

# Stereospecific Synthesis of 2-Iminothiazolidines via Domino Ring-Opening Cyclization of Activated Aziridines with Aryl- and Alkyl Isothiocyanates

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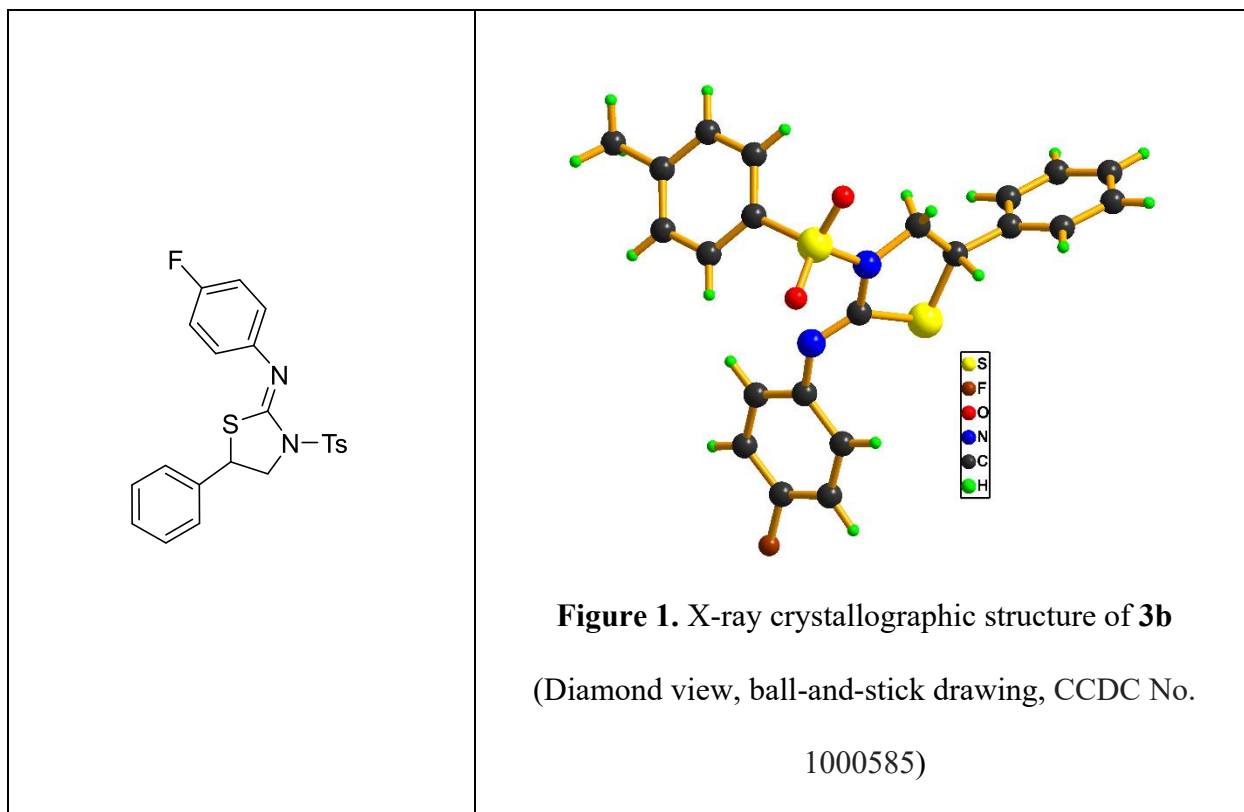
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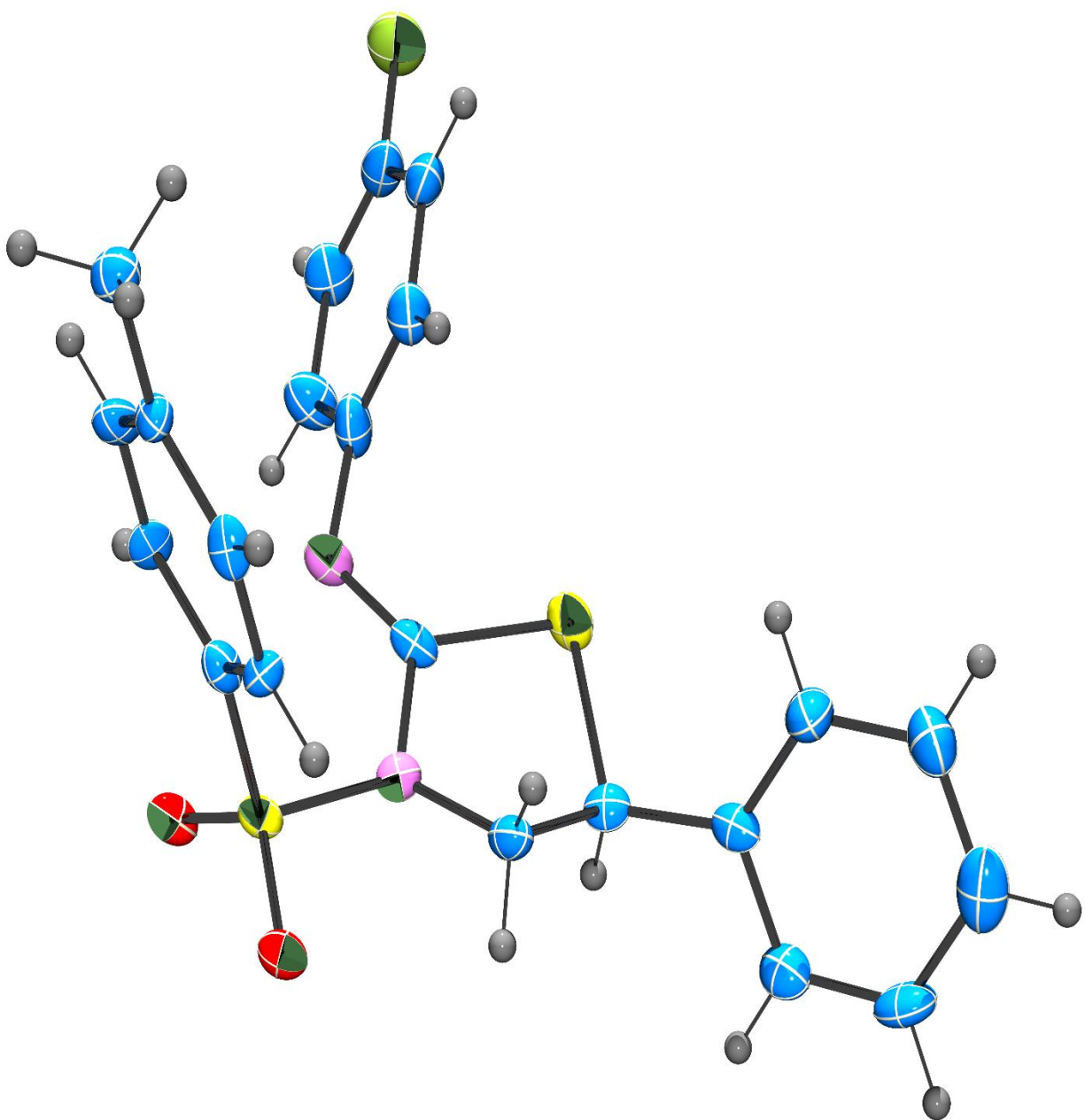
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## 1. X-ray crystallographic studies:

The crystals used in the analyses were glued to a glass fiber and mounted on CCD diffractometer. The instrument was equipped with CCD area detector and data were collected using graphite-monochromated Mo K $\alpha$  radiation ( $\lambda = 0.71073$ ) at low temperature (100K). Cell constants were obtained from the least-squares refinement of three-dimensional centroids through the use of CCD recording of narrow  $\omega$  rotation frames, completing almost all-reciprocal space in the stated  $\theta$  range. All data were collected with SMART 5.628 and were integrated with the SAINT<sup>1</sup> program. An empirical absorption correction was applied to collect reflections with SADABS<sup>2</sup> using XPREP.<sup>3</sup> The structure was solved using SIR-97<sup>4</sup> and refined using SHELXL-97.<sup>5</sup> The space group of the compounds was determined based on the lack of systematic absence and intensity statistics. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms of the hydroxyl groups were located by differential Fourier map, all other hydrogen atoms are fixed by using geometrical constraints using idealized geometries. All the hydrogen atoms have been defined isotropically.

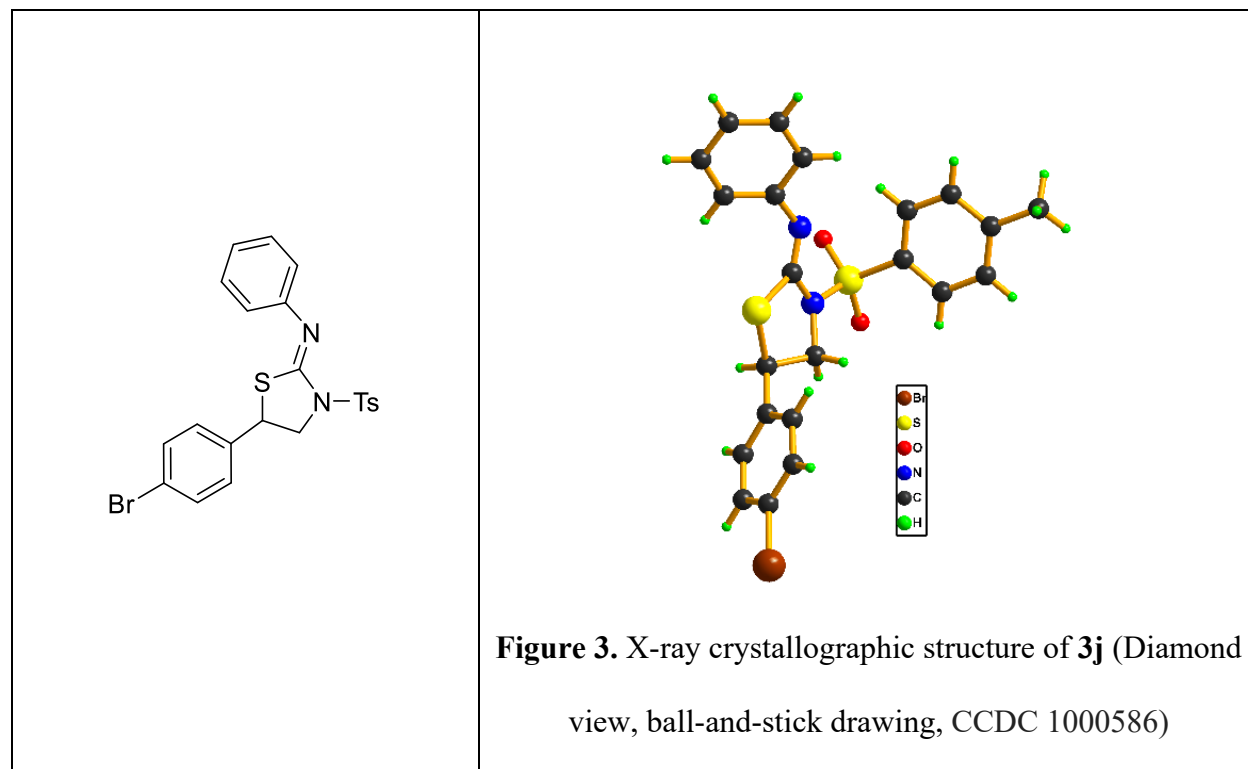
## 2. X-ray crystallographic structure of 3b.

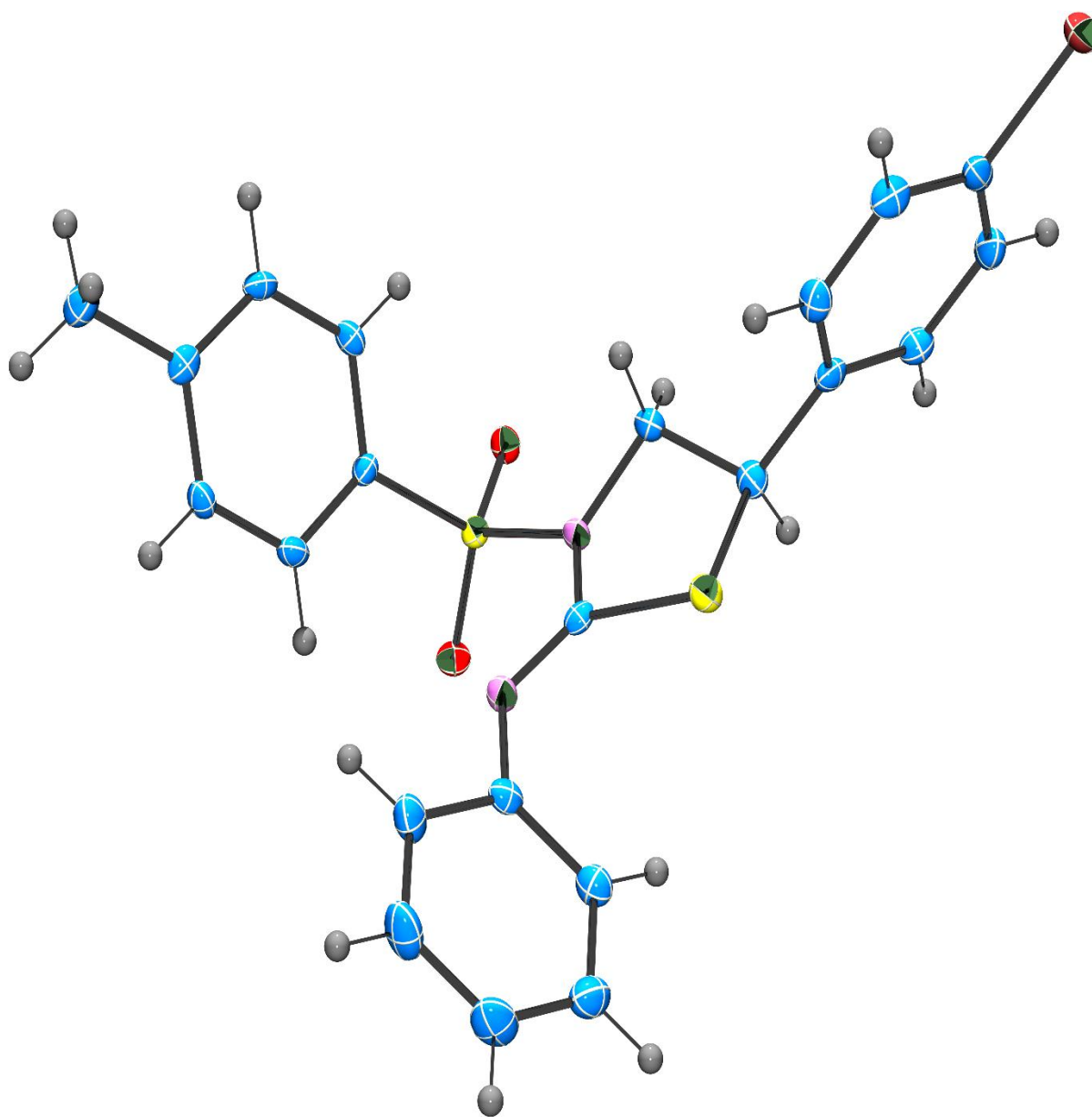




**Figure 2.** X-ray crystallographic structure of **3b** (ORTEP view with 50% thermal ellipsoid contour probability, CCDC 1000585)

### 3. X-ray crystallographic structure of 3j.





**Figure 4.** X-ray crystallographic structure of **3j** (ORTEP view with 50% thermal ellipsoid contour probability, CCDC 1000586)

#### 4. X-ray crystallographic data and structure refinement:

Compound	<b>3b</b> (CCDC 1000585)	<b>3j</b> (CCDC 1000586)
Formula	C <sub>22</sub> H <sub>19</sub> FN <sub>2</sub> O <sub>2</sub> S <sub>2</sub>	C <sub>22</sub> H <sub>19</sub> BrN <sub>2</sub> O <sub>2</sub> S <sub>2</sub>
Formula weight	426.53	487.42
Crystal system	Orthorhombic	Monoclinic
Space group	P2(1)2(1)2(1)	P21/c
T, K	273(2)	293(2)
Z	8	4
a, Å	12.068(5)	14.3343(7)
b, Å	13.052(5)	12.9414(6)
c, Å	26.055(5)	12.2133(6)
α, deg	90.000(5)	90
β, deg	90.000(5)	114.1340(10)
γ, deg	90.000(5)	90
V, Å <sup>3</sup>	4104(2)	2067.60(17)
d <sub>calcd</sub> , g/cm <sup>3</sup>	1.3814	1.566
μ, mm <sup>-1</sup>	0.289	2.212
θ range, deg	2.21–25.99	2.21–26.00
GOF (F <sup>2</sup> )	1.039	1.015
R <sub>1</sub> <sup>b</sup> (wR <sub>2</sub> <sup>c</sup> ), %	0.0974 (0.1712)	0.0564 (0.0772)
[a] <sup>a</sup> Mo Kα radiation, <sup>b</sup> R <sub>1</sub> = $\sum   F_o  -  F_c   / \sum  F_o $ , <sup>c</sup> wR <sub>2</sub> = $\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}^{1/2}$		

## References:

1. SAINT+ 6.02ed.; Bruker AXS, Madison, WI, 1999.
2. Sheldrick, G. M. SADBAS, Empirical Absorption Correction Program, University of Göttingen, Göttingen, Germany, 1997.
3. XPREP, 5.1ed. Siemens Industrial Automation Inc., Madison, WI, 1995.
4. Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Cryst.* **1999**, 32, 115.
5. Sheldrick, G. M. SHELXL-97: Program for Crystal Structure Refinement (University of Göttingen, Göttingen, Germany, 1997).



## 2. Copies of NMR spectra:

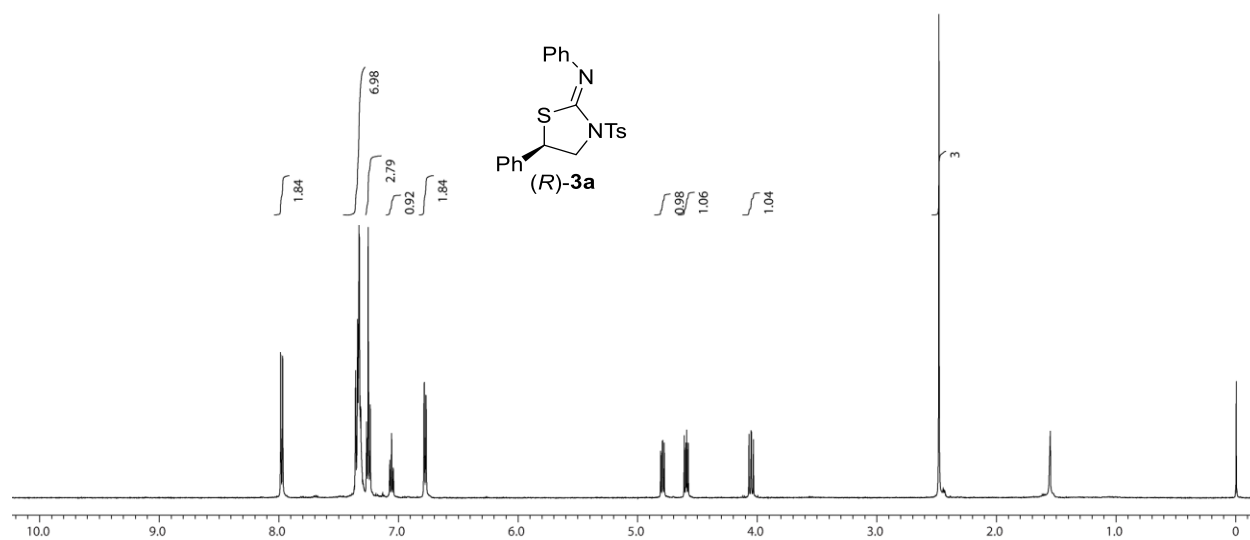


Figure 5. <sup>1</sup>H NMR spectrum of 3a (500 MHz, CDCl<sub>3</sub>)

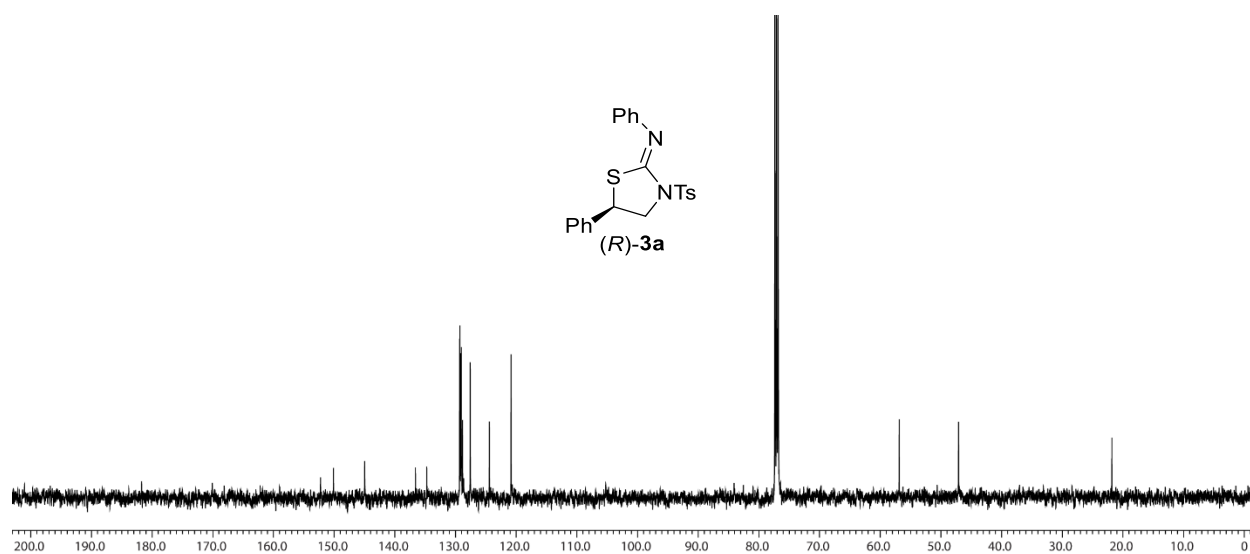
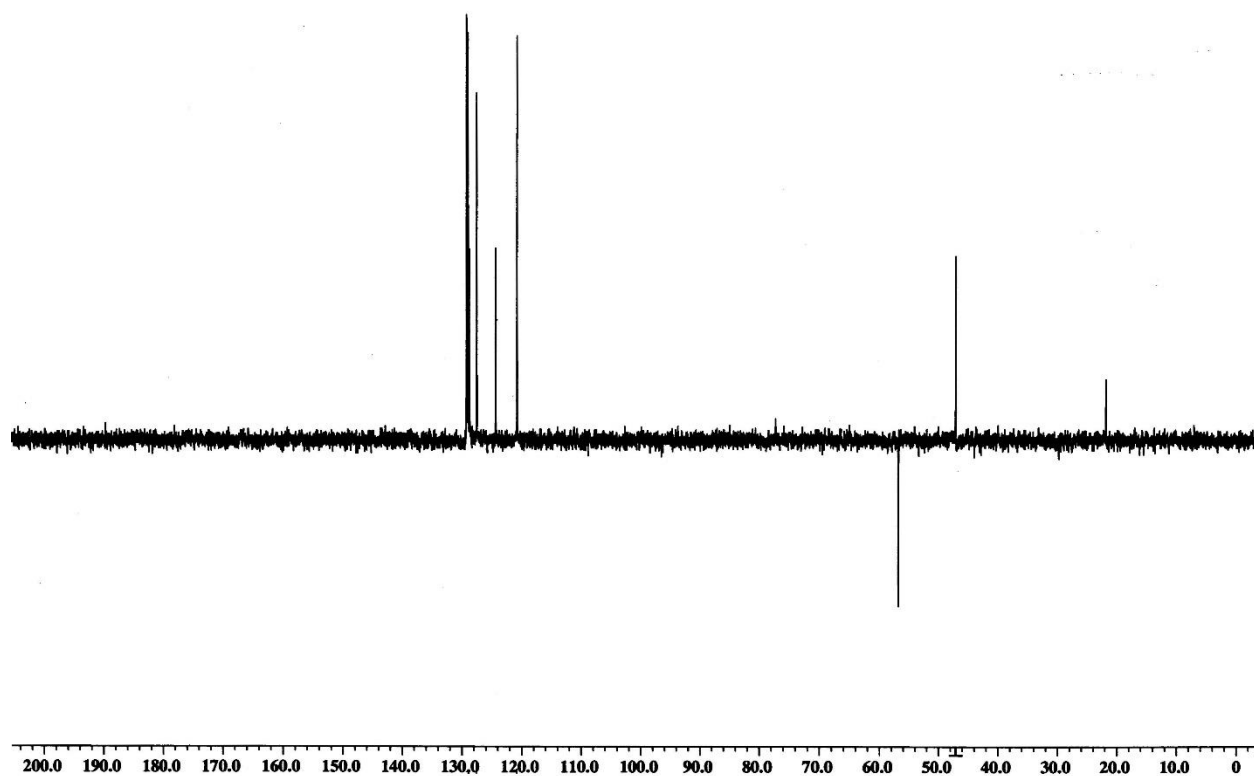
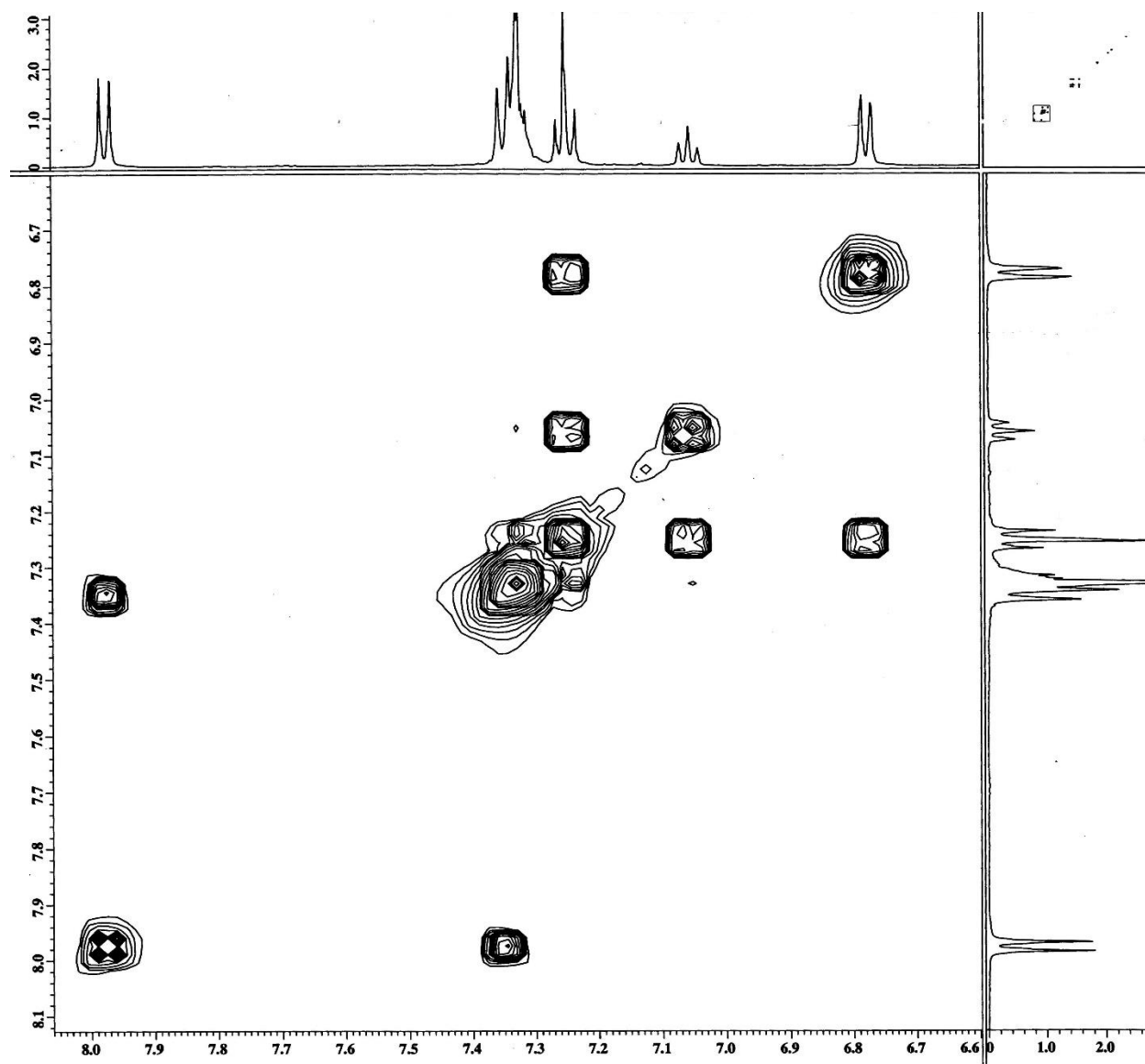


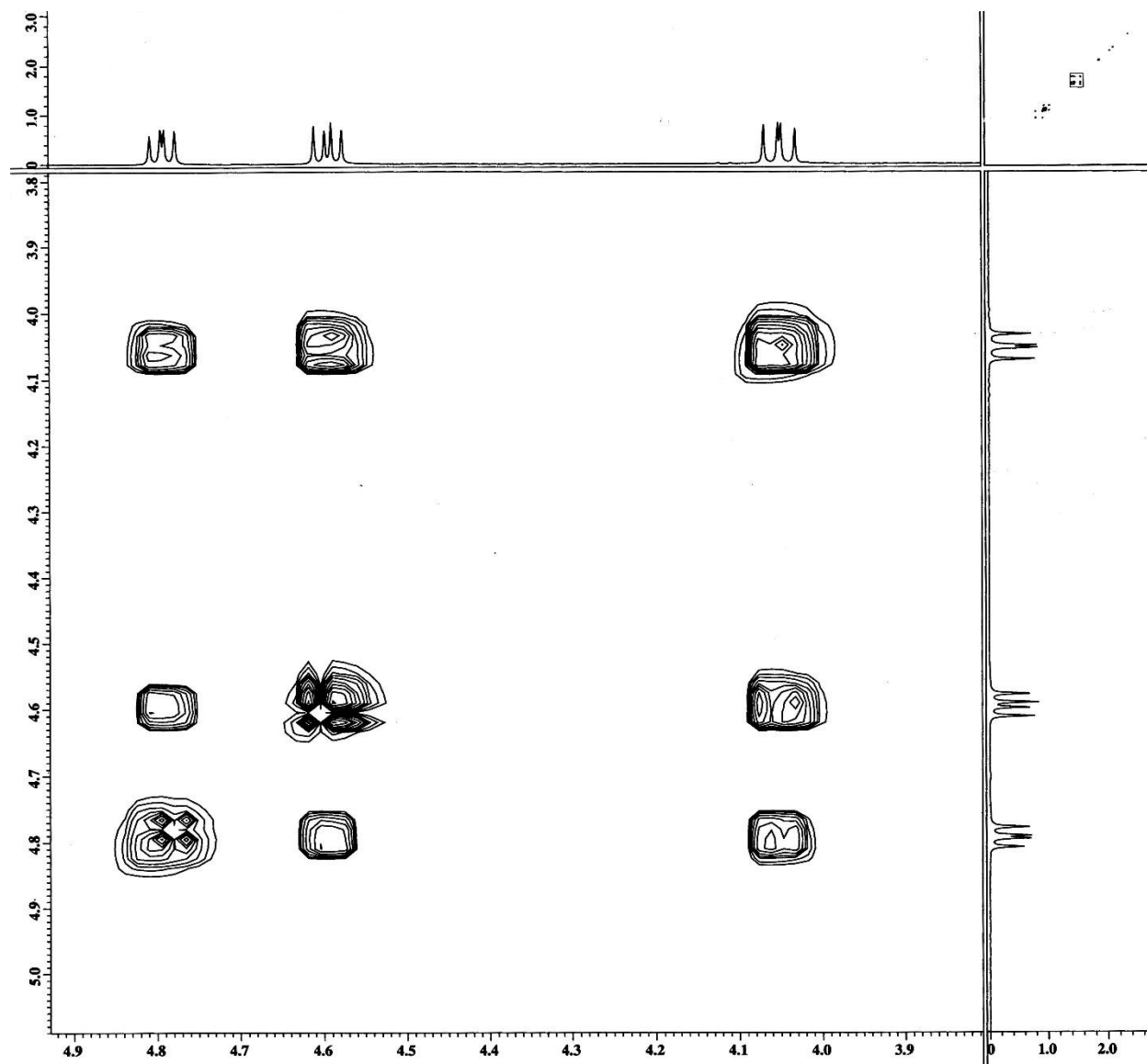
Figure 6. <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of 3a (125 MHz, CDCl<sub>3</sub>)



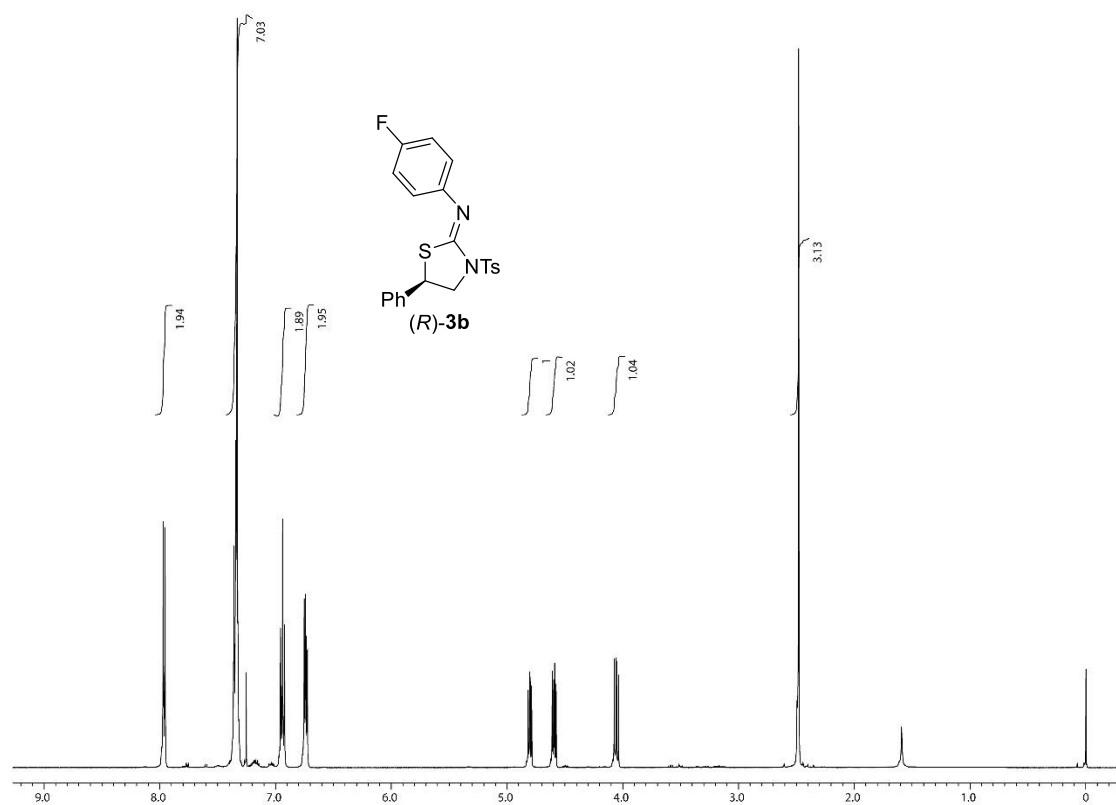
**Figure 7.** DEPT-135 spectrum of **3a** (125 MHz, CDCl<sub>3</sub>)



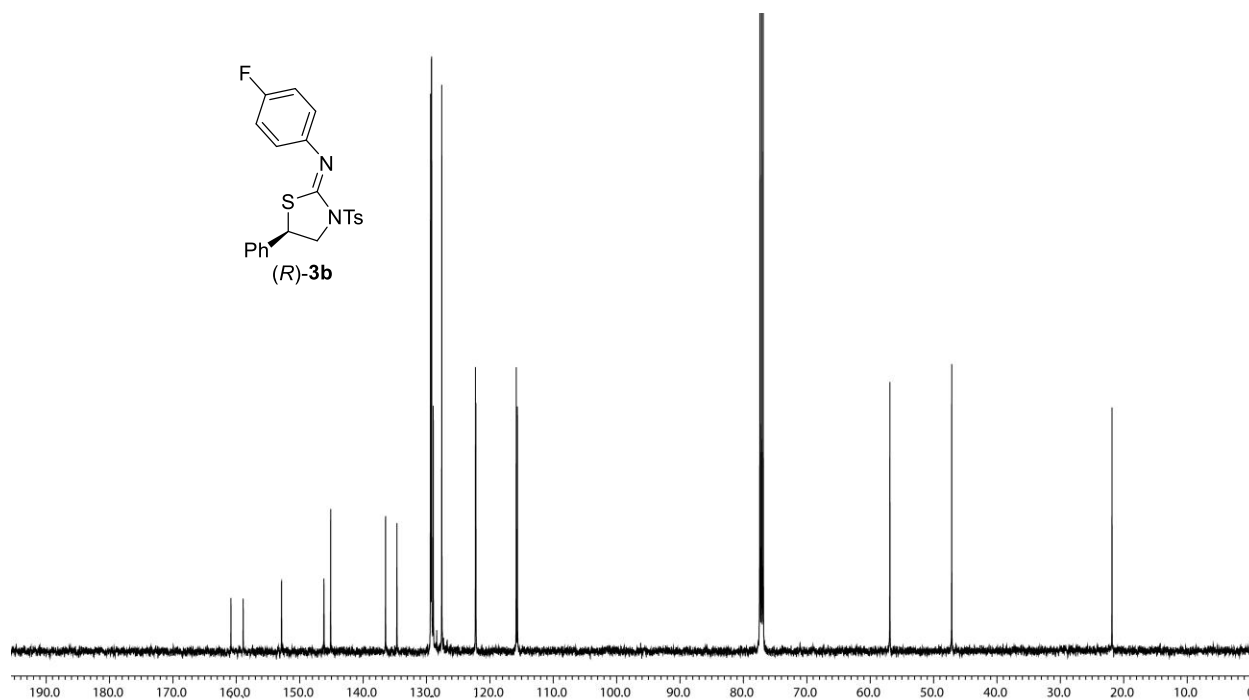
**Figure 8.** COSY spectrum of **3a** (500 MHz, CDCl<sub>3</sub>)



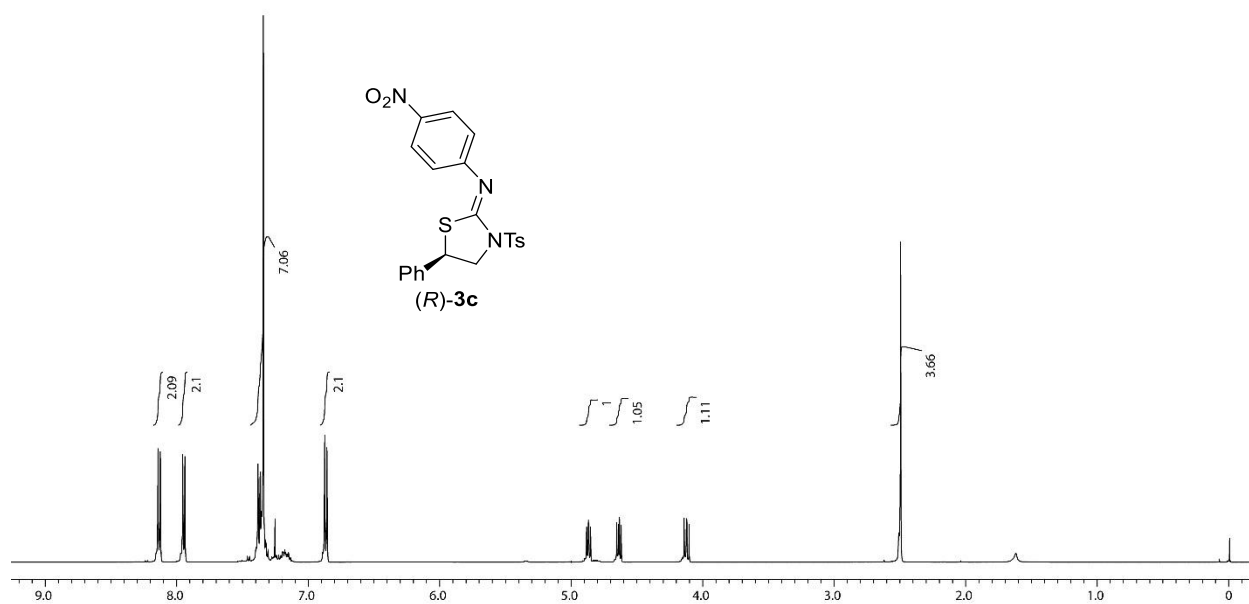
**Figure 9.** COSY spectrum of **3a** (500 MHz, CDCl<sub>3</sub>)



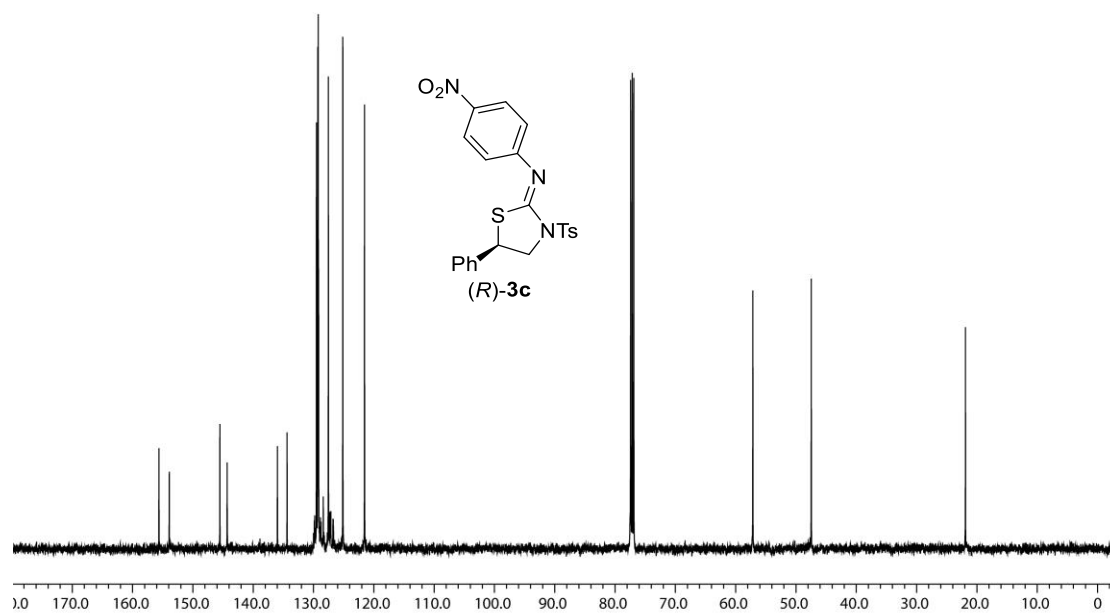
**Figure 10.** <sup>1</sup>H NMR spectrum of **3b** (500 MHz, CDCl<sub>3</sub>)



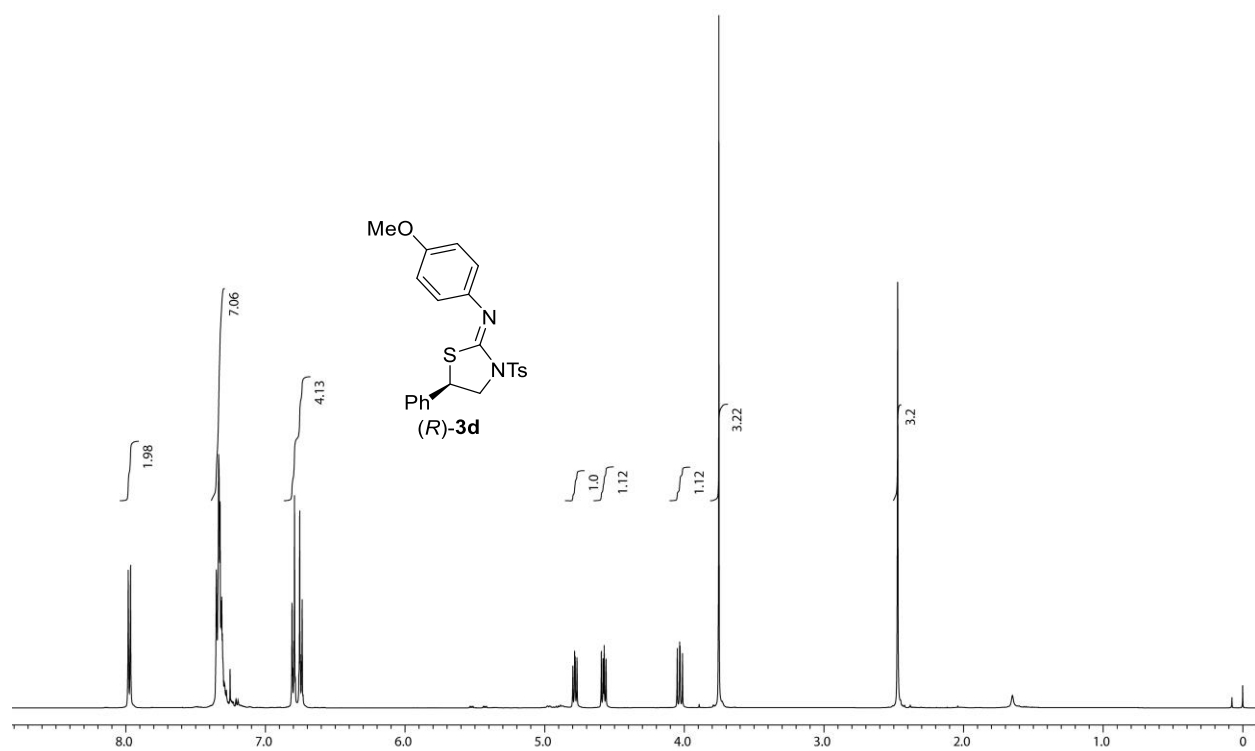
**Figure 11.** <sup>13</sup>C {<sup>1</sup>H} NMR spectrum of **3b** (125 MHz, CDCl<sub>3</sub>)



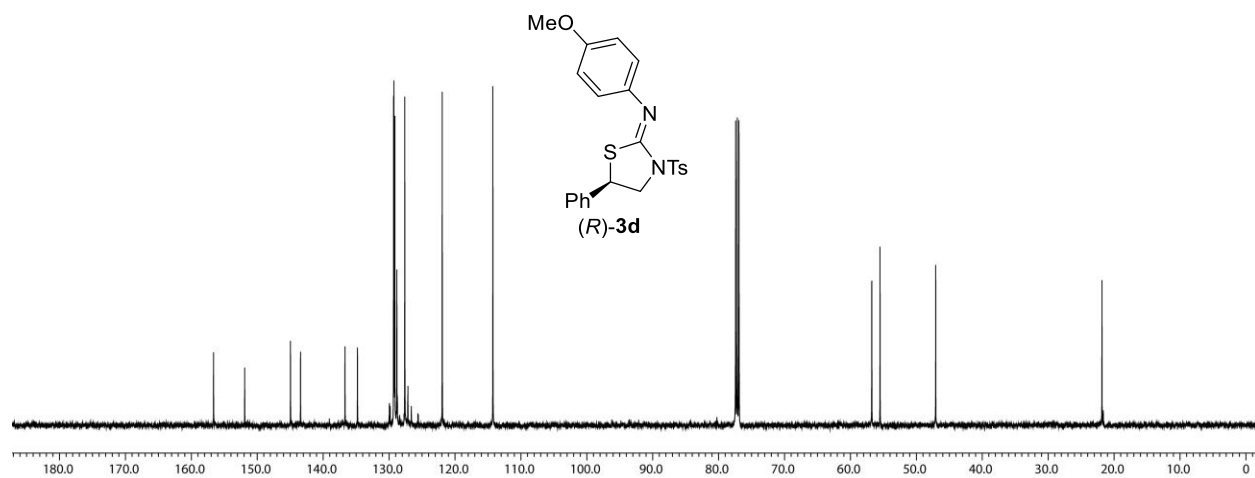
**Figure 12.**  $^1\text{H}$  NMR spectrum of **3c** (500 MHz,  $\text{CDCl}_3$ )



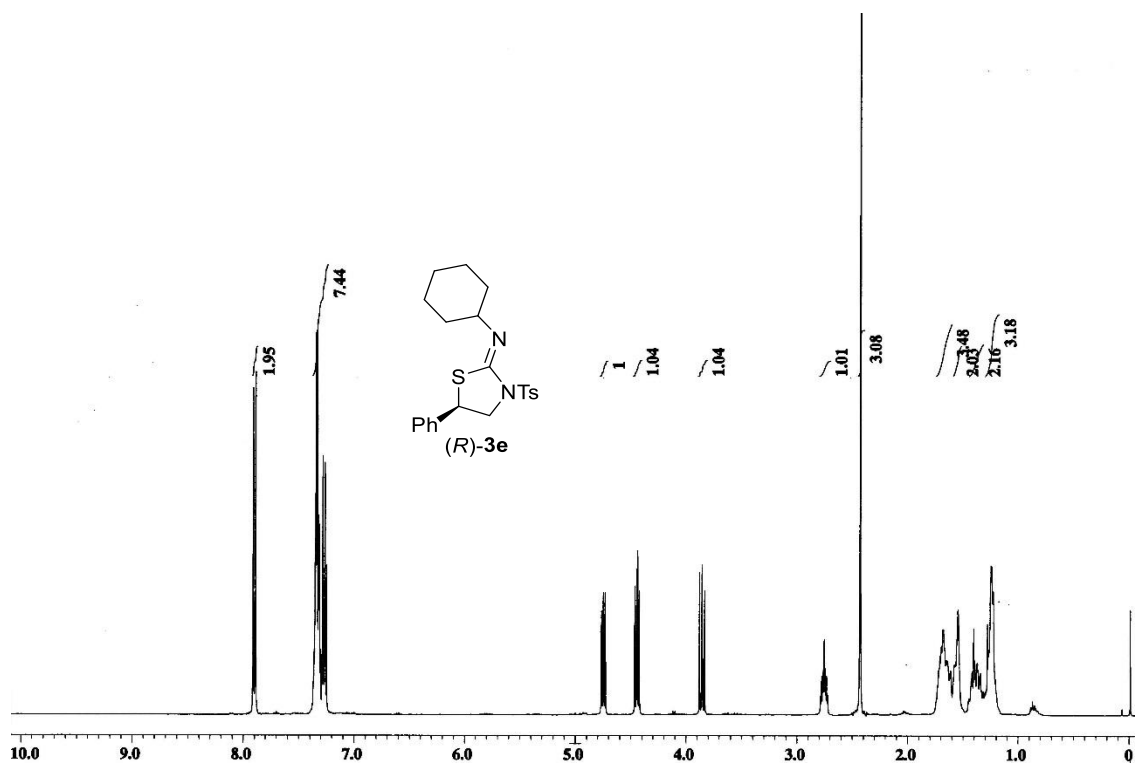
**Figure 13.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **3c** (125 MHz,  $\text{CDCl}_3$ )



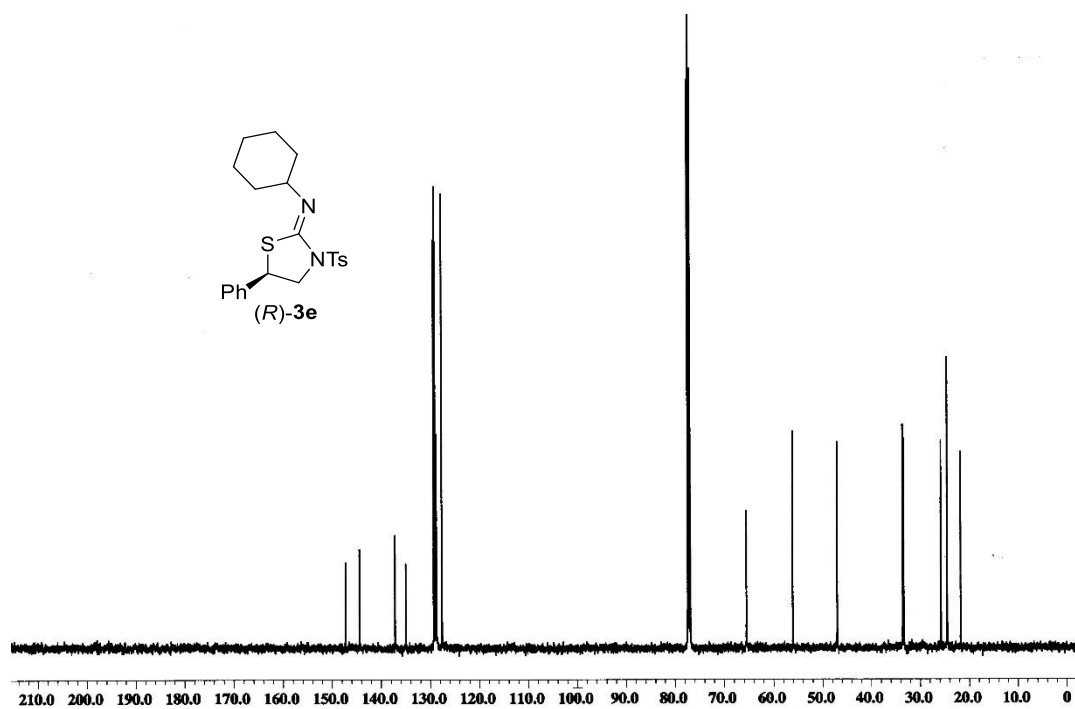
**Figure 14.**  $^1\text{H}$  NMR spectrum of **3d** (500 MHz,  $\text{CDCl}_3$ )



**Figure 15.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of **3d** (125 MHz,  $\text{CDCl}_3$ )

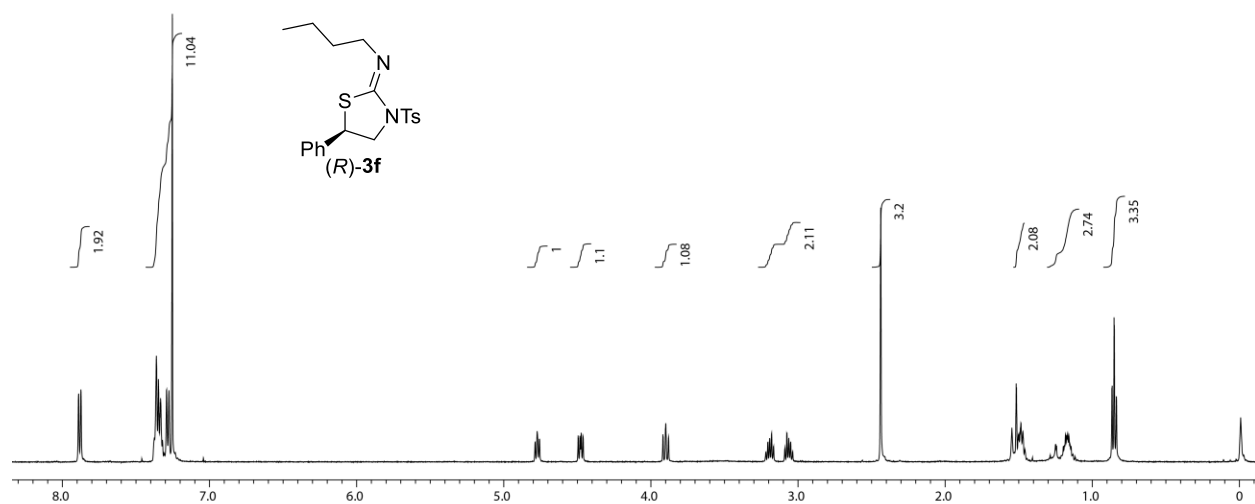


**Figure 16.** <sup>1</sup>H NMR spectrum of **3e** (500 MHz, CDCl<sub>3</sub>)

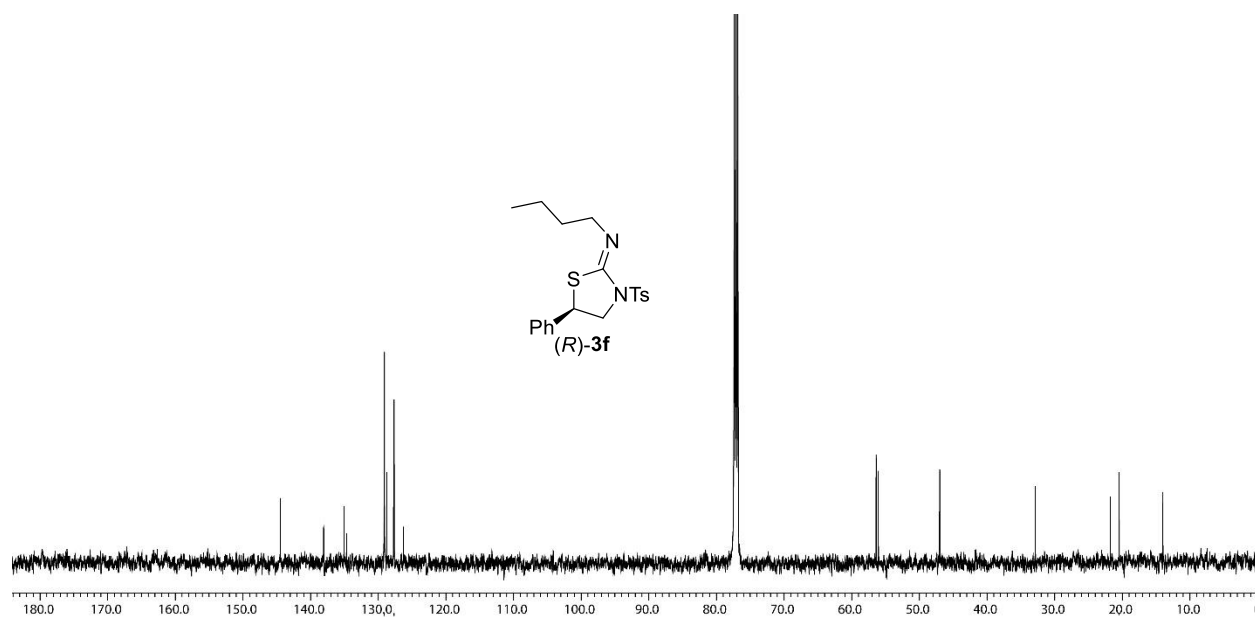


**Figure 17.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of **3e** (125 MHz, CDCl<sub>3</sub>)

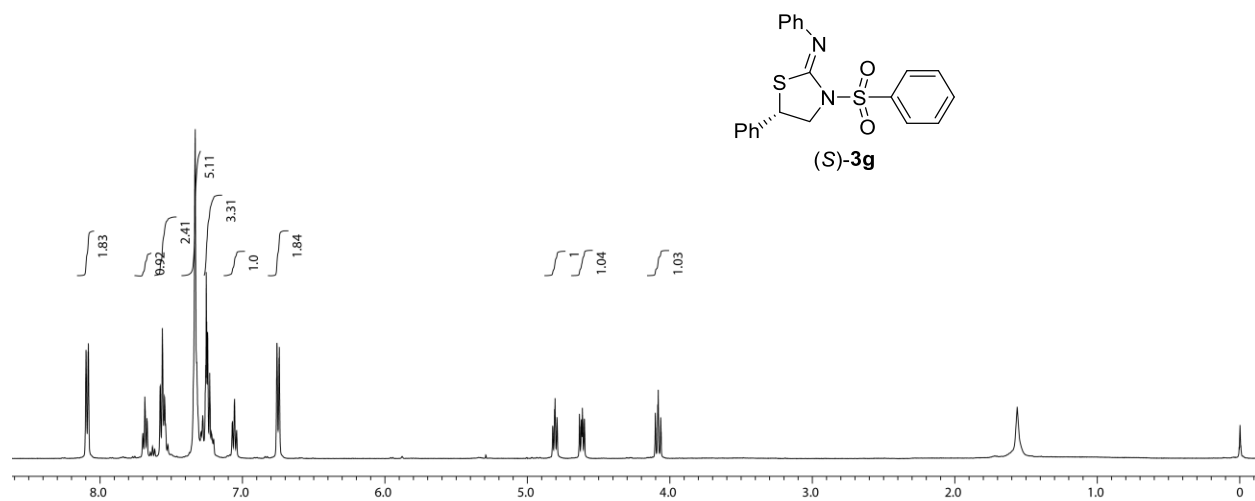




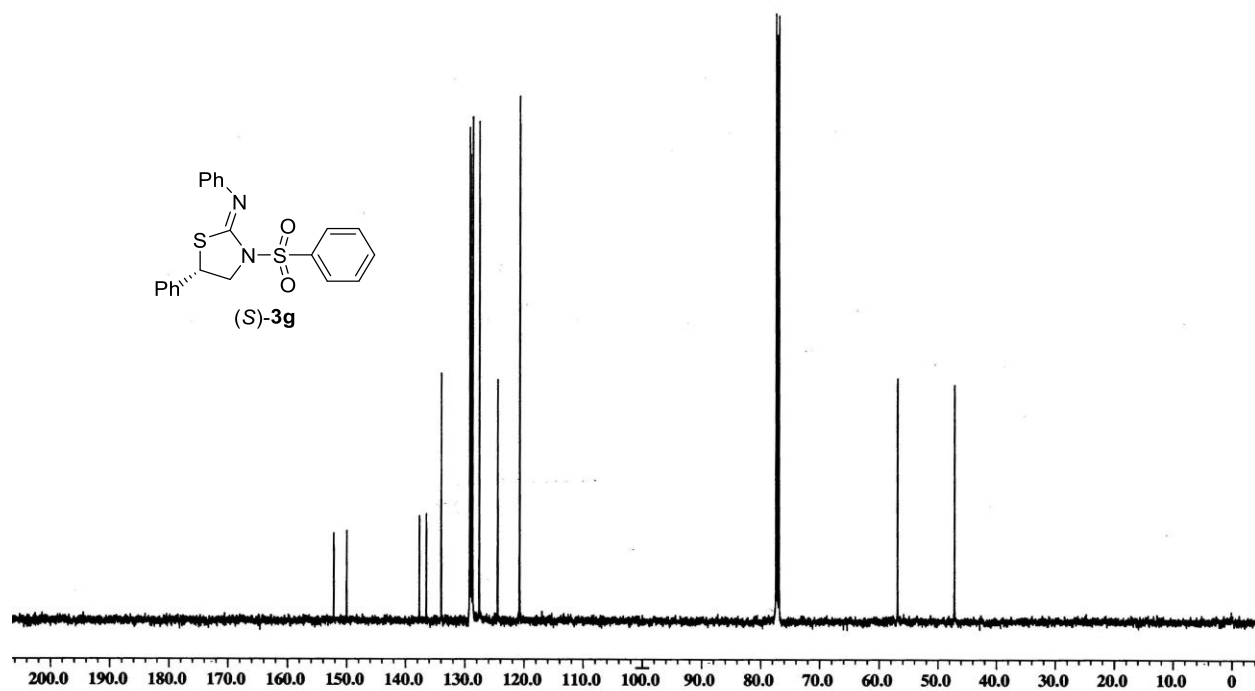
**Figure 18.** <sup>1</sup>H NMR spectrum of (*S*)-3f (500 MHz, CDCl<sub>3</sub>)



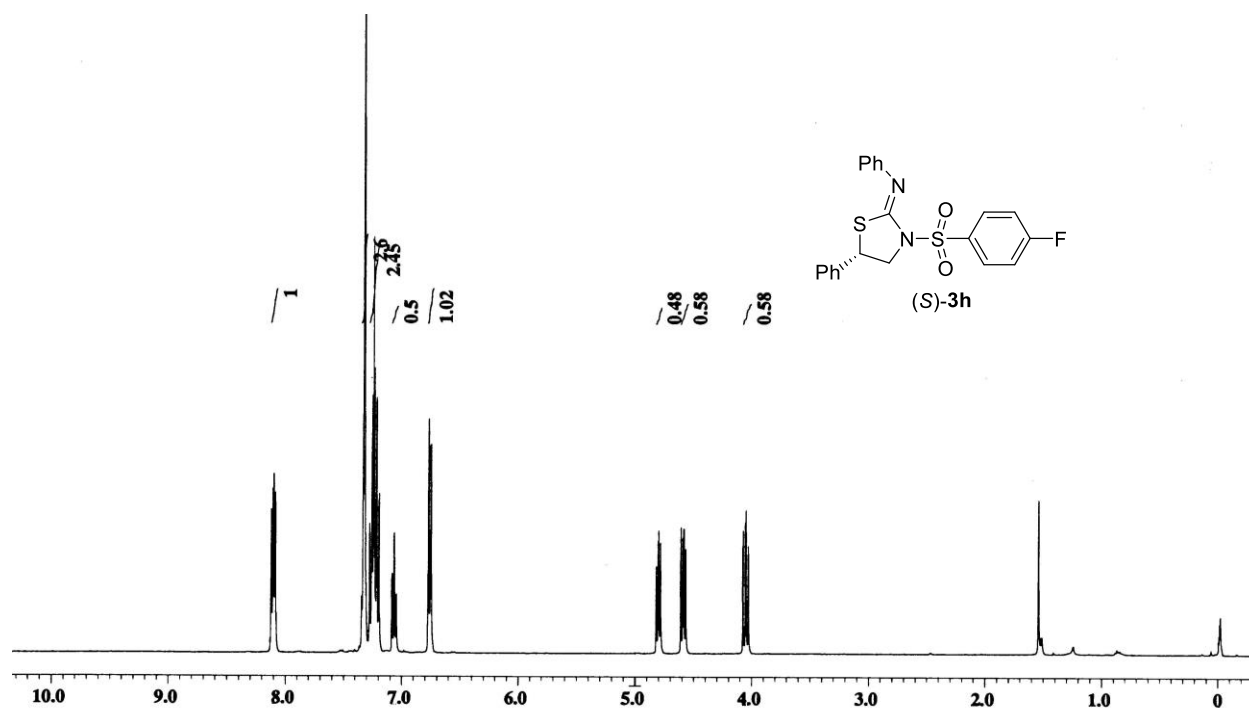
**Figure 19.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of (*S*)-3f (125 MHz, CDCl<sub>3</sub>)



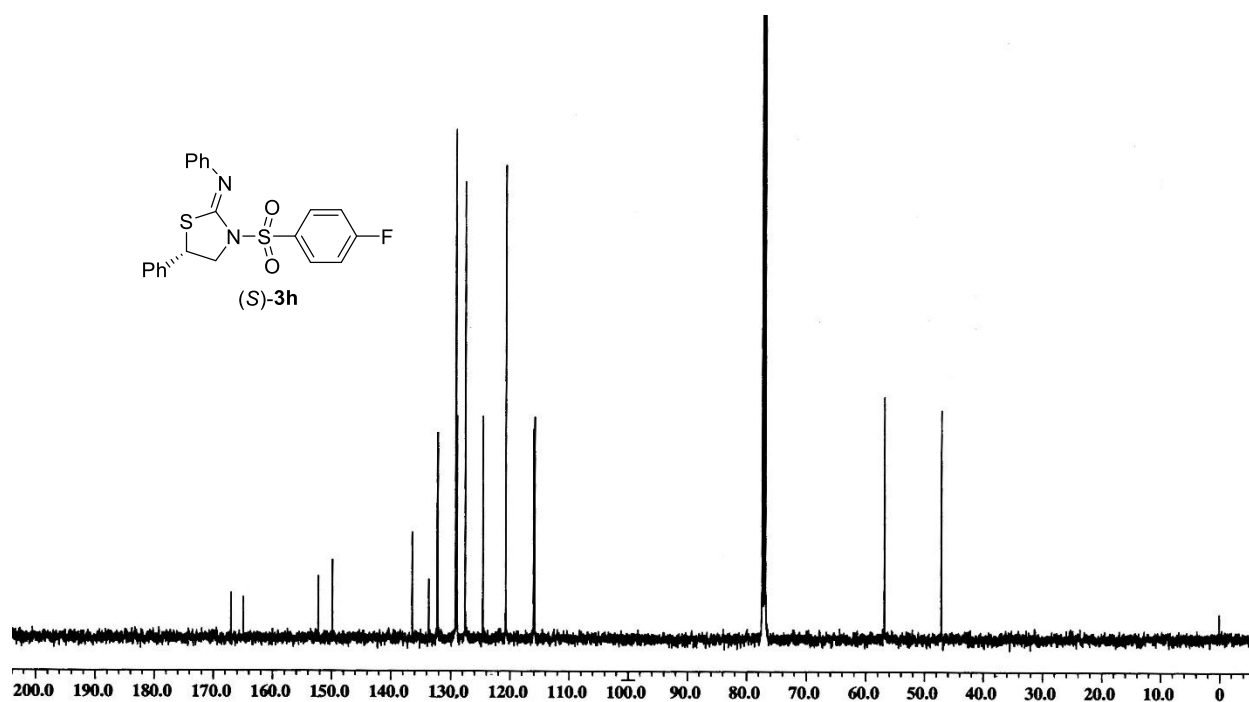
**Figure 20.** <sup>1</sup>H NMR spectrum of (S)-3g (500 MHz, CDCl<sub>3</sub>)



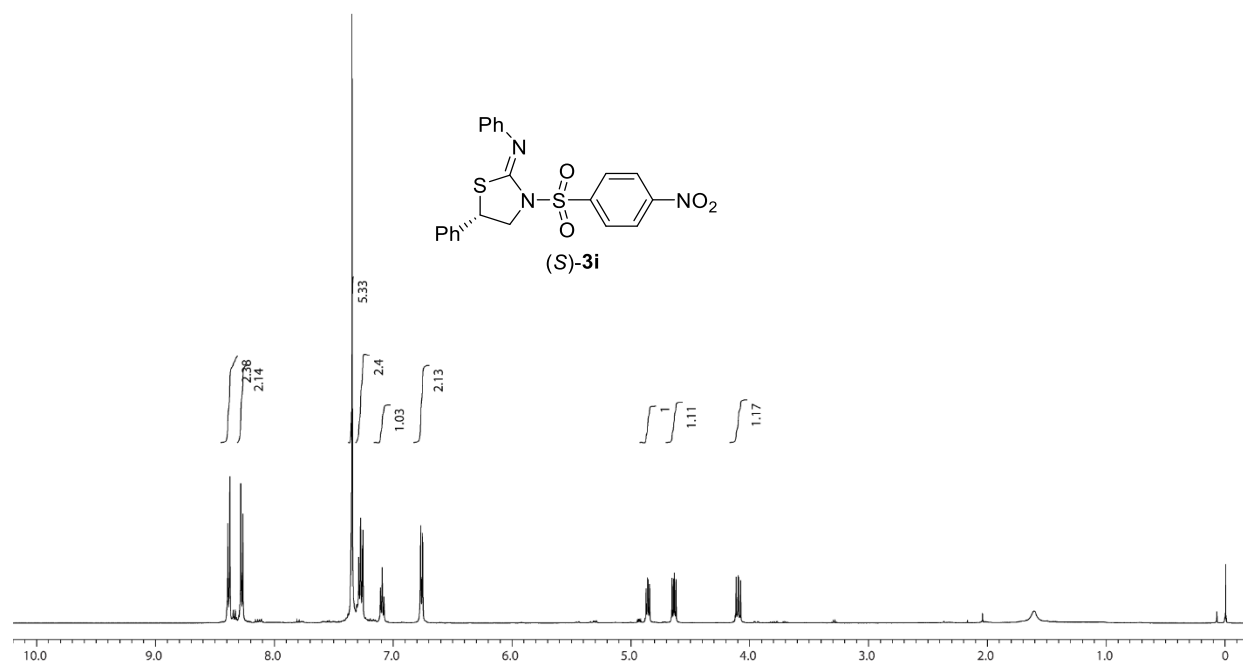
**Figure 21.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of (S)-3g (125 MHz, CDCl<sub>3</sub>)



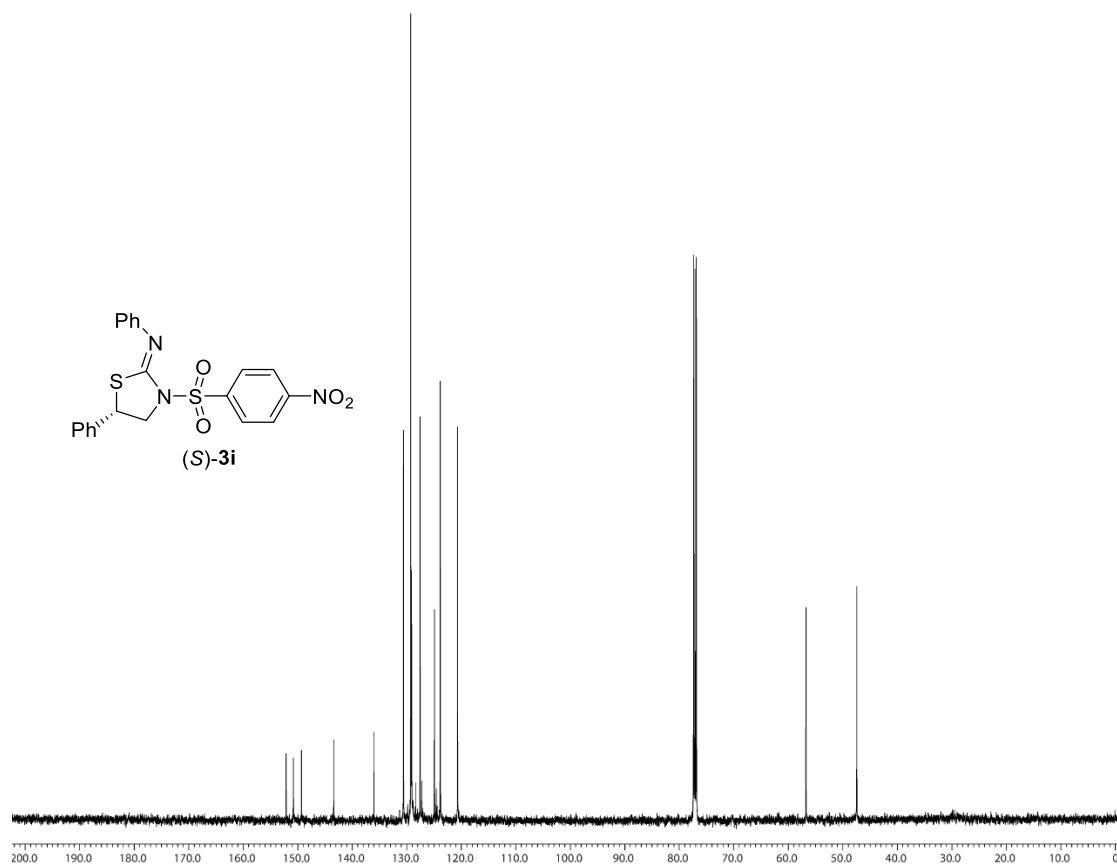
**Figure 22.** <sup>1</sup>H NMR spectrum of (S)-3h (400 MHz, CDCl<sub>3</sub>)



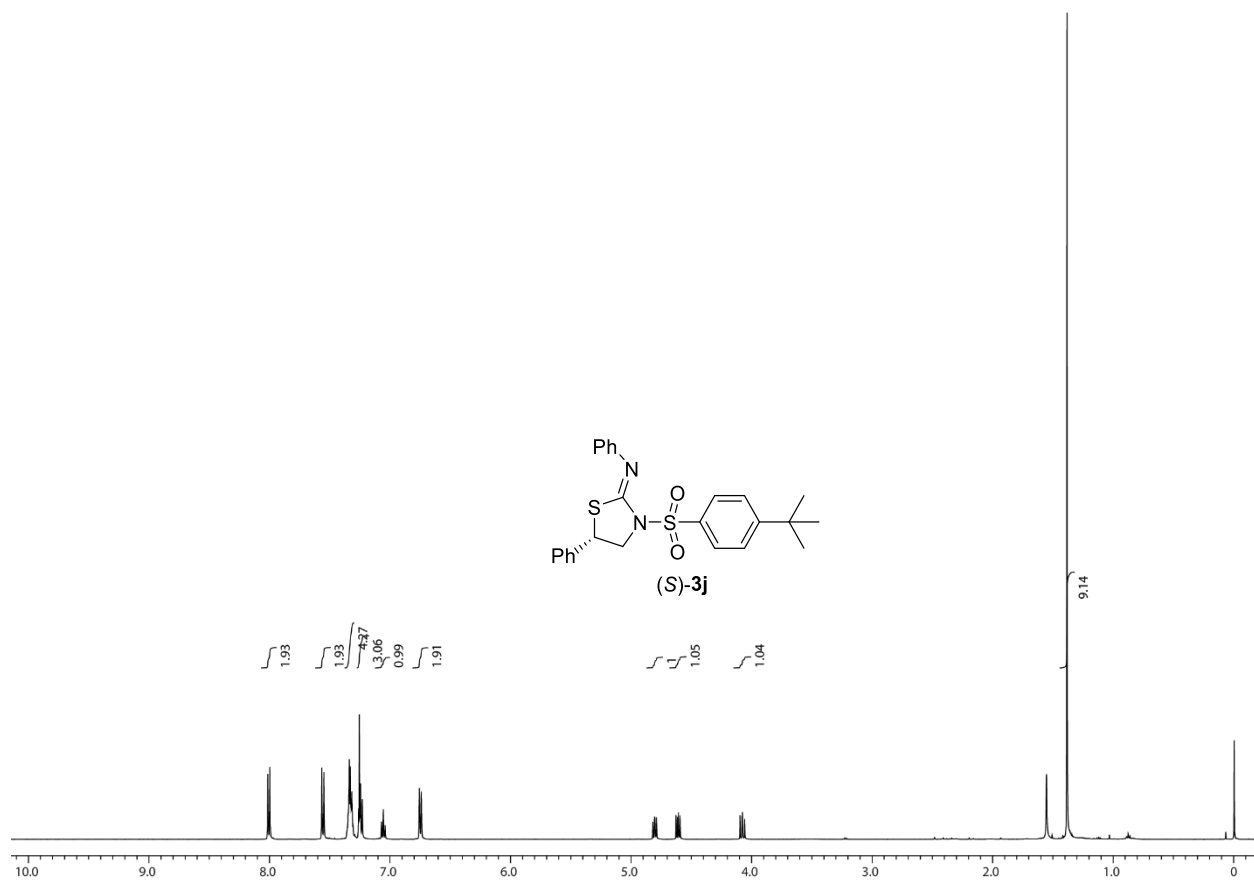
**Figure 23.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of (S)-3h (125 MHz, CDCl<sub>3</sub>)



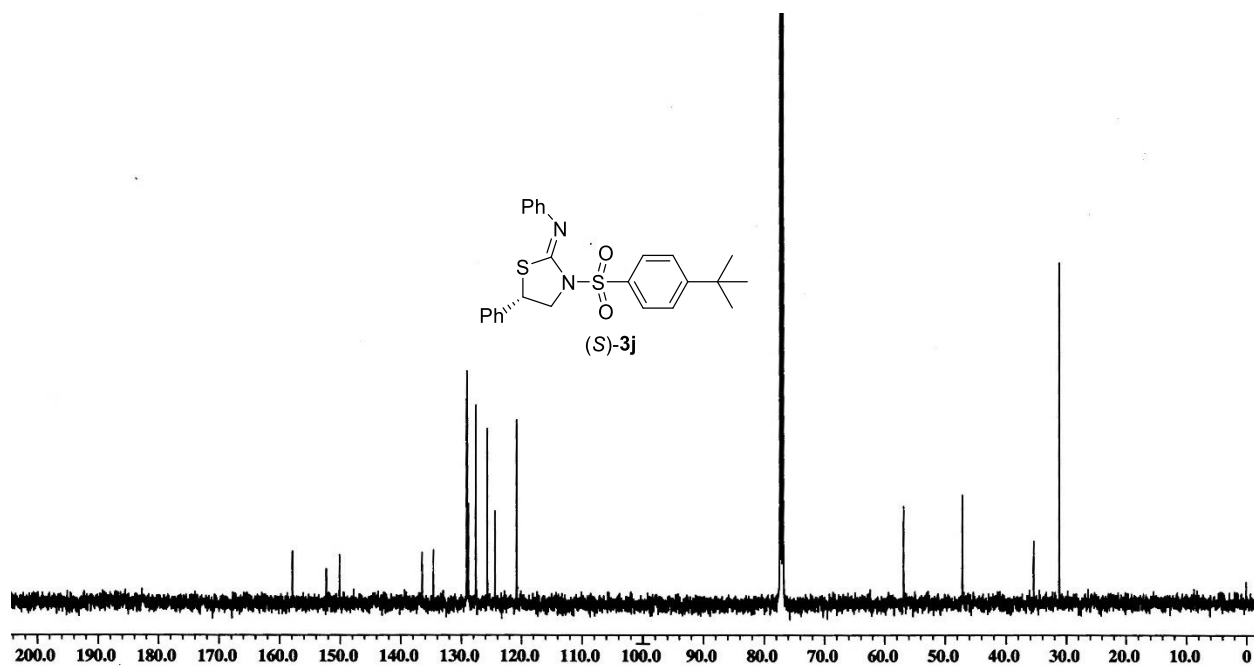
**Figure 24.** <sup>1</sup>H NMR spectrum of (S)-3i (500 MHz, CDCl<sub>3</sub>)



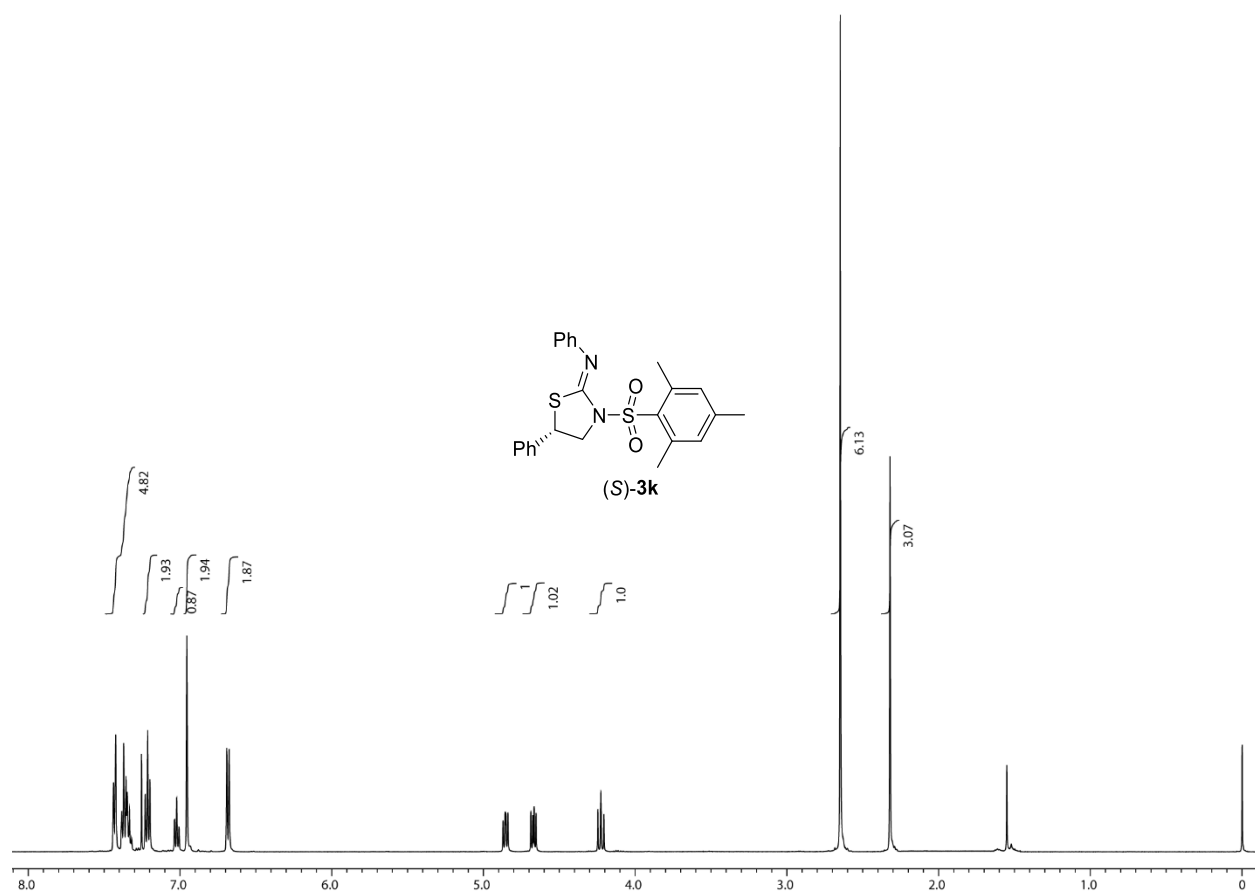
**Figure 25.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of (S)-3i (125 MHz, CDCl<sub>3</sub>)



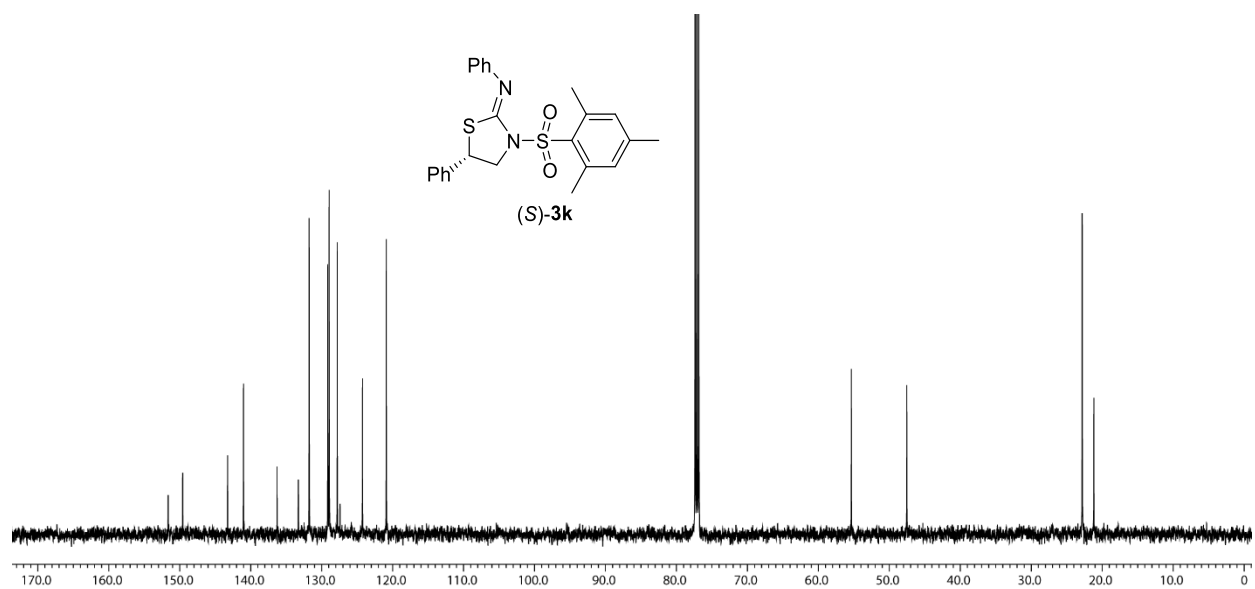
**Figure 26.**  $^1\text{H}$  NMR spectrum of (S)-3j (500 MHz,  $\text{CDCl}_3$ )



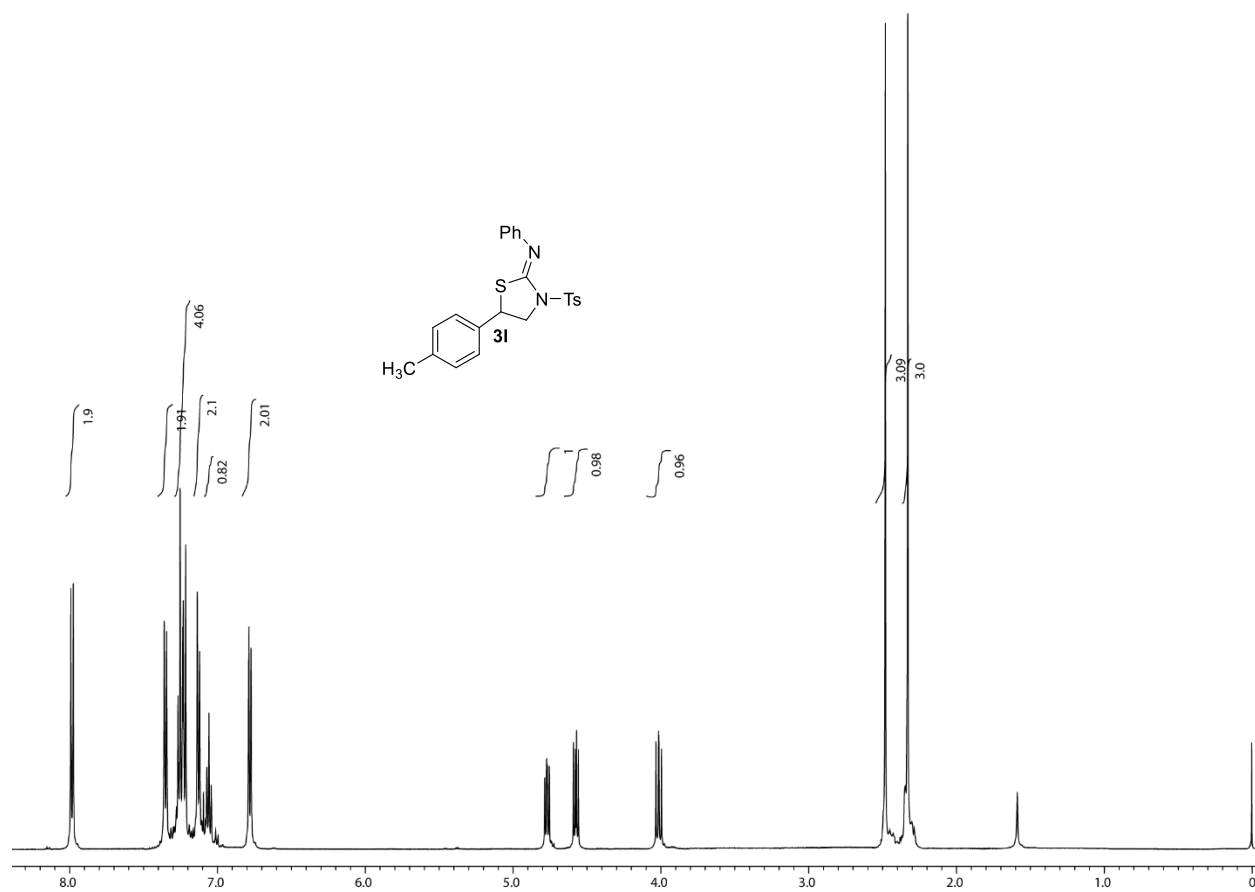
**Figure 27.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of (S)-3j (125 MHz,  $\text{CDCl}_3$ )



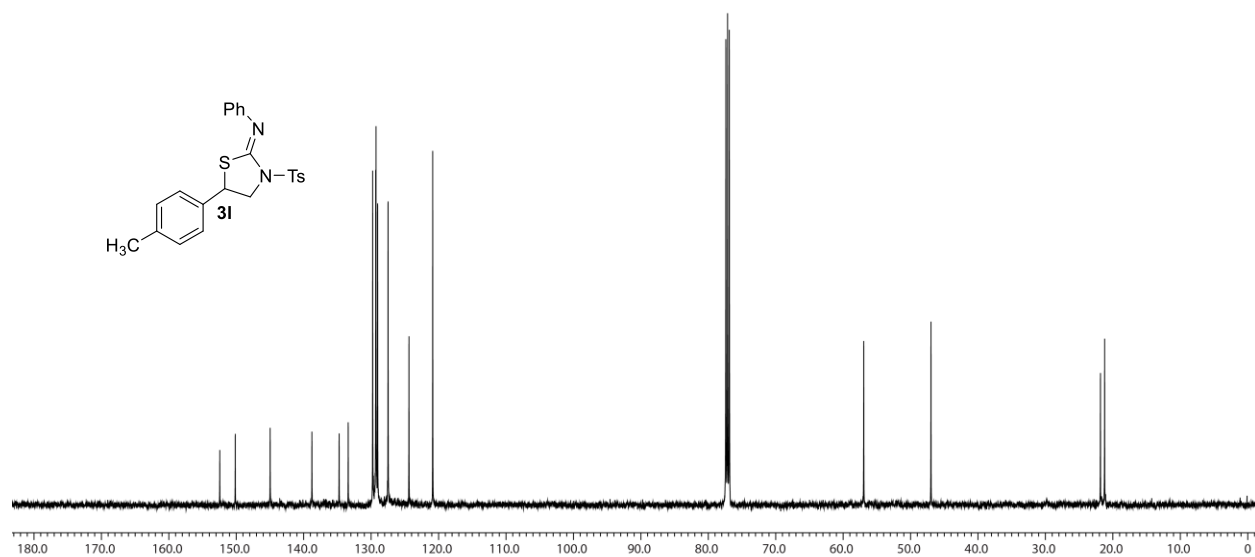
**Figure 28.** <sup>1</sup>H NMR spectrum of (S)-3k (500 MHz, CDCl<sub>3</sub>)



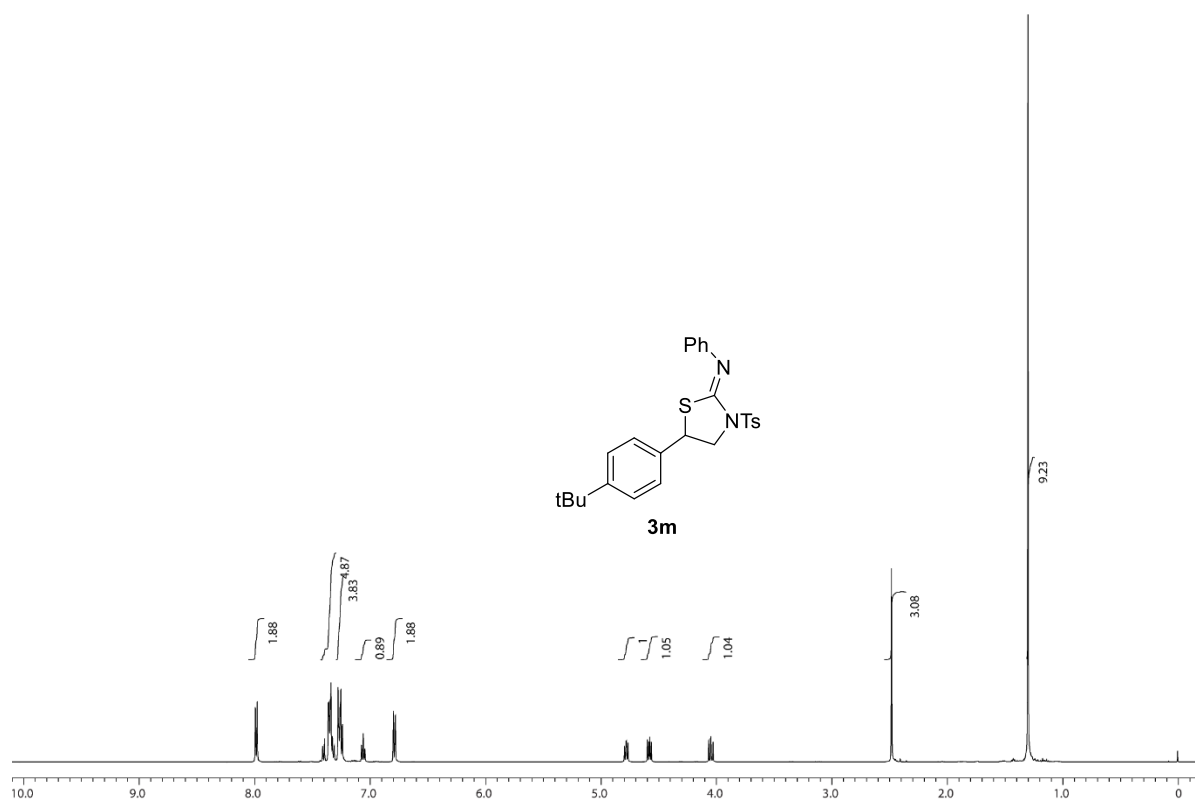
**Figure 29.** <sup>13</sup>C {<sup>1</sup>H} NMR spectrum of (S)-3k (125 MHz, CDCl<sub>3</sub>)



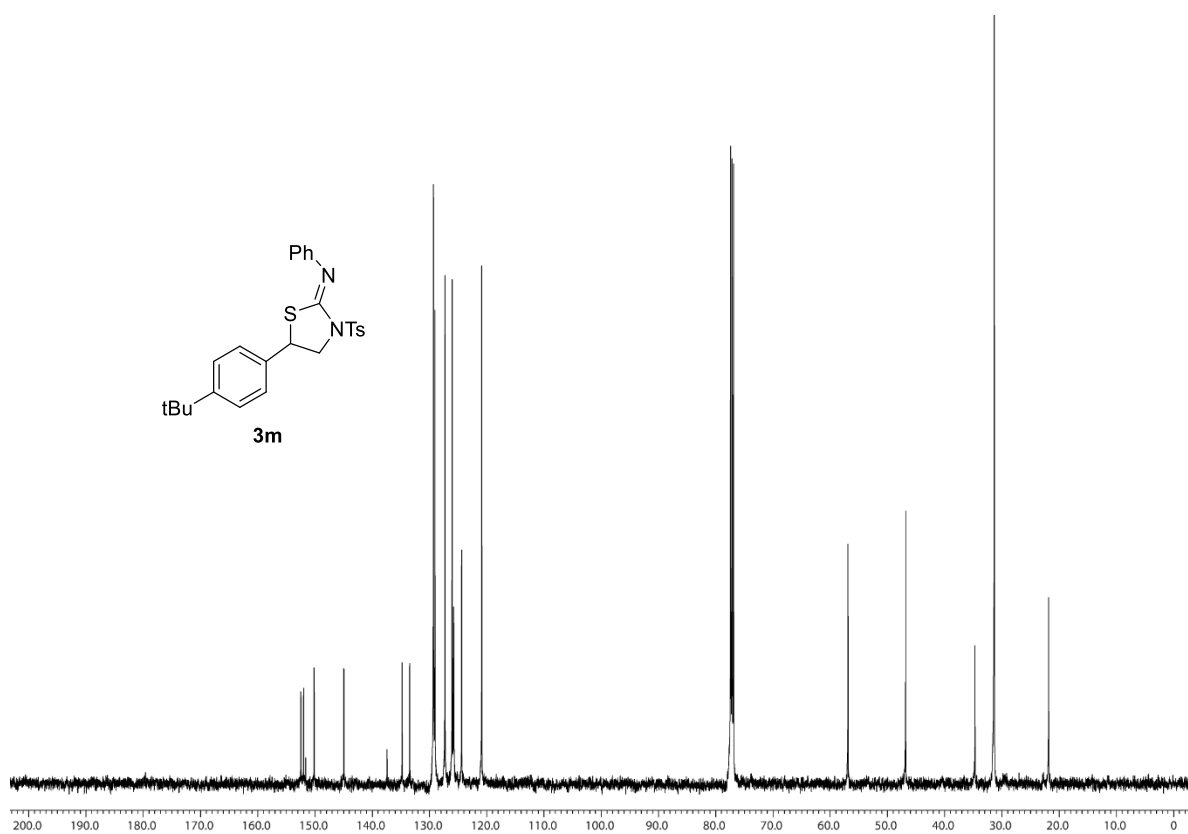
**Figure 30.** <sup>1</sup>H NMR spectrum of **3I** (500 MHz, CDCl<sub>3</sub>)



**Figure 31.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of **3I** (125 MHz, CDCl<sub>3</sub>)

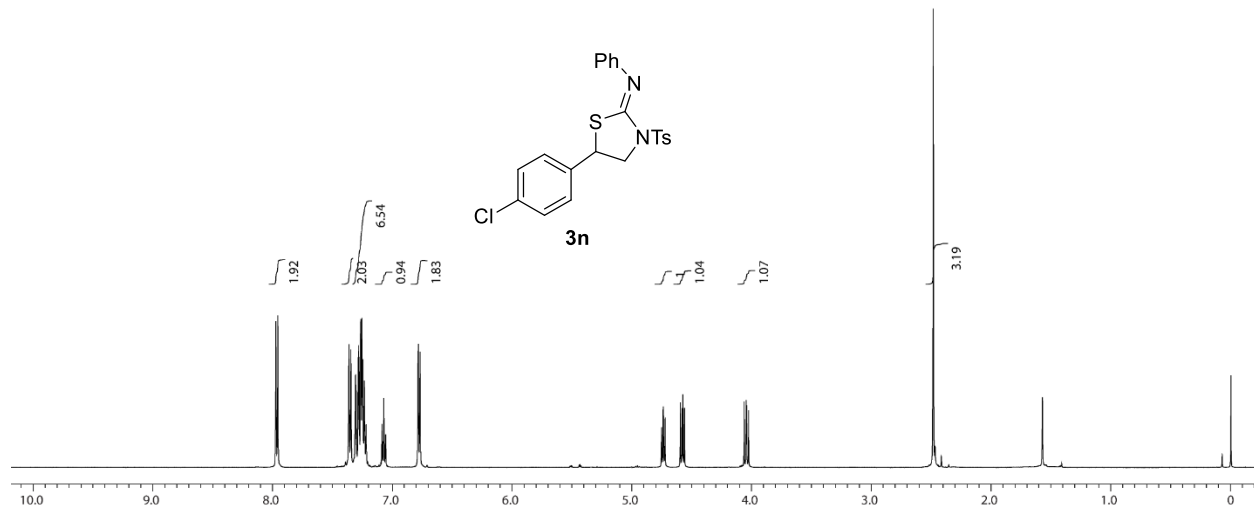


**Figure 32.** <sup>1</sup>H NMR spectrum of **3m** (500 MHz, CDCl<sub>3</sub>)

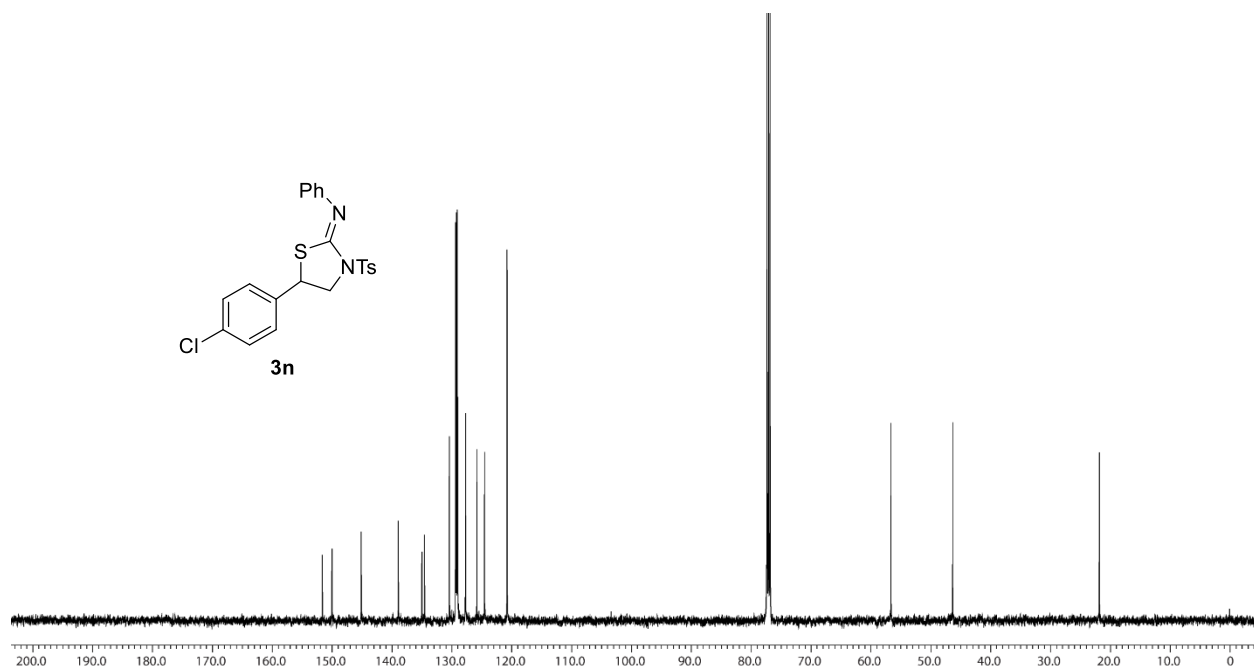


**Figure 33.** <sup>13</sup>C {<sup>1</sup>H} NMR spectrum of **3m** (125 MHz, CDCl<sub>3</sub>)

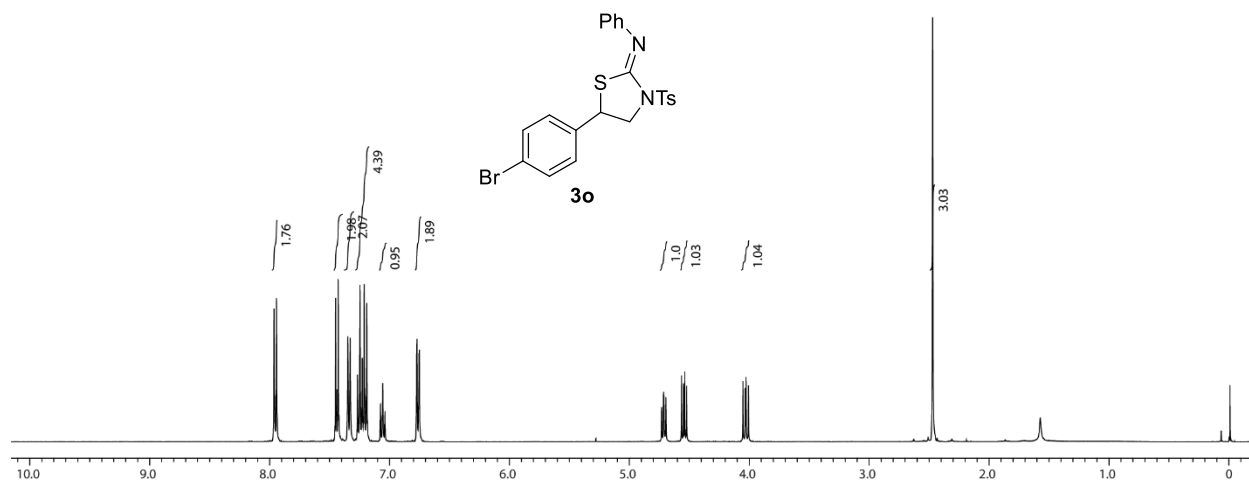




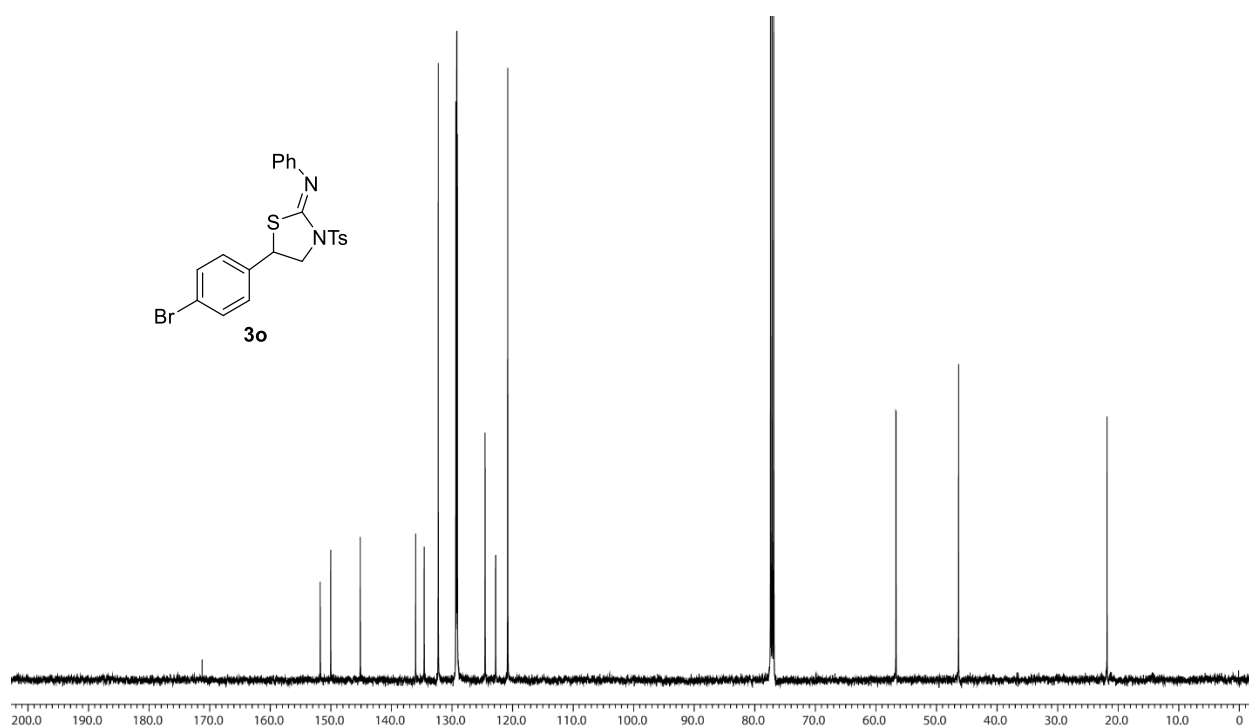
**Figure 34.** <sup>1</sup>H NMR spectrum of **3n** (500 MHz, CDCl<sub>3</sub>)



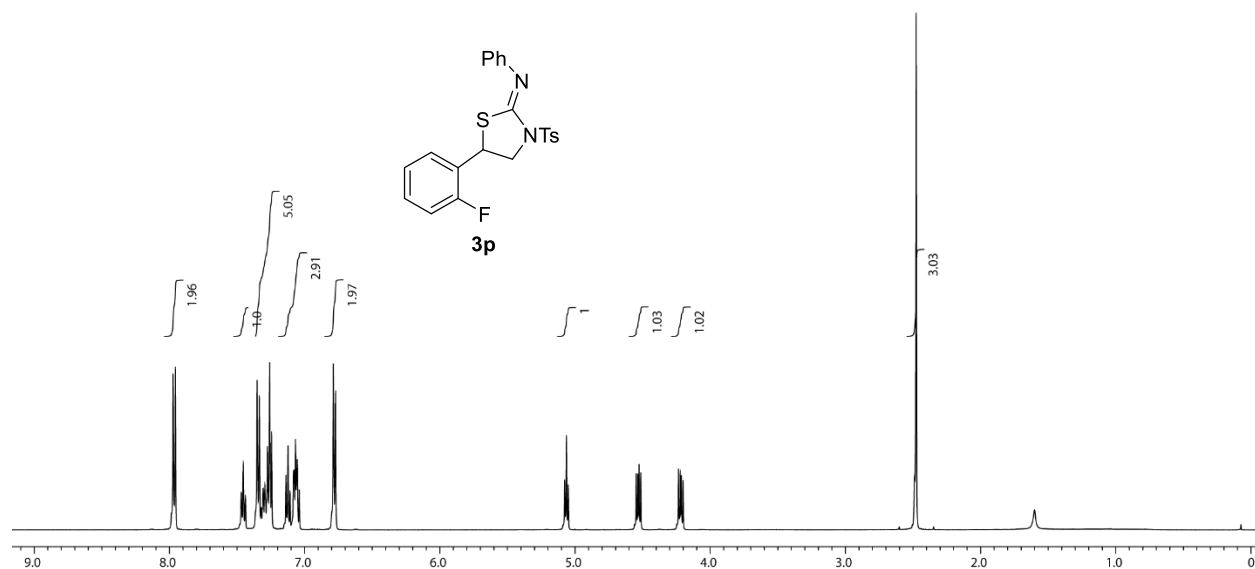
**Figure 35.** <sup>13</sup>C {<sup>1</sup>H} NMR spectrum of **3n** (125 MHz, CDCl<sub>3</sub>)



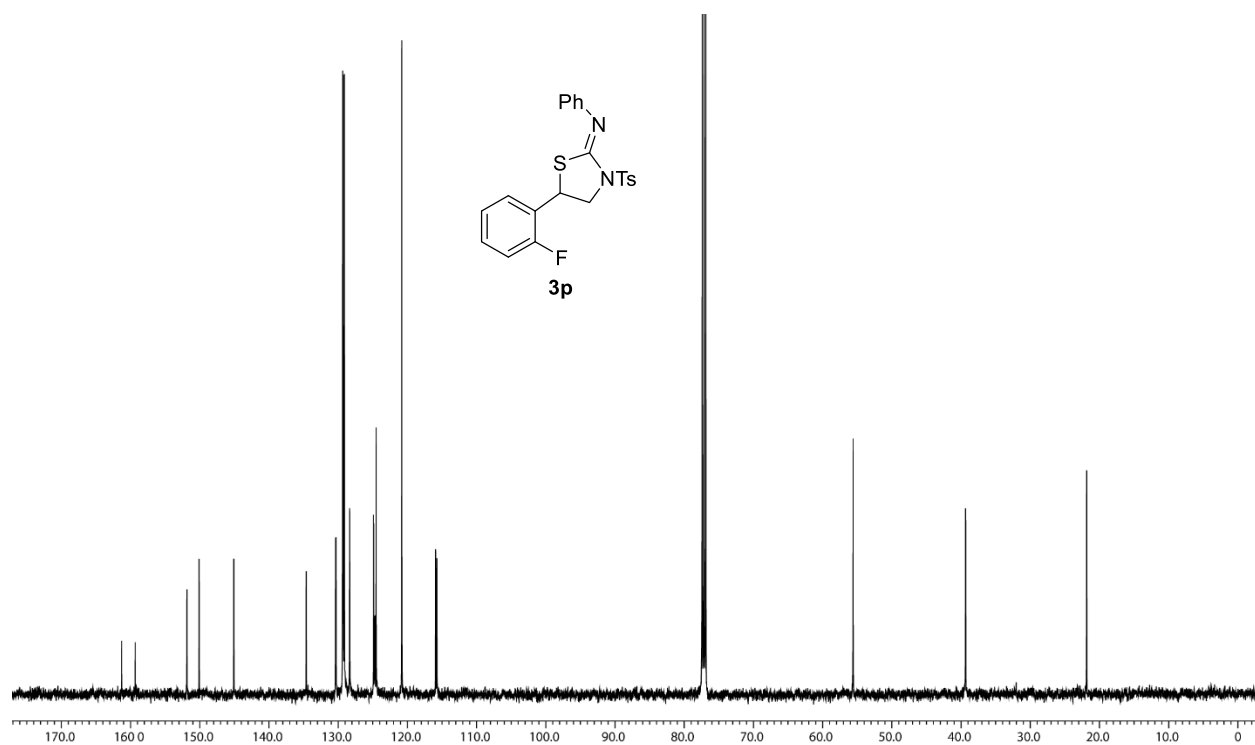
**Figure 36.** <sup>1</sup>H NMR spectrum of **3o** (500 MHz, CDCl<sub>3</sub>)



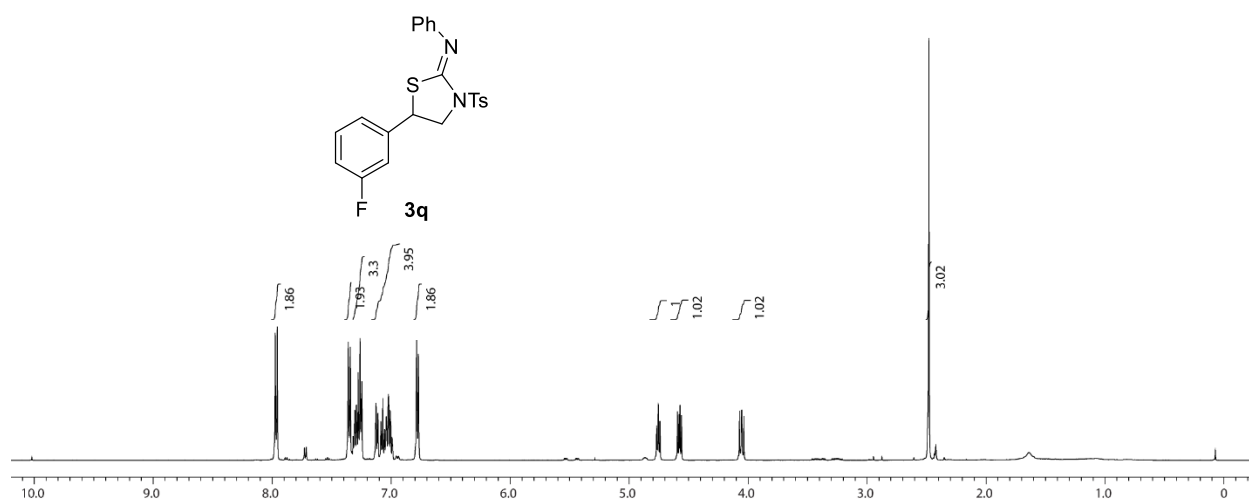
**Figure 37.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of **3o** (125 MHz, CDCl<sub>3</sub>)



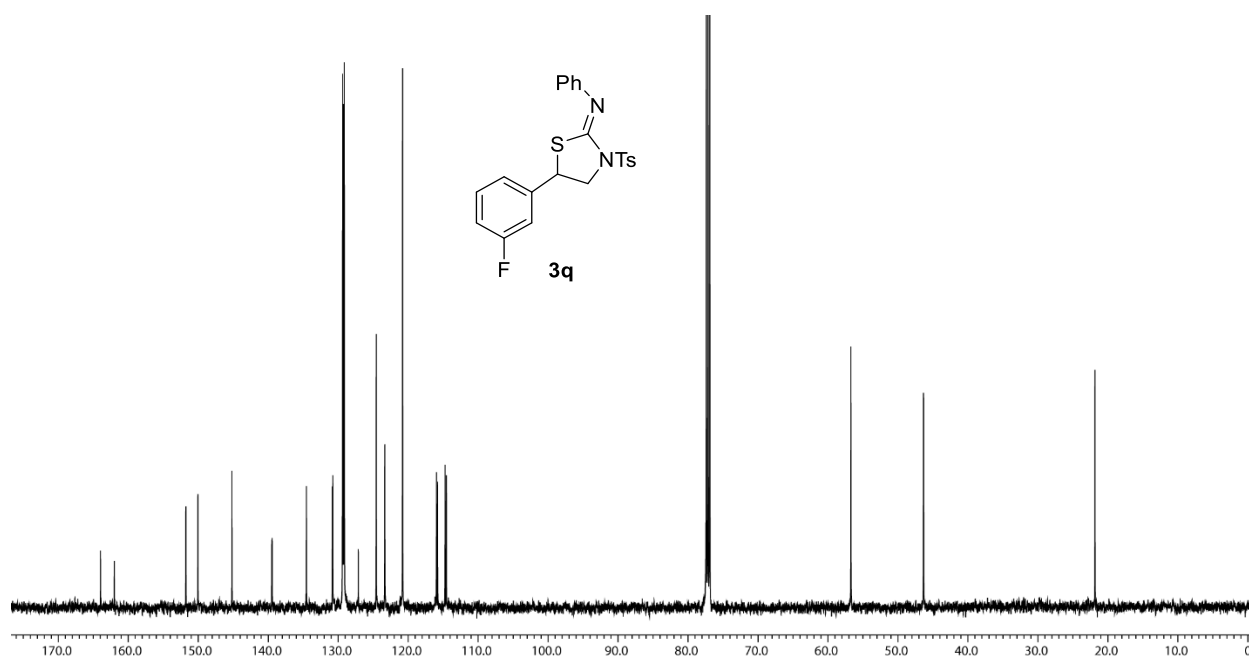
**Figure 38.** <sup>1</sup>H NMR spectrum of **3p** (500 MHz, CDCl<sub>3</sub>)



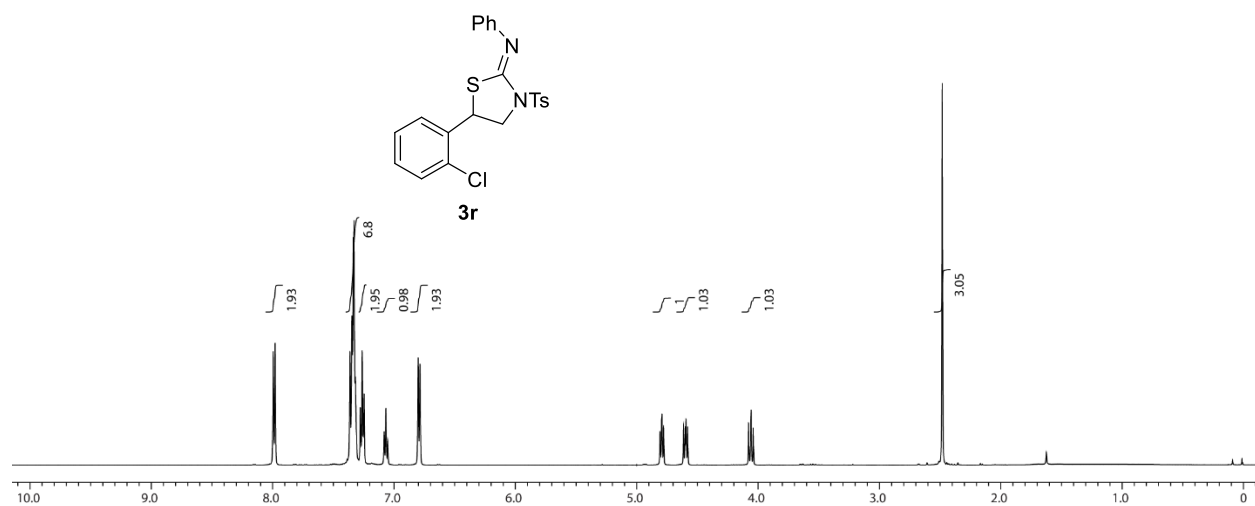
**Figure 39.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of **3p** (125 MHz, CDCl<sub>3</sub>)



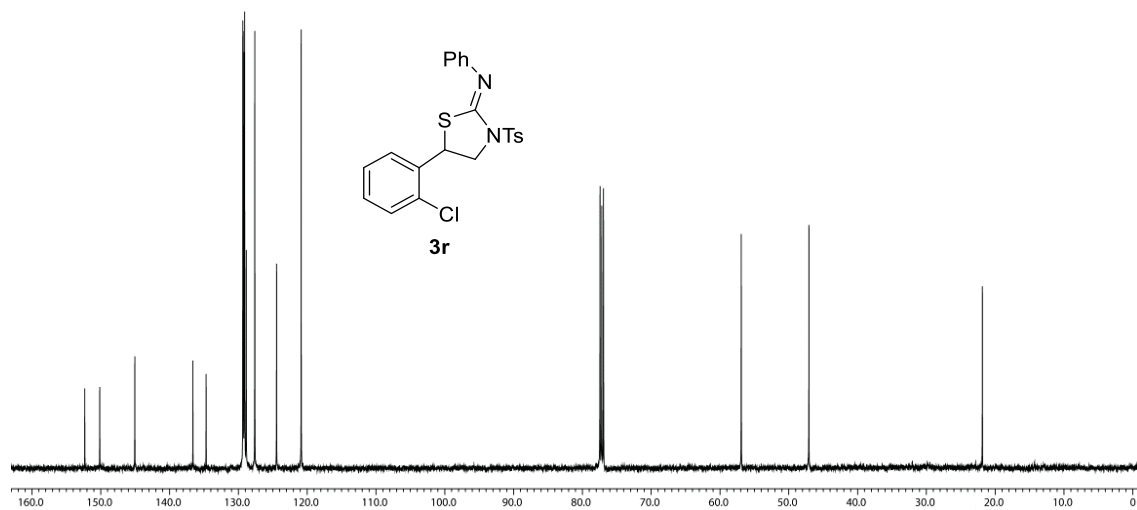
**Figure 40.** <sup>1</sup>H NMR spectrum of **3q** (500 MHz, CDCl<sub>3</sub>)



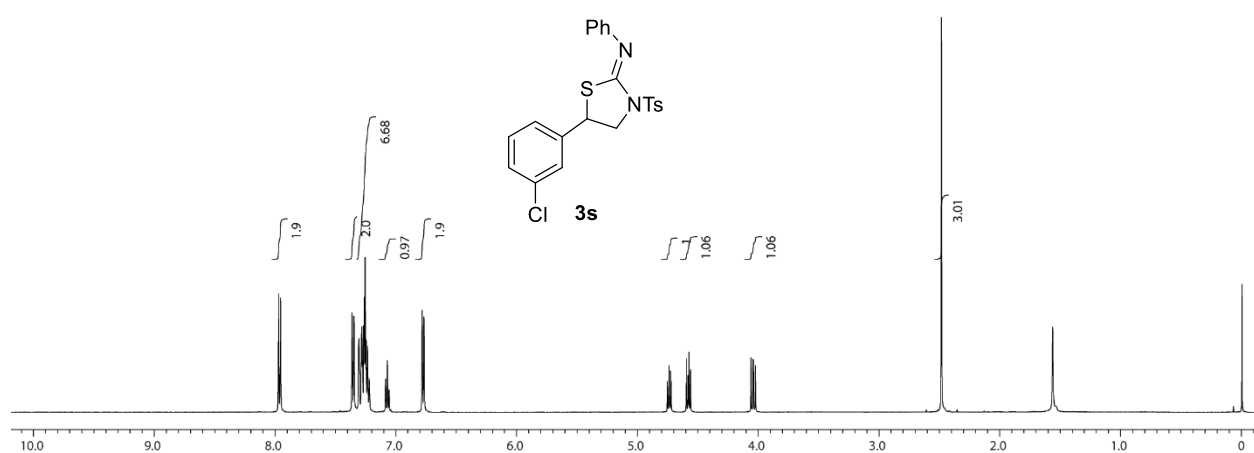
**Figure 41.** <sup>13</sup>C {<sup>1</sup>H} NMR spectrum of **3q** (125 MHz, CDCl<sub>3</sub>)



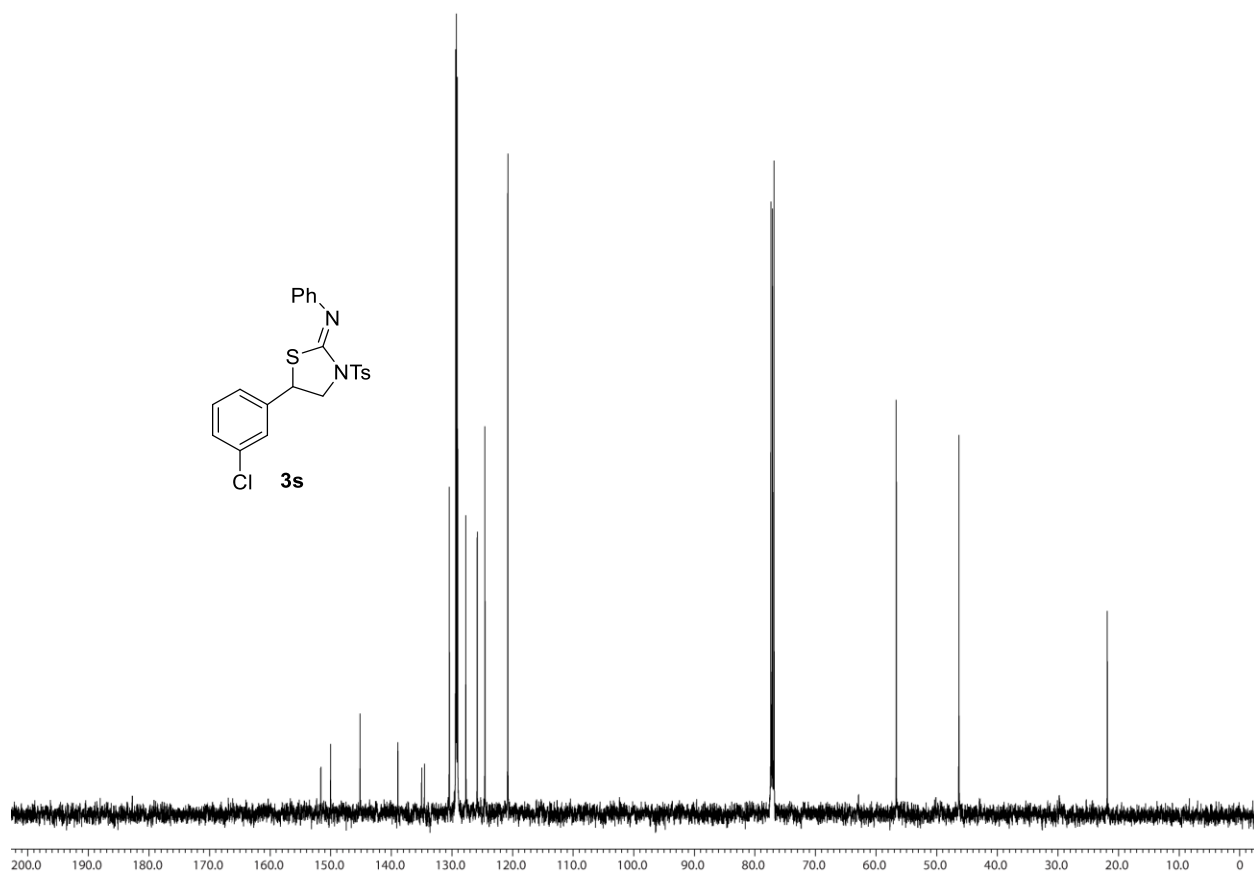
**Figure 42.** <sup>1</sup>H NMR spectrum of **3r** (500 MHz, CDCl<sub>3</sub>)



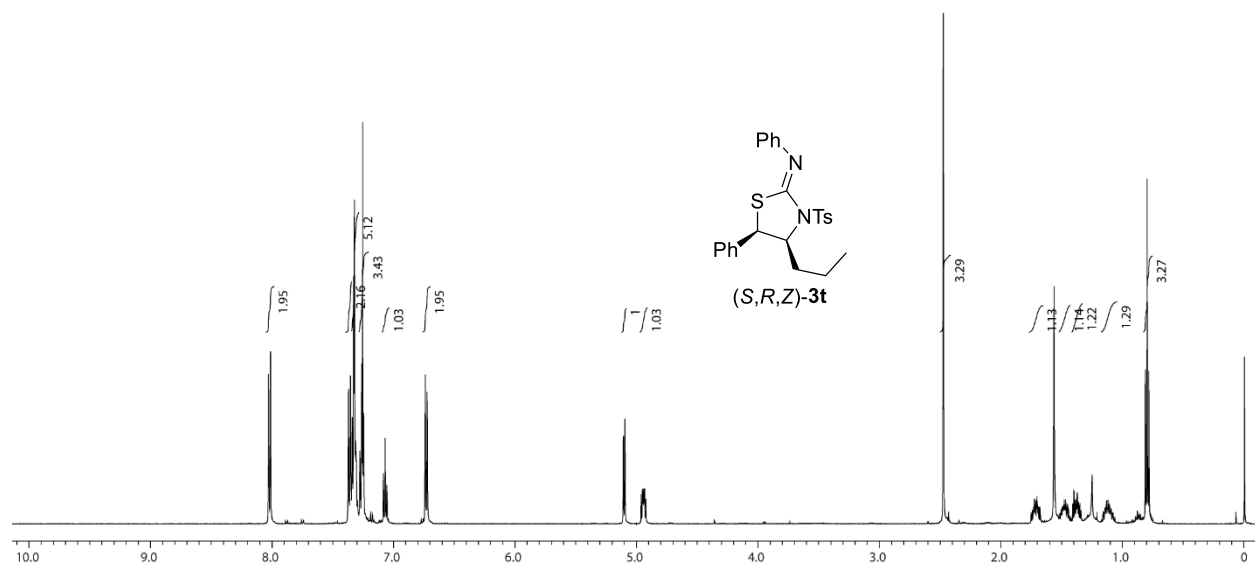
**Figure 43.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of **3r** (125 MHz, CDCl<sub>3</sub>)



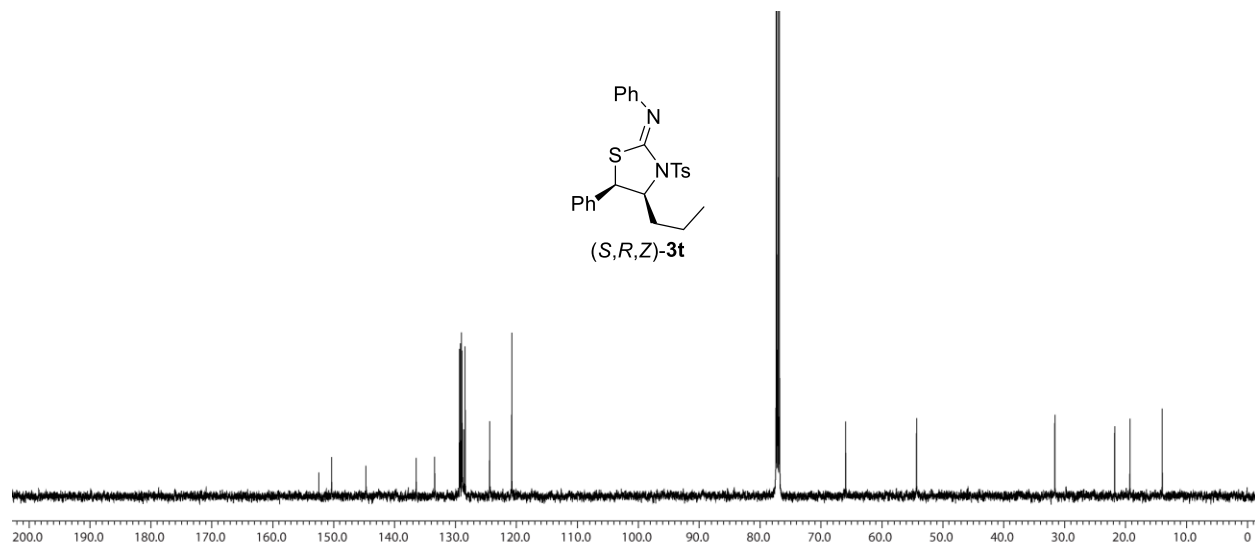
**Figure 44.** <sup>1</sup>H NMR spectrum of **3s** (500 MHz, CDCl<sub>3</sub>)



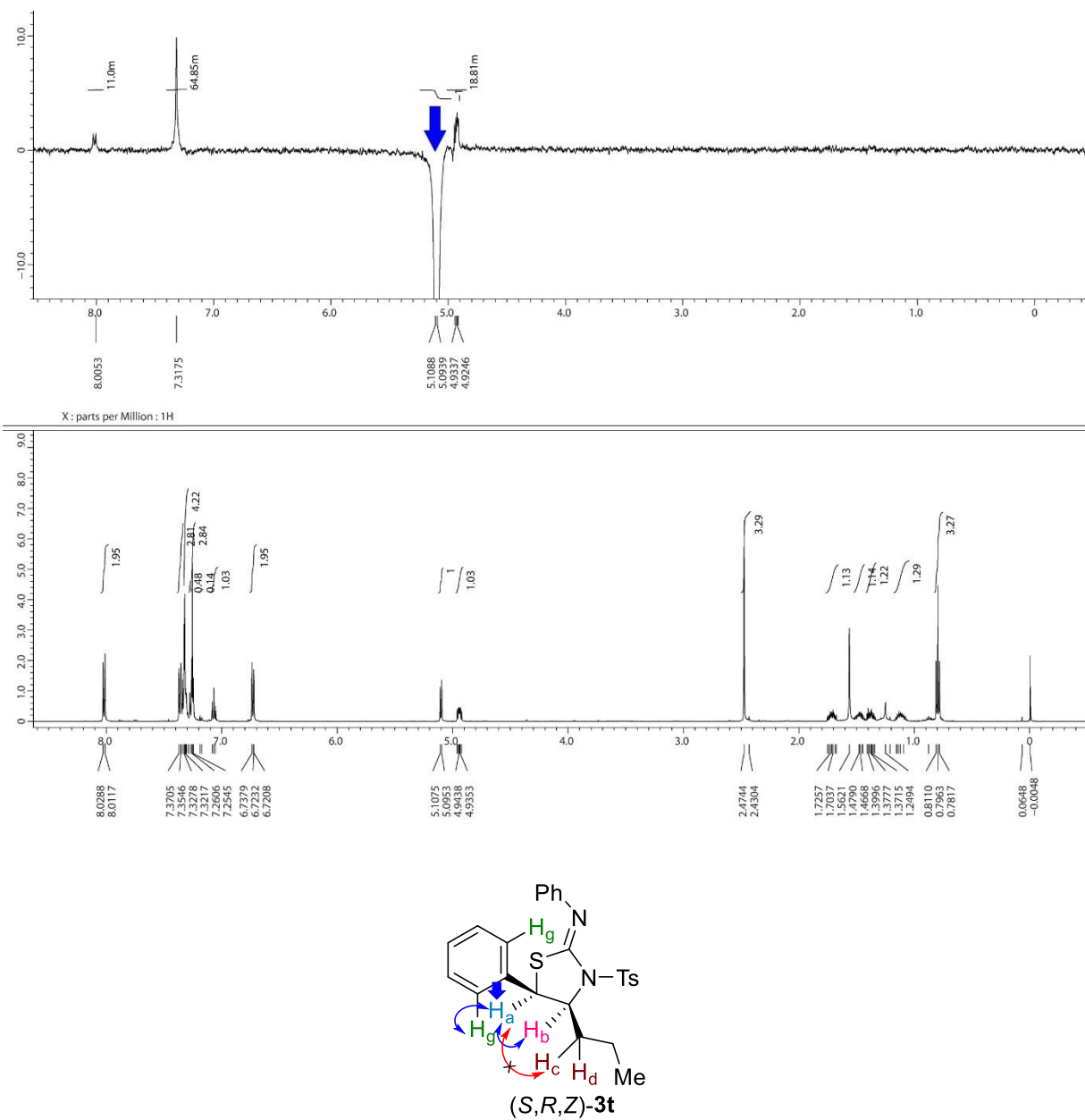
**Figure 45.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of **3s** (125 MHz, CDCl<sub>3</sub>)



**Figure 46.**  $^1\text{H}$  NMR spectrum of  $(S,R,Z)$ -**3t** (500 MHz,  $\text{CDCl}_3$ )

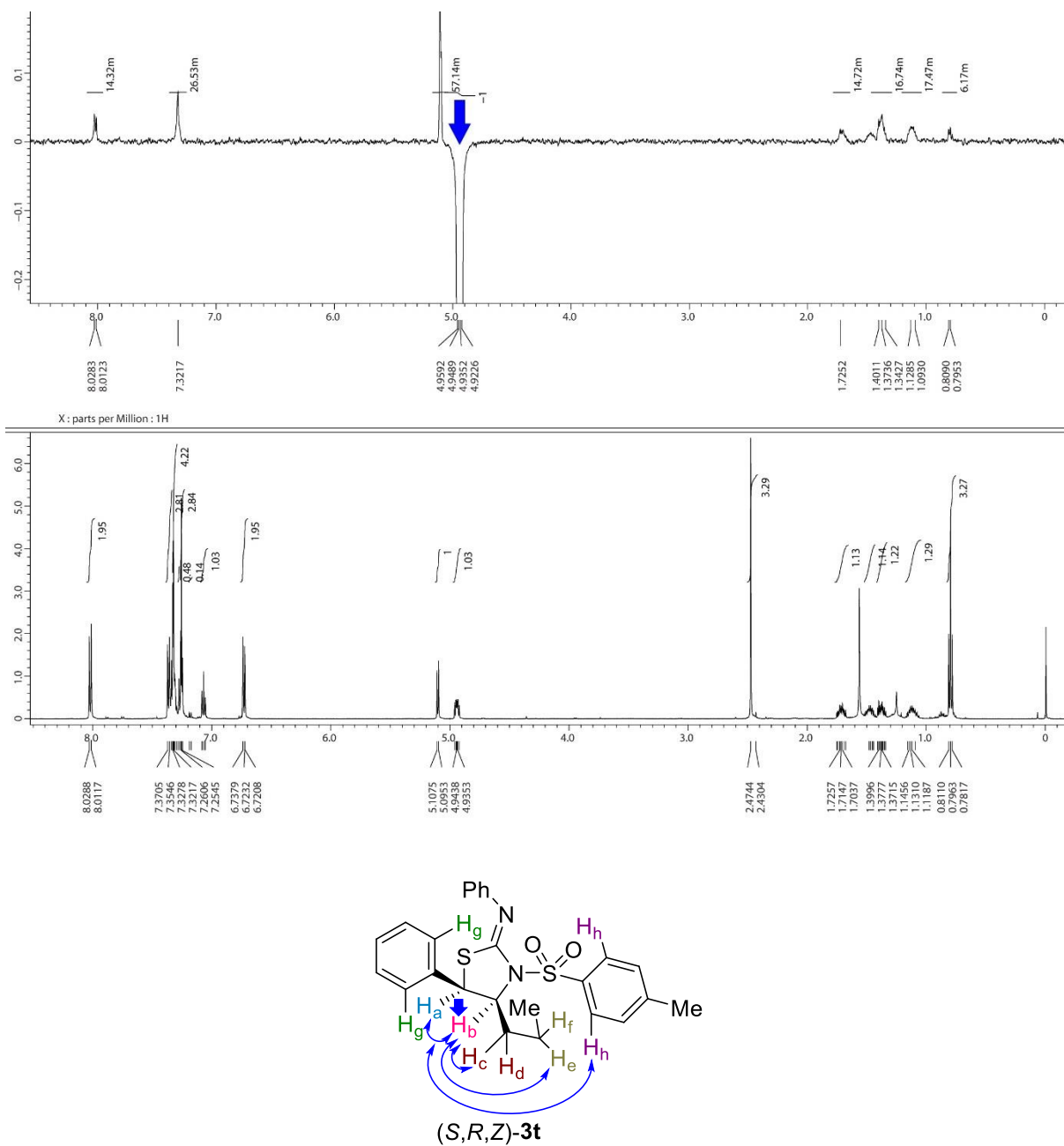


**Figure 47.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of  $(S,R,Z)$ -**3t** (125 MHz,  $\text{CDCl}_3$ )

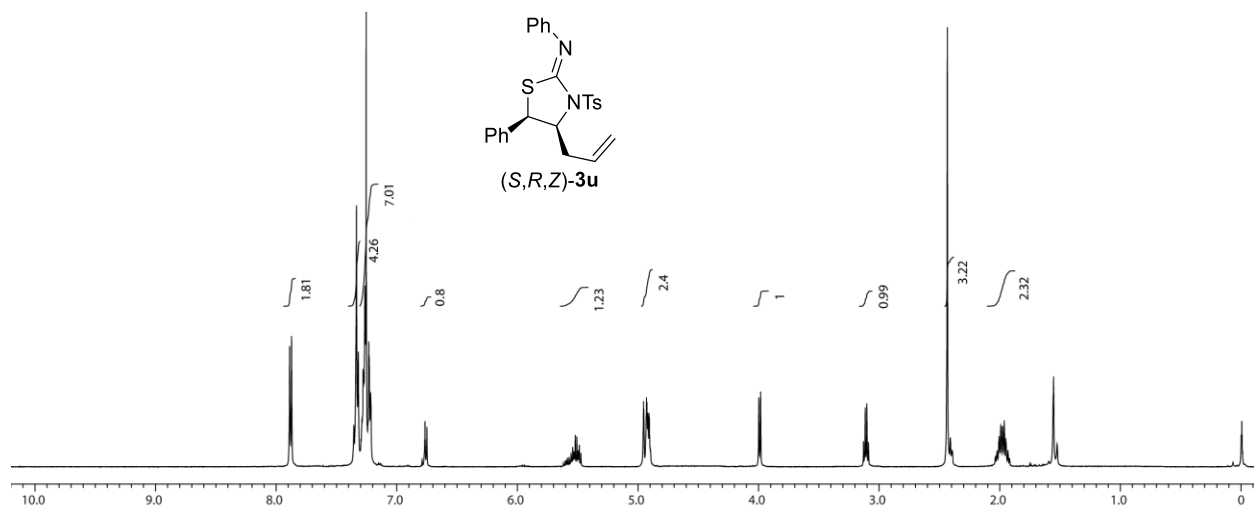


**Figure 48.** NOE spectrum of  $(S,R,Z)$ -**3t** with irradiation of  $H_a$  at 5.10 ppm (500 MHz,  $CDCl_3$ )

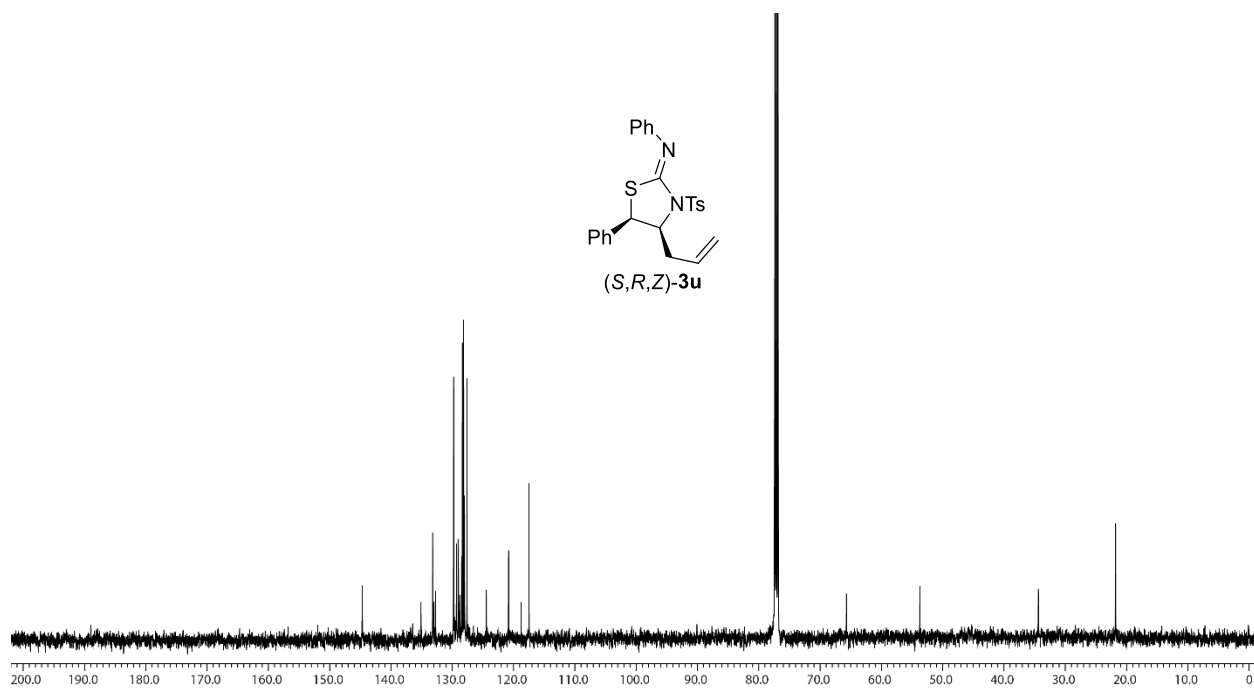




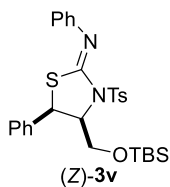
**Figure 49.** NOE spectrum of *(S,R,Z)*-**3t** with irradiation of H<sub>b</sub> at 4.94 ppm (500 MHz, CDCl<sub>3</sub>)



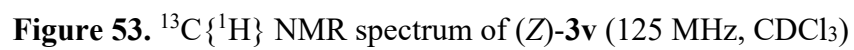
**Figure 50.** <sup>1</sup>H NMR spectrum of **(S,R,Z)-3u** (500 MHz, CDCl<sub>3</sub>)

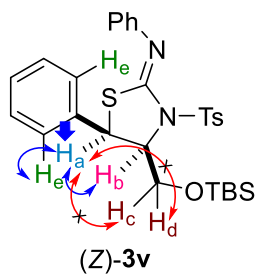


**Figure 51.** <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of **(S,R,Z)-3u** (125 MHz, CDCl<sub>3</sub>)

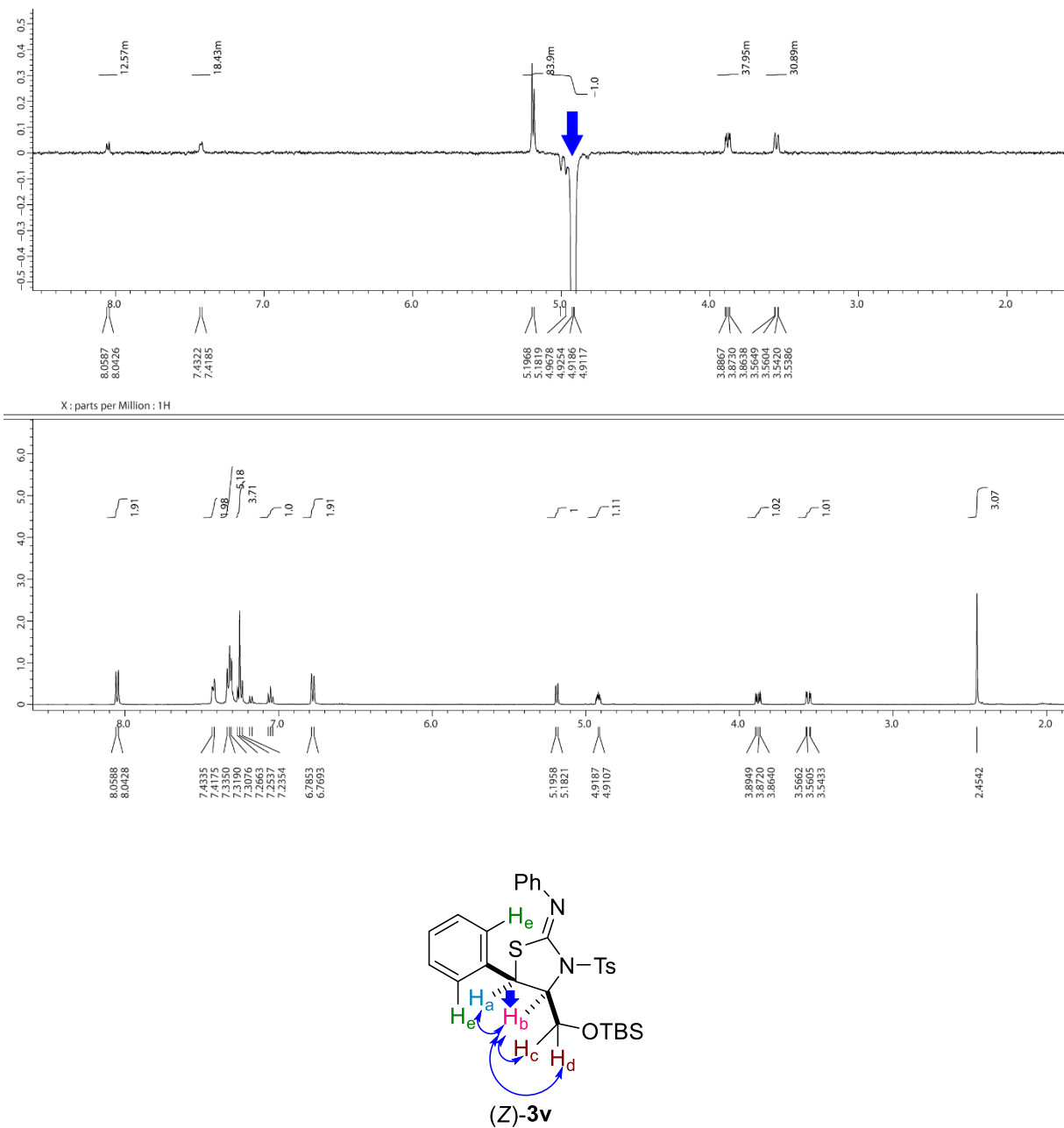


**(Z)-3v**

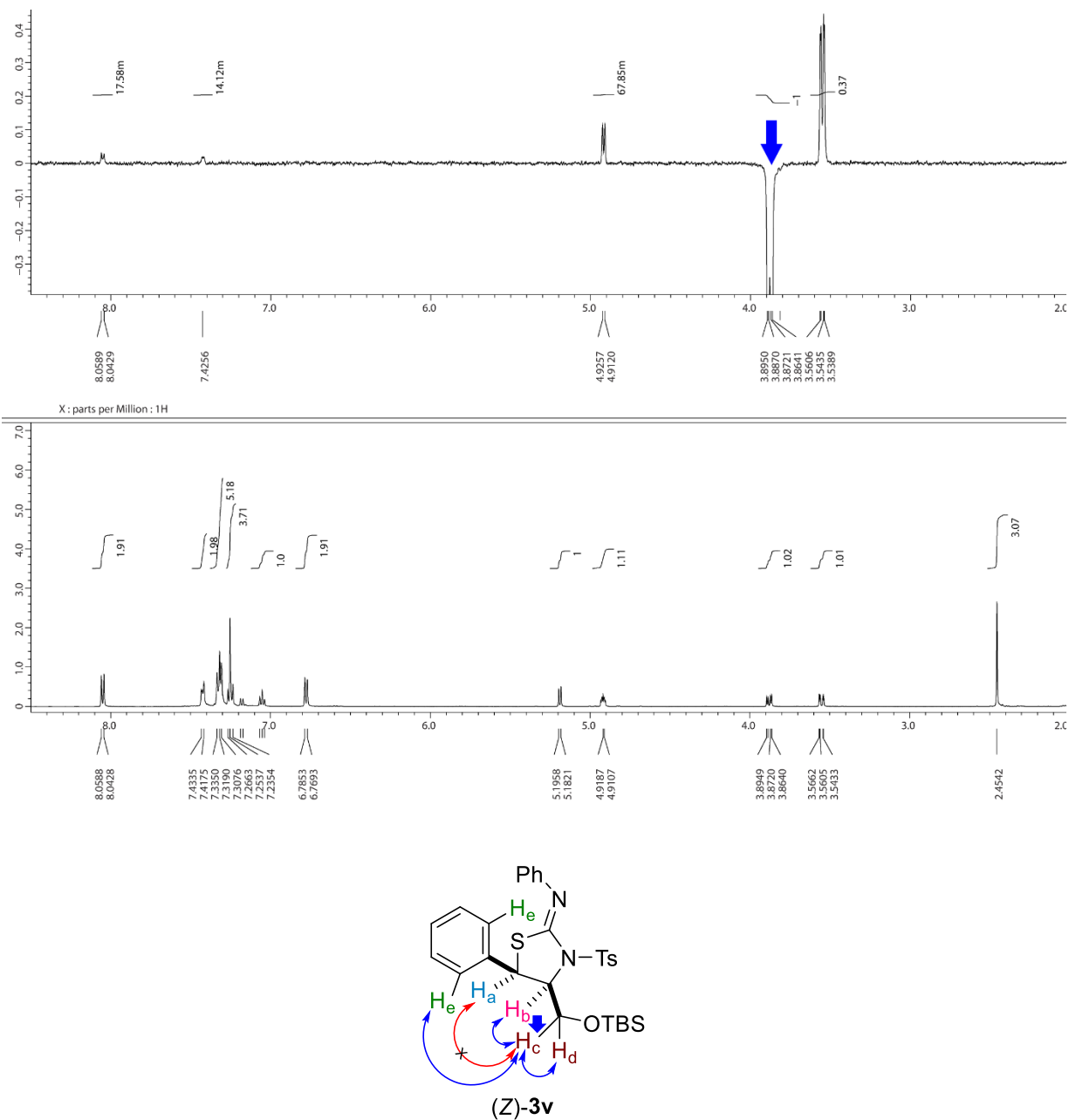




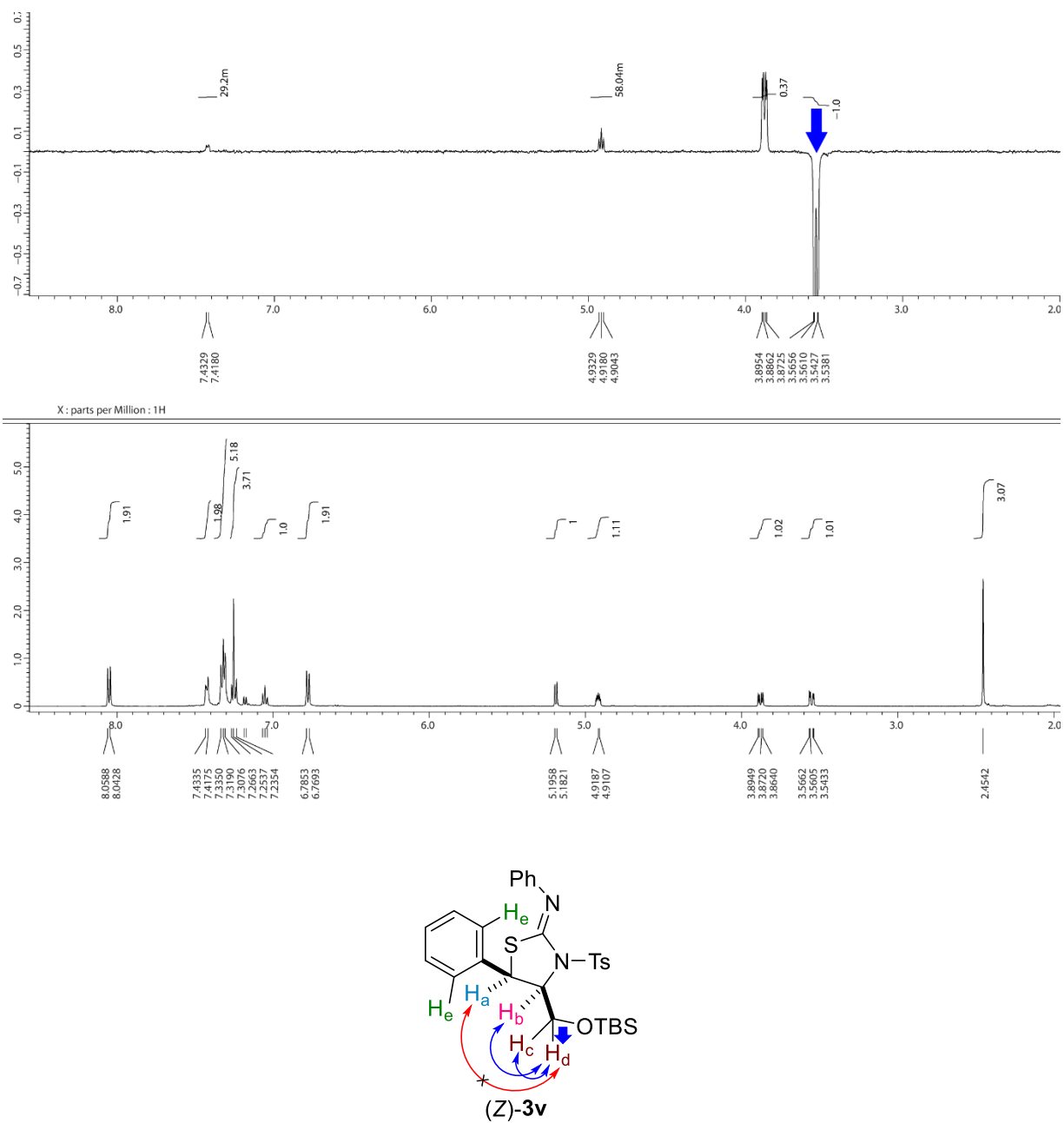
S36



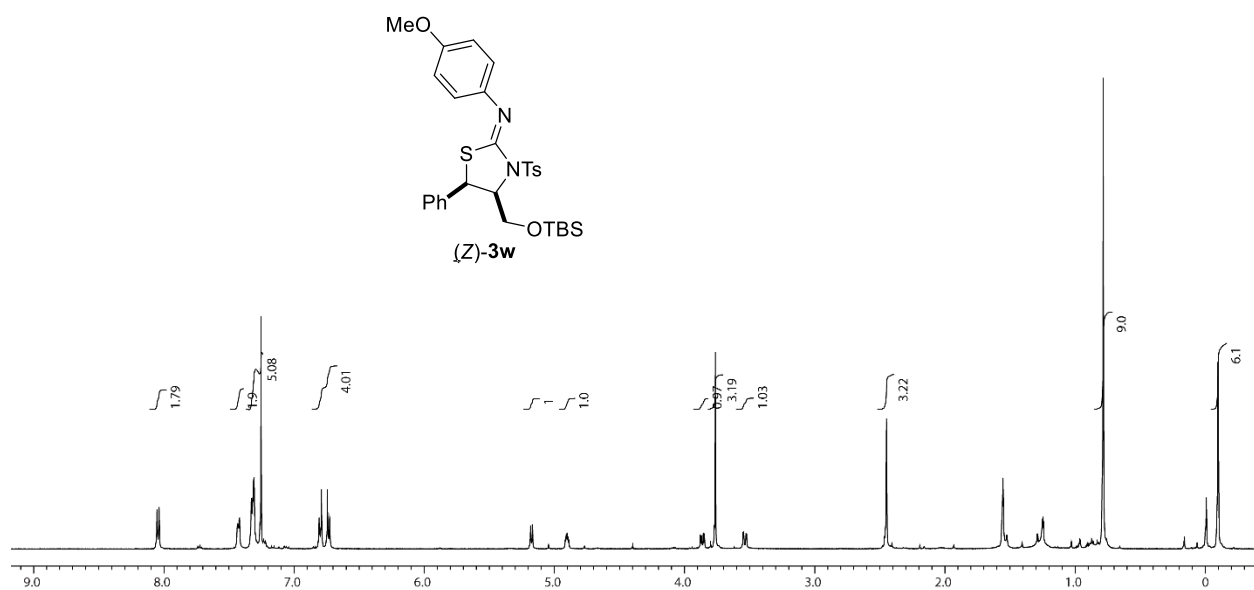
**Figure 55.** NOE spectrum of (Z)-3v with irradiation of H<sub>b</sub> at 4.92 ppm (500 MHz, CDCl<sub>3</sub>)



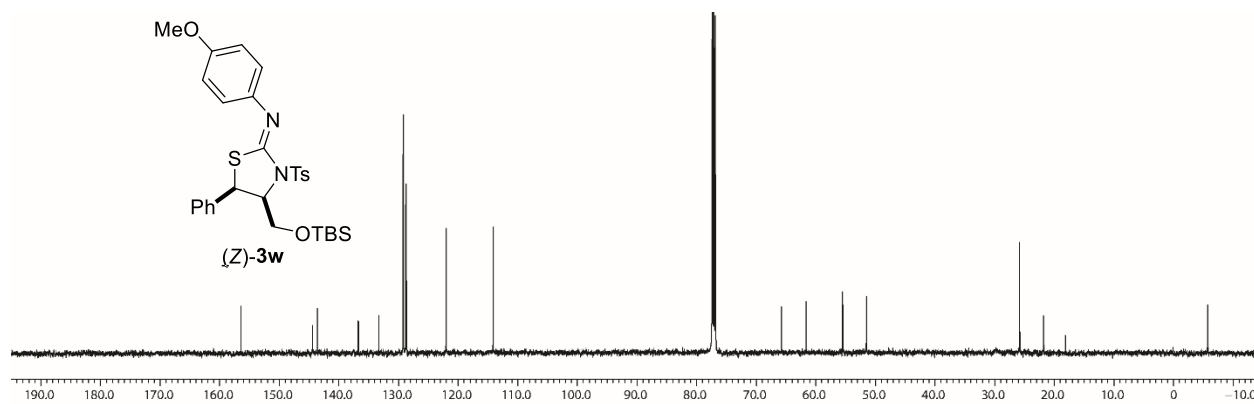
**Figure 56.** NOE spectrum of (Z)-3v with irradiation of H<sub>c</sub> at 3.88 ppm (500 MHz, CDCl<sub>3</sub>)



**Figure 57.** NOE spectrum of (Z)-3v with irradiation of H<sub>d</sub> at 3.55 ppm (500 MHz, CDCl<sub>3</sub>)



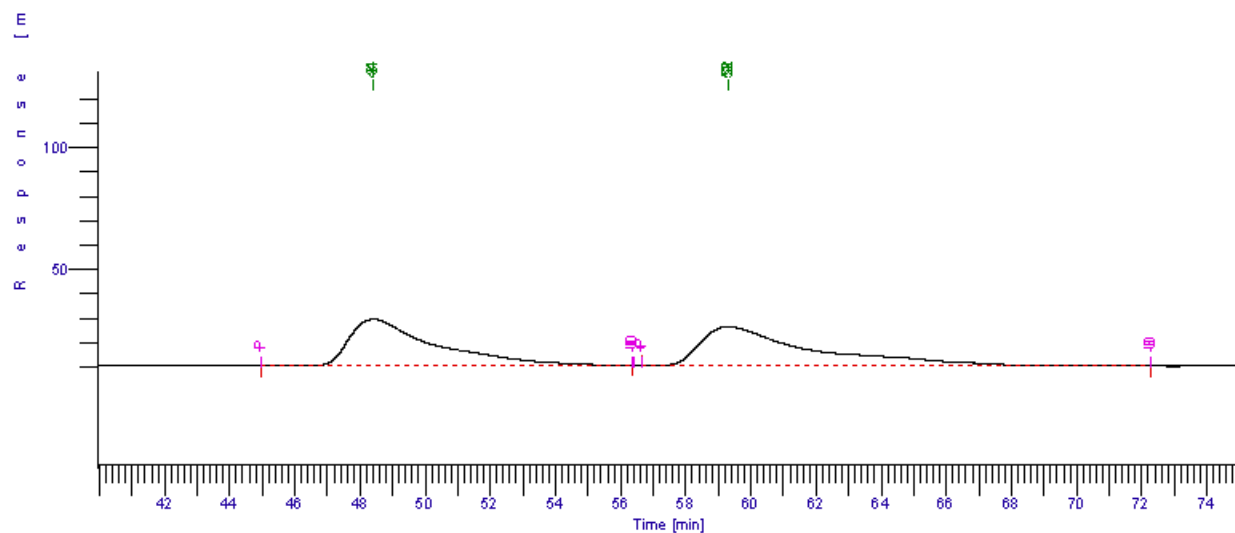
**Figure 58.** <sup>1</sup>H NMR spectrum of compound (Z)-3w (500 MHz, CDCl<sub>3</sub>)



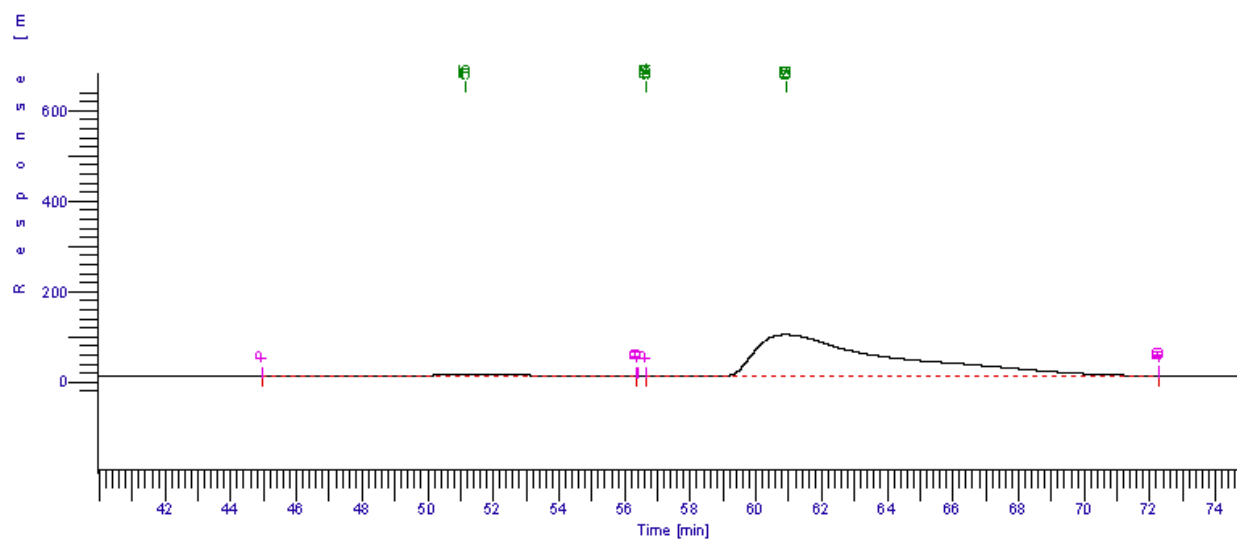
**Figure 59.** <sup>13</sup>C {<sup>1</sup>H} NMR spectrum of compound (Z)-3w (125 MHz, CDCl<sub>3</sub>)



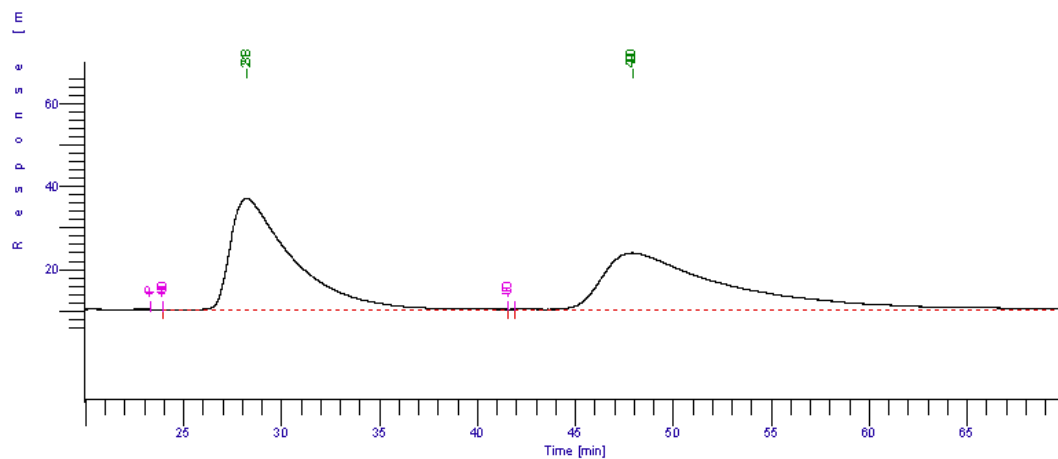
## 7. Copies of HPLC Chromatograms for ee Determination:



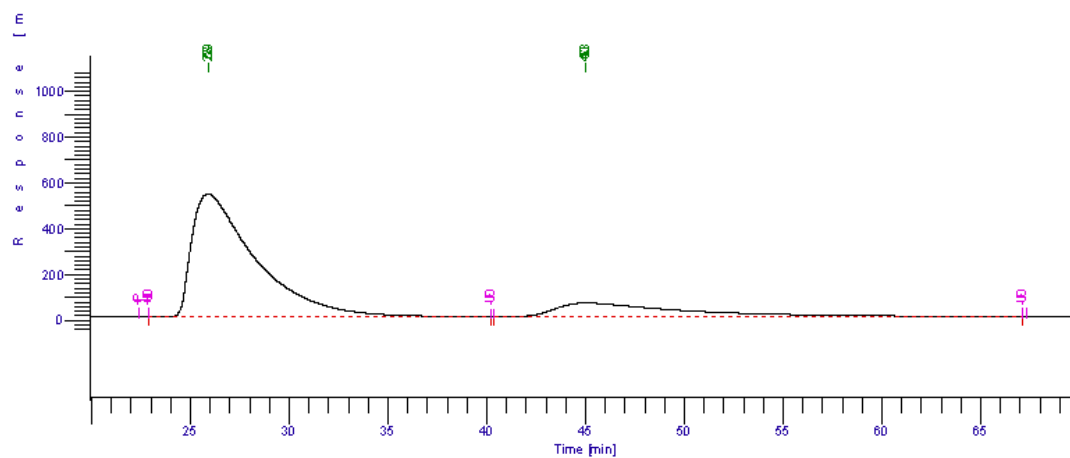
**Figure 60.** HPLC chromatogram of racemic **3a** (Cellulose 1, hexane:isopropanol 98:2, 0% ee)



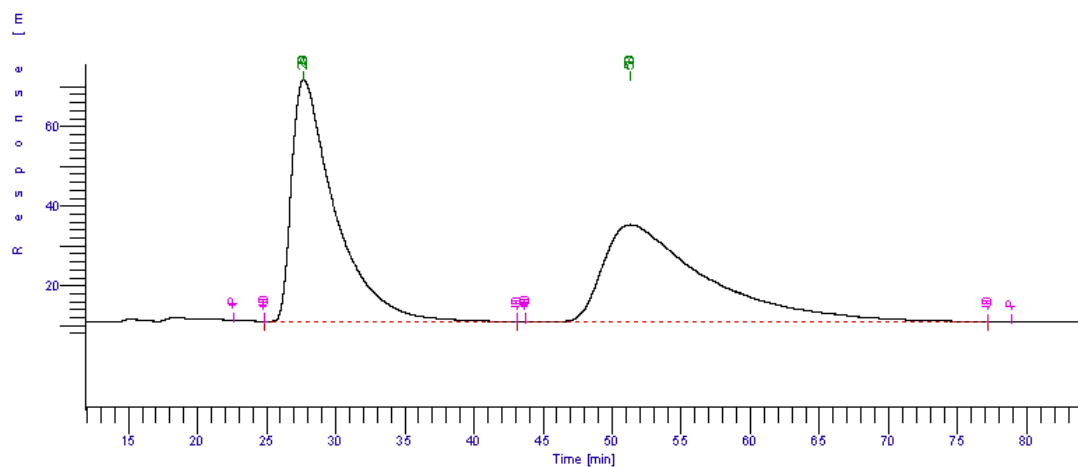
**Figure 61.** HPLC chromatogram of non-racemic (*R*)-**3a** (Cellulose 1, hexane:isopropanol 98:2, 98% ee)



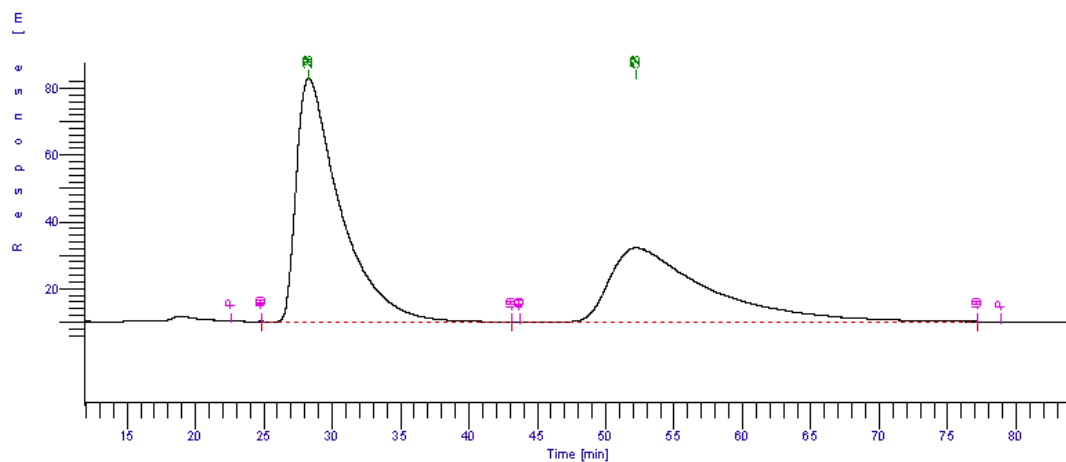
**Figure 62.** HPLC chromatogram of racemic **3b** (Chiralpak AS-H, hexane:isopropanol 90:10)



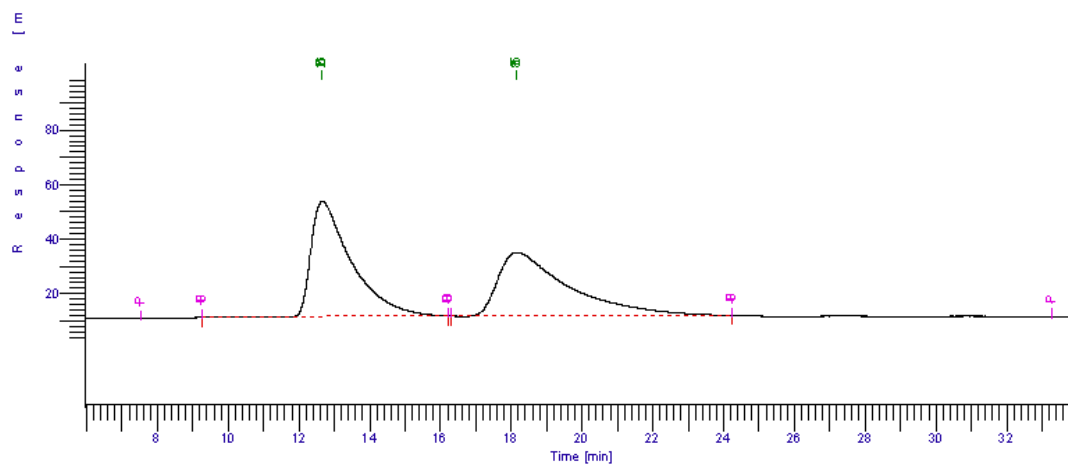
**Figure 63.** HPLC chromatogram of non-racemic (*R*)-**3b** (Chiralpak AS-H, hexane:isopropanol 90:10, 66% ee)



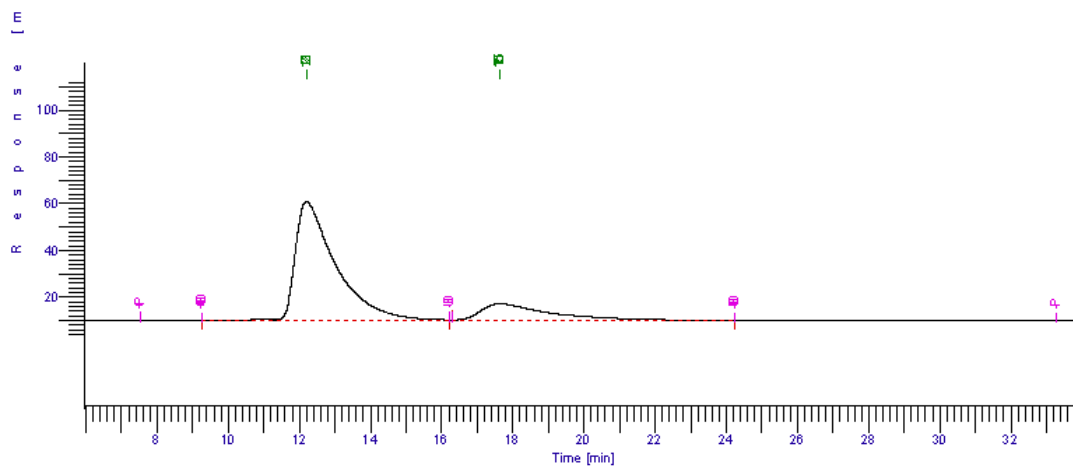
**Figure 64.** HPLC chromatogram of racemic **3d** (Chiralpak AS-H, hexane:isopropanol 80:20)



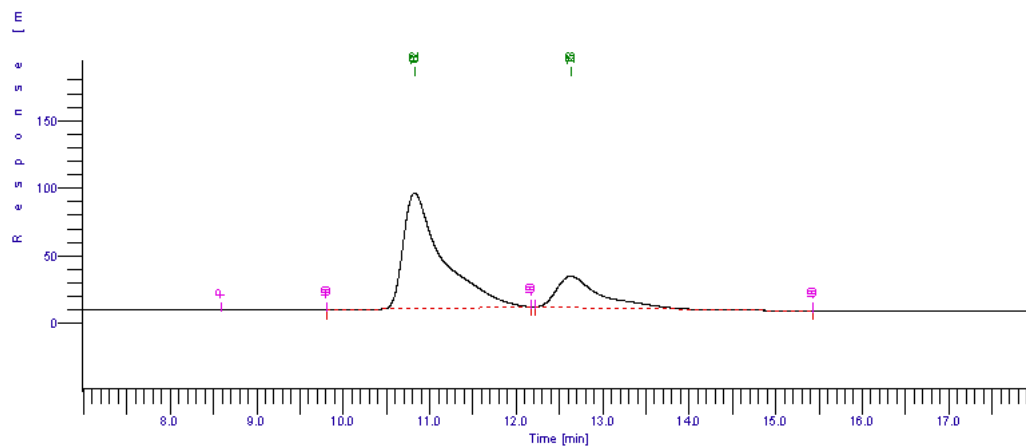
**Figure 65.** HPLC chromatogram of non-racemic (*R*)-**3d** (Chiralpak AS-H, hexane:isopropanol 80:20, 20% ee)



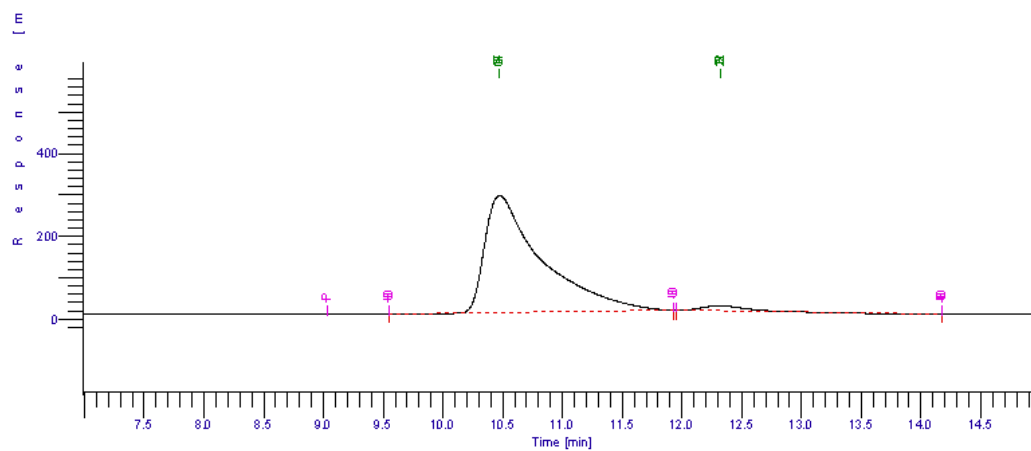
**Figure 66.** HPLC chromatogram of racemic **3e** (Chiralpak AS-H, hexane:isopropanol 90:10)



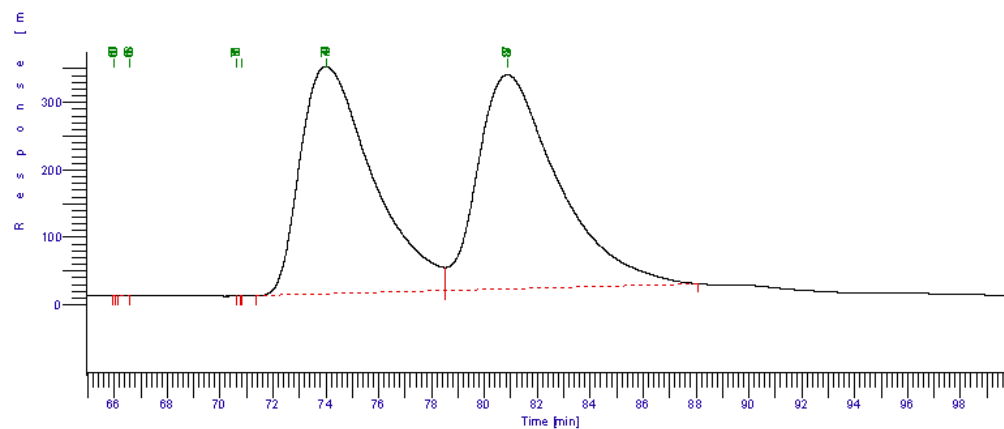
**Figure 67.** HPLC chromatogram of non-racemic (*R*)-**3e** (Chiralpak AS-H, hexane:isopropanol 90:10, 63% ee)



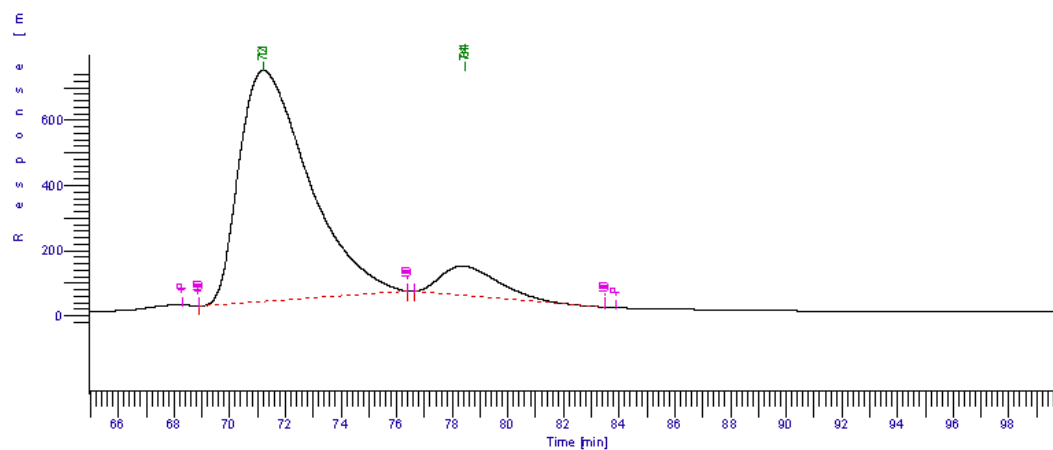
**Figure 68.** HPLC chromatogram of racemic **3f** (Cellulose-1, hexane:isopropanol 90:10)



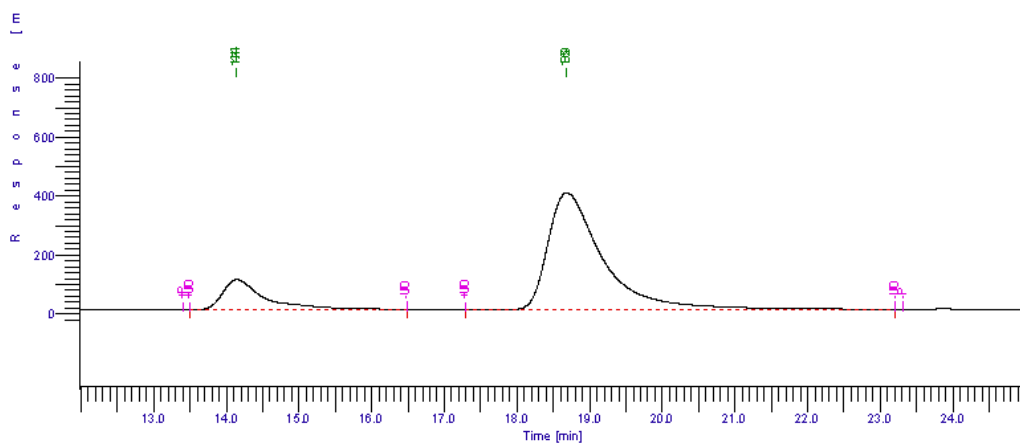
**Figure 69.** HPLC chromatogram of non-racemic (*R*)-**3f** (Cellulose-1, hexane:isopropanol 90:10, 93% ee)



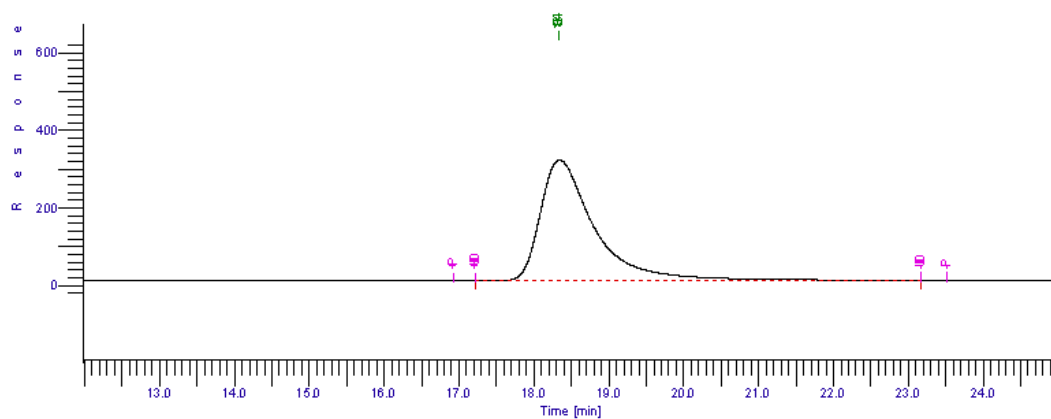
**Figure 70.** HPLC chromatogram of racemic **3g** (Cellulose 2, hexane:isopropanol 98:2)



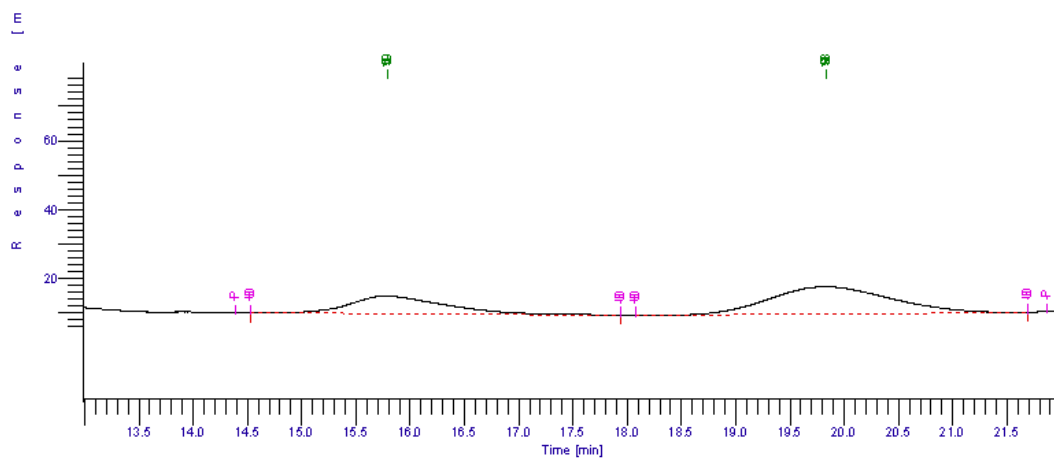
**Figure 71.** HPLC chromatogram of non-racemic (*S*)-**3g** (Cellulose 2, hexane:isopropanol 98:2,  
80% ee)



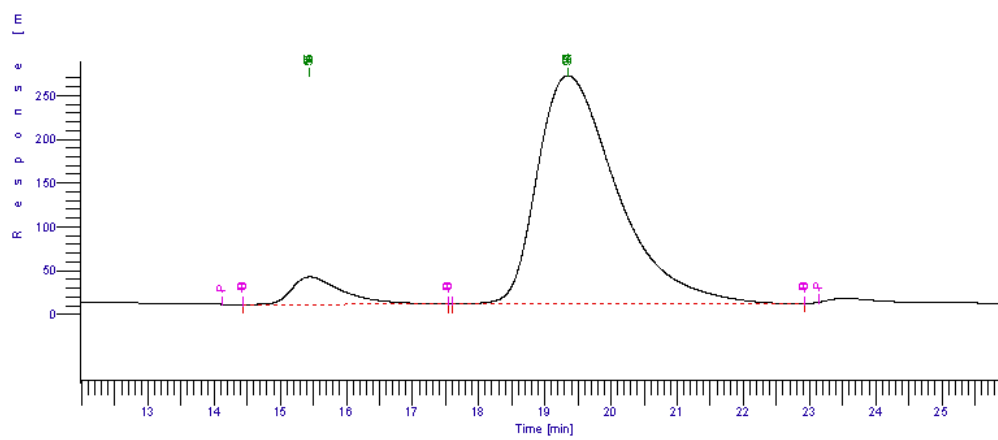
**Figure 72.** HPLC chromatogram of non-racemic (*S*)-**3h** (Cellulose 2, hexane:isopropanol 98:2, 67% ee)



**Figure 73.** HPLC chromatogram of non-racemic (*S*)-**3h** (Cellulose 2, hexane:isopropanol 98:2, >99% ee)

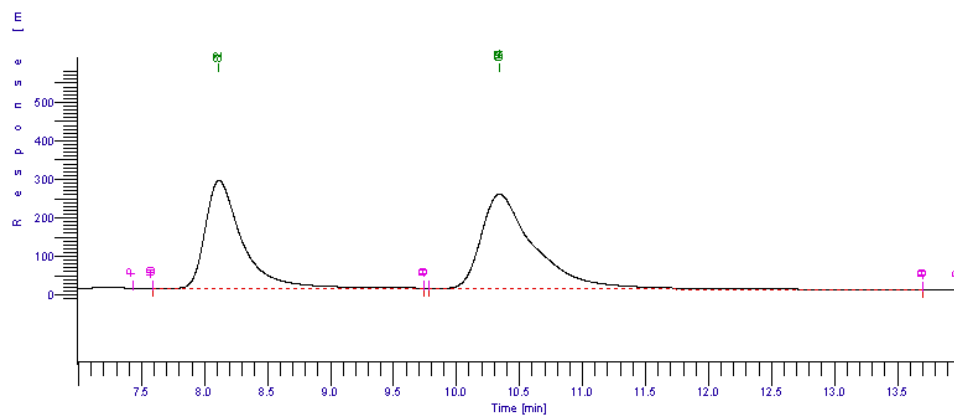


**Figure 74.** HPLC chromatogram of non-racemic (*S*)-**3j** (Chiralcel OD-H, hexane:isopropanol 95:5, 30% ee)

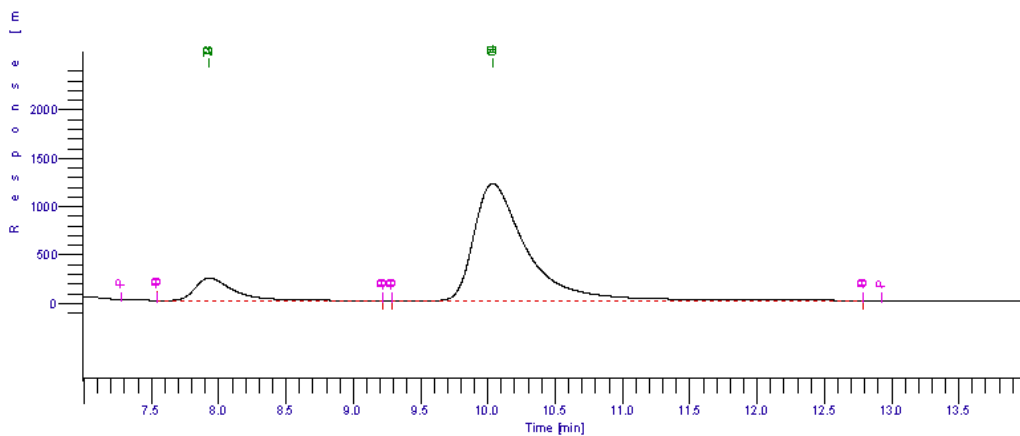


**Figure 75.** HPLC chromatogram of non-racemic (*S*)-**3j** (Chiralcel OD-H, hexane:isopropanol 95:5, 86% ee)





**Figure 76.** HPLC chromatogram of non-racemic (*S*)-**3k** (Cellulose-2, hexane:isopropanol 90:10, 11% ee)



**Figure 77.** HPLC chromatogram of non-racemic (*S*)-**3k** (Cellulose-2, hexane:isopropanol 90:10, 76% ee)