Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting information

One-Pot Cascade Synthesis of Fused Heterocycles from Furan-tethered Terminal Alkynes and Aldehydes in the Presence of Amines and CuBr

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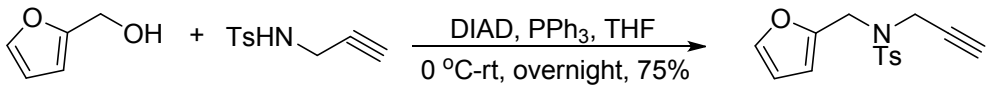
CONTENTS

1. General Remarks. All reagents were obtained commercially and used without further purification. Toluene was distilled from sodium (Na) under argon (Ar) atmosphere. Organic solvents used were dried by standard methods when necessary. Unless otherwise noted, all reaction mixtures were stirred with a magnetic stir bar in flame-dried glassware under argon atmosphere. All the temperatures were referred to the used oil baths. Extracts were dried over $MgSO_4$ or Na_2SO_4 and solvents were removed in a rotary evaporator. TLC analysis of reaction mixtures was performed on Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300-400 mesh silica gel under increased pressure. MP was obtained with a Yanagimoto micro melting point apparatus and is uncorrected. Infra-red spectra were measured on a spectrometer. ^1H NMR spectra were recorded for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. *J*-values are in Hz. Mass and HRMS spectra were recorded by EI, ESI, or MALDI method.

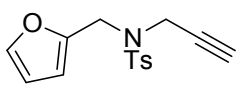
2. General procedure for synthesis of substrates 1.

Scheme 1 Representative procedure: synthesis of **1**.



S1 **S2** **1a**

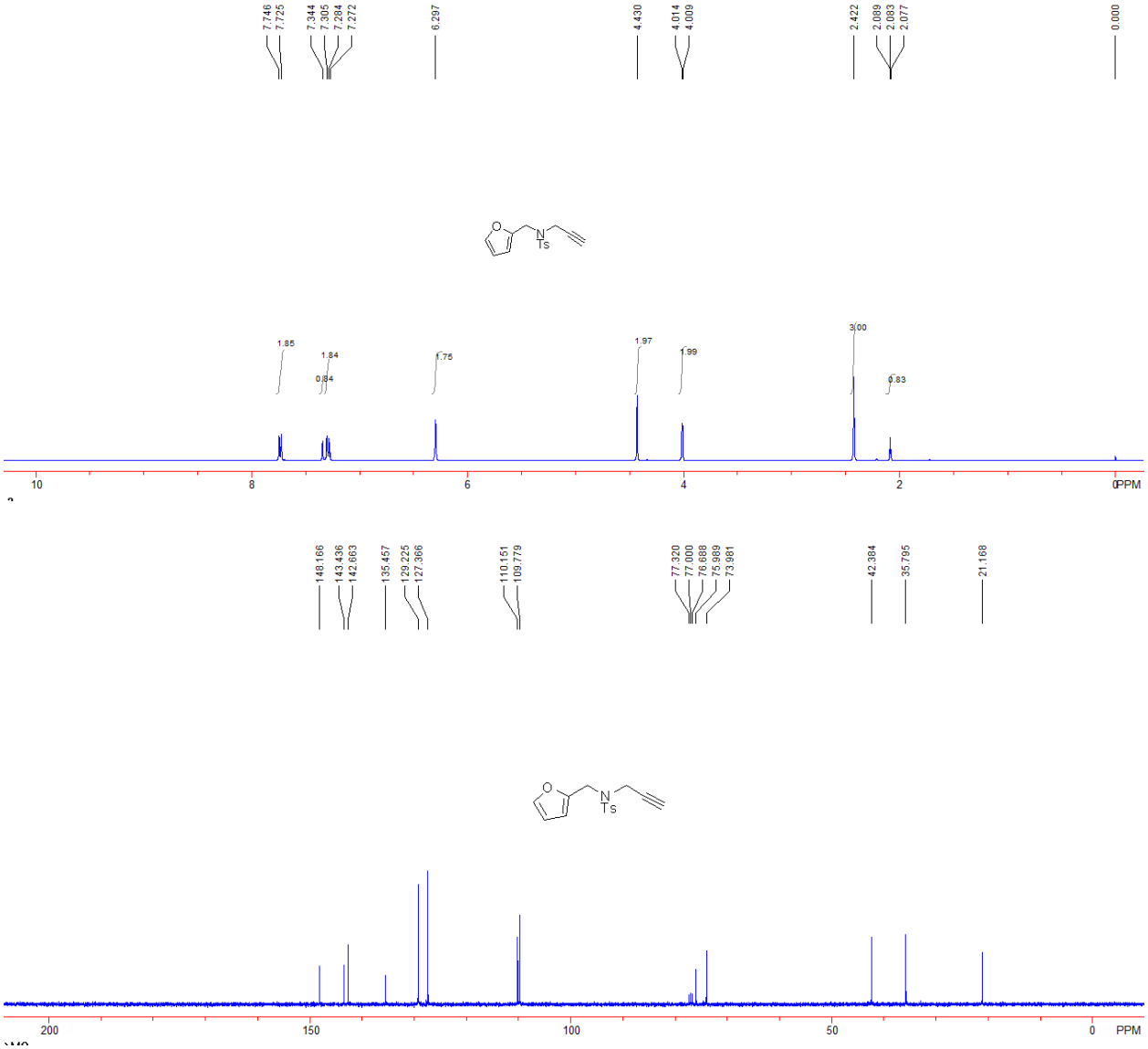
This compound was prepared by a procedure reported by Hsung.[1] To a 100 mL flame and vacuum dried flask was added furfuryl alcohol **S1** (1.08 g, 11 mmol), *N*-propargyl tosyl amine **S2** (2.09 g, 10 mmol), triphenylphosphine (2.88 g, 11 mmol), and anhydrous THF (11 mL) under Ar. Then, DIAD (2.17 mL, 11 mmol) was added dropwise at 0 °C and the resulting solution was warmed to room temperature and stirred overnight. When the reaction was complete as monitored by TLC, the solution was concentrated under reduced pressure and the crude residue was purified via silica gel flash column chromatography (PE/EA = 15/1) affording propargyl amide **1a** (2.18 g, 7.55 mmol) in 75% yield.



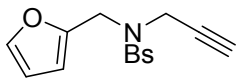
***N*-(furan-2-ylmethyl)-4-methyl-*N*-(prop-2-yn-1-yl) benzenesulfonamide 1a**

A white solid, 75% yield (2.18 g). M.p.: 67-69 °C. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.08 (t. *J* = 2.4 Hz, 1H, CH), 2.42 (s, 3H, CH_3), 4.01 (d, *J* = 2.4 Hz, 2H, CH_2), 4.43 (s, 2H, CH_2), 6.30 (s, 2H, ArH), 7.28 (d, *J* = 8.0 Hz, 2H, ArH), 7.33 (s, 1H, ArH), 7.73 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.2, 35.8, 42.4, 74.0, 76.0, 109.8, 110.2, 127.4, 129.2, 135.5,

142.7, 143.4, 148.2. IR (CH_2Cl_2) ν 3290, 2923, 1597, 1495, 1348, 1330, 1186, 1159, 1092, 914, 813, 704, 657 cm^{-1}. MS (ESI) *m/z* (%): 307.1 (100) [M^++NH_4]; HRMS (ESI) Calcd. For $C_{15}H_{19}N_2O_3S^{+1}$(M^++NH_4) requires 307.1111, Found: 307.1116.



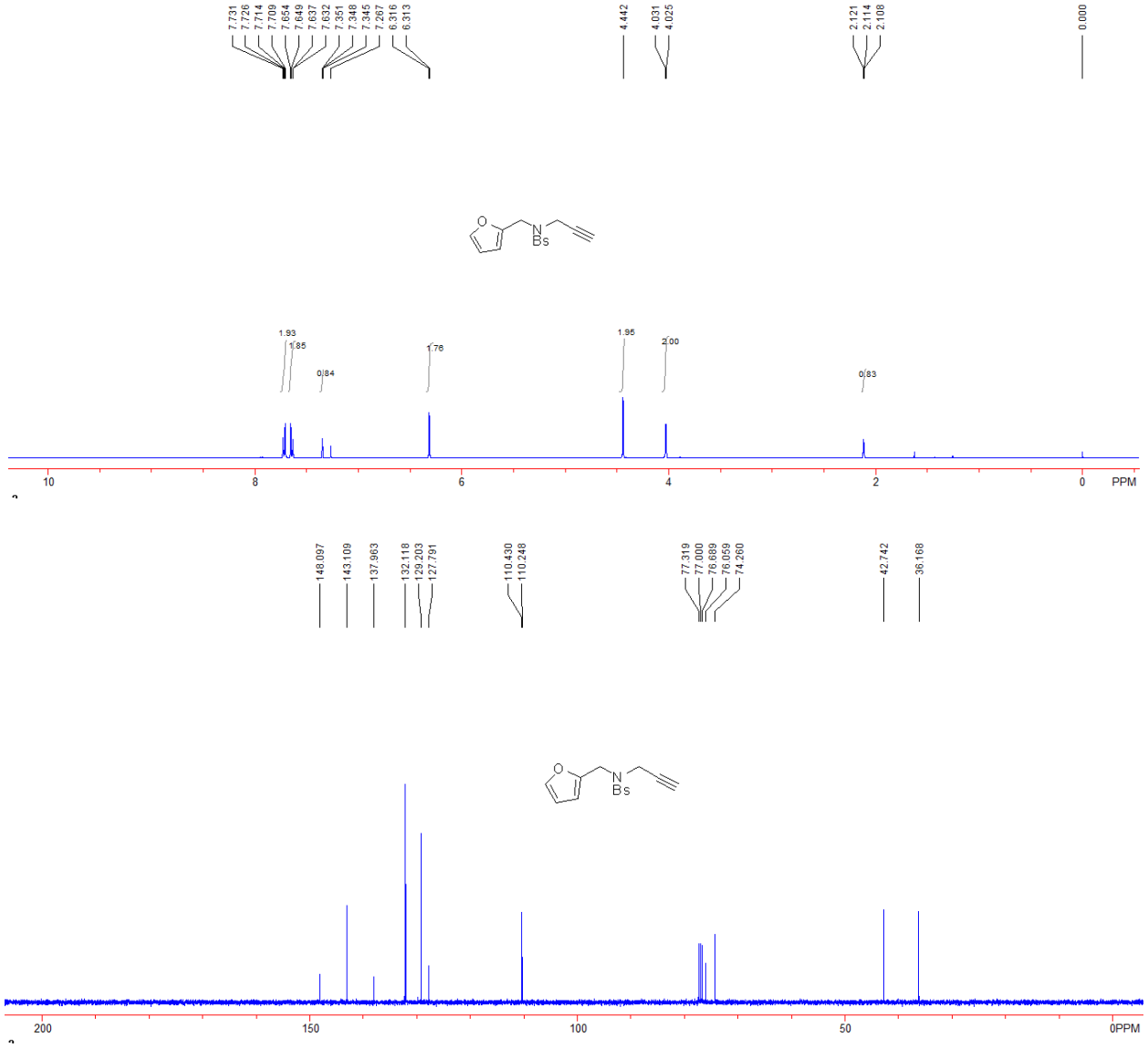
Compounds **1b** and **1c** were prepared in the similar method as that of **1a**.

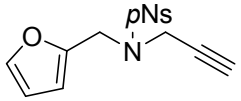


4-bromo-*N*-(furan-2-ylmethyl)-*N*-(prop-2-yn-1-yl) benzenesulfonamide 1b

A white solid, 67% yield (777 mg). M.p.: 89-91 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.11 (t, *J* = 2.4 Hz, 1H, CH), 4.03 (d, *J* = 2.4 Hz, 2H, CH_2), 4.44 (s, 2H, CH_2), 6.31 (d, *J* = 1.2 Hz, 2H, ArH), 7.35 (t, *J* = 1.2 Hz, 1H, ArH), 7.64 (d, *J* = 8.8 Hz, 2H, ArH), 7.72 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 36.2, 42.7, 74.3, 76.1, 110.2, 110.4, 127.8, 129.2, 132.1,

138.0, 143.1, 148.1. IR (CH_2Cl_2) ν 3291, 1574, 1471, 1351, 1332, 1161, 1091, 1067, 1009, 914, 891, 766, 741, 722 cm^{-1}. MS (ESI) *m/z* (%): 353.9 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{14}H_{13}BrNO_3S^{+1}$(M^++H) requires 353.9794, Found: 353.9776.

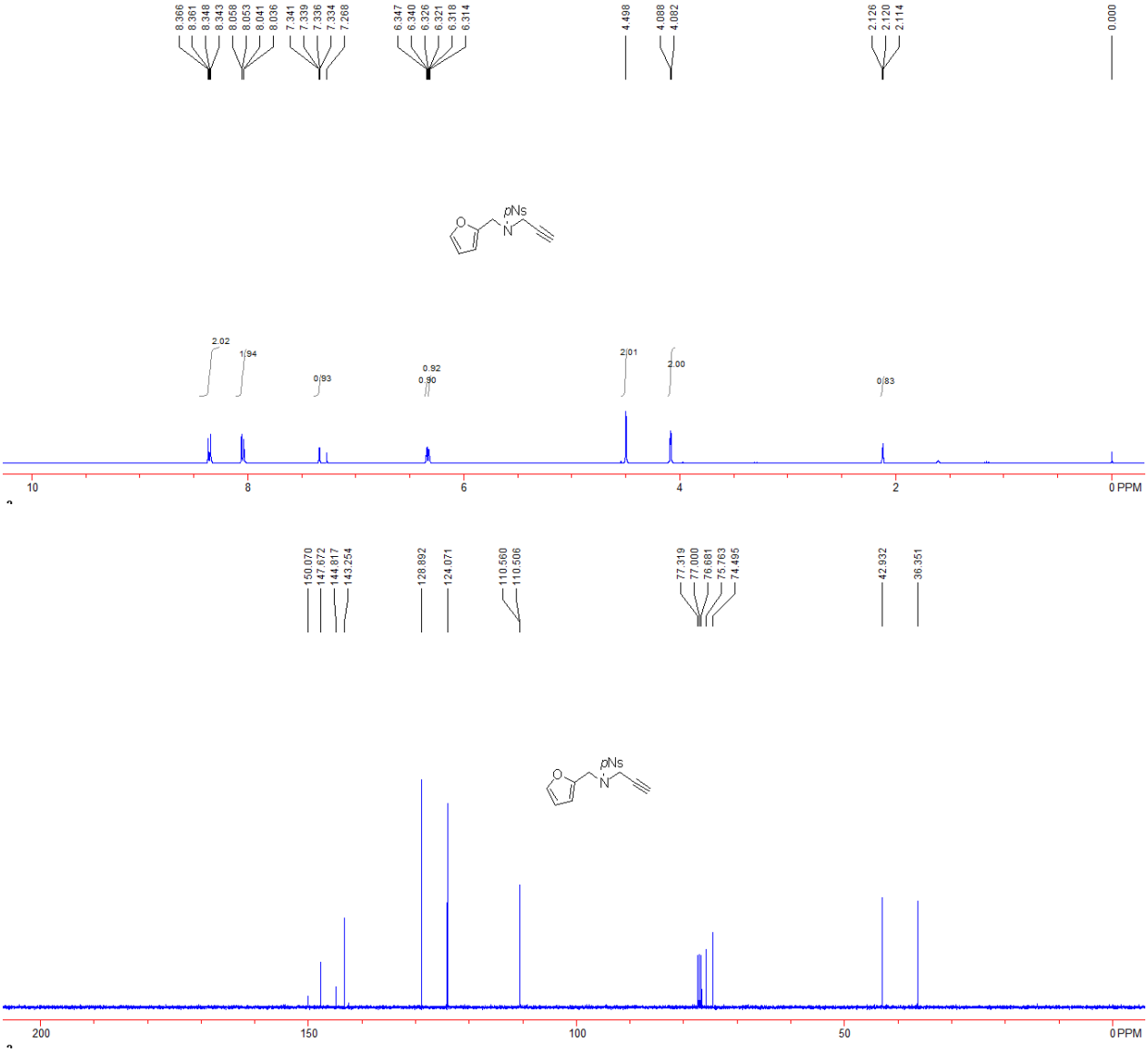




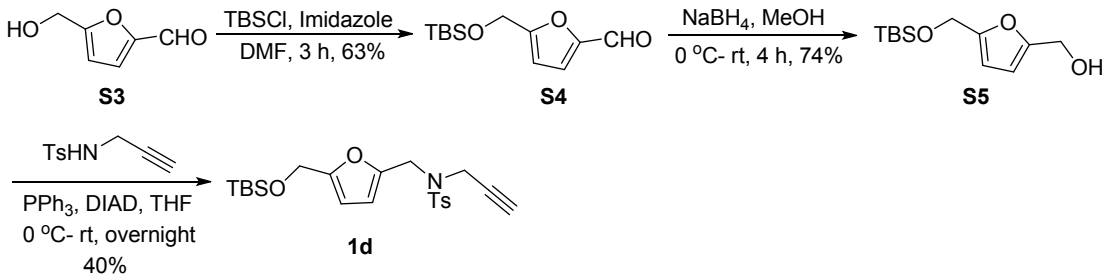
_N_-(furan-2-ylmethyl)-4-nitro-_N_-(prop-2-yn-1-yl)benzenesulfonamide 1c

A pale yellow solid, 78% yield (432 mg). M.p.: 120-122 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.12 (t. *J* = 2.4 Hz, 1H, CH), 4.08 (d, *J* = 2.4 Hz, 2H, CH_2), 4.50 (s, 2H, CH_2), 6.32 (dd, *J* = 2.8, 2.0 Hz, 1H, ArH), 6.34 (d, *J* = 2.8 Hz, 1H, ArH), 7.34 (dd, *J* = 2.0, 0.8 Hz, 1H, ArH), 8.04 (d, *J* = 8.8 Hz, 2H, ArH), 8.35 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 36.4, 42.9, 74.5, 75.8, 110.5, 110.6, 124.1, 128.9, 143.3, 144.8, 147.7, 150.1. IR (CH_2Cl_2) ν 3288,

3106, 1606, 1527, 1504, 1348, 1162, 1108, 1092, 854, 738, 719,B 683 cm^{-1}. MS (ESI) *m/z* (%): 321.0 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{14}H_{13}N_2O_5S^{+1}$(M^++H) requires 321.0540, Found: 321.0538.



Scheme 2. Synthesis of **1d**.



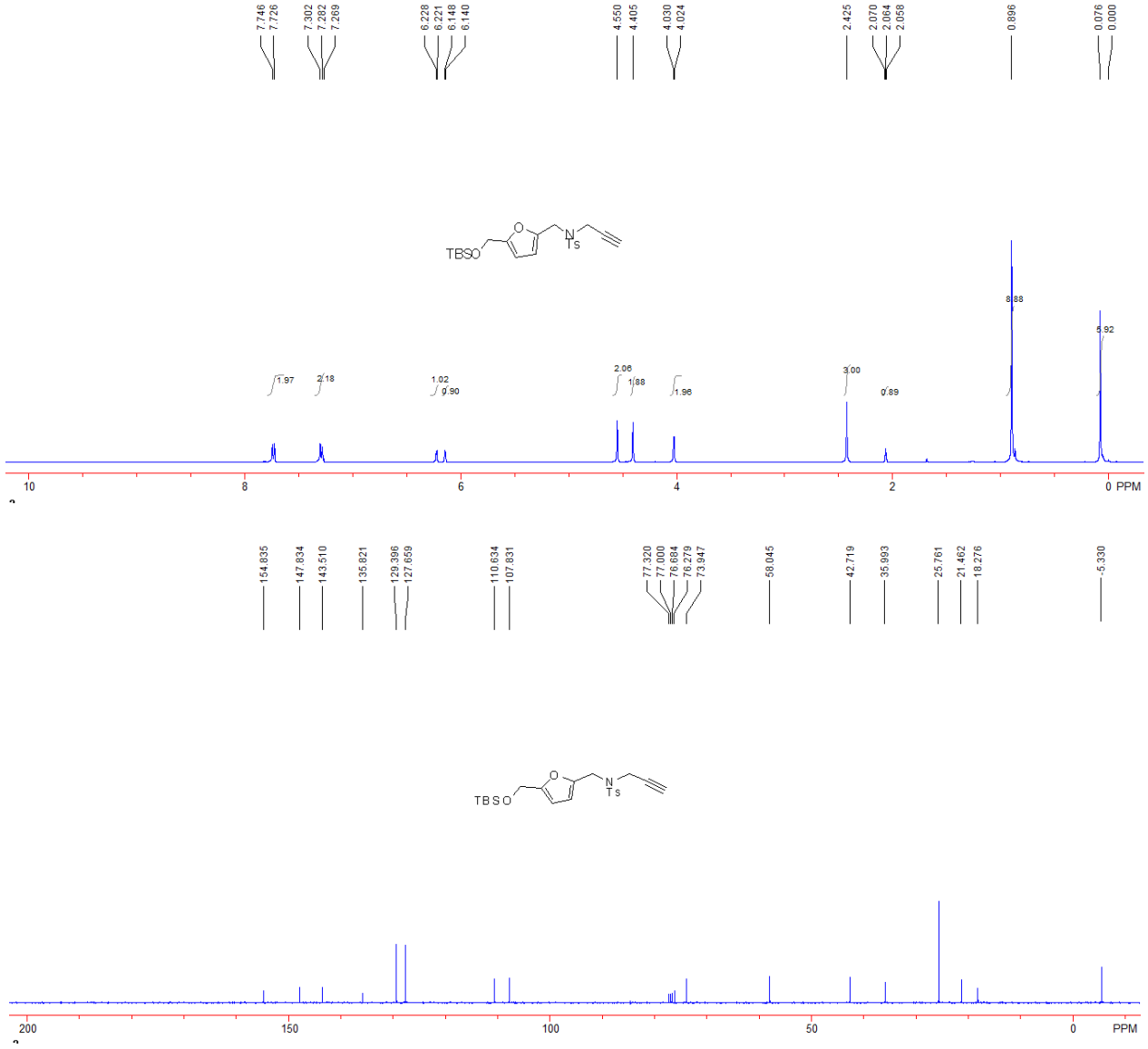
Compound **S4** was synthesized by a procedure reported by MacPhail.[2]

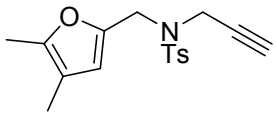
Compound **S5** was prepared according to the previous literature.[3]

Compound **1d** was prepared in the similar method as that of **1a**

***N*-((5-(((tert-butyldimethylsilyl)oxy)methyl)furan-2-yl)methyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide 1d**

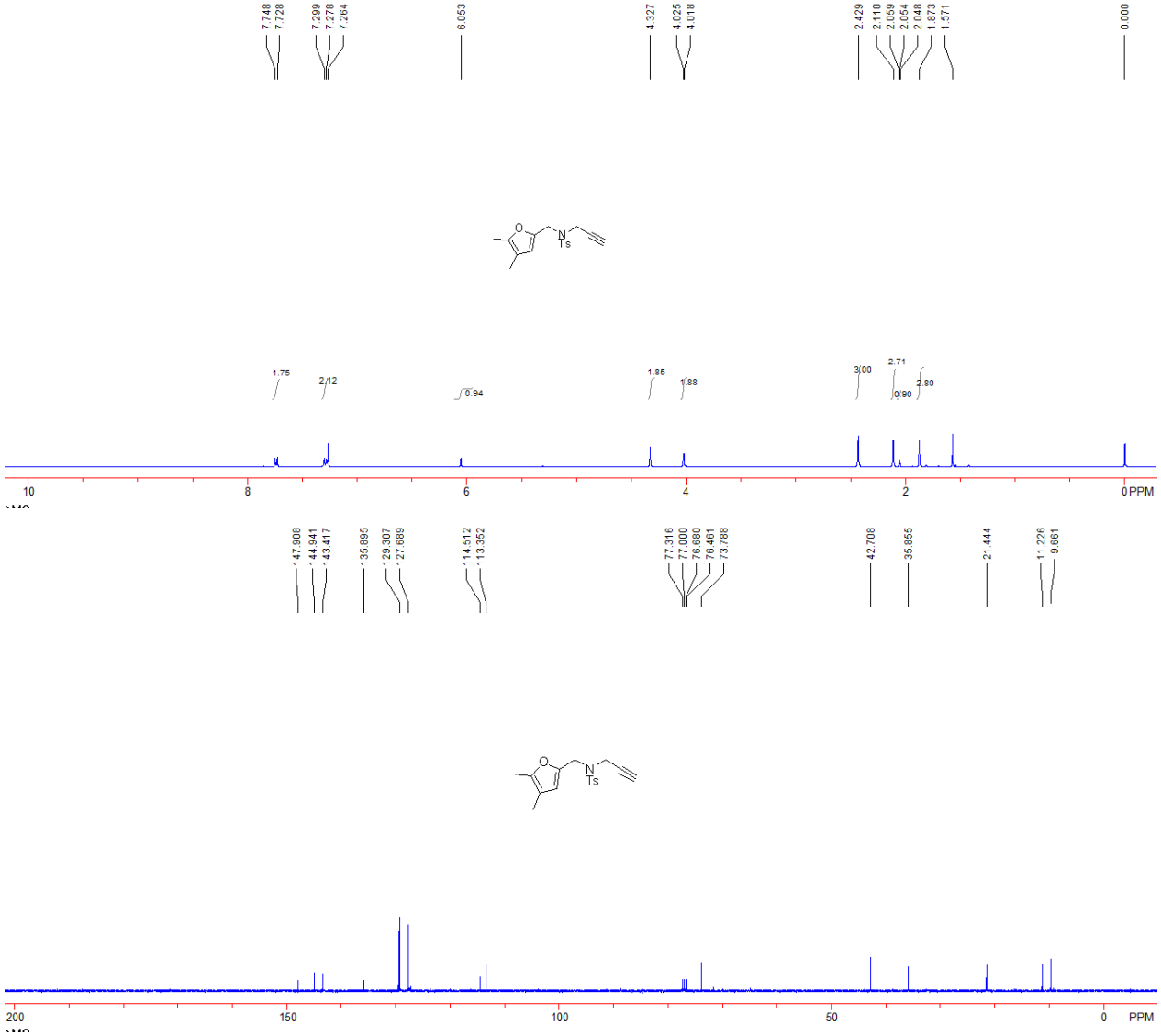
A yellow liquid, 40% yield (121 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.08 (s, 6H, CH_3), 0.90 (s, 9H, CH_3), 2.06 (t, J = 2.4 Hz, 1H, CH), 2.43 (s, 3H, CH_3), 4.03 (d, J = 2.4 Hz, 2H, CH_2), 4.41 (s, 2H, CH_2), 4.55 (s, 2H, CH_2), 6.15 (d, J = 3.2 Hz, 1H, ArH), 6.23 (d, J = 3.2 Hz, 1H, ArH), 7.29 (d, J = 8.0 Hz, 2H, ArH), 7.73 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ -5.3, 18.3, 21.5, 25.8, 36.0, 42.7, 58.0, 73.9, 76.3, 107.8, 110.6, 127.7, 129.4, 135.8, 143.5, 147.8, 154.8. IR (CH_2Cl_2) ν 3279, 2926, 1724, 1597, 1494, 1347, 1158, 1016, 972, 838, 751, 660 cm^{-1}. MS (ESI) *m/z* (%): 451.2 (100) [M^++NH_4]; HRMS (ESI) Calcd. For $C_{22}H_{35}N_2O_4SSi^{+1}$($M^+$+$NH_4$) requires 451.2081, Found: 451.2092.



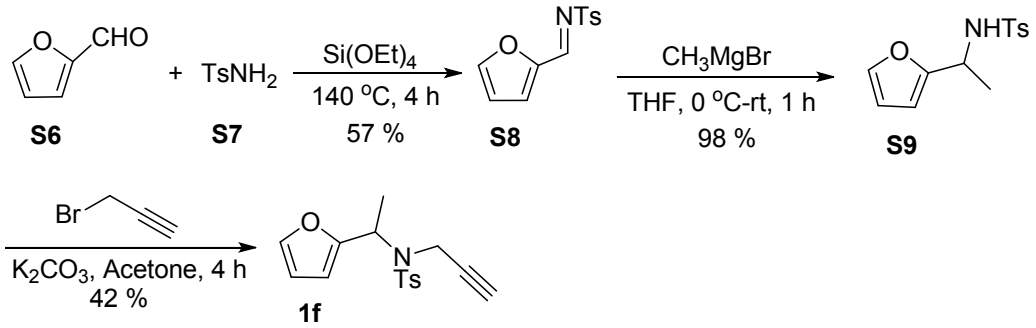


***N*-((4,5-dimethylfuran-2-yl)methyl)-4-methyl-*N*-(prop-2-yn-1- yl)benzenesulfonamide 1e**

A yellow liquid, 54% yield (171 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.87 (s, 3H, CH_3), 2.06 (t, J = 2.4 Hz, 1H, CH), 2.11 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 4.02 (d, J = 2.4 Hz, 2H, CH_2), 4.33 (s, 2H, CH_2), 6.05 (s, 1H, ArH), 7.28 (d, J = 8.0 Hz, 2H, ArH), 7.73 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 9.7, 11.2, 21.4, 35.9, 42.7, 73.8, 76.5, 113.4, 114.5, 127.7, 129.3, 135.9, 143.4, 144.9, 147.9. IR (CH_2Cl_2) ν 3285, 2923, 1598, 1348, 1160, 1119, 706, 654 cm^{-1}. MS (ESI) *m/z* (%): 318.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{17}H_{20}NO_3S^{+1}$(M^++H) requires 318.1158, Found: 318.1161.



Scheme 3. Synthesis of **1f**.

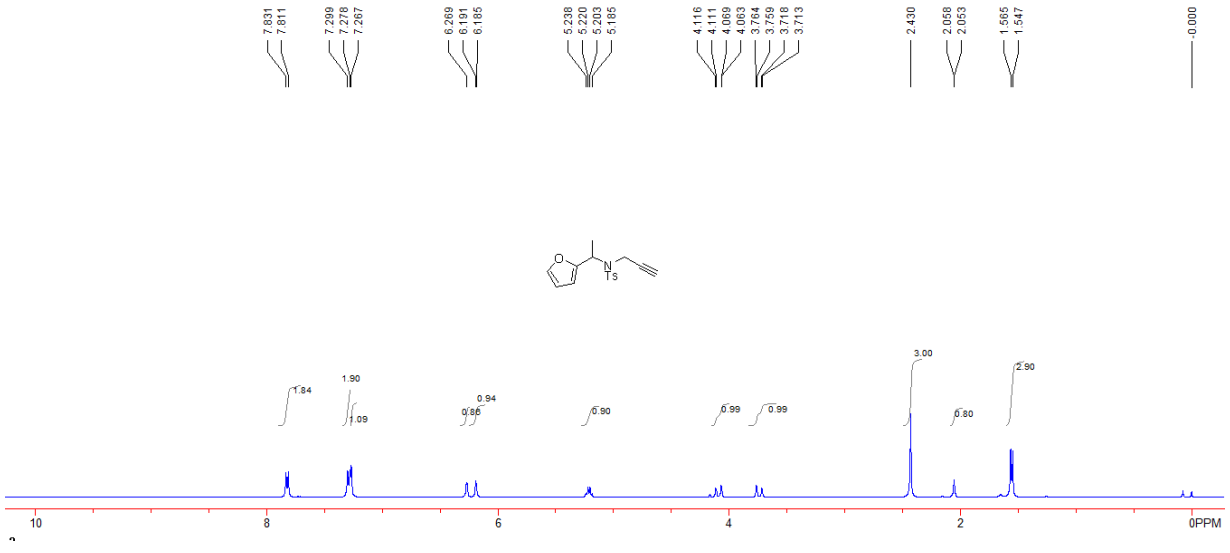


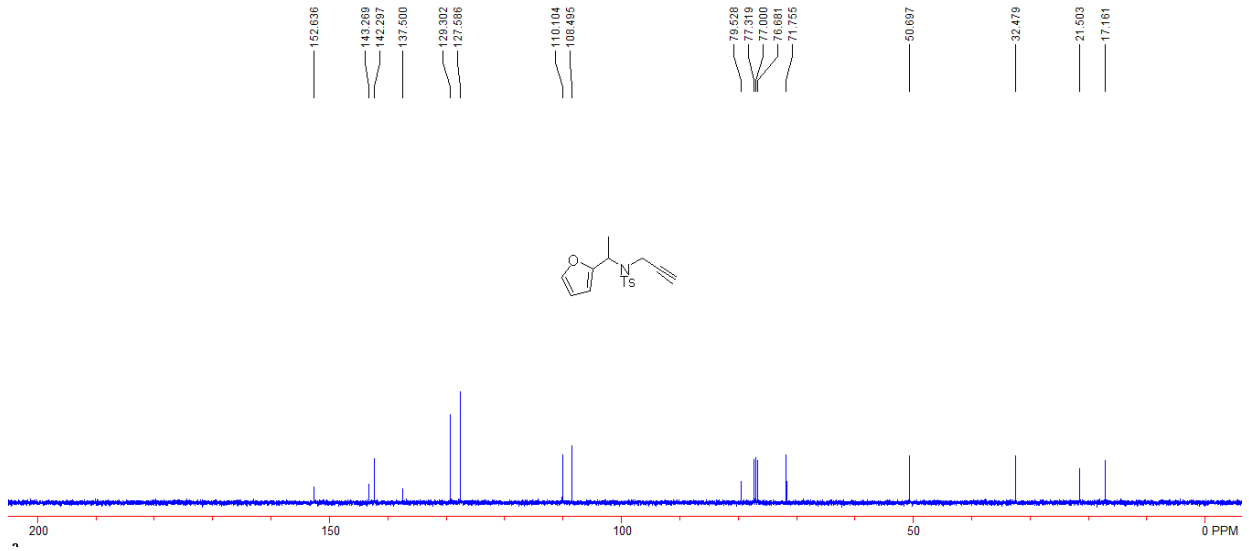
Compound **S9** was prepared according to previous literature.[4]

Compound **1f** was prepared according to previous literature.[5]

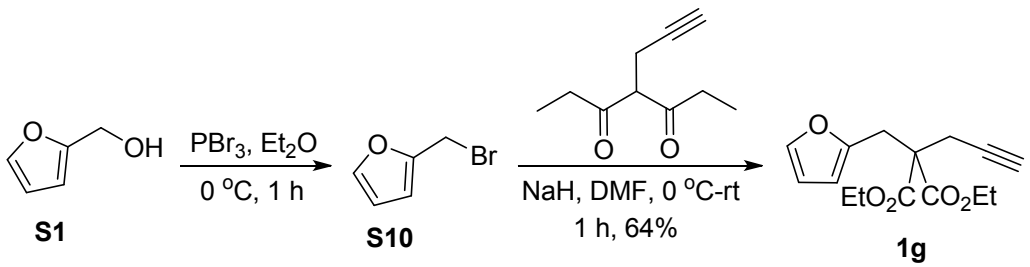
***N*-(1-(furan-2-yl)ethyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide 1f**

A White solid, 41% yield (355 mg). M.p.: 78-80 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.55 (d, J = 7.2 Hz, 3H, CH_3), 2.05 (t, J = 2.0 Hz, 1H, CH), 2.43 (s, 3H, CH_3), 3.74 (dd, J = 2.0, 18.4 Hz, 1H, CH_2), 4.09 (dd, J = 2.0, 18.4 Hz, 1H, CH_2), 5.21 (q, J = 7.2 Hz, 1H, CH), 6.19 (d, J = 2.4 Hz, 1H, ArH), 6.27 (s, 1H, ArH), 7.27 (s, 1H, ArH), 7.29 (d, J = 8.0 Hz, 2H, ArH), 7.82 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 17.2, 21.5, 32.5, 50.7, 71.8, 79.5, 108.5, 110.1, 127.6, 129.3, 137.5, 142.3, 143.3, 152.6. IR (CH_2Cl_2) ν 3289, 2922, 2853, 1598, 1456, 1334, 1154, 1091, 1057, 1035, 876, 742, 657 cm^{-1}. MS (ESI) *m/z* (%): 321.1 (100) [M^++NH_4]; HRMS (ESI) Calcd. For $C_{16}H_{21}N_2O_3S^{+1}$(M^++NH_4) requires 321.1273, Found: 321.1253.

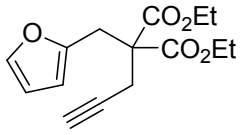




Scheme 4. Synthesis of **1g**.

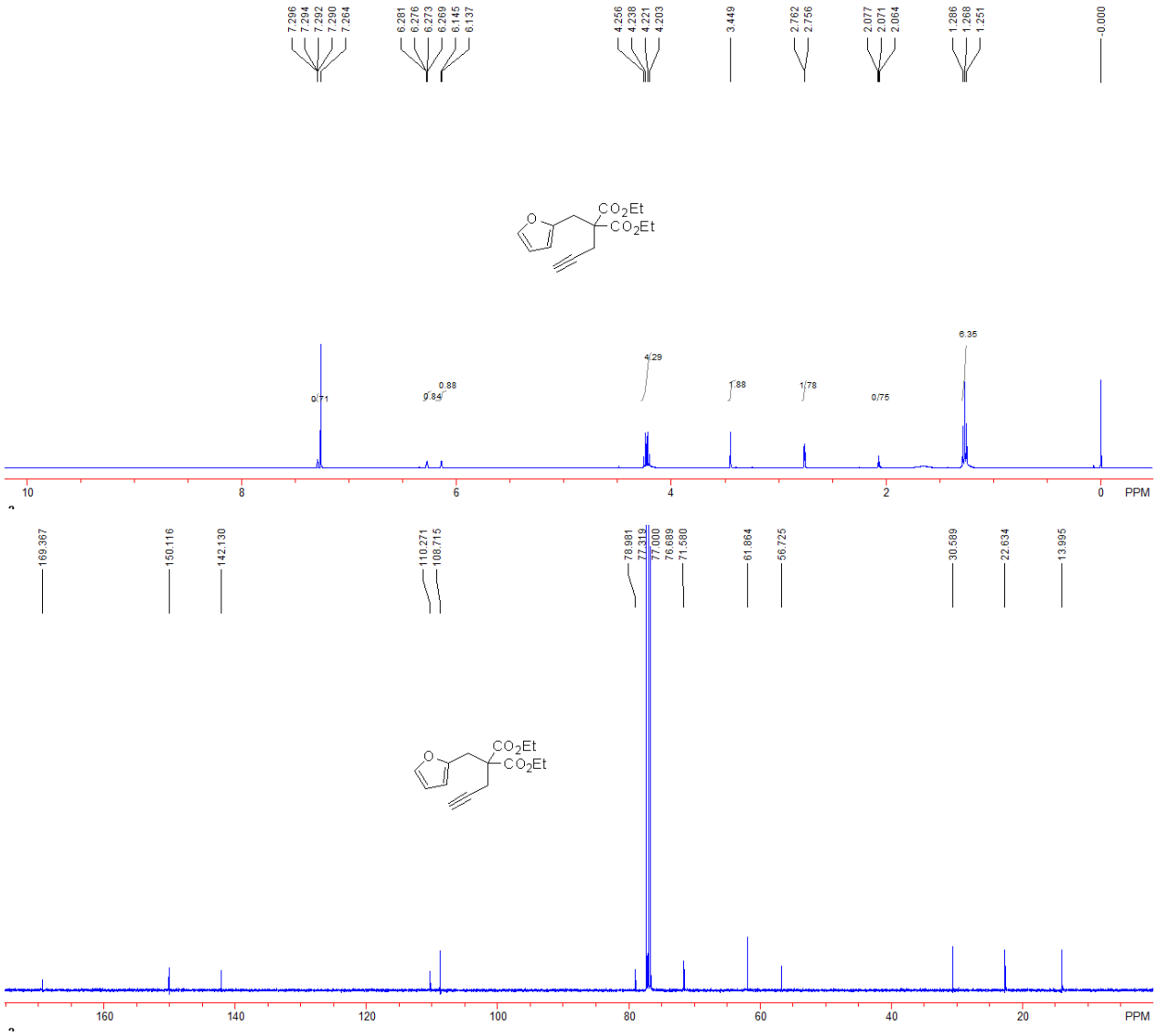


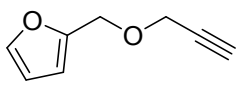
To a solution of **S1** (980 mg, 10 mmol) in Et_2O (50 mL) at 0 °C was added dropwise PBr_3 (2.168 g, 8 mmol), the reaction mixture was warmed to room temperature and stirred for 1 hour. The reaction was quenched with water, and the organic layers were separated and the aqueous phase was washed with Et_2O (3 x 20 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated via a rotary evaporator to afford a yellow oil. The crude product was directly used in next step. To a stirred suspension of NaH (120 mg, 3 mmol; 60% in mineral oil) in dry DMF (15 mL) was added dropwise diethyl propargylmalonate (448 mg, 2.70 mmol) at 0°C. After being stirred for 10 min, 2-(bromomethyl)furan **S10** was added and the mixture was stirred for 5 h at room temperature. Water (20 mL) was added to the flask and the product was extracted with Et_2O (3 x 20 mL) and dried over Na_2SO_4. The solvent was evaporated and the crude product was purified by a column chromatography (PE/EA = 10/1) to yield **1g** (479 mg, 64%) as a yellow oil.



Diethyl 2-(furan-2-ylmethyl)-2-(prop-2-yn-1-yl)malonate 1g

A yellow oil, 64% yield (479 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.27 (t, J = 6.8 Hz, 6H, CH_3), 2.07 (t. J = 2.4 Hz, 1H, CH), 2.76 (d, J = 2.4 Hz, 2H, CH_2), 3.45 (s, 2H, CH_2), 4.23 (q, J = 7.2 Hz, 4H, CH_2), 6.14 (d, J = 3.2 Hz, 1H, ArH), 6.27 (dd, J = 1.6, 3.2 Hz, 1H, ArH), 7.29 (dd, J = 0.8, 1.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 22.6, 30.6, 56.7, 61.9, 71.6, 79.0, 108.7, 110.3, 142.1, 150.1, 169.4. IR (CH_2Cl_2) ν□ 3290, 3107, 2982, 1734, 1531, 1350, 1165, 1012, 856, 740, 721, 683 cm^{-1}. MS (ESI) *m/z* (%): 279.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{15}H_{19}O_5^{+1}$(M^++H) requires 279.1227, Found: 279.1232.



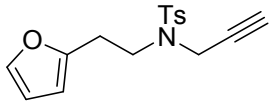


2-((prop-2-yn-1-yloxy)methyl)furan 1h

Colorless liquid, 73% yield (248 mg).

The preparation of substrate **1h** has been detailed in Reference.[6]

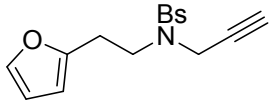
3. General procedure for synthesis of substrates 4.



***N*-(2-(furan-2-yl)ethyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide 4a**

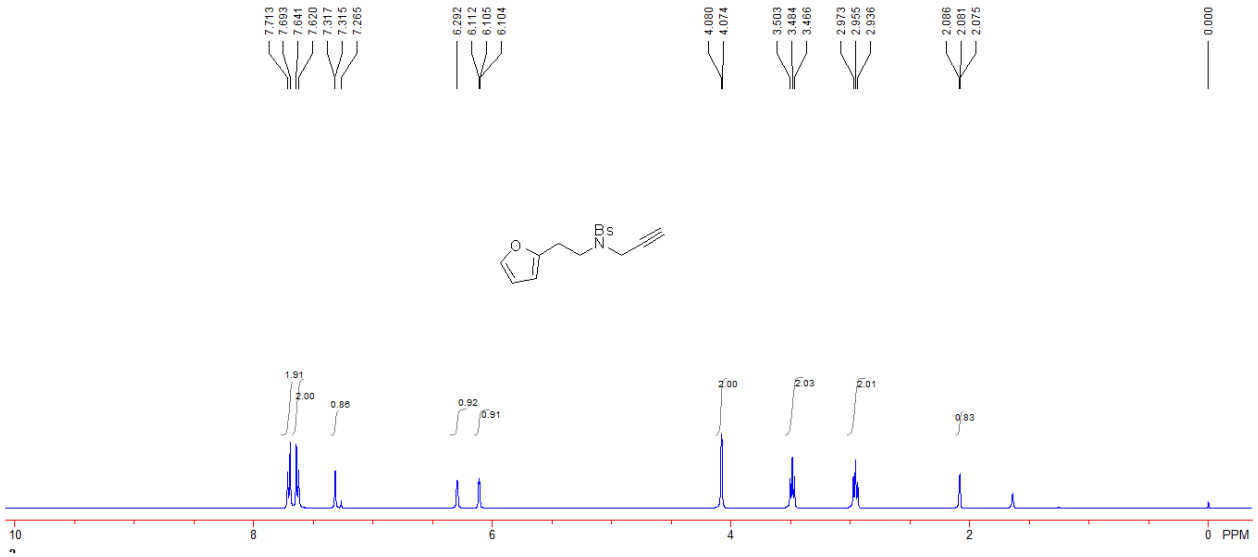
A pale yellow solid, 44% yield (2.109 g).

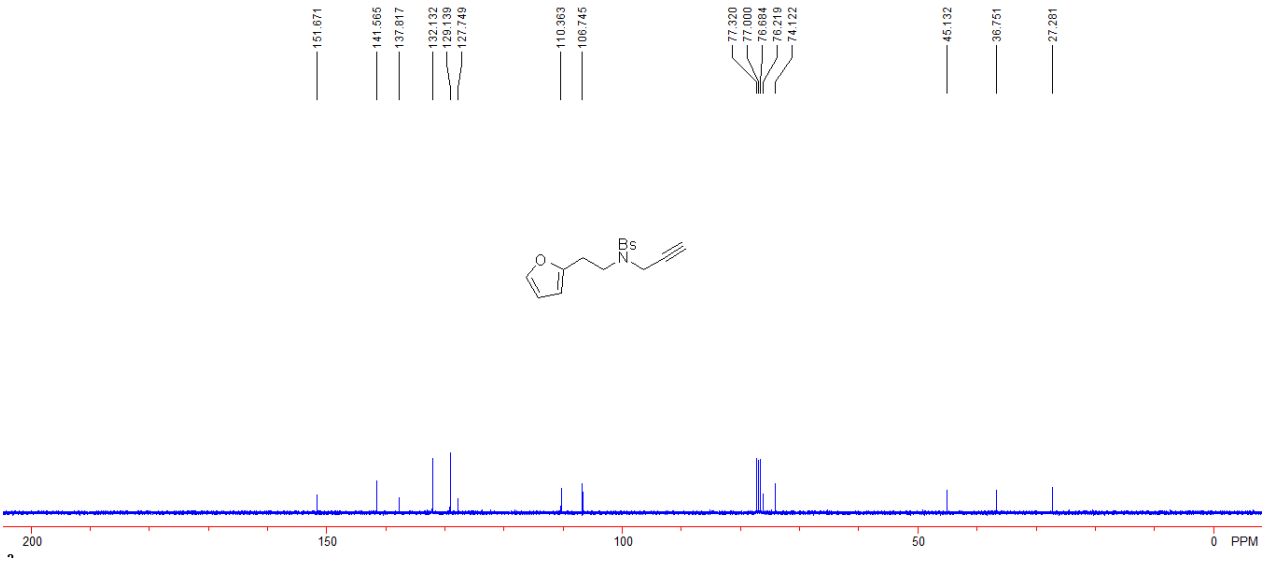
For preparation and characterization of **4a**, see reference.[1]

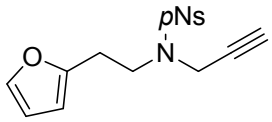


4-bromo-*N*-(2-(furan-2-yl)ethyl)-*N*-(prop-2-yn-1-yl)benzenesulfonamide 4b

A yellow solid, 71% yield (550 mg). M.p.: 69-70 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.08 (t, *J* = 2.4 Hz, 1H, CH), 2.95 (t, *J* = 7.6 Hz, 2H, CH_2), 3.48 (t, *J* = 7.6 Hz, 2H, CH_2), 4.08 (d, *J* = 2.4 Hz, 2H, CH_2), 6.11 (d, *J* = 3.2 Hz, 1H, ArH), 6.29 (s, 1H, ArH), 7.31 (d, *J* = 0.8 Hz, 1H, ArH), 7.63 (d, *J* = 8.0 Hz, 2H, ArH), 7.70 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 27.3, 36.8, 45.1, 74.1, 76.2, 106.7, 110.4, 127.7, 129.1, 132.1, 137.8, 141.6, 151.7. IR (CH_2Cl_2) ν 3292, 2926, 1574, 1471, 1349, 1160, 1068, 1009, 907, 738, 712 cm^{-1}. MS (ESI) *m/z* (%): 367.9 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{15}H_{15}BrNO_3S^{+1}$(M^++H) requires 367.9951, Found: 367.9954.



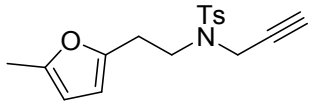




_N_-(2-(furan-2-yl)ethyl)-4-nitro-_N_-(prop-2-yn-1-yl)benzenesulfonamide 4c

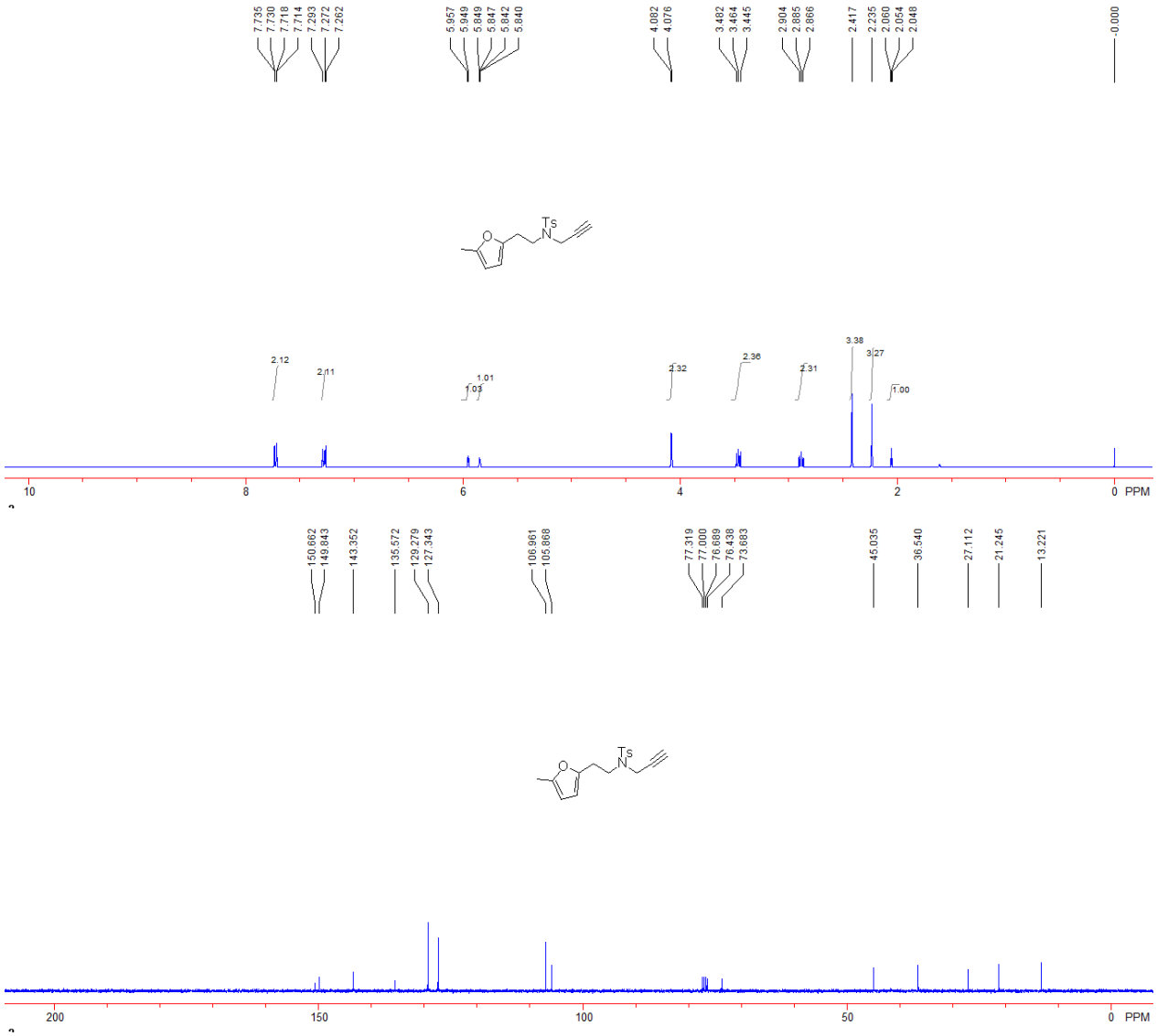
A pale yellow solid, 80% yield (454 mg).

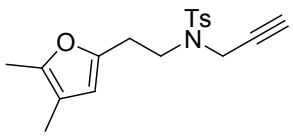
For preparation and characterization of **4c**, see reference.[1]



4-methyl-_N_-(2-(5-methylfuran-2-yl)ethyl)-_N_-(prop-2-yn-1-yl)benzenesulfonamide 4d

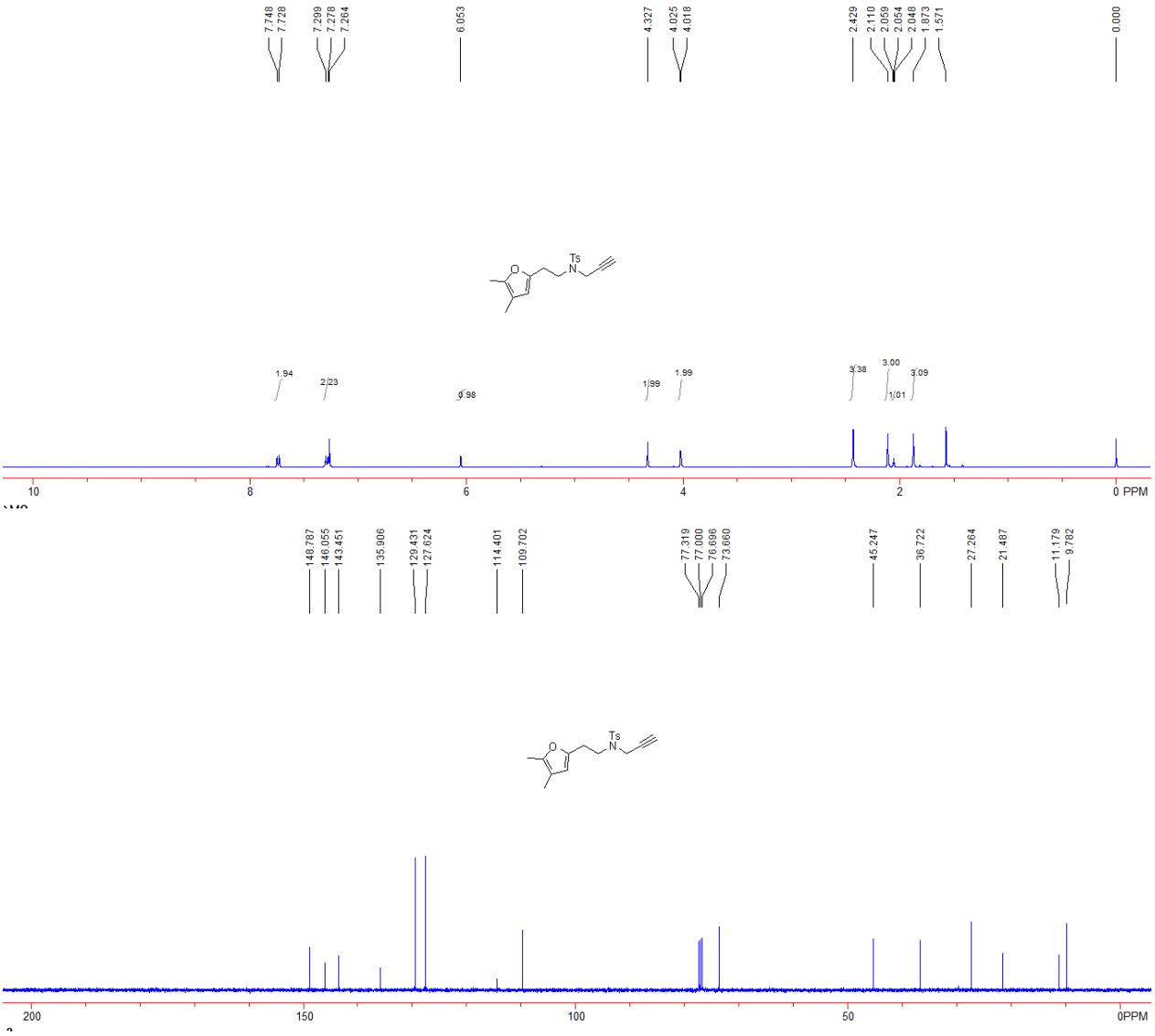
A colorless liquid, 92% yield (640 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.05 (t, J = 2.4 Hz, 1H, CH), 2.24 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.89 (t, J = 7.6 Hz, 2H, CH_2), 3.46 (t, J = 7.6 Hz, 2H, CH_2), 4.08 (d, J = 2.4 Hz, 2H, CH_2), 5.84 (dd, J = 0.8, 2.8 Hz, 1H, ArH), 5.95 (d, J = 2.8 Hz, 1H, ArH), 7.28 (d, J = 8.0 Hz, 2H, ArH), 7.74 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.2, 21.2, 27.1, 36.5, 45.0, 73.7, 76.4, 105.9, 107.0, 127.3, 129.3, 135.6, 143.4, 149.8, 150.7. IR (CH_2Cl_2) ν 3283, 2922, 1597, 1569, 1346, 1185, 1157, 1092, 906, 784, 723, 658 cm^{-1}. MS (ESI) *m/z* (%): 318.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{17}H_{20}NO_3S^{+1}$(M^++H) requires 318.1158, Found: 318.1162.

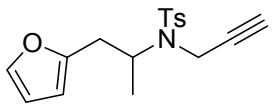




_N_-(2-(4,5-dimethylfuran-2-yl)ethyl)-4-methyl-_N_-(prop-2-yn-1-yl)benzenesulfonamide 4e

A colorless liquid, 41% yield (268mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.88 (s, 3H, CH_3), 2.05 (t. J = 2.4 Hz, 1H, CH), 2.14 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.84 (t, J = 7.6 Hz, 2H, CH_2), 3.45 (t, J = 7.6 Hz, 2H, CH_2), 4.08 (d, J = 2.4, 2H, CH_2), 5.85 (s, 1H, ArH), 7.27 (d, J = 8.4 Hz, 2H, ArH), 7.71 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 9.8, 11.2, 21.5, 27.3, 36.7, 45.2, 73.7, 76.7, 109.7, 114.4, 127.6, 129.4, 135.9, 143.5, 146.1, 148.8. IR (CH_2Cl_2) ν 3284, 2923, 2855, 1727, 1346, 1306, 1158, 1092, 1018, 747, 657 cm^{-1}. MS (ESI) *m/z* (%): 332.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{18}H_{22}NO_3S^{+1}$(M^++H) requires 332.1315, Found: 332.1317.

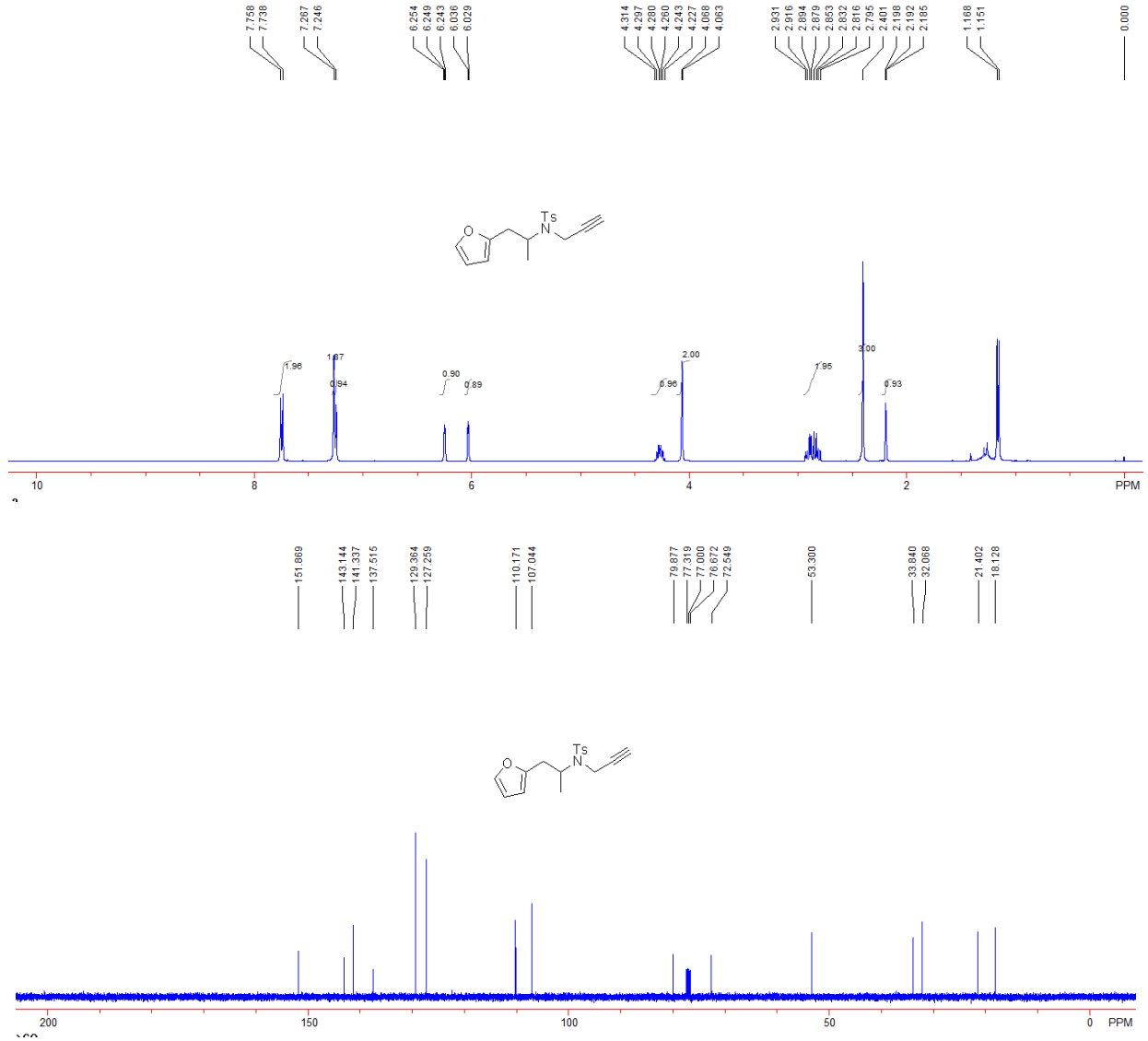


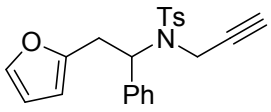


_N_-(1-(furan-2-yl)propan-2-yl)-4-methyl-_N_-(prop-2-yn-1-yl)benzenesulfonamide 4f

A yellow liquid, 16% yield (305 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.16 (d, J = 6.8 Hz, 3H, CH_3), 2.19 (t, J = 2.4 Hz, 1H, CH), 2.40 (s, 3H, CH_3), 2.82 (dd, J = 8.4, 14.8 Hz, 1H, CH_2), 2.90 (dd, J = 6.0, 14.8 Hz, 1H, CH_2), 4.07 (d, J = 2.4 Hz, 2H, CH_2), 4.27 (sep, J = 6.8 Hz, 1H, CH), 6.03 (d, J = 2.8 Hz, 1H, ArH), 6.25 (t, J = 2.4 Hz, 1H, ArH), 7.25 (s, 1H, ArH), 7.26 (d, J = 8.0 Hz, 2H, ArH), 7.74 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 18.1, 21.4, 32.1, 33.8, 53.3, 72.5, 79.9, 107.0, 110.2, 127.3, 129.4, 137.5, 141.3, 143.1, 151.9. IR (CH_2Cl_2) ν 3284, 2962, 1717, 1598, 1332, 1306, 1155, 1092, 813, 799, 658 cm^{-1}. MS (ESI) *m/z*

(%): 318.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{17}H_{20}NO_3S^{+1}$(M^++H) requires 318.1158, Found: 318.1163.

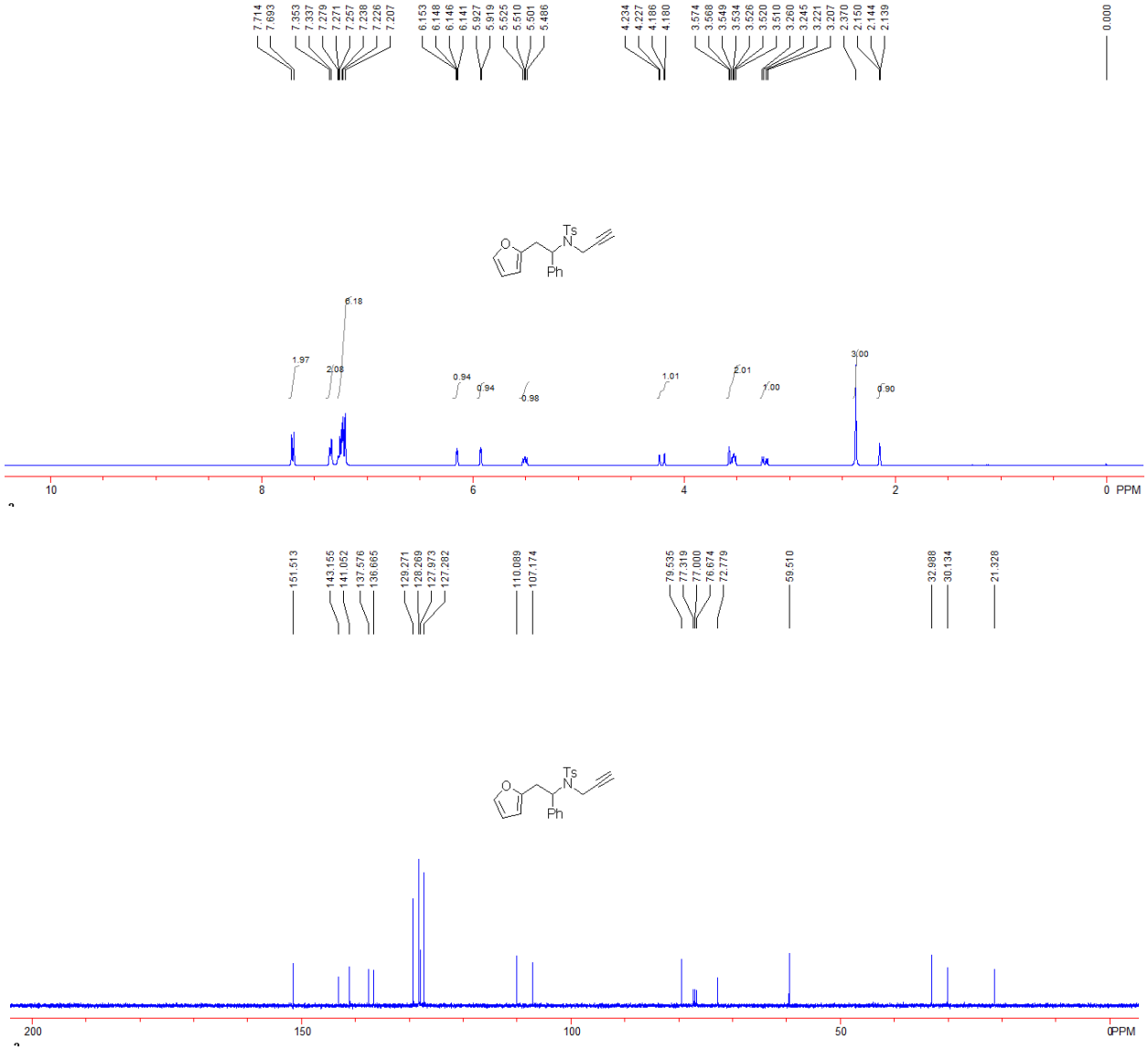


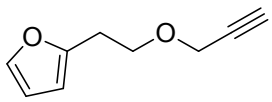


***N*-(2-(furan-2-yl)-1-phenylethyl)-4-methyl-*N*-(prop-2-yn-1-yl) benzenesulfonamide 4g**

A yellow solid, 50% yield (529 mg). M.p.: 90-92 ^oC. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.14 (t, J = 2.4 Hz, 1H, CH), 2.37 (s, 3H, CH_3), 2.23 (dd, J = 5.6, 15.2 Hz, 1H, CH_2), 3.51-3.58 (m, 2H, CH_2), 4.21 (dd, J = 2.4, 18.8 Hz, 1H, CH_2), 5.51 (dd, J = 6.0, 9.6 Hz, 1H, CH), 5.92 (d, J = 3.2 Hz, 1H, ArH), 6.15 (dd, J = 2.0, 2.8 Hz, 1H, ArH), 7.20-7.28 (m, 6H, ArH), 7.34 (d, J = 8.0 Hz, 2H, ArH), 7.70 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.3, 30.1, 33.0, 59.5, 72.8, 79.5, 107.2, 110.1, 127.3, 128.0, 128.3, 129.3, 136.7, 137.6, 141.1, 143.2, 151.5.

IR (CH_2Cl_2) ν 3290, 2922, 1597, 1496, 1333, 1154, 1092, 812, 772, 716, 657 cm^{-1}. MS (ESI) *m/z* (%): 397.1 (100) [M^++NH_4]; HRMS (ESI) Calcd. For $C_{22}H_{25}N_2O_3S^{+1}$(M^++NH_4) requires 397.1580, Found: 397.1585.





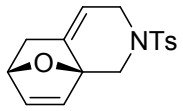
2-(2-(prop-2-yn-1-yloxy)ethyl)furan 4h

For preparation and characterization of **4h**, see reference.[7]

4. General procedure for synthesis of 2, 3, 5 and 7 as well as their characterization

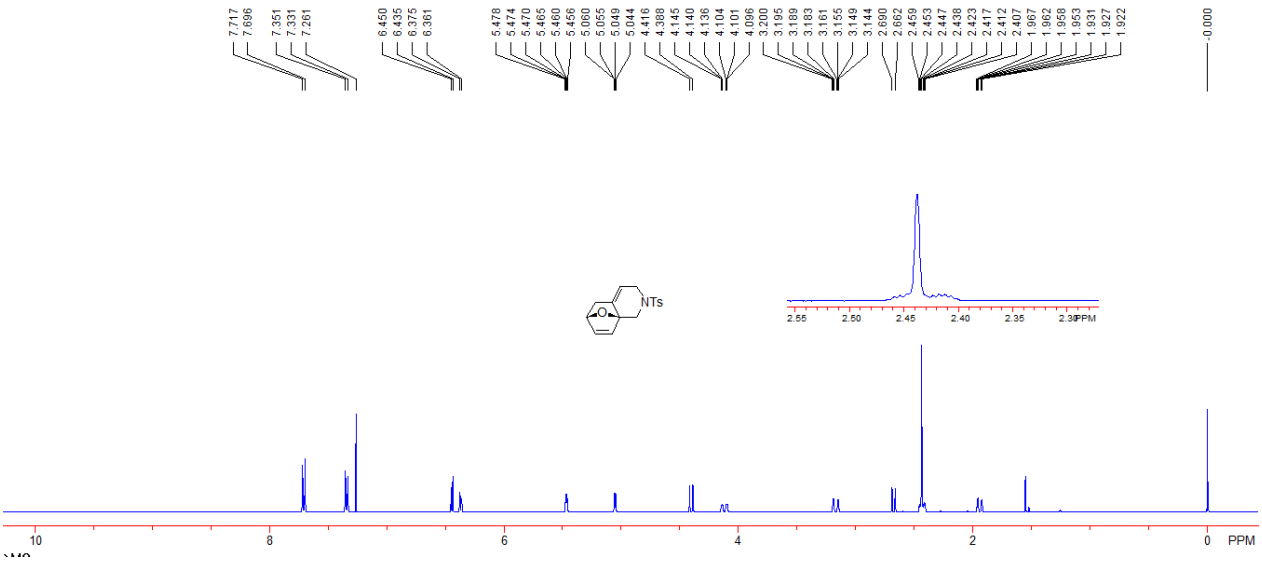
To a dried reaction tube with a reflux condenser was added CuBr (0.06 mmol), paraformaldehyde (0.50 mmol). Then, alkyne (0.20 mmol), dicyclohexylamine (0.36 mmol), and toluene (1.00 mL)

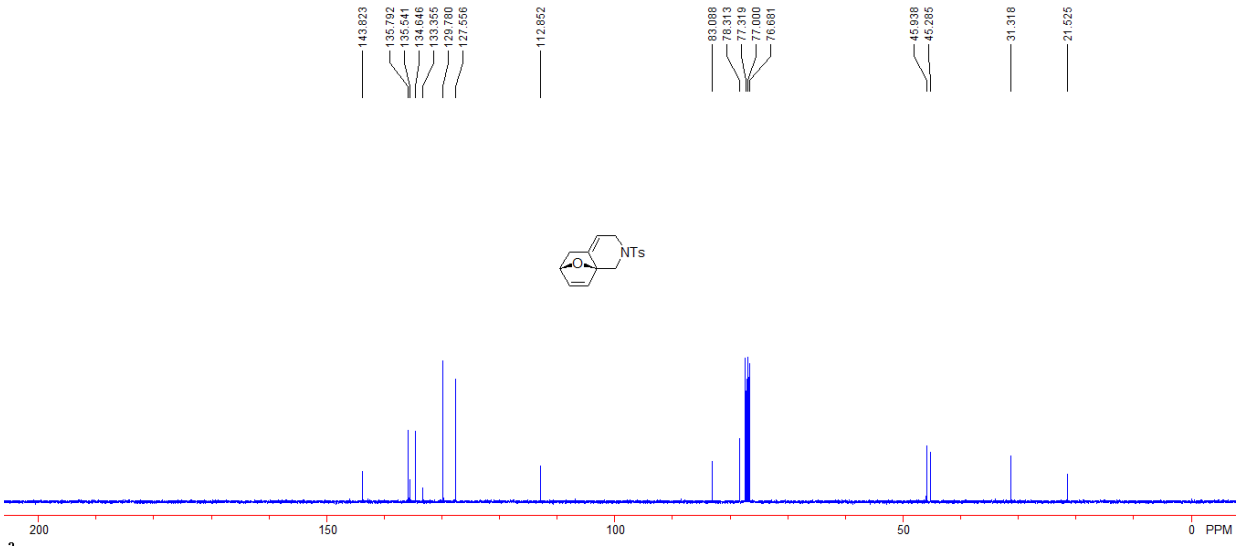
were added sequentially into this dried reaction tube under an argon atmosphere and the resulting mixture was stirred at 110 °C. Compound **7d** was stirred at 130 °C in a sealed tube. Compound **7e** and **7f** were stirred at 150 °C in a sealed tube. When the reaction was complete as monitored by TLC, the solution was concentrated under reduced pressure and the crude residue was purified by a silica gel flash column chromatography (eluent: petroleum ether / ethyl acetate = 15/1) to give the cycloadducts **2**, **3**, **5** and **7**.

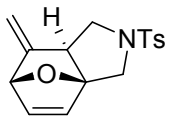


(6S,8aS)-2-tosyl-2,3,5,6-tetrahydro-1H-6,8a-epoxyisoquinoline 2a

A white solid, 18% yield (11 mg). M.p.: 163-165 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.95 (ddd, *J* = 2.0, 3.6, 14.0 Hz, 1H, CH_2), 2.43 (ddd, *J* = 2.0, 4.0, 14.0 Hz, 1H, CH_2), 2.44 (s, 3H, CH_3), 2.68 (d, *J* = 11.2 Hz, 1H, CH_2), 3.15 (ddd, *J* = 2.4, 5.6, 16.0 Hz, 1H, CH_2), 4.10 (ddd, *J* = 1.6, 3.6, 16.0 Hz, 1H, CH_2), 4.40 (d, *J* = 11.2 Hz, 1H, CH_2), 5.05 (dd, *J* = 1.6, 4.4 Hz, 1H, CH), 5.47 (ddd, *J* = 2.0, 3.6, 5.6 Hz, 1H, =CH), 6.37 (d, *J* = 6.0 Hz, 1H, =CH), 6.44 (d, *J* = 6.0 Hz, 1H, =CH), 7.34 (d, *J* = 8.0 Hz, 2H, ArH), 7.71 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.5, 31.3, 45.3, 46.0, 78.3, 83.1, 112.9, 127.6, 129.8, 133.4, 134.6, 135.5, 135.8, 143.8. IR (CH_2Cl_2) ν 2939, 2853, 1598, 1341, 1301, 1194, 1163, 1136, 1088, 1040, 1000, 945, 915, 830, 735, 709, 694, 662 cm^{-1}. MS (ESI) *m/z* (%): 304.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{16}H_{18}NO_3S^{+1}$(M^++H) requires 304.1002, Found: 304.1009.

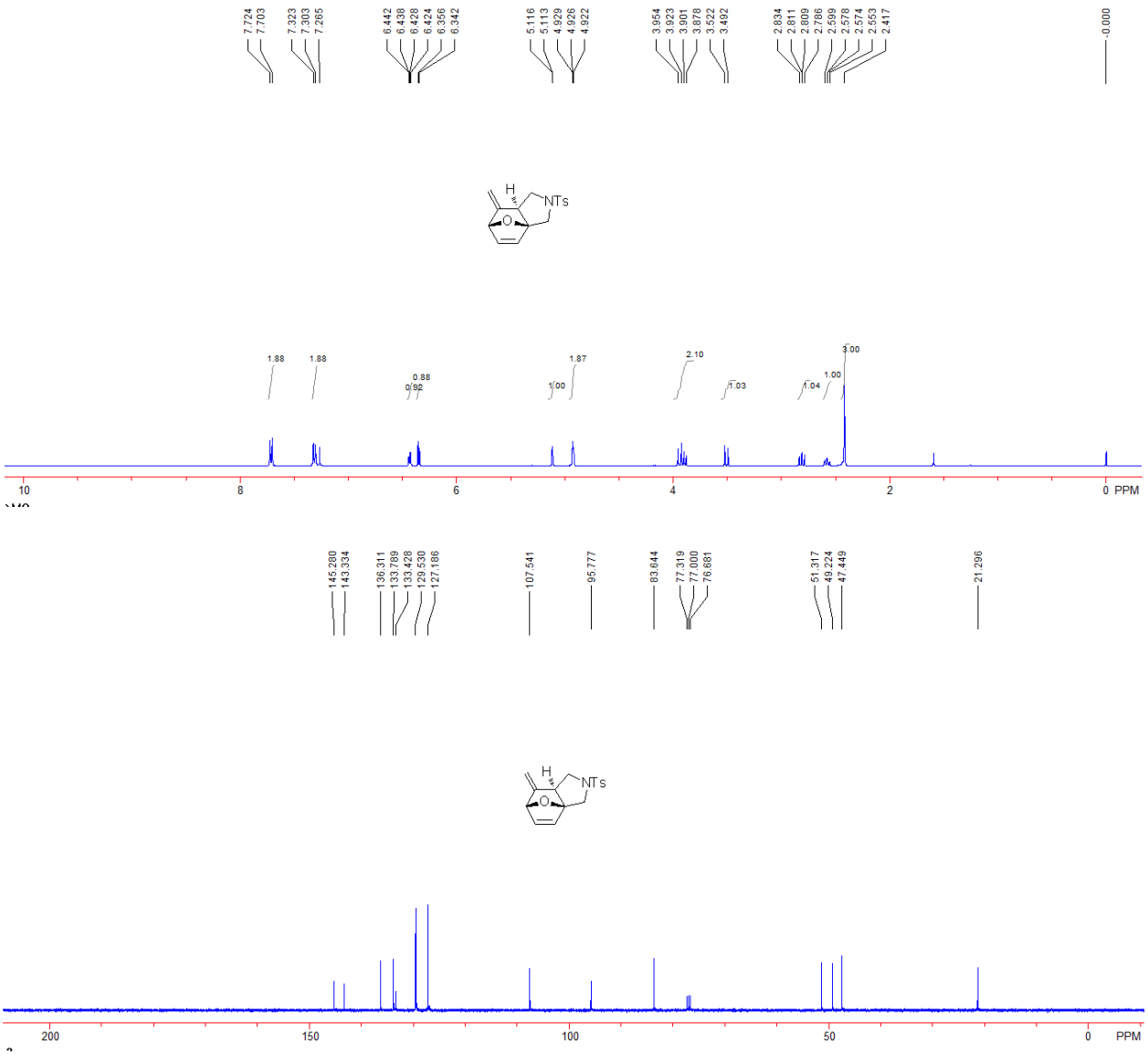


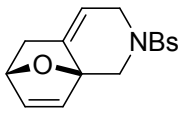




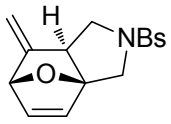
(3aS,6R,7aS)-7-methylene-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole 3a

A white solid, 68% yield (41 mg). M.p.: 171-174 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.42 (s, 3H, CH_3), 2.58 (dd, *J* = 9.2, 9.2 Hz, 1H, CH), 2.81 (dd, *J* = 9.2, 9.2 Hz, 1H, CH_2), 3.51 (d, *J* = 12.0 Hz, 1H, CH_2), 3.90 (dd, *J* = 9.2, 9.2 Hz, 1H, CH_2), 3.94 (d, *J* = 12.0 Hz, 1H, CH_2), 4.92 (d, *J* = 1.2 Hz, 2H, =CH_2), 5.12 (s, 1H, CH), 6.35 (d, *J* = 6.0 Hz, 1H, =CH), 6.43 (d, *J* = 6.0 Hz, 1H, =CH), 7.31 (d, *J* = 8.0, 2H, ArH), 7.71 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.3, 47.4, 49.2, 51.3, 83.6, 96.0, 107.5, 127.2, 129.5, 133.4, 133.8, 136.3, 143.3, 145.3. IR (CH_2Cl_2) ν 2929, 2875, 1676, 1597, 1492, 1455, 1371, 1339, 1306, 1289, 1181, 1163, 1106, 1062, 998, 924, 898, 818, 708, 664, 656 cm^{-1}. MS (ESI) *m/z* (%): 304.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{16}H_{18}NO_3S^{+1}$(M^++H) requires 304.1002, Found: 304.1009.





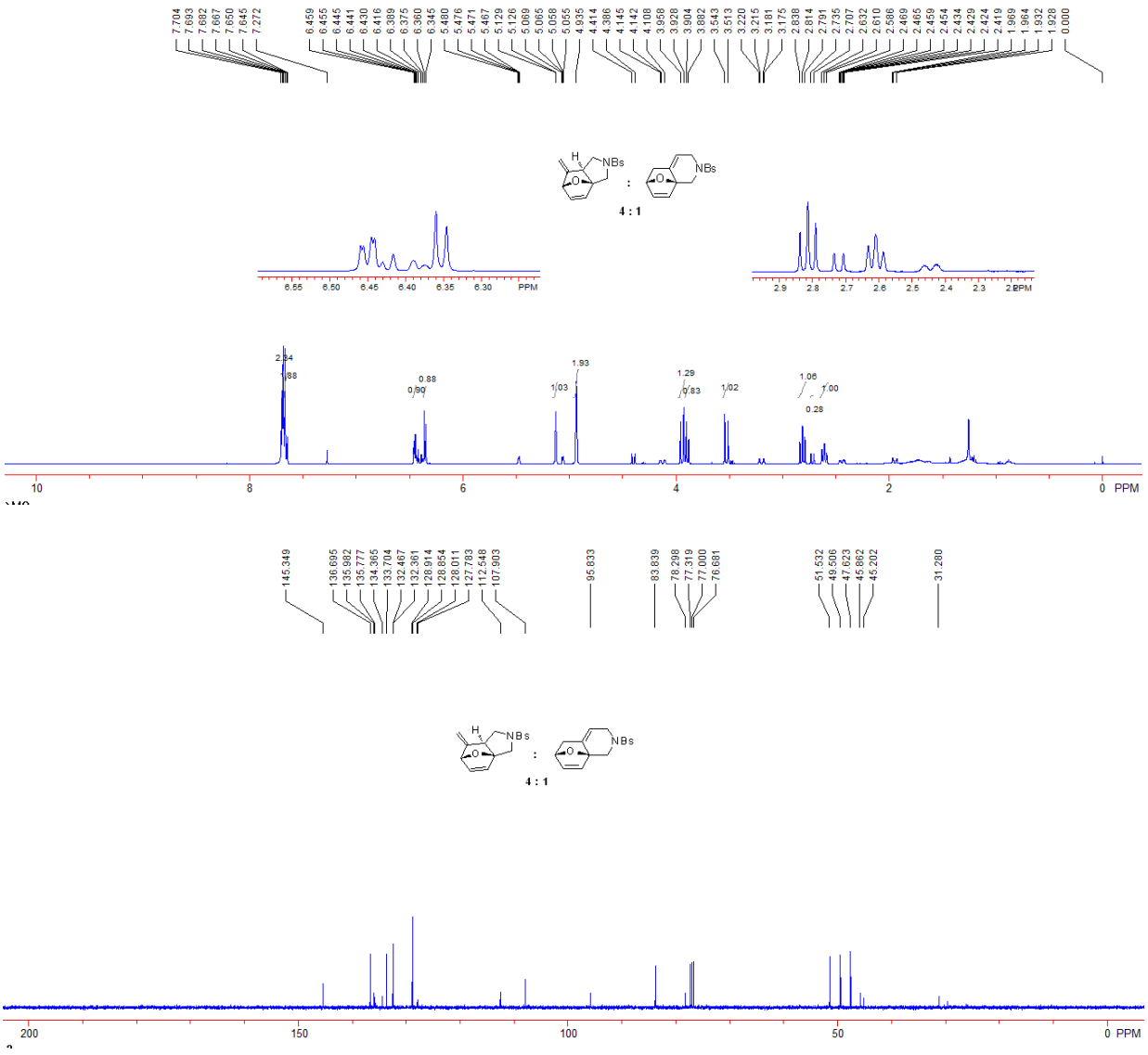
(6S,8aS)-2-((4-bromophenyl) sulfonyl)-2,3,5,6-tetrahydro-1H-6,8a-epoxyisoquinoline 2b

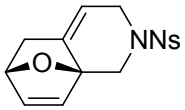


(3aS,6R,7aS)-2-((4-bromophenyl)sulfonyl)-7-methylene-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole 3b

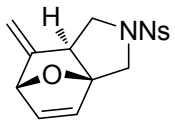
A White solid, 63% yield (46 mg). Ratio (**2b**/**3b**) = 1/4. M.p.: 160-163 ^{o}C. Minor product **2b**, diagnostic peaks: ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.95 (dd, J = 1.6, 14.0 Hz, 1H, CH_2), 2.43 (ddd, J = 2.0, 4.0, 14.0 Hz, 1H, CH_2), 2.72 (d, J = 11.2 Hz, 1H, CH_2), 3.19 (dd, J = 2.0, 16.0 Hz,

1H, CH_2), 4.12 (dd, *J* = 1.6, 16.0 Hz, 1H, CH_2), 4.39 (d, *J* = 11.2 Hz, 1H, CH_2), 5.06 (dd, *J* = 1.6, 4.0 Hz, 1H, CH), 5.47 (dd, *J* = 1.6, 4.0 Hz, 1H, =CH), 6.38 (d, *J* = 5.6 Hz, 1H, =CH), 6.42 (d, *J* = 5.6 Hz, 1H, =CH), 7.65 (d, *J* = 8.8 Hz, 2H, ArH), 7.69 (d, *J* = 8.8 Hz, 2H, ArH). Major product **3b**: ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.61 (dd, *J* = 9.2, 9.2 Hz, 1H, CH), 2.81 (dd, *J* = 9.2, 9.2 Hz, 1H, CH_2), 3.52 (d, *J* = 12.0 Hz, 1H, CH_2), 3.91 (dd, *J* = 9.2, 9.2 Hz, 1H, CH_2), 3.94 (d, *J* = 12.0 Hz, 1H, CH_2), 4.94 (s, 2H, $=CH_2$), 5.12 (d, *J* = 1.2 Hz, 1H, CH), 6.35 (d, *J* = 6.0 Hz, 1H, =CH), 6.45 (dd, *J* = 1.2, 6.0 Hz, 1H, =CH), 7.65 (d, *J* = 8.8 Hz, 2H, ArH), 7.69 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 47.6, 49.5, 51.5, 83.8, 95.8, 107.9, 127.8, 128.9, 132.4, 133.7, 134.4, 136.7, 145.3. IR (CH_2Cl_2) ν 2954, 2924, 2853, 1574, 1470, 1389, 1347, 1165, 1068, 1009, 996, 772, 741, 705 cm^{-1}. MS (MALDI) *m/z* (%): 367.9 (100) [M^++H]; HRMS (MALDI) Calcd. For $C_{15}H_{15}NO_3BrS^{+1}$(M^++H) requires 367.9951, Found: 367.9948.



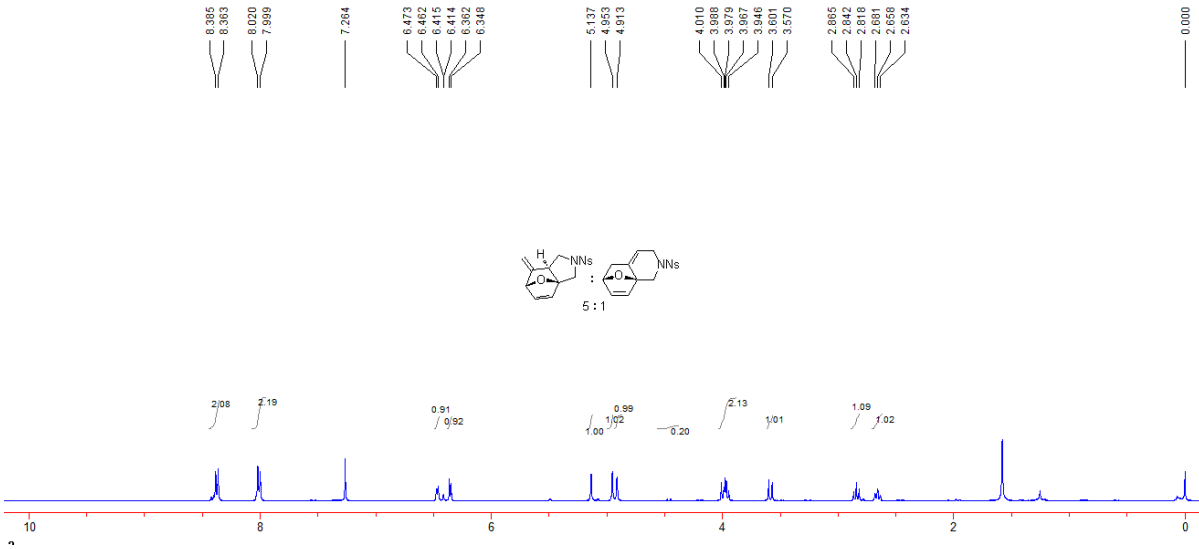


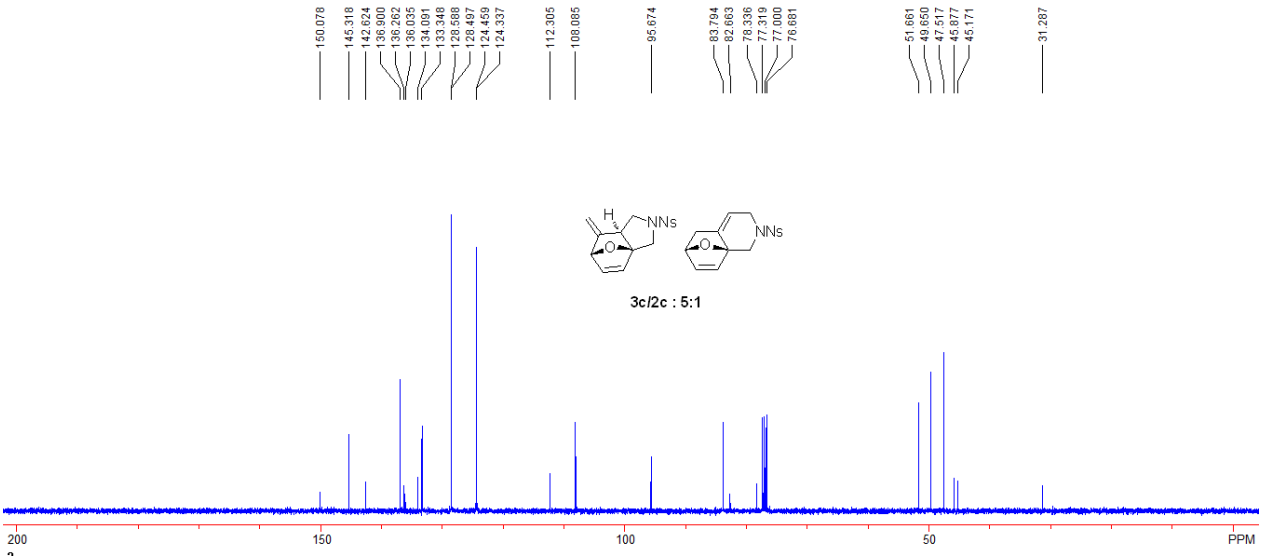
(6S,8aS)-2-((4-nitrophenyl)sulfonyl)-2,3,5,6-tetrahydro-1H-6,8a-epoxyisoquinoline 2c

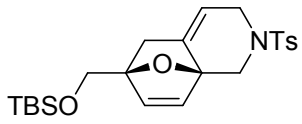


(3aS,6R)-7-methylene-2-((4-nitrophenyl)sulfonyl)-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole 3c

A Yellow solid, 80% yield (51 mg). Ratio (**2c**/**3c**) = 1/5. M.p.: 175-178 °C. Minor product **2c**, diagnostic peaks: ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.96 (dd, *J* = 1.6, 14.0 Hz, 1H, CH_2), 2.45 (ddd, *J* = 2.0, 4.0, 14.0 Hz, 1H, CH_2), 2.80 (d, *J* = 11.6 Hz, 1H, CH_2), 3.27 (dd, *J* = 2.0, 16.0 Hz, 1H, CH_2), 4.19 (d, *J* = 16.0 Hz, 1H, CH_2), 4.46 (d, *J* = 11.6 Hz, 1H, CH_2), 5.07 (d, *J* = 4.0 Hz, 1H, CH), 5.49 (dd, *J* = 1.6, 4.4 Hz, 1H, =CH), 6.38 (d, *J* = 5.6 Hz, 1H, =CH), 6.42 (d, *J* = 5.6 Hz, 1H, =CH), 8.01 (d, *J* = 8.8 Hz, 2H, ArH), 8.40 (d, *J* = 8.8 Hz, 2H, ArH). Major product **3c**: ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.66 (dd, *J* = 9.2, 9.6 Hz, 1H, CH_2), 2.84 (dd, *J* = 9.2, 9.2 Hz, 1H, CH_2), 3.59 (d, *J* = 12.4 Hz, 1H, CH_2), 3.97 (dd, *J* = 9.2, 9.2 Hz, 1H, CH), 3.99 (d, *J* = 12.4 Hz, 1H, CH_2), 4.91 (s, 1H, =CH_2), 4.95 (s, 1H, =CH_2), 5.14 (s, 1H, CH), 6.35 (d, *J* = 5.6 Hz, 1H, =CH), 6.46 (d, *J* = 5.6 Hz, 1H, =CH), 8.01 (d, *J* = 8.8 Hz, 2H, ArH), 8.37 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 47.5, 49.6, 51.7, 83.8, 95.7, 108.1, 124.3, 128.5, 133.3, 134.1, 136.9, 142.6, 145.3. IR (CH_2Cl_2) ν 3105, 2934, 2874, 1528, 1349, 1308, 1166, 1108, 1044, 998, 855, 830, 738, 699 cm^{-1}. MS (MALDI) *m/z* (%): 357.0 (100) [M^++Na]; HRMS (MALDI) Calcd. For $C_{15}H_{14}N_2O_5NaS^{+1}$($M^+$+Na) requires 357.0516, Found: 357.0511.

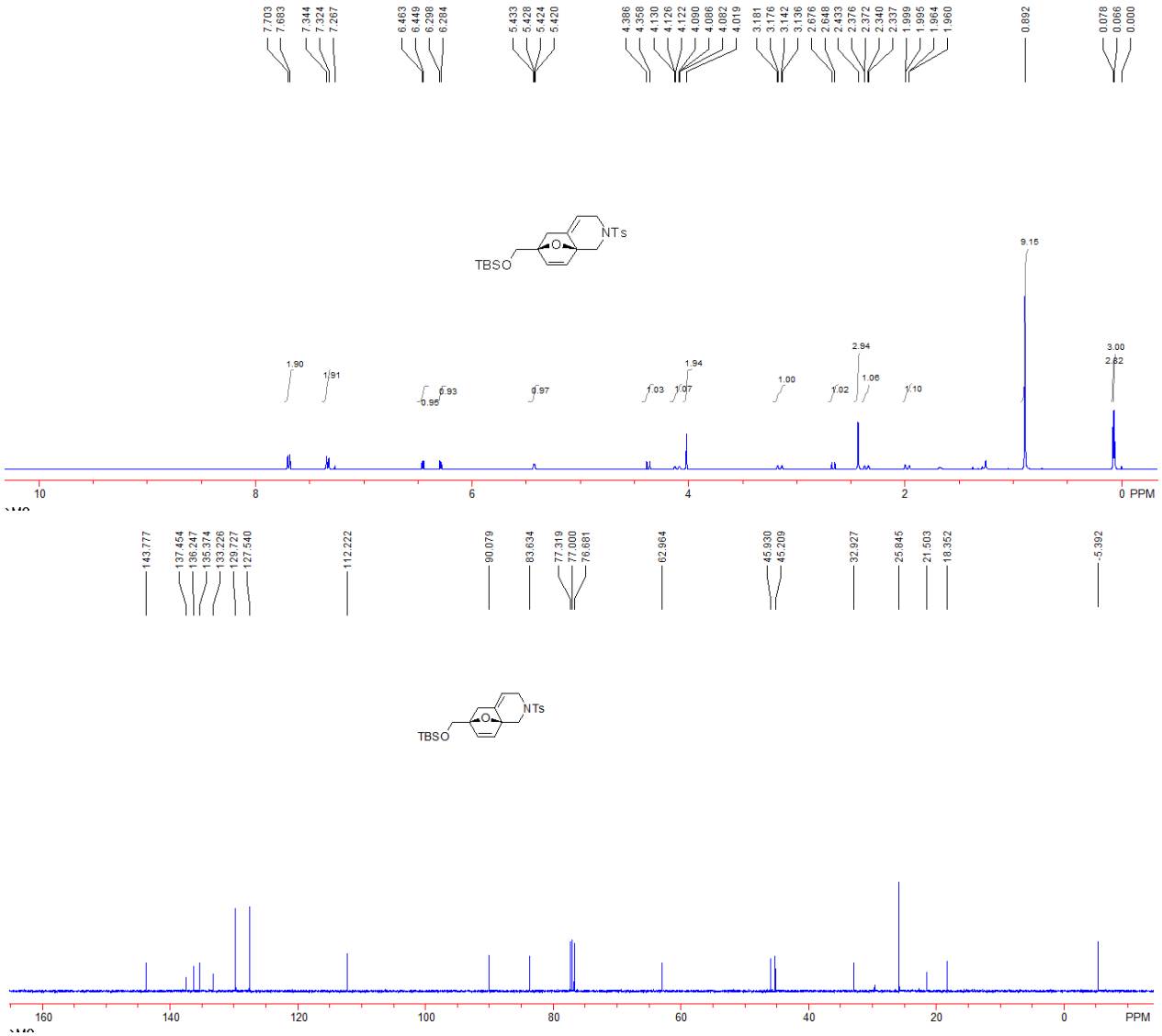


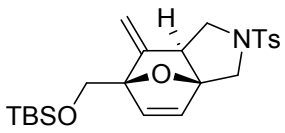




(6S,8aS)-6-(((tert-butyldimethylsilyl)oxy)methyl)-2-tosyl-2,3,5,6-tetrahydro-1H-6,8a-epoxyisoquinoline 2d

A White solid, 30% yield (29 mg). M.p.: 81-83 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.07 (s, 3H, CH_3), 0.08 (s, 3H, CH_3), 0.90 (s, 9H, $C(CH_3)_3$), 1.98 (dd, *J* = 1.6, 14.0 Hz, 1H, CH_2), 2.36 (dd, *J* = 1.6, 14.0 Hz, 1H, CH_2), 2.43 (s, 3H, CH_3), 2.66 (d, *J* = 11.2 Hz, 1H, CH_2), 3.16 (dd, *J* = 2.0, 16.0 Hz, 1H, CH_2), 4.02 (s, 2H, CH_2), 4.09 (d, *J* = 1.6 Hz, 1H, CH_2), 4.37 (d, *J* = 11.2 Hz, 1H, CH_2), 5.43 (dd, *J* = 1.6, 3.2 Hz, 1H, =CH), 6.29 (d, *J* = 5.6, 1H, =CH), 6.45 (d, *J* = 5.6 Hz, 1H, =CH), 7.33 (d, *J* = 8.0 Hz, 2H, ArH), 7.69 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ -5.4, 18.4, 21.5, 25.8, 32.9, 45.2, 45.9, 63.0, 83.6, 90.1, 112.2, 127.5, 129.7, 133.2, 135.4, 136.2, 137.5, 143.8. IR (CH_2Cl_2) ν 2955, 2927, 2856, 1597, 1461, 1354, 1331, 1258, 1169, 1090, 1053, 1029, 949, 839, 813, 765, 749, 712, 667 cm^{-1}. MS (ESI) *m/z* (%): 465.2 (100) [M^++NH_4]; HRMS (ESI) Calcd. For $C_{23}H_{37}N_2O_4SSi^{+1}$($M^+$+$NH_4$) requires 465.2238, Found: 465.2239.

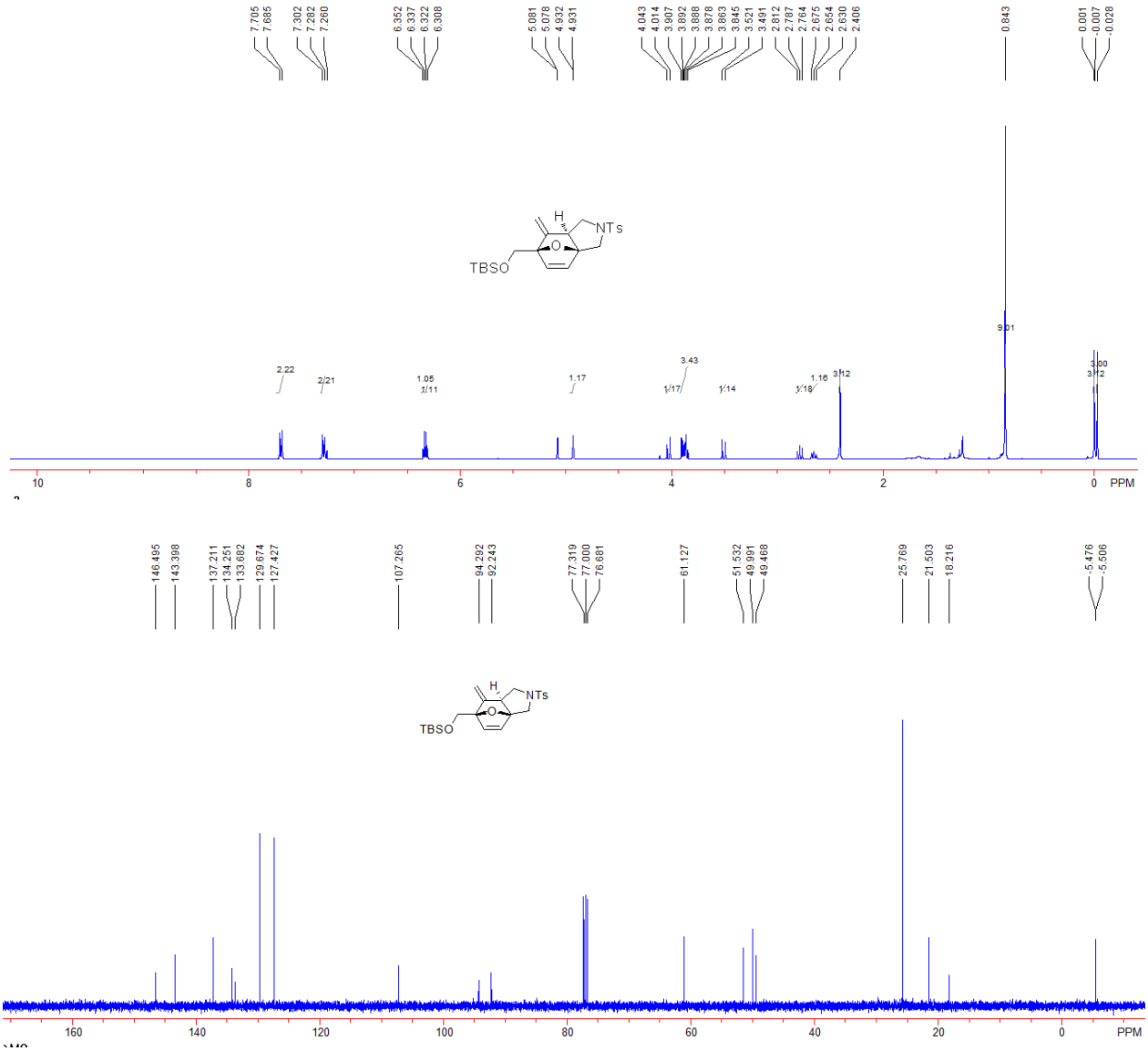


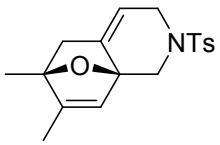


(3aS,6R,7aS)-6-(((tert-butyldimethylsilyl)oxy)methyl)-7-methylene-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole 3d

A White solid, 30% yield (29 mg). M.p.: 120-123 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ -0.03 (s, 3H, CH_3), -0.01 (s, 3H, CH_3), 0.84 (s, 9H, CH_3), 2.41 (s, 3H, CH_3), 2.65 (dd, J = 8.4, 9.6 Hz, 1H, CH_2), 2.79 (dd, J = 9.6, 10.0 Hz, 1H, CH_2), 3.51 (d, J = 12.0 Hz, 1H, CH_2), 3.84-3.91 (m, 3H, CH_2), 4.03 (d, J = 12.0 Hz, 1H, CH_2), 4.93 (d, J = 0.4 Hz, 1H, =CH_2), 5.08 (d, J = 1.2 Hz, 1H, =CH_2), 6.31 (d, J = 5.6, 1H, =CH), 6.34 (d, J = 5.6 Hz, 1H, =CH), 7.29 (d, J = 8.0 Hz, 2H, ArH), 7.69 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ -5.5, -5.47, 18.2, 21.5, 25.8, 49.5, 50.0, 51.5, 61.1, 92.2, 94.3, 107.3, 127.4, 129.7, 133.7, 134.3, 137.2, 143.4, 146.5. IR

(CH_2Cl_2) ν 2925, 2853, 1598, 1462, 1340, 1288, 1163, 1120, 1094, 999, 882, 859, 836, 814, 782, 697, 665 cm^{-1}. MS (ESI) *m/z* (%): 465.2 (100) [M^++NH_4]; HRMS (ESI) Calcd. For $C_{23}H_{37}N_2O_4SSi^{+1}$($M^+$+$NH_4$) requires 465.2238, Found: 465.2237.

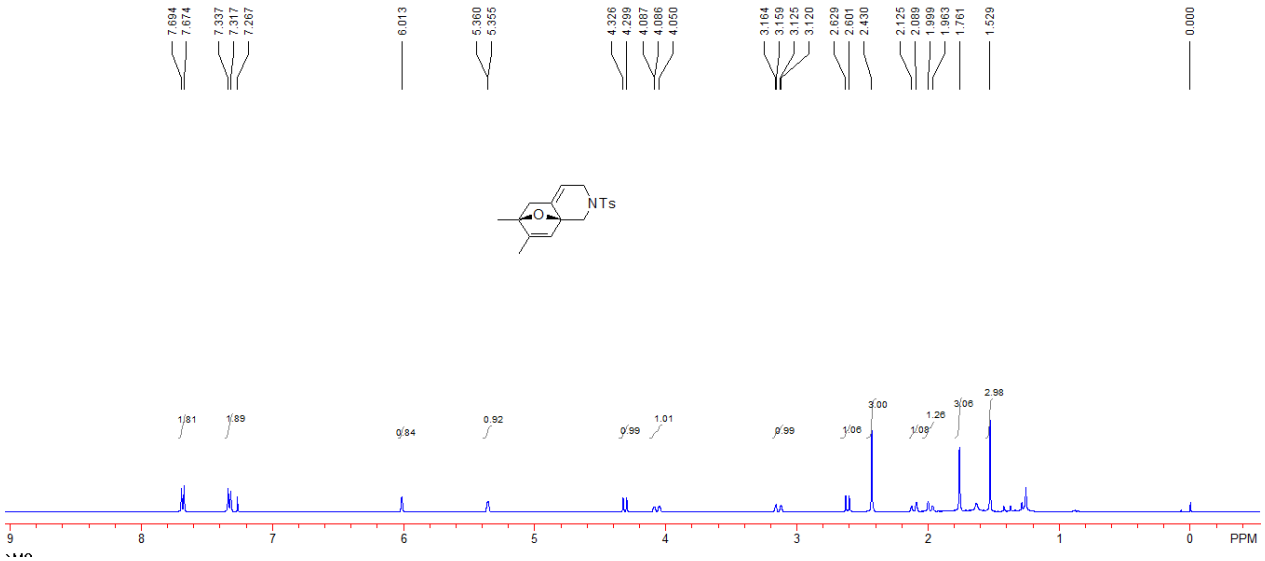


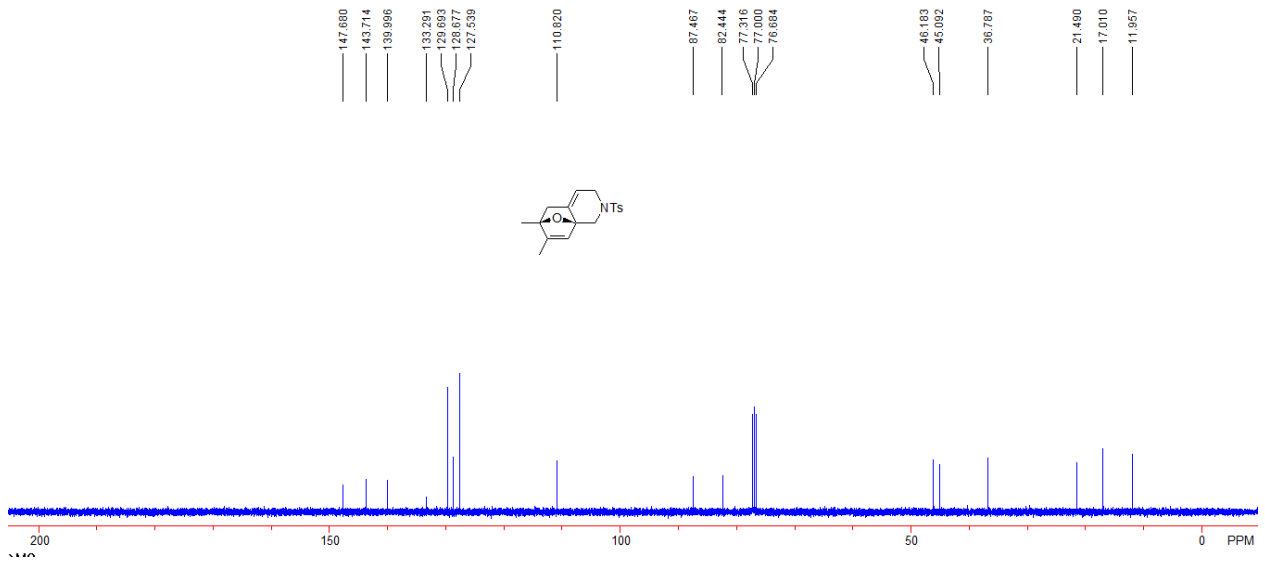


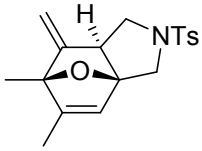
(6S,8aS)-6,7-dimethyl-2-tosyl-2,3,5,6-tetrahydro-1H-6,8a-epoxyisoquinoline 2e

A White solid, 12% yield (9 mg). M.p.: 121-124 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.53 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 1.98 (d, *J* = 14.4 Hz, 1H, CH_2), 2.10 (d, *J* = 14.4 Hz, 1H, CH_2), 2.43 (s, 3H, CH_3), 2.62 (d, *J* = 12.0 Hz, 1H, CH_2), 3.14 (dd, *J* = 2.0, 15.6 Hz, 1H, CH_2), 4.07 (dd, *J* = 0.4, 15.6 Hz, 1H, CH_2), 4.31 (d, *J* = 10.8 Hz, 1H, CH_2), 5.36 (d, *J* = 2.0 Hz, 1H, =CH), 6.01 (s,

1H, =CH), 7.32 (d, J = 8.0 Hz, 2H, ArH), 7.68 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 12.0, 17.0, 21.5, 36.8, 45.1, 46.2, 82.4, 87.5, 110.8, 127.5, 128.7, 129.7, 133.3, 140.0, 143.7, 147.7. IR (CH_2Cl_2) ν 2922, 2852, 1597, 1457, 1378, 1348, 1328, 1165, 1142, 1029, 1000, 948, 889, 831, 713, 695, 663 cm^{-1}. MS (ESI) *m/z* (%): 349.1 (100) [M^++NH_4]; HRMS (ESI) Calcd. For $C_{18}H_{25}N_2O_3S^{+1}$(M^++NH_4) requires 349.1580, Found: 349.1590.

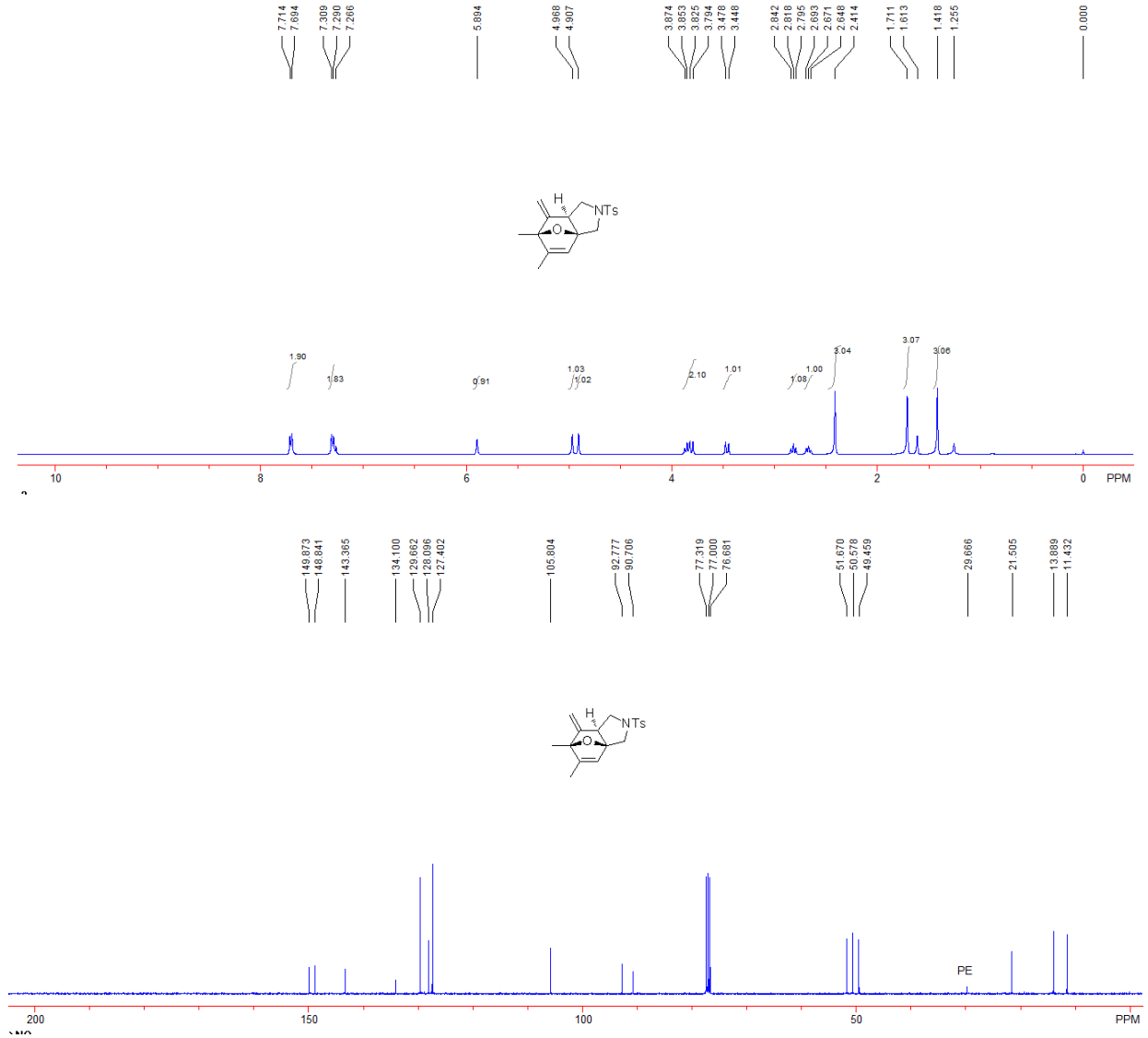


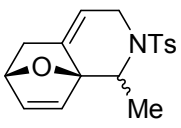




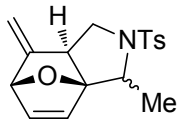
(3aS,6R,7aS)-5,6-dimethyl-7-methylene-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole 3e

A white solid, 48% yield (31 mg). M.p.: 156-159 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.42 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.67 (dd, J = 8.8, 9.2 Hz, 1H, CH_2), 2.82 (dd, J = 9.2, 9.6 Hz, 1H, CH_2), 3.46 (d, J = 12.0 Hz, 1H, CH_2), 3.81 (dd, J = 8.8, 9.2 Hz, 1H, CH), 3.86 (d, J = 12.0 Hz, 1H, CH_2), 4.91 (s, 1H, =CH_2), 4.97 (s, 1H, =CH_2), 5.89 (s, 1H, =CH), 7.30 (d, J = 8.0 Hz, 2H, ArH), 7.70 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 11.4, 13.9, 21.5, 49.5, 50.6, 51.7, 90.7, 92.8, 105.8, 127.4, 128.1, 129.7, 134.1, 143.4, 148.8, 149.9. IR (CH_2Cl_2) ν 2933, 1670, 1598, 1494, 1454, 1343, 1290, 1162, 1108, 1093, 1000, 886, 817, 781, 668 cm^{-1}. MS (ESI) *m/z* (%): 332.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{18}H_{22}NO_3S^{+1}$(M^++H) requires 332.1315, Found: 332.1322.



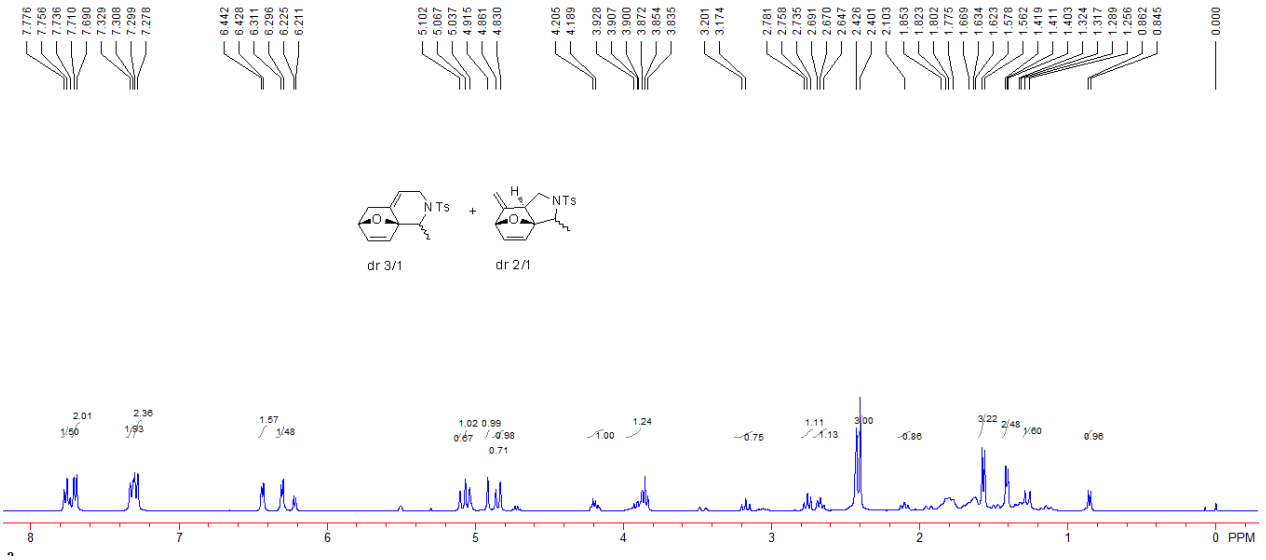


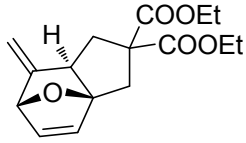
(6S,8aS)-1-methyl-2-tosyl-2,3,5,6-tetrahydro-1H-6,8a-epoxyisoquinoline 2f



(3aS, 6R, 7aS)-3-methyl-7-methylene-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole 3f

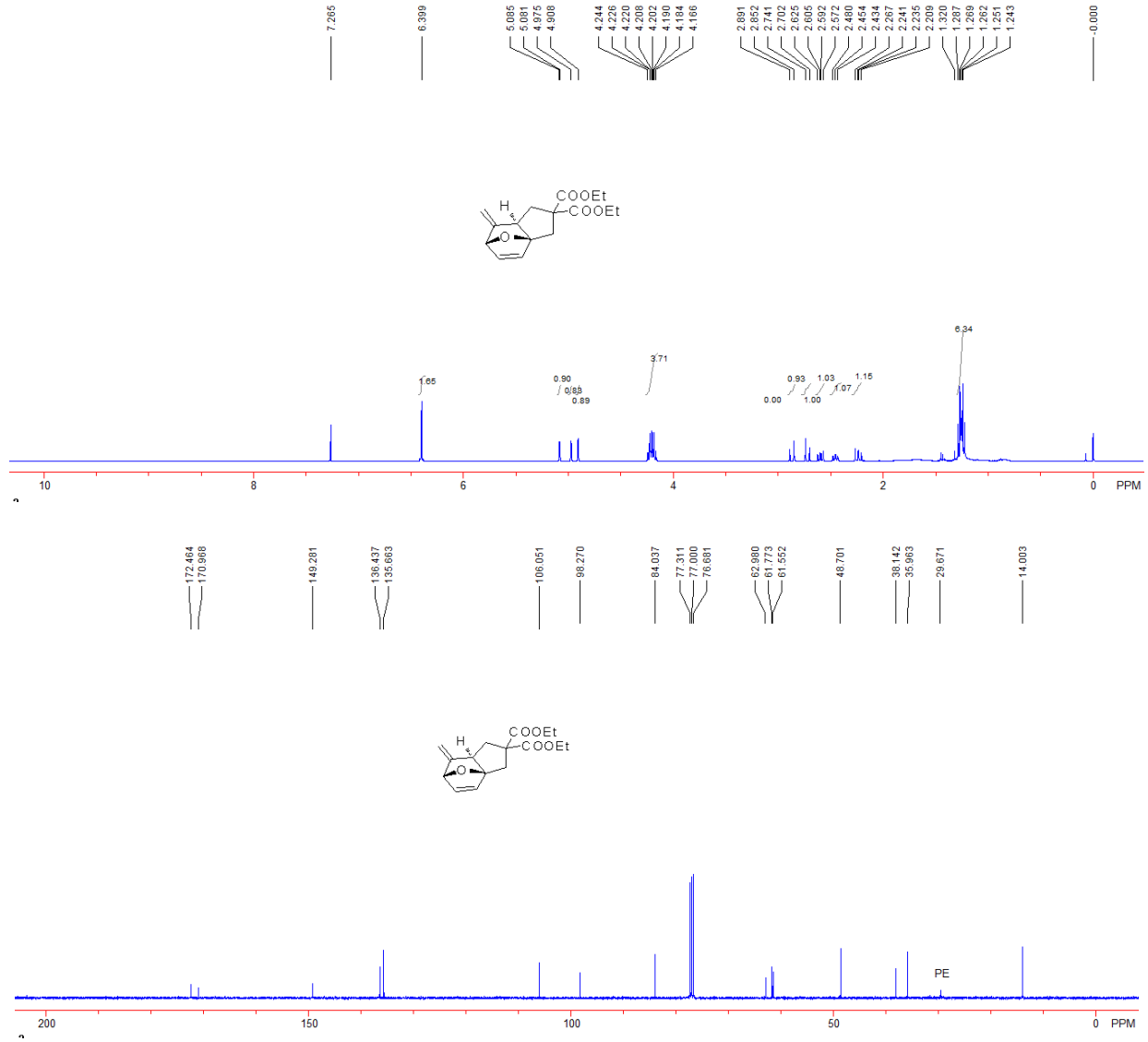
A white solid. 81% yield (51 mg). Ratio (**2f**/**3f**) = 1/2. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) select resonances for **2f** (showing as a mixture of diastereomers in 3/1 ratio) δ 0.85 (d, *J* = 6.8 Hz, 3H, CH_3), 1.93 (ddd, *J* = 2.0, 3.6, 14.0 Hz, 1H, CH_2), 2.44 (s, 3H, CH_3), 2.45-2.49 (m, 1H, CH_2), 3.46 (ddd, *J* = 2.4, 5.6, 16.0 Hz, 1H, CH_2), 4.19 (ddd, *J* = 1.6, 3.6, 16.0 Hz, 1H, CH_2), 4.72 (q, *J* = 6.8 Hz, 1H, CH), 5.03 (d, *J* = 3.6 Hz, 1H, CH), 5.51 (dd, *J* = 1.6, 3.6 Hz, 1H, =CH), 6.30 (s, 2H, =CH), 7.32 (d, *J* = 8.0 Hz, 2H, ArH), 7.74 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) not recorded for mixture. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) select resonances for **3f** (showing as a mixture of diastereomers in 2/1 ratio) δ 1.41 (d, *J* = 6.8 Hz, 3H, CH_3), 2.12 (dd, *J* = 9.2, 10.0 Hz, 1H, CH_2), 2.43 (s, 3H, CH_3), 3.17 (dd, *J* = 10.4, 11.2 Hz, 1H, CH_2), 3.92 (dd, *J* = 10.4, 11.2 Hz, 1H, CH_2), 4.20 (q, *J* = 6.8 Hz, 1H, CH), 4.86 (s, 1H, =CH_2), 5.04 (s, 1H, CH), 5.10 (d, *J* = 1.2 Hz, 1H, CH), 6.22 (d, *J* = 5.6 Hz, 1H, =CH), 6.44 (d, *J* = 5.6 Hz, 1H, =CH), 7.31 (d, *J* = 8.0 Hz, 2H, ArH), 7.76 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) not recorded for mixture. IR (CH_2Cl_2) ν 2925, 1672, 1598, 1452, 1341, 1161, 1094, 1045, 960, 931, 779, 746, 699, 666, 655 cm^{-1}. MS (ESI) *m/z* (%): 318.1 (100) [M^++H]; HRMS (ESI) Calcd. For $C_{17}H_{20}NO_3S^{+1}$(M^++H) requires 318.1158, Found: 318.1161.

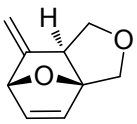




(3aS,6R,7aR)-diethyl-7-methylene-1,6,7,7a-tetrahydro-3a,6-epoxyindene-2,2(3H)-dicarboxylate 3g

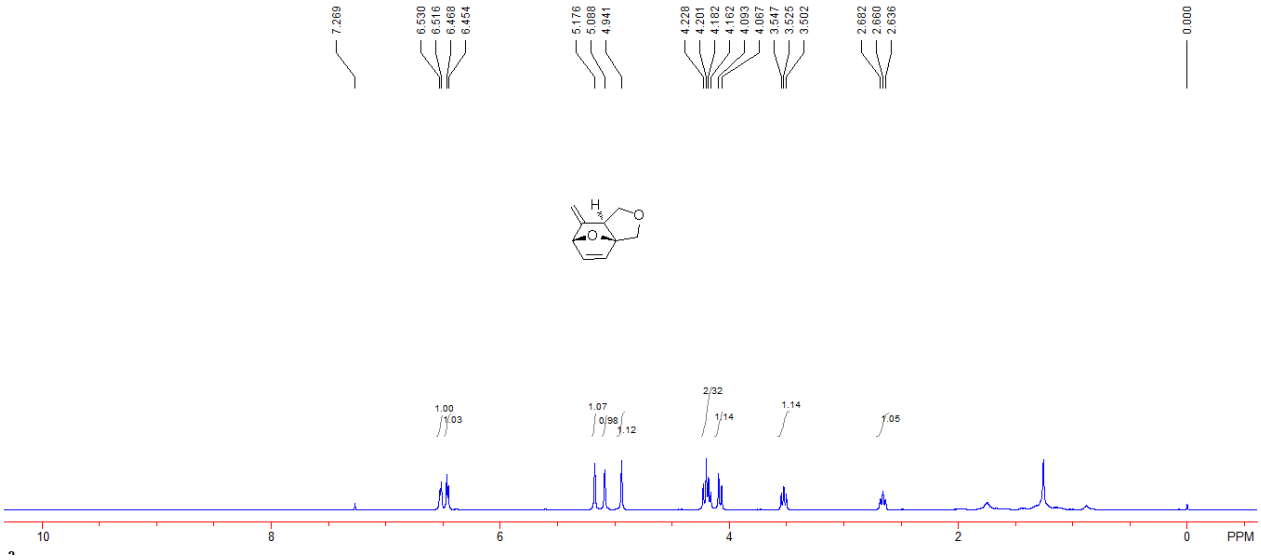
A yellow liquid, 46% yield (28 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.25 (t, *J* = 6.4 Hz, 3H, CH_3), 1.26 (t, *J* = 6.4 Hz, 3H, CH_3), 2.23 (dd, *J* = 10.8, 12.8 Hz, 1H, CH_2), 2.45 (dd, *J* = 8.4, 10.8 Hz, 1H, CH_2), 2.60 (dd, *J* = 8.4, 12.8 Hz, 1H, CH_2), 2.72 (d, *J* = 15.2 Hz, 1H, CH_2), 2.87 (d, *J* = 15.2 Hz, 1H, CH_2), 4.16-4.25 (m, 4H, CH_2), 4.91 (s, 1H, CH), 4.98 (s, 1H, $=CH_2$), 5.09 (s, 1H, $=CH_2$), 6.40 (s, 2H, =CH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 36.0, 38.1, 48.7, 61.6, 61.8, 63.0, 84.0, 98.3, 106.1, 135.7, 136.4, 149.3, 171.0, 172.5. IR (CH_2Cl_2) ν 2984, 2934, 2854, 1729, 1447, 1366, 1254, 1215, 1093, 931, 899, 766, 694 cm^{-1}. MS (ESI) *m/z* (%):293.0 (100) $(M+H)^+$; HRMS (ESI) Calcd. for $C_{16}H_{21}O_5^{+1}(M+H)^+$ requires 293.1384, Found: 293.1381.

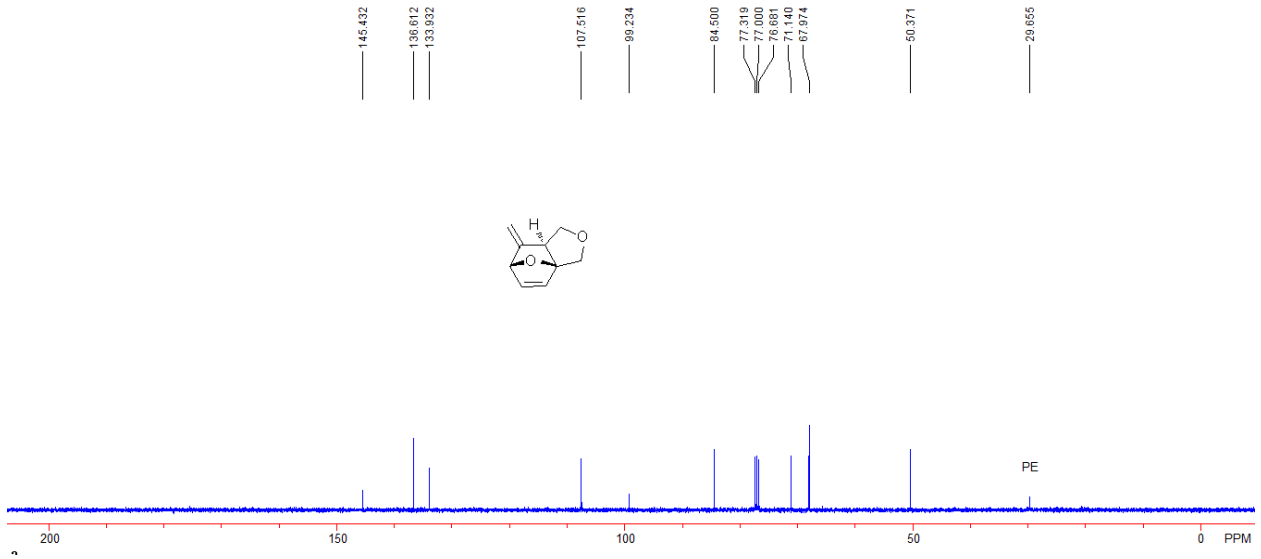


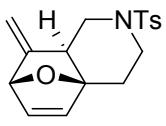


(3aS,6R,7aS)-7-methylene-3,6,7,7a-tetrahydro-1H-3a,6-epoxyisobenzofuran 3h

A yellow liquid, 14% yield (4 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.66 (dd, *J* = 8.8, 9.2 Hz, 1H, CH), 3.53 (dd, *J* = 8.8, 9.2 Hz, 1H, CH_2), 4.08 (d, *J* = 10.4 Hz, 1H, CH_2), 4.18 (dd, *J* = 8.8, 8.8 Hz, 1H, CH_2), 4.21 (d, *J* = 10.4 Hz, 1H, CH_2), 4.94 (s, 1H, CH), 5.09 (s, 1H, $=CH_2$), 5.18 (s, 1H, $=CH_2$), 6.46 (d, *J* = 5.6 Hz, 1H, =CH), 6.52 (d, *J* = 5.6 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 50.4, 68.0, 71.1, 84.5, 99.2, 107.5, 134.0, 136.6, 145.4. IR (CH_2Cl_2) ν 2923, 2853, 1717, 1653, 1507, 1452, 1149, 1080, 1014, 894, 799, 725, 695 cm^{-1}. MS (EI) *m/z* (%): 81 (78), 91 (100), 92 (58), 120 (19), 121 (16), 150 (2) [M^+]; HRMS (EI) Calcd. for $C_9H_{10}O_2$ [M^+] requires 150.0681, Found: 150.0683.

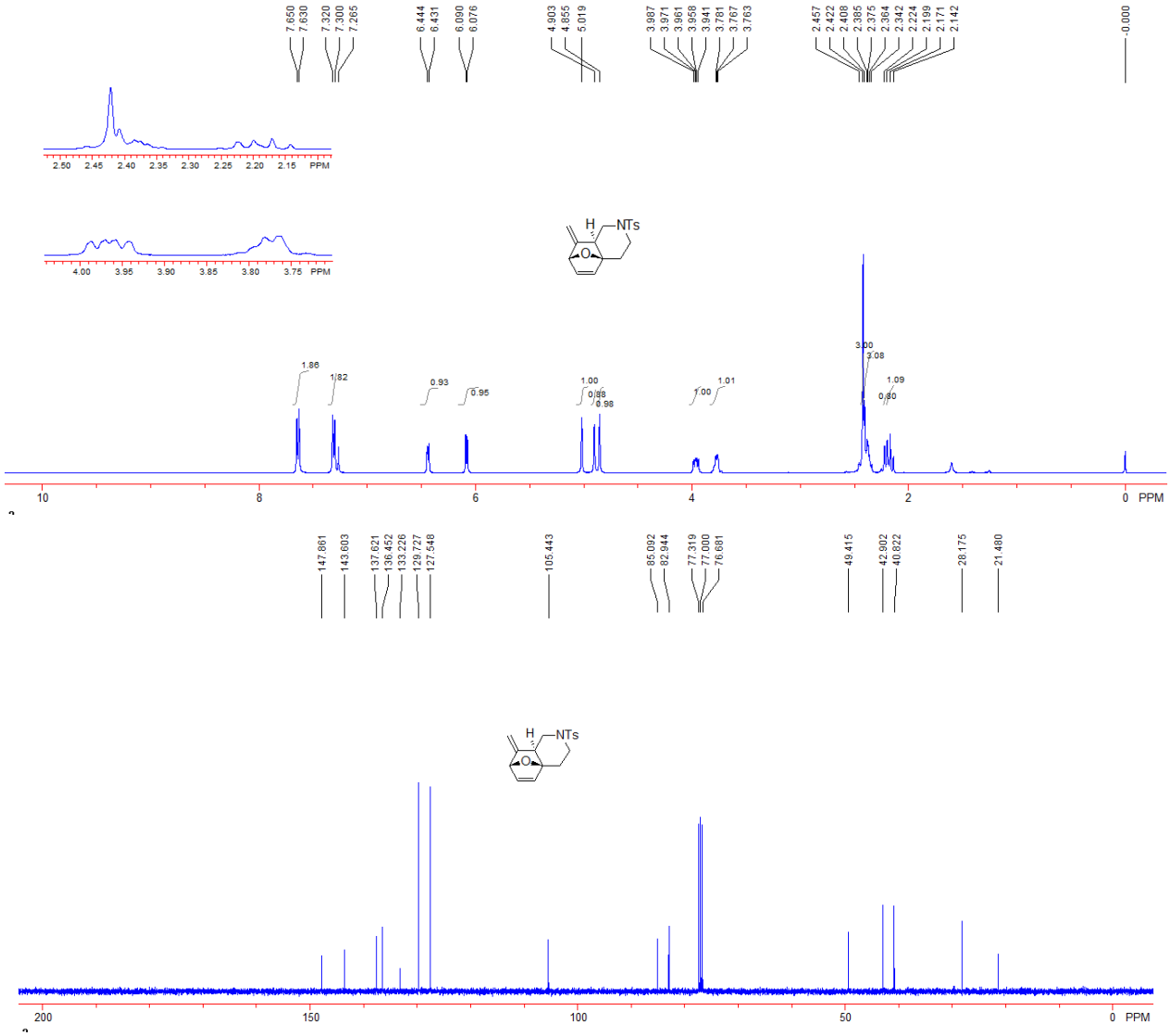


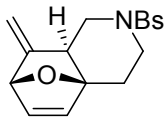




(4aS,7R,8aS)-8-methylene-2-tosyl-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 5a

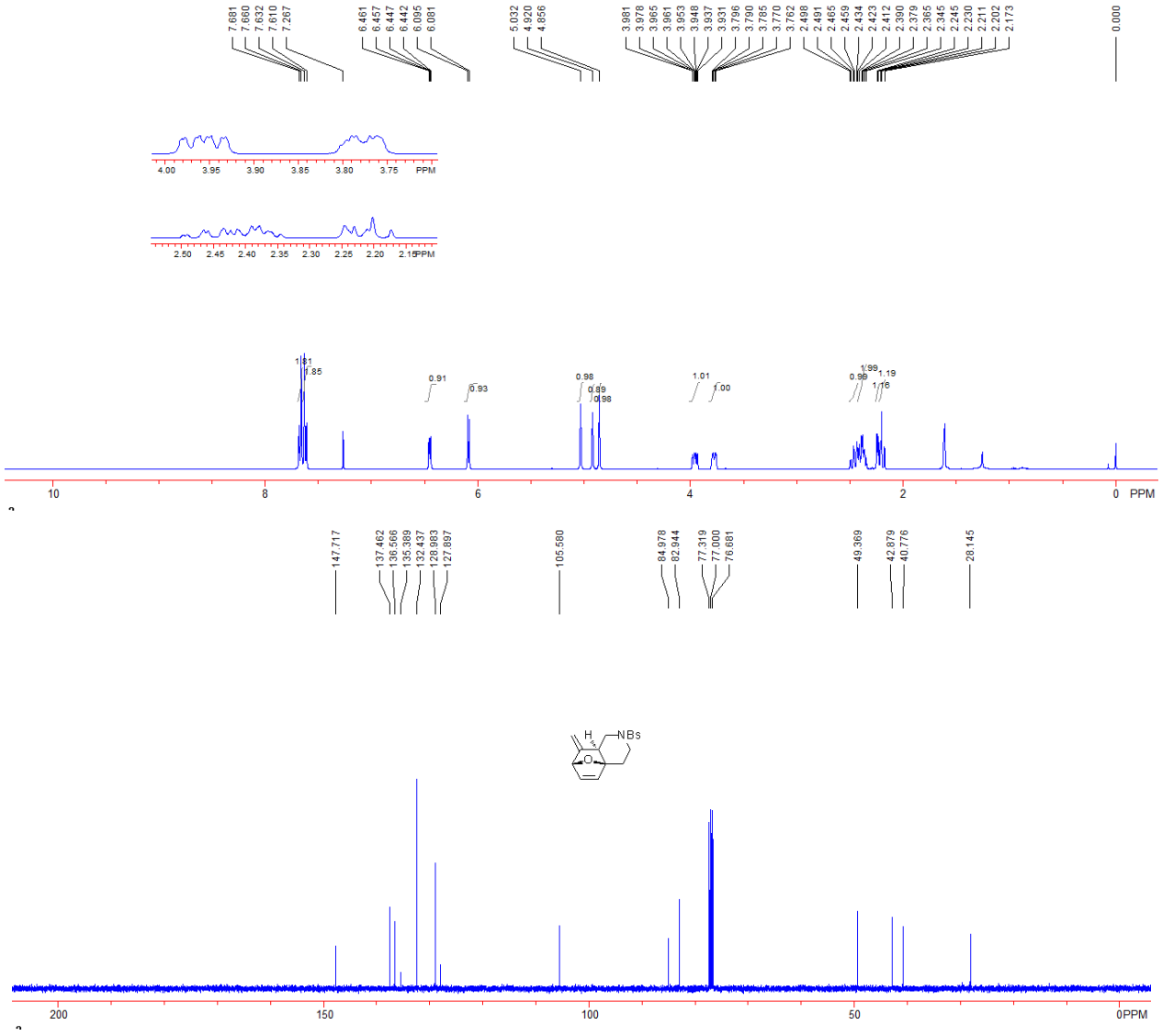
A white solid, 85% yield (54 mg). M.p.: 123-126 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.17 (dd, *J* = 11.6, 11.6 Hz, 1H, CH_2), 2.19-2.23 (m, 1H, CH_2), 2.36-2.41 (m, 3H, CH_2), 2.42 (s, 3H, CH_3), 3.76-3.79 (m, 1H, CH_2), 3.97 (ddd, *J* = 1.6, 7.2, 10.0 Hz, 1H, CH_2), 4.86 (s, 1H, =CH_2), 4.90 (s, 1H, =CH_2), 5.02 (s, 1H, CH), 6.08 (d, *J* = 5.6 Hz, 1H, =CH), 6.44 (d, *J* = 5.6 Hz, 1H, =CH), 7.31 (d, *J* = 8.0 Hz, 2H, ArH), 7.64 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.5, 28.2, 40.8, 42.9, 49.4, 82.9, 85.1, 105.4, 127.6, 129.7, 133.2, 136.5, 137.6, 143.6, 147.9. IR (CH_2Cl_2) ν 2928, 2857, 1661, 1593, 1463, 1341, 1302, 1165, 1140, 1090, 1016, 956, 928, 816, 740, 680, 659 cm^{-1}. MS (ESI) *m/z* (%): 318.1 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{17}H_{20}NO_3S^{+1}(M+H)^+$ requires 318.1158, Found: 318.1159.

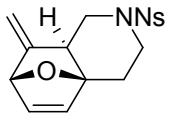




(4aS,7R,8aS)-2-((4-bromophenyl)sulfonyl)-8-methylene-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 5b

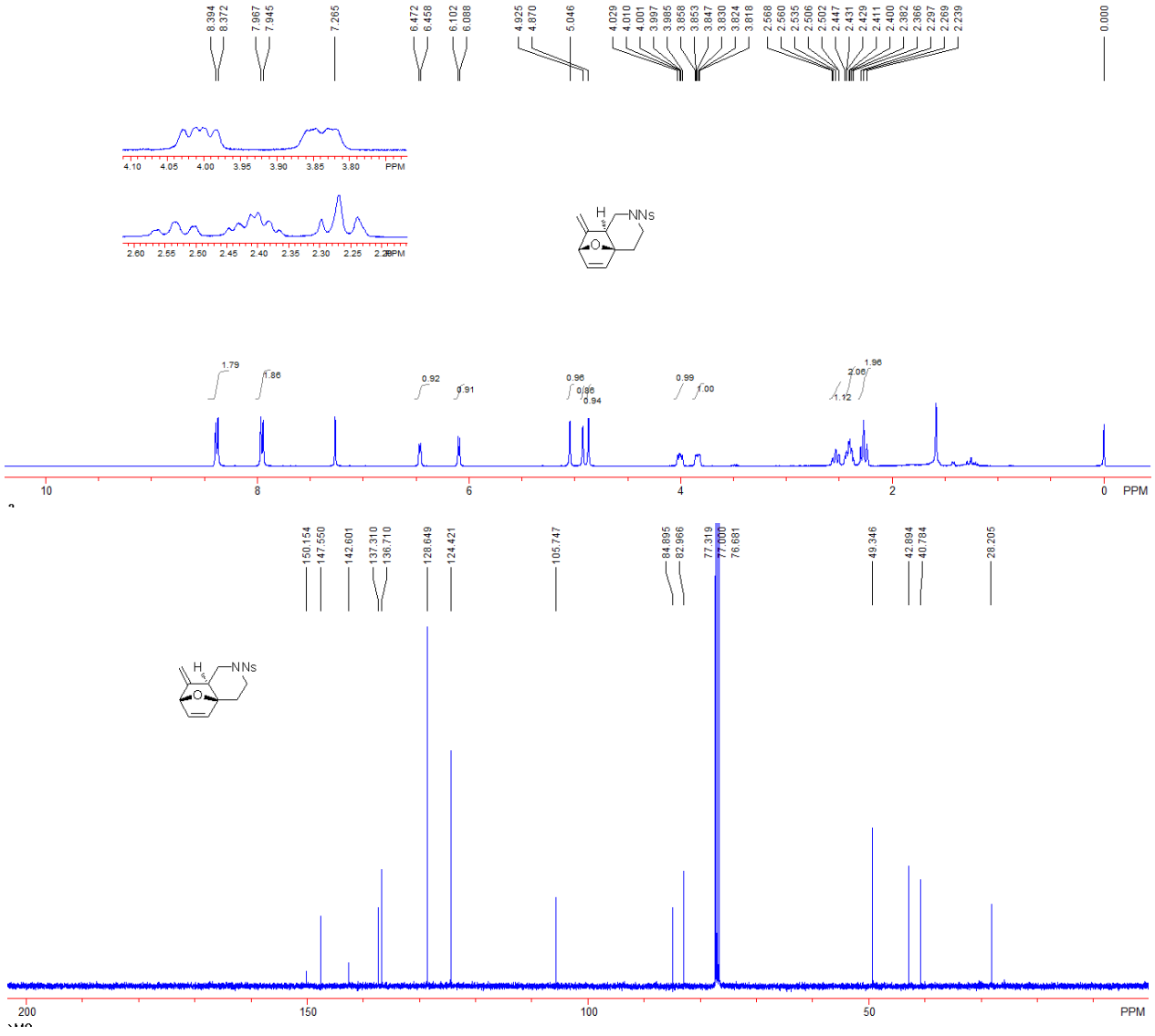
A white solid, 80% yield (61 mg). M.p.: 135-138 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.18 (dd, *J* = 11.2, 11.6 Hz, 1H, CH_2), 2.21-2.25 (m, 1H, CH_2), 2.34-2.43 (m, 2H, CH_2), 2.46 (td, *J* = 2.4, 13.2 Hz, 1H, CH_2), 3.76-3.80 (m, 1H, CH_2), 3.95 (ddd, *J* = 2.0, 7.6, 10.8 Hz, 1H, CH_2), 4.86 (s, 1H, =CH_2), 4.92 (s, 1H, =CH_2), 5.03 (s, 1H, CH), 6.09 (d, *J* = 5.6 Hz, 1H, =CH), 6.43 (dd, *J* = 1.6 Hz, 5.6 Hz, 1H, =CH), 7.62 (d, *J* = 8.8 Hz, 2H, ArH), 7.67 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.1, 40.8, 42.9, 49.4, 82.9, 85.0, 105.6, 127.9, 129.0, 132.4, 135.4, 136.6, 137.5, 147.7. IR (CH_2Cl_2) ν 2927, 2856, 1660, 1574, 1463, 1349, 1165, 1087, 955, 927, 772, 751, 728, 678 cm^{-1}. MS (EI) *m/z* (%): 42 (42.9), 81 (61.73), 134 (100), 162 (82.04), 221 (26.87), 302 (16.35), 381.0 (3.69) [M^+]; HRMS (EI) Calcd. for $C_{16}H_{16}NO_3SBr^{+1}$(M^+) requires 381.0034, Found: 381.0033.

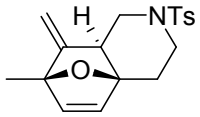




(4aS,7R,8aS)-8-methylene-2-((4-nitrophenyl)sulfonyl)-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 5c

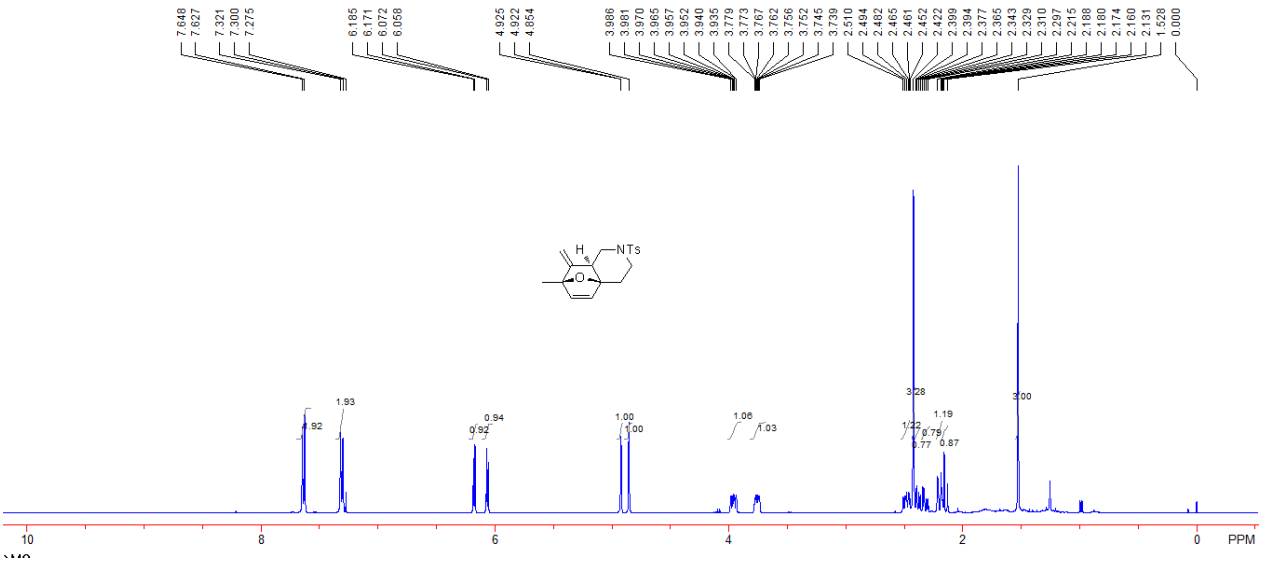
A pale yellow solid, 56% yield (39 mg). M.p.: 175-178 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.23-2.30 (m, 2H, CH_2), 2.36-2.45 (m, 2H, CH_2), 2.53 (td, J = 1.6, 12.4 Hz, 1H, CH_2), 3.81-3.86 (m, 1H, CH_2), 4.00 (ddd, J = 1.6, 6.4, 10.0 Hz, 1H, CH_2), 4.87 (s, 1H, =CH_2), 4.93 (s, 1H, =CH_2), 5.05 (s, 1H, CH), 6.09 (d, J = 5.6 Hz, 1H, =CH), 6.46 (d, J = 5.6 Hz, 1H, =CH), 7.95 (d, J = 8.8 Hz, 2H, ArH), 8.38 (d, J = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.2, 40.8, 42.9, 49.3, 83.0, 84.9, 105.7, 124.4, 128.6, 136.7, 137.3, 142.6, 147.6, 150.2. IR (CH_2Cl_2) ν 2926, 1674, 1575, 1471, 1347, 1166, 1069, 1010, 825, 742, 705 cm^{-1}. MS (EI) *m/z* (%): 81 (100), 134 (70.86), 162 (52.45), 215 (26.71), 267 (40.59), 348 (4.7) [M^+]; HRMS (EI) Calcd. for $C_{16}H_{16}N_2O_5S^{+1}(M^+)$ requires 348.0780, Found: 348.0778.

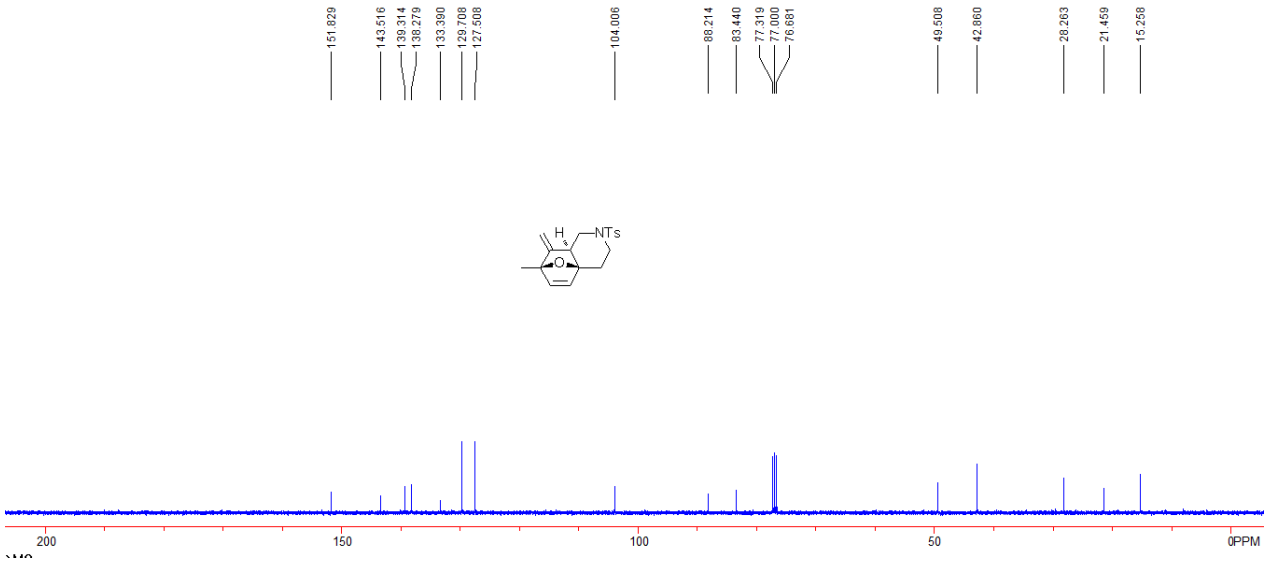


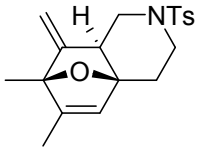


(4aS,7R,8aS)-7-methyl-8-methylene-2-tosyl-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 5d

A white solid, 83% yield (55 mg). M.p.: 145-148 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.53 (s, 3H, CH_3), 2.16 (dd, J = 11.2, 11.6 Hz, 1H, CH_2), 2.18 (dt, J = 2.4, 14.0 Hz, 1H, CH_2), 2.30 (td, J = 2.4, 14.0 Hz, 1H, CH_2), 2.42 (s, 3H, CH_3), 2.39-2.45 (m, 1H, CH_2), 2.48 (ddd, J = 2.8, 6.4, 9.2 Hz, 1H, CH_2), 3.76 (ddd, J = 2.0, 5.6, 8.0 Hz, 1H, CH_2), 3.97 (ddd, J = 2.0, 8.0, 11.2 Hz, 1H, CH_2), 4.85 (s, 1H, =CH_2), 4.92 (s, 1H, =CH_2), 6.06 (d, J = 5.6 Hz, 1H, =CH), 6.18 (d, J = 5.6 Hz, 1H, =CH), 7.31 (d, J = 8.0 Hz, 2H, ArH), 7.63 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 15.3, 21.5, 28.2, 42.8, 49.5, 83.4, 88.2, 104.0, 127.5, 129.7, 133.3, 138.3, 139.3, 143.5, 151.8. IR (CH_2Cl_2) ν 2930, 2857, 1667, 1463, 1341, 1165, 1120, 935, 709, 660 cm^{-1}. MS (ESI) *m/z* (%): 332.1 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{18}H_{22}NO_3S^{+1}$(M^++H) requires 332.1315 Found: 332.1317.

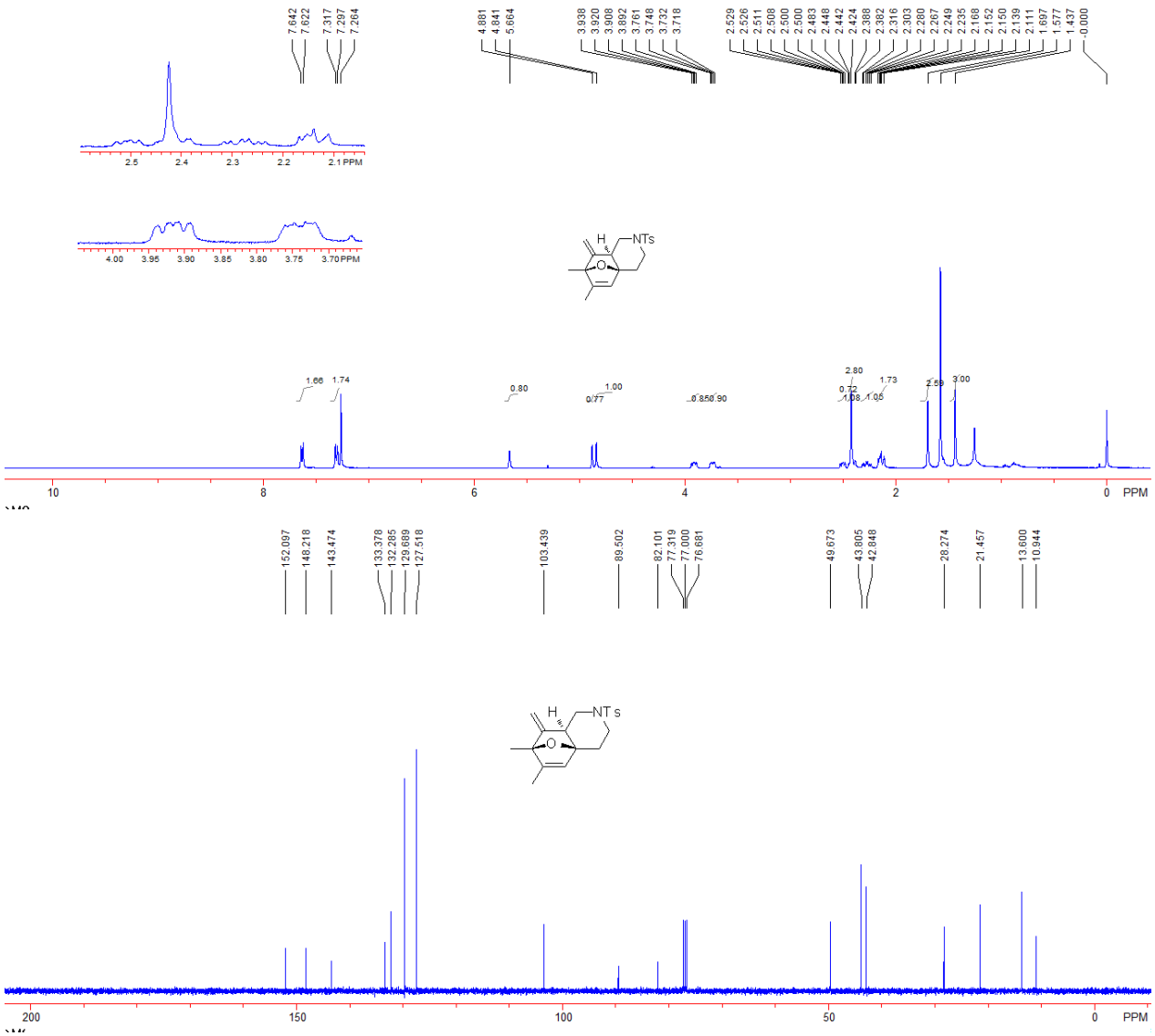


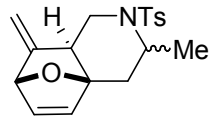




(4aS,7R,8aS)-6,7-dimethyl-8-methylene-2-tosyl-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 5e

A white solid, 87% yield (60 mg). M.p.: 112-115 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.44 (s, 3H, CH_3), 1.69 (s, 3H, CH_3), 2.11-2.18 (m, 2H, CH_2), 2.27 (td, *J* = 5.2, 13.2 Hz, 1H, CH_2), 2.38-2.46 (m, 1H, CH_2), 2.42 (s, 3H, CH_3), 2.50 (ddd, *J* = 2.0, 6.8, 10.8 Hz, 1H, CH_2), 3.71-3.77 (m, 1H, CH_2), 3.92 (ddd, *J* = 1.6, 7.6, 10.8 Hz, 1H, CH_2), 4.84 (s, 1H, =CH_2), 4.88 (s, 1H, =CH_2), 5.66 (s, 1H, =CH), 7.31 (d, *J* = 8.4 Hz, 2H, ArH), 7.63 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 10.9, 13.6, 21.5, 28.3, 42.8, 43.8, 49.7, 82.1, 89.5, 103.4, 127.5, 129.7, 132.3, 133.4, 143.5, 148.2, 152.1. IR (CH_2Cl_2) ν 2930, 2855, 1664, 1452, 1377, 1349, 1167, 1144, 1014, 919, 815, 744, 671 cm^{-1}. MS (ESI) *m/z* (%): 346.1 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{19}H_{24}NO_3S^{+1}$(M^++H) requires 346.1471, Found: 346.1475.

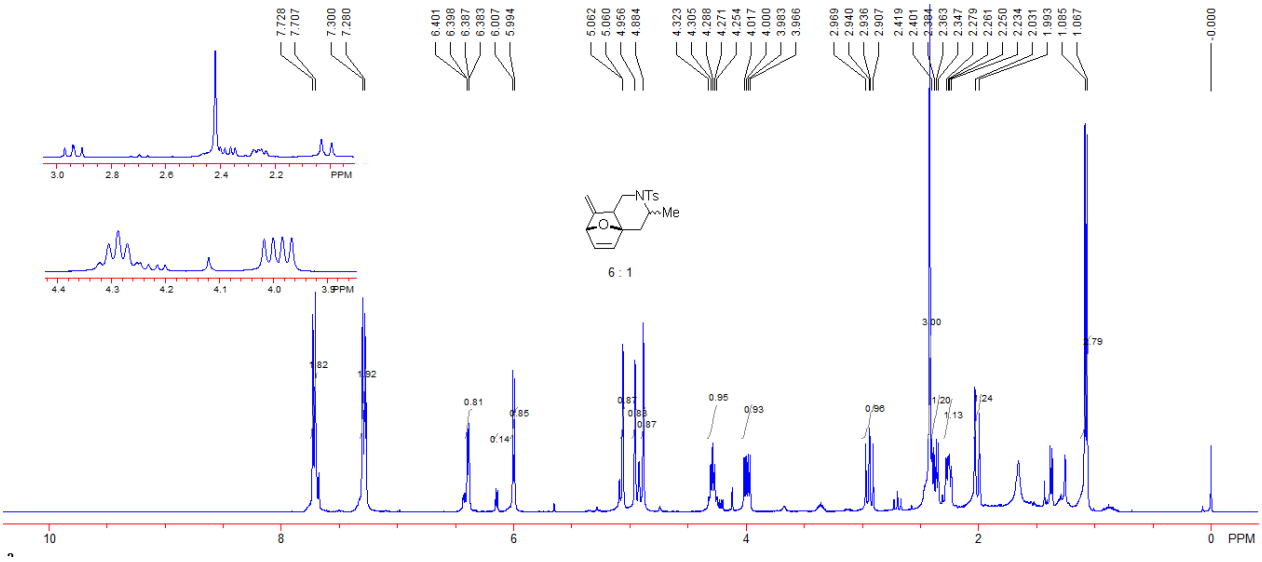


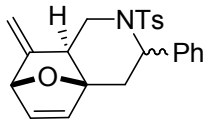


(4aS,7R,8aS)-3-methyl-8-methylene-2-tosyl-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 5f

A pale yellow solid, 61% yield (40 mg). M.p: 140-142 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) (showing as mixture of diastereomers in ~6:1 ratio) major diastereomer δ 1.07 (d, J = 7.2 Hz, 3H, CH_3), 2.02 (d, J = 15.2 Hz, 1H, CH_2), 2.25 (dd, J = 6.8 Hz, 11.6 Hz, 1H, CH), 2.37 (dd, J = 6.8 Hz, 15.2 Hz, 1H, CH_2), 2.42 (s, 3H, CH_3), 2.94 (dd, J = 11.6 Hz, 13.6 Hz, 1H, CH_2), 3.99 (dd, J = 6.8 Hz, 13.6 Hz, 1H, CH_2), 4.29 (qd, J = 7.2, 7.2 Hz, 1H, CH), 4.88 (s, 1H, =CH_2), 4.96 (s, 1H, =CH_2), 5.06 (d, J = 1.2 Hz, 1H, CH), 6.00 (d, J = 5.6 Hz, 1H, =CH), 6.39 (dd, J = 1.2 Hz, 5.6Hz, 1H, =CH), 7.29 (d, J = 8.0 Hz, 2H, ArH), 7.71 (d, J = 8.0 Hz, 2H, ArH). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) minor diastereomer δ 1.37 (d, J = 7.2 Hz, 3H,

CH_3), 2.02 (d, J = 15.2 Hz, 1H, CH_2), 2.45 (dd, J = 6.0 Hz, 15.2 Hz, 1H, CH_2), 2.70 (dd, J = 11.6, 13.4 Hz, 1H, CH_2), 4.22 (dd, J = 6.0, 12.4 Hz, 1H, CH_2), 4.92 (s, 2H, =CH_2), 5.09 (d, J = 1.6 Hz, 1H, CH), 6.15 (d, J = 5.6 Hz, 1H, =CH), 6.42 (dd, J = 1.6, 5.6 Hz, 1H, =CH), 7.29 (d, J = 8.0 Hz, 2H, ArH), 7.71 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) not recorded for mixture. IR (CH_2Cl_2) ν 2924, 1670, 1451, 1368, 1338, 1153, 1086, 960, 920, 762, 728, 657 cm^{-1}. MS (ESI) *m/z* (%): 332.1 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{18}H_{22}NO_3S^{+1}$(M^++H) requires 332.1315, Found: 332.1314.

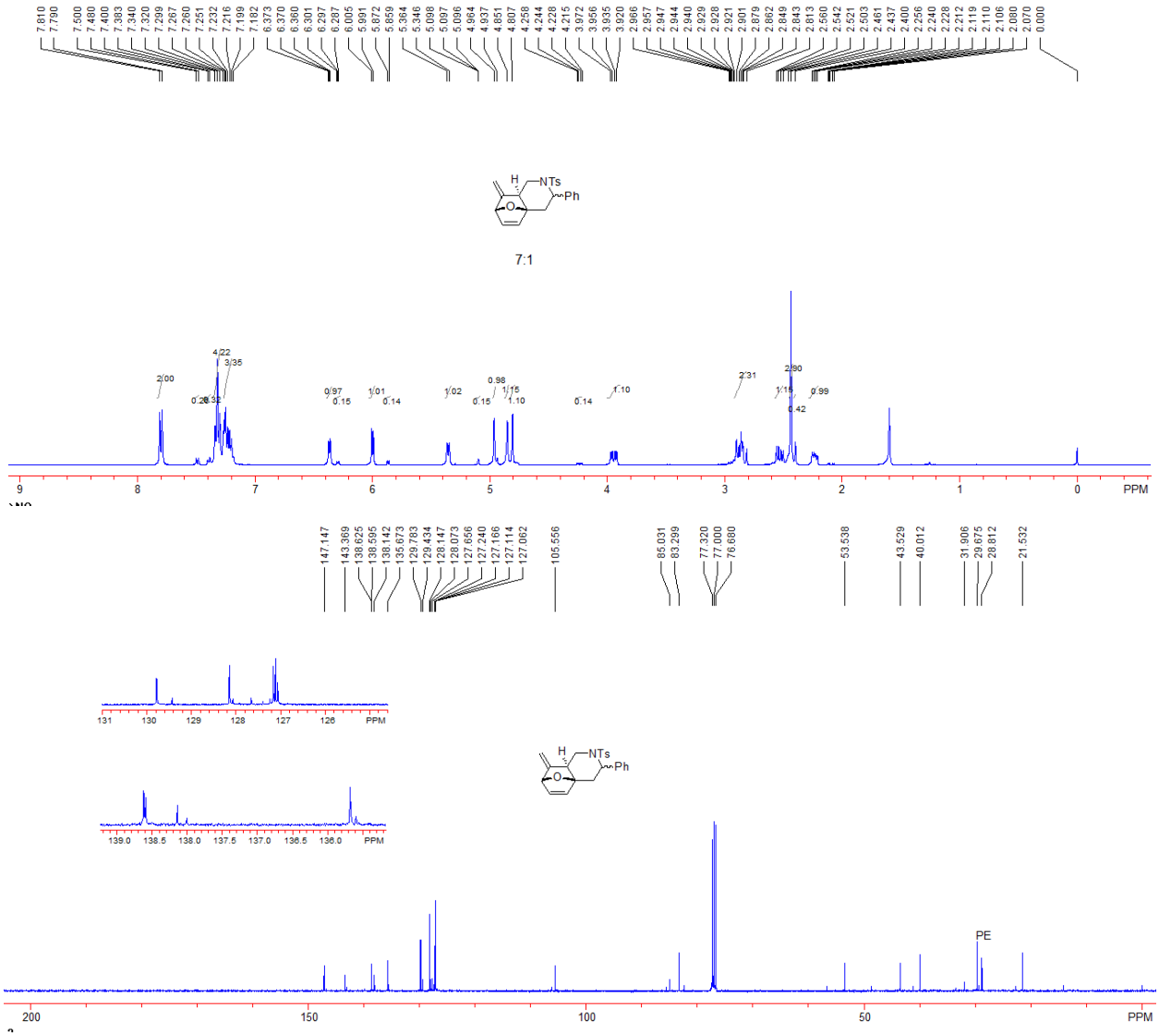


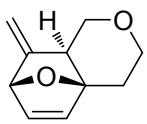


(4aS,7R,8aS)-8-methylene-3-phenyl-2-tosyl-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 5g

A pale yellow solid, 71% yield (56 mg). M.p.: 173-176 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) (showing as mixture of diastereomers in ~7:1 ratio) major diastereomer δ 2.22 (dd, J = 6.4, 11.2 Hz, 1H, CH_2), 2.46 (s, 3H, CH_3), 2.53 (dd, J = 7.2, 15.6 Hz, 1H, CH_2), 2.81-2.91 (m, 2H, CH_2), 3.94 (dd, J = 6.4, 14.4 Hz, 1H, CH_2), 4.81 (s, 1H, CH), 4.85 (s, 1H, =CH_2), 4.96 (s, 1H, =CH_2), 5.35 (d, J = 7.2 Hz, 1H, CH), 6.00 (d, J = 5.6 Hz, 1H, =CH), 6.37 (d, J = 5.6 Hz, 1H, =CH), 7.19-7.30 (m, 3H, ArH), 7.32-7.39 (m, 4H, ArH), 7.80 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.5, 32.0, 40.0, 43.5, 53.5, 83.3, 85.3, 105.6, 127.06, 127.11, 127.17, 128.1, 129.8, 135.7, 138.1, 138.59, 138.63, 143.4, 147.1. Minor diastereomer: ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) select resonances: δ 2.09 (dd, J = 4.0, 16.0 Hz, 1H, CH_2), 2.38 (s, 3H, CH_3), 2.92-2.97 (m, 2H, CH_2), 4.23 (dd, J = 5.2, 12.0 Hz, 1H, CH_2), 4.85 (s, 1H, =CH_2), 4.94 (s, 1H, =CH_2), 5.10 (s, 1H, CH), 5.86 (d, J = 5.6 Hz, 1H, =CH), 6.29 (dd, J = 1.6, 5.6 Hz, 1H, =CH), 7.39 (d, J = 8.0

Hz, 2H, ArH), 7.49 (d, J = 8.0 Hz, 2H, ArH). IR (CH_2Cl_2) ν 2927, 1671, 1598, 1448, 1368, 1340, 1158, 1116, 854, 768, 743, 707, 694, 663 cm^{-1}. MS (ESI) *m/z* (%): 394.1 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{23}H_{24}NO_3S^{+1}$(M^++H) requires 394.1471, Found: 394.1472.

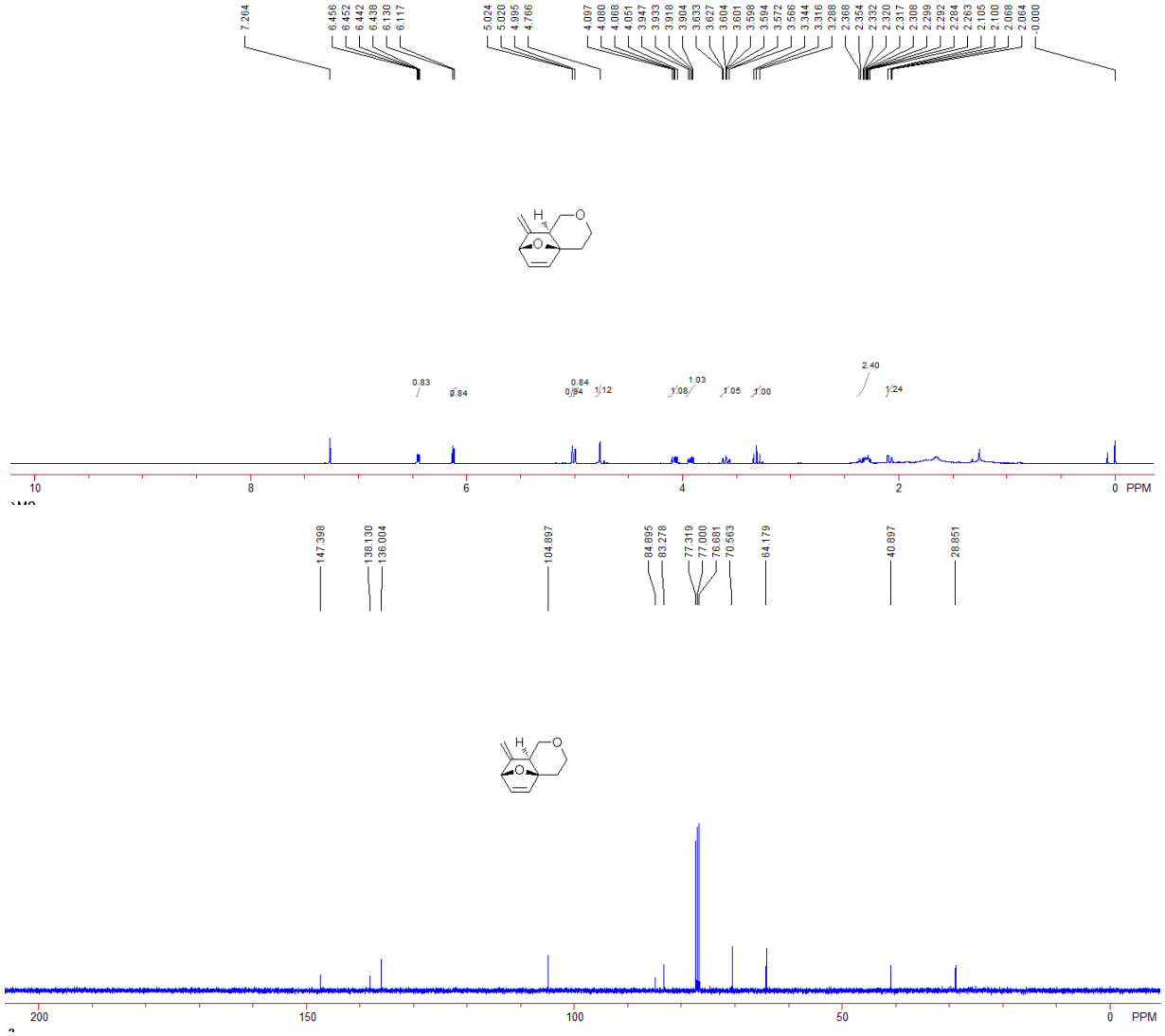


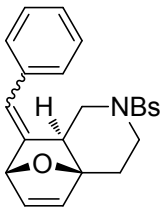


(4aS,7R,8aS)-8-methylene-1,3,4,7,8,8a-hexahydro-4a,7-epoxyisochromene 5h

A Yellow liquid, 9% yield (8 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.08 (dd, J = 2.0, 14.4 Hz, 1H, CH_2), 2.26-2.37 (m, 2H, CH_2), 3.32 (dd, J = 11.2, 11.2 Hz, 1H, CH_2), 3.60 (td, 1H, J = 2.0, 11.2 Hz, 1H, CH_2), 3.92 (dd, J = 1.6, 11.6 Hz, 1H, CH_2), 4.07 (dd, J = 6.8, 11.6 Hz, 1H, CH_2), 4.77 (s, 1H, =CH_2), 5.00 (s, 1H, =CH_2), 5.02 (d, J = 1.6 Hz, 1H, CH), 6.12 (d, J = 5.6 Hz, 1H, =CH), 6.45 (dd, J = 1.6, 5.6 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.9, 40.9, 64.2, 70.6, 83.3, 84.9, 104.9, 136.0, 138.1, 147.4. IR (CH_2Cl_2) ν 2927, 2856, 1710, 1668, 1449,

1376, 1263, 1084, 1011, 971, 943, 927, 889, 817, 769, 702, 678 cm^{-1}. MS (EI) *m/z* (%):81 (100), 91 (66), 92 (58), 105 (43), 134 (41), 149 (27), 164 (9) [M^+]; HRMS (EI) Calcd. for $C_{10}H_{12}O_2^{+1}(M+H)^+$ requires 164.0837, Found: 164.0838.

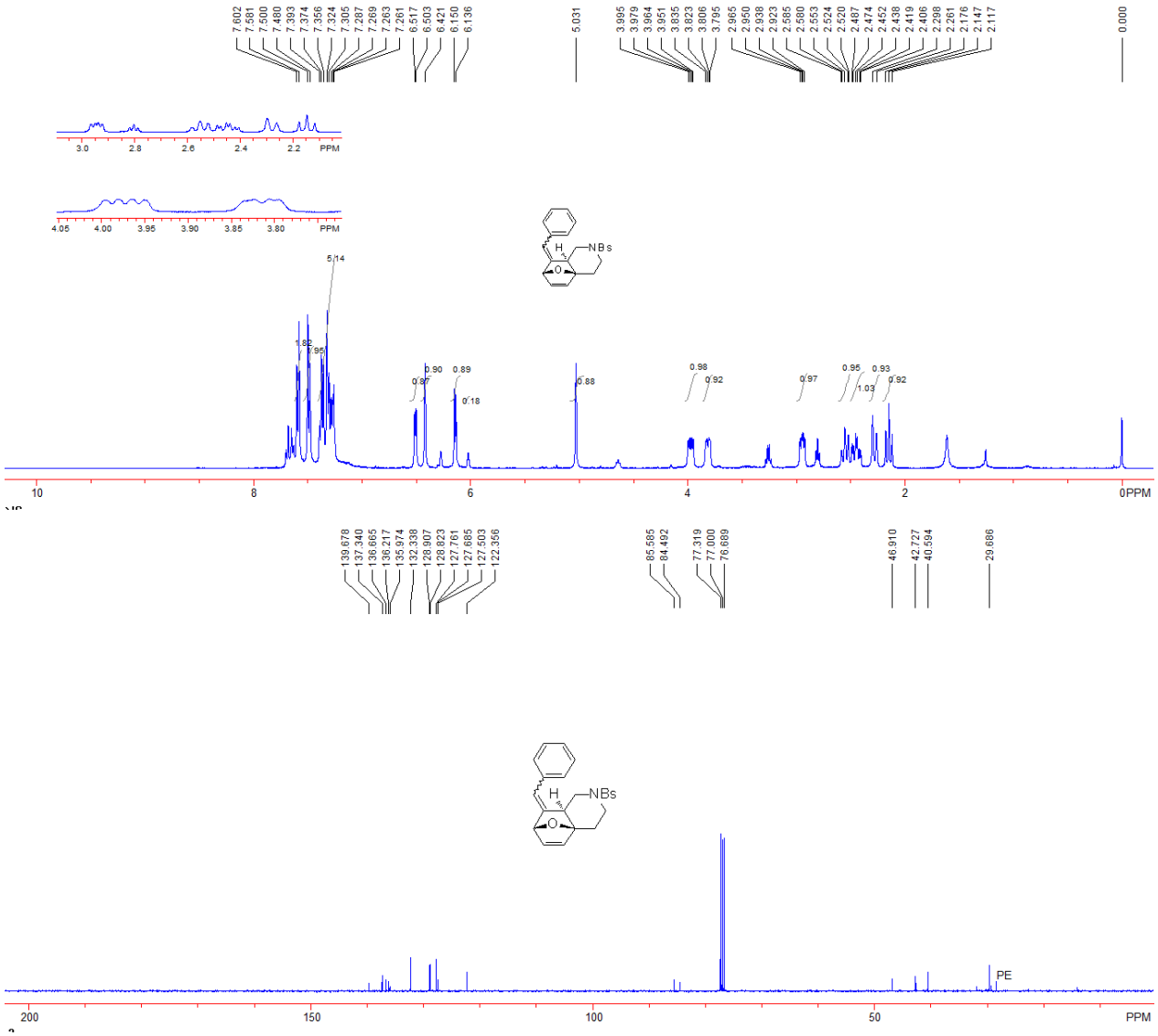


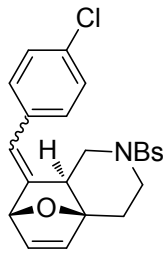


(4aS,7R,8aS)-8-benzylidene-2-((4-bromophenyl)sulfonyl)-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 7a

A white solid, 55% yield (50 mg). M.p.: 122-125 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.15 (dd, *J* = 11.6, 12.0 Hz, 1H, CH_2), 2.44 (dt, *J* = 5.6, 12.8 Hz, 1H, CH_2), 2.56 (td, *J* = 2.8, 12.8 Hz, 1H, CH_2), 2.56 (td, *J* = 2.8, 12.8, Hz, 1H, CH_2), 2.94 (ddd, *J* = 1.6, 6.4, 10.0 Hz, 1H, CH_2), 3.79-3.84 (m, 1H, CH_2), 3.97 (ddd, *J* = 2.0, 6.8, 11.2 Hz, 1H, CH_2), 5.03 (d, *J* = 1.6 Hz, 1H, CH), 6.14

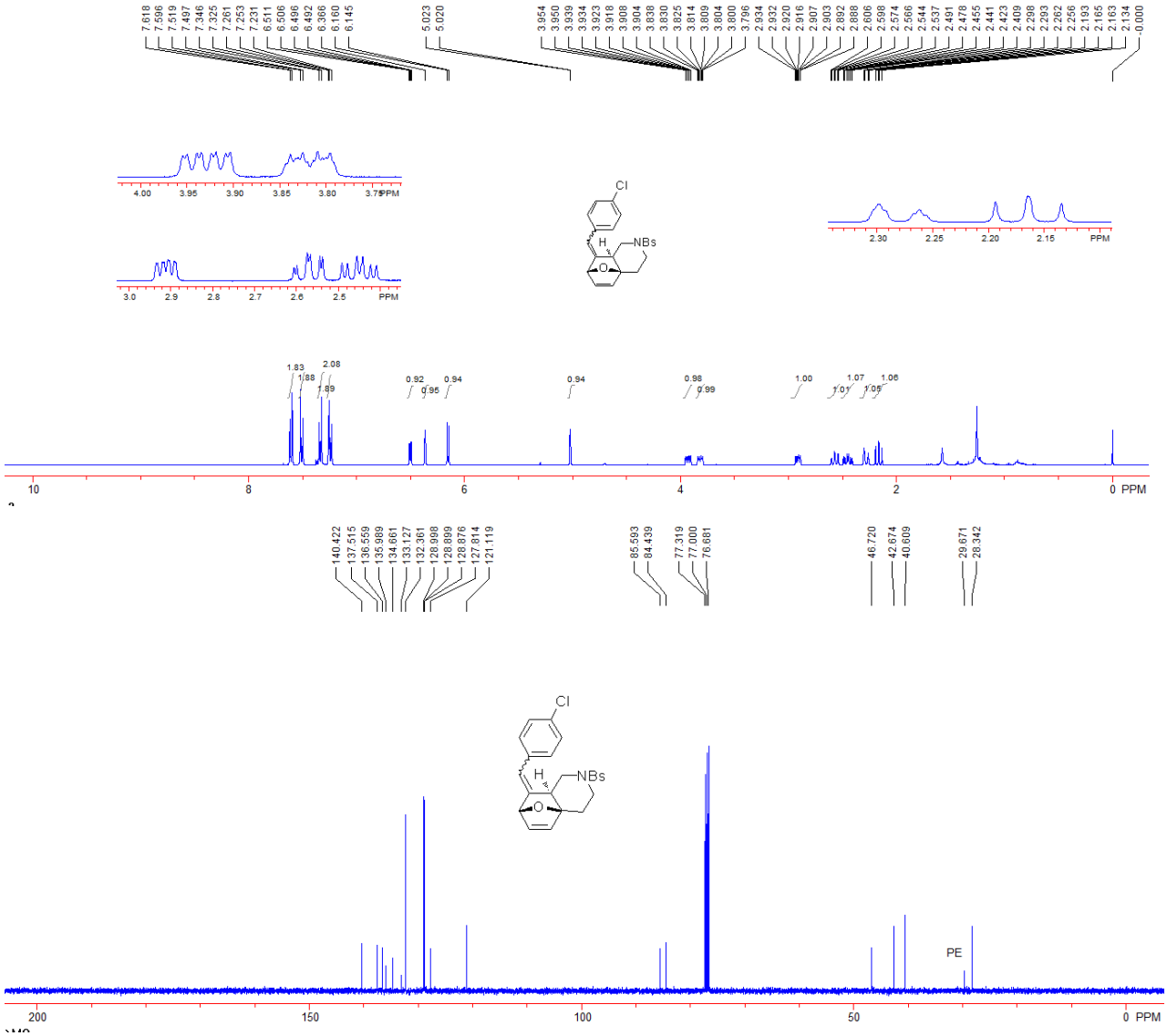
(d, J = 5.6 Hz, 1H, =CH), 6.42 (s, 1H, =CH), 6.51 (dd, J = 1.6, 5.6 Hz, 1H, =CH), 7.27-7.40 (m, 5H, ArH), 7.49 (d, J = 8.8 Hz, 2H, ArH), 7.59 (d, J = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 29.7, 40.6, 42.7, 46.9, 84.5, 85.6, 122.4, 127.5, 127.7, 127.8, 128.8, 128.9, 132.3, 136.0, 136.2, 136.7, 137.3, 139.7. IR (CH_2Cl_2) ν 2923, 2853, 1574, 1352, 1166, 1068, 771, 750, 718, 696 cm^{-1}. MS (ESI) *m/z* (%): 458.0 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{22}H_{21}NO_3BrS^{+1}$(M^++H) requires 458.0420, Found: 458.0413. (*note: by-product: 10%. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.80, 3.25, 4.63, 6.02, 6.28, 7.64, 7.69 ppm*).





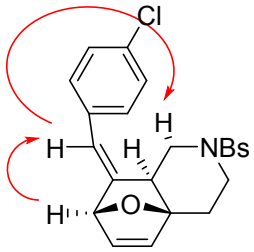
(4aS,7R,8aS)-2-((4-bromophenyl)sulfonyl)-8-(4-chlorobenzylidene)-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 7b

A white solid, 47% yield (46 mg). M.p.: 216-218 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.16 (dd, *J* = 11.6, 12.4 Hz, 1H, CH_2), 2.28 (dt, *J* = 2.4, 14.8 Hz, 1H, CH_2), 2.45 (td, *J* = 5.6, 12.8 Hz, 1H, CH_2), 2.57 (td, *J* = 2.8, 12.0 Hz, 1H, CH_2), 2.91 (ddd, *J* = 1.6, 6.8, 10.4 Hz, 1H, CH_2), 3.79-3.85 (m, 1H, CH_2), 3.93 (ddd, *J* = 1.6, 6.8, 11.2 Hz, 1H, CH_2), 5.02 (d, *J* = 1.2 Hz, 1H, CH), 6.15 (d, *J* = 6.0 Hz, 1H, =CH), 6.37 (s, 1H, =CH), 6.50 (dd, *J* = 1.6, 6.0 Hz, 1H, =CH), 7.24 (d, *J* = 8.8 Hz, 2H, ArH), 7.33 (d, *J* = 8.8 Hz, 2H, ArH), 7.51 (d, *J* = 8.8 Hz, 2H, ArH), 7.61 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.3, 40.6, 42.7, 46.7, 84.4, 85.6, 121.1, 127.8, 128.88, 128.90, 129.0, 132.4, 133.1, 134.7, 136.0, 136.6, 137.5, 140.4. IR (CH_2Cl_2) ν 3088, 2923, 2853, 1574, 1491, 1349, 1166, 1053, 1037, 884, 771, 754, 723, 704 cm^{-1}. MS (MALDI) *m/z* (%): 492.0 (100) [M^++H]; HRMS (MALDI) Calcd. for $C_{22}H_{20}O_3NBrClS^{+1}$($M^+$+H) requires 492.0030, Found: 492.0028.

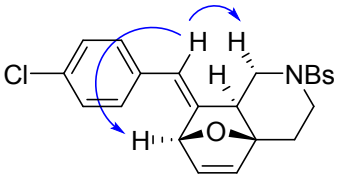


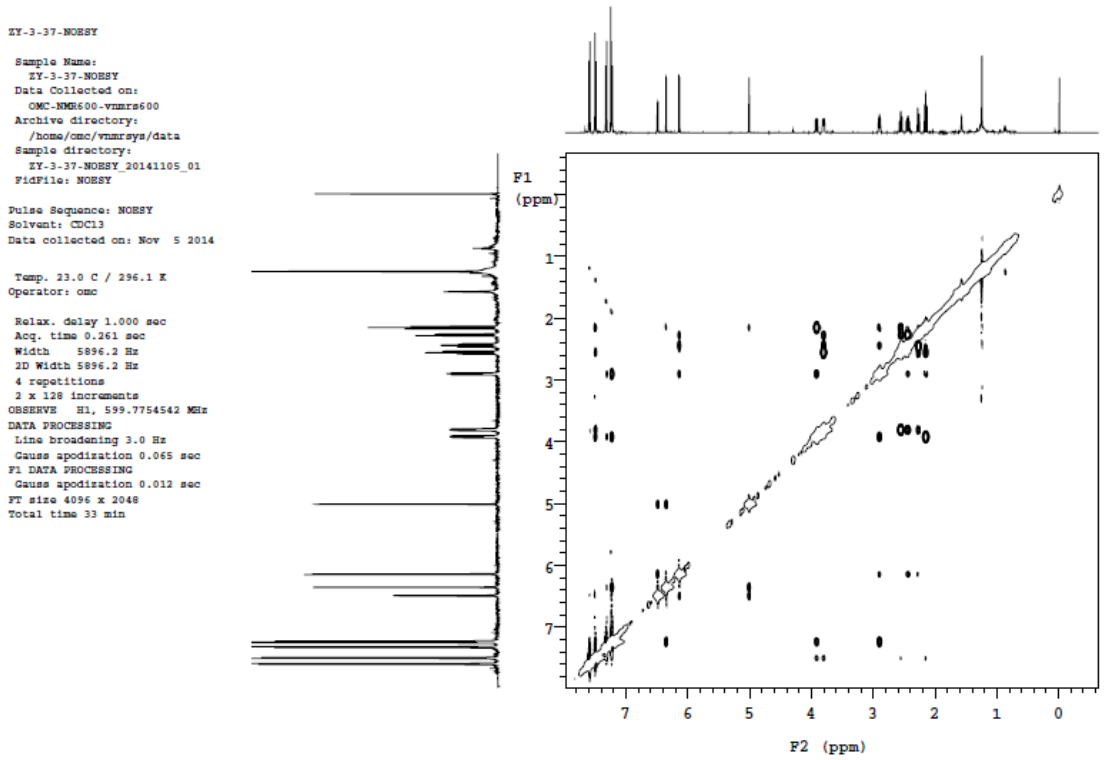
NOE of **7b** (600 MHz, $CDCl_3$)

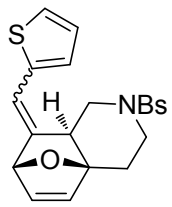
major



minor



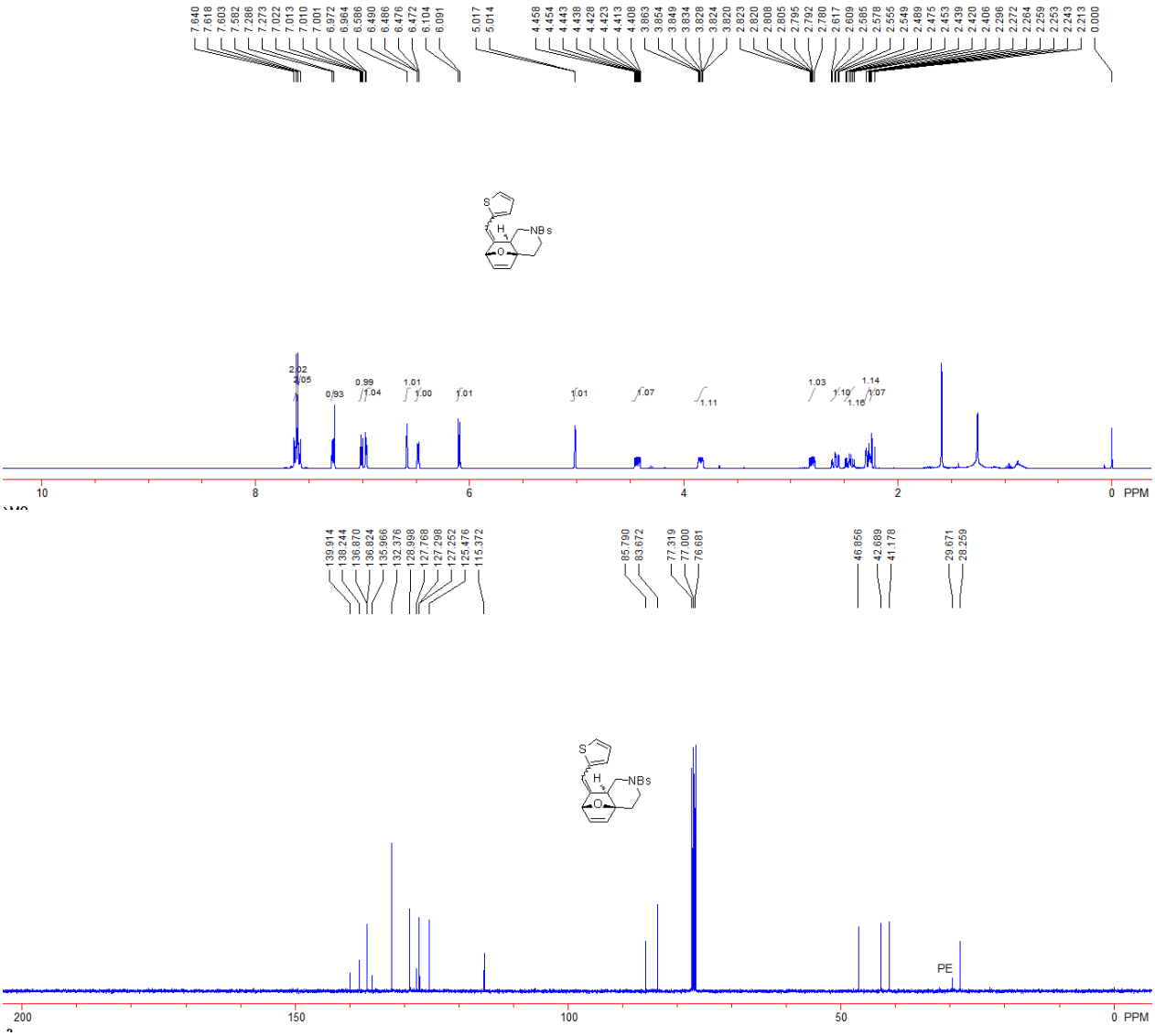


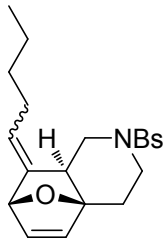


(4aS,7R,8aS)-2-((4-bromophenyl)sulfonyl)-8-(thiophen-2-ylmethylene)-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 7c

A white solid, 32% yield (30 mg). M.p.: 217-219 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.24 (dd, J = 11.6, 12.0 Hz, 1H, CH_2), 2.28 (dt, J = 2.0, 14.8 Hz, 1H, CH_2), 2.44 (td, J = 5.6, 13.2 Hz,

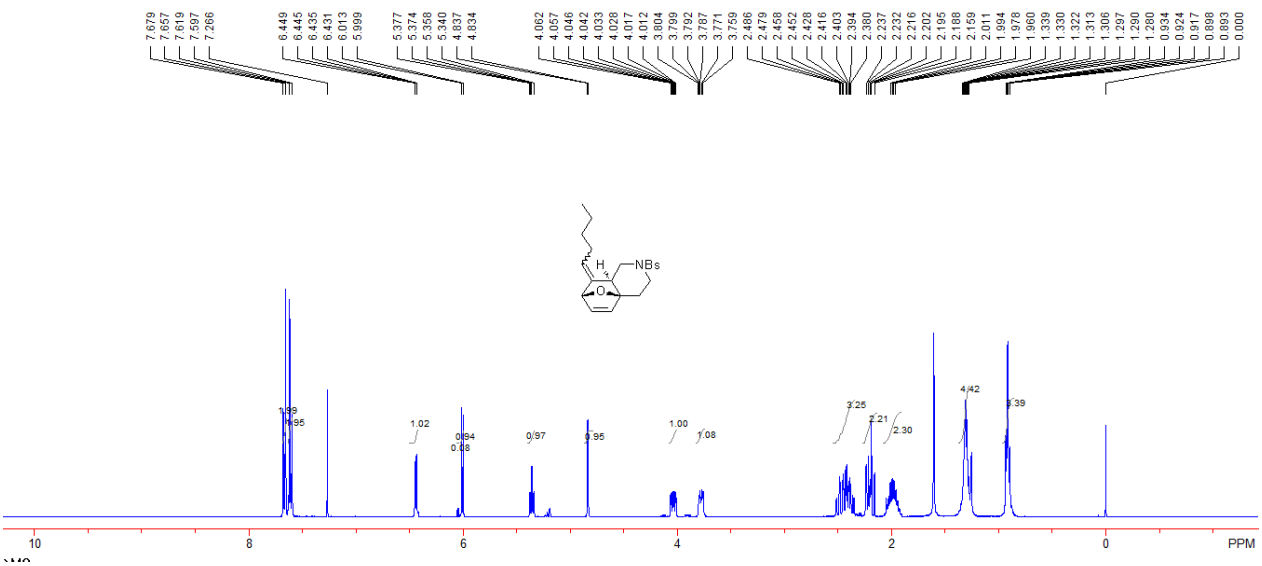
1H, CH_2), 2.58 (td, *J* = 2.8, 12.0 Hz, 1H, CH_2), 3.80 (ddd, *J* = 1.2, 6.8, 10.8 Hz, 1H, CH_2), 3.82-3.87 (m, 1H, CH_2), 4.43 (ddd, *J* = 2.0, 6.8, 10.8 Hz, 1H, CH_2), 5.01 (d, *J* = 1.2 Hz, 1H, CH), 6.10 (d, *J* = 5.2 Hz, 1H, =CH), 6.48 (dd, *J* = 2.0, 5.6 Hz, 1H, =CH), 6.59 (s, 1H, =CH), 6.96 (d, *J* = 3.2 Hz, 1H, ArH), 7.01 (dd, *J* = 1.2, 3.6 Hz, 1H, ArH), 7.28 (d, *J* = 5.2 Hz, 1H, ArH), 7.59 (d, *J* = 8.8 Hz, 2H, ArH), 7.63 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.3, 41.2, 42.7, 46.9, 83.7, 85.8, 115.4, 125.5, 127.25, 127.30, 127.8, 129.0, 132.4, 136.0, 136.8, 136.9, 138.2, 140.0. IR (CH_2Cl_2) ν 2925, 2856, 1574, 1643, 1353, 1167, 1008, 941, 776, 852, 719, 703 cm^{-1}. MS (MALDI) m/z (%): 485.9 (100) $[M+Na]^{+1}$; HRMS (MALDI) Calcd. for $C_{20}H_{18}NO_3BrNaS_2^{+1}[M+Na]^{+1}$ requires 485.9804, Found: 485.9806.

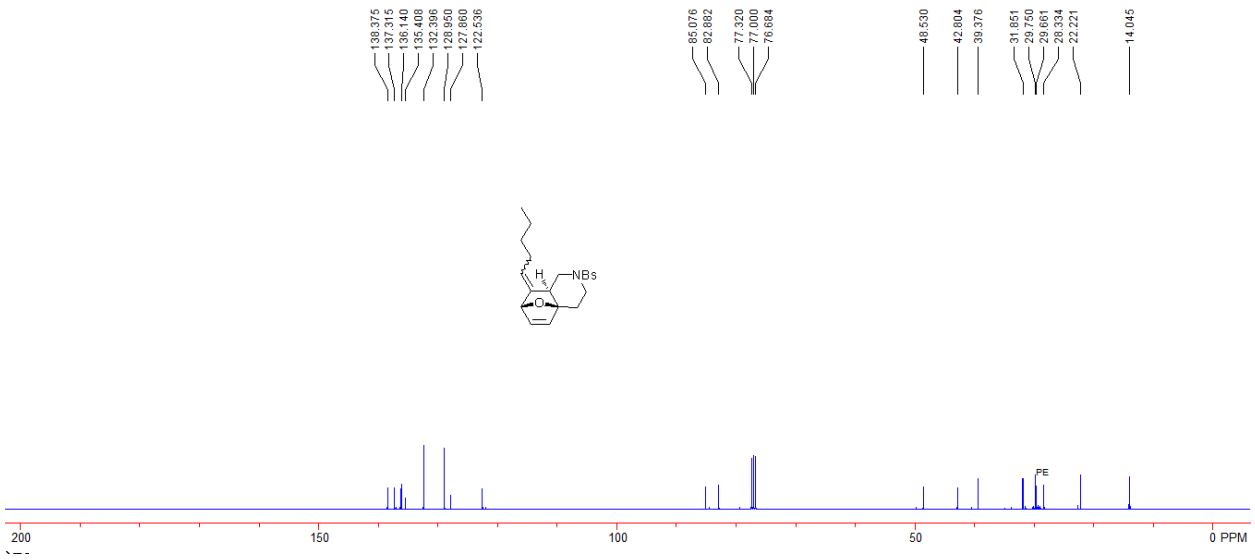




(4aS,7R,8aS)-2-((4-bromophenyl)sulfonyl)-8-pentylidene-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 7d

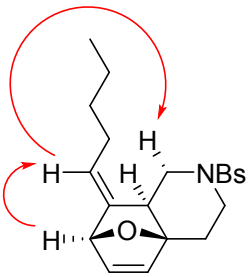
A white solid, 37% yield (32 mg). M.p.: 129-131 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.89-0.94 (m, 3H, CH_3), 1.28-1.34 (m, 4H, CH_2), 1.92-2.05 (m, 2H, CH_2), 2.15-2.24 (m, 2H, CH_2), 2.34-2.52 (m, 3H, CH_2), 3.75-3.79 (m, 1H, CH_2), 4.03 (ddd, J = 2.0, 6.8, 10.4 Hz, 1H, CH_2), 4.83 (d, J = 1.2 Hz, 1H, CH), 5.37 (t, J = 7.2 Hz, 1H, =CH), 6.01 (d, J = 5.6 Hz, 1H, =CH), 6.44 (dd, J = 1.6, 5.6 Hz, 1H, =CH), 7.61 (d, J = 8.8 Hz, 2H, ArH), 7.66 (d, J = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 22.2, 28.3, 29.7, 31.9, 39.4, 42.8, 48.5, 82.9, 85.1, 122.5, 127.9, 129.0, 132.4, 135.4, 136.1, 137.3, 138.4. IR (CH_2Cl_2) ν 2926, 2857, 1575.1352, 1166, 1088, 913, 750, 703 cm^{-1}. MS (MALDI) m/z (%): 438.0 (100) $[M+H]^{+1}$; HRMS (MALDI) Calcd. for $C_{20}H_{25}O_3NBrS^{+1}$(M+H) $^{+1}$requires 438.0733, Found: 438.0739.



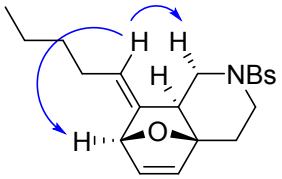


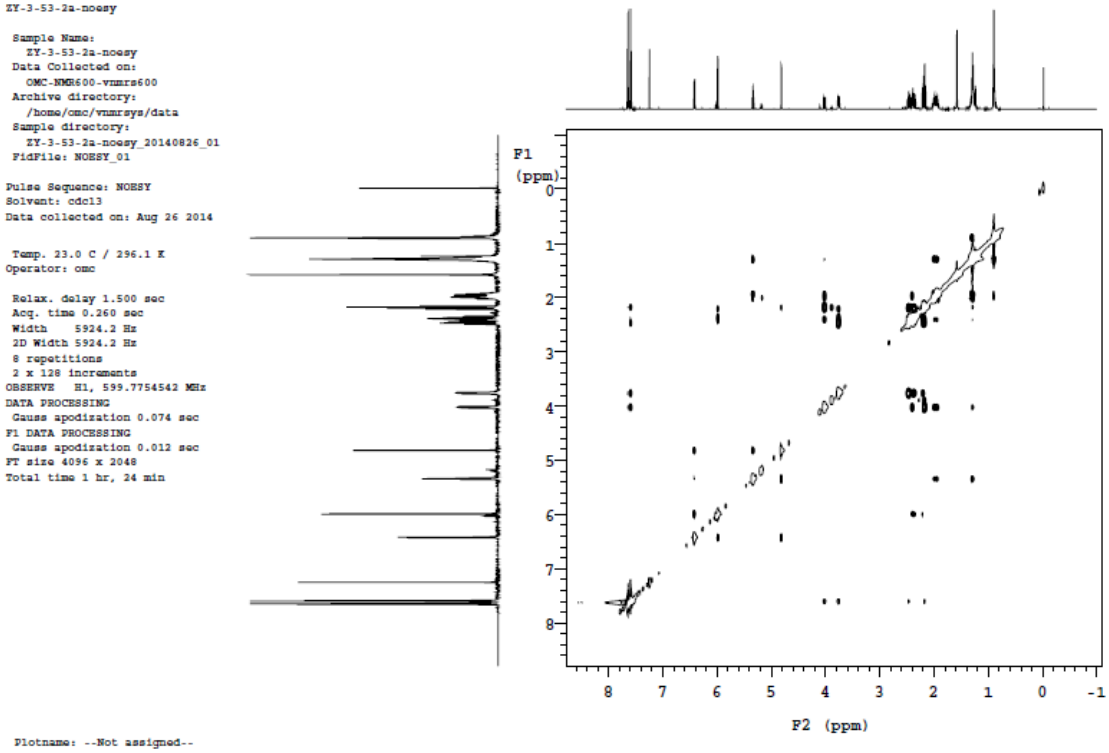
NOE of **7d** (600 MHz, $CDCl_3$)

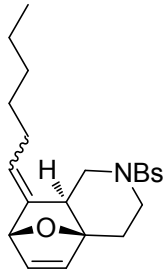
major



minor

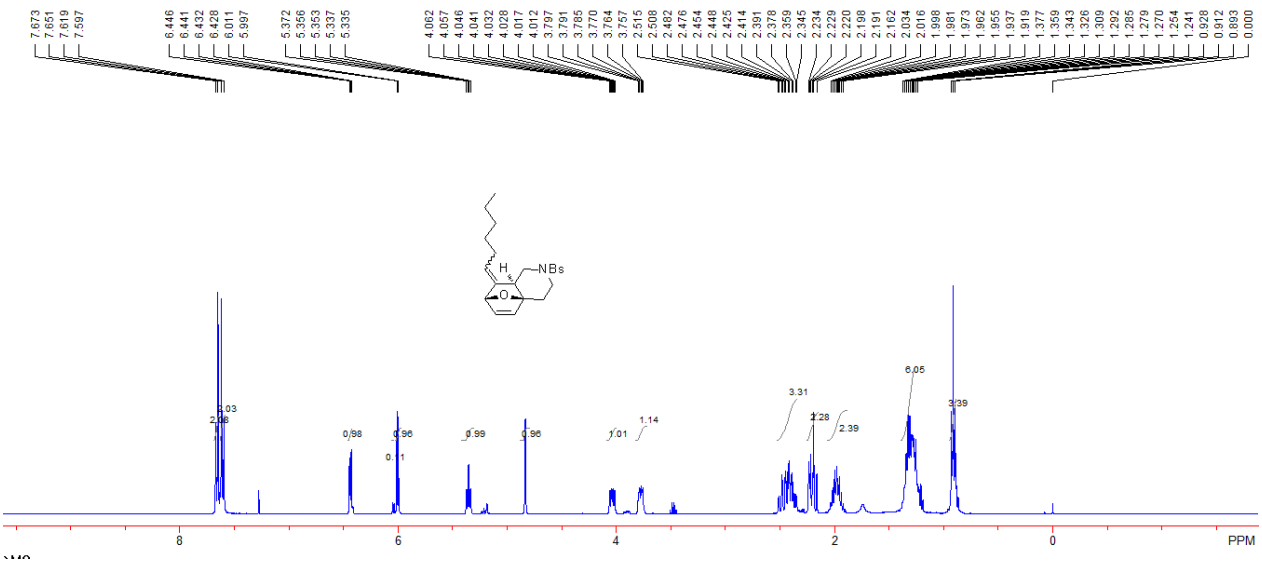


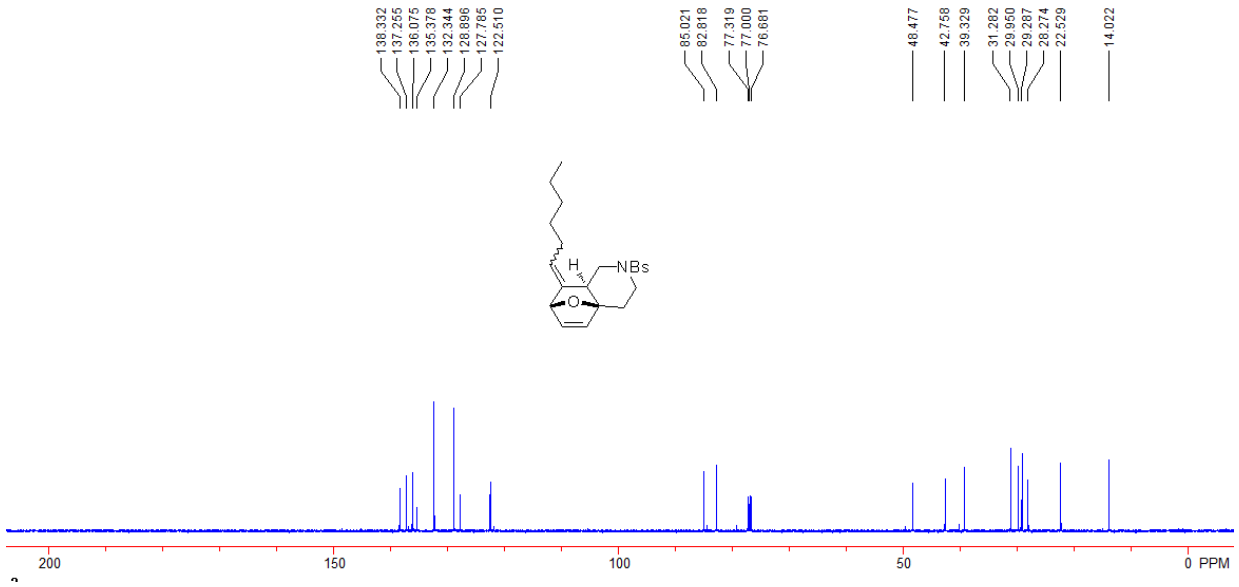


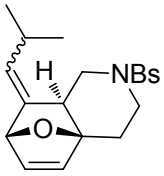


(4aS,7R,8aS)-2-((4-bromophenyl)sulfonyl)-8-hexylidene-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 7e

A white solid, 43% yield (39 mg). M.p.: 139-141 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.91 (t, *J* = 6.4 Hz, 3H, CH_3), 1.25-1.38 (m, 6H, CH_2), 1.91-2.03 (m, 2H, CH_2), 2.16-2.24 (m, 2H, CH_2), 2.34-2.52 (m, 3H, CH_2), 3.75-3.80 (m, 1H, CH_2), 4.03 (ddd, *J* = 2.0, 6.4, 10.4 Hz, 1H, CH_2), 4.83 (s, 1H, CH), 5.36 (td, *J* = 0.8, 7.2 Hz, 1H, =CH), 6.00 (d, *J* = 5.6 Hz, 1H, =CH), 6.44 (dd, *J* = 2.0, 5.6 Hz, 1H, =CH), 7.60 (d, *J* = 8.8 Hz, 2H, ArH), 7.66 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 22.5, 28.3, 29.3, 30.0, 31.3, 39.3, 42.8, 48.5, 82.8, 85.0, 122.5, 127.8, 128.9, 132.3, 135.4, 136.1, 137.3, 138.3. IR (CH_2Cl_2) ν 2960, 2925, 2856, 1575, 1352, 1166, 1008, 914, 751, 705 cm^{-1}. MS (MALDI) m/z (%): 474.0 (100) $[M+Na]^{+1}$; HRMS (MALDI) Calcd. for $C_{21}H_{26}NO_3BrNaS^{+1}[M+Na]^{+1}$ requires 474.0709, Found: 474.0709.

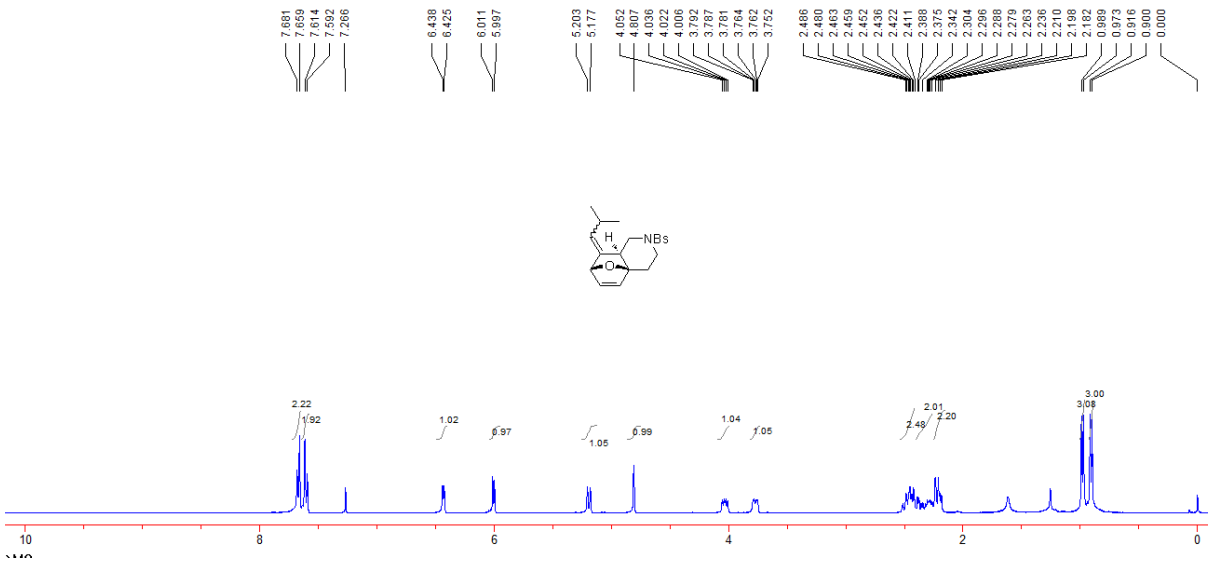






(4aS,7R,8aS)-2-((4-bromophenyl)sulfonyl)-8-(2-methylpropylidene)-2,3,4,7,8,8a-hexahydro-1H-4a,7-epoxyisoquinoline 7f

A white solid, 33% yield (28 mg). M.p.: 175-178 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.91 (d, J = 6.4 Hz, 3H, CH_3), 0.98 (d, J = 6.4 Hz, 3H, CH_3), 2.18-2.24 (m, 2H, CH_2), 2.26-2.39 (m, 2H, CH_2), 2.41-2.52 (m, 2H, CH_2), 3.75-3.80 (m, 1H, CH_2), 4.03 (ddd, J = 2.0, 6.4, 12.0 Hz, 1H, CH_2), 4.81 (s, 1H, CH), 5.18 (d, J = 10.4 Hz, 1H, =CH), 6.00 (d, J = 5.6 Hz, 1H, =CH), 6.43 (d, J = 5.6 Hz, 1H, =CH), 7.60 (d, J = 8.8 Hz, 2H, ArH), 7.67 (d, J = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 22.8, 23.4, 28.4, 29.9, 39.5, 42.8, 48.9, 82.9, 85.1, 127.9, 128.9, 129.8, 132.4, 135.4, 135.8, 136.2, 137.3. IR (CH_2Cl_2) ν 2955, 2926, 2859, 1728, 1575, 1352, 1166, 1041, 914, 752, 724, 705 cm^{-1}. MS (MALDI) m/z (%): 446.0 (100) $[M+Na]^{+1}$; HRMS (MALDI) Calcd. for $C_{19}H_{22}NO_3BrNaS^{+1}[M+Na]^{+1}$ requires 446.0396, Found: 446.0396.


7.681
7.659
7.614
7.592
7.266
6.438
6.425
6.011
5.997
5.203
5.177
4.052
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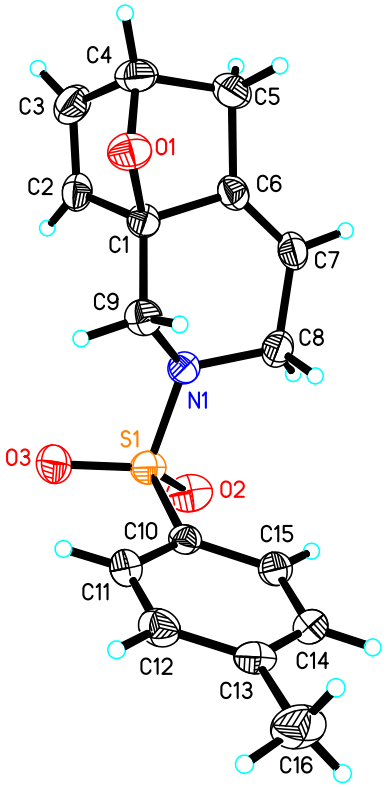
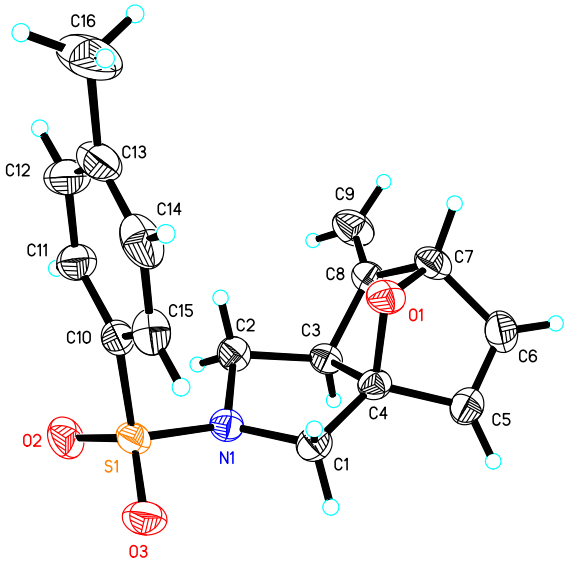
4.036
4.022
4.006
3.792
3.787
3.781
3.764
3.762
3.752
2.486
2.480
2.463
2.459
2.452
2.436
2.422
2.411
2.388
2.375
2.342
2.304
2.296
2.288
2.279
2.263
2.236
2.210
2.198
2.162
0.989
0.973
0.916
0.900
0.000
NBs
2.22
1.92
1.02
0.97
1.05
0.99
1.04
1.05
2.48
2.01
2.20
3.00
3.08
10
8
6
4
2
0
PPM
137.335
136.220
135.795
135.438
132.431
129.780
128.915
127.888
85.101
82.901
77.319
77.000
76.685
48.852
42.818
39.523
29.905
28.373
23.435
22.832
NBs
200
150
100
50
0
PPM

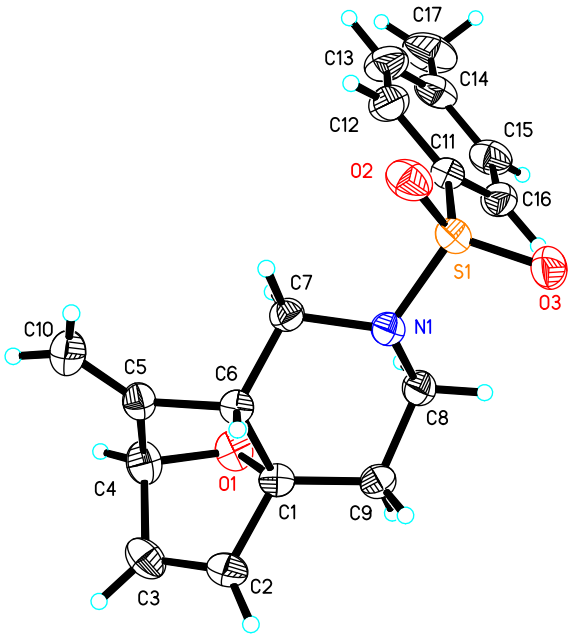
7. X-ray crystallographic information of product 2a, 3a and 5a



The crystal data of **2a** have been deposited in CCDC with number 999306. Empirical formula: $C_{16}H_{17}NO_3S$, Formula weight: 303.36, Temperature: 293(2) K, Crystal system: Triclinic, Space group: P-1, Unit cell dimensions: a = 8.3878(16) Å, = 76.354(4)°; b = 9.8582(18) Å, = 84.421(4)°; c = 19.139(3) Å, = 73.985(4)°. Volume: 1477.3(5) $Å^3$, Z = 4, Density (calculated): 1.364 Mg/m^3, F(000): 640, Crystal size: 0.211 x 0.175 x 0.123 mm^3, Final R indices [I>2sigma(I)]: R1 = 0.0513, wR2 = 0.1322.



The crystal data of **3a** have been deposited in CCDC with number 995122. Empirical formula: $C_{16}H_{22}NO_3S$, Formula weight: 308.40, Temperature: 293(2) K, Crystal system: Triclinic, Space group: P-1, Unit cell dimensions: a = 6.2097(13) Å, = 104.782(4)°; b = 11.272(2) Å, = 101.238(4)°; c = 11.547(3) Å, = 100.235(4)°. Volume: 744.2(3) $Å^3$, Z = 2, Density (calculated): 1.376 Mg/m^3, F(000): 330, Crystal size: 0.211 x 0.176 x 0.123 mm^3, Final R indices [I>2sigma(I)]: R1 = 0.0656, wR2 = 0.1786.



The crystal data of **5a** have been deposited in CCDC with number 1009701. Empirical formula: $C_{17}H_{19}NO_3S$, Formula weight: 317.39, Temperature: 293(2) K, Crystal system: Monoclinic, Space group: P 21/c, Unit cell dimensions: a = 14.5933(18) Å, = 90°; b = 9.6858(12) Å, = 92.745(3)°; c = 11.3977(14) Å, = 90°. Volume: 1609.2(3) $Å^3$, Z = 4, Density (calculated): 1.310 Mg/m^3, F(000): 672, Crystal size: 0.211 x 0.145 x 0.112 mm^3, Final R indices [I>2sigma(I)]: R1 = 0.0432, wR2 = 0.1107.

6. Reference

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