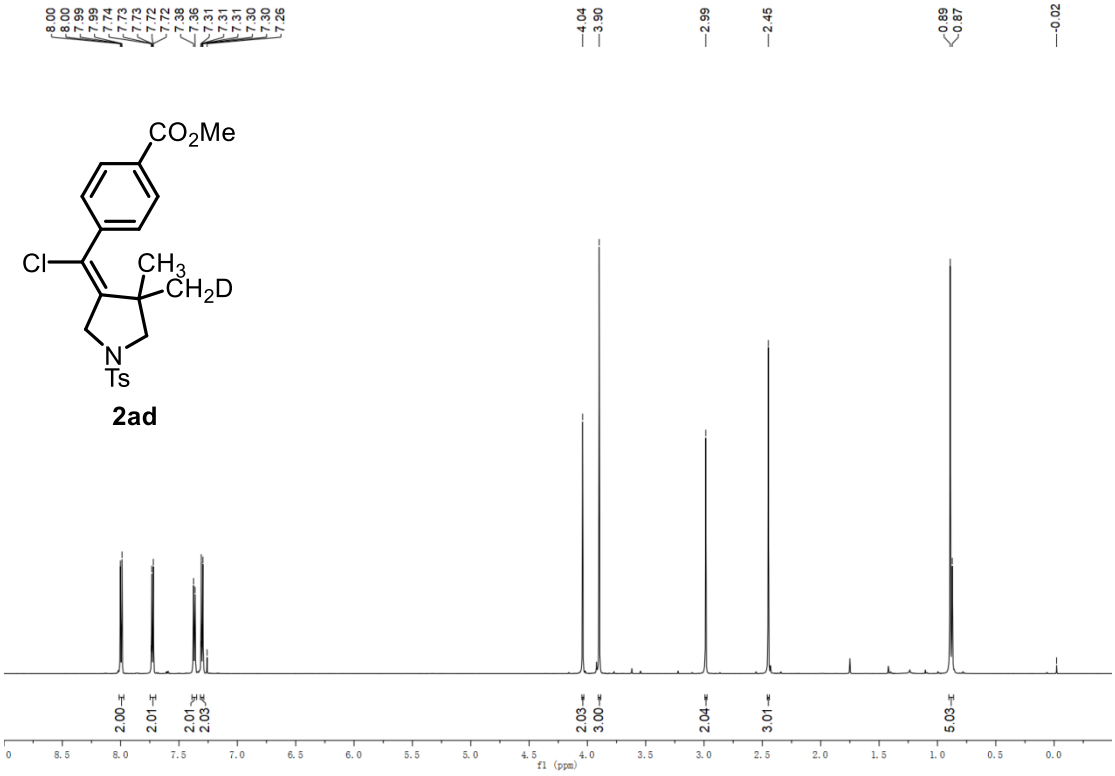
^{1}H NMR of **2ac** (600 MHz, $CDCl_3$)



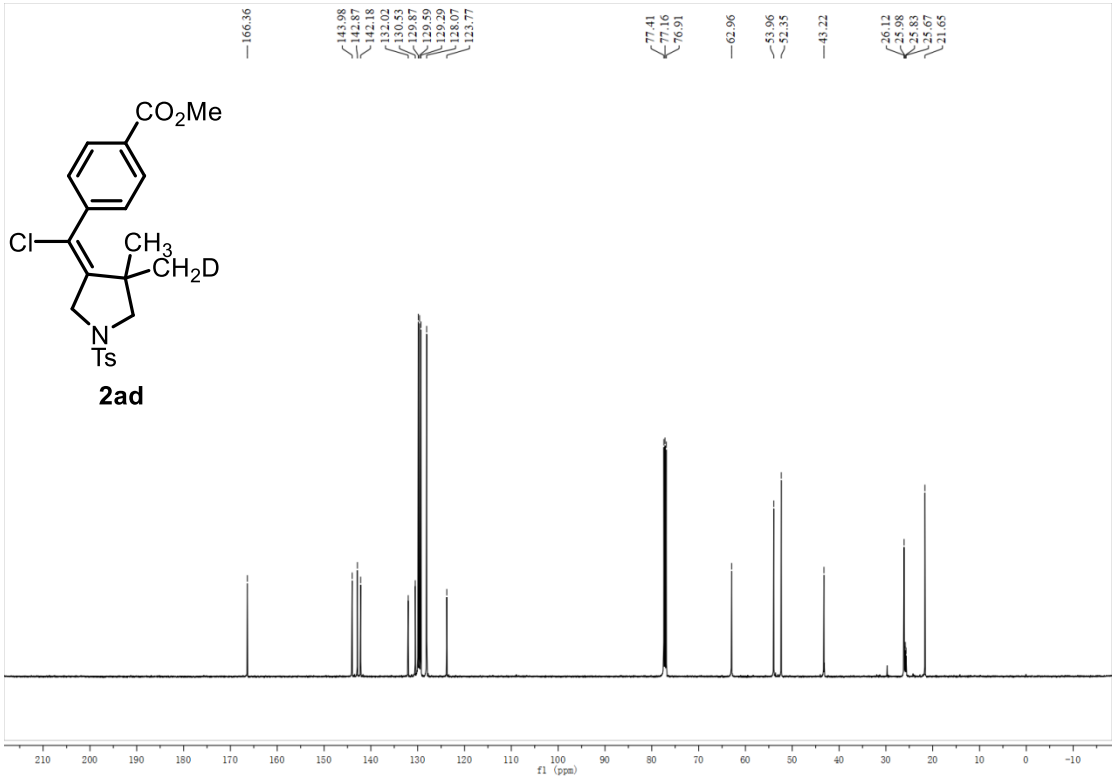
^{13}C NMR of **2ac** (151 MHz, $CDCl_3$)



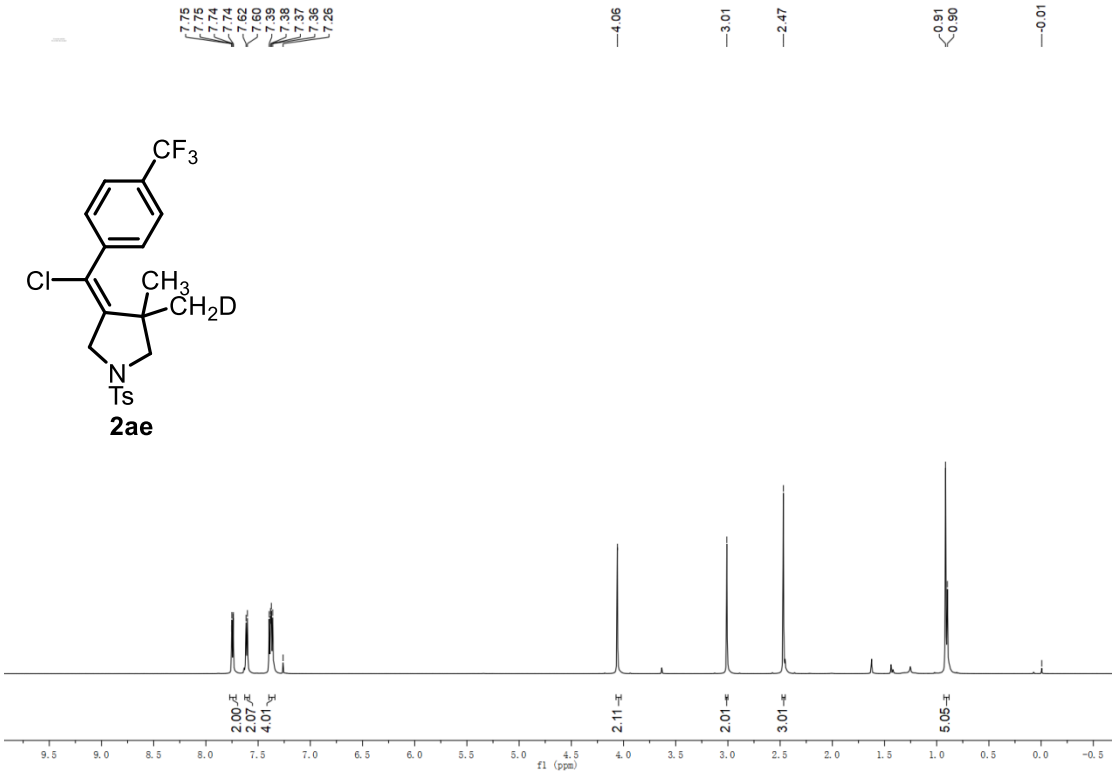
^{1}H NMR of **2ad** (600 MHz, $CDCl_3$)



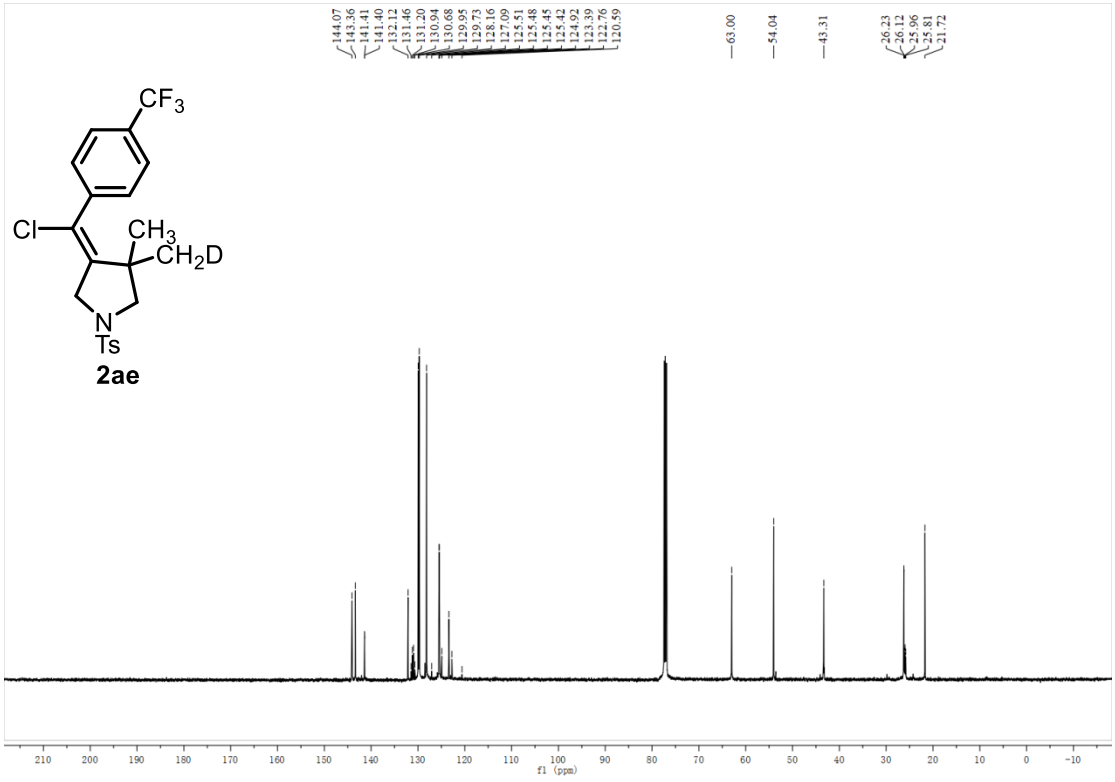
^{13}C NMR of **2ad** (126 MHz, $CDCl_3$)



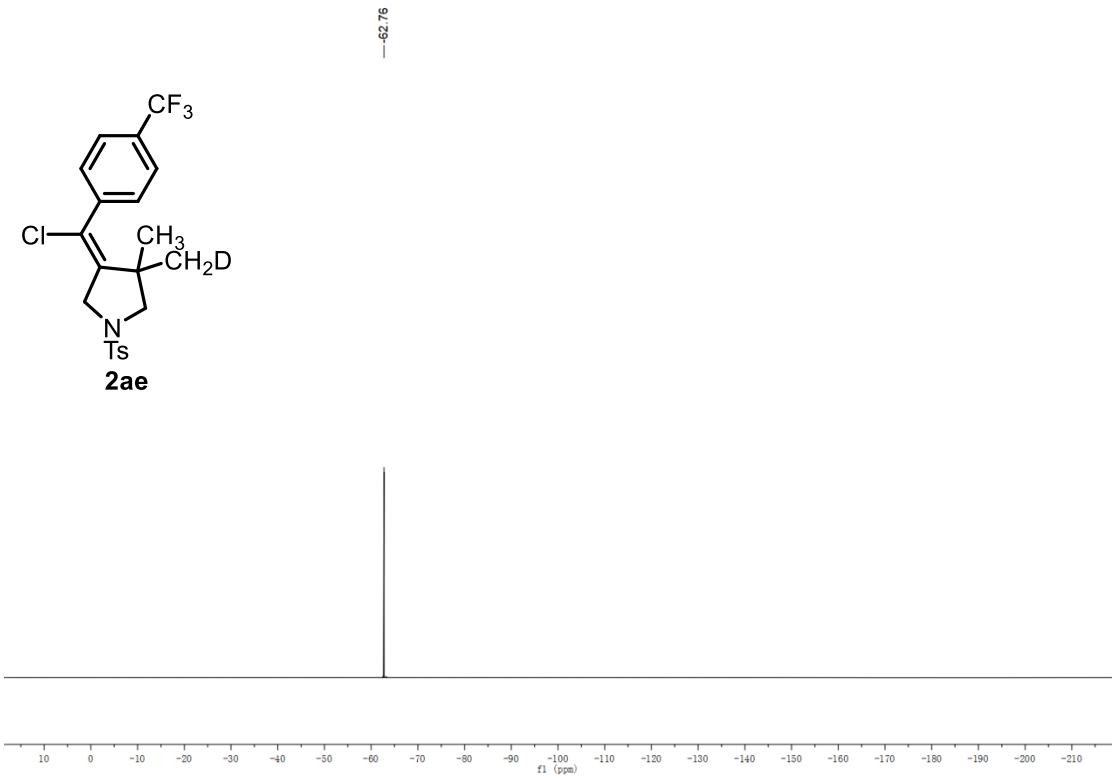
^{1}H NMR of **2ae** (600 MHz, $CDCl_3$)



^{13}C NMR of **2ae** (126 MHz, $CDCl_3$)

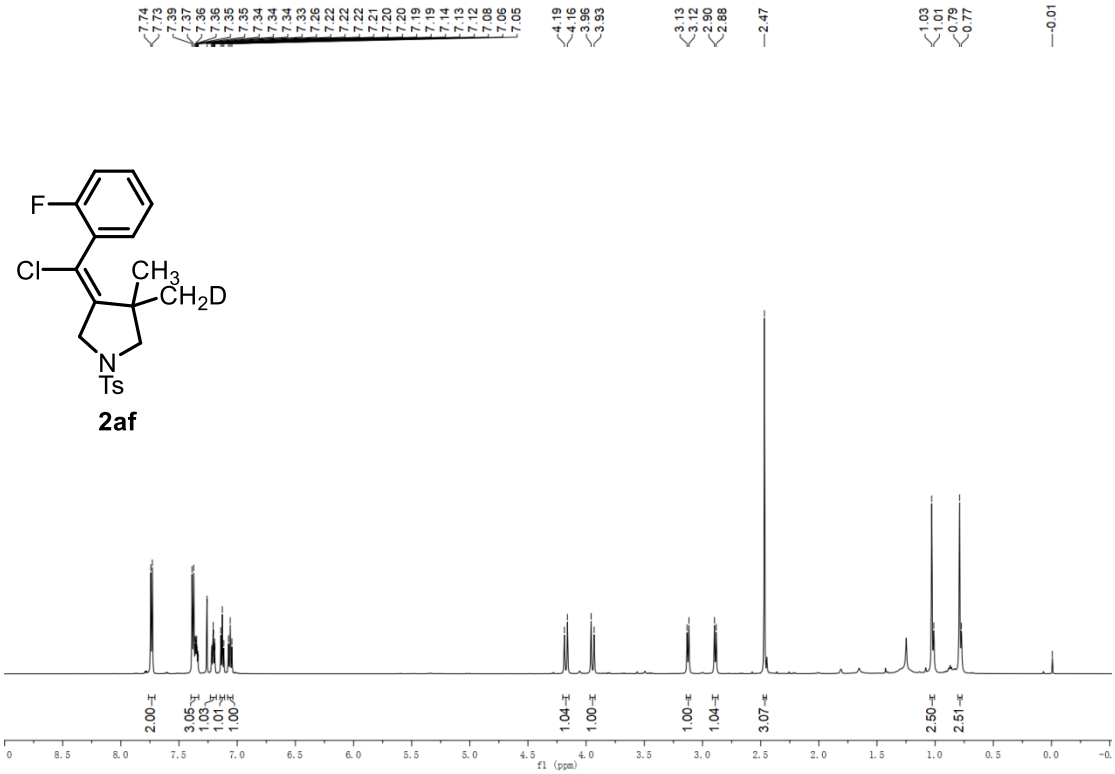


^{19}F NMR of **2ae** (377 MHz, $CDCl_3$)

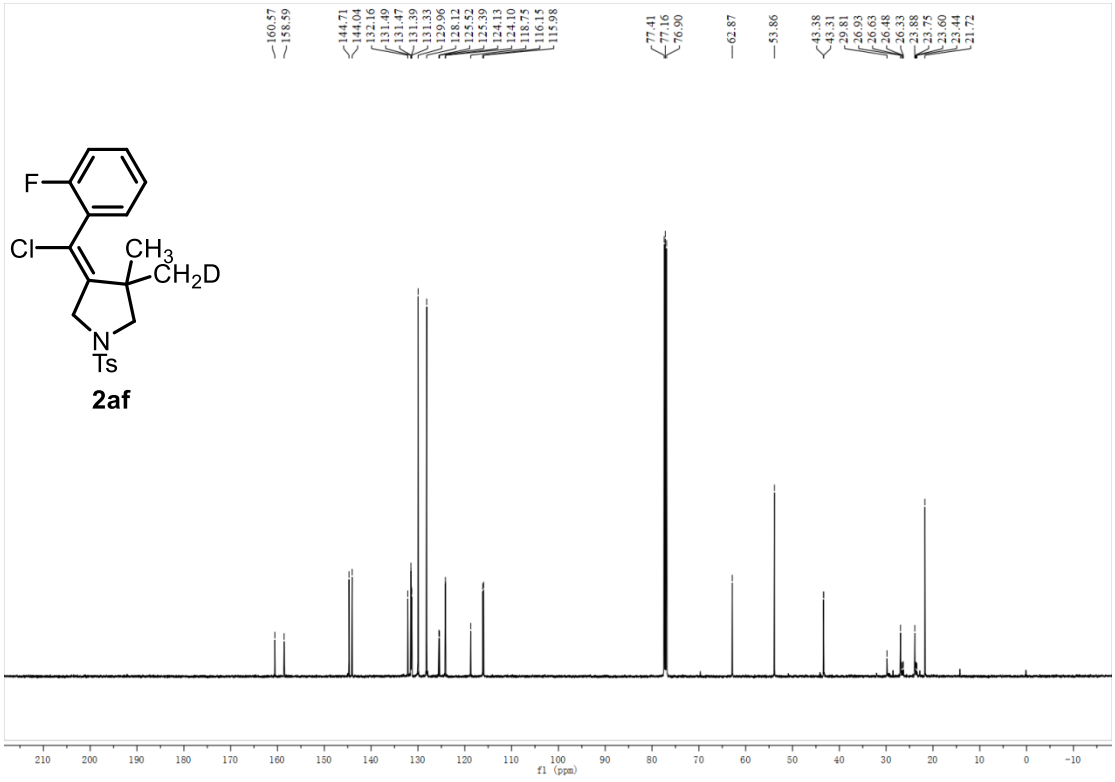


2ae

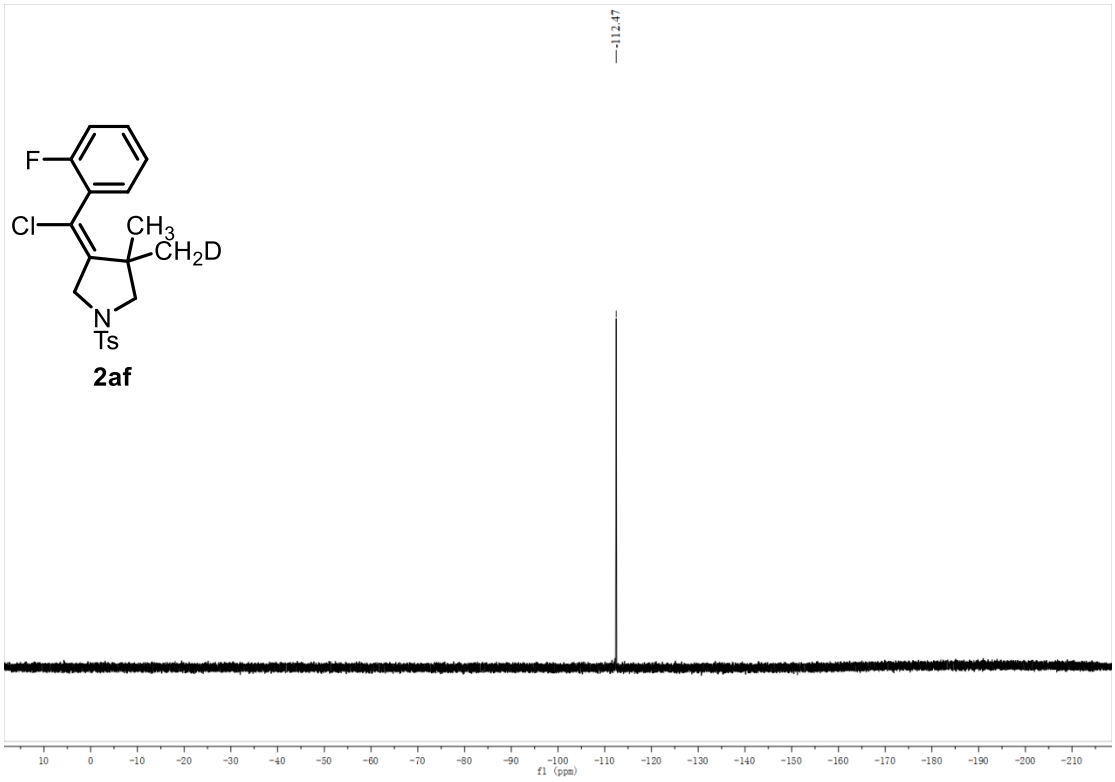
^{1}H NMR of **2af** (600 MHz, $CDCl_3$)



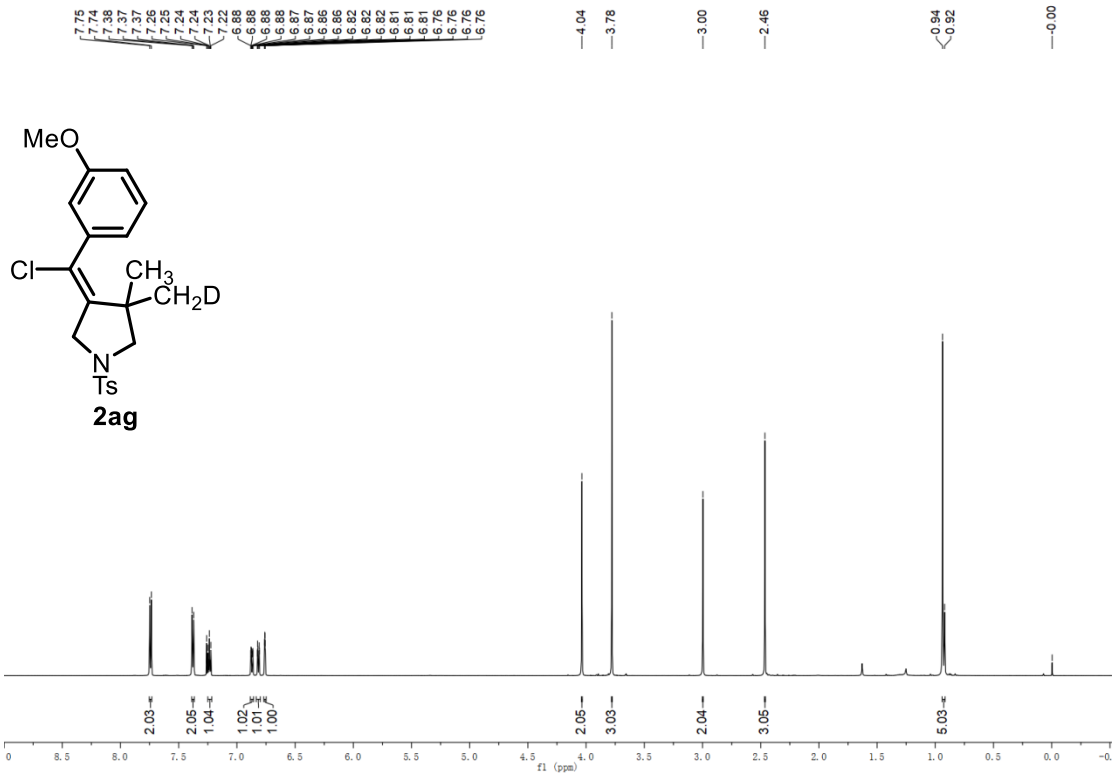
^{13}C NMR of **2af** (126 MHz, $CDCl_3$)



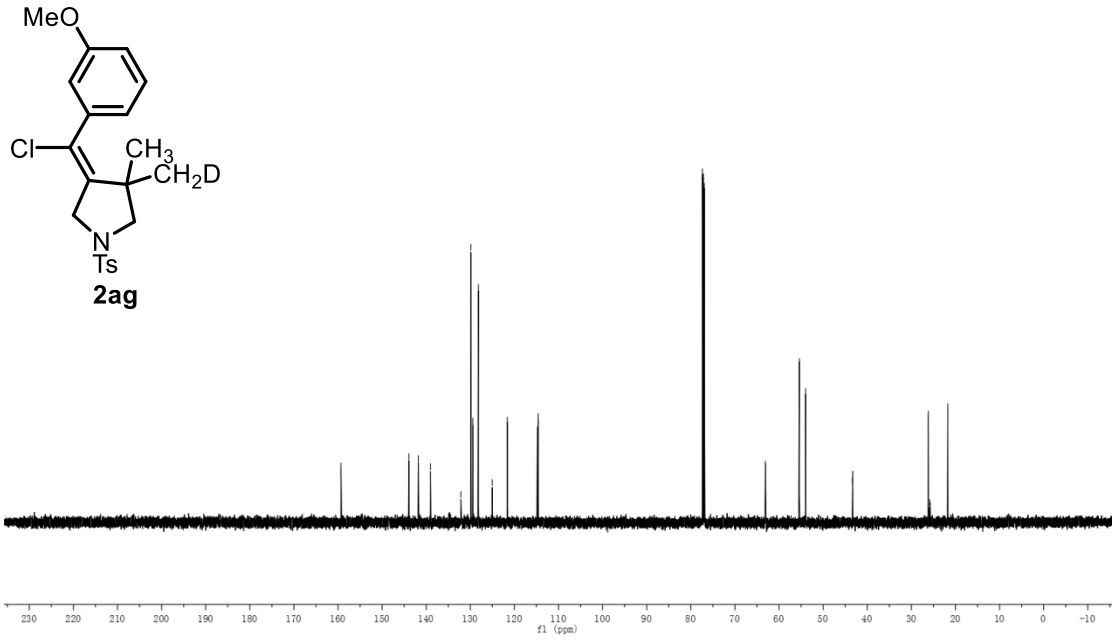
^{19}F NMR of **2af** (377 MHz, $CDCl_3$)



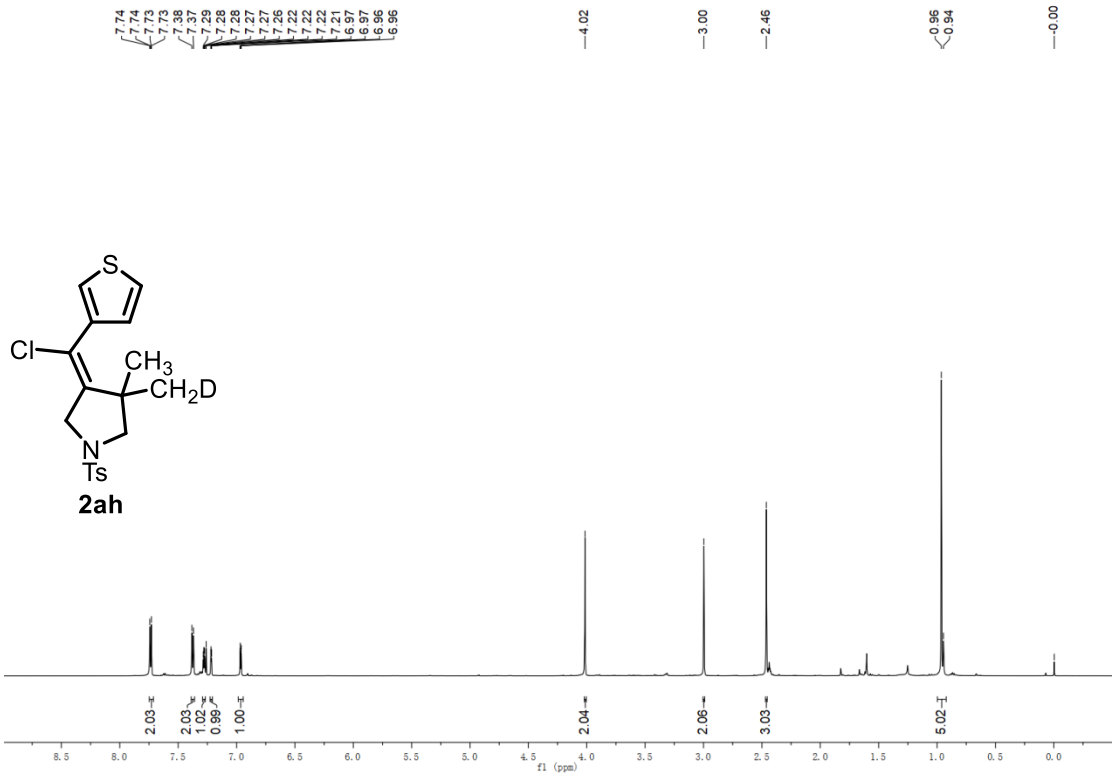
^{1}H NMR of **2ag** (600 MHz, $CDCl_3$)



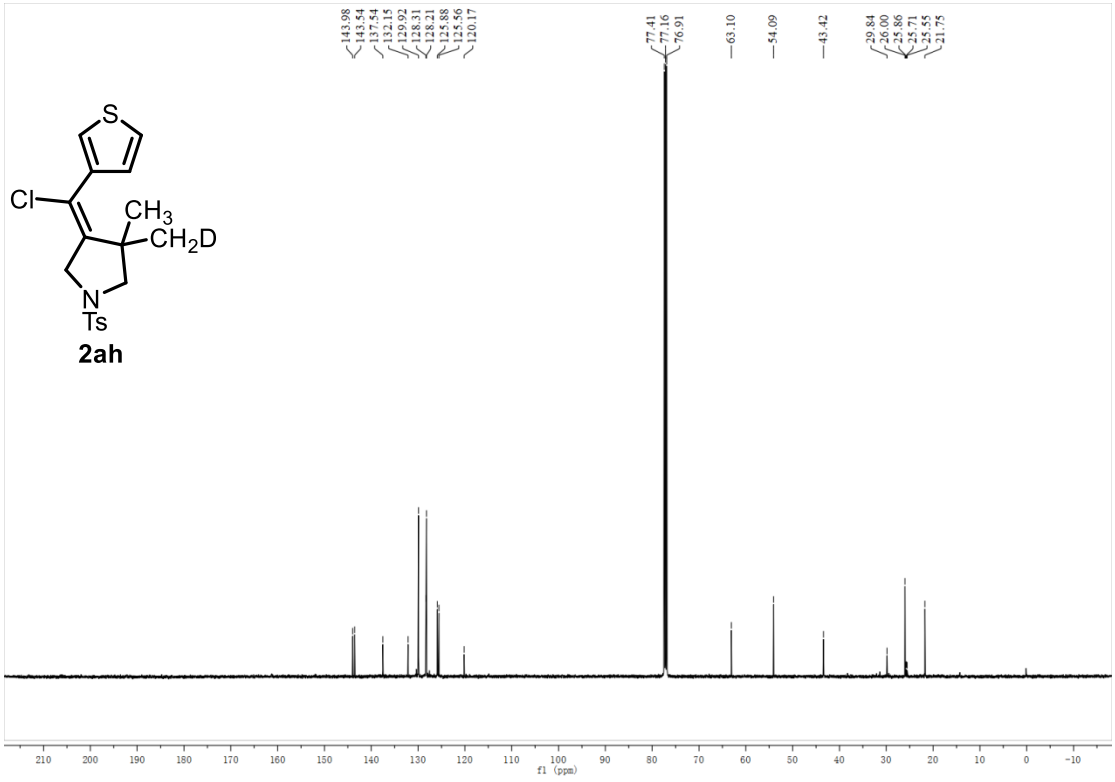
^{13}C NMR of **2ag** (151 MHz, $CDCl_3$)



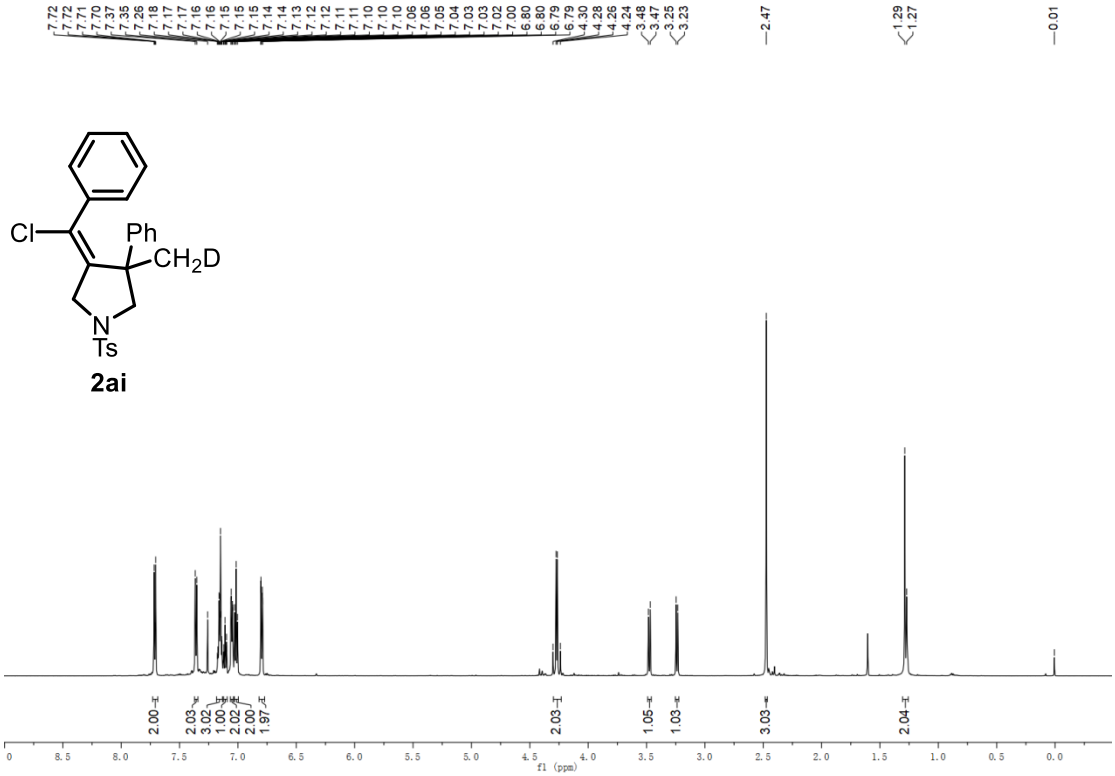
^{1}H NMR of **2ah** (600 MHz, $CDCl_3$)



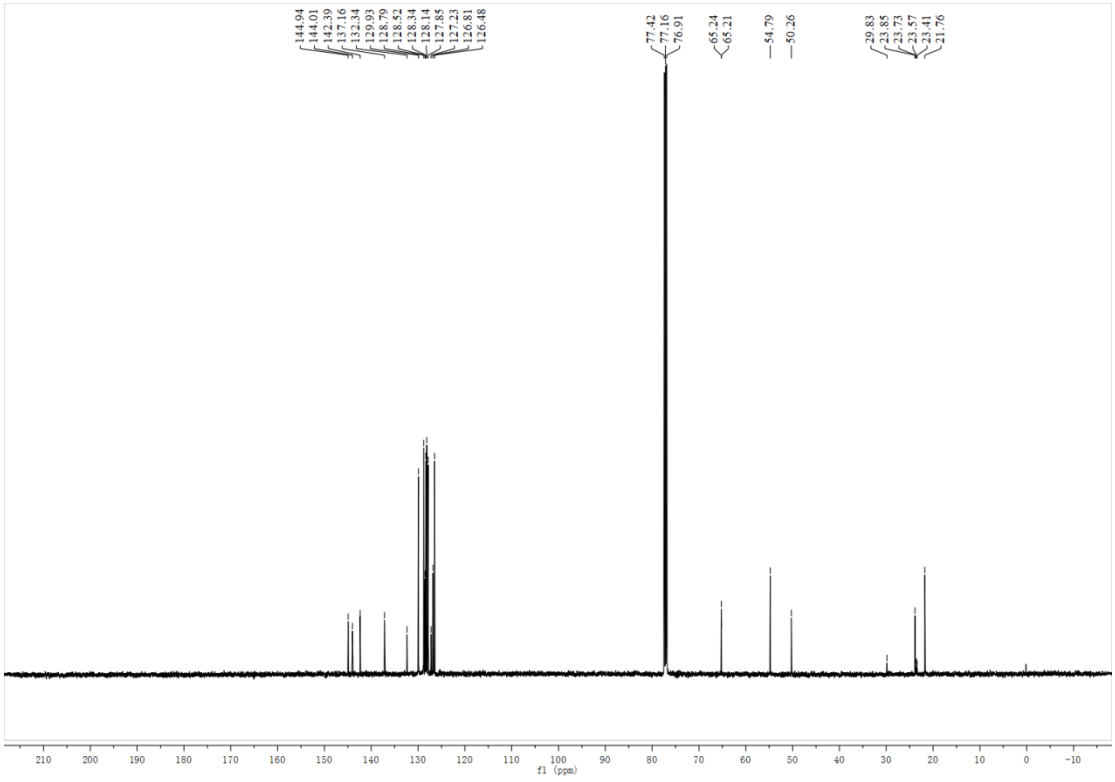
^{13}C NMR of **2ah** (126 MHz, $CDCl_3$)



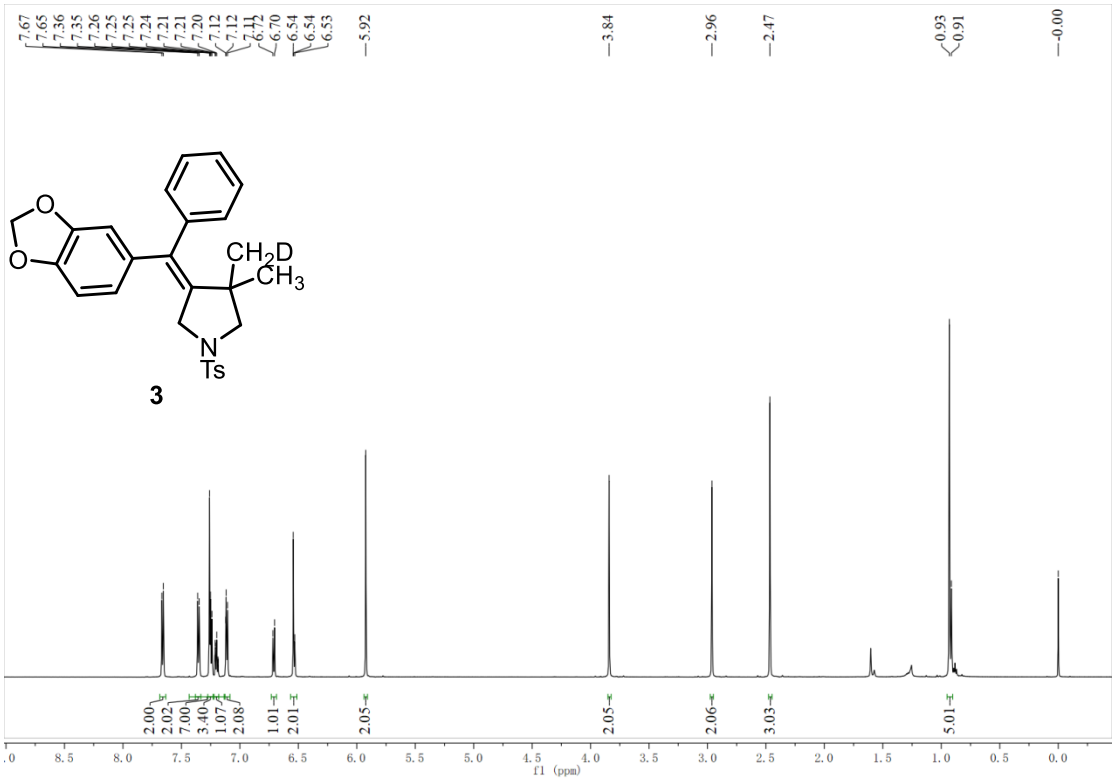
^{1}H NMR of **2ai** (600 MHz, $CDCl_3$)



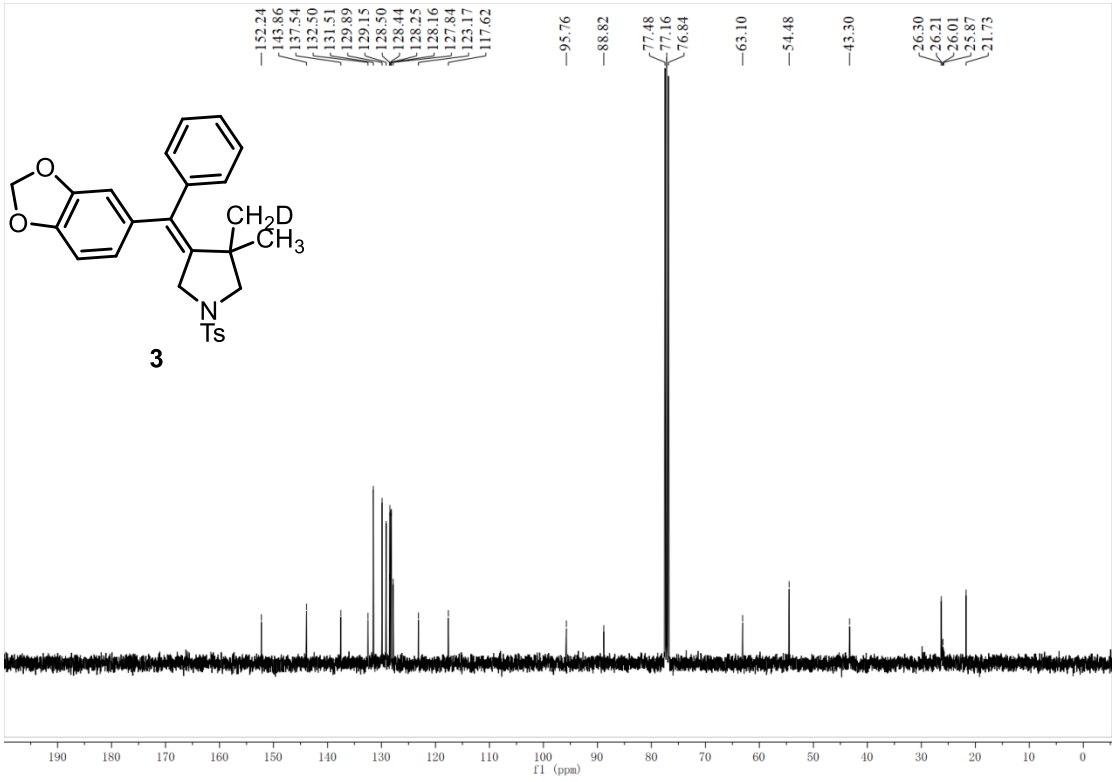
^{13}C NMR of **2ai** (126 MHz, $CDCl_3$)



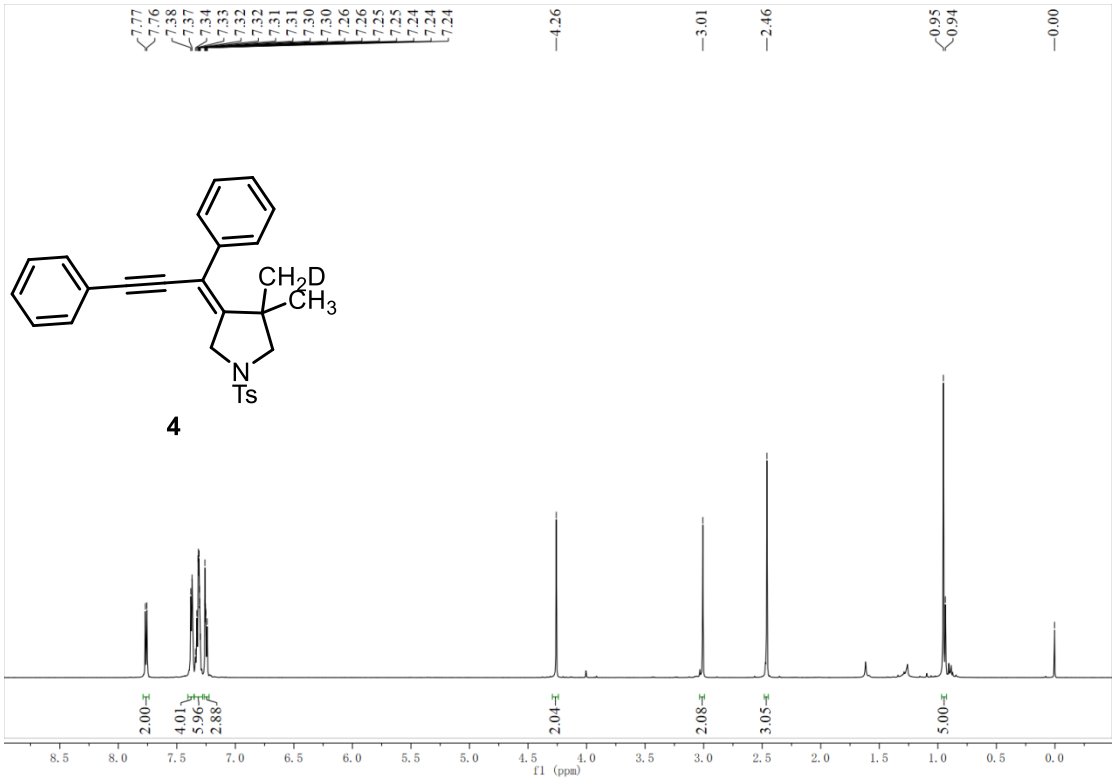
^{1}H NMR of **3** (600 MHz, $CDCl_3$)



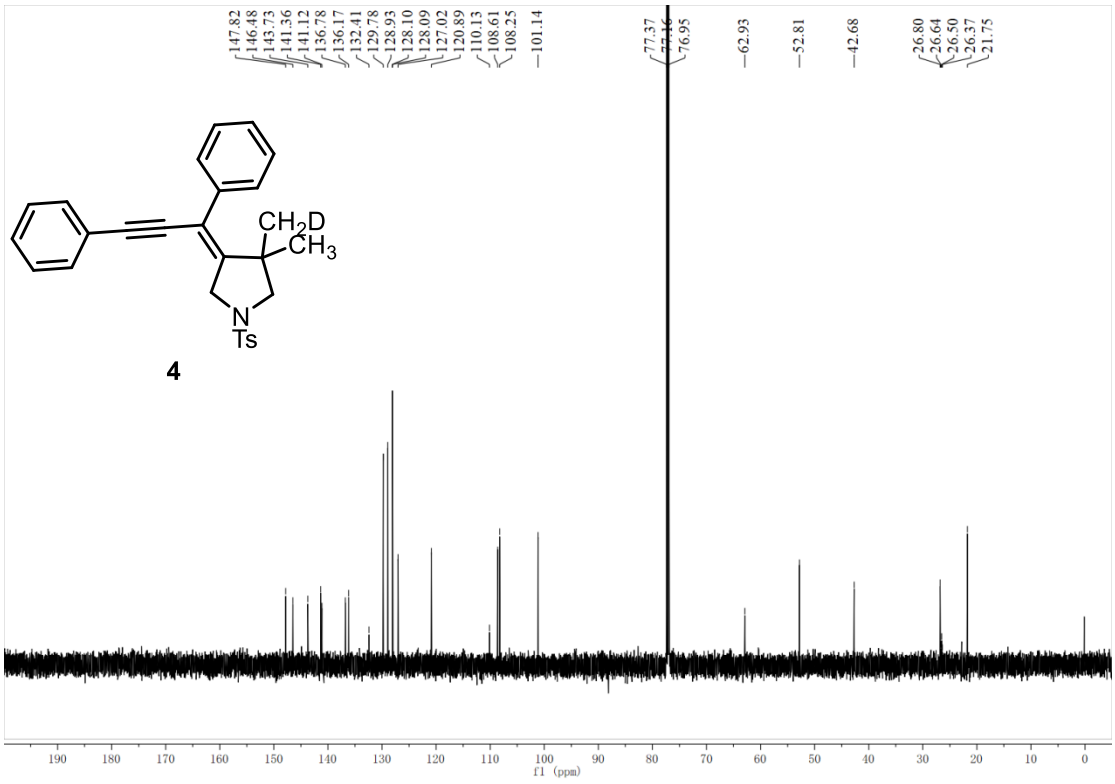
^{13}C NMR of **3** (151 MHz, $CDCl_3$)



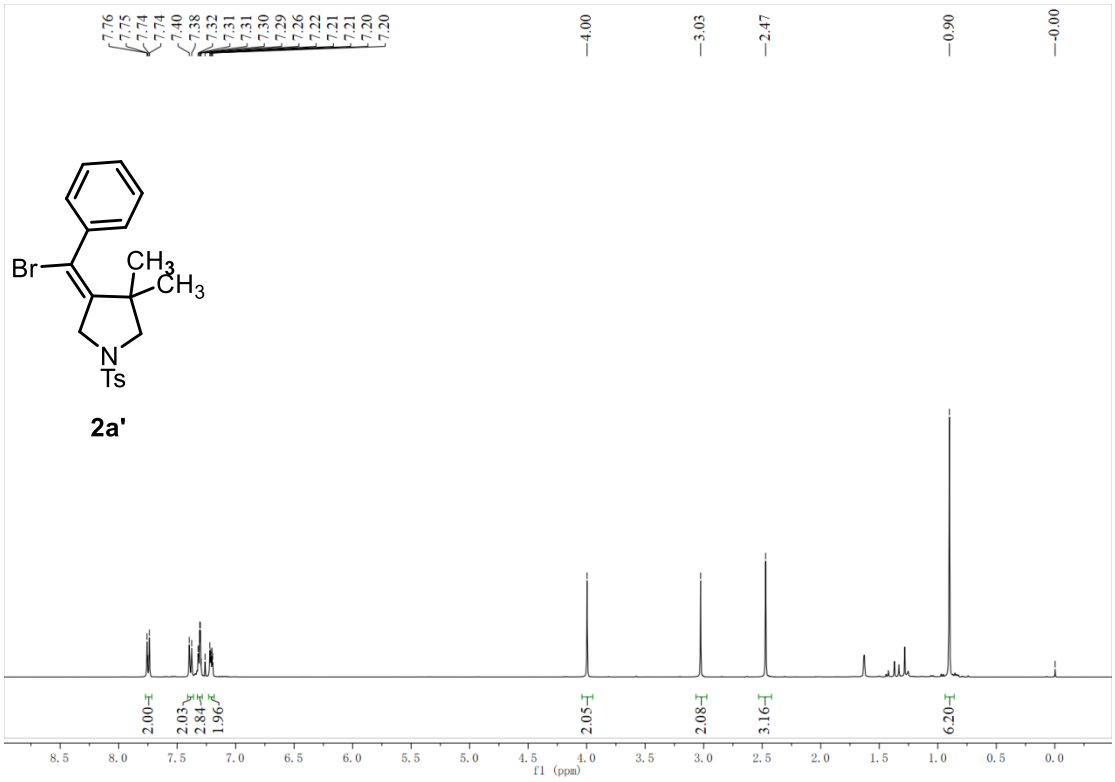
^{1}H NMR of **4** (600 MHz, $CDCl_3$)



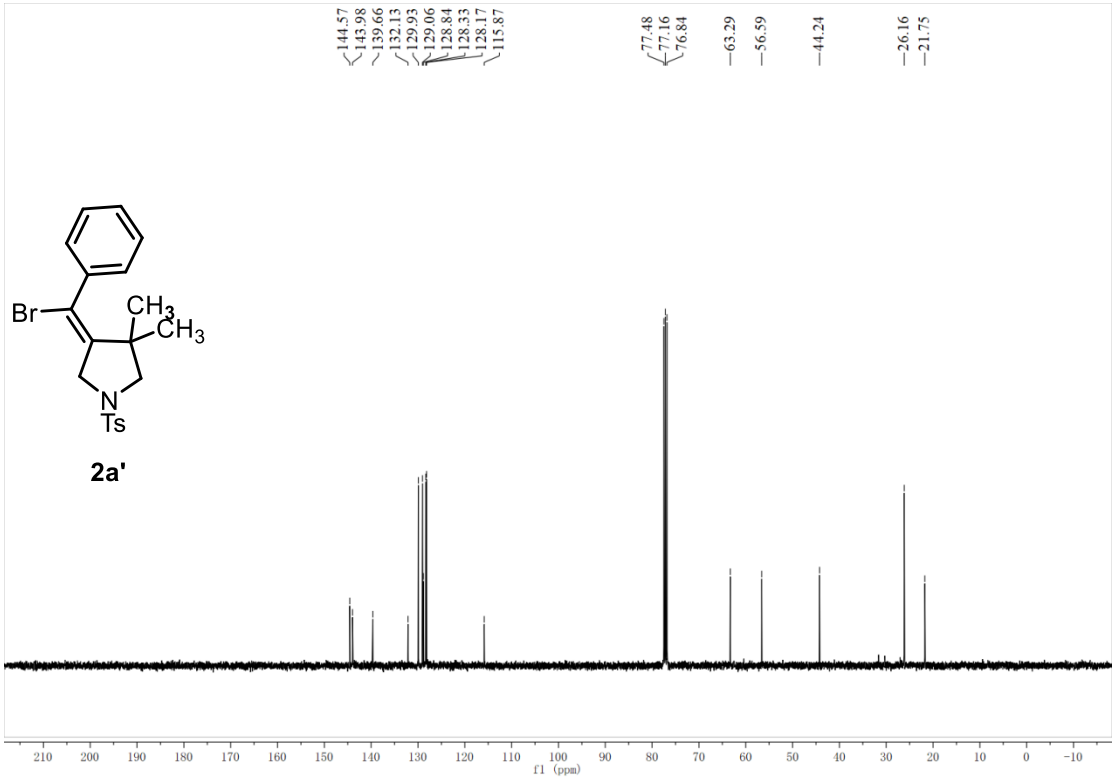
^{13}C NMR of **4** (151 MHz, $CDCl_3$)



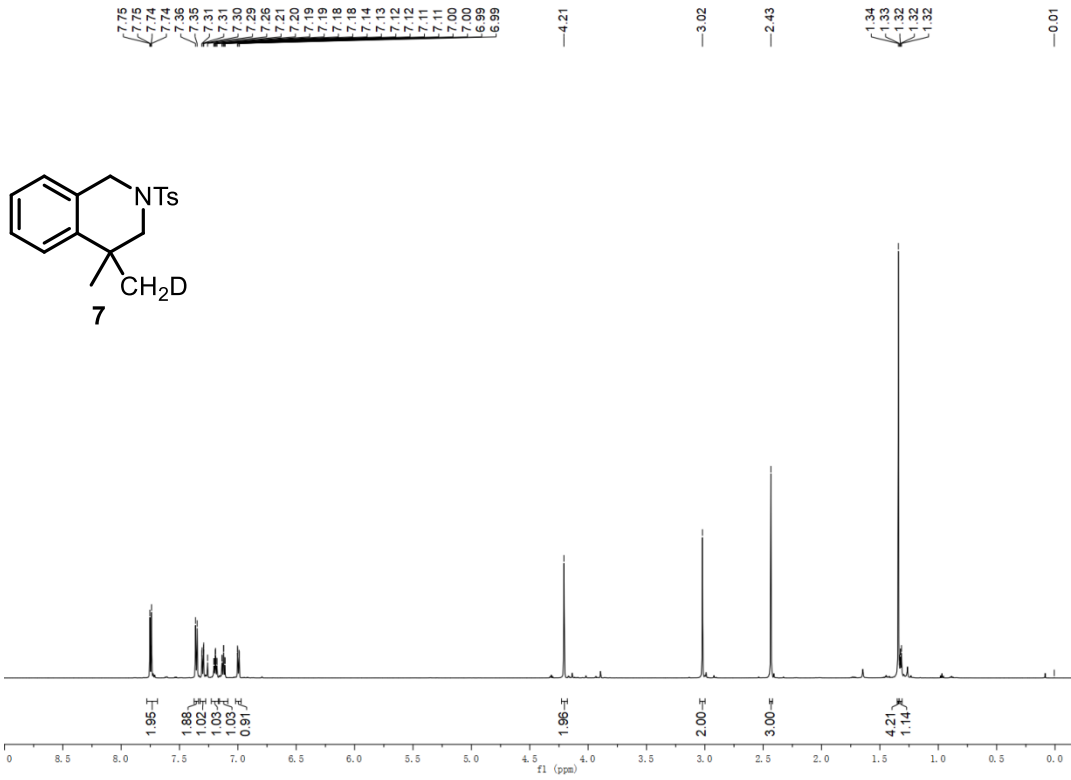
^{1}H NMR of **2a'** (400 MHz, $CDCl_3$)



^{13}C NMR of **2a'** (101 MHz, $CDCl_3$)



^{1}H NMR of **7** (600 MHz, $CDCl_3$)



^{13}C NMR of **7** (101 MHz, $CDCl_3$)