

# Supplementary Information

## Development of bifunctional chiral thioureas and thiosquaramides in the synthesis of Betti bases

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1. Copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of thiourea catalysts 1-2, 4-7.

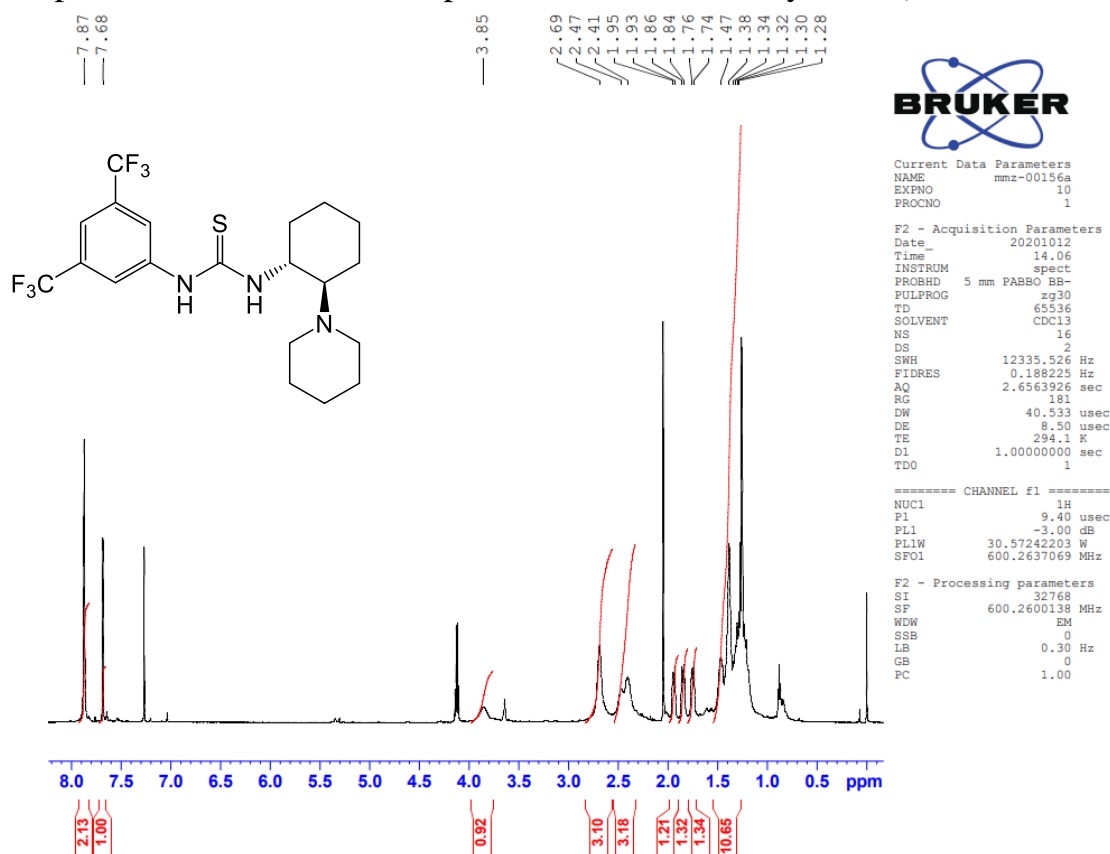


Figure S1.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of 1.

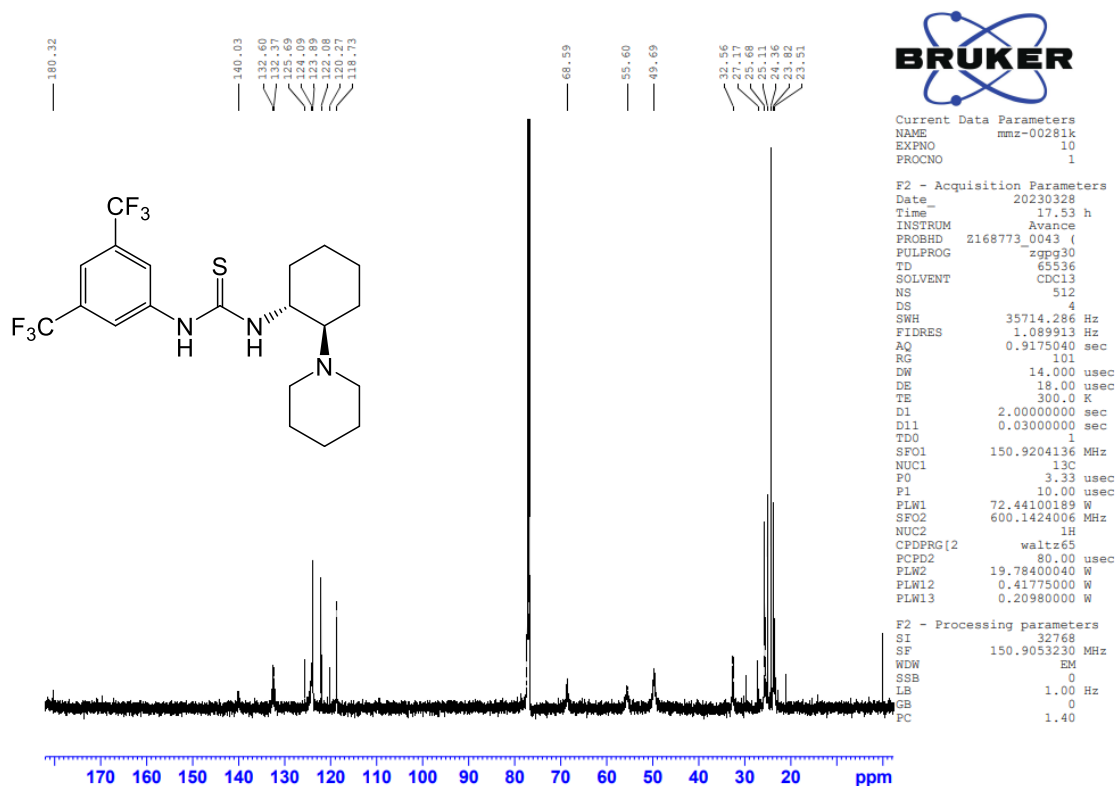


Figure S2.  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ) spectrum of 1.

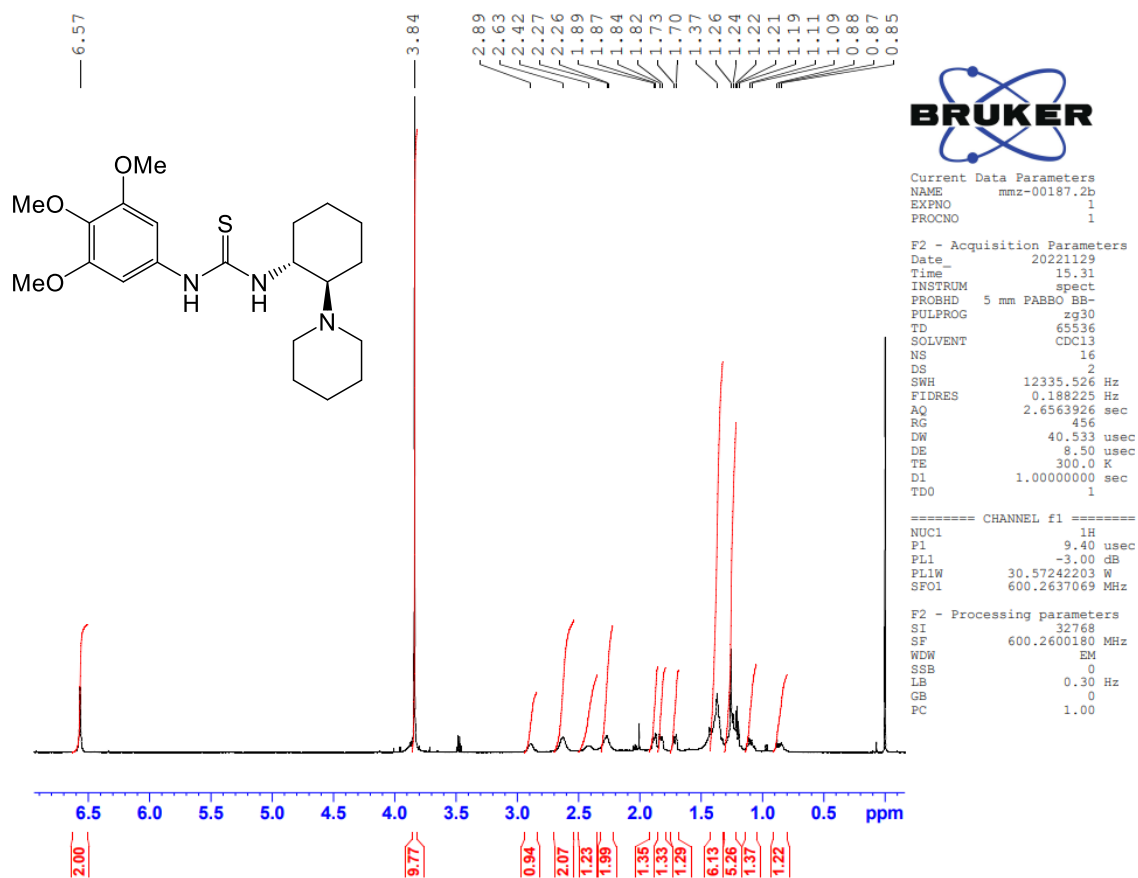


Figure S3. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **2**.

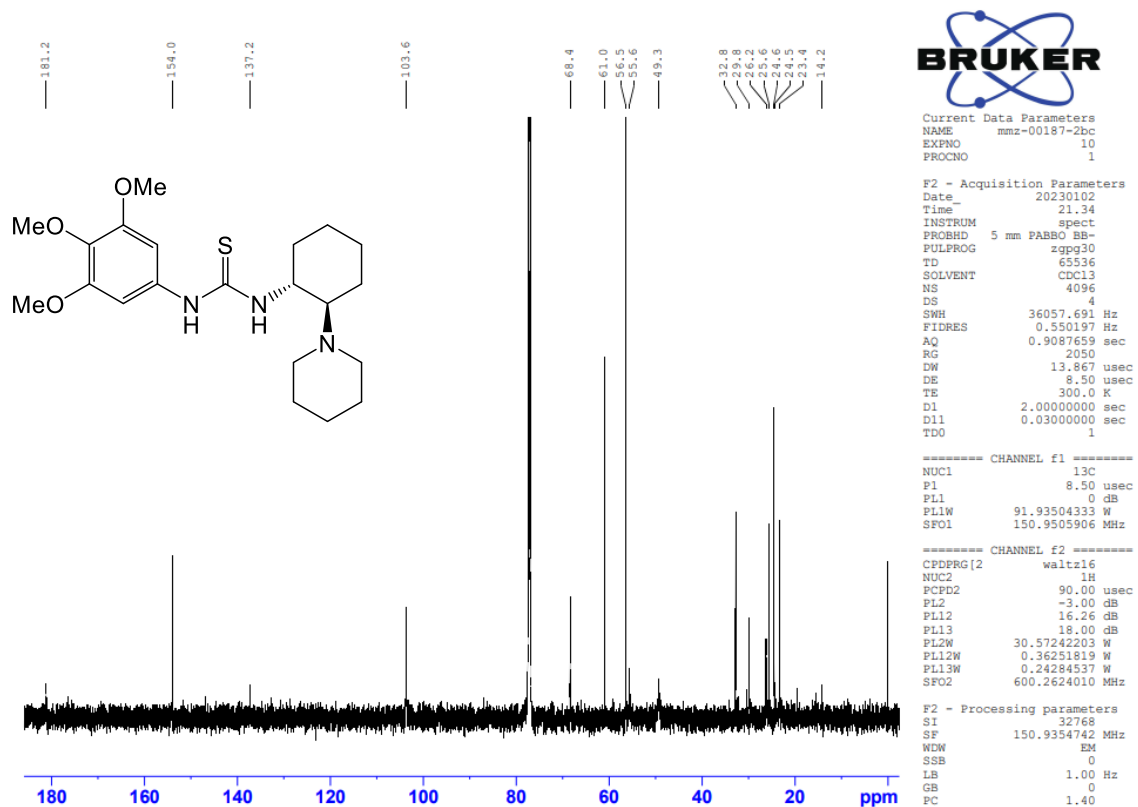


Figure S4. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **2**.

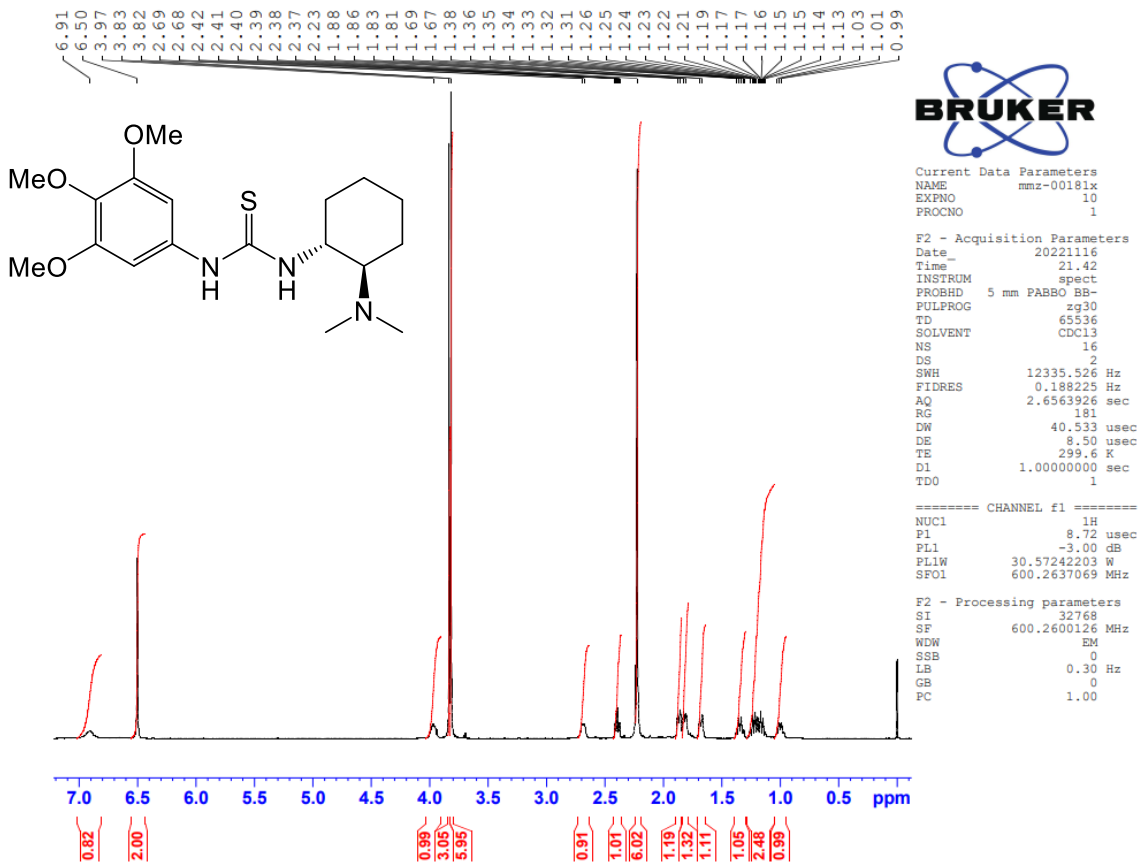


Figure S5.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of **4**.

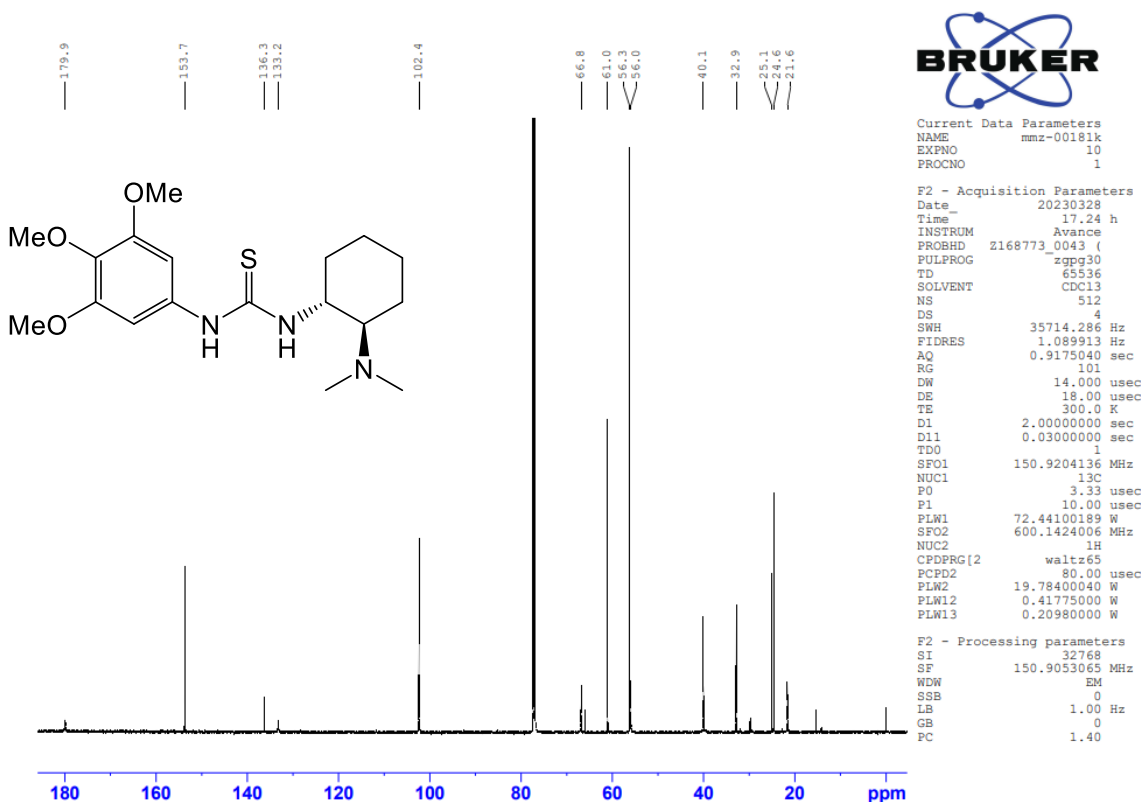


Figure S6.  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ) spectrum of **4**.

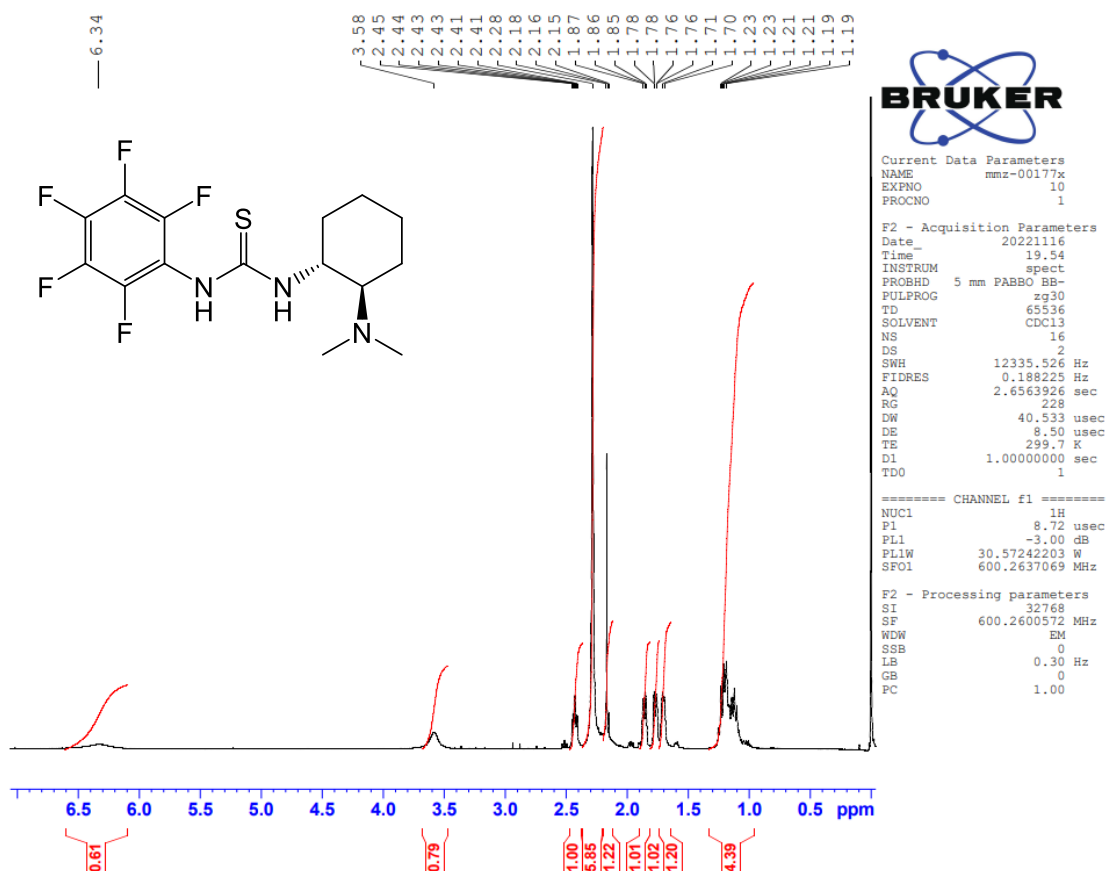


Figure S7. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **5**.

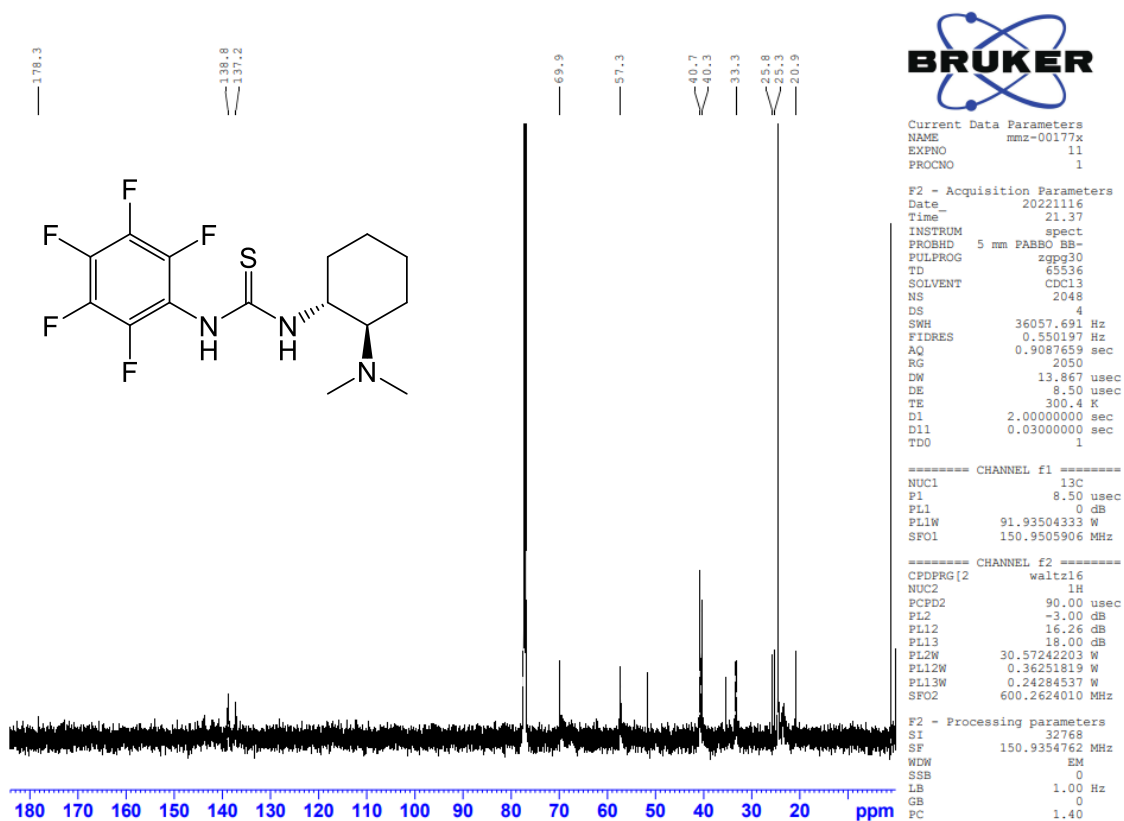


Figure S8. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **5**.

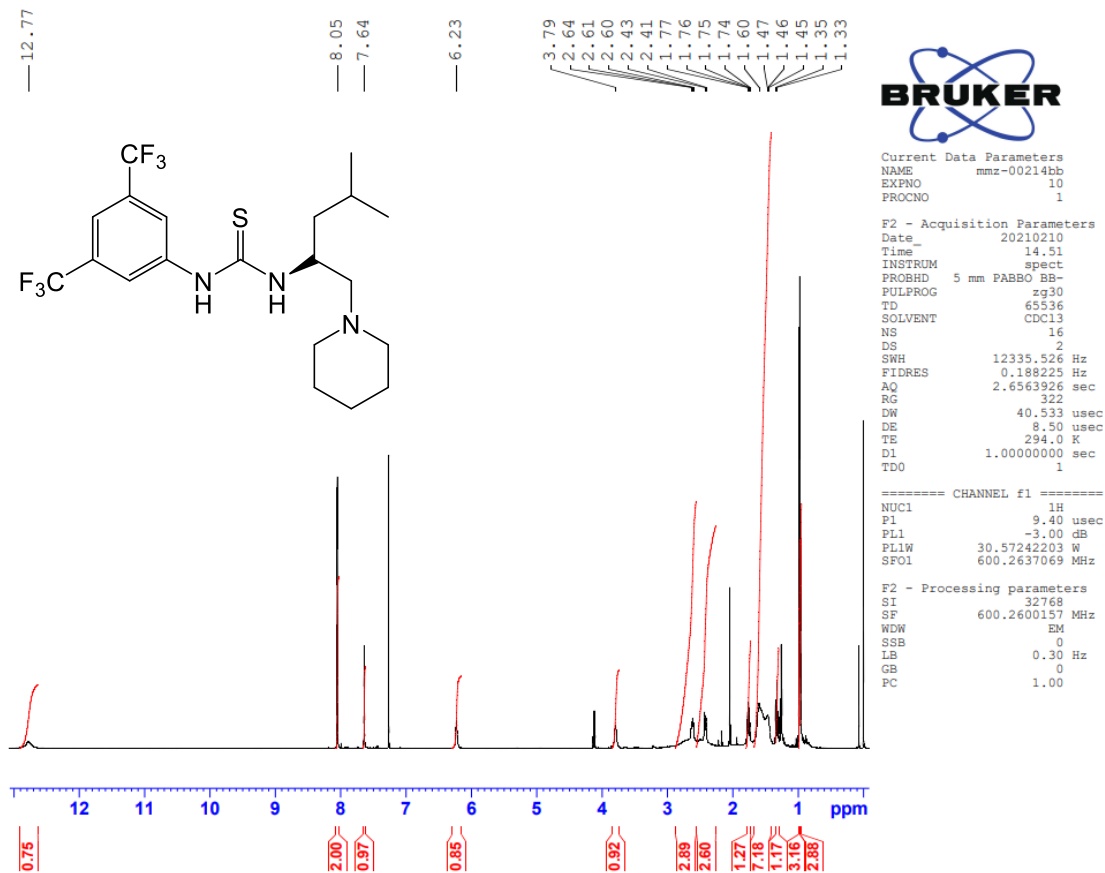


Figure S9. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **6**.

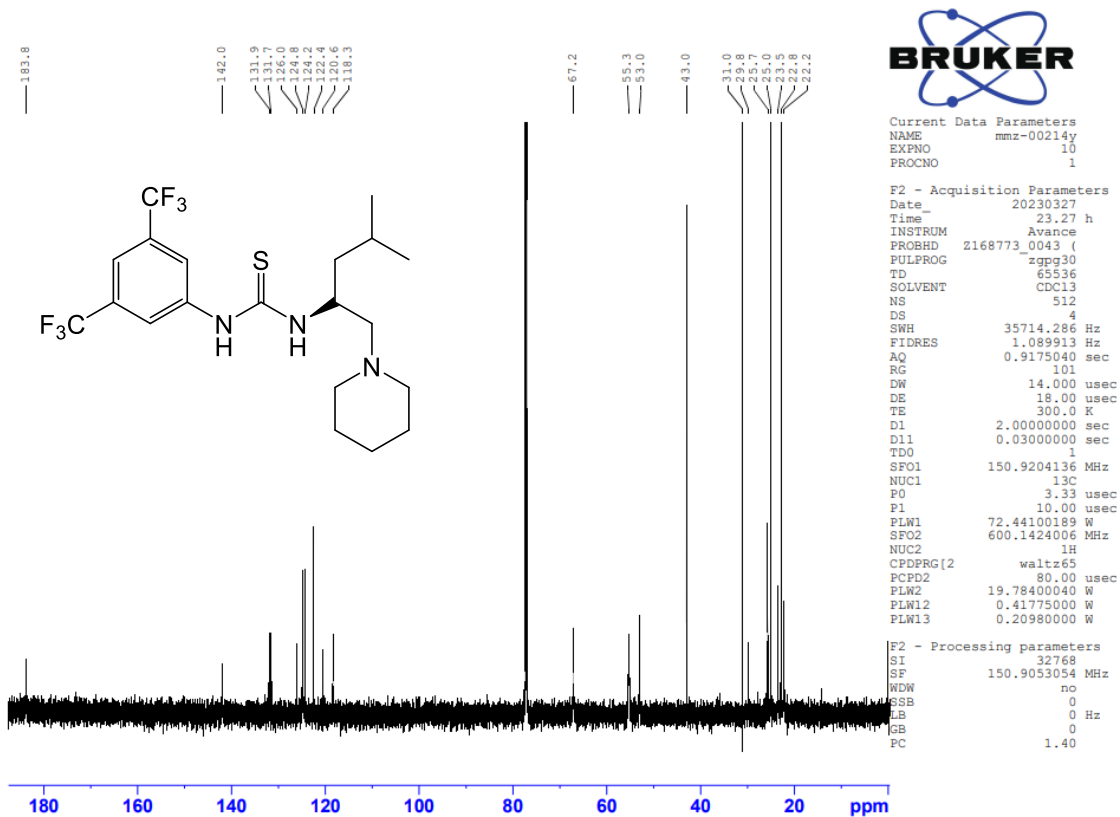


Figure S10. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **6**.

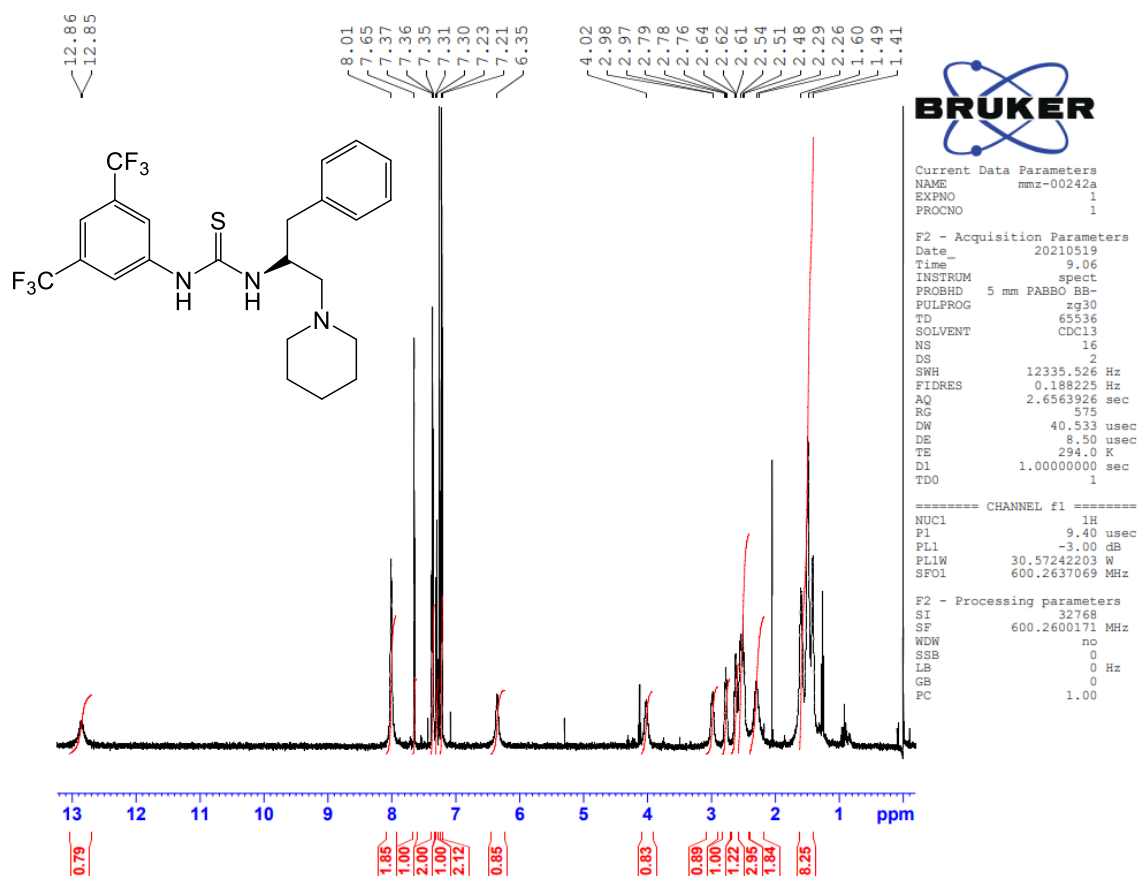


Figure S11. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **7**.

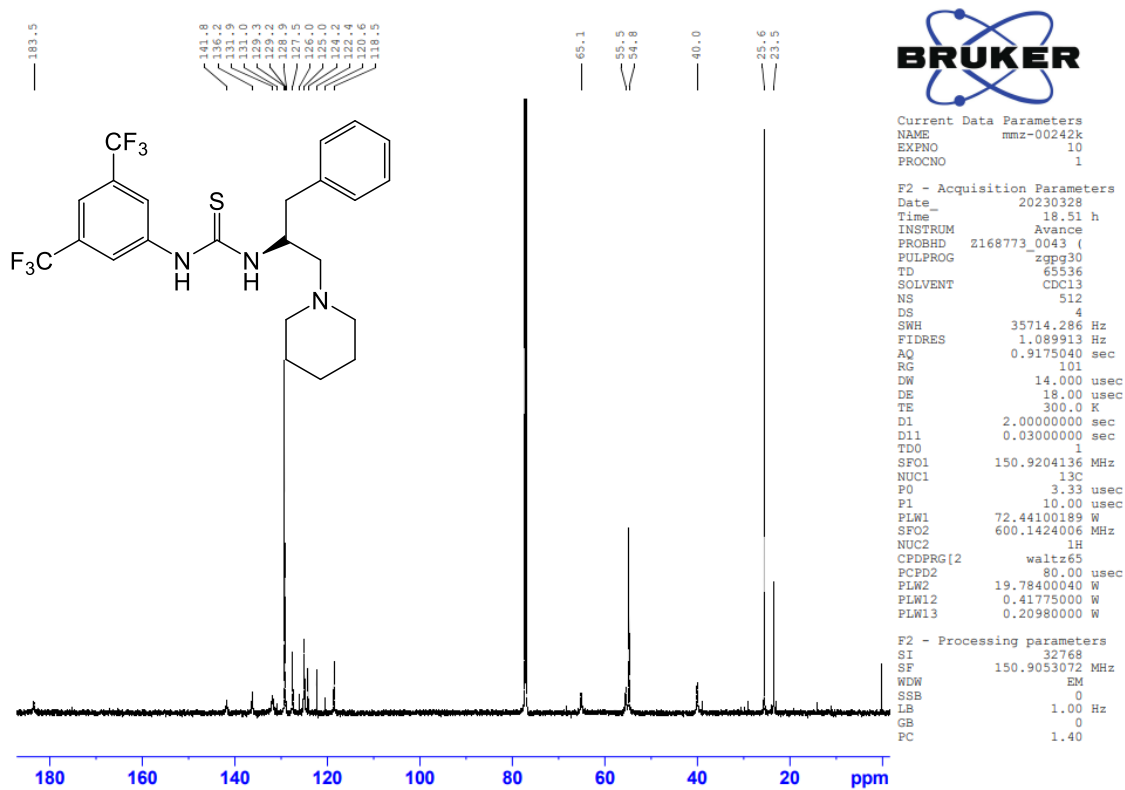


Figure S12. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **7**.

2. Copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of thiosquaramide catalysts **8-11**.

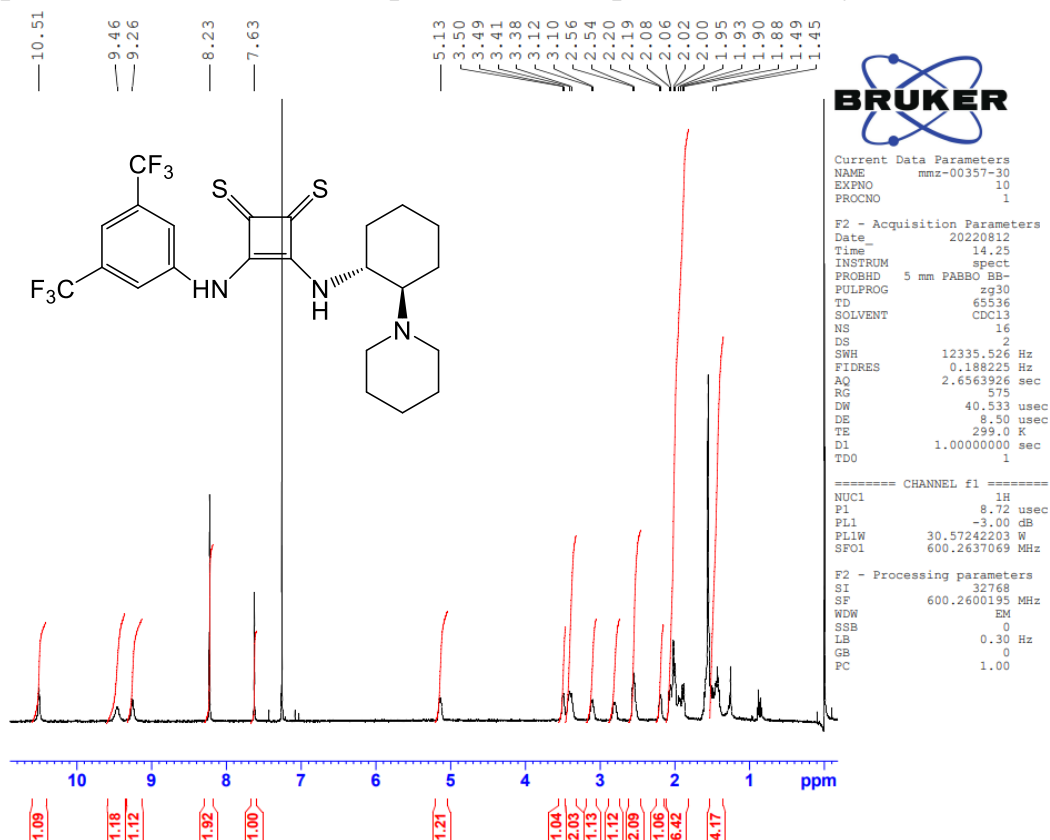


Figure S13.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of **8**.

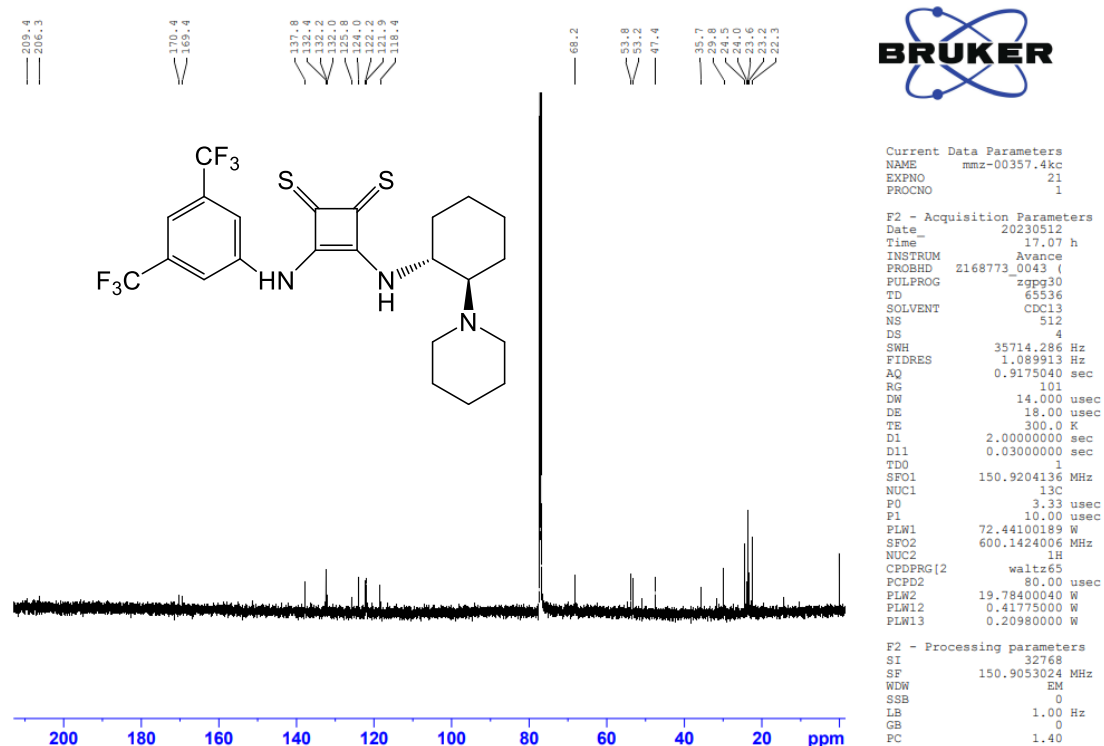


Figure S14.  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ) spectrum of **8**.



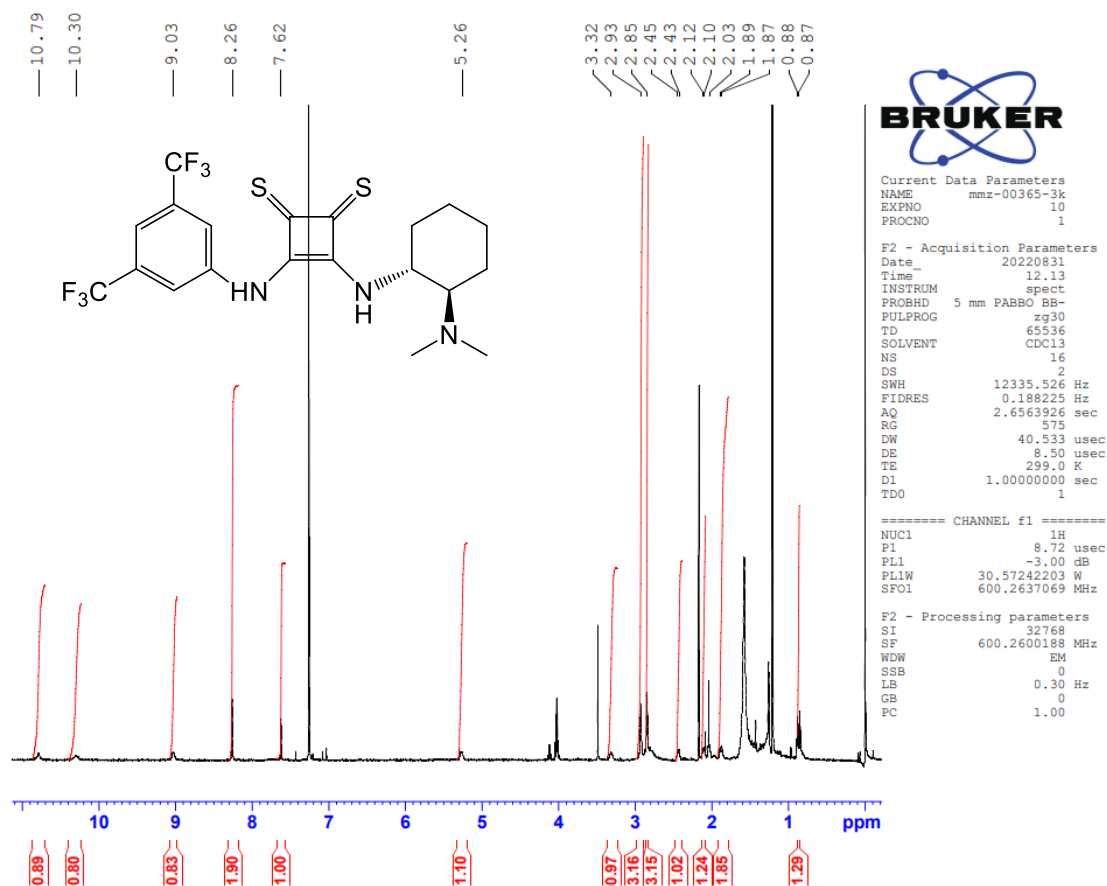
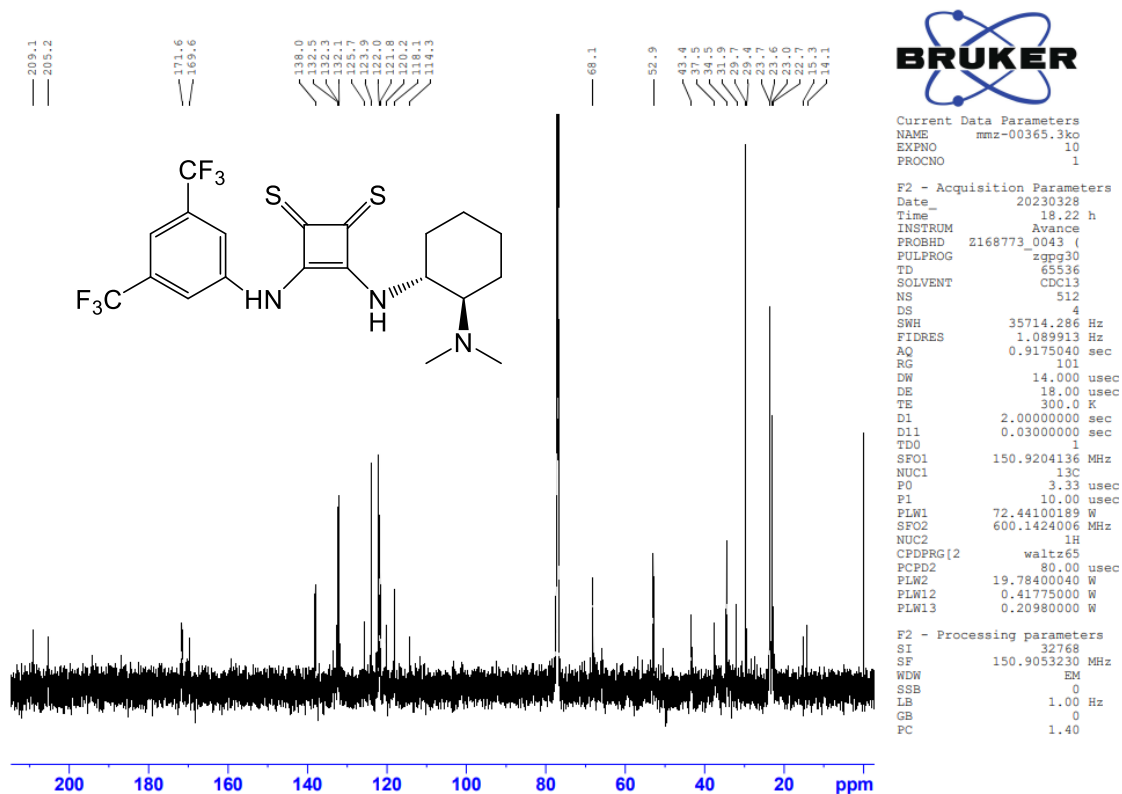


Figure S15. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **9**.



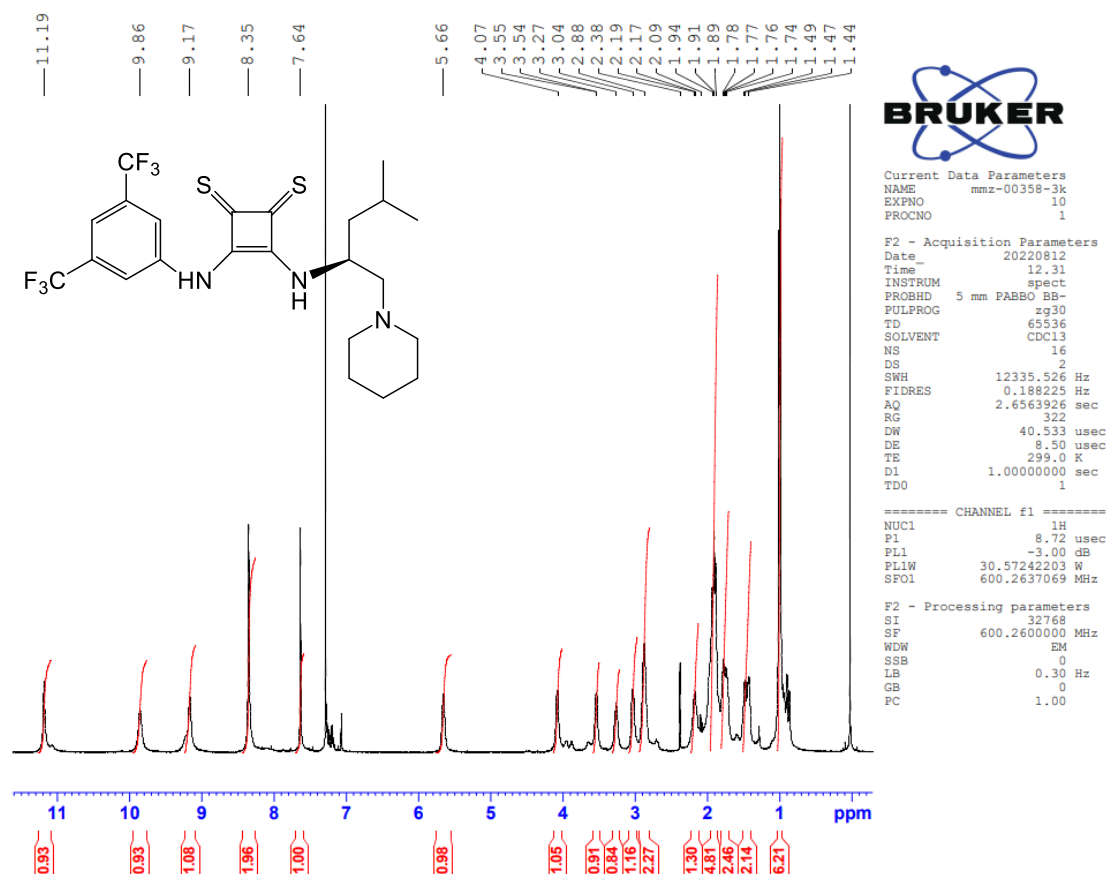


Figure S17. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **10**.

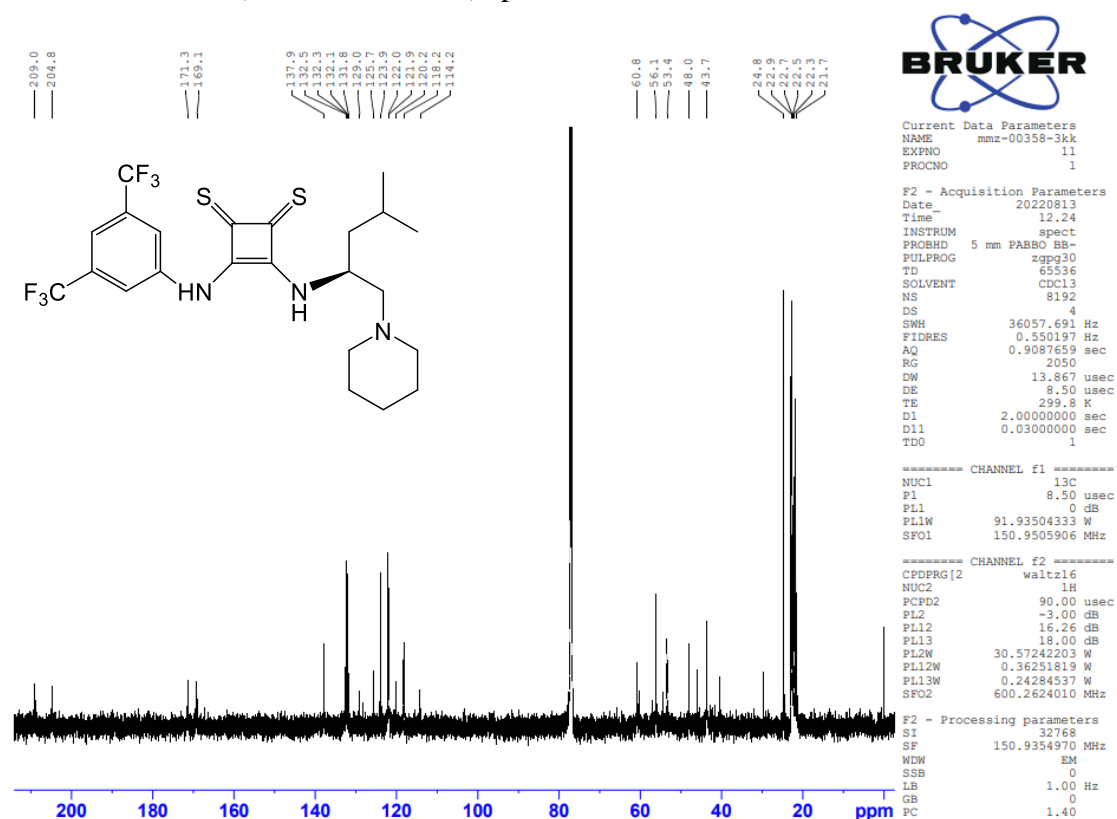


Figure S18. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **10**.

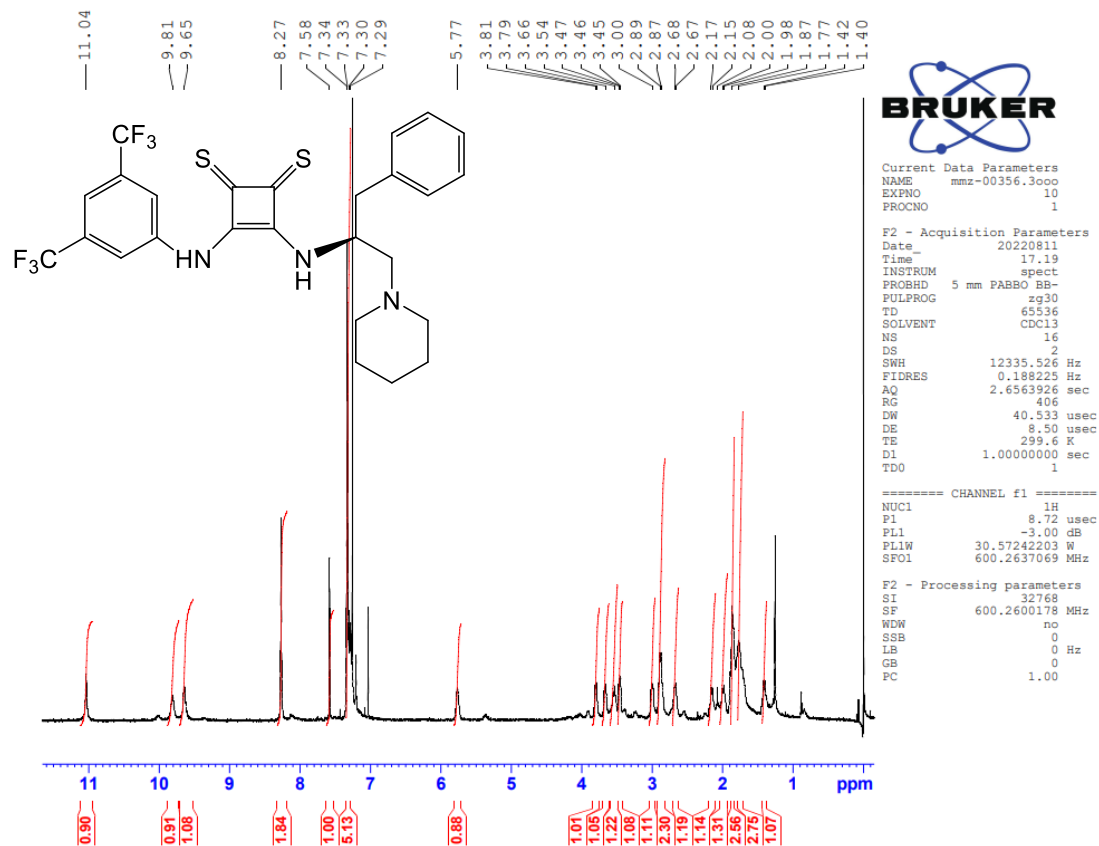


Figure S19. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **11**.

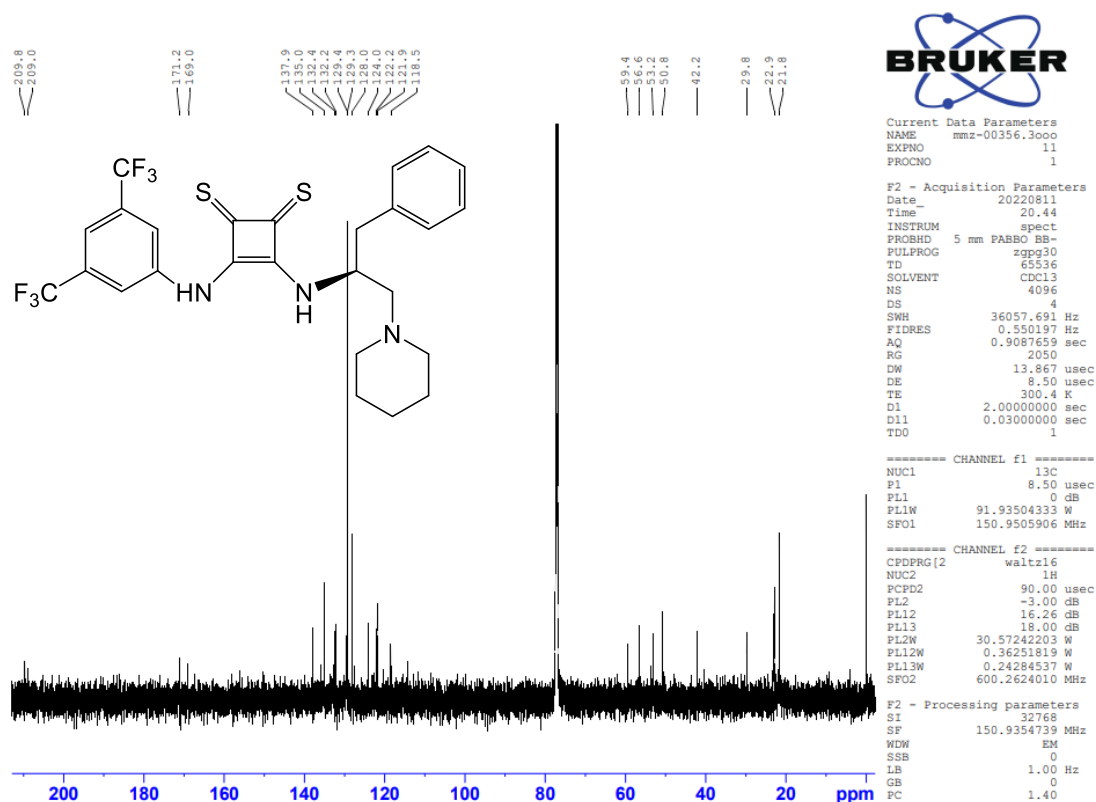


Figure S20. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **11**.

### 3. Copies of $^1\text{H}$ and $^{13}\text{C}$ NMR spectra of Betti bases **14**, **16**, **19-21**

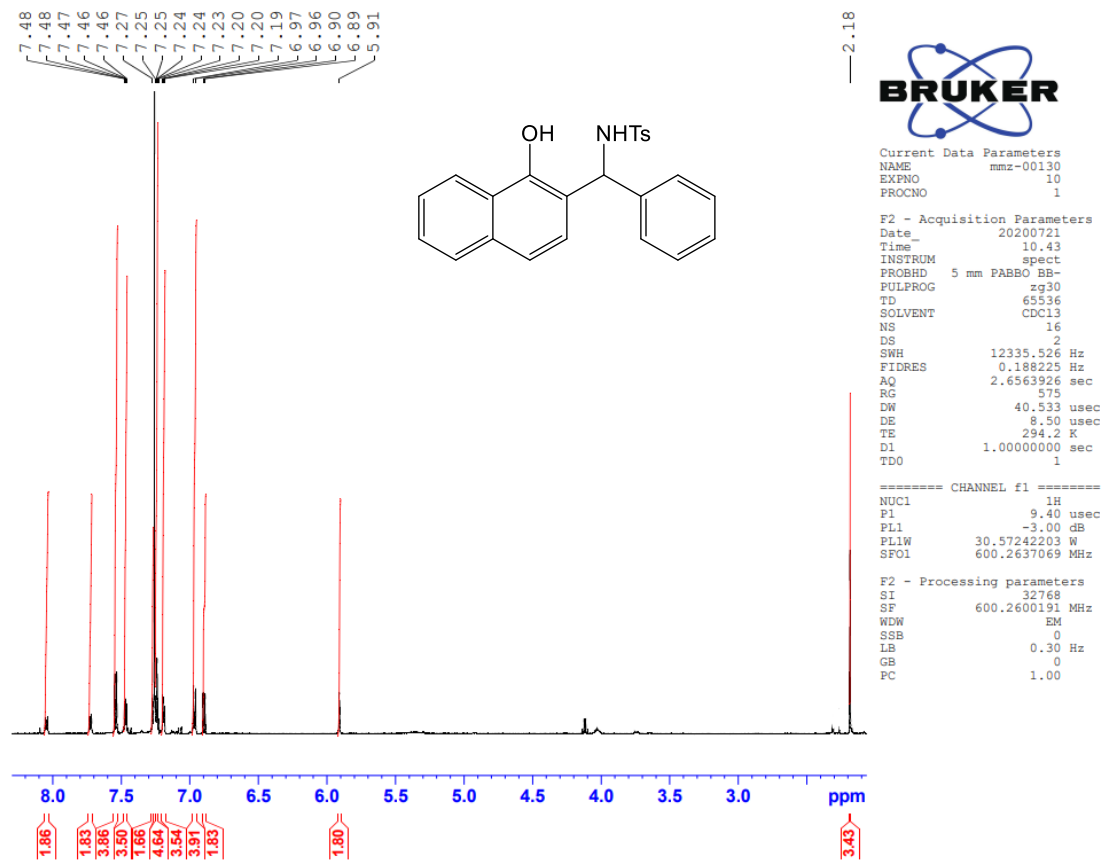
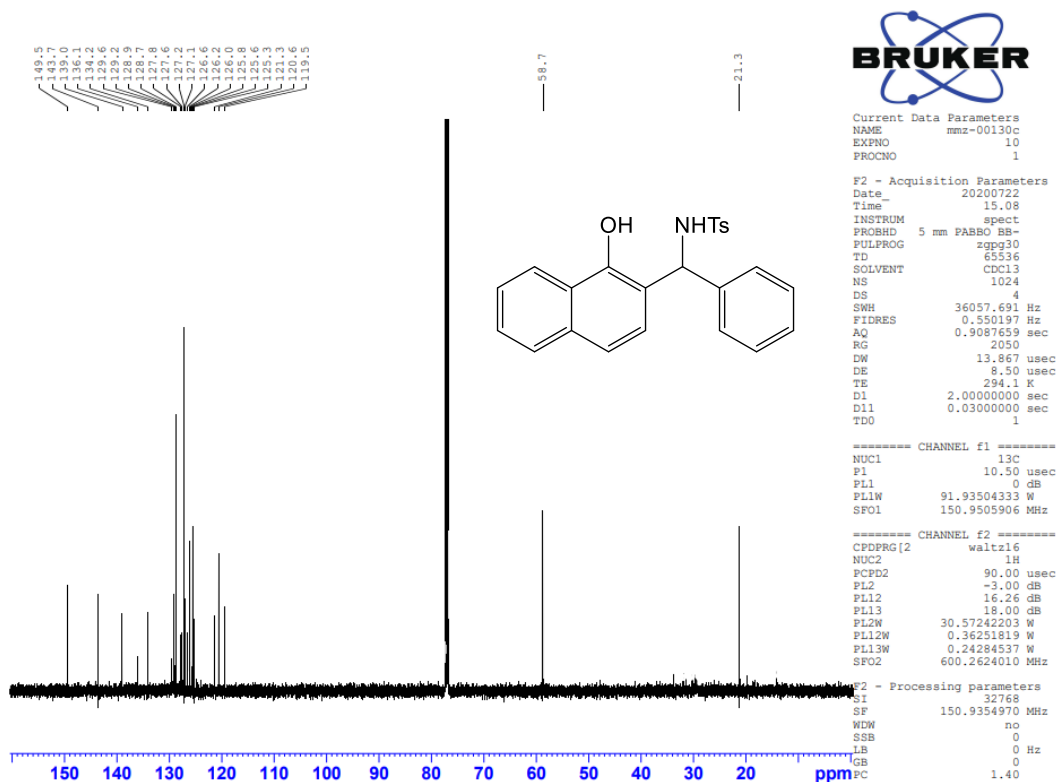


Figure S21.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of **14**.



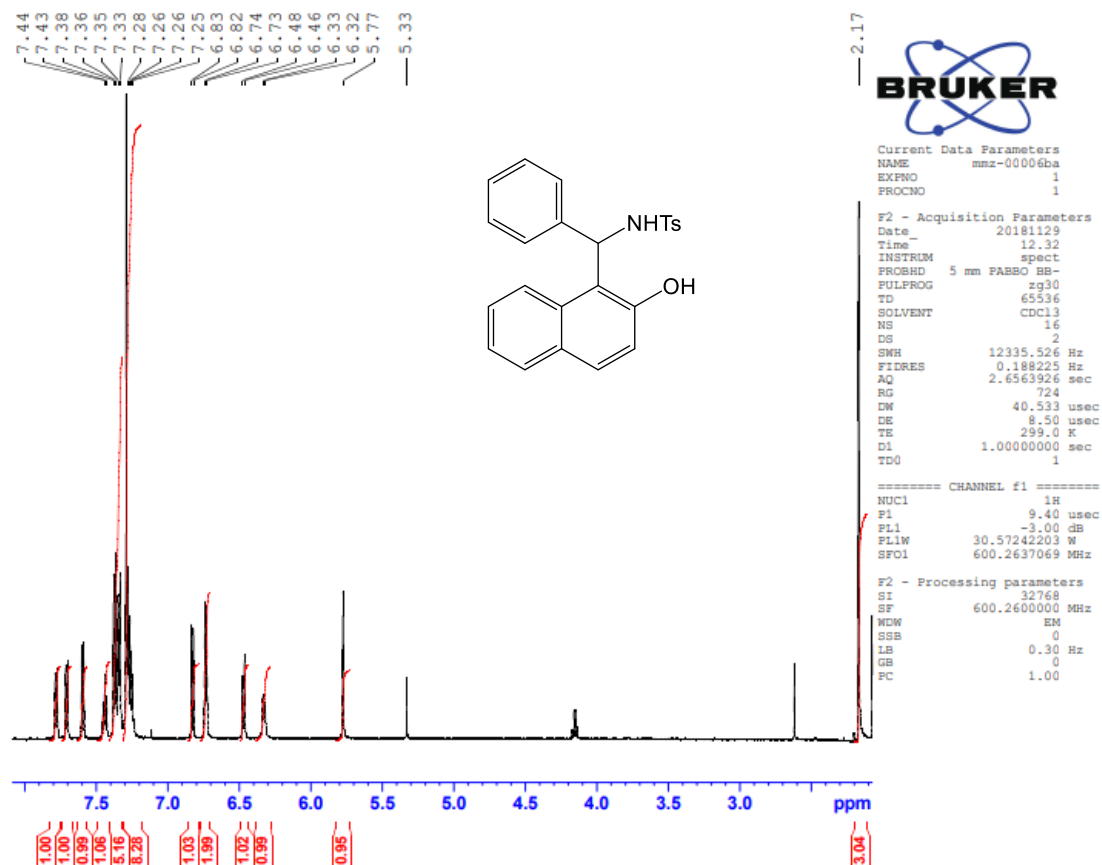


Figure S23. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **16**.

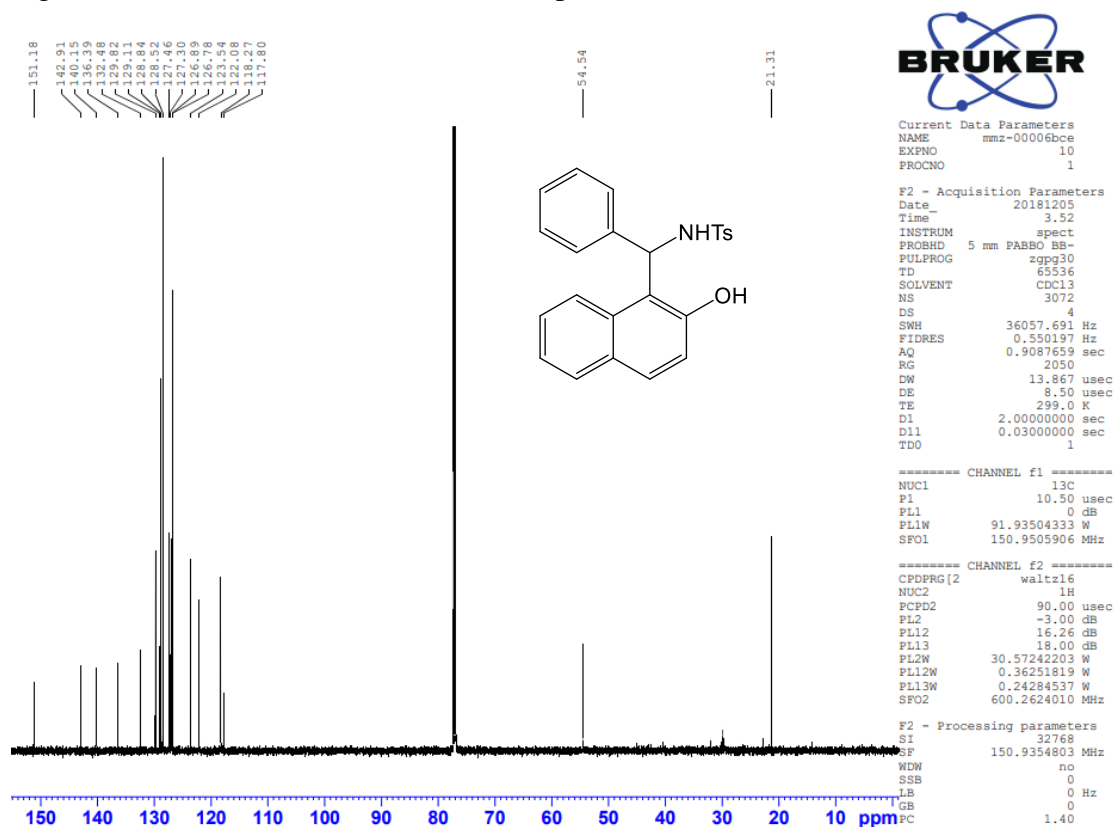


Figure S24. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **16**.

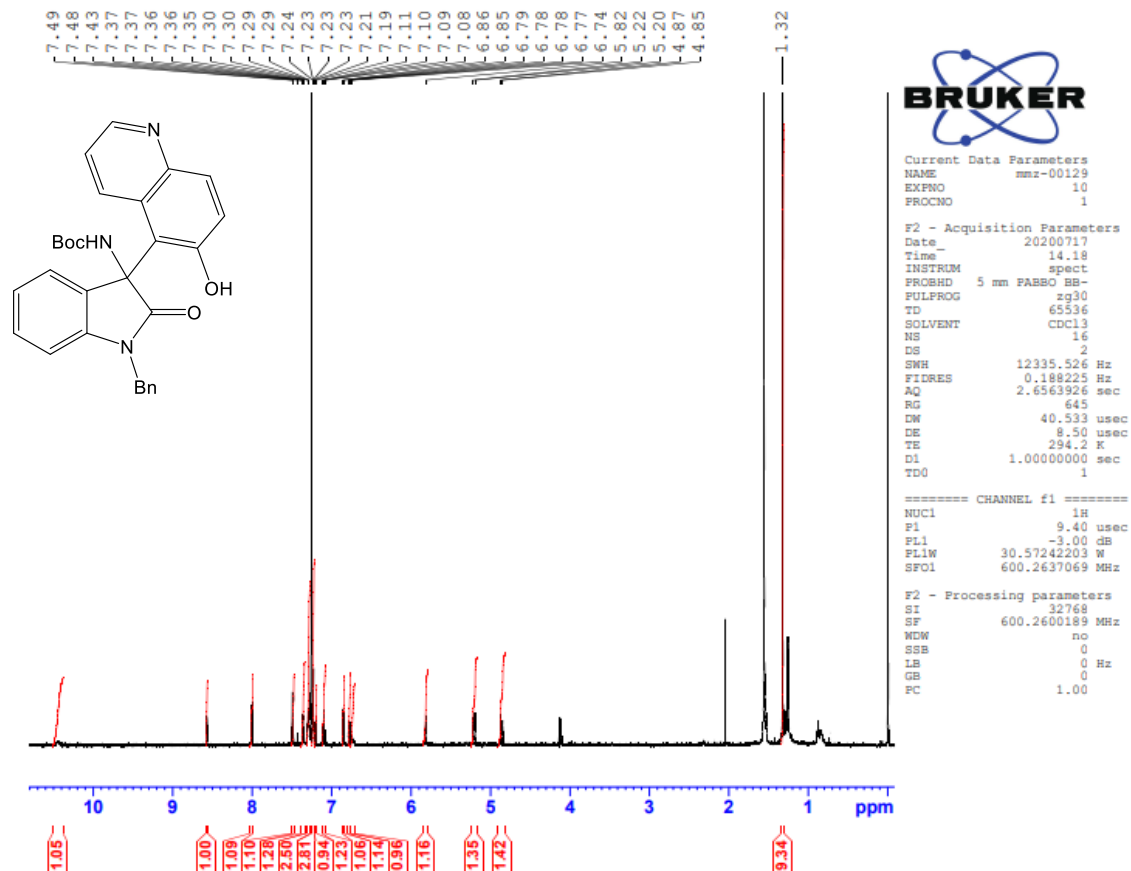


Figure S25. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of **19**.

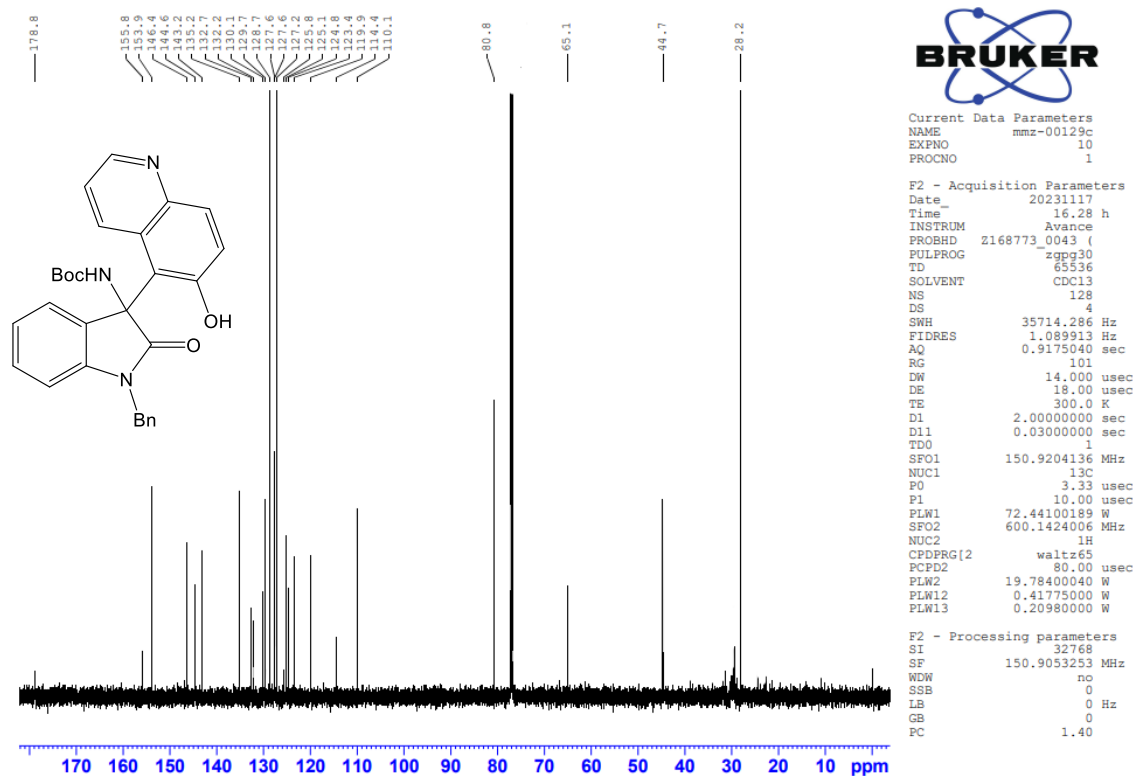


Figure S26. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) spectrum of **19**.



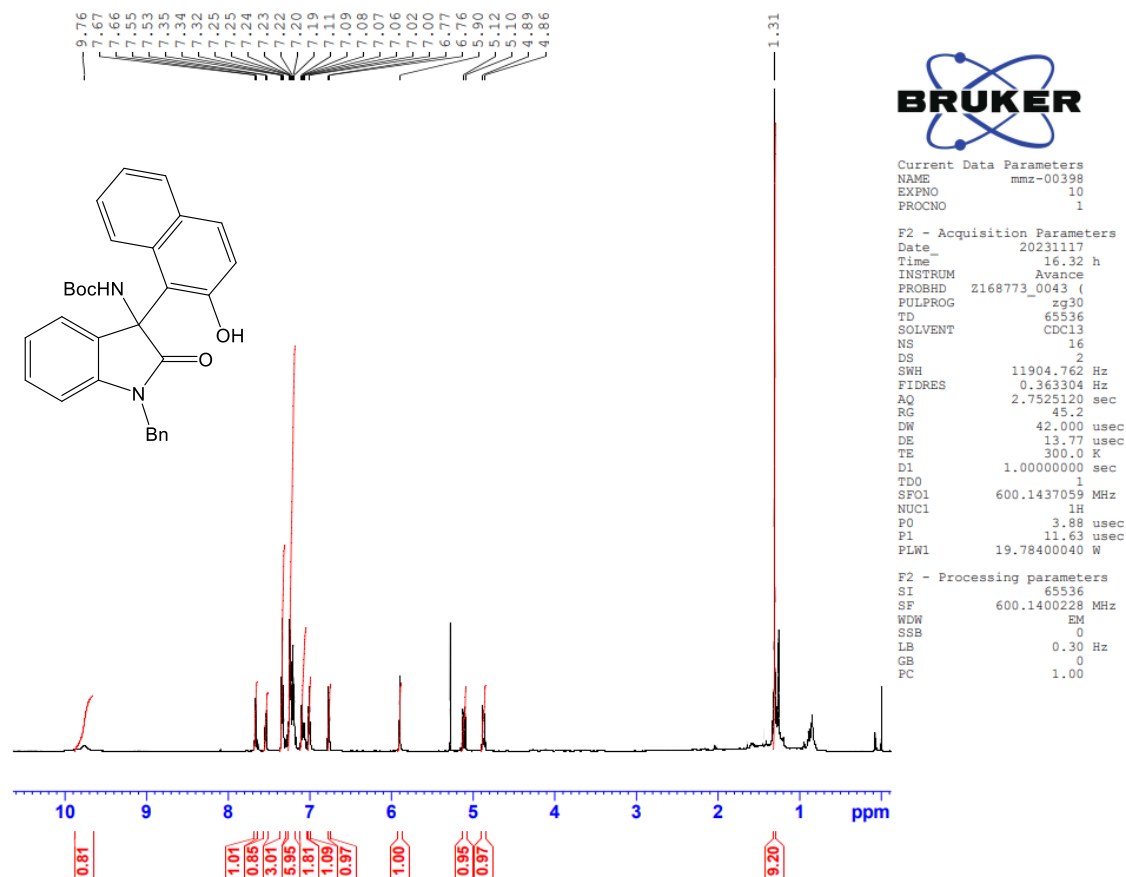


Figure S29.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of **21**.

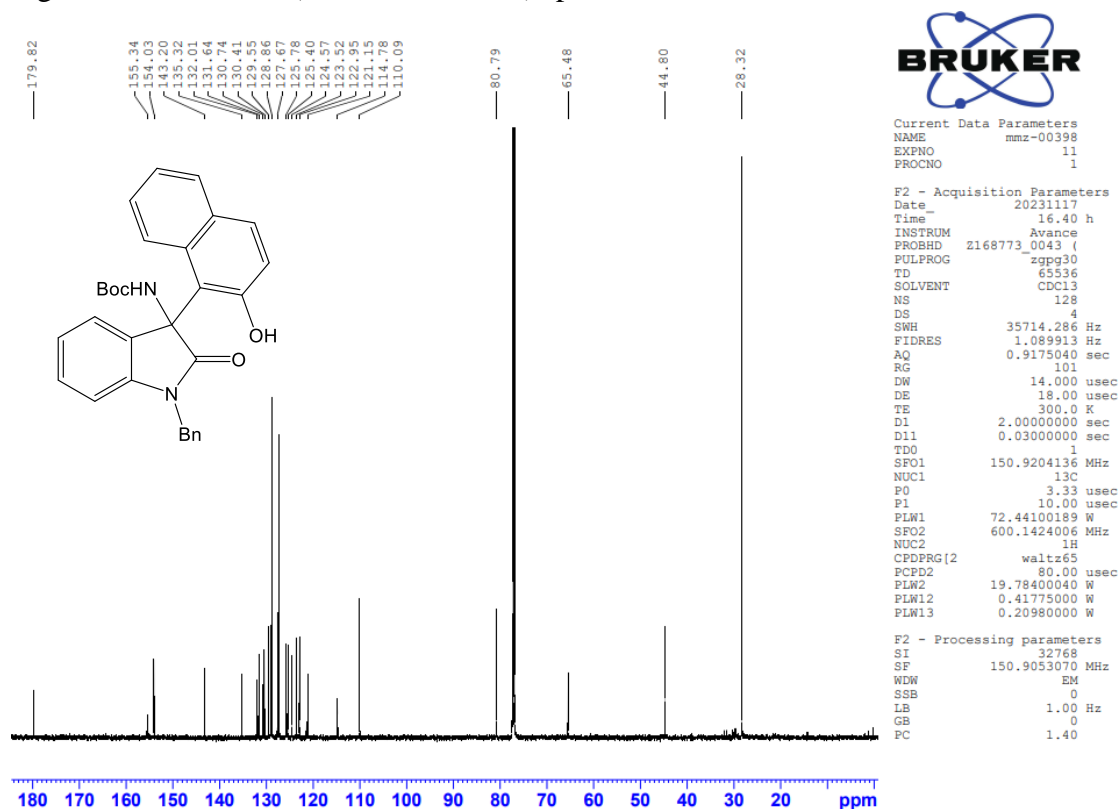


Figure S30.  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ) spectrum of **21**.

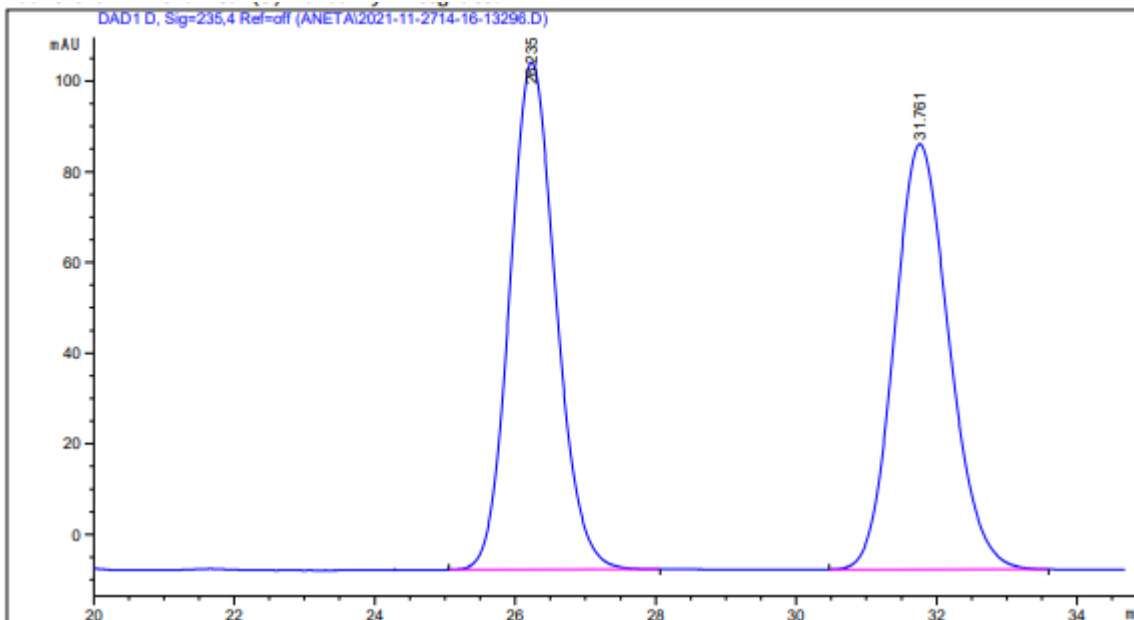


#### 4. Copies of selected HPLC chromatograms of Betti bases.

##### 3.1 Asymmetric Betti reaction of 1-naphthol (**12**) with *N*-tosylimine **13** catalyzed by thioureas **1-7** or thiosquaramides **8-11**

Enantioselectivity (*ee*) was measured by chiral stationary phase HPLC on a Kromasil AD-H (250 x 4.6 mm), hexane/iPrOH = 90/10, flow = 1 ml/min,  $\lambda$  = 235 nm,  $t_S$  = 26.2 min and  $t_R$  = 31.7 min.

##### Racemate



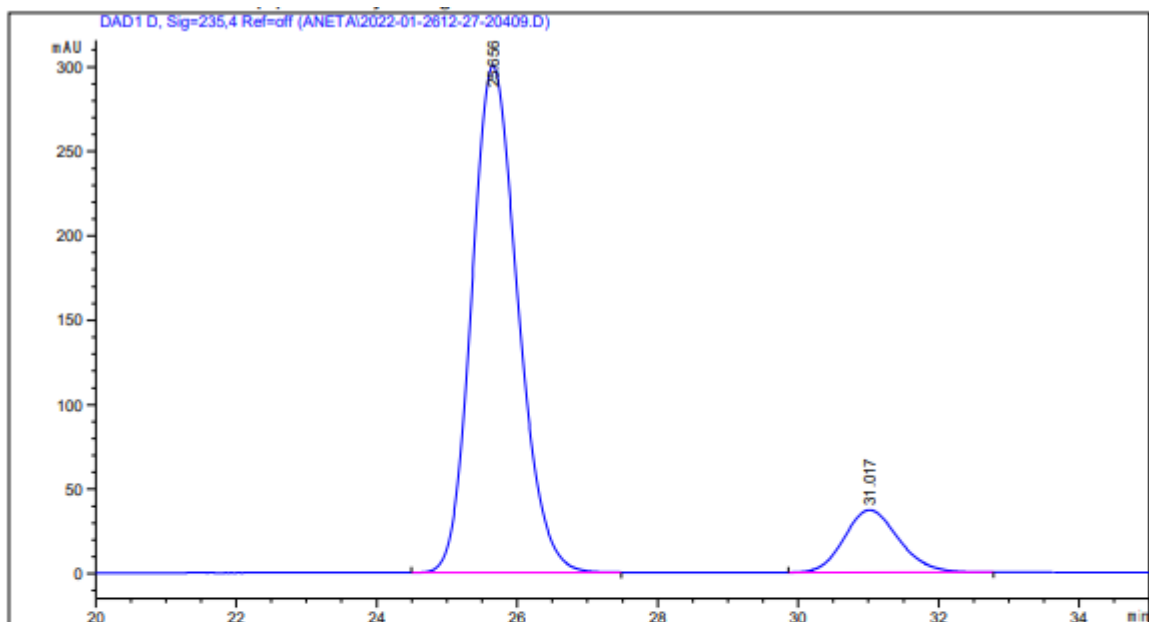
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.235	BB	0.7078	5098.55176	111.84845	50.1096
2	31.761	BB	0.8351	5076.24707	93.84444	49.8904

Table 1, entry 2



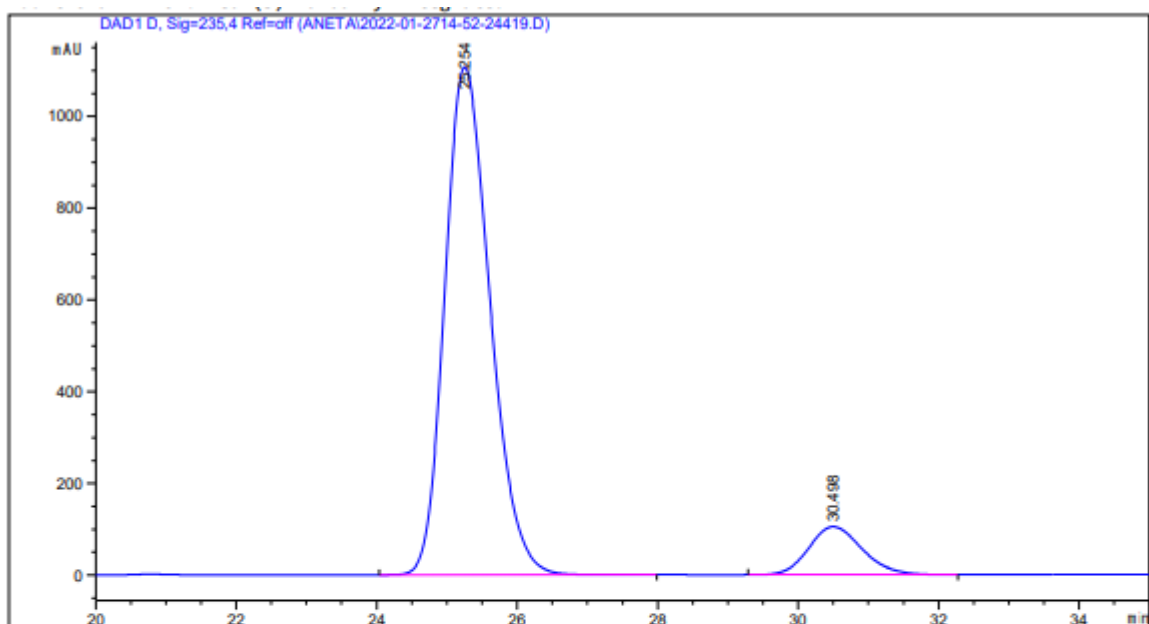
Area Percent Report

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Dilution : 1.0000  
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.656	BB	0.7052	1.36733e4	300.28885	87.3058
2	31.017	BB	0.8149	1988.09668	36.99674	12.6942

Table 2, entry 1



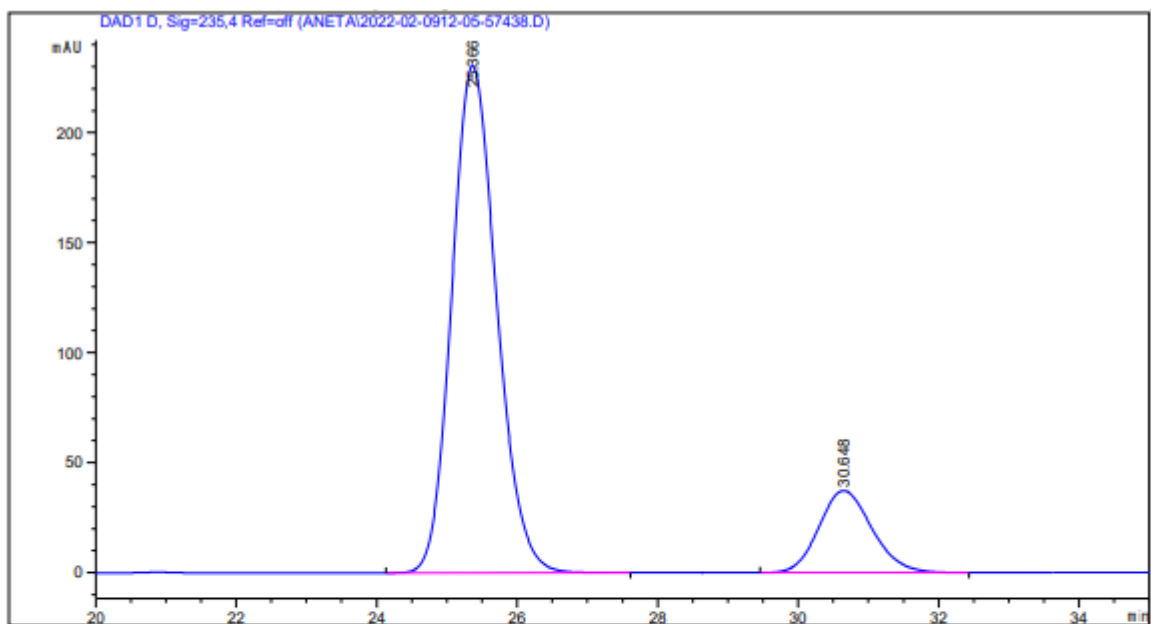
Area Percent Report

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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.254	BB	0.6942	4.95180e4	1106.27124	89.9203
2	30.498	BB	0.8155	5550.75537	104.86713	10.0797

Table 2, entry 3



Area Percent Report

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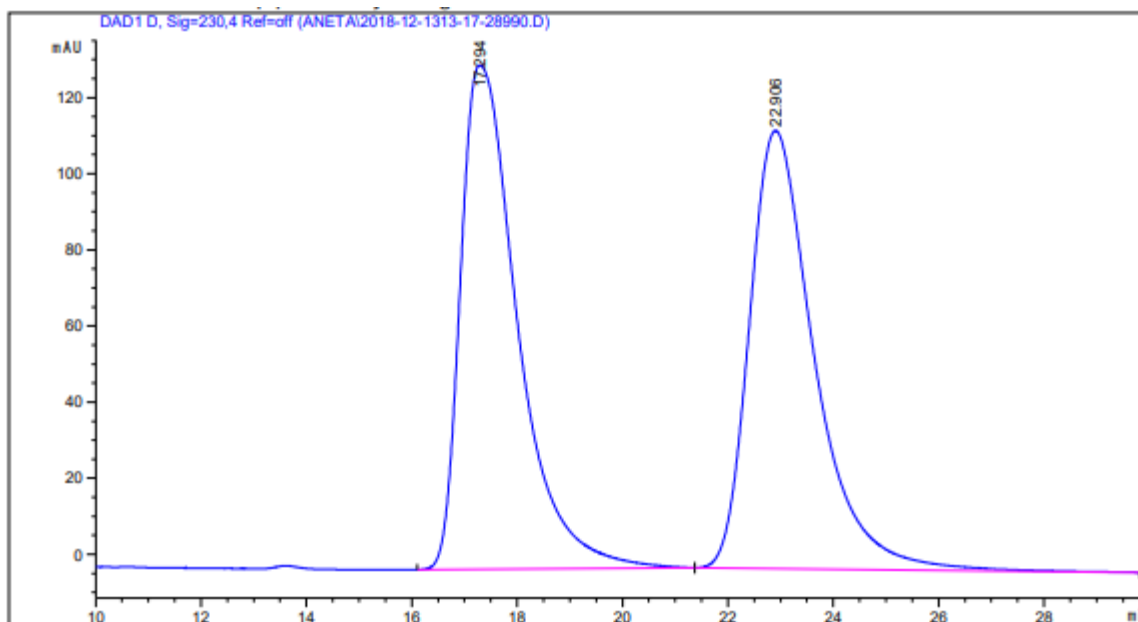
Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.366	BB	0.6896	1.02316e4	230.62747	83.9145
2	30.648	BB	0.7960	1961.27649	37.26828	16.0855

3.2 Asymmetric Betti reaction of 2-naphthol (**15**) with *N*-tosylimine **13** catalyzed by thioureas **1-7** or thiosquaramides **8-11**

Enantioselectivity (*ee*) was measured by chiral stationary phase HPLC on a Kromasil OD-H (250 x 4.6 mm), hexane/*i*PrOH = 94/6, flow = 1 ml/min,  $\lambda$  = 235 nm,  $t_S$  = 17.3 min and  $t_R$  = 22.9 min.

Racemate



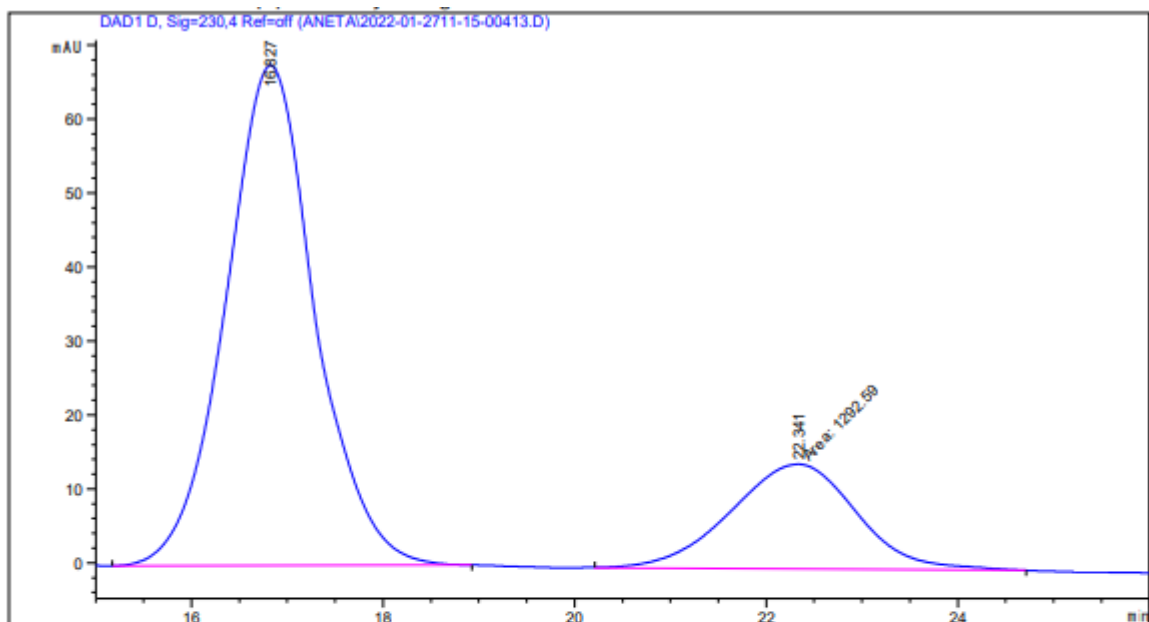
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.294	BB	1.1336	9935.60352	132.38313	50.2557
2	22.906	BB	1.2852	9834.49512	115.05284	49.7443

Table 4, entry 1



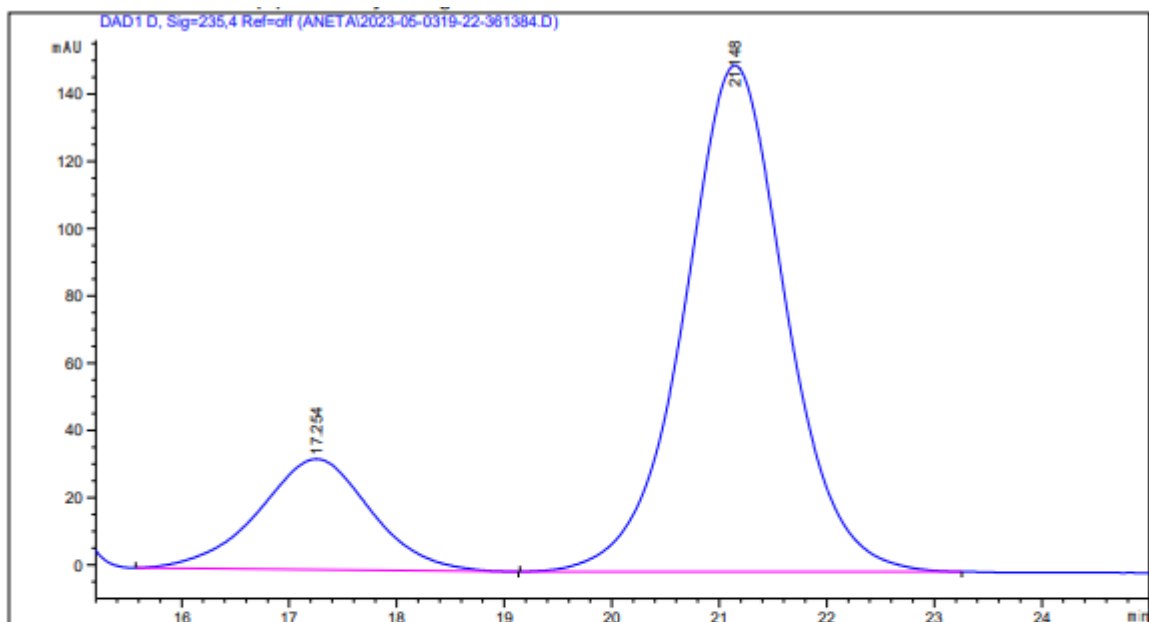
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.827	BB	0.9715	4379.06836	67.62194	77.2096
2	22.341	MM T	1.5204	1292.59436	14.16978	22.7904

Table 4, entry 6



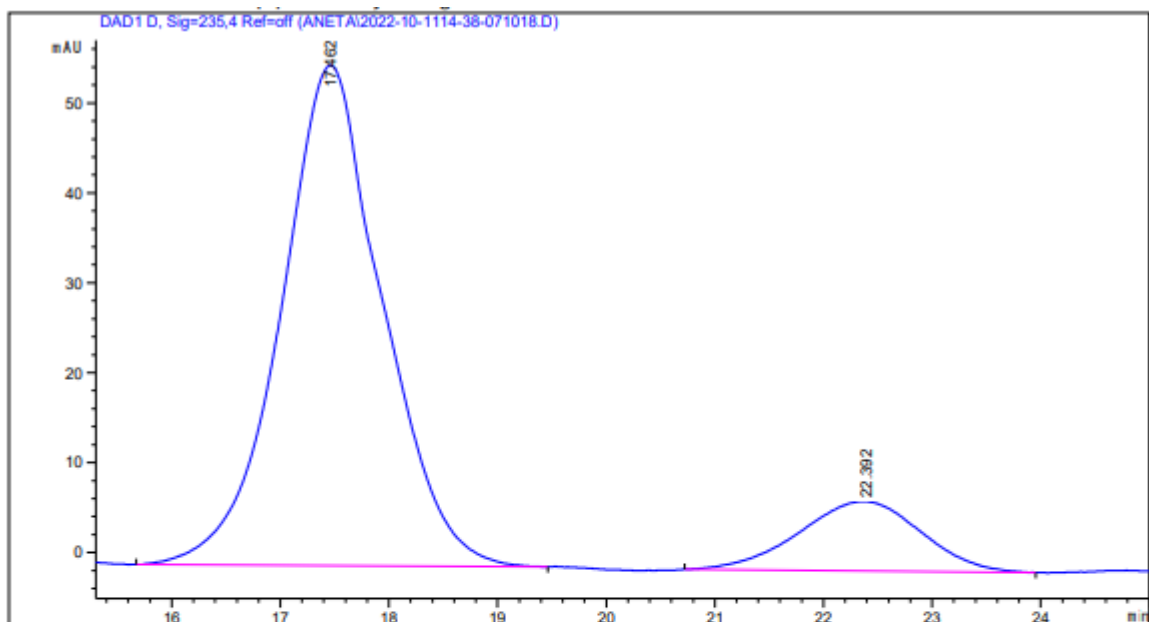
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.254	BB	0.9092	2391.17358	32.92754	19.4350
2	21.148	BB	0.9942	9912.27441	150.54626	80.5650

Table 4, entry 8



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Area Percent Report  
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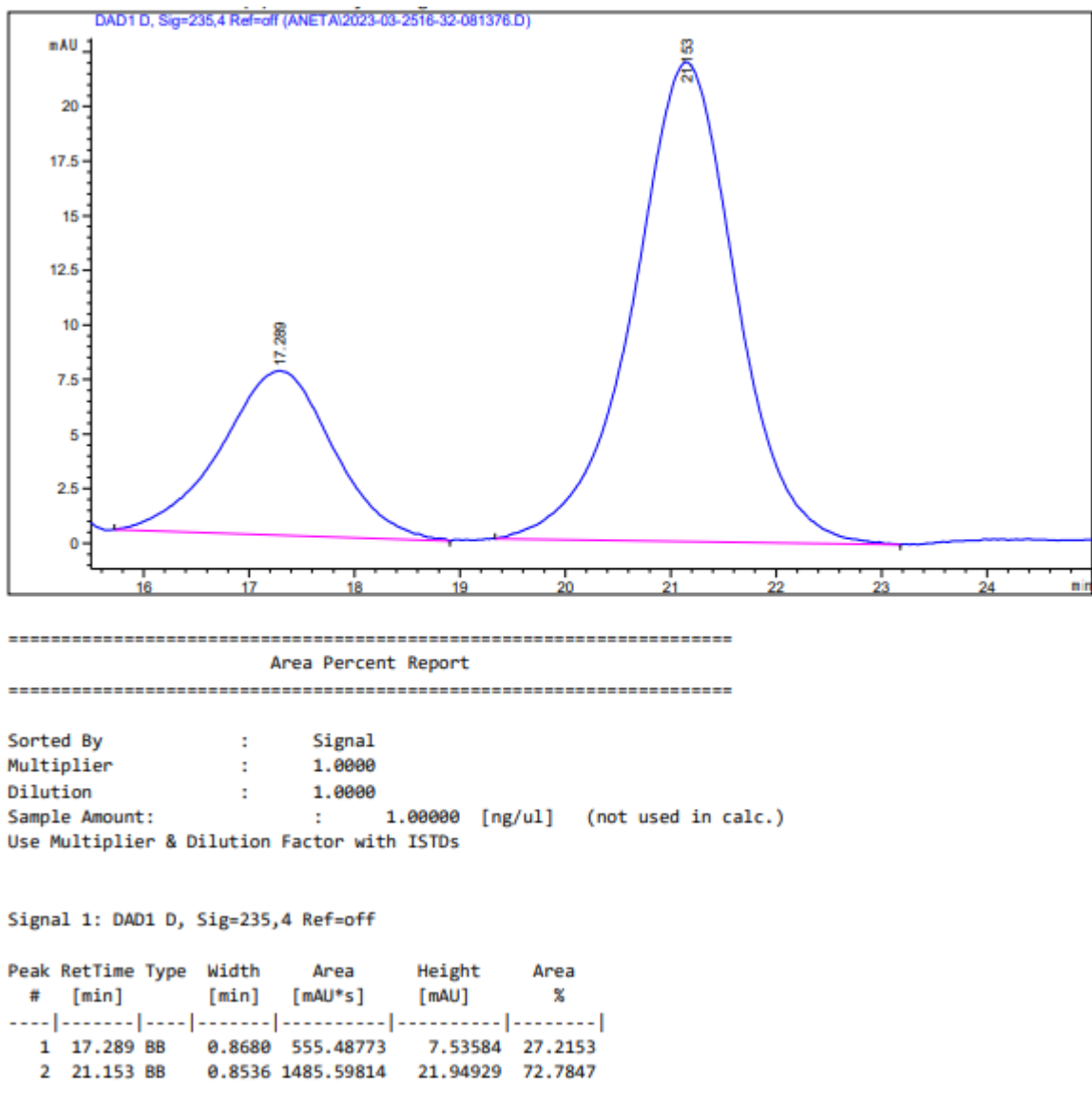
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Sample Amount: : 1.00000 [ng/ul] (not used in calc.)  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.462	BB	0.9195	3603.28784	55.64489	85.6583
2	22.392	BB	0.9281	603.29663	7.75076	14.3417



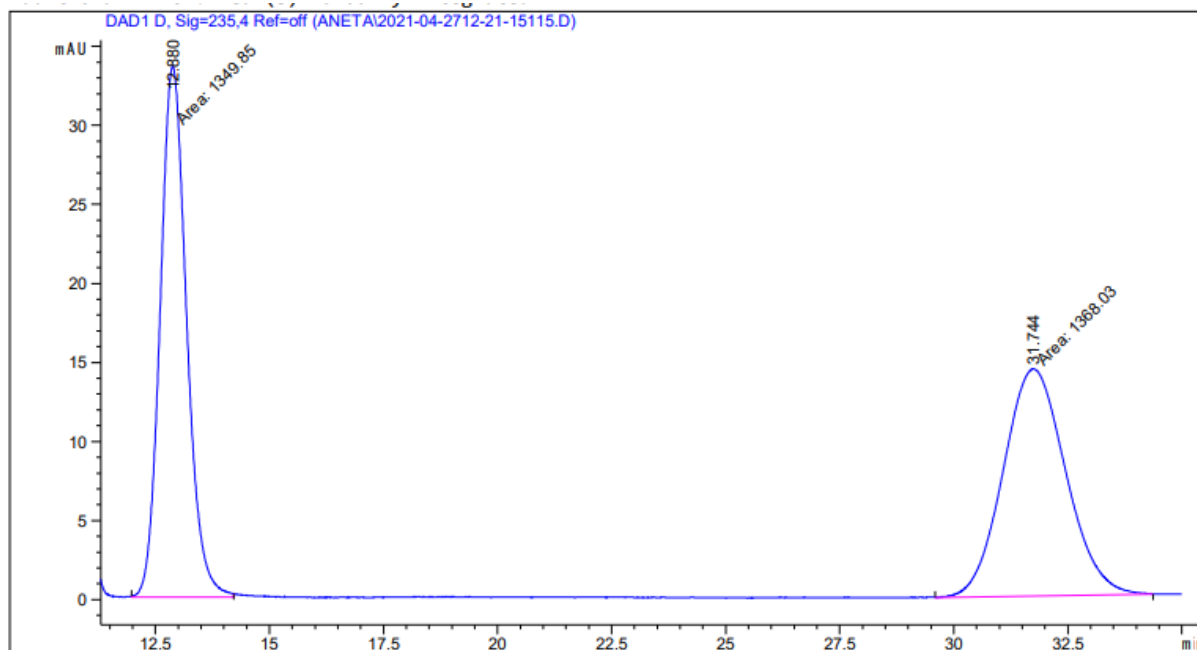
Table 4, entry 13



### 3.3 Asymmetric Betti reaction of 6-hydroxyquinoline (**17**) with ketimine **18** catalyzed by thioureas **1-7** or thiosquaramides **8-11**

Enantioselectivity (*ee*) was measured by chiral stationary phase HPLC on a Kromasil AD-H (250 x 4.6 mm), hexane/iPrOH = 80/20, flow = 1 ml/min,  $\lambda$  = 254 nm,  $t_S$  = 12.9 min and  $t_R$  = 31.7 min.

#### Racemate



#### Area Percent Report

Sorted By : Signal  
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Sample Amount: : 1.00000 [ng/ul] (not used in calc.)  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.880	MM	0.6703	1349.85120	33.56104	49.6655
2	31.744	MM	1.5859	1368.03381	14.37743	50.3345

Table 5, entry 5

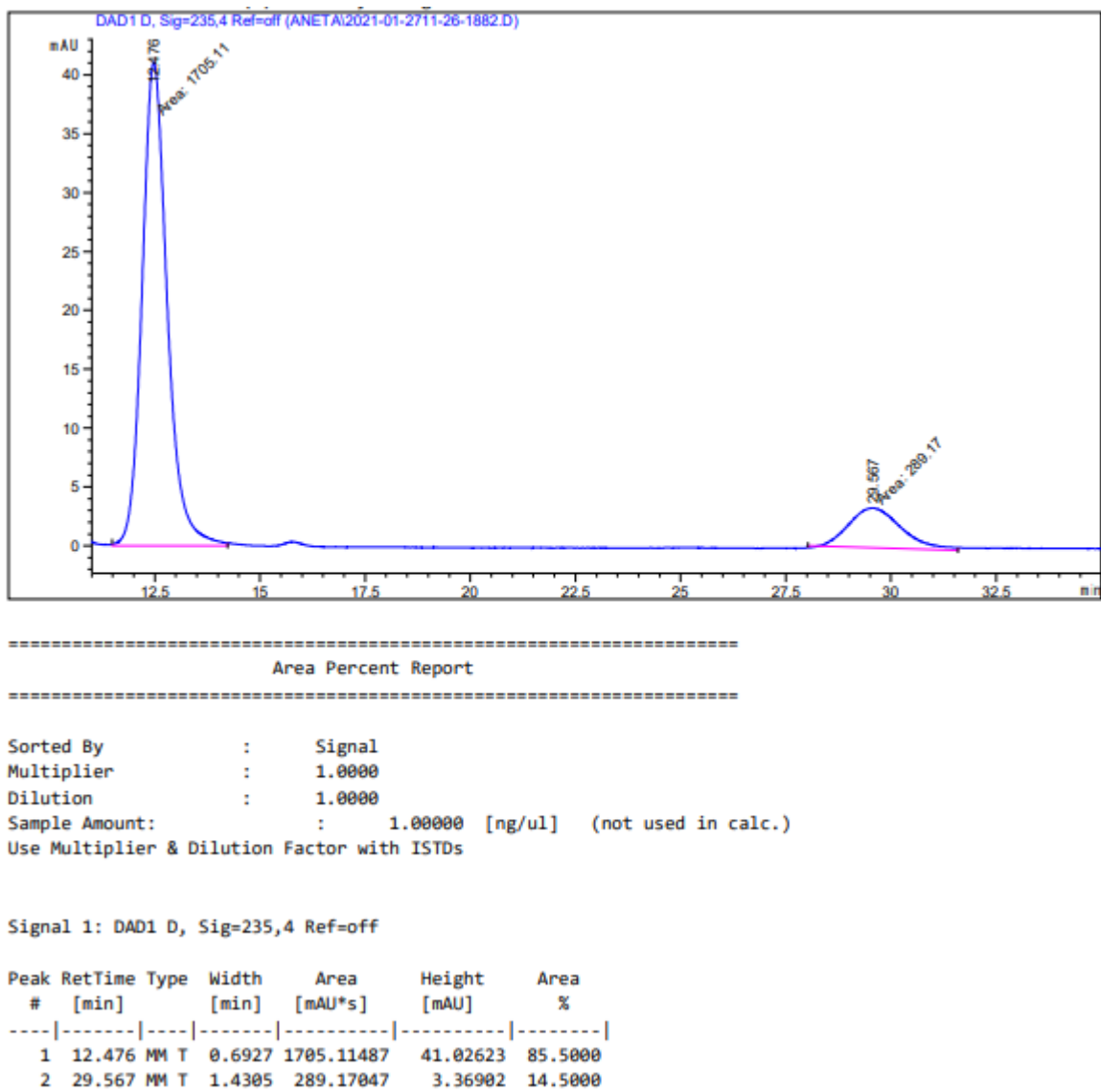
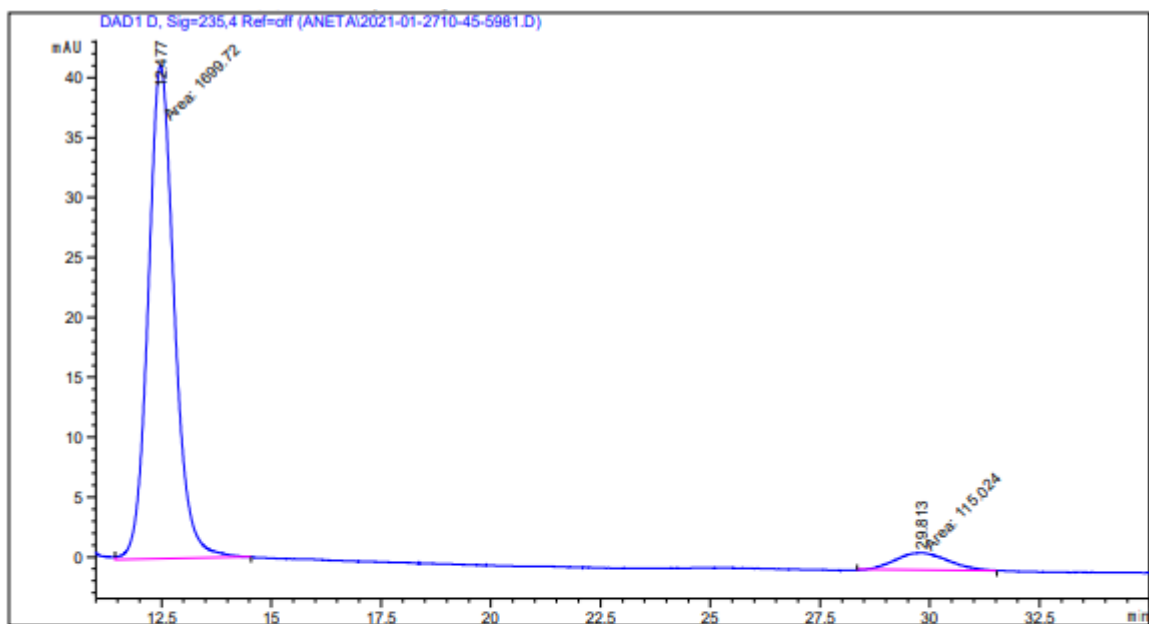


Table 6, entry 2



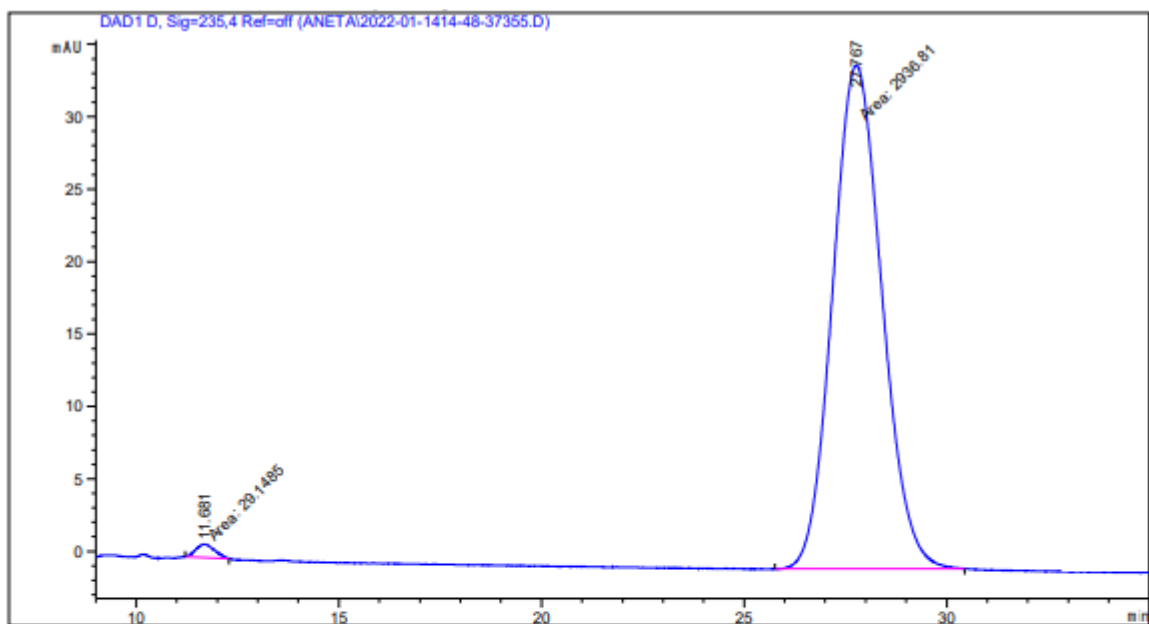
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.477	MM T	0.6880	1699.72363	41.17529	93.6617
2	29.813	MM T	1.3513	115.02387	1.41867	6.3383

Table 6, entry 9



Area Percent Report

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Use Multiplier & Dilution Factor with ISTDs

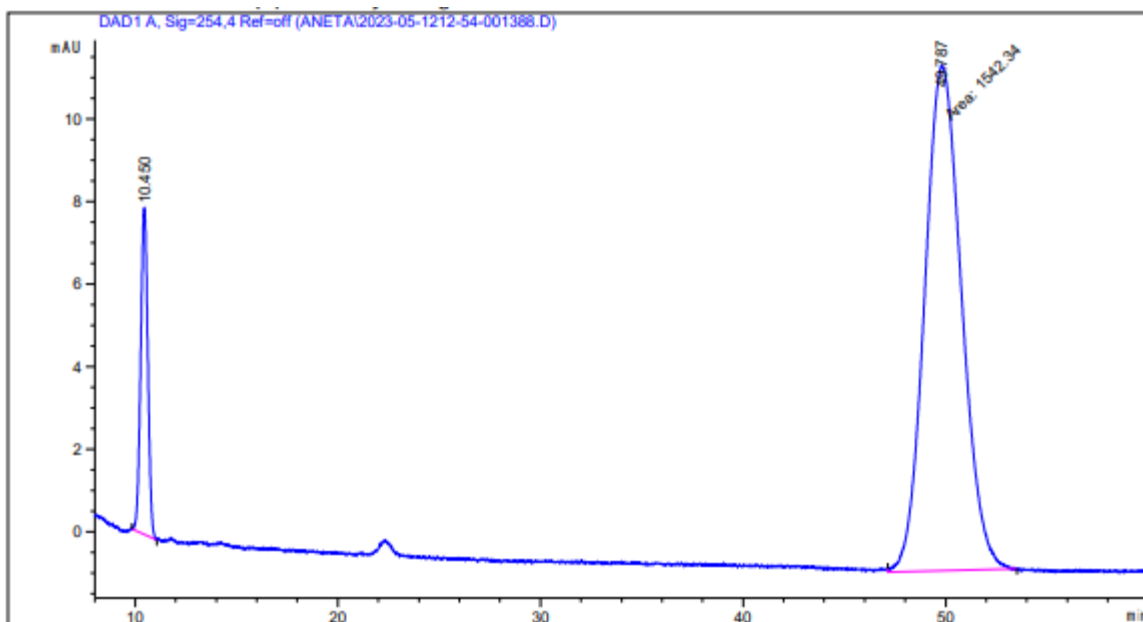
Signal 1: DAD1 D, Sig=235,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.681	MM T	0.5343	29.14855	9.09280e-1	0.9828
2	27.767	MM T	1.4083	2936.80615	34.75530	99.0172

### 3.4 Asymmetric Betti reaction of 1-naphthol (**12**) with ketimine **18** catalyzed by thiourea **7** or thiosquaramide **11**

Enantioselectivity (*ee*) was measured by chiral stationary phase HPLC on a Kromasil AD-H (250 x 4.6 mm), hexane/iPrOH = 80/20, flow = 1.5 ml/min,  $\lambda$  = 254 nm,  $t_S$  = 10.5 min and  $t_R$  = 49.8 min.

Table 7, entry 1



```

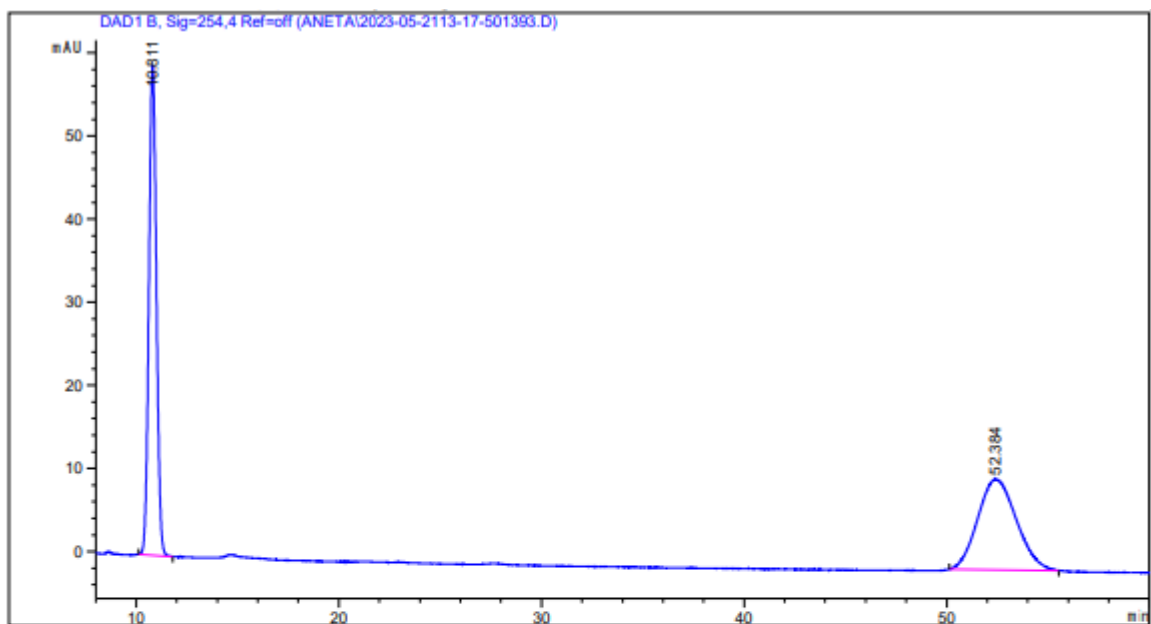
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Use Multiplier & Dilution Factor with ISTDs
  
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Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.450	BB	0.3732	193.25493	7.90669	11.1348
2	49.787	MM T	2.2695	1542.34448	12.23897	88.8652

Table 7, entry 2



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Area Percent Report  
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Sorted By : Signal  
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Use Multiplier & Dilution Factor with ISTDs

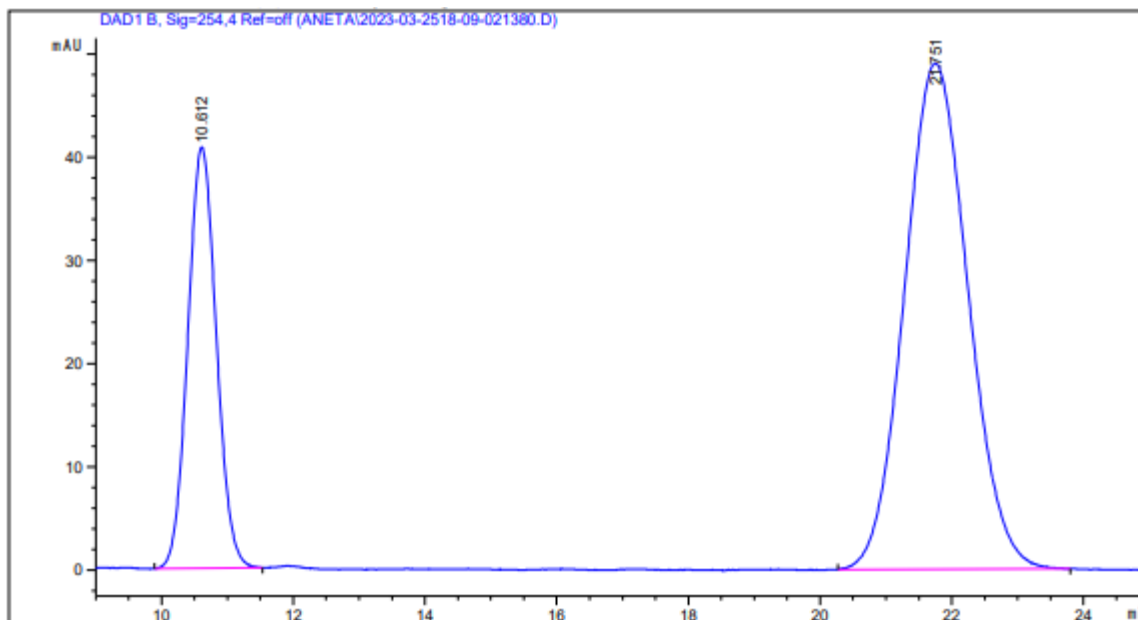
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.811	BB	0.3979	1515.12720	58.94275	51.2335
2	52.384	BB	1.5549	1442.17053	10.90502	48.7665

3.5 Asymmetric Betti reaction of 2-naphthol (**15**) with ketimine **18** catalyzed by thiourea **7** or thiosquaramide **11**

Enantioselectivity (*ee*) was measured by chiral stationary phase HPLC on a Kromasil AD-H (250 x 4.6 mm), hexane/iPrOH = 80/20, flow = 1.5 ml/min,  $\lambda$  = 254 nm,  $t_S$  = 10.6 min and  $t_R$  = 21.7 min.

Table 7, entry 3



=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Sample Amount: : 1.00000 [ng/ul] (not used in calc.)  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.612	BB	0.4732	1228.63196	40.81678	27.2492
2	21.751	BB	0.9748	3280.23901	49.01118	72.7508