Supporting Information

Aza-Prins Type Cyclisation of Vinyl *Bis*-Sulfide-Tethered Amines for the Collective Synthesis of Piperidine, Indolizidine and Isoindolone Natural Products

Santosh J. Gharpure, * Rakhi Yadav, Krishna S. Gupta, Girish P. Kadam

Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India.

Fax: +91-22-2576 7152; Tel: +91-22-2576 7171; E-mail: sjgharpure@iitb.ac.in

Table of Contents

• Optimisation table …….... S2

• General……S3

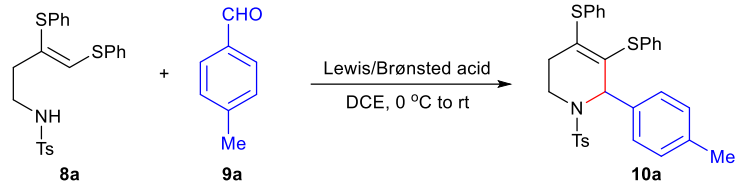
• Experimental and Characterization of compounds……... S4-S32

• References……S32

• Spectra and X-Ray crystallographic analysis……S32-S79

Optimisation table for 2-monosubstituted piperidine cyclisation reaction

Table S1: Optimisation of the 2-monosubstituted piperidine cyclisation reaction [a]



entry	acid	equiv	yield (%)[b]
1	TMSOTf	1.0	58[c]
2	$MeSO_3H$	1.0	70
3	**$MeSO_3H$**	**2.0**	**80**
4	$MeSO_3H$	3.0	74
5	TfOH	1.0	46
6	AgOTf	0.1	-[d]
7	$Cu(OTf)_2$	0.1	-[d]
8	$BF_3{\cdot}OEt_2$	1.0	-[d]

[a]Reaction carried out using **8a** (0.25 mmol) and aldehyde **9a** (0.38 mmol) in 3 mL of dry solvent at rt. [b]Isolated yield. [c]51% yield of **10a** with TMSOTf in DCM. [d]Starting material recovered.

General experimental:

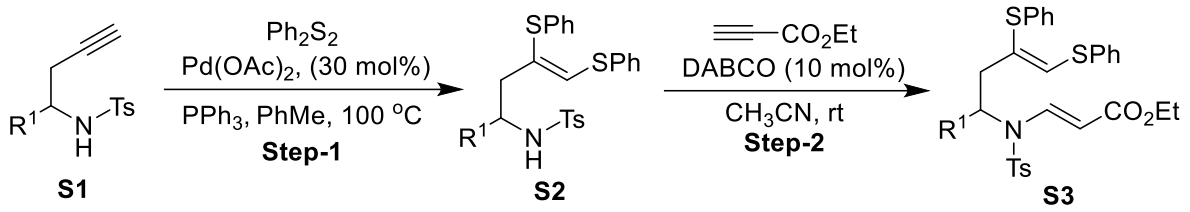
Melting points are recorded using dbk programmable melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on Nicolet 6700 spectrophotometer. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on Bruker Avance 400 spectrometer. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on Bruker Avance 500 spectrometer. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane or residual $CHCl_3$ (7.26 ppm for ^{1}H) or the central line (77.16 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment, and is given in parentheses.

High resolution mass measurements were carried out using Maxis impact (bruker) instrument using direct inlet mode. X-ray diffraction studies were carried out using Bruker Single Crystal Kappa Apex II. Analytical thin-layer chromatography (TLC) were performed on glass plates (7.5 × 2.5 and 9 × 5.0 cm) coated with Merck or Acme's silica gel G containing 13% calcium sulfate as binder or on pre-coated 0.2 mm thick Merck 60 F_{245} silica plates and various combinations of ethyl acetate and Petroleum ether were used as eluent. Visualization of spots was accomplished by either exposure to iodine vapour or $KMnO_4$ stain or vanillin stain. All small-scale dry reactions were carried out using standard syringe septum technique. Dry dichloromethane and dichloroethane was prepared by refluxing over anhydrous P_2O_5 and distillation on to calcium hydride. Dry DMF was prepared by stirring on CaH and distillation on to molecular sieves. $BF_3{\cdot}OEt_2$, $Cu(OTf)_2$, TMSOTf, TfOH, AgOTf, and CuI, were obtained from Aldrich. All other Lewis/Bronsted acids, NaH (60a% dispersion in mineral oil), benzyl bromide, cyclohexene oxide and propargyl bromide (80% in toluene), Mg turning, DMP, $Pd(OAc)_2$ are commercial reagents and were used as such without further purification.

(Note: *In the cases where ca. 1:1 mixture of diastereomers was formed, all the peaks are mentioned*.)

Experimental and Characterization of Compounds:

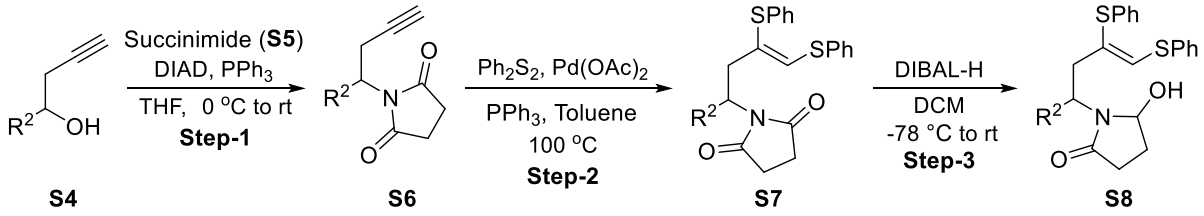
General procedure for synthesis of vinylogous carbamates S3:



Step 1: To a stirred solution of tosyl protected alkyne amine **S1** (500 mg, 2.239 mmol), Ph_2S_2 (538 mg, 2.463 mmol), PPh_3 (352 mg, 1.343 mmol) in 20 mL of degased dry toluene was added $Pd(OAc)_2$ (15 mg, 0.067 mmol). The reaction was performed in a reaction tube for overnight at 100 °C. The reaction mixture was concentrated and the residue was chromatographed on a silica gel column using EtOAc: Petroleum ether as an eluent furnished vinyl-*bis* sulfide amine **S2**.

Step 2: Amine **S2** (500 mg, 1.097 mmol) was dissolved in dry CH_3CN (5 mL) at room temperature, followed by the addition of DABCO (12 mg, 0.11 mmol) and ethyl propiolate (134 µL, 1.317 mmol). The reaction mixture was stirred at room temperature for 12 h and monitored by TLC. Upon completion, the solvent was removed under reduced pressure, and the crude residue was purified by silica gel column chromatography using EtOAc/petroleum ether as the eluent to afford the desired vinylogous carbonate **S3**.

General procedure for synthesis of 5-hydroxypyrrolidin-2-one S8:



Step 1: To a solution of Succinimide **S5** (4.2 g, 42.802 mmol) in anhydrous THF (100 mL) was added alkynol **S4** (3.2 mL, 42.802 mmol) followed by PPh_3 (11.2 g, 42.802 mmol). Then the temperature of the reaction mixture was reduced to 0 °C and DIAD (8.4 mL, 42.802 mmol) was added dropwise. The reaction mixture was then stirred at room temperature up to the completion of the reaction (TLC control). After the complete consumption of starting material, the solvent was removed in vacuo followed by purification of the residue over a silica gel column using ethyl acetate-petroleum ether (1/1: v/v) as an eluent furnished corresponding terminal alkynyl pyrrolidine-2,5-dione **S6**.

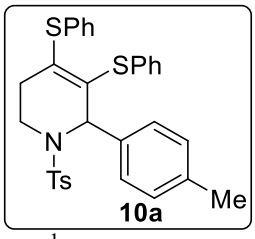
Step 2: Refer procedure as described for **S2**

Step 3: To a solution of vinyl *bis*-sulfide substituted pyrrolidine-2,5-dione (1.2 g, 3.157 mmol) **S7** in DCM was added DIBAL-H (3.6 mL, 6.314 mmol). After the complete consumption of starting material, the reaction was quenched by rochelle salt and products were extracted with DCM (3 x 5 mL) and dried over anhydrous Na_2SO_4. Then the solvent was removed in vacuo followed by purification of the residue over a silica gel column using ethyl acetate-petroleum ether (1:1 v/v) as an eluent furnished corresponding vinyl *bis*-sulfide substituted 5-hydroxypyrrolidin-2-one **S8**.

General procedure for the synthesis of piperidine derivatives:

***4,5-bis(phenylthio)-6-(p-tolyl)-1-tosyl-1,2,3,6-tetrahydropyridine* (10a)**:

To a cold (0 ºC) magnetically stirred solution of the tosyl protected vinyl sulphide amine **8a** (53 mg, 0.120 mmol) and 4-methylbenzaldehyde **9a** (22 µL, 0.180 mmol) in dry $(CH_2Cl)_2$ (3 mL) was added CH_3SO_3H (16 µL, 0.240 mmol) at 0 ºC and the resulting mixture was slowly warmed up to rt and stirred for completion for overnight. The reaction mixture was then quenched with saturated aq. $NaHCO_3$ (2 mL), extracted with CH_2Cl_2 (3 × 5 mL) and combined organic layer was washed with brine sol. and dried (*anhyd.* Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc: Petroleum ether (1:9) as an eluent furnished the tetrahydropyridine derivative **10a** (52.0 mg, 80%) as a white solid.



10a

Physical appearance: white solid.

Melting Point: 143-145 °C.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 3055, 2921, 1580, 1474, 1327, 1158, 1096, 813, 749, 692, 669 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.35-7.24 (m, 12H), 7.13-7.65 (m, 4H), 5.34 (s, 1H), 3.68 (dd, *J* = 14.8, 6.4 Hz, 1H), 3.13-3.05 (m, 1H), 2.49 (s, 3H), 2.35 (s, 3H), 2.19-2.10 (m, 1H), 1.94 (dd, *J* = 17.6, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 143.3 (C), 138.2 (C), 137.9 (2 × C), 135.5 (2 × C), 134.0 (2 × CH), 132.6 (2 × CH), 132.3 (C), 131.5 (C), 129.6 (2 × CH), 129.2 (2 × CH), 129.1 (4 × CH), 128.8 (2 × CH), 128.4 (CH), 128.1 (CH), 127.3 (2 × CH), 59.7 (CH), 37.8 (CH_2), 29.8 (CH_2), 21.7 (CH_3), 21.3 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{31}H_{30}NO_2S_3$ is 544.1433, found 544.1434.

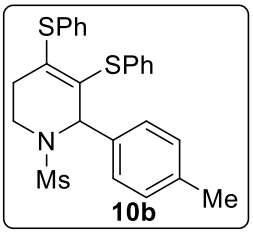
***1-(methylsulfonyl)-4,5-bis(phenylthio)-6-(p-tolyl)-1,2,3,6-tetrahydropyridine* (10b)**:

Reaction of the mesyl protected vinyl sulfide amine **8b** (101 mg, 0.277 mmol) and 4-methylbenzaldehyde **9a** (49 µL, 0.416 mmol) and CH_3SO_3H (36 µL, 0.554 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 ºC as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10b** (98.0 mg, 75%) as a white solid.

Physical appearance: white solid.

Melting Point: 138-140 °C.

R_f: 0.6 (1:4 ethyl acetate-pet ether).



10b

IR (neat): 3055, 2921, 1580, 1474, 1327, 1158, 1096, 813, 749, 692, 669 cm^{-1}.

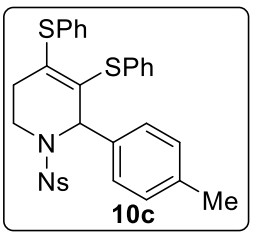
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.54 (m, 2H), 7.40-7.38 (m, 3H), 7.30-7.27 (m, 5H), 7.17-7.12 (m, 4H), 5.29 (s, 1H), 3.60 (dd, *J* = 13.6, 6.8 Hz, 1H), 3.14-3.07 (m, 1H), 2.59-2.54 (m, 1H), 2.44 (s, 3H), 2.36 (s, 3H), 2.20 (dd, *J* = 17.6, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 139.5 (C), 138.5 (C), 134.7 (C), 134.6 (2 × CH), 132.9 (C), 131.4 (C), 131.2 (2 × CH), 129.5 (2 × CH), 129.4 (2 × CH), 129.3 (2 × CH), 128.9 (2 × CH), 128.9 (CH), 127.7 (CH), 126.8 (C), 60.1 (CH), 39.3 (CH_3), 37.9 (CH_2), 31.1 (CH_2), 21.3 (CH_3).

HRMS (ESI, M+Na^+): m/z calcd. for $C_{25}H_{25}NNaO_2S_3$ is 490.0940, found 490.0937.

***1-((4-nitrophenyl)sulfonyl)-4,5-bis(phenylthio)-6-(p-tolyl)-1,2,3,6-tetrahydropyridine* (10c)**:

Reaction of the *p*-nosyl protected vinyl sulfide amine **8c** (153 mg, 0.323 mmol) and 4-methylbenzaldehyde **9a** (57 µL, 0.485 mmol) and CH_3SO_3H (42 µL, 0.647 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 ºC as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10c** (97.0 mg, 52%) as a white solid.



Physical appearance: white solid.

Melting Point: 123-125 °C.

R_f: 0.6 (1:4 ethyl acetate-pet ether).

IR (neat): 2924, 2855, 1529, 1474, 1348, 1163, 1099, 940, 749, 692 cm^{-1}.

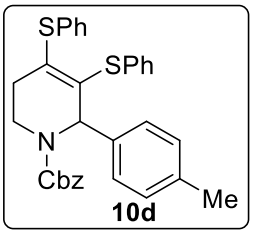
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.38-7.30 (m, 10H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 5.35 (s, 1H), 3.69 (dd, *J* = 14.0, 4.4 Hz, 1H), 3.18-3.13 (m, 1H), 2.34 (s, 3H), 2.09-2.05 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 149.8 (C), 146.6 (C), 138.6 (C), 138.5 (C), 134.8 (C), 134.5 (2 × CH), 133.0 (2 × CH), 132.3 (C), 131.1 (C), 129.4 (2 × CH), 129.3 (2 × CH), 129.3 (2 × CH), 129.0 (CH), 128.8 (2 × CH), 128.5 (CH), 128.3 (2 × CH), 126.9 (C), 124.2 (2 × CH), 60.1 (CH), 38.3 (CH_2), 30.1 (CH_2), 21.2 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. for $C_{30}H_{27}N_2O_4S_3$ is 575.1127, found 575.1129.

benzyl 4,5-bis(phenylthio)-6-(p-tolyl)-3,6-dihydropyridine-1(2H)-carboxylate **(10d)**:

Reaction of the vinyl sulfide amine **8d** (114 mg, 0.270 mmol) and 4-methylbenzaldehyde **9a** (48 µL, 0.405 mmol) and CH_3SO_3H (35 µL, 0.540 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10d** (110.0 mg, 78%) as a colourless liquid.



10d

Physical appearance: colourless liquid.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 3059, 2926, 1697, 1581, 1423, 1303, 1103, 1022, 987, 744, 695 cm^{-1}.

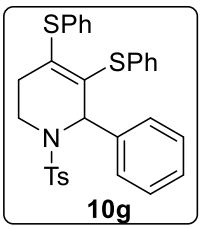
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.51 (m, 2H), 7.37-7.31 (m, 6H), 7.24-7.21 (m, 7H), 7.09 (bs, 4H), 5.68 (s, 1H), 5.11 (s, 2H), 3.95 (bs, 1H), 3.01 (td, *J* = 13.6, 4.0 Hz, 1H), 2.51-2.42 (m, 1H), 2.34 (s, 3H), 2.17 (dd, *J* = 13.2, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 154.6 (C), 137.7 (2 ×C), 136.8 (C), 136.5 (C), 134.2 (C), 131.2 (C), 129.3 (3 × CH), 129.2 (4 × CH), 129.1 (4 × CH), 128.8 (2 ×CH), 128.6 (2 × CH), 128.5 (CH), 128.1 (CH), 128.0 (2 × CH), 127.3 (C), 67.5 (CH_2), 58.9 (CH), 37.0 (CH_2), 31.4 (CH_2), 21.2 (CH_3).

HRMS (ESI, M+Na^+): m/z calcd. for $C_{32}H_{29}NNaO_2S_2$ is 546.1532, found 546.1528.

6-phenyl-4,5-bis(phenylthio)-1-tosyl-1,2,3,6-tetrahydropyridine **(10g):**

Reaction of the vinyl sulfide amine **8a** (140 mg, 0.317 mmol) and benzaldehyde **9b** (49 µL, 0.476 mmol) and CH_3SO_3H (41 µL, 0.634 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10g** (128 mg, 76%) as a white solid.



10g

Physical appearance: white solid.

Melting Point: 162-163 °C.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 2923, 2852, 1583, 1328, 1160, 1097, 815, 693, 669 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.33-7.24 (m, 15H), 7.16 (bs, 2H), 5.36 (s, 1H), 3.67 (dd, *J* = 14.8, 6.4 Hz, 1H), 3.11-3.04 (m, 1H), 2.49 (s, 3H), 2.17-2.10 (m, 1H), 1.93 (dd, *J* = 17.6, 4.0 Hz, 1H).

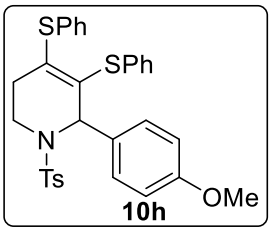
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 143.4 (C), 138.5 (2 ×C), 137.9 (2 ×C), 134.0 (2 × CH), 132.8 (2 × CH), 132.2 (C), 131.5 (C), 129.7 (2 × CH), 129.2 (2 × CH), 129.1 (2 × CH),

128.9 (2 × CH), 128.5 (CH), 128.4 (2 × CH), 128.2 (CH), 128.1 (CH), 127.3 (2 × CH), 59.9 (CH), 37.9 (CH_2), 29.8 (CH_2), 21.7 (CH_3).

HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{30}H_{27}NNaO_2S_3$ is 552.1094, found 552.1094.

***6-(4-methoxyphenyl)-4,5-bis(phenylthio)-1-tosyl-1,2,3,6-tetrahydropyridine* (10h):**

Reaction of the vinyl sulfide amine **8a** (94 mg, 0.213 mmol) and *p*-anisaldehyde **9c** (39 µL, 0.319 mmol) and CH_3SO_3H (28 µL, 0.425 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10h** (88 mg, 74%) as a white solid.



Physical appearance: white solid.

Melting Point: 140-142 °C.

R_f: 0.4 (1:4 ethyl acetate-pet ether).

IR (neat): 3057, 2928, 1607, 1510, 1328. 1252, 1160, 817, 752 cm^{-1}.

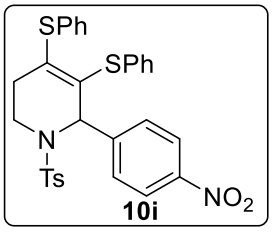
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.30-7.21 (m, 12H), 7.04 (d, *J* = 8.0, Hz, 2H), 6.79 (d, *J* = 8.0, Hz, 2H), 5.28 (s, 1H), 3.78 (s, 3H), 3.64 (dd, *J* = 14.4, 6.4 Hz, 1H), 3.08-3.00 (m, 1H), 2.46 (s, 3H), 2.16-2.07 (m, 1H), 1.90 (dd, *J* = 17.6, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 159.4 (C), 143.3 (C), 138.0 (C), 137.5 (C), 133.9 (2 × CH), 132.8 (2 × CH), 132.2 (C), 131.6 (C), 130.6 (C), 130.2 (2 × CH), 129.7 (2 × CH), 129.2 (4 × CH), 128.4 (CH), 128.2 (CH), 127.9 (C), 127.4 (2 × CH), 113.8 (2 × CH), 59.4 (CH), 55.4 (CH_3), 37.8 (CH_2), 29.9 (CH_2), 21.8 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{31}H_{30}NO_3S_3$ 560.1382, found 560.1391.

***6-(4-nitrophenyl)-4,5-bis(phenylthio)-1-tosyl-1,2,3,6-tetrahydropyridine* (10i)**:

Reaction of the vinyl sulfide amine **8a** (115 mg, 0.260 mmol) and *p*-nitrobenzaldehyde **9d** (59 mg, 0.390 mmol) and CH_3SO_3H (34 µL, 0.520 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10i** (134 mg, 90%) as a light-yellow solid.



Physical appearance: light yellow solid.

Melting Point: 163-165 °C.

R_f: 0.3 (1:4 ethyl acetate- pet ether).

IR (neat): 2920, 2850, 1596, 1519, 1347, 1160, 1096, 750, 693, 658 cm^{-1}.

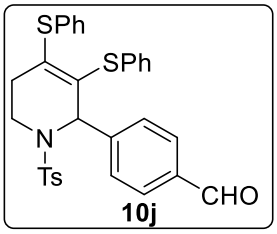
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.36-7.28 (m, 12H), 7.26-7.24 (m, 2H), 5.41 (s, 1H) 3.70 (dd, *J* = 14.8, 6.4 Hz, 1H), 3.03-2.95 (m, 1H), 2.51 (s, 3H), 2.10-2.02 (m, 1H), 1.92 (dd, *J* = 17.6, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 147.7 (C), 146.0 (C), 143.9 (C), 140.0 (C), 137.5 (C), 134.5 (2 × CH), 132.8 (2 × CH), 131.7 (C), 130.8 (C), 129.9 (2 × CH), 129.8 (2 × CH), 129.5 (2 × CH), 129.3 (2 × CH), 128.9 (CH), 128.7 (CH), 127.3 (2 × CH), 124.9 (C), 123.7 (2 × CH), 59.1 (CH), 38.2 (CH_2), 29.6 (CH_2), 21.8 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{30}H_{27}N_2O_4S_3$ is 575.1127, found 575.1129.

***4-(3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl)benzaldehyde* (10j):**

Reaction of the vinyl sulfide amine **8a** (199 mg, 0.450 mmol) and terephthalaldehyde **9e** (90 mg, 0.675 mmol) and CH_3SO_3H (58 µL, 0.900 mmol) in dry $(CH_2Cl)_2$ (4.0 mL) at 0 ºC as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10j** (210 mg, 84%) as a viscous liquid.



10j

Physical appearance: viscous liquid.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 3056, 2925, 1699, 1580, 1475, 1329, 1159, 1096, 750, 692, 656 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.01 (s, 1H), 7.81 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.35-7.26 (m, 14H), 5.40 (s, 1H), 3.69 (dd, *J* = 14.8, 6.0 Hz, 1H), 3.13-2.98 (m, 1H), 2.50 (s, 3H), 2.08-2.04 (m, 1H), 1.93 (dd, *J* = 17.8, 4.0 Hz, 1H).

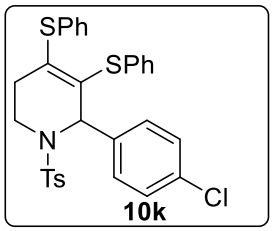
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 192.0 (CH), 145.4 (C), 143.7 (C), 139.2 (C), 137.6 (C), 136.0 (C), 134.3 (2 × CH), 132.8 (2 × CH), 131.9 (C), 131.0 (C), 129.9 (2 × CH), 129.8 (2 × CH), 129.6 (2 × CH), 129.4 (2 × CH), 129.2 (2 × CH), 128.8 (CH), 128.6 (CH), 127.3 (2 × CH), 125.7 (C), 59.5 (CH), 38.1 (CH_2), 29.7 (CH_2), 21.8 (CH_3).

HRMS (ESI, M+ H$^+$): m/z calcd. for $C_{31}H_{28}NO_3S_3$ is 558.1226, found 558.1233.

***6-(4-chlorophenyl)-4,5-bis(phenylthio)-1-tosyl-1,2,3,6-tetrahydropyridine* (10k):**

Reaction of the vinyl sulfide amine **8a** (151 mg, 0.342 mmol) and 4-chlorobenzaldehyde **9f** (58 mg, 0.513 mmol) and CH_3SO_3H (44 µL, 0.684 mmol) in dry $(CH_2Cl)_2$ (4.0 mL) at 0 ºC as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10k** (164 mg, 85%) as a white solid.

Physical appearance: white solid.



Melting Point: 155-156 °C.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 3058, 2923, 1582, 1439, 1341, 1161, 1095, 749, 692, 665 cm^{-1}.

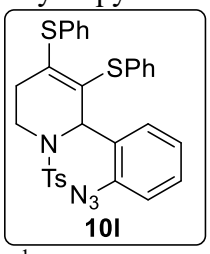
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.36-7.24 (m, 14H), 7.10 (d, *J* = 8.4 Hz, 2H), 5.32 (s, 1H), 3.68 (dd, *J* = 14.8, 6.4 Hz, 1H), 3.06-2.98 (m, 1H), 2.50 (s, 3H), 2.15-2.05 (m, 1H), 1.91 (dd, *J* = 17.6, 4.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 143.6 (C), 138.4 (C), 137.8 (C), 137.2 (C), 134.1 (2 × CH), 134.0 (C), 132.9 (2 × CH), 131.9 (C), 131.2 (C), 130.3 (2 × CH), 129.8 (2 × CH), 129.3 (2 × CH), 129.2 (2 × CH), 128.6 (3 × CH), 128.4 (CH), 127.3 (2 × CH), 126.6 (C), 59.2 (CH), 37.9 (CH_2), 29.8 (CH_2), 21.8 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. for $C_{30}H_{27}ClNO_2S_3$ is 564.0887, found 564.0892.

***6-(2-azidophenyl)-4,5-bis(phenylthio)-1-tosyl-1,2,3,6-tetrahydropyridine* (10l):**

Reaction of the vinyl sulfide amine **8a** (63 mg, 0.143 mmol) and 2-azidobenzaldehyde **9g** (32 mg, 0.215 mmol) and CH_3SO_3H (19 µL, 0.286 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 ºC as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10l** (33 mg, 41%) as a white solid.



Physical appearance: white solid.

Melting Point: 146-148 °C.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 3058, 2923, 2124, 1580, 1481, 1324, 1157, 1090, 750, 693, 728 cm^{-1}.

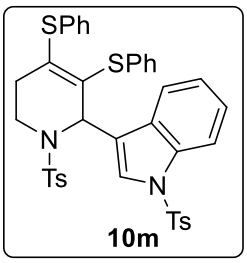
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 6.8 Hz, 2H), 7.46-7.45 (m, 2H), 7.38-7.28 (m, 10H), 7.24-7.20 (m, 2H), 7.10 (t, *J* = 6.0 Hz, 1H), 6.94 (d, *J* = 6.4 Hz, 1H), 5.47 (s, 1H), 3.72 (dd, *J* = 12.0, 5.6 Hz, 1H), 3.21-3.15 (m, 1H), 2.55-2.48 (m, 1H), 2.41 (s, 3H), 2.08 (dd, *J* = 14.4, 3.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 143.5 (C), 138.8 (C), 137.2 (C), 136.1 (C), 133.6 (2 × CH), 133.0 (2 × CH), 131.9 (C), 131.8 (C), 130.6 (CH), 129.7 (CH), 129.3 (C), 129.3 (4 × CH), 129.1 (C), 129.0 (2 × CH), 128.3 (CH), 128.0 (3 × CH), 124.4 (CH), 118.6 (CH), 54.9 (CH), 38.6 (CH_2), 30.5 (CH_2), 21.6 (CH_3).

HRMS (ESI, M+Na^+): m/z calcd. for $C_{30}H_{26}N_4NaO_2S_3$ is 593.1110, found 593.1112.

***3-(3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl)-1-tosyl-1H-indole* (10m):**

Reaction of the vinyl sulfide amine **8a** (158 mg, 0.358 mmol) and 1-Tosyl-indole-3-carbaldehyde **9h** (160 mg, 0.536 mmol) and CH_3SO_3H (46 µL, 0.716 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10m** (203 mg, 78%) as a white solid.



10m

Physical appearance: white solid.

Melting Point: 117-119 °C.

R_f: 0.3 (1:4 ethyl acetate-pet ether).

IR (neat): 2923, 1596, 1446, 1371, 1329, 1160, 1095, 1021, 748, 667 cm^{-1}.

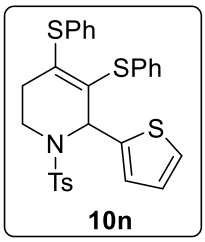
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.45-7.43 (m, 2H), 7.36-7.33 (m, 3H), 7.30-7.28 (m, 3H), 7.27-7.23 (m, 5H), 7.19-7.11 (m, 5H), 5.60 (s, 1H), 3.62 (dd, *J* = 14.8, 6.8 Hz, 1H), 3.18-3.10 (m, 1H), 2.49 (s, 3H), 2.33 (s, 3H), 2.09-2.00 (m, 1H), 1.87 (dd, *J* = 18.0, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 145.3 (C), 143.7 (C), 137.5 (C), 136.4 (C), 135.4 (C), 135.0 (C), 134.1 (2 × CH), 133.5 (2 × CH), 131.4 (C), 131.2 (C), 130.0 (2 × CH), 129.7 (2 × CH), 129.5 (C), 129.2 (2 × CH), 129.1 (2 × CH), 128.6 (2 × CH), 127.4 (2 × CH), 127.2 (C), 127.0 (2 × CH), 126.9 (CH), 125.1 (CH), 123.6 (CH), 120.6 (C), 120.6 (CH), 113.5 (CH), 52.6 (CH), 38.2 (CH_2), 29.2 (CH_2), 21.7 (CH_3), 21.6 (CH_3).

HRMS (ESI, M+Na^+): m/z calcd. for $C_{39}H_{34}N_2NaO_4S_4$ is 745.1294, found 745.1297.

***4,5-bis(phenylthio)-6-(thiophen-2-yl)-1-tosyl-1,2,3,6-tetrahydropyridine* (10n):**

Reaction of the vinyl sulfide amine **8a** (176 mg, 0.398 mmol) and thiophene-2-carbaldehyde **9i** (56 µL, 0.597 mmol) and CH_3SO_3H (52 µL, 0.796 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10n** (160 mg, 75%) as a viscous liquid.



10n

Physical appearance: viscous liquid.

R_f: 0.5 (1:4 ethyl acetate- pet ether).

IR (neat): 3058, 2923, 1580, 1326, 1156, 1096, 933, 747, 691, 658 cm^{-1}.

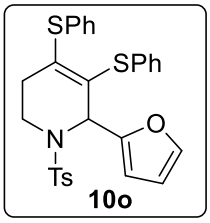
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.0 Hz, 2H), 7.35-7.34 (m, 10H), 7.22-7.20 (m, 3H), 6.93-6.90 (m, 2H), 5.61 (s, 1H), 3.76 (dd, *J* = 14.0, 7.2 Hz, 1H), 3.28-3.20 (m, 1H), 2.44 (s, 3H), 2.31-2.22 (m, 1H), 1.99 (dd, *J* = 17.6, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 143.4 (C), 141.8 (C), 139.8 (C), 137.4 (C), 134.1 (2 × CH), 133.0 (C), 132.8 (C), 131.5 (2 × CH), 131.4 (C), 129.6 (2 × CH), 129.3 (2 × CH), 129.2 (2 × CH), 128.6 (CH), 128.0 (CH), 127.8 (CH), 127.3 (2 × CH), 126.6 (CH), 126.0 (CH), 55.6 (CH), 38.3 (CH_2), 30.4 (CH_2), 21.7 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{28}H_{26}NO_2S_4$ is 536.0841, found 536.0844.

***6-(furan-2-yl)-4,5-bis(phenylthio)-1-tosyl-1,2,3,6-tetrahydropyridine* (10o):**

Reaction of the vinyl sulfide amine **8a** (112 mg, 0.254 mmol) and furan-2-carbaldehyde **9j** (32 µL, 0.380 mmol) and CH_3SO_3H (33 µL, 0.508 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10o** (92 mg, 70%) as a viscous liquid.



10o

Physical appearance: viscous liquid.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 3055, 2924, 1579, 1476, 1328, 1159, 1096, 750, 691, 656 cm^{-1}.

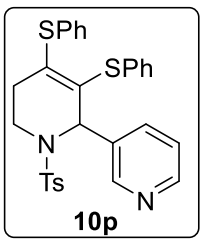
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.35-7.28 (m, 10H), 7.22-7.17 (m, 3H), 6.24 (dd, *J* = 3.2, 1.6 Hz, 1H), 6.15 (d, *J* = 3.2 Hz, 1H), 5.45 (s, 1H), 3.75 (dd, *J* = 14.0, 6.4 Hz, 1H), 3.32-3.24 (m, 1H), 2.42 (s, 3H), 2.32-2.22 (m, 1H), 2.00 (dd, *J* = 17.6, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 151.3 (C), 143.2 (C), 142.4 (CH), 141.6 (C), 137.2 (C), 134.4 (2 × CH), 133.1 (C), 131.2 (C), 130.6 (2 × CH), 129.5 (2 × CH), 129.2 (4 × CH), 128.7 (CH), 127.4 (CH), 127.2 (2 × CH), 123.9 (C), 110.3 (CH), 110.1 (CH), 54.5 (CH), 39.2 (CH_2), 30.6 (CH_2), 21.6 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{28}H_{26}NO_3S_3$ is 520.1069, found 520.1070.

***3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydro-2,3'-bipyridine* (10p):**

Reaction of the vinyl sulfide amine **8a** (980 mg, 2.219 mmol) and nicotine-3-carbaldehyde **9k** (312 µL, 3.329 mmol) and CH_3SO_3H (720 µL, 11.095 mmol) in dry $(CH_2Cl)_2$ (10.0 mL) at 0 °C as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10p** (530 mg, 45%) as a sticky solid.



10p

Physical appearance: sticky solid.

R_f: 0.5 (3:7 ethyl acetate- pet ether).

IR (neat): 3055, 2924, 1579, 1476, 1328, 1159, 1096, 812, 750, 691, 656 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52-8.51 (m, 1H), 8.32 (bs, 1H), 7.48-7.46 (m, 3H), 7.34-7.20 (m, 13H), 5.34 (s, 1H), 3.71 (dd, *J* = 14.4, 6.0 Hz, 1H), 3.03-2.95 (m, 1H), 2.48 (s, 3H), 2.18-2.09 (m, 1H), 1.94 (dd, *J* = 17.6, 4.0 Hz, 1H).

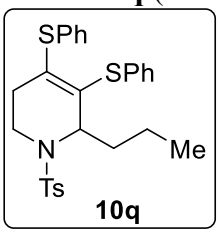
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 150.0 (CH), 149.3 (CH), 143.8 (C), 138.8 (C), 137.5 (C), 136.4 (CH), 134.3 (C), 134.1 (2 × CH), 132.9 (2 × CH), 131.7 (C), 131.2 (C), 129.8 (2 × CH), 129.4 (2 × CH), 129.2 (2 × CH), 128.7 (CH), 128.5 (CH), 127.3 (2 × CH), 125.8 (C), 123.4 (CH), 57.9 (CH), 38.0 (CH_2), 29.8 (CH_2), 21.8 (CH_3).

HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{29}H_{26}N_2NaO_2S_3$ is 553.1049, found 553.1055.

Note: In the case of aliphatic aldehydes, trace amounts of a regioisomeric impurity were observed, as exemplified by compounds **10q** and **10r**.

***4,5-bis(phenylthio)-6-propyl-1-tosyl-1,2,3,6-tetrahydropyridine* (10q):**

Reaction of the vinyl sulfide amine **8a** (157 mg, 0.356 mmol) and butyrlaldehyde **9l** (99 µL, 1.066 mmol) and CH_3SO_3H (46 µL, 0.711 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 ºC as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10q** (117 mg, 66%) as a sticky liquid.



10q

Physical appearance: sticky liquid.

R_f: 0.6 (1:5 ethyl acetate- pet ether).

IR (neat): 3057, 2957, 1581, 1475, 1329, 1156, 748, 715, 693, 1097, 925, 657 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.43-7.33 (m, 5H), 7.29-7.22 (m, 5H), 7.11 (d, *J* = 6.8 Hz, 2H), 4.19 (d, *J* = 10.4 Hz, 1H), 3.82 (dd, *J* = 15.2, 6.8 Hz, 1H), 3.23-3.15 (m, 1H), 2.48 (s, 3H), 2.04-1.91 (m, 2H), 1.74 (dd, *J* = 17.6, 4.4 Hz, 1H), 1.69-1.51 (m, 1H), 1.50-1.26 (m, 1H), 1.19-1.14 (m, 1H), 0.78 (t, *J* = 7.6 Hz, 3H).

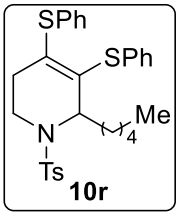
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 143.3 (C), 138.0 (C), 137.8 (C), 133.9 (2 × CH), 133.2 (C), 131.5 (C), 131.3 (2 × CH), 129.6 (2 × CH), 129.5 (C), 129.3 (2 × CH), 129.0 (2 × CH), 128.4 (CH), 127.7 (CH), 127.4 (2 × CH), 57.5 (CH), 38.0 (CH_2), 35.1 (CH_2), 29.5 (CH_2), 21.7 (CH_3), 19.6 (CH_2), 13.6 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{27}H_{30}NO_2S_3$ is 496.1433, found 496.1438.

***6-pentyl-4,5-bis(phenylthio)-1-tosyl-1,2,3,6-tetrahydropyridine* (10r):**

Reaction of the vinyl sulfide amine **8a** (126 mg, 0.285 mmol) and hexanal **9m** (105 µL, 0.856 mmol) and CH_3SO_3H (37 µL, 0.570 mmol) in dry $(CH_2Cl)_2$ (3.0 mL) at 0 ºC as described for the tetrahydropyridine derivative **10a** followed by purification on a silica gel column using

EtOAc: Petroleum ether (1:9) as eluent furnished the tetrahydropyridine derivative **10r** (149 mg, 71%) as a light-orange solid.



Physical appearance: light-orange solid.

Melting Point: 109-111 °C.

R_f: 0.5 (1:4 ethyl acetate- pet ether).

IR (neat): 3058, 2926, 1581, 1475, 1329, 1157, 1092, 747, 714, 693, 658 cm^{-1}.

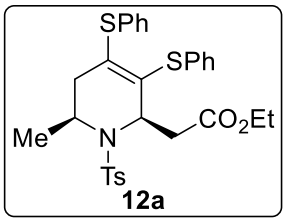
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.44-7.23 (m, 10H), 7.15-7.13 (m, 2H), 4.16-4.14 (m, 1H), 3.84 (dd, *J* = 14.8, 6.8 Hz, 1H), 3.23-3.15 (m, 1H), 2.48 (s, 3H), 2.07-1.95 (m, 2H), 1.76 (dd, *J* = 17.6, 4.4 Hz, 1H), 1.50-1.49 (m, 1H), 1.30-1.06 (m, 6H), 0.82 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 143.3 (C), 138.0 (C), 137.8 (C), 133.9 (2 × CH), 133.2 (C), 131.6 (C), 131.3 (2 × CH), 129.6 (C), 129.6 (2 × CH), 129.3 (2 × CH), 129.0 (2 × CH), 128.3 (CH), 127.7 (CH), 127.4 (2 × CH), 57.7 (CH), 38.1(CH_2), 33.0 (CH_2), 31.4 (CH_2), 29.7 (CH_2), 26.0 (CH_2), 22.6 (CH_2), 21.7 (CH_3), 14.1 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{29}H_{34}NO_2S_3$ is 524.1746, found 524.1746.

***Ethyl 2-((2R,6S)-6-methyl-3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-l) acetate* (12a):**

To a cold (0 °C), magnetically stirred solution of the vinylogous carbamate **11a** (140 mg, 0.253 mmol) in dry $(CH_2Cl)_2$ (4 mL) was added CH_3SO_3H (33 μL, 0.506 mmol). The reaction mixture was slowly allowed to warm up to rt, stirred for overnight and quenched by adding sat. $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent followed by purification of the residue on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent to furnished the required piperidine derivative **12a** (106 mg, 75%) as a sticky solid.



Physical appearance: sticky solid.

R_f: 0.5 (1:4 ethyl acetate- pet ether).

[α]$_D$ ^{25}: -61.522 (c 0.420, $CHCl_3$).

IR (neat): 3058**,** 2980, 1733, 1581, 1335, 1154, 1022, 747, 664 cm^{-1}.

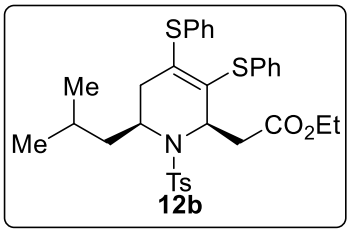
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.4 Hz, 2H), 7.36-7.24 (m, 10H), 7.16-7.14 (m, 2H), 4.95-4.91 (m, 1H), 4.24 (qd, *J* = 6.8 ,1.6 Hz, 1H), 4.09 (qd, *J* = 7.2, 1.2 Hz, 2H), 3.08 (dd, *J* = 14.8, 6.0 Hz, 1H), 2.71 (dd, *J* = 14.4, 7.2 Hz, 1H), 2.48 (s, 3H), 2.04 (ddd, *J* = 17.6, 7.2, 2.8 Hz, 1H), 1.75 (dd, *J* = 17.6, 0.8 Hz, 1H), 1.29 (d, *J* = 6.8 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.6 (C), 143.4 (C), 141.6 (C), 137.4 (C), 134.4 (2 × CH), 133.7 (C), 131.4 (C), 129.8 (2 × CH), 129.6 (2 × CH), 129.4 (2 × CH), 129.2 (2 × CH), 128.8 (CH), 127.3 (2 × CH), 127.2 (CH), 125.0 (C), 61.0 (CH_2), 54.1 (CH), 46.9 (CH), 42.3 (CH_2), 35.2 (CH_2), 22.3 (CH_3), 21.8 (CH_3), 14.1 (CH_3).

HRMS (ESI, M+Na$^+$): m/z calcd. For $C_{29}H_{31}NNaO_4S_3$ 576.1307, found 576.1304.

***Ethyl 2-((2R,6S)-6-isobutyl-3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl) acetate* (12b):**

Reaction of the vinylogous carbamate **11b** (95 mg, 0.159 mmol) with CH_3SO_3H (21 μL, 0.318 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the required piperidine **12b** (64 mg, 67%) as a white solid.



12b

Physical appearance: white solid.

Melting Point: 118-120 °C.

[α]$_D$ ^{25}: -94.125 (c 0.420, $CHCl_3$).

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 3058, 2957, 1734, 1581, 1474, 1324, 1157, 747, 691 cm^{-1}.

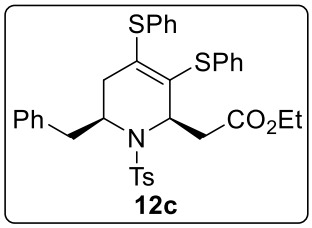
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.33-7.24 (m, 8H), 7.21-7.17 (m, 4H), 4.92-4.90 (m, 1H), 4.16-4.04 (m, 3H), 3.08 (dd, *J* = 14.8, 6.0 Hz, 1H), 2.66 (dd, *J* = 14.8, 6.4 Hz, 1H), 2.48 (s, 3H), 2.05 (ddd, *J* = 16.8, 6.8, 2.4 Hz, 1H), 1.78-1.74 (m, 1H), 1.65-1.57 (m, 3H), 1.18 (t, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.0 Hz, 3H), 0.85 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.7 (C), 143.4 (C), 142.7 (C), 137.4 (C), 134.5 (2 × CH), 133.9 (C), 131.4 (C) 129.8 (2 × CH), 129.3 (2 × CH), 129.3 (2 × CH), 129.2 (2 × CH), 128.8 (CH), 127.4 (2 × CH), 127.0 (CH), 124.1 (C), 61.0 (CH_2), 53.8 (CH), 49.2 (CH), 43.9 (CH_2), 42.4 (CH_2), 34.1 (CH_2), 24.6 (CH_3), 22.6 (CH_3), 22.4 (CH), 21.8 (CH_3), 14.1 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. For $C_{32}H_{38}NO_4S_3$ 596.1957, found 596.1956.

***Ethyl 2-((2R,6S)-6-benzyl-3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl) acetate* (12c):**

Reaction of the vinylogous carbamate **11c** (89 mg, 0.141 mmol) with CH_3SO_3H (18 µL, 0.282 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the required piperidine **12c** (62 mg, 65%) as a syrupy liquid.



12c

Physical appearance: syrupy liquid.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

[α]$_D$ ^{25}: -110.730 (c 1.085, $CHCl_3$).

IR (neat): 3059, 2926, 1733, 1582, 1476, 1329, 1160, 745, 693 cm^{-1}.

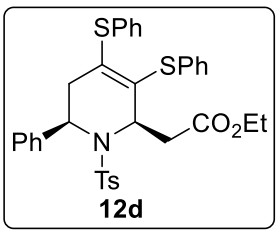
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.37-7.17 (m, 15H), 7.04 (d, *J* = 6.8 Hz, 2H), 4.98 (t, *J* = 6.4 Hz, 1H), 4.29-4.26 (m, 1H), 4.16-4.09 (m, 2H), 3.19 (dd, *J* = 14.8, 6.0 Hz, 1H), 3.12 (dd, *J* = 12.8, 3.2 Hz, 1H), 2.80-2.73 (m, 2H), 2.47 (s, 3H), 1.90-1.85 (m, 1H), 1.78 (ddd, *J* = 17.6, 6.4, 1.6 Hz, 1H), 1.21 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.4 (C), 143.4 (C), 142.4 (C), 138.0 (C), 137.2 (C), 134.8 (2 × CH), 133.7 (C), 130.7 (C), 129.8 (2 × CH), 129.3 (2 × CH), 129.2 (2 × CH), 129.1 (2 × CH), 129.0 (2 ×CH), 128.9 (CH), 128.6 (2 × CH), 127.2 (2 × CH), 127.0 (CH), 126.7 (CH), 124.0 (C), 60.9 (CH_2), 53.9 (CH), 52.8 (CH), 42.8 (CH_2), 41.8 (CH_2), 31.2 (CH_2), 21.6 (CH_3), 14.0 (CH_3).

HRMS (ESI, M+Na$^+$): m/z calcd. For $C_{35}H_{35}NNaO_4S_3$ 652.1620, found 652.1617.

***Ethyl 2-((2R,6R)-6-phenyl-3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl) acetate* (12d):**

Reaction of the vinylogous carbamate **11d** (98 mg, 0.159 mmol) with CH_3SO_3H (21 µL, 0.318 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the required piperidine **12d** (64 mg, 66%) as a sticky solid.



12d

Physical appearance: sticky solid.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

[α]$_D$ ^{25}: 102.251 (c 0.340, $CHCl_3$).

IR (neat): 3060, 2926, 1732, 1581, 1475, 1332, 1162, 748, 695, 675 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.56-7.33 (m, 8H), 7.32-7.28 (m, 9H), 5.30 (d, *J* = 6.8 Hz, 1H), 4.93-4.89 (m, 1H), 3.99 (q, *J* = 7.2 Hz, 2H), 2.52 (s, 3H), 2.15

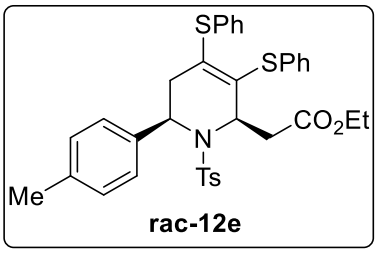
(ddd, *J* = 18.0, 7.2, 2.4 Hz, 1H), 2.43-2.41 (m, 1H), 2.38-2.37 (m, 1H), 1.75 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.5 (C), 143.5 (C), 141.6 (C), 138.9 (C), 137.3 (C), 135.0 (2 × CH), 133.5 (C), 130.7 (C), 129.9 (2 × CH), 129.8 (2 × CH), 129.2 (4 × CH), 129.1 (CH), 128.6 (2 × CH), 128.1 (CH), 128.0 (2 × CH), 127.3 (3 × CH), 125.2 (C), 60.6 (CH_2), 54.7 (CH), 52.3 (CH), 40.1 (CH_2), 31.2 (CH_2), 21.7 (CH_3), 14.0 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. For $C_{34}H_{34}NO_4S_3$ 616.1644, found 616.1640.

***Ethyl 2-((2R*,6R*)-3,4-bis(phenylthio)-6-(p-tolyl)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl) acetate* (*rac*-12e):**

Reaction of the vinylogous carbamate **11e** (150 mg, 0.238 mmol) with CH_3SO_3H (31 μL, 0.476 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the required piperidine **rac-12e** (65 mg, 43%) as a white solid.



rac-12e

Physical appearance: white solid.

Melting Point: 148-150 °C.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 2980, 2922, 1731, 1581, 1476, 1329, 1157, 1092, 812, 748, 961 cm^{-1}.

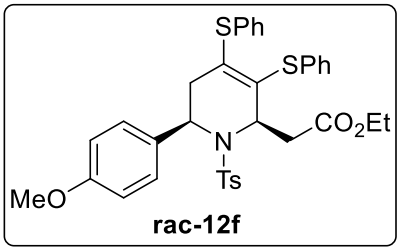
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.2 Hz, 2H), 7.39-7.36 (m, 2H), 7.33-7.28 (m, 4H), 7.27-7.25 (m, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.77-6.74 (m, 4H), 5.15 (dd, *J* = 8.8, 4.4 Hz, 1H), 4.78 (dd, *J* = 9.2, 4.0 Hz, 1H), 4.10-3.98 (m, 2H), 3.17-3.08 (m, 2H), 2.92 (dd, *J* = 14.8, 8.8 Hz, 1H), 2.46 (dd, *J* = 16.8, 4.0 Hz, 1H), 2.28 (s, 3H), 2.25 (s, 3H), 1.20 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.7 (C), 142.3 (C), 140.2 (C), 138.5 (C), 137.3 (C), 133.9 (2 × CH), 133.5 (C) 132.6 (C), 131.5 (2 × CH), 129.3 (2 × CH), 129.2 (C, 2 × CH), 128.8 (C), 128.5 (4 × CH), 128.4 (CH), 128.3 (2 × CH), 127.7 (CH), 127.4 (2 × CH), 60.8 (CH_2), 57.0 (CH), 55.5 (CH), 40.0 (CH_2), 34.5 (CH_2), 21.5 (CH_3), 21.2 (CH_3), 14.2 (CH_3).

HRMS (ESI, M+Na$^+$): m/z calcd. For $C_{35}H_{35}NNaO_4S_3$ 652.1620, found 652.1616.

***Ethyl 2-((2R*,6R*)-6-(4-methoxyphenyl)-3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl) acetate* (*rac*-12f):**

Reaction of the vinylogous carbamate **11f** (185 mg, 0.286 mmol) with CH_3SO_3H (37 µL, 0.572 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the required piperidine **rac-12f** (100 mg, 54%) as a white solid.



rac-12f

Physical appearance: white solid.

Melting Point: 141-142 °C.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 2930, 2837, 1733, 1583, 1512, 1330, 1253, 1162, 1095, 749, 670 cm^{-1}.

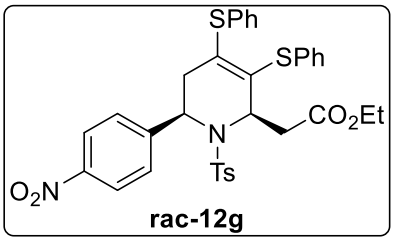
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.35-7.26 (m, 12H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 5.25 (d, *J* = 6.4 Hz, 1H), 4.87 (t, *J* = 6.0 Hz, 1H), 3.98 (q, *J* = 6.8 Hz, 2H), 3.80 (s, 3H), 2.52 (s, 3H), 2.42-2.33 (m, 2H), 2.14 (dd, *J* = 18.0, 5.6 Hz, 1H), 1.78 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.7 (C), 159.4 (C), 143.5 (C), 141.8 (C), 137.5 (C), 135.1 (2 × CH), 133.6 (C), 130.8 (C), 129.9 (4 × CH), 129.3 (4 × CH), 129.2 (4 ×CH), 127.4 (2 × CH), 127.3 (C), 125.2 (C), 114.0 (2 × CH), 60.7 (CH_2), 55.4 (CH_3), 54.6 (CH), 51.9 (CH), 40.2 (CH_2), 31.5 (CH_2), 21.8 (CH_3), 14.1 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. For $C_{35}H_{36}NO_5S_3$ 646.1750, found 646.1753.

***Ethyl 2-((2R*,6R*)-6-(4-nitrophenyl)-3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl) acetate* (*rac*-12g):**

Reaction of the vinylogous carbamate **11g** (152 mg, 0.230 mmol) with CH_3SO_3H (30 µL, 0.460 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the required piperidine **rac-12g** (100 mg, 66%) as a light-yellow solid.



rac-12g

Physical appearance: light yellow solid.

Melting Point: 160-162 °C

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 2924, 1731, 1598, 1520, 1345, 1159, 751, 694, 672 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.8 Hz, 2H), 7.58-7.55 (m, 2H), 7.44-7.22 (m, 8H), 7.02-6.98 (m, 4H), 6.92 (d, *J* = 8.0 Hz, 2H), 5.02 (dd, *J* = 8.0, 4.4 Hz, 1H), 4.94 (dd, *J* =

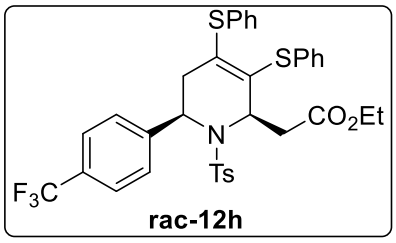
8.4, 4.8 Hz, 1H), 4.13-3.92 (m, 2H), 3.14 (dd, *J* = 15.2, 4.8 Hz, 1H), 3.02-2.91 (m, 2H), 2.63 (dd, *J* = 16.8, 4.4 Hz, 1H), 2.32 (s, 3H), 1.21 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.4 (C), 147.1 (C), 145.5 (C), 143.6 (C), 138.4 (C), 137.6 (C), 134.0 (2 × CH), 132.5 (2 × CH), 132.1 (C), 131.1 (C), 129.6 (C), 129.5 (2 ×CH), 129.4 (2 × CH), 129.0 (2 × CH), 128.9 (2 × CH), 128.8 (CH), 128.3 (CH), 127.4 (2 × CH), 122.9 (2 × CH), 61.0 (CH_2), 56.8 (CH), 55.4 (CH), 40.2 (CH_2), 34.4 (CH_2), 21.5 (CH_3), 14.2 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. For $C_{34}H_{33}N_2O_6S_3$ 661.1495, found 661.1493.

***Ethyl 2-((2R*,6R*)-3,4-bis(phenylthio)-6-(p-tolyl)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl) acetate* (*rac*-12h):**

Reaction of the vinylogous carbamate **11h** (200 mg, 0.292 mmol) with CH_3SO_3H (38 µL, 0.585 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent furnished the required piperidine **rac-12h** (104 mg, 52%) as a white solid.



rac-12h

Physical appearance: white solid.

Melting Point: 141-143 °C.

R_f: 0.5 (1:4 ethyl acetate-pet ether).

IR (neat): 2925, 1732, 1582, 1324, 1160, 1124, 1068, 745, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.36-7.32 (m, 5H), 7.31-7.25 (m, 7H), 5.25 (d, *J* = 6.4 Hz, 1H), 4.92-4.89 (m, 1H), 4.00 (q, *J* = 7.2 Hz, 2H), 2.52 (s, 3H), 2.48-2.47 (m, 2H), 2.39 (dd, *J* = 18.0, 1.6 Hz, 1H), 2.16 (ddd, *J* = 18.0, 6.8, 2.0 Hz, 1H), 1.75 (dd, *J* = 14.8, 8.0 Hz, 1H),1.16 (t, *J* = 7.2 Hz, 3H).

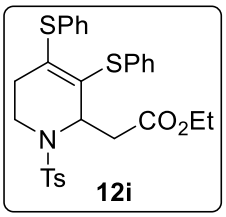
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.2 (C), 143.9 (C), 143.4 (C), 140.5 (C), 136.9 (C), 134.8 (2 × CH), 133.1 (C), 130.8 (C), 130.5 (2 × CH), 130.3 (q, *J* = 32.0 Hz, C), 130.0 (2 × CH), 129.4 (2 ×CH), 129.3 (2 × CH), 129.2 (CH), 128.4 (2 × CH), 127.7 (CH), 127.5 (2 × CH), 126.4 (CH), 125.6 (q, *J* = 3.9 Hz, 2 × CH), 124.0 (q, *J* = 271.0 Hz, C), 60.8 (CH_2), 55.0 (CH), 52.6 (CH), 40.3 (CH_2), 31.4 (CH_2), 21.8 (CH_3), 14.1 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.52

HRMS (ESI, M+Na$^+$): m/z calcd. For $C_{35}H_{32}NNaO_4S_3F_3$ 706.1338, found 706.1334.

***(±)-Ethyl 2-(3,4-bis(phenylthio)-1-tosyl-1,2,5,6-tetrahydropyridin-2-yl)acetate* (12i):**

Reaction of the vinylogous carbamate **11i** (179 mg, 0.332 mmol) with CH_3SO_3H (43 µL, 0.664 mmol) in dry $(CH_2Cl)_2$ (4 mL), as described for the piperidine **12a** followed by purification on a silica gel column using EtOAc:Petroleum ether (1:9) as eluent furnished the required piperidine **12i** (149 mg, 83%) as a white solid.



12i

Physical appearance: white solid.

Melting Point: 111-113 °C.

R_f: (1:4 ethyl acetate-pet ether).

IR (neat): 2981, 2925, 1731, 1581, 1475, 1330, 1157, 748, 719, 693, 655 cm^{-1}.

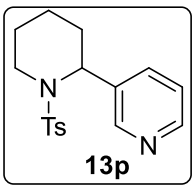
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46-7.38 (m, 6H), 7.33-7.24 (m, 4H), 7.22-7.18 (m, 4H), 4.76-4.74 (m, 1H), 4.04-3.92 (m, 2H), 3.80 (dd, *J* = 15.2, 6.8 Hz, 1H), 3.26-3.18 (m, 1H), 3.05 (dd, *J* = 14.4, 3.2 Hz, 1H), 2.57 (dd, *J* = 14.4, 9.2 Hz, 1H), 2.44 (s, 3H), 2.07-1.98 (m, 1H), 1.78 (dd, *J* = 18.0, 4.0 Hz, 1H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.0 (C), 143.3 (C), 141.5 (C), 137.5 (C), 134.5 (2 × CH), 132.8 (C), 130.8 (2 × CH), 129.6 (2 × CH), 129.3 (2 × CH), 129.0 (2 × CH), 128.7 (CH), 127.6 (2 × CH), 127.3 (2 × CH), 125.8 (C), 60.7 (CH_2), 54.9 (CH), 39.3 (CH_2), 38.3 (CH_2), 29.5 (CH_2), 21.6 (CH_3), 14.0 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. For $C_{28}H_{30}NO_4S_3$ 540.1331, found 540.1334.

***3-(1-tosylpiperidin-2-yl) pyridine* (13p):**

A solution of tetrahydropyridine **10p** (250 mg, 0.624 mmol) in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (1 mL) at reflux conditions. The suspension was stirred for 5h, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the piperidine **13p** (95.0 mg, 81% yield) as a colourless liquid.



13p

Physical appearance: colourless liquid.

R_f: 0.5 (1:1 ethyl acetate-pet ether).

IR (neat): 2932, 2861, 1587, 1455, 1355, 1158, 1100, 943, 815, 676 cm^{-1}.

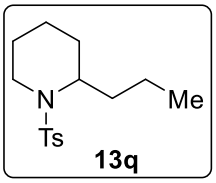
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52-8.48 (m, 2H), 7.74-7.72 (m, 3H), 7.30-7.28 (m, 3H), 5.25 (m, 1H), 3.84-3.80 (m, 1H), 2.95 (t, *J* = 12.0 Hz, 1H), 2.42 (s, 3H), 2.17 (d, *J* = 14.0 Hz, 1H), 1.71-1.64 (m, 1H), 1.54-1.51(m, 1H), 1.47-1.24 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 148.5 (CH), 148.3 (CH), 143.4 (C), 138.3 (C), 135.4 (CH), 134.8 (C), 129.9 (2 × CH), 127.1 (2 × CH), 123.6 (CH), 53.8 (CH), 42.1 (CH_2), 27.2 (CH_2), 24.2 (CH_2), 21.6 (CH_3), 19.0 (CH_2).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{17}H_{21}N_2O_2S$ is 317.1318, found 317.1320.

2-propyl-1-tosylpiperidine **(13q):**

A solution of tetrahydropyridine **10q** (149 mg, 0.300 mmol) in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (1 mL) at reflux conditions. The suspension was stirred for 5h, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the piperidine **13q** (66.0 mg, 78% yield) as a colourless liquid.



13q

Physical appearance: colourless liquid.

R_f: 0.5 (4:6 ethyl acetate- pet ether).

IR (neat): 2934, 2868, 1451, 1382, 1151, 1092, 931, 771 cm^{-1}.

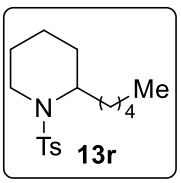
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 4.02-4.01 (m, 1H), 3.73 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.01-2.94 (m, 1H), 2.41 (s, 3H), 1.59-1.17 (m, 10H), 0.88 (t, *J* = 7.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 142.8 (C), 139.2 (C), 129.7 (2 × CH), 127.1 (2 × CH), 52.9 (CH), 40.7 (CH_2), 31.8 (CH_2), 27.5 (CH_2), 24.6 (CH_2), 21.6 (CH_3), 19.8 (CH_2), 18.5 (CH_2), 14.0 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{15}H_{24}NO_2S$ is 282.1522, found 282.1527

2-pentyl-1-tosylpiperidine **(13r):**

A solution of tetrahydropyridine **10r** (96 mg, 0.183 mmol) in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (1 mL) at reflux conditions. The suspension was stirred for 5h, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the piperidine **13r** (42.0 mg, 75% yield) as a viscous liquid.



13r

Physical appearance: viscous liquid.

R_f: 0.5 (4:6 ethyl acetate- pet ether).

IR (neat): 2927, 2860, 1332, 1150, 1092, 928, 809, 724, 697, cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 3.95 (dd, *J* = 11.2, 8.0 Hz, 1H), 3.70 (dd, *J* = 14.0, 3.6 Hz, 1H), 2.96-2.89 (m, 1H), 2.36 (s, 3H), 1.56-1.38 (m, 6H), 1.21-1.19 (m, 8H), 0.82 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 142.6 (C), 139.0 (C), 129.5 (2 × CH), 126.9 (2 × CH), 52.9 (CH), 40.5 (CH_2), 31.6 (CH_2), 29.3 (CH_2), 27.4 (CH_2), 26.1 (CH_2), 24.4 (CH_2), 22.5 (CH_2), 21.4 (CH_3), 18.4 (CH_2), 14.0 (CH_3).

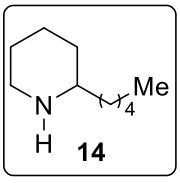
HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{17}H_{27}NNaO_2S$ is 332.1646, found 332.1655.

***2-pentylpiperidin*e (14):**

To a magnetically stirred solution of naphthalene (718 mg, 5.604 mmol) in dry THF (5.0 mL) was added sodium metal (129 mg, 5.604 mmol). The reaction mixture was stirred at room temperature for 45 minutes until a deep blue color formed. The reaction tube cooled at - 78 ° C and piperidine **13r** (289 mg, 0.934 mmol) in THF (5.0 mL) was added dropwise. Reaction was monitored by TLC, quenched with saturated aq. solution of NH_4Cl upon completion, extracted with EtOAc (3 × 5 mL) and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product obtained was purified on a basic alumina silica gel using ethyl acetate-petroleum ether as eluent furnished the piperidine derivative **14** (106 mg, 73%).

Physical appearance: colourless liquid.

R*f*: 0.5 (4:6 ethyl acetate- pet ether).



14

IR (neat): 2922, 2856, 1453, 1320, 1155, 876, 733 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.06-3.03 (m, 1H), 2.60 (dt, *J* = 11.6, 2.8 Hz, 1H), 2.42-2.39 (m, 1H), 1.85 (bs, 1H), 1.78-1.74 (m, 1H), 1.65-1.55 (m, 2H), 1.44-1.26 (m, 10H), 1.14-0.99 (m, 1H), 0.87 (t, *J* = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 57.0 (CH), 47.4 (CH_2), 37.6 (CH_2), 33.1 (CH_2), 32.2 (CH_2), 26.7 (CH_2), 25.7 (CH_2), 25.0 (CH_2), 22.8 (CH_2), 14.2 (CH_3).

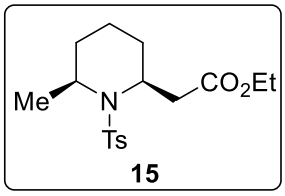
HRMS (ESI, M+H$^+$): m/z calcd. for $C_{10}H_{22}N$ is 156.1747, found 156.1749.

***Ethyl 2-((2S,6S)-6-methyl-1-tosylpiperidin-2-yl) acetate* (15):**

A solution of tetrahydropyridine **12a** (500 mg, 0.903 mmol) in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (5 mL) at reflux conditions. The suspension was stirred for overnight, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the piperidine **15** (245.0 mg, 80% yield) as a white solid.

Physical appearance: white solid.

Melting Point: 78-80 °C



15

R_f: 0.5 (1:4 ethyl acetate- pet ether).

$[\alpha]_D$ ^{25}: -11.272 (c 0.750, $CHCl_3$).

IR (neat): 2933**,** 2863, 1730, 1324, 1162, 1021, 602, 550 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 4.44-4.40 (m, 1H), 4.21-4.16 (m, 1H), 4.15-4.06 (m, 2H), 2.79-2.67 (m, 2H), 2.39 (s, 3H), 1.64-1.40 (m, 4H), 1.36-1.24 (m, 8H).

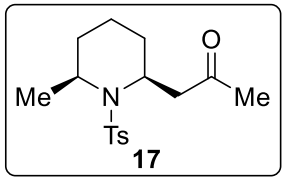
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 171.2 (C), 142.9 (C), 138.6 (C), 129.7 (2 ×CH), 126.8 (2 ×CH), 60.7 (CH_2), 48.7 (CH), 47.9 (CH), 40.3 (CH_2), 29.5 (CH_2), 27.5 (CH_2) 22.0 (CH_3), 21.6 (CH_3), 14.2 (CH_3), 13.4 (CH_2).

HRMS (ESI, M+Na^+): m/z calcd. For $C_{17}H_{25}NO_4SNa$ 362.1397, found 362.1405.

1-((2S,6S)-6-methyl-1-tosylpiperidin-2-yl) propan-2-one **(17):**

To a cold (-20 °C), magnetically stirred solution of ester **15** (185 mg, 0.545 mmol) and N,O-dimethylhydroxylamine hydrochloride in dry THF (10 mL) was added freshly prepared isopropyl magnesium bromide (240 mg, 1.635 mmol). The reaction mixture was stirred at the same temperature for 2 h and then allowed to warm to room temperature. The reaction mixture was extracted with EtOAc (3 × 5 mL), washed with brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent furnished the crude Weinreb amide.

The crude mixture was then subjected to reaction with freshly prepared methyl magnesium iodide (154 mg, 0.926mmol) (prepared from iodomethane and magnesium in Et_2O) in dry THF at −78 °C. The reaction mixture was stirred at this temperature for 2 h and then allowed to warm to room temperature for another 14 h. The reaction mixture was extracted with EtOAc (3 × 5 mL), washed with brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by purification of the residue by silica gel column chromatography using EtOAc/petroleum ether (1:9) as eluent furnished the required ketone derivative **17** (94 mg, 56%) as a colourless liquid over two steps.



17

Physical appearance: colourless liquid.

R_f: 0.6 (1:4 ethyl acetate- pet ether).

$[\alpha]_D$ ^{25}: -6.557 (c 0.220, $CHCl_3$).

IR (neat): 2927**,** 2857, 2360, 1712, 1324, 1162, 662 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 4.40 (m, 1H), 4.20 (t, *J* = 6.4 Hz, 1H), 2.95-2.81 (m, 2H), 2.39 (s, 3H), 2.15 (s, 3H), 1.59-1.20 (m, 9H).

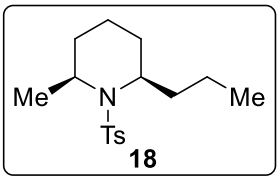
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 206.4 (C), 143.0 (C), 138.5 (C), 129.7 (2 × CH), 126.7 (2 × CH), 49.5 (CH_2), 48.0 (CH), 47.6 (CH), 30.4 (CH_3), 29.6 (CH_2), 27.6 (CH_2), 22.1 (CH_3), 21.6 (CH_3), 13.4 (CH_2).

HRMS (ESI, M+Na$^+$): m/z calcd. For $C_{16}H_{23}NO_3SNa$ 332.1291, found 332.1297.

***(2S,6R)-2-methyl-6-propyl-1-tosylpiperidine* (18):**

To a cold (0 ºC), magnetically stirred solution of the ketone **17** (77 mg, 0.249 mmol) in dry (CH_2Cl_2) (3 mL) was added 1,2-ethanedithiol (21 µL, 0.249 mmol) and $BF_3{\cdot}OEt_2$ (31 µL, 0.249 mmol). The reaction mixture was slowly allowed to warm up to rt, stirred for another 3h. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4) which afforded crude dithiane. Crude dithiane was subjected to Raney-Ni in 5 mL EtOH. The suspension was stirred for 2h, then the mixture was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the piperidine **18** (46.0 mg, 63% yield) as a colourless liquid over two steps.

Physical appearance: colourless liquid.



18

R_f: 0.5 (1:4 ethyl acetate- pet ether).

[α]$_D$ ^{25}: -5.773 (c 0.715, $CHCl_3$).

IR (neat): 2937**,** 2866, 1457, 1330, 1335, 1163, 1022, 661, 547 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 2H), 4.16-4.09 (m, 1H), 4.01-3.96 (m, 1H), 2.40 (s, 3H), 1.73-1.47 (m, 5H), 1.42-1.24 (m, 7H), 0.92 (t, *J* = 7.2 Hz, 3H).

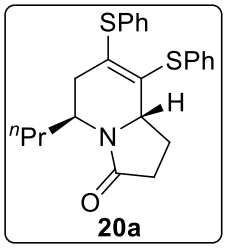
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 142.6 (C), 139.2 (C), 129.7 (2 × CH), 126.9 (2 × CH), 52.6 (CH), 48.1 (CH), 37.9 (CH_2), 29.4 (CH_2), 27.4 (CH_2), 21.9 (CH_3), 21.6 (CH_3), 20.7 (CH_2), 14.1 (CH_3), 13.8 (CH_2).

HRMS (ESI, M+Na$^+$): m/z calcd. For $C_{16}H_{25}NO_2SNa$ 318.1498, found 318.1503.

***(5S*,8aS*)-7,8-bis(phenylthio)-5-propyl-1,5,6,8a-tetrahydroindolizin-3(2H)-one* (20a):**

To a cold (0 ºC), magnetically stirred solution of the hydroxypyrrolidine-2-one **19a** (167 mg, 0.404 mmol) in dry ($CH_2Cl)_2$ (4 mL) was added CH_3SO_3H (26 µL, 0.404 mmol). The reaction mixture was slowly allowed to reflux to 80 ºC, stirred for overnight and quenched by adding sat. $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent followed by purification of the residue

on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent to furnished the required tetrahydroindolizine derivative **20a** (111 mg, 70%) as a viscous liquid.



Physical appearance: viscous liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2956, 2928, 1689, 1577, 1474, 1436, 744, 693 cm^{-1}.

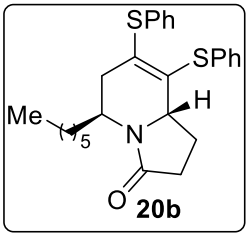
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.31 (m, 9H), 7.24-7.22 (m, 1H), 4.30-4.25 (m, 1H), 4.10 (t, *J* = 7.2 Hz, 1H), 2.45 (ddd, *J* = 17.2, 6.4, 2.8 Hz, 1H), 2.35-2.25 (m, 3H), 2.05-2.00 (m, 1H), 1.79-1.70 (m, 1H), 1.60-1.50 (m, 1H), 1.40-1.31 (m, 1H), 1.26-1.12 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 173.1 (C), 140.2 (C), 134.1 (C), 134.0 (2 × CH), 131.8 (C), 129.4 (2 × CH), 129.3 (4 × CH), 128.6 (CH), 127.0 (CH), 126.8 (C), 56.0 (CH), 45.7 (CH), 35.2 (CH_2), 33.6 (CH_2), 31.4 (CH_2), 26.5 (CH_2), 19.4 (CH_2), 13.9 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{23}H_{26}NOS_2$ is 396.1450, found 396.1451.

(5S*,8aS*)-5-hexyl-7,8-bis(phenylthio)-1,5,6,8a-tetrahydroindolizin-3(2H)-one **(20b):**

To a cold (0 ^oC), magnetically stirred solution of the hydroxypyrrolidine-2-one **19b** (173 mg, 0.379 mmol) in dry $(CH_2Cl)_2$ (4 mL) was added CH_3SO_3H (25 μL, 0.379 mmol). The reaction mixture was slowly allowed to reflux to 80 ^oC, stirred for overnight and quenched by adding sat. $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent followed by purification of the residue on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent to furnished the required tetrahydroindolizine derivative **20b** (125 mg, 75%) as a viscous liquid.



Physical appearance: viscous liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 3057, 2925, 2855, 1691, 1577, 1409, 744, 692 cm^{-1}.

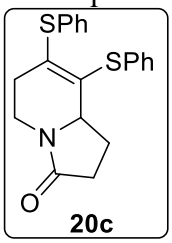
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.29 (m, 9H), 7.24-7.20 (m, 1H), 4.27-4.23 (m, 1H), 4.10-4.07 (m, 1H), 2.44 (ddd, *J* = 17.6, 6.4, 3.2 Hz, 1H), 2.34-2.26 (m, 3H), 2.04-2.00 (m, 1H), 1.76-1.71 (m, 1H), 1.56-1.49 (m, 1H), 1.41-1.32 (m, 1H), 1.27-1.08 (m, 8H), 0.85 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 173.0 (C), 140.1 (C), 134.0 (C), 134.0 (2 × CH), 131.7 (C), 129.3 (2 × CH), 129.2 (4 × CH), 128.6 (CH), 128.2 (C), 126.9 (CH), 126.7 (C), 55.9 (CH), 45.9 (CH), 35.1 (CH_2), 31.6 (CH_2), 31.3 (2 ×CH_2), 29.0 (CH_2), 26.5 (CH_2), 25.9 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{26}H_{32}NOS_2$ is 438.1920, found 438.1938.

***7,8-bis(phenylthio)-1,5,6,8a-tetrahydroindolizin-3(2H)-one* (20c):**

To a cold (0 °C), magnetically stirred solution of the hydroxypyrrolidine-2-one **19c** (239 mg, 0.569 mmol) in dry $(CH_2Cl)_2$ (4 mL) was added CH_3SO_3H (18 μL, 0.284 mmol). The reaction mixture was slowly allowed to warm up to rt, stirred for overnight and quenched by adding sat. $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent followed by purification of the residue on a silica gel column using EtOAc: Petroleum ether (1:9) as eluent to furnished the required tetrahydroindolizine derivative **20c** (100 mg, 50%) as a colourless liquid.



20c

Physical appearance: colourless liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 3060, 2985, 2926, 1685, 1571, 1422, 1310, 1193, 746, 694 cm^{-1}.

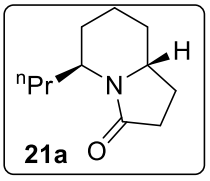
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.20 (m, 10H), 4.20-4.08 (m, 2H), 2.82 (td, *J* = 12.4, 4.4 Hz, 1H), 2.36-2.25 (m, 4H), 2.14-2.01 (m, 1H), 1.80-1.69 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 173.0 (C), 141.5 (C), 134.1 (2 × CH), 133.9 (C), 131.4 (C) 129.3 (6 × CH), 128.7 (CH), 127.5 (C), 126.9 (CH), 59.0 (CH), 36.6 (CH_2), 31.4 (CH_2), 31.0 (CH_2), 26.5 (CH_2).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{20}H_{20}NOS_2$ is 354.0981, found 354.0991.

***(5S*,8aR*)-5-propylhexahydroindolizin-3(2H)-one* (21a):**

A solution of tetrahydroindolizine **20a** (548 mg, 0.510 mmol) in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (1 mL) at reflux conditions. The suspension was stirred for 5h, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the indolizidine **21a** (186.0 mg, 74% yield) as a colourless liquid.



21a

Physical appearance: colourless liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2958, 2870, 1665, 1570, 668, 646 cm^{-1}.

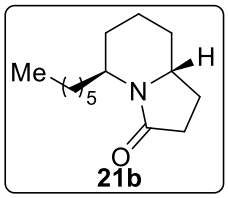
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.18-4.13 (m, 1H), 3.55-3.47 (m, 1H), 2.32-2.28 (m, 2H), 2.16-2.08 (m, 1H), 1.80-1.77 (m, 1H), 1.59-1.43 (m, 6H), 1.39-1.28 (m, 1H), 1.26-1.16 (m, 2H), 1.14-1.03 (m, 1H), 0.86 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 173.6 (C), 53.2 (CH), 47.8 (CH), 33.9 (CH_2), 32.3 (CH_2), 30.4 (CH_2), 27.5 (CH_2), 25.3 (CH_2), 19.6 (CH_2), 19.0 (CH_2), 14.0 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{11}H_{20}NO$ is 182.1539, found 182.1547.

***(5S*,8aR*)-5-hexylhexahydroindolizin-3(2H)-one* (21b):**

A solution of tetrahydroindolizine **20b** (129 mg, 0.295 mmol) in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (1 mL) at reflux conditions. The suspension was stirred for 5h, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the indolizidine **21b** (50.0 mg, 76% yield) as a colourless liquid.



21b

Physical appearance: colourless liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2926, 2853, 1688, 1463, 1416, 637, 614 cm^{-1}.

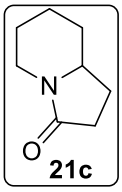
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.19-4.15 (m, 1H), 3.57-3.52 (m, 1H), 2.35-2.30 (m, 2H), 2.19-2.12 (m, 1H), 1.83-1.81 (m, 1H), 1.61-1.38 (m, 7H), 1.27-1.25 (m, 8H), 1.16-1.08 (m, 1H), 0.85 (t, *J* = 5.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 173.7 (C), 53.3 (CH), 48.2 (CH), 34.0 (CH_2), 31.9 (CH_2), 30.5 (CH_2), 30.2 (CH_2), 29.4 (CH_2), 27.5 (CH_2), 26.4 (CH_2), 25.4 (CH_2), 22.7 (CH_2), 19.1 (CH_2), 14.2 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{14}H_{26}NO$ is 224.2009, found 224.2009.

***hexahydroindolizin-3(2H)-one* (21c):**

A solution of tetrahydroindolizine **20c** (135 mg, 0.381 mmol) in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (1 mL) at reflux conditions. The suspension was stirred for 5h, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the indolizidine **21c** (45.0 mg, 85% yield) as a colourless liquid.



21c

Physical appearance: colourless liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2966, 2848, 1590, 1485, 1219, 772, 672 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.12-4.07 (m, 1H), 3.41-3.37 (m, 1H), 2.60 (t, *J* = 12.8 Hz, 1H), 2.37-2.32 (m, 2H), 2.22-2.16 (m, 1H), 1.88-1.83 (m, 2H), 1.69-1.54 (m, 2H), 1.41-1.23 (m, 2H), 1.18-1.08 (m, 1H).

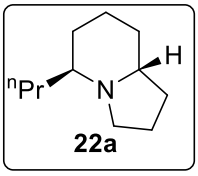
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 173.9 (C), 57.5 (CH), 40.4 (CH_2), 33.7 (CH_2), 30.4 (CH_2), 25.4 (CH_2), 24.5 (CH_2), 23.8 (CH_2).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_8H_{14}NO$ is 140.1070, found 140.1069.

***(5S*,8aR*)-5-propyloctahydroindolizine* (22a):**

To a cold (0 ºC), magnetically stirred solution of the indolizidine **21a** (138 mg, 0.760 mmol) in dry THF (4 mL) was added LAH (87 mg, 2.280 mmol). The reaction mixture was slowly allowed to warm up to rt, stirred for overnight and quenched by adding 2-3 drops of sat. Na_2SO_4. The reaction mixture was filtered off with ethyl acetate. Evaporation of the solvent furnished the required indolizidine **22a** (115 mg, 91%) as a colourless liquid.[1]

Physical appearance: colourless liquid.



22a

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2954, 2835, 1588, 1491, 772, 674 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.90-2.87 (m, 1H), 2.77 (td, *J* = 8.8, 3.2 Hz, 1H), 2.62-2.56 (m, 1H), 2.42-2.40 (m, 1H), 1.79-1.68 (m, 3H), 1.62-1.52 (m, 3H), 1.51-1.40 (m, 3H), 1.38-1.21 (m, 3H), 1.16-1.10 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H).

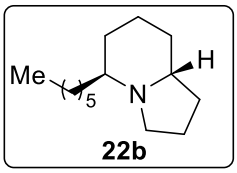
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 55.3 (CH), 55.2 (CH), 48.8 (CH_2), 31.4 (CH_2), 30.7 (CH_2), 27.7 (CH_2), 25.8 (CH_2), 21.0 (CH_2), 20.9 (CH_2), 19.4 (CH_2), 14.5 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{11}H_{22}N$ is 168.1747, found 168.1748.

***(5S*,8aR*)-5-hexyloctahydroindolizine* (22b):**

To a cold (0 ºC), magnetically stirred solution of the indolizidine **21b** (30 mg, 0.134 mmol) in dry THF (3 mL) was added LAH (15 mg, 0.403 mmol). The reaction mixture was slowly allowed to warm up to rt, stirred for overnight and quenched by adding 2-3 drops of sat. Na_2SO_4. The reaction mixture was filtered off with ethyl acetate. Evaporation of the solvent furnished the required indolizidine **22b** (29 mg, 90%) as a colourless liquid.[1]

Physical appearance: colourless liquid.



22b

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2924, 2854, 1584, 1465, 772, 668 cm^{-1}.

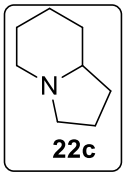
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.92-2.89 (m, 1H), 2.82 (td, *J* = 8.8, 3.2 Hz, 1H), 2.67-2.60 (m, 1H), 2.48-2.46 (m, 1H), 1.83-1.72 (m, 3H), 1.66-1.56 (m, 3H), 1.55-1.41 (m, 3H), 1.40-1.25 (m, 10H), 1.18-1.13 (m, 1H), 0.88 (t, *J* = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 55.7 (CH), 55.3 (CH), 49.0 (CH_2), 32.0 (CH_2), 31.3 (CH_2), 30.8 (CH_2), 29.8 (CH_2), 27.8 (CH_2), 27.7 (CH_2), 23.7 (CH_2), 22.8 (CH_2), 21.0 (CH_2), 19.5 (CH_2), 14.2 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{14}H_{28}N$ is 210.2216, found 210.2216.

***Octahydroindolizine* (22c):**

To a cold (0 ºC), magnetically stirred solution of the indolizidine **21c** (29 mg, 0.208 mmol) in dry Et_2O (4 mL) was added LAH (16 mg, 0.417 mmol). The reaction mixture was slowly allowed to warm up to rt, stirred for overnight and quenched by adding 2-3 drops of sat. Na_2SO_4. The reaction mixture was filtered off with Et_2O. Evaporation of the solvent furnished the required octahydroindolizine **22c** (22 mg, 84%) as a colourless liquid.



Physical appearance: colourless liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2954, 2923, 2853, 1463, 771, 699 cm^{-1}.

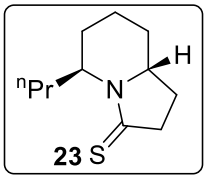
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.12-3.03 (m, 2H), 2.08 (q, *J* = 9.0 Hz, 1H), 1.98 (td, *J* = 11.2, 3.2 Hz, 1H), 1.85-1.73 (m, 5H), 1.67-1.57 (m, 3H), 1.46-1.39 (m, 1H), 1.28-1.16 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 64.6 (CH), 54.3 (CH_2), 53.2 (CH_2), 31.0 (CH_2), 30.6 (CH_2), 25.5 (CH_2), 24.6 (CH_2), 20.8 (CH_2).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_8H_{16}N$ is 126.1277, found 126.1279.

***(5S*,8aR*)-5-propylhexahydroindolizine-3(2H)-thione* (23):**

To a magnetically stirred solution of lactam **21b** (76 mg, 0.419 mmol) in toluene, lawesson reagent (136 mg, 0.335 mmol) was added at room temperature and reaction mixture was allowed to heat at 120 ºC for 2 h, then solvent was evaporated to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:3) gave thio lactam **23** (74.0 mg, 88% yield) as a sticky liquid.[2]



Physical appearance: sticky liquid.

R_f: 0.5 (1:3 ethyl acetate- pet ether).

IR (neat): 2938, 2862, 1470, 1304, 1123, 790 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.96-4.91 (m, 1H), 3.86-3.79 (m, 1H), 3.02-2.82 (m, 2H), 2.21-2.16 (m, 1H), 1.92-1.72 (m, 1H), 1.69-1.17 (m, 10H), 0.89 (t, *J* = 7.6 Hz, 3H).

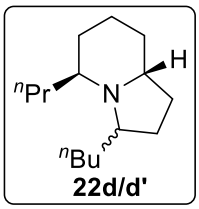
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 198.7 (C), 61.2 (CH), 53.1 (CH), 43.5 (CH_2), 33.7 (CH_2), 31.6 (CH_2), 26.7 (2 ×CH_2), 19.5 (CH_2), 18.2 (CH_2), 14.0 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{11}H_{20}NS$ is 198.1311, found 198.1315

***(5S*,8aR*)-3-butyl-5-propyloctahydroindolizine* (22d/d'):**

Thiolactam **23** (85 mg, 0.431 mmol) was dissolved in anhydrous THF (3mL) then iodomethane was added to the solution for 14h, and then excess iodomethane was evaporated. To a cooled solution (-20 °C) of CuI (246 mg, 1.293 mmol) in anhyd. THF was added (1.6mL, 2.586 mmol) *n*-BuLi. Mixture was cooled to -60 °C and stirred for an hour. Then, iminium

salt solution was added and the mixture was stirred at -60 °C for 5 min, then temperature was increased to -10 °C followed by addition of $NaBH_4$ (65 mg, 1.724 mmol) and glacial acetic acid (0.5 mL). After that, the reaction was quenched with solid Na_2CO_3. The reaction mixture was extracted with ethyl acetate (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent followed by purification of the residue on a basified silica gel column using EtOAc: Petroleum ether (1:1) as eluent to furnished the required indolizidine derivatives **22d/22d'** (52.0 mg, 54%) with dr = 1.2:1 as a colourless liquid. [2]



22d/d'

Physical appearance: colourless liquid.

R_f: 0.5 (ethyl acetate).

IR (neat): 2957, 2924, 2855, 1587, 1501, 817, 621cm^{-1}.

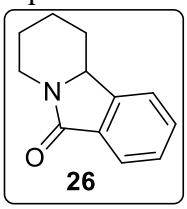
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.26-3.20 (m, 0.8H), 3.07-3.03 (m, 1H), 2.95-2.88 (m, 0.8H), 2.72-2.67 (m, 0.8H), 2.58-2.51 (m, 1H), 2.44-2.37 (m, 1H), 2.03-1.93 (m, 2H), 1.80-1.69 (m, 8H), 1.59-1.41 (m, 7H), 1.40-1.08 (m, 21H), 0.93-0.87 (m, 10.8H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 58.6 (CH), 56.4 (CH), 55.1 (CH), 52.6 (CH), 52.5 (CH), 36.1 (CH_2), 35.6 (CH_2), 32.6 (CH_2), 29.6 (CH_2), 29.2 (CH_2), 28.9 (2 ×CH_2), 28.7 (CH_2), 28.4 (CH_2), 27.9 (CH_2), 27.3 (CH_2), 23.3 (CH_2), 23.2 (CH_2), 23.0 (2 ×CH_2), 20.9 (CH_2), 20.5 (CH_2), 19.5 (CH_2), 19.4 (CH_2), 14.6 (CH_3), 14.4 (CH_3), 14.3 (2 ×CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{15}H_{30}N$ is 224.2373, found 224.2372.

***1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one* (26):**

To a cold (0 ºC), magnetically stirred solution of the hydroxypyrrolidine-2-one **24** (239 mg, 0.569 mmol) in dry $(CH_2Cl)_2$ (4 mL) was added CH_3SO_3H (18 μL, 0.284 mmol). The reaction mixture was slowly allowed to come to room temperature, stirred for overnight and quenched by adding sat. $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent furnished the required crude tetrahydroindolizine derivative **25** as a pale-yellow sticky solid. Then, solution of crude tetrahydroindolizine **25** in EtOH (5 mL) was added in one portion to a stirred suspension of Raney-Ni (W2) (approximate weight) in the same solvent (3 mL) at reflux conditions. The suspension was stirred for 5h, then the solid was filtered off and washed with EtOH. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography on silica gel using Ethyl acetate: Petroleum ether (1:9 gave the indolizidine **26** (66.0 mg, 62% yield) as a viscous liquid.



26

Physical appearance: viscous liquid.

R_f: 0.5 (3:7 ethyl acetate-pet ether).

IR (neat): 2934, 2858, 1653, 1410, 1291, 982, 763, 727 cm^{-1}.

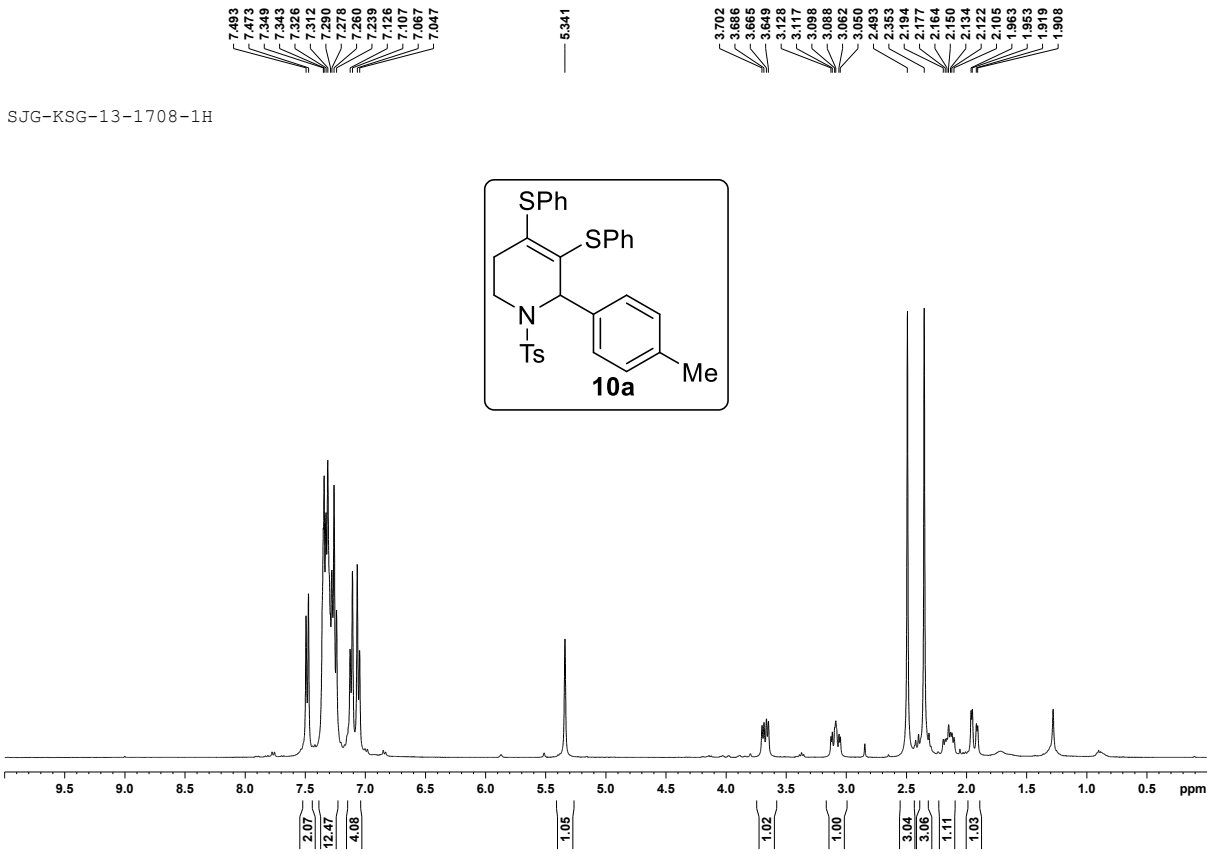
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 6.0 Hz, 1H), 7.50 (t, *J* = 5.6 Hz, 1H), 7.45-7.39 (m, 2H), 4.47 (dd, *J* = 10.4, 4.0 Hz, 1H), 4.25 (dd, *J* = 9.6, 2.8 Hz, 1H), 2.96 (td, *J* = 10.4, 2.8 Hz, 1H), 2.36-2.32 (m, 1H), 2.00-1.97 (m, 1H), 1.82-1.79 (m, 1H), 1.70-1.60 (m, 1H), 1.43-1.33 (m, 1H), 1.10 (qd, *J* = 10.0, 2.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 166.3 (C), 145.8 (C), 132.5 (C), 131.2 (CH), 128.1 (CH), 123.8 (CH), 121.7 (CH), 59.0 (CH), 39.7 (CH_2), 31.8 (CH_2), 25.4 (CH_2), 23.8 (CH_2).

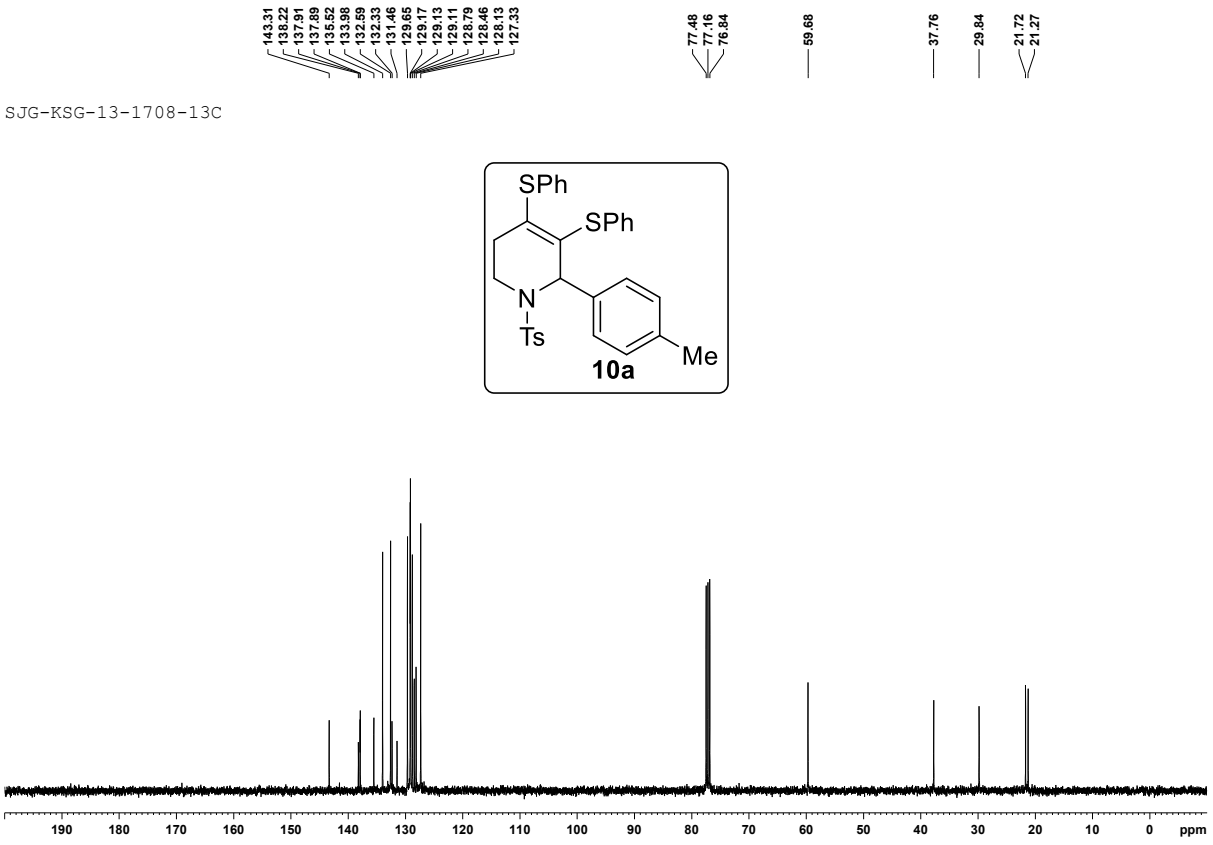
HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{12}H_{14}NONa$ is 210.0889, found 210.0889.

References

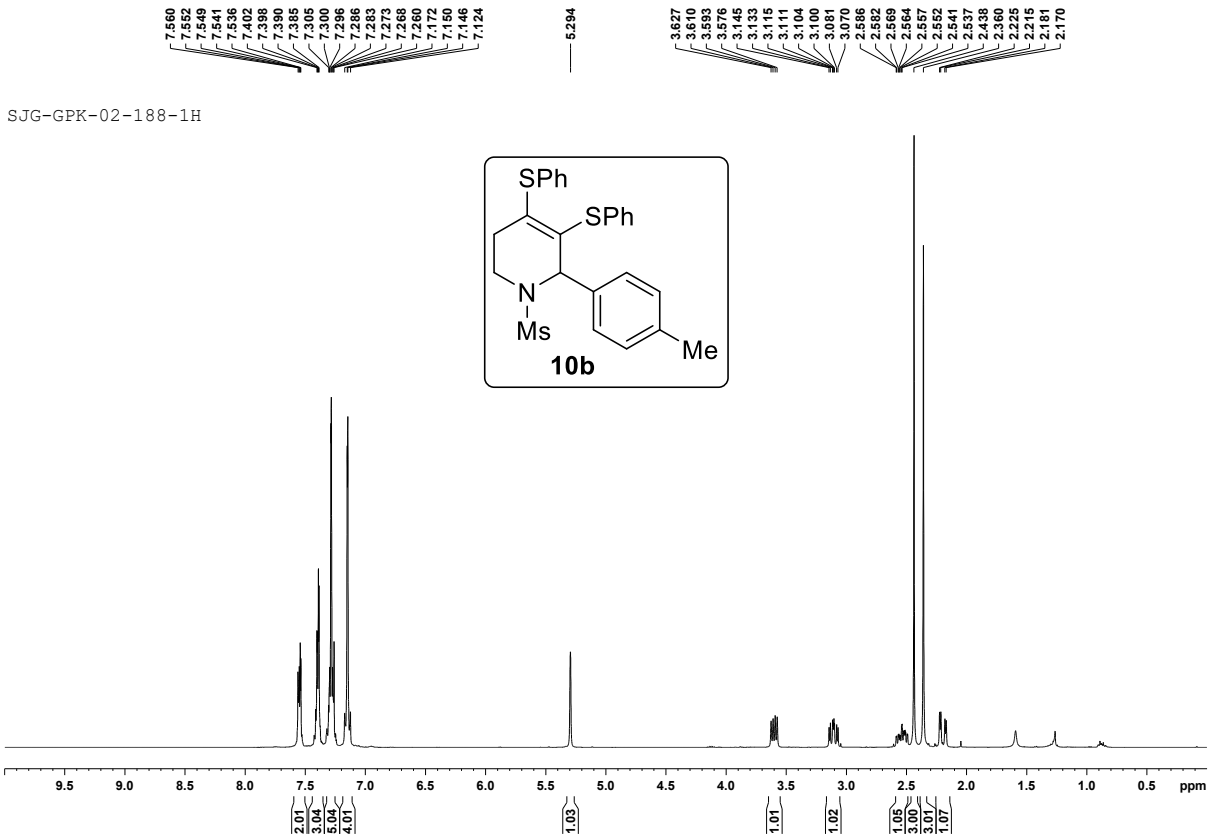
1. Saikia, A. K.; Indukuri, K.; Das, J. Stereoselective Synthesis of O-Tosyl Azabicyclic Derivatives via Aza Prins Reaction of Endocyclic *N*-Acyliminium Ions: Application to the Total Synthesis of (±)-*Epi*-Indolizidine 167B and 209D. *Org. Biomol. Chem.* **2014**, *12* (36), 7026–7035.
2. Chang, K.-C.; Wang, L.-Y.; Li, C.-C.; Huang, R.-J.; Zhang, Z.-F.; Liang, Y.-F.; Su, M.-D.; Li, Y.-J. Total Synthesis of Poison Dart-Frog Alkaloids (−)-209D, (−)-209B, (−)-223V, 3-Epi-(−)-223AB. *ChemSelect.* **2024***, 9* (33)*,* e202403037



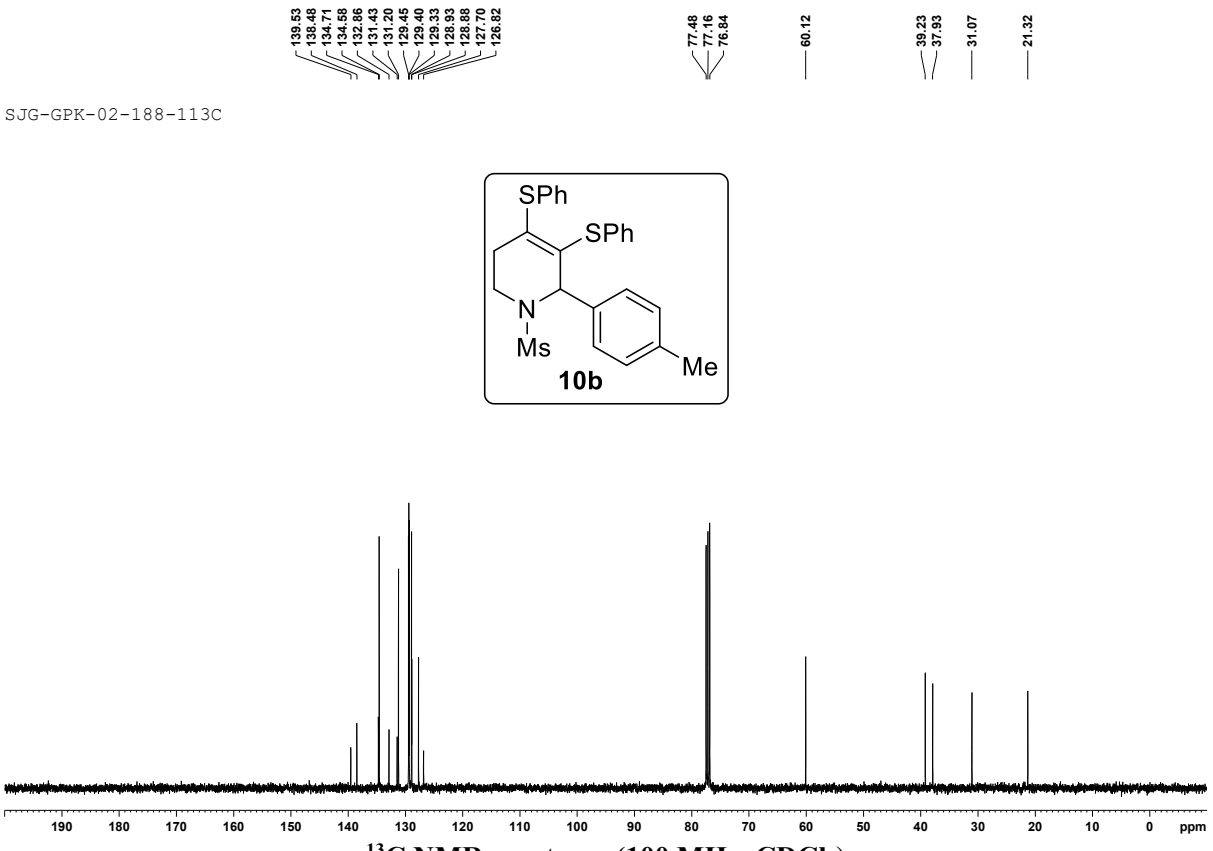
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



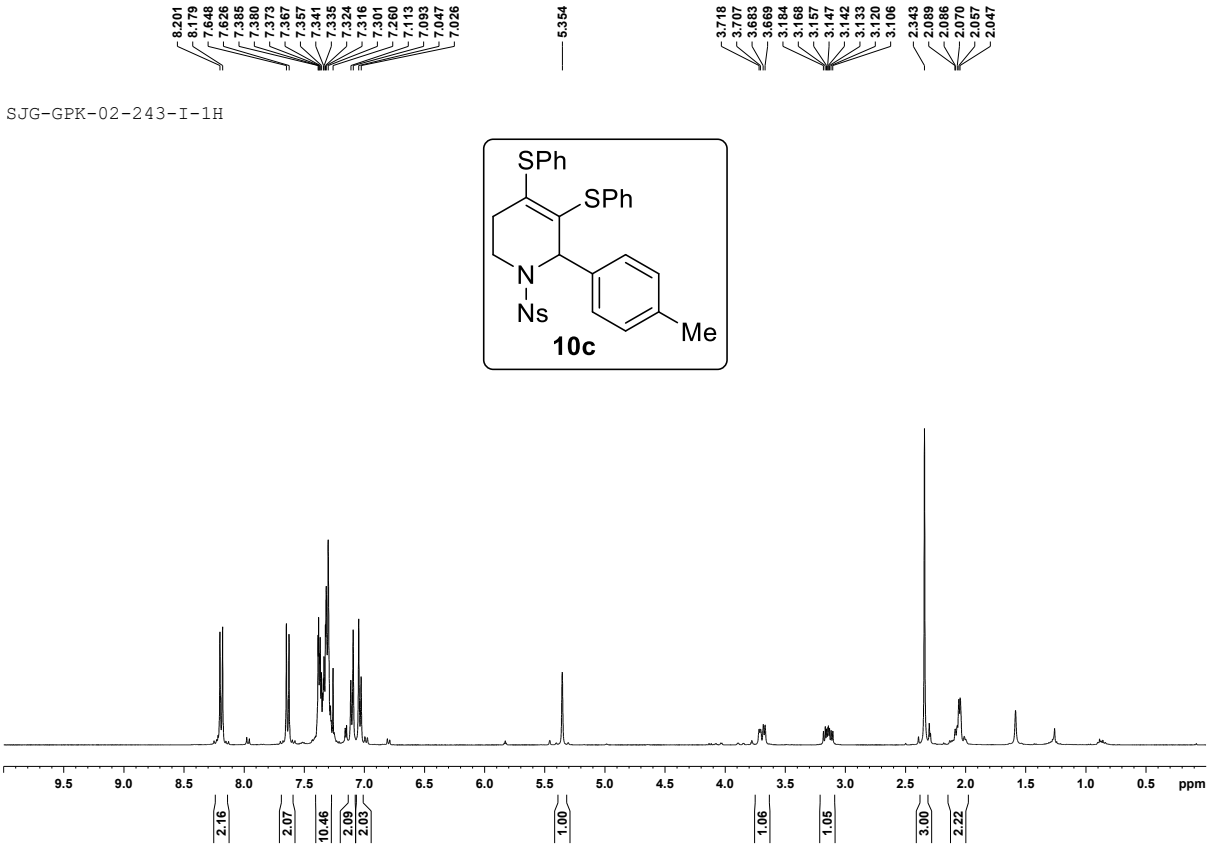
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



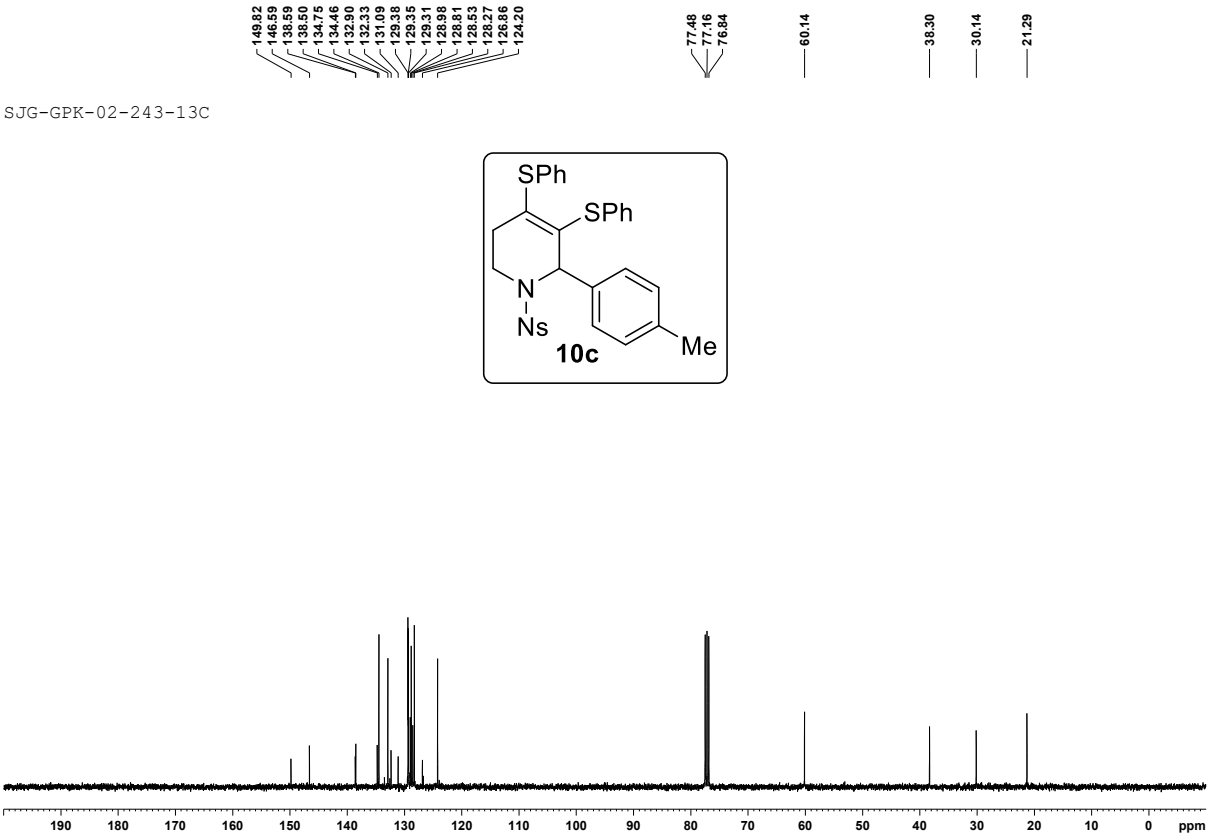
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



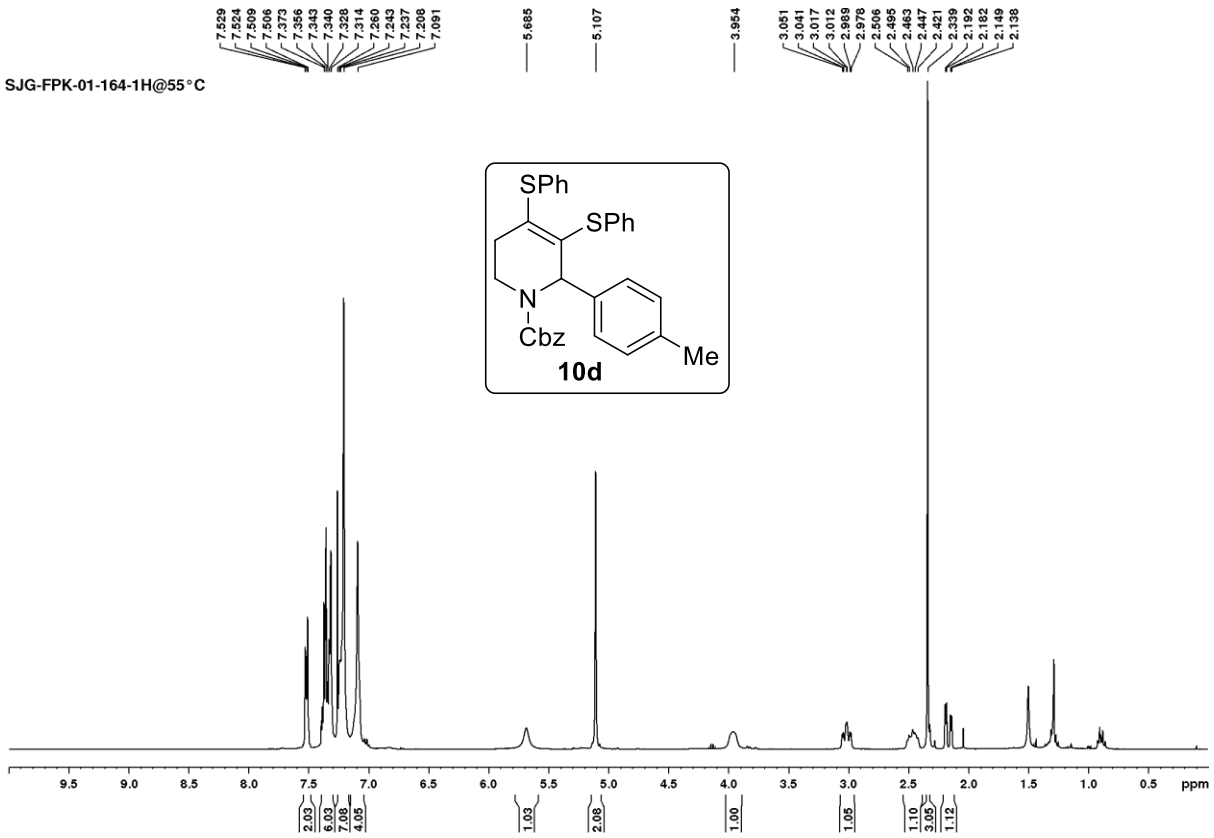
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



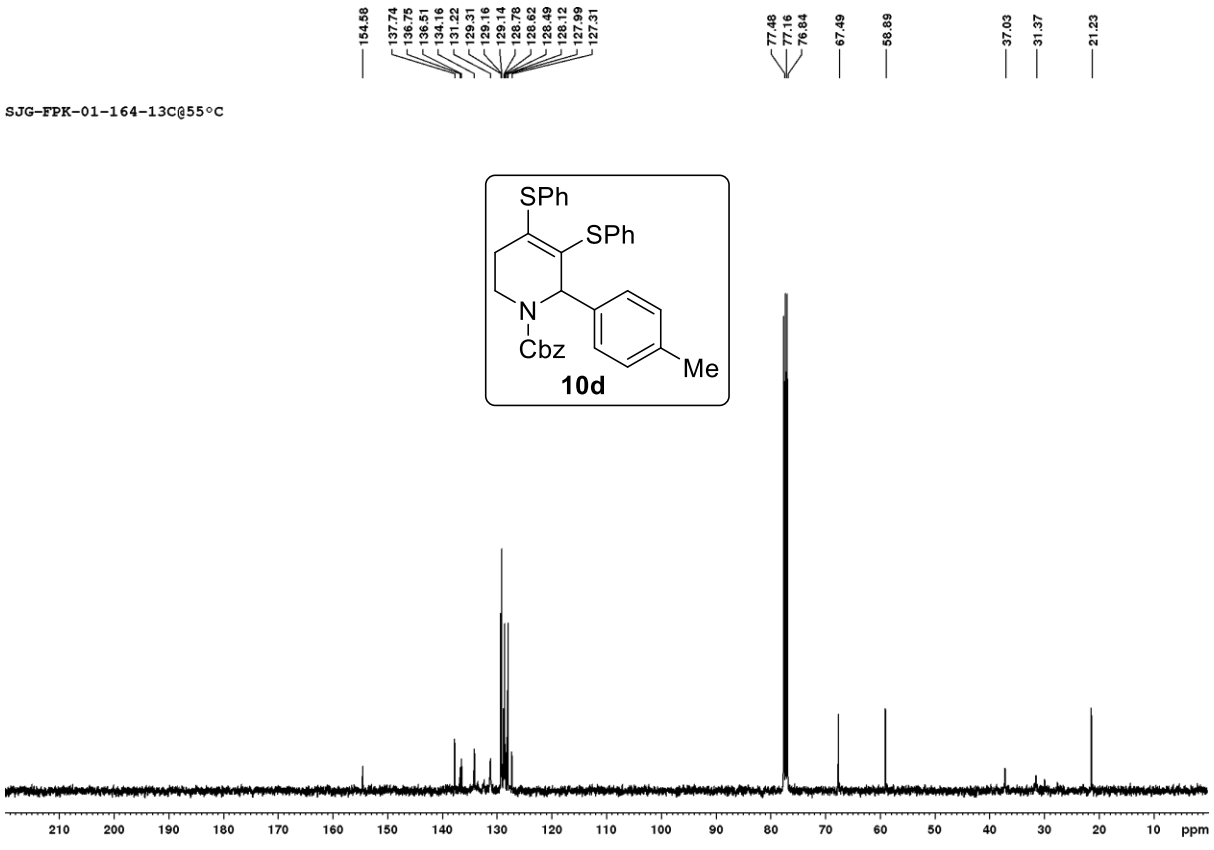
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



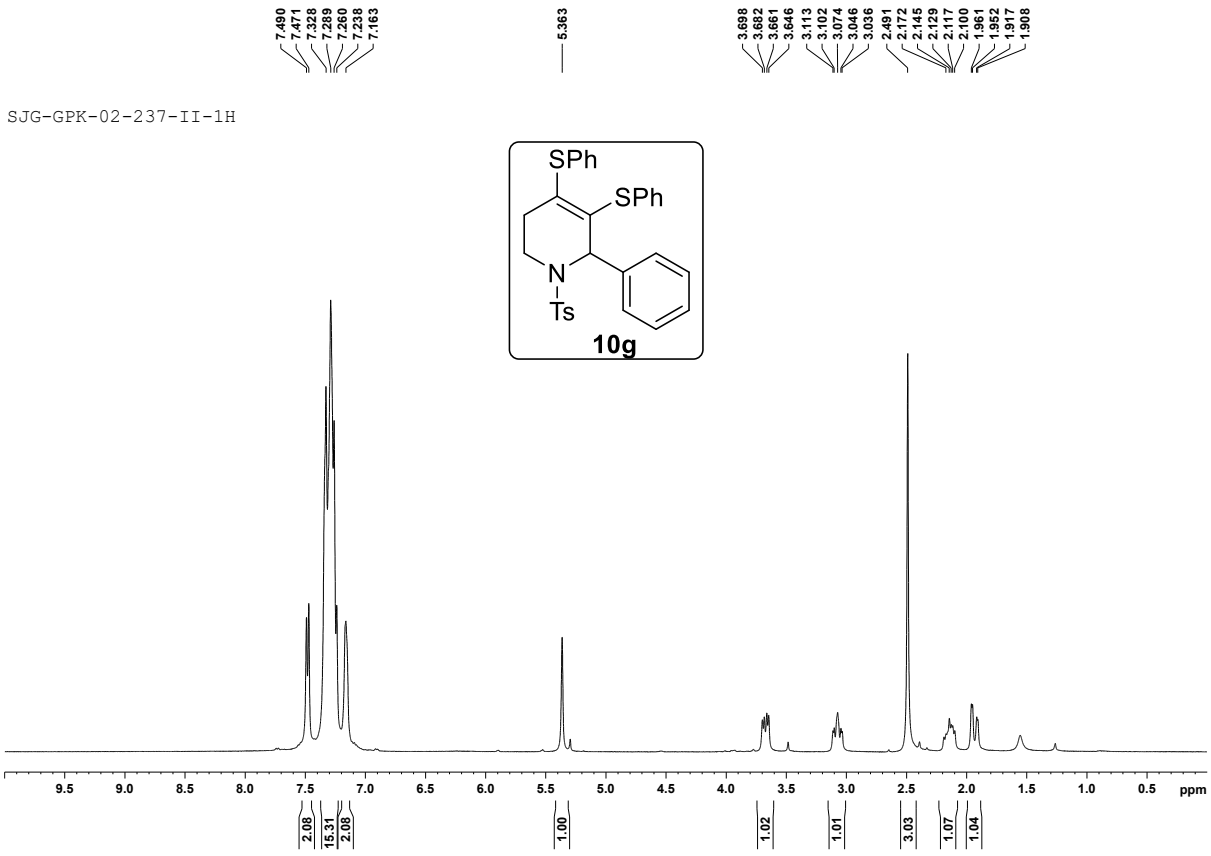
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



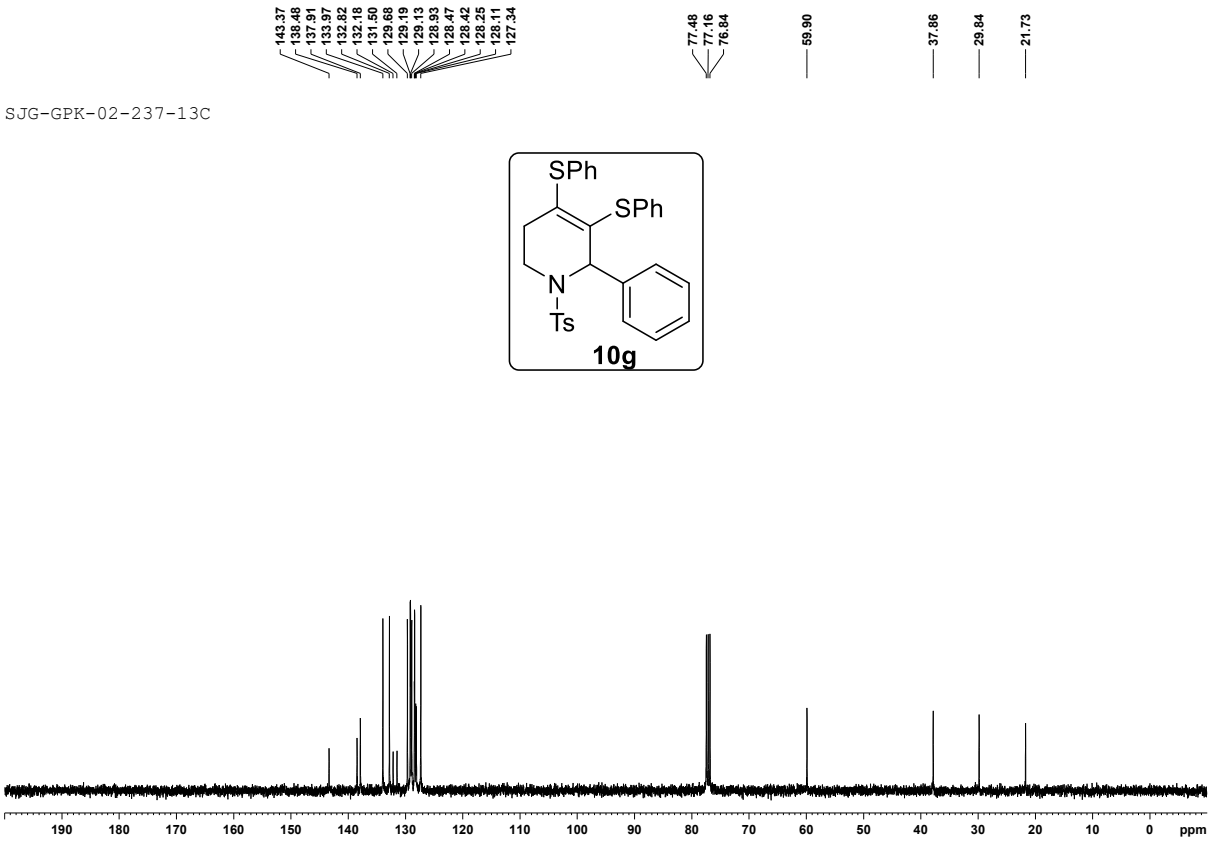
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



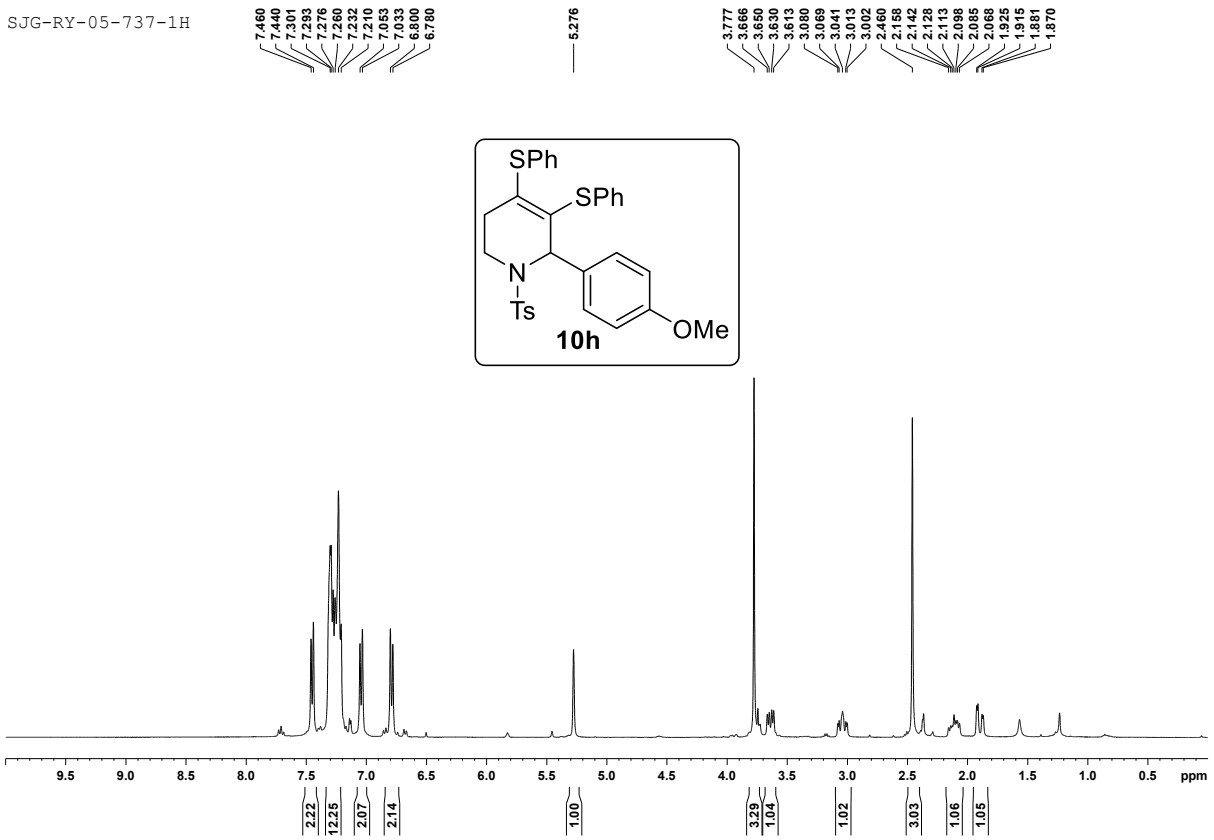
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



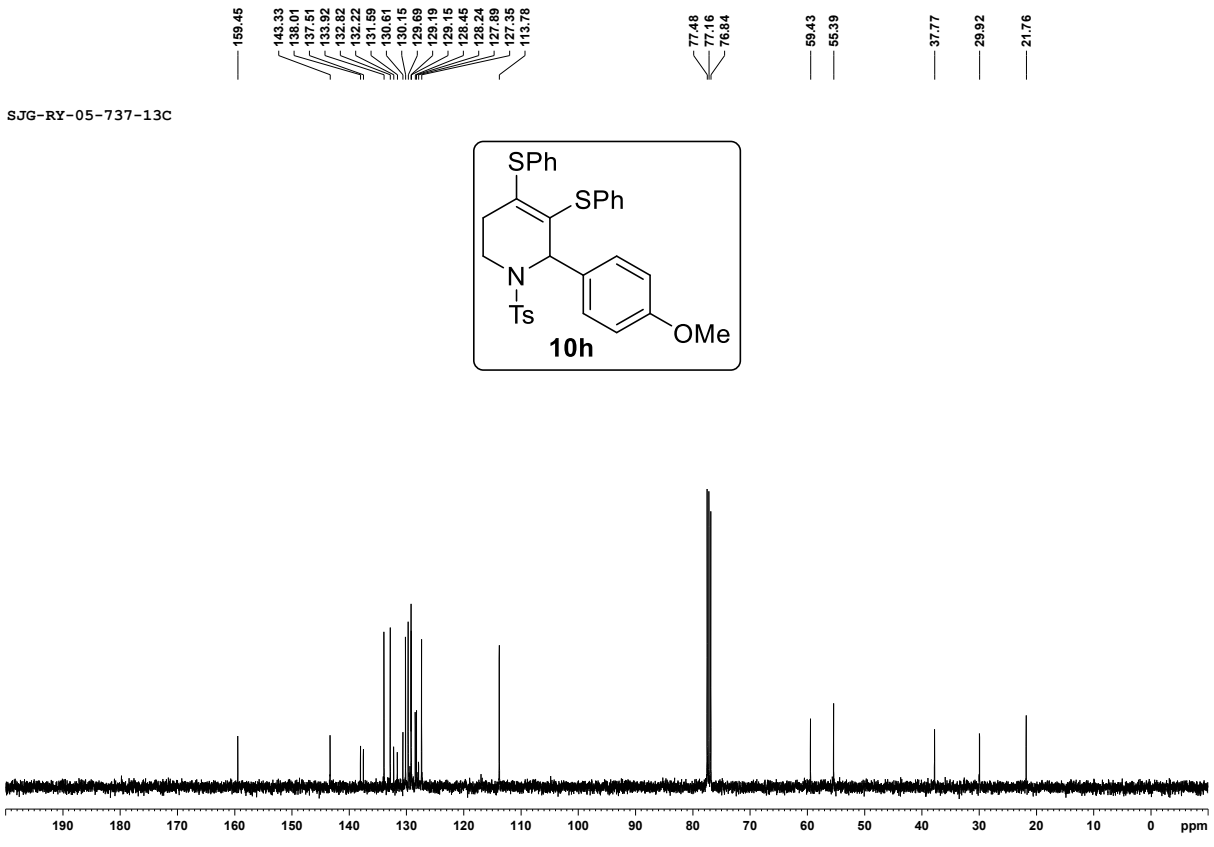
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



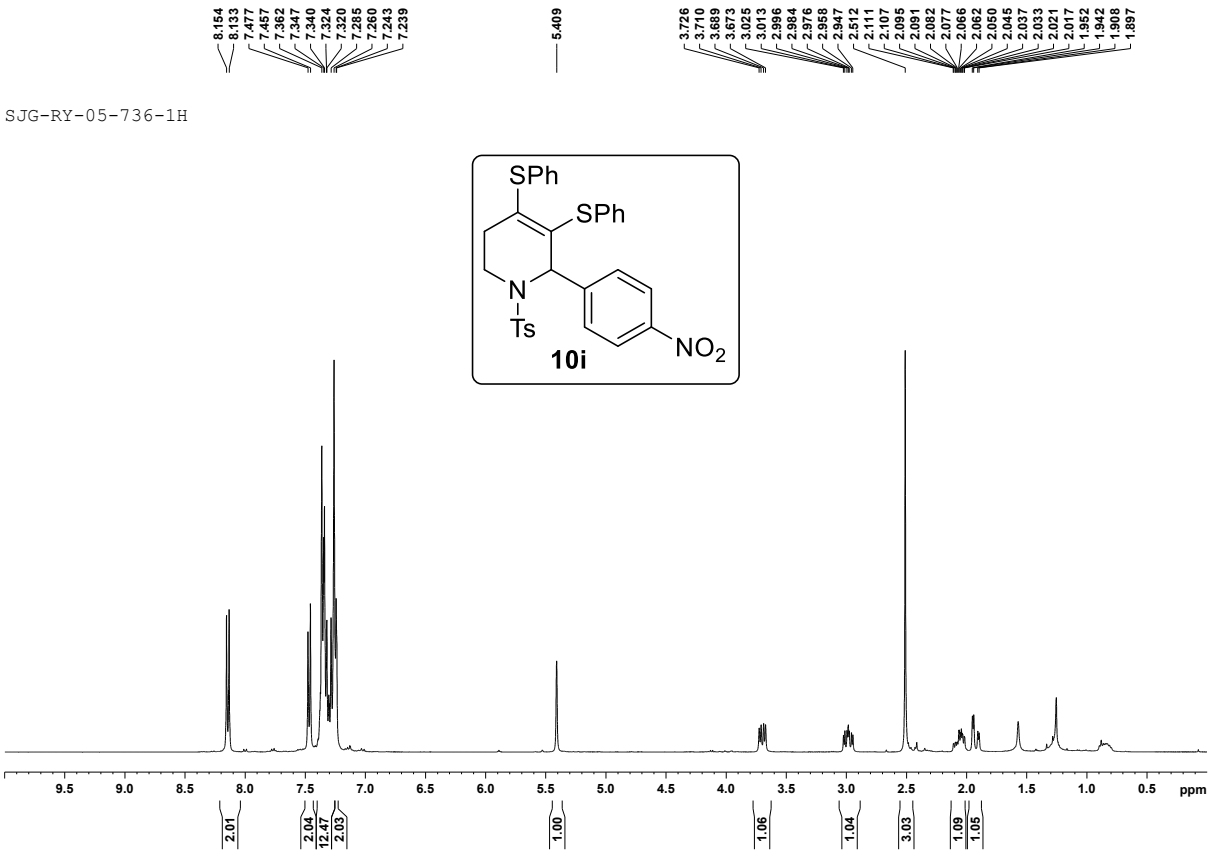
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



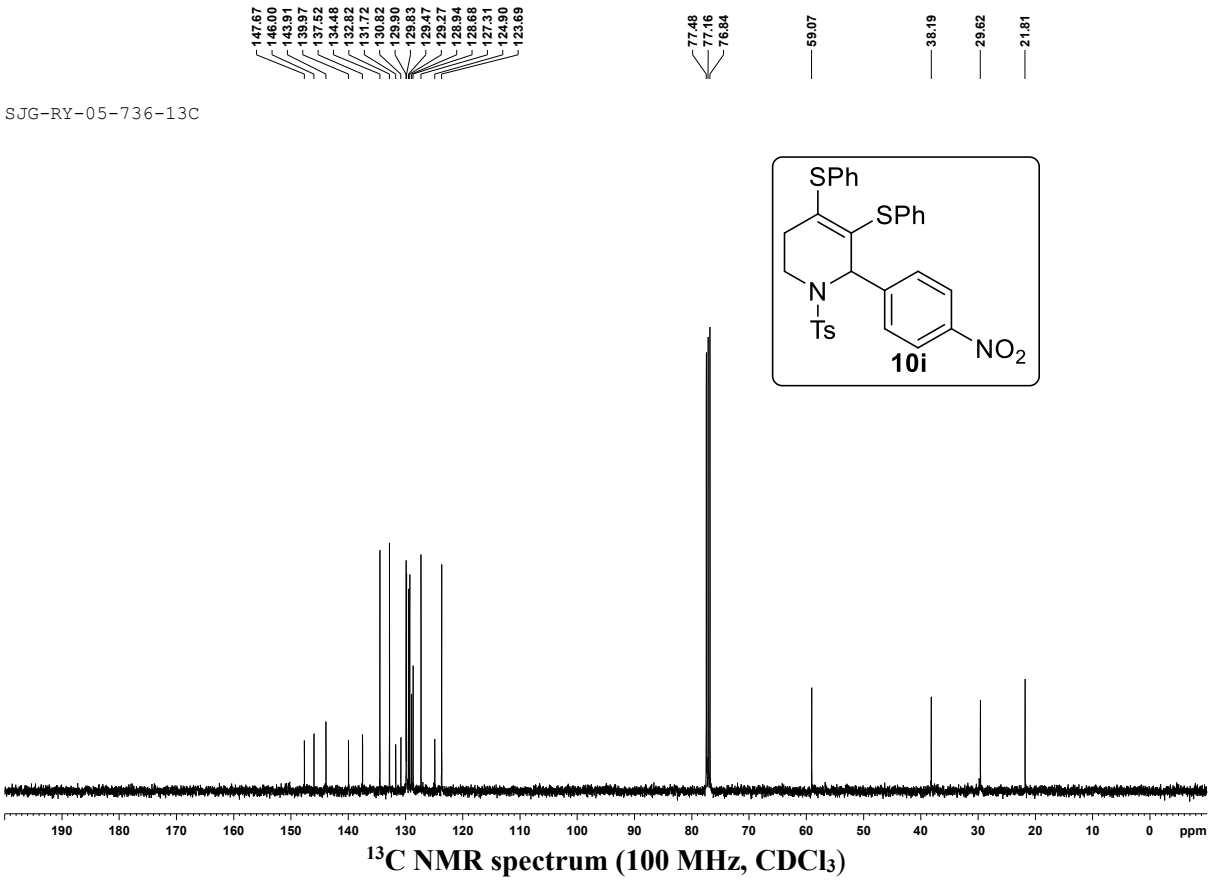
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



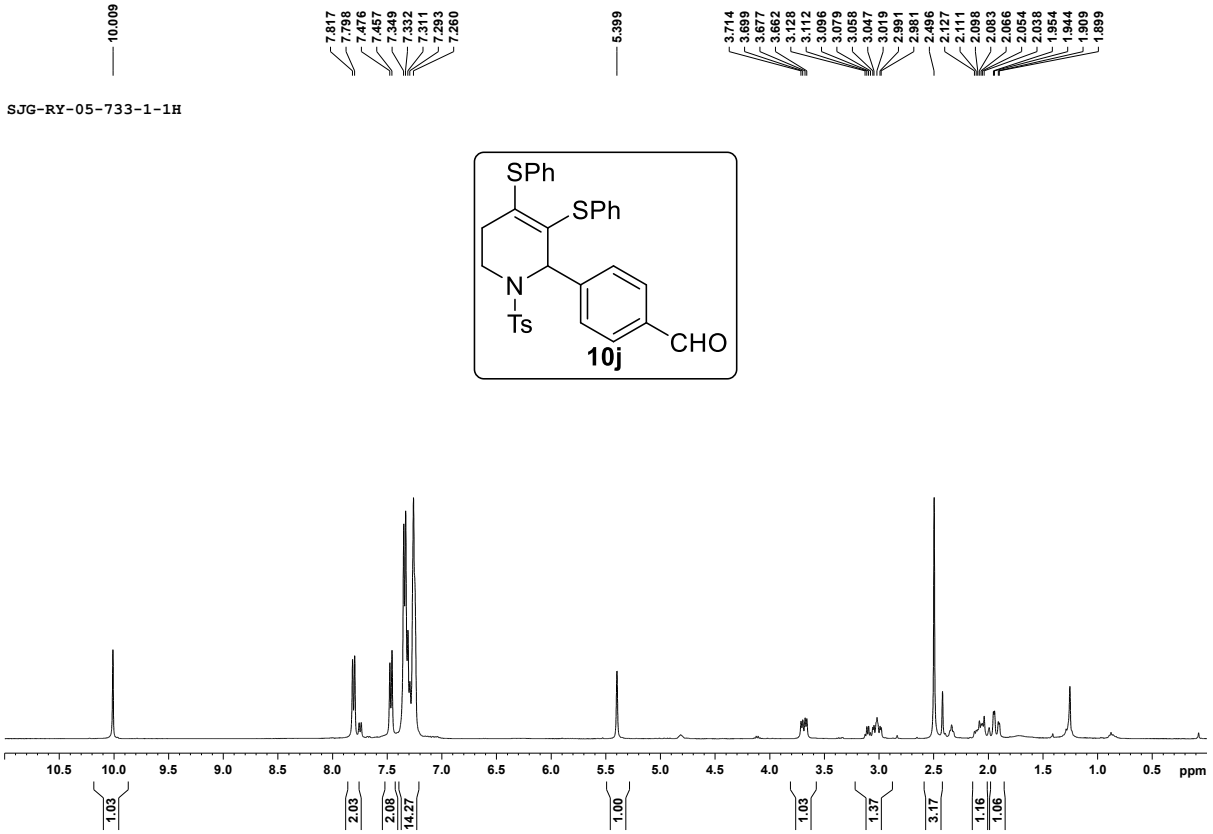
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



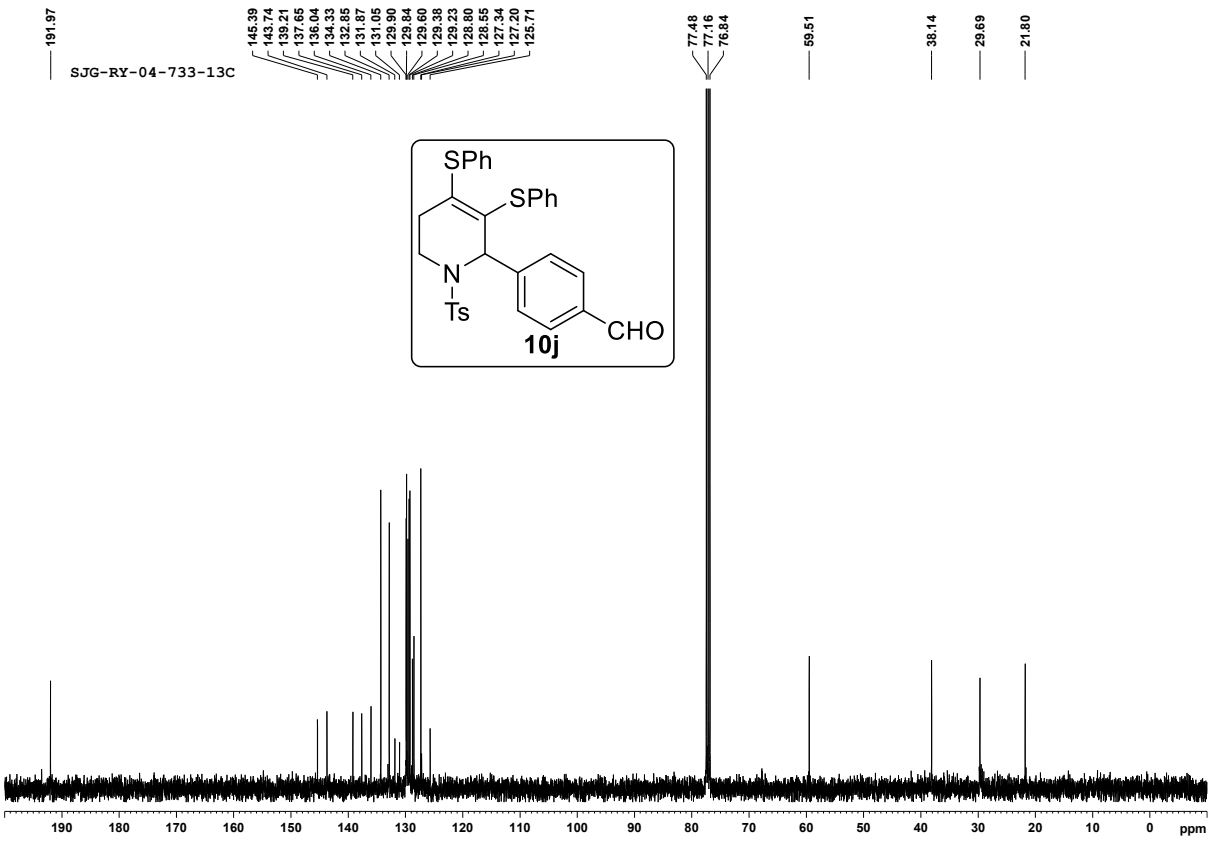
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



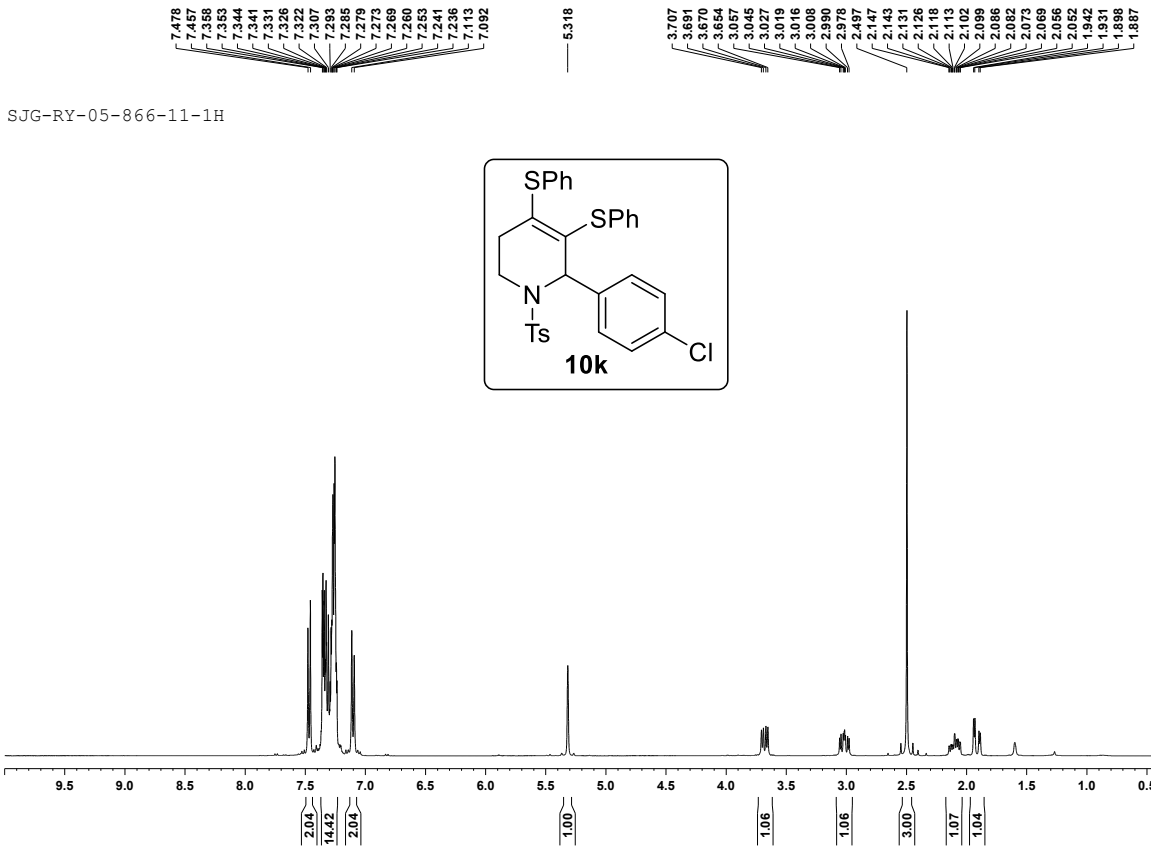
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



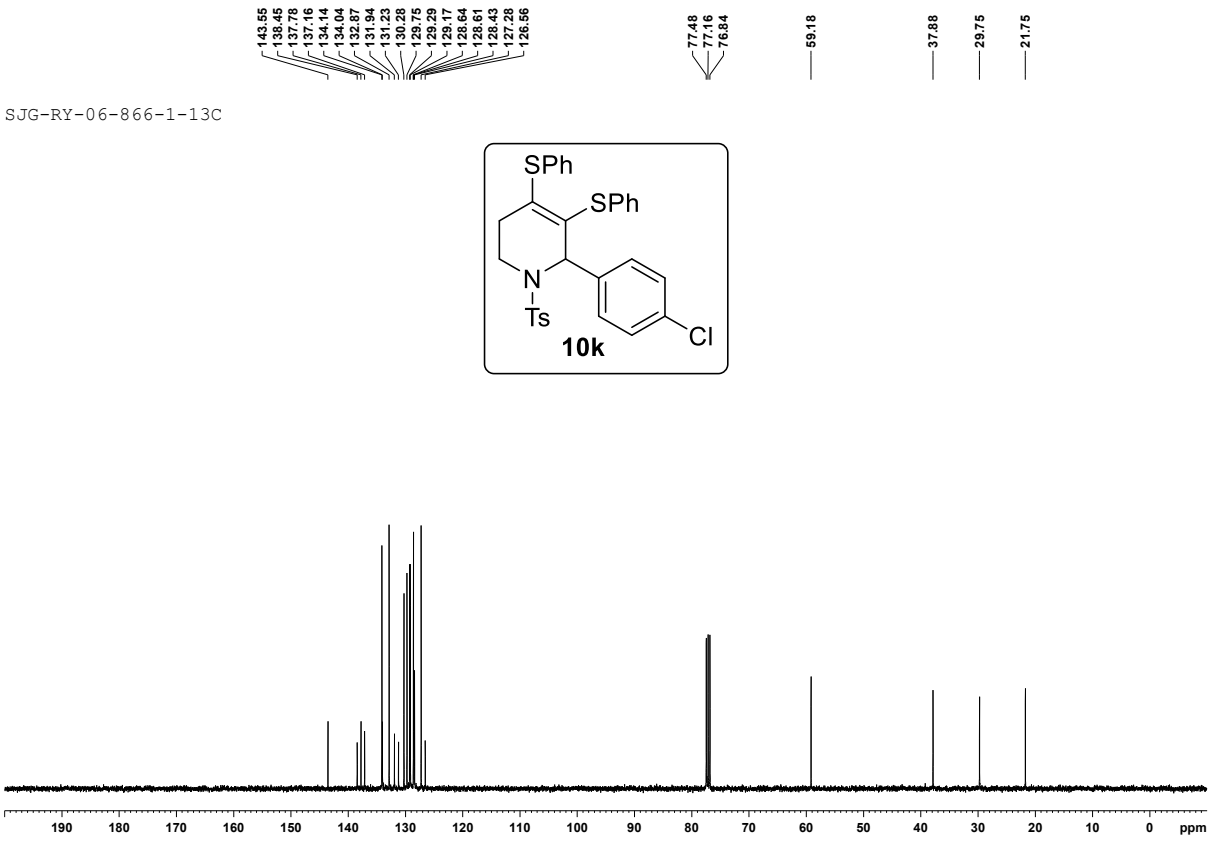
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



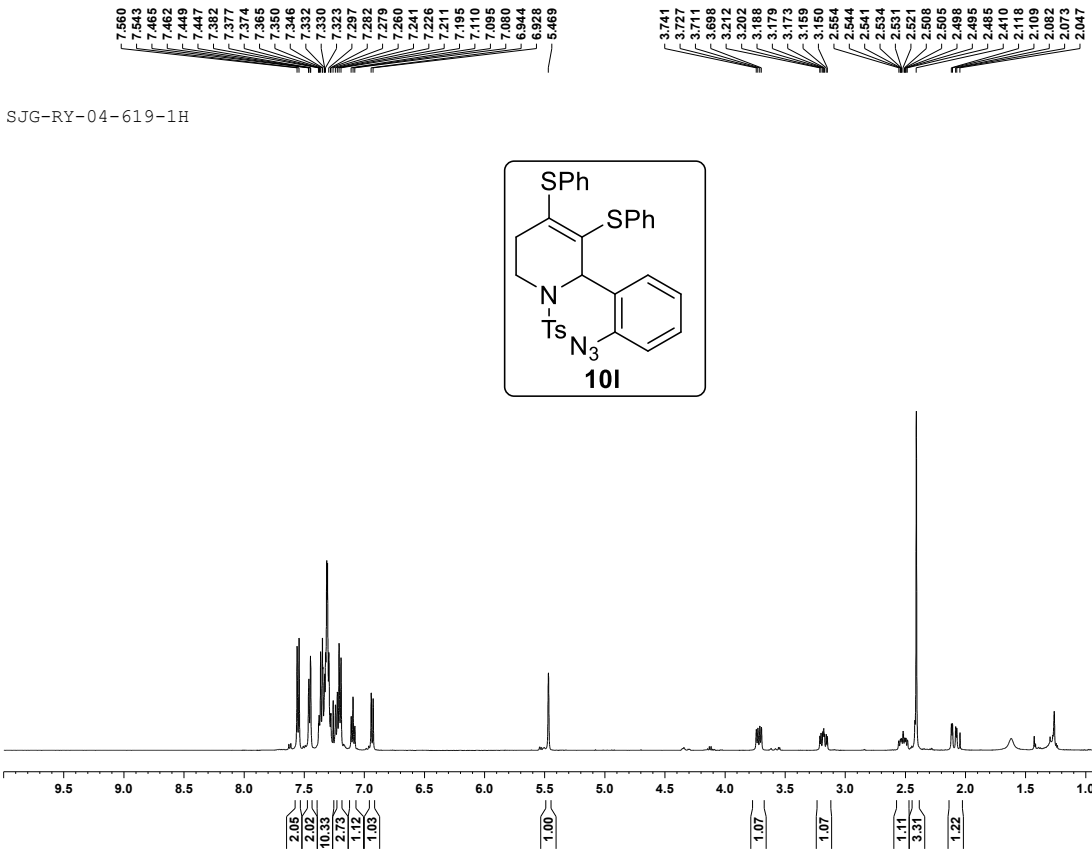
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



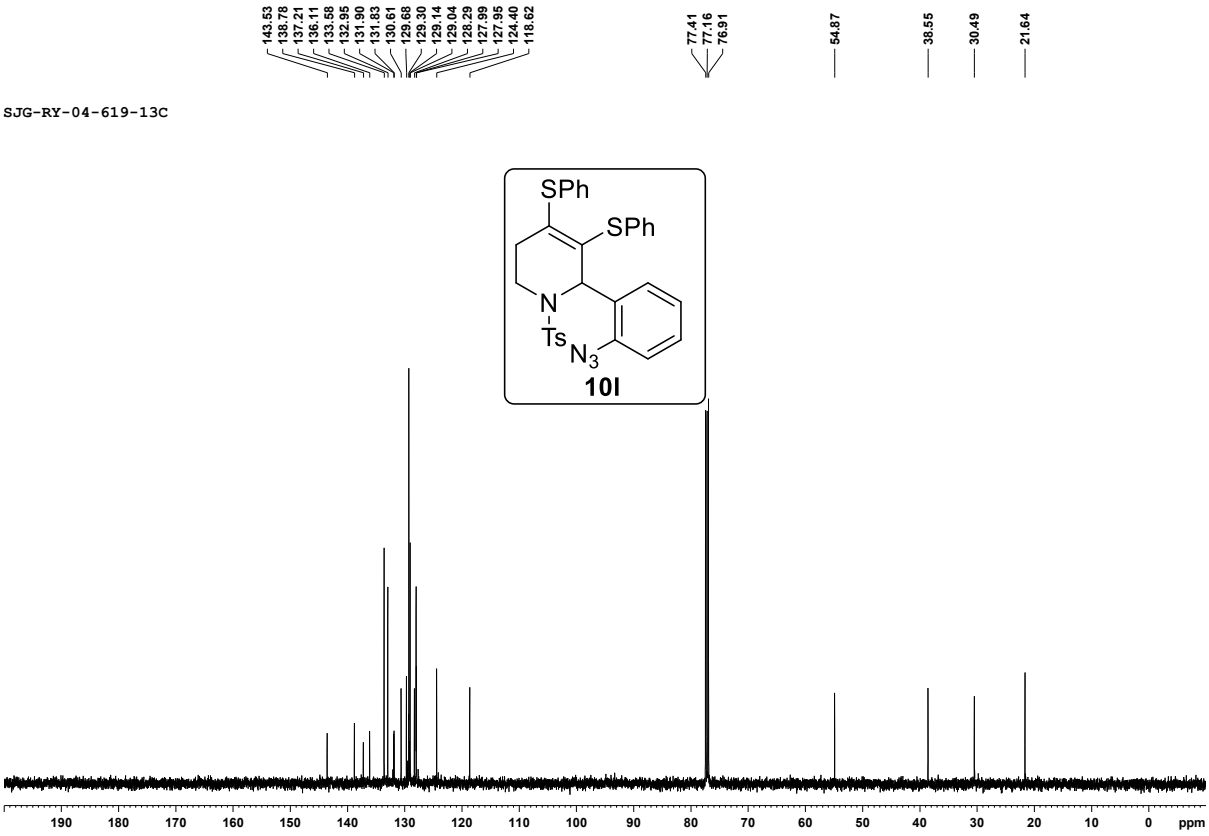
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



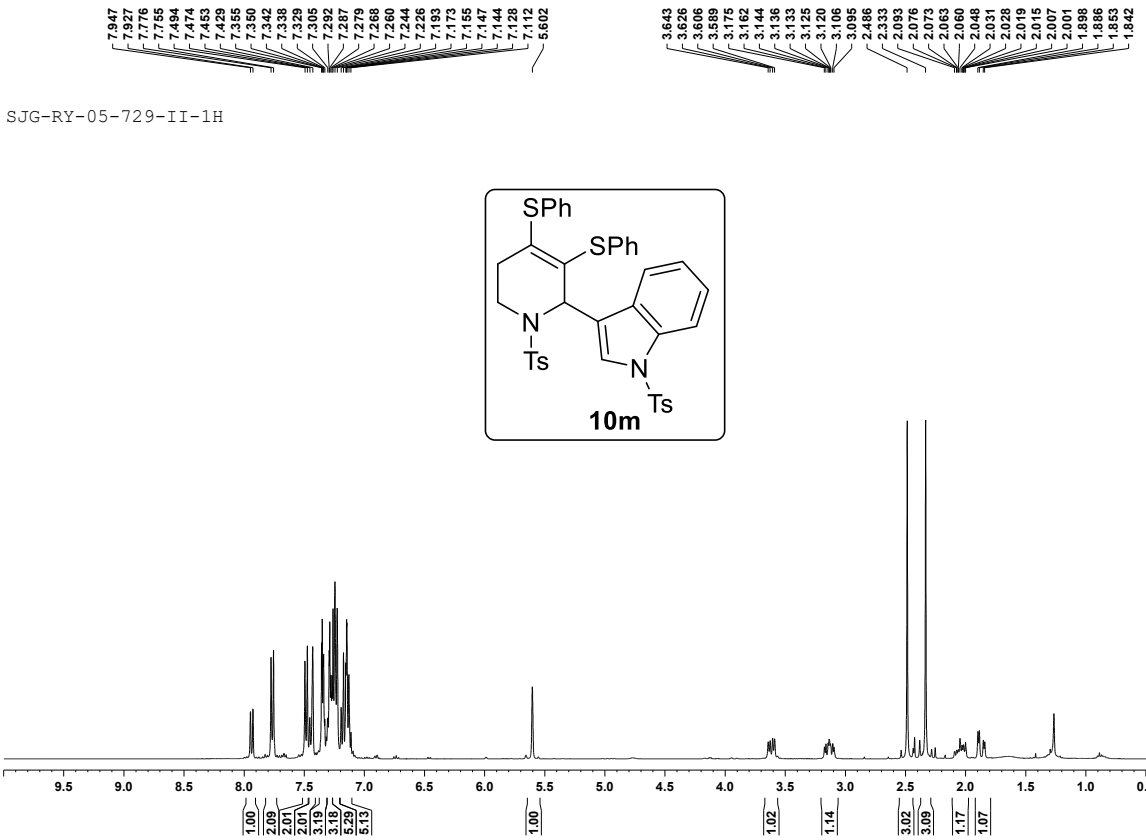
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



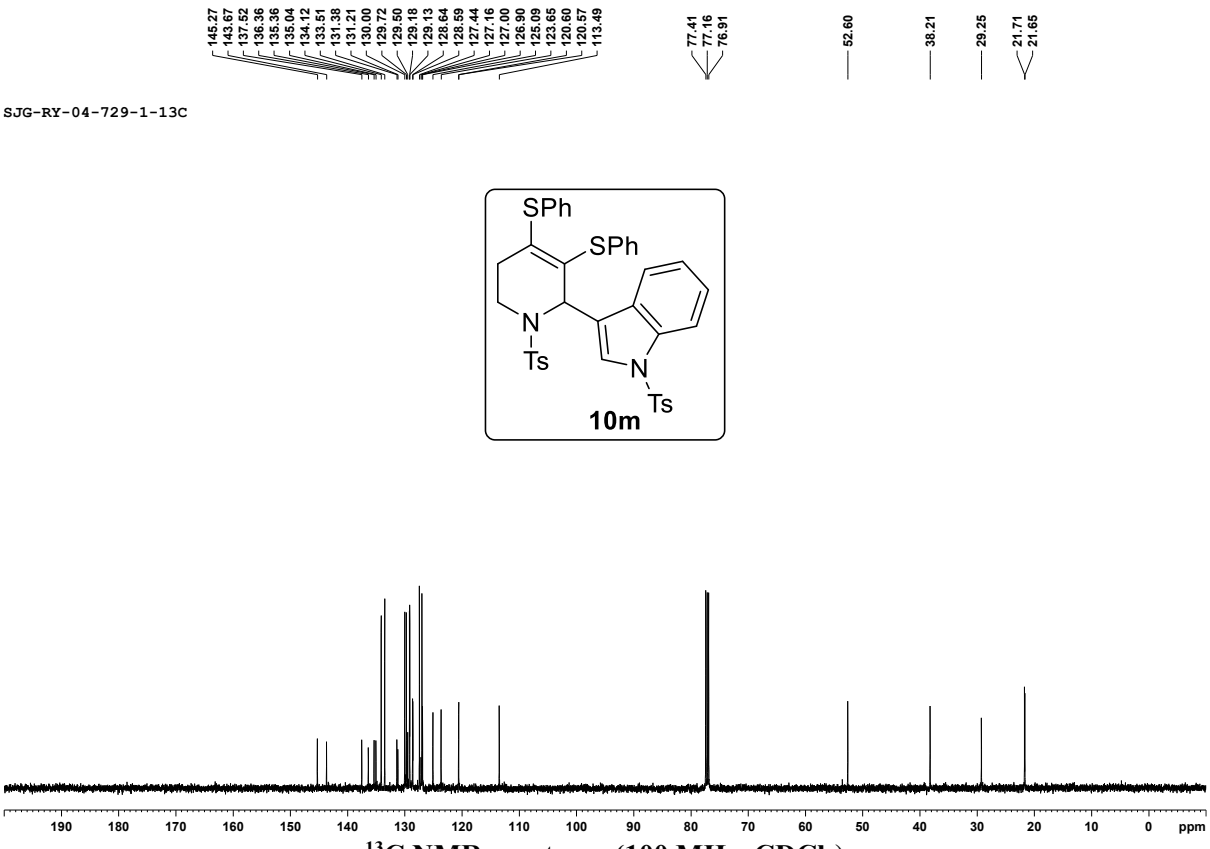
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



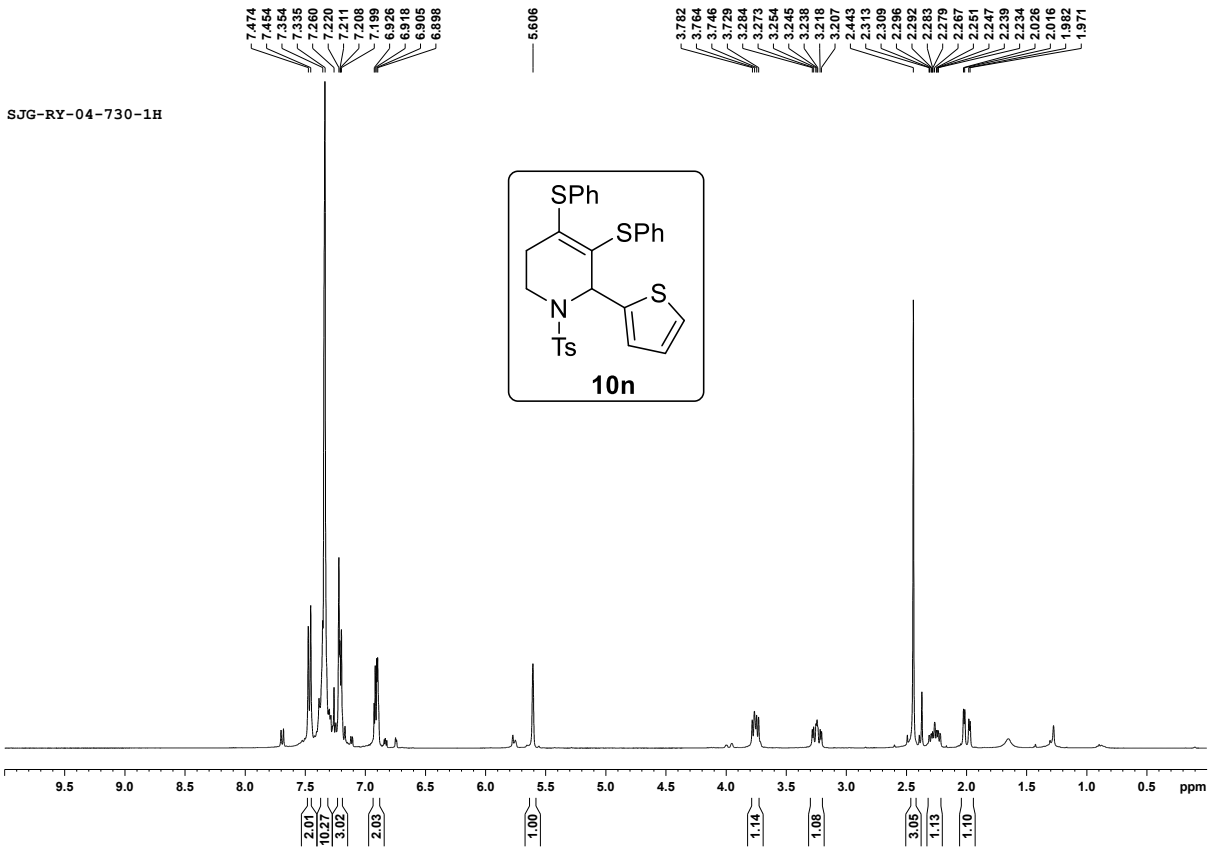
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



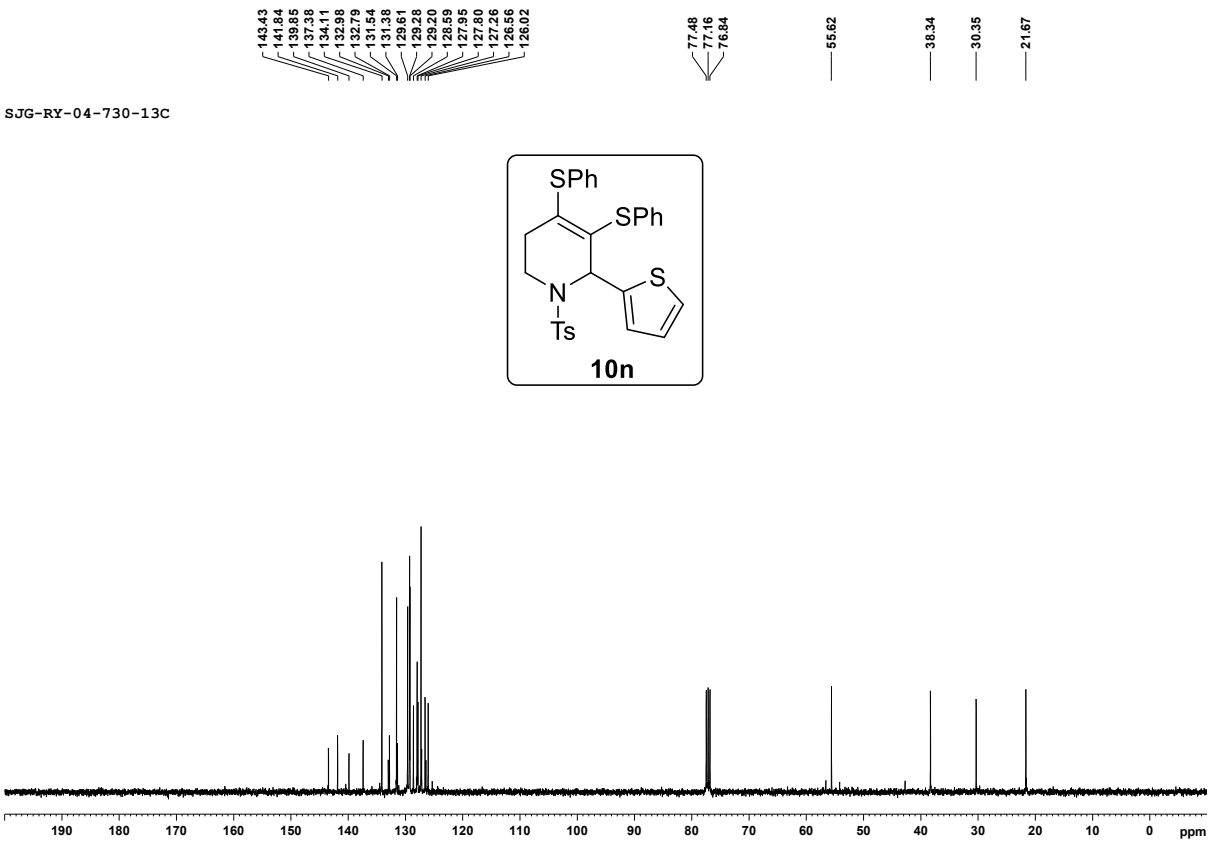
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



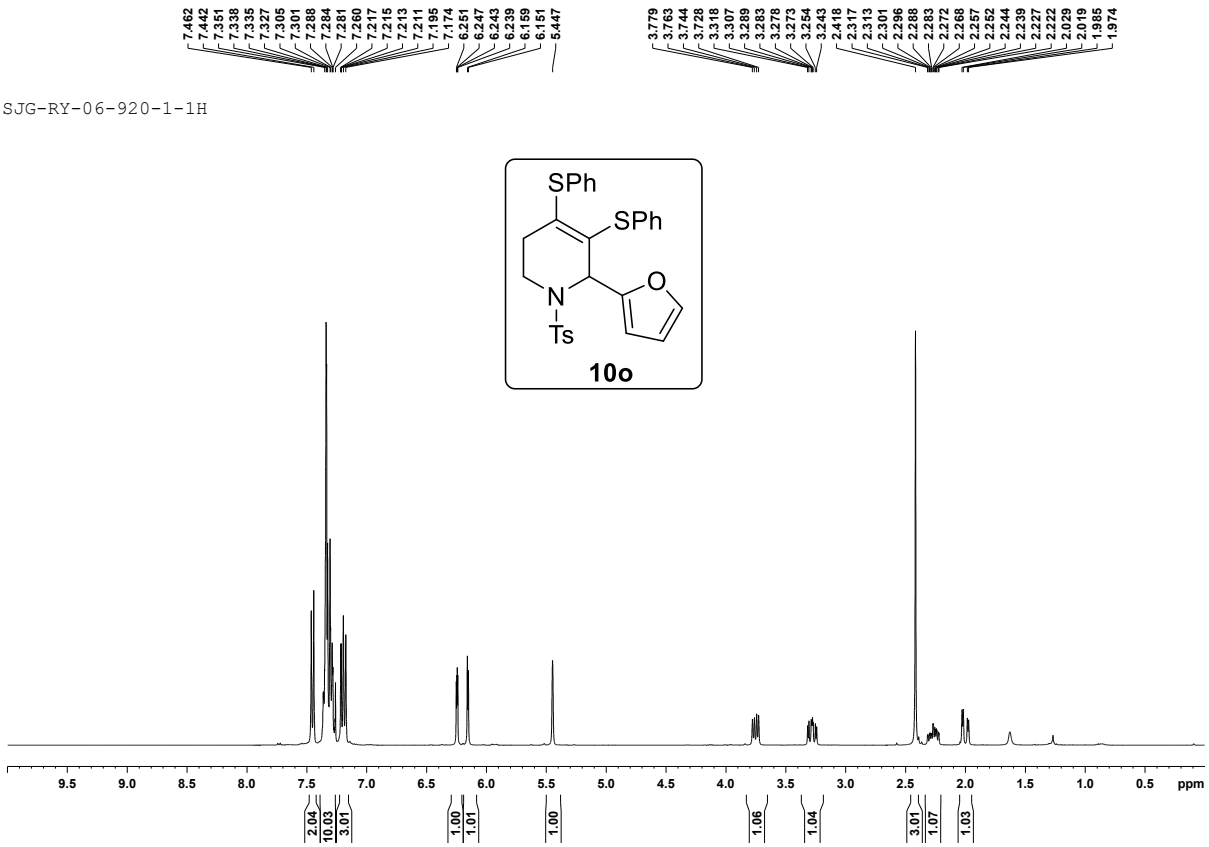
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



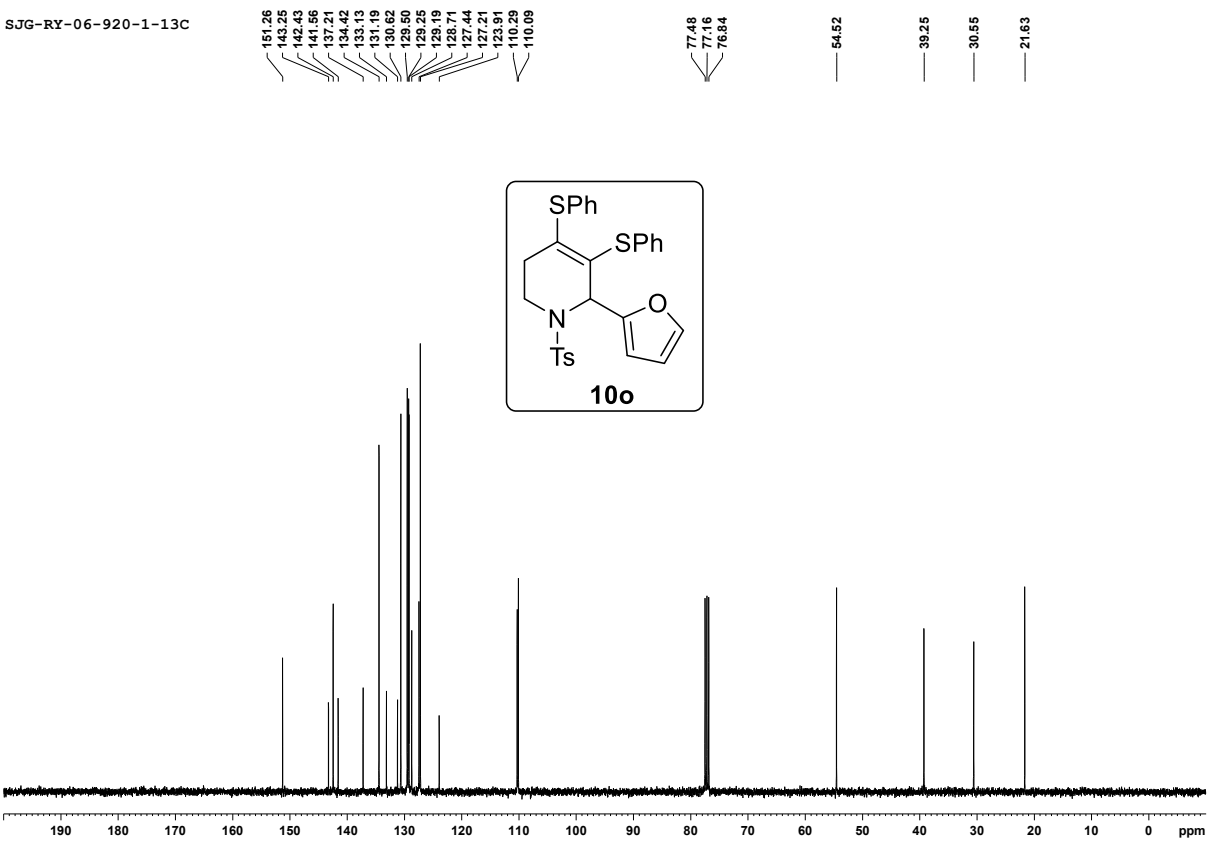
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



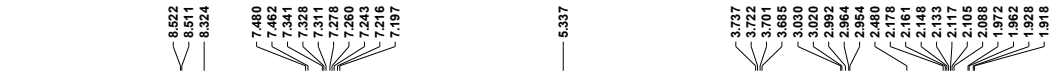
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



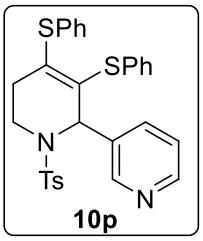
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

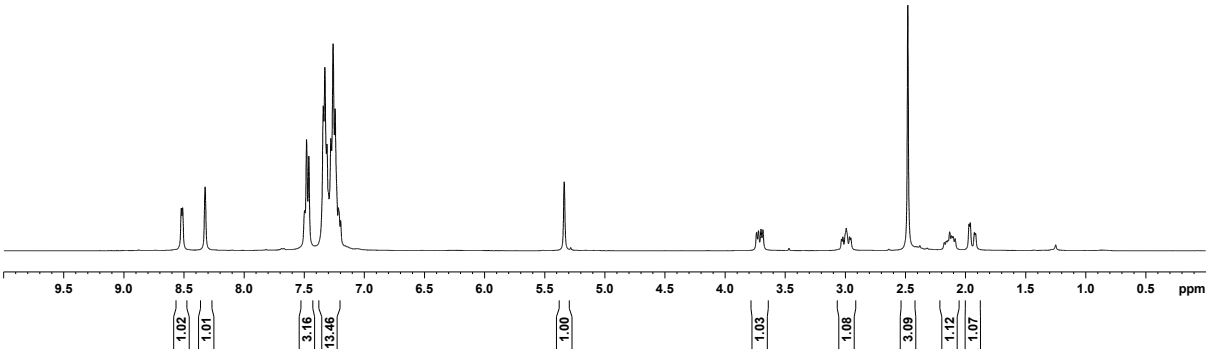


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



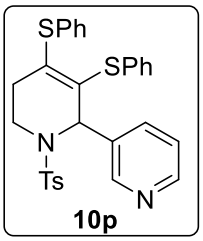
SJG-RY-05-558RE-1H

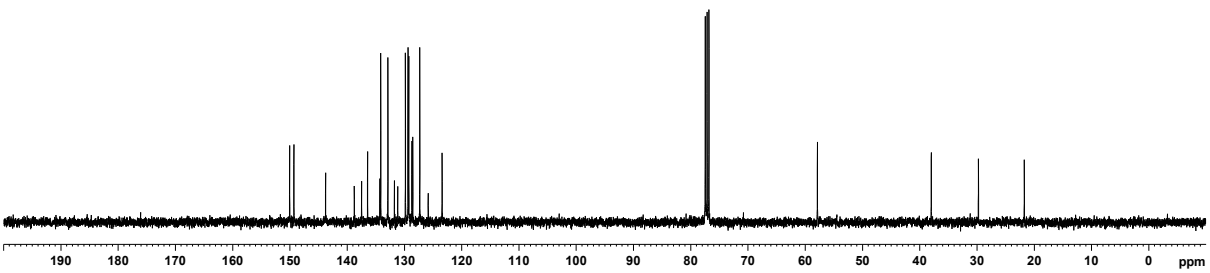




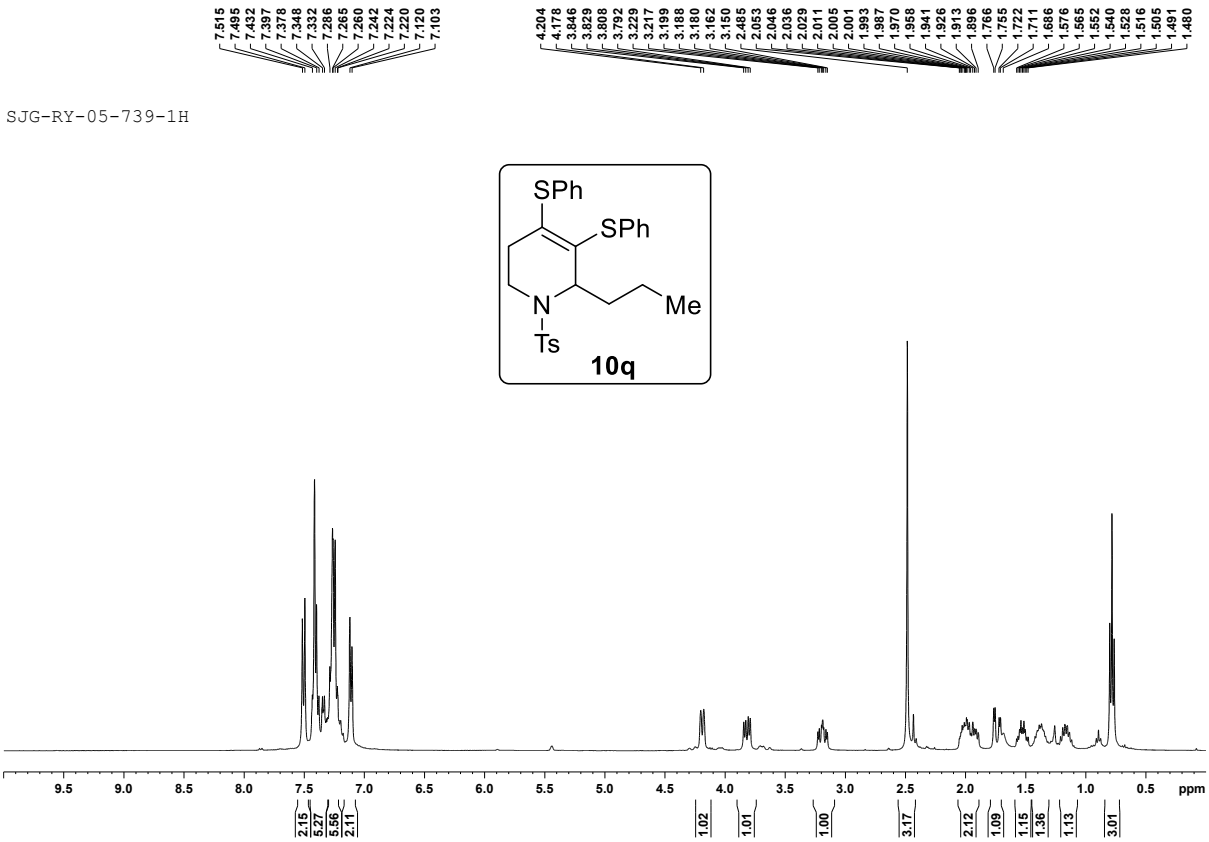
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

SJG-RY-05-558RE-13C

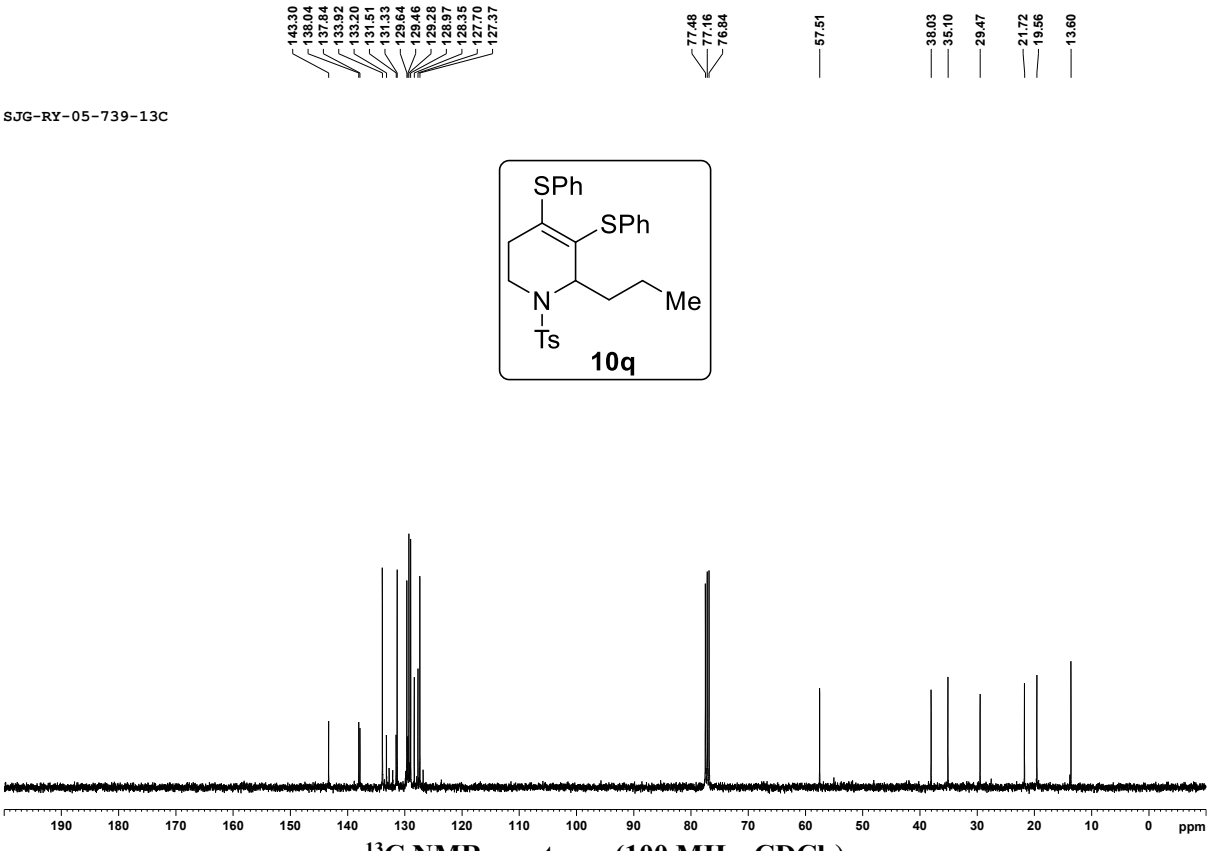




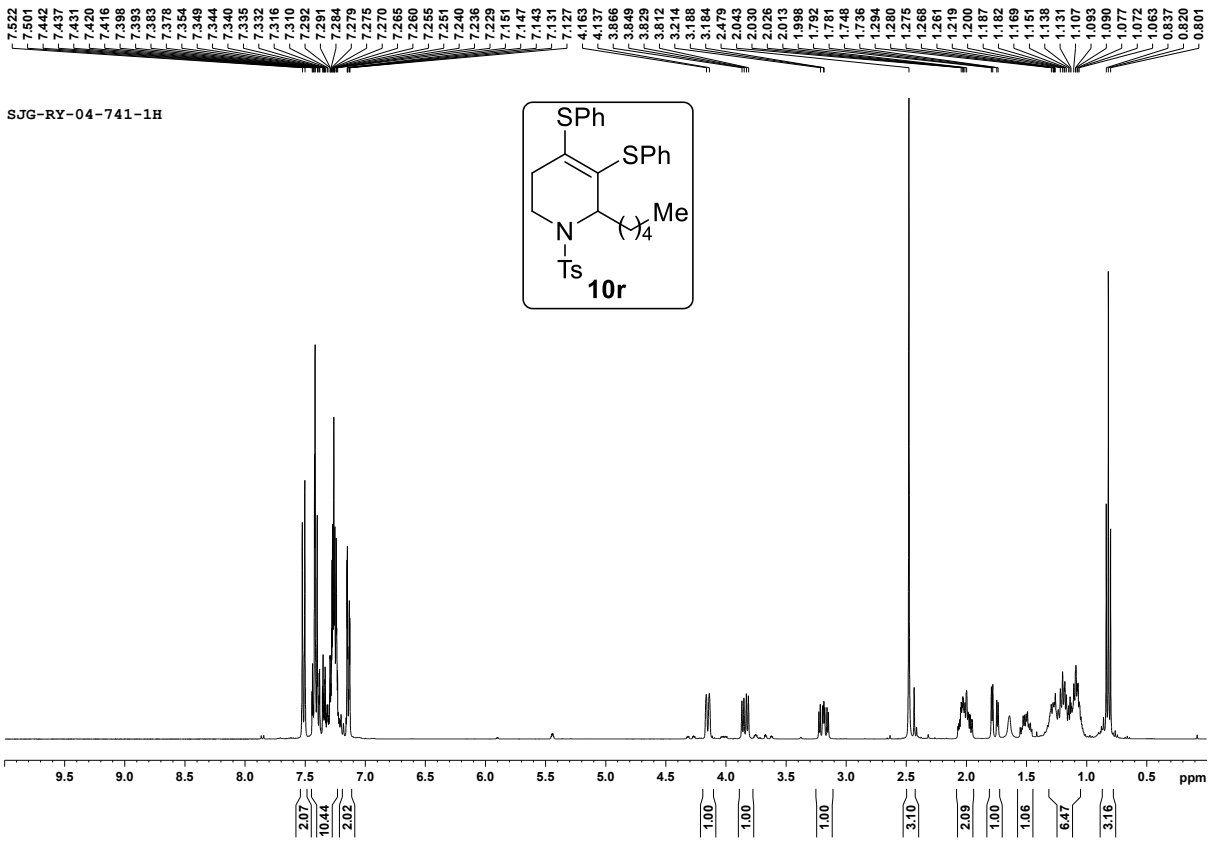
^{13}C NMR spectrum (100MHz, $CDCl_3$)



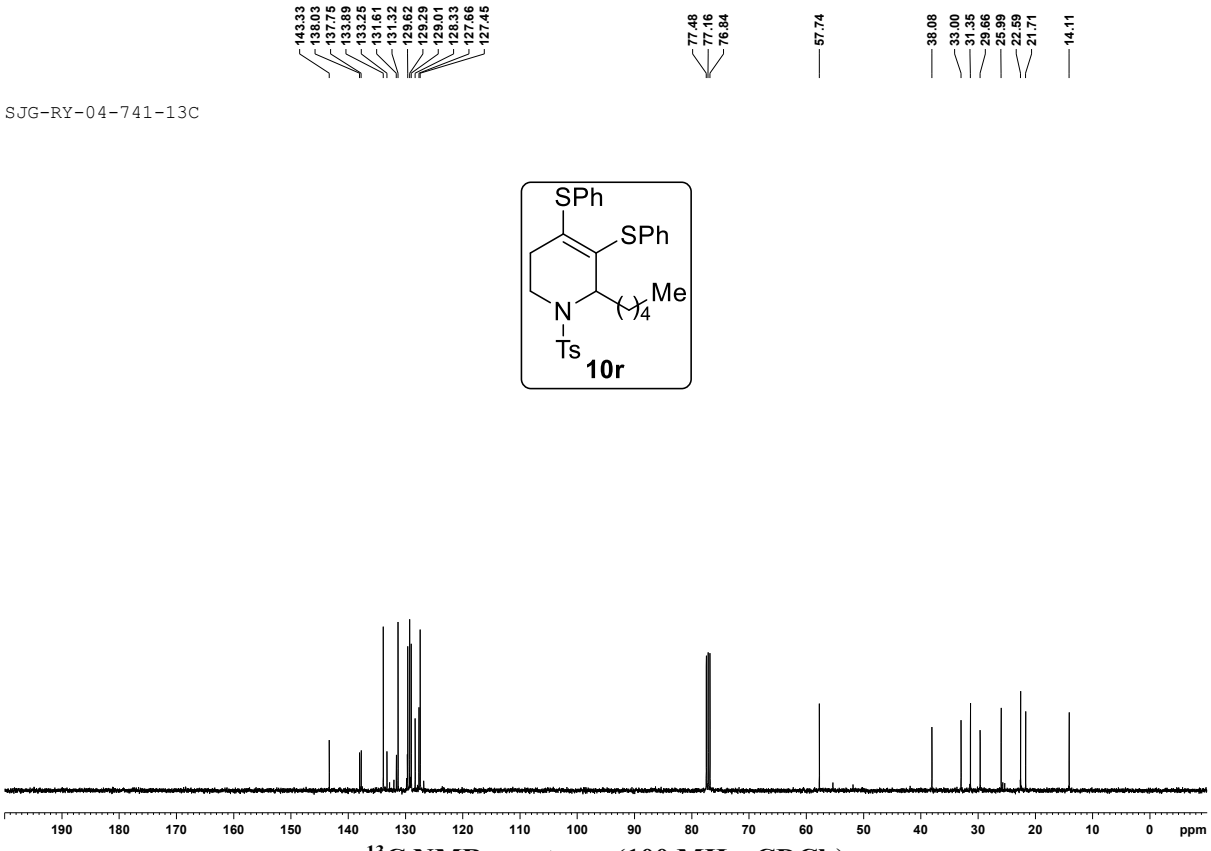
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



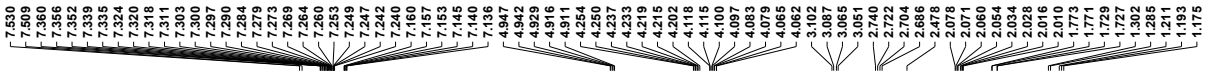
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



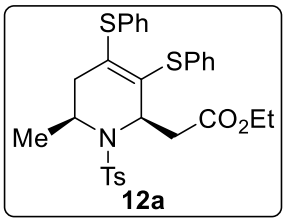
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

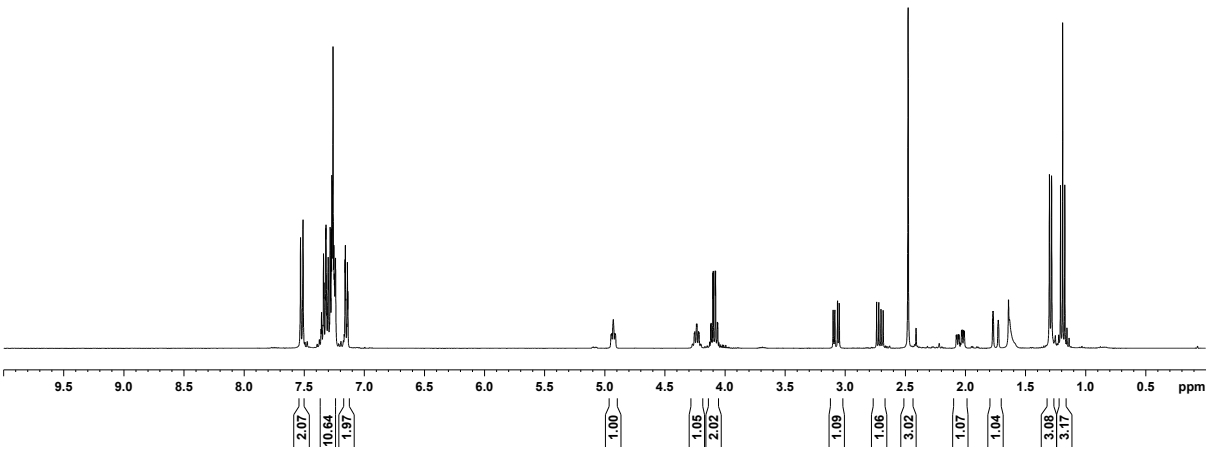


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



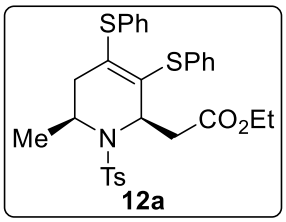
SJG-RY-05-771-1H

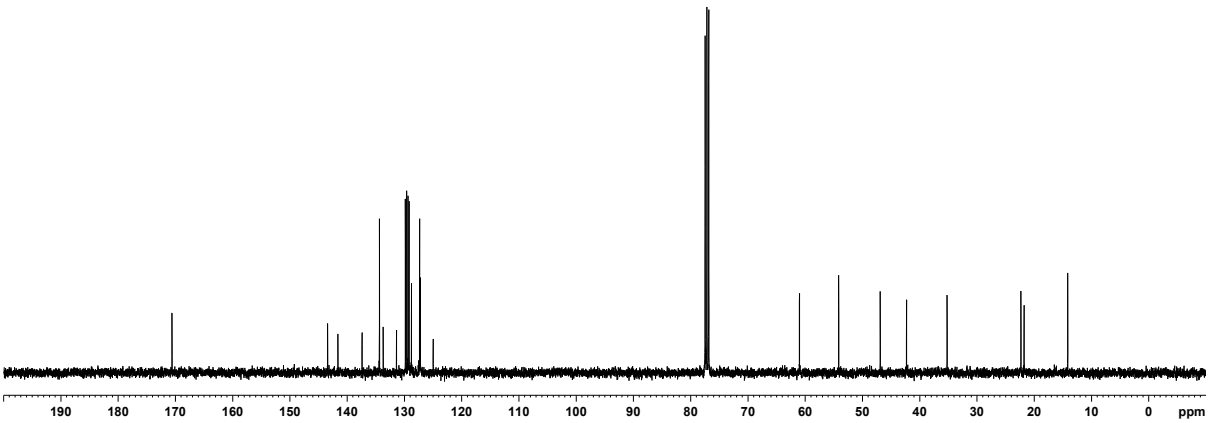




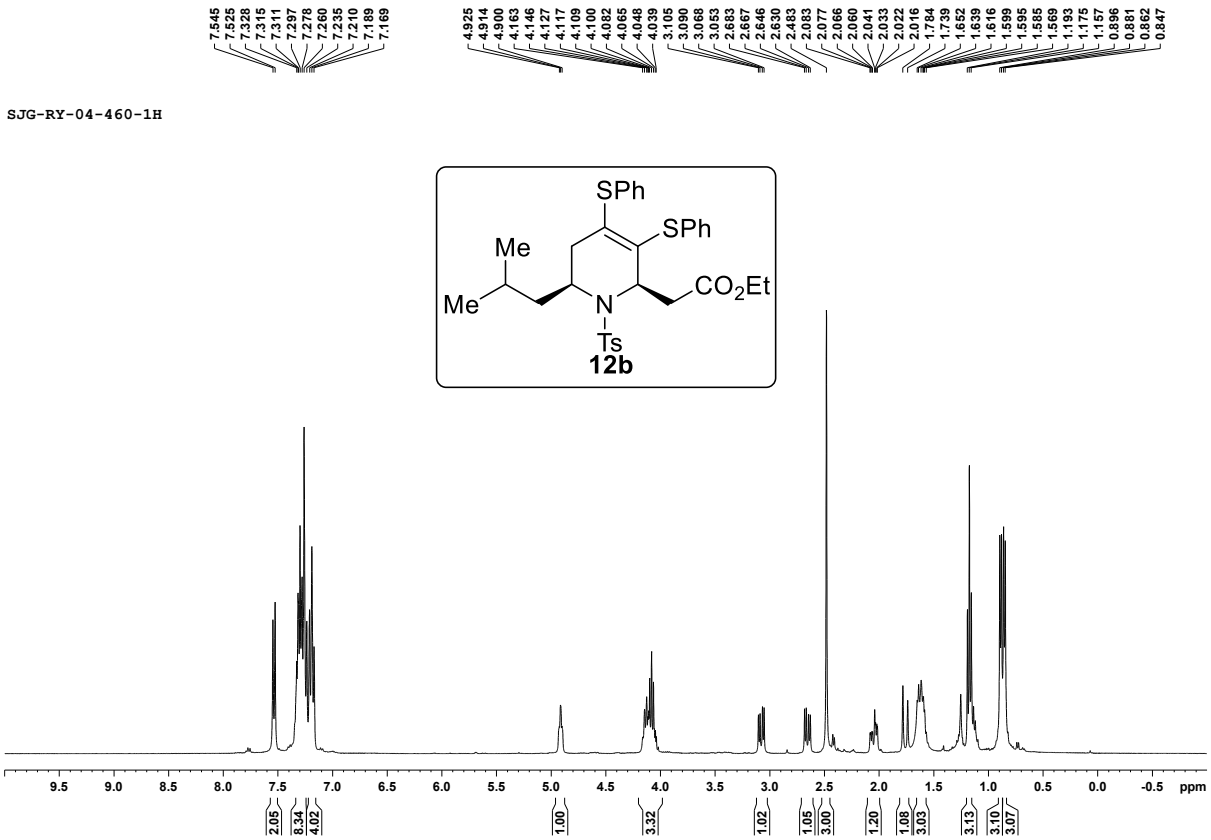
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

SJG-RY-05-771-13C

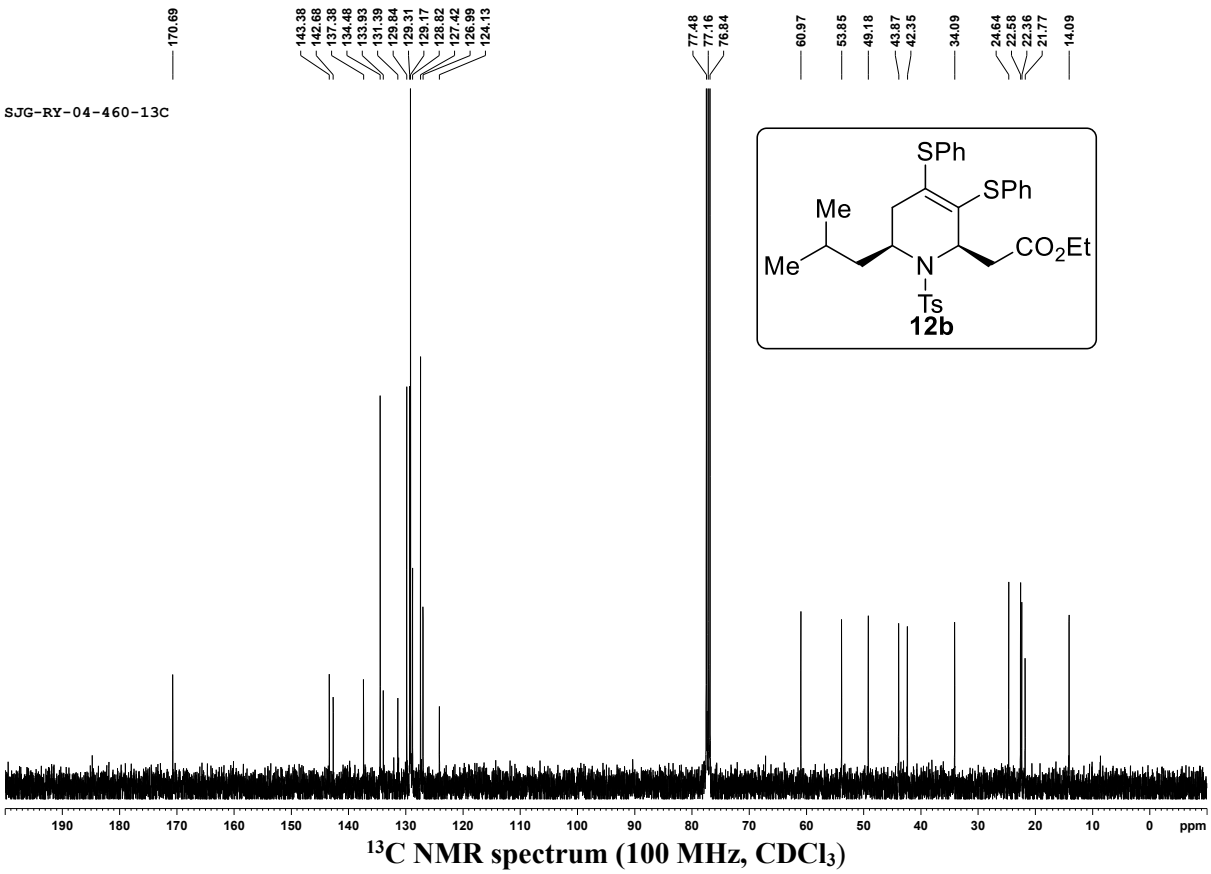




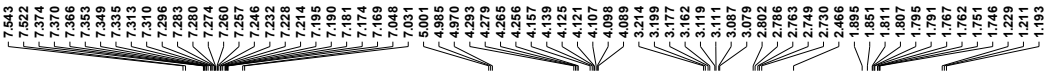
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



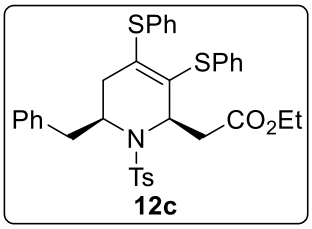
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

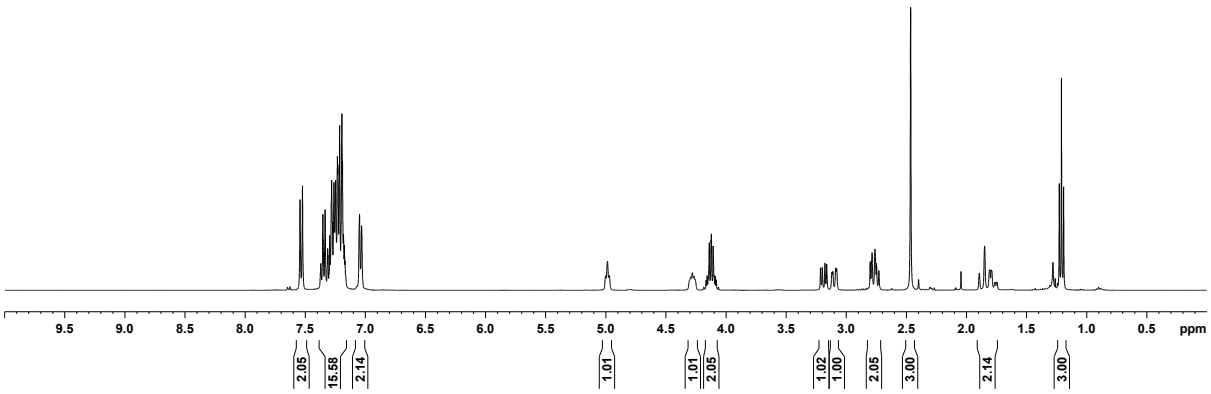


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



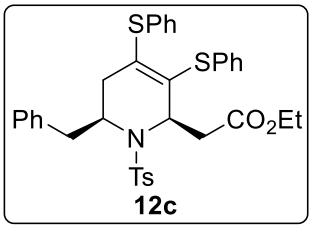
SJG-GPK-02-232-1H

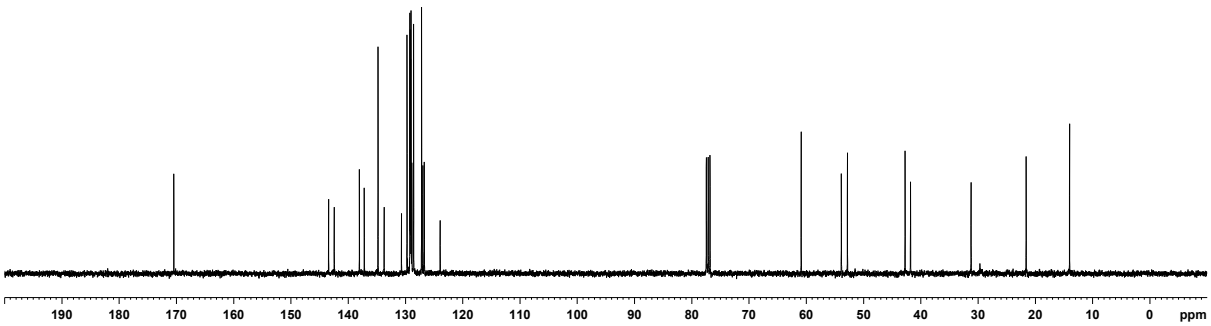




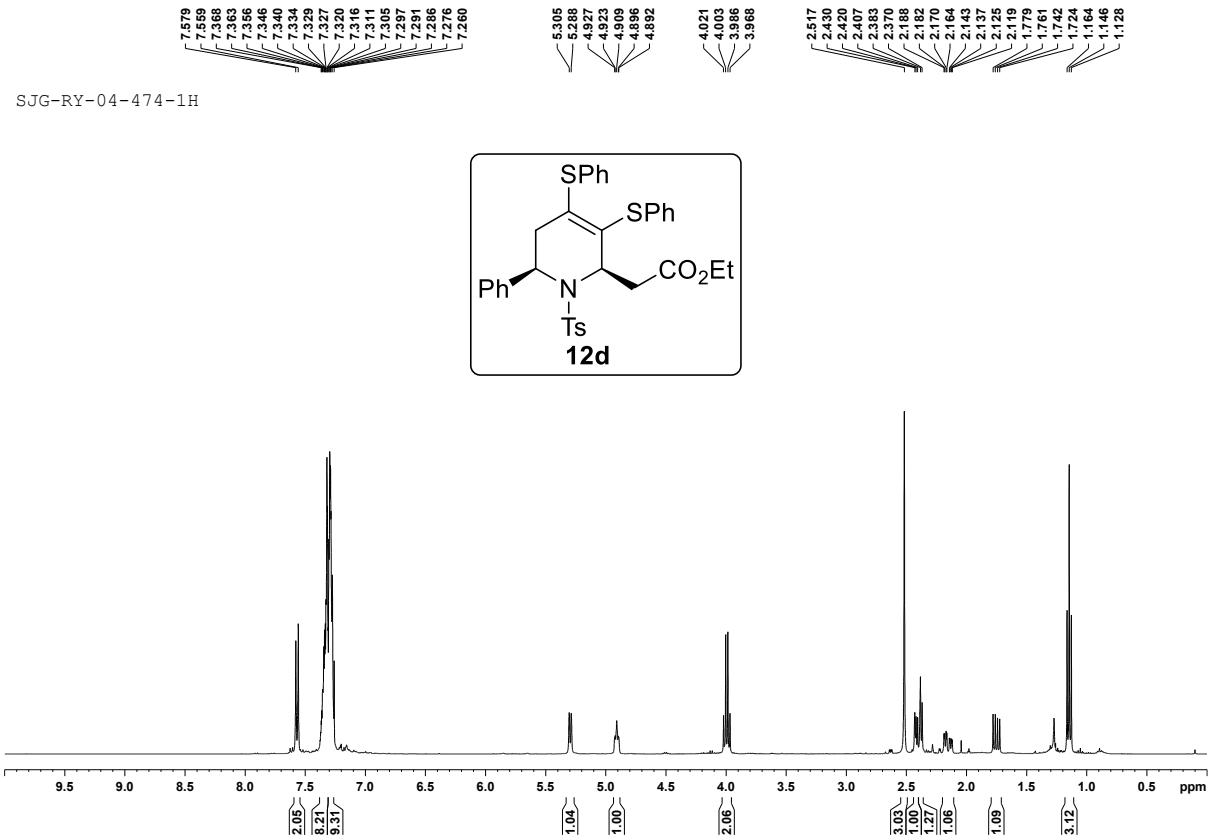
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

SJG-GPK-02-13C

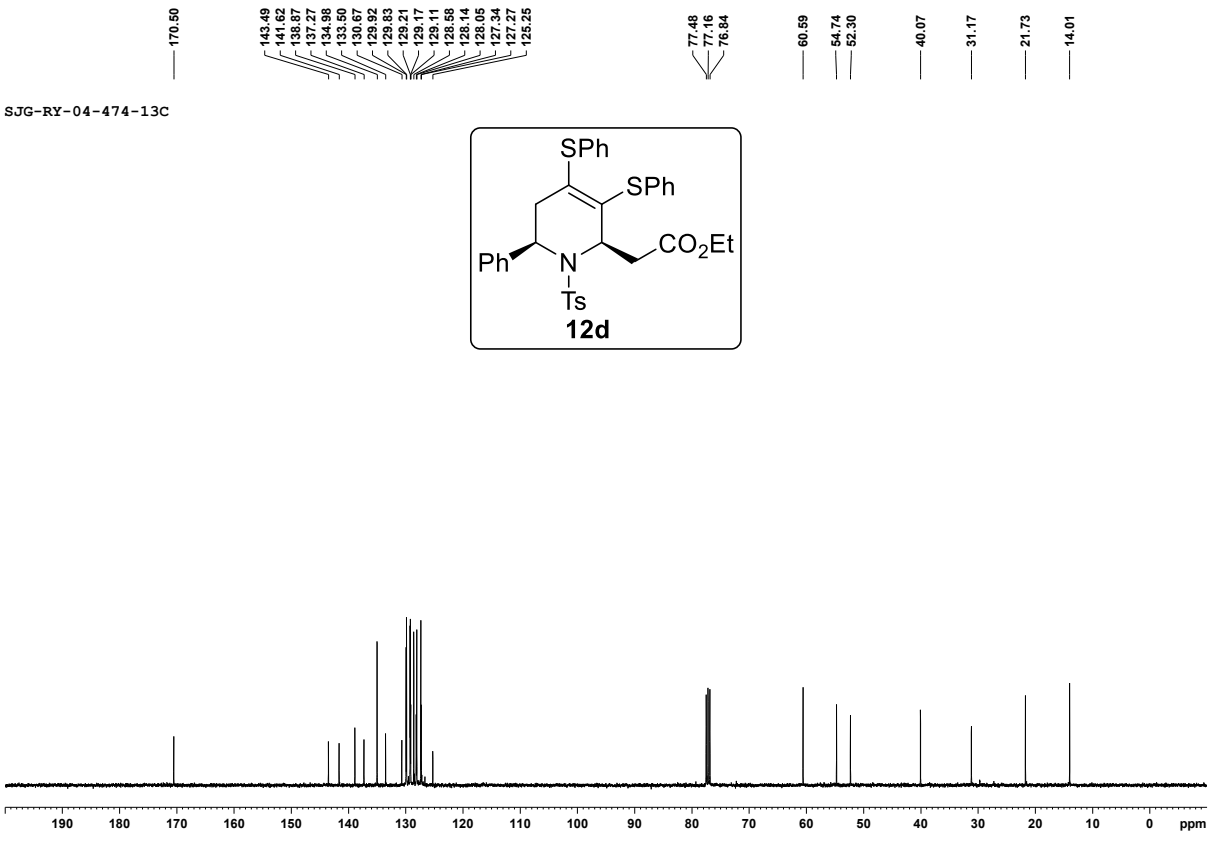




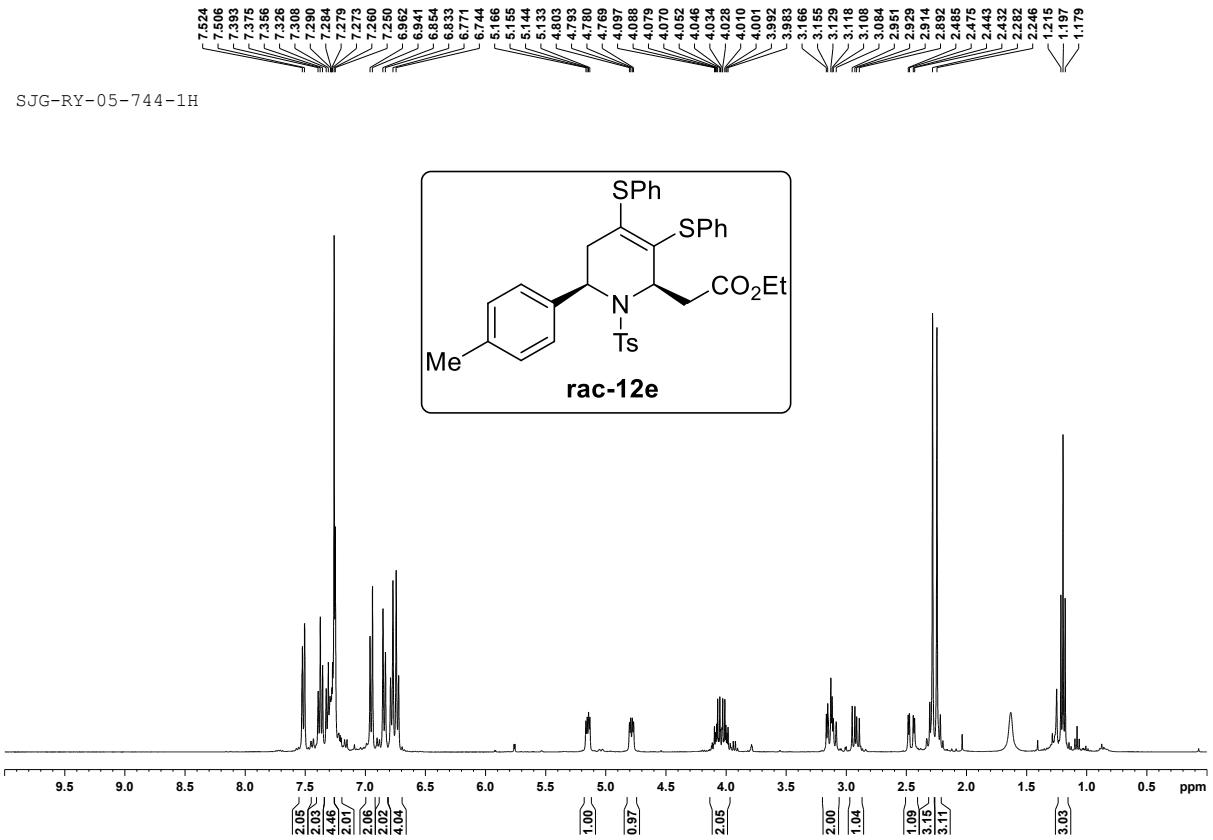
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



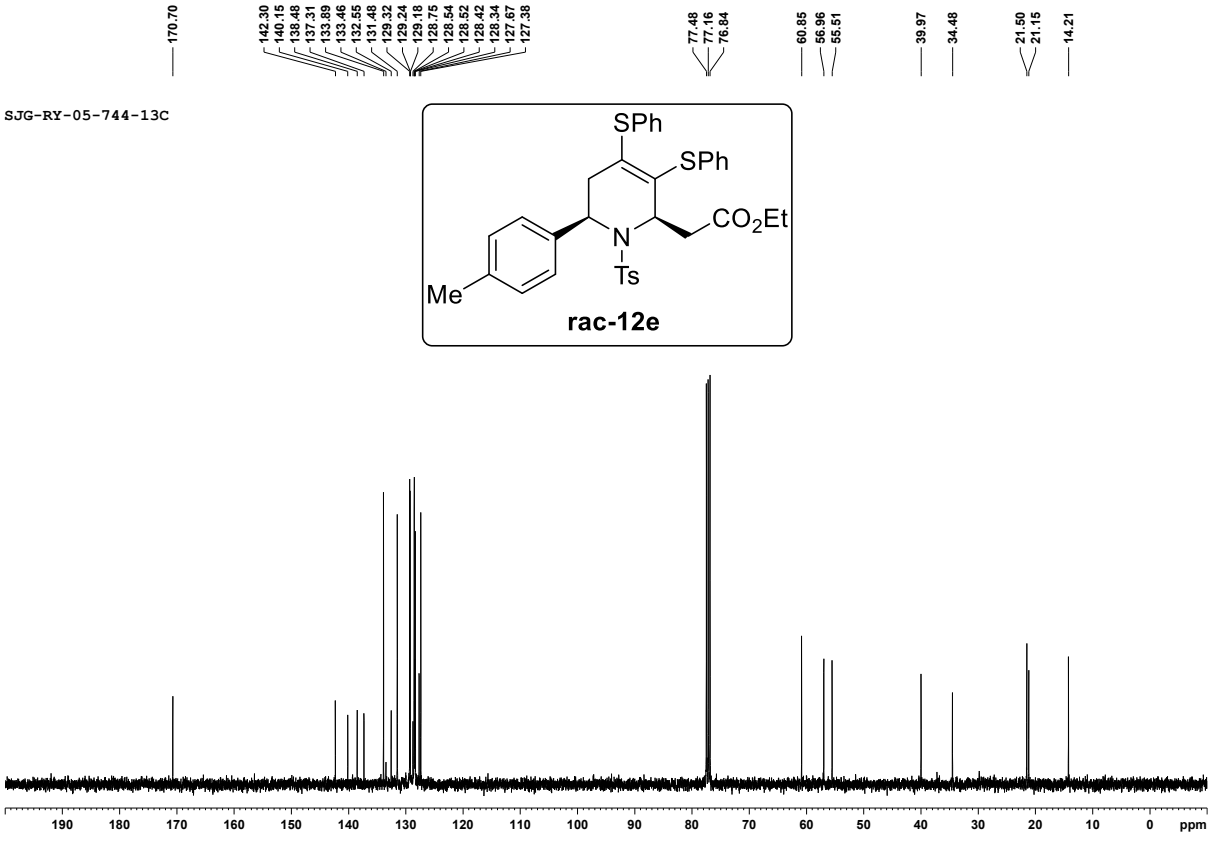
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



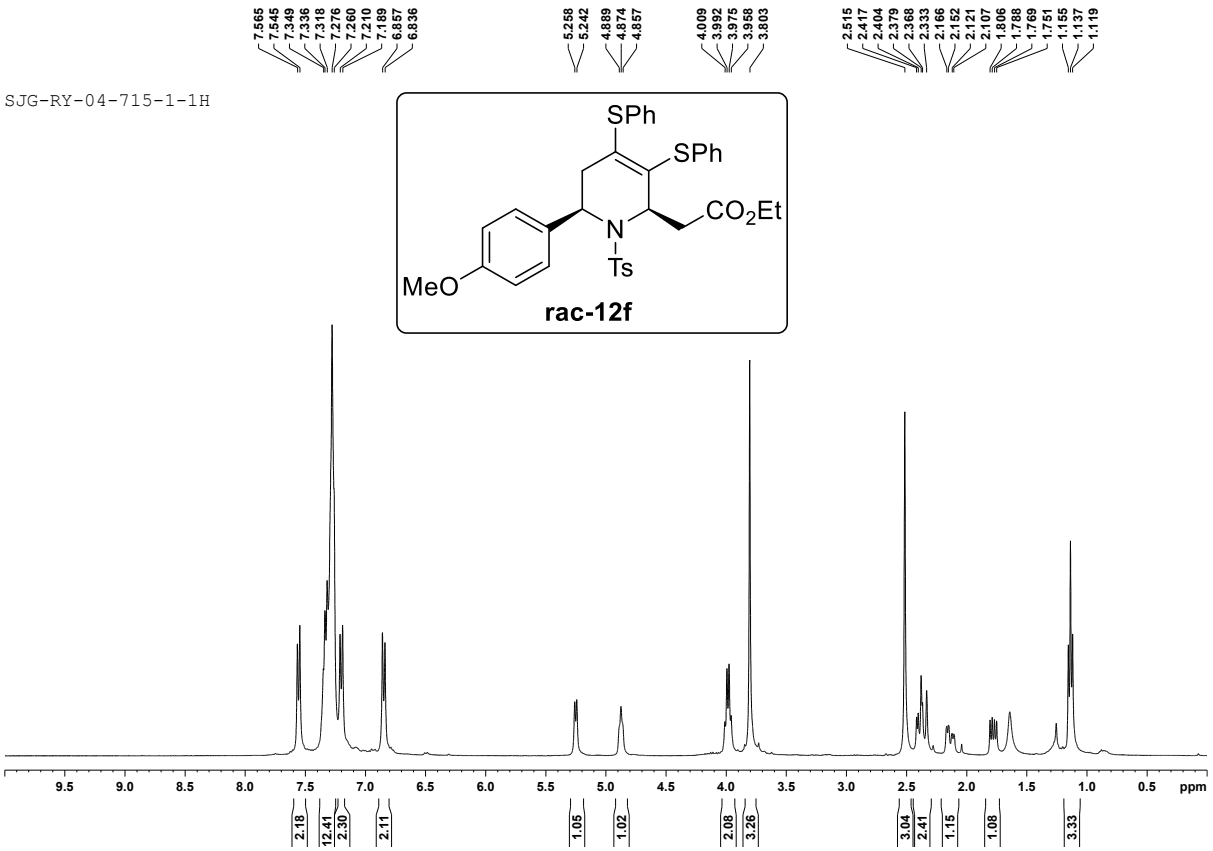
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



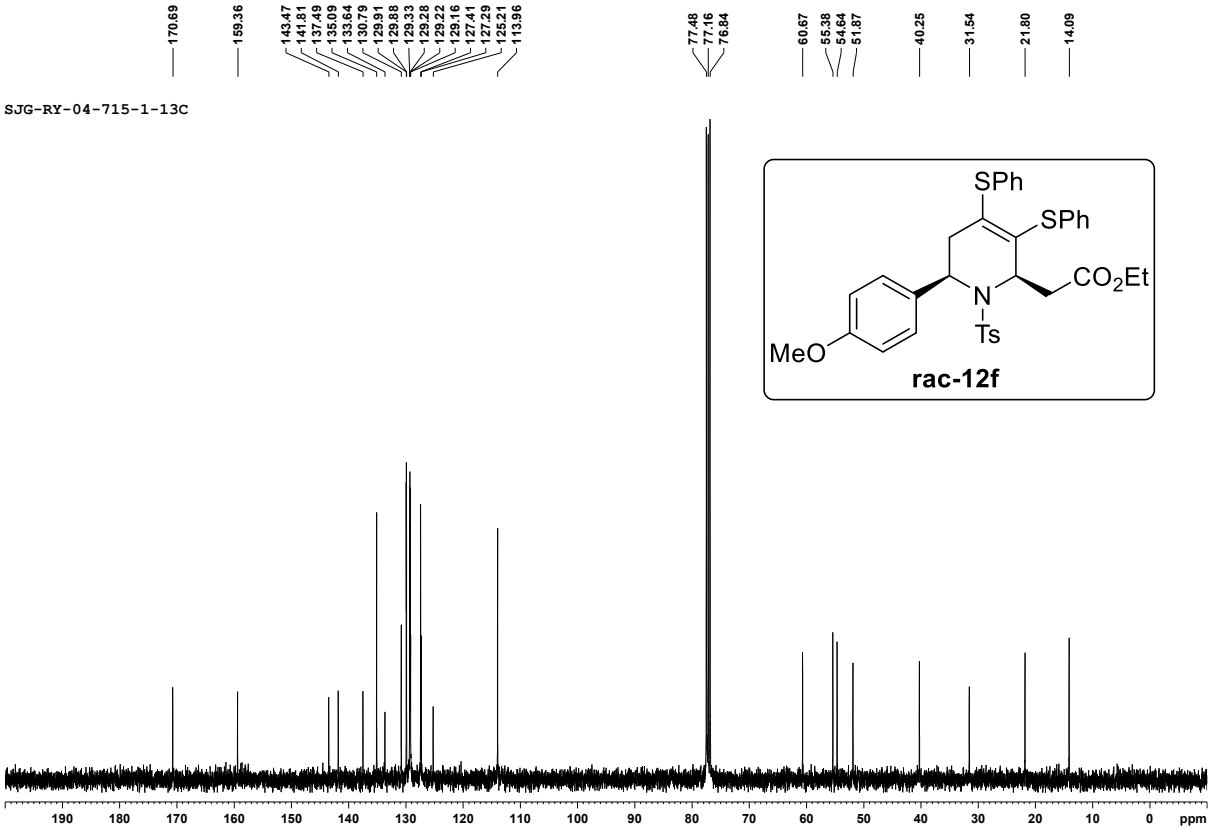
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



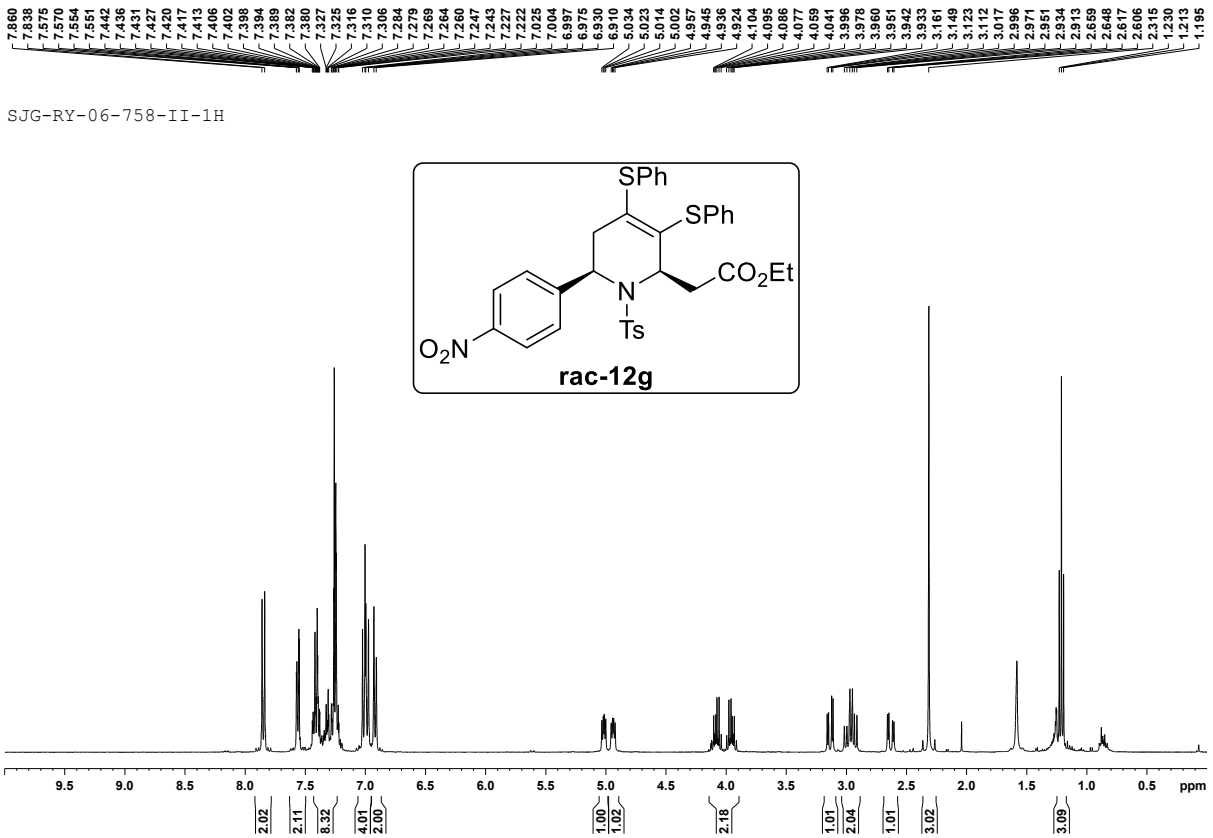
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



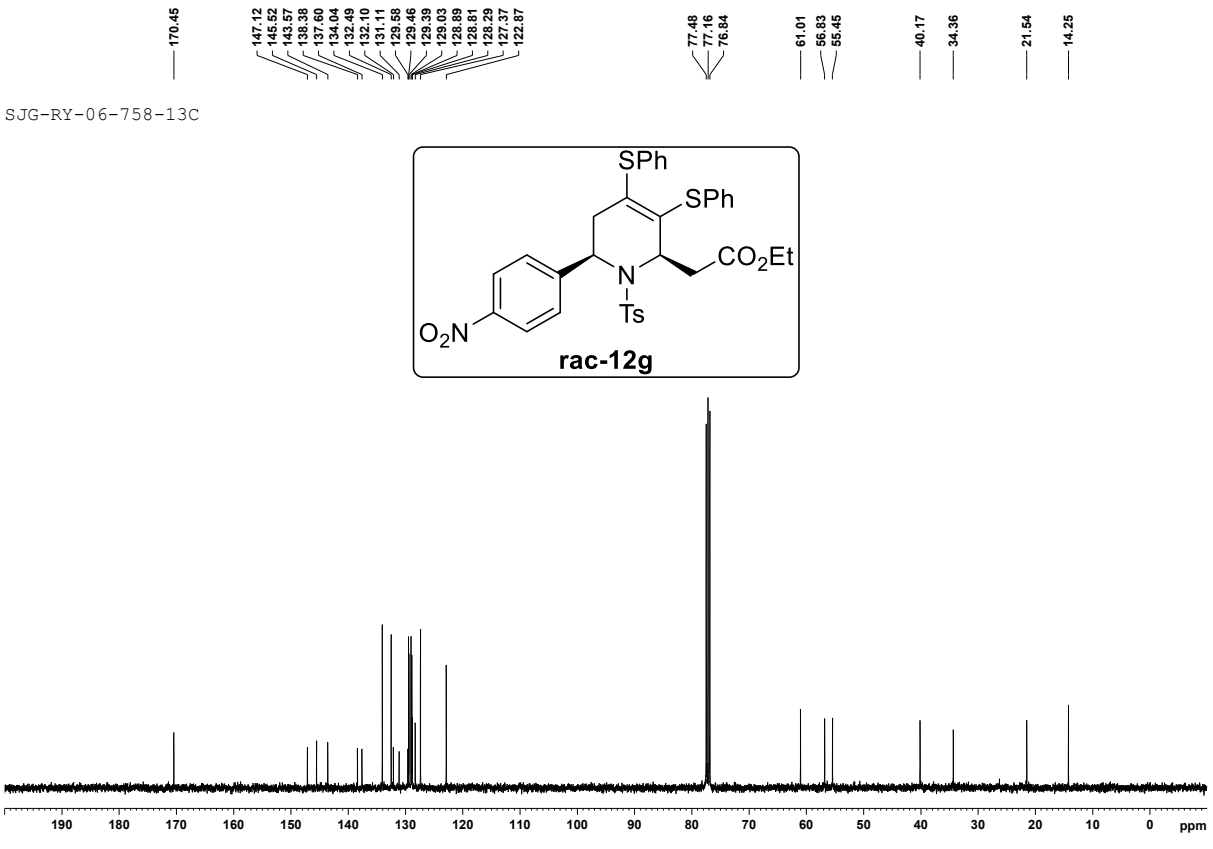
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



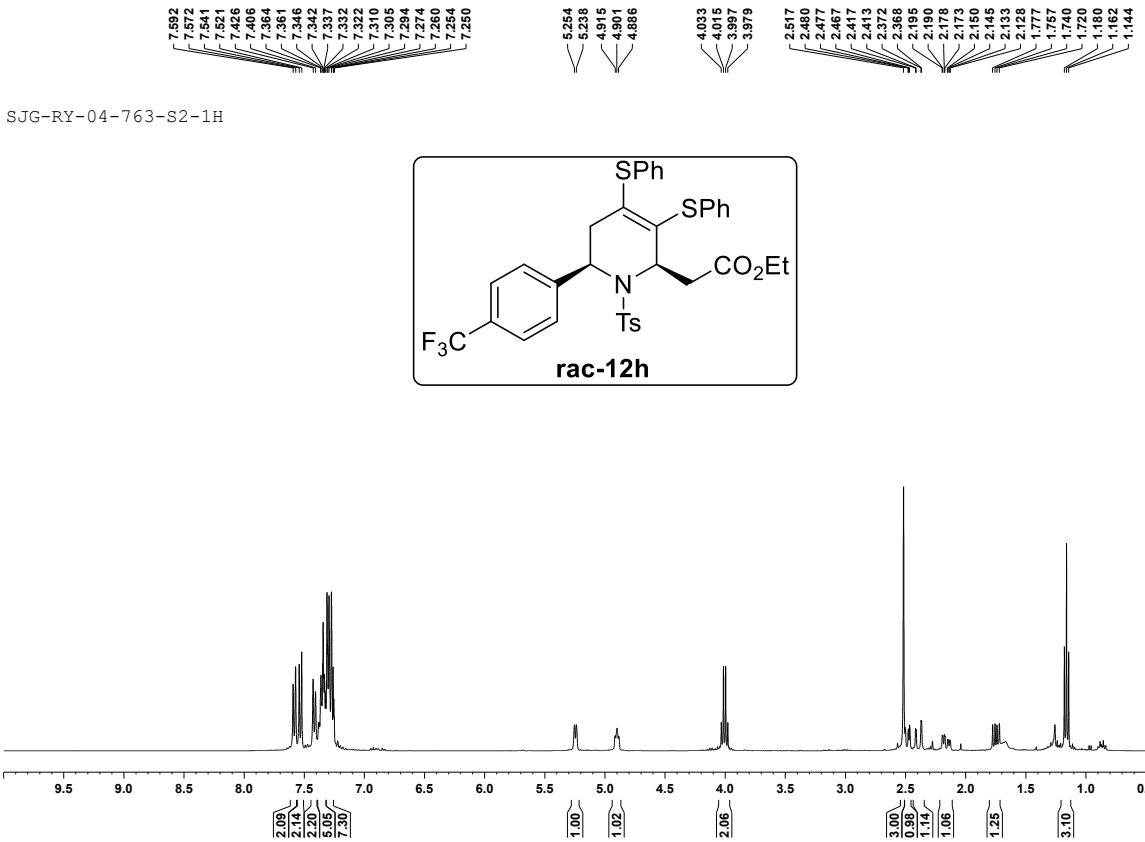
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



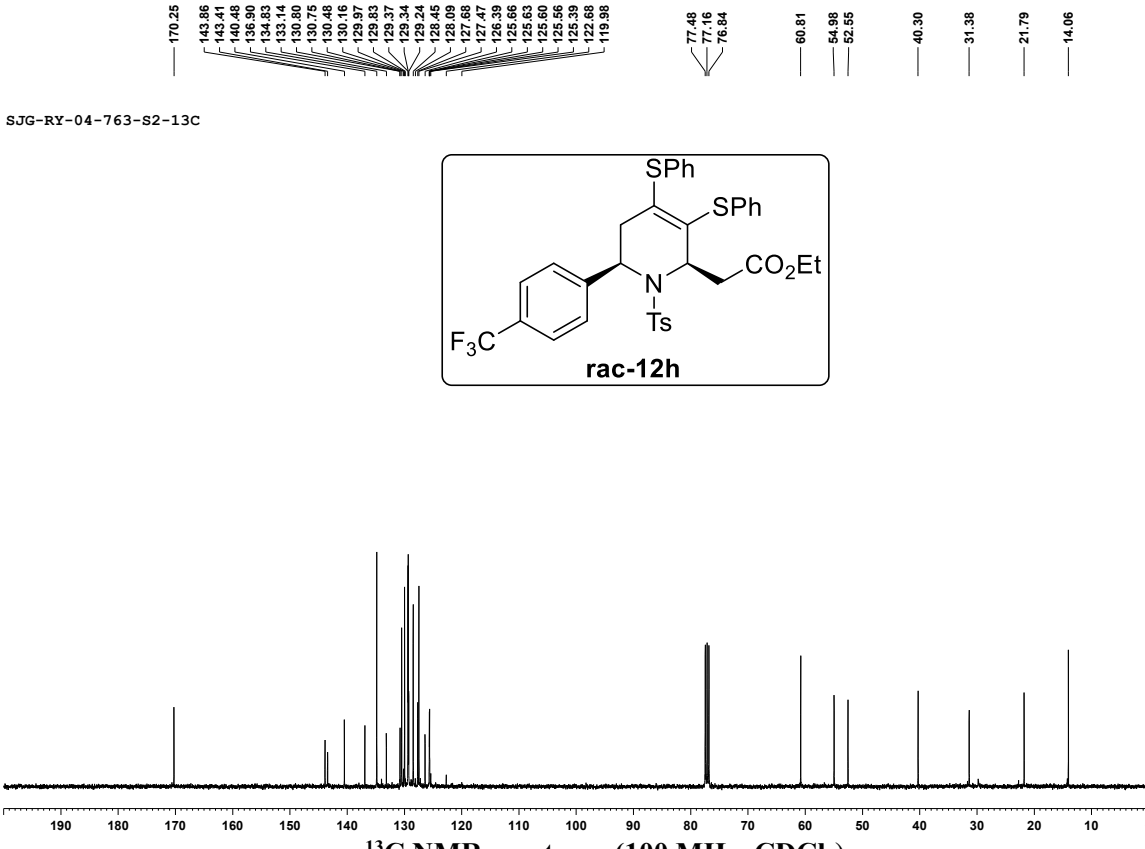
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



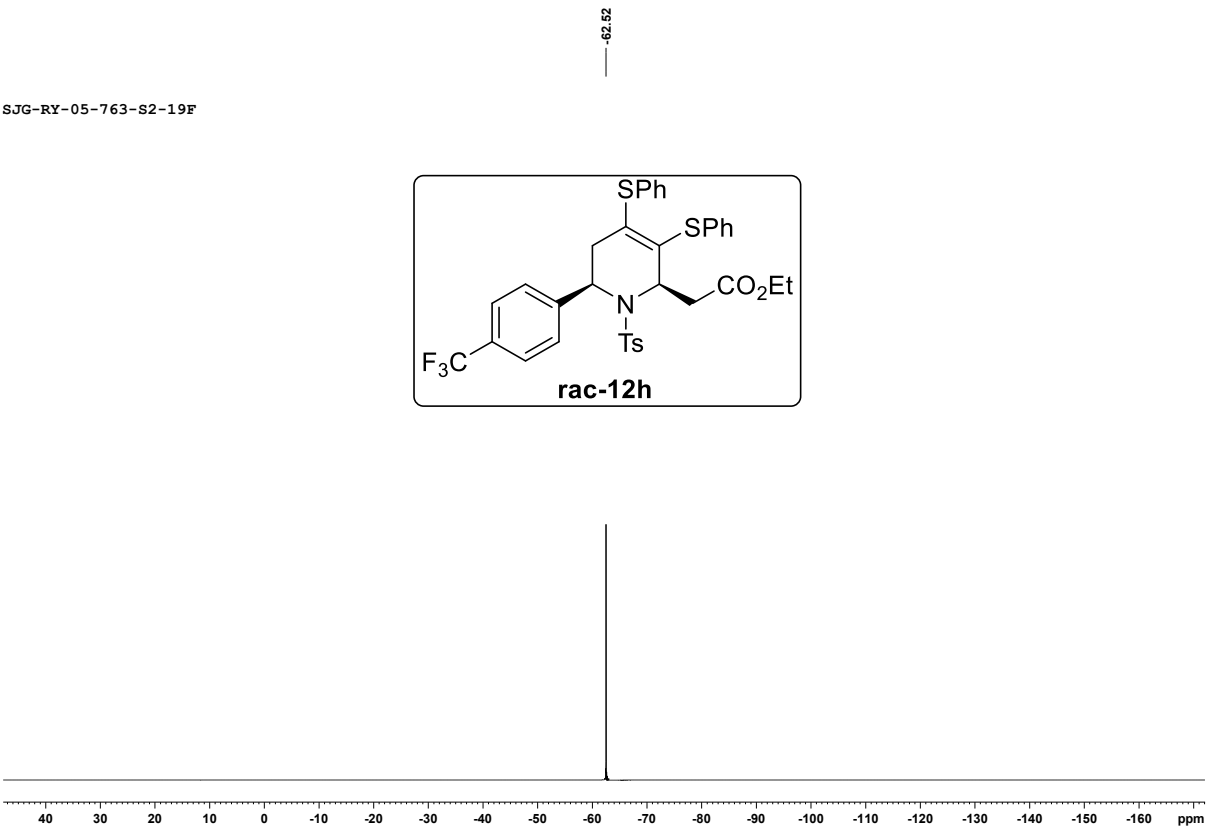
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



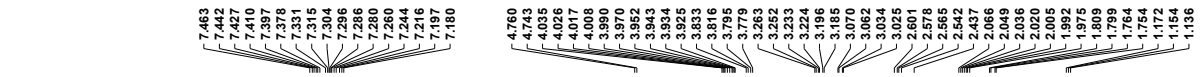
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



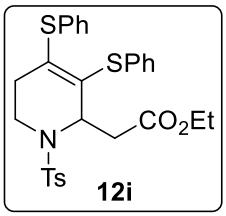
^{13}C NMR spectrum (100 MHz, $CDCl_3$)

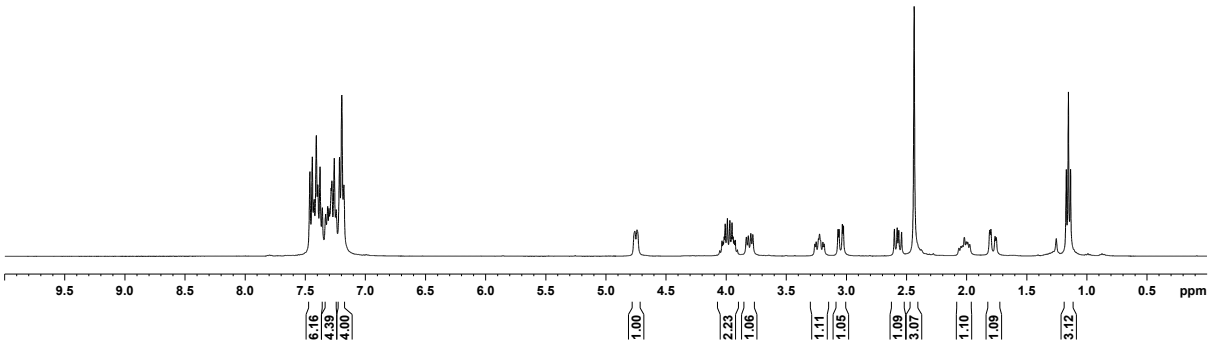


^{19}F NMR spectrum (376 MHz, $CDCl_3$)



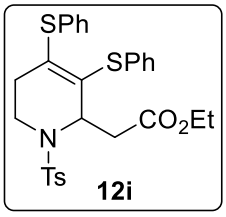
SJG-RY-04-538-1H



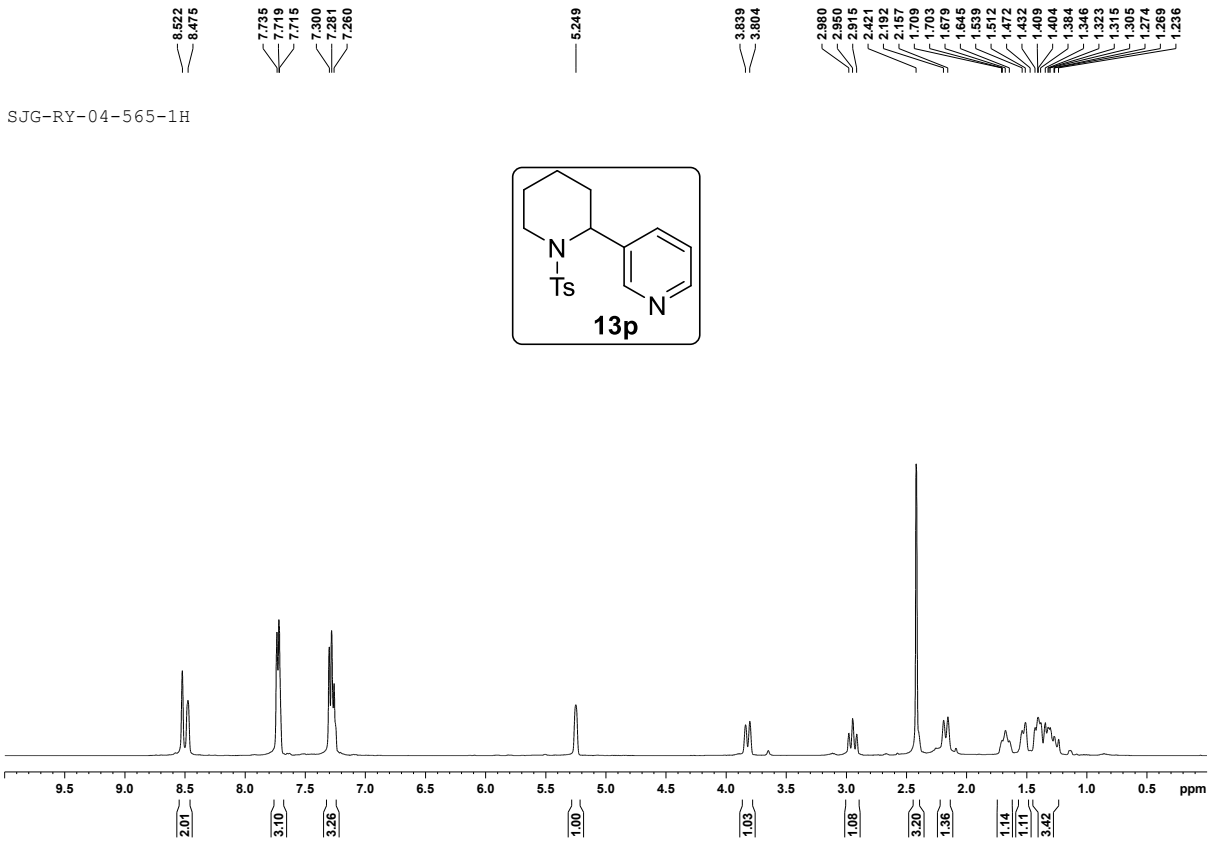


^{1}H NMR spectrum (400 MHz, $CDCl_3$)

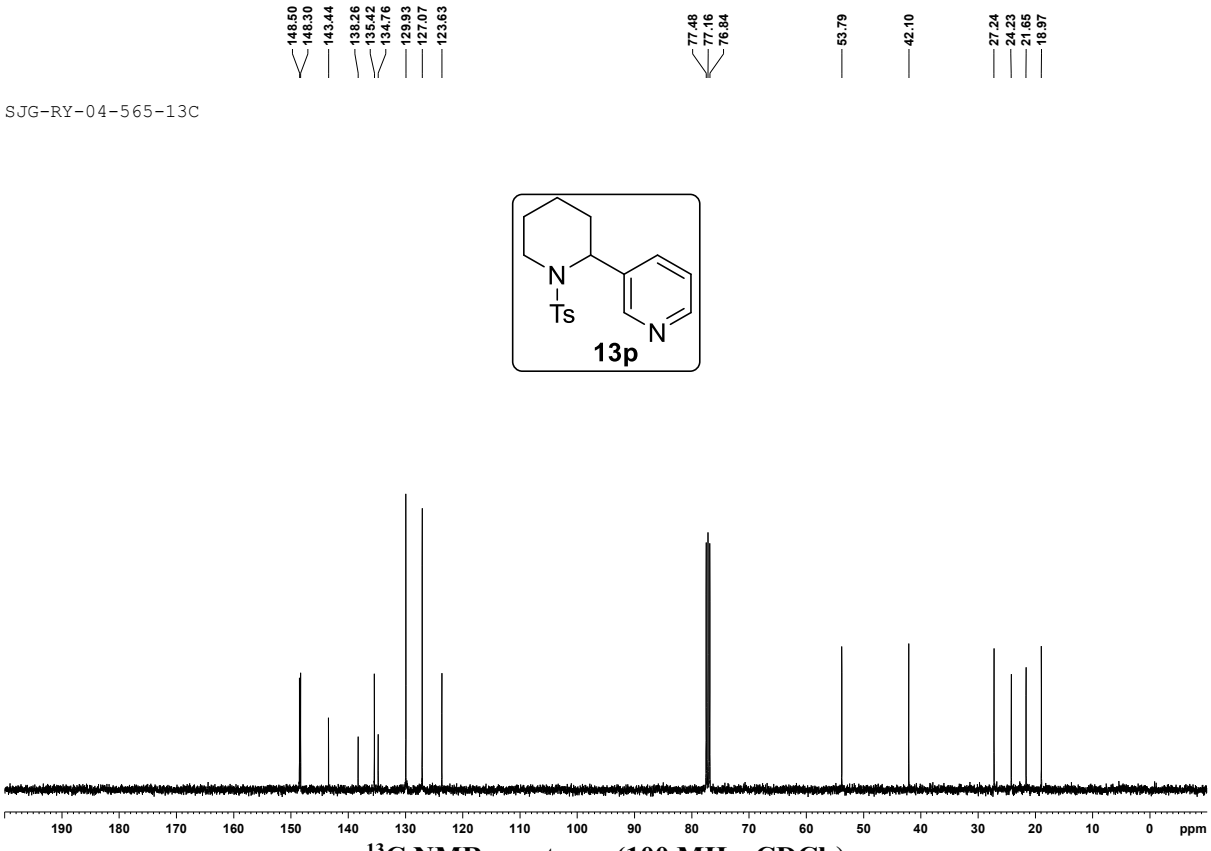
SJG-RY-04-538-13C



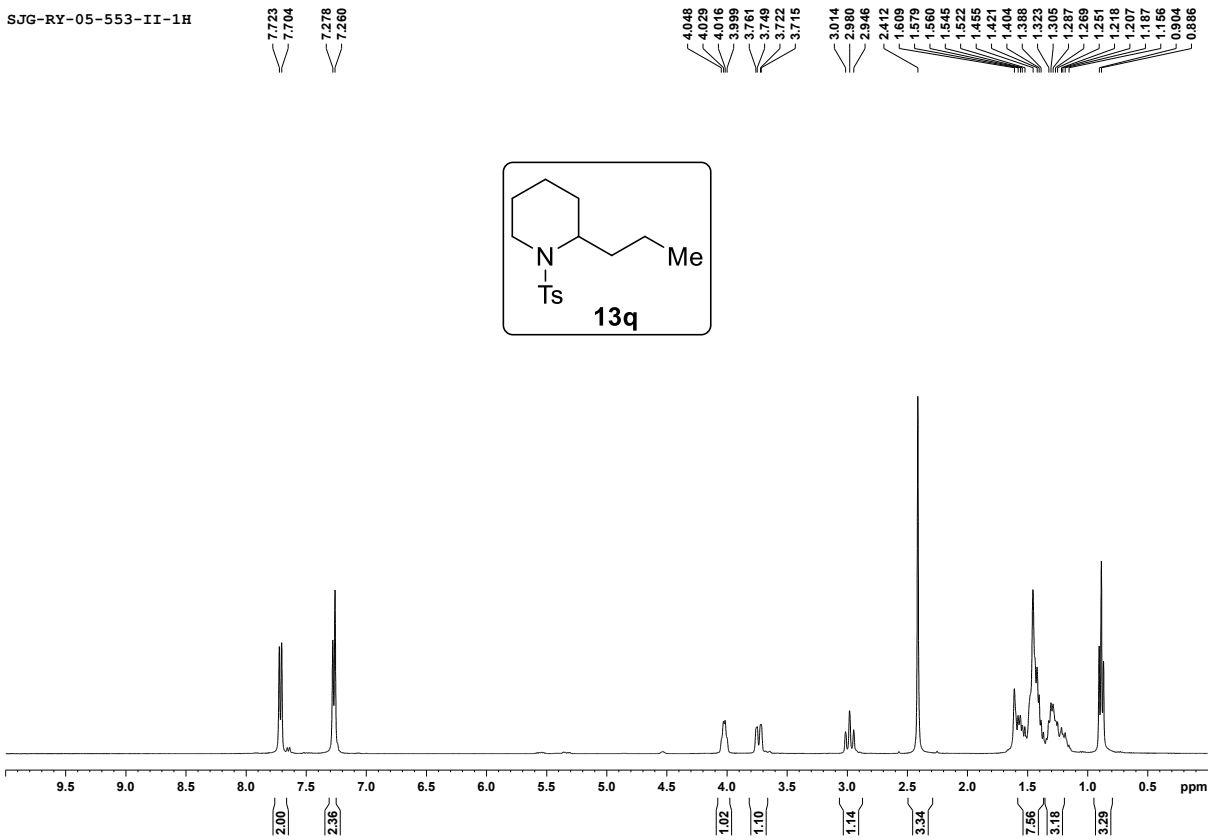
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



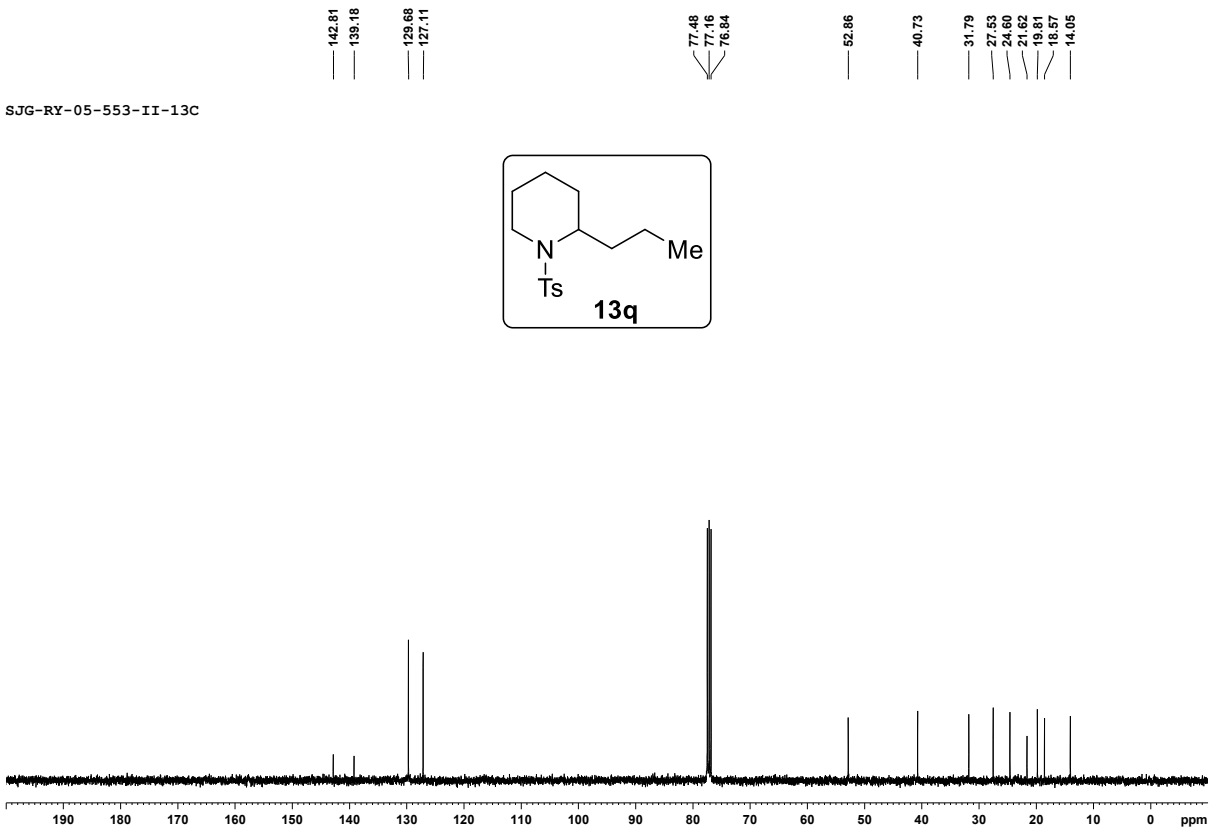
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



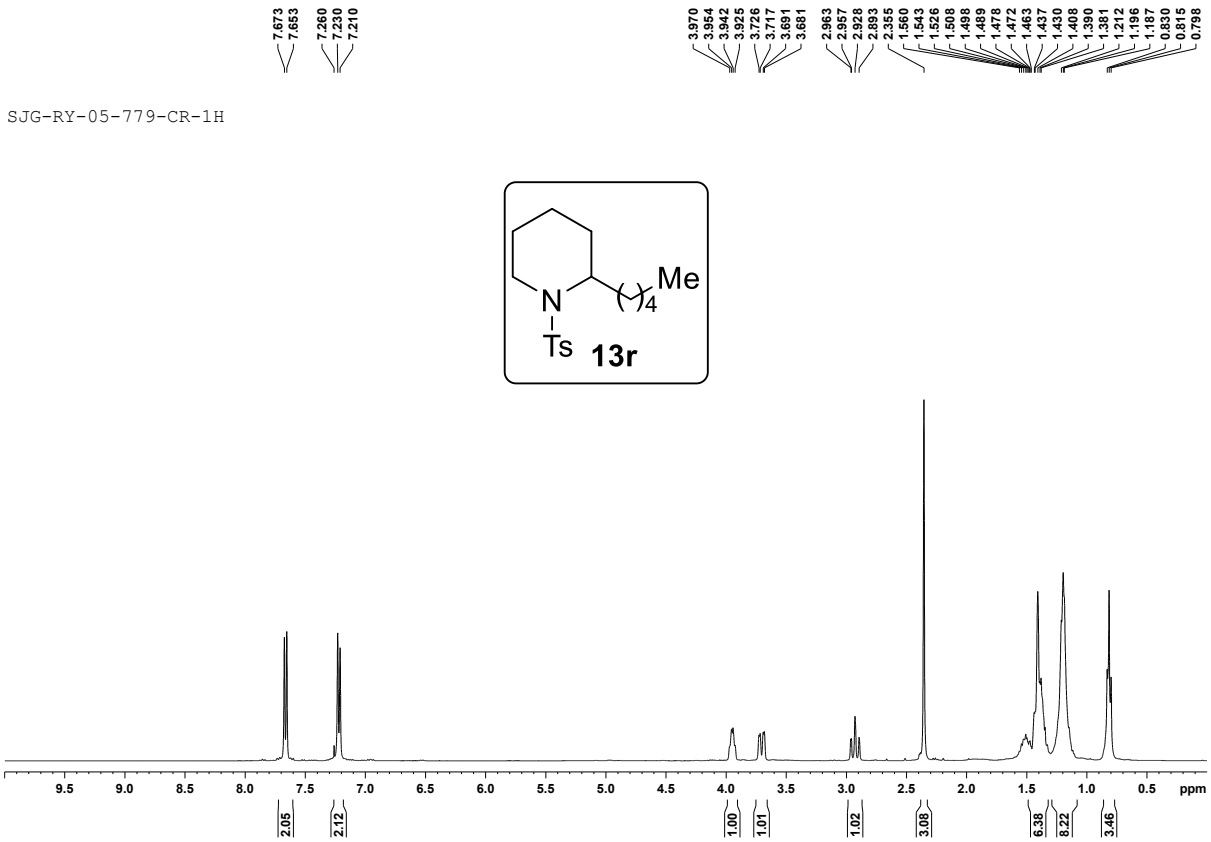
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



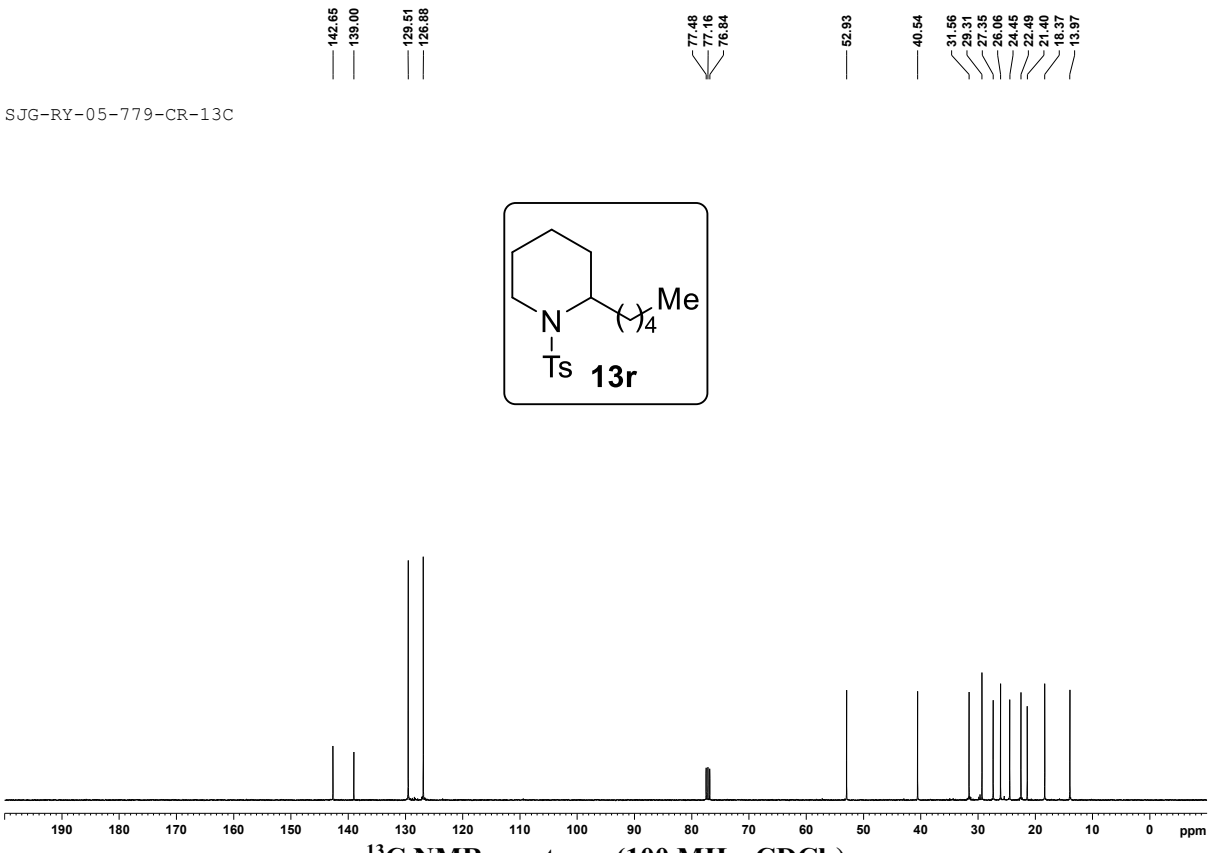
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



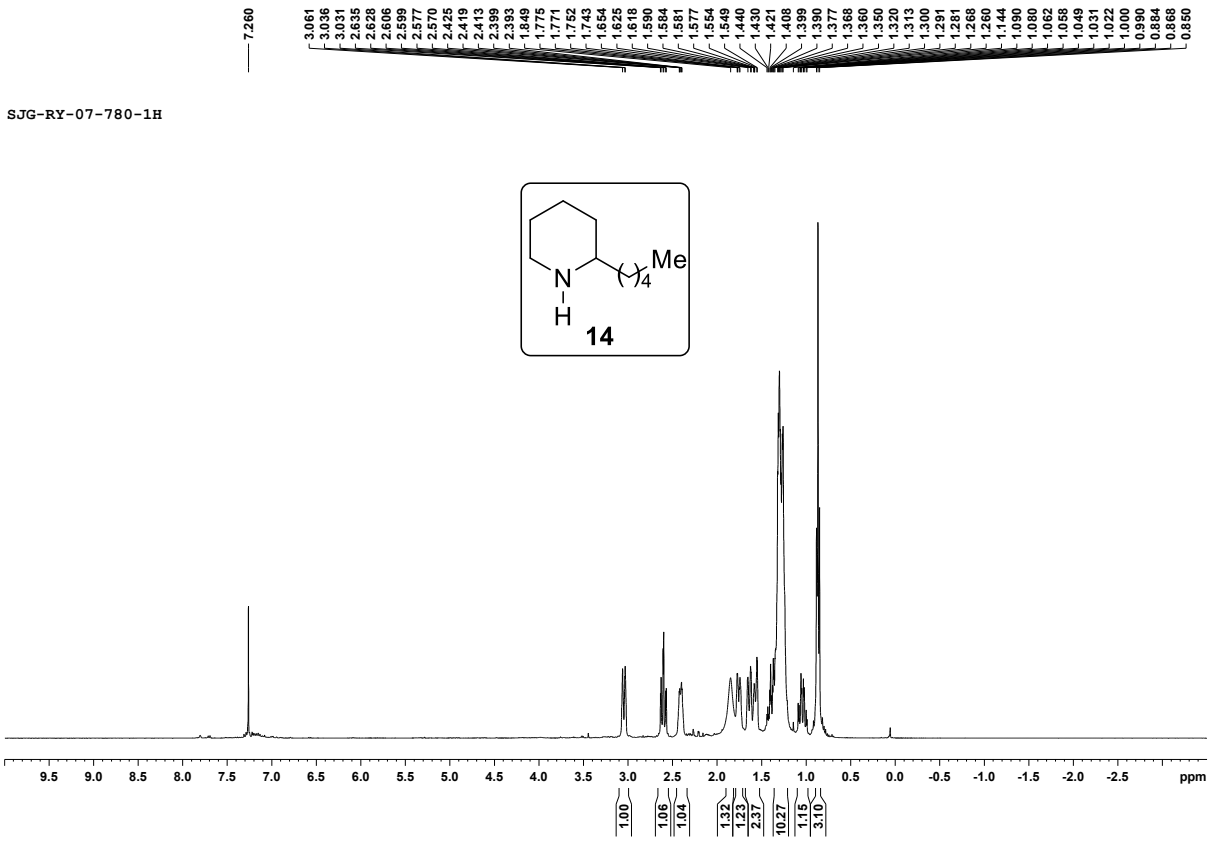
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



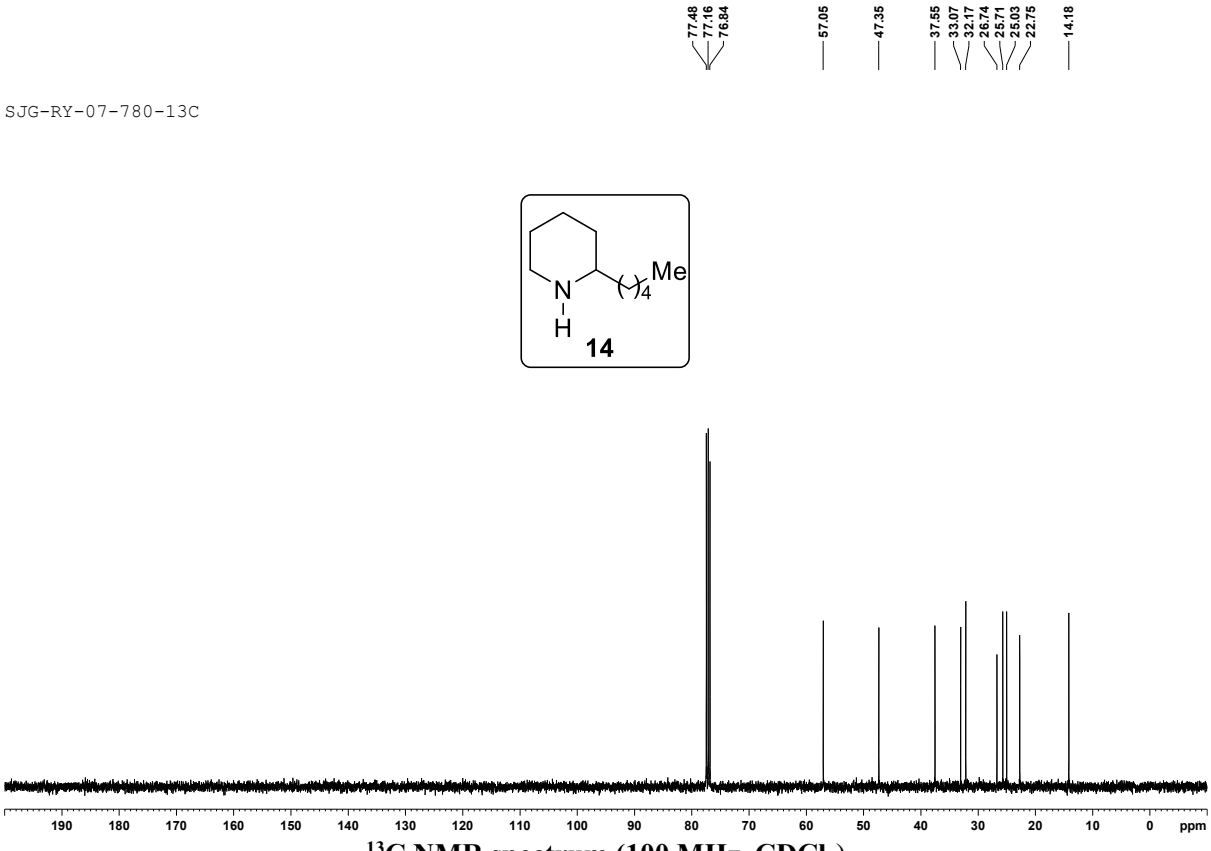
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



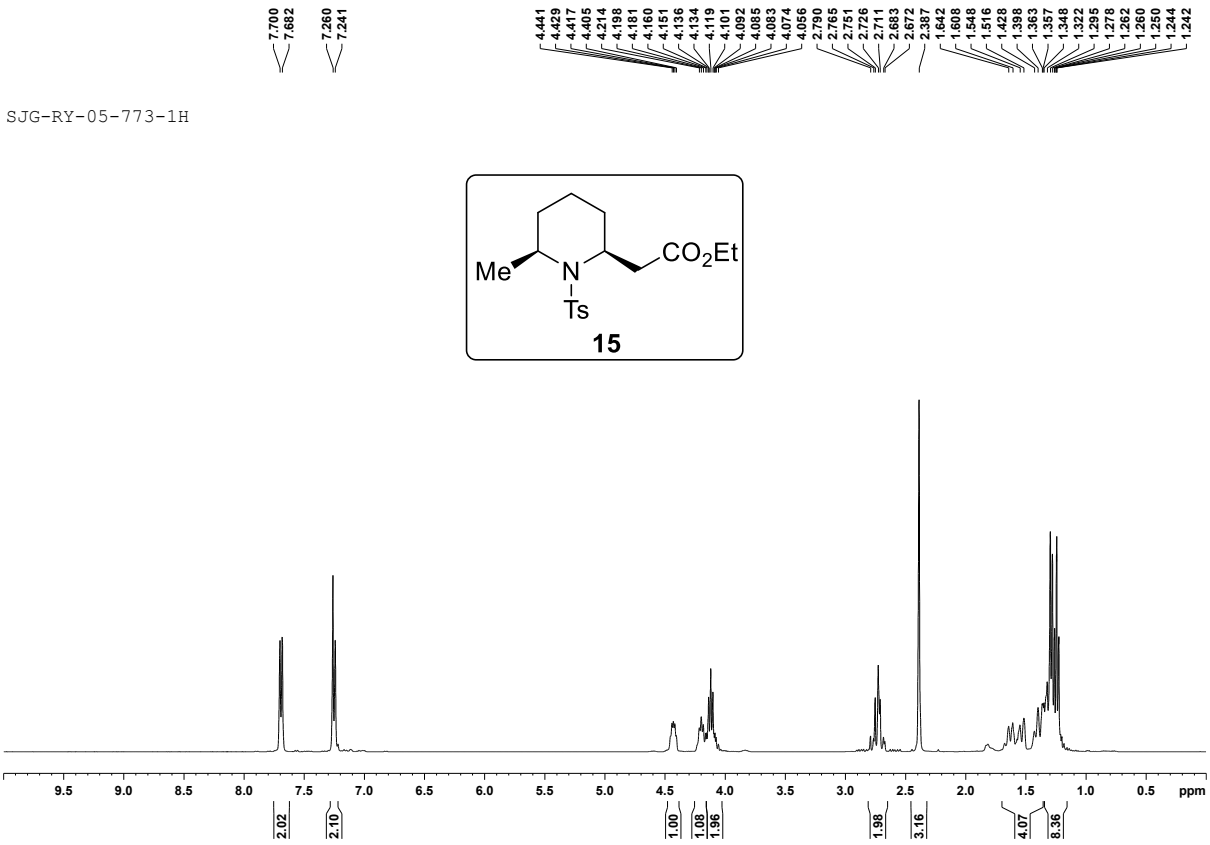
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



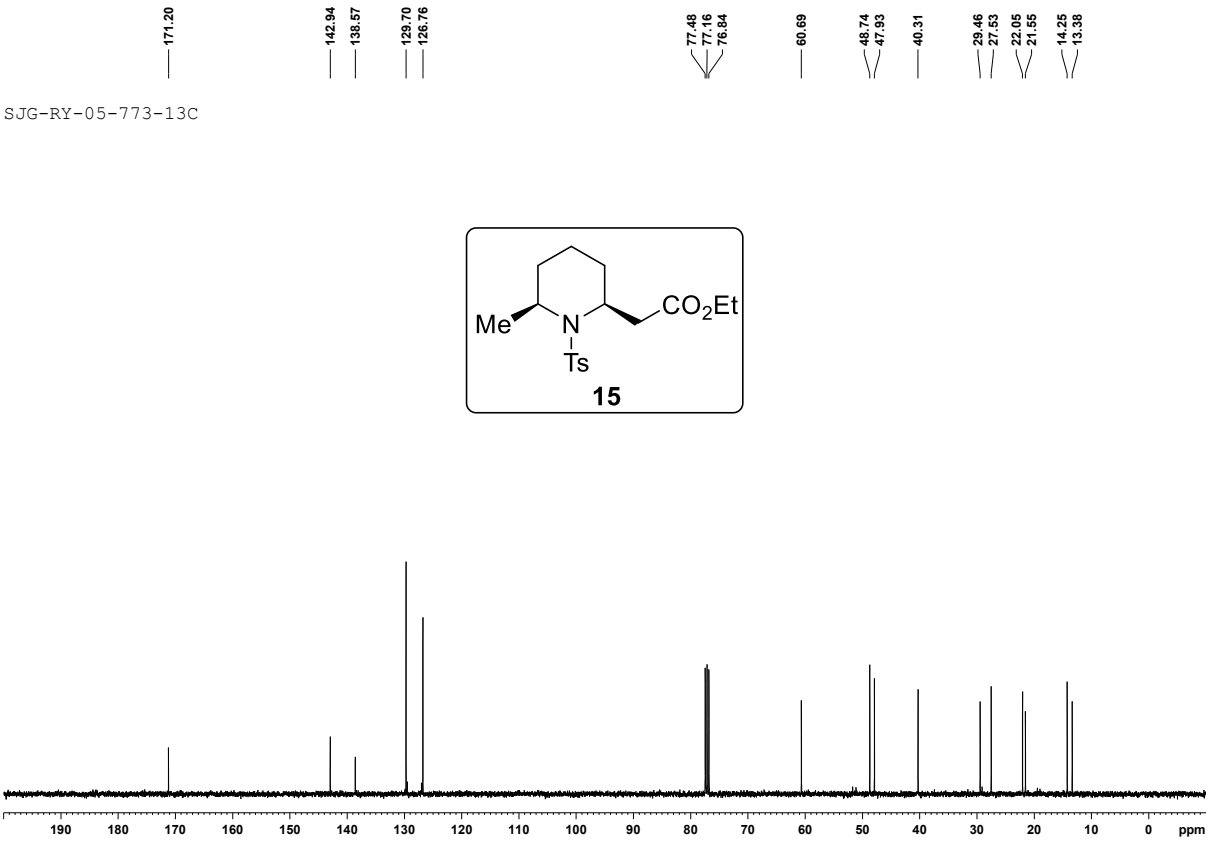
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



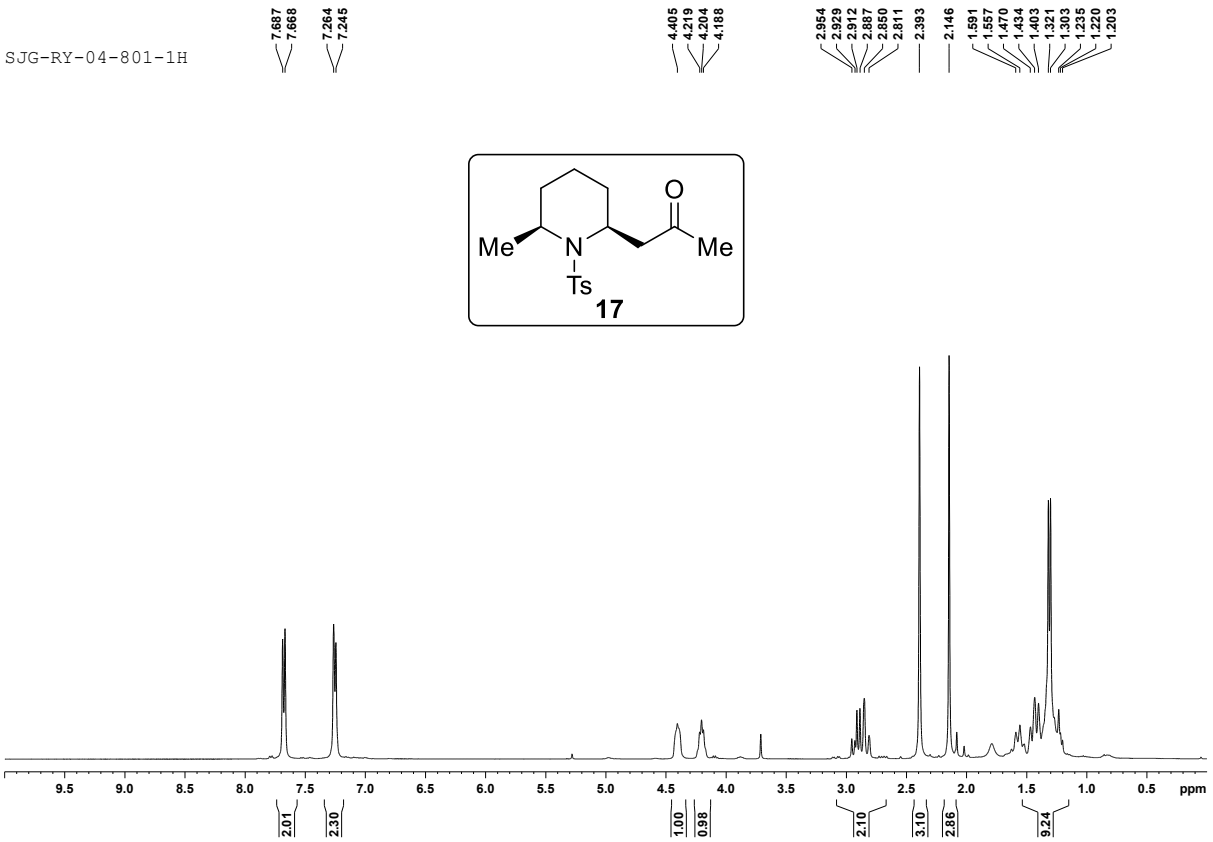
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



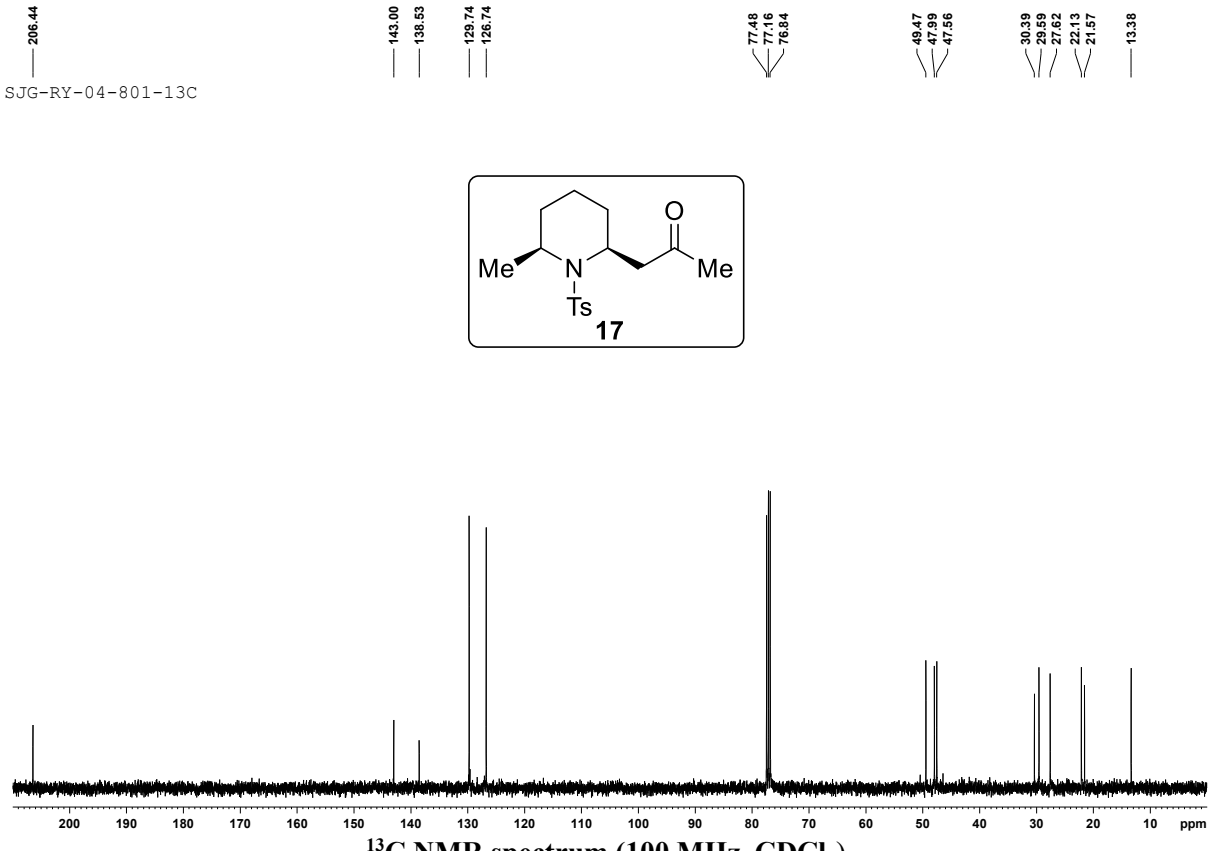
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



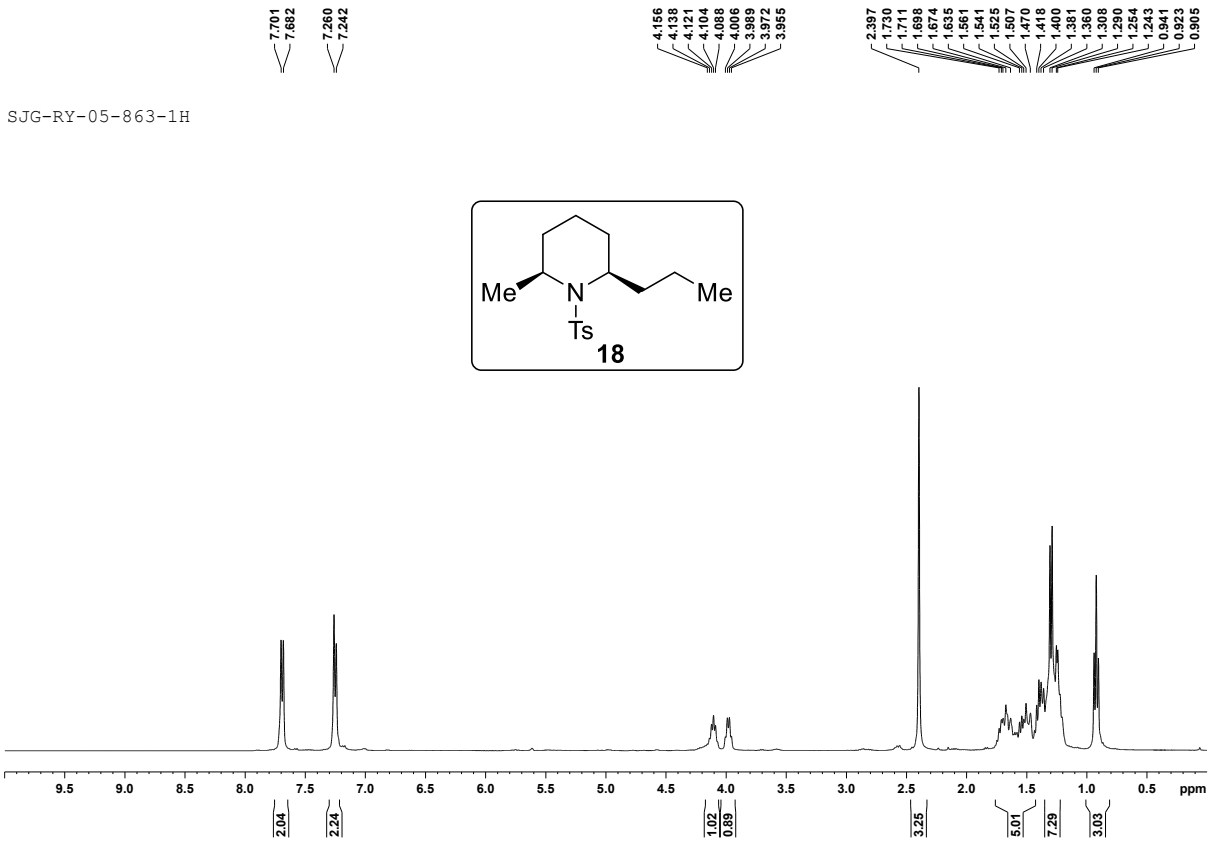
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



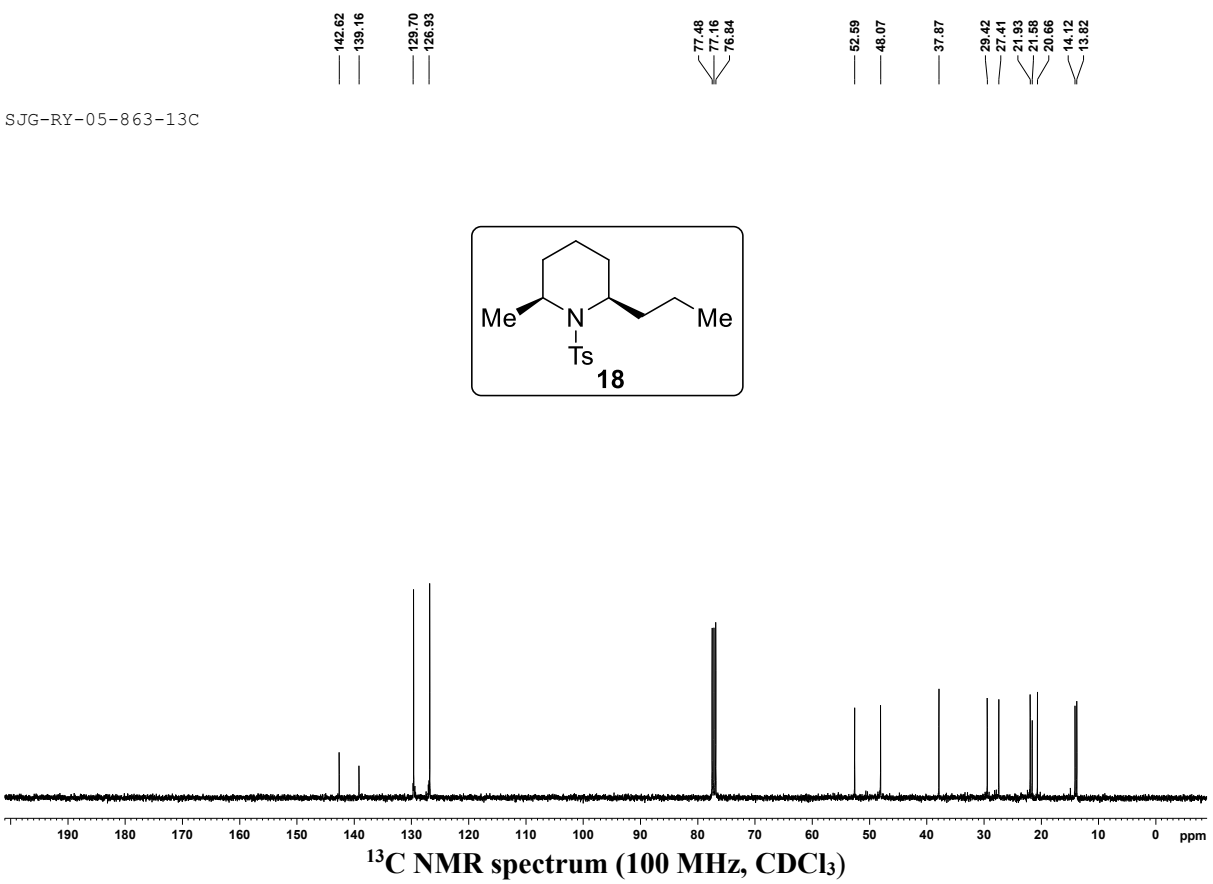
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



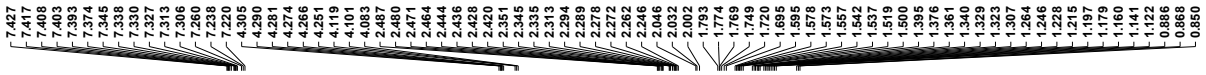
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



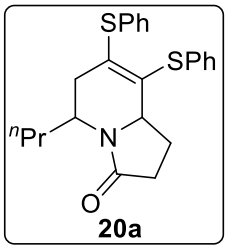
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

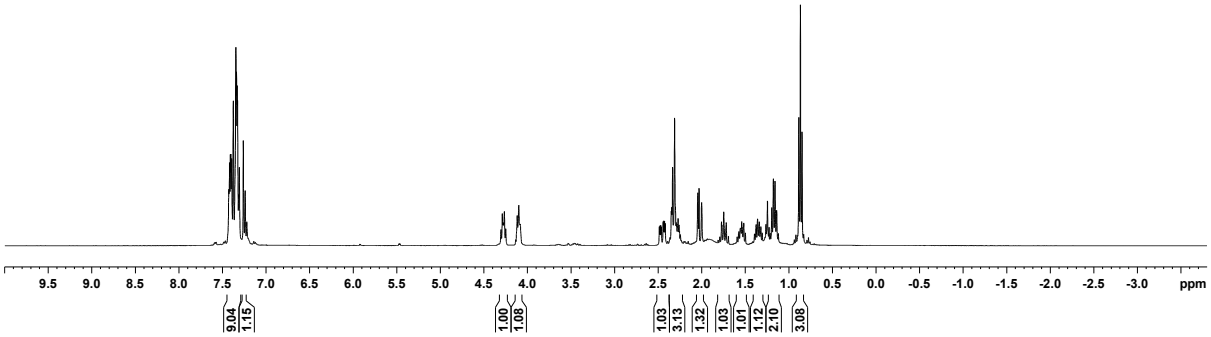


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



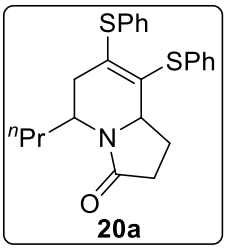
SJG-RY-04-621-1H

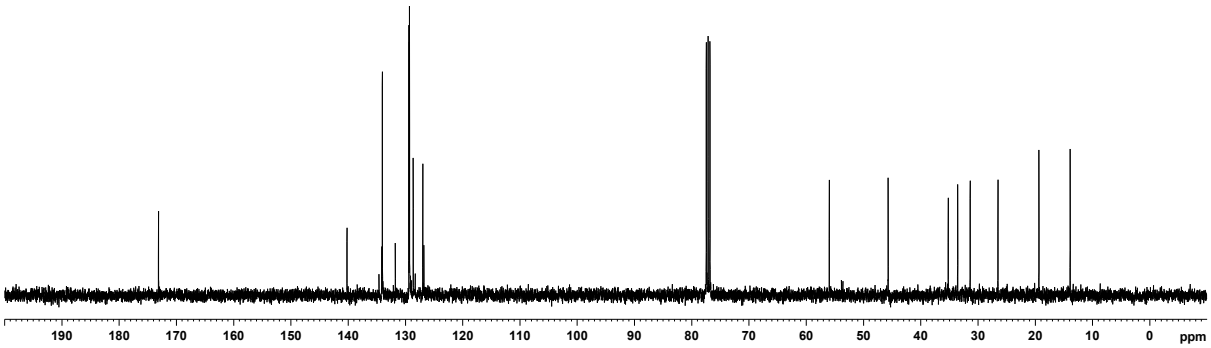




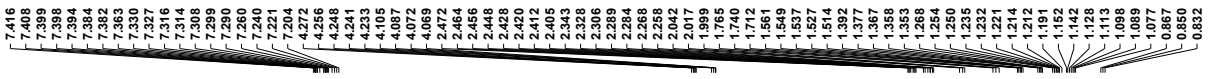
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

SJG-RY-04-621-13C

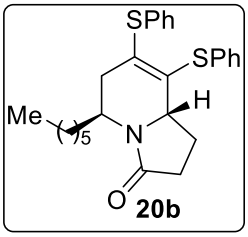


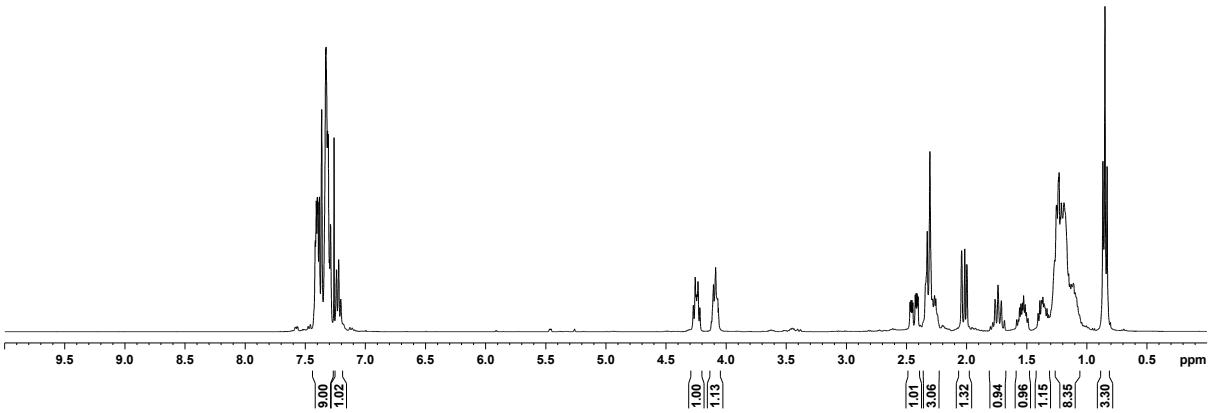


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



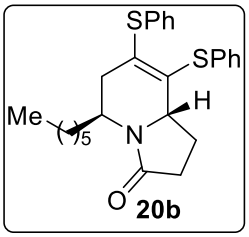
SJG-RY-04-615-1H

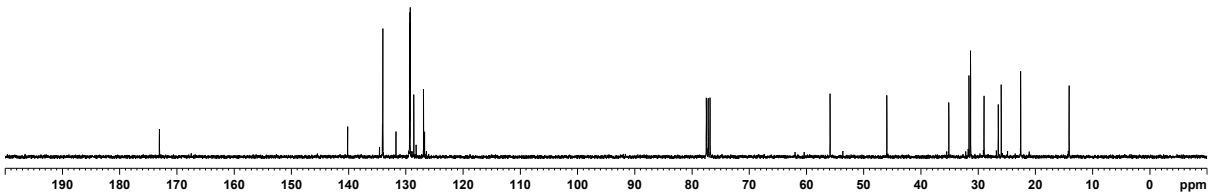




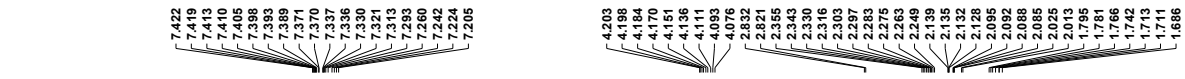
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

SJG-RY-04-615-13C

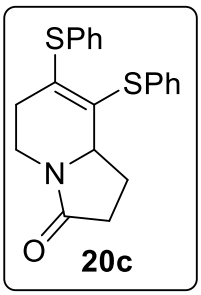


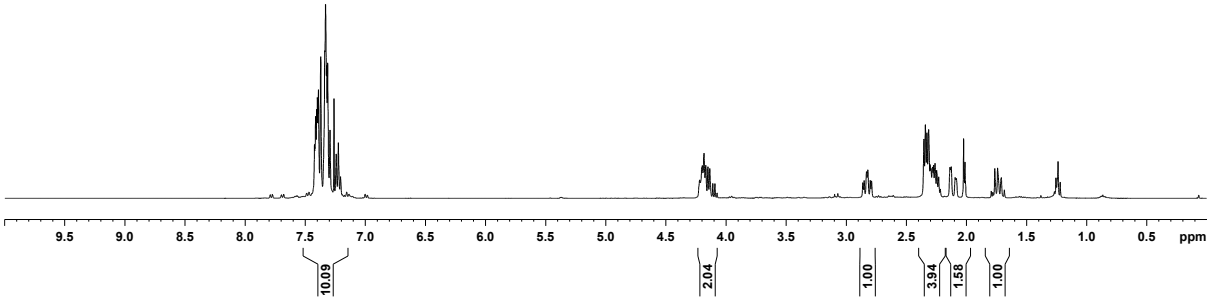


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

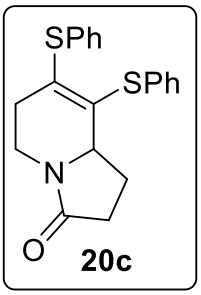


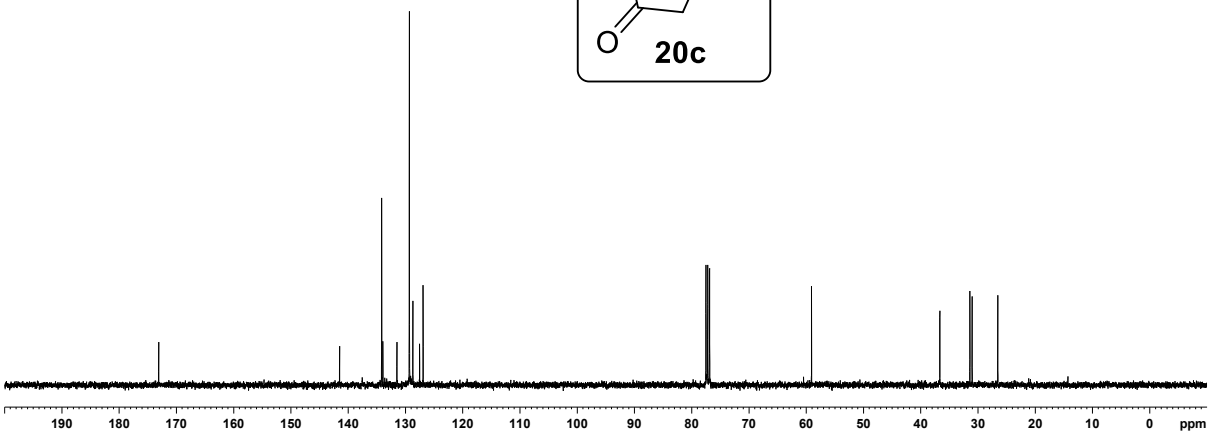
SJ-RY-04-678-S1-1H



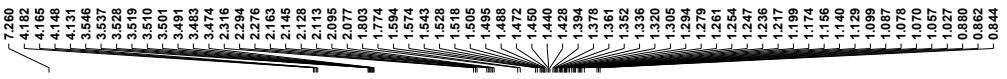


^{1}H NMR spectrum (400 MHz, $CDCl_3$)

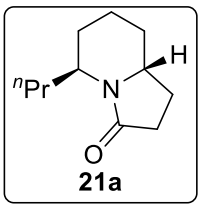




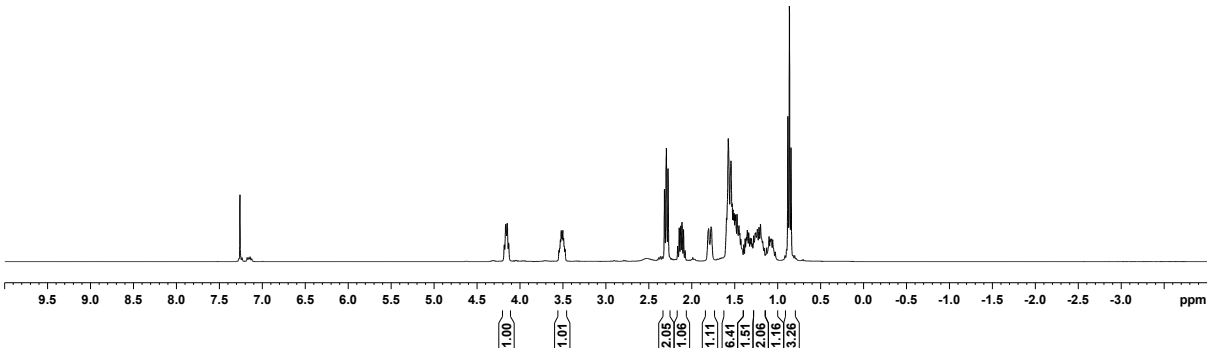
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



SJG-RY-04-598-1H

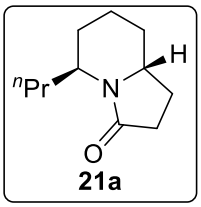


21a

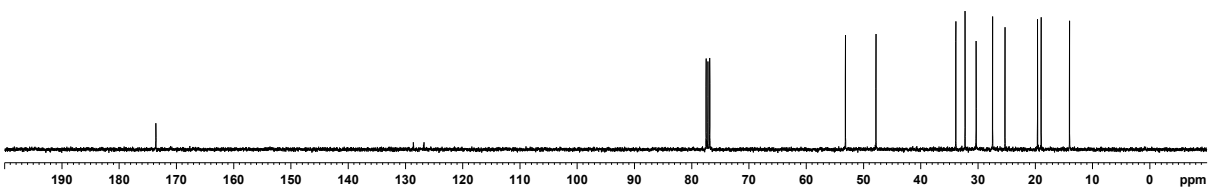


^{1}H NMR spectrum (400 MHz, $CDCl_3$)

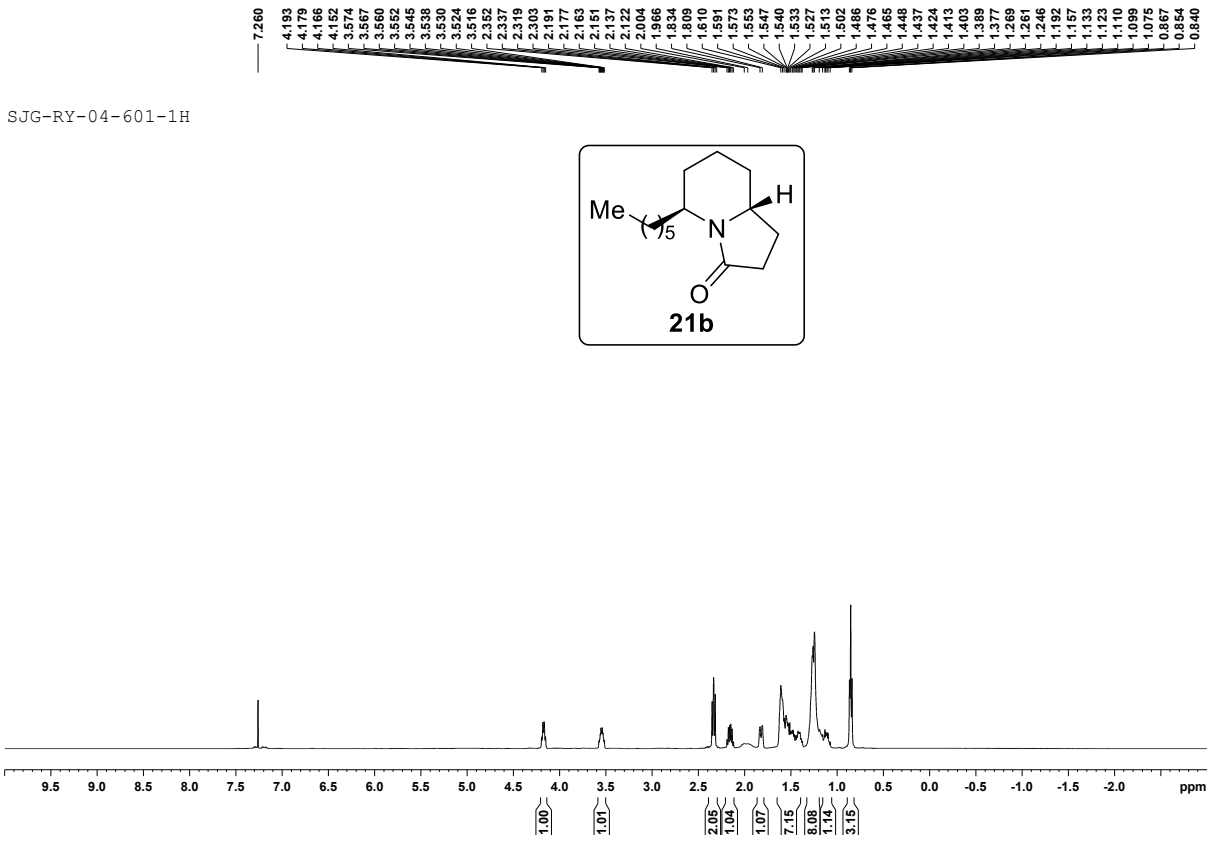
SJG-RY-04-598-13C



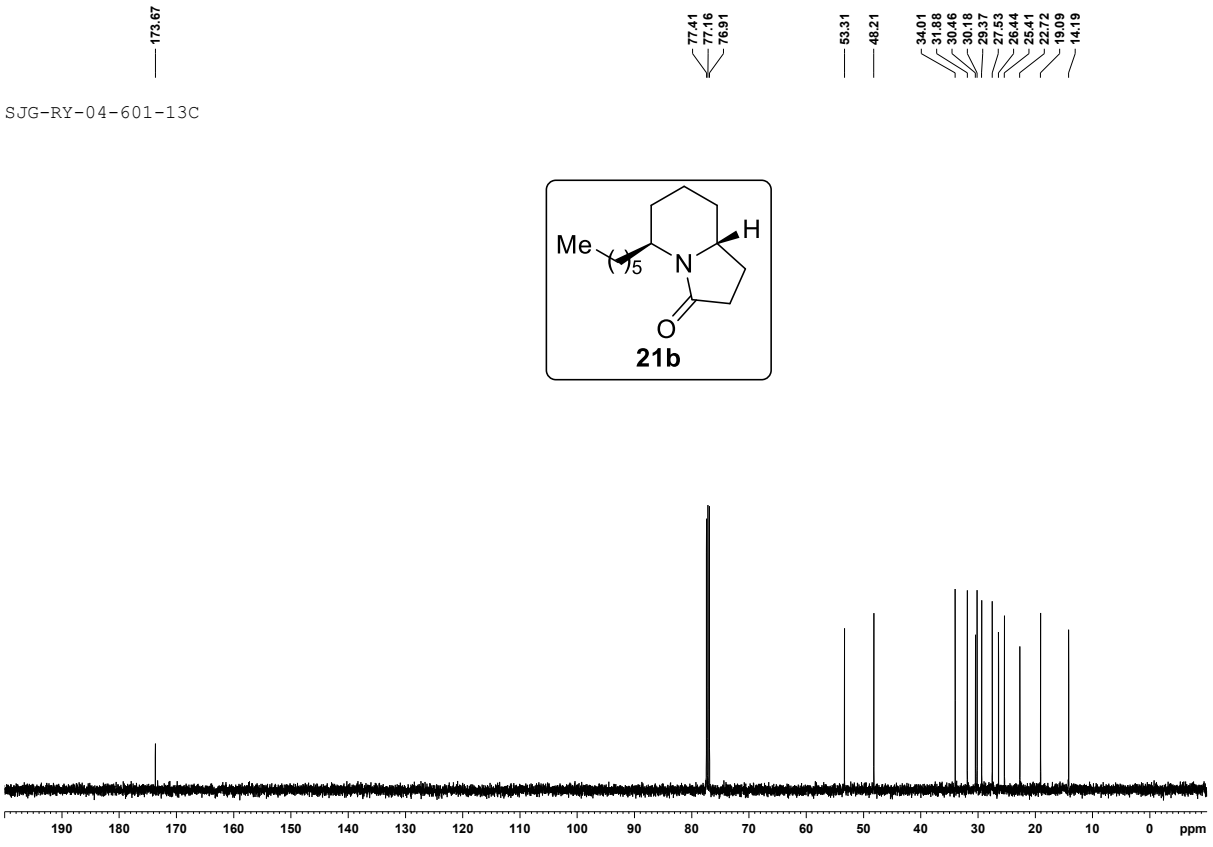
21a



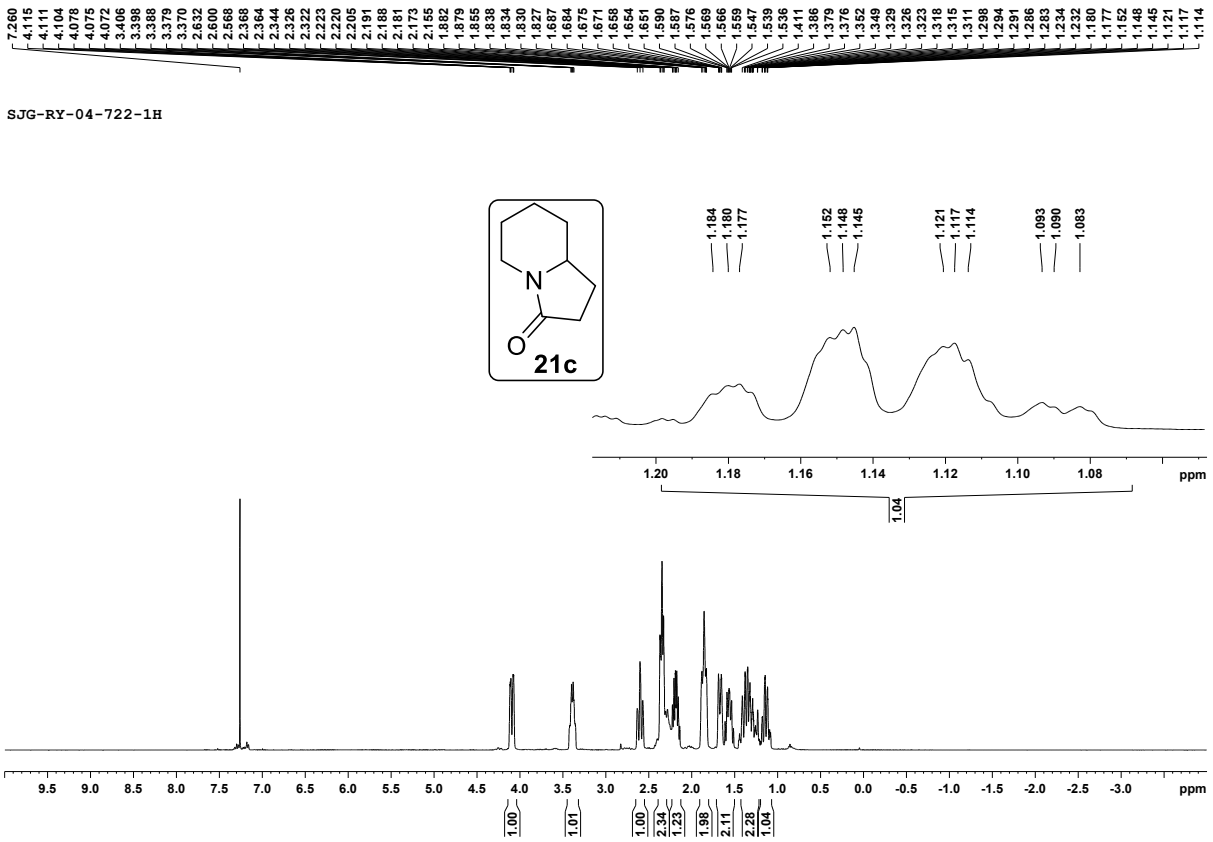
^{13}C NMR spectrum (125 MHz, $CDCl_3$)



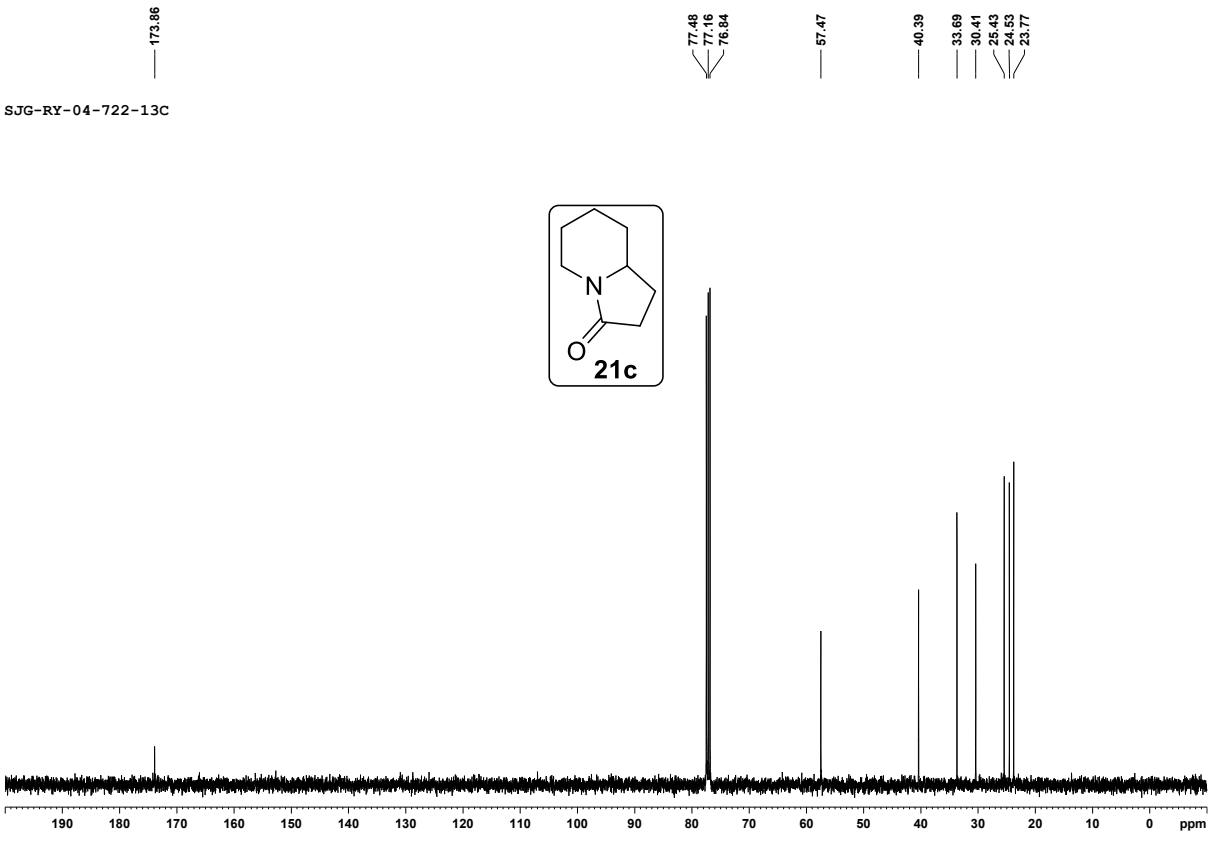
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



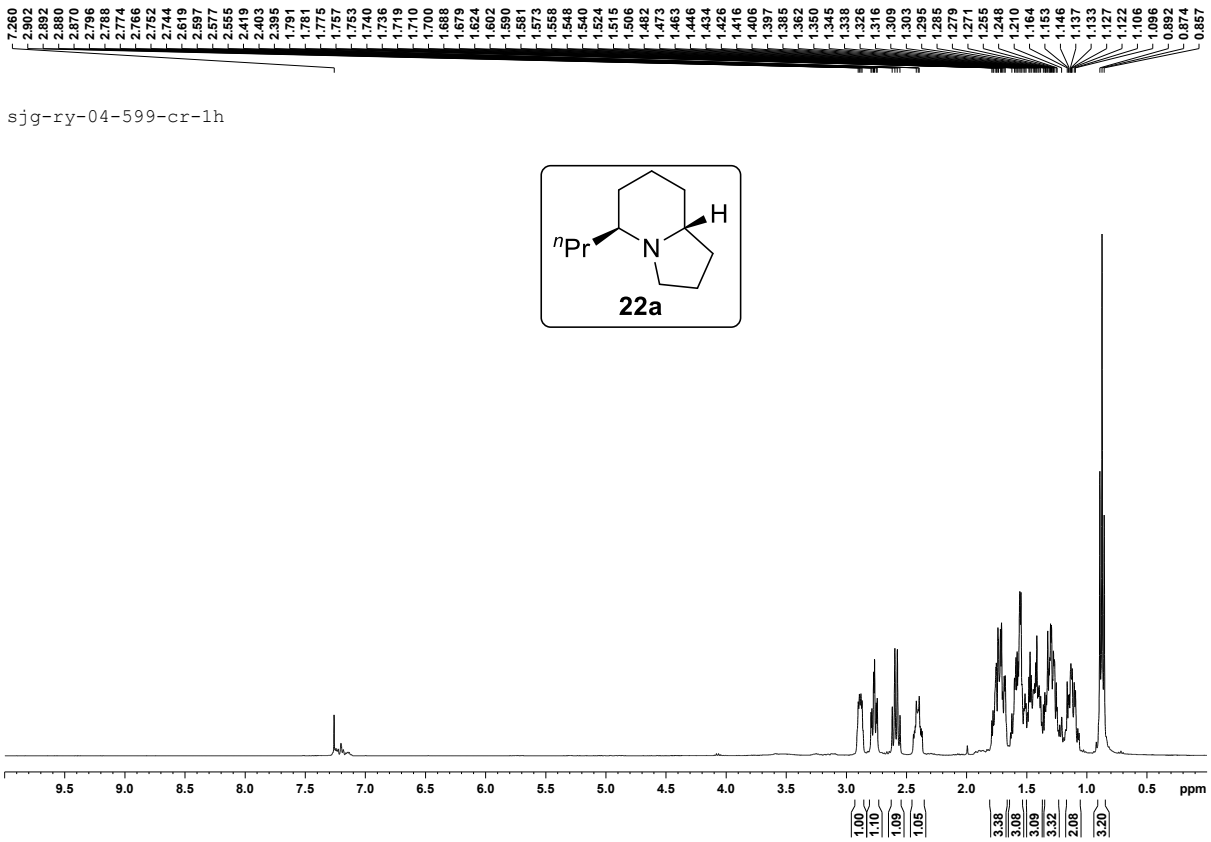
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



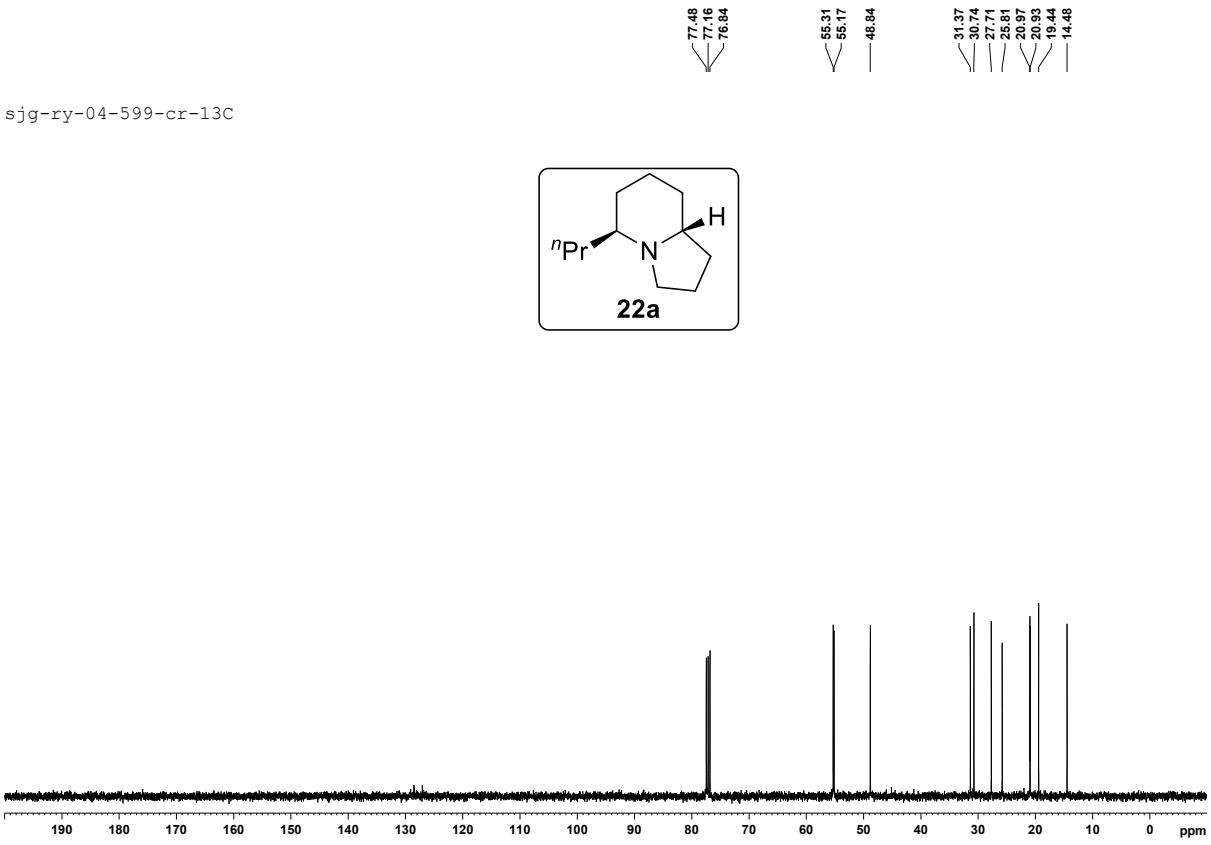
^{1}H NMR spectrum (400 MHz, $CDCl_3$)



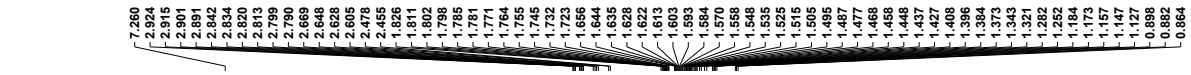
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



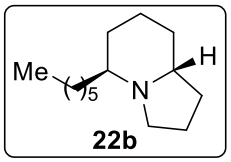
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

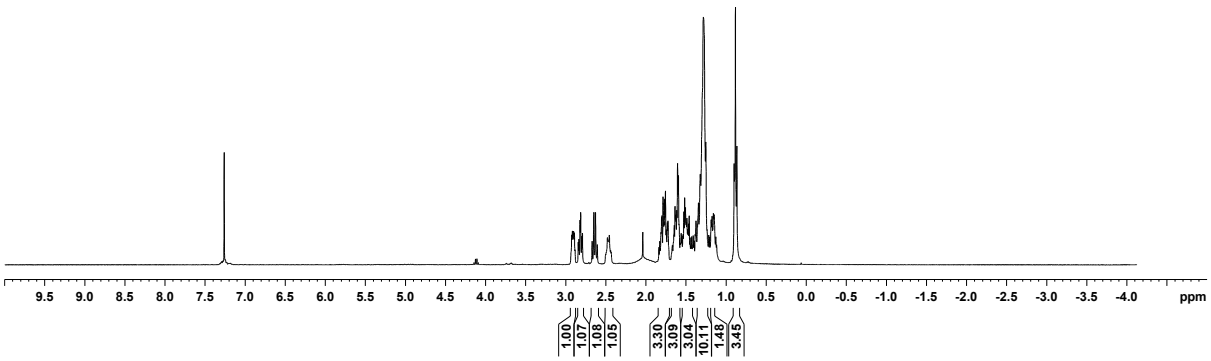


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

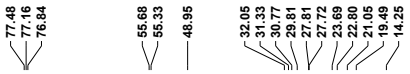


SJG-RY-04-602-1H

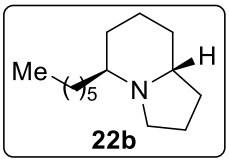


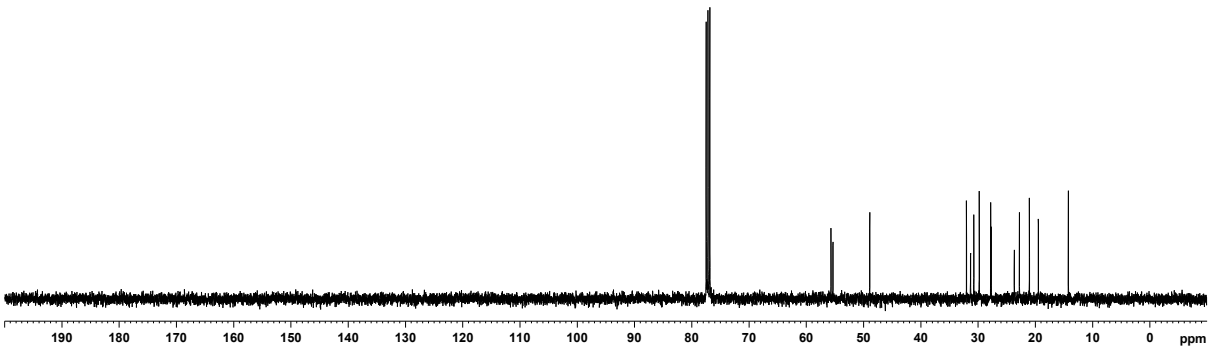


^{1}H NMR spectrum (400 MHz, $CDCl_3$)

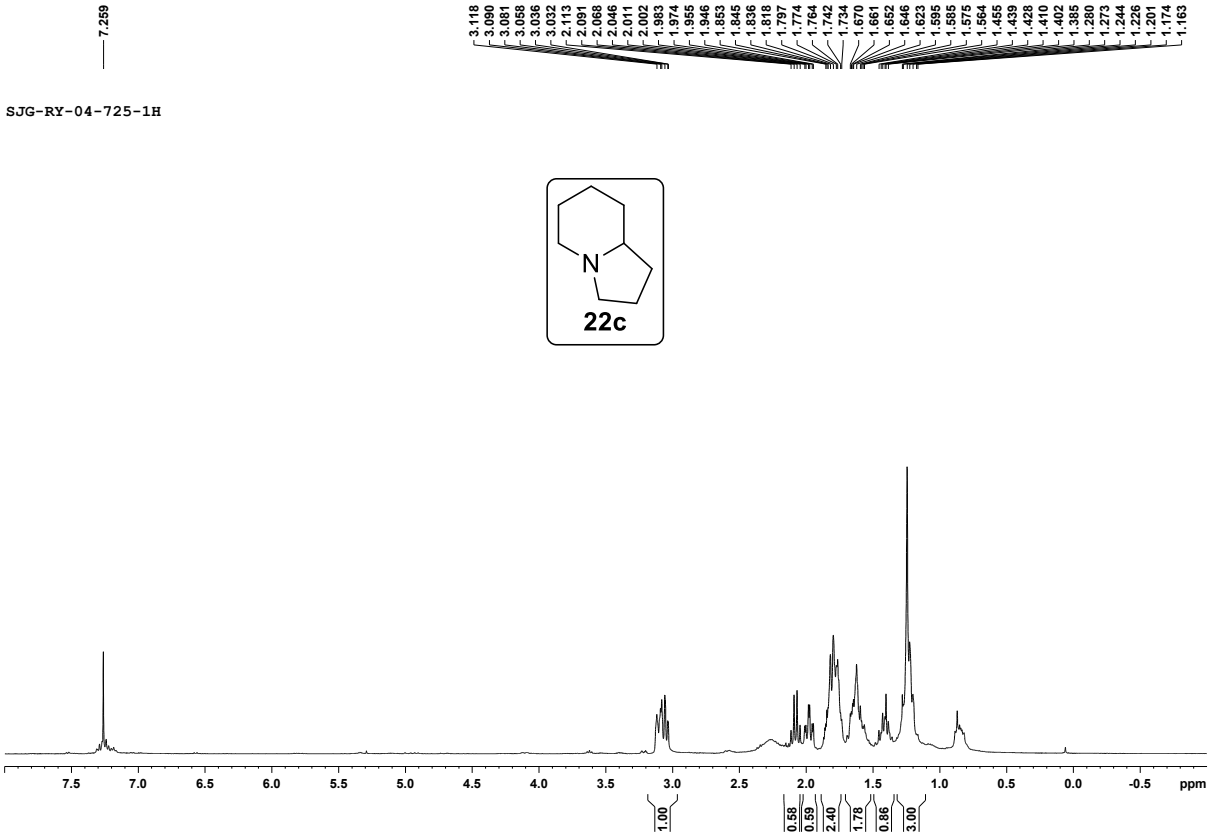


SJG-RY-04-602-13C

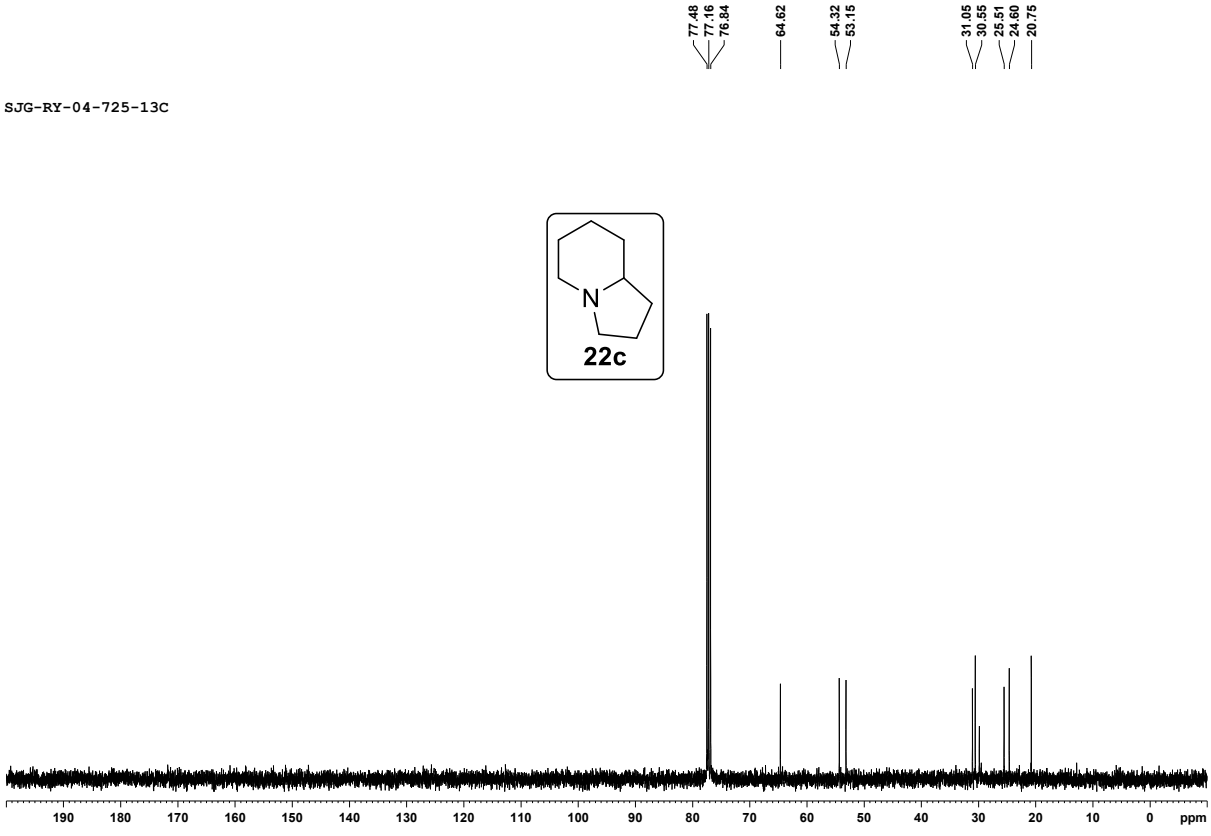




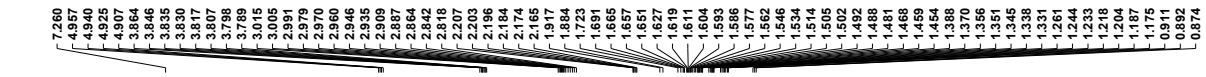
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



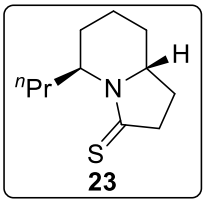
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

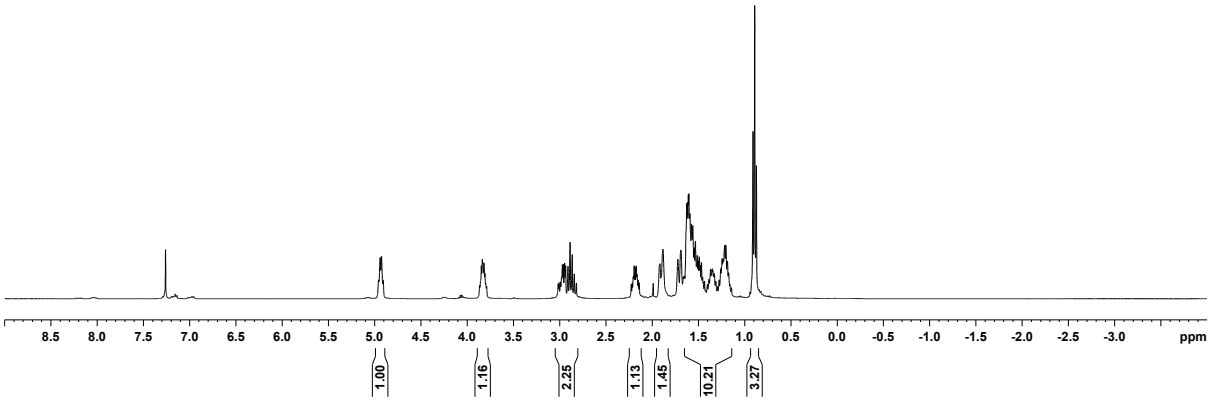


^{13}C NMR spectrum (100 MHz, $CDCl_3$)

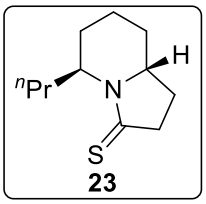


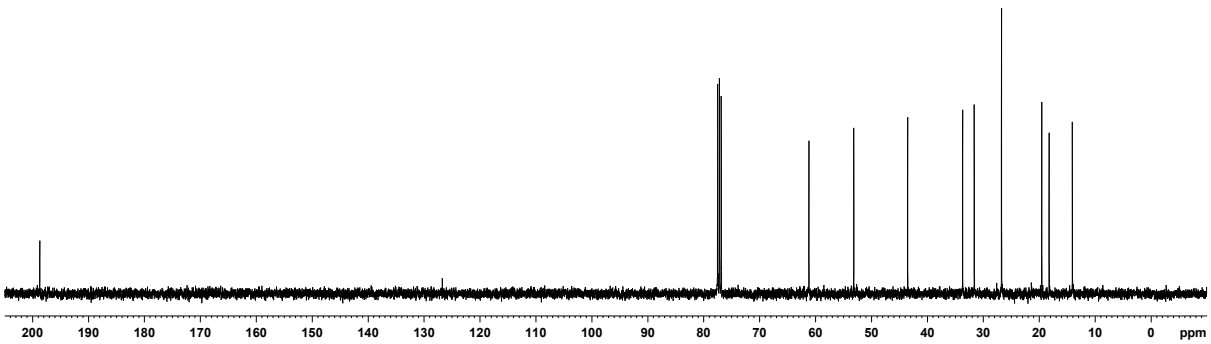
SJG-RY-04-660-1H



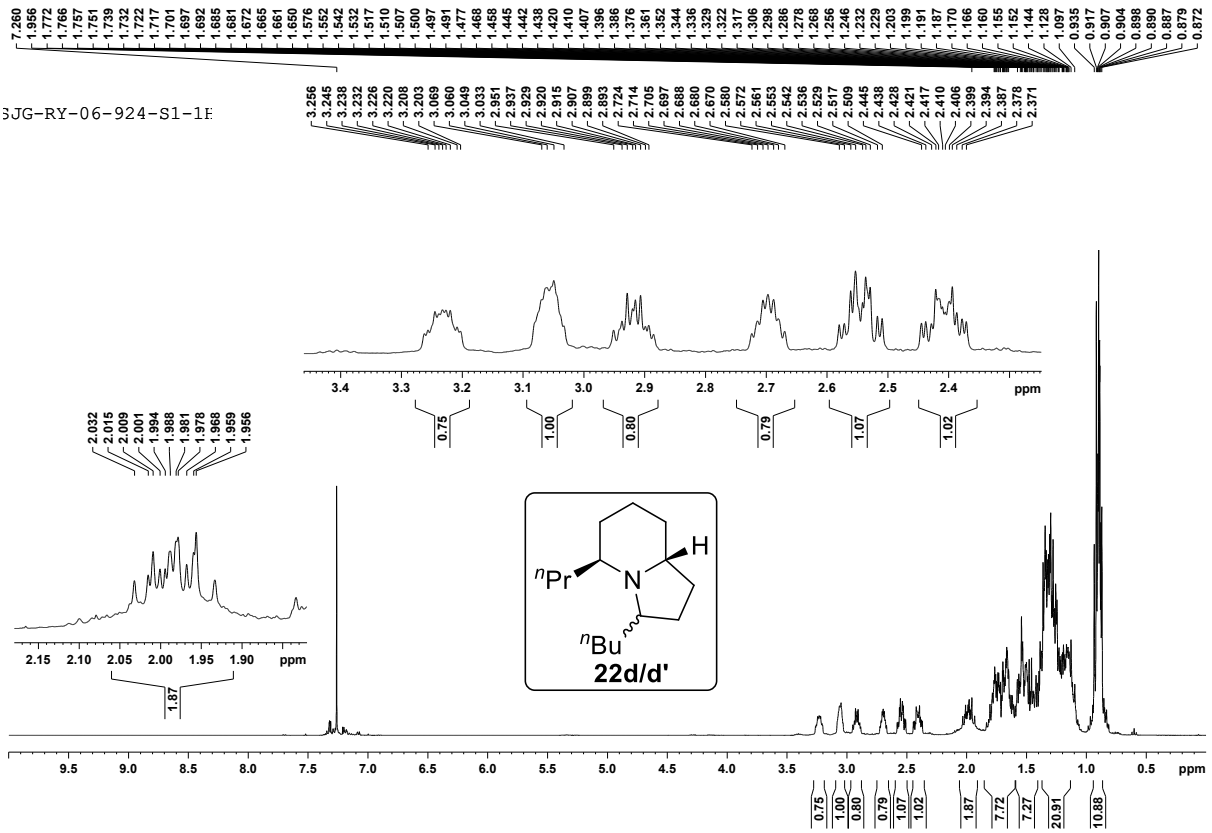


^{1}H NMR spectrum (400 MHz, $CDCl_3$)

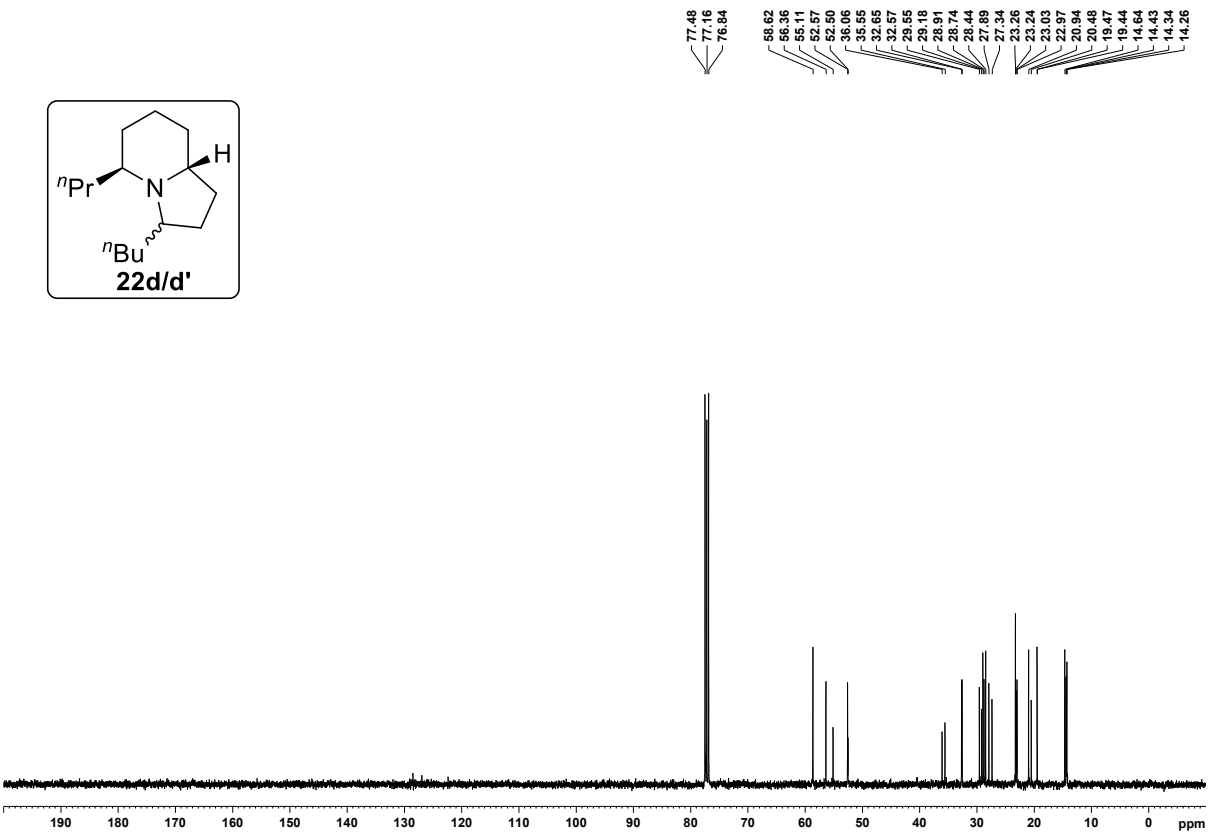




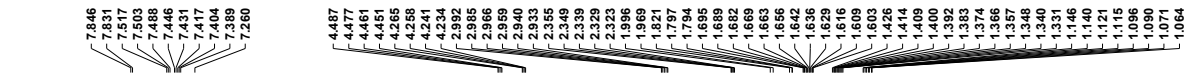
^{13}C NMR spectrum (100 MHz, $CDCl_3$)



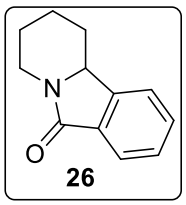
^{1}H NMR spectrum (400 MHz, $CDCl_3$)

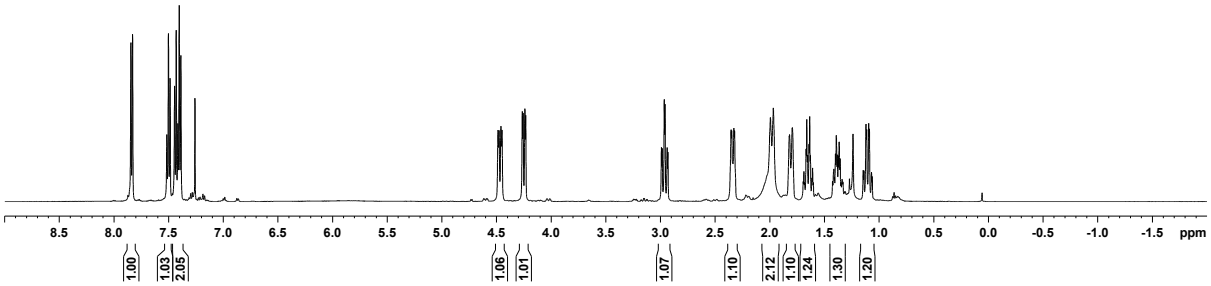


^{13}C NMR spectrum (100 MHz, $CDCl_3$)



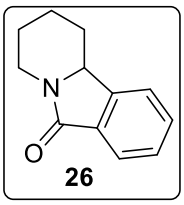
SJG-RY-04-695-S1-1H

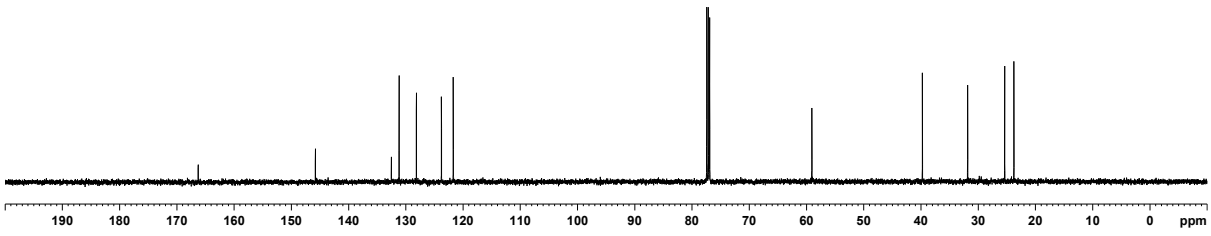




^{1}H NMR spectrum (400 MHz, $CDCl_3$)

SJG-RY-04-695-S1-13C

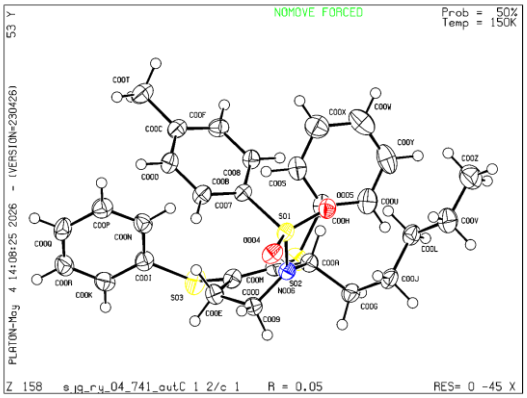




^{13}C NMR spectrum (100 MHz, $CDCl_3$)

X-Ray crystallographic analysis

Crystal data and structure refinement for 10r (ellipsoid is drawn at the 50% probability level):



Identification code	**10r**		
Solvent	CH_2Cl_2		
CCDC	2551281		
Bond precision:	C-C = 0.0033 A		Wavelength=0.71073
Cell:	a=32.7633(9)	b=9.4879(3)	c=17.0617(6)
	alpha=90	beta=102.720(3)	gamma=90
Temperature: 150 K			

	Calculated	Reported
Volume	5173.6(3)	5173.5(3)
Space group	C 2/c	C 1 2/c 1
Hall group	-C 2yc	-C 2yc
Moiety formula	C29 H33 N O2 S3	C29 H33 N O2 S3
Sum formula	C29 H33 N O2 S3	C29 H33 N O2 S3
Mr	523.74	523.74
Dx,g cm-3	1.345	1.345
Z	8	8
Mu (mm-1)	0.315	0.315
F000	2224.0	2224.0
F000'	2227.72	
h,k,lmax	38,11,20	38,11,20
Nref	4556	4553
Tmin,Tmax	0.886,0.907	0.453,1.000
Tmin'	0.797	

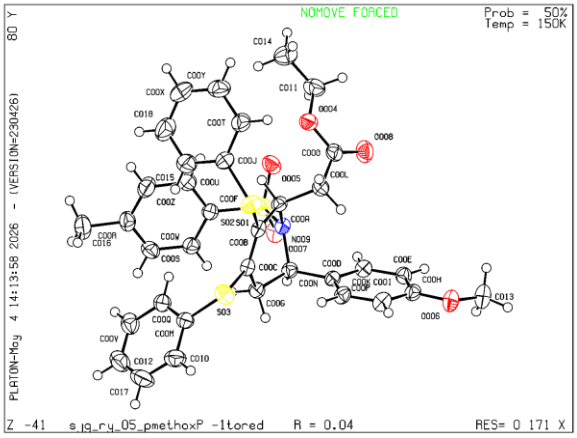
Correction method= # Reported T Limits: Tmin=0.453 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.999 Theta(max)= 24.995

R(reflections)= 0.0455(3781) wR2(reflections)= 0.1428(4553)

S = 1.097 Npar= 318

Crystal data and structure refinement for 12f (ellipsoid is drawn at the 50% probability level):



Identification code	**12f**
Solvent	CH_2Cl_2
CCDC	2551281
Bond precision:	C-C = 0.0033 A Wavelength=0.71073
Cell:	a=11.8441(3) b=12.1655(3) c=12.5634(3)
	alpha=64.953(3) beta=78.227(2) gamma=76.682(2)
Temperature: 150 K	

	Calculated	Reported
Volume	1584.22(8)	1584.22(8)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C35 H35 N O5 S3	C35 H35 N O5 S3
Sum formula	C35 H35 N O5 S3	C35 H35 N O5 S3
Mr	645.82	645.82
Dx,g cm-3	1.354	1.354
Z	2	2
Mu (mm-1)	0.278	0.278
F000	680.0	680.0
F000'	681.02	
h,k,lmax	14,14,14	14,14,14
Nref	5577	5574
Tmin,Tmax	0.902,0.928	0.535,1.000
Tmin'	0.821	

Correction method= # Reported T Limits: Tmin=0.535 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.999 Theta(max)= 25.000

R(reflections)= 0.0406(4626) wR2(reflections)= 0.1110(5574)

S = 1.044 Npar= 400