Electronic Supplementary Information

Palladium-Catalyzed Heck-type Reaction of Oxime Ether Bearing a Pendant Vinyl Iodide Moiety

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I. General information

Unless otherwise noted, all reagents were obtained commercially and used without further purification.

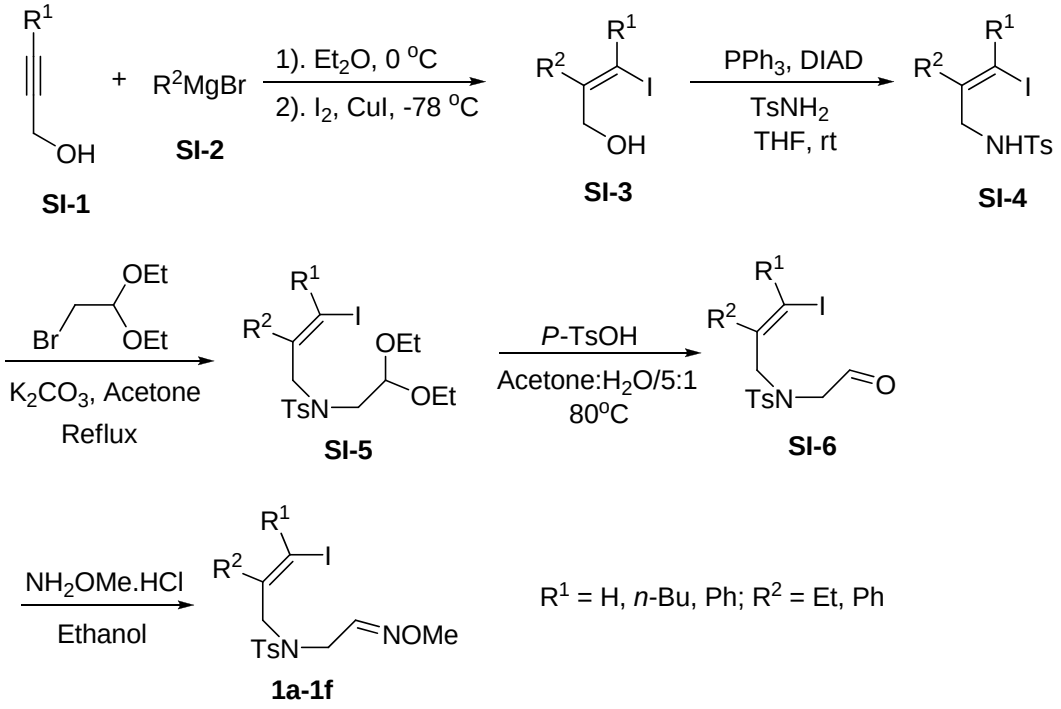
NMR spectrum: ^{1}H and ^{13}C spectra were recorded on a Bruker AVANCE 400 spectrometer, operating at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR. For ^{1}H NMR, chemical shifts were reported downfield from $CDCl_3$ (δ: 7.28 ppm). For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent of $CDCl_3$ (δ: 77.0 ppm) used as an internal reference.

Mass spectroscopy: Mass spectra were in general recorded on an AMD 402/3 or a HP 5989A mass selective detector.

Chromatography: Column chromatography was performed with silica gel (200-300 mesh ASTM).

II. The Procedure for Substrate Synthesis

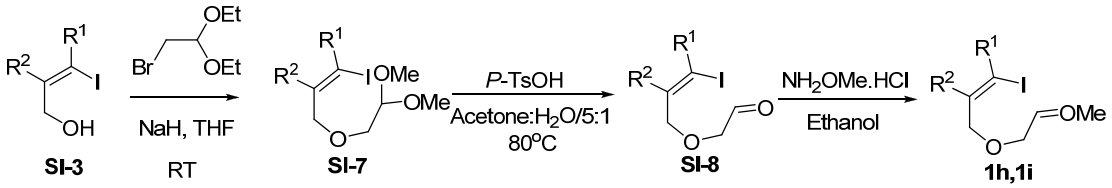
Procedure A: synthesis of compounds 1a-1f



To a stirred solution of alcohol **SI-1** (50 mmol) in anhydrous ether (70 mL) under an N_2 atmosphere was added CuI (10 mol%, 5 mmol, 0.952 g) and the resulting pink suspension was cooled to -78°C. Grignard reagent **SI-2** (2.5 equiv., 125 mmol), which had been freshly prepared in anhydrous ether, was then added via cannula, at such a rate as to maintain the temperature below -60°C. The resulting dark green suspension was allowed to slowly warm to room temperature over 18 hours. The reaction was again cooled to -78°C and treated with I_2 (13 g, 1.1 equiv.) in anhydrous THF (40 mL). After warming up to room temperature and stirring at rt for additional 1hr, the reaction mixture was kept in refrigerator at about 0-3°C overnight. The mixture was cooled to 0°C and was quenched with saturated aqueous NH_4Cl. The two phase mixture was separated by a separatory funnel. The aqueous layer was extracted by ether (3x50 mL) and the combined organic layers were washed with saturated aqueous $Na_2S_2O_3$ and saturated aqueous NaCl (100ml), and dried over Na_2SO_4. It was purified by column chromatography to give **SI-3**. Following the general procedure of Mitsunobu reaction, **SI-4** was obtained. [Reference: Richard C. Larock, Mark J. Doty, and Xiaojun Han. *J. Org. Chem.*, **1999**, *64*, 8770–8779.]

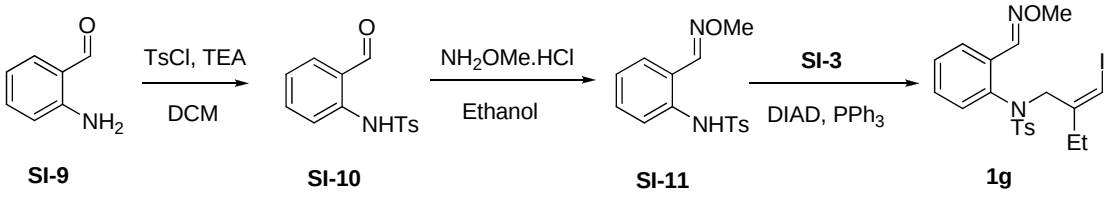
SI-4 (1.0 equiv.), 2-bromo-1,1-diethoxyethane (1.5 equiv.) and K_2CO_3 (1.5 equiv.) were dissolved in acetone. The reaction mixture was refluxed overnight. After standard work-up, compound **SI-5** was obtained, which was hydrolyzed with *P*-TsOH (10 mol%) in acetone:H_2O(5:1) at 80 °C to afford crude product **SI-6**. Compound **SI-6** was directly used without further purification. The mixture of **SI-6** (1.0 equiv.) and $NH_2OMe.HCl$ (2.0 equiv.) in ethanol was stirred at RT for 6 hours. After standard work-up, compound **1a-1f** was obtained.

Procedure B: synthesis of 1h and 1i



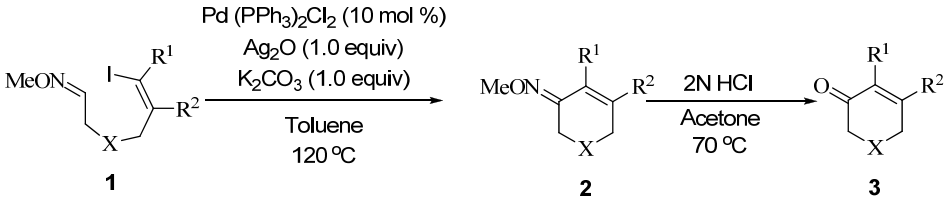
SI-3 (1.0 equiv.) was added dropwise to NaH (1.2 equiv.) suspension in THF at 0 ^{o}C. After 30 min, the solution of 2-bromo-1,1-diethoxyethane (1.5 equiv.) in THF was added dropwise. The mixture was stirred overnight. The reaction was quenched with water, and extracted with EA. It was purified by column chromatography to give **SI-7**. Compounds **1h** and **1i** were obtained just following the **Procedure A**.

Procedure C: synthesis of 1g



TsCl (110 mmol, 1.1 equiv.) was added to the solution of **SI-9** (100 mmol, 1.0 equiv.) in DCM in one portion. Then, TEA was added dropwise. The mixture was stirred overnight. After removing the solid, **SI-10** was obtained by column chromatography. Then, **SI-11** was obtained just following the **Procedure A**. Following the general procedure of Mitsunobu reaction, **1g** was obtained.

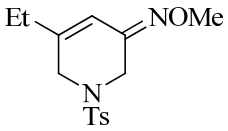
III. The Procedure for Catalytic Reaction and the Data for Compounds 2 and 3



1 **2** **3**

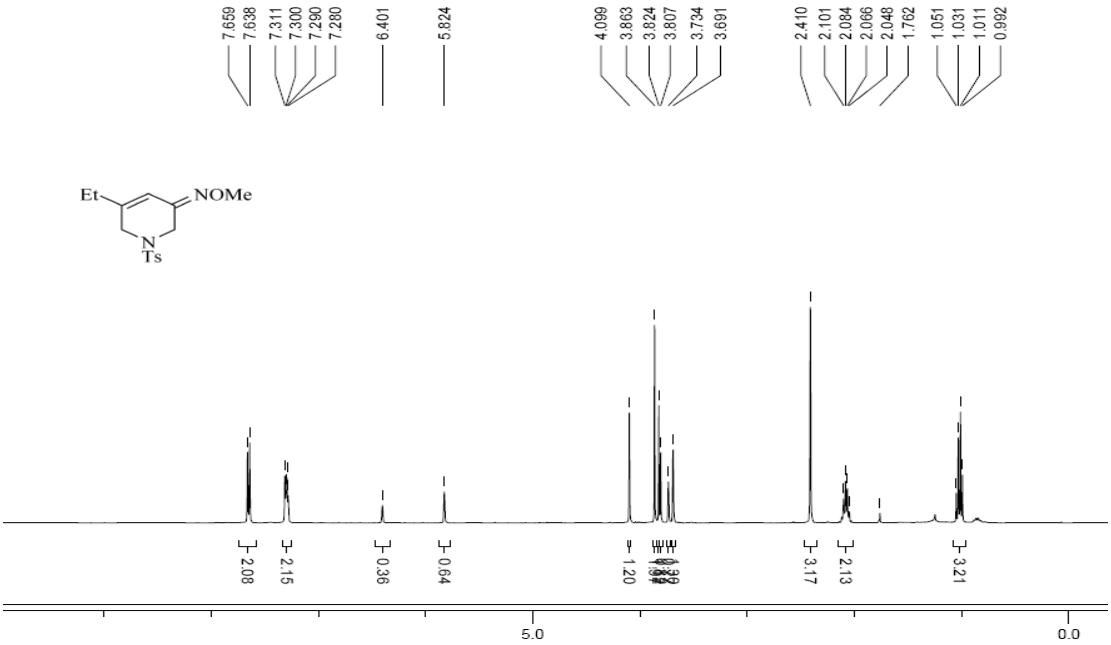
In a 25 mL Schlenk tube, substrate **1** (0.30 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), Ag_2O (0.3 mmol), and K_2CO_3 (0.30 mmol) were dissolved in 4 mL toluene under N_2. The mixture was heated to 120°C for 24h. The reaction mixture was cooled to room temperature and directly subjected to column chromatography to give **2**.

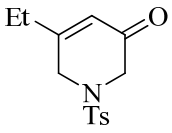
To the mixture of acetone (5 mL) and 2 N HCl (2mL) was added compound **2**. The mixture was heated to 70 °C overnight. The reaction mixture was cooled to room temperature and then was extracted by ether (3 x 10 mL). The combined organic layers were dried over Na_2SO_4. After evaporation of solvent, the residue was directly purified by column chromatography to give **3.**



2a (isomer ratio: 36 : 64)

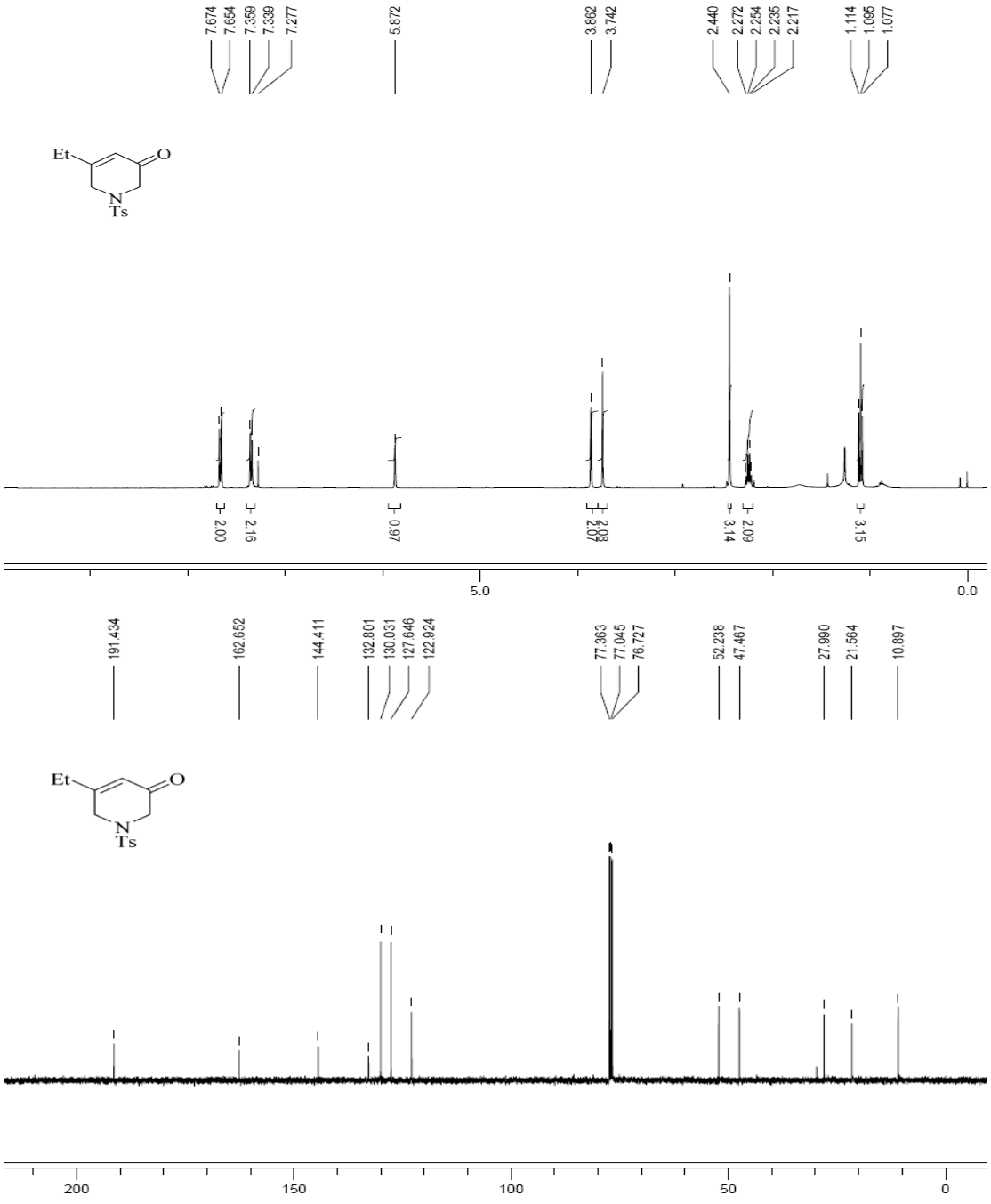
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.02 (t, *J* = 8.0 Hz, 3H), 2.05-2.10 (q, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 3.69 (s, 1.30H), 3.73 (s, 0.77), 3.81 (s, 0.82H), 3.82 (s, 1.12H), 3.86 (s, 1.97H), 4.10 (s, 1.20H), 5.82 (s, 0.64H), 6.40 (s, 0.36H), 7.28-7.31(m, 2H), 7.65 (d, *J* = 8.4 Hz, 2H)

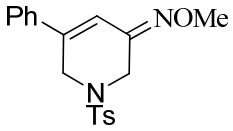




3a

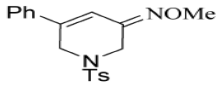
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.10 (t, *J* = 7.2 Hz, 3H), 2.24 (q, *J* = 7.2 Hz, 2H), 2.44 (s, 3H), 3.74 (s, 2H), 3.86 (s, 2H), 5.87 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 10.9, 21. 6, 28.0, 47.5, 52.2, 122.9, 127.6, 130.0, 132.8, 144.4, 162.6, 191.4; HRMS Calcd for $C_{14}H_{17}NO_3S$ 279.0929, Found 279.0933.

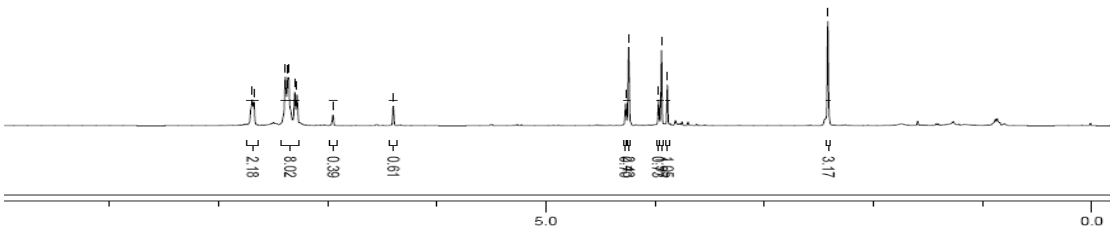


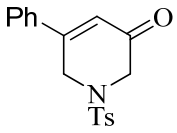


2b (isomer ratio: 39 : 61)

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (s, 3H), 3.89 (s, 1.05H), 3.94 (s,1.97H), 3.97 (s, 0.73H), 4.24 (s, 2.43H), 4.27 (s, 0.70H), 6.40 (s, 0.61H), 6.95 (s, 0.39H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.36-7.38 (m, 5H), 7.68 (d, *J* = 7.6 Hz, 2H).

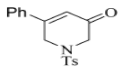


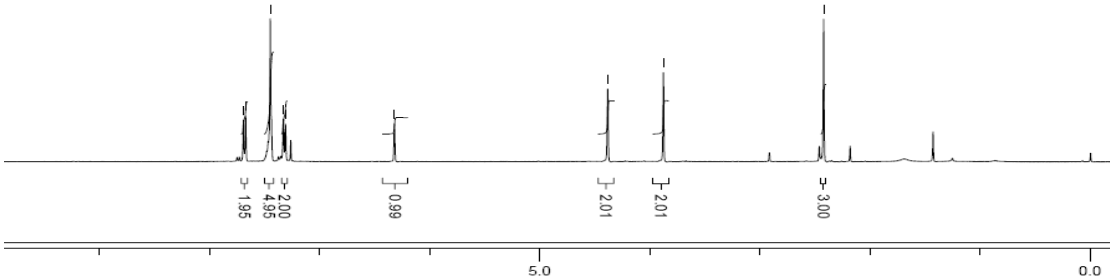


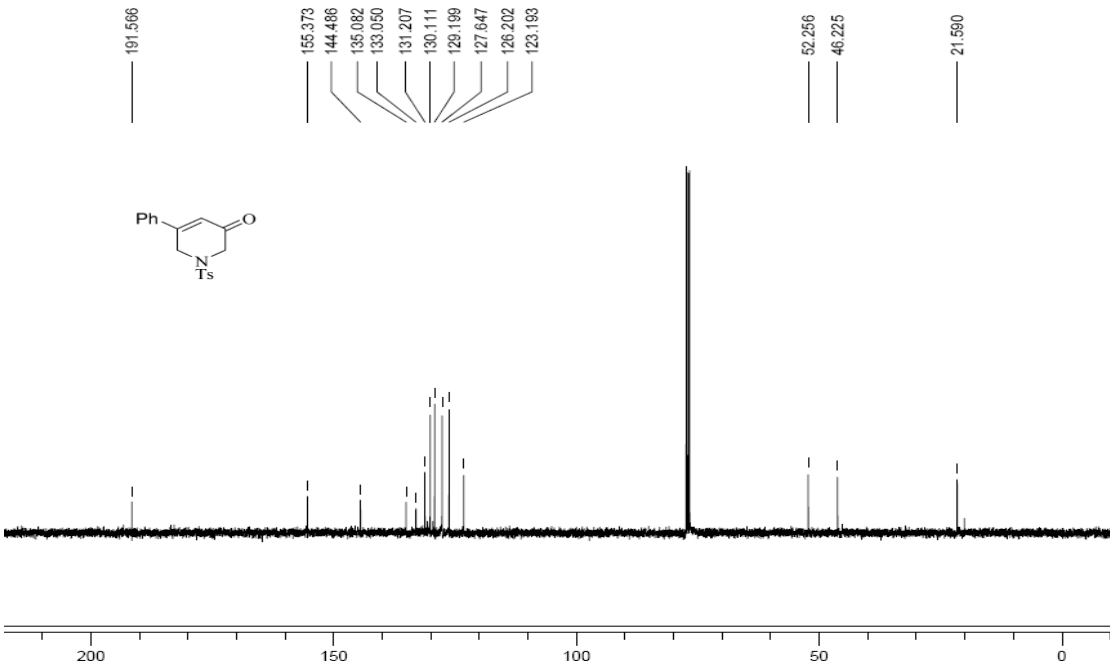


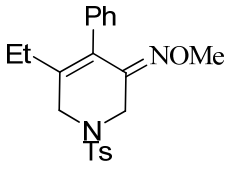
3b

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (s, 3H), 3.87 (s, 2H), 4.38 (s, 2H), 6.32 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.45-7.48 (m, 5H), 7.68 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 21.6, 46.2, 52.3, 123.2, 126.2, 127.6, 129.2, 130.1, 131.2, 133.0, 135.1, 144.5, 155.4, 191.6; HRMS Calcd for $C_{18}H_{15}NO_3S$ 325.0773, Found 325.0776.



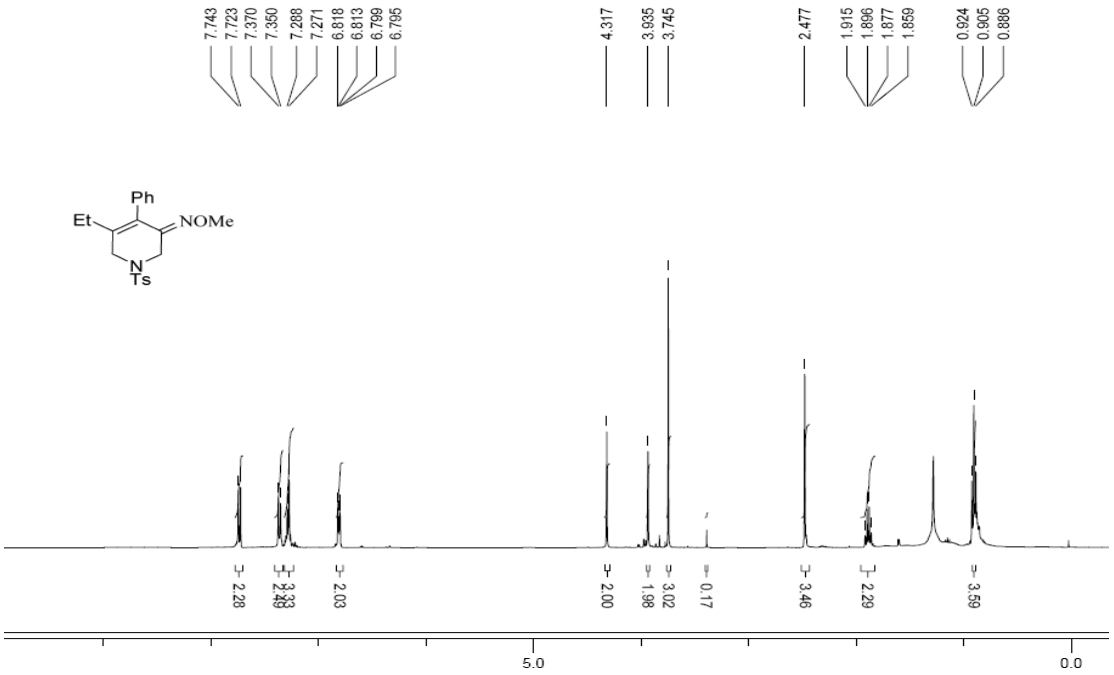


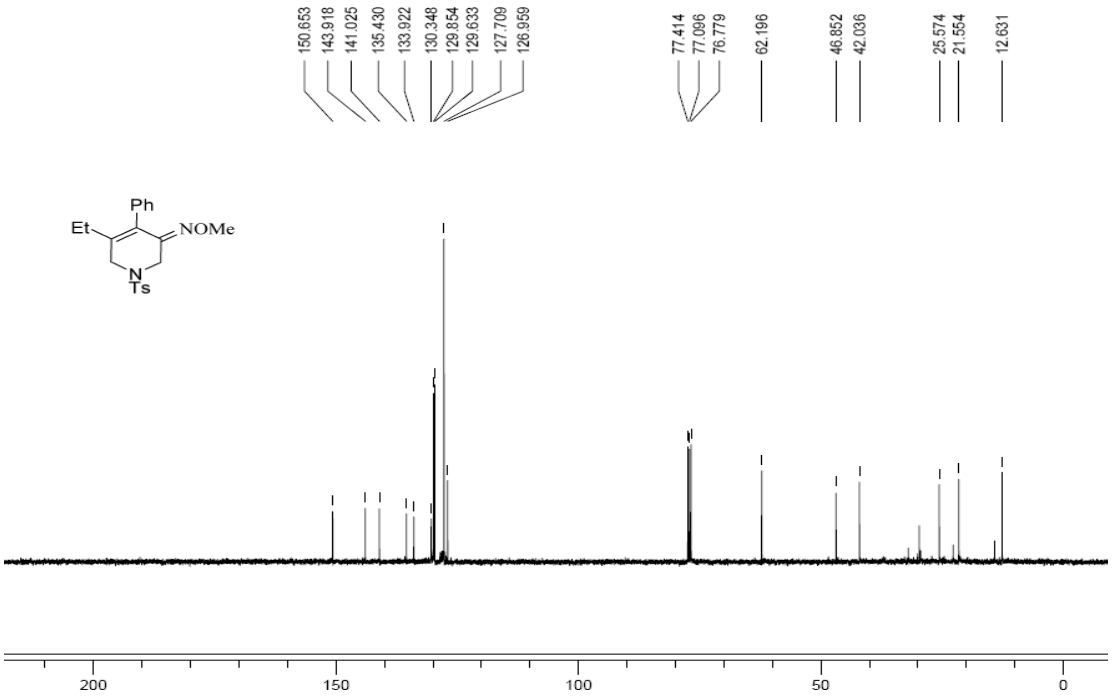


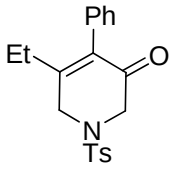


2e (single isomer)

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, *J* = 7.6 Hz, 3H), 1.89 (q, *J* = 7.6 Hz), 2.48 (s, 3H), 3.74 (s, 3H), 3.94 (s, 2H), 4.32 (s, 2H), 6.80-6.82 (m, 2H), 7.27-7.29 (m, 3H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 12.6, 21.6, 25.6, 42.0, 46.8, 62.2, 127.0, 127.7, 129.6, 129.8, 130.4, 133.9, 135.4, 141.0, 143.9, 150.6.

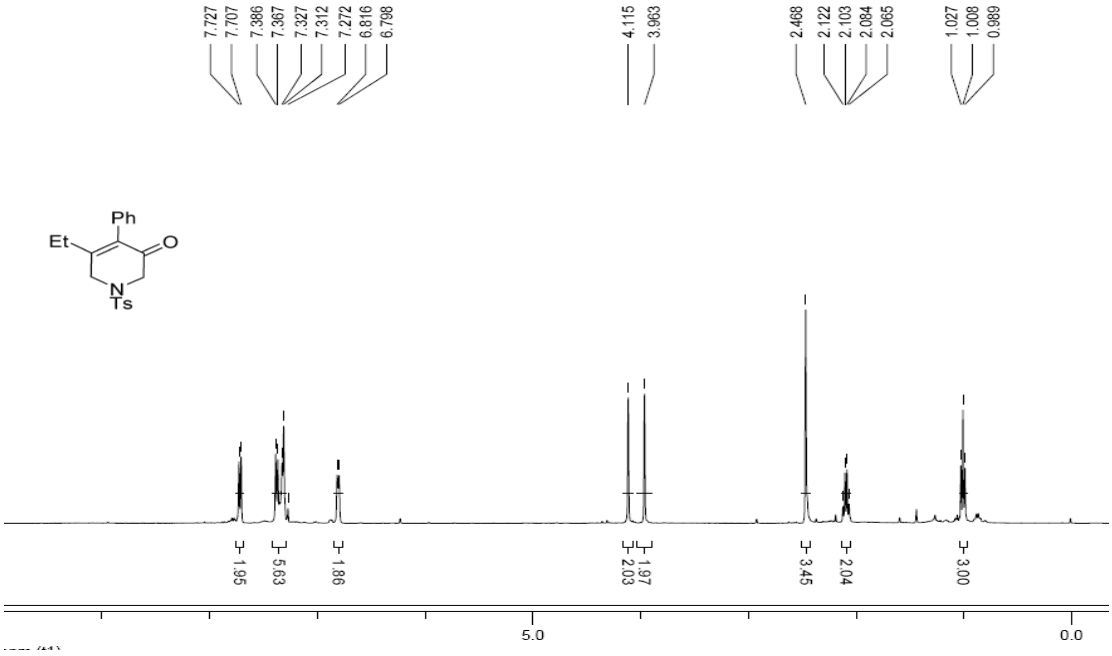


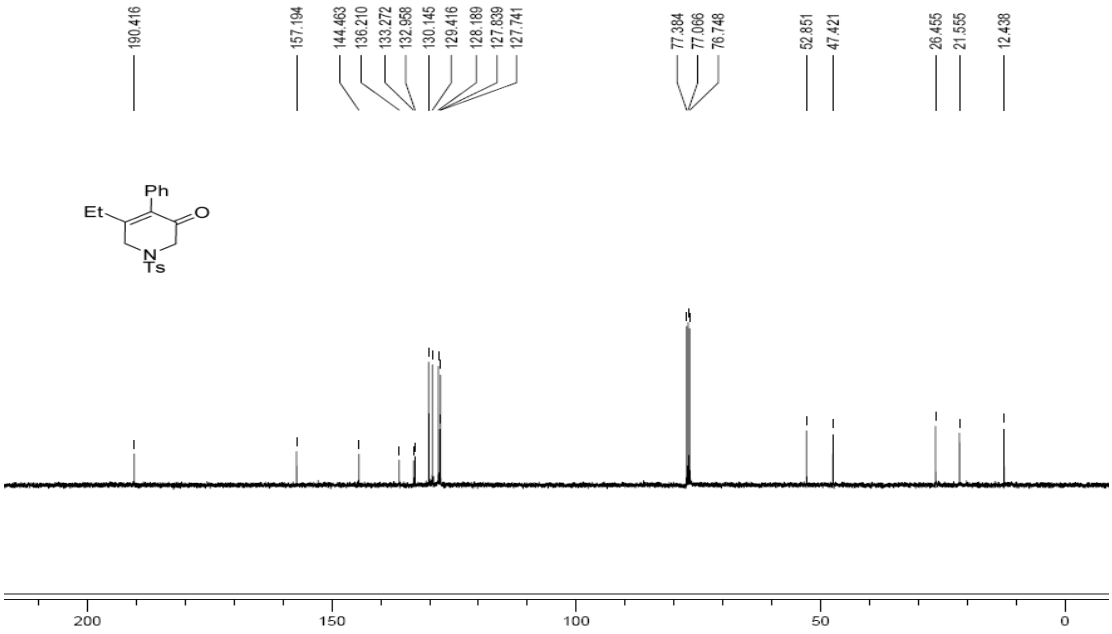


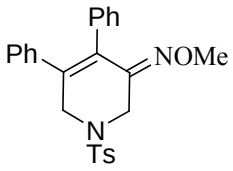


3e

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (t, J = 7.6 Hz, 3H), 2.09 (q, J = 7.6 Hz, 2H), 2.47 (s, 3H), 3.96 (s, 2H), 4.12 (s, 2H), 6.81 (d, J = 7.2Hz, 2H), 7.27-7.39 (m, 5H), 7.71-7.73 (d, J = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 12.4, 21.6, 26.5, 47.42, 52.8, 127.7, 127.8, 128.2, 129.4, 130.1, 133.0, 133.3, 136.2, 144.5, 157.2, 190.4; HRMS Calcd for $C_{20}H_{21}NO_3S$ 355.1242, Found 355.1241.

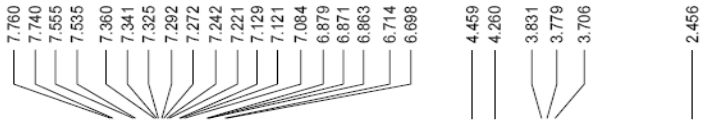


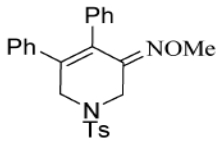


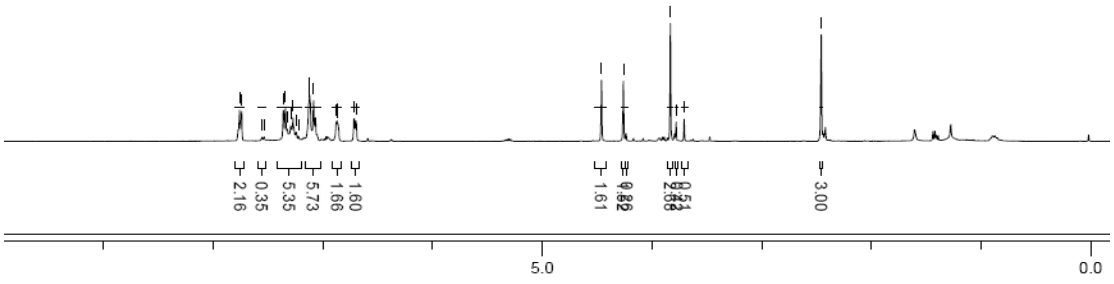


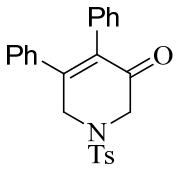
2d (isomer ratio: 20 : 80)

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 3.71 (s, 0.51H), 3.78 (s, 0.42H), 3.83 (s, 2.68H), 4.26 (s, 1.52H), 4.46 (s, 1.61H), 4.26 (s, 2H), 4.46 (s, 1.61H), 6.70 (d, *J* = 6.4 Hz, 1.60H), 6.86-6.88 (m, 1.66H), 7.08-7.13 (m, 5.73H), 7.22-7.36 (m, 5H), 7.54 (d, *J* = 8.0 Hz, 0.35H), 7.75 (d, *J* = 8.0 Hz, 2H).



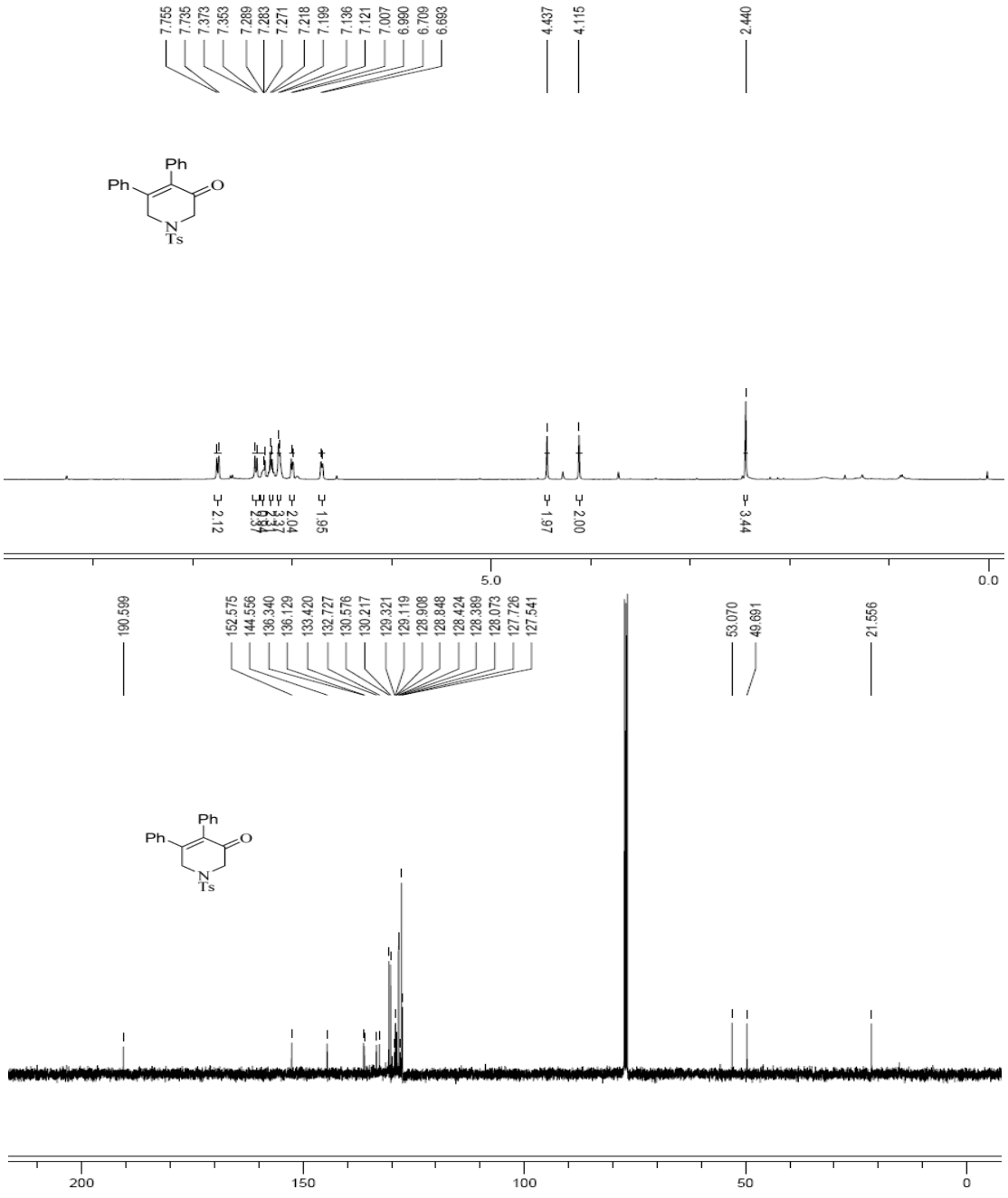


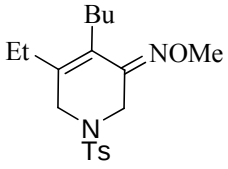




3d

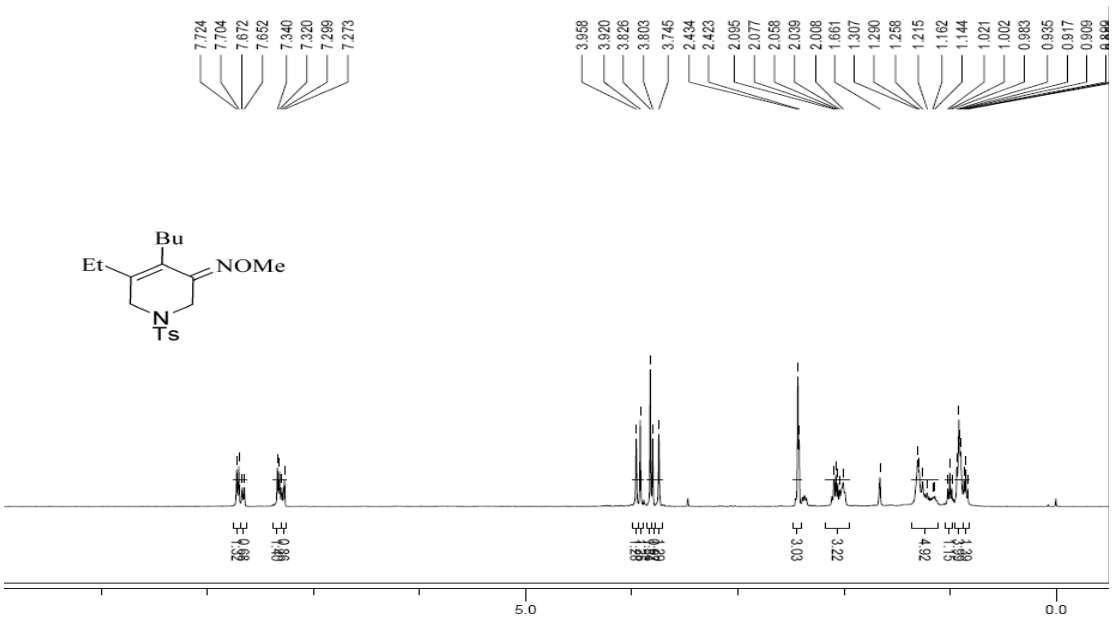
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 4.12 (s, 2H), 4.44 (s, 2H), 6.70 (d, *J* = 6.4 Hz, 2H), 7.00 (d, *J* = 6.8 Hz, 2H), 7.12-7.14 (m, 3H), 7.20-7.22 (m, 2H), 7.28-7.29 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 21.6, 49.7, 53.1, 127.5, 128.1, 128.4, 128.4 128.8, 128.9, 129.1, 129.3, 130.2, 130.6, 132.7, 133.4, 136.1, 136.3, 144.6, 152.6, 190.6; HRMS Calcd for $C_{24}H_{21}NO_3S$ 403.1242, Found 403.1243.

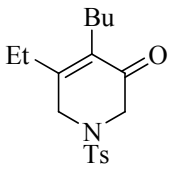




2c (isomer ratio: 34 : 66)

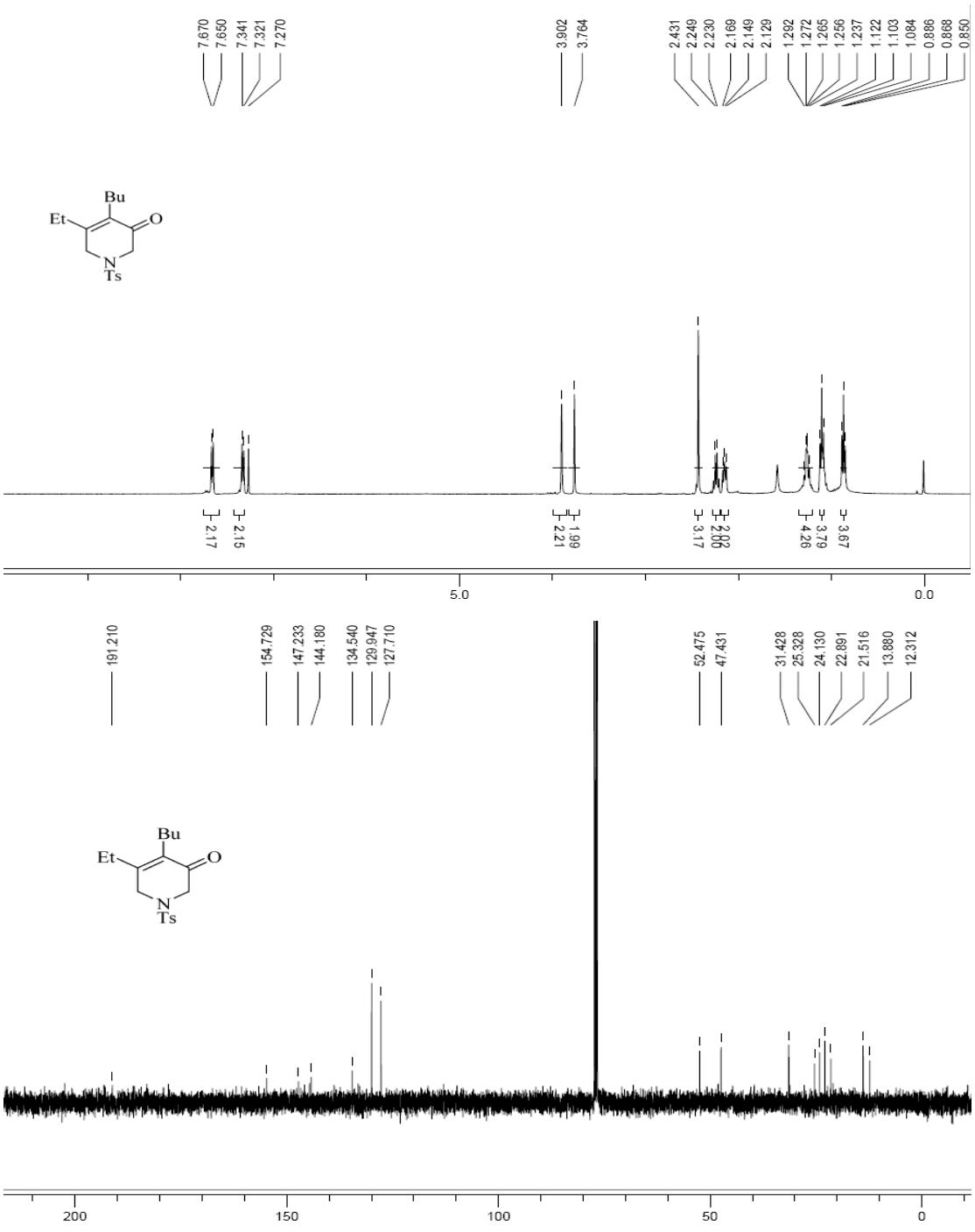
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, *J* = 7.2 Hz, 1.39H), 0.90-0.94 (m, 3.99H), 1.00 (t, *J* = 7.6 Hz, 1.15H), 1.14-1.31 (m, 4.92H), 2.01-2.11 (m, 3.22H), 2.42-2.46 (m, 3.03H), 3.74 (s, 1.29H), 3.80 (s, 0.92H), 3.83 (s, 1.84H), 3.92 (s, 1.25H), 3.96 (s, 1.28H), 7.29 (d, *J* = 8.0 Hz, 0.86H), 7.33 (d, *J* = 8.0 Hz, 1.40H), 7.66 (d, *J* = 8.0 Hz, 0.68H), 7.71 (d, *J* = 8.0 Hz, 1.32H).

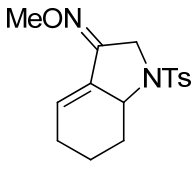




3c

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.6 Hz, 3H), 1.24-1.29 (m, 4H), 2.15 (t, *J* = 8.0 Hz, 2H), 2.24 (q, *J* = 7.6 Hz, 2H), 2.43 (s, 3H), 3.76 (s, 2H), 3.90 (s, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 12.3, 13.9, 21.5, 22.9, 24.1, 25.3, 31.4, 47.4, 52.5, 127.7, 130.0, 134.5, 144.2, 147.2, 154.7, 191.2; HRMS Calcd for $C_{18}H_{25}NO_3S$ 335.1555, Found 335.1556.

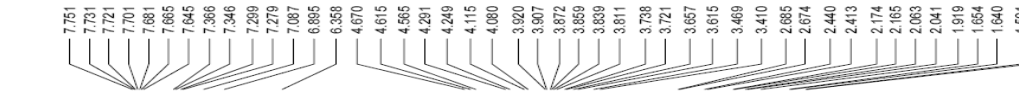


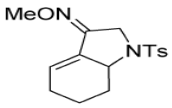


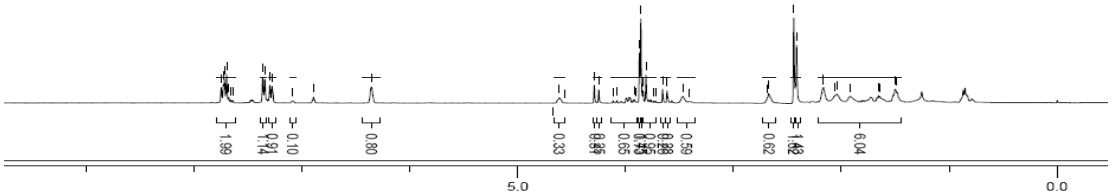
2f (not determined)

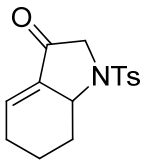
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.49-2.17 (m, 6.04H), 2.41(s, 1.43H), 2.44 (s, 1.62H), 2.67-2.68 (m, 0.62H), 3.41-3.47 (m, 0.59H), 3.62 (s, 0.28H), 3.66 (s, 0.26H), 3.72-3.84 (m, 0.95H), 3.86 (s, 1.54H), 3.87 (s, 0.73H), 3.91-4.12 (m, 0.65H), 4.25 (s,

0.25H), 4.29 (s, 0.31H), 4.56-4.67 (m, 0.33H), 6.36 (s, 0.80H), 7.09 (s, 0.10H), 7.29 (d, *J* = 8.0 Hz, 0.91H), 7.36 (d, *J* = 8.0 Hz, 1.14H), 7.64-7.75 (m, 1.99H)



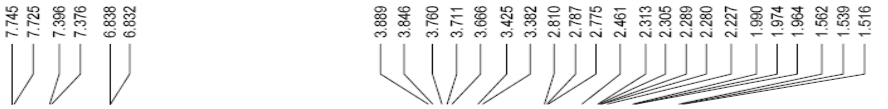


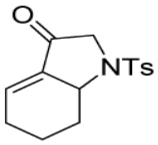


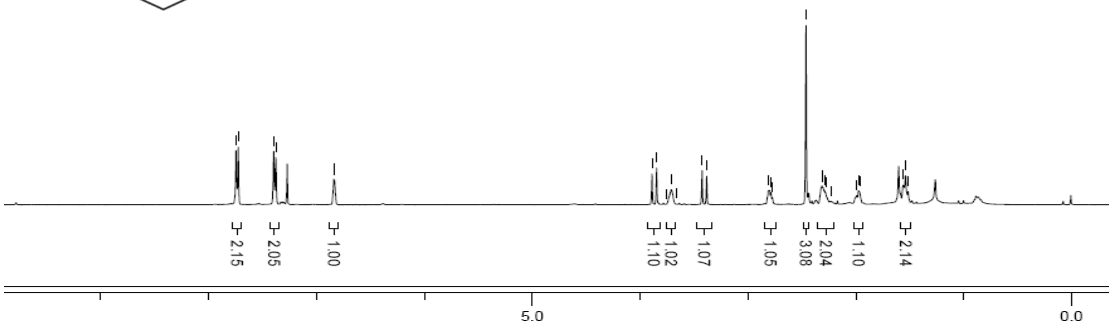


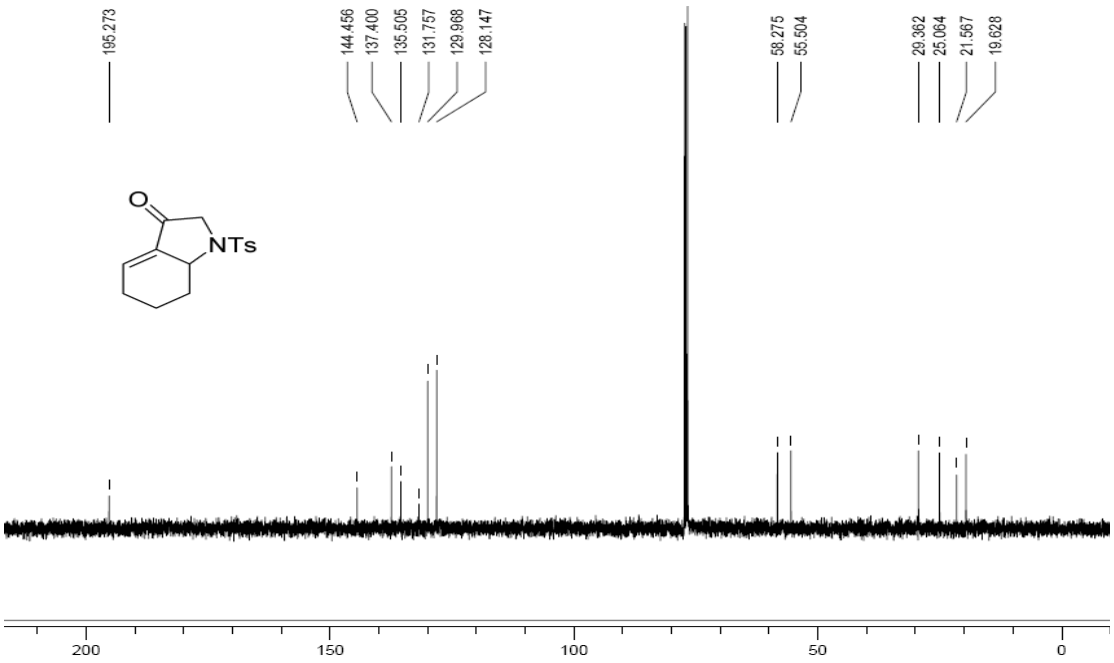
3f

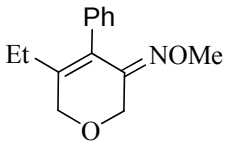
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48-1.56 (m, 2H), 1.96-1.99 (m, 1H), 2.27-2.31 (m, 2H), 2.46 (s, 3H), 2.78-2.81 (m, 1H), 3.40 (d, *J* = 17.2 Hz, 1H), 3.67-3.76 (m, 1H), 3.86 (d, *J* = 17.2 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 19.6, 21.6, 25.1, 29.4, 55.5, 58.3, 128.2, 130.0, 131.8, 135.5, 137.4, 144.5, 195.3; HRMS Calcd for $C_{24}H_{21}NO_3S$ 291.0929, Found 291.0931.





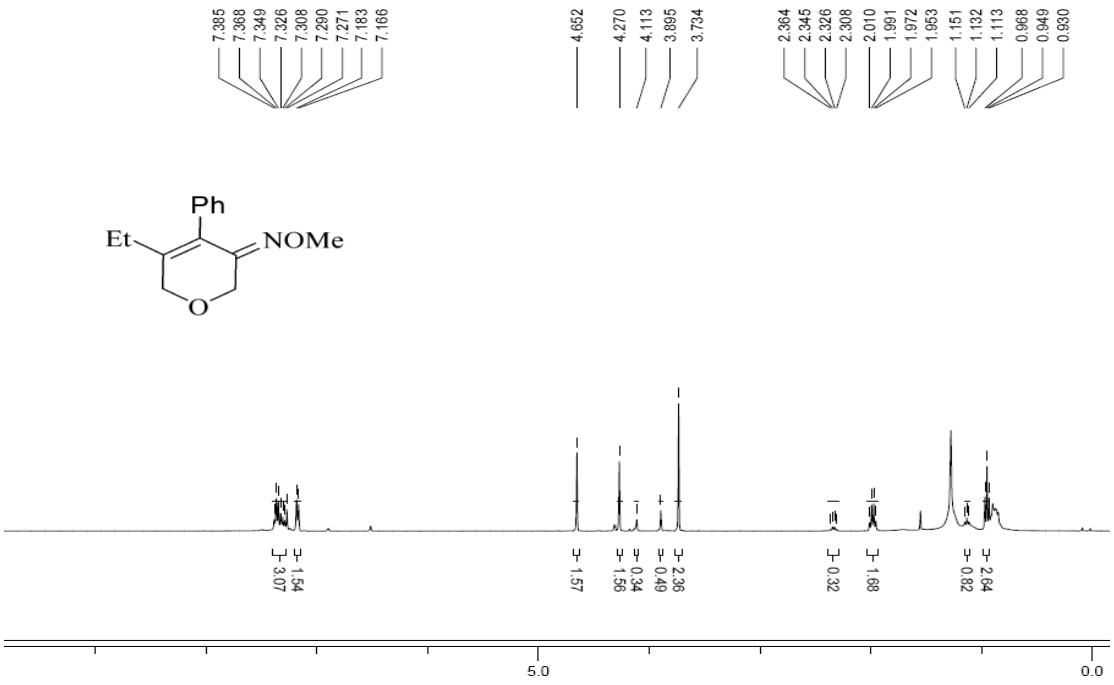


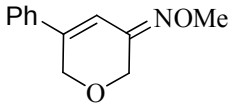




2h (isomer ratio: 16 : 84)

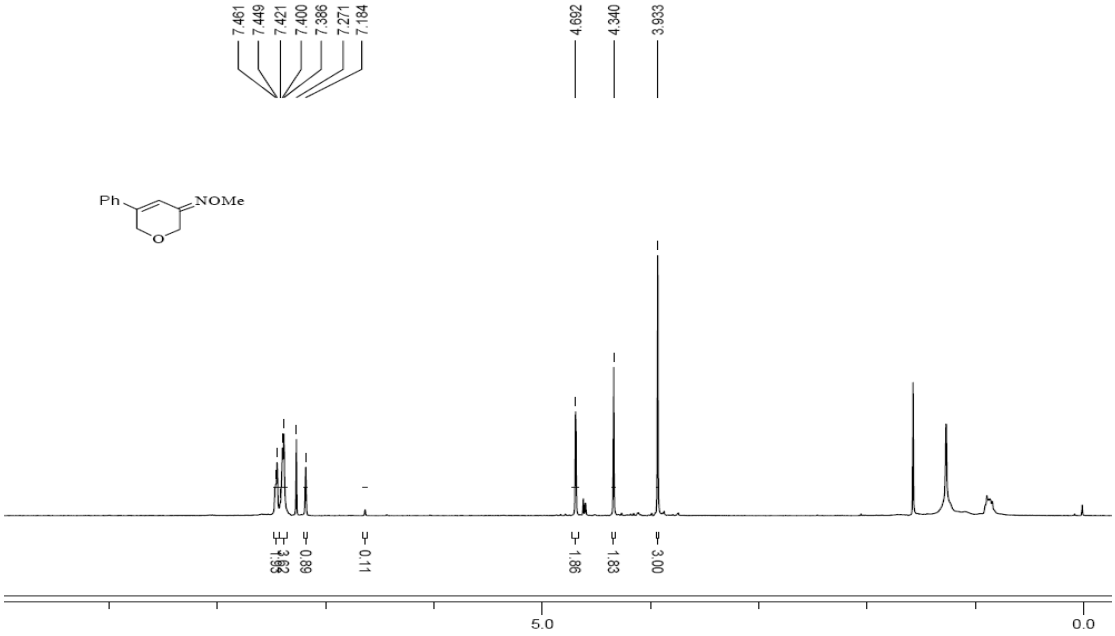
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (t, *J* = 7.6 Hz, 2.64H), 1.13 (t, *J* = 7.6 Hz, 0.82H), 1.98 (q, *J* = 7.6 Hz, 1.68H), 2.34 (q, *J* = 7.6 Hz, 0.32H), 3.73 (s, 2.36H), 3.90 (s, 0.49H), 4.11 (s, 0.34H), 4.27 (s, 1.56H), 4.65 (s, 1.57H), 7.17 (d, *J* = 6.8 Hz, 1.54H), 7.29-7.38 (m, 3.07H); HRMS Calcd for $C_{14}H_{17}NO_2$ 231.1259, Found 231.1258.

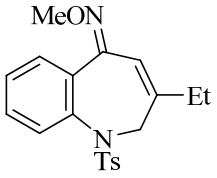




2i (isomer ratio: 11: 89)

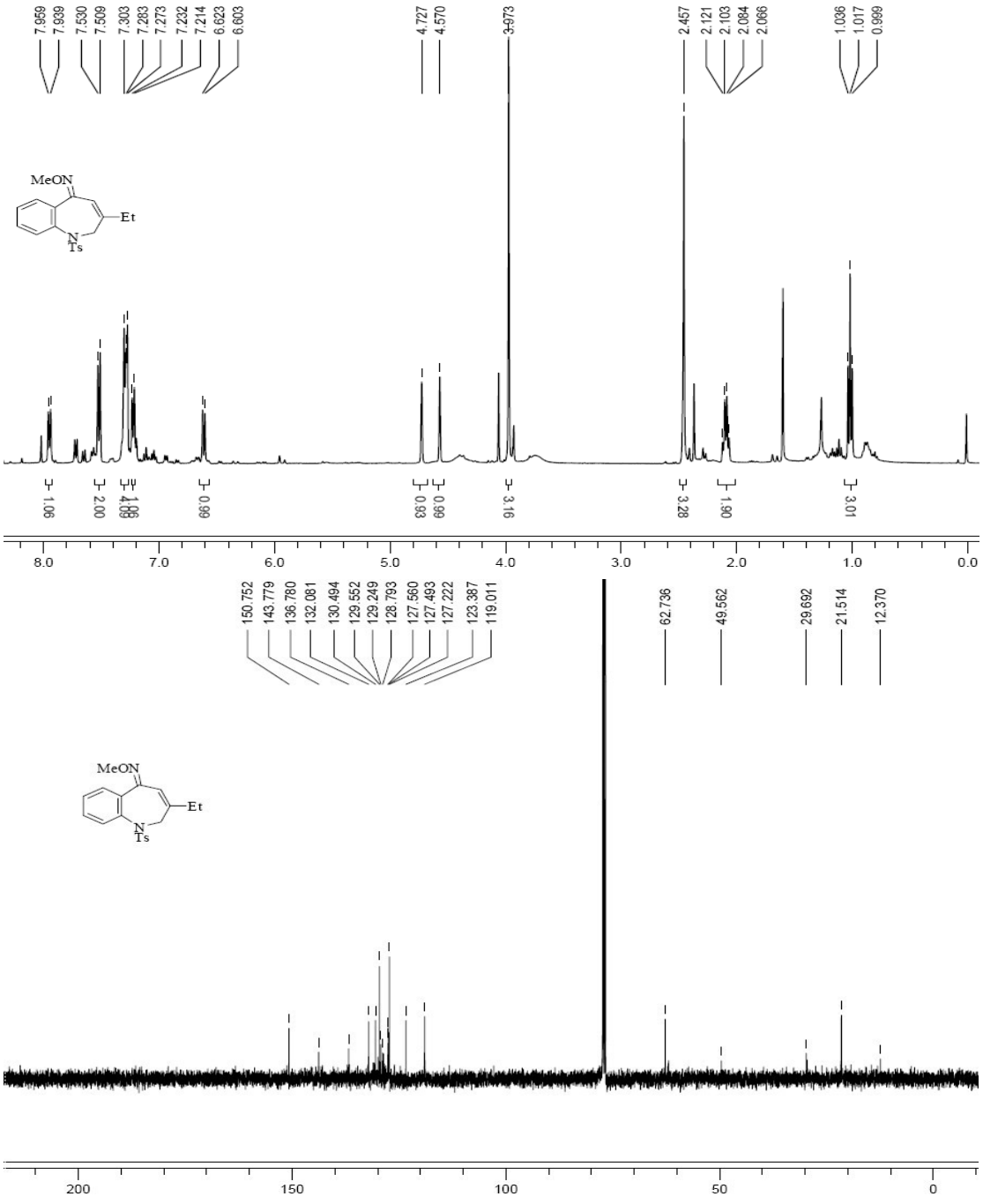
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.93 (s, 3H), 4.34 (s, 2H), 4.69 (s, 2H), 7.18 (s, 1H), 7.39-7.46 (m, 5H); HRMS Calcd for $C_{12}H_{13}NO_2$ 203.0946, Found 203.0947.



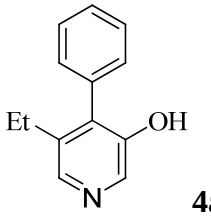


2g (not determined)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.02 (t, J = 7.2 Hz, 3H), 2.09 (q, J = 7.2 Hz, 2H), 2.46 (s, 3H), 3.97 (s, 3H), 4.57 (s, 1H), 4.73 (s, 1H), 6.61 (d, J = 8.0 Hz, 1H), 7.21-7.30 (m, 5H), 7.52 (d, J = 8.0 Hz, 2H), 7.95 (d, J = 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 12.4, 21.5, 29.7, 49.6, 62.7, 119.0, 123.4, 127.2, 127.5, 127.6, 128.8, 129.2, 129.6, 130.5, 132.1, 136.8, 143.8, 150.8; HRMS Calcd for $C_{20}H_{22}N_2O_3S$ 370.1351, Found 370.1351.


7.959
7.939
7.530
7.509
7.303
7.283
7.273
7.232
7.214
6.623
6.603
4.727
4.570
3.973
2.457
2.121
2.103
2.084
2.066
1.036
1.017
0.999
MeON
Et
N
Ts
1.06
2.00
1.98
1.98
0.99
0.93
0.99
3.16
3.28
1.90
3.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
150.752
143.779
136.780
132.081
130.494
129.552
129.249
128.793
127.560
127.493
127.222
123.387
119.011
62.736
49.562
29.692
21.514
12.370
MeON
Et
N
Ts
200
150
100
50
0

IV. The data for 4



4a

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06 (t, *J* = 7.6 Hz, 3H), 2.47 (q, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 6.8 Hz, 2H), 7.43-7.46 (m, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 8.05 (s, 1H), 8.29 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 15.2, 23.8, 128.2, 128.8, 129.3, 134.0, 134.4, 137.0, 138.8, 140.2, 151.6; HRMS Calcd for $C_{13}H_{13}NO$ 199.0997, Found 199.0985.